CAMPBELL BIOLOGY IN FOCUS

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37

Neurons, Synapses, and Signaling

Lecture Presentations by Kathleen Fitzpatrick and Nicole Tunbridge, Simon Fraser University

SECOND EDITION

Overview: Lines of Communication

- The cone snail kills prey with venom that disables neurons
- **Neurons** are nerve cells that transfer information within the body
- Neurons use two types of signals to communicate: electrical signals (long distance) and chemical signals (short distance)

- Interpreting signals in the nervous system involves sorting a complex set of paths and connections
- Processing of information takes place in simple clusters of neurons called **ganglia** or a more complex organization of neurons called a **brain**

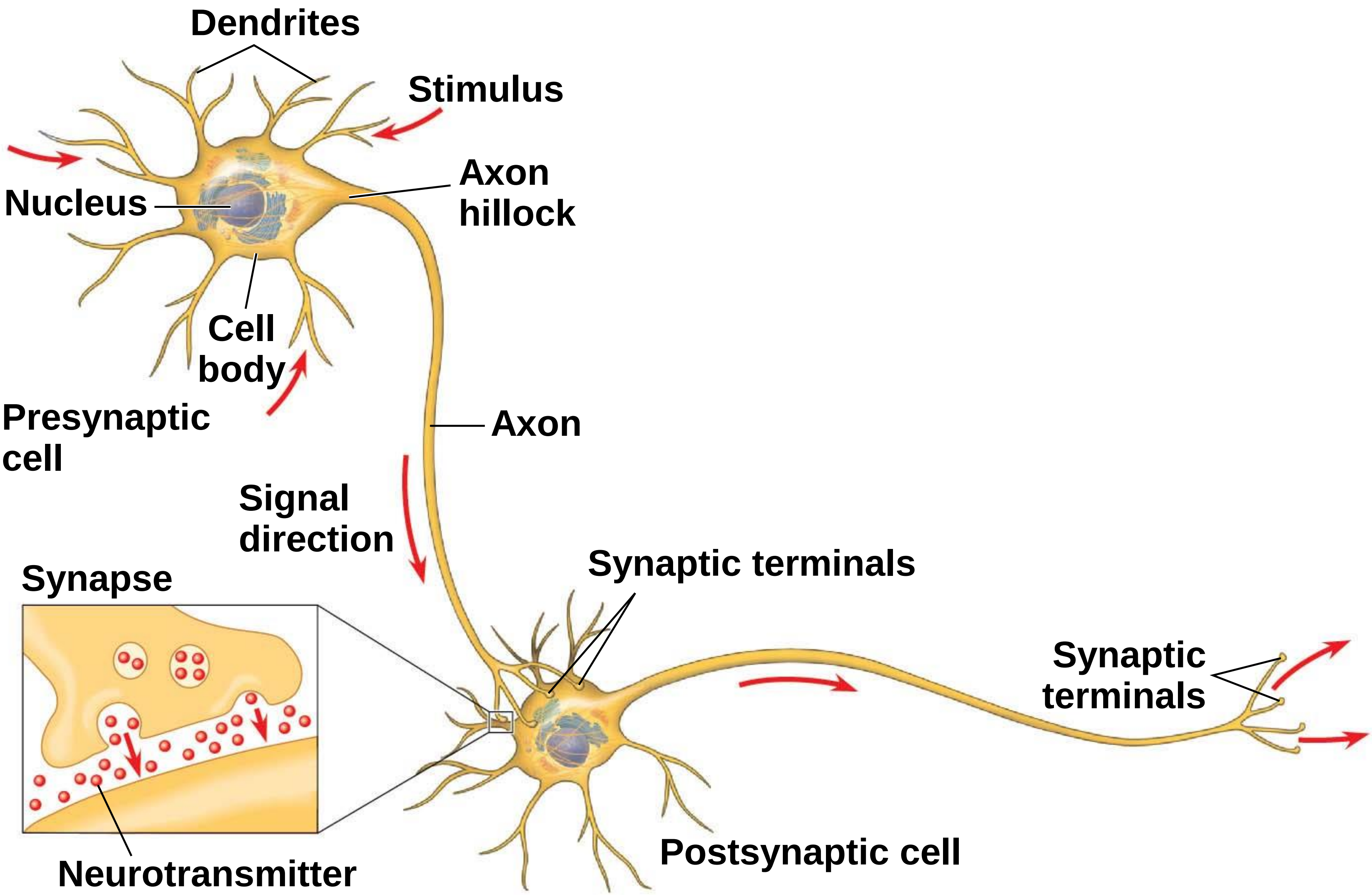
Concept 37.1: Neuron structure and organization reflect function in information transfer

- The neuron is a cell type that exemplifies the close fit of form and function that often arises over the course of evolution

Neuron Structure and Function

- Most of a neuron's organelles are in the **cell body**
- Most neurons have **dendrites**, highly branched extensions that receive signals from other neurons
- The single **axon**, a much longer extension, transmits signals to other cells
- The cone-shaped base of an axon, where signals are generated, is called the axon hillock

Figure 37.2


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

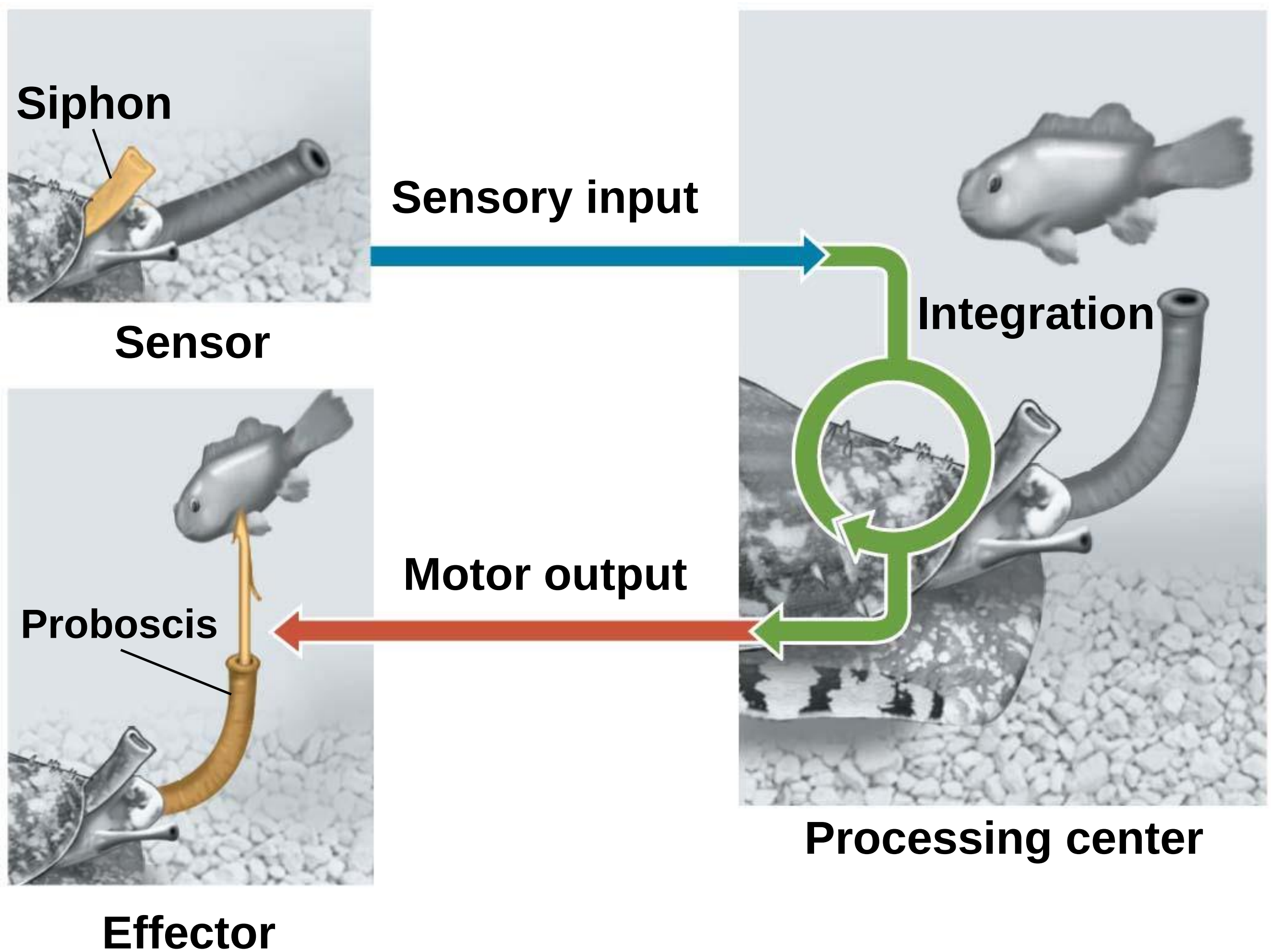
- The branched ends of axons transmit signals to other cells at a junction called the **synapse**
- At most synapses, chemical messengers called **neurotransmitters** pass information from the transmitting neuron to the receiving cell

- Neurons of vertebrates and most invertebrates require supporting cells called **glial cells**
- In the mammalian brain, glia outnumber neurons 10- to 50-fold

Introduction to Information Processing

- Nervous systems process information in three stages
  - Sensory input
  - Integration
  - Motor output

Figure 37.4

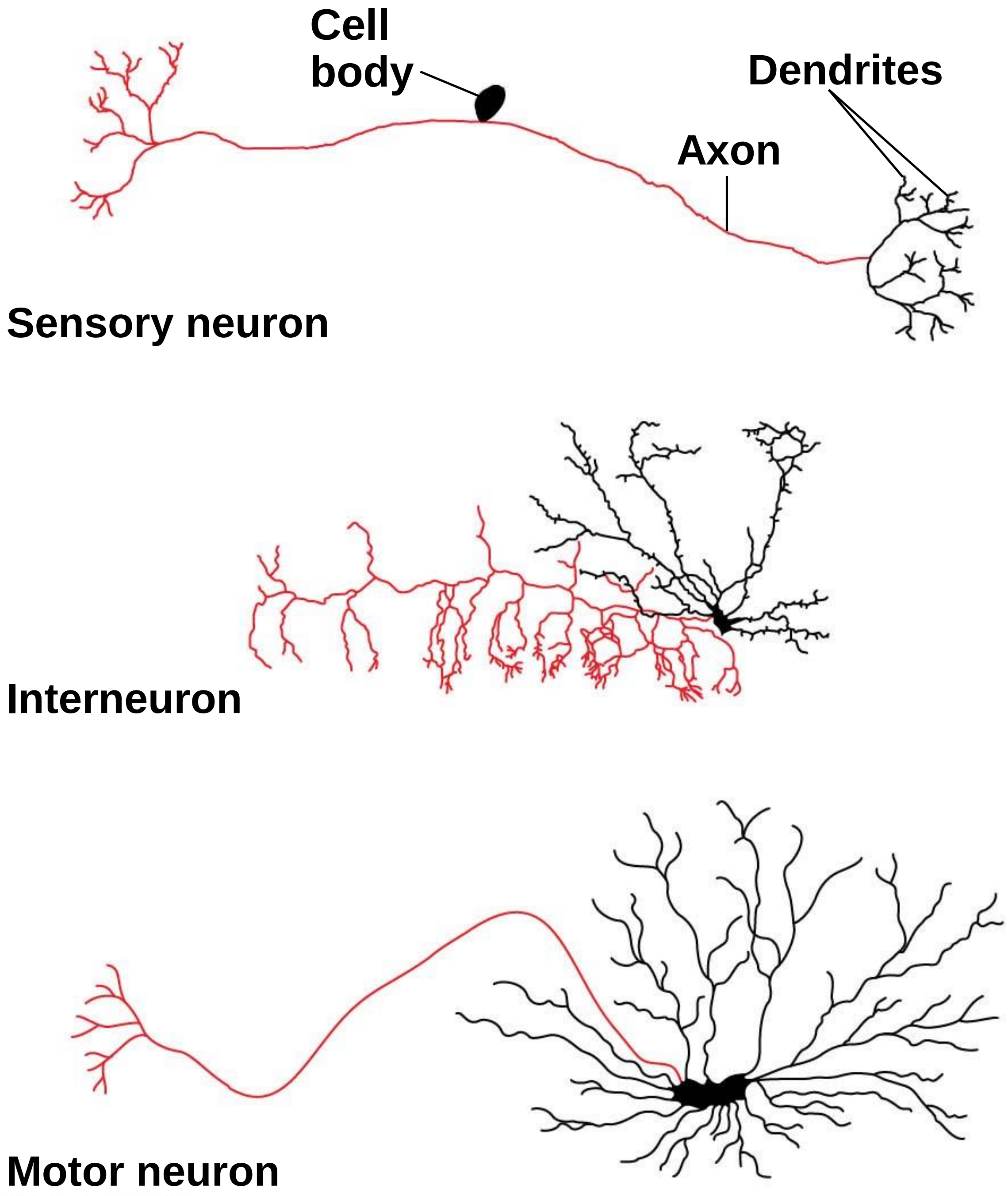


Siphon
Sensor
Sensory input
Integration
Motor output
Proboscis
Effector
Processing center

- **Sensory neurons** transmit information about external stimuli or internal conditions
- This information is sent to the brain or ganglia, where **interneurons** integrate (analyze and interpret) the sensory input
- Neurons that extend out of the processing centers trigger muscle or gland activity
- For example, **motor neurons** transmit signals to muscle cells, causing them to contract

- The neurons that carry out integration are often organized in a **central nervous system** (**CNS**)
- The neurons that carry information into and out of the CNS form the **peripheral nervous system** (**PNS**)
- PNS neurons, bundled together, form **nerves**

Figure 37.5


Cell
body
Dendrites
Axon
Sensory neuron
Interneuron
Motor neuron

Concept 37.2: Ion pumps and ion channels establish the resting potential of a neuron

- The inside of a cell is negatively charged relative to the outside
- This difference is a source of potential energy, termed **membrane potential**
- The **resting potential** is the membrane potential of a neuron not sending signals
- Changes in membrane potential act as signals, transmitting and processing information

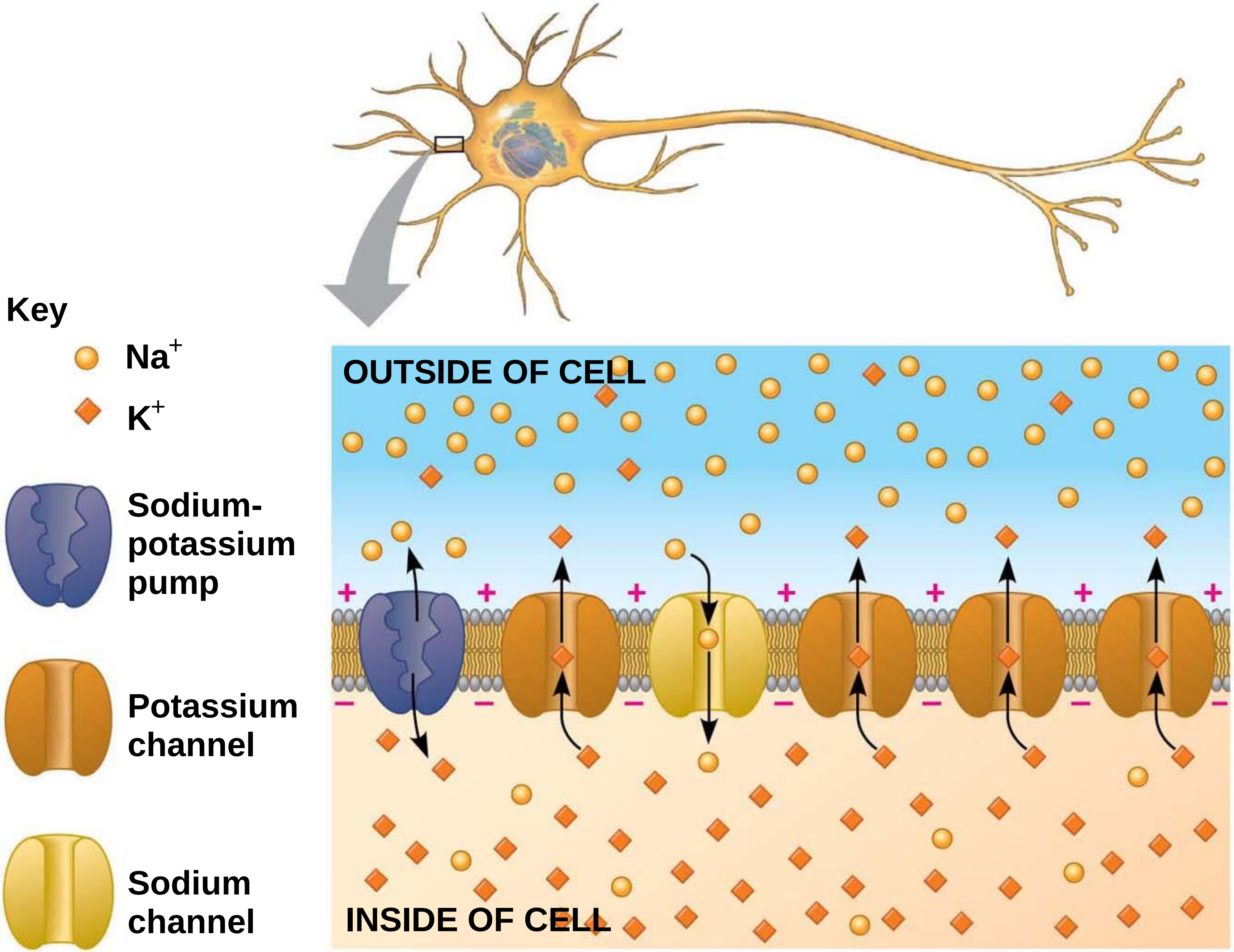
Formation of the Resting Potential

- K^+ and Na^+ play an essential role in forming the resting potential
- In most neurons, the concentration of K^+ is higher inside the cell, while the concentration of Na^+ is higher outside the cell
- **Sodium-potassium pumps** use the energy of ATP to maintain these K^+ and Na^+ gradients across the plasma membrane

