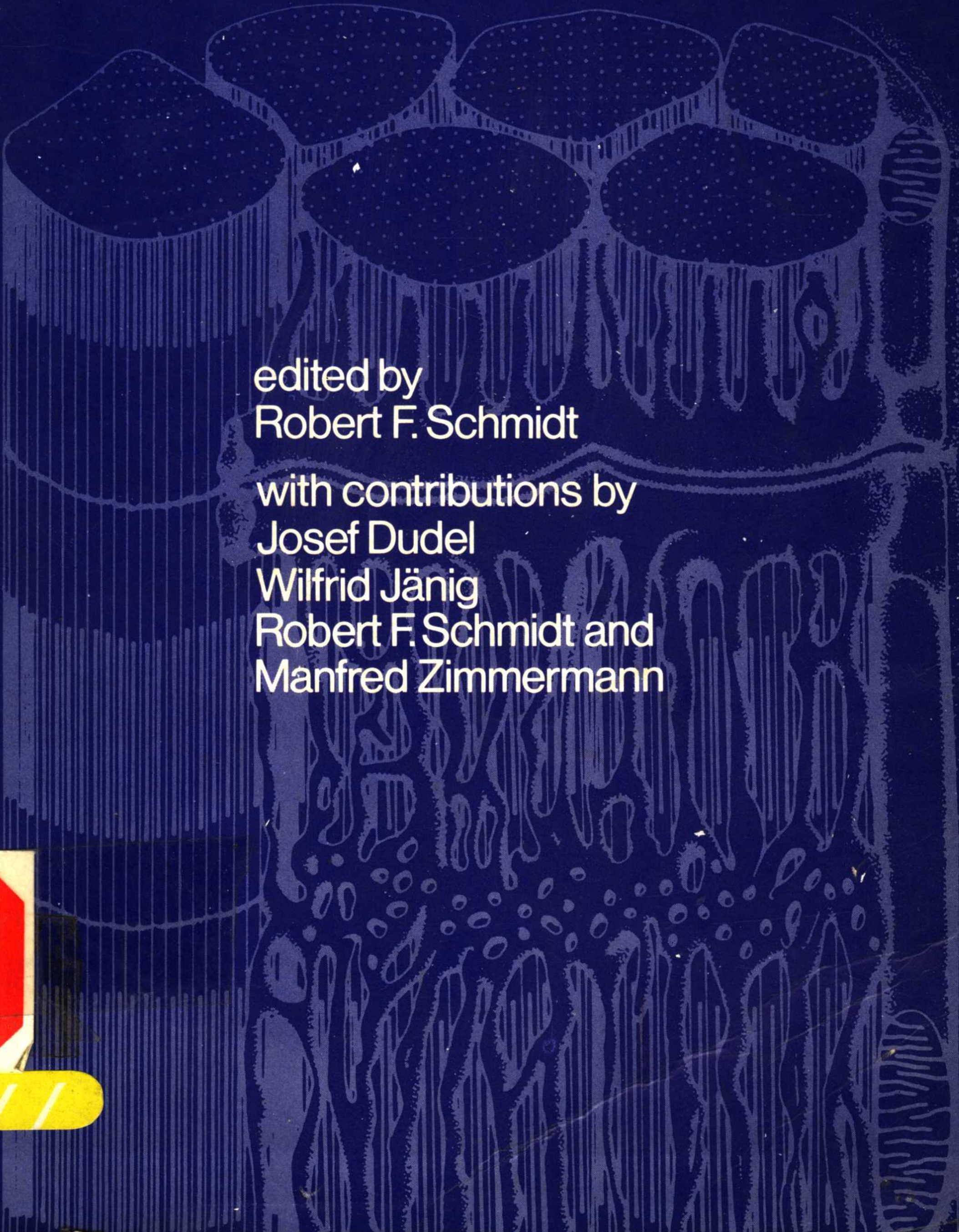
Fundamentals of Neurophysiology



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PREFACE

The English edition of this book has been prepared from the third German edition published in December 1974. The first two German editions, published in 1971 and 1972, respectively, were very well received in Germany. We hope that this English version will enjoy a similar popularity by students wishing to understand the essential concepts relevant to the fascinating field of neurophysiology.

