Chapter 2. The Cellular and Molecular Basis of Cognition

Cognitive Neuroscience: The Biology of the Mind, 3rd Ed.,
M. S. Gazzaniga, R. B. Ivry, and G. R. Mangun, Norton, 2008.

Summarized by
B.-W. Ku, E. S. Lee, and B.-T. Zhang
Biointelligence Laboratory, Seoul National University
http://bi.snu.ac.kr/

Introduction (motivating questions)

- Schizophrenia – The problem of chemical transmitter systems in brain
- "How do neurons communicate?"
- "What are the chemical signals that mediate that communication?"
- "How do drugs modify these interactions?"

Contents

- Cells of the Nervous System
- Neuronal Signaling
- Synaptic Transmission

Cells of the Nervous System

Cells of the Nervous System

- Two main classes of cells in the nervous system
  - Neurons
  - Glial cells

The Structure of Neurons (1/4)

- The structure of a neuron (Fig. 2.2).

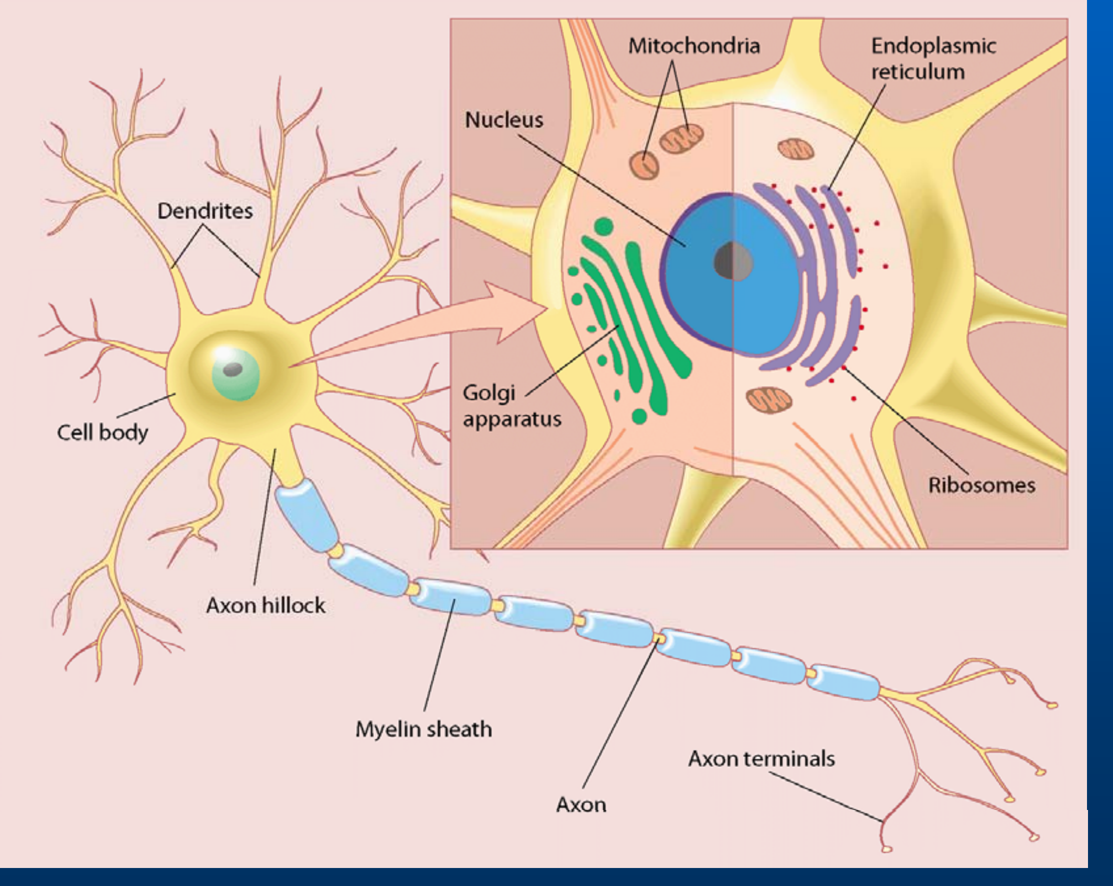


Fig. 2.2: Idealized mammalian neuron

The Structure of Neurons (2/4)

- The dendritic spines

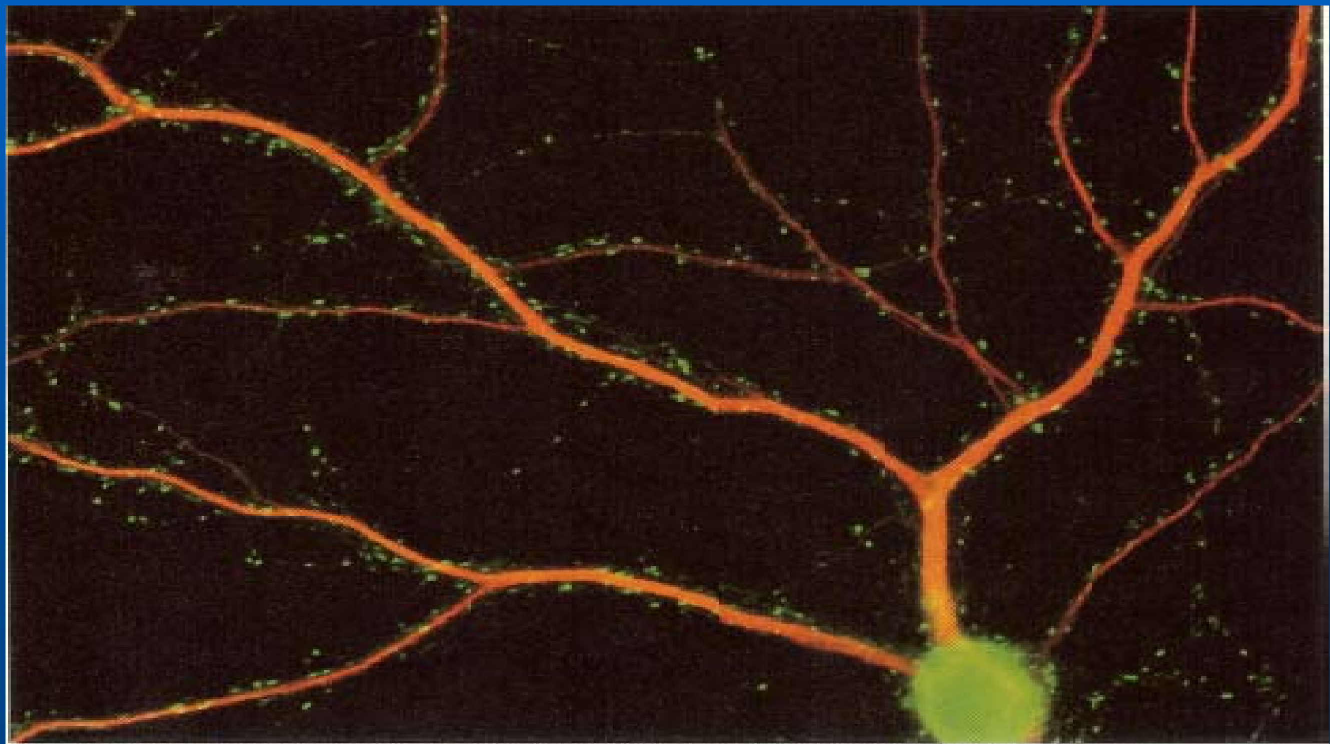


Fig. 2.5: Cultured rat hippocampal neuron double labeled using immunofluorescent methods. Presynaptic terminals (green dots) making contact with spines located on the dendrite

The Structure of Neurons (3/4)

- Neuron: take in information, make a '*decision*' by a rule, and pass it to other neurons
- Cell body (soma): *the metabolic center* of a neuron
- Dendrites and axon: extended processes to take in and pass information
  - Dendrites: the short processes emanating from the cell body, receiving information from other neurons
  - Axon: the long, narrow process that leaves the cell body, sending signals to other neurons
- Synapses: a location where neurons' axon and dendrites meets
  - Postsynaptic neuron: the neuron after the synaptic cleft
  - Presynaptic neuron: the neuron before the synaptic cleft
  - Most neurons are both presynaptic and postsynaptic
- Neurotransmitters: chemicals released by axon terminals

The Structure of Neurons (3/4)

- Unipolar
  - only 1 process. 1 dendrite or 1 axon
- Bipolar
  - 2 processes. 1 axon and 1 dendrite
- Multipolar
  - 1 axon, but many dendrites
- Pseudounipolar
  - Appears unipolar, though originally bipolar

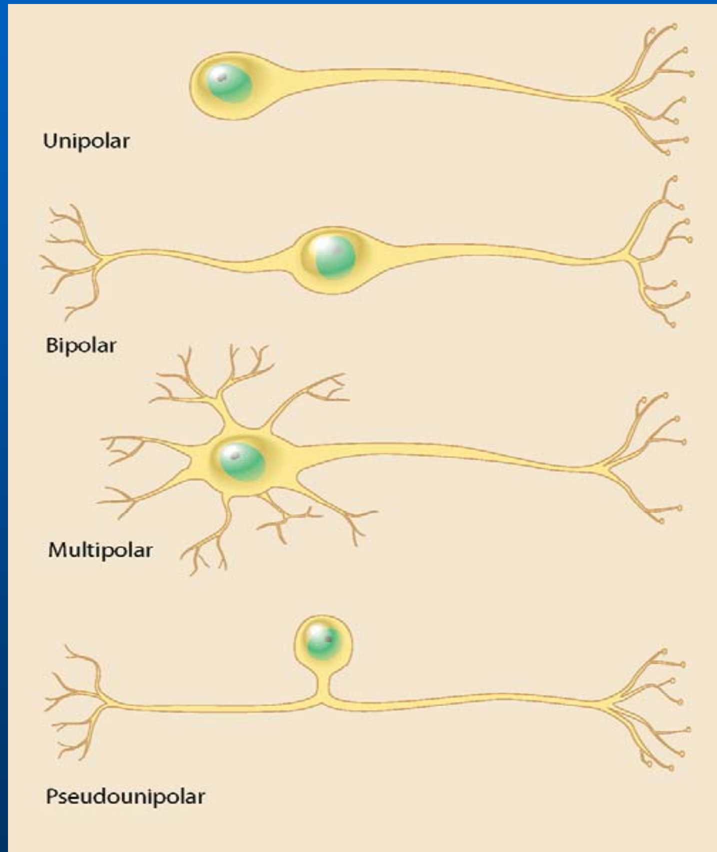


Fig. 2.6: Various forms that mammalian neurons may take.

Major Types of Neurons and Their Functions

- Sensory neurons
  - Sensitive to stimulation, such as light, sound waves, touch, or chemicals.
- Interneurons
  - Receives information from other neurons and sends it to either motor neurons or more interneurons.
- Motor neurons
  - Receives excitation from other neurons and conducts impulses from its soma in the C.N.S. to muscles.

Glial Cells

- Glial cells
  - Do not conduct signals,
  - But without them, the functionality of neurons would be severely diminished.
- In the central nervous system (CNS)
  - Astrocytes
  - Oligodndrocytes
  - Microglia
- In the peripheral nervous system (PNS)
  - Schwann cells

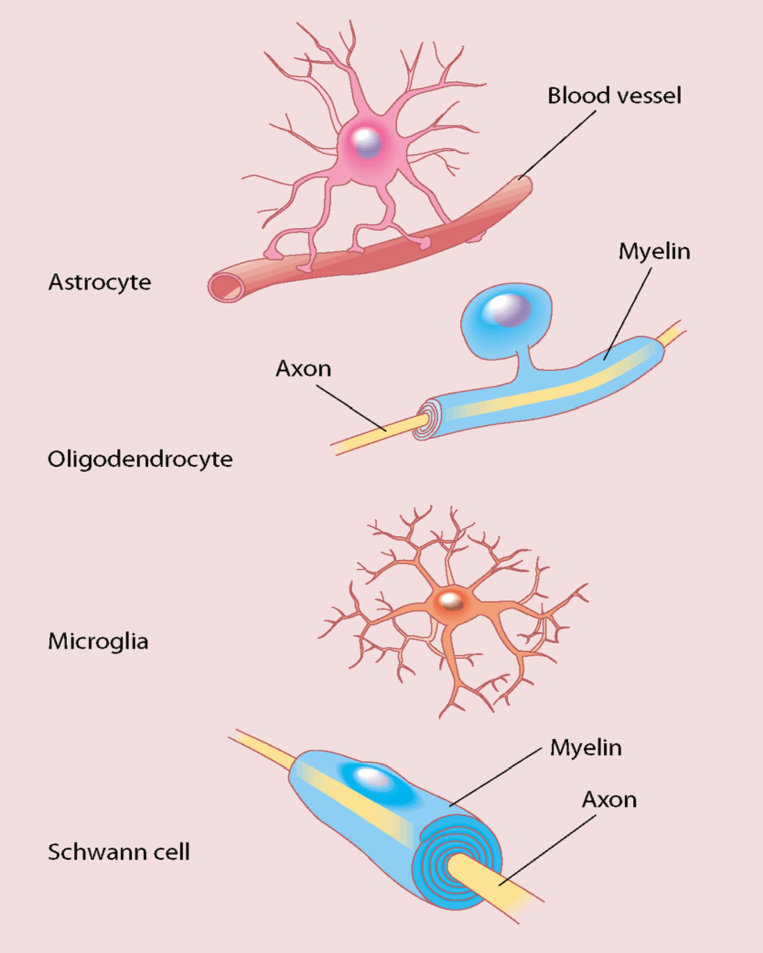


Fig. 2.7: Various types of glial cells

The Role of Glial Cells (1/2)