Table 37.1 Ion Concentrations Inside and Outside of Mammalian Neurons

Ion	Intracellular Concentration (m*M*)	Extracellular Concentration (m*M*)
Potassium (K^+)	140	5
Sodium (Na^+)	15	150
Chloride (Cl^-)	10	120
Large anions (A^-) inside cell, such as proteins	100	Not applicable

Figure 37.6

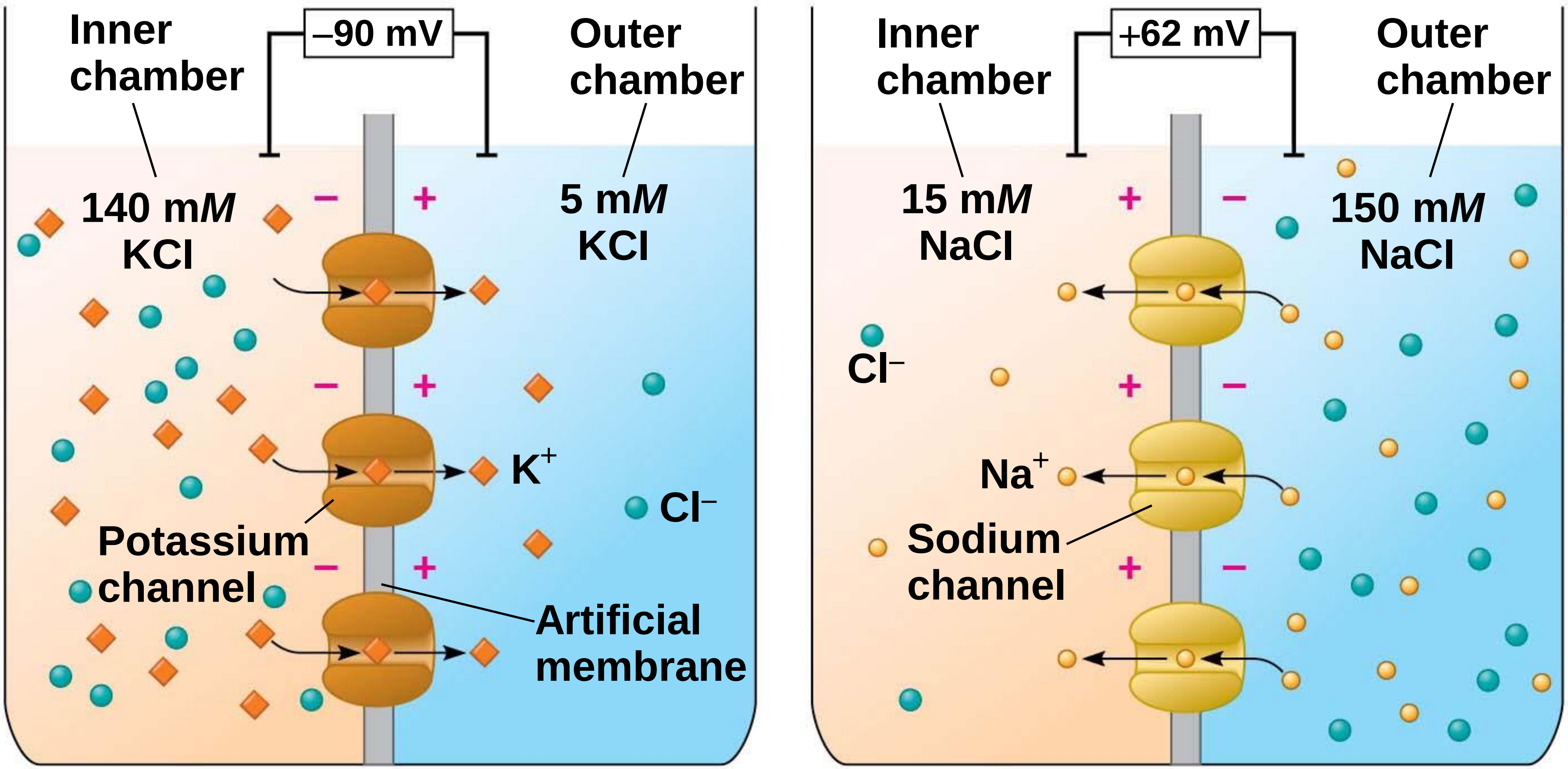

Key
Na+
K+
Sodium-potassium pump
Potassium channel
Sodium channel
OUTSIDE OF CELL
INSIDE OF CELL

- The opening of **ion channels** in the plasma membrane converts the chemical potential energy of the ion gradients to electrical potential energy
- Ion channels are selectively permeable, allowing only certain ions to pass through
- A resting neuron has many open potassium channels, allowing K^+ to flow out
- The resulting buildup of negative charge within the neuron is the major source of membrane potential

Modeling the Resting Potential

- Resting potential can be modeled by an artificial membrane that separates two chambers
  - The concentration of KCl is higher in the inner chamber and lower in the outer chamber
  - K^+ diffuses down its gradient to the outer chamber
  - Negative charge (Cl^-) builds up in the inner chamber
- At equilibrium, both the electrical and chemical gradients are balanced

Figure 37.7



(a) Membrane selectively permeable to K^+

$$E_K = 62 \text{ mV}\left(\log \frac{5 \text{ m}M}{140 \text{ m}M}\right) = -90 \text{ mV}$$

(b) Membrane selectively permeable to Na^+

$$E_{Na} = 62 \text{ mV}\left(\log \frac{150 \text{ m}M}{15 \text{ m}M}\right) = +62 \text{ mV}$$

- The **equilibrium potential** (***E***$_{\mathbf{ion}}$) is the membrane voltage for a particular ion at equilibrium and can be calculated using the Nernst equation

$$E_{ion} = 62 \text{ mV} \left(\log \frac{[\text{ion}]_{outside}}{[\text{ion}]_{inside}} \right)$$

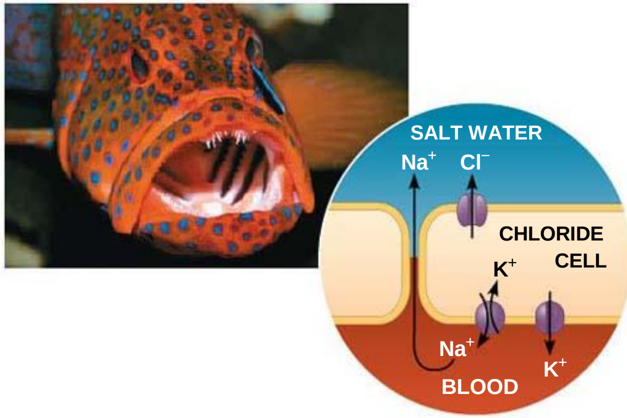
- The equilibrium potential for K^+ is –90 mV
- The resting potential of an actual neuron is about –60 to –80 mV because a small amount of Na^+ diffuses into the cell

- In a resting neuron, the currents of K^+ and Na^+ are equal and opposite, and the resting potential across the membrane remains steady

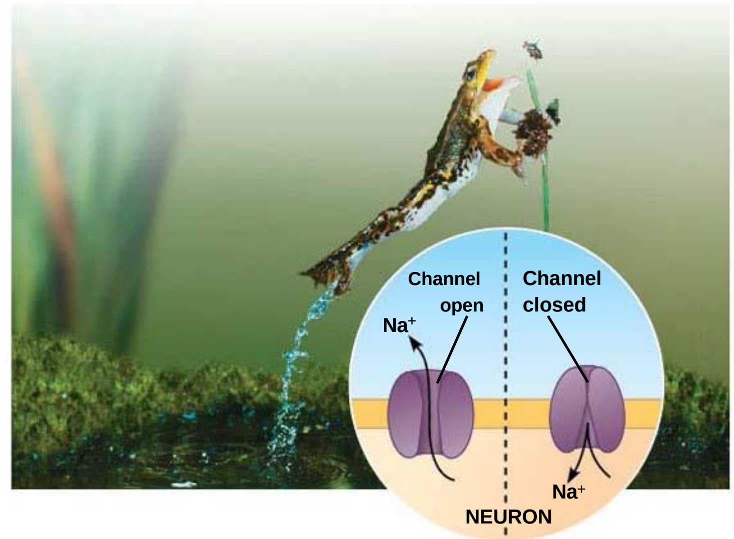
Figure 37.8

MAKE CONNECTIONS: Ion Movement and Gradients

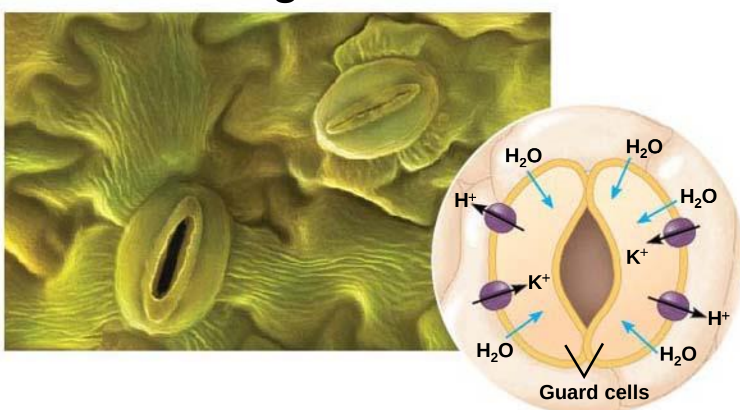
Osmoregulation



Information Processing



Gas Exchange



Locomotion

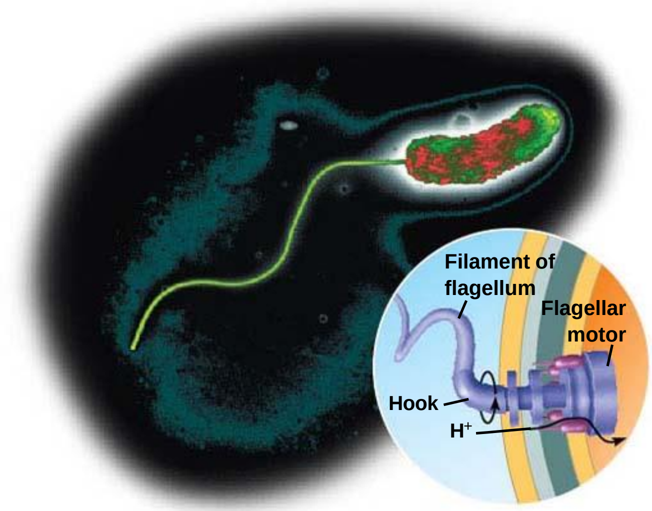
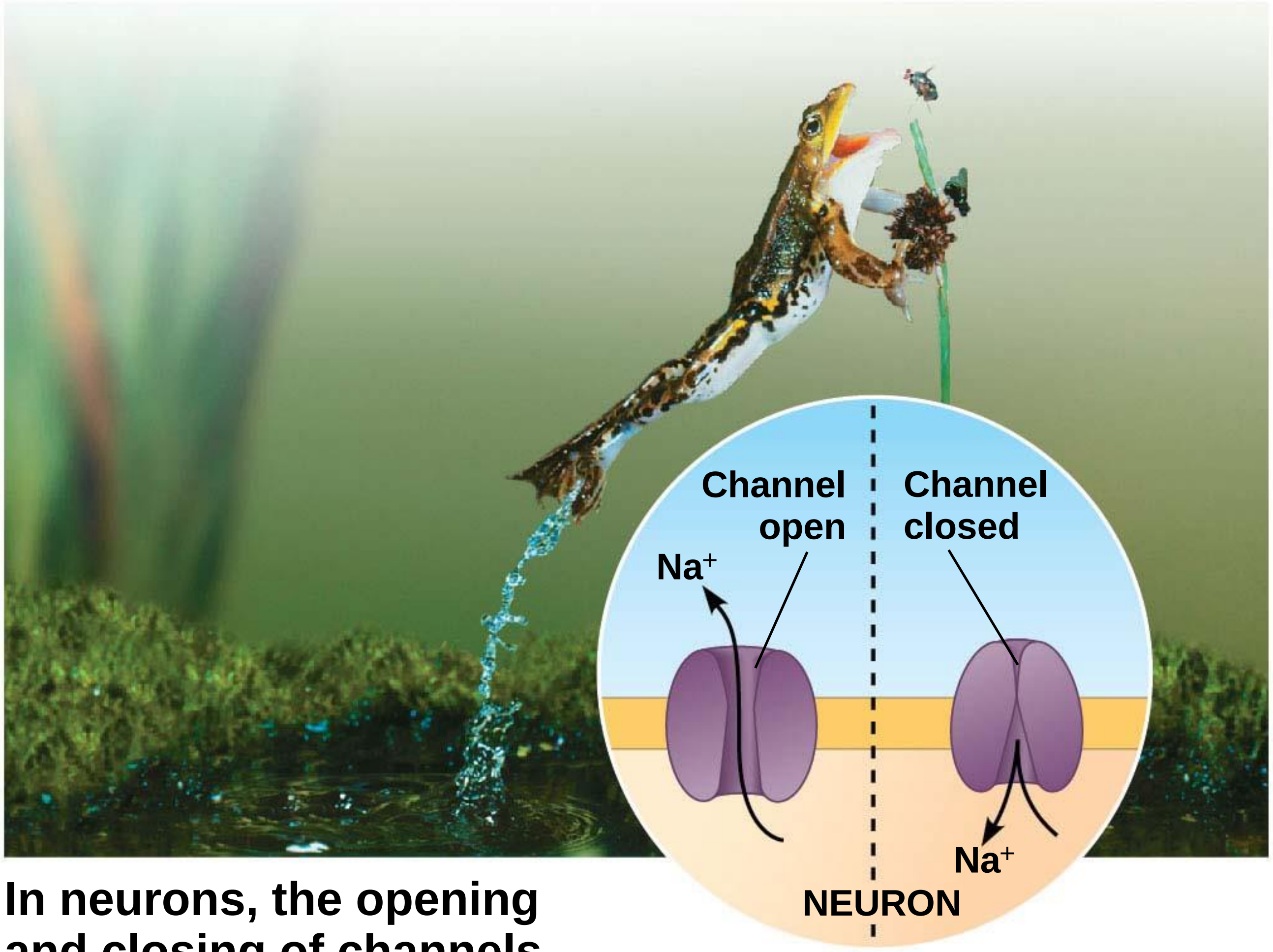


