single membrane-bounded osmiophilic vacuoles and granules are identical with those we have observed. Many of the new organelles described in these early studies were in close proximity to the Golgi apparatus; since acid phosphatase staining in some of our cultured cells was also localized in the perinuclear area, it is possible that these newly formed, lysosome-like structures arise from the Golgi apparatus, as suggested by Novikoff (*5*).

Cellular enlargement and mitotic activity can also be induced in 5 to 40 percent of human lymphocytes by culturing them in the presence of specific antigens to which the donor of the cells has been sensitized (*2*); such cells contain granules and vacuoles (*13*) resembling those described by Tanaka. From these studies and from our observations of tuberculin-stimulated cultures it would appear, therefore, that both nonspecific (PHA) and specific (antigen) stimulants induce the formation of lysosome-like structures before mitosis.

If these granules containing acid phosphatase resemble the lysosomes of other tissues, it may be that such organelles participate in the remodeling processes immediately preceding cell division.

ROCHELLE HIRSCHHORN
J. MARTIN KAPLAN
ARTHUR F. GOLDBERG
KURT HIRSCHHORN
GERALD WEISSMANN

Department of Medicine, New York University School of Medicine, New York, New York

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Foveal Receptors of the Monkey Retina: Fine Structure

Abstract. *The outer segments of the foveal cones of the rhesus monkey are about 40 microns long and 0.9 microns wide. They consist of stacks of membrane-limited, transverse discs about 140 Å thick, surrounded by a plasma membrane. The inner segments are about 30 microns long and 2.5 to 3 microns wide at the base, and they taper gradually to a tip diameter of about 1.5 microns. They contain many long mitochondria which are oriented lengthwise and are concentrated in the distal portion of the segment. The terminal pedicles show many synaptic contacts, probably as many as 36 per pedicle.*

The central portion of the primate fovea contains receptor cells of only one type, classified physiologically as cones (*1*). The gross structure of the foveal cone-cells presents something of an enigma, however, since they appear more like rods than cones when observed with the light microscope (*1*, p. 249). They have thin, cylindrical outer segments which show no taper and are the longest outer limbs in the retina, extending some 40 to 60 μ in length (*1*, p. 448). The inner segments of the foveal cones are likewise thin and elongated and also resemble rod inner segments. No detailed studies of the fine structure of the foveal receptors have been reported as yet, although there have been several studies of the fine structure of rods and extrafoveal cones in primates (*2*). This report describes the foveal receptors in the rhesus monkey.

Eyes were obtained from small rhesus monkeys (*Macaca mulata*) anesthetized with nembutal. The cornea and lens were cut away, along with the more peripheral retina, and the back of the eye was immersed in 2-percent osmium tetroxide buffered to *p*H 7.8 with veronal acetate and containing 1 percent calcium chloride and sucrose at 45 mg/ml. The eyes were fixed for 1 hour, dehydrated in graded acetone-water mixtures, and embedded in Araldite in a flat aluminum pan. After hardening, the pan was cut away and the clear plastic disc containing the tissue was examined under the dissecting microscope to locate the fovea.

The fovea was not easily distinguished in the densely-staining tissue, but the optic disc, retinal blood-vessels, and nerve fibers on the surface of the retina were easily seen and provided marks to locate the fovea. When the approximate foveal position was found, thick sections were cut with a razor blade until the fovea was found. Then thin sections were cut on a Porter-Blum microtome, stained with lead citrate, and examined in an RCA EMU-3F electron microscope.

A portion of a typical outer segment of a central foveal cone is shown in Fig. 1. The diameter of the foveal cone is approximately 0.9 μ, and no tapering of the outer segment structure is evident throughout its length. As is the case with rods and cones from all vertebrates (*3*, *4*), the internal structure of the outer segments of the foveal cone consists of a stack of flattened, membrane-limited discs piled one atop the other. Each disc is approximately 140 Å thick, the bounding membranes are about 50 Å wide, and the intra-disc space is about 40 Å. The inter-disc space

