Vision's Brain

Arrangements, connections and activities of cells add up to a three-dimensional plan for the first steps of visual processing

BY JULIE ANN MILLER

Ten billion nerve cells, tightly packed and highly interconnected, make up the machinery of thought. Just what are all those cells doing in a person's everyday life? "For most of the brain, we haven't the foggiest idea," says David H. Hubel of Harvard Medical School. Yet in work during the past twenty years, Hubel and Torsten N. Wiesel have explained much of the nuts and bolts workings, the cellular functions and organization, of one section of the brain — the primary visual cortex.

Functional architecture is the label Hubel and Wiesel give to the three-dimensional cell patterns they and their colleagues have discovered. Starting with the retina of the eye, investigators have traced how each cell that processes visual information converts its input to output. A combination of anatomical and physiological techniques reveals groups of functionally related cells, juxtaposed and superimposed, in a sometimes complex, but presumably efficient, structure.

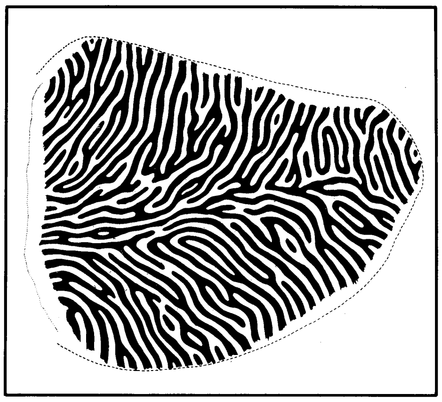
The basic physiological experiment, repeated thousands of times over the years, is to eavesdrop on a single brain cell while presenting the eyes with a visual pattern. The animal gazes with immobilized eyes at spots, edges and moving bars while the researchers observe what shape, position and motion most effectively stimulates the cell to fire.

"To make such extracellular records from single cells for periods of many hours is today relatively easy," Hubel says. "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 behavior 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 structural arrangement of brain cells is investigated with anatomical techniques. The classical methods show how the cells in the brain are packed: The primary visual cortex is made up of six major layers. More recent methods demonstrate cell connections. For example, researchers can destroy a group of cells and trace the degenerating material, or they can follow a radioactive compound that is transferred between connected cells.

Actual activity of nerve cells in the brain can now be measured simultaneously in all areas of the brain with an anatomical method developed at the National Institutes of Health by Louis Sokoloff and coworkers (SN: 11/11/78, p. 324). Application of his 2-deoxyglucose technique has confirmed previous physiological work and supplied new information.

To understand the excitement over the complex, but intriguing, arrangement of functionally identified brain cells, it is necessary to follow the story from the retina into the brain.



LeVay, Hubel and Wiesel

Zebra stripes show the ocular dominance pattern over the entire exposed surface of right striate cortex. Black areas are dominated by one eye, white by the other.

In general, cells respond to a more and more complicated signal the further they are along the information processing track. The first cells in the retina simply signal when they sense light. But those signals are locally processed, so that the retinal ganglion cells, which send output to the brain, are actually spot detectors. By weighing the excitatory signals from some retinal cells and inhibitory signals from others, each retinal ganglion cell is found to be most responsive to either a circular spot of light surrounded by darkness or to a dark disk surrounded by light. Each ganglion cell responds only if the appropriate disk is presented in a given position of the animal's visual field.

At the lateral geniculate body, the visual input's first stop in the brain, each cell again responds best to a disk of light or darkness. The lateral geniculate consists of six layers, each many cells thick, stacked one above the other like, Hubel says, a club sandwich. Each layer receives and sends signals from only one eye. Thus the lateral geniculate is sometimes considered simply a relay for sensory information.

