Casagrande, V. **A.** and J.M. Ichida (2002) The visual cortex. In *Physiology* of *the eye*. F. H. Adler, C.V. Mosby Co, St. Louis, pp. 669-685.

CHAPTER 29

THE PRIMARY VISUAL CORTEX

VIVIEN A. CASAGRANDE AND JENNIFER M. ICHIDA

OVERVIEW. PRIMARY VISUAL CORTEX CONSTRUCTS LOCAL IMAGE FEATURES

The visual system is designed to provide a description of the location and identification of objects that have survival value to the species. These descriptions must be made accurately not in a static world but in a dynamic one in which gaze is constantly shifting and in which objects move. Beginning in the retina the visual system selects what is needed to accomplish this goal. The retina contributes to this selection process by throwing away information about absolute light intensity, emphasizing local image contours, and compressing the visual signal information into a manageable size during a manageable time period to be transmitted to the lateral geniculate nucleus (LGN). The LGN contributes by regulating the flow of visual signals so that only the most relevant signals reach cortex. Primary visual cortex (also called *V1* or *striate cortex),* as described in this section, contributes by coding important aspects of local image features, 'including their size, orientation, local direction of movement, and binocular disparity. All of these local descriptions of stimulus quality are critical for the more global and complex identification of objects ("what") and spatial relations ("where") that will take place in extrastriate areas. At one level, one can think of V1 as an area where information provided by the separate channels within the LGN is combined in different ways before it is sent to extrastriate visual areas for further processing. To do its job, V1 must solve the geometry puzzle of representing all stimulus qualities necessary for the subsequent steps of analyses within the different parts of the visual field map. V1 accomplishes this goal by a division of labor between different layers and different iterated modules within each layer. The following sections describe how visual signals are put together in V1 by first providing a review of the gross anatomy and laminar structure of V1 and illustrating how the visual world is mapped onto the layers. The next two subsections delineate the connections, cell types, and basic receptive field properties of V1 cells. Later in this chapter we consider how microcircuits within V1 have been proposed to work together and how parallel inputs to V1 relate to the output channels that are constructed in V1. The final section of this chapter summarizes key points.

OVERVIEW OF CORTICAL ORGANIZATION: GENERAL ROAD MAP

The primary visual cortex in humans is an area the size of a large index card, is about 2 mm thick, and, is located within the occipital lobe extending from the posterior pole along the medial wall of the hemisphere[16] (Figure **29-1).** (Also see Figure 28-1.) Like the rest of the cerebral cortex, primary visual cortex contains six principle layers. This area is often called *striate cortex* in recognition of its original identification by the Italian medical student Francesco Gennari more than 200 years ago. Gennari observed that at the posterior pole, the cortex contains a striking white stripe visible in both raw and fixed brain tissue, which is known as the *stria* of *Gennari.* The stria of Gennari actually marks one heavily myelinated layer in the middle of the gray matter of this area of cortex. Primary visual cortex also is referred to by several other names, including, most commonly, *area* 17 of

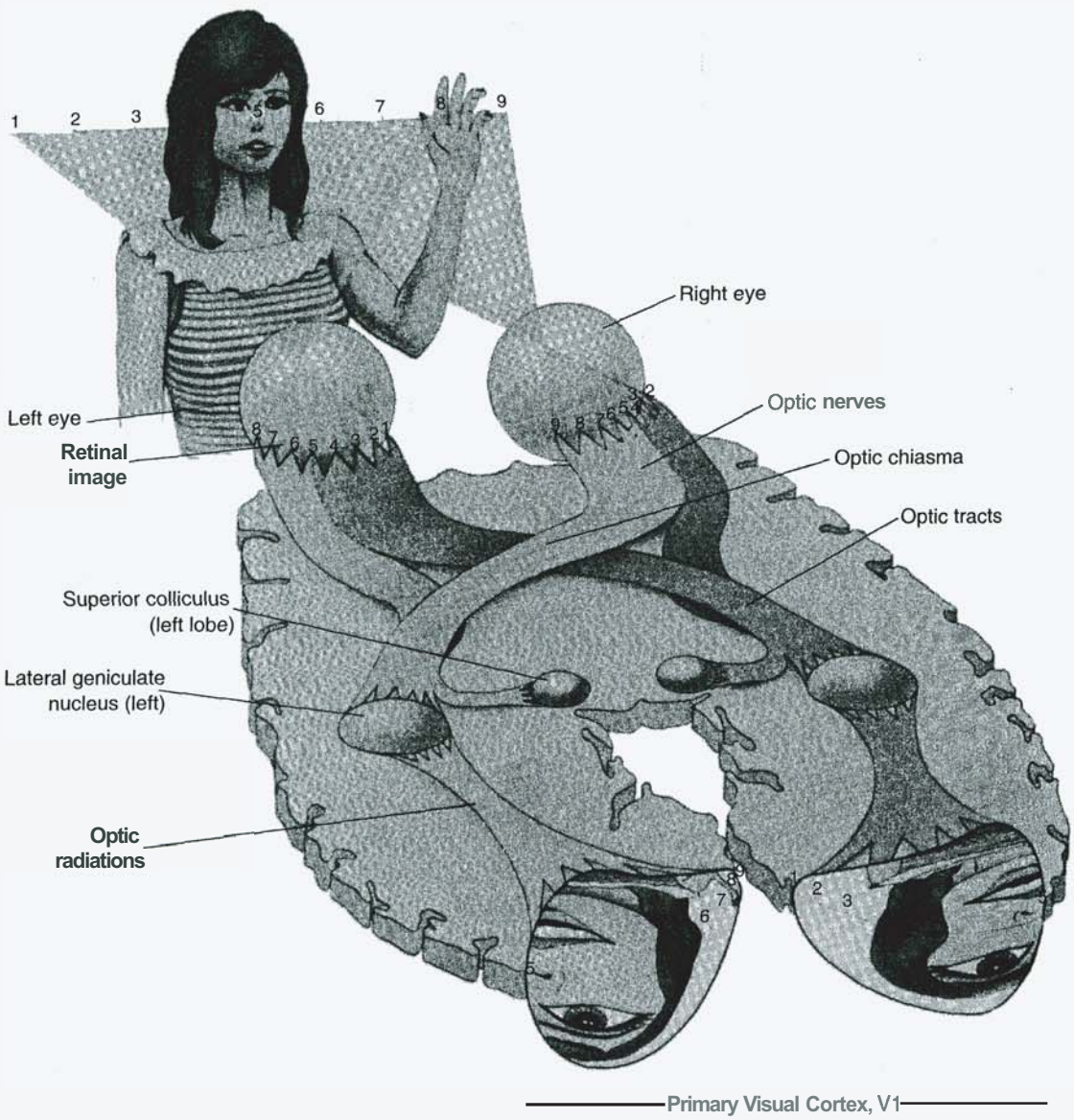


FIGURE 29-1 Schematic illustration of two important visual pathways, one from the eyes to V1 and one from the eyes to the superior colliculus. The messages in the first pathway begin in the retina of each eye, travel from each eye via an optic nerve, pass through structures called the ***optic chiasm*** and the ***lateral geniculate nuclei,*** proceed on their way via the optic radiations, and finally arrive in a region of the cerebrum at the back of the head called the ***primary visual cortex*** or *V1.* (From Frisby J P ***Seeing: illusion brain and mind,*** New York, **1979,** Oxford University Press.)

Brodmann or ***area V1***. For convenience, we use the latter term for the remainder of this section.

As discussed in Chapter ***26,*** damage to V1 results in a hole (scotoma) or blind spot in one visual hemifield. Also, as in the LGN, the location of damage to V1 can be predicted based on the topographic map of the opposite visual hemifield that is known to exist in this region in all mammalian species. In humans, detailed knowledge about the manner in which the visual field is mapped onto V1 has been obtained from a variety of sources, including clinical assessments of damage, results of electrical stimulation, and more recently, functional maps using magnetic resonance imaging (MRI) and positron emission tomography (PET).[11,15,20] Knowledge about the retinotopic organization of V1 in humans is relevant not only to the clinical evaluation of damage but also to research efforts designed to develop visual prosthetic devices involving visual cortical electrical stimulation for individuals with incurable retinal

