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SPECIFICITY OF RESPONSES OF CELLS IN THE VISUAL CORTEX

DAVID H. HUBEL

Department of Neurobiology, Harvard Medical School, Boston, Massachusetts

LOOKING at the human brain from the outside, the most striking feature, by far, is the cerebral cortex, partly because it is on the outside, and partly because of its sheer size. A student approaching the nervous system for the first time is bound to be struck by the paucity and unevenness of present-day knowledge of this impressive structure. Despite a century of study by neurologists, neuroanatomists and neurophysiologists, only a very small fraction of the cortex is understood in any detail, and much of it is not understood at all. This ignorance is not confined to the cortex, but is common to a large part of the deeper structures of the brain.

Considering how much is known about most organs of the body, such as the pituitary, pancreas, or kidney, our slowness in coming to grips with the nervous system may seem puzzling. The main source of the difficulty is to be found in the very nature of the nervous system. For most other organs it is enough, broadly speaking, to know the functions of a few classes of cells. If you understand the actions of one salivary gland cell, plus the architecture of the gland's circulation and duct system, you have a reasonable grasp of the whole organ. In the nervous system it is not enough to know how a single cell works, though of course that is essential. One must also study the connections and interrelations between enormous numbers of cells, and this is a matter of comprehending an architecture vastly more complicated than the salivary gland duct system.

In the past few decades much progress has been made in working out what might be called the general cellular physiology of the nervous system, including the ionic mechanisms of impulse conduction and synaptic transmission. This has opened the way towards an attack on the functional architecture of the central nervous system. Today we are in the position of someone who has a reasonable understanding of the components of a radio circuit, the resistors, condensers, transistors and so on, but for the most part does not know how they are strung together, or what the electrical signals passing through them signify, or how the signals are being analysed or transformed.

One difficulty here is that the problem requires a study of many single cells in the intact animal. It does not get us very far to study the pooled activity of many cells at a time—for example with large electrodes placed on or in the brain—since neighbouring cells even if morphologically similar may perform entirely different tasks. Studies of populations of cells in general tell us little about the individuals. Until very recently methods for studying single

cells in the intact brain did not exist, and it was not until around 1950 that single cortical cells were first recorded. Probably the first finding of profound interest was Mountcastle's discovery that somatosensory cells are aggregated into columnar groups according to modality. This was the first indication of a parcellation of cells on a scale smaller, by an order of magnitude, than the cortical filelds which the architectonic anatomists and localization neurophysiologists had fought so hard to establish in the previous decades.

In the past 10 or 15 years techniques have advanced rapidly and much progress has been made, especially in the sensory systems, where one can examine regions not too remote, in terms of numbers of synapses, from the input to the nervous system. The visual system, despite its great analytic capabilities and consequent complexity, has turned out to be especially amenable to study. This is partly because it has a fairly simple anatomic path, with flow of information directed mainly from periphery centrally over a number of relatively discrete stages. In the present paper I wish to illustrate one type of work that is being done by describing two cells in the visual cortex, one situated in area 18 in the cat, the other in 17 in the Rhesus monkey. These are not special or exceptional cells, but typical ones both in their specificity and their great individuality. The experiments were done at Johns Hopkins and later at Harvard by TORSTON WIESEL and myself.[1,2] In a sense they are a continuation of studies begun by Hartline in frog and Limulus, and by Kuffler in the cat retina.

Let me begin with a brief word about methods, some of which were originally developed for awake unrestrained animals while I was at Walter Reed. We now mainly use anesthetized animals because for this type of experiment it is very much easier and more efficient. In the past few years, however, most of the results have been shown to hold in awake unrestrained animals by WURTZ.[3] The animal (cat or monkey) has its head firmly supported in a head holder, and the eyes are held open facing a screen one and a half meters away. Visual stimuli of various shapes, colors and rates of movement are projected upon this screen and hence onto the retinas. Records are made extracellularly from a tungsten microelectrode introduced through a small hole in the skull. With these methods it is possible, in a good experiment, to record over a hundred cells as one penetrates through 2 mm of cortex. A single cell can if necessary be studied for several hours.

