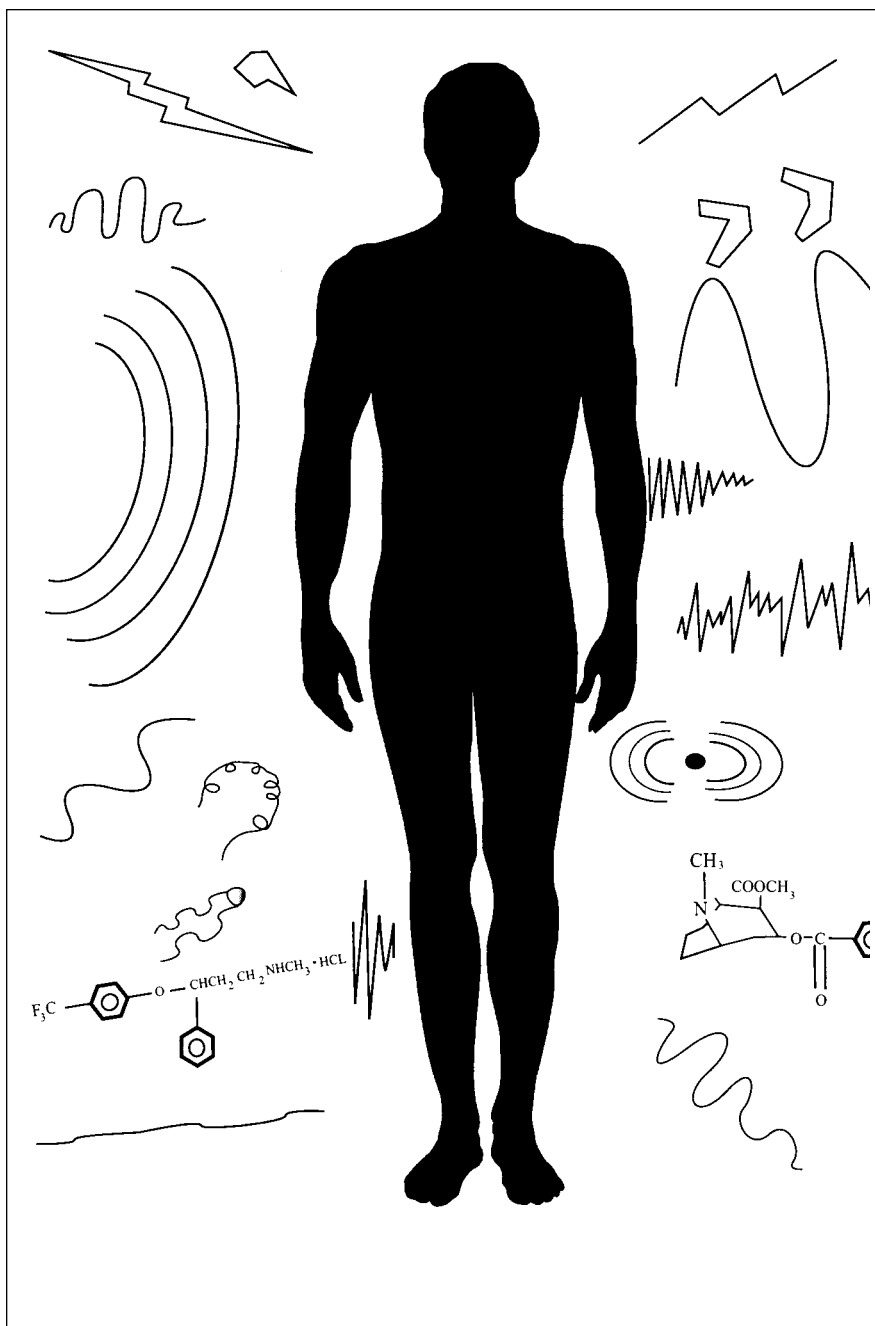


# Introduction to the Nervous System

**T**he world is mostly unknown. This statement immediately emphasizes the point that we are not conscious of most of the environmental events that occur around us. The world consists of stimuli of which we may or may not be aware. These stimuli are pressure variations, chemicals, electromagnetic radiation, temperature, and even gravity. Figure 1.1 emphasizes this situation. This world of ours contains many events we do not focus on but also some we simply cannot perceive. We process the sensory information we interpret automatically each moment. However, we overlook many interesting aspects of our existence. For example, there are different types of pain. If you pause and think about it, you can recognize this. Remember the day you bumped your head. The immediate pain, sharp and crisp, was followed by a duller but still acutely painful ache and throb. You may even recall being told to “rub it, it’ll feel better.” The light rubbing usually does reduce the pain, but what happens if you rub too hard? It does not feel better. Pain is a confusing sensation when examined closely. Another example is to stare at a waterfall for a minute and then look at the grass. You would see the grass grow upward right in front of you. This illusion is the response of an active and normal visual system.

In this chapter, we examine the human nervous system and some principles that govern its operation. The nervous system can be understood more easily by first partitioning it in smaller components. Even when the nervous system is partitioned, however, it is cumbersome when first encountered. The goal of this chapter, and the one that follows, is to provide the knowledge



**Figure 1.1.** The Physical Energy in Our Surrounding Environment

necessary to appreciate the sensory systems discussed in later chapters. This chapter concludes with a discussion of some nervous system dysfunctions.

## The Nervous System

The old adage that says “You are what you eat” can be more correctly stated, from a neurological perspective, as “You are what your nervous system permits.” This simply means, in an emphatic way, that your thoughts, feelings, emotions, sensations, desires, dreams, ideas, creative urges, language, and life itself are under the control of the most complex structure in the world—your brain. This, of course, does not mean that there are no other physical structures or systems having important roles in your life—for example, digestive processes, internal organs, glands, and hormones. However, the nervous system is undoubtedly in control. It is no overstatement to say that the function of 100 to 120 billion neurons composing the nervous system is one of the most elusive mysteries of science today. The task of understanding the brain has been difficult but rewarding. The study of the nervous system is one of the most intellectually stimulating fields of study. Indeed, it is intriguing to realize that the nervous system investigates the nervous system. This is a simple matter of one brain investigating itself—a unique situation.

The immense magnitude of the nervous system requires, or demands, that investigators limit themselves to the study of relatively small and restricted features. Even by investigating small regions at a time, however, investigators are continually amazed at the bewildering complexity. The intricacy occurs in the realms of functions—what the nervous system does, and structure—how the nervous system is put together. It is our goal to examine the operation of the nervous system from only one of the multitude of different perspectives, namely, how does the nervous system receive information from the environment and, once the information is received, how does it process the information? In other words, how do we “sense” the stimuli in our environment? Because our lives depend on well-functioning sensory systems, we seek to understand what the nervous system does to provide us with a “real” world. The real-world environment also includes internal bodily activities such as stomachaches and joint movements. The nervous system monitors, reacts to, and interprets the world external to the body while continually monitoring the shifting environment within.

The nervous system is commonly partitioned in two parts: the **peripheral nervous system (PNS)** and the **central nervous system (CNS)**. These two interacting and communicating systems are in actuality a continuous entity.

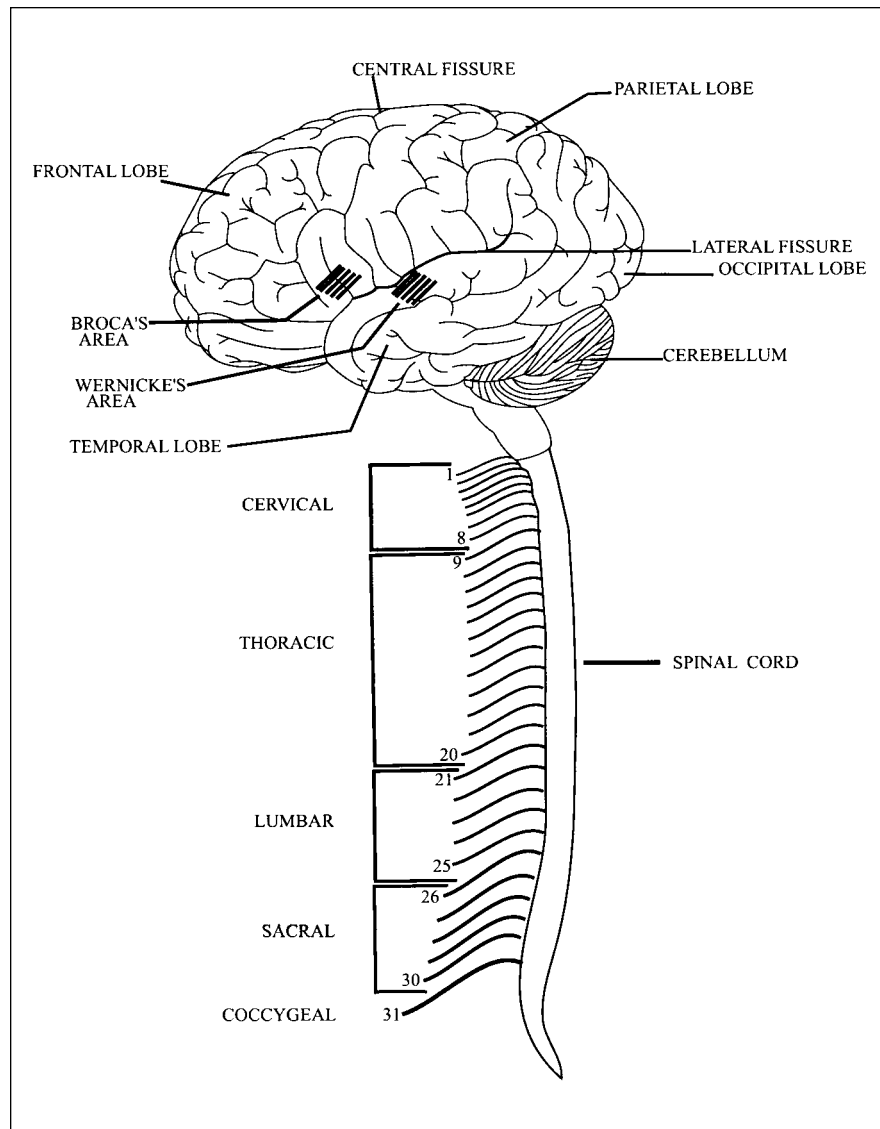
The peripheral nervous system effectively merges into the central nervous system so dividing the nervous system in two separate parts is, in fact, an artificial partition. For the sake of description, however, it is a necessity. Furthermore, the central nervous system is usually partitioned in two additional sections: the brain and the spinal cord. The sectioning of the central nervous system is a useful procedure that is adhered to for our purpose of exposition. Figure 1.2 shows, diagrammatically, the division of the human nervous system into the peripheral nervous system and the central nervous system. We discuss each in turn.

### The Peripheral Nervous System

The peripheral nervous system in Figure 1.2 shows the 31 pairs of **spinal nerves**. They are called “spinal” because they carry information to and from the spinal cord (Heimer, 1983). There are also 12 **cranial nerves** that conduct information to and from the brain more directly; that is, they do not involve the spinal cord. We discuss the cranial nerves associated with sensory systems as we examine each sensory modality. We focus here on the spinal and peripheral nerves and their organization.

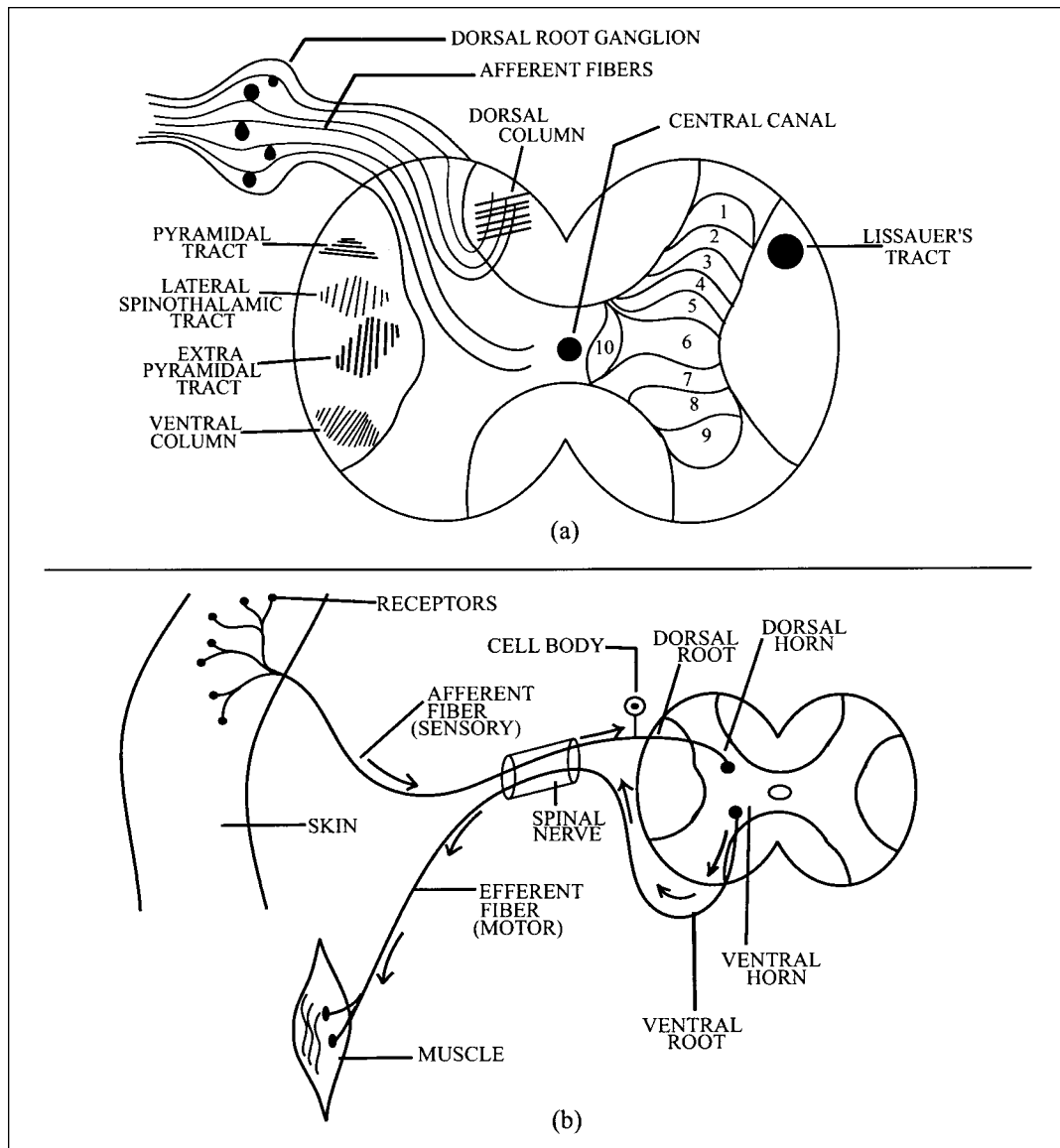
Before we discuss the plan of the peripheral nervous system, it is important at the outset to briefly examine the idea of a nerve. All **nerves** are composed of thousands of small strands of fibers called **axons**. The axon is the conducting portion of a neuron. The peripheral nervous system and central nervous system process the neural impulses conducted by each axon. Many of these axons are individually wrapped with a covering called **myelin**. The axons are often gathered together to make a nerve. An analogy may be useful. We can compare a nerve with a telephone cable. A telephone cable (the nerve) consists of thousands of individually insulated wires (the axons). Each wire (axon) is capable of carrying a separate message. The insulation around each wire is the myelin. In addition, the insulation for each wire in the cable is often color coded, as is the myelin; it appears white when viewed with a microscope. The white appearance indicates to investigators that they are viewing a pathway of the nervous system. Neurons themselves appear gray.

The spinal nerves emerge from both sides of the spinal cord in a very specific manner. They emerge from the **dorsal** and **ventral horns**. The words *dorsal* and *ventral* refer to the back and belly of the spinal cord, respectively. The ventral portion of the spinal nerve sends information to muscles and glands and thus has an **effluent** function. *Efferent* refers to the conveying of information away from the central nervous system. The ventral portion of the nerve is also referred to as a “motor” nerve because it is often concerned with the



**Figure 1.2.** The Divisions of the Nervous System and an External View of the Brain and Spinal Cord

movement of the skeletal muscles. The dorsal portion of the spinal nerve is **afferent** in nature and carries information toward the central nervous system. The afferent portion of the spinal nerve provides the sensory information while the efferent axons allow the central nervous system to send messages to muscles, internal organs, and glands. Figure 1.3 shows a simplified diagram of this arrangement.



**Figure 1.3.** The Spinal Cord and Pathways

NOTE: (a) Cross-section of the spinal cord showing pathways and laminae within the cord and (b) Overview of the afferent and efferent paths.

