

The Physiology of Color Vision

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6.1 INTRODUCTION

Most of what we know about color vision has been learned from psychophysical investigations, most of what we know about the underlying physiology has been discovered with the explicit guidance of theories grounded in psychophysical observation, and mostly the physiological findings have confirmed expectations. One might therefore be forgiven for supposing that to discuss the physiology of color vision is merely to provide an account of the mechanics of systems whose operating principles we understand well. To some extent that is true, particularly for the earliest stages of color vision, but modern physiological investigations have also revealed an organization that could not be suspected from psychophysical observations.

This chapter first reviews briefly the gross anatomy of the visual pathway, from the retina to

the occipital cortex. Then it examines the physiology of the different stages, beginning with a look at the techniques used to explore it. Relatively little of this work has been undertaken on the human visual system, but a great deal has been done on the visual system of the macaque monkey, which, because its structure is similar to that of the human, is widely thought to be a good model.

6.1.1 BASIC ANATOMY OF THE VISUAL SYSTEM

6.1.1.1 The retina

The image is formed on the retina, shown in vertical cross-section in Figure 6.1. This highlights very clearly the layers that comprise a structure less than 0.5 mm thick.

The general organization of the retina is broadly the same in all vertebrates: there are

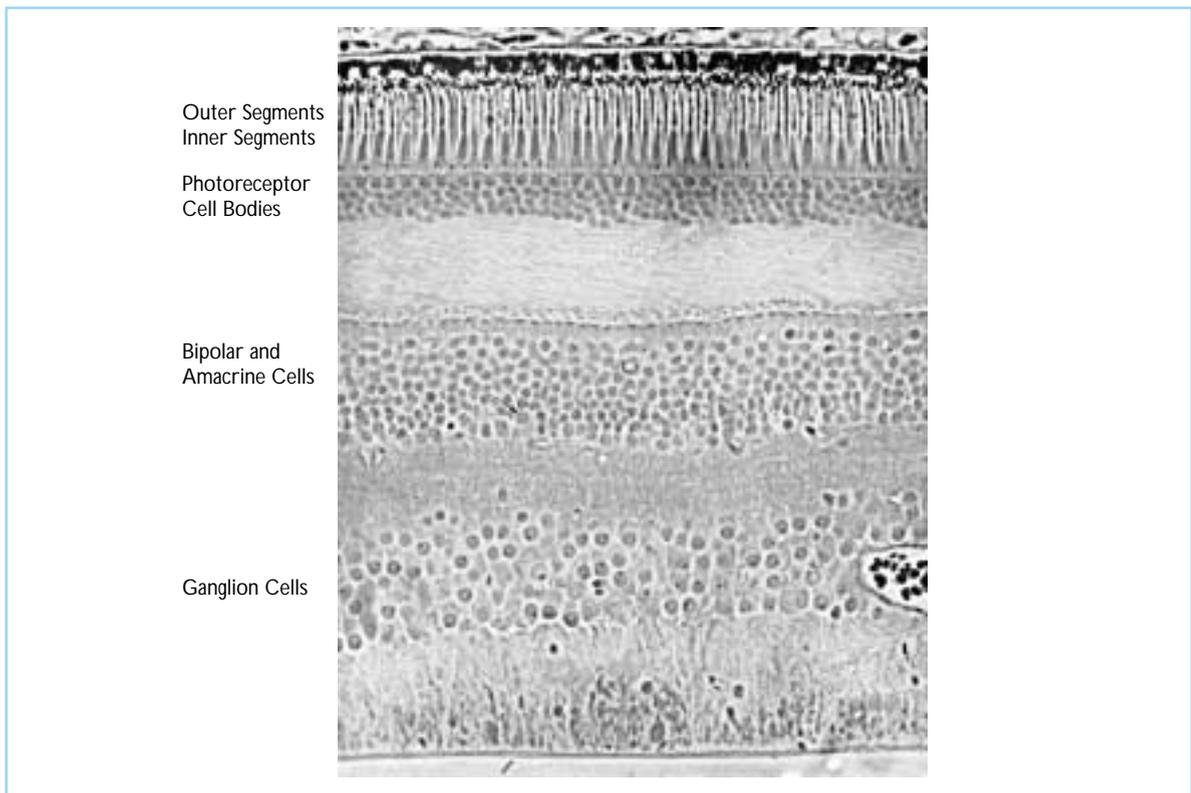


Figure 6.1 Vertical section through the primate retina, showing its layered structure. Light enters the retina from the bottom of the picture, passing through all layers before being absorbed in the outer segments of photoreceptors. The three principal layers of cells are identified. The rods and the cones lie nearest the top of the figure, with their different parts identified. Bipolar cells and amacrine cells lie in the inner nuclear layer. Ganglion cells lie in the ganglion cell layer. (From Boycott and Dowling, 1969.)

three vertical stages, with interconnecting horizontal pathways at the junctions between stages. Figure 6.2 shows this diagrammatically. The photoreceptors, rods and cones, which form the most peripheral stage, lie farthest from the pupil, and light must pass through the thickness of the retina before being absorbed. Since the neural retina is transparent, this is visually inconsequential. The inverted organization seems to be an adaptation to the demands of the photoreceptors – metabolically the most active cells in the body – which derive their nutrients from the nearby choroid. Structurally, rods and cones are grossly similar, consisting of two clearly defined parts, the inner and outer segments. The outer segment, nearest the choroid, contains the photopigment, and within it originate the light-

evoked signals. The inner segment contains the biological support mechanisms.

Until relatively recently most anatomical work on the retina used vertical sections of the kind shown in Figure 6.1. These make clear the vertical strata and also some structural features such as the fovea (Figure 6.3), which contains no rods and where all neurons beyond the cones are displaced, forming a pit over the very densely packed cones.

Although neuroanatomists working with vertical sections have been able to identify some sub-classes of the major neuron groups identified in Figure 6.2 (principally through scrutiny of the levels at which their dendrites and axons branch), the clearest indications of different sub-classes have often emerged through examination

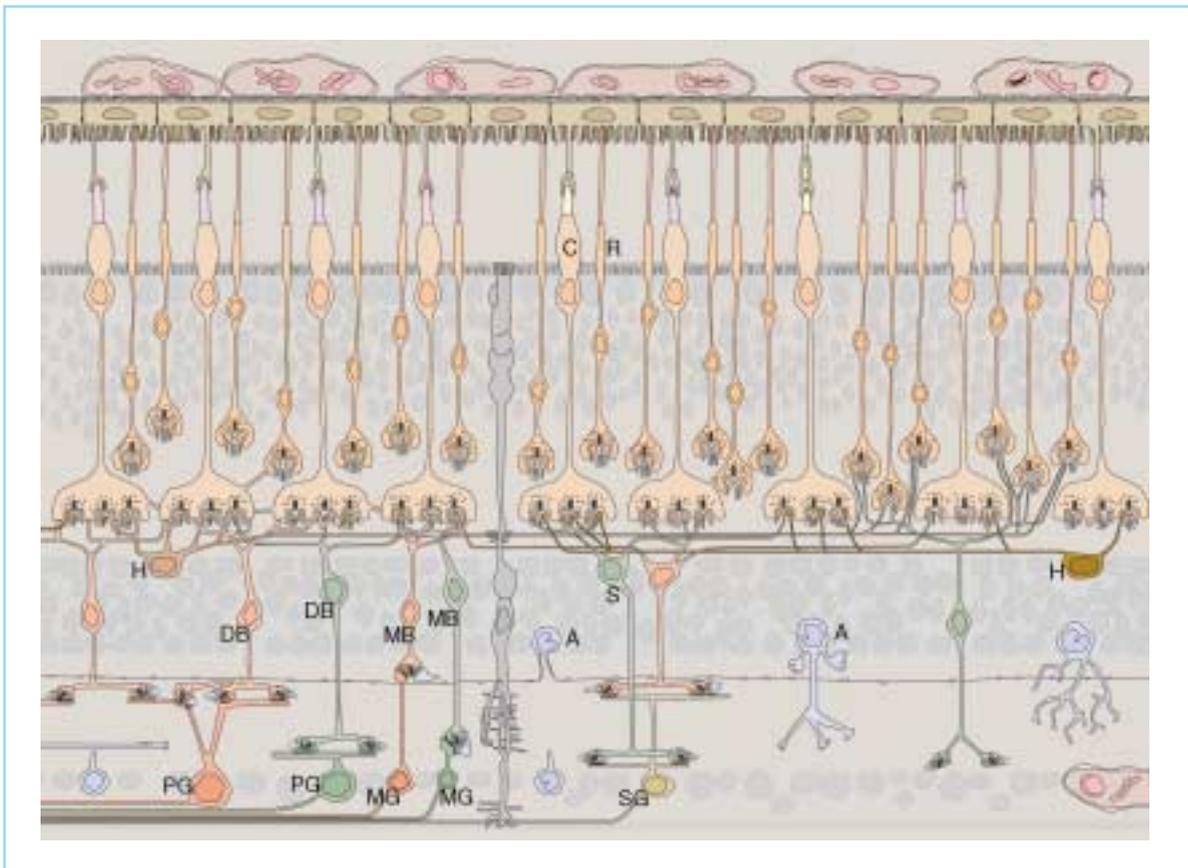


Figure 6.2 Diagram of the neurons and their principal connections in the primate retina. C, cone; R, rod; MB, midget bipolar cell; DB, diffuse bipolar cell; S, S cone bipolar cell; H, horizontal cell; A, amacrine cell; MG, midget ganglion cell; PG, parasol ganglion cell; SG, S cone ganglion cell. Bipolar cells and ganglion cells colored red are off-center types; those colored green are on-center types. (Adapted from Rodieck, 1998, with corrections by R.W. Rodieck.)

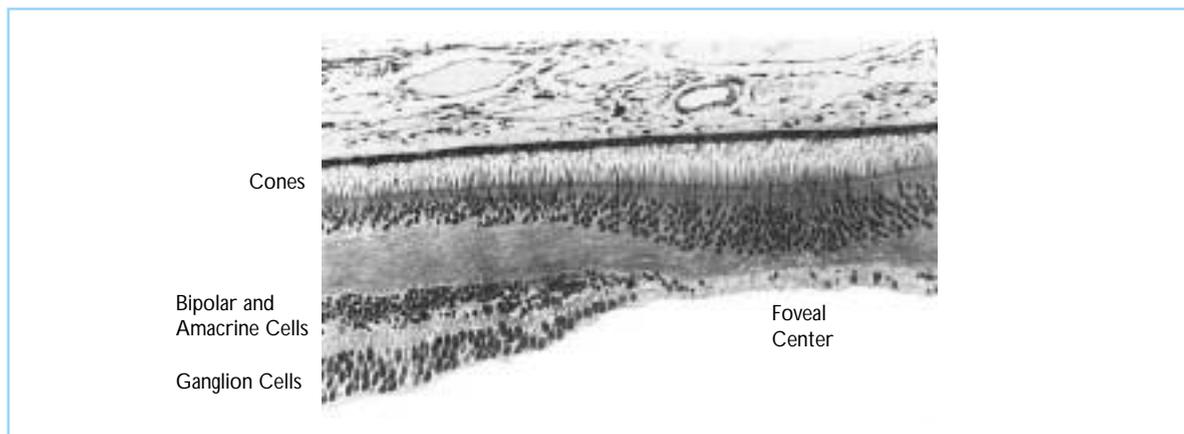


Figure 6.3 Vertical section through the human fovea, showing the elongation of the cones, and the absence of the other neurons, which lie outside the center of the fovea and to which the cones are connected through long fibers. (Photograph courtesy of Anita Hendrickson.)

of horizontal sections of retina – sometimes whole-mounted retinas – in which one can view the retina in the plane of the image, and which reveal the pattern and spread of a neuron’s dendritic field.

It is now clear that the primate retina contains several kinds of bipolar cells, several kinds of horizontal cells, several kinds of ganglion cells, and perhaps many kinds of amacrine cells. We will consider some of these in detail later, but for the moment the important idea is that the existence of several types among each major class of cell suggests the retina forms multiple representations of the image. This idea draws clear support from an examination of ganglion cells, whose axons form the optic nerve. Anatomical classes of ganglion cells are characterized principally by the pattern, horizontal extent, and depth of branching of their dendritic fields. The characteristic dimensions vary, of course, with position on the retina, but at any one spot cells of different classes can be robustly distinguished. Ganglion cells of the different classes form quasi-regular mosaics of sampling elements, each of which conveys a (presumably) different representation of the image to the brain. These different arrays project differently into the brain. Their relevance to color vision stems from the fact that different classes of ganglion cells are connected in different ways to the cone photoreceptors.

In the primate retina there are two major and several minor classes of ganglion cells. The two

major classes, now widely known as *P cells* and *M cells*,¹ together constitute about 90% of the 1.25 million ganglion cells in each eye. P cells alone probably constitute 80% of all ganglion cells. The most distinctive anatomical difference between them is size: at any one eccentricity the P cells have much smaller cell bodies, smaller dendritic fields, and smaller axons. P and M cells are connected to cones through different kinds of bipolar cells (they both also make indirect connections with rods, but these are not relevant here). In and near the fovea each P cell contacts a single *midget bipolar cell*, which in turn contacts a single cone (Wässle and Boycott, 1991). In the fovea, there are two midget ganglion cells and two midget bipolar cells for every cone. Each cone drives two midget bipolar cells, which in turn drive two P cells. These dual contacts made by a single cone seem to be the origin of distinct pathways, for the two midget bipolar cells are anatomically different, and they in turn contact their counterpart P cells in different planes in the retina. As we shall see, these pathways have different physiological properties. There are corresponding pathways feeding two kinds of M cells. Each M cell contacts a single *diffuse bipolar cell*, which in turn contacts several cones. Other, rarer, kinds of ganglion cells are clearly distinguished anatomically (Rodieck *et al.*, 1993), but except for a bistratified cell that is associated with signals from S cones (Dacey and Lee, 1994), little is known about their function, and their

central projections, discussed below, suggest that most have no substantial role in color vision.

The horizontal pathways in the retina, represented by horizontal cells and (to some extent) amacrine cells, seem to be organized to permit the infusion of remote signals into the direct vertical pathways. Horizontal cells, of which there are at least two types, make connections directly with cones at their junctions with bipolar cells, and near the fovea each horizontal cell makes contact with most of the cones that lie in its dendritic field (Wässle *et al.*, 1989; Ahnelt and Kolb, 1994). Amacrine cells exist in many more discernible forms than do other retinal neurons. Some have an identified special role in the transmission of rod signals from bipolar cells to ganglion cells, but beyond some involvement in shaping the responses of ganglion cells, the roles of most are unclear.

