

Circuitry, Architecture, and Functional Dynamics of Visual Cortex

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A fundamental understanding of the mechanisms of cortical processing requires an examination of the relationships of cortical circuitry, functional architecture, and receptive field properties. Ultimately, this kind of analysis can be utilized to explore the neurobiological basis of psychophysics and perception. At the outset our studies were intended to account for the then known receptive field properties of cortical cells in terms of their underlying circuitry, but surprisingly a good part of the cortical circuit appeared to be in violation of the principles of cortical architecture, and this led us to explore the possibility of new, more complex properties of cortical cells. It has become increasingly possible to relate the responsive specificity of cortical cells, and the circuitry underlying this specificity, to the perceptual capabilities of the visual system by performing analogous experiments on single cells and in human psychophysics.

Cortical Circuitry and Projection Patterns

The cortical circuit can be divided into its excitatory components, generated by pyramidal and spiny stellate cells, and its inhibitory components, formed by smooth stellate cells. Classically, much of the cortical circuit had been delineated using the Golgi silver impregnation technique (Ramon y Cajal, 1911; O'Leary, 1941; Lorente de Nò, 1944; Lund, 1973; Lund and Boothe, 1975). We used a different approach, involving intracellular recording and dye injection, for the several advantages it offers: it allows one to relate the functional properties of cells to their dendritic morphology and axonal projection pattern, and it reveals more about the extent of axonal connections than the Golgi technique (Gilbert and Wiesel, 1979, 1983). The excitatory cells form a series of connections running across the cortical layers. The set of connections in cat primary visual cortex is summarized in Figure 1. Input from the lateral geniculate nucleus (LGN) arborizes within layer 4 and the upper part of layer 6. Layer 4 spiny stellate cells project up to the superficial layers of cortex, superficial layer pyramidal cells project down to layer 5, layer 5 projects to layer 6, and layer 6 cells project back up to layer 4, closing a loop of intrinsic excitatory connections. In addition to these spiny neurons, there is a population of smooth stellate cells, comprising approximately 20% of cortical neurons, that mediate inhibition within the cortex. At each stage in the cortical circuit the spiny cells are tapped for output to other areas, superficial layer cells projecting to other cortical areas (Fig. 2), layer 5 cells projecting to the superior colliculus, and layer 6 cells projecting to the LGN (Gilbert and Kelly, 1975).

The functional properties of cells in any cortical layer are well suited to the functions of the structures to which they project, and they reflect the characteristics of the inputs to the layer in which they reside (Gilbert, 1977). Layer 4 cells, as well as cells in the superficial part of layer 6, receive input from the LGN, and have simple receptive field properties, supporting the idea that the simple cell represents the first stage in visual cortical processing (Hubel and Wiesel, 1962). Cells in layer 2/3 have complex receptive fields, with small diameters, that are end-inhibited, which is appropriate for the higher resolution and analysis of form that higher cortical areas mediate. Cells in layer 5 have larger receptive fields, tend to be directionally selective, and are sensitive to movement of small ob-

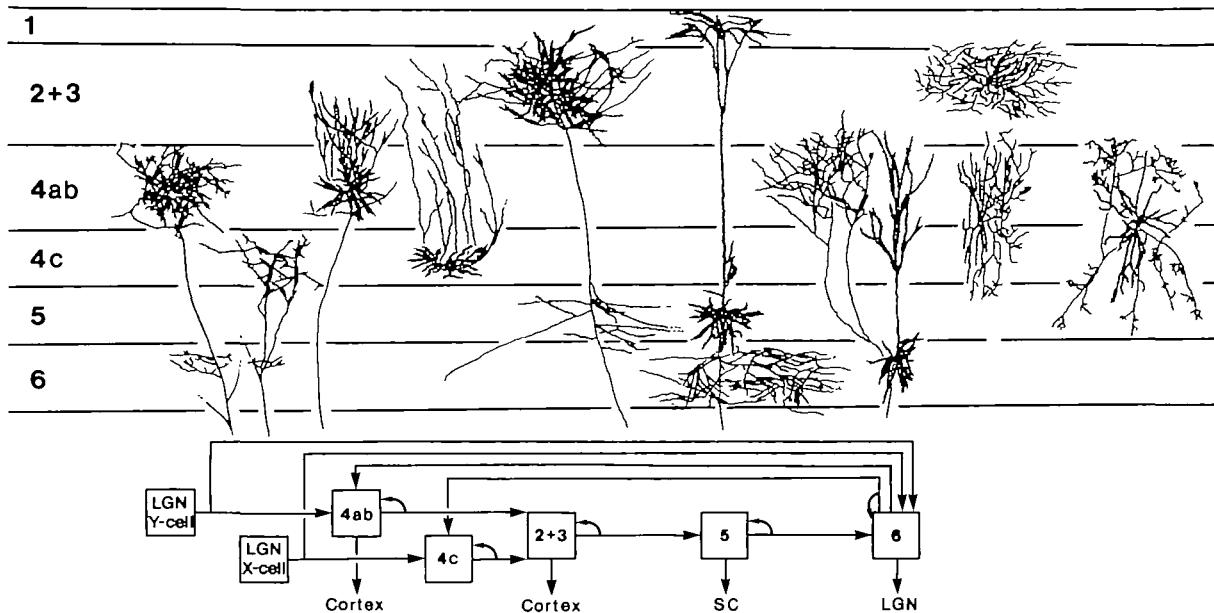


Figure 1. Schematic diagram of the intracortical connections of the cat's striate cortex, determined by intracellular HRP injections (Gilbert and Wiesel, 1979). The spiny stellate and pyramidal cells are responsible for excitatory connections, and their intracortical and efferent connections are summarized in the block diagram below. Smooth stellate cells, several types of which are shown at upper right, mediate inhibitory interactions in the cortex (Gilbert and Wiesel, 1983).

jects within the receptive field. Since these cells project to the superior colliculus, which helps direct the movement of the eyes to track moving objects, they are likely to provide the colliculus with information about the direction of object movement. Cells in layer 6 form a major feedback projection to the LGN, but the role of this projection remains largely unknown. They also project to layer 4, and play an important role in the generation of the property of end-inhibition.

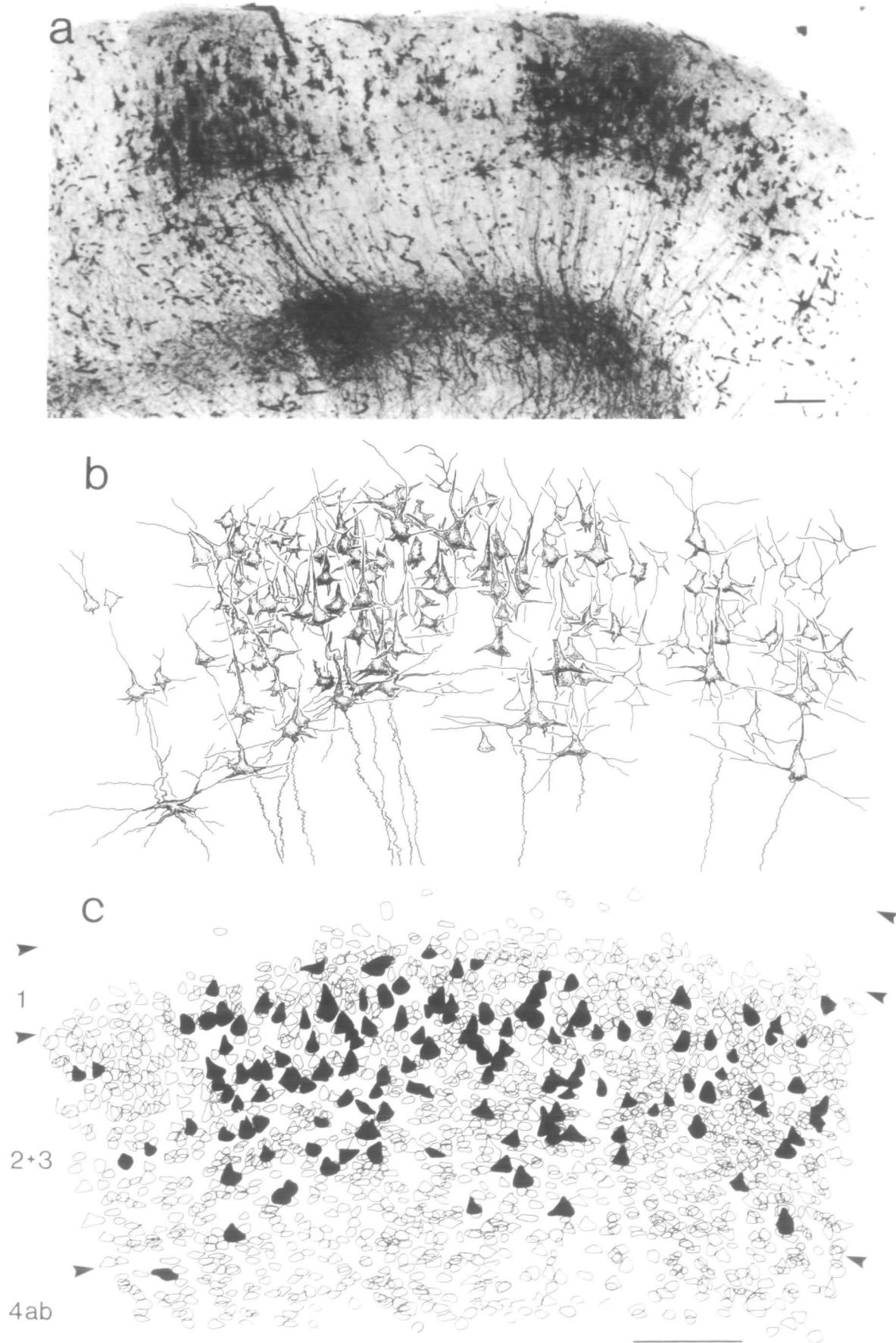
Functional Roles of Interlaminar Connections

