

Neurons of the Human Retina: A Golgi Study

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ABSTRACT

Golgi techniques have been applied to post mortem specimens of human retina. Analysis was possible on 150 human retinas processed and viewed by light microscopy as whole mounts. Camera lucida drawings and photography were used to classify the impregnated neurons into 3 types of horizontal cell, 9 types of bipolar cell, 24 basic types of amacrine cell, a single type of interplexiform cell, and 18 types of ganglion cell.

We have distinguished two types of midget bipolar cell: fmB (flat) and imB (invaginating). In central retina, both types are typically single-headed, each clearly contacting a single cone. Peripherally, they may be two- or even three-headed, obviously contacting more than one cone. Two types of small-field diffuse cone bipolars occurring as flat and invaginating varieties are found across the entire retina from fovea to far periphery. The single rod bipolar type appears about 1 mm from the fovea and increases in dendritic tree diameter from there into the far periphery. The putative "ON-center" blue cone bipolar and the giant bistratified bipolar first described by Mariani are also present in human retina and we add two previously undescribed bipolar cell types: a putative giant diffuse invaginating and a candidate "OFF-center" blue cone bipolar.

Taking into account the variation of cell size with eccentricity at all points on the retina, we observed three distinct varieties of horizontal cell. The HI is the well known, long-axon-bearing cell of Polyak. HII is the more recently described multibranching, wavy-axoned horizontal cell. The third variety, HIII, introduced here, has been separated from the HI type on morphological criteria of having a larger, more asymmetrical dendritic field and in contacting 30% more cones than the HI at any point on the retina.

Amacrine cells proved to be most diverse in morphology. Many of the amacrine cell types that have been described in cat retina (Kolb et al., '81: *Vision Res.* 21:1081-1114) were seen in this study. Where there are no equivalent cells in cat, we have adopted the descriptive terminology used by Mariani in monkey retina. Thus eight varieties of small-field amacrines (under 100 μm dendritic trees), eight varieties of medium-field cells (100-500 μm dendritic span), and eight large-field varieties (over 500 μm dendritic trees) have been classified. Often a broadly described variety of amacrine cell can be subdivided into as many as three subtypes dependent on stratification levels of their dendrites in the inner plexiform layer.

Only a single morphological type of interplexiform cell has been seen in this study. Its diffusely branched dendritic tree in the inner plexiform layer and loosely branched, appendage-laden process in the outer plexiform layer suggest that it is homologous to the GABAergic interplexiform cell of the cat retina.

As with amacrine cells, wherever possible, ganglion cells in human retina have been classified according to the scheme in cat retina. However, the major groups of ganglion cells are unique to the primate. Ganglion cells with the smallest dendritic trees, originally called midget ganglion cells, are herein called P1 cells, to denote that they are a type of ganglion cell that projects to the parvocellular layers of the lateral geniculate nucleus. P1 ganglion cells occur in high branching (a-type) and low branching (b-type) pairs across the entire retina. They have dendritic trees varying from 5 μm at the fovea to 20 μm diameter at 10 mm eccentricity. P1 cells of peripheral retina can become double-headed presumably to contact two midget bipolar cells. P2 cells are so named because they also project to the parvocellular layers of the LGN and occur

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as a- and b-types. In human retina this cell type has a dendritic tree ranging from 10 to 100 μm in size over an eccentricity of 14 mm. In contrast, the magnocellular projecting ganglion cells, herein called M cells, have dendritic trees increasing in diameter from 20 to 330 μm with eccentricity to 14 mm. All but six of the ganglion cell types G3 to G23 of cat have also been seen in the human retina.

Key words: bipolar cells, horizontal cells, amacrine cells, ganglion cells

Over the past few years there has been an explosion of knowledge concerning retinal architecture in various vertebrate species mainly because newly developed techniques, such as dye-injection of single cells or immunostaining showing whole populations of neurons, are built upon descriptive morphology from Golgi studies. Yet, the one retina that all vision scientists are trying to understand, namely the human retina, has been rather little studied by this classical neuroanatomical technique; thus there is no background information available on which to proceed with the more modern approaches. We still know little about the specific morphologies of the multitude of neurons constituting our own retinas. The problem has always been one of acquiring human tissue in either sufficient amounts or after short enough post mortem times to be sure of success with temperamental silver-staining procedures such as the Golgi method. The rare Golgi studies that have employed human material have concentrated on only one or two cell types (Rodieck et al., '85). Polyak ('41) included some examples of human cells in his monumental treatise on the neurons of the primate retina, but by far the greater proportion of the latter work is devoted to the macaque monkey. The monkey visual system is thought to be the closest of any vertebrate to the human and we naturally expect to find the same neural types and architecture of pathways in the human as in the monkey retina. Thus at the present time our assumptions concerning the organization of the human retina are based on knowledge of anatomy and function in the monkey retina.

It was a great advance for our knowledge of the organization of retinal neurons in monkey retina and vertebrate retinas in general when a wholemount technique for Golgi was developed (Boycott and Kolb, '73; Ogden, '74; Stell and Witkovsky, '73). This enabled us, for the first time, to see the full expanse of neurons with large dendritic trees, which, outside of the private midget systems peculiar to primate retinas, form the major components of the neural retina (Ramón y Cajal, 1892). Monkey retinas have been studied anew since Polyak's time, at first by traditional vertical sectioning techniques but more recently and, to better advantage, by wholemount techniques (Boycott and Dowling, '69; Boycott and Kolb, '73; Kolb, '70; Kolb et al., '69, '80; Mariani, '81, '82, '83, '84b, '90; Ogden, '74; Rodieck, '89). Thus a great many new neural types have been added to Polyak's original inventory. However, the wealth of facts detailed in his book, even from vertical section analysis, have often been poorly cited and substantially ignored; therefore we suggest that his work merits closer scrutiny particularly where applicable to cell types found only in primate retinas.

In this study we have been fortunate enough to acquire a large number of human eye specimens in good enough condition to have success with the Golgi method. Most of the neural types previously described by Polyak and later

authors in monkey retina have been revealed, and, furthermore, several new varieties in all neuronal classes can be added. Thus we have identified in human retina all the bipolar cells described in rhesus monkey by others and have seen two new types. Furthermore, we have enlarged upon the original classification of horizontal cells into first one type (Polyak, '41) and then into two types (Kolb et al., '80) by presenting evidence for a third type. A dizzying number of amacrine cells, many of which were recently described in rhesus monkey from Golgi studies (Mariani, '90), with a few from intracellular dye-injection studies (Dacey, '89a, '90), have been seen and classified in the human retina. Some new varieties are presented here for the first time. We have also described more ganglion cell types in human than have been described by either Polyak ('41) or others (Boycott and Dowling, '69; Perry and Cowey, '81, '84; Perry et al., '84; Rodieck, '88; Rodieck et al., '85) in the monkey retina. We have reemphasized Polyak's original classification scheme for the ganglion cells unique to primate retina that project through the geniculate-striate pathways and probably subserve trichromatic color vision and high acuity, i.e., the parvocellular-projecting (P) and magnocellular-projecting (M) cells to the lateral geniculate nucleus (Kaplan et al., '90; Shapley and Perry, '86).

Some aspects of our Golgi classification scheme for human retinal neurons have been reported previously in abstract form and in review articles and chapters (Fisher et al., '86; Kolb, '91a,b; Kolb et al., '86, '89; Kolb and DeKorver, '91; Kolb and Lipetz, '91; Linberg et al., '86, '87).

MATERIALS AND METHODS

Eye specimens

The posterior poles of 150 human donor eyes were obtained from several local southern Californian eye banks (UCLA, Loma Linda, Lions Doheny, Orange County, and San Diego). All were corneal donor eyes free of retinal pathology. The protocols for obtaining and handling these eyes had all been passed by the U.C. Santa Barbara human subjects committee. Most of our successful impregnations occurred in specimens obtained within 4 hours of death. Occasional specimens that were up to 8 hours post mortem yielded usable cells. It is our impression that eyes donated to the hospital-associated eye banks after respirator deaths did not impregnate as reliably.

Fixation and Golgi procedures

After the anterior segments, lens, and vitreous of these eyes had been removed, the posterior eye cups were immersed in 1% formaldehyde, 1–2% glutaraldehyde in 0.1 M phosphate buffer (pH 7.2) by the eye bank technicians using fixatives supplied to them in advance. Eye cups were shipped to us periodically and remained in fixative for periods as short as 4 days to up to 8 months. Most, however,

were kept in fixative at 4°C for between 1 and 3 weeks. Once in the laboratory, retinas were carefully peeled from the choroid and pigment epithelium. Each retina was then sandwiched between two pieces of Whatman #50 (hard) filter paper moistened with fixative. A stack of such sandwiched retinas, each sandwich separated by Whatman #2 (soft) filter paper were held between two large glass slides tied together with thread. This ensemble was transferred to a solution composed of 5% glutaraldehyde and 4% potassium dichromate for 1 week, kept at room temperature in the dark. The bundled retinas were then washed in several changes of 0.75–1% aqueous silver nitrate until the red reaction product no longer appeared, after which they remained immersed in this solution for 3 days in the dark at room temperature. After a brief wash in distilled water, the sandwiched retinas were dehydrated in an ascending ethanol series until the 70% alcohol stage at which point they were untied and separated. Dehydration continued and retinas were cleared for 10–15 minutes in cedar wood oil and infiltrated with xylene for 5 minutes. Each retina was then mounted on a large glass slide with Permount (Fisher Scientific), ganglion cell side up. Cover slips were placed over the wholemounts and small lead weights were placed on top of them to help flatten the tissue. Shrinkage of the retinas is not very great with sandwich techniques. We estimate no more than 10% occurs.

Methods of analysis

Retinas were examined by light microscopy and cells of interest were drawn with the aid of a camera lucida. Some cells were photographed. In some cases groups of cells were drawn and analyzed by quantitative computer methodology with a Zeiss MOP digital analyzer. When possible the exact eccentricity of the cells was recorded but frequently the fovea had been removed for other investigators' experiments and/or the foveal pit was folded or distorted so that exact measurements were difficult to obtain. Under these circumstances we could only estimate eccentricity vaguely as central (within 5 mm of the fovea) versus midperipheral (5–10 mm eccentricity) versus far-peripheral retina (10–20 mm eccentricity). Scales and dendritic tree sizes were established by using an eyepiece graticule in the microscope binocular head.

The arborization levels within the inner plexiform layer (IPL) of dendritic trees of amacrine and ganglion cells and axon terminals of bipolar cells have been judged in whole-mount views by measuring the plane of the impregnated profiles in relationship to the inner nuclear layer and ganglion cell layer borders. We use Ramón y Cajal's (1892) division of the IPL into five equal thickness strata, with stratum 1 beginning under the amacrine cells and stratum 5 ending on the ganglion cell layer. In some cases we also use the bisublamination scheme, first introduced by Famiglietti and Kolb ('76) to denote whether neurons branch in the OFF layer (sublamina a, strata 1 and 2) or ON layer (sublamina b, strata 3, 4, and 5).

RESULTS

Bipolar cells of the human retina

Eight different cone bipolar types and one rod bipolar type were seen in this study (Table 1). Cone bipolars are readily distinguishable from rod bipolars by their characteristic of having unbranched (in the case of foveal midget

TABLE 1. Bipolar Cell Types of the Human Retina and Possible Equivalent Cell Types in Other Mammalian Retinas¹

Type	Sample size	Axon Stratification in IPL	Monkey	Cat	Rabbit
RBb	Many	S5	Mop bipolar ² Rod bipolar ³	rb ⁸	rb ⁹
fmB	Many	S1/2	Midget bipolar short axon ² Flat midget bipolar ⁴	cb1 ⁸	na1,2,3 ¹⁰
imB	Many	S5	Midget bipolar long axon ² Invaginating midget bipolar ⁴	cb5 ⁸	nb1,2 ¹⁰
DBa	Many	S2	Flat bipolar ^{2,3}	cb2 ⁸	ma ¹⁰
DBb	Many	S4	Brush bipolar ² Diffuse invaginating bipolar ⁵	cb6 ⁸	wb ¹⁰
BBa	Few	S1	—	—	wa ¹⁰
BBb	Several	S5	Blue cone bipolar ⁶ CCK-IR ¹¹	—	wb ¹⁰
GBa,b	Several	S1,S4	Giant bistratified bipolar ⁷	cb4 ⁸	—
GBb	Several	S3	—	cb8 ⁸	—

¹IPL, inner plexiform layer; RBb, rod bipolar cells; fmB, flat midget bipolar cells; imB, invaginating midget bipolar cells; DB, diffuse cone bipolar cells; BB, blue cone bipolar cells; GBa,b, bistratified giant bipolar cells. GBb, giant diffuse bipolar cells. CCK-IR, cholecystokinin-immunoreactive.

²Polyak ('41).

³Boycott and Dowling ('69).

⁴Kolb et al., ('69).

⁵Mariani ('81).

⁶Mariani ('84b).

⁷Mariani ('83).

⁸Kolb et al. ('81).

⁹Dacheux and Raviola ('86).

¹⁰Famiglietti ('81).

¹¹Kouyama and Marshak ('92).

bipolars) or branched (in the case of diffuse bipolars) apical dendrites ending in clusters of terminals on the plane of the cone pedicles in the outer plexiform layer (OPL). Rod bipolars, on the other hand, have multiple spiky dendrites, usually arising from a single stout apical dendrite, extending past the layer of cone pedicles to reach the more sclerated tiers of rod spherules.

Midget cone bipolar cells. Two types of midget bipolar cell, reflecting the nature of their contacts with their respective cone pedicles, are recognizable in the human as in monkey retinas (Kolb et al., '69; Kolb, '70). Figure 1 (top) shows examples of both types. The midgets, as well as the rest of the bipolar cell types in Figures 1 and 2, are depicted in two views showing their dendrites at one level of focus, and their axon terminal arborization at the other. Flat midget bipolars (fmB) are characterized by their axon terminals ending in sublamina a (Famiglietti and Kolb, '76) of the IPL. The fmB cells have a small dendritic bouquet of fine terminals fitting the size of a single cone pedicle. In central retina (4.5 mm from the fovea) (Fig. 1, fmB) their axon terminals end as small compact groups of varicosities restricted to the border of strata 1 and 2 (sublamina a) of the IPL. In peripheral retina (Fig. 1, fmB, 12 mm; Fig. 26f), fmB cells frequently appear to have two or even three dendritic clusters, thus clearly contacting two or three neighboring cone pedicles. This finding of multiple-headed midget bipolar cells in primate retina has been described by both Polyak ('41) and Ogden ('74) and more recently by Boycott and Hopkins ('91). As the midget bipolar dendritic tree expands to innervate two or three cones, the axon terminal broadens in lateral extent too. At peripheral locations fmB axon terminals have a 20 µm spread (Figs. 1, 26g).

The other midget bipolar cell type, the invaginating midget bipolar cell (imB) (Kolb et al., '69), appears superficially similar to the fmB type. However, its major difference from fmB lies in the level of its axon termination in the IPL. The imB cells have compact bulbous endings that terminate

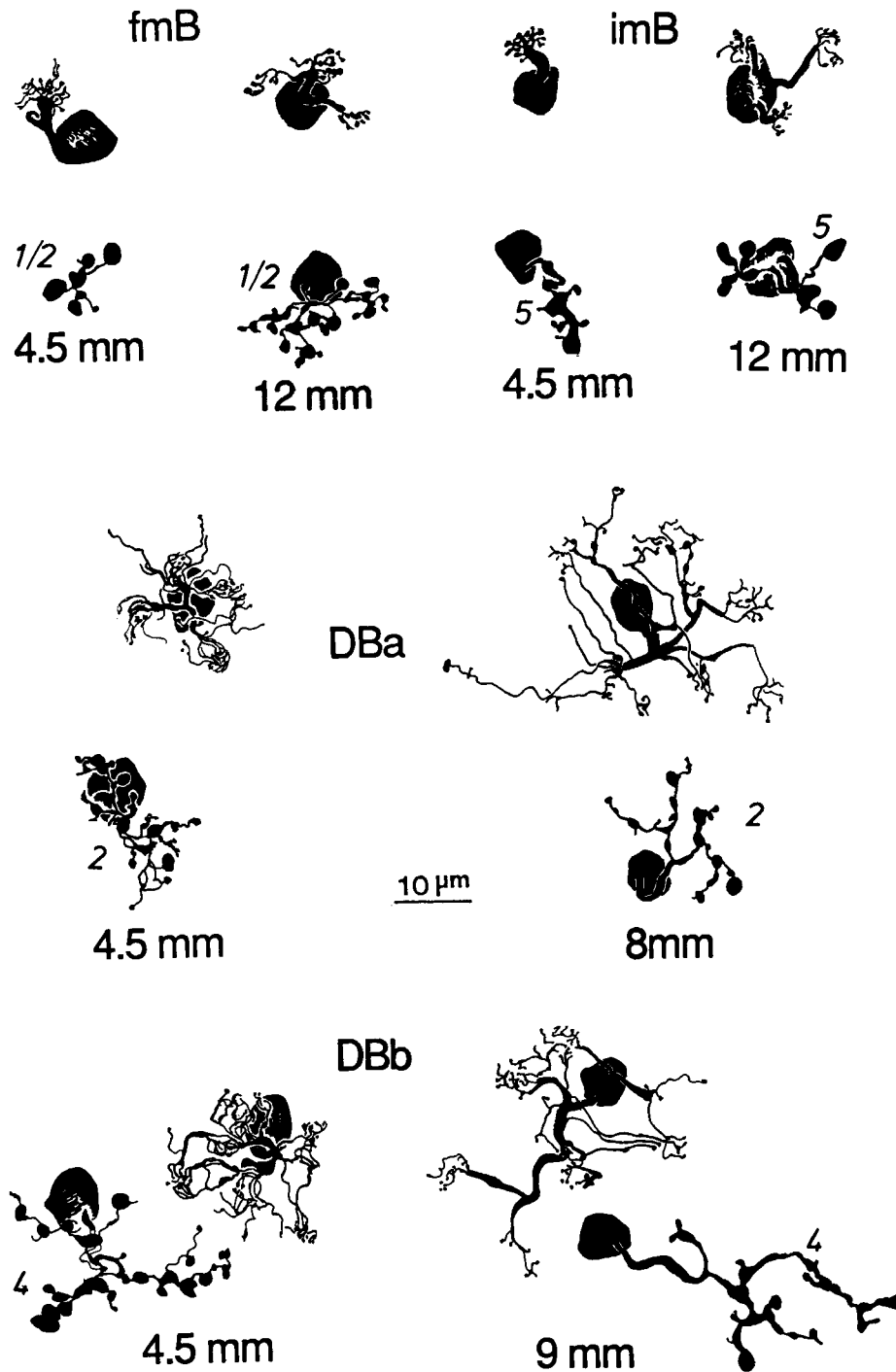


Fig. 1. Camera lucida drawings of cone bipolar cells of the human retina as seen in wholemount Golgi preparations. Each cell is drawn at two levels: the dendritic tree in the outer plexiform layer (OPL) (above) and the axon terminal in the inner plexiform layer (IPL) (below). The stratification of the axon terminal in whichever of the five strata of the

IPL is applicable is given by the adjacent italicized number. Positions on the retina in millimeters of eccentricity are indicated for each cell illustrated. Midget bipolar cells, fmB and imB varieties, are indicated above the diffuse small-field bipolar types, DBa and DBb. See text for further detailed descriptions. Scale bar = 10 μm.

deep in sublamina b of the IPL next to the ganglion cells (Fig. 1, imB, 5). Also the perikarya of the imB cells tend to lie more sclerad in the inner nuclear layer (INL) than those of the fmB cell type. Like the fmB type, the dendritic bouquets of imB cells, which usually have more easily

resolvable individual terminals, are the size of single cone pedicles in central retina (Fig. 1, imB, 4.5 mm) and may become multiple-headed (up to three heads) in peripheral retina (Fig. 1, imB, 12 mm). Both midget bipolar cell types have been seen as single-headed as far peripheral as 15 mm

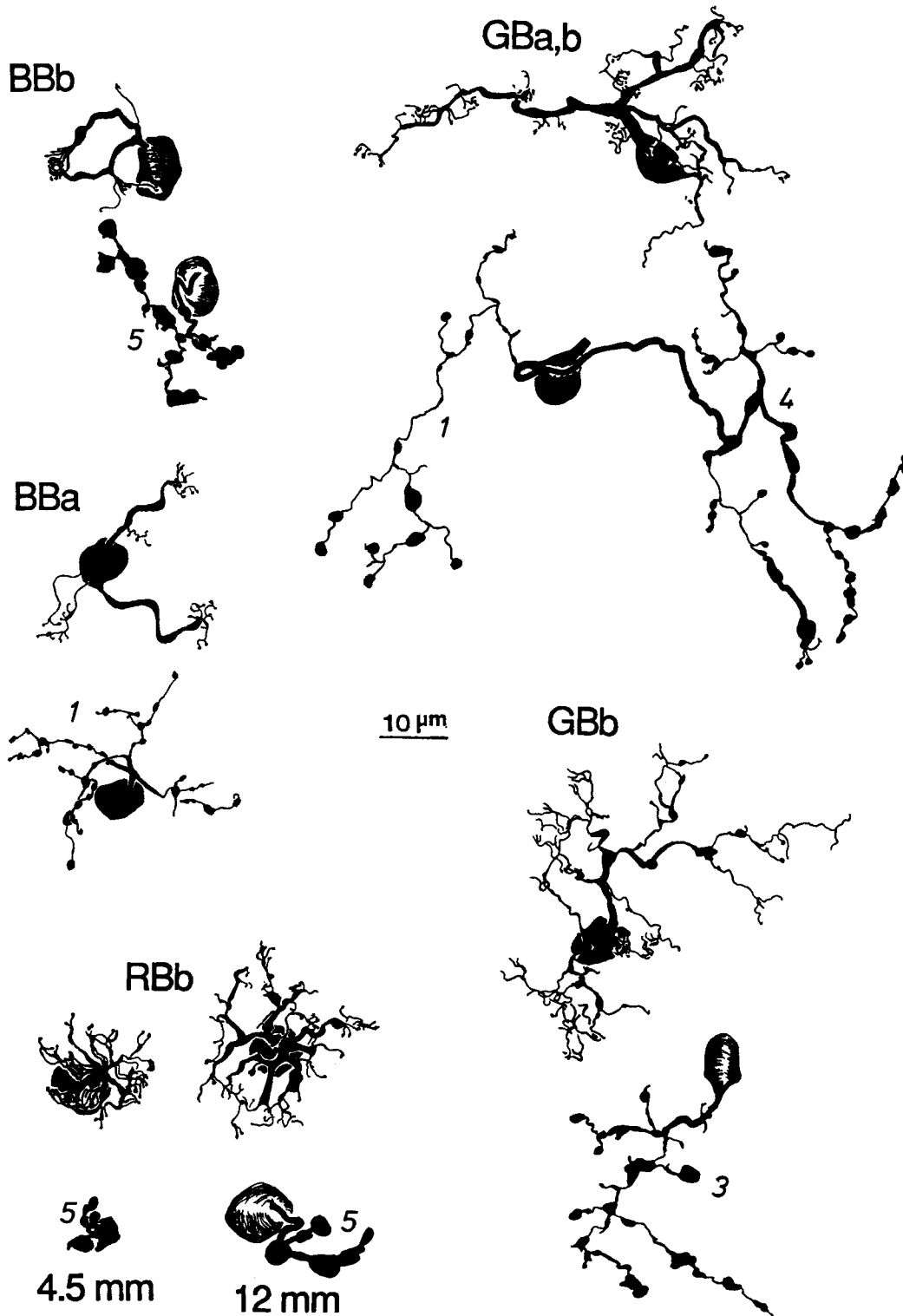


Fig. 2. Unusual cone bipolar cells and the single morphological type of rod bipolar cell of the human retina as seen in wholemounts. BBb is a bipolar cell specific for blue cones with its axon terminating in sublamina b of the IPL. A putative blue cone-specific bipolar, BBa, with its axon terminating in sublamina a of the IPL is drawn below. The two

varieties of large-field cone bipolars, giant bistratified (GBa,b) and giant diffuse (GBb) are on the right. GBb is a cone bipolar type newly added to the primate classification. A central and a peripheral example of the rod bipolar cell type RBb is illustrated at lower left. Scale bar = 10 μm.

(see Fig. 26c, single-headed midget found at 8 mm eccentricity near the two-headed example in Fig. 26f).

In central retina, the midget bipolar axon terminals for both types are only 4–10 μm in spread. With increasing eccentricity and with increasing numbers of dendritic heads, the axon terminal expands correspondingly to reach a maximum spread of 20 μm (Fig. 1).