Cell I: A 'hypercomplex' cell of area 18 *(visual II) in the cat*

This cell was recorded from area 18, a region which, in the cat, is situated just lateral to area 17, and which receives a topographically ordered set of connections both from 17 and from the lateral geniculate body. The cell, like the great majority of cells in the visual cortex, gave no detectable response to changes in diffuse light; even shining a bright flashlight into the eyes of the animal produced no obvious change in spontaneous firing. There were, however, strong and predictable responses to a specific stimulus within an area of visual field about 2° by 4° in size, located about 15° below and to the contralateral side of the center of gaze. (The moon subtends ½° to an observer on earth, and 1° of visual angle corresponds to about 250μ on the cat retina.) After much trial and error we found that the most effective stimulus was an edge, oriented in a 2 o'clock—8 o'clock direction, with dark below and light above, swept slowly up across the rectangular region outlined by dotted

lines in Fig. 1. As the edge's position was varied to include more and more of the left half of the rectangle, the responses became increasingly vigorous, in terms of impulses per second and total number of impulses (Fig. 1, A–C). On extending the edge still further to the right, however, the response began to get weaker, and when it covered the entire dotted region there was no response at all (D–E). It was as if stimulating the right hand area with an edge

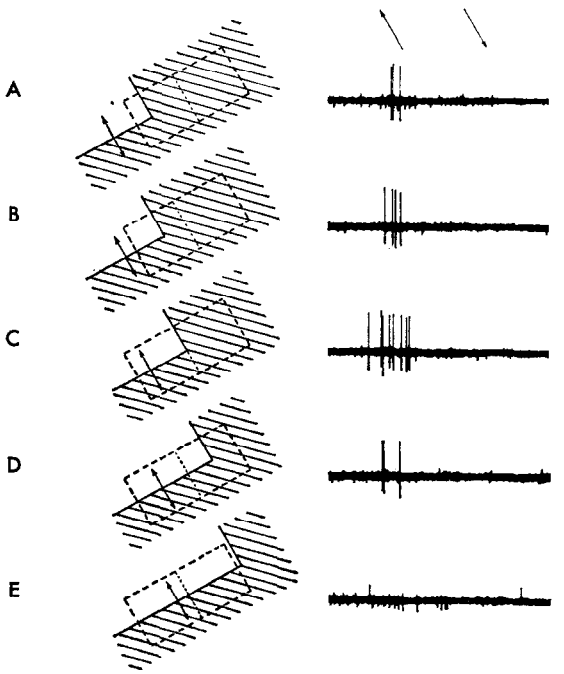

FIG. 1. Records from a hypercomplex cell in cat visual II. Stimulation of right (ipsilateral) eye. Receptive field, 2° × 4°, indicated by interrupted rectangle. Stimulus consisted of an edge oriented at 2:00, with dark below, terminated on the right by a second edge intersecting the first at 90°. A–C: up-and-down movement across varying amounts of the activating portion of the field: D–E: movement across all of the activating portion and varying amounts of the antagonistic portion. Rate of movement 4°/sec. Each sweep, 2 sec (See Ref. 1, Fig. 8).

was able to block the response that would normally have been produced by stimulating the left area. Both regions were orientation specific. If the optimal orientation for the left region was kept constant at 2:00–8:00, while varying the part of the edge crossing the right hand region, it was possible to show that here too a 2:00–8:00 orientation was specific, this time for a complete blocking of the response (Fig. 2).

This cell was maximally responsive, then, to a specifically oriented moving edge terminated on the right at a specific point. If the edge extended to the right of that point the response failed, whereas it could be extended without penalty any distance to the left.