The evolution of this book has been unique. The first edition was based on a series of lectures presented for many years to first-year physiology students at the Universities of Heidelberg and Mannheim. These lectures were converted into a series of 38 programmed texts, and after extensive testing, published as a programmed textbook of neurophysiology (Neurophysiologie programmiert, Springer-Verlag Heidelberg, 1971). Thereafter the present text was written and thoroughly brought up to date. Throughout this period all of the authors were members of the Department of Physiology in Heidelberg allowing for maximum cooperation at all stages of this endeavor.

With regard to the English edition, I wish to express my appreciation to Mr. Derek Jordan and Mrs. Inge Jordan for translating this book, and to my colleagues Dr. Mark Rowe and Dr. Dean O. Smith for their valuable comments and suggestions on the English manuscript. I express my grateful thanks to the publishers, both in Heidelberg and New York, for their unfailing courtesy and for their extraordinary efficiency.

Kiel, Germany, 1975 ROBERT F. SCHMIDT

CONTENTS

1

THE STRUCTURE OF THE NERVOUS SYSTEM

1.1 The Nerve Cells

Neurons. The building blocks of the nervous system are the *nerve cells*, which are also called *ganglion cells* but usually referred to as *neurons*. It is estimated that the human brain possesses 25 billion cells. Like all animal cells, each neuron is bounded by a cell membrane that encloses the contents of the cell, that is, the cytoplasm (cell fluid) and the nucleus. The size and shape of these neurons fluctuate widely, but the structural plan is always the same (Fig. 1-1): a cell body, or *soma*, and the processes from this cell body, namely, an *axon* (neurite) and usually several *dendrites*. The neuron shown in diagrammatic form in Fig. 1-1 has one axon and four dendrites. The axon and the dendrites normally divide into a varying number of branches (collaterals) after emerging from the soma.

The classification of the neuronal processes into an axon and several dendrites is made on the basis of *function*: the axon links the nerve cell with other cells. The axons of other neurons terminate on the dendrites and also on the soma. In order to make sure that you know the three important terms—soma, axon, and dendrite—draw Fig. 1-2 on a sheet of paper and give the correct names of the various parts indicated by the letters *a* to *g*. The answers are given on page 277, where the key to all the exercises begins.

Figure 1-3 illustrates various types of neurons. Notice in particular the great variation in the dendritic formations. Some neurons, for

Note: In this chapter a brief anatomical-histological introduction to the structure of the nervous system is given. These introductory remarks are intended only for students who have no previous knowledge of neuroanatomy. Anyone possessing such knowledge should check it immediately by working through test questions Q 1.1 to 1.5 on page 5, Q 1.6 on page 7, Q 1.7 to 1.9 on page 10, and Q 1.10 to 1.14 on page 15; and then continue with Chapter 2.

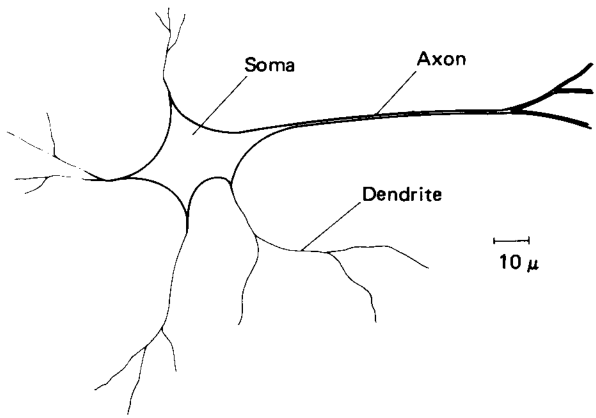

Fig. 1-1. Schematic diagram of a neuron showing the names of the various parts of the cell. The scale is intended to give an indication of the approximate dimensions.

example, neuron c, possess profusely branched dendrites, but in others, for example, neurons a and b, the ratio of soma surface to dendrite surface is somewhat more balanced. Finally, there are also neurons (d, e) that have no dendrites. The diameter of the neuronal cell bodies is in the order of magnitude of 5 to 100 μ (1 mm = 1,000 μ). The dendrites can be several hundred microns long.

