MICROCIRCUITRY OF THE CAT RETINA

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INTRODUCTION

As a device for extracting information from a visual image, the vertebrate retina is unparalleled in its range, reliability, and compactness. Signaling in the retina is slower by six orders of magnitude than in an integrated digital circuit. The advantage of the biological structure must therefore derive from the variety of its fundamental elements and from the subtlety of their connections. Each of the five major classes of retinal neuron, whose synaptic contacts were first described systematically by Dowling & Boycott (1966), is now known to have multiple types, totaling in the cat about 60. Specific local circuits involving about one-third of these neurons have been recognized in the electron microscope. Physiological responses have also been documented for about one-third of the types, and evidence regarding the neural transmitter, or at least the sign of the synapse, has accumulated also for about one-third.

These discoveries have abundantly supported certain concepts of retinal function developed in the 1960s by Letvin & Maturana. The function of the retina, they proposed, "is not to transmit information about the point-to-point distribution of light and dark in the image, but to analyze this image at every point in terms of... arbitrary contexts..." (Maturana et al 1960). Each of these "contexts," they suggested, corresponds to some operation on the local image performed by a ganglion cell of particular size and shape (Letvin et al 1961). This idea, based on studies of the frog, seemed for a time inapplicable to the cat, which was thought to have a "simple" retina with only center-surround type ganglion cells. Subsequent studies to be reviewed here have firmly established for the cat the validity of this idea.
In describing a cell type 1 infer, where the data permit, its "birefringence factor." The physiological coverage factor is the number of neurons of a particular type whose receptive fields overlap a particular point on the retina. It is calculated for a given point as the receptive field areas (mm²) X the cell density (cells/mm²). The anatomical coverage factor is similar; the number of cells of a given type whose dendritic fields overlap a particular point. It is calculated similarly, as the dendritic field areas (mm²) X the cell density (cells/mm²). The coverage factor for a given eccentricity appears to be characteristic for each cell type. Another useful analytic expression introduced by Wiesel & Riemann (1970) as a measure of regularity in a pattern is the ratio, mean/standard deviation. The higher this ratio, the greater the regularity. This ratio, too, is apparently characteristic for a given feature of a specific cell type.

Receptors

RODS. Only two types of photoreceptor have been identified in the cat retina, rods and cones. The rod has an extremely fine outer segment, which increases in diameter (0.5 μm to 1.6 μm) and length (25 μm to 50 μm) from the periphery to the central area (A. Lalos, cited by Barlow & Hill 1971; C. Steinberg et al 1973). The rod soma is small (4.5 by 6 μm) and the inner segment is narrow (2 μm). The axon is extremely fine (0.25 μm), ending in a "spherule." The axon of the outer half of the outer plexiform layer. The spherule, which contains mitochondria and 1-2 synaptic ribbons, is invaginated by 2-3 laterally placed processes from horizontal cells and two centrally placed processes from rod bipolar cells (Figure 1; Beycoat & Kohl 1973, Kohl 1974, Kohl 1977). The rod spherule receives 4-6 punctate gap junction contacts from the same processes of neighboring cone pedicles (Kohl 1977).

The response of the cat rod to light must be inferred from the responses of rods in other species and from responses of neurons postsynaptic to rods in cat. In darkness, according to Penn & Hagan (1972), a steady depolarizing chloride current flows in the interstitial space and enters the rod outer segment (RDS). This "dark current" is suppressed transiently by a flash of hyperpolarizing light, which reduces the chloride current. The amplitude of the rod photoreceptor increases with light intensity until the dark current is just balanced. Beyond this point, which corresponds psychophysically to the rod saturation, increases in light intensity increase the photoreceptor's rate of rise and greatly prolong its duration (to more than 30 min; Penn &
example, chromatic differences between cones are associated with morphological differences (Sebba 1975, Stell & Lightfoot 1975). Such correlations have not been observed in the cat, nor has the mosaic distribution of the chromatic types been determined as in goldfish (Mace & Sperling 1976) and monkey (Mace & Sperling 1977, DeMonasterio et al 1981). The retinotopic
situation demonstrated for cones in the turtle (Baylor et al 1971) has not been found in cat, possibly for technical reasons (Nelson 1977).

Among the more astonishing of recent findings is the discovery that cones have input from rods (Nelson 1977). The main lines of evidence, illustrated in Figure 2, are as follows: The threshold of the 556 nm cone to a rod stimulant (blue, 441 nm) is the same as the rod's threshold and about 3 log units below the cone's threshold to a cone stimulant (red, 647 nm). The cone's response function to blue light of increasing intensity shows a break at rod-saturation, whereas its response function to red light is smooth. Finally, the rod after-effect is recorded in cones. This rod input is presumably mediated by the rod-cone gap junctions. Evidence of the reverse pathway, passage of the cone signal to rods, has not been obtained from rod bipolar, where it might have been anticipated (Nelson et al 1976). Whether this reflects rectification at the gap junction or simply dilution of the cone signal among the rods, which are at least ten times more numerous, is unknown. It seems clear, however, that rod and cone signals mix in the cone pedicle before transmission to the horizontal cells.

**MOSAIC DISTRIBUTION OF RODS AND CONES**

The rods are arranged in well-defined rows; each rod is surrounded by six others (Figure 1). Their density reaches a maximum of 460,000/mm² at an eccentricity of 10–15° and is high (275,000/mm²) even in the central area (Steinberg et al 1972). The cone density reaches a maximum of about 20,800/mm² in the central area, where the rod/cone ratio is 10.6, and falls to 3100/mm² in the periphery, where the rod/cone ratio is 90 (Steinberg et al 1972; see also Hill and Stone 1972, Wässle & Riemann 1978). The distribution of cones appears upon simple inspection to form a regular pattern (Figure 2). The reason for this impression, expressed by Wässle & Riemann (1978), is that the distances of each cone to its nearest neighbors are regular. The distribution of those distances is Gaussian and the ratio, mean standard deviation, is relatively low. A standard of comparison is the distribution of nearest neighbor distances for a random dot pattern of the same density. This distribution is skewed and the ratio, mean/standard deviation, is relatively low. Wässle & Riemann made their measurements on what is almost certainly a heterogeneous population. When these measurements can be repeated on distributions for individual cone types, the degree of regularity may be even greater. This

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**Figure 2**

Retinal microcircuitry. Density for cones, 18 X 10⁶/mm², for rod, 33 X 10⁶/mm². About 1 mm from central area. Density for cones, 11 X 10⁶/mm², for rod, 57 X 10⁶/mm². Reprinted from Steinberg et al 1975.

