CHAPTER III

NEURONS: SIZE AND GENERAL MORPHOLOGY

Any neural center, no matter how complex, consists of only two intimately intermingled cell types: neurons, with their conducting process or axon, and glial cells. The general histology of the nervous system is therefore based entirely on studies of these two elements, including such anatomical features as size, shape, and fine structure, as well as the functional properties associated with them.

We shall start with the fundamental unit of the nervous system, the nerve cell, or as Waldeyer has called it, the neuron.

NEURONAL SIZE

Neurons differ greatly in size from cells in other tissues. In fact, their cell bodies can attain diameters of 70 μm or more (even when the proximal parts of dendrites are excluded). Examples include large motor neurons in the bovine spinal cord and even larger cells in the torpedo electric lobe. However, not all neurons attain such dimensions: many are quite small indeed. Granule cells of the cerebellum and olfactory bulb, whose diameters range between 6 and 8 μm, are good examples of small cells.

Are these size variations entirely fortuitous? Comparative studies of cells in similar regions of homologous neural centers have established that this is not so. Instead, one principle emerges from this work: nerve cell volume decreases progressively from higher to lower animals, and this is true even if one considers only vertebrates.

At first glance, two factors would seem to account for this decrease in size: the small size of the animal, and the morphological simplicity of the cell.

These relationships are not strictly causal, however, and decreases in the size and morphological complexity of cells are not always strictly proportional to decreases in the size of cell bodies. Whatever the cause may be, the reduction involves both factors, and, within certain limits, cells can adapt to decreases in the volume of the central nervous system without affecting either the structure or the behavioral repertoire of the whole animal. Thus, the brains of fish, amphibians, and reptiles are not nearly as simple as the small size of their bodies would lead one to assume. And similarly, the brains of rabbits, guinea pigs, and rats show only insignificant behavioral and structural differences, despite large differences in body size.

Do other factors play a role in determining the size of neurons? The functional role of the cell has been suggested as one possibility. However, this can be excluded. For example, although motor neurons are usually quite large, many small ones have also been observed. Furthermore, large size is not the sole prerogative
of motor neurons; spinal ganglion sensory cells and one major group of retinal ganglion cells are among the largest neurons.

Another possibility, commonly attributed to Pierret, was that there may be a correlation between the size of a neuron and the length of its axonal trunk. At first glance, and from a superficial examination of the issue, this seems to be true. It is common knowledge that motor cells in the cervical and lumbar enlargements of the spinal cord (whose axons have to traverse much of the length of the limbs) are larger than motor cells in other parts of the cord.

Nevertheless, it is important to examine this question in more depth and look more closely at other parts of the nervous system. In the retina, we may find small ganglion cells adjacent to very large ganglion cells, and truly enormous amacrines cells immediately adjacent to dwarf amacrines. Are the axons, which are the major process of these different cell types, either shorter or longer? By no means. Similarly, there are Golgi cells with extremely short axons in the cerebellum, and yet these cells are much larger than other cerebellar neurons with axons that extend much farther. It is also interesting to compare several different species from this point of view. Fish and amphibians have certain monstrously large cells and axons that were first described by Mauthner. They are considerably larger, even in embryos, than most comparable cells in the largest vertebrates. And even in invertebrates, nerve cells may often attain colossal sizes, although their axons must travel relatively short distances. Surely these exceptions are enough to tip the scales against Pierret's rule, rendering it invalid as a general principle.

In our opinion, one must compare the size of a nerve cell to the diameter of its axonal trunk, and more especially to the number and thickness of its collateral and terminal branches. Again let us cite a few examples. Motor neurons of the spinal cord, giant neurons of the torpedo electric lobe, Golgi type II cells of the cerebellum, and large horizontal cells of the retina are all large, and their axon ramifies profusely and contacts many other neurons. In contrast, granule cells of the cerebellum, bipolar cells of the retina, granule cells of the fascia dentata, and so on are all pygmy neurons, and their axon is remarkable precisely because it branches so rarely. In summary, the dimensions of the neuronal cell body are proportional to the number of axonal ramifications they generate and to the number of cells they contact.