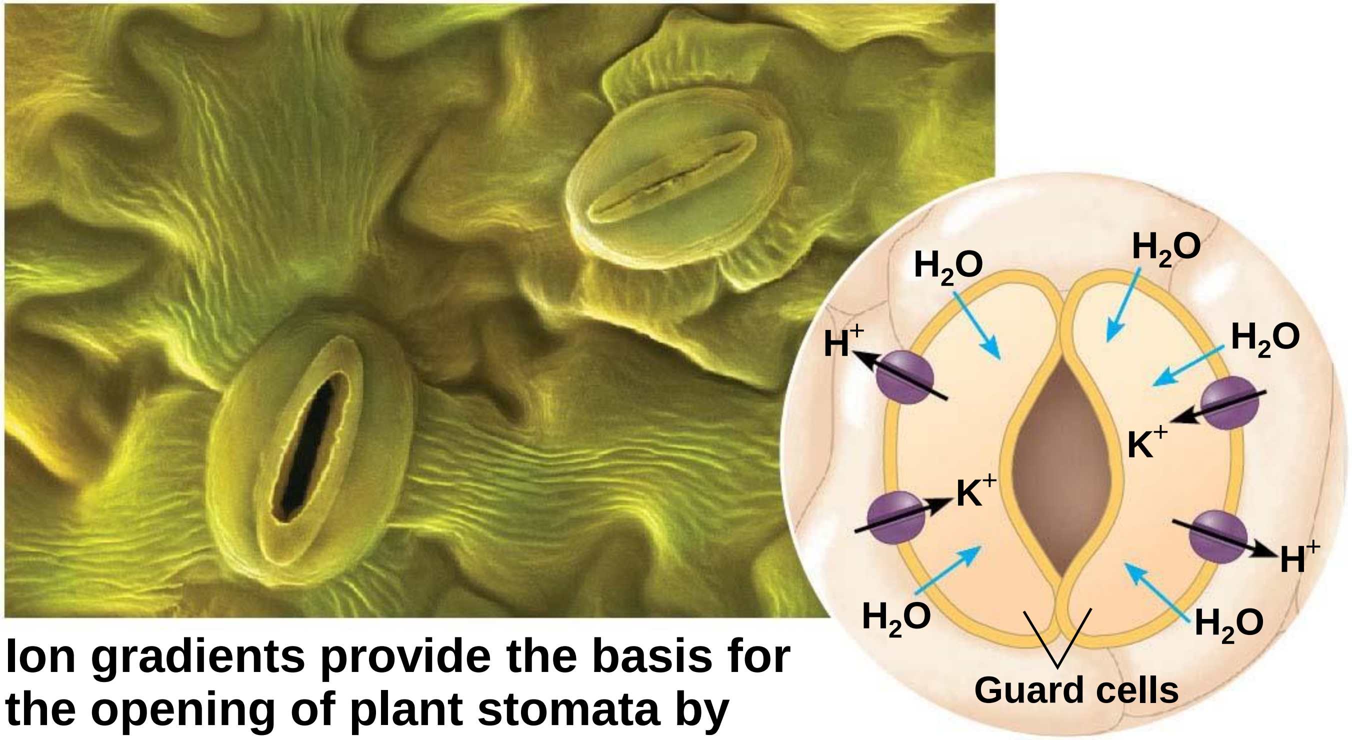
Figure 37.8-2

Information Processing



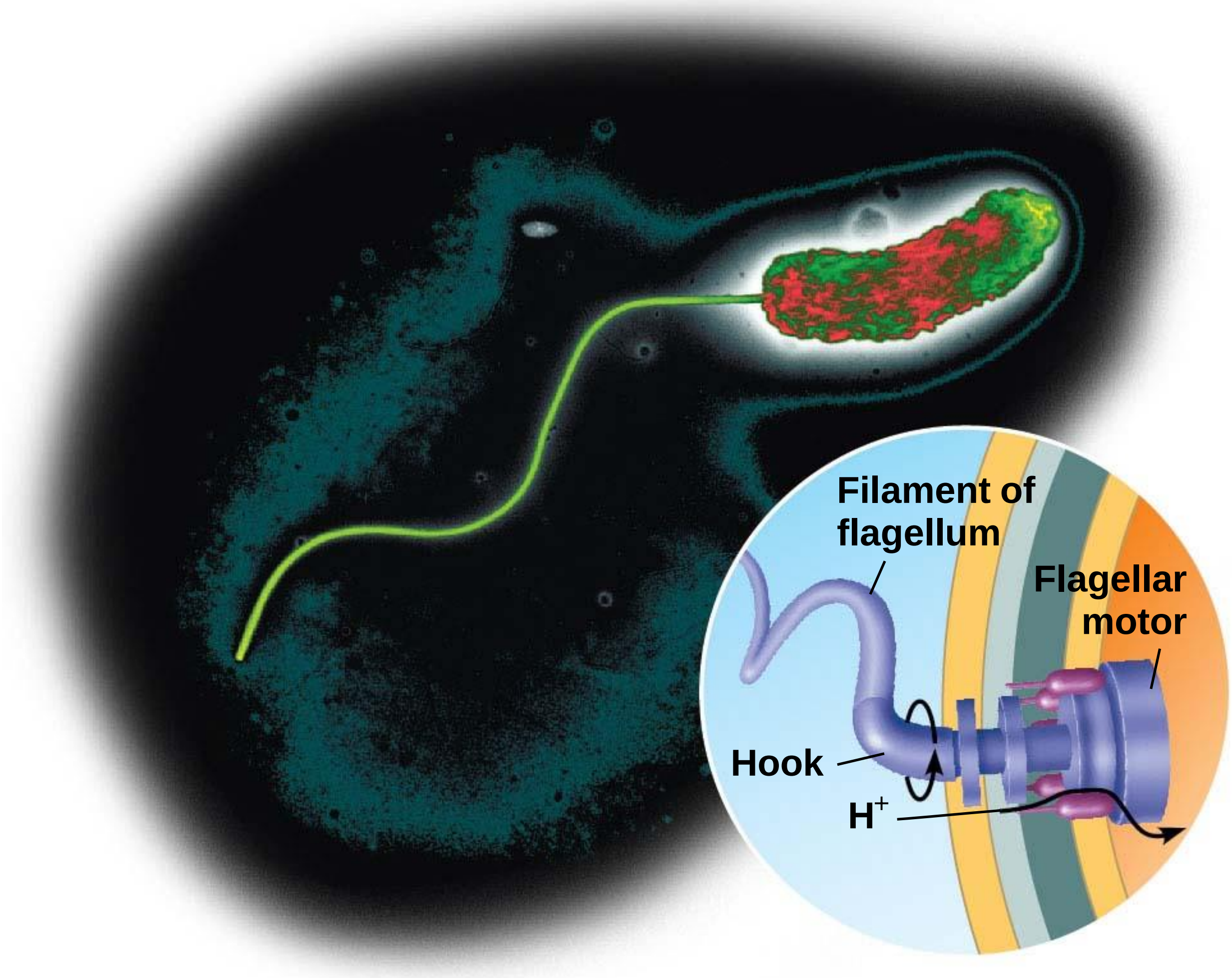
In neurons, the opening and closing of channels selective for sodium or other ions underlies the transmission of information as nerve impulses.

Gas Exchange



Ion gradients provide the basis for the opening of plant stomata by surrounding guard cells.

Locomotion

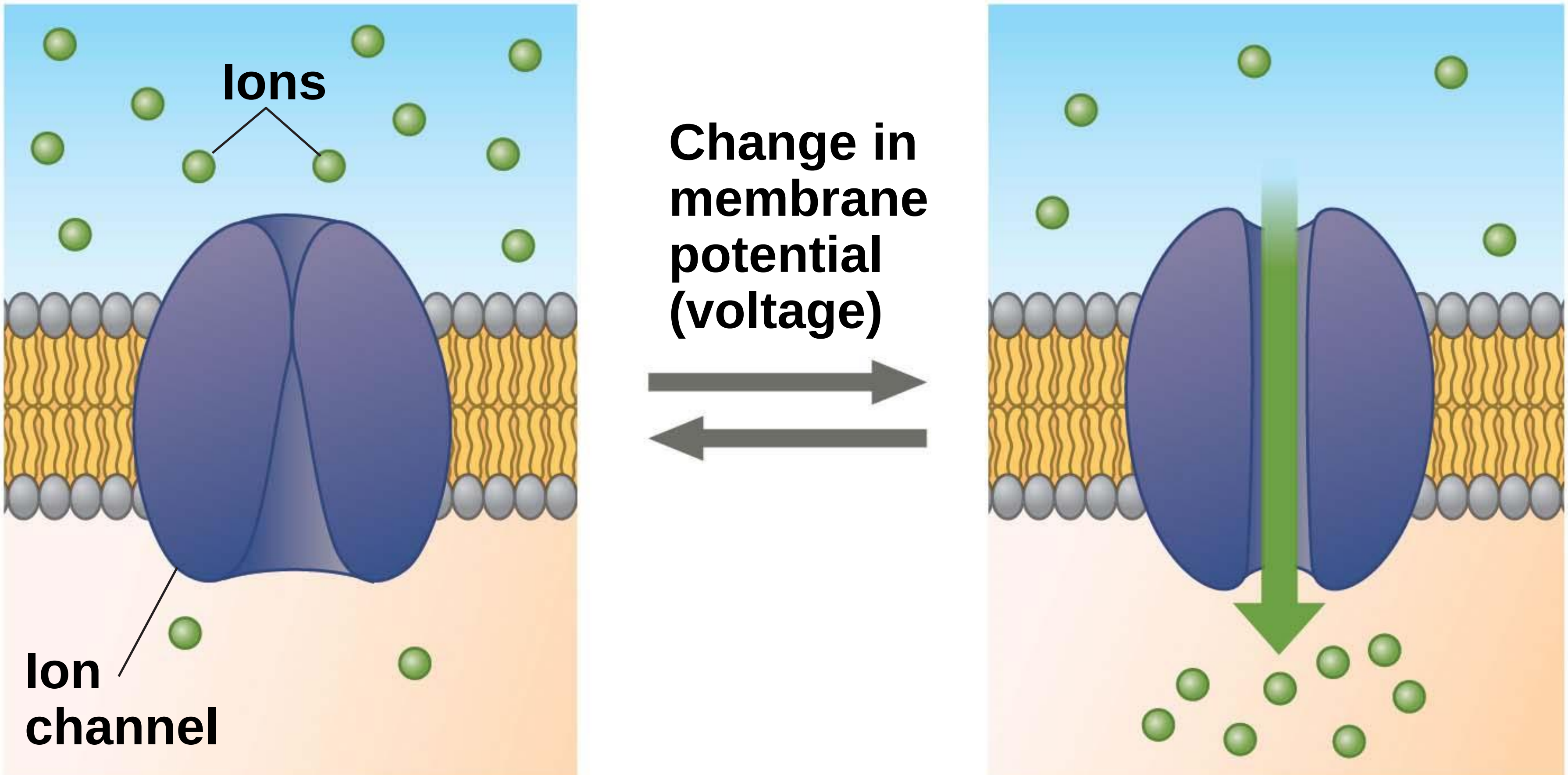


A gradient of H^+ ions powers the bacterial flagellum.

Concept 37.3: Action potentials are the signals conducted by axons

- Researchers can record the changes in membrane potential when a neuron responds to a stimulus
- Changes in membrane potential occur because neurons contain **gated ion channels** that open or close in response to stimuli
- A **voltage-gated ion channel** opens or closes in response to a shift in the voltage across the plasma membrane of the neuron

Figure 37.10



Gate closed: No ions flow across membrane.

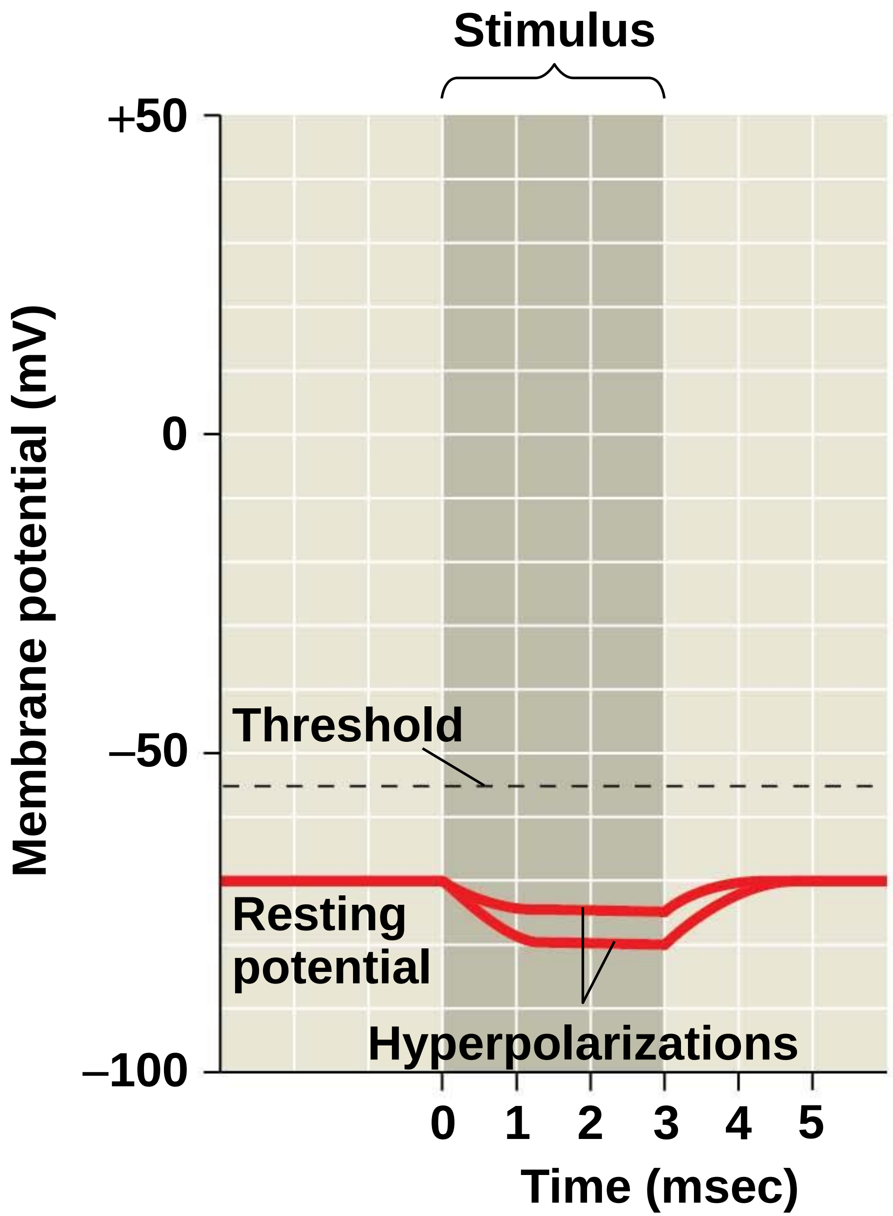
Gate open: Ions flow through channel.

Hyperpolarization and Depolarization

- When gated K^+ channels open, K^+ diffuses out, making the inside of the cell more negative
- This is **hyperpolarization**, an increase in magnitude of the membrane potential

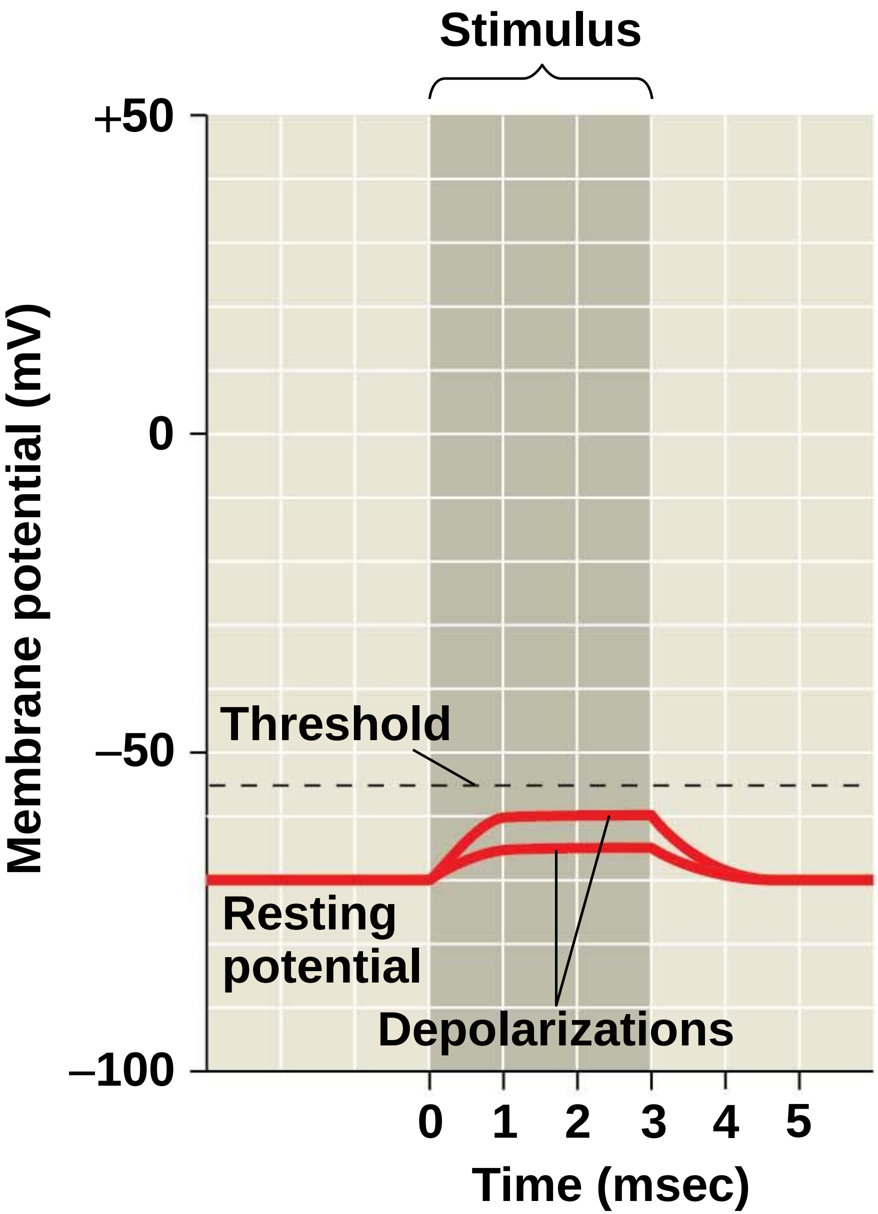
Figure 37.11-1

(a) Graded hyperpolarizations produced by two stimuli that increase membrane permeability to K^+



