Nonpyramidal Neurons
General Account

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1. Introduction

Much information about nonpyramidal cells was available by the turn of the century, in the earliest writings by Ramón y Cajal. His contributions, based on the extensive use of the Golgi methods, are summarized in his 1911 book. This book seemed to have closed an era of an extremely promising endeavor, as Ramón y Cajal himself rather bitterly complained in 1921. His approach, in fact, was not widely followed by students of cortical architecture during the first half of the present century, although there were outstanding exceptions such as his pupil Lorente de Nó (1922, 1933, 1934, 1949) and O’Leary (O’Leary and Bishop, 1938; O’Leary, 1941). A lucid analysis of the circumstances that may have led to such a situation is given by Schiestel and Schiessell (1970). For the cerebral cortex, a significant factor was that, due to the intricacy of its neuronal circuits, no schemes of interneuronal connectivity could emerge from the analysis of Golgi preparations alone (Van der Loos, 1976), although masterly insights were

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variants seem to indicate that with these techniques the impregnation is selective and bears some, as yet unclarified, relationships to the conditions in which the reaction takes place, e.g., aldehyde perfusion vs. direct immersion-fixation in the chromating solution, and duration of chromation and silvering. If impregnation is selective, it follows that negative findings, such as absence of a given cell type in a given cortex, are meaningless. Additionally, selectivity of impregnation makes the Golgi method not ideally suited to study distribution, or frequency of occurrence, of neurons in a given brain area.

Completeness of impregnation was generally believed to be related to the overall quality of the impregnations, but Golgi-electron microscope studies have made us aware of the fact that incomplete impregnations are not rare (e.g., Peters and Fairén, 1978) and confirmed the suspected fact that myelinated axons do not stain (e.g., Somogyi, 1978; Peters and Proskauer, 1980a,b; Peters and Kimerer, 1981). Recent studies using intracellular injections of markers (e.g., Gilbert and Wiesel, 1979) have also suggested that axonal impregnation may be incomplete in Golgi preparations. The use of young specimens permits better axonal impregnations but the possibility of synaptic rearrangements during early postnatal life must be considered (e.g., Somogyi et al., 1982; see Section 3.5.2).

Whether local synaptic connections may be predicted from Golgi observations has been a matter of controversy, but fortuitous contacts may be occasionally seen, the Golgi impregnation revealing both the pre- and postsynaptic elements; and the real synaptic nature of some of these contacts has been confirmed recently (e.g., Peters and Proskauer, 1980a; Peters and Kimerer, 1981; Fairén et al., 1982). However, light microscopy alone is unreliable as a means of identifying synaptic relationships.

Computer technology has offered a complementary approach to the study of Golgi-stained material (Glaser and Van der Loos, 1965; Garvey et al., 1973; Wann et al., 1973; Llinás and Hillman, 1975; and see Jones and Hartman, 1978, and Woolsey and Dierker, 1982, for reviews). The use of these procedures has been useful in defining the general trends of the tangential distribution of neuronal processes in the cerebral cortex (e.g., Glaser et al., 1979; Steffen and Van der Loos, 1980; but also see Colonnier, 1964, and Wong, 1967). Their application to the characterization of nonpyramidal cell groups (Martin-Falda and Sibilia, 1974; Jones, 1975; Martin-Falda, 1975; Woolsey et al., 1975; Valverde, 1976, 1978; Fairén and Valverde, 1980; Peters and Regidor, 1981) shows promise, but the potential of these methods to quantitatively define dendritic (e.g., Woolsey et al., 1978; Uylings et al., 1981) and axonal branching patterns, as an aid to classification of nonpyramidal cells in the cerebral cortex, has not been fully exploited.

2.1. General Comments on Methodology: The Value of the Golgi Methods in Defining Nonpyramidal Cell Populations

Since most available data on morphology of nonpyramidal neurons in the cerebral cortex have derived from the use of the Golgi methods, a few comments on the powers and limitations of these procedures are pertinent. First of all, the Golgi methods, by their very nature, are unpredictable (Valverde, 1970; Scheibel and Scheibel, 1978). There are some indications that, in the Golgi-Cox method, impregnation occurs at random (Sem and Colon, 1969; Pasternak and Woolsey, 1975), but common experience with the rapid Golgi method or the K opinobtained by Lorente de Nó (1949). For a time, very simple classifications of cortical neurons, such as that by Sholl (1956), dominated the scene, but in 1966 Colonnier anticipated the real importance of reevaluating the old descriptions and, from this time on, there has been a renewed interest in Golgi studies of cortical organization. The present chapter aims at reviewing the wealth of information these studies have provided on the morphology of nonpyramidal cells in the neocortex, and at integrating these data, whenever possible, with other pieces of information that have emerged recently. In line with a recent review (Fairén and Valverde, 1979), it was deemed important to try to assemble a catalog of neuronal types to serve as a basis for the interpretation of experimental results, even if such a goal cannot be fully attained as yet. Additionally, an attempt is made at determining whether each type of nonpyramidal neuron is a constant cellular component of all areas of the neocortex and through mammalian phylogeny.

2. Methodological Considerations

This review has largely been based on the study of our own collection of Golgi preparations of young mice, rabbits, and cats. Mice were approximately 3 weeks old, and rabbits and cats 8 months old. Additional material from hedgeshogs, rats, and monkeys has been made available to us for comparisons, and we have examined some of the preparations of human specimens made by Ramón y Cajal himself (Cajal Museum, Madrid). Golgi drawings from the literature have constituted a second, significant source of information.

In the present account, as in most Golgi studies, a certain degree of subjectivism has been unavoidable, when defining criteria for different neuronal types (see Chapter 4). Taxonomy of neurons (Tyner, 1975; Rowe and Stone, 1977, 1980; Mann, 1979) relies on the selection of certain characteristics which may define neuronal subsets. In the present account, the choice has been to consider primarily the forms of the axonal arborizations, but other features such as the morphology of the dendritic trees have also been taken into account. Axonal geometry is, in certain cases, very distinct and facilitates comparisons with published drawings. It is obviously related to the local effector connectivity of the cells, a feature of functional significance on which we shall dwell.

2.2. Novel Approaches to Nonpyramidal Cell Organization

Many of the uncertainties associated with a Golgi analysis can often be resolved through the application of techniques which allow correlations of morphology, pharmacology, and physiology of nonpyramidal cells in the cerebral cortex. These include electron microscopy, transmitter localization, and intracellular recording and are dealt with in Chapter 4.
2.2.1. The Ultrastructural Features of Nonglial Neurons

A basic dichotomy in synaptic organization between spine-free or sparsely spined and spiny-laden cell types (comprising both pyramidal cells and layer IV spiny stellate cells) was established by LeVay (1975) in the visual cortex. Subsequent studies have clearly established that spine-free or sparsely spined cells do not constitute a unique category. With a single exception, the different synapses formed by the axonal arborizations of these cells are of the type II (Gray, 1959) or asymmetrical type (Colonetti, 1968), as established by LeVay (1973) and Parnavelas et al. (1977b), but subtle variations seem to exist among the different types of neurons in the morphologies of these synapses (Peters and Fairén, 1978; Peters and Proskauer, 1980a; Somogyi and Cowey, 1981). In addition, the distribution of different synapses made by individual cell types is often very distinct, as will emerge below. It is also important to note that the relative proportions of different synapses from different sources can also vary among the different types of nonglial neurons (Davis and Sterling, 1975; Hersch and White, 1981a; White and Rock, 1980, 1981).

Golgi–electron microscope studies, by correlating geometrical aspects revealed by the Golgi stain with these different patterns of synaptic connections, have established a firm basis for characterizing a number of nonglial cell groups on morphological grounds, though not all classes have yielded to this sort of analysis yet.

2.2.2. Localization of Neurotransmitters in Nonglial Neurons

Immunocytochemical studies have shown that many nonglial cells contain material which co-reacts with antibodies against glutamic acid decarboxylase (GAD), vasoactive intestinal polypeptide (VIP), cholera toxin (CCK), avian pancreatic polypeptide (APP), or somatostatin (SRIF).

GABAergic neurons, demonstrated by GAD immunocytochemistry (Ribak, 1978; Ribak et al., 1979, 1982; Emson and Hunt, 1981; Hendrickson et al., 1981; Hendrickson, 1982; Hendry et al., 1983a; Houser et al., 1983) or the selective uptake of [$^{3}H$]-GABA (Hökfelt and Ljungdahl, 1972; Chornwall and Wolff, 1978, 1980; Hendry and Jones, 1981; Somogyi et al., 1981a,b; Wolff and Chornwall, 1982), constitute a heterogeneous population, but all of them are intrinsic neurons (Hendry and Jones, 1981) and, as we will show, some correlations can be made with morphological types (see also Chapters 8–10, and Chapter 5 in Volume 2).

Immunocytochemical identification of peptide-containing nonglial neurons may give clues to the interpretation of certain nonglial cell groups which have not been sufficiently defined in Golgi-based studies (see McDonald et al., 1982a; also Chapters 11, and Chapters 8 and 9 in Volume 2). In addition, coexistence of peptides in cortical neurons (e.g., APP and SRIF; see Vincent et al., 1982a,b) must be taken into account to evaluate the presence of a given peptide as a distinguishing characteristic of a certain neuronal population.

Nonglial neurons which co-react with antisera to VIP (Loren et al., 1979; Fabrènkrug, 1980; Simal et al., 1980; Emson and Hunt, 1981; McDonald et al., 1982a; Morrison 1982) are morphologically similar to bipolar neurons of the rat visual cortex (Feldman and Peters, 1978; Peters and Kimerer, 1981), but other VIP-containing neurons are multipolar. CCK has been localized to certain nonglial neurons (Emson and Hunt, 1981; McDonald et al., 1982b; Hendry et al., 1983b; Peters et al., 1983) which are bistratified or bipolar in form; multipolar morphologies are also found. More extensive studies on the localizations, overall morphologies, and synaptic properties of nonglial neurons have proven to be particularly difficult to establish.

