5. THE ARCHITECTURE OF THE VISUAL CORTEX

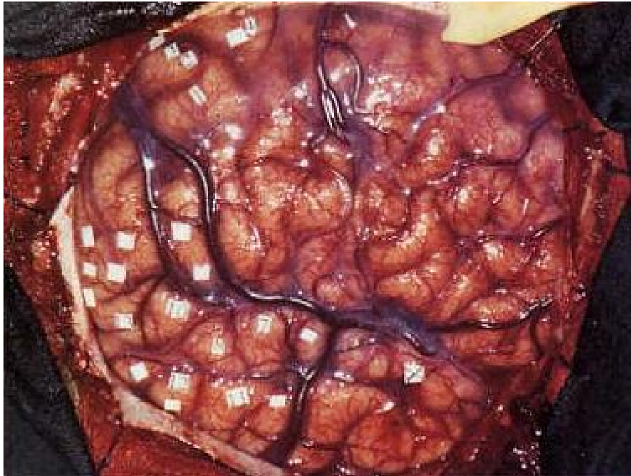
The primary visual, or striate, cortex is a far more complex and elaborate structure than either the lateral geniculate body or the retina. We have already seen that the sudden increase in structural complexity is accompanied by a dramatic increase in physiological complexity. In the cortex we find a greater variety of physiologically defined cell types, and the cells respond to more elaborate stimuli, especially to a greater number of stimulus parameters that have to be properly specified. We are concerned not only with stimulus position and spot size, as we are in the retina and geniculate, but now suddenly with line orientation, eye dominance, movement direction, line length, and curvature. What if anything is the relation between these variables and thestructural organization of the cortex? To address this question, I will need to begin by saying something about the structure of the striate cortex.

Ocular-dominance columns are seen in this section through a macaque monkey's left striate cortex, taken perpendicular to the surface in a left-to-right direction. As we follow the part of the cortex that is exposed to the surface from left to right (top of photo), it bends around forming a buried fold that extends from right to left. Radioactive amino acid injected into the left eye has been transported through the lateral geniculate body to layer 4C, where it occupies a series of half-millimeter-wide patches; these glow brightly in this dark-field picture. (The continuous leaflet in the middle is white matter, containing the geniculo-cortical fibers.)

ANATOMY OF THE VISUAL CORTEX

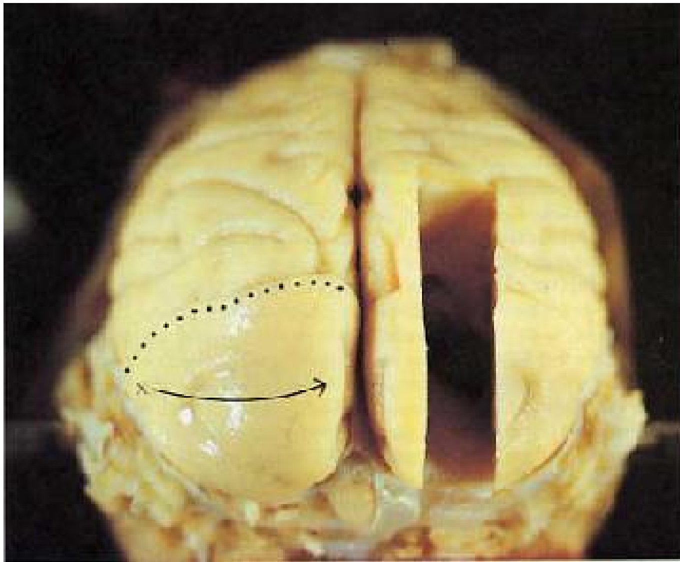
The cerebral cortex, which almost entirely covers the cerebral hemispheres, has the general form of a plate whose thickness is about 2 millimeters and whose surface area in humans is over i square foot. The total area of the macaque monkey's cortex is much less,

probably about one-tenth that of the human. We have known for over a century that this plate is subdivided into a patchwork of many different *cortical areas*; of these, the primary visual cortex was the first to be distinguished from the rest by its layered or striped appearance in cross section—hence its classical name, striate cortex. At one time the entire careers of neuroanatomists consisted of separating off large numbers of cortical areas on the basis of sometimes subtle histological distinctions, and in one popular numbering system the striate contex was assigned the number 17. According to one of the more recent estimates by David Van Essen of Caltech, the macaque monkey primary visual cortex occupies 1200 square millimeters—a little less than one-third the area of a credit card. This represents about 15 percent of the total cortical area in the macaque, certainly a substantial fraction of the entire cortex.



A large part of the cerebral cortex on the right side has been exposed under local anesthesia for the neurosurgical treatment of seizures in this fully conscious human patient. The surgeon was Dr. William Feindel at the Montreal Neurological Institute. The scalp has been opened and retracted and a large piece of skull removed. (It is replaced at the end of the operation.) You can see gyri and suici, and the large purplish veins and smaller, red, less conspicuous arteries. The overall pinkish appearance is caused by the finer branches of these vessels. Filling the bottom third of the exposure is the temporal lobe; above-the prominent, horizontally running veins arc the parietal lobe, to the left, and frontal lobe, to the right. At the extreme left we sec part of the occipital lobe. This operation, for the treatment of a particular type of epilepsy, consists of removing diseased brain, which is only permissible if it does not result in impairment of voluntary movement or loss of speech. To avoid this, the neurosurgeon identifies speech, motor, and sensory areas by electrical stimulation, looking for movements, sensations related precisely to different parts of the body, or interference with speech. Such tests would obviously not be possible if the patient were not conscious. Points that have been stimulated have been labeled by the tiny numbered sterile patches of paper. For example, stimulation of these regions gave the following results: (1) tingling sensation in the left thumb; (2) tingling in the left ring finger; (3) tingling in the left middle and ring finger; (4) flexion of left fingers and wrist. The regions labeled 8 and 13 gave more complex memory-like sensations typically produced on stimulation of the temporal lobe in certain types of epileptic patients.

A rear view of the brain of a macaque monkey is seen in the photograph on this page. The skull has been removed and the brain perfused for preservation with a dilute solution of formaldehyde, which colors it yellow.

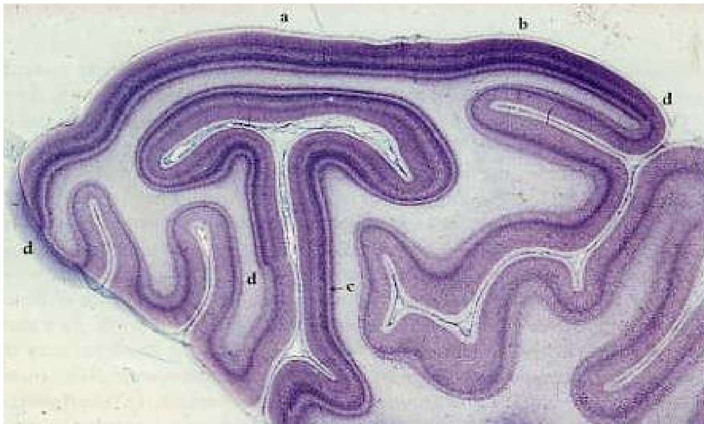


This view of a macaque monkey's brain, from behind, shows the occipital lobe and the part of the striate cortex visible on the surface (below the dotted line).

Blood vessels normally form a conspicuous web over the surface, but here they are collapsed and not visible. What we see in this rear view is mostly the surface of the occipital lobe of the cortex, the area that is concerned with vision and that comprises not only the striate cortex but also one or two dozen or more *prestriate* areas. To get a half-millimeter-thick plate of nervous tissue that is the area of a large index card into a box the size of the monkey's skull necessitates some folding and crinkling, the way you crinkle up a piece of paper before throwing it into the waste basket; this produces fissures, or *sulci*, between which are ridges, or *gyri*. The area behind (below, in this photograph) the dotted line is the exposed part of the striate cortex. Although the striate cortex occupies most of the surface of the occipital lobe, we can see only about one-third to one-half of itin the photograph; the rest is hidden out of sight in a fissure. The striate cortex (area 17) sends much of its output to the next cortical region, visual *area 2*, also called *area 18* because it is next door to area 17. Area18 forms a band of cortex about 6 to 8 millimeters wide, which almost completely surrounds area 17. We can just see part of area 18 in the photograph, above the dotted line, the boundary between 17 and 18, but most of it extends down into the deep sulcus just in front of that line. Area 17 projects to area 18 in a plate-to-plate, orderly fashion. Area 18 in turn projects to at least three postage-stamp-size occipital regions, called MT (for medial temporal), visual area 3, and visual area 4 (often abbreviated V3 and V4). And so it goes, with each area projecting forward to several other areas. In addition, each of these areas projects back to the area or areas from which it receives input. As if that were not complicated enough, each of the areas projects to structures deep in the brain, for example to the superior colliculus and to various subdivisions of the thalamus (a complex golfball-size mass of cells, of which the lateral geniculate forms a small part). And each of these visual areas receives input from a

thalamic subdivision: just as the geniculate projects to the primary visual cortex, so other parts project to the other areas. In the same photograph, X indicates the part of area 17 that receives information from the foveas, or centers of gaze, of the two retinas. As we move from X, in the left hemisphere, toward the arrowhead, the corresponding point in the right half of the visual field starts in the center of gaze and moves out, to the right, along the horizon. Starting again from X, movement to the right along the border between areas 17 and 18 corresponds to movement down in the visual field; movement back corresponds to movement up. The arrowhead marks a region about 6 degrees out along the horizon. The visual field farther out than 9 degrees is represented on the part of area 17 that is folded underneath the surface and parallel to it.

To see what the cortex looks like in cross section, we have cut a chunk from the visual cortex on the right side of the photograph on the previous page. The resulting cross section, as in the photomicrograph on this page, is stained with cresyl violet, a dye that colors the cell bodies dark blue but does not stain axons or dendrites. With the photomicrograph taken at this low power, we cannot distinguish individual cells, but we can see dark layers of densely aggregated cells and lighter layers of more thinly scattered ones. Beneath the exposed part of the cortex, we see a mushroom-shaped, buried part that is folded under in a complicated way, but these two parts are actually continuous. The lightly stained substance is white matter; it lies under the part of the cortex that is exposed to the surface, separating it from the buried fold of cortex, and consists mainly of myelinated nerve fibers, which do not stain. The cortex, containing nerve-cell bodies, axons, dendrites, and synapses, is an example of gray matter.



