A PROBABILITY APPROACH TO CERTAIN NEUROELECTRIC PHENOMENA

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TECHNICAL REPORT 307

MARCH 1, 1956

RESEARCH LABORATORY OF ELECTRONICS
MASSACHUSETTS INSTITUTE OF TECHNOLOGY
CAMBRIDGE, MASSACHUSETTS

The Research Laboratory of Electronics is an interdepartmental laboratory of the Department of Electrical Engineering and the Department of Physics.

The research reported in this document was made possible in part by support extended the Massachusetts Institute of Technology, Research Laboratory of Electronics, jointly by the Army (Signal Corps), the Navy (Office of Naval Research), and the Air Force (Office of Scientific Research, Air Research and Development Command), under Signal Corps Contract DA36-039 sc-42607, Project 102B; Department of the Army Project 3-99-10-022.

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Lawrence S. Frishkopf

This work was presented as a thesis submitted to the Department of Physics, M.I.T., 1956, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

Abstract

When an acoustic click is presented to the ear of an anesthetized cat, an electrode, placed near the round window of the cochlea, detects a superposition of microphonic and neural components. The first neural component (N_1) represents a sum of action potentials of first-order auditory neurons. We have studied the N_1 response amplitude as a function of click intensity and observed that this "intensity function" characteristically exhibits a two-stage growth. This behavior suggests that the contributing neural elements might be usefully classified as "sensitive" or "insensitive."

A model is developed in which properties of "neural units" are defined: units obey the all-or-nothing principle; the threshold of a unit is a fluctuating parameter describable by a probability density function. Populations of statistically independent identical units are postulated. The model is related to the data by defining an intensity function that depends linearly on the number of units in each population that respond.

The results of two experiments are compared with the predictions of the model. First, we have studied the amplitude variability of N_1 as a function of stimulus intensity. Second, we have investigated the effect of a continuous noise background on the amplitude of the N_1 response to a click ("masking" of N_1). In both cases the data and the predictions of the model are in good agreement over the first interval of amplitude growth (the sensitive range). Over the insensitive interval the data are incompatible with a single-population hypothesis in one case; in the other case they are inconclusive. The size of the sensitive population and the characteristic rate of threshold fluctuations of a sensitive unit are estimated.

We conclude (a) that a relatively homogeneous population of neural units, characterized by rapidly fluctuating thresholds, is responsible for the initial component of growth of the intensity function and (b) that over the remaining interval of the intensity function a single-population hypothesis will not account for the data within the framework of the model.

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I. INTRODUCTION

We shall first consider the anatomical, physiological, and electro-physiological characteristics of the neuron and of groups of neurons, as disclosed by gross and microscopic techniques (2,3). Our purpose is to provide a background for the material of the following sections; the topics below were selected with this object in mind.

1. Brief Description of a Neuron

A neuron is a highly differentiated cell. Anatomically, it is grossly characterized by its extreme length compared to its dimensions in cross section. Physiologically, it is notable for its ability to transmit excitation, initiated at one point, along its length.

A neuron is, for purposes of reference, conveniently separated into three parts: cell body, axon, and dendrites. Figure 1 shows, schematically, the relationship of these parts for one type of neuron (bipolar). The cell body contains the cell nucleus; the dendrites, axon, and axon terminals are specialized for the reception and transmission of excitation.

Reception of a pulse from another fiber or from a sense cell occurs in the dendritic terminals or on the surface of the cell body. The region of interneuronal junction is called a synapse. Excitation is transmitted, transsynaptically, from the axonal terminals of one neuron to the dendritic endings of another; the impulse then propagates through the cell body and along the axon to the branched axonal terminals, which then synapse with other neurons or with muscle fibers.

In many fibers the axon is covered with a layer or sheath of a fatty material called myelin, which gives to nerve bundles their characteristic white appearance. Myelin has the electric properties of an insulator.

2. Classification of Fibers

It is useful to classify fibers, first, on the basis of function and, second, on the basis of such physical properties as axon diameter, conduction velocity, and presence or absence of myelin (4). It is found that larger fibers are more heavily myelinated, conduct faster, and yield larger responses (5). The values of fiber diameters in a bundle will generally tend to cluster around one or more of three values. The A fibers subserve the somatic (sensory and motor) system and are the largest; the medium-sized or B fibers subserve visceral sensation and muscle; the C fibers, smallest of the three, are connected with perception of pain and warmth (6, 7, 8). These are rough classifications with respect to size and there is a considerable amount of overlapping. The A fibers have diameters of one to twenty microns; B fibers are less than three microns in diameter; and C fibers are less than 1 micron.

All three kinds of fibers may, as has been indicated, run together in a single bundle. In this case the composition may be analyzed by recording the response from the bundle at a point some distance from the site of excitation (9). The dispersion of

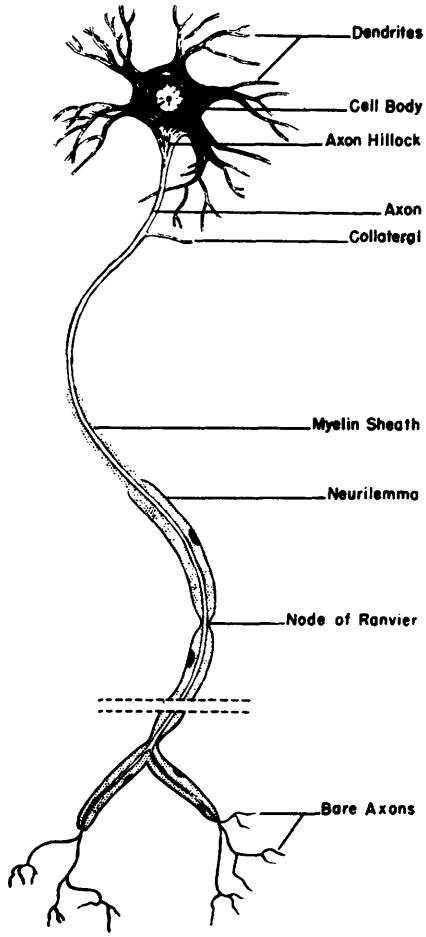

Fig. 1. Schematic drawing of a neuron. Some dimensions are grossly exaggerated for diagrammatic representation of the structures mentioned in the text. (From Brazier, The Electrical Activity of the Nervous System, Pitman, London, 1951, and Macmillan, New York, 1953.)

the response into three components reflects the distribution of conduction velocities and thereby the distribution of diameters in the bundle.

3. Conduction Velocity

The conduction velocity in a fiber is thought to be approximately proportional to its diameter (4, 10). For a fiber with a diameter of twenty microns, the conduction velocity is about 160 meters per second, under normal conditions. The C fibers may conduct at velocities of less than two meters per second.

Velocities in dendritic and axonal terminals are, of course, much smaller than in the axon of the same neuron, owing to the much reduced diameters of these branches.

4. Cell Excitability

The gross structural elements of a cell consist of a nucleus surrounded by cytoplasm, the whole enclosed by the cell membrane. It is a property common to all cells that this membrane is polarized and, therefore, that a potential difference exists across it (11). This potential has its source in a separation of ions across the membrane. Excess positive ions are maintained on the outside; negative ions on the inside. When appropriately stimulated, the effective resistance of the membrane drops, and a current flows across it.

5. Propagation of the Nerve Impulse (12)

The existence of this potential plays a primary role in the functioning of a neuron as an element of a communication system; for the neuron has the property that excitation initiated at one point of the cell is normally propagated along its entire length. The situation prior to stimulation is illustrated in Fig. 2a. This is the so-called resting state of the nerve. Now a stimulus is applied at some point B along the axon. The membrane resistance at B drops, and current flows into the fiber (Fig. 2b, c). In adjacent sections A and C, the current flow is outward. The consequent drop in resting potentials at A and C act as stimuli for these regions. By repetition of this process, propagation is effected in both directions from the initial point of excitation. It is seen that eddy currents play an essential role in the excitation and propagation processes. Electric spread in a conductive medium (electrotonus) also plays an important role in the interaction of adjacent parallel fibers and in conduction across a synapse.

The degree of stimulation produced upon an adjacent region by the propagating impulse must be suprathreshold to cause further propagation. Along an axon this is no problem, for the system has a large safety factor. One can, however, produce

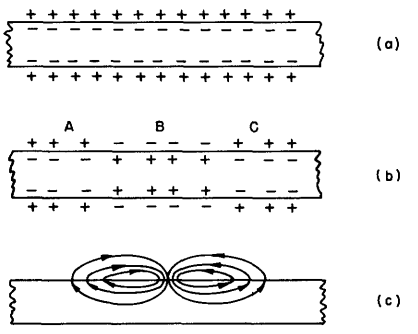

Fig. 2. Schematic drawings of (a) the distribution of charge along a nerve fiber in the resting state; (b) the distribution of charge along a nerve fiber immediately following excitation at point B. (At B the potential across the membrane has reversed sign, while at adjacent points A and C it is reduced in magnitude.); (c) the flow of current near the point of excitation B. (Current flows into the fiber at B, out at A and C.)

artificial situations in which this requirement is not fulfilled. If, for example, we anesthetize a short length of axon, that portion can no longer conduct. If the anesthetized interval is sufficiently short, however, conduction can jump across it (see ref. 12 and Fig. 3) by the physical spread of eddy currents, as described above. As this interval is extended, the effect of the eddy currents becomes weaker, until it is subthreshold and conduction ceases. Such considerations obviously govern the conduction velocity in a normal fiber.

Extinguishing effects like these may have physiological importance in the functioning of the central nervous system. Axons and dendrites terminate in many fine branches; the fiber bifurcates and rebifurcates and becomes narrower each time. The dendritic endings of a 20-micron axon are less than one micron in diameter. Narrow fibers have small resting potentials and high thresholds; threshold therefore becomes a function of position along the fiber. Conduction velocity into the terminals decreases, and under some circumstances the impulse may be extinguished altogether.

6. The All-or-Nothing Principle

From the discussion above it is clear that the energy for the propagation of an impulse comes from the nerve itself, and not from the stimulus which initiates the impulse. The stimulus acts as a trigger; the impulse results from the abolition of the resting potential (although the story is somewhat more complicated than that), which is then restored by metabolic processes within the fiber. It also follows that if a fiber is stimulated and propagates an impulse, the amplitude and velocity of that impulse are independent of the strength of the stimulus. In other words, with respect to the nerve impulse, a neuron behaves like a binary element; a stimulus either fires the cell or fails to do so. This is a statement of the so-called "all-or-nothing" principle of nerve physiology, first enunciated in 1871 by Bowditch (13). It has been extensively verified by experiment (4, 14).

Finally, it is clear that, at a given point along the fiber and at a given time, there exists a least stimulus which will produce a propagated impulse. This value of the stimulus is called the threshold of the fiber (with respect to that mode of stimulation).

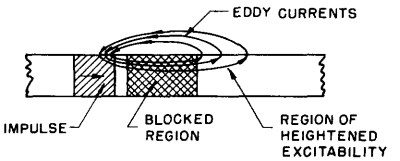

Fig. 3. Schematic diagram of the spread of eddy currents from an approaching impulse across a blocked region of nerve. The eddy currents heighten the excitability of the region beyond the block. If the blocked interval is small, the impulse may "jump" the block and propagate into the region beyond. (After Hodgkin, J. Physiol. 90, 183, 1937, Cambridge University Press, London and New York.)

For electric stimulation, commonly employed, the threshold can be expressed as the least voltage across the stimulating electrodes which will produce firing.

Stimuli which lie below threshold are called subliminal (15). Such stimuli can have important effects. This is especially true at a synapse, where several impulses, separately subliminal in their effect on a transsynaptic neuron, may, through their combined effect in space or time, produce excitation (16, 17). Also, the effects of electrotonus on an axon that neighbors active ones, although insufficient in itself to fire that axon, may change its threshold and thereby affect its activity (18, 19).

It should be pointed out that the all-or-nothing principle makes no statement about the amplitude of response or about the threshold value. These depend upon the instantaneous state of the fiber. Briefly, the all-or-nothing principle may be restated as follows: a nerve fiber, stimulated, will fire to the maximum of its instantaneous ability if it fires at all.

It seems hardly necessary to make these qualifications if the model of a neuron described above is kept in mind. However, the all-or-nothing principle was enunciated before much was known about individual nerve fibers, and for many years it was applied without restrictions. Its discovery represented a landmark in the understanding of the nervous system and it has dominated the thinking of neurophysiologists ever since. It remains, today, the bedrock of neurophysiological theories, and only very recently is the complementary aspect of neural activity – i.e., slow potentials, analogical rather than digital in character – beginning to assume comparable importance.

7. Response of Single Neuron (4, 20)

Figure 4 shows the response from a single axon, excited by electric shock. The duration of the response, that is, the time it takes for the activity to propagate under the active electrode, is about 1 msec. This value is fairly typical for axons. To some extent it depends on the propagation velocity in the fiber, but less than one might think, since in a slow fiber the threshold is high and the activated region consequently small (2). The shortest spike durations are about 0.5 msec in large A fibers (conduction velocity approximately 160 meters per second); the longest, about 2 msec, in C fibers (conduction velocity 2 meters per second). The activated region is thereby calculated to range from about 8 cm in fast A fibers to about 0.4 cm in the slow C fibers.

