BHARATHIDASAN UNIVERSITY

Tiruchirappalli- 620024

Tamil Nadu, India

Programme: M.Sc., Biochemistry

Course Title : Biochemistry of Signal Transduction

Course Code : BC203CR

Unit-3

Signaling in nerve impulse transmission, vision and muscle contraction

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Professor

Topics :-

- Nerve cells
- Synapses
- Resting membrane potential
- Action potential
- Voltage gated ion channels
- Impulse transmission
- Neurotransmitters
- Neurotransmitter receptors

The Cells of the Nervous System

- The human nervous system is comprised of two kinds of cells:
  - Neurons
  - Glia
- The human brain contains approximately 100 billion individual neurons.
- Behaviour depends upon the communication between neurons.

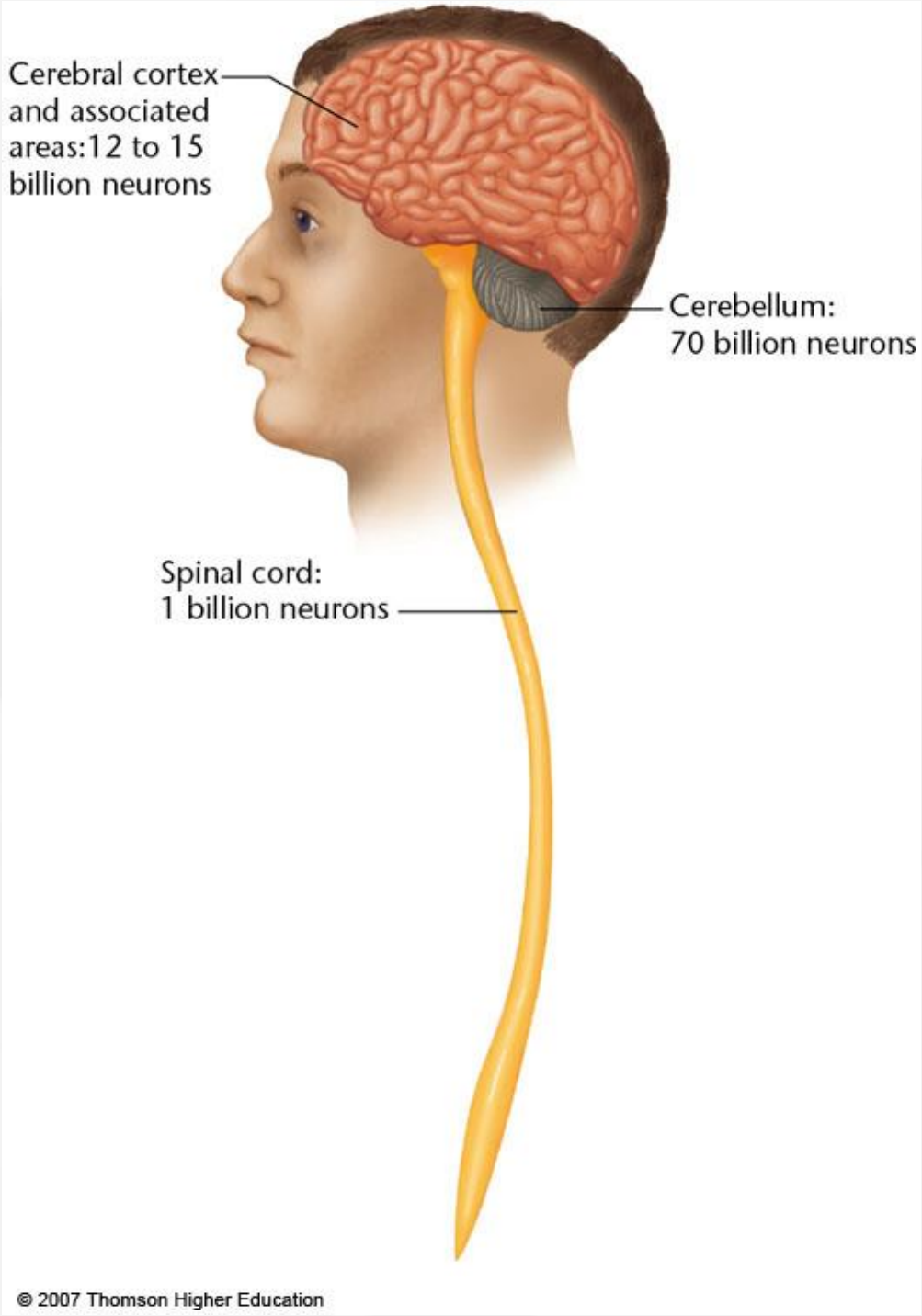
Cerebral cortex and associated areas:12 to 15 billion neurons
Cerebellum: 70 billion neurons
Spinal cord: 1 billion neurons
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Fig. 2-1, p. 30

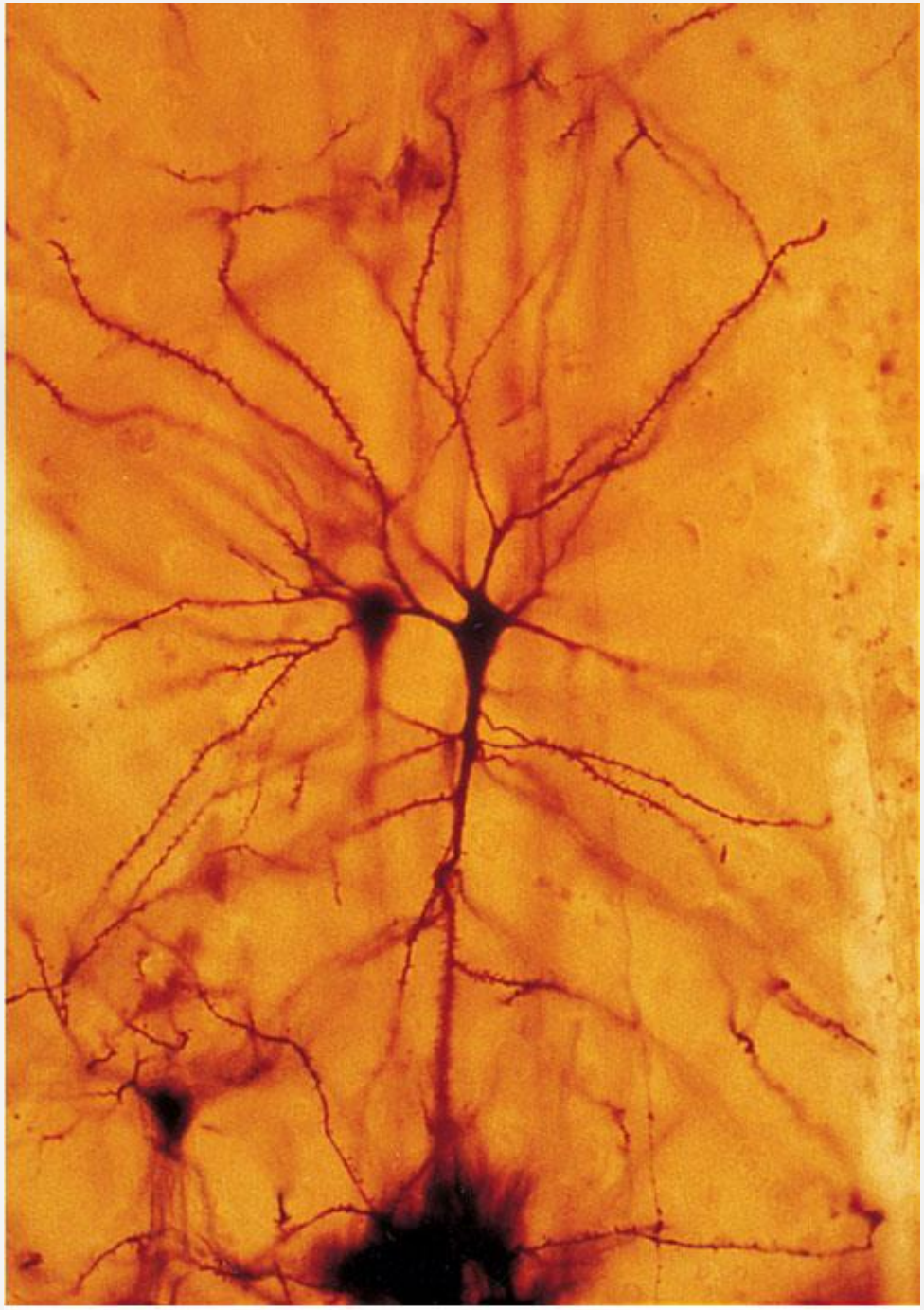

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Fig. 2-4, p. 32

The Cells of the Nervous System

- Spaniard Santiago Ramon y Cajal (1852-1934) was the first to demonstrate that the individual cells comprising the nervous system remained separate.
- He showed that they did not grow into each other as previously believed.

The Cells of the Nervous System

- Like other cells in the body, neurons contain the following structures:
  - Membrane
  - Nucleus
  - Mitochondria
  - Ribosomes
  - Endoplasmic reticulum

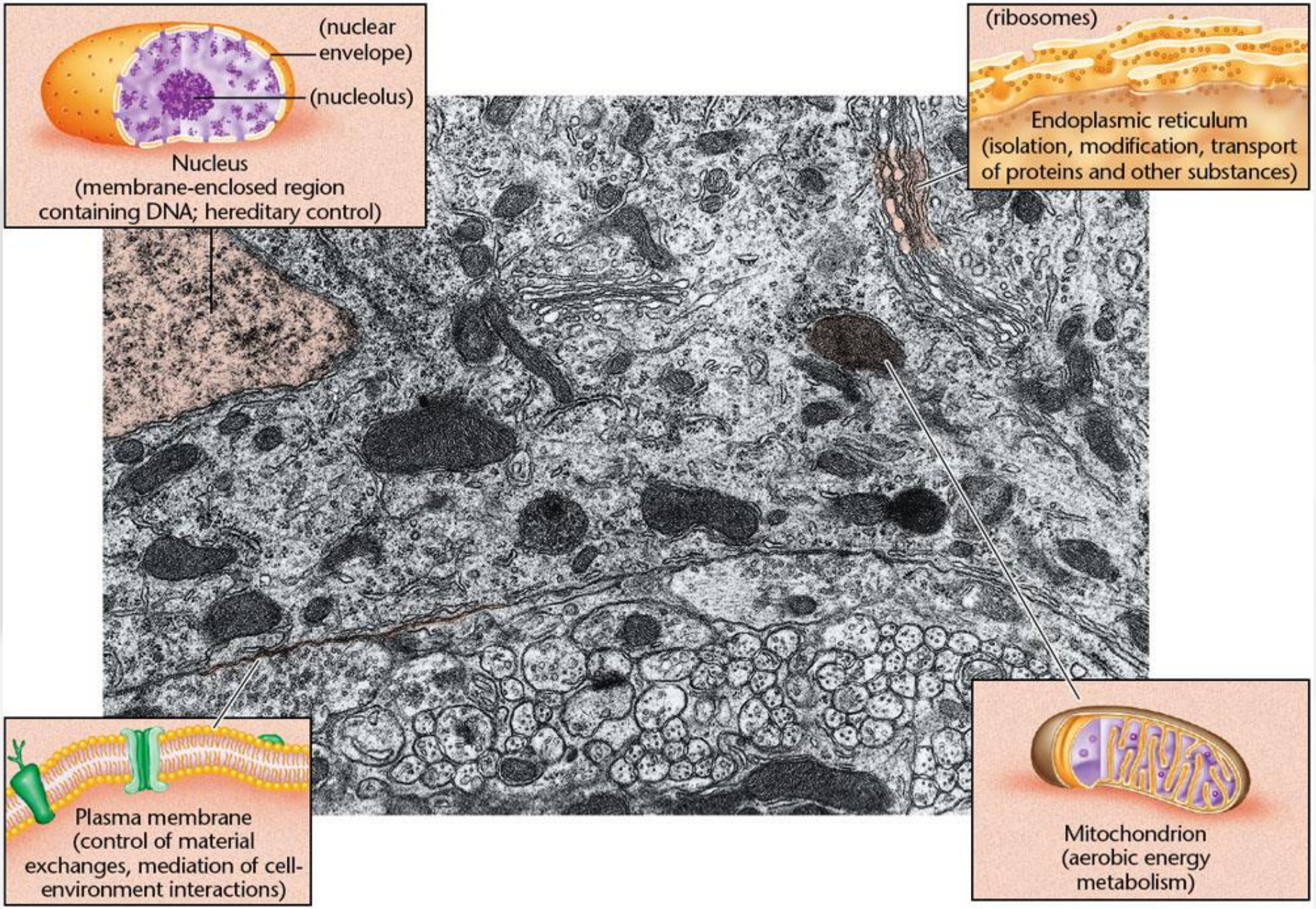

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Fig. 2-2, p. 31

The Cells of the Nervous System

- The membrane refers to the structure that separates the inside of the cell from the outside environment.
- The nucleus refers to the structure that contains the chromosomes.
- The mitochondria are the strucures that perform metabolic activities and provides energy that the cells requires.
- Ribosomes are the sites at which the cell synthesizes new protein molecules

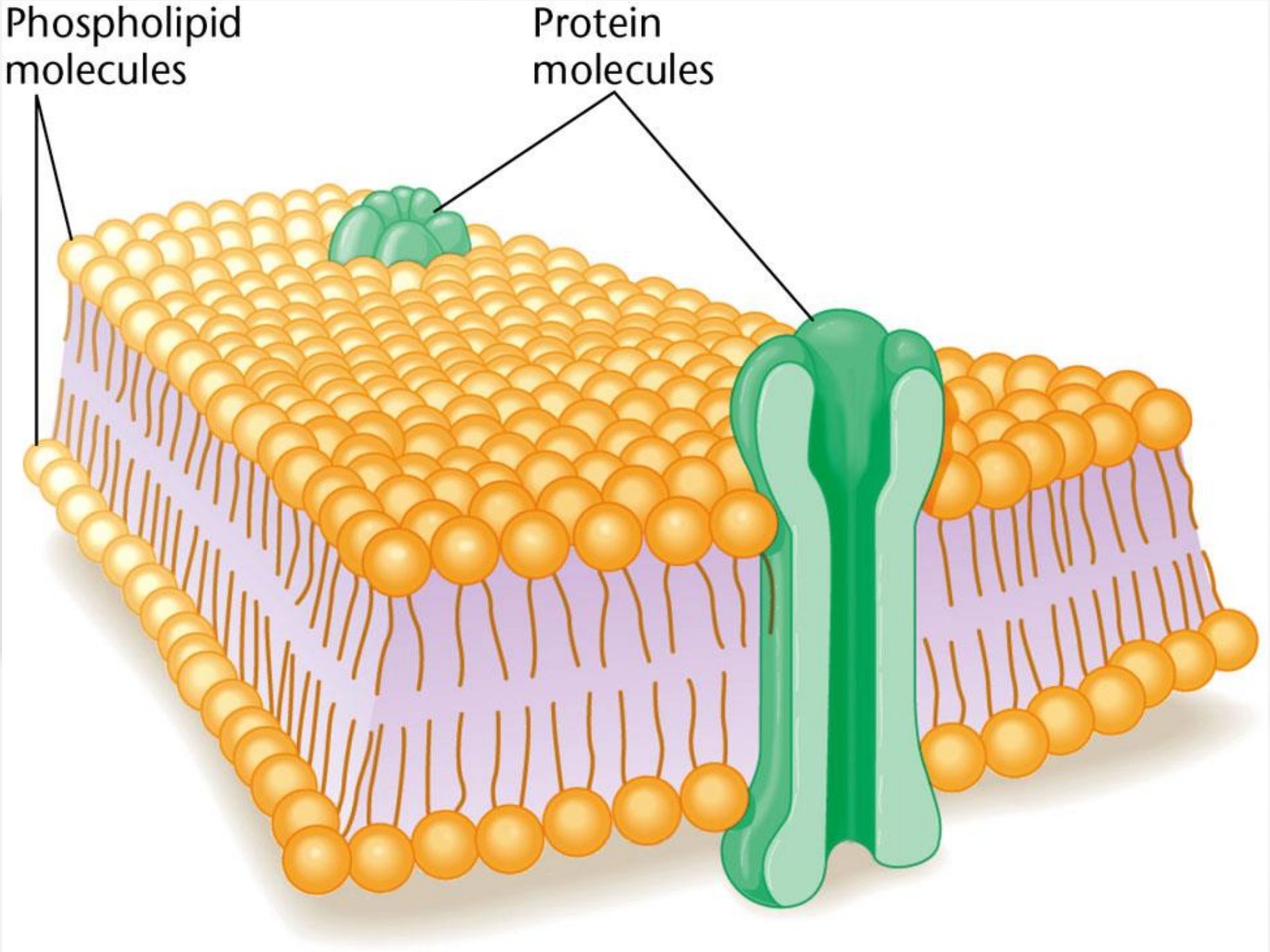

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Fig. 2-3, p. 32

The Cells of the Nervous System

- Neuron cells are similar to other cells of the body but have a distinctive shape.
- A motor neuron has its soma in the spinal cord and receives excitation from other neurons and conducts impulses along it axon to a muscle.
- A sensory neuron is specialized at one end to be highly sensitive to a particular type of stimulation (touch, temperature, odour etc.)

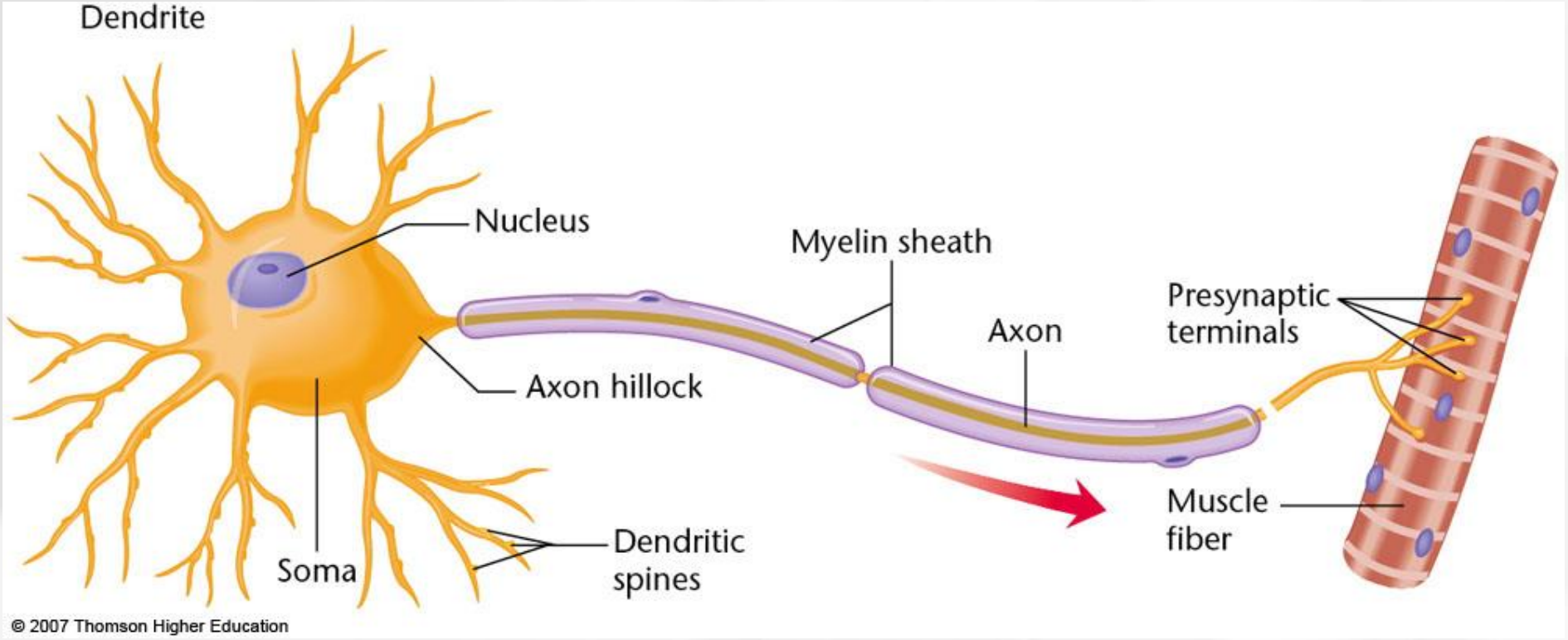
Dendrite
Nucleus
Myelin sheath
Axon
Presynaptic terminals
Axon hillock
Muscle fiber
Soma
Dendritic spines
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Fig. 2-5, p. 32

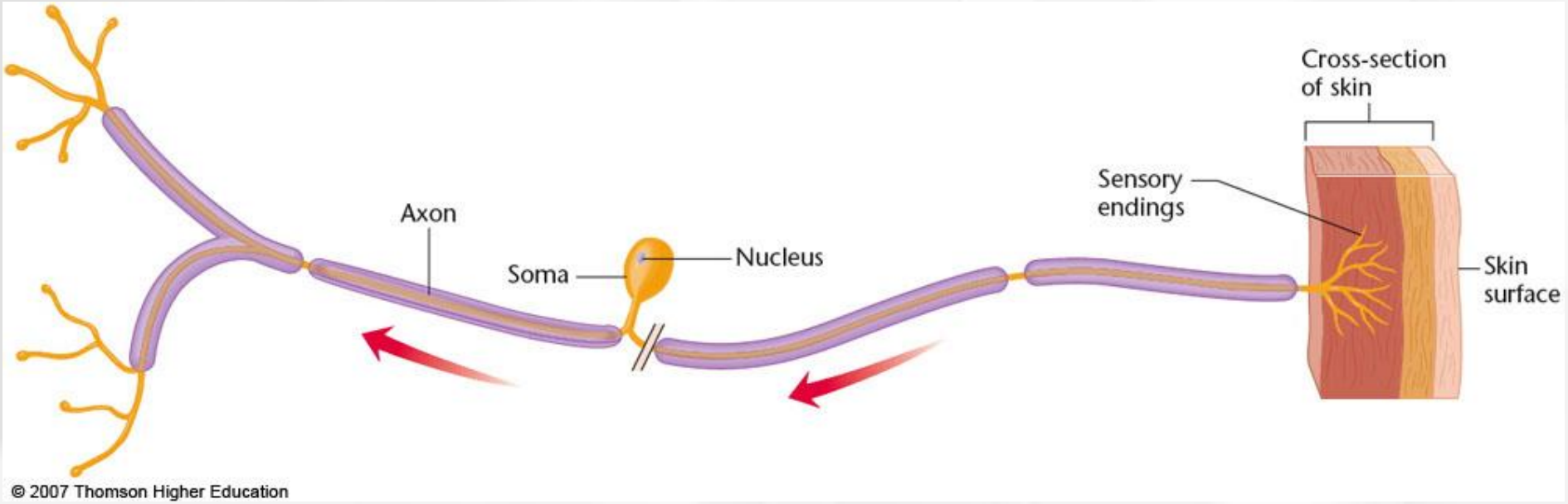

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Fig. 2-6, p. 33

The Cells of the Nervous System

- All neurons have the following major components:
  - Dendrites.
  - Soma/ cell body.
  - Axon.
  - Presynaptic terminals.

The Cells of the Nervous System

- Dendrites- branching fibers with a surface lined with synaptic receptors responsible for bringing in information from other neurons.
- Some dendrites also contain dendritic spines that further branch out and increase the surface area of the dendrite.

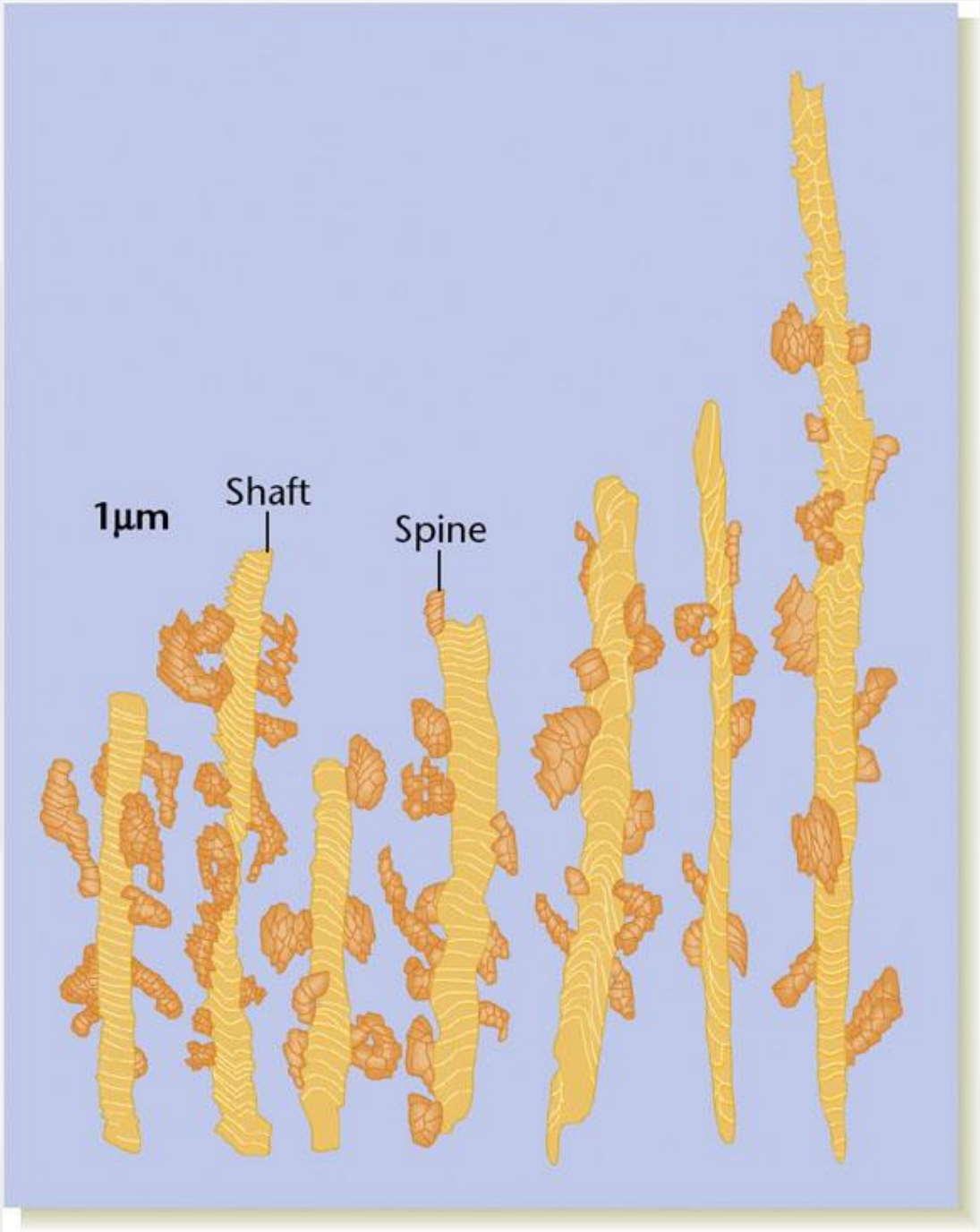

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Fig. 2-7, p. 33

The Cells of the Nervous System

- Soma - contains the nucleus, mitochondria, ribosomes, and other structures found in other cells.
  - Also responsible for the metabolic work of the neuron.