Small-field diffuse cone bipolar cells. Two different morphological types of diffuse cone bipolar cell (DB) have been impregnated in the human retina: DBa, with its axon terminal branches in sublamina **a** of the IPL and DBb, with its axon terminal branches in sublamina **b** (Fig. 1, middle and lower pairs of cells). DBa is the cone bipolar type originally called the “flat bipolar” (Polyak, '41; Boycott and Dowling, '69) (Table 1) and is known from electron microscope studies to contact cone pedicles at superficial or basal junctions (Kolb, '70; Missotten, '65). In wholmount view, DBa cells of central retina (Fig. 1, DBa, 4.5 mm) have a branching apical dendrite passing to a minimum of five neighboring cones as judged by the distinct clusters of dendritic terminals. The axon terminal ends in stratum 2 of the IPL in a branched, laterally spreading group of varicosities covering 20–25 μm . At peripheral eccentricities the dendrites reach out to contact 10–15 cone pedicles with a wider spreading dendritic field (Fig. 1, DBa, 8 mm; Fig. 26b). It appears that all cones in the field are contacted. Correspondingly, the axon terminals of peripheral cells span an area similar to the dendrites in the OPL, about 25–50 μm .

The other diffuse cone bipolar type we have seen was originally described by Polyak in primate retina as a brush bipolar cell (Polyak, '41) (Table 1). Mariani renamed it the diffuse invaginating bipolar cell based on his ultrastructural study of its contacts with cone pedicles (Mariani, '81) (Table 1). The DBb type is most readily distinguished from the DBa type in wholmount views of retina by its axon terminal stratification in the IPL. DBb cells have axons ending in laterally spreading terminals in stratum 4 of sublamina **b**. The dendritic fields of DBb cells are typically 20 μm in diameter in the central retina, and the individual bouquets of terminals appear to contact all overlying cones in the field (usually five pedicles) (Fig. 1, DBb, 4.5 mm). In peripheral retina 10–15 cones seem to be innervated by DBb cells with dendritic field sizes of 35–40 μm (Fig. 1, DBb, 9 mm; Fig. 26d). Again, all the cones in the dendritic field appear to be contacted. The axon terminals become correspondingly wider spreading with eccentricity, always having about the same dimensions as the dendritic field coverage (Fig. 1, DBb, 4.5 and 9 mm).

“Blue cone” bipolar cells. Like the diffuse bipolar cells, the putative blue cone bipolar cells (BB) innervate more than one cone pedicle lying above their dendritic arbors. Unlike the commonly seen diffuse cone bipolar pair, however, the rarely impregnated BB cells innervate only a *subpopulation* of overlying pedicles. We have also observed the blue cone bipolar type described by Mariani ('84b) in the human material. It has an axon terminal arborizing in stratum 5 of the IPL (Fig. 2, BBb) and thus by the criteria applied in cat retina (Famiglietti and Kolb, '76), it is hypothesized to be an ON-center variety. In addition we have found a cell type that we are herein suggesting might be an OFF-center variety of the blue-specific cone bipolar since its axon terminal ends in stratum 1 of sublamina **a** (Fig. 2, BBa) (Table 1).

The critical distinction between ordinary diffuse cone bipolar cells and those specific for blue cones, is the manner in which the dendrites target certain widely spaced cones in the OPL (Mariani, '84b; Kouyama and Marshak, '92). Thus the BBb occurring at 4 mm eccentricity (Fig. 2, BBb) has a divided apical dendrite diverging to end in widely spaced bouquets. The typical description of Mariani's blue-specific bipolar fits the BBb here (Fig. 2). This cell has two sturdier dendrites converging on the same cone and finer, wispy branches ending either on another cone or in the neuropil of the OPL. The axon terminal is also characteristic, being a widely ramifying varicose structure ending in stratum 5 of the IPL. The BBb axon terminal extends over a 30 μm area compared with a comparable midget bipolar cell at the same eccentricity (4 mm from the fovea) that has a mere 4–10 μm spread (Fig. 1, imB and fmB).

The putative BBa type was encountered in more peripheral retina (10 mm eccentricity) than the BBb type illustrated. It does, however, appear unique when compared to neighboring fmB or DBa cells. It has the characteristics of the BBb cells in that its dendrites target only a few widely spaced cones in the overlying field, compared with neighboring DBa cells, which contact all the overlying cones (Fig. 1, DBa, 8 mm). The axon of the putative BBa bipolar ends as a very thin, widely spreading axon terminal running in stratum 1 immediately under the amacrine cell bodies (compare DBa cells that have sturdier axons running lower in sublamina **a** in stratum 2). Unfortunately we have only encountered a few of these putative BBa type cells in our 150 specimen collection, so we extend this descriptive classification with caution.

Giant cone bipolars. We have seen two types of cone bipolar that could be categorized as “giant” in dendritic spread. Bipolars in primate are considered “giant” if their dendritic spread exceeds 50 μm in central retina and 100 μm in peripheral retina (Mariani, '83; Rodieck, '88). Figure 2 shows an example of a giant bistratified bipolar like the type first described by Mariani ('83) and below it lies an example of a giant diffuse cone bipolar cell, which we are introducing here (Fig. 2, GBa,b, GBb). Both have very large dendritic trees 60 μm across, which for cone bipolar cells of midperiphery (8 mm eccentricity) is outside the size range (30 μm maximum) for the narrow field DBa and DBb types. Giant cells such as these illustrated herein were always compared in dendritic tree size with neighboring small-field diffuse cone bipolar varieties to make sure of the classification, particularly when the eccentricity of their retinal location was not known exactly.

The GBa,b type has a thick major dendrite that branches into three sinuous and long dendrites covering an asymmetrical dendritic tree of 60 μm diameter. Dendritic clusters, the sizes of the cone pedicles, project off each of the three main dendrites and appear to innervate most of the likely cones above their dendrites. A bistratified axon terminal (Fig. 2) branches with the upper, thin, pronouncedly beaded terminal in stratum 1 and the thicker, lower axon terminal running in stratum 4 of the IPL. The axon terminal, particularly the lower branch, appears to cover the same diameter of the retina as the dendrites, i.e., 60 μm . The giant diffuse cone bipolar, (GBb) resembles the narrow-field DBb cell in overall morphology. However, at the same eccentricity, approximately 7–9 mm from the fovea, neighboring narrow field bipolars had only 30 μm dendritic field diameters. GBb has a 60 μm dendritic field within which are seen several ill-defined groups of dendritic terminals.

The impression is that these terminals innervate the majority of the cones overlying the dendrites. The uniform, unbranching axon descends from the cell body into the IPL to give rise to a very wide, laterally spreading axon terminal in mid-IPL in stratum 3. The axon terminal appears similar to that of the DBb bipolar except that the larger varicosities are more spread out along finer caliber processes. Small branches tipped with boutons sprout from the main axonal branch (Fig. 2, GBb).

Rod bipolar cells. Rod bipolar cells (RBb) of the human retina have the overall appearance of rod bipolar cells of all mammalian retinas (Ramón y Cajal, 1892). They have a characteristic spray of spiky dendrites with terminals reaching up to different levels to get to rod spherules, and they have a large tuberos axon terminal ending in the IPL in strata 4 and 5 (Fig. 2, RBb; Fig. 26e). As described by others for the primate retina (Boycott and Dowling, '69; Mariani, '84a; Polyak, '41; Rodieck, '88), there appears to be only a single morphological type of rod bipolar cell, which doubles in dendritic tree diameter and axonal expanse from central to peripheral retina (Fig. 2, RBb, 4.5 and 12 mm). Their large perikarya (10 μm diameter) lie in the outer half of the INL, some even lie between horizontal cell bodies bordering the OPL (Linberg and Fisher, '88; Missotten, '65). It is difficult to estimate how many rods a single RBb may contact, because impregnation of the finest terminals is not always reliable. However, rough estimates from counting the fine wispy profiles on the dendrites suggest 30–35 rods may be contacted in central retina and 40–45 in peripheral retina (Fig. 2, RBb, 4.5 and 12 mm).

Horizontal cells of the human retina

Polyak ('41) described a single horizontal cell type in primate retina. This long-axoned cell type was further characterized by Boycott and Dowling ('69) and the connectivity of its dendrites and axon terminals with photoreceptors was established by electron microscopy (Kolb, '70). In the human retina we commonly see this type of horizontal cell and have called it the HI type (Fig. 3, HI). HI cells are very small in the foveal region, with a dendritic span of 18–20 μm (Fig. 3, HI, 0.5 mm). They have interwoven clusters of dendritic terminals that are difficult to distinguish into individual cone-specific groups because of the crowding of cone pedicles in this thick region of retina. However, by 2.5 mm eccentricity the HI cells have the definite, thick, radiating dendrites giving rise to distinct clusters destined for seven individual cone pedicles in a 25–30 μm diameter field (Fig. 3, HI, 2.5 mm). At greater eccentricities, the radiating dendrites and clusters of terminals contact seven to nine neighboring cones in a 40–60 μm dendritic field, and by peripheral retina they are contacting 15–20 cones with a dendritic tree diameter of 75–80 μm (Fig. 3, HI, 16 mm). It appears as though HI cells contact all the cone pedicles in their dendritic field at all eccentricities.

A stout axon (2 μm thick) typically arises from the large cell body or from one of the main dendrites and can be traced for a few micrometers to 100 μm or more before impregnation fails. Very few complete HI type horizontal cells of primate retina have ever been illustrated (Mariani, '85; Ogden, '74; Rodieck, '88) and we have not yet seen any ourselves in human retina. However, the axon, judging from the complete example shown by Mariani ('85), maintains a uniformly thick diameter to its ending as a fan-shaped group of distinctive terminals (Fig. 3, HIAT). The individual "lollipop" terminals are quite large (0.5–1 μm)

and often disc-shaped. They are, of course, known to innervate rod spherules (Kolb, '70; Linberg and Fisher, '88).

The second type of horizontal cell described in 1980 by Kolb and coauthors ('80) and later confirmed by Boycott, et al. ('87) has been called the HII cell. It is typically more woolly in appearance, with many intertwining, overlapping fine dendrites, and has a short, curled axon. Figure 3 shows the Golgi-impregnated appearance of HII cells in human retina as seen at different eccentricities from the fovea. At the fovea HII is difficult to tell from HI as the overlapping dendrites passing up to overlying crowded cone pedicles are difficult to distinguish into individual clusters in either horizontal cell type. With greater eccentricity (Fig. 3, HII, 2.5 mm) the woolly appearance of HII differentiates it from HI. Its fine dendrites converging on overlying cones or ending in single wispy terminals are never clearly arranged in cone-innervating clusters. In peripheral retina, HII cells have a particularly randomized dendritic tree and individual cone clusters are still difficult to distinguish. The dendritic tree diameter of HII cells appears to be slightly larger than HIs until 5 mm eccentricity, at which point the trend reverses and HIIs are slightly smaller (Fig. 3, compare HII to HI, at 16 mm). This conforms to what has been described before in monkey retina (Boycott et al., '87; Kolb et al., '80).

HII cells, in human retina as in monkey retina, bear a distinctly thinner diameter axon (0.5 μm) than the HI cells. Their axons usually arise from the end of dendrites and curl around in the OPL over a 300 μm length emitting occasional fine terminals (Fig. 3, HII, arrows), known from electron microscope studies to innervate cone pedicles (Kolb et al., '80, '89).

A new horizontal cell category is introduced here for the first time. We split this HIII type off from the HI type, with which it has been included previously, on morphological criteria of dendritic field size and shape. At points beyond 3 mm eccentricity in the retina the HIII cell has a distinctly larger dendritic tree size. Figure 4 shows this observation graphically. The figures represent an analysis by digitized and computer methods of 650 horizontal cells in 12 well-impregnated human retinas. In the first 3 mm from the fovea the cell type we consider to be HIII is not distinguishable in size from the HI, but beyond that the two cell types clearly fall into different size categories, the one group (triangles, Fig. 4) having a dendritic field area and regression line fit that is significantly different from the group with the smaller dendritic field area (circles, Fig. 4). Thus by objective statistical analysis the two groups are separable.

Morphologically, the HIII cell is most clearly distinguished when seen in midperipheral or peripheral retina and occurring among a group of well-impregnated neighboring HI cells for comparison (Fig. 26a). The HIII cell has a slightly larger cell body (e.g., 13 μm diameter at 16 mm eccentricity, compared with the HI with a 10 μm diameter; Fig. 3). When compared with a neighboring HI cell, the HIII has a much wider spread, heavier set arrangement of long, radiating dendrites. The HIII cells are usually highly asymmetrical with one or two primary dendrites being distinctly longer than the others (Figs. 3, 26a). In comparison, the HI cell type is more uniformly radial in dendritic tree shape and the individual cone clusters of terminals are more regularly spaced, contacting all the overlying cones of the mosaic (Fig. 26a). HIII cells appear to miss cones,

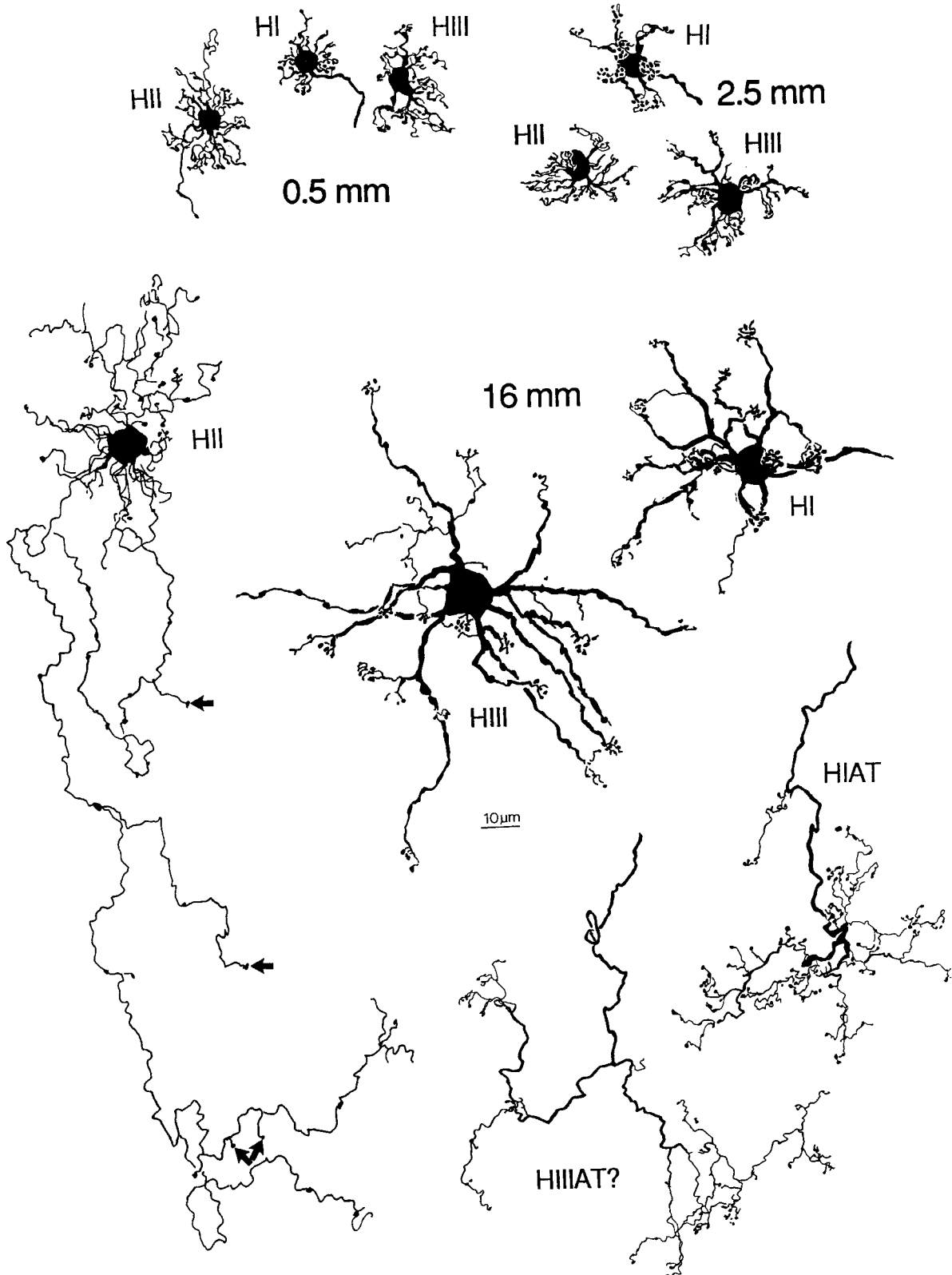


Fig. 3. Wholemout views of the horizontal cells of the human retina. Cells of the fovea (0.5 mm) are small and difficult to distinguish into the three types but nevertheless are recognizable to the trained eye. By 2.5 mm eccentricity HI, HII, and HIII types are discernable from each other. In peripheral retina (16 mm) HIII is clearly a bigger cell than HI and has an asymmetric dendritic field. HII cells have a

wooly appearance distinguishing them readily from HI and HIII. The short curled axon of the HII type gives rise to occasional terminals (arrowed). The HI axon terminal ends as a fan-shaped structure with many "loollipop" terminals HIAT, while a finer, more loosely clustered terminal is putatively assigned to the HIII horizontal cell type HIIIAT?. See text for detailed descriptions. Scale bar = 10 μm.

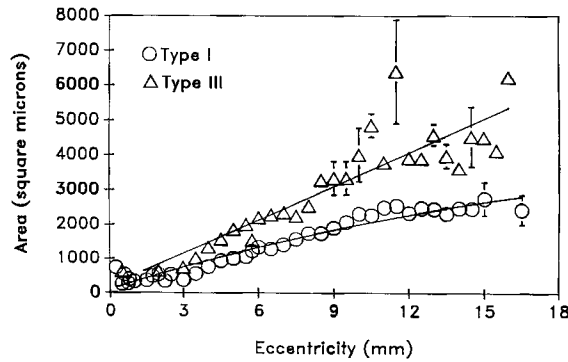


Fig. 4. Graph shows how the dendritic field areas increase for HI and HIII types of horizontal cell with increasing eccentricity from the fovea. Data are pooled from 12 retinas and represent 680 cells that were analyzed by digitized computer methodology. F test for difference between the regression lines is significant ($P < 0.001$).

especially between the larger primary dendrites, but also apparently over their major dendrites. Counting clusters of terminals, HIIs appear to contact about 30–40% more cones than adjacent HI cells (see Fig. 3, where the HIII cell has 20 clusters of terminals compared with the HI that has only 13). Even in central retina, where the statistical analysis could not separate the HI from HIII, we think that we are able to select the two types on the same criteria of dendritic size, asymmetry, and cone contacts. Thus cells at 500 μm and 2.5 mm from the fovea can be seen to fall into these distinct types with experienced observation, e.g., in Figure 3, HIII cells at 2.5 mm appear to contact nine cones, compared to HIs, which contact seven cones.

HIII cells also emit an axon from their cell body or a primary dendrite (Fig. 26a, arrows). Like the HI axon, these have not been followed to their termination. In whole-mount views of the OPL, isolated axon terminals are commonly impregnated, often overlapping and crossing each other. The fan-shaped relatively compact, clustered, densely branched type of axon terminal we know belongs to HI cells (Mariani, '85; Rodieck, '88). In contrast, more loosely organized, sprawling-type axonal arborizations, broken up into patches of terminals with less defined "lollipop" endings, may belong to HIII cells (Fig. 3, HIIIAT?). HIII type horizontal cells have quite commonly been seen to emit a stout descending process from their cell bodies to reach the level of, and even branch somewhat in, the outer levels of the IPL (not shown).

Amacrine cells of the human retina

We have divided amacrine cells into three basic categories based on dendritic field size: small-field, 25–100 μm in diameter; medium-field, 100–500 μm ; and large-field, over 500 μm diameter. Twenty four basic types of amacrine cell emerge from this classification. Even some of these types can be further subdivided on criteria of differing stratification levels for their dendrites in the IPL. All the amacrine cells seen in this study are summarized in Table 2.

Small-field amacrine cells. Eight different types of small-field amacrine cell can be distinguished primarily on the basis of their stratification in the IPL. In wholemounts, these cells look superficially very similar (Fig. 5). Seven of the eight types correspond almost exactly to the same named types in cat retina (Kolb et al., '81). All of the first

TABLE 2. Amacrine Cell Types of the Human Retina and Possible Equivalent Cell Types in Other Mammalian Retinas

Type	Sample size	Axon stratification in IPL	Monkey	Cat	Rabbit
A1	Many	S1/2	Knotty 1 ¹	A1 ² glycine ⁴	
A2	Many	S2	Stratified ⁶ Knotty bistratified ²¹	A2 ² GABA ⁴	
A3	Many	S2-3	Knotty 2 ¹	A3 ² Glycine ⁵	
A4	Many	S2,3,4	Knotty 2 ¹	A4 ² Glycine ⁵	
A5	Few	S4,5	Knotty 3 ¹ Knotty bistratified ²¹ Stratified narrow field ⁶	A5 ²	
Small diffuse	Few	S1-5			
AII	Several	a,b	AII ¹ Narrow diffuse ⁶ Bistratified ⁶	AII ² Glycine ⁵ A8 ² Glycine ⁵	NFB ³
A8	Few	a,b		A12 ² Substance P-IR ¹¹	Substance P-IR ⁸
A12	Several	S5		A14 ²	
A14	Few	S2,4/5	Wavy multi-stratified ¹		
Tristratified	Few	S1/2, 2/3,4/5	Wavy multi-stratified ¹		DAPI-3 ⁹
Woolly	Many	S1-5			
A13	Many	S1-5	A13 ¹	A13 ² GABA ⁴	
Spiny	Several	S3	Spiny ¹ Axon-bearing ¹⁵ Unistratified ⁶		
Spiny varicose	Several	S3			
ACH	Several	S2, S4	Sa, Sb ¹	Starburst ¹⁰ Indoleamine ¹⁹	Starburst ^{7,14}
Thorny 1	Several	S1	Thorny 1 ¹ Dopaminergic ¹⁶	A15 ²	
Thorny 2	Several	S3	Thorny 2 ¹		
Wavy	Few	S1	Unistratified ⁶		
A18	Many	S1	Type 1 CA ¹	A18 ² TOH-IR ¹⁷	TOH-IR ¹⁸
Semilunar 1	Several	S1	Semilunar 1 ¹		
Semilunar 2	Several	S2	Semilunar 2 ¹ Large unistratified ⁶	A19 ² GABA ⁴	
Semilunar 3	Several	S4/5	Semilunar 3 ¹	A22 ²	
Stellate wavy	Few	S3-4	Stellate wavy ¹		
Stellate varicose	Few	S2-3	Stellate varicose ¹		
A17 spidery	Many	S1-5	Spidery 1 ¹ Wide-field diffuse ⁶	A17 ² GABA ⁴	Serotonin ²⁰ S2 ¹²
Wiry	Few	S3	Wiry 2 ¹	A20 ² Indoleamine ¹⁹	

¹Mariani ('90).
²Kolb et al. ('81).
³Dacheux and Raviola ('86).
⁴Pourcho and Goebel ('83).
⁵Pourcho and Goebel ('85).
⁶Boycott and Dowling ('69).
⁷Famiglietti ('83).
⁸Vaney et al. ('89).
⁹Vaney ('90).
¹⁰Pourcho and Osman ('86).
¹¹Pourcho and Goebel ('88).
¹²Vaney ('86).
¹³Mariani and Hokoc ('88).
¹⁴Tauchi and Masland ('84).
¹⁵Dacey ('89a).
¹⁶Dacey ('90).
¹⁷Kolb et al. ('90).
¹⁸Brecha et al. ('84).
¹⁹Wässle et al. ('87).
²⁰Sandell and Masland ('86).

five types we describe here were called "knotty" amacrine cells by Mariani ('90) (Table 2). A1 and A2 (both examples from 9 mm eccentricity) have small-diameter dendritic fields (approximately 60 μm ; Fig. 5) of fine intertwined dendrites bearing small varicosities and appendages. A1 has

