BLY122

Chapter 45 Electrical Signals in Animals

I. Principles of Electrical Signaling

A. Neurons transmit information through electrical impulses.
1. The speed of transmission may be as rapid as 100 m/sec (225 mph).
2. Sensory receptors receive information about the external environment and body interior.
   a. Sensory cells on the periphery of the body transmit information about the external environment.
   b. Sensory cells inside the body monitor conditions that are important in homeostasis.
3. The pathway of information flow in the nervous system in vertebrates:
   a. Sensory neurons send information to the central nervous system (CNS).
   b. The CNS integrates information from many sensory neurons.
   c. The CNS stimulates a motor neuron, which sends signals to effector cells in glands or muscles.
4. The peripheral nervous system (PNS) consists of all components of the nervous system that are outside the CNS.
5. A reflex bypasses the brain and travels directly to an effector.
   a. The reflex makes it possible to have rapid automatic responses.
   b. A connection is made between a sensory neuron and a motor neuron in the spinal cord.

B. The Anatomy of a Neuron
1. Neurons are small, transparent, and morphologically complex.
2. C. Golgi discovered that silver nitrate solution makes some neurons visible.
   a. Most neurons have dendrites, a cell body, and one or more axons.
   b. Dendrites are highly branched but are generally no more than 2 mm long.
   c. Axons can be over 1 meter long.
   d. The number and arrangement of dendrites varies in different neurons.
   e. Many brain neurons have only dendrites and lack axons.
3. Hypothesis: Dendrites receive electrical signals and axons pass them on.
   a. Golgi—Neurons are directly connected to each other; they form a continuous network.
   b. Cajal—Neurons are distinct, and the membranes of axons and dendrites meet at synapses.
   c. 1950s—Electron microscopy showed that, for most neurons, Cajal was correct.

C. An Introduction to Membrane Potentials
1. Cells are inherently electrical in nature.
   a. Ions carry an electric charge, and extracellular fluids contain ions.
   b. If an imbalance of ions occurs across the membrane, a voltage, or electrical potential, is created.
   c. Membrane potential is a separation of charge across a membrane.
   d. Membrane voltage is large if the charge difference across the membrane is large.
2. If a membrane potential exists, the ions on either side of the membrane have potential energy.
   a. Ions move across membranes in response to charge and concentration gradients, that is, an electrochemical gradient.
   b. A flow of charge is called an electric current.

D. The Resting Potential
1. The membranes of neurons at rest have a voltage, called a resting potential.
   a. Inside neurons, there are many negatively charged large organic acids.
   b. The major positively charged ion inside neurons is K^+.
   c. The extracellular fluid is rich in Na^+ and Cl^- ions.
2. Resting potential is the potential across the membrane when Na^+, K^+, and Cl^- ions are at equilibrium in a resting neuron.
   a. K^+ ions can move through a channel down their concentration gradient and exit the neuron.
   b. As K^+ leaves the cell, the interior of the cell becomes more negatively charged.
   c. Buildup of negative charge inside the cell eventually begins to attract K^+.
   d. The membrane reaches a voltage at which there is equilibrium between the concentration gradient that moves K^+ out, and the electrical gradient that moves K^+ in.

e. This equilibrium is the equilibrium potential for K^+.
f. Na^+ and Cl^- cross the membrane more slowly than K^+ does, but some exchange occurs.
g. The Na^+/K^+ pump moves 3 Na^+ out of the cell and 2 K^+ ions into the cell.

3. The Nernst equation—calculating the equilibrium potential for ions
   a. The equilibrium potential (E_{ion}) is the voltage that counteracts the movement of an ion across a membrane in response to a concentration gradient.
   b. E_{ion} = the valence of the ion times the thermodynamic potential (*RT/F*) times the natural logarithm (*l*) times the concentration of the ion outside divided by the concentration of the ion inside ($[ion]_o/[ion]_i$).
   c. The membrane potential that results when K^+, Na^+, and Cl^- are each at their E_{ion} depends on the permeability of the membrane to each ion.

E. Using Microelectrodes to Measure Membrane Potentials
1. Hodgkin and Huxley pioneered use of giant squid axon in electrical signaling studies (1930s–1940s).
   a. The giant axon conducts signals to contract muscles that expel water from a cavity to give the squid jet-propulsion motion.
   b. Squid giant axon is particularly large; about 500 µm in diameter.
   c. A wire could be inserted down the giant axon; or later, glass microelectrodes were used (Ling and Gerard).
2. Hodgkin and Huxley recorded membrane potentials in the giant axon.
   a. The axon was bathed in seawater or a solution of known composition.
   b. Result: The squid axon has a resting potential of –45 mV (although most other axons are –70 mV).
   c. The resting potential can be disrupted by an action potential.