The Cells of the Nervous System

- Axon - thin fiber of a neuron responsible for transmitting nerve impulses away to other neurons, glands, or muscles.
- Some neurons are covered with an insulating material called the myelin sheath with interruptions in the sheath known as nodes of Ranvier.

The Cells of the Nervous System

- Presynaptic terminals refer to the end points of an axon responsible for releasing chemicals to communicate with other neurons.

The Cells of the Nervous System

- Terms used to describe the neuron include the following:
  - Afferent axon - refers to bringing information into a structure.
  - Efferent axon - refers to carrying information away from a structure.
  - Interneurons or Intrinsic neurons are those whose dendrites and axons are completely contained within a structure.

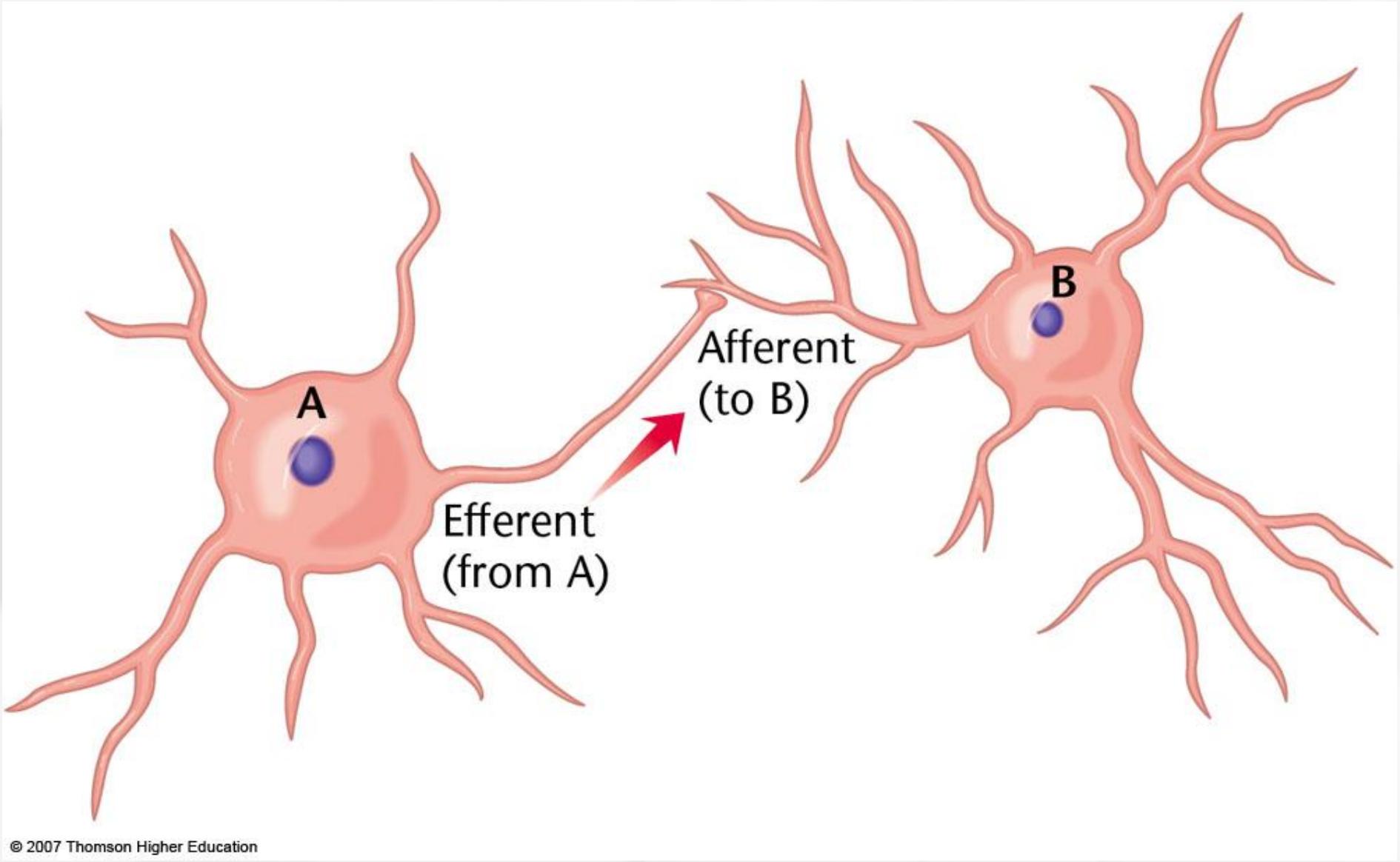
A
B
Afferent
(to B)
Efferent
(from A)
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Fig. 2-8, p. 34

The Cells of the Nervous System

- Neurons vary in size, shape, and function.
- The shape of a neuron determines its connection with other neurons.
- The function is closely related to the shape of a neuron.
  - Example: Pukinje cells of the cerebellum branch extremely widely within a single plane

The Cells of the Nervous System

- Glia are the other major component of the nervous system and include the following:
  - Astrocytes helps synchronize the activity of the axon by wrapping around the presynaptic terminal and taking up chemicals released by the axon.
  - Microglia - remove waste material and other microorganisms that could prove harmful to the neuron.

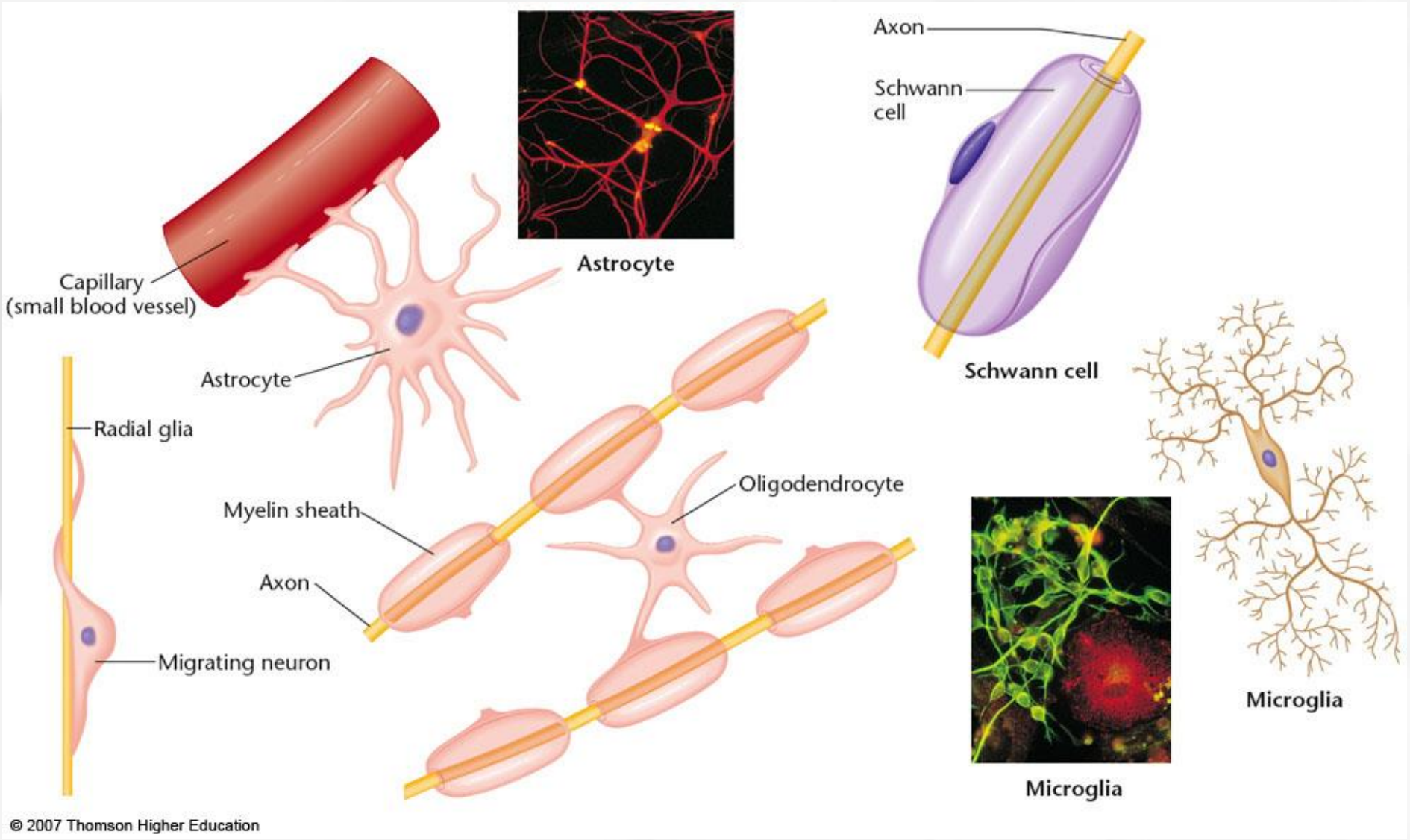

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Fig. 2-10, p. 35

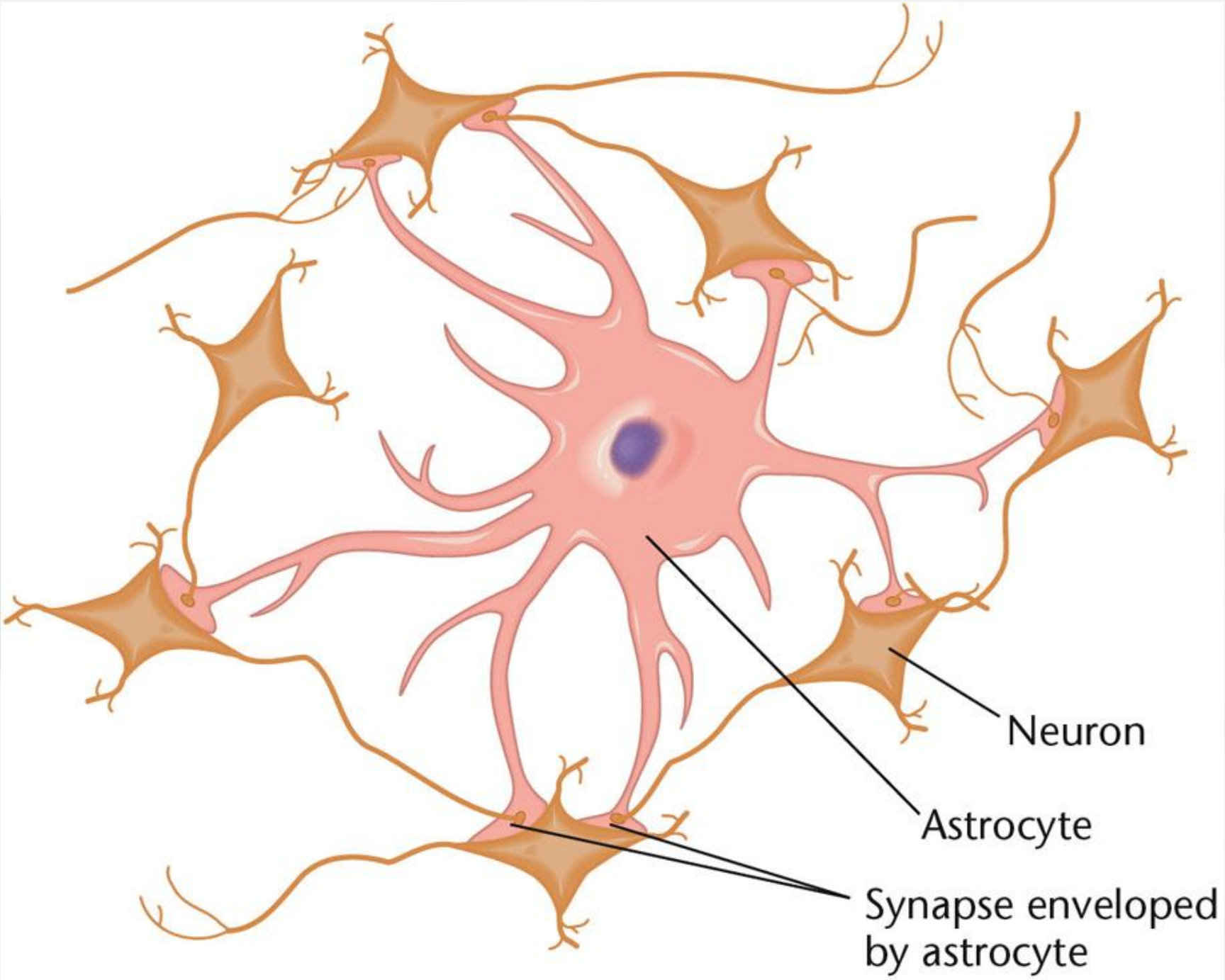

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Fig. 2-11, p. 36

The Cells of the Nervous System

- (Types of glia continued)
  - Oligodendrocytes & Schwann cells- build the myelin sheath that surrounds the axon of some neurons.
  - Radial glia- guide the migration of neurons and the growth of their axons and dendrites during embryonic development.

The Cells of the Nervous System

- The blood-brain barrier is a mechanism that surrounds the brain and blocks most chemicals from entering.
- Our immune system destroys damaged or infected cells throughout the body.
- Because neurons in the brain generally do not regenerate, it is vitally important for the blood brain barrier to block incoming viruses, bacteria or other harmful material from entering.

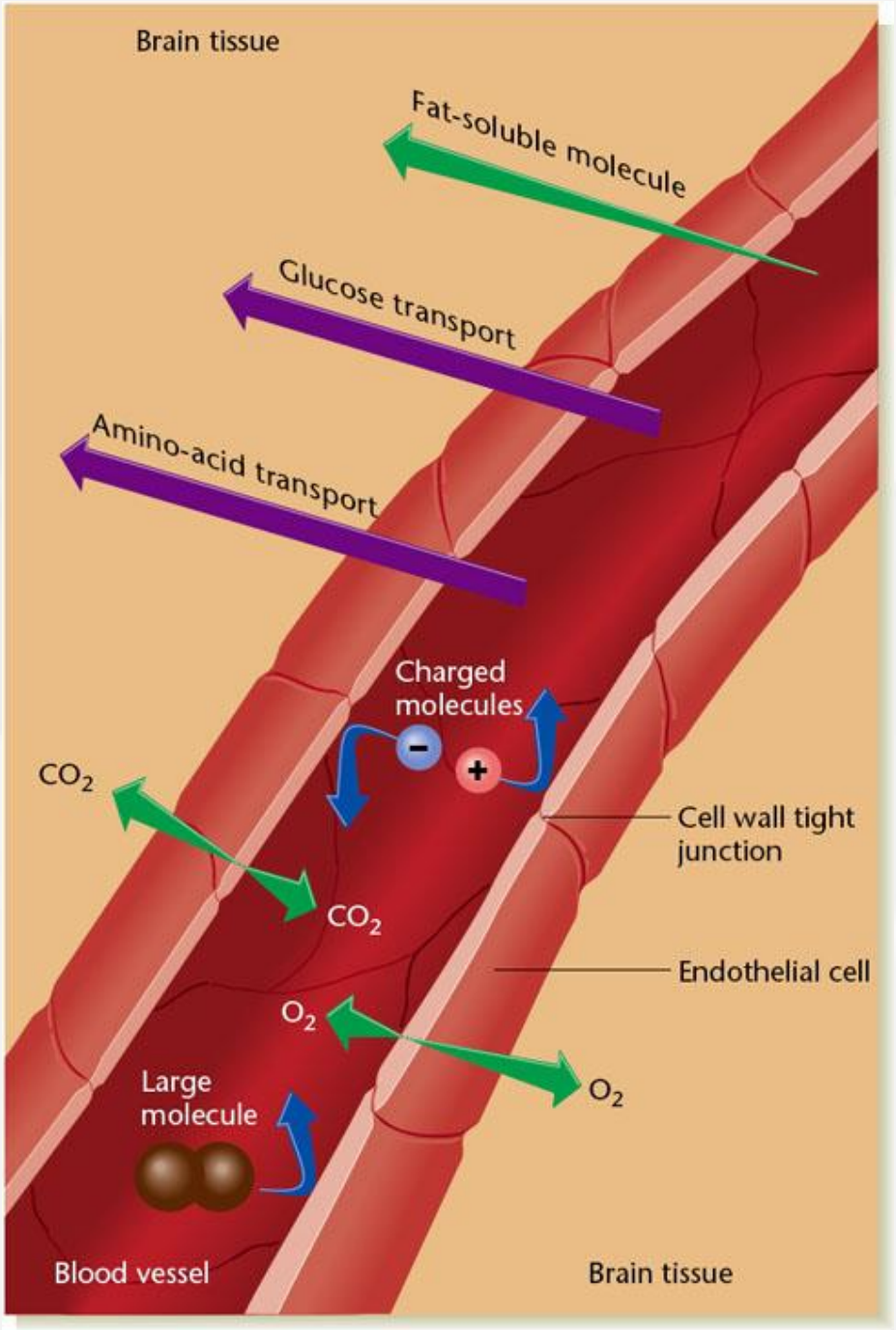

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Fig. 2-12, p. 37

The Cells of the Nervous System

- Active transport is the protein mediated process by which useful chemicals are brought into the brain.
- Glucose, hormones, amino acids, and vitamins are brought into the brain via active transport.
- Glucose is a simple sugar that is the primary source of nutrition for neurons.
  - Thiamine is a chemical that is necessary for the use of glucose.

The Nerve Impulse

- A nerve impulse is the electrical message that is transmitted down the axon of a neuron.
- The impulse does not travel directly down the axon but is regenerated at points along the axon.
- The speed of nerve impulses ranges from approximately 1 m/s to 100 m/s.

The Nerve Impulse

- The resting potential of a neuron refers to the state of the neuron prior to the sending of a nerve impulse.
- The membrane of a neuron maintains an electrical gradient which is a difference in the electrical charge inside and outside of the cell.

The Nerve Impulse

- At rest, the membrane maintains an electrical polarization or a difference in the electrical charge of two locations.
  - the inside of the membrane is slightly negative with respect to the outside. (approximately -70 millivolts)

The Nerve Impulse

- The membrane is selectively permeable, allowing some chemicals to pass more freely than others.
- Sodium, potassium, calcium, and chloride pass through channels in the membrane.
- When the membrane is at rest:
  - Sodium channels are closed.
  - Potassium channels are partially closed allowing the slow passage of sodium.

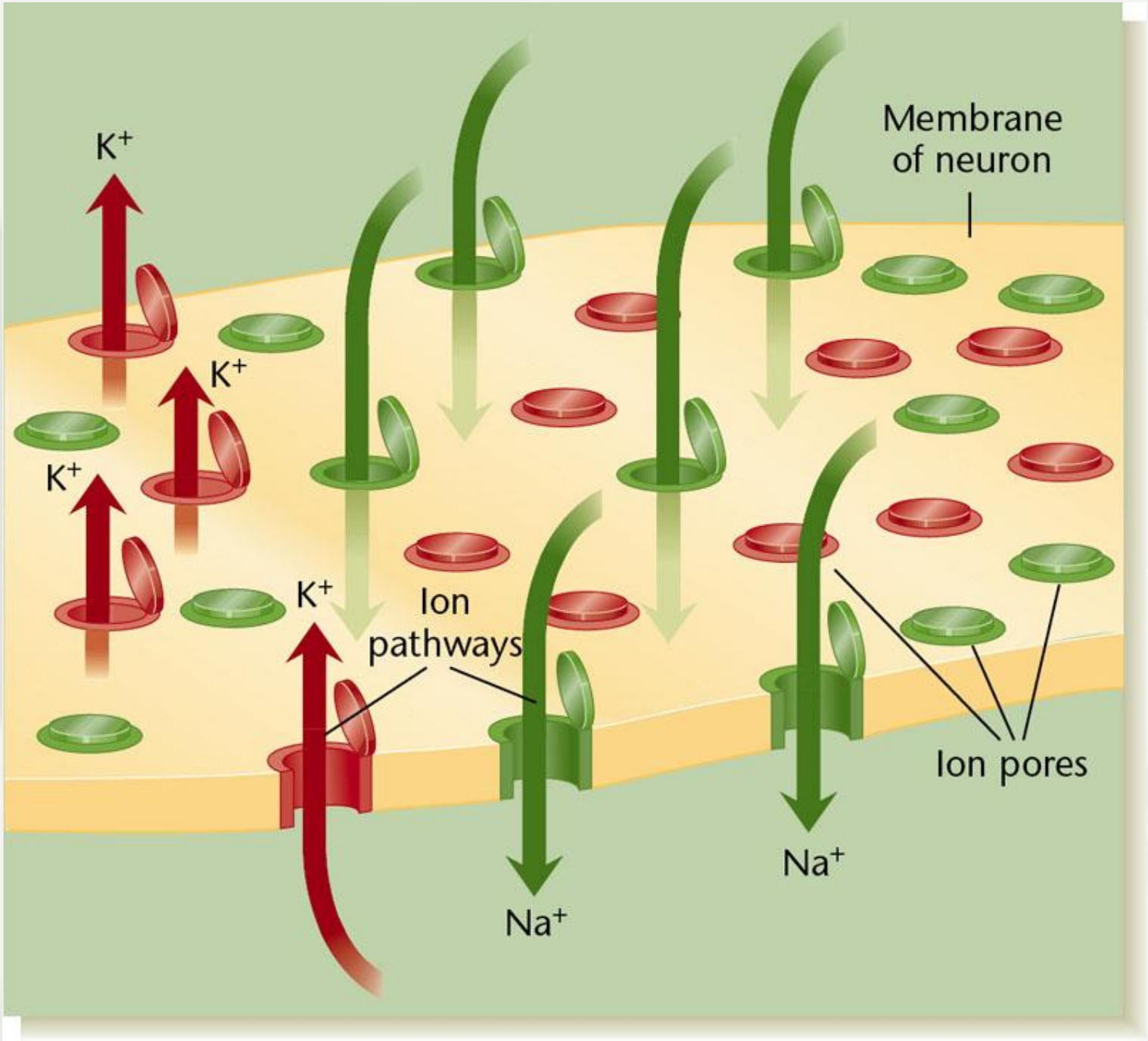

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Fig. 2-14, p. 40

The Nerve Impulse

- The sodium-potassium pump is a protein complex that continually pumps three sodium ions out of the cells while drawing two potassium ions into the cell.
  - helps to maintain the electrical gradient.
- The electrical gradient and the concentration gradient work to pull sodium ions into the cell.
- The electrical gradient tends to pull potassium ions into the cells.

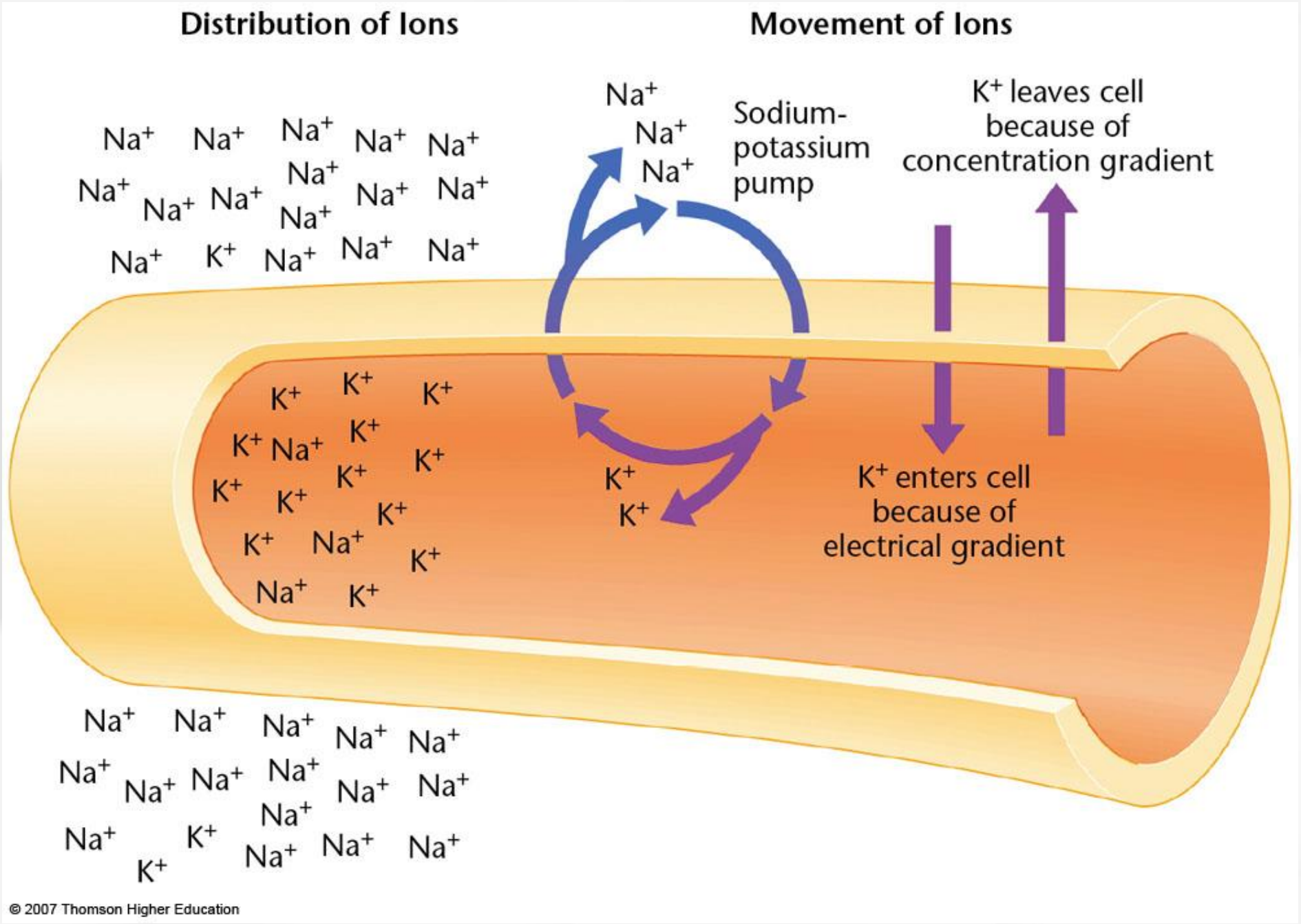
Distribution of Ions
Movement of Ions
Na+
Na+
Na+
Sodium-potassium pump
K+ leaves cell because of concentration gradient
K+ enters cell because of electrical gradient
K+
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Fig. 2-15, p. 41

- The resting potential remains stable until the neuron is stimulated.
- Hyperpolarization refers to increasing the polarization or the difference between the electrical charge of two places.
- Depolarization refers to decreasing the polarization towards zero.
- The threshold of excitement refers any stimulation beyond a certain level and results in a massive depolarization.