Obviously these dimensions cannot exceed certain limits, a principle governing not only neurons but cells in all other tissues. The limit is the amount of cytoplasm compatible with the maintenance of a viable cell; in other words, it is related to the amount of cytoplasm necessary for adequate cellular metabolism and respiration. As Bullot has pointed out, excessive size (especially in the absence of all processes) would prevent the rapid penetration of oxygen and metabolites throughout the cytoplasm. At the same time it would be virtually impossible to rid the cell of carbonic acid and the other by-products of cellular catabolism rapidly enough. A corollary is that nutrient exchange ought to be much faster in small cells such as granule neurons than in large cells such as spinal motor neurons.

**NEURONAL MORPHOLOGY**

One of the basic features of neurons is that they generate and conduct nerve impulses, and naturally their morphology or shape is adapted to serve these two functions. In addition to the cell body, which is a factory that generates or trans-
forms impulses, neurons give rise to a thread-like axon that directly or indirectly links the sensory surfaces of the organism (through receptors, which detect environmental changes in the skin and other sense organs) to the effector organs of movement and secretion, muscles and glands. Shape is thus an important feature because it reflects the relationships of neurons to other cells. It would, of course, be expecting too much to think that the form of cells would by itself reveal the nature of neural excitation. However, by directing us to the various neural centers that lie along specific functional pathways, and by demonstrating how excitation passes from one neuron to another, it has already performed a noteworthy service.

Nevertheless, it seems logical to think of neurons as responding so that the number of inputs is proportional to the complexity of their axonal ramifications, and it is not unreasonable to formulate this hypothesis a priori. In vertebrates, where associational connections in the gray matter are most abundant, the form of neurons is more complex than in invertebrates, where there are relatively few neuronal connections.

Comparative histology has transformed this a priori assumption into an indisputable fact: There appears to be a distinct morphological hierarchy among neurons as one passes from invertebrates, to mammals, to humans, with unipolar cells at the bottom and multipolar cells at the top. However, let us leave aside for the moment such evolutionary considerations and view neurons strictly from a morphological perspective. When we do this, it becomes clear that they may be divided into three classes: unipolar, bipolar, and multipolar cells.

The first class, unipolar cells, has, as the name implies, only one process. This process at times generates a rich arborization, as in the case of retinal amacrine cells; or it may simply bifurcate into two branches that run in opposite directions, as in the case of spinal ganglion cells.

Bipolar cells are characterized by two processes that arise from opposite poles of the cell body. One of these processes is usually thicker than the other and is directed toward a sensory surface; the other, thinner process extends through underlying tissues, and at times reaches as far as the central nervous system. Examples of bipolar neurons include receptor cells of the olfactory mucosa, bipolar cells of the retina, spiral ganglion cells in the cochlea, and various sensory cells in fish and invertebrates.

Multipolar cells predominate in the spinal cord, cerebellum, cerebrum, and sympathetic trunk. The name is derived from the multiplicity of dendrites that these cells issue. The number of dendrites can range from three or four to many more; they are usually branched, and always end freely.

Is it worthwhile to formulate a more natural classification of the various kinds of neuron? If so, it should be based on the structure, length, branching pattern, and connections—in short, on the functions—of the axon, as well as on the shape of the cell body and the number of its dendrites.

As Deiters first pointed out on anatomical grounds, and modern physiological thinking confirms, there are clearly two distinct types of neuronal process. One is thin, flexible, and often covered with a myelin sheath that transforms it into a tube-like structure over the greater part of its course. In addition, this type of process gives rise to many branches that normally leave at right angles and at times terminate at considerable distances from the parent process. This type of process conducts nerve impulses toward its terminal arborizations, or, to use Van Gehuchten's expression, in a cellulifugal direction. It was called the neural prolongation by Gerlach, the axis-cylinder by Deiters, the neuraxon and axon by Kölliker.
and Lenhossek, \(^5\) and the *principal process* by Kallius. \(^6\) The second type of process is thick, has an irregular surface, usually branches at acute angles, and ends abruptly near its origin from the cell body. The direction of conduction in such processes is toward the cell body, or, to be more precise (for reasons we shall consider later), toward the origin of the axon. They are in essence celluipetal, or better yet, *axopetal*, and are variously called *protoplasmic processes or dendrites*, as suggested by His. \(^7\)

On the basis of these different anatomical and functional characteristics, we have devised the following more natural and more complete classification of neurons.