One can account for some of the functional properties of cortical cells by the connections between layers. By comparing the receptive field properties of intracellularly injected neurons with those in the layers to which they project, we developed models of how particular connections would contribute specific receptive field properties.

An important interlaminar connection is that originating in layer 6 and synapsing with neurons in layer 4 (Fig. 3). Cells in layer 4 show selectivity for the length of a line stimulus, having inhibitory flanks along the orientation axis of the receptive field, a property referred to as end-inhibition. In addition to orientation selectivity, this property may play an important role in the analysis of form, giving cells a sensitivity to local curvature. Cells with end-inhibited receptive fields respond better to curved lines than to long,

straight lines (Fig. 4, left). In contrast to this property, layer 6 cells show the opposite behavior: a short bar produces little or no response, and as the bar is lengthened, the response improves progressively up to lengths of 10–15°. The size of the receptive fields of layer 4 cells, including their inhibitory flanks, is roughly comparable to the receptive fields of layer 6 cells. It would be plausible, therefore, that the inhibition in layer 4 is produced by the projection from layer 6 to layer 4 by means of an inhibitory neuron (Fig. 4, middle). This idea was supported by the finding that the population of neurons targeted by layer 6 cells are preponderantly smooth stellate cells (McGuire et al., 1984). When layer 6 cells are inactivated by local injection of GABA, the cells in layer 4 overlying the injection site lose the property of end-inhibition (Fig. 4, right; Bolz and Gilbert, 1986). The direct projection from layer 6 to layer 4 is therefore the most likely source of end-inhibition. Since, however, layer 6 cells project both to layer 4 and down to the LGN, some of their effects might be mediated by the corticothalamic feedback. Though cortical ablation reduces some of the surround inhibition seen in neurons in the LGN (Murphy and Sillito, 1987), local injection of GABA in layer 6, while eliminating end-inhibition in cortex, has little effect on LGN surrounds (Bolz et al., 1989). This supports the idea that cortical end-inhibition is mediated by the direct pathway from layer 6 to layer 4.

Figure 2. Corticocortical connections, viewed by retrograde transport of extracellularly injected HRP. *a*, Following a focal HRP injection in area 19, the retrogradely labeled cells in area 17 are found in the superficial cortical layers, and are distributed widely, indicating highly convergent connections. The cells are grouped in clusters, reflecting columnar specificity of the connections. *b*, Camera lucida reconstruction of the retrogradely labeled cells in the right cluster in *a*, which all had pyramidal morphology. *c*, The labeled cells (black) represent roughly 20% of the total population (Gilbert and Kelly, 1975, reprinted from Gilbert and Wiesel, 1981). Scale bars, 100 μm.



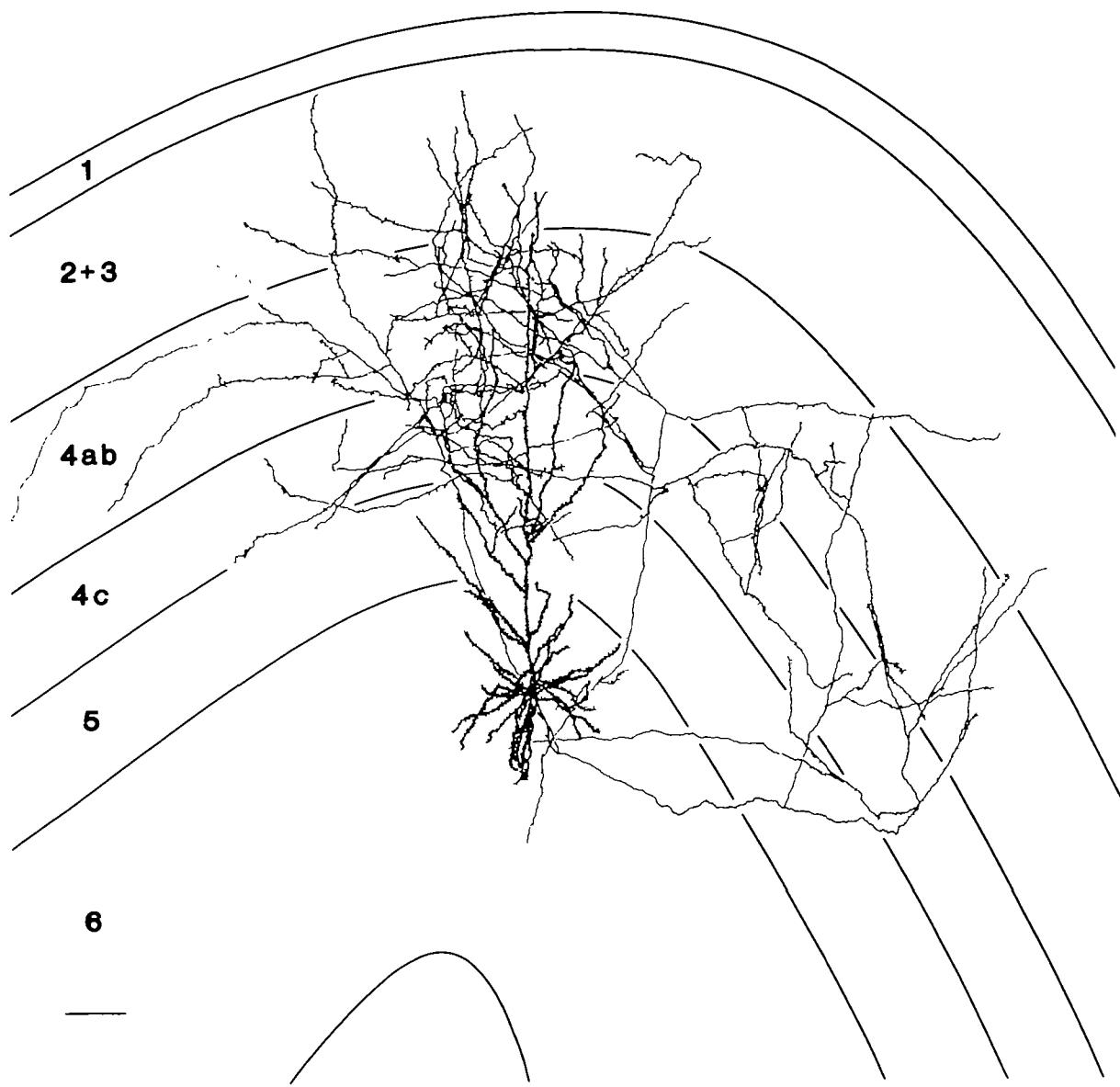


Figure 3. Layer 6 pyramidal cell projecting to layer 4. The apical dendrite ramifies within layer 4, and the axon collaterals are distributed widely within layer 4. The cell had a simple receptive field, as is characteristic of upper layer 6 cells, located at 7° eccentricity, 4° in length and 1.5° in width, vertically oriented and directional for leftward movement. Scale bar, 100 μ m.