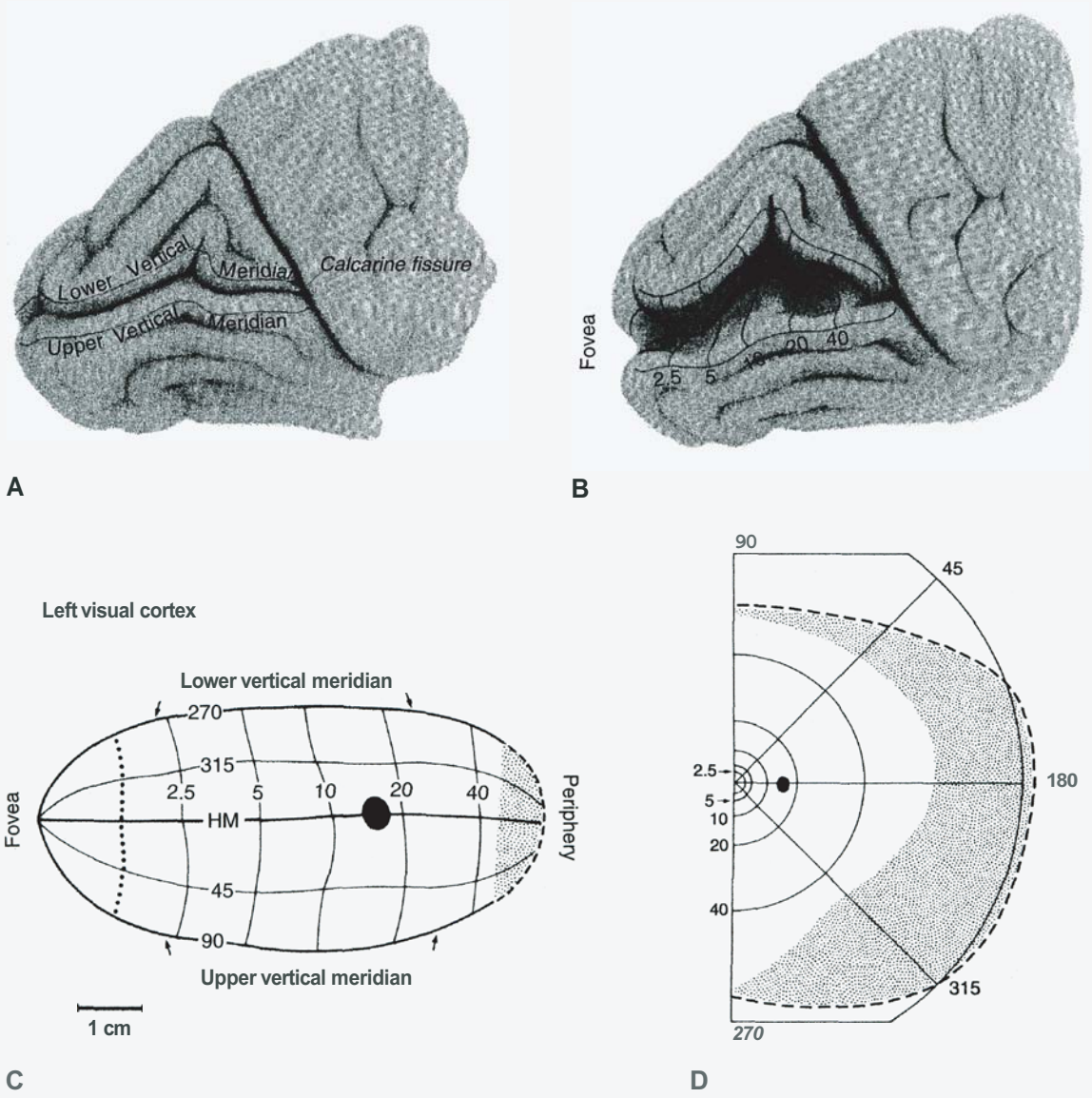


FIGURE 29-2 **A,** Left occipital lobe showing the location of V1 within the calcarine fissure. **B,** View of V1 after opening the lips of the calcarine fissure. The lines indicate the coordinates of the visual field map. The representation of the horizontal meridian runs approximately along the base of the calcarine fissure. The vertical lines mark the isoeccentricity contours from 2.5 to 40 degrees. V1 wraps around the occipital pole to extend about 1 cm onto the lateral convexity, where the fovea is represented. ***C,*** Schematic map showing the projection of the right visual hemifield on the left visual cortex by transposing the map illustrated in B onto a flat surface. The row of dots indicates approximately where V1 folds around the occipital tip. The black ovals mark the region of V1 corresponding to the contralateral eye's blind spot. It is important to note that considerable variation occurs among individuals in the exact dimensions and location of V1. *HM,* Horizontal meridian. **D,** Right visual hemifield plotted with a Goldmann perimeter. The stippled region corresponds to the monocular temporal crescent, which is mapped within the most anterior 8% to 10% of V1. (From Horton JC, Hoyt WF: *Arch Ophthalmol* 109:816, 1991.)

diseases. All of the methods used to understand the map of the visual field in V1 are in general agreement, showing, as illustrated in Figure 29-2, that the fovea is represented in the occipital pole and the far periphery is represented in the anterior margin of the calcarine fissure with the upper and lower visual fields being mapped onto the lower (lingual gyrus) and upper (cuneus gyrus) banks, respectively.[20] As in the LGN, the visual field map in human cortex is distorted such that the representation of central vision

occupies much more tissue than does peripheral vision. Whether or not the foveal representation in V1 is expanded over what would be predicted simply by assigning each retinal ganglion cell or LGN cell the same amount of cortical tissue has been the subject of considerable debate. Some investigators[3] have argued that foveal ganglion cells are allocated between three to six times more space than are peripheral ganglion cells; others[43] argue that there is no further magnification over that predicted by ganglion cell number alone. One explanation for these differences of opinion is that the proportion of cortex devoted to central vision has been shown to be highly individually variable at least in macaque monkeys.[41] The latter finding suggests that the relative amount of tissue devoted to the fovea could, indeed, be magnified at the cortical level relative to the retina in some individuals but not in others.

LAYERS AND CONNECTIONS OF V1: INPUTS, OUTPUTS, AND GENERAL WIRING

As in other cortical areas, V1 has six main layers that can be identified in a cell stain as shown in Figure 29-3. The layers and sublayers of V1 have been named in different ways depending on investigator interpretation. The most common laminar scheme is the one adopted by Brodmann,[6] whose designations for the V1 layers are shown in parenthesis in Figure 29-3. The key difference between Brodmann's laminar scheme and that of others

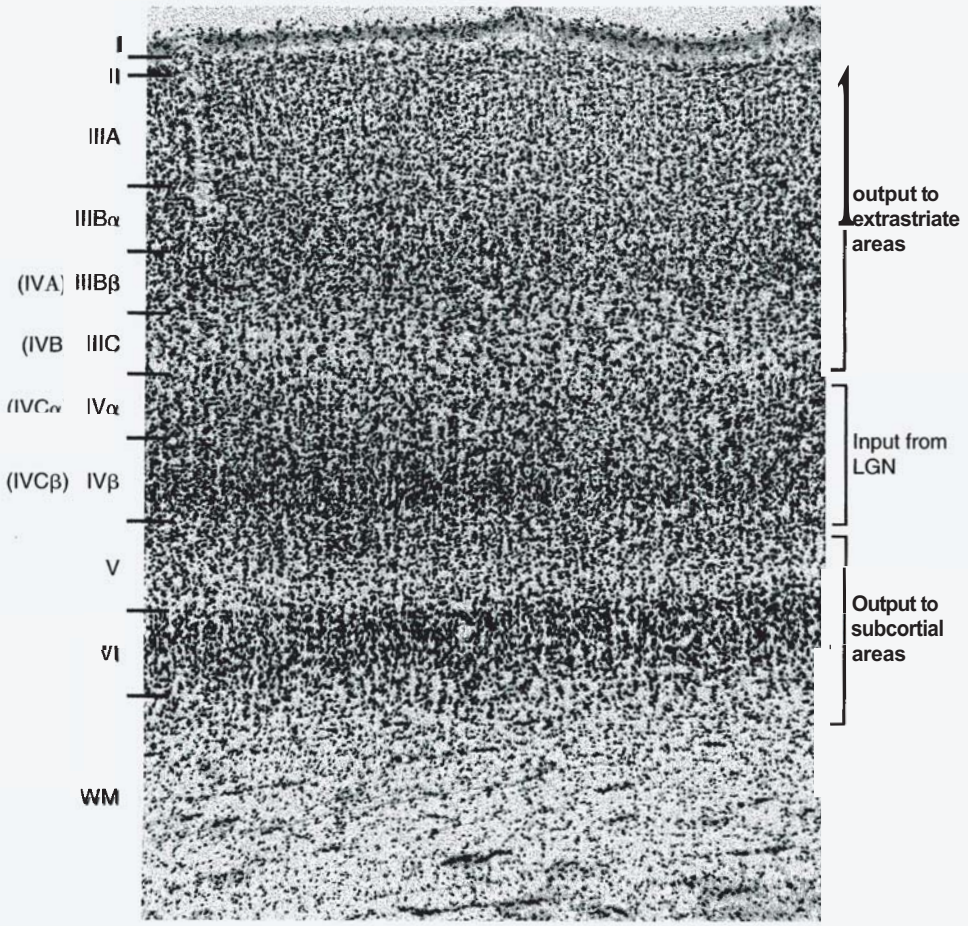


FIGURE 29-3 Nissl-stained section through V1 of macaque monkey. The layers are numbered according to a modification of Hassler's nomenclature with Brodmann's nomenclature in parentheses (see text for details). As indicated by the brackets, layer IV receives the main input from the lateral geniculate nucleus (*LGN*), the layers above IV send projections to other cortical areas, and the layers below IV send projections to subcortical areas (see text for details). *WM*, White matter.

concerns what is included as part of layer IV. Brodmann's definition of layer IV included subdivisions that are interpreted by others as part of layer III (for review, see reference 9). The latter scheme, originally suggested by Hässler,[18] is more in keeping with the laminar schemes used in all other areas of sensory cortex. Hence, as in other cortical areas, the bulk of the input from the thalamus (LGN) to V1 terminates within layer IV (IVC of Brodmann); the main output to other cortical areas exits from the layers above layer IV, mainly layer III (IVB, IVA, and III of Brodmann); and the main output to subcortical areas exits from layers V and VI (Figure 29-3).

