CHAPTER

27

Vision

OVERVIEW

Vision is the most studied and perhaps the best understood topic in sensory neuroscience. This chapter is concerned primarily with vision in mammals and focuses on the pathway in the visual system that has to do with perception: from the retina to the lateral geniculate nucleus of the thalamus (LGN) and on to the multiple areas of visual cortex. Other regions of the brain that receive visual input (such as the superior colliculus) are dealt with briefly in this chapter and more extensively in the chapter on eye movements (Chapter 36).

Studying vision provides the opportunity to explore the brain at many different levels, from the physical and biochemical mechanisms of phototransduction (Chapter 24) to the boundary between psychology and physiology (Chapters 52 and 53). At each of these levels, the visual system has evolved to solve a number of difficult problems. In terms of the physical stimulus, vision operates over extremely wide ranges of illumination. The visual system detects single photons in the dark but can also see clearly in bright sunlight, when the retina is bombarded with over 10^{14} photons per second. At a much higher level of complexity, ensembles of neurons in the cerebral cortex are able to solve extremely difficult problems, such as extracting the three-dimensional motion of an object from two-dimensional retinal images.

At every moment, the visual system is confronted with the vast amount of information present in visual scenes. The complex circuitry of the retina has evolved so that much of this information is extensively processed and relayed to the rest of the central nervous system, both efficiently and with great fidelity. Vision, however, has not evolved to treat all of this information equally; instead, it appears to be best suited to extract the sort of information that may be useful to animals, including humans, in a natural environment. Vision allows animals to navigate in the world; to judge the speed and distance of objects; and to identify food, members of other species and familiar or unfamiliar members of the same species.

In many animals, primates in particular, more of the brain is devoted to vision than to any other sensory function. This is perhaps because of the extreme complexity of the task required of vision: to classify and to interpret the wide range of visual stimuli in the physical world. At the highest levels of processing, the cerebral cortex extracts from the world the diverse qualities experienced as visual perception: from motion, color, texture and depth to the grouping of objects, defined by the combination of simple features.

The Receptive Field Is the Fundamental Concept in Visual Physiology

The strategies that the brain uses to solve the problems of vision can be understood at a very intuitive level. The most useful concept to aid this intuition is that of the *receptive field*, which is the cornerstone of visual physiology. As defined by H. K. Hartline in 1938 (Ratliff, 1974, p. 167), a visual receptive field is the "region of the retina which must be illuminated in order to obtain a response in any given fiber." In this case, "fiber" refers to the axon of a retinal neuron, but any visual neuron, from a photoreceptor to a visual cortical neuron, has a receptive field. The definition was later extended to include not only the region of the retina that excited a neuron, but also the specific properties of the stimulus that evoked the strongest

response. Visual neurons can respond preferentially to the turning on or turning off of a light stimulus—termed *on*-and-*off* responses—or to more complex features, such as color or the direction of motion. Any of these preferences can be expressed as attributes of the receptive field.

Sensory Systems Detect Contrast or Change

In the 1930s and 1940s, Hartline developed the concept of the receptive field with studies of the axons of individual neurons that project from the lateral eye of the horseshoe crab (*Limulus*) and from the frog's eye (Ratliff, 1974). The lateral eye of the *Limulus* is a compound eye made up of about 300 *ommatidia* arranged in a roughly hexagonal array. Each ommatidium contains optical elements, photoreceptors and a single neuron whose axon joins the optic nerve. Hartline found that when an isolated ommatidium was illuminated, the firing rate of its axon increased. More surprisingly, the firing of the same axon was decreased by a light stimulus in any adjacent ommatidium. This form of antagonistic behavior, known as *lateral inhibition*, serves to enhance responses to edges while reducing responses to constant surfaces. Without it, visual neurons would be just as sensitive to a featureless stimulus, such as a clean white wall, as to stimuli defined by edges, such as a white square on a black wall. Similar spatially antagonistic visual responses were found in mammals, as first demonstrated by Kuffler (1953) in the retina of the cat (Box 27.1).

Lateral inhibition represents the classic example of a general principle: most neurons in sensory systems are best adapted for detecting changes in the external environment. This principle can be explained in behavioral terms. As a rule, it is change that has the greatest significance for an animal, e.g., the edge of an extended object or a static object beginning to move. This principle can also be explained in terms of information processing. Given a world that is filled with constants—with uniform objects, with objects that move only rarely—it is most efficient to respond only to changes.

Several types of visual responses can be discussed in terms of the detection of change, or of *contrast:* defined as the fractional difference in luminance between two stimuli. There are several forms of contrast. The first is spatial contrast, the detection of which is enhanced by neurons in the retina that have lateral inhibition (center-surround organization, see Box 27.1). Next, there is temporal contrast, or change over time. Starting in the retina, visual neurons are affected very little by slow changes in illumination, but are extremely sensitive to more rapid changes. Finally, there is motion, which is distinguished by characteristic changes in a stimulus over both space and time. Many neurons in the visual system are excited selectively by objects that have a certain rate or direction of motion. In summary, contrast sensitivity can take on at least three forms: sensitivity to spatial variations in a stimulus (spatial contrast), sensitivity to changes over time (temporal contrast) and sensitivity to changes in both space and time (motion; see Box 27.4).

Receptive Fields Encode Increasingly High-Order Features of the Visual World

From the photoreceptors to the multiple visual cortical areas, the visual system is hierarchical. One level provides input to the next in a feedforward progression, although lateral interactions and feedback are almost always present as well. As a general rule, receptive fields at successive stages of processing (from photoreceptors, bipolar cells, ganglion cells and geniculate neurons, through neurons in multiple visual cortical areas) encode increasingly high-level features of the visual stimulus. The outer segment of a photoreceptor, which contains the visual pigment, is influenced only by a small point in visual space. It is therefore almost entirely insensitive to the spatial structure of a stimulus. At the opposite extreme, neurons in the inferior parietal region of visual cortex seem to respond best when the animal is viewing a specific face (see Chapter 55).

These two extremes of visual responses illustrate the visual system's dual task: to maintain generality—the ability to respond to any stimulus—while also being able to represent specific, environmentally important classes of stimuli. High-level neurons classify visual stimuli by integrating information that is present in the earlier stages of processing, but also by ignoring information that is independent of that classification. For instance, motion-sensitive neurons in area MT of the cerebral cortex (see later) are exquisitely sensitive to the direction and rate of motion of an object, but very poor at distinguishing the object's color or its position. This lack of localization is quite common in high-level neurons: receptive fields become larger as the features they represent become increasingly complex. Thus, for instance, neurons that respond to faces typically have receptive fields that cover most of visual space. For these cells, large receptive fields have a distinct advantage: the preferred stimulus can be identified no matter where it is located on the retina.

Summary

The mammalian visual system is a complex, hierarchical system that can be studied from a number of different viewpoints. This chapter concentrates on the physiology of visual neurons, which is based on the study of receptive fields. Originally, receptive fields were defined as the area of the retina that could evoke responses in a visual neuron. The concept has evolved to include the stimulus attributes that lead to a neural response, such as color, motion, or even the complex features of a specific physical object. Within the hierarchy of the visual system—from retina to the multiple areas of the visual cortex—neurons are selective for increasingly complex or high-order features.

THE EYE AND THE RETINA

The Optics of the Eye Project an Inverted Visual Image on the Retina

The study of vision begins with the eye (Fig. 27.1), whose refractive properties are determined by the curvature of the cornea and the lens behind it. These optical elements act to focus an inverted image on the retina, where the first stages of neural visual processing take place. The curvature of the cornea is fixed, but the curvature of the lens is adjusted by smooth muscles that flatten the lens when they contract, thus bringing more distant objects into focus. The amount of light that reaches the retina is controlled by the iris, whose aperture is the pupil. The iris, which is situated between the cornea and the lens in the *anterior chamber* of the eye, contracts at high light levels and expands in the dark. It is thus partially responsible for the ability to see over a broad range of light levels, but this ability is primarily due to light and dark adaptation, two complex processes that take place in the retina (see Chapter 24).

The Retina Is a Three-layered Structure with Five Types of Neurons

The anatomy of the retina has an almost crystalline beauty, a beauty that is enhanced by the clear relationships between form and function (Dowling, 1997). It is composed of five principal layers: three layers of cell bodies separated by two layers of neural pro-

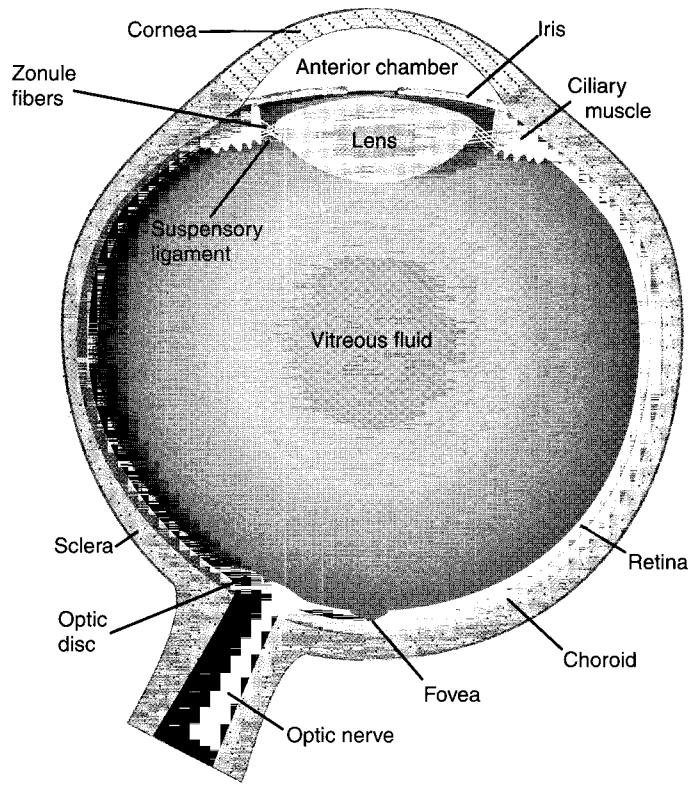


FIGURE 27.1 Schematic diagram of the human eye.

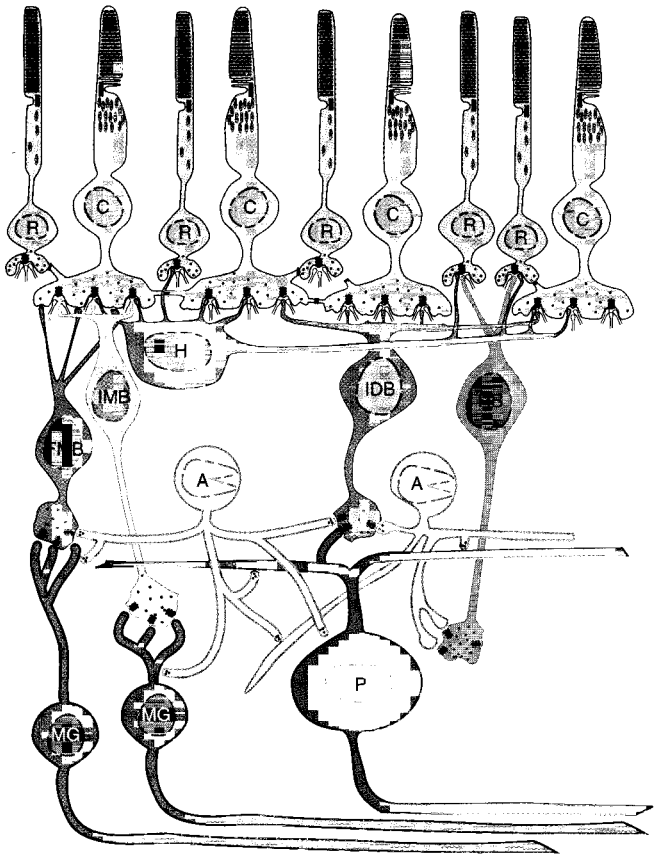


FIGURE 27.2 Summary diagram of the cell types and connections in the primate retina. R, rod; C, cone; H, horizontal cell; FMB, flat midget bipolar; IMB, invaginating midget bipolar; IDB, invaginating diffuse bipolar; RB, rod bipolar; A, amacrine cell; MG, midget ganglion cell; P, parasol cell. Adapted from Dowling (1997).

cesses, dendrites and axons (Fig. 27.2). The vertebrate retina is oriented within the eye so that light must travel through the entire thickness of the neuropil to reach the photoreceptors. Of the three cell layers, the first is farthest from the center of the eye and is thus called the *outer nuclear layer.* It contains the cell bodies of the photoreceptors, the rods and cones (Chapter 24). The next cell layer is the *inner nuclear layer*, which contains the cell bodies of the interneurons of the retina, both excitatory and inhibitory. These include horizontal cells, bipolar cells, and amacrine cells. Finally, the *ganglion cell layer* is home to the retinal neurons whose axons form the optic nerve, the sole pathway from the retina to the rest of the central nervous system. Interposed between the cell body layers are two layers of cell processes: *inner* and *outer plexiform layers.* The two plexiform layers are the sites of all interactions between the neurons of the retina.

The retina is one of the few circuits in the nervous system simple enough that cell types and connections can be learned without great effort. This is made even easier since the role of each of the five cell types can be placed within a simple functional scheme. The two main attributes of the output of the retina—the point-to-point representation of the visual image and the spatially antagonistic center-surround interactions in the receptive field (see Box 27.1)—can be understood in terms of the anatomy. The direct pathway, photoreceptor → bipolar cell → ganglion cell, is the substrate for the center of the receptive field of the ganglion cell and thus for its spatial resolution. Lateral interactions in the retina, most notably the center-surround antagonism, or lateral inhibition, are mediated by horizontal cells and amacrine cells.

