Visual Perception Begins in the retina and occurs in two stages. Light entering the cornea is projected onto the back of the eye, where it is converted into an electrical signal by a specialized sensory organ, the retina. These signals are then sent through the optic nerve to higher centers in the brain for further processing necessary for perception. In this chapter we describe the neural processing of visual signals in the retina. The next three chapters explain, in cell-physiological terms, how processing in higher centers underlies the perception of form, motion, and color.

The retina bears careful examination for several reasons. First, it is useful for understanding sensory transduction in general because photoreceptors in the retina are perhaps the best understood of all sensory cells. Second, unlike other sensory structures, such as the cochlea or somatic receptors in the skin, the retina is not a peripheral organ but part of the central nervous system, and its synaptic organization is similar to that of other central neural structures. At the same time, the retina is relatively simple compared with other brain regions. It contains only five major classes of neurons, linked in an intricate pattern of connections but with an orderly, layered anatomical arrangement. This combination of physiological diversity and relatively simple structural organization makes the retina useful for understanding how information is processed by complex neural circuits in the brain.

For these reasons we describe neural processing in the retina in considerable detail. This chapter is divided into two parts. In the first part we describe how photoreceptors transduce light into an electrical signal. In the second we consider how these signals are shaped by other retinal neurons before being sent to the brain and...
Figure 26-1 Photoreceptors are located in the retina. The location of the retina within the eye is shown at left. Detail of the retina at the fovea is shown on the right (the diagram has been simplified by eliminating lateral connections mediated by interneurons; see Figure 26-6). In most of the retina light must pass through layers of nerve cells and their processes before reaching the photoreceptors. In the center of the lower circle, these proximal neurons are shifted to the side so that has a direct pathway to the photoreceptors. As a result, the visual image received at the fovea is the least distorted.

how synaptic connections among the retinal neurons are organized to accomplish this processing. Before discussing phototransduction, however, we shall review the organization of the retina and the basic physiological properties of the photoreceptor cells.

The Retina Contains the Eye’s Receptor Sheet

The eye is designed to focus the visual image on the retina with minimal optical distortion. Light is focused by the cornea and the lens, then traverses the vitreous humor that fills the eye cavity before reaching photoreceptors in the retina (Figure 26-1). The retina lies in front of the pigment epithelium that lines the back of the eye. Cells in the pigment epithelium are filled with the black pigment melamin, which absorbs any light not captured by the retina. This prevents light from being reflected off the back of the eye to the retina again (which would degrade the visual image).

Because the photoreceptors lie in the back of the eye, immediately in front of the pigment epithelium, all other retinal cells lie in front of the photoreceptors, closer to the lens. Therefore, light must travel through layers of other retinal neurons before striking the photoreceptors. Slow light to reach the photoreceptors without being absorbed or greatly scattered (which would distort the visual image), the axons of neurons in the proximal of the retina are unmyelinated so that these layers are relatively transparent. Moreover, in one region of the retina, the fovea, the cell bodies of the proximal neurons are shifted to the side, enabling the photoreceptors there to receive the visual image in its least distorted form (Figure 26-1). This shifting is most pronounced in the center of the fovea, the foveola. Humans have constantly move their eyes so that scenes of interest are projected onto the fovea. The retina also contains a region called the optic disc, where the optic nerve leaves the retina. This region has no photoreceptors and therefore is a blind spot in the visual field (see Figure 2). The projection of the visual field onto the two hemispheres is described in Chapter 27.

There Are Two Types of Photoreceptors: Rods and Cones

The human retina contains two types of photoreceptors: rods and cones. Cones are responsible for day
### Differences Between Rods and Cones and Their Neural Systems

<table>
<thead>
<tr>
<th>Cones</th>
<th>Rods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower sensitivity, specialized for day vision</td>
<td>Higher sensitivity, specialized for night vision</td>
</tr>
<tr>
<td>Less photopigment</td>
<td>More photopigment</td>
</tr>
<tr>
<td>Lower amplification</td>
<td>Higher amplification</td>
</tr>
<tr>
<td>High temporal resolution; fast response, short integration time</td>
<td>Low temporal resolution; slow response, long integration time</td>
</tr>
<tr>
<td>Most sensitive to direct axial rays</td>
<td>Most sensitive to indirect, scattered light</td>
</tr>
<tr>
<td>Cone system</td>
<td>Rod system</td>
</tr>
<tr>
<td>High acuity; concentrated in fovea, dispersed retinal pathways</td>
<td>Low acuity; distributed throughout the retina</td>
</tr>
<tr>
<td>Chromatic: three types of cones, each with a distinct pigment that is most sensitive to a different part of the visible light spectrum</td>
<td>Dichromatic: two types of cones, sensitive to red and blue light</td>
</tr>
</tbody>
</table>

Rods mediate night vision; total loss of rods produces night blindness. Rods are exquisitely sensitive and therefore function well in the dim light present at dusk or at night, when most stimuli are not strong enough to excite the cones.