Lateral Geniculate Nucleus Inputs

Studies done in anesthetized monkeys have shown that activation of V1 neurons depends completely on input from the LGN because if the LGN is inactivated, visually evoked potentials in V1 are blocked.[33] As discussed in the last section, LGN axons carrying signals from the left and right eyes and from koniocellular (K), magnocellular (M), and parvocellular (P) layers remain segregated at the first synapse in V1 in primates. As shown in Figure 28-6, K, M, and **P** axons terminate within layers IVα, IVβ, and layers III and I, respectively. In some primates, such as macaque monkeys, the P layers send additional input to layer IIIBβ (IVA of Brodmann), but data suggest that this input does not exist in other primates, such as humans.[19] KLGN axons are somewhat different in their termination pattern from M and P axons in that they terminate within segregated patches of high cytochrome oxidase (CO) density known as the CO *blobs* located within layer IIIB, as well as within layer I.

In addition, input arriving from left and right eye LGN layers remains segregated in the form of *ocular dominance columns* both in humans and in other primates, although the degree of segregation varies greatly between primate species.[13,14] Figure 29-4 shows the complete pattern of ocular dominance columns on a flattened reconstruction through layer IV of V1 in a macaque monkey. In this case the pattern of eye input was revealed by using a histochemical stain to show the downregulation of CO mitochondrial enzyme activity associated with the loss of one eye. CO staining is normally dark in all layers of V1 that receive input from the LGN; therefore loss of one eye results in lighter staining in areas connected to that eye. The result is shown in Figure 29-4 in tangential sections through layer IV of V1 following flattening of the tissue. Black regions depict CO-dense areas in cortex. As can be seen in Figure 29-4, ocular input is segregated into bands within V1 that are less regular in the portions of V1 representing central vision.

The fact that input from the left and right eye remains segregated at the first synapse in V1 raises an interesting question concerning the retinotoyic map. Recall that in the LGN, each layer contains a continuous map of the opposite visual hemifield. This means that in the cortex, there must be *two* topographic maps, one for each eye, within the *same* layer, at least at the first synapse from the LGN. This is exactly what was found in layer IV of the macaque monkey using detailed electrophysiologic recordings.[24] Tangential recordings made

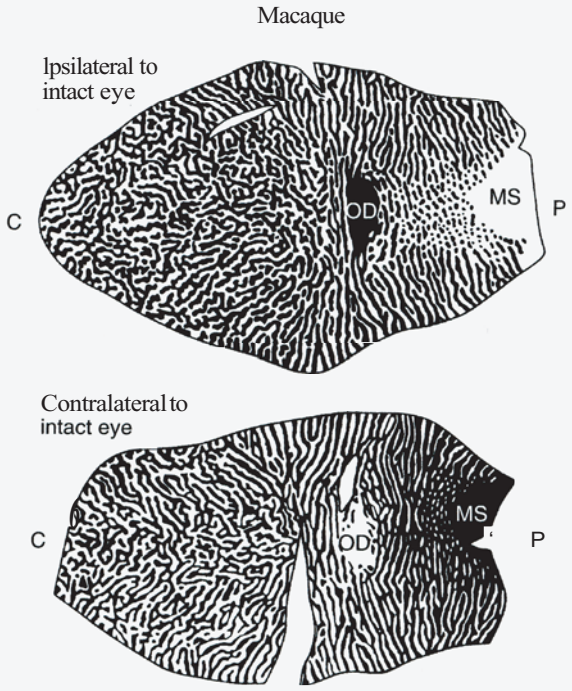


FIGURE 29-4 Distributions of ocular dominance columns in a macaque monkey ipsilateral and contralateral to the intact eye. These drawings were made from photographic montages. Black regions depict cytochrome oxidase (CO)–dense reactivity related to the intact eye. The ocular dominance patterns in the two hemispheres are highly similar, although not identical. Splits that occurred during the flattening process are shown. The visual field is represented from central (C) to the peripheral (P) as indicated. The representation of the optic disc *(OD)* of the nasal retina is centered 17 degrees from the fovea. The unbanded segments to the right correspond to the monocular temporal segment *(MS)* of the visual field. (Scale bar = 5 mm.) (From Florence SL, Kaas JH: *Vis Neurosci* 8:449, 1992.)

within layer IV revealed that the segments of the visual field mapped in one ocular dominance column for one eye were also represented in the adjacent column that received input from the other eye. As shown later, information from the two eyes and from K, M, and P cells is combined in different ways within other layers of V1 so that most cells in V1 receive a combination of many extrinsic and intrinsic inputs.

Other Inputs to V1

Besides the LGN, V1 receives a variety of other modulatory inputs both from subcortical and cortical areas. These inputs include serotonergic, noradrenergic, and cholinergic inputs from the brainstem and basal forebrain nuclei, respectively.[26] The latter inputs appear to show differences in density within the V1 layers but show a much less specific pattern of innervation than do LGN inputs. Other input sources include the intralaminar nuclei of the thalamus and pulvinar, both of which send broad projections most heavily to layer I of V1. In addition, there are retinotopically more specific sources of input to V1, many of which also receive projections from V1, including the claustrum and visual areas 2, 3, 4, and 5 (V4 and V5 are also commonly referred to as areas *DL* and *MT*).[9,31] Many higher-order visual areas in the temporal and parietal lobes that do not receive direct projections from V1 nevertheless send axons to V1. With the exception of the claustrum, whose axons also terminate within layer IV of V1, all of the other extrastriate visual inputs to V1 terminate outside of layer IV.

So why are there so many other inputs to V1 if the main drive comes from the LGN? As described earlier with the LGN, the numerous nongeniculate inputs to V1 regulate which visual signals will be transmitted to higher-order visual areas. An example of the impact that these non-LGN connections to V1 can have has been demonstrated using fMRI methods. With use of these imaging methods in humans, it has been shown that topographic regions of V1 can be activated simply by asking normal subjects to imagine (with eyes closed) visual objects within particular areas of the visual field (i.e., in the *absence* of any direct stimulus to the retina).[10] These findings argue that non-LGN inputs can have a strong effect on activity in V1.

Output Pathways from V1

As mentioned previously, many cells in the layers that lie outside of layer IV (IVC of Brodmann) send axons to other areas of the brain (for review, see reference 9). The lower layers, V and VI, send axons back to the thalamus and to the midbrain and pons. Layer VI is unique in that cells in this layer provide direct feedback to the LGN and, as discussed in Chapter 28, provide a major pathway for V1 to regulate its own input. Cells in layer VI also send axons to the visual sectors of the thalamic reticular nucleus (see Chapter 28) and the claustrum. Cells in layer V provide the major driving input to many cells in the pulvinar nucleus of the thalamus in monkeys; the pulvinar in turn provides input to a number of extrastriate areas that also feed signals back to V1. In addition, cells in layer V send a major projection to the superficial layers of the superior colliculus and other midbrain areas such as the pretectum, as well as nuclei in the pons that are concerned with eye movements. Thus V1 is in a position to inform these structures of its activities and be informed by them indirectly through connections with the LGN that were discussed earlier or through feedback from extrastriate areas.

As listed earlier, the superficial cortical layers of V1 provide output connections to a number of extrastriate cortical areas (Figure 29-5). These connections emerge from different layers or modules within layers, suggesting that they carry different messages. In macaque monkeys the largest output connection is to visual area 2 (V2). Connections to V2 emerge from three populations of cells. Cells within the CO-rich blobs of layer IIIA and IIIB send a major input to thin CO-rich bands in V2 (Figure 29-6), and the cells between the CO blobs (the interblobs) send projections to CO pale bands of cells (the interbands) in V2.[28] Finally, cells in layer IIIC (also called the *stria of Gennari* or *layer IVB of Brodmann)* send axons to the thick CO bands in V2.

In addition to these connections, there are direct connections from layer IIIB to the dorsal medial visual area (DM) and from patches of cells that lie below the CO blobs in layer IIIC directly to extrastriate area MT.[5] Other output connections of layer III of V1 include projections to areas V3 and V4 (for review, see reference 9).

CELL TYPES AND RECEPTIVE FIELD PROPERTIES: HOW IS V1 DIFFERENT FROM THE LGN?

Examination of the receptive field properties of V1 neurons suggests that visual signals are transformed from those seen in the retina and LGN. In other words, new properties emerge in V1, such as