Some of the spinal nerves are referred to as mixed nerves because they contain a mix of sensory (afferent) and motor (efferent) fibers. The classical division of the spinal nerve in two parts, shown in Figure 1.3(b) as the **dorsal** and **ventral roots**, is known as the **Bell-Magendie law**—the dorsal root is sensory and the ventral root is motor. Recent evidence has shown, however, that

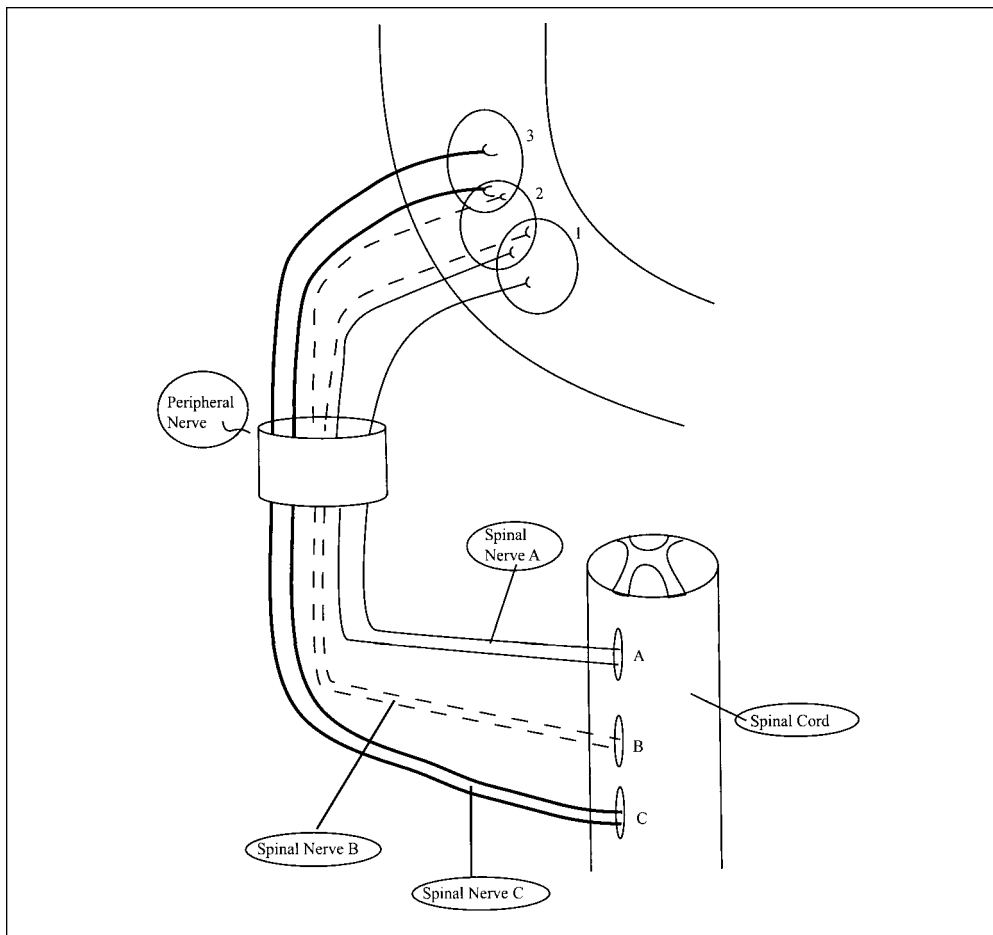
some afferent fibers enter the ventral horn, so the Bell-Magendie “law” may be more of a rule of thumb than a law.

Figure 1.3(a) shows the dorsal root ganglion as an enlargement of the sensory nerve. The axon fibers that compose the nerve require a **cell body** or **perikaryon** as a means of life support. The cell body is the main protoplasmic mass of a cell. The cell body produces an internal constituent called **axoplasm**. The axoplasm provides the axon with the metabolic means of existence. The dorsal root ganglion is a gathering together of the cell bodies associated with each sensory fiber in the spinal nerve. Because the cell bodies are not covered with myelin, visual inspection yields the gray appearance. Thus, to repeat, one of the first general rules of the nervous system is that pathways are white and cell bodies are gray. There is no ganglion for the efferent fibers. The cell bodies for the efferent fibers are located within the spinal cord itself.

Examination of Figure 1.3(b) shows that the distal end of axons, the end farthest from the central nervous system, often have special **arborizations** or treelike branching near their terminals. In the case of the sensory or afferent fibers, the arborizations enable the neural element to receive stimulation simultaneously from several sources in the environment. In addition, the axon often has additional arborizations that permit a single axon to send impulses to and communicate with many other cells. At the distal end of the neural element, there is often a specialized modification. The modification is a receptor (discussed in the next chapter). The rule to remember at this point is simple: No receptor = no sensation.

### *Peripheral and Spinal Nerves*

Until now, we have not differentiated between the spinal nerves and the peripheral nerves. The situation is, at first glance, somewhat confusing. It can be readily understood, however, by noting that the spinal nerves come directly from the spinal cord and combine to form a peripheral nerve, see Figure 1.4. As the spinal nerve begins its journey toward the periphery of the body, a number of **plexuses** occur. *Plexus* is Latin for “braid.” This means that the sensory portions of the spinal nerves are composed of individual fibers that diverge to different peripheral nerves. Each peripheral nerve, as a result, is made up of fibers from several spinal nerves. The peripheral nerves then continue to specific areas of the body. It is this very organization of the peripheral nervous system that causes differences in sensitivity as a function of different types of physiological insult—that is, an injury or surgical procedure. If a peripheral nerve is severed, the sensations are eliminated from a fixed and relatively small, circumscribed area of the body. Each peripheral nerve serves a



**Figure 1.4.** An Example of the Spinal and Peripheral Nerve Configuration

NOTE: Spinal nerves A, B, and C form a peripheral nerve and synapse on dermatomes 1, 2, and 3.

restricted portion of the body surface. If, on the other hand, a spinal nerve is cut there may be very little loss in feeling because fibers from other spinal nerves innervate the same surface area of the body. Figure 1.4 shows, diagrammatically, how this can occur. If spinal nerve A were severed, there would be little loss of sensitivity at the body surface labeled 1. This is because the innervations provided by spinal nerve B overlaps with the body surface previously served by spinal nerve A. In short, the loss of the fibers due to the severing of spinal nerve A is offset by the innervations provided by spinal nerve B. If, however, you were to cut the peripheral nerve, then all three body surfaces shown in Figure 1.4 would be devoid of innervations. The entire body area served by the peripheral nerve would be numb.



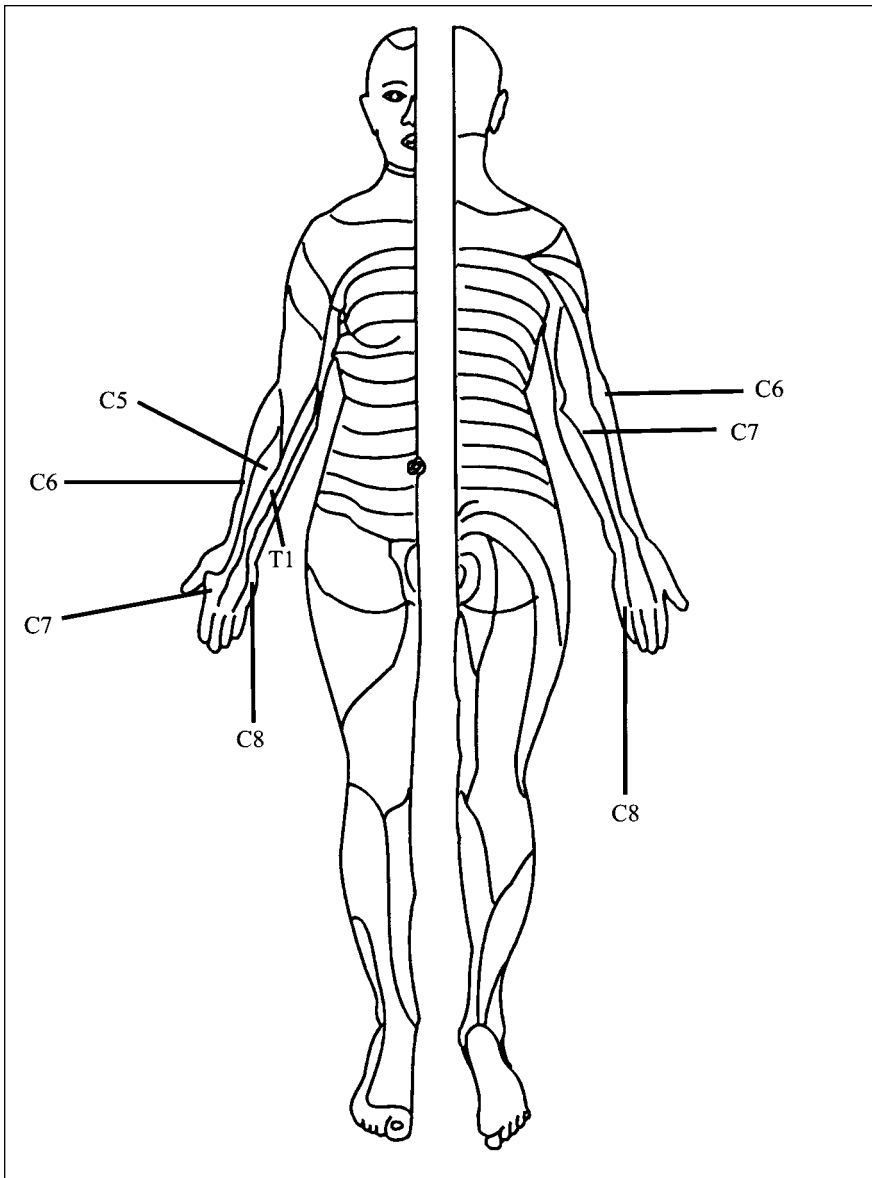
Each circular area of the body surface shown in Figure 1.4 is innervated by a spinal nerve. Specifically, spinal nerves A, B, and C innervate body surfaces 1, 2, and 3, respectively. The body surface innervated by the dorsal root of a spinal nerve is called a **dermatome**. Although each dorsal root (recall that there are 31 pairs) innervates its own specific dermatome (body surface) the dermatomes overlap to a large degree.

What this means, most simply, is that the entire surface of the body is partitioned and subdivided into specific areas served by spinal nerves. Figure 1.5 shows the dermatomes of the body associated with the spinal nerves. The dermatomes shown in Figure 1.5 do not overlap as indicated by the previous discussion. Figure 1.5 examines the spinal innervations and the spinal nerves of the arm. The cervical spinal nerve, labeled C6, innervates the area associated with the thumb. If you were to cut this spinal nerve, the area associated with the thumb and associated forearm would be incapable of sending information to the central nervous system. Because the peripheral radial nerve, composed of several spinal nerves, also innervates the thumb, it should be clear that there still would be some feeling in the thumb. In other words, cutting spinal nerve C6 does not eliminate all feeling and sensations from the thumb because there are other spinal nerves serving the thumb area via the radial nerve. There is a decrease in sensitivity, but not a complete loss of sensation.

## The Central Nervous System

As mentioned previously, the central nervous system is composed of two parts: the spinal cord and the brain. We begin by describing the afferent and efferent portions of the spinal cord and some of the intricate interactions within the cord.

We can assume that every pain you perceive depends on information within your brain. The maxim to remember here is a simple one: No brain, no pain. There are pathways within the spinal cord that transmit pain information from the extremities of the body. If the spinal cord were severed (a transection), you could obtain an idea of how the pathways within the spinal cord are organized. Figure 1.3(a) shows such a cross section with the incoming fibers arriving at the dorsal horn. The interior of the cord is shaped like a butterfly and is gray in appearance. This grayness is a clear cue that one is viewing millions of unmyelinated cell bodies. The cell bodies, and the myelinated pathways, have been extensively studied and labeled. The diagram shown in Figure 1.3(a) briefly introduces the terminology necessary to discuss the conduction and function within the spinal cord. Once we have this overview, we can continue our discovery within the brain itself.



**Figure 1.5.** Dermatomes of the Body Associated With the Spinal Nerves

### *Spinal Gray Matter*

The butterfly shape within the spinal cord is divided into three areas. Two of the classifications have already been discussed: the dorsal and ventral

horns. The third is the intermediate area lying between the two extremes. The intermediate zone consists of a dense grouping of cells known as **interneurons**. Interneurons are small neurons that interact with each other within the layers of the spinal cord. The dorsal horn, intermediate area, and ventral horn have been further divided in 10 separate layers (see Figure 1.3[a]). There are five **laminae** or layers within the dorsal horn, three laminae within the intermediate zone, and two laminae in the ventral horn. There are only about 5 of the 10 that are directly concerned with the transmission and integration of sensory information. These five are the laminae located in the dorsal horns. For clarity, the laminae are only shown on the right half of the spinal cord in Figure 1.3(a). For the time being, we label them from 1 to 5. When we discuss pain in a later chapter, more details of the function and interaction of these cellular layers will be apparent. Our goal at this point is to be aware of the fact that the cellular center of the spinal cord is fairly well defined and has distinctive structural and functional layers.

### *Spinal Pathways*

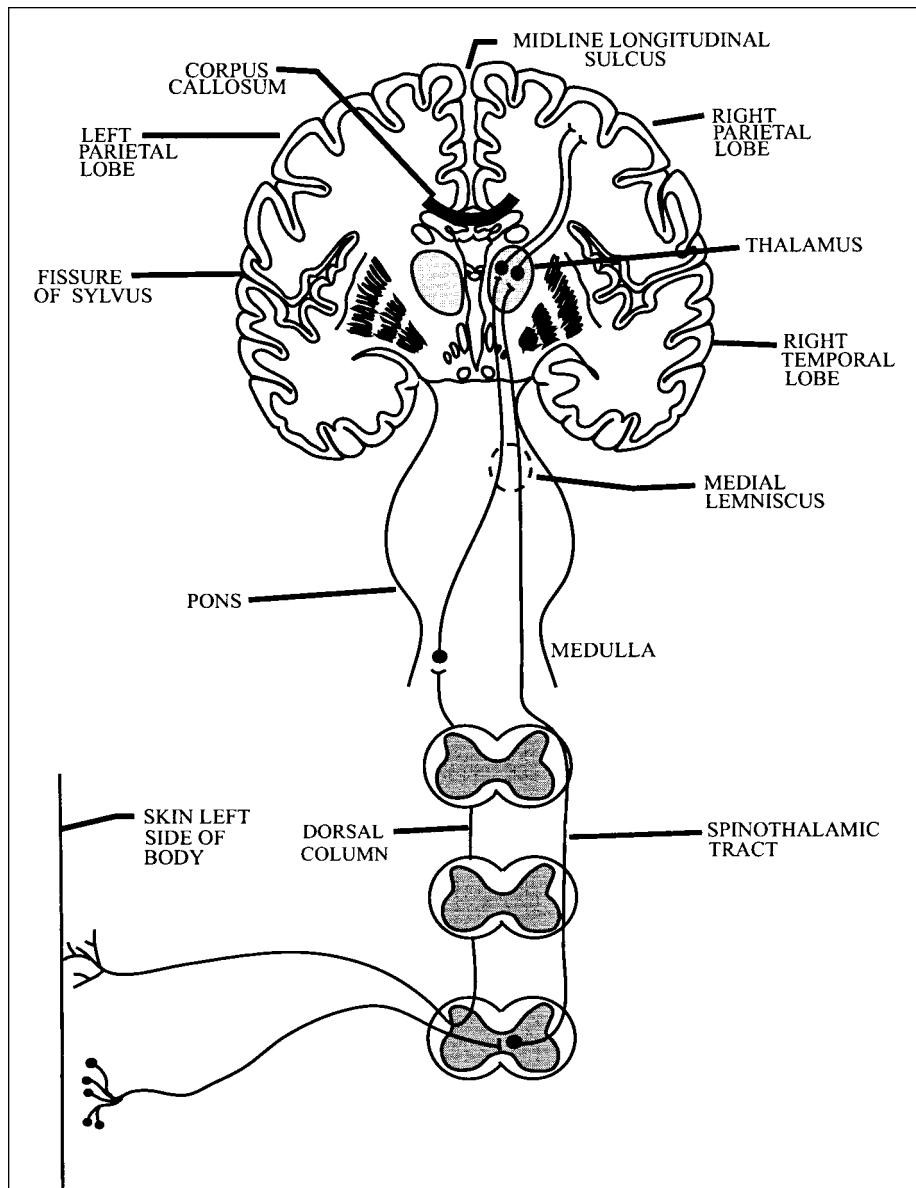
The pathways that surround the central gray matter conduct information to the brain—the afferent pathways—and away from the brain—efferent pathways. Figure 1.3(a) shows, in the white area surrounding the central butterfly, the two major afferent pathways: the **dorsal column** and the **lateral spinothalamic tract**. The afferent pathways are only shown on the left of the diagram. The pathways in reality, of course, ascend and descend throughout the area surrounding the butterfly central core. In addition to the afferent pathways, there are three major descending paths coming from higher centers in the brain: the **pyramidal tract**, the **extrapyramidal tract**, and the **ventral column**. At first glance, these paths may appear difficult to remember. However, once you get a feel for how these paths got their names, you can recall more easily their destination and location. The fibers in the dorsal column travel throughout the spinal cord and are named according to their dorsal location, near the back. Likewise, the fibers in the lateral spinothalamic tract are located laterally, to the side, of the spinal cord and conduct information from the spinal cord to an area within the brain called the thalamus. The lateral spinothalamic tract has also been called the anterolateral funiculus, the neospinothalamic tract, paleospinothalamic tract, and the spinoreticular tract. For our purposes of discussion, we retain the more descriptive nomenclature of the lateral spinothalamic tract.

