markers and by the relatively few frames of film spanned by the contraction. The anterior region of *Stentor* contracts little, and it is harder to determine the arrival of the contractile wave in this area. Measurements of propagation velocity in anterior segments (segments a to I and I to II in Fig. 1A) have higher uncertainties than those in the stalk. With these values included, the calculated velocities in nine different animals have ranged from 5 to 25 cm/sec.

It is possible to initiate contraction locally in the stalk region with a mechanical stimulus, as is illustrated in Fig. 2. A graphical analysis of this contraction (Fig. 1B) shows that the contractile wave is capable of spreading in both anterior and posterior directions. The mechanism responsible for such propagation, at least in the longitudinal direction, is not polarized.

A distinctly different picture of contraction emerges when electrical stimulation is used. Figure 1C displays an example of electrically induced contraction in which all segments begin to contract within the same 0.38-msec interval. This interval is too short to be due to a propagated contractile wave originating from a distinct initiation point as shown by examples of mechanically induced contraction that take several milliseconds to spread across the animal. Electrical stimulation is capable of initiating contraction in many areas of *Stentor* simultaneously.

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8. I thank Dr. J. Lettvin for inspiring this study and for his many suggestions and insights. I also thank Drs. H. Edgerton and S. Raymond for their assistance and encouragement. Supported in part by an Alfred P. Sloan Foundation grant to H. L. Teuber, Department of Psychology, M.I.T., in part by a grant from Bell Telephone Laboratories Inc., and in part by NIH grant 5 PO1 GM14940-05.

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Single Cell Activity in the Auditory Cortex of Rhesus Monkeys: Behavioral Dependency

Abstract. *The response to repetitive stimulation of single cells in the auditory cortex of the monkey is dependent upon behavioral performance and training of the subject in a simple auditory discrimination task. In the trained, performing animal, single cells are more responsive than in the animal that is trained but not performing in the task. In the naive monkey, evoked responses are labile and are maintained only with nonrepetitive auditory stimuli.*

The central auditory system, from the eighth nerve to the cortex, has been examined extensively by means of acute (*1*) extracellular recordings from single units (*2*), and patterns of neural response to a variety of acoustic stimuli throughout the auditory pathway have thus been specified. However, certain limitations must be placed on data obtained with this approach. For example, anesthetics greatly alter single cell responsiveness (*3*). Moreover, chronic (*1*) electrophysiological techniques yield data that indicate a dependence of single cell activity within the auditory system upon behavior or "attentiveness" of the animal (*4*). Thus, the contribution of data obtained in acute studies to the understanding of neural functioning in awake, behaving animals is to some degree restricted. Chronic recording techniques for investigation of neural activity provide a more nearly normal physiological preparation than that offered by the anesthetized subject. Coupled with behavioral procedures for training nonverbal animals, these techniques allow investigation of single cell activity in unanesthetized, behaving animals, and in animals trained to report the occurrence of stimuli presented to them.

We report observations of single cell responsiveness in the auditory cortex of rhesus monkeys (*Macaca mulatta*) with emphasis on the effects of three behavioral conditions: (i) trained animals performing an auditory discrimination task; (ii) animals trained to the auditory task, but not performing; and (iii) awake, untrained animals.

Training and both electrophysiological and behavioral testing took place in sound-attenuated experimental chambers (Industrial Acoustics 400A or 1200A), with subjects restrained in primate chairs. Head movement was eliminated during testing sessions by rigidly fixing the head at three anchor points (*5*). During aseptic surgery a stainless steel chamber was anchored permanently to the skull over the middle-posterior extent of the Sylvian fissure.

For electrophysiological testing, tungsten microelectrodes were driven through the intact dura into cortex by a remotely controlled micromanipulator (Trent Wells), which was attached to the steel chamber on the monkey's head. With this preparation, isolated cells may routinely be studied for 1 to 2 hours. At termination of some of the penetrations into the cortex, small marking lesions were made to aid in later identification of recording sites. Standard electronic equipment was used in amplification and recording of the electrophysiological activity and in generation and control of acoustic stimuli. Auditory stimuli included clicks, bursts of white noise, bursts of pure tone, and verbal utterances. These auditory stimuli were delivered through a PDR-600 ear speaker (Permaflux) adjacent to the ear contralateral to the cortical recording site. Calibration of pure tone and white noise acoustic signals was performed with a Brüel and Kjaer ½-inch condenser microphone and a calibrated probe tube. Probe tube measurements were made at the entrance to the external auditory meatus. Intensities are given in decibels referred to 0.0002 dyne/cm^2.

Subjects were trained, by techniques described (*6*), to perform in a simple auditory reaction time (RT) task. This task involved depressing a telegraph key at the onset of a light stimulus, maintaining the key depressed for a variable duration (1- to 4-second foreperiod), and releasing the key rapidly at onset of the acoustic stimulus. Key release responses of brief latency were positively reinforced by delivering a dollop of applesauce to the animal's mouth. Final performance of monkeys in this task is similar to that of humans in a simple auditory RT task.