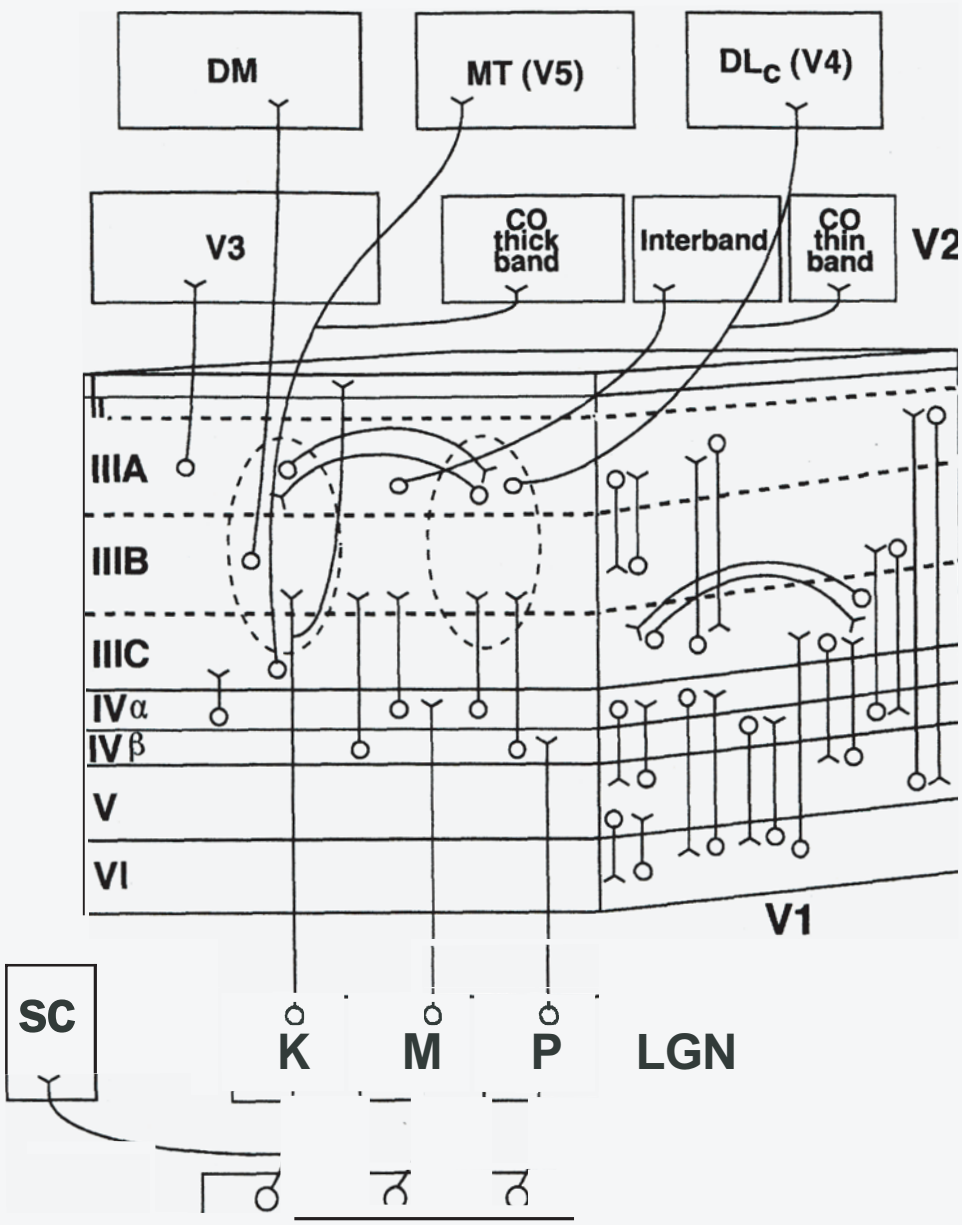


FIGURE 29-5 Schematic indicating some of the main intrinsic and extrinsic connections of VI in primates, as described in the text. No effort is made to define the strength of connections or to indicate true axon collaterals or species-unique features. Feedback connections to V1 and the lateral geniculate nucleus (*LGN*), as well as connections between extrastriate areas, are not shown. The major input to VI is from the LGN, which arrives via three pathways: the koniocellular (*K*), magnocellular (*M*), and parvocellular (P) pathways. The retina also projects to other targets, one of which, the superior colliculus (SC), is shown. Within VI, cell layers are heavily interconnected, not only by some of the axonal Pathways shown but also by dendritic arbors (not shown). The main ipsilateral connections to extrastriate cortex exit from layer 111. In layer IIIA, the cells within cytochrome oxidase (*CO*)–rich blobs, indicated by dotted ovals, and CO-poor interblobs send information to different target cells within bands in V2. In layer IIIB, cells within the CO blobs send projections to the dorsomedial area (*DM*). Cells that lie under the CO blobs in layer IIIC send information to the middle temporal area (*MT*), also called V5. Although the connection between V1 and V3 has been documented, it is not known from which layer/module this connection arises. DL_c (*V4*), Dorsolateral caudal. (Modified from Casagrande VA, Kaas JH: The afferent, intrinsic and efferent connections of primary visual cortex in primates. In Peters **A,** Rockland KS [eds]: *Cerebral cortex,* vol 10, New York, 1994, Plenum Press.)

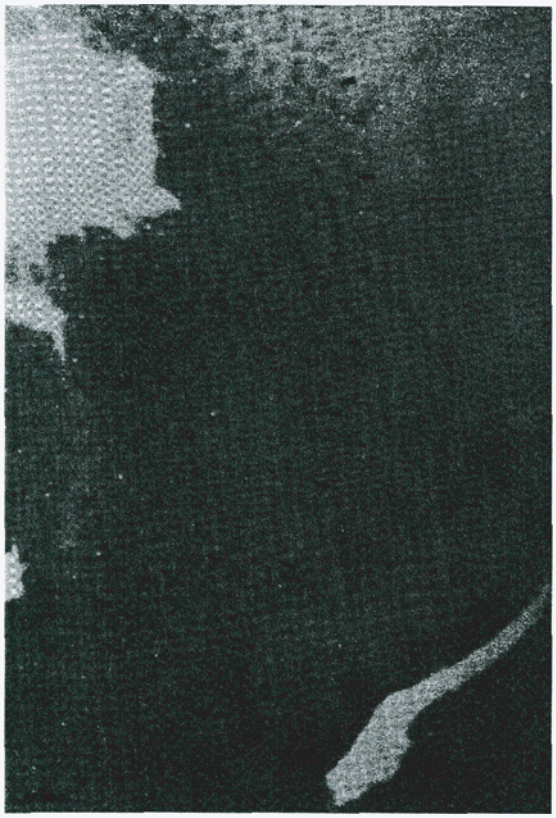


FIGURE 29-6 Tangential section through layer III of squirrel monkey V1. This section has been stained with cytochrome oxidase (CO) to reveal the CO blobs in V1 and the CO stripes in V2 (see text for details). The boundary between V1 and V2 is indicated by arrowheads. (Scale bar = 500 μm.) (From Lachica EA, Beck PD, Casagrande VA: J *Comp Neurol* 329:163, *1993.)*

binocularity and sensitivity to stimulus orientation and movement direction. At the same time, V1 cells retain the retinotopic selectivity of their LGN cell inputs, although receptive fields are a bit larger.

In the late 1950s and early 1960s, Hubel and Wiesel[22,23] began to characterize the properties of V1 receptive fields in cats and monkeys using a variety of patterns, including line segments and spots of light displayed at discrete locations on a screen. In these seminal studies, they showed that V1 cells could be subdivided on the basis of their responses to light. Hubel and Wiesel[25] proposed that the cell types in V1 were arranged in serial order of complexity, beginning with those that receive input directly from the LGN, which they termed *simple* cells. They originally proposed that simple cell responses could best be explained by assuming that the receptive fields of a number of LGN cells were aligned as shown in Figure 29-7 (see also reference 42). Simple cells differ from LGN and retinal ganglion cells, many of which have more or less circularly symmetric receptive fields. Simple cells have elongated receptive fields with adjacent excitatory and inhibitory regions. Hubel and Wiesel called these cells *simple* because it appeared that the responses of these cells to complex shapes could be predicted by linear summation of their responses to individual spots of light.

As can be appreciated by examining Figure 29-7, simple cells can give different responses depending on the spatial arrangement of their inhibitory and excitatory regions. For example, although all the cells shown in Figure 29-7 respond to the same orientation, cells with longer receptive fields, such as shown in Figure 29-7, *C,* will respond to a narrower range of orientations than those with shorter receptive fields, as shown in Figure 29-7, A. As this figure also illustrates, the receptive fields of simple cells require that LGN ON- and OFF-center cells are aligned because it is the center responses of these cells that dominate the subfield response of simple cells within V1. Hubel and Wiesel also identified other cell classes with more complex response properties. These cells, generally called *complex cells,* are different from simple cells in that their responses to stimuli cannot be predicted on the basis of linear addition of the cell's response to spots of light presented in different parts of the receptive field; complex cells do not have discrete regions of excitation and inhibition. Instead, complex cells respond to preferred orientations like simple cells, but complex cells respond equally well to a preferred stimulus anywhere in their receptive field" (Figure 29-8).

A special type of V1 cell, referred to as an *end-stopped cell,* responds only if the correctly oriented stimulus is of appropriate length. Extending the length of a bar beyond the field into an inhibitory zone of an end-stopped cell diminishes the cell's responses, suggesting that these cells may signal more complex shapes. Hubel and Wiesel originally proposed that the receptive fields of each cell class (namely, LGN, simple, complex, and end-stopped cells) built on the properties of their predecessors in serial order. Scientists know now that connections are more complex, that complex cells can receive input directly from the LGN, and that end-stopped cells can either be simple or complex cells.