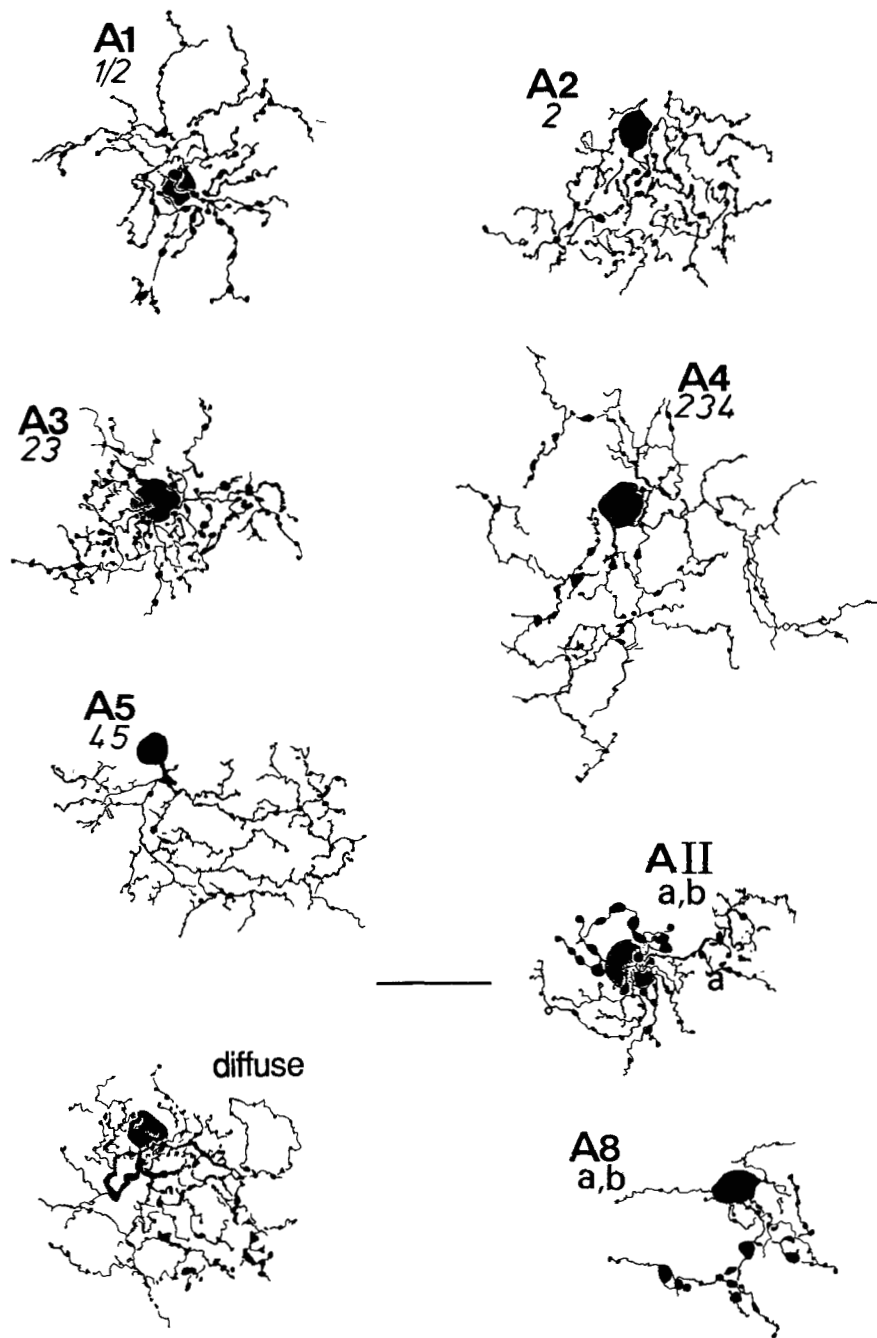


Fig. 5. Small-field amacrine cells of the human retina. Most of the small-field cells have correlates in the cat retina and the nomenclature of the cat is thus used. These cell types have dendritic trees less than $100\ \mu\text{m}$ across at any point on the retina and their dendrites are small, compact, and overlapping. AII and A8 cells are the small-field bistratified amacrine cells well described in cat retina and, as in cat, they arborize in both sublamina *a* and *b* of the IPL. The diffuse small-field amacrine may not have a counterpart in the cat. Strata in the IPL

where the dendrites ramify are indicated by italicized numbers. Narrowly stratified cells are indicated by a single number, or if their dendrites ramify on the border between two strata, by the numbers separated by slashes. More broadly stratifying cells are indicated by a sequence of numbers. Bi- and tristratified cells are shown by commas separating the strata numbers. Diffusely ramifying cells, with dendrites passing through all layers of the IPL, are labeled "diffuse." Scale bar = $25\ \mu\text{m}$.

its dendrites in stratum 1 to the 1/2 border, while A2 has the majority of its dendrites in stratum 2. A3 (4 mm eccentricity) has a $50\text{--}60\ \mu\text{m}$ dendritic tree size but its dendrites are slightly heavier with more pronounced beading and, furthermore, stratify broadly through strata 2 and 3 of the IPL. A4

in Figure 5 was from 11 mm eccentricity and it was larger than the others in dendritic span at $96\ \mu\text{m}$. The dendrites bearing varicosities and appendages branch broadly in the three central strata of the IPL, 2, 3, and 4 (Fig. 5). The A5 illustrated (Fig. 5) is also fairly peripheral (10 mm eccentric-

ity) but has a small dendritic span of 75 μm of rather fine cobweb-like, discrete dendrites ramifying in strata 4 and 5. The diffuse small-field cell described here merely as diffuse may not have an equivalent in the cat. The diffuse nature of the dendritic tree of the human example can be appreciated in wholmount views by the characteristic crossing and looping of its dendrites (Fig. 5).

AII and A8 are small-field bistratified amacrine cells clearly equivalent to their counterparts first described in detail in the cat retina (Famiglietti and Kolb, '75; Kolb et al., '81) (Table 2). AII cells have the characteristic lobular appendages in sublamina **a** and finer, spiky dendrites throughout sublamina **b** of the IPL. In midperipheral retina (exact eccentricity is unknown for the AII and A8 cell in Fig. 5), AII cells have a span of 25–30 μm for their distal lobular appendage field, while the proximal dendrites are 55–60 μm across. In peripheral retina, AII cells have dendritic tree sizes of 70–80 μm (Fig. 28c). The A8 cell, as first described in cat, has the opposite morphology of the AII. The processes in sublamina **a** are thin and spiky, and measure 50 μm in span, while the dendrites in sublamina **b** are markedly varicose and beaded and have a similar 50 μm span.

Medium-field amacrine cells. Eight different morphological types of amacrine cell with dendritic trees ranging from approximately 100 to 500 μm in diameter have been seen. This particular group of amacrines is the most difficult to classify on dendritic tree size alone, because at their extremes they overlap both the small-field group and the large-field group. Thus cells of this group near the fovea have 100 μm dendritic field sizes but by far peripheral retina they can be as big as 600 μm . The cell we call A12, because of its similarity to A12 in cat, has a simple, sparsely branched dendritic tree of beaded dendrites running in stratum 5 covering approximately 185 μm (Fig. 6, A12, 7 mm eccentricity, displaced cell body). A14 is also probably equivalent to an amacrine in cat retina. In human retina this cell appears to be more clearly bistratified in that the finer dendritic terminals emitted from the major dendritic tier in lower stratum 2 (solid profiles, Fig. 6) of sublamina **a** go on to end on the stratum 4/5 border in sublamina **b** (dashed profiles, Fig. 6). The dendrites, like those of the cat A12, are particularly fine and curled and bear only a few appendages over a 140 μm dendritic field (Fig. 6, A14).

Two types of medium-field amacrine in the human retina have no equivalents yet described in cat retina. The first type is a tristratified medium-field cell, with a 170 μm dendritic field composed of three tiers of fine, beaded, curled dendrites spreading on the strata 1/2, 2/3, and 4/5 borders (Fig. 6, tristratified). The woolly diffuse amacrine cell, illustrated in Figure 6 and also by another example in the micrograph of Figure 27f, is very commonly impregnated in human retina. This cell is remarkably complex in its overlapping dendrites that are rather sturdy but clearly looping and retroflexive through all strata of the IPL. Some beads and appendages adorn some of the looping dendrites but on the whole they are smooth. The cell of Figure 6 occurred 8 mm from the fovea and had a 145 μm dendritic tree diameter.

Commonly seen in human retina is an amacrine with a characteristic large cell body (14–16 μm diameter) and very fine, crinkly dendrites bearing large beads every 10 μm or so that pass diffusely through all strata of the IPL (Fig. 7). This cell is very similar to one called A13 in cat retina so we retain this name for it. In midperipheral retina (Fig. 7,

upper right) the dendritic tree measures 290 μm across while in peripheral retina it has increased to 500 μm (Fig. 27d). The spiny and spiny-varicose medium-field amacrine cells have no equivalents yet in cat retina so we use the descriptive terms for these cells introduced by Mariani in monkey retina (Mariani, '90). These spiny amacrine cells have fairly coarse and tapering dendrites, bearing some fine long spines and branches. The primary dendrites splay out in tufted fashion from three trunks off the cell body to stratify broadly in stratum 3 of the IPL. The "spiny varicose" variety may be the same cell type as the "spiny" type in Figure 7 although it has a much more beaded, varicose character to its primary dendrites. We think it has this appearance due to variations in fixation and in Golgi impregnation between specimens. Both varieties exhibit very fine processes arising from their primary dendrites that appear not to be impregnated beyond a few micrometers (Fig. 7, arrows). Dacey ('89a) described this cell type as an axon-bearing amacrine cell type and noted the further development of these fine smooth branches into axon-like processes. His HRP-injected examples were spectacular in showing these fine, smooth branches becoming long-ranging and indeed "axon-like," running for distances as great as 3 mm. Both of our examples in Figure 7 have about the same dendritic field size (400 μm across in midperipheral retina) as the central dendritic tree portion of Dacey's axon-bearing amacrine cells in macaque.

Amacrine cells with the "starburst" appearance ascribed to cholinergic amacrine cells in other species, (i.e., rabbit and cat, Famiglietti, '83; Tauchi and Masland, '84; Vaney, '90) have also been seen in human retina (Table 2). Rodieck ('88) showed the same cell type in macaque retina. These ACh amacrines occur in mirror-symmetric pairs; the type with the normally placed cell body in the amacrine cell layer branches in stratum 2, while the other, which has a displaced cell body, branches typically in stratum 4 (Fig. 8, ACh; Fig. 27c). The smaller field ACh cell of Figure 8 is from central retina (3 mm eccentricity) and has a 10 μm cell body diameter and a 250 μm dendritic tree span. Typically, five fine primary dendrites radiate out and branch only twice more to end in the thicker, beaded tertiary dendrites characteristic of this cell. The more peripheral cells (Fig. 8; Fig. 27c, larger ACh cells are at 8.5 mm eccentricity) have an 11 μm cell body diameter and a 400–500 μm dendritic tree size. We noticed that the distally branching ACh amacrine of stratum 2 is much simpler in terms of numbers of branches and branch points and somewhat smaller in dendritic tree diameter than its counterpart branching in stratum 4 (Fig. 8, ACh, 2).

Large-field amacrine cells. The first large-field type of amacrine that we describe for human retina is one of the "thorny amacrines" of Mariani ('90). These cells in human, like in monkey, appear to occur in two subtypes according to stratification of their dendrites. Thorny type 1 cells (Fig. 9) have three thick primary dendrites, arising from largish cell bodies (12 μm diameter), which run in stratum 1 for more than 500 μm . The primary dendrites are covered with small but heavy-set spines thus giving the dendrites a thorny appearance (Fig. 27a,b shows details of the thorny type 1 dendrites). Finer secondary dendrites bearing spines and appendages range in close proximity to the main dendrites. Very fine caliber dendrites that appear to be smooth with occasional beads are also seen (Fig. 9, fine arrows; Fig. 27b, arrows), but the full extent of these has

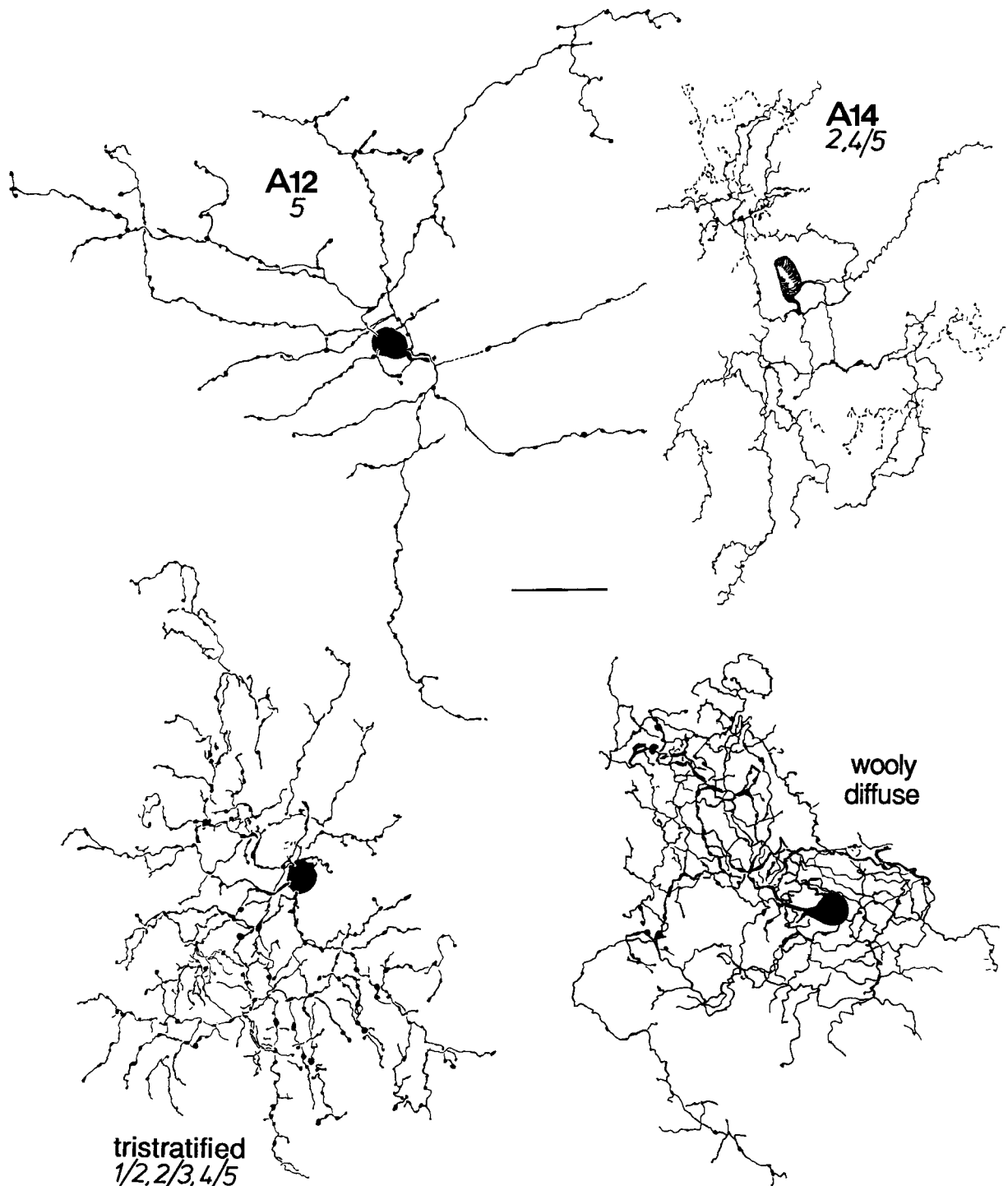


Fig. 6. Medium-field amacrine cells of the human retina. These amacrine cells have dendritic fields 100–500 μm in diameter. They are characterized by small-diameter dendrites, often profusely branched

and intertwined, with the exception of A12. The tristratified and wooly amacrine cells are new additions to primate amacrine cell types. See text for detailed descriptions. Scale bar = 25 μm .

not been seen on our examples. Other authors (Dacey, '90; Mariani, '90) illustrate more completely stained examples of thorny amacrine cells than ours, in which these finest smooth branches, called "axon-like," run for hundreds of microns radiating away from the cell body.

The thorny type 2 cells, in human retina, are clearly branching at a lower level in the IPL than the type 1. This is particularly clearly illustrated when both of the thorny amacrine cell types are impregnated together (Fig. 27a,b). The peripherally located thorny type 2 amacrine shown

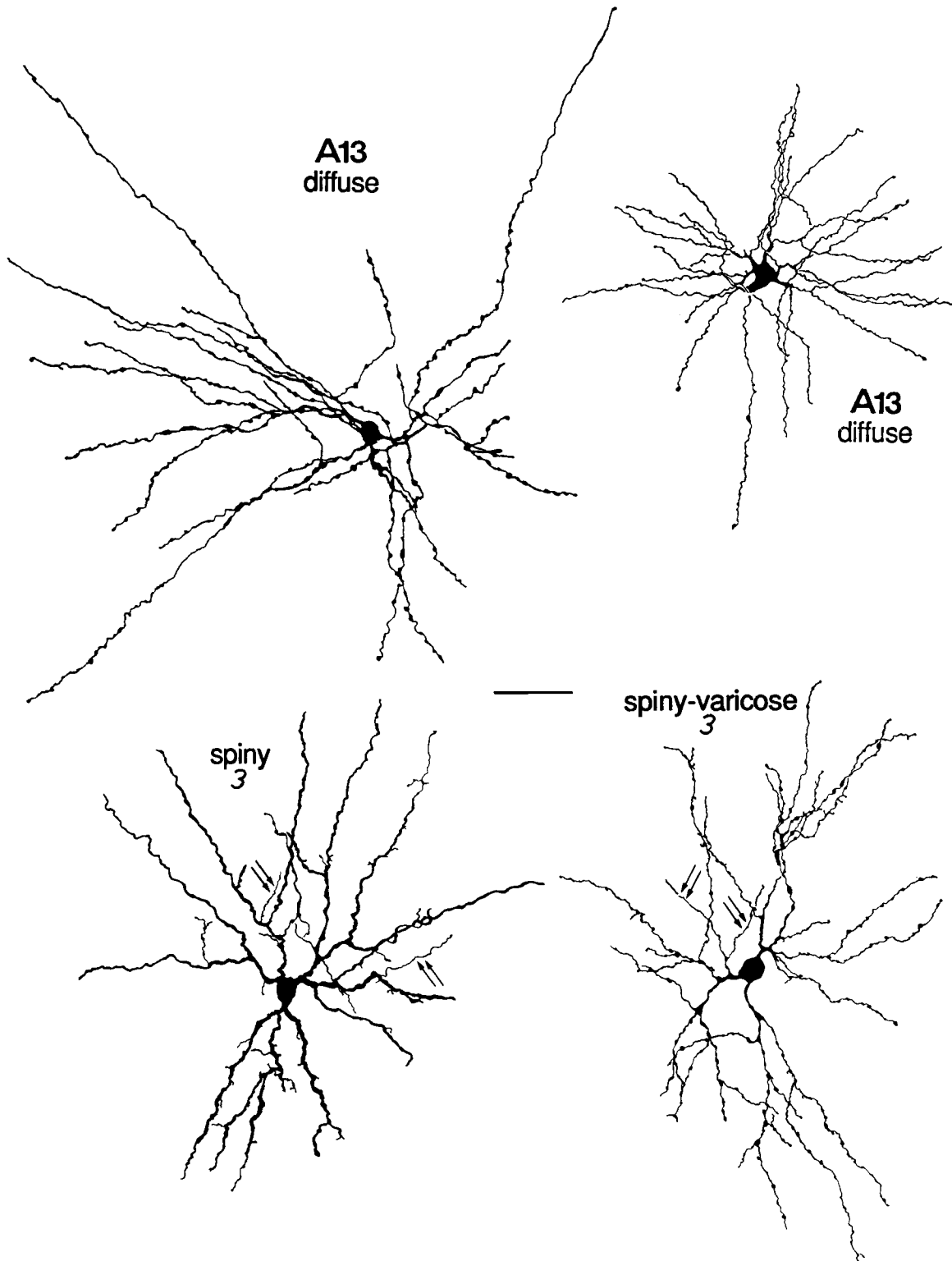


Fig. 7. Medium-field amacrine cells of the human retina. A13 amacrine cells are similar to cat A13s. In central retina (top right) they have a considerably smaller dendritic field than in peripheral retina (top left). A13 cells have particularly large cell bodies. The spiny and

spiny-varicose amacrine cells have been described in monkey retina. They have axon-like processes (double arrows) arising from the primary dendrites that have not been impregnated to their full extent. See text for more details. Scale bar = 50 μ m.

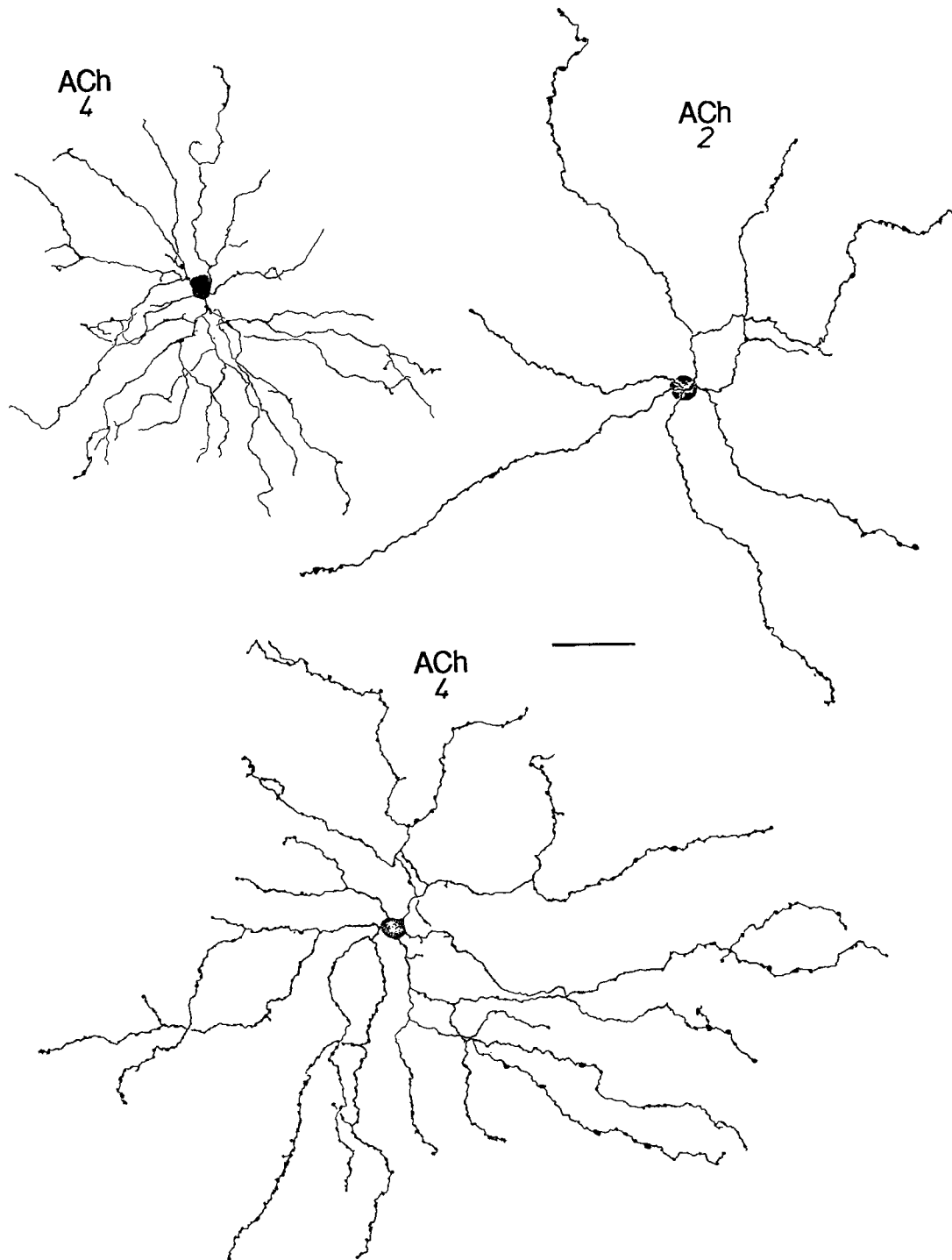


Fig. 8. The putative cholinergic (ACh) or "starburst" amacrine cells of the human retina. They occur as mirror-symmetric pairs branching either in sublamina **a** or in sublamina **b** of the IPL. The sublamina **a**

variety (top right) has a simpler dendritic branching pattern than the displaced variety (bottom) in sublamina **b**. A more centrally located ACh cell is illustrated at top left. Scale bar = 50 μm .

here (Fig. 9, thorny type 2) seems to have a larger dendritic tree (800 μm in longest extent) and the dendrites running in stratum 3 appear to have longer and more complex secondary dendrites coming off the main dendrites. They also appear to be less thorny but we cannot discount staining variations for this difference. The more centrally

occurring thorny type 2 cell shown in Figure 10 is illustrated to show that where they are smaller in dendritic field (450 μm diameter) they do not have as characteristic and asymmetric a dendritic tree, and could be possibly confused with the A14 bistratified medium-field cell of Figure 6 on superficial inspection. However, we are confident that the