6.1.1.2 Central projections

Ganglion cells project to several centers in the brain, notably the superior colliculus (SC) in the midbrain and the lateral geniculate nucleus (LGN) in the thalamus (Figure 6.4). Each optic nerve branches at the optic chiasm, and approximately half of the nerve fibers (representing ganglion cells in the nasal retina) cross to the other hemisphere. The representation of the retinal image is split vertically through the fovea, each half being represented in one hemisphere. The peculiarity of the projection results in the left visual field being represented in the right hemisphere, and *vice-versa*. This brings the representation of visual space broadly into register with the representations provided by other senses, which are all crossed.

The SC is phylogenetically older, and is the more important center in lower mammals; in primates it receives inputs from only a small fraction of the retinal ganglion cells. These cells are of the rarer types found in the retina (i.e., neither P nor M cells). The SC has clear roles in directing eye movements and in intersensory localization (Sparks and Nelson, 1987), but all that we know about it, including the physiology of neurons in it, suggests that it has no consequential role in color vision.

The LGN in primates is a highly developed, laminated, structure to which the retinal P cells and M cells project. The prototypical LGN in the

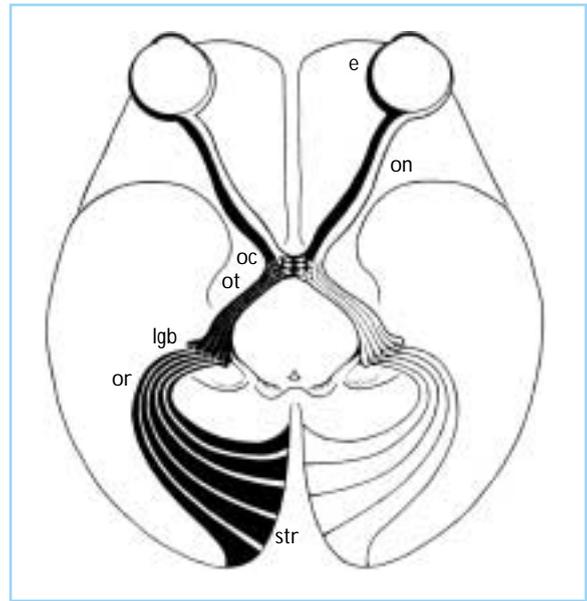


Figure 6.4 Major visual centers in the brain. The optic nerve (ON) from each eye (E) divides at the optic chiasm (OC), sending half its fibers into the optic tract (OT) of each hemisphere, which projects to the lateral geniculate nucleus (LGB). The lateral geniculate nucleus in turn projects to the striate cortex (STR). The projection into each hemisphere originates in the half-retina on that side of the head. (From Polyak, 1957.)

primate has six layers, organized in two distinct groups (Figure 6.5).

The four dorsal, *parvocellular*, layers receive inputs from the retinal P cells, with those from the left and right eyes being interleaved. The two ventral, *magnocellular*, layers receive inputs from the M cells, separately from each eye. There are no discernible connections among layers, and physiological evidence suggests no functional connections. The topography of the retinal image is preserved on the LGN, each layer of which contains an orderly though distorted map. The distortions in the map are broadly consistent with each projecting ganglion cell occupying a fixed territory in the LGN, so that the representation of the central visual field is large – a convenience for physiologists.

6.1.1.3 Visual cortex

Neurons in the LGN project to *striate cortex* (also known as *primary visual cortex* or *V1*), an anatomically distinctive cortical region in the occipital

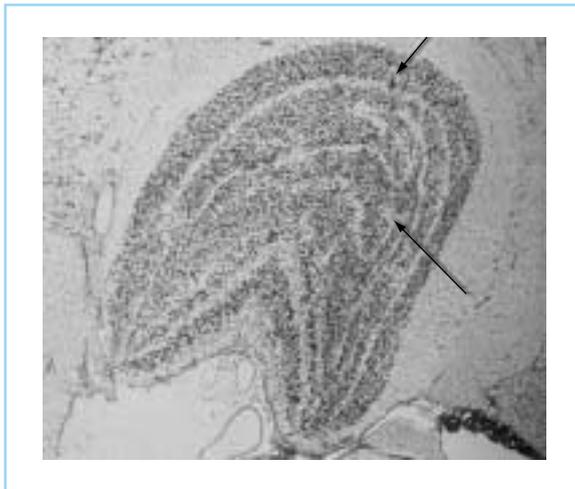


Figure 6.5 Section through the lateral geniculate nucleus (LGN), showing its laminated structure. The prototypical LGN has six layers – four dorsal (parvocellular) layers and two ventral (magnocellular) layers – though this arrangement is not always present. The magnocellular layers are thinner and contain larger cells. The LGN contains a topographical map of the half of the retina that projects to it. The arrows in this figure mark the path of a microelectrode that recorded the discharges of individual neurons. (From Wiesel and Hubel, 1966.)

lobe, at the back of the brain. The cortex as a whole is a large, thin (~2 mm) sheet containing several clearly defined layers of neurons, and in the human brain (and to a lesser extent the monkey brain) is deeply folded to fit into the cranial cavity. Cortex is functionally specialized, but, with a few exceptions, its structure provides little evidence of this and almost everywhere is similar anatomically. Figure 6.6 shows the major laminar subdivisions of striate cortex. It differs from cortex elsewhere in the brain by having a much thicker layer 4, to which the incoming fibers from the LGN project.

The general organization of cortex is as follows: inputs from lower levels of the visual pathway arrive in layer 4, ascending outputs to higher levels of the pathway arise in the upper layers (above layer 4), and descending (feedback) outputs to lower levels arise in the lower layers (below layer 4).

The anatomical distinctiveness of striate cortex (the thick layer 4 produces a texture visible to the naked eye) makes it relatively easy to discover that in each hemisphere it contains a

single map of the left or right half of the visual field. As would be expected from the topography of the earlier map in the LGN, this contains a large representation of the central visual field and a progressively reduced representation of the peripheral field. Beyond this cortex lies a great deal more that is intimately coupled to vision. Because it is not structurally distinctive, its organization has been less easy to discern, but modern work, using both anatomical and physiological methods, shows unequivocally that it contains multiple maps of the visual field. These maps (at least twenty-two have now been identified) cover the whole of the occipital lobe of the brain, and substantial parts of the temporal and parietal lobes. The fraction of the brain they occupy, and their general arrangement, are most easily seen in representations that unfold the cortex and lay it flat. Figure 6.7 (Felleman and Van Essen, 1991) shows this done for the macaque monkey, and makes clear how large a fraction (around 50%) of cortex is devoted to visual analysis. In the human brain the fraction is considerably smaller, perhaps around 15%.

By tracing the connections among visual areas, and knowing from which layers in cortex these connections originate and to which layers they project, it becomes possible to discover a hierarchical structure that can accommodate, somewhat loosely, all the areas (Figure 6.8). This hierarchy has its origin in striate cortex, ascends through the second visual area, V2, and then on through perhaps seven further levels. Beyond V2 each level contains more than one area, so the general picture that emerges is one of multiple parallel streams organized hierarchically.

The parallel organization of cortical streams reflects to some degree, but by no means fully, the parallel organization of signals conveyed by the M and P pathways through the LGN. The M and P cells project to different subdivisions of layer 4, and these in turn project to other layers within striate cortex. The separate identities of the pathways are generally not well-preserved beyond this level, although a small but distinctive projection that appears to be dominated by signals from the M pathway has been traced from striate cortex to an extrastriate region known as the middle temporal area (MT).

Within the collection of extrastriate cortical areas concerned with vision, there appears to be

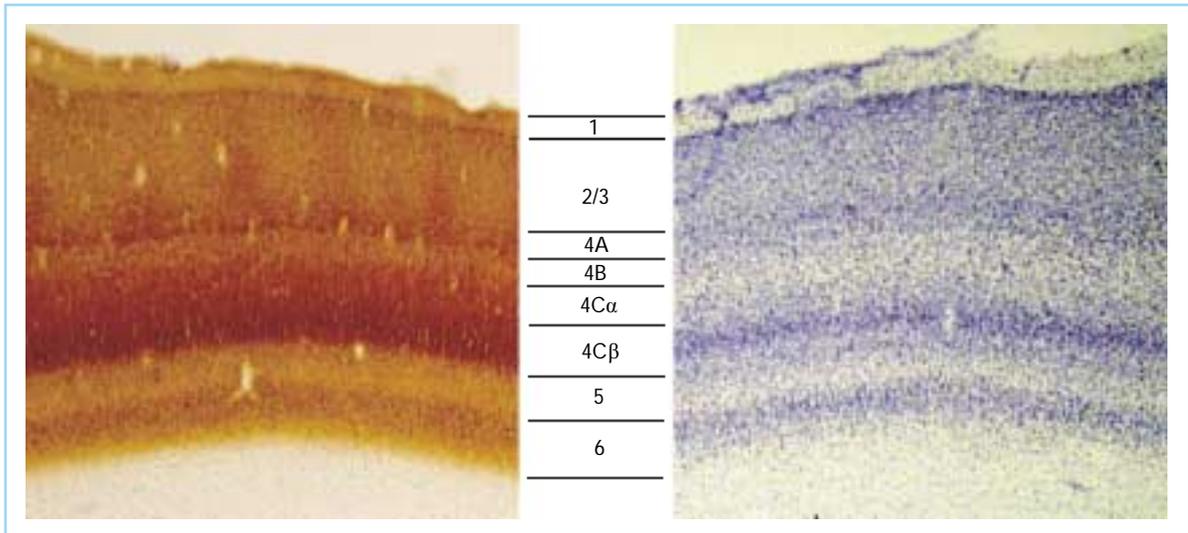


Figure 6.6 The arrangement of layers in striate cortex, revealed by two stains that highlight different aspects of the organization. (Right) A stain that reveals the locations of the cell bodies of neurons. (Left) A stain for the enzyme cytochrome oxidase, which labels densely the input layers in the middle of cortex, and also shows the 'blobs' in layer 2/3 that are a distinctive feature of the upper layers.

a broad division into two groups. One contains a set of hierarchically connected areas that form a conduit from striate cortex, through area V2, into the parietal lobe of the brain. The other contains a set of areas that carry information from striate to the temporal lobe. Experimental and clinical studies of parietal cortex show it to have important roles in spatial orientation and visual localization, and perhaps also with the analysis of self-movement, but there are no indications that it is important for color vision. Temporal cortex is for object vision, and damage to it, or to the visual areas that lead to it, can bring about profound disruption of various aspects of object vision, including color vision.

6.1.2 EXPLORING FUNCTION

Some useful inferences about function can be drawn from our knowledge of the structure of the visual pathway (for example, one can infer that P cells are probably important for visual acuity), but a great deal more can be learned by examining activity in the nervous system. Physiologists have available to them a powerful armament of methods. For the purposes of understanding mechanisms of color vision, and particularly how these give rise to perceptual

phenomena, most of the activity we need to pursue occurs on a time scale of tens of msec, and on a spatial scale that involves groups of neurons. The following paragraphs review briefly some of the more important methods that are relevant to exploration on these scales, and outline their strengths and weaknesses.

6.1.2.1 Recording signals from individual neurons

Within an individual neuron signals are propagated electrically, and between neurons, chemically, via *neurotransmitters*. In their resting states most neurons maintain a steady potential difference of ~60 mv across the cell membrane. A reduction in this potential difference (depolarization) constitutes the neural signal. The membrane potential is controlled by neurochemical events at the synapses (junctions) between the cell and those from which it receives signals. A neuron receives most of its synaptic connections on its dendrites and soma (Figure 6.9).

Each neuron receives thousands of synaptic connections from other neurons, and each synapse, when active, gives rise to a brief event, a *postsynaptic potential*, that tends either to excite (depolarize) or inhibit (hyperpolarize) the neuron. The aggregate weight of the postsynaptic

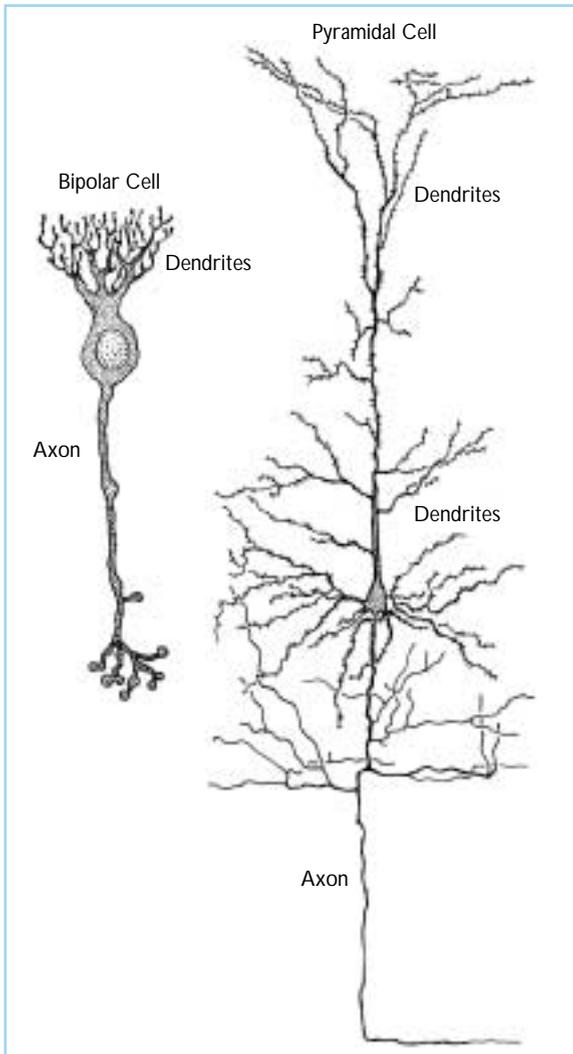


Figure 6.9 Diagram of the general structure of neurons, and their specializations. (Left) Bipolar cell in the retina. (Right) Pyramidal cell in cortex. The neuron accumulates signals from other cells mostly through synaptic connections on its dendrites. The action potential usually originates at the junction of the cell body and axon, and is propagated down the axon to the axon terminal system where it causes the release of neurotransmitter at synapses. (Adapted from Kuffler and Nichols, 1976.)

used by all retinal neurons except ganglion cells. It provides neurons with a larger dynamic range than would be possible were action potentials used, but at the cost of slower and less reliable signal transmission over distances.