The propagated response of a single nerve fiber is called the action potential; the term nerve impulse is often used equivalently. Since the fiber in the resting state is charged positively on the outside and negatively on the inside, the action potential is seen as a potential drop by an external electrode. This negative potential is conventionally recorded in electrophysiology as an upward deflection.

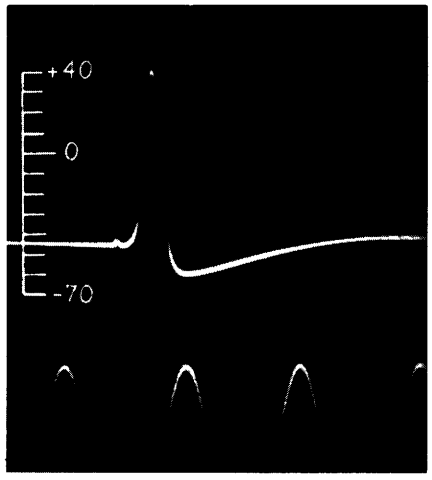

Fig. 4. Action potential recorded between the inside and the outside of a squid axon. The vertical scale indicates the potential of the internal electrode in mv, the seawater outside being taken as zero potential. Time marker, 500 cps. (From Hodgkin and Huxley, J. Physiol. 104, 176, 1945, Cambridge University Press, London and New York.)

8. Sources of the Resting and Action Potentials

Discussion is in order concerning the nature of the resting and action potentials, and the mechanism of excitation. These are subjects that have produced much controversy and many competing theories. The main questions are these: How is the resting potential maintained? How does a stimulus affect the system to permit the development of an action potential? How is the resting potential restored after propagation of an impulse?

It is well known that the concentrations of certain ions are very different within the cell and in the intercellular fluid. It is generally believed that these concentration gradients play an essential role in producing the cellular potentials. Extensive work on this subject has been done by Hodgkin and Huxley (21-26) on the squid axon. (This is a very large axon – diameter, about 50 microns – into which an electrode can be inserted and the various potentials studied directly under a variety of experimental conditions.) Their studies indicate that two ions, K^+ and Na^+, are central in producing the resting and action potentials, respectively. It is known that, in the resting state, the nerve membrane is permeable to potassium but not to sodium (24). From the measured potassium ion cencentrations, a potential has been calculated whose magnitude accords quite well with that actually observed in the resting squid axon – about 40 mv (22). It also appears that the action potential is not simply the result of abolishing the resting potential and that it depends critically on the presence of the sodium ion; the absence of sodium prevents the development of an action potential altogether (27). Moreover, Hodgkin and Huxley have shown that, following excitation, sodium enters the nerve, rendering the outside finally negative with respect to the inside. The action potential

is therefore considerably larger than the resting potential; in squid axon the resting potential is about 40 mv, the action potential about 75 mv (Fig. 4). The difference can be quantitatively accounted for on the basis of the measured sodium ion concentrations.

The membrane theory (28), tacitly assumed above, requires that we postulate a change in the specific permeability properties of a nerve following stimulation, and a restoration of these properties following the passage of an impulse. How this process might be mediated has been the subject of much debate. There is some reason to believe that the resting potential is maintained in whole or in part by metabolic processes in the fiber (29).

9. Refractoriness and Recovery of a Nerve Fiber

After a neuron fires, its threshold and its response amplitude to a second stimulus are altered for a short time while recovery to the resting state takes place (30). The detailed sequence of changes in threshold and after-potentials depends, to a considerable extent, on the kind of nerve we are dealing with and on the part of the neuron that we are considering. In general, recovery is slower in the smaller fibers: A fibers recover more quickly than C fibers, and the axon of a given neuron faster than its dendrites.

Following the excitation of an impulse in a fiber, the application of a second stimulus will make apparent the following changes (31, 32). For the first millisecond after firing the neuron will respond to no stimulus, however strong. This is called the absolute refractory period of the fiber. In A fibers it may be as short as 0.4 msec, in C fibers as long as 2 msec. There follows a period of so-called relative refractoriness, lasting about 4 msec, during which the cell will fire, but its threshold is elevated and the amplitude of response is reduced. Conduction velocity is also reduced in this period. At the end of this time, amplitude of response has fully recovered but the threshold is still elevated. Persistent threshold effects, accompanied by small characteristic slow potentials, are observed in mammalian A fibers out to 60 msec, in B fibers to 300 msec, and in C fibers to 1 sec. It should be emphasized that these properties have been determined in bundles of peripheral axons or in single isolated peripheral fibers. No corresponding data are available for dendritic terminals or for the neurons of the central nervous system, spinal neurons excepted.

10. Neural Mechanisms (3, 33)

Up to this point we have been concerned with results obtained by stimulating single fibers by brief shocks. This is not a normal physiological situation. Those sensory stimuli which we ordinarily encounter and whose differentiation is a primary task of the nervous system, are, in general, diffuse in space and time. One may well ask: What are the primary mechanisms by which the most peripheral neural elements carry out their task of coding? A partial answer can be given.

If we consider, for example, just one stimulus dimension, that of intensity, two such

mechanisms can be definitely stated. On the one hand, an increase in stimulus intensity will produce an increase in the rate of firing in individual fibers. This mechanism is utilized in touch, pressure, pain, olfactory, visual, and other sensory fibers. In A fibers, the absolute refractory period is approximately 0.5 msec, so that the maximal response frequency theoretically available is about 2000 impulses per second. Such rates are rarely if ever evoked. A very intense tactile stimulus may evoke impulses at the rate of 500 per second.

A second mechanism of coding information in the peripheral sensory system depends upon the number of units that fire: more intense stimulation excites more neurons. Under physiological conditions of stimulation, it is rare that one neuron alone is excited; such a signal would probably be disregarded by a system accustomed to considerable spontaneous activity.

11. Fatigue and Adaptation

As a result of very rapid firing of a neuron, its refractory period increases; thus a unit stimulated at near maximal rate may soon find itself able to respond only to every second or third event. Even at slower rates of stimulation, fibers will show decremental responses over a period of several seconds. These effects are relatively long-lasting; recovery to a normal resting state requires many seconds. In this situation it can be shown that oxygen consumption and heat production fall. Such a condition is called "fatigue" (32, 34).

A property which all external sensory fibers exhibit is that of adaptation. If these fibers are presented with a continuing stimulus, the impulse rate in a fiber is initially maximal; then it decreases, often to zero. The fiber seems somehow to change its threshold level to coincide with the stimulus present. This is not fatigue, for any change in stimulus, increasing or decreasing, if sufficiently rapid, will "alert" the cell and produce a barrage of impulses. The necessity of such an adaptation mechanism is clear. The peripheral nervous system is primarily designed to detect changes in environment, and this function cannot be efficiently performed if the detecting channels are continually occupied with activity induced by a constant background level.

12. Composition of a Nerve Trunk

Strong shock applied to a bundle of fibers will produce firing of all neurons in the bundle. Such a shock is known as a maximal stimulus. The composition of the bundle with regard to the distribution of fiber velocities, and thereby (indirectly) fiber types and diameters, can be determined in the following manner (4). A recording electrode sufficiently removed from the source of stimulation will see a succession of impulses, each corresponding to a group of fibers that conduct at about the same velocity. Thus it has been observed that in mixed trunks containing A, B, and C fibers, three response components are present. Of course the bundle must be long enough to resolve these velocities. If the stimulus is reduced, the high-threshold C fibers stop firing,

and only two response components are observed. Further reduction results in the elimination of the B fibers as well. In this way thresholds are also resolved. In theory, one could investigate the fine structure of threshold and velocity composition within a single grossly resolved group by similar methods.

13. Spontaneous Activity

Neurons, in the organism, are often observed to fire without external stimulation. Such activity is said to be spontaneous. The origin of this behavior is uncertain. Statistical fluctuations in ion concentrations, metabolic fluctuations, activity of other cells, or persistent after-potentials may produce local threshold variations. At any rate, this property implies a certain degree of variability of threshold properties, of a sort that cannot be controlled or predicted by the observer.

14. The Synapse

In the nervous system, communication depends on chains of neurons. Transmission is effected from one neuron to another at the junction region, or synapse, of the two cells.

A synapse generally consists of a complex interlacing of the axonal terminal fibers of one neuron with the dendritic endings of a second neuron, transmission occurring only from axon to dendrites. In a second arrangement, the axon terminals end in bulb-like structures, called boutons, which synapse directly onto the surface of the cell body. On the basis of available evidence, it is generally believed that transmission occurs across the synapse by electrotonus, initiating an impulse in the dendrites which is then transmitted down the fiber. The situation is similar to that, described earlier (12) for a single axon, in which excitation occurs across a blocked interval of nerve.

In general, synaptic connection is not a one-to-one but a many-to-many relation. That is, each presynaptic neuron has connections to many postsynaptic neurons, and conversely. The many resulting possibilities account in large measure for the versatility and flexibility of the nervous system. We now examine some of the transsynaptic mechanisms that are known to be available to the nervous system (29, 35, 36).

First, it should be noted that transmission across a synapse requires a time of the order of a millisecond. Since the transsynaptic distance is negligible compared to the distance an impulse in an axon would move in that time, a synapse may be functionally regarded as a delay element. An explanation that accounts, at least in part, for this delay is that the transmission velocity in the fine axonal terminals is much smaller than in the axon. The further out along the terminal fibers the impulse must go to produce transsynaptic excitation, the longer the delay.

This brings us to a second property, namely, that the transsynaptic delay is a function of the number of presynaptic fibers simultaneously active, and therefore of the stimulus intensity. Each postsynaptic fiber has, in general, connections from many presynaptic ones. Presumably there is some minimal field at the dendrites or cell body

which produces excitation; this value is, of course, independent of the source of the field. The summed effect of a large number of presynaptic fibers will produce this minimal value when the impulses in the axonal terminals are relatively farther from the postsynaptic endings. Thus the transsynaptic delay is shortened.

Whereas the firing of a single presynaptic fiber may be insufficient to cause excitation in a neuron with which it synapses, the simultaneous excitation of several neurons having terminals on the same postsynaptic cell may, through the summing of their fields, produce transsynaptic conduction. This phenomenon is called spatial summation (36).

A similar phenomenon occurs in response to a series of appropriately spaced impulses in a single fiber, where each impulse is separately subliminal to a transsynaptic cell. Long-lasting effects induced in the neighborhood of the synapse by a subliminal impulse make the postsynaptic cell more susceptible to excitation, so that, after the arrival of a number of such impulses, the cell fires. This phenomenon is called temporal summation or facilitation (35). Since the effect occurs over times much longer than one could expect electrotonic potentials to persist, it is necessary to seek other explanations. There is a group that believes that synaptic conduction is mediated chemically and that long-lasting effects are attributable to the persistence of the chemical mediators (37). Another explanation postulates long-lasting local excitatory processes at the surface of the transsynaptic cell (38); yet another proposes reverberatory chains of neurons (39). There is some evidence for each of these explanations, generally based on work in different areas. It is clear that some such mechanism is necessary.

Inhibition, or blocking of impulses, may occur at a synapse. Consider the following simple example. A chain of impulses is set up in a fiber, at a rate that will result in each impulse falling in the relative refractory period of the previous one. Thus, after the first, all responses are reduced in amplitude. A postsynaptic cell that responds to the first impulse will, under suitable threshold conditions, fail to respond to any of the sequence that follows. This is called Wedensky inhibition (40). If the impulse rate is decreased, amplitude is restored, and transsynaptic conduction occurs at every impulse (2).

A second example is found in the common situation in which neurons A and B synapse with the same third cell C. If A is activated very shortly before B, the neuron C may respond only to A, provided the excitation from B falls in its phase of elevated threshold. Thus the presence of an impulse in A effectively inhibits a response to B (41). Variations of this mechanism are probably employed by the nervous system in reflex inhibition and in sensory masking. That inhibition in one form or another plays an important role in the functioning of the nervous system cannot be doubted, and it is reassuring that demonstrable mechanisms for it are available.

The paramount role of the synapse in neural organization is clear. The synapses are effectively the "switching" elements of this communication system. All the logical elements necessary for building the most complex automata are available in the properties of synaptic junctions noted above (42, 43).

II. PROPERTIES OF THE AUDITORY SYSTEM

The auditory system subserves a sensory modality whose function is the detection and discrimination of acoustic vibrations. In all higher species, it provides one of the chief links with the environment. The auditory system extends from periphery to cortex, ascending through at least four intermediate nuclei (Fig. 14) and embracing little-explored descending and nonspecific pathways as well. We are concerned mainly with the peripheral structures.

A. THE PERIPHERAL AUDITORY SYSTEM

1. A Brief Description (44-47)

In mammals, the peripheral auditory structures are highly differentiated. The ear consists of three major parts: the external ear, which provides direct coupling to the air; the inner ear or cochlea, which contains the sensory endings of the auditory nerve; and the middle ear, which mechanically links the first two structures. The system is schematized in Fig. 5.