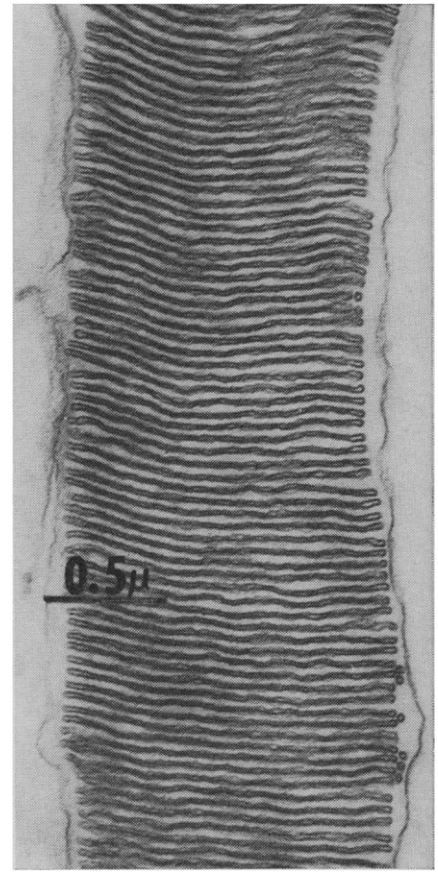

Fig. 1. Portion of the outer segment of a cone from the central fovea of a rhesus monkey. The outer segment consists of a pile of membrane-limited discs piled one atop the other. (× 52,000)

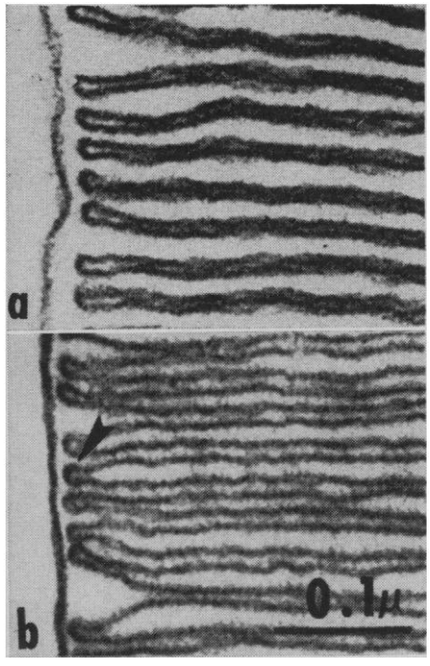

Fig. 2. Highly magnified portion of a foveal cone (*a*) and rod (*b*) from the same preparation. The disc membranes of the rod appear slightly thinner than the plasma membrane, except at the very edges of the discs (arrow), while the membranes of the cone discs are about as thick as the plasma membrane. The intra-disc space in the rods is larger than in the cones; the inter-disc space, smaller. (× 162,000)

is about 180 Å, so that the repeating distance is 310 Å. Thus there are about 30 discs per micron and 1200 discs in an outer segment measuring 40 μ long.

In the monkey retina, foveal cones are readily distinguished from rods by their fine structure. Figure 2 shows a highly magnified portion of a foveal cone (*a*) and a peripheral rod (*b*) from the same preparation. The disc membranes of the cones are about as thick as the plasma membrane (50 Å); the disc membranes of the rods appear somewhat thinner (35 Å), except at the edges of the disc where a slightly thickened, button-like ending is characteristic of rod discs (Fig. 2*b*, arrow) (*5*). The intra-disc space in the rods is larger than in the cones (110 Å as opposed to 40 Å), while the inter-disc space is smaller (110 Å as opposed to 180 Å). The repeating unit distance is about the same in both foveal cone and rod outer-segments (310 Å and 320 Å, respectively), so that both contain approximately the same number of discs per micron. Their thick disc-membranes, however, make the cones appear generally denser than the rods, especially when viewed at medium and low magnifications in the electron microscope. An additional difference between rods and foveal cones is striking when the outer segments are slightly swollen: in rods, the intra-disc space swells, leaving the inter-disc space intact; in cones the intra-disc space remains intact, and the inter-disc space swells. There is a suggestion of this in Fig. 2: in the rod it is the intra-disc space which is quite variable in width from disc to disc; in the cone it is the inter-disc space that shows the more variation. It should be noted that only one fixation procedure was used when these observations were made. To elucidate further differences in structure between rods and cones, other fixatives and preparative conditions will have to be tried.

It is now well established that the discs of the outer segments of both rods and cones are formed by infoldings of the plasma membrane (*4*, *6*). In the cones of lower vertebrates, the discs retain continuity with the plasma membrane in the differentiated retina, while in rods and in cones of higher mammals the discs tend to pinch off from the plasma membrane and appear free-floating in the outer segment (*4*). At the very base of the outer segments of mammalian cones, and occasionally in rods, continuity of disc with plasma membrane is seen in the adult eye, but the majority of the discs appear not confluent with the plasma membrane. In foveal cones, continuity of the discs with the plasma membrane is seen only occasionally, and then only at the very base of the segment. Confluences extend no farther than 5 μ from the base of the outer segment, so that the great majority of the segment shows no contact between disc and plasma membrane (Fig. 1).