The pyramidal tract is actually triangular or pyramidal in shape when viewed in cross section. The extrapyramidal tract is, therefore, just another pyramidal tract when viewed in cross section. Hence, it is an “extra” pyramidal pathway. The ventral column conducts information down the spinal cord in the ventral horn, near the belly. Finally, Figure 1.3(a) shows a small pathway called **Lissauer’s tract**, named after the individual who first described it. Many functional aspects of the nervous system got their names from their discoverers. Lissauer’s tract is relatively short in comparison with the other pathways. It is located dorsal and lateral to the dorsal horn. The fibers that enter this tract travel a short distance, both up and down, and then reenter the spinal cord. Thus, information that comes in at one level of the spinal cord makes contact with other levels of the spinal cord by way of Lissauer’s tract.

Although Figure 1.3 is instructive in terms of providing structural labels and an overall view of the organization of the spinal cord, it is far from complete. If we move on to Figure 1.6, we see a larger perspective of the sensory path from skin to brain.

Figure 1.6 shows a fiber entering the spinal cord via the dorsal root. Once the fiber has entered the cord, it joins other fibers already ascending in the dorsal column. For clarity, the other fibers are not shown. These first-order fibers (first in the sequence) travel upward, enter the brain stem, and make a connection within an area known as the **medulla**. Once the first-order fiber has made this connection the second-order axons leave the medulla and cross the midline to the opposite side of the body. The ascent then continues toward the **thalamus** through the pathway called the **medial lemniscus** (band or ribbon of fibers). The second-order fibers that enter the thalamus make a connection with the third and last group of fibers in the sequence. These third-order fibers then ascend to the cortex and terminate within the primary somatosensory cortex on the **postcentral gyrus** of the **parietal lobe**. A **gyrus** is a convolution or bump in contrast with a **sulcus** that is a groove or fissure. The entire pathway consists of just three sequences: first-, second-, and third-order neurons, and two connections. An important aspect of the dorsal column pathway is that the fibers enter the spinal cord and ascend **ipsilaterally** (on the same side). The fibers do not cross the midline until they have ascended to the brain stem in the medulla. Once they arrive at the brain stem, they cross the midline and continue their journey to the cortex. The right hemisphere receives the sensory activity from the left side, and the left hemisphere receives sensory input from the right side.

The course traveled by the fibers within the lateral spinothalamic tract differs from that in the dorsal column. Figure 1.6 also shows the lateral



**Figure 1.6.** Dorsal Column and Lateral Spinothalamic Tract

NOTE: The dorsal column travels ipsilaterally to the medulla and then crosses the midline. The spinothalamic tract synapses in the spinal cord and crosses the midline before ascending to the cortex.

spinothalamic path. The first-order sensory fibers that make up the lateral spinothalamic tract connect with the second-order fibers in the ipsilateral dor-

sal horn of the spinal cord. Following this first connection, the second-order fibers immediately cross the midline in the spinal cord to the contralateral side of the body. The second-order fibers then ascend, via the lateral spinothalamic tract, to the thalamus. Once in the thalamus, the third-order fibers are contacted to continue the ascent to the postcentral gyrus of the cortex.

Referring back to Figure 1.2, you can see additional information about the brain structure itself. This view shows the four lobes in the left hemisphere of the brain: the **frontal lobe** is behind the forehead, the **temporal lobe** is on the side near the temple, the **occipital lobe** is at the back of the head, and the parietal lobe is anterior to the occipital lobe and behind the frontal lobe. The fissure of Rolando, also called the **central fissure**, separates the frontal and parietal lobe. The central fissure is, from the side view shown in Figure 1.2, located near the central part or center of the brain. The area immediately behind or posterior to the central fissure, postcentral, is the parietal lobe. The postcentral gyrus is the final destination of afferent sensory information regarding bodily sensations such as touch or pressure on the skin. These portions of the parietal lobe are, therefore, directly associated with the somesthetic experiences. The particulars of this portion of the cortex are discussed in more detail in a later chapter.

Immediately in front, anterior, of the central fissure is the motor cortex that initiates the commands for movement. The occipital lobe is the final destination for visual sensations. The temporal lobe has functions for auditory sensations as well as the capacity to process visual information. In summary, the pathways for somesthesia terminate at the highest level in the postcentral gyrus of the parietal lobe. The primary visual processes terminate within the occipital lobe, and auditory and visual sensations reside within the temporal lobe. The fissure that runs laterally and divides the temporal lobe from the frontal and parietal lobes is the fissure of Sylvius. The fissure of Sylvius is also known as the **lateral fissure**.

Referring back to Figure 1.2, you can see two functional areas of the brain known as **Broca's area** and **Wernicke's area**. These two portions of the brain are discussed in detail in later chapters. For the moment, it is only necessary to note that Broca's area has motor-speech functions and is located in the frontal lobe adjacent to the motor cortex. Broca's area is directly associated with phonation, articulation, and facial expression. Speech is directly under the neural control of a specific area of the brain—namely, Broca's area. Wernicke's area, on the other hand, appears to be responsible for the comprehension and understanding of language. The two areas have connecting pathways. Actually, the complete linguistic dominance of Broca's and Wernicke's

areas within the left hemisphere is not entirely correct. The language functions are within the left hemisphere for about 90% of right-handed individuals. Left-handed people, however, have their linguistic dominance, speech production, and comprehension, in the left hemisphere only about 60% of the time. As usual, the brain and nervous system have shown their typical complexity.

The description of the nervous system to this point is exceptionally sketchy. Because there are more than 120 billion cells in the nervous system, perhaps many more, this is surely an understatement. In addition, there have been deliberate omissions of specific nuclei, cell groups, and pathways. This was done to simplify the discussion and still introduce structures, functions, and nomenclature needed in future chapters. As we proceed, the basic structures of the nervous system are expanded and modified for each sensory system. The meticulous details and the elegant organization of the nervous system are, unfortunately, beyond the scope of a single introductory text. Nevertheless, the goal is to entice you to examine and wonder about the most complex and intricate mechanism on earth: your brain.

### The Neuron

Thoughts, memories, and all sensations are based on the same brain process. They all operate and depend on the transmission of neural impulses. As a straightforward analogy, consider the nervous system to be like a giant telephone system. What makes memories, thoughts, vision, speech, hearing, and pain different is that each system has a different area code and telephone number. Some of the memories have toll-free “800” numbers. Some of the numbers are occasionally busy, and some are misdialed. The numbers are all different but they all work on the same principle—the conductance of electrical impulses along neural pathways. The telephone system has calls going everywhere simultaneously. Some are routed through the local exchange, some through an intermediate system, some through communication satellites. The brain uses this same basic idea. The brain has pathways (axons), local exchanges (interneurons), intermediate substations (thalamus), and higher-level communication satellites (cortex). The points of exchange in the brain, however, are vastly more complex than any telephone or computer system. Facilitation of transmitted information, inhibition of information, and modulation or changes in the information occur at billions and billions of points along the brain’s communication lines. In addition, the neural paths are monitored by literally millions of other neural paths. Shifts in the

information can and do occur because of such monitoring. The bottom line is that the brain, pathways, and neurons, all operate on the same principle: electrical-chemical impulses.

### *A Brief Overview*

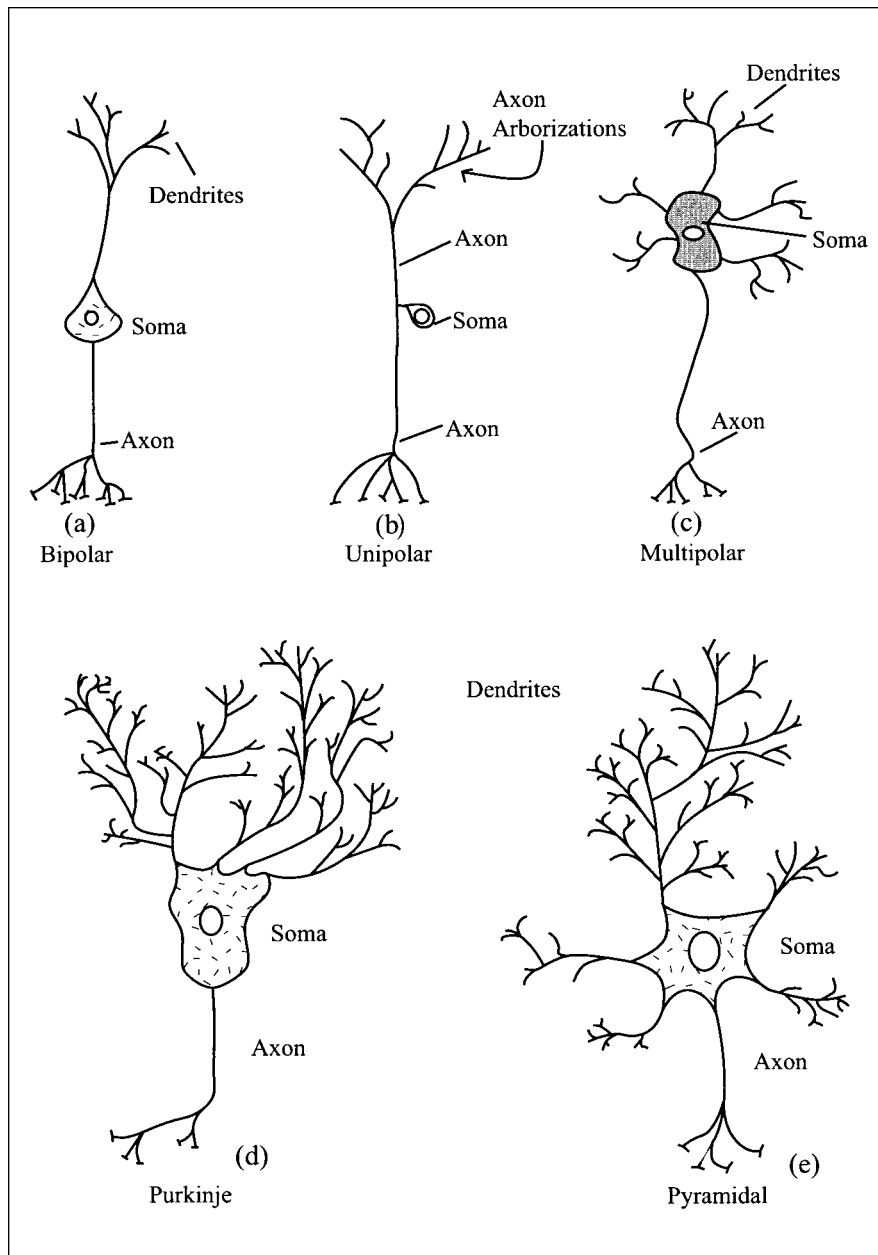
In this section, we extend our view by focusing on the small neural elements that comprise the central nervous system. These individual parts, the neurons, provide the foundation for the construction of perceptions. The uniqueness of the neuron has some similarities with the common digital computer. Both the computer and the neuron operate on a binary system. Our brain and the individual cells are, however, several magnitudes more versatile than any computer. No computer, in existence now or even planned for the future, can ever match the processing abilities of our brain. After describing the distinctive characteristics of neurons, we consider some methods of recording and measuring their activity.

Neurons, remember, are both the paths to the brain and the centers used to produce sensory perceptions of the world. Knowledge of their operation is critical to understanding sensory processes and daily interactions with the environment. Any error or misfortune in their normal activity affects our perceptions, thoughts, and memories. It is important that we have this background. All sensory systems are based on these cells operating smoothly. When neurons fail, we fail.

### *The Anatomy of a Neuron*

The nervous system is based on the electrical-chemical conductance of impulses over a multitude of paths. The neuron, the basic element of the nervous system, is a physiological structure and a unique entity in itself. Each neuron or cell is alive and independent, to some degree, of all other cells. It processes information that impinges on it by integrating (summing) all the messages it receives and then makes a “decision” whether to send the message on to other neurons. Even though all the cells operate on the same basic principle, they differ in size, shape, number of arborizations, number of receptive fibers (dendrites), and chemical messengers (neurotransmitters). In addition, we need to clarify an important element of the analogy. The neuron does operate on electrical charges and the conduction of impulses; however, the impulses are dependent on the chemical environment internal and external to the cell. The role of chemistry is examined more fully in a later section when we examine the origin of the electrical impulses.





**Figure 1.7.** Example of Neurons in the Nervous System

NOTE: (a) bipolar cell, (b) unipolar cell, (c) multipolar cell, (d) Purkinje cell, (e) a pyramidal cell.

Figure 1.7 is a schematic drawing of neurons found in different parts of the nervous system. The cells, although they differ radically in shape, have

several important features in common. Each neuron generally has four morphological regions:

1. The cell body (also called the soma or perikaryon)
2. Dendrites
3. Axon
4. The terminal end bouton

The end bouton is also referred to as the “presynaptic terminal” at the end of the axon arborizations. Each part of the neuron has a function of its own. Before we examine the common features, it is useful to examine the neurons shown in Figure 1.7 more closely.

Figure 1.7(a) shows a **bipolar neuron**. The name, as you may suspect, comes from the two fibers that originate from the cell body. One of the fibers is the dendrite and the other the axon. Based on the classical neuron theory, the dendrite and axon have two distinctively different functions. The function of the dendrite is to receive information from other cells whereas the axon conducts the information to the next cell in the sequence. The information flows in a unidirectional path from dendrite to axon. In respect to the bipolar cell shown in Figure 1.7(a), the dendrite receives the information and the axon sends it on. The bipolar cell can, for example, be found in the visual system at the back of the eye within the retina. More is said about this type of neural element when we discuss the visual system.

Figure 1.7(b) shows a neuron that we have discussed, although not specifically by name. This neuron is unipolar and has no dendrites; rather, it has a single axon emerging from the perikaryon that receives information at one end and sends it to the other end. This neuron is the common element in the conductance of information from the skin to the spinal cord. The cell body is located in the dorsal root ganglion.

A much more common neuron found within the nervous system is the multipolar cell shown in Figures 1.7(c), 1.7(d), and 1.7(e). Figure 1.7(c) shows a multipolar cell typical of the interneuron found in the central gray matter of the spinal cord and brain. The view of the multipolar neuron is much more complex than the previous two types of cells. There are several dendrites leaving the cell body. Each dendrite, in turn, has several branches and collaterals extending from its trunk. The branches also have small dendritic spines to which other neurons make functional contact. The multipolar

cell, then, has most of its function devoted to the dendritic reception of inputs from other cells.

When you consider the fact that a neuron's soma also receives information in a manner similar to that of the dendrites, the function of the multipolar cell immediately appears to be primarily for reception and integration. Once the information is integrated, the cell makes a decision. The cell either forwards the message to the next cell or does not. Figure 1.7(d) and 1.7(e) show different multipolar neurons. These are the Purkinje cell from the cerebellum and the pyramidal cell from the cortex.

When you think about these cells, particularly the multipolar cells with their vast number of inputs, the complexity of the brain and nervous system becomes almost overwhelming. For example, we have already pointed out that the central nervous system contains an estimated 100 to 120 billion neurons, or more.

When you consider the fact that each multipolar cell probably makes about 1,000 connections with other cells (the axon has its collaterals and arborizations) and in turn receives literally thousands of inputs from other cells, the total number of possible functional connections within a human brain becomes truly astonishing. Scientists estimate the number of connections is as large as 10,000,000,000,000,000—ten quadrillion, and it is probably an underestimate. This estimate is larger than the estimated number of stars in our galaxy.

The neurons shown in Figure 1.7 are representative of the diversity found within the nervous system. Just as in the case of snowflakes, no two neurons are alike. This single fact makes the nervous system utterly unknowable in minute detail. Fortunately, the differences among neurons lie primarily in their morphology, not their basic functional operation. Because of this functional similarity, the telephone cable analogy is quite correct when it comes to the basic principle that all neurons conduct impulses along predetermined paths. This principle has allowed scientists to discover the neurological functions that permit an individual to sense the environment, think, have emotions, learn, remember, and be alive.

Our discussion has thus far touched on the function of three of the four features of a neuron. These are the dendrite, soma, and axon. What remains to be discussed is the presynaptic terminal or end bouton found at the end of the axon arborizations. This portion of the neuron is, perhaps, the most important because communication occurs at this point.