*Type A* and *B* are two types of horizontal cell in the cat retina (Dowling et al 1966, Fisher & Boycott 1974, Kolb 1977, Boycott et al 1978). Type A has a large soma (12 by 15 um), an indented nucleus, and 4-6 thick, filament-packed dendrites radiating to form a circular or oval field about 80 µm in diameter. Type B has a smaller soma, an unindented nucleus, and densely branched, relatively slender dendrites radiating to form a circular field about 50 µm in diameter. Clusters of terminals from the micro dendrites of both cell types lie in register with the overlying cone pedicles to form the lateral elements of the triad. In each triad one lateral element: is from type A and the other from type B (Kolb 1974, Boycott et al 1978). Neither type of horizontal cell makes or receives typical chemical synaptic contacts. The type A cells, however, commonly form gap junctions with each other and, less commonly, 'basal junction' type contacts with cone bipolar cells (Kolb 1977), at least one of which is the type B of McGugan et al (1980). The type B horizontal cell emits a fine (0.5 µm) axon.

*Cell sizes and dendritic diameters, unless otherwise noted, are given for the central area.
that meanders for 300–500 \( \mu m \) before producing an elaborate arborization whose terminals penetrate the rod sphere to form the lateral elements of the triad. Each triad receives from two different axons (Kolb 1974, Nelson et al 1975, Boycott et al 1978).

**MOSAIC DISTRIBUTION** The mosaic distribution of each horizontal cell type is regular and independent of the other. The densities of both types peak centrally and decline peripherally, though their ratio (2.7 B/A) remains constant. This decline is offset, however, by a corresponding increase in dendritic field diameter so that the coverage factor (see above) for each type remains constant at about 4 (Figure 5), except in the central area where the coverage by type B increases to 7 (Wassle et al 1978). In a four-force of quantitative light microscopy, Wassle et al (1978a) estimated that each type A cell contacts 120–170 cones and each type B cell contacts 60–90. (Every cone is connected with several horizontal cells of each type.) They argued that since each horizontal cell contacts at least 80% of the cones in its field, at least 80% of the cones must be contacted by both types and there can be no strict selectivity of each type. The axon of type B contacts 2000–3000 rods (Wassle et al 1978a).

![Figure 4](Image)

**PHYSIOLOGY** Intracellular recordings followed by dye injection (Nelson et al 1975, Nelson 1977) show that the A and B somas and also the B axon respond to a flash of light with a sharp, sustained hyperpolarization, called the "S-potential" (Steinberg 1969a, 1971, Steinberg & Schmidt 1970, Nelmayer & Gouras 1973). To a dim flash the response is rod-generated with a spectral sensitivity peaking at 500 nm, coincident with the absorption peak of rhodopsin (Steinberg 1969a). The amplitude of the S-potential increases with intensity to about 2.5 log units above threshold. At higher intensities (3 log units or more above threshold) the peak amplitude is saturated but the S-potential's return to baseline is greatly prolonged, and this is the rod after-effect whose basis is described above.

Rod input to the B type B axon terminal probably comes directly from the rod sphere in which it is housed. This, however, is probably not the source of rod input to the type B somas because the connecting axon does not spike and seems too thin to conduct much of the rod signal passively (Nelson et al 1975). Further, were the B axon to convey rod signals, the soma's rod receptive field would be offset from its cone receptive field, but in fact they are almost exactly superimposed (Nelson 1977). The rod signal to the A and B somas is believed to be conveyed from rod sphere to cone pedicle and thence to the dendrites of these horizontal cells.

To a bright flash, three log units or more above rod threshold, the S-potential in the type A and B somas is cone-driven (Figure 6). Experiments with chromatic adaptations indicate the input to be overwhelmingly from the 556 nm cone with no evidence of contributions from the 430 or 500 nm types (Nelson 1977). The axon terminal of type B shows relatively little response to cone stimuli (Nelson et al 1975).

The horizontal cell receptive fields show spatial summation over 1.0–1.7 mm for rod stimuli and over 0.8–1.0 mm for cone stimuli (Steinberg 1969a).
with space constants ranging from 210–410 μm (Nelson 1977). The larger space constants probably belong to the type A cells with their larger dendritic fields and gap-junction interconnections (Nelson 1977). Intracellular recordings in vivo provide evidence for three classes of response based on the critical flicker frequency, but their assignment to the three anatomical types of horizontal cell process is not yet established (Foerster et al. 1972a,b).

In species other than cat the horizontal cell hyperpolarization induced by a broad field stimulus feeds back to the cone as a depolarization, thereby providing the cone with an antagonistic surround (Bayly et al. 1971). Cone bipolars, which share the cone triad with horizontal cell dendrites, also have antagonistic surrounds (Werbin & Dowling 1969, Kaneko 1970, Schwartz 1974). Whether the cone bipolar surrounds arise directly from horizontal cell input or indirectly via the cone's surround is unknown (reviewed by Kaneko 1979).

To assign distinct functions to the A and B horizontal cells in the cat is at this point speculative. One might suggest that the type A horizontal cell, activated either by rod or cone input, provides the antagonistic surrounds of the cones and/or cone bipolars. The axonal terminals of the type B horizontal cell might conceivably perform a corresponding function for rods and/or rod bipolar input, but there is no evidence for any species that rods or rod bipolars have surrounds. On the contrary, rods show broad spatial summation (see above), apparently maximizing sensitivity at the expense of contrast-enhancing mechanisms. The dendritic terminals of type B might act in a similar fashion to those of type A, but this would not explain why the two types should inhabit the same cone, nor would it offer a role for the axonal pathway connecting the axonal and dendritic terminals of type B.

