The transretinal pathway of optic nerve fibers in the retinas of cynomolgus and bonnet monkeys was studied by light microscopy following small intraretinal injections of horseradish peroxidase (HRP). Injections of HRP into nerve bundles at the optic disc labeled a few ectopic ganglion cells, in addition to those in the related retinal sector. Injections into nerve bundles in the retina labeled long (more than 3 mm) fibers of passage, most of which remained close to the vitreal surface as they crossed the retina. These long fibers mingled with short (less than 1 mm) peripapillary fibers at the disc margin and in the prelaminar part of the disc. Axons of intermediate ganglion cells (1–3 mm in length) were added to the fiber layer at its scleral border, beneath long fibers of more peripheral origin. These findings demonstrate a retinotopic organization of macaque nerve fiber bundles with long fibers vitreal and shorter fibers more scleral in position. Intermingling of fibers of disparate origin is extensive at the optic disc where a decussation of long and short fibers occurs. Invest Ophthalmol Vis Sci 24:85–98, 1983.

Retinotopy implies that neighboring retinal areas project in an orderly manner onto neighboring areas of central nervous system structures. The nature of retinotopy in the retinal nerve fiber layer is controversial. There is an obvious horizontal nerve fiber layer retinotopic organization based on the collection of the axons from wedge-shaped retinal areas in bundles.1 Thus, each nerve fiber bundle contains fibers from a radial sector of retina that extends from disc to equator, and it is claimed that there is normally little if any lateral dispersion of fibers among bundles.2 The retinal path of a fiber varies in length with the position of its cell of origin; fibers of peripapillary ganglion cells are short, fibers of equatorial cells are very long. For retinotopy to be present within a given bundle, long fibers must be separated from short fibers by fibers of intermediate length. Thus, the long fibers might be found as a lamina on the vitreal surface or deeply placed on the scleral surface of the nerve fiber layer. Either arrangement would be consistent with a retinotopic organization of fibers within the nerve fiber bundles.

The older literature on the question of nerve fiber layer retinotopy is summarized by Wolff and Penman,3 who conclude on the basis of their own experimental studies in rabbits and on clinical observations that long retinal fibers are segregated and lie deep within the nerve fiber layer, beneath the shorter fibers of peripapillary origin. This view has received recent support from experimental studies in monkeys by Radius and Anderson2 and Minckler.4 Polyak1 states a contrary view: “Fibers from the far periphery, while within the retinal fiber layer, are necessarily situated close to the vitreal surface.” This conclusion is supported by the observation that axonal growth cones in the developing chick retina are only found close to the vitreal surface.5 As the retina develops, new ganglion cells are added at its margin only. The axons of these young cells grow toward the disc along the axons of older cells, forming the bundles. Thus, the presence of growth cones, the growing tip of the new axons, only near the vitreous, suggests layering of nerve fibers with the longest axons most superficial.

The possibility that the nerve fiber layer lacks a retinotopic organization was suggested by Traquair6 in his treatise on perimetry: “It is probable that fibers are mingled in the retina. . . .” Fiber mingling is supported by studies of monkey ganglion cell axons labeled by the uptake of radioactive amino acid injected into a retinal area giving rise to long arcuate fibers. The path of the labeled fibers to the disc was clearly identified in these studies, and cross-sections of the retina revealed label scattered throughout the full thickness of the nerve fiber layer near the disc.7

The morphologic techniques used in past studies...
of nerve fiber layer retinotopy involved large populations of fibers and did not permit the course of individual fibers to be followed across the retina. The data produced are thus ambiguous in terms of fine organization. Also, those studies that involved creation of retinal lesions and subsequent evaluation of degenerating fibers may be misleading if there is a discrepancy among fibers in their rate of degeneration. Thus, failure of superficial fibers to degenerate as fast as deep fibers, or vice versa, could lead to the erroneous conclusion that the nerve fiber layer is retinotopically organized. Finally, the studies that were based on intraretinal injection of radioisotope did not involve electron microscopy, so it was not proven that the label was entirely intra-axonal. Extracellular diffusion of the isotope could have masked layering due to retinotopy. Therefore, the results of previous studies of nerve fiber layer retinotopy are inconclusive.