Results in this report are based on responses of approximately 150 single cells examined in seven unanesthetized monkeys. In animals trained and performing in an auditory RT task, single cells were readily isolated and studied which exhibited a consistent maintained response to repetitive auditory stimuli. Some cells were excited by onset and offset of the auditory stimulus, and

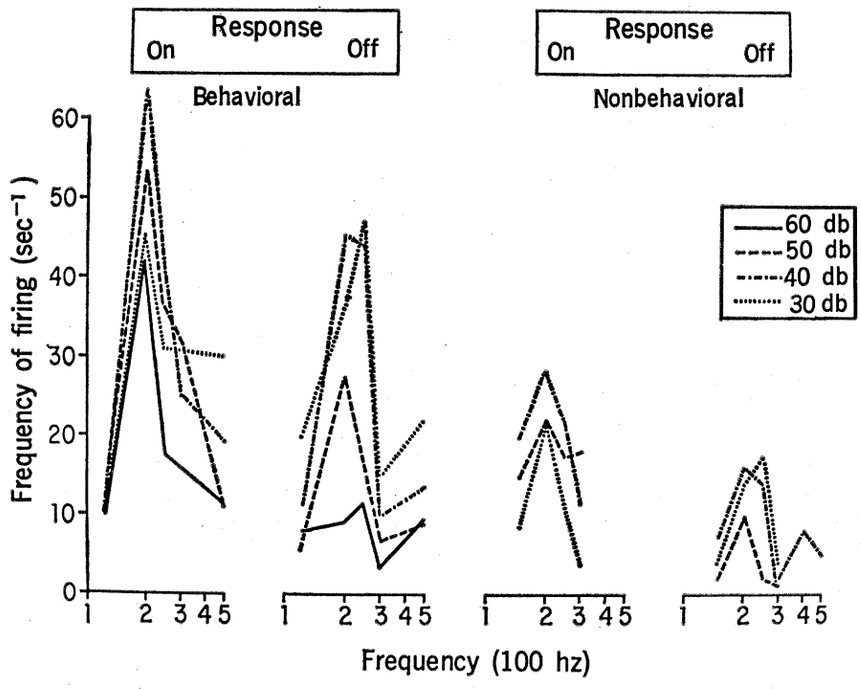

Fig. 1. Firing frequency of a cell excited by stimulus onset and offset. Observations were made (left) while the animal performed in the behavioral task, and (right) while the animal was not performing. In the inset, decibels are referred to 0.0002 dyne/cm².

others were suppressed by stimulus onset. The latter group exhibited a decrease in firing rate with onset of the auditory stimuli. Cells were found with either broad or narrow response fields throughout the frequency range of hearing for this primate (*7*).

In order to examine the relation between single cell activity and behavioral performance in this auditory task, we studied cells both when the animal was performing the behavioral task and when no performance was required. In the nonperforming condition, the light, telegraph key, and feeder were inactivated, and "free" tones were presented to the animal at a rate commensurate with that generated when he was working normally in the task. For each cell examined, the performing and nonperforming conditions were repeatedly alternated. Typical effects of behavioral performance on cellular activities are illustrated in Fig. 1. In this example, response contours are shown for one cell excited by stimulus onset and offset (*8*).

The cell exhibited a narrow receptive field, with the best frequency at approximately 200 hz. It responded with a nonmonotonic change in firing frequency to increases in the intensity of stimulation. These observed characteristics, including small differences in the receptive fields of the responses to stimulus onset and offset, remained identical under the performing and nonperforming conditions. However, the firing frequency of the cell when the animal was performing was far greater than that elicited when the animal was not responding to the tones in the behavioral task (*9*).

In animals untrained in the auditory RT task, we found few cells that were consistently responsive to repetitive clicks, white noise bursts, or tonal stimulation. Of approximately 50 cells that responded to acoustic stimuli in the untrained animal, more than 85 percent exhibited a maintained responsiveness only to nonrepetitive acoustic stimulation. Thus, consistent evoked responding from these cells was observed only with simple stimuli, such as pure tones presented randomly in time, or with complex stimuli, such as verbal utterances.

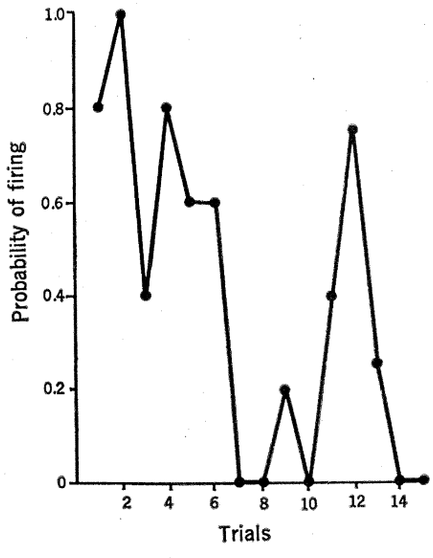

Fig. 2. Probability of response to repetitive tonal stimulation in one cell of an untrained animal. These data were obtained by examining the response of this cell to five different successive sets of pure tone stimuli of 15 trials each.

