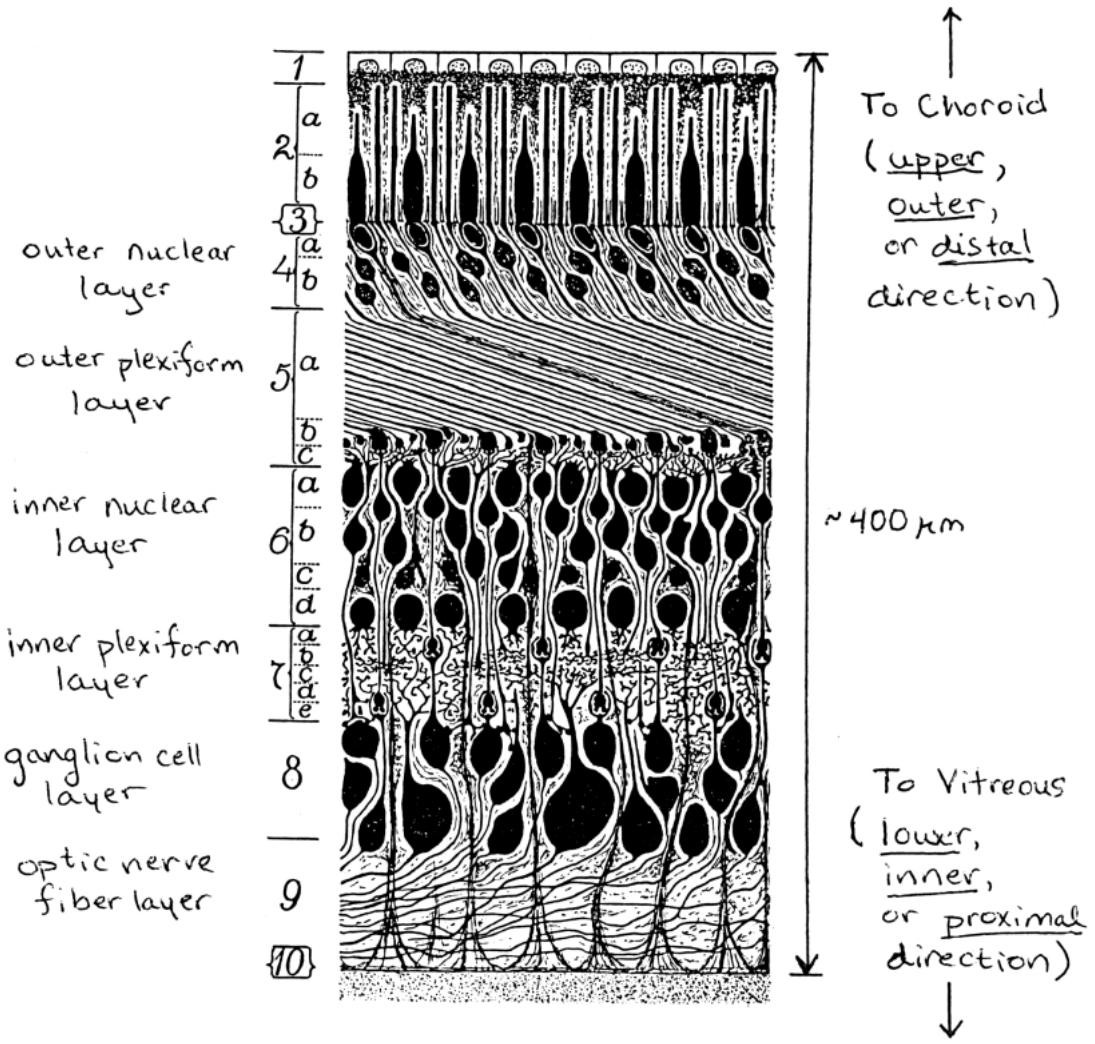


Figure 2-3: Cross-section through the adult human retina in the periphery of the central area. From Polyak [42]. Labeling: (1) pigment epithelium; (2) bacillary layer; (3) outer limiting membrane; (4) outer nuclear layer; (5) outer plexiform layer; (6) inner nuclear layer; (7) inner plexiform layer; (8) ganglion cell layer; (9) optic nerve fiber layer; (10) inner limiting membrane. The pigment epithelial cells (1) are found at the back of the retina, closest to the choroid membrane (*ch* in Figure 2-1), while the inner limiting membrane (10) is closest to the vitreal chamber (*vitr*).