The external ear consists of the auricle, or pinna; the ear canal, or external meatus; and the ear drum, or tympanic membrane. The first two channel the sound waves to the drum, a tough translucent membrane which completely separates the outer and middle ears and whose vibrations form the input to the rest of the system.

Across the tympanic membrane is the middle ear, consisting of an air-filled cavity containing a chain of three small bones, the ossicles. These are firmly suspended from the bony walls of the cavity by muscles and ligaments. The first of these bones, the malleus, is attached at one end to the ear drum. The last in the chain, the stapes, is attached to a membranous window of the inner ear. The middle bone, the incus, serves, in lever fashion, to couple the relatively large displacements of the drum to those of the much smaller oval window of the cochlea. Together then, the ossicles function as a mechanical transmitter and impedance-matching device between the drum and cochlea. The middle ear structures have the additional function of protecting the cochlea from overly intense stimulation (48). A loud sound produces reflex contraction of the muscles that are attached to the ossicles, thereby attenuating their motion.

Of the three structures that make up the ear, the cochlea is the most complex. Externally, the cochlea is a bony spiral, coiling upon itself in turns of decreasing diameter along a central core into the temporal bone of the skull. In mammals there are about three such turns. A drawing of a section through the middle of the human cochlea is shown in Fig. 7. In many mammals, the cochlea protrudes in part into an air-filled cavity of the temporal bone called the bulla. The bulla is separated from the middle-ear cavity by a thin bony partition. In the outer or basal turn of the cochlear spiral are two membranous apertures (Fig. 5): the oval window, opening into the middle ear and containing the foot plate of the stapes; and the round window, opening

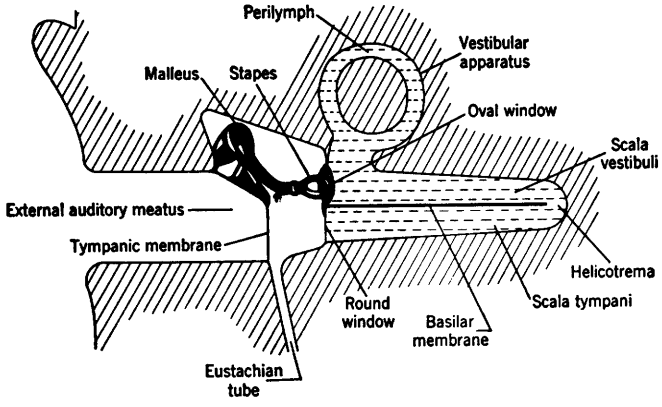

Fig. 5. Schematization of the ear, showing tympanic membrane, ossicles, and cochlea. For simplicity, the cochlea is represented as uncoiled. (From Békésy and Rosenblith, Handbook of Experimental Psychology (editor, S. S. Stevens), John Wiley and Sons, Inc., N. Y., 1951, p. 1076.)

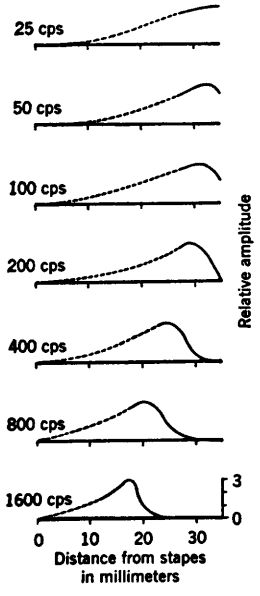

Fig. 6. Envelopes of the traveling waves produced along the cochlear partition by various input frequencies. The stapes was driven at a constant amplitude, and the amplitude of vibration of the cochlear partition was measured. (From Békésy and Rosenblith, Handbook of Experimental Psychology (editor, S. S. Stevens), John Wiley and Sons, Inc., N. Y., 1951, p. 1097.)

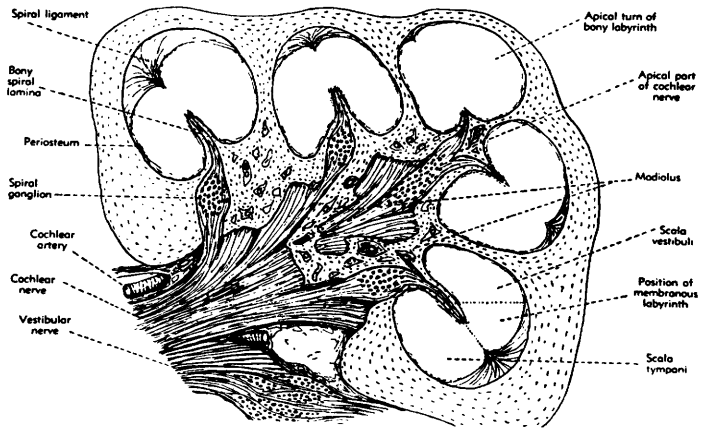

Fig. 7. Drawing of a section through the middle of the human cochlea. (From Rasmussen, Outlines of Neuroanatomy, William C. Brown Co., Dubuque, Ia., 3rd edition, 1943.)

into the middle ear cavity or into the bulla, when this structure is present.

Internally, the cochlea is divided longitudinally into three parts by two partitions that run the length of the spiral. A drawing of a section through one turn of the cochlea is seen in Fig. 8. The partitions are called Reissner's membrane and the basilar membrane; the three resulting divisions of the cochlea are called the scala vestibuli, scala media, and scala tympani. All three are fluid-filled. The first and last are connected through a small opening, called the helicotrema, at the tip or apex of the spiral. Two fluids are distinguished: the perilymph of the scala vestibuli and scala tympani, and the endolymph of the scala media. These fluids have very different properties, mechanically and chemically, a fact that plays an important role in the detailed functioning of the organ.

The oval window opens into the scala vestibuli, the round window into the scala tympani. Vibrations introduced at the oval window from the stapes are transmitted through the perilymph, and thereby to the endolymph and the basilar membrane. A compression at the oval window produces a movement of the basilar membrane away from scala vestibuli; a rarefaction produces a movement away from scala tympani. The round window serves to equalize the pressure in the perilymph, and its motion complements that of the oval window.

Sensory cells of the auditory system are imbedded in a structure known as the organ of Corti, which lies on the basilar membrane within the scala media (Fig. 9). Two sets of sensory cells have been distinguished, each running the length of the basilar membrane. These are the inner and outer hair cells; their bristle-like endings protrude from the surface of the organ of Corti, and may be attached to, or touch, the tectorial membrane, which is suspended like a canopy above them. The outer hair cells are the more numerous, lying in three or four parallel rows; there seems to be just a single row of inner hair cells. In all, there are about 20,000 outer hair cells

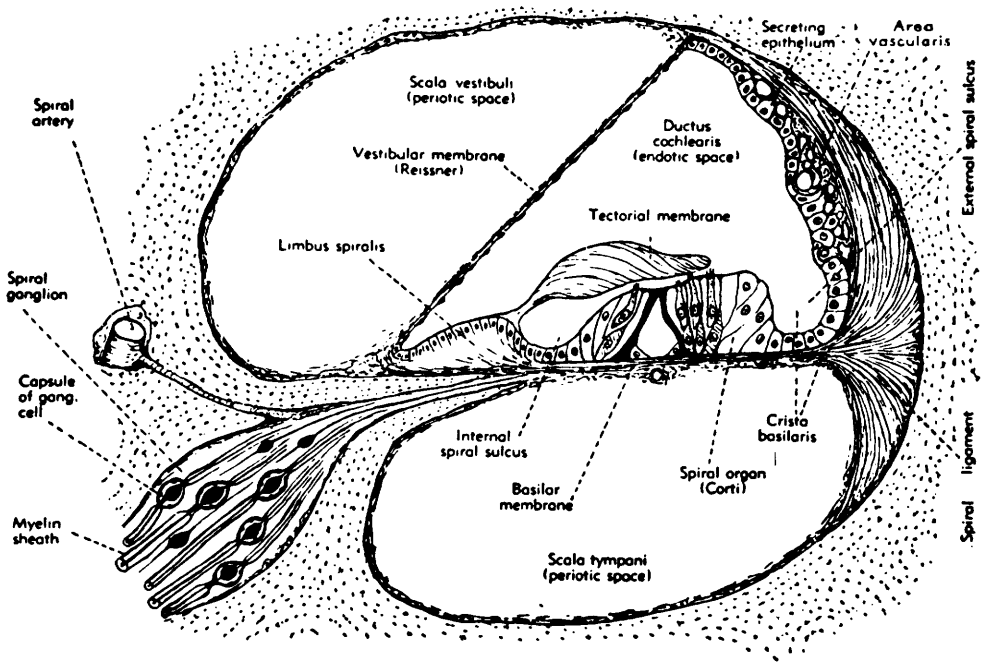

Fig. 8. Drawing of a vertical section through one turn of the human cochlea. (From Rasmussen, Outlines of Neuroanatomy, William C. Brown Co., Dubuque, Ia., 3rd edition, 1943.)

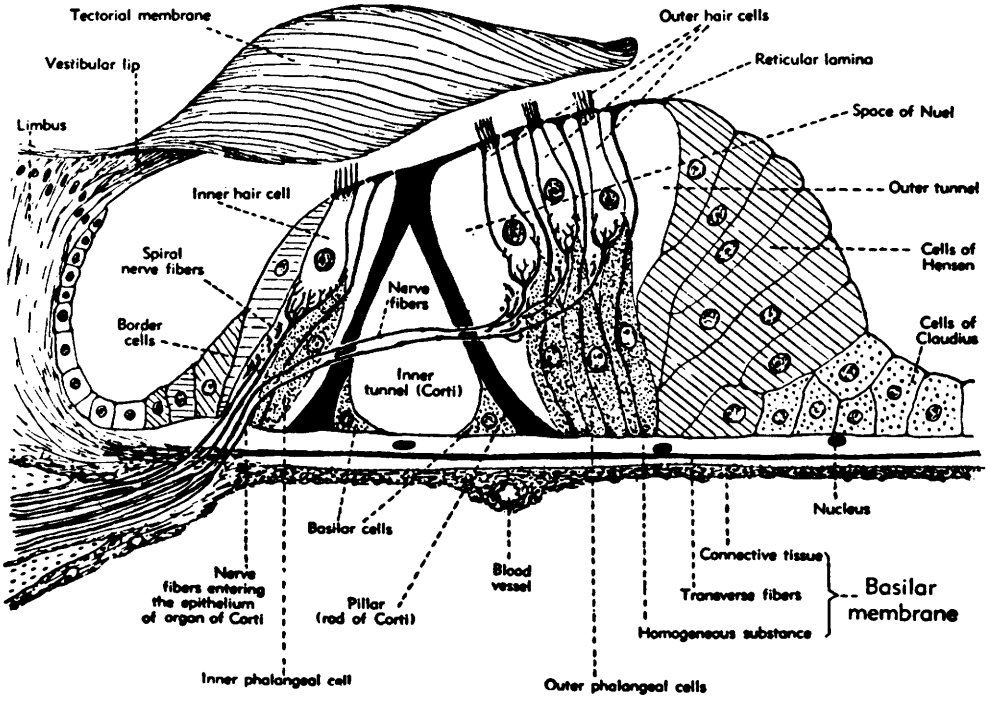

Fig. 9. The organ of Corti and the basilar membrane in greater magnification (compare Fig. 8). (From Rasmussen, Outlines of Neuroanatomy, William C. Brown Co., Dubuque, Ia., 3rd edition, 1943.)

and 3500 inner hair cells (44).

The hair cells appear to "synapse" with the very fine dendritic terminals of the auditory fibers, which then run through the basilar membrane and to the central core of the cochlea. There they merge in a spiraling bundle to form the auditory part of the eighth nerve (Fig. 7), which makes its exit from the cochlea beneath the first turn through a bony aperture known as the internal meatus. The cell bodies of the fibers from each turn occur in clusters, or ganglia, shortly before the fibers enter the central core. It is characteristic that in this spiraling bundle, adjacent sections along the basilar membrane give rise to adjacent fibers. In this way the topography of the cochlea is largely preserved in the cochlear bundle. The innervation of hair cells by fibers appears to be nearly one-to-one for inner hair cells and many-to-many for outer hair cells (44).

There has been much speculation about the mechanism of excitation at the hair cells. It has at various times been suggested (a) that the motion of the basilar membrane relative to the tectorial membrane produces mechanical movement of the hair tuft which, through the hair cell, brings pressure to bear on the terminal fibers, thus exciting them mechanically; (b) that the motion of the hair tufts causes the cell to produce a chemical that excites the fiber endings; and (c) that the motion of the hair tuft serves either to produce or modulate a potential across the hair cell, and that the potential change thereby produced excites the dendrites (49, 50). However, it is generally agreed that excitation occurs through the hair cell, and that motion of the hair tuft is somehow essential to this process.

2. The Electric Potentials of the Cochlea

A great deal of effort has been expended in exploring the electric potentials of the cochlea. This subject is complex, and a comprehensive survey would carry us far afield. Briefly, the facts are these. In 1930, Wever and Bray (51), recording from the eighth nerve of the cat, detected an electric response to auditory stimulation which they assumed to be the response of the auditory nerve. Amplified and led to a loudspeaker, this response reproduced reasonably faithfully the acoustic input to the ear. Speech could be understood and music recognized. As a result, it was at first thought that the eighth nerve reproduced auditory input waveforms in the envelope of its neural response. It was not until 1934 that Davis and his associates, by differentially recording from the eighth nerve, showed conclusively that two separate potentials were involved (52, 53). One, a local potential, originating in the cochlea and reproducing the mechanical input, they named the cochlear microphonic. The second component, the response of the eighth nerve, was shown to have all the properties of a well-behaved sum of action potentials.