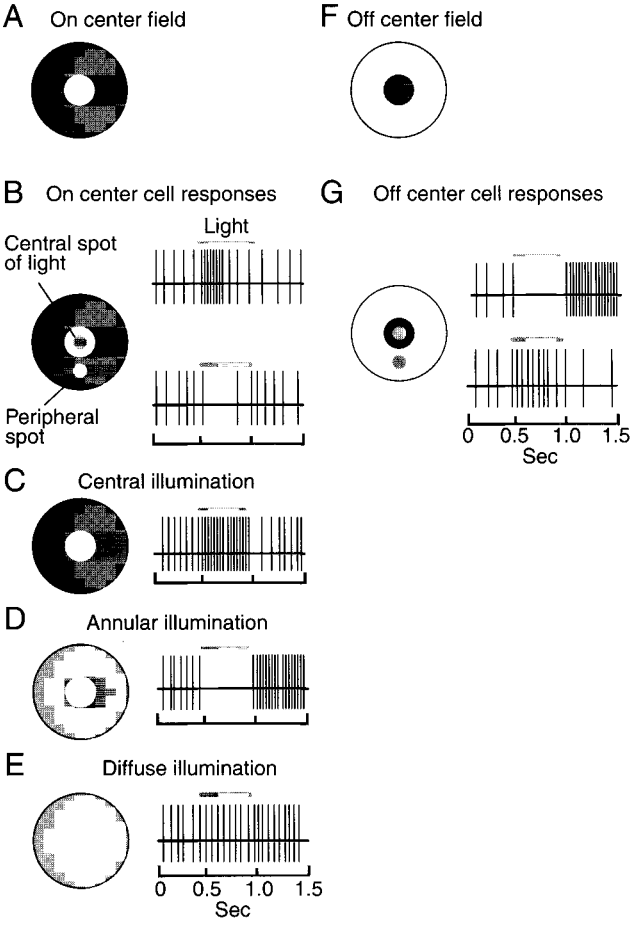
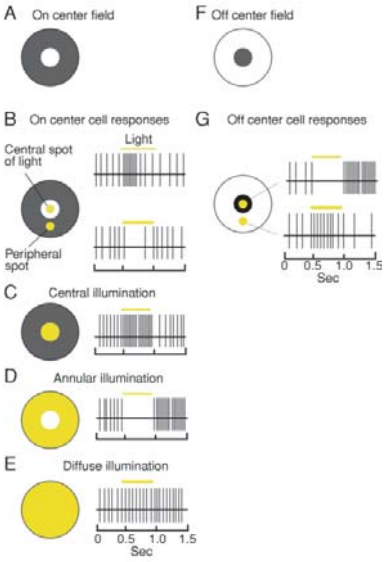


FIGURE 27.3 Visual responses of *on*-center (white) and *off*-center (dark gray) retinal ganglion cells. Visual stimuli are indicated in yellow, and the responses to these stimuli are shown to the right. See text for details.

FIG 28.3



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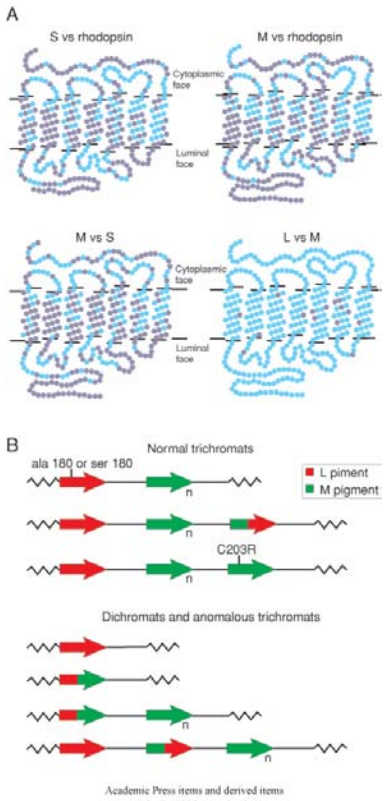

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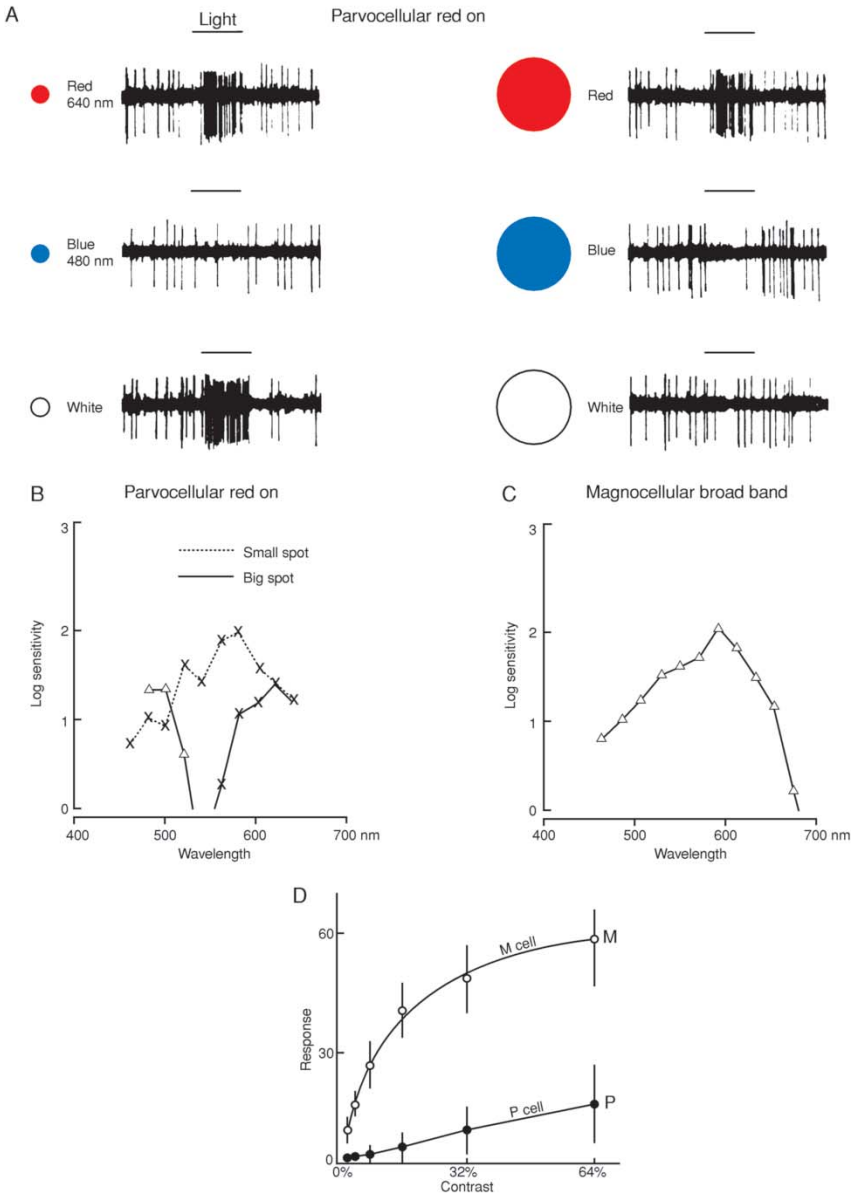

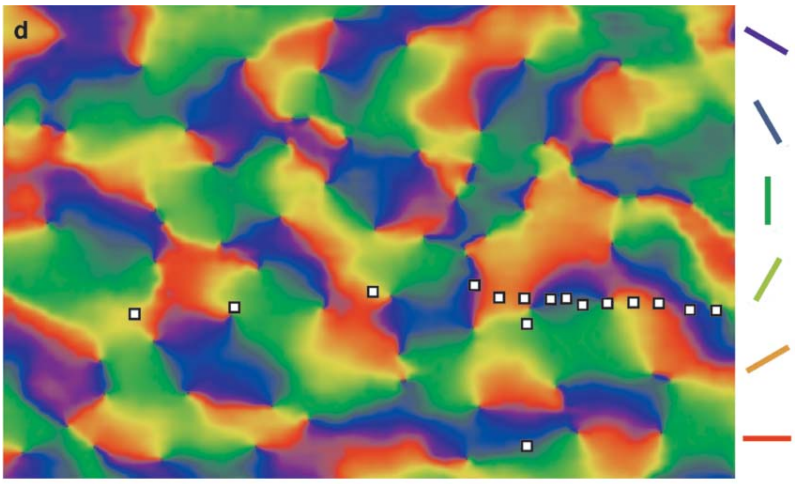

Photoreceptors Are Hyperpolarized by Light

Photoreceptors have been discussed at length elsewhere (Chapter 24). Here it is important to note that unlike most cells in the nervous system, the majority of cells in the retina—photoreceptors, bipolar cells, horizontal cells, and, arguably, most amacrine cells—do not normally fire action potentials. Instead, they have continuously graded membrane potentials that are modulated around a mean level. Photoreceptor cells have a tonic level of depolarization and of neurotransmitter release. They are hyperpolarized by an increment in light via a cGMP-gated process that closes sodium channels. This light-induced hyperpolarization acts to decrease the amount of neurotransmitter released by photoreceptors.

Bipolar Cells Can Be Hyperpolarized or Depolarized by Light

Bipolar cells are divided into two broad classes, termed *on* and *off* bipolars, that respond to light stimuli with depolarization and hyperpolarization, respectively. *On* bipolars are also known as *invaginating bipolars*, and *off* bipolars are known as *flat bipolars* because of the shape of the synaptic contacts they receive from photoreceptors (Fig. 27.2). Because all photoreceptors use glutamate as their neurotransmitter, these opposite responses require that *on*-and-*off* bipolar cells respond to the same neurotransmitter in opposite ways (Wu, 1994). Glutamate, typically an excitatory transmitter, is inhibitory for *on* bipolars. It acts by closing a cGMP-gated sodium channel, similar to that seen in photoreceptors. The depolarization of

BOX 27.1

KUFFLER'S STUDY OF CENTER-SURROUND RETINAL GANGLION CELLS

The classic experiments that Kuffler (1953) performed on retinal ganglion cells have formed the foundations for much of the subsequent physiological analysis of the mammalian visual system. Even beyond the study of vision, they represent a model for understanding the neurobiology of sensory systems. These experiments were performed *in vivo* in anesthetized cats. The first step in this sort of experiment is the careful placement of a fine microelectrode close to a single neuron so that action potentials can be recorded extracellularly. An oscilloscope trace of the firing pattern of this neuron is important, but the sound of action potentials on an audio monitor is even more critical. This immediate feedback allows the researcher to search for visual stimuli that excite or inhibit the neuron. Kuffler's first finding was that there were two categories of ganglion cells, as Hartline had seen in the retina of the frog. The cells were either *on*, i.e., excited by light increment, or *off*, i.e., excited by light decrement.

One of Kuffler's most important contributions was the careful mapping of lateral interactions in the retina, or what he termed the *center-surround* structure of the receptive field. When an *on* ganglion cell was being studied, a small light spot placed in the center of its receptive field would cause an immediate increase in firing rate of the cell (Fig. 27.3B, top). The center of the receptive field of an *on* ganglion cell was defined as all positions where the small spot evoked an *on* excitatory response. When the same spot was placed just beyond the center, in the region termed the *surround*, the neuron decreased its firing rate (Fig. 27.3B, bottom). Kuffler mapped the spatial extent of the regions that evoked excitation or inhibition simply by listening to the responses to spots flashed at many different locations. Alternatively, Kuffler studied receptive fields by searching for an optimal stimulus—one that increased the firing of a ganglion cell most effectively. The strongest stimulus for an *on* center cell was a spot of light that filled the receptive field center entirely (Fig. 27.3C). Similarly, the most effective inhibitory stimulus was a bright annulus shown to the surround alone. Following such strong inhibition, the cell had an excitatory response when the stimulus was turned off (Fig. 27.3D). Finally, Kuffler studied interactions between receptive field subregions. A large bright stimulus that covered both center and surround was found to evoke a much weaker response than a smaller spot confined to the center; the surround inhibition weakened or altogether eliminated the central excitation (Fig. 27.3E).

Kuffler's early experiments, along with those of Hartline, established the technical and conceptual foundations for the field of visual physiology. Almost all subsequent work in this field can be seen as falling into the three broad categories of experiments, exemplified by Kuffler's 1953 study: (1) the mapping of responses with isolated, suboptimal stimuli, (2) the search for an optimal stimulus, and (3) the study of interactions between responses evoked by two or more stimuli.

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on bipolars by light results not from excitation, but from the removal of inhibition, which occurs when photoreceptors are hyperpolarized by light. *Off* bipolars are excited by glutamate via more typical kainate receptors (named for the pharmacological agent that selectively activates them; see Chapter 10). When these cells are inhibited by light, the inhibition is in fact due to the removal of tonic excitation, which again occurs when the photoreceptors are hyperpolarized.

The functional importance of the *on* and the *off* pathways can best be understood in terms of contrast. From the bipolar cells onward, i.e., once *on*-and-*off* pathways have been established, visual neurons respond best to spatial and temporal contrast rather than to absolute light levels. Objects in the world are visible by the light they reflect; their borders are discerned usually because of different degrees of reflectance, which leads to contrast (changes in illumination, except for shadows, tend to be much more

BOX 27.2

QUANTITATIVE METHODS IN THE STUDY OF VISUAL NEURONS: CLASSIFICATION OF RETINAL GANGLION CELLS

Although neuroscientists have learned a tremendous amount about the visual system using the tools developed by Kuffler, researchers have been following a parallel line of studies of the visual system by asking different sorts of questions with the aid of more quantitative methods. In Kuffler's experiments and, most notably, many of Hubel and Wiesel's (see later), easily produced stimuli (such as spots, edges, and bars) were used to stimulate visual neurons. Action potentials were detected primarily with an oscilloscope and audio monitor. In the more quantitative studies of visual physiology, stimuli are shown primarily on video monitors and data are recorded with computers. The quantitative study of visual physiology constitutes a large field, which stems from the work of Hartline, Ratliff, Campbell, Barlow, and others (see Ratliff, 1974; Wandell, 1993). Analysis of the receptive fields of retinal ganglion cells in the cat performed by Enroth-Cugell and Robson (1966) represents an early and influential example of this line of research.