- Astrocyte
  - Make contact with blood vessels
  - Transport ions across the vascular wall
  - Blood-Brain Barrier: protective layer for certain substances (e.g. no dopamine, no norepinephrine, but permit L-dopa)
- Microglia
  - Invade into damaged regions
  - Devours damaged cells

The Role of Glial Cells (2/2)

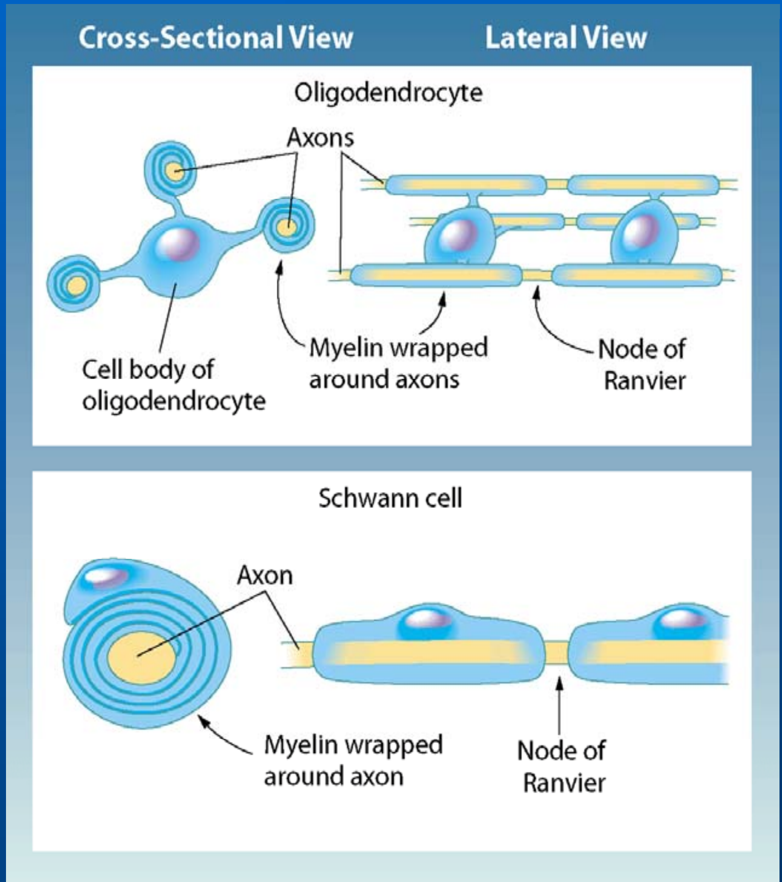


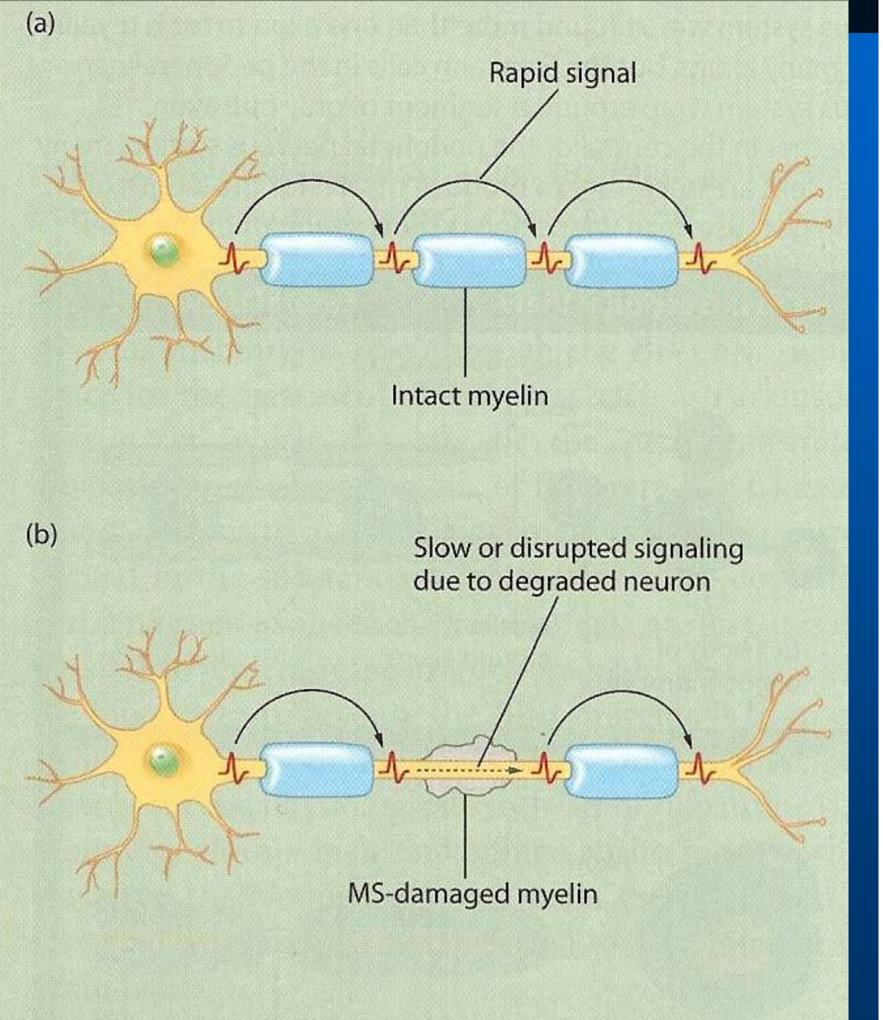
Fig. 2.8: Oligodendrocytes and Schwann cells produce myelin around axons.

Table 2.1 Major Differences Between the Two Types of Myelin-Producing Cells

Cell Type	Location	Number of Axons Myelinated by One Cell
Schwann cell	Peripheral nervous system	One
Oligodendrocyte	Central nervous system	Many

Myelin and Disease

- *Multiple sclerosis*
  - Damage to myelin sheaths.
  - Slowing or complete disruption of action potential propagation.



(a) Healthy neuron. **(b)** Neuron of a person with multiple sclerosis.

Neuronal Signaling

Properties of the neuronal membrane and membrane potential

- Neuronal membrane: bilayer of lipid molecules
- Water-dissolved thing does not dissolve in the membrane's lipids.

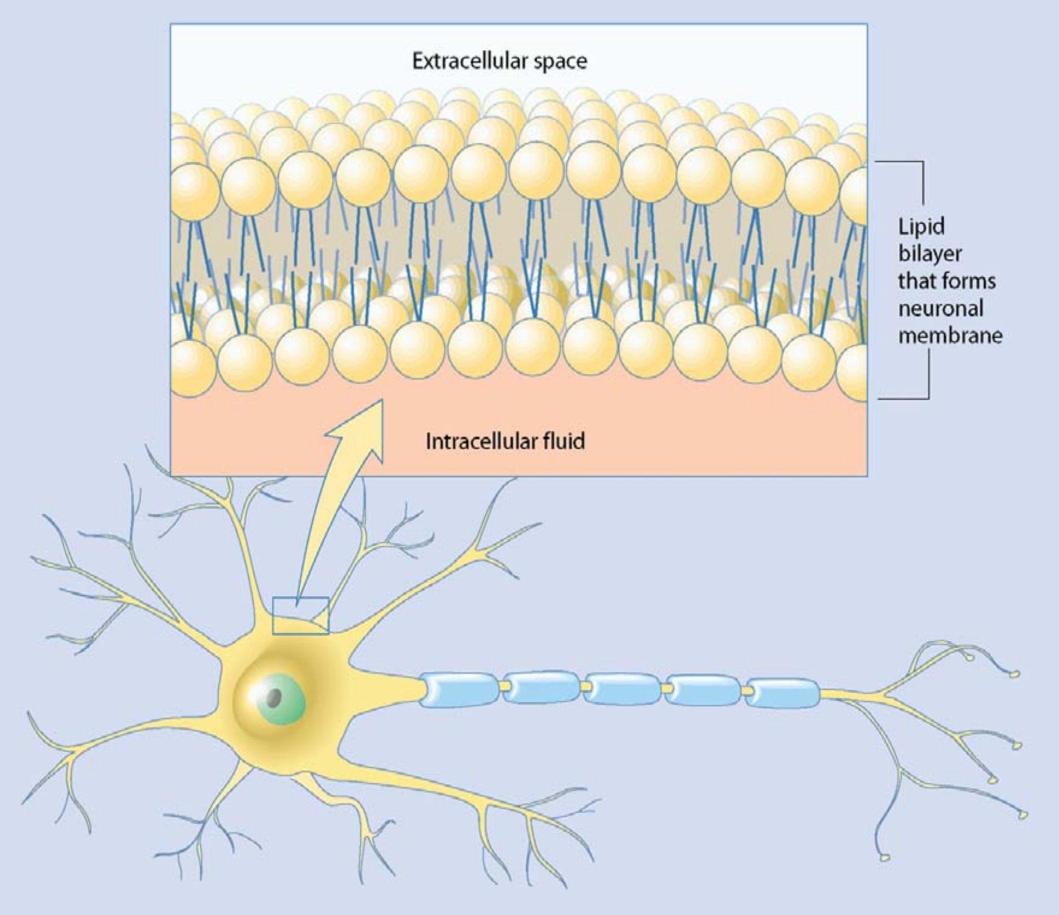


Fig. 2.9: Neuron and the lipid bilayer seperating intra & extra cellular space

The basis of the resting membrane potential (1/2)

- Resting potential
  - Electrical potential difference in a resting neuron

  ($V_{in} – V_{out}$ = -65~-70 mV)

- Relatively negative electrical potential in the inside of the membrane.

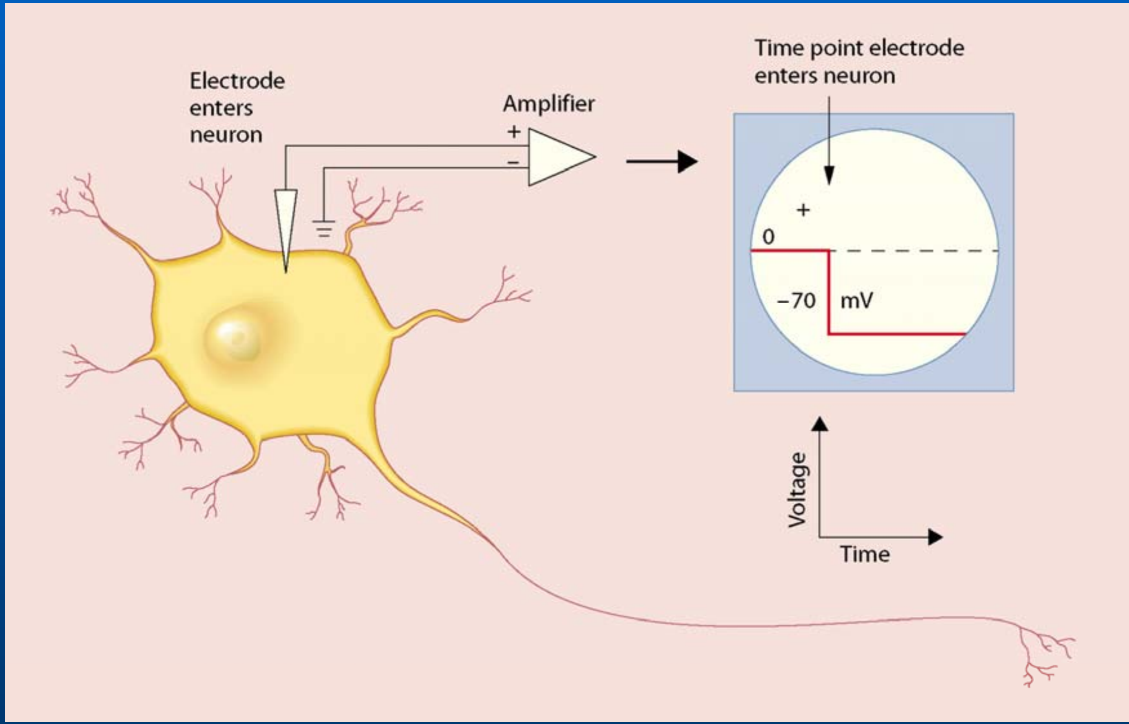


Fig. 2.10: Intracellular recordings are used to measure the resting membrane potential.

