Receptive Fields of Single Cells and Topography in Mouse Visual Cortex

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ABSTRACT The visual cortex was studied in the mouse (C57 Black/6J strain) by recording from single units, and a topographic map of the visual field was constructed. Forty-five percent of the neurons in striate cortex responded best to oriented line stimuli moving over their receptive fields; they were classified as simple (17%), complex (25%) and hypercomplex (3%). Of all preferred orientations horizontal was most common. Fifty-five percent of receptive fields were circularly symmetric: these were on-center (25%), off-center (7%) and homogeneous on-off in type (23%). Optimal stimulus velocities were much higher than those reported in the cat, mostly varying between 20° and 300°/sec. The field of vision common to the two eyes projected to more than one-third of the striate cortex. Although the contralateral eye provided the dominating influence on cells in this binocular area, more than two-thirds of cells could also be driven through the ipsilateral eye. The topography of area 17 was similar to that found in other mammals: the upper visual field projected posteriorly, the most nasal part mapped onto the lateral border. Here the projection did not end at the vertical meridian passing through the animal's long axis, but proceeded for at least 10° into the ipsilateral hemifield of vision, so that at least 20° of visual field were represented in both hemispheres. The magnification in area 17 was rather uniform throughout the visual field. In an area lateral to area 17 (18a) the fields were projected in condensed mirror image fashion with respect to the arrangement of area 17. Medial to area 17 a third visual area (area 18) was again related to 17 as a condensed mirror image.

Neurophysiologists have devoted little attention to the mouse and have particularly neglected its visual system. This is not only due to the difficulties in handling a small animal in a long lasting neurophysiological experiment, but rather because such a study does not fit with two of the most widely accepted practices in neurophysiology: either to investigate a very simple animal having only a small number of identifiable neurons, with the prospect of understanding its whole nervous system in terms of the interaction of all its components, or to study one subsystem, such as the visual pathway, in an animal in which that system is developed to a very refined stage. The mouse is neither a simple animal nor is its visual capability outstanding; on the contrary there is no doubt from behavioral studies that its visual sense is not the dominating one and indeed is rather coarse (for references, see Fuller and Wimer, '66). One argument for a study of the mouse visual system stems from an interest in comparative physiology, given the extensive studies already available in the cat, monkey and also the more closely related rabbit. But the strongest motivation for a functional analysis of the mouse central nervous system is the availability of genetically pure strains and of many well-identified neurological mutants (Sidman et al., '65). Since the visual pathway represents perhaps the most thoroughly investigated part of the mammalian central nervous system, it seemed easiest to take advantage of existing knowledge and to work out a part of the mouse visual pathway as a basis for future studies of mutant mice. For such a study it does not primarily matter

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how well the visual sense is developed or how important it may be for the mouse, as long as an order of any kind is revealed.

METHODS

Included in the analysis of this paper are recordings from 56 mice of the C57 Black/6J strain obtained from the Zentralinstitut für Versuchstierzucht in Hannover, and two mice that were a cross between the local wild mouse and several laboratory strains. The mice were about 4 to 8 months old and their weights ranged between 20 and 26 grams. There was no obvious difference between the two strains in the results to be reported.

The mouse was anesthetized with an initial dose of 60 mg/kg of pentobarbital intraperitoneally; this was supplemented later, as required, by additional 0.02 mg doses. Atropine (0.03 ml of a 1% solution) was used to counteract vagotonic effects of the anesthetic. To prevent cerebral edema, which is easily caused merely by mechanical vibrations from drilling the skull, about 1 mg of prednisolon was injected intramuscularly. Later a single dose of 0.12 mg of chlorprothixene (Truxal) was given intramuscularly; this is a tranquilizer whose effect is synergistic with that of pentobarbital. With this combination at optimal anesthetic levels for recording from single cells, the mouse sits quietly without moving but reacts vigorously if pinched. The anesthetic level must be light if cells are to respond well. Even when no artificial respiration was used the trachea was always cannulated, since otherwise it tended to become clogged with salivary secretions. Rectal temperature was maintained at 36.5°C by a manually controlled heating pad. The head was supported by a holder that was clamped to an LPC stereotaxic system for cats. The horizontal plane of this holder lies between the intraaural line and a point 2 mm above the incisor bar and provides the same inclination as that used by Montemurro and Dukelow ('72) in their stereotaxic atlas. The skull over the visual cortex on one side was removed cautiously by first drilling away the external and spongy layers of bone and then tearing off the internal layer with forceps. Great care was taken to leave the dura intact. To protect the cortex against drying and to dampen pulsations the best method was to cement the skin to a ring cut from a silicone tube using a water-binding glue (Cyanolit), and to fill the well so formed with agar.

To keep the optics transparent in mice presented a major problem. Various anesthetics, cold, anoxia, or other stress can lead to a reversible cataract in the anterior capsule of the lens. Fraunfelder and Burns ('70) found that the osmotic pressure in the anterior chamber increases and recommended using contact lenses. In the first experiments the eyes were protected with silicone fluid (1,000 sc. Dow Corning); later contact lenses of a variety of sizes were used. Most animals were best fitted with lenses with a radius of curvature between 1.50 and 1.55 mm. The mouse eye as measured with an ophthalmoscope is highly hyperopic, about +15 diopters. This is probably an error due to the distance between the light reflecting layer and the receptor layer (Brückner, '51; Glickstein and Millodot, '70), a distance that remains fairly constant among different species, but becomes increasingly important with decreasing eye size. Here it was presumed that the mouse is emmetropic, and contact lenses were selected so as not to change the appearance of the fundus when viewed with an ophthalmoscope. No attempt was made to correct for focus on the screen, since the depth of focus in such a small eye was assumed to be large; with ophthalmometric methods such a correction would have been most difficult.

The mouse was placed 27 cm from a 1 × 1.4 meter translucent tangent screen. The long axis of the mouse formed an angle of 65 degrees with the screen; this angle was chosen as a compromise, given the laterally positioned eyes and a possibly larger central representation of the anterior field of vision. The arrangement was kept constant in all experiments. The screen covered a rather large sector of the field of vision through one eye (120 × 130 degrees), but the peripheral parts were projected in a somewhat distorted manner. As a retinal landmark the optic disc was projected on the screen with an ophthalmoscope. It projected roughly 60 degrees lateral to the animal's midline and 40 degrees above the horizontal. No cen-

tral retinal area could be determined ophthalmoscopically.

Most recordings were performed with laquer coated tungsten electrodes. In a few experiments glass pipettes were used; these were filled with 1.5 molar potassium citrate and had a resistance of 3–6 megohms. In several experiments with tungsten electrodes the recording tracks were marked by electrolytic lesions made by passing 3 μA for 2 seconds through the electrode tip (DC, electrode negative). Animals were perfused at the end of the experiment and their brains prepared for histology. Impulses from single cells were recorded and amplified by conventional recording methods, displayed on an oscilloscope, monitored by a loudspeaker, and sometimes stored on an Ampex tape recorder. For immediate analysis a two channel electronic counter was used.

Various stimuli were projected manually on the screen by a Zeiss handlamp or a slide projector. Automatically generated stimuli consisted of circles of various diameters flashed by means of an electromagnetic shutter driven by a Hivotronic impulse generator. To generate moving stimuli a servo-driven oscillating projector system was used, in which different stimuli could be moved back and forth over the screen with variable speed and amplitude and rotated in any direction. The screen was indirectly illuminated from a distance by two tungsten bulbs; background illuminance was about 0.5 cd/m^2 and stimulus intensity ranged between 2 and 10 cd/m^2.

In several mice direct measurements were made to determine whether eye movements were a serious problem in the lightly anesthetized animals. For that purpose a tiny mirror (about ½ mm^2) was glued to one eye with water-binding cement, and a narrow beam of light was reflected from this mirror to the screen. Under these conditions there was a continuous vibration of about 0.25° to 0.5° synchronous with respiratory excursions, but no large rapid eye movements were visible. In some mice there was a slow continuous drift in eye position of up to 15° in three hours. This may have been partly an artifact due to the irritation by the glue and the weight of the mirrow compared to that of the small eye. In actual recording experiments several small receptive fields were observed for up to three hours; during this time large rapid eye movements were never seen and slow drifts never exceeded 2–3° per hour, a negligible error compared to the average size of the receptive fields.

Many preliminary experiments were nevertheless performed to achieve relaxation by curarizing with Flaxedil and respirating artificially by means of a rodent respirator. It was found that relaxation was possible but rather tedious, since the cortex tended to become unresponsive or give epileptiform discharges unless the respiration volume was very carefully regulated. The few good units recorded in respirated animals were similar to the ones recorded without relaxation and are included in the results without special reference. As residual eye movements and the continuous administration of anesthetics did not to any serious degree interfere with the study most experiments were done without relaxation.