The presynaptic terminal, by its very name, suggests that it is only a part of a more complex structure. This is exactly the case. The functional connec-

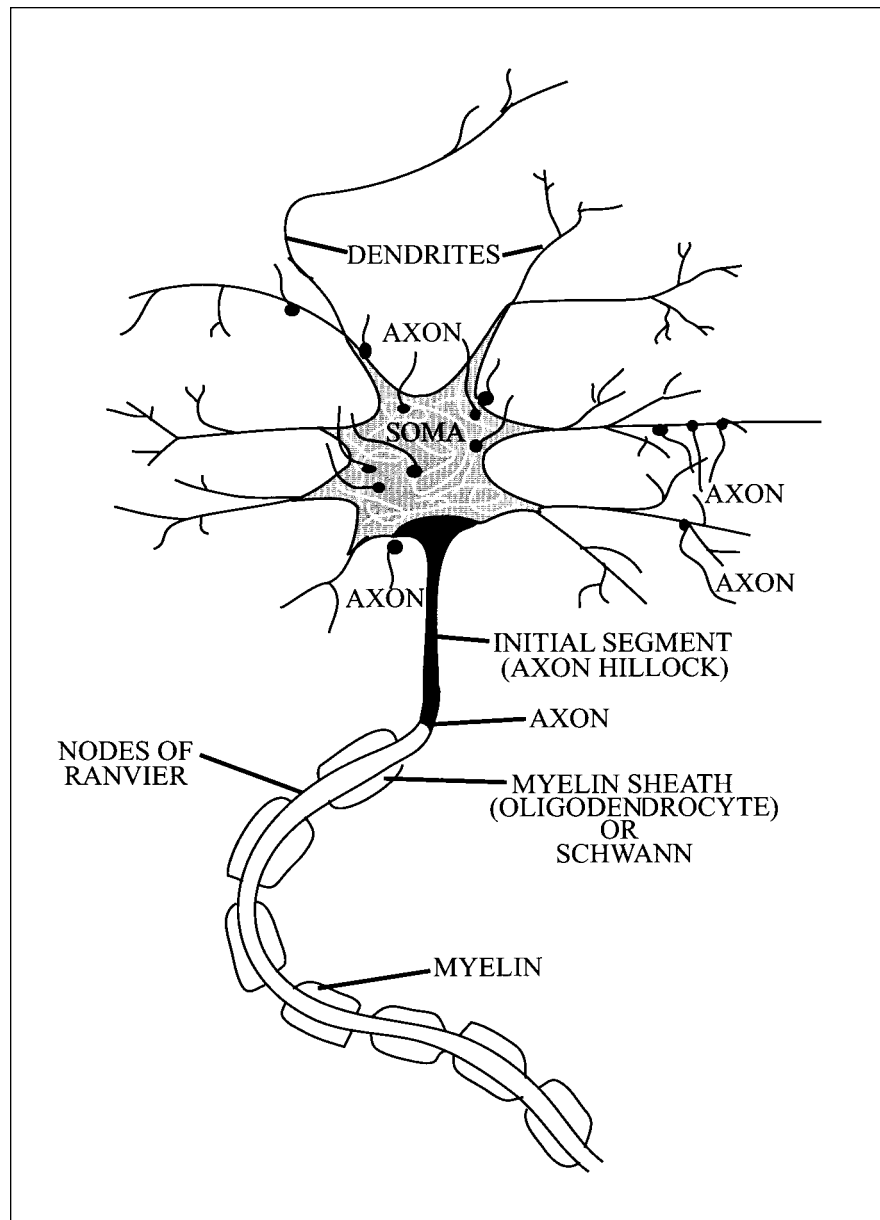
tion between neurons is called a **synapse**. The synapse consists of three parts. The initial part is the structural **end bouton** found at the end of the axon. The second part of the synapse is in reality not a physical structure at all; rather, it is the gap between the axon end terminal and the neural structure on which the end bouton is functionally attached. The gap is known as the **synaptic cleft**. The post side of the synaptic cleft (the end bouton is the presynaptic side) is referred to as the postsynaptic portion of the functional connection. Thus, when a synapse is discussed it is in terms of the presynaptic terminal, the cleft, and the postsynaptic portion of the connection.

You should keep in mind several aspects of the synapse. The vast majority of synapses occur when an axon connects with a dendrite, **axodendritic**, or a soma **axosomatic**. Often there is a dendritic spine formed on a dendrite for the synaptic formation. Two other synaptic designations are the **axoaxonic**, synapse of one axon on another, and the axoaxonic and axodendritic combination, respectively.

A closer view of a representative neuron is provided in Figure 1.8 that shows a schematic of a multipolar neuron with several synaptic connections from other neurons. The synapses are axodendritic and axosomatic. Surrounding the single long axon is a myelin sheath. There are separations or interruptions in the myelin called nodes. These nodes, named after the individual who first observed them, are the **nodes of Ranvier**. The myelin sheath, as noted previously, is not found on every axon. However, when myelin is present it is the result of a specialized supporting cell. Within the central nervous system, myelin is formed by a glial cell known as an **oligodendrocyte**. This cell wraps itself around the axon in a tight spiral. In the peripheral nervous system, the myelin sheath is the result of a different glial cell called the **Schwann cell**. The general effect of having an axon wrapped in the myelin is to improve the speed of conduction of neural impulses. Unmyelinated fibers conduct their messages at a much slower rate. The swiftness of conduction in the myelinated fibers is the result of a process called **saltatory conduction**. When an axon is myelinated, the electrical impulses functionally leap from node to node along the axon.

This “leapfrogging,” from one node of Ranvier to the next, increases the speed of conduction by a factor of six. At the end of the axon, which in humans may be over a meter in length, are the arborizations and synapses. One need exert very little intellectual effort to imagine the length of some of the axons in giraffes or pachyderms.

The shaded area of Figure 1.8, the point at which the axon leaves the soma, is known as the **axon hillock** or the **initial segment**. This particular sec-



**Figure 1.8.** A Myelinated Multipolar Neuron With the Nodes of Ranvier and Multiple Axodendritic and Axosomatic Synapses

tion of the neuron plays a key role in determining whether the cell initiates an impulse within the axon. This section of the neuron is examined more closely in a following section of this chapter.

### *The Supporting Glia Cells*

The nervous system is not an entity that consists entirely of neurons. In fact, the nervous system has another group of cells that is 9 to 10 times more numerous than neurons. (Can you imagine 900 to 1,000 billion more cells in the brain?) This group of cells is known as **glia** or sometimes **neuroglia**.

There are several different subclassifications of glia cells. For our purposes, we need only be concerned with astrocytes, oligodendrocytes, microglia, and Schwann cells. As noted previously, the oligodendrocytes and Schwann cells act primarily to provide myelin covering to the axons within the central nervous system and peripheral nervous system, respectively. The astrocytes, on the other hand, apparently have nutritive functions (Kimelberg & Norenberg, 1989). They make contact with neurons while simultaneously in contact with blood capillaries. In addition, when an injury occurs in the nervous system both the microglia and the astrocytes become actively engaged in the removal of the debris produced by the trauma and degeneration of the nerve cells. It is the glia cells, primarily the astrocytes and microglia, which react to the trauma and energize the recovery process. Unfortunately, the proliferation of the astrocytes and microglia can also lead to a **glial scar**. The glial scar is a possible reason for the lack of axon regeneration within the central nervous system following an injury. The fact that most central nervous system neurons are no longer capable of cell division accounts for the lack of new neurons. Some recent evidence suggests that the formation of new neurons in adult mammals is possible.

### *A Little History*

Let us take a few moments to review the past endeavors of scientists who have given us the current panorama of the synapse and the neuron. The synapse is perhaps one of the most interesting aspects of the nervous system.

The history of the discovery and understanding of the synapse covers several decades of intellectual debate and experimentation. There were, before the advent of the electron microscope and direct observation, differences of opinion regarding the manner in which electrical impulses crossed from one neuron to the next. According to the classical neural theory espoused earlier, there is a one-way path from the transmitting axon to a receptive dendrite or cell body. In the view of one group of investigators, a chemical diffuses across a synaptic cleft, a gap that was yet to be observed, to accomplish transmission from cell to cell. The chemical hypothesis said that the presynaptic end

bouton released a chemical that, when it reached the postsynaptic side, initiated activity in the receiving neuron. Many individuals supported this view. If there is to be a controversy, however, it is important to have colleagues who support your theory and a group of colleagues who believe otherwise. Thus, the opposing camp reported strong and convincing arguments that the synapse is not chemically mediated; rather, they contended that information was passed from neuron to neuron by the electrical impulse simply being passed on by a physically present conductor among cells.

The debate continued until the weight of the evidence began to suggest that the chemical hypothesis was correct. One bit of evidence, for example, to support the latter position was that the time required for an impulse to cross a synapse was too long to support the electrical hypothesis. The time required to cross the synapse was measured to be in the neighborhood of 0.3 to 0.5 milliseconds (0.0003 to .0005 of a second). Although this appears to be a very short time, it is about the amount of time that is necessary for chemical release, diffusion, and the postsynaptic contact. This and other types of evidence continued to act as instigators for scientists to find a chemical that permits the transmission of an impulse from one neuron to the next. The search has yielded several chemical mediators. These chemical transmitters, discussed later, are critically important in the functioning of the nervous system and the sensory processes we take for granted every day.

The story, however, does not end here. The recognition of chemical transmitter substances and the direct observation of a synaptic gap between the neurons have secured the chemical mediation hypothesis. This conclusion does not eliminate the possibility of an electrical conductance by a direct structural connection between the neurons. The electron microscopist not only provided evidence to support the chemical mediation but also discovered the evidence for the electrical conductance. There are, in fact, physical connections called **gap junctions** between some neurons. These gap junctions provide the necessary conduit for the flow of electrical impulses. The gap junctions act like a pipeline between neurons. Thus, as is often the case in science, both of the synaptic hypotheses are correct. The electrical synapse is in the minority, however. The chemically mediated synapse is far more abundant within the nervous system. The electrical synapse, also called **electrotonic** transmission, has been known to exist in invertebrates and more recently was found in vertebrates. However, their occurrence is rare in humans.

A final bit of history important in the study of the nervous system is one that concerns many people. How do scientists determine what neurons, glia, synapses, and pathways look like and how did they discover the brain's organization and function?

The answer, which seems so obvious, is more complex than you might suspect. The obvious conclusion is that they looked with a microscope and drew pictures of what we saw. However, about 150 years ago anatomy was done painstakingly by dissection and macroscopic study of the parts. It was not until the 1800s that the appearance of the microscope and methods to stain tissue with dyes such as silver nitrate were found, and great strides were made in the morphological study of the nervous system. The microscope greatly enhanced the anatomist's ability to trace and follow pathways within the animals examined. It was well-known at that time that when central nervous system tissues were injured they degenerated. The degeneration of injured tissue provided, then as now, a built-in method of learning about nervous structure and function. When an axon is cut, an **axotomy**, it begins to degenerate distally and proximally from the site of the lesion. The initial degeneration is in the direction of impulse flow, away from the cell body and toward the axon terminal. This is known as anterograde degeneration, also called **Wallerian degeneration** and **orthograde degeneration**. **Retrograde degeneration** refers to the degeneration proximal from the zone of trauma, toward the cell body and dendrite. The loss of myelin, axon, dendrite, and soma can be mapped by the use of stains and dyes that differentially mark the degenerating parts of the cell. In this way, the origin and destination of the cut fiber can be determined.

Advances in cell study in the 1970s have used enzymes and radioactive markers to trace the fibers and reveal the morphological details of neurons. These substances are taken up by the metabolic activity of the neuron. Two important substances used to delineate the neural elements of a cell are the enzyme **horseradish peroxidase (HRP)**, and radioactive  $^{14}\text{C}$ -deoxyglucose. The dendrites, soma, and axon are then identified and inspected. Tracing techniques have yielded the line drawings and photographs published in scientific journals. Knowledge concerning neural structure and pathways continues to grow in quantum leaps.

### *Single-Cell Recording*

You already know by the heading of this section that the study of individual neuronal activity is possible. What is described here is a brief overview of endeavors that have led to Nobel prizes for scientists, cures for diseases, and intellectual pursuits for hundreds of people, including you.

When we speak of single-cell recording, or unit response, it is important to keep in mind that there are two basic procedures used to study the activity of living neurons. Both procedures detect and measure electrical voltage or



current and variations in voltage or current. The variations may occur because of normal spontaneous activity or because of deliberate external stimulation under experimenter control. In either case, the objective is to record neural activity.

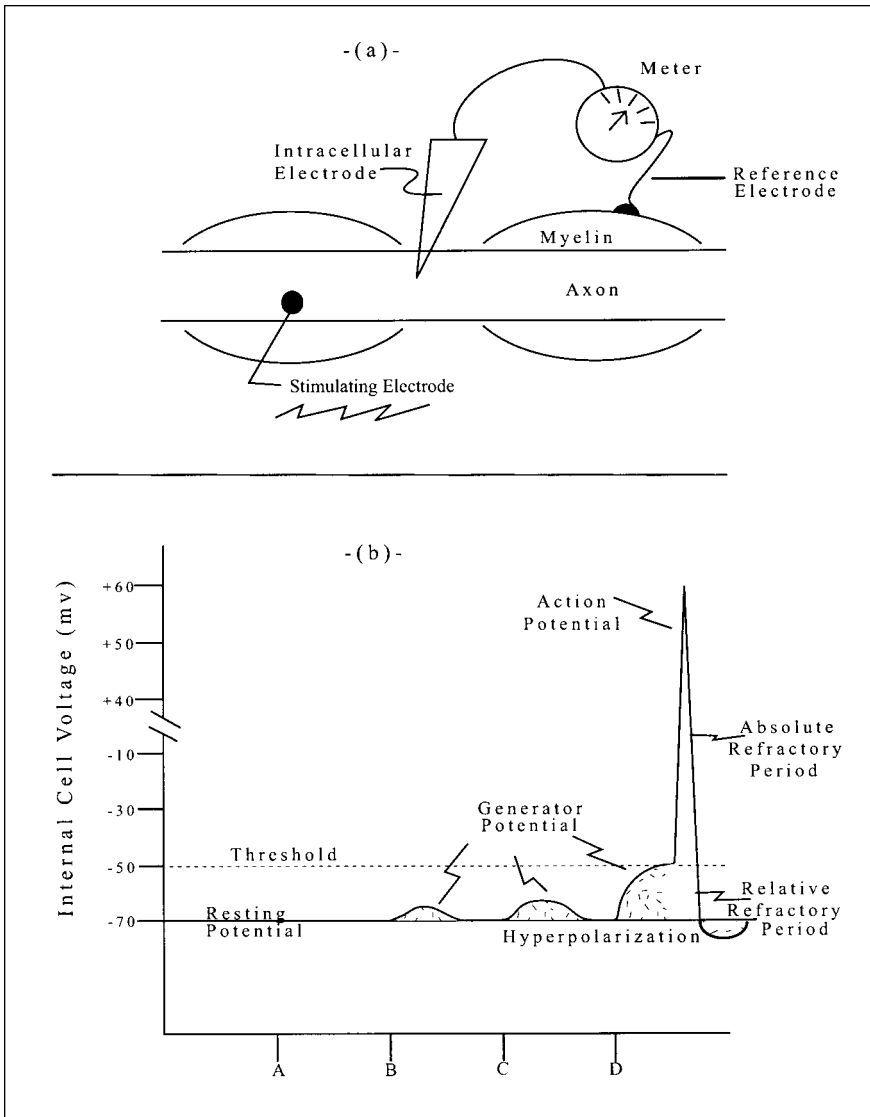
The first procedure entails recording electrical activity from outside the cell. The placement of a small microelectrode, approximately 10 microns in diameter at the tip, is placed near a living and active cell. This is the extracellular procedure because the electrode does not enter the cell from which it is recording. When the electrode is placed close to a cell, it is possible to record the electrical activity of the cell as the response flows by the electrode. Extracellular recordings do not reveal the small voltage variations within the neuron; rather, they reveal the relatively large impulses, about 100 millivolts (mv), that are conducted past the electrode. These impulses are formally known as the **action potentials** and are based on the transmission of information from one neuron to another. The action potentials are a large part of the secret to the nervous system, sensation, movement, thought, memories, and life itself (Hodgkin, 1964, 1992; Peters, Palay, & Webster, 1991).

The second method of examining the neural activity is intracellular recording. In this procedure, an electrode 1.0 micron or less in diameter is inserted directly into a cell. The electrode may be placed in the soma or within an axon. When the microelectrode tip is inside the cell, without damaging the cell, you can examine not only the larger action potentials that are recordable by the extracellular electrode but also the low-level electrical activity that leads to action potential generation. These small electrical changes are of different types and are known by various labels, but for the time being we call these smaller voltage variations, approximately 20 to 25 mv, **generator potentials**. This label is, in many ways, quite descriptive of these small electrical changes. These intracellular recordings are more difficult to obtain and reveal different types of information than does the extracellular procedure. Both techniques, however, are extremely important in the investigation of the nervous system and sensory processes.

### *Electrical Potentials of the Neuron*

The stage is set now for the details of neural activity. The morphology has been explained, and the electrodes are waiting for our attention. So let us begin by examining Figure 1.9(a).

This schematic diagram shows an axon with an intracellular electrode within an axon. The electrode is attached to a meter to indicate changes in voltage. There must be, as any physics major knows, another electrode placed



**Figure 1.9.** Physiological Recording of Neural Activity

NOTE: (a) example of intracellular recording electrodes and (b) results of four experiments that depolarize the cell.

somewhere if an electrical circuit is to be completed. This latter electrode, the reference electrode, is placed outside the cell membrane. This recording system, if it is sensitive enough, should measure the voltage difference across the cell membrane. Specifically, the two electrodes provide a quantitative differ-

ence, in millivolts, between the inside of the cell where the intracellular electrode is placed, and the outside of the cell where the reference electrode is located.