In the experimental primate study described below, HRP was injected into individual fibers or fiber bundles of the nerve fiber layer of the macaque monkey. The course of the fibers across the retina was followed in serial cross-sections that revealed the locations of the stained fibers without ambiguity.

**Materials and Methods**

Ten adult cynomolgus (*Macaca irus*) and two juvenile bonnet (*Macaca radiata*) monkeys were used in these studies. HRP was injected into the nerve fiber layer of the retina of both eyes of each animal. After a 12- to 24-hour period to permit transport of the label to the optic nerve head, the animals were killed, and the retinas were processed histologically, first as flat whole mounts, then in serial cross-sections.

Anesthesia was induced with ketamine (8 mgm/kgm) and phenylcyclidine (1 mgm/kgm). The pupils were dilated with topical tropicamide and neosynephrine. Following tracheostomy and paralysis with curare, the animals were ventilated artificially with a mixture of oxygen (30%) and nitrous oxide (70%). End-tidal carbon dioxide was continuously monitored and maintained at 5% by appropriate adjustment of respiratory tidal volume and rate.

Intraretinal recording was accomplished as described previously. Micropipettes filled with 5% HRP in 0.5 M KCL were introduced into the vitreous through a hypodermic needle channel in the pars plana. The electrode was attached to a hydraulic advancer and guided to the selected retinal region under direct ophthalmoscopic control. A 100-micron spot of white light was flashed on the retina in a position appropriate to drive ganglion cell discharge at the recording site. The glass pipettes were positioned within the nerve fiber layer, and HRP was injected by combined pressure and electrophoresis. Intraretinal potentials were monitored during penetration of the retina and served to signal accurately retinal depth of the electrode during the injection.

Twenty-three of 59 injections were successful in that nerve fibers were labeled throughout their intraretinal extent. The retinal locations of these injections, which involved both eyes, are illustrated in Figure 1.
Fig. 2. Diagram of optic disc injection number 6 into the superior arcuate bundles. Labeled ganglion cells were found entirely within the outlined area (arrows) except for ten heavily stained cells whose locations are indicated by the filled circles. D, optic disc; F, fovea; Calibration bar, 1 mm.

Figure 1. Injections 1-4 involved nasal retina; 5-7 involved the optic disc; 8-15 and 18-23 involved the arcuate nerve fiber bundles; and 16 and 17 involved the maculopapillar bundles. Disc injections 5-7 stained fibers of all lengths; injections 16, 17, and 19 stained intermediate and long fibers; the other retinal injections stained only long fibers. Injections 2, 8, 21, and 22 involved only a few fibers, the remainder labeled one or more bundles. Thirty-six of the 59 injections failed to label fibers from their cells of origin to the disc margin and are not included in the results presented below.

Of particular interest in this study were the relative positions within the nerve fiber layer of fibers whose cells of origin lay at different distances from the optic disc. To distinguish among these fibers, the following terminology is used: "short" is arbitrarily used to designate fibers originating within 1 mm of the disc; "intermediate length" refers to fibers originating from 1-3 mm from the disc, and fibers whose cells of origin lie more than 3 mm from the optic disc are called "long." This terminology is based on the intraretinal length of nerve fibers, not on the position of the cell of origin with respect to fixation. The terms "central" and "peripheral," usually applied with reference to fixation, are ambiguous as descriptors of fiber length. Fibers that originate 20° nasal to fixation are short while those that arise 20° temporal to fixation are very long, yet the receptive fields of both are equally "peripheral."

The animals were maintained under anesthesia until they were killed, at which time the eyes were enucleated, hemisected, and immersed in 2% glutaraldehyde in phosphate buffer (pH 7.4). The retinas were gently detached and flattened, receptor side down, with the aid of peripheral incisions, onto filter paper. The disc was cross-sectioned carefully with a sharp blade and, in most cases, the prelaminar portion of the disc was obtained with the retina. Vitreous was removed by sharp dissection under a dissecting microscope, then fixation was continued for 1 hr in 2% glutaraldehyde. Following a 1-hr wash in the phosphate buffer, HRP histochemistry was done as described by Graham and Karnovsky.10 The progress of the reaction was monitored under the dissecting microscope and halted when staining was observed at the optic disc in fully stained bundles, or in 30 minutes in the case of single fiber injections and retinas with partially stained bundles.