In many parts of the nervous system individual neurons are large enough to withstand penetration by a microelectrode that can record the

potential difference across the membrane. Even where this is not the case microelectrodes that sit just outside the membrane can record (extracellularly) the local electrical disturbance produced by an action potential, though not any slow potentials. Intracellular methods are usually most practicable *in vitro*, when the neurons are not subject to movement by the pulse and other small body movements, but extracellular methods are much more robust, and can record signals from individual neurons in moving animals. The small size of neurons in the primate retina makes it exceptionally difficult to record their activity with intracellular electrodes. Some special techniques have been developed for studying the signals generated by photoreceptors (see the next section), but apart from photoreceptors only ganglion cells have been studied exhaustively in primates, because they generate action potentials that can be recorded with extracellular electrodes. Much of what we know directly about the function of other retinal neurons has been learned through studying reptiles and fish, in which cells are much larger. Elsewhere in the primate's visual system, extracellular recordings provide valuable information about the characteristics of individual neurons.

6.1.2.2 Recording larger scale electrical activity

Gross electrical activity evoked by light can be recorded from several places in the nervous system. The electroretinogram (ERG) is a composite signal that can be recorded either with electrodes placed on the retina, or with surface electrodes on the intact eye. Elements of the composite light-evoked signal can be attributed to different stages of signal analysis in the nervous system. The ERG has been particularly helpful in the analysis of signals generated by photoreceptors.

Gross electrical signals evoked by visual stimuli can be recorded with electrodes placed on the scalp, or on the surface of the cortex. Although large signals can be evoked by time-varying changes in color, they are often difficult to interpret, because the source of the signals is hard to localize.

6.1.2.3 Direct imaging of activity

Active neurons consume more oxygen than inactive ones, and as a result provoke local

increase in the circulation of blood. Several recently developed techniques can record these stimulus-induced local changes in the circulation, and have been exploited in attempts to reveal cortical structures that might be involved in the analysis of color. In cortex that can be viewed directly following removal of the skull, one can record changes in the composition of light reflected from the cortical surface to produce a map that shows local regional specialization (Roe and Ts'o, 1995). Positron emission tomography can be used to measure local changes in circulation in the human brain, and has been used to identify regions that are engaged in the analysis of color. The attraction of this method, and similar methods that exploit magnetic resonance imaging (Engel *et al.*, 1997), is that they reveal activity on a scale of millimeters. The drawback is that they measure changes in circulation occurring on a time scale of seconds.

6.2 PHOTORECEPTORS

6.2.1 RECEPTOR SIGNALS

Many of the important steps in the transduction of light to electrical signals in the nervous system are now understood, and have been clearly described (see, for example, Baylor 1987; Torre *et al.*, 1995). The general functional principles are the same in rods and cones, although there are important differences of detail between them, notably in the speed of responses, and in their time-courses. In the dark the receptor maintains a steady potential of ~ -40 mv across its membrane. When the receptor is illuminated, the potential becomes hyperpolarized to as much as -70 mv. This hyperpolarization by an effective stimulus makes photoreceptors unique among vertebrate neurons, which normally become depolarized when excited. Primate cones are too small to accommodate microelectrodes that can measure change in membrane potential, but Baylor and colleagues (Schnapf *et al.*, 1990) have characterized the electrical responses *in vitro* by drawing the outer segment of a cone into a micropipette and measuring the current flow through the outer segment. In darkness, there is a steady inward current (the *dark current*)

of 30–50 pA. This arises from the flow of Na^+ ions through the permeable membrane of the outer segment, and a flow of K^+ ions out of the inner segment. The current is maintained by pumps in the inner segment that drive Na^+ ions out and K^+ ions in. During illumination, the Na^+ permeability of the outer-segment membrane is reduced, and the current flow correspondingly reduced, resulting in hyperpolarization of the membrane. These light-induced changes in outer-segment membrane conductance result from a recently discovered cascade of biochemical events inside the outer segment (Pugh and Lamb, 1993; Torre *et al.*, 1995). In darkness, the photoreceptors release neurotransmitter continuously from their terminals, which contact bipolar cells and horizontal cells. The absorption of light and consequent hyperpolarization of the cell reduces the amount of transmitter released.

6.2.2 VISUAL PROPERTIES

Figure 6.10 shows the change in current flowing through the outer segment of a single monkey cone induced by a series of brief flashes of progressively increased intensity, at three wavelengths.

Several important principles can be inferred. First, over a substantial range of progressively increasing flash intensities, the cone's responses have exactly the same shape, and can be superimposed if scaled by the flash intensity. This linear relationship between light intensity and response breaks down at high flash intensities, where the responses saturate. Second, the cones generate sets of responses of identical shape regardless of the wavelength of light that excites them – they are univariant. Third, the responses are biphasic, and last considerably longer than the flash.

6.2.2.1 Spectral sensitivity

Given the univariance of a cone, demonstrated very clearly by Baylor *et al.* (1987), its spectral sensitivity can be readily measured by finding, at each of several wavelengths, the flash intensity required to evoke a response of a specified size. Figure 6.11 shows the result of essentially this kind of measurement made on a sample of cones from the macaque retina (Baylor *et al.*, 1987).

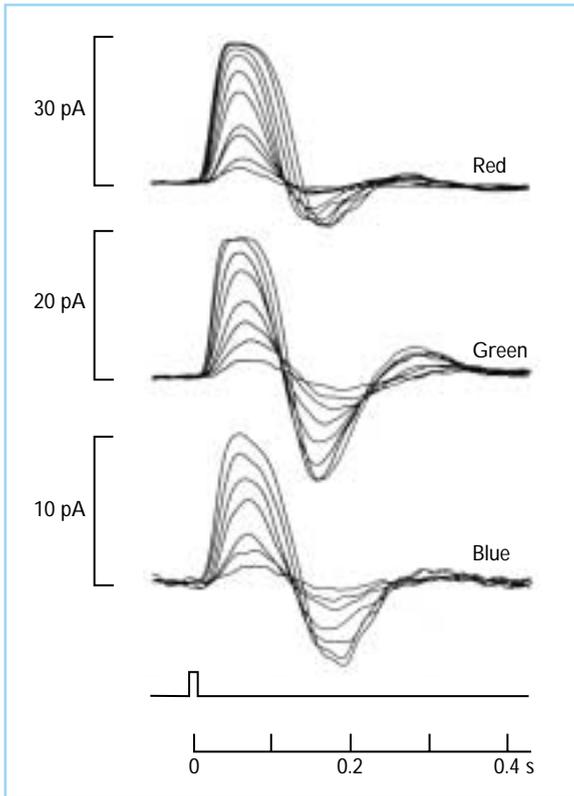


Figure 6.10 Current flow induced in the outer-segment of the three kinds of primate cones. Each set of traces shows the responses to brief flashes (identified by the pulse at bottom) at a series of intensities stepped by factors of 2. The responses of low and middle amplitudes would be superimposed if scaled by the flash intensity. (From Schnapf *et al.*, 1990.)

These measurements, remarkable for the range of wavelengths over which they can be made, show higher sensitivity at short wavelengths than is found in curves of cone fundamentals measured psychophysically. Differences of this kind would be expected from the different circumstances under which measurements are made – the psychophysically derived fundamentals include the effects of selective absorption of light by passive filters in the eye, and of self-screening by photopigment. After correcting for the effects of these other absorbing filters, a linear transformation of the cone spectral sensitivities describes well the shapes of the color-matching functions measured by Stiles and Burch (1959).

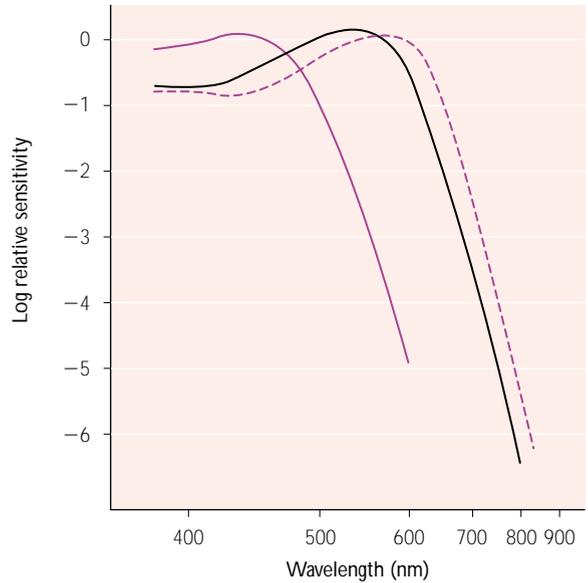


Figure 6.11 Spectral sensitivities of cones in the retina of the macaque monkey. From left to right the curves show the averaged spectral sensitivities of small samples of S, M, and L cones. (From Baylor *et al.*, 1987.)

The measurements in Figure 6.11 are averages from populations of cones that fall very tightly into three distinct groups. No electrophysiological measurements have revealed cones with *anomalous* spectral sensitivities, neither have spectrophotometric methods that measure directly the absorption spectrum of the photopigment in the outer segment, and which have been applied to larger numbers of cones from retinas of old-world primates. Anomalous pigments have been found in the cones of new-world primates (Mollon *et al.*, 1984).

6.2.2.2 Light adaptation

The small dynamic range of impulse-discharging neurons requires that the retina map an enormous range of light levels on to a small range of signal amplitudes in optic nerve fibers. We know something of the general principles that govern this relationship between output and input: the retina as a whole preserves little information about the absolute level of illumination, and at any moment the range of outputs is mapped on to a small part of the input range around the ambient level of illumination; the input range represented in the output is larger at higher levels of illumination. The upshot is that the signal enter-

ing the optic nerve conveys information about the local *contrast* in the image. To achieve this requires two kinds of regulating mechanisms: a subtractive one to discard the signal about the ambient level of illumination, and a multiplicative one to reduce the gain of signal transmission (Walraven *et al.*, 1989). Cones contribute something to the normalization of these signals.

Because each cone – at least in and near the fovea – appears to have an essentially private pathway through the retina, and does not pool its signals with those from other cones, there would appear to be some advantage in regulating sensitivity at the receptors. Psychophysical measurements demonstrate light-adaptation in mechanisms that have spectral sensitivities close to those of individual cones (Stiles, 1939); physiological measurements, made by recording extracellular current flow across outer segments (Valeton and van Norren, 1983), *in vivo*, measurements of current flow in single cones *in vitro* (Schnapf *et al.*, 1990), and measurements of the *a*-wave of the electroretinogram (Hood and Birch, 1993) show that steady illumination reduces the sensitivity of cones through a multiplicative gain reduction, and possibly also some response compression. At high levels of illumination (above 10^4 td), photopigment bleaching contributes substantially to the reduction in sensitivity. It is not clear from physiological measurements that the regulation of sensitivity within cones is sufficient to explain gain changes measured psychophysically; the latter are evident at low levels of illumination that do not desensitize cones, and implicate mechanisms beyond cones, perhaps at the synaptic connections between cones and bipolar cells.

There appears also to be some subtractive mechanism within the cones, for over much of their operating range the *steady-state* responses to standing background illumination vary little with level of illumination. Figure 6.12, which shows how flash responses vary with the strength of background and flash, illustrates the effects of both desensitizing gain changes and subtractive changes that stabilize the responses to standing backgrounds.

6.2.2.3 Dynamics

A cone's biphasic response to a flash (Figure 6.10) implies a band-pass frequency characteristic. The

Fourier transform of the response to a pulse can be used to reveal a cone's sensitivity to different temporal frequencies. When this is done to a moderately light-adapted cone (Figure 6.13) we see that it has a pass-band that peaks near 5 Hz, with sensitivity falling on either side.

The extent to which cones limit the temporal resolving power of the visual system is unclear. The temporal characteristics of vision depend on the spatial (Robson, 1966), and chromatic

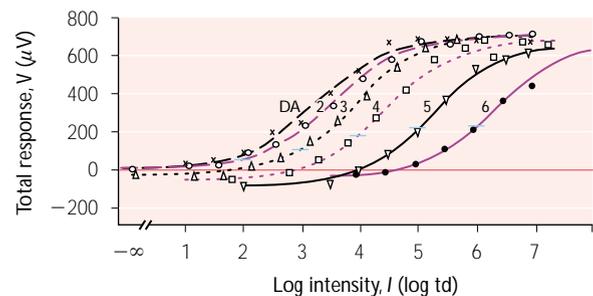


Figure 6.12 Responses of primate cones to a series of flashes of different intensity, recorded in the presence of backgrounds at a range of intensities. Each curve represents the set of responses obtained on a single background, whose intensity is marked by the short horizontal bar on that curve. Points to the left of the bar represent responses to decremental flash, points to the right, responses to incremental flashes. The operating range of the cones is set by the background. (From Valeton and van Norren, 1983.)

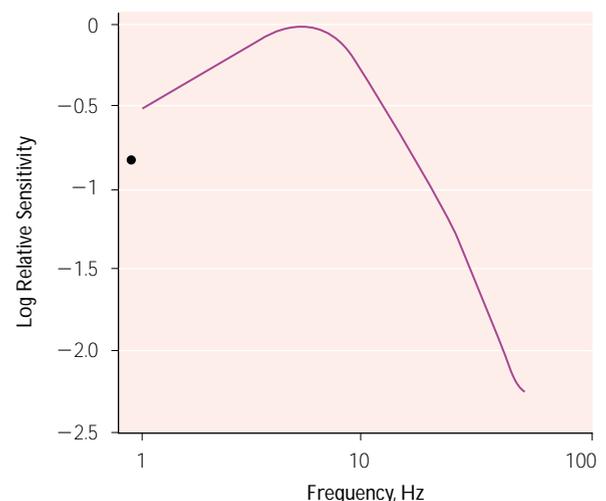


Figure 6.13 Temporal modulation transfer function of primate cones, obtained by Fourier transform of the impulse response. (Courtesy of W. Makous.)

(Estévez and Spekreijse, 1974) attributes of stimuli in ways that suggest that cones seldom limit the temporal resolving power of the visual system; measurements of the late receptor potential (a component of the electroretinogram attributed to photoreceptors) point to the same conclusion (Boynton and Baron, 1975).

The kinetics of the cone's photocurrent response to flashes vary little with level of light-adaptation (Schnapf *et al.*, 1990), so the adaptation-dependent changes observed psychophysically (Kelly, 1961) apparently must reflect action at later sites.

6.3 INTERMEDIATE RETINAL NEURONS

6.3.1 HORIZONTAL CELLS AND BIPOLAR CELLS

6.3.1.1 Connections to cones

Horizontal cells and bipolar cells make synaptic contacts with cones through a specialized connection (the 'triad') that seems designed to permit horizontal cells to regulate the transmission of signals from cones to bipolar cells. The triad consists of a central bipolar cell dendrite flanked by two horizontal cell dendrites. Each cone accommodates 20–30 triads in invaginations in its pedicle (foot).