3. A Comparative Overview of Nonglial Cells in the Neocortex

During the preparation of the present account, our main concern has been to try to define homologies between comparable populations of nonglial neurons in different cortical areas of different mammalian species. We were painfully aware of the fact that sound criteria are largely nonexistent. Nevertheless, we have tried to assemble the sets of data available with the hope that our comments, tentative as they are, will stimulate future research into the organization of nonglial neurons. The rationale of our intent has not been followed consistently. It is based on the consideration of the nonglial neurons as entities that may have essential features independent of the particular context (i.e., layer and area) where they happen to occur. Obviously, nonglial neurons entirely comparable on the basis of a number of criteria will differ radically in their connectivities if they are located in different cortical areas or in different cortical layers and the functional roles they accomplish may necessarily be different. What we will try to analyze are the intrinsic properties of the pieces of a puzzle. How these pieces are to be assembled together in order to complete a picture of the local circuitry of a given cortical area is another concern.

The review that follows is restricted to the nonglial neurons located in layers II through V of the cerebral cortex, where our best Golgi impregnations have occurred and give us a basis for comparisons with the contributions made by other authors.

A definition of the term nonglial has been deliberately avoided. It must be pointed out, however, that nonglial cells are not always nonprojecting neurons (see Section 5.5) and, on the other hand, that certain pyramidal cells may possess exclusively intracortical axons (Ramón y Cajal, 1899b, 151; Lorente de Nó, 1949; Valverde, 1971; Luer et al., 1979), but these neurons have not been considered in the present review.

To present our data, we had to choose a classification of nonglial neurons. Dendritic arborizations may suitably be described on the basis of the terminology devised by Feldman and Peters (1978). How to compare axonal arborizations has posed more problems and, finally, we have adopted a descriptive classification which has its roots in Lorente de Nó (1949) and is not dissimilar to some of the ones proposed in recent studies (Jones, 1975; Noita and Ka-
descending branches have also been described. In addition to this terminal arborization, it is not infrequent to observe a relatively dense local plexus originating from the initial portion of the axon (Ruiz-Marcos and Valverde, 1970; Valverde, 1976; Fairén and Valverde, 1979), which, occasionally, may be rather rich (Valverde, 1976, his Fig. 6). But, given the possibility of incomplete impregnations, it is difficult to judge how extensive a local axonal arborization should be before it can be considered characteristic. It is of interest to note that, as already suggested by Ramón y Cajal (1921, 1922), the axons of Martinotti cells may be myelinated in adult specimens.

Martinotti cells seem to be present in many species and in many cortical areas. Reports include the mouse somatosensory (Lorente de Nó, 1922) and visual cortices (Ruiz-Marcos and Valverde, 1970; Valverde, 1976, his type II axons; Fairén and Valverde, 1979); the rat visual (Feldman and Peters, 1976, their Fig. 20C) and circulate cortices (Vogt and Peters, 1981); the rabbit visual cortex (O’Leary and Bishop, 1958; Shkolnik-Yarros, 1971); the cat visual cortex (Ramón y Cajal, 1921, 1922; O’Leary, 1941) and other neocortical areas in the cat (Marín-Padilla, 1972, 1978); and the human somatosensory (Ramón y Cajal, 1911) and motor cortices (Marín-Padilla and Marín-Padilla, 1982). On the basis of these reports, it can be concluded that Martinotti cells are ubiquitous components of the mammalian neocortex. Their role in the cortical circuitry remains unknown, although it is clear, since they must represent an important synaptic input to layer I neurons, that information on the connectivity of these cells must be obtained. Here is the suggestion by Szentágothai (1978) that Martinotti axons might contribute asymmetrical synapses to the dendritic spines in layer I.

To complete the group of cells with ascending axons entering layer I, we will refer to a type of cell that Ramón y Cajal described, for the first time, in the human sensory motor cortex (1899c). In his Fig. 9G, he illustrates a “cortízculo estrellado axona,” a small multipolar or bifurcated cell located in layer II, possessing an ascending axon which arborizes profusely in the supragranular layer I. The term “axon tuft cell” coined by Szentágothai (1978) expresses accurately the essential features of this neuronal variety. Drawings of layer II cells with the axon arborizing in layer I are given by Lorente de Nó (1922) in the somatosensory (his Fig. 7H) and entorhinal cortices of the mouse (Lorente de Nó, 1933, his Fig. 4 I); these cells, however, do not form the typical dense axonal tuft. A recent example is given by Lund (1973) in her account of the monkey area 17 (her Fig. 39X). According to Szentágothai (1975), axon tuft cells would form symmetrical synapses on dendritic spines in layer I, but more direct evidence is necessary to substantiate this proposal.

A second conspicuous variety of cells with ascending axons may be recognized; two examples from the cat auditory cortex are shown in Fig. 1. These are large bifurcated or multipolar cells, located in layers III-V; in some cases (as in cell B of Fig. 1A), the perikaryon has the form of an inverted triangle. As in

* In this figure, as in the other original Golgi drawings, the axons (in solid black) have been drawn in such a way that all their collaterals appear as if they were superficial to the dendritic arborization.

This has been done in order to enhance the patterns of axonal distribution. To facilitate comparison of sizes, all the original illustrations of Golgi-stained cells have been reproduced at the same final magnification, with the exception of Fig. 8A.
the case of Martinotti cells, the axon stems from the upper aspect of the cell body or from the base of a dendrite and then ascends, occasionally, to layer I. One differential characteristic, however, is the presence of conspicuous, long horizontal collaterals which give origin, in turn, to short vertical branches. This neuronal variety has been known since the earliest studies of Ramón y Cajal on the cerebral cortex of the mouse (1891, his Fig. 6c) but, according to that author, they are also present in the human visual cortex (1911, his Fig. 384P). Other examples found in the earliest literature are from the somatosensory cortex of the mouse (Lorente de Nó 1922) describes them there as “células cosasoles,” gigantic cells, in his Figs. 11 A, B, F. They have also been seen in the rabbit visual cortex (O’Leary and Bishop, 1938, their Figs. 9-2 and 14-5) and in the visual cortex of the cat (O’Leary, 1941, his Fig. 9-8). These data, obtained in rather different species, seem to indicate that such cells might be present in all mammalian cortices. It is remarkable that, with some exceptions, modern reports do not mention the existence of such nonpyramidal neurons. In their account of the rat visual cortex, Parnavelas et al. (1977a) illustrate, in their Fig. 6, a cell that may be comparable. Another example is the cell shown by Valverde (1976) in his Fig. 6, which has been commented on above. Since, in this latter case, the axon arborizes within layer I, it must be considered as a Martinotti cell but the great number of horizontal branches in layers III and IV induces one to consider this cell as different. However, there are, at present, no valid arguments to justify a separation of these cells into a well-defined group different from Martinotti cells. What must be considered, nevertheless, is the morphology of the axonal plexus, excluding the layer I component. In fact, it resembles the axonal arborization of the classical basket cells (see Section 3.4).

Other neurons with ascending axons do not project to layer I. An outstanding variety is represented by cells with a bifurcated or, less frequently, multipolar morphology, located in the middle or lower layers of the cortex. They form an axon that usually bifurcates into thick, ascending branches, which end in layer II–III in the form of a dense plexus. Abundant examples are found in the earliest literature: Ramón y Cajal (1911) depicted them in layer IV of the human visual cortex (e.g., his Fig. 388, reproduced here as Fig. 1, cell B) and in the cortex of the temporal lobe (his Fig. 401M); Lorente de Nó (1922, his Figs. 226, D) in the mouse somatosensory cortex; O’Leary and Bishop (1938, their Figs. 13-3, 13-5, and 14-5) in the visual cortex of rabbits. In these figures, a relatively sparse local plexus is observed and, in addition, an axonal tuft in lamina II–III, whose richness varies in the different renditions. It is our opinion, however, that these differences merely represent an effect of the varying qualities of the Golgi impregnation. If this is true, the sparsely prinuous bifurcated cell shown in Fig. 2 of the present report might be included in this category. In this example taken from the cat auditory cortex, the axon originates from the lower aspect of the perikaryon and initially descends; then it soon turns upwards to end in layer II–III.

Although similar cells are not frequently reported in recent papers, there are examples illustrated by Lund et al. (1979) which deserve mention. Perhaps, the most typical example is shown in their Fig. 5 (cell labeled B), but cell A in

* This figure has been reproduced as Fig. 4 in the present account.
their Fig. 4, though possessing a denser, local axonal plexus, might be considered comparable. The suggestion put forward by Lund (1973) and Lund et al. (1979), and earlier by Lorente de Nó (1949), that some types of nonpyramidal stellate cells might establish highly specific interlaminar connections justifies the necessity for systematic studies of the axonal geometry and synaptology of these cells.

3.2. Cells with Columnar Axons: Double Bouquet and Bipolar Cells

A distinct population of nonpyramidal cells have axonal arborizations which distribute themselves within narrow, radially oriented columns of cortical tissue. These cells have commonly been referred to as double bouquet cells, a term which only defines the forms of the dendritic arborizations. A review of the pertinent literature reveals that neurons of rather variable dendritic morphology, even somewhat multipolar in form, have been considered to be double bouquet cells, on the basis of their columnar axonal plexuses. Therefore, a search for the origin of the term may be worthwhile, as it is to explore whether the cells so named constitute a homogeneous population.