With repetitive stimulation, most of these cells exhibited high initial probability of response, which decreased during the first four to ten stimulus presentations. Figure 2 illustrates an example of this change in responsiveness. Nonsystematic changes in excitability were seen both during and after the initial decrease in responsiveness. Neither the initial change in probability of response nor subsequent changes could be related to variation in spontaneous activity or to other obvious fluctuations in cellular activity, or to the state of the preparation.

Because the cells in the untrained monkey exhibited no consistently maintained response with repetitive stimulation, detailed study of their characteristics was difficult. In response to onset of the auditory stimulus, some cells within this group were excited and others were suppressed. Moreover, all cells examined within this group exhibited some response selectivity dependent upon frequency of tonal stimulation.

Cell response in the untrained monkey may be contrasted with the responsiveness of cells in the trained but nonperforming monkey. Whereas in the untrained, awake animal the probability of cell response diminished rapidly with repetitive stimulation, no similar decrease in response probability was observed in cells studied in monkeys trained to perform in the RT task. Cell responses to repetitive stimulation presented during the nonperforming condition were consistent and showed none of the marked variability in cells of the untrained animal. Thus, it appears that differences in neuron activity can be found which reflect not

only conditions of performance and nonperformance but also the long-term effects of training.

Our observations indicate a clear dependence of cortical cell activity on the behavioral state of the animal (*10*). On the basis of these results we argue that the interpretation of electrophysiological data in sensory systems must take into consideration not only the physiological state of the preparation but also the training and current behavioral state of the awake animal. We suggest that interpretation of cellular activity in sensory behavior requires, beyond the traditional analysis of neuronal response to stimulus manipulation, the specification of rigidly defined behavioral contexts within which stimuli are presented. The effects on cell activity of systematic changes in the animal's behavior can then be assessed. A number of conditioning procedures, such as the RT method, are available for the precise measurement of sensory function in animals (*11*). Coupled with available chronic electrophysiological procedures and adequate control of the sensory stimuli, these procedures satisfy the requirements of such an approach. They permit the systematic independent control of both the peripheral input to the animal and the behavioral context within which it is presented. It is proposed that such an approach is necessary if we are to evaluate the role of central structures in behavior (*12*).

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9. We have also noted a decrease in amplitude in auditory evoked primary potentials when monkeys are switched from a performing to a nonperforming condition in this simple RT task.
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13. We are indebted to R. Smith for invaluable technical assistance. Supported by PHS grants RR 00166 and NS 08181.

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Nucleotide Conformations

Rubin *et al.* (*1*) in comparing the conformations of uridylyl-(3′,5′)-adenosine phosphate (UpA) (*2*) and A-RNA (*3*) have perpetuated errors in Sundaralingam's earlier dihedral angle calculations (*4*) from A-RNA coordinates. The correct values of the conformations are shown in the first column of Table 1. In any case, these RNA coordinates, from a manual model-building study, have for some time been superseded by the more accurate results of linked-atom least-squares refinements (*5*, *6*), the second of which utilized high quality data from a synthetic, complementary double-helical RNA that provided almost twice as many x-ray reflections as the original (isostructural) viral RNA. Rubin *et al.* (*1*) were concerned also to emphasize the conformational differences between UpA and A-RNA. Use of the erroneous angles or even the corresponding correct, but inaccurate, values obscures some striking similarities in conformation.

Rather than compare the UpA conformations with a single polymer structure determination (however accurate), we show in Table 1 the mean values (and estimated standard deviations from the mean) of conformation angles (Fig. 1) found in eight appropriate (*7*), helical, polynucleotide structure determinations. We also show corresponding data derived from x-ray analyses of monomer crystals (*8*).

Twenty values for conformation angles in two structurally distinct UpA molecules are available (Table 1). Except in three instances (ϕ of one molecule and ψ, ϕ of the second) the values, or average values where appropriate, differ by less than two standard deviations from the corresponding average values observed for polynucleotides to date. The three exceptional values are equally similar to conformational alternatives noted in monomers (*9*). In the great majority of its conformation-angles, therefore, UpA has values no more different from any particular

Table 1. A comparison of the backbone conformations in UpA, double-helical polynucleotides and monomers. The angles are defined in Fig. 1. No estimated standard deviation (E.S.D.) from the mean is shown for σ in the case of the polymer structures (*) since the sugar ring was kept fixed in the linked-atom, least-squares refinements.

Conformation angles	Early A-RNA results (deg)	(UpA) I (deg)		(UpA) II (deg)		UpA mean (deg)	Mean values (and E.S.D.)	
		A	U	A	U		Linear polymers (deg)	Monomers (deg)
χ	62	108	80	98	69	89	89(9)	79(10)
σ	75	94	81	83	87	86	83(*)	77(13)
ξ	69	52	54	57	49	53	53(3)	52(8), −179(9), −67(2)
θ	165	−167		−159		−163	−169(17)	176(13)
ψ	−78	−88		84			−69(17)	60(15), −179(9), −60(14)
ϕ	−83	164		84				
ω	−136	−138		−159		−149	−166(19)	−108(16)