Two morphological classes of horizontal cells (H1, H2) have been identified in the primate retina; a third class (H3) might also be present (Kolb *et al.*, 1994). The H2 cell contacts only cones; the H1 horizontal cell contacts both rods and cones: dendrites contact cones, axon terminals contact rods. The axon is long and thin and apparently provides rather poor communication between the two ends of the cell, which are often considered to operate relatively independently. Each horizontal cell appears to contact every L and M cone within its dendritic field (in the fovea covering perhaps six or seven cones, in the periphery perhaps two to three times as many), but only H2 cells contact all S cones (Wässle *et al.*, 1989; Ahnelt and Kolb, 1994). H1 cells make very few contacts with S cones (Ahnelt and Kolb, 1994; Goodchild *et al.*, 1996).

Two morphologically distinctive types of bipolar cells contact cones: *diffuse* bipolar cells and

midget bipolar cells (other types contact rods). Diffuse bipolars contact 5–7 cones (Boycott and Wässle, 1991); a midget bipolar cell contacts a single cone, everywhere in the retina (Wässle *et al.*, 1994). Each class of bipolar cell appears to exist in two sub-types, named for the characteristic morphology of their cone connections. An *invaginating* bipolar cell inserts a dendritic terminal into the cone pedicle, forming the central element of a triad; a *flat* bipolar cell makes contacts with the surface of the pedicle. In the central retina each cone probably makes contact with four bipolar cells, one of each kind (Wässle and Boycott, 1991).

6.3.1.2 Functional organization

Primate horizontal cells have not been studied *in vivo*, but single-unit recordings in cat, where horizontal cells resemble in form and connections the H1 type in primate, show some mixing of rod and cone signals at levels of illumination where both receptor types are active (Lankheet *et al.*, 1991). *In vitro* recordings from H1 cells in primate (Verweij *et al.*, 1999) show that they too receive rod input.

The dense connections horizontal cells make with the cones underlying their dendritic fields implies mixing of signals from cones of different types. *In vitro* recordings from horizontal cells in the intact retina (Dacey, 1996; Dacey *et al.*, 1996) show that H1 cells receive signals of the same polarity from L cones and M cones, but not S cones; H2 cells receive signals from all cone classes, with that from S cones being conspicuous.

Bipolar cells receive direct signals from cones and perhaps directly from horizontal cells. Each bipolar cell is connected to a region of retina (or, equivalently, it views a region of visual space) within which light will evoke some physiological response. This is known as the *receptive field*. Receptive fields in vertebrates typically consist of two concentrically organized regions, a circular center and enclosing, overlapping, surround (Naka, 1976), and the primate is no exception (Dacey *et al.*, 2000). Center and surround generate signals of opposite polarity, so that when both are illuminated together, the bipolar cell responds poorly. The receptive field surround appears to originate in H1 horizontal cells, which influence the bipolar cell either directly, or by regulating transmission of signals from cones

(Dacey *et al.*, 2000). The midget bipolar cell in the primate will therefore have a receptive field in which the center and surround have different spectral sensitivities: the spectral sensitivity of the center is that of a single cone, while the spectral sensitivity of the surround is that of horizontal cells that accumulate signals from both L and M cones. The spectral sensitivities of the center and surround of a diffuse bipolar cell are probably more alike, because each mechanism draws inputs from several cones.

L and M cones, and their associated pathways, are not distinguishable by modern histological methods, but Kouyama and Marshak (1992) have identified an immunocytochemically distinct class of invaginating midget bipolar cells that are connected only to S cones. In most instances each bipolar cell contacts a single cone, although each S cone contacts more than one bipolar cell (Mariani, 1984; Kouyama and Marshak, 1992).

There are two functional types of bipolar cells: one in which illumination of the center depolarizes the cell and illumination of the surround hyperpolarizes it (often known as ON-bipolar cells), another in which illumination of the center hyperpolarizes the cell, and illumination of the surround depolarizes it (OFF-bipolar cells). These two fundamental types seem to exist in all retinas, and provide the first stages of on- and off-pathways that remain distinct as far as visual cortex.

The on- and off- types of bipolar cell appear to be the physiological expression of an anatomical distinction we noted earlier: on-bipolar cells make invaginating contacts with cones; off-bipolar cells make flat contacts with cones (Stell *et al.*, 1977). In general, each cone therefore provides a signal to two on-pathways (midget and diffuse), and two off-pathways. The organization of connections to S cones might be different: a presumed on-pathway is known to exist, but although a counterpart off-pathway might be inferred from the presence of some flat bipolar cell contacts that appear on S cones (Kouyama and Marshak, 1992), the bipolar cells making these contacts have not been identified.

6.3.1.3 Amacrine cells

Amacrine cells (named by Cajal for their lack of an axon) lie in the inner retina and make con-

nections with bipolar cells and ganglion cells. They exist in a wide variety of morphological types (Masland, 1988; Wässle and Boycott, 1991). With rare exceptions, little is known about their roles. Some amacrine cells might have little to do directly with vision, instead controlling functions such as eye-growth (Schaeffel *et al.*, 1995). One class of amacrine cell (AII) provides an essential link in the chain from rod photoreceptor to ganglion cell: it links the rod bipolar cell through an inhibitory synapse to a diffuse cone off-bipolar cell, and through an excitatory synapse to an on-bipolar cell. These cone bipolar cells in turn contact ganglion cells (Sterling *et al.*, 1988). Amacrine cells that contact midget bipolar cells and midget ganglion cells make indiscriminate contacts with all midget bipolar cells within reach. These include bipolar cells driven by both L and M cones (Calkins and Sterling, 1996). Most types of amacrine cells are not directly interposed between bipolar and ganglion cells, and the general organization of their connections suggests that they modulate the transmission of information from bipolar cells to ganglion cells, or add components to the receptive fields of ganglion cells.

No physiological recordings have been obtained *in vivo* from amacrine cells in primates, but where recordings have been obtained from other species amacrine cells have often exhibited complex behaviors (for example giving depolarizing responses to both light onset and light offset) that suggest an important role in the formation of some distinctive nonlinear behaviors in kinds of ganglion cells that project to the superior colliculus (see below). Where receptive fields have been characterized (Kaneko, 1973) they are circular, but have no center-surround organization.

6.4 GANGLION CELLS AND LGN CELLS

Neurons in LGN are, in their general behavior, almost indistinguishable from the ganglion cells that drive them, so it is convenient to consider both kinds together. Because different classes of LGN neuron are segregated in different layers of the nucleus, and can be selected for study, LGN neurons are more often studied than ganglion cells.

6.4.1 STRUCTURAL ISSUES

In primate retina the principal classes of bipolar cells, midget and diffuse, make specific connections in the *inner plexiform layer* (IPL) with the two kinds of ganglion cells known as parasol and midget cells. A midget bipolar cell in the fovea (Calkins *et al.*, 1994), and to eccentricities of perhaps 6° , makes exclusive contact with a single midget ganglion cell, providing each cone with a private pathway through the retina. A parasol cell in the fovea receives inputs, via diffuse bipolar cells, from perhaps 30–50 cones (Grünert *et al.*, 1993).

The on- and off- types of each of the major classes of bipolar cell contact their counterpart ganglion cells at different depths within the retina, permitting the identification of on- and off-center ganglion cells in anatomical sections (Perry *et al.*, 1984; Watanabe and Rodieck, 1989). The on-bipolars contact on-center ganglion cells in a stratum of the IPL closer to the ganglion cells (Famiglietti and Kolb, 1976).

Recent anatomical evidence points to reliable structural differences among midget pathways that might be associated with the L and M cones. Calkins *et al.* (1994) found that (within each of the major classes, on- and off-) most midget bipolar cells in the monkey retina made one of two different kinds of synaptic connections with midget ganglion cells: either the synapse had around 50 synaptic ribbons, or it had around 30, with no overlap between the distributions. There is a corresponding disparity in the numbers of synaptic ribbons each kind of bipolar cell makes with the cone that drives it. The bipolar cells making the two kinds of connections were randomly distributed on the retina. Among the bipolar-ganglion connections studied, 44% had the larger number of synaptic ribbons. These different synaptic connections might reflect differences between the pathways conveying signals from L and M cones, although it is not known which kind of cone might be associated with each pathway.

It is not known if any midget ganglion cells convey S cone signals, but these signals are known to be carried by another, relatively rare, kind of ganglion cell described by Rodieck (1991) and Dacey (1993). This *small bistratified* cell has dendrites that branch in two planes in

the IPL, one in the region where off-bipolars contact midget ganglion cells, and the other in the region where on-bipolars contact midget ganglion cells. The span of the bistratified cell's dendrites matches that of the parasol cell, so in the fovea might cover 30–50 cones, and the cell might receive signals from 3–5 S cones. Small bistratified cells constitute less than 2% of ganglion cells in and near the fovea (Dacey, 1994), and probably provide a mosaic that is too coarse to account for the spatial resolving power of the S cone system measured psychophysically (Williams and Collier, 1983). This and other evidence to be reviewed below suggests that the retina must contain additional S cone pathways.

Parasol and midget cells project respectively to the magnocellular and parvocellular divisions of the LGN (Perry *et al.*, 1984); small bistratified cells project to the parvocellular layers (Rodieck, 1991). The internal organization of the LGN is locally complex with afferent fibers from ganglion cells making contact with relay neurons that convey signals to cortex, and with interneurons. The LGN also receives projections from several other parts of the brain. Nothing that we know of the internal organization helps us understand color vision.

6.4.2 FUNCTION ORGANIZATION

The action potentials discharged by a ganglion cell or LGN cell can be recorded with an electrode that sits outside the neuron, and this makes it possible to record from individual neurons in an intact animal, and to study their visual sensitivities. Where the visual properties of ganglion cells have been compared with those of the LGN neurons to which they project, they have been found to be essentially identical, except perhaps for differences in sensitivity that probably reflect the action of regulatory mechanisms in the LGN (Sherman, 1996). In the following discussion ganglion cells and LGN neurons are therefore distinguished only when their properties are known to differ. The physiological counterparts of the anatomically identified parasol and midget cells are named for their projections to magnocellular and parvocellular layers in the LGN, and are known as M and P cells, respectively. This terminology provides some potential for confusion, for it does not accommodate

the small bistratified cells that project to the parvocellular layers.

6.4.2.1 Receptive field organization

Both P (parvocellular) and M (magnocellular) cells have receptive fields organized into two concentric antagonistic regions: a center (on- or off-) and a surrounding region of opposite sense. This arrangement is common in vertebrates. The receptive fields of small bistratified cells appear to lack clear center-surround organization (Dacey and Lee, 1994).

The distributions of sensitivity within center and surround mechanisms are usually represented by Gaussian profiles of different extents and opposite polarity (Figure 6.14A; Rodieck, 1965); the properties of these mechanisms are commonly inferred from a neuron's spatial modulation transfer function (or contrast-sensitivity function (Enroth-Cugell and Robson, 1966)) measured with grating patterns whose luminance is modulated sinusoidally about a constant mean (see Figure 6.14B).

Neurons respond to moving or counterphase-flickering gratings with a modulated discharge that reflects the time-varying changes of luminance locally within the receptive field. Contrast sensitivity is typically measured by finding, as a function of the spatial frequency of a grating, the contrast required to evoke a modulated discharge of specified amplitude (Figure 6.14C). Such measurements show that, to a close approximation, both center and surround accumulate cone signals linearly, and the cell responds to the sum of the signals aggregated from the two mechanisms (Kaplan and Shapley, 1982; Derrington and Lennie, 1984). It is important to note that this linear behavior is observed when neurons are stably adapted to the average luminance of the grating and are driven by modulations about this mean; changing mean luminance leads to the expression of nonlinearities (see below).

As one would expect from the anatomy of their connections, M cells have larger receptive fields than P cells. Although anatomical evidence points to the center of a P cell receptive field originating in a single cone, conventional measurements of contrast sensitivity only rarely hint at this (Derrington and Lennie, 1984; Blakemore and Vital-Durand, 1986). Measurements made with interference fringes formed directly on the

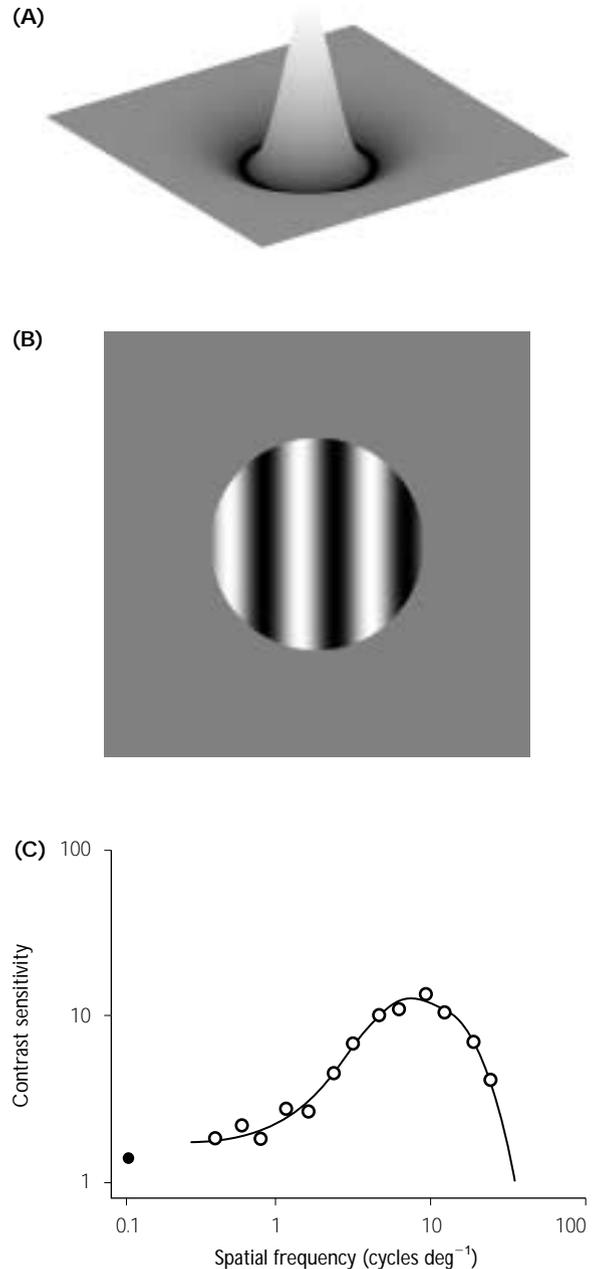


Figure 6.14 (A) Diagram showing the distribution of sensitivity within the center and surround mechanisms of a ganglion cell's receptive field. The peak sensitivity of the center greatly exceeds that of the surround, but because the center is much smaller than the surround, the center only slightly dominates when both regions of the receptive field are illuminated. (B) Sinusoidal grating patterns of the kind used to explore the spatiotemporal transfer characteristics of visual neurons. (C) Contrast sensitivity function obtained from a parvocellular neuron in LGN. (From Derrington and Lennie, 1984.)

retina (by-passing the optics of the eye) are consistent with the center receiving signals from a single cone (McMahon *et al.*, 2000).