Long-range Horizontal Connections

In any vertical column, cells have overlapping receptive fields with similar orientation specificity and eye preference (Hubel and Wiesel, 1962). From considerations of functional architecture, it made a lot of sense that there would be a systematic series of connections between layers, relating cells with similar functional properties. It was therefore quite surprising to find extensive horizontal connections traveling parallel to the cortical surface, relating sites representing disparate locations in the visual field. These are the axon collaterals of cortical pyramidal cells (Gilbert and Wiesel, 1979, 1983, 1989; Rockland and Lund, 1982, 1983; Martin and Whitteridge, 1984). An example of one of these cells, with its characteristic horizontally projecting clustered collateral arbor, is shown in Figure 5. These connections allow the target

cells to integrate information from a wide area of cortex, and as a consequence of the topographical architecture of cortex, from a large part of the visual field, including loci outside their receptive fields. Taking together the receptive field area and the scatter in receptive field position, the receptive fields of all the cells in the column will cover a tiny fraction of the visual field. A rough rule of thumb governing topographic order in this area is that there is no overlap in the receptive fields of cells separated by a distance of 1.5 mm, a distance corresponding to two complete cycles of orientation columns, or two "hypercolumns" (Hubel and Wiesel, 1974). Thus, horizontal connections spanning 6–7 mm allow communication between cells with widely separated receptive fields. This represents puzzling evidence for cells' ability to integrate information over a larger part

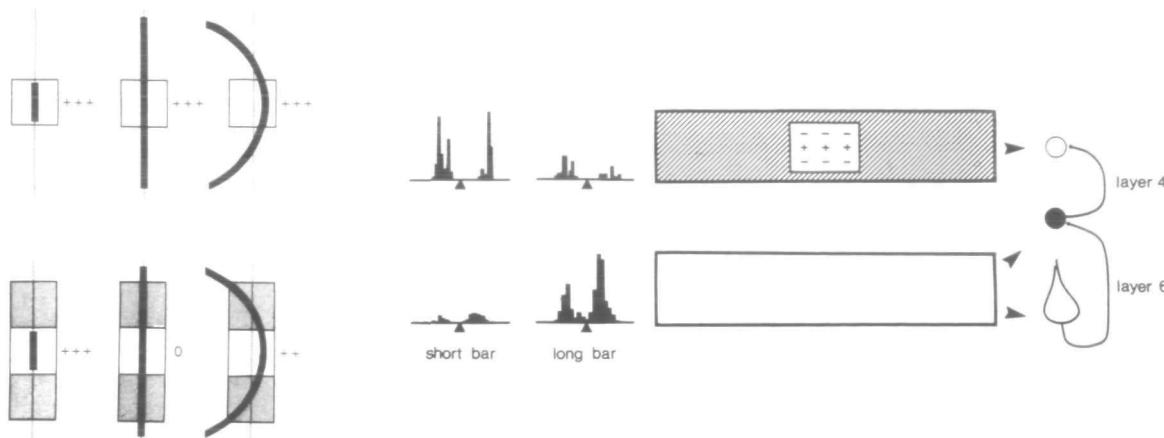


Figure 4. Schematic diagrams of the functional role of end-inhibition (*left*) and the mechanism for its generation (*right*). Non-end-inhibited cells do not respond differentially to short lines, long straight lines, or curved lines. End-inhibited cells respond well to short fine segments and poorly to long, straight lines. Curved lines with the appropriate radius of curvature, however, can be effective stimuli, since, as shown here, the part of the curve passing through the receptive field center is of the optimal orientation for the excitatory part of the field but is at an ineffective orientation for the inhibitory flanks, leaving the cell with a net excitation. The property of end-inhibition can be generated by the long receptive fields of layer 6 cells, which, by connecting inhibitory interneurons in layer 4, can contribute the end-inhibitory flanks to layer 4 simple cells. This circuit would lead to a reciprocal behavior in the response of the layer 6 and layer 4 cells to short and long bars, as shown (Gilbert and Wiesel, 1978; Balz and Gilbert, 1986).

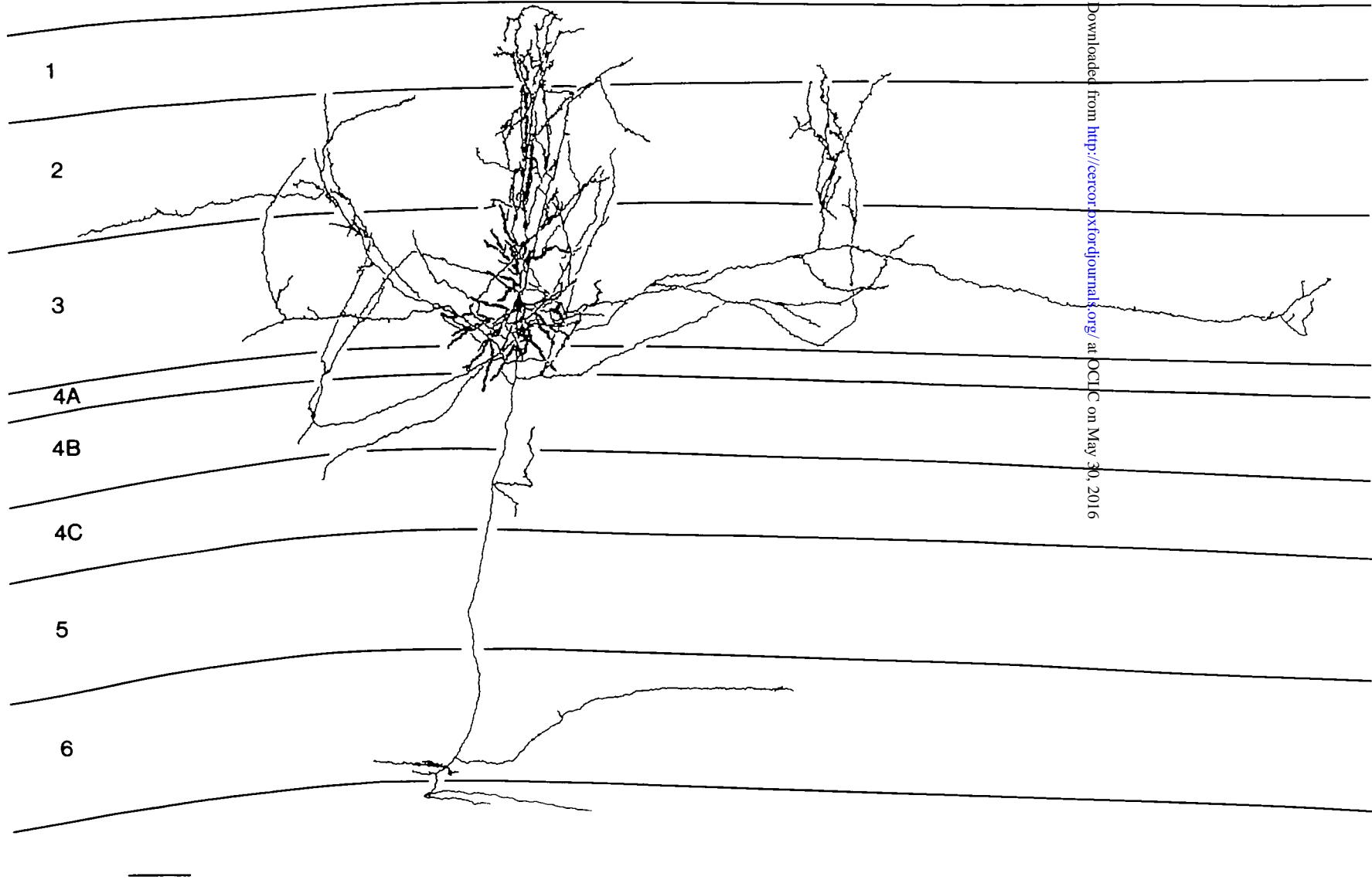
of visual space than that covered by their receptive fields, and calls into question the very definition of receptive field. The explanation for this seeming contradiction between cortical topography and receptive field structure is that the definition of the receptive field is stimulus dependent, and that a cell's response can be modulated by stimuli lying outside the classical receptive field. Put another way, a cell's response to a complex visual stimulus cannot be fully predicted from its response to a simple stimulus, such as a single short line segment.

Though the horizontal connections are very widespread, they are quite specific in terms of the functional properties of the target cells. Rather than contacting all cells within a certain radius, the axon collaterals of the horizontally projecting cells are distributed in discrete clusters. The clustering implied a possible relationship to the functional architecture of the cortex: the tendency of cells with similar functional properties to be grouped into columns of similar functional specificity. In the primary visual cortex, cells with common orientation specificity and ocular dominance are distributed in this fashion. Several lines of evidence show that the clustering of the horizontal axon collaterals allows them to mediate communication between columns of similar orientation preference. The spacing between clusters is roughly the same distance as that required to run though a full cycle of orientation columns (or one hypercolumn for orientation, which is about 750 μm wide). A physiological technique, known as cross-correlation analysis, demonstrated the functional relationship of cells communicating via the horizontal connections. A cross-correlation is a histogram of differences in the spike times for a pair of cells. Cells that are connected, or that share a common input, will show a peak in this histogram at a particular delay. Looking across a population of cells, cross-correlation analysis shows that cells in columns of similar functional specificity showed correlated firing, even when separated by dis-

tances as great as 2 mm (Ts'o et al., 1986; Ts'o and Gilbert, 1988).