One function for the type B horizontal cell might be to regulate the direct rod → cone pathway. This pathway might be open under mesopic illumination, giving rods access to high-sensitivity, cone bipolar pathways, and closed at the end of dark adaptation when rod bipolars are thought to take over and acuity is sacrificed for the last degree of sensitivity (see Microcircuitry of the Beta Ganglion Cell Receptive Field, below; Sterling & Megill 1983). The rod after-effect recorded in the type B axon terminal, when the rods are saturated, might represent the state of adaptation. This prolonged hyperpolarization might be transduced to a chemical signal that might be conveyed by axoplasmic transport to the type B dendritic terminals in the cone pedicle. Here, the hypothetical substance would hold the rod → cone pathway open. This signal would decay during dark adaptation, consequent to the decay of the rod after-effect, allowing the rod-cone pathway to close after about an hour in the dark. Such chemical signaling would require an axoplasmic transport rate of about 12 mm/day which is well within the known rates. This speculation is unsupported by evidence but links several physiological and anatomical observations for which at present there is no other interpretation.

**Bipolar Cells**

Cajal (1893) observed that certain bipolars in mammals are associated exclusively with rods (rod bipolars) and others exclusively with cones (cone bipolars). Boycott & Kolb (1973), examining Golgi-imregnated bipolars by electron microscopy, showed that in the cat rod bipolar dendrites do indeed form the central elements of the triad in rod spherules (Figure 1A). Rod bipolar spherule terminals end in sublamina 9 of the inner plexiform layer where they receive input from reciprocal and nonreciprocal amacrine and send output to reciprocal and AII amacrine (Kolb & Famiglietti 1974, Kolb 1979, McGuire et al. 1983b).

 Cone bipolar dendrites were shown by Boycott & Kolb (1973) to be associated only with cones (Figure 1B). They found the dendrites of certain cone bipolars, called "imagining," to form the central element of the cone pedicle triad and the dendrites of other cone bipolars, called "flat," to form superficial contacts with the cone pedicle at some distance from the synaptic ribbon. This distinction proved good evidence when rod fibers from other species showed that invaginating cone bipolars depolarize to illumination of their receptive field centers, whereas flat cone bipolars are hyperpolarized (reviewed by Kaneko 1979). Surprisingly, the rod bipolar, despite its invaginating, ribbon-related dendrite, is hyperpolarizing (Figure 7A; Nelson et al. 1976).

It was believed at first that axons of flat (hyperpolarizing) bipolars terminate exclusively in the outer third of the inner plexiform layer (sublamina a) and those of invaginating (depolarizing) bipolars exclusively in its inner two-thirds (sublamina b) (Famiglietti & Kolb 1976). This fit the observation that ganglion cells branching exclusively in sublamina b are retin
Figure 7 A. Hyperpolarizing response of rod bipolar in r-5-staining, blue (441 nm) stimulus of increasing intensity (roughly half log unit series). Note similarity to cone response (Figure 2A). B. Ressponse of All-association to similar stimuli (intensity increasing from top to bottom). Note all-or-none response followed by prolonged de-polarization. Arrows mark "cone mode" seen at stimulus "off." Calibrating pulse 2 sec, flash length 500 msec. Reprinted from Nelson et al. (1976).

A   B

Figure 8 Five types of bipolar partially reconstructed from electron micrographs of serial sections. a, CB1b, flat, cone bipolar ending in sublamina c; CB2a, invaginating cone bipolar also ending in c; CB3b, cone bipolar invaginating, ending in sublamina c; CB4a, cone bipolar terminating fast, mixing in; & a Nerve cell bipolar ending in sublamina a; & b, CB5a, cone bipolar terminating slowly, mixing in. Reprinted from McGuire et al. (1983b).
Table 1 Characteristics of four types of cerebellar 

<table>
<thead>
<tr>
<th>Type</th>
<th>Cerebellar Type</th>
<th>Inputs</th>
<th>Outputs</th>
</tr>
</thead>
<tbody>
<tr>
<td>CB1a</td>
<td>F</td>
<td>All</td>
<td>NRES, BRES, NRES, BRES, DBS, TCRS</td>
</tr>
<tr>
<td>CB1b</td>
<td>J</td>
<td>NRES, BRES</td>
<td>DBS, TCRS</td>
</tr>
<tr>
<td>CB2a</td>
<td>J</td>
<td>NRES, BRES</td>
<td>DBS, TCRS</td>
</tr>
<tr>
<td>CB2b</td>
<td>F</td>
<td>All</td>
<td>NRES, BRES, DBS, TCRS</td>
</tr>
</tbody>
</table>

Both types have outputs in different proportions, to reciprocal and non-reciprocal amacrine and to stellate (on-beta) and amacrine (probably on-alpha) ganglion cell dendrites. CB2b may accumulate excessive H-glycine (McGuire et al. 1983b, Sterling et al. 1983).

Amacrine Cells

Golgi-impregnated amacrine neurons in the cat retina have been sorted into at least 22 types based on differences in soma size and in the length, stratification, and morphology of their processes in the inner plexiform layer (Kob et al. 1981). The expectation by now is strong that each morphological type will also have a specific wiring pattern and physiology. Anatomical support for this belief comes from partial EM reconstructions of amacrine processes that show consistent correlations between the morphology and synaptic patterns (Kob 1979, Sterling & Meghill 1983). Simultaneous physiological and anatomical mapping for the view comes from intracellular recordings in three amacrine types followed by electron microscopy of their HRP-injected processes (Kob & Nelson 1981).

Amacrine types have also been identified by their association with a particular neuronal transmitter (Table 2). Such data can and yet be perfectly integrated with the Golgi and physiological studies but we shall see (see section below on Microcircuity of the Inner Field) that where integration is possible, rather specific hypotheses emerge regarding function.