As can be seen from the illustrations, one axon (synonyms: neurite, axon cylinder, axis cylinder) originates in each case from the soma of every neuron. This axon then usually splits up into branches called *collaterals*. The axons vary greatly in length. Often they are only a few microns long, but occasionally, for example, in the case of certain neurons in humans and other large mammals, they are much more than a meter long (for more details see Sec. 3 of this chapter).

Synapses. As already mentioned, the axon and all its collaterals join the nerve cell with other cells, which can be other nerve cells,

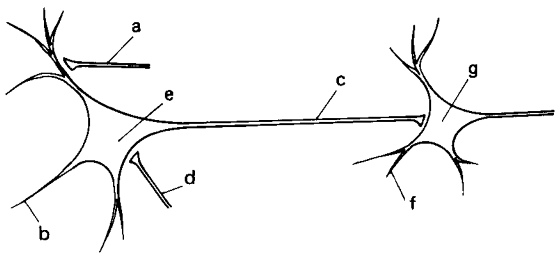

Fig. 1-2. Schematic diagram of two neurons. Give the names of the parts of the cells indicated by letters *a* to *g* (see text).

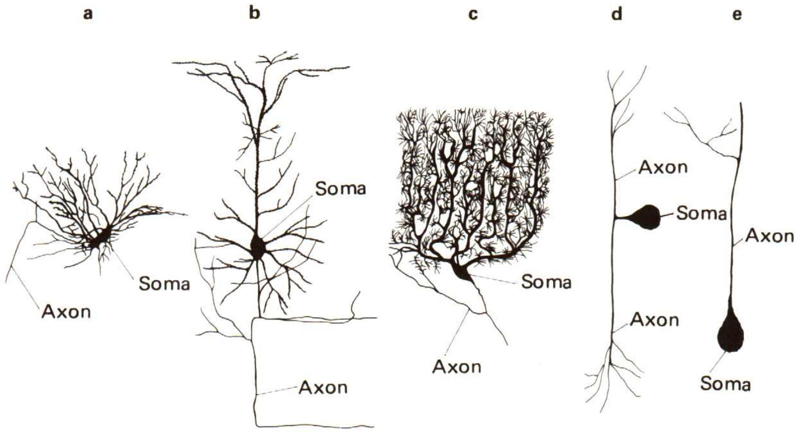

Fig. 1-3. Examples of the variety of shapes of neurons. See text for discussion. (After Ramon y Cajal.)

muscle cells, or glandular cells. The *junction of an axonal ending with other cells is called a synapse.* Figure 1-4 shows examples of neuronal junctions. If an axon or an axon collateral ends on the soma of another neuron, then we speak of an *axo-somatic synapse*. Correspondingly, a synapse between an axon and a dendrite is called an *axo-dendritic* synapse, and a synapse between two axons is called an *axo-axonic* synapse. If an axon ends on a skeletal muscle fiber, then this particular synapse is called a *neuromuscular end plate* (see Fig. 3-2). Synapses on muscle fibers of the intestines (smooth muscles) and on glandular cells have no special names.

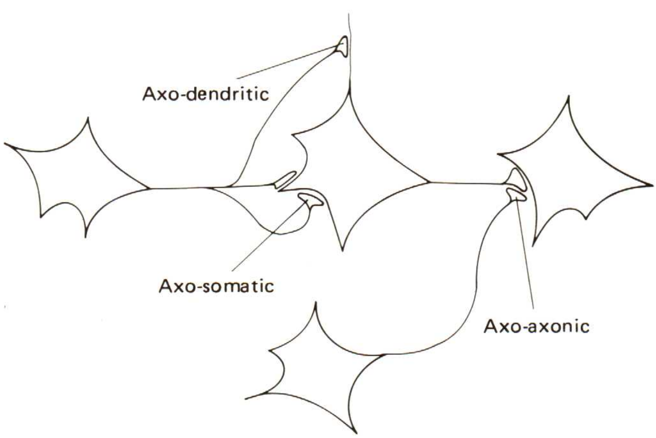

Fig. 1-4. Schematic diagram of synapses. See text for discussion.

Effectors. So far, we have learned that the nervous system is composed of individual cells called neurons. Most neurons are connected by synapses to other neurons to form neuronal circuits. However, the axons of a small number of neurons do not contact other neurons but, instead, connect with muscle cells or glandular cells. The striated skeletal muscles, the smooth muscles of the intestines, and the glands are thus the executive organs, or *effectors*, of the nervous system. We will deal with the structure of the effectors, as far as is necessary, in the relevant chapters.