An anatomical technique, combining retrograde tracing with 2-deoxyglucose autoradiography, confirmed the functional specificity of the horizontal connections. Injecting a retrograde tracer, such as rhodamine-filled latex microspheres, reveals the distribution of cells projecting to the injection site. After such an injection, cells are labeled across 8 mm of cortex, which represents an area roughly an order of magnitude larger than the receptive fields of the recipient cells. Within the labeled area the cells are distributed in discrete clusters, reminiscent of the pattern of axon collaterals seen in intracellular injections. When the retrograde tracing technique is combined with the 2-deoxyglucose technique, one can compare the distribution of the labeled cells with the distribution of orientation columns. These experiments showed that the horizontal connections run between columns of similar orientation specificity (Gilbert and Wiesel, 1989).

The functional nature of the horizontal connections depends on a complex set of interactions with their target neurons. Since the cells of origin are pyramidal and the principle targets are other pyramidal cells, one might expect the net effect of the horizontal connections within the overall circuit to be excitatory. Although inhibitory interneurons constitute only 20% of the targets (McGuire et al., 1991), the inhibitory component of the horizontally evoked synaptic potentials could be larger than this proportion might indicate. A number of factors, such as the relative excitability and the density of local collaterals of inhibitory and excitatory cells, could increase the influence of one population over another. In fact, as observed in an *in vitro* cortical slice preparation, the balance between excitation and inhibition generated by activating the horizontal connections varies widely, from cell to cell and also according to the level of recruitment of the horizontal inputs (Hirsch and Gil-



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Figure 6. Example of a horizontally projecting pyramidal cell in macaque striate cortex. The cell is a layer 3 pyramidal cell whose axon extended for more than 4 mm parallel to the cortical surface. The dendrite is seen as the thicker, darker lines in the center, and is studded with dendritic spines. The axon gives off several clusters of collaterals within the superficial layers, as well as projecting out of the immediate cortical area (adapted from McGuire et al., 1991).

bert, 1991). Consequently, horizontal inputs may be responsible for inhibitory as well as facilitatory receptive field properties.

The widespread connections seen within each cortical area are also reflected in the highly convergent and divergent corticocortical connections between successive stages in the visual pathway. The connections between different cortical areas have a similar distribution to the intrinsic horizontal connections, in that they are widespread and their terminal arbors are clustered. Conversely, a site in a given cortical area receives input from clusters of cells in the antecedent cortical area (Fig. 2). The clustered intrinsic and extrinsic corticocortical connections have been seen in other visual areas, including V2, V3, and MT, and in somatosensory, auditory and frontal cortex (Gilbert and Kelly, 1975; Zeki, 1976; Goldman and Nauta, 1977; Imig and Brugge, 1978; Jones et al., 1978; Gilbert and Wiesel, 1979, 1983; Imig and Reale, 1981; Tigges et al., 1981; Rockland and Lund, 1982; Weller et al., 1984; DeFelipe et al., 1986; Rockland and Virga, 1990; Ojima et al., 1991, 1992; Lund et al., 1993). Just as the horizontal connections show columnar specificity in visual cortex, similar specificities are observed in auditory cortex (Imig and Reale, 1981).

The picture that emerges is a sequence of convergent pathways mediating integration over progressively larger parts of visual space. Even in primary visual cortex, however, this convergence enables cells' stimulus specificities to be influenced by the context within which a local feature is presented.

Contextual Influences on Receptive Field Properties

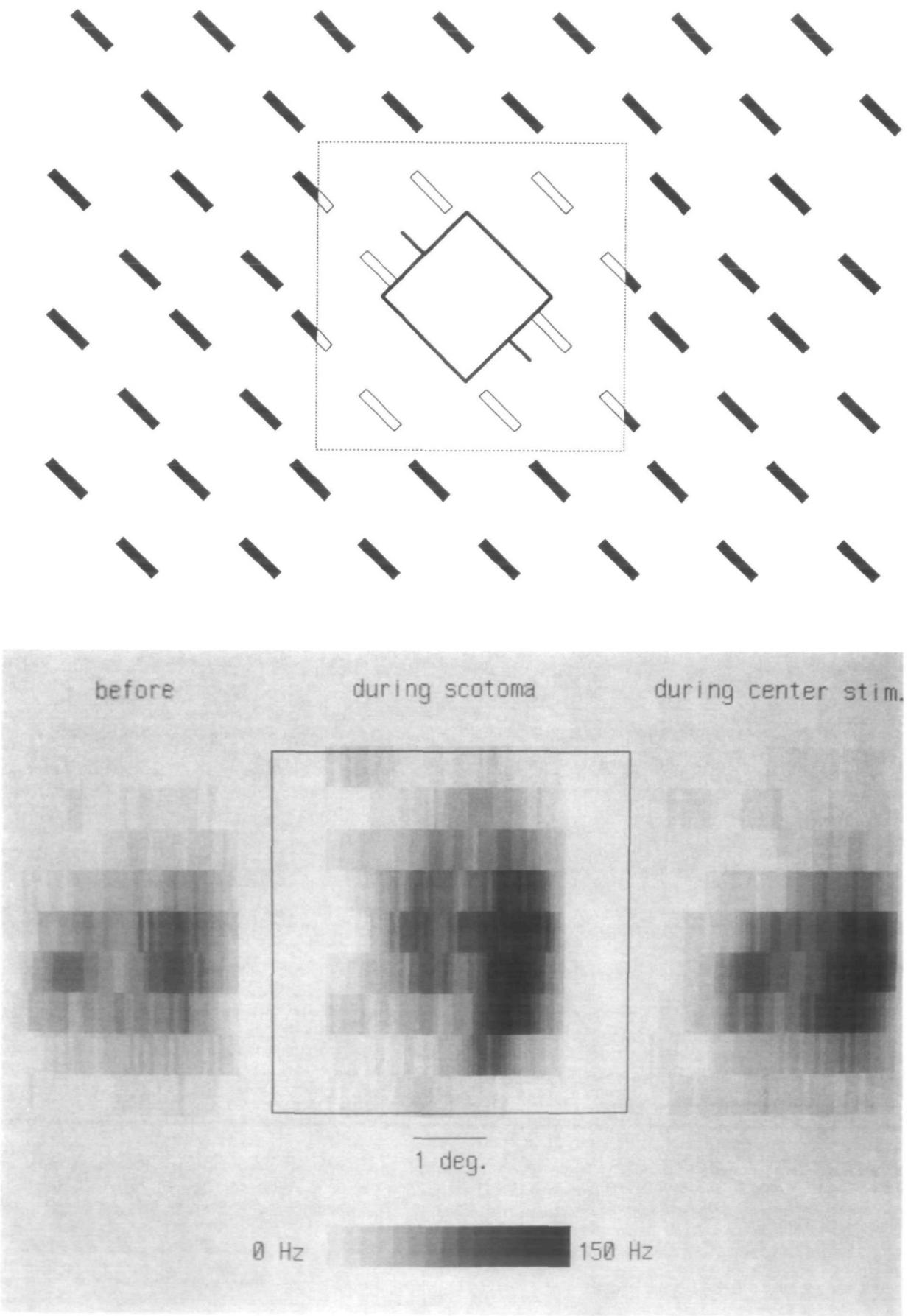
Given the picture of the horizontal plexus, its distribution, relationship to functional architecture, and synaptic physiology, one is left with the question of functional role in influencing receptive field properties and the perceptual consequences of these influences. An increasing body of evidence now shows that the size and orientation specificity of receptive fields can be changed by context, the presence of contours or textures outside the receptive field. These changes can be induced in several ways. The concurrent presence of the surrounding contours can alter the functional specificity (or "filter characteristics") of a cell, indicating a differential response between simple and complex stimuli. Even more surprisingly, stimulation in the receptive field surround can induce lasting changes in the responsiveness of the cell to the original simple stimulus, even after the surrounding pattern is removed. These effects may be related to observations of visual psychophysics, which have long established that the perceived attributes of a local feature can be influenced by the context in which that feature is presented.