BIOGENIC AMINES, NEUROPEPTIDES, AND ACETYLCHOLINE

One type of amacrine in the cat retina fluoresces for catecholamines (Elgin 1966, Boycott et al. 1975) and is apparently dopaminergic (Kramer 1971, Kramer et al. 1971). Tögel & Stoos (1979) described this type as a large cell distributed at a density of 40-20/ mm², whose interwoven dendrites form rings of catecholamine fluorescence at the base of another amacrine type. Kob et al. (1981) argue convincingly that this dopamine amacrine corresponds to the wide-field (about 500 µm) amacrine, A10. The coverage factor at a density of 40/ mm² and a field diameter of 300 µm is 7.9. Pierce (1981) has shown that the cells enclosed by the dopaminergic rings and postsynaptic to them is the A11 amacrine. An iodolamine amacrine was described along with its synaptic contacts by Hofmein et al. (1974), and amacrine immunoactive for substance P, vasoactive intestinal polypeptide, and possibly choleptokhinin have been observed by H. Karten and N. Brecha (unpublished observations). Choline acetyltransferase activity in the cat retina is less than a tenth that in the rabbit (Roth & McDougal 1976), whereas Maldonado & Mills (1979) have identified choline amacrine. The enzyme in the cat retina is high, however, in the amacrine and inner plexiform layers, thus suggesting that at least one amacrine type is cholinergic.

Table 2 Amacrine transmitters

<table>
<thead>
<tr>
<th>Transmitter</th>
<th>Cell density</th>
<th>Field depth</th>
<th>Coverage</th>
<th>Percentage of total area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopamine²</td>
<td>400/µm²</td>
<td>200 µm²</td>
<td>7.9</td>
<td>1</td>
</tr>
<tr>
<td>GABA accum.</td>
<td>900/µm²</td>
<td>200 µm²</td>
<td>4.4</td>
<td>28</td>
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<tr>
<td>GABA IV</td>
<td>500/µm²</td>
<td>150 µm²</td>
<td>4.8</td>
<td>25</td>
</tr>
<tr>
<td>GABA IV</td>
<td>500/µm²</td>
<td>150 µm²</td>
<td>4.8</td>
<td>25</td>
</tr>
<tr>
<td>A12</td>
<td>5000/µm²</td>
<td>35 µm²</td>
<td>10.6</td>
<td>67</td>
</tr>
</tbody>
</table>

Indoleamine

Substance P

Vasoactive intestinal polypeptide

Choleptokhinin

Acetylcholine (no morphological identification)}
AMINO ACIDS. Gamma aminobutyric acid (GABA) and glycine are widely considered to be transmitters in the mammalian retina because of their high endogenous levels, the presence of the GABA synthetic enzyme glutamic acid decarboxylase (Graham 1972, Wood et al 1976, Hramov et al 1976), the light-evoked, calcium-dependent release of glycine (Elzinga & Lindberg-Bauer 1976), and the potent physiological effects of their agonists (Kirby & Elzinga-Currell 1976, Kirby 1976, Saito 1974, Caldwell & Daw 1978). Many neurons in the cat amacrine layer accumulate 3H-GABA or 3H-glycine following intravitreal injections (Dreyer & Elzinga 1974, Marshall & Vassan 1975), and the problem since this discovery has been to determine which specific amacrine types are involved and the nature of their circuitry.

Five cell types accumulating GABA have been described by partial reconstructions from serial, electron microscope autoradiograms (Fried et al 1985), and one of these has been identified more specifically as the interplexiform cell (Nakamura et al 1980). This type is known from Golgi studies (GALA1971, Hoycott et al 1976) to ramify in the outer and inner plexiform layers. The dendritic field diameter of the best Golgi-impregnated interplexiform cell is about 30 µm (Figure 8, Hoycott et al 1976), and the type is distributed near the central area at a density of about 90/mm². The coverage factor calculated from these figures is about 4.4. The cut interplexiform cell receives amacrine input and has output to amacrine. The cell also provides output in both the outer and inner plexiform layers to rod bipolar and cone bipolar cells of both the fast and interstimulating types (Koizl & West 1977, Nakamura et al 1980, McGuire et al 1983B). One might well wonder what the function of such a cell could be that innervates, and perhaps affects simultaneously, all bipolar cells of the opposite responses to light. One possibility is that the interplexiform cell might function in dim light as part of a gain-control system for bipolars.

ALL AMACRINE. The best characterized amacrine in the cat retina is the AII, first described from Golgi and electron microscopic studies (Kolb & Famiglietti 1974, Famiglietti & Kolb 1975) and later from detailed reconstructions (Sterling & Megill 1983). The AII cell, with a medium soma (about 9 µm) and narrow dendritic field (about 35 µm near the central area), sends a distinctly different set of processes to each sublamina. To sublamina b it sends radially a single stumpy process that branches to at least the eighth order and contains large mitochondria. To sublamina a it sends laterally fine processes that swell into large varicosities ("lobular appendage") and contain large mitochondria and synaptic vesicles.

The base of the AII soma bears a dozen synaptic contacts (Sterling & Megill 1983) that are apparently from the dopaminergic amacrine (Fou-

![Figure 9. All amacrine and its synaptic connections partially reconstructed from electron micrographs of 10,000 serial sections. Radial process branches to sublamina b, and receives two aspects of the AII soma.](image-url)
bipolar CB4, and to a lesser extent with types CB6 and CB8 (McGuire et al. 1983b). Aminergic staining, underestimated in its origin, distributes sparsely over the AII dendrites in subalbina (Sterling & Magill 1983). The AII lobular appendages in subalbina appear to receive input from cone bipolar CB4a (McGuire et al. 1983b) and the dopamine aminecrine (Fountas 1981). The chemical synaptic output of the lobular appendage is directed to other aminecrine, ganglion cells, and cone bipolar, specifically type CB8 (Famiglietti & Kobs 1975, Kobs 1979, McGuire et al. 1983b).