Figure 1.9(b) shows the results of a set of four experiments. Each experiment is an independent study with a different stimulus intensity. The four stimuli are applied to the neuron at four different times. The stimuli vary in their strength. Let us assume that the investigator has chosen four values of increasing magnitude. They are Stimulus A (no stimulus), Stimulus B (weak intensity), Stimulus C (moderate intensity), and Stimulus D (high intensity).

The experiment is discussed in four stages. Each stage is associated with one of the four stimulus intensities. We record the voltage across the membrane starting at the point when the stimulus is turned on (a brief electrical impulse) and stopping when the voltage returns to the starting value. The astute observer notes that there are actually two questions being asked by the investigator in this experiment. First, how does the voltage in millivolts change as stimulus intensity changes? Second, how does the voltage in millivolts change as time passes?

*Stage I.* The initial recording is done with Stimulus A. In this condition, we prepare the neural fiber for an electrical shock in the usual manner. However, the intensity of the stimulus is set to 0.0. In this condition, it is assumed that the voltage measured across the cell membrane is representative of the cell when it is in an unstimulated or resting state. It is important to emphasize that the procedures used to record the activity of a neuron with a stimulus intensity equal to 0.0 must be the same procedures as those used when a non-zero stimulus intensity is applied. If valid conclusions are to be drawn from the experiment, all stimulus conditions must be the same except for stimulus intensity.

The results of the experiment using Stimulus A is shown in Figure 1.9(b). The voltage is recorded at a constant  $-70$  mv. The  $-70$  mv is interpreted to mean that the inside of the cell is negative relative to the outside of the cell. The neuron, regardless of how you measure it, has a value of  $-70$  mv when it is inactive and at rest. This voltage is called, not surprisingly, the neuron's **resting potential** when it is nonconducting, and unstimulated. This resting potential is the baseline you use when examining the effects of other stimulus values.

Because the inside of the cell is negative and the outside is positive, the cell is considered to be **polarized** in its resting condition. In other words, the cell has two poles, one negative inside and one positive outside. If you were to

**depolarize** the cell, you need to move the  $-70$  mv potential toward  $0.0$ . If a stimulus event occurred that caused the voltage difference across the membrane to move toward zero, you could say that the cell was in the process of depolarizing. Any event that depolarizes a cell moves the voltage more positive—that is, toward  $0.0$  from a  $-70$  mv. Any event that caused the resting potential to become more negative could make the cell more polarized. The cell, in this latter case, is **hyperpolarized**.

You should keep this terminology firmly in mind as you progress through the book. A neuron's momentary state is always considered relative to its normal resting state. Thus, the terminology of hyperpolarization and depolarization should become second nature as you proceed. If a cell is depolarized, the internal potential is more positive than the resting value; if the cell is hyperpolarized it has become more negative within the cell.

*Stage II.* Stage II of our experiment proceeds exactly as before. However, in this case a weak stimulus, Stimulus B, is applied. The results are shown in Figure 1.9(b) as a depolarization of the cell. The application of the stimulus caused the voltage to move from  $-70$  mv toward  $0.0$ . The magnitude of the depolarization is small. In a period of approximately 10 milliseconds (msec), the cell changed from the resting state of  $-70$  mv to  $-67$  mv and back again to  $-70$  mv. This is the first appearance of the generator potential. Let us try a more intense stimulus.

*Stage III.* The experiment is repeated exactly as before. This time the stimulus to activate the cell is increased to a moderate value, Stimulus C. Figure 1.9(b) shows the results for this condition. These data are very similar to those in Stage II with the weak stimulus. The exception is in the magnitude of the depolarization. The depolarization is 7 mv in Stage III (from  $-70$  mv to  $-63$  mv). If a conclusion were to be drawn from the data collected thus far it could run along the following lines: The size of the generator potential is a direct function of the stimulus intensity. The more intense the stimulus, the greater the depolarization.

*Stage IV.* The last stage of the experiment is conducted using Stimulus D, the most intense of the four levels. The recording begins, as before, when the stimulus impulse is turned on. The data are collected continuously until the cell has returned to its resting level of  $-70$  mv. What do the data look like now?

Figure 1.9(b) shows the variation in voltage across the cell membrane as a function of time after stimulus onset. Figure 1.9(b) shows an initial depolarization when Stimulus D is turned on. It is similar to that seen in Stages II and III. That is, there is a relatively slow depolarization from  $-70$  mv to  $-50$  mv during the first few milliseconds following the stimulus onset. This portion of the data is the generator potential. Following this relatively slow depolarization, a unique feature of the data begins. At  $-50$  mv the internal voltage of the cell makes a brief and rapid positive-going spike. This rapid depolarization, and its immediate return to a polarized state, lasts about a millisecond and is, as previously noted, the action potential. *Spike, impulse, or neural impulse* are used interchangeably with action potential. The action potential begins at  $-50$  mv as indicated by the label *threshold*. The spike is considered complete after it has returned to the threshold value. The period of time required for an action potential to occur, 1 msec, is the **absolute refractory period**. The portion of the curve immediately following the spike is the **relative refractory period**. A portion of this latter interval consists of a period of hyperpolarization.

The experiment is now complete and the results can be interpreted. The first thing to note is the difference in voltage for the first three stages of the experiment in contrast with the change in voltage in Stage IV with Stimulus D. In the latter situation, when the most intense stimulus was used, an action potential occurred. The spike was nonexistent in the first three stages of the investigation. If we were to repeat the final stage of the experiment, we could find the same result every time. Each time Stimulus D, or a stimulus more intense than D, was presented a spike could occur. The interesting aspect of the replications is that the spike could be initiated at the same voltage level every time,  $-50$  mv. A fixed amount of depolarization is required to generate a neural impulse. If a spike is to be produced, the cell must be depolarized to a threshold value. This threshold is  $-50$  mv. If the slow depolarization, the generator potential, does not reach this threshold value, no impulse is produced. The action potential, then, either occurs or it does not; it is an all-or-none phenomenon. When the depolarization reaches the threshold value, the impulse is initiated. It completes the cycle from threshold-to-maximum depolarization and back to threshold in a millisecond. The size of the action potential is always the same for any one neuron.

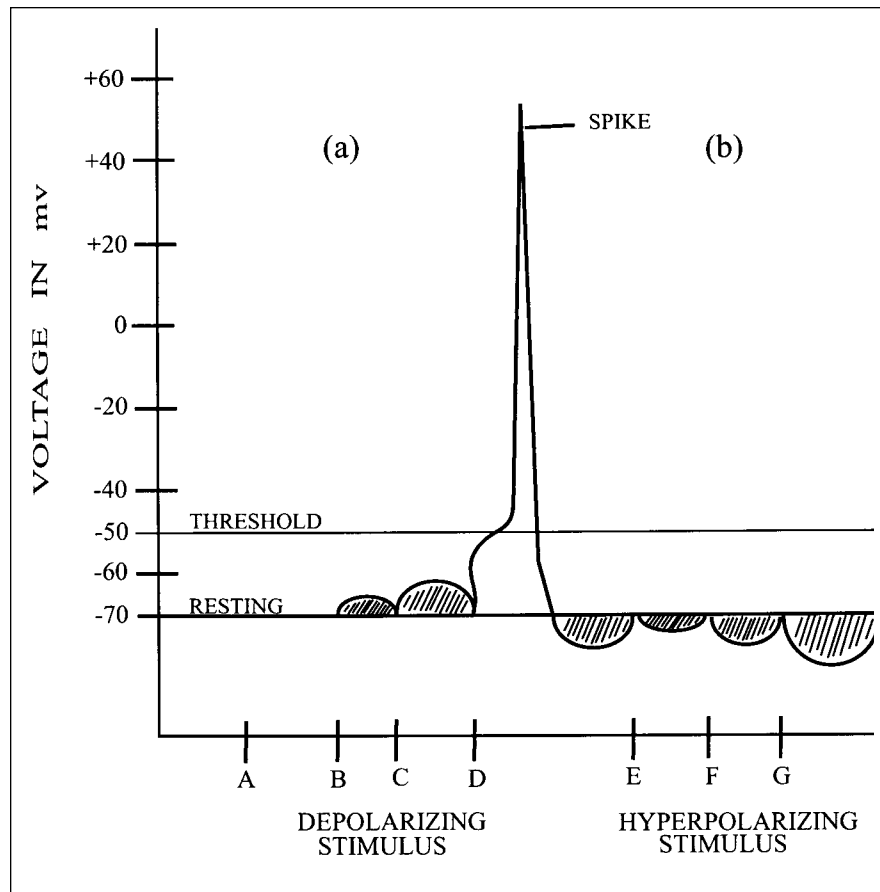
The conclusions of the experiment may be summarized by noting that action potentials fire (are generated) on an all-or-none basis and are initiated when the generator potential reaches the threshold value. The magnitude of the generator potential is dependent on the stimulus intensity. A weak stimu-

lus produces a small generator potential, also referred to as an electronic depolarization; a stronger stimulus produces a larger generator potential. The intensity of the stimulus does not affect the size of the action potential. Every action potential produced by any one neuron is the same magnitude.

### *Excitation and Inhibition*

Thus far, the experiment has worked out well. The results are clear-cut. The conclusions are straightforward and easily interpreted. The stimulus that was used to generate the potential variations across the cell membrane was, however, somewhat loosely defined in the previous paragraphs. The stimuli were simply defined as electrical shocks with different intensities. The fact of the matter is, however, that the parameters of the stimulus are critically important in obtaining the observed results. It should come as no surprise that there are several ways in which the stimulus is applied. We used just one of them; namely, we applied a brief electrical shock so that the cell depolarized. The stimuli could be presented in such a way that they increase the negativity of the cell. If these latter stimuli were used, the results would have been remarkably different. Figure 1.10(a) demonstrates the results of the experiment we just completed, depolarization and action potential generation, and shows a new outcome in Figure 1.10(b). This experiment assumes that the stimulus was reversed in its effect. The internal portion of the cell became more negative. The stimuli are labeled E, F, and G and represent negative stimulus intensities in an increasing order of magnitude. The results of such an experiment are clear: The cell becomes increasingly hyperpolarized and action potentials never occur.

The results of the entire experiment, including the negative stimulus condition, show that the internal voltage can vary both above and below the resting value of  $-70$  mv. When a stimulus depolarizes the cell, it is possible to generate a spike. When a stimulus causes the cell to become hyperpolarized, there is no spike generation. It may have occurred to you that if a cell happens to be hyperpolarized when confronted with a depolarizing stimulus, the cell is less likely to generate an impulse. This is indeed the case. The further removed from the critical threshold potential ( $-50$  mv) the cell is, the less likely it is that the cell becomes depolarized enough to initiate an impulse. If, for example, a cell is hyperpolarized to  $-75$  mv, the amount of depolarization required to initiate a spike is 25 mv (from  $-75$  to  $-50$  mv). If the cell is at resting potential, it requires just 20 mv of depolarization to initiate the spike ( $-70$  to  $-50$  mv). A cell that is hyperpolarized is in a state of **inhibition**, and the inhibition must



**Figure 1.10.** Depolarizing and Hyperpolarizing Activity in a Neuron

be overcome if a spike is to be initiated. In contrast with inhibition is the idea of **excitation**. As you have already guessed, excitation is associated with the depolarization of the cell. A stimulus, then, can lead to depolarization (excitation) or hyperpolarization (inhibition).

The ideas of inhibition and excitation are extremely important in understanding the nervous system and sensory processes. The complexity of the system is almost overwhelming when you consider the fact that each neuron is at any moment in time in a continuous state of agitation. Furthermore, as you already know, there are literally thousands of synapses attached to each neuron. Each one of these synapses is shouting at the top of its “chemical” voice. Some synapses are excitatory and urgently request that the post-synaptic cell depolarize to immediate activity (excitation). Other synapses are inhibitory in nature and request an urgent message of inhibition and

hyperpolarization. You might think that the cacophony of such a situation, repeated billions of times, would be utter chaos. This, fortunately, is not the case. Each neuron makes a calm and rational decision. The decision is made at the initial segment or axon hillock of the neuron (see Figure 1.8) through a process similar to algebraic summation. That is, excitation (depolarization) and inhibition (hyperpolarization) are “added up” by the cell with depolarization considered as positive and hyperpolarization as negative. If the result of the summation is a depolarization to threshold ( $-50$  mv), at the axon hillock, then an action potential is initiated. This summation is a continuous algebraic integration of all synaptic inputs. An action potential is generated only when the generator potential reaches the threshold value at the initial segment.

### *Intensity Coding*

It may have occurred to you that the generation of a single action potential, as discussed in the previous experiment, is not sufficient to produce a sensation, movement, or thought. This is certainly the case. A single impulse from a single neuron is an insignificant event in the operation of the entire brain. There are literally billions of action potentials being generated in your brain and nervous system at this very moment. This occurs even while you sleep. There is a continuous bombardment of activity from one neuron to the next, via the synapses, which gives rise to life and active organisms—humans, cats, dogs, insects, frogs, and so on.

The interesting aspect concerning the brain activity and the sensations that occur is that everything is done by action potentials. However, the end result of neural activity is clearly not the same. Vision is not the same as touch. Hearing is certainly different from taste. Yet, all these sensations are based on the same brain process: the neural impulse and the associated synaptic activity. The reason for the different sensations is, to a large degree, the result of where the impulses originate and where they are sent. Impulses that originate from the skin and end up in the somesthetic area of the brain do not produce a visual perception. Impulses from the auditory nerve do not end up in the visual cortex. Thus, the telephone analogy is accurate in many respects. This “direct line” concept of neural operation is often referred to as the **specificity theory**. This theory is encountered repeatedly as we progress through the book.

Although the specificity theory can help account for intermodality differences, differences between different sensory systems, a question still exists



concerning intramodality differences, differences within the same sensory system. We all acknowledge that sounds are seldom of equal loudness. The difference in loudness, an intramodality difference, raises the question: What is the neural cause for the variation of intramodality sensations? Neuroscientists, physicians, engineers, and sensory psychologists (among others) are interested in the processes that cause these various sensations.

The examination of sensory systems has resulted in a variety of procedures and techniques. One fruitful methodological attack was represented by our previous experiment: The direct neurological or physiological approach. A second very useful procedure is psychophysics (Kandel, Schwartz, & Jessel, 1995; Posner, 1989). Psychophysics, for the moment, may be briefly introduced by noting that it is a methodological procedure directed toward elucidating the relationship between a stimulus and a sensory response. The stimulus, for example, may be a light or sound of a certain magnitude. The response may be a simple button press, a verbal response, or an animal's behavior. Psychophysics finds its primary use in laboratories directed toward sensory questions using humans and intact organisms. Seldom are invasive procedures used—for example, no ablation, lesion, axotomy, or single-cell recording. Because you seldom find a human volunteer for a neurological ablation or single-cell recording investigation, the psychophysical procedure is extensively used with humans. Furthermore, ethical and moral obligations clearly take precedence with investigations using both human and animal participants.

Thus, much of the human and animal data come primarily from experiments that use psychophysical procedures. Although there are experiments that have used human participants with nonpsychophysical procedures, these latter investigations have occurred under strict ethical conditions, legal and medical. These latter experiments were accomplished during necessary brain operations. They are discussed in later chapters. Our aim now is to examine the relationship between the stimulus intensity and the organism's response, both psychophysically and physiologically.