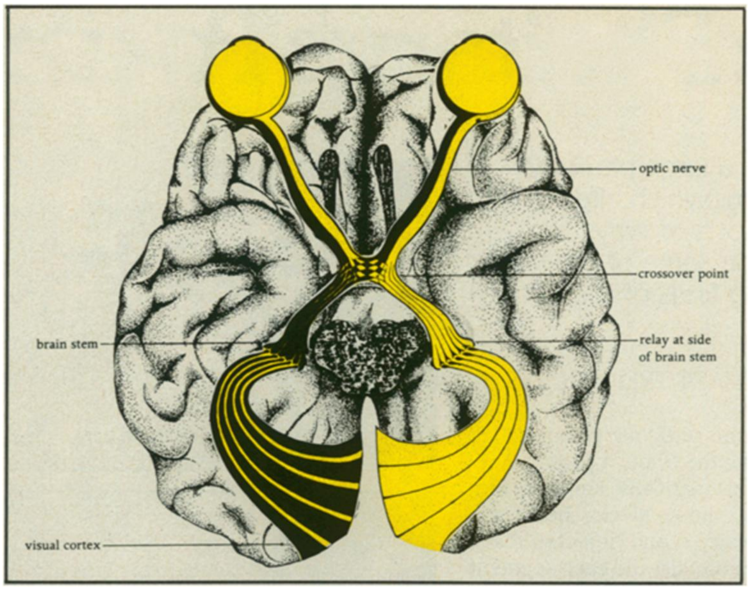
The primary visual (or striate) cortex is an area of obvious information processing, with several cells involved in converting input to output, which travels to nearby and distant brain regions. Although study of cells in the striate cortex has taken years and has revealed several steps in information processing, that region is not in any sense the end of the visual path (SN: 11/11/78, p. 324). "It is probably very close to the beginning," Hubel says. "All of the single cell physiology in fact suggests that area 17 [striate cortex] is concerned simply with building blocks for perception."

Two important block building operations of the striate cortex are now known. First, it is the area where input from the two eyes first converges on a single cell. Second, the striate cortex rearranges input so that cells respond preferentially, not to spots of light as in the lateral geniculate, but to short line segments with particular orientations. Those two functions have similar architectural elements.

"The primary visual cortex is the first stage where the two eyes get together," Hubel explains. The simpler cells within the cortex are monocular. However, among cells further along in information processing, more than half (at least in the macaque monkey) receive input arising in both eyes.

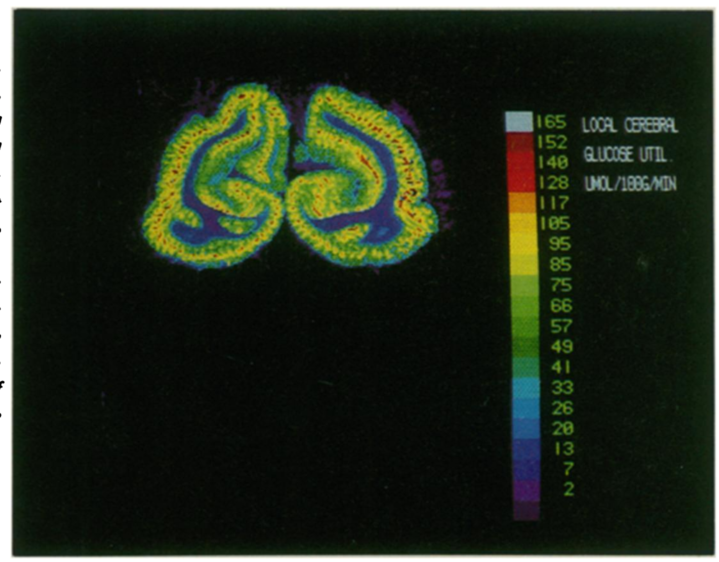
The cells with binocular input are wired in such a way that the information from the two eyes is basically identical. With either eye closed, a cell will respond best to stimuli in the same part of the receptive field, with the same linear orientation and moving in the same direction, if the cell prefers a moving line. "In short," says Hubel, "everything one learns about the cell through one eye matches precisely what one learns through the other."

But in one respect there is a difference in the input from the two eyes. The density of inputs from each eye to a given cell is not necessarily the same, so that identical stimuli detected by each eye can give a quantitatively different response. Among cortical cells, the researchers find all varieties of left eye-right eye balance and imbalance. Some cells receive most of their input from one eye, some from the other and still other cells receive nearly equal amounts of input from each eye. That characteristic of a cell, its relative



after Hubel

Seen from beneath the brain, visual input runs from the eyes to the lateral geniculate relay to the visual cortex at the back of the brain.



Sokoloff

Dashed red line reveals the increased activity of cell columns receiving input from one stimulated eye. A computer has assigned colors to areas of the brain slice on the basis of 2-deoxyglucose uptake.

input from each eye, is called the ocular dominance.

The brain cell community in the macaque monkey brain is subdivided into sharp ocular dominance neighborhoods. If one cell receives the greater proportion of its input from the left eye, chances are that its neighbor will do the same. High-rise apartment buildings, each with a homogeneous group of tenants, might be the best analogy to cortical organization. When investigators sink an electrode vertically into the cortex, all the cells encountered usually respond preferentially to the same eye. However, if the electrode is inserted horizontally or at an oblique angle, it will detect first cells dominated by one eye, then cells dominated by the other, then by the first, and so on. The stacks of cells responding best to one eye have been named ocular dominance columns, but recent work has shown them to be shaped less like pillars and more like curved slabs, each about 0.4 millimeters thick.