The AII response to light is an all-or-none, depolarizing transient followed by a sustained depolarization (Figure 7b, Nelson et al. 1976). This response, as anticipated from the circuitry, is strongly rostro-dorsal. There is also evidence at higher stimulus levels for a small cone bipolar (Nelson et al. 1976) suggested may enter the AII via its gap junction with cone bipolar. The AII accumulates 3H-glycine (Nakamura et al. 1974, Porroco 1980, Sterling & Magill 1983). Its lobular appendages may, therefore, be glycergic (inhibitory). The AII is the most numerous of the aminecrine types, representing more that one quarter of all cells in the amacrine layer (Sterling & Magill 1983). Its distribution near the central area is quite regular, with a density of about 500 neurons/0.25 mm^2. Potential morphological types, including an axon of about 4.7, possible, and morphological types, many of which have been illustrated by Cejal (1982), but whether these represented discrete types or a continuum was unclear (Brown & Majes 1986).

The number of recognized physiological types doubled in 1966 when Enroth-Cugel & Robson distinguished on- and off-center X and Y type ganglion cells. These were later described also by Chelran et al. (1971) as "brisk-sustained" and "brisk-transient." By 1974 fully a dozen physiological types had been described (reviewed by Rodieck 1979, Rowe & Stone 1977, Stone et al. 1979), and in that year as well the problem of morphological-typing was essentially clarified. The crucial step in defining discrete morphological types of ganglion cell was to compare neurons at equivalent retinal positions (Boyce & Wadsell 1974). With this approach, two fundamental types, termed alpha and beta, suddenly became obvious (Table 7). The alpha has a large soma and a wide-field (180-2000 mm diameter) swardly branched dendritic tree. The beta has a medium soma and axon, and a narrowly (20-300 mm diameter), densely branched, dendritic tree (Figure 10). Each type is represented at all eccentricities and increases in size from center to periphery. Evidence that alpha cells are physiologically brisk-transient (Y) while beta cells are brisk-sustained (X) was obtained from comparisons at a given eccentricity between soma and dendritic field size on the one hand, and axonal conduction velocity and receptive field center size on the other (Chelran & LeVick 1974).
Table 3: Characteristics of alpha and beta ganglion cells in central retina

<table>
<thead>
<tr>
<th>Cell type</th>
<th>Size</th>
<th>Density</th>
<th>Physical coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>on-alpha</td>
<td>17 μm^2</td>
<td>848 pm^2</td>
<td>52 pm^2</td>
</tr>
<tr>
<td>off-alpha</td>
<td>20 μm^2</td>
<td>66 pm^2</td>
<td>3250 pm^2</td>
</tr>
</tbody>
</table>

Input: from... Output: to...

<table>
<thead>
<tr>
<th>Cell type</th>
<th>Cb_{1-4}</th>
<th>Cb_{5-9} +</th>
<th>All spines (a,b)</th>
<th>All spines (a,b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>on-alpha</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>off-alpha</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

*Wassle et al. 1984b.*

Cleland et al. (1975) mapped the position of every brisk-transient cell in a small patch of retina. Subsequently they identified all the alpha cells in the same patch and showed the correspondence to be essentially complete. They showed further that over a wide range of eccentricities every retinal locus is covered by the receptive fields of 3–7 alpha cells. Although the distribution density of alpha cells declines from the central area outward, at each locus they are a constant fraction (about 4%) of the total ganglion cell population (Wässle et al. 1972). Their increase in dendritic field diameter with eccentricity offsets their decline in numbers; this is the reason the coverage factor is constant.

When Boycott & Wässle (1974) pointed out the resemblance between a central alpha cell and a peripheral beta cell, the roof of much cloud and confusion was exposed. Since then, anatomical observations have been reported in the context of their ecentricity and the conclusion of Kolb et al. (1981) that there are several dozen types of ganglion cell is consistent. Boycott & Wässle (1974) also described several types of smaller ganglion cells with radially dendritic trees, termed gamma and delta, and to this Leventhal et al. (1980) have added the epsilon cell. Kolb et al. (1981) have

Figure 10: Micrograph from retina flat-mount stained with Golgi-Cox. Dako phase thymo... sufusin B of outer plexiform layer. Narrow-field cell with bushy dendrites on left is an...n-beta ganglion cell. Dorsal retina in right with dendrites cut out of focus. In奢usin B is...a beta. Sparsely-branched dendrites, belonging to two on-alpha cells, overlap the whole field. Reproduced from Wässle et al. (1984b).
exclusively in a, they proposed that ganglion cells branching in b are on-center, while those branching in c are off-center. Intracellular recordings from ganglion cells followed by dye injection confirmed this conjecture (Nelson et al. 1975). Only later was it learned that flat and invaginating cone bipolar interneurons both sublaminated (see Section above on Bipolar Cells). In summary, dendrites of off- and on-center ganglion cells stratify, respectively, in sotluminae a and b (see also Pichl & Wässle 1981, Wässle et al. 1981b), and appear in each sublamina to receive input from both depolarizing and hyperpolarizing bipolar cells (McGuire et al. 1982b,c).

**ALPHA CELLS** Knowledge of the on- and off-alpha cells' dendritic stratification permitted Wässle et al. (1981a) to work out, using neurofibrillary stains selective for alpha cells, their detailed distributions in the retinal mosaic. The on-alpha was found to be slightly smaller and less numerous than the off-alpha, and the coverage factor for each type, respectively, was 1.4 and 1.7. The distribution of somas formed a regular lattice independently for each alpha type. For such a lattice the ratio, mean/s.d., for the distribution of nearest neighbor distances is about 0.5 whereas this ratio for a random distribution of the same density is 2.4. By this measure (mean/s.d.) the distribution of on-alpha dendritic field diameters for a small patch of retina is also extremely regular, (as numerical value being 10.9 (Wässle et al. 1981a); Pichl & Wässle (1989) found similar regularity in the size of receptive field centers within a small patch of retina.