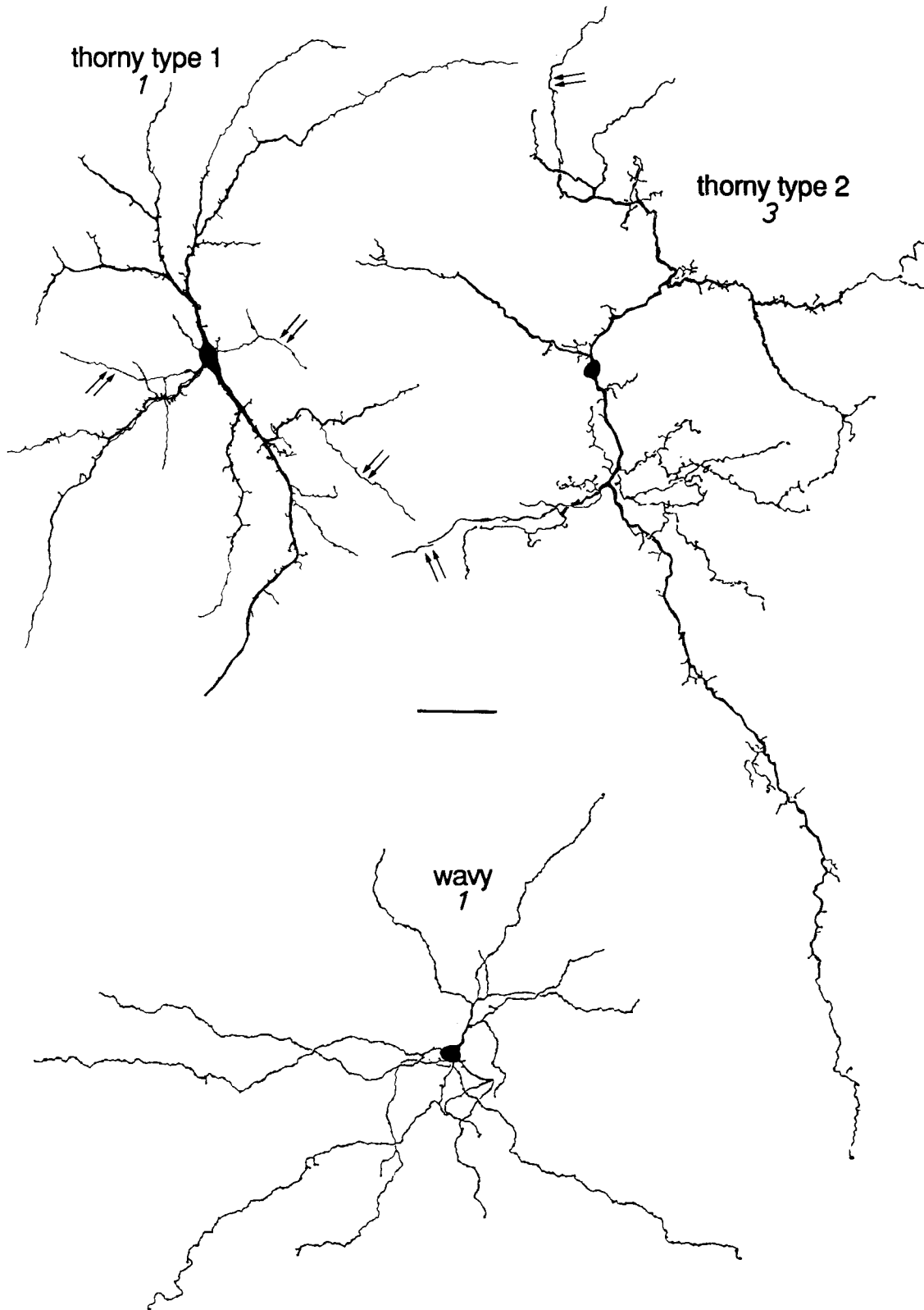


Fig. 9. Large-field amacrine cells of the human retina. Thorny types 1 and 2 are subvarieties of the same type that branch at different levels of the IPL. Both are "axon-bearing" types although in our examples the axons (double arrows) are only impregnated for a short distance. The wavy cell has not been reported before in primate retina. See text for further details. Scale bar = 50 μ m.

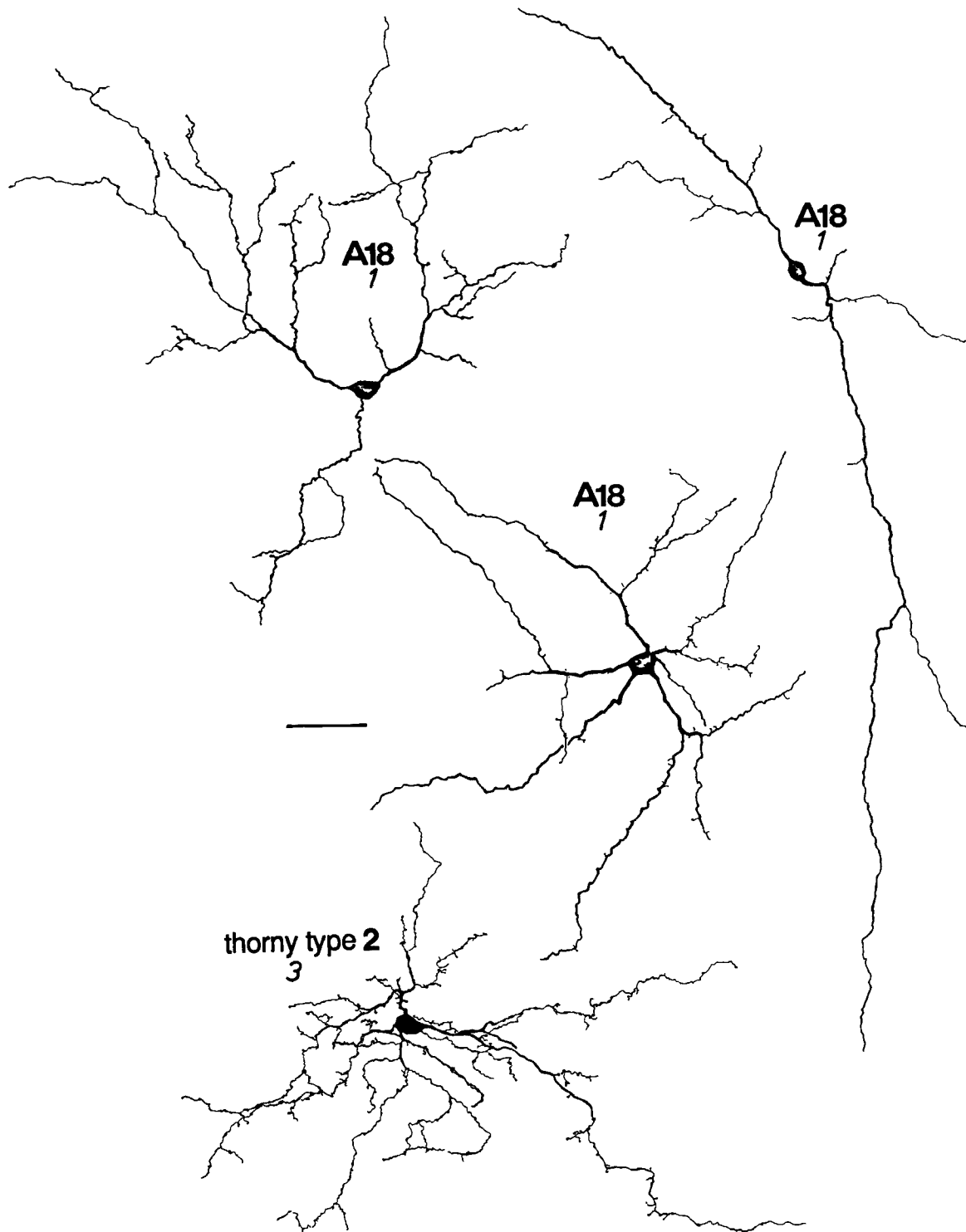


Fig. 10. Large-field amacrine cells of the human retina. A18 amacrine cells are putatively the dopaminergic amacrine cell demonstrated by immunocytochemical staining in other preparations. We show three examples to illustrate their diverse cell body shapes and dendritic arbor

asymmetries. A second thorny type 2 cell from central retina can be compared with the larger-diameter varieties of peripheral retina. Scale bar = 50 μm .

spiny dendrites with many appendages profusely branched in stratum 3 of the IPL and larger dendritic field size make this cell fall into the thorny type 2 category.

A new type of amacrine that we call simply "wavy" has no known counterpart in cat or monkey. As can be seen in Figure 9, this amacrine has a rather simple dendritic tree of gently waving dendrites that bear only occasional beads and appendages. Its medium-sized cell body (11 μm diameter) gives rise to several slim dendrites that maintain the same caliber throughout and cover a 500 μm diameter field in stratum 1 of the IPL.

We illustrate three examples of the A18 type of amacrine cell in Figure 10 to show the variability in their appearance in whole mounts. A18 in the cat retina is known to be the type 1 dopaminergic amacrine cell that stains strongly for tyrosine hydroxylase in both cat and monkey (Kolb et al., '81, '90; Mariani and Hokoc, '88). The appearance of this cell is rather typical in Golgi preparations. The cell body is very large, 15–18 μm diameter, and often angular in appearance. Two to five primary dendrites arise from the cell body to run under the amacrine cell bodies in stratum 1 of the IPL. The main dendrites taper over a 500 μm dendritic tree, which can be round or elongate in shape. The primary dendrites bear occasional appendages or fine, beaded dendrites of varying lengths. The "rings" characteristic of fluorescence- or tyrosine hydroxylase-stained A18 cells in cat (Oyster et al., '85; Törk and Stone, '79) are not evident in isolated Golgi-impregnated examples in either cat or human retina.

Figure 11 shows two types of semilunar amacrine cell as described by Mariani ('90) in Golgi-impregnated monkey retina. We illustrate two of the three types in Figure 11 (semilunar types 1 and 3) and the other in Figure 12 (semilunar type 2). A semilunar type 1 is also shown in the micrograph of Figure 27e. As noted by Mariani, these amacrines have medium to large-sized cell bodies (12–15 μm diameter) and give rise to two to three thick dendrites that project straight out from the cell body branching only once or twice. Their major dendrites often appear kinky and then taper to finer smooth dendrites. Occasional appendages and beads occur along their length. Type 1 cells stratify in stratum 1 of the IPL and appear to have the finest caliber dendrites of all three types. Their dendritic trees cover a 700 μm diameter. The type 2 semilunar cells give the appearance of being the coarsest and most kinky of the three, with dendrites running for 600–700 μm in lower stratum 2 of the IPL. The dendrites may not be completely impregnated in the example shown in Figure 12. This type 2 semilunar cell is similar to what we called an A19 amacrine in cat retina (Kolb et al., '81). Type 3 cells also have kinky dendrites, can be displaced, as is the example illustrated (Fig. 11), and are striking large-field amacrine cells (800 μm diameter dendritic fields) when seen in isolation as this one was, 8–9 mm from the fovea. Their dendrites in strata 4–5 of the IPL appear to end in a rather obvious string of beads (Fig. 11, double arrows).

Stellate-wavy and stellate-varicose large-field amacrine cells are also described in rhesus monkey retina by Mariani ('90) (Table 2). In human retina we often see these amacrine cell types (Figs. 12, 13). Both varieties have rather small cell bodies (10 μm diameter) that give rise to three to four dendrites that branch within a few microns into a radiating splay of finer dendrites. The stellate-wavy cell's dendrites run relatively unbranched to cover a 600 μm field in strata 3 and 4. The fine-caliber dendrites have some

subtle swellings but these are not nearly as obvious as those on the stellate-varicose variety. This latter feature, in addition to a different branching level in strata 2 and 3, distinguishes stellate-varicose from stellate-wavy varieties. The stellate-varicose cell we illustrate here (Fig. 13) had an 800 μm diameter dendritic field of seemingly more branched and more clustered dendrites than the stellate wavy variety. Cells of both Figures 12 and 13 were found in peripheral retina and thus have larger dendritic trees than Mariani described for these cells in monkey retina.

Spidery-diffuse amacrine cells are the largest field amacrine cells we have seen in human retina, excluding cells that have uniquely long "axon-like" processes adding to their dimensions. Spidery amacrine cells are equivalent to those described in cat as A17 cells. Our example from central retina (Fig. 14) has an oddly shaped cell body of about 12 μm diameter that emits two large and one finer primary dendrites. These branch immediately into a tuft of fine-caliber dendrites that run off in all directions without too much more branching. They often cross each other and descend slowly through all the strata of the IPL to run ultimately in stratum 5. The dendrites bear definite beads at 10–15 μm intervals. Mariani ('90) considered one type of spidery amacrine in monkey to have a proportion of its dendrites remaining in stratum 1, which we cannot claim to have verified for any of our cells in human. We consider the impregnation to be incomplete in most of the examples we have seen and we cannot exclude the possibility that all dendrites finally end up in stratum 5. The largest field spidery cell that we observed and that appeared to be completely impregnated occurred in peripheral retina (10 mm eccentricity, Fig. 15). Its amazingly large number of far-ranging slender dendrites covered a 1 mm diameter field in the IPL (in Fig. 15 the full length of some of the dendrites had to be cropped to fit the page).

Wiry amacrine cells are the final type of wide-field amacrine cells that we have impregnated in the human retina. These are very simple in dendritic tree design, usually consisting of only two to seven dendrites that simply run straight out for at least 600 μm (Fig. 14) off a single primary dendrite emitted from the cell body. The type we illustrate here stratifies narrowly in stratum 3 of the IPL, had a displaced cell body, and was found in central retina at 2.5 mm eccentricity from the fovea. Other varieties stratify either in stratum 1 or 5 according to Mariani ('90). The type that stratifies in stratum 1 commonly exhibits a simple bipolar shape to its dendritic tree.

Interplexiform cells of the human retina.

We have only observed one morphological type of interplexiform cell in the human retina as of this writing. This cell appears very comparable in morphology to the interplexiform cell of cat retina that is known to be GABAergic (Boycott et al., '75; Pourcho and Goebel, '83). Similar appearing cell types have been illustrated more recently in macaque retina (Rodieck, '88). The cell looks like a diffuse amacrine cell type until the ascending profiles to the OPL are discerned. The cell body is medium-sized (11 μm) and the loosely organized wavy dendrites in the IPL bear occasional beads and appendages and ramify essentially throughout the IPL, but more distinct tiers of dendrites occur in strata 1, 3, and 5. The dendritic tree in the IPL is 210 μm across in the cell illustrated (Fig. 16). The cell occurred in midperipheral retina. A beaded process, which splits into two immediately, arises from the cell body and

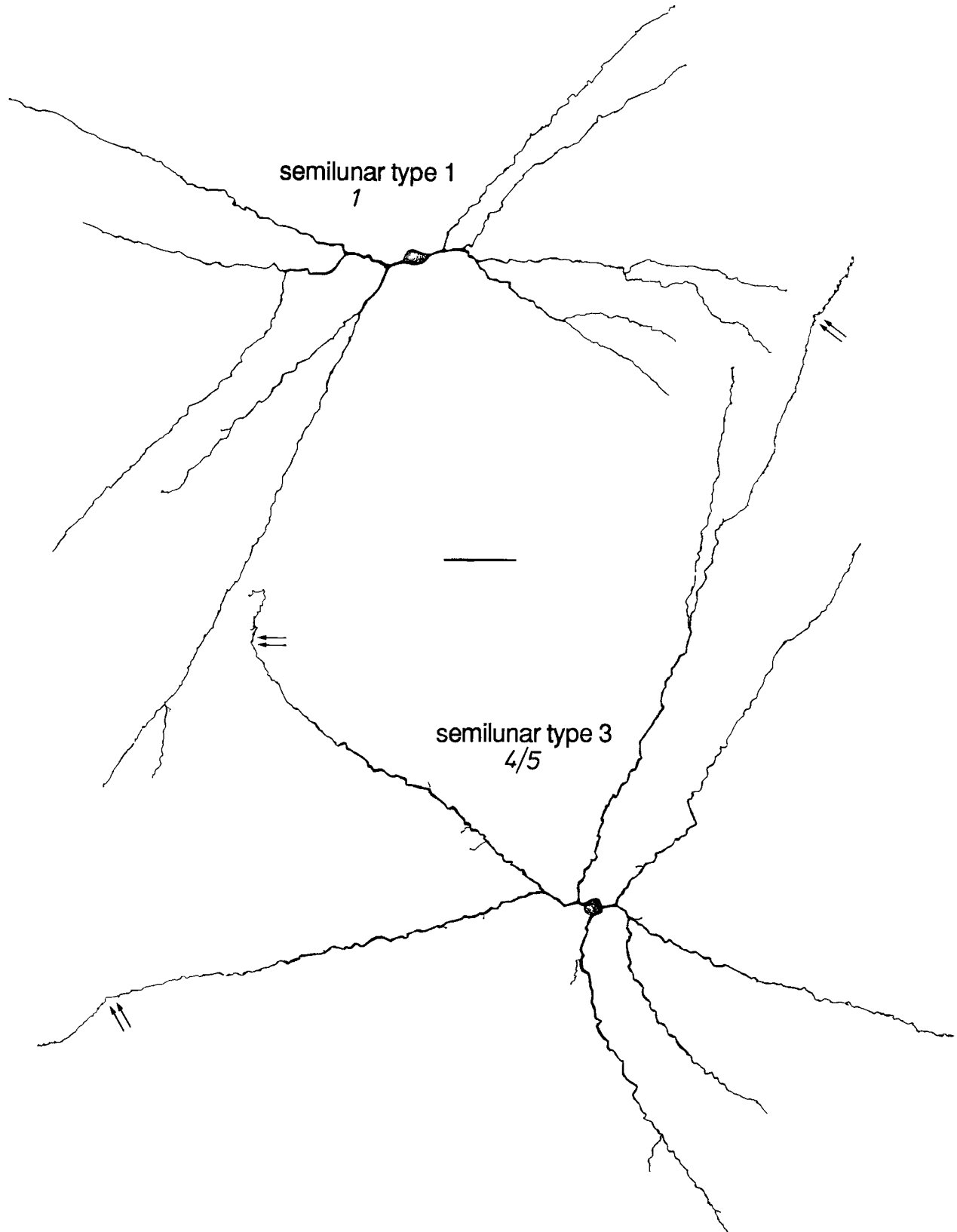


Fig. 11. Large-field amacrine cells of the human retina. These amacrine cells with a simple dendritic tree morphology are classified as the semilunar types. Type 1 and type 3 stratify in strata 1 and the border

of 4/5 are illustrated in this figure. Type 2 is found in Figure 12. The arrows indicate the string of beads at the dendritic extremities of the displaced type 3 semilunar amacrine. Scale bar = 50 μm .

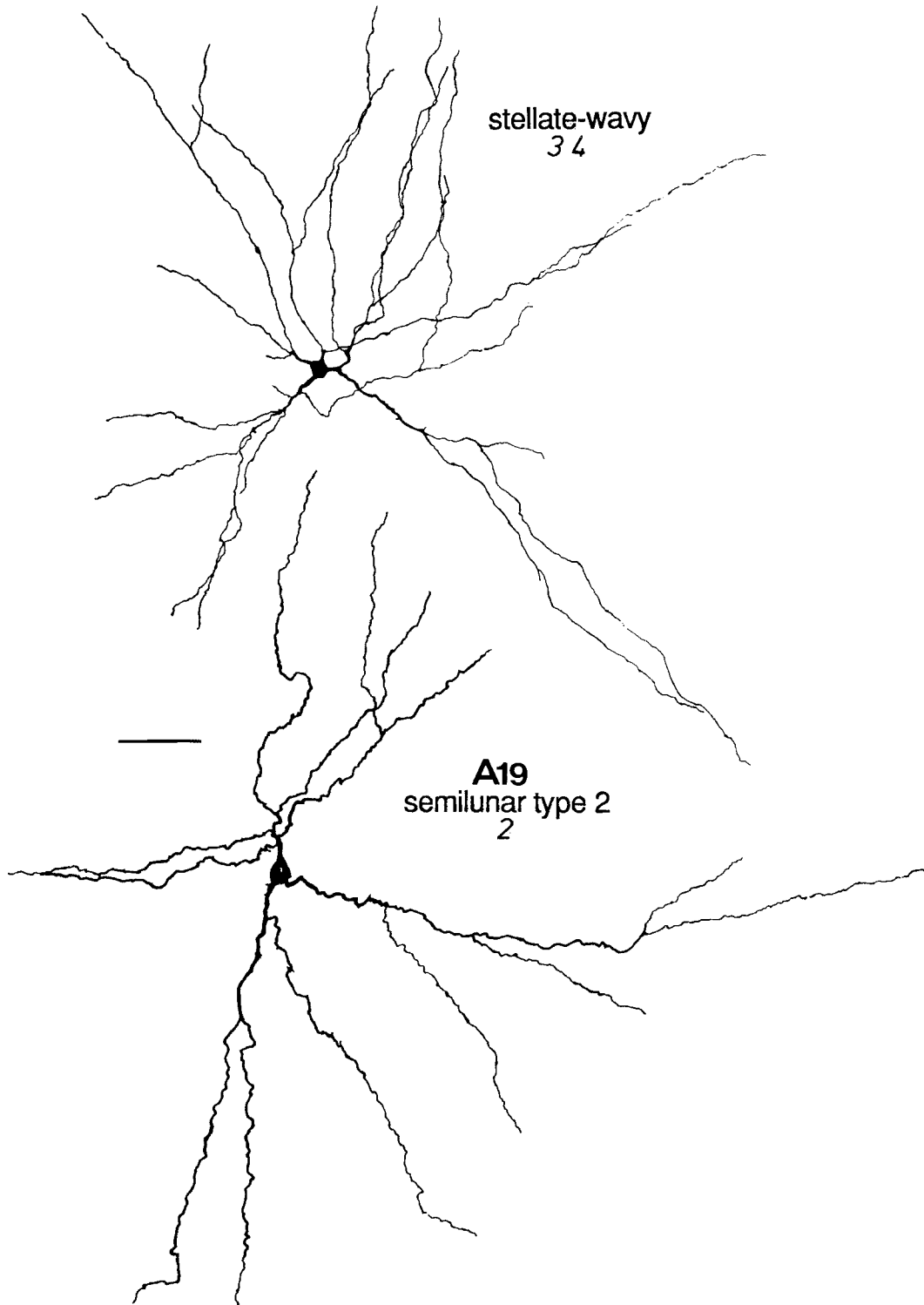


Fig. 12. Large-field amacrine cells of the human retina. A semilunar type 2 cell is a cell type similar to one named A19 in the cat retina. The stellate wavy amacrine has simple, long-ranging dendrites running broadly in strata 3 and 4. Scale bar = 50 μ m.