Stimuli used by Enroth-Cugell and Robson, and in many studies that followed theirs, consisted of *gratings*: light and dark bands whose luminance varied in a sinusoidal fashion across a screen. Gratings were not designed to be the most effective stimuli for visual neurons. The broad goal of this sort of experiment is to study not just what makes neurons respond best, but to study how they would respond to *any* stimulus and to probe what mechanisms they use to produce these responses. The analytical framework that goes along with these experiments is called *systems theory*, the study of input–output (or stimulus–response) systems. *Linear systems*, those that simply add up all of their inputs to produce an output, constitute an important part of this theory.

Enroth-Cugell and Robson used a simple test of linearity in their study of retinal ganglion cells in the cat. A grating was presented at different positions (called phases), and the responses to its introduction and removal were recorded. Two questions were addressed for each cell studied: (1) If a certain phase (whose bars were arranged white, black, and white; as in Fig. 27.4, 0°) excited the cell, did the opposite grating (black, white, and black; Fig. 27.4, 180°) inhibit it? (2) More importantly, were there null positions for the grating that evoked no response, as excitation and inhibition were perfectly balanced (Fig. 27.4, 90 and 270°)?

One class of ganglion cells, called *X cells*, passed these tests for linear spatial summation (Fig. 27.4, left) A second class of cells, *Y cells*, behaved differently. Like X cells, these cells also had a center-surround receptive field when mapped with spots and annuli. When studied with two opposite gratings, however, the responses evoked were not equal and opposite. Instead, the introduction and removal of the gratings at all positions resulted in two peaks of excitation, and no null position could be found (Fig. 27.4, right).

The use of systems theory and quantitative techniques in the study of the visual system has had a number of notable successes. It has helped in the classification of different families of visual neurons, such as X and Y cells. Further, it has been used to elucidate some of the mechanisms responsible for the responses of visual neurons (such as directionally selective cells, see Box 27.4). Perhaps most importantly, along with a large body psychophysical experiments that employ the same stimuli, it has helped create a common framework in which the responses of neurons can be related to perception.

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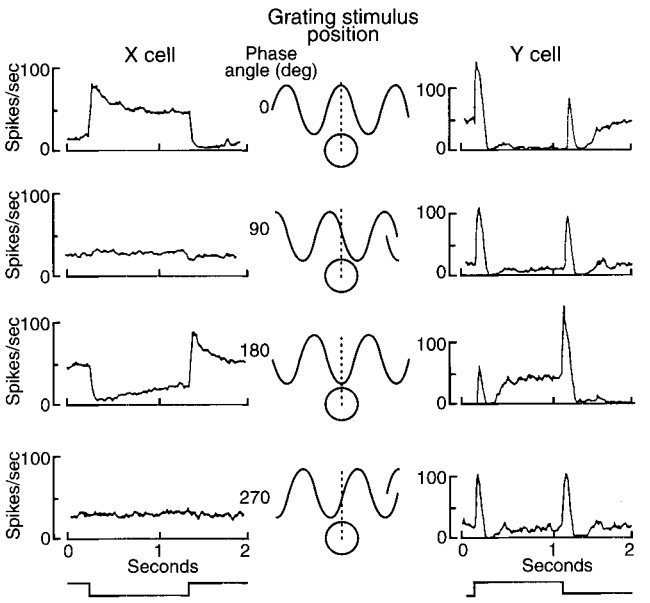


FIGURE 27.4 Visual responses of X and Y cells to contrast-reversing sine-wave gratings at different spatial phases (different positions, indicated schematically in the middle column). Visual responses, in spikes per second, are shown as poststimulus time histograms synchronized to the repetitive stimulus. Upward deflection of the lowest trace indicates introduction of the grating pattern (contrast on), and downward deflection indicates removal of the pattern (contrast off, but no change in mean luminance). Adapted from Enroth-Cugell and Robson (1966).

gradual). Because the visual system is adapted for seeing objects that can be either brighter or darker than their backgrounds, it is not too surprising that it is equally sensitive to positive and negative contrast steps.

Most ganglion cells, the output cells of the retina, receive their main excitatory input from bipolar cells. Thus these ganglion cells also have either *on* or *off* responses in the center of their receptive fields, according to which class of bipolar cells provide their input (see Box 27.1). Other ganglion cells, known as *on–off* cells, respond to both light onset and to light offset. These latter cells receive input from both classes of bipolar cells. Many of these cells respond preferentially to stimuli moving in a particular direction of motion (see Box 27.4).

Horizontal and Amacrine Cells Mediate Lateral Interactions in the Retina

There is a complex three-way synaptic relationship among the terminals of the photoreceptors, the processes of horizontal cells and the dendrites of bipolar cells (Fig. 27.2). Horizontal cells are inhibitory (GABAergic) and, as the name implies, they contact photoreceptors over a much larger horizontal extent of retina than bipolar cells. Thus, because they are the only neurons that sample over a sufficiently large area in the outer plexiform layer, horizontal cells are thought to be responsible for the antagonistic surround seen in the receptive fields of bipolar cells.

The second family of lateral interneurons in the retina, the amacrine cells (literally, cells with no axons), is a diverse class of cells that exhibits a wide range of morphologies. As is true of horizontal cells, all processing takes place on the dendrites of amacrine cells (in the inner plexiform layer), which contain both pre- and postsynaptic elements (Fig. 27.2). Most amacrine cells use GABA, glycine, or both acetylcholine and GABA as neurotransmitters, but it is thought that virtually every transmitter found in the brain is used by some amacrine cell. The functions of most of these diverse subclasses remain poorly understood. In addition to a possible role in the creation of the antagonistic surround, it has been proposed that some amacrine cells are responsible for the nonlinear responses in Y cells of the cat (see Box 27.2) or for the direction selectivity seen in the rabbit retina (see Box 27.4).

Retinal Ganglion Cells Provide the Output of the Retina

Visual information leaves the eye via the optic nerve, which is composed of the axons of all of the different classes of ganglion cells. The optic nerve begins at the *optic disc* (see Fig. 27.1). Because there are no photoreceptors at the optic disc, this circular region constitutes a blind spot in the retina. The routing of ganglion cell axons to different parts of the brain provides a number of interesting problems for developmental neurobiology (Chapters 19 and 22). The routing of axons is both macroscopic—different types of ganglion cells project to different regions of the brain—and microscopic: within any given target region, axons are sorted out in a precise manner. In each of two principal targets of retinal axons, the superior colliculus and lateral geniculate nucleus of the thalamus (LGN), a topographical map of visual space is created in which spatial relations are maintained between neighboring neurons.

This chapter is concerned primarily with the classes of retinal ganglion cells that project to LGN neurons, which in turn project to the primary visual (striate) cortex. Although cells in the LGN are more than mere relays of information from the retina, their receptive fields are quite similar to those of their ganglion cell inputs. The following discussion of retinal

receptive fields, therefore, can serve equally well to describe receptive fields in the LGN.

Parallel Pathways Are Composed of Distinct Classes of Retinal Ganglion Cells in the Cat

Kuffler found that retinal ganglion cells in the cat have a stereotyped center-surround organization. Similar cells (both *on* and *off*) were found at every position across the entire retina. Researchers later discovered, however, that there are in fact several different functional classes of ganglion cells, each with distinct response properties. Although different cell classes have been found in different species, in none is the retina composed of a single mosaic of identical cells. The fact that there are multiple types of output from the retina has had a profound effect on the study of visual processing in the brain. The degree to which these *parallel pathways* (Livingstone and Hubel, 1984; Merigan and Maunsell, 1994) are combined or kept separate has been a major theme in the study of central visual pathways, particularly the visual cortex.

The idea that there are parallel sensory pathways into the brain is not new. At the beginning of the 19th century, both Bell and Müller argued for what Müller termed the "specific energy of nerves." This term is a precursor of the idea that axon sensory neurons are "labeled lines," each of which conveys distinct signals to the brain. A surprisingly modern version of this idea was given in 1860 by Helmholtz in the "*Handbook of Physiological Optics*" (2000) in which he expressed Thomas Young's theory of color vision (1807) in the following manner: "The eye is provided with three distinct sets of nervous fibers. Stimulation of the first excites the sensation of red, stimulation of the second the sensation of green, and stimulation of the third the sensation of violet."

In one of the earlier studies using a quantitative approach to receptive field mapping (see Box 27.2), Enroth-Cugell and Robson (1966) found that cat retinal ganglion cells could be classified into two categories: X and Y (more categories have been found subsequently). This classification was based on a simple criterion: did ganglion cells simply add together all of their excitatory and inhibitory inputs (linear summation) or were the interactions between inputs more complicated (nonlinear summation)? The linear/nonlinear distinction between X and Y cells (see Box 27.2) may seem fairly abstract, but these cells turned out to be different in a number of other ways. Most notably, Y cell receptive fields are, on average, three times larger than those of neighboring X cells. X cells are therefore far more numerous, because many more X cell receptive fields are needed to effectively tile, or cover, the retina. One view is that the large, nonlinear receptive fields of Y cells make them well suited to detect change, at the cost of their ability to signal the exact location or nature of the stimulus; similarly, X cells are better at localizing more specific stimulus features, but less sensitive in detecting change.

Primate Ganglion Cells Project to Three Subdivisions of the Lateral Geniculate Nucleus: Parvocellular, Magnocellular, and Koniocellular

Primates have a number of different classes of retinal ganglion cells, each with distinct cellular morphology, projection patterns, and visual response properties. This discussion focuses on ganglion cells that project to the lateral geniculate nucleus (LGN). There are many differences among primate species (nocturnal versus diurnal, Old World versus New World); this section concentrates on the macaque; a diurnal, Old World primate. The macaque visual system has been studied extensively with anatomical, physiological, and behavioral methods. Most importantly, macaque vision is very similar to human vision.

The most numerous class of ganglion cells in the macaque retina are sometimes referred to as *P cells*, so called because they project to the dorsal-most layers of the LGN, the *parvocellular layers* (small cells; Fig. 27.9). *M cells*, which project to the two ventral layers of the LGN, the *magnocellular layers* (large cells), constitute a second class of retinal neurons. P and M cells have distinct morphologies (Fig. 27.2). P cells (also known as $P\beta$ or, in the central retina, midget ganglion cells) have very small dendritic fields. M cells (also known as $P\alpha$ or parasol cells) have much larger dendritic fields. Finally, members of a third class of retinal cells project to the *intercalated layers* between principal parvocellular and magnocellular layers. These intercalated layers are also termed *koniocellular* (dust-like, or tiny cells). There are roughly 1,000,000 P cells in the retina and parvocellular neurons in the LGN; there are 100,000 M and magnocellular neurons. Although the intercalated layers appear quite sparse and thin in standard histological sections (Fig. 27.9), there are as many intercalated cells as there are magnocellular cells. Due to their size and location, intercalated cells have been difficult to study and little is known about them in the macaque. Therefore the following section discusses only the functional properties of P and M pathways.

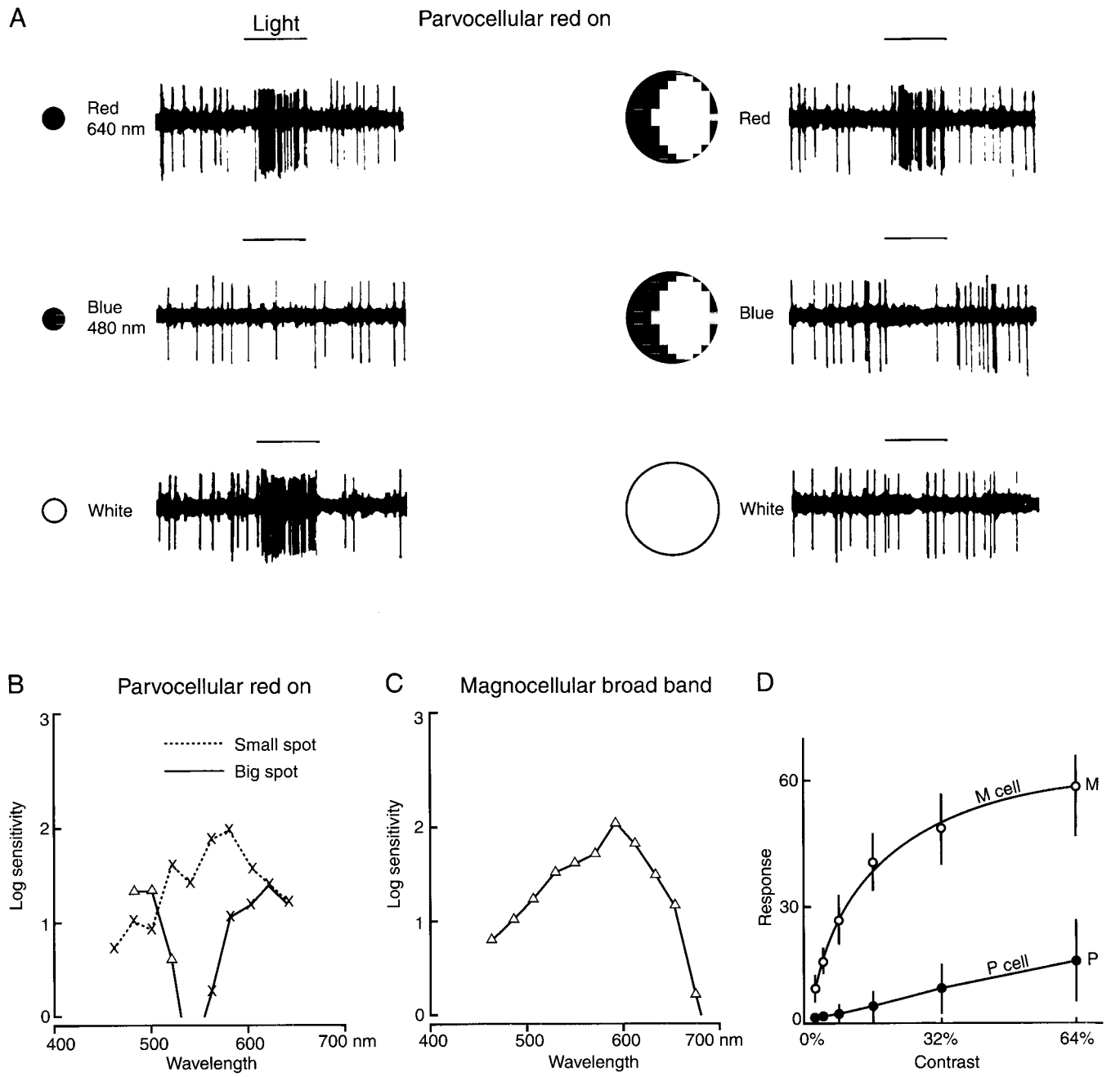
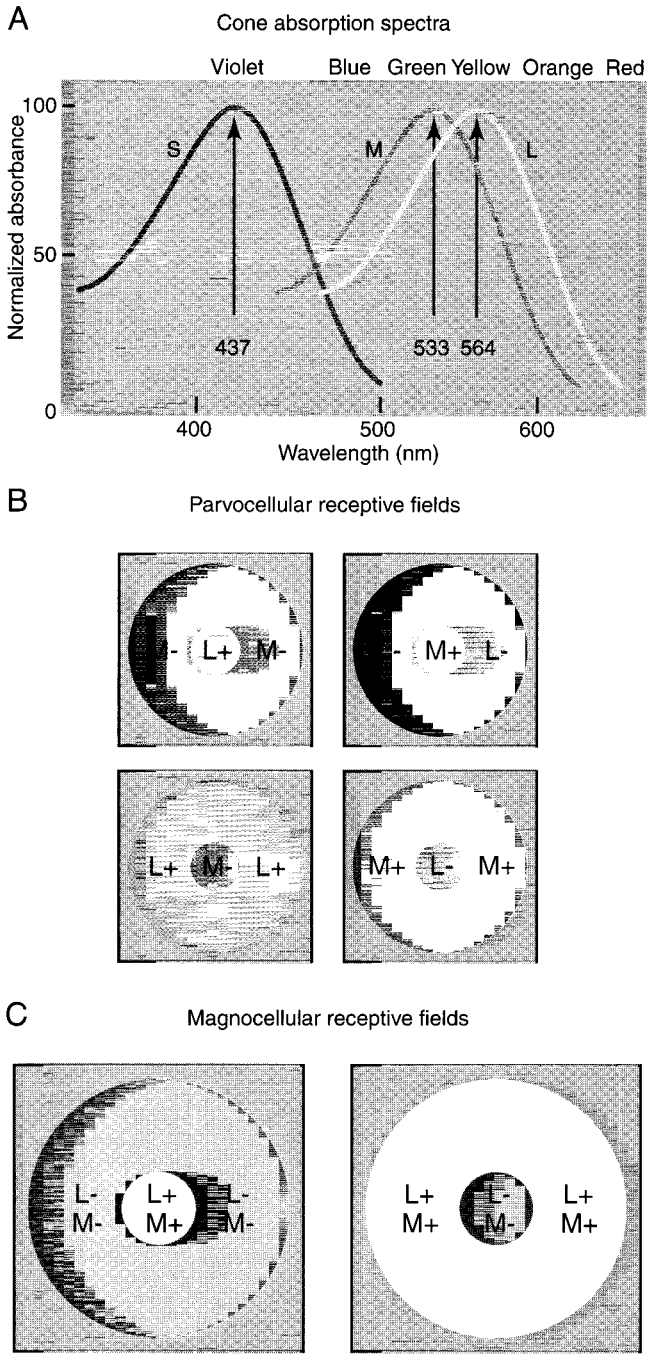