In cross section, the outer-segments of the foveal cones are circular; they do not show the lobulations or incisions found in mammalian rods (*4*), and, except at the base of the outer segment, there is no continuity between disc and plasma membrane.

The inner segments of the foveal receptors also are thin and elongated (Fig. 3). They taper in width from about 2.5 to 3 μ at the base to about 1.5 μ at the tip, where they connect with the thinner (0.9 μ) outer segments. Rushton recently reported measurements of pigment (chlorolabe) from the foveal cones of man, by the technique of retinal densitometry (*7*). He found the apparent photosensitivity of the pigment to be some 5 times that of rhodopsin in the rods. This result seems unlikely, since it is thought that the photosensitivity of rhodopsin is close to the theoretically possible limit. To explain this discrepancy, Rushton postulates that the apparent great photosensitivity of chlorolabe is due to a funneling factor, the inner segments capturing a large fraction of the incident light and transmitting the light in-

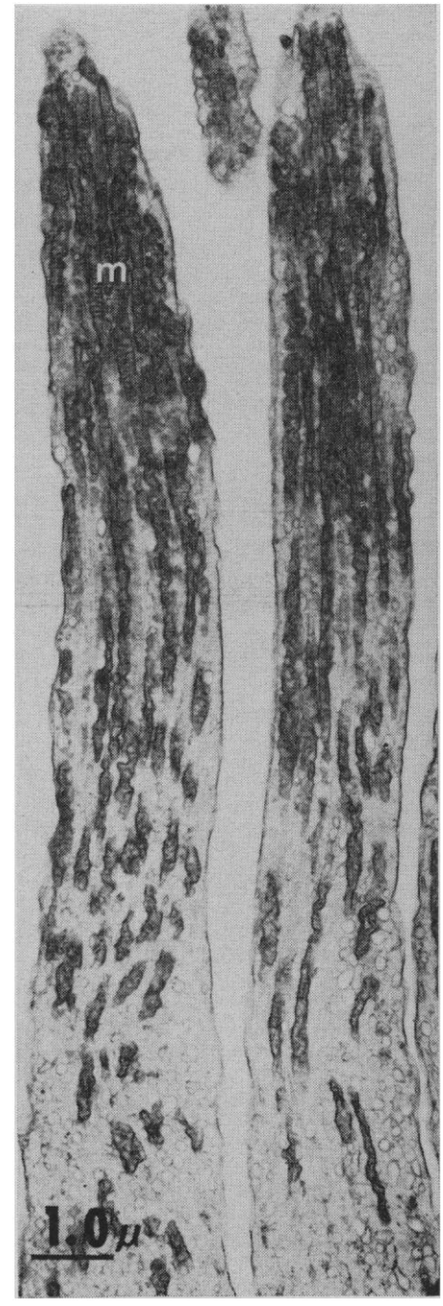

Fig. 3. Inner segments of foveal cone near the edge of the fovea. The inner segment contains many mitochondria (*m*), which are oriented lengthwise and concentrated in the distal portion of the outer segment. The inner segments taper from a base diameter of about 2.5 μ to 1.5 μ at the tip. (× 8820)

tact to the much thinner outer segments. In the extra-foveal regions of the retina this is clearly possible, since the base of the inner segments is considerably wider than the mean diameter of the outer segments (4 to 6 μ as opposed to 1.4 to 1.9 μ) (*1*, pp. 211–217). In the central fovea the inner segments are much thinner and taper only slightly. However, our measurements in the monkey show that even the thinnest inner segments of the fovea are still considerably thicker at the base than the outer segments (2.5 μ as opposed to 0.9 μ); so that, if, as Rushton suggests, two-thirds of the light reaching the inner segments is funneled into the outer segment, this could explain an apparent increase of photosensitivity of more than 5 times. If funneling does occur, it should also aid in single-cell microspectrophotometry, making possible the longitudinal measurement of single cells in the fovea with light beams having the diameters of the inner segments (2.5 to 3 μ) rather than that of the outer segments (0.9 μ) (*8*).

The inner segments contain many very long mitochondria, which are oriented longitudinally and concentrated in the distal portion of the structure. In favorably oriented sections, thin processes from the inner segment extend along the length of the outer segment, as has been described with other visual cells (*9*). The extent of these processes along the outer segments has not been determined. The inner segments of the foveal cones markedly resemble nearby rod inner-segments. Looking only at inner segments, one cannot tell when one moves out of the rod-free area of the fovea; looking at outer segments, however, the rods are instantly recognized as the viewer strays from the center of the fovea.