The reacted retinal flat mounts were then rapidly dehydrated in alcohol and embedded in epon-araldite. Linear shrinkage was determined by measuring the distances between prominent retinal landmarks in the freshly fixed and embedded specimens, and was less then 15% as reported previously.11 Stained fiber bundles were easily observed and photographed in the whole mount. Individual fibers were followed with the use of a 63× oil immersion lens, and their path across the retina was recorded in camera lucida drawings. The drawings also showed the location of all stained ganglion cells, and thus revealed the approximate "receptive field" of the stained bundles. The extent of HRP diffusion around the injection site was clearly indicated by the presence of the label in other retinal elements, particularly ganglion and amacrine cells, whose processes extended across the retina beneath the electrode. Absence of such staining in a particular region provided proof that significant amounts of HRP had not diffused into it.

Following these detailed studies, the whole mount was serially cross-sectioned at 100 microns with a sliding microtome, and the sections were mounted in epon-araldite on teflon-coated microscope slides. Examination of these cross-sections revealed the position within the nerve fiber layer of the stained fibers, but definition was poor because of the thickness of
the sections. Selected sections from the serial series were removed from the slide, re-embedded, and re-sectioned at 1- to 2-micron thickness on an LKB-V ultramicrotome. The latter sections, stained with toluidine blue, showed the HRP-labeled fibers clearly and were used to determine their position with respect to the internal limiting membrane.

Results

Fiber Bundle Injections into the Optic Disc

The presence of a precise retinotopic organization in a nerve fiber bundle implies that all its fibers originate in one retinal area. HRP injections into the optic disc margin were used to reveal the retinal area that contributed fibers to a particular bundle. These injections resulted in heavy labeling of a bundle and by retrograde transport of the HRP, heavy labeling of a population of ganglion cells whose axons comprised the bundle (Fig. 2). The retinal distribution of the labeled ganglion cells corresponded in a sense to the "receptive field" of the labeled bundle. Most of the stained cells were found immediately beneath the bundle and in a wedge-shaped sector of retina that extended into the periphery. This primary area of labeling was clearly in the retinotopic domain of the bundle and is indicated by arrows in the diagram of Figure 2, which illustrates the results of injection 6 (see Fig. 1). This heavily labeled area was surrounded by a much larger region in which a few scattered ganglion cells were stained (solid circles in Fig. 2). Each of these cells in this surrounding area was heavily labeled and contributed its axon to the injected bundle. These cells, however, were retinotopically outside the primary area of labeling. This result suggests that nerve fiber bundles are not retinotopically perfectly homogeneous. Rather, the bundles contain some axons, less than 2% in the case of injection 6, whose cells of origin are not topographically closely related to the bulk of the cells whose fibers make up the bundle.

Small fascicles of nerve fibers are often seen to be interchanged among adjacent bundles as they cross the retina. Figure 3 shows a retinal whole mount in which many nasal bundles were stained as a result of injection 5 into the optic disc (Fig. 1). The macroscopic bundles (large arrow) seen in the whole mount probably correspond to the fiber layer striations seen by ophthalmoscopy. The small arrows in Figure 3 indicate a few of the many fiber bridges that can be seen between adjacent bundles. It seems likely that the fibers of the ectopic cells labeled by disc injection 6 and shown in Figure 2 were transferred to the injected bundles through such fiber bridges as these.