RESULTS

Four hundred units and some unit clusters were recorded in area 17 and the directly adjoining visual cortex of 57 mice. Many units in the early experiments and some in the later experiments were not completely investigated. For some the only information obtained was the location of the receptive field on the screen, and in some the preferred direction of movement was determined, but too little information was obtained to permit further classification. Not all cells were tested with both eyes. In experiments in which glass electrodes were used there were sometimes doubts concerning the identification of the point of contact with the cortical surface and consequently the depth of a recorded cell. The samples of neurons tested for different characteristics thus vary slightly in number.

For construction of the topographic map unit clusters as well as isolated units were used. For all other purposes all units had to be well enough isolated to permit distinction between fiber and cell spikes (Hubel, '60); of these only cells were analyzed and classified. Additional evidence that the cell classes to be reported represent cortical cells and not fibers is the observation that some of the units in all

classes were binocular or showed prolonged injury discharges. The following detailed analysis of single units applies only to area 17. Too few units were identified in areas 18 and 18a to provide more than a general impression of the population in these areas.

Units in mouse area 17, like those in cat and monkey, reacted poorly to changes in overall illumination. Moving patterns of various shapes and contrast were usually the most effective stimuli, but for purposes of mapping separate field subdivisions stationary stimuli were commonly flashed on (+) and off (−).

Two main groups of cortical cells were found. Cells of one group responded equally well to all directions of movement and were not concerned with stimulus orientation. A second smaller group of cells strongly preferred a properly oriented elongated stimulus swept across the field in one or both of the two opposite directions.

A. Cells with non-oriented receptive fields

In this group three subtypes were found: on-center cells, off-center cells, and a heterogenous group of on-off cells which are here called "fast cells" because of their common characteristic of reacting to rapid movement.

On-center cells

On-center cells constituted 25% of all classified cells in mouse area 17. In figure

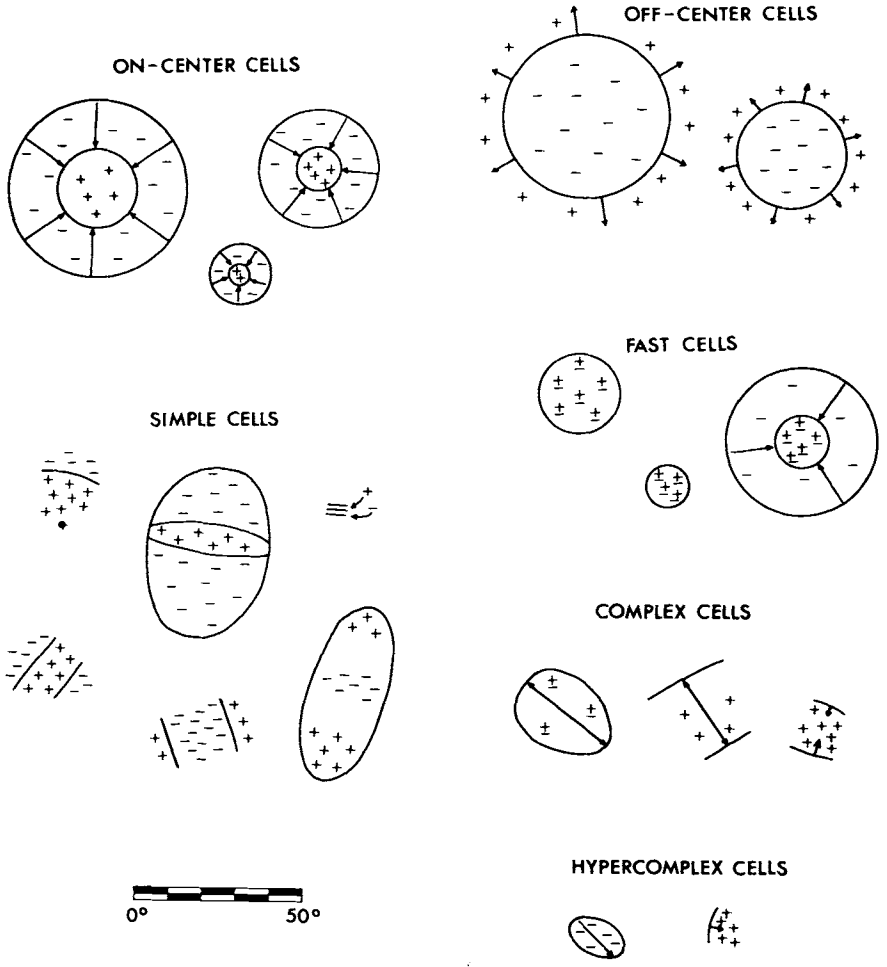

Fig. 1 Maps of the different receptive field types found in mouse area 17, drawn to scale.

1 a few on-center fields are drawn; the average diameter of their center plus surround was 35° and ranged from 18° to 50°; the mean diameter of field centers was 15°, ranging from 6° to 35°. On-center cells reacted with maximum response to a light spot flashed in the field center and filling it. Responses to flashed stimuli were transient, and this was found for all cells in mouse area 17. The power of the surround in suppressing the center response was very striking: in contrast e.g. to on-center cells in cat lateral geniculate these cells reacted poorly to a very long slit moved over the whole field and responded either weakly or not at all to changes in diffuse illumination. Despite this strong influence of the surround over the center, it was not easy to obtain an off-response from the surround with flashed stimuli. A carefully placed annulus of light flashed in the surround usually evoked only a weak off-discharge, and for determining the extent of the surround the best method was to produce a large spot of light with an iris diaphragm, and to close the diaphragm abruptly in small steps. The off-surrounds in figure 1 were obtained by this method. A spot of light smaller than the field center moved from the surround into the center was also usually a much more effective stimulus than a flash. The optimal speed for such a spot was about 30° to 150°/sec and for a given cell the speed was often quite critical. On-center cells were easy to find since they had a high spontaneous activity (about 50 to 150 spikes per minute) and generally responded vigorously.

Off-center cells

Off-center cells were rare; only 15 were found in area 17 (7% of the total sample). Their receptive fields were very large, with an average center diameter of 51°, ranging from 15° to 80°. Spontaneous activity was low (5–10 spikes/min), and the cells were rather difficult to drive, giving only a few spikes even to the most effective stimulus. A spot of light flashed into the center evoked a transient off-response; a stimulus flashed within the surround produced a weak on-discharge. The best way to stimulate these cells was to move a light stimulus outwards from the center into the surround with a velocity of about 50° to 150°/sec.

"Fast cells" (on-off cells)

This group of cells comprised 23% of the total sample of classified cortical cells. Their common characteristic was a homogenous receptive field without any obvious subareas but with a substructure with complex properties. The average field size was 22°, ranging from 12° to 45°. These cells were easy to find mainly because of their characteristic spontaneous high-frequency bursting firing pattern, which in some cells reached levels as high as 15 spikes per second. The best stimulus was an edge or restricted spot of any shape moved very rapidly over the receptive field at rates of 100–1,000°/sec. Many of these cells also reacted to slow movement (in the range of 20° to 50°/sec.), but they then responded with a series of high-frequency bursts that could easily be confused with their spontaneous activity. The stimulus form and size were not critical; for optimal response a slit or edge had to cover the entire field, but it could also be much longer. When a light square was used most cells reacted preferentially to the leading edge and less to the trailing edge. A restricted light stimulus was usually better than a dark one, but some cells were highly sensitive even to the faintest moving shadow. When tested with a moving grid some of the fast cells could resolve a spacing finer than the field size; for example, one cell with a field 12° in diameter could resolve a grid frequency of 6°. As with other cortical cells, fast cells re-

TABLE 1

Frequency of 224 cells in area 17

Simple cells	Complex cells	Hypercomplex cells	On-center cells	Off-center cells	Fast cells
38	56	6	56	15	53
=17%	=25%	=3%	=25%	=7%	=23%