Cones perform better than rods in all visual tasks that depend on the detection of dim stimuli. Cone-mediated vision is limited to the fovea, a small area at the center of the retina, and is characterized by high acuity. Although the rod system is more light-sensitive than the cone system, it is achromatic. These differences in performance are due partly to properties of cones themselves and partly to the connections they make with other neurons in the retina (the cone systems).

The most important factors that contribute to these differences are summarized in Table 26-1 and discussed further in more detail below.

#### Cones Mediate Color Vision

There are three types of cones, each containing a visual pigment that is sensitive to a different part of the light spectrum (see below). As we shall see in Chapter 29, the brain obtains information about color by comparing the responses of the three types of cones. In contrast, rods contain only one type of pigment and therefore respond in the same way to different wavelengths.

Although rods outnumber cones by roughly 20 to 1, the cone system has better spatial resolution for two reasons. First, because many neighboring rods converge onto a single bipolar cell, differences in the responses of the rods are averaged out in the interneuron. Second, cones are concentrated in the fovea, where the visual image is least distorted.

Like some other sensory receptors, rods and cones do not fire action potentials. Instead, they respond to light with graded changes in membrane potential. Rods respond slowly, so that the effects of all the photons absorbed during a 100 ms interval are summed together. This helps rods detect small amounts of light, but prevents them from resolving light that is flickering faster...
A. Morphology of photoreceptors

Figure 28-2. The two types of photoreceptors, rods and cones, have similar structures. (Adapted from O'Brien 1982 and Young 1970.)

A. Both rod and cone cells have inner and outer segments connected by a cilium. The inner segment contains the cell’s nucleus and most of its biosynthetic machinery. The outer segment contains the light-transducing apparatus.

B. Outer segments of photoreceptors

B. The outer segment consists of a stack of membranous discs, which contain the light-absorbing photopigments. Different types of cells these discs are formed by invaginations of the plasma membrane. In rods, however, the folds pinch off from the membrane so that the discs are free-floating within the outer segment, whereas in cones the discs remain part of the plasma membrane.

Light Is Absorbed by Visual Pigments in the Photoreceptors

Both rods and cones have three major functional regions (Figure 26-2):

1. The outer segment, located at the outer or distal surface of the retina, is specialized for phototransduction.
2. The inner segment, located more proximally within the retina, contains the cell’s nucleus and most of its biosynthetic machinery.
3. A synaptic terminal makes contact with the photoreceptor’s target cells.

The outer segments of rods and cones are filled with light-absorbing visual pigments. Each pigment molecule comprises a small light-absorbing molecule attached to a large membrane-spanning protein. Rods and cones can contain a remarkably large number of these membrane proteins (as many as 10^6 in each cell), because they have evolved an elaborate system of stacked membranous discs in their outer segments that dramatically increase the surface area of the membrane in cells (Figure 26-2B). These discs develop as a series of invaginations of the cell’s plasma membrane, ultimately arranging themselves like a roll of pennies in aluminum wrapper. In rods the discs are continuous with the plasma membrane, while in rods they pinch off from the plasma membrane and become intracellular organelles.

Like other neurons, photoreceptors do not die but their outer segments are constantly renewed. New discs are formed at a rapid rate; in rods about the discs are synthesized every hour. Old discs are discarded by the tips of photoreceptors and removed by the phagocytic activity of the pigment epithelial cells.

Phototransduction Results from a Three-Stage Cascade of Biochemical Events in the Photoreceptors

The absorption of light by visual pigments in rods and cones triggers a cascade of events that leads to changes in ionic fluxes across the plasma membrane of these cells, and consequently a change in membrane potential. A key molecule in the cascade is the nucleotide cyclic guanosine 3'-5' monophosphate (cGMP). When light hits rods, the (cGMP) molecule acts as a second messenger for the photopigments, causing the photoreceptor to hyperpolarize.
Phototransduction then occurs in three stages: (1) Light activates visual pigments; (2) these activated molecules stimulate cGMP phosphodiesterase, an enzyme that reduces the concentration of cGMP in the cytoplasm; and (3) the reduction in cGMP concentration closes the cGMP-gated channels, thus hyperpolarizing the photoreceptor. We shall now examine these events step by step.