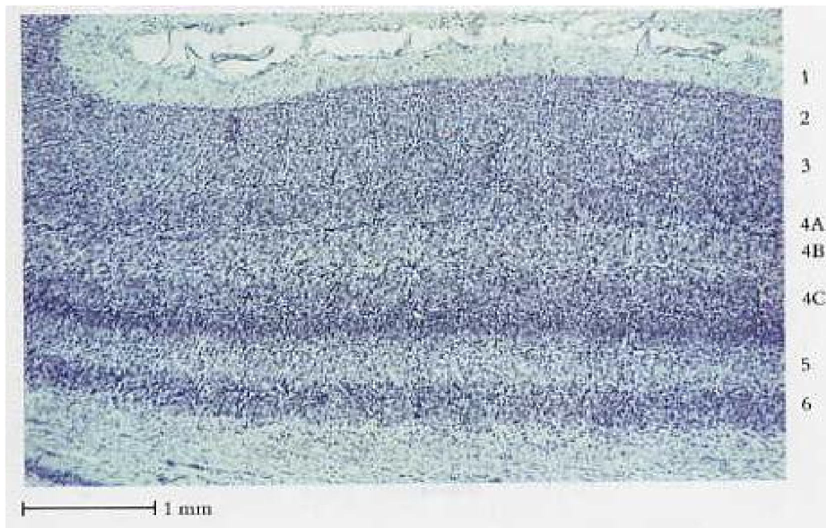
This cross section through the occipital lobe was made by cutting out a piece as shown in the photograph on the previous page. It is what we would see if we were to walk into the groove and look to the left. The letter a corresponds to a point halfway between X and the arrowhead. The Nissi stain shows cell bodies only; these are too small to make out except as dots. The darker part of the top and the mushroom-shaped part just below are striate cortex. The three letter d's mark the border between areas 17 and 18.

For anatomical richness, in its complexity of layering, area 17 exceeds every other part of the cortex. You can see an indication of this complexity even in this low-magnification cross section when you compare area 17 with its next door neighbor, area 18, bordering area 17 at d. What is more, as we look along the cross section from the region marked a, which is a few degrees from the foveal projection to the cortex, toward the region marked b, 6 degrees out, or toward c, 80 to 90 degrees out, we see very little change in the

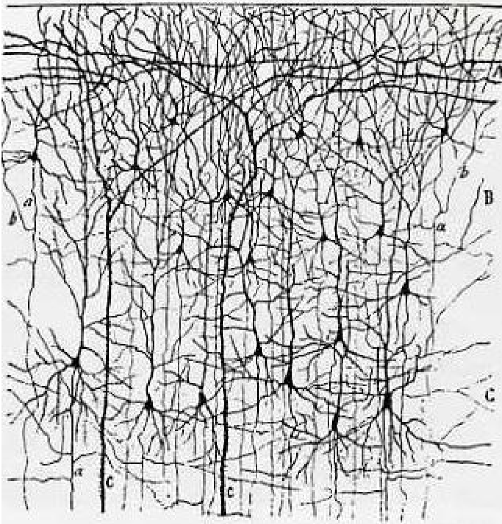
thickness or the layering pattern. This uniformity turns out to be important, and I will return to it in Chapter 6.

LAYERS OF THE VISUAL CORTEX

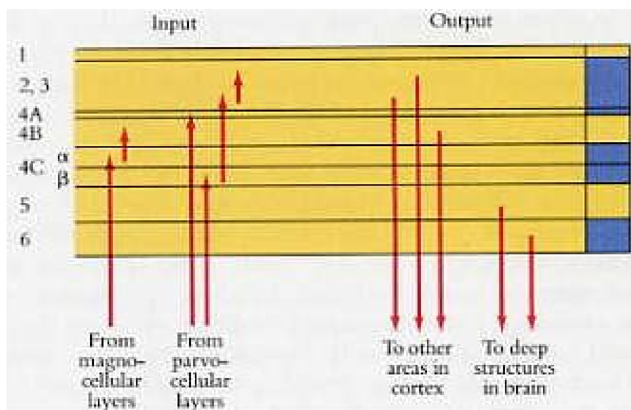
A small length of area 17 appears at higher magnification in the photomicrograph on this page. We can now make out the individual cell bodies as dots and get some idea of their size, numbers, and spacing. The layering pattern here is partly the result of variations in the staining and packing density of these cells. Layers 4C and 6 are densest and darkest; layers 1, 4B, and 5 are most loosely packed. Layer 1 contains hardly any nerve cells but has abundant axons, dendrites, and synapses. To show that different layers contain different kinds of cells requires a stain like that devised by Camillo Golgi in 1900. The Golgi stain reveals only occasional cells, but when it does reveal a cell, it may show it completely, including its axons and dendrites. The two major classes of cortical cells are the pyramidal cells, which occur in all layers except i and 4, and the stellate cells, which are found in all layers. You have seen an example of a pyramidal cell and a stellate cell on page 6 in Chapter 1. We can get a better idea of the distribution of pyramidal cells witnin the cortex in another drawing from Ramon y Cajal's *Histologie* (on the next page), which shows perhaps 1 percent of pyramds instead of only one or two cells.



A cross section of the striate cortex taken at higher magnification shows cells arranged in layers. Layers 2 and 3 are indistinguishable; layer 4A is very thin. The thick, light layer at the bottom is white matter.



A Golgi-stained section from the upper layers, 1, 2, and 3, of the visual cortex in a child several days old. Black triangular dots are cell bodies, from which emanate an apical dendrite ascending and dividing in layer 1, basal dendrites coming off laterally, and a single slender axon heading straight down.



The main connections made by axons from the lateral geniculate body to the striate cortex and from the striate cortex to other brain regions. To the right, the shading indicates the relative density of Nissl staining, for comparison with the illustration on page 5.

The fibers coming to the cortex from the lateral geniculate body enter from the white matter. Running diagonally, most make their way up to layer 4C, branching again and again, and finally terminate by making synapses with the stellate cells that populate that layer. Axons originating from the two ventral (magnocellular) geniculate layers end in the upper half of 4C, called 4C alpha; those from the four dorsal (parvocellular) geniculate layers end in the lower half of 4C (4C Bata). As you can see from the diagram on this page, these subdivisions of layer 4C have different projections to the upper layers: 4C alpha sends its output to 4.B; 4Q Bata, to the deepest part of 3. And those layers in turn differ in their projections. Seeing these differences in the pathways stemming from the two sets of geniculate layers is one of many reasons to think that they represent two different systems. Most pyramidal cells in layers 2, 3, 4A, 5, and 6 send axons out of the cortex, but side-branches, called "collaterals", of these same descending axons connect

locally and help to distribute the information through the full cortical thickness.

The layers of the cortex differ not only in their inputs and their local interconnections but also in the more distant structures to which they project. All layers except 1, 4A, and 4C send fibers out of the cortex. Layers 2 and 3 and layer 4B project mainly to other cortical regions, whereas the deep layers project down to subcortical structures: layer 5 projects to the superior colliculus in the midbrain, and layer 6 projects mainly back to the lateral geniculate body. Although we have known for almost a century that the inputs from the geniculate go mostly to layer 4, we did not know the differences in outputs of the different cortical layers until 1969, when Japanese scientist Keisuke Toyama first discovered them with physiological techniques; they have been confirmed anatomically many times since.

Ramon y Cajal was the first to realize how short the connections within the cortex are. As already described, the richest connections run up and down, intimately linking the different layers. Diagonal and side-to-side connections generally run for 1or 2 millimeters, although a few travel up to 4 or 5 millimeters. This limitation in lateral spread of information has profound consequences. If the inputs are topographically organized—in the case of the visual system, organized according to retinal or visual-field position—the same must be true for the outputs. Whatever the cortex is doing, the analysis must be local. Information concerning some small part of the visual world comes in to a small piece of the cortex, is transformed, analyzed, digested—whatever expression you find appropriate—and is sent on for further processing somewhere else, without reference to what goes on next door. The visual scene is thus analyzed piecemeal. The primary visual cortex cannot therefore be the part of the brain where whole objects—boats, hats, faces—are recognized, perceived, or otherwise handled; it cannot be where "perception" resides. Of course, such a sweeping conclusion would hardly be warranted from anatomy alone. It could be that information is transmitted along the cortex for long distances in bucket-brigade fashion, spreading laterally in steps of i millimeter or so. We can show chat this is not the case by recording while stimulating the retina: all the cells in a given small locality have small receptive fields, and any cell and its neighbor always have their receptive fields in very nearly the same place in the retina. Nothing in the physiology suggests that any cell in the monkey primary visual cortex talks to any other cell more than 2 or 3 millimeters away.

For centuries, similar hints had come from clinical neurology. A small stroke, tumor, or injury to part of the primary visual cortex can lead to blindness in a small, precisely demarcated island in the visual field; we find perfectly normal vision elsewhere, instead of the overall mild reduction in vision that we might expect if each cell communicated in some measure with all other cells. To digress slightly, we can note here that such a stroke patient may be unaware of anything wrong, especially if the defect is not in the foveal representation of the cortex and hence in the center of gaze—at least he will not perceive in his visual field an island of blackness or greyness or indeed anything at all. Even if the injury has destroyed one entire occipital lobe, leaving the subject blind in the entire half visual field on the other side, the result is not any active sensation of the world being blotted out on that side. My occasional migraine attacks (luckily without the headache) produce transient blindness, often in a large part of one visual field; if asked what I see there, I can only say, literally, nothing—not white, grey, or black, but just what I see directly be-hind—nothing.

Another curious feature of an island of localized blindness, or scotoma, is known as "completion". When someone with a scotoma looks at a line that passes through his blind region, he sees no interruption: the line is perfectly continuous. You can demonstrate the same thing using your own eye and blind spot, which you can find with no more apparatus than a cotton Q-tip. The blind spot is the region where the optic nerve enters the eye, an oval about 2 millimeters in diameter, with no rods and cones. The procedure for mapping it is so childishly simple that anyone who hasn't should! You start by closing one eye, say the left; keeping it closed, you fix your gaze with the other eye on a small object across the room. Now hold the Q-tip at arm's length directly in front of the object and slowly move it out to the right exactly horizontally (a dark background helps). The white cotton will vanish when it is about 18 degrees out. Now, if you place the stick so that it runs through the blind spot, it will still appear as a single stick, without any gap. The region of blindness constituting the blind spot is like any scotoma; you are not aware of it and cannot be, unless you test for it. You don't see black or white or anything there, you see nothing.