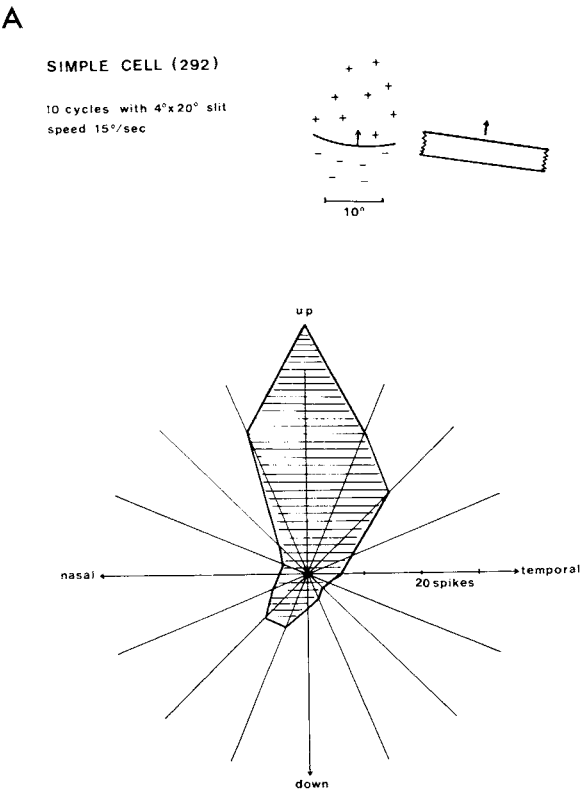

Figure 2A

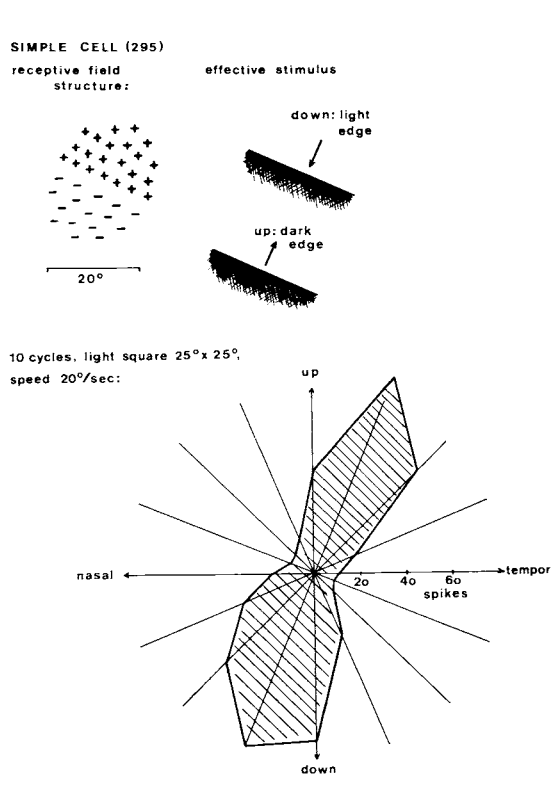

Figure 2B

sponded poorly or not at all to changes in background illumination. Flashing a light spot evoked a transient on-off response all over the receptive field. Usually the on-component was stronger, but in cells preferring a moving dark stimulus the off-response dominated. The on-off structure was hard to demonstrate in some cells and easy in others. When it was easy the cells could be triggered by flickering a light spot within their field, some following a flicker frequency of up to 14/sec. Usually fast cells had no surround. In some cells the field borders appeared indistinct, attenuating gradually in the periphery. When tested by closing or opening an iris diaphragm, a few cells had a weak surround of either on-, off-, or on/off-type, and a few cells seemed to be intermediate in form between this group and on-center cells.

B. Cells with oriented receptive fields

Cells in this group fell into three subtypes; simple, complex and hypercomplex. These categories appeared to be similar to those described in visual cortex of other mammals.

Simple cells

Thirty-eight cells of the 224 included in table 1, or 17% of all classified cells in area 17, were categorized as simple. By flashing slits or squares of light the receptive fields could be shown to consist of an excitatory area flanked by inhibitory areas on one or both sides, or more rarely an inhibitory area flanked by two excitatory areas. Unless the flashing stimulus was exactly placed to fill a whole area, most cells did not respond at all. Usually it was more difficult to evoke an off-response from inhibitory flanks than to demonstrate excitatory areas, but the existence of inhibitory flanks could be demonstrated indirectly, since flashing light on both areas simultaneously abolished the on-response from excitatory areas. As in all other cortical cell types the reaction to changes in

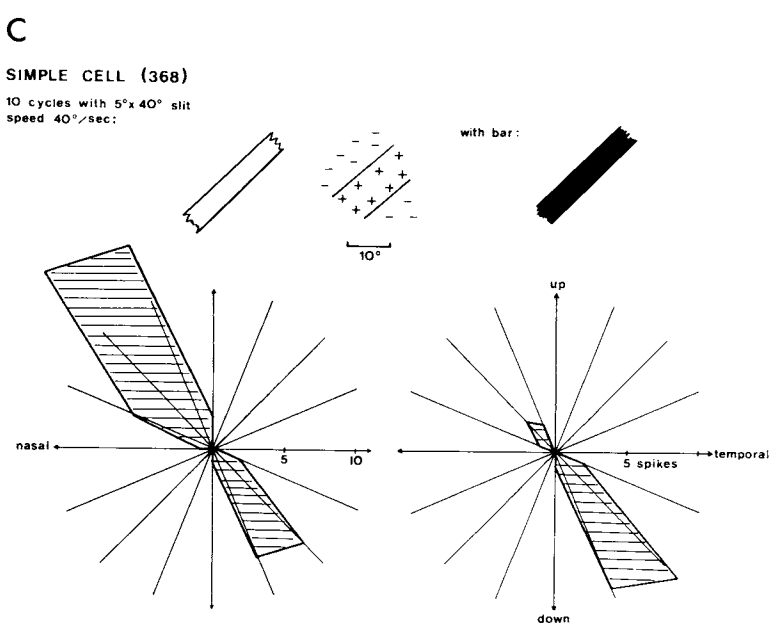

Figure 2C

Fig. 2 Responses of three simple cells to moving line stimuli in various orientations. For each cell receptive field map is shown at the top. Responses are plotted in polar coordinates. For each point plotted, distance from origin represents number of spikes/10 sweeps, direction from origin represents direction of movement. A. Cell responding best to an upward moving slit. Diagram appears somewhat distorted since field projected on the periphery of the tangent screen. B. Cell responding best to edge with dark below. C. Cell responding to slit and dark bar; for this cell optimum direction of movement reversed with contrast reversal.

diffuse illumination was generally inconsistent or rather poor in simple cells. When there was a reaction it was dominated by the strongest subarea: the cells tended to give a weak on-response to diffuse light if the optimal stimulus was a slit, and a weak off-reation when it was a bar.

Figure 1 shows a representative sample of all receptive-field types found in area 17, drawn to the same scale. The mean diameter of the total receptive fields of simple cells was 23.5°, ranging from 6° to 55°. The mean width of the main area was 10°, ranging from 2° to 30°. The extent of the field along the orientation axis was usually shorter than along the line perpendicular to this (the movement direction), particularly in large fields. It was sometimes difficult to determine the exact extent of the field along the axis, because a stimulus was only effective when it virtually filled a field subdivision. Similarly the expanse of the side flanks in a direction perpendicular to the orientation might have been larger in some fields than could be demonstrated. The most effective stimulus was a slit, or less frequently a dark bar or a light–dark edge, moved at right angles to the orientation of the subareas of the receptive field. To evoke an optimal response the stimulus had to be long enough to cover the entire length of the field, but it could be much longer without loss of effectiveness. The optimal speed of motion ranged from 5 to about 200 degrees per second and was critical for each cell. The thickness of a bar or slit, on the other hand, was not very critical: optimally it was about one-half to two-thirds of the width of the main area.

To document the cells' reactions to oriented movement, diagrams like those in figure 2 were made by sweeping a line, bar or edge over the receptive field and counting the number of spikes for each direction: the curves of response (in impulses per 10 sweeps) versus movement direction are plotted in polar coordinates. In some

curves (e.g., figs. 2A, 3A,C) the two preferred directions are not exactly 180° apart. This is probably a distortion related to the eccentric position of the receptive fields on the tangent screen. Simple cells usually had a low spontaneous activity, at least in the anesthetic state used in these experiments and compared to other cell types; they usually generated 2 to 10 spikes per minute spontaneously and only responded with a few spikes even to the optimal stimulus. This sluggish behavior made the detailed mapping of some fields difficult. The inhibitory flanks were often especially hard to demonstrate with a stationary stimulus, but their presence could usually be shown indirectly by comparing the response to a slit confined to the excitatory region with the response to a larger slit that included some or all of the inhibitory regions. In those cells in which separate "on" and "off" subareas could clearly be demonstrated, the orientation of a moving line and the most effective direction of back and forth movement could very often be predicted from the arrangement of subareas. Some cells with a side by side arrangement of two antagonistic areas responded only to a simple contrast moved in either direction. One example is the cell in figure 2B: this cell responded only when a light edge was moved from above into the on-area or when a dark edge was moved from below into the off-area — that is, it reacted to moving a light-above-dark contrast in both directions. Of cells responding specifically to edges, including simple and complex cells, the great majority preferred horizontal edges with dark below. Slits were very ineffective in activating such cells.