- An action potential is a rapid depolarization of the neuron.
- Stimulation of the neuron past the threshold of excitation triggers a nerve impulse or action potential.

Ion Channels

- When ion channels are open, they allow specific ions to move across the plasma membrane, down their **electrochemical gradient—a concentration difference (chemical + electrical**).
- Ion channels open and close due to the presence of “gates.” The gate is a part of the channel protein that can seal the channel pore shut or move aside to open the pore
- The electrical signals produced by neurons and muscle fibers rely on four types of ion channels: leakage channels, ligand-gated channels, mechanically gated channels, and voltage-gated channels

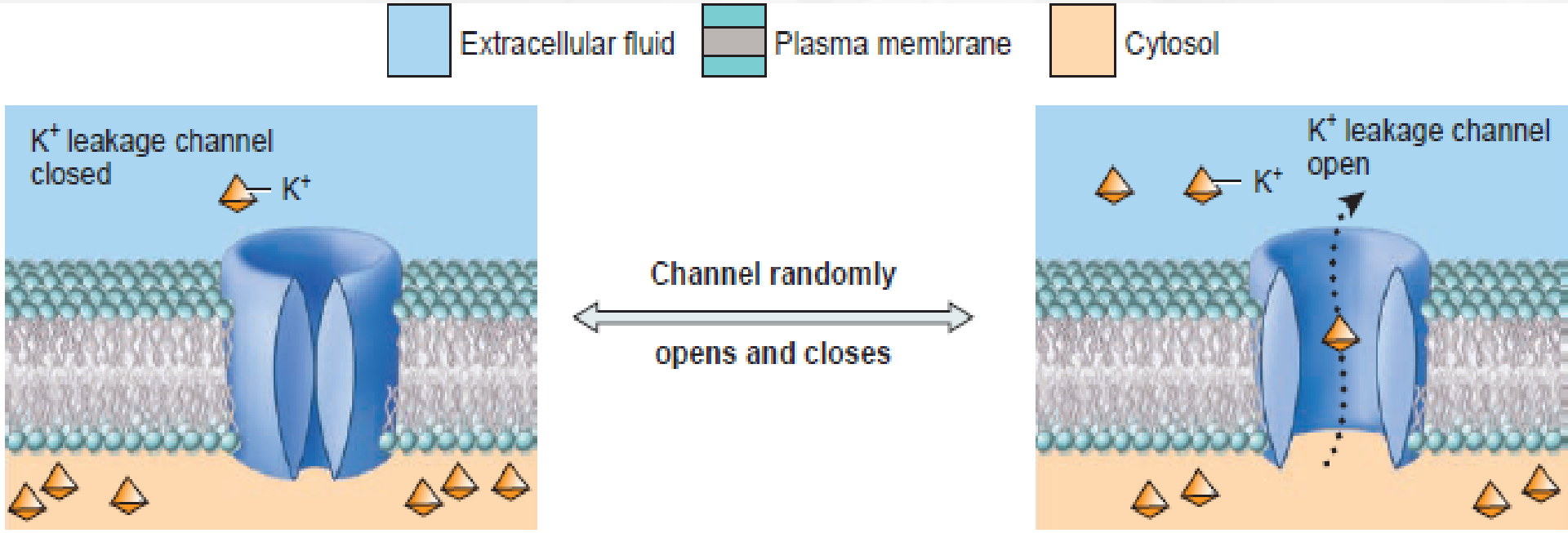
TABLE 12.1

Ion Channels in Neurons

TYPE OF ION CHANNEL	DESCRIPTION	LOCATION
Leakage channels	Gated channels that randomly open and close.	Found in nearly all cells, including the dendrites, cell bodies, and axons of all types of neurons.
Ligand-gated channels	Gated channels that open in response to the binding of a ligand (chemical) stimulus.	Dendrites of some sensory neurons such as pain receptors and dendrites and cell bodies of interneurons and motor neurons.
Mechanically gated channels	Gated channels that open in response to the binding of a mechanical stimulus (such as touch, pressure, vibration, and tissue stretching).	Dendrites of some sensory neurons such as touch receptors, pressure receptors, and some pain receptors.
Voltage-gated channels	Gated channels that open in response to a voltage stimulus (change in membrane potential).	Axons of all types of neurons.

Leakage channels

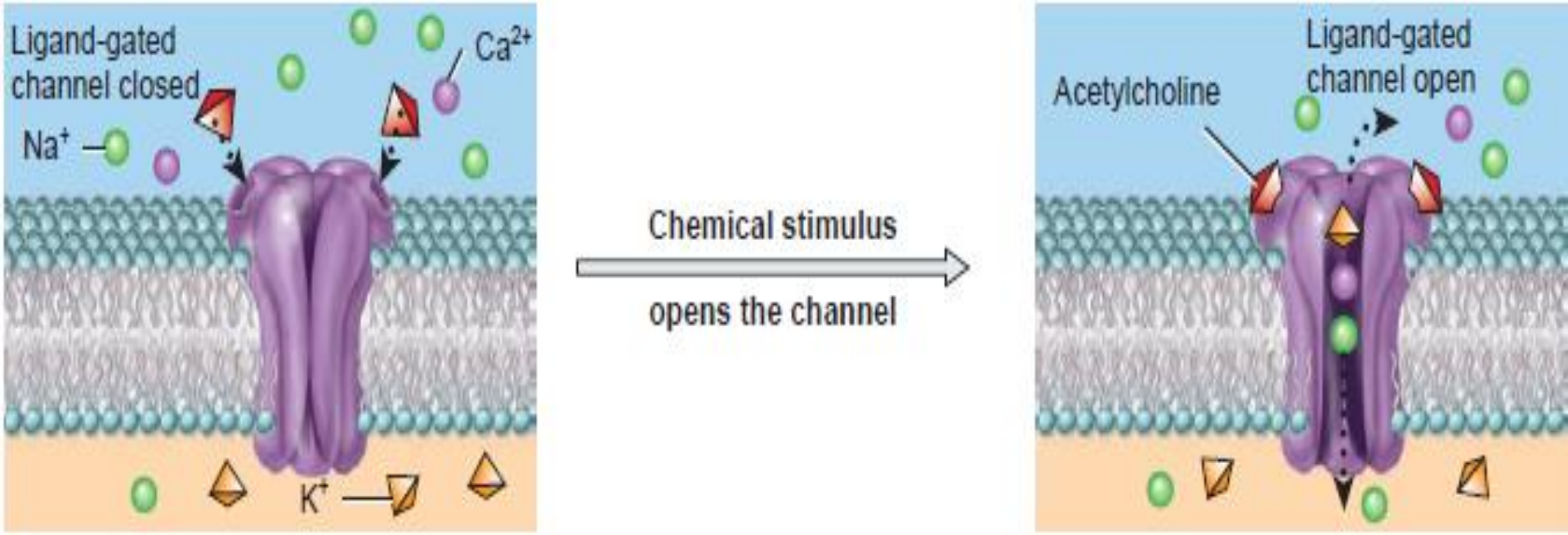
- The gates of leakage channels randomly alternate between open and closed positions
- Plasma membranes have many more potassium ion (K) leakage channels than sodium ion (Na) leakage channels
- Thus, the membrane’s permeability to K is much higher than its permeability to Na.



(a) Leakage channel

Ligand-gated channel

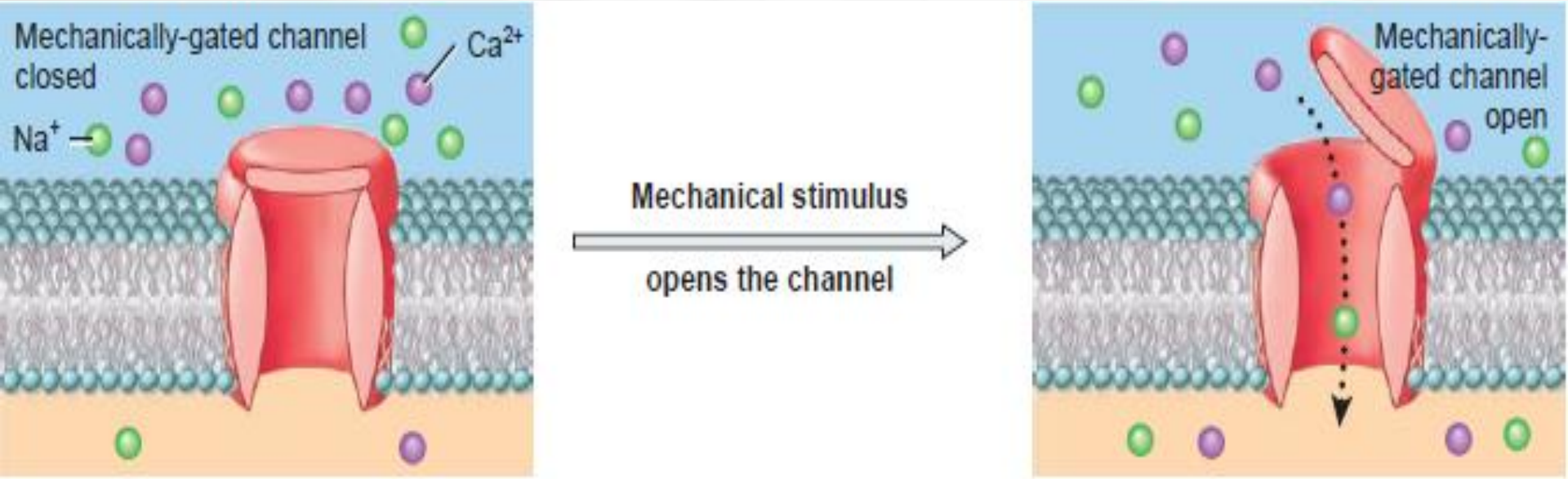
- A ligand-gated channel opens and closes in response to a specific chemical stimulus.
- A wide variety of chemical ligands—including neurotransmitters, hormones, and particular ions—can open or close ligand-gated channels.
- The neurotransmitter acetylcholine opens cation channels that allow Na and Ca^2 to diffuse inward and K to diffuse outward



(b) Ligand-gated channel

Mechanically gated channel

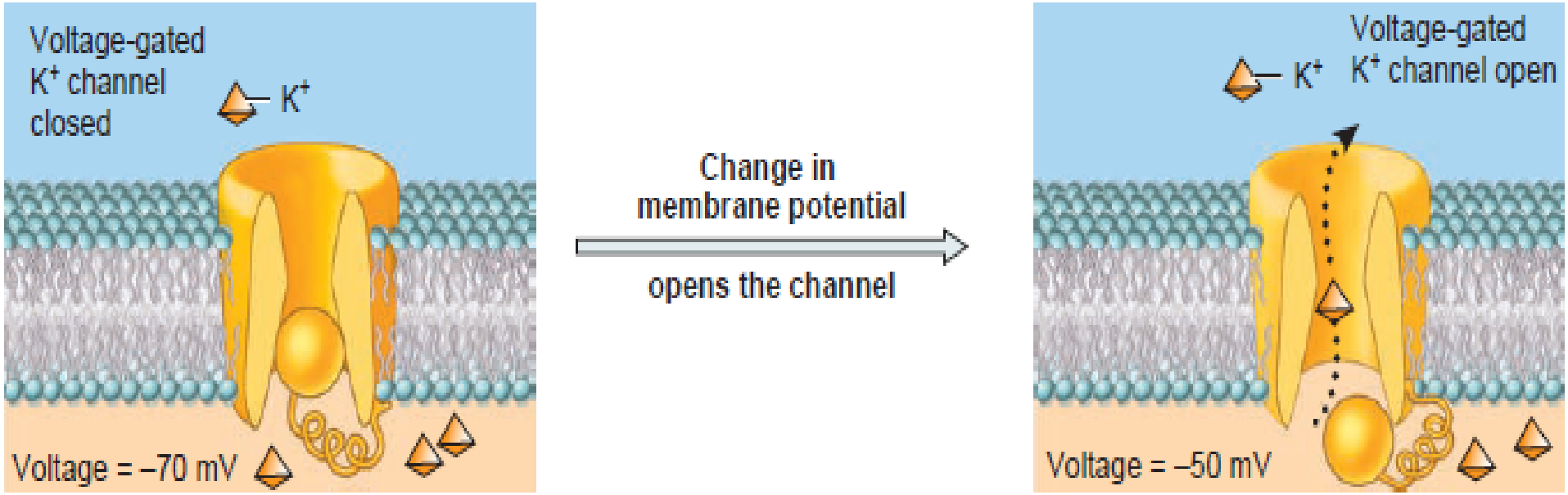
- A mechanically gated channel opens or closes in response to mechanical stimulation in the form of vibration (such as sound waves), touch, pressure, or tissue stretching
- The force distorts the channel from its resting position, opening the gate.
- Examples - auditory receptors in the ears, receptors that monitor stretching of internal organs, and touch receptors and pressure receptors in the skin



(c) Mechanically-gated channel

Voltage-gated channel

- Voltage-activated channels are membrane channels whose permeabililty depends upon the voltage difference across the membrane.
  - Sodium channels are voltage activated channels.
- When sodium channels are opened, positively charged sodium ions rush in and a subsequent nerve impulse occurs.

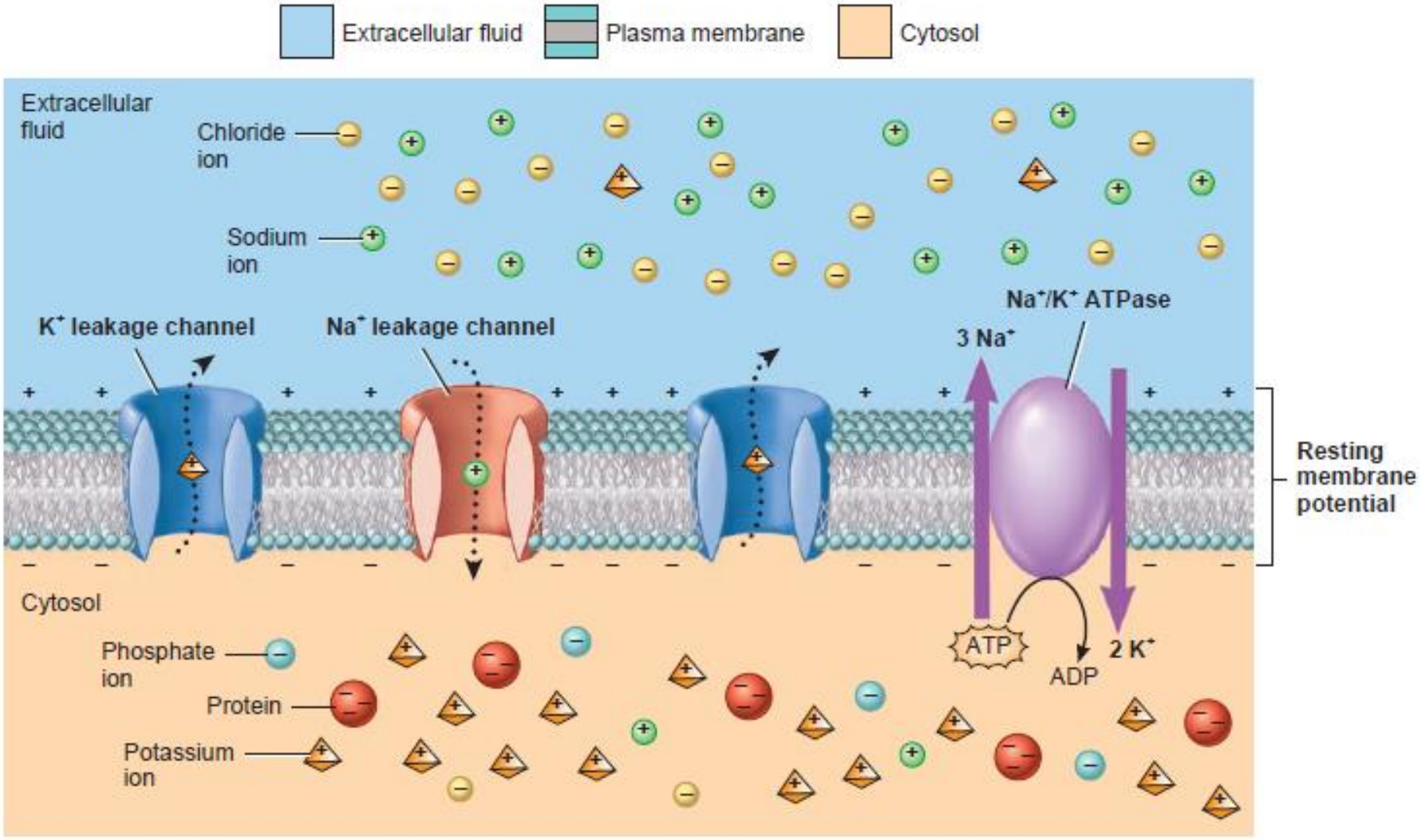


(d) Voltage-gated channel

Resting Membrane Potential

- In neurons, the resting membrane potential ranges from -40 to -90 mV. A typical value is -70 mV. The minus sign indicates that the inside of the cell is negative relative to the outside.
- A cell that exhibits a membrane potential is said to be **polarized**

- The resting membrane potential is determined by three major factors: (1) unequal distribution of ions in the ECF and cytosol; (2) inability of most anions to leave the cell; and (3) electrogenic nature of the Na^+/K^+ ATPases.



Resting Membrane Potential

- **Unequal distribution of ions in the ECF and cytosol-** Extracellular fluid is rich in Na and chloride ions (Cl). In cytosol, however, the main cation is K,and the two dominant anions are phosphates attached to molecules,such as the three phosphates in ATP, and amino acids in proteins
- **Inability of most anions to leave the cell.**
- **Electrogenic nature of the Na/K ATPases** -These pumps help maintain the resting membrane potential by pumping out Na as fast as it leaks in. At the same time, the Na/K ATPases bring in K. Na/K ATPases expel three Na for each two K imported. Since these pumps remove more positive charges from the cell than they bring into the cell, they are electrogenic, which means they contribute to the negativity of the resting membrane potential

Graded Potential

- A graded potential is a small deviation from the membrane potential that makes the membrane either more polarized (inside more negative) or less polarized (inside less negative) ie *hyperpolarizing graded potential or depolarizing graded potential*

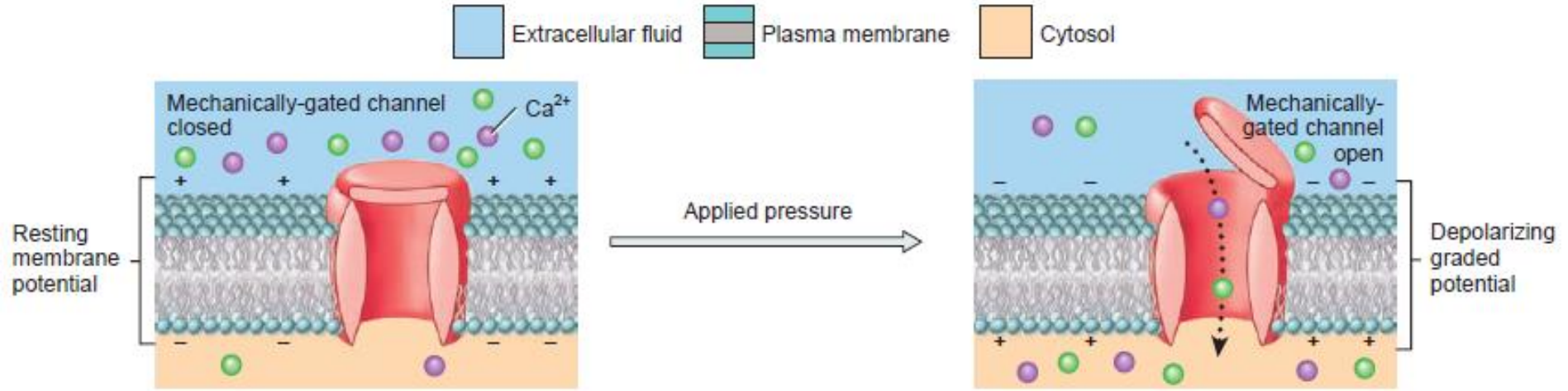
TABLE 12.2

Comparison of Graded Potentials and Action Potentials in Neurons

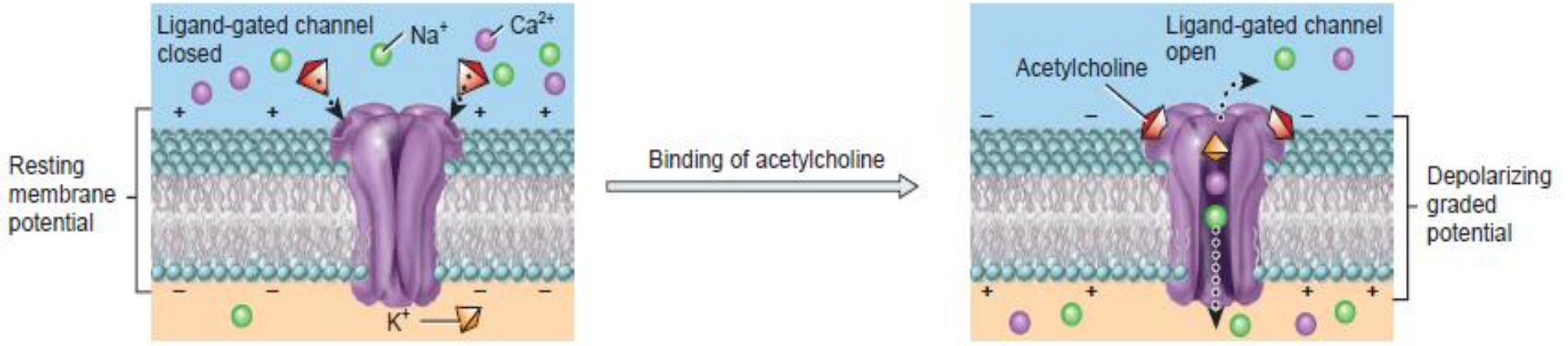
CHARACTERISTIC	GRADED POTENTIALS	ACTION POTENTIALS
Origin	Arise mainly in dendrites and cell body.	Arise at trigger zones and propagate along the axon.
Types of channels	Ligand-gated or mechanically gated ion channels.	Voltage-gated channels for Na^+ and K^+.
Conduction	Decremental (not propagated); permit communication over short distances.	Propagate and thus permit communication over longer distances.
Amplitude (size)	Depending on strength of stimulus, varies from less than 1 mV to more than 50 mV.	All-or-none; typically about 100 mV.
Duration	Typically longer, ranging from several msec to several min.	Shorter, ranging from 0.5 to 2 msec.
Polarity	May be hyperpolarizing (inhibitory to generation of an action potential) or depolarizing (excitatory to generation of an action potential).	Always consists of depolarizing phase followed by repolarizing phase and return to resting membrane potential.
Refractory period	Not present, thus summation can occur.	Present, thus summation cannot occur.

Figure 12.16 **Generation of graded potentials in response to the opening of mechanically gated channels or ligand-gated channels.** (a) A mechanical stimulus such as pressure opens a mechanically gated channel that allows passage of cations (mainly Na^+ and Ca^{2+}) into the cell, and a depolarizing graded potential occurs because the membrane potential becomes inside less negative than at rest. (b) The neurotransmitter acetylcholine (a ligand stimulus) opens a cation channel that allows passage of Na^+, K^+, and Ca^{2+}, but Na^+ inflow is greater than either Ca^{2+} inflow or K^+ outflow and a depolarizing graded potential occurs because the membrane potential becomes inside less negative than at rest. (c) The neurotransmitter glycine (a ligand stimulus) opens a Cl^- channel that allows passage of Cl^- ions into the cell, and a hyperpolarizing graded potential occurs because the membrane potential becomes inside more negative than at rest.

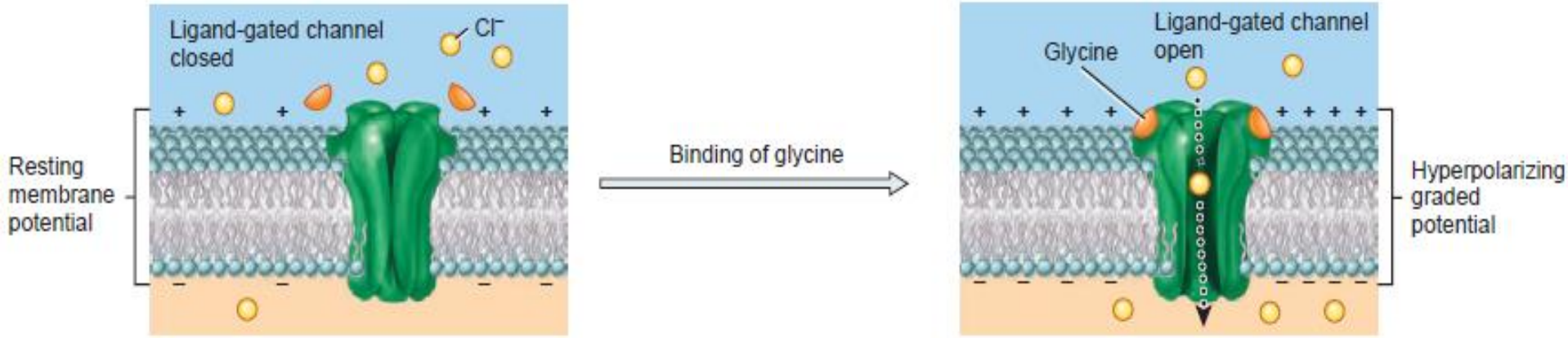
6 A graded potential forms in response to the opening of mechanically gated channels or ligand-gated channels.