Fiber Bundle Injections into the Retina

Intraretinal injection of HRP resulted in heavy labeling of a high percentage of fibers that passed
through the injection site. The HRP spread in a retrograde direction back to the cells of origin that were also heavily labeled. As the stained (long) fibers approached the optic disc they were joined by a large number of unstained (shorter) fibers that greatly increased the thickness of the fiber layer. The distinction between the stained and unstained fibers was striking and revealed the position of the HRP-filled long fibers without ambiguity. Diffusion of HRP from the injection site toward the disc was clearly evident from the location of stained ganglion cells. Thus, all stained fibers found near the optic nerve head, following a retinal injection, originated at or distal to the most proximal stained ganglion cells. Extracellular spread of the HRP from the injection site toward the optic disc, sufficient to cause ganglion cell staining, was slight, never more than 0.5 mm.

Arcuate bundles labeled by injection 11 are shown diagrammatically in Figure 4A. The area of labeled ganglion cells is indicated in this figure by stippling. Photomicrographs of a series of 0.1-mm thick cross-sections through the stained bundles are shown in Figure 5. The mass of stained fibers filled the nerve fiber layer near the injection site (Fig. 5A). As the optic disc was approached (Figs. 5B–F), the nerve fiber layer became thicker from the addition of shorter (unstained) fibers. Near the disc, the fiber layer had more than doubled in thickness, and it is seen...
that most of the unstained fibers are scleral in position; the mass of stained long fibers is in the vitreal half of the nerve fiber layer. Segregation of long from short fibers was imperfect, however, as some unstained fibers are seen in the vitreal half, and some stained fibers are seen in the scleral half of the layer.

The course taken by the stained fibers as they entered the optic disc was followed in sections cut along
Fig. 6. Photomicrographs of 1 micron-thick sections through stained bundles shown in Figure 5 (injection 11). A and B show sections obtained just peripheral and central to the injection site. The full thickness of the fiber layer (double arrows) contains HRP-stained fibers. C-F, sections obtained progressively closer to the optic disc at about 0.5 mm intervals. Note that most labeled fibers remain in the vitreal half of the layer as it increases in thickness. G, section from the disc margin shows wide dispersal of fibers, but most remain in the vitreal half of the fiber layer. Sections stained with toluidine blue. Magnification: 362X.
the axis of the fibers enclosed in the rectangular area shown in Figure 4A (heavy arrow). Figures 5G–I show low-power photomicrographs of three of these sections. Individual fibers were easily distinguished with high power microscopy. Camera lucida drawings of 92 of these fibers were made from eight serial sections across the disc margin. The drawings are shown superimposed in Figure 4B. The stained fibers were largely in the vitreal half of the fiber layer (double arrows) as the disc was approached, but spread throughout the layer as they turned into the disc at its margin (D). Many of the fibers followed a meandering course as was suggested by Horton et al.13 for optic nerve fibers of the cat. The labeled fibers were confined mostly to four adjacent bundles near the injection site (see below), but spread to involve a segment of disc that extended from its margin half the distance to its center. These long peripheral fibers must pass through many different pores of the lamina cribrosa within this segment of the optic disc.

The thick sections shown in Figure 5 were excellent for tracing fibers over long distances across the retina, but were too thick to reveal accurately fiber position in the bundles. Therefore, sections were re-embedded and resectioned at a thickness of 1–2 microns. The photomicrographs shown in Figures 6A,B were obtained just distal and proximal to the injection site shown in Figure 4. It is seen that the nerve fiber layer was stained throughout its full thickness. A number of large profiles are evident. These correspond to swollen fiber endbulbs and are probably analogous to cytoid bodies,4 representing organelle accumulation as a result of axoplasmic flow obstruction at the injection site. The sections illustrated in Figures 6C–F, each progressively closer to the optic disc, clearly show segregation of the stained fibers in the vitreal half of the fiber layer. The segregation is imperfect, and a few stained fibers are seen in the scleral half of the layer. Figure 6G shows the situation adjacent to the disc margin. The nerve fiber layer is greatly thickened from the addition of unstained fibers, many of which are interspersed among the stained fibers. The stained long fibers are relatively confined to the vitreal half of the layer, but a few are seen much deeper.