The basis of the resting membrane potential (2/2)

- Ion channels (or gates)
  - Sodium (Na^+), potassium (K^+) and chloride (Cl^-) channels
  - Electrochemical force onto ions
  - Selective permeability
- Na^+/K^+ pump
  - Move ions across the membrane.
  - Maintain the concentration gradients of Na^+ and K^+ .
  - ATP (adenosine triphosphate) provides fuel.
- Net current = 0

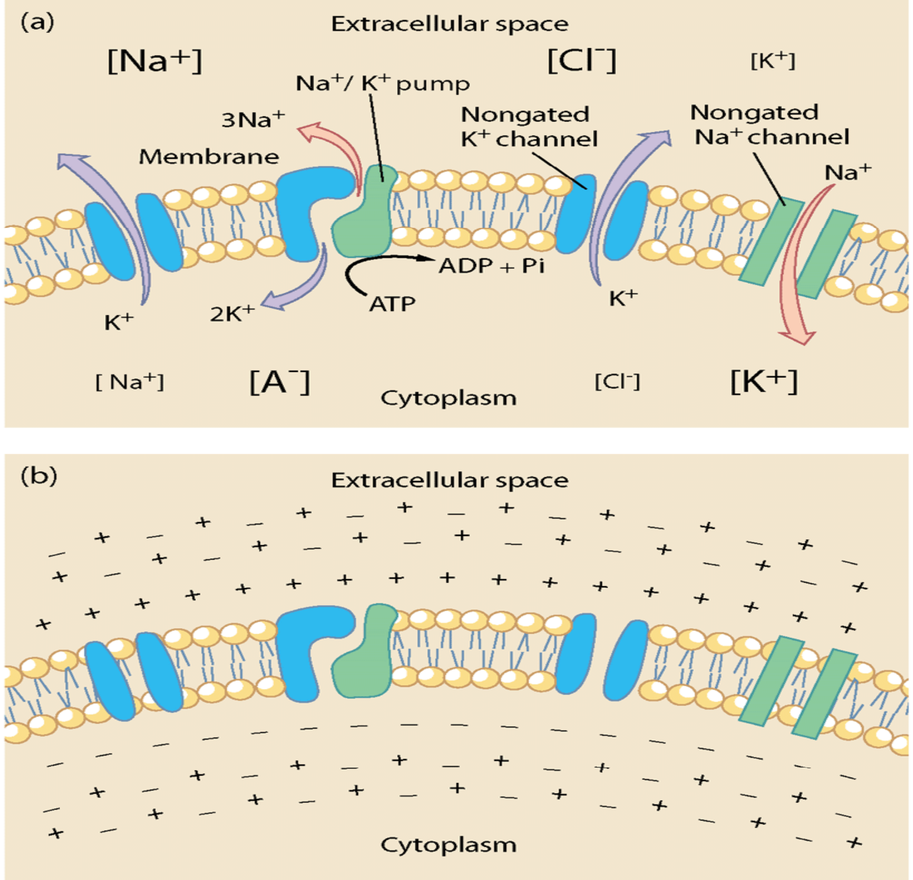


Fig. 2.11: (a) Active transporters (Na+/K+ ATPase pump) and non-gated ion channels (b) The electrical potential across the membrane

Electrical Conduction in Neurons (1/2)

- Events occurred immediately after action potentials reach the presynaptic axon terminal
  ① Releases neurotransmitter
  ② Changes in ionic currents in membrane of postsynaptic ne uron (sodium ions rush into the inside of the membrane)
  ③ Changes in membrane potential
  ④ Increased membrane potential (in the action potential triggering zone) triggers action potential
  ⑤ Action potential travels down the axon to its terminal

Electrical Conduction in Neurons (2/2)

- Injection of electrical current changes the membrane potential
  ① Electrodes pass current into the neuron.
  ② Current effect on the membrane potential can be measured.
  ③ Depolarizing current is injected by making electrode inside the neuron more positive.
  ④ This depolarizes the membrane

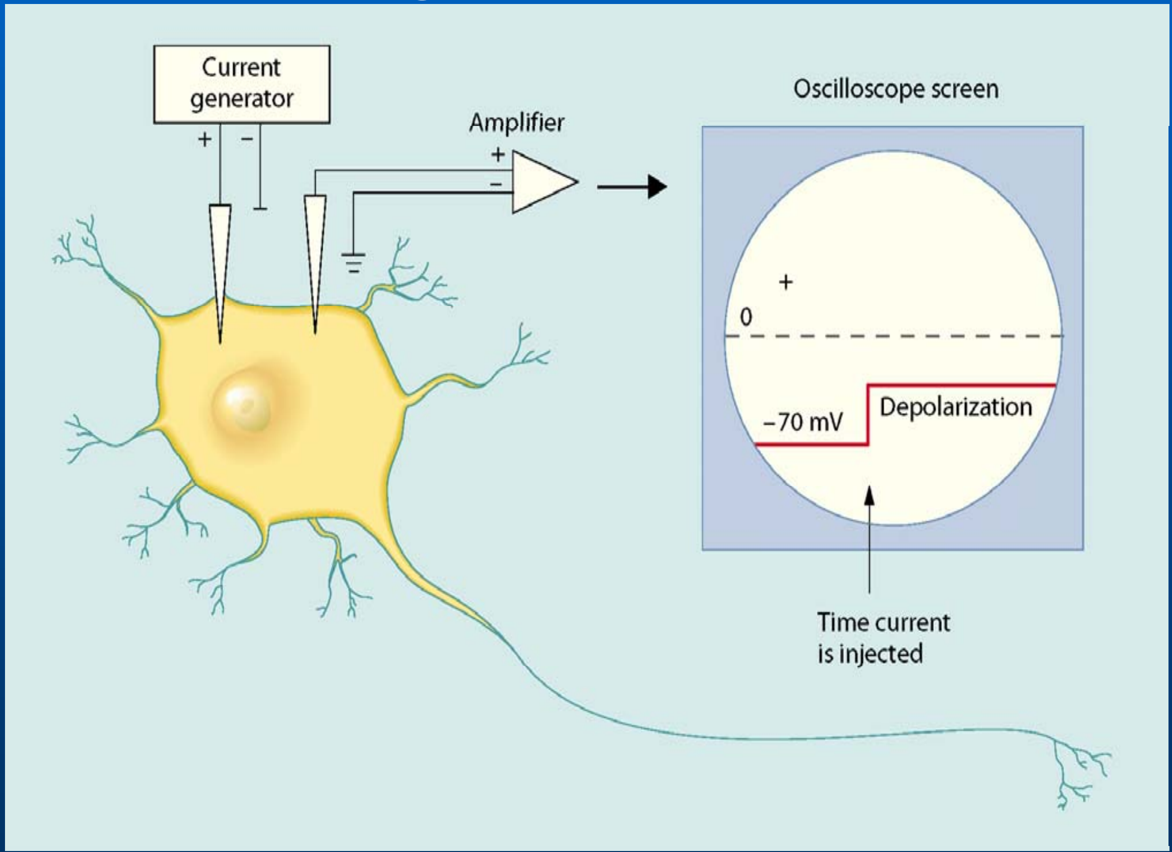


Fig. 2.13: Intracellular recording and intracellular injection of current.

Signaling between Neurons

- Overview of signaling between neurons
  - ① Synaptic inputs
  - ② Synaptic inputs make postsynaptic current.
  - ③ Passive depolarizing currents
  - ④ Action potential: depolarize the membrane, and trigger another action potential.
  - ⑤ The inward current conducted down the axon .
  - ⑥ This leads to depolarization of adjacent regions of membrane
- Action Potential: for long distance communication

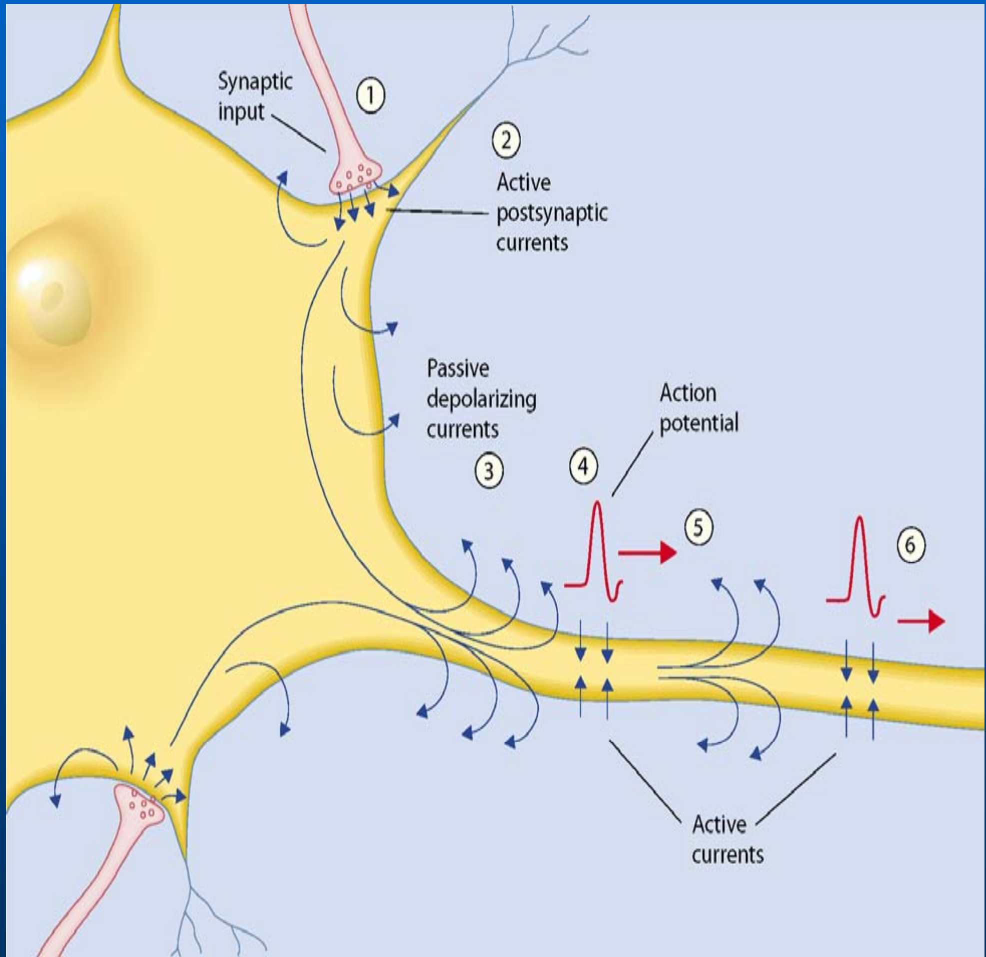


Fig. 2.14: Overview of signaling between neurons.

Graded vs. Action Potentials

Table 2.2 Major Differences Between Graded and Action Potentials

Feature	Graded Potentials	Action Potentials
Amplitude	Varies with stimulus	All or none; always same amplitude
Summation	Can be summed (compare to an analog code)	Cannot be summed (compare to a digital code)
Threshold	No	Yes
Refractory period	No	Yes, both relative and absolute
Conduction	Decremental	Nondecremental
Duration	Varies	Constant for given type of cell under constant conditions
Polarization	Can be depolarization or hyperpolarization	Can be only depolarization
Initiation	Initiated by signal transduction and neurotransmission	Initiated by a graded potential
Channels	Not voltage-gated (mostly ligand-gated)	Voltage-gated

Active Electrical Properties of Neurons (1/5)

- The membrane potential can become either more (hyperpolarized) or less (depolarized) negative with respect to the resting membrane potentials.

- Excitatory and inhibitory inputs influence the membrane potentials

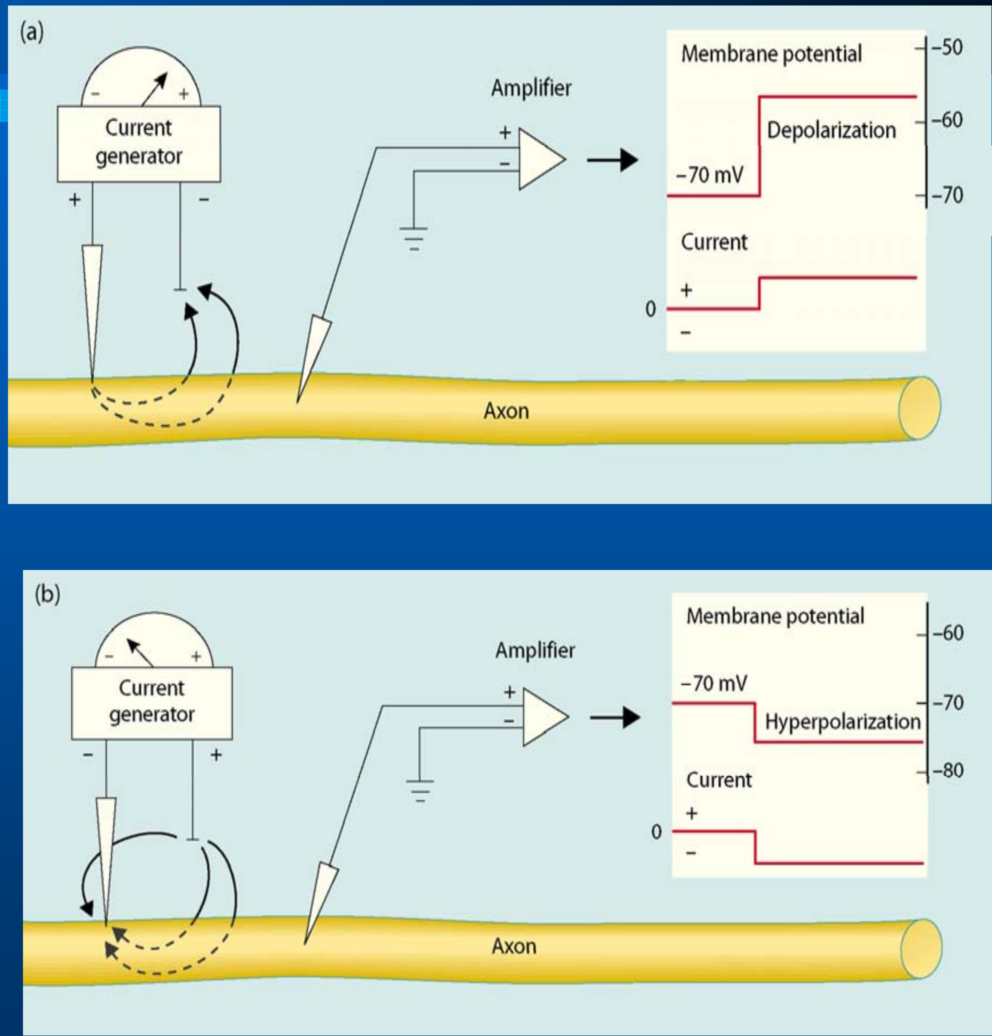


Fig. 2.18: An axon with stimulating and recording electrodes placed inside.