FIGURE 27.5 Visual responses of magnocellular and parvocellular neurons in the macaque. (A) Responses of a color-opponent (red-*on*/green-*off*) parvocellular neuron to small and large stimuli. For small spots, roughly the size of the receptive field center, the neuron was excited by both red and white and was weakly inhibited by blue. The responses to large spots were more selective. Red was excitatory, blue was strongly inhibitory, and white stimuli were ineffective. (B) Responses of the same red-*on*/green-*off* parvocellular neuron to different wavelengths of light. For small spots, the neuron was excited (X) for a broad range of wavelengths. For big spots, it was excited above 550 nm, from yellow to red, and inhibited (D) below 550 nm, from blue to green. (C) Responses of a magnocellular neuron to different wavelengths of light presented in the receptive field center. The neuron had *off* (D) responses at all wavelengths, i.e., no wavelength specificity was found. (D) Average contrast response functions of P (•) and M (o) cells measured in spikes per second. P cells respond poorly to low contrasts and do not saturate at high contrasts. M cells respond better to low contrasts, but saturate by 20–30%. A–C: from Wiesel and Hubel (1966). D: from Kaplan and Shapley (1986).

P and M Pathways Have Different Response Properties

As noted earlier, the receptive field properties of the LGN relay cells match closely those of their retinal afferents, but the two parallel pathways, P→ parvocellular and M→ magnocellular, are quite different. Five main characteristics distinguish the responses of P cells and M cells (see Figs. 27.5 and 27.6). (1) P cell receptive fields are smaller than M cell receptive fields at the same retinal position. (2) M cell axons conduct impulses faster than P cell axons. (3) The responses of P cells to a prolonged visual stimulus, particularly a color stimulus, can be very sustained, whereas M cells tend to respond more transiently. (4) Most P cells are sensitive to the color of a stimulus; M cells are not (Figs. 27.5A–27.5C). (5) M cells are much more sensitive than P cells to low-contrast, black-and-white stimuli (Fig. 27.5D). These last two differences, which have strong implications for the functional role of these pathways, are discussed next.



Color-Selective Responses in the P Pathway Are Derived from Antagonistic Inputs from L and M cones

Color vision depends on the distinct sensitivities of the three classes of cone photoreceptors to different wavelengths of light (the rods are active only under low light levels and are not involved in color vision). Although fine distinctions can be made between different wavelengths, it is important to emphasize that each of the light-sensitive pigments in the three cone classes is sensitive to a broad range of wavelengths. The spectral sensitivities of these pigments overlap considerably (Fig. 27.6A). Consequently, the names sometimes used for these pigments—red, green, and blue sensitive—are inaccurate. For instance, the "red" pigment is most sensitive to light whose wavelength is 564 nm, or yellow, although it is more sensitive than the other pigments to red light. A more accurate terminology, one that identifies the relative sensitivities of the three cone absorption spectra, is usually employed: long, middle, and short wavelength sensitive (or L, M, and S).

FIGURE 27.6 Aspects of color vision. (A) Absorption spectra of the three cone photoreceptors in humans: long, middle and short wavelength sensitive (L, M, and S). L and M cones in particular are sensitive to overlapping ranges of wavelengths. (B) Receptive field of the four types of red–green parvocellular cells in the macaque (labeled L+ and M+ or L- and M- according to their on-or-off centers, respectively). Classically, these small receptive fields have been described as receiving antagonistic input from L cones in their centers and M cones in their surrounds, or vice versa. When probed with color stimuli, L-*on* center and M-*off* center cells are excited by red and inhibited by green (and some blues: see Fig. 27.5 A). M-*on* and L-*off* cells are excited by green and inhibited by red. When probed with small white spots, L-on and M-on cells are excited when the stimulus is turned on; L-*off* and M-*off* cells are excited when the stimulus is turned off. (C) Receptive fields of the two main types of magnocellular cells. These larger receptive fields receive mixed L and M input to both center and surround. There are two types: *on* center (M+L+) and *off* center (L-M-).

BOX 27.3

INHERITED AND ACQUIRED DEFECTS OF COLOR VISION: RETINAL AND CORTICAL MECHANISMS

Inherited defects of color vision have been studied for over 200 years, originally with psychophysical methods but more recently with the tools of molecular genetics. Normal color vision is *trichromatic* (literally, three colored) because there are three different classes of cone photoreceptors. In the most common form of color vision defect, there are three pigments, but one of them is abnormal, or anomalous. More severe defects are found in *dichromats*, who lack a single cone type entirely. The current terminology for the three types of dichromacy was proposed by von Kries in 1897: *protanopia* (literally, the first type of blindness, or "red-blindness"), *deuteranopia* (second type, or "green-blindness"), and *tritanopia* (third type, or "blue-blindness"). While dichromats are unable to make certain color distinctions, only the very rare *monochromats*—people with one cone type or only rods—are truly color blind.

The genetics of red–green defects have long been known to be X linked: they are inherited from the mother and are fairly common in men, but they are uncommon in women. Roughly 2% of European white males are protanopes or deuteranopes and, depending on the population, between 2 and 6% are trichromats with a single anomalous pigment (either protanomalous or, more commonly, deuteranomalous). In contrast, only 0.4% of women in similar populations have red–green defects. Tritanopia, found equally in men and women, is significantly rarer. It is inherited as an autosomal-dominant trait thought to occur at low frequencies, estimated variously between 1 in 500 and 1 in over 10,000.

Because of the overlap in cone pigments, inherited color vision defects are not as simple as terms such as "red blindness" might suggest. In broad terms, protanopes and deuteranopes are unable to make specific discriminations along the red–green axis. Depending on the defect, they are unable to distinguish certain reds and greens from gray or from each other. Tritanopes are unable to discriminate between colors with and without a short wavelength component, such as between gray and certain shades of violet or yellow.

In the 1980s, Nathans, Hogness, and colleagues cloned and sequenced the three cone pigment genes and related them to color defects in humans. The cloning strategy was based on the pigments predicted close homology to rhodopsin (Fig. 27.7B). As expected from the genetics of protanopia and deuteranopia, two very similar genes for L and M pigments were found on the X chromosome. The third gene, which codes for the S pigment, was found on chromosome 7. In subsequent work by this group and others, molecular genetics of the inherited color defects, including anomalous trichromacy, have been studied in great detail.

While the inherited color deficiencies are fairly simple and well understood, acquired defects in color vision—found in a number of ocular, neurological, and systemic diseases—are far more varied. One such syndrome, *cerebral achromatopsia*, was described in the neurological literature in the 1880s. In rare patients with certain cortical lesions, the discrimination of colors and the naming of colors were severely impaired. In the majority of cases, there were other associated deficits—either an area of complete blindness (a scotoma) or an inability to recognize faces (prosopagnosia)—but in some cases, vision was otherwise quite normal. From the location of the lesions, some neurologists early on inferred the existence of a region of cortex required for color, vision, near the inferior border of the primary visual cortex.

The literature of cerebral achromatopsia, quite developed in the late 19th century, fell into eclipse for the first half of the 20th century when highly specific functional divisions of the cortex were questioned. With the discovery in the 1970s of multiple visual areas in primate cerebral cortex (Felleman and Van Essen, 1993), however, the existence of a cortical region devoted to color in humans seemed less farfetched. With recent advances in noninvasive brain imaging there is little doubt that such regions exist in humans, although their homology to brain regions in non-human primates remains controversial.

R. Clay Reid

Because green light will excite both long and middle wavelength cones, the color green can be distinguished only by the fact that it excites middle wavelength cones more strongly than it excites long wavelength cones. This distinction can be made by neurons that are sensitive to the difference between the signals from two cone classes, or neurons that are *color opponent*. In the retina and LGN, there are two categories of color-opponent cells: red–green and blue–yellow (yellow is made of the sum of long and middle wavelength cone signals; Dacey, 2000). These are sometimes also termed red-minus-green cells and blue-minus-yellow cells. The

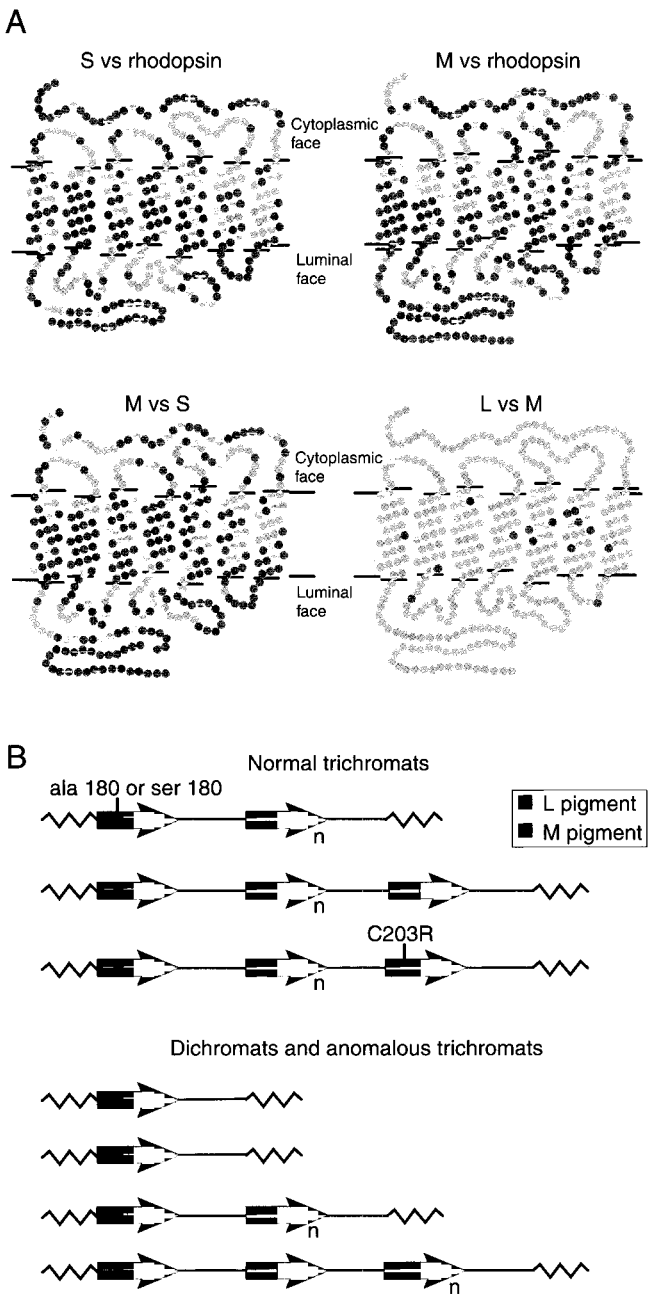


FIGURE 27.7 Molecular biology of photopigment genes. (A) Transmembrane model of cone photopigments. Homologies between the different photopigments are shown, with differences between proteins highlighted. The amino acid sequences of M and S cone pigments and rhodopsin are all approximately 40% identical (and 75% homologous), whereas L and M pigments are 96% identical (99% homologous). (B) Structure of the portion of the X chromosome coding for L and M pigments. Normally, there is one L pigment gene and several M pigment genes. Because not all of these genes are expressed, different variants can result in normal color vision (top). Many different patterns of recombination and deletion can be associated with a defect in red–green vision: either dichromacy or anomalous trichromacy (bottom). A: from Nathans *et al.*, 1986; B: from Nathans (1994).

most numerous color-opponent neurons in the primate retina are red–green opponent P cells. These cells receive antagonistic input from long and middle wavelength-sensitive (L and M) cones.