The description of double bouquet cells by Ramón y Cajal (1911, pp. 388-394, and his Fig. 348, reproduced here as Fig. 3) is well known and has been summarized, notably by Golowinski (1960) and Szentágothai (1973). The difficulty, however, arises from the fact that Ramón y Cajal, in 1911, described additional, distinct varieties of neurons under the common denomination of double bouquet cells (Jones, 1975; Peters and Regidor, 1981; see Chapter 7). It seems that not only are there cells with apparently comparable axonal arborizations, but showing different dendritic morphologies (see, e.g., in Ramón y Cajal, 1911, his Fig. 384, reproduced here as Fig. 4, cell labeled E), but there are others whose axonal arborizations do not fit at all with his first descriptions of double bouquet cells (Ramón y Cajal, 1899a.d). In these earlier writings, it is evident that while the essential traits was the axonal distribution, their dendritic morphology was considered by Ramón y Cajal to be consistent. The axonal patterns he defines as a very distinctive one (Fig. 3), formed of extremely thin and very long collaterals (Ramón y Cajal states that only one-third of their total vertical span is represented in his figure), which are both ascending and descending. On the other hand, the dendritic patterns, identical in cells A and B of Fig. 3, justify the name of *células bifurcadas*—literally, bifurcated cells—given by Ramón y Cajal (1899a).

However, these neurons have two polar dendrites as do bipolar cells defined in the rat visual cortex by Feldman and Peters (1978) and Peters and Kimerer (1981). In fact, Peters and Regidor (1981) have considered the cells in the figure by Ramón y Cajal (Fig. 3) as being bipolar in nature.

Aiming to clarify the concept of the double bouquet cell, we have thoroughly examined original preparations made by Ramón y Cajal himself, preparations which were made available to us at the Cajal Museum in Madrid. In Fig. 5, we represent two examples; in A, a layer III cell (human somatosensory cortex) with two long dendritic tufts which span from layers II to V. In B, also taken from layer III of the human somatosensory cortex has a larger cell body but the dendritic morphology is comparable to that of cell A; however, the vertical span is more limited (layers II-III). The axon also forms a vertical plexus, but

Figure 2. Sparsely spiny bitufted neurone from the first auditory area of the cat. The perikaryon is located in layer V and gives rise to a descending axon which soon recurs and, during its ascent, bifurcates to distribute sparsely in the middle of layer II-III. The two main ascending branches are continuous at a and b.
it is principally constituted by descending collaterals which make it similar to a horsetail (Szentágothai, 1973). In addition, axonal side branches are conspicuous. Cell A shows characteristics which are compatible with those shown by cells in Fig. 3. Cell B, on the other hand, has an axonal arborization more similar to those shown by cells E and F in Fig. 4, and may correspond to some of the cells analyzed by Somogyi and Cowey (1981) (see Chapter 9).

To give an idea of the excellent preservation of cells in these preparations, in Fig. 6 we present a photomontage of part of cell B in Fig. 5. Incidentally, in this photomicrograph some axonal branches are seen to approach the apical
dendrite of a layer V pyramid very intimately; it is most likely that similar observations prompted Ramón y Cajal (1899a) to suggest a functional relationship between the axonal arborization of his double bouquet cells and the cell bodies and apical dendrites of pyramids. It has been suggested, furthermore, that these contacts would be established onto the apical dendritic spines of pyramidal cells (Colonnier, 1966; Szentágothai, 1959, 1973), and consequently that
double bouquet cells might be excitatory. Such an assumption has recently been contested by Somogyi and Cowey (1981), who have examined double bouquet cells with vertical axonal plexuses in the visual cortices of cats and monkeys which form symmetrical synapses and, in the visual cortex of monkeys, Somogyi et al. (1981b) have suggested that it is these cells that can be labeled by retrograde
transport of [3H]-GABA from deeper layers (see Chapter 5). Additionally, however, Somogyi and Cowey (1981) present a neuron in layer IV of the monkey area 17 which forms asymmetrical contacts; they interpret that neuron as being a spiny stellate cell (another neuron variety which produces columnar axonal patterns; see Section 3.5). Another interpretation is tenable, however, for Peters and Kimerer (1981) have described, in the rat visual cortex, bipolar cells which produce efferent synapses of the asymmetrical variety (see Chapter 11). Some of the bipolar cells reported by these authors have axons that form vertically oriented plexuses, as also do examples shown by Voigt and Peters (1981, their Figs. 15c, d) and McMullen and Glazer (1982, their Fig. 13), or the cell shown in Fig. 7, taken from our rabbit material. Whether bipolar cells must be considered as a distinct subgroup of double bouquet cells awaits further study, but some data seem to support the idea that two main groups of double bouquet cells must be considered.

3.2.1. Double Bouquet Cells with Ascending and Descending Axonal Collaterals

This group contains bifurged or bipolar cells with very elongate dendritic fields and perikarya located in layers II through V, but they seem to be more frequent in supragranular layers. The characteristics of the axon have been summarized above. In brief, the axon originates from the cell body or from a proximal dendrite and generates a plexus of ascending and descending collaterals. The collaterals are thin and the plexuses, as far as one can judge from the Golgi drawings, are not very dense. This description corresponds to cells A and B in Fig. 8 or to cell F in Fig. 5 of Ramón y Cajal (1900). Ramón y Cajal (1899a, 1900, 1911) stated that, in cats and dogs, these cells are less frequent than in the human cortex; he showed examples of what he considered to be their homologs in his Figs. 21G (1899a) and 347d (1911), although no comparable cells are illustrated in his study of the cat visual cortex (1921, 1922). Other examples in the literature of what we believe are similar cells are reported by O'Leary and Bishop (1938) in their Fig. 10 (rabbit visual cortex); O'Leary (1941) in his Figs. 9-11 and 10-2 (cat visual cortex); Norita and Kawamura (1981) in their Fig. 1a (Clare–Bishop area of the cat); and Lund et al. (1981) in their Fig. 3c (area 18 of the monkey). It is interesting to note that Jones (1975) apparently does not include similar cells in his type 3 and that they were probably not sampled by Somogyi and Cowey (1981) in their study of double bouquet cells (see Section 3.2.2).

We have chosen a few additional examples from our own material which seem to fit into this group. Besides the cell shown in Fig. 5A, which we have referred to above, there is a neuron in the cat visual cortex (Fig. 8A) with a comparable dendritic morphology but a poorly arborizing axon arising from the main descending dendritic trunk. In Figs. 9A and C, there are two neurons, also from the cat visual cortex, with more complete axonal impregnations: they are strikingly similar to cell d in Fig. 7 of Ramón y Cajal (1911). Cell B in Fig. 9 is from the rat visual cortex; though showing a similar dendritic morphology, its identity is difficult to establish since the axonal arborization is looser.

Figure 7. Bipolar cell from layer IV of the visual cortex of a rabbit. It shows an axonal plexus with vertically oriented ascending and descending axonal collaterals.

Since, as pointed out by Peters and Regidor (1981), some of the neurons considered here may be envisaged as bipolar cells, it might be of interest to know whether the synapses formed by their axons are asymmetrical, as they are in bipolar cells of the rat visual cortex (Peters and Kimerer, 1981). That this is indeed the case has been found for the cells shown in Figs. 8 and 9A. In Figs. 8B and C, two axonal boutons are presynaptic, at asymmetrical synaptic junctions (open arrows), to dendritic spines. Figure 10 shows some of the synapses formed...
Figure 8. (A) Gold-purified fusiform neurons from deep layer III of cat area 17. Dendritic morphology suggests it could be a bipolar cell and it also resembles cell A in Fig. 5. Although impregnation was incomplete, the nature of the synapses formed by its axon could still be identified. In B and C, examples of asymmetrical synapses (open arrows) on dendritic spines are shown. Calibration bars: A, 50 μm; B and C, 0.5 μm.

By axonal collaterals of the cell in Fig. 9A. In the two serial sections shown in Figs. 10A and B, two boutons are seen to contact dendritic spines; note that the postsynaptic density is not recognizable as being of an asymmetrical synapse in one of the cases (open arrow in A), whereas its nature is obvious in a serial section (B). Two more asymmetrical synapses on spines are seen in C. Since these results are preliminary, no information regarding the sources of these dendritic spines is available, and similarly, no other postsynaptic targets as reported by Peters and Kimerer (1981) for the rat bipolar neurons (shafts of apical dendrites and somata and dendrites of nonpyramidal cells) have been found in our material (see Chapter II). The difficulty of staining the axons of bipolar...
cells by the Golgi method is notorious and has made attempts at correlations between species particularly troublesome. It is hoped that further analyses of their synaptology at the electron microscope level, together with immunocytochemical studies, will help to solve the problem.

3.2.2. Double Bouquet Cells with Mainly Descending Axonal Arborizations

The cell variety is exemplified by cells E and F in Fig. 4 (taken from Ramón y Cajal, 1911, Fig. 384). As mentioned above, Ramón y Cajal did not separate these cells from his first type of double bouquet cell, but there are reasons to believe that they represent a different subtype of neurons (see, e.g., Peters and Regidor, 1981). Similar cells have frequently been shown in the literature, as they appear in rather diverging species and cortical areas: the mouse somatosensory (Lorente de Nó, 1922, his Fig. 7C) and visual (Ruiz-Marcos and Valverde, 1970, their Fig. 1c) cortices; the cat visual cortex (Peters and Regidor, 1981, Figs. 5K, L) and Clare–Bishop area (Noriita and Kawamura, 1981, Figs. 1b, c); the monkey somatosensory (Jones, 1975, Fig. 8) and visual (area 18) cortices (Valverde, 1978, Fig. 3a). Besides the cell shown in Fig. 5B, drawn from preparations of Ramón y Cajal’s, one example taken from our material of the cat area 17 is represented in Fig. 11A, to facilitate comparisons. It is clear that the examples listed above possess the same configurations as some of the neurons selected by Somogyi and Cowey (1981) in their Golgi–electron microscope study of double bouquet cells (e.g., their Fig. 1, from the cat, and Fig. 13, from the monkey area 17; see also Fig. 2 in Chapter 9). Excellent descriptions and illustrations of these cells are found in Jones (1975), who includes them in his type 3, and in Valverde (1978), who names them “cells with vertical axonal bundles and grape-like terminal knobs.” Also, the cells with horsetail-shaped axons of Szentágothai (1975, 1975) seem to correspond to this group. The essential features of these cells are their location in superficial layers, their multipolar or binate dendritic trees, and their descending axonal bundles. There is, in some instances, a tendency for the superficial dendrites to form an ascending tuft which gives a peculiar appearance to some of these cells, but the ascending tufts are not exclusive to these cells. The axonal plexuses are essentially descending and clearly pass beyond the dendritic domain. Axonal collaterals become thick along their descending trajectory and intertwine together forming one or more compact fascicles of fibers, in which short-side appendages are conspicuous. Overall, these morphological characteristics are peculiar and allow them to be distinguished from the ones we have described in the preceding subsection. Some collaterals, however, take an ascending course, as in Fig. 4F.

