



Ferrier Lecture: Functional Architecture of Macaque Monkey Visual Cortex

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FERRIER LECTURE

Functional architecture of macaque monkey visual cortex

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Of the many possible functions of the macaque monkey primary visual cortex (striate cortex, area 17) two are now fairly well understood. First, the incoming information from the lateral geniculate bodies is rearranged so that most cells in the striate cortex respond to specifically oriented line segments, and, second, information originating from the two eyes converges upon single cells. The rearrangement and convergence do not take place immediately, however: in layer IVc, where the bulk of the afferents terminate, virtually all cells have fields with circular symmetry and are strictly monocular, driven from the left eye or from the right, but not both; at subsequent stages, in layers above and below IVc, most cells show orientation specificity, and about half are binocular. In a binocular cell the receptive fields in the two eyes are on corresponding regions in the two retinas and are identical in structure, but one eye is usually more effective than the other in influencing the cell; all shades of ocular dominance are seen.

These two functions are strongly reflected in the architecture of the cortex, in that cells with common physiological properties are grouped together in vertically organized systems of columns. In an ocular dominance column all cells respond preferentially to the same eye. By four independent anatomical methods it has been shown that these columns have the

form of vertically disposed alternating left-eye and right-eye slabs, which in horizontal section form alternating stripes about 400 μm thick, with occasional bifurcations and blind endings. Cells of like orientation specificity are known from physiological recordings to be similarly grouped in much narrower vertical sheet-like aggregations, stacked in orderly sequences so that on traversing the cortex tangentially one normally encounters a succession of small shifts in orientation, clockwise or counterclockwise; a 1 mm traverse is usually accompanied by one or several full rotations through 180° , broken at times by reversals in direction of rotation and occasionally by large abrupt shifts. A full complement of columns, of either type, left-plus-right eye or a complete 180° sequence, is termed a hypercolumn. Columns (and hence hypercolumns) have roughly the same width throughout the binocular part of the cortex.

The two independent systems of hypercolumns are engrafted upon the well known topographic representation of the visual field. The receptive fields mapped in a vertical penetration through cortex show a scatter in position roughly equal to the average size of the fields themselves, and the area thus covered, the aggregate receptive field, increases with distance from the fovea. A parallel increase is seen in reciprocal magnification (the number of degrees of visual field corresponding to 1 mm of cortex). Over most or all of the striate cortex a movement of 1–2 mm, traversing several hypercolumns, is accompanied by a movement through the visual field about equal in size to the local aggregate receptive field. Thus any 1–2 mm block of cortex contains roughly the machinery needed to subserve an aggregate receptive field. In the cortex the fall-off in detail with which the visual field is analysed, as one moves out from the foveal area, is accompanied not by a reduction in thickness of layers, as is found in the retina, but by a reduction in the area of cortex (and hence the number of columnar units) devoted to a given amount of visual field: unlike the retina, the striate cortex is virtually uniform morphologically but varies in magnification.

In most respects the above description fits the newborn monkey just as well as the adult, suggesting that area 17 is largely genetically programmed. The ocular dominance columns, however, are not fully developed at birth, since the geniculate terminals belonging to one eye occupy layer IVc throughout its length, segregating out into separate columns only after about the first 6 weeks, whether or not the animal has visual experience. If one eye is sutured closed during this early period the columns belonging to that eye become shrunken and their companions correspondingly expanded. This would seem to be at least in part the result of interference with normal maturation, though sprouting and retraction of axon terminals are not excluded.

INTRODUCTION

Anyone who glances at a human brain can hardly fail to be impressed by the degree to which it is dominated by the cerebral cortex. This structure almost completely envelopes the rest of the brain, tending to obscure the other parts.

Though only 2 mm thick it has a surface area, when spread out, of about 2000 cm². Even more impressive is the number of elements it contains. Under every square millimetre there are some 10⁵ nerve cells, making a total of around 10¹⁰ cells. The number of synaptic connections in the cortex is certainly several orders of magnitude greater than this. For sheer complexity the cortex probably exceeds any other known structure.

To reveal this complexity special methods are necessary. Certain stains such as the Nissl make it possible to count and classify the cells, but help little in unravelling the wiring diagram, to say nothing of revealing what the cells are doing in the daily life of the animal. For these problems one needs a combination of approaches such as the Golgi method, autoradiography and the electron microscope, in anatomy, and single-cell recordings in physiology. Since many of these methods have been developed only recently, it is not surprising that beginnings have been made in understanding only a few areas of cortex.

Much of the work on cortex in the past 20 years has concentrated on sensory areas, which are more accessible to the neurophysiologist since they are close to the input end of the nervous system. For these few cortical regions some understanding of function in terms of structure seems to be evolving. An interesting and certainly a surprising result of this work is the discovery of structural patterns that were not apparent at all with the standard morphological techniques. One particular type of order, which we term 'functional architecture', seems only to be revealed by a combination of physiological and morphological approaches. What we mean by functional architecture will, we hope, become evident in the course of this paper, which presents a description of the known functional architecture of the primary visual cortex of the macaque monkey.

The geniculo-cortical pathway

Cells in the visual cortex tend to be grouped together according to their physiological properties. On the crudest level, all of the cells in this part of the cortex are obviously concerned primarily with vision. But within the visual cortex finer functional groupings of several kinds also occur, and the functional architecture is a description of these groupings. To understand the architecture one must therefore have some knowledge of the physiological properties of the individual cells. We accordingly begin with a summary of the single-cell physiology of the striate cortex, as it is presently understood. We propose to give only a rough sketch of the subject: those who wish to read further may consult the original papers (Kuffler 1953; Hubel & Wiesel 1959, 1962, 1968).

The position occupied by the striate cortex in the visual pathway is illustrated in figure 1, a diagram taken from Polyak (1957). The brain in this figure is seen from below. It is from a human rather than a macaque, but the pathways are very similar in the two species. The main components of the visual pathway are the retinas, the lateral geniculate bodies, and the striate cortex. About a million optic nerve fibres (axons of retinal ganglion cells) issue from each eye and pass

uninterrupted through the optic chiasm to the lateral geniculate bodies. (Some of the fibres end in the brain stem, especially in the superior colliculus.) At the chiasm a little over half of the optic fibres cross, and the other half (or slightly less) remain uncrossed. The redistribution takes place in such a way that the left lateral

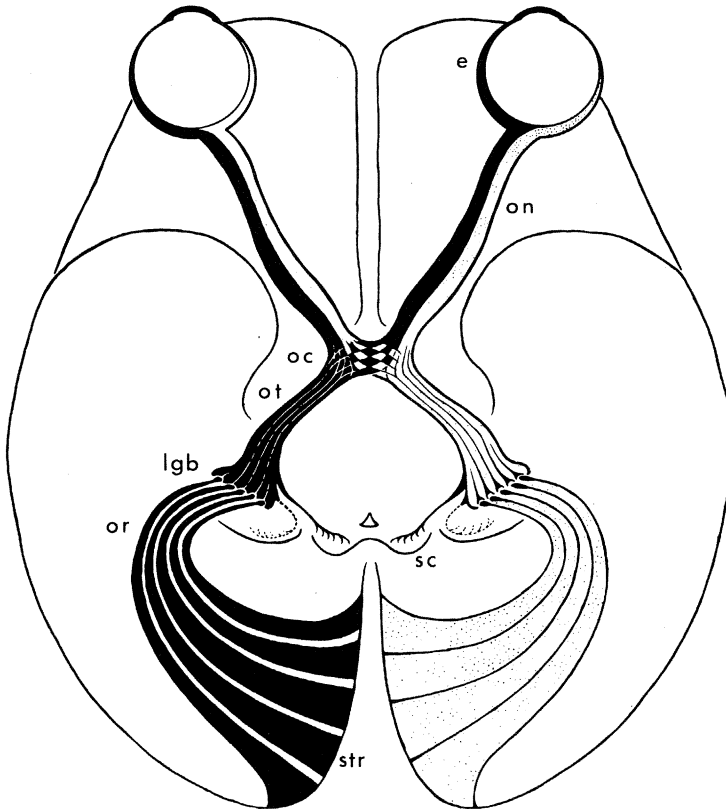


FIGURE 1. Diagram of the retino-geniculo-cortical pathway in a higher mammal. The brain is viewed from below; by skilful dissection the eyes and optic nerves have been removed from the orbits, and kept in their normal relationship to the brain. Up, in the diagram, is anterior. The right halves of each retina, shown in black, project to the right hemisphere (to the left, in the figure, since it is viewed from below): thus the right hemisphere receives input from both eyes and is concerned with the left half-field of vision. e, eye; on, optic nerve; oc, optic chiasm; ot, optic tract; lgb, lateral geniculate body; sc, superior colliculus; or, optic radiations; str, striate cortex. (Figure from Polyak, 1957.)

geniculate body receives axons from retinal ganglion cells in the two left half retinas, and hence is concerned with the right visual field; the right geniculate is similarly concerned with the left visual field. The lateral geniculate is in some respects quite complex; anatomically there are several cell types, and a variety of synaptic categories are seen (Guillery & Colonnier 1970). But compared with many other structures in the brain, and in particular with the cortex, the lateral geniculate body is simple: most geniculate cells receive synaptic input directly

from optic nerve fibres, and most of these cells in turn send their axons directly to the cortex. Thus it is not unfair to say that it is basically a one-synapse station.

The axons that form the output of the geniculates pass back in the white matter of the cerebral hemispheres to the striate cortex. The striate cortex is clearly more complicated, with at least 3 or 4 synapses interposed between the input and the output. The organization of this structure will be the subject of most of this paper. Finally, the axons that leave the cortex make their way to a number of different destinations: to other nearby cortical regions such as area 18, to the optic tectum, and, in a recurrent path, to the lateral geniculate bodies. The striate cortex should thus not be regarded in any sense as the end of the visual path – in fact it is probably very close to the beginning, and, as we will see, the behaviour of the cells, though it tells us the outcome of the first five or six steps in the processing of visual information, does not take us very far toward solving the ultimate problem of visual perception.

In studying the physiology of the visual pathway we have made use of methods developed by Hartline (1940), Kuffler (1953), Talbot & Marshall (1941), and others. Our general strategy has been to stimulate the retina in a natural way (i.e. with patterns of light) and to record the responses of single cells at one stage after the next, starting with retina, going on to the geniculate, and finally to the cortex. In this type of work we record with extracellular microelectrodes because our main interest is in the all-or-none impulses of the cells, and because firing patterns tend to be seriously distorted if a cell is penetrated by an electrode; to make such extracellular records from single cells for periods of many hours is today relatively easy. At any given stage one studies cell after cell, observing how each reacts to spots and patterns of light, gradually forming an overall idea of the behaviour of the cells in that structure. The procedure is then repeated at the next stage, and by comparing the two sets of results one may learn what kinds of analysis the second stage has made upon the input that it received from the first.

The primary visual cortex (also called 'striate cortex' and 'area 17' – the three terms are synonymous) can be said to have two main functions – there are certainly others, some known and perhaps many still to be discovered, but the two to be described here are very important. First, the visual input from the lateral geniculate body is rearranged in such a way as to make the cortical cells responsive to specifically oriented short line segments. Second, the cortex is the first point in the retino-geniculo-cortical path at which fibres carrying information from the two eyes converge upon single cells. Let us discuss each of these functions in turn.

Receptive field orientation

A retinal ganglion cell or a geniculate cell responds best to a roughly circular spot of light, the optimal size of spot varying from cell to cell, and for any one cell the spot must be presented in a particular part of the visual field (i.e. of the retina). The response may consist of a speeding up of the resting train of impulses,

or a slowing down. Because of the concentric, mutually antagonistic centre-surround receptive field arrangement (Kuffler 1953), a spot occupying exactly the centre of the receptive field is always more effective than one of larger size, and consequently more effective than diffuse light. The responses to various shapes of stationary stimuli are to a large extent predictable from the receptive-field maps;

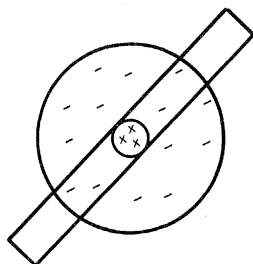


FIGURE 2. Centre-surround receptive field of a typical on-centre retinal ganglion cell. The diagram represents a small portion of the retina, or, what is equivalent, a small portion of the visual field. In the case of the retina, the retinal ganglion cell body is situated close to the centre of the region, and the region itself is the territory of retina containing receptors that make functionally effective connections (via other interposed retinal cells) with the ganglion cell. In a monkey the entire receptive field occupies a region a degree or so in diameter (about 0.3 mm, on the retina). The field centre varies from a few minutes of arc, for cells near the fovea, up to a degree or so, for peripheral cells. Shining light anywhere within the centre region (x) causes the cell to increase its firing rate, whereas shining light in the annular surround (—) produces a slowing in firing rate, with a transient discharge when the light is turned off (the off-response). Because of this antagonism between the two regions, a light shining over the entire field gives a much weaker response than light confined to the centre; the centre usually dominates, so that the response is 'on' in type. The slit-shaped stimulus illustrated gives a strong on-response, since it covers all of the centre region and only a fraction of the opposing surround. Cells in the lateral geniculate body have similar receptive fields. Many cells in retina and geniculate have just the reverse configuration, with inhibition from the centre of the receptive field and excitation from the surround.

for example a slit whose width is the same as the diameter of the receptive field centre will excite an on-centre cell (figure 2) even though some of the surround is illuminated. Apparently the centre and surround interact in such a way that a stimulus covering all the centre but only a fraction of the surround produces a strong centre-type response. These cells have fields with circular symmetry, and consequently respond roughly equally to all orientations of a line stimulus.

In the cortex we first find cells with orientation specificity. By this we mean that a cell responds to a specifically oriented stationary or moving straight line segment presented within a restricted receptive field. An example of the behaviour of such a cell is shown in figure 3. This cell, recorded, say, from the right hemisphere, responds only to stimuli within a roughly rectangular area in the left half field of vision. To evoke consistent strong responses it is not enough to use a circular spot of light, however: the region must be crossed by a slit of light in 01h30–07h30 orientation. The slit may be kept stationary and presented anywhere within the

rectangle, or it may be swept across the receptive field in the direction of the arrow. Changing the orientation so that the slit is misoriented by more than 10° – 20° usually results in a marked decline in the response. The sensitivity to variations in orientation differs to some extent from cell to cell, but almost all cells fail to respond long before the misorientation reaches 90° . A moving stimulus is

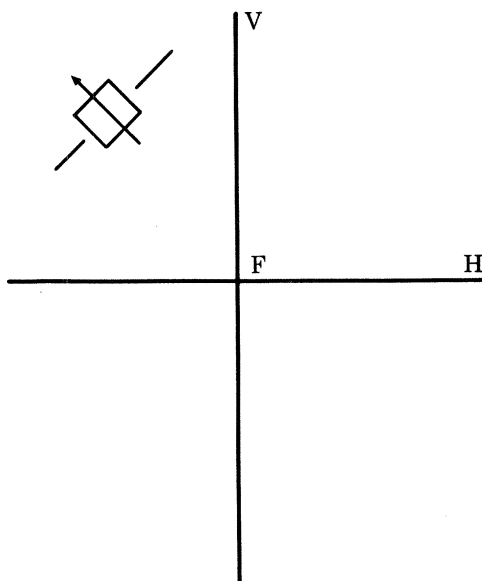


FIGURE 3. Receptive field of a complex cell in the striate cortex. Axes represent the vertical (V) and horizontal (H) meridian of the visual field, crossing at the centre of gaze F (the projection of the fovea). The cell is recorded from the right hemisphere, so that the receptive field, represented by the rectangle, is in the left field of vision. No responses are observed when this region is illuminated diffusely, and small circular spots produce at most only weak or inconstant responses. An appropriate line, however, gives strong reproducible responses. The cell in this example gives optimal responses to a long narrow slit oriented in a 01 h30–07 h30 manner; responses are especially strong if the line is swept over the area in the direction indicated by the arrow.

generally very powerful in evoking a discharge (i.e. in raising the impulse frequency of the cell above the resting level). In many cells movement of a slit, or even a small spot, in one direction (here, up-and-left) evokes a much more vigorous response than movement in the reverse direction (down-and-right), and often movement in one of the two directions will evoke no response at all. The mechanism for this directional selectivity for movement is still unknown, but must depend on connections within the cortex, since in cat and monkey such selectivity has not been described at the geniculate level (see, for example, Wiesel & Hubel 1966). In lower vertebrates such as frog (Lettvin, Maturana, McCulloch & Pitts 1959), and even in some mammals such as the rabbit (Barlow, Hill & Levick 1964) and cat (Cleland & Levick 1974; Stone & Fukuda 1974), some retinal ganglion cells show directional selectivity, but these cells probably project mainly to the

superior colliculus. The ideas proposed by Barlow *et al.* to explain directional selectivity in the rabbit retina may also apply to the cat and monkey cortex, but there are important differences which make it unlikely that exactly the same mechanisms are used. While retinal cells in frog and rabbit may be directionally selective, they show no selective responses to specifically oriented line segments. In cat and monkey cortex, directional selectivity is intimately bound up with orientation specificity, since the optimum orientation of a slit is always 90° to the optimum direction of movement.

The optimal orientation of the line varies from cell to cell, some cells preferring vertical, others horizontal, and still others oblique. All possible orientations are represented roughly equally – there being no obvious preponderance of cells tuned, for example, to vertical or horizontal stimuli. The line stimulus may be produced in any one of three ways: most cells respond best to a light line on a dark background; many others, however, respond selectively to dark lines on a light background, and some prefer borders between light and dark.

Cells in the primary visual cortex are not all specifically sensitive to particular orientations. Roughly four classes of cells can be distinguished, in a series of ascending complexity (Hubel & Wiesel 1959, 1962, 1965, 1968). These are termed ‘circularly symmetric’, ‘simple’, ‘complex’ and ‘hypercomplex’. We assume that cells at each stage receive their major input from cells at the previous stage, with the circularly symmetric cells receiving their inputs predominantly from geniculate cells. Circularly symmetric cells, as their name implies, show no preference to any particular orientation of lines, and, indeed, seem similar in their properties to geniculate cells. Simple cells are the first in the hierarchy to show orientation specificity, so that the rearrangements responsible for orientation specificity are presumed to take place between the circularly symmetric and the simple cells. A simple cell responds to an optimally oriented line in some narrowly defined position: even a slight displacement of the line to a new position, without change in orientation, renders the line ineffective. A complex cell, on the contrary, is probably just as specific in its orientation requirements as the simple cell, but is far less particular about the exact positioning of the line. Such a cell will respond wherever a line is projected within a rectangle such as that of figure 3; if the cell responds to a dark or light line (rather than to an edge), increasing the line’s thickness beyond some value that is far less than the width of the receptive field renders it ineffective. Thus a patch of light as large as the entire receptive field evokes no response at all. This is equivalent to saying that diffuse light is ineffective. As mentioned above, sweeping the line over the receptive field usually evokes a sustained discharge from the cell. Hypercomplex cells, finally, resemble complex cells in all respects but one: extending a line beyond the region from which responses are evoked produces a marked reduction or complete abolition of the response. A few years ago Bishop & Henry (1972) described in cat cortex a type of cell whose properties resembled those of simple cells, except that extending the line led to a drop in the response. Schiller, Finlay & Volman (1976) and we have seen such cells in

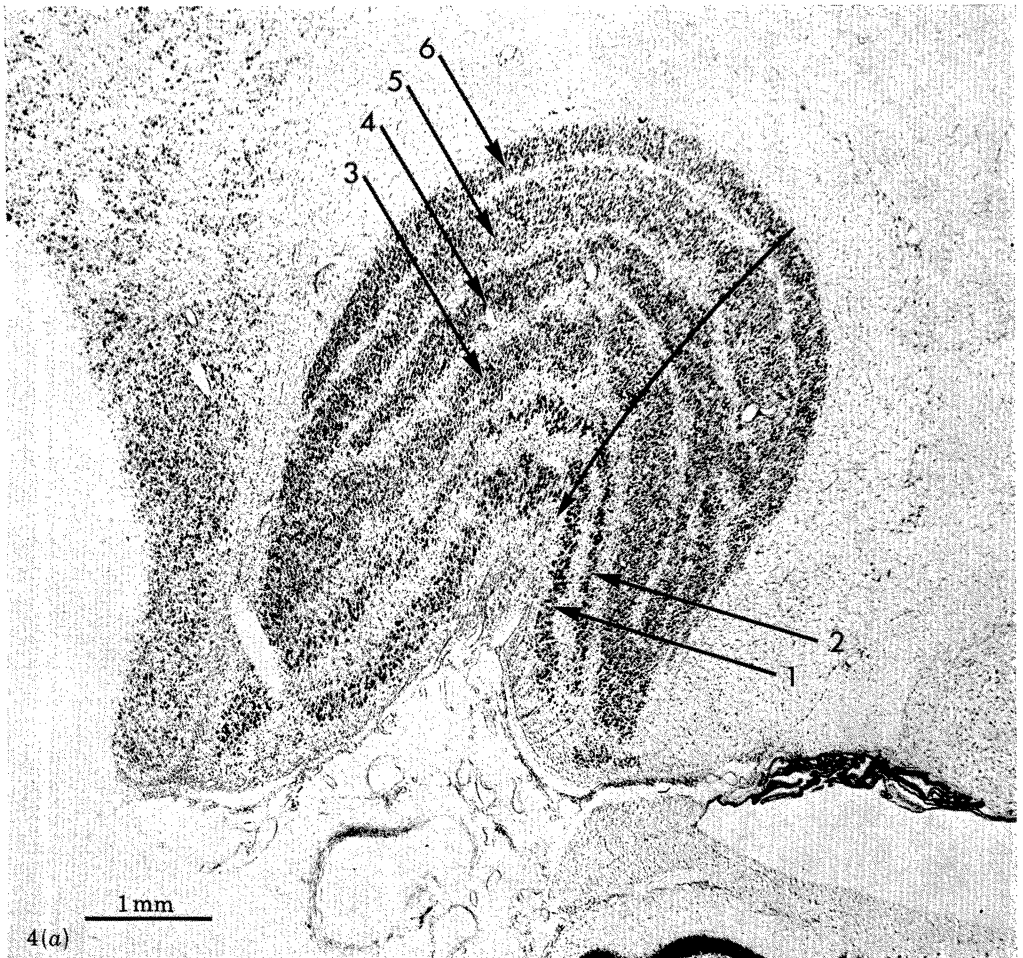


FIGURE 4. (*a*) Coronal section through the right lateral geniculate body of a normal adult macaque monkey, cresyl violet stain. Cells are divided into six layers: Nos. 1, 4, and 6 receive input from contralateral (left) eye; 2, 3, and 5 from the ipsilateral. Each layer contains a detailed and orderly representation of the contralateral field of vision; moving along one layer thus implies a movement through the visual field dictated by this representational map. The six maps of the visual field are in precise register, so that corresponding to movement along a radial line, such as the arrow, there is no movement in the visual field. (*b*) One form of evidence that certain geniculate layers receive input from the contralateral eye, and others from the ipsilateral. The right eye of this rhesus monkey was removed at the age of 2 weeks, and the brain examined at 19 months. Coronal sections, Nissl stain (cresyl violet). On each side cells in layers with input from the right eye are markedly atrophic and appear pale. Compare figure 4*a*. (From Hubel, Wiesel & LeVay 1977.)

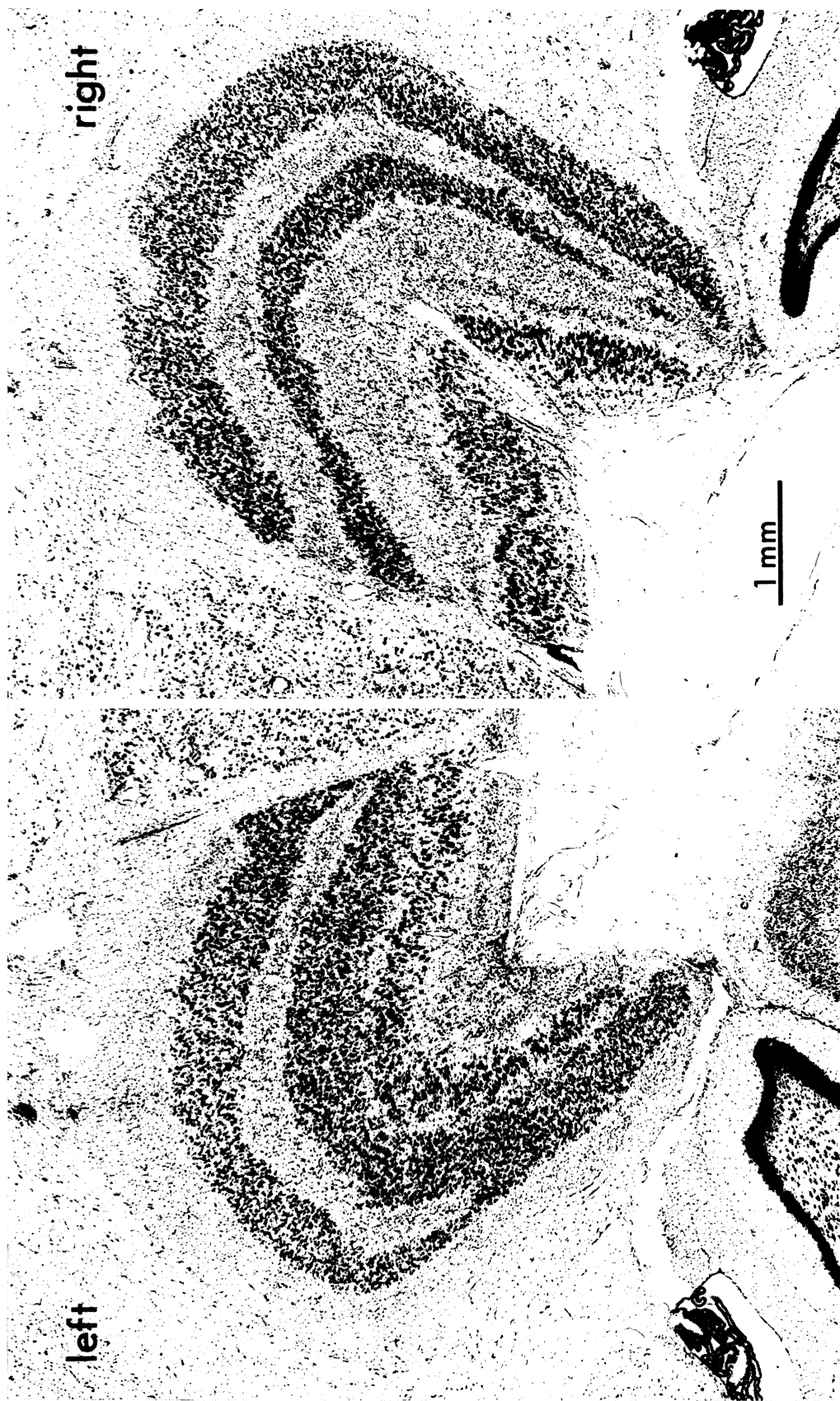


FIGURE 4. (b) For description see previous page.

monkey cortex, and Gilbert (1977) has confirmed their presence in the cat striate cortex. It is thus clear that there are two categories of hypercomplex cells. Different cells show different degrees of suppression when a line is made very long, suggesting that the distinction between hypercomplex cells on the one hand and simple and complex on the other may not be very sharp; rather there seems to be a continuum, from cells that respond very well to cells that do not respond at all, to long lines.