Near the fovea, the center of the retina, a P cell receives input from only one bipolar cell. This *midget bipolar* in turn receives input from a single cone (Fig. 27.2). This arrangement ensures not only that the center of the ganglion cell's receptive field is as small as possible, but also that the center receives input from only one cone type: L or M. Classically, the antagonistic surround of these P cells (or their counterparts in the LGN) has been thought to be dominated by the other main cone class, M or L, respectively (Wiesel and Hubel, 1966). Although the exact nature of the surround in red–green P cells has been somewhat controversial in recent years (Dacey, 2000), this classical view is shown in Fig. 27.6B.

There are four different types of red–green opponent P cells in the retina (Fig. 27.6B), and hence parvocellular neurons in the LGN. L-*on* center and M-*off* center cells are excited by red and inhibited by green (and some blues; see Fig. 27.5A). M-*on* and L-*off* cells are excited by green and inhibited by red. As Wiesel and Hubel showed (1966), parvocellular neurons in the LGN are sensitive to small bright spots presented in their receptive field centers, but they are most selective for the color of the stimulus when larger stimuli are used (see Figs. 27.5A and 27.5B). This is because only larger stimuli are effective in stimulating simultaneously the color-opponent center and surround. Because they absorb a broad range of wavelengths (Fig. 27.6), single cones are not very color selective. Parvocellular neurons are most color selective when the stimulus evokes antagonistic influences from two cone classes: one found in the center and the other found only in the surround.

M Cells Are Highly Sensitive to Contrast

Because of their marked color sensitivity and small receptive fields, P cells have long been thought to be involved with the ability to make color discriminations and to see the finest details. When tested with black-and-white stimuli, however, P cells responded to low contrast very poorly compared to M cells. In a study that used the quantitative methodology similar to Enroth-Cugell and Robson's (see Box 27.2), Kaplan and Shapley (1986) measured the responses of P and M cells to sine-wave gratings of various contrasts (Fig. 27.5D). Perceptually, stimuli can be detected that have less than 1% contrast (i.e., 1% luminance deviation from the mean). Kaplan and Shapley (1986) found that M cells often responded well to contrasts of under

5% and that they gave their strongest responses at contrasts as low as 20%. P cells tended to respond poorly to contrasts below 10%, a stimulus that is quite salient, and rarely reached their strongest responses below 64%. From this, Kaplan and Shapley concluded that the ability to see low contrasts is due primarily to the M cell system.

The relatively poor sensitivity of P cells to low-contrast stimuli is not well understood, but it may be partially the result of two factors: receptive-field centers receive input from a very small region of the retina, and the inputs from different cone classes are subtracted from each other, rather than added together. Whatever the reason, the poor performance of the P pathway in detecting low contrast implies an important role for M cells in the detection of the form of objects (which is robust at low contrasts), in addition to their role in the motion pathway (discussed later).

Summary

The retina, part of the central nervous system, is a self-contained neuronal circuit whose anatomy and physiology have been studied in great detail. There are five types of cells in the retina. Photoreceptors, bipolar cells, and ganglion cells constitute the direct, feed-forward pathway. Horizontal cells and amacrine cells subserve lateral interactions within the retina. Photoreceptors are all hyperpolarized by light, but bipolar cells can be either hyperpolarized (*off* cells) or depolarized by light (*on* cells). There is a great variety of retinal ganglion cells, but most have an antagonistic center-surround organization. In the primate, the two best studied classes of ganglion cells are P cells and M cells, which project to the parvocellular and magnocellular layers of the LGN, respectively. P cells have small receptive fields, are sensitive to the color of a stimulus, and are relatively insensitive to low contrasts. M cells have larger receptive fields, are insensitive to color, and are very sensitive to low contrasts.

THE RETINOGENICULOCORTICAL PATHWAY

Visual Information Is Relayed to the Cortex via the Lateral Geniculate Nucleus

In mammals with forward-facing eyes, such as most carnivores and the primates, retinal axons are routed so that visual information from the same points in space coming from the two eyes can be combined. From both eyes, ganglion cells whose receptive fields are in one half of the visual field project to the opposite cerebral hemisphere (Fig. 27.8). This cross-routing occurs at the optic chiasm (from the Greek letter *chi*, χ). Here, axons from the medial (nasal, or nearer the nose) half of one retina cross over to join the axons from the lateral (temporal, or nearer the temples) half of the other retina. In other words, the temporal retina projects to the *ipsilateral* (same-side) hemisphere and the nasal retina projects to the *contralateral* (opposite-side) hemisphere. Unlike somatic sensation, which is entirely crossed (see Chapter 26), only half of the retinal axons cross. Like somatic sensation, however, the crossing of retinal axons results in each half of the external visual field being represented in the opposite cerebral hemisphere.

The LGN Is a Layered Structure That Receives Segregated Input from the Two Eyes

As they leave the optic chiasm, retinal axons from the two eyes travel together in the optic tract, which terminates in the LGN (Fig. 27.8). The LGN is com-

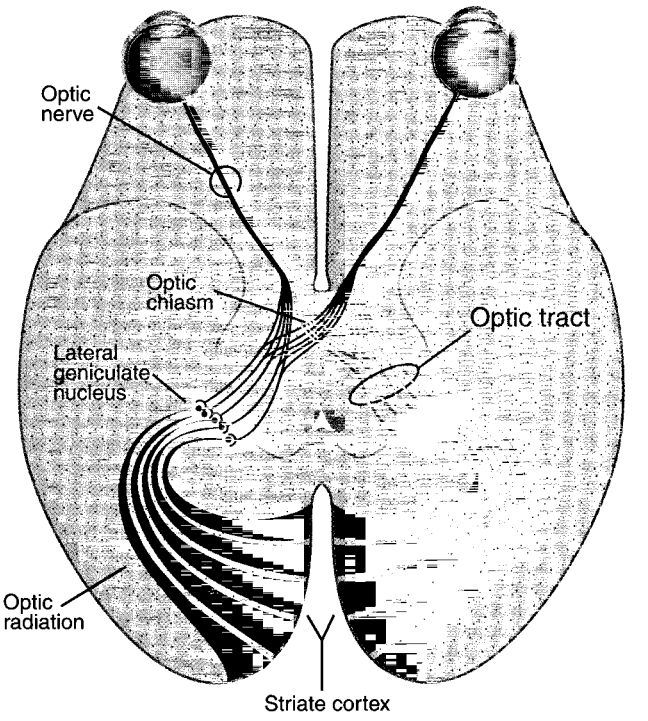


FIGURE 27.8 The retino-geniculo-cortical pathway in the human. Optic nerve axons from the nasal retina cross at the optic chiasm and join axons from the temporal retina of the other eye. Together, these contralateral and ipsilateral axons make up the optic tract, which projects to the LGN. Each of the six layers of the LGN receives input from only one eye. Axons from the LGN make up the optic radiations, which project to the striate cortex. Adapted from Polyak (1941).

posed of layers, each of which receives input from only one eye, although the number varies between species. In the macaque, the six principal layers contain most of the relay cells to primary visual cortex (Fig. 27.9). The four parvocellular layers are found dorsally. They receive P cell input from the contralateral and ipsilateral eye in the order of contra, ipsi, contra, and ipsi. The magnocellular layers are found more ventrally. They receive M cell input in the order of ipsi and contra. Interposed between these principal layers are the intercalated layers, populated by koniocellular neurons.

In the cat, the LGN has only two principal layers, called A and A1, which receive input from the contralateral and ipsilateral retinas, respectively. The neurons are again quite similar to either the retinal X cells or the Y cells that innervate them.

The Primary Visual Cortex in the Cat Is an Example of a Functional Hierarchy

Cat primary visual cortex (area 17) is perhaps the best understood neocortical area in any species. The first studies of Hubel and Wiesel (1962) form the foundation of this understanding. Hubel and Wiesel found cells whose responses differed dramatically from those in the retina and thalamus. Many of these cells could be excited by stimuli presented to either eye. The primary visual cortex thus represents the first level of the visual system at which binocular interactions could form a substrate for depth perception. Most strikingly, Hubel and Wiesel found that the vast majority of cortical cells respond best to elongated stimuli at a specific orientation and give no response at the orthogonal orientation. This is in sharp contrast to cells in the retina and LGN, which are not selective for orientation.

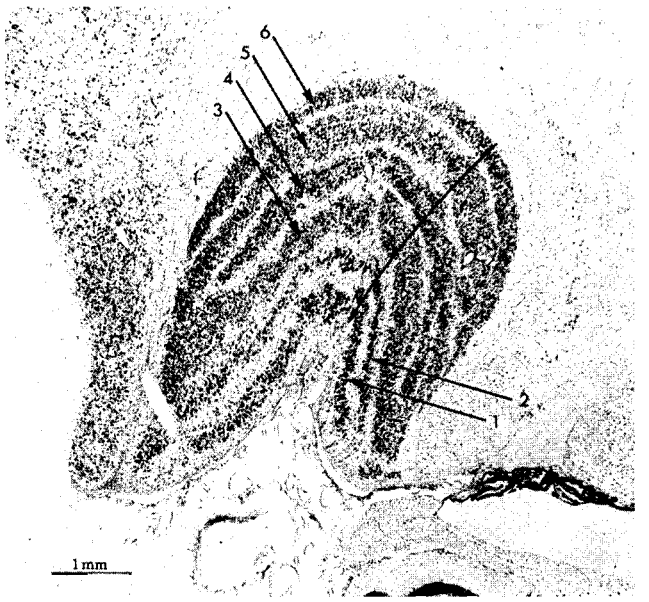


FIGURE 27.9 The six-layered LGN of the macaque monkey. The top four parvocellular layers (6, 5, 4, and 3) receive input from the ispilateral and contralateral eye in the order of contra, ipsi, contra, and ipsi. The bottom two magnocellular layers (2 and 1) receive ipsi and contra input, respectively. In between these principal layers are intercalated or koniocellular layers. The arrow from layer 6 to 1 indicates organization of the precisely aligned retinotopic maps of the six layers. The receptive fields of neurons found along this line are located at the same position in visual space. From Hubel and Wiesel (1977).

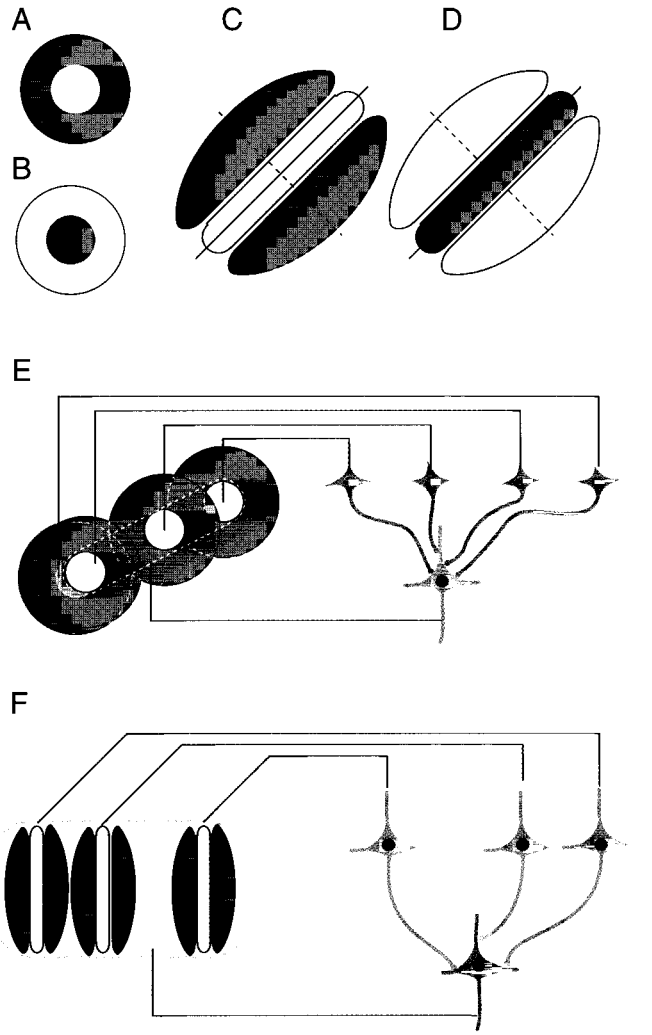


FIGURE 27.10 Hubel and Wiesel's original models of visual cortical hierarchy. (A and B) Receptive field maps of center-surround receptive fields in LGN. White: *on* responses; dark gray: *off* responses. (C and D) Receptive field maps of simple cells. (E) Model of convergent input from LGN neurons onto the cortical simple cell. (F) Model of convergent input from simple cells onto complex cells. Adapted from Hubel and Wiesel (1962).

Hubel and Wiesel described two broad classes of neurons in area 17: *simple cells* and *complex cells*. The receptive fields of simple cells were segmented into oriented *on*-and-*off* subregions (Figs. 27.10C and 27.10D) and were therefore most sensitive to similarly oriented stimuli. In these receptive field subregions, responses were evoked by turning a light stimulus *on* or *off*, but not by both. Given these well-defined *on*-and-*off* subregions in simple cells, Hubel and Wiesel suggested a straightforward hierarchical model to explain orientation selectivity: neurons in the lateral geniculate nucleus whose receptive fields are arranged in a row could all converge to excite a specific simple cell (Fig. 27.10E). Although this model has generated much controversy over the ensuing years, many of its elements have been demonstrated directly (Reid and Alonso, 1995; Ferster *et al.*, 1996).