**BETA CELLS** Across most of the retina the beta cells constitute about 55% of the ganglion cells, the on-betas being slightly less numerous than the off-betas (Pichl & Wässle 1979, Wässle et al. 1981b). Their density is highest in the central area (about 3250 cells/mm² for each type; Pichl & Wässle 1979) and their dendritic fields the smallest (about 30 µm diameter; Boycott & Wässle 1974). Each beta type forms a regular lattice (Figure 15) that is independent of other, and provides an anatomical covariance factor in the central area of about one. The minimum diameter of the physiological receptive field center is about 66 µm, providing a physiological coverage factor for each type of about 11 (Pichl & Wässle 1979). This spacing and field size matches closely, according to Higashiyama (1981), the optimum predicted from clamping theory for a system that can resolve about 6 cycles/deg. using elements with the cut-off frequencies of the beta cells (Cleland et al. 1979). Thus the evidence suggests that the maximum spatial resolution demonstrated behaviorally is in the order of 7 cycles/deg. (Higashiyama 1981) depends on the simultaneous reports from these two types of beta ganglion cells. This is consistent with the observation of Berkeley & Sprague (1979) that the major effect of removing area 17 (in which beta cells project via the lateral geniculate nucleus) is a loss of spatial resolution.

![Diagram](Figure 11) (a) Retinotopy grid showing 150 of all beta cells in a small field. (b) Same field with only on-betas drawn. Note regularity of mosaic. Binning indicates (dendritic field of a beta cell from Origin material as were accessibility. Below, distributions of distances to nearest neighbor for drawings of all (c) Mean/s.d. for all beta cells. (d) Mean/s.d. for on-betas only. (e) Reproduced from Wässle et al. 1981b).

**CIRCUITRY OF ALPHA AND BETA GAMMONT CELLS** Once the alpha and beta types of ganglion cell were defined by light microscopy, they could be recognized in serial sections at the electron microscope level and a start could be made in defining their circuitry. The first observations showed that the inputs to each type are not on the soma but are concentrated on the dendrites in the sublamina of the cell's major arborization (Kolb 1978, Stevens et al. 1981). Beta cells receive over 70% of their input from cone bipolar cells, whereas the alpha cells get relatively more of their input from amacrines (Kolb 1979). McGuire et al. (1982b) found that all four cone bipolar types in sublamina a (CBa, CBc) and all three types in sublamina b (CBa, CBc) contact dark ganglion cell dendrites (presumed beta) and pale ganglion cell dendrites (some probably alpha). Thus, whatever information is conveyed to the inner plexiform layer by this heterogeneous group of bipolar neurons, it all appears to reach both the alpha and beta ganglion cells.
The convergence onto on- and off-beta cells from two pairs of cone-bipolars was reconstructed in more detail (McGuire et al. 1985c). The partially reconstructed beta cells had adjacent somas near the central area and overlapping dendritic fields estimated to be 50–40 μm diameter. The on-beta reconstructed to its sixth order branches received a total of 69 synaptic contacts from three C8β cells and 34 contacts from a single C8β cell (Figure 13). The contacts from C8β were concentrated on the proximal dendrites in strata 4–5, while those from C8β were concentrated more distally in strata 3–4. The off-beta, reconstructed to its seventh order branches, received 23 contacts from a single C8β, and 14 from a C8β. The actual proportions of input from the different bipolar types cannot be read from these data, because the reconstructions were incomplete. It was estimated, for example, that the on-beta might actually collect as many as 400 contacts from up to six cone bipolars. Clearly, however, each type of beta cell receives substantial input from at least two types of cone bipolar. The possible functions of these arrangements are discussed below (See Microcircuitry of the Beta Ganglion Cell Receptive Field).

The diameter of the receptive field center of an alpha cell corresponds almost exactly to the diameter of its dendritic field. In contrast, the receptive field center of the beta cell is about three times larger than its dendritic field (Polish & Wilke 1979). According to Huchstein & Shapley (1975), the alpha's receptive field center contains nonlinear subunits corresponding roughly in size to the beta's receptive field center. These authors suggested that both the subunits of the alpha cell and the full receptive field center of the beta cell might correspond to the receptive field of a single bipolar.

Although it is now clear that each beta cell receives from several bipolars, this basic idea may still have merit. The relationship between a single cone bipolar and its target beta cell is strong, the narrow-field bipolar richly enveloping the beta's dendritic tree and investing it with multiple contacts (Kolb 1979, McGuire et al. 1985c). These contacts distribute widely over the beta's dendritic tree, which might contribute to the linear summation of their postsynaptic effects (Rall 1967). The relation of the same cone bipolar and its target alpha cell is both weaker and more punctate, the bipolar contributing a smaller number of contacts to a relatively short segment of the alpha dendrite. The postsynaptic effects of these contacts, which are locally concentrated, might tend to sum nonlinearly (Rall 1967). Obviously, more detail must be gathered on the alpha cells' circuitry before this argument can be pursued.

**Summary of Retinal Cell Types**

The crucial insight emerging from the work reviewed here is that the neurons in the cat retina belong to discrete types. A “type” has come to be defined by the regular association of particular morphological, cytological, connectional, chemical, and physiological features. Thus, among ganglion cells, neither soma size nor dendritic branching pattern alone defines a fundamental type. The strict association, however, of medium size and “busky” dendritic branching restricted to sublamina b, and the physiological properties, “K-isms,” brisk-sustained, and on-center, define what is almost certainly a fundamental type, the on-center beta/X cell. Similarly, the accumulation of a particular neural transmitter does not define a type because neurons of several different morphologies accumulate the same transmitter. But a strict association between accumulation of a particular transmitter, such as glycine, and a distinctive morphology, connectivity, and physiology does define a fundamental type, the glycine-accumulating, depolarizing, All amacrine. Each type, so defined, turns out to have a characteristic stoichiometry and distribution in the retinal mosaic; thus further supporting the idea that the type is fundamental.

In certain respects, the definition of a type is not absolute but relational. Thus, the on-alpha cell cannot be defined by its absolute dendritic field.
diameter because this increases about five-fold from center to periphery. Nor can the alpha be defined by its absolute distribution density, because this falls from center to periphery by about sixteen-fold. The relation between these two features is strong, however, so that coverage factor at every retinal locus is the same and this becomes a defining feature of the type. Furthermore, although the on-alpha's absolute density changes, its fractional relationship to the other ganglion cells remains constant across the retina at about 40%, and falls, too, in a defining feature. The same is true physiologically. Absolute receptive field size is from center to periphery, but the fundamental properties, y gap, brisk latency, and on-center, can be recognized as varying eccentricity. This is probably because the synaptic relationships are constant between the on-alpha and the various cell types that provide its input. Direct evidence on this point is badly needed.