Stage 1: Light Activates Pigment Molecules in the Photoreceptors

In rod cells the visual pigment, rhodopsin, has two parts. The protein portion, opsin, is embedded in the
Figure 26-4 Phototransduction involves the closing of cation channels in the outer segment of the photoreceptor membrane. In the absence of light these cation channels are kept open by intracellular cGMP and conduct an inward current, carried largely by Na⁺.

When light strikes the photoreceptor (illustrated here by a rod cell) the cGMP-gated channels are closed by a three-step process. (1) Light is absorbed by and activates pigment molecules (rhodopsin in rods) in the disc membrane (the green rectangle in the rhodopsin molecule represents the light-absorbing portion, retinal). (2) The activated pigment then activates a G protein (transducin in rods), which in turn activates cGMP phosphodiesterase. This enzyme catalyzes the breakdown of cGMP to 5′-GMP. (3) As the cGMP concentration is lowered, the cGMP-gated channels close, thereby reducing the inward current and causing the photoreceptor to hyperpolarize.

disc membrane and does not by itself absorb light. The light-absorbing portion, retinal, is a derivative of vitamin A. Retinal can assume several different isomeric conformations, two of which are important in different phases of the visual cycle. In its nonactivated form rhodopsin contains the 11-cis isomer of retinal, which fits snugly into a binding site in the opsins molecule (Figure 26-3A).

Activation of rhodopsin starts with the absorption of light, which causes retinal to change from the 11-cis to the all-trans configuration (Figure 26-3B). This reaction is the only light-dependent step in vision. As a result of this conformational change, retinal no longer fits into the binding site in opsins. The opsins, therefore, undergoes a conformational change to a semistable conformation called metarhodopsin II, which triggers the second step of phototransduction discussed below.

Metarhodopsin II is unstable and splits within minutes, yielding opsins and all-trans retinal. The all-trans retinal is then transported from the rods to pigment epithelial cells, where it is reduced to all-trans retinol (vitamin A), the precursor in the synthesis of 11-cis retinal, which is transported back to the rods. All-trans retinol is thus a crucial compound in the visual system and, because it cannot be synthesized by humans, must be supplied in the diet. Deficiencies of vitamin A can lead to night blindness and, if untreated, to a deterioration of receptor outer segments and eventually total blindness.

In the retina of primates each of the three cone cells contains a different pigment optimized for absorption of light in a different part of the visible spectrum. As in rods, the visual pigments in cones are composed of two parts: a protein called coneopsin and a light-absorbing portion, 11-cis retinal. Each cone pigment contains a different isoform of coneopsin that interacts with 11-cis retinal in a distinct way, making it to be most sensitive to a particular part of the visible spectrum. The existence of three types of cones with different absorption characteristics underlies the color vision in humans (see Chapter 29).

Stage 2: Activation of Pigment Molecules Reduces the Cytoplasmic Concentration of Cyclic GMP

The activation of pigment molecules by light leads to a reduction in the cytoplasmic concentration of the second messenger cGMP. The concentration of cGMP is controlled by two enzymes. It is synthesized inside the cell by guanylyl cyclase, and it is broken down outside the cell by cGMP phosphodiesterase, a protein peripheral to the disc membrane (see Figure 26-2A). The concentration of cGMP is affected by light. When cGMP phosphodiesterase is itself controlled by visual pigments, in darkness cGMP phosphodiesterase is weakly active, and the concentration of cGMP is therefore relatively high. Activation of pigment molecules by light leads to the activation of the phosphodiesterase.
## 26.4. The Dark Current

There are two currents that predominate in a photoreceptor. An inward current flows through cGMP-gated channels, which are activated in the outer segment, while an outward current flows through non-gated $K^+$-selective channels, which are like those of other neurons and are concentrated in the inner segment. The outward current carried by the depolarization of the photoreceptor toward the potassium potential for $K^+$ (around $-70 \text{ mV}$). The inward current tends to depolarize the photoreceptor. The photoreceptor is able to maintain steady intracellular concentrations of $Na^+$ and $K^+$ in the face of these large fluxes because its inner segment has a high density of $Na^+-K^+$ pumps, which pump out $Na^+$ and pump in $K^+$ (Figure 26-5A).

In darkness the cytoplasmic concentration of cGMP is high, thus maintaining the cGMP-gated channels in an open state and allowing a steady inward current, called the dark current (Figure 26-5B). As a result, in darkness the photoreceptor's membrane potential is around $-40 \text{ mV}$, significantly more depolarized than that of most neurons. When light reduces the level of cGMP, thus closing cGMP-gated channels, the inward current that flows through these channels is reduced and the cell becomes hyperpolarized (Figure 26-5C).

**Figure 26-5A.** An inward current flows into a photoreceptor through cGMP-gated channels and out of the cell, through non-gated channels. Active transport ($Na^+-K^+$) pumps maintain $Na^+$ and $K^+$ concentrations at steady levels.

