*Journée du 4 juillet 1969*

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*Deuxième séance*

# INFORMATION ET SYSTÈMES BIOLOGIQUES

## III - STOCKAGE DE L'INFORMATION DANS LES SYSTÈMES NERVEUX

PRESIDENT J. Z. YOUNG

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*De la Physique théorique à la Biologie, C.N.R.S., 1971.*

# INTRODUCTION

J.Z. YOUNG

Our topic is called "Information storage in the nervous system" and I would like to call your attention to the ambiguity of our title. I think it is something that all of us, physicists, chemists, biologists and mathematicians can well discuss together. Words like "information" and "storage" are far from clear. I do not propose now to proceed to try to define them but I think it should be in our minds, that this is part of the area in which we could all perhaps contribute to understanding of nervous systems and others. I would like however to say a few words about the third part of our title "Information storage in the nervous system", because that is my particular subject. As Kandel says, the nervous system is a genetically programed system, pre-programed to take some appropriate action. I think we have been in some danger of forgetting this in the abstractions of talking about associative memory and other matters, we've tended to forget the nervous system as an adaptive device, pre-programed by its DNA, of course, to produce adaptive reactions. It's a multichannel system, as we've been often reminded of although one sometimes tends to forget it and to forget the problem which it brings to the theoretician. We are so used to talking about simple, single channel systems — computers and the like, where there are few processors of information and the information is passed along a small number of channels — that to think about a system which has this very large number of channels is a challenge that I think we have not always met in our discussions. There will be a divergence of opinion, today as to the encoding system of the nervous system. I think that some of you who are not biologists should realize that the points of view this afternoon will differ. My own view is that we can say rather firmly that the nervous system encodes by putting information about separate events into distinct channels. Certainly one of our speakers this afternoon will take an opposite view. But it is a very important difference from the encoding system with which perhaps you are more familiar. In the nervous system the mechanism of encoding is in general to put each item of information into a separate channel. It may seem a fantastically inefficient, indeed an absurd way, of proceeding, if you think about it. Nevertheless, at least in a large part, this seems to be the way the nervous system operates.

Now as to the memory, the memory also is a pre-programed part of the nervous system, programed by its DNA, to select between possible alternate actions those which are most appropriate in the light of past events. Therefore we have always to bear in mind the fact that the nervous system is informed not only by the outside world, but also by its own internal receptors (I don't think they've been mentioned yet : receptors for taste, for example, or for pain) which tell it what have been the results of the actions that have taken place in the past. This is a form of association, which is perhaps the most important for the nervous system, to associate an event with its results and to act appropriately in the future. In this way the nervous system builds what we can call a model of the events in the environment that are likely to happen and what their consequences are likely to be and hence can forecast and produce appropriate action in the future. I make no apology for this teleological formulation, which of course is quite commonplace in biology, I think we are all able to use these words without *arrière-pensée* now.

Finally, each species has its own type of memory system. Again a point we must remember : the organism does not always remember everything. It remembers only that which is relevant to its own particular form of life. Our own memory is so complex as is that of mammals with which we shall mostly be dealing this afternoon, that it is very salutory to be reminded of simpler forms of memory such as Dr. Kandel's beautiful example this morning. And we shall hear further about the memory of goldfishes and I may have a moment or two to say a word about octopuses — just to remind us that these are special purpose memories, each tailored to do a particular job for the animal. It's rather amusing for you to know that many of you have been walking on some highly programed memory systems if you've been to see the Palace of Versailles ! I wonder if any of you noticed — perhaps Dr. Maynard Smith did — the diggerwasps all over the courtyard here in front of the palace. There are thousands upon thousands of diggerwasps there, with their nests between the stones. Each of those wasps must remember the appearance of its hole, to which it brings back grubs, to feed the offspring which will presently emerge. If you wished to, you could study that particular memory system. I don't suppose it can remember much, but it must remember its particular hole and distinguish it from the holes made by all the other wasps there. Now with that diversion may I call upon Dr. Morrell.

*De la Physique théorique à la Biologie, C.N.R.S., 1971.*

# NEURONAL INTEGRATIONS IN VISION

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## Introduction

When a cat learns to associate a click with a light or a touch with a particular visual stimulus or discriminates one kind of visual stimulus from another, as judged by appropriate quantitative behavioral tests, we assume that there has occurred in the cat's nervous system an alteration in the relationship between, for instance, the auditory and visual systems or the visual and somatosensory systems, as the case may be. The present research is aimed at discovering the mechanisms of such a change in relationships.

It has now been clearly established that there are at least two stages, and probably many more, of information storage in the nervous system. Short-term memory in the range of 20-30 minutes is apparently subserved by electrical activity in nerve cells. It may be abolished by any intervention, i.e. electroconvulsive shock, concussion, deep anesthesia, etc., which interferes with the electrical activity of the brain. In contrast, long-term or permanent memory is resistant or impervious to all the interventions which suppress electrical activity. The development of the permanent stage is dependent upon the prior occurrence of the electrically sensitive stage. Thus, if electrical activity is blocked within a few minutes after exposure to a stimulus, all memory of that stimulus is erased. However, if electrical activity is allowed to continue normally for 15-20 minutes after stimulation and then blocked, subsequent testing reveals that memory for that particular event is quite preserved (Bures and Buresova, 1963; Deutsch, 1962; Gerard, 1961; John, 1961, 1967a, 1967b; McGaugh and Petrinovich, 1965; Morrell, 1961a, 1961b, 1963; Morrell and Naitoh, 1962; Russell and Ochs, 1963).

Our studies are concerned exclusively with the analysis of the neural mechanisms involved in short-term storage of information.

The mammalian visual system is especially well suited to an analysis of sensory coding. The elementary details of stage by stage connectivity have been extensively studied (Clare and Bishop, 1954; Doty, 1958; Hubel and Wiesel, 1959, 1961, 1962, 1963; Kuffler, 1953; Otsuka and Hassler, 1962; Polley and

Dirkes, 1963; Polyak, 1927; Talbot and Marshall, 1941; Thompson *et al.*, 1950; Vastola, 1961). An extraordinary degree of order and specificity has been found, not only at the lower levels, but extending into the cortical regions and even beyond the primary receiving area. Single cells have been shown to be extremely selective in their stimulus preferences and the required stimuli are generally quite complex (Barlow and Levick, 1965; Hill, 1966; Hubel and Wiesel, 1963; Lettvin *et al.*, 1959, 1961; McIlwain and Buser, 1968; Sterling and Wickelgren, 1969; Wickelgren and Sterling, 1969; Wurtz, 1969). Furthermore, polysensory interactions at single units have been shown by Jung and his co-workers (1958, 1961, 1963; Baumgarten and Jung, 1952) and Murata *et al.* (1965) to be an extremely pervasive feature of visual physiology.

Visual areas II and III have been described anatomically by Otsaka and Hassler (1962) and by Hubel and Wiesel (1965) as the zone immediately anterior and lateral to the primary visual area or striate cortex. These authors consider these areas homologous with areas 18 and 19 of Brodmann or parastriate cortex in man. Hubel and Wiesel (1965) have reported physiological observations on these cells which indicate highly complex receptive field organizations and highly selective stimulus preferences. In particular, these cells respond best to appropriately oriented lines, bars, edges or contours. We have confirmed these observations in detail. In addition, however, we have examined : a) the detailed microstructure of the cellular response pattern; b) sensitivity to non-visual modalities of sensation; c) the specificity of non-visual interactions; and d) modifiability of response pattern as a consequence of " prior experience ". " Prior experience " is herein defined as simultaneous presentation of two different stimuli, each of which, individually, elicited different response patterns.

The experimental preparation was the curarized, unanesthetized cat. Before the experiment, a sterile operative procedure was performed for implantation of a nylon receptacle which could be opened when desired for insertion of the microelectrode. At the same time, the animals were fitted with a cap of dental cement especially molded to receive the ear bars of the stereotaxic instrument. The arrangement was a modification of the " semichronic " technique of Hayward *et al.* (1964) described by Lindsley, Chow and Gollander (1967). Animals were immobilized with Flaxedil and artifically respired. Pupils were dilated with 0.5 % atropine and contact lenses were fitted to each eye. The " semichronic " technique (Hayward *et al.*, 1964; Lindsley *et al.*, 1967) permits rigid fixation of the head and eyes without any pressure upon the animal. Tungsten microelectrodes were used for extracellular single unit recording (Hubel, 1957).

All stimuli were 50 msec. in duration. Visual stimuli were projected on a screen 30 cm. distant from the eyes and could be delivered to each eye separately. Acoustic stimuli were 10 msec. clicks repeated for 50 msec. Tactile stimuli

were 10 msec. electric shocks lasting 50 msec. to the contralateral hind limb. Vestibular stimuli were produced by D.C. polarization of the labyrinth (anodal or cathodal) of 0.05 mamps through a Ag-AgCl electrode at the round window (Jung, 1963).

The interstimulus interval was randomly varied around a mean of 22.5 sec.

Data analysis was accomplished by playing tape recorded electrical activity through a LINC computer programmed to compute and display PST histograms (bin width manually selectable) out to 250 msec. after stimulus onset or 300 msec. after a prepulse placed on tape 50 msec. before stimulus onset.