These results, which show a qualitative segregation of long fibers in the vitreal portion of nerve fiber bundles as they travel across the retina toward the optic disc, were obtained with every intraretinal injection shown in Figure 1. Figure 7 shows the results of injection 10 (Fig. 1) that labeled a more peripheral segment of the arcuate fibers. The entire thickness of the nerve fiber layer contained stained fibers near the injection site and several bundles were involved (Figs. 7A,B). Closer to the disc, only the central bundle was heavily labeled, and the stained fibers were separated from the ganglion cell layer by unstained short fibers of peripapillary origin (Fig. 7C). The epon block containing the disc was rotated 90° to permit longitudinal sectioning of the fiber bundles at the disc margin. Figure 7D shows such a section. The stained fibers were vitreal in position until they reached the disc margin where substantial dispersion into deeper regions of the fiber layer occurred. Camera lucida drawings were made of 14 fibers whose path across the disc margin could be traced through a series of 11 such longitudinal serial sections. These drawings are shown superimposed in Figure 7E. Close to the disc margin, where the fiber layer had doubled in thickness, the stained long fibers were entirely vitreal in position. They were separated from the ganglion cell layer by unstained fibers. Note that stained fibers diverged throughout the layer at the disc margin, but were mainly evident in the vitreal portion. In this case, segregation of long from short fibers was maintained across the retina and only became imperfect near the disc margin.

The papillomacular bundle was stained widely, but incompletely by injection 16 (Fig. 1). Figure 8A shows a photomicrograph of a section obtained from the vicinity of the injection and shows labeling of many fibers throughout the full thickness of the fiber layer over a broad area. Figure 8B shows the stained fibers about 1 mm closer to the disc and reveals a clear zone beneath the labeled fibers. This clear zone of unlabeled fibers became even more pronounced as the disc was approached (Fig. 8C), and the stained fibers were entirely confined to the vitreal half of the fiber layer. Near the disc margin, however, as with the other bundle injections, some stained fibers migrated to the scleral portions of the fiber layer. This is shown in a longitudinal section, with the disc margin to the right, in Figure 8D.

Single Fiber Injections in the Retina

In all retinal regions, an intermixing of a few fibers of retinotopically disparate origins occurred as a result of meandering of fibers. This was revealed best by injections 2, 8, 21, and 22 (Fig. 1) that labeled only a few fibers, each of which could be followed in retinal whole mounts and serial sections across the retina to the optic disc. A diagram of injection 2, which labeled four fibers, is shown in Figure 9. Three of the fibers remained approximate neighbors as the retina was crossed, the fourth meandered considerably (Fig. 9, arrows). Cross sections, which reveal the stained fibers at retinal locations A–C (Fig. 9), are shown in Figure 10.

Close to the injection site, it is seen that three of
the fibers are in two adjacent bundles and the fourth is three bundles away (Fig. 10A). All of the fibers are in the scleral half of the bundles. At position B (Fig. 10B), the nerve fiber layer was doubled in thickness and the fibers were located in three adjacent bundles. Three of the fibers were vitreal, one was scleral in position. At position C (Fig. 10C), the fiber layer doubled again in thickness and all of the fibers were in the same bundle, three were vitreal, and the fourth scleral in position.

These results are typical of each of the small injections in showing a loose retinotopy with substantial
Fig. 8. Photomicrographs of retinal cross-sections through maculopapillary fibers stained by intraretinal injection 16 (Fig. 1). A, full thickness of the nerve fiber layer (vertical bar) is labeled near the injection site; B, C, sections 2 and 1.5 mm from the disc, show addition of unlabeled peripapillary fibers to the scleral part of the bundles (double arrows); D, longitudinal section at the disc margin (to the right) shows some stained fibers are dispersed to a scleral position in the fiber layer (arrow). G, ganglion cell layer. Calibration, 50 microns.
meandering of individual fibers, but with a definite tendency for long fibers to remain in the vitreal portion of the fiber layer as the retina is traversed.

**Discussion**

The results of this study of the macaque monkey show: (1) A horizontal topographic organization of nerve fiber bundles made imperfect by inclusion in the bundles of a few fibers of a retinotopically remote origin. (2) A vertical topographic organization within each bundle with long fibers, which originate at a distance from the optic disc, vitreal in position. This organization, well defined away from the disc, is degraded in the peripapillary retina as some long fibers take up a scleral position in the bundles. (3) Extensive intermingling of long and shorter fibers in the prelaminar portion of the disc. (4) A relatively meandering course of individual fibers across the retina.