**Figure 26-5B.** A reduction in the cytoplasmic concentration of cGMP closes the cGMP-gated channels.

**Figure 26-5C.** An inward current of $-50 \text{ pA}$ is suppressed by a bright light, hyperpolarizing the cell to $-70 \text{ mV}$, the equilibrium potential for $K^+$. A light of intermediate intensity would hyperpolarize the cell to potentials between $-40$ and $-70 \text{ mV}$. 
Box 26-2 Calcium and Light Adaptation

Calcium modulates the function of several proteins of the phototransduction pathway. The recovery of the cone membrane potential and the desensitization of the cone that underlies light adaptation are mediated by a slow decrease in \( Ca^{2+} \) concentration in the cone outer segment during prolonged illumination (the opposite changes occur during dark adaptation).

In darkness \( Ca^{2+} \) constantly flows into the outer segment of the cone through the cGMP-gated channels. (Calcium accounts for about one-seventh of the current that flows through these channels.) The \( Ca^{2+} \) that enters is extruded by a specialized \( Ca^{2+} \) carrier in the outer segment membrane, and this process maintains a constant \( Ca^{2+} \) concentration in the outer segment. During prolonged illumination the cGMP-gated channels close, thus reducing the influx of \( Ca^{2+} \). This reduction in influx leads to a slow decrease in the intracellular \( Ca^{2+} \) concentration because the extrusion of \( Ca^{2+} \) continues.

The slow decrease in \( Ca^{2+} \) concentration allows the cone membrane potential to recover from its initial hyperpolarizing response to bright illumination because \( Ca^{2+} \) inhibits guanylyl cyclase, the enzyme that synthesizes cGMP from GTP, and, in darkness, when the \( Ca^{2+} \) level is relatively high, guanylyl cyclase is maintained in a partially inhibited state. The decrease in \( Ca^{2+} \) concentration during illumination reduces the inhibitory effect of \( Ca^{2+} \) on guanylyl cyclase. As a result, cGMP is synthesized, and the concentration of cGMP increases. This results in the reopening of cGMP-gated channels and, consequently, slow depolarization of the cone.

The slow decrease in \( Ca^{2+} \) concentration also causes desensitization of the cone during light adaptation partly through effects on the visual pigments and cGMP-gated channels. Lowering the \( Ca^{2+} \) concentration helps to speed up the inactivation of the visual pigments, thereby improving the effectiveness of a given light flash in activating cGMP phosphodiesterase. A lower concentration of \( Ca^{2+} \) decreases the sensitivity of the cGMP-gated channels to changes in cGMP. Because of these effects of \( Ca^{2+} \), an intense light stimulus is required to close the same number of cGMP-gated channels. Whether these effects entirely explain for the desensitization is unknown.

cyclic AMP, which breaks down cGMP and lowers its concentration.

Photoactivation of a single rhodopsin molecule can lead to the hydrolysis of more than \( 10^5 \) molecules of cGMP per second. An activated rhodopsin molecule diffuses within the disc membrane and activates hundreds of molecules of the regulatory protein transducin, each of which stimulates a phosphodiesterase molecule. Each phosphodiesterase molecule in turn is capable of hydrolyzing over \( 10^7 \) molecules of cGMP per second.

The biochemical cascade initiated by the photoactivation of rhodopsin resembles the cascades triggered by the binding of many hormones and neurotransmitters to their receptors. Indeed, the rod and cone opsins show a high degree of structural similarity with the family of hormone and transmitter receptors that couple to G proteins (see Chapter 13). Moreover, transducin is a member of the trimeric G protein family. As with other G proteins, the activation of transducin involves a characteristic interaction with guanine nucleotides (see Figure 13-3). Inactive transducin binds a molecule of GDP tightly; upon interaction with activated rhodopsin in the disc membrane, however, transducin exchanges GDP for GTP and itself becomes active. Transducin becomes inactivated because it also has GTPase activity, which breaks down the bound GTP molecule into GDP (see Figure 13-4).

Two mechanisms terminate the light response as described, transducin inactivates itself by hydrolyzing bound GTP. Also, once activated, rhodopsin becomes a target for phosphorylation by a specific protein kinase; the phosphorylated rhodopsin then acts with a specific regulatory protein called cGMP phosphodiesterase, leading to its rapid inactivation.