Other receptive field properties that emerge within area V1 are direction selectivity and binocularity. Although in some mammals, such as rabbits,

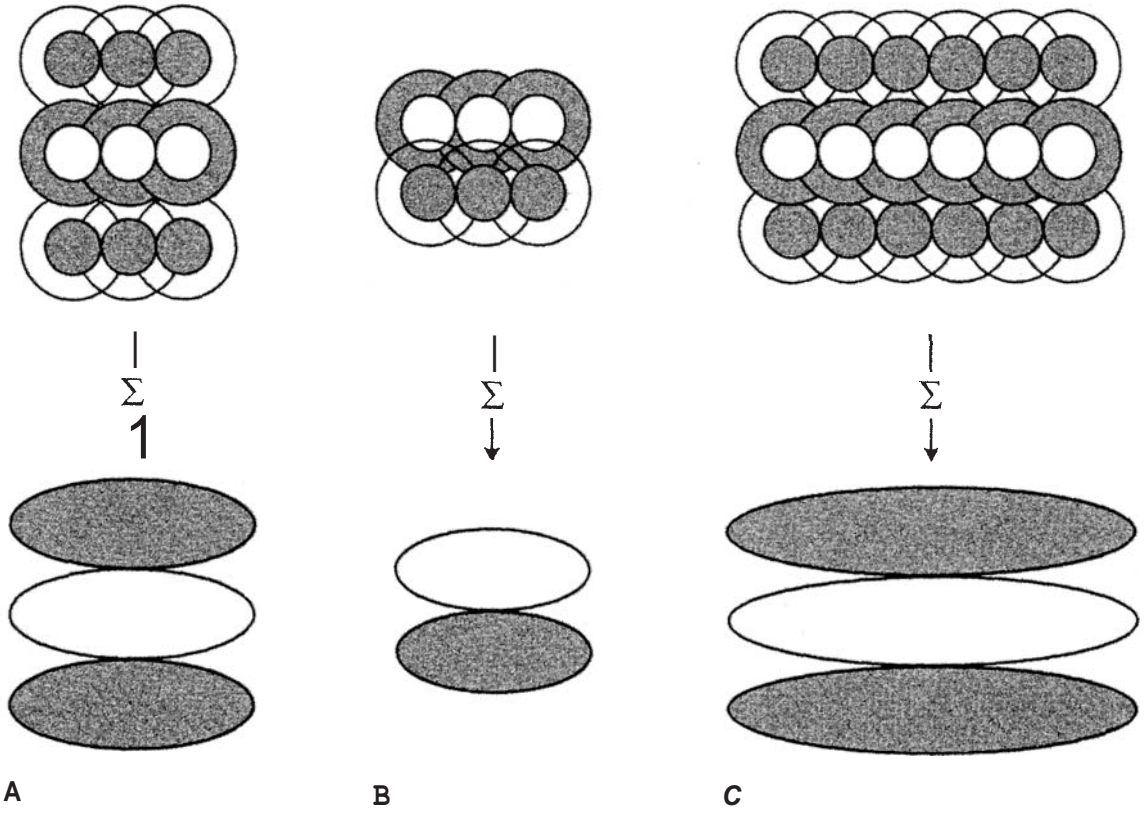


FIGURE 29-7 Orientation-selective receptive fields can be created by summing the responses of neurons with nonoriented, circularly symmetric receptive fields. The receptive fields of three hypothetical neurons are shown. Each hypothetical receptive field has adjacent excitatory and inhibitory regions. **A** comparison of **A, B,** and **C** illustrates that the degree of orientation selectivity can vary depending on the number of neurons combined along the main axis. (From Wandell B: *Foundations of vision,* Sunderland, Mass, 1995, Sinauer Associates.)

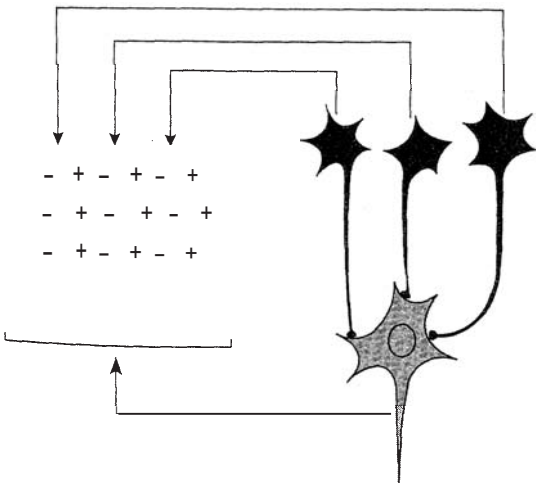


FIGURE 29-8 The complex cell in this diagram receives input from three simple cells. Each simple cell responds optimally to a vertically oriented edge of light. The receptive fields are scattered in overlapping fashion throughout the rectangle, which represents the receptive field of the complex cell. An edge falling anywhere within the rectangle evokes a response from a few simple cells; this in turn evokes a response in the complex cell. Because there is adaptation at the synapses, only a moving stimulus will keep up a steady bombardment of the complex cell. (From Hubel DH: *Eye, bruin and vision,* New York, 1988, Scientific American Library.)

direction selectivity is a characteristic of many retinal ganglion cells, in primates there are very few retinal ganglion and LGN cells that exhibit this property.[2] In V1 there are many cells that respond best to one direction of motion of a stimulus. One explanation for how this property is constructed is that there is a temporal delay between two adjacent connected cortical neurons with the same orientation selectivity, such that one cell either enhances or suppresses the response of the other.

In addition to orientation and direction selectivity, many cortical neurons in cats and monkeys are binocular (i.e., receive signals from both eyes). V1 is the first place where visual information from the two eyes is brought together (Figure 29-9). In binocular V1 neurons, there exists a range of cells, with many responding somewhat more to one eye than to the other. The bias in ocular response is such that ocular preference within a column extending from layer I to layer VI tends to reflect the preference of cells in layer IV within that column. This is because cortical cells tend to be connected preferentially in vertical columns. Binocular cells with slightly displaced monocular fields (i.e., cells with a disparity between the receptive fields of the left and right eye) have been proposed as the possible substrate for stereoscopic vision. Some readers may recall seeing three-dimensional images with small stereoviewers as a child. The impression of depth requires that each view of the image be slightly different, just as it would be for binocular V1 cells with disparate monocular fields.

CORTICAL MICROCIRCUITRY: WHO TALKS TO WHOM IN V1?

Of all cortical areas, V1 has been studied in the most detail. The numbers of cell classes and complexity of connections of this area that have been identified, and the controversies over the functional significance of the many circuits identified in V1 are beyond the scope of this short chapter (for recent review, see reference 7). The diagram shown in Figure 29-5 provides an overview of some of the intrinsic connections within V1 in primates. What such a diagram does not convey is the relative strength of connections and which types of cells are involved.

Cell Classes in V1

In V1, as in the LGN, cells containing glutamate account for the vast majority (approximately 80%) with the remaining cells containing γ-aminobutyric

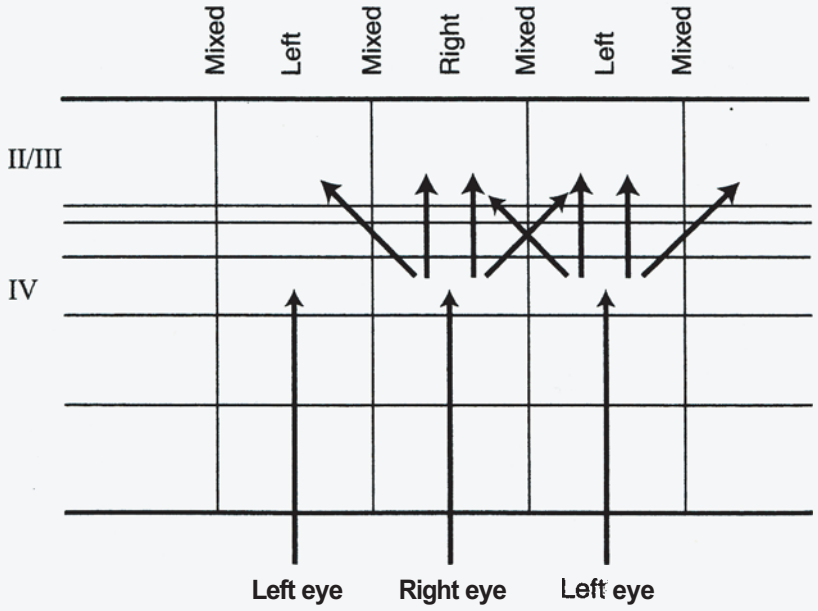


FIGURE 29-9 Information from the two eyes remains segregated until it reaches V1. Within layer IV, information from the right and left eye are still segregated, but connections between layers IV and III combine inputs from both eyes through horizontal and diagonal connections. This combination of inputs results in cells in V1 that respond to input from both eyes (see text for details). (From Hubel D H *Eye, bruin and vision,* New York, 1988, Scientific American Library.)

acid (GABA).[12] These two main cell classes are morphologically distinct[27,40] (Figure 29-10). Two types of cells contain glutamate: the spiny stellate cells that occur mainly in layer IV and the pyramidal cells that occur in all of the layers. Both of these glutamate-containing neurons have a high density of dendritic spines. Although pyramidal cells are the only class of cell that sends axons outside of V1, many pyramidal cells have only local axons within V1. In contrast to the pyramidal cells, the inhibitory GABA-ergic cells have few to no spines on their dendrites. The latter are multipolar neurons whose dendritic arbors come in a variety of shapes. Many subclasses of GABA-ergic interneurons have been

A B

FIGURE 29-10 A, Camera lucida drawings of three examples of pyramidal cells in primary visual cortex of rhesus monkey. Note that examples *a* and *b* are in layer III, and *c* (*far* right) is in layer II. The diagram of the coronal section on the left denotes the portion of primary visual cortex from which the material was taken. All three have the relatively classic morphology of a pronounced apical dendrite, an axon that exits from the cortical gray matter, and several recurrent collaterals that extend for a millimeter or more in the horizontal plane (a, *b*). The drawings are based on a Golgi stain. B, Major classes of aspiny nonpyramidal cells in the primate cerebral cortex as seen in Golgi preparation. Group 1 cells, represented by a neurogliaform cell (A) and chandelier cell (*B*), form local connections. Cells in Group 2 have long horizontal axon collaterals and include Cajal-Retzius neurons (*C*) and large basket cells (D). Group 3 neurons form vertical connections and are represented by a Martinotti cell with an ascending axonal arbor (*E*) and a double bouquet cell with both ascending and descending axonal arbor that can extend for up to a mm or more in the radial domain (*F*). All of these neurons use GABA as their neurotransmitter, as well as several peptides; in addition, calcium-binding proteins are colocalized in different combinations of these morphologic classes. (A from Valverde F: The organizing principles of the primary visual cortex in the monkey. In Peters A, Jones EG [eds]: *Cerebral cortex*, vol 3, New York, 1985, Plenum Press; B from Jones EG et al: GABA neurons ans their role in activity-dependent plasticity of adult primate visual cortex. In Peters A, Rockland KS [eds]: *Cerebral* cortex, vol 10, New York, 1994, Plenum Press.)

identified on the basis of morphology, the presence of different calcium-binding proteins such as calbindin and parvalbumin, or various peptides (see Figure 29-10, *B*). The proportion of glutamate/GABA cells remains fairly constant across layers, at least in macaque monkeys.[12]

Connections within V1

Connections between layers can be made by both excitatory and inhibitory neurons (for review, see references 7 and **32).** Efforts to trace the general flow of information using pharmacologic manipulations have suggested that layer IV becomes active first and after this the upper layers followed by the lower laye r ~Circuits that connect layers III and V are especially robust, as are circuits that connect layers IV and VI (at least from VI to IV, see reference 7).