**Lateral Dispersion of Fibers**

Separate injections of HRP into nasal, arcuate, and maculopapillary fiber bundles at the disc margin resulted in heavy labeling of the injected bundles and their ganglion cells of origin. Each injection labeled a large group of related and a small population of unrelated cells. The disc injections were sharply localized, and it is considered unlikely that involvement of fibers within remote bundles occurred because of unrecognized diffusion of HRP at the disc. Uptake of HRP by fibers of passage probably requires direct or indirect damage to the fiber membrane. Obviously, such damage can occur at a distance from the injection site since the micropipettes used were very small compared to the volume of tissue stained. Uptake, however, is graded with distance from the injection site and the ectopic cells found here were heavily stained. This suggests that their axons were heavily injected, ie, were located in the injected bundles. Thus, it appears that the axons of these cells had dispersed laterally to the injected bundles.

Numerous small fascicles of fibers pass among neighboring fiber bundles, and this was more commonly observed near the disc than in the periphery. Clearly this interchange of fibers among adjacent bundles must degrade the topographic integrity of each bundle. The extent of lateral dispersion is probably small, amounting to less than 2% of the fibers stained in disc injection 6 (Fig. 1). Lateral dispersion of nerve fibers from a particular retinal location has been suggested as an explanation for the presence of arcuate scotomata in some glaucoma patients who show no evidence of nerve fiber bundle defects and could also explain the absence of arcuate scotomata in some patients with ophthalmoscopically evident arcuate fiber bundle defects.

**Fiber Bundle Retinotopy**

Every intraretinal injection made in this study resulted in labeling of long nerve fibers that tended to remain vitreal to shorter fibers. Vertical nerve fiber bundle retinotopic organization has been unequivo-
Fig. 10. Photomicrographs of retinal cross-sections obtained at positions A to C and showing the four fibers illustrated in Figure 9. The fibers (arrows) are spread among five bundles in A, are in two adjacent bundles in B, and are in the same bundle in C, where three are vitreal and the fourth is scleral within the nerve fiber layer (double arrows). Calibration, 20 microns.

Cally demonstrated and follows the pattern suggested by Polyak and others. In the peripapillary region, and in the prelaminar part of the disc, substantial intermingling of long and short fibers occurred. Long nerve fibers eventually pass to the circumference of the anterior optic nerve. Reordering of these long fibers is required at the disc margin where they are separated from the circumference of the optic
nerve by short nerve fibers of more central origin. The intermingling of fibers observed must represent this reordering. Had the long fibers been scleral in position at the disc margin, as suggested by Radius and Anderson⁷ and Minckler⁴, they could pass to their final position on the circumference of the optic nerve directly. Under these circumstances, fiber intermingling at the disc would not be expected. The observed intermixing of fibers at the disc is consistent with the vitreal position of most of the long fibers as they approach the disc.

The difference between these results and those of Radius and Anderson,⁷ Minckler,⁴ and Ogden⁷ requires some comment. Radius and Anderson⁷ observed a layer of degenerating fibers at the scleral border of the nerve fiber layer following peripheral retinal photocoagulation and concluded that long fibers cross the retina on the scleral surface of fiber bundles. They studied both owl and macaque monkeys, but apparently their results were obtained mainly from the owl monkey since they comment that they “consistently saw less dramatic stratification of degeneration in the eyes of rhesus monkeys.” The owl monkey has a highly evolved, rod-dominated retina without a fovea, and its nerve fiber layer organization is quite different from that of the macaque. Nasal bundles lack a retinotopic organization. Arcuate bundles of the owl monkey are organized retinotopically, as described by Radius and Anderson,⁷ with the long fibers in a scleral position.⁴ Minckler⁴ based his conclusion that long fibers of the macaque are scleral in position on the observation of decussating fibers near the disc. He clearly showed vertical passage of peripapillary ganglion cell axons through the overlying fibers in the region of long and short fiber intermixing observed above. He did not observe the transretinal course of the long fibers and had no direct evidence of their position in the bundles.