In this paper no attempt will be made to describe these different cell types in detail. It is enough to point out that a complex cell can most easily be understood by supposing that it receives inputs from many simple cells, all with the same orientation preference. Similarly a hypercomplex cell's properties can be explained by assuming that it receives inputs from complex cells (or, for the less common type, from simple cells) all with the same preferred orientation. One would therefore predict that cells whose fields are in a particular part of the visual field and which prefer the same stimulus orientation would be highly interconnected, whereas cells of different orientation preference would not be expected to be interconnected except possibly by inhibitory synapses. These predictions will be referred to again in interpreting the significance of the orientation columns described below.

One may add, parenthetically, that the organization suggested here, while hierarchical in a rough sense, is certainly not rigidly so. For example, complex cells probably do not all project to hypercomplex cells; many of those situated in layer V, for example, project to tectal cells (Palmer & Rosenquist 1974; Toyama, Matsunami, Ohno & Takashiki 1974), while many VIth layer cells project back to the lateral geniculate body (Gilbert & Kelly 1975; Lund *et al.* 1975). Despite a certain degree of dissension over the idea of an underlying hierarchy, there is considerable evidence to support it (Kelly & Van Essen 1974; Gilbert (1977).

Binocular convergence

To understand the second main function of the striate cortex, the combining of influences from the two eyes, we must return for a moment to the lateral geniculate body, for this, as already mentioned, is the first structure in the path to receive input from both eyes. The geniculate nevertheless seems to go well out of its way to avoid any significant mixing of the inputs from the two eyes. Figure 4*a*, plate 1, shows a coronal section through the right lateral geniculate of a macaque monkey, in which cell bodies are stained by the Nissl method. The geniculate consists of six layers stacked one above the other rather like a club sandwich, each plate being many cells thick. The terminals coming in from the two eyes distribute themselves to these six layers in such a way as to produce six topographic maps of the contralateral half field of vision; all six maps are in register so that in a radial pathway traversing the six layers, as indicated by the arrow, all the receptive fields of the cells encountered will have virtually identical positions in the visual fields (Brouwer & Zeeman 1926; Bishop, Kozak, Levick & Vakkur 1962; Hubel & Wiesel 1961).

In the geniculate of many primates including man the distribution of the

terminals from the two eyes takes a very special form. Each of the six layers receives input from one eye only. For the right lateral geniculate the most dorsal layer has input from the left eye, and beginning with this layer the sequence proceeds left-right, left-right, right-left. Why a reversal should occur between the dorsal four and the ventral two layers is a mystery, but, for that matter, why there is any sequence at all is still an unsolved riddle. The important point for our present purposes is that each layer, and consequently each individual cell in each layer, receives input from only one eye. The geniculate in the monkey, then, consists almost entirely of monocular cells. Layer VI of the visual cortex sends a strong projection to the geniculate (Lund *et al.* 1975), and many cells in that layer are binocular. There is therefore some reason to expect an indirect influence of some kind on a geniculate cell from both eyes, by way of the cortex. Such an influence has been demonstrated in the cat geniculate, where there are also opportunities for direct interchange of information across the layers (Sanderson, Darian-Smith & Bishop 1969; Guillery 1966), but not, so far, in the monkey. The original evidence that the different layers correspond to single eyes was based on the degeneration of cells that occurs on eye removal, as shown by Minkowski in 1920. An example of a result similar to Minkowski's is shown in figure 4*b*. There is now very much additional evidence to support Minkowski's finding, both physiological and anatomical (see figure 21).

The fibres carrying information to the cortex are thus for all practical purposes strictly monocular. The process of convergence of information from the two eyes occurs first in the primary visual cortex. It is, however, delayed to a point beyond the first two cortical stages, for the circularly symmetric cells and the simple cells are almost all monocular, whereas among the complex and hypercomplex cells binocular input is very common. Nevertheless even at these stages binocular cells make up only a little more than half of the population.

Now we can ask a very specific question designed to reveal more about the way in which the inputs from the two eyes combine. If we record from a binocular cortical cell, a complex cell for example, we may map its receptive field in one eye, meanwhile keeping the animal's other eye closed. Suppose the result is a map like that of figure 3. We then transfer the mask to the other eye and repeat the procedure. If the cell is a binocular cell, how similar will the receptive fields be in the two eyes? The answer is that they are practically identical (Hubel & Wiesel 1959; 1968). This is illustrated in figure 5. The positions of the receptive fields in the two retinas match as perfectly as one can measure: the fields are the same distance from the fovea and in the same direction, and thus in the visual fields the two receptive fields are superimposed. The receptive-field complexity is the same, the orientations are identical, the direction preferences, if any, are the same. In short, everything one learns about the cell through one eye matches precisely what one learns through the other. It is therefore no surprise to find that when both eyes are used together and properly lined up, a stimulus usually evokes a much more vigorous response than when either eye is used alone.

We can say, then, that the cell receives inputs from the two eyes and that these inputs are qualitatively virtually identical – which means that the wiring in the two paths, up to their point of convergence, must be very similar. Only in one respect are there differences: the responses that are obtained on comparing identical stimuli in the two eyes may not be equal. For many cells the responses from one of the two eyes are consistently greater than those from the other; some cells,

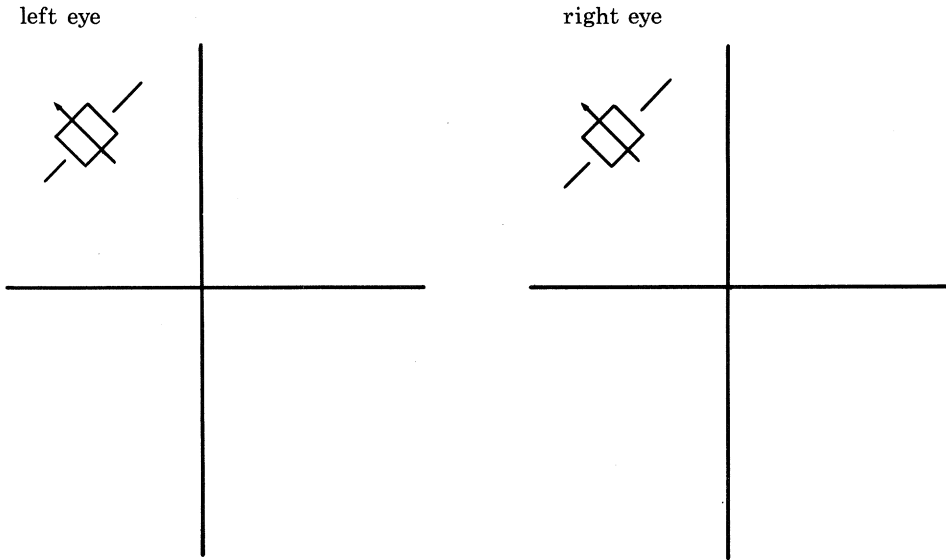


FIGURE 5. Receptive fields of a binocular cell in area 17. Each diagram shows the visual field as seen by one eye; normally the two would be superimposed, but they are drawn separately here for clarity. The fields in the two eyes are, as closely as one can measure, similar in size, shape, position and orientation, and respond to the same form of stimulus, in this case a moving slit.

the monocular ones, receive input only from one of the eyes; some receive equal inputs. There are, in fact, all shades of relative ocular dominance in the population, from complete dominance by one eye, through equality, to complete dominance by the other. We can sum this up by saying that cortical cells receive qualitatively similar inputs from the two eyes but that for any given cell the densities of the two inputs are not necessarily the same.

Everything we have said up to now applies not only to the normal adult macaque monkey, but, with one minor exception to be discussed below, also to the newborn monkey, lacking any visual experience (Wiesel & Hubel 1974). It is hard to escape the conclusion that the connections responsible for the findings so far outlined, and indeed also for the architecture to be described, are genetically determined. At least their formation is not dependent on visual experience. This will be discussed in more detail later in the paper.

To sum up this abbreviated account of the physiology, we may think of a cell in

area 17 of the monkey as responding optimally when a number of stimulus variables are correctly specified. The cell may be described, then, by its degree of complexity, the $x-y$ coordinates of the position of the receptive field, the receptive field orientation, the ocular dominance, and the degree to which there is directional preference to movement. Such a list of specifications is analogous to the tag showing the price, sleeve length, percentage of wool, and so on, attached to a suit in a department store.

The drawing up of such a list allows us to pose a key question that leads to new information on the architecture of the cortex. Are cells with similar qualities – similar orientations or similar field positions – aggregated together in the cortex, (as suits often are in a store), or are they scattered at random through the cortex with respect to these variables? The answer to this question provides some strong hints as to how the cortex carries out its functions.

FUNCTIONAL ARCHITECTURE

1. *Anatomy*

Before addressing directly the subject of functional architecture we must look briefly at the anatomy of the striate cortex. The entire cortex is a plate of cells about 2 mm thick and in the macaque monkey about 13 cm² in surface area. Figure 6*a*, plate 3, shows a view of the macaque brain from behind. The visual cortex is partly buried, and partly exposed on the outer surface of the occipital lobe and visible in the picture. The exposed part extends forward to the dotted line (the 17–18 border), which lies a millimetre or so behind the lunate sulcus (L). As one proceeds medially to the midline the striate area bends around and continues as a complicated buried fold, some of which is roughly parallel to the exposed surface but one level deeper. The contralateral half visual field is mapped systematically onto the striate cortex, just as it was in the case of the lateral geniculate. The foveal projection is far lateral, roughly at x in figure 6*a*, and as one moves from x in the direction of the arrow the corresponding points in the visual field move out from the foveal projection along the horizon. As one moves medially from x along the dotted 17–18 border the corresponding points in the visual field move downwards from the fovea along the vertical midline.

The deep groove in the right hemisphere represents a knife cut made in blocking the cortex for histology. If one were to stand in this groove and look to the left one would see in cross section the smooth outer part of area 17 as well as the buried fold: this is shown, in a Nissl stained section, in figure 6*b*, plate 4. The arrows mark the 17–18 boundaries. The outer convexity (A) and the buried fold (B) are of course all part of the same folded continuous surface.

The topography of the macaque visual cortex is in itself not of major interest, but the landmarks just pointed out will be needed in the descriptions that follow.

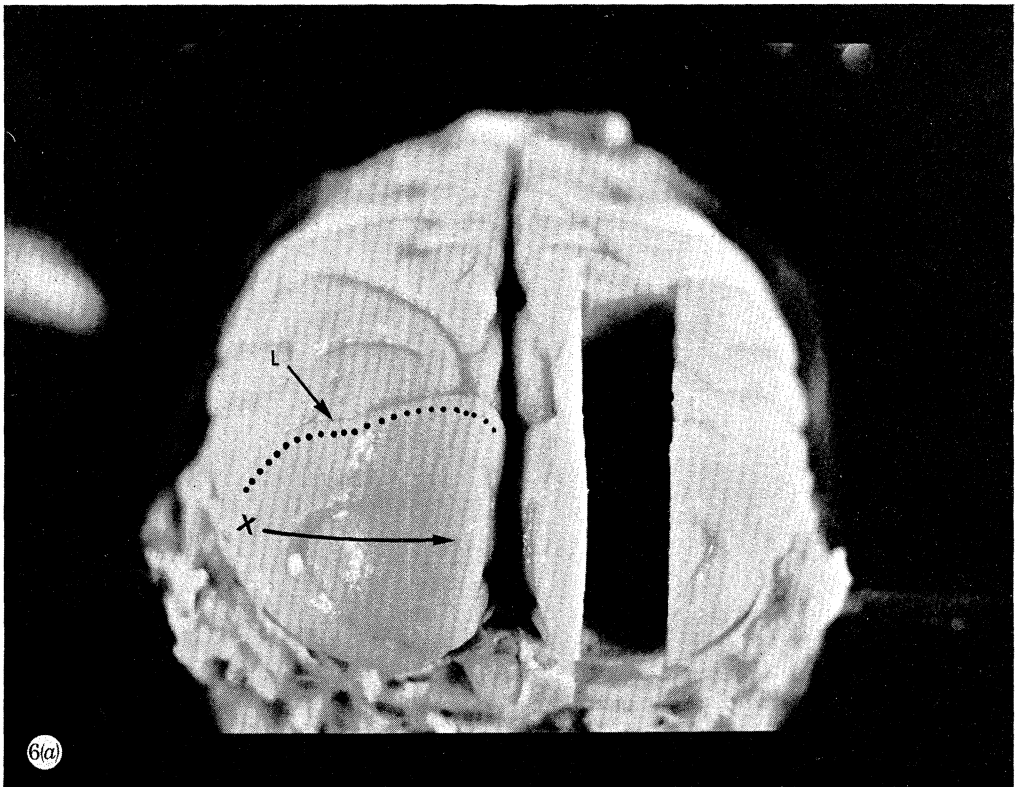


FIGURE 6. (*a*) Brain of a macaque monkey, perfused with formalin, viewed from above and behind. The occipital lobe is demarcated in front by the lunate sulcus (L) and consists mainly of the striate cortex, which occupies most of the smooth surface, extending forward to the dotted line (the 17–18 border). If followed medially area 17 curves around the medial surface of the brain and continues in a complex buried fold, a part of which lies underneath the convexity and parallel to it. X marks the projection of the fovea; movement in the direction of the arrow corresponds to movement out along the horizon; movement along the dotted line, to movement down along the vertical midline of the visual field. The groove in the right hemisphere was made in removing a parasagittal block of tissue to produce the cross section of figure 6*b*. (*b*) Low power Nissl-stained section from a parasagittal block such as that of figure 6*a*. It is what would be seen if one could stand in the groove of 6*a* and look to the left. A marks the outer convexity; B the buried fold, and arrows indicate the 17–18 borders, the upper right one of which is indicated by the dotted line in figure 6*a*.

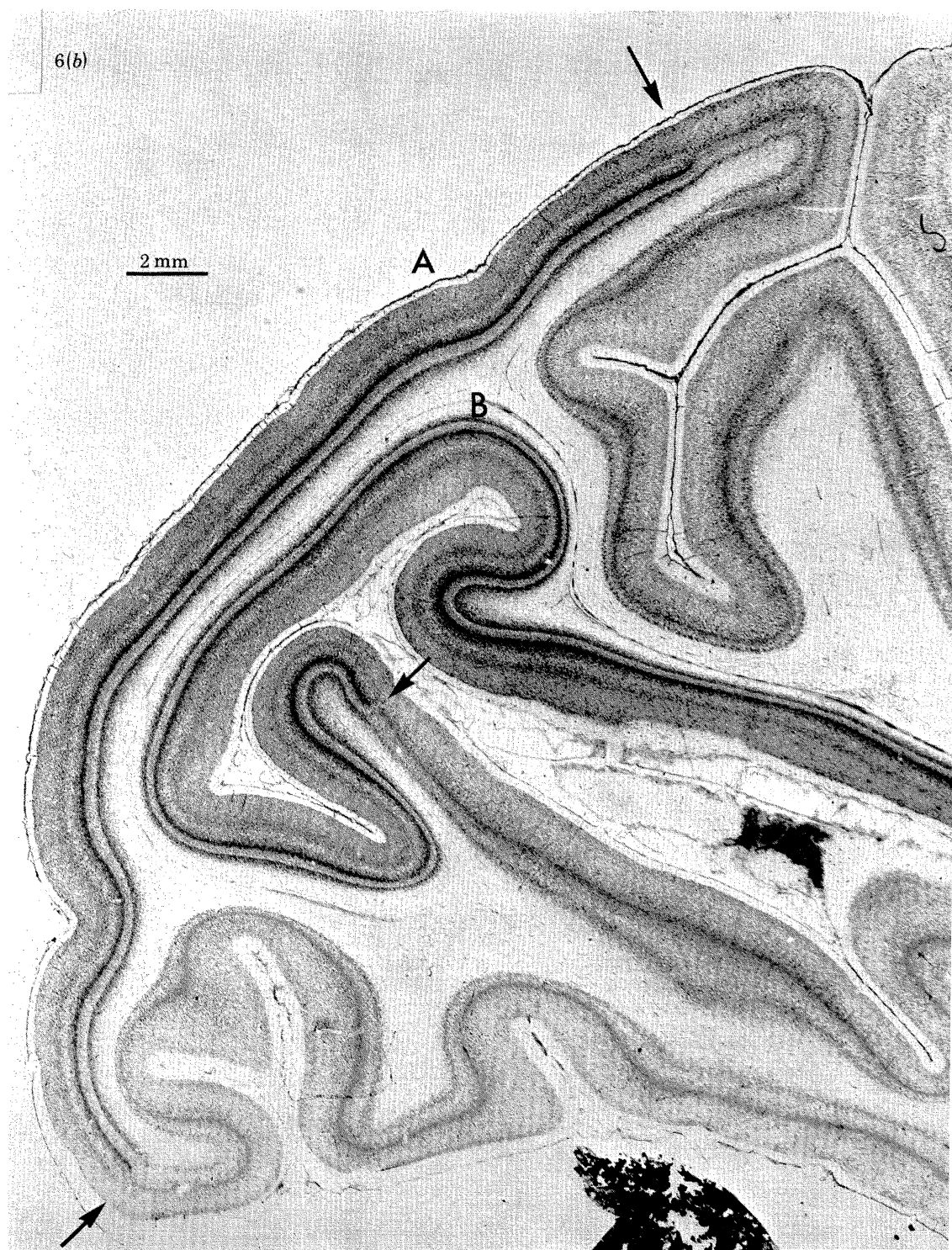


FIGURE 6(b). For description see previous page.

2. Position in the visual field

Besides the richness of the layering pattern formed by alternating zones of concentration and rarefaction of cells, the most striking feature of this part of the cortex is its remarkable uniformity as one proceeds in a direction parallel to the surface. There are no great differences in layering pattern or thickness that cannot be accounted for by the folding or by the oblique angle at which the cortex is inevitably cut in some regions. This uniformity is at first glance surprising. Physiologically it is clear that at every level up to and including area 17 the visual fields are analysed in much more detail in regions near the fovea than in the periphery. The most obvious manifestation of this non-uniformity of analysis is the variation of receptive field size with distance from fovea (with 'eccentricity'). In retinal ganglion cells and in cells of the geniculate, for example, the receptive fields, and especially the receptive-field centres, are very small in the most central region and become progressively larger with increasing eccentricity (Wiesel 1960; Hubel & Wiesel 1960, 1961; Wiesel & Hubel 1966; Hoffman, Stone & Sherman 1972). This of course has a psychophysical parallel in the greatly heightened visual acuity in the foveal region compared with the periphery. From all of this it is only to be expected that the neural machinery necessary to take care of one square degree of fovea should be much more massive than that subserving the same area of visual field periphery. In the retina the difference is obvious histologically. Figure 7, plate 5, shows that near the primate fovea the ganglion cell layer is many cells thick, whereas peripherally there are not enough cells to make up a single continuous layer (Van Buren 1963). In the cortex one might similarly expect a relative thickening in parts subserving regions of visual field in or near the fovea, but if there is any at all it is so subtle that careful control of plane of sectioning would be required to be certain of it: certainly there is no variation in thickness remotely approaching what is seen in the layer of retinal ganglion cells.

The cortex, in fact, finds an entirely different way of devoting proportionately more machinery to central visual field areas than to peripheral. The amount of retinal surface devoted to a degree of visual field is of course constant; it must be for obvious optical reasons. In the cortex the corresponding amount of surface is far from constant, being large in the foveal region and falling off progressively as eccentricity increases. This variation in magnification (mm cortex/degree visual field) was first systematically analysed by Daniel & Whitteridge (1961). Magnification in fact seems to vary with eccentricity in such a way as to guarantee a uniform thickness of cortex (Hubel & Wiesel 1974*b*). Instead of being heaped up in the region representing central vision, the cortex is spread out, to just the amount required to preserve uniformity.

The orderliness of this arrangement can be seen by examining the positions of receptive fields as an electrode moves through the cortex sampling cell after cell. In a vertical penetration (here and elsewhere we mean vertical not in a literal sense, but simply in the sense of perpendicular to the surface) the fields are all

clustered in some particular part of the visual field – not surprisingly, given the precise map of the field of vision on the cortex. The receptive fields recorded in a vertical penetration in fact show considerable overlap. They are not precisely superimposed, however: there is not only some variation in size, but also a certain amount of apparently random scatter in position. In any one penetration the fields collectively cover an area several times the size of an average receptive field, as illustrated in figure 8*a*. For convenience we can refer to this areas as the *aggregate field* of any point on the cortical surface.

Both field size and the amount of scatter vary from layer to layer, being smallest in layer IVc, largest in layer V and intermediate in the others. Thus for any point on the cortex we can obviously speak of the aggregate field for an individual layer. (The aggregate field for the full cortical thickness will then be about the same as the aggregate field for layer V.)

Now consider what happens as an electrode is moved not vertically, but horizontally through the cortex, sampling cell after cell in a given layer. Over a short distance one will again find a random scattering of receptive fields, again over a territory several times the size of any one field; the exact size, as just mentioned, will vary with the layer one is traversing. Let us suppose, to be specific, that the electrode is recording from layer III, where the field sizes and scatter are not huge, as in layer V, nor tiny as in IVc, but somewhere in between. As the penetration progresses one begins to detect an overall drift in field position, superimposed on the random scatter, in a direction dictated by the topographic map of the visual field upon the cortex. It requires a traverse of about 1–2 mm through the cortex to produce a drift equal to the size of the aggregate field, that is, a drift sufficient to produce a displacement of the receptive fields into territory completely distinct from the original one (figure 8*b*). The interesting thing is that 1–2 mm is what is required for such a displacement regardless of where in area 17 the penetration is made (figure 9). For a more peripheral part of the visual field, receptive-field sizes and scatter are both larger and consequently the aggregate field is larger; a 1–2 mm traverse along the cortex gives a drift in fields that is likewise larger, in exact proportion. At an eccentricity of 45° the aggregate field is about 3° and a 1–2 mm displacement shifts this territory by about 3° . At 22° the figure is $1\frac{1}{2}^\circ$, at 7° it is about 0.5° , and in the fovea about 0.1° . The overall law is that for this layer a 1–2 mm displacement along the cortex is about enough, on the average, to displace the aggregate field into an entirely new terrain. The figure of 1–2 mm will be somewhat greater if one studies the deep part of layer III or layer V, and much less for layer IVc or layer II. This suggests that over the entire visual field a region whose size is that of the aggregate field is subserved by the machinery contained in a block of cortex with a surface area of about $2\text{ mm} \times 2\text{ mm}$. The block everywhere subserves the same function – the field sizes and scatter for the incoming geniculate fibres vary, but the number of fibres is probably constant (Clark 1941), and what is done with the input by the cortical machine is probably the same everywhere. Thus diagrams such as those of figure 8 will be similar

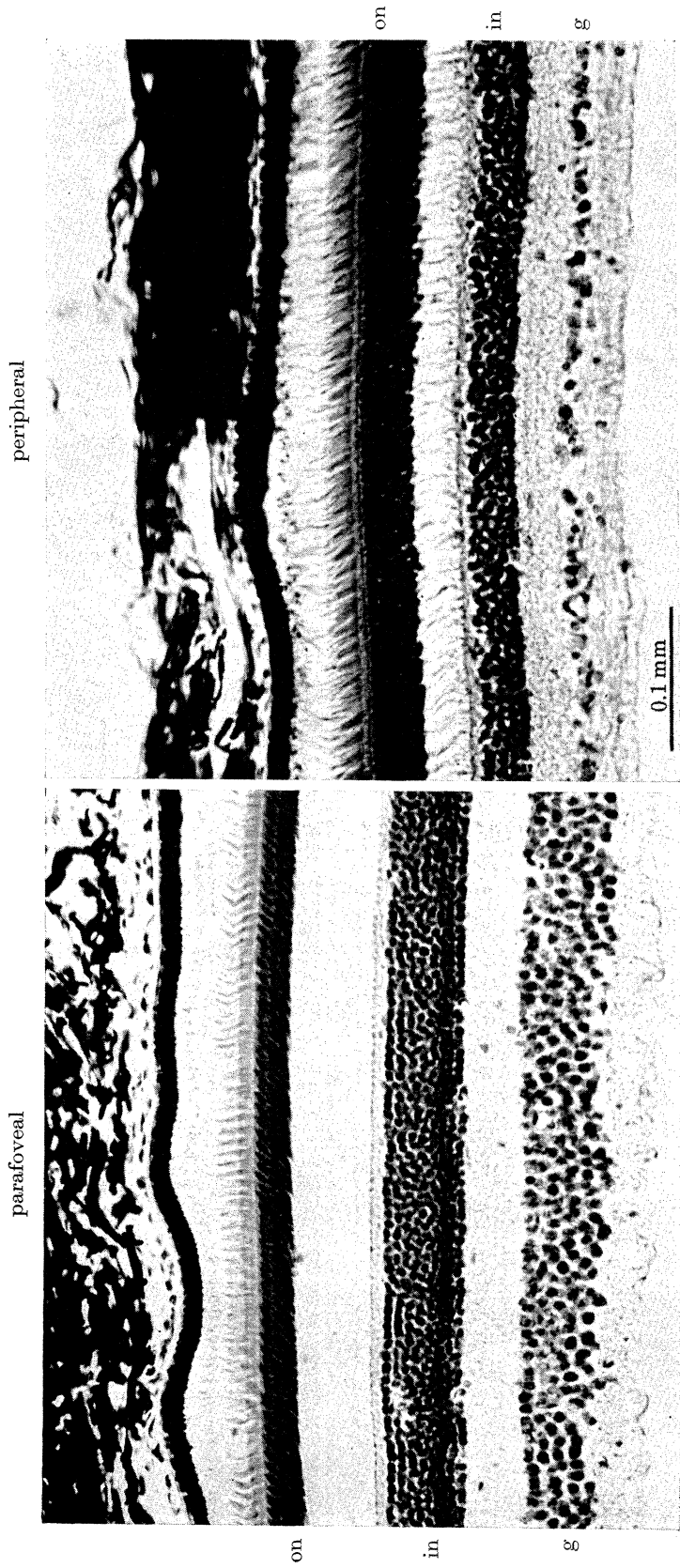


FIGURE 7. Comparison of ganglion cell layer of monkey retina near fovea and in the periphery. Cross sections of a macaque monkey retina, stained with hematoxylin-eosin, from the parafoveal region and the far periphery. on, outer nuclear layer; in, inner nuclear layer; g, ganglion cell layer. Note how retinal ganglion cells form a layer about five cells deep in the parafoveal region, but constitute only a thinly populated layer in the periphery.