The general plan of the experiment was as follows : For each cell encountered, the visual field was scanned manually with a 2 mm lighted baton or torch, much in the manner used in the clinical ophthalmological examination. All quadrants of gaze were covered. The response looked for was a change in the spontaneous discharge of the monitored cell. Such change could, of course, be excitatory or inhibitory (or both, one occurring after the other). In practice, it was easier to define a response where an excitatory component predominated. The excitatory portion of the receptive field was then carefully plotted and, in most cases, the inhibitory surround was also measured. Thereafter, the configuration of the target (now presented only within the excitatory receptive field) was changed repeatedly until one was found which gave the most vigorous discharge. That target was then selected as the optimum or " preferred " visual stimulus for the cell in question. Immediately following the determination of optimal visual stimulus, the cell's responsiveness to acoustic, tactile and vestibular input was examined. Out of the total of 890, 871 visually excitable cells also responded to one of the other three modalities of sensation. Very few cells responded to more than one non-visual modality; a few were trisensory in the sense of Buser and Bignall (1967), Buser and Imbert (1961) and Imbert *et al.* (1966) and of Jung (1961, 1963), Kornhuber and DaFonseca (1964) and Murata *et al.* (1965).

The receptive fields identified confirm quite precisely those measurements already published by Hubel and Wiesel (1965). The " preferred " stimulus configuration was extremely complex (yet still simple when compared to real life) consisting of edges, bars or lines of various lengths and orientation. When the optimal stimulus was used, mean cellular responses were quite stable (as measured by PST histograms of sums of 20 trials) even though there was obvious trial-to-trial variability and scatter of " latencies " and sometimes omission of some components.

Figure 1 illustrates the first 12 trials of the total of 20 used to compute the histogram shown in the lower half of the figure. There are obviously two bursts of activity evident when the tracings are displayed this way, i.e. looked at simultaneously, and, of course, two peaks in the histogram. Note, however, that if the tracings were examined individually, the second burst might not be

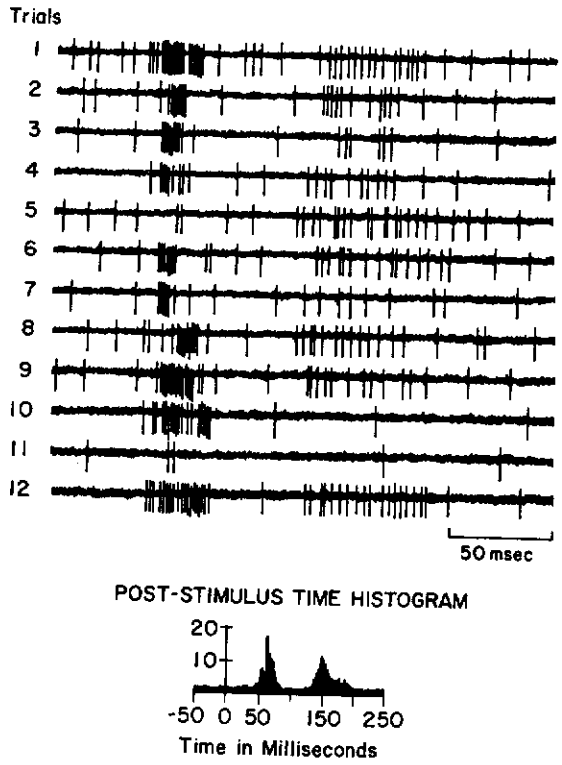


Fig. 1. Single unit extracellular records of the first successive 12 trials of the 20 trials which were summed to compute the PST histogram shown at the bottom of the figure. Each trial (250 msec segment of record triggered by stimulus onset) was displayed on a Tektronix 564 storage oscilloscope with the beam stepped down after each trace. When arrayed in this manner, i.e.: one above the other, it was obvious that there were two bursts of activity distinguishable from the relatively high rate of background spiking and these were reflected in the two peaks of the PST histogram. The different organization of each burst was also reflected by differences in amplitude and slope of the two histogram peaks. The portion of the histogram labeled — 50 msec to 0 represents unstimulated activity; the computation in this case having been initiated by the pre-pulse. It is important to note that if the single traces had been examined individually, the second burst might not be detected on trials 3, 7 and 10. On trial 5, the early burst failed to occur and on trial 11 there was no evidence at all of stimulus related discharge. Thus, in 5 out of the first 12 occasions the full pattern failed to appear. Binwidth equals 5 msec in this and all other illustrations in this paper. The calibration bar (the abscissa) at time zero equals 20 spikes in this and other figures unless separately specified. The cellular activity shown was this cell's response to its " preferred " visual stimulus. The latter was an obliquely oriented light slit in the right upper quadrant of gaze extending from 10° to 13° lateral to the vertical meridian. The excitatory visual receptive field is illustrated by the cross-hatched area in Figs. 9 and 10. Stimulus duration in this and all other figures was 50 msec.

detected in trials 3, 7 and 10; on trial 5 the early burst was undetectable and in trial 11 neither burst occurred. Each oscilloscope sweep was triggered by stimulus onset. The portion of the histogram labeled —50 msec. to 0 msec. represents " spontaneous " unstimulated activity, the computation in this instance having been initiated by the prepulse.

The PST histogram has the virtue of preserving the true time course of events (in contrast to the interval histogram) and, most important, preserves the trial-to-trial variability (in contrast to an " average " measurement).

When a stable response to a non-visual modality was discovered (or in a few cases a second visual but non-preferred stimulus configuration), the preferred stimulus was paired, i.e. presented simultaneously over the 50 msec. stimulus duration for 40 trials. These paired trials are what we herein define as " prior experience ". After the paired trials, the preferred visual stimulus was presented alone (testing for modification of response pattern). In most neurons (769), there was no effect on the post-pairing firing pattern, i.e. the " preferred " visual stimulus elicited a response virtually identical with that which occurred on initial presentation.

Thus, in the experiment illustrated by Fig. 2, the preferred visual stimulus evoked the discharge pattern summed in 20 trial blocks (1-20 and 21-40 of Fig. 2). Vestibular stimulation (Fig. 2, trials 41-60 and 61-80) yielded an entirely different pattern. Concomitant presentation of visual and vestibular stimulation (Fig. 2, trials 81-100 and 101-120) resulted in a third and quite distinctive histogram pattern. Nevertheless, upon retesting with the preferred visual stimulus, we obtained (Fig. 2, trials 121-140) exactly the same pattern originally elicited by that stimulus. Several reinterpolations of paired stimulation failed to induce a change in the cells' response pattern to visual or vestibular stimulation when the latter were presented alone. When such stability was encountered, as many reinterpolations of combined stimuli as were possible were attempted as time and the preparation would allow. In no single case was such " reinforcement " successful in eliciting modification; i.e. if modification was not evident after the first paired trials, it never occurred.

However, in 102 cells relatively striking and reliable changes in response pattern did occur after the initial pairing. All cells exhibiting response modification exhibited the alteration during the first testing sequence. Thus, there was no ambiguity about which cells would and which would not exhibit the change. More specifically, in these modifiable cells the histogram yielded by the testing stimulus alone resembled that elaborated by combined stimulation more than it did the control histogram for " preferred " stimuli upon initial presentation. Thus, there was a clear distinction, under the conditions of our experiment, of two separate populations : a majority of cells could be classified as extraordinarily stable cells reporting faithfully the stimulus configuration regardless of past history; and a smaller population, equally distinct, in which response

histograms were influenced by a specific past history. The degree of specificity will be illustrated below.

## A prototypical example of modifiability

Figure 3 illustrates a prototypical example of response modification. This cell (64-128) was preferentially activated by a diagonal line of light at about

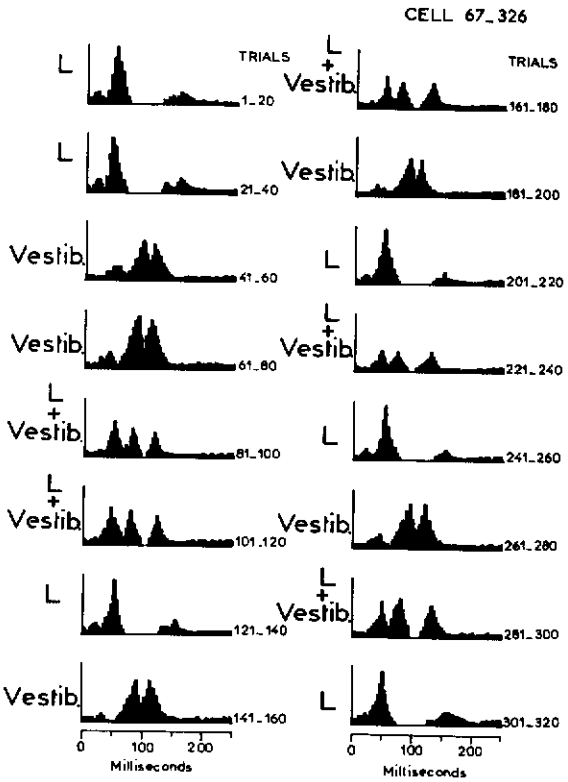


Fig. 2. Typical responses in a polymodal but non-modifiable neuron. Visual stimulation yielded a response configuration consisting of a sharp early peak, an inhibitory interval and very small late activity peaking about 150 msec after stimulus onset. Notations to the left of the histograms indicate the type of stimulation; trial numbers are listed to the right. The sequence of events should be read from the top to bottom on the left and then top to bottom on the right. This cell was typical in that it responded differently to visual (L) and non-visual (Vestib.) modalities and with a third pattern when the two (L + Vestib.) were combined. But the experience of paired stimulation had no effect on patterns subsequently elicited by either L or Vestib. alone. Visual stimulus was an obliquely oriented light slit in the left lower quadrant of gaze. Intensity of slit: 2.3 $\log_{10}$ cd/m$^2$; background: 0.03 $\log_{10}$ cd/m$^2$. Vestibular stimulus was a cathodal DC current 0.05 mA at the round window of the left ear. Its duration was 50 msec as with all other stimuli. Depth of the cell was 900 $\mu$.

six degrees to the left of the vertical meridian. When so stimulated twenty times, the spike train summation yielded the uppermost histogram in Fig. 3. The single trace above the histogram was the response to the preferred stimulus which was most typical of the sum of twenty used to compute the histogram.