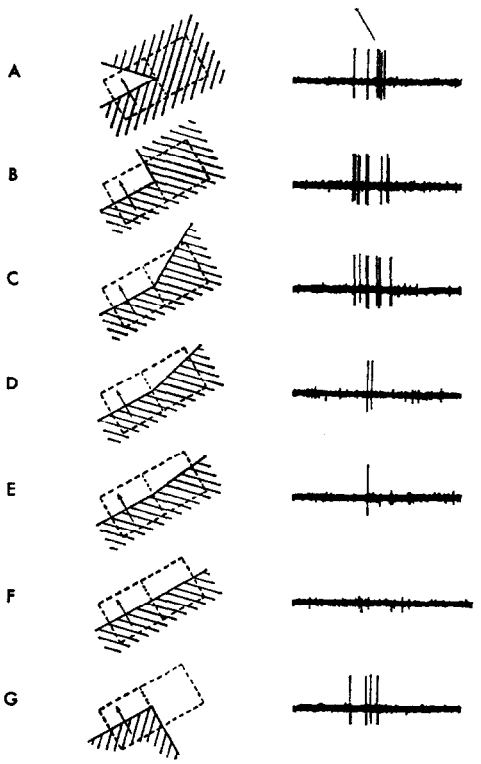

FIG. 2. Same cell as in Fig. 1. Stimulation with two intersecting edges moved up across the receptive field as shown. Inhibition is maximum when the right (antagonistic) half of the receptive field is stimulated with an edge having the same orientation as the optimum edge for the left (activating) half (F). Duration of each sweep, 2 sec. (See Ref. 1, Fig. 9.)

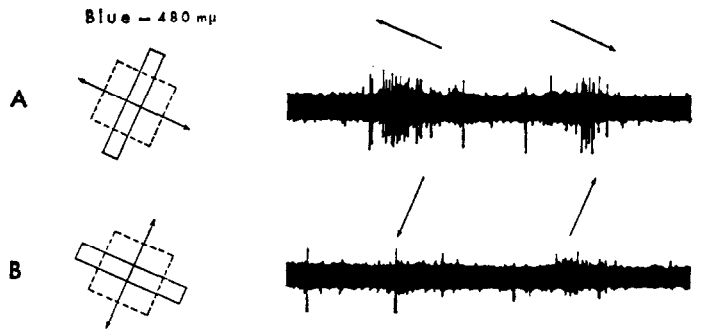

FIG. 3. Complex cell with color coded properties recorded in layer II of monkey striate cortex. Responses to two orthogonal stimulus orientations; wavelength of light, 480 mμ (blue). Size of receptive field, ½° × ½°. Time for each record, 5 sec. (See ref. 2, Fig. 6.)

Cell II: A complex color coded cell in monkey cortex

This cell was recorded from monkey striate cortex. Like a typical cell of the type we term 'complex' it gave a brisk, sustained response as a properly oriented line was swept over a restricted region of retina. Here the optimal orientation was 1 o'clock–7 o'clock; a vertical orientation or more oblique ones such as 2 o'clock–8 o'clock, or 4 o'clock–10 o'clock were quite ineffective (Fig. 3). The remarkable feature of this cell was its wavelength specificity. The best responses were obtained with a moving blue line, about 480 mμ in wavelength. Wavelengths of 520 mμ (blue green) or longer were virtually without effect, at any available brightness (Fig. 4). What was especially striking was the ineffectiveness of a *white* line, which could be obtained simply by removing the blue filter from the slide projector, i.e. by adding in the longer wavelengths that the filter had been holding back. It was as if this longer wavelength light was in some way blocking the response the blue light would have produced.