Most of the connections between V1 cells are local, either within a layer or within a vertically defined column of cortex approximately 350 to 500 μm wide. There are, however, longer connections of up to *3* mm in macaque monkeys that occur typically between cells with similar properties (e.g., selectivity for the same orientation or ocular preference). These long tangential connections are found most commonly in layers I, 111, and V.[38] The effect of these longer connections has been noted in the responses of V1 cells when areas beyond the classical receptive field are stimulated. Studies have shown that although V1 cells do not respond directly to stimuli presented outside of their receptive fields, if these cells are actively responding to a preferred stimulus within their classical receptive field, this response can be modulated by stimuli presented simultaneously at other locations in the field.[29] Such interactions suggest a means whereby responses to local features might begin to be put together to represent the global features of objects.[17]

Comment on Processing Dynamics

What is difficult to appreciate from descriptions of wiring alone is that the visual system is highly dynamic in the living animal. The problem is that the visual system must maintain stability while animals are constantly looking around and often moving through their environments. Therefore the receptive fields of V1 neurons can provide only useful snapshots within short windows of time. A good

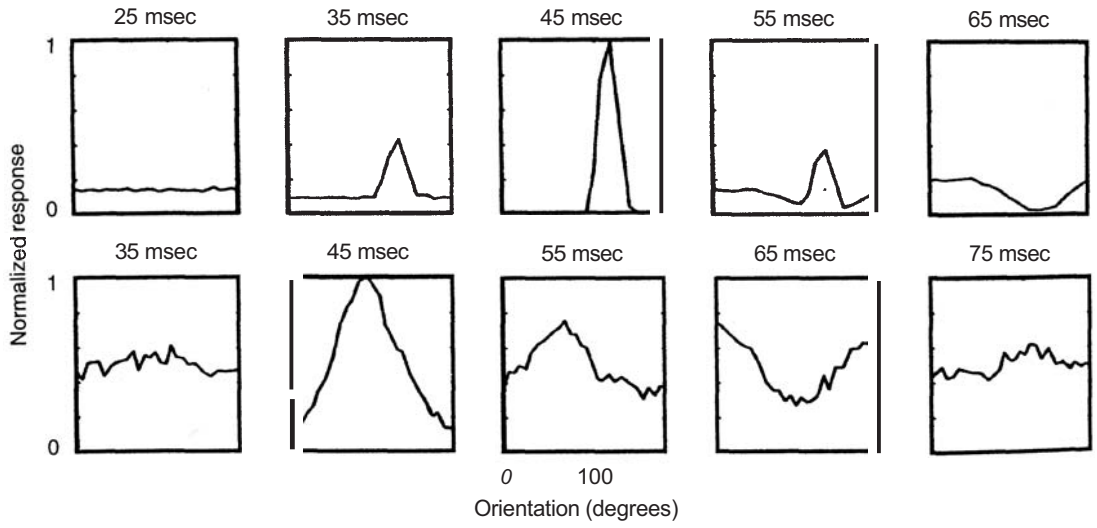


FIGURE 29-11 Reverse correlation measurements of the time evolution of orientation tuning in macaque V1 neurons (Ringach, Hawken, and Shapley, unpublished results). Here the results are obtained by reverse correlation in the orientation domain. To study the dynamics of orientation tuning, they used as stimuli the set of sine gratings of optimal spatial frequency at many orientations (around the clock in 10-degree steps). The dynamic stimuli used consisted of a rapidly changing sequence of sinusoidal gratings. The responses of the neurons are the cross-correlations of their spike trains with the sequence of images; this gives the neurons' orientation-tuning functions as functions of time. In each graph the horizontal axis goes from 0- to 180-degree orientation. This figure displays orientation-tuning functions for two neurons in macaque V1 layer IIIC. Results for each cell occupy a different row. The five different panels for each neuron correspond to give different delays between neural response and stimulus onset. Note that the response to orientation has a dynamic nature; the same cell responds differently to the same orientation at different times (see text for details). (From Shapley R: The receptive fields of visual neurons. In De Valois KK [ed]: *Seeing,* New York, 2000, Academic Press.)

example showing that receptive fields are highly dynamic can be appreciated by examining the evolution of orientation tuning in a single V1 cell in a macaque monkey (Figure 29-11). (See reference **39.)** Two cells located in layer IIIC were stimulated with rapidly changing sequences of differently oriented sinusoidal gratings. The horizontal axis represents orientation preference from 0 to 180 degrees, and the vertical axis represents the normalized response of the cells. The responses of the cells are measured as the cross-correlations of their spike train outputs against the sequence of images. These cross-correlations show the orientation preference of the cell as a function of time. Each panel represents a period (in milliseconds) after stimulus onset. The main point is that averaging responses over long periods (i.e., 500 milliseconds), as is typically done in most experiments, masks the complex dynamics that take place over time. The cell in the top row shows clear evidence of a peak excitatory response at 45 milliseconds at one orientation but inhibition at that same orientation 20 milliseconds later. The second cell *(bottom* ***row)*** not only shows similar evidence of inhibition but also appears to show a shift in orientation preference at ***65*** milliseconds after stimulus onset compared with the peak shown 10 milliseconds earlier. As techniques for sampling from many neurons over time in awake monkeys become more sophisticated, it is clear from this example that the concept of how V1 cells contribute to vision will have to move from static pictures of single simple cell receptive fields to a more dynamic view involving network relations between many cells.

COLUMNS AND MODULES: OUTLINING THE FUNCTIONAL ARCHITECTURE OF V1

As shown, V1, like the LGN, is arranged in layers containing cells of different types. Unlike the LGN, new receptive field properties such as selectivity for stimulus orientation, movement direction, and binocularity are constructed at the level of V1. In addition, information about spatial frequency, temporal frequency, brightness, and color contrast, sent by cells of the LGN, must be either preserved or incorporated into the coding of V1 cells. Given the precision of the visuotopic map in V1, this means that critical stimulus attributes must be coded in an iterated manner to cover each location in visual space so that form and movement can be appreciated equally well without holes or gaps at different locations.

How is this accomplished? Hubel and Wiesel[25] were cognizant of the problem that local stimulus attributes would need to be represented again and again at each locale. What they noticed early on in their studies was that orientation preference in cat and monkey V1 changes regularly as one moves an electrode tangentially within any layer (Figure 29-12). An advance of 1 to 2 mm was usually found to be sufficient to rotate twice through 180 degrees of orientation preference. This distance was also found to be sufficient to include at least one left and right eye ocular dominance column. From this information, Hubel and Wiesel constructed a model in which they proposed that the cortex is composed of repeating modules called *hypercolumns.* They argued that each hypercolumn, whose exact boundaries were not fixed, should contain all of the machinery necessary to analyze one portion of visual space. More recently, Livingstone and Hubel[30] argued that CO blobs should be added to this modular organization as zones uniquely equipped to transmit color signals to