Receptors. To react properly to its environment and to supervise the activity of the effectors, the nervous system also needs sensing elements that respond to changes in the environment and the organism and that transmit these responses to the nervous system. For this task the body possesses specialized nerve cells called *receptors*. We can therefore state that *specialized nerve cells that respond to certain changes in the organism or in its environment and that transmit these responses to the nervous system are called receptors.*

Each of these receptors responds to practically one particular form of stimulus only. The receptors of the eye, for example, react only to the stimulus of light or, more accurately, to electromagnetic radiation with a wavelength of 400 to 800 mμ (violet to red). These stimuli to which the receptors of the eye specifically react are called *adequate stimuli.* For most of the body's receptors we can say to which stimuli they are specially (specifically) sensitive, that is, we know their adequate stimuli. For example, sound waves (longitudinal fluctuations in air pressure) from 16 to 16,000 Hz (Hertz, cycles per second) constitute the adequate stimulus of the ear. High frequency sound waves are perceived as high-pitched sounds and low frequency waves as low-pitched sounds. (Receptors sometimes can also react to stimuli other than their adequate stimuli. However, in such cases, these *inadequate stimuli* must act on the receptor with a much greater amount of physical energy, for example, the "stars" that one sees when hit in the eye.)

It is through the receptors that the nervous system senses the events occurring in our environment and our bodies. In functional terms the receptors provide information on (1) our distant environment (eye, ear: teleceptors), (2) our immediate environment (skin receptors: exteroceptors), (3) the attitude and the position of the body in space (receptors of the muscles, the tendons, and the joints: proprioceptors), and (4) events in the intestines (interoceptors or visceroceptors).

The following questions will enable you to check your newly acquired knowledge. When answering them you should avoid as far as possible checking back in the text.

Q 1.1 Which of the following statements are correct (one or more possibilities)? Note your answers on a sheet of paper and compare them with the answer key on page 277.
a. Receptors react to all environmental stimuli.
b. Each receptor has an adequate stimulus.
c. Receptors are specialized nerve cells.
d. The receptor is much more responsive to nonadequate (inadequate) than to adequate stimuli.
e. Muscles and glands are the effectors of the nervous system.

Q 1.2 *Neuromuscular end plate* means the junction of an axon with a
a. Smooth muscle fiber.
b. Glandular cell.
c. Skeletal muscle fiber.
d. Nerve cell.
e. Statements a to d are all incorrect.

Q 1.3 Draw a diagram of a neuron and label its various parts.

Q 1.4 Draw diagrams of and label the three typical junctions that are possible between two nerve cells.

Q 1.5 The cell bodies (somata) of the nerve cells range in diameter from
a. 400 to 800 mμ.
b. 5 to 100 μ.
c. 0.1 to 1.0 mm.
d. 16 to 16,000 Hz.
e. they are more than 1 m in diameter.

1.2 Supporting and Alimentary Tissue

Glia cells. While functionally the neurons are the most important building blocks of the nervous system, they are not the only cells of which the brain is composed. The neurons are encased in a special supporting tissue composed of *glia cells*, also known as neuroglia. In other organs of the body, this supporting tissue is generally referred to as connective tissue. Thus, the glia cells form the connective tissue of the nervous system. Besides their function as connective tissue, the glia cells are also thought to play a role in neuronal metabolism to some extent in certain processes of nervous excitation. However, there is considerable controversy surrounding these functions of the glia cells, and consequently these problems will not be examined in any further detail.

Extracellular space. When examined under the light microscope the neurons and the glia cells look as if they abut each other in the nervous system without any interspace, like bricks laid without any mortar. Under the electron microscope, however, it is easy to see that a very narrow gap (average width: 200 Å = 20 mμ = 2 × 10^{-5} mm) separates the cells. All these interspaces are linked with one another to form the fluid-filled *extracellular space* of the neurons and the glia cells. At several points in the brain, known as the ventricles, the extracellular space widens to form large cavities. For more details, consult a book on neuroanatomy, examine anatomical specimen, or ask a butcher for an intact brain from a pig or calf which can then be cut into longitudinal and transverse sections to gain some idea of the arrangement of these cavities.