### *Physiological Recording*

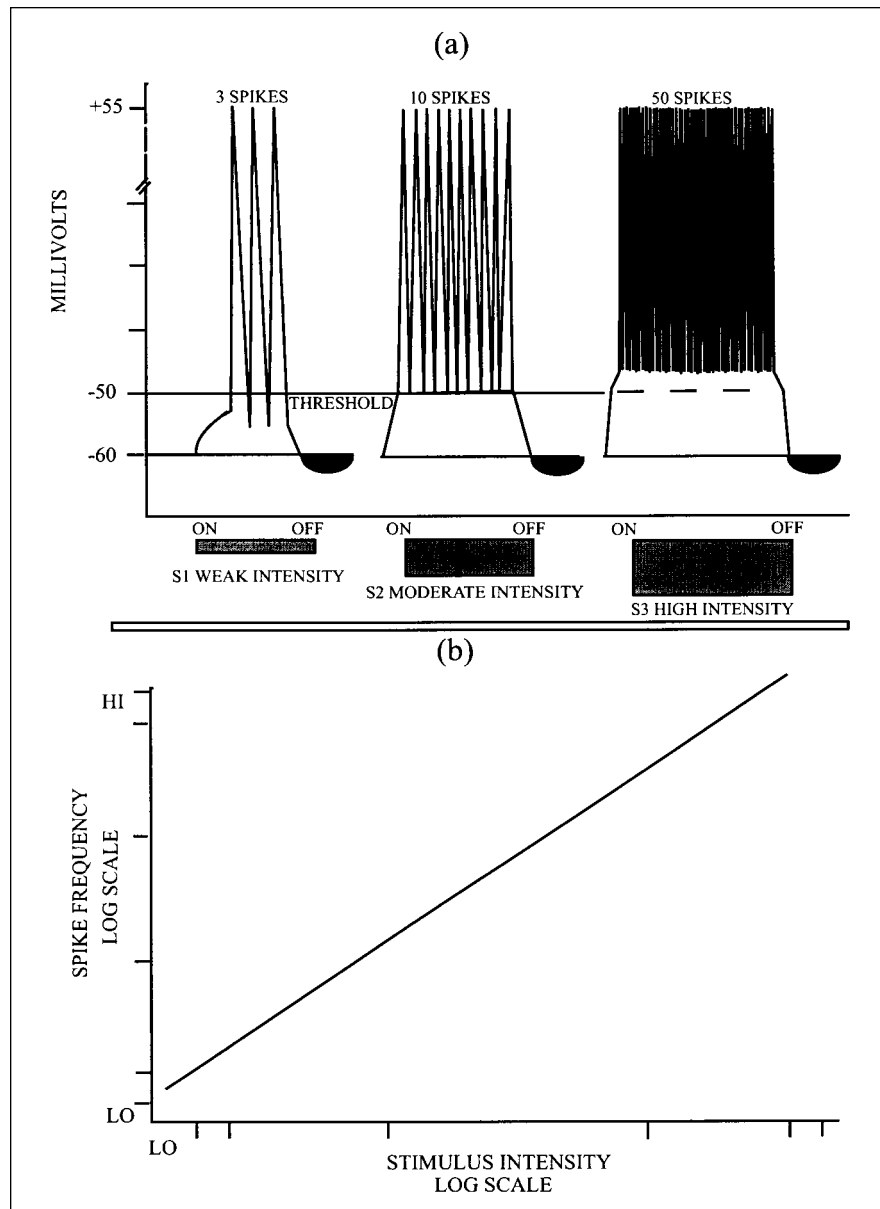
Because we know that sensations are dependent on action potentials, stimulus intensity must somehow be encoded in the form of neural impulses. The impulses are dependent on stimulus intensity first because the stimulus must be intense enough to cause the generator potential to reach threshold and generate a spike. Thus, one of the goals of investigations in sensory pro-

cesses is to break the neural code and discover how the nervous system generates the multiplicity of sensations from action potentials. A first step in this enterprise is to examine more thoroughly the relationship between neural impulses and stimulus intensity.

The procedure we use is the one we are familiar with from the previous single-cell experiment. The intracellular electrode is implanted within the cell, and the neutral electrode is placed outside the cell membrane. The independent variable is stimulus intensity. The dependent variable is the variation in voltage across the cell membrane recorded intracellularly in response to stimuli of different magnitudes. There is, however, a difference in the duration of the stimulus. In the previous experiment, we had a very brief stimulus shock. In the present experiment, the stimulus, a depolarizing one, is turned on and remains on for a longer period. The longer duration of the intracellular recording not only allows us to examine the voltage changes we saw before but also permits us to count the number of impulses that occur as a function of the stimulus intensity and duration.

The previous experiment was somewhat artificial because it was assumed that the stimulus generated only a single action potential. In practice, this is seldom the case. Any stimulus that evokes a spike, nearly always evokes more than one. Figure 1.11 shows, diagrammatically, the responses of a neuron to a stimulus that is long in duration at three different intensities. The stimulus is denoted by the rectangles below the data in Figure 1.11(a). The most obvious result is that the number of spikes increases as a function of stimulus intensity. This conclusion is further shown in Figure 1.11(b). The size of the action potential, as noted previously, does not increase as the stimulus intensity increases; rather, the intensity affects the number or frequency of spikes that occur during the interval. The stronger or more intense the stimulus, the more neural impulses there are. Part of the neural code, then, is that as the stimulus in the environment increases in strength, the nervous system increases the number of action potentials generated. This is the **frequency-intensity** principle.

Close inspection of Figure 1.11(a) reveals the manner in which the action potentials are increased in frequency. The spikes occur more often with more intense stimuli because each impulse is initiated earlier in the cycle. That is, after a spike has been generated, the action potential does not completely dissipate or return to resting level before the next impulse is generated. This means that the interval between spikes decreases as the stimulus intensity increases and, as a result, there are more spikes within the same interval of time. This results in the increase in the number of action potentials as the intensity of the stimulus increases. You should note, however, that there is a limit to the



**Figure 1.11.** The Frequency of Impulses Increases as a Function of Increasing the Intensity

NOTE: (a) the effect of increasing stimulus level on neural activity and (b) a plot of the frequency-intensity principle.

number of action potentials a neuron can produce. At some point, as the stimulus intensity continues to intensify, the neuron will stop increasing its

spike production. At this point, the neuron has reached its maximum activity or its saturation point.

Note, once again, that the axis for Figure 1.11(b) is logarithmic. These data are representative of a power function. There is a linear relationship when the data are plotted on the log-log scale within the neuron's dynamic range. A log-log scale refers to data plotted logarithmically on both the X and Y axis.

It may appear possible to infer from these data that sensations such as brightness and loudness are dependent on the frequency-intensity principle. That is, the sensation depends on the frequency of the neural impulses. For example, the number of impulses received by the brain within a second indicates the loudness of the sound. This is generally known as a strong inference, based on reasoned logic and suggestive data. It should be emphasized, however, that the data presented here do not, by themselves, support such an inference. You must be extremely careful in drawing conclusions from data. The task of finding relationships between sensory experience and neural activity requires data from several different experiments.

What then can be concluded from the data? What does the coding of intensity to frequency of neural firing show? The acknowledged relationship in sensory physiology is that a single neuron's activity is dependent on the stimulus intensity. When several neural fibers increase their activity, there is a perceptual increase in the experienced sensation. So, the frequency-intensity principle is clearly related to our perceptions.

## Action Potentials

This section outlines how neurons process and conduct information. If environmental events are to be sensed and perceived it is important to understand how a neuron conducts its daily routine. The neuron's operation includes topics such as passive and active transport, sodium pumps, and action potentials. The activity that occurs between neurons, at synapses, is the topic of the next chapter.

The voltage variations across a cell membrane, from a resting potential near  $-70$  mv to a positive potential near  $+55$  mv has been introduced and discussed. The task now is to explain, as simply as possible, a complex system of electrical and chemical events. The events provide the basis for the observed changes across the neural membrane. To be more specific, the question we are going to address is: What occurs within a cell to maintain a polarized resting state ( $-70$  mv) and how does depolarization occur during an action potential ( $+55$  mv)?

The discovery of neural operation has followed a normal course of scientific investigation. Considerable curiosity, perseverance, skill, luck, and intellectual brilliance have led to the present state of knowledge. The breadth of this knowledge is, of course, still evolving. Experiments are currently underway in laboratories throughout the world that undoubtedly will suggest new directions and understanding.

### *Ions and Ionic Flow*

The cellular examination of living matter, whether it is nervous tissues or oak trees, necessitates some knowledge of chemistry and electricity. For our purposes, the chemical and electrical ideas are relatively simple. For example, if we put common table salt, NaCl, (called a solute) into a glass of water (called a solvent) the result is not only a glass of salty tasting water but also the production of electrically charged substances called ions. The ionic theory states that, in particular circumstances, the salt molecules dissociate in two parts called ions. An **ion** is simply an atom that has gained or lost an extra electron (or two). When the molecule of salt breaks apart in water, the chloride ion retains an extra orbiting electron that was previously shared. Because electrons have a negative charge, the chlorine atom takes on a negative charge,  $\text{Cl}^-$ . The loss of the electron by the sodium results in a positive ion ( $\text{Na}^+$ ). Furthermore, these positive and negative ions are attracted by electrical potentials with opposite charges because opposite charges attract and like valences repel. The movement of ions creates **ionic flow** and is the basis for *ion*, the Greek verb that means “to move.”

The internal constituents of a neuron reveals that the cytoplasm or **axoplasm** of a neuron contains potassium ( $\text{K}^+$ ), sodium ( $\text{Na}^+$ ), chlorine ( $\text{Cl}^-$ ), calcium ( $\text{Ca}^{2+}$  has lost two electrons), and large amino acids and proteins that have a negative charge, labeled  $\text{A}^-$ , and called anions.

The concentration of these different ions within the cell, however, is not equal. There are fewer sodium ( $\text{Na}^+$ ), chlorine ( $\text{Cl}^-$ ) and calcium ( $\text{Ca}^{2+}$ ) ions inside the cell than there are potassium ( $\text{K}^+$ ) ions. The concentration of  $\text{K}^+$  within the cell is approximately 20 times higher than outside it. The  $\text{Na}^+$  distribution, moreover, is almost 9 times more concentrated outside of the cell. The  $\text{Cl}^-$  distribution across the cell membrane (inside relative to the outside) is nearly 5 times greater outside the cell. Finally, the  $\text{Ca}^{2+}$  ions have a greater concentration outside the cell than inside it. These unequal distributions of ions with their associated electrical charges are shown in Table 1.1. These charges and ion distributions are the basis of the negative resting potential and the action potential. The cell membrane contains “channels” or “pores”

TABLE 1.1 Distribution of Ions Across the Cell Membrane

<i>Ion</i>	<i>Concentration Inside</i>	<i>Concentration Outside</i>	<i>Ratio</i>
Na <sup>+</sup>	50	440	1:9
K <sup>+</sup>	400	20	20:1
Cl <sup>-</sup>	40-150	560	1:6
Ca <sup>2+</sup>	$0.3 \times 10^{-3}$	10	—

through which ions can flow under certain conditions. This movement of ions is the aforementioned ionic flow. The flow can be either an **influx** of ions into the interior of the cell, or an **efflux** when ions exit the cell.

When ion channels are open, ionic flow occurs for two reasons—namely, concentration and electrical gradients. These two gradients form the basis for passive ion movement. The ions, in turn, determine the resting and action potentials in all neurons.

### *Concentration and Electrical Gradients*

Concentration gradients begin with diffusion, a simple nonmetabolic process in which there is no expenditure of energy by the cell. Diffusion is the process by which ions tend to equalize themselves throughout a solution. If, for example, there were nine ions on the inside of a cell and only one ion on the outside, this difference could generate a concentration gradient and diffusion could occur provided they could cross the membrane. In an axon, the uneven distribution of K<sup>+</sup> ions on the inside relative to the outside of the cell leads to diffusion and an ionic flow. The ions attempt to diffuse and equalize the number of ions on each side of the membrane. When there is a difference in concentration, an inequality exists. The inequality in ion concentrations on each side of the membrane results in a **concentration gradient**. The diffusion of ions from an area of high concentration to an area of low concentration reduces the concentration gradient.

Another reason for ionic flow is electrical. As noted previously, like charges repel, and unlike charges attract. In terms of ions, a positive area repels positively charged ions such as K<sup>+</sup> and Na<sup>+</sup>. A negatively charged area attracts the positively charged ions and repels ions like Cl<sup>-</sup>. When differences in

electrical charge exist between areas, for example, the inside and the outside of a cell, there is an electrical inequality known as an **electrical gradient**. For example, an electrical gradient causes the  $\text{Na}^+$  ions to flow from an area with a positive valence or charge to an area with a negative valence. The  $\text{Na}^+$  influxes from the outside of the cell to the inside.

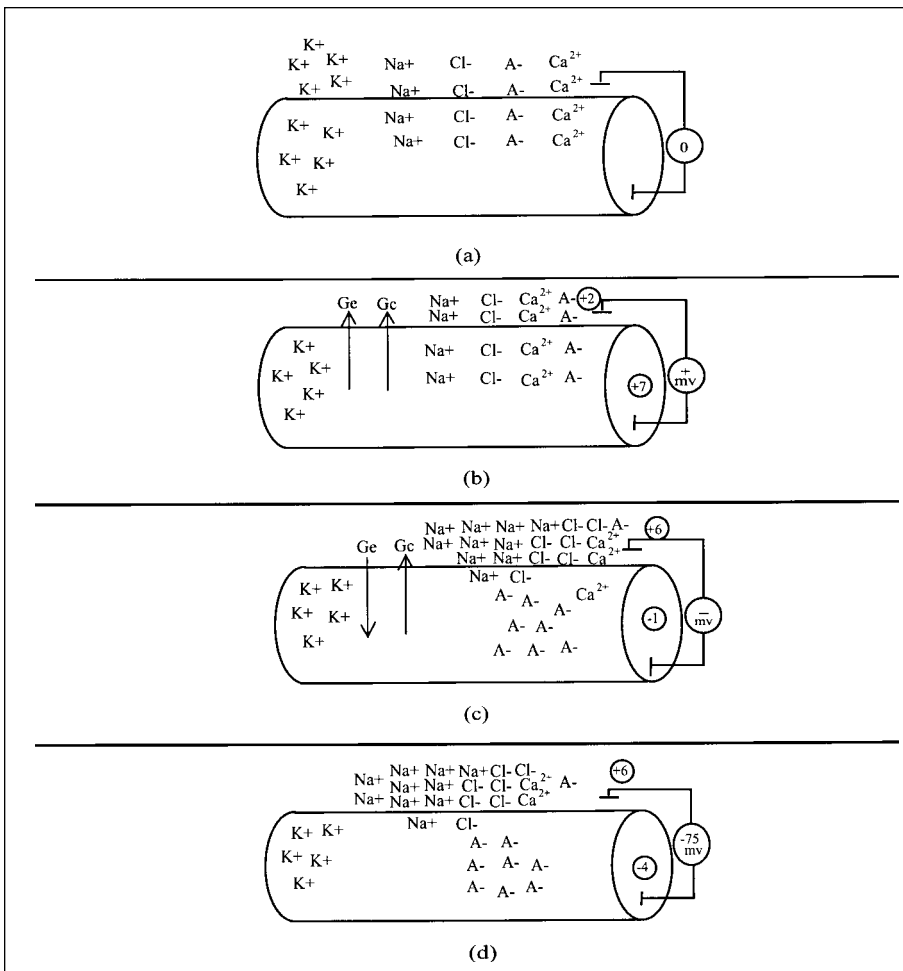
The flow of ions may be viewed as analogous to the flow of electrons in a flashlight. A flashlight battery is a polarized cell, like a neuron. Indeed, the flashlight battery is called, for example, a “D cell,” an “AA cell,” or a “C cell.” The voltage, as measured from one pole of the battery to the other, is like the electrical gradient across a neural membrane. The flow of electrons through a bulb in the flashlight is analogous to the ionic flow across the cell membrane. The flow in both cases is due to an electrical gradient.

### *Passive Transport*

It is time to consider a neuron’s charge when the ions are not distributed equally on both sides of the cell membrane. That is, when the cell is at rest near  $-70$  mv, what keeps it there and how does it get negatively charged in the first place?

Similarly, what happens to the ions when an action potential occurs and the inside of the cell spikes to a value near  $+55$  mv? To answer these questions, we need to consult Figure 1.12. The sketch is, of course, highly diagrammatic and inaccurate in terms of how an axon appears. Nevertheless, we can get a solid feeling for the processes and the general operation of **passive transport** by considering the simplified view. Passive transport refers to the movement of ions without metabolic cell involvement. The neuron does not actively move the ions across its membrane.

Figure 1.12(a) shows the membrane when there is an equal number of  $\text{K}^+$ ,  $\text{Na}^+$ ,  $\text{Cl}^-$ ,  $\text{Ca}^{2+}$ , and anions inside and outside the cell. The voltage across the membrane is, in this case, balanced because both the concentration and electrical gradients are equal. If we were to arbitrarily remove the  $\text{K}^+$  ions from the outside, as shown in Figure 1.12(b), an imbalance is apparent. The inside of the cell would become positive due to the abundance of the  $\text{K}^+$ . In addition, there would be both a concentration gradient and an electrical gradient across the membrane. These gradients tend to draw out the  $\text{K}^+$  from the cell passively. This is shown by the arrows and the notation  $G_c$  and  $G_e$  in Figure 1.12(b). In other words, the concentration gradient,  $G_c$ , causes the  $\text{K}^+$  ions to diffuse out through the membrane and the electrical gradient,  $G_e$ , repels the  $\text{K}^+$  toward the outside. If nothing occurred to change this situation, the  $\text{K}^+$



**Figure 1.12.** Ion Distribution Within an Axon and the Concept of Passive Conduction

NOTE: (a) Equal distribution of ions on each side of the membrane results in a zero membrane potential, (b) unequal distribution of  $K^+$  produces an electrical and concentration gradient for  $K^+$  efflux, (c) a more realistic ion configuration results in electrical influx and efflux gradients for different ions, and (d) ion concentrations leading to a  $-75$  mV resting potential across the cell membrane.

ions eventually distribute themselves equally on each side of the membrane. The cell is then similar to the one shown in Figure 1.12(a).

If the  $Na^+$ ,  $Cl^-$ ,  $Ca^{2+}$ , and anion concentrations were distributed across the membrane as shown in Figure 1.12(c), the situation changes. In this case, the



distribution of ions reflects a more realistic situation. It is based on the data given in Table 1.1.