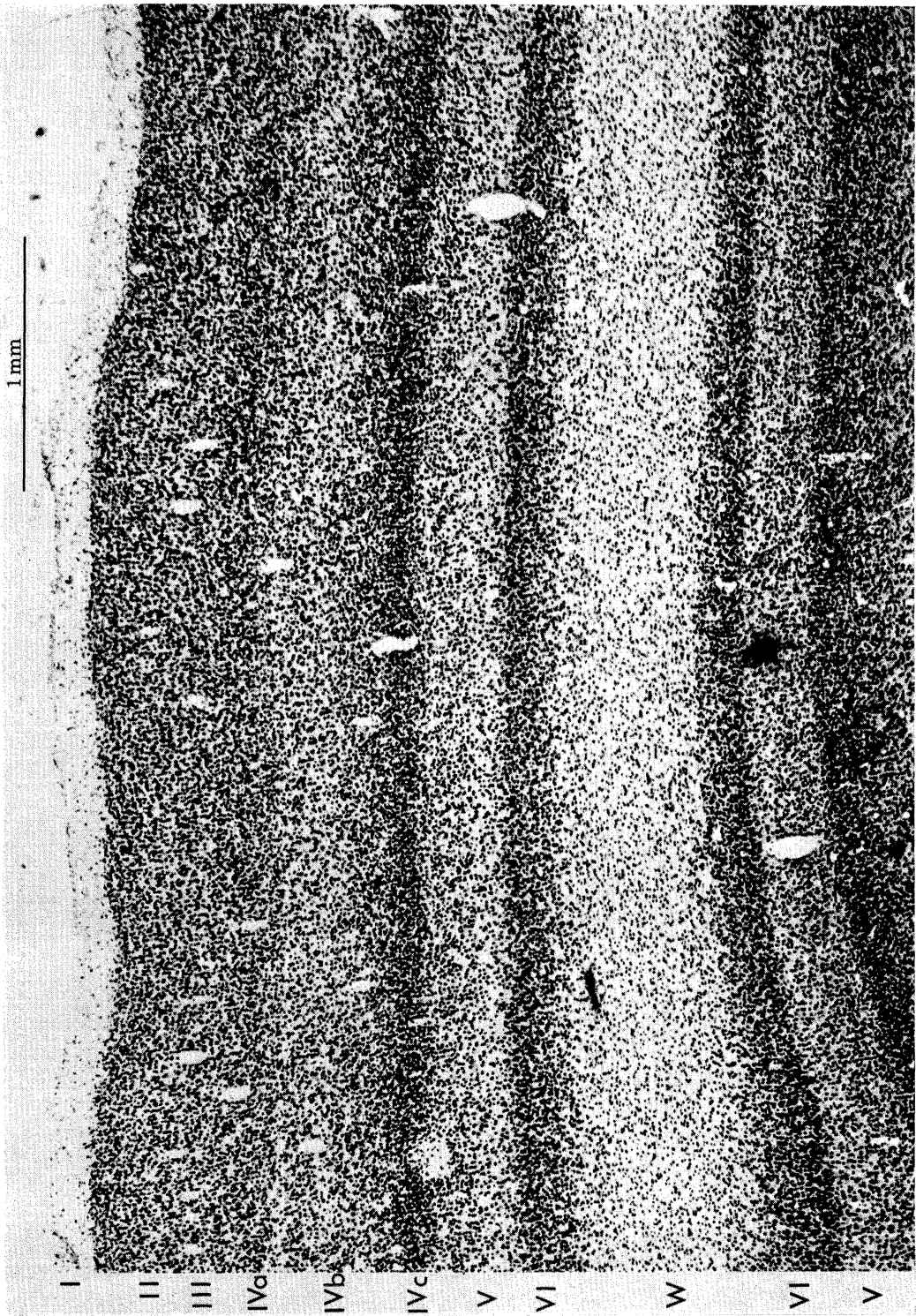


FIGURE 10. Cross section through monkey striate cortex showing conventional layering designations. W, white matter. Deeper layers (VI, V) of the buried fold of cortex are shown in the lower part of the figure (compare figure 6*b*). Cresyl violet.

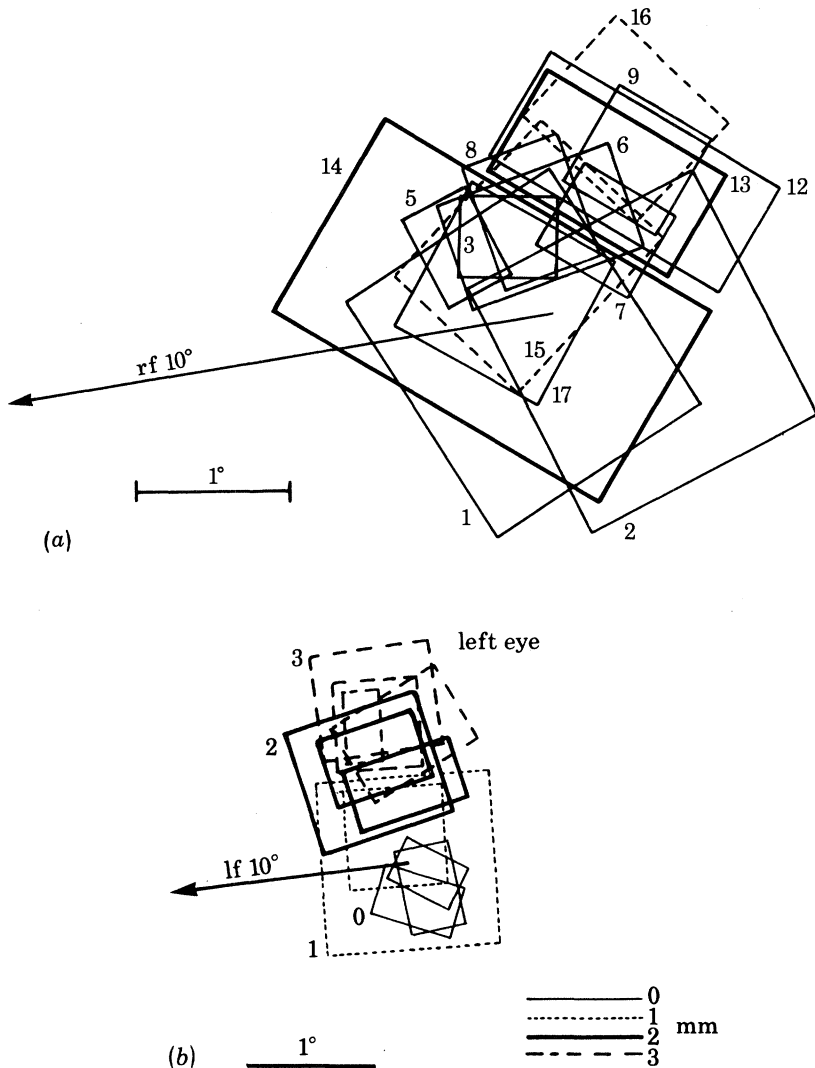


FIGURE 8. (a) Receptive-field scatter: Receptive-field boundaries of 17 cells recorded in a penetration through monkey striate cortex, in a direction perpendicular to the surface. Note the variation in size, and the more or less random scatter in the precise positions of the fields. The penetration was made in a part of the cortex corresponding to a visual field location 10° from the centre of gaze, just above the horizontal meridian. Fields are shown for one eye only. Numbers indicate the order in which the cells were recorded. (From Hubel & Wiesel 1974*b*.) (b) Receptive-field drift: Receptive fields mapped during an oblique, almost tangential penetration through striate cortex, in roughly the same region as in *a*. A few fields were mapped along each of four $100\ \mu\text{m}$ segments, spaced at $1\ \text{mm}$ intervals. These four groups of fields were labelled 0, 1, 2 and 3. Each new set of fields was slightly above the other, as predicted from the direction of movement of the electrode. Roughly a $2\ \text{mm}$ movement through cortex was required to displace the fields from one region to an entirely new region. (From Hubel & Wiesel 1974*b*.)

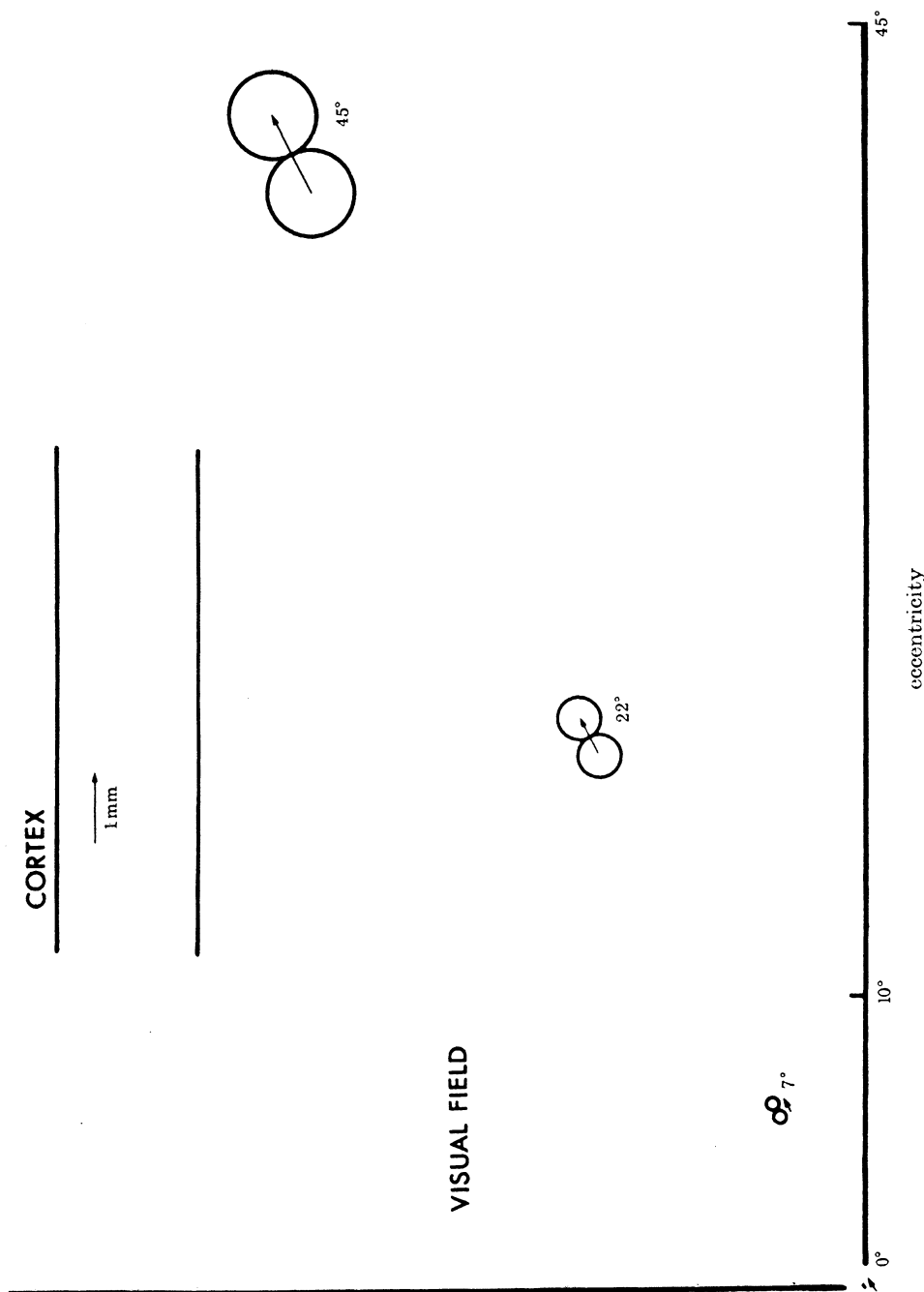


FIGURE 9. Variation of receptive-field drift with eccentricity: The diagram represents one quadrant of the field of vision, and the circles represent aggregate receptive fields, the territory collectively occupied by receptive fields of cells encountered in a micro-electrode penetration perpendicular to the cortical surface. Each pair of circles illustrates the movement in aggregate receptive field accompanying a movement along the cortex of 1–2 mm. Both the displacement and the aggregate field size vary with distance from the fovea (eccentricity), but they do so in parallel fashion. Close to the fovea the fields are tiny, but so is the displacement accompanying a 1–2 mm movement along the cortex. The greater the distance from the fovea, the greater the two become, but they continue to remain roughly equal. (From Hubel & Wiesel 1974*b*.)

wherever the penetration is made in the striate cortex, except that the scale will differ.

The dimension of 1–2 mm is an interesting one, for studies of the cortex by silver degeneration methods (Fisken, Gary & Powell 1973) show that the longest intracortical connections extend only for a few millimetres, and most are under 1–2 mm. (The longest connections probably involve cells of layer V and deep III, and the shortest, cells in IVc.) This means that there is little or no opportunity for signals entering the cortex in one place to make themselves felt at points more than 1–2 mm away. As a corollary to this it may be added that the striate cortex must be analysing the visual world in piecemeal fashion: information about some region in the visual field is brought to the cortex, digested, and the result transmitted on with no regard to what is going on elsewhere. Visual perception, then, can in no sense be said to be enshrined in area 17 – the apparatus is simply not made to analyse a percept that occupies more than a small region of visual field. All of the single cell physiology in fact suggests that area 17 is concerned simply with what may be thought of as building blocks for perception.

To sum up, a 1–2 mm square of cortex subserves an area of visual field roughly equal to the aggregate field in that part of the cortex. In this way magnification is adjusted to receptive field size so that the cortex can be everywhere uniform. In the paragraphs that follow it will be shown that each 1–2 mm block of cortex contains just enough machinery to analyse its region of visual field, for all line orientations and for both eyes.

3. Complexity and binocularity according to laminae

We turn now to the layering of area 17, which is shown at higher power in figure 10, plate 6. The afferents coming from the lateral geniculate terminate at several levels – layers IVa, IVc and VI, and perhaps also layer I (Hubel & Wiesel 1972). The great majority of terminations are, however, in IVc. The subsequent wiring is not fully known, but several synapses are required before the information reaches cells whose axons project out of the cortex (Lund 1973). If we examine the properties of cells layer by layer, two salient findings emerge. First, there is a correlation between complexity and layering, at least to the extent that the least complicated cells, the circularly symmetric geniculate-like cells, are located mainly in layer IVc. Simple cells seem to be located mainly in IVb; they are perhaps also present in VI – at least they have been found there in the cat (Hubel & Wiesel 1962; Gilbert 1977). Complex and hypercomplex cells are found, in our experience, only in II, III, V, and VI. It is a relief, at any rate, to find the simplest cells at the input end of the cortex.

The second fact about lamination involves binocular convergence. Cells in layer IVc are almost exclusively monocular. This of course is consistent with our previous statement that the concentric cells are almost all monocular. Cells in IVb, including the simple cells found there, are predominantly monocular, whereas over half of those in II, III, V, and VI are binocular.

4. Ocular dominance columns

We next consider the distribution of cells in the cortex according to ocular dominance. We begin by asking whether two cells sitting side by side in the cortex are likely to have the same ocular dominance. The answer is that they almost always do. Either both prefer the left eye or both prefer the right eye. Furthermore, if an electrode penetration is made perpendicular to the cortical surface all of the

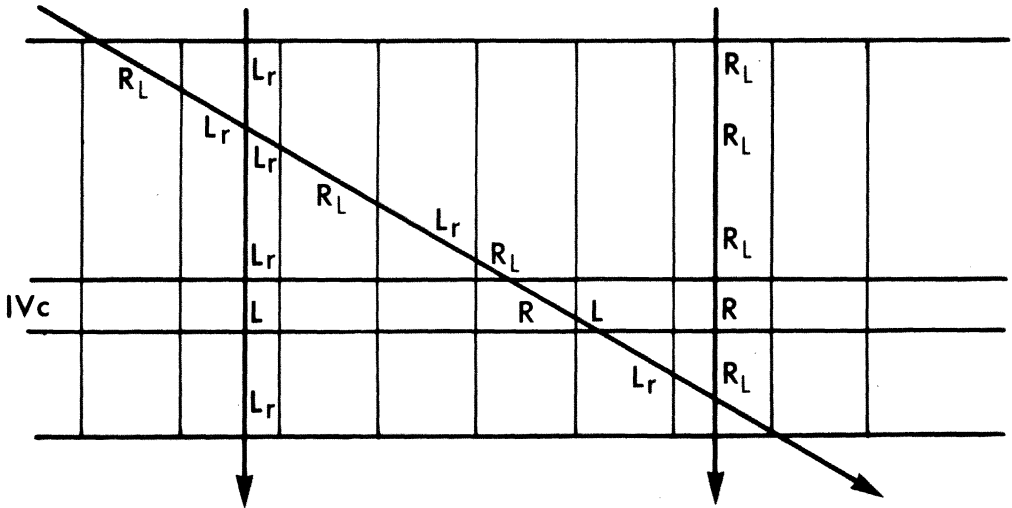


FIGURE 11. Illustration of ocular dominance columns in macaque monkey. The diagram represents a cross section through striate cortex, with surface at top and border between layer VI and white matter below. Two vertical penetrations and one oblique are illustrated. Letters refer to expected eye dominance at various stages in each penetration. R_L stands for a region in which there is a mixture of binocular cells preferring the right eye, and monocular cells responding to the right eye. R stands for a region containing only cells driven exclusively from the right eye. Layer IVc contains only monocular cells, grouped separately in patches according to eye affiliation. Layers above and below IVc contain binocular cells, grouped in columns according to eye preference. When a vertical penetration reaches IVc the eye that has been preferred all along comes to monopolize. In an oblique or horizontal penetration there is a regular alternation of eye preference as the electrode goes from column to column.

cells encountered, from the surface to the white matter, will with high probability respond preferentially to the same eye (figure 11). If we pull out the electrode and reinsert it at a point a millimetre or so away, the same eye may again be dominant all the way down, or the other eye may now dominate. In a horizontal or oblique penetration there is an alternation of eye dominance: first one eye prevails, then the other. By making a large number of penetrations in various directions one reaches the conclusion that the striate cortex is subdivided into regions whose cross-sectional width is in the order of 0.4 mm and whose walls are perpendicular to the cortical surface and to the layers. We term these subdivisions *ocular dominance columns*. The word 'column' as applied to vertically organized cortical

subdivisions was coined by Mountcastle (1957) for a system of aggregations in the somatosensory cortex, corresponding to cutaneous versus deep sensory sub-modalities. The cross-sectional appearance of the ocular dominance columns does indeed suggest a pillar-like three-dimensional shape, but as we will see the actual shape in area 17 is not at all pillar-like. In retrospect, for the visual system, the term 'column' may be somewhat misleading, but to change the term seems

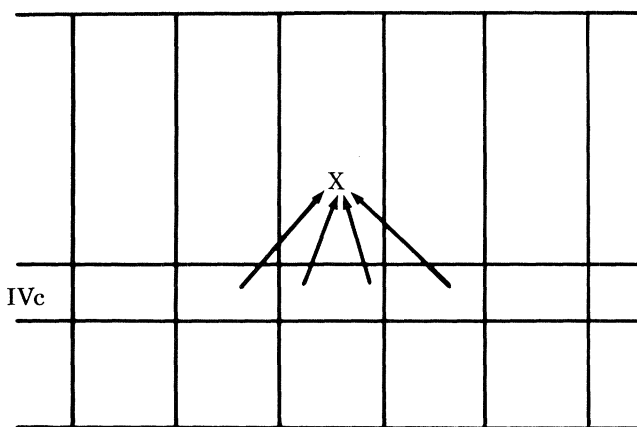


FIGURE 12. Scheme to illustrate the wiring of a binocular cell in a layer above (or below) layer IVc. The bulk of the afferents to the striate cortex from the lateral geniculate body, themselves monocular, are strictly segregated by eye affiliation in layer IVc, and thus the cells in this layer are strictly monocular. A cell outside of IVc, labelled X in the diagram, receives its input connections, directly or indirectly, by one or more synapses from cells in IVc (to some extent also, perhaps, from layers IVa and VI). Cells in IVc will be more likely to feed into X the closer they are to it; consequently X is likely to be binocular, dominated by the eye corresponding to the nearest patch in IVc. The degree of dominance by that eye is greater, the closer X is to being centred in its ocular dominance column, and cells near a boundary may be roughly equally influenced by the two eyes (see also figure 13).

undesirable, since whatever the exact geometric shape there is no doubt that the subdivisions in the visual and somatosensory systems are to a large extent analogous. In both systems, one may add, the discovery of the subdivisions came as a complete surprise, since the classical neurophysiological procedures, Golgi, Nissl and fibre stains, had given no hint of their presence.

Given these ocular dominance columns, we may imagine that a binocular cell results from wiring of the sort shown, very schematically, in figure 12. Suppose a cell X in layer II or III lies above the centre of a right-eye ocular-dominance patch. We know from the Golgi anatomy that this cell receives its input, either directly or over a few synapses, from a region of layer IV having a horizontal extent of 1 or a few millimetres. The cell will be most richly connected to cells in IVc lying directly below it. It can therefore be predicted that cell X will have stronger links with the eye that feeds the IVc patch directly beneath it, than with the other eye. The nearer X is to being centred over (or under) a particular patch the stronger will

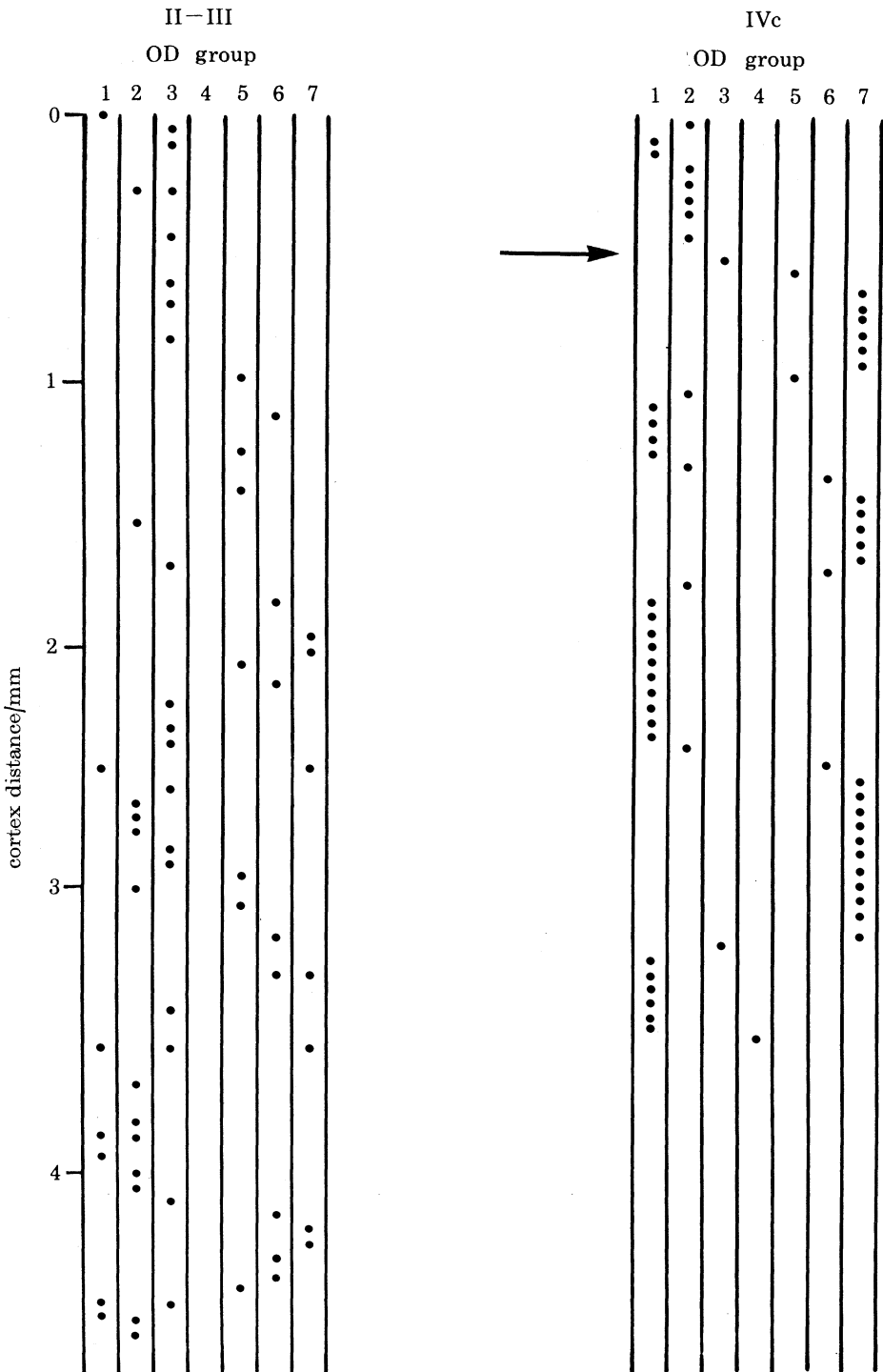


FIGURE 13. For description see opposite.

be its domination by the corresponding eye; the closer to a columnar border, the more nearly equal will be the influence of the two eyes. This expectation is borne out experimentally, for in a horizontal penetration through the upper or lower layers (i.e. the layers above or below layer IV) there is a strong tendency to systematic fluctuation in dominance back and forth, from one extreme through equality to the other extreme. This is illustrated in the left part of figure 13, which shows the variations in ocular dominance with electrode distance for a penetration passing horizontally along layer III. It should be stressed that the ocular-dominance column, as we define it, refers to the full thickness of cortex and is defined by eye *preference*. The part of the column in layer IVc contains monocular cells only; at the borders of the columns in IVc there is little intermixing of the two cell populations, and the borders themselves are consequently very sharp, more so than in the other layers. This is illustrated in the right half of figure 13. Even outside of IVc, however, the boundaries are far from nebulous, and can generally be specified to within 50–100 μm .