- Opening other types of ion channels triggers a **depolarization**, a reduction in the magnitude of the membrane potential
- For example, depolarization occurs if gated Na^+ channels open and Na^+ diffuses into the cell

(b) Graded depolarizations produced by two stimuli that increase membrane permeability to Na^+



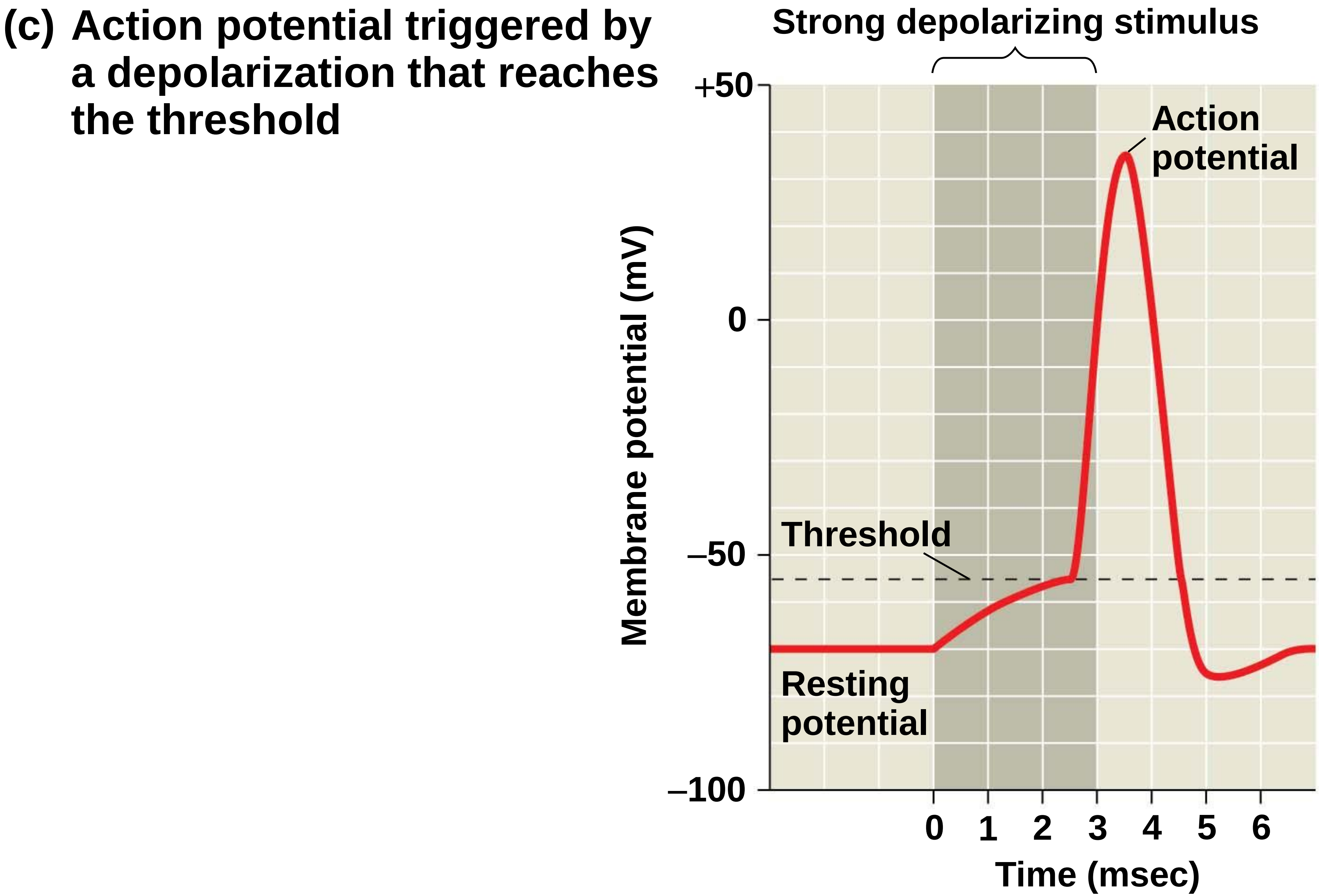
Graded Potentials and Action Potentials

- **Graded potentials** are changes in polarization where the magnitude of the change varies with the strength of the stimulus
- Graded potentials decay with distance from the source

- If a depolarization shifts the membrane potential sufficiently, it results in a massive change in membrane voltage, called an **action potential**
- Action potentials have a constant magnitude and transmit signals over long distances

- Action potentials occur whenever a depolarization increases the membrane potential to a particular value, called the **threshold**
- Action potentials are all or none

Figure 37.11-3

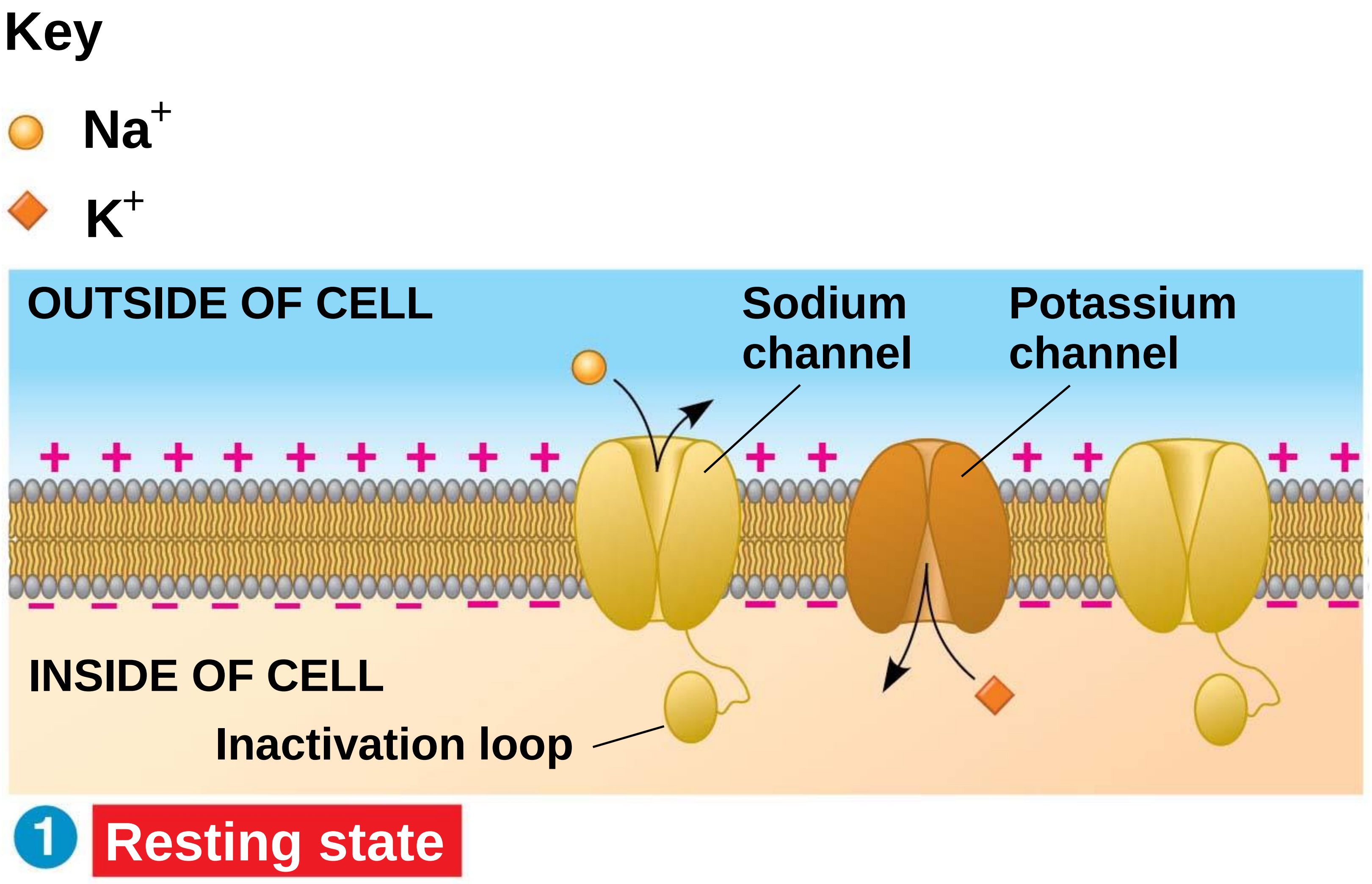


Generation of Action Potentials: *A Closer Look*

- An action potential can be considered as a series of stages
- At resting potential

1. Most voltage-gated sodium (Na^+) channels are closed; most of the voltage-gated potassium (K^+) channels are also closed

Figure 37.12-1



- When stimulus depolarizes the membrane

2. Some gated Na^+ channels open first, and Na^+ flows into the cell
3. During the *rising phase*, the threshold is crossed, and the membrane potential increases
4. During the *falling phase*, voltage-gated Na^+ channels become inactivated; voltage-gated K^+ channels open, and K^+ flows out of the cell

Figure 37.12-2

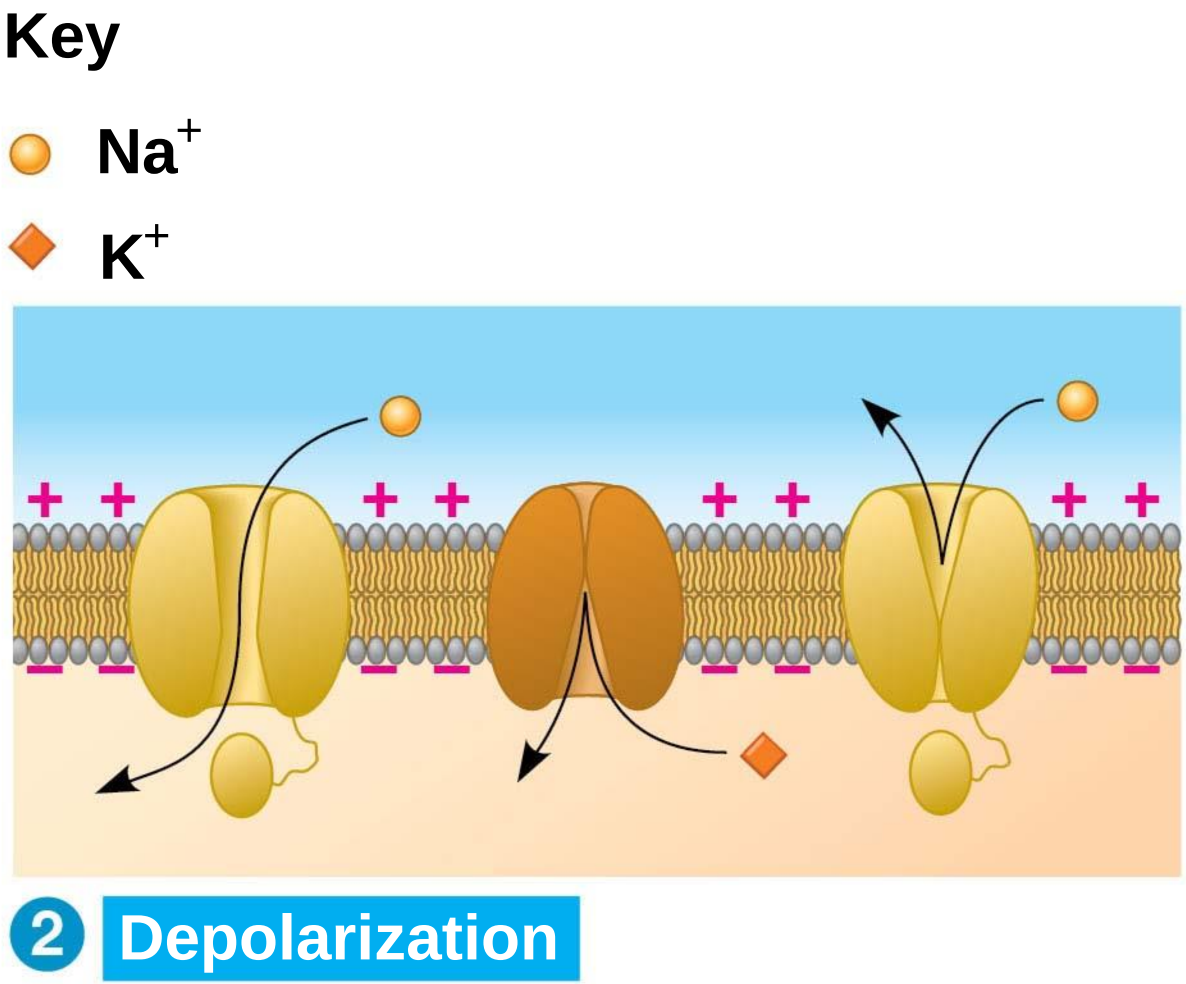
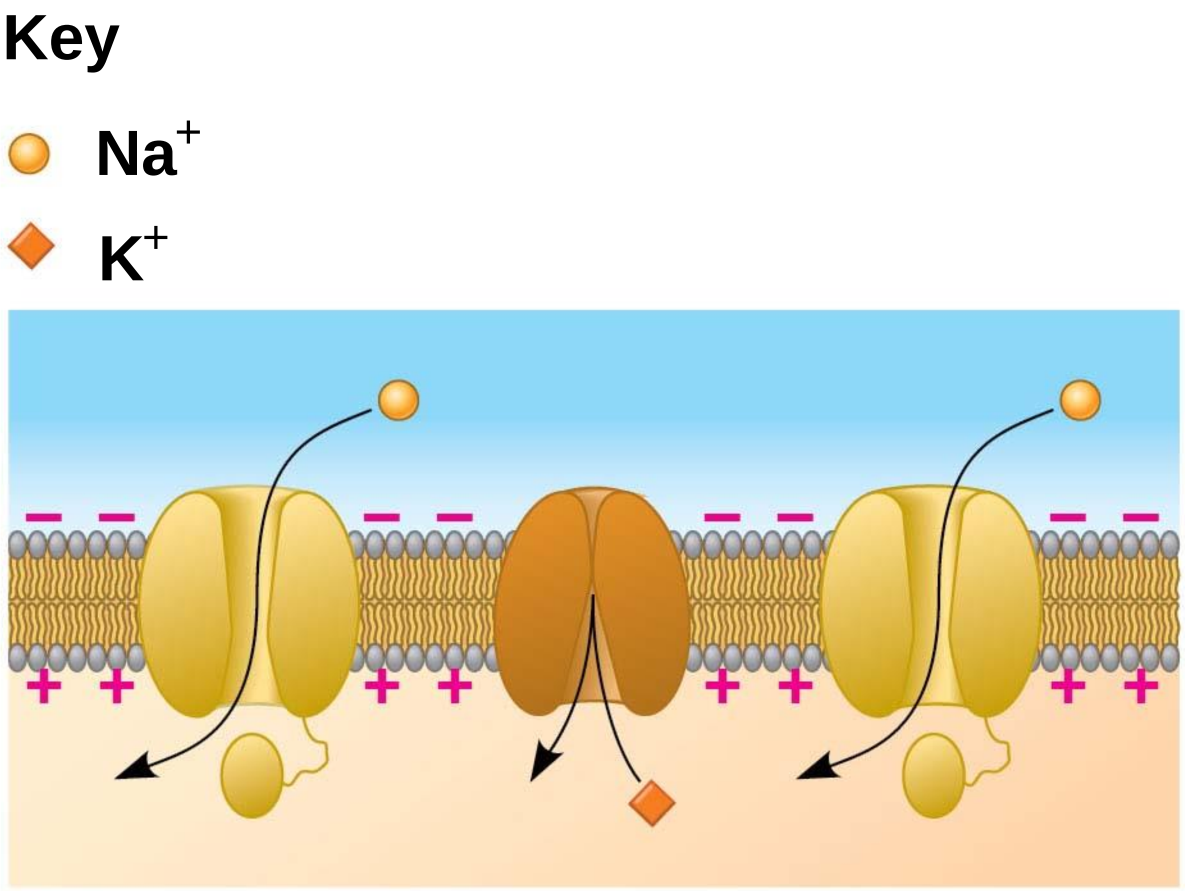
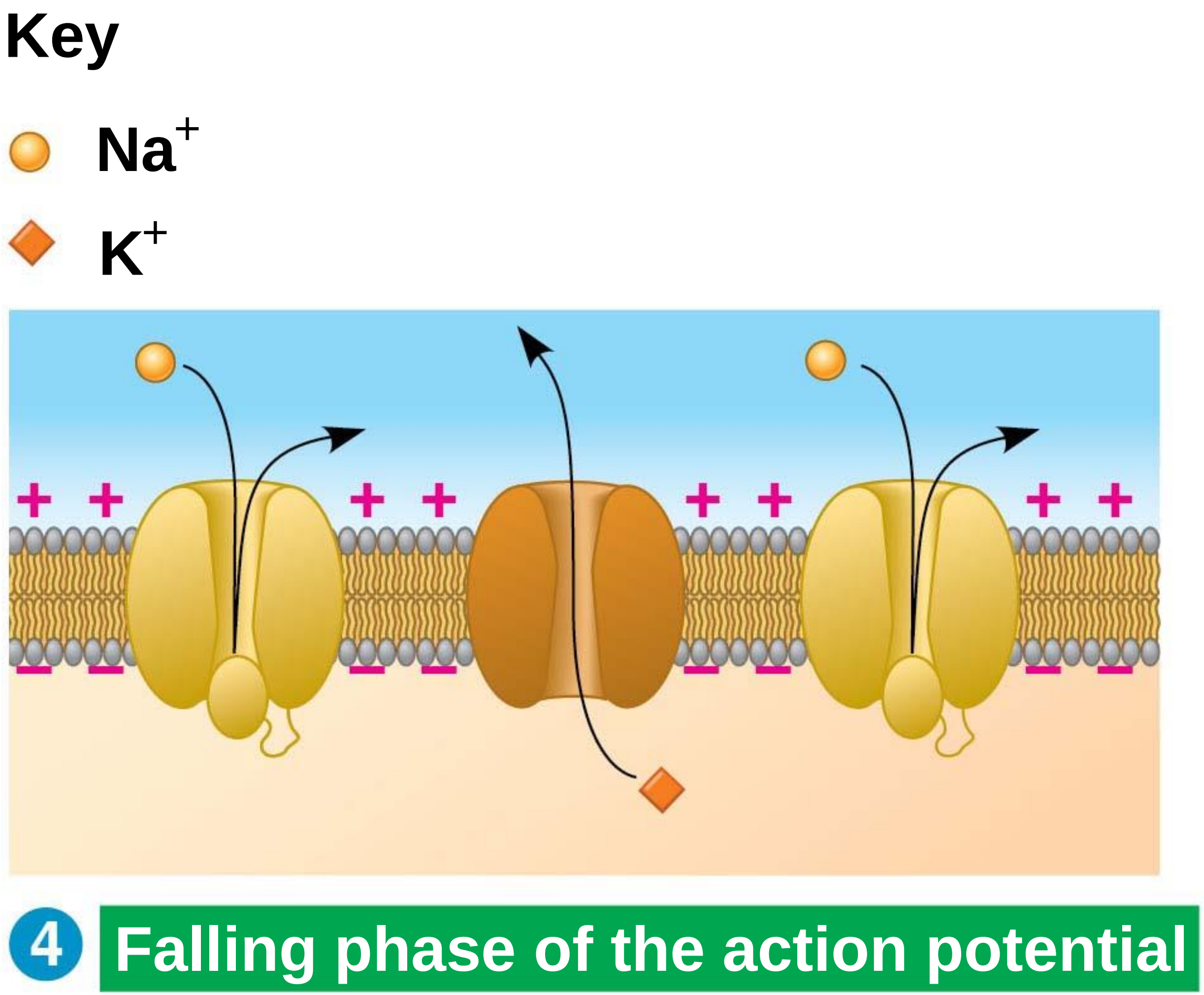


