Instructor's Answer Key

Chapter 7: The Nervous System: Neurons and Synapses

Answers to Test Your Understanding of Concepts and Principles

1. Action potentials are caused by voltage-regulated gates that open in response to depolarization and that produce increasing depolarization in a positive feedback fashion. Action potentials are all-or-none events that peak at a membrane potential of about +40 mV, and occur with increasing frequency in response to increasing strength of stimulation, up to a maximum frequency determined by the length of the refractory periods. Because of the refractory periods and the all-or-none nature of action potentials, they cannot summate. Action potentials originate at the axon hillock (initial segment) portion of the neuron axon where threshold is determined and are conducted without decrement because they are regenerated along the axon. By contrast, synaptic potentials occur at a synapse such that formed on the dendrite or cell body and are created by chemical ligands such as neurotransmitters, hormones, or drugs binding to specialized receptor proteins. Synaptic potentials are graded (no threshold), can be excitatory (EPSP) or inhibitory (IPSP), can be summated temporally or spatially, and travel with decremental decay.
   [Note: This question is also answered in the Student Study Guide.]

2. Voltage-regulated gates located along the length of the neuron axon open in response to a depolarization stimulus (usually a threshold stimulus at the axon hillock). First the voltage-regulated Na^+ gates open, permitting Na^+ to enter the axon by diffusion. Since Na^+ is positively charged this causes further depolarization, which in turn opens more Na^+ gates. A positive feedback loop is thus created, resulting in an explosive change in the membrane potential toward the Na^+ equilibrium potential (+60 mV). It is this positive feedback loop that makes action potentials all-or-none events. As the equilibrium potential rises the Na^+ gates begin to close (actually inactivated) while the K^+ gates begin to open and K^+ begins to diffuse rapidly out of the axon (repolarization). Continued outward movement of K^+ produces a slight overshoot of the membrane potential (after-hyperpolarization). Closure of the gated K^+ channels leads to reestablishment of the resting membrane potential and completion of the negative feedback loop.

3. During the production of an action potential at one region of an unmyelinated axon the membrane potential reverses (usually at the axon hillock), so that the inside of the membrane is positively charged compared to the outside. Since the membrane potential has the opposite polarity at the adjacent region of the axon membrane, electrical currents are created between the first region and the second. This depolarizes the second region, and when this second region is depolarized to threshold its voltage-regulated gates open and serve as a depolarization stimulus for a new action potential in the third region, and so on.

4. In an unmyelinated axon, new action potentials are produced a fraction of a *micrometer* apart along every patch of the axon membrane. In a myelinated axon, the myelin sheath insulates the axon, preventing movements of ions through the membrane. Therefore, new action potentials are produced about 1-2 *millimeters* apart only at the nodes of Ranvier. This axon conduction by cable properties along myelinated axons is faster than the time required for the generation and conduction of action potential at every patch along the unmyelinated axon membrane. The rapid jump in action potentials from node to node is called saltatory conduction in myelinated fibers and is much faster than conduction in unmyelinated fibers. In addition, axons with a larger diameter have less resistance to the spread of charges by cable properties and conduct impulses at a higher velocity. Larger diameter axons tend to be myelinated.

5. The **nicotinic** ACh receptor consists of five polypeptide subunits that enclose the ion channel. Two of these subunits contain ACh binding sites. When both sites are bound to ACh molecules, the ion channel opens. The opening of this channel permits the simultaneous diffusion of Na^+ inward and the outward diffusion of K^+. Because of the steeper electrochemical gradient, the inward flow of Na^+ predominates and a depolarization is produced in the postsynaptic membrane. This causes an EPSP (known as a EPP or end plate potential in skeletal muscle). This EPSP (EPP) forms action potentials at the motor end plate that stimulate skeletal muscle contraction.