### Photoreceptors

The photoreceptor cells are named after their function; these cells capture light and transduce it to neural signals. Since no other type of retinal cell can perform this feat, only the photoreceptors are stimulated directly by light. When the light-evoked responses of other cell types are discussed below, it should be remembered that these responses are secondary to photoreceptor stimulation. Transduction occurs at the outermost portion of the retina, where incoming light is absorbed by the outer segments of the photoreceptors (layer 2a in Figure 2-3). Since light entering the eye impinges on the retina at the layer of optic nerve fibers, it must travel through the tissue's transparent layers in order to reach the rod and cone outer segments.

There are two types of photoreceptors: rods and cones. The inner segments (see layer 2b) of cones are typically thicker than those of nearby rods. The cell bodies of both types of cells are found in the outer nuclear layer. The photoreceptor terminals extend into the outer plexiform layer, where they make well-characterized synapses onto horizontal and bipolar cell dendrites. Photoreceptors are also known to make contacts with one another, typically via electrical gap junctions.

Rods and cones exhibit distinct types of light sensitivity. The rods are responsible for dim-light or *scotopic* vision, while the cones mediate bright-light or *photopic* vision. In addition, cones are sensitive to the different wavelengths of the visible light spectrum, allowing us ultimately to perceive color. Rods, on the other hand, are not color-sensitive.

Both types of photoreceptors hyperpolarize in response to light. The amount of hyperpolarization produced by a photoreceptor is proportional to the logarithm of light intensity. For this reason, the responses are called *graded potentials*. Photoreceptor responses are also *sustained* in the sense that, barring adaptation effects, the graded hyperpolarizing potentials are maintained as long as a stimulus is present.

### Horizontal cells

Cell bodies of horizontal cells are found at the outer edge of the inner nuclear layer (6a in Figure 2-3). These cells extend their dendritic processes to form a dense network in the outer plexiform layer. There are two basic morphological types of horizontal cells found in vertebrates. The first has a relatively short axon which is several hundred microns long and ends in a prominent terminal expansion. Several subtypes of this cell have been observed and classified in different species. The second type of horizontal cell, which has not been found in primates (as of 1987), is axonless.

Horizontal cells of the same class are known to make contacts with one another via electrical gap junctions. The probable effect of such contacts is to increase the total retinal area over which a given cell is sensitive to light. This area, termed the horizontal cell's *receptive field*, is generally much larger than the area spanned by its dendrites. In addition to making connections amongst themselves, there is substantial physiological evidence indicating that horizontal cells make inhibitory synapses onto photoreceptors.

Horizontal cells generally respond to illumination of the retina with graded, sustained hyperpolarization.

### Bipolar cells

The cell bodies of bipolar cells are found in the inner nuclear layer, usually in layer 6b (Figure 2-3). Bipolar cells spread their dendrites in the outer plexiform layer, and extend

their axons into the inner plexiform layer. This fact suggests a simple functional polarity, whereby information is conducted away from the outer plexiform layer by the bipolar cell and delivered as input to the inner plexiform layer.

Based on both anatomical and physiological evidence, three types of bipolar cells have been identified. The first type, the *rod* bipolar cell, receives input exclusively from rods at characteristic, invaginating synapses and has a relatively large dendritic field. The other two types of cells receive input exclusively from cones. *On-center* bipolar cells connect to cones at characteristic, invaginating synapses and extend their axons to the inner portion of the inner plexiform layer. *Off-center* bipolar cells connect to cones at characteristically flat synapses and extend their axons to the outer portion of the inner plexiform layer.

Bipolar cells of all three types make synapses onto two postsynaptic processes at a structure called a dyad. The postsynaptic processes are most often either a ganglion cell dendrite and an amacrine cell process, or two amacrine cell processes.

The two types of cone bipolar cells are named after their responses to light stimuli. On-center bipolar cells respond to illumination of their receptive field centers with graded, sustained depolarizing potentials. Off-center bipolar cells respond with graded, sustained hyperpolarizing potentials. For both types of cells, the center response is reduced, and in some cases reversed, by illumination of a region surrounding the center of the receptive field. The On/Off dichotomy of cone bipolar cell responses has a known pharmacological basis (see section 2.1.3). The antagonistic center/surround receptive field organization is thought to stem from opposing influences produced by inputs from the two types of retinal neurons described above. In this scheme, direct interactions between photoreceptors and bipolar cells produce a center response, while the surround response is mediated by horizontal cells. Rod bipolar cells have been found in some mammalian retinas to depolarize in response to illumination.