Injection of radioactive amino acid into the retina by Ogden⁷ was used to label long fibers of the arcuate nerve fiber bundles of rhesus monkeys. Autoradiography of retinal cross-sections revealed label throughout the thickness of the nerve fiber layer and showed no evidence of lamination. The diffuse nature of the labeling was particularly evident near the optic disc. In view of the present results, it seems likely that the region of fiber intermingling was sampled near the disc in the previous study. Diffuse labeling of the fiber layer away from the disc could have resulted from diffusion of the label in the extracellular space along the fiber bundles. This would not have been recognized since the resolution of the light microscopic technique used was insufficient to associate the silver grains with individual fibers.

The above results of studies of single HRP stained fibers showed substantial meandering in their course across the retina. This was previously noted by Polylak²⁰ who wrote “... the axis cylinder joins the layer of optic nerve fibers, where its course, often twisted and meandering, may be followed for a considerable distance.” The fibers wandered within a given bundle and passed among adjacent bundles through the fiber bridges. A single fiber was seen to occupy as many as five separate bundles in its transretinal passage. This constant shifting of position has the effect of reducing contact between neighboring fibers. Most nerve fibers in the nerve fiber bundles are in apposition to other nerve fibers.²¹ If this contact were continued over long distances, the activity in one fiber could influence the activity in an adjacent fiber through ephaptic transmission. This possibility, which would degrade information transmission along these unmyelinated nerve fibers, seems obviated by the variable path of individual fibers. Meandering of fibers could also explain the common observation of the absence of demonstrable functional deficits following a small peripheral retinal lesion, since some fibers from retina peripheral to such a lesion may bypass it and therefore be spared.

The present results, which show a gross retinotopy of fiber bundles in the retina but meandering of individual fibers, are consistent with recent studies of optic nerve and tract retinotopy in cats. The extreme view of Horton et al¹³ that no retinotopy is present in the optic nerve resulted from their analysis of only a few fibers. Such studies fail to reflect gross retinotopy involving large segments of the visual map. The very small injections of the present study also yielded results that suggest much more fiber variability than the results of the large injections. Large and small injections are complementary and should be used together to reveal the course of both a large population and individuals within a population of fibers. It is clearly unwarranted to conclude that a retinotopic organization is absent on the basis of single fiber studies. More recent experiments by Torrealba et al²² suggest the presence of several overlapping, but out of register, retinotopic maps in the cat optic tract and these most probably reflect an ordering of fibers within the nerve of substantial complexity.

The pathogenesis of visual loss in glaucoma is poorly understood. Recent studies of optic nerve fibers in monkey eyes with abnormal intraocular pressures have shown blockade of nerve fiber axoplasmic transport in the region of the lamina cribrosa pars scleralis.²³⁻²⁶ This is the first direct evidence that the site of primary nerve fiber damage in glaucoma may be in the intralaminar portion of the optic disc. Visual field loss in glaucoma, associated with loss of nerve fibers, often begins in the Bjerrum area as a peripheral island that may eventually spread to the blind spot. This reflects heightened sensitivity of long fibers to
the adverse effects of glaucoma, and a theory of glaucomatous field loss must account for this peculiar sensitivity. Explanations of field loss that invoke mechanical compression or ischemia of selected nerve fibers at the disc are based on the assumption that a high order of retinotopic organization is present at the point of injury. The results of the present study indicate that such organization is lacking in the prelaminar portion of the disc. It is the intralaminar part of the disc, however, where injury is most likely to occur and this part was not examined in this study. Intermingling of long and short fibers was extensive in the prelaminar disc, and it seems unlikely that the required high order of retinotopy could be established within the narrow width of the lamina; thus some property of long nerve fibers, other than retinotopy, may be responsible for their selective damage in glaucoma and other disease states.

Key words: macaque, retina, nerve fiber layer, retinotopy, horseradish peroxidase

References