In an analogous way, if looking at a big patch of white paper activates only cells whose fields are cut by the paper's borders (since a cortical cell tends to ignore diffuse change in light), then the death of cells whose fields are within the patch of paper should make no difference. The island of blindness should not be seen—and it isn't. We don't see our blind spot as a black hole when we look at a big patch of white. The completion phenomenon, plus looking at a big white screen and verifying that there is no black hole where the optic disc is, should convince anyone that the brain works in ways that we cannot easily predict using intuition alone.

ARCHITECTURE OF THE CORTEX

Now we can return to our initial question: How are the physiological properties of cortical cells related to their structural organization? We can sharpen the question by restating it: Knowing that cells in the cortex can differ in receptive-field position, complexity, orientation preference, eye dominance, optimal movement direction, and best line length, should we expect neighboring cells to be similar in any or all of these, or could cells with different properties simply be peppered throughout the cortex at random, without regard to their physiological attributes? Just looking at the anatomy with the unaided eye or under the microscope is of little help. We see clear variations in a cross section through the cortex from one layer to the next, but if we run our eye along any one layer or examine the cortex under a microscope in a section cut parallel to the layers, we see only a gray uniformity. Although that uniformity might seem to argue for randomness, we already know that for at least one variable, cells are distributed with a high degree of order. The fact that visual fields are mapped systematically onto the striate cortex tells us at once that neighboring cells in the cortex will have receptive fields close to each other in the visual fields. Experimentally that is exactly what we find. Two cells sitting side by side in the cortex invariably have their fields close together, and usually they overlap over most of their extent. They are nevertheless hardly ever precisely superimposed. As the electrode moves along the cortex from cell to cell, the receptive-field positions gradually change in a direction predicted from the known topographic map. No one would have doubted this result even fifty years ago, given what was known

about geniculo-cordcal connections and about the localized blindness resulting from strokes. But what about eye dominance, complexity, orientation, and all the other variables? It took a few years to learn how to stimulate and record from cortical cells reliably enough to permit questions not just about individual cells but about large groups of cells. A start came when, by chance, we occasionally recorded from two or more cells at the same time. You already saw an example of this on page 30 of Chapter 4. To record from two neighboring cells is not difficult. In experiments where we ask about the stimulus preferences of cells, we almost always employ extracellular recording, placing the electrode tip just outside the cell and sampling currents associated with impulses rather than the voltage across the membrane. We frequently find ourselves recording from more than one cell at a time, say by having the electrode tip halfway between two cell bodies. Impulses from any single cell in such a record are all almost identical, but the size and shape of the spikes is affected by distance and geometry, so that impulses from two cells recorded at the same time are usually different and hence easily distinguished. With such a two-cell recording we can vividly demonstrate both how neighboring cells differ and what they can have in common. One of the first two-unit recordings made from visual cortex showed two cells responding to opposite directions of movement of a hand waving back and forth in front of the animal. In that case, two cells positioned side by side in the cortex had different, in fact opposite, behaviors with respect to movement. In other respects, however, they almost certainly had similar properties. Had I known enough to examine their orientation preferences in 1956, I would very likely have found that both orientation preferences were close to vertical, since the cells responded so well to horizontal movements. The fact that they both responded when the moving hand crossed back and forth over the same region in space means that their receptive-field positions were about the same. Had I tested for eye dominance, I would likely have found it also to be the same for the two cells. Even in the earliest cortical recordings, we were struck by how often the two cells in a two-unit recording had the same ocular dominance, the same complexity, and most striking of all, exactly the same orientation preference. Such occurrences, which could hardly be by chance, immediately suggested that cells with common properties were aggregated together. The possibility of such groupings was intriguing, and once we had established them as a reality, we began a search to learn more about their size and shape.

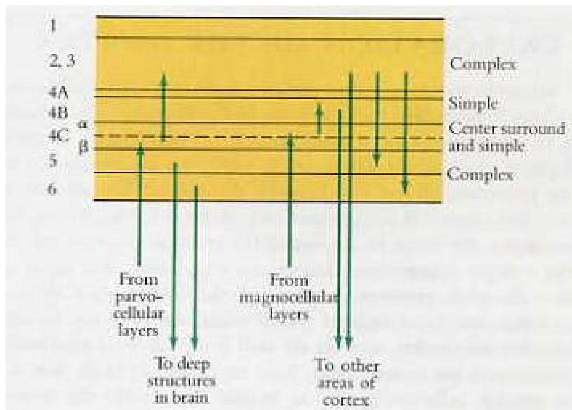
EXPLORATION OF THE CORTEX

Microelectrodes are one-dimensional tools. To explore a three-dimensional structure in the brain, we push an electrode slowly forward, stop at intervals to record from and examine a cell, or perhaps two or three cells, note the depth reading of the advancer, and then go on. Sooner or later the electrode tip penetrates all the way through the cortex. We can then pull the electrode out and reinsert it somewhere else. After the experiment, we slice, stain, and examine the tissue to determine the position of every cell that was recorded. In a single experiment, lasting about 24 hours, it is usual to make two or three electrode penetrations through the cortex, each about 4 to 5 millimeters long, and from each of which some 200 cells can be observed. The electrodes are slender, and we do well if we can even find their tracks under a microscope; we consequently have no reason to think that in a long penetration enough cells are injured to impair measurably the

responses of nearby cells. Originally it was hard to find the electrode track histologically, to say nothing of estimating the final position of the electrode tip, and it was consequently hard to estimate the positions of the cells that had been recorded. The problem was solved when it was discovered that by passing a tiny current through the electrode we could destroy cells in a small sphere centered on the electrode tip and could easily see this region of destruction histologically. Luckily, passing the current did no damage to the electrode, so that by making three or four such lesions along a single penetration and noting their depth readings and the depth readings of the recorded cells, we could estimate the position of each cell. The lesions, of course, kill a few cells near the electrode tip, but not enough to impair responses of cells a short distance away. For cells beyond the electrode tip, we can avoid losing information by going ahead a bit and recording before pulling back to make the lesion.

VARIATIONS IN COMPLEXITY

As we would expect, cells near the input end of the cortex, in layer 4, show less complicated behavior than cells near the output. In the monkey, as noted in this chapter, cells in layer 4C Bata, which receive input from the upper four (parvocellular) geniculate layers, all seem to have center-surround properties, without orientation selectivity. In layer 4C alpha, whose input is from the ventral (magnocellular) pair of geniculate layers, some cells have center-surround fields, but others seem to be orientation-specific, with simple receptive fields. Farther downstream, in the layers above and below 4C, the great majority of cells are complex. End-stopping occurs in about 20 percent of cells in layers 2 and 3 but seldom occurs elsewhere. On the whole, then, we find a loose correlation between complexity and distance along the visual path, measured in numbers of synapses.



A rough indication of physiological cell types found in the different layers of the striate cortex.

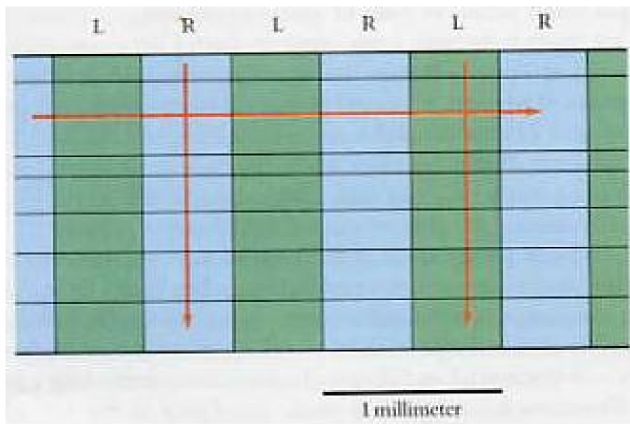
Stating that most cells above and below layer 4 are complex glosses over major layer-to-layer differences, because complex cells are far from all alike. They all have in common the defining characteristic of complex cells—they respond throughout their receptive field to a properly oriented moving line regardless of its exact position—but they differ in other ways. We can distinguish four subtypes that tend to be housed in different layers. In layers 2 and 3, most complex cells respond progressively better the longer the slit (they

show length summation), and the response becomes weaker when the line exceeds a critical length only if a cell is end stopped. For cells in layer 5, short slits, covering only a small part of the length of a receptive field, work about as well as long ones; the receptive fields are much larger than the fields of cells in layers 2 and 3. For cells in layer 6, in contrast, the longer an optimally oriented line is, the stronger are the responses, until the line spans the entire length of the field, which is several times greater than the width (the distance over which a moving line evokes responses). The field is thus long and narrow. We can conclude that axons running from layers 5, 6, and 2 and 3 to different targets in the brain (the superior culliculus, geniculate, the other visual cortical areas) must carry somewhat different kinds of visual information.

In summary, from layer to layer we find differences in the way cells behave that seem more fundamental than differences, say, in optimal orientation or in ocular dominance. The most obvious of these layer-to-layer differences is in response complexity, which reflects the simple anatomical fact that some layers are closer than others to the input.

OCULAR-DOMINANCE COLUMNS

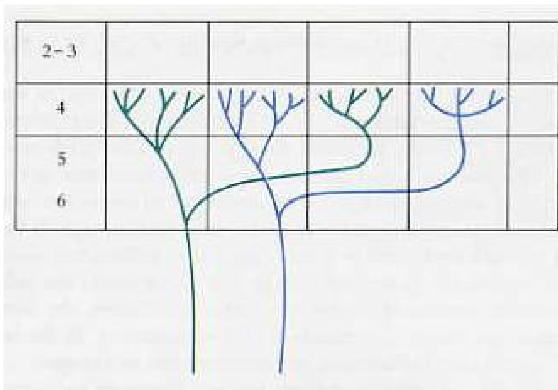
Eye-dominance groupings of cells in the striate cortex were the first to be recognized, largely because they are rather coarse. Because we now have many methods for examining them, they are now the best-known subdivision. It was obvious soon after the first recordings from monkeys that every time the electrode entered the cortex perpendicular to the surface, cell after cell favored the same eye, as shown in the illustration on this page. If the electrode was pulled out and reinserted at a new site a few millimeters away, one eye would again dominate, perhaps the same eye and perhaps the other one. In layer 4C, which receives the input from the geniculates, the dominant eye seemed to have not merely an advantage, but a monopoly. In the layers above and below, and hence farther along in the succession of synapses, over half of the cells could also be influenced from the nondominant eye—we call these cells binocular.