For a particular cell type at a given retinal locus there is evidence, though still fragmentary, for a surprising degree of regularity of feature. Thus, the distances between neighboring cellss of a particular type form a relatively narrow, Gaussian distribution, the ratio, mean/SD, (see Cell Types above) ranging from 3.5-4.5 (Table 4). The same distances for a particular type at a particular locus are similarly regular, the ratio, mean/SD, for each of five types ranging from 3.4 to 7.7 (Table 4). Similar regularity has been observed for the dendritic-field diameters of on- and off-alpha ganglion cells; the mean/SD for their distributions is about seven (Table 4). The synaptic relationships between particular cell types may be even more highly regular (Table 4; McIlwain et al 1983b). Thus, inputs to adjacent rod bipolar from retinopetal and nonretinopetal sources form rather constant fractions of the total input, and rod bipolar outputs to each of these amacrine form rather constant fractions of the total output (mean/SD, 10.3-54.4). Inputs and outputs of the same bipolar CGB are similarly regular (mean/SD, 4.0-15.3).

Considered simply as nervous tissue, a small patch of cat retina resembles in some ways an invertebrate ganglion. Both tissues are composed of many discrete cell types, each highly regular in size, distribution, synaptic connections, and neural transmitter. Just as the developmental rules for forming an invertebrate ganglion are repeated for each segment with appropriate modification, so the rules for forming a piece of the mosaic seem to be repeated with appropriate modification across the retina. Possibly, mammalian neurons are wired with a precision similar to that for which the invertebrates are famous (Sterling 1982). If so, perhaps there exist wide similarities across phyla in the principles, if not the detailed instructions, by which nervous tissue is formed. Such speculation aside, an appreciation of retinal tissue as composed of many definite types has sharpened the confidence of microscopists that even subtle differences between cells can have meaning and has led to a renewed and truly inspired microscopy.

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Coverage</th>
<th>Dend.</th>
<th>Total Input Size (%)</th>
<th>Total Output Size (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>on-alpha</td>
<td>4.0/4.5</td>
<td>10.3</td>
<td>54.4</td>
<td>14.7</td>
</tr>
<tr>
<td>off-alpha</td>
<td>4.0/4.5</td>
<td>10.3</td>
<td>54.4</td>
<td>14.7</td>
</tr>
<tr>
<td>CGB</td>
<td>4.0/4.5</td>
<td>10.3</td>
<td>54.4</td>
<td>14.7</td>
</tr>
<tr>
<td>CGB</td>
<td>4.0/4.5</td>
<td>10.3</td>
<td>54.4</td>
<td>14.7</td>
</tr>
</tbody>
</table>

COVERAGE FACTOR: the coverage factor (see Cell Types, above) has been determined for nine cell types (Tables 2-4). In every case coverage is complete. It has been determined for six types that the coverage is largely constant across the retina from center to periphery. Because cell density falls continuously across the retina while dendritic-field diameter rises, a constant coverage factor implies a close matching of these two parameters at every eccentricity. This appears to be a large scale regularity that should perhaps be distinguished in our thinking from local regularities such as dendritic-field diameter, cell spacing, and synaptic connections.

Certain cell types, the wide-field, sparsely distributed, alpha ganglion cells, for example, have small coverage factors (1.4-1.7), close to the minimum required for completeness. Other types, such as the narrow field, densely distributed, beta ganglion cells, have much larger coverage factors (as large as 11 in the ventral area). It is believed that the beta cell's large coverage is not redundant. Rather, the particular combination of receptive field size and density that produces such a coverage appears matched to the optimin precipitated by sampling theory for a system resolving about 6 cycles/deg (Wasile et al 1971b, Hughes 1981). The distribution density of the narrow-field, All amacrine resembles that of the beta ganglion cells, and this is probably because the All serves the beta cell's dark-adapted receptive field (see below). On the other hand, the dopamine amacrine, a cell that...
provides input to the AII, is wide-field and sparse, suggesting that the information it conveys to the AII is poor in spatial detail. Such observations as a whole suggest that the coverage factor for each cell type reflects the specific role that type and that coverage beyond the minimum has little to do with automatic sensations of "unateness" (Sterling 1983).

**MICROSCIRCUITRY OF THEBETA GANGLION CELL RECEPTIVE FIELD**

The preceding sections described individual elements and anatomical circuits linking photoreceptors to ganglion cells. An obvious next step is to infer which of these circuits form the actual physiological pathways that generate the ganglion cell receptive fields. With this aim I consider for the beta cell a circuit involving 13 neuron types. Connections between eight of these types, reconstructed directly from a series of 189 thin sections, are shown in Figure 13. Two ganglion cell somas, an on- and an off-beta, about each other is the seres, and their dendritic fields overlap, but in Figure 13 they are teased apart for clarity.

Major input to each beta cell is from a pair of cone bipolars, each of which is presumed to have a center and an antagonistic surround. The bipolars seem to be strung in "push-pull" fashion such that excitation delivered from one bipolar to the beta cell is accompanied by withdrawal of inhibition delivered by the other, and vice-versa (Figure 14). For the on-beta cell, one member of the cone bipolar pair (CBL) is believed to be depolarizing and excitatory, and the other (CBL) is believed to be hyperpolarizing and inhibitory. Turning on a spot in the on-beta cell's receptive field center should depolarize CBL, delivering excitation, and simultaneously hyperpolarize CBL, withdrawing inhibition. Turning off a spot or turning on an annulus in the surround should cause the opposite response withdrawal of excitation by CBL, and delivery of inhibition from CBL. For the off-beta cell, one member of the cone bipolar pair (CBL) is believed to be hyperpolarizing and excitatory and the other (CBL) is believed to be depolarizing and inhibitory. Turning off a spot in the center should cause excitation from CBL and withdrawal of inhibition from CBL.