6. The **muscarinic** ACh receptors are formed by a single subunit and do *not* contain ion channels. When ACh binds to the muscarinic receptor, it activates a complex of proteins in the plasma membrane known as G-protein subunits, which are named because their activity is influenced by guanosine nucleotides (GDP and GTP). In response to the binding of ACh to its membrane receptor protein, the alpha subunit of the G-protein complex dissociates from the beta-gamma complex. Depending on the receptor location in the body, either the alpha subunit or the beta-gamma subunit complex then diffuses laterally through the membrane until it binds to an ion channel or membrane-bound enzymes, causing the channel to open or activation of enzymes. A short time later, the G-protein subunit dissociates from the channel and moves back to its previous position as the ion channel closes. In heart muscle the beta-gamma complex causes the ion channels to open and K^+ diffuses out of the postsynaptic cell. The heart cell becomes hyperpolarized, producing an IPSP. However, in other tissues (smooth muscle, for example) the binding of ACh to its muscarinic receptors releases a different type of G-protein alpha subunit that indirectly causes the K^+ channels to close rather than to open. As a result, the outward diffusion of K^+ is reduced below resting levels, which causes a depolarization (resulting in stomach muscle contractions, for example).

7. The EPSP is a graded depolarization that must spread by cable properties from its site of production at the synapse usually on a dendrite to the axon hillock. Upon arrival at the axon hillock, the depolarization produced by the EPSP will, if it is at least equal to some threshold level, open voltage-regulated gates and stimulate the production of an action potential. Since the EPSP decreases in amplitude with distance, and since its initial amplitude depends on the amount of neurotransmitter released at the synapse, it may not have sufficient amplitude by the time it reaches the axon hillock to stimulate action potential production. Such subthreshold EPSPs will not result in action potentials. A number of EPSPs, however, can add together by spatial and temporal summation, so that the level of depolarization that occurs at the axon hillock can be sufficient to generate action potentials.

8. An IPSP is a hyperpolarization of the postsynaptic membrane in which the membrane potential moves farther from the threshold depolarization required to produce action potentials. An IPSP can be caused by the release of a particular inhibitory neurotransmitter (such as glycine or GABA) that increases the membrane permeability to the inward diffusion of chloride ion through open Cl^- channels, but not to Na^+. This results in inhibition, because when the postsynaptic membrane is hyperpolarized, a greater amount of excitatory neurotransmitter will be required to produce an adequate depolarization to threshold in the postsynaptic neuron.

9. The endogenous opioids in the brain and pituitary gland have been identified as a family of polypeptides including β-endorphin, enkephalins, and dynorphin. It has been proposed that activation during stress releases endogenous opioids that block the transmission of pain perhaps by blocking the release of substance P. This is a form of presynaptic inhibition in which depolarization of the pain neuron axon terminals decreases the inflow of Ca^{2+} and thus inhibits the release of neurotransmitter involved in pain transmission. Opioids may also provide pleasant sensations and thus mediate reward or positive reinforcement pathways.

10. When a presynaptic neuron is stimulated at a high frequency, for even as short a time as a few seconds, the excitability of the synapse is enhanced – or potentiated – when this neuron pathway is subsequently stimulated. The improved efficacy of synaptic transmission may last for hours or even weeks and is called *long-term potentiation*. Long-term potentiation may favor transmission along frequently used neural pathways and thus represent a mechanism of neural "learning." Observed LTP in the hippocampus region of the brain is of interest since this area has been implicated in memory storage. Nitric oxide may be a retrograde messenger released from the postsynaptic neuron in long-term potentiation and appears to improve synaptic transmission.

Answers to Test Your Ability to Analyze and Apply Your Knowledge

1. The white matter of the peripheral nerve includes the surrounding living sheath of Schwann cells known as the neurilemma, or sheath of Schwann. The gray matter of the spinal cord (CNS) is composed of high concentrations of cell bodies and dendrites that lack a continuous neurilemma (myelin sheath). The Schwann cells of the peripheral graft can form a regeneration tube as the part of the axon that is connected to the cell body begins to grow and exhibit amoeboid movement. Schwann cells of the regeneration tube are believed to secrete chemicals that attract the growing axon tip and guide the regenerating axon of the spinal cord to the grafted peripheral nerve. The inability to regenerate central axons is partly due to the absence of a continuous neurilemma and also due to at least three growth-inhibiting protein molecules produced by oligodendrocytes and to physical axon blockade of glial scars formed by astrocytes in the injured spinal cord. These growth-inhibiting proteins bind to a receptor (called the *Nogo* receptor) on the severed axon. Furthermore, injury to the spinal cord has been shown to cause apoptosis (cell suicide) in neurons that were *not* directly damaged by the injury.