Our first observation in this regard was made in the domain of orientation. When a line is presented within the receptive field in isolation, one can determine the orientation specificity of the cell by measuring its response to lines of different orientations, and deriving an orientation tuning curve. This tuning

curve can be altered when lines are presented in the surround, and the nature of the influence depends on the relationship between the orientation of the surround lines and the optimum orientation of the cell. With certain surround orientations the tuning curve may be either inhibited or potentiated, and with others one sees other effects including shifts in optimum orientation and changes in the bandwidth of the tuning curve. Some of the changes can be quantitatively compared to measurements of shifts in perceived orientation induced by context, a phenomenon known as the tilt illusion (Gibson and Radner, 1937; Westheimer, 1990). To make such a comparison one has to make a population model in which the estimate of orientation is based on the relative firing levels of a set of cells, each cell tuned to a different orientation. One such model makes a vector representation of the cells: each cell is represented by a vector, pointing in the direction of its optimum orientation and whose length represents its level of firing. Since the cells within the ensemble have overlapping tuning curves, any given stimulus will activate many cells within the ensemble, and the estimate of orientation can be derived as the vector sum of the entire ensemble. Using such a model, we found that several of the observed effects of contextual lines, including iso-orientation inhibition, shifts in the tuning curves toward the orientation of the surrounding lines, and changes in the bandwidth of orientation tuning could all account for the perceptual changes (Gilbert and Wiesel, 1990). Further experiments are required to ascertain which of these changes most consistently account for the psychophysical measurements.

A second example of the context dependency of receptive field properties is in the domain of receptive field size. Not only can receptive field properties be modulated by the presence of contours in the area surrounding the receptive field, but the surround influences can alter receptive field structure over time. When an area several times the diameter of the receptive field is occluded, and the surrounding area is stimulated with lines or random dots, the receptive fields within the occluded area expand severalfold in diameter. When stimuli are then placed within the receptive field, the field collapses down to its original size. By alternately putting in and removing the mask from the conditioning stimulus, the field can go through several cycles of expansion and shrinkage (Fig. 6; Pettet and Gilbert, 1992).

The mechanism of this reorganization is found in processes that are intrinsic to the cortex, and are not found at antecedent levels in the visual pathway. One piece of evidence in support of this is the fact that it shows interocular transfer: if the conditioning stimulus, the artificial scotoma, is presented to one eye, one finds expansion of the receptive field in the other eye (Volchan and Gilbert, 1992). This suggests that the source of the expansion is cells with binocular receptive fields, or at least ones receiving binocular input. The next step is to ascertain the synaptic mechanism of the change. Evidence of changes in synaptic weight that is correlated with the receptive field ex-



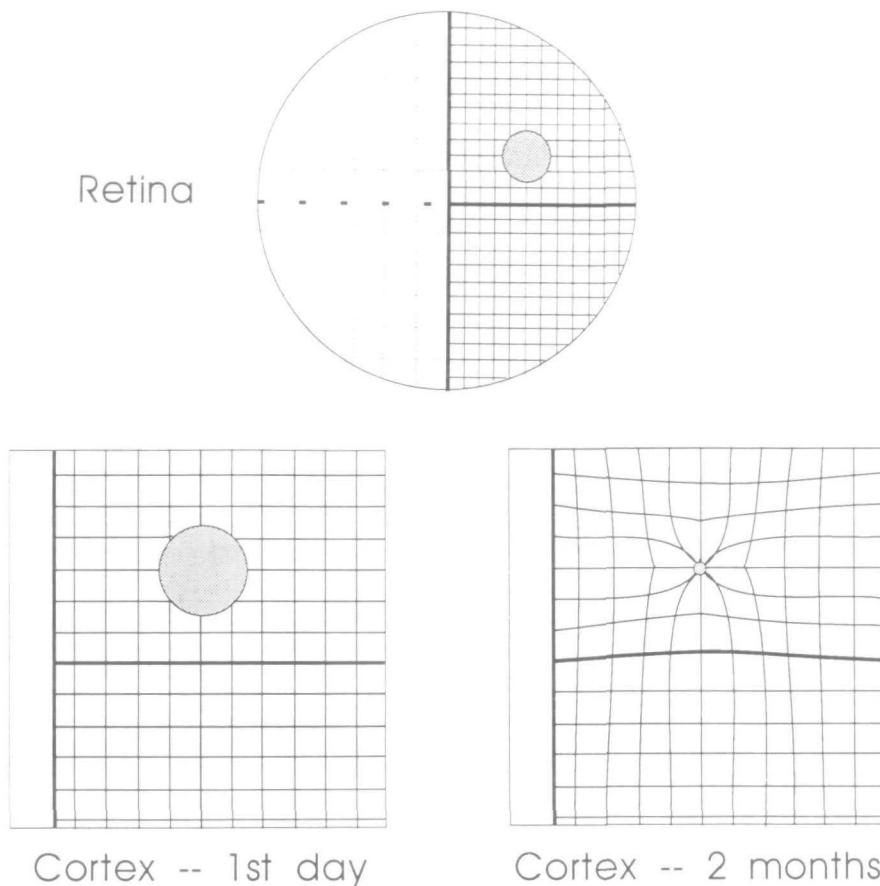


Figure 7. Effect of making retinal lesions on cortical topography. The visuotopic axes are represented as the Cartesian grid superimposed on the retina, and the corresponding maps on the cortex in surface view. A lesion, made with a diode laser, destroys the photoreceptor layer in a restricted part of the retina (shaded area, top), effectively removing visual input from the cortical region representing that retinal area (lower left). To get an idea of the dimensions involved, in the primate, a lesion subtending 5° of visual field, centered about 4° in the periphery, silences an area of cortex 10 mm in diameter. Over a period of 2 months the topography of the cortex is reorganized (lower right), with a decreased representation of the silenced input, and an increased representation of the nonlesioned retina (Gilbert and Wiesel, 1990, 1992; Kaas et al., 1990; Hennen and Skavenski, 1991; reprinted from Gilbert, 1992).

pansion comes from cross-correlation analysis. Ordinarily, cells with similar receptive field properties, such as common orientation preference, show correlated firing. A cross-correlogram provides a measure of the strength of connectivity between cells. If one records from a pair of cells with adjacent receptive fields, the strength of correlation, and hence the synaptic weight, increases as the receptive fields expand and the amount of overlap increases. *In vitro* recordings in cortical slices show that the strength of the horizontally evoked synaptic potentials becomes greater with use. The supposition is that the receptive field plasticity observed with conditioning with an artificial scotoma may have a corresponding increase

in synaptic weights of excitatory connections, perhaps the horizontal connections, in the cortical circuit.

Other demonstrations of sensitivity for context include response to illusory contours, which has been shown in primate area 18 (Von der Heydt and Peterhans, 1989), response of supposedly "monocular" cells in the cortical representation of the optic disk to stimulation of the other eye by lines passing through and extending beyond the optic disk, a form of perceptual completion (Fiorani et al., 1992), and sensitivity to movement outside of the receptive field, altering cells' responses to moving stimuli within the receptive field (Allman et al., 1985; Tanaka et al., 1986; Gulyás et al., 1987).

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Figure 6. Effect of an artificial scotoma on receptive field size. Just as the retinal lesions are capable of producing a considerable expansion in receptive field size within minutes after making the lesion (Gilbert and Wiesel, 1992), mimicking the lesion by occluding a small part of the visual field also causes receptive fields located within the occluded area to expand (Pettet and Gilbert, 1992). The upper part shows the conditioning stimulus: a pattern of lines moving outside the receptive field (the square with a solid outline, with the orientation specificity indicated by the two lines protruding from the square). The lines disappear when they move within the masked area (the mask is indicated by the dotted line, but is not explicitly drawn in the stimulating pattern; the stimulating lines are shown as the blackened rectangles, and their disappearance is indicated by the open rectangles). After 10 min of conditioning, the receptive field expands. This is illustrated in the lower part, which gives a two-dimensional response profile of the cell, with the darker portions showing the greater response. The size and position of the occluder are indicated by the outline in the center, and the enlarged receptive field is indicated within the outline. Stimulating the center of the receptive field causes it to collapse in size, as indicated in the lower right. The receptive field can be caused to expand and contract alternately by a sequence of surround stimulation followed by center stimulation. Adapted from Pettet and Gilbert (1992, their Figs. 1, 4); reprinted from Gilbert (1992).