So far in our discussion, we have assumed that the membrane is impervious to  $\text{Na}^+$ ,  $\text{Cl}^-$ ,  $\text{Ca}^{2+}$ , and anions and only  $\text{K}^+$  could pass through. In this situation the inside of the cell is, as noted in Figure 1.12(c), slightly negative relative to the outside. This can be verified in the example by counting the positive and negative charges on each side of the membrane. The negativity and the high concentration of  $\text{K}^+$  inside the cell produce an interesting milieu. The  $\text{K}^+$  is, as expected, drawn out of the cell because of the concentration gradient, labeled  $G_c$  in Figure 1.12(c). As each  $\text{K}^+$  ion leaves the cell, due to the diffusion, it takes with it a positive charge. The more the efflux of the  $\text{K}^+$  ions continues, due to the concentration gradient “drawing” them out, the more electrically negative the inside of the cell becomes. Eventually there is an electrical gradient set up across the membrane that equals the concentration gradient, but in the opposite direction. The electrical gradient is labeled  $G_e$  in Figure 1.12(c). The negative valence within the cell draws the  $\text{K}^+$  ions into the cell because the  $\text{K}^+$  ions are positive; simultaneously, the concentration gradient forces the  $\text{K}^+$  to leave the cell. The result is a stalemate. The concentration gradient draws  $\text{K}^+$  out, but only to a certain point. The point of equilibrium is reached when the  $\text{K}^+$  no longer diffuses outward because the negativity within the cell acts as a magnet to draw them back in. When a balance is reached between the concentration gradient and the electrical gradient, the voltage drop across the membrane is  $-75$  mv, only 5 mv away from the neural resting potential.

Figure 1.12(d) shows the situation when the cell is near the resting potential. Ignoring the other ions for a moment, it is clear that the resting potential of  $-70$  mv is primarily the result of a balance of two forces: the concentration gradient drawing the  $\text{K}^+$  out and the electrical gradient, which draws the  $\text{K}^+$  back in. The  $\text{K}^+$  ionic flow yields a negative interior of  $-75$  mv, a value very close to the resting potential. An important point concerning the  $\text{K}^+$  flow is that the potential of  $-75$  mv is done without any active help from the cell itself. The cell is, in this sense, passive. As noted earlier, the process of ionic flow without metabolic cell activity defines passive transport. Before we consider the flow of ions during an action potential, it is necessary to digress slightly and consider an important mechanism known as the sodium-potassium pump. Once this phenomenon is understood, we can more clearly understand the ionic flow that produces the maintenance of the  $-70$  mv resting potential and the observed difference of 5 mv.

### *The Sodium-Potassium Pump*

The situations depicted in Figure 1.12 are somewhat artificial. When a more realistic situation is examined in which the concentrations of  $\text{Na}^+$ ,  $\text{Ca}^{2+}$ , and  $\text{Cl}^-$  are higher on the outside of the cell than within, it becomes apparent that there is a strong tendency for the  $\text{Na}^+$  and  $\text{Ca}^{2+}$  to attempt to cross the membrane and enter the cell. The high concentration of  $\text{Cl}^-$  also sets up a concentration gradient for  $\text{Cl}^-$  to enter the cell. However, this  $\text{Cl}^-$  concentration gradient is offset by the opposite force of the electrical gradient;  $\text{Cl}^-$  is driven out of the cell due to the high negative charge in the cell (due to the  $A^-$ ). We focus, for the moment, on the  $\text{Na}^+$  and  $\text{Ca}^{2+}$  ions.

Returning to Figure 1.12(d), we see the large number of  $\text{Na}^+$  and  $\text{Ca}^{2+}$  ions concentrated outside the cell, and the interior of the cell has a negative resting potential. Both the concentration and electrical gradients for the  $\text{Na}^+$  and  $\text{Ca}^{2+}$  are producing an influx force to move the  $\text{Na}^+$  and  $\text{Ca}^{2+}$  inward. The electrical gradient produces an influx gradient because the negative resting potential within the cell attracts the positive sodium and calcium ions. The concentration gradient is an influx force because of the difference in ions inside and outside the cell. At this point it is time to acknowledge that the cell membrane is not completely impervious to  $\text{Na}^+$  and  $\text{Ca}^{2+}$ . The strong influx gradients force a leakage of  $\text{Na}^+$  and  $\text{Ca}^{2+}$  through the membrane. The consequence of the leakage is a decrease in the negativity of the cell interior. The continual leakage of positive ions into the cell makes the interior of the cell more positive and slowly depolarizes it. Furthermore, as the inside of the cell starts to become positively charged, the  $\text{K}^+$  tend to efflux. The  $\text{K}^+$  leaves because like charges repel and because there is a concentration gradient attracting the  $\text{K}^+$  ions outward.

In summary, there is a constant influx of  $\text{Na}^+$  and  $\text{Ca}^{2+}$  ions into the cell and an efflux of  $\text{K}^+$ . This constant leakage of ions moves the electrical potential of the cell interior from negative toward positive. If this leakage continues unabated, the negative resting potential dissipates and eventually becomes zero. The polarization is removed and the cell “runs down” analogous to a flashlight that has been turned on all night. If nothing is done by the cell to recharge and prevent the  $\text{Na}^+$  and  $\text{Ca}^{2+}$  ions from leaking in and the  $\text{K}^+$  ions from leaving, the negative potential within the cell continues to decrease and eventually becomes zero just as is shown in Figure 1.12(a).

The manner in which the leakage is counteracted entails the active participation of the neuron. The cell transports the  $\text{Na}^+$  ions back to the outside of the cell while moving the  $\text{K}^+$  back inside. This involvement of the cell in the transport of  $\text{Na}^+$  and  $\text{K}^+$  is called **active transport**. To be more specific, the active

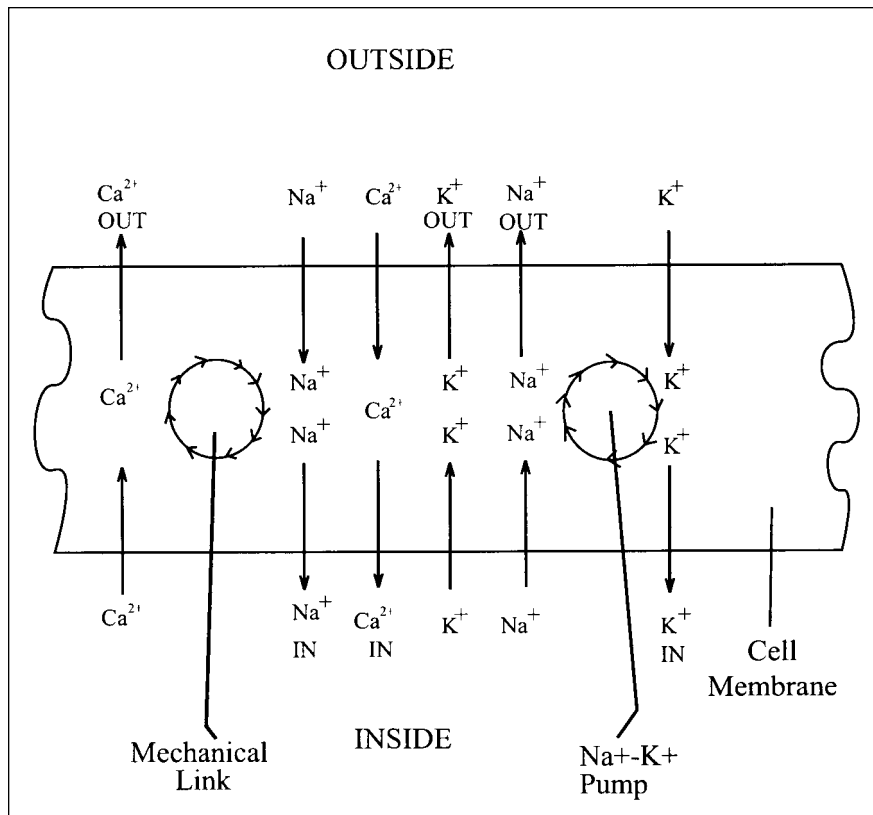
transport of  $\text{Na}^+$  from the inside of the cell to the outside and the active transport of  $\text{K}^+$  into the cell is accomplished by a metabolic process known as the **sodium-potassium pump**. The sodium-potassium pump not only removes the  $\text{Na}^+$  from the inside of the cell but simultaneously ensures that the concentration of  $\text{K}^+$  is maintained at the appropriate level by pumping  $\text{K}^+$  into the cell. The sodium-potassium pump does not exchange ions equally, however. The ratio of exchange is near 3:2; three ions of  $\text{Na}^+$  are removed for each insertion of two  $\text{K}^+$ . This inequality, however, causes no problem because the leakage of  $\text{Na}^+$  and the outflow of  $\text{K}^+$  is at the same rate. Three  $\text{Na}^+$  ions leak in for every two  $\text{K}^+$  ions that leave. Thus, the exchange ratio of the sodium-potassium pump matches the leakage. The sodium-potassium pump is shown diagrammatically in Figure 1.13. The figure shows the clockwise movement of the pump as it removes  $\text{Na}^+$  from the cell and brings  $\text{K}^+$  into the cell.

### *Calcium Removal*

You have probably noted by now that the active transport system of the sodium-potassium pump has not handled the infusion of the  $\text{Ca}^{2+}$  ions. The removal of the  $\text{Ca}^{2+}$  is done by a different method. Briefly, the  $\text{Ca}^{2+}$  removal is a by-product of the influx of the  $\text{Na}^+$ . That is, as the  $\text{Na}^+$  leaks into the cell there is an automatic and continual removal of  $\text{Ca}^{2+}$ . An analogy may help to simplify the concept. The in-pouring of the  $\text{Na}^+$  ions may be viewed as a continuous stream of water that turns a waterwheel. The waterwheel is mechanically coupled to a large millstone in a flour mill. As the waterwheel is turned, the millstone grinds the grain to flour. In this analogy, the  $\text{Na}^+$  ions represent the water that turns the waterwheel. The mechanical linkage to the millstone is analogous to an automatic linkage in the cell membrane. The influx of  $\text{Na}^+$  ions is the “power” that “mechanically” removes the  $\text{Ca}^{2+}$  ions. There is no special active transport system for the  $\text{Ca}^{2+}$  removal. Figure 1.13 shows a situation in which the  $\text{Na}^+$  and  $\text{Ca}^{2+}$  leak into the cell and the sodium-potassium pump transports the  $\text{Na}^+$  back out. The sodium-potassium pump also replaces the  $\text{K}^+$  that has “escaped” to the outside. The mechanical removal of the  $\text{Ca}^{2+}$  occurs when the  $\text{Na}^+$  leaks into the cell.

### *Chlorine Distribution*

The concentration of  $\text{Cl}^-$  is predominantly outside the cell relative to the inside. This, at first glance, tends to cause some concern about their effect on the potential of the cell. Surprisingly, the effect of  $\text{Cl}^-$  is relatively small. The primary reason for such a state of affairs is that the membrane of the cell is



**Figure 1.13.** Diagram of the Active Transport System Using the Sodium-Potassium Pump to Remove the  $\text{Na}^{+}$  and Return the  $\text{K}^{+}$

NOTE: The mechanical removal of  $\text{Ca}^{2+}$  by  $\text{Na}^{+}$  influx and  $\text{K}^{+}$  and  $\text{Ca}^{2+}$  leakage is also shown.

“open” to the free movement of the  $\text{Cl}^{-}$  ions. This freedom of movement allows the  $\text{Cl}^{-}$  ions to arrange themselves in such a manner that they balance, and the concentration and electrical gradients are equalized at the value of the resting potential. Said differently, the sodium-potassium pump maintains a fixed ionic concentration for  $\text{Na}^{+}$  and  $\text{K}^{+}$  but the  $\text{Cl}^{-}$  ions are free to “settle” at an equilibrium across the membrane that is at the value set by the sodium-potassium pump.

### *The 5 mv Difference*

To visualize why the resting potential of the cell is  $-70$  mv rather than  $-75$  mv requires that we acknowledge the actual permeability of the cell

membrane and the activity of the sodium-potassium pump. Let us review the situation briefly.

When the membrane is permeable only to  $K^+$ , then the potential across the membrane is  $-75$  mv. The assumption is that the membrane is permeable only to  $K^+$ . The assumption is incorrect. There is a tendency for  $Na^+$  to leak into the cell because of the concentration and electrical gradients. Like most biological systems, the neural membrane is imperfect, it leaks. Consequently, the membrane is not likely to remain at  $-75$  mv. The influx of  $Na^+$  and the leakage of  $K^+$  across the membrane results in a decrease in the internal potential of the cell from the  $-75$  mv. The sodium-potassium pump, of course, operates to offset the leakage of  $Na^+$  and  $K^+$ , but the pump can only do so if it has been activated. When the sodium-potassium pump begins operation, it maintains the membrane potential at a relatively stable value. For our purposes, we can assume that the sodium-potassium pump begins once the cell has been depolarized from  $-75$  mv to  $-70$  mv. In other words, the sodium-potassium pump “kicks in” when the potential of the cell reaches  $-70$  mv due to the  $Na^+$  and  $K^+$  leakage. As an analogy, ideally, a ship is watertight. In reality, however, ships do leak. A slight leakage is acceptable if it is maintained at a low level. If the leakage becomes too great, however, it is important to eliminate it. The water pumps (bilge pumps) are activated to do the job. In a very leaky boat the bilge pumps are turned on when the water inside the boat reaches the maximum allowable limit. Once the pumps are active, the water level is maintained at a constant level. In the analogy, the sodium-potassium pump is activated when enough  $Na^+$  and  $K^+$  ions have leaked in to increase the internal potential from  $-75$  mv to  $-70$  mv. The sodium-potassium pump maintains a constant resting state by pumping the leaking  $Na^+$  out and returning the  $K^+$  to the inside. The sodium-potassium pump is nearly always active. The only time the active transport system is not working is during the brief durations when action potentials are being produced. The generation of the action potential is the next discussion.

### *Conductance and the Action Potential*

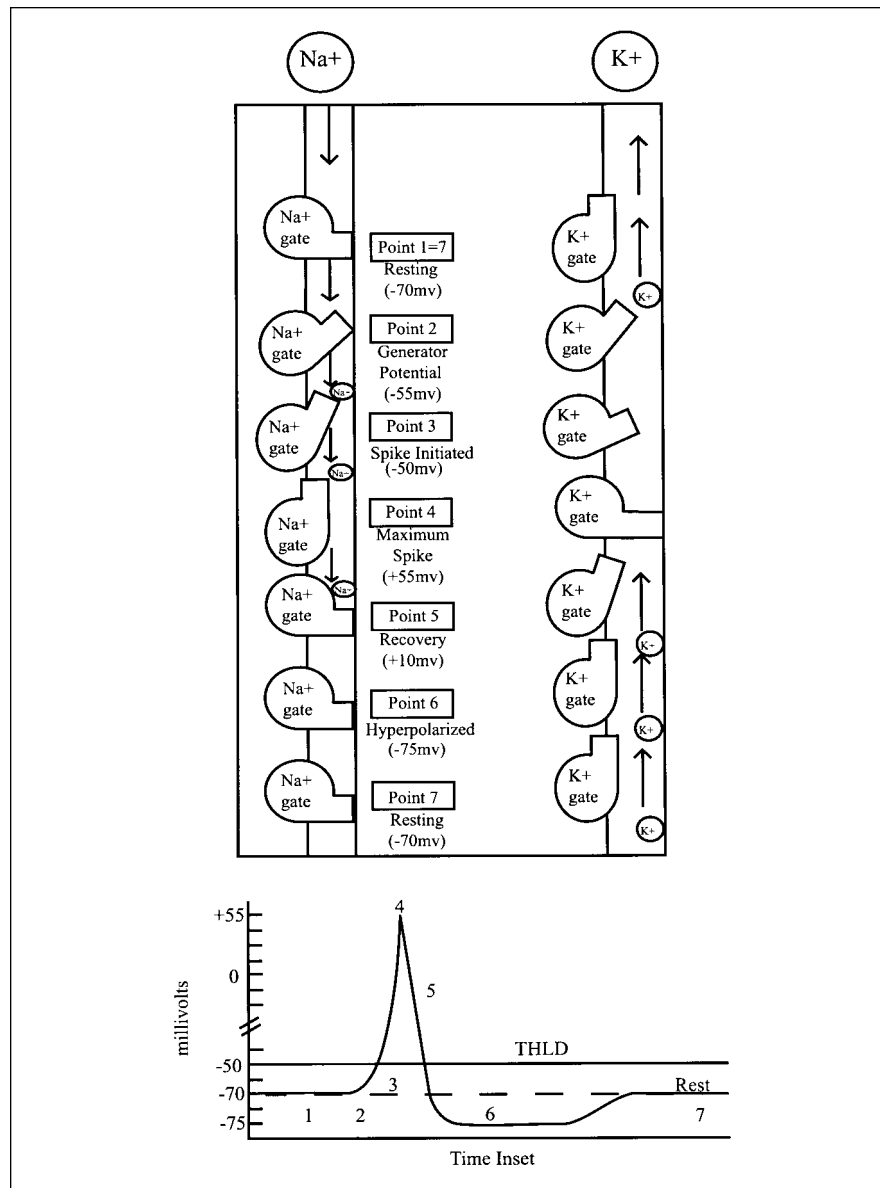
One of the important aspects of the neural operation has been alluded to but not addressed specifically. It should be apparent that ionic movements across the membrane determine both the resting potential and the action potential. However, what has not been stated is that the membrane of the axon itself is sensitive to the voltage differential across it. The axon membrane is **potential sensitive**. This means that the “pores” or gates that allow the differ-

ent ions to pass through the membrane are opened or closed as a function of the potential across the membrane.