There are, in addition, other cells which have commonly been included in this group, characterized by their being multipolar and by the distribution of their axons. Examples are shown by Lorente de Nó (1922, his Fig. 7A), Jones

Figure 10. Synapses formed by the axon of the gold-stained neuron shown in Fig. 5A. A and B show two serial sections in which a vertically oriented axonal branch, labeled by its content of gold particles, forms a synaptic junction on a dendritic spine (open arrows), its asymmetrical nature being evident in B; another bouton forms an asymmetrical synaptic junction on a dendritic profile of unidentifiable nature (arrow). C. Asymmetrical synapses on dendritic spines. Calibration bars, 1 μm.
3.3. Cells with No Preferred Axonal Orientation

We include in this group a rather heterogeneous population of neurons, defined by a common geometrical property of their axonal fields, i.e., the lack of a preferred orientation in either the vertical (ascending or columnar) or the tangential directions. Within this group, there are some cells which can be considered as generalized (Fairen and Valverde, 1979), whereas the others are specialized. Precise differences between generalized types are difficult to establish, either on the basis of size or on the basis of subtle differences in the axonal branching patterns.

The group contains cells showing a strictly local axonal arborization (GOLGI type II cells) but, also, others which display axonal arborizations with diverse degrees of dispersion around the perikarya or origin. For some of these cells, especially those with large perikarya and rather extended dendritic fields, the term local applied to their axonal trees would seem inappropriate. Depending on the size of the axonal domain, some cells may be confined to a single lamina or encompass two or more adjacent ones. A discussion of some of these cells is also presented in Chapter 15.

5.3.1. Small Multipolar Cells with Strictly Local Axonal Arborizations

These cells correspond to the "neurogliaform cells" of Ramón y Cajal (1899b,c,d, 1900, 1911, 1921, 1922; see Chapter 12). They are small cells provided with short, smooth, and finely beaded dendrites which branch at obtuse angles, not far from their points of origin; there are instances, however, in which the dendrites ramify less and are recurving. The axon is slender and is studded with dilations; it arborizes richly within the dendritic domain, in a strictly local

Figure 11. Double bouquet cells with descending axonal arborizations. Both have multipolar dendritic fields. A is taken from the upper tier of layers II-III of area 17 and shows a columnar axonal plexus in which the descending branches interlace together; inset shows the continuation of the descending axons at a. B is a similar cell from layers II-III of the visual area of a rabbit. It shows a comparable descending axonal plexus but differs in the overall distribution of the more appositional branches.
manner. Thus, neurogliaform cells are the only true Golgi type II cell in the cerebral cortex. These cells have been reported in a number of species and cortical areas (Ramón y Cajal, 1911, 1921, 1922; Lorente de Nó, 1922, 1949; Ramón-Moliner, 1961; Valverde, 1971, 1978; Shkol'nik-Yarros, 1971; LeVay, 1973; Lund, 1973; Szentágothai, 1973, 1978; Jones, 1975; Lund et al., 1977; Tömböl, 1978b; Fairén and Valverde, 1979; Werner et al., 1979; Norita and Kawamura, 1981; Peters and Regidor, 1981; see Chapter 12). In the published drawings, the morphological characteristics that define this cell group are easily recognizable, and no new details need to be added to the previous descriptions. As defined here, the essential trait is the strictly local organization of their dendritic and axonal trees. They may be more or less compact, however. It seems that in the primary sensory areas of primates, including man, neurogliaform cells are small and possess a dense axonal plexus; this makes arborization patterns difficult to analyze, as for instance in the original drawings of Ramón y Cajal. In cats and dogs (Ramón y Cajal, 1911, 1921, 1922; Fairén and Valverde, 1979; Norita and Kawamura, 1981; Peters and Regidor, 1981) or in rabbits (Tömböl, 1978b) the cells are larger and the axonal arborizations looser; they may spread out of the dendritic domain slightly. The same seems true for local cells in area 18 of monkeys (Valverde, 1978, and compare Fig. 6b in Lund et al., 1981).

In the visual cortex of rodents, the presence of local neurons seems to be absent or minimal in rats of different ages, but abundant in young rats of the same age. In the somatosensory cortex of mice (Lorente de Nó, 1922; Woolsey et al., 1975) there is a type of smooth stellate cell which is, in its distribution, confined to a single layer IV barrel (Woolsey and Van der Loos, 1970). The cells shown in Figs. 6C and 71 of Lorente de Nó (1922) are comparable to local axon cells in other species (Valverde, 1971). In layers V and VI, Lorente de Nó (1922, 1949) represented cells with similar shapes, but less restricted in space (cf. Fig. 73, cells 24, 25, and 26, in Lorente de Nó, 1949).

Neurons with strictly local axons are present in all cortical layers (Ramón y Cajal, 1911; Ramón-Moliner, 1961; Peters and Regidor, 1981), including layer I (LeVay, 1973). Some reports, however, indicate that they are typical of layer IV in the somatosensory cortex (Jones, 1975) and in area 17 (Valverde, 1971) and 18 (Valverde, 1978; Lund et al., 1981) of monkeys. It may be, however, that these layer IV cells—those in the rodent barrel field—constitute a peculiar type, akin to Valverde's (1951) clew cells, whereas other cells may correspond more directly, on account of their dendritic branching patterns, to the classical neurogliaform cells (cf. Szentágothai, 1973). A further account of neurogliaform cells is given in Chapter 12.

3.3.2. Chandelier Cells

These interneurons were first described by Szentágothai and Arbib (1974) in the cingulate cortex of the cat. Prior to this description, no such interneurons had been represented in any account of neurons of the cerebral cortex. This illustrates the limitations of the Golgi method for describing the distribution of the presence of a particular type of neuron in a given cortical area. There can be some debate about whether some of the interneurons described in the literature as small basket cells (e.g., Figs. 17-4 and 73 in Shkol'nik-Yarros, 1971) are chandelier cells. In any case, we have not found convincing examples after an examination of a large number of preparations from the Ramón y Cajal collection; most probably, chandelier cells were very infrequently impregnated and escaped recognition.

The name given to these cells derives from the peculiar morphology of their overall axonal distribution and of their terminal, vertical rows of axonal boutons, which Fairén and Valverde (1980) have named specific terminal portae. Even if there are certain differences among species and areas (e.g., Fig. 12), the basic pattern, reminiscent of a chandelier fixture, can easily be recognized (see Chapter 10).

Chandelier cells are unique among the cortical nonpyramidal cells in that they are, in absolute terms, target selective. In all Golgi-EM studies reported so far, their vertical axonal terminal portions have been found to contact only the axon initial segments of pyramidal cells, forming symmetrical synaptic specializations (Somogyi, 1977, 1979; Somogyi et al., 1979, 1982, 1983, Fairén and Valverde, 1980; Fairén et al., 1981; Peters et al., 1982). In addition, Somogyi et al. (1982) have added that those individual boutons, not belonging to the specific terminal portions, also form axo-axonic synapses. This unique type of synaptic relationship has prompted the formal proposal by Somogyi et al. (1982) that chandelier cells should be renamed axo-axonic cells. While this point of view may be correct, the study of Fairén and Valverde (1980) showed that cells identical, in the Golgi picture, to the ones shown by Szentágothai (1975, 1979) behave in exactly the same way as Somogyi's axo-axonic cells. We believe that the name chandelier cells should be maintained because this term best describes their axonal morphology. Changing the name to reflect the synaptic target might force us to change the names of many other cells once their synaptology is accurately determined. However, most of the local axons studied so far in the cerebral cortex have postsynaptic targets that are rather diversified.

Somogyi et al. (1982) have questioned the identity of their axo-axonic cells to many of the chandelier cells that have been illustrated in the literature, in which electron microscopy evidence of the axonal distribution has no been given. Indeed, the apical shafts of pyramidal cells, proposed by Szentágothai and Arbib (1974) and Szentágothai (1975, 1978, 1979) as the postsynaptic targets for chandelier cells, do receive multiple innervation by boutons forming symmetrical synapses (Szentágothai and Arbib, 1974; Szentágothai, 1975; Herrick and White, 1981b). The cells of origin of these boutons have not been identified. Somogyi et al. (1982) report preliminary data on interneurons forming multiple symmetrical synapses on this location, but they do not give any information regarding their morphology at the light microscope level. In passing, reference should also be made to the report by Müller-Pachinger et al. (1985) who, on the sole basis of Golgi observations, suggest that axon terminals of chandelier cells in the rabbit sensory cortices may contact virtually all portions of the pyramidal neurons. Most of the terminal boutons of chandelier cells tend to form clusters around the most distal part of the axon initial segments of pyramidal cells, although
some may be more proximal. There are, in addition, other interneurons whose axonal boutons occasionally contribute with similar axo-axonic synapses to the axon initial segment (Peters and Fairén, 1978; Peters and Proskauer, 1980a; DeFelipe and Fairén, 1981; Somogyi et al., 1982). However, the distribution of chandelier cell axonal boutons is so typical that they can be recognized using GAD immunocytochemistry. This led Peters et al. (1982) to the important conclusion that they are GAD-positive and, thus, that chandelier cells are inhibitory, as had been suggested earlier (Somogyi, 1977; Fairén and Valverde, 1980) on the basis of the morphology of the synaptic contacts they produce. See Chapter 12 for additional discussion of this point.