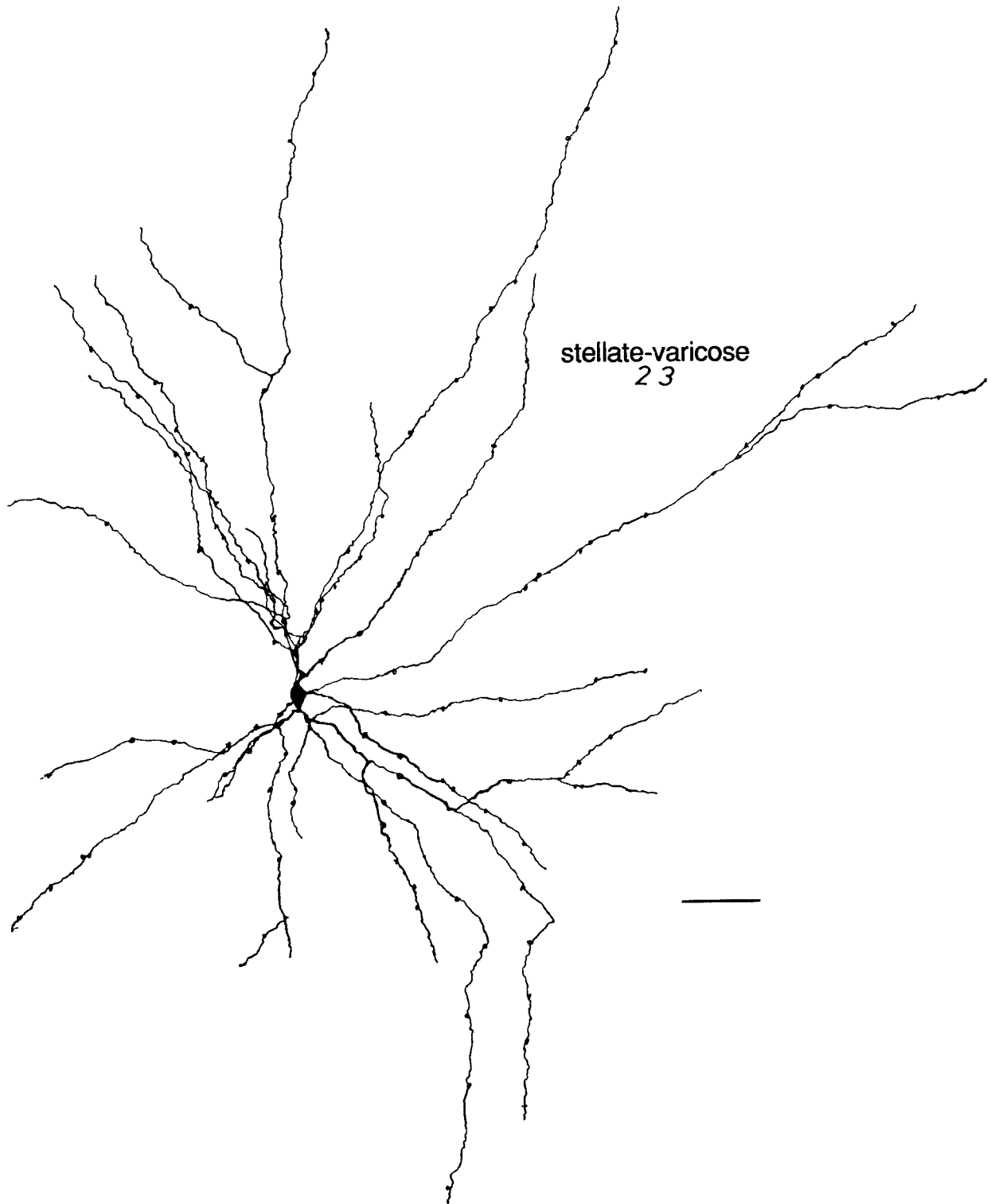


Fig. 13. Large-field amacrine cell of human retina. The stellate-varicose amacrine has a huge dendritic spread, which, like the stellate-wavy type, stratifies broadly in strata 2 and 3. However, it has pronounced beads or varicosities on its dendrites. It is drawn at the same scale as all the other large-field amacrine cells. Scale bar = 50 μ m.

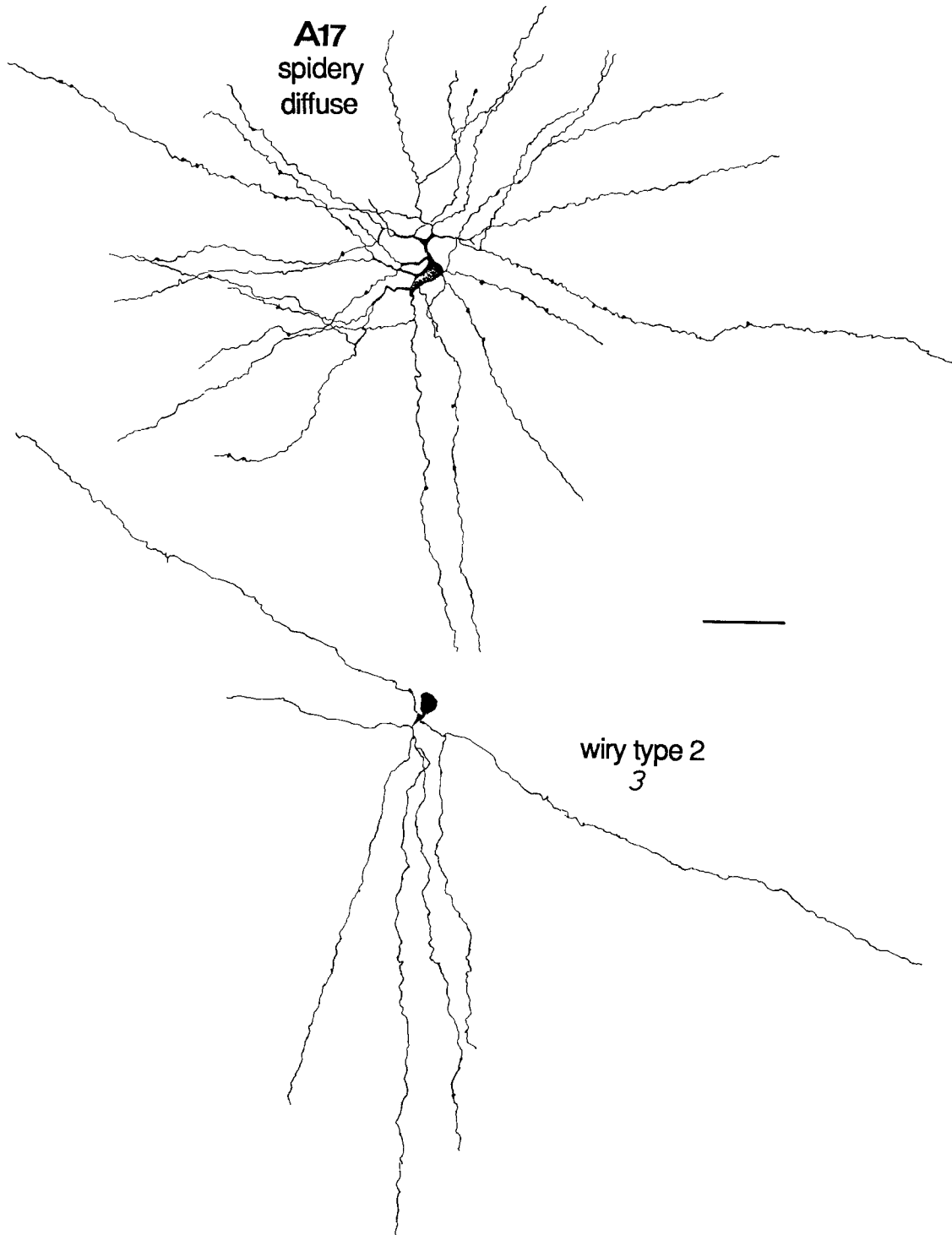


Fig. 14. Large-field amacrine cells of the human retina. Spidery diffuse amacrine cells have very large dendritic trees widely ramifying through all the strata of the IPL. These cells are probably equivalent to A17 cells of cat retina. A larger, far peripheral example occupies all of

Figure 15. Wiry amacrine cells have the simplest dendritic trees of all amacrine cells. The type 2 cell narrowly stratifies in stratum 3. Other varieties of this type of amacrine run in strata 1 and 5 (not illustrated). Scale bar = 50 μ m.

another one arises from a dendrite in stratum 1 of the IPL (Fig. 16, double arrows). These processes pass through the INL to the OPL and there branch and run for up to 300 μ m.

Ganglion cells of the human retina.

Polyak ('41) described one group of primate ganglion cells as "diffuse," meaning that they have sufficiently large

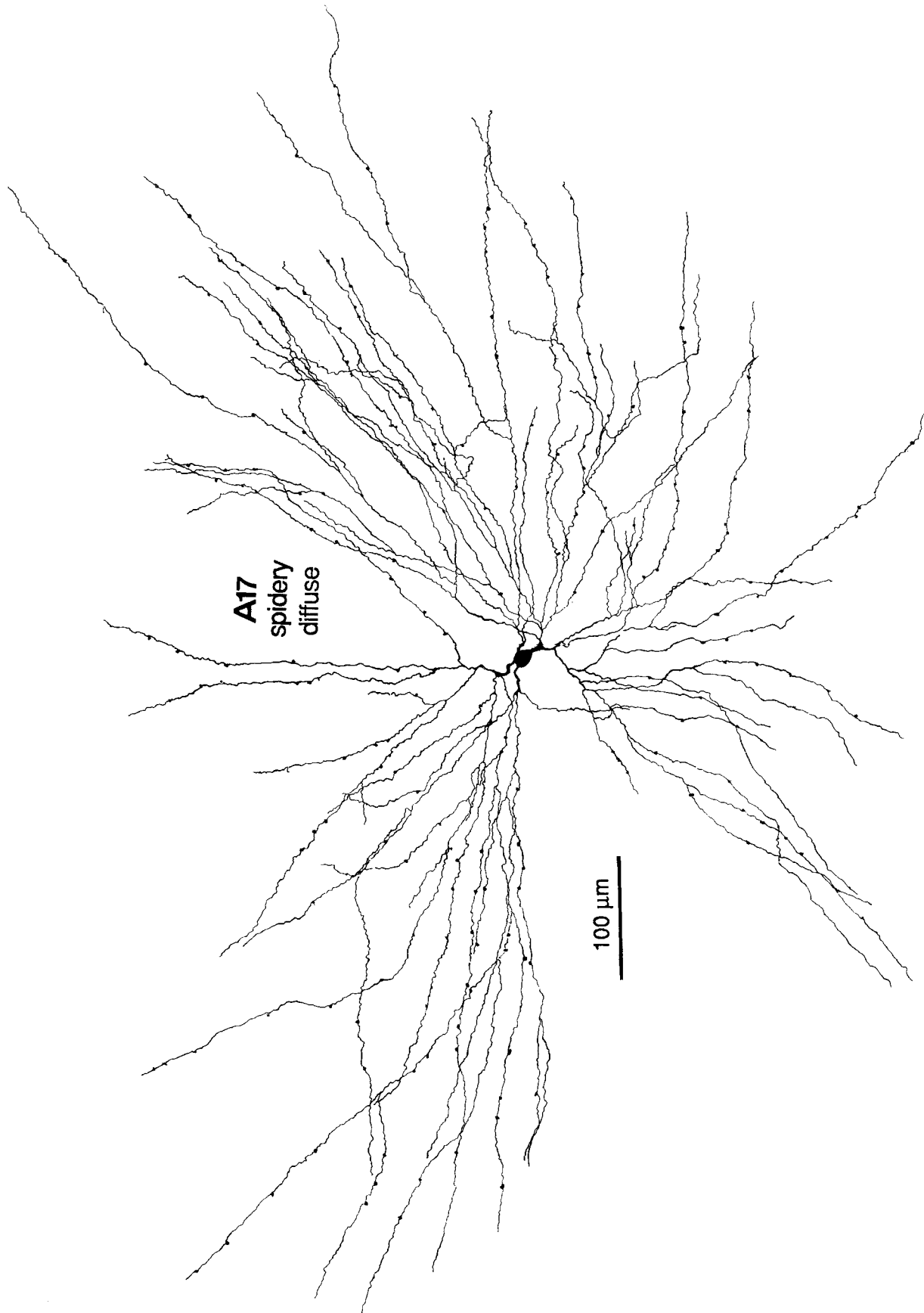


Fig. 15. Large-field amacrine cell of the human retina. A17 is the largest spidery diffuse amacrine we have impregnated nearly completely. It lies in far peripheral retina and has a dendritic field close to 1,000 μm in diameter. Scale bar = 100 μm .

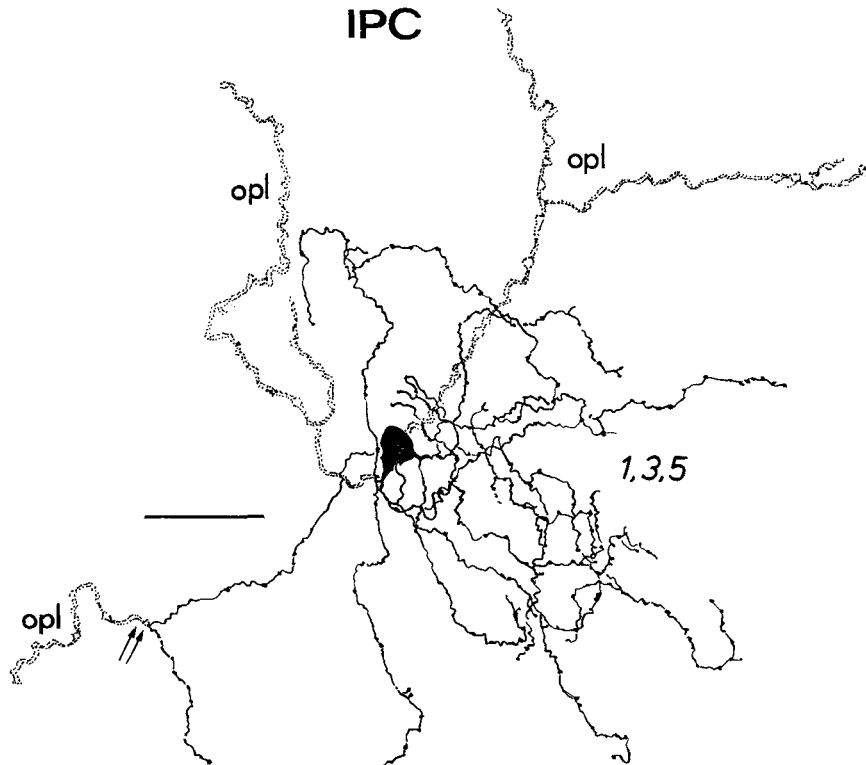


Fig. 16. An interplexiform cell of the human retina (IPC). This cell has its major dendritic tree in the IPL with dendrites obvious at strata 1, 3, and 5. Two ascending processes from the cell body and one from a dendrite in stratum 1 (arrows) pass to the outer plexiform layer (opl) to

run therein over approximately the same distance as the dendritic span in the IPL. The ascending and OPL-running processes are indicated by dashed outlines. Scale bar = 25 μm .

dendritic trees that they would be contacted by several bipolar cells. In the "diffuse" group he named ganglion cell types as parasol, shrub, small diffuse, garland, and giant types. He contrasted the diffuse ganglion cells with the type "midget" ganglion cells that he considered to be in one-to-one or individual relationships with the midget bipolars. The midget ganglion cell is unique to the primate retina while the diffuse types might be expected to have counterparts in other mammals such as the cat. We have divided the ganglion cells we have seen in the human retina into the "primate types," which include parasols as well as midget types, and into "cat types," in which we found obvious counterparts. The latter are then named after those we have previously described in the cat retina (Kolb et al., '81). Table 3 summarizes our findings on ganglion cells in the human retina.

P1 type ganglion cells or midget ganglion cells. We have adopted the nomenclature of Shapley and Perry ('86) for small-field ganglion cells that have been proved by retrograde transport studies to project to the parvocellular layers of the lateral geniculate nucleus (LGN). Thus we are calling these cells P cells. Our Golgi study indicates that P cells consist of two subclasses, P1 and P2, divided primarily on dendritic tree size. Within each of these two subclasses are found two varieties divided on dendritic stratification level in the INL. P1 cells are without doubt the midget ganglion cells and P2 cells the small parasol ganglion cells of Polyak ('41).

P1 cells have the smallest dendritic trees of all ganglion cells in the human retina. They occur in the two varieties, a

and b, that are presumed to subserve OFF- and ON-center pathways, respectively, by virtue of their branching either in sublamina a or sublamina b of the IPL. The P1a types have their dendritic trees restricted to strata 1 and 2 of the IPL whereas the P1b types branch immediately above the ganglion cell layer in stratum 5 of the IPL (Table 3) (Kolb and DeKorver, '91). In the fovea (Fig. 17, P1s, arrows) these ganglion cells have elongated cell bodies measuring approximately $8 \times 12 \mu\text{m}$, a single apical dendrite, and a minute group of dendritic terminals forming a bouquet of $5-7 \mu\text{m}$ across. Their cell bodies enlarge with increasing distance from the fovea to reach a maximum size of about $14 \times 16 \mu\text{m}$ by 8 mm. P1 cells have dendritic bouquets always composed of a handful of varicosities enlarging to $8-10 \mu\text{m}$ diameter by 0.5 and 1.5 mm, respectively (Fig. 17, 0.5, 1.5). A steady increase in dendritic bouquet size then occurs for these P1 ganglion cells over the course of 8 mm of eccentricity as can be seen from the examples of these cells in the figures (Fig. 17; Fig. 26i, 3 mm; Fig. 18, 8 mm). Their dendritic bouquets, filled with a small spray of varicosities, measure $9-12 \mu\text{m}$ diameter at 3 mm and $20 \mu\text{m}$ by 8 mm eccentricity.

The dendritic tree sizes of a large sample of P1 cells are displayed graphically in Figure 19. Thus it can be seen that P1 ganglion cells, originally called midget ganglion cells by Polyak, are not just restricted to the fovea and central primate retina, but instead extend at least to 10 mm of eccentricity and possibly further. In fact, Polyak indicated that midget ganglion cells with dendritic tree sizes of the same small diameter as we have documented (i.e., less than

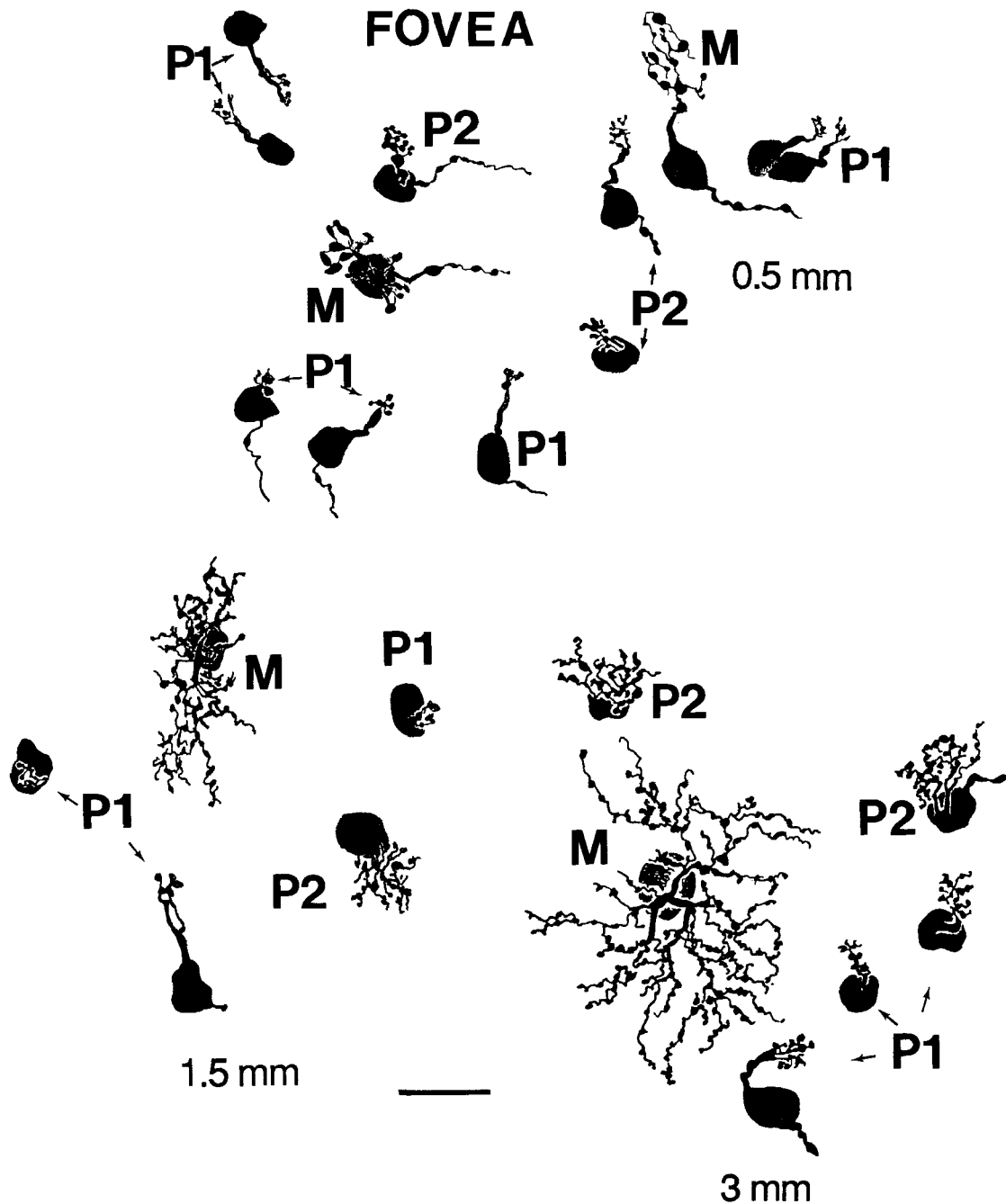


Fig. 17. P1, P2, and M ganglion cells of foveal and central human retina. The three types can be distinguished on dendritic tree size when they occur adjacent to each other. P1 ganglion cells have the minutest dendritic trees at the fovea, which expand to be no more than a small bouquet of varicosities 9–12 μm across by 3 mm eccentricity. P2

ganglion cells have dendritic trees about double the size of P1 cells. M ganglion cells are on average three times the size of P2 cells in dendritic extent. All three types occur as a and b subtypes dependent on levels of their dendritic trees in sublamina a or sublamina b of the IPL. Scale bar = 25 μm .

20 μm) occurred in extra-areal periphery (outside of the central 5 mm radius). The open circles on the graph (Fig. 19) indicate the cells drawn in Figures 17 and 18 amongst neighboring examples.

In our material we observed, on several occasions, that P1 ganglion cells in midperipheral retina may be double headed. This was also noticed by Polyak ('41, p. 323). Thus we have illustrated an example in Figure 18 (circles around

the two dendritic bouquets) in which a double-headed P1 (midget) ganglion cell sits next to a common single-headed P1 cell.

P2-type ganglion cells or small parasol ganglion cells. Polyak ('41) introduced the name parasol for a ganglion cell type in the primate retina that had a densely branched, compact dendritic tree spreading horizontally like an "open Chinese umbrella or parasol." We suggest that by using

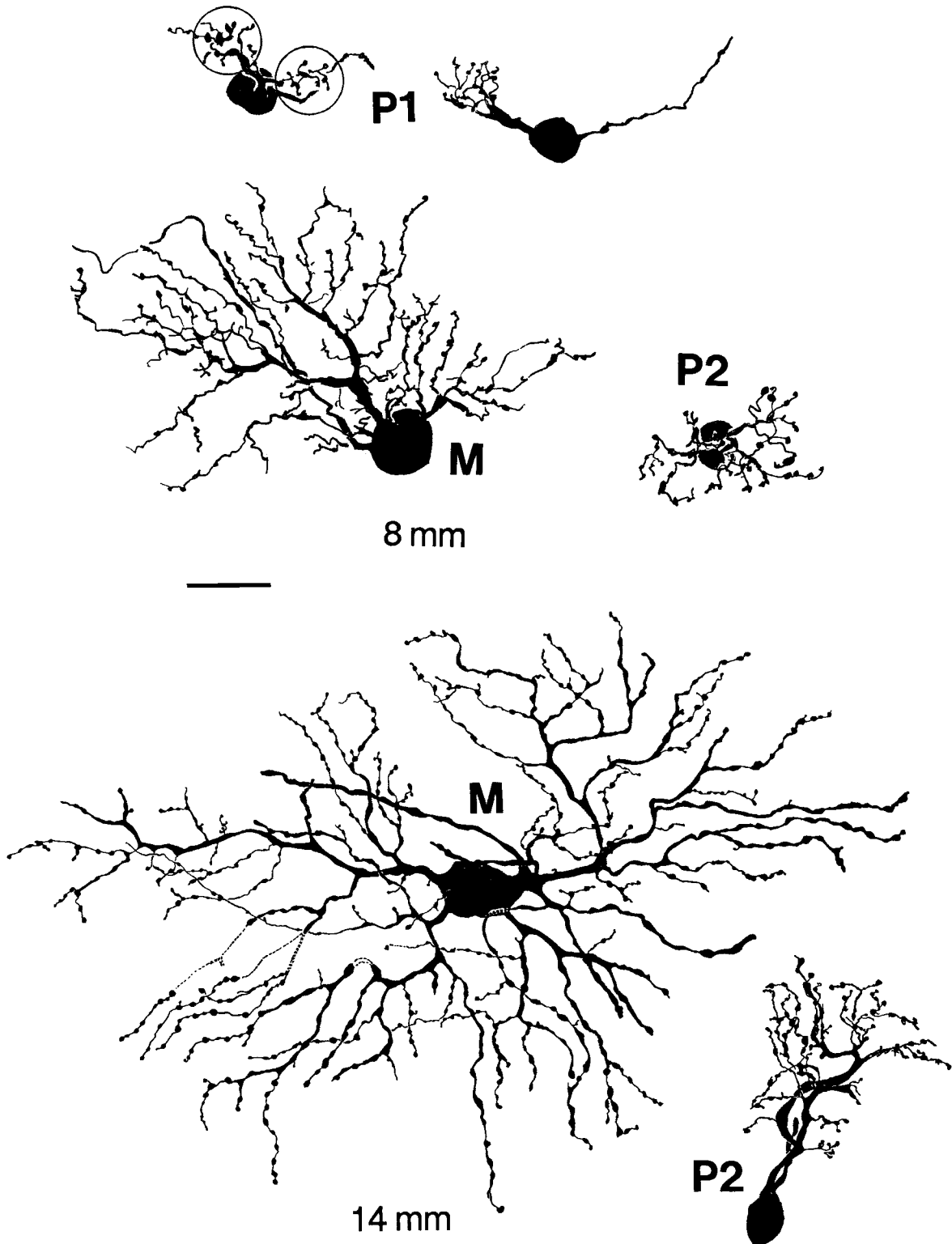


Fig. 18. P1, P2, and M ganglion cells of mid- and far peripheral retina. These cells show a continuation, from Figure 17, of their increasing dendritic tree sizes at greater eccentricities. P1 cells have not been seen in our material much past midperipheral retina (10 mm). Many of the P1 cells in this region have two dendritic heads (circled).