Anatomical work confirms the existence of the ocular dominance groupings. Destruction of cells in a right-eye layer of the lateral geniculate produces alternating patches of cortical degeneration. Injecting a radioactive amino acid into one eye shows patches of radioactivity in slices of the cortex.

In 1976, when Sokoloff and co-workers wanted to test their 2-deoxyglucose method on a brain region with an intricate pattern of functional organization, they chose the monkey binocular vision system. They injected monkeys with 2-deoxyglucose and then stimulated one eye with light for 45 minutes. The result was a striking demonstration of the columns, evident through the full cortical thickness (the other techniques had shown the alternation only in the layer of the lateral geniculate input). Together, the anatomical and physiological methods revealed a cortex in which ocular dominance groupings form a set of parallel bands, which are usually straight, but in places form loops, whorls, bifurcations and blind endings.

Differentiating the orientation of line stimuli, the second recognized function of the striate cortex, also depends on columns or slabs of functionally related cells. The information processing in the primary visual cortex depends on four classes of cells, the simpler generally feeding their output to the more complex. The least complex cells, called "circularly symmetric," are similar in their properties to the lateral geniculate cells. The next class, "simple" cells, respond to a specifically oriented line in a narrowly defined position. "Complex" cells, in contrast, are far less particular about the exact positioning of the stimulus line. And finally, hypercomplex cells resemble complex cells, except they are fussy about the length of the stimulus line.

The properties of the cortical cells hint at their organization in the brain—slabs of similar orientation preference. A complex cell can most easily be understood by supposing it receives inputs from many simple cells, all with the same preferred orientation. Similarly, a hypercomplex cell's properties can be explained by assuming that it receives inputs from complex cells, again with the same orientation preference. "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," Hubel says.

The existence of orientation columns is a rare case in which physiological data, rather than anatomical, led the way to a structural description. Hubel and Wiesel found, as in the case of ocular dominance, that neighboring cells almost always favor the same stimulus orientation. And an electrode perpendicular to the cortical surface encounters cells preferring the same orientation; while a horizontal or oblique penetration records from cells with a succession of orientation preferences.

In that succession, the preferred orientation shifts are generally small (about 10°) and orderly, adding up to a total rotation of 180° or more. (The researchers, however, cannot completely rule out the possibility that preferred orientations vary continuously across the cortex.) Throughout, a rotation of 180° in preferred stimulus corresponds approximately to a 1-millimeter displacement along the cortex.

Until last year, no anatomical method could confirm the orientation columns. The difficulty was that, unlike the ocular dominance columns, the orientation columns are produced by interconnections within the cortex, not by a special distribution of incoming fibers. But now, Hubel, Wiesel and Michael P. Stryker, instructed by Sokoloff and his group, have succeeded in using the 2-deoxyglucose method to anatomically reveal the second set of columns in an anesthetized monkey presented with moving vertical stripes for 45 minutes.