Ocular dominance remains constant in vertical microelectrode penetrations through the striate cortex. Penetrations parallel to the surface show alternation from left eye to right eye and back, roughly one cycle every millimeter.

If instead of placing the electrode perpendicular to the surface, we introduced it

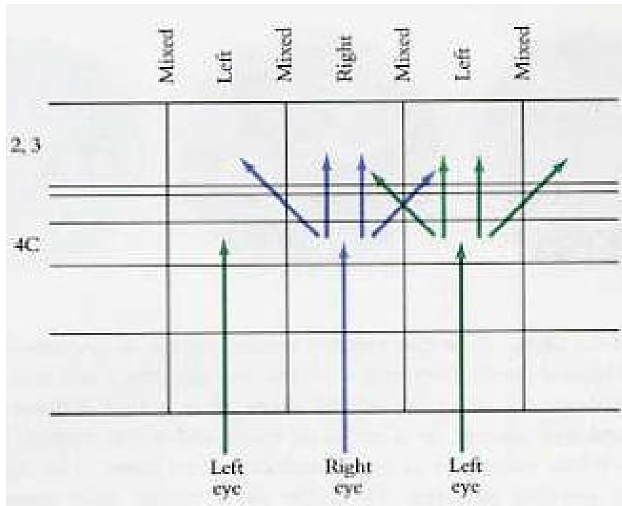
obliquely, as close to parallel to the surface as could be managed, the eye dominance alternated back and forth, now one eye dominating and now the other. A complete cycle, from one eye to the other and back, occurred roughly once every millimeter. Obviously, the cortex seen from above must consist of some kind of mosaic composed of left-eye and right-eye regions. The basis of the eye alternation became clear when new staining methods revealed how single geniculo-cortical axons branch and distribute themselves in the cortex. The branches of a single axon are such that its thousands of terminals form two or three clumps in layer 4C, each 0.5 millimeter wide, separated by o. 5-millimeter gaps, as shown in the illustration of synapse endings on this page. Because geniculate cells are monocular, any individual axon obviously belongs either to the left eye or the right eye. Suppose the green axon in the illustration is a left-eye fiber; it turns out that every left-eye fiber entering the cortex in this region will have its terminal branches in these same 0.5-millimeter clumps. Between the clumps, the 0.5-millimeter gaps are occupied by right-eye terminals. This special distribution of geniculo-cortical fibers in layer 4C explains at once the strict monocularity of cells in that layer. To select one fiber and stain it and only it required a new method, first invented in the late 1970s. It is based on the phenomenon of axon transport. Materials, either proteins or larger particles, are constantly being transported, in both directions, along the interior of axons, some at rates measured in centimeters per hour, others at rates of about a millimeter per day. To stain a single axon, we inject it through a micropipette with a substance that is known to be transported and that will stain the axon without distorting the cell. The favorite substance at present is an enzyme called horseradish peroxidase. It is transported in both directions, and it catalyzes a chemical reaction that forms the basis of an exceedingly sensitive stain. Because it is a catalyst, minute amounts of it can generate a lot of stain and because it is of plant origin, none of it is normally around to give unwanted background staining.



Each geniculate axon ascends through the deep layers of the striate cortex, subdividing repeatedly, finally terminating in 4C in 0. 5 millimeter-wide clusters of synapticendings, separated by blank areas, also 0.5 millimeter wide. All fibers from one eye occupy the same patches: the gaps are occupied by the other eye. The horizontal extent of the patches from a single fiber may be 2 to 3 millimeters for magnocellular terminals in 4Calpha; a parvocellular fiber branches in a more restricted area in 4QBata and generally occupies only one or two patches.

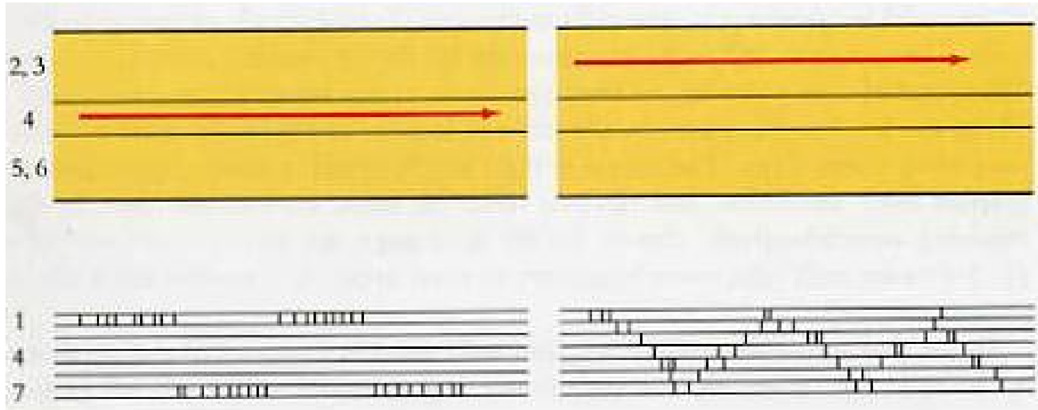
The microelectrode penetrations in the vertical axis, by showing the cortex subdivided

into ocular-dominance columns extending from the surface to the white matter, confirmed anatomical evidence that a patch of cells in layer 4C is the main supplier of visual information to cell layers above and below it. The existence of some horizontal and diagonal connections extending a millimeter or so in all directions must result in some smudging of the left-eye versus right-eye zones in the layers above and below 4C, as shown in the diagram on this page. We can expect that a cell sitting directly above the center of a layer-4 left-eye patch will therefore strongly favor that eye and perhaps be monopolized by it, whereas a cell closer to the border between two patches may be binocular and favor neither eye. Microelectrode penetrations that progress horizontally through one upper cortical layer, or through layer 5 or 6, recording cell after cell, do indeed find a progression of ocular dominance in which cells first favor one eye strongly, then less strongly, are then equally influenced, and then begin to favor the other eye progressively more strongly. This smooth alternation back and forth contrasts sharply with the sudden transitions we find if we advance the electrode through layer 4C.



The overlap and blurring of ocular-dominance columns beyond layer 4 is due to horizontal or diagonal connections.

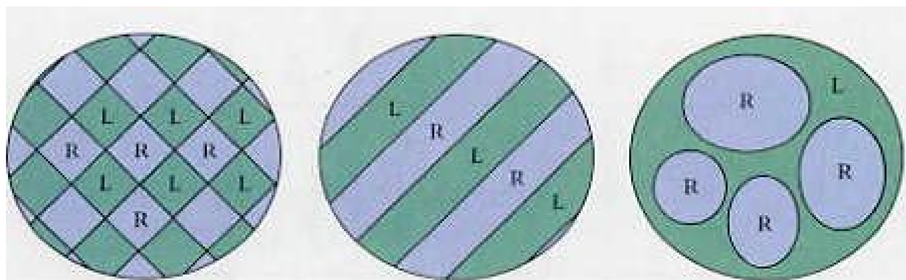
Viewed from the side, the subdivisions in layer 4 appeared as patches. But we wanted to know how the pattern would appear if we stood above the cortex and looked down. Suppose we have two regions, black and white, on a surface; topologically, we can partition them off in several different ways: in a checkerboard-like mosaic, in a series of black and white stripes, in black islands on a white ocean, or in any combination of these. The figures above show three possible patterns. To tackle the problem with microelectrodes alone amounts to using a one-dimensional technique to answer a three-dimensional question. That can be frustrating, like trying to cut the back lawn with a pair of nail scissors. One would prefer to switch to a completely different type of work, say farming, or the law. (In the early 1960s, when Torsten Weisel and I were more patient and determined, we actually did try to work out the geometry, with some success. And I actually did cut our back lawn once in those days, admittedly with kitchen scissors rather than nail scissors, because we could not afford a lawn mower. We were poorer than modern graduate students, but perhaps more patient.)



The ocular-dominance column borders in upper (2, 3) and lower (5, 6) layers are blurred, compared to the sharp boundaries in layer 4. The arrows illustrate electrode tracks made in layer 4 (upper left) and layer 2 or 3 (upper right). The lower diagrams plot ocular dominance of cells recorded along the tracks. In layer 4, we find abrupt alternation between group1 (contralateral eye only) and group 7 (ipsilateral eye only). In other layers, we find binocular cells, a the eye dominance alternates by going through the intermediate degrees of eye preference. (1, 4, and 7 refer to ocular dominance.)

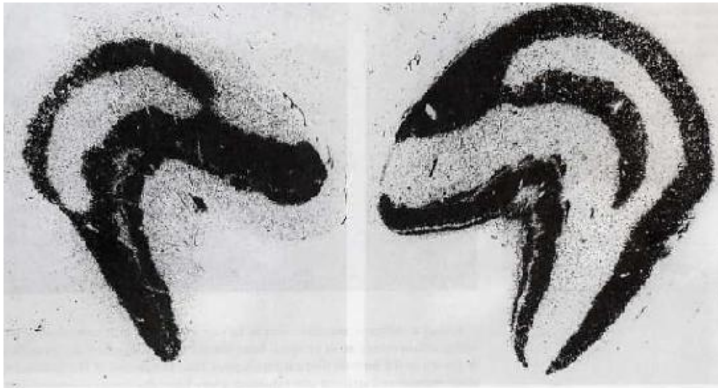
Luckily, neuroanatomical methods have been invented in breathtaking succession in the past decade, and by now the problem has been solved independently in about half a dozen ways. Here I will illustrate two.