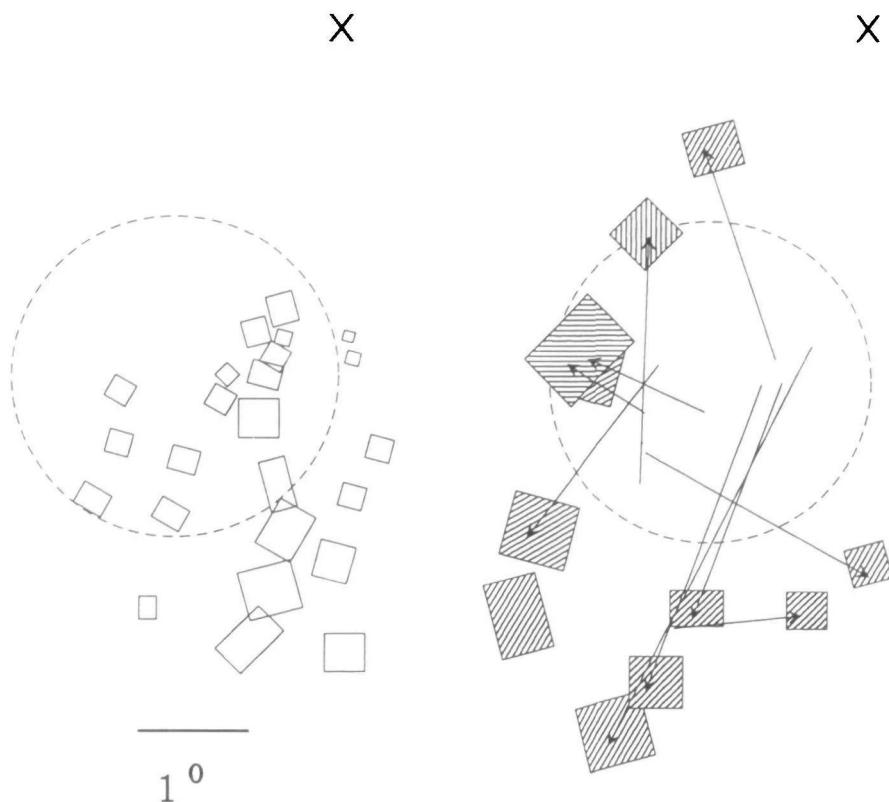


Figure 8. Receptive field maps in a region of monkey cortex deafferented by a retinal lesion, immediately before the lesion was made (*left*) and 2 months following the lesion (*right*). All recorded sites had cells with receptive fields located outside the lesioned retinal area. Though some arrows are crossed, overall the shifts maintained a rough retinotopic order, with fields that were originally located in the lower part of the scotoma shifting down, and those located in the upper part shifting up. Note that for one site where the receptive field was initially located *outside* the lesion, the field shifted horizontally. This result was observed in several experiments, and indicates that the effects of the perturbation caused by the lesion are propagated beyond the deafferented area of cortex. There was also receptive field enlargement: the field areas averaged 0.036 ± 0.022 degrees 2 before the lesion and 0.100 ± 0.025 degrees 2 2 months later ($p < 0.01$). The Xs mark the foveal position. Reprinted from Gilbert and Wiesel (1992).

It has long been known that one's perception of the attributes of localized features, such as brightness or color, orientation, and position, can be influenced by the context within which these features are presented (Westheimer et al., 1976; Westheimer and McKee, 1977; Butler and Westheimer, 1978; Badcock and Westheimer, 1985; Westheimer, 1986). Under certain circumstances, context can induce the perception of brightness, color, lines, or textures at points in the image where there is no physical stimulus present. These phenomena are referred to as perceptual fill-in or illusory contours (Yarbus, 1957; Krauskopf, 1961; Kanizsa, 1979; Crane and Piantanida, 1983; Paradiso and Nakayama, 1991; Ramachandran and Gregory, 1991). The visual system also tends to integrate along contours, facilitating the salience of a contour composed of a series of similarly oriented line segments (Fields et al., 1993). This principle is related to the idea of "good continuation," one of the Gestalt laws of perceptual grouping, and may be related to visual segmentation. Which of these observations can be related to the context dependency and mutability of receptive fields seen in striate cortex remains to be established, but at least in the domains of orientation and position there appears to be a strong link.

We studied spatial localization around an artificial scotoma in human psychophysical experiments (M. Kapadia, C. D. Gilbert, and G. Westheimer, unpub-

lished observations). In experiments analogous to the physiological studies, we asked subjects to determine the position of short line segments in the vicinity of an artificial scotoma. Lines located near the boundary of the scotoma appear to be shifted toward the center of the scotoma. The perceived shift may be related to expansion of receptive fields within the scotoma: if each cell represents a "labeled line" for a particular visuotopic location, for example, the center of their receptive fields, when a group of cells expand their fields, stimuli located near the scotoma boundary cause activation of more cells located near the center of the scotoma than the outside the scotoma. This would result in an estimate of visual field position shifting toward the center of the scotoma. If the psychophysical experiments do reflect the same processes as the physiological observations, then they provide a useful measure of the time course of the changes: the positional shifts occur within one sec of conditioning with the artificial scotoma.

Long-term Changes in Cortical Topography

When the visual system receives changes in sensory experience for an extended period of time, even more dramatic alterations in receptive fields and cortical functional architecture can be seen. This is most dramatically shown when one makes lesions of the pe-