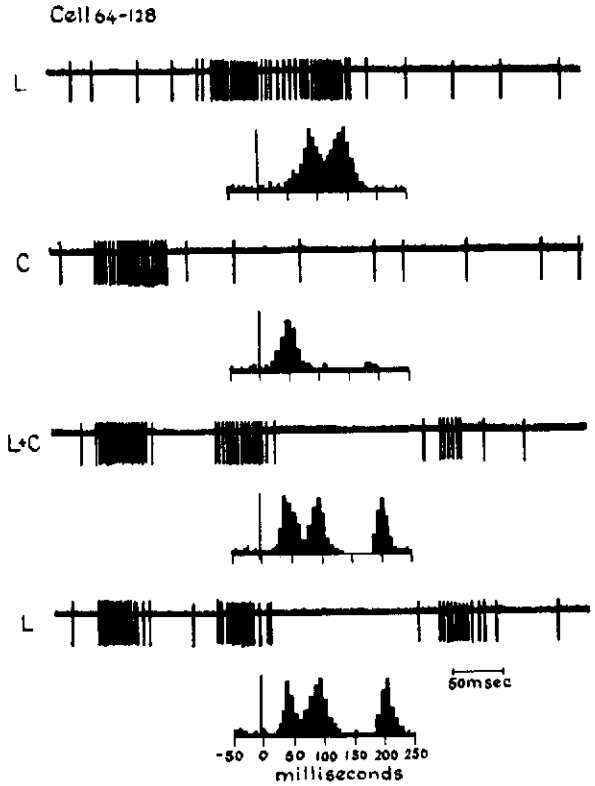


Fig. 3. A prototypical example of modifiability. This cell was encountered at a depth of 540 μ. It was preferentially activated by a diagonal line of light at about six degrees to the left of the vertical meridian. Intensity of the light: 1.8 $\log_{10}$ cd/m$^2$; background: 0.03 $\log_{10}$ cd/m$^2$. Above each histogram is shown the original record of a single trial (selected as the most representative of the 20 trials used to compute the histogram). Visual stimulation (L) yielded a particular temporal pattern of discharge. Acoustical stimulation (C, 30 db SPL at the cat's ear) resulted in a different pattern of firing having a single peak with a latency even shorter than the response to light. When the two stimuli were delivered simultaneously (L + C) an additional pattern was seen which appeared not to be a simple linear combination of responses to the two single stimuli but rather a total reorganization of firing pattern. After 40 such paired trials, the same visual stimulus as that used initially (L, lower) elicited a response pattern similar to that elicited by the paired stimuli (L + C) and unlike that which the stimulus had provoked on initial exposure (L, upper). The altered response lasted about 30 min, i.e.: time for 3 blocks of 20 trials each and then reverted to the original configuration of the response to light (L, upper).

The histogram had a late bi-phasic peak which is well illustrated in the single response (Fig. 3, L). The second histogram (Fig. 3, C) was the result of acoustic stimulation and had a single peak appearing even earlier than the response to light. When light and click were delivered simultaneously (Fig. 3, L + C), a reorganization of the temporal pattern of discharge took place which contained inhibitory intervals not seen before (especially between peak 2 and 3, Fig. 3, L + C) and which was difficult to regard as a simple summation of the effects of light and sound individually. Again, the single response above the histogram was chosen as that most representative of the sum of twenty used to compute the histograms. Following the paired trials, the preferred visual stimulus was presented alone (Fig. 3, L, fourth trace). The pattern of firing was similar to that elicited by the paired trials and relatively unlike that elicited by the same preferred visual stimulus before the pairing occurred.

**Response modification in " polymodal " cells**

The true time course of these events may be illustrated in Fig. 4. Visual stimulation resulted in a long, slow discharge of the cell, (Fig. 4, trials 1-40). Acoustical stimulation yielded a sharp, early peak (Fig. 4, trials 41-80). Repeated stimulation (Fig. 4, trials 81-100) resulted in a histogram identical with that which occurred on first exposure (Fig. 4, trials 1-40). Thus, the presentation of sound alone (Fig. 4, trials 41-80), or of time itself did not alter the cellular response as manifested in the post stimulus time histogram. Yet when light and sound were presented together (Fig. 4, L + C, trials 101-140) a third histogram type was obtained. Following the paired trials, the light alone elicited a response similar to that resulting from paired stimulation (Fig. 4, trials 141-200). As unreinforced visual stimulation continued (Fig. 4, 201-220), the pattern of discharge became gradually more and more similar to that originally elicited by the visual stimulus (Fig. 4, trials 241-260). However, acoustic stimulation (Fig. 4, trials 221-240) resulted in no change in the temporal discharge pattern (compare Fig. 4, trials 221-240 with trials 41-80) to acoustic stimulation when first applied (Fig. 4, trials 41-80). Since the light-evoked response was then similar to the initial response (compare Fig. 4, trials 1-40 with trials 241-260), a reintroduction of light-click pairing was instituted for twenty trials (Fig. 4, trials 261-280). The result of such reintroduction was the reappearance of the modified response (Fig. 4, trials 281-320) which persisted for as long as the cell was held in view.

**Response modification in the case where the second stimulus elicits no overt response**

Cell 64-196 (Fig. 5) was responsive to illumination of the contralateral eye (Fig. 5, trials 1-40) but not to illumination of the ipsilateral eye (Fig. 5, trials

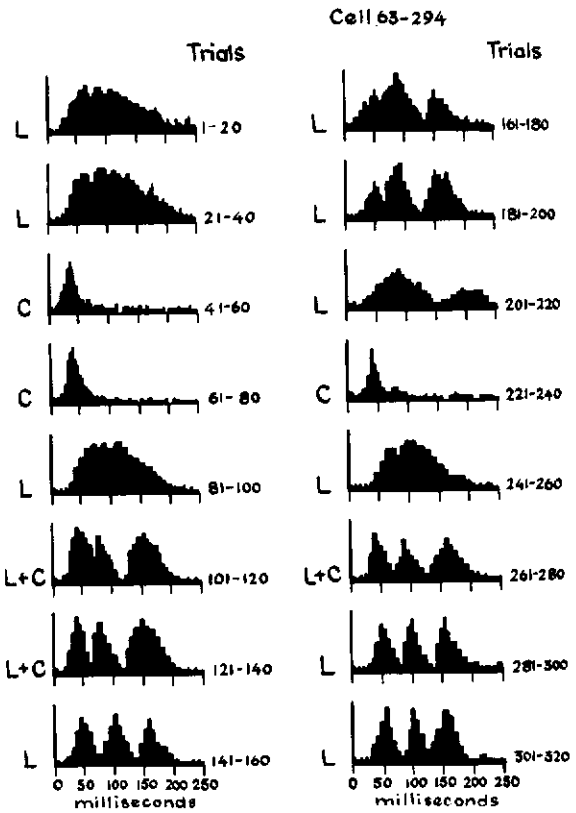


Fig. 4. Response modification in a polymodal cell. " Preferred " visual stimulus (L) for this cell, encountered at a depth of 1 mm, was a light line, light line : 1.5 $\log_{10}$ cd/m$^2$; background : 0.03 $\log_{10}$ cd/m$^2$, oriented from : 2:00 to 8:00 in its receptive field in the left lower quadrant of gaze. Click stimulus (C), 30 db above human auditory threshold in open field conditions, was also effective athough with a different pattern. This figure illustrates the PST histograms obtained throughout the entire course of observation of this cell. L + C indicates " preferred " visual and acoustic stimuli combined. Further explanation in text.
From : Morrell, 1967.

41-80). Yet when both eyes were stimulated (Fig. 5, trials 81-120) the response pattern differed from that attributable to stimulation of either eye individually. Thereafter, for some eighty trials (Fig. 5, trials 121-200) the response to contralateral eye stimulation differed from that obtained originally (Fig. 5, trials 1-40). There was still no response to ipsilateral eye stimulation (Fig. 5, trials 221-240). But after a brief repeated introduction of bilateral stimulation (Fig. 5, trials 261-280), the contralateral eye stimulus yielded, again, a pattern which approximated that resulting from paired stimulation (Fig. 5, trials 281-320).