6.4.2.2 Contrast sensitivity

M and P cells differ in their sensitivities to contrast, M cells having several times greater contrast sensitivity to achromatic gratings (Kaplan and Shapley, 1982; Derrington and Lennie, 1984). Over a range of low to moderate contrasts, the responses of both M and P cells to stimuli of optimal spatial frequency grow linearly with contrast, but the greater sensitivity of M cells leads to their giving responses of saturating amplitude to high-contrast stimuli (Derrington and Lennie, 1984). Moreover, the temporal frequency at which sensitivity peaks is around 20 Hz in M cells and around 10 Hz in P cells (Derrington and Lennie, 1984). This, coupled with the higher contrast sensitivity of M cells, results in M cells responding to a range of high frequency signals that are apparently never seen by P cells.

Signals from the center and surround of a receptive field travel through different pathways to reach a neuron, and are subject to different delays and attenuation, so it is not surprising that the interaction between center and surround varies with the temporal frequency of visual stimulation. As temporal frequency is raised, center-surround antagonism is apparently reduced, so the spatial contrast sensitivity curve (Figure 6.14C) tends to lose its distinctive band-pass shape, becoming instead low-pass. This behavior is consistent with surround signals lagging center signals by several milliseconds (Derrington and Lennie, 1984).

6.4.3 CHROMATIC PROPERTIES

In the M cell's receptive field, center and surround generally have different spectral sensitivities, although the differences are not often conspicuous. The center has a spectral sensitivity close to that of $V\lambda$ (see Chapter 2), therefore drawing its inputs from L and M cones, while the surround draws on some different mix of cone signals (Derrington *et al.*, 1984; Kaiser *et al.*, 1990), possibly even having some local chromatically opponent structure within it (Schiller and Colby, 1983; Lee *et al.*, 1989).

In the P cell's receptive field, center and surround have overtly different spectral sensitivities (Wiesel and Hubel, 1966; Gouras, 1968; Dreher *et al.*, 1976; Derrington *et al.*, 1984). The different spectral sensitivities of center and surround endow the P cell with curious properties: the spatial contrast sensitivity curve measured with achromatic gratings has a characteristic bandpass shape that reflects that antagonistic interaction between center and surround (Figure 6.14), but the curve measured with chromatic gratings (sinusoidal modulation of chromaticity rather than luminance) has a lowpass shape, so that sensitivity to chromatic modulation is highest when a spatially uniform field of light is modulated in time. For this reason a spatially uniform field is now often used to characterize the chromatic properties of receptive fields. The luminance and/or chromaticity of this field are usually modulated in time about some point near the center of the chromaticity diagram.

P cells fall into two chromatic classes, loosely red-green and yellow-blue (De Valois *et al.*, 1966; Wiesel and Hubel, 1966; Gouras, 1968). The analysis of cone inputs reveals one class that receives opposed inputs from L and M cones only, and a second class that receives inputs from S cones opposed to some unspecified combination of signals from L and M cones (Derrington *et al.*, 1984; Figure 6.15).

The techniques now used to characterize the chromatic properties of P cells show that the neurons receive opposed inputs from different cone classes, but do not reveal the spatial distribution of these inputs. Until recently, it was presumed that the different kinds of cones whose signals were opposed were cleanly segregated in center and surround of the receptive field (bearing in mind possible exceptions for cells driven by S cones), but several lines of evidence have recently prompted a closer look at alternatives. First, if indeed the P cell receives its center input from a single cone, it will have a chromatically opponent receptive field even if its surround draws indiscriminately on all cone classes (Lennie, 1980). Second, the recently discovered similarity of the genes that encode L and M cone pigments, and the very similar structures of the cone pigments themselves (Nathans *et al.*, 1992), raise the possibility that the visual system might not distinguish them during development; third,

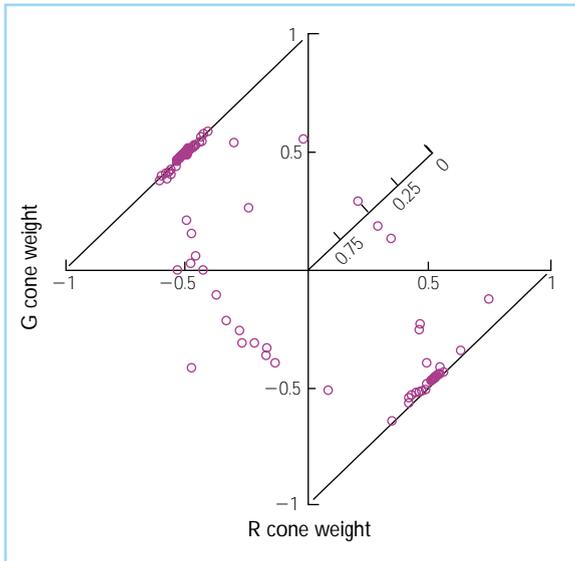


Figure 6.15 Distribution of weights that P cells in LGN attach to inputs from the different classes of cones. The weights attached to signals from L and M cones are represented explicitly; cells that receive inputs from only L and M cones are represented by points that lie on the unit diagonals; cells that receive inputs from S cones are represented by points inside the diagonals. The unsigned S cone weight can be read from the internal scale. (From Derrington *et al.*, 1984.)

the connections horizontal cells make with cones (Wässle *et al.*, 1989), and the physiological signals recorded from horizontal cells (Dacey, 1996) suggest that they receive mixed signals from the different classes of cones. Fourth, the amacrine cells that contact midget bipolar cells and midget ganglion cells make indiscriminate contact with the bipolar cells driven by both kinds of cones (Calkins and Sterling, 1996). Lennie *et al.* (1991) showed that the properties of L–M opponent neurons were consistent with either pure cone input to the surround, or mixed cone input from L and M cones, but not S cones. Reid and Shapley (1992) have argued that the P cell's surround receives inputs from a single class of cone. Given the mixing of cone signals present in horizontal cells and amacrine cells, this would require some elaborate organization that segregates cone signals again. *In vitro* recordings from midget ganglion cells in the periphery show mixed cone input to both center and surround (Dacey and Lee, 1999); no recordings have yet been made from central retina.

Dacey and Lee (1994) showed that the small

bistratified ganglion cell that projects to parvocellular LGN receives 'on' (depolarizing) signals from S cones and 'off' signals from L and M cones. Neurons that receive strong 'off' (hyperpolarizing) signals from S cones, and 'on' signals from L and M cones, also exist, although they are encountered less frequently (de Monasterio and Gouras, 1975; Derrington *et al.*, 1984; Valberg *et al.*, 1986). Their anatomical substrate has not yet been found. As was noted in an earlier section, there are probably yet other kinds of neurons that carry signals from S cones, for in and near the fovea the sampling density of the small bistratified system is too low to account for the visual acuity of the S cone system.

Just as the different temporal characteristics of center and surround make the spatial properties of receptive fields depend on the temporal frequency of visual stimulation, so too do they affect the chromatic properties. At high temporal frequencies the phase difference between center and surround signals is reduced, so the mechanisms tend to act synergistically rather than antagonistically. In P cells this leads to some loss of chromatic opponency (Gouras and Zrenner, 1979; Derrington *et al.*, 1984; Smith *et al.*, 1992). However, up to frequencies of 20 Hz or more the effect is small (Derrington *et al.*, 1984; Lee *et al.*, 1990) – too small to contribute significantly to the rapid decline in sensitivity to chromatic flicker found psychophysically (Wisowaty and Boynton, 1980), which must therefore originate in cortex.

6.4.3.1 Chromatic adaptation

The two-color adaptation methods developed by Stiles (1939) to isolate chromatic mechanisms psychophysically have been used to isolate the chromatic mechanisms in ganglion cells and LGN cells (Wiesel and Hubel, 1966; Gouras, 1968), but have not been employed to explore details of chromatic adaptation. We know that a change in mean illumination causes a ganglion cell's sensitivity to decline approximately in proportion to the level of illumination (Purpura *et al.*, 1990; Lee *et al.*, 1990). The mechanism almost certainly lies before the ganglion cells themselves, for the gain change proceeds independently in rod and cone pathways that converge on the same ganglion cells. Less attention has been paid to the changes in ganglion cell behavior that result from changing the mean

chromaticity of illumination. DePriest *et al.* (1991) found that, at constant luminance, a modest step change in the chromaticity of a background brought about a long-lasting change in the maintained discharge of a P cell, a step in the ‘on’ color direction increasing the discharge, a step in the ‘off’ color direction decreasing the discharge. A step in luminance that provided a similar change in cone excitation had little effect upon the maintained discharge. Yeh *et al.* (1996) described similar behavior. These long-lasting changes in discharge provide cortex with a persisting signal about the ambient chromaticity.

In addition to changing the maintained discharge, the step change in background color perturbs the cell’s sensitivity, although different investigations do not fully agree on the nature of the change. DePriest *et al.* (1991) found a rapid, paradoxical, increase in sensitivity to chromatic probe stimuli following a change in background that would have been expected to reduce sensitivity. Yeh *et al.* (1996), who used larger background steps, found prolonged disturbances of sensitivity, possibly reflecting saturation of an opponent site. These experiments point to possibly complex mechanisms of sensitivity regulation involving sites at which signals from the different classes of cones have converged.

6.4.4 CANDIDATE CHROMATIC AND ACHROMATIC PATHWAYS

The two different types of chromatically opponent P cells, a ‘red–green’ one and a ‘blue–yellow’ one, together with M cells, whose spectral sensitivities are close to that of $V\lambda$, provide plausible substrates of the three kinds of post-receptoral mechanisms postulated by psychophysicists.

There seems little doubt that the P cells provide signals to two chromatically opponent visual channels, but the role of M cells in the third channel is less secure. Modern psychophysical work attributes to this mechanism high spatial and temporal resolution, and a spectral sensitivity close to that of $V\lambda$ (for a review, see Lennie *et al.*, 1993). The temporal resolving power of M cells (and also of P cells) considerably exceeds that measured psychophysically, but the spatial resolving power of the mosaic of M cells is demonstrably too low to explain psychophysical performance (Lennie, 1993).

Moreover, having a $V\lambda$ -like spectral sensitivity does not necessarily implicate M cells as the third post-receptoral mechanism. Lennie *et al.* (1993) argue that although M cells are a plausible substrate of luminous efficiency functions measured with heterochromatic flicker photometry, similar functions can be obtained from linear transformations of the signals carried by P cells, and this provides a more probable account of luminous efficiency functions derived by other means, such as acuity measurements.

The above considerations encourage one to explore the possibility that the P pathway carries signals for all three chromatic dimensions of vision. Several observations, puzzling when considered in isolation, become more intelligible in that context. First, around 90% of P cells (about 80% of all ganglion cells) are of the ‘red–green’ type that receive opponent signals from L and M cones – many more than are needed to account for visual acuity for colored objects, but the right number to explain visual acuity for achromatic objects. Second, the center-surround organization of their receptive fields ensures that they respond well to chromatic changes at low spatial frequencies and to achromatic stimuli at high spatial frequencies. Simply put, a single P cell is equally capable of conveying information about the chromatic and achromatic content of the image, albeit in different frequency bands. Its response is ambiguous, but this ambiguity can be resolved by comparing, at some higher level, signals from different neurons (Lennie and D’Zmura, 1988). This kind of account leaves M cells little role in color vision, save possibly in heterochromatic flicker matches. Lee (1996) attributes to M cells a larger role in object vision.

6.5 CORTEX

6.5.1 STRUCTURAL ISSUES

In primates, V1 is the only cortical area that receives projections from LGN. Those from magnocellular and parvocellular layers arrive in different anatomical subdivisions of layer 4: M cells project principally to layer 4C α , and P cells project mainly to layers 4C β and 4A (see Figure 6.6). The incoming fibers from the LGN are segregated

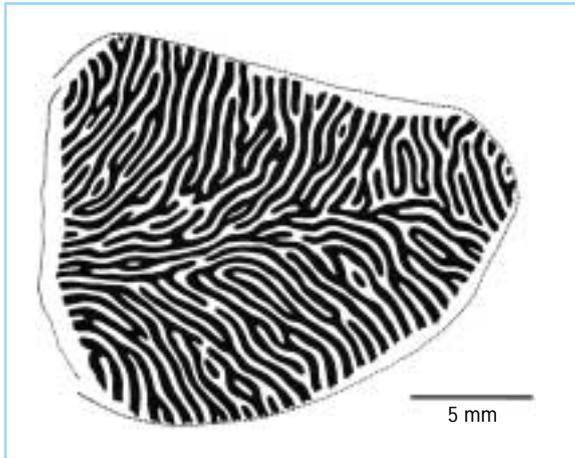


Figure 6.16 The organization of ocular dominance columns in striate cortex of the macaque monkey. The cortex here has been unfolded as a flat sheet. Radioactive tracer injected into one eye is deposited in striate cortex, in regions to which that eye projects. This results in the distinctive pattern of stripes. (From Hubel and Wiesel, 1977.)

by eye of origin into strips about 0.5 mm wide. These strips, known as *ocular dominance columns*, can be readily identified anatomically by examining the uptake in cortex of the radioactive amino acid proline injected into one eye. This is transported to cortex and deposited in layer 4 (Figure 6.16). This anatomical segregation of signals from the two eyes is not well maintained in layers above and below layer 4, and ocular dominance columns are less sharply defined.

V1 contains a topographically organized map of half of the visual field, with a large representation of the fovea and a much smaller representation of the periphery. Most of the distortion in the map can be explained by the variation in the density of retinal ganglion cells from fovea to periphery; each ganglion cell projects, via LGN, to a roughly constant volume of cortex. The arrangement and size of distinctive anatomical features such as ocular dominance columns does not vary from place to place in the map.