Stage 3: The Reduction in Cyclic AMP Concentration Closes cGMP-Gated Ion Channels Thus Hyperpolarizing the Photoreceptor

The light-evoked decrease in cGMP results in the closure of cGMP-gated ion channels in the photoreceptor (Figure 26-4). Cyclic GMP gates these channels leading directly to the cytoplasmic face of the channel. The channel is activated by the cooperative binding of at least three molecules of cGMP. The cGMP-gated channel in photoreceptors was the first known example of a channel regulated by a cyclic nucleotide acting directly on the channel rather than through a protein. Similar channels are also present in some bipolar cells (see below) and in olfactory neurons (Chapter 32).

In the absence of a light stimulus the cGMP-gated channels conduct an inward current that tends to depolarize the photoreceptor. The light-evoked closure
The retina has three major functional classes of photoreceptors (rods and cones) lie in the outer nuclear layer, neurons (bipolar, horizontal, and amacrine cells) in the inner nuclear layer, and ganglion cells in the ganglion cell layer. Photoreceptors, bipolar cells, and horizontal cells make connections with each other in the outer plexiform layer. The bipolar, amacrine, and ganglion cells make contact in the inner plexiform layer. Information flows vertically from photoreceptors to bipolar cells to ganglion cells, as well as laterally via horizontal cells in the outer plexiform layer and amacrine cells in the inner plexiform layer. (Adapted from Dowling 1979.)

The first change in cones during light adaptation is the slow recovery of the membrane potential. A very bright light closes all cGMP-gated channels, hyperpolarizing the cones to $-70 \text{ mV}$, the equilibrium potential for $K^+$. In this state the cones cannot respond to further increases in light intensity. If this illumination is maintained, the cones slowly depolarize to a membrane potential between $-70$ and $-40 \text{ mV}$ (the resting potential), and are once again capable of hyperpolarizing in response to further increases in light intensity—the bright light is no longer blinding. The second change in cones during light adaptation is the desensitization of the receptor. During prolonged illumination by a background light, the smallest increment in light intensity capable of evoking a detectable change in membrane potential increases in proportion to the background intensity, in accordance with Weber's law (Chapter 21). Both changes in the responses of cones—slow recovery of the membrane potential and desensitization—are due to a slow...
Figure 26-7 Retinal ganglion cells respond optimally to contrast in their receptive fields. Ganglion cells have circular receptive fields, with specialized center (pink) and surround (gray) regions. On-center cells are excited when stimulated by light in the center and inhibited when stimulated in the surround; off-center cells have the opposite responses. The figure shows the responses of both types of cells to five different light stimuli (the stimulated portion of the receptive field is shown in yellow). The pattern of action potentials fired by the ganglion cell in response to each stimulus is also shown in extracellular recordings. Duration of illumination is indicated by a bar above each record. (Adapted from Kuffler 1953.)

A. On-center cells respond best when the entire central part of the receptive field is stimulated (3). These cells also respond well, but less vigorously, when only a portion of the cell field is stimulated by a spot of light (1). Illumination of the surround with a spot of light (2) or ring of light (4) reduces the cell firing, which resumes more vigorously a short period after the light is turned off. Diffuse illumination of the entire receptive field (5) elicits a relatively weak discharge because the center and surround oppose each other strongly.

B. The spontaneous firing of off-center cells is suppressed when the central area of the receptive field is illuminated but accelerates for a short period after the stimulus turns off. Light alone onto the surround of the receptive field also excites the cell (2, 4).
The output of the Retina Is Conveyed by Ganglion Cells

The second topic of this chapter: How do the retina modify and process the signals evoked by light in photoreceptors before sending them to the brain? The output of the retina is conveyed by ganglion cells. Unlike photoreceptors, which respond to light with graded changes in membrane potential, ganglion cells transmit information as trains of action potentials. The axons of these cells form the optic nerve, which projects to the lateral geniculate nucleus of the thalamus and the superior colliculus as well as to thepretectum and other targets (see Chapter 27).

Between the photoreceptors and the ganglion cells are several classes of interneurons, bipolar, horizontal, and amacrine cells (Figure 26-6). These cells do not simply relay signals from the photoreceptors to the ganglion cells but also combine signals from several photoreceptors in a way that the electrical responses evoked in the ganglion cells depend critically on the precise spatial and temporal patterns of the light that stimulates the retina. In this section we examine the responses of ganglion cells to spatial patterns of light. In the final section of this chapter, we discuss how the synaptic connections among photoreceptors, interneurons, and ganglion cells are organized for carrying out the processing of the visual scene. Central and peripheral ganglion cells are not silent even in the absence of light; spontaneous activity is modulated by the activity of the ganglion cells themselves. The inputs to a ganglion cell originate from neighboring photoreceptors in the same area of the retina, the receptive field for that ganglion cell. In effect, the ganglion cell’s receptive field is a map of the retina that the ganglion cell monitors. The receptivefields of ganglion cells have two important features.