Complexity of the specific terminal portions is variable, and some reports on the cat cerebral cortex (Szentágothai, 1975, 1979; Lund et al., 1979; Fairén and Valverde, 1980; Fairén et al., 1981) describe very complex ones, made occasionally by the convergence of several collaterals from the same axonal arborization into a unique terminal portion (see, e.g., Figs. 6 and 7, taken from a 3-month-old specimen, in Fairén and Valverde, 1980). Other terminal formations in the cat are simpler, formed of a single row of boutons, as in the case of chandelier cells of rats and mice. It was tentatively suggested by Fairén and Valverde (1980) and Fairén et al. (1981) that this might be the expression of an evolutionary trend, but reports of chandelier cells in the monkey neocortex show simple rows of terminal boutons (e.g., Jones, 1975; Somogyi et al., 1982; Valverde, 1983). The alternative hypothesis that complex specific terminal portions are immature structures has been advanced by Somogyi et al. (1982), but Somogyi et al. (1983) show complex axonal terminations of similar cells in the hippocampus of adult monkeys. Clearly, the issue cannot be considered completely settled and an examination is required of terminal axonal formations of chandelier cells in immature specimens of species, such as rats or mice, where they have been reported to be simple in all cases.

Examples of chandelier cells, with or without electron microscope evidence, have been reported in different species and cortical areas, including the mouse, the visual (Tómböl, 1978a; Lund, 1981; Lund et al., 1981; Somogyi et al., 1982; Valverde, 1983), somatosensory (Jones, 1975; Szentágothai, 1975), and auditory cortices (Szentágothai, 1975). In the cat, examples have been found in the visual cortex (Tómböl, 1976, 1978b; Fairén and Valverde, 1979, 1980; Lund et al., 1979; Somogyi, 1979; Peters and Regidor, 1981; Somogyi et al., 1982), the Clare–Bishop area (Norita and Kawamura, 1981), the somatosensor (Tómböl, 1978b), and motor (Somogyi et al., 1982) cortices, the cortex of the anterior ectosylvian sulcus (Valverde, 1983, and unpublished observations by the present authors), and the cingulate cortex (Szentágothai and Arbib, 1974; Szentágothai, 1975). In rabbits, they have been reported in the visual area (Valverde, 1983) and in other sensory cortices (Müller-Raschinger et al., 1985). Chandelier cells in the rat have been encountered in the visual cortex (Somogyi, 1977; Somogyi et al., 1979, 1982; Werner et al., 1979; Peters et al., 1982) and in the cingulate cortex (Vogt and Peters, 1981) and, in the mouse, in the visual cortex (Valverde, 1983), auditory cortex (Fairén et al., 1981), and premotor cortex (unpublished observations). As shown in Fig. 12, taken from Valverde (1983), cells with identical terminal axonal portions are present in a primitive cortex, that of the hedgehog Erinaceus europaeus; Valverde has found them in the parietal region

![Figure 12. Examples of chandelier cells in diverse mammalian species and cortical areas. Reproduced from Valverde (1983) with permission.](image-url)
and in the interhemispheric and entorhinal cortices. Somogyi et al. (1982) have described chandelier cell axons in the subiculum and pyriform cortex of the rat, and, additionally, Somogyi et al. (1983) have provided light and electron microscopic evidence that similar chandelier cells exist in the stratum pyramidale of the monkey hippocampus, which is not surprising if the synaptology of the axon initial segments of hippocampal pyramidal cells (Kosaka, 1980) is considered. Therefore, it seems that chandelier cells occur in all mammals and are present in all cortical areas, and not exclusively in the neocortex, so that they must be regarded as an essential cellular component of the cerebral cortex.

A point of interest is whether chandelier cells distribute uniformly in the areas where they appear. In the visual cortex of cats and rats, Fairen and Valverde (1980) and Peters et al. (1982) have reported a greater occurrence of chandelier cells at the border of areas 17 and 18 (or 17 and 18a); while this might be due to the capriciousness of the Golgi method, it appears that certain pyramidal cells receive only a few synaptic contacts on their axon initial segments (Peters et al., 1982), thus indicating that they might not be innervated by chandelier cells. An indirect approach to solve the problem of the suspected discreteness in distribution of chandelier cells may be found by reconstructing entire initial axonal segments of diverse populations of pyramidal cells identified according to their projections by using retrograde labels. Combination of HRP retrograde labeling with the Golgi staining in the same material (Somogyi et al., 1976) is of interest, but it is subjected to the vagaries of the Golgi impregnation. This combined method, however, has generated the interesting observation that one of the targets of chandelier cells are callous-projecting neurons (Somogyi et al., 1979), a fact that might explain the preferential impregnation of chandelier cells at the periphery of area 17.

Similarly, new efforts are required to analyze the distribution of chandelier cells according to cortical layers. Most reports indicate that chandelier cells are more abundant in supragranular layers and there are reports that indicate, at least in the monkey somatosensory and motor cortices, a richer synaptic supply to axon initial segments of pyramidal cells located in supragranular layers (Sloper and Powell, 1979). Nevertheless, chandelier cells indeed exist in the infragranular layers (Tomabechi, 1976, 1978a, b; Fairen and Valverde, 1980), and unpublished results in the cat visual cortex. Occasionally, the descending axonal collaterals of superficially located chandelier cells may arborize in these layers (Lund et al., 1979; Fairen and Valverde, 1980).

5.3.3. Small Basket Cells

Ramón y Cajal (1899, 1911) described a medium-sized variety of his "cellules à double bouquet dendritique," located in the supragranular layers of the human sensory motor cortex. One such cell, taken from this last publication, is reproduced here as Fig. 13B. The peculiarity of the axon of these cells is that they form nests about the cell bodies of small-sized pyramidal cells (Fig. 13A). Comparable cells are described by O'Leary and Bishop (1982) and O'Leary (1984) in the visual cortices of rabbits and cats, respectively, but, as pointed out by Peters and Regidor (1981), the dendritic and axonal arborizations of the examples shown by O'Leary (1941) resemble those of chandelier cells. However, other interpretations of the drawings by Ramón y Cajal have been advanced (Marín-Padilla and Sáez, 1974; Marín-Padilla, 1975), but it is interesting to note that this is the first formulation, in Ramón y Cajal's writings, of the concept of the neocortical basket, i.e., a cell which contributes synaptic contacts, preferentially, to cell bodies of pyramids.

There are several varieties of basket cells (Ramón y Cajal, 1911, 1915; Marín-Padilla, 1969, 1970b; Séjourné, 1973; Jones, 1973, and see Chapter 8), and in this section, we will refer only to what Séjourné (1969, 1975) has named small or short-range basket cells. Golgi-EM evidence for the existence of such a variety of cells in the visual cortex of the cat has been given recently (DeFelipe and Fairen, 1982). The basic criterion for identification of small basket cells in that study was the analysis of their patterns of different connections, to determine whether there were signs of target selectivity (cf. Fairen and Valverde, 1979). In a preliminary evaluation of local interneurons in layer II-III of the cat area 17, using semithin sections of Golgi-stained material, some cells were found which consistently produce multiple contacts on cell bodies and proximal dendrites of pyramidal cells (Fig. 14). The synaptic nature of these contacts was demonstrated electron microscopically, but it was also found that nonpyramidal cells receive multiple synaptic contacts (DeFelipe and Fairen, 1982). In addition, multiple axoaxonic autapses have recently been described in one such cell (Fairen et al., 1992). In all cases, the identified synapses were of the symmetrical variety.

This type of connectivity was not evident in the preliminary light microscope evaluation of the Golgi preparations: no visible basket formations were present. Nevertheless, the cells that, according to the above criteria, proved to be basket cells show a well-defined morphology. They are multipolar cells with rather wide dendritic fields, sometimes showing a predominant dendritic tuft oriented to-
Figure 14. Phase-contrast photomicrograph of a semithin section from a Golgi preparation. Multiple axonal button of a common origin, traced back to a small basket cell, are seen in close apposition (arrows) to the perikaryon and apical dendrite (ap) of a pyramidal cell. Calibration bar, 20 μm.

ward the pial surface (Fairén et al., 1981, and Fig. 15). In all the cases analyzed (see examples in Figs. 15 and 16), the axon is primarily descending and forms a rich local plexus through diverging, recurrent collaterals. There are some variations, however, both in the form of descending axonal branches as in Fig. 16, which resembles the cell labeled 5 in Peters and Fairén (1978), and in the presence of relatively long horizontal collaterals (Fig. 15), as in type 6 cells of Jones (1975). It may be that horizontal branches are lost, in certain cases, due to the orientation of cells in the preparations (see Section 3.3.4). Overall, the local axonal plexus is characterized by its curving preterminal axonal branches, provided with "en passant" boutons, which were later found to contact neuronal perikarya or proximal dendrites.