Active Electrical Properties of Neurons (2/5)

- Depolarizing potentials can generate action potentials.

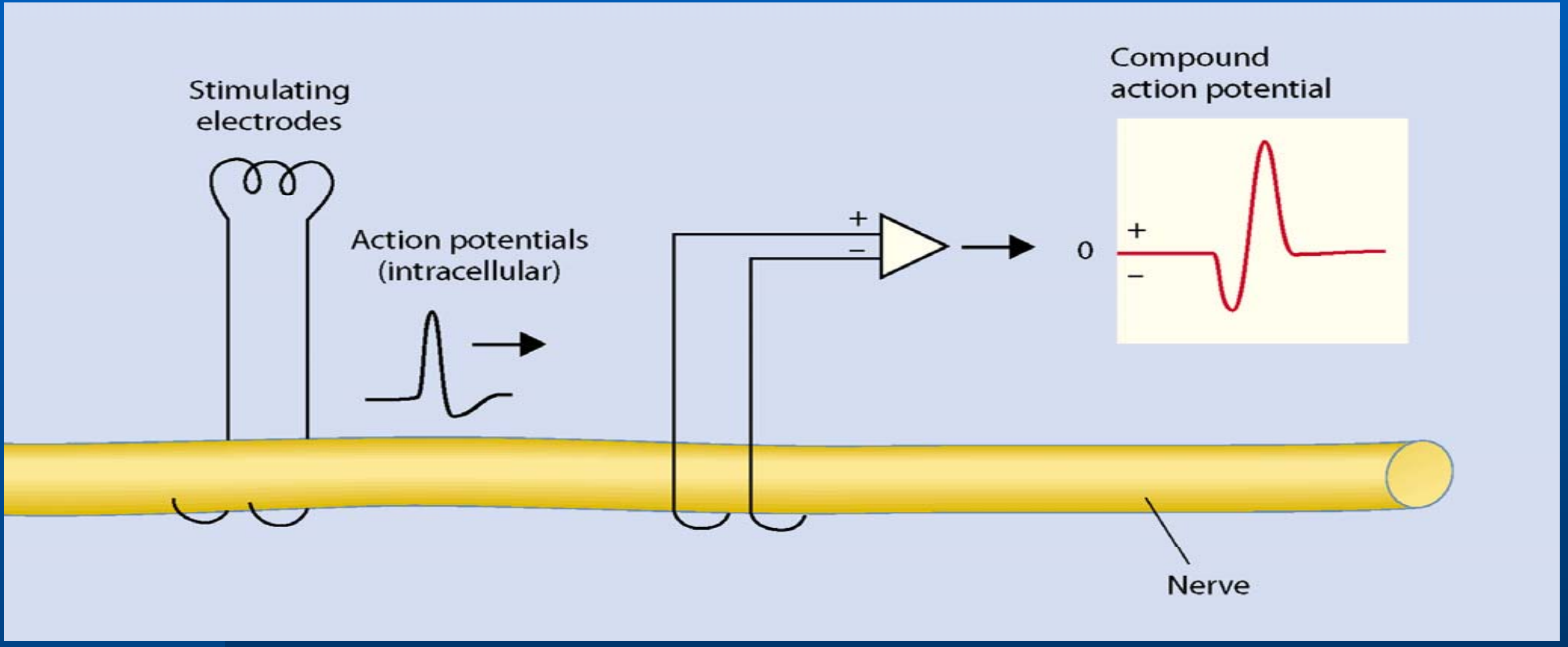


Fig. 2.19: Extracellular stimulating and recording electrodes and recorded compound action potentials.

Active Electrical Properties of Neurons (3/5)

- The action potential is a rapid depolarization of the membrane in a localized area.
  - Injection of positive current into an axon, its depolarization, then action potential.
  - Compare the membrane depolarizations 1~3 and the size of the injected current above.
  - The action potential is not related to the size of the original depolarizing current.
  - The action potential is said to be all or none.

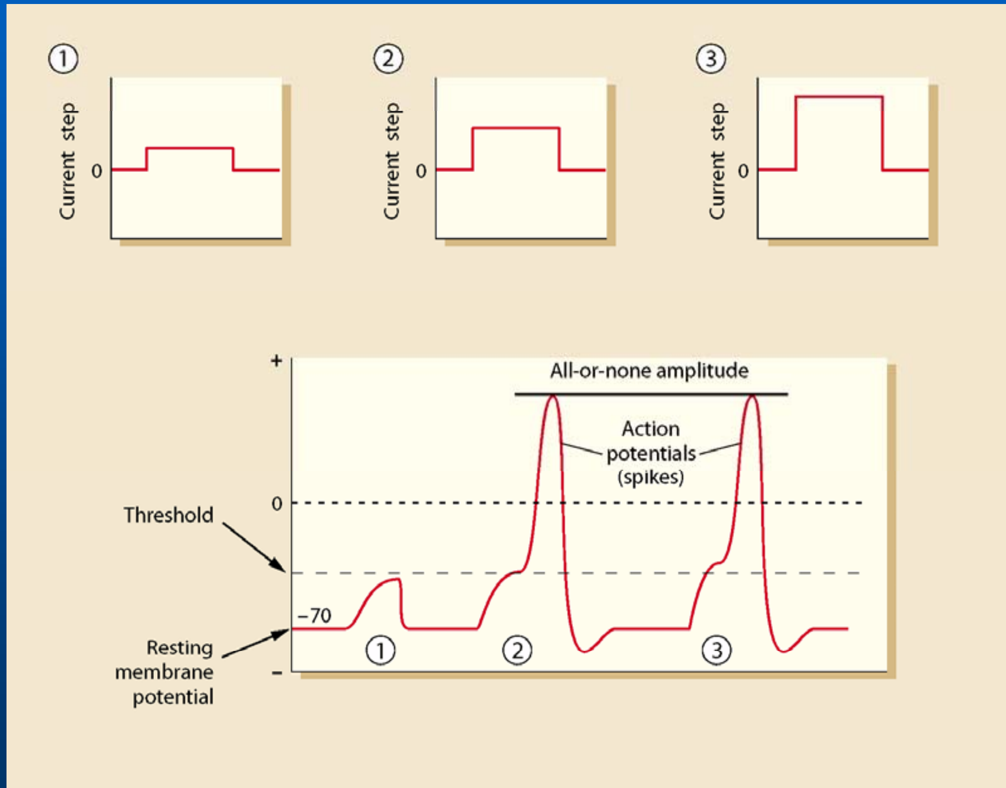


Fig. 2.20: Injection of positive current into an axon leads to depolarization, which, if large enough, triggers an action potential.

Active Electrical Properties of Neurons (4/5)

- The Hodgkin-Huxley cycle (Fig. 2.21)
  - Voltage-gated ion channels open and close according to the membrane potential.
  - Rapid and self-reinforcing cycle (positive feedback)

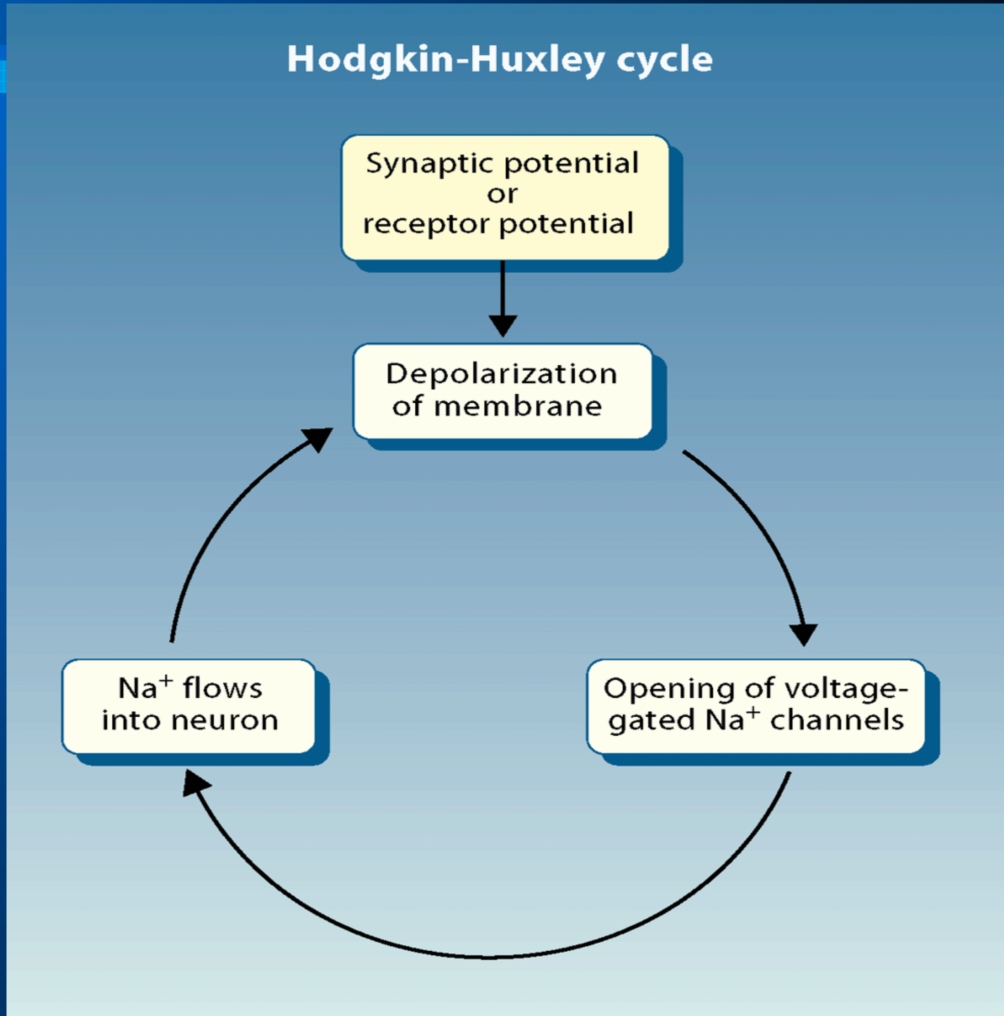


Fig. 2.21: The Hodgkin-Huxley cycle.

Active Electrical Properties of Neurons (5/5)

- Ionic movements during an action potential
- Steps:
  - Resting potential period: more sodium outside of the neuron, more potassium inside.
  - Early period of action potential: sodium ions rush into the neuron.
  - Late period of action potential: potassium ions are driven out from the neuron.
  - The neuron is hyperpolarized.
  - The resting potential is reestablished, which restores the original ion distribution

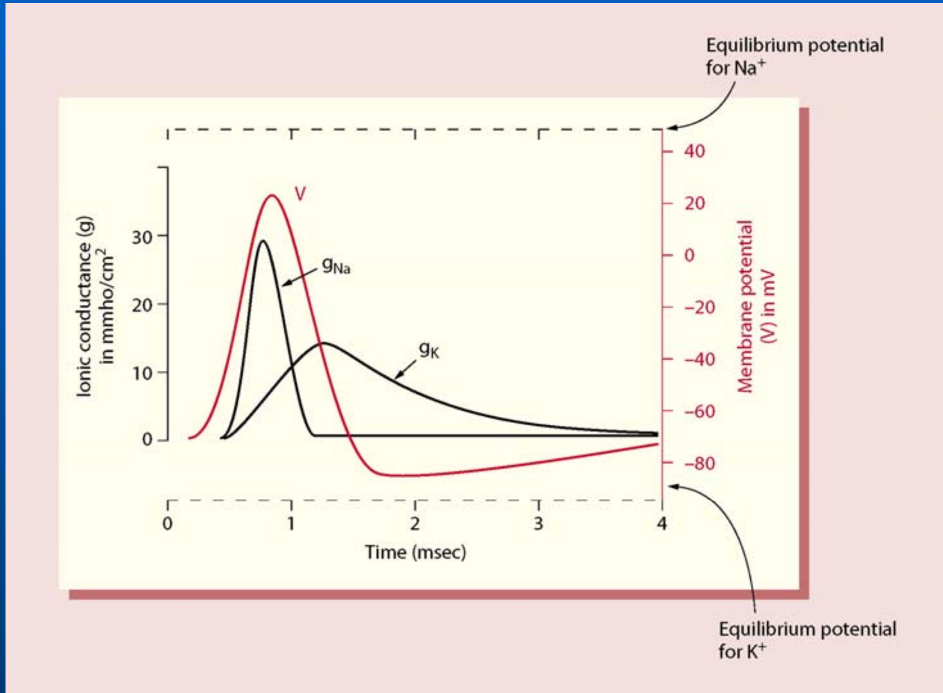


Fig. 2.22 The relative time course of changes in membrane voltage during an action potential, and the underlying causative changes in membrane conductance to Na^+ (g_{Na}) and K^+(g_K)

- Ex: Anesthetic drug such as Novocain attaches to the sodium gates of the membrane, preventing sodium ions from entering. In doing so, such drug blocks action potentials in the affected area.