First, when small spots of light on the retina are turned on or off, the receptive properties of ganglion cell receptive fields change, and the receptive fields prove to be roughly circular. Second, in most ganglion cells the receptive field is divided into two parts: a circular zone at the center, the receptive field center, and the remaining area of the receptive field called the surround. Ganglion cells respond optimally to differential illumination of the receptive field center and surround.

Two classes of ganglion cells can be distinguished by their responses to a small spot of light applied to the center of their receptive field (Figure 26-7). On-center ganglion cells are excited when light is directed to the center of their receptive field. Light applied to the surround inhibits the cell; the most effective inhibitory stimulus is a ring of light on the entire surround. Off-center ganglion cells are inhibited by light applied to the center of their receptive field. However, their firing rate increases for a short period of time after the light is removed; that is, they are excited when the spot of light on the center is turned off. Light excites an off-center ganglion cell when it is directed to the surround of the receptive field. In both types of cells the response evoked by a ring of light on the entire surround cancels the response evoked by light directed to the center almost completely. For this reason, diffuse illumination of the entire receptive field evokes only a small response in either type of cell (Figure 26-7). Not all ganglion cells have a center-surround receptive field organization. For example, a few ganglion cells respond to changes in the overall luminance of the visual field and are important in controlling pupillary reflexes (see Chapter 27).

On-center and off-center ganglion cells are present in roughly equal numbers, and every photoreceptor sends output to both types. Thus, ganglion cells provide two parallel pathways for the processing of visual information. In addition, their receptive fields vary in size across the retina. In the foveal region of the primate retina, where visual acuity is greatest, the receptive fields are small, with centers that are only a few minutes of arc (60 min = 1 degree). At the periphery of the retina, where acuity is low, the fields are larger, with centers of 3°–5° (1° on the retina is equal to about 0.25 mm).
Box 26-3 The Center-Surround Receptive Field of Bipolar Cells

Cone cells in the center of the receptive field of a bipolar cell synapse directly on the bipolar cell. Each cone cell synapses on both on-center and off-center bipolar cells. Cone cells release a single neurotransmitter, glutamate, which inhibits (hyperpolarizes) on-center bipolar cells and excites (depolarizes) off-center cells.

In the dark the cones are depolarized (around -40 mV), so that voltage-gated Ca^{2+} channels in their synaptic terminals are open, allowing Ca^{2+} to enter the terminals and trigger the release of glutamate. This constant release of glutamate in the dark maintains the on-center bipolar cells in a hyperpolarized state. When illuminated, however, the cones become hyperpolarized, and the voltage-gated Ca^{2+} channels close, reducing the Ca^{2+} influx and therefore the amount of glutamate the cells release; as a result, the on-center bipolar cells depolarize.

Conversely, cone cells maintain off-center bipolar cells in a depolarized state in the dark. When glutamate release is reduced by light the off-center bipolar cells hyperpolarize (Figure 26-9).

Glutamate produces different responses in the two classes of bipolar cells by gating different cation channels. In off-center bipolar cells glutamate opens a type of cation channel that carries an inward (depolarizing) Na^+ current into the cells. In on-center bipolar cells the mechanism by which glutamate hyperpolarizes the cell is unusual and may be different for rods and cones. At some synapses the transmitter appears to act by opening K^+-selective ion channels. At others it closes a cGMP-gated channel that carries an inward Na^+ current. In the absence of transmitter this type of channel is kept open by a high intracellular concentration of cGMP. Glutamate appears to cause the closure of these channels in precisely the same way that light causes the closure of cGMP-gated channels in photoreceptors—by activating a specific glutamate receptor that activates a G protein, which in turn activates cGMP phosphodiesterase and lowers the cytoplasmic concentration of cGMP.

Cones in the surround of a bipolar cell's receptive field synapse on horizontal cells. Horizontal cells do not make direct synaptic contact with the bipolar cells, however. Instead, they have synapses on cones in the center of the bipolar cell's receptive field. When the surround is illuminated, the horizontal cells depolarize the cones in the center, the opposite effect of light absorption by these cones (Figure 26-10). Whether this mechanism alone accounts for the antagonism between center and surround in bipolar cells is not yet known.