Just why the two eyes should be brought together in this elaborate but incomplete way is not yet clear. What the ocular dominance columns appear to achieve is a partial mixing of influences from the two eyes, with all shades of ocular dominance throughout the entire binocular field of vision. The columns may represent a way of making sure that this special kind of mixing occurs in the same way everywhere. That monocular complex cells are kept aside in all parts of the visual fields is perhaps related to stereoscopy. It seems that cells whose fields in the two eyes show positional disparity in a horizontal direction are absent or rare in area 17 but rather common in 18 (Hubel & Wiesel 1970; 1973). Area 17 projects in a topographically faithful way to 18. To build up such depth cells in 18, with all the degrees of disparity required for stereopsis, probably requires keeping aside monocular cells in area 17 which can later be combined in various ways, producing a complete range of field disparities: to commit all cells in area 17 by combining them with zero disparity would preclude this procedure later. Presumably the machinery required to produce all degrees of disparity is too ponderous for it to be included in area 17, which perhaps has enough to worry

FIGURE 13. Variation of ocular dominance with distance in two penetrations made at a very oblique angle to area 17, in the parasagittal plane in macaque monkey striate cortex. The part of the penetration illustrated on the left side is entirely in layers II and III. The portion of the penetration illustrated on the right begins in IVb, but enters IVc at the arrow and remains in IVc to the end. The two penetrations were about 1 mm apart. In layers II and III (and also in V and VI) most cells are binocular but show some eye preference. As the electrode passes through 8 or 9 dominance columns, the cells first show marked preference for one eye, then are more nearly equally driven by the two eyes, and finally the other eye gains the ascendancy; the dominance thus swings back and forth in a smooth fashion. In IVc, on the other hand, the transitions are more abrupt and complete, from regions dominated exclusively by one eye to regions monopolized by the other.

about as it is. While stereopsis provides a plausible explanation for the existence of monocular cells at the output end of area 17, the question of why binocular cells should exist in all shades of eye preference remains an open one.

5. Orientation columns

Let us now turn to the final variable on our list, receptive-field orientation. Here again we first ask whether neighbouring cells tend to favour the same stimulus orientation. Again, the answer is that they almost invariably do. And as with ocular dominance, a penetration exactly perpendicular to the cortical

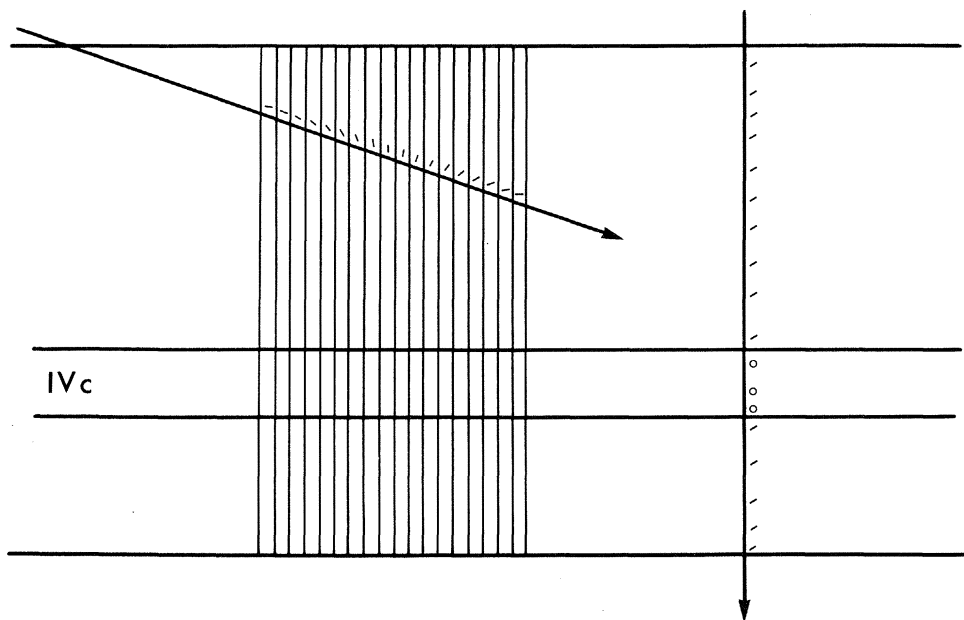


FIGURE 14. Diagram to illustrate orientation columns in monkey striate cortex. Two penetrations are illustrated, one vertical, the other oblique. In the vertical penetration orientation is clearly defined and constant, from cell to cell, in layers above and below IVc. In layer IVc the cells have fields with circular symmetry, and there is no orientation preference. In an oblique penetration there is a systematic variation in orientation, clockwise or counterclockwise, in steps of about 10° or less, that occur roughly every $50\ \mu\text{m}$. (That the variation is in some sense continuous is not ruled out – see text.)

surface and to the layers reveals cells all of which favour the same orientation, except of course those in layer IVc, which have no orientation preference at all (figure 14). In a horizontal or oblique penetration one sees a succession of preferred orientations. The shifts occur so frequently that even the smallest advance one can make, and be sure that the electrode has indeed moved (that is about $20\ \mu\text{m}$), is accompanied by a detectable change in optimal orientation (Hubel & Wiesel 1974a). The shifts are generally small and occur usually, though not always, in an amazingly orderly sequence, with many clockwise or counterclockwise steps that

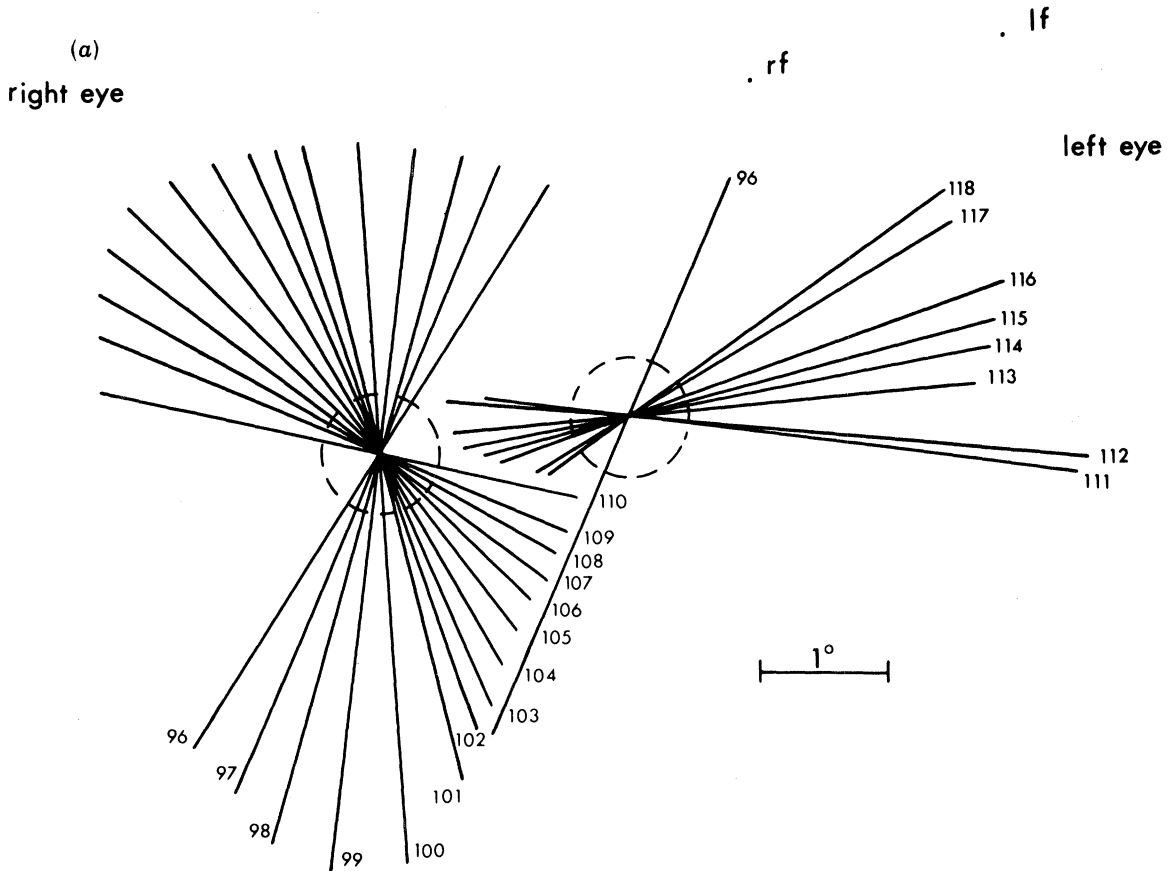


FIGURE 15. (a) Illustration of results obtained in a typical experiment during part of an almost tangential penetration through area 17 in the right hemisphere. The figure represents the tangent screen on which fields were mapped. rf and lf represent projections of the two foveas – the paralysed eyes had their axes crossed at a point in front of the screen. Receptive fields, collectively occupying the regions outlined in dashed circles, were about 4° below and to the left of the centre of gaze. At the beginning of the sequence shown here (cell no. 96) the orientation was about 1 o'clock–7 o'clock, and responses were evoked from both eyes, the right better than the left. As the electrode was advanced the orientation shifted in a counterclockwise direction in small steps at a rate of about $280^\circ/\text{mm}$. The right eye continued to dominate, and fields were therefore mapped only in that eye, up to cell no. 111. Here eye dominance abruptly changed to favour the left eye, and fields were mapped in that eye up to no. 118, when the penetration was terminated. Note that when eye dominance changed there was no interruption of the orientation sequence.

add up finally to total rotations of up to 180° or more. From time to time, unpredictably, the direction of rotation may reverse.

A typical sequence is shown in figure 15a. Here the anaesthetized and paralysed monkey was facing a tangent screen $1\frac{1}{2}$ m distant. The directions of gaze for the two eyes in these circumstances are seldom parallel, and here they even crossed so that the left foveal projection (lf) lay to the right of the right projection (rf) (as

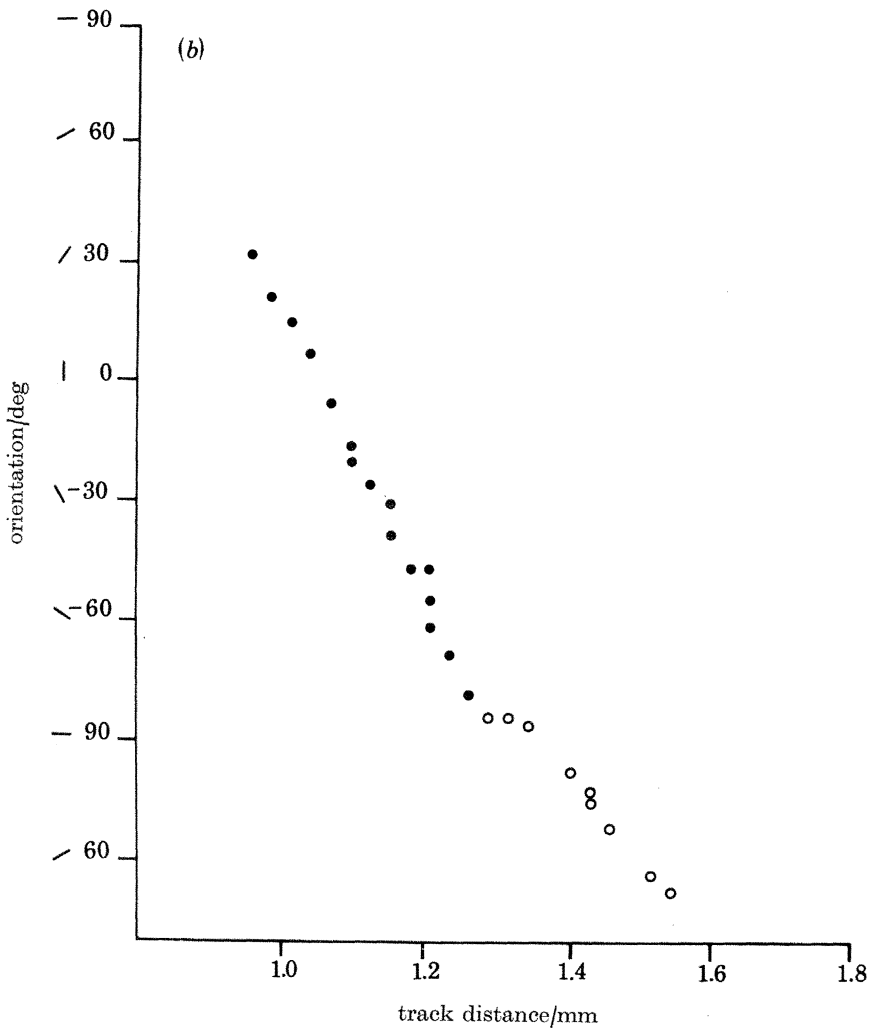


FIGURE 15(b). Graph of orientation in degrees plotted against electrode track distance in millimetres, for the sequence illustrated in 15a. ●, cells dominated by right eye; ○, left eye.

determined with an ophthalmoscope). The recording was almost tangential to the surface of the striate cortex of the right side, so that the aggregate receptive fields in the two eyes were in the left visual fields, as indicated by the interrupted circles. The first unit recorded (which happened to be the 96th in this entire experiment) was binocular but with the right eye dominant, and for this cell the fields were mapped in both eyes. The preferred orientations were almost identical, roughly 1 o'clock - 7 o'clock. Advancing the electrode produced a slight counterclockwise shift (no. 97), and from this point on each advance was accompanied by a similar shift, always counterclockwise. To save time, from cell 97 on we mapped fields only in the dominant eye. At no. 111 the eye dominance suddenly shifted to the

left eye, indicating that the electrode had crossed over into a new eye-dominance column: the orientation sequence nevertheless went its own way, quite unaffected by the dominance shift. By the end of the sequence the orientation had rotated through some 160° .

This result is shown as a graph in figure 15*b*, where orientation is plotted against distance traversed by the electrode. The relation is virtually linear, with only a small offset where the dominance changed from right eye (filled circles) to left eye (open circles), caused by a slight relative eye rotation in the equatorial plane. Figure 16 shows a second graph from a different experiment. The penetration was long and very oblique, almost tangential, as shown in the reconstruction at the upper right. Several reversals were seen, with the largest uninterrupted sequence totalling 267° .

The conclusion from these results is that the cortex is subdivided by a second set of vertical partitions into columns which are very slender. For technical reasons (see Hubel & Wiesel 1974*a*) one cannot be sure that orientation does not vary in some sense continuously with horizontal position (see also Albus 1975). If the steps are discrete they occur every 20–50 μm and correspond to orientation shifts of about 10° . Whether or not they are discrete, one can say that roughly 180° rotation corresponds to a 1 mm displacement along the cortex. To judge from a number of penetrations made in different parts of area 17, this law probably holds true throughout the cortex. Thus the columns probably have the same thickness everywhere.

It is hard to imagine that such an elaborate and highly patterned organization as this would have evolved if orientation were not important. The significance of the organization is suggested by the physiology. Within each column are housed cells with concentric fields together with simple, complex, and hypercomplex cells, having the same orientation preference and all having more or less the same receptive-field position. These are the very cells which the physiology tells us are probably interconnected – certainly there is no suggestion that cells with very different receptive field positions or very different orientations have major excitatory interconnections. One may thus look upon a column as a functional unit of cortex, a means of bringing into one place the cells that are to be interconnected, and of separating them from cells with which they have few or no connections. The alternative, of having cells mixed at random without regard to preferred orientation, would surely be less efficient in terms of length of connections and specificity, for any cell could then not simply reach out to its nearest neighbour or to cells directly above or below, but would instead have to search out the axons or dendrites of other cells having just the correct orientation, while ignoring all the others. It is indeed hard to contemplate the nightmare of interconnections that would have to exist if the cells were distributed at random with respect to orientation.

Probably there is functional importance not only in the orientation columns themselves, but also in the regularity of their arrangement. Having such a

regularity presumably guarantees that all orientations are represented everywhere in the field of vision, with no omissions or redundancies. There is probably also an improved economy in the connections that are required to manufacture simple cells from circularly symmetric ones (Hubel & Wiesel 1974*a*). Finally, orientation specificity may be enhanced by mutual inhibition between cells whose orientations differ by a small angle (Blakemore & Tobin 1972); having such cells close together in neighbouring columns would shorten the connections responsible for this inhibition.

In a cross section such as that represented in figure 14 the orientation columns appear as pillar-like structures, just as the ocular dominance columns do, but several lines of evidence indicate that they are not columns at all, in the usual sense of that word. Direct observation by means of multiple parallel electrode tracks, which can be reconstructed in three dimensions (Hubel & Wiesel 1974*a*), indicate that the shape is actually that of narrow parallel slabs lined up vertically (perpendicular to the surface) like slices of bread. Cross sections of such arrays would then give the appearance of figure 14 unless the plane of section happened to be parallel to the slabs. Only rarely, in fact, does orientation remain constant in a horizontal penetration (resulting in a zero slope in graphs of the type shown in figures 15*b* and 16), and such constancy would indeed be expected only rarely, given the unlikelihood of an electrode's threading its way along such narrow slabs. Moreover, the slabs may be swirls rather than parallel planes, and a swirling pattern would easily explain the reversals in direction of rotation seen in figure 16.

An entirely different argument that the columns are actually slabs comes from considerations of continuity. If we suppose that throughout a particular region of cortex there is order everywhere – that for all directions of penetrations the orientation changes in small steps, or does not change at all – then the regions of constant orientation must be slabs. The argument runs as follows: When we say there is order everywhere, geometrically we mean that if orientation in degrees is plotted on the z -axis against the two-dimensional $x-y$ cortical surface position, the graph forms some kind of surface. The surface is smooth if orientation is a continuous function of position along the cortex, as discussed above, and finely terraced if orientation changes in small steps. Such a surface in a three-dimensional graph yields the curves of figures 15*b* and 16, when cut by any plane perpendicular to the cortex. On the other hand if the surface in the three-dimensional graph is cut by a plane parallel to the cortical surface, corresponding to a particular z -value of orientation, the intersection between surface and plane yields a contour line of constant orientation. Sets of such contour lines correspond to the tops of the slabs, as seen when one looks down on the cortex from above. The shape of the surface would of course be fascinating to know. The reversals seen in figure 16 could be produced by mountains and valleys, corresponding to the swirling columns mentioned above, or by a surface with ridges like a washboard or a camera bellows or a series of mountain ranges.

These two lines of evidence, from parallel penetrations and from the argument

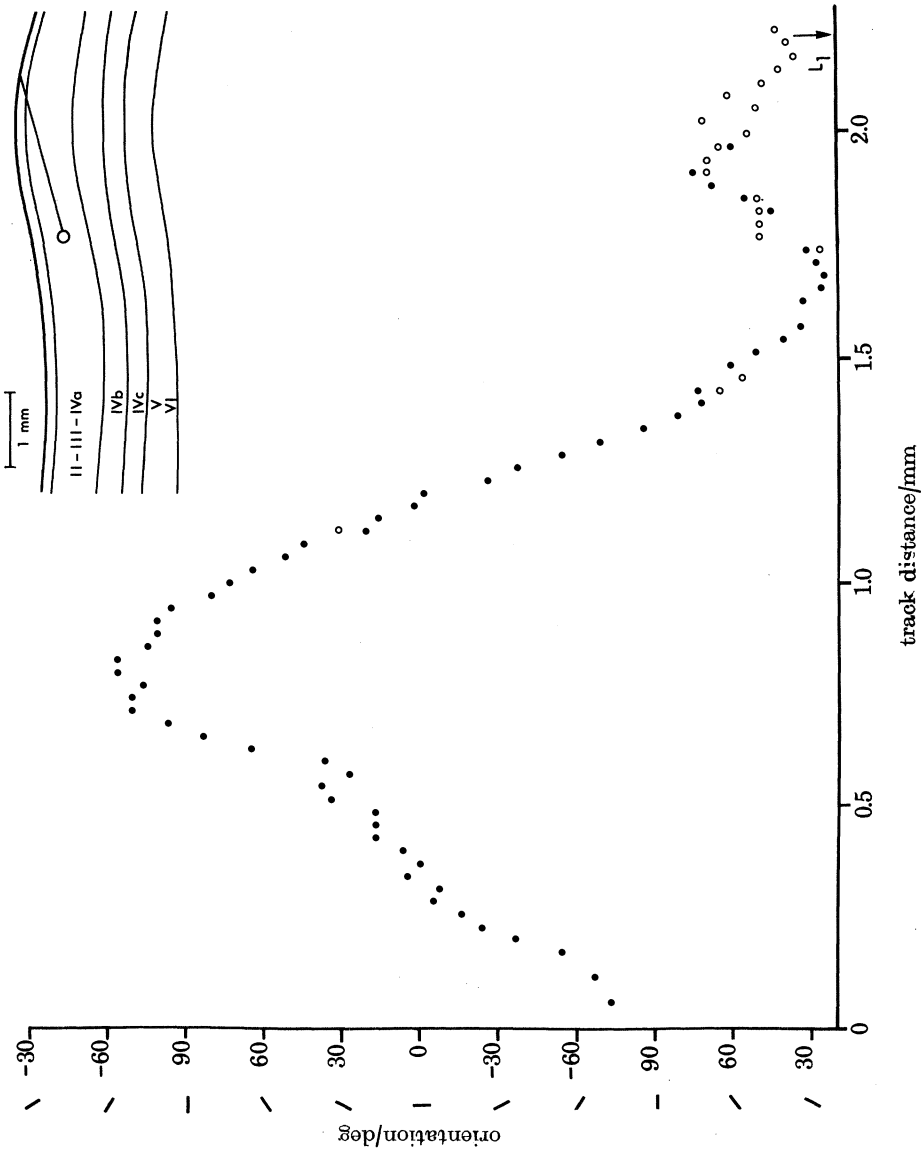


FIGURE 16. Graph similar to that of figure 15b, but from a different experiment. Again, the penetration was almost horizontal and was restricted to layers II and III (see inset). Several reversals in the direction of rotation occur, with two very long, almost linear, sequences followed by two short ones. The right eye was dominant until almost the end of the sequence.

based on the orderliness of the shifts, are obviously less direct than an actual anatomical visualization of the slabs, but so far no such anatomical method has been found. This is in part because the orientation columns (or slabs, as we may now term them) are produced not by any special distribution of the afferent terminals, but by interconnections within the cortex. What the precise connections are that lead to orientation specificity is not known, and as mentioned already none of the common methods for examining nervous tissue, such as Nissl or Golgi or fibre stains, or the use of the electron microscope, has yet shown anything that could be convincingly construed as representing the orientation columns. The ocular dominance columns, on the other hand, actually result from the specific patchy terminal distribution of afferents from the geniculate to layer IV. In this respect they differ profoundly from the orientation columns, and are more akin to the superficial vs. joint columns described for the somatosensory cortex by Mountcastle. This dependence on afferent distribution has made it possible to visualize the dominance columns anatomically, as we shall describe in the next section.

6. *Geometry of ocular dominance columns*

Here again our problem was to determine the three-dimensional shape of columns when the physiological recordings told us only that the walls separating the columns were perpendicular to the surface. A cross-sectional appearance of the sort indicated in figure 11 might result from several very different geometries. The columns seen from above could, for example, consist of alternating squares of right and left eye affiliation, forming a sort of checker board (figure 17*a*). They could consist of islands of right-eye dominance in a sea of left-eye dominance, or the reverse, or of some combination of these two (figure 17*b*). Or, finally, they could consist of a set of alternating left-eye and right-eye stripes (figure 17*c*). Cut in cross section any of these topologies would result in the alternating sequence of figure 11. To distinguish among the three possibilities (or any others that one might conjure up) with a microelectrode is possible in principle, for example with reconstructions of multiple parallel penetrations, but to attack such a three-dimensional problem with a one-dimensional weapon is a dismaying exercise in tedium, like trying to cut the back lawn with a pair of nail scissors. And so it turned out – after one or two attempts we decided that it would be more rewarding to turn to farming (with modern implements) as a career.