This "push-pull" hypothesis, which stems directly from the microcircuitry illustrated in Figure 13, might have several advantages for a cell designed to detect local contrast at high spatial resolution. First, it would allow a cell to fire at high frequencies under some conditions and be totally suppressed under others. This may be what enables ganglion cells such as the on-beta (detecting local brightness) and the off-beta (detecting local darkness) to operate over such a wide range of spike frequencies (0-700/second; Kuffler 1953). The push-pull mechanism should also quicken the beta's
response to change in contrast and that may contribute to one of the beta's notable physiological attributes, "tinkliness" of response.

Figure 15 shows that under metopic illumination the beta ganglion cell receptive field still has a center and an antagonistic surround, both of which are rod-driven (Barlow et al. 1977, Kaplan et al. 1979). The operative pathway suggested in Figure 16 is the rod from the rod spherules to midget cone pedicles (Kolb 1979, Nelson 1977). A dot spot (below the cone threshold) causes a contrast effect or rods from rods into the cone pedicle. This current may activate the horizontal cell mechanism contained in the pedicle for generating the center-surround fields of cone bipolar and thence the center-surround receptive fields of beta cells. This might be the mechanism by which the center-surround organization, so crucial to the beta cell's spatial resolution, is maintained even in dim illumination.

After an hour or so in total darkness, the beta cell's sensitivity increases still further (Figure 15), to the point where a single photon can cause several extra impulses (Barlow et al. 1971). But now spatial resolving power is sacrificed as the receptive field center enlarges by two-fold and the antagonistic surround drops out (Figure 15; Barlow et al. 1957, Enroth-Cugel & Robson 1966, Kaplan et al. 1979). The primary pathway suggested for this condition is no longer rod → cone → cone bipolar, but rod → rod bipolar → All amacrines (Figure 16). The depolarization evoked in the All by a rod (Nelson et al. 1976) may spread via gap junctions to the Chb, axon terminals, causing them to excite the on-beta cell. The on-beta cell's enlarged receptive field center would correspond in diameter to the aggregate field of all the All cells that feed it (Sterling & Megill 1982). It could, perhaps, be even a little larger than this, because the Alls are interconnected by gap junctions. The antagonistic surround is lost from the beta cell apparently because it is converted from the outer plexiform layer by the cone bipolar dendrites, which under complete dark adaptation may carry no signal.

The same depolarization of the All that excites the on-beta ganglion cell may suppress the off-beta cell by two mechanisms. The depolarized bipolar apposition of the All, as it is probably glycinegic, may cause postsynaptic inhibition via its contact with off-beta dendrites (Kolb 1979) and presynaptic inhibition via its contacts with the axon terminal of Chb (Figure 16; McGurk et al. 1983b, Sterling & Megill 1983). Because for both types of beta cell the push-pull arrangement is sacrificed in the dark, one would anticipate a loss in temporal as well as spatial resolution, and this is in accord with the physiological observations of Kaplan et al. (1979). The circuitry in Figure 16 is also in accord with the reported effects of strychnine, a glycine blocker, as beta cell receptive fields (Kirby 1979, Salto 1981).

The two rod pathways discovered by Famiglietti, Kolb, and Nelson thus may serve different functions, and one wonders whether there are mecha-
niens to regulate which pathway is active. It would not be surprising if the rod → cone pathway serving metopic vision were switched off at the end of dark adaptation and the rod → All pathway were switched on. The pattern of the rod → cone pathway might be regulated by the 3 horizontal cells as described above (Horizontal Cells, Physiology). The rod bipolar → All pathway might be regulated by the dopamine amacrine. One would not expect the All to be totally suppressed by dopamine at photopic levels because the All can carry a cone signal (Figure 7). However, the rod bipolar pathway into or out of the All might be regulated by dopamine in a more specific fashion (Sterling & Maglil 1983).

CONCLUSION

Hubel & Wiesel proposed in 1962 a hierarchical architecture for the cet visual system. A particular proposition was that a retinal mosaic, established at one level, sharpened at successively higher levels, and generalized to a larger region of visual field. Their idea developed from studies of single units at the third through sixth levels (ganglion cells to complex cells in area 17). The student reviewing has strongly supported their concept and applied to the first through third levels (receptors to ganglion cells). In return to simple and complex cortical cells, the hierarchical model has been strongly criticized (Stone et al 1979). However, if we are anything like the retina, it probably contains many discrete cell types connected in specific ways. These probably do not form a single simple-to-complex hierarchy but rather parallel hierarchies to further abstract and generalize the "qualitative contexts" relayed there from the many types of retinal ganglion cells. Axon collaterals and physiological evidence grows that a single sublayer of area 17 does have many discrete types (Davis & Starling 1979, Schlicht 1981, Hannos et al 1983), and new "context" apparent to us may be in the same sublayer or sublayer (Hubel & Wiesel 1962) and spatial frequency (Movshon et al 1978). What is needed to identify the continuation of the retinal hierarchy into area 17 is more detailed knowledge of the cortical cell types and their circuitry (Gilbert 1983, this volume).

Strong concepts have emerged to guide research on microcircuitry of the cet retina. It is now believed that certain cell types are discrete and number roughly 60. Each type is believed to have a particular transmitter, set of connections, and mosaic distribution. As knowledge of circuitry becomes very detailed, hypotheses regarding function emerge. These hypotheses are quite specific and testable: whether they are correct seems less important than that they can be read directly from the circuitry. Powerful technologies to extend our knowledge of circuitry in cet retinas exist and are still developing. We may expect, in addition to the approaches already noted, to have monoclonal antibodies specific for particular cell types (Boscling & Lampson 1983). Further, since natural activity is strongly reflected in oxidative metabolism and this can be recognized at the electron microscope level (Wong-Riley et al 1979) it is possible to determine by electron microscopy what pathways are active under particular conditions. Where concepts and methods are strong, one may expect progress to be rapid. At a recent meeting of the Society for Neuroscience, D. H. Hubel declared, "The good old days are right now." Those who work on cet retinas will not argue.

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