Figure 26-9 On-center and off-center bipolar cells have parallel pathways for the signal of a single cone. Each bipolar cell makes an excitatory connection with a ganglion cell of the same type. When the cone is hyperpolarized by light the on-center bipolar cell is excited and the off-center bipolar cell is inhibited. These opposite and simultaneous actions are mediated by the transmitter glutamate. In the dark the cone releases large amounts of transmitter because it is depolarized and hyperpolarizing the cone causes a reduction in transmitter release. The same transmitter has different actions on the two types of bipolar cells because the two types of bipolar cells have different postsynaptic densities that gate different types of ion channels. The responses of ganglion cells are largely determined by the input from bipolar cells. The on-center bipolar cell, which becomes depolarized by illumination of its receptive field center, will depolarize the on-center ganglion cells; the off-center cell shows the opposite response.
Ganglion Cells Are Specialized for the Detection of Contrasts and Rapid Changes in the Visual Image

Why do ganglion cells have a center-surround receptive field organization, and why are there parallel on-center and off-center pathways?

As we have just seen, ganglion cells respond only weakly to uniform illumination because of the center-surround structure of their receptive fields. They respond best when the light intensities in the center and surround are quite different. They therefore report principally the contrasts in light, rather than its absolute intensity.

Most of the useful information in a visual scene is, however, contained in the pattern of contrasts. The absolute amount of light reflected by objects is relatively uninformative because it is largely determined by the intensity of the light source. Doubling the ambient light intensity will double the amount of light reflected by objects but does not alter contrasts between the objects. The center-surround organization of the receptive field of ganglion cells is therefore an adaptation for detecting useful information in the visual scene.

As we shall see in Chapters 28 and 29, perception of the brightness and color of objects relies mainly on information about contrast rather than the absolute amount of light and can therefore be influenced by the contrast between an object and its surroundings. For example, the same gray ring looks much lighter against a black background than against a white one (Figure 26-8).

Why does the detection of contrast start in the retina? In principle the information from photoreceptors could be sent directly to higher centers for this processing. However, signals transmitted through several relay steps to the cortex inevitably become slightly distorted. One way of minimizing the effect of transmission errors is for the retina itself to measure the difference and to transmit that information. This, in effect, is what the ganglion cell does. The firing rate of a ganglion cell provides a measure of the difference in the intensities of light illuminating the center and surround. In this way information about small differences in intensities is directly transmitted to higher centers.

Parallel on-center and off-center pathways also enhance the performance of the visual system because each type of ganglion cell responds best to either rapid increases or decreases in illumination. On-center ganglion cells have a low rate of firing under dim illumination; rapid increases in firing thus signal rapid increases in light intensity in their receptive field center. In contrast, off-center ganglion cells discharge at a low rate in the light; rapid increases in firing in these cells therefore signal rapid decreases in light intensity in their receptive field center.
field center. This specialization has been demonstrated by experiments in which the function of on-center ganglion cells in awake monkeys was blocked using a pharmacological agent, aminophosphorobutyrinate (APB), which selectively antagonizes transmission from photoreceptors to on-center bipolar cells. Detection of rapid increases, but not decreases, in illumination was severely impaired in these animals.

Specialized Ganglion Cells Process Different Aspects of the Visual Image

In addition to contrast and rapid changes in illumination, the visual system also analyzes several other aspects of the visual image, such as color, form, and movement. As we discussed briefly in the preceding chapter and will discuss again in more detail in subsequent chapters, these features are processed in the visual cortex in parallel pathways. This parallel processing begins in the retina with parallel networks of ganglion cells.

Each region of the retina has several functionally distinct subsets of ganglion cells that convey, in parallel pathways, signals from the same photoreceptors. Most ganglion cells in the primate retina fall into two functional classes, M (for magni, or large) and P (for parv, or small). Each class includes both on-center and off-center cells.

M cells have large receptive fields (reflected in their large dendritic arbors) and respond relatively transiently to sustained illumination. They respond optimally to large objects and are able to follow rapid changes in the stimulus. As we shall see in Chapter 27, they appear therefore to be concerned with the analysis of the gross features of a stimulus and its movement. The smaller P cells, which are more numerous, have small receptive fields, respond selectively to specific wavelengths, and are therefore involved in the perception of form and color. P cells are thought to be responsible for the analysis of fine detail in the visual image, although some M cells may also be involved in this function.

The primate retina also contains ganglion cells that do not fall into the P or M classes. The functions of these cells are largely unknown, although one type is known to report on the overall ambient light intensity.

Signals From Photoreceptors Are Relayed to Ganglion Cells Through a Network of Interneurons

How do the relatively simple signals provided by photoreceptors give rise to the complex responses of the ganglion cells? Although the circuitry connecting these seems complicated, on close examination it is rather simple. Each type of retinal interneuron (horizontal, bipolar, and amacrine) plays a specific role in the photoreceptor signals transmitted through the retina. The role of retinal interneurons is best illustrated by focusing on the bipolar cells, as they represent the direct pathway between receptors and ganglion cells. As a further simplification, we restrict our attention to the circuitry for cones, the circuitry that mediates visual function during normal daylight.