(a) Depolarizing graded potential caused by pressure, a mechanical stimulus



(b) Depolarizing graded potential caused by the neurotransmitter acetylcholine, a ligand stimulus

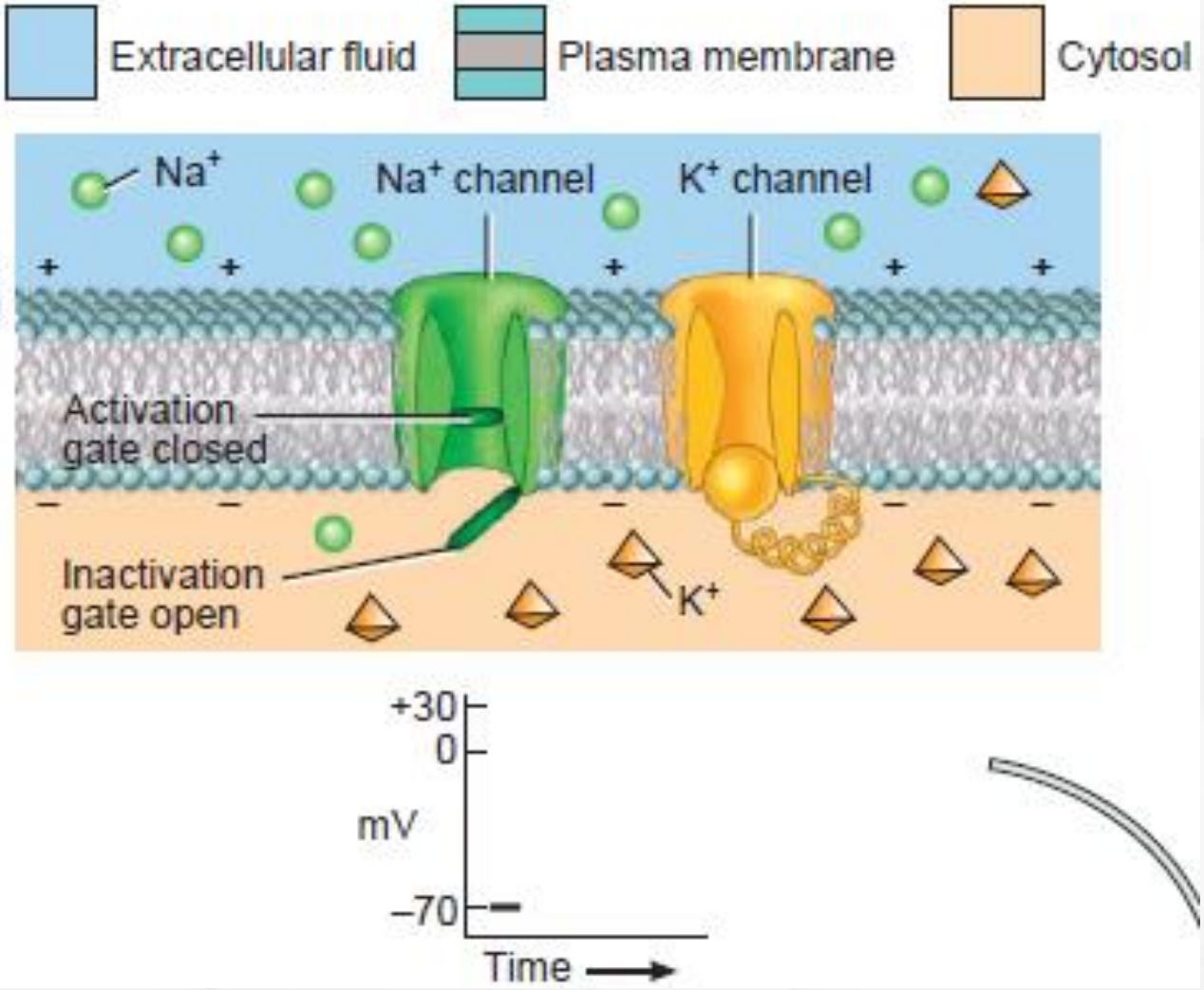


(c) Hyperpolarizing graded potential caused by the neurotransmitter glycine, a ligand stimulus

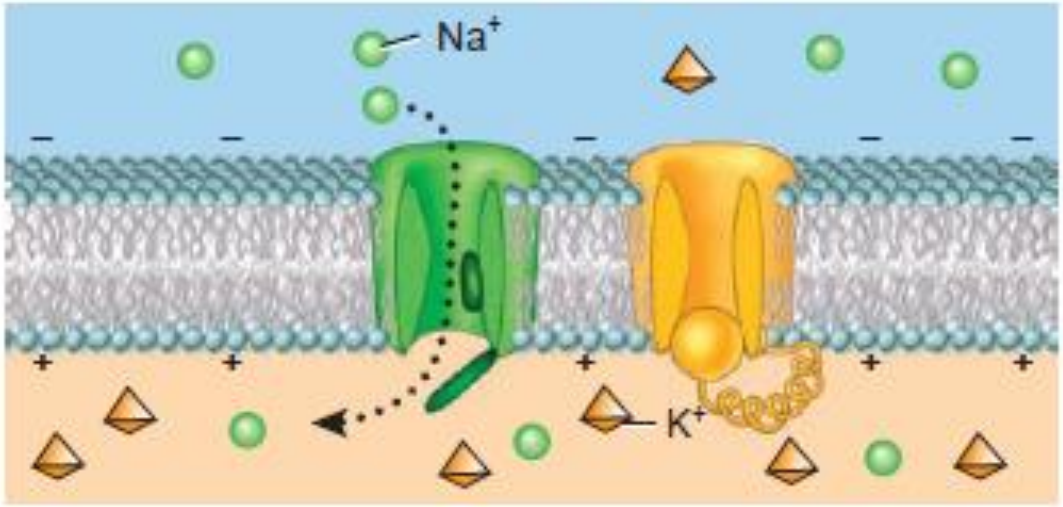
Generation of Action Potentials

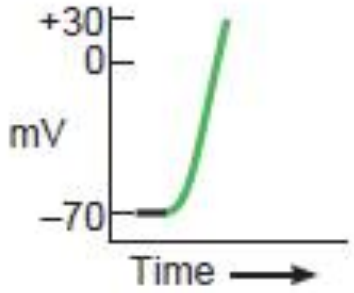
- An action potential (AP) or impulse is a sequence of rapidly occurring events that decrease and reverse the membrane potential and then eventually restore it to the resting state.
- An action potential has two main phases: a depolarizing phase and a repolarizing phase

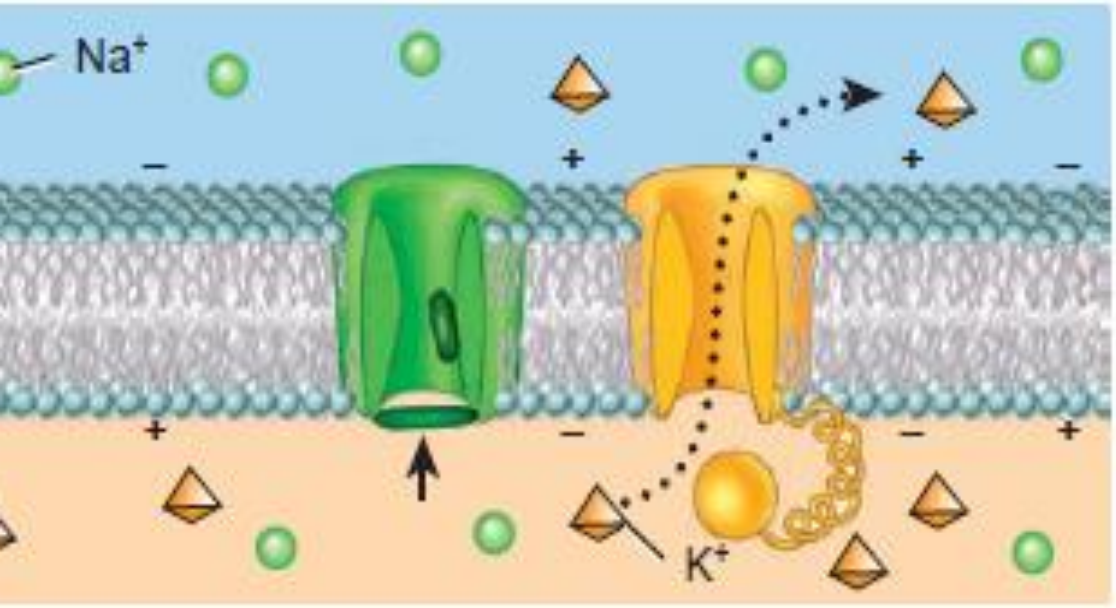
Inflow of sodium ions (Na^+) causes the depolarizing phase, and outflow of potas
the repolarizing phase of an action potential.



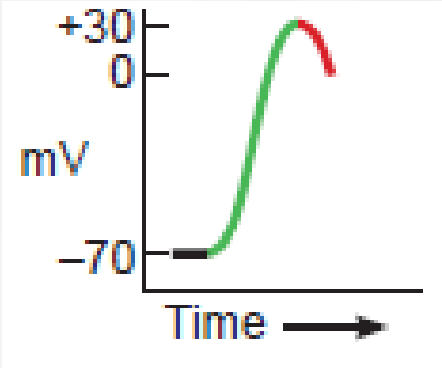
2. **Depolarizing phase:** When membrane potential of axon reaches threshold, the Na^+ channel activation gates open. As Na^+ ions move through these channels into the neuron, a buildup of positive charges forms along inside surface of membrane and the membrane becomes depolarized.

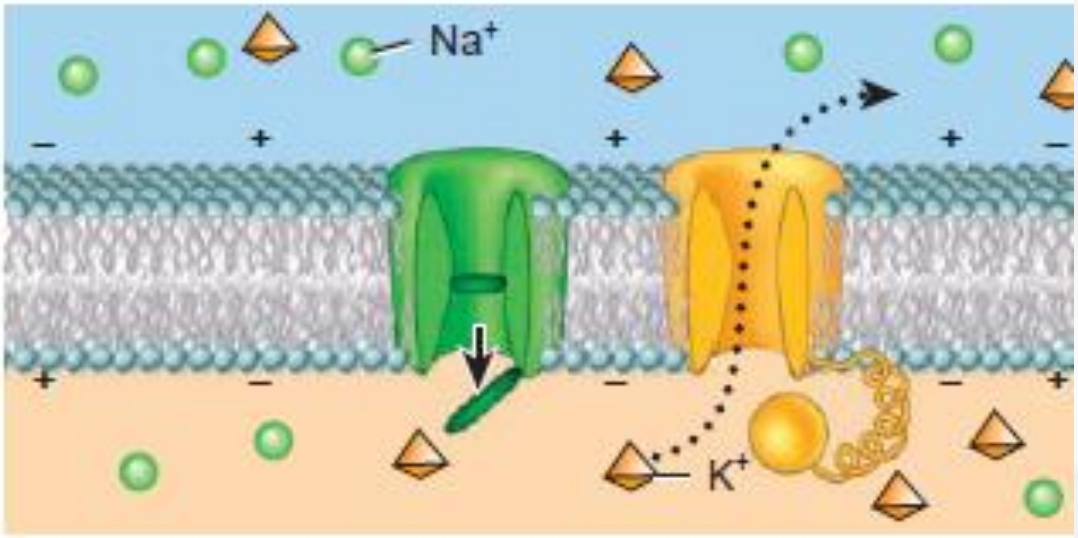


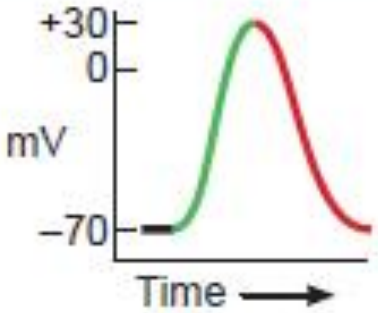




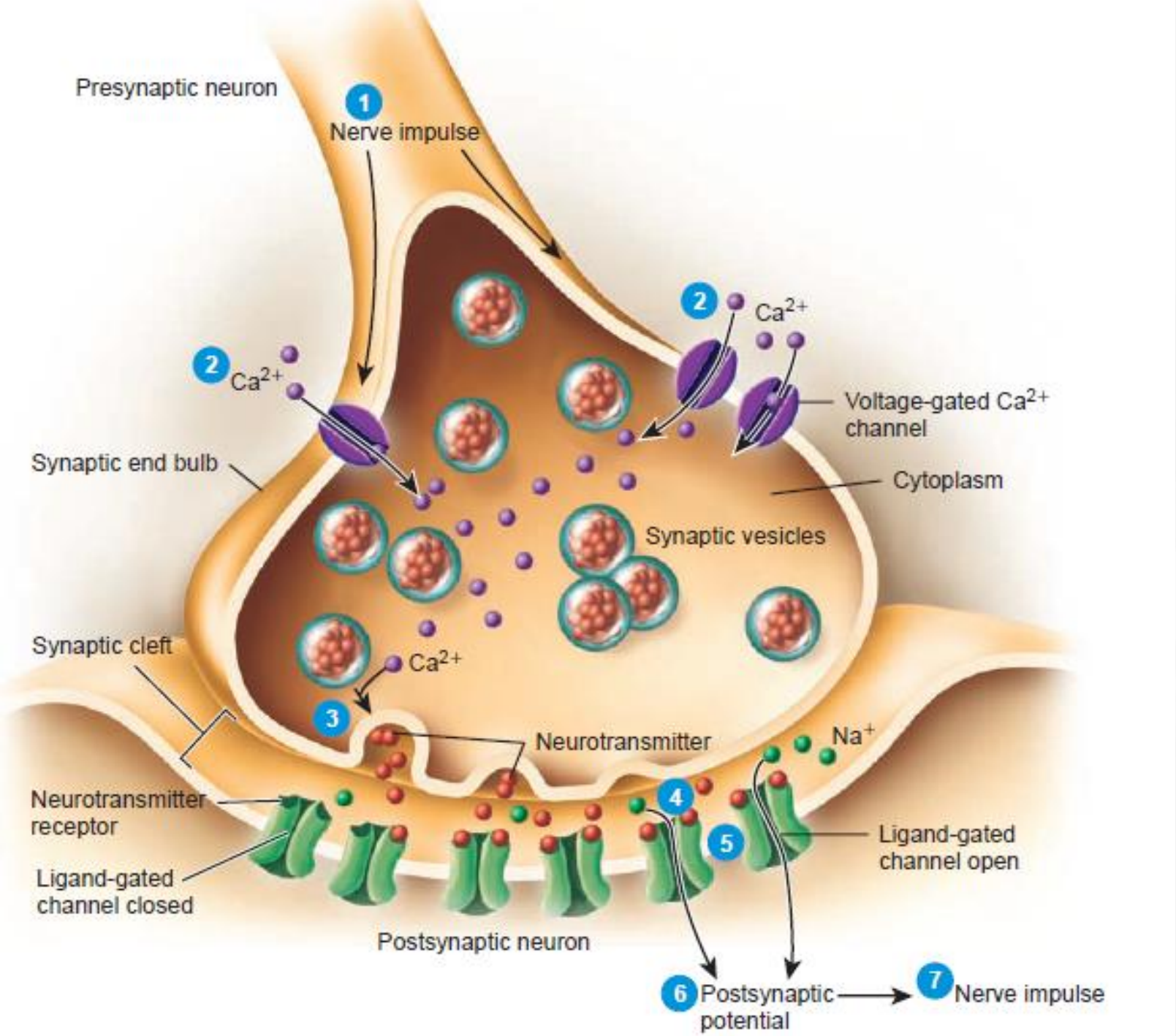
3. **Repolarizing phase begins:** Na^+ channel inactivation gates close and K^+ channels open. The membrane starts to become repolarized as some K^+ ions leave the neuron and a few negative charges begin to buildup along the inside surface of the membrane.







4. **Repolarization phase continues:** K^+ outflow continues. As more K^+ ions leave the neuron, more negative charges build up along inside surface of the membrane. K^+ outflow eventually restores resting membrane potential. Na^+ channel inactivation gates open. Return to resting state when K^+ gates close.


Presynaptic neuron
1
Nerve impulse
2
Ca^{2+}
2
Ca^{2+}
Voltage-gated Ca^{2+} channel
Synaptic end bulb
Cytoplasm
Synaptic vesicles
Synaptic cleft
Ca^{2+}
3
Neurotransmitter
Na^{+}
Neurotransmitter receptor
4
5
Ligand-gated channel open
Ligand-gated channel closed
Postsynaptic neuron
6
Postsynaptic potential
7
Nerve impulse

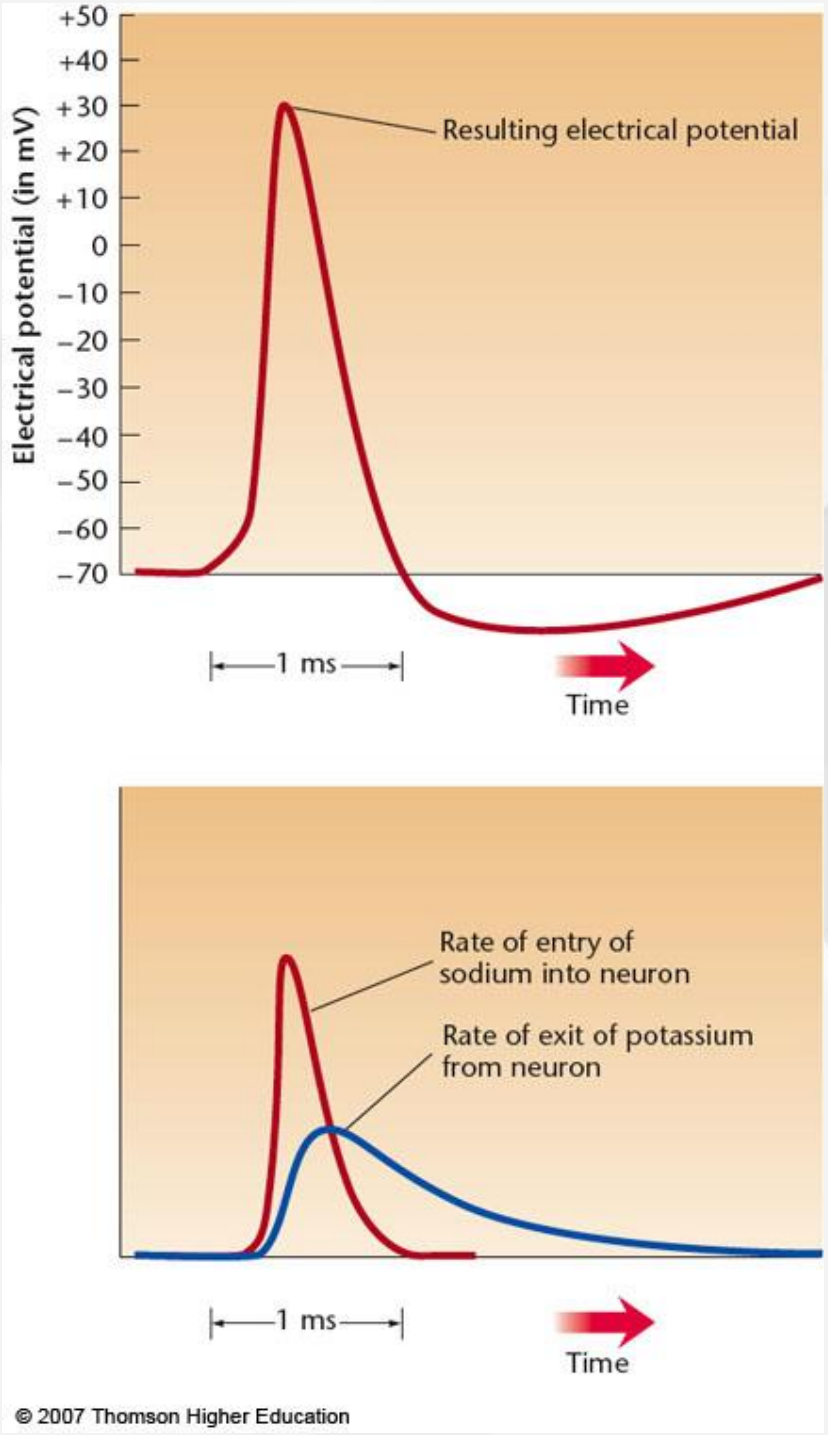


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Fig. 2-16, p. 43

The Nerve Impulse

- After an action potential occurs, sodium channels are quickly closed.
- The neuron is returned to its resting state by the opening of potassium channels.
  - potassium ions flow out due to the concentration gradient and take with them their positive charge.
- The sodium-potassium pump later restores the original distribution of ions.

The Nerve Impulse

- Local anesthetic drugs block sodium channels and therefore prevent action potentials from occurring.
  - Example: Novocain

The Nerve Impulse

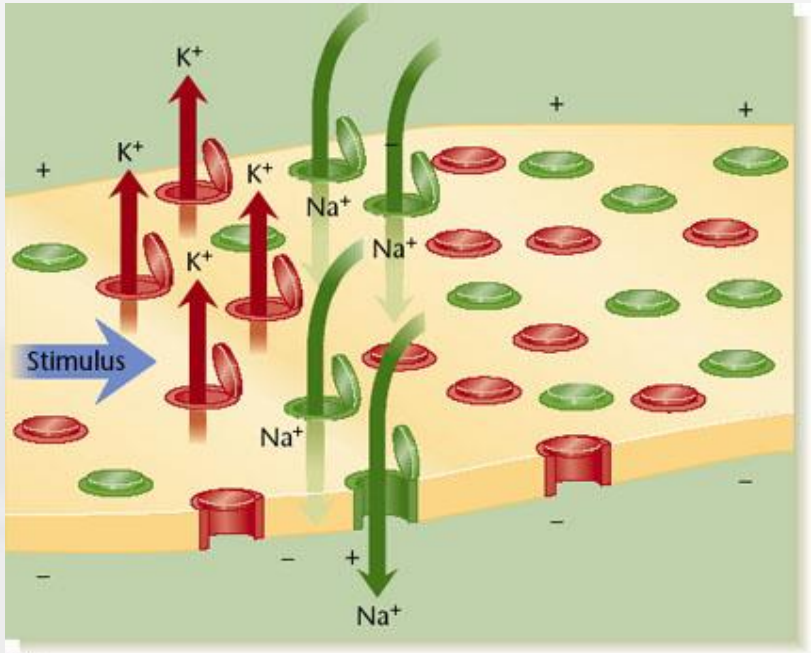
- The all-or-none law states that the amplitude and velocity of an action potential are independent of the intensity of the stimulus that initiated it.
  - Action potentials are equal in intensity and speed within a given neuron.

The Nerve Impulse

- After an action potential, a neuron has a refractory period during which time the neuron resists another action potential.
- The absolute refractory period is the first part of the period in which the membrane can not produce an action potential.
- The relative refractory period is the second part in which it take a stronger than usual stimulus to trigger an action potential.

The Nerve Impulse

- In a motor neuron, the action potential begins at the axon hillock (a swelling where the axon exits the soma).
- Propagation of the action potential is the term used to describe the transmission of the action potential down the axon.
  - the action potential does not directly travel down the axon.



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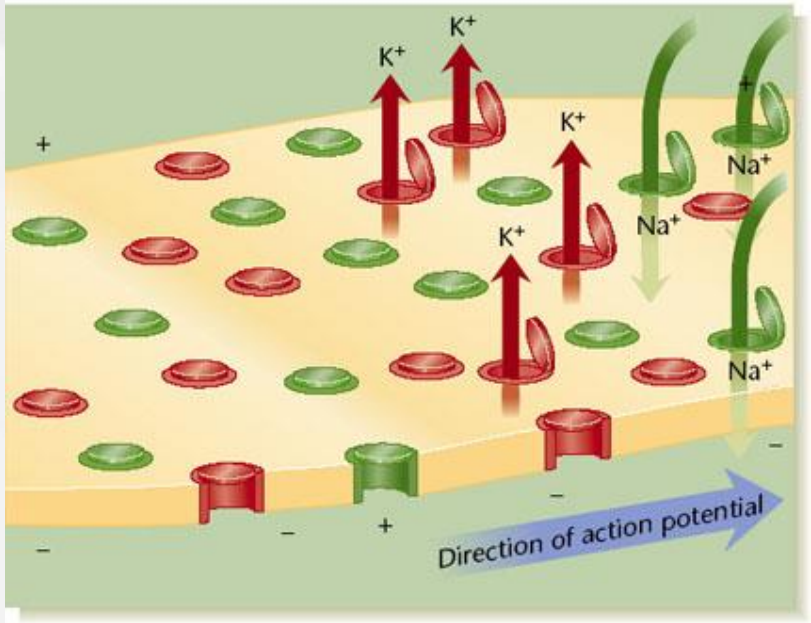

(b)

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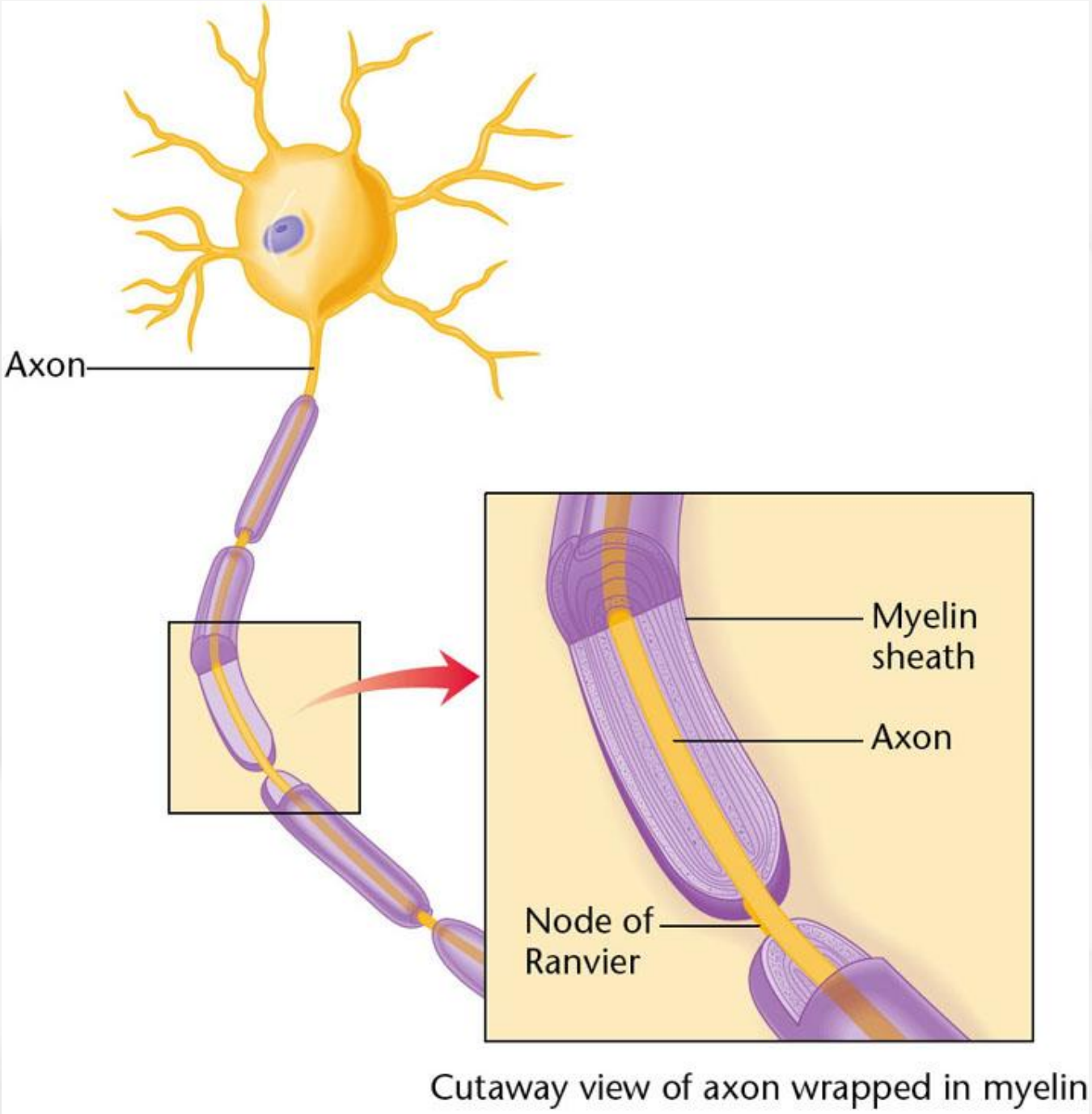
Fig. 2-17, p. 45

The Nerve Impulse

- The myelin sheath of axons are interrupted by short unmyelinated sections called nodes of Ranvier.
- At each node of Ranvier, the action potential is regenerated by a chain of positively charged ion pushed along by the previous segment.