Saltatory Conduction and the Role of Myelin

- Saltatory conduction: meaning "to jump," by which nerves can transmit action potential.
- Myelination holds the key: Myelin wrapping around the axons of neurons increases membrane resistance.

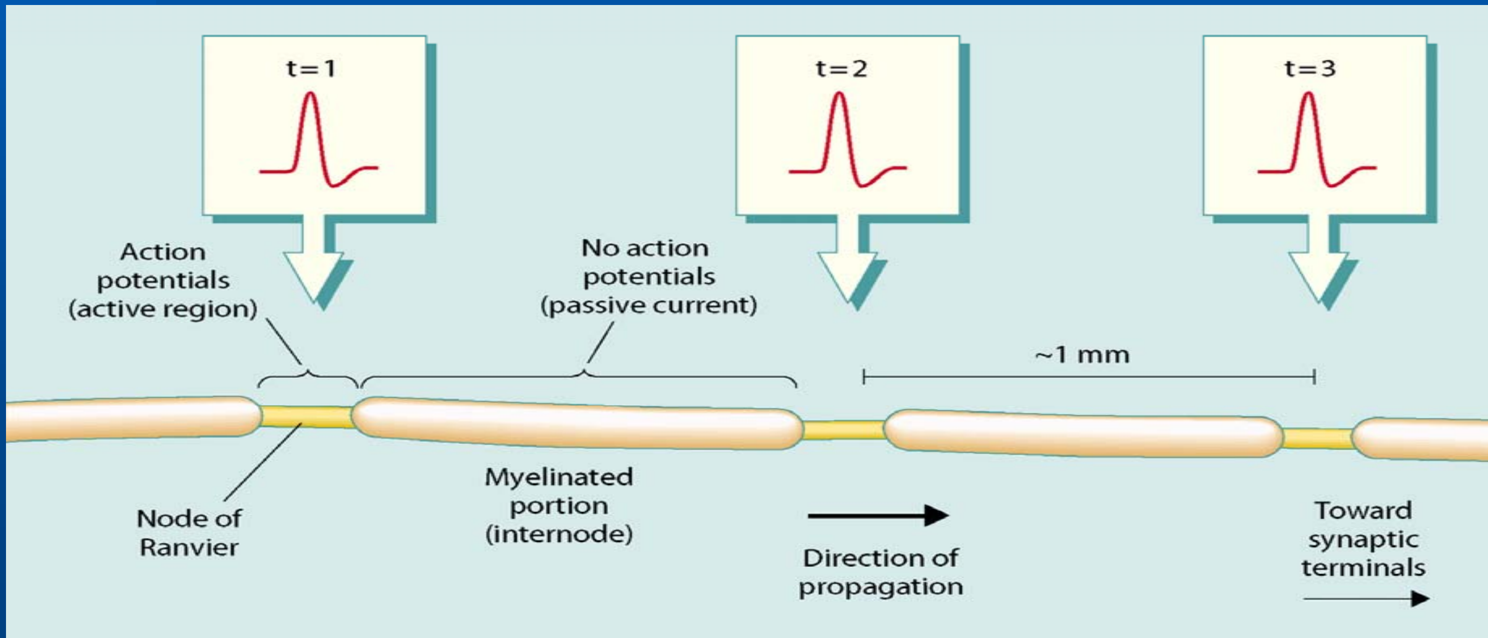


Fig. 2.24: Saltatory conduction in a myelinated nerve.

Transmembrane Proteins: Ion Channels and Pumps

- Ion channels are proteins. (Fig. 2.25, 2.26)
- The size and polarity of the pore helps certain size of ions to cross the membrane. (Fig. 2.26)

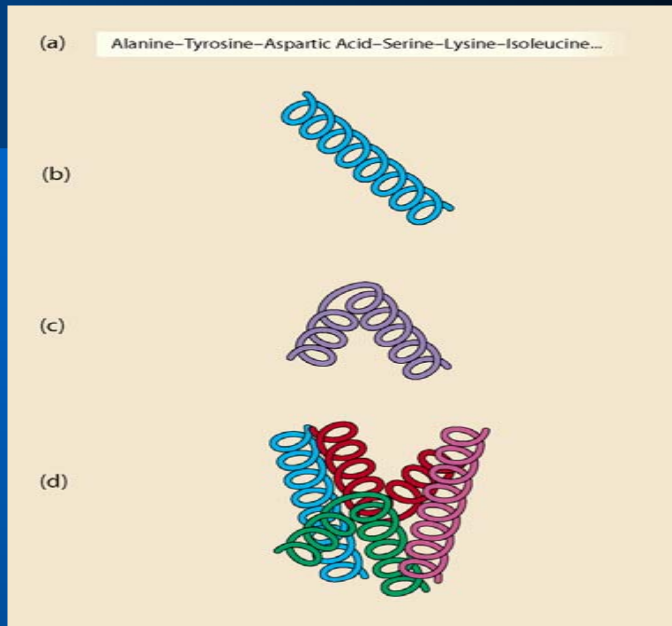


Fig. 2.25: General structure of proteins.

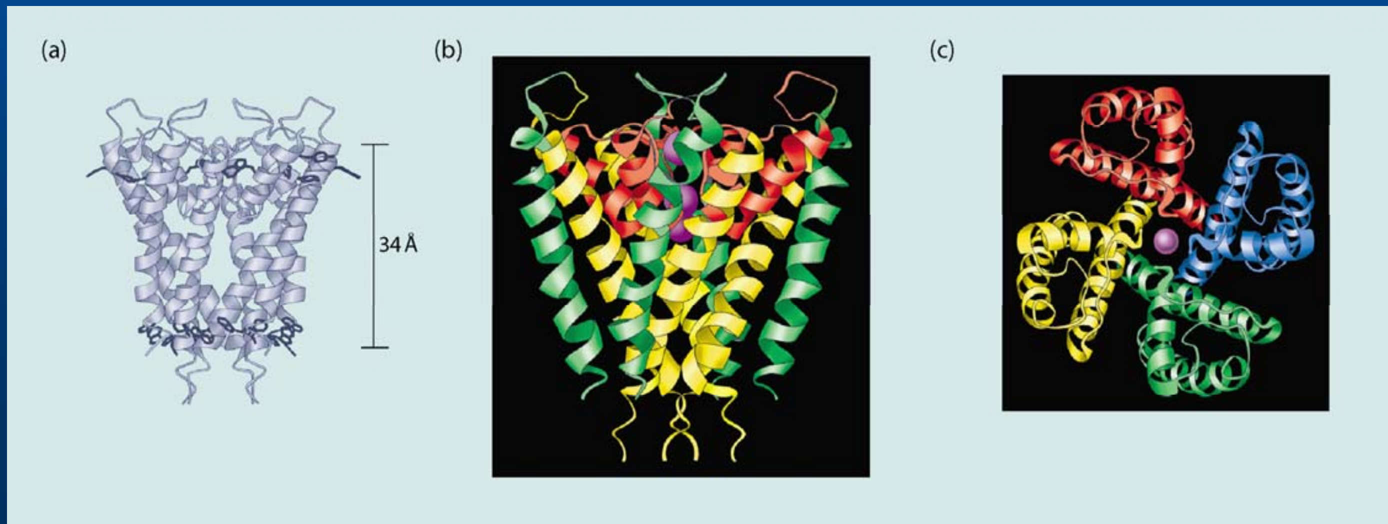


Fig. 2.26: The helical structure of the K+ ion channel.

Transmembrane Proteins: Ion Channels and Pumps (2/2)

- Characteristics of gated and non-gated ion channels (Fig. 2.28, 29)
  - The Na+ and K+ channels involved in the generation of the action potential are voltage-gated channels.
  - Voltage-gated channels exist for Na+, K+, Cl-, and Ca2+.
  - Voltage-gated Cl- channels are involved in homeostatic processes, including stabilization of the membrane potential.
  - Voltage-gated Ca2+ channels are relevant for the release of neurotransmitters from presynaptic terminals.
  - Changes in the transmembrane potential influence the size of pore (open or closed).
  - Receptors are specialized ion channels that mediate signals at synapses.

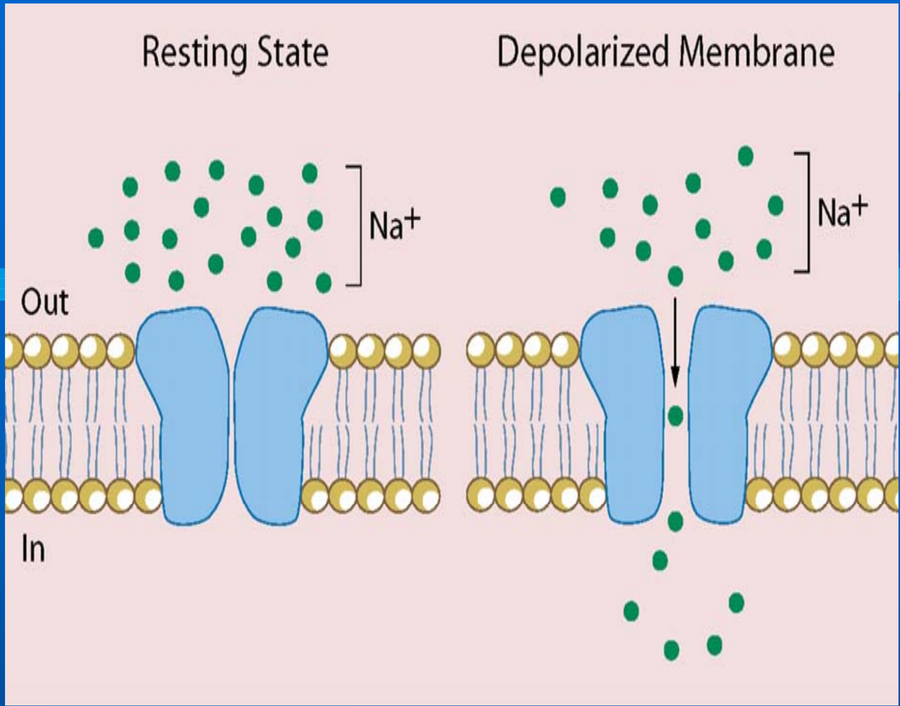


Fig. 2.28: Voltage-gated channel in the neuronal membrane.

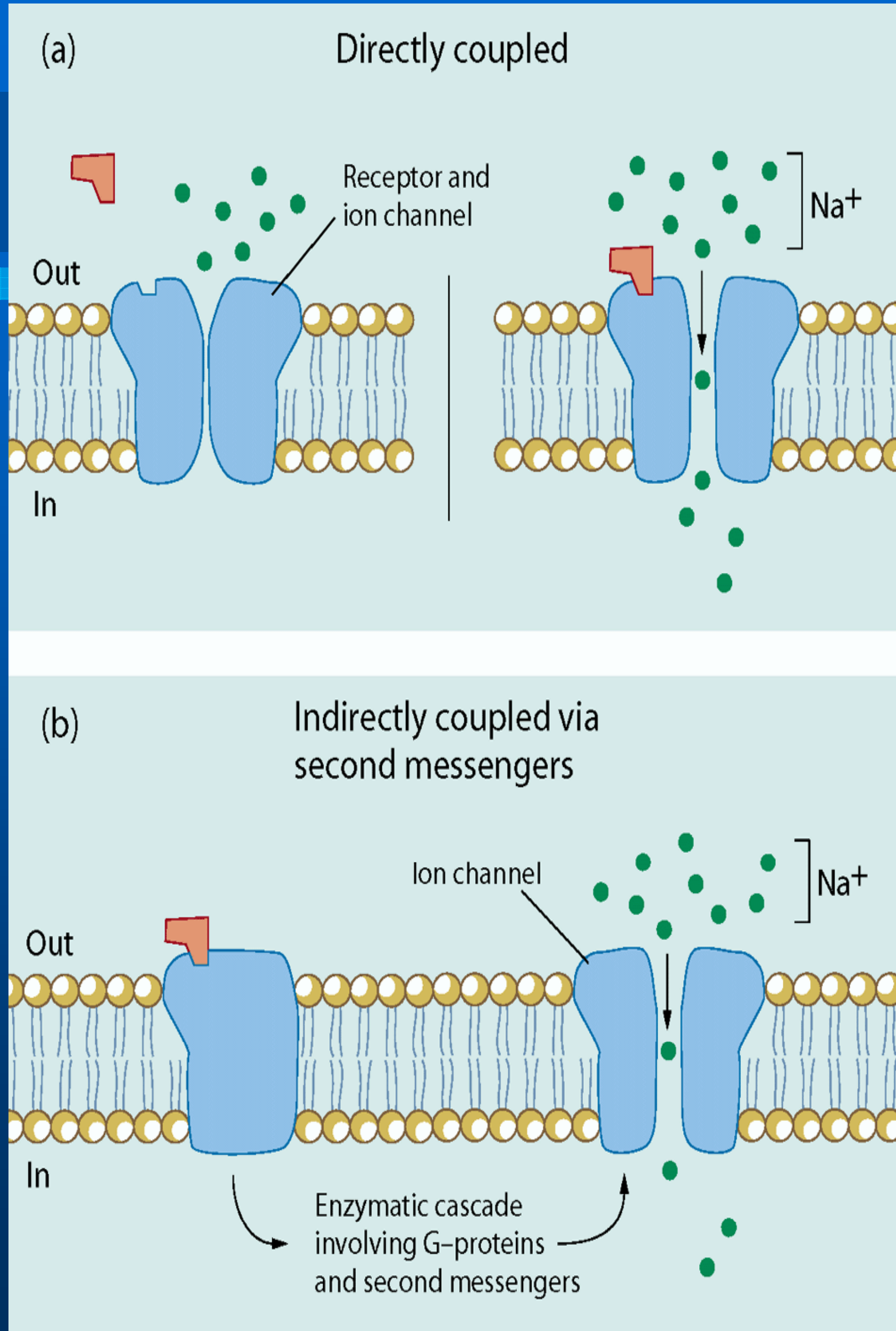


Fig. 2.29: Mechanisms of neurotransmitter receptor molecules.