The orientation columns seen with

Continued on page 376

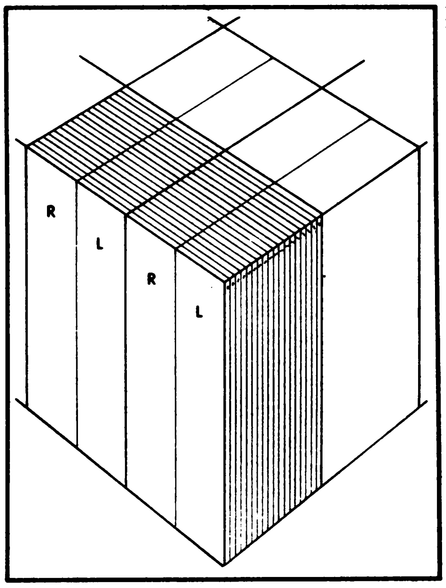
. . . Vision

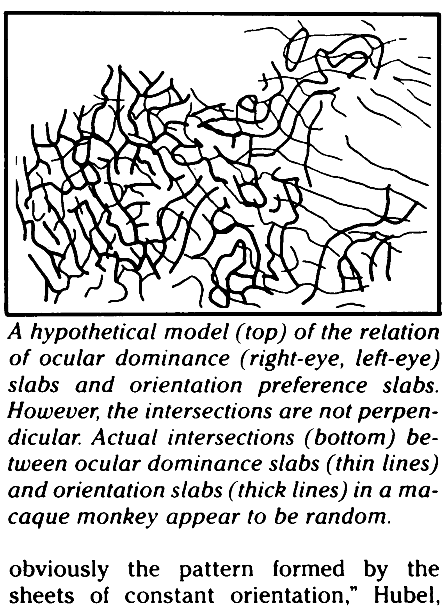
2-deoxyglucose were similar to ocular dominance columns, with one obvious difference. One layer of cells, layer IVc, is continuous instead of striped. Physiological recording from that layer had already indicated that the cells there are circularly symmetric and thus do not have any orientation specificity.

"The main new finding in this study is

Hubel and Wiesel

Ocular dominance columns are revealed by stripes of radioactive label (white areas) after an injection of radioactive tracer to one eye. Section shows striate cortex surface and the underlying fold.





Hubel, Wiesel, Stryker

A hypothetical model (top) of the relation of ocular dominance (right-eye, left-eye) slabs and orientation preference slabs. However, the intersections are not perpendicular. Actual intersections (bottom) between ocular dominance slabs (thin lines) and orientation slabs (thick lines) in a macaque monkey appear to be random.

obviously the pattern formed by the sheets of constant orientation," Hubel, Wiesel and Stryker say in the JOURNAL OF COMPARATIVE NEUROLOGY (Volume 177, pp. 361-380, 1978). The distance between the stripes, representing cells responding to vertical stimuli, is strikingly uniform, as it was for the ocular dominance columns. Although they are of constant thickness, the orientation sheets are not in strict register, but instead curve in complex and, so far, unpredictable ways. A major goal of current research, Hubel says, is to examine more monkeys and some other animals to try to find whether or not there is any consistent, orderly pattern.

Fitting together the two known components of primary visual cortex architecture is like doing a puzzle. The pieces are sets of two ocular dominance columns, each about 0.4 millimeters wide, and of 18 orientation columns, each about 0.05 millimeters wide. Thus, in each case the complete set of columns, which the researchers call a hypercolumn, subserving all orientations or both eyes, is approximately 1 millimeter. How do they fit with respect to each other?

Theoretically, the most efficient system would be to have the sets of columns intersect, like woven cloth with ocular dominance as the warp and orientation preference as the woof. In that case, the binocular cells, whatever their orientation preference, would neighbor simpler cells with input from each eye, to make the wiring as simple as possible. Intersections of the columns are evident from a study where, in a single monkey, orientation columns were labeled with 2-deoxyglucose and ocular dominance columns were labeled with a different radioactive tracer transported from one eye. But the intersections are certainly not orthogonal, as in woven cloth; they seem as random as the craft of a drunken weaver working without a loom. "Apparently, random intersection is enough to guarantee that the two sets intersect frequently and never remain parallel over long distances, and that is probably what is important," the researchers conclude. They will continue to look for a pattern in further examination of monkeys and other animals.

Macaque monkeys have been the subjects of the most extensive experiments on the functional architecture of the visual cortex. Yet it is necessary to survey a broad range of mammals to avoid making false generalizations before extrapolating to the human brain. Ocular dominance columns, for example, are much more striking in some primates (and lower animals) than in others. Hubel suggests that the differences may relate to the mechanisms of depth perception at a more advanced processing station in the brain.

"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 [of the visual field]. Undoubtedly the picture is incomplete," Hubel concludes. Orientation specificity, for example, might be just one, albeit an important characteristic, among twenty or thirty competing properties of cortical cells. Although researchers have looked for columns in the striate cortex related to other properties, such as color perception, the evidence is not yet convincing.

Development of the intricate cortical connections that organize the two recognized sets of columns is also a field of lively research. "We ask whether this beautiful machine is present at birth, and is genetically determined, or whether it depends on the postnatal period, and the visual experience the animal has during this period," Wiesel explains. Experiments on newborn monkeys demonstrate that at birth the cortex, at least in the primary visual area, is very similar to that of the adult. The newborn already has both ocular dominance and orientation columns.

Column development is not, however, complete at birth. Experiments in which the lids of one monkey eye are stitched closed during a crucial period in early life show competition between the input from the two eyes. If the right eye is closed, for example, the pathway belonging to the left eye takes over some of the right eye's territory. (Closing both eyes for that time, in contrast, has little effect.) Anatomical studies have confirmed that fibers from the lateral geniculate layer associated with the normal, unstitched eye come to occupy the space in the cortex normally allotted to the deprived eye. The columns of the normal eye get thicker and those of the deprived eye get thinner. "It is a striking change," Hubel says.