The first method depends again on axon transport. A small amount of an organic chemical, perhaps an amino acid, is labeled with a radioactive element such as carbon-14 and injected into one eye of a monkey, say the left eye. The amino acid is taken up by the cells in the eye, including the retinal ganglion cells. The ganglion-cell axons transport the labeled molecule, presumably now incorporated into proteins, to their terminals in the lateral geniculate bodies. There the label accumulates in the left-eye layers. The process of transportation takes a few days. The tissue is then thinly sliced, coated with a photographic silver emulsion, and allowed to sit for some time in the dark. In the resulting autoradiograph, shown on this page, we can see the three left-eye layers on each side, complementary in their order, revealed by black silver grains.



Here are three different ways that a surface can be partitioned off into two kinds of regions: the possible patterns are a checker-board, stripes, and islands in an ocean. In this case, the surface is the cortex, and the regions are left-eye and right-eye.

To see this geniculate pattern requires only modest amounts of radioactivity in the injection. If we inject a sufficiently large amount of the labeled amino acid into the eye, the concentration in geniculate layers becomes so high that some radioactive material leaks out of the optic-nerve terminals and is taken up by the geniculate cells in the labeled layers and shipped along their axons to the striate cortex. The label thus accumulates in the layer-4C terminals in regular patches corresponding to the injected eye. When the autoradiograph is finally developed (after several months because the concentration of label finally reaching the cortex is very small), we can actually see the patches in layer 4C in a transverse section of the cortex, as shown in the photograph on this page. If we slice the cortex parallel to its surface—either flattening it first or cutting and pasting serial sections—we can at last see the layout, as though we were viewing it from above. It is a beautiful set of parallel stripes, as shown on page 17 in in a single section (top) and a reconstruction (bottom). In all these cortical autoradiographs, the label representing the left eye shows up bright, separated by dark, unlabeled regions representing the right eye. Because layer 4 feeds the layers above and below mainly by up-and-down connections, the regions of eye preference in three dimensions are a series of alternating left- and right-eye slabs, like slices of bread, as shown in the bottom diagram on page 17.
Using a different method, Simon LeVay succeeded in reconstructing the entire striate cortex in an occipital lobe; the part of this exposed on the surface is shown in the bottom illustration on page 17.

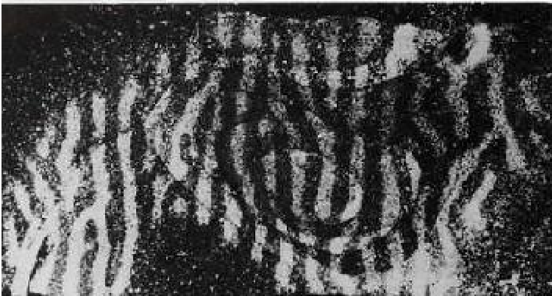


These sections through the left and right lateral geniculate bodies show autoradiographic label in the three left-eye layers on each side. The left eye had been injected with radioactive label (tritiated proline) a week earlier. The labeled layers are the dark ones.

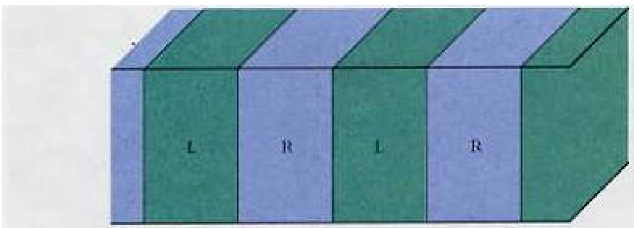
The stripes of the pattern are most regular and striking some distance away from the foveal representation. For reasons unknown, the pattern is rather complex near the fovea, with very regular periodicity but many loops and swirls, hardly the regular wallpaper-like stripes seen farther out. The width of the stripes is everywhere constant at about 0.5 millimeter. The amount of cortex devoted to left and right eyes is nearly exactly equal in the cortex representing the fovea and out to about 20 degrees in all directions. LeVay and David Van Essen have found that owing to the declining contribution of the eye on the same side, the ipsilateral bands shrink to 0.25 millimeter out beyond 20 degrees from the fovea. Beyond 70 or 80 degrees, of course, only the contralateral eye is represented. This

makes sense, because with your eyes facing the front, you can see with your right eye farther to the right than to the left.
A second method for demonstrating the columns reveals the slabs in their full thickness, not just the part in layer 4. This is the 2-deoxyglucose method, invented by Louis Sokoloff at the National Institutes of Health, Bethesda, in 1976. It too depends ultimately on the ability of radioactive substances to darken photographic film. The method is based on the fact that nerve cells, like most cells in the body, consume glucose as fuel, and the harder they are made to work, the more glucose they eat. Accordingly, we might imagine injecting radioactive glucose into an animal, stimulating one eye, say the right, with patterns for some minutes—long enough for the glucose to be taken up by the active cells in the brain—and then removing the brain and slicing it, coating the slices with silver emulsion, and exposing and developing, as before. This idea didn't work because glucose is consumed by the cells and converted to energy and degradation products, which quickly leak back out into the blood stream. To sidestep the leakage, Sokoloffs ingenious trick was to use the substance deoxyglucose, which is close enough chemically to glucose to fool the cells into taking it up: they even begin metabolizing it. The process of breakdown goes only one step along the usual chemical degradation path, coming to a halt after the deoxyglucose is converted to a substance (2-deoxyglucose-6-phosphate) that can be degraded no further. Luckily, this substance is fat insoluble and can't leak out of the cell; so it accumulates to levels at which it can be detected in autoradiographs. What we finally see on the film is a picture of the brain regions that became most active during the stimulation period and took up most of this fake food. Had the animal been moving its arm during that time, the motor arm area in the cortex would also have lit up. In the case of stimulating the right eye, what we see are the parts of the cortex most strongly activated by that stimulus, namely, the set of right ocular-dominance columns.

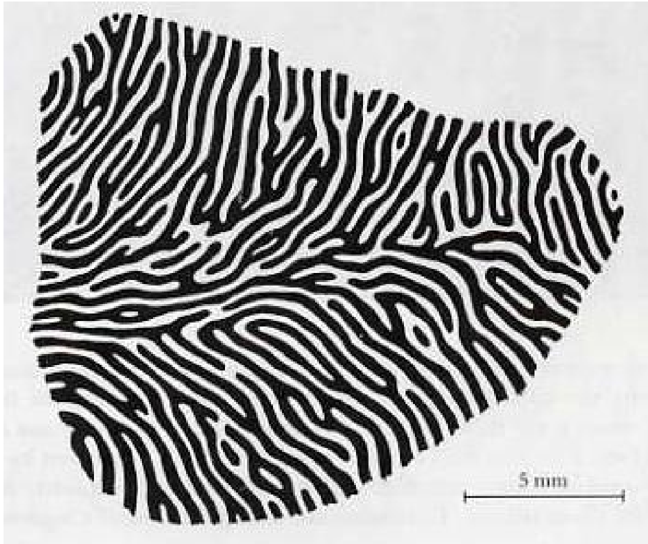
In this autoradiograph through the striate cortex, the white segments are the labeled patches in layer 4 representing the injected left eye; these patches are separated by unlabeled (dark) right-eye regions.



Top: A single section through the dome-shaped cortex is made parallel to the surface. It cuts through layer 4 in a ring. Bottom: A reconstruction of many such rings from a series of sections—the deeper the section, the bigger the ring—made by cutting out the rings and superimposing them. (Traces of the rings can be seen because it was difficult to get all the sections exposed and photographed equally, especially as I am strictly an amateur photographer.)



In three-dimensional view, the ocular- dominance columns are seen to be, not Greek pillars, but slabs perpendicular to the surface, like slices of bread.



Seen here in LeVay's reconstruction are the ocular-dominance columns in the part of area 17 open to the surface, right hemi- sphere. Foveal representation is to the right. (Compare right side of photograph on page 3.)

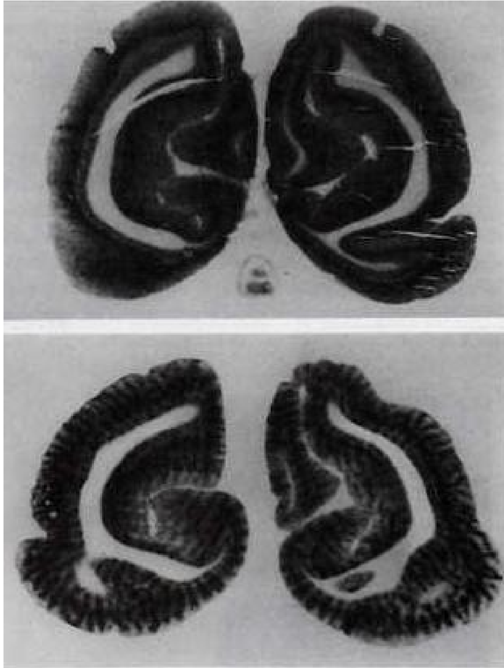
You see the result in the photographs on the next page.

In a very pretty extension of the same idea, Roger Tootell, in Russel De Valois's laboratory at Berkeley, had an animal look with one eye at a large pattern of concentric circles and rays, shown in the top image of the figure on the next page. The resulting pattern on the cortex contains the circles and rays, distorted just as expected by the variations in magnification (the distance on the cortex corresponding to i degree of visual field), a phenomenon related to the change in visual acuity between the fovea and periphery of the eye. Over and above that, each circle or ray is broken up by the fine ocular-dominance stripes. Stimulating both eyes would have resulted in continuous bands. Seldom can we illustrate so many separate facts so neatly, all in a single experiment.