Within the overall pattern established by the ocular dominance columns, other repeating structures can be discerned in V1. Cortex stained for the presence of the enzyme cytochrome oxidase displays a regular pattern of patches where the enzyme is concentrated (Figure 6.17). These 'blobs,' which are more prominent above and

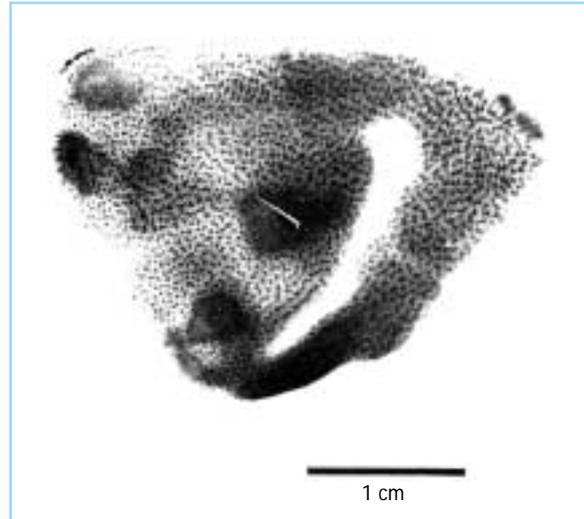


Figure 6.17 Distribution of cytochrome oxidase 'blobs' in the unfolded striate cortex of the macaque monkey. The blobs are spaced almost uniformly throughout striate cortex, and fall within the separate ocular dominance columns that define the territories dominated by the two eyes. (From Livingstone and Hubel, 1984.)

below layer 4, lie securely within the separate domains of left- and right-eye columns.

The existence of repeating structures in V1 suggests a modular organization, assembled from units of a certain size. It is widely believed that the fundamental organizing unit spans the width of a pair of adjacent strips of input from left and right eyes, and therefore occupies about 1 mm² of cortical surface and has a depth of about 2 mm. This unit, known as a *hypercolumn* (Hubel and Wiesel, 1974), contains perhaps 200 000 cells. Within a hypercolumn there are further organizational regularities that can be discerned physiologically but not anatomically.

Signals from different subdivisions of layer 4 are delivered to different places within V1. Layer 4C α , which receives its input from M cells, makes a distinctive projection to layer 4B, which sends an equally distinctive projection out of striate cortex to extrastriate regions that appear to be particularly concerned with the analysis of image movement (Zeki, 1974; Newsome *et al.*, 1985), and which ultimately send major projections to the parietal lobe. Neurons in layers 4C β and 4A, which receive input from P cells, project principally to the upper layers of striate cortex.

Neurons in the upper layers of striate cortex send projections principally to area V2.

6.5.2 FUNCTIONAL ORGANIZATION

6.5.2.1 Striate cortex

The earliest studies showed that receptive fields of V1 neurons often differ profoundly from those of neurons in retina and LGN. The most prominent differences lay in the spatial organization of receptive fields, which instead of being concentrically organized, were often elongated, sometimes having no distinct excitatory and inhibitory regions (Hubel and Wiesel, 1977). The result is that most neurons in V1 are selective for the orientation of visual stimuli that fall within their receptive fields; they are also often sharply selective for the size of the stimulus (Figure 6.18), and for its direction of movement. The uniformity of receptive field properties in retina and LGN thus gives way to great heterogeneity in cortex.

Hubel and Wiesel (1962, 1968) drew a broad distinction, generally upheld by subsequent work, between two major kinds of cortical cell

that they called *simple* and *complex*. These have similar orientation, spatial, and directional selectivities, but differ sharply in the form of their responses. A simple cell generates a response that reflects the quasi-linear addition of signals (excitatory or inhibitory) arising in different parts of the receptive field. A map of the excitatory and inhibitory regions in a simple receptive field provides a reasonable guide to the visual selectivity of the cell. A complex cell is inherently nonlinear: the receptive field generally cannot be parsed into distinct excitatory and inhibitory regions, and the cell will respond with an increased discharge to either a localized increase or decrease in illumination. The behavior of the complex cell represents an important change in the way the visual system analyzes the image, for, unlike the simple cell or a neuron at an earlier stage in the pathway, it gives a response from which the image cannot be reconstructed. It is unclear whether or not complex cells derive their inputs from simple cells, or receive the same inputs as simple cells.

Cells with different properties tend to be concentrated at different depths within cortex. Complex cells are most often found in layers 2/3 and in layer V. Simple cells are found in layers 2/3 and in layer 4. Neurons with concentrically organized receptive fields are found in layer 4, where inputs from LGN arrive. Above and below layer 4, neurons can often be excited by stimulation through either eye, although rarely are both eyes equally effective. If a cell can be driven binocularly, it is often sensitive to the relative position of the stimuli presented to the two eyes, responding well when the stimuli fall on corresponding points, much less well otherwise. This makes neurons sensitive to binocular depth (Poggio and Talbot, 1981).

Neurons with different visual preferences are placed in an orderly arrangement in cortex. From any point on the cortical surface, extending perpendicularly through the depth of the cortex, neurons prefer stimuli of the same orientation. On an adjacent, parallel, trajectory neurons prefer a slightly different orientation. A set of 'orientation columns,' covering the range of orientations around the circle, is contained within the width of a pair of ocular dominance columns (a hypercolumn; Hubel and Wiesel, 1977).

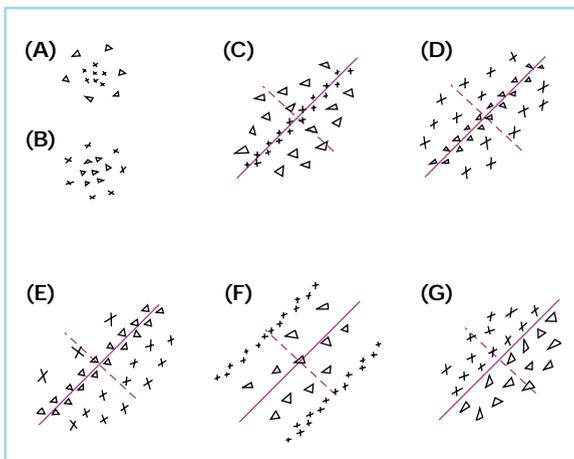


Figure 6.18 Diagram of the receptive field organization often found in cells in striate cortex. Crosses represent excitatory regions giving 'on' responses; triangles represent inhibitory regions giving 'off' responses. (A) and (B) illustrate the arrangement of regions in concentrically-organized receptive fields typical of ganglion cells and LGN cells, but relatively rare in cortex. (C–G) represent arrangements of excitatory and inhibitory regions in different simple cells. (From Hubel and Wiesel, 1962.)

Beyond layer 4 of striate cortex the distinct identities of the incoming M and P pathways are not well preserved. Neurons in layer 4B tend to have higher contrast sensitivities than neurons elsewhere (Hawken and Parker, 1984), presumably reflecting their close association with inputs from the sensitive M cells, but neurons in other layers give few explicit indications of the sources of their driving signals.

Neurons in striate cortex respond best to contrast modulations at temporal frequencies distributed around 12 Hz, a lower and more variable frequency than characterizes neurons in LGN (Hawken *et al.*, 1996), but one that better matches psychophysical measurements. As temporal frequency is lowered below the peak, the sensitivity of a cortical neuron often declines sharply.

6.5.2.2 Extrastriate cortex

The visual characteristics of neurons in regions beyond striate cortex have been less thoroughly studied, but some general characteristics are well known. Among the collection of visual areas that lead toward the temporal lobe, and are the most likely to be important for color vision, receptive fields of neurons grow progressively larger as one moves towards the temporal lobe, and nearly all neurons can be driven by inputs through either eye, but the general properties of receptive fields – spatial selectivity, orientation, and direction selectivity – change little from area to area. There is some physiological evidence that different areas are specialized for different kinds of analysis; this issue is taken up in a later section.

6.5.3 CHROMATIC PROPERTIES

In exploring the properties of cortical neurons, investigators have concentrated on aspects of color vision that cannot be easily explained by the known properties of neurons at earlier stages in the pathway.

6.5.3.1 Separation of chromatic and achromatic signals

It was noted earlier that P cells driven by signals from L and M cones must be the substrate of the achromatic pathway that supports visual acuity, and presumably also a red–green opponent

pathway, but that in any individual cell the chromatic and achromatic signals are confounded. In cortex one might expect to find mechanisms whose behavior better reflects what is observed psychophysically, namely substantial independence of chromatic and achromatic mechanisms.

There is a profound change in the general chromatic characteristics of cells as one moves from LGN to cortex. The ubiquitous color-opponent P cells in LGN give way to a dearth of overtly color-opponent neurons in V1. Hubel and Wiesel (1968) commented on this in their first investigation of primate visual cortex, and it has been confirmed regularly since (Gouras, 1974).

Neurons with receptive fields in and near the fovea often have sharply defined preferences for stimuli containing relatively high spatial frequencies – high enough that chromatic aberration removes much of the chromatic contrast from the image. This preference for high spatial frequencies undoubtedly accounts for the weak responses of many neurons to stimuli containing spatio-chromatic contrast, and as a result, most investigations of the chromatic properties of neurons concentrate on cells that prefer stimuli containing low spatial frequencies.

Overtly color-opponent neurons are found in all layers of striate cortex, but more often in layer 4 than elsewhere. In layer 4 and layer 6 particularly, the most responsive neurons often, but by no means always, have receptive fields with poorly defined orientation selectivity, and low-pass spatial frequency tuning (Lennie *et al.*, 1990). These receptive fields are reminiscent of receptive fields in LGN, with the following important difference: their chromatic characteristics depend little upon the spatial configuration of the stimulus. Cortical neurons therefore do not confound different dimensions of stimulus variation in the way that LGN neurons do.

In the upper layers of cortex, where simple and complex cells predominate, few neurons are overtly color-opponent. Most of those that can be excited by colored patterns can also be excited by patterns defined by brightness contrast; cells that respond best to isoluminant chromatic contrasts are rare (Gouras and Krüger, 1979; Thorell *et al.*, 1984; Lennie *et al.*, 1990). When a neuron's receptive field properties can be established with stimuli defined by either color or brightness contrast, the spatial and orientational selectivities

are generally similar (Thorell *et al.*, 1984; Lennie *et al.*, 1990).

The general picture to emerge from studies of striate cortex is that for the first time there appear in large numbers neurons whose receptive field properties are indifferent to the chromatic composition of the stimulus – they may be conceived as analyzing spatial structure with little regard for the spectral composition of the stimulus. Most of these neurons respond best when stimulus patterns are defined by brightness rather than color contrast. In this sense cortex might be viewed as having formed an achromatic pathway. The standing of independent chromatic pathways is less clear.

Neurons that respond preferentially to stimuli defined by color rather than brightness contrast are also found in areas V2, V3, and V4, and in parts of the temporal lobe.

6.5.3.2 Number of chromatic channels

Psychophysical evidence reviewed in Chapter 3 grants a special status to two chromatic axes in color space (loosely a red–green axis and a yellow–blue one), but at the same time that evidence is not consistent on the locus of these special (cardinal) directions. Moreover, studies that have examined aftereffects of habituating to modulations of chromaticity along different directions in color space (Krauskopf *et al.*, 1986; Webster and Mollon, 1991) reveal more mechanisms than just the two tuned to the cardinal directions – mechanisms tuned to intermediate directions exist too.

P cells in LGN fall neatly into just two chromatic classes. Moreover, their sensitivities are not changed by prolonged exposure to habituating stimuli of the kind used to reveal multiple chromatic mechanisms in psychophysical experiments. These multiple mechanisms must originate in cortex.

Several studies have examined the distribution of chromatic preferences among cells in striate cortex. Although they do not agree on details, these investigations do agree that chromatic preferences are not clustered in two groups. Vautin and Dow (1985), in recordings made from awake monkeys, found that, when chromatic preferences were explored with monochromatic lights, neurons in layer 4 fell

into four loosely defined clusters (blue, green, yellow, red), identified by their wavelengths of peak excitability. Thorell *et al.* (1984) and Lennie *et al.* (1990) found a similar modest tendency for cells' chromatic preferences to be aligned along the red–green and yellow–blue axes (properly an axis of exclusively L and M cone modulation and one of exclusively S cone modulation) of color space. In the upper layers of cortex, chromatic preferences are broadly distributed.

To the extent that cells' chromatic preferences are broadly distributed, neurons in striate cortex are a candidate substrate for the multiple chromatic mechanisms inferred from psychophysical experiments. However, it is hard to tell from physiological observations which of the neurons that respond to colored stimuli are important for color vision – that is, which neurons might have a role in perceptual judgments about color. Attempts to identify the relevant neurons have generally sought to demonstrate physiological properties that mirrored those of the psychophysical mechanisms. One such attempt, to explore habituation to chromatically modulated stimuli, showed that although some cortical neurons habituate (and neurons in LGN never do), others become more responsive following prolonged stimulation (Lennie *et al.*, 1994). Another approach has been to examine whether or not color-opponent neurons are concentrated in particular places – pathways specialized for the analysis of color.

6.5.3.3 Spatial contrast effects

Some of the most distinctive phenomena of color vision – for example, the uniform color induced in a neutral patch by enclosing it in a colored region – depend upon spatial interactions between nearby regions of visual field. These remote influences have a longer reach than can plausibly be associated with any mechanisms in retina or LGN, and have generally been thought to originate in cortex. In area V1, long-range contrast effects have been observed in the domains of orientation and direction of movement (Blakemore and Tobin, 1972; Knierim and Van Essen, 1992; Lamme, 1995), but not consistently in the domain of color. In their first discussion of neurons in striate cortex, Hubel and Wiesel (1968) described a rare 'double-opponent' receptive field, in which a core region with co-extensive

color-opponent mechanisms (for example, red-on, green-off) was enclosed by an outer region containing color-opponent mechanisms of the opposite sense. Neurons with such properties could perhaps account for induced color phenomena (Daw, 1984), but they are rare, and their receptive fields are small. Livingstone and Hubel (1984) and Ts'o and Gilbert (1988) later studied neurons, perhaps differing from those explored by Hubel and Wiesel, in which the region enclosing the core of the receptive field was not itself color-opponent, but always suppressed the response to a stimulus applied to the core region. It is unclear what such cells might do for color vision.

In seeking physiological accounts of color induction, physiologists have looked most carefully at area V4 (the fourth visual cortical area). Zeki (1973, 1977) discovered that this contains an unusually large proportion of cells with sharp chromatic selectivities. Moreover, Zeki (1983) later found that the response of a V4 cell to a colored stimulus in the middle of its receptive field depended on the color of light falling in surrounding regions, in a manner that was correlated with the colored appearance the stimulus to a human observer. Schein and Desimone (1990) later described a mechanism that might be responsible for this behavior: the receptive field of a V4 cell is enclosed by a region that has the same spectral characteristics as the receptive field proper, but when illuminated always suppresses the response to a stimulus falling within the receptive field.