Synaptic Transmission

Chemical Transmission (1/2)

- Release and diffusion of transmitters (Fig. 2.30, next slide)
  - Action potentials reach the end of axon
  - The depolarization changes the voltage across the membrane
  - The calcium gates open
  - Increased calcium (Ca2+) concentration inside the presynaptic cell membrane.
  - Axon terminal releases a certain amounts of its neurotransmitters in the next 1 or 2 milliseconds.
  - The chemicals diffuse across the synaptic cleft to the postsynaptic membrane, where it attaches to a receptor.

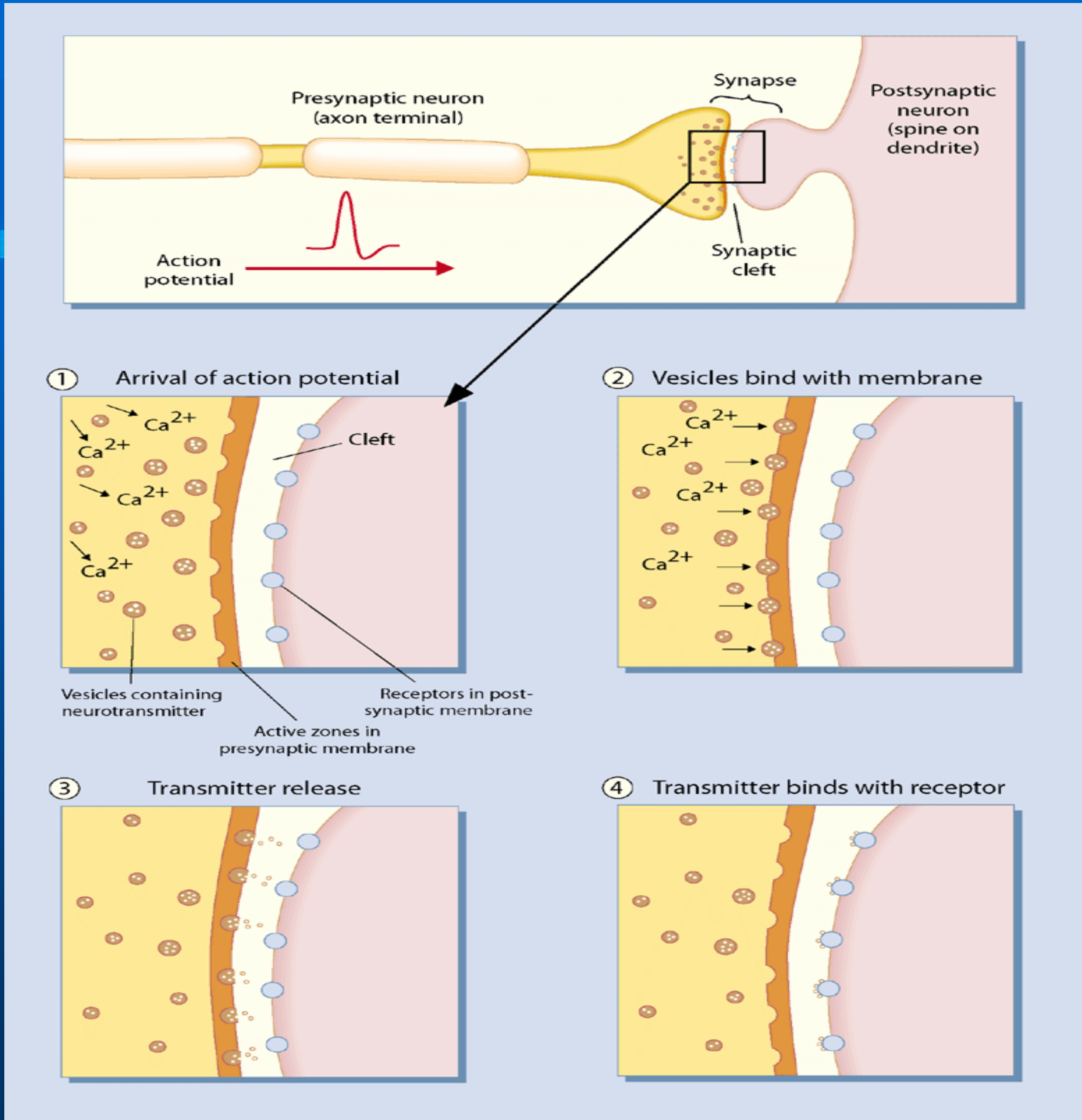


Fig. 2.30: Neurotransmitter release at the synapse

Chemical Transmission (2/2)

- Vesicle docking (Fig. 2.32b)
- Neurotransmitter release (Fig. 2.32c)

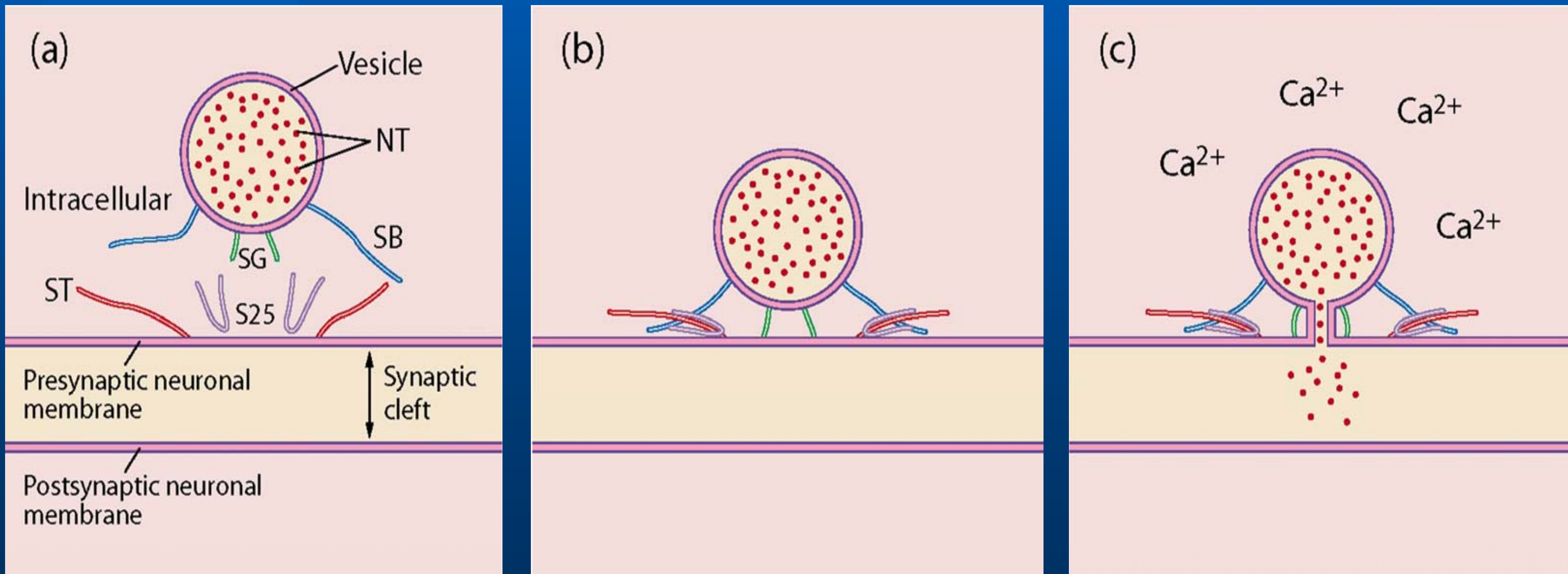


Fig. 2.32: Release of neurotransmitter (NT) from the presynaptic terminal.

Neurotransmitters

- More than 100 neurotransmitters are recognized today.
- Criteria for identifying a neurotransmitter:
  - Be synthesized by and localized within the presynaptic neuron, and stored in the presynaptic terminal.
  - Be released by the presynaptic neuron when action potentials invade and depolarize the terminal.
  - Contain receptors that are specific for the substance.
  - When applied to the postsynaptic cell, it should lead to same response that stimulating the presynaptic neuron would lead to.
- Each neuron typically produces one, two, or more neurotransmitters, which may be released together or separately depending on stimulations.

Classes of Neurotransmitters

- Neurotransmitters could be classfied biochemically as particular substances like:
  - *Ach* (acetylcholine)
  - Amino acids
    - *GABA*(γ-aminobutyric acid), *glutamate*, glycine
  - Biogenic amines
    - catecholamins (*dompamine*, norepinephrine, epinephrine), serotonin, histamine
  - Neuropeptides
    1) tachykinins (substance P, …)
    2) neurophypophyseal hormones (oxytosine, vasopression, …)
    3) hypothalamic releasing hormones (corticotropin-releasing hormone, somatostatin …)
    4) opioid peptides (endorphins, enkephalins, …)
    5) the others

Synthesis of Neurotransmitters

- Large molecule transmitters (peptides)
  - Produced in the cell body
- Small molecule transmitters
  - Produced in the synaptic terminals
  - Enzymes necessary for synthesis are produced in the cell body

- Synthesis of the catecholamines (e.g. dopamine) has important implication in the treatment of Parkinson's disease.

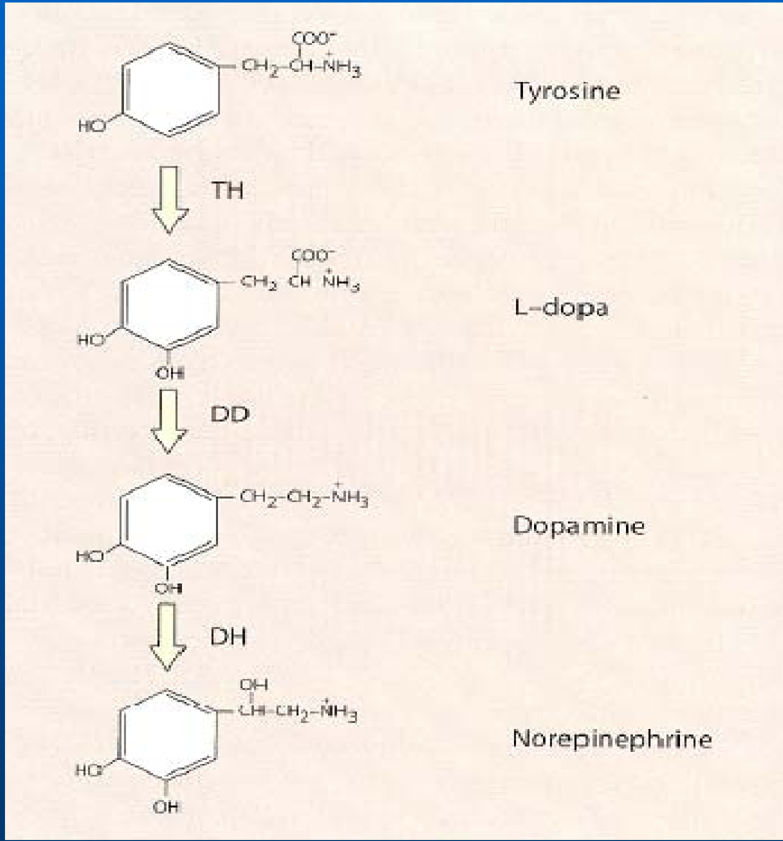


Fig. 2.33: Biochemical synthesis of dopamine and norepinephrine from the amino acid tyrosine.

Inactivation of Neurostrnsmitters after Release

- Reuptake
- Enzymatic breakdown
- Diffusion

Anatomical Pathways of the Biogenic Amines

- Biogenic amines are specifically localized.

  (cf. glutamate is located almost everywhere in the brain.)