Figure 37.12-3



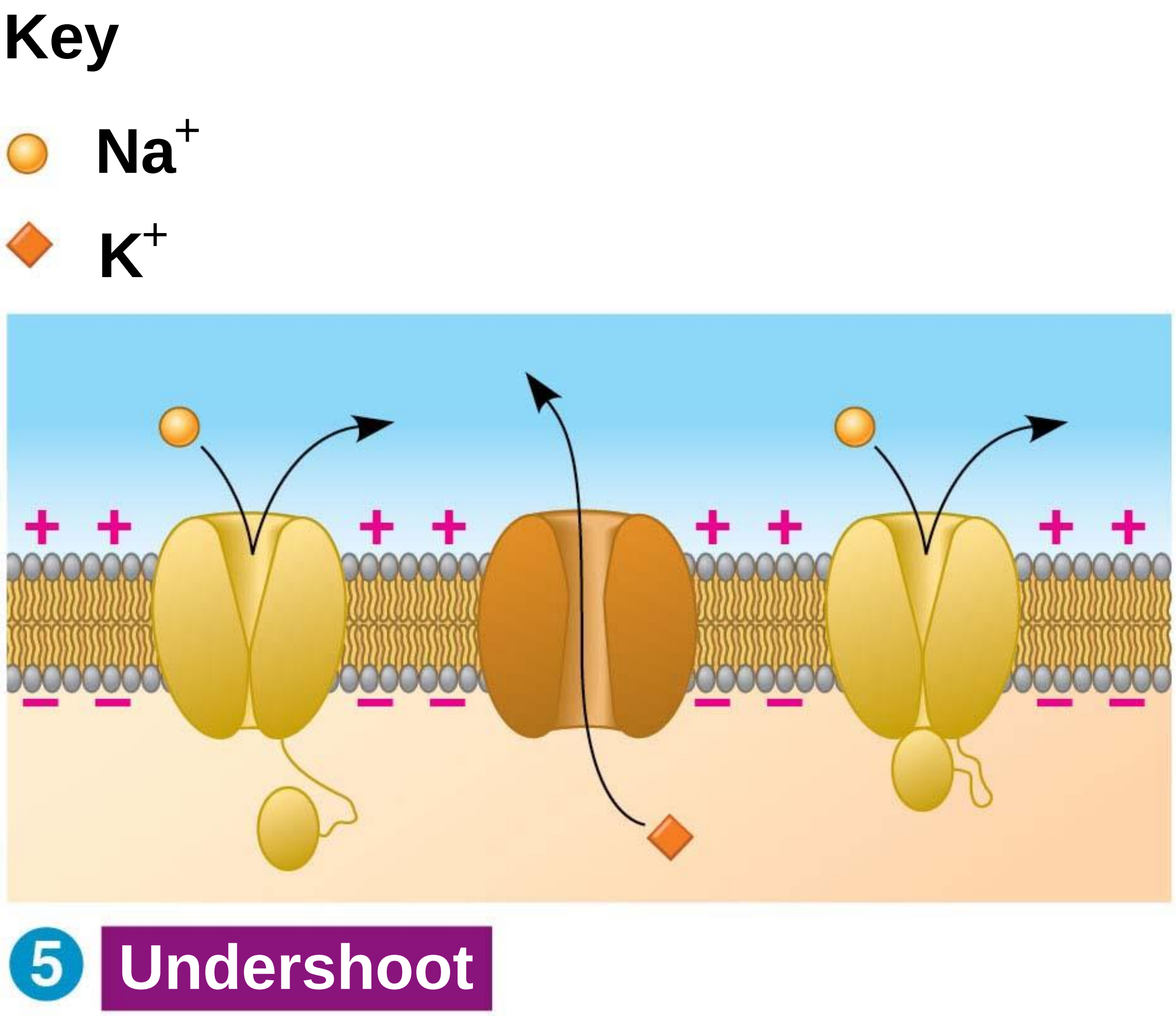
3 Rising phase of the action potential

Figure 37.12-4



5. During the *undershoot*, membrane permeability to K^+ is at first higher than at rest, and then voltage-gated K^+ channels close and resting potential is restored

Figure 37.12-5



- During the **refractory period** after an action potential, a second action potential cannot be initiated
- The refractory period is a result of a temporary inactivation of the Na^+ channels

Conduction of Action Potentials

- At the site where the action potential is initiated (usually the axon hillock), an electrical current depolarizes the neighboring region of the axon membrane
- Action potentials travel only toward the synaptic terminals
- Inactivated Na^+ channels behind the zone of depolarization prevent the action potential from traveling backward

Figure 37.13-s1

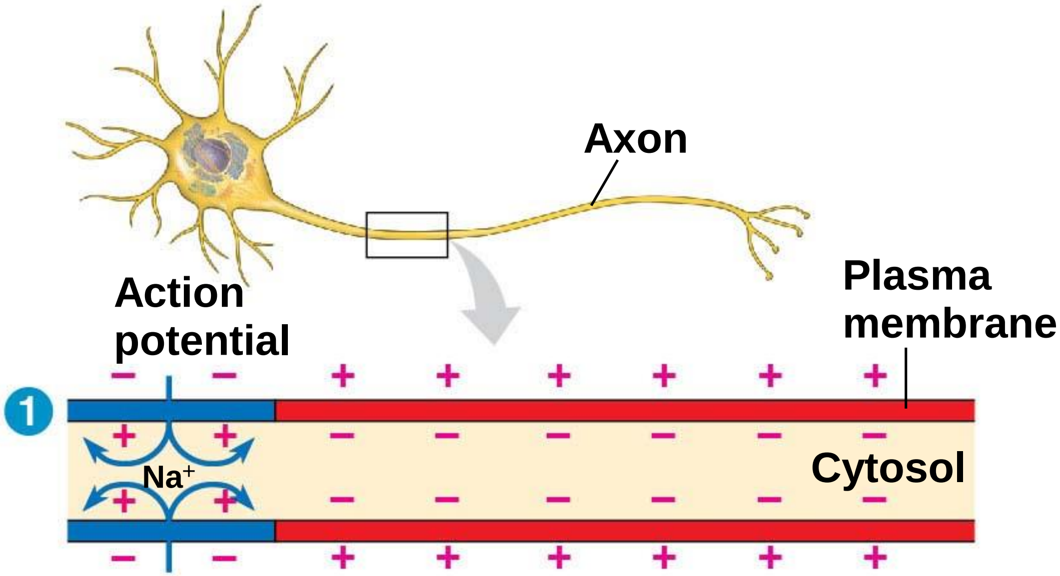


Figure 37.13-s2

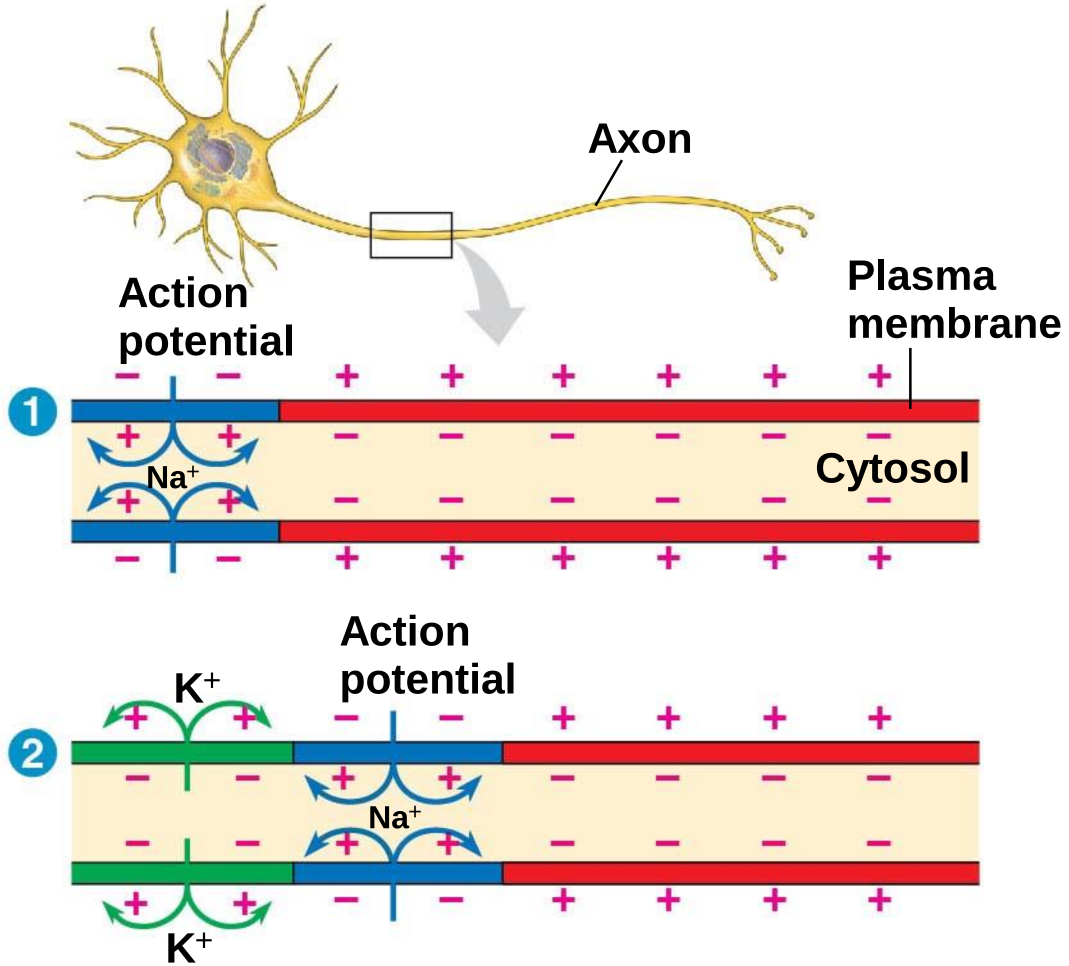
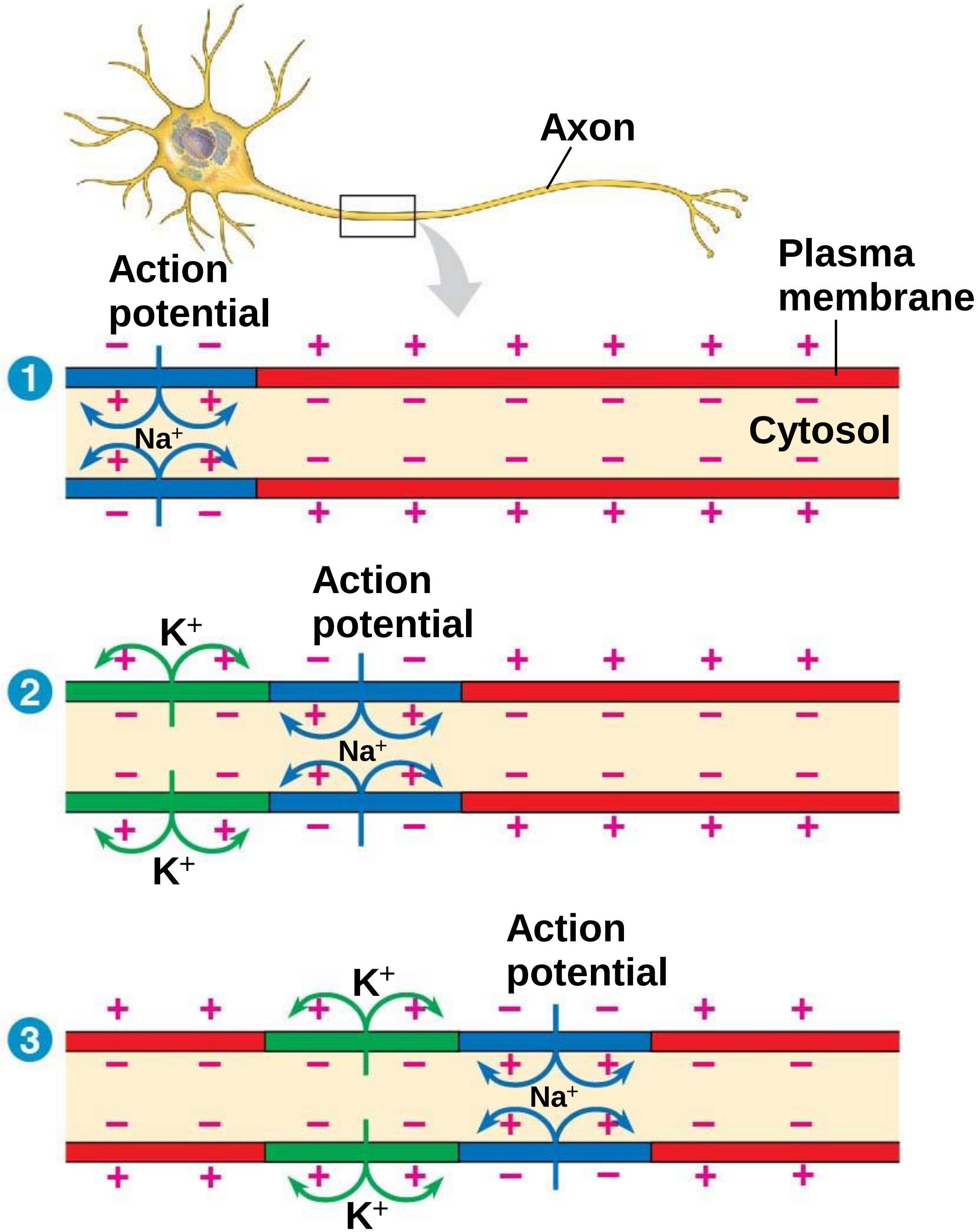