6.5.3.4 Private pathways for color

Two kinds of evidence bear on the question of whether there exist cortical pathways specialized for color. The first comes from physiological studies that have looked for special concentrations of color-opponent cells in different parts of cortex. The second comes from studies that have attempted to localize color centers in human cortex.

All investigators seem to agree that area V4 contains neurons with interesting chromatic properties, but there is much less agreement on whether V4 is an area specialized for analysis of the chromatic attributes of objects. V4 is the principal conduit of information from lower visual cortical regions to the temporal lobe, a

region crucially involved in all aspects of object vision, not just the analysis of color (Heywood and Cowey, 1987; Heywood *et al.*, 1992). It therefore seems unlikely that V4 could be devoted exclusively to the analysis of color. Nevertheless, subdivisions of V4 might have differently specialized functions, undertaking analyses of different attributes of the image; one of these might be the analysis of color.

This issue has been explored in studies that have traced pathways projecting from earlier stages of visual cortex to V4. Most of the work that has attempted to trace a specialized color pathway has concentrated on the projections that originate in the cytochrome oxidase 'blobs' in V1. Livingstone and Hubel (1984) first drew attention to properties of cells in blobs, finding that they tended to have concentrically organized receptive fields, more than half being color-opponent – a much higher proportion than is typically found elsewhere in V1. Neurons in the blobs project to the second visual area, V2. When stained for cytochrome oxidase, V2 shows a pattern not of blobs, but of three alternating stripes, often called thick, thin, and pale (Tootell *et al.*, 1983). The projections from blobs in V1 end preferentially in the thin stripes (Livingstone and Hubel, 1983). Neurons in the thin stripes and the pale stripes project to V4 (Shipp and Zeki, 1985; DeYoe and Van Essen, 1985), where their terminations seem to be segregated (DeYoe *et al.*, 1994).

Physiological explorations of the pathway that originates in blobs are equivocal on the question of it being specialized for color. Ts'o and Gilbert (1988) corroborated Livingstone and Hubel's (1984) finding of a concentration of color-opponent cells in blobs, but Lennie *et al.* (1990) and Leventhal *et al.* (1995) found no concentrations of this kind. In area V2, Hubel and Livingstone (1987) described a concentration of color-opponent cells in the thin stripes to which blobs project. Later studies in which cells were characterized quantitatively (Levitt *et al.*, 1994; Gegenfurtner *et al.*, 1996) have found only a slight tendency for cells with different properties to be clustered in different stripes.

Although work on monkeys provides no firm pointers to the existence of a specialized color pathway, studies of people with cortical lesions (usually resulting from stroke) that cause selective impairment of color vision, without (or with

little) concomitant impairment of other dimensions of vision, suggest the existence of a cortical region specialized for the analysis of color (Zeki, 1990). However, it is often unclear from these studies whether the impairment affects the capacity to identify colors, or the capacity to distinguish surfaces of different color. Where this question has been examined (Mollon *et al.*, 1980; Victor *et al.*, 1989; Barbur *et al.*, 1994), achromatopsic subjects often are able to use chromaticity to segment surfaces, and sometimes have near normal hue discrimination, but are much impaired in naming colors and grouping of items of similar color.

Recently developed methods can identify in cortex the local changes in blood flow and blood volume associated with increased neural activity. Two of these kinds of measurement, positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), have been used to investigate whether or not mechanisms of color vision are localized in particular cortical regions (Zeki *et al.*, 1991; Corbetta *et al.*, 1991). The results show that a region in the fusiform gyrus, which lies between the occipital and temporal lobes, seems to be unusually active during the perception of colored patterns, though the degree to which it is specialized for the analysis of color has not been fully explored.

6.6 ACKNOWLEDGMENTS

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6.7 NOTES

1 Other terms are sometimes used. The cell types were originally distinguished by Polyak (1941), who called them 'midget' and 'parasol' cells. Perry *et al.* (1984) have called them $P\beta$ and $P\alpha$ cells.

6.8 REFERENCES

- Ahnelt, P. and Kolb, H. (1994) Horizontal cells and cone photoreceptors in primate retina: a Golgi-light microscope study of spectral connectivity. *Journal of Comparative Neurology*, 343, 387–405.
- Barbur, J.L., Harlow, A.J., and Plant, G.T. (1994) Insights into the different exploits of colour in the visual cortex. *Proceedings of the Royal Society of London B*, 258, 327–34.
- Baylor, D.A. (1987) Photoreceptor signals and vision. *Investigative Ophthalmology and Visual Science*, 28, 34–49.
- Baylor, D.A., Nunn, B.J., and Schnapf, J.L. (1987) Spectral sensitivity of cones of the monkey *Macaca fascicularis*. *Journal of Physiology (London)*, 390, 145–60.
- Blakemore, C. and Tobin, E.A. (1972) Lateral inhibition between orientation detectors in the cat's visual cortex. *Experimental Brain Research*, 15, 439–40.
- Blakemore, C. and Vital-Durand, F. (1986) Effects of visual deprivation on the development of the monkey's lateral geniculate nucleus. *Journal of Physiology (London)*, 380, 493–512.
- Boycott, B.B. and Dowling, J.E. (1969) Organization of the primate retina: light microscopy. *Philosophical Transactions of the Royal Society of London B*, 255, 109–94.
- Boycott, B.B. and Wässle, H. (1991) Morphological classification of bipolar cells of the primate retina. *European Journal of Neuroscience*, 3, 1069–88.
- Boynton, R.M. and Baron, W.S. (1975) Sinusoidal flicker characteristics of primate cones in response to heterochromatic stimuli. *Journal of the Optical Society of America*, 65, 1091–100.
- Calkins, D.J., Schein, S.J., Tsukamoto, Y., and Sterling, P. (1994) M and L cones in macaque fovea connect to midget ganglion cells by different numbers of excitatory synapses. *Nature*, 371, 70–2.
- Calkins, D.J. and Sterling, P. (1996) Absence of spectrally specific lateral inputs to midget ganglion cells in primate. *Nature*, 381, 613–15.
- Corbetta, M., Miezin, F.M., Dobmeyer, S., Schulman, G.L., and Petersen, S.E. (1991) Selective and divided attention during visual discriminations of shape, color and speed: functional anatomy by positron emission tomography. *Journal of Neuroscience*, 11, 2383–402.
- Dacey, D.M. (1993) Morphology of a small-field bistratified ganglion cell type in the macaque and human retina. *Visual Neuroscience*, 10, 1081–98.
- Dacey, D.M. (1994) Physiology, morphology and spatial densities of identified ganglion cell types in primate retina. In *Higher-order Processing in the Visual System*. Chichester: Wiley, pp. 12–28.
- Dacey, D.M. (1996) Circuitry for color coding in the primate retina. *Proceedings of the National Academy of Sciences (USA)*, 93, 582–8.
- Dacey, D.M. and Lee, B.B. (1994) The blue-on opponent pathway in the primate retina originates from a distinct bistratified ganglion cell. *Nature*, 367, 731–5.
- Dacey, D.M. and Lee, B.B. (1999) Functional architecture of cone signal pathways in the primate retina. In K.R. Gegenfurtner and L.T. Sharpe (eds), *Color Vision: From Genes to Perception*. Cambridge: Cambridge University Press, pp. 181–202.
- Dacey, D.M., Lee, B.B., Stafford, D.K., Pokorny, J., and Smith, V.C. (1996) Horizontal cells of the

- primate retina: cone specificity without spectral opponency. *Science*, 271, 656–9.
- Dacey, D., Packer, O.S., Diller, L., Brainard, D., Peterson, B., and Lee, B. (2000) Center surround receptive field structure of cone bipolar cells in primate retina. *Vision Research*, 40, 1801–11.
- Daw, N.W. (1984) The psychology and physiology of colour vision. *Trends in Neuroscience*, 7, 330–35.
- de Monasterio, F.M. and Gouras, P. (1975) Functional properties of ganglion cells of the rhesus monkey retina. *Journal of Physiology (London)*, 251, 167–95.
- De Valois, R.L., Abramov, I., and Jacobs, G.H. (1966) Analysis of response patterns of LGN cells. *Journal of the Optical Society of America*, 56, 966–77.
- DePriest, D.D., Lennie, P., and Krauskopf, J. (1991) Slow mechanisms of chromatic adaptation in macaque. *Investigative Ophthalmology and Visual Science*, 32 (Suppl.), 1252.
- Derrington, A.M., Krauskopf, J., and Lennie, P. (1984) Chromatic mechanisms in lateral geniculate nucleus of macaque. *Journal of Physiology (London)*, 357, 241–65.
- Derrington, A.M. and Lennie, P. (1984) Spatial and temporal contrast sensitivities of neurones in lateral geniculate nucleus of macaque. *Journal of Physiology (London)*, 357, 219–40.
- DeYoe, E.A., Felleman, D.J., Van Essen, D.C., and McClendon, E. (1994) Multiple processing streams in occipitotemporal visual cortex. *Nature*, 371, 151–4.
- DeYoe, E.A. and Van Essen, D.C. (1985) Segregation of efferent connections and receptive field properties in visual area V2 of the macaque. *Nature*, 317, 58–61.
- Dowling, J.E. and Boycott, B.B. (1966) Organization of the primate retina: electron microscopy. *Proceedings of the Royal Society of London B*, 166, 80–111.
- Dreher, B., Fukuda, Y., and Rodieck, R.W. (1976) Identification, classification and anatomical segregation of cells with X-like and Y-like properties in the lateral geniculate nucleus of old-world primates. *Journal of Physiology (London)*, 258, 433–52.
- Engel, S., Zhang, X., and Wandell, B. (1997) Color tuning in human visual cortex measured with functional magnetic resonance imaging. *Nature*, 388, 68–71.
- Enroth-Cugell, C. and Robson, J.G. (1966) The contrast sensitivity of retinal ganglion cells of the cat. *Journal of Physiology (London)*, 187, 517–52.
- Estévez, O. and Spekreijse, H. (1974) A spectral compensation method for determining the flicker characteristics of the human colour mechanisms. *Vision Research*, 14, 823–30.
- Famiglietti, E.V., Jr and Kolb, H. (1976) Structural basis for on- and off-center responses in retinal ganglion cells. *Science*, 194, 193–5.
- Felleman, D.J. and Van Essen, D.C. (1991) Distributed hierarchical processing in the primate cerebral cortex. *Cerebral Cortex*, 1, 1–47.
- Gegenfurtner, K.R., Kiper, D.C. and Fenstemaker, S.B. (1996) Processing of color, form, and motion in macaque area V2. *Visual Neuroscience*, 13, 161–72.
- Goodchild, A.K., Chan, T.L. and Grünert, U. (1996) Horizontal cell connections with short wavelength sensitive cones in macaque monkey retina. *Visual Neuroscience*, 13, 833–45.
- Gouras, P. (1968) Identification of cone mechanisms in monkey ganglion cells. *Journal of Physiology (London)*, 199, 533–47.
- Gouras, P. (1974) Opponent-colour cells in different layers of foveal striate cortex. *Journal of Physiology (London)*, 238, 583–602.
- Gouras, P. and Krüger, J. (1979) Response of cells in foveal visual cortex of the monkey to pure color contrast. *Journal of Neurophysiology*, 42, 850–60.
- Gouras, P. and Zrenner, E. (1979) Enhancement of luminance flicker by color-opponent mechanisms. *Science*, 205, 587–9.
- Grünert, U., Greferath, U., Boycott, B.B., and Wässle, H. (1993) Parasol ($P\alpha$) ganglion-cells of the primate fovea: immunocytochemical staining with antibodies against GABAA-receptors. *Vision Research*, 33, 1–14.
- Hawken, M.J. and Parker, A.J. (1984) Contrast sensitivity and orientation selectivity in lamina IV of the striate cortex of old world monkeys. *Experimental Brain Research*, 54, 367–72.
- Hawken, M.J., Shapley, R.M., and Grosof, D.H. (1996) Temporal-frequency selectivity in monkey visual cortex. *Visual Neuroscience*, 13, 477–92.
- Heywood, C.A. and Cowey, A. (1987) On the role of cortical visual area V4 in the discrimination of hue and pattern in macaque monkeys. *Journal of Neuroscience*, 7, 2601–16.
- Heywood, C.A., Gadotti, A., and Cowey, A. (1992) Cortical area V4 and its role in the perception of color. *Journal of Neuroscience*, 12, 4056–65.
- Hood, D.C. and Birch, D.G. (1993) Human cone receptor activity: the leading edge of the a-wave and models of receptor activity. *Visual Neuroscience*, 10, 857–71.
- Hubel, D.H. and Livingstone, M.S. (1987) Segregation of form color and stereopsis in primate area 18. *Journal of Neuroscience*, 7, 3378–415.
- Hubel, D.H. and Wiesel, T.N. (1962) Receptive fields, binocular interactions, and functional architecture in the cat's visual cortex. *Journal of Physiology (London)*, 160, 106–54.
- Hubel, D.H. and Wiesel, T.N. (1968) Receptive fields and functional architecture of monkey striate cortex. *Journal of Physiology (London)*, 195, 215–43.
- Hubel, D.H. and Wiesel, T.N. (1974) Sequence regularity and geometry of orientation columns in the monkey striate cortex. *Journal of Comparative Neurology*, 158, 267–94.
- Hubel, D.H. and Wiesel, T.N. (1977) The Ferrier lecture. Functional architecture of macaque monkey visual cortex. *Proceedings of the Royal Society of London B*, 198, 1–59.
- Kaiser, P.K., Lee, B.B., Martin, P.R., and Valberg, A. (1990) The physiological basis of the minimally distinct border demonstrated in the ganglion cells of the macaque retina. *Journal of Physiology (London)*, 422, 153–83.