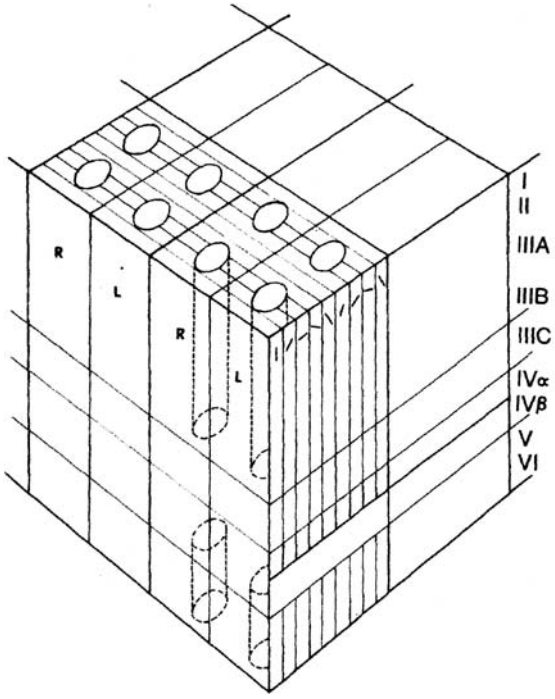
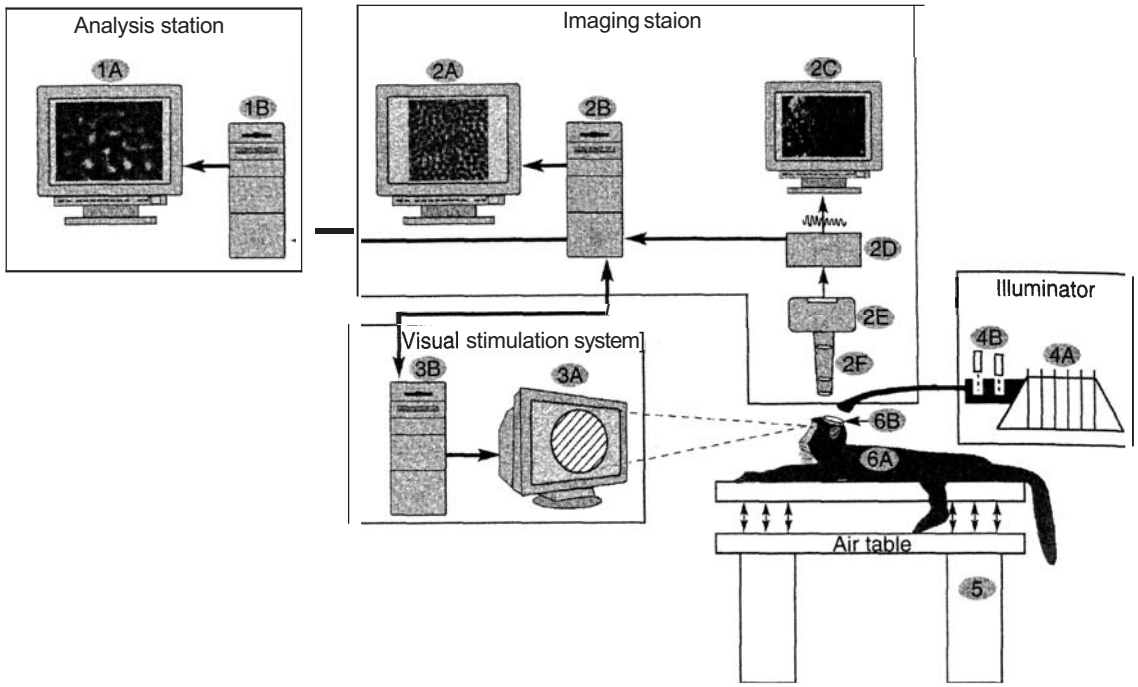


FIGURE *29-12* Schematic diagram of the modular organization of V1. Each module (or hypercolumn; see text for details) consists of two ocular dominance columns (representing right *[R]* and left *[L]* eyes), a series of orientation columns (representing 180 degrees of rotation), and cytochrome oxidase blobs ***(dotted*** columns; representing color information). (From Livingstone MS, Hubel DH. *J Neurosci* 4309, 1984.)



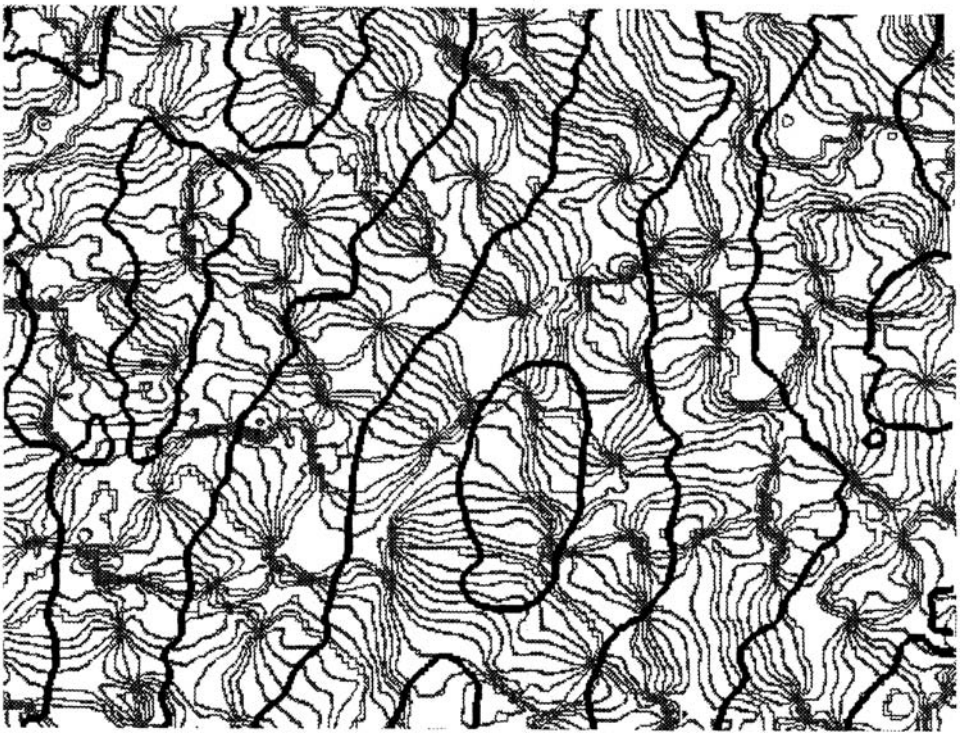
A

FIGURE 29-13 **A,** Computer-generated stimuli presented on a display monitor *(3A)* activate functionally specific regions of monkey (*6A*) cortex. Stimulus-evoked activity in regions near the brain surface modulates reflectance of light (from [*4A, 4B*]) off the brain, a phenomenon mediated by an increase in the oxyhemoglobin/deoxyhemoglobin ratio in regions of greater metabolic activity. The illuminated brain surface is imaged through a cranial window chamber (*6B*) by a magnifying lens *(2F)* onto the charge coupled device (CCD) of a low-noise camera (*2E*), which converts the optical image of the brain to an analog video electrical signal. **A** video-enhancement amplifier *(20)* boosts image contrast (*2C*). Images sampled on repeated trials are stored and averaged by the imaging computer (*2B*), and the results are presented pictorially on a monitor (*2A*). Subsequent analyses of averaged data are performed on the analysis station (*1A, 1B*). Because images are averaged over repeated trials, the images must be aligned and the camera must not move with respect to the brain. **A** mechanically isolating air table *(5)* reduces movement induced by floor vibration.

Continued

the next level (see Figure 29-5). Although there is considerable debate as to whether CO blobs are actually uniquely designed for color processing because they appear to exist in all primates, even nocturnal species with only a single cone type, the fact that these modules are the targets of LGN input from a separate class of cells, the K cells, suggests that CO blobs do something special.[8] Moreover, there appear to be enough CO blobs so that whatever is processed within these modules can clearly be represented across all topographic areas. Because CO blobs are positioned in the centers of ocular dominance columns in macaque monkeys, they were added as another dimension to be included within a V1 hypercolumn (Figure 29-12). The geometric problem is not so difficult for the cortex to solve when only three stimulus properties-orientation, ocular dominance, and color—must be constrained by topography, but when more properties, such as spatial frequency, direction selectivity, and binocular disparity are added, the task becomes more challenging.

Recently, optical imaging of intrinsic signals has been used to try to determine the relationship between maps of different stimulus properties in single animals. Figure 29-13, **A,** shows the basic set up and procedures used.[36] The signals imaged using this technique are tiny differences in the reflected light from cortex based on dynamic differences in oxygenated and deoxygenated blood that occur as a result of the relative activity of cells. This technique has several advantages, including excellent spatial resolution (approximately 50 μm) and the ability to image several different stimulus properties in one experiment, as well as the ability to be combined with anatomic and single-unit electrophysiologic methods. Of course, the disadvantages are



B

FIGURE 29-13, CONT'D B, Example of a contour plot of orientation preferences in overlay with the borders of ocular dominance bands imaged from macaque monkey V1. Isoorientation lines *(gray)* are drawn in intervals of 11.25 degrees. ***Black*** *lines* indicate the border of ocular dominance bands. (From Obermayer K, Blasdel GG: *J Neurosci* 13:4114,

that it is invasive, has poor temporal resolution, and is limited to surface structure. With use of this technique, it has been found that changes in orientation selectivity are represented mainly in pinwheel formation, with some regions also showing more gradual linear or abrupt fractures in the orientation map. The structure of orientation maps in different primates and in other species shows a great deal of similarity, suggesting that orientation-selective cells are organized the same way in humans. Maps of different stimulus qualities also suggest that, although not organized exactly as originally envisioned in the hypercolumn model of Hubel and Wiesel,[25] maps of stimulus attributes are nevertheless iterated in such a manner that there are no "holes" in the map across space (Figure 29-13, *B*).

How Do Parallel Inputs Relate to Parallel Outputs?

It has been popular to suggest that there is a direct link between the input and output pathways of V1. There is considerable support for the idea that two hierarchies of extrastriate visual areas exist: one devoted to object vision or *what* something is and one to support spatial vision or complex tasks related to *where* items are in space relative to ourselves. The "what" and "where" pathways, also called the *ventral* and *dorsal streams,* consist of projections through V2 to **V4** and into areas of temporal cortex and projections through area MT to regions in the parietal cortex, respectively.[34] It is less clear whether they are directly linked to the K, M, and P LGN pathways. The best evidence for such a direct link comes from studies in which input from the M and P pathways and associated K cells were temporarily blocked in macaque monkeys with microinjections of GABA.[35] These studies clearly demonstrated that the majority of input to area MT comes either from M cells or M and neighboring K cells; K and M cells could not be inactivated separately in these studies. Despite these results, some MT cells could still be driven by the remaining P and/or K cells within the LGN. The importance of M input to area MT is not surprising given the importance of the ability to detect rapidly moving stimuli. **A** fairly direct pathway for signals from M LGN cells to area MT has also been demonstrated anatomically given that cells in

layer IVα, the target layer for LGN M cells, send axons directly to cells in layer IIIC, which, in turn, can send signals to area MT. Nevertheless, cells in layer IIIC that project to MT do not reflect the receptive field properties of M cells; instead, most are complex direction selective cells whose receptive fields are constructed through circuits within cortex.[37]

Even more opportunity for integration between pathways seems to exist before signals enter the ventral stream ("what" pathway). Blockade of the P layers and surrounding K layers does not silence cells within output layers IIIA and IIIB, both of which respond well with either M or P layers blocked.' Moreover, anatomically, much of the output to the ventral stream leaves from layer IIIA, which gets no direct input from layer IV but receives signals only after they have passed to other layers. Thus both the wiring and physiology suggest that considerable integration of signals takes place in V1 before they are transmitted into the ventral stream for further analysis of object identity. Finally, as discussed in Chapter 28, the fact that lesions of either M or P layers in the LGN (together with associated K layers) do not eliminate either form or motion vision reinforces the view that it is inappropriate to equate complex visual behavior with the threshold properties of retinal and LGN cells.