F. What Is an Action Potential?
1. An action potential consists of a rapid depolarization/repolarization across the membrane.
   a. Depolarization—the membrane becomes less polarized.
   b. When the membrane reaches +40 mV, rapid repolarization begins.
   c. An action potential takes less than 1 millisecond.
2. Other observations about action potentials (Hodgkin and Huxley):
   a. It is an all-or-none event; partial action potentials do not exist.
   b. All action potentials for a given neuron are identical in shape and magnitude.
   c. Action potentials can be triggered by injecting a cell with electrical current, using a microelectrode.
   d. Action potentials are propagated down the length of the axon, with no change in shape or magnitude.
3. These observations suggest a mechanism for electrical signaling:
   a. Information is in the form of action potentials that travel down neurons.
   b. The frequency of action potentials, not their magnitude, is meaningful.

II. Dissecting the Action Potential

A. Which ions are involved in the currents that constitute the action potential?
1. Initial hypothesis: The action potential results from a temporary breakdown of the selective permeability of the neuron membrane.
   a. Channels open and allow a free flow of Na^+, K^+, and Cl^-.
   b. Problem: If Na^+, K^+, and Cl^- flow freely, the peak of the action potential should be at 0 mV.
   c. The observed peak of the action potential was +50 mV.
2. Hodgkin found that +50 mV corresponds to the equilibrium potential for Na^+.
   a. Revised hypothesis: The depolarization phase of the action potential results from an influx of sodium ions.
   b. The next step was to test this hypothesis.

B. Distinct ion currents are responsible for depolarization and repolarization.
1. Hodgkin and Huxley tested the ion currents that cause an action potential.
   a. Electrical activity was recorded in axons bathed in seawater.
   b. Seawater was replaced with dextrose and electrical activity was recorded.

d. Conclusion: The data support the hypothesis that an action potential begins when Na^+ flows into the neuron.
2. What ion flow is responsible for repolarization?
   a. If radioactive K^+ is used, a strong outward flow of K^+ is detected during repolarization.
   b. Conclusion: An action potential consists of a strong inward flow of Na^+ followed by a strong outward flow of K^+.

C. Voltage-Gated Channels
1. Voltage-gated channels open and close in response to changes in membrane voltage.
   a. The conformation of the channel protein changes in response to the charges present at the membrane surface.
   b. Conformational changes lead to opening or closing of the channel.
   c. Cole et al. devised a way to hold the membrane potential of a neuron constant, while ions were flowing through channels in the membrane.
      d. Hodgkin and Huxley performed voltage clamping of squid giant axons.
   e. If Na^+ flows in and K^+ flows out, why don't the two currents cancel each other out?
2. Patch clamping and studies of single channels
   a. Neher and Sakmann perfected the patch-clamping technique.
   b. Positive feedback explains why the action potential is an all-or-none event:
3. Using neurotoxins to identify channels and dissect currents
   a. Many toxins produced by poisonous animals cause convulsions, paralysis, or unconsciousness.
   b. Hypothesis: These toxins affect neuron function.
   c. Puffer-fish toxin specifically blocks the voltage-gated Na^+ channels of neurons.
   d. The neurotoxin of black mamba snakes affects the K^+ channel.

D. The Role of the Sodium-Potassium Pump—If enough action potentials occurred, the concentration gradients of Na^+ and K^+ across the neuron membrane would eventually dissipate.
1. To maintain the concentration gradients, a protein that hydrolyzes ATP must pump Na^+ out of neurons and K^+ in.
2. J. Skou succeeded in isolating a protein from crab neurons that began hydrolyzing ATP if both Na^+ and K^+ were present.
3. Hypothesis: The ATP-hydrolyzing pump is responsible for establishing the resting potential of neuron membranes.
4. The compound ouabain, from foxglove plants, abolishes the resting potential of neurons.
   a. Does ouabain poison the pump?
   b. The activity of the pump stopped when ouabain was added.
5. Na^+/K^+-ATPase establishes the resting potential of neurons.
   a. Na^+/K^+-ATPase restores normal concentrations of Na^+ and K^+ after an action potential has brought Na^+ into the neuron and sent K^+ out.
   b. Na^+/K^+-ATPase maintains the gradients responsible for the resting potential.