Cells with a similar morphology are present in the rat visual cortex (Fig. 17) and in the somatosensory cortex of the mouse. Further work is needed, however, to confirm the identity of these cells in the rodent cortex as small basket cells, and this can only be achieved by a detailed analysis of their efferent connections. It is also important to determine if small basket cells are present in different cortices. Perhaps the spherical, multipolar neurons with a local axonal

plexus described by Peters and Regidor (1981) in the cat visual cortex and the type 6 cells of Jones (1975) in the somatosensory cortex of monkeys are neurons of this type. Other examples deserving mention include the cells shown by Lund (1973) in her Fig. 31z (monkey area 17); Szentágothai (1978) in his Fig. 5 (cat visual cortex); Norita and Kawamura (1981) in their Fig. 5 (Clar–Bishop area of the cat); McMullen and Glaser (1989) in their Fig. 5 (rabbit auditory cortex); and Lorente de Nó (1922) in his Fig. 6A (mouse barrel cortex). It seems, therefore, that small basket cells might be present in rather different cortices. Finally, it must be mentioned that there are examples in the literature of purported small basket cells which show different appearances. See, for instance, Fig. 9 in Valverde (1985) from the hedgehog neocortex, in which bushy terminal axonal formations enter the "accentuated layer II" (Sanides and Sanides, 1974) typical of that cortex.

3.3.4. Cells with Relatively Extended, Generalized Axonal Arborizations

This group is formed of multipolar or binucleated cells with rather extended, smooth or sparsely spinous dendrites which may invade two or more contiguous layers. Their axonal plexuses are predominantly local in nature, but not as compact as in the case of neuroglial cells, and may exceed the limits of the dendritic fields. Descending axonal branches are not uncommon and the plexuses may appear somewhat columnar (Jones, 1975; Peters and Fairén, 1978; Norita and Kawamura, 1981) but not as clearly as in the cell category reviewed in Section 3.2. Moreover, unlike cells with ascending axons (see Section 3.1) or the large basket cells (Section 3.4), their axons lack a well-defined trend to form vertically or horizontally oriented plexuses outside the dendritic domain. In
common with these cell types, the axon collaterals do not possess specialized terminal formations.

Defining this cell group is difficult, since there is a rather broad range of morphological diversity and one fears that the group as a whole might represent a common pool in which rather different types of cells are included. This is illustrated by Figs. 18 and 19. Cell A in Fig. 18 is from layer IV of the cat area 17; it shows a multipolar morphology, with sparsely spinous dendrites and somatic spines. The ascending axon forms a loose plexus in which recurving axonal arcs are visible. Cell B is a bitufted cell from layer II–III of the rat area 17 and shows a similar plexus, not strictly confined to the dendritic domain; some of the axonal branches enter layer I. Figure 19 shows a multipolar cell located in the middle layers of the cortex of the anterior ectosylvian sulci of the cat. In this case, the perikaryon and the span of the dendrites are larger; the axon ascends and forms a plexus in which horizontal and vertical collaterals are clearly discernible. By its size and the form of its axonal arborization, this neuron resembles the ones described by Jones (1975) as type I cells, and it is reminiscent of a cell type reported by Valverde (1983, his Fig. 5) in the neocortex of the hedgehog. The question now arises as to whether some of the multipolar neurons with apparently generalized axonal arborizations might not be true basket cells (see Section 3.4). In fact, Martin-Padilla and Subitz (1974), Martin-Padilla (1975), and Jones (1975) have shown that axonal patterns of basket cells vary drastically when viewed in the direction of the long horizontal collaterals, and Peters and Regidor (1981) have specifically pointed out that multipolar cells with elongated dendritic trees and horizontal axons in the cat visual cortex display recurring axonal arcs after a 90° rotation in the vertical axis. These observations clearly indicate that a bias may be introduced in previous reports of multipolar cells with generalized axonal arborizations being different from basket cells.

Clearly, the issue requires the study of the synapses formed by the axon terminals of these cells. This has been done in the rat visual cortex of Peters and
Fairen (1978) have examined, with the Golgi-EM method, smooth or sparsely spinous multipolar cells, with spherical or ovoid dendritic fields, which possess axonal arborizations similar to the examples shown in Fig. 18. The axon of these cells do not have preferred postsynaptic targets, for they contact perikarya of stellate and pyramidal neurons, shafts of apical dendrites, dendrites of smooth stellate cells, and, in one case, the axon initial segment of a pyramidal cell, always forming symmetrical synapses. On the other hand, Peters and Proskauer (1980a) have examined, also in the rat visual cortex, the synaptic relationships between the axon of a layer III multipolar cell with smooth dendrites and a Golgi-impregnated pyramidal cell, and report a substantial number of synapses formed by the stellate cell axon on the cell body and proximal dendrites of the pyramidal cell; in addition, the axon forms synapses with other pyramids, including the axon initial segment of one of them, and with cell bodies and dendrites of other aspyny nonpyramidal neurons (also see Chapter 13). As discussed in Section 3.3.3, multiplicity of the synaptic input on the same postsynaptic neuron indicates a certain degree of target selectivity; this feature differentiates small basket cells from other nonpyramidal neurons present in the superficial layers of the rat visual cortex. Whether this is also the case for the classical basket cells is not yet known, but our observation of the reality of the small basket cells and the Golgi evidence, as far as it goes (see, e.g., Fig. 17 in Jones, 1981; and Fig. 6c in Peters and Regidor, 1981), indicate that this is a most likely possibility.

It seems that a sharp distinction between the basket cells and the cells with relatively extended axonal arborizations does not exist. Several important pieces of evidence are wanting: first, a complete account of the distribution of axon terminals from basket cells, to see if they exclusively contact neuronal cell bodies and proximal dendrites; second, whether nonpyramidal cell bodies are also contacted by the axons of the large basket cells; and, third, a definition of the ratio of the axon terminals emanating from generalized multipolar neurons vs. basket cells, converging on a given postsynaptic cell. Since it has been firmly established that axosomatic synapses on pyramidal cells are GABAergic (see Chapter 8), it would be of interest to determine whether or not these terminals

Figure 18. Nonpyramidal cells with extended axon arborization. A is from layer IV of cat area 19, and B from upper layer II-III of rat area 17.

Figure 19. Aspyny multipolar neuron with extended axonal arborization from middle layers of the anterior ectosylvian sulcus of the cat.
derive from the axonal arborizations of a uniform population of nonpyramidal neurons.

With these reservations in mind, it appears that multipolar neurons with relatively extended axonal arborizations are a common cellular component of the mammalian neocortex. They correspond to type 2 cells (Jones, 1976) or "common cells with axonal arborizations" (Jones, 1971) in the monkey sensory motor cortex, but there are some doubts about their correspondence to the cells Szentágothai (1973) includes in his "category II cells with widely distributed axonal arborizations." Similar to Jones type 2 are cells which have been represented in monkey area 17 (Lund, 1973, her Figs. 34, 27, and 36) and 18 (Lund et al., 1971, their Fig. 5), cat area 17 (Tomboh, 1978), her Fig. 1a; Lund et al., 1979, their Fig. 6b, and Clare-Bishop area (Norita and Kawamura, 1971, their Fig. 2); and rat area 17 (Feldman and Peters, 1978, their Fig. 19). Examples in the human neocortex are given by Ramón y Cajal (e.g., cells A and G in Fig. 4 of the present report), and an early observation in a newborn rabbit is reported in Fig. 9 of Ramón y Cajal (1881).

Valverde and Ruiz-Marcos (1969), Valverde (1976), and Fairén and Valverde (1979) have represented similar neurons in the visual cortex of the mouse, as did Lorente de Nó (1922) in the somatosensory cortex of the same species (e.g., his Fig. 1a, but see also Fig. 3 in Lorente de Nó, 1949, where he represents diverse types of cells with intracortical axons). Valverde (1976) distinguishes two types of axonal configurations, which either distribute within a cylindrical volume of tissue, above the perikaryon of origin (type I), or are flattened and arborize both above and below the cell body (type III). The morphology of these axonal plexuses, with obvious axonal arborizations, reminds one of a weeping willow tree, but as discussed in Section 3.2.2, somewhat similar cells in the monkey area 18 (Valverde, 1976), and also in other species and areas, form additional compact axonal bundles descending to lower layers and have been included by Somogyi and Cowey (1981) in the group of double bouquet cells (see Chapter 15 for an additional discussion of this point). One such interneuron, in the cat visual cortex, analyzed by Delépine and Fairén (1981), showed a pattern of efferent connectivity compatible with that reported by Somogyi and Cowey (1981). This implies an additional landmark to be established for the cell category we are discussing.

3.4. Cells with Horizontal Axons: The Basket Cells

As discussed in the preceding section, one of the known sources of the symmetrical GABAergic synapses on the perikarya of pyramidal cells in the rat visual cortex are multipolar cells with smooth or sparsely spined dendrites (see Chapter 8). However, the existence of a characteristic type of nonpyramidal cell which contributes more substantially, by multiple synapses, to the afferent connectivity of pyramidal cell bodies has been postulated for higher species, and doubts arise on whether such cells do appear in more primitive cortices.

* As already mentioned, Peters and Regidor (1981) consider similar cells in the cat visual cortex to be basket cells seen on edge.

Ramón y Cajal (1899b, c, 1911) observed, in the human visual and motor cortices and in the visual cortex of the cat, the presence of rich axonal plexuses (nest or, according to Marin-Padilla (1969), baskets) surrounding the cell bodies of (unimpregnated) pyramidal cells, located in layers III and V. In his Fig. 301 (Ramón y Cajal, 1911) he represents a number of these plexuses, in which there is convergence of several axon collaterals originating from horizontally running axons. Later, Marin-Padilla (1969, 1970a, b, 1974) and Valverde (1963) in man, and Szentágothai (1973) and Holländer and Vanegas (1981) in cat, have represented similar plexuses and confirmed the convergence of multiple fibers into an individual pericellular plexus (see also Szentágothai, 1975, 1978). The work by Holländer and Vanegas (1981), based on the uptake of locally injected HRP, has provided electron microscopy evidence that the pericellular baskets form symmetrical synapses on the pyramidal cell perikarya and proximal dendrites and, additionally, that afferent fibers may be myelinated. This agrees well, as will be shown later, with the observation by Jones (1975) of large multipolar cells of his type I cells which lack axonal impregnation in adult specimens.