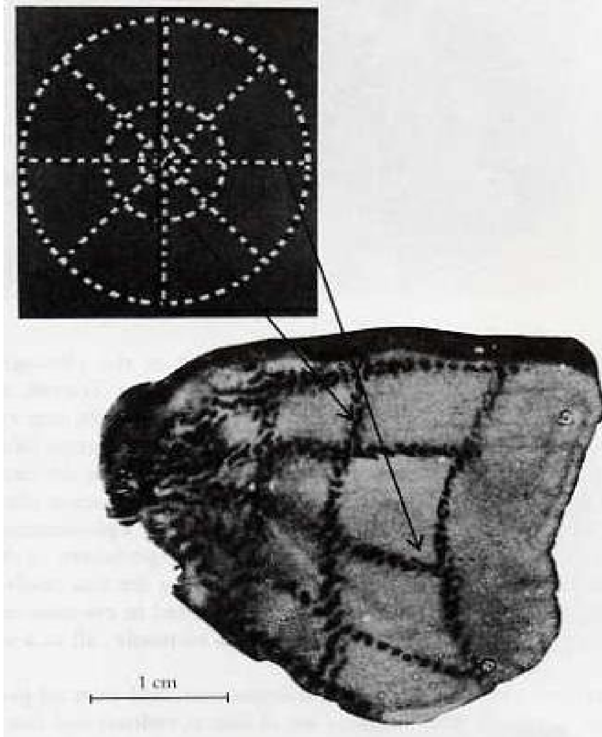
Cats, several kinds of monkeys, chimpanzees, and man all possess ocular-dominance columns. The columns are absent in rodents and tree shrews; and although hints of their presence can be detected physiologically in the squirrel monkey, a new world monkey, present anatomical methods do not reveal the columns. At present we don't know what purpose this highly patterned segregation of eye influence serves, but one guess is that it has something to do with stereopsis (see Chapter 7).

Subdivisions of the cortex by specialization in cell function have been found in many regions besides the striate cortex. They were first seen in the somato-sensory cortex by Vernon Mountcastle in the mid-1950s, in what was surely the most important set of observations on cortex since localization of function was first discovered. The somatosensory is to touch, pressure, and joint position what the striate cortex is to vision. Mountcastle showed that this cortex is similarly subdivided vertically into regions in which cells are sensitive to touch and regions in which cells respond to bending of joints or applying deep pressure to a limb. Like ocular-dominance columns, the regions are about half a millimeter across, but whether they form stripes, a checkerboard, or an

ocean-and-islands pattern is still not clear. The term column was coined by Mountcastie, so one can probably assume that he had a pillarlike structure in mind. We now know that the word slab would be more suitable for the visual cortex. Terminology is hard to change, however, and it seems best to stick to the well-known term, despite its shortcomings. Today we speak of columnar subdivisions when some cell attribute remains constant from surface to white matter and varies in records taken parallel to the surface. For reasons that will become clear in the next chapter, we usually restrict the concept to exclude the topographic representation, that is, position of receptive fields on the retina or position on the body.



Two experiments using radioactive deoxyglucose. Top: A cross section of the two hemispheres through the occipital lobes in a control animal that had its visual field stim ulated with both eyes open following the intravenous injection. Bottom: After injec tion, an animal viewed the stimulus with one eye open and the other closed. This experiment was done by C. Kennedy, M. H. Des Rosiers, 0. Sakurada, M. Shinohara, M. Reivich, J. W. Jehle, and L. Sokoloff.

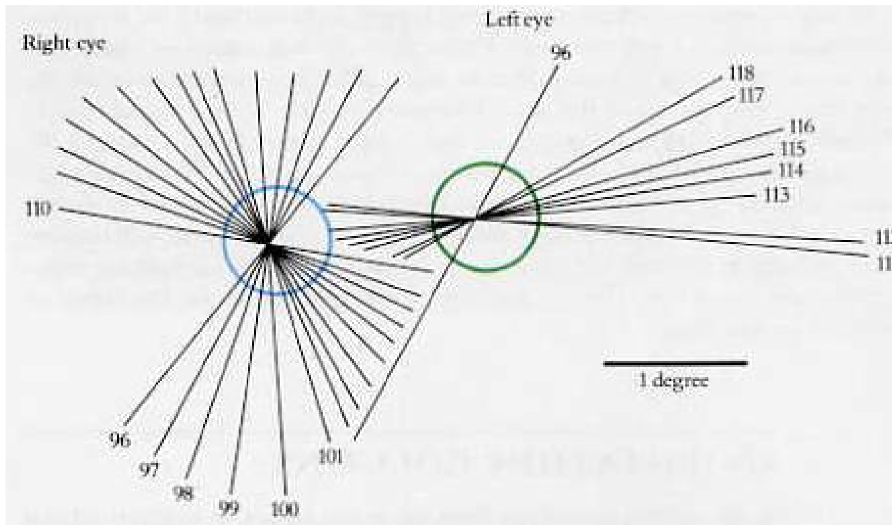


In this experiment by Roger Tootell, the target-shaped stimulus with radial lines was centered on an anesthetized macaque mon-key's right visual field for 45 minutes after injection with radioactive 2-deoxyglucose. One eye was held closed. The lower picture shows the labeling in the striate cortex of the left hemisphere. This autoradiograph shows a section parallel to the surface; the cortex was flattened and frozen before sectioning. The roughly vertical lines of label represent the (semi)circular stimulus lines; the horizontal lines of label represent the radial lines in the right visual field. The hatching within each line of label is caused by only one eye having been stimulated and represents ocular-dominance columns.

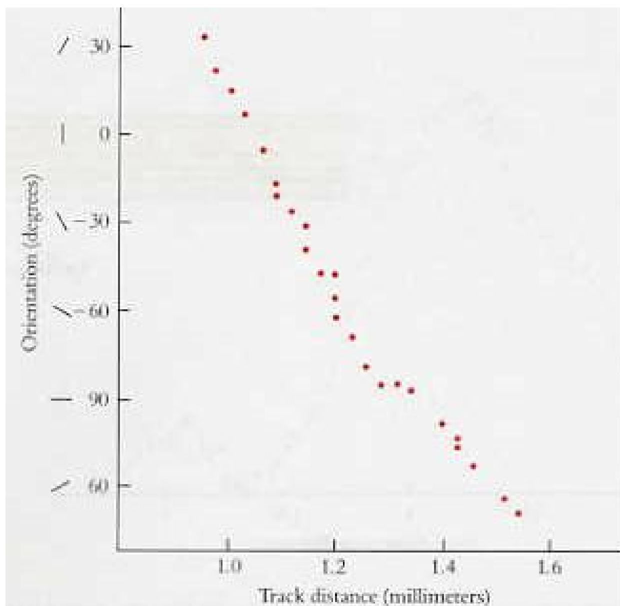
ORIENTATION COLUMNS

In the earliest recordings from the striate cortex, it was noticed that whenever two cells were recorded together, they agreed not only in their eye preference, but also in their preferred orientation. You might reasonably ask at this point whether next-door neighboring cells agree in all their properties: the answer is clearly no. As I have mentioned, receptive-field positions are usually not quite the same, although they usually overlap; directional preferences are often opposite, or one cell may show a marked directional preference and the other show none. In layers 2 and 3, where end-stopping is found, one cell may show no stopping when its neighbor is completely stopped. In contrast, it is very rare for two cells recorded together to have opposite eye preference or any obvious difference in orientation.
Orientation, like eye preference, remains constant in vertical penetrations through the full cortical thickness. In layer 4C Bata, as described earlier, cells show no orientation preference at all, but as soon as we reach layer 5, the cells show strong orientation preference and the preferred orientation is the same as it was above layer 4C. If we pull out the electrode and reinsert it somewhere else, the whole sequence of events is seen again, but a different orientation very likely will prevail. The cortex is thus subdivided

into slender regions of constant orientation, extending from surface to white matter but interrupted by layer 4, where cells have no orientation preference.
If, on the other hand, the electrode is pushed through the cortex in a direction parallel to the surface, an amazingly regular sequence of changes in orientation occurs: every time the electrode advances 0.05 millimeter (50 micrometers), on the average the preferred orientation shifts about 10 degrees clockwise or counterclockwise. Consequently a traverse of 1 millimeter typically records a total shift of 180 degrees. Fifty micrometers and 10 degrees are close to the present limits of the precision of measurements, so that it is impossible to say whether orientation varies in any sense continuously with electrode position, or shifts in discrete steps.



A very oblique penetration through area 17 in a macaque monkey reveals the regular shift in orientation preference of 23 neighboring cells.

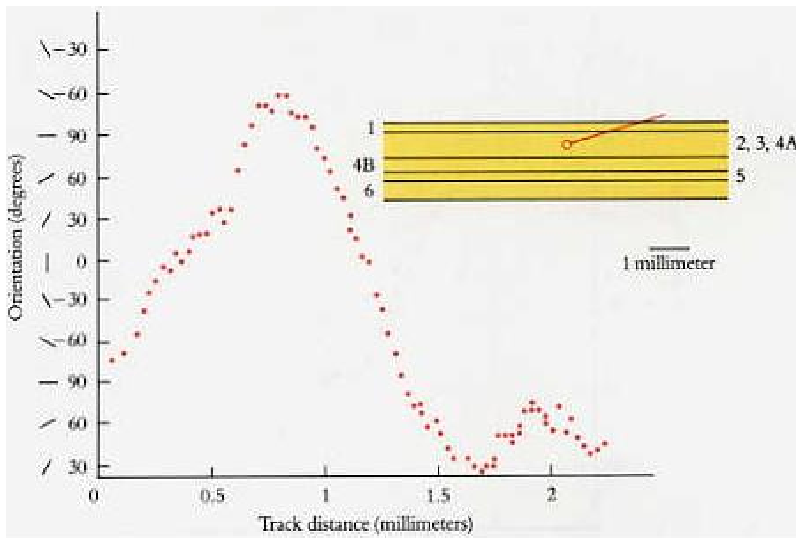


The results of the experiment shown above are plotted in degrees, against the distance the electrode had traveled. (Because the electrode was so slanted that it was almost parallel to the cortical surface, the track distance is almost the same as the distance along the surface.) In this experiment 180 degrees, a full rotation, corresponded to about 0.7 millimeter.

In the two figures on the previous page, a typical experiment is illustrated for part of a close-to-horizontal penetration through area 17, in which 23 cells were recorded. The eyes were not perfectly aligned on the screen (because of the anesthetic and a muscle-relaxing agent), so that the projections of the foveas of the two eyes were separated by about 2 degrees. The color circles in the figure above represent roughly the sizes of the receptive fields, about a degree in diameter, positioned 4 degrees below and to the left of the foveal projections—the records were from the right hemisphere. The first cell, 96, was binocular, but the next 14 were dominated strongly by the right eye. From then on, for cells in to 118, the left eye took over. You can see how regularly the orientations were shifting during this sequence, in this case always counterclockwise. When the shift in orientation is plotted against track distance (in the graph on the previous page), the points form an almost perfect straight line. The change from one eye to the other was not accompanied by any obvious change either in the tendency to shift counterclockwise or in the slope of the line. We interpret this to mean that the two systems of groupings, by eye dominance and by orientation, are not closely related. It is as though the cortex were diced up in two completely different ways. In such penetrations, the direction of orientation shifts may be clockwise or counterclockwise, and most penetrations, if long enough, sooner or later show shifts in the direction of rotation; these occur at unpredictable intervals of a few millimeters. The graph on the next page shows an example of a sequence with several such reversals.