The second class of cortical neurons, complex cells, also responded best to oriented stimuli, but their receptive fields were not elongated along a preferred orientation, nor were they divided into distinct *on*-and-*off* subregions. It would therefore be difficult to imagine how the responses of these neurons could be constructed directly from the center/surround receptive fields in the thalamus. Given the properties of simple cells, Hubel and Wiesel proposed a hierarchical scheme. Complex cells receive their orientation selectivity from convergent input from simple cells whose receptive fields have the same orientation preference, but have slightly different spatial locations (Fig. 27.10F).

This original model is hierarchical or serial; information flows from one level to the next in a well-defined series. In contrast to this hierarchical model

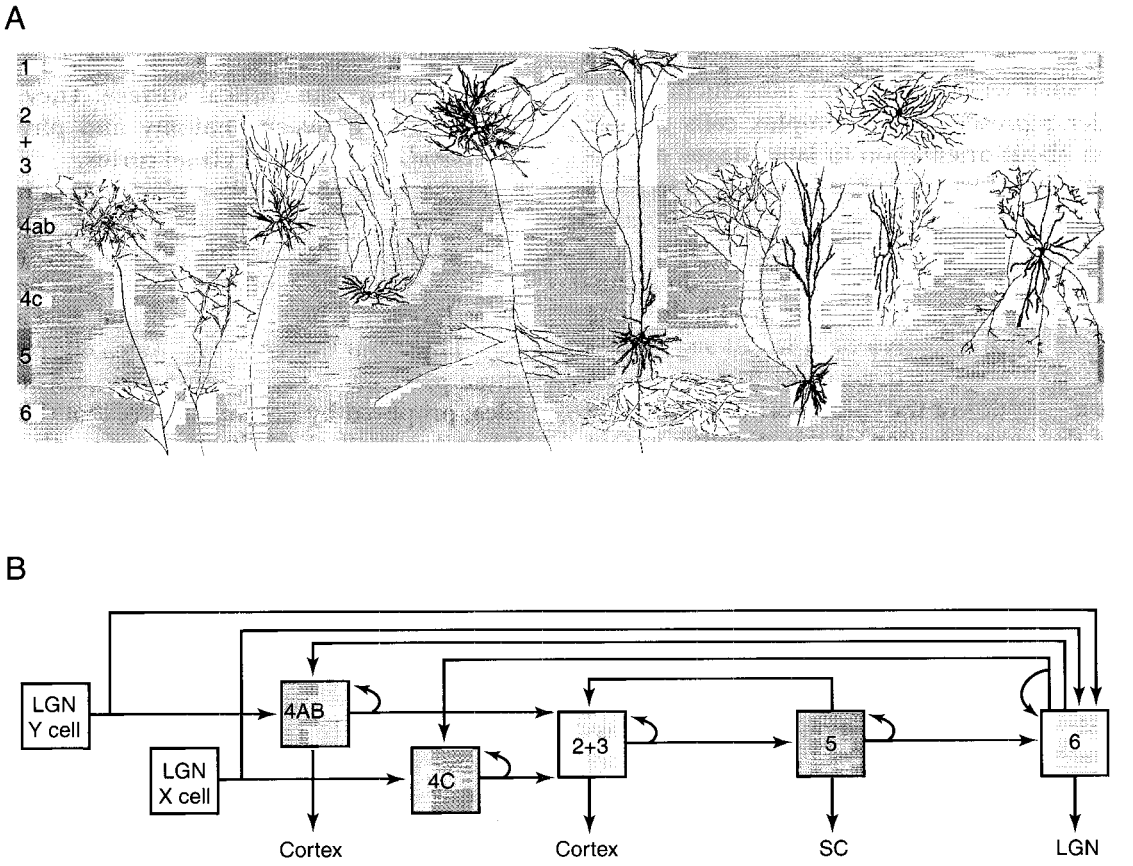


FIGURE 27.11 Circuitry of cat cortical area 17. (A) Morphology of individual cells stained with horseradish peroxidase. Thick lines: dendrites; thin lines: axons. (B) Schematic diagram of connections. Most thalamic (LGN) input is concentrated in layer 4 and, to a lesser degree, in layer 6. Y cells tend to project more superficially in layer 4 than X cells (note that sublayers 4ab and 4c are not strictly analogous to 4A, 4B, and 4C in the macaque). There is a fairly strict hierarchical pathway from layers 4 Æ 2+3 Æ 5 Æ 6 with feedback connections from 5 Æ 2+3 and 6 Æ 4. There are also many lateral connections between neurons within the same layer. Adapted from Gilbert and Wiesel (1985).

of cortical processing, it has also been proposed that each region of the cerebral cortex is made up of several different streams of information that are all processed in parallel. As with most dichotomies, elements of both hierarchical and parallel processing have been found in the visual cortex of all mammals studied. For simplicity, an outline of the organization of visual cortex in the cat is discussed here in terms of a hierarchical model. Parallel processing will be illustrated with the example of a primate visual cortex.

The hierarchical scheme has received support from several correlations between anatomy and physiology of area 17. In broad terms, simple cells are more common in the layers of cortex that receive direct input from the thalamus (layer 4 and, to a lesser extent, layer 6). Complex cells are found more frequently in layers that are more distant from the thalamic input in layers 2+3, which receive input primarily from layer 4, and in layer 5, which receives most of its input from layers 2+3 (Gilbert and Wiesel, 1985; Fig. 27.11).

In terms of their probable function in perception, the receptive fields of complex cells furnish an early example of what was meant in the introduction by a higher order representation. Complex cells convey information about orientation to later stages of processing, but that information has been combined and generalized. A simple cell responds to an oriented stimulus of a specific configuration and a specific location; in particular, it has separate *on*-and-*off* subregions. A complex cell also responds to stimuli at one orientation, but the receptive field is not segregated into *on*-and-*off* subregions. Instead, it can respond to a light or dark stimulus of the correct orientation, independent of the exact location of the stimulus within the receptive field. This sort of generalization is a recurrent theme in the cortical processing of visual information.

Several Parallel Streams Are Found in the Macaque Primary Visual Cortex

In the macaque primary visual cortex (V1, or striate cortex), a hierarchical organization is certainly present, but it is also clearly composed of several parallel streams. As discussed earlier, at least three types of inputs to visual cortex (parvocellular, magnocellular, and koniocellular) are first segregated within the LGN. Each class of neurons projects to a specific subdivision of primary visual cortex. Most thalamic afferents terminate in layer 4C, which is split into two divisions. 4Cα receives its input from magnocellular neurons and 4Cβ from parvocellular neurons. Intercalated, or koniocellular, geniculate neurons project to layers 2+3, specifically to regions known as "blobs" (discussed later) that stain densely for the enzyme cytochrome oxidase (Livingstone and Hubel, 1984)

Thus visual information from functionally and anatomically distinct M and P retinal neurons are kept separate through the LGN and at least up to the cortical neurons that receive direct thalamic input. The degree to which these pathways—as well as the more poorly understood koniocellular pathway—are kept separate within visual cortex remains an area of active research (see Fig. 27.15).

Functional Architecture Can Be Seen in the Columnar Structure of the Visual Cortex

So far, the physiology of the visual cortex has been considered in terms of individual neurons and their response properties. Another major contribution of Hubel and Wiesel was their demonstration that cells with similar receptive field properties tend to be found near each other in the cortex. Further, they found that physiological response properties, such as orientation selectivity, are organized in an orderly fashion across the cortical surface. They termed the relationship between anatomy and physiology the *functional architecture* of visual cortex.

Hubel and Wiesel's key observation in this arena was that when an electrode is advanced through the cortex perpendicular to its surface, all neurons encountered have similar response properties. If a cell near the surface has a specific orientation and is dominated by input from one eye, then cells below it share these preferences. This finding is consistent with the idea, proposed by Lorente de Nó, that the fundamental unit in cortical architecture is a vertically oriented *column* of neurons. Hubel and Wiesel proposed that a cortical column is both a physiological and an anatomical unit, as had Mountcastle in his study of somatosensory cortex (see Chapter 26). A second observation was that the property of orientation preference varies smoothly over the cortical surface. If an electrode takes a tangential path through the cortex through many different columns, the orientation preference generally changes in a steady clockwise or counterclockwise progression, although occasionally there are discontinuous jumps (Fig. 27.12A).

In addition to orientation, at least two other parameters are mapped smoothly across the cortical surface. Cells in the visual cortex receive inputs from the two eyes in varying proportion, a property that Hubel and Wiesel termed *ocular dominance.* In tangential microelectrode penetrations, cells are found that are dominated first by input from one eye and then the other. This provides evidence for *ocular dominance columns,*

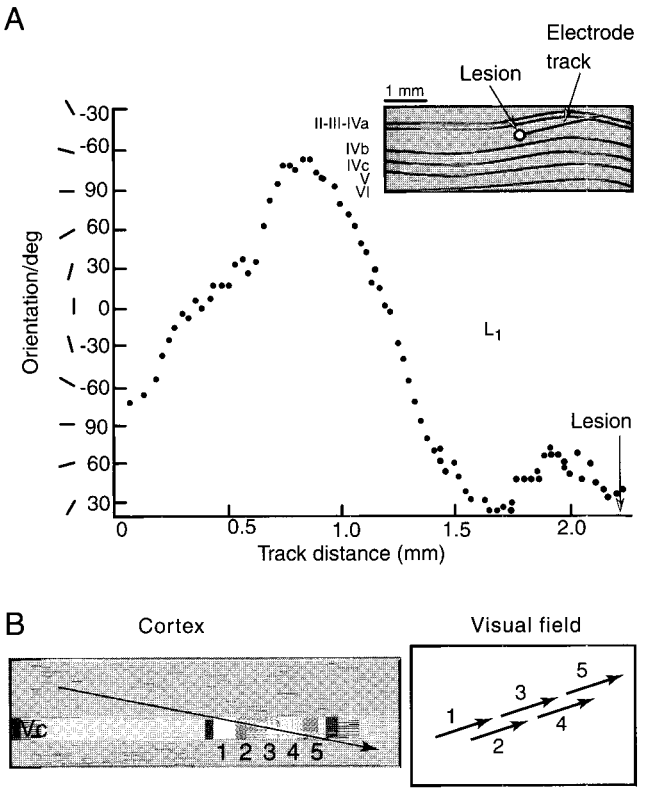


FIGURE 27.12 Two aspects of the functional architecture of the macaque primary visual cortex. (A) Graph of the preferred orientation of neurons encountered in a long microelectrode penetration through layers 2+3 (inset). There was an steady, slow progression of preferred orientations, although there were a few positions where the orientations changed more abruptly. (B) Schematic diagram of an electrode penetration through layer 4C (left) and the retinotopic positions of receptive fields (right). Numbers (1–5) indicate regions dominated by input from alternating eyes. At the border between ocular dominance columns (e.g., instance between 1 and 2), the location of receptive fields jumps back to a point represented near the middle of the previous ocular dominance column. There is a complete representation of visual space in columns dominated by each eye (1,3,5 or 2,4) and these representations are spatially interleaved. Adapted from Hubel and Wiesel (1977).

which have subsequently been demonstrated anatomically as well as physiologically. Second, prior to Hubel and Wiesel's work, a precise map of visual space across the surface of the cortex had been demonstrated. For any cortical column, receptive fields are all located at roughly the same position on the retina. Nearby columns represent nearby points in visual space in a precise and orderly arrangement. The position of a stimulus on the retina is termed its *retinotopy;* thus a region of the brain (such as the superior colliculus, LGN, or the visual cortex) that maintains the relations between adjacent retinal regions is said to have a *retinotopic map.*

Given the existence of multiple functional maps, the obvious question is: How do these maps relate to each other? This question has been answered most definitively for the relationship between retinotopy and ocular dominance. Layer 4 in the primate is ideal for studying this question, as the receptive fields are quite small and the borders between ocular dominance columns are well defined. By making long, tangential penetrations through layer 4 of the striate cortex, Hubel and Wiesel found a precise interdigitating map from each eye. When eye dominance shifts, the receptive field location shifts to a point corresponding to the middle of the previous ocular dominance column (Fig. 27.12B). Thus there is a 50% overlap in the spatial locations represented by adjacent ocular dominance columns. In this manner, a complete representation of space is attained for both eyes while ensuring that cells that respond to overlapping points in visual space are always nearby within the cortex.

Ocular Dominance and Orientation Columns Can Be Revealed with Optical Imaging

The technique of optical imaging has proven extremely useful in the study of the functional architecture of the visual cortex. Optical imaging allows direct visualization of the relative activity of small cortical ensembles rather than relying on inferences made from single-unit studies (Blasdel and Salama, 1986; Grinvald *et al.*, 1986). The technique uses dyes that change their optical properties with neural activity. Even if no dyes are used, brain activity can be mapped with an intrinsic signal, caused primarily by changes in blood flow and blood oxygenation.