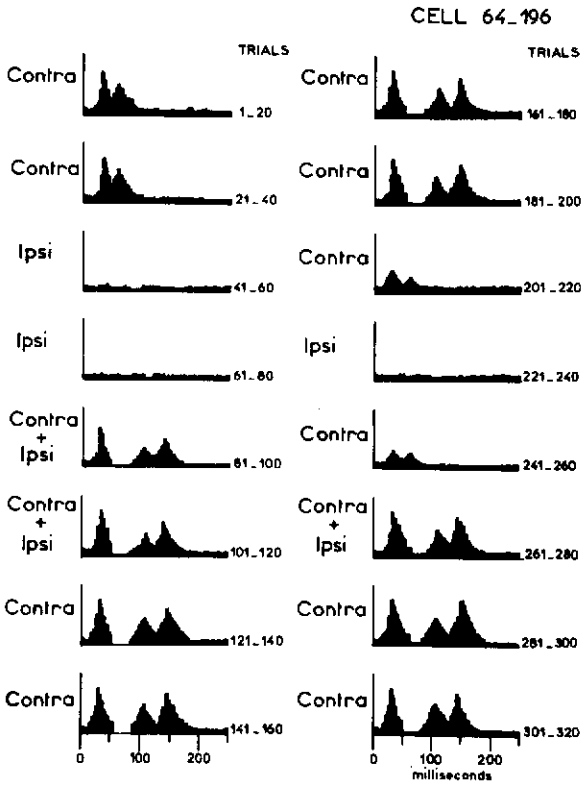


Fig. 5. Response modification in the case where the non-preferred stimulus was ineffective. Cell encountered at depth of 1 mm. Preferred visual stimulus for this cell was a light spot (2.8 $\log_{10}$ cd/m$^2$; background: 0.03 $\log_{10}$ cd/m$^2$) presented to the left or contralateral (contra) eye in the appropriate portion of the receptive field. Stimulation of the corresponding receptive field for the right eye (Ipsi) evoked no response at all. Nevertheless, binocular stimulation (Contra + Ipsi) yielded a different response pattern than had resulted from contralateral eye stimulation originally (Contra, trials 1-40). Following 40 trials of binocular stimulation, the response to stimulation of the contralateral eye alone (Contra, trials 121-200) shifted to the pattern first elicited by binocular stimulation. The alteration lasted 40 min or 4 blocks of 20 trials each before reverting to its original configuration. Further explanation in text.

## Vestibular interaction

The preferred stimulus for cell 66-241 was a light line oriented from 11:00 to 5:00 in its receptive field. The vestibular stimulus was a 0.05 mAmp D.C. pulse, either anodal (A) or cathodal (C), applied to the left semicircular canals. The cell (Fig. 6) responded to the visual and to both types of vestibular stimulation — each with a different pattern. Combining the visual stimulus with vestibular A yielded a fourth histogram type (Fig. 6, trials 61-100). Following the paired presentations, the visual stimulus alone elicited a pattern (Fig. 6,

trials 101-160) closer to that resulting from paired stimulation (Fig. 6, trials 61-100) than to that yielded by visual stimulation alone (Fig. 6, trials 1-20) before pairing. Response to vestibular A alone (Fig. 6, trials 181-200) was unchanged. After some time, the discharge elicited by visual stimulation reverted to its original type (Fig. 6, trials 161-180 and 201-220). However, reintroduction of paired trials (Fig. 6, trials 221-240) restored the capacity of the visual stimulus to provoke a modified response (Fig. 6, trials 241-260 and 281-300).

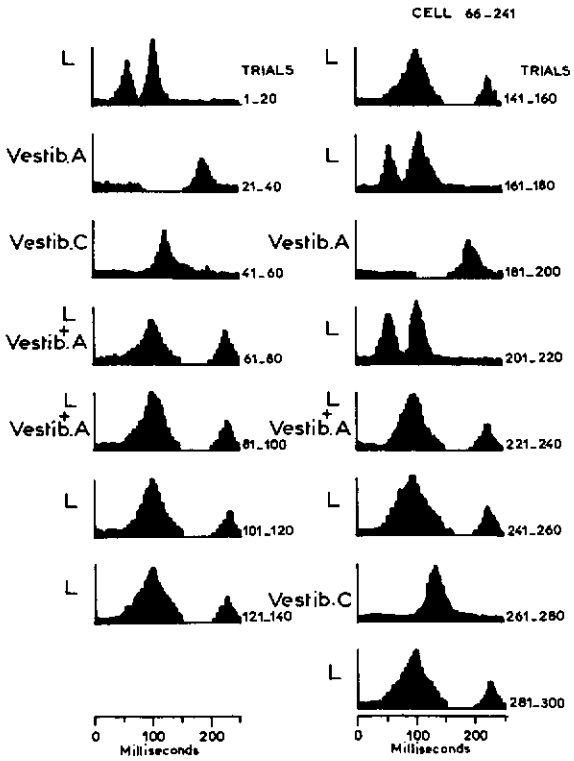


Fig. 6. Vestibular interaction. Cell 66-241 was encountered at a depth of 840 μ. Preferred visual stimulus was a light line oriented from 11:00 to 5:00 in a receptive field in the left upper quadrant. Luminance: 1.5 $\log_{10}$ cd/m$^2$; background, 0.03 $\log_{10}$ cd/m$^2$. Vestibular stimulus was a 0.05 mA D.C. pulse, either anodal (Vestib. A) or cathodal (Vestib. C) applied to the left semicircular canals. The cell responded to the visual (L) and to both types of vestibular stimulation - each with a different pattern. Combining the visual stimulus with Vestib. A resulted in a fourth histogram type. Following the paired presentations (trials 61-100), the visual stimulus alone elicited a pattern closer to that resulting from paired stimuli (trials 101-160) than to that originally evoked by the same visual stimulation. The entire time course of this effect is depicted in the serial PST histograms of this figure.

## Differential specificity

Cell 64-107 (Fig. 7) was encountered at a depth of 1.3 mm below the pial surface. It had an extraordinarily rich response repertoire. There was a different response histogram for each of the following stimuli: a vertical bar (2.8 $\log_{10}$ cd/m$^2$) 6° in length moving from left to right in a dark room (VR-D); the same stimulus moving in the opposite direction (VL-D); the same stimulus

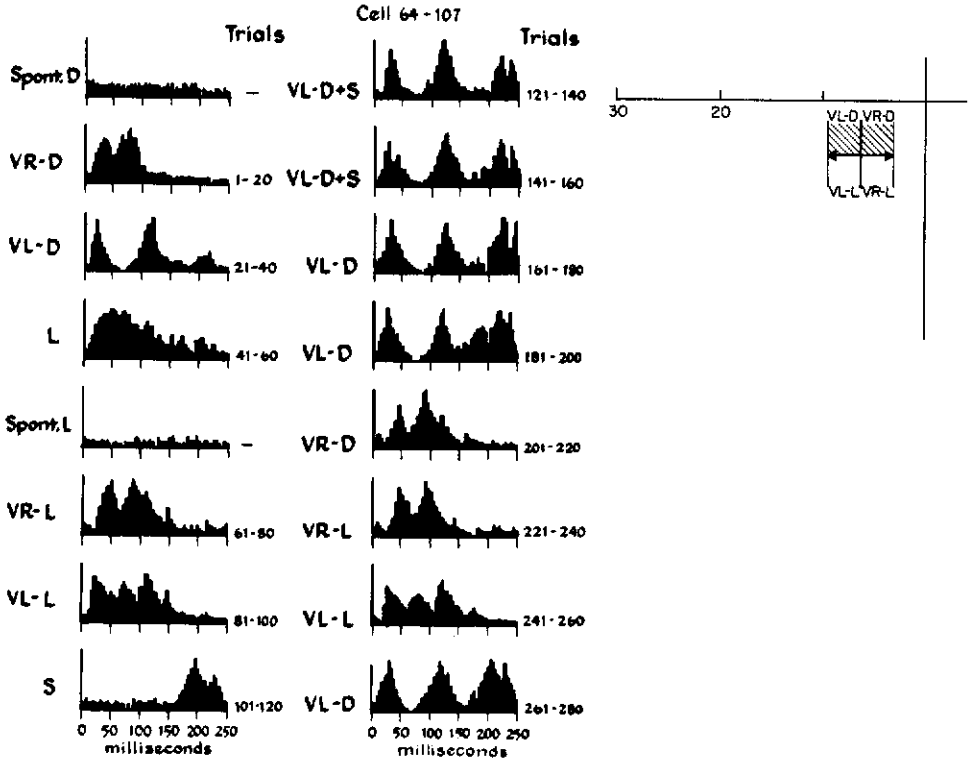


Fig. 7. Differential specificity. Cell 64-107 was encountered at a depth of 1.3 mm. Different response histograms were evoked when the vertical light bar, shown on the diagram to the left, in the receptive field also illustrated, having a luminance of 2.8 $\log_{10}$ cd/m$^2$, was moved to the right with the room lights dimmed (0.01 $\log_{10}$ cd/m$^2$, (VR-D); the same stimulus moving in the opposite direction (VL-D); the same stimulus moving to the right but with the room lights on (1.1 $\log_{10}$ cd/m$^2$) (VR-L); and the same stimulus moving to the left with the room lit (VL-L). The cell also responded simply to diffuse illumination of the room (L) and to an electric shock to the contralateral hindlimb (S). One of these stimulus configurations (VL-D) was paired with shock (S). The others served as controls for specificity. Histograms marked " Spont. L " and " Spont. D " represent sums of randomly chosen, 250 msec segments of record when the cell was unstimulated either in the dark room (D) or with the room lighted (L). See text for further explanation.
Modified from Morrell, 1967.

moving from left to right with the room lights on (1.1 $\log_{10}$ cd/m$^2$), (VR-L); and the same stimulus moving from right to left with the room lights on (VL-L). The cell also responded simply to diffuse illumination of the room (L) and to an electric shock to the contralateral hind limb (S). One of these stimulus configurations (VL-D) was paired with shock (S). The others served as controls for specificity. Histograms labeled " Spont. D " and " Spont. L " represent sums of randomly chosen 250 msec segments of record when the cell was unstimulated either in the dark room (0.01 $\log_{10}$ cd/m$^2$) (D) or with the room lit (L). The receptive field is shown in the diagram to the left in Fig. 7.