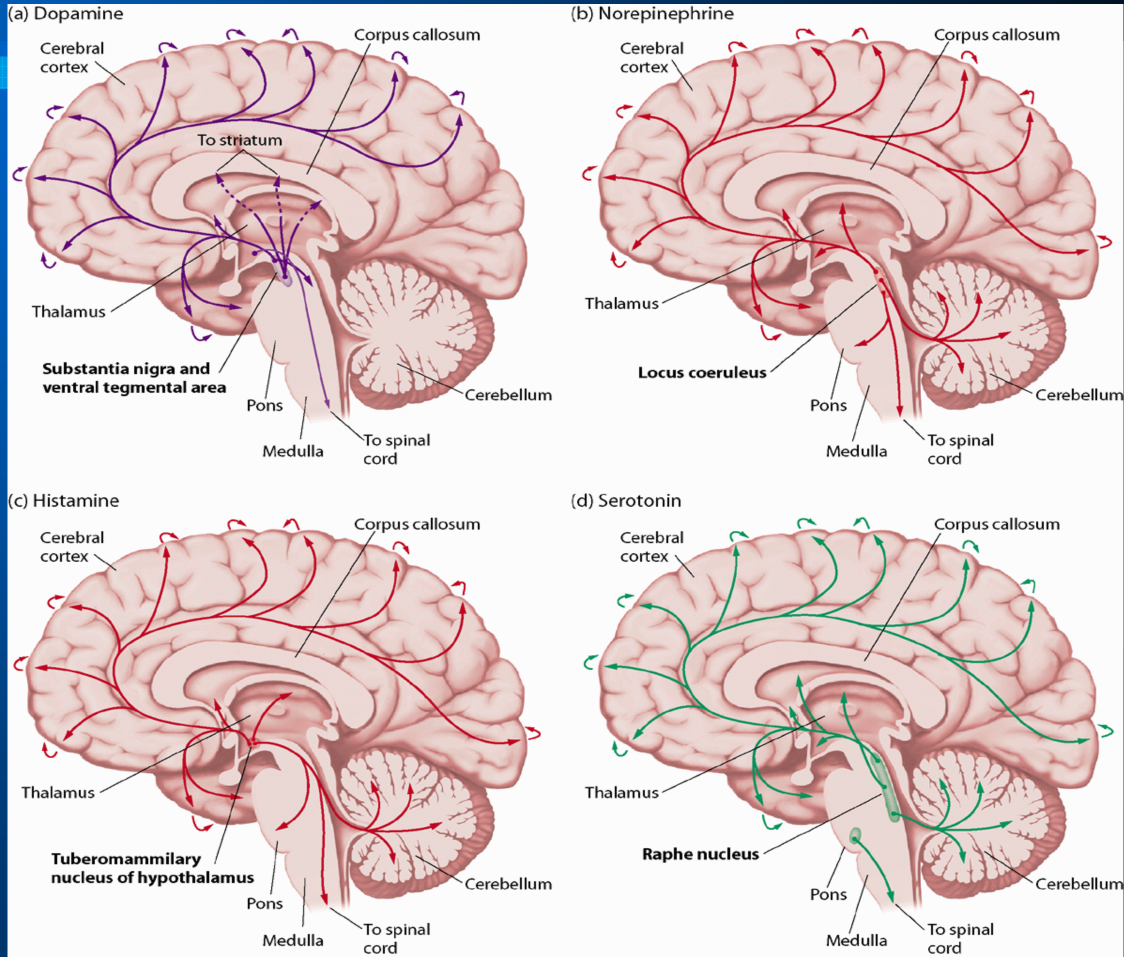


Fig. 2.34: Major projection pathways of the biogenic amine neurotransmitter systems.

Electrical Transmission (1/2)

- Some neurons communicate via electrical synapses.
- These two neurons are essentially continuous.
- This continuity occurs via specialized transmembrane channels called 'gap junctions' that create pores connecting the cytoplasms of the two neurons.

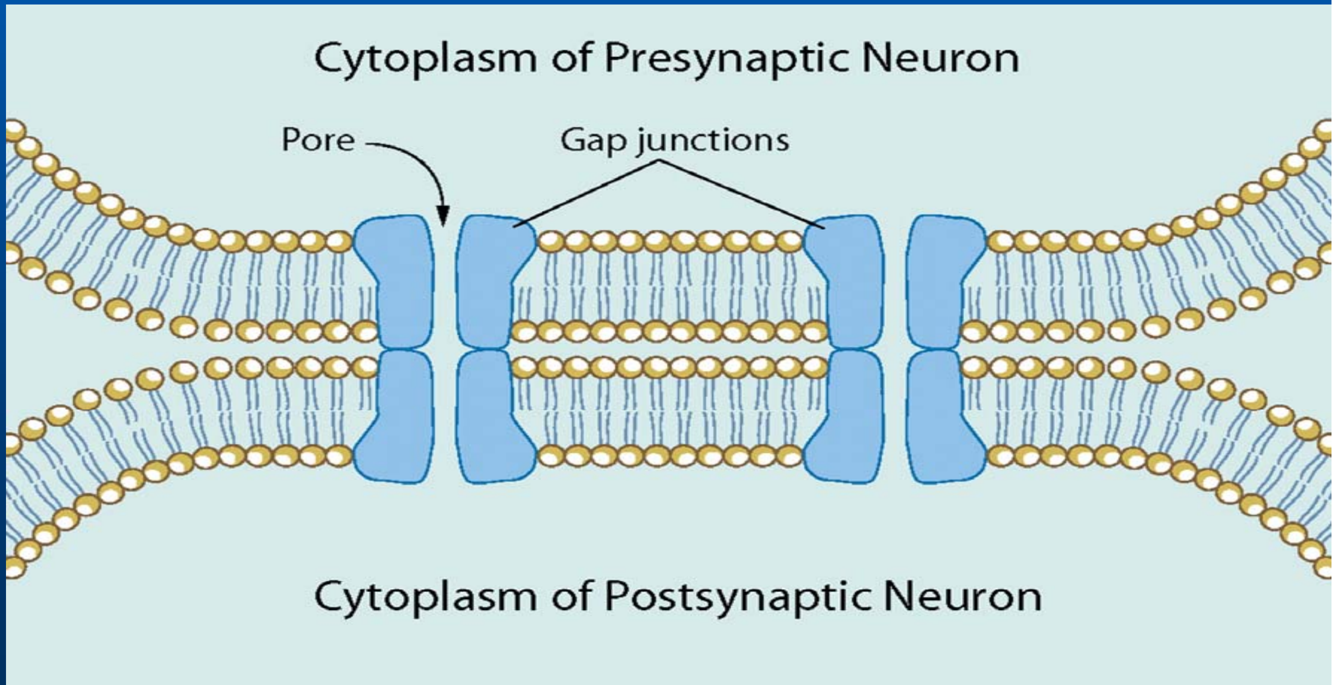


Fig. 2.35: Electrical synapse between two neurons.

Electrical Transmission (2/2)

- Rapid information conduction
- Synchronous neuron operation

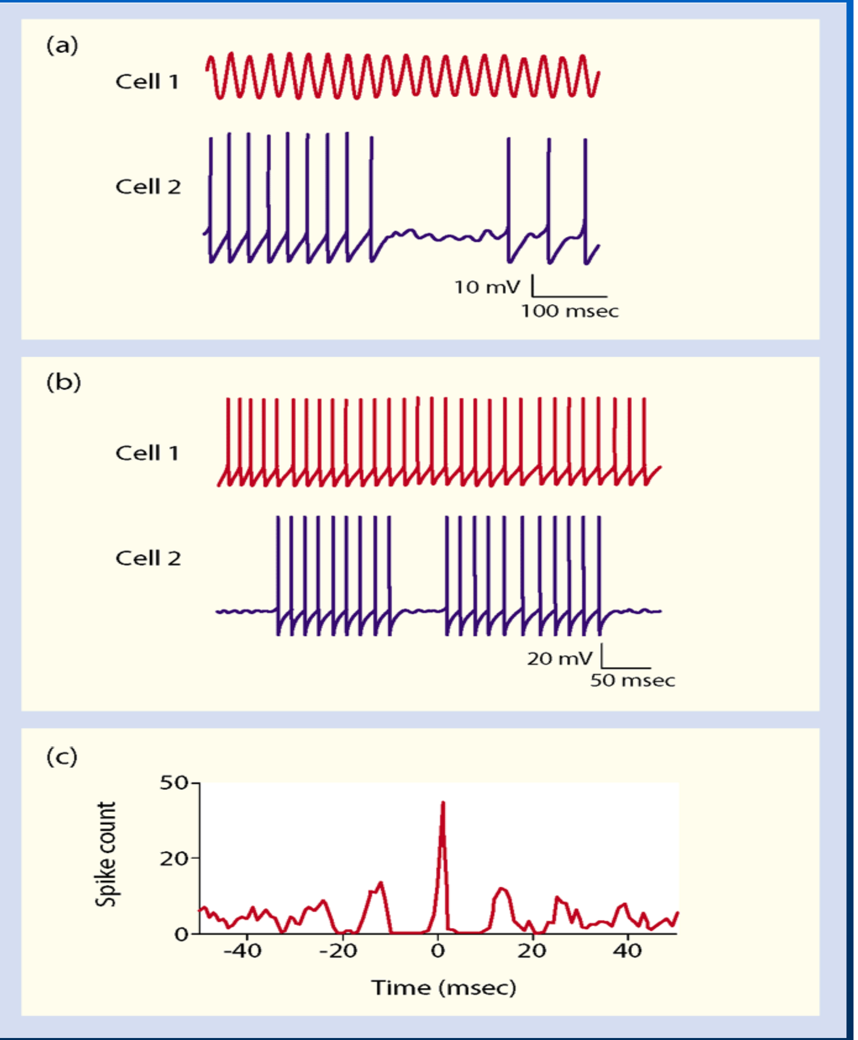


Fig. 2.35: Activity of two cortical interneurons in the rat somatosensory cortex connected by electrical synapses.

Summary

- Neuron: information processing cell
- Resting neuron → different ions at in-or-out side of membrane → electrical potential difference → electrical currents generated → action potentials as energy → travel through cell body to axon → axon releasing chemicals (neurotransmitters) → diffusing chemicals around synaptic cleft → postsynaptic neuron receives chemicals → currents generated → continuation of signals through neural circuits
- Ion channels: mediators of membrane potential.
- Neurotransmitters: media chemicals leading to changes around membrane.

Key Terms

action potentials
axon
blood-brain barrier (BBB)
dendrite
electrical gradient
electrotonic conduction
equilibrium potential
glial cell
hyperpolarization
ion channel

myelin
neuron
neurotransmitter
nodes of Ranvier
permeability
postsynaptic
presynaptic
propagation
receptor
receptor potential
refractory period

resting membrane potential
saltatory conduction
second messenger
soma
spike-triggering zone
spine
synapse
synaptic potential
threshold
vesicle

Thought Questions

1. If action potentials are all or none, how does the nervous system code differences in sensory stimulus amplitudes?
2. What property (or properties) of ion channels makes them selective to only one ion such as K+, and not another such as Na+? Is it the size of the channel, other factors, or a combination?
3. Given that synaptic currents produce electrotonic potentials that are decremental, how do inputs located distantly on a neuron's dendrites have any influence on the firing of the cell?
4. What would be the consequence for the activity of a postsynaptic neuron if reuptake or degradation systems for neurotransmitters were damaged?
5. How do drugs modify brain chemistry to alleviate disorders such as shizophrenia?