Two lines of investigation have since developed, one centering on the neural response and the problem of the coding of auditory signals, the other seeking the source and function of the cochlear microphonic. The obvious speculation that the microphonic is the immediate stimulus of the action potential has never been conclusively demonstrated.

The time relations involved appear to be wrong, the onset of the neural response coming 0.2 msec to 1.0 msec later than the peak of the microphonic. This could, however, be accounted for by the conduction time in terminal fibers.

Attempts to discover the source of the microphonic have led to a number of interesting developments. At first it was thought that some mechanical-electrical transformation, attributable to the distortion of the hair cell, was involved (47). It was shown, however, that the size of the resultant potential (about 800 μv maximum) is too great to be accounted for if the energy source were simply the acoustic wave (54). Then followed the discovery that there exists across the basilar membrane, between the endolymph and perilymph, a large potential difference (about 75 mv) (55). This result led to the hypothesis that the movement of the hair tufts changes the resistance or capacitance of the hair cells, thereby modulating the potential difference across the basilar membrane. Only the resultant modulation is observed through capacity-coupled amplifiers, and this constitutes the microphonic response (49).

That the cochlear microphonic originates in the neighborhood of the hair cells appears to be fairly well established (49). The proponents of the theory of electrical excitation claim that the current flow connected with this potential variation across the hair cells stimulates the dendritic terminals of the auditory neurons. There is also some incomplete evidence that when the cochlear microphonic is artificially modified, the neural response changes in the expected direction. But whether this indicates a parallel or a causal relation between the two phenomena is as yet uncertain. Other local potentials have been observed whose relations in time to the neural response make them candidates for the excitatory role (56).

3. Frequency Response of the Cochlear Partition*

As a result of the important role that pitch has in hearing, there has been a great deal of interest in the frequency response characteristics of the cochlear partition. Helmholtz viewed the cochlear partition as a collection of sharply tuned bands, each running the width of the cochlear spiral. In this way the cochlea could function as a Fourier analyzer, the amplitude of vibration of each band being proportional to the Fourier coefficient of the corresponding frequency. This view was entirely upset by the experiments of Békésy, who showed that the basilar membrane is not under tension (45, 57). His observations indicate that sinusoidal excitation at the oval window produces a traveling wave, rather than a resonance, along the cochlear partition (45, 58, 59). Békésy demonstrated directly that there is some frequency selectivity along the length of the cochlear partition (see Fig. 6 and refs. 45, 58). The basal end is more responsive

*The cochlear partition consists of the scala media and the two membranes which bound it (the basilar membrane and Reissner's membrane); the auditory receptors or hair cells are within the cochlear partition, embedded in the organ of Corti on the basilar membrane (see Fig. 9). It is in terms of the excitation patterns evoked in these receptor cells that the response characteristics of the cochlear partition are important.

to high frequencies; the apical end, to low frequencies. But the tuning is not very sharp. Starting with a very low frequency, the whole partition is excited, but maximally at the apical end. As the frequency is increased, the displacement maximum of the response envelope moves toward the oval window. The amplitude cutoff on the apical side of the maximum is quite sharp; on the basal side it is very slow. Indeed, the basal end responds to all frequencies within the range of hearing.

In summary, the result of sinusoidal excitation at the oval window is a traveling wave, along the cochlear partition, whose point of maximum amplitude along the partition is a function of the input frequency. Superposition of two inputs of different frequencies does not result simply in a superposition of amplitude characteristics. In other words, we are dealing with a nonlinear response system.

4. The Neural Response

An electrode placed on the round window in the cat, and in other mammals, detects a response that is predominantly microphonic (Fig. 12). If one wishes to study the neural response, it is first necessary to reduce the microphonic. This can be accomplished in several ways. Davis employed a concentric bipolar electrode for this purpose (52). Another technique, used in conjunction with pure tone stimulation, consists of recording from the round window and of introducing into the response signal a sine wave of the same frequency as that of the stimulus; its phase and amplitude are then adjusted until cancellation of the microphonic is achieved, leaving only the neural component (60). Finally, it has been found that there are locations outside of and within the bulla of the cat at which the microphonic response is substantially eliminated, whereas the neural is left intact (61). The success of this method depends on the fact that the sources of the two components are in different places and differently oriented. Thus a neutral position with respect to one of them can be found.

All of these methods have advantages and disadvantages. The second is perhaps best for pure tones but is difficult to apply in the case of arbitrary stimuli. The first method is the most direct and gives results that are most easily interpreted. However, it involves exposing the eighth nerve (not a simple operation), whereupon questions of damage from electrode placement and from drying arise. The last method leaves the animal intact and is suitable in a fairly wide range of stimuli; however, its success depends on the conductivity of the interior surface of the bulla. If that surface is wet, the microphonic is conducted to all locations.

The method used in the series of experiments described in the following sections of this report is the last one discussed above, that of electrode placement.

5. Neural Mechanisms of Frequency Coding

As we mentioned, Davis used a bipolar electrode to record directly from the auditory nerve. Having isolated the neural component of the response, he was interested in exploring the response characteristics of the auditory bundle as a function of the

frequency of a sinusoidal stimulus. The results he obtained were compatible with the known properties of A fibers (52, 53). Up to a stimulus frequency of about 800 cps, the response followed the stimulus in frequency and maintained nearly a constant amplitude; at about 800 cps the response amplitude abruptly dropped in half, although still following in frequency; near 1600 cps another abrupt change in amplitude was noted. The interpretation was clear: up to 800 cps, each stimulated fiber in the auditory bundle was responding to every cycle; from 800 cps to 1600 cps each fiber was able to respond only to every other cycle, because of the absolute refractory period; and so on.

Other investigators have confirmed these results. It has also been found that above 2000 cps (approximately), responses to single cycles can no longer be observed. Instead, only a response to the onset of the tone is seen. Whether this involves a real change in the mechanism of frequency coding or indicates the limitations of our detecting methods is not clear.

The apparent dichotomy of mechanism noted above, occurring in the cat at about 2000 cps, has a bearing on a controversy of long standing (46). The question is this: Is frequency information coded into the eighth nerve in terms of the place on the basilar membrane excited, or on the basis of the frequency of impulses in individual fibers? For a long time, as a consequence of Helmholtz's dominant position, the place theories held sway. The Wever-Bray effect and then Davis' work gave impetus to the frequency theories. Békésy's investigations did much to clarify the situation. At low frequencies no place theory is likely to hold, since the entire partition is excited. At high frequencies, however, where the system apparently can no longer follow the stimulus, there is an amplitude peak and a sharp amplitude cutoff on the cochlear partition. The tendency today, then, is to acknowledge both coding methods, one predominating at low frequencies, the other at high frequencies, and both, perhaps, involved in the middle range.

6. Neural Responses to Clicks

A click is a brief acoustic stimulus, produced by introducing an electric pulse of rectangular shape into an earphone. The resultant acoustic pulse is not rectangular but has a waveform that is characteristic of the phone and of the acoustic coupler. Figure 10 shows the acoustic waveform produced by introducing an electric pulse of 0.1-msec duration into an earphone (PDR-10), coupled to a one-cubic-centimeter cavity. (This phone was used throughout this series of experiments.)

The present investigation is concerned with the ensemble response of first-order auditory neurons, without regard to their frequency selectivity. For this purpose it seemed to us that an acoustic click was an appropriate stimulus (62). Its rapid rise evokes a coherent response from the neural population; its broad frequency character precludes the interpretation of these results on a frequency basis. In Fig. 10 we see that, with a 0.1-msec electric pulse, the initial rise of the acoustic stimulus occurs in about 0.1 msec, a time considerably shorter than the period of natural vibration of

the ossicles (about 0.5 msec). Under these conditions, the rising phase of the acoustic stimulus appears to the ossicles as an impulse; it is our feeling that this rising phase alone is effective in producing firing of neural elements.

In Fig. 11 is shown an electrophysiological response to the acoustic click of Fig. 10; the recording electrode was located near the round window. The microphonic is labeled M. Note that it begins about 0.3 msec after the delivery of the electric pulse (the latter coincides with the beginning of the trace). This is just about the time required for the stimulus to travel from the phone to the eardrum of the cat (about 8 cm). Following this, at an interval of about 0.6 msec, is the onset of the response labeled N_1, resulting from the coherent firing of first-order auditory neurons. The component labeled N_2 is probably, at least in part, the response of second-order auditory neurons (63). There is some evidence that a portion of the N_2 response results from the repetitive firing of first-order elements (64).

7. Noise as a Stimulus

Like a click, noise has a broad frequency character; unlike a click, it is incoherent, and the excitation it may produce is unsynchronized, and, by our recording methods, undetectable for measurement. Nevertheless, its effect can be measured indirectly.

If the response to a click in the presence of audible noise is compared to the response to a click of the same intensity, presented alone, one finds a sizable reduction in the amplitude of the neural response (62, 65, 66); the microphonic component, however, remains unchanged. Some of these results are shown in Fig. 37. This "masking" effect was first discovered by Davis (53). Davis' theoretical interpretation is simple. Neurons are continually being excited by the noise; when a click comes along, some fibers which ordinarily would have responded are refractory, in threshold or in amplitude, and thus are unable to respond or to respond fully. The phenomenon is therefore sometimes called the "line busy" effect.

8. Methods of Distinguishing Neural from Microphonic Components

Masking may be used to distinguish microphonic from neural responses, since the microphonic, being the response of a transducer, is left substantially unchanged by noise, while the neural is reduced by it. Still another method of distinguishing neural from microphonic components consists of simply reversing the click polarity. The microphonic reverses sign; the neural, the sum of negative action potentials regardless of the character of the stimulus, is left substantially unchanged. This effect is illustrated in Fig. 12, where the highly microphonic responses to two clicks of equal intensities and opposite polarities are shown, together with their sum. The latter clearly has the character of a neural response, the microphonic components having cancelled under addition.

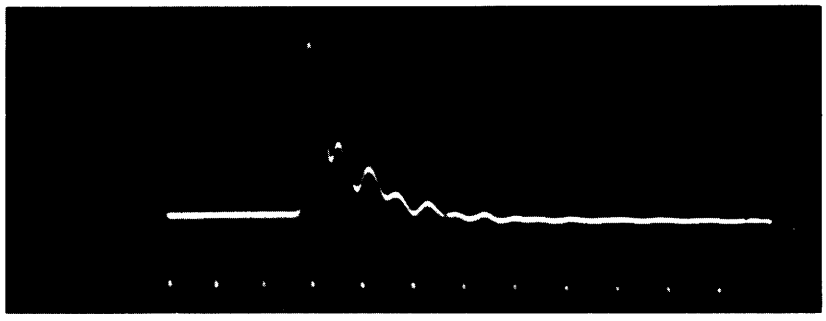

Fig. 10. The acoustic output of the PDR-10 earphone into a 1-cc cavity, when the input to the phone is a rectangular pulse of 0.1-msec duration. The response was measured with a Western Electric 640 AA microphone. Time marker, 2000 cps.

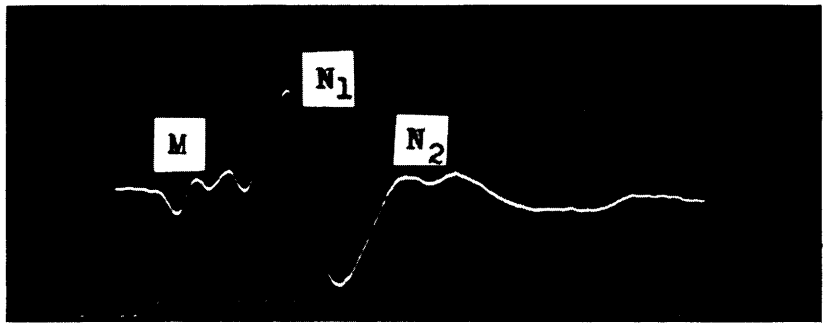

Fig. 11. An electrophysiological response to the acoustic click shown in Fig. 10, recorded from the cat at a relatively microphonic-free location near the round window. The microphonic and neural components of the response are labeled M and N, respectively. Time marker, 10,000 cps.