Response to paired stimulation (Fig. 7, VL — D + S, trials 121-160) appeared to be a simple summation of the light evoked activity (Fig. 7, VL-D, trials 21-40) and that produced by the shock alone (Fig. 7, S, trials 101-120). Nevertheless, following the paired trials, the VL-D stimulus alone (Fig. 7, trials 161-200) provoked response patterns similar to those elicited by combined stimulation. Thereafter, the response to each of the other three stimulus configurations (VR-D, VL-L and VL-D) could be compared to that obtained before pairing, i.e. in Fig. 7 compare trials 201-220 with trials 1-20; trials 221-240 with trials 61-80; and trials 241-260 with trials 81-100. Finally, the stimulus VL-D was again presented (Fig. 7, trials 261-280) and resulted in a histogram comparable to that of combined stimulation and different from that originally provoked by VL-D (Fig. 7, trials 21-40). In this case the modified pattern persisted for almost sixty minutes, 30 minutes having been employed to test the unreinforced or control stimuli.

Another cell exhibited another form of differential modifiability. It was encountered at a depth of 760 μ. The preferred visual stimulus was a light line (1,8 $\log_{10}$ cd/m$^2$) against a dark background (0.01 $\log_{10}$ cd/m$^2$). However, there were two effective orientations of the line (see diagram, Fig. 8). The orientation which was designated L.A. was within 2° of vertical; the other effective orientation was 5° from the horizontal and was designated L.B. The intermediate positions tested (shown as dotted lines in Fig. 8) did not alter the cellular firing pattern. Stimulus L.A. elicited the histograms shown in Fig. 8) (trials 1-20 and 21-40). Stimulus L. B. gave rise to a quite different temporal pattern of discharge (Fig. 8, trials 41-60 and 61-80) which was characterized by burst activity which had an earlier peak than that caused by L.A. and was followed by a pronounced inhibitory interval lasting 60-75 msec. The cell was also responsive to vestibular stimulation (0.8 mA D.C. applied to the contralateral round window), either anodal (A) (Fig. 8, trials 81-100) or cathodal (C) (Fig. 8, trials 121-160). Following the pairing, stimulus L.A. was applied alone for three groups of 20 trials each (Fig. 8, trials (161-220). A late component, apparently derived from vestibular C (see Fig. 8, trials 101-120) persisted in the patterned response provoked by the L.A. visual stimulus alone. The control visual stimulus, L.B., did not elicit such a change (Fig. 8, trials

221-240 compared with trials 41-80), the response being essentially like that which occurred on first application. Nor was there any change of response to vestibular A (Fig. 8, trials 241-260) or vestibular C (Fig. 8, trials 261-280) when each was presented separately and without combination with light. However, repairing of vestibular C with L.A. (Fig. 8, trials 281-300) again yielded

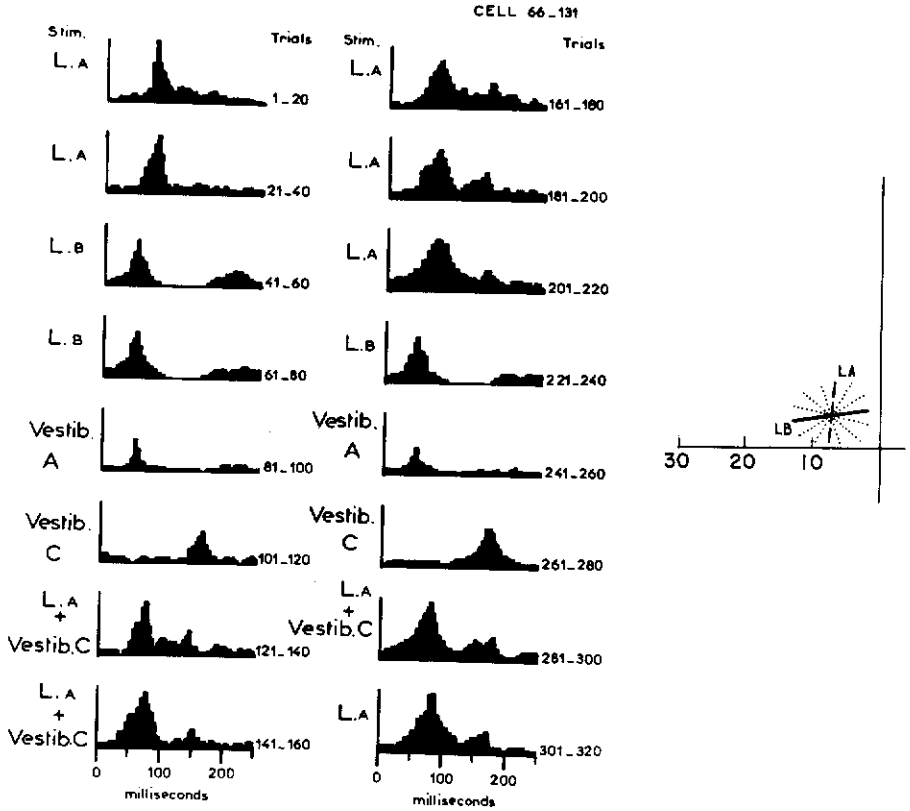


Fig. 8. Further differential specificity. Cell 66-131 was encountered at a depth of 780 μ. Preferred visual stimuli for this cell consisted of light lines (1.8 $\log_{10}$ cd/m$^2$) (background: 0.01 $\log_{10}$ cd/m$^2$). Two orientations L. A (dashed line) and L. B (solid line) were differentially effective while intermediate positions (shown as dotted lines in the diagram) were ineffective. The cell also responded to vestibular stimulation, anodal (Vestib. A) or cathodal (Vestib. C) differentially (0.8 mA D.C. to contralateral round window). Stimulus L. A was paired with Vestib. C (trials 121-160), stimulus L. B serving as a control for specificity. Subsequent testing with L. A alone (trials 161-220) revealed the usual evidence of modifiability. Testing with L. B alone revealed (trials 221-240) no evidence of modified histogram pattern. Furthermore, testing with Vestib. A alone or Vestib. C alone yielded no evidence of change consequent to the pairing experience. Thus, only the response to the visual stimulus which had been combined with stimulation via another modality exhibited a change in cellular discharge pattern.

the modified histogram and the modification persisted for the next set of 20 trials when L.A. was presented alone (Fig. 8, trials 301-320). Here, again, it seems that only the particular visual stimulus that had been combined with the vestibular activation was capable of eliciting the modified response pattern. Vestibular stimulation, either the one which had been combined with light (vestibular C) or the " control " stimulus, (Vestibular A) failed to produce the modified response. The latter was also true of the " control " visual stimulus (L.B.).

**The specificity of non-visual input of visual cells : the dimension of acoustical space**

Most investigators have regarded non-visual input to visual cells as being conducted through pathways, e.g., reticular formation of thalamus and mesencephalon, classically considered to be non-sensory specific (Abrahamian *et al.*, 1963; Bergamini and Bergamasco, 1967; French, 1960; Jasper, 1960, 1961; John, 1961; Kornhuber and Da Fonseca, 1964; Lomo and Mollica, 1962; Machne and Segundo, 1956; Moruzzi and Magoun, 1949; Rose and Lindsley, 1968; Scheibel et al., 1955; Scheibel and Scheibel, 1967; Segundo and Machne, 1956; Skrebitskii and Gapich, 1967, 1968; Steriade, 1970; Thompson *et al.*, 1963a, 1963b). These are pathways in which the quality and sign of the sensation was thought to be essentially lost and the function of such afference to be the modulation of arousal, attention, etc. We, ourselves, regarded the matter in the same way and that is why we chose to use trains of clicks, electric shocks to the hind limb and vestibular polarization as the non-visual stimuli. These were as unspecific as possible while still representing activity of another sensory modality. Moreover, there is no doubt that sleep, wakefulness, or the various stages of sleep (Evarts, 1963, 1967; Hubel, 1959a, 1959b, 1960; Huttenlocher, 1960, 1961; Jouvet, 1967; Wurtz, 1969) as well as administration of barbiturates (Erulkar *et al.*, 1956; Jarcho, 1949; Lömo and Mollica, 1962; McIlwain, 1964, Mountcastle et al., 1963; Murata *et al.*, 1965; Poggio and Mountcastle, 1963; Robertson, 1965; Verzeano *et al.* 1955; Wurtz, 1969) drastically alter the responsiveness of cells at both the lateral geniculate nucleus (LGN) and at the cortical level in a very general way. On the other hand, Spinelli *et al.* (1968) reported that there was tonal or frequency specificity in the acoustical input to striate cells; acoustically driven striate cells each had a " best-frequency " to which it responded and showed relatively little response to other frequencies. This result suggested that rather specialized attributes of the acoustical stimulus were being conveyed to the visual system.