Because of its great functional importance, it must be stressed that there is no exchange of ions or nutrients directly between two neurons or a neuron and a glia cell. Such an exchange occurs always between the extracellular fluid and the neurons or glia cells. The fluid contained in the extracellular space is called *cerebrospinal fluid* or *liquor cerebrospinalis* (cerebrum = brain, spina = spine).

The extracellular space also surrounds the extremely thin branches of the blood vessels in the brain, the capillaries, and an exchange of material takes place between these and the extracellular space. Figure 1-5 shows diagrammatically the path of the oxygen (O_2) and the nutrients from the blood into the neuron and of the carbon dioxide (CO_2) and other metabolites from the neuron into the blood. A drug injected intravenously must therefore pass through the wall of the blood vessel (capillary membrane) and then through the cell membrane before it can take effect in a neuron. The capillary membrane of the cerebral

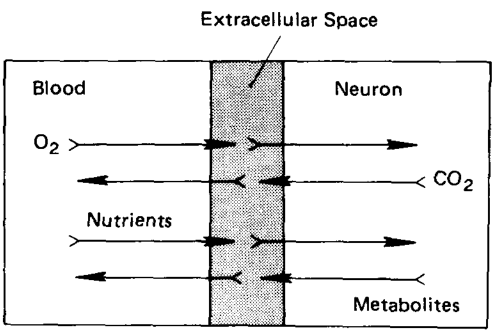

Fig. 1-5. Neuronal supply pathways. The capillary blood vessel (*left*) and the neuron (*right*) are separated by the extracellular space. The arrows indicate the direction in which the nutrients and metabolites diffuse into and out of the extracellular space.

blood vessels seems to be impermeable to many substances, which is why pharmacologists speak of a "blood-brain barrier."

The neurons of the central nervous system, particularly those of the higher sections of the human brain (cerebral cortex), depend on a constant supply of oxygen. An interruption in the blood flow (for example, cardiac arrest, severe strangulation of the neck) for 8 to 12 sec is enough to cause unconsciousness. After 8 to 12 min irreversible brain damage usually has been sustained. When breathing stops, these times are considerably longer because the oxygen supply in the circulating blood can still be utilized.

Q 1.6 Which of the following statements is/are correct?
a. Glia cells form the connective tissue of the nervous system.
b. The fluid in the extracellular space and in the ventricle of the brain is called plasma.
c. Complete lack of oxygen leads to irreversible brain damage only after several hours have elapsed.
d. The extracellular space encloses all neurons but not the glia cells.
e. The glia cells are filled with cerebrospinal fluid.
f. None of the above statements is correct.

1.3 The Nerves

The *central nervous system* (CNS) consists of the *brain* and the *spinal cord.* All the remaining nervous tissue is referred to as the *peripheral nervous system.* The nerves in the periphery of the body are bundles of axons that are enclosed in their sheaths of connective tissue. Their structure, origin, and classification according to morphological and functional considerations will now be described.

The nerve fibers. A single axon is termed a *nerve fiber.* "Axon" and "nerve fiber" are thus synonyms, although the latter expression is more commonly used when referring to axons in the peripheral nerves. A *nerve* is a bundle of nerve fibers. If a nerve is big enough to be seen easily with the naked eye, it can contain as many as several hundred nerve fibers. In even thicker nerves the number of fibers can be tens of thousands. Upon emerging from the soma of the neuron, about 50 percent of all nerve fibers become encased in a sheath of lipoprotein (fat-protein mixture) called the *myelin*. In cross section such a nerve fiber resembles a wire encased in a thick insulating covering. Nerve fibers "insulated" in this way are called *myelinated* or *medullated nerve fibers.*

Unlike an insulated wire, the *medullary sheath* does not surround

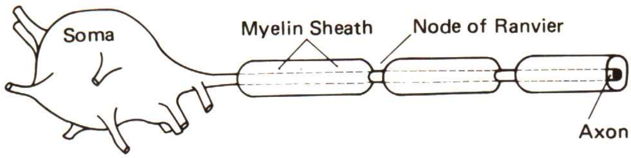

Fig. 1-6. Schematic three-dimensional diagram of a neuron with a medullated nerve fiber. The dendrites have been cut off. The medullary sheath, consisting of myelin, is interrupted at regular intervals by the nodes of Ranvier.