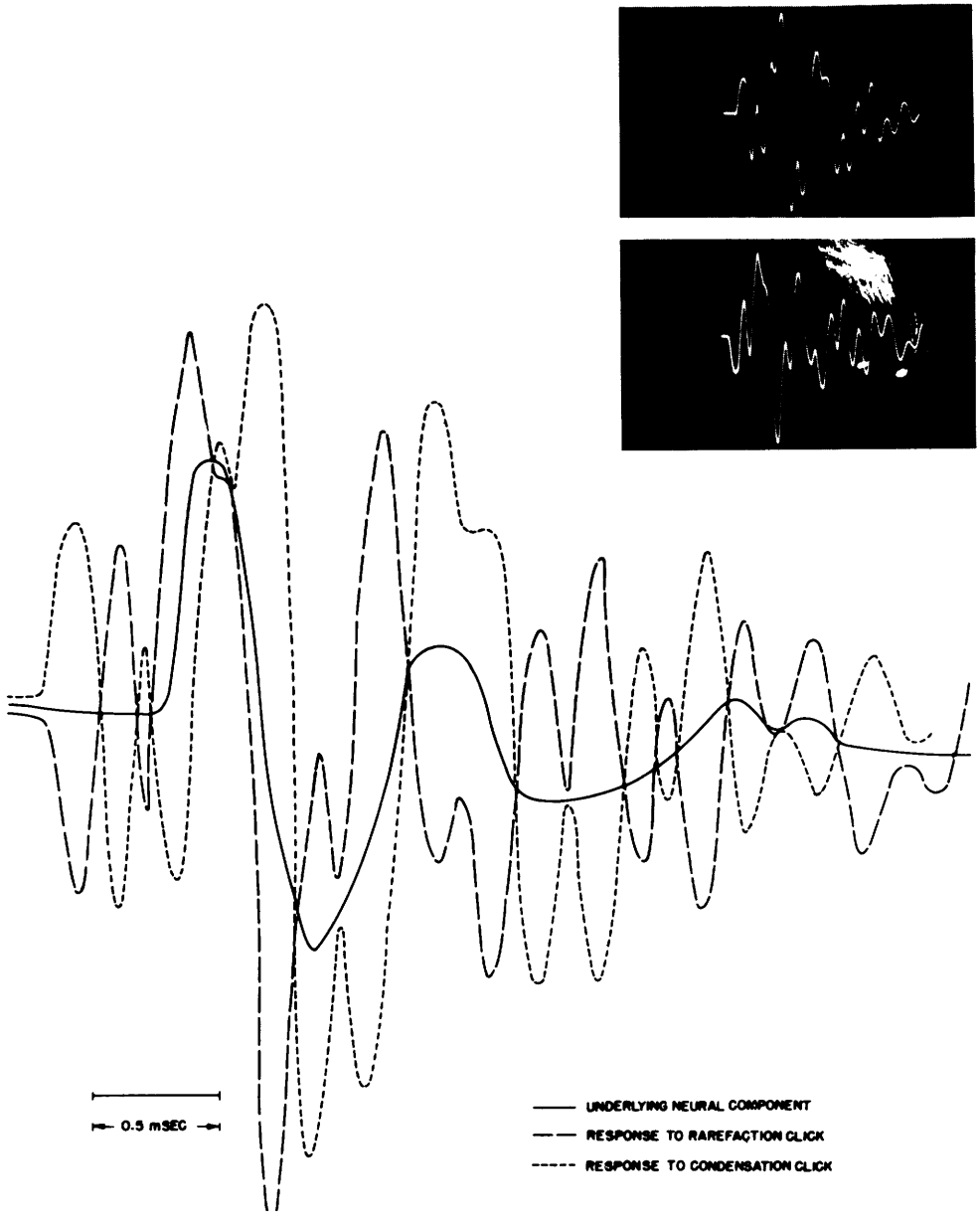

Fig. 12. Upper right: Photographs of the highly microphonic responses to two clicks of equal intensity but opposite polarity. The electrode was located on the round window. Center: Traces of the responses shown in the photographs above, together with their sum (solid line). The microphonic components are approximately mirror images of each other and therefore cancel under addition; the neural components add constructively.

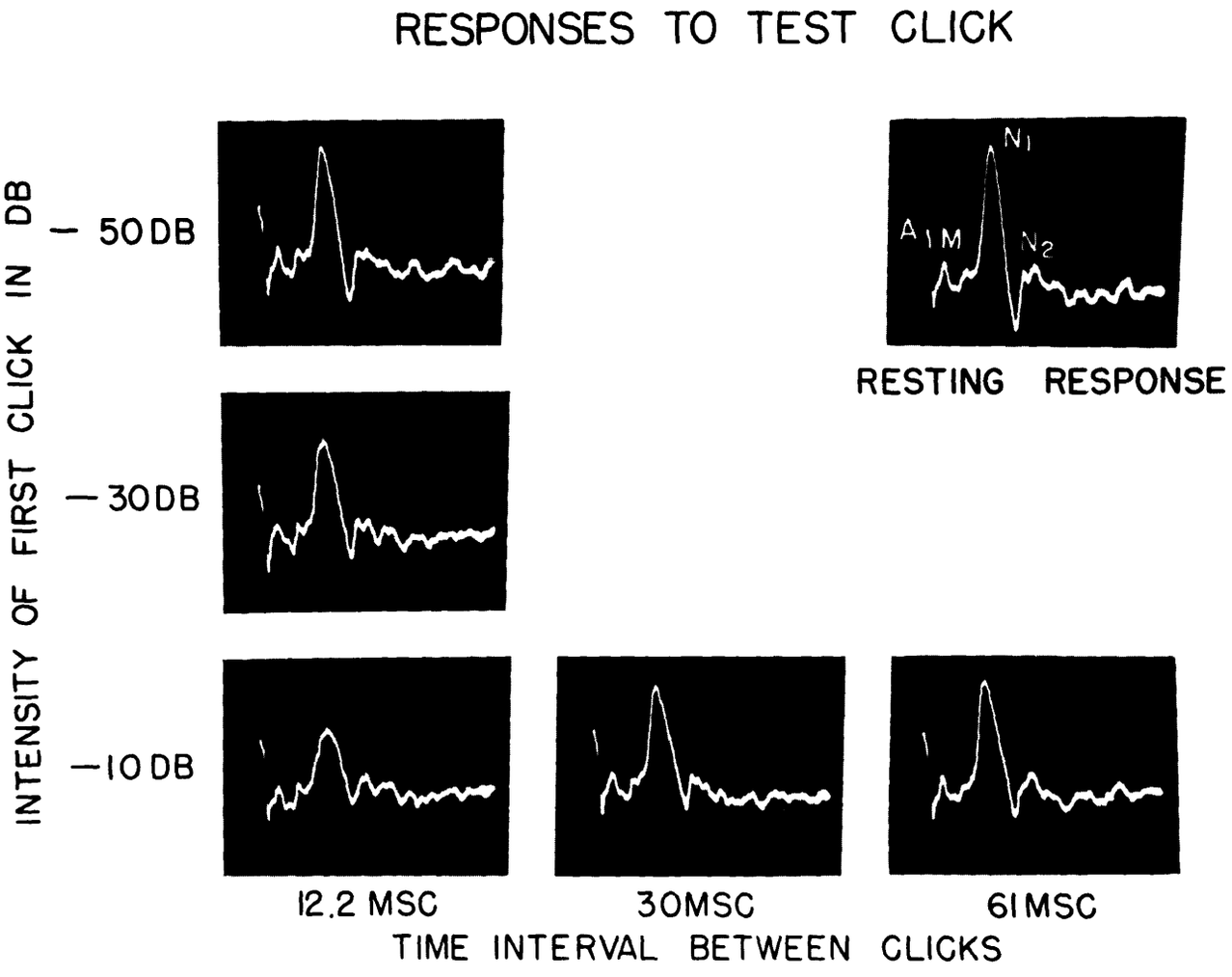

Fig. 13. Two-click paradigm: the responses shown are to a constant-intensity (-45 db) second click. The vertical set shows the effect of varying the first click intensity; the horizontal set shows the effect of varying the interval between the pair. Upper right: Response to a -45 db click presented alone. (From W. J. McGill, Ph. D. thesis, Harvard University, 1952.)

9. Two-Click Experiments

Another set of experiments studies the effect of a first click on the response to a second click. This is the classic condition-test paradigm. It was used by McGill and Rosenblith (67, 68) to investigate the effect of firing on the thresholds of peripheral auditory elements. Their results (some of them are given in Fig. 13) show that the response to a test click is smaller than the response to the same click presented alone, even when the conditioning and test clicks are separated by as much as 100 msec. These long-lasting effects may reflect threshold changes in the hair cell, in the terminal fibers, or in the hair cell-terminal junction; it is unlikely that threshold changes of the necessary magnitude could persist for so long a time in the axons of the auditory nerve.

B. THE HIGHER AUDITORY CENTERS (3)

The following is a very brief description of the auditory nervous system above the most peripheral station. This is the subject of a very large literature. The material presented here is very selective and is meant simply to provide a certain over-all perspective; it is related only indirectly to the material of the following sections.

We have discussed at considerable length the cochlea, hair cells, and the eighth nerve. We have pointed out that the ganglia of the peripheral auditory neurons are situated just before the fibers enter the central core of the cochlea, and that the bundle then passes through a channel in the temporal bone called the internal meatus. Thereafter these neurons synapse in the medulla with second-order cells, which synapse, in turn, at the midbrain level; the chain continues through several stages, terminating finally at the cerebral cortex. A typical chain from cochlea to cortex consists of five neurons and four synapses. At several of these levels, fibers from one side cross to the other, so that at the level of the medulla and above, each ear is represented bilaterally. Figure 14 shows the well-known pathways of the ascending specific auditory system in the cat (69). Table 1 gives the approximate number of cells at each auditory level in the monkey, as determined by Chow (70). From 30,000 first-order fibers, the system expands to ten million at the level of the cortex.

Responses to clicks can be recorded at every level. A few of these are shown in Fig. 15 (62). The increase in latencies following the stimulus are attributable to neural transmission and synaptic delay times. Little simultaneous recording has been done at different levels. What has been done (at cortex and periphery, for example) serves to emphasize the lack of apparent correlation between what may be regarded in some sense as the input and output stages of a network; it also points up the extreme nonlinearity of the system we are dealing with and the need for more relevant measures of "coded information." The relationships of these physiological responses to the psychological phenomena of hearing have only been worked out to the point where we can say that such relationships exist. It should be borne in mind, in regard to the latter point, that most electrophysiological work has been done in

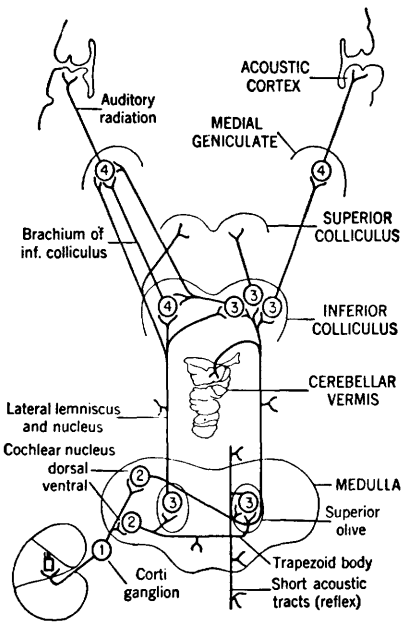

Fig. 14. Schematic representation of the well-known pathways of the ascending specific auditory nervous system of the cat. (From Davis, Handbook of Experimental Psychology (editor, S. S. Stevens), John Wiley and Sons, Inc., N. Y., 1951, p. 1120.)

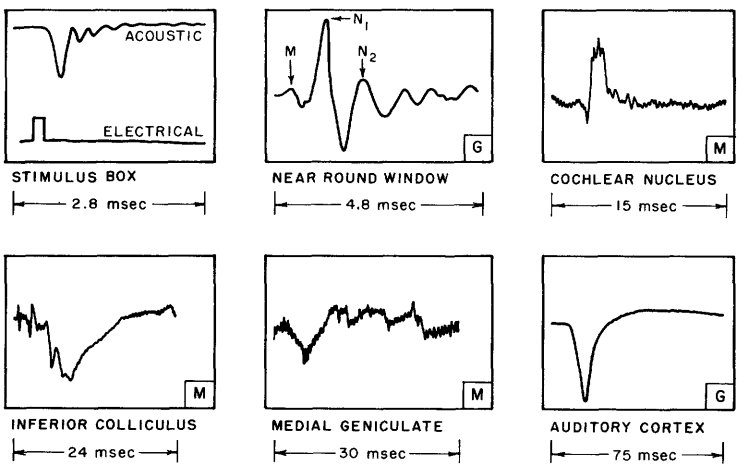

Fig. 15. Responses to acoustic clicks recorded at five stations of the ascending auditory system of the cat. Responses marked G were recorded with a gross electrode; those marked M, with a microelectrode. The acoustic stimulus is also shown. (From Rosenblith, Proceedings of the Symposium on Information Networks, Polytechnic Institute of Brooklyn, 1954.)

Table 1

Approximate Number and Density of Cells at Each Level of the Ascending Auditory System of the Monkey.

Level of the Auditory System	Total Number of Cells (approx.)	Average Number of Cells in 0.002 mm^3
Cochlear nucleus	88,000	31
Superior olivary complex	34,000	29
Lateral lemniscus	38,000	--
Inferior colliculus	390,000	84
Medial geniculate (Parvocellular)	360,000	65
Medial geniculate (Magnocellular)	58,000	38
Auditory cortex	10,200,000	186

Note: These data were obtained by Chow (70) from cell counts on the central auditory systems of two monkeys. No data on the number of ganglion cells in the cochlear nerve of the monkey are available; in man, there are about 30,000 such ganglion cells. According to Chow, the monkey may have the same number and probably does not have more.

anesthetized rather than in behaving animals.