Fortunately (for American agriculture) over the last few years four entirely independent anatomical methods have become available, and it has been possible to approach the problem of dominance-column geometry directly and answer it unequivocally. The first of these was the Nauta silver-degeneration method, which relies on the possibility of staining selectively axons that degenerate when they are cut proximally or when the parent cell bodies are injured. A subsequent modification of this method, by Fink & Heimer (1967) and later by Wiitanen (1969), made possible the selective staining of degenerating axon terminals. With this method a large lesion in the lateral geniculate body would be expected to produce

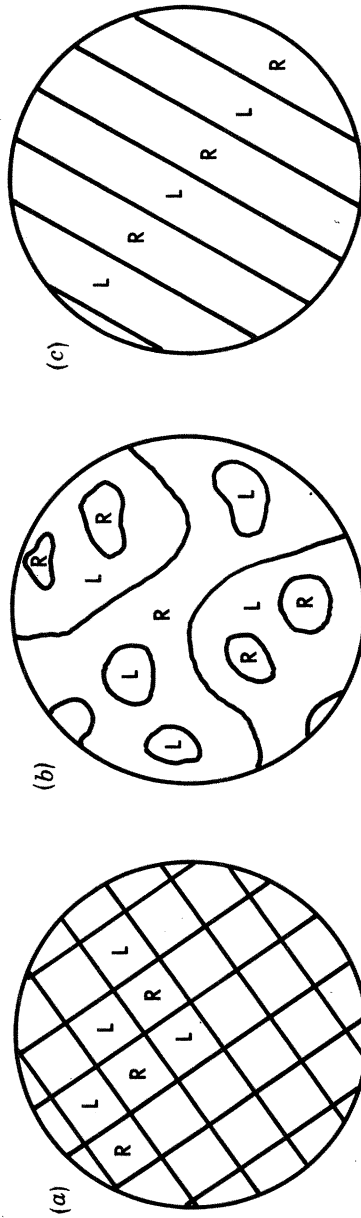


FIGURE 17. Three possible ways in which a plane surface might be partitioned into two types of region; here, left eye (L) and right eye (R).

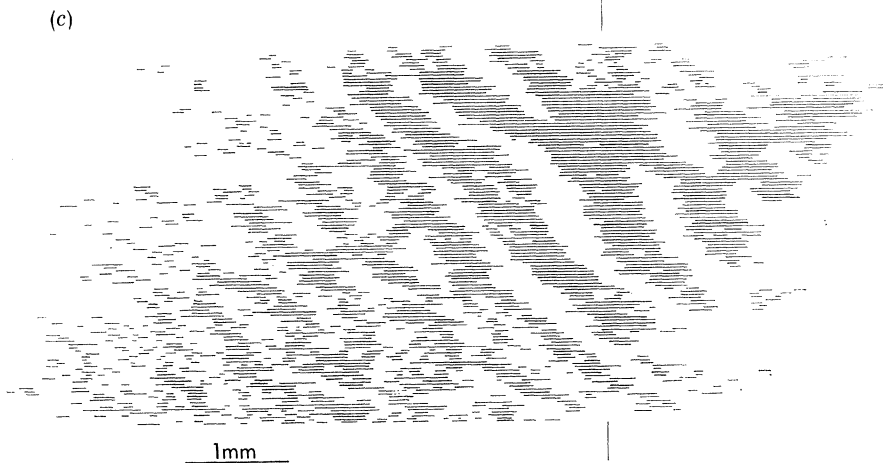
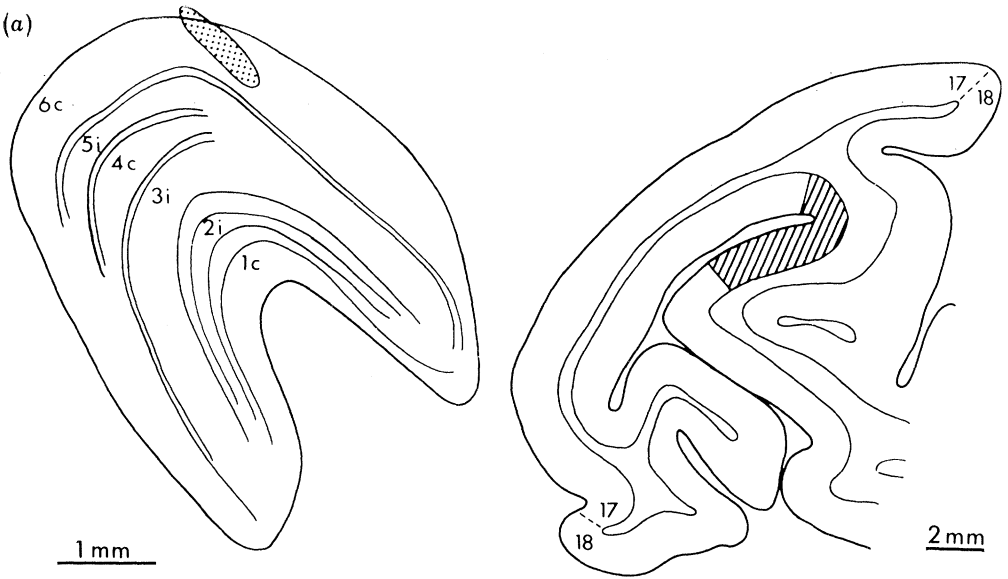
a forest of stained terminals, appearing as dense 5–10 μm brown dots, precisely in layer IV. In 1965 (Hubel & Wiesel) we had begun to adapt the Nauta method to microelectrodes, making minute lesions in single cortical layers or single subdivisions of deep nuclei, recording from the electrode to help guide its precise placement prior to making the lesion. It occurred to us that if we were to place a small lesion in a single geniculate layer (corresponding to a single eye) the degeneration of terminals in IVc of the cortex should be in discrete regular patches with gaps between, unless our deductions from the physiology were completely faulty.

The results of one of our first attempts at this are shown in figure 18, plate 7 (Hubel & Wiesel 1972). The geniculate penetration was luckily almost tangential to the most dorsal of the geniculate layers, which allowed us to make a long cigar-shaped lesion entirely within this layer. This produced a rather wide region (4×8 mm) of cortical degeneration in the mushroom-like buried fold of cortex, shown diagrammatically in the upper right of figure 18*a*. A photomicrograph of a typical section is shown in figure 18*b* in dark field; here regions rich in degenerating terminals glow brightly. The existence of regular alternations of patches of terminals and terminal-free gaps was thus confirmed. Now to get at the three-dimensional shape of these patches it was only necessary to prepare a few hundred serial sections and stack them next to each other at the correct spacing. This was done graphically as shown below in figure 18*c*. Each horizontal broken line in the diagram represents the patches and gaps from a single section, artificially (graphically) straightened out into a line. The entire reconstruction thus represents a face-on view of the cortex, or, to be more specific, of the degenerating terminals in layer IVc.

From this reconstruction and a number of others it was clear that to a first

DESCRIPTION OF PLATE 7

FIGURE 18. (*a*) Distribution of degenerating terminals in macaque monkey striate cortex following a focal lesion confined to the most dorsal layer (no. 6) of the left lateral geniculate body. At the upper left the position of the lesion is shown (stippled) on a tracing of a coronal section through the geniculate. At the top right the shaded region indicates the part of area 17 in which degenerating terminals were found, in layers IVa and c; this drawing is traced from a parasagittal section through the occipital lobe (compare figure 6). Within the shaded region the degenerating terminals occurred in patches about 0.5 mm wide, separated by terminal free gaps of about the same size; each section contained about 5–6 patches and gaps. (*b*) Dark field photomicrograph through region of cortex to which degenerating fibres projected. Bands of densely packed degenerating endings can be seen as light patches in the highly curved portion of the buried part of area 17. (*c*) Reconstruction drawn from 118 sections parallel to the one in *b*, and including it. Each horizontal interrupted line is obtained from a photograph like that shown in *b*, by graphically flattening the part of layer IVc containing degenerated terminals and tracing the patches of degeneration. The resulting pattern represents the view one would get looking at layer IVc face on. The columns are thus for the most part parallel stripes. The vertical lines indicate the position of the crease in the cortex. (Hubel & Wiesel 1972, figures 8–10.)



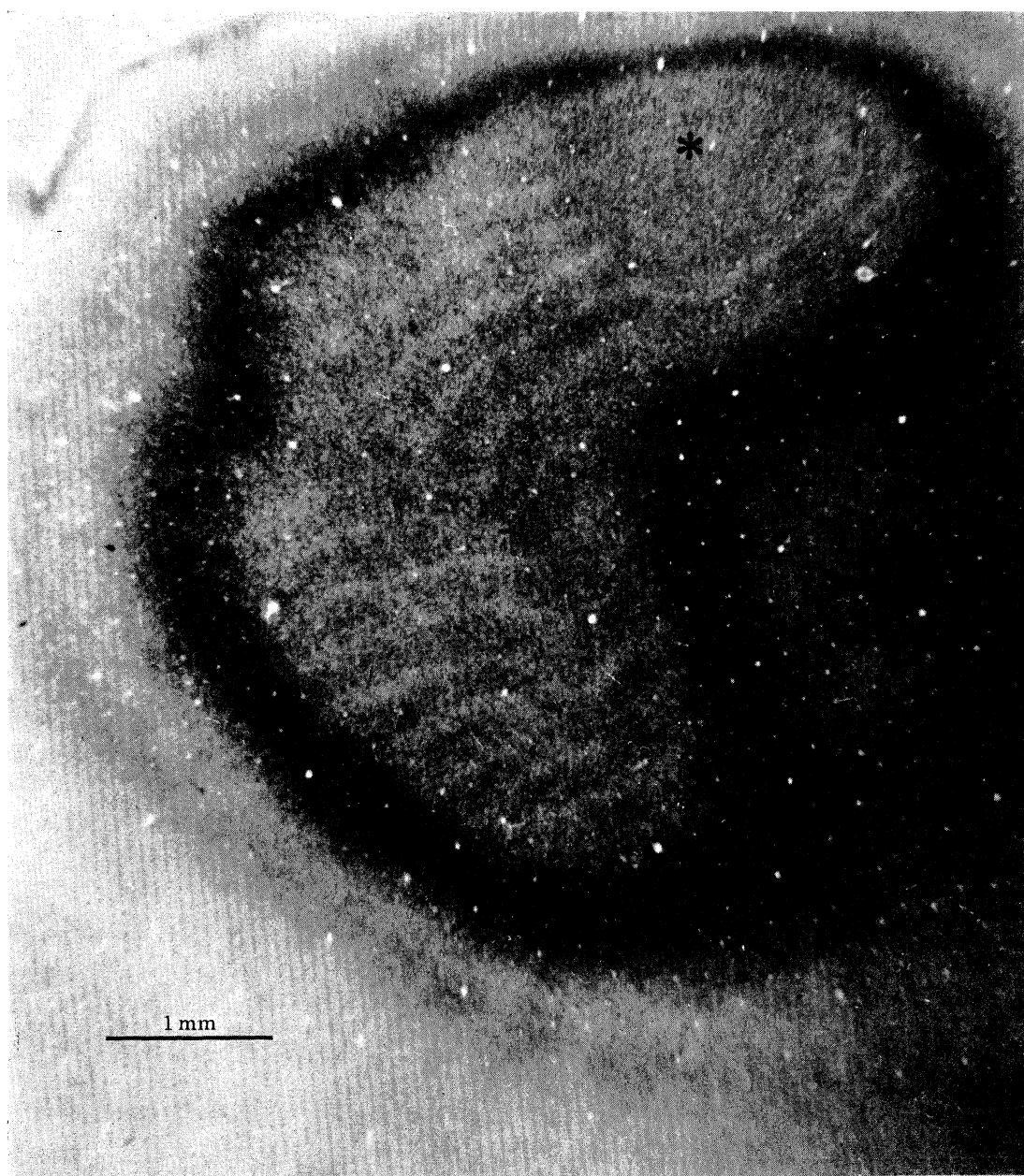


FIGURE 20. Pattern of ocular dominance columns seen in a tangential section through layer IVc of normal macaque striate cortex, stained by the reduced-silver method of Liesegang. The cortical surface is seen on the upper left of the figure. The very dark ring is layer IVb, the line of Gennari. Within this is layer IVc with the alternating dark and light bands, except for a small area marked by the asterisk, which grazes layer V. The dark bands represent the columns. These contain relatively fewer horizontally running fibres near their borders, resulting in the light bands. The actual column boundaries are thus the centre lines of these light bands (LeVay *et al.* 1975, Fig. 2).

approximation the IVth layer terminals have the distribution of parallel stripes. The stripes have a width of about 0.4 mm and are in most regions remarkably regular. There is, to be sure, a certain degree of irregularity, especially a tendency for two stripes corresponding to one eye to join, leaving the intervening stripe from the other eye to end blindly. Near the fovea the anastomoses are very frequent and form a lattice-like series of cross linkings (figure 19). Perhaps the most striking

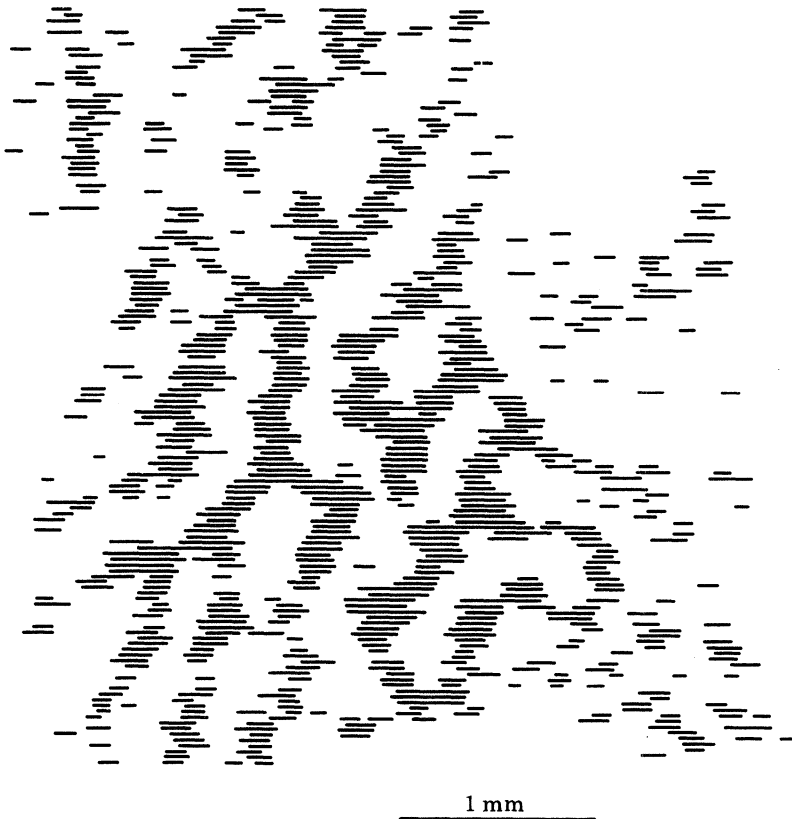


FIGURE 19. Reconstruction similar to that of figure 18c, but here the geniculate lesion was made a few degrees from the foveal representation in the most ventral geniculate layer (no. 1). The lattice-like appearance, with a large number of blind endings and cross linkings, seems to be a characteristic of the foveal and parafoveal region. (Hubel & Wiesel, 1972, Fig. 17.)

feature of the stripes is the regularity of their spacing; it is difficult to find a point in layer IVc that is more than about 0.2 mm from the nearest stripe border.

As a by-product of these experiments it was shown that geniculate terminals do not occur in layer IVb (Line of Gennari), confirming an old observation of Clark & Sunderland (1939), and that the parvocellular layers (the four dorsal layers) project to layer IVa and to the deeper half of IVc, whereas the magnocellular (ventral two) layers project to the superficial half of IVc. This was the first evidence

that the ventral and dorsal layers have different projections. The significance of this pattern of projection is still quite obscure.

The Nauta method as applied to this problem had one severe limitation. For a lesion to be confined strictly to a single geniculate layer it had to be small, so that the consequent overall size of the corresponding region of striate cortical degeneration was only a few mm in diameter. To visualize a wider area, to say nothing of the entire striate cortex, a new method was needed. One day Simon LeVay, who had recently joined our laboratory, was examining tangentially sectioned striate cortex of macaque using a reduced silver stain, in the hope of seeing something that might correlate with orientation columns. He noticed high in layer IVc a series of dark parallel stripes about 400 μm wide, separated by narrow paler interbands about 50 μm wide (figure 20, plate 8). Clearly these dark bands could not be orientation columns – they were much too wide. Could they represent the eye dominance columns? Close examination showed that occasionally two dark stripes joined, but never two adjacent ones; there was always a dark stripe between the two, which ended blindly. LeVay recognized that this was just what was to be expected in a twofold system, since by definition if two columns joined they must correspond to the same eye. To establish that the stripes were, in fact, the dominance columns we made very oblique penetrations down to layer IVc, cutting it tangentially or nearly so, and then made lesions each time the electrode tip crossed from a region dominated by one eye to a region dominated by the other. When the brain was later sectioned tangentially and stained by the reduced silver method the lesions matched precisely the narrow pale regions separating the dark bands. This established beyond any doubt that the dark bands do indeed represent the eye dominance columns. The bands are produced by large and medium sized horizontally running fibres in upper IVc; they are somewhat more concentrated in the dark bands than in the narrow lighter interbands. Exactly what these fibres are is not known; some of them are probably geniculate afferents, since some of the afferents run in this region and are more numerous within columns than between them (LeVay, Hubel & Wiesel 1975).

At the same time as LeVay's method was developed a third method for demonstrating the columns became available, this one based on autoradiography and axonal transport. The method of mapping pathways by injecting radioactive amino acids or other compounds in the vicinity of nerve cell bodies, and identifying the axon terminals autoradiographically, was already well known (Goldberg & Kotani 1967; Lasek, Joseph & Whitlock 1968; Cowan *et al.* 1972). In applying it to the monkey visual system one simply injected the label into the vitreous humour of the eye, whereupon the retinal cells took it up and in the case of retinal ganglion cells transported it (probably in the form of proteins) down their axons. An accumulation of radioactive compounds in the axon terminals led to the dense accumulation of silver grains on autoradiographs in the layers receiving input from the injected eye. A typical result for macaque monkey is shown in figure 21, plate 9, confirming once again the original deduction of Minkowski. (The power

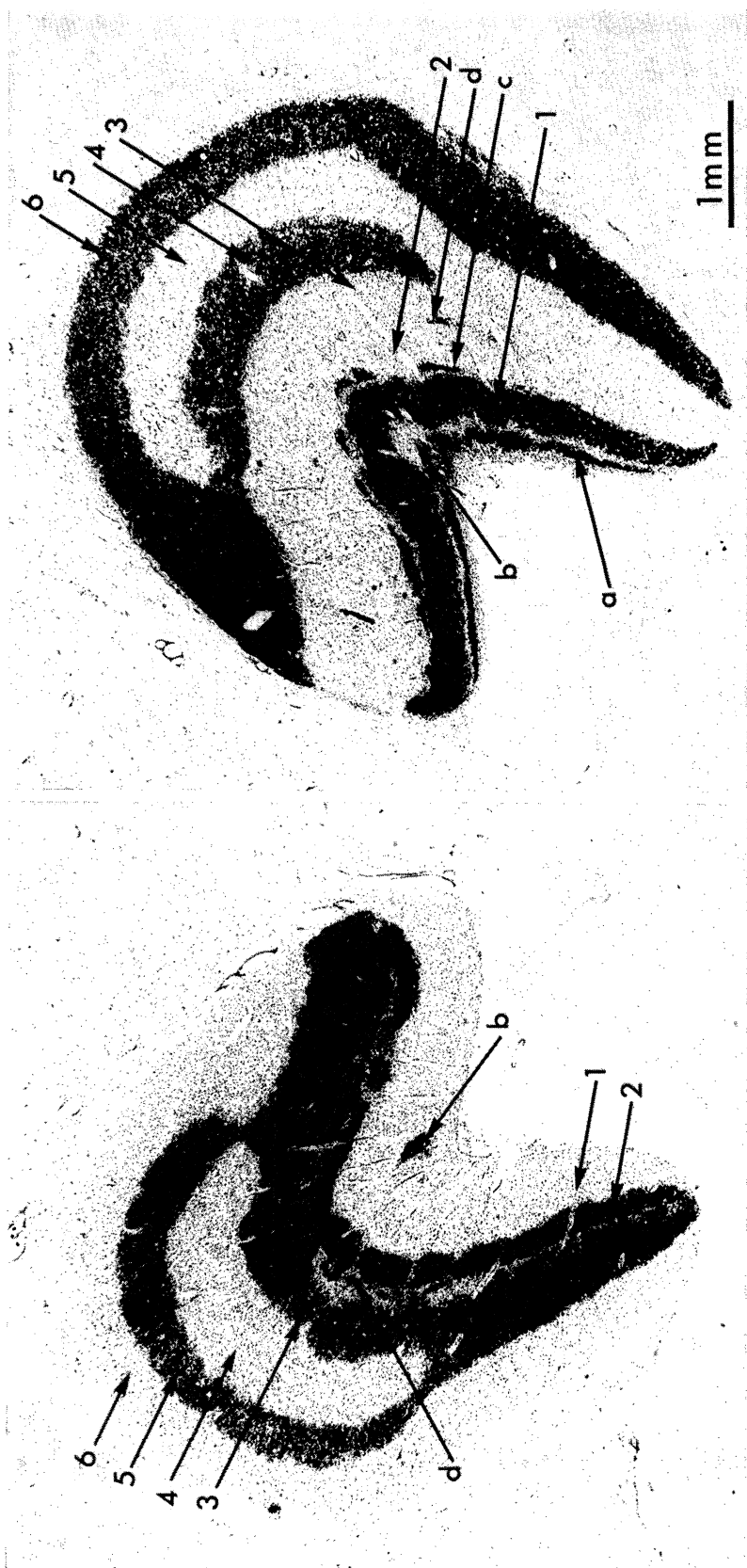


FIGURE 21. Autoradiographs of left and right lateral geniculate bodies of a 1-week-old monkey whose left eye was injected at birth with tritiated fucose. Light field: labelled regions are black. 1-6 are the classical six layers, numbered from ventral dorsally. a-d represent four additional regions of input: a and c are supplied from the contralateral eye, b from ipsilateral, and d is apparently supplied by both eyes, possibly as alternating band-like monocular regions.



of the autoradiographic method is shown by its ability to reveal four aggregations of optic nerve terminals besides the six classical layers. These are described in figure 21 (Hubel *et al.* 1976). The targets to which these aggregations project are unknown, and their significance is quite obscure.)

A few years before our studies, Grafstein & Laurenco (1973) had observed that in a mouse whose eye had been injected with a mixture of radioactive proline and fucose, some of the label was transported all the way to the striate cortex of the opposite hemisphere. Since in the mouse the visual pathway is predominantly crossed, they concluded that some of the radioactive compounds had passed out of the optic nerve terminals in the geniculate, had been taken up by the cell bodies there and transported by the geniculate-cell axons to the striate cortex. We reasoned that if the same thing could be made to happen by using autoradiography in the monkey we should be able to see the distribution, in layer IV, of the geniculate-cell terminals corresponding to the injected eye. These should then appear in cross section as patches of silver grains, about 0.4 mm wide, separated by gaps corresponding to the eye that had not been injected.

The result of such an experiment is shown in figure 22, plate 10 (Hubel *et al.* 1976). Dark-field techniques had to be used since the grains were too sparse to be obvious on cursory inspection by light field illumination. The layer IVc columns stand out clearly everywhere, and this section by itself shows some 56 pairs of columns.

Though requiring an eye injection and the use of large amounts of radioactive substances, which are expensive and not free of danger, this method has several advantages over LeVay's reduced silver technique, for the latter only reveals stripes in sections that are tangential or almost tangential to layer IV, and does not seem to work at all in monkeys under about 6 months old.

To reconstruct the pattern of columns over a wide area and to visualize them *en face*, one can stack many serial sections such as that of figure 22 one above the other just as was done in preparing figures 18c and 19. A more direct alternative is to section the cortex tangentially – something that was impractical in the Nauta studies because one never knew exactly where in the cortex the small patch of degenerating terminals would be found. If the microtome knife cuts the dome-shaped exposed part of area 17 so as to graze layer IVc, this layer appears as an oval. A slightly deeper section cuts layer V in an oval, and layer IVc then appears as an annulus. Such a section, showing layer IVc as an annulus, is shown in

DESCRIPTION OF PLATE 10

FIGURE 22. Dark-field autoradiograph of striate cortex in an adult macaque in which the ipsilateral eye had been injected with tritiated proline-fucose 2 weeks before. Labelled areas show as white. Section passes for the most part in a plane perpendicular to the surface. Photograph shows part of the exposed surface of the striate cortex and the buried part immediately beneath; some of the buried part has fallen away during sectioning. In all, some 56 columns can be counted in layer IVc.

figure 23*a*, plate 11, from the same monkey as that of figure 20, but the opposite hemisphere. By taking deeper and deeper sections a series of larger and larger annuli results. These can then be cut and superimposed, giving the reconstruction shown in figure 23*b*. Again the general arrangement of the layer IVc patches as parallel stripes is very clear, as are the occasional bifurcations and blind endings.

By using LeVay's reduced-silver technique (the autoradiographic technique could have been used equally well) it has been possible to reconstruct the columns over the entire exposed part of the occipital lobe (the operculum), and, with small gaps where curvature is extreme, their continuation in the calcarine fissure. The reconstruction of the operculum is shown in figure 24*a* (LeVay *et al.* 1975). This diagram represents the same part of area 17 as is shown in the right side of figure 6*a*, with the foveal representation to the extreme right and the left boundary representing roughly a semi-circle 9° distant from the fovea. To visualize more easily the actual size of the stripes in figure 24, a fingerprint of one of us (D.H.) is reproduced in figure 24*b*, to the same scale.