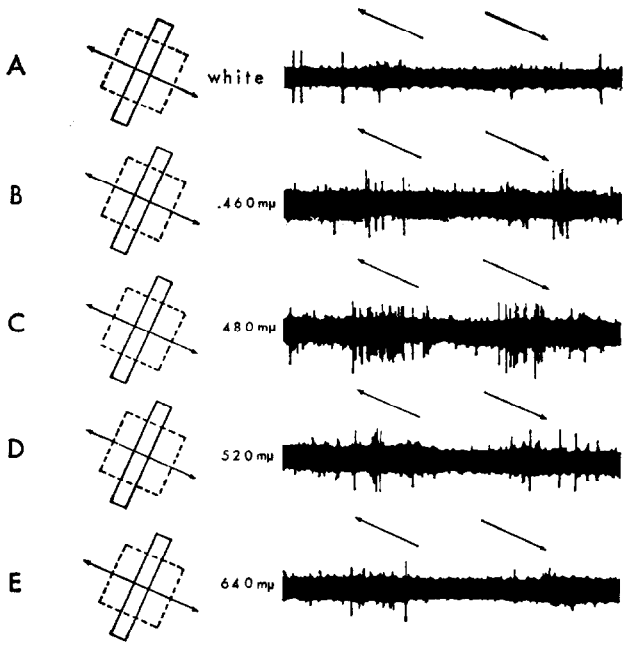

FIG. 4. Same cell as in Fig. 3. Responses to movement of optimally oriented slits of white light and monochromatic light at various wave-lengths. Monochromatic light made by interposing interference filters in a beam of white light. Stimulus energies are greatest for A, and progressively less for E, D, C and B. None of the responses was improved by lowering the intensity. (See Ref. 2, Fig. 5.)

My main purpose in describing these cells has been to illustrate the characteristic specificity that one finds in cells of the visual path in higher mammals. Frequently this specificity seems to be the result of converging excitatory and inhibitory influences that can cancel each other. In the first example an edge crossing the left area excites, whereas

an edge crossing the right area, if presented simultaneously, precisely antagonizes and cancels out this response. A plausible scheme to illustrate the mechanism is given in Fig. 5. It is as if the cell received an excitatory input from a cell with a receptive field in the left area, and an inhibitory input from a second cell with its field in the right hand area. A long line would be expected to fire both these lower order cells, and their influences on the cell we are discussing would cancel, resulting in no response. In the second example a similar antagonism exists between the effects of short and long wavelengths, and we may imagine that a similar convergence of inputs is responsible for the observed behavior. The result of such transformations is that a single cell may possess specificity of response to a large number of variables, such as position on the retina, orientation, speed of movement, wavelength, line length, and so on. All of these may have to be precisely adjusted for the stimulus to work. Our impression is that for each combination of values of these variables there corresponds a cell or set of cells. Of course this calls for a vast number of cells, but that is exactly what a structure like the visual cortex possesses, given many square centimeters of cortex, and some 10^5 cells beneath each square millimeter of surface.

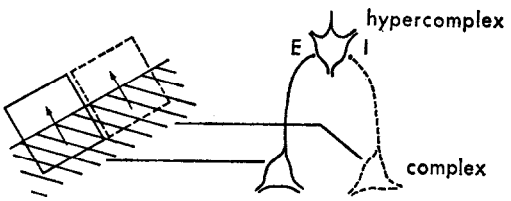

FIG. 5. Wiring diagram that might account for the properties of a hypercomplex cell. Cell responding to single stopped edge (as in Figs. 1 and 2) receives projections from two complex cells, one excitatory to the hypercomplex cell (*E*), the other inhibitory (*I*). The excitatory complex cell has its receptive field in the region indicated by the left (continuous) rectangle; the inhibitory cell has its field in the area indicated by the right (interrupted) rectangle. The hypercomplex field thus includes both areas, one being the activating region, the other the antagonistic. Stimulating the left region alone results in excitation of the cell, whereas stimulating both regions together is without effect.

By using methods such as those illustrated here to analyse a large number of cells in the visual cortex it has been possible to obtain further insight into the functions of this structure. Little by little one learns what attributes of a visual image are important in producing responses from cortical cells, and one begins to form an idea of how images are analysed. By comparing the properties of neighbouring groups of cells it is also possible to learn something of the functional architecture of the cortex, and to correlate this with morphology. At present we can thus list a number of specific functions of this part of the brain, and give definite and testable suggestions as to how these functions are carried out.

Fortunately for our livelihoods, the work is just beginning. The detailed ultrastructure of the cortex seems vastly more complex than any of the circuits we can propose, and it is likely that the gold in the mine greatly exceeds any that has already been removed. The encouraging thing is that known methods seem to be equal to the task. Moreover, to understand the cortex, despite its complexity, seems well within man's capabilities.

Getting the information is often difficult and sometimes exasperating, but the results are usually simple and elegant. The monkey's solution to the problem of analysing the visual environment is more ingenious than anything a neurophysiologist could possibly dream up.

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