Others are normal single headed. P1 cells reach a maximum dendritic tree size of 25 μ m. P2 and M cells occur into the far periphery and are clearly distinguished on both cell body size and dendritic tree size. Scale bar = 25 μ m.

Golgi wholemounts we are better able to characterize the dendritic tree of this ganglion cell type than Polyak could from vertical sections. Thus we can differentiate the smaller variety of parasol ganglion cell from the larger diameter type that he also included as a parasol type and that, in our judgement, is continuous with a further cell type he called "giant." Thus our P2-type ganglion cells are the equivalents of the smaller breed of parasol ganglion cells described by Polyak. Like the P1 types, P2 ganglion cells have been seen in our material to come in two varieties, P2a, branching in stratum 2 of the IPL and P2b, branching more broadly through strata 3 and 4 (Table 3).

P2 ganglion cells are difficult to distinguish from P1 cells in the fovea but we suggest that a cell with a 9 μm diameter dendritic tree composed of a cluster of terminals, compared to a neighboring P1 cell with a 5–6 μm diameter dendritic bouquet, could represent this type (Fig. 17, P2, fovea). By 1.5 mm and 3 mm P2 cells are obviously larger than P1 cells in dendritic expanse measuring 30–35 μm across and composed of a large cluster of varicosities and appendages (see Fig. 26j and compared with Fig. 26i). At 8 mm from the fovea the P2 cells have 60 μm dendritic tree spans (Fig. 18, P2, 8 mm). The largest P2 cell dendritic trees were just below 100 μm in diameter as shown in the example in Figure 18 from 14 mm eccentricity. A larger number of P2 cell dendritic tree measurements are depicted on the graph (Fig. 19) so that the general relationship of this cell's size with eccentricity can be compared with the P1 ganglion cells. Clearly, the two groups of cells do not overlap in our analysis and at any point on the retina out to 10 mm at least, the P1 population is significantly smaller in dendritic tree size than the P2 cells. Interestingly, the cell body sizes of P1 and P2 ganglion cells appear to be very comparable out to 8 mm from the fovea (Figs. 17, 18).

M-type ganglion cells or large parasol and giant cells.

Until recently, ganglion cells that project to the magnocellular layers of the LGN were not thought to be present in the primate fovea. Silveira and Perry ('91) have proved conclusively that the large-bodied ganglion cell type presumed to be the large parasols or giants of Polyak peak in density close to the fovea as do P-type ganglion cells. We have also impregnated what we are calling M cells in the foveal region: this cell type increases in size to become the more familiar M cells of peripheral retina. In our material the M cells at the fovea have larger cell bodies than surrounding P1 and P2 cells and have dendritic tree diameters of 25–30 μm , again significantly larger than surrounding P1s and P2s (Fig. 17, M). M cell dendritic trees are composed of much coarser varicose dendrites bearing many more spines and appendages than surrounding P cells. By 1.5 mm eccentricity the M cells have elliptical dendritic trees, measuring 40 \times 70 μm , perhaps reflecting an orientation parallel to the concentric rim of the fovea (Fig. 17, M, 1.5 mm). At 3 mm and beyond into peripheral retina, M cells become familiarly "large parasol" in appearance (Fig. 26h) (Polyak, '41) and increase steadily in dendritic tree diameter from 110 μm (Fig. 17, M, 3 mm), through 160 μm (Fig. 18, M, 8 mm) to "giant-sized" with a 270 μm diameter at 14 mm (Fig. 18, M). In peripheral retina M cells are strikingly obvious (Fig. 26k). Their large cell bodies (25–30 μm diameter) give rise to two or more large thick dendrites that branch many times and are beaded, varicose, and appendage laden. The dendrites appear to be very planar and branch either in sublamina **a** (stratum 2) or sublamina **b** (stratum 3) (Table 3). As expected for a magnocellular

projecting ganglion cell, and as described by Polyak ('41), M cells have very stout axons 1.5–2 μm thick.

Figure 19 shows a plot of a group of M cells' dendritic trees as measured at different eccentricities from the fovea. This ganglion cell population is clearly significantly different in dendritic tree size from the two P cell groups and at no place on the retina do they overlap. The clear diamonds represent a group of M cells including the cells of Figures 17 and 18 to show where these particular examples fall on the graph. Similarly the P1 and P2 cells of Figures 17 and 18 are denoted by open symbols.

Ganglion cells of the human retina similar to ganglion cells of cat retina. Wide-field planar ganglion cells with smallish cell bodies are seen in human retina as in cat. In cat these were named gamma cells by Boycott and Wässle ('74), and later G3 by Kolb and coauthors ('81) since G1 and G2 were allotted to the alpha and beta classes, respectively. In human retina, G3 cells come in two subtypes, the G3a having dendrites running in strata 1 and 2 of sublamina **a**, while G3b types have dendrites stratifying in stratum 3 of sublamina **b** (Fig. 20). Both have cell bodies measuring 15 \times 18 μm and dendritic field diameters of 600–800 μm in these examples from peripheral retina. The G3 variety appears to have slightly smaller diameter dendrites bearing occasional spines while the b-types have coarse, smooth dendrites. We did not impregnate axons on any of our G3 cells and we admit to wondering whether they could not be amacrine cells of the semilunar type (see Figures 11 and 12 for comparison). However, their much larger cell bodies and prominent, large-diameter dendrites make us favor an interpretation that these are ganglion cells.

The G4 ganglion cell is very similar to its counterpart in the cat. It has a small cell body (14 μm diameter) but a large dendritic tree (625 μm diameter) made up of wavy, simple, tapering dendrites that occasionally bear spines and rise diffusely through the IPL from the cell body in the ganglion cell layer to stratum 1 (Fig. 21, G4). Another diffuse ganglion cell type, named G5, has a large cell body (20 μm diameter) but a smaller dendritic tree than the G4 variety. Its thick dendrites branch diffusely through the IPL and exhibit a few spines and varicosities. The G5 cell of Figure 21 comes from midperipheral retina (9 mm from the fovea). The axon is indicated in this and the following plates by an arrowhead.

G7 has an interesting appearance (Fig. 22, G7). Its cell body is large (30 \times 20 μm) and sits in the amacrine cell layer in this example. The two major branches spread first in stratum 1 and then fall to branch many times in curled, wavy fashion in stratum 3. Probably the small nubbin on one side of the cell body indicates where another dendrite should arise. The dendritic tree spans 440 μm of the IPL. G8, by comparison, has a much smaller cell body (16 μm diameter), which also is displaced. The fine-caliber dendrites bear numerous beads and appendages and spread in planar fashion across 330 μm in stratum 2 (Fig. 22, G8). It is very similar to a G8 described in cat retina (Table 3). The same cell is also illustrated in Figure 28c.

G10 has a large cell body (23 μm diameter) and a clearly impregnated axon (Fig. 22, G10). It occurred in peripheral retina 11 mm from the fovea. The large-caliber, tapering, unadorned dendrites are very simple in branching pattern. They meander broadly through strata 1 and 2. The total dendritic tree is just over 400 μm across. The bistratified cell G11, from midperipheral retina, exhibits a similar large cell body (22 μm diameter) and possesses coarse, crinkly

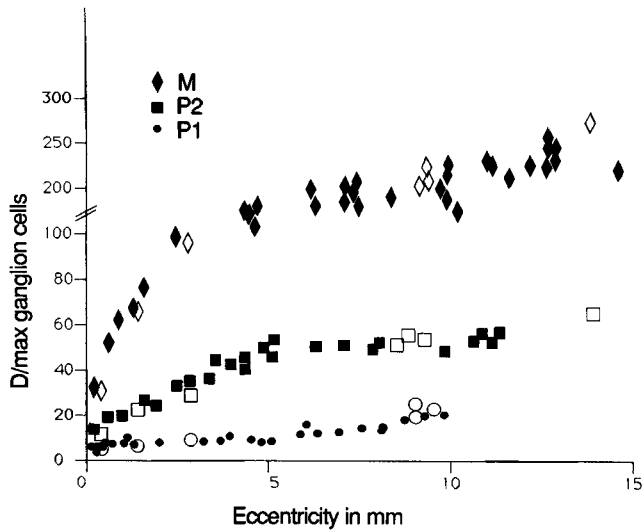


Fig. 19. Graph showing a plot of maximum dendritic tree diameter for P1, P2, and M cells against eccentricity, in the human retina. Three distinct dendritic tree size groups are apparent at all regions of the retina. Measurements of cell dendritic trees are all taken from one well-impregnated retina and represent 103 cells. The actual cells depicted in Figures 17 and 18 are indicated by the open symbols. Scale bar = 50 μ m.

TABLE 3. Ganglion Cell Types of the Human Retina and Possible Equivalent Cell Types in Other Mammalian Retinas

Type	Sample size	Stratification of dendrites	Monkey	Cat	Rabbit
P1a, P1b	Many	S1-2, S5	Midget ganglion long ¹ Midget ganglion short ¹		
P2a, P2b	Many	S2, S3-4	Midget ganglion ³ Shrub, small parasol ¹ Midget ganglion ³		
Ma, Mb	Many	S2, S3	Parasol, giant ¹ Parasol ³	Beta cells ⁴	
G3a, G3b	Several	S1-2, S3		Gamma cells ²	
G4	Several	S1-5		G4 ²	OFF—sluggish ⁸
G5	Few	S1-5	Small diffuse ¹	G5 ²	
G7	Few	S1, S3		G7 ²	ON-sluggish ⁸
G8	Few	S2	Garland ¹	G8 ²	Orientation ⁷
G10	Few	S1, S2	Unistratified ⁵	G10 ²	
G11	Few	S2, S4	Diffuse ⁵	G11 ²	ON-OFF-DS ^{7,10}
G12	Few	S3		G12 ²	
G16	Few	S5	Garland ¹ Unistratified ⁵	G16 ²	
G17	Few	S2, S4		G17 ²	Uniformity ⁷
G19	Few	S1		G19, delta ²	
G20	Several	S4-5		G20 ²	
G21	Several	S3		G21 ²	
G22	Few	S1-5		G22 ²	ON-DS ⁷
G23	Few	S4-5		G23 ² , epsilon ⁹	

¹Polyak ('41).
²Kolb et al. ('81).
³Rodieck et al. ('85).
⁴Shapley and Perry ('86).
⁵Boycott and Dowling ('69).
⁶Dacey ('89b).
⁷Amthor et al. ('89b).
⁸Amthor et al. ('89a).
⁹Leventhal et al. ('80).
¹⁰DS, directionally selective.

dendrites branching in stratum 4 while the finer, smoother and beaded dendrites curl around in stratum 2 of the IPL (Fig. 22, G11).

G12 has a small 15 μ m diameter cell body but its thin axon makes it unequivocally a ganglion cell. Its dendritic tree is just under 400 μ m in diameter and consists of fine, curled dendrites occupying stratum 3 (Fig. 22, G12). G16 was larger bodied at 20 μ m across, and produced three large-caliber dendrites bearing many spines. The dendrites branch repeatedly into a planar array of fine, retroflexive dendrites filling in space (Fig. 22, G16). At 3 mm from the fovea this centrally located retinal ganglion cell has a very large diameter axon and may appear superficially similar to an M cell. On closer analysis G16 has quite a different character to its dendrites in their being finer caliber with many small appendages, and the whole dendritic field being larger (350 μ m diameter) than any M cells at this eccentricity.

Figure 23 shows two large-field ganglion cells very similar to cells in the cat retina (Table 3). G17 has a 28 \times 18 μ m diameter cell body, a stout axon, and a bistratified dendritic tree. The thick, kinky dendrites stratify in stratum 4 while the finer dendrites pass up to stratum 2 to run for some distance. The total dendritic field size is 450 μ m across. The cell was found in close proximity to G11 in midperipheral retina but its larger proportions and less branched, unadorned dendrites distinguish it from the smaller bistratified G11. The other large-field cell, G19, has a 21 μ m diameter cell body, a definite axon, and a highly planar dendritic tree branching in stratum 1 of the IPL (Fig. 23, G19). This cell was found very peripherally at 18 mm from the fovea, and thus may be at the extreme of dendritic tree size range for this ganglion cell type (700 μ m across). Its dendritic tree is characteristic of this cell type in cat, in being planar, curled, and filled in, with overlapping, sparsely beaded dendrites. This cell type is also known as a delta cell type in cat retina (Boycott and Wässle, '74).

G20 and G21 are very large-field ganglion cells that look rather similar (Fig. 24, G20, G21). However, the G20 with a 20 μ m diameter cell body has two major dendrites exiting from opposite poles of the cell body that divide almost immediately into a tuft of large diameter, relatively smooth dendrites. These bifurcate twice more to produce long, rangy, tapering dendrites that remain in lower sublamina b (strata 4 and 5), covering a 650 μ m diameter field, in this example from midperipheral retina (8 mm eccentricity). The same G20 cell is also pictured in Figure 28d. In comparison, G21 has different characteristics from G20 (Figs. 24, 28b). It has a spindle-shaped cell body, 27 \times 17 μ m across, that produces, like G20, two primary dendrites from each side. These primary dendrites are very large in caliber (5 μ m) and adorned with spines. The primary dendrites branch only twice and give rise to extremely long, tapering dendrites that bear obvious spines and appendages. The dendrites rise to the middle of the IPL (stratum 3) and there run for 700 μ m. The dendrite passing to the left (Fig. 24, G21) is clearly not completely impregnated. Therefore, the dendritic tree is probably much larger, possibly 1,000 μ m or more. The cell is also shown in Figure 28b.

Figure 25 shows the final two ganglion cell types that we have observed in this Golgi study. G22 is very similar to a counterpart in cat retina. It has a smallish cell body at 18 μ m diameter, but its dendritic tree consists of thick dendrites covering a large area (650 μ m span) in far peripheral retina (18 mm from the fovea). The four primary dendrites branch immediately after they arise from the cell body into

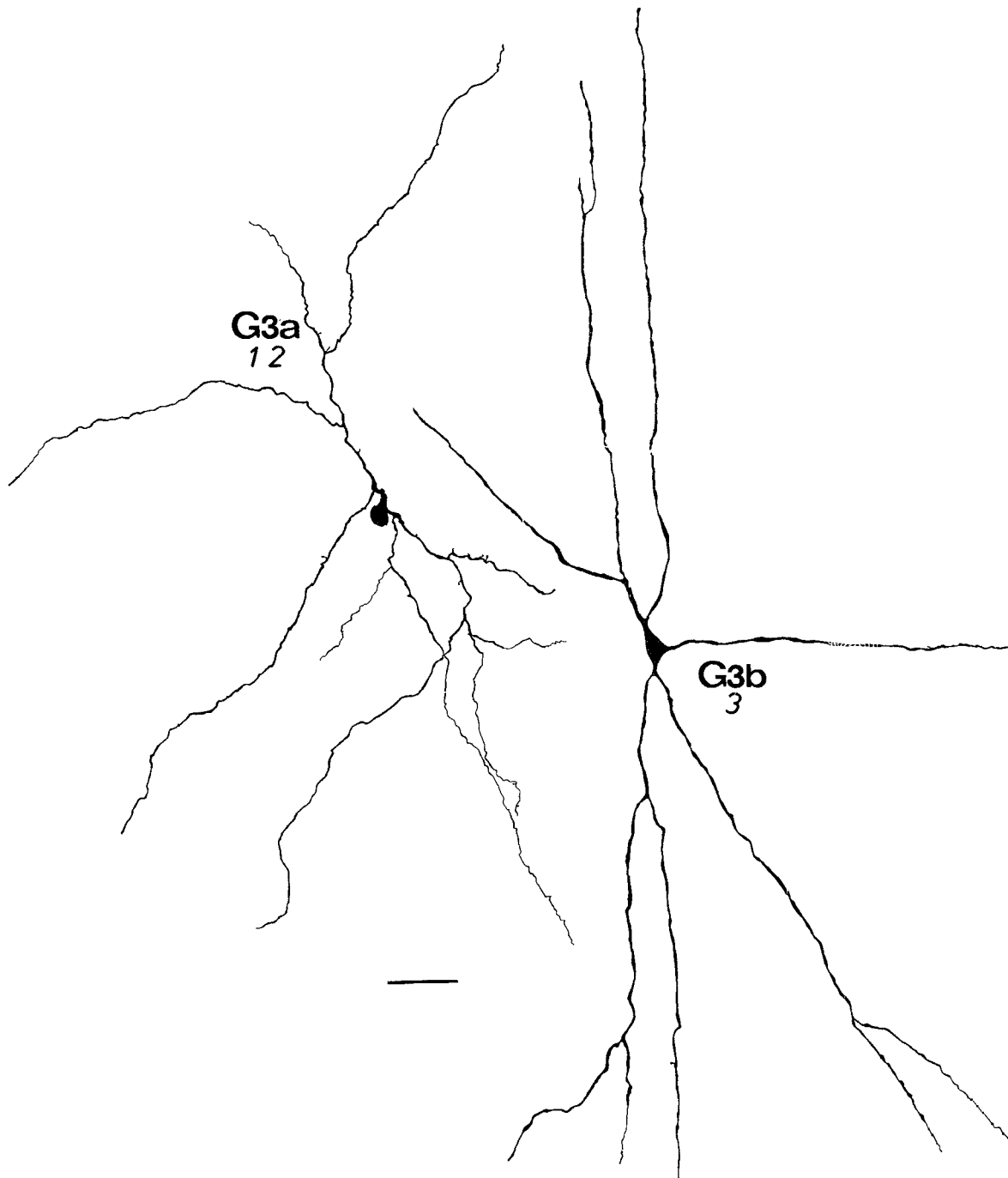


Fig. 20. Wide-field small-bodied ganglion cells of the human retina most like the gamma cells of cat. Scale bar = 50 μm .

a tuft of relatively smooth, thick dendrites that pass slowly up to the top of the IPL to stratum 1 (Fig. 25, G22).

G23 is a monstrous cell with a 36 μm diameter cell body, a thick axon, and a very conspicuous, heavy-set dendritic tree of 550 μm diameter. The large-diameter dendrites branch and curl to fill in space, with the finest branches being quite beaded in appearance. The dendrites lie close to the plane of the ganglion cell layer in strata 4 and 5 as can be appreciated in the micrograph (Fig. 28a), in which all parts of the cell are seen in the same plane of focus. Figure 28 also shows some other ganglion cell types photographed

at the same scale to illustrate the enormity of the G23 type. Also, an M cell of the far peripheral retina in Figure 26k, photographed at the same magnification as G23 in Figure 28a, affords a good size comparison of ganglion cells that might both fit the category of "giant" types (Polyak, '41) of human retina.

DISCUSSION

The present study of Golgi-impregnated wholemounts of human retina has demonstrated that all the neural types

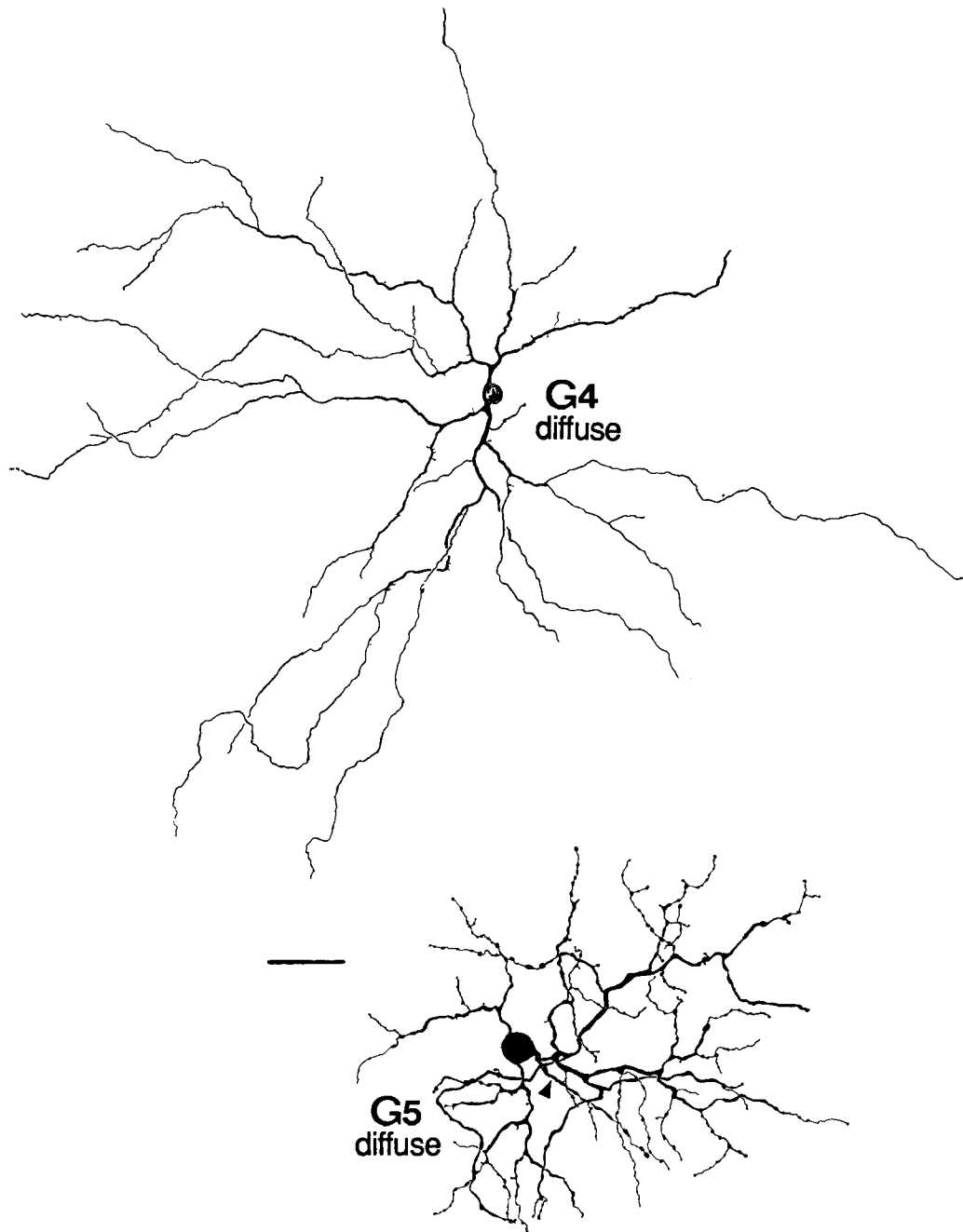


Fig. 21. Large-field (G4) and a smaller field (G5) diffuse ganglion cells of the human retina. Where impregnated, the axon on this and following ganglion cells is pointed out by an arrowhead. Scale bar = 50 μm .

that have been described before in monkey retina can be found in the human retina as well. Thus we have been able to distinguish in our human material 9 different types of bipolar cell (Table 1), 3 distinct types of horizontal cell, 24 different morphological types of amacrine cell (Table 2), a single type of interplexiform cell, and 18 varieties of ganglion cell (Table 3). This was made possible in part by the successful application of the Golgi method to whole-mounted human retinas. This technique allowed us to analyze large numbers of cells, most of which were impregnated through the full extent of their dendritic trees. We

have been able to add new cells to almost every class of retinal neuron, and to confirm and extend to humans the descriptions of cells known to exist in both monkey and retinas of other mammals.