An attempt has been made to suggest the intricacy of this system. In the following, we confine ourselves to the relatively simple and more accessible peripheral stage of the auditory nervous system.

III. EXPERIMENTAL PROCEDURES

The data and conclusions of the following sections are based on the electric responses to auditory clicks obtained from nine anesthetized adult cats. The preparation of the animals and the stimulating and recording techniques are discussed below.

1. Preparation of the Animal

Adult cats were anesthetized by intraperitoneal injection of dial in urethane (0.75 cc per kilogram body weight). If, after waiting thirty minutes to an hour, the animal was still unanesthetized, an additional 0.3 cc was injected intramuscularly or intravenously. At frequent intervals during the course of an experiment, the approximate level of anesthesia was checked by testing corneal, pinna, and withdrawal reflexes. Respiration rate was used as an additional criterion. Our object was to maintain the animal at as constant a level of anesthetization as possible with the crude indicators at our disposal. When one or several of these reflexes appeared, it was our practice to administer an additional 0.2 cc or 0.3 cc of dial. This procedure was at times overruled by other considerations.* Fortunately, the peripheral response with which we are concerned is relatively insensitive to the state of anesthesia, within wide limits. Moreover, dial is an extremely long-lasting anesthetic; the initial dosage will often render the animal unconscious for several days. Therefore, in an experiment performed over a period of a few hours, the state of the animal may be assumed not to change radically, in the absence of contrary evidence.

In about half of the cases, following anesthetization, the trachea was exposed and a canula inserted. This helped to prevent subsequent respiratory difficulties. In particular, we were interested in minimizing the noise of breathing, which would have a masking effect on the responses to clicks. The animal was then placed, with a heating pad under it, in a prone position with the head mounted rigidly in a head holder.

A thermometer was inserted rectally. The heating pad was regulated to maintain the cat's temperature at about 37° C. The temperature and humidity of the anechoic chamber, in which the animal was placed for recording, could also be controlled. In several animals, a thermistor, inserted beneath the collar bone, turned the heating pad on and off and thus automatically maintained the animal's temperature at a preset value.

An incision about three inches long was made along the midline of the head and extended at both ends away from the medial line. The skin was then laid back, and the external meatus, or ear canal, exposed. A hemostat was inserted under the meatus, and a length of heavy thread drawn under it. Thereafter, the canal was cut halfway through, close to the skull, and a plastic tube inserted far enough to allow the thread

*The task of maintaining a relatively constant state of anesthesia is a very difficult one, since the operational aspects of this conceptual "state" cannot at present be precisely defined; moreover, the effects of anesthesia upon the internal condition of the animal are known only in their grosser aspects.

about the meatus to be tied over it so that a tight seal was formed. Care was taken not to insert the tube too far, lest the drum be damaged. The other end of the tube was fitted with a coupler, to which the earphone could be attached later.

With the meatus exposed, an approach was made to the bulla, along the nuchal ridge. The bony covering of the bulla cavity was broken away in order to bring into view the round window and part of the cochlea.

The earphone was connected to the plastic tube in the meatus. An electrode was placed in contact with the interior surface of the bulla, and the reference electrode attached at an exposed place at the back of the neck. This completed the preparation of the animal for stimulation and recording.

2. Stimulation

A rectangular pulse, 0.1 msec in duration, was used to drive an earphone (PDR-10, No. A1604). The driving pulse was produced by a Grason-Stadler pulse generator, model 876-8-1, and amplified by a McIntosh power amplifier.

Attenuators allowed a total voltage range at the input to the phone of 145 db* (from 0 db to -145 db), in 1-db steps. At the reference level of 0 db, the voltage across the input terminals to the phone was 1.29 volts, and the peak output pressure of the phone into a rigid 1-cc coupler was about 125 db, with reference to 0.0002 dyne/cm^2.

Figure 10 shows the acoustic output of the phone when excited by the pulse described above; the phone was coupled to a 1-cc rigid cylindrical cavity, 1.85 cm in diameter, 0.38 cm deep; the response was measured with a Western Electric 640 AA microphone. The resonant frequency of the cavity was approximately the same as the resonant frequency of the ossicles, as estimated from the frequency of the microphonic component (compare resonance and microphonic frequencies in Figs. 10 and 11). It should be understood, however, that because of differences in shape and rigidity the acoustic response properties of the middle ear differ from those of the cavity used here in many other respects.

The phone has been shown to be linear ($\pm$0.5 db) up to the reference level of 0 db, the maximum stimulus level used.

The frequency response of the phone into the 1-cc coupler was measured under two conditions: (a) with the plastic tubing that connects the phone and coupler empty, and (b) with one section of tubing filled with cotton yarn. Both of these conditions were used in this set of experiments. There were two sections of tubing, each 3.3 cm long, with an inside diameter of 0.4 cm. The cotton filled the section nearest the phone. Figure 16 shows the frequency response characteristics of the phone, with and without cotton, as measured with a Western Electric 640 AA microphone. It is seen that the response of the earphone falls off sharply in the neighborhood of 7 kc. The effect of the

*Let A and B be voltage amplitudes. Then $A(db) - B(db) = 20 \log_{10} \frac{A(volts)}{B(volts)}$

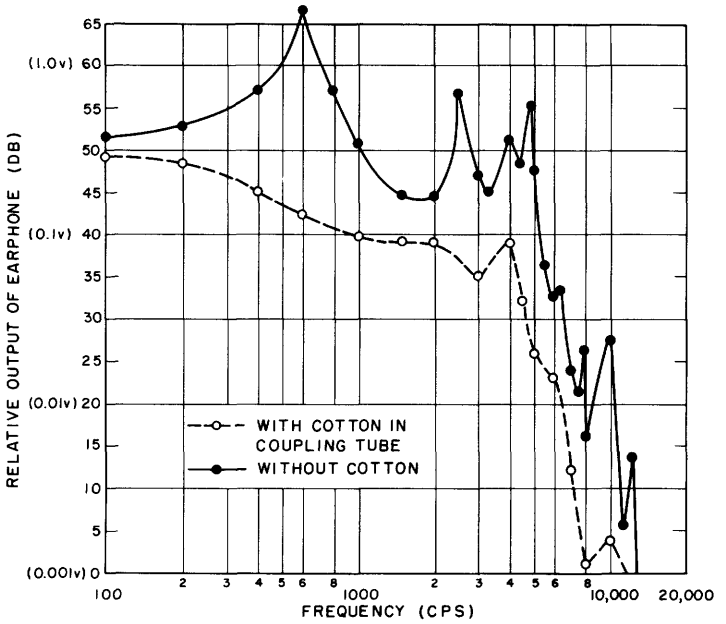

Fig. 16. Frequency response characteristics of the earphone (PDR-10) used throughout these experiments, under the two conditions (with and without cotton) described in the text. The earphone response was measured with a Western Electric 640 AA microphone.

cotton is to flatten the response curve, eliminating peaks caused by resonances in the connecting tube.

Our noise generator is a 6D4 gas tube in a magnetic field. The noise it produces is "white"; that is, it is characterized by equal energy in equal frequency intervals. In the early experiments, unfiltered noise was used; later, two filter sections were placed in series, set for 7 kc, low-pass; attenuation above this frequency was 36 db per octave. Finally, in a control experiment, filtered and unfiltered noise were peak-clipped. The clipping level was always equal to the rms amplitude of the noise being clipped.

The value 0 db for the noise was chosen so that, at the input to the phone, the rms amplitude of the noise was equal to the amplitude of a 0-db click. For unfiltered noise, this calibration requires correction, since the response of the phone falls off sharply for frequencies above 7 kc. By measuring the energy in the noise above 7 kc, we have shown that to effect this correction 12 db should be subtracted from the level settings.

3. Recording

Our electrodes were made of platinum wire, 0.2 mm in diameter. Records were taken from a number of locations within the bulla. A particularly favorable placement for microphonic free recording was found a few millimeters above the round window. As we have stated before, the reference electrode was generally placed in exposed neck muscle. These electrodes were connected to a differential input amplifier (Grason-Stadler model 221A) whose maximum gain is about 30,000. The response was filtered

20 cps high-pass (6 db per octave) and 5 kc low-pass (12 db per octave).

The amplifier output was used to drive a four-gun oscilloscope. The trace was triggered from the stimulus pulse. Two output channels were available, so that we were able to record simultaneously from two locations when it was desirable.

Responses were photographed with a Grass 35-mm camera on continuously moving film. The stimulus repetition rate was either one per second or 0.4 per second, and the rate of film transport was adjusted to prevent overlap of successive traces. Measurements were made on a microfilm reader.

In two of the early experiments, part of the data was analyzed directly, without photographing the responses, by means of an amplitude quantizing device (78) developed by Klaus Putter, formerly of the Research Laboratory of Electronics, M.I.T. Although this device greatly aided data analysis, certain aspects of its operation retarded the experiment, and for this reason its use has been reluctantly abandoned until appropriate modifications can be made.

IV. THE INTENSITY FUNCTION

1. Choice of Parameters

In Section II we discussed in some detail the response to an acoustic click, recorded from within the bullar cavity (Fig. 11). It was pointed out that the first neural component of this response, N_1, probably represents the sum of action potentials of first-order auditory neurons, or a transformation on such a sum. The problem of interpretation becomes extremely important when one attempts to quantify the stimulus-response relationship in terms of the number of neurons firing.

In Fig. 17 is shown a sequence of responses to clicks over a 90-db intensity range, obtained from Cat 307 (C-307). The location is essentially microphonic free. We observe that as the stimulus intensity is increased, the shape of the N_1 response changes. The most apparent change is an increase in the amplitude of N_1. In Fig. 18 we have plotted as a function of stimulus intensity the average values of a number of parameters which, to a considerable extent, characterize the N_1 response. Each point is the median of ten measurements on successive responses to identical stimuli (Fig. 17 shows one set of the ten)*. We call these curves intensity functions.

Let us return again to the basic problem of relating the N_1 response to the number of peripheral auditory neurons that fire. One might surmise that as the stimulus intensity increases, the number of neurons excited increases, and that this fact is reflected in a tendency for the relevant parameters of N_1 to increase. In Fig. 18 we have plotted the intensity functions in such a way that their near identity under a linear (proportional) transformation is emphasized. One might readily conclude that whatever these parameters do measure, they all measure approximately the same thing.

We shall make the assumption at this point that the parameters A_{pp}, A_{bp}, and α, all vary directly as the number of active neurons. This assumption may be regarded as a purely heuristic step, whose credibility depends on the consistency and success of the theory growing out of it. We shall hereafter confine our attention to the intensity function determined by the peak-to-peak amplitude of N_1. Frequently we shall speak interchangeably about the number of active neurons and the amplitude A_{pp}; in such cases, the discussion above will be understood to apply.

Figure 19 shows intensity functions recorded simultaneously from one animal at several locations. Again, each plotted point is the average of ten amplitudes. This and similar data suggest that the shape of the intensity function is substantially independent of electrode location.

In general, intensity functions recorded from a single electrode location show great

*Clicks were delivered at one per second. Ten responses were taken at -90 db; then the stimulus was changed to -80 db, and ten more responses were recorded; and so on, up to 0 db. The entire sequence was over in less than five minutes.