E. How Is the Action Potential Propagated?
1. Hodgkin and Huxley hypothesis: The influx of Na^+ causes charges to spread away from sodium channels.
   a. Negative charges inside the neuron are attracted by entering Na^+.
   b. Positive charges inside the neuron are repulsed by the entering Na^+.
2. Why don't action potentials propagate back up the axon?
   a. Once Na^+ channels have opened and closed, they inactivate and will not open again for a short time.
   b. The undershoot phase of the action potential means that the most recently fired portion of the axon is briefly hyperpolarized, which inhibits opening of Na^+ channels.
3. The squid's axon is large because charge spreads farther in a membrane with a large surface area.
   a. Large surface area means more channels and more charge.
   b. Giant axons propagate action potentials more quickly than smaller axons.
   c. Vertebrates do not have giant axons; instead, they have myelinated axons.

III. The Synapse

A. An indirect mechanism transmits electrical signals from neuron to other neurons or effectors.
   1. Most neurons are not directly connected.
   2. Otto Loewi showed that chemical neurotransmitters are the indirect mechanism.
      a. Hypothesis: The signal from nerve to muscle is delivered by a chemical.
      b. Experiment: Investigate the stimulus to the vagus nerve and heart of a frog.
      c. Conclusion: A neurotransmitter chemical was probably released from the vagus nerve into the solution, causing the heartbeat to slow down.
   3. How are neurotransmitters delivered?
      a. Transmission electron microscopy revealed the nature of the synapse.
      b. Model of synaptic transmission based on anatomical and chemical studies:

B. What Do Neurotransmitters Do?
   1. Patch-clamping studies using radioactive neurotransmitters showed that many receptors for neurotransmitters are ligand-gated channels.
      a. Ligand-gated channels open and close in response to the binding of a chemical compound to the receptor portion of the molecule.
      b. Binding of a neurotransmitter to a ligand-gated ion channel in the membrane of the postsynaptic neuron, the channel opens.
      c. Ions enter the cell, immediately transducing the chemical signal of the neurotransmitter into a change in the membrane potential of the postsynaptic neuron.
   2. Some receptors for neurotransmitters are not ligand-gated channels.
      a. These receptors activate enzymes that produce second messengers in the postsynaptic neuron.
      b. Second messengers are chemicals that travel through the cell and induce changes in enzyme activity, gene transcription, or membrane potential.

C. Postsynaptic Potentials, Summation, and Integration
   1. Two general types of synapses occur in neurons.
      a. Binding of the neurotransmitter induces an influx of Na^+ ions.
      b. Binding of the neurotransmitter induces an efflux of K^+ or an influx of Cl^-.
   2. Unlike action potentials, EPSPs and IPSPs are not all-or-none events.
      a. They are graded in size and short lived.
      b. The size of an EPSP or IPSP depends on the amount of neurotransmitter released.
      c. The length of the EPSP or IPSP depends on how quickly the neurotransmitter is inactivated or removed from the synapse.
      d. Street drugs cocaine and amphetamine alter neuron activity by inhibiting the uptake and removal of neurotransmitters from the synapse.
   3. Summation of the EPSPs and IPSPs in a given neuron determine if an action potential fires.
      a. Each neuron has hundreds or thousands of synapses with other neurons.
      b. EPSPs and IPSPs that are occurring at any of the synapses lead to short-lived surges in charge in the dendrites and cell body.
      c. The changes in membrane potential are additive.
      d. An action potential begins at the axon hillock.

D. What Happens When Ligand-Gated Channels Are Defective?
   1. Are defects in neurotransmitters and/or receptors involved in drug addictions and mental illnesses?
      a. Hypothesis: Defects in a ligand-gated channel are involved in schizophrenia.
      b. Schizophrenia patients exhibit positive and negative symptoms.
      c. People intoxicated with phenylcyclidine (PCP, “angel dust”) exhibit many symptoms of schizophrenia.
      d. Mohn et al. generated mice that produce only 5% of the normal amount of a key subunit of the NMDA receptor, and the mice exhibited behaviors similar to those induced by PCP.
      e. Researchers compared brain slices of normal and schizophrenic humans.
   2. Conclusion: Schizophrenia has not yet been decisively linked to a specific defect in an NMDA receptor, although the data implicate the NMDA receptor.