Most cells were much more sensitive to a slit than to a dark bar; those preferring dark stimuli usually had one or two exceptionally strong inhibitory areas in their fields. For any given cell the preferred direction of movement was generally the same for a dark bar as for a slit. The cell

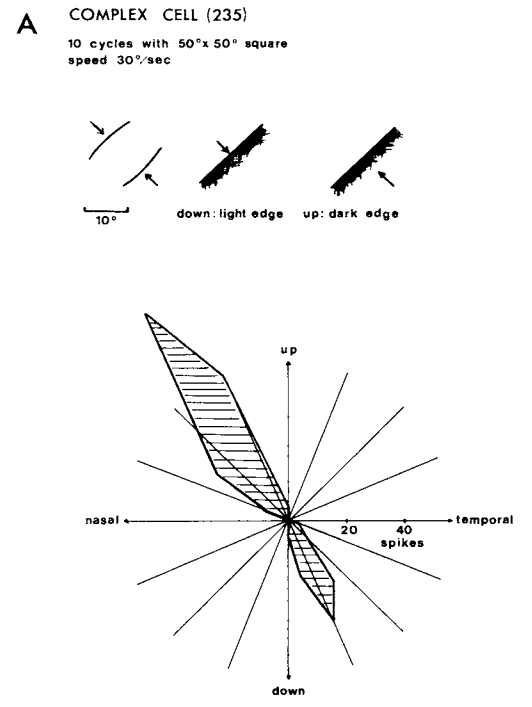

Figure 3A

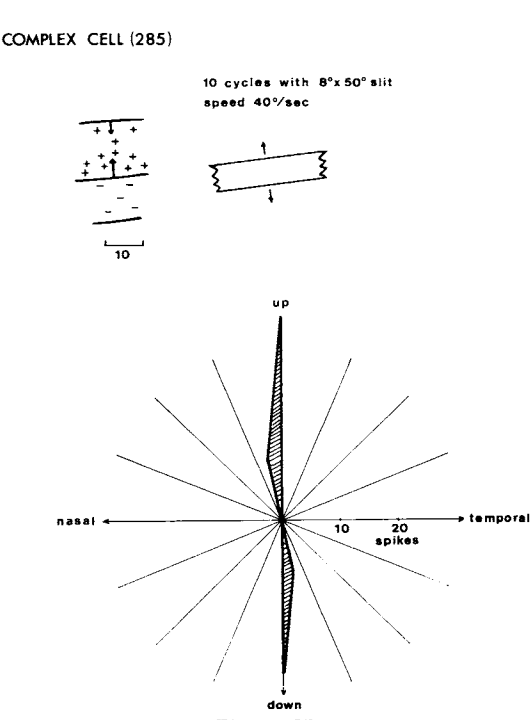

Figure 3B

Fig. 3 Polar plots of responses of four complex cells. A. Cell responding best to a moving edge. B. Complex cell whose field could be subdivided, by flashing stationary stimuli, into an upper area which gave "on" responses and a lower area giving "off" responses. The tuning curve of this cell was the narrowest recorded in this series. C. Cell responding best to a dark bar. D. Cell responding best to a narrow slit of light.

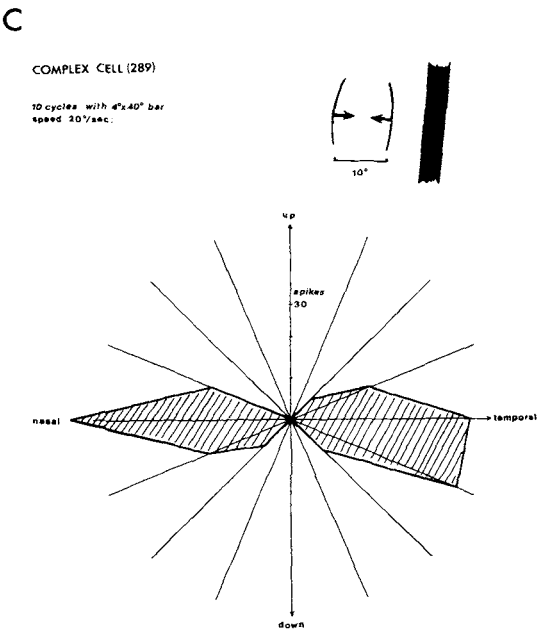

Figure 3C

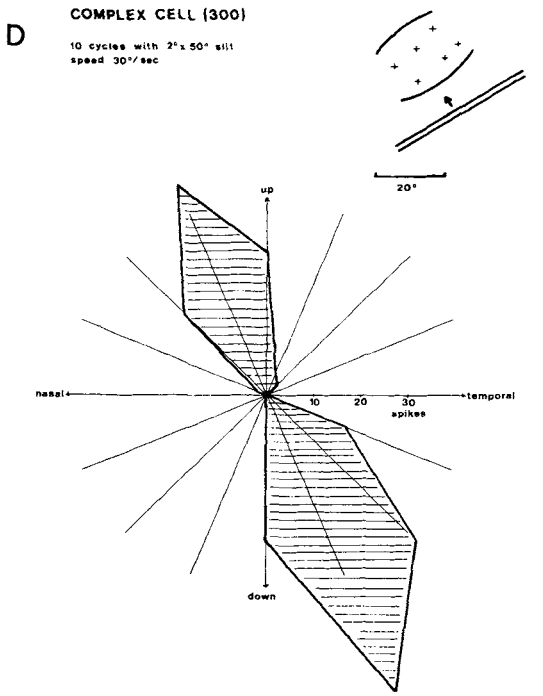

Figure 3D

in figure 2C was the only exception; here a bar and a slit had diametrically opposite optimal movement directions.

Complex cells

Complex cells constituted about 25% of the total sample. They were distinguished from simple cells by a substructure requiring an oriented stimulus within an apparently homogenous receptive field. A few complex fields are outlined in figure 1; the mean receptive field diameter was 20° along the optimal direction of movement. A typical complex cell responded everywhere within its receptive field to a properly oriented slit or bar of a certain width, or to an edge moved in a direction perpendicular to its orientation. The optimal width of the slit was much less than the width of the field. Lengthening the slit gave summation up to a maximum when the slit extended over the whole field; further lengthening it made no difference. Flashing a light stimulus was generally rather ineffective in driving a cell; it could evoke a weak on- or off-response throughout the receptive field, but for most cells no distinct on- or off-subareas could be demonstrated. Cells that responded optimally to a moving edge responded also to a flashed edge uniformly all over their fields. Spontaneous activity was usually higher than that seen in simple cells, and an optimal stimulus moved over the field typically evoked several short bursts. Polar diagrams looked similar to those obtained from simple cells; figure 3 gives four examples. The receptive fields of some complex cells had an inhibitory area flanking their main area on one side, as shown for the cell in figure 2B. This cell responded everywhere within its 15° wide excitatory area to a moving narrow slit of 1° width, something that would be unusual for a simple cell with that field size; it could also resolve a grid frequency below the width of the excitatory area. This cell had the narrowest tuning curve of all recorded cells with oriented receptive fields.

It was sometimes difficult or impossible to decide whether a cell was simple or complex. Frequently the width of the stimulus was not a critical requirement for driving the cell. Also a level of anesthetic that was slightly too deep could cause a simple cell to respond with a bursting fir-

ing pattern which resembled closely that of complex cells. For this reason the relative numbers of simple and complex cells given in table 1 must be taken as an approximation.

Hypercomplex cells

By definition a hypercomplex cell responds to a specifically oriented line stimulus moved in one or both of the two opposite directions over its receptive field, but in contrast to complex cells the line must not exceed a certain length since the field is bordered by one or two antagonistic areas to either side of the receptive field. In the present series only six such cells were found. These showed strong preference for one direction of movement and responded only to a short stimulus. One of the cells responded only to an exactly oriented corner moved with a certain critical speed into the field. The cell whose polar diagram is shown in figure 4A required a short oriented light slit moving upwards. Three cells were not particularly concerned about the orientation and form of the stimulus, as long as it was short enough. Their tuning curves were as broad as the curve in figure 4B. Although the orientation specificity of the whole group was rather variable, it seemed convenient to call them hypercomplex cells. It is possible, however, that the term "directionally selective units" might be more suitable for some of them, in the sense the term has been used by Barlow et al. ('64) for certain ganglion cells in the rabbit retina which lack orientation specificity. It will be necessary to record from more of these rare cells before it is possible to make definite statements about their classification. To flashed stimuli these cells either responded very poorly or their fields consisted of a homogenous on- or off-area. The antagonistic areas were purely suppressive, giving no reaction at all to flashed stimuli or to any stimulus moved within them. Spontaneous firing rates varied from 5 to