We see in some experiments a final peculiarity called a *fracture*. Just as we are becoming mesmerized by the relentless regularity, observing shift after shift in the same direction, we see on rare occasions a sudden break in the sequence, with a shift of 45 to 90 degrees. The sequence then resumes with the same regularity, but often with a reversal from clockwise to counterclockwise. The graph on page 25 shows such a fracture, followed a few tenths of a millimeter later by another one.

The problem of learning what these groupings, or regions of constant orientation, look like if viewed from above the cortex has proved much more difficult than viewing ocular-dominance columns from the same perspective. Until very recently we have had no direct way of seeing the orientation groupings and have had to try to deduce the form from microelectrode penetrations such as those I have shown here. The reversals and fractures both suggest that the geometry is not simple. On the other hand, the linear regularity that we see, often over millimeter after millimeter of cortex, must imply a regularity at least within small regions of cortex; the reversals and fractures would then suggest that the regularity is broken up every few millimeters. Within these regions of regularity, we can predict the geometry to some extent. Suppose that the region is such that wherever we explore it with an electrode parallel to the surface, we see regularity—no reversals and no fractures—that is, everywhere we obtain graphs like the one on page 24. If we had enough of these graphs, we could ultimately construct a three-dimensional graph, as in the illustration shown on the page 25, with orientation represented on a vertical axis (z) plotted against cortical distance on horizontal axes (x and y). Orientations would then be represented on a surface such as the tilted plane in this illustration, in cases where the graphs were straight lines, and otherwise on some kind of curved surface. In this three-dimensional graph horizontal planes (the x-y plane or planes parallel to it) would intersect this surface in lines, contour lines of constant orientation (iso-orientation lines) analogous to lines of constant height in a contour map in geography.



In still another experiment where we graph orientation against track distance, three reversals separated long, straight progressions.

Undulations—hills, valleys, ridges—in the 3-D graph would give reversals in some orientation-versus-distance plots; sudden breaks in the form of cliffs would lead to the fractures. The main message from this argument is that regions of regularity imply the possibility of plotting a contour map, which means that regions of constant orientation, seen looking down on the cortex from above, must be stripes. Because orientations plotted in vertical penetrations through the cortex are constant, the regions in three dimensions must be slabs. And because the iso-orientation lines may curve, the slabs need not be flat like slices of bread. Much of this has been demonstrated directly in experiments making two or three parallel penetrations less than a millimeter apart, and the three-dimensional form has been reconstructed at least over those tiny volumes.

If our reasoning is right, occasional penetrations should occur in the same direction as contour lines, and orientation should be constant. This does happen, but not very often. That, too, is what we would predict, because trigonometry tells us that a small departure from a contour line, in a penetration's direction, gives a rather large change in slope, so that few graphs of orientation versus distance should be very close to horizontal.

The number of degrees of orientation represented in a square millimeter of cortex should be given by the steepest slopes that we find. This is about 400 degrees per millimeter, which means a full complement of 180 degrees of orientation in about o. 5 millimeter. This is a number to have in mind when we return to contemplate the topography of the cortex and its striking uniformity. Here, I cannot resist pointing out that the thickness of a pair of ocular-domi-nance columns is 0.4 plus 0.4 millimeter, or roughly 1 millimeter, double, but about the same order of magnitude, as the set of orientation slabs.

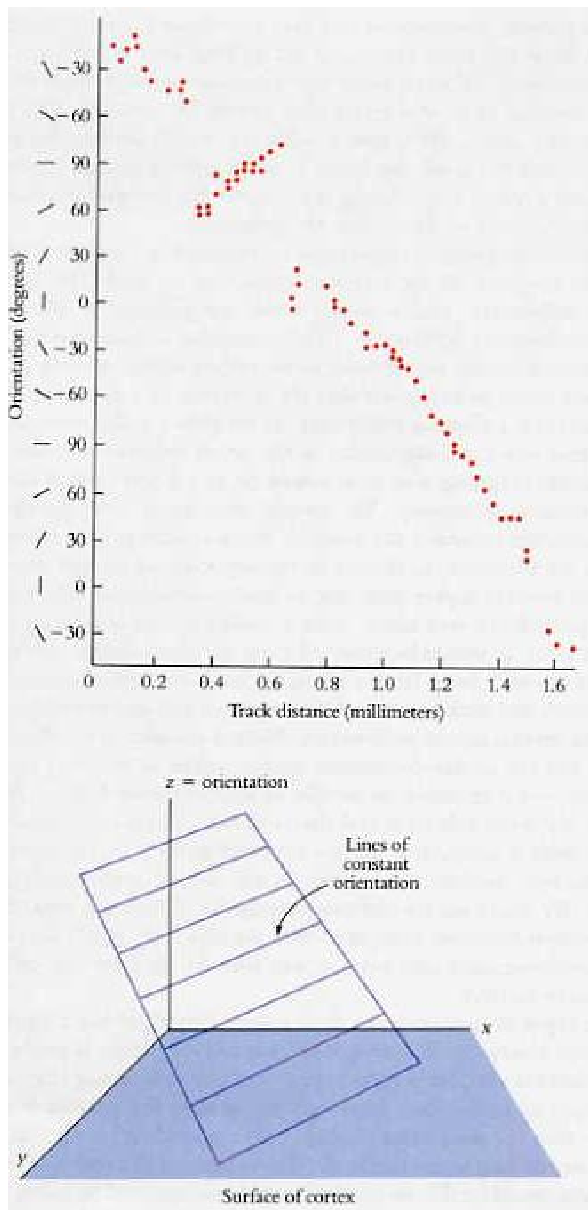
Deoxyglucose mapping was soon seized on as a direct way of determining orientation-column geometry. We simply stimulated with parallel stripes, keeping orientation constant, say vertical, for the entire period of stimulation. The pattern we obtained, as shown in the top autoradiograph on page 26, was far more complex than that of ocular-

dominance columns. Nevertheless the periodicity was clear, with i millimeter or less from one dense region to the next, as would be expected from the physiology—the distance an electrode has to move to go from a given orientation, such as vertical, through all intermediates and back to vertical. Some places showed stripelike regularity extending for several square millimeters. We had wondered whether the orientation slabs and the ocular-dominance stripes might in any way be related in their geometry—for example, be parallel or intersect at 90 degrees. In the same experiment, we were able to reveal the ocular-dominance columns by injecting the eye with a radioactive amino acid and to look at the same block of tissue by the two methods, as shown in the second autoradiograph on page 26. We could see no obvious correlation. Given the complex pattern of the orientation domains, compared with the relatively much simpler pattern of the ocular-dominance columns, it was hard to see how the two patterns *could* be closely related.

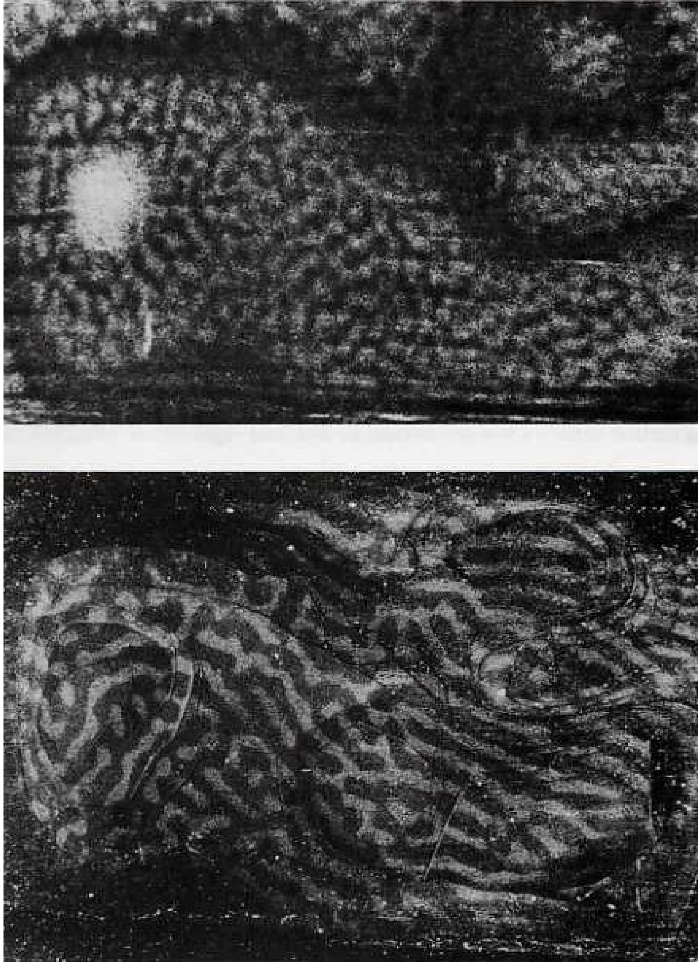
For some types of questions the deoxyglucose method has a serious limitation. It is hard always to be sure that the pattern we obtain is really related to whatever stimulus variable we have used. For example, using black and white vertical stripes as a stimulus, how can we be sure the pattern is caused by verticality—that the dark areas contain cells responding to vertical, the light areas, cells responding to nonvertical?

The features of the stimulus responsible for the pattern could be the use of black-white, as opposed to color, or the use of coarse stripes, as opposed to fine ones, or the placing of the screen at some particular distance rather than another. One indirect confirmation that orientation is involved in the deoxyglucose work is the absence of any patchiness or periodicities in layer 4C, where cells lack orientation preference. Another comes from a study in which Michael Stryker, at the University of California at San Fransisco, made long microelectrode penetrations parallel to the surface in cat striate cortex, planted lesions every time some particular orientation was encountered, and finally stimulated with stripes of one orientation after injecting radioactive deoxyglucose. These experiments showed a clear correlation between the pattern and stimulus orientation.