Figure 37.13-s3



Evolutionary Adaptations of Axon Structure

- The speed of an action potential increases with the axon's diameter
- In vertebrates, axons are insulated by a **myelin sheath**, which enables fast conduction of action potentials
- Myelin sheaths are produced by glia—**oligodendrocytes** in the CNS and **Schwann cells** in the PNS

Figure 37.14

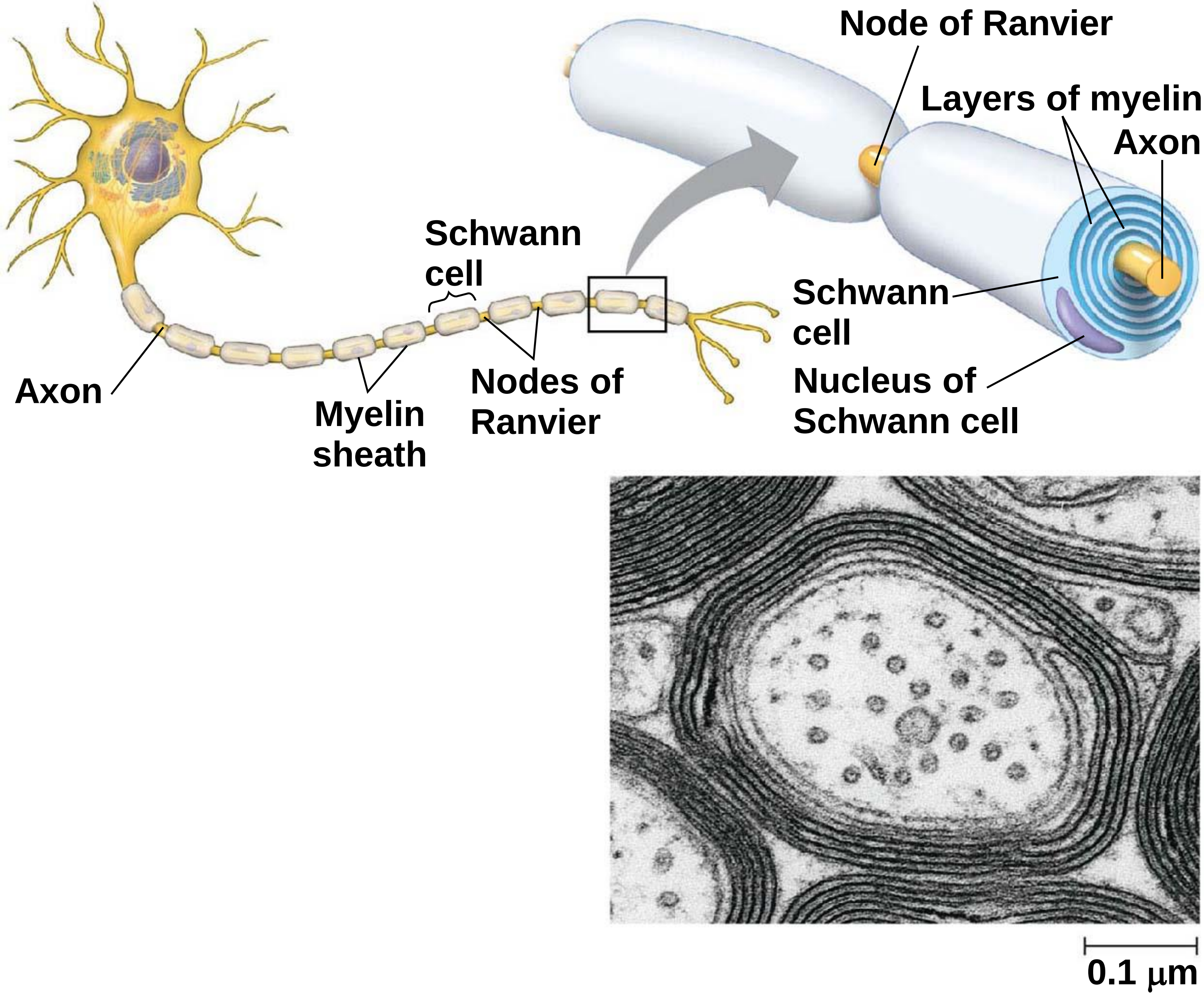
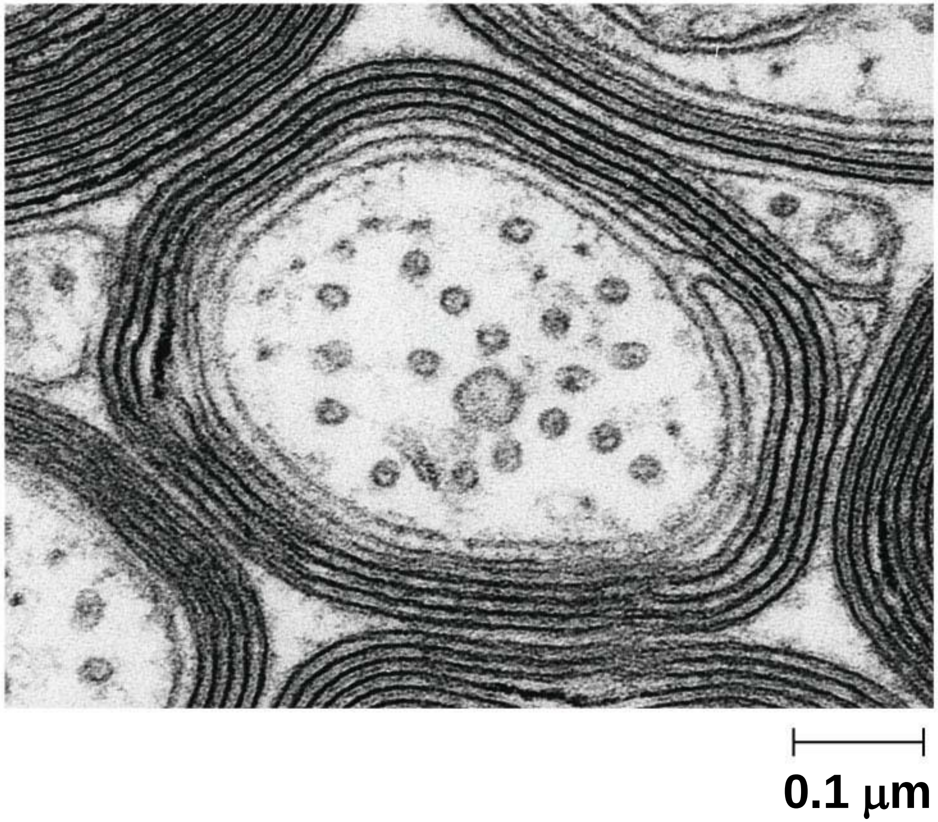
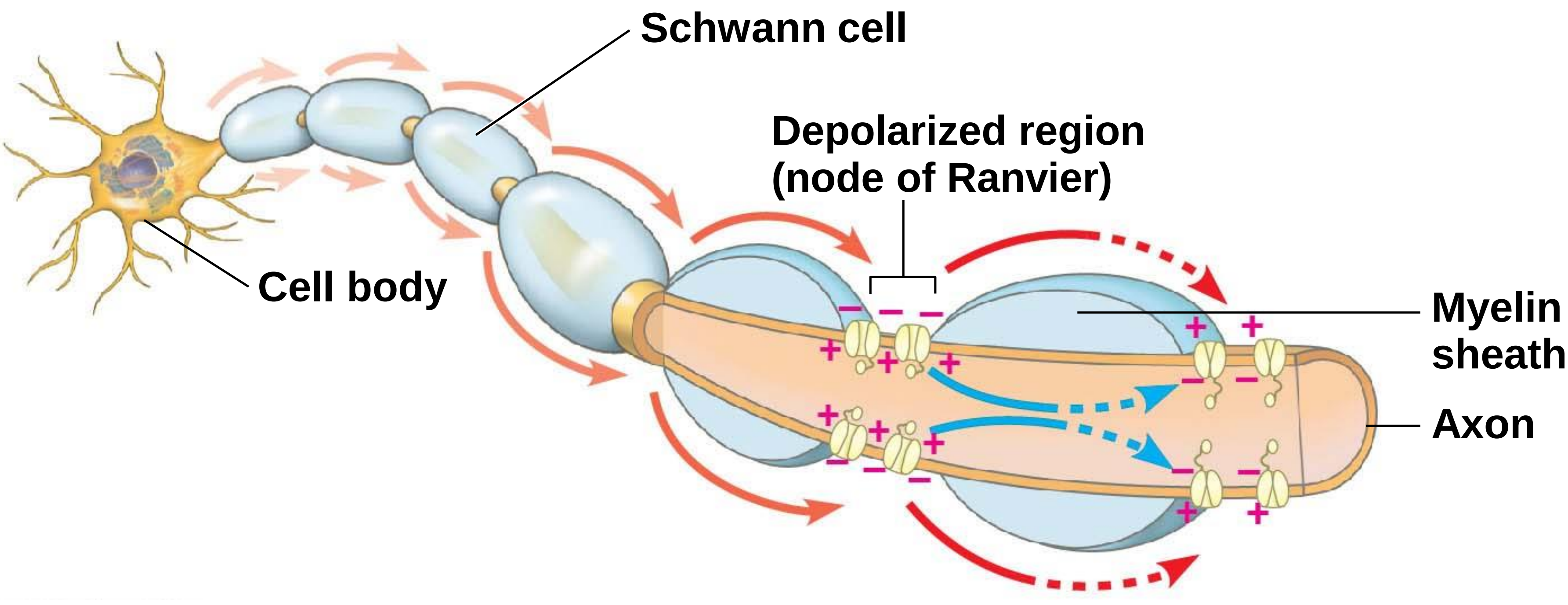

Node of Ranvier
Layers of myelin
Axon
Schwann cell
Schwann cell
Nucleus of Schwann cell
Axon
Myelin sheath
Nodes of Ranvier
0.1 μm

Figure 37.14-1



- Action potentials are formed only at **nodes of Ranvier**, gaps in the myelin sheath where voltage-gated Na^+ channels are found
- Action potentials in myelinated axons jump between the nodes of Ranvier in a process called **saltatory conduction**
- A selective advantage of myelination is space efficiency

Figure 37.15

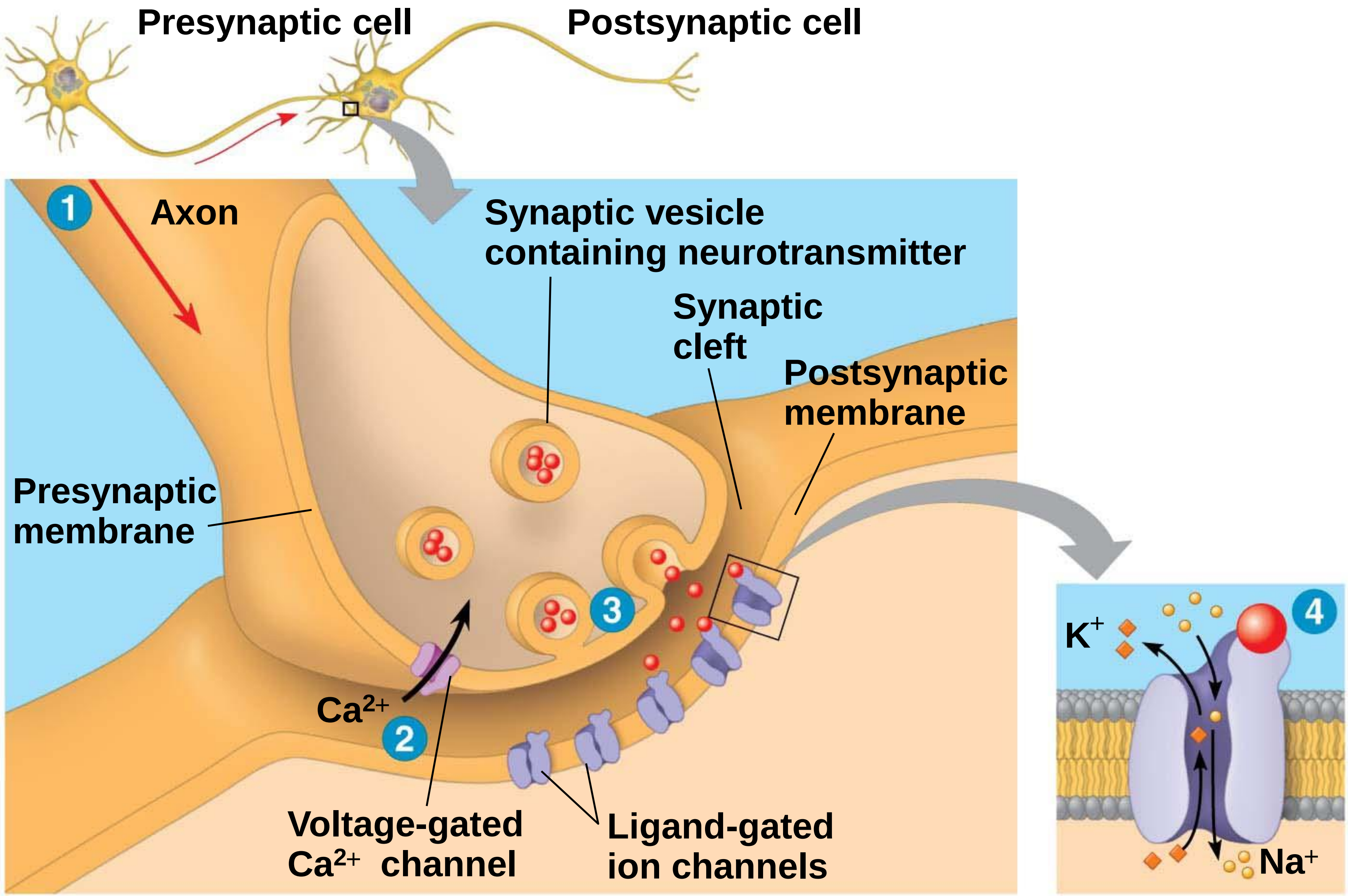

Schwann cell
Depolarized region
(node of Ranvier)
Cell body
Myelin
sheath
Axon

Concept 37.4: Neurons communicate with other cells at synapses

- In most cases, action potentials are not transmitted from one neuron to another
- Information is transmitted, however, at synapses
- Most synapses are chemical synapses, in which a chemical neurotransmitter carries information from the presynaptic neuron to the postsynaptic cell

- The presynaptic neuron synthesizes and packages the neurotransmitter in synaptic vesicles located in the synaptic terminal
- The arrival of the action potential causes the release of the neurotransmitter
- The neurotransmitter diffuses across the synaptic cleft and is received by the postsynaptic cell

Figure 37.16



Presynaptic cell
Postsynaptic cell
1
Axon
Synaptic vesicle containing neurotransmitter
Synaptic cleft
Postsynaptic membrane
Presynaptic membrane
3
Ca2+
2
Voltage-gated Ca2+ channel
Ligand-gated ion channels
4
K+
Na+