Skipped Figures

Figure 2.15

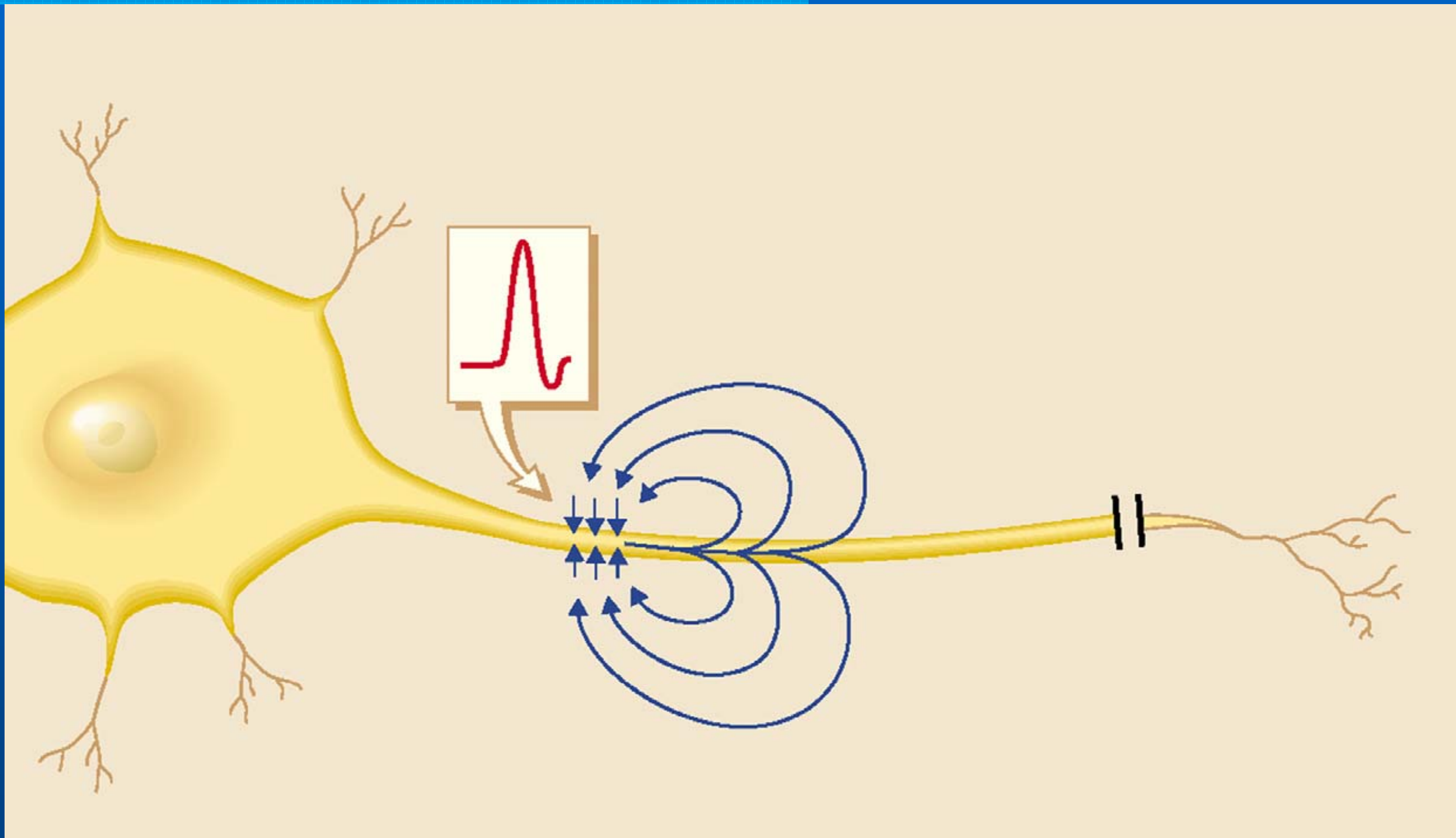


Figure 2.16

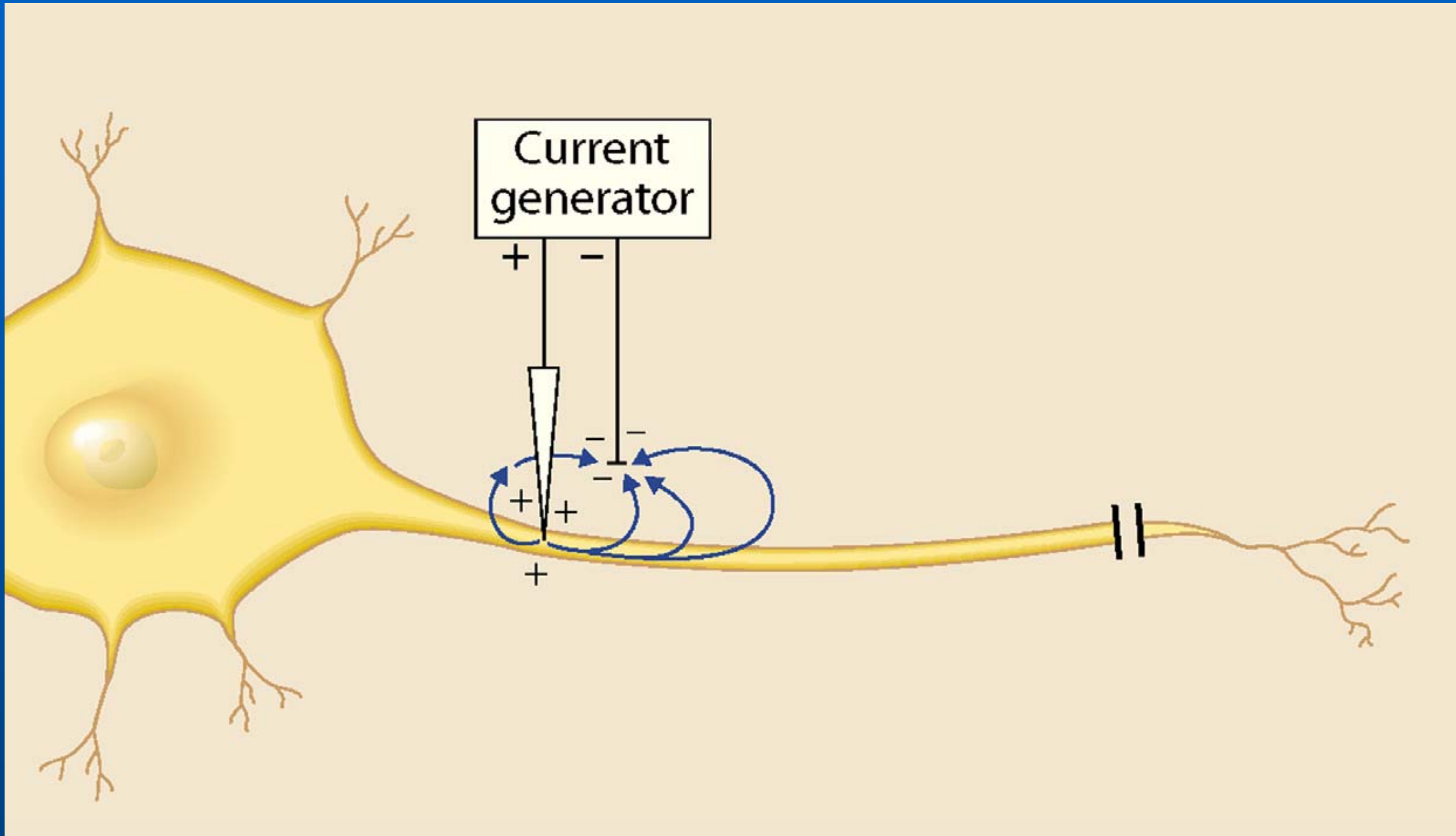
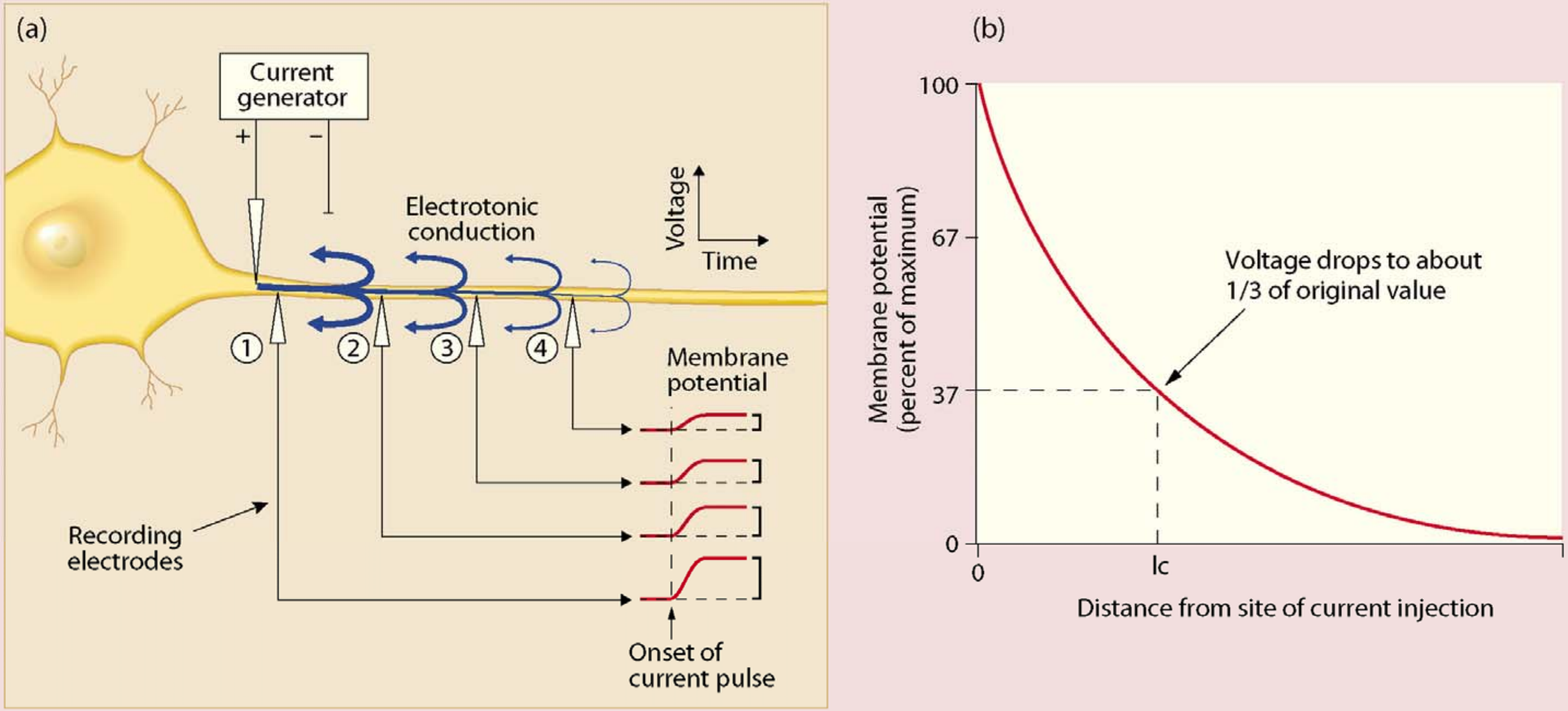
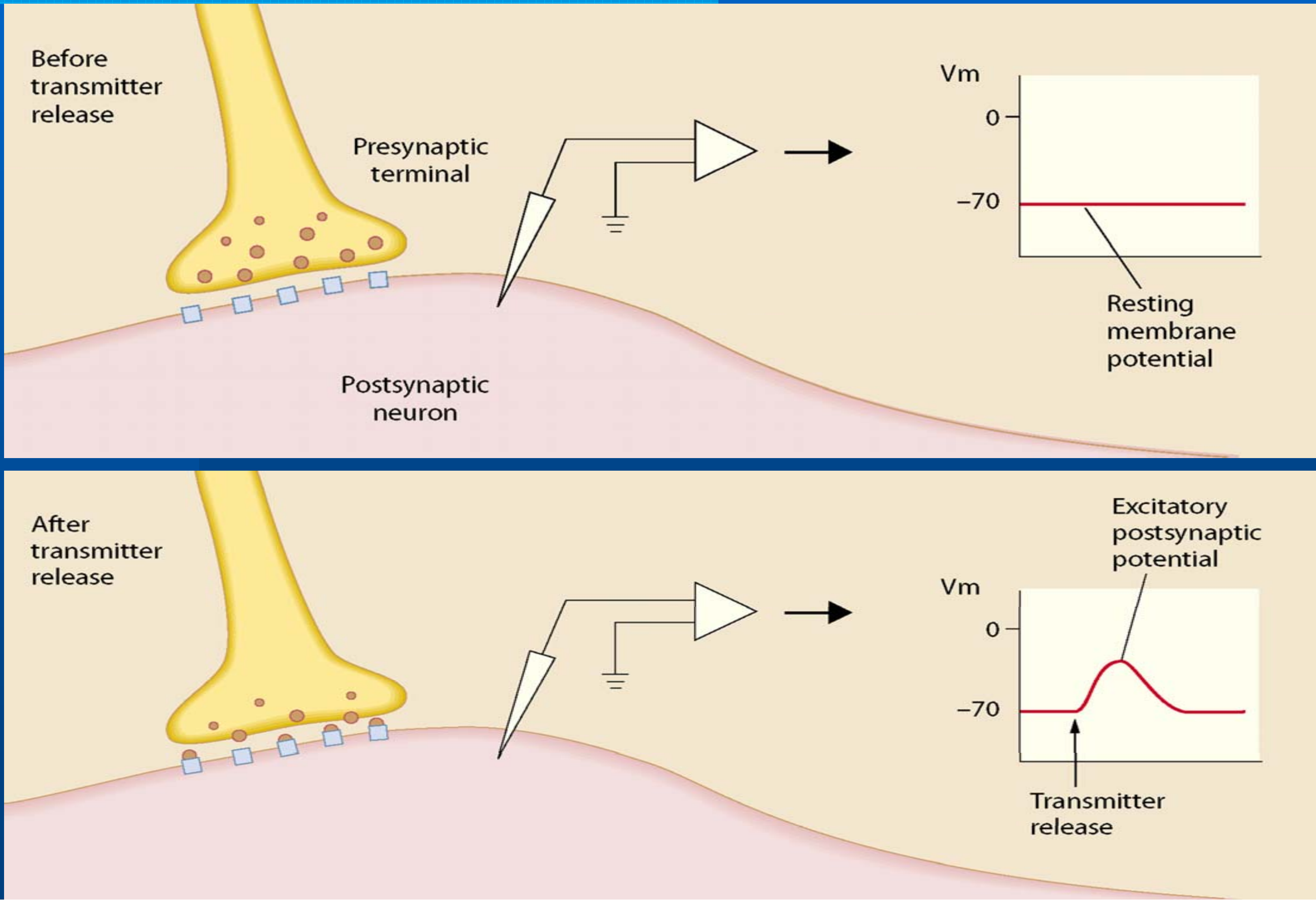


Figure 2.17



(a)
Current generator
+
−
Electrotonic conduction
Voltage
Time
1
2
3
4
Membrane potential
Recording electrodes
Onset of current pulse
(b)
100
67
37
0
Membrane potential (percent of maximum)
Voltage drops to about 1/3 of original value
0
lc
Distance from site of current injection

Figure 2.31



Before transmitter release
Presynaptic terminal
Postsynaptic neuron
Vm
0
–70
Resting membrane potential
After transmitter release
Excitatory postsynaptic potential
Vm
0
–70
Transmitter release