Ramón y Cajal attributed the origin of the horizontal fibers entering the baskets to large stellate cells located in layers III and V (see Fig. 360 in Ramón y Cajal, 1911, and Fig. 20 of the present account, taken from Ramón y Cajal, 1899b).
1899)). That the origin of perisomatic axonal boutons must be local was shown by Szentagothai (1965), since they persist in isolated cortical slabs. Convincing Golgi evidence was given, in the human motor cortex, by Marin-Padilla (1969, 1970a,b). Thus, basket cells are large multipolar cells which, in immature specimens, show a sparse population of dendritic spines (also see Chapter 8). The poorly arborizing dendrites radiate in all directions but the vertical ones predominate. The axons are either ascending or descending and soon form long branches coursing horizontally over distances of up to 1-2 mm, but additional long oblique branches are present. Besides these general characteristics, a conspicuous feature is the component of short vertical collaterals which, in Marin-Padilla's drawings, are seen to join Golgi-stained, pericellular baskets. Perhaps, the failure to simultaneously impregnate these plexuses and the axons of individual basket cells has somewhat jeopardized the interpretation of the short, vertically oriented collaterals of these cells, for these structures are not easily recognizable as specialized terminal formations in the absence of impregnation of the axonal plexuses to what they contribute, and, also, because the contribution of an individual basket cell to a given pyramidal cell perikaryon is likely to be less dense, as pointed out by Jones (1981; see, for instance, his Fig. 17), than in the case of the cerebellar basket cells. Consequently, many reports of Golgi-impregnated cells with long horizontal axons in diverse species fail to recognize them as true basket cells. One interesting point, already noted by Ramón y Cajal, is that each basket cell contributes to the pericellular plexuses of a number of pyramidal cells.

Two examples, drawn from preparations of the Ramón y Cajal collection, are presented in Fig. 21, mainly to compare the dimensions of the cells reported by Ramón y Cajal (1899c, 1911) with those of more recent accounts. Cell A is from deep layer III of the visual cortex of a 27-day-old infant, and B from layer III of the motor cortex of a newborn. Both of them fit well with the description given above, both in their dendritic morphology and in that their axons form long horizontal or oblique collaterals, with short-side appendages.

In the sensory motor cortex of monkeys, Jones (1975) has described, as type 1 cells, similar large multipolar neurons with long horizontal axons. In adult specimens, the axons are myelinated, but the cells can still be recognized on the basis of somal size and dendritic distribution. Type 1 cells vary in their dimensions according to their locations, the ones in area 2 and in area 4 being the largest. There is also a size segregation according to layers, the deeper cells being larger than the superficial ones, as also pointed out by Ramón y Cajal (1911) and Marin-Padilla (1969, 1970b). In spite of the fact that the smallest ones, such as the "short-range basket cells" (Szentagothai, 1969, 1973), similar to type 6 cells of Jones (1975), must be considered as a variety of basket cells, we have chosen to consider them separately (see Section 3.3.3).

Whether basket cells are present in all mammalian species has not been definitely settled. In the following selection of examples published by different authors, their identification of the neurons as putative basket cells is based on the presence of the basic morphological patterns just discussed; but it must be pointed out that, in certain cases, the identification is based on the present authors' concepts. In the monkey, such cells are illustrated in area 17 by Lund (1975, her Fig. 29), and by Lund et al. (1981, their Fig. 18b) in area 18. There are no doubts that the neocortex of carnivores contains basket cells (e.g., in cat area 17, Tömböl, 1978a, her Fig. 7; Lund et al., 1979, their Fig. 8A; Peters and Regidor, 1981, their Figs. 5F, H; Gilbert and Wiesel, 1979, their Fig. 2b; in Clare-Bishop area of the cat, Norita and Kawamura, 1981, their Figs. 4a and 5a; in area 17 of the dog, Sikolniki-Varros, 1971, her Figs. 36 and 57; in cat auditory cortex, Sousa-Pinto, 1973, his Figs. 17F, H). Examples drawn from our own material of cats are shown in Figs. 19 and 22A. The cell in Fig. 19 could be considered to be a basket cell by virtue of its similarity to a drawing by Jones (1975) of a type 1 cell in the monkey somatosensory cortex (his Fig. 21), but their vertical axonal branches are striking. Figure 22A represents a more typical example, even if the long axonal collaterals are oblique. In rabbits, reports include the visual (O'Leary and Bishop, 1938, their Figs. 14-4 and 14-11; Tömböl, 1978b, her Fig. 8) and auditory cortices (McMullen and Glaeser, 1982, their Fig. 12). As pointed out by Peters and Regidor (1981), the possibility must be considered that some of the examples we have included in our review of cells with relatively extended axonal arborizations (see Section 3.3.4) might in fact be basket cells, but this must await further studies.

Whether basket cells are present in rodents is an unsettled question. It has been suggested earlier (Peters and Fairén, 1978; Peters and Proskauer, 1980; 1981).

Figure 21. Two large multipolar neurons with long horizontal axons (presumably large basket cells) drawn from original preparations of Ramón y Cajal. See text for details.
Peters and Regidor, 1981) that in these species, they could be represented by the smooth or sparsely spiny multipolar neurons. In fact, the axons of certain of these cells are myelinated (Peters and Proskauer, 1960b), a characteristic common to basket cells of higher species, but these cells with myelinated axons may well represent a heterogeneous population. Looking for nonpyramidal cells with long horizontal axons, we have examined preparations of the rat visual cortex. In Fig. 22B is a multipolar neuron, located in layer II–III of area 18a.

The axon stems from the side of the perikaryon and tends to form horizontally oriented collaterals. However, there are certain differences with respect to the typical cases found in other species by other authors. A case in point is the cell labeled H in Fig. 7 by Lorente de Nó (1922), as are some interneurons present in phylogenetically older cortices, such as the interhemispheric cortex (Iwahori and Mizuno, 1981, their Figs. 3F and 5). On the other hand, Lorente de Nó (1935) in the mouse entorhinal cortex has represented multipolar cells with horizontal axons having vertical collaterals, which may resemble basket cells.

Finally, some doubts on the interpretation of the cell shown in Fig. 5 by Valverde (1983) have been commented upon in the preceding section.

Axonal geometry is an interesting feature of basket cells. Marin-Padilla (1969, 1970b) and Jones (1975) have found that the axons distribute within narrow slabs of tissue, precisely oriented in a plane perpendicular to the long axis of the pre- and postcentral gyri. The possible correlation between this spatial arrangement and certain properties of the functional columns has been suggested by Marin-Padilla (1970b) and stressed by Jones (1975, 1981) and Peters and Regidor (1981) (see Chapter 8).

Thus, in the sensory motor cortex, the basket cells may mediate the inhibition of the columns adjacent to the one which is excited by a peripherally applied stimulus (Powell and Mountcastle, 1959). In the visual cortex, a similar flattened distribution in tissue slabs has been recognized (Peters and Regidor, 1981), but their precise spatial orientation is not yet known in that cortex. However, as discussed by Jones (1975, 1981), Peters and Regidor (1981), and in Chapter 8, basket cells in that cortex might play a role in the determination of orientation columns (Hubel and Wiesel, 1974; Hubel et al., 1978).

3.5. Spiny Stellate Cells

Several types of nonpyramidal cells from immature specimens are more or less richly endowed with dendritic spines; especially in the old literature, many types of nonpyramidal cells which are recognized today as smooth or sparsely spined are represented with conspicuous spiny dendrites. It is customary, however, to reserve the term spiny stellate cells (LeVay, 1973; Lund, 1973) to a type of nonpyramidal cell specifically located in layer IV (or in any of its subdivisions) of the primary sensory areas (see Chapter 7). Jones (1975) reports them, however, in the motor cortex. Spiny stellate cells do not seem to constitute a uniform population, for substantial differences have been reported to exist between species, the cortical area or even the sublayer in which they are located. Nevertheless, it is useful to consider these cells as a group. In general, they are defined as multipolar neurons with spiny dendrites comparable to those of pyramidal cells, but they lack a typical apical dendrite. The density of spines, however, is less than that of pyramidal cells (Jones, 1975; see Chapter 4), and visible differences exist in this respect among the subtypes present in layer IV of the monkey visual cortex (see, e.g., Figs. 3 and 5A in Fairén and Valverde, 1979).

It may be that some of the cells reported as spiny stellate cells are in fact true pyramidal cells in which the apical dendrite failed to impregnate or was not included in the Golgi section during tissue processing. In some instances, some of the dendrites are not confined to layer IV, but instead enter supragranular layers, as in the case of star pyramids, a term coined by Lorente de Nó (1949).

Perhaps, the distinction Lorente de Nó (1949) made between star pyramids and star cells is most evident in the barrel field of rodents, i.e., the cortical representation of the mystacial vibrissae of the animal's snout. In his initial account of this cortex (Lorente de Nó, 1922), both differences and similarities between the two types are obvious (see his Figs. 3 and 9), for there are patterns of local dendrite distribution clearly related to the presence of "glomeral" (barrels; Woolsey and Van der Loos, 1970) and perhaps to the termination of thalamocortical fibers in discrete territories (Lorente de Nó, 1922; Killackey, 1973; Steffen, 1976; White, 1979). The patterns vary according to whether the cells are located in the periphery of a "glomeral" (barrel wall or septum) or in its center (barrel hollow). Thus, the patterns of distribution of the dendrites are "context-dependent characteristics" (Woolsey et al., 1975) that allow for straightforward differentiation between star pyramids and true pyramidal cells.
On the other hand, star pyramids differ from star cells in that they possess a thin and poorly arborizing ramifications ascending dendrite which may reach layer 1.