The most dramatic demonstration of orientation columns comes from the use of voltage-sensitive dyes, developed over many years by Larry Cohen at Yale and applied to the cerebral cortex by Gary Blasdel at the University of Pittsburgh. In this technique, a voltage-sensitive dye that stains cell membranes is poured onto the cortex of an anesthetized animal and is taken up by the nerve cells. When an animal is stimulated, any responding cells show slight changes in color, and if enough cells are affected in a region close enough to the surface, we can record these changes with modern TV imaging techniques and computer-aided noise filtration. Blasdel stimulated with stripes in some particular orientation, made a photograph of the pattern of activity in a region of cortical surface a few centimeters in area, and repeated the procedure for many orientations. He then assigned a color to each orientation—red for vertical, orange for one o'clock, and so on—and superimposed the pictures. Because an iso-orientation line should be progressively displaced sideways as orientation changes, the result in any one small region should be a rainbowlike pattern. This is exactly what Blasdell found. It is too early, and the number of examples are still too few, to allow an interpretation of the patterns in terms of fractures and reversals, but the method is promising.



This penetration showed two fractures, or sudden shifts in orientation, following and followed by regular sequences of shifts. The surface of the cortex is plotted on the x-y plane in this three dimensional map; the vertical (z) axis represents orientation. If for all directions of electrode tracks straight line orientation-versus-distance plots are produced, the surface generated will be a plane, and intersections of the surface (whether planar or not) with the x-y plane, and planes parallel to it, will give contour lines. (This sounds more complicated than it is! The same reasoning applies if the x-y plane is the surface of Tierra del Fuego and the z axis represents altitude or average rainfall in January or temperature.)



Top: After the injection of deoxy glucose, the visual fields of the anesthetized monkey were stimulated with slowly moving vertical black and white stripes. The resulting autoradiograph shows dense periodic labeling, for example in layers 5 and 6 (large central elongated area). The dark gray narrow ring outside this, layer 4C(3, is uniformly labeled, as expected, because the cells are not orientation selective. Bottom: In the same animal as above, one eye had been injected a week earlier with radioactive amino acid (proline), and after washing the section in water to dissolve the 2-deoxyglucose, an autoradiograph was prepared from the same region as in the upper autoradiograph. Label shows ocular-dominance columns. These have no obvious relationship to the orientation columns.

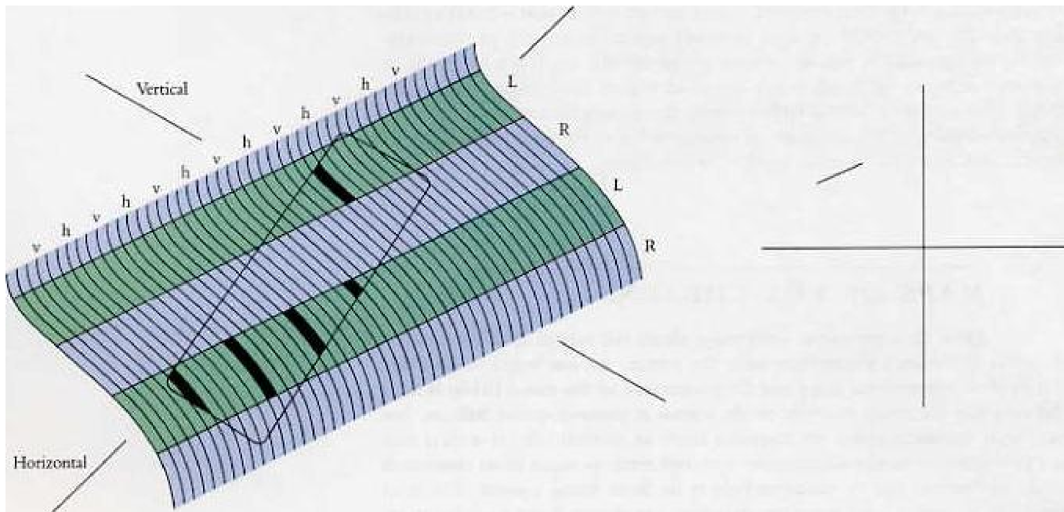
In this experiment Gary Blasdel applied a voltage-sensitive dye to a monkey's striate cortex and stimulated the visual fields with stripes of one orientation after the next, while imaging the cortex with TV techniques. Using computers, the

results are displayed by assigning a color to each set of regions lit up by each orientation. For any small region of cortex the orientation slabs are parallel stripes, so that a complete set of orientations appears as a tiny rainbow.

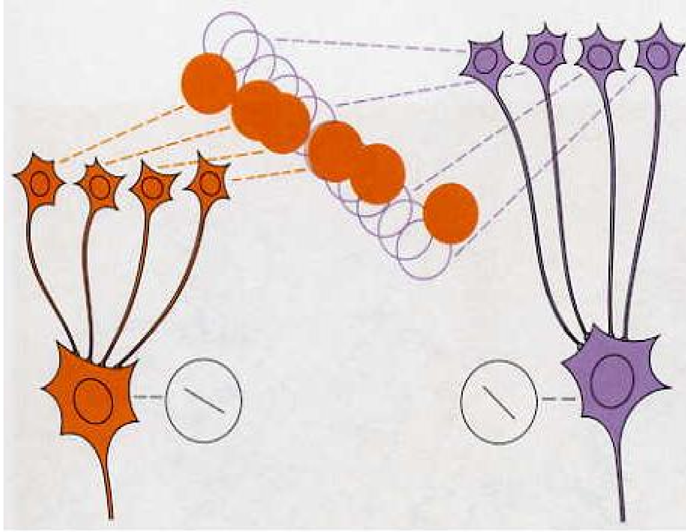
MAPS OF THE CORTEX

Now that we know something about the mapping of orientation and ocular-dominance parameters onto the cortex, we can begin to consider the relation between these maps and the projections of the visual fields. It used to be said that the retina mapped to the cortex in point-to-point fashion, but given what we know about the receptive fields of cortical cells, it is clear that this cannot be true in any strict sense: each cell receives input from thousands of rods and cones, and its receptive field is far from being a point. The map from retina to cortex is far more intricate than any simple point-to-point map. I have tried in the figure on the next page to map the distribution of regions on the cortex that are activated by a simple stimulus (not to be confused with the receptive field of a single cell). The stimulus is a short line tilted at 60 degrees to the vertical, presented to the left eye only. We suppose that this part of the visual field projects to the area of cortex indicated by the rounded-corner rectangle. Within that area, only left-eye slabs will be activated, and of these, only 6o-degree slabs; these are filled in in black in the illustration. So a line in the visual field produces a bizarre distribution of cortical activity in the form, roughly, of an array of bars. Now you can begin to see how silly it is to imagine a little green man sitting up in our head, contemplating such a pattern. The pattern that the cortex happens to display is about as relevant as the pattern of activity of a video camera's insides, wires and all, in response to an outside scene. The pattern of activity on the cortex is anything but a reproduction of the outside scene. If it were, that would mean only that nothing interesting had happened between eye and cortex, in which case we would indeed need a little green man. We can hardly imagine that nature would have gone to the trouble of grouping cells so beautifully in these two independently coexisting sets of columns if it were not of some advantage to the animal. Until we work out the exact wiring responsible for the transformations that occur in the cortex, we are not likely to understand the groupings completely. At this point we can only make logical guesses. If we suppose the circuits proposed in Chapter 4 are at all close to reality, then what is required to build complex cells from simple ones, or to accomplish end-stopping or directional selectivity, is in each case a convergence of many cells onto a single cell, with all the interconnected cells having the same receptive-field orientation and roughly the same positions. So far, we have no compelling reasons to expect that a cell with some particular receptive-field orientation should receive inputs from cells with different orientations. (I am exaggerating a bit: suggestions have been made that cells of different orientation affiliations might be joined by inhibitory connections: the evidence for such connections is indirect and as yet, to my mind, not very strong, but it is not easily dismissed.) If this is so, why not group together the cells that are to be interconnected? The alternative is hardly attractive: imagine the problem of having to wire together the appropriate cells if they were scattered through the cortex without regard to common properties. By far the densest interconnections should be between cells having common orientations; if cells were distributed at random, without regard to orientation, the tangle of axons necessary to interconnect the appropriate cells would be massive. As it is, they are, in fact, grouped together. The same argument applies to ocular-dominance domains.

If the idea is to pack cells with like properties together, why have sequences of small orientation steps? And why the cycles? Why go through all possible orientations and then come back to the first, and cycle around again, instead of packing together all cells with 30-degree orientation, all cells with 42-degree orientation, and indeed all left-eye cells and all right-eye cells? Given that we know how the cortex is constructed, we can suggest many answers. Here is one suggestion: perhaps cells of unlike orientation do indeed inhibit one another. We do not want a cell to respond to orientations other than its own, and we can easily imagine that inhibitory connections result in a sharpening of orientation tuning. The existing system is then just what is wanted: cells are physically closest to cells of like orientation but are not too far away from cells of almost the same orientation; the result is that the inhibitory connections do not have to be very long. A second suggestion: if we consider the connections necessary to build a simple cell with some particular opitimal orientation out of a group of center-surround layer-4 cells, more or less the same inputs will be required to build a nearby simple cell with a different, but not a very different, orientation. The correct result will be obtained if we add a few inputs and drop a few, as suggested in the illustration on the next page. Something like that might well justify the proximity of cells with similar orientations. The topic to be considered in the next chapter, the relationship between orientation, ocular dominance, and the projection of visual fields onto the cortex, may help us understand why so many columns should be desirable. When we add topography into the equation, the intricacy of the system increases in a fascinating way.



A tilted line segment shining in the visual field of the left eye (shown to the right) may cause this hypothetical pattern of activation of a small area of striate cortex (shown to the left). The activation is confined to a small cortical area, which is long and narrow to reflect the shape of the line; within this area, it is confined to left oc-ular-dominance columns and to orientation columns representing a two o'clock-eight o'clock tilt. Cortical representation is not simple! When we consider that the orientation domains are not neat parallel lines, suggested here for simplicity, but far more complex, as shown in the upper, deoxyglucose figure on page 26 and Blasdel's figure on same page, the representation becomes even more intricate.



The group of center-surround layer 4 cells that is needed to build a simple cell that responds to an oblique four o'clock—ten o'clock slit is likely to have cells in common with the group needed to build a 4:30-10:30 cell: a few inputs must be discarded and a few added.