Generation of Postsynaptic Potentials

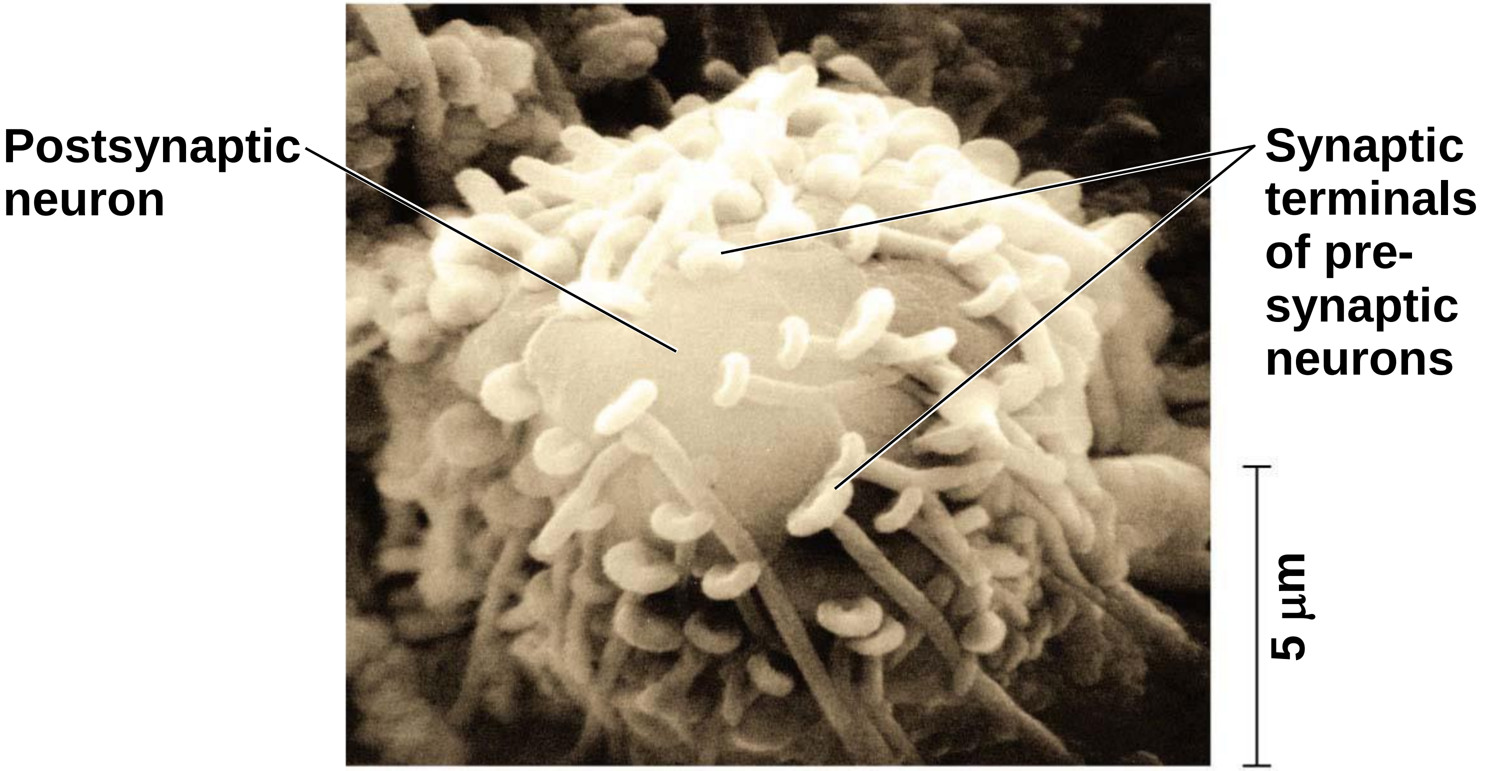
- Direct synaptic transmission involves binding of neurotransmitters to **ligand-gated ion channels** in the postsynaptic cell
- Neurotransmitter binding causes ion channels to open, generating a postsynaptic potential

- Postsynaptic potentials fall into two categories
  - **Excitatory postsynaptic potentials** (**EPSPs**) are depolarizations that bring the membrane potential toward threshold
  - **Inhibitory postsynaptic potentials** (**IPSPs**) are hyperpolarizations that move the membrane potential farther from threshold

Summation of Postsynaptic Potentials

- The cell body of one postsynaptic neuron may receive inputs from hundreds or thousands of synaptic terminals
- A single EPSP is usually too small to trigger an action potential in a postsynaptic neuron

Figure 37.17

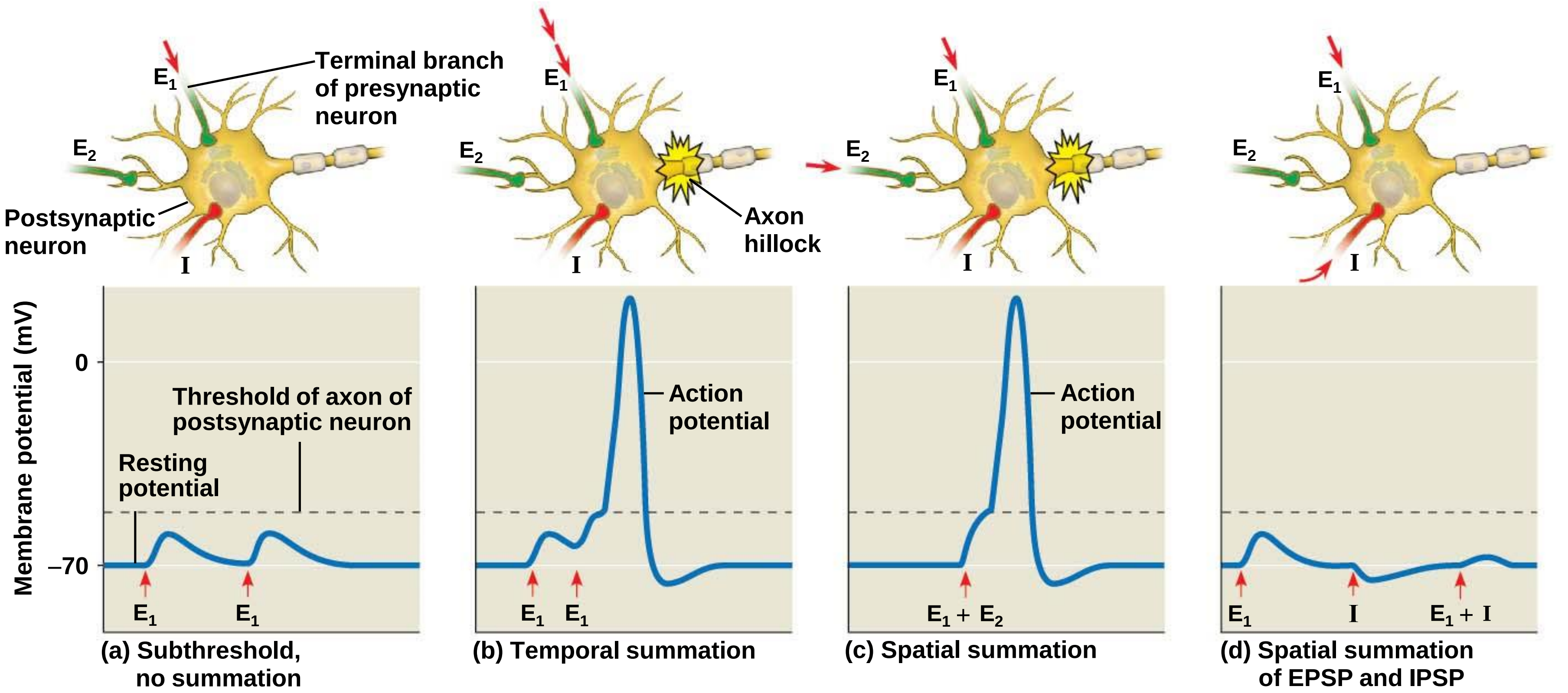


Postsynaptic neuron
Synaptic terminals of pre-synaptic neurons
5 µm

- Individual postsynaptic potentials can combine to produce a larger postsynaptic potential in a process called **summation**
- If two EPSPs are produced in rapid succession, an effect called temporal summation occurs

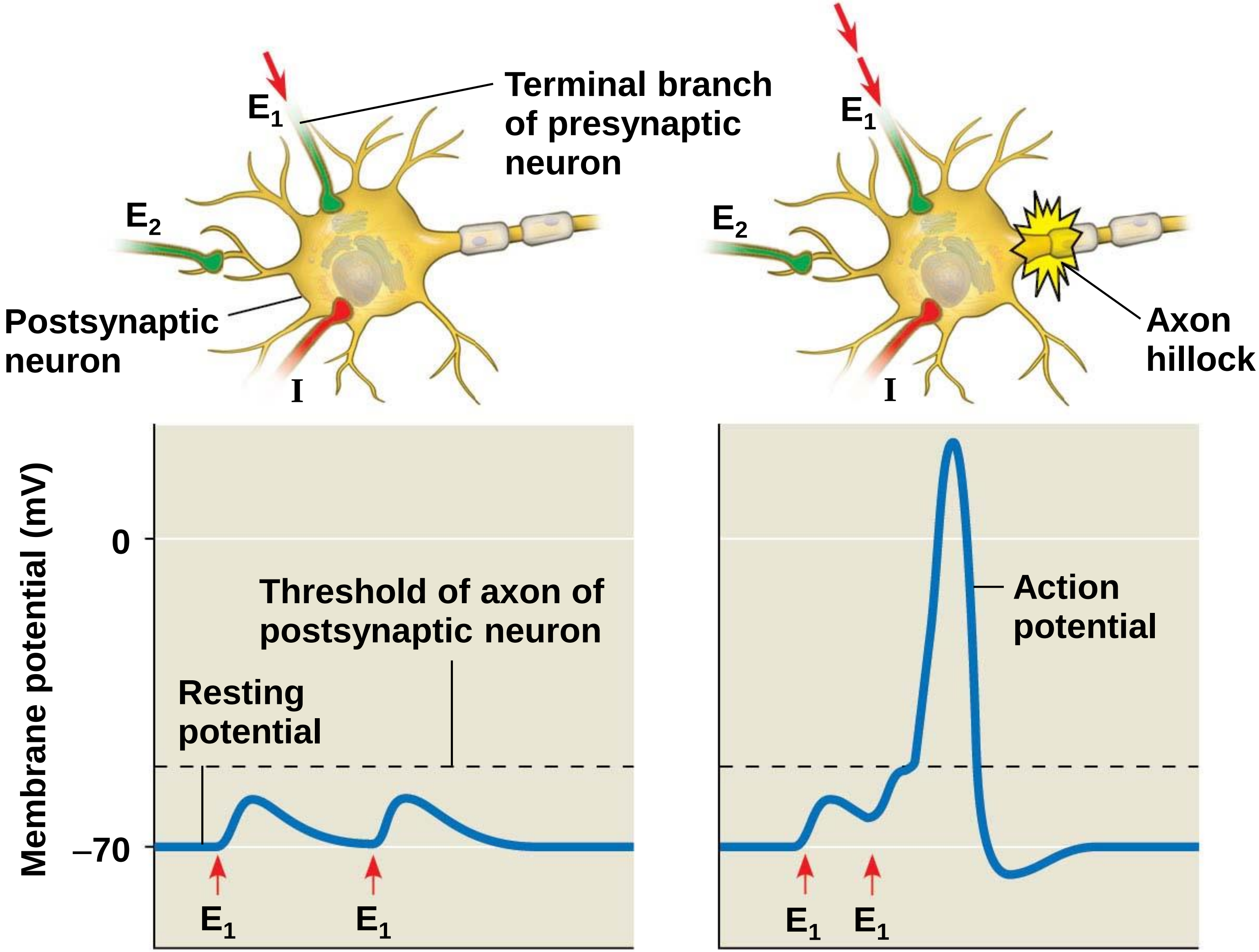
- In spatial summation, EPSPs produced nearly simultaneously by different synapses on the same postsynaptic neuron add together
- The combination of EPSPs through spatial and temporal summation can trigger an action potential

Figure 37.18



Terminal branch of presynaptic neuron
Postsynaptic neuron
Axon hillock
E1
E2
I
Membrane potential (mV)
0
–70
Threshold of axon of postsynaptic neuron
Resting potential
Action potential
E1 + E2
E1 + I
(a) Subthreshold, no summation
(b) Temporal summation
(c) Spatial summation
(d) Spatial summation of EPSP and IPSP

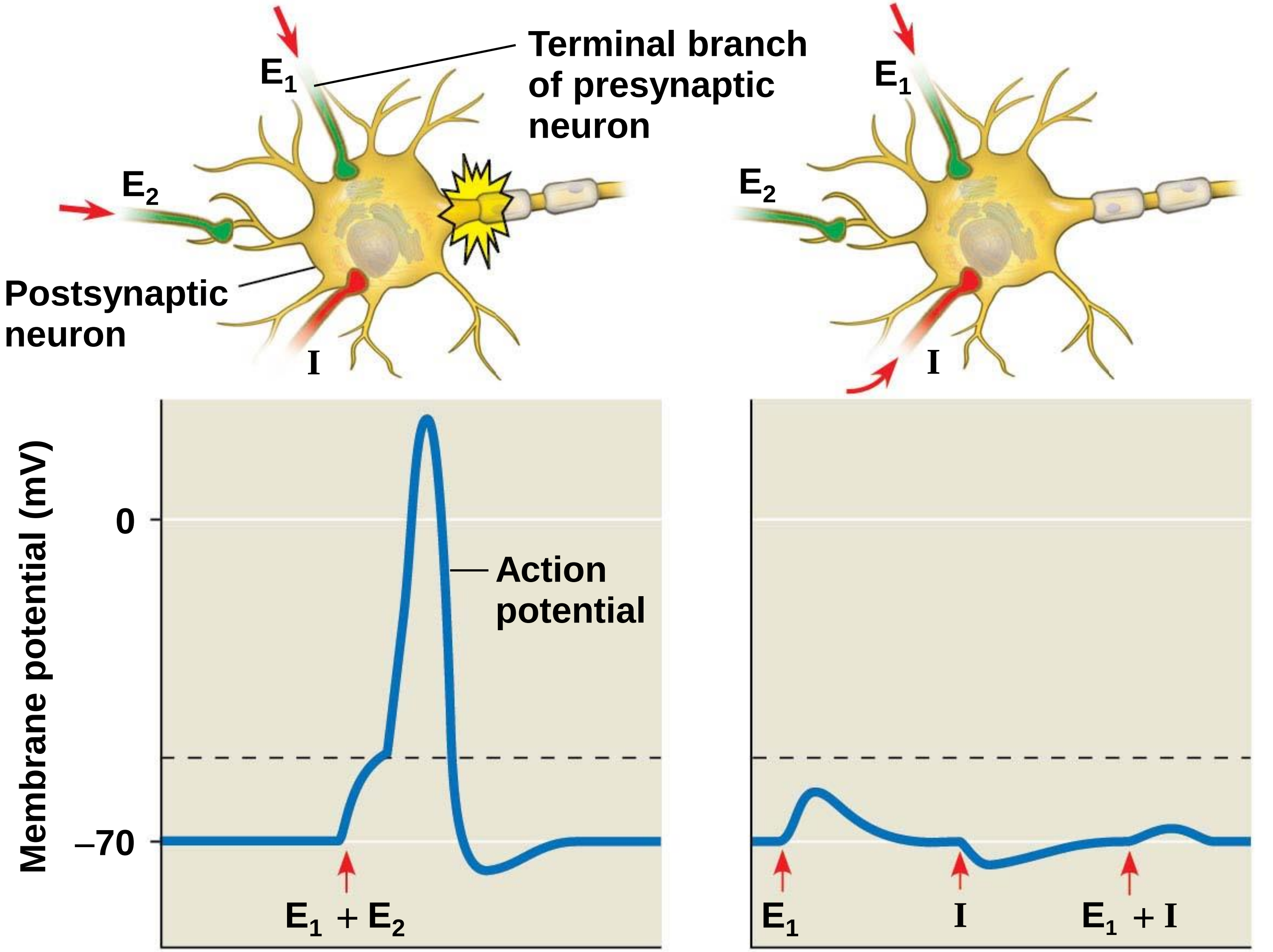
Figure 37.18-1



(a) Subthreshold, no summation

(b) Temporal summation

Figure 37.18-2



(c) Spatial summation

(d) Spatial summation of EPSP and IPSP

- Through summation, an IPSP can counter the effect of an EPSP
- The summed effect of EPSPs and IPSPs determines whether an axon hillock will reach threshold and generate an action potential

Modulated Signaling at Synapses

- In some synapses, a neurotransmitter binds to a receptor that is metabotropic
- In this case, movement of ions through a channel depends on one or more metabolic steps

- Binding of a neurotransmitter to a metabotropic receptor activates a signal transduction pathway in the postsynaptic cell involving a second messenger
- Compared to ligand-gated channels, the effects of second-messenger systems have a slower onset but last longer

Neurotransmitters

- Signaling at a synapse brings about a response that depends on both the neurotransmitter from the presynaptic cell and the receptor on the postsynaptic cell
- A single neurotransmitter may have more than a dozen different receptors
- **Acetylcholine** is a common neurotransmitter in both invertebrates and vertebrates

Acetylcholine

- Acetylcholine is vital for functions involving muscle stimulation, memory formation, and learning
- Vertebrates have two major classes of acetylcholine receptor, one that is ligand gated and one that is metabotropic

- The best understood function of the ligand-gated ion channel is in the vertebrate neuromuscular junction
- When acetylcholine released by motor neurons binds to this receptor, the ion channel opens and an EPSP is generated
- This receptor is also found elsewhere in the PNS and in the CNS

- A number of toxins disrupt neurotransmission by acetylcholine
- These include the nerve gas sarin and a bacterial toxin that causes botulism
- Acetylcholine is one of more than 100 known neurotransmitters

Table 37.2

Table 37.2 Major Neurotransmitters

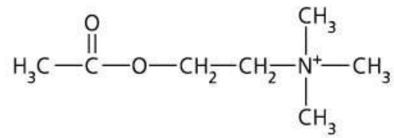
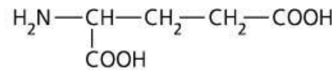
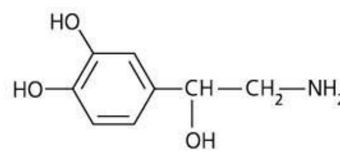
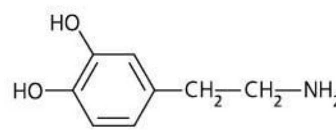
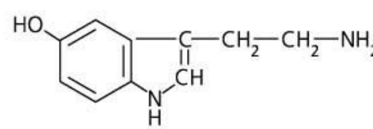
Neurotransmitter	Structure
Acetylcholine	
Amino Acids	
Glutamate	
Glycine	$H_2N—CH_2—COOH$
GABA (gamma-aminobutyric acid)	$H_2N—CH_2—CH_2—CH_2—COOH$
Biogenic Amines	
Norepinephrine	
Dopamine	
Serotonin	
Neuropeptides (a very diverse group, only two of which are shown)	
Substance P	Arg—Pro—Lys—Pro—Gln—Gln—Phe—Phe—Gly—Leu—Met
Met-enkephalin (an endorphin)	Tyr—Gly—Gly—Phe—Met
Gases	
Nitric oxide	N=O