**CLASS**

**SUBCLASS**

(a) Cells with relatively short processes.

(b) Cells with a long axon.

(c) Cells with a long myelinated axon.

(a) Sensory cells with a receptor process and an axon.

(b) Cells with multiple dendrites and a long axon.

(c) Cells with multiple dendrites and a short axon.

(d) Cells with multiple dendrites and a long axon that branches and sends many collaterals through the white matter.

**TYPES**

- Retinal amacrine cells.
- Olfactory granule cells.
- Interstitial cells in glands and the enteric system of the gut.
- Unipolar cells in the mesencephalic nucleus of the trigeminal nerve.
- Olfactory bipolar neurons, retinal ganglion cells, and neurons in the spiral ganglion of the cochlea, in Scarpa’s ganglion, and in spinal ganglia.
- Motor, autonomic, and association neurons.
- Golgi type I cells in the cerebellum, cerebrum, and so on.
- Cells with a T-shaped axon in the cerebellum and spinal cord, other cells with a complex axon.

Admittedly, this purely morphological classification is much less useful than one based on the function of each cell type. In fact, the morphology of neurons with the same general function clearly differs in descending the animal series. Unfortunately, because we do not yet know the function of a great many neurons, we are forced to rely entirely on their external morphology or shape.

Bearing these serious reservations in mind, let us now examine in detail the classification that we have just proposed.

**A. Cells with Only Cellulifugal Processes.** The clearest examples of cells without dendrites or axopetal processes are retinal amacrine cells, olfactory bulb granule
cells, certain autonomic cells in the intestine and glands, and cells in the mesencephalic nucleus of the trigeminal nerve.

The retinal spongioblasts we have called amacrine cells display a variety of shapes. Some are unipolar, with a descending trunk-like process that ramifies within the inner plexiform layer; whereas others seem to be multipolar, although this appearance is deceptive because the terminal arborizations arise directly from the cell body, rather than from a common trunk. The terminal branches of these processes are sometimes long and thin and sometimes short, thick, and tortuous. But these subtle differences should not obscure the true character of the branches, which are all essentially the same. Without knowing the connections made by these processes, it is difficult to identify exactly what their nature may be. However, because we do know that the cell bodies generating them are contacted (and presumably activated) by the central processes of photoreceptors, conduction in amacrine cell processes is undoubtedly cellulifugal, and in this sense they function as axons.

Neurons in the interstitial tissue of glands and those associated with smooth muscle fibers seem to provide another example of dispossessed cells with an axon and no dendrites.

If one examines sections that have been cut through superficial parts of the intestine and stained with Ehrlich’s methylene blue, here and there one observes (in regions not occupied by the ganglia of Auerbach’s plexus) fusiform, triangular, or stellate cells with slender varicose processes winding between groups of muscle fibers, upon which at least some of them appear to end. It is impossible to distin-
guish more than one type of process arising from these cells. We first observed them in the intestine and pancreas, and they were later found in various glands by E. Müller, and in Auerbach's plexus by Dogiel, who referred to them as Cajal cells. They have also been observed by Lavilla (Fig. 5).

Granule cells of the olfactory bulb are constructed along the same general pattern, and appear to fall into the same category.

There is one striking feature common to these cells with only one type of process: Despite the fact that their processes are undoubtedly axonal, none of their branches have myelin sheaths. However, there is one exception to this general rule, namely, the pear-shaped unipolar cells discovered by Golgi in the mammalian brain that Kölliker, Lugaro, and we have identified as giving rise to the mesencephalic root of the trigeminal nerve. The single process of these cells (Fig. 6) is covered with myelin, distinguishing it as a true axon. Moreover, during its course, the process gives rise to abundant collaterals that ramify within the motor nucleus of the trigeminal nerve.