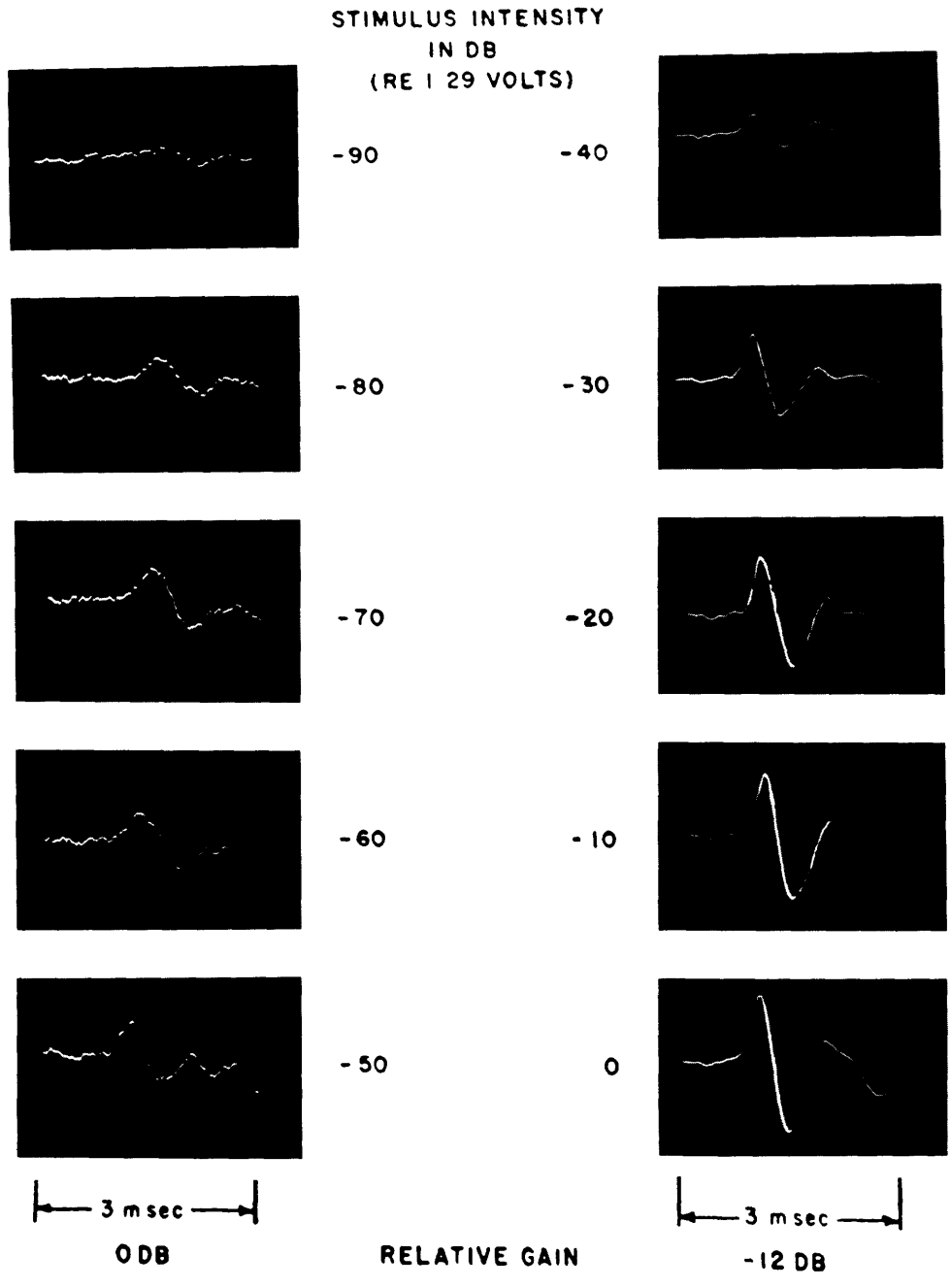

Fig. 17. Responses to clicks over a 90-db range (C-307). The electrode was at a nearly microphonic-free location above the round window. Note that the voltage gain of the recording equipment was reduced by 12 db (factor of 1/4) for stimulus intensities above -40 db.

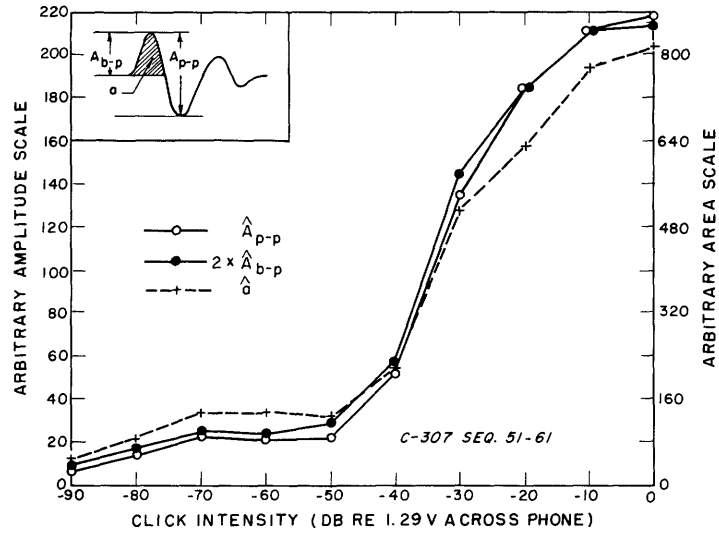

Fig. 18. Intensity functions (C-307). The quantities plotted are shown on the inset drawing at the upper left. Each plotted point is the median of about ten such measurements. The scales were chosen in such a way that the similarity of the different functions under a proportional transformation would be emphasized.

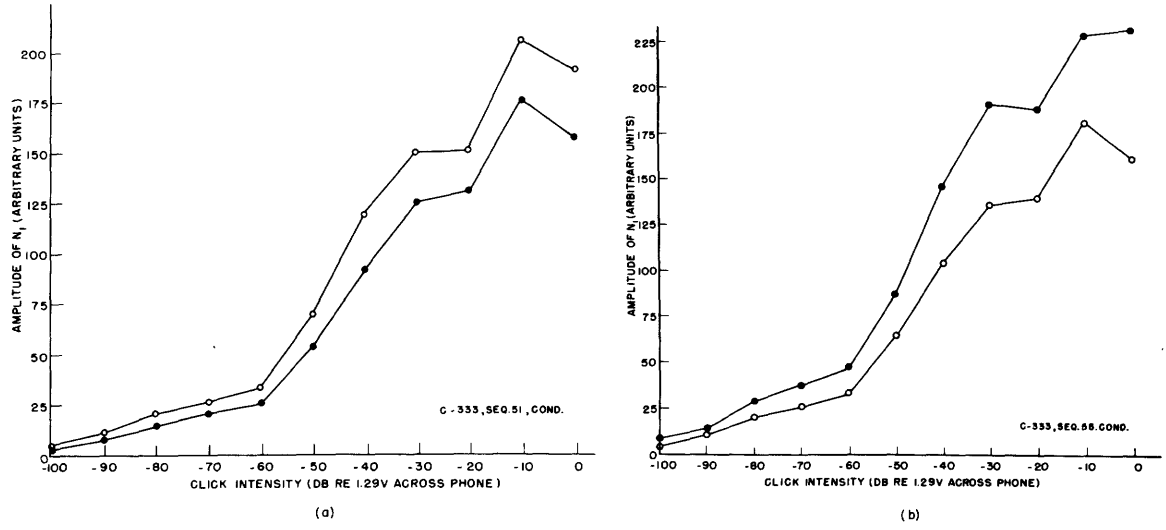

Fig. 19. (a) Intensity functions simultaneously recorded from two locations within the bulla of a cat (C-333). Each point is the median of about ten measurements. (b) Repetition of (a) with one of the electrodes (solid circles) at a new location.

stability when observed at different times. This stability was used as an empirical monitor of the constancy of the physiological state of the preparation.

2. Independence of Successive Responses

It is known that the response to the second of two successive stimuli will be reduced in amplitude for time intervals up to 0.1 sec and perhaps more (67, 68). In the experiments described here and in the following sections, we are delivering without interuption up to a hundred identical clicks at a fixed rate. Since it is essential to our interpretation (Section V) that each response reflect the resting state of the system, the interval between successive presentations must be sufficiently great to rule out the possibility of fatigue or other interaction. On the other hand, one cannot spread the clicks out too much without running the risk that, in the course of the total experiment, which consists of many such sequences, the physiological state of the animal will change considerably. That is, we require (a) that successive data be statistically independent, and (b) that their statistical character not change during an experiment.

We used clicks at both one per second and 0.4 per second. In neither case did we note any significant correlation between successive response amplitudes. Where intensity functions were obtained from very long sequences (100 takes per stimulus setting) and many stimulus values, a check on the stability of the preparation was maintained by comparing abbreviated intensity functions (3 to 5 takes per setting), run at intervals during the course of the experiment.

3. Character of the Intensity Function

Intensity functions from a single animal tend to be similar, but considerable variations are observed from one animal to another. Figure 20 shows intensity functions for each of the animals studied, obtained at relatively microphonic-free locations. In general, there is little microphonic present up to about -50 db; beyond this value, as we pointed out before, one must find locations that are neutral with respect to the source of the microphonic.

If the interior of the bulla is wet, as it sometimes is, the electrical spread on the surface renders all locations highly microphonic. In such cases suitable locations can often be found outside the bullar cavity (61); since the response here is greatly attenuated, such locations are useful only at medium and high intensities (greater than -60 db). Thus we are sometimes faced with the problem of fitting together two overlapping intensity functions. Needless to say, whenever it was possible, an entire experiment was completed at a single location. The most favorable microphonic-free locations are found a few millimeters above the round window, at a position of approximately one o'clock.

As seen in Fig. 17, the response first becomes visually detectable at a stimulus intensity between -90 and -100 db. The level at which visual detection of a response is first possible will be referred to as the response threshold. Since N_1 is nearly always

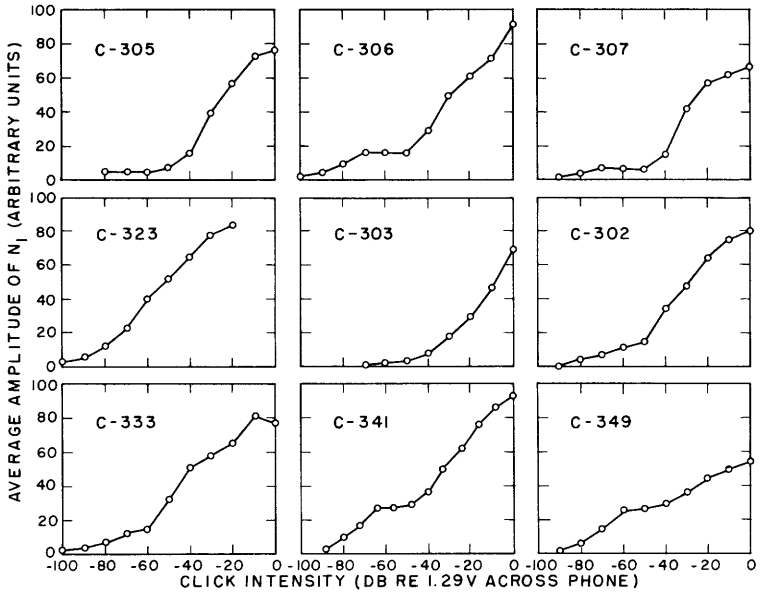

Fig. 20. Intensity functions of each of the animals studied. In all cases, the electrode locations at which these data were taken were selected so that the microphonic content of the response would be minimized.

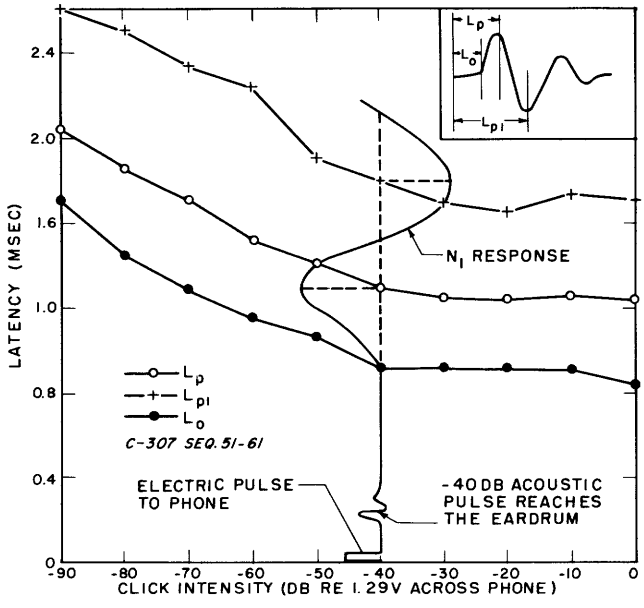

Fig. 21. Latencies of the onset, peak, and negative peak of N_1 as a function of stimulus intensity (C-307). The inset drawing at the upper right identifies these quantities. Latencies are measured from the time of the stimulus pulse to the earphone. Each plotted point is the average of about ten such measurements.

the first component to appear, the N_1 threshold will generally be identical with the response threshold.

It is assumed that animals with response thresholds above -90 db do not possess "normal" hearing, and these were, in most cases, arbitrarily eliminated from consideration. A few such animals were retained and studied. The intensity function of one of these (C-303) is shown in Fig. 20.

Despite their considerable differences, there are significant features which all of the functions of Fig. 20 have in common. In particular, nearly all of them exhibit a two-stage growth, the point of inflection between the two growth components occurring at about -60 db. In some preparations the two components are separated by a very definite plateau that extends over a range of approximately 10 db. This behavior suggests the possibility that the contributing neurons might be usefully classified as "sensitive" or "insensitive." This line of thought is developed further in the following section; its consequences are examined in Sections VI and VII.

4. The N_2 Response

Following N_1 is a second, and sometimes a third and fourth peak, neural in origin. These have variously been reported as being the result of (a) repetitive firing of first-order neurons and (b) the response of higher order fibers. Our data indicate that the N_2 response in the cat is to a large extent the response of second-order (cochlear nucleus) elements. This conclusion is based primarily on the fact that by moving the electrode from above the round window toward the cochlear nucleus (along the nuchal ridge), we find that we can differentially affect N_1 and N_2. One finds locations where N_2 is larger than N_1, just the reverse of the situation at the round window. If N_1 and N_2 originated in the same elements, one would expect that changing the location of a distant electrode could have no effect on their relative size.

There is the possibility that N_2 represents a superposition of effects (a) and (b) above. This is made plausible by the double peak of N_2 which is frequently observed (Figs. 11 and 17).

Finally, the time interval between the peaks of N_1 and N_2 was, in some cases of intense stimulation, found to be as short as 0.4 msec; the length of the absolute refractory period alone makes repetitive firing implausible under these circumstances. The interval is, on the other hand, consistent with the synaptic delay time that might be encountered between first- and second-order auditory neurons in response to a strong stimulus.