Cutaway view of axon wrapped in myelin

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Fig. 2-18, p. 46

The Nerve Impulse

- Saltatory conduction is the word used to describe this “jumping” of the action potential from node to node.
  - Provides rapid conduction of impulses
  - Conserves energy for the cell
- Multiple sclerosis is disease in which the myelin sheath is destroyed and associated with poor muscle coordination.

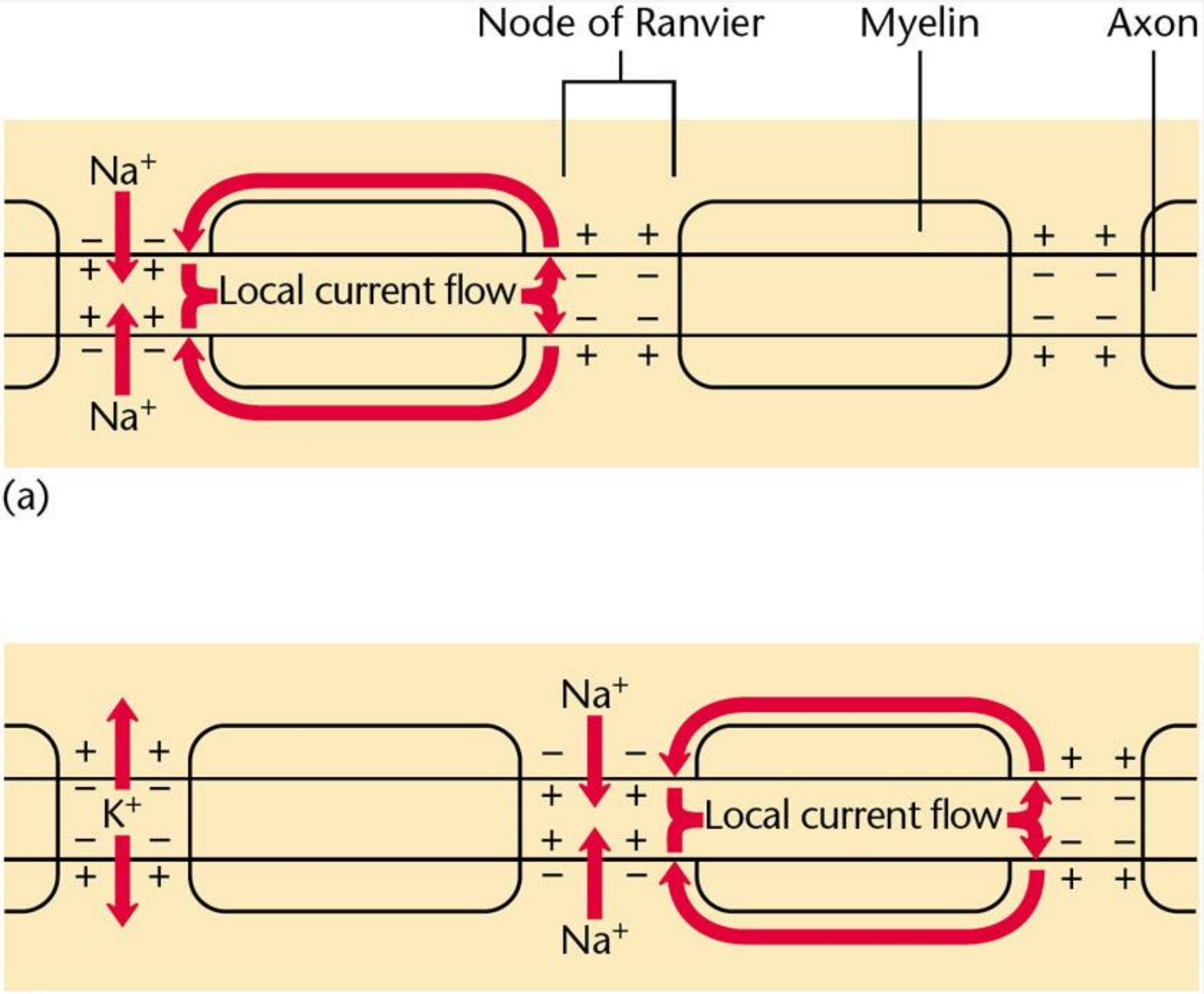

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Fig. 2-19, p. 46

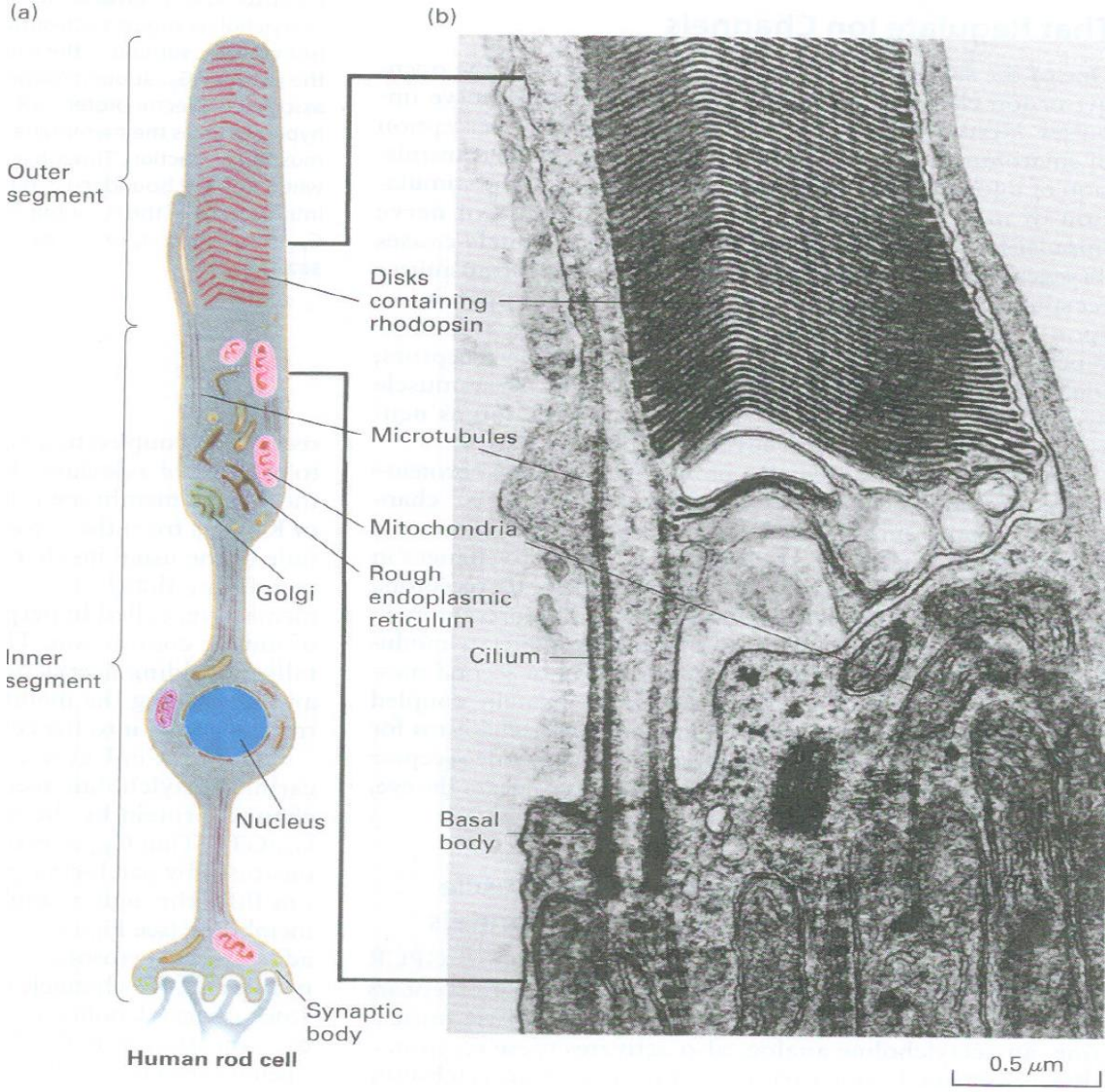
The Nerve Impulse

- Not all neurons have lengthy axons.
- Local neurons have short axons, exchange information with only close neighbours, and do not produce action potentials.
- When stimulated, local neurons produce graded potentials which are membrane potentials that vary in magnitude and do not follow the all-or-none law.
- A local neuron depolarizes or hyperpolarizes in proportion to the stimulation.

Light Activates G Protein-Coupled Rhodopsins in Rod Cells of the Eye

- Human retina contains two types of photoreceptor cells, *rods and cones, which are the primary recipients of visual* stimulation.
- Cones are involved in color vision, while rods are stimulated by weak light such as moonlight over a range of wavelengths.
- Signals are processed and interpreted by the part of the brain called the *visual cortex.*
- Rod cells sense light with the aid of a light-sensitive GPCR known as *rhodopsin.*
- *Rhodopsin consists of the protein* opsin, which has the usual GPCR structure, covalently linked to a light-absorbing pigment called retinal.

- A human rod cell contains about 4 X 10^7 molecules of rhodopsin.
- The trimeric G protein coupled to rhodopsin, called *transducin (G_t), contains* a Gα unit referred to as $G_{\alpha t}$; like rhodopsin, $G_{\alpha t}$ is found only in rod cells.

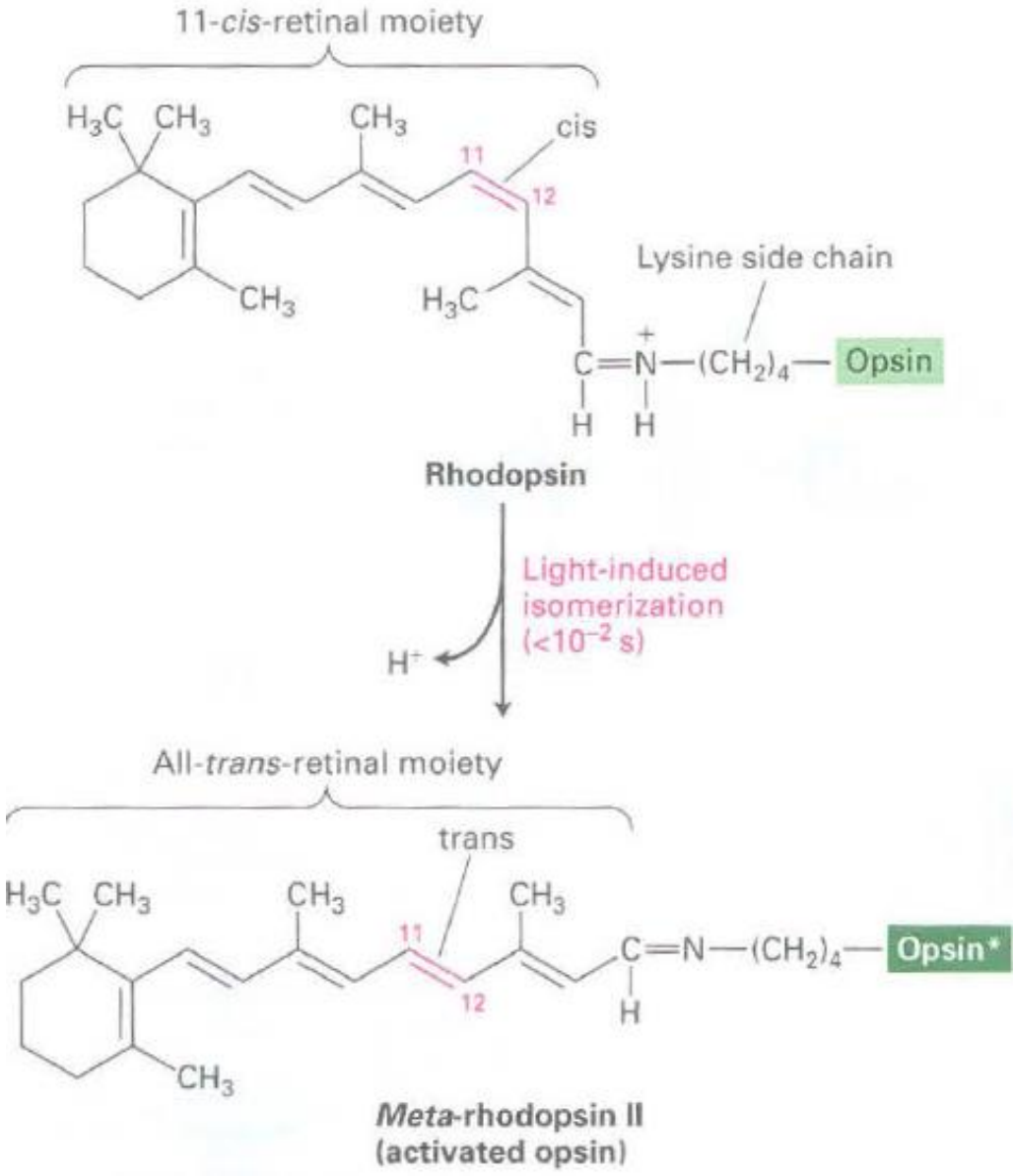


1. Activating signal - Absorption of a photon of light by the bound retinal

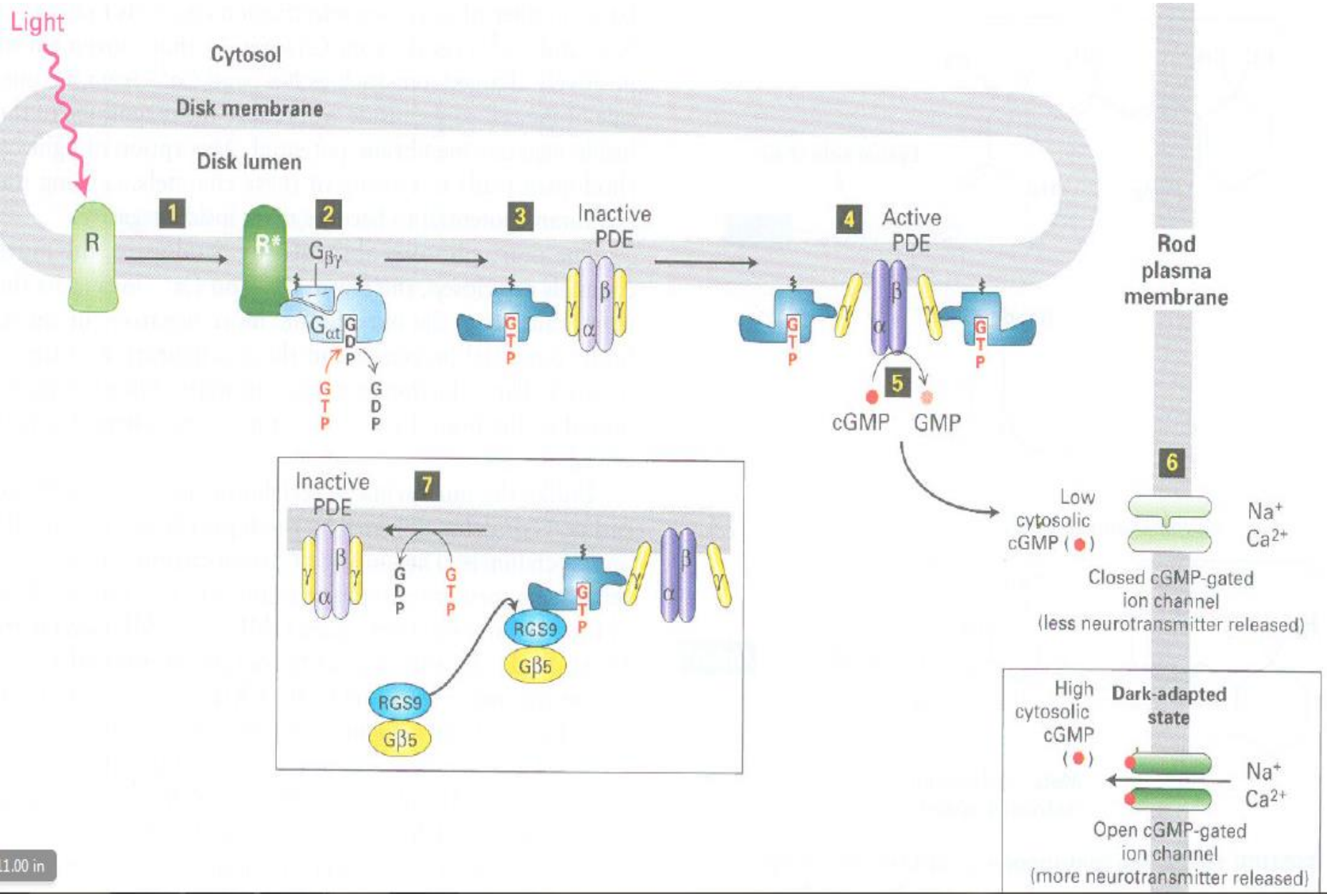
2. Retinal moiety of rhodopsin is immediately converted from the cis form (known as 11-cisretinal) to the all-trans isomer, causing a conformational change in the opsin protein

3. Form an unstable intermediate meta-rhodopsin II or activated opsin which activates G_t proteins .

4. Within seconds, all-trans-retinal dissociates from opsin and is converted by an enzyme back to the cis isomer, which then rebinds to another opsin molecule



Activation of Rhodopsin by light leads to Closing of cGMP-Gated Cation Channels



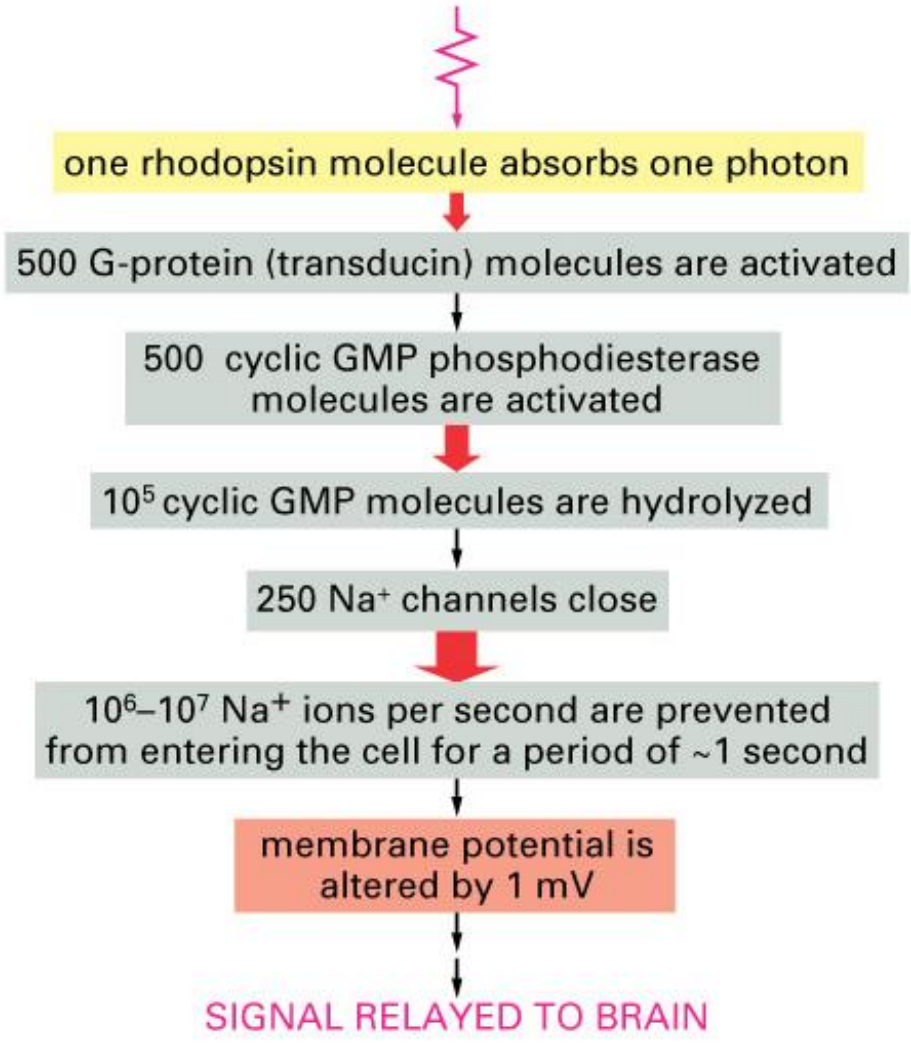
Light-activated rhodopsin pathway and the closing of cation channels in rod cells.

- In dark-adapted rod cells, a high level of cGMP keeps nucleotide-gated non-selective cation channels open, leading to depolarization of the plasma membrane and neurotransmitter release. Light absorption generates activated rhodopsin, R
- Rhodopsin binds inactive GDP-bound $G_{\alpha t}$ protein and mediates replacement of GDP with GTP
- The free $G_{\alpha t}$·GTP generated then activates cGMP phosphodiesterase (PDE) by binding to its inhibitory γ subunits and dissociating them from the catalytic α and β subunits.
- Relieved of their inhibition, the α and β subunits of PDE hydrolyze cGMP to GMP

- The resulting decrease in cytosolic cGMP leads to dissociation of cGMP from the nucleotide-gated channels in the plasma membrane and closing of the channels.
- The membrane then becomes transiently hyperpolarized, and neurotransmitter release is reduced.
- The complex of G_{α}-GTP and the PDE γ subunits binds a GTPase activating complex termed RGS9-Gβ5 ; by hydrolyzing the bound GTP, this triggers the physiologically rapid inactivation of the phosphodiesterase

Signal Amplification Makes the Rhodopsin Signal Transduction Pathway Sensitive

Absorbance of a single photon-yielding a single activated opsin molecule-can trigger closing of thousands of ion channels in the plasma membrane and a measurable change in the membrane potential of the cell

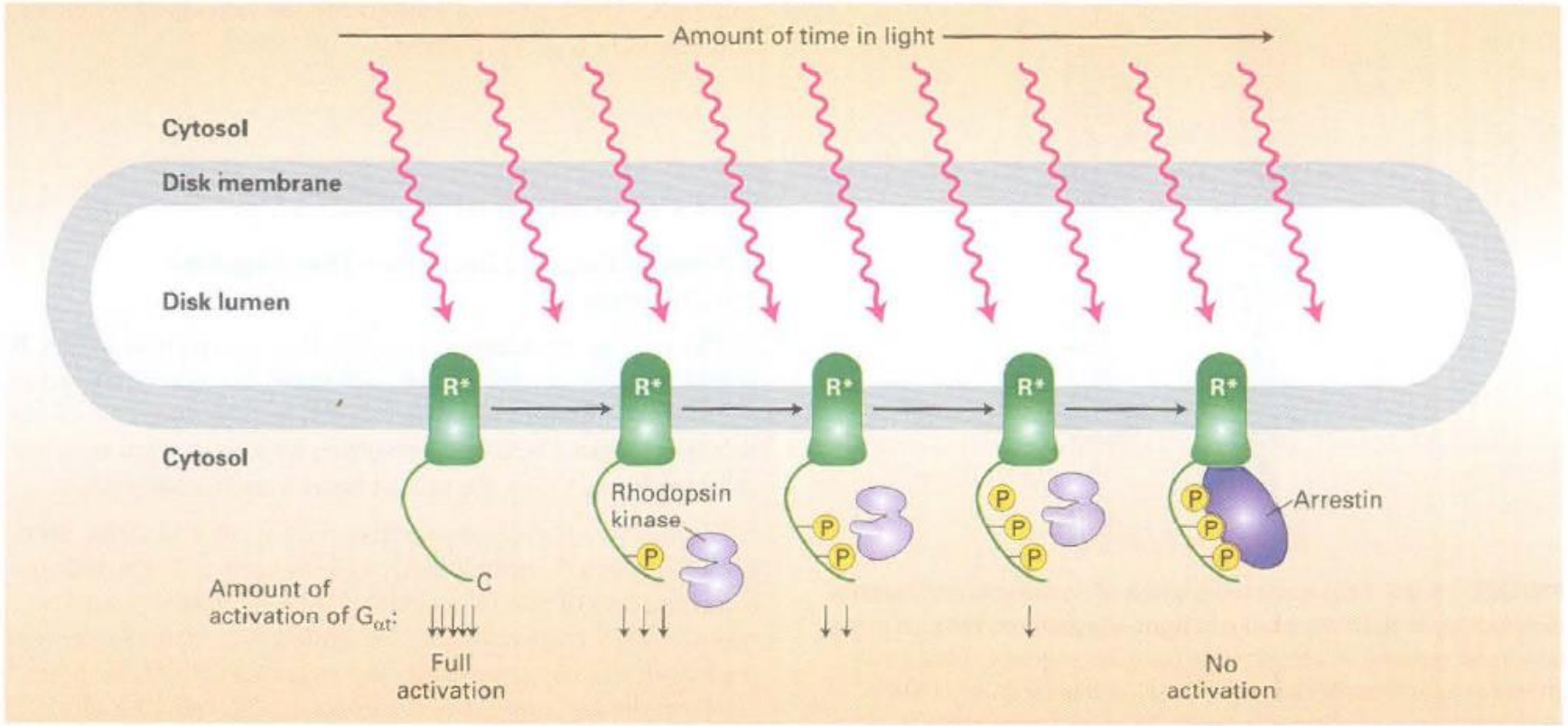


Rapid Termination of the Rhodopsin Signal Transduction Pathway Is Essential for Acute Vision