Two mechanisms are invoked to explain the effect of deprivation on the dominance columns. At birth, Wiesel and Hubel find, the fibers entering the cortex send branches over a much wider area than they do in the adult. Thus the effect of deprivation might be that the fibers carrying information from the deprived eye retract more than normal, and those of the normal eye retract less. In addition, the process known as "sprouting" may play a part. In sprouting, the cells carrying information from the normal eye grow new terminals that spread beyond their usual territory when the competing terminals are at a disadvantage.

The primary visual cortex is now the area most thoroughly mapped in terms of cell functions and organization. Yet the findings should be applicable to other parts of the brain. "Columns occur all over the cortex," Hubel says. In the somatosensory area of the brain, there are alternating areas of deep and of superficial sensation. Even in the auditory area, regions receiving sound information predominantly from the left ear appear to alternate with areas receiving sound from the right.

The take-home message, as the researchers would say, is that the primary visual cortex, and probably other regions of the cortex, consists of many small working subdivisions, all or more or less identical structure. While in some brain regions researchers have good ideas of what the repetitive units might be, in others, such as the speech area, the key properties are still difficult to imagine.

"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," Hubel and Wiesel say. And researchers will then know what a small proportion of the brain's 10 billion cells are doing in everyday life. □

The Brain: What's It For?

Armed with scalpels, chemicals and electrodes, thousands of scientists are assaulting the brain and carrying away clues to its mysteries. How do we think? How do we generate emotions? And why do those crucial functions sometimes go wrong? The research progress is impressive, and yet the most important answers aren't nearly in. In Washington in September a group of scientists and National Institutes of Health administrators got together to project where the research is headed and how it can be boosted along the way.

One obvious trend among brain and nervous system researchers is increased teamwork. The cost of the most elaborate equipment and the need for knowledge of disparate disciplines dictate cooperation. Some scientists welcome continual collaborations, while others fear a loss of the "American frontier" individualistic spirit and rue the day when brain research, like high-energy physics, will be the territory of scientific "empires." Ray Guillery, a neuroanatomist at the University of Chicago, said, "Interdisciplinary marriages have expensive dowries."

Perhaps neuroscience teams should include an engineer who would know when solid-state electronics would solve a problem. And a chemist who would be able to synthesize analogs and radioactive tags for molecules under study. And a tissue culture expert to grow nerve cells in the laboratory and to raise cells that produce antibodies. Some groups do include electrical engineers, chemists or tissue culture experts, but most, so far, do not.

As in the past, the brain remains a problem waiting for techniques. Radical advances in scientific understanding followed development of the micropipette (for detecting electrical activity inside cells), methods for mapping cell connections and immunological methods for localizing nerve cell transmitter chemicals and receptors. Neuroscientists expect further advances from recent discoveries of ways to produce selected, pure antibodies, to record electrical activity in conscious, behaving animals and to scan the biochemistry and activity of a living, human brain. The most desirable, as yet unavailable, method that those who attended the meeting would imagine is a device to simultaneously record electrical activity from large numbers of cells, for further investigation of the nervous system's information processing.

Where will the research lead? W. Maxwell Cowan of Washington University in St. Louis and president of the Society for Neuroscience expects within our lifetime to see scientists assemble a sound account of brain perception and control of motor activity. And he expects greater understanding of "the real purpose of brains — how they control behavior" and that long-term puzzle — learning. Analysis of brain chemicals, Cowan predicts, someday will alleviate, if not eliminate, major forms of mental illness.

Predictions are conservative because the very areas included in neuroscience are increasing. Recently the brain has been implicated in regulating processes with which it had never before been associated. For example, the brain appears important in control of blood pressure. Roger Guillemin of the Salk Institute in San Diego reportedly responds to increasing brain importance by quipping, "Endocrinology is now a branch of neuro-endocrinology."

So as more and more researchers face the brain, examining it with varied techniques, more complex will become the answer to a question asked of Cowan on his way to testify before a Senate committee hearing. The guard checked inside Cowan's briefcase, found a human brain and immediately asked: "Good god, what's it for?"

It's for, at least, thinking and sensing and learning and emotional feeling, and in this special issue of Science News we describe some of the research exploring the bases of those functions.

—Julie Ann Miller