Lorentze de Nô (1922) considers his star cells to be equivalent to the long-axonated star cells that Ramón y Cajal (1911) described in the human visual cortex and in the visual cortex of the cat (Ramón y Cajal, 1911, 1921, 1922). Ramón y Cajal gave the first description of these large cells in 1899 (Ramón y Cajal, 1899a,b), insisting that their axons project out of the cortex, a fact that has been confirmed for some such neurons in the visual cortex of the cat (Innocenti and Fiore, 1976; Slatz, 1977; Sanides and Donato-Oliver, 1978; Innocenti, 1979; Sanides, 1979; Hornung and Garey, 1980, 1981; Meyer and Albus, 1981), as well as in layer IVb of the visual cortex of the monkey (Lund et al., 1975; Lund, 1981). However, the distant target areas are not the same for the cat as for the primate (see Lund et al., 1979; Lue, 1981; and see Chapter 16).

Spiny stellate cells in layer IV of the visual cortex are Ramón y Cajal's star cells (Ramón y Cajal, 1909b, 1911, 1921, 1922; O'Leary, 1941; Shkolnik-Yarros, 1971; LeVay, 1975; Szentágothai, 1973; Lund et al., 1975; Fairén and Valverde, 1979; Peters and Regidor, 1981). They are large cells with long dendrites richly supplied with spines; cells located in the lower tier of layer IV are smaller (Garey, 1971; Lund et al., 1975; Hornung and Garey, 1981b; Peters and Regidor, 1981).

The axon originates from the lower pole of the perikaryon, initially descends and gives off horizontal or recurrent collaterals. Although an idea of the axonal distribution can be obtained with the Golgi method, it is apparent that innervations are not complete (see Lund et al., 1979); the intracranial HRP injection by Gilbert and Wiesel (1979, 1981) of one such cell in layer IVb shows a very extensive arborization through layers IVb and II–III, not restricted to the dendritic tree. The axonal arborization of layer IVC spiny stellate cells seems to be much more restricted (Lund et al., 1979; Gilbert and Wiesel, 1979, 1981).

In the monkey area 17, several varieties of spiny stellate cells are present (Valverde, 1971; Lund, 1975; Lund and Boothe, 1975; Fairén and Valverde, 1979; Lund, 1981), but they have been reported to be absent of area 18 (Valverde, 1978; Lund et al., 1981). In area 17, morphology varies according to the sublayer in which the cells are located. First, there is a type of long-projecting, spiny stellate cell in layer IVb (Lund et al., 1975; Lund, 1981) which seems to be the homolog of the large star cell of Ramón y Cajal, which is also present in human visual cortex (Ramón y Cajal, 1899a,b). On the other hand, in layers IVa and IVC there are distinct populations of spiny stellate cells which have a lesser spine density (see Fig. 3 in Fairén and Valverde, 1979) and possess intracortical axons (Valverde, 1971; Lund, 1975; Lund and Boothe, 1975; Fairén and Valverde, 1979; Lund, 1981). The most conspicuous type, apparently absent from the visual cortex in nonprimates, is located in the lower part of layer IVc: the axon first descends but soon forms recurrent branches which ascend in a strictly columnar fashion. An interesting, additional feature of spiny stellate cells in the primate visual cortex is the existence of quite specific, differential patterns of axonal projections to the suprageniculate layers, depending on the parent cell at the different levels of layer IV (see Lund, 1981, and Chapter 7 for a review). Given, however, that this is based solely on Golgi studies, where there are no guarantees of complete axonal staining, complementary evidence must be sought to fully substantiate the reality of these differential projections. Unlike the situation in the rodent barrel field, in the visual cortex of primates (and also in case) there are no indications of dendritic asymmetries which could reflect a spatial relationship between the distribution of chalmoconteric axons and that of spiny dendrites (Lund, 1981, and Chapter 7). The application of a recently developed technique (Botteri et al., 1982) might shed some light on this issue.

An interesting discussion on spiny stellate cells in the monkey somatosensory cortex is given by Jones (1975). It seems that the majority of these cells possess dendrites entering layer III and, thus, they may be classified as star pyramids; their axons are not dissimilar to those of spiny stellate cells in layer IVC of the monkey visual cortex in that their strongly recurrent collaterals distribute in a columnar fashion. Spiny stellate cells with dendrites confined to layer V (more commonly impregnated in area 3) have axons with a relatively wider distribution through their recurrent ascent. In addition, a descending branch of the axon may be present in both subtypes.

In the rodent visual cortex, Golgi studies usually refer to the apparent scarcity of spiny stellate cells; this is somewhat surprising, since such cells are an outstanding component of the somatosensory cortex in such species. Typical examples are shown by Valverde (1968) in his Fig. 7 and by Feldman and Peters (1976) but, clearly, the problem of identification of these cells in the visual cortex of rodents is not settled yet (cf. Parnavelas et al., 1977b; Somogy, 1978).

4. Concluding Remarks

The present account attempts to describe the different sets of nonpyramidal neurons present in the neocortex of a variety of mammalian species. Basically, morphological criteria have been employed, but data on synaptology and cytochemistry have been useful in defining characteristics within this rather diverse group of neurons. We offer a general overview which may serve as a body of reference for more specific studies dealing with the neuronal composition of particular cortical areas. An additional step has been to explore whether the differences between cortical areas in diverse mammalian species can be based on differences in the types of neuronal units they contain. After compiling this overview, our conclusion is that, along the evolutionary scale, each one of the well-defined nonpyramidal cell classes is basically stable: similarities between the neuronal components of the various areas in the diverse species are more evident than their dissimilarities. Of course, exceptions exist and these have been discussed in the preceding sections.

Is there a basic uniformity in the cellular composition of the cerebral neocortex? The answer must await further analyses. It must be emphasized that we have deliberately looked for basic structural patterns which would permit comparisons to be made, and we have intentionally underestimated certain morphological details, when comparing cells in different species. It is uncertain whether we have succeeded in selecting the essential features which define non-
pyramidal cell groups. It is discouraging to realize that even after more than a century of possessing suitable methods to reveal the forms of neurons, morphological criteria to define neuronal groups are not established. There are many examples of neurons, both in our preparations and in the literature, whose interpretation largely evades us. Moreover, it is an everyday experience of many Golgi workers that new types appear each time a successful preparation is examined; this has prompted the common trend to consider higher brains as more diversified in cell types than the most primitive ones are. The conclusion is clear: glimpses at neuronal geometry now need to be complemented by other approaches if valid criteria are to emerge. In addition, the fact must be seriously considered that Golgi observations have covered but minute parts of the neocortical mantle. Very little has been said about the association cortices.

The question of the basic uniformity in the composition of the cerebral cortex has been the subject of countless discussions; it was already embedded in the early efforts by Ramón y Cajal to disclose the structural basis of the cortical parcellations made by the cytoarchitectonic schools, and it still pervades much of the contemporary Golgi-based literature. It is our hope that by studying the particularities of organization of nonpyramidal cells in the different cortical fields, the nature and fundamental significance of cytoarchitectonic distinctions will become clearer.

The idea that nonpyramidal neurons or, in general terms, local circuit neurons increase in number and diversity in phylogeny was advanced by Ramón y Cajal (1911) (see Rakic, 1975, for a restest). Modern concepts on the modular organization of the cerebral cortex (Mountcastle, 1957, 1979; Hubel and Wiesel, 1962, 1977; Szentagothai, 1975, 1978; Jones, 1981) suggest that the cellular components of the modules are basically unvaried; what makes for differences are the number of modules and their connections (Rockel et al., 1980).

Two converging lines of evidence support the idea of uniformity. First, neuron counting (Rockel et al., 1974, 1980; Powell, 1981; Powell and Hendrickson, 1981) reveals that the total number of neurons in narrow columns of uniform width through the full depth of the cortex, in diverse species and areas, is remarkably constant. There is an exception, however, in both the monocular and the binocular segments of the area 17 of monkeys, in which the number of cells is more that twice that in other cortical areas.* The second line of evidence comes from the comparison of the ratio between pyramidal and nonpyramidal neurons, identified according to conventional electron microscope criteria. The ratio is remarkably constant in monkeys (Slaper, 1975; Tömböl, 1974; Sloper et al., 1979) and in rats and cats (Winfield et al., 1980).

Within the modules, elaboration of the neuropil differs in the various species (e.g., Mountcastle, 1979). The idea that cells with specialized axonal arborizations are more abundant in higher species (Fairén and Valverde, 1979) could only reflect an elaboration of dendritic and axonal processes. Uniformity of the basic types of nonpyramidal cells along the evolutionary scale has been suggested by various authors using the Golgi methods (e.g., Szentagothai, 1979), and the

* Besides the possibility that certain nonpyramidal neurons only appear in area 17 of primates (e.g., some varieties of stellate cells; see Section 3.3), there are biochemical indications of a unique organization of this cortex (Hendrickson et al., 1981; Horton and Hubel, 1981; Livingstone and Hubel, 1982; Hsu, 1982).

The present reexamination of the problem strongly favors this point of view. The most noticeable fact is that most of the nonpyramidal cell varieties have been found in all species of mammals which so far have been examined by the present authors or by others, and little variation has been found even for certain of the cell types previously considered as specialized (Fairén and Valverde, 1979). A reevaluation of what is meant by specialized axonal arborizations is needed. Our proposal is that the qualification of specialized must be reserved for those cells whose axonal arborizations are selective for their postsynaptic partners (see Fairén and Valverde, 1988), and DeFelipe and Fairén, 1982, for additional discussion. An outstanding example of specialized cell is the chandelier cell, and this cell type is present all along the evolutionary scale, from insectivores to primates. Perhaps, another strong candidate is the basket cell, but data about its constancy in phylogeny are still scarce.

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