A typical optical imaging experiment works as follows (Fig. 27.13A). First, a series of digitized images is taken of a region of visual cortex (Fig. 27.13B) while the animal is presented with visual stimuli through the left eye. Next, a similar series is captured during right eye stimulation. When the right eye images are subtracted digitally from the left eye images, a striking picture is created that reveals the functional architecture of ocular dominance (Fig. 27.13C). Previously, anatomical methods had been used to produce maps of ocular dominance, and these maps appear similar to those found with optical imaging, but an important feature of optical imaging is that multiple images can be obtained from the same region of the cortex. For instance, in addition to ocular dominance, maps of the preferred orientation can also be made. A useful way to present these data is in terms of a color code, in which each color represents a different preferred orientation (Fig. 27.13D). The orientation columns revealed by optical imaging were consistent with earlier microelectrode studies (compare Fig. 27.13E

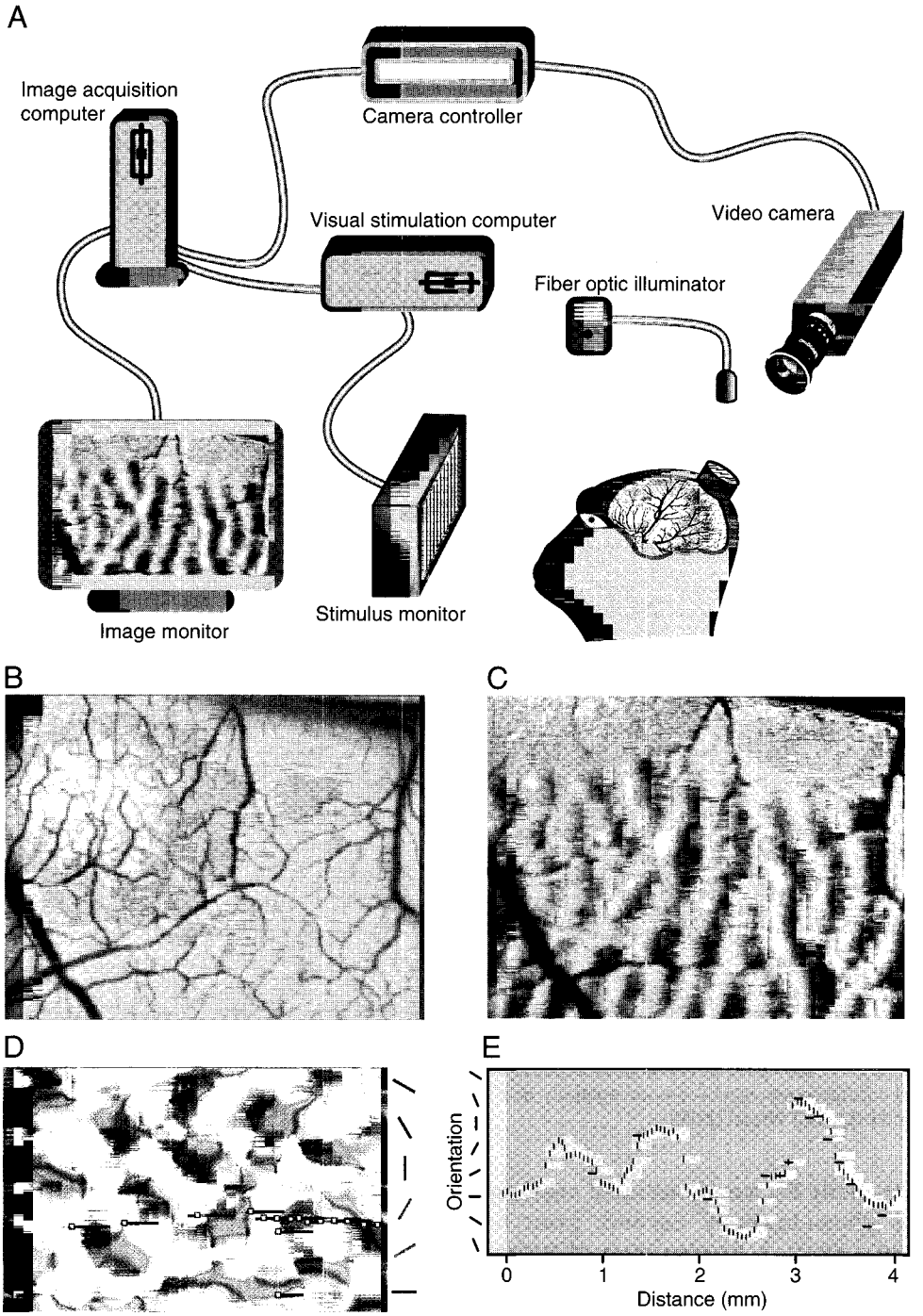


FIGURE 27.13 Optical imaging of functional architecture in the primate visual cortex. (A) Schematic diagram of the experimental setup for optical imaging. Digitized images of a region of visual cortex (as in B) are taken with a CCD camera while the anesthetized, paralyzed animal is viewing a visual stimulus. These images are stored on a second computer for further analysis. (B) Individual image (9 by 6 mm) of a region of V1 and a portion of V2 taken with a special filter so that blood vessels stand out. (C) Ocular dominance map. Images of the brain during right-eye stimulation were subtracted digitally from images taken during left-eye stimulation. (D) Orientation map. Images of the brain were taken during stimulation at 12 different angles. The orientation of stimuli that produced the strongest signal at each pixel is color coded, as indicated to the right. The key at the right gives the correspondence between color and the optimal orientation. (E) Comparison of the preferred orientation of single neurons with the optical image. At each of the locations indicated by squares in D, single neurons were recorded with microelectrodes. The preferred orientations of the neurons (dashes) were compared with the preferred orientations measured in the optical image, sampled along the line connecting the recording sites (dots). A: adapted From Grinvald *et al.* (1988); B and C: adapted from Ts'o *et al.* (1990); D and E: adapted From Blasdel and Salama (1986).

with Fig. 27.12A), but the images for the first time gave a detailed picture of the layout of orientation across the cortical surface. Details of these orientation maps—and their relationships with ocular dominance—were entirely new and had not been demonstrated with previous techniques.

Cytochrome Oxidase Staining Reveals Blobs and Stripes in Cortical Areas V1 and V2

In the primate, there is a fourth feature of the functional architecture of visual cortex in addition to retinotopy, orientation, and ocular dominance columns. When stained for the enzyme cytochrome oxidase (a metabolic enzyme whose presence indicates high activity), histological sections of V1 reveal a regular pattern of patches, or blobs (Fig. 27.14). In layers 2+3, these blobs were reported to contain neurons whose receptive fields are color selective, poorly oriented, and monocular (Livingstone and Hubel, 1984).

In V2, the second visual area in the cerebral cortex (see later), cytochrome oxidase staining reveals regions of high and low activity arranged in parallel stripes (Fig. 27.14, along the top). The anatomical connections between V1 and V2 are strongly constrained by the subdivisions revealed by cytochrome oxidase staining. Layer 4B of V1 projects to thick stained stripes; in layers 2+3, the interblob areas project to unstained stripes and blobs project to thin stained stripes.

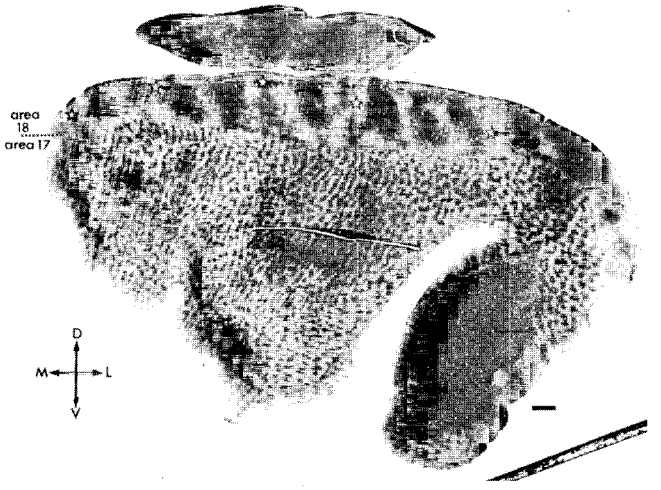


FIGURE 27.14 Macaque visual cortex stained for the metabolic enzyme, cytochrome oxidase. A tangential section through layers 2+3 of V1 (below) and V2 (above) is shown. In V1, blobs are seen in a regular array with a spacing of 400 mm. In V2, there are cytochrome oxidase-rich stripes with much coarser spacing. The distinction between thick and thin stripes (see text) is seen less readily in the macaque than in the owl monkey. Scale bar: 1 mm. From Livingstone and Hubel (1984).

The anatomy and physiology of the regions defined by cytochrome oxidase staining in V1 and V2 have been the objects of much research since the 1980s, and of much controversy. It is agreed that blobs in layers 2+3 are the sites of termination of the koniocellular thalamic afferents, but the relationship between cytochrome oxidase staining and magnocellular and parvocellular pathways, originally thought to be straightforward, is still an open question (reviewed in Merigan and Maunsell, 1994). Consensus has been reached on one point, however: magnocellular inputs dominate the pathway from 4Cα to 4B in V1; 4B then projects, both directly and indirectly (via the thick stripes in V2), to regions of the brain that process visual motion signals. Magnocellular neurons, with their rapidly conducting axons and high sensitivity to luminance contrast, are well suited to providing input to the motion-sensitive neurons in cortical areas MT and MST (see later).

Many Extrastriate Visual Areas Perform Different Functions

In early studies of the cytoarchitecture of cerebral cortex, the visual cortex was divided into three areas according to Brodmann's classification: areas 17, 18, and 19. These divisions were based on differences in cell cytoarchitecture, or differences in the size, morphology, and distributions of cells within the six cortical laminae. Area 17 is primary visual cortex, or striate cortex, so named because of a heavily myelinated sublamina within layer 4 (4Cα), prominently visible as a stripe in transverse section. Areas 18 and 19 were known simply as the visual association cortex. An assumption behind these designations was that areas defined by anatomical criteria would ultimately prove to be functionally specialized.

The demonstration of multiple visual cortical areas has been one of the important discoveries of the past quarter century in the field of sensory neurobiology. A vast expanse of cerebral cortex—greater than 50% of the total in many primate species—is involved primarily or exclusively in the processing of visual information. The extrastriate cortex now includes areas 18 and 19, as well as large regions of the temporal and parietal lobes (see Fig. 27.15 for a diagram of the four main regions of cerebral cortex: occipital, parietal, temporal, and frontal). It is composed of some 30 subdivisions that can be distinguished by their physiology, cytoarchitecture, histochemistry, and/or connections with other areas (Felleman and Van Essen, 1991). Each of these extrastriate visual areas is thought to make unique functional contributions to visual perception and visually guided behavior.

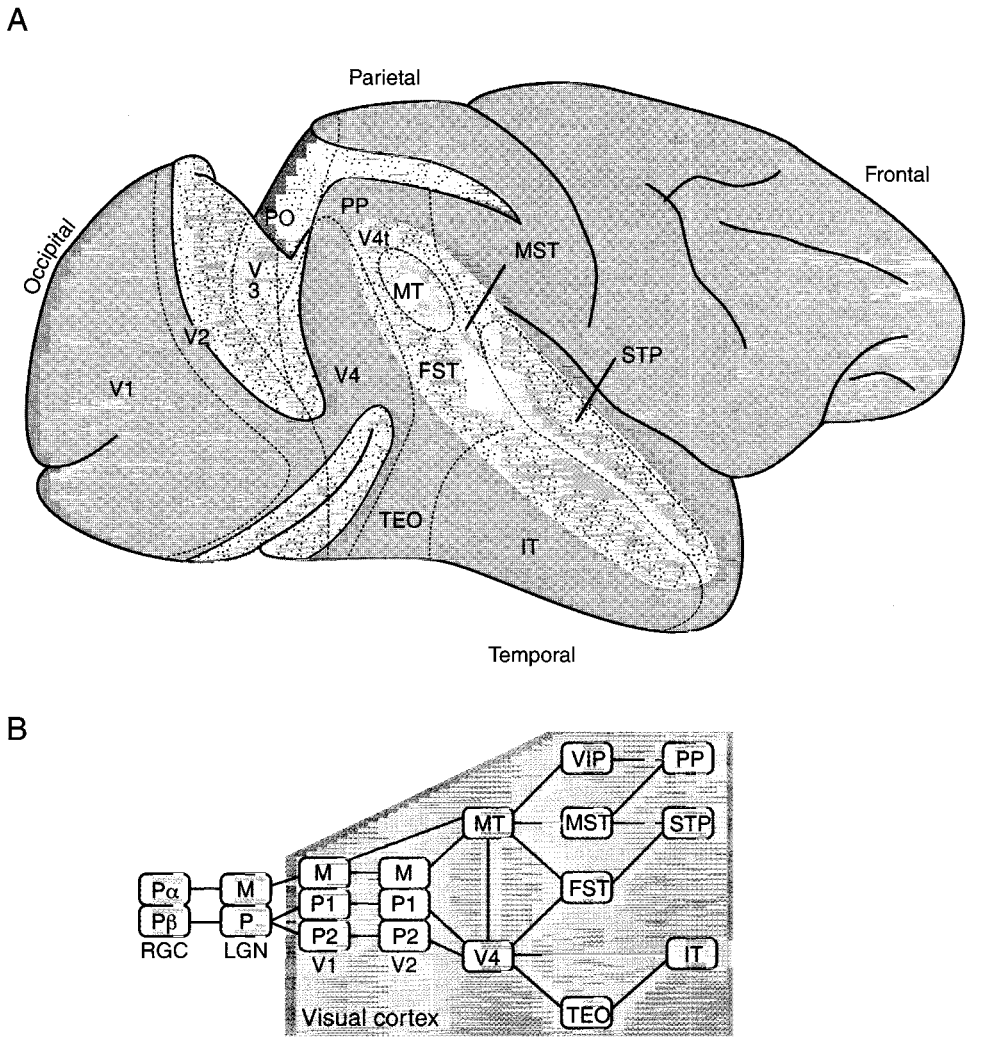


FIGURE 27.15 Extrastriate cortical regions. (A) Lateral view of the macaque brain, with the sulci partially opened to expose the areas within them. Shown are the rough outlines of the main visual areas, which take up all of the occipital cortex and much of the parietal and temporal cortex. (B) Partial diagram of the connections between visual areas. Emphasis is placed on the hierarchical organization of the connections and on the partially segregated P parvocellular and M magnocellular pathways. Adapted from Albright (1993).

As a testament to the increasing complexity of the field, the naming of visual areas (see Fig. 27.15) has progressed from the use of simple labels—V1 through V4—to the use of more complex terms specifying anatomical location of each new area, such as MT (medial temporal, or V5), MST (medial superior temporal), or IT (inferotemporal, itself made up of several distinct areas).

The dual themes of parallel and hierarchical processing are central to the understanding of the extrastriate cortex. Figure 27.15 is a vastly simplified version of a wiring diagram between visual areas (Felleman and Van Essen, 1991). Several criteria have been used to define new visual cortical areas. First, extrastriate regions have retinotopic maps of the visual world that can be demonstrated by physiological recordings. Second, a clear hierarchy between many cortical areas can be demonstrated anatomically. There is a stereotyped pattern of projections from one visual area to the next. Where strong connections between two areas exist, these connections tend to be bidirectional. The feedforward and feedback connections are distinguished by the layers that send and receive the connections. In such a manner, a clear hierarchy can be traced, for instance, along the pathway V1→ V2→ V3→ MT→ MST (with several shortcuts, such as V1→ MT).