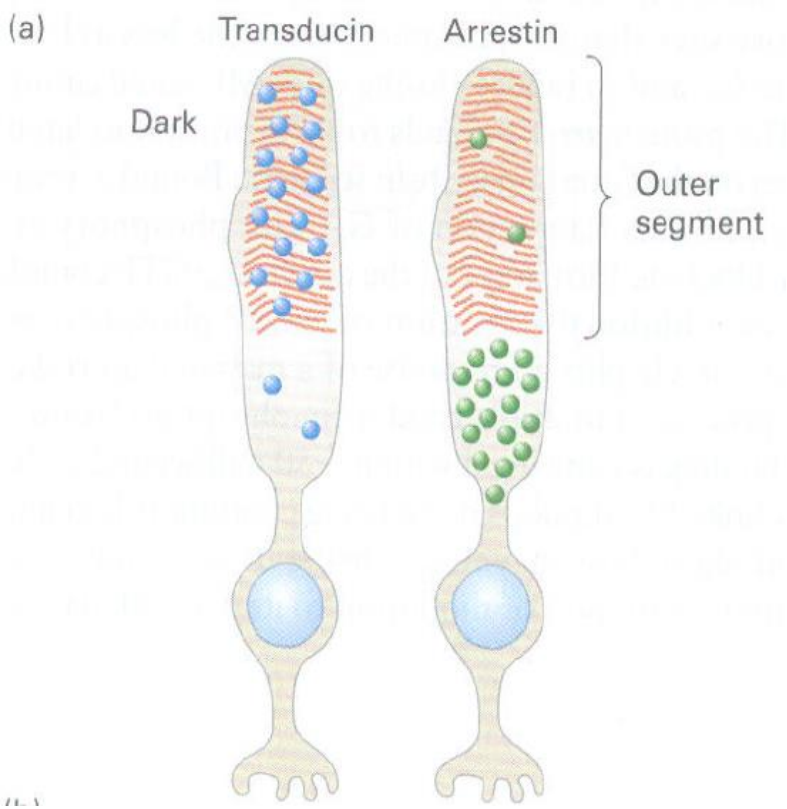
- GAP Proteins That Inactivate $G_{\alpha t}$·GTP-
  - The complex of the inhibitory γ phosphodiesterase subunit and $G_{\alpha t}$·GTP recruits a complex of two proteins, RGS9 and Gβ5, that together act as a GAP protein and hydrolyze the bound GTP to GDP. This releases the inhibitory γ subunit and terminates phosphodiesterase activation.
- Ca^{2+} -Sensing Proteins That Activate Guanylate Cyclase
  - Light-triggered closing of the cGMP-gated Na and Ca2+ channel will cause a drop in the cytosolic Ca2 concentration. The fall in intracellular *Ca2+ is sensed by Calcium -binding proteins called guanylate cyclase*- activating proteins, or GCAPs. This results in a rapid stimulation of cGMP synthesis by guanylate cyclase, causing the ion channels to reopen

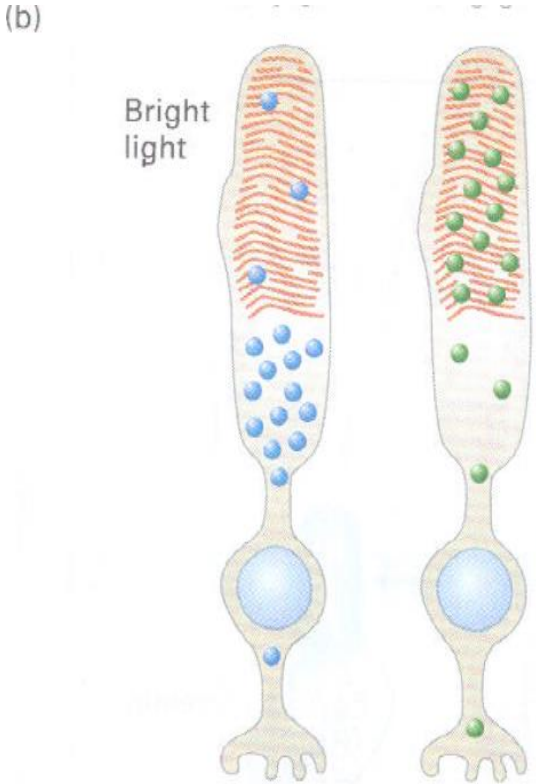
- Rhodopsin Phosphorylation and Binding of Arrestin
  - Phosphorylation of rhodopsin in its active conformation (R *) by *rhodopsin kinase terminates the visual response.*
  - *Each opsin molecule has three principal serine phosphorylation sites on its cytosol-facing C-terminal C4 segment.*
  - *Protein arrestin binds to three phosphorylated serine residues on the C-terminal opsin segment, prevents interaction of Gαt with phosphorylated R *,totally blocking formation of the active Ga,·GTP complex and stopping additional activation of cGMP phosphodiesterase*

Inhibition of rhodopsin signaling by rhodopsin kinase



1. Light-activated rhodopsin (R*), but not dark-adapted rhodopsin, is a substrate for rhodopsin kinase.
2. The extent of rhodopsin phosphorylation is proportional to the amount of time each rhodopsin molecule spends in the light-activated form and reduces the ability of R* to activate transducin.
3. Arrestin binds to the completely phosphorylated opsin, forming a complex that cannot activate transducin at all.





1. In the dark, most transducin is localized to the outer segment, while most arrestin is found in other parts of the cell; in this condition vision is most sensitive to very low light levels.
2. In bright light, little transducin is found in the outer segment and abundant arrestin is found there; in this condition vision is relatively insensitive to small changes in light. Coordinated movement of these proteins contributes to our ability to perceive images over a 100,000-fold range of ambient light levels.

Muscles

Muscles are effectors which enable movement to be carried out

Muscle

- It is responsible for almost all the movements in animals
- 3 types

Cardiac muscle	**Involuntary controlled by autonomic nervous system**
Smooth muscle	
Skeletal muscle (aka striped or striated muscle)	**voluntary controlled by somatic nervous system**

Muscles & the Skeleton

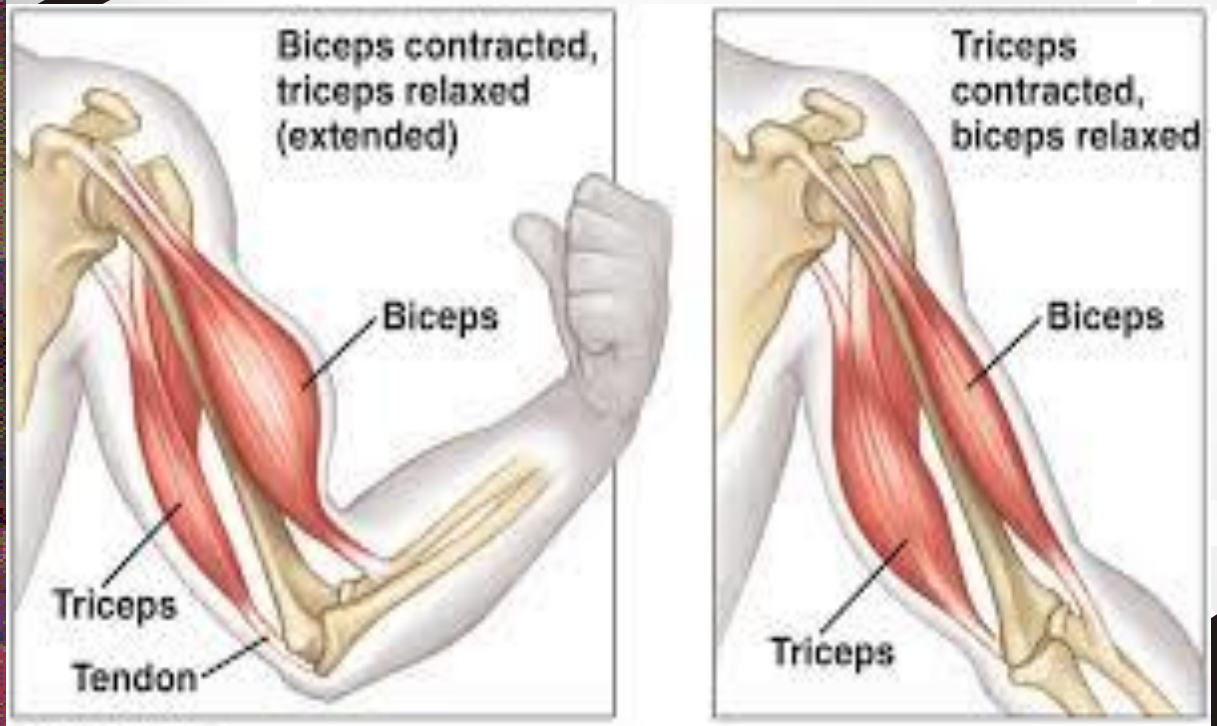
- Skeletal muscles cause the skeleton to move at joints
- They are attached to skeleton by tendons.
- Tendons **transmit** muscle force to the bone.
- Tendons are made of collagen fibres & are very strong & stiff

Antagonistic Muscle Action

- Muscles are either contracted or relaxed
- When contracted the muscle exerts a pulling force, causing it to shorten
- Since muscles can only pull (not push), they work in pairs called *antagonistic muscles*
- The muscle that bends the joint is called the *flexor* muscle
- The muscle that straightens the joint is called the *extensor* muscle

Elbow Joint

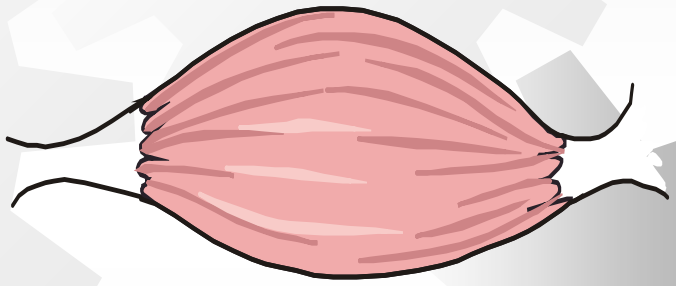
- The best known example of antagonistic muscles are the bicep & triceps muscles



Muscle Structure

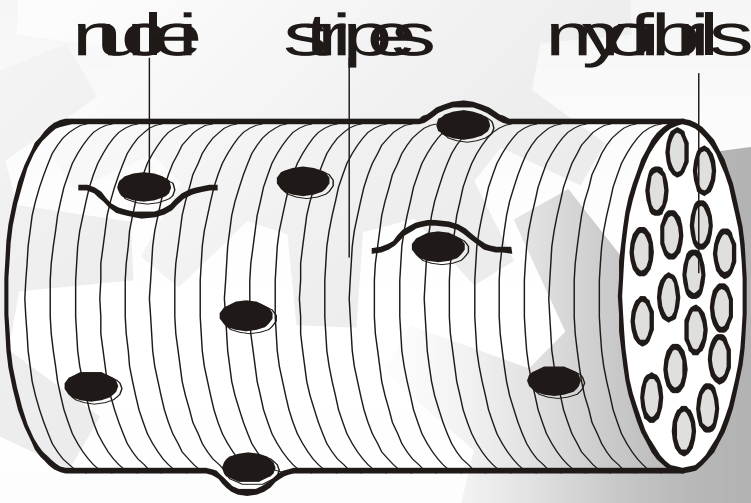
- A single muscle e.g. biceps contains approx 1000 muscle fibres.
- These fibres run the whole length of the muscle
- Muscle fibres are joined together at the tendons

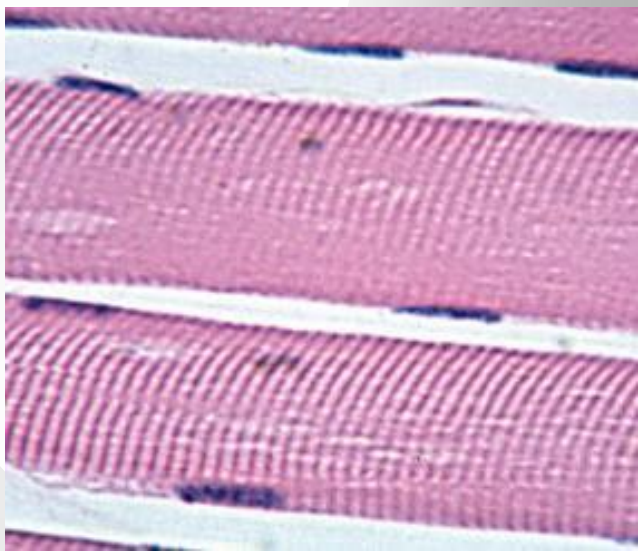
Bicep Muscle

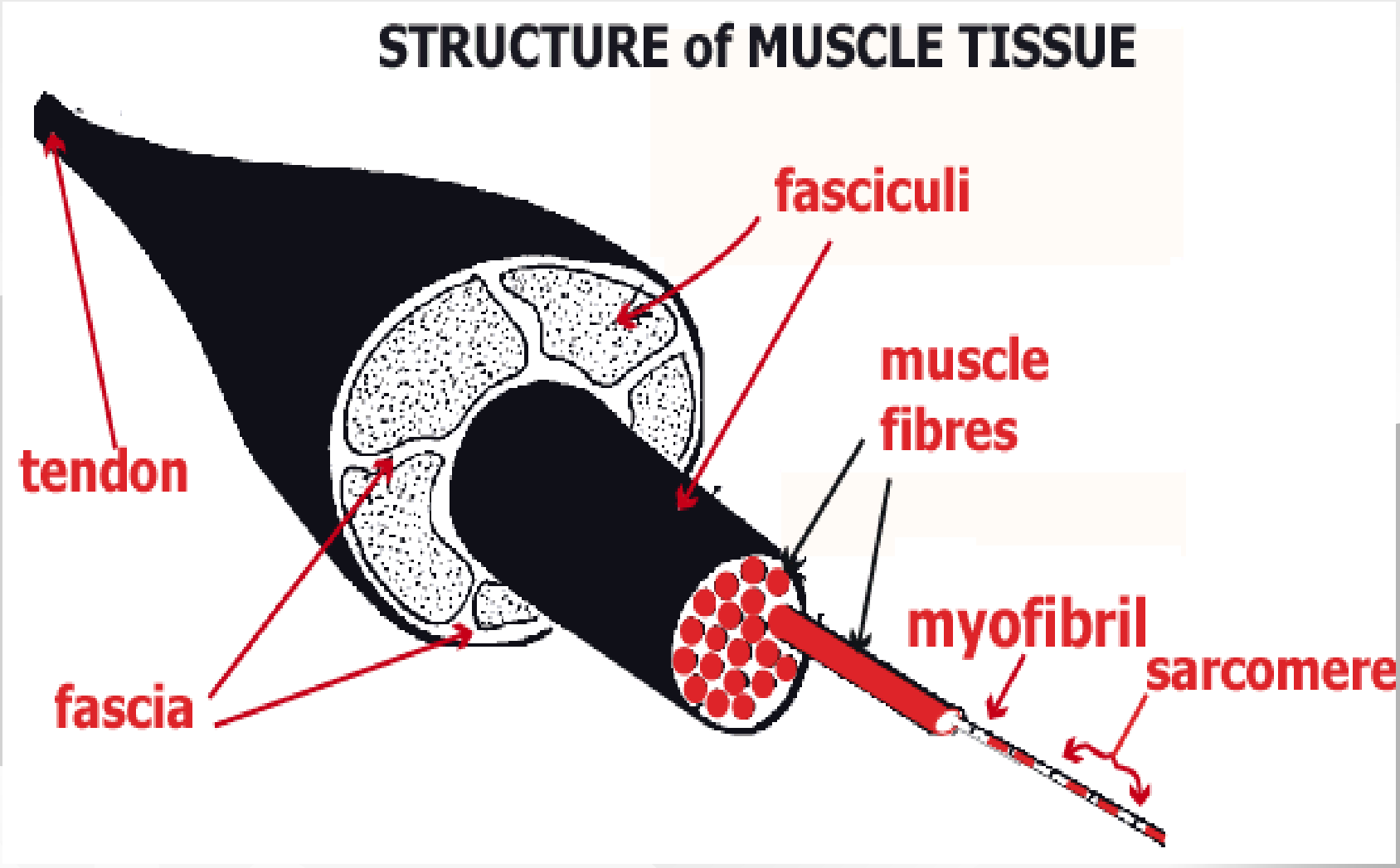


Muscle Structure

- Each muscle fibre is actually a single muscle cell
- This cell is approx 100 □m in diameter & a few cm long
- These giant cells have many nuclei
- Their cytoplasm is packed full of *myofibrils*
- These are bundles of protein filaments that cause contraction
- Sarcoplasm (muscle cytoplasm) also contains mitochondria to provide energy for contraction







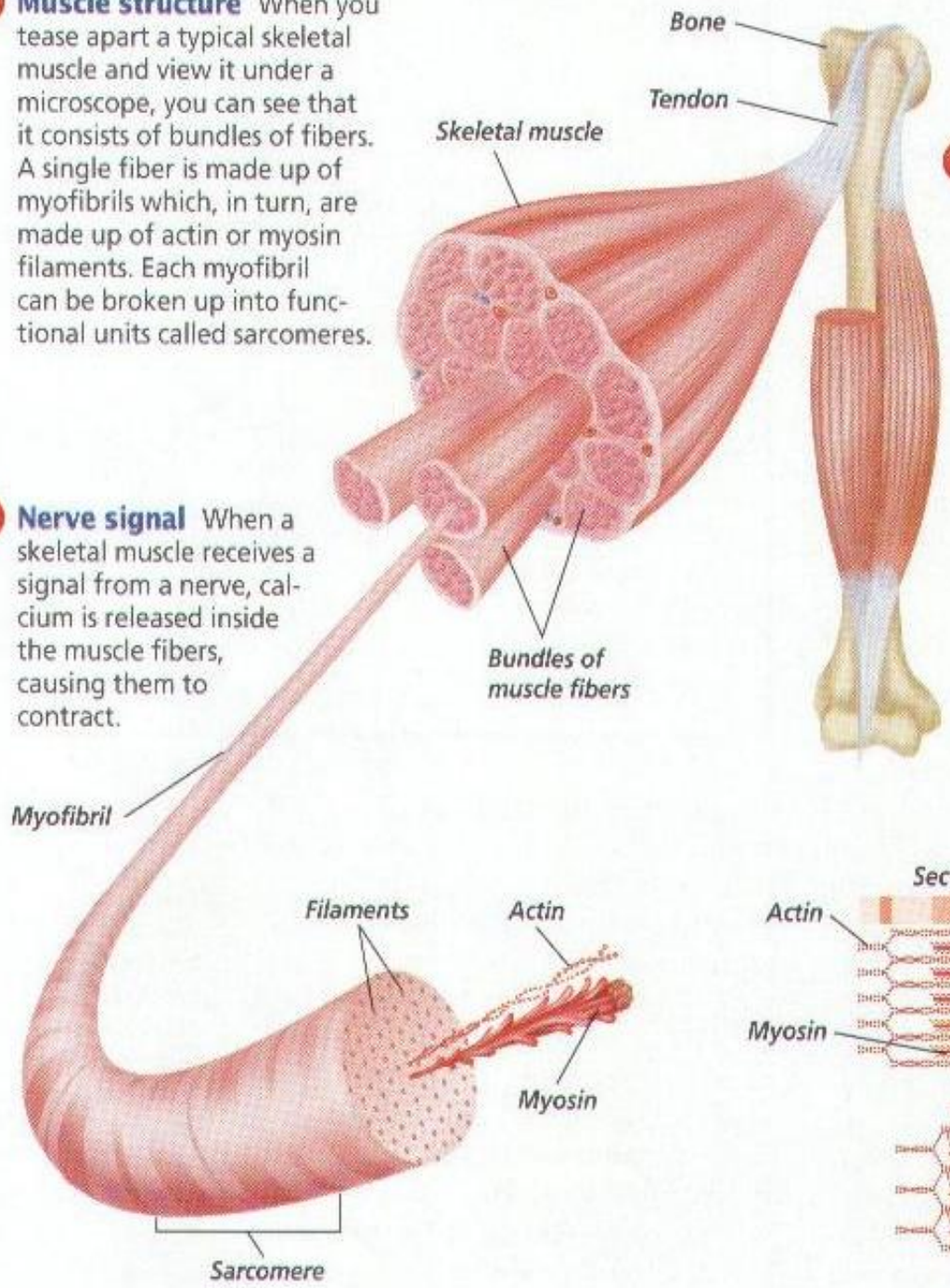
Sarcomere = the basic contractile unit

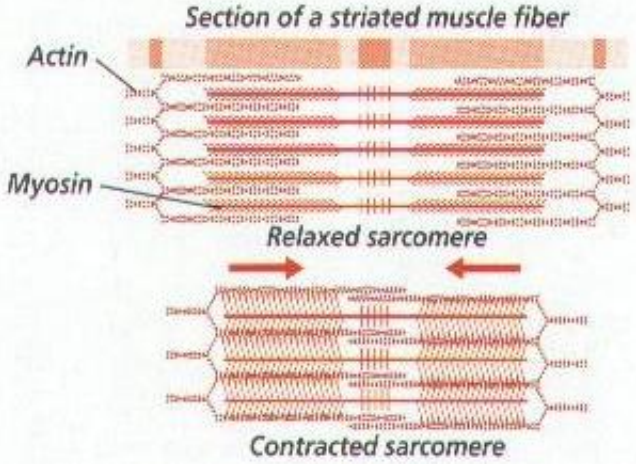
for moving your bones.

1 Muscle structure When you tease apart a typical skeletal muscle and view it under a microscope, you can see that it consists of bundles of fibers. A single fiber is made up of myofibrils which, in turn, are made up of actin or myosin filaments. Each myofibril can be broken up into functional units called sarcomeres.

2 Nerve signal When a skeletal muscle receives a signal from a nerve, calcium is released inside the muscle fibers, causing them to contract.

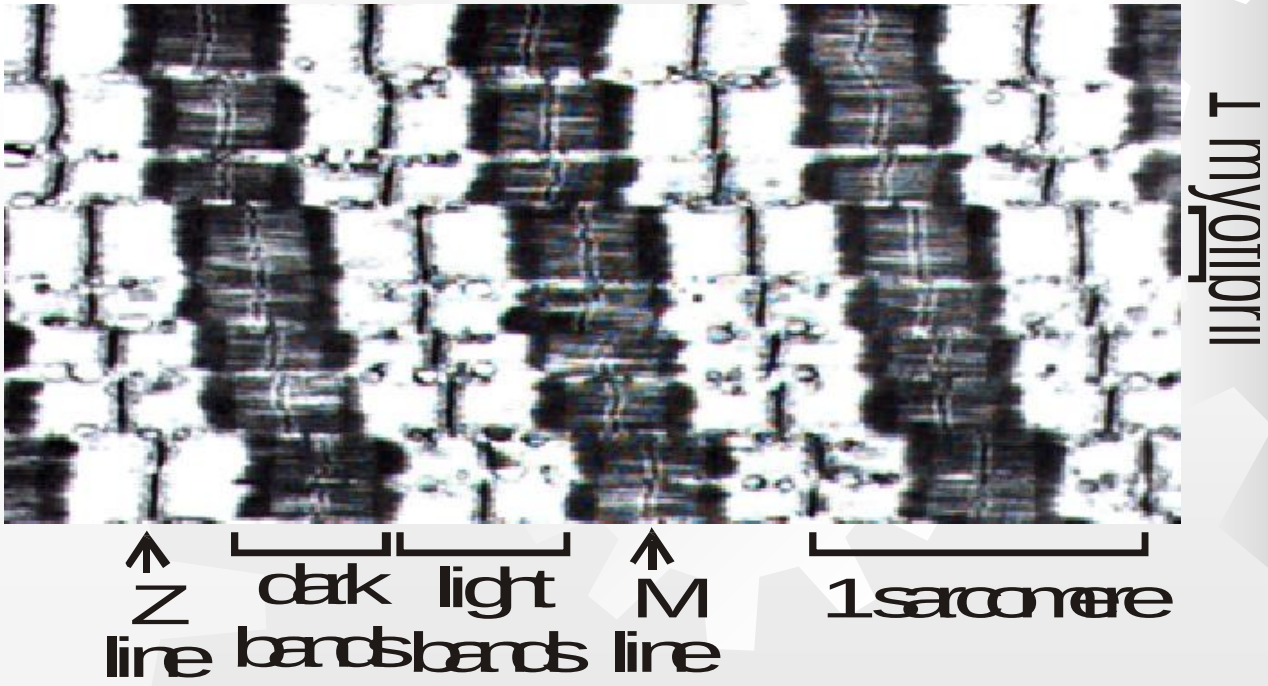
3 Contraction The presence of calcium causes attachments to form between the thick myosin and thin actin filaments. The actin filaments are then pulled inward toward the center of each sarcomere, shortening the sarco-mere and producing a muscle contraction. When the muscle relaxes, the filaments slide back into their original positions.