During the resting state, the potential-sensitive gates of the membrane are open only to the flow of  $K^+$  ions (ignoring leakage). The onset of an action potential begins when a graded potential at the axon hillock reaches the threshold value of  $-50$  mv. At threshold, the potential-sensitive  $Na^+$  gates open wide to allow a rapid influx of  $Na^+$  into the cell. The initial increase in internal potential closes the potential-sensitive  $K^+$  gates. The rapid influx of  $Na^+$  into the cell continues until the depolarization reaches the  $+55$  mv peak spike value. The consequent rapid increase in potential has an almost immediate second effect on the potential-sensitive gates for  $Na^+$  ions. At the peak of the spike ( $+55$  mv), the gates close to the passage of  $Na^+$ . An instant later, the gates open for the efflux of  $K^+$  ions from the cell. The efflux of  $K^+$  returns the cell to near resting potential. Said differently, the  $K^+$  gates are open and the  $Na^+$  gates are closed when the cell is at rest ( $-70$  mv). When the neuron is depolarized and reaches threshold, because of the graded potential at the axon hillock, the  $Na^+$  gates open and the  $K^+$  gates almost immediately close. This sequence is then reversed when the internal potential reaches  $+55$  mv. At the peak of the spike, the  $Na^+$  gates close and the  $K^+$  gates reopen. The recovery portion of the action potential that follows the maximum spike potential ( $+55$  mv) is due to the efflux of the  $K^+$ .

Figure 1.14 shows a hypothetical view of the potential-sensitive gates during rest (Point 1), during a generator potential (Point 2), during the initiation of an action potential (threshold at Point 3), during the action potential (Point 4), and during the recovery or decline of the action potential (Point 5). Although the gates are shown diagrammatically opening and closing in unison, this simultaneity does not actually occur. It is just difficult to draw gates opening and closing with microsecond offsets. The insert at the bottom of Figure 1.14 indicates the electrical activity at the various points. The result is, of course, an action potential. The hyperpolarization is shown at Point 6. This hyperpolarization occurs where the internal potential becomes more negative than the resting potential. This is due to the “overshoot” of  $K^+$  ion efflux. Point 7 reflects a state of rest identical to that at Point 1.

The conductance of an action potential is a relatively simple concept. It is like the burning of a fuse. Once a fuse has been lit, the heat of the ignited portion raises the temperature of the area adjacent to it. When the powder in the zone next to the flame reaches its flash point, it too bursts in flame. The flame at this new point then raises the temperature of the powder next to it, and this powder now ignites. The flame, therefore, moves steadily down the fuse burn-



**Figure 1.14.** Diagrammatic View of Na<sup>+</sup> and K<sup>+</sup> Gates and the Movement of Ions During the Generation of an Action Potential

ing the powder as it goes. The activity of the neural impulse is similar. During the occurrence of a spike, the influx of Na<sup>+</sup> causes a voltage change across the cell membrane as it flows into the cell. The voltage change affects the membrane permeability to Na<sup>+</sup> in the neighboring area and Na<sup>+</sup> begins to enter.

When the threshold value of  $-50$  mv is reached the  $\text{Na}^+$  gates open wide, and the spike is conducted to the neighboring area of the membrane. In sum, the influx of  $\text{Na}^+$  causes the gates for  $\text{Na}^+$  to open in the area of the axon next to the spike. The influx of  $\text{Na}^+$  is followed by an efflux of  $\text{K}^+$ . The exchange of ions flows down the membrane in a manner analogous to that of the fuse.

It is interesting to note another analogy of membrane conductance and fuses—namely, conductance time. The speed at which the flame moves down the fuse is dependent, to some degree, on the actual size of the fuse. The larger the fuse, the faster it conducts the flame to the dynamite. In neural conduction, the size of the axon is also a factor in the speed of conduction. The larger the axon diameter, the faster it conducts.

There is, finally, one comment necessary to complete the story. Some neurons have myelination and nodes of Ranvier. The flow of action potentials in myelinated neurons is increased in speed because of the special mechanism of saltatory conduction. The myelin acts as a cover that is resistant to the passage of ions through the membrane. Thus, for the neuron to conduct, the action potential must leap from node to node. The speed of conduction is increased when a neuron has myelin. Finally, the size of the neural impulse (spike) is nondecremental. This simply means that the magnitude of the spike does not decrease as it is conducted down the axon. In the present example, the “height” of the spike is maintained at  $+55$  mv from beginning to end.

## Dysfunctions

The nervous system is a very delicate and tender structure. As we progress through the book, selected diseases and accidents are discussed relative to a normal functioning system. The common everyday experiences and news reports, unfortunately, cover a large range of neurological problems. It is not the goal of this section to examine the vast array of situations and conditions that can occur. Rather, these sections of the book, found in nearly every chapter, are directed toward a brief introduction and excursion into some commonly known, and some not so commonly known, dysfunctions (Brodal, 1981).

A serious neurogenic problem is the **cerebrovascular accident (CVA)**, commonly known as a stroke. The irretrievable loss of neural tissue because of a stroke is one of the most serious problems an individual can encounter. The brain, which makes up approximately 2% of the total body weight, requires 17% of all the cardiac output and uses 20% of the oxygen consumption. Nearly 2 million U.S. citizens suffer neurological impairment because of



cardiovascular disease alone. The brain is quite susceptible to interruptions in the blood and oxygen supply.

A CVA refers to neurological symptoms and signs that occur because of diseases from blood vessels that serve the brain. The CVA can occur because the vessels become closed (occlusive CVA), or because the vessels burst (hemorrhagic CVA). In either case, the effect on brain cells can be life threatening and traumatic. The occlusive CVA is thought generally to be due to atherosclerosis (clogging of the arteries due to fatty deposits) and thrombosis (blood clots). The hemorrhagic CVA is due to genetic aneurysm, weaknesses in the vessel wall, or hypertension (high blood pressure). Often when a hemorrhagic CVA occurs there is a loss in consciousness, possibly due to changes in the intracranial pressures.

The symptoms of a CVA vary according to the region of the brain in which it occurs. The symptoms presented by the patient provide clues for diagnosing the location of the CVA within the brain. For example, if the loss of neural cells occurs in the right parietal lobe, there is often a loss of perceptual abilities with disturbances in the ability to accomplish spatial tasks such as copying maps, pictures, or diagrams. Occasionally there is a severe difficulty in finding your way around in the environment, called topographagnosia. You should keep in mind that the functions affected seldom are controlled by a single region of the brain. The specificity you find for particular functions refers to certain regions of the brain that are more concerned with one set of functions than others. Most functions require integrated actions from several regions of the cortex as well as lower centers within the brain. Broca's and Wernicke's areas (see Figure 1.2) are examples of specificity, yet it is clear that without the input from the auditory sensory system, the areas are restricted in their function. It should be clear at this point that if a CVA were to occur in the area that produces speech, Broca's area, the individual's speech is drastically affected. A similar CVA within Wernicke's area results in the loss of the ability to understand verbal communication.

A loss of neural cells within the precentral gyrus, just in front of the central fissure in the frontal lobe, results in the loss of voluntary movement. A stroke within the motor area of the left hemisphere, for example, results in the loss of movement in the right half of the body. A lesion or a loss of cells due to CVA, or a heavy hit to the head by a boxer, in the posterior parietal cortex usually leave deficits in learning tasks associated with somesthesia. For example, a CVA in the left hemisphere often shows verbal and language deficits, agnosia or the inability to perceive even though the sensory channel is functional.

Loss of neural cells in the right hemisphere can result in striking effects. There sometimes is a complete lack of appreciation for all sensory inputs from the contralateral side of the body and from the opposite portions of the environment. Patients often fail to dress, wash, and undress the side of the body that is contralateral to the neural loss. Such a behavior is called the neglect syndrome.

A final example of a CVA within the temporal lobe is that the loss of neural cells, whether they are few or many, is a serious event. The loss of central neural cells is permanent. The peripheral nervous system, on the other hand, has regenerative capabilities. Peripheral nerves do regenerate.

A CVA within the superior temporal lobe in the right hemisphere usually leads to deficits in auditory pattern recognition. Should the stroke occur within the medial or inferior portion of the right temporal lobe the result is a visual learning deficit for patterns. The general outcome of temporal lobe losses is that loss in the left lobe eliminates the ability to process verbal material and loss in the right hemisphere eliminates the ability to process sensory pattern information.

A short comment or two needs to be inserted here regarding the regeneration or replacement of central nervous system cells. The first statement has to do with the “tenderness” of neural lifetimes. You are born with the maximum number of neurons you will ever have. The only sure thing in your life is that you continue to lose neural cells through the normal attrition of everyday living.

Second, a question is probably hanging around at this point concerning how it is that people can recover after a traumatic insult to the central nervous system. Not many years ago very little was known about how such “repairs” came about. This does not mean that we now fully understand how the brain comes to take up the slack of injured and destroyed neurons. What is recognized, however, is that the brain has a remarkable ability to take over functions of the neural cells that are destroyed. Not all functions, of course, are recoverable. It depends on the extent of the injury or stroke. The brain has shown a high degree of what is called **neural plasticity**—that is, the ability to do some considerable reorganizing or remodeling, both structurally and functionally. Because the brain may not produce new nerve cells after a stroke, lesion, or other disease, it is necessary to examine other mechanisms of recovery. It has long been recognized that the initial improvement, over the first few days or weeks, is likely due to the decrease in the edema (i.e., retention of fluid or swelling of the brain), resorption of the blood, and the recovery of

the injured cells. The continual recovery of a patient over an indeterminate period requires another explanation.

Without doubt, many people have viewed the recovery following severe brain damage with amazement. The reasons for partial or total recovery of literally millions of damaged brain cells require some explanation. A complete answer, however, is not yet available, although research on brain functions and structures has suggested three possibilities to account for recovery.

One idea is that the neural elements that have not been affected by the insult or damage caused by the CVA take up the slack by sprouting new collaterals. The new collaterals make both structural and functional connections with neural elements that, before the damage, were in contact with the destroyed cells. That is, there may be a new pathway provided and thus the functions may be reintroduced.

A second alternative for the recovery is that of “unmasking.” This idea simply means that the death of brain cells can lead to the revelation of unknown or seldom used pathways that accomplish the same function as the cells that were destroyed by the CVA. Pathways and cells, which were functional before the death of the cells, come to be primary rather than secondary when the initial primary group of cells is destroyed.

The third possibility, one that surely is involved to some extent, is that of learning. If learning occurs in normal individuals, as we certainly know it does, it requires that the brain be capable of modifying its structure and circuitry in some manner. It makes sense to assume that the improvement that comes about is the result of such learning processes even if it is in a defective or damaged nervous system. What the exact rewiring is and how plasticity is accomplished still remains to be determined. There are, certainly, amazing things on the horizon when it comes to the brain.

The problems that can occur with the neuron are mostly degenerative diseases and viral invasions. One of the more unfortunate, and fatal, of such degenerative diseases is that commonly referred to as Lou Gehrig’s disease or amyotrophic lateral sclerosis (ALS). This disease progressively attacks the motor neuron and causes muscle atrophy due to the lack of innervations. The cause of the disease is presently unknown. *Amyotrophic* is derived from the neurogenic atrophy of the muscle. *Lateral sclerosis* refers to the hardened spinal cord observed during autopsy. This is due to the proliferation of the glia cells, astrocytes, and the scarring of the lateral columns. The disease does not affect sensory neurons or, somewhat surprisingly, the motor neurons associated with the viscera and glands. The search for the cause and a cure

continues. The investigations are presently focused more in the exploratory and understanding stage than in the preventative and or curing position.

## Summary

The nervous system is a continuous entity that is partitioned, for the sake of discussion and study, in two parts: the peripheral and central nervous systems. The peripheral nervous system is made up of 12 cranial and 31 pairs of spinal nerves. The spinal nerves each innervate a particular part of the body surface. The body surface served by a single spinal nerve is called a dermatome. The spinal nerves diverge and mix with peripheral nerves so that the severance of a single spinal nerve causes only a partial loss of sensitivity.

The central nervous system is partitioned in two parts: the spinal cord and the brain. These two parts function as a unit and are, in fact, structurally a single continuous system. The spinal cord receives information from the environment via the afferent axons that enter the dorsal horn. Efferent information is sent to muscles and glands via the ventral horn. The division of the spinal nerves in two functional sections is known as the Bell-Magendie law. The spinal cord both conducts as well as integrates information it receives. The conductive aspect of the cord is done by the pathways that ascend and descend via the dorsal column, spinothalamic tract, pyramidal tract, lateral spinothalamic tract, extrapyramidal tract, ventral column, and Lissauer's tract. Both the dorsal column and the lateral spinothalamic tract are sensory in nature and send information to higher nervous centers via the thalamus. The dorsal column first-order afferents enter the spinal cord and ascend ipsilaterally to the medulla within the brain stem. The second-order fibers then cross the midline and ascend via the medial lemniscus. Each hemisphere of the brain, therefore, processes sensory information from the contralateral side of the body; the left hemisphere processes information from the right side of the body and the right hemisphere receives and processes information from the left side of the body. The third-order fibers leave the thalamus and project to their final destination in the postcentral gyrus of the cortex. The integrative aspects of the cord are done by the interneurons within the spinal gray matter (butterfly shaped). Layers 1 through 5 of the interneurons integrate and modulate the information as it passes through the cord on its way toward or away from the higher centers of the brain.

The two hemispheres of the cortex, separated by the **longitudinal fissure** are structurally and functionally connected via a large band of fibers called the **corpus callosum**. Each hemisphere is composed of four lobes: frontal,

parietal, occipital, and temporal. Each lobe has been identified with sensory and motor functions. The motor system is found in the frontal lobes (precentral gyrus) and the somesthetic sense is in the parietal lobes (postcentral gyrus). The fissure of Rolando (central fissure) divides the frontal and parietal lobes. The occipital lobes, located posterior to the parietal lobes, process visual information. The temporal lobes, separated from the parietal and frontal lobes by the Sylvian sulcus, processes auditory information.

This chapter has taken a rather large, complex, and continually growing body of literature and presented a very simplified story of the chemical and electrical events that are the basis of neural operation. Because the story is necessarily brief and incomplete, some liberties were occasionally taken to ensure, within the author's capabilities, that the fascinating operation of neurons were clear. As an aid for your understanding, an overview of the cell operation is given next to highlight the main points discussed:

1. The neural membrane is semipermeable. It contains gates or channels through which positive and negative ions may flow.
2. The voltage potential across the membrane, from inside to outside, is approximately  $-70$  mv when the neuron is not "active." The  $-70$  mv within the cell, relative to the outside, is determined by the  $K^+$  ions. The cell, at this point, is at the resting potential.
3. The difference between the  $-75$  mv and the resting potential of  $-70$  mv is due to the leakage of  $Na^+$  and  $K^+$  ions into and out of the cell.
4. When the leakage is sufficient to increase the  $-75$  mv to a value of  $-70$  mv, the cell initiates an active process to maintain the resting state. The active transport of the  $Na^+$  and  $K^+$  ions— $Na^+$  out and  $K^+$  in—by the sodium-potassium pump ensures that the cell does not become depolarized (go to zero).
5. The positive value of  $+55$  mv occurs at the maximum point of the action potential because of the sodium influx.
6. Chlorine does not enter the activity of the neuron in terms of the resting potential and action potential. Calcium also does very little to affect the state of the neuron. The  $Ca^{2+}$  ions are important, however, when it comes to synaptic transmission.
7. The membrane changes permeability in response to voltage changes across it. In other words, changes in potential across the membrane opens the  $Na^+$  channel to allow  $Na^+$  to rush in because

of concentration and electrical gradients (passive transport). The  $K^+$  channels are almost immediately closed during the  $Na^+$  influx. The brief influx of  $Na^+$  is approximately a millisecond in duration. At the peak of the spike (+55 mv), the  $Na^+$  gates close immediately followed by the reopening of  $K^+$  channels.

8. The reopening of the  $K^+$  channels allows the  $K^+$  ions to “escape” to the outside due to high electrical and concentration gradients. The efflux of the  $K^+$  to the outside of the cell causes the return of the negative internal potential.
9. The efflux of the  $K^+$ , in fact, results in a hyperpolarization of the cell to a value below the  $-70$  mv resting state.
10. The sodium-potassium pump begins operation following the action potential to prevent the eventual “running down” of the cell. The tremendous number of ions inside and outside the cell almost ensures that there can be thousands of spikes before the cell becomes depleted and all the  $Na^+$  and  $K^+$  become equal across the cell membrane. The sodium-potassium pump is not in operation at the point when an action potential is being actively generated.
11. The conductance of the action potential down the axon is dependent on the size of the axon and whether or not it is covered with myelin. The large myelinated neurons conduct the action potential, nondecrementally, at a rapid rate. Small diameter unmyelinated neurons conduct at a slower rate.

### Suggested Readings

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