Bipolar Cells Convey Cone Signals to Ganglion Cells Through Direct or Indirect Pathways

Visual information is transferred from cones to ganglion cells along two types of pathways in the retina. One is the center of a ganglion cell's receptive field makes synaptic contact with bipolar cells that in turn can contact the ganglion cells; these connections are termed as direct or vertical pathways. Signals from cones are conveyed to the ganglion cell through bipolar cells directly only indirectly by means of horizontal and one amacrine cells; these indirect connections are called lateral pathways. Horizontal cells, which have large dendritic trees, transfer information from distant bipolar cells. (Horizontal cells are also electrically coupled to each other by gap junctions and thus respond to inputs from even more distant cones that contact neighboring horizontal cells.) Curiously, these horizontal cells do not appear to convey information to the bipolar cells directly, but rather by feeding back cones in the center of the bipolar cell's receptive field (see Figure 26-10). Some types of amacrine cells transfer information from distant bipolar cells to ganglion cells (see Figure 26-6).

Most synaptic contacts in the retina are grouped into two plexiform (network-like) layers. The outer plexiform layer contains the processes of receptor, bipolar, and horizontal cells, while the inner plexiform layer contains the processes of bipolar, amacrine, and ganglion cells (see Figure 26-6). Thus the bipolar cells bridge the two plexiform layers by having processes on both.

We have seen that photoreceptors respond to light with graded changes in membrane potential rather than by firing action potentials. The same is true of horizontal and bipolar cells. These cells lack voltage-gated ion channels capable of generating action potentials; instead they transmit signals passively (see Chapter 24). Because these cells are small and have short processes, the signals spread to their synaptic terminals.
The receptive field properties of a ganglion cell largely determine those of the bipolar cells connected to it, because the type of bipolar cell (on-center or off-center) makes only synaptic connections with the corresponding type of ganglion cell. When on-center bipolar cells are excited by light, they depolarize on-center ganglion cells (see Figure 26–9 in Box 26–3). Although the responses of ganglion cells are largely determined by these direct inputs from bipolar cells, they are also shaped by amacrine cells, a group of interneurons with processes in the inner plexiform layer (Figure 26–6). There are over 20 morphologically distinct types of amacrine cells that use at least 8 different neurotransmitters. Some amacrine cells function like retinal cells: They mediate antagonistic inputs from cells in the ganglion cell’s surround. Others have been implicated in shaping the complex receptive field properties of specific classes of ganglion cells, such as type ganglion cells that process orientation information (see Chapter 28).

An Overall View

The detection of light and its transduction into electrical signals is carried out by the photoreceptors. Visual information is then transferred from the receptors to the ganglion cells via the bipolar cells. The ganglion cells in turn project to the brain; their axons form the optic nerve. Two types of interneurons (horizontal cells and amacrine cells) provide lateral inputs to bipolar cells and ganglion cells.

The cyclic nucleotide cGMP plays a central role in phototransduction. Absorption of light by the photosensitive visual pigments in the photoreceptor triggers a second-messenger cascade. The activated pigment molecules stimulate a G protein, transducin, which in turn activates a phosphodiesterase that catalyzes the hydrolysis of cGMP. Light absorption therefore causes a reduction in the cytoplasmic concentration of cGMP. In darkness cGMP opens specialized ion channels that carry a depolarizing current into the cell, so that the reduction in the level of cGMP makes the photoreceptor hyperpolarize.

Signals from photoreceptors to ganglion cells are conveyed in parallel on-center and off-center pathways. An on-center ganglion cell is excited when light stimulates the center of its receptive field and inhibited when light stimulates its surround. An off-center ganglion cell exhibits the opposite responses; it is inhibited when light stimulates its center and excited by light on its surround. These transformations of the visual signal assist higher centers in detecting weak contrasts and rapid changes in light intensity. In addition, ganglion cells are specialized for processing different aspects of the visual image such as movement, fine spatial detail, or color.

The pattern of synaptic connections in the retina explains how the various responses of ganglion cells arise. Interposed between the photoreceptors and ganglion cells are interneurons, the bipolar cells. Bipolar cells, like ganglion cells, fall into two classes, on-center and off-center. The transmitter released by cones excites bipolar cells of one class and inhibits the others. Each cone makes contact with both types of bipolar cells. Cones in the receptive-field center of a ganglion cell synapse onto bipolar cells that make direct contact with the ganglion cell. Inputs from cones in the receptive-field surround are relayed along lateral pathways by horizontal and amacrine cells.

As we shall see in subsequent chapters, the segregation of information into parallel processing pathways and the shaping of response properties by inhibitory lateral connections are pervasive organizational principles in the visual system.
Selected Readings


References