Our own observations on cells of areas 18 and 19 revealed another specific aspect of the acoustical stimulus, namely its location is space. This feature had been ignored in all of our previous studies in which the sound was delivered

from a loudspeaker mounted high on the wall contralateral to the exposed visual cortex. A rearrangement of the equipment resulted in positioning of the loudspeaker on the opposite or ipsilateral wall. In subsequent experiments the effectiveness of the acoustical stimulus dropped precipitously; the only variable

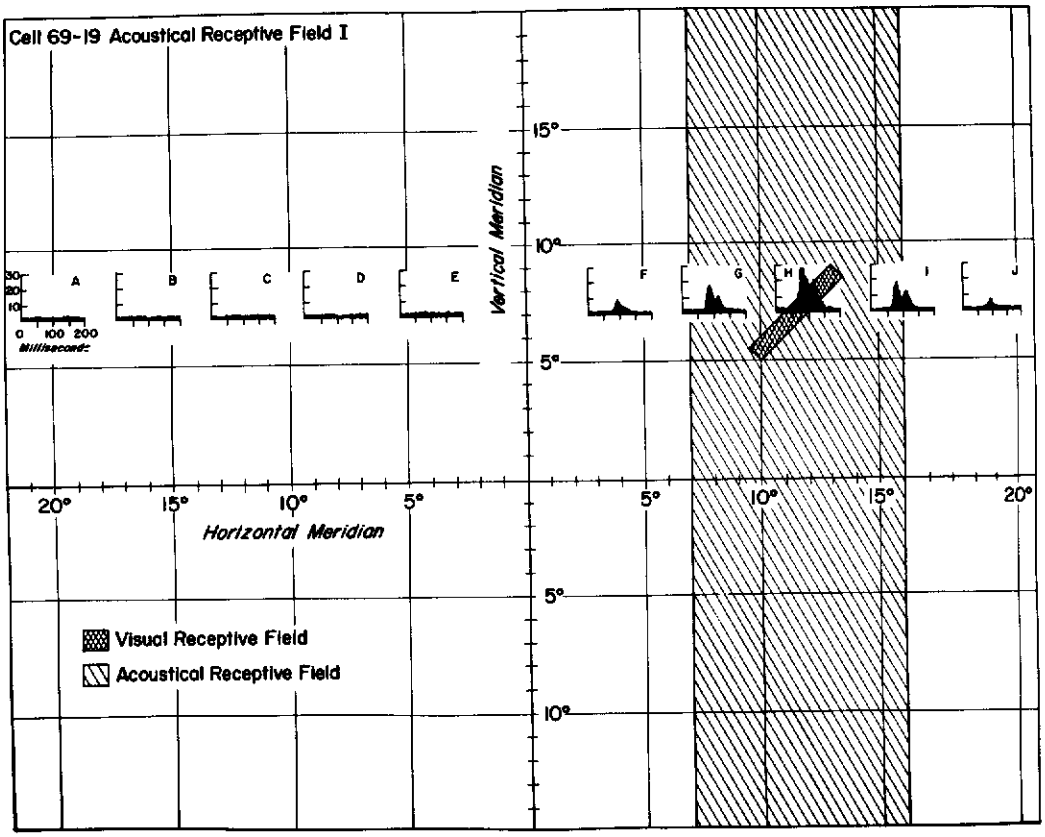


Fig. 9. Visual and acoustical receptive fields superimposed. Horizontal dimension. PST histograms to acoustical stimulation (50 msec train of 10 msec clicks) delivered from small focused loudspeakers mounted on the wall immediately behind the tangent screen on which the visual images were projected. The center of the histogram display corresponds to the site of the sound source as projected on the tangent screen. Thus, the histogram labeled " A " was located 20° to the left; " B " was 16° left; " C " was 12° left; " D " was 8° left, " E " was 4° left; " F " was 4° right; " G " was 8° right; " H " was 12° right; " I " was 16° right; " J " was 20° right. All sites were 7° above the horizontal meridian. Excitatory visual receptive field was an obliquely oriented light line in the right upper quadrant and is indicated by the cross-hatched area. The area marked by diagonal lines represents what we herein call an acoustical receptive field. The PST histograms of acoustical responses in this and the succeeding three figures, i.e.: Figs. 9-12, were composed of sums of 40 trials (as compared with 20 trial sums in the preceding 8 figures) and the calibration bar at time zero represents 30 counts (instead of 20). Analysis interval: 200 msec.

having changed being the location of the sound source. We then obtained a small focused loudspeaker mounted in a metal sleeve of 2.5 cm diameter which could be positioned at any site behind, above or below the screen on which the visual images were projected. Without dwelling on details, since the full data will be presented elsewhere, it was clearly evident that the most effective sound source for acoustical activation of visual neurons was one located in that cell's receptive field for visual stimuli. For example, a cell having an excitatory

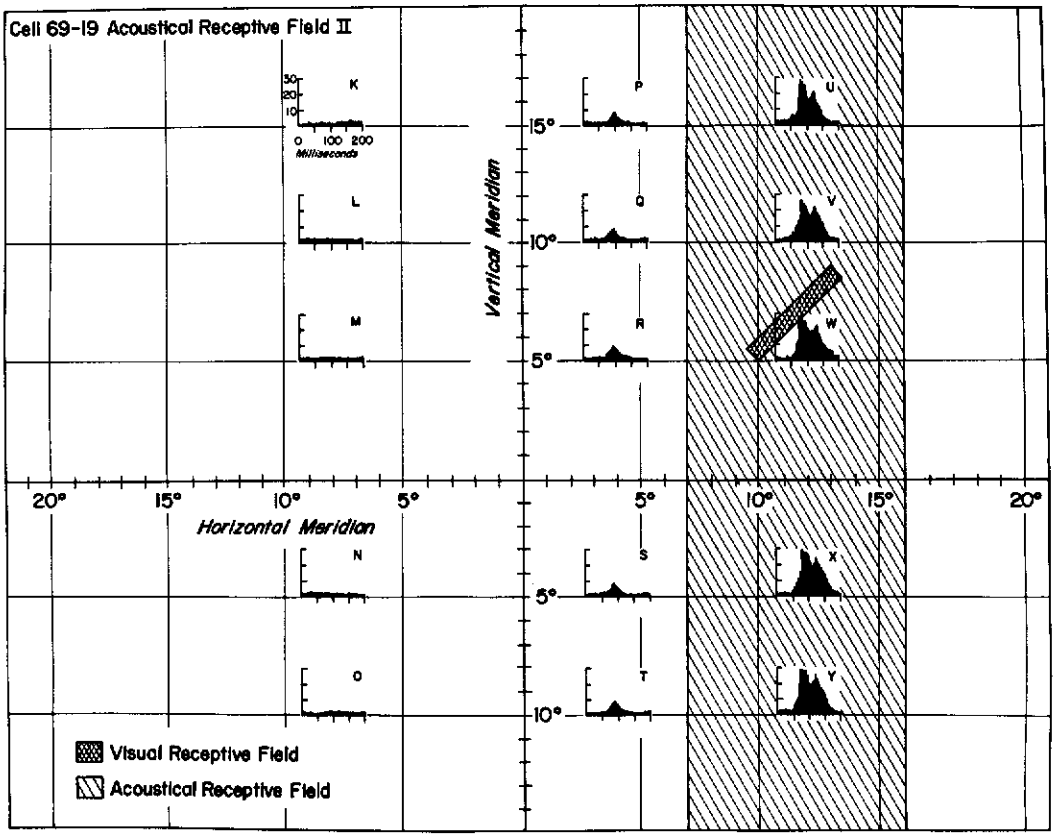


Fig. 10. Visual and acoustical receptive fields superimposed. Vertical dimension. Same cell as in Fig. 9. PST histograms of acoustical responses elicited by focused loudspeakers placed at sites on the tangent screen corresponding to the center of the histogram. Thus, sites " K ", " L ", " M ", " N " and " O " were all 8° left lateral and at, respectively, 15°, 10° and 5° above the horizontal meridian and 5° and 10° below it. Sites " P ", " Q ", " R ", " S " and " T " were all 4° right lateral and at, respectively, 15°, 10°, 5° above the horizontal meridian and 5° and 10° below it. Sites " U ", " V ", " W ", " X " and " Y " were all 12° right lateral and at, respectively, 15°, 10°, 5° above the horizontal meridian and 5° and 10° below it. The visual receptive field is indicated by cross-hatching. Visual responses from a light slit placed in the indicated region may be seen in Fig. 1, which illustrates the visual responses from the same cell.

receptive field 10-12° lateral to the vertical meridian gave its most vigorous acoustical response when the sound source was also 10-12° lateral to the vertical meridian. The borders of the receptive field for sound were not as precise as those for light and we failed to demonstrate a true inhibitory surround. Maximal acoustic response occurred when the loudspeaker was within the excitatory visual receptive field but weaker responses were detectable over a range of at least ± 5°. Responses invariably disappeared when the sound source was placed on the other side of the vertical meridian. Only the lateral dimension was significant. Displacements of the sound source above or below the horizontal meridian while maintaining the same deviation from the vertical meridian had no additional effect.

Figure 9 exhibits PST histograms of the cellular discharge to acoustical stimuli (in each case 40 presentations of 50 msec click trains) as a function of position on the tangent screen used to project visual images. The " preferred " visual stimulus was an obliquely oriented light slit in the right upper quadrant of the field extending from 10°-13° lateral to the vertical midline. When the light slit was positioned slightly to the right or left of site indicated, there was a pronounced inhibition of discharge; other sites had no effect whatsoever. As can be seen from the accompanying histograms the borders of the acoustically responsive zone were not as sharp and there was no evidence of an inhibitory surround. The shaded area of Fig. 9 represents the zone of effective acoustic stimulation. It is notable that within that zone stimulations above and below the horizontal meridian gave similar results (Fig. 10). Another cell in the same penetration was activated by a differently oriented visual stimulus (Fig. 11) and had a smaller receptive field closer to the vertical meridian. Histograms of acoustically-evoked activity are displayed at various sites along the horizontal meridian (Fig. 11 A, B, C, D, E). Similarly, the histograms of cellular firing at various sites along the vertical meridian are illustrated in Fig. 12 F through Q. The acoustical receptive field is shown as the shaded area superimposed on the tangent screen map (Figs. 9, 10, 11, 12). The cell shown in Figs. 11 and 12 had a narrower zone of acoustic sensitivity than the cell in Figs. 9 and 10. It is important to stress that the boundaries are not as sharp as they appear in the diagram and such relative differences as were noted between these two cells depend upon the use of the small focused loudspeaker mentioned above for their demonstration. Moreover, a certain subjective element enters into the determination of what constitutes an acoustical receptive field boundary. This is well exemplified by the histogram patterns in Fig. 9. The histogram for position " H " had the largest number of counts. Histograms " G " and " I " contained fewer counts but maintained the basic shape of histogram " H ". Therefore, " G ", " H " and " I " were all considered within the acoustical receptive field. The histograms for positions " F " and " J " do, in fact, reveal an acoustical response but it was very small and did not have the same shape

as " G ", " H " and " I ". The decision to place " F " and " J " outside the boundary of the receptive field was purely arbitrary and may have to be reconsidered as more parametric details become available.