The terminal pedicles of the central foveal receptors look like those of other cones, except that they are somewhat smaller (Fig. 4*a*). Each pedicle is displaced laterally from the fovea and connects with the rest of its cell by a long fiber running outward from the central fovea. The pedicles are filled with synaptic vesicles and usually show multiple synaptic contacts, in any one section (Fig. 4*a*). The invaginated synaptic contacts are characteristically arranged in triads, with an accompanying synaptic ribbon surrounded by a cluster of synaptic vesicles (*9*) (Fig. 4*b*). In any one section, there appears to be a maximum of about four triads per pedicle; so that, if the triads are evenly distributed in the pedicle, they probably total about 12 triads per pedicle, or a minimum of 36 synaptic contacts per pedicle.

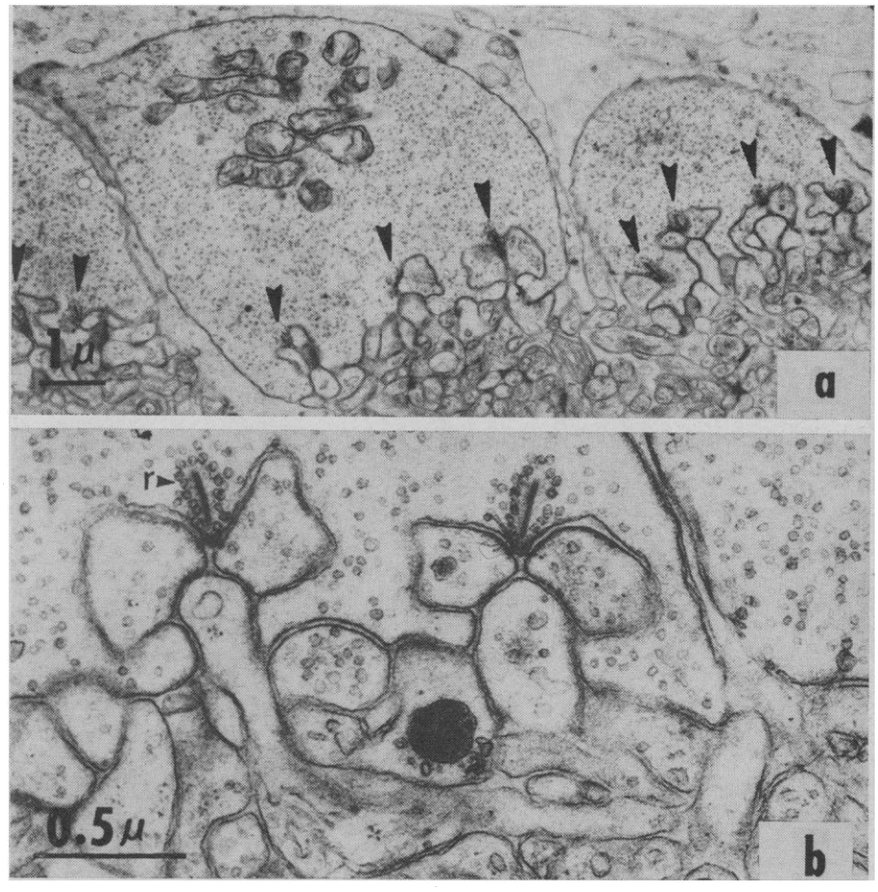

Fig. 4. (*a*) The synaptic pedicles of the foveal cones. The structure contains a few mitochondria and many synaptic vesicles. Several synaptic contacts are seen in each pedicle (arrows). (× 9000). (*b*) A blow-up showing triad arrangement of synaptic contacts and synaptic ribbon (*r*) with its surrounding cluster of synaptic vesicles. (× 40,000)

Polyak suggests that foveal cones connect with only a single bipolar cell (the midget bipolar cell), and that each midget bipolar cell synapses several times with its "private" cone (*1*, p. 280); but it is difficult to understand why a single bipolar cell would need to synapse so many times with the same cone pedicle. Some of the contacts may be horizontal-to-receptor cell contacts, but it seems unlikely that these would account for a substantial number of the contacts seen. Furthermore, there may very well be other contacts that do not invaginate into the pedicle (*10*). I have also searched for receptor-to-receptor contacts between cone pedicles, which have been reported to occur in retinas of other species (*11*) and which are clearly seen in extra-foveal regions of the monkey retina; I have found none. However, proving that receptor-to-receptor contacts do not exist in the fovea, or that foveal cones synapse with more than one bipolar cell, will require study of serial sections; this is yet to be done.

JOHN E. DOWLING

Alan C. Woods Research Building, The Wilmer Institute, Johns Hopkins Hospital, Baltimore, Maryland 21205

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