Table 37.2 Major Neurotransmitters

Neurotransmitter	Structure
Acetylcholine	$H_3C-C(=O)-O-CH_2-CH_2-N^{+}(CH_3)_3$
Amino Acids	
Glutamate	$H_2N-CH(COOH)-CH_2-CH_2-COOH$
Glycine	H_2N-CH_2-COOH
GABA (gamma-aminobutyric acid)	$H_2N-CH_2-CH_2-CH_2-COOH$

Table 37.2 Major Neurotransmitters

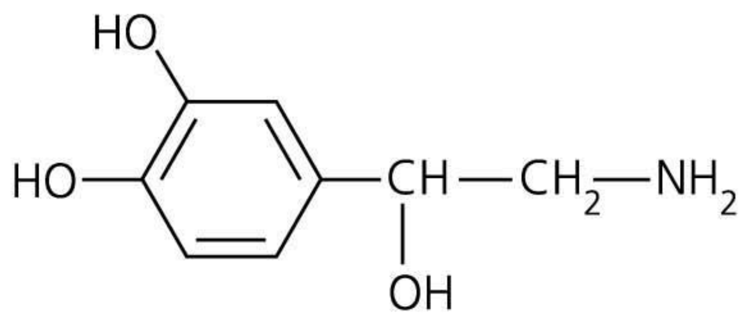
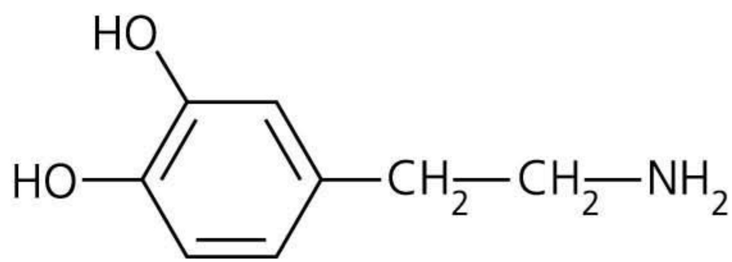
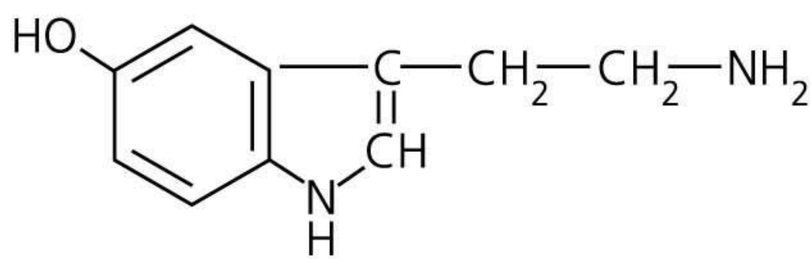
Neurotransmitter	Structure
Biogenic Amines	
Norepinephrine	
Dopamine	
Serotonin	

Table 37.2 Major Neurotransmitters

Neurotransmitter	Structure
Neuropeptides (a very diverse group, only two of which are shown)	
Substance P	
Arg—Pro—Lys—Pro—Gln—Gln—Phe—Phe—Gly—Leu—Met	
Met-enkephalin (an endorphin)	
Tyr—Gly—Gly—Phe—Met	
Gases	
Nitric oxide	N=O

Amino Acids

- Glutamate (rather than acetylcholine) is used at the neuromuscular junction in invertebrates
- Glycine also acts at inhibitory synapses in the CNS that lies outside of the brain
- Gamma-aminobutyric acid (GABA) is the neurotransmitter at most inhibitory synapses in the brain

Biogenic Amines

- Biogenic amines include
  - Norepinephrine and the chemically similar ephinephrine
  - Dopamine
  - Serotonin
- They are active in the CNS and PNS
- Biogenic amines have a central role in a number of nervous system disorders and treatments

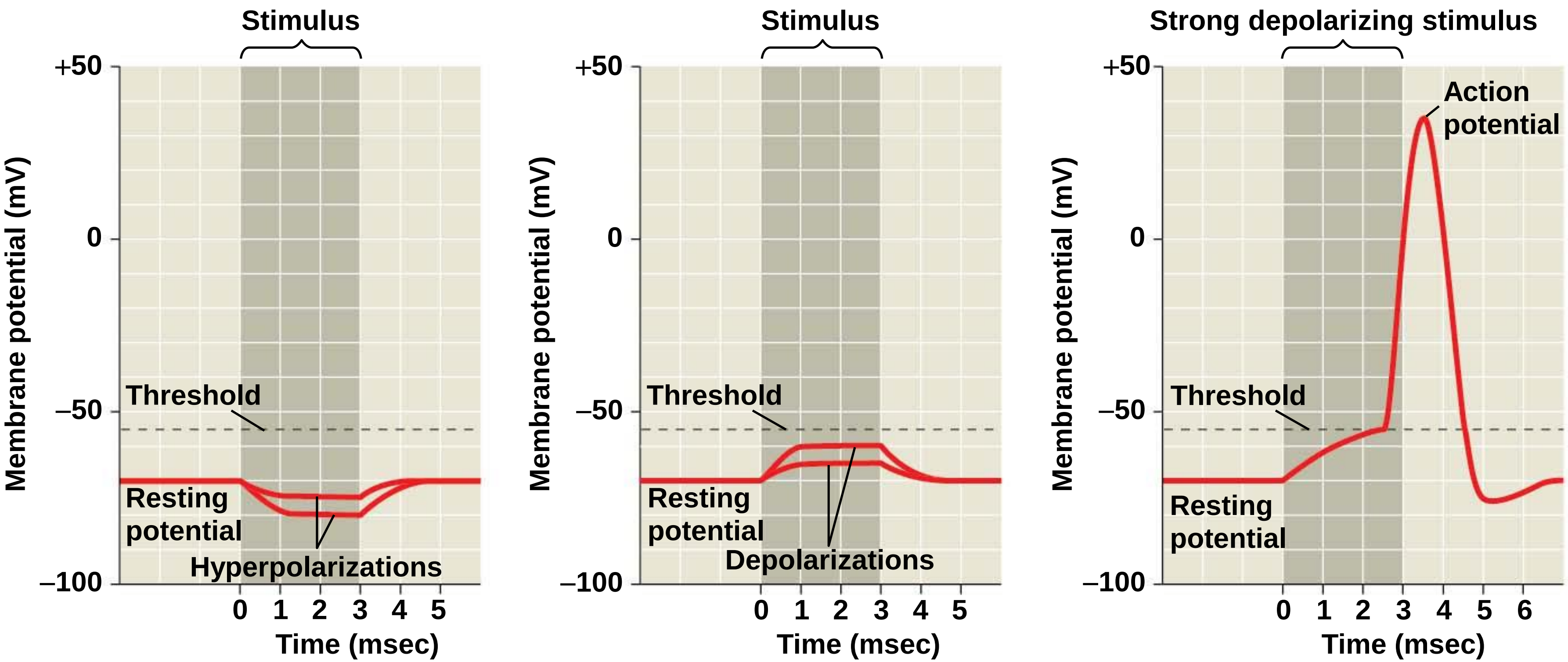
Neuropeptides

- Several **neuropeptides**, relatively short chains of amino acids, also function as neurotransmitters
- Neuropeptides include substance P and **endorphins**, which both affect our perception of pain
- Opiates bind to the same receptors as endorphins and produce the same physiological effects

Gases

- Gases such as nitric oxide (NO) and carbon monoxide (CO) are local regulators in the PNS
- Unlike most neurotransmitters, these are not stored in vesicles but are instead synthesized as needed

Figure 37.11

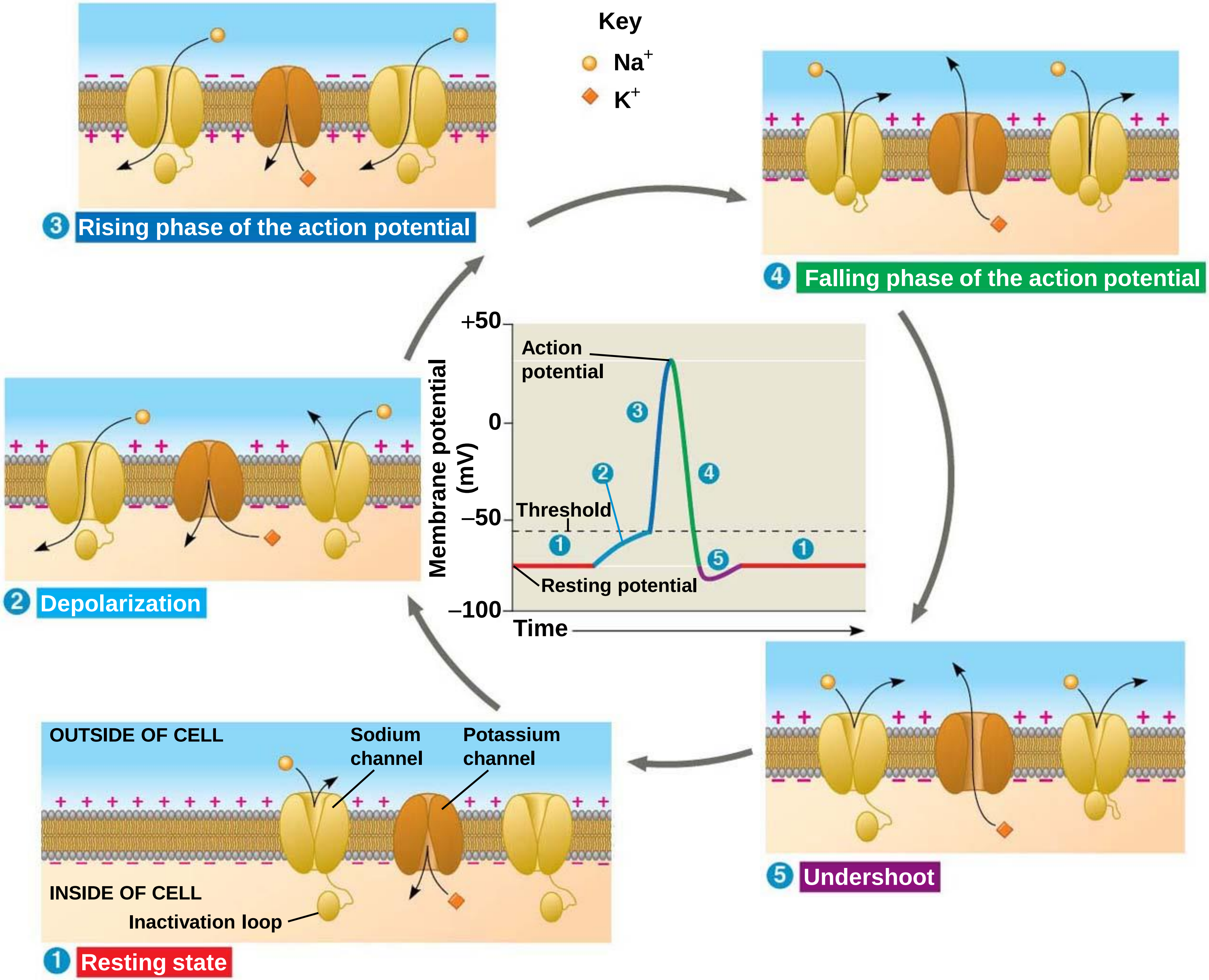


(a) Graded hyperpolarizations produced by two stimuli that increase membrane permeability to K^+

(b) Graded depolarizations produced by two stimuli that increase membrane permeability to Na^+

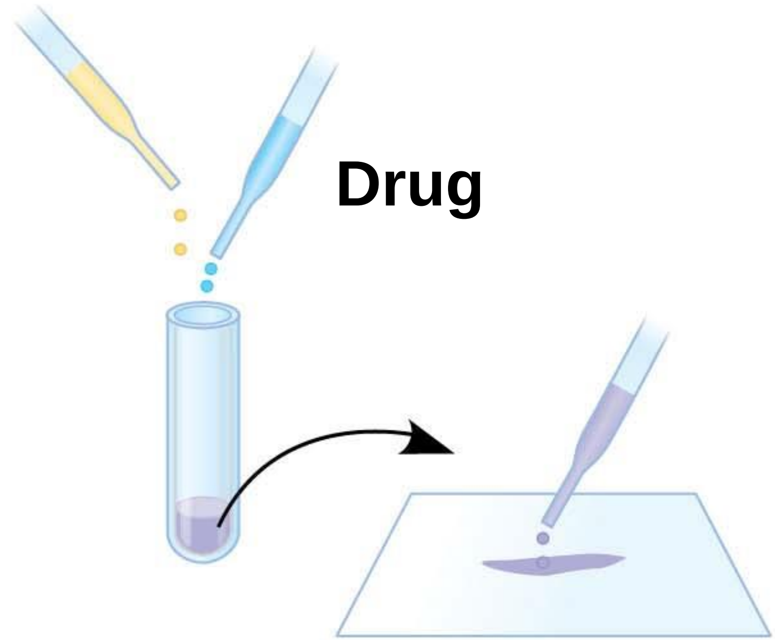
(c) Action potential triggered by a depolarization that reaches the threshold

Figure 37.12



Key
Na+
K+
3 Rising phase of the action potential
4 Falling phase of the action potential
2 Depolarization
+50
0
–50
–100
Membrane potential (mV)
Action potential
Threshold
Resting potential
Time
OUTSIDE OF CELL
Sodium channel
Potassium channel
INSIDE OF CELL
Inactivation loop
1 Resting state
5 Undershoot

Figure 37.UN01-1



1 Radioactive naloxone and a test drug are incubated with a protein mixture.

2 Proteins are trapped on a filter. Bound naloxone is detected by measuring radioactivity.

Figure 37.UN01-2

Drug	Opiate	Lowest Concentration That Blocked Naloxone Binding
Morphine	Yes	6×10^{-9} *M*
Methadone	Yes	2×10^{-8} *M*
Levorphanol	Yes	2×10^{-9} *M*
Phenobarbital	No	No effect at 10^{-4} *M*
Atropine	No	No effect at 10^{-4} *M*
Serotonin	No	No effect at 10^{-4} *M*

Data from C. B. Pert and S. H. Snyder, Opiate receptor: Demonstration in nervous tissue, *Science* 179:1011–1014 (1973).

Figure 37.UN02

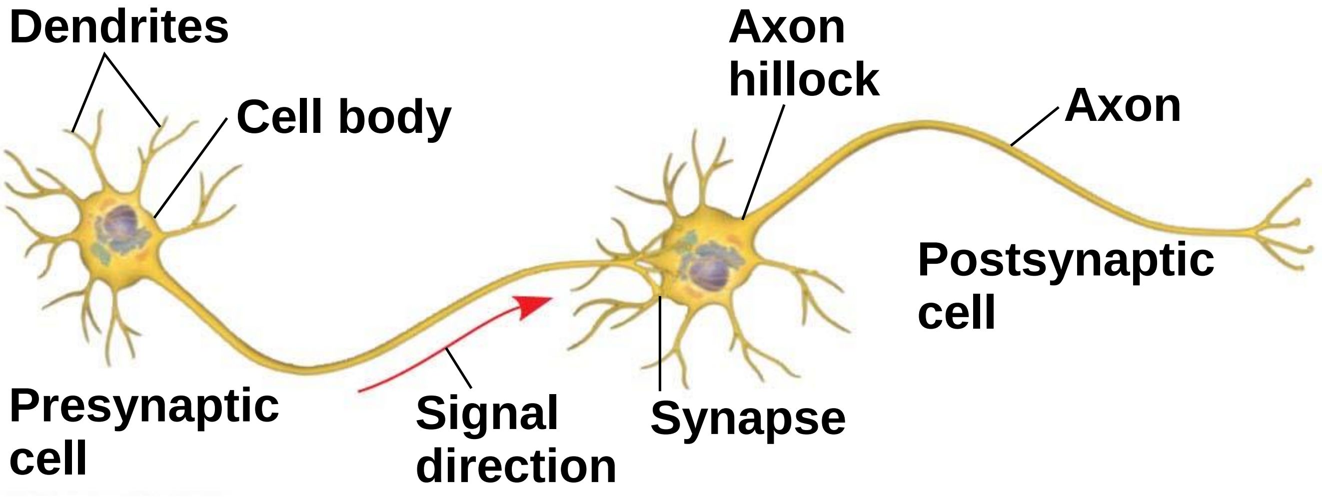


Figure 37.UN03