B. Cells with Two Kinds of Process. A majority of the cells listed under this class in the accompanying table may be divided into four groups, but for simplicity we shall consolidate them into just two. The first group consists of sensory cells and includes all cells with only one axon and one dendrite; it corresponds to the first subdivision in the table. The second group consists of multipolar cells in the central nervous system that have many of the same features as cells in the first group—including a single axon—but also have a rich complement of dendrites; this group encompasses the last three subdivisions in the table.

1. Sensory Cells or Neurons with One Axon and One Dendrite. Neurons in this category are among the best defined, and their principal characteristics are already displayed in the earliest forms of neural tissue in the animal kingdom. They may lie in the skin and mucous membranes, or in ganglia some distance from the neuraxis. Their cell bodies are almost always fusiform and give rise to one process from either end. One process can be thought of as central and the other as peripheral. The latter generally extends toward an epithelial surface, where it generates a sheaf of thin terminal branches. Conversely, the central (and usually longer) process extends either toward the neuraxis or toward other cells that lie deeper within the organism. Both
processes may conduct nerve impulses, but in opposite directions. The relationships can be deduced from a knowledge of the contacts established by the terminals of each type of process. The peripheral process is in contact with the external environment and can respond to environmental stimuli and transmit them to the cell body; in other words, it is a cellulipetal process, or dendrite. The deep process is a conduit for transmission between the stimulated cell body and the as yet inactive central nervous system. It serves only to transmit transformed or untransformed excitations from one cell to another, and is thus a cellulifugal process or axon (Fig. 7).

At times both the peripheral and central processes lack myelin sheaths, as in retinal bipolar cells, unipolar cells of the vertebrate olfactory mucosa, and various sensory cells of invertebrates. At other times, as in bipolar cells of the auditory (spiral) and vestibular (Scarpa’s) ganglia, and in the spinal ganglia, both processes have an insulating myelin sheath. It is thus clear that myelin is not an essential feature of sensory cells, nor, for that matter, is the site from which the processes emerge from the cell body. Not all sensory cells present a bipolar shape; we know, for example, that, whereas spinal ganglion cells in certain fish are bipolar, the homologous cells in amphibians, birds, and mammals become unipolar and yet continue to function perfectly well as sensory cells. The transformation from a bipolar to a unipolar shape—whose functional significance will be discussed later—seems to have no effect on either the course or relationships of the peripheral and central processes, which, in higher vertebrates, arise from a common, short, initial process generated by the sensory cell body.¹⁰

Only one of the characteristics of sensory neurons just listed is constant and truly unique: the existence of two conducting processes, one cellulipetal and the other cellulifugal.

II. Multipolar Cells of the Central Nervous System with an Axon and Many Dendritic or Cellulipetal Processes. These cells have two kinds of process, and are so common that they form much of the framework of the central nervous system, as well as the autonomic ganglia.

There is a truly immense number of such cells. And while the group as a whole is characterized by the presence of multiple dendrites, individual cells may be distinguished on the basis of a number of secondary features. We thus feel justified in subdividing the group, along lines suggested by the disposition and characteristics of the two kinds of process.

(a) This subdivision is based on the form and orientation of dendrites.

1. Stellate Cells. This cell type displays highly branched dendrites (often with irregular contours and covered with delicate spines) that diverge from one another while radiating in all directions from the cell body. Examples of cells in this cate-
gory include motor neurons, various projection cells in the spinal cord and brain-stem, autonomic neurons, and so on (see Fig. 11).

2. Cells with a Simple Apical Dendrite. These cells have a massive, long dendrite arising from one side of the perikaryon and ending as a tuft of small branches in a more superficial layer or, more generally, in a molecular layer. The best examples of this cell type are pyramidal cells of the cerebral cortex (Fig. 8) and mitral cells of the olfactory bulb.

P. Ramón also discovered this cell type in the optic lobe of reptiles and amphibians, where the apical dendrites synapse in a complex, knot-like arrangement with incoming axons from the retina. The branches of their apical dendrites are short, tortuous, varicose, and free of spines, and are distributed within the various concentric molecular layers.