SUMMARY OF KEY POINTS

- *All* visual signals necessary for conscious visual perception are processed in V1 before being sent to other visual areas.
- Primate V1 contains a complete map of the opposite hemifield, in which the representation of central vision is greatly magnified.
- As in the LGN, inputs from K, M, and P and left and right eye remain separate at the first synapse. M and P axons terminate within the upper and lower tier of layer IV, where left and right eye input is segregated into ocular dominance columns. K axons terminate within the CO blobs of layer IIIB and layer I.
- Activation of V1 neurons depends completely on LGN input, but V1 also receives many other cortical and subcortical modulatory inputs.
- V1 subcortical output axons originate within the lower two layers. Layer VI provides the main feedback to the LGN, and layer V axons provide the main drive to cells of the pulvinar, which, in turn, sends axons to extrastriate areas. Each layer also sends axons to other subcortical visual targets.
- V1 cortical output axons originate mainly from layer III; each extrastriate area receives input from different layer III sublayers and from CO blob and interblob compartments within layer 111. V1 projects to extrastriate areas concerned with both the "what" (portions of V2 and V4) and "where" (V3 and V5) components of vision.
- New receptive field properties are created within the complex circuitry of V1 and involve both excitatory spiny pyramidal cells and a variety of nonspiny inhibitory interneurons. The new receptive fields code for local image features, including orientation, direction of motion, and binocular disparity.
- The functional geometry of V1 is organized such that each stimulus property is mapped in an iterated fashion to provide each point in the visual field with all necessary stimulus information.

REFERENCES

1. Allison JD et al: Differential contributions of magnocellular and parvocellular pathways to the contrast response of neurons in bush baby primary visual cortex (V1), *Vis Neurosci* 17:71, 2000.
2. Amthor FR, Grzywacz NM: Directional selectivity in vertebrate retinal ganglion cells, *Rev Oculomot Res* 5:79, 1993.
3. Azzopardi P, Cowey A Preferential representation of the fovea in the primary visual cortex, *Nature* 361:719, 1993.
4. Bolz J, Gilbert CD, Wiesel TN: Pharmacological analysis of cortical circuitry, *Trends Neurosci* 12:292, 1989.
5. Boyd JD, Casagrande VA Relationships between cytochrome oxidase (CO) blobs in primate primary visual cortex (V1) and the distribution of neurons projecting to the middle temporal area (MT), *J Comp Neurol* 409:573, 1999.
6. Brodmann K *Localization in the cerebral cortex,* London, 1994, Smith-Gordon and Co Ltd (Translated and edited by LJ Garey from *Vergleichen lokalisationslehre der grosshirnrinde in ihren prinzipien dargestellt* auf *grund des zellenbaues,* Leipzig, 1909, Johann Ambrosius Barth).
7. Callaway EM: Local circuits in primary visual cortex of the macaque monkey, *Annu Rev Neurosci* 21:47, 1998.
8. Casagrande VA A third parallel visual pathway to primate area V1, *Trends Neurosci* 17:305, 1994.
9. Casagrande VA, Kaas JH: The afferent, intrinsic and efferent connections of primary visual cortex in primates. In Peters A, Rockland KS (eds): *Cerebral cortex,* vol 10, New York, 1994, Plenum Press.
10. Chen W et al: Human primary visual cortex and lateral geniculate nucleus activation during visual imagery, *Neuroreport* 9:3669, 1998.
11. Engel SA et al: fMRI of human visual cortex, *Nature* 369: 525, 1994.
12. Fitzpatrick D et al: Distribution of GABAergic neurons and axon terminals in the macaque striate cortex, *J Comp Neurol* 264:73, 1987.
13. Florence SL, Casagrande VA: Changes in the distribution of geniculocortical projections following monocular deprivation in tree shrews, *Brain Res* 374:179, 1986.

14. Florence SL, Kaas JH: Ocular dominance columns in area 17 of Old World macaque and talapoin monkeys: complete reconstructions and quantitative analyses, *Vis* Neurosci 8:449, 1992.
15. Fox PT et al: Retinotopic organization of human visual cortex mapped with positron-emission tomography, *J* Neurosci 7:913, 1987.
16. Frisby JP: Seeing: illusion brain and mind, New York, 1979, Oxford University Press.
17. Gilbert C et al: Interactions between attention, context and learning in primary visual cortex, *Vis* Res 40:1217, 2000.
18. Hässler R: Comparative anatomy of the central visual systems in day- and night-active primates. In Hassler R, Stephen S (eds): Evolution of the forebrain, Stuttgart, Germany, 1967, Thieme.
19. Horton JC, Hedley-Whyte ET Mapping of cytochrome oxidase patches and ocular dominance columns in human visual cortex, Phil Trans R *Soc* Lond B 304:255, 1984.
20. Horton JC, Hoyt WF: Quadrantic visual field defects: a hallmark of lesions in extrastriate (V2/V3) cortex, Brain 114:1703, 1991.
21. Hubel DH: Eye, bruin and vision, New York, 1988, Scientific American Library.
22 Hubel DH, Wiesel TN: Receptive fields, binocular interaction and functional architecture in the cat's striate cortex, *J Physiol* 154:572, 1962.
23. Hubel DH, Wiesel TN: Receptive fields and functional architecture of monkey striate cortex, *J Physiol* 195:215, 1968.
24. Hubel DH, Wiesel TN: Laminar and columnar distribution of geniculo-cortical fibers in the macaque monkey, *J Comp Neurol* 146:421, 1972.
25. Hubel DH, Wiesel TN: Ferrier lecture. Functional architecture of macaque monkey visual cortex, Proc *R Soc Lond B* 198:1, 1977.
26. Jones EG: The thalamus of primates. In Björklund A, Hokfelt T (eds): Handbook of chemical neuroanatomy, vol 14, New York, 1998, Elsevier.
27. Jones EG et al: GABA neurons ans their role in activity-dependent plasticity of adult primate visual cortex. In Peters A, Rockland KS (eds): Cerebral cortex, vol 10, New York, 1994, Plenum Press.
28. Lachica EA, Beck PD, Casagrande VA: Intrinsic connections of layer III of striate cortex in squirrel monkey and bush baby: correlations with patterns of cytochrome oxidase, *I Comp Neurol* 329:163, 1993.
29. Levitt JB, Lund J S Contrast dependence of contextual effects in primate visual cortex, Nature 387:73, 1997.
30. Livingstone MS, Hubel DH: Anatomy and physiology of a color system in the primate visual cortex, *J* Neurosci 4:309, 1984.
31. Lyon DC, Kaas JH: Connectional and architectonic evidence for dorsal and ventral V3, and dorsomedial area in marmoset monkeys, *J Neurosci* 21: 249,2001.
32. Lund JS: Anatomical organization of macaque monkey striate visual cortex, *Annu Rev* Neurosci 11:253, 1988.
33. Malpeli JG, Schiller PH, Colby C L Response properties of single cells in monkey striate cortex during reversible inactivation of individual lateral geniculate laminae, *J Neurophysiol* 46:1102, 1981.
34. Merigan WH, Maunsell JH: How parallel are the primate visual pathways? *Annu* Rev Neurosci 16:369, 1993.
35. Nealey TA, Maunsell JH: Magnocellular and parvocellular contributions to the responses of neurons in macaque striate cortex, *J* Neurosci 142069, 1994.
36. Obermayer K, Blasdel GG: Geometry of orientation and ocular dominance columns in monkey striate cortex, *J* Neurosci 13:4114, 1993.
37. Recanzone GH, Wurtz RH, Schwarz U Responses of MT and MST neurons to one and two moving objects in the receptive field, *J Neurophysiol* 78:2904, 1997.
38. Rockland KS, Lund JS: Widespread periodic intrinsic connections in the tree shrew visual cortex, Science 215:1532, 1982.
39. Shapley R: The receptive fields of visual neurons. In De Valois KK (ed): Seeing, New York, 2000, Academic Press.
40. Valverde F: The organizing principles of the primary visual cortex in the monkey, In Peters A, Jones EG (eds): *Cerebral* cortex, vol 3, New York, 1985, Plenum Press.
41. Van Essen DC, Newsome WT, Maunsell JH: The visual field representation in striate cortex of the macaque monkey: asymmetries, anisotropies, and individual variability, Vis Res 24:429, 1984.
42. Wandell B: Foundations of vision, Sunderland, Mass, 1995, Sinauer Associates.
43. Wassle H et al: Retinal ganglion cell density and cortical magnification factor in the primate, *Vis Res* 30:1897, 1990.