So far we have been unable to demonstrate tuning curves for these cells; the spatial distributions described obtained for clicks and also for pure tone bursts from 10khz to 50khz. Therefore, these cells appear to be a separate population from that discovered by Spinelli *et al.* (1968) in that they are sensitive to acoustical space rather than to pitch. Other possible parameters have not yet been investigated. In particular, it should be noted that since the visual

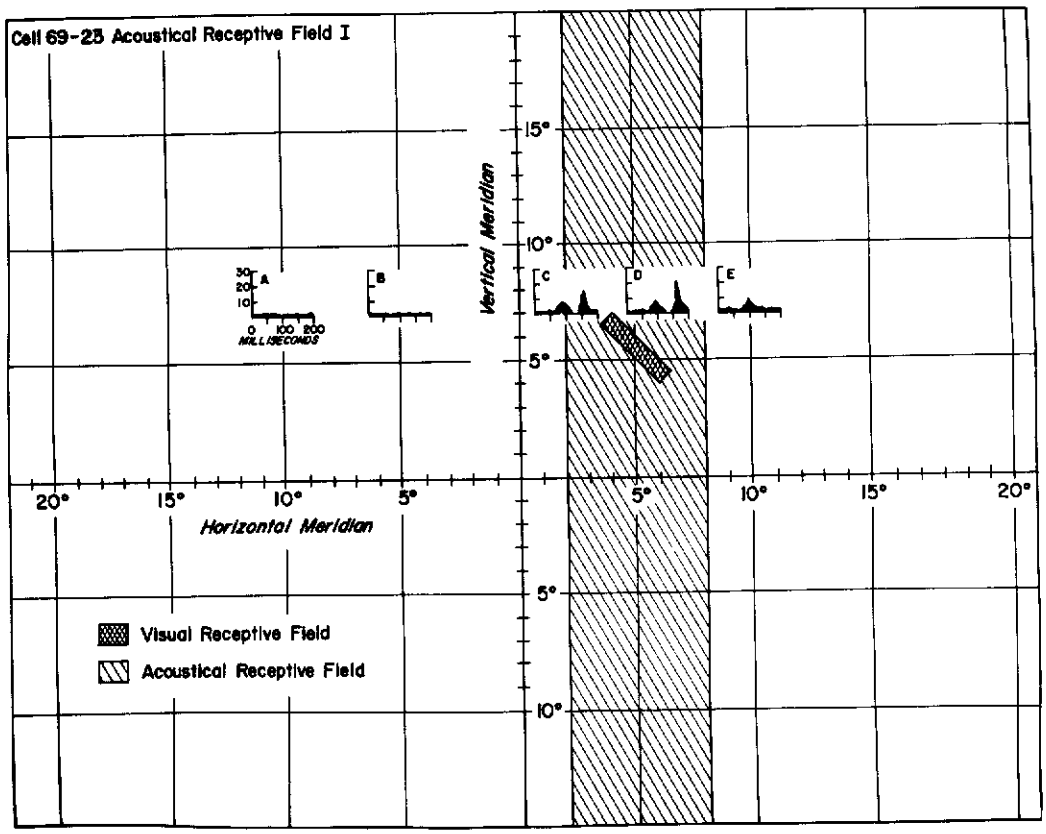


Fig. 11. Visual and acoustical receptive fields superimposed. Horizontal dimension. Another cell in the same penetration. Visual receptive field extends from 6° to 4° right lateral with an obliquity opposite from that of the preceding cell (Figs. 9 and 10). PST histograms to acoustical stimulation from focused loudspeakers placed at sites indicated by the center of the histogram display. Thus, sites " A ", " B ", " C ", " D " and " E " were all at 7° above the horizontal meridian, and were at, respectively, 10° and 5° left lateral and 2°, 6° and 10° right lateral. Visual receptive field indicated by cross-hatching; acoustical field by diagonal lines.

displays were designed for tangent screen projection rather than for a perimeter and the acoustical stimulus sites were superimposed upon the visual field coordinates, all sites were not equidistant from the ears. Nevertheless, in Fig. 9, for instance, loudspeaker positions " C " and " H " were both displaced 12° from the vertical meridian, yet the difference between the two histograms was striking. Position " F " was nearer to the animal than position " H " and position " J " much further away. Yet the loudspeaker at position " H " yielded

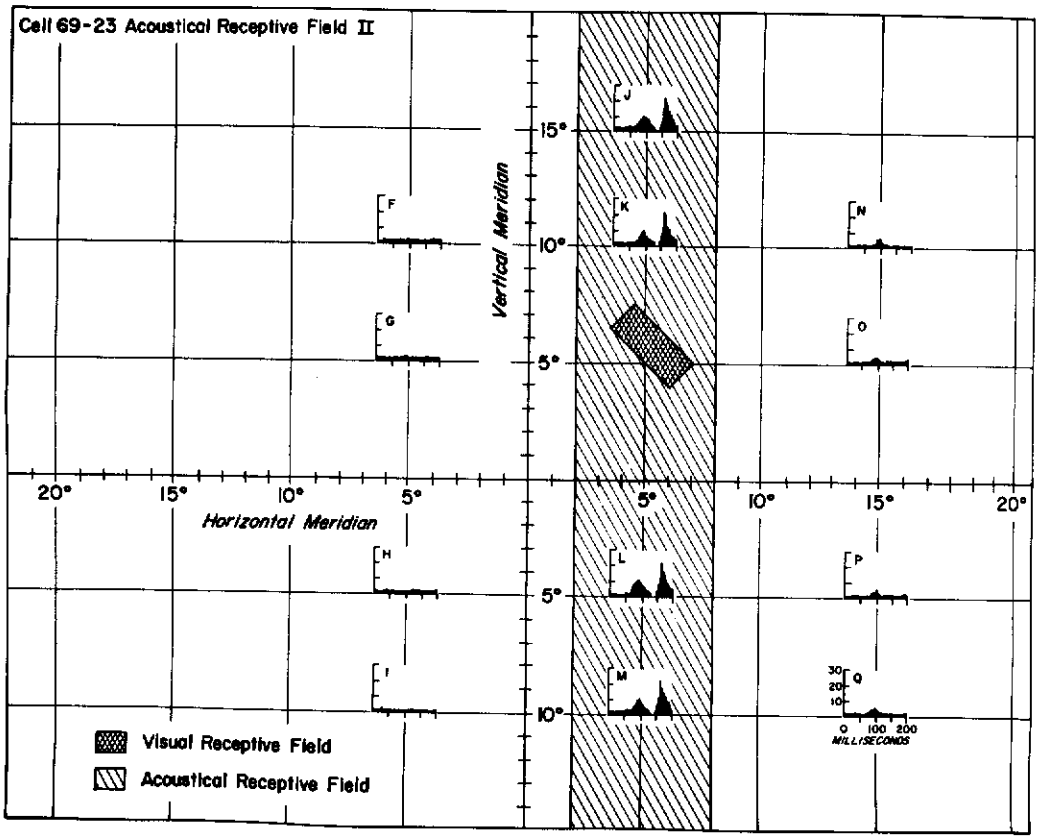


Fig. 12. Visual and acoustical receptive fields superimposed. Vertical dimension. Same cell as in Fig. 11. PST histograms to acoustical stimulation from focused loudspeakers placed at sites upon the tangent screen indicated by the center of the histogram display. Thus, sites " F ", " G ", " H " and " I " were all 5° above and 5° and 10° below the horizontal meridian. Sites " J ", " K ", " L " and " M " were all at 5° right lateral and were, respectively, 15° and 10° above and 5° and 10° below the horizontal meridian. Sites " N ", " O ", " P " and " Q " were all 15° right lateral and were, respectively, 10° and 5° above and 5° and 10° below the horizontal meridian. The acoustical receptive field in this cell was narrower than in the example of Figs. 9 and 10, but shares with the latter the property that the cellular responsiveness does not discriminate stimuli displaced along the vertical dimension but does so sharply along the horizontal.

the most vigorous discharge, while stimulations at " F " and " J " evoked very similar and smaller activity patterns. Thus, it seems unlikely that the spatial differences observed can be accounted for by any simple scale for distance of sound source.