3. Arboriform or Bipolar Cells. These tree-like cells have “roots” or descending dendrites (one of which normally gives rise to the axon), and a more or less elongated “trunk” or ascending dendrite that emerges from the apex of the cell and then branches profusely. The branches and roots bristle with silky spines, like shaggy caterpillars. The most appealing examples of this elegant cell type are found in Ammon’s horn, particularly in smaller mammals, and in olfactory regions of the cerebral cortex (see Fig. 14). They are also abundant in the optic lobes of birds, reptiles, and amphibians, where their elegance is enhanced by an unusual histological feature: The axon commonly arises from the trunk or one of the ascending dendrites and has a characteristic bend in its initial course. We have referred to them as Shepherd’s crook cells (see Fig. 36).

4. Unipolar Cells with Highly Branched Dendrites. The processes of these cells are distinctly polarized and arise from a more or less spherical perikaryon. Either a single dendritic trunk, or a cluster of dendritic shafts, arise from the superficial pole of the soma, and immediately generate an espalier-like arrangement of branches. In contrast, the thread-like axon emerges from the opposite pole of the

---

**Fig. 8.** A pyramidal cell from the rabbit cerebral cortex. This cell type has an elaborate dendritic tree. Golgi method.

a, basal dendrites; b, dendritic trunk and its branches; c, axon collateral; d, long axon; e, white matter.
cell body. Although this verbal portrait could be mistaken for a description of the sensory cells considered above, the two cell types are actually quite different. A cursory glance at the illustration of a Purkinje cell from the human cerebellum (Fig. 9) is more helpful than any verbal description. One cannot help being astounded by the complex dendritic arborizations of such cells, and others of this general class, such as granule cells of the fascia dentata and ganglion cells of the retina. It is difficult to imagine how the terminal branches of axons find their way in this web of densely intertwined branches.

(b) The various types of multipolar neuron can also be analyzed on the basis of axonal features. The most variable characteristic of axons is undoubtedly their length. Golgi, and many later workers, remarked on this in the cerebral cortex, cerebellum, and spinal cord. Golgi was so impressed by differences in axonal length that he advanced a dualist theory of nerve cell function based primarily on this feature. Following Golgi, we shall use axon length as our primary guide.

Type II Cells or Cells with a Short Axon (Fig. 10). The axon of this cell type ends near its origin in a terminal arborization often consisting of an indescribably tangled mass of tortuous branches that surrounds adjacent neurons. Such cells are common in the cerebellum, cerebral cortex, corpus striatum, and spinal cord, but seem to be absent in the autonomic and spinal ganglia. For some obscure reason, Golgi regarded this cell type as sensory in his dualist functional theory, a notion we have challenged and shown to be incorrect.

To avoid prejudging their function, and instead rely solely on anatomical obser-
vations, we have referred to them as neurons with a short axon. Retzius called them Golgi cells, and in what follows only these two terms will be used.

Type I Cells or Cells with a Long Axon (Fig. 11). In this cell type, the axon arises from a stellate, pyramidal, or bipolar cell body, or in some cases even a dendrite. It leaves the gray matter more or less directly from its point of origin and enters the neighboring white matter, where it continues either as a myelinated association fiber or as a fiber in the root of a motor nerve. If it arises from an association or projection neuron in the brain, it courses toward other neural centers; if it arises from a motor neuron in the spinal cord or brainstem, it projects toward muscle fibers. At its destination, the axon generates a shower of freely ending, varicose terminal branches contacting the appropriate cells. Before terminating, however, such axons usually generate (commonly at right angles) innumerable collateral

---

**Fig. 10.** A neuron with a short axon in the cerebral cortex. Golgi method.

**Fig. 11.** Motor neuron of the spinal cord; cat fetus. Golgi method.

A, ventral sulcus of the spinal cord; c, axon; a, axon collaterals; b, d, f, and g, dendrites.
branches in both the gray and white matter; these collateral branches are directed toward other neurons.

This type of cell with a long axon was among the first discovered in the central nervous system and is the most common type of neuron in the spinal cord, brainstem, cerebral cortex, autonomic ganglia, and so on. Although they were christened motor cells by Golgi, we need hardly take the time to show how inappropriate such a designation is. Instead, the term cell with a long axon will be used exclusively because it carries no functional implications.

Cells with a long axon comprise such a vast group that the following subdivisions—based again on axonal morphology—may be proposed.