New findings on bipolar cells

All the bipolar cell types that have been described in monkey retina have been seen in this study of human retina (Table 1). Thus midget bipolars of the two varieties thought to subservise ON- and OFF-center chromatic pathways, i.e.,

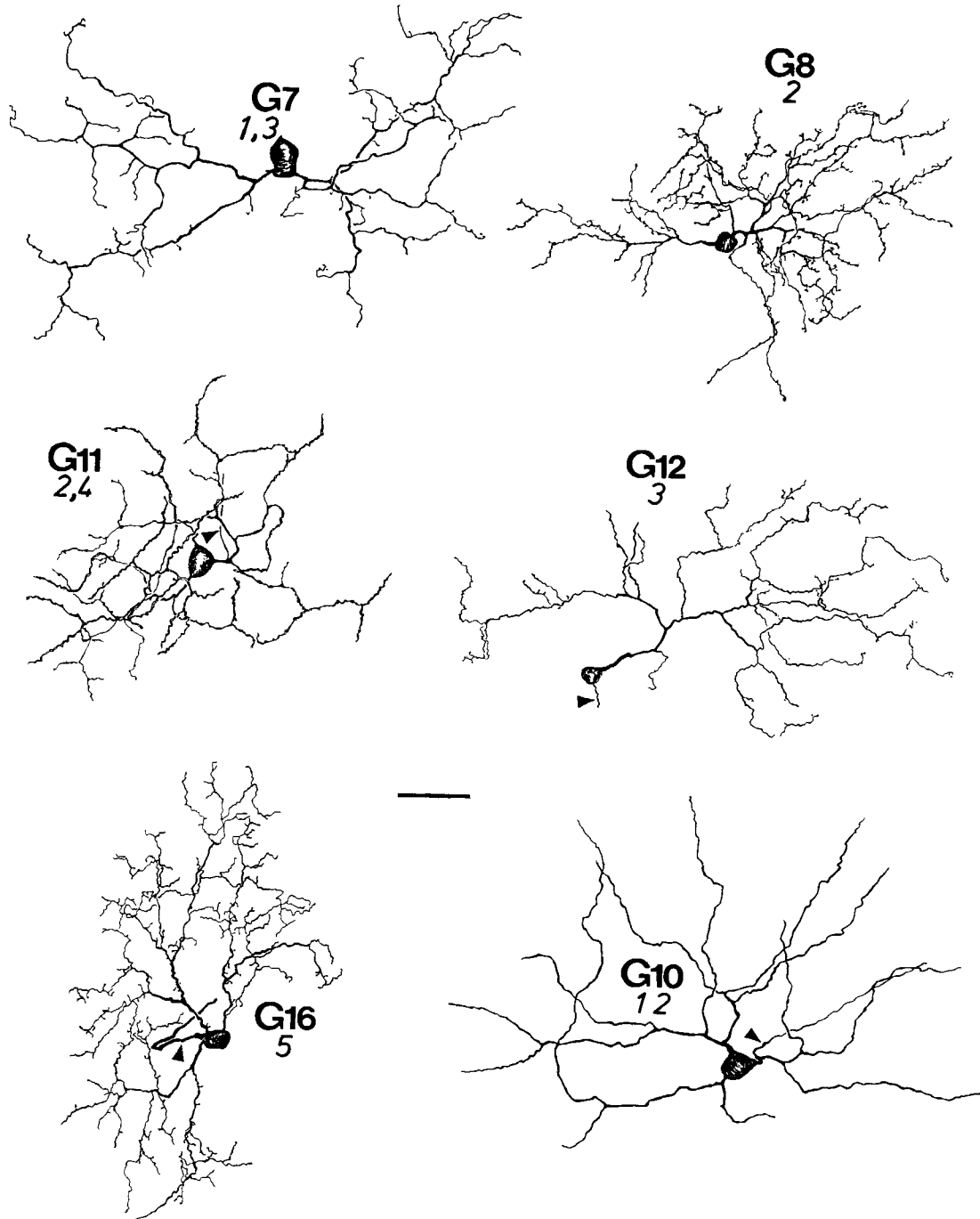


Fig. 22. Small-field ganglion cell varieties of the human retina. All have rather bushy dendritic trees except G10, but the dendrites are all of fine caliber and delicate. Scale bar = 50 μ m.

flat and invaginating midget types (fmB and imB, Table 1), are well represented in humans. Midget bipolar cells have been seen all the way out to the far peripheral retina. However, starting around 4 mm from the fovea we have consistently observed midget bipolar cells to become two- or even three-headed. Each dendritic head presumably innervates separate cone pedicles. Two-headed midget bipolars were noted by Polyak ('41) in peripheral monkey retina and

apparently they are fairly common in the nocturnal owl monkey (Ogden, '74), which might suggest that they are prevalent in rod-dominated primate retinas. As they appear to be frequent in human retina they too must be important for the trichromatic, cone-dominant visual pathways. They seem to allow for convergence of two or three cones in retina just beyond the region of the high-acuity, single-channel pathways of the fovea. The significance of this for

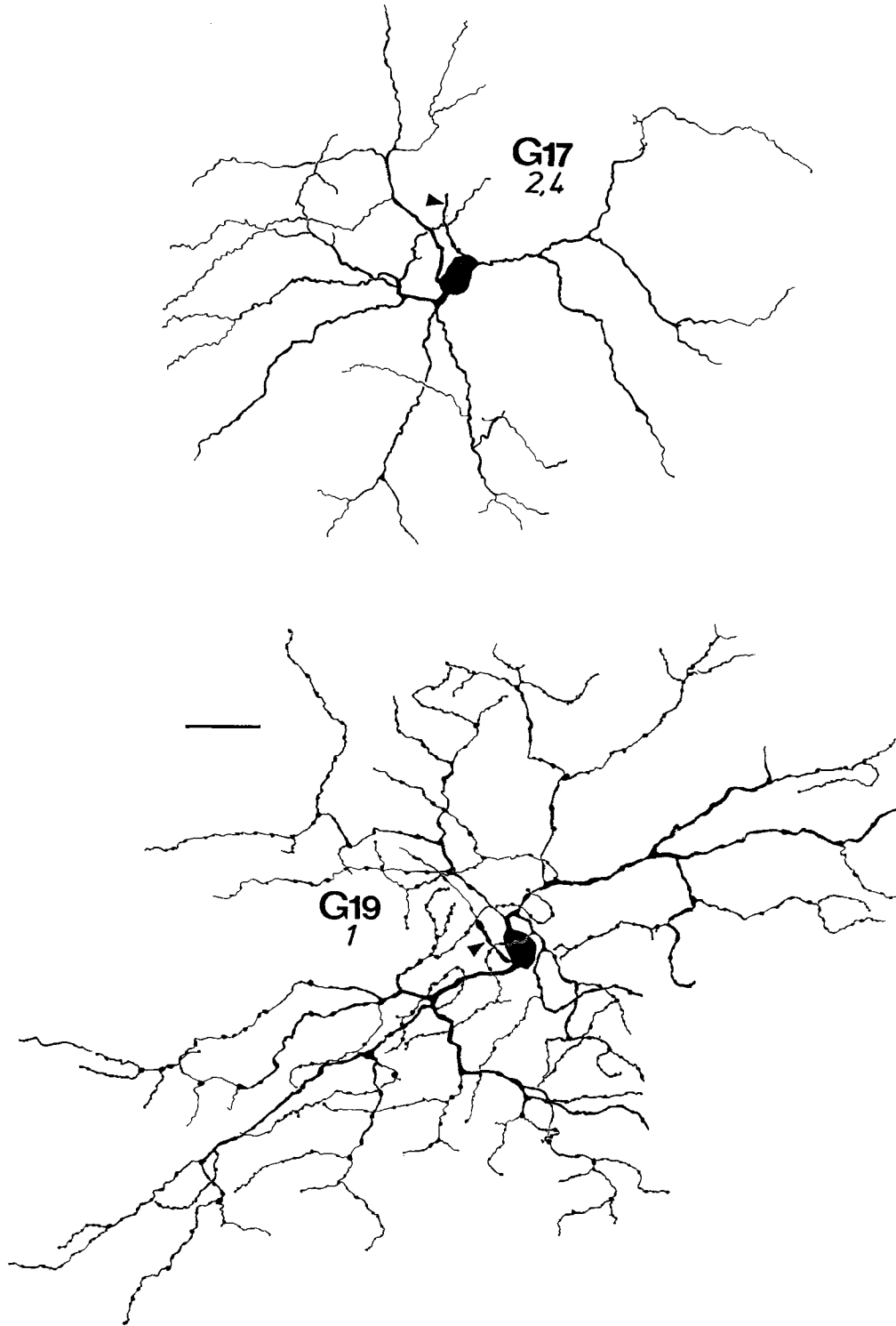


Fig. 23. G17 is a large-field bistratified ganglion cell branching in strata 2 and 4. G19 has the appearance of the delta cell type in cat and stratifies high in the IPL in stratum 1. Scale bar = 50 μ m.

color vision remains intriguing. For instance do multiple-headed midget bipolar cells contact the same spectral type of cone?

Another interesting aspect of this finding of midget bipolars innervating more than one cone, apart from the

effect on acuity and color specificity, is the consequences on cone pedicle microcircuitry. It is known from electron microscope studies that dendritic terminals of invaginating midget bipolars occupy central positions at most of the ribbon triads in cone pedicles (Kolb, '70). Does the finding

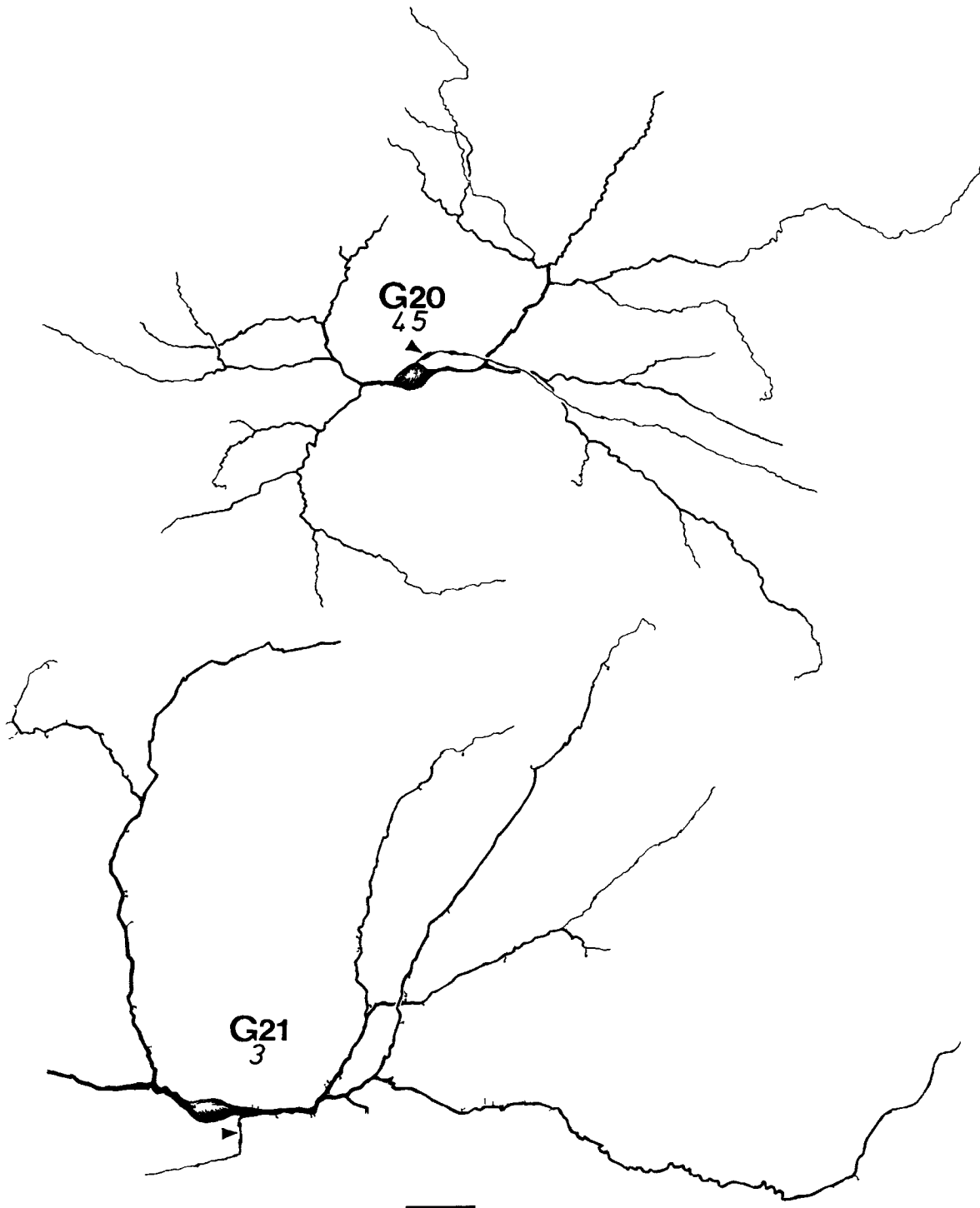


Fig. 24. G20 and G21 are large-field ganglion cells with large-diameter dendrites with few branches. G21 may have the largest dendritic tree of all ganglion cells, as only half of its arbor is impregnated in this example. Scale bar = 50 μ m.

of multiple dendritic heads on midget bipolars mean that each midget bipolar distributes an even number of dendritic contacts to its innervated cone pedicles, or does one cone pedicle remain the focus of the dendrites with only limited input from other cones? Furthermore, the diffuse invaginating variety of cone bipolar cell has also been shown to have

dendritic contacts in the central element position of cone triads in several cone pedicles (Mariani, '81). We have certainly seen examples of the diffuse invaginating cone bipolar type, our DBb, all over the human retina too, even in the foveal region (Table 1). Thus this cell type is also occupying some of the central element positions in cone

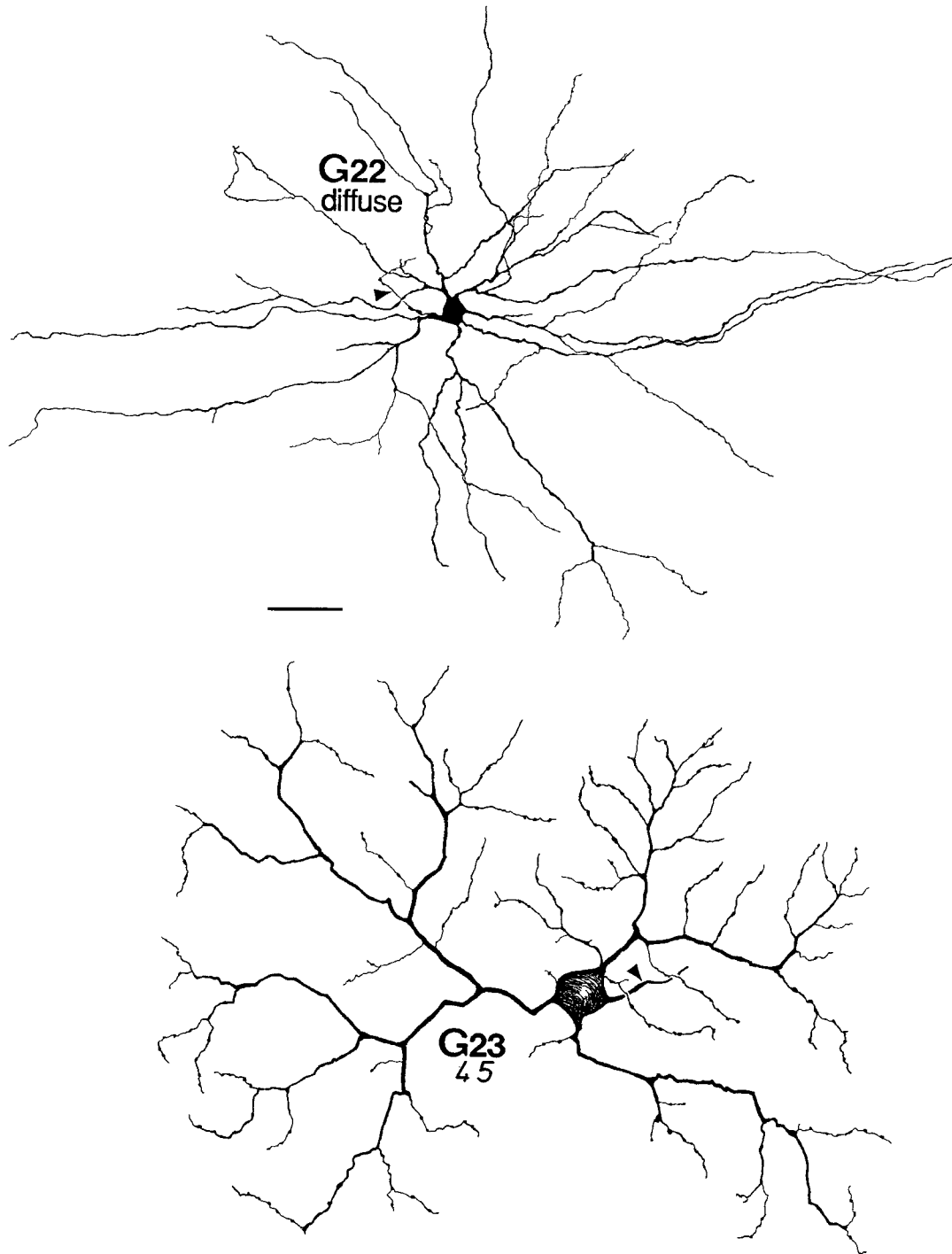


Fig. 25. G22 is a large-field diffuse ganglion cell equivalent to G22 in cat. G23 is the "monster" cell of the human retina. It has the largest cell body of any ganglion cell. Scale bar = 50 μ m.

triads. Furthermore, we have proposed in this study the existence of another diffuse variety of bipolar, the giant diffuse type, GBb (Fig. 2) that has its axon stratifying in sublamina **b** and could conceivably also be an invaginating type (Table 1). This bipolar cell type would add to the congestion of cone bipolar pathways initiated at the invaginating ribbon synapses in cones. The exact relationship of single-headed midgets, multiple-headed midgets, and diffuse invaginat-

ing and giant diffuse types to the ribbon triads will have to be resolved by electron microscope studies of the sort already in progress (Boycott and Hopkins, '91).

The bipolar specific for blue cones that was originally described by Mariani ('84b), has also been seen in this study on human retina and is herein called BBb (Table 1). By virtue of its axon terminals running in sublamina **b** and its dendrites making contacts with blue cone pedicles at invagi-

nating synapses (Kouyama and Marshak, '92), it is suspected to be an ON-center bipolar variety. Blue ON-center ganglion cell types have been recorded from electrophysiological investigations in both the retina and LGN of the monkey (DeMonasterio, '79; Malpeli and Schiller, '78). OFF-center blue pathways have also been identified in the LGN (Gouras, '91) so it is only reasonable that an OFF-center blue specific bipolar pathway should exist in the primate retina. We illustrate an example of a bipolar cell type that might be a candidate for an OFF-center blue cone bipolar cell, BBa (Fig. 2, Table 1). It is a type of bipolar that appears to be seeking out widely dispersed cones to contact in the OPL and it has a widely ramifying axon terminal in sublamina **a** of the IPL, rather different in dimensions and appearance from the neighboring flat diffuse bipolar DBa with which it might be confused. We await further confirmation of this finding in future Golgi studies in both humans and other primates.

Three types of horizontal cell in human retina?

In addition to, but distinct from the classic long-axoned HI-type horizontal cell of primate retina first described by Polyak ('41), and the second, short, curly-axoned HII type added by Kolb and coauthors ('80), we here introduce a third type, HIII. As described in the text, the salient feature of this new horizontal cell type that differentiates it from the similar but smaller relative, HI type, is its asymmetrical and consistently larger dendritic field across the whole retina. Additionally, HIII cells appear to contact approximately 30% more cones than HIs in the same area of retina. However, their morphology as seen in Golgi-impregnated examples suggests that HIII cells lack clusters of terminals in positions where there are cone pedicles overlying their long asymmetrical dendrites. Thus we get the impression that HIII cells *miss* a subpopulation of cones in their dendritic field compared with HI types, which are known to provide full coverage to all overlying cone pedicles (Boycott et al., '87; Kolb, '70; Wässle et al., '89).

This finding suggests that there is some chromatic selectivity at work for the HIII cells compared with the HIs. We have, in fact, some preliminary evidence from electron microscopy that HIII cells are selective for red and green cones and avoid blue cones (Kolb et al., '89). On the other hand, HII cells have been shown to be relatively *blue-cone* specific in their contacts when examined by electron microscopy (Kolb et al., '89). Although light microscope examination of mosaic arrangements and overlap of HI and HII cells do not reveal any obvious chromatic selectivity (Wässle et al., '89), the addition of another horizontal cell type to the primate repertoire makes sense (Kolb, '91b) if trichromatic color selectivity is to be initiated at the OPL in the same manner, with three horizontal cell types, as in submammalian species with good color vision (Fuortes and Simon, '74; Stell and Lightfoot, '75; Stell et al., '75).

We have seen that all HIII cells, like HI cells, give rise to axons that run for short distances in the OPL before staining fails. Our identification of a possible HIII axon terminal as being less densely organized and less "lollipop laden" than the HI axon terminal, is offered tentatively here. Interestingly, similar differences in axon terminal morphologies were once before pointed out in monkey OPL by Boycott and Dowling ('69) and returned to as possible differences between monkey and human horizontal cell axon terminals by Rodieck ('88). Another feature that we

mention in passing is that HIII cells frequently produce a thick process from the bottom of their cell body descending through the INL to branch in stratum 1 of the IPL. Such descending processes have been described in horizontal cells in a variety of retinas (Ramón y Cajal, 1892; Silveira et al., '89) but their significance is presently uncertain.

Amacrine cell diversity in human retina

We have shown in this study that the human retina joins a growing list of vertebrate retinas having a complexity and multiplicity of amacrine cell types not suspected before. These numerous types differ from each other in dendritic tree size, morphology, and branching patterns as well as in dendritic stratification levels in the IPL. Of the 24 types that we have described in human retina, four are introduced here for the first time in a primate species. The remainder have been described in cat retina (Kolb et al., '81) and/or in macaque monkey retina in a recent, elegant, Golgi study by Mariani ('90). Table 2 summarizes the amacrine cell types seen in this study and compares them with amacrine cells of similar morphology in the monkey, cat, and (where relevant) rabbit retinas.

Fig. 26. Photomicrographs of horizontal, bipolar, and specific "primate-type" ganglion cells of the human retina. **a**: A group of HI horizontal cells occurs next to a single HIII cell. The outline around their respective dendritic trees emphasizes the differences in dendritic tree sizes for the two cell types. HIII has an asymmetric dendritic tree. Its axon is pointed out (double arrows). **b**: The dendritic tree of a small-field diffuse cone bipolar (DBa) in the OPL. **c**: The small dendritic bouquet, the size of a cone pedicle, of a single-headed imB-type midget bipolar in midperipheral retina close to the other bipolar dendrites illustrated in b-f. **d**: The dendritic tree, in the OPL, of a small-field DBb diffuse cone bipolar cell. **e**: The dendritic tree of a rod bipolar cell (RBb). **f and g**: The dendritic bouquets in the OPL and the axon terminal (at) in sublamina **a** of the IPL of a two-headed fmB midget bipolar cell. Arrows point to the two separate dendritic bouquets, one of which clearly consists of more dendritic terminals. **h-j**: Dendritic tree of an M-ganglion cell (M) of central retina (3-4 mm eccentricity) (h) to be compared in size to neighboring P1 (i) and P2 (j) ganglion cell dendritic trees. **k**: M-ganglion cell of far peripheral retina taken at lower magnification to show its striking morphology and size in comparison to ganglion cells illustrated in Figure 28a-d. All but k $\times 600$; k, $\times 240$.

Fig. 27 (page 182). Photomicrographs of amacrine cell varieties of the human retina. **a**: Thorny type 1 amacrine cell lies in focus while a thorny type 2 cell (arrows) has dendrites running deeper in the IPL. **b**: Higher magnification of the thorny type 1 cell of **a** to show details of the thorns on the major dendrites and the emergence of a thin "axon-like" process (arrows). **c**: Example of a cholinergic "starburst" amacrine (ACh2) branching in sublamina **b** and with a displaced cell body in the ganglion cell layer. **d**: A field of three overlapping A13 amacrine cells in peripheral retina. **e**: A semilunar type 1 wide-field amacrine cell with dendrites in stratum 1. DBa type bipolar axon terminals are also seen in this plane of focus. **f**: A woolly diffuse medium-field amacrine cell of the human retina. All but b $\times 240$; b, $\times 600$.

Fig. 28 (page 183). Photomicrographs of the unusual ganglion cells that have counterparts in the cat retina. **a**: G23 is the largest bodied ganglion cell we encountered in human retina. Its large-diameter dendrites branch on a plane just above the cell body in strata 4 and 5. **b**: G21 is a very large-field ganglion cell with simple dendritic morphology and may have the largest dendritic field of all ganglion cell types. **c**: A medium-field ganglion cell, G8, which by comparison with the other wide-field types looks particularly petite. An AII amacrine cell is seen in the left corner. **d**: G20 looks similar to G21 but is of much smaller caliber and stratifies slightly differently. All $\times 240$.