the nerve fiber continuously but, as illustrated in Fig. 1-6, is interrupted at regular intervals. Under the light microscope these unmedullated portions look like constrictions. They are therefore called the *nodes of Ranvier* after their discoverer. In myelinated nerve fibers a node of Ranvier occurs approximately every 1 to 2 mm. Nerve fibers without a medullary sheath are termed *unmedullated* or, since they are not covered by a myelin sheath, *unmyelinated nerve fibers*. Both types of nerve fibers, the medullated and the unmedullated, are enclosed in a sheath of special glia cells called *Schwann cells* after their discoverer. So, the axon is encased first in myelin, if it is myelinated, and then always in Schwann cells. Cross-sectional views through one myelinated and three unmyelinated nerve fibers and their associated Schwann cells are shown in Fig. 1-7. The Schwann cells surround the nerve fibers over their entire length, with each cell occupying approximately the space between two nodes. As Fig. 1-7 shows, in the case of the unmedullated nerve fibers a single Schwann cell often encloses several axons.

Physiologically, the medullated nerve fibers differ from the unmedullated fibers chiefly because of the different velocities at which both are capable of transmitting action potentials. For reasons explained in detail later, the conduction velocity is very high in myeli-

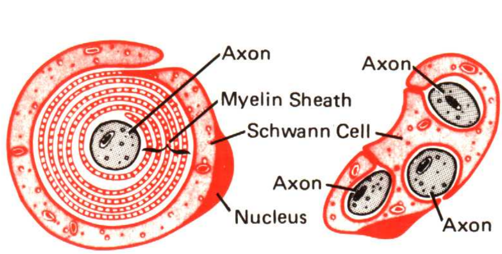

Fig. 1-7. Cross sections through medullated and unmedullated nerve fibers. The names of the two types of sheaths (myelin sheath, Schwann cells) are shown.

Table 1-1. Classification of Nerve Fibers.

Fiber Group			Diameter (μ)
Medullated fibers (diam. = axon + medullary sheath)	I	A fibers	18–10
	II	A fibers	10–5
	III	A fibers	5–1
Unmedullated fibers (diam. of axon)	IV	C fibers	1–0.1

nated nerve fibers and low in unmyelinated fibers. Within each group the conduction velocity also depends on the diameter of the axons: as the diameter increases the conduction velocity increases. Consequently, the various proposed anatomical and physiological classifications of nerve fibers coincide reasonably well. Medullated fibers are often referred to as *A fibers* and unmedullated fibers as *C fibers*. Table 1-1 shows the commonest classification according to diameter. The most frequently occurring diameters among the A fibers are those with values approximately equal to the mean values of the three ranges indicated, that is, 14, 7.5, and 3 μ.

Functional classification of nerve fibers. Apart from the conduction velocity and the diameter, a number of other functional characteristics are used to categorize nerve fibers. The most important of these are presented in Fig. 1-8. The nerve fibers of the receptors are called *afferent nerve fibers*, or, more succinctly, *afferents* (left side in Fig. 1-8). They lead to the CNS and transmit information from the receptors about changes in the environment or the body. Afferent nerve fibers from the intestines are termed *visceral afferents*, while all other afferents in the body—from muscles, joints, skin, and sensory organs of the head (eyes, ears, etc.)—are called *somatic* afferents.

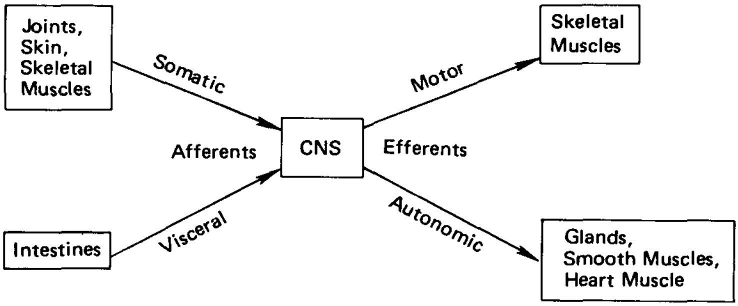

Fig. 1-8. Diagram of the classification of nerve fibers according to origin and function. See text for detailed discussion.