## Discussion

The microstructure of the temporal pattern of cellular discharge as examined by computation of PST histograms revealed an extraordinary richness and diversity of detail as well as a remarkable stability of pattern when the same stimulus was applied in serial replications. For most cells the stability of response for given stimuli persisted despite applications of combined stimuli which, in a small proportion of cells, resulted in response modification. The most important observation which the use of the PST histogram allowed was that in polymodal cells each and every qualitatively different stimulus resulted in a different and distinctive temporal pattern of discharge. Thus, a visual cortical neuron, which was also responsive to acoustical stimulation, responded in a different manner depending on the location of the sound source (Fig. 9, compare F or J with G. H. or I. Cells responsive to more than one visual stimulus (Figs. 7 and 8) produced unique histograms for each effective stimulus configuration and, furthermore, non-visual stimuli impinging on the same cells (tactile or pain, in the case of Fig. 7 and vestibular in the example of Fig. 8) elicited still further unique and characteristic histogram patterns. Even the direction of vestibular polarization affected response patterns in different ways (Figs. 6 and 8). The same acoustical stimulation provoked one kind of response in one cell (Fig. 4) and other kinds in other cells (Figs. 9 and 11). In short, cellular discharge patterns appear to be quite specific both for each particular cell and for each effective stimulus.

When looked at in this manner, it seems extremely hazardous to classify the various afferent drives engaging visual neurons into simply "specific" and "unspecific" influences. In an early paper, Jung (1961) cogently summarized the argument for a specific vestibulovisual interaction as necessary to the precise regulation of visual function. This was quite apart from any diffuse, non-specific arousal. Furthermore, at that time Jung suggested that many of the neural mechanisms mediated by the brain stem reticular formation and loosely termed "non-specific" were, in fact, highly specific behaviors. That suggestion has received ample experimental confirmation, both in man (Morrell, 1967) where the topological distribution of cortical desynchronization was precisely concordant with the primary geniculocalcarine afferents activated by a localized visual stimulus (Polyak, 1927) and in several animal species (Gumnit, 1960; Jasper, 1960, 1961; Jasper *et al.*, 1960; Morrell, 1961 *a*).

Indeed, it often seems that when so-called "unspecific" neural systems are challenged in physiological ways and their ensuing responses thoroughly exa-

mined, some surprisingly specific features may be detected. This may not always be the specific quality intitially expected as shown, for instance, in Figs. 9-12, where the specificity lies in the spatial rather than the frequency dimension of acoustical stimuli. Certainly, in these examples of non-visual input to visual cells, the term "unspecific" seems inappropriate. The rough anatomical distinctions derived from work with gross evoked potentials (for reviews, see Albe-Fessard and Fessard, 1961; French, 1960; Jasper, 1960, 1961; Rose and Mountcastle, 1959) led to the hypothesis made explicit by Abrahamian *et al.* (1963), Bergamini and Bergamasco (1967), Rose and Lindsley (1968) and Uttal and Cook (1964), that short latency responses are of "lemniscal" origin while long latency responses arise from parallel activation of "extralemniscal", bilaterally projecting, modality non-specific, mesencephalic and thalamic reticular systems. The same distinctions were applied to single unit studies by Kornhuber and Da Fonseca (1964) but to this writer, they no longer seem adequate to encompass the vast range, variety and complexity of observations now becoming available through the application of computer technology to the analysis of single unit activity. A case in point is the very different picture observed by Dubner and Rutledge (1964) when they examined single units of the same association cortex in which Thompson *et al.* (1963 *a*, 1963 *b*) concluded that there was a "central association system" which was modality non-specific and was activated by extralemniscal pathways. However, examination of single units receiving biomodal or trimodal convergence revealed that each cell had biases in terms of what modality most effectively engaged it and that cellular response patterns differed depending upon which stimulus modality was used to activate the cell (see also Dow and Dubner, 1969).

The case is similar in parastriate neurons. Thus, although the parastriate area is clearly a zone having mainly visual function organized on a receptive field plan, even visual afferents do not command the cell's behavior in a simple reflex manner. Non-visual afferents impinging on visual cells elicit different output patterns and, presumably, themselves have a specificity along some dimension. Responses to other modalities which engage visual neurons are not distinguishable by latency, duration or maximal initial reaction (to use the criteria set forth by Kornhuber and Da Fonseca, 1964). There are only two criteria by which we can distinguish the effect of non-visual from visual input to visual cells. These are 1) sensitivity to barbiturate anesthesia, respiratory and cardiac distress and sleep (Abrahamian *et al.*, 1963; Erulkar *et al.*, 1956; Murata *et al.*, 1965), all of which diminish the response to non-visual input but leave the response to visual input relatively unaltered (Hubel and Wiesel, 1965 *b*; Robertson, 1965), and 2) the one-way character of results on cellular modification described above and discussed below.

In short, none of our results suggest a lack of specificity either for cell or for signal. Therefore, we prefer the more neutral terms primary and secondary as used by Buser (Buser and Bignall, 1967; Buser and Borenstein, 1959; Buser and Imbert, 1961), Albe-Fessard (Albe-Fessard and Fessard, 1963; Albe-Fessard and Rongeul, 1958, Mallart *et al.,* 1961), Amassian (Amassian, 1953, 1954; Amassian and De Vito, 1954), and Jung (1961). Until more experimental data enabling a detailed and meaningful classification becomes available, we consider that for visual cells the preferred visual stimulus is primary and all non-visual activations are secondary. For some cells, there was more than one "preferred" visual stimulus (Figs. 7 and 8).

Yet even this distinction is unsatisfactory. The designation of a "preferred" stimulus is limited by the investigator's inventiveness in compiling a stimulus repertoire and by a subjective estimate of the response magnitude. Magnitude, in turn, is hardly a meaningful scale on which to compare patterns. As noted above, the stimuli we use are relatively complex but still extremely simple when compared to those of real life. How will the cell having an active discharge to a certain orientation of line or edge respond to a picture of a mouse. Or, even better, a live mouse, with its olfactory, tactile and motile features? Similar difficulties apply to the selection of non-visual, interaction stimuli. The previously unguessed specificity of the spatial aspect of acoustical stimuli (Figs. 9-12) raises the question of whether specificities exist in some dimension for tactile, noxious and vestibular input to visual cells. No answer to that question can yet be given because the required experiments have not been done.

Auditory physiologists generally have devoted much more attention to mechanisms of pitch discrimination than to those for localization of a sound. Nevertheless, there is a considerable body of literature relating to the latter problem (Brugge *et al.,* 1969; Erulkar *et al.,* 1956; Galambos *et al.,* 1959; Geisler *et al.,* 1969; Goldberg and Brown, 1968, 1969; Kass *et al.,* 1967; Masterton and Diamond, 1964; Masterton *et al.,* 1968; Moushegian *et al.,* 1967; Neff, 1962; Neff and Diamond, 1958; Nelson and Erulkar, 1963; Rose *et al.,* 1966; Rosenzweig, 1954; and for an excellent and comprehensive review of the clinical literature, see Walsh, 1957). In general, it appears that stimulus coding for the location of sound depends upon very small differences in time of arrival at each ear. Cells in the superior olivary complex are sensitive to time differences in the range of microseconds. Such information must then be relayed to visual cortex, perhaps through auditory cortex or, possibly, via the inferior colliculus to superior colliculus and then on to visual cortex. To our knowledge, there has been no investigation of any kind of acoustical response in the superior colliculus, let alone responses depending upon directionality of sound source.

Whatever the pathway, there is a certain biological sense about the fact that many parastriate cells are sensitive to spatial features of the acoustical input

and, in particular, are concerned with sound sources roughly coincident with the same sector of space which contains that cell's visual receptive field.

The equally obvious lack of discrimination in the up-down dimension is consistent with the observation that the intact, behaving cat cannot learn a discrimination based upon altitude alone unless it tilts the head, thereby adding a lateral dimension to the stimuli. (Our cats were paralyzed with heads rigidly fixed in the horizontal plane.) It is also possible that "feature-detector" cells for altitude of sound source are present but in such small numbers that we failed to encounter them.

The notion that temporal pattern of discharge may provide a code by which the nervous system preserves qualitative features, local sign and modality specificity in polymodal cells is not new and has been suggested by many investigators (Adey *et al.*, 1954; Adrian, 1949; Amassian, 1953, 1954; Amassian and De Vito, 1954; Burns, 1955, Granit, 1955; Machne and Segundo, 1956; Segundo and Machne, 1956; Tove and Amassian, 1958; von Békésy, 1959; Wall, 1959, 1961). The statistical homogeneity of the typical patterns (For a cell and for a stimulus) shown in the preceding figures affords strong support for that notion. Nevertheless, it must be clearly stated that these cells do not exhibit the kind of synaptic security which was demonstrated by Mountcastle *et al.* (1963) and Poggio and Mountcastle (1963) for cells of the ventrobasal complex. Although all could be driven by particular visual stimuli within well-defined receptive fields as previously noted (Morrell, 1967), each stimulation did not yield exactly the same cellular discharge pattern. Thus, in Fig. 1 the PST histogram clearly indicates two peaks of activity. Yet, when examined individually, trials 3, 7 and 10 failed to show the second burst; in trial 5 the early burst was not detectable and in trial 11 neither discharge occurred. Clearly, therefore, at any given time, on any particular occasion, the responsiveness of a nerve cell cannot be relied upon to specify the nature of an experience. Obviously any complex organism must rely on parallel processing in thousands of elements along hundreds of channels to adequately analyze an external event. No single channel need be depended upon for most activities of everyday life. The observed relationship between the input and the output of a cell has been described as "probabilistic" (Morrell, 1967), i.e.; as having a statistical stability in the time course of firing with respect to a stimulation. The term "probabilistic" is descriptive only and does not imply any particular conclusion about the nature of the "noise" in the system. It is possible that a completely deterministic system, but one in which many variables are unknown, would appear probabilistic to the limited viewpoint of a microelectrode sampling the output of one single cell. Nor, of course, do these observations exclude the possibility of some fundamental stochastic property operating at the level of synaptic transmission. All that can be said at this stage is that it is not necessary to