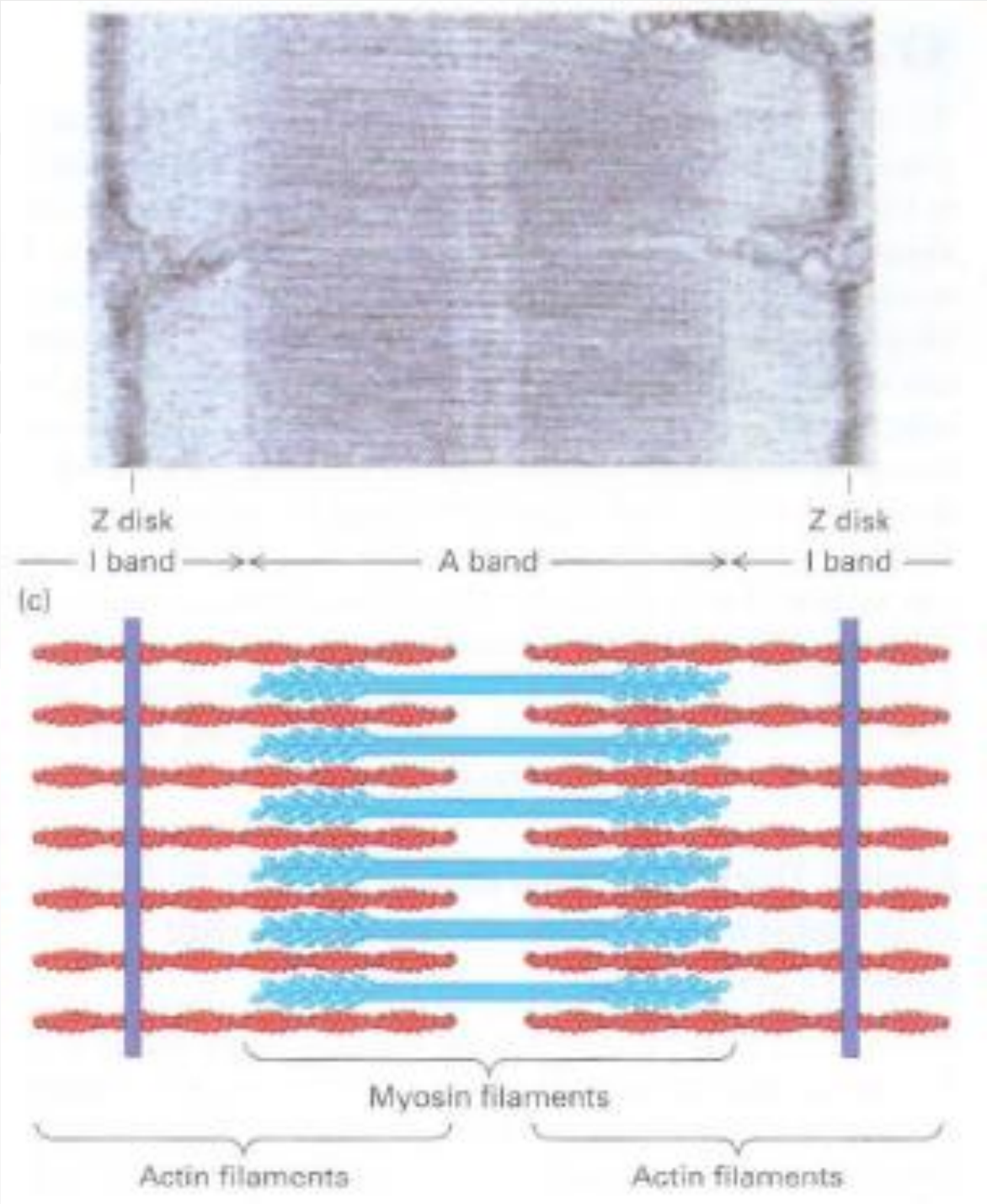




Muscle Structure

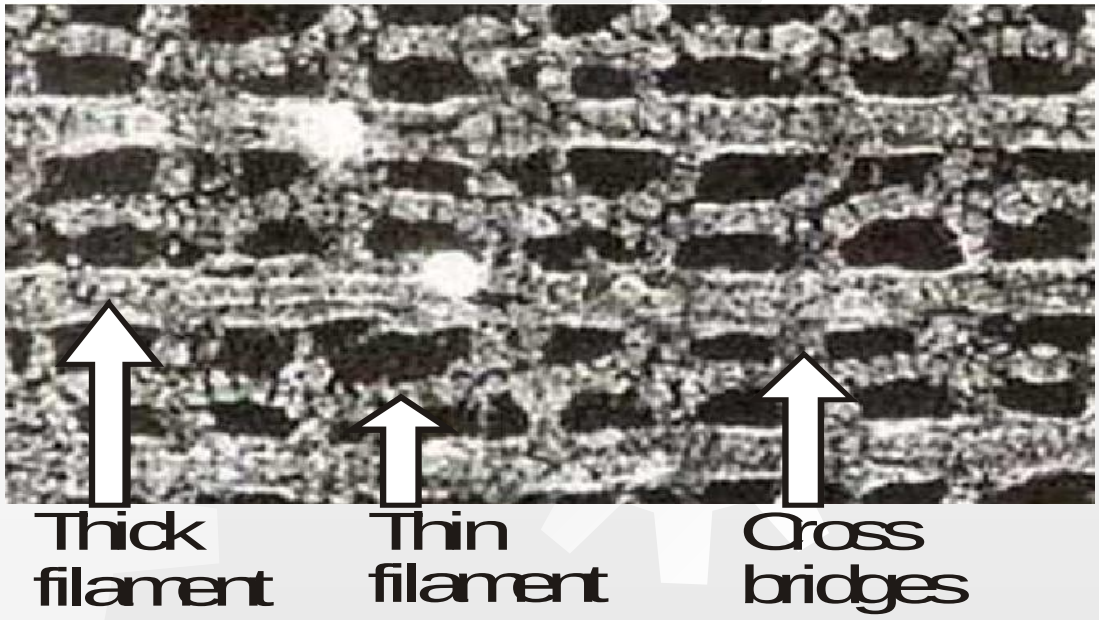
- The E.M shows that each myofibril is made up of repeating dark & light bands
- In the middle of the dark band is the M-line
- In the middle of the light band is the Z-line
- The repeating unit from one Z-line to the next is called the sarcomere




Z disk
Z disk
I band
A band
I band
(c)
Myosin filaments
Actin filaments
Actin filaments

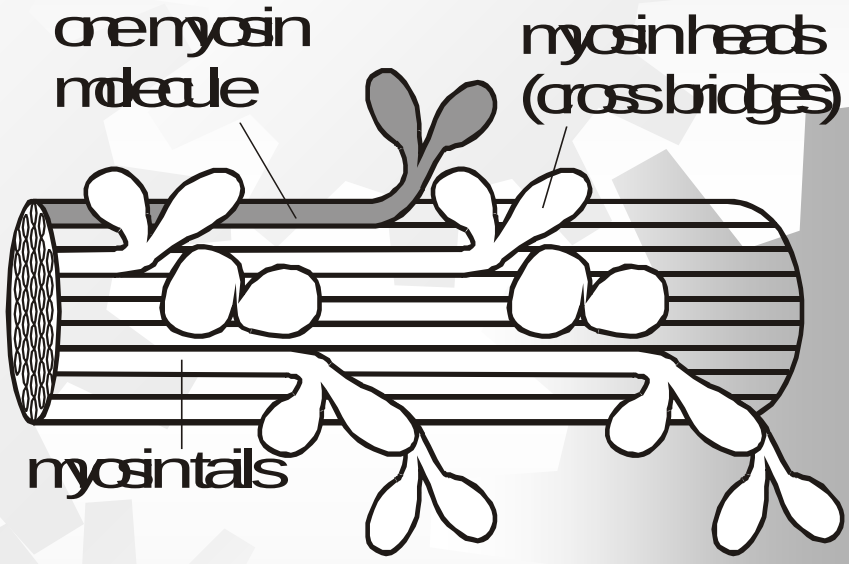
Muscle Structure

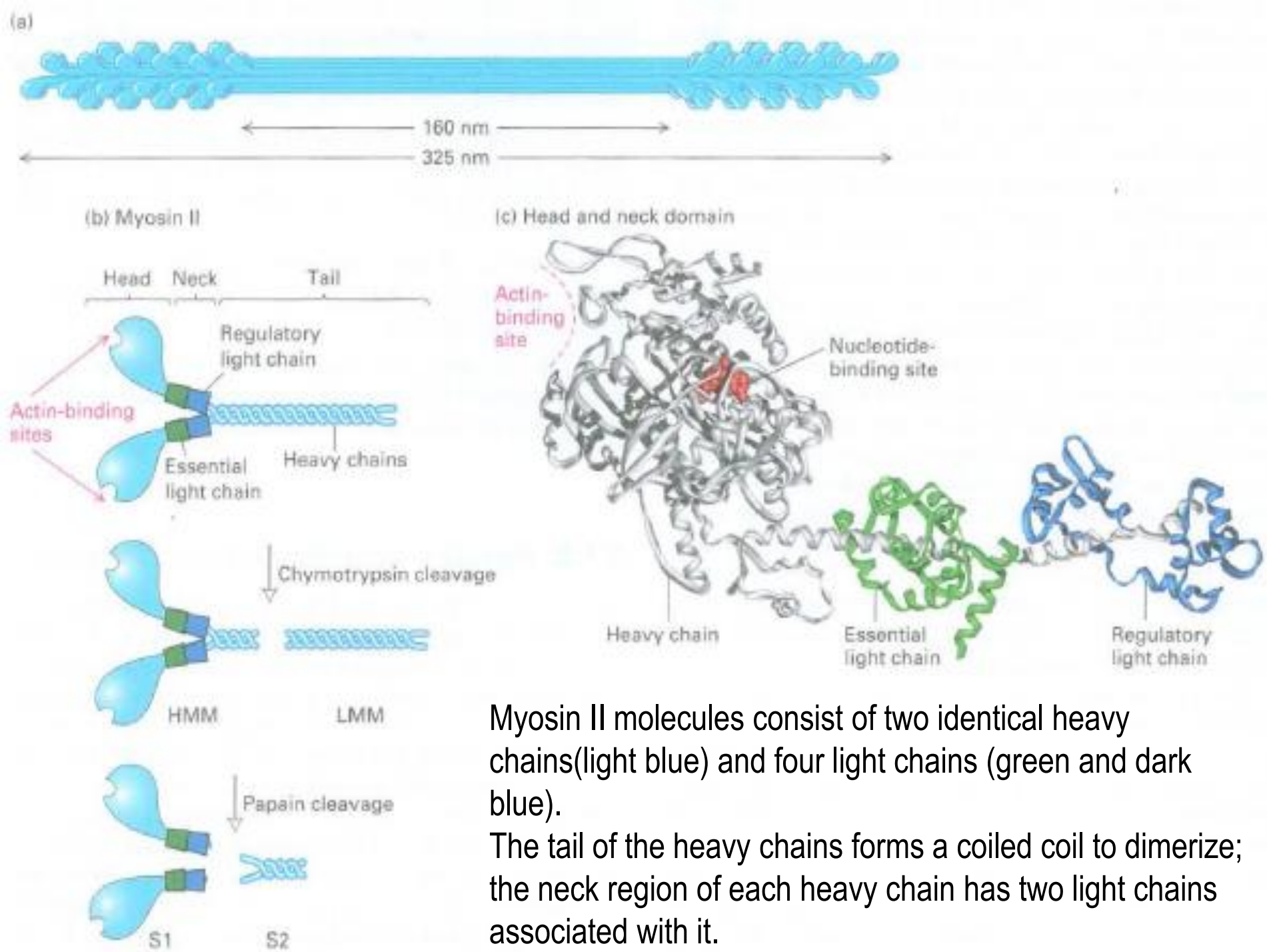
- A very high resolution E.M reveals that each myofibril is made up of parallel filaments.
- There are 2 kinds of filament called thick & thin filaments.
- These 2 filaments are linked at intervals called *cross bridges*, which actually stick out from the thick filaments



The Thick Filament (Myosin)

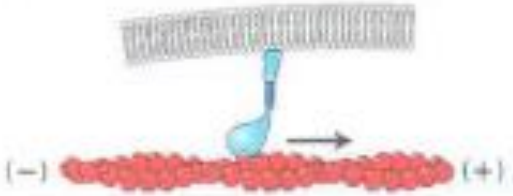
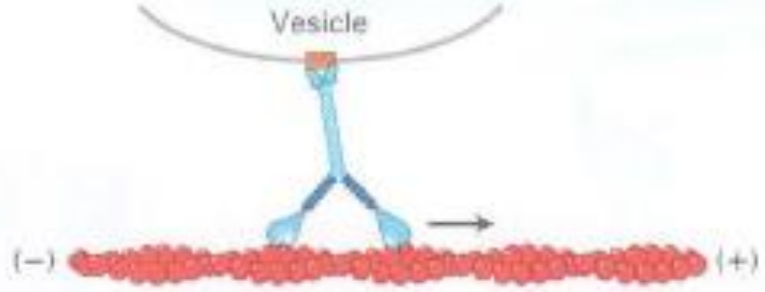
- Consists of the protein called myosin.
- A myosin molecule is shaped a bit like a golf club, but with 2 heads.
- The heads stick out to form the cross bridge
- Many of these myosin molecules stick together to form a thick filament





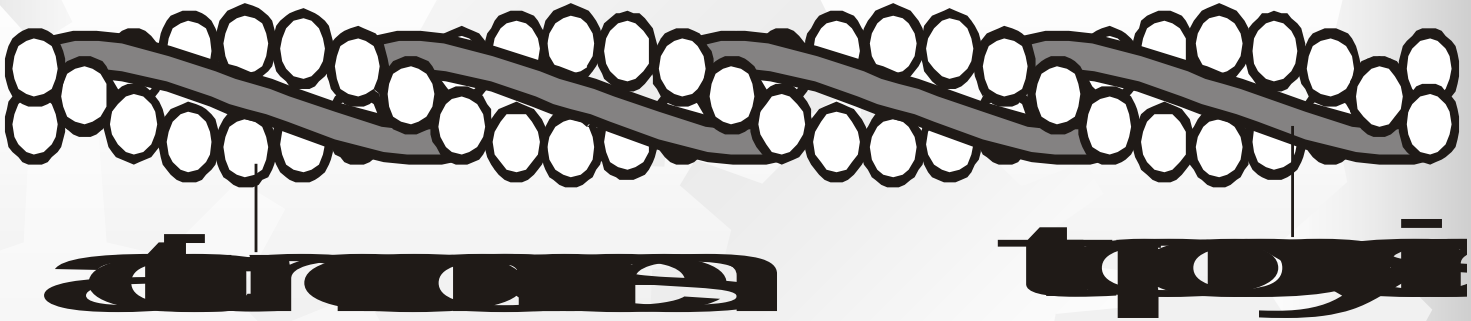
Myosin II molecules consist of two identical heavy chains(light blue) and four light chains (green and dark blue).

The tail of the heavy chains forms a coiled coil to dimerize; the neck region of each heavy chain has two light chains associated with it.

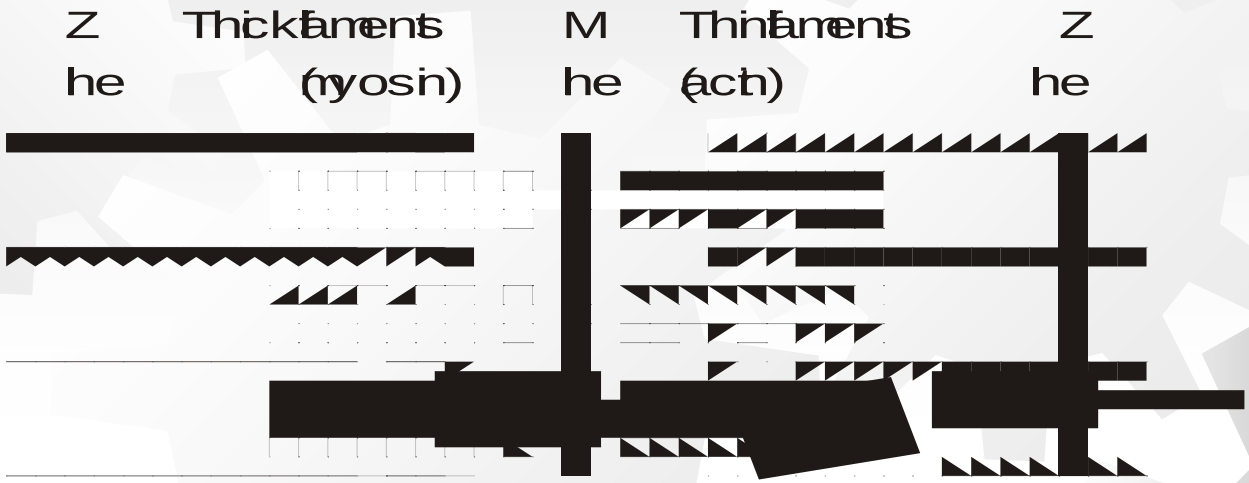
Class	Step size		Function
I	10–14 nm		Membrane association, endocytosis
II	8 nm		Contraction
V	36 nm		Organelle transport

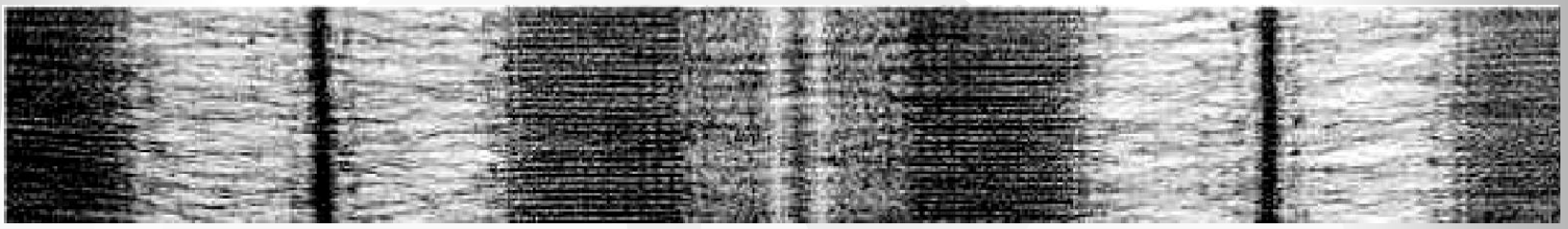
Thin Filament (Actin)

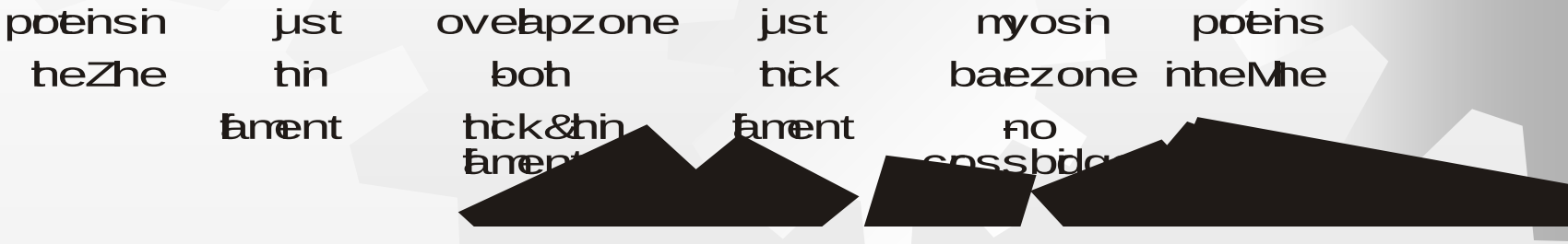
- The thin filament consists of a protein called actin.
- The thin filament also contains *tropomyosin*.
- This protein is involved in the control of muscle contraction

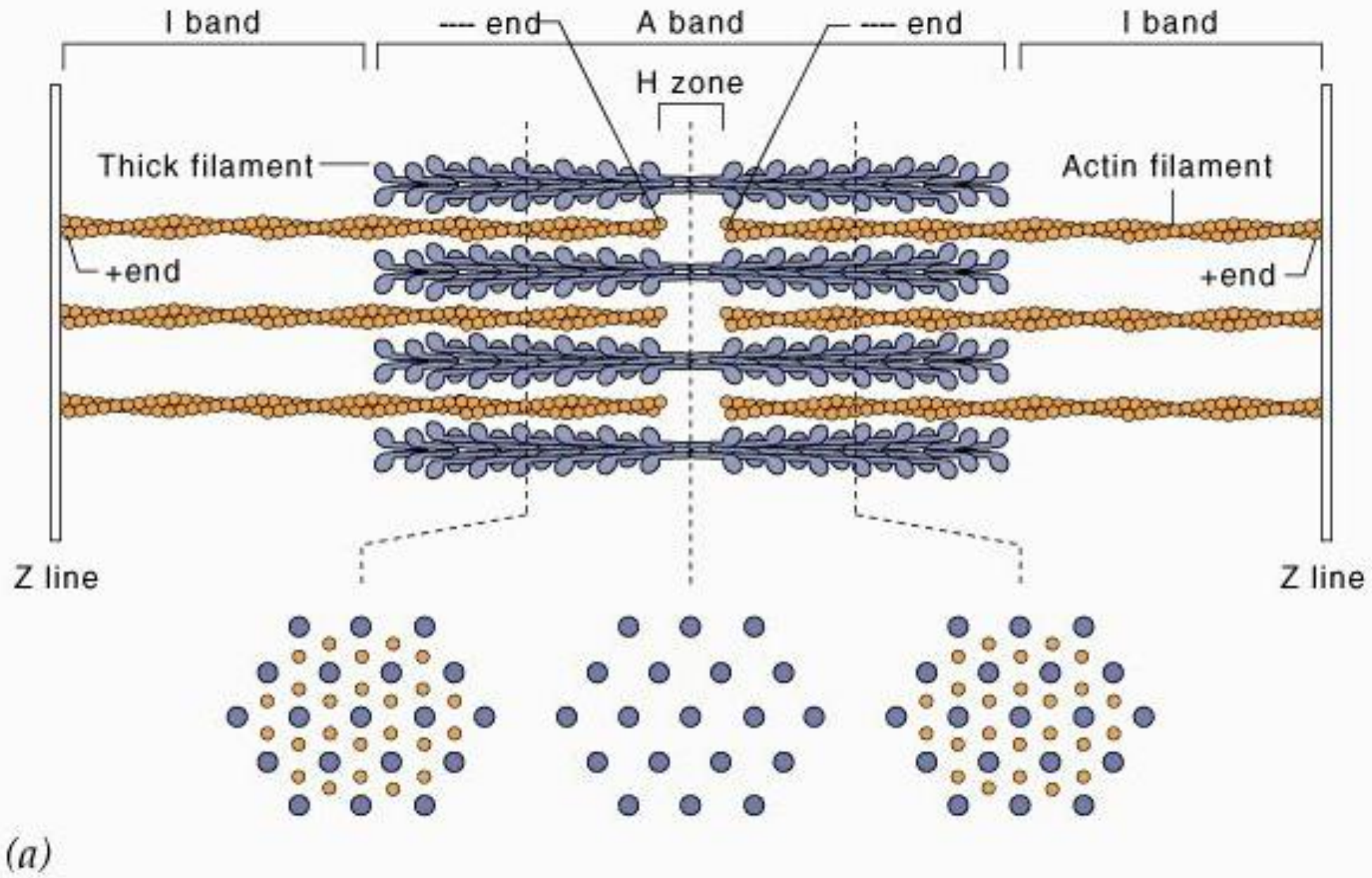


The Sarcomere









(a)

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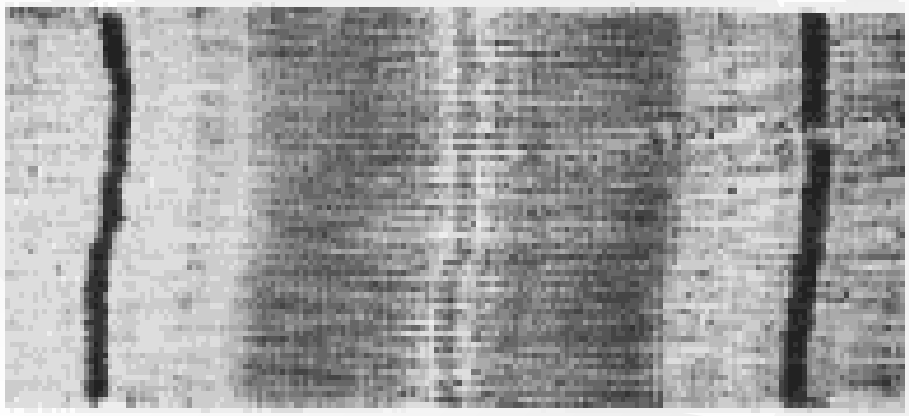
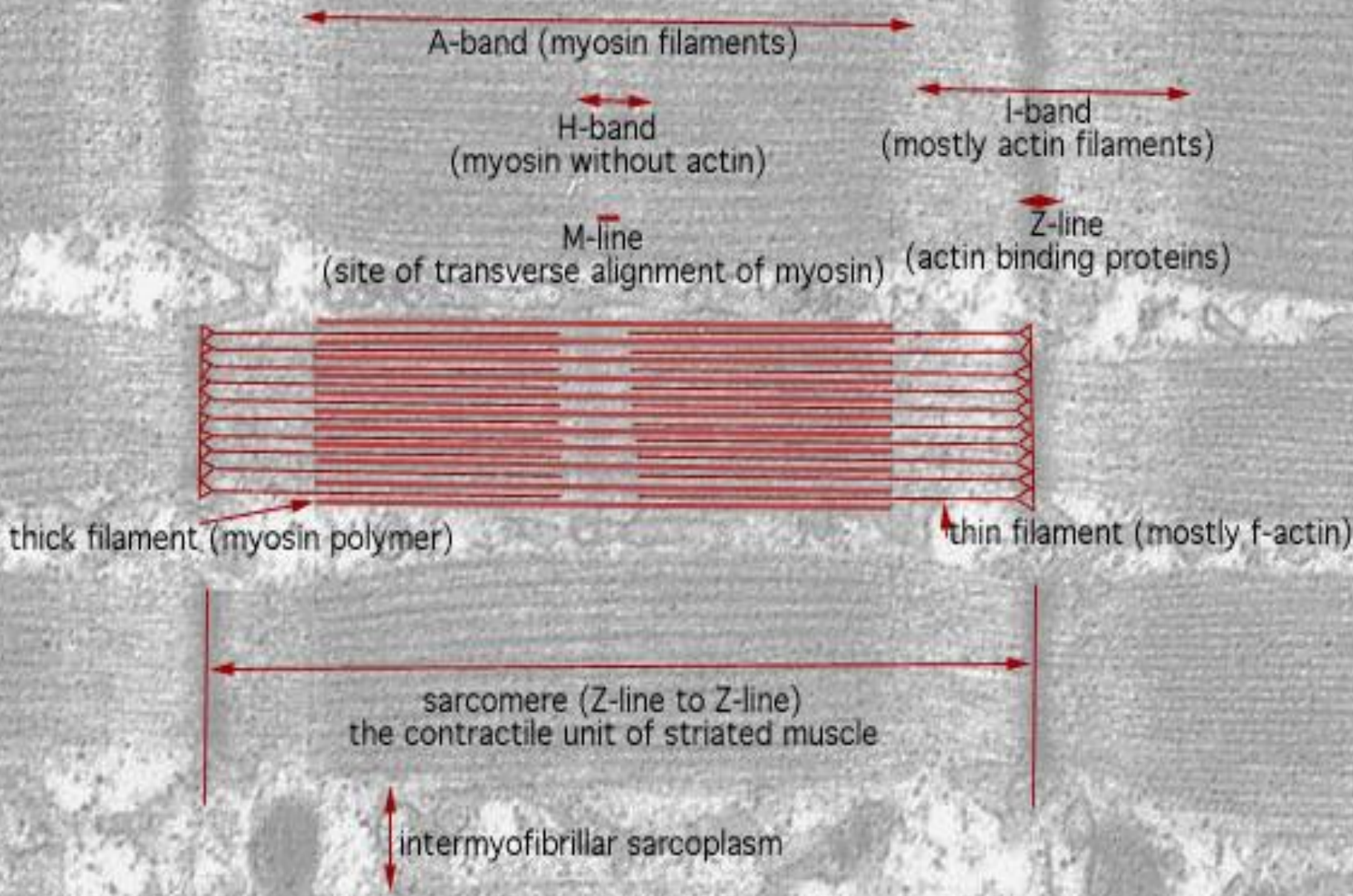
I Band = actin filaments