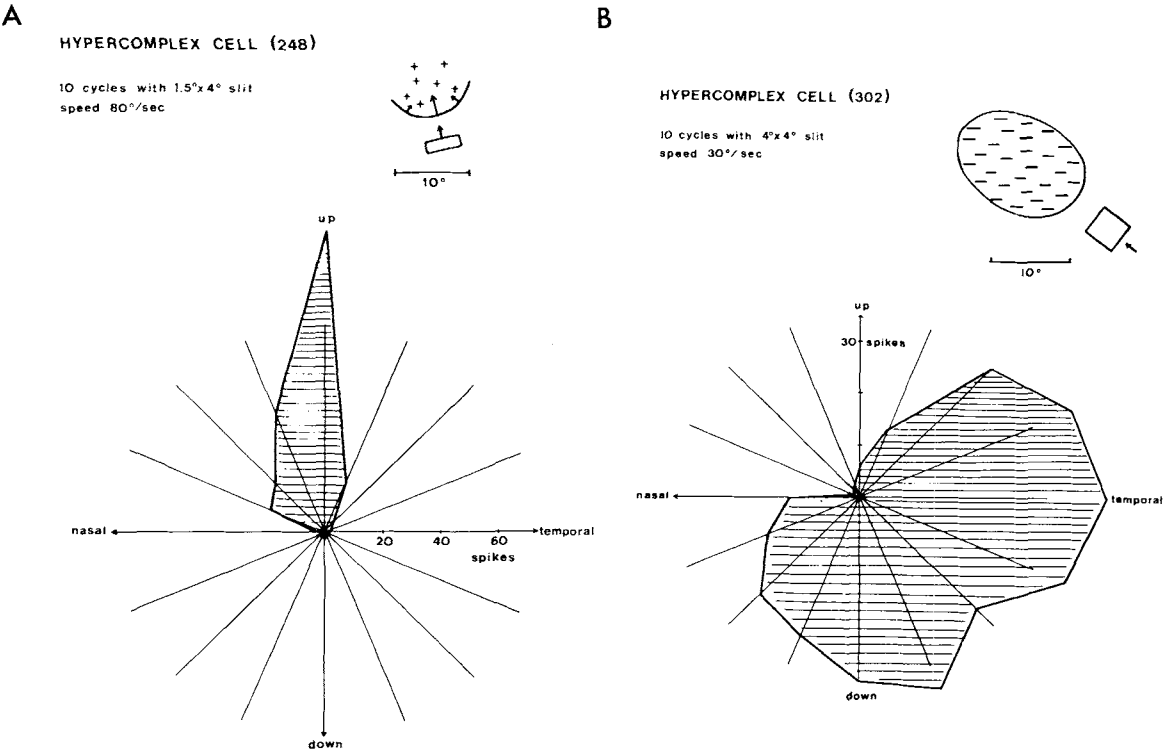

Fig. 4 Polar plots of responses of two hypercomplex cells. A. Cell responding best over a narrow range of orientations to a short slit. A long slit evoked no response. B. Cell giving unidirectional responses over a wide range of orientations. A long slit was completely ineffective.

30 spikes per minute, and an appropriate stimulus could evoke a rather vigorous reaction (up to 10 spikes per sweep).

Unidentified neurons

About 10% of the total number of well-isolated cells could not be classified. They were not grouped as a separate category, because their occurrence was highly dependent on the state of the animal or the experimenter. Most of them reacted in some way to light. There is no reason to believe there are non-visual cells in mouse visual cortex. No systematic testing was made for specific input from other sensory modalities.

Preferred directions of movement

It seemed worth enquiring whether some directions of movement stimulate a larger population of neurons than others, as is described for the visual system in the rabbit. Figure 5 shows the distribution of preferred directions of movement of 117 cells with orientation selectivity: simple, complex and hypercomplex cells are counted together. Of these 117 cells 43 reacted only to a stimulus moving in one direction; the remaining 74 were bidirectional. In figure 5A each unidirectional cell is drawn as a single radius from the center pointing towards the preferred direction, and each bidirectional cell is shown as a whole diameter. Figure 5B gives the same data as figure 5A, only as a polar histogram: in this representation it becomes obvious that cells responding to vertical movement (and hence with horizontally oriented fields) were distinctly more frequent.

Distribution of cells by depth in the cortex

The depth of a cell within the cortex was estimated from the readings of the micromanipulator. Because the point of contact with the cortical surface, estimated by watching the electrode tip through an operating microscope, is not very exact, and because there can be some dimpling during penetration of the dura, no attempt was made to determine the distribution of cell types according to cortical layers. Figure 6 shows the distribution of the percentage of all neurons with oriented receptive fields as opposed to circularly symmetric fields, at intervals of 50 μ through the depth of the cortex. Whereas in the upper layers both cell groups were found

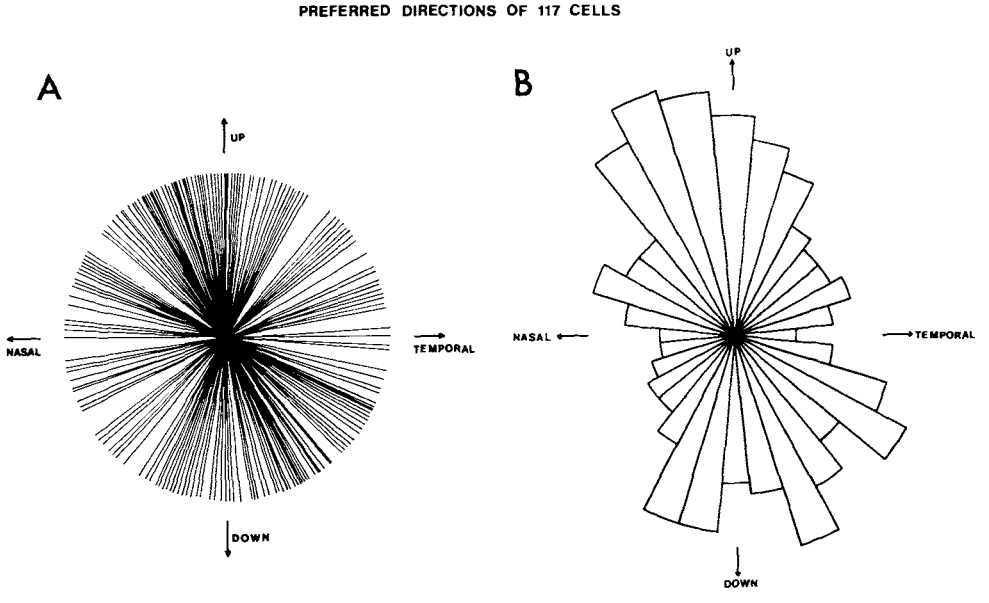

Fig. 5 Preferred directions of movement of 117 cells in area 17. A. Unidirectional cells are represented by a line pointing from the center towards the optimal direction of movement and bidirectional cells by a diameter indicating directions of movement. B. Polar histogram of the same data grouped into 32 bins of 11° each.

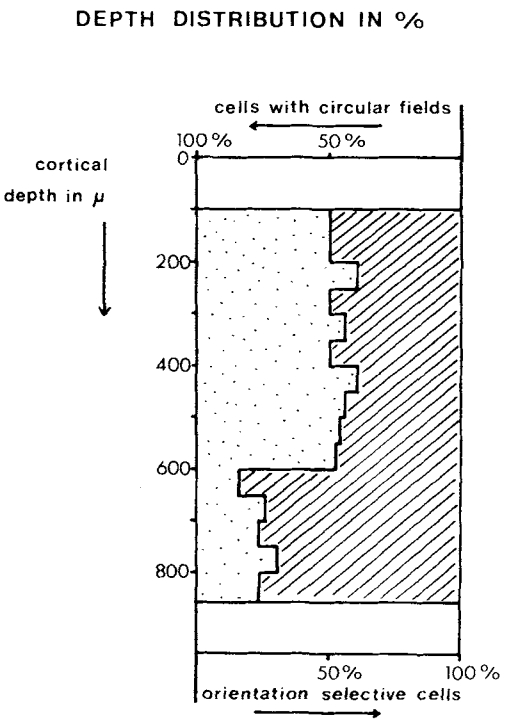

Fig. 6 Distribution by per cent of cells with oriented receptive fields versus cells with circularly symmetric fields, at different depths in cortex. Total number of cells, 175.

with about equal frequency, in the lower layers cells with circularly symmetric fields predominated.

Grouping of cortical cells according to functional characteristics

For technical reasons it remains doubtful whether in mouse striate cortex cells with similar properties are grouped together in vertical columns comparable to the orderly arrangement found in cats or monkeys. The evidence for columnar grouping of cells with similar orientations in cat or monkey depends largely on the reconstruction of penetrations in which cells are recorded in a sequence, and on the observation that the unresolved background and a simultaneously recorded cell almost always respond preferentially to the same orientation. To be sure that in the mouse records were from cell somata and not from fibers required sufficient resolution to allow identification by spike form; for this reason it was rare to record more than six cells in a vertical penetration. Cells with similar orientations definitely tended to occur in clusters: of 31 cases in which two oriented receptive fields were mapped in sequence within 300 μ, the difference in orientation was less than 30° in 23 pairs and greater than 30° in eight pairs. In contradistinction to this, when a cell with an oriented field was recorded, the background responded in the same area on the screen but seemed not to have any orientation preference. Cells with circularly symmetric fields were randomly interposed between recordings of oriented cells. No clustering of on-center cells was noted, but fast cells tended to appear together. Whenever a fast cell was isolated the background responded with a similar briskly bursting activity and followed equally well or even better to fast movement. Cells preferring dark stimuli seemed also to be grouped together in the cortex: most cells reacted much better to a stimulus lighter than the background, but when a cell preferring a dark bar was encountered the cells immediately following usually favored a dark stimulus too, regardless of cell type.