Several conclusions can be drawn from this reconstruction and from results using the other two anatomical methods. First, the stripes are roughly of equal width in all parts of 17, except for a few stripes at the extreme peripheral binocular region and, of course, the monocular region. Thus it seems that for both systems of columns the widths are constant throughout most of the cortex. For the monocular part of the cortex, i.e. the representation of the outlying temporal parts of the visual field, which can be seen by one eye but not the other (the temporal crescents), there is in the autoradiographs the expected continuous band of label in the hemisphere opposite the injected eye, and nothing on the ipsilateral side. We have not sectioned this part of the cortex tangentially and stained with the reduced silver method because tangential sections here are difficult to obtain. We will refer again to the temporal crescent representation in discussing effects of deprivation.

Secondly, from hemisphere to hemisphere, even on the two sides in the same monkey, the patterns of stripes differ in their details. Identical patterns would indeed not be expected, any more than one would expect the stripes of all zebras to be identical. Nevertheless, as with zebras' stripes (Portmann 1948) certain general rules seem to be obeyed in all the monkeys we have so far looked at. For example, the stripes seem always to intersect the 17–18 border at approximately 90°. At least in the mid-periphery and periphery of the visual fields the stripes when projected into the visual fields turn out to be approximately semi-circles (figure 25); see also Hubel & Freeman (1977). This figure also shows strikingly the distortion in size that occurs as a consequence of the variation in magnification with eccentricity. The number of dominance columns in each hemisphere is about 150.

A final demonstration of ocular dominance columns comes from the 2-deoxyglucose method developed in recent years by Sokoloff's group (Sokoloff 1975, 1977). The method is based on the increase in uptake of glucose or deoxyglucose by active cells, and the inability of the metabolic end product of deoxyglucose to

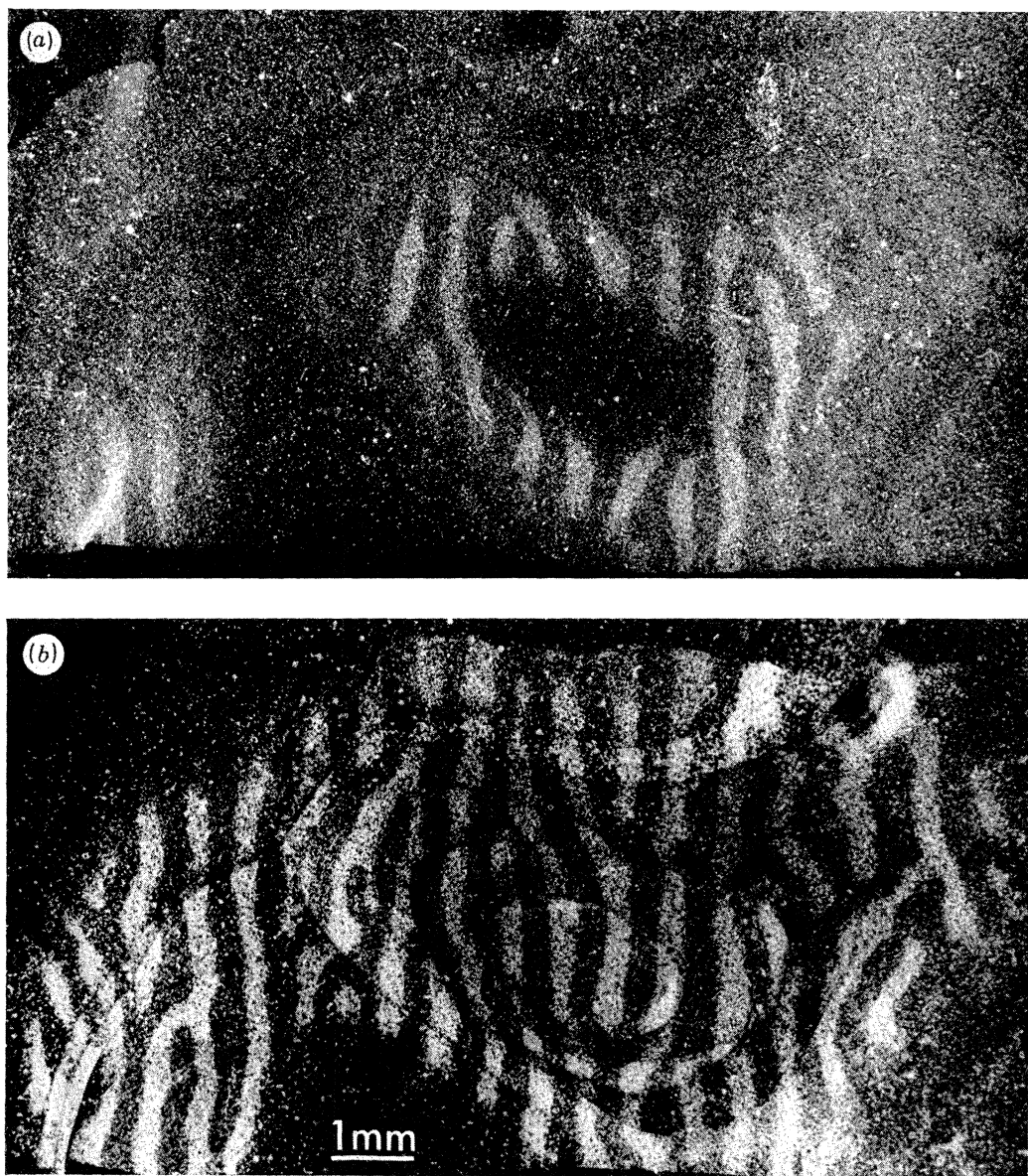


FIGURE 23. Autoradiograph from the same (normal) animal as figure 22, but hemisphere contralateral to the injected eye (dark field). (a) shows a section tangential to the exposed dome-like surface of the occipital lobe, just grazing layer V, which appears as an oval, surrounded by layer IVc, which appears as a ring containing the labelled parallel bands; these appear as light against the dark background. (b) a composite made by cutting out layer IVc from a number of parallel sections such as the one shown in (a), and pasting them together to show the bands over an area some millimetres in extent.

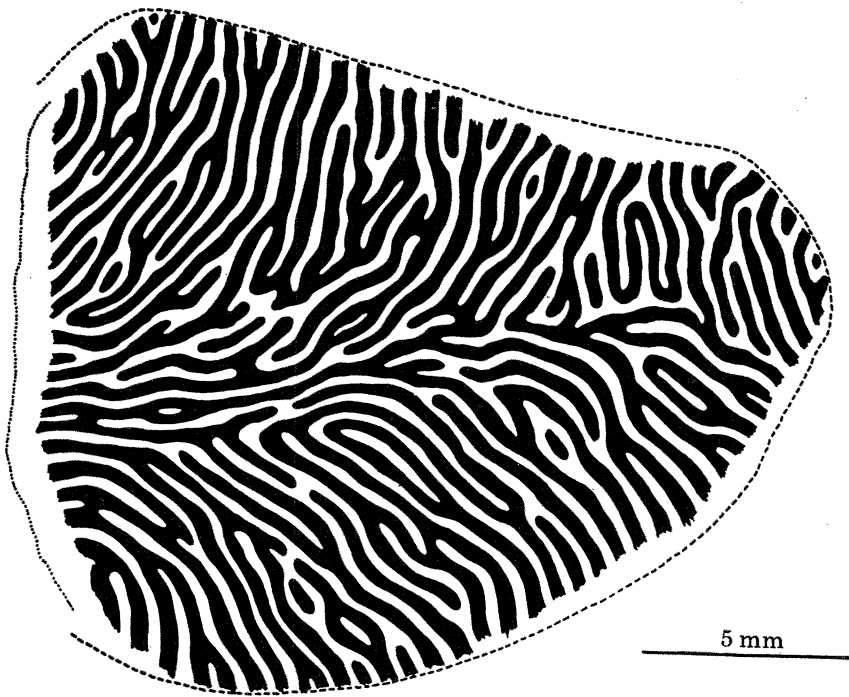


FIGURE 24. (a) Reconstruction of layer IVc ocular dominance columns over the entire exposed part of area 17 in the right occipital lobe, made from a series of reduced-silver sections (LeVay *et al.* 1975). Dotted line on the left represents the midsagittal plane where the cortex bends around. Dashed c-shaped curve is the 17-18 border, whose apex, to the extreme right, represents the fovea. Every other column has been blackened in, so as to exhibit the twofold nature of the set of subdivisions. Note the relative constancy of column widths. (b) Fingerprint of human index finger, to scale, for comparison.



FIGURE 25. Translation of the reconstruction of figure 24*a* into the visual field. Since this is the right hemisphere, the translation is into the left visual field. With the aid of a computer each point along the diagram in figure 24*a* has been projected into the visual field. Note that projected stripes are narrowest around the point of fixation and become progressively broader with increasing eccentricity. The projection is shown out to 9°. (Hubel & Freeman 1977.)

pass out of a cell. In animals injected intravenously with radioactive glucose, previously active cells thus show on autoradiography a surfeit of silver grains. Macaque monkeys in which one eye has been removed or closed show in area 17 a beautiful pattern of ocular dominance columns (Sokoloff 1975; Kennedy *et al.* 1975). In contrast to the eye injection technique, this method reveals the entire column from layer I down to layer VI, rather than just the part in layers IVa and c.

7. *Representation of visual fields in layer IVc*

In one important respect figure 25 may be misleading, since taken literally it could give the impression that only half of the visual field is represented in each eye. If black stripes represent right eye, for example, one could infer that the right eye sees the black regions but is blind to the white, which are seen only by the left eye. Intuitively, this would seem most unlikely. To resolve the problem the most direct procedure is to ask what happens to the positions of receptive fields as an electrode moves horizontally through the cortex from one eye dominance column to the next.

In the layers above and below IVc, in crossing through the 0.4 mm occupied by a single column, it is very difficult to make out any appreciable drift in receptive field position against the random scatter; one records a number of binocular cells all dominated by one eye, intermixed with some monocular cells especially near the column borders, all of these cells varying slightly and rather unpredictably in receptive-field position. As described above, a displacement in the cortex several times this size is required to detect any clear overall movement in the visual field. In the upper and lower layers, at least, there is no doubt that any given part of the visual field is represented in both eyes.

In layer IV, however, the receptive field centres are very much smaller than the fields in the upper and lower layers. The positions of the individual fields can therefore be specified far more accurately. The scatter in field positions is also very much less – the cells seem to obey the rule that we have found to apply wherever we have recorded in the visual system, namely that receptive-field scatter is of the same order of magnitude as the size of the fields that are scattered, so that the aggregate field for any one layer is several times the size of an average field. It occurred to us that in crossing from one side of an ocular dominance slab to the other, within layer IVc, the precision of representation might be sufficient to permit the detection of a corresponding movement through the visual field. Experimentally this is, in fact, possible (Hubel, Wiesel & LeVay 1974) and there turns out to be a very special and highly ordered topography within layer IVc. As an electrode crosses from one side to the other of a single column there is a clear progression through the visual field in a direction predicted by the topographic map of the visual fields. All of this movement of course takes place in one eye only; as long as the electrode tip is within a layer IVc column no responses are detected from the other eye. When the border of the column is reached the eyes switch, and one now looks to see the positions of the receptive fields of the first

cells recorded in the newly dominant eye. If the receptive fields were to continue their march through the visual field uninterrupted by the change of eyes, and if this were to occur at every column border crossing, then the visual field would obviously end up being shared by the two eyes in the manner suggested by figure 25. This is not at all what happens. As the border is crossed there is an abrupt discontinuity in the visual-field representation. The position of the receptive fields suddenly jumps back in the visual field through a distance equal to about half of that crossed in the preceding column, when the other eye was used. As the electrode is advanced the fields resume their march forward, recovering the lost territory and then going on for an equal distance into new ground. This is illustrated in figure 26. The visual field is traversed completely in each eye, but in an intermittent 'two steps forward and one step back' fashion, in which each eye must take its turn. The corollary of this is that within a single column the magnification – the number of degrees traversed for each millimetre of cortex – must be double the overall local cortical magnification: in crossing column after column each eye is heard from only half the time, and if the fields are to keep up with the movement of the receptive fields in the other layers the movement must occur at twice the overall rate. Across a given column magnification (mm cortex/degree visual field) must be half that along the length.

The main point, however, is that the field of vision in layer IV is represented completely in each eye. The peculiar interlaced way in which this is accomplished is necessitated by the very special side-by-side manner in which the cortex is shared by the two eyes.

8. *The cortical machinery*

If we now step back and survey the different components of area-17 architecture just reviewed, we find that they fit together rather like the pieces of a Chinese puzzle. The orientation columns, if discrete, are some 50 μm in width, and each represents a shift in angle of about 10° . To cover the full 180° therefore requires a movement across the cortex of the order of 1 mm. Similarly each ocular dominance column is about 0.4 mm in width, and to take care of both eyes requires two such columns – again roughly 1 mm. In each case we designate one complete set of columns, subserving all orientations on the one hand or both eyes on the other, as a *hypercolumn* (Hubel & Wiesel 1974*b*). We now ask what happens to the position of receptive fields in the visual field as an electrode moving horizontally through the cortex traverses one hypercolumn, of either type. Obviously, it would make no sense at all if movement through one orientation hypercolumn were associated with a movement through the visual field that was large compared to aggregate field size, for that would mean that some regions of visual field must be specialized to handle certain orientations and others other orientations. There is certainly no hint, from psychophysics, of any such specialization in our own visual fields. Similarly crossing a single eye-dominance column outside of layer IVc produces a displacement of aggregate field considerably less than the local

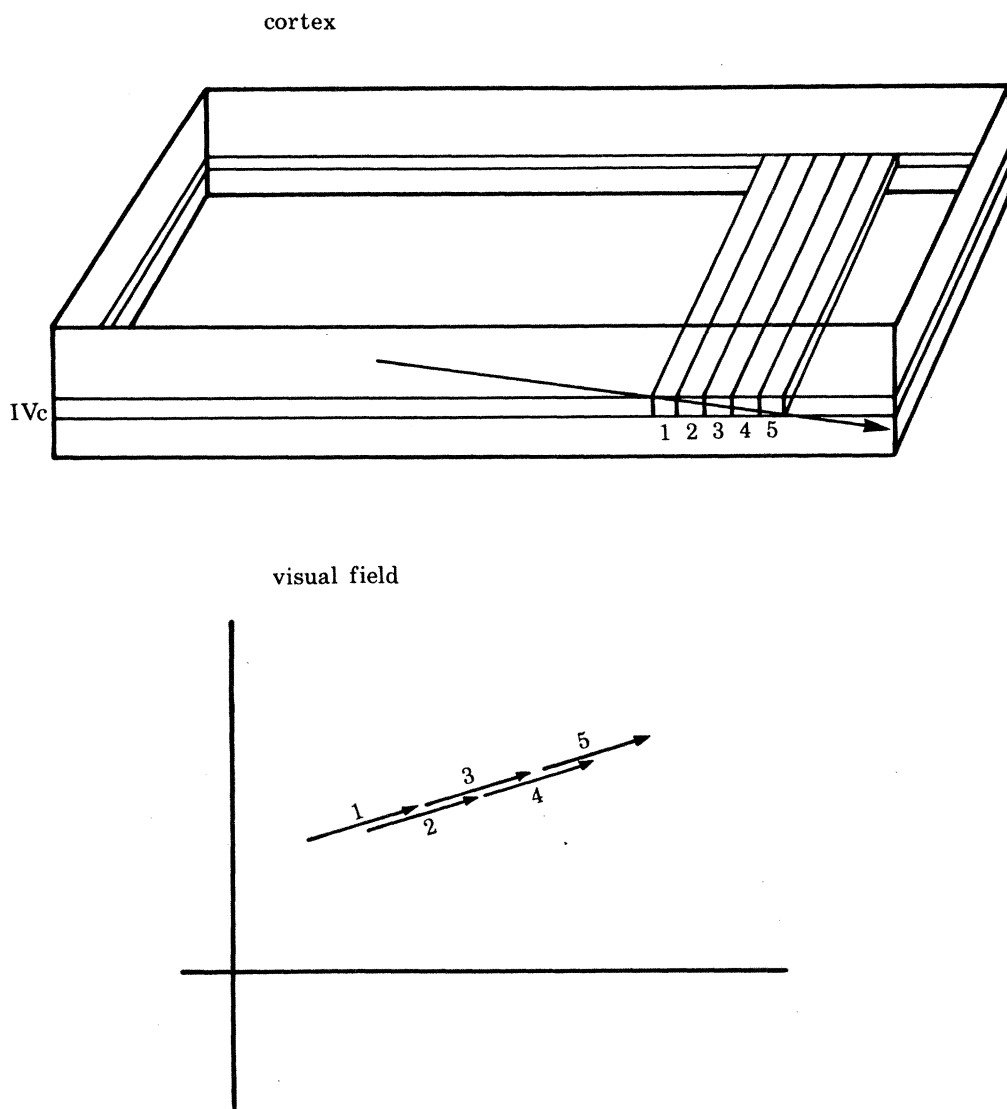


FIGURE 26. Diagram to illustrate topographic representation in layer IVc. An electrode passes through cortex obliquely, almost parallel to the layers; it enters layer IVc, crosses five ocular dominance stripes, and then leaves that layer. During this traverse there is a progressive movement of receptive-field centres through the visual field: the fields in this layer are small enough, and the topography precise enough, to make this movement obvious. Suppose arrow 1, in the lower part of the figure, represents the movement as measured in the eye that feeds into column 1 – say the left eye. On crossing over to column 2, the right eye becomes the one that evokes responses. The receptive-field position jumps back in the visual field by half the distance just traversed, moves forward so as to retrace the lost ground and then an equal distance further (arrow 2). The left eye then takes over again, with a jump back to its previous position and a similar progression (arrow 3) – and so on. The overall rate of movement is the same as that measured in the upper and lower layers (figure 8b). Thus layer IVc has a complete representation of the visual fields.

aggregate field size. In fact, as we have seen, it takes a 1–2 mm traverse through the cortex to produce a movement in the visual field that is comparable to the aggregate field size. What this means is that contained in a 2 mm × 2 mm block there is more than enough machinery to digest such a region of visual field (the aggregate size), examining it for light–dark contours in all orientations and with both eyes.

A block of cortex containing a hypercolumn of each type is illustrated schematically in figure 27. For purposes of illustration we have drawn the two sets of columns orthogonal to each other, but it should be stressed that there is at the moment no direct evidence to suggest how the two sets are related, if indeed there is any consistent relation. There would seem to be advantages, however, for them to intersect at some angle, and preferably at 90°. There is good reason to expect cells that are interconnected to have the same orientation preference, at least if the connections are excitatory, and our notion of the significance of the orientation column is that it houses together groups of cells with like orientation preference in the interests of efficiency of connections. At the same time we imagine that a binocular cell in the cortex, complex or hypercomplex, receives its input directly or otherwise from two sets of simple monocular cells, one set for each eye (figure 12). The connections subserving this binocular convergence must by definition extend beyond the borders of a single ocular dominance column. If the two column systems were parallel these connections would at the same time have to link up at least two orientation columns with the same orientation affiliation, separated by all the intervening orientation columns. This cumbersome wiring could largely be obviated if the two sets of columns were to intersect, since then the fibres could cross ocular dominance columns while remaining within the same orientation column.

The probable pattern of activity of cells in area 17 in response to a contour in the visual field is illustrated in figure 28. We suppose that the contour is a short horizontal line segment, and is viewed by the left eye only: this is shown to the right in figure 28. For the sake of specificity we place the line in the upper left visual quadrant. The general region of cortex affected is predictable from the topographic map of the visual field; let us suppose the line projects to the elongated region in the right striate cortex shown by the broken lines in the left part of the figure. Within this area the dispositions of the boundaries of the two types of columns will, given the limitations of our present knowledge, be unpredictable; let us assume that the boundaries are more or less orthogonal and have the shape shown – for the present discussion the precise shape and relationship to the cortical topography are immaterial. The regions of cortex maximally affected will be those areas within the broken-line boundary that represent horizontal lines and also represent the left eye. The pattern produced by the active cells should therefore be something like that shown in heavy lines. Of course, a truer representation would show fuzziness both at the edges, since orientation specificity is for most cells relaxed enough so that neighbouring columns will be weakly stimulated, and at the ends, since many cells in the right-eye columns will be influenced from the

left eye, though again rather weakly. (In layer IVc, of course, the ocular dominance column boundaries are rigidly respected, but the orientation columns are irrelevant, so here all of the left-eye territory within the broken lines will be active, instead of only the territory belonging to one specific orientation, and no right-eye territory will be affected.) Such a diagram can, in principle, be prepared for any line or curve

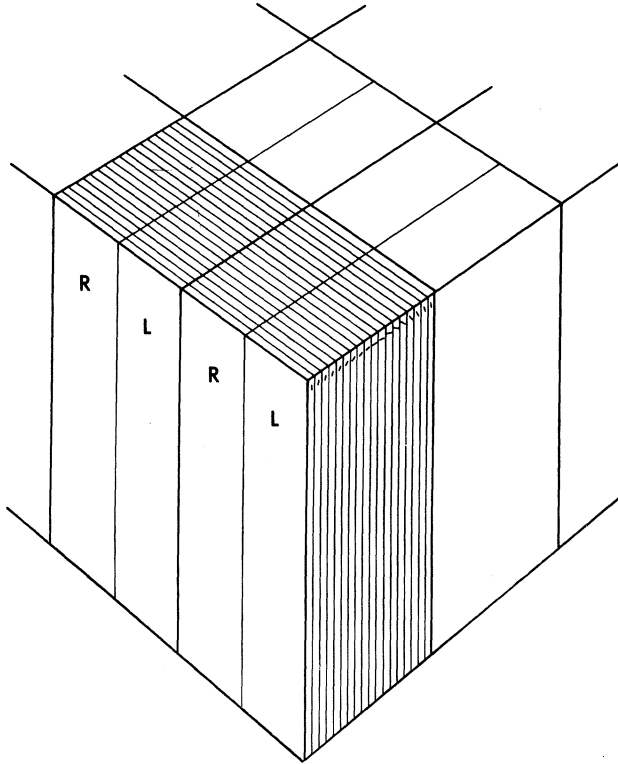


FIGURE 27. Model of the striate cortex, to show roughly the dimensions of the ocular dominance slabs (L, R) in relation to the orientation slabs and the cortical thickness. Thinner lines separate individual columns; thicker lines demarcate hypercolumns, two pairs of ocular dominance columns and two sets of orientation columns. The placing of these hypercolumn boundaries is of course arbitrary; one could as well begin at horizontal or any of the obliques. The decision to show the two sets of columns as intersecting at right angles is also arbitrary, since there is at present no evidence as to the relationship between the two sets. Finally, for convenience the slabs are shown as plane surfaces, but whereas the dominance columns are indeed more or less flat, the orientation columns are not known to be so, and may when viewed from above have the form of swirls.

in the visual scene: one first draws the swath of activated territory on the cortex, as determined from the topographic map, and then fills in the squares according to the local orientation and the eye that is being used. The interesting conclusion is that a continuous line in the visual field produces a very discontinuous activity pattern in area 17.

Parenthetically we may emphasize here how absurd it is to think of a simple or

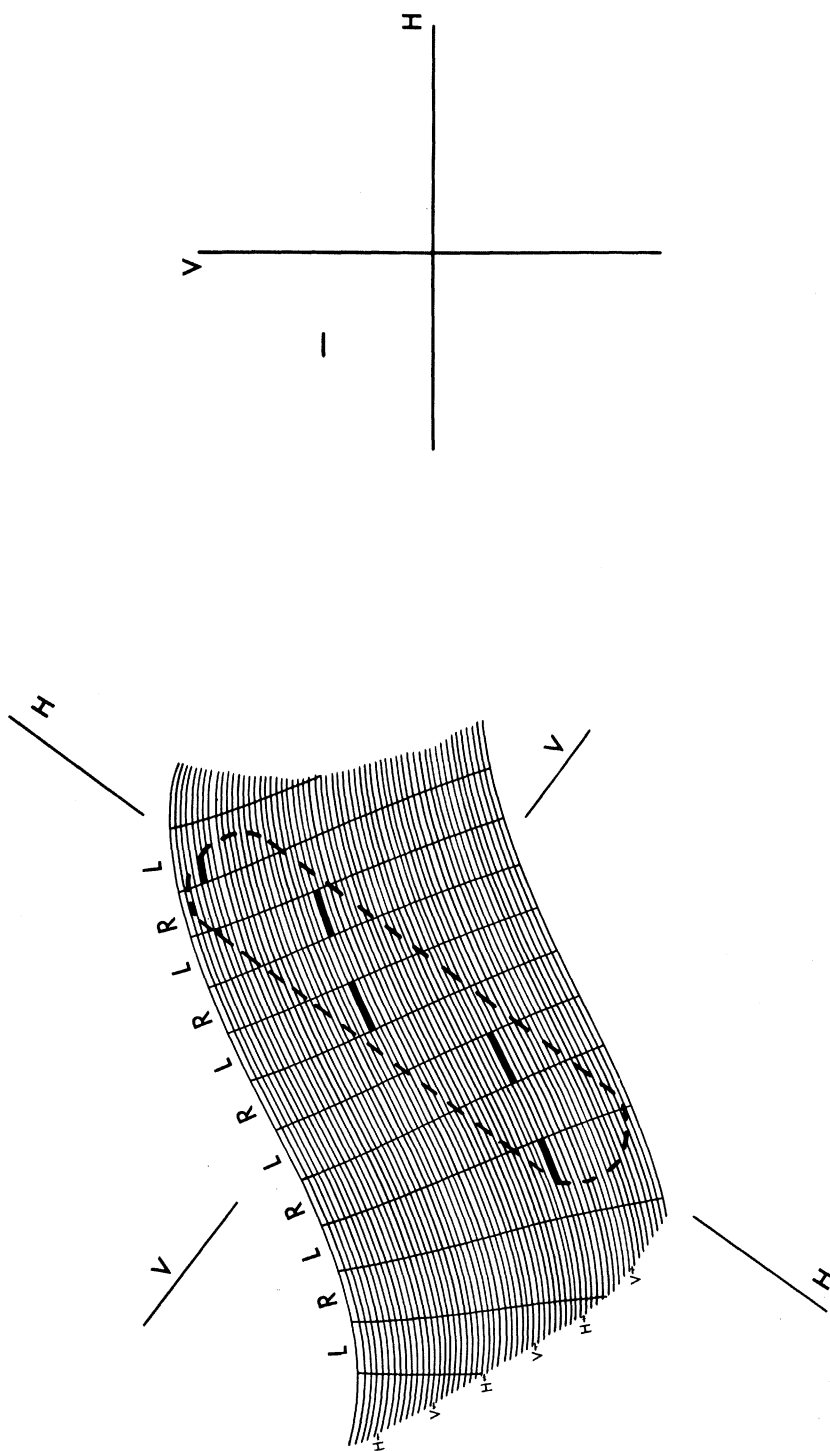


FIGURE 28. Diagram illustrating the pattern of cortical activity that might follow from stimulation of the left eye with a short line in the visual field, say a horizontal line in the left visual field, as shown in the diagram on the right. To the left is drawn an area of cortex including the activated region as it might appear if one stood above and looked down at it. Let V and H represent the vertical and horizontal directions – their position will of course be determined by the topographic map of the visual field (i.e. the sum of aggregate fields of all the points along the line stimulus). Suppose, finally, that the eye-dominance and orientation columns are as shown; for the argument, any other directions would do just as well; as in figure 27, the decision to make the boundaries of the two sets of columns orthogonal is arbitrary. Then the regions of activation will be those marked by heavy lines – the areas corresponding to horizontal stimuli and left eye. See text for additional comments.

complex cell as a 'straight-line detector'. What is detected is the orientation of a short line-segment. A straight line long enough to be seen as straight (or for that matter a curved line) would have to be 'detected' by some cell receiving input from populations of area-17 cells, presumably scattered in regions such as those shown in figure 28. Whether such cells exist is not known.