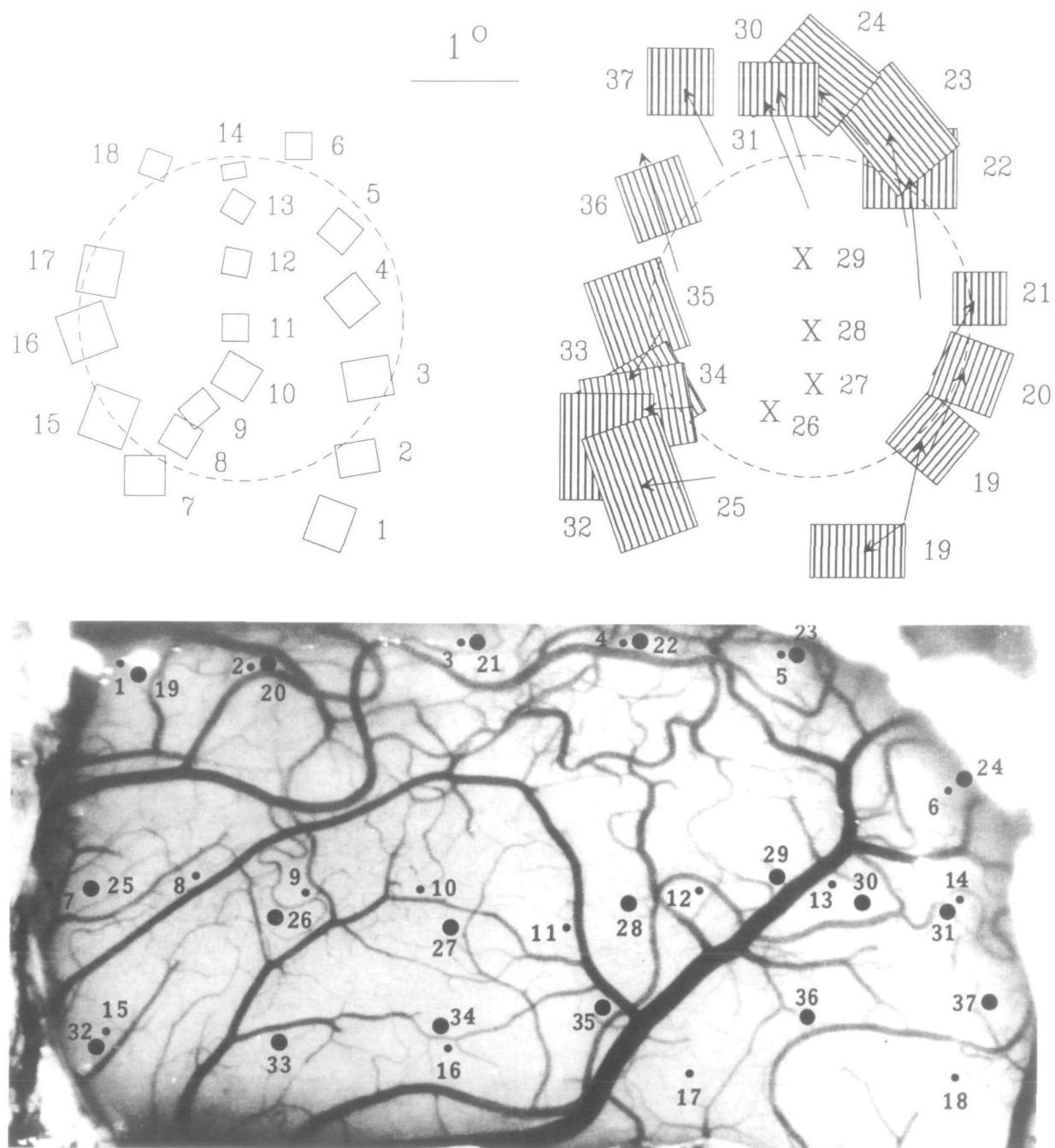


Figure 9. Receptive fields of cells encountered in vertical electrode penetrations in the superficial layers of monkey area V1 before and immediately after binocular retinal lesions at retinotopically corresponding sites. The first sets of receptive field maps, made before the lesion, are shown on the top left, with the subsequently made lesion included for reference (dashed lines). The size and retinotopic positions of the receptive fields encountered in one animal within minutes after making the lesion are shown on the top right. Using the cortical vasculature for reference (bottom), the same recording sites were visited before and after the lesion so one could make a direct comparison of the receptive fields of cells encountered at these sites at the different time points. The recording sites made before the lesion (small dots) and after the lesion (large dots) are numbered, with the corresponding receptive fields numbered accordingly. On the same day of the lesion a number of the originally recorded cortical sites were unresponsive to visual stimuli (as indicated by the Xs at the top right). The most striking effect was that receptive fields originally located near the boundary of the lesion expanded considerably, on average reaching five times their original area: before the lesion, the average field area at the recording sites was 0.07 ± 0.03 degrees 2 , and 0.37 ± 0.26 degrees 2 immediately after the lesion was made ($p < 0.01$). In addition, there was a suggestion of a shift in receptive field position, from immediately inside to just outside the boundary of the lesion, though this shift was less than 1°. The arrows at the top right indicate the relative positions of the receptive field centers of cells at nearby cortical sites recorded before and after the lesion, with the starting center position of each receptive field indicated by the tail of the arrow, and the ending position by the arrowhead. A few of the arrow positions were interpolated at points where the before and after recording sites were not sufficiently close. The position of the fovea is indicated by the Xs at the top right. Reprinted from Gilbert and Wiesel (1992).

periphery. Initially, when sensory input is removed by retinal lesions, an area of cortex is left silenced, devoid of functioning input. Over a period of a few months the silenced area recovers function, and it

develops a representation of a different part of the retina than it represented before the lesion. The result is an enlarged representation of the area of retina outside the lesion (Fig. 7; Gilbert and Wiesel, 1992).

For individual cortical cells the receptive fields shift from positions within the lesioned part of the retina to loci surrounding the lesion. In cortical terms the size of the shift is on the order of 3–4 mm, similar in extent to the horizontal connections. In receptive field terms this of course depends on the retinotopic location of the lesion, but in primates, at about 5° eccentricity, the receptive field shift is on the order of 6° (Fig. 8; Gilbert and Wiesel, 1992).

Though the magnitude of the shift corresponds closely to the extent of horizontal connections, one has to establish whether the reorganization is occurring within the cortex or at antecedent steps in the visual pathway, and to ascertain which sets of connections are responsible for propagating visual information from outside to within the cortical scotoma. We approached the first question by mapping the scotoma in the LGN at a time when the cortical scotoma had filled in. These experiments show that little reorganization occurs in the LGN, which retains a large area that cannot be activated by visual stimuli (Gilbert and Wiesel, 1992). The size of this area corresponds to the normal representation of the lesioned retina, indicating that most of the reorganization seen in cortex is intrinsic to the cortex (Darian-Smith et al., 1992). Within the cortex, several classes of connections are potentially responsible: thalamic afferents, horizontal intrinsic connections arising from pyramidal cells, and feedback connections from higher cortical areas. The thalamic input is more restricted in its lateral spread than the horizontal connections, so by itself would be insufficient to account for the degree of reorganization observed. Sprouting of thalamocortical connections could, however cause the effect. When one maps the extent of the thalamocortical input to cortex by injection of multiple fluorescent retrograde tracers, there appears to be no such increase in its lateral spread. This leaves us with the horizontal connections and feedback connections, which are normally long enough to account for the observed reorganization.

Even if the horizontal connections do not need to become more widespread to allow for the reorganization, they do appear to become strengthened in order to cause the shift in receptive field position. The strengthening might involve various mechanisms, from potentiation of excitatory connections to adaptation of inhibitory connections. From experiments with cortical slices we know that the horizontal inputs can be strengthened by use (Hirsch and Gilbert, 1993), but this strengthening takes place after a few seconds of conditioning, and is not something normally requiring months to bring about. It is plausible that changes of this sort might be involved with the receptive field alterations observed with an artificial scotoma, since these do occur in minutes. Something else might differentiate short- from long-term changes, for example, morphological changes such as synaptic proliferation. At this stage we have preliminary evidence indicating that there might be an increase in the number of axon collaterals in the distant axon collateral clusters of cells projecting from

outside the cortical scotoma toward the center of the scotoma (Darian-Smith and Gilbert, 1993).

Though the full-scale reorganization of cortical topography following retinal lesions takes a few months to occur, one can observe dramatic changes within minutes after making the lesions. Cells whose receptive fields are originally located near the boundary of the scotoma greatly increase their receptive field size, expanding into the part of visual field outside the lesioned area, with topographical shifts on the order of 1–2 mm (Fig. 9; Gilbert and Wiesel, 1992). Similarly, when a lesion is made in one eye, the cortex is initially silenced, but small areas of inactivated cortex, about 2 mm in diameter, can recover visual input a few hours after enucleation of the unlesioned eye (Chino et al., 1992). These findings might reflect the fact that under ordinary circumstances cells are capable of integrating information over a large part of visual space. Usually the inputs from outside the classic receptive field serve to modulate the response of the cell, but under the appropriate pattern of stimulation they can be boosted to a suprathreshold level. Removing the input that contributes to the receptive field center, for example, might allow the more peripheral inputs to be potentiated.

In summary, the functional consequences of the horizontal connections can be seen over several time scales. The longest-term effects can mediate recovery following lesions of the CNS. Shorter-term changes, occurring within minutes, either after retinal lesions or after conditioning with an artificial scotoma, reflect a normal process of adaptation to changes in sensory experience. The functional role of this adaptation may, in primary visual cortex, be a normalization or calibration of the system to analysis of various visual attributes. In higher-order cortical areas the same mechanisms may be applied to acquisition and storage of visual percepts. It may be that changes may occur on an even shorter time scale, as suggested by the psychophysical experiments. If so, receptive fields may adjust their specificity dynamically, as one assimilates and analyzes each view. Any model of visual processing will have to take into account that receptive field properties are dynamic, subject to the context within which features are presented and capable of being shaped by visual experience. Importantly, this mutability starts at the earliest cortical stages of visual processing, including primary visual cortex.

Notes

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References

- Allman JM, Miezin F, McGuinness E (1985) Direction and velocity specific surround in three cortical visual areas of the owl monkey. *Perception* 14:105–126.
- Badcock DR, Westheimer G (1985) Spatial location and hyperacuity: the centre-surround localization function has two substrates. *Vision Res* 25:1259–1269.