Binocularity

The region of overlap of the visual fields seen through the two eyes of the mouse is quite large. It widens considerably from anterior to above the mouse: in the horizontal plane it measures 35° across, 30° higher it is 80°, and on a level 60° above the horizontal line it is 120° wide. This is the minimal extent of the binocular visual field, measured as the projection of the corneal vertex in a dead mouse. In an awake mouse the binocular field is occasionally even larger, because mice, like many other mammals, have a musculus retractor bulbi; in an excited mouse the eyes protrude. In the histogram of figure 7 the relative influence of the two eyes on single cells is rated for 95 cells recorded in the binocular part of the striate cortex. Here group 1 cells are defined as receiving exclusive contralateral input; group 5 cells are driven only through the ipsilateral eye; group 3 cells are driven roughly equally from the two eyes, and cells in group 2 and 4 are binocular but not equally driven. Given the variability of the binocular field of vision, some cells may have

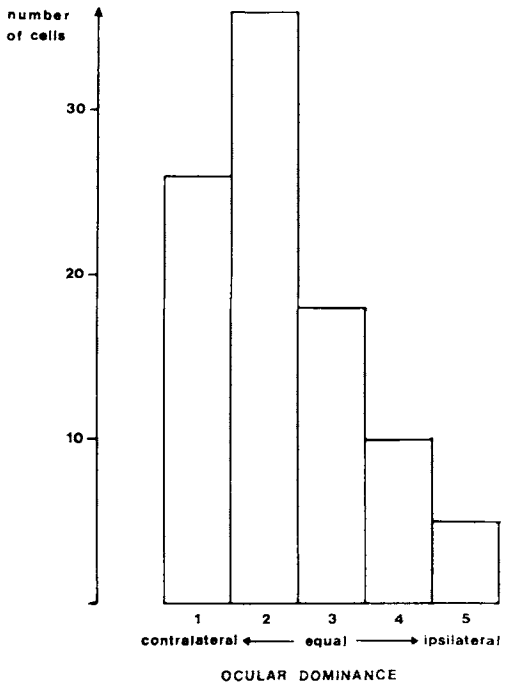

Fig. 7 Ocular dominance distribution of 95 cells in the binocular part of mouse striate cortex. Cells in group 1 were driven exclusively by contralateral eye; group 5, ipsilateral eye; cells in group 2–4 were binocular, those in group 2 favoring the contralateral eye, in group 4 the ipsilateral eye; in group 3 the influence was about equal.

been classed as group 1 when in fact access to the ipsilateral eye was occluded due to eye retraction. In this histogram a cell was only included in group 1 if its receptive field projected clearly within the geometrically determined binocular visual field or, when it projected near the borders, only if it was preceded or followed in the same penetration by cells or background noise which showed some influence through the ipsilateral eye.

It was surprising, in view of the predominance of crossed fibers in mouse optic tracts (90%: Valverde, '68; 96%: Grafstein, '71), to find that more than one third of the part of striate cortex recorded from receives binocular input and that 73% of the cells in this area could be driven through the ipsilateral eye. The two receptive fields of a binocular cell, in each eye, always belonged to the same field type, but there could be minor discrepancies besides the difference in strength of input. Figure 8 shows polar plots of two binocular cells, a simple and a complex cell recorded through each eye separately. For each cell the two preferred directions are not identical, but are slightly rotated against each other, probably because of rotation of the eyes in the equatorial planes (the two cells are from different animals). For the simple cell (fig. 8A) the optimal direction of movement was diametrically opposite through both eyes, a phenomenon that was only seen once. On-center cells sometimes had a stronger center through one eye and a relatively more prominent off-surround through the other eye. Fast cells frequently followed a higher speed of movement when driven through the dominating eye than through the other eye.

Map of the visual field projected onto the cortex

Figure 9 gives a map of area 17 and shows the position of the two adjoining areas, called 18 and 18a in analogy to the terminology introduced by Krieg ('46) for the rat. As it was not possible with single unit recordings to obtain a complete map in one animal, the topology of the visual field projection was constructed from about 350 points recorded in 31 mice. The points represent the geometric centers of fields of single cells and some unit clusters. There was always some variation in the stereotaxic zero mark, probably due to slight variations in brain size. The positions recorded from each mouse were therefore assumed to be consistent only within themselves, and the coordinates from each experiment were transferred to an average normal map using the positions of the optic disc and spatial coordinates of receptive fields. Since in any given perpendicular penetration there was a considerable scatter of receptive field positions (up to $\pm 15°$), the mean center of all the fields of one penetration was taken; if only one cell was recorded, its position was considered as less representative than the average of many. In addition, eye movements could never be ruled out. Because of these technical restrictions the map shown in figure 9 is to be regarded as an average, with a possibility that some details may have been smoothed out. Since the visual field is a sector of a sphere its

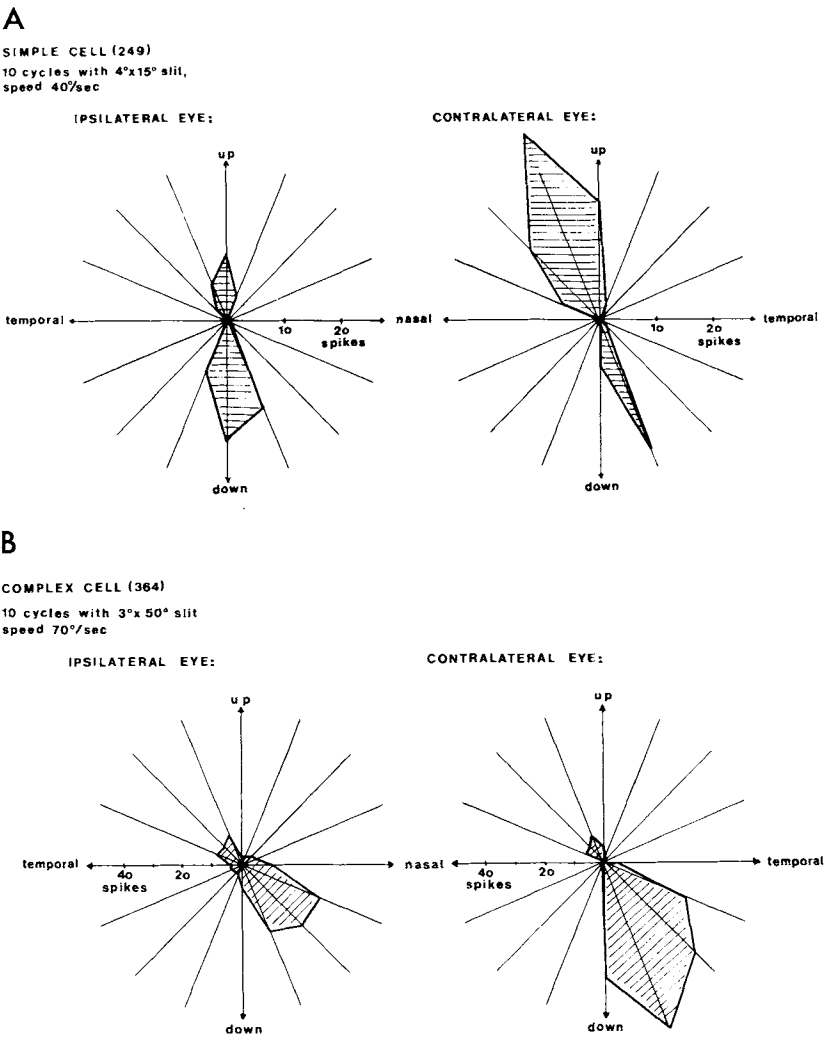

Fig. 8 Polar plots of two binocular cells, a simple cell (A.) and a complex cell (B.); each eye stimulated separately. For each cell, the two polar histograms are slightly rotated against each other, probably due to eye rotation.

projection on a two-dimensional plane has to be specified: the lines drawn in the cortical map represent the projections of the horizontal and vertical lines tangent to circles concentric about the point on the screen closest to the mouse eye.