It is perhaps worth stressing once more that the cortical machinery is highly uniform, as far as is known, at least throughout the binocular part of the cortex. Both sets of columns have roughly constant width. In the temporal crescent representation, where only the contralateral eye has input, there are obviously no ocular dominance columns. It is also likely that certain kinds of analysis, for example those involving colour, are selectively emphasized in the fovea, while others, like movement, are best developed in the periphery. Thus the uniformity may not be absolute. Aside from these probable differences, what seem to be the main preoccupations of area 17, orientation selectivity and binocular convergence, probably depend on the same apparatus throughout. This is supported, as mentioned earlier, by the similarity of the histology everywhere, and the tailoring of aggregate field size to magnification.

The cortex, then, seems to solve the problem of analysing the visual field in great detail centrally and in much less detail peripherally, in a very special way. The same basic units of cortical function (figure 27) seem to be used throughout, but more of them are used per degree of visual field the greater the detail of analysis. The alternative to this would be to vary the machinery, for example by having a thicker cortex in the region subserving the fovea, with more cells and more connections in a unit area. Intuitively one suspects that that would be a far more difficult and cumbersome solution. The disparity in magnification between fovea and periphery is very large, so that if magnification were uniform the corresponding regions of cortex would presumably have to be very different in thickness.

The development of the cortex, finally, must pose a much easier problem if the structure is uniform, since the instructions need only be specified once, for a block roughly $2\text{ mm} \times 2\text{ mm}$; and then repeated again and again – perhaps about 300–400 times, since the surface area of the macaque striate cortex is probably in the neighbourhood of $1300\text{--}1400\text{ mm}^2$ (Clark 1941; Daniel & Whitteridge 1961).

STUDIES IN NEWBORN MONKEYS

In addressing the problem of the development of area 17, it seemed to us that the first question to ask was whether the system as we know it in the adult, with its hierarchy of cells, its topographic map and its intricate architecture, is all present at birth and thus presumably determined genetically, or whether some or all of the specificity depends on the details of postnatal experience. Our previous work in cats (Hubel & Wiesel 1963) had led us to conclude that in that species genetics was the main, if not the sole determinant in the formation of area 17, but the problem was complicated by the immaturity of the cat's visual system at

birth and a difficulty in knowing whether binocular deprivation effects were a result of holding back postnatal maturation or of withholding specific experience. By now almost everyone seems to agree that one can find cells with strict orientation specificity in visually naïve cats (Blackemore & Van Sluyters 1975), but it is still difficult to interpret the large number of non-oriented cells in these animals. Any slight deterioration in an animal's condition during recording can lead to a disappearance of orientation specificity, and very young animals are especially hard to keep in good condition during acute experiments.

The newborn macaque monkey is visually much more advanced than the cat. The eyes are open, and by the day after birth the baby monkey fixes visually and follows objects with its eyes. One would expect, then, that for interpretations of deprivation effects the problems of postnatal maturation might be less troublesome in the monkey than in the cat.

Recordings from newborn monkey cortex are in fact very similar to those obtained in the adult (Wiesel & Hubel 1974). Cells in layers outside IVc occur in simple, complex and hypercomplex types, with orientation and directional specificity that appear to be about as well developed as in the adult. To be certain that there are *no* differences between newborn and adult would require a statistical survey, with automated stimuli and averaged responses. This has not yet been done. Histologically the cortex of the newborn macaque is indeed not fully mature (though it is far advanced by comparison with the cortex of the newborn cat), so that some differences between it and adult cortex might well be expected. Receptive field size, for example, may be larger. But what strikes one most forcibly in these records is the similarity to the adult, not the differences. One exception to this, in the case of ocular dominance columns, is taken up below.

To record in area 17 from a monkey on the day of its birth is technically difficult and risky. In most cases we have therefore sutured the eyes closed at birth, to avoid visual experience, and recorded after about 2–4 weeks. The eye closures allow some diffuse light to reach the retinas but almost certainly exclude any light–dark contours. Records from area 17 in these animals were virtually indistinguishable from those of adults. One problem posed by this procedure was the delay between the birth of the monkey and our notification of the birth, during which time the animal usually received a few hours of visual exposure. It seemed hardly likely that a few hours' experience in dim light would by itself produce an adult-like cortex, but it seemed important to avoid all possibilities of this. We accordingly did a Caesarean section in a mother monkey near term, immediately sutured the eyes of the baby, and waited 2 weeks before recording. This animal's primary visual cortex showed just as high a degree of specificity as was seen in the cortex of other less stringently controlled monkeys. A graph of optima orientation against track distance in this monkey is shown in figure 29. The graph points up another aspect of the recordings: in addition to the regular small orientation shifts indicated by the graph, there were periodic alternations in ocular dominance. This indicates that both the orientation and ocular dominance columns

are present, though, as we will see, the development of the dominance columns is not quite complete at birth. That area 17 is in so many respects wired up and ready to go when the animal is born is perhaps not so surprising if one remembers that the machinery of area 17 represents building blocks of vision, used in a

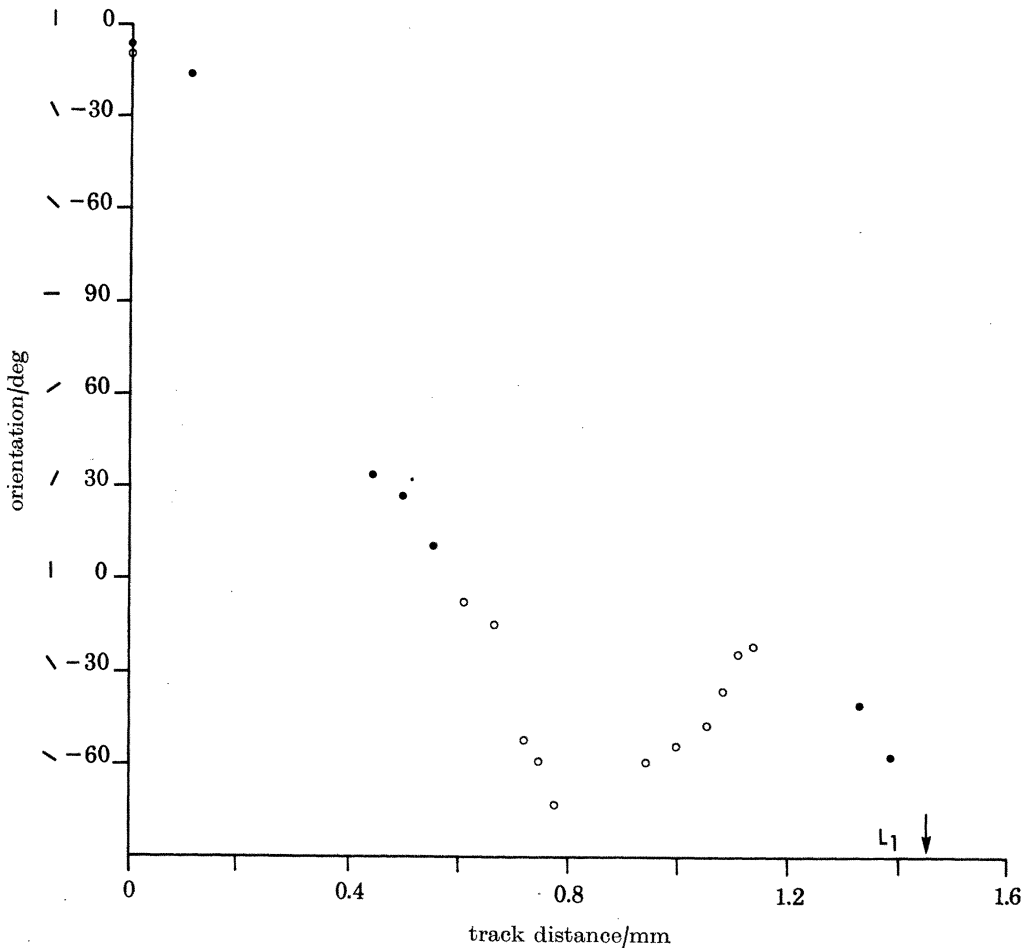


FIGURE 29. Graph of orientation plotted against electrode position similar to those of figures 15b and 16, but for a 30-day-old monkey that was delivered at term by Caesarean section and both eyes immediately sewn shut. The animal thus had no patterned visual experience. Orientation specificity in this animal showed no obvious lack of precision, compared with what is seen in the adult.

piecemeal analysis of the visual fields and required whatever the detailed environment of the animal is to be. One would not expect experience to be important in the development of area 17 any more than it is in the development of retinal connections: the striate cortex extends the kinds of analysis already begun in the retina, and what takes place there is not much more sophisticated, relative to the tasks that still remain to be solved in perception. Nevertheless, our original finding that

specificity of various types, particularly orientation specificity, was already present in the newborn was greeted with surprise and some considerable scepticism. The reason for this is a partly justified conviction that the cerebral cortex of all parts of the brain is the structure most important for perception, memory, and in fact for mentation in general. A structure that is involved in learning must change in some way with experience. Hence to find some part of the cortex for all intents and purposes formed at birth seems to fly in the face of all one's preconceptions about that structure. Too little is known about other cortical areas to permit guesses as to the importance of experience in forming and organizing them, but, to take an extreme case, one would certainly expect regions such as the speech areas of man to be modified by the details of postnatal experience. The striate cortex seems to represent an extreme in the other direction, and the lesson, if any, is that very different rules may apply in the development of different regions of the cerebral cortex.

DEPRIVATION STUDIES

A detailed account of the studies we and others have made on the effects of early deprivation on the visual system is beyond the scope of this article. Some recent results, nevertheless, bear strongly on the problem of the origin of the ocular dominance columns, and illustrate the possibility of deforming the columns. To describe these results it will be necessary to review at least some of the deprivation work. Some years ago we observed that if one eye of a kitten was sewn closed for the first few months of life a marked change occurred in the cortical physiology (Wiesel & Hubel 1963). Instead of most cells' responding to both eyes, the great majority of cells lost all ability to respond to the eye that had been closed, while remaining normally responsive to the eye that had been open. Recordings from retina and geniculate were relatively normal, so that the major defect was clearly in the cortex. We found that to obtain the changes the eye had to be closed some time during the first few months, and the most marked changes were produced by closures between about the fourth and eighth week of life. Closures in adults produced no obvious defects. Our first guess was that the defects resulted simply from disuse of the closed eye. This guess was incorrect, as we found on examining cats in which both eyes had been sewn shut from birth, for here there were far less severe defects than would have been predicted on any naïve expectation that the separate lid-closure effects add in a simple way (Wiesel & Hubel 1965). Evidently monocular closures produced such striking results because of some kind of binocular competition; if the right eye was closed the pathway belonging to the left eye could presumably take over the right eye's territory at some point along the pathway. The idea of a competitive interaction between the two paths was subsequently reinforced by anatomical findings at the geniculate level by others (Guillery & Stelzner 1970; Guillery 1972; Sherman 1973; Sherman, Guillery, Kaas & Sanderson 1974).

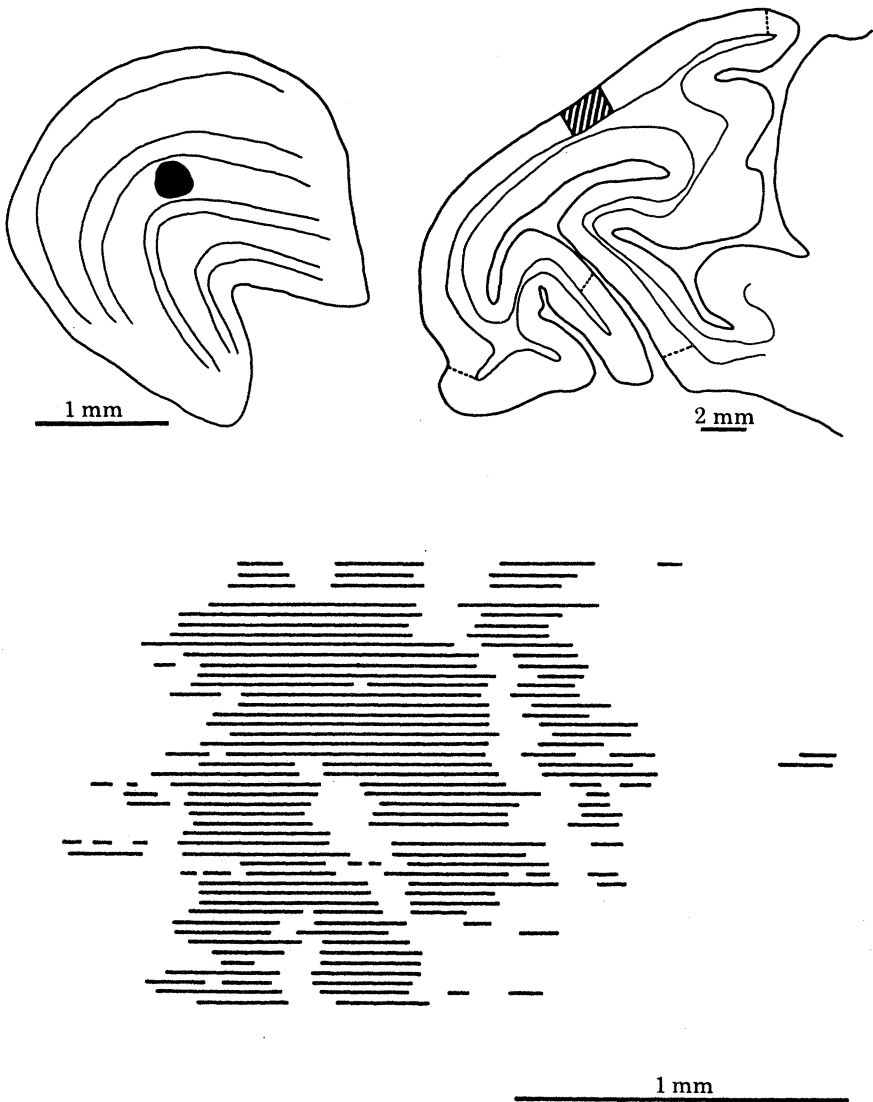


FIGURE 30. Distribution of degenerating terminals in layer IVc of a macaque monkey whose right eye was removed at 2 weeks of age and the experiment carried out at an age of 18 months. At that age lesions were made in two layers of the left lateral geniculate body, and the brain sectioned 5 days later and stained by the Fink-Heimer method (compare figure 18). Here the lesion was made in layer 3, whose input was from the surviving eye. Bands of terminal degeneration are wider than normal, whereas gaps between the bands, corresponding to the eye that was removed, are markedly shrunken.

Similar experiments in monkeys have given almost the same results. The critical period for monocular-closure effects is probably the first 6 weeks or so, though eye closure produces defects for a period of up to a year or more if the closure is sufficiently prolonged.

The macaque monkey provides an opportunity to test the idea of binocular competition, since in area 17, as described in the first part of this paper, convergence of inputs from the two eyes does not occur until after the first two stages of integration. There is thus little or no convergence in layer IV, and one might

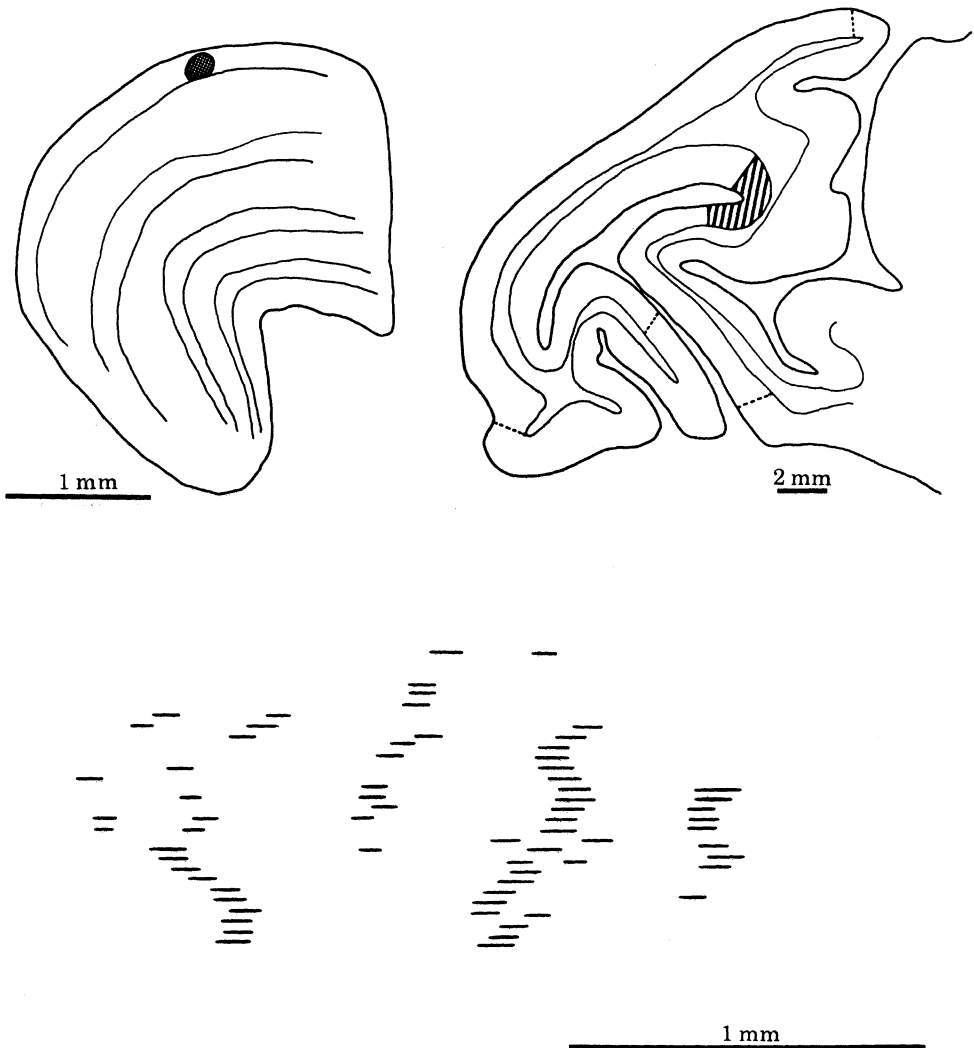


FIGURE 31. Same monkey as in figure 30. Lesion in layer 6, the most dorsal layer, deafferented. Bands of degeneration in IVc are markedly shrunk, and the gaps between widened. This is thus the complement of figure 30. (Figures 30 and 31 are from Hubel *et al.* (1977).)

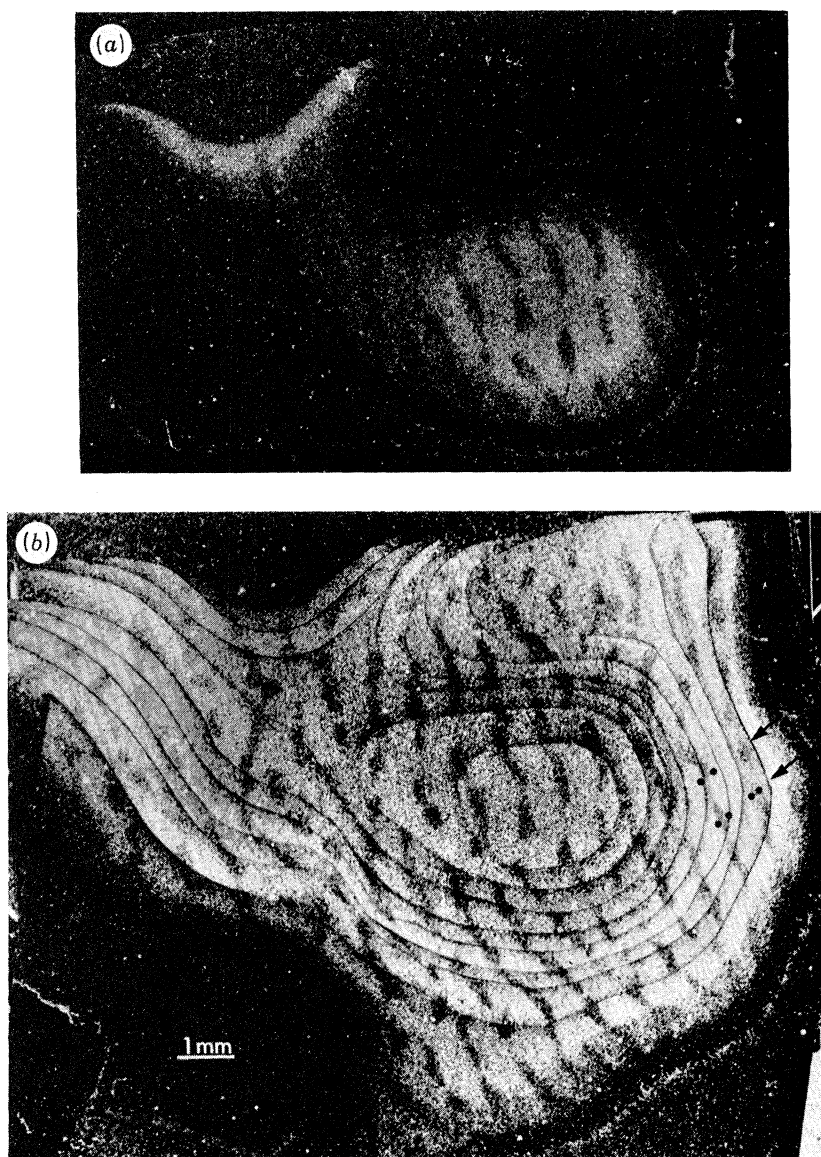


FIGURE 32. Transneuronal autoradiography of left occipital lobe of macaque monkey whose right eye was sutured closed at 2 weeks, and studied at 18 months. Left (normal) eye injected with tritiated proline-fucose mixture 2 weeks before brain was sectioned. (a) Section tangential to layer IVc, dark field, as in figure 23. Note expansion of labelled columns and shrinkage of the gaps. The serial reconstruction, (b), was made from a number of sections parallel to *a* and including *a*. The positions of six lesions, determined from neighbouring sections, are shown near the right border. These lesions were made during the electrical recordings, in two penetrations (arrows), at points of eye transition. Note how each lesion falls on a column border. (From Hubel *et al.* 1977.)



FIGURE 33. Autoradiograph of transverse sections through striate cortex of a 7-month-old macaque monkey whose right eye was closed at 2 days of age, for a period of 7 weeks; the eye was then reopened and kept open till an age of 7 months, when the right (deprived) eye was injected with radioactive proline-fucose mixture and the brain examined 2 weeks later. The labelled columns in layer IVc are shrunken, and the gaps between enlarged. (Label is seen at two distinct horizontal levels, thin in layer IVa above and thicker in IVc below.) This figure forms the complement of figure 32, in which the normal eye was injected. (From Hubel *et al.* 1977.)

not expect to see a profound disturbance of responses in this layer following monocular deprivation. For the layers above and below IVc our early studies in monkeys had shown a takeover by the normal eye that was just as impressive as that which occurs in the cat, but until a few years ago we had not looked specifically at layer IV itself. Obviously the time was ripe to study layer IV in deprived monkeys, using the same tools we had employed in the normal physiological recordings, i.e. tangential penetrations, the Nauta method, the reduced silver method and transneuronal autoradiography (Hubel, Wiesel & LeVay 1977).

We began with the rather radical procedure of removing one eye in each of two 2-week-old monkeys and waiting $1\frac{1}{2}$ years before experimenting. We felt that if this did not produce a change in layer IV nothing would! We were not disappointed, for when we made long tangential penetrations through the cortex we found that there was in layer IVc almost continuous activity evoked from the normal eye as the electrode moved forward, instead of responses for about 0.4 mm alternating with silence for 0.4 mm, as would be expected if no change had occurred. This suggested that there had been a rearrangement in layer IVc, with the retinogeniculate fibres belonging to the normal eye occupying space normally allotted to the deprived eye.