While physiological studies of cortical areas revealed profound differences between them, a series of studies by Ungerleider and Mishkin (1982) uncov-

ered a higher order dichotomy between two types of processing in the extrastriate cortex. Using behavioral analyses of animals with anatomically defined cortical lesions, Ungerleider and Mishkin found a strong dissociation between the types of deficits exhibited by animals with lesions in either their parietal cortex or their temporal cortex (see Fig. 27.15). Animals with temporal lesions were often much worse at recognizing objects visually, although lower level visual function, such as acuity, was not appreciably lessened. Parietal lesions led to little or no deficit in object recognition, but visuospatial tasks, such as visually

BOX 27.4

THREE TYPES OF SELECTIVITY FOR MOTION

Motion is one of the most important aspects of the visual world. It is a powerful cue for navigating in the world, for segregating figures from their background, and for predicting the trajectory of objects. It is not surprising, therefore, that sensitivity to motion is a highly developed feature of the mammalian visual system. At the lowest level, a class of neurons in the retina respond best to stimuli moving in a specific direction (Barlow *et al.*, 1964). These neurons give *on–off* responses to flashed lights (denoted ± in Fig. 27.16 A), but are best excited by the motion of an object anywhere in their receptive fields. They can signal that motion in a particular range of directions is present, but because their receptive fields are relatively large and have both *on*-and-*off* responses, they cannot resolve the details of an object. Directionally selective retinal neurons do not project to the LGN so directional neurons found in the visual cortex (Hubel and Wiesel, 1962) create their selectivity independently and with a different mechanism.

Unlike directionally selective ganglion cells, which signal that motion is present somewhere within a large region, directionally selective simple cells in the visual cortex maintain detailed spatial information as well. A moving stimulus, such as a light bar moving to the left (Fig. 27.16B, left), is described by its trajectory in space over time. If the trajectory is plotted in space versus time, the slope represents the direction and velocity of the object. For instance, a bar moving to the right traces an oblique trajectory (up and to the left) in such a space–time plot (Fig. 27.16B, middle). When represented in a similar plot, the receptive fields of directionally selective simple cells can show a similar orientation (Fig. 27.16B, right). This plot is exactly analogous to Kuffler's maps of ganglion cell receptive fields. It represents the responses of the cell to a bright or dark bar at different positions, but it includes the time course of the responses as well. The *on* responses of this receptive field (the responses to a bright bar) are indicated with solid contour lines and are shown in white for added emphasis; *off* flanks (the responses to dark bars) are indicated with dotted contour lines.

For directionally selective simple cells, the timing of the response is directly related to the position of the stimulus. In the illustration, the cell is sensitive to a bright bar at a range of positions, but the timing of the peak response changes with position. These responses to flashed bars explain the responses to moving stimuli. Just as *on*-center/*off*-surround ganglion cells respond best to a bright spot on a dark background (Fig. 27.3C), a directionally selective simple cell responds best to a bar moving in a specific direction. A moving bar is the stimulus that best matches the template formed by its receptive field. In this manner, simple cell receptive fields can be strongly direction selective, but their responses preserve precise information about the position and structure of the stimulus.

A third kind of directionally selective cell is found in cortical area MT of the macaque. Receptive fields of individual neurons in MT integrate motion information over large regions of visual space. By comparison, receptive fields in the retina, LGN, and V1 can be thought of as viewing the world through much smaller apertures. If the goal of vision is to extract the properties of objects, rather than isolated features, then the existence of small receptive fields can lead to what is known as the *aperture problem.* As illustrated in Figure 27.16C, two objects moving in different directions can appear to have the same direction of motion when viewed through an aperture. In a dual study of perception in humans and of MT neurons in macaques, Movshon and colleagues (1985) analyzed the responses to complex stimuli whose components moved in different directions (such as the edges of the square in the bottom half of Fig. 27.16C), but which were perceived as coherent patterns moving in an intermediate "pattern direction." Unlike neurons in V1, many neurons in MT responded to the pattern direction rather than to the components. This would imply that these MT neurons combine their inputs in a complex manner to achieve a selectivity for the motion of extended objects rather than primitive features.

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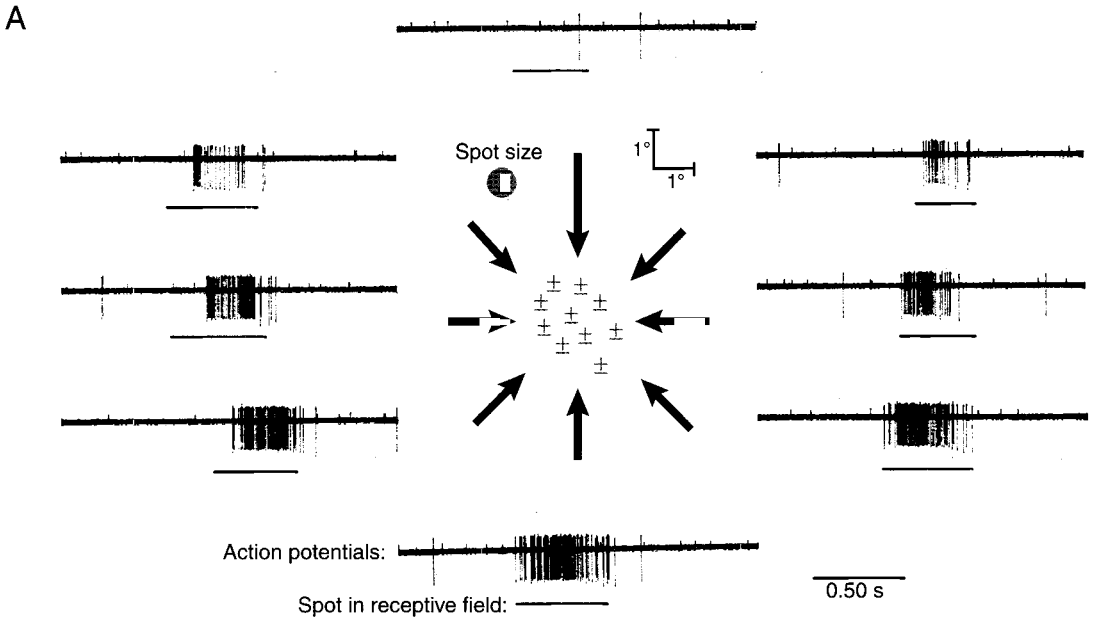
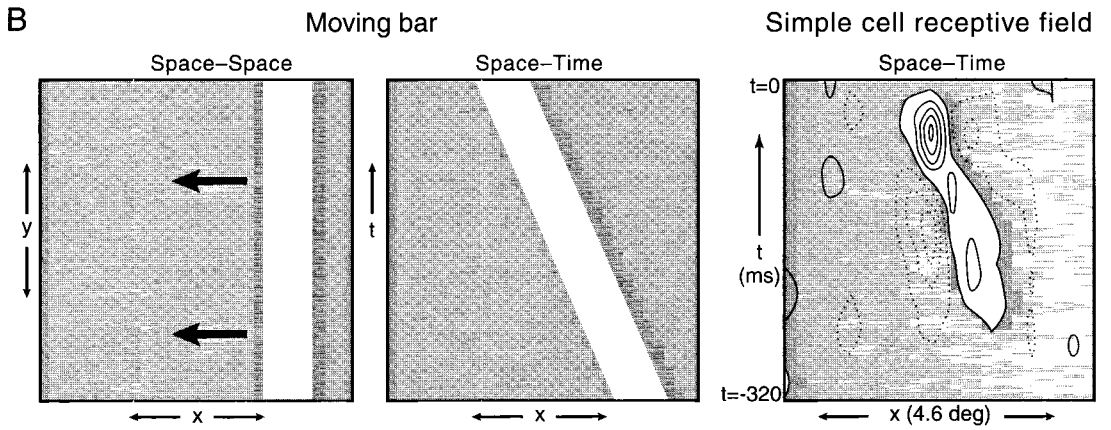
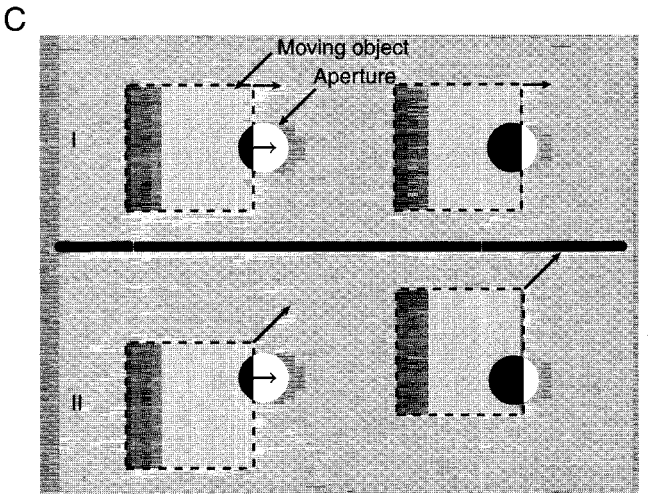

A
Spot size
1°
1°
Action potentials:
Spot in receptive field:
0.50 s


B
Moving bar
Simple cell receptive field
Space–Space
Space–Time
Space–Time
y
x
t
x
t=0
t
(ms)
t=-320
x (4.6 deg)


C
Moving object
Aperture
I
II

guided behavior, were impaired profoundly. From these studies and the growing body of physiological evidence, two distinct streams were postulated: a *temporal* or *ventral stream* devoted to object recognition and a *parietal* or *dorsal stream* devoted to action or spatial tasks. Ungerleider and Mishkin termed these the "what" and "where" pathways.

The temporal stream, V1→ V2→ V3→ V4→ IT ..., is discussed elsewhere (Chapter 55). This chapter considers only the parietal stream, V1→ V2→ MT→ MST .... The parietal stream is dominated by magnocellular cells and the temporal stream by parvocellular inputs, although the segregation is far from strict (Merigan and Maunsell, 1994).

In the Parietal Cortex, Neurons Are Selective for Higher Order Motion Cues

MT, or V5, is perhaps the best understood of the extrastriate visual areas. It has held particular interest ever since its was discovered in 1971 (Allman and Kaas, 1971; Dubner and Zeki, 1971), primarily because it was the first area found that was strongly dominated by one visual function. Fully 95% of the neurons in MT are highly selective for the direction of motion of a stimulus (Dubner and Zeki, 1971). In V1, a significant fraction of neurons are selective for the direction of motion, but the optimal speed may vary depending on the spatial structure of the object that is moving. In MT, speed tuning is less dependent on other stimulus attributes. Receptive fields of individual neurons in MT integrate motion information over large regions of visual space and are qualitatively less selective than neurons in the primary visual cortex. This generalization of motion signals can be achieved in a simple manner, such as by adding together inputs over space or, in a complex manner, by combining two component motions in different directions into a single coherent motion (see Box 27.4). Of even greater interest, neurons in MT (and, to a greater extent, those in MST) appear to be sensitive to more complex aspects of visual motion, such as the motion of extended objects rather than isolated features (Albright, 1993).

The range of stimuli that a given MT neuron can respond to is impressively broad—the attributes, or form cues, that define a figure can be luminance, texture, or relative motion—but the preferred direction and speed are always the same for that neuron (Albright, 1993). This is an extreme example of what were termed high-order responses in the introduction to this chapter. Neurons at lower levels in the visual system are sensitive to isolated and specific features in visual scenes. Higher visual areas respond to very specific attributes, but these attributes are increasingly remote from the physical stimulus. Instead, they represent increasingly complex concepts, such the motion of an extended object or the identity of a face.

Summary

The lateral geniculate nucleus of the thalamus is a layered structure that receives segregated input from the two eyes and projects to the primary visual cortex (V1). Geniculate neurons have center-surround receptive fields that are similar to those of their retinal inputs. In contrast, most neurons in the primary visual cortex are sensitive to the orientation of a stimulus. In mammalian species, there are elements of both hierarchical and parallel processing in the primary visual cortex. This section has emphasized that the visual cortical circuit in the cat can be seen as a functional hierarchy that transforms geniculate input into simple and then complex receptive fields. In the macaque monkey the focus has been on the parallel pathways that are kept relatively separate in the striate and extrastriate cortex.

The visual cortex has an orderly functional architecture. Neurons within a cortical column have similar receptive field attributes, such as orientation selectivity, ocular dominance, and receptive field location. Each of these receptive field attributes varies smoothly

◀ **FIGURE 27.16** Three types of direction selectivity. (A) Receptive field map of a directionally selective ganglion cell in the rabbit (± indicates where neuron responded in an *on–off* manner). Surrounding it are individual responses to stimuli moving in eight different directions. The smooth traces below each train of action potentials correspond to the position of the stimulus as it moves in the indicated direction. Horizontal bars indicate when the spot was in the receptive field. (B) Direction selectivity in cortical simple cells of the cat. A bar moving to the left (shown in a space–time plot in the middle panel) matches the template formed by a directionally selective simple receptive field (shown in a space–time plot at right). The vertical time axis in the right-hand panel corresponds to the stimulus location 0 to 320 ms *before* the neuron fired. Bright regions in the receptive field correspond to the best location for a bright stimulus at each delay between stimulus and response. (C) The ambiguous motion of an extended object when viewed through a small aperture—known as the aperture problem—is partially resolved by some neurons in macaque cortical area MT. The squares in I and II (each shown at two successive time points) are moving in different directions, but they appear identical when viewed through a small aperture. A: adapted from Barlow *et al.* (1964); B: far right adapted from McLean *et al.* (1994).

over the cortical surface. The organization of ocular dominance columns and orientation columns across the cortical surface can be visualized with optical imaging.

Finally, in the macaque monkey, there are more than 30 extrastriate visual cortical regions, each of which performs different functions. These extrastriate regions can be divided into two pathways: the temporal stream, devoted to form recognition, and the parietal stream, devoted to action or to spatial tasks. Areas in each stream form a functional and anatomical hierarchy. Neurons in successive visual areas respond to increasingly high-order or abstract features of the visual world.

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