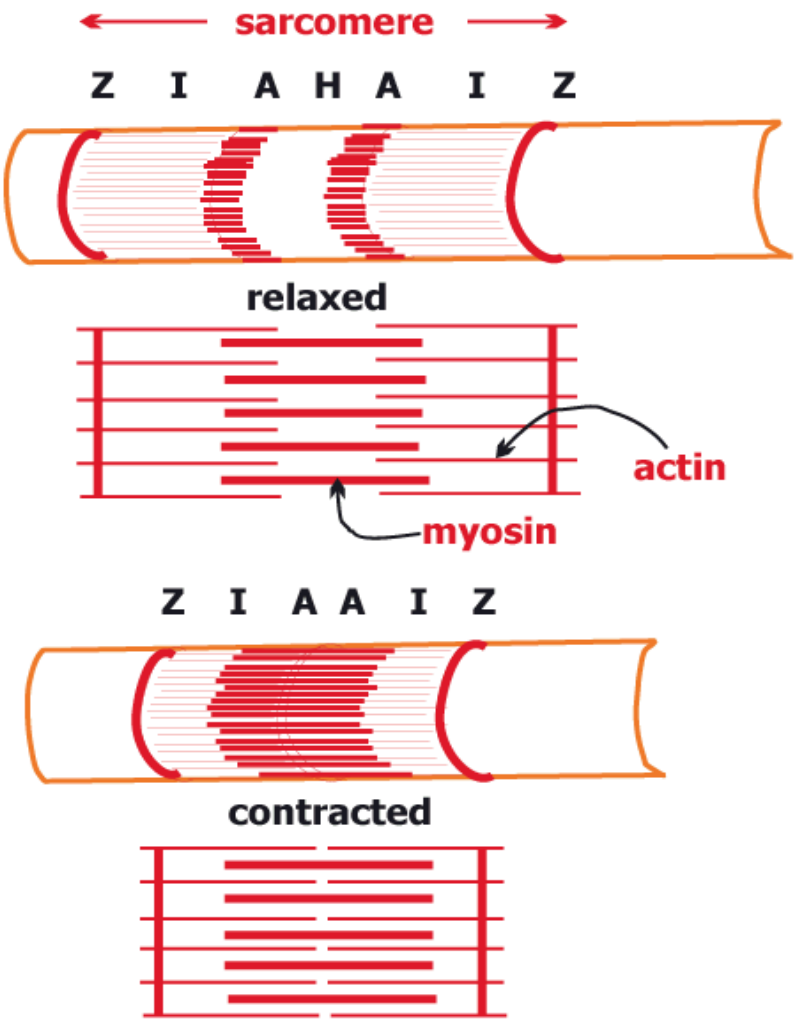

A-band (myosin filaments)
H-band
(myosin without actin)
I-band
(mostly actin filaments)
M-line
(site of transverse alignment of myosin)
Z-line
(actin binding proteins)
thick filament (myosin polymer)
thin filament (mostly f-actin)
sarcomere (Z-line to Z-line)
the contractile unit of striated muscle
intermyofibrillar sarcoplasm

Anatomy of a Sarcomere

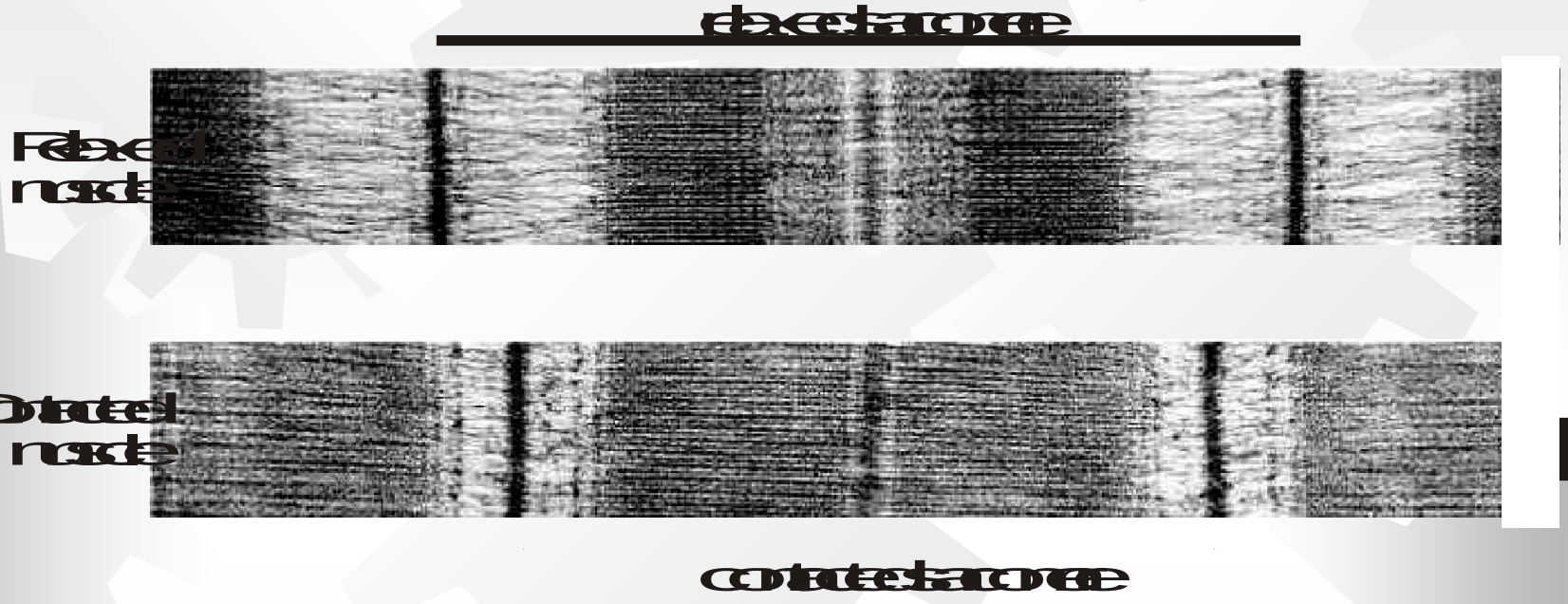
- The **thick filaments** produce the dark **A band**.
- The **thin filaments** extend in each direction from the Z line.
- Where they do not overlap the thick filaments, they create the light **I band**.
- The **H zone** is that portion of the A band where the thick and thin filaments do not overlap.
- The entire array of thick and thin filaments between the Z lines is called a **sarcomere**

Sarcomere shortens when muscle contracts

- Shortening of the sarcomeres in a myofibril produces the shortening of the myofibril
- And, in turn, of the muscle fibre of which it is a part



Mechanism of muscle contraction



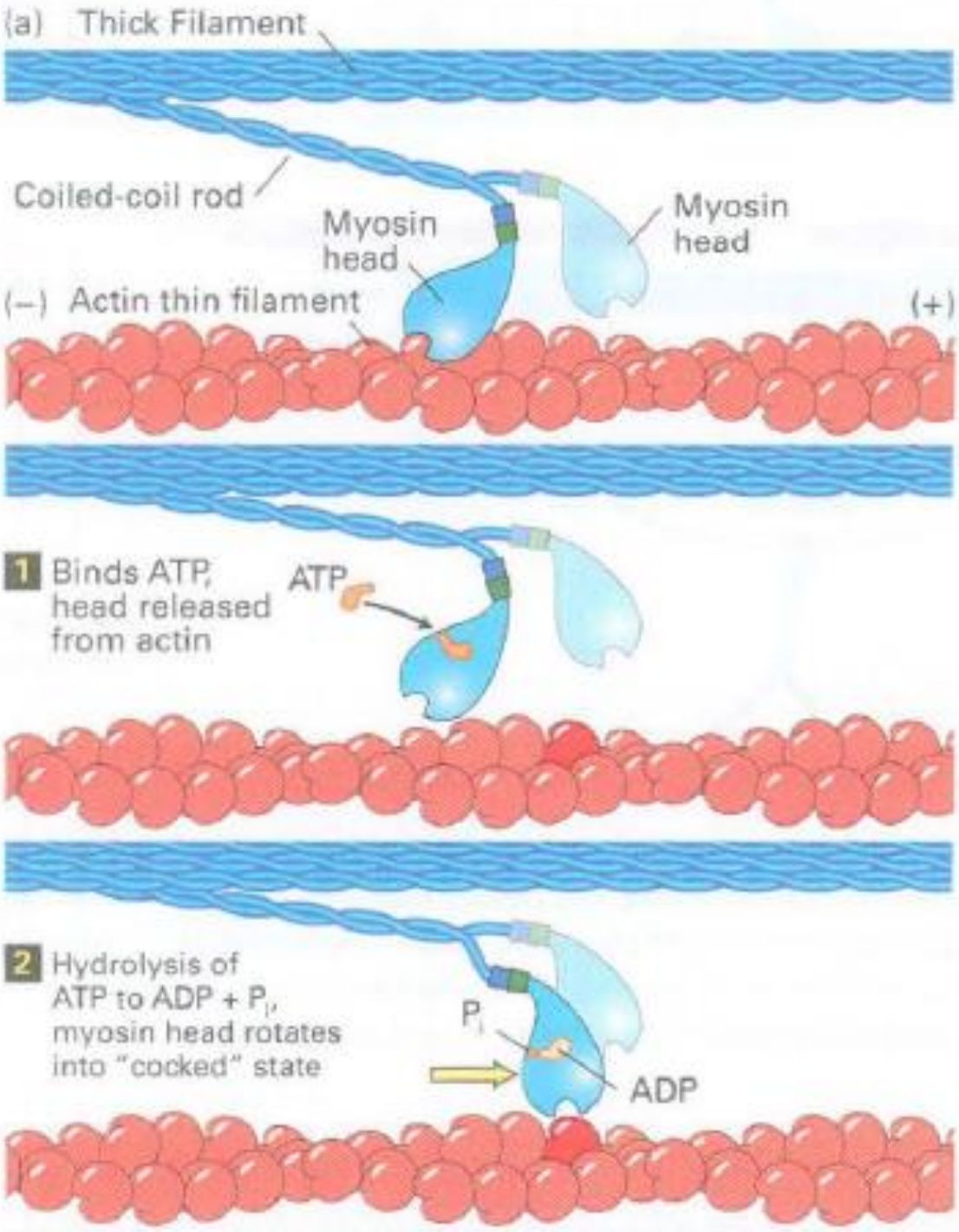
- The above micrographs show that the sarcomere gets shorter when the muscle contracts
- The light (I) bands become shorter
- The dark bands (A) bands stay the same length

The Sliding Filament Theory

- So, when the muscle contracts, sarcomeres become smaller
- However the filaments do not change in length.
- Instead they slide past each other (overlap)
- So actin filaments slide between myosin filaments
- and the zone of overlap is larger

Repetition of the cycle

- One ATP molecule is split by each cross bridge in each cycle.
- This takes only a few milliseconds
- During a contraction 1000’s of cross bridges in each sarcomere go through this cycle.

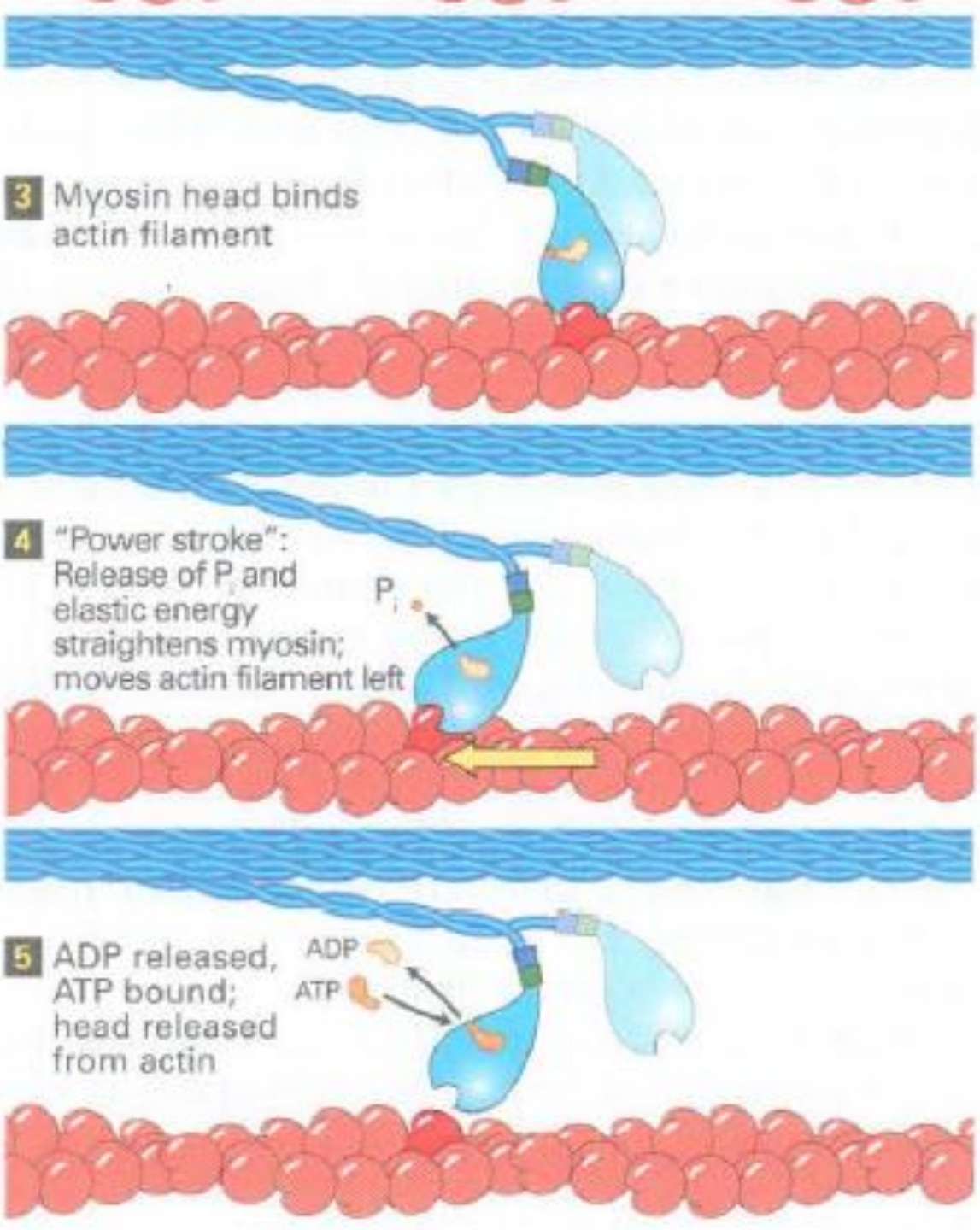


ATP-driven myosin movement along actin filaments

In the absence of ATP, the myosin head is firmly attached to the actin filament. Although this state is very short-lived in living muscle, it is the state responsible for muscle stiffness in death (rigor mortis).

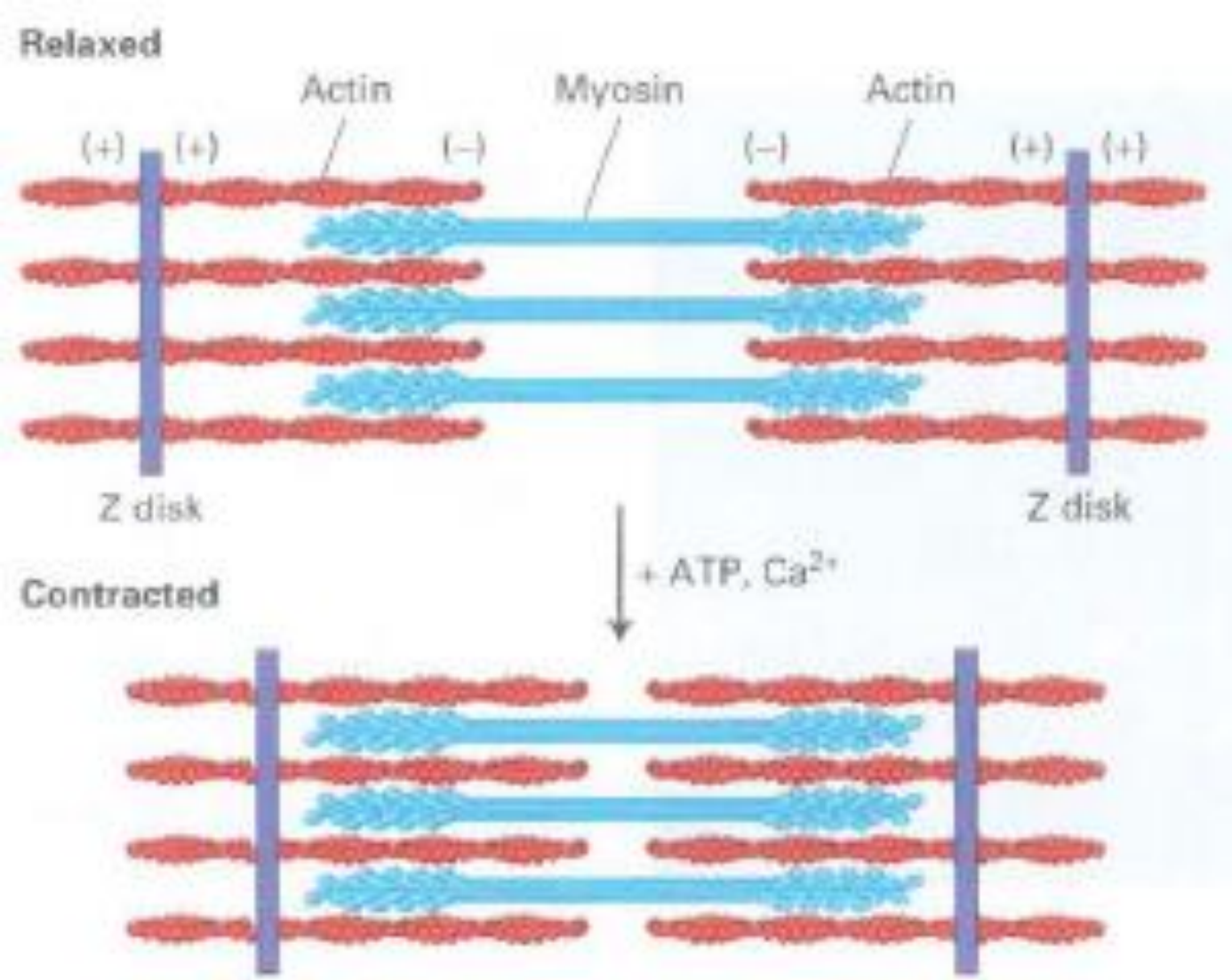
On binding ATP, the myosin head releases from the actin filament.

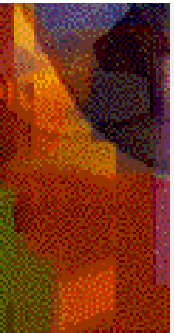
- The head hydrolyzes the ATP to ADP and Pi, which induces a rotation in the head with respect to the neck. This "cocked state" stores the energy released by ATP hydrolysis as elastic energy, like a stretched spring.
- Myosin in the "cocked" state binds actin



When it is bound to actin, the myosin head couples release of P with release of the elastic energy to move the actin filament. This is known as the "power stroke," as it involves moving the actin filament with respect to the end of the myosin neck domain.

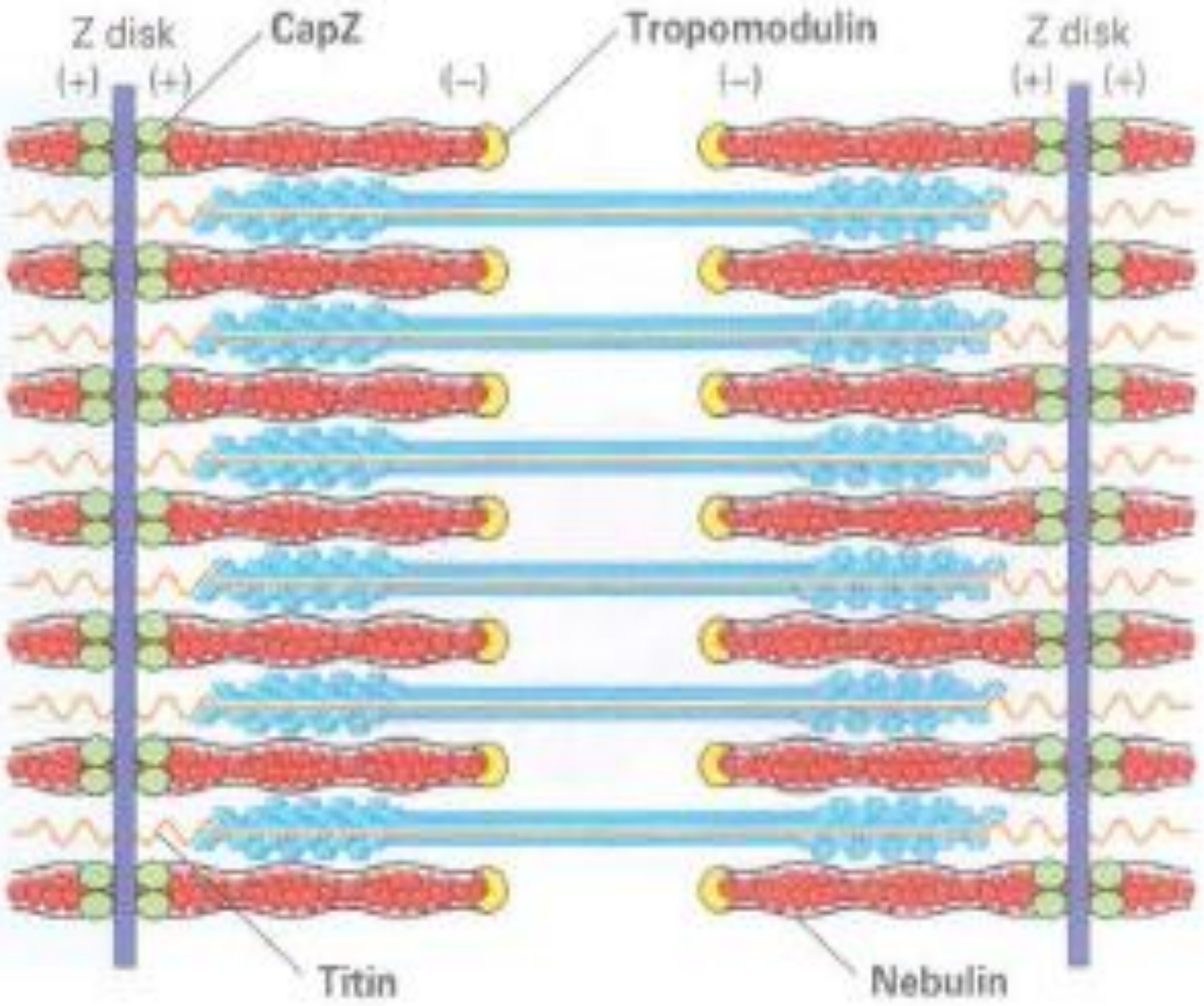
The head remains tightly bound to the filament as ADP is released and before fresh ATP is bound by the head





In the presence of ATP and Ca^{2+}, the myosin heads extending from the thick filaments walk toward the (+)ends of the thin filaments. Because the thin filaments are anchored at the Z disks (purple), movement of myosin pulls the actin filaments toward the center of the sarcomere,shortening its length in the contracted state

Accessory proteins found in skeletal muscle.



To stabilize the actin filaments, CapZ caps the (+)end of the thin filaments at the Z disk, whereas tropomodulin caps the(-) end. The giant protein titin extends through the thick filaments and attaches to the Z disk. Nebulin binds actin subunits and determines the length of the thin filament.

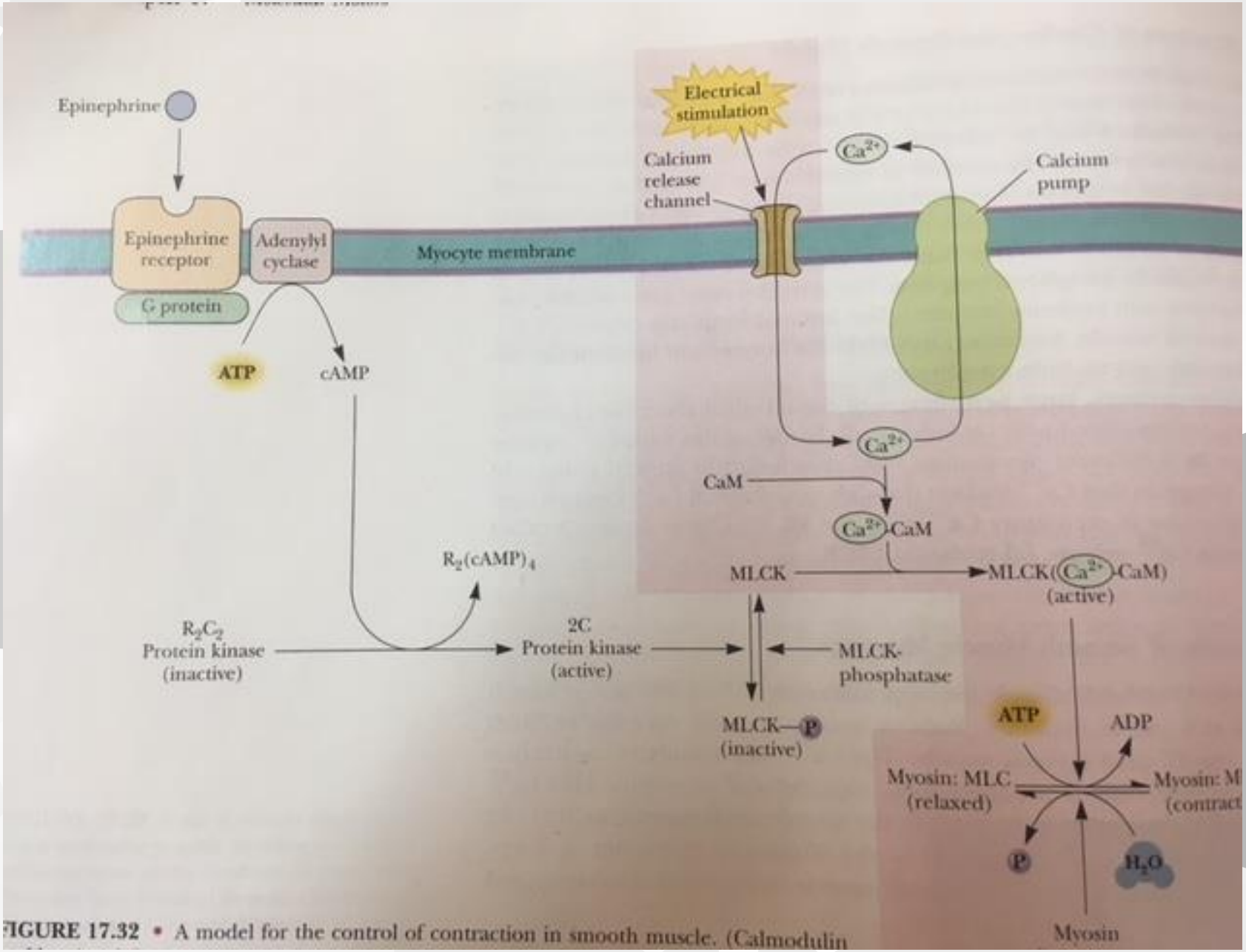


FIGURE 17.32 • A model for the control of contraction in smooth muscle. (Calmodulin