This was confirmed anatomically. In one of the animals, for example, we made several geniculate lesions 5 days before the recording; some were made in layers fed by the normal eye, some in the deafferented layers, which were electrically silent. On examining the cortex with Nauta stain we were able to find the projections from two of the normal-layer lesions and from one of the deprived-layer lesions. The reconstruction of two of these projections is shown in figures 30 and 31; they are analogous to the reconstructions from a normal monkey shown in figure 18. What the diagrams show is that the terminals from the geniculate layers fed by the normal eye have occupied virtually the entire extent of layer IVc, instead of exactly half of it, while the bands representing the removed eye are less than one-third normal size. This anatomical result was obtained in both monkeys, and confirms the physiological findings.

We have done similar experiments over the past few years in monkeys with monocular eye suture from an early age. The results have been generally similar to those obtained after eye removal. For example, one monkey had its right eye sutured closed at 2 weeks of age and was allowed to live for 18 months. Two weeks before the records were made, the left (normal) eye was injected with radioactive amino acids, and a week before recording, geniculate lesions were made for Nauta studies. The results of making several tangential penetrations were similar to what we had found after eye removal, but not so extreme; rather to our surprise there were regions in layer IVc in which brisk responses were obtained only from the right (closed) eye. The spans over which these responses were recorded were clearly short compared with the normal 0.4 mm. In striking contrast, the regions dominated by the normal eye were much wider than normal. At each point where a shift of eyes occurred a small electrolytic lesion was made in order to

correlate the points of transition, in the recordings, with the autoradiographic results.

Transneuronal autoradiography fully confirmed this impression of an extreme departure from the normal balance in the distribution of geniculate terminals. Figure 32*a*, plate 12, shows a photograph of a section made tangential to layer IVc, analogous to the normal section of figure 23*a*. The picture is again taken under dark-field illumination, so that the bright regions produced by silver grains represent terminals of afferent geniculate fibres belonging to the injected, normal eye. A montage from a number of sections parallel to this one is shown in figure 32*b*. The deprived columns not only show marked shrinkage, but seem in places to be pinched off entirely. Actual measurements of area in this montage indicate a shrinkage of about 50 %. To the right in (*b*) the lesions made during the recording are indicated, traced from neighbouring fibre-stained sections. Each lesion is just where the recordings had predicted it should be, on the border separating two bands. The agreement between the physiologic and anatomic results tends to strengthen one's confidence in both approaches.

Finally, another monkey had its right eye sutured at 2 days of age, for a period of only 7 weeks; the eye was then reopened and the animal kept to an age of 7 months, at which time the right (deprived) eye was injected with a tritiated proline-and-fucose mixture and the brain examined two weeks later. A transverse section through the left striate cortex is shown in figure 33, plate 13. Here the labelled portions of layer IVc, corresponding to the deprived eye, are markedly shrunk. This experiment thus forms the complement of the previous one. In addition, in agreement with other anatomical and physiological studies, it shows that even a very brief closure is enough to disturb the columns, and further that the recovery resulting from simply reopening the eye is very disappointing.

DOMINANCE COLUMNS IN NEWBORN MONKEYS

On first seeing the results described in the preceding section our natural tendency was to assume that monocular closures had led to an invasion of the deprived columns by geniculate terminals belonging to the eye that had been open. A process of proliferation of terminals and spread beyond their normal territory when

DESCRIPTION OF PLATE 14

FIGURE 34. Autoradiographs through striate cortex of a baby monkey whose right eye was injected with radioactive fucose the day after birth, and the brain examined at 1 week of age. (From Hubel *et al.* 1977.) (*a*) Transverse section through hemisphere contralateral to injected eye, shows virtually no hint of fluctuation in label density along layer IVc. (The extreme lower left tail of label, deep in the calcarine fissure, is temporal crescent representation; here no fluctuations are expected.) (*b*) Tangential section through top of mushroom-like part of calcarine fissure, intersecting layer IVc in an oval. A strong suggestion of stripes is seen, but the entire region is labelled, rather than having virtually label-free gaps between dense stripes, as was seen in the normal adult (figure 23).

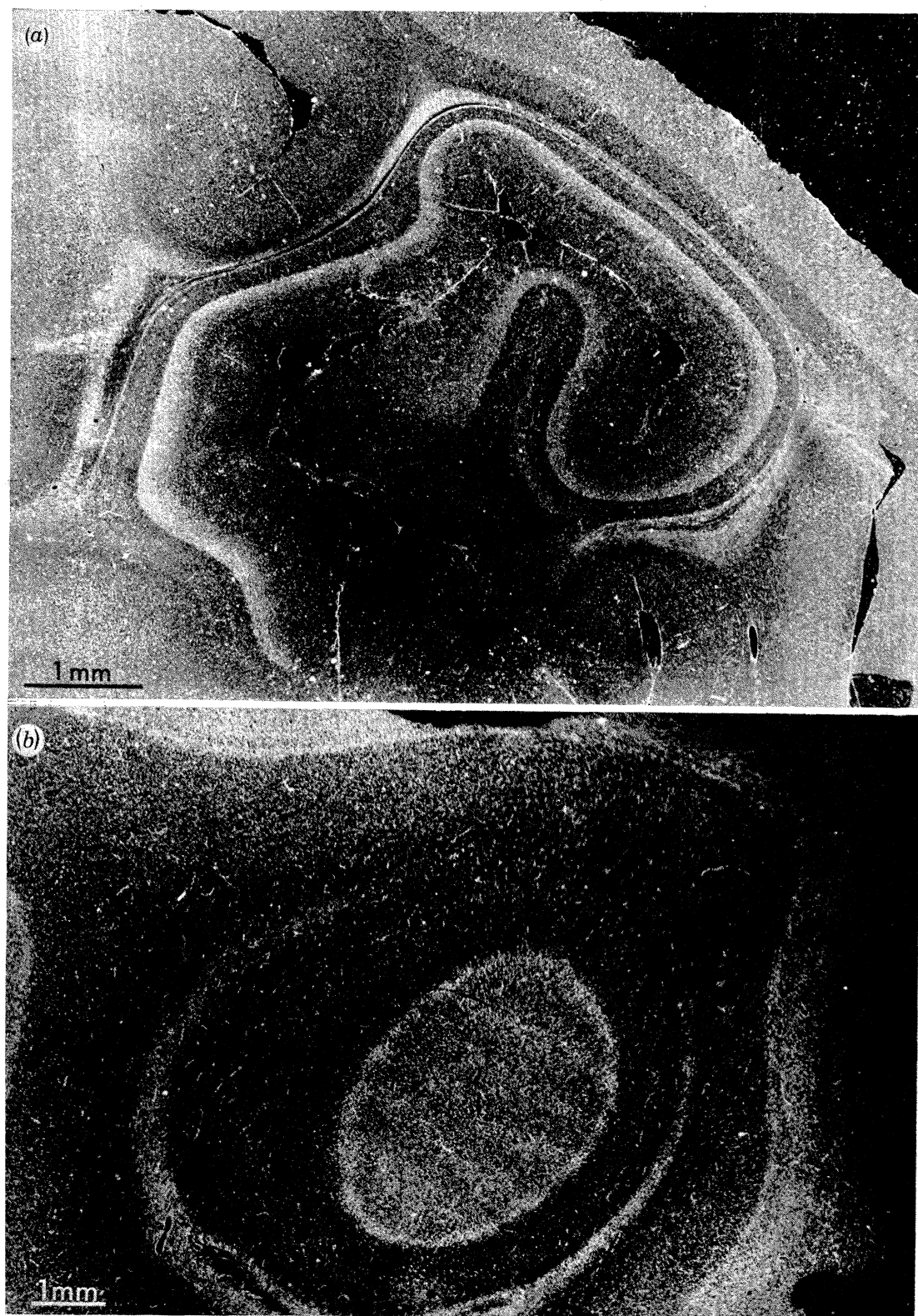


FIGURE 34. For description see opposite.

(Facing p. 50)

a competing set of terminals is put at a disadvantage has been observed in many situations, and is usually termed 'sprouting', though that term has normally been used in cases where the competition has been destroyed by a lesion, surgical or electrolytic. The notion that sprouting can occur by an insult as mild as merely covering one eye would in itself be of considerable interest. If this were indeed a matter of sprouting one would have to modify the idea of competition, for here one can obviously only talk about competition between columns, i.e. sets of terminals in layer IVc, and not about competition between two inputs for territory on a single cell. How one set of terminals would know that it should extend its domain, whether by a chemical signal or some other action at a distance, is a matter for speculation.

A recent set of findings (Hubel *et al.* 1977) has made us reconsider the whole question of sprouting. In accounting for the IVth layer changes following deprivation we had assumed that the ocular dominance columns were present at birth, or at least at 2 weeks, when the closures were made. There was some reason for this assumption, since recordings from layers outside IVc in newborn animals had shown regular fluctuations in ocular dominance. What we needed, however, was autoradiographic proof that in the newborn monkey the geniculate terminals were sharply segregated in layer IVc. Accordingly, we injected the eye of a monkey the day after birth and examined the visual pathway autoradiographically at one week. The lateral geniculate bodies were well labelled, and showed a layering as distinct as in the adult. This result has already been illustrated in figure 21. The cortical picture was, on the contrary, not at all what we had expected. Layer IVc, as seen in transverse section, was virtually continuously labelled, with only the vaguest of fluctuations in density here and there (figure 34*a*, plate 14). Tangential sections did, however, show periodic stripe-like variations in density, but with levels of label that were well above background throughout (figure 34*b*), suggesting that at that age terminals belonging to one eye were not restricted in any clear-cut way to one set of stripes. This would mean that a particular geniculocortical fibre, which in the adult would enter the cortex, subdivide, and have its branches run selectively to several stripes of its own set, over an area of perhaps 1–2 mm, would in the newborn distribute its branches over the entire area, perhaps favouring its own set of stripes but not confining itself to them.

In a series of eye injections of foetal monkeys Rakic (1977) has extended these observations by showing that when the geniculate afferents from one eye grow into the cortex they occupy layer IVc continuously, whereas a week or so before term there are periodic fluctuations in density too subtle to see by naked eye, but obvious from grain counts.

Interpretation of these eye-injection experiments is complicated by the likelihood that a smearing of input to the cortex from one eye results from leakage of label at the geniculate level by diffusion from one set of layers to the other. We have therefore felt it necessary to crosscheck the results in the newborn in as many ways as possible. For example, physiological recordings in the first days

after birth support the anatomical results in showing a binocular input to layer IVc at most points along its extent. By 6 weeks, however, this binocularity has disappeared, and the distribution of input from the two eyes seems to be identical to that found in the adult. (This postnatal change, incidentally, takes place even

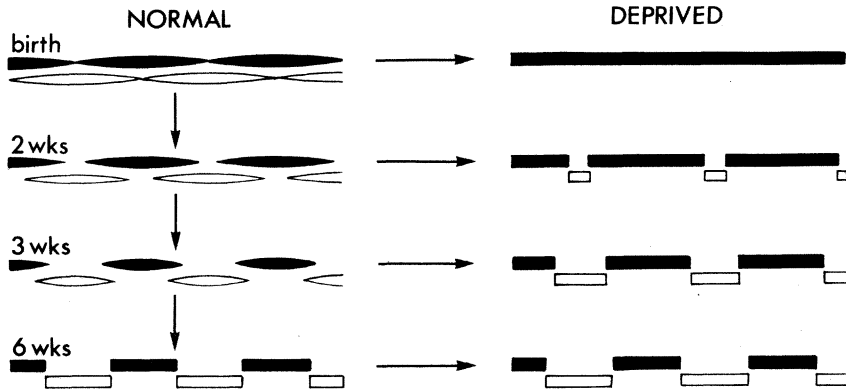


FIGURE 35. Scheme that might explain the effects of eye closures on columns in layer IVc, on the assumption that the segregation of the eyes is not complete until some weeks after birth. The solid lines represent the terminations of geniculate afferents in layer IVc corresponding to one eye; the open lines, the terminations from the other eye. In each, the width is intended to represent the presumed density of the terminals. The left half of the diagram illustrates the course of normal development suggested by our results. At birth there is some periodic variation in density (see figure 34): it is unlikely that the minimum is zero, as suggested here, and the fluctuations may be different in different parts of the striate cortex. In this scheme we suppose that competition normally occurs between the eyes, with the weaker input declining progressively and the stronger becoming fortified. The result is a progressive retraction as the sparse terminals die out entirely. For purposes of the drawing we assume that the retraction process takes about 6 weeks, but the exact times are not known. On the right, the illustration shows what happens if at any stage in this process one eye (here, the eye corresponding to open lines) is sutured closed. We suppose that this inflicts a competitive disadvantage on the terminals from the closed eye so that they die out at those places where terminals from the normal eye are still present. Where normal-eye terminals have already retracted, their adversaries meet no competition and survive. The final outcome thus depends on when the deprivation was inflicted. (From Hubel *et al.* 1977.)

if both eyes are sutured closed, and hence is not dependent on visual experience.) The physiological findings thus appear to support the autoradiography.

In the normal development of ocular dominance columns, then, what seems to happen first is a complete occupation of layer IVc all along its length by fibres from both eyes and, with time, a gradual retraction and segregation until the process is complete, at about 6 weeks. What produces the orderly retraction is not known, but one might imagine a competition between terminals from the two eyes, in which the rules are that the denser of the two sets proliferates and the less dense regresses. In such an unstable equilibrium the final result would be complete segregation. This is schematized in the left half of figure 35.

To explain the deprivation effects, then, one need only suppose that closing one eye puts the corresponding IVc terminals at a competitive disadvantage, so that they retract completely from any point provided their adversaries have not themselves already retracted. The later the closure in the first 6 weeks the less would be the final apparent shrinkage. This process is shown in figure 35 on the right.

Thus there seems to be a good possibility that the monocular deprivation results involve not so much a pathological proliferation of terminals as a persistence and perhaps strengthening of inputs that are present at birth and normally regress in the first 6 weeks. If this proved to be true it would neatly explain two otherwise puzzling problems. First, the 'sensitive period' would become simply the time of normal consolidation of columns, the period between birth and the final maturation of this part of the visual system. Second, if at and shortly after birth layer IVc were supplied all along its length by fibres from both eyes, it would be possible to explain the effects of monocular deprivation on a model that presupposes competition for space on the postsynaptic cell. Such a model would assume that a large number of afferent fibres make transitory synaptic contacts in IVc. One should emphasize, however, that the existence of temporary synapses in IVc is not established. Competition is in any case easier to imagine among fibres that are interwoven than between groups that are separated by a sizeable fraction of a millimetre.

Meanwhile, we do not exclude sprouting as a contributing mechanism in the process of columnar shrinkage and expansion. Eye closures after the sixth week seem not to affect the columns in layer IVc, but whether sprouting can be produced by removals or reversing the suturing – opening the closed eye and closing the open one – remains to be tested.

COMPARATIVE STUDIES OF ARCHITECTURE

Obviously an important motive for investigating the brains of mammals is the possibility of understanding the brain of man. It is partly for this reason that one seeks to learn as much as possible about the brains of higher mammals, especially of primates. To avoid making false generalizations it is important to survey as broad a range of mammals as possible. We were therefore interested in looking at physiology and architecture in striate cortex of a number of other species.

Our experiments in cats preceded the work in monkeys, but since about 1962 the two sets of studies have gone in parallel. In striate cortex of adult cats orientation specificity is just as common as in monkeys, and indeed it is likely that some cells in layer IVc have simple receptive fields (with orientation specificity) rather than circularly symmetric ones. Orientation columns are well developed. Ocular dominance columns, on the other hand, while present, are more subtle, and it was only after seeing accentuated versions of them in cats brought up from an early age with artificial squint that we were fully convinced of their presence. Eye

injection studies (Shatz, Lindström & Wiesel 1977) have since revealed their presence clearly (figure 36, plate 15). They are well defined on the ipsilateral side, but less well on the contralateral, where the input is stronger but also more diffuse. In tangential section they are less stripe-like, more chaotic, than those of the macaque. The cat is unique among known mammals in having a strong projection to area 18 from the geniculate. Eye dominance columns are seen also in 18 where they are well defined and probably coarser than in 17.

In the mouse (Dräger 1975) cells with orientation specificity are common but in contrast to the cat and monkey form only about 50% of the population. There may be some kind of grouping of cells with like orientation preference, but no clear columns have been observed. Compared with cat and monkey, the mouse has a much higher proportion of fibres crossing in the optic chiasm. Eye injection studies (Dräger 1974) show the expected disparity on the two sides, with the contralateral hemisphere far more strongly labelled (figure 37, plate 16). There is no hint, from physiology or autoradiography, of dominance columns. Results in the rat (Dräger, unpublished) are similar to those in mouse except that the ipsilateral input seems even weaker (figure 38, plate 17).

The tree shrew shows no hint of ocular-dominance columns (Hubel 1975; Casagrande & Harting 1975). The main difference in labelling on the two sides is an absence of label in the narrow cell-sparse cleft which subdivides layer IVc into three sublaminae (figure 39, plate 18).

In the prosimian, Galago, orientation specificity is as common as in macaque, and orientation columns are well developed and orderly (Hubel & Ginzler, unpublished). Both studies with Nauta degeneration (Glendenning & Kofron 1974) and eye injection (Hubel, unpublished) reveal clear eye dominance columns, again better defined ipsilaterally (figure 40, plate 19). Finally in the squirrel monkey, a New World species, one animal whose eye was injected showed no hint at all of eye-dominance columns, both hemispheres showing uniform label in layer IVc (Hubel *et al.* 1976). If this result is confirmed physiologically it will form an

DESCRIPTION OF PLATES 15 AND 16

FIGURE 36. Distribution of label in layer IV of cat cortex following injection of left eye with a tritiated proline-fucose mixture. Autoradiograph, coronal section through postlateral gyri; darkfield. The label in most of the dorsal part of the postlateral gyrus and sulcus is in area 18; the medial surfaces (which face each other) are area 17. Columns are more obvious ipsilaterally (i). On the contralateral side (c) the label is in places almost continuous. The intensely and continuously labelled inferior portion on the contralateral side is the temporal crescent representation; it is of course absent ipsilaterally.

FIGURE 37. Coronal section through mouse brain; autoradiograph, dark field, showing visual cortex following injection of a tritiated proline-fucose mixture into the left eye. Label in layer IV of contralateral cortex (c) is very obvious, in contrast to the ipsilateral cortex (i) in which the label is only barely visible. There is no suggestion of ocular dominance columns. There is probably some label in area 18 (which in the mouse is termed 18a), just lateral to the densely labelled area 17 on the side contralateral to the injection. The optic tectum as expected is intensely labelled. (From Dräger 1974.)



FIGURE 36. For description see opposite.



FIGURE 37. For description see page 54.



FIGURE 38. Autoradiograph of rat brain; right eye was injected with a tritiated proline-fucose mixture; coronal section, dark field. As in the mouse the cortical label is much heavier in the contralateral cortex (c), and no columns are present. (Indeed, in this section there is virtually no label in the ipsilateral cortex (i).) Label in contralateral area 17 is concentrated mainly in layer IV, but some faint label may be seen in layers I and VI (Ribak & Peters 1975). Lateral to area 17 two fainter areas of label can be made out. Again, the contralateral optic tectum is intensely labelled. (Dräger, unpublished.)



FIGURE 39. For description see opposite.

amazing departure from what otherwise seemed like a tendency for columns to be better defined the higher one looked in phylogeny. One is reluctant to accept this result without physiological confirmation, however, since the lamination of the lateral geniculate in this animal is not so well defined as in the old world monkey, and opportunity for label to leak from one set of layers to the other is greater.

In man the methods of physiology and autoradiography are of course unavailable and will remain so. We had hoped that LeVay's reduced silver technique might be used to demonstrate bands, but so far the method has failed to show any. The apparent difference between squirrel monkey and macaque should, however, make one cautious in assuming that all higher primates have ocular dominance columns.

CONCLUSION

We end up, then, with a view of the cortex as containing a thousand small machines of more or less identical structure. Each machine contains two types of hypercolumns, whose functions are dovetailed with each other and with the topographical map. This dicing up into subdivisions is the way the cortex handles or represents two variables (orientation and ocular dominance) besides the two obvious visual-field positional variables. Undoubtedly the picture is incomplete and, given the indirectness of much of the evidence, perhaps in places also incorrect. Colour information is not taken into account at all, for example, nor is black vs. white. Both of these may be associated with columns. What makes the architecture encouraging and attractive to us, however, has nothing to do with the relative completeness of the picture but the reinforcement it gives to much of the physiological findings. Orientation specificity, for example, might be just a curious property of cortical cells, shown, to be sure, by the majority of cells, but merely one among twenty or thirty competing properties. The existence of such an intricate edifice of orderly columns subserving this variable suggests, on the contrary, that it is of very great importance in area 17.

Another interesting aspect is the very orderliness of the architecture. It would be surprising if other regions of cortex did not use some similar orderly principles. If area 18 is largely devoted to mechanisms related to stereopsis (Hubel & Wiesel 1970), one might expect to see the eyes brought together in a whole range of different horizontal disparities in all parts of the visual field, and it would seem

DESCRIPTION OF PLATE 18

FIGURE 39. Autoradiograph of the brain of a tree shrew whose right eye was injected with a tritiated proline-fucose mixture; dark field, coronal section (Hubel 1975). On the contralateral side (c) layer IVc is labelled throughout its entire thickness; an upper tier of label can be seen in layer IVa (to use a terminology analogous to that employed in the macaque). Ipsilaterally (i) there is a narrow label free cleft dividing layer IVc, and IVa is not labelled. In the optic tectum label is almost confined to the contralateral side; only a few tiny clusters of label are seen ipsilaterally.

reasonable to find this done again in repetitive units. At the moment there is no conclusive evidence for such an arrangement but it would surely be reasonable to look for one. What orderly arrangements one should expect in a structure like auditory cortex, where time sequences might conceivably be expected to form some vague counterpart to orientation, is difficult to imagine; on the other hand, our ideas about frontal lobes or speech areas are so vague as to make the auditory cortex seem like home territory. At least it can be said that with some years of work a few regions of cortex are capable of being understood, even if incompletely.

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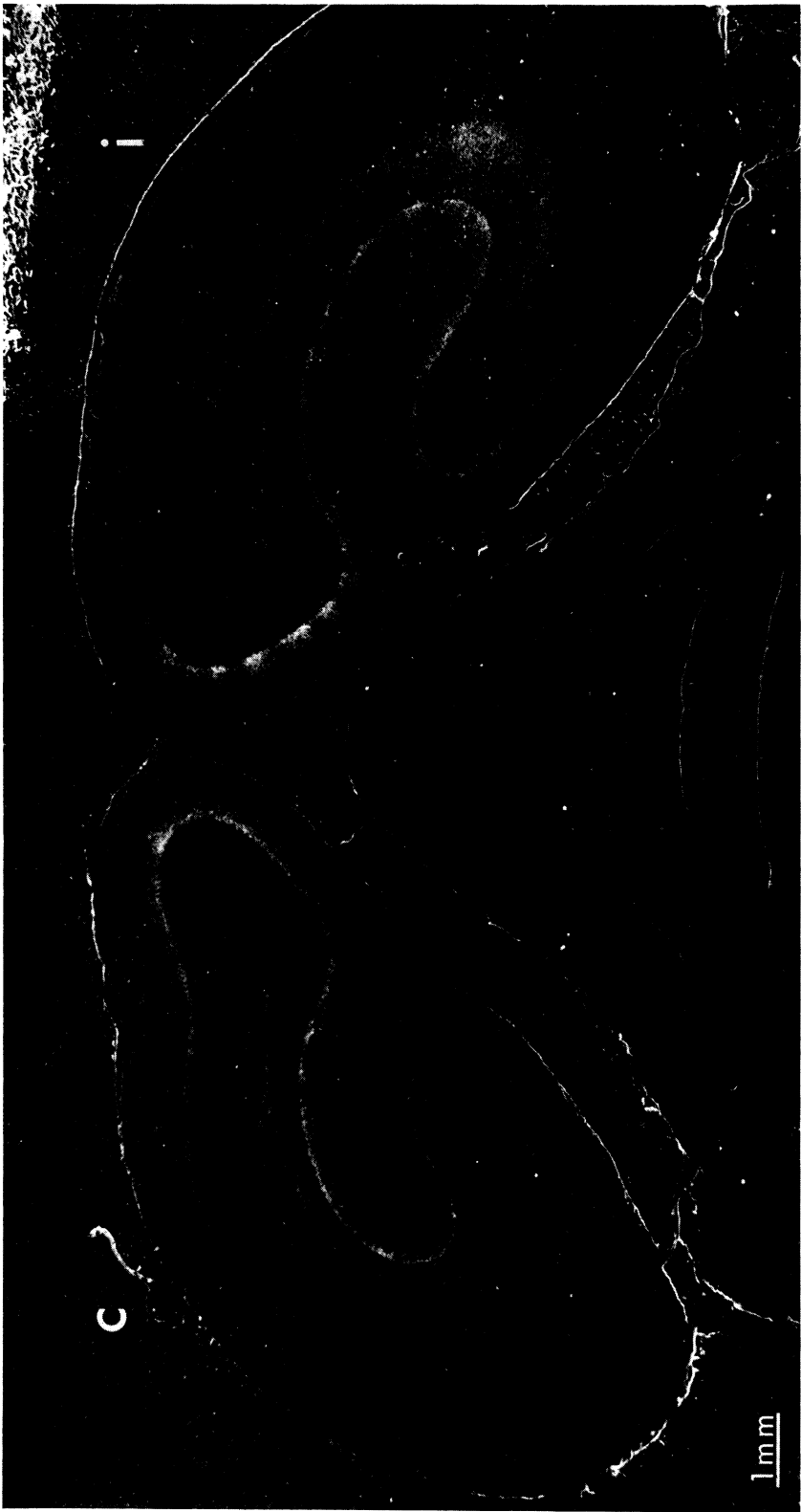


FIGURE 40. Autoradiograph of the brain of an old world prosimian, *Galago crassicaudatus*, whose right eye was injected with a tritiated proline-fucose mixture. Ocular dominance columns are obvious in both hemispheres, but, as in the cat, are better defined ipsilaterally (i).

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