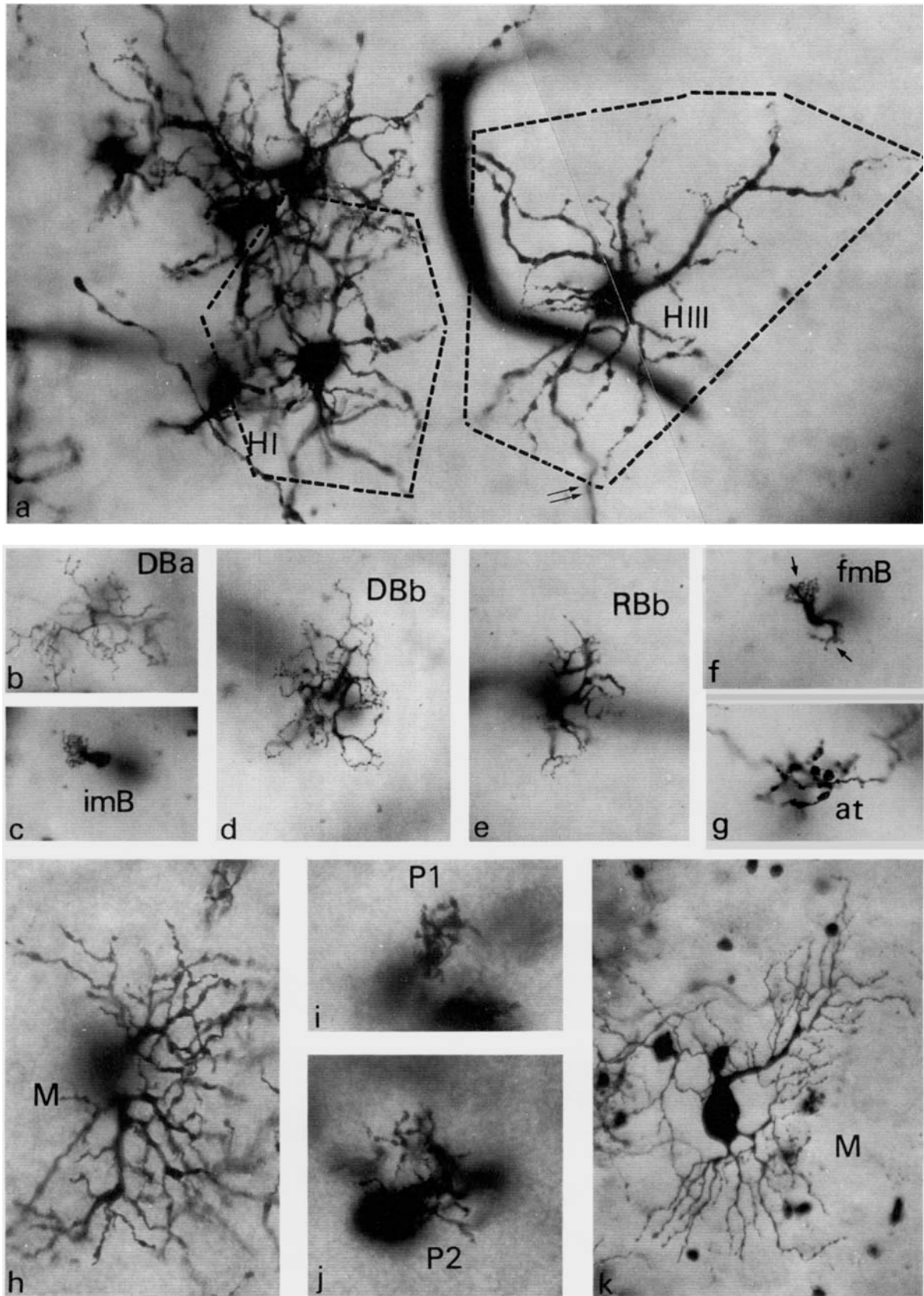


Figure 26

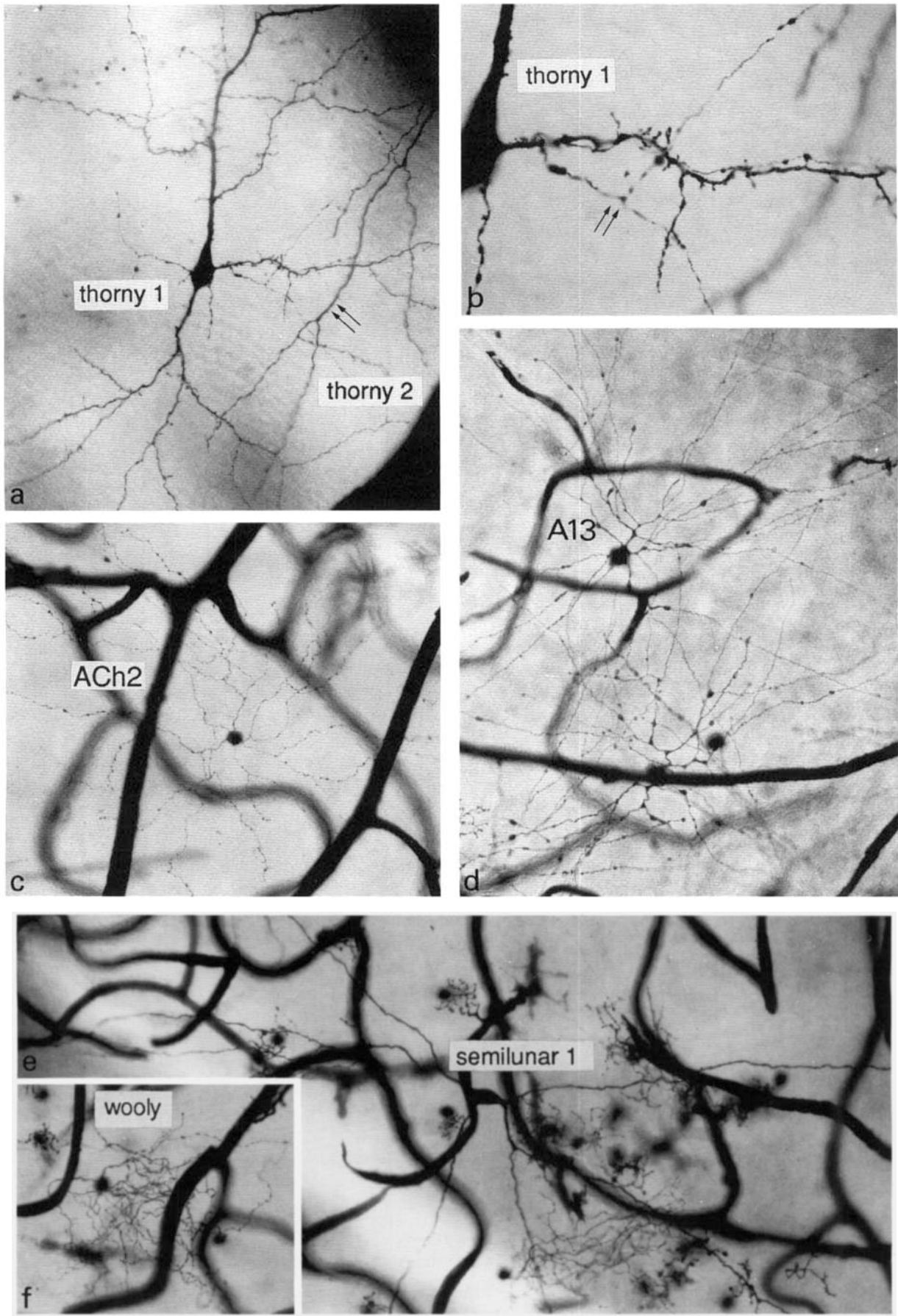


Figure 27

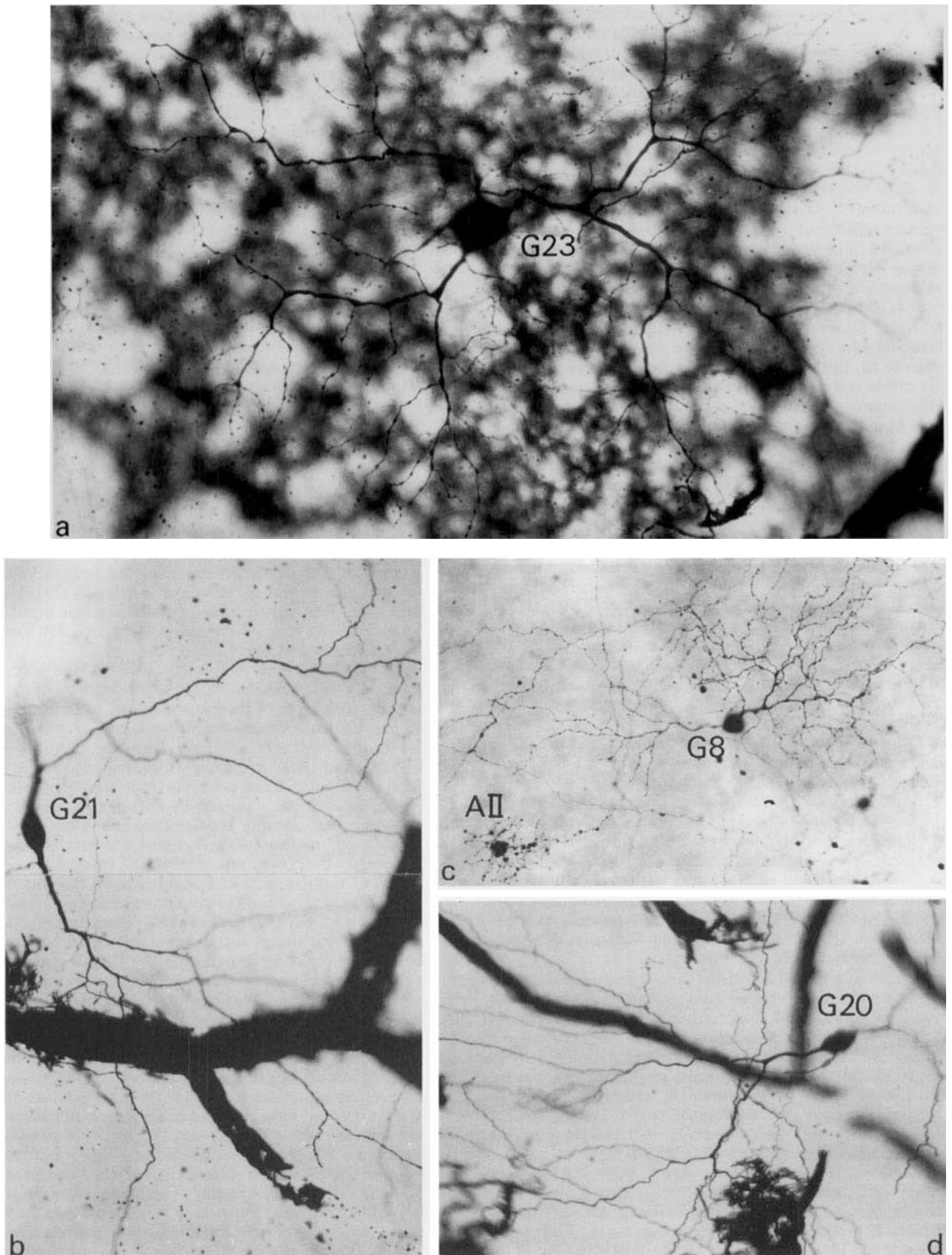


Figure 28

All but one of the small-field cells described in cat retina have counterparts in human retina (Table 2). Particularly noteworthy is the occurrence of the two bistratified narrow-field amacrine cells generally known to be important in the rod/cone pathways of mammalian retinas. The one that has now become known as the AII amacrine is clearly identifiable in human retina. It was probably already seen by both Polyak ('41) and Boycott and Dowling ('69) in earlier years (Table 2), but now that we know so much more concerning this cell's functional anatomy and neurochemistry in the rod-dominated retinas of cats and rabbits, its presence becomes significant in the more cone-dominated primate retina. We have not impregnated that many AII amacrine cells by Golgi methods. Immunocytochemical and autoradiographic studies, however, have certainly demonstrated their presence in monkey and human retina (Crooks and Kolb, '92; Frederick et al., '82; Hendrickson et al., '88; Marc and Liu, '85). Similarly, the A8 is known from cat retina to be, like AII, a glycinergic amacrine cell (Table 2) that mixes rod and cone pathway information in the IPL before innervating ganglion cells. It is pleasing to see that these important amacrine cell types occur in the human retina, implying that conservation of basic retinal wiring patterns has been maintained across species.

Though most of the amacrine cell types described in cat retina have been seen in the human retina (Table 2), those that have not may simply not yet have been impregnated by Golgi procedures. Many of the amacrine cells that we have seen here have been studied by physiology combined with dye-marking techniques such that we have an understanding of their roles in retinal wiring in the cat retina at least. For example, we have some knowledge of the response characteristics and synaptic connectivity of amacrine cells A4, AII, A8, A13, A17, and A19 in cat retina (Freed et al., '90; Kolb and Nelson, '84, '85; Nelson, '82; Nelson and Kolb, '85) and many of these appear to be almost identical in the rabbit (Dacheux and Raviola, '86; Raviola and Dacheux, '87). We can only presume that amacrine cells with such similar appearances to these mammalian examples have similar connectivities and functions in the human retina.

In this study we have seen all but one of the amacrine cell classes described by Mariani ('90) in monkey retina. Some of these are unknown for the cat retina and may, therefore, represent specializations of the human visual system (Table 2). Indeed, we have seen several varieties with complex multistratified dendritic trees, perhaps more reminiscent of amacrine cells in turtle and fish retinas—animals with good color vision (Kolb, '82; Wagner and Wagner, '88)—than those of rabbit and cat.

We have not seen the "wispy" amacrine cell of Mariani's ('90) classification, which he suggests corresponds to the type-2 catecholaminergic amacrine cell (CA2) (Mariani and Hokoc, '88). The CA2 amacrine cell has been described in human retina by immunocytochemical staining (Crooks and Kolb, '92), so we know it must be present in the retina and should have a Golgi equivalent. It may indeed be the "wispy" amacrine, but we suggest that it is equally likely that any of the wide-field amacrine cell types ranging from semilunar, wiry, stellate-wavy or stellate-varicose could be the CA2 cell in human retina, due to their cell body size characteristics and stratification levels. Obviously, further morphological and histochemical investigations are needed to identify this cell type more positively.

Some confusion has arisen in the literature as to the exact morphology of the CA1 dopaminergic amacrine in the

primate retina. Beautiful dye-injection studies by Dacey ('90) have revealed an amacrine cell type claimed by him to be the dopaminergic amacrine. Yet Dacey's ('90) dye-injected amacrine is characterized by having a large cell body and markedly branched *spine-invested* dendrites that stratify in stratum 1 of the IPL and emit long "axon-like" processes. The thorny type 1 amacrine cell that we show here and that is reported in monkey by Mariani ('90) is almost certainly the candidate for Dacey's dye-injected amacrine cell. Probably the latter amacrine is indoleaminergic (Wässle et al., '87) instead of dopaminergic. Other authors' double-staining experiments with dye-injection and immunocytochemical labeling (Voigt and Wässle, '87) and straight immunocytochemical staining (Mariani and Hokoc, '88) repeatedly reveal that the dopaminergic amacrine cell is A18- or CA1-like in morphology with relatively smooth and unbranched dendrites (Kolb et al., '81; Mariani, '90). Such confusions have appeared in the literature because there has been a lack of detailed Golgi-impregnated classifications for investigators who use intracellular dye techniques to consult.

Specialized ganglion cells for primate vision: P1, P2, and M cells

We have seen 18 different morphological types of ganglion cell in the human retina. All but three of these closely correspond to cells in the cat retina and we have classified them accordingly with the same names (Table 3). Of particular interest for organization of the human visual system are the P and M ganglion cell types that have recently been determined to comprise the major input to the geniculostriate areas (Perry and Cowey, '81, '84; Perry et al., '84; Shapley and Perry, '86).

Polyak ('41) stressed the importance of the midget ganglion cells and considered them to form the majority of the ganglion cell types of the central retina. Ascertaining a reliable comparison of numbers of ganglion cells from Golgi studies is obviously difficult since one can only get an impression from their frequency of impregnation. Midget ganglion cells were thus probably the most commonly Golgi-impregnated ganglion cell in Polyak's hands. More recent retrograde staining studies indicate that ganglion cells with medium-size cell bodies and the smallest dendritic trees, putting them into a "midget" category of cell, form 80% of the ganglion cell population in the monkey retina, and form the complete projection to the parvocellular layers of the LGN (Perry et al., '84). The question then arises as to how many cell types correspond to these parvocellular projecting ganglion cells. Polyak describes midget ganglion cells quite clearly as the ganglion cells with the smallest dendritic trees, never much exceeding the diameter of their *cell body*, which is 9–12 μm in his preparations. We, in this study, concur with Polyak's description and thus our data suggest that the maximum size reached by midget ganglion cell dendritic trees is 20 μm in the peripheral retina (see Figs. 17–19). Rodieck has classified any small-field ganglion cell with a dendritic tree diameter of as much as 100 μm as a "midget" ganglion cell (Rodieck et al., '85; Watanabe and Rodieck, '89). It is almost certain then that Rodieck's midget class of ganglion cell also includes the small parasol variety of ganglion cell of Polyak ('41). We, like Polyak, have seen the coexistence at all points on the retina of the true midget ganglion cells with the small parasol ganglion cell types. Thus, we prefer to subdivide the small-field ganglion cells that project exclu-

sively to the parvocellular layers of the LGN (Shapley and Perry, '86) into P1 and P2 subtypes: P1 are then the classical midgets of Polyak and the smallest variety of Rodieck's "midget" group, while the P2 cells correspond to a distinctly larger dendritic-sized group that were called "small parasols" by Polyak and contribute to the upper size limits of "midglets" by Rodieck (Rodieck et al., '85; Watanabe and Rodieck, '89).

From Golgi preparations we cannot tell what percentage of the physiological P cells the true midglets, our P1 cells, would contribute. We suspect, however, that they do predominate over P2 cells in the foveal projection to the LGN parvocellular layers and are the opponent chromatic units, or type-1 cells of Weisel and Hubel ('66) and Gouras ('68, '71, '91). The P2 cells would be less frequent at the fovea but may then gradually assume dominant numbers in peripheral retina and be equivalent to the spectrally broadband types recorded physiologically in the LGN (Gouras, '91).

We suspect that the single-headed P1 midget ganglion cells, as apposed to the double-headed midget ganglion cells (Fig. 18), always maintain a one-to-one relationship with the midget bipolar cells across the retina because the diameters of their dendritic trees exactly match the diameters of midget bipolar axon terminals, also increasing with eccentricity. This leaves the double-headed midget ganglion cells, first described by Polyak ('41), to receive input from two midget bipolar axon terminals. The double-headed midget ganglion cells are presumably not found in the fovea and allow a convergent midget pathway in peripheral retina. Whether double-headed midget ganglion cells are connected to two single-headed or two multiple-headed midget bipolar cells or what might be the consequences for color specificity remain intriguing questions. We suggest that the larger field P2 cells maintain a relationship across the whole retina, from fovea to periphery, with the narrow-field diffuse cone bipolar types and would thus probably never be chromatically specific.

There is general agreement that the magnocellular-projecting ganglion cells are the very large variety of parasol cells that Polyak saw (Polyak, '41). Unfortunately, Polyak probably described as "parasol" a mixture of what we consider the smaller parasol variety, here called P2s, and the larger field variety, here called M cells, because he was viewing primate retina in sections where it is difficult to make dendritic tree size comparisons. Due to their cell body size and dendritic tree size characteristics some of Polyak's giant cells are undoubtedly the equivalent of our Golgi-impregnated M cells in far peripheral retina (see Figs. 18, 26k, Table 3), of Rodieck's parasol ganglion cells (Rodieck et al., '85; Watanabe and Rodieck, '89) and of the large-bodied, multibranching reduced silver-stained cells of Silveira and Perry ('91).

Many ganglion cell types, apart from those forming the primate's geniculostriate projections, were Golgi impregnated in this study on human retina (Table 3). Presumably most of these ganglion cells project to the midbrain and correspond to some of those retrogradely filled by Perry and Cowey ('84). Two of these varieties in macaque retina are large-bodied and have large-diameter dendrites filled with neurofilaments, making them stainable by reduced silver techniques like the M cells (Silveira and Perry, '91). We suspect they may correspond to G22 and G23 of this study. Some correlations between physiologically examined ganglion cells and morphological varieties demonstrated by

both Golgi impregnation and intracellular dye injection are becoming available for the more commonly studied mammalian retinas (Amthor et al., '89a,b; Dacey, '89b; Fukuda et al., '84; Leventhal et al., '80; Nelson et al., '78; Stanford, '87). Thus the G19 variety that we illustrate here in Golgi wholemounts has an equivalent in cat that has been stained by intracellular dye injection and is apparently monoamine-accumulating (Dacey, '89b) (Table 3). It will be fascinating to see if the human G19 has the same neurochemical signature.

Although not commonly recorded in primate retina or geniculate, ganglion cells with complex receptive fields may also be present in smaller numbers in human retina. We suggest this notion because ganglion cells have occasionally been seen in this study that resemble the complex ganglion cell types of the rabbit retina (Table 3). Most likely such ganglion cell types would project to the midbrain rather than to the geniculate. Thus G11 is a bistratified cell that could correspond to the rabbit ON-OFF directionally selective (DS) cell and G22 to an ON-DS cell (Amthor et al., '89b). Ganglion cells selective for orientation and uniformity could correspond to G8 and G17, respectively, in human retina (Amthor et al., '89b). Several of the concentric sluggish cells of the rabbit could also have Golgi-impregnated counterparts. For example, G3 and G20 could be ON-center varieties and G7 and G4 OFF-center varieties (Amthor et al., '89a). Naturally it is going to be difficult to get intracellular recordings and stainings to make unequivocal physiomorphological determinations of ganglion cell types in the human retina. The monkey retina is more likely to yield answers to such questions but has been rather refractory to date. Only one physiologically recorded and stained monkey ganglion cell has been reported so far, and, ironically, it proves to be the most puzzling ganglion cell ever described in any vertebrate retina. This is the biplexiform ganglion cell reported by Zrenner and coauthors ('83) and illustrated to be present in primate retina by Golgi techniques (Mariani, '82). We have not yet encountered such a cell type in our material.

How many types of interplexiform cell are there in human retina?

To date in this Golgi study of human retina we have only observed one morphological type of interplexiform cell (IPC). Several fragmentary examples and one more or less complete specimen were impregnated (Fig. 16). The medium-field size and multistratified organization of this cell's dendritic tree in the IPL suggests that it is the same type as has been described in car and monkey retina (Gallego, '71; Boycott et al., '75) and later examined for circuitry in detail in the cat (Kolb and West, '77). Its function is to integrate information between the two plexiform layers of the retina using gamma-aminobutyric acid (GABA) as a neurotransmitter (Nakamura et al., '80; Pourcho and Goebel, '83; Ryan and Hendrickson, '87). An electron microscope study of an IPC in human retina (Linberg and Fisher, '86) revealed connectivity similar to the IPC studied in the cat retina (Kolb and West, '77). Thus we suspect that the EM study was looking at the same cell that we have now impregnated by Golgi stain. Recently a very similar appearing cell type was also reported in monkey retina (Rodieck, '88).

It seems clear that the putative GABAergic IPC of the human retina has been revealed by the Golgi study, but we have not yet seen any cell in human retina that could be the

equivalent of the putative "dopaminergic" IPC seen by other authors in primate retina (Frederick et al., '82; Laties, '72). Tyrosine hydroxylase (Toh+) immunostaining in monkey and human indicates that two clear amacrine cell types are stained (Mariani's CA1 and CA2 types) (Crooks and Kolb, '92; Mariani and Hokoc, '88). However, none of these studies have been able to show the existence of long-ranging Toh+-stained profiles running in the OPL, either coming off the stained cell body or even from stained dendrites in the IPL. On the other hand, dopaminergic amacrine cells in human retina appear to emit many fine processes that insinuate themselves between cell bodies of the INL like the INL-fluorescent plexus described for *Cebus* monkeys (Boycott et al., '75; Dowling and Ehinger, '75). It will be intriguing to understand the synaptology of this INL plexus and possibly to find processes more distinctly "interplexiform cell-like" in the OPL from a dopaminergic cell in the human.

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