- Kaneko, A. (1973) Receptive field organization of bipolar and amacrine cells in the goldfish retina. *Journal of Physiology (London)*, 235, 133–53.
- Kaplan, E. and Shapley, R.M. (1982) X and Y cells in the lateral geniculate nucleus of the macaque monkey. *Journal of Physiology (London)*, 330, 125–44.
- Kelly, D.H. (1961) Visual responses to time-dependent stimuli. II. Single-channel model of the photopic visual system. *Journal of the Optical Society of America*, 51, 747–54.
- Knierim, J.J. and Van Essen, D.C. (1992) Neuronal responses to static texture patterns in area V1 of the alert macaque monkey. *Journal of Neurophysiology*, 67, 961–80.
- Kolb, H., Fernandez, E., Schouten, J., Ahnelt, P., Linberg, K.A., and Fisher, S. K. (1994) Are there three types of horizontal cell in the human retina? *Journal of Comparative Neurology*, 343, 370–86.
- Kouyama, N. and Marshak, D.W. (1992) Bipolar cells specific for blue cones in the macaque retina. *Journal of Neuroscience*, 12, 1233–52.
- Krauskopf, J., Williams, D.R., Mandler, M.B., and Brown, A.M. (1986) Higher order color mechanisms. *Vision Research*, 26, 23–32.
- Kuffler, S.W. and Nicholls, J.G. (1976) *From Neuron to Brain*. Sunderland: Sinauer.
- Lamme, V.A.F. (1995) The neurophysiology of figure-ground segregation in primary visual cortex. *Journal of Neuroscience*, 15, 1605–15.
- Lankheet, M.J.M., van Wezel, R.J.A., and van de Grind, W.A. (1991) Effects of background illumination on cat horizontal cell responses. *Vision Research*, 31, 919–32.
- Lee, B.B. (1996) Receptive field structure in the primate retina. *Vision Research*, 36, 631–44.
- Lee, B.B., Martin, P.R., and Valberg, A. (1989) Nonlinear summation of M- and L-cone inputs to phasic ganglion cells of the macaque. *Journal of Neuroscience*, 9, 1433–42.
- Lee, B.B., Pokorny, J., Smith, V.C., Martin, P.R., and Valberg, A. (1990) Luminance and chromatic modulation sensitivity of macaque ganglion cells and human observers. *Journal of the Optical Society of America A*, 7, 2223–6.
- Lennie, P. (1980) Parallel visual pathways: a review. *Vision Research*, 20, 561–94.
- Lennie, P. (1993) Roles of M and P pathways. In R.M. Shapley and D.M.K. Lam (eds), *Contrast Sensitivity*. Cambridge, MA: MIT Press, pp. 201–13.
- Lennie, P. and D'Zmura, M. (1988) Mechanisms of color vision. *CRC Critical Reviews in Neurobiology*, 3, 333–400.
- Lennie, P., Haake, P.W., and Williams, D.R. (1991) The design of chromatically opponent receptive fields. In M.S. Landy and J.A. Movshon (eds), *Computational Models of Visual Processing*. Cambridge, MA: MIT Press, pp. 71–82.
- Lennie, P., Krauskopf, J., and Sclar, G. (1990) Chromatic mechanisms in striate cortex of macaque. *Journal of Neuroscience*, 10, 649–69.
- Lennie, P., Lankheet, M.J.M., and Krauskopf, J. (1994) Chromatically selective habituation in monkey striate cortex. *Investigative Ophthalmology and Visual Science (Supplement)*, 35, 1662.
- Lennie, P., Pokorny, J., and Smith, V. C. (1993) Luminance. *Journal of the Optical Society of America A*, 10, 1283–93.
- Leventhal, A.G., Thompson, K.G., Liu, D., Zhou, Y., and Ault, S. J. (1995) Concomitant sensitivity to orientation, direction, and color of cells in layers 2, 3, and 4 of monkey striate cortex. *Journal of Neuroscience*, 15, 1808–18.
- Levitt, J.B., Kiper, D.C., and Movshon, J.A. (1994) Receptive fields and functional architecture of macaque V2. *Journal of Neurophysiology*, 71, 2517–42.
- Livingstone, M.S. and Hubel, D.H. (1983) Specificity of cortico-cortical connections in monkey visual system. *Nature*, 304, 531–4.
- Livingstone, M.S. and Hubel, D.H. (1984) Anatomy and physiology of a color system in the primate visual cortex. *Journal of Neuroscience*, 4, 309–56.
- Mariani, A.P. (1984) Bipolar cells in monkey retina selective for the cones likely to be blue-sensitive. *Nature*, 308, 184–6.
- Masland, R.H. (1988) Amacrine cells. *Trends in Neuroscience*, 11, 405–10.
- McMahon, M.J., Lankheet, M.J.M., Lennie, P., and Williams, D. (2000) Fine structure of parvocellular receptive fields in the primate fovea revealed by laser interferometry. *Journal of Neuroscience*, 20, 2043–53.
- Mollon, J.D., Bowmaker, J.K., and Jacobs, G.H. (1984) Variations of colour vision in a New World primate can be explained by a polymorphism of retinal photopigments. *Proceedings of the Royal Society of London B*, 222, 373–99.
- Mollon, J.D., Newcombe, F., Polden, P.G. and Ratcliff, G. (1980) On the presence of three cone mechanisms in a case of total achromatopsia. In G. Verriest (ed.), *Colour Vision Deficiencies*. Bristol: Hilger, pp. 130–5.
- Naka, K.I. (1976) Functional organization of the catfish retina. *Journal of Neurophysiology*, 40, 26–43.
- Nathans, J., Merbs, S.L., Sung, C.H., Weitz, C.J., and Wang, Y. (1992) Molecular genetics of human visual pigments. *Annual Review of Genetics*, 26, 403–24.
- Newsome, W.T., Wurtz, R.H., Dürsteler, M.R., and Mikami, A. (1985) Deficits in visual motion processing following ibotenic acid lesions of the middle temporal visual area. *Journal of Neuroscience*, 5, 825–40.
- Perry, V.H., Öhler, R., and Cowey, A. (1984) Retinal ganglion cells that project to the dorsal lateral geniculate nucleus in the macaque monkey. *Neuroscience*, 12, 1101–23.
- Poggio, G.F. and Talbot, W.H. (1981) Mechanisms of static and dynamic stereopsis in foveal cortex of the rhesus monkey. *Journal of Physiology (London)*, 315, 469–92.
- Polyak, S.L. (1941) *The Retina*. Chicago: University of Chicago Press.
- Polyak, S.L. (1957) *The Vertebrate Visual System*. Chicago: University of Chicago Press.

- Pugh, E.N., Jr and Lamb, T.D. (1993) Amplification and kinetics of the activation steps in phototransduction. *Biochim Biophys Acta*, 1141, 111–49.
- Purpura, K., Tranchina, D., Kaplan, E., and Shapley, R.M. (1990) Light adaptation in the primate retina: analysis of changes in gain and dynamics of monkey retinal ganglion cells. *Visual Neuroscience*, 4, 75–93.
- Reid, R.C. and Shapley, R.M. (1992) Spatial structure of cone inputs to receptive fields in primate lateral geniculate nucleus. *Nature*, 356, 716–18.
- Robson, J.G. (1966) Spatial and temporal contrast sensitivity functions of the visual system. *Journal of the Optical Society of America*, 56, 1141–2.
- Rodieck, R.W. (1965) Quantitative analysis of cat retinal ganglion cell response to visual stimuli. *Vision Research*, 5, 583–601.
- Rodieck, R.W. (1991) Which cells code for color? In A. Valberg and B.B. Lee (eds), *From Pigments to Perception*. New York: Plenum Press, pp. 83–94.
- Rodieck, R.W. (1998) *The First Steps in Seeing*. Sunderland: Sinauer Associates.
- Rodieck, R.W., Brening, R.K., and Watanabe, M. (1993) The origin of parallel visual pathways. In R. Shapley and D. M.-K. Lam (eds), *Contrast Sensitivity*. Cambridge, MA: MIT Press, pp. 117–47.
- Roe, A.W. and Ts'o, D.Y. (1995) Visual topography in primate V2: multiple representation across functional stripes. *Journal of Neuroscience*, 15, 3689–715.
- Schaeffel, F., Bartmann, M., Hagel, G., and Zrenner, E. (1995) Studies on the role of the retinal dopamine/melatonin system in experimental refractive error in chickens. *Vision Research*, 35, 1247–64.
- Schein, S.J. and Desimone, R. (1990) Spectral properties of V4 neurons in the macaque. *Journal of Neuroscience*, 10, 3369–89.
- Schiller, P.H. and Colby, C.L. (1983) The responses of single cells in the lateral geniculate nucleus of the rhesus monkey to color and luminance contrast. *Vision Research*, 23, 1631–41.
- Schnapf, J.L., Nunn, B.J., Meister, M., and Baylor, D.A. (1990) Visual transduction in cones of the monkey *Macaca fascicularis*. *Journal of Physiology (London)*, 427, 681–713.
- Sherman, S.M. (1996) Dual response modes in lateral geniculate neurons: mechanisms and functions. *Visual Neuroscience*, 13, 205–13.
- Shipp, S. and Zeki, S.M. (1985) Segregation of pathways leading from area V2 to areas V4 and V5 of macaque monkey visual cortex. *Nature*, 315, 322–5.
- Smith, V.C., Lee, B.B., Pokorny, J., Martin, P.R., and Valberg, A. (1992) Responses of macaque ganglion cells to the relative phase of heterochromatically modulated lights. *Journal of Physiology (London)*, 458, 191–221.
- Sparks, D.L. and Nelson, J.S. (1987) Sensory and motor maps in the mammalian superior colliculus. *Trends in Neuroscience*, 10, 312–17.
- Stell, W.K., Ishida, A.T., and Lightfoot, D.O. (1977) Structural basis for on- and off-center responses in retinal bipolar cells. *Science*, 198, 1269–71.
- Sterling, P., Freed, M.A., and Smith, R.G. (1988) Architecture of rod and cone circuits to the ON-beta ganglion cell. *Journal of Neuroscience*, 8, 623–42.
- Stiles, W.S. (1939) The directional sensitivity of the retina and the spectral sensitivities of the rods and cones. *Proceedings of the Royal Society of London B*, 127, 64–105.
- Stiles, W.S. and Burch, J.M. (1959) NPL colour-matching investigation: final report. *Optica Acta*, 6, 1–26.
- Thorell, L.G., De Valois, R.L. and Albrecht, D.G. (1984) Spatial mapping of monkey V1 cells with pure color and luminance stimuli. *Vision Research*, 24, 751–69.
- Tootell, R.B.H., Silverman, M.S., De Valois, R.L., and Jacobs, G.H. (1983) Functional organization of the second cortical visual area (V2) in the primate. *Science*, 220, 737–9.
- Torre, V., Ashmore, J.F., Lamb, T.D., and Menini, A. (1995) Transduction and adaptation in sensory receptor cells. *Journal of Neuroscience*, 15, 7757–68.
- Ts'o, D.Y. and Gilbert, C.D. (1988) The organization of chromatic and spatial interactions in the primate striate cortex. *Journal of Neuroscience*, 8, 1712–27.
- Valberg, A., Lee, B.B., and Tigwell, D.A. (1986) Neurones with strong inhibitory S-cone inputs in the macaque lateral geniculate nucleus. *Vision Research*, 26, 1061–4.
- Valeton, M.J. and van Norren, D. (1983) Light adaptation of primate cones: an analysis based on extracellular data. *Vision Research*, 23, 1539–47.
- Vautin, R.G. and Dow, B.M. (1985) Color cell groups in foveal striate cortex of the behaving macaque. *Journal of Neurophysiology*, 54, 273–92.
- Verweij, J., Dacey, D.M., Peterson, B.B., and Buck, S.L. (1999) Sensitivity and dynamics of rod signals in H1 horizontal cells of the macaque monkey retina. *Vision Research*, 39, 3662–72.
- Victor, J.D., Maiese, K., Shapley, R., Sidtis, J., and Gazzaniga, M.S. (1989) Acquired central dyschromatopsia: analysis of a case with preservation of color discrimination. *Clinical Vision Sciences*, 4, 183–96.
- Walraven, J., Enroth-Cugell, C., Hood, D.C., MacLeod, D.I.A., and Schnapf, J. (1989) The control of visual sensitivity: receptor and postreceptor processes. In L. Spillmann and J. Werner (eds), *Visual Perception: The Neurophysiological Foundations*. New York: Academic Press, pp. 53–101.
- Wässle, H. and Boycott, B.B. (1991) Functional architecture of the mammalian retina. *Physiological Reviews*, 71, 447–80.
- Wässle, H., Boycott, B.B., and Röhrenbeck, J. (1989) Horizontal cells in the monkey retina: cone connections and dendritic network. *European Journal of Neuroscience*, 1, 421–35.
- Wässle, H., Grünert, U., Martin, P.R., and Boycott, B.B. (1994) Immunocytochemical characterization and spatial distribution of midget bipolar cells in the macaque monkey retina. *Vision Research*, 34, 561–79.
- Watanabe, M. and Rodieck, R.W. (1989) Parasol and midget ganglion cells of the primate retina. *Journal of Comparative Neurology*, 289, 434–54.

- Webster, M.A. and Mollon, J.D. (1991) Changes in colour appearance following post-receptor adaptation. *Nature*, 349, 235–8.
- Wiesel, T.N. and Hubel, D.H. (1966) Spatial and chromatic interactions in the lateral geniculate body of the rhesus monkey. *Journal of Neurophysiology*, 29, 1115–56.
- Williams, D.R. and Collier, R.J. (1983) Consequences of spatial sampling by a human photoreceptor mosaic. *Science*, 221, 385–7.
- Wisowaty, J.J. and Boynton, R.M. (1980) Temporal modulation sensitivity of the blue mechanism: measurements made without chromatic adaptation. *Vision Research*, 20, 895–909.
- Yeh, T., Lee, B.B., and Kremers, J. (1996) The time course of adaptation in macaque retinal ganglion cells. *Vision Research*, 36, 913–31.
- Zeki, S.M. (1973) Colour coding in rhesus monkey prestriate cortex. *Brain Research*, 53, 422–7.
- Zeki, S.M. (1974) Functional organization of a visual area in the posterior bank of the superior temporal sulcus of the rhesus monkey. *Journal of Physiology (London)*, 236, 549–73.
- Zeki, S.M. (1977) Colour coding in the superior temporal sulcus of rhesus monkey visual cortex. *Proceedings of the Royal Society of London B*, 197, 195–223.
- Zeki, S.M. (1983) Colour coding in the cerebral cortex: the responses of wavelength-selective and colour-coded cells in monkey visual cortex to changes in wavelength composition. *Neuroscience*, 9, 767–81.
- Zeki, S.M. (1990) A century of cerebral achromatopsia. *Brain*, 113, 1721–77.
- Zeki, S.M., Watson, J.D.G., Lueck, C.J., Friston, K.J., Kennard, C., and Frackowiak, R.S.J. (1991) A direct demonstration of functional specialization in human visual cortex. *Journal of Neuroscience*, 11, 641–9.