2. Voltage-gated ion channels can open and close in response to alterations in the membrane potential. When ion channels are closed, the plasma membrane is less permeable, and when the channels are open, the membrane is more permeable to an ion. There appears to be two kinds of K^+ channels – one type is not gated; these channels are always open (K^+ diffuses out, called *leakage channels*) whereas the other type is gated and closed in the resting cell. Channels for Na^+, by contrast, are all gated and always closed in the resting cell. Yet, some Na^+ does leak slightly into the cell resulting in a resting potential that is a little less negative than the equilibrium potential for K^+. Molecular biology/biochemistry efforts have clarified the chemical nature of these "gates" that are part of the proteins that comprise the channels. Knowledge of the protein structures of these channels allows a better understanding of when and how the gates open in response to voltage changes both in the laboratory and in vivo. Such studies, for example, have shown that the local anesthetics (procaine, lidocaine, and tetracaine) block the conduction of action potentials in sensory neurons by reversibly binding to specific sites within the voltage-gated Na^+ channels and thereby inhibiting depolarization.

3. Voltage-regulated Ca^{2+} channels are located in the axon terminal adjacent to the docking sites for the synaptic vesicles containing excitatory neurotransmitter molecules. When an axon terminal is stimulated normally, the arrival of an action potential opens these channels, causing an inward diffusion of $Ca2^+$ that triggers the rapid fusion of the synaptic vesicle with the axon terminal membrane and the release of neurotransmitters. In the experiment with the drug that blocks the Ca^{2+} channels, motor neuron-muscle transmission will be blocked on the presynaptic side of the synapse, resulting in *flaccid* (limp) muscle paralysis. In a similar fashion, opiates are thought to promote analgesia by inhibiting the release of pain neurotransmitters. Tetanus toxin by contrast, is produced by bacteria and causes a *spastic* form of paralysis by blocking synaptic transmission of inhibitory neurons, primarily glycine-releasing or GABA-releasing neurons in the spinal cord (CNS). Blocking the neuromuscular inhibitory influence will cause relatively greater stimulation of the excitatory motor neuron transmission that will result in uncontrolled muscle spasms.

4. G-proteins are a complex of postsynaptic cell membrane receptor proteins whose activity is influenced by guanosine nucleotides (GDP and GTP). There are three G-protein subunits, designated alpha, beta, and gamma. In response to a neurotransmitter or other regulatory molecule binding to the G-protein receptor complex, one or more of the subunits dissociate and diffuse laterally through the membrane to bind with membrane ion channels. Depending on the effector cell type, the ion channel may open (opening of K^+ channels in heart muscle causes hyperpolarization) or close (closing of K^+ channels in smooth muscle causes depolarization). In this way, the complexity and variability of the G-protein membrane receptor proteins creates a variety of possible response options by the target postsynaptic cell. One neurotransmitter can result in directing different responses in the postsynaptic cell depending the chemistry and physiology of the G-protein receptor.

5. Several studies have already been done involving human twins separated at birth and reared in different environments. The hypothesis is that a gene that codes for one subtype of dopamine receptor (D_2) is more prevalent in the mesolimbic dopamine system of alcoholics than non-alcoholic people who express other dopamine receptor subtypes. These emotional reward pathways involve neurons that originate in the midbrain and send axons to structures in the forebrain that are part of the limbic system. Similar studies using genetically bred rats have also been done exploring the emotion-reward connection in rats. Gene knockout studies in mice in which the dopamine receptor (D_2) gene has been deleted would also shed light on the physiological role of dopamine in behavior and reward. Furthermore, drugs such as those prescribed to treat schizophrenia (neuroleptics) act as antagonists of the D_2 subtype of dopamine receptor and could be used either in twin studies as mentioned earlier or in larger group clinical studies.