In the mouse, as in other mammals such as cat, rabbit and rat, the upper visual field is represented in the anterior part of area 17, the lower field in the posterior parts, and the most temporal visual field projects medially. The vertical midline is represented laterally in area 17, running slightly obliquely from posterior and lateral to anterior and medial. But here, at the lateral border of area 17 in the mouse, the visual field representation did not stop at the projection of the vertical meridian, but the geometric centers of receptive fields progressed for at least 10° into the ipsilateral hemifield of vision before the topography reversed in area 18a (see below). The vertical midline was defined as the projection of the long body axis of the mouse corrected for squint: in the recording situation all mice had a divergent

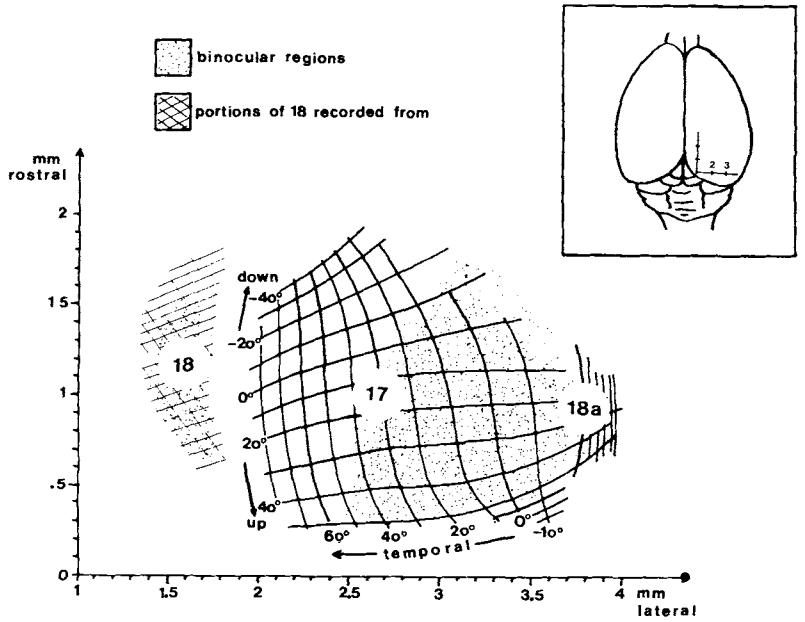

Fig. 9 Topographic map of visual field representation in area 17. Position of the axes, relative to the brain, are indicated in the inset. The positions of the adjoining areas 18 and 18a are merely indicated.

squint as shown by the fact that receptive fields of binocular cells were always separated horizontally by about 5–20°. It was assumed that this divergent strabismus was symmetric.

The magnification in area 17 was rather uniform throughout the visual field. Although there might have been a slight tendency for the smallest receptive fields to occur in the anterior field of vision, there was no statistically significant correlation between receptive field size and eccentricity.

Area 18a

The position of area 18a can only be hinted at in this map, because as far lateral as this the cortex slopes down, and the map was not corrected for surface curvature. When the electrode moved laterally, starting in area 17, fields moved slowly to the vertical midline and probably beyond it into the ipsilateral visual field for at least 10°, as mentioned above; they then rather rapidly moved out again into the temporal (contralateral) field of vision, as is shown in the upper graph of figure 10. Area 18a thus seems to be arranged in a representation that is a condensed mirror image of the area 17 projection. This area is presumably the analogue of areas 18 in cat and monkey. Plate 1 shows an oblique penetration crossing the 17/18a border from medial to lateral. The middle lesion, in layer V, marks the point where the topography started to reverse. In the cytoarchitectonic atlas of Rose ('29), who did not distinguish a lateral visual area, the 17/18a border is described as the transition from striate cortex to ectorhinal cortex.

Area 18

As an electrode moved medially within area 17 the receptive fields moved out progressively to the temporal field periphery. Fields of enormous size could then be recorded, enclosing a large area of the temporal periphery and sometimes extending anteriorly almost up to the midline. Still more medially, successively recorded fields became progressively smaller and moved medially, until they again occupied the midline. Here there were many binocular cells, just as in the binocular part of area 17 and 18a. The lower graph of figure 10 demonstrates a series of vertical electrode tracks at successively more me-

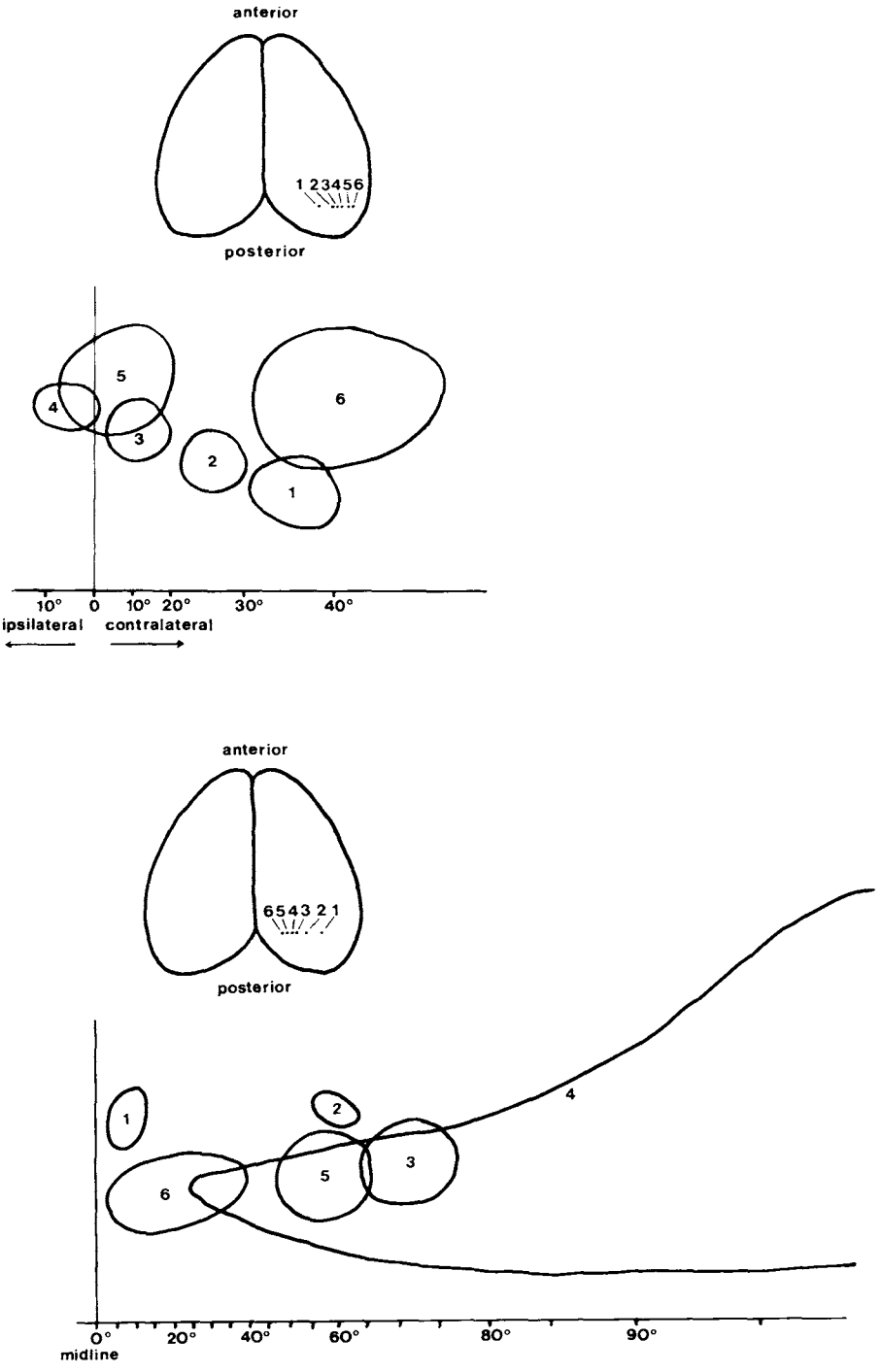

Fig. 10 Upper part: Receptive field positions, as mapped on the tangent screen, corresponding to six successive penetrations made in the same coronal plane, progressing mediolaterally from area 17 into area 18a. Origin represents a point 30° below the intersection of the animal's long axis with the screen. Lower part: Six penetrations moving from area 17 into area 18.

dial positions in the visual cortex. The hatched area in figure 9 includes sites where visually driven cells in a reversed topology have been recorded; not enough data were collected in area 18 to construct a map of it. Histologic lesions in this medial area seemed to be located in the region named peristriate cortex by Rose. The exact border between this area and area 17 was difficult to determine histologically.

DISCUSSION

Cells in mouse striate cortex were found to be of two main general types, those with and those without orientation-specific responses. All three types of oriented receptive fields, simple, complex and hypercomplex, are described as occurring in the visual cortex of every mammalian species so far studied, e.g., the cat (Hubel and Wiesel, '62), monkey (Hubel and Wiesel, '68), rabbit (Chow et al., '71), tree shrew (Kaufman et al., '73), and opossum (Rocha-Miranda et al., '73). Oriented cells in the mouse have a similar field structure and their response to moving stimuli can be as sharply tuned as in the cat or monkey. As for other species, mouse cortical cells react poorly or not at all to changes in overall illumination.