### Amacrine cells

Amacrine cell bodies are found in both the inner nuclear layer (6d in Figure 2-3) and in the ganglion cell layer (8). The latter group are referred to as *displaced* cells. As a literal translation of their name would imply, amacrine cells do not have axons.

While as many as 30 distinct morphological types of amacrine cells have been found in some species, a simple binary classification scheme can often be applied. *Diffuse* amacrine cells extend processes throughout the inner plexiform layer, while the processes of *stratified* amacrine cells are usually confined to a single plane. This scheme has been further subdivided in some cases to include narrow- and wide-field diffuse amacrine cells and mono-, bi-, and multi-stratified cells. Another way to classify amacrine cells is through the neurotransmitters they use. Examples of a *glycinergic* and a *cholinergic* cell are given below[3]. As these examples will indicate, correspondences have been found between the two classification schemes discussed here.

In the inner plexiform layer, amacrine cell processes make synaptic contacts with ganglion cell dendrites, bipolar cell terminals, interplexiform cell processes, and other amacrine cell processes. While these cells do not have axons in the conventional sense, their processes can both transmit and receive information through synapses. In some cases, sites of synaptic input and output occur over very short distances along the length of a process. One example of this is the *reciprocal* synapse, whereby a bipolar cell makes a synapse

[3]A cell which either releases or is activated by neurotransmitter X is referred to as X-ergic.

onto an amacrine cell, which in turn makes a synapse back onto the bipolar at a nearby location. Reciprocal synapses between two adjacent amacrine cells have also been found (i.e. amacrine 1 synapses onto amacrine 2, which in turn synapses back onto amacrine 1). The wiring scheme inherent in the reciprocal synapse suggests a local feedback interaction. Another local interaction is the *serial* synapse, whereby an amacrine cell synapses onto another amacrine cell, which in turn synapses onto a third process at a nearby location. The functional nature of amacrine cell processes which make reciprocal and serial synapses is somewhat ambiguous; the processes exhibit properties of both axons and dendrites.

On the other hand, some types of amacrine cells exhibit a characteristic segregation of synaptic interaction, suggesting a functional polarity. For example, the AII amacrine cells found in the cat are glycinergic, have diffuse dendritic fields, and make well-characterized contacts with three types of retinal neurons. AII amacrine cells receive input from rod bipolar cells in the inner half of the inner plexiform layer, form electrical gap junctions with On-center cone bipolars in the middle portion of the layer, and make synapses onto either ganglion cell dendrites, Off-center cone bipolar terminals, or other amacrine cell processes in the outer portion of the layer. Thus the AII amacrine cell might be thought of as conducting information from the inner to the middle and outer portions of the inner plexiform layer. The starburst amacrine cell also exhibits functional polarity. This cell type has been found in all mammalian species in which it has been looked for, including humans. Starburst cells are cholinergic and have stratified, radially symmetric dendritic fields. Starburst amacrine cells receive inputs throughout their dendritic fields, but only make output synapses along the fields' outer edges. This synaptic arrangement suggests a functional polarity which points radially outward from the cell body.

In most cases, amacrine cell responses are either transient or, less frequently, sustained. Transient amacrine cell responses are depolarizing, and usually are produced at both the onset and cessation of illumination. The amount of depolarization is graded with stimulus intensity, though over a much narrower range of intensities than bipolar, horizontal, and photoreceptor cells. Action potentials are often superimposed on the transient potentials. The number of superimposed spikes is usually small - one or two - and is not sensitive to changes in stimulus intensity.

Transiently responding amacrine cells are very responsive to moving stimuli. Unlike bipolar cells, these cells do not usually have antagonistic center/surround receptive field organization. Sustained responses generated by amacrine cells can be both depolarizing and hyperpolarizing, and a number of these have antagonistic center/surround receptive field organization. Finally, some amacrine cells exhibit responses containing both transient and sustained components.

### Interplexiform cells

The cell bodies of interplexiform cells are found among those of amacrine cells. The main difference between these cells and their neighbors is that interplexiform cells extend processes into the outer plexiform layer, where they make output synapses. This suggests a functional polarity opposite to that of bipolar cells. Interplexiform cells receive input mainly from, and synapse rarely onto, amacrine cell processes.

Interplexiform cells are not stained well by the Golgi method - a fact that accounts for their relatively recent discovery. These cells have been studied less extensively than the other cells discussed above, though there are indications that they respond to illumination of the retina with both transient and sustained components [14].