**Cells with a Simple Axon.** We need not describe again motor and association neurons, except to say that they are paradigmatic of this cell type, their long, single parent axon generating many collaterals. Instead, we shall point out two other varieties: cells with a bifurcated axon and cells with a complex axon.

**Cells with a Bifurcated Axon.** The axon of these cells gives rise to a T- or Y-shaped bifurcation. Examples of such neurons that we first provided include cerebellar granule cells, many spinal funicular cells, certain cortical pyramidal cells, and a variety of brainstem neurons. The branches resulting from this bifurcation may be of equal or unequal diameter, and may proceed in opposite directions. In general, both branches are myelinated and course through the white matter, so that they transmit nerve impulses to widely separated regions, and end by way of more or less complex terminal arborizations; furthermore, each branch may give rise to collaterals that contact other cells in the gray matter.

**Cells with a Complex Axon.** Finally, certain neurons in the spinal cord, brainstem, and cerebral cortex give rise to an axon that, after coursing through the gray matter for some distance, divides into two, three, or even more branches. Each of the branches usually enters a different fiber tract, becomes myelinated, and ends in a remote and often quite different neural region.

On general anatomical principles, it is evident that neurons with a short or long axon must play significantly different roles in the organization and function of the central nervous system. Thus, cells with a short axon usually exert their influence upon similar neurons within the same neural center, whereas cells with a long axon are able, through their initial collaterals, to influence adjacent neurons, but at the same time they can activate neurons in more distant parts of the central nervous system through their collaterals in the white matter and the terminal arborizations of their parent axon. Thus, the former (type II) form short intranuclear pathways, whereas the latter (type I) form intercentral or internuclear pathways.

The axon of a multipolar cell is not always distinct enough to classify it with certainty as either a cell with a short axon or a cell with a long axon. There are also multipolar neurons with an axon that is intermediate in character and often difficult to classify. Among these intermediate forms, we might call attention to stellate cells in the molecular layer of the cerebellum (see Fig. 21) (the basket cells of Kölliker) and certain neurons with an ascending axon in the cerebral cortex and Ammon's horn that were discovered by Martinotti. The axon of each cell type has features characteristic of types I and II mentioned above. And while they do not leave the region in which they arise, they often extend over enormous distances within the region, grasping neurons encountered along the way in the claws of innumerable collaterals.
NOTES


5. V. Lenhossek, Der feinere Bau des Nervensystems im Lichte neuester Forschungen, etc. Berlin, 1895.


10. The general idea of forming a special group of neurons that includes all sensory neurons and is characterized by neurons with two precisely oriented processes was first advanced in an article we wrote entitled Comexión general de los elementos nerviosos, which appeared in Medicina práctica in 1889.

To include the unipolar cells of spinal ganglia in this synthesis, so they are considered homologous with olfactory and auditory bipolar cells from both the ontogenetic and phylogenetic points of view, we assume here that their peripheral process is a dendrite.

The reduction of such apparently disparate elements to a single group was greeted with such enthusiasm by Retzius that he extended it to include invertebrate sensory cells. At the same time, he showed that receptor and sensory cells differ only in their topographic location (Retzius, Biologische Untersuchungen, Neue Folge, Bd. IV, 1892). Von Lenhossek, with his magnificent discovery of sensory cells in worms, and Van Gehuchten with his views on the function of dendrites, have confirmed the foundations of this theory, which at first glance appeared so daring. In this short historical overview we should not forget to mention how much of the important research of His on the histogenesis of ganglia, which has been confirmed by our own work and that of Lachi, Lenhossek, Van Gehuchten, Retzius, and others. (His, Die Neuroblasten und deren Entstehung im embryonalen Marke. Arch. f. Anat. u. Entwickelung, 1887). By demonstrating the transformation of bipolar cells into unipolar cells in spinal ganglia, and by pointing out that sensory nerve roots are formed by the central processes of peripheral ganglion cells that enter the brainstem and spinal cord, these various studies have prepared the way for our important generalization.

11. Cajal's original text is confusing to the modern reader because he refers to type I Golgi cells as having a short axon, and type II Golgi cells as having a projection axon. In the translation, we have adhered to Golgi's original designation (and modern usage) of type I cells as having a long axon—LWS.