IV. The Vertebrate Nervous System

A. A Closer Look at the Peripheral Nervous System
   1. The PNS is divided into two systems:
      a. The afferent system carries information to the CNS.
      b. The efferent system carries information away from the CNS.
   2. The efferent system of the PNS is further divided into two systems:
      a. The somatic system responds to external stimuli and results in movement.
      b. The autonomic system responds to internal stimuli and controls the activity of internal organs.
   3. Two distinct types of autonomic nerves serve many glands and organs.
      a. Parasympathetic nerve signals promote relaxation and digestion by
      b. Sympathetic nerve signals prepare organs for stressful situations by

B. Functional Anatomy of the CNS
   1. The spinal cord collects and transmits information from throughout the body.
      a. Parasympathetic nerves originate at the base of the brain or spinal cord.
      b. Most sympathetic nerves originate in the spinal cord.
      c. Most sensory and motor neurons project to or from the spinal cord.
      d. Other than reflexes, all the information that travels to or from the spinal cord is sent to the brain for processing.
   2. The brain is the most complex organ found in animals and is divided into four structures.
      a. The cerebrum is the largest portion of the brain.
      b. The cerebellum coordinates motor patterns.
      c. The pons relays sensory information to the cerebrum.
      d. The medulla connects the brain to the spinal cord and regulates the heart, lung, and digestive systems.
   3. Electrical stimulation of conscious patients
      a. W. Penfield pioneered the study of brain function in conscious patients.
      b. Some patients reported that electrical stimulation triggered vivid memories.

C. How Does Memory Work?
   1. Memory is the retention of learned information.
      a. Learning and memory are closely related.
      b. Studies of memory generally involve tandem studies of learning.
   2. Recording from single neurons during memory tasks
      a. Ojemannn and Schoenfield-McNeill—As learning and memory take place, how do the action potentials generated by a neuron change?
      b. Results: Neurons in the temporal lobe were active when the patient was remembering, but quiet when the patient was naming objects.
      c. How could action potentials from specific cells make memory possible?
   3. Documenting changes in synapses
      a. Research on the molecular basis of memory is based on two ideas:
         (1) Some type of short-term or long-term change in neurons must occur during learning and memory.
         (2) Understanding the changes is easier if an extremely simple system of neurons is studied.
            b. Kandel et al. studied the sea slug *Aplysia californica*.
      c. Most researchers now agree that long-term memory involves changes in gene expression.

Chapter Vocabulary

central nervous system (CNS)
peripheral nervous system (PNS)
neuron
cell body/soma
dendrite
axon
sensory neuron
interneuron
motor neuron
effector
reflex

ions
extracellular fluid
voltage
millivolt
electric current
potential energy
electrical potential
membrane potential
electrochemical gradient

resting potential
ion channels
selectively permeable
leak channels
equilibrium potential
Nernst equation
gas constant (*R*)
absolute temperature (*T*)
faraday constant (*F*)
thermodynamic potential
natural logarithm (*l*)

squid giant axon
dextrose
glass microelectrode
millivolts (mV)

action potential
polarization
depolarization
threshold
excitable membranes
repolarization
refractory

voltage-gated channels
voltage clamping
inward-directed current
outward-directed current
patch clamping

positive feedback

neurotoxin
tetrodotoxin
puffer fish
black mamba snake venom
ouabain
Na^+/K^+-ATPase
myelination
Schwann cells
glia
node of Ranvier
multiple sclerosis

neurotransmitters
synapse
synaptic cleft
synaptic vesicles
ligand
ligand-gated ion channels
second messenger

presynaptic neuron
postsynaptic neuron
excitatory postsynaptic potentials (EPSPs)

inhibitory postsynaptic potentials (IPSPs)
summation
axon hillock

schizophrenia
positive symptoms
negative symptoms
phencyclidine (PCP)
n-methyl-D-aspartic acid (NMDA) receptor
glutamate

afferent division
efferent division
autonomic system
somatic system
parasympathetic nerve
sympathetic nerve

cerebrum
frontal lobe
temporal lobe
parietal lobe
occipital lobe
left hemisphere
right hemisphere
corpus callosum
cerebellum
pons
medulla
Aplysia californica
siphon
gill
serotonin (5-HT)
synaptic plasticity
Parkinson's disease
substantia nigra
dopamine
xenografting
xenotransplantation