Non-oriented cells are reported to be absent or rare in the cat (Baumgartner et al., '65), and in the rhesus monkey they are probably confined to layer IV. In the rabbit, tree shrew and opossum, however, they constitute a considerable portion of striate cortical neurons. All non-oriented receptive fields described in cat and monkey visual cortex have a concentric center-surround organization. In the rabbit, besides finding concentric center-surround fields, Chow et al. ('71) have described two non-oriented field types without a surround: "uniform cells" and "movement selective cells." In the mouse these classes seem to correspond to the third non-oriented field type, "fast cells" with homogeneous on-off fields. These cells responded to a moving stimulus or contrast everywhere within their field and may perhaps therefore be regarded as a non-oriented analogue to the complex cells. Many of these cells required or were most easily driven by very fast moving stimuli. Like the "movement selective cells" of Chow et al., these mouse "fast cells" form a rather heterogeneous group: some were rather specific for a certain stimulus speed; others followed over a very wide range of velocities; some showed brisk on-off responses to flashed light spots; in others the on-off receptive field structure was hard to demonstrate, responses occurring almost exclusively to movement.

Receptive field organization of cortical neurons in the mouse does not seem to be basically different from that of other mammals. The way receptive fields are built up in mammalian visual cortex may indeed be universal. Perhaps the most striking difference between cat or monkey and mouse striate cortex cells, besides the much larger size of receptive fields in the mouse, was the requirement of much higher stimulus velocities. While this may reflect some difference in cortical organization, it may on the other hand merely be a reflection of the difference in the size of the eyes. The mouse eye has a very strong, almost spheric lens that projects the image of the outer world on a very reduced scale on the retina (about 7 times smaller compared to the cat retina). Thus the image of a stimulus moving with a given speed over the screen travels over a much greater distance in absolute terms in the cat retina compared to the mouse retina. If one cell is wired up so that it is optimally excited when points a given distance apart on the retina are stimulated with a certain time delay, then the optimal stimulus speed should be much higher for the mouse.

In cat or monkey striate cortex no angle of receptive field orientation occurs more often than others, but in the rabbit the orientations of simple cells are reported to run predominantly parallel to the visual streak (Chow et al., '71). The histogram of preferred directions of movement of mouse striate cortex cells (fig. 5) shows a mild but clear preference for vertical movements, horizontally oriented cells being more frequent than others. Histologically the mouse retina is described as not having any central area or streak-like structure (e.g., Chievitz, 1891).

The topologic projection of the visual field onto the primary visual cortex is similar to the known projection in other mammals, with the upper visual field represented posteriorly and the visual midline projecting most laterally within area 17 (Thompson et al., '50; Daniel and Whit-

teridge, '61; Bilge et al., '67; Adams and Forrester, '68; Kaas et al., '70; Hall et al., '71; Allman and Kaas, '71; Kass et al., '72). Lateral to area 17 lies an area homologous to area 18 in cat and monkey, which is organized in a condensed mirror image fashion relative to the area 17 projection. In analogy to the terminology introduced for the rat by Krieg ('46), this area is usually referred to as area 18a. On the medial side of area 17 some recordings were made in a third visual area, which was also organized in a mirror image fashion relative to the area 17 projection: as one moved medially within this area receptive fields moved back from the peripheral temporal field of vision to the midline, where most recorded receptive fields were binocular. This area was described by Rose ('29) as peristriate cortex and is now usually referred to as area 18 (e.g., Valverde and Esteban, '68). In his evoked potential study of mouse cerebral cortex, T. A. Woolsey ('67) reported that there might have been two foci of visually evoked potentials. Recently in the cat Kalia and Whitteridge ('73) have described an area located medial to area 17 in the splenial sulcus. This area is probably analogous to mouse area 18.

One peculiar finding in the mouse cortical projection was made at the border between area 17 and 18a: the geometric centers of receptive fields progressed for at least 10° into the ipsilateral hemifield of vision, so that at least 20° of visual field (or 500 μ on the retinae) are represented in both cerebral hemispheres. In the cat the naso-temporal overlap of the optic tract, and presumably also of the cortical input, is only 0.9° (Stone, '66), in the monkey about 1° (Stone et al., '73).

Another surprising finding was the large extent of the binocular cortical area. More than one third of the cortical area recorded from received input from both eyes, and more than 70% of the cells in this area could be influenced through the ipsilateral eye (fig. 7). Using silver degeneration methods, Valverde ('68) reported 10% of uncrossed fibers in the optic tracts. Grafstein ('71) found after injection of tritiated amino acids in one eye that the radioactivity in the ipsilateral optic tract was only 4% of the radioactivity in the contralateral tract. These few uncrossed fibers have to subserve a rather large field of vision: about one-third of the visual field looked at through one mouse eye is viewed simultaneously by the other eye, i.e., about one-third of retinal area projects to binocular area in the visual cortex. It may be that most of the cortical input through the ipsilateral eye is mediated via the corpus callosum, but in the rat sectioning of the corpus callosum is reported to have little effect on the evoked responses in the binocular area (Adams and Forrester, '68). An additional explanation would be to assume that most ipsilateral fibers in the optic tract project to the lateral geniculate body and avoid the superior colliculus; this would increase the percentage of ipsilateral fibers projecting to the cortex.

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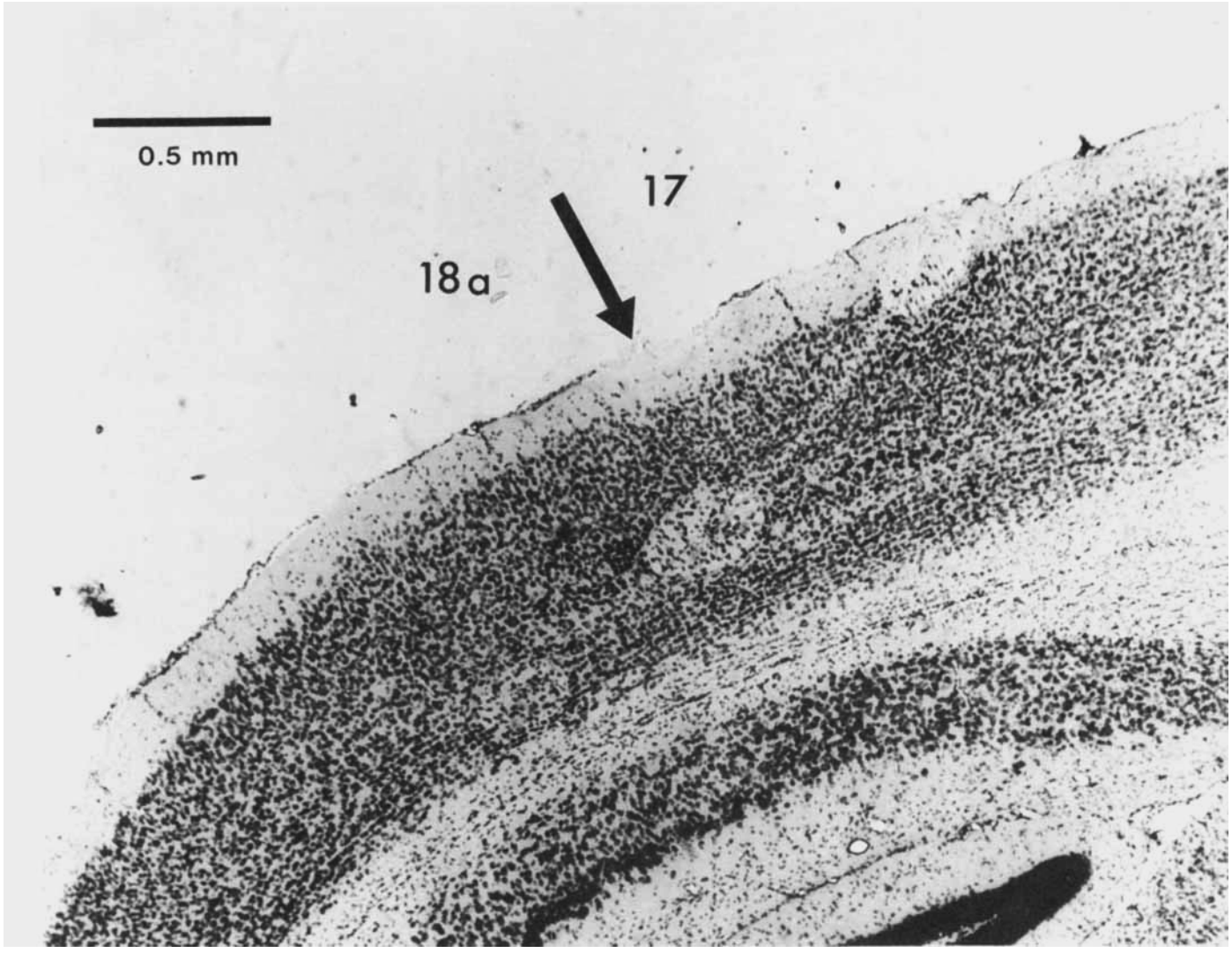
PLATE 1

EXPLANATION OF FIGURE

Coronal section through striate cortex, showing oblique penetration beginning in area 17 and crossing over into area 18a. Three lesions were made during the penetration. The middle lesion, in layer V, marks the point of reversal of the topographic representation. Nissl stain.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18a