Transmission of information from the CNS to the periphery takes place by *efferent nerve fibers*, or, more succinctly, *efferents* (right side in Fig. 1-8). Efferents to the skeletal muscle fibers are called *motor* efferents. All the rest belong to the vegetative, or autonomic, nervous system and are therefore called *autonomic* efferents. The latter supply information to the smooth muscles of the intestines and in the walls of the blood vessels, as well as to the cardiac muscle and to all the glands in the body.

In the preceding paragraph we considered only the functional classification of individual nerve fibers. But, as we have already seen, a nerve contains large numbers, often many tens of thousands, of nerve fibers. In practically all nerves, for example, the Nervus ischiadicus, which innervates the greater part of the leg, afferent and efferent nerve fibers are bundled together. The types of nerve fiber contained in the nerve depend on the area (skin, muscles, intestines) it serves. It is now important to learn the names and the composition of these various nerves.

Classification of nerves. The nerves to the skin, the skeletal muscles, and the joints form the group known as *somatic* nerves. The nerves leading to the intestines are called *splanchnic nerves* (synonyms: autonomic nerves, visceral nerves, vegetative nerves; these terms are sometimes used with slightly different meanings, but we will not go into that here). A *cutaneous nerve* is thus a somatic nerve. It contains somatic afferents (afferent nerve fibers) from the receptors of the skin, but it also contains autonomic efferents to the blood vessels, the sweat glands, and the skin hair. A skeletal muscle nerve, usually called a *muscle nerve* for short, is also a somatic nerve. It contains motor efferents as well as somatic afferents from the receptors of the muscles and autonomic efferents to the blood vessels. A *joint nerve* is also a somatic nerve with somatic afferents from the receptors of the joints and autonomic efferents to the blood vessels of the joints and the joint capsule. The thick nerves, for example, Nervus ischiadicus, are usually *mixed nerves* that later branch into their component cutaneous, muscle, and joint nerves. Finally, we must mention that the *splanchnic nerves* contain visceral afferents and autonomic efferents.

You should now be able to give the correct answers to the following questions:

Q 1.7 Which of the following statements is/are correct?

a. Cutaneous, muscle, and splanchnic nerves form a group known as somatic nerves.

b. Unmedullated fibers are always larger in diameter than the medullated type.

c. "Somatic afferents" and "somatic nerves" are synonymous terms.
d. A cutaneous nerve has no motor efferents.

Q 1.8 By "nodes of Ranvier," we mean
a. The points where an axon branches into its collaterals.
b. The indentations in the Schwann cells caused by the unmedullated nerve fibers embedded in them.
c. The regular interruptions in the medullary sheath in the case of myelinated nerve fibers.
d. The gaps, filled with cerebrospinal fluid, between the cells of the CNS.
e. The point of transition of the receptor into the afferent nerve fiber.

Q 1.9 The diameter of medullated nerve fibers is in the order of magnitude of
a. 0.1–1 μ
b. 1–20 μ
c. 20–100 μ
d. 0.1–1.0 mm
e. 1–10 mm

1.4 The Anatomy of the Central Nervous System (CNS)

Of the two parts of the CNS, the brain and the spinal cord, the latter is phylogenetically by far the older and is relatively simple and stereotyped in structure. We will now study the structure of the spinal cord and, at the same time, gain an initial impression of the arrangement of the neurons in the CNS.

The structure of a spinal segment. The brain and the spinal cord are enclosed in bony protective casings (Fig. 1-9), the *skull* and the *vertebral canal*, respectively. As a result of this design the soft tissue of the CNS is optimally protected from mechanical damage. One section of the spinal cord, a *spinal segment*, corresponds to each vertebra. This uniform structure has been determined by evolutionary factors. As a person grows, however, the growth of the spinal segments falls behind that of the vertebrae so that, as the longitudinal (sagittal) section in Fig. 1-9 shows, in adult humans the spinal cord ends at approximately the level of the top lumbar vertebrae, although the segmented structure is fully retained.

The uniform structure of the spinal cord in the longitudinal direction, that is, the way it is built up of spinal segments, is matched by a uniform cross-sectional structure in all parts. Figure 1-10 illustrates such a cross section. The cell bodies of the neurons are located in the inner region of the spinal cord, and the ascending and the descending