- Bolz J, Gilbert CD (1986) Generation of end-inhibition in the visual cortex via interlaminar connections. *Nature* 320:362-364.
- Bolz J, Gilbert CD, Wiesel TN (1989) Pharmacological analysis of cortical circuitry. *Trends Neurosci* 12:292-296.
- Butler T, Westheimer G (1978) Interference with stereoscopic acuity: spatial, temporal, and disparity tuning. *Vision Res* 18:1387-1392.
- Chino YM, Kaas JH, Smith EL III, Langston AL, Cheng H (1992) Rapid reorganization of cortical maps in adult cats following restricted deafferentation in retina. *Vision Res* 32:789-796.
- Crane HD, Piantanida TP (1983) On seeing reddish green and yellowish blue. *Science* 221:1078-1079.
- Darian-Smith C, Gilbert CD (1993) Role of laterally projecting intrinsic fibers in topographic reorganization of visual cortex in adult cats. *Soc Neurosci Abstr*, in press.
- Darian-Smith C, Gilbert CD, Wiesel TN (1992) Cortical reorganization following binocular focal retinal lesions in the adult cat and monkey. *Soc Neurosci Abstr* 18:11.
- DeFillipe J, Hendry SHC, Jones EG (1986) A correlative electron microscopic study of basket cells and large GABAergic neurons in the monkey sensory-motor cortex. *Neuroscience* 17:991-1009.
- Field DJ, Hayes A, Hess RF (1993) Contour integration by the human visual system: evidence for a local "association field." *Vision Res* 33:173-193.
- Fiorani M Jr, Rosa MGP, Gattass R, Rocha-Miranda CE (1992) Dynamic surrounds of receptive fields in primate striate cortex: a physiological basis for perceptual completion? *Proc Natl Acad Sci USA* 89:8547-8551.
- Gibson JJ, Radner M (1937) Adaptation, after-effect and contrast in the perception of tilted lines. *J Exp Psychol* 20:453-467.
- Gilbert CD (1977) Laminar differences in receptive field properties of cells in cat primary visual cortex. *J Physiol (Lond)* 268:381-421.
- Gilbert CD, Kelly JP (1975) The projections of cells in different layers of the cat's visual cortex. *J Comp Neurol* 163:81-106.
- Gilbert CD, Wiesel TN (1979) Morphology and intracortical projections of functionally identified neurons in cat visual cortex. *Nature* 280:120-125.
- Gilbert CD, Wiesel TN (1983) Clustered intrinsic connections in cat visual cortex. *J Neurosci* 3:1116-1133.
- Gilbert CD, Wiesel TN (1989) Columnar specificity of intrinsic horizontal and corticocortical connections in cat visual cortex. *J Neurosci* 9:2432-2442.
- Gilbert CD, Wiesel TN (1990) The influence of contextual stimuli on the orientation selectivity of cells in primary visual cortex of the cat. *Vision Res* 30:1689-1701.
- Gilbert CD, Wiesel TN (1992) Receptive field dynamics in adult primary visual cortex. *Nature* 356:150-152.
- Goldman PS, Nauta WJH (1977) Columnar distribution of cortico-cortical fibers in the frontal association, limbic and motor cortex of the developing rhesus monkey. *Brain Res* 122:393-413.
- Gulyas B, Orban GA, Duyssens J, Maes H (1987) The suppressive influence of moving texture background on responses of cat striate neurons to moving bars. *J Physiol (Paris)* 57:1767-1791.
- Heinen SJ, Skavenski AA (1991) Recovery of visual responses in foveal V1 neurons following bilateral foveal lesions in adult monkey. *Exp Brain Res* 83:670-674.
- Hirsch JA, Gilbert CD (1991) Synaptic physiology of horizontal connections in the cat's visual cortex. *J Neurosci* 11:1800-1809.
- Hirsch J, Gilbert CD (1993) Long-term changes in synaptic strength along specific intrinsic pathways in the cat's visual cortex. *J Physiol (Lond)* 461:247-262.
- Hubel DH, Wiesel TN (1962) Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. *J Physiol (Lond)* 160:106-154.
- Hubel DH, Wiesel TN (1974) Uniformity of monkey striate cortex: a parallel relationship between field size, scatter and magnification factor. *J Comp Neurol* 158:295-306.
- Imig TJ, Brugge JF (1978) Sources and terminations of callosal axons related to binaural and frequency maps in primary auditory cortex of the cat. *J Comp Neurol* 182:637-660.
- Imig TJ, Reale RA (1981) Ipsilateral corticocortical projections related to binaural columns in cat primary auditory cortex. *J Comp Neurol* 203:1-14.
- Jones EG, Coulter JD, Hendry SHC (1978) Intracortical connectivity of architectonic fields in the somatic sensory, motor and parietal cortex of monkeys. *J Comp Neurol* 181:291-348.
- Kaas JH, Krubitzer LA, Chino YM, Langston AL, Polley EH, Blair N (1990) Reorganization of retinotopic cortical maps in adult mammals after lesions of the retina. *Science* 248:229-231.
- Kanizsa G (1979) Organization in vision. *Essays on Gestalt perception*. New York: Praeger.
- Krauskopf J (1961) Heterochromatic stabilized images: a classroom demonstration. *Am J Psychol* 80:632-637.
- Lorente de Nò R (1944) Cerebral cortex: architecture, intracortical connections, motor projections. In: *Physiology of the nervous system* (Fulton JF, ed), pp 291-325. London: Oxford UP.
- Lund JS (1973) Organization of neurons in the visual cortex, area 17, of the monkey (*Macaca mulatta*). *J Comp Neurol* 147:455-496.
- Lund JS, Boothe RG (1975) Interlaminar connections and pyramidal neuron organization in the visual cortex, area 17, of the macaque monkey. *J Comp Neurol* 159:305-334.
- Lund JS, Yoshioka T, Levitt JB (1993) Comparison of intrinsic connectivity in different areas of macaque monkey cerebral cortex. *Cereb Cortex* 3:148-162.
- Martin KAC, Whitteridge D (1984) Form, function and intracortical projections of spiny neurones in the striate visual cortex of the cat. *J Physiol (Lond)* 353:463-504.
- McGuire BA, Hornung J-P, Gilbert CD, Wiesel TN (1984) Patterns of synaptic input to layer 4 of cat striate cortex. *J Neurosci* 4:3021-3033.
- McGuire BA, Gilbert CD, Rivlin PK, Wiesel TN (1991) Targets of horizontal connections in macaque primary visual cortex. *J Comp Neurol* 305:370-392.
- Murphy PC, Sillito AM (1987) Corticofugal feedback influences the generation of length tuning in the visual pathway. *Nature* 329:727-729.
- Ojima H, Honda CN, Jones EG (1991) Patterns of axon collateralization of identified supragranular pyramidal neurons in the cat auditory cortex. *Cereb Cortex* 1:80-94.
- Ojima H, Honda CN, Jones EG (1992) Characteristics of intracellularly injected infragranular pyramidal neurons in cat primary auditory cortex. *Cereb Cortex* 2:197-216.
- O'Leary JL (1941) Structure of the area striata of the cat. *J Comp Neurol* 75:131-161.
- Paradiso MA, Nakayama K (1991) Brightness perception and filling-in. *Vision Res* 31:1221-1236.
- Pettet MW, Gilbert CD (1992) Dynamic changes in receptive field size in cat primary visual cortex. *Proc Natl Acad Sci USA* 89:8366-8370.
- Ramachandran VS, Gregory TL (1991) Perceptual filling in of artificially induced scotomas in human vision. *Nature* 350:699-702.
- Ramon y Cajal S (1911) *Histologie du système nerveux de l'homme et des vertébrés*. Reprint. Madrid: CSIC, 1972.
- Rockland KS, Lund JS (1982) Widespread periodic intrinsic connections in the tree shrew visual cortex. *Brain Res* 169:19-40.
- Rockland KS, Lund JS (1983) Intrinsic laminar lattice connections in primate visual cortex. *J Comp Neurol* 216:303-318.
- Rockland KS, Virga A (1990) Organization of individual cortical axons projecting from area V1 (area 17) to V2 (area 18) in the macaque monkey. *Vis Neurosci* 4:11-28.
- Tanaka K, Hikosaka K, Saito H, Yukie M, Fukada Y, Iwai E (1986) Analysis of local and wide-field movements in the superior temporal visual areas of the macaque monkey. *J Neurosci* 6:134-144.

- Tigges J, Tigges M, Anschel S, Cross NA, Letbetter WD, McBride RL (1981) Areal and laminar distribution of neurons interconnecting the central visual cortical areas 17, 18, 19 and MT in squirrel monkey (*Saimiri*). *J Comp Neurol* 202:539–560.
- Ts'o D, Gilbert CD (1988) The organization of chromatic and spatial interactions in the primate striate cortex. *J Neurosci* 8:1712–1727.
- Ts'o D, Gilbert CD, Wiesel TN (1986) Relationships between horizontal and functional architecture in cat striate cortex as revealed by cross-correlation analysis. *J Neurosci* 6:1160–1170.
- Volchan E, Gilbert CD (1992) Cortical mechanisms of receptive field expansion in the cat striate cortex. *Soc Neurosci Abstr* 18:209.
- Von der Heydt R, Peterhans E (1989) Mechanisms of contour perception in monkey visual cortex. I. Lines of pattern discontinuity. *J Neurosci* 9:1731–1748.
- Weller RE, Wall JT, Kaas JH (1984) Cortical connections of the middle temporal visual area (MT) and the superior temporal cortex in owl monkeys. *J Comp Neurol* 228:81–104.
- Westheimer G (1986) Spatial interaction in the domain of disparity signals in human stereoscopic vision. I. Lines of pattern discontinuity. *J Physiol (Lond)* 370:619–629.
- Westheimer G (1990) Simultaneous orientation contrast for lines in the human fovea. *Vision Res* 30:1913–1921.
- Westheimer G, McKee SP (1977) Spatial configurations for visual hyperacuity. *Vision Res* 17:941–949.
- Westheimer G, Shimamura K, McKee S (1976) Interference with line orientation sensitivity. *J Opt Soc Am* 66:332–338.
- Yarbus AL (1957) The perception of an image fixed with respect to the retina. *Biophysics* 2:683–690.
- Zeki SM (1976) The projections to the superior temporal sulcus from areas 17 and 18 in the rhesus monkey. *Proc R Soc Lond [Biol]* 193:199–207.