5. Latency Intensity Functions

The temporal parameters of the response are all far more stable than are those associated with amplitude. In Fig. 21 we have plotted the latency of the peak of N_1 against stimulus intensity for C-307. We have also obtained from the same data the latency of the onset of N_1 and the latency of the negative peak as a function of stimulus

intensity. The inset in the same figure shows the relation of these parameters to the response. We note that as the stimulus intensity increases, the latency decreases, reaches a minimum, and remains there. It would actually be more appropriate to measure latency from the onset of the microphonic, since this represents the time at which the stimulus reaches the hair cells. This time is stimulus-independent, however, so that the shape of the curve remains intact.

V. THE MODEL

A natural way of describing the response behavior of a nerve bundle is in terms of the response characteristics of the neurons of which it is composed. An approach of this sort will be taken here. Properties of hypothetical neural units will be defined; the behavior of aggregates of such units will then be deduced and interpreted in terms of the N_1 response. It should be pointed out that the neural unit is not to be regarded as a model of the neuron. We are dealing here with the response of a system consisting of hair cells, neurons, and hair cell - neural junctions. The characteristics of the N_1 response are determined by properties of all of these. It should also be recalled that the hair cells and neurons are not connected in a one-to-one fashion. The difficulty of singling out a definite element or group of elements that can be assigned a unitary role becomes apparent. The simplest procedure is to define the neural unit abstractly by its properties alone, and to relate it only loosely to physical structures.

1. Properties of the Neural Unit

The following properties are postulated:

(a) A neural unit is capable of responding to suitable stimuli. In so doing, it obeys the all-or-nothing principle. That is, it is characterized by only two states: maximal response or no response.

(b) The neural unit fails to respond to stimuli $S < S_T$ and will respond to any stimulus $S > S_T$. A threshold property is thereby defined; S_T is the threshold of the unit with respect to the mode of stimulation S.

(c) The threshold S_T of a unit fluctuates in time. No attempt is made to specify the detailed time course of this fluctuation. Rather, the description is limited to a specification of the fraction of the time the unit's threshold is to be found in any stimulus interval ΔS. Reinterpreting this, we may state that the threshold properties of a unit are given by specifying the probability of finding its threshold in any stimulus interval – that is, by a probability distribution. This distribution is assumed to be stationary for a resting unit. It is, in addition, assumed that the characteristic time of threshold fluctuation is very small compared with the interval (approximately 1 sec) between stimulus presentations, and that successive responses of a single unit are, at this rate of stimulation, statistically independent.

(d) The firing of a unit alters its threshold distribution, which then becomes a function of the time $\Delta\tau$ since firing. For times $\Delta\tau$ that are sufficiently long (greater than 0.1 sec), the unit's threshold returns to the resting distribution. For a sufficiently small $\Delta\tau$ (taken here as less than 2 msec), the unit will respond to no stimulus, whatever its intensity. This time interval is called the absolute refractory period of the neural unit.

(e) We assume, moreover, that if a unit responds at all, it always does so with the same response amplitude. This is a somewhat stronger assumption than the

all-or-nothing principle. It is made for the sake of convenience, since it greatly simplifies the calculations.

2. Populations of Neural Units

We define a population of neural units as an aggregate of units whose properties (a) to (e) involve identical parameters. All units of a single population are therefore characterized by the same threshold probability distribution. It is assumed, moreover, that the threshold fluctuations of any pair of units are statistically independent. This constitutes what we might call the zero-order interaction approximation.

Units that fire in response to a stimulus are assumed to fire synchronously, so that the total response amplitude is simply the sum of all the unit response amplitudes. Within a single population, all units are characterized by the same response amplitude. If $n_1, \ldots, n_k$ represent the number of fired units in k populations, $r_1, \ldots, r_k$ the unit response amplitudes, and A the total response amplitude, we have

$$A = n_1 r_1 + n_2 r_2 + \ldots + n_k r_k = \sum_{1}^{k} n_i r_i \tag{5.1}$$

Considerations of latency and duration of response have been entirely omitted in this development. This evidently is another possible dimension along which the model could be extended.

3. Development of the Intensity Function

We wish to determine the response characteristics of a system of neural units as a function of stimulus intensity.

(a) One population. Consider a population of N neural units, all characterized by the probability distribution function D(S) of Fig. 22. The probability that, at a given instant, the threshold of a given unit lies between S_1 and S_2 is equal to the area under

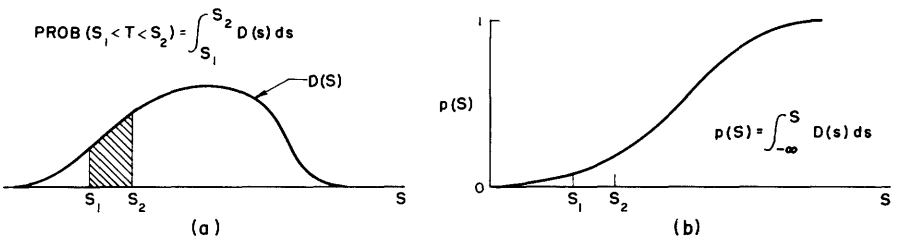

Fig. 22. (a) A probability distribution D(S). The probability of finding the unit's threshold between S_1 and S_2 is given by the area (shaded) under D(S) between those values. (b) The probability p that the same unit will respond to a stimulus S, given by the integral of the distribution function D(S) from minus infinity to S.

D(S) between those values.

$$p(S_1 < T < S_2) = \int_{S_1}^{S_2} D(s)\, ds \tag{5.2}$$

D(S) satisfies the conditions $D(S) \geqslant 0$ and

$$\int_{-\infty}^{\infty} D(s)\, ds = 1 \tag{5.3}$$

We present this system with a stimulus S. The probability that the threshold of a given unit lies below S, and therefore the probability that it will fire to S, is given by

$$p(S) = p(T < S) = \int_{-\infty}^{S} D(s)\, ds \tag{5.4}$$

Each of the N units of the population has then, independently, the probability p(S) of firing to a stimulus S. It follows that the average number of units that will fire upon repeated presentation of a stimulus S is

$$\bar{n}(S) = Np(S) \tag{5.5}$$

and that the average response amplitude is

$$\bar{A}(S) = rNp(S) \tag{5.6}$$

Obviously, the response amplitude on a single trial cannot be precisely predicted, finite probability attaching to all integral multiples of r from zero to N.

The function $\bar{A}(S)$ is to be interpreted in this theory as the intensity function for one population. If the intensity function is known, the probability distribution can be obtained from it by differentiation.

(b) Two or more populations. For the independent populations that we are considering, the extension of the formulation above to several populations is straightforward. Assume populations of sizes $N_1, \ldots, N_k$ with distributions $D_1(S), \ldots, D_k(S)$; also $D_i(S) \geqslant 0$ and

$$\int_{-\infty}^{\infty} D_i(s)\, ds = 1 \qquad i = 1, \ldots, k \tag{5.7}$$

Single units of the populations are characterized by response amplitudes $r_1, \ldots, r_k$.

The probability that a unit of the i^{th} population will respond to a stimulus S is given by

$$p_i(S) = \int_{-\infty}^{S} D_i(s)\, ds \qquad i = 1, \ldots, k \tag{5.8}$$

The average response amplitude of the system of k populations is therefore given, as a function of stimulus intensity, by

$$\overline{A}(S) = \sum_{1}^{k} r_i N_i p_i(S) \tag{5.9}$$

This is the general intensity function for k independent populations. $\overline{A}(S)$ is seen to be a nondecreasing function.

Only when the distribution functions do not overlap (disjoint case) can one infer the distribution functions from the intensity function by differentiation. Even in this case, it is necessary to know, independently, how many populations there are. That a single intensity function is compatible with a multitude of population structures is illustrated in Fig. 23. The intensity function, however, does provide a constraint on the possible choice of populations; that is, Eq. 5.9 must be satisfied.

4. Choice of a Population Structure

It is clear from the discussion above that the model developed in this section is capable of accounting for intensity functions of the sort presented in Section IV. This is, of course, a basic requirement of the model but one readily satisfied, since the

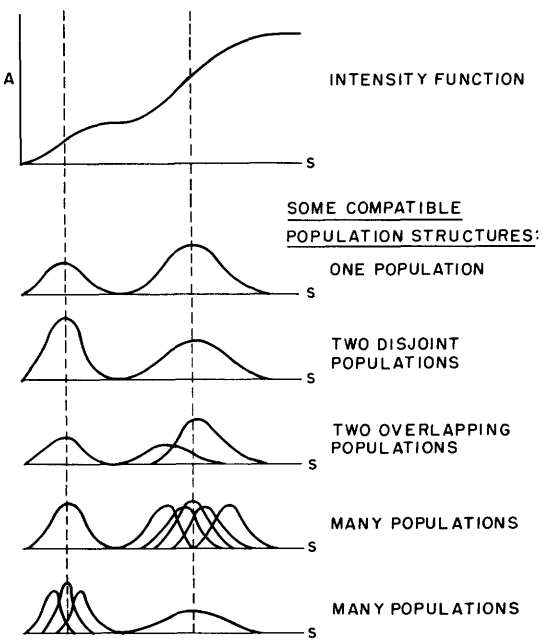

Fig. 23. A typical intensity function, together with a number of compatible population structures.

only restriction which the model places on the intensity function is that it be non-decreasing. The lack of a unique determination of population structure from the intensity function further minimizes the importance of this result.

One can nevertheless attempt to use the observed intensity function as the basis of a first guess at the population structure of the system, a guess whose value is simply to provide some working hypothesis. As we pointed out in Section IV, nearly all of the observed intensity functions show a two-component growth, with the components separated by a relatively flat plateau. If, as suggested by the data of Rosenblith (71) and of Pecher (72), discussed in the following subsection, the distribution function for a single unit is single-peaked, then one population could not give rise to such a two-component function. The simplest hypothesis, and the one that we tentatively adopt, is that two approximately disjoint populations are involved. It is, of course, possible that one or both components represent a superposition of overlapping subpopulations. These alternatives will be explored in Sections VI and VII.

In Fig. 24 intensity functions from several animals are analyzed on the basis of a two-population hypothesis.

5. Basis for the Hypothesis of a Fluctuating Threshold

We have established that the form of the intensity function can be accounted for within the framework of the model. But there are other reasonable models that could account for the intensity function data equally well. We could, for example, simply assume a collection of fixed-threshold elements whose threshold values are so distributed that they lead at once to the intensity function.

A number of earlier results have led us to base the model on the hypothesis of a fluctuating threshold. Direct evidence of fluctuating thresholds in second-order auditory elements was obtained by Rosenblith (71), recording from single units in the cochlear nucleus of the cat. A sequence of identical clicks (between ten and forty at each intensity) was presented at the ear of an anesthetized cat; the element near which the electrode sat sometimes responded and sometimes failed to respond to successive stimuli. The relative frequency of response at a given stimulus level is plotted as a function of stimulus intensity in Fig. 25. These data show clearly that the excitability of an element varies over an interval of 15 db to 20 db. If threshold were a fixed parameter, the resultant data would have had the character of a step function. This frequency function approximates directly the response probability function p(S), discussed in subsection 3.

Pecher (72), in a series of experiments employing electric stimulation of single sciatic nerve fibers, also found that a fiber will sometimes respond and sometimes fail to respond to the same stimulus; he reached a similar conclusion, namely, that the excitability of a nerve fiber fluctuates in time.

Lloyd and McIntyre (73) and Hunt (74), recording monosynaptic reflex responses of motoneurons to repeated afferent volleys, have observed variability in the responses of

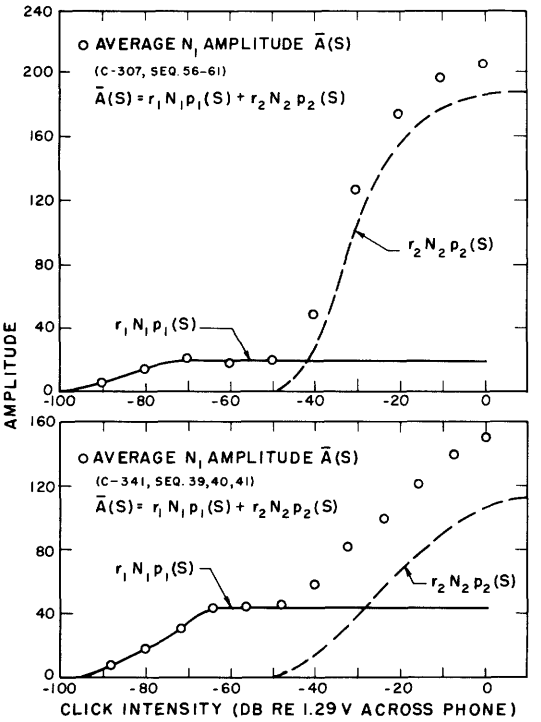

Fig. 24. Intensity functions of C-307 and C-341 analyzed on a two-population basis. The circles are data points. The solid curve is fitted to the first component of amplitude growth; the dashed curve is obtained by subtracting the solid curve from the over-all intensity function (as defined by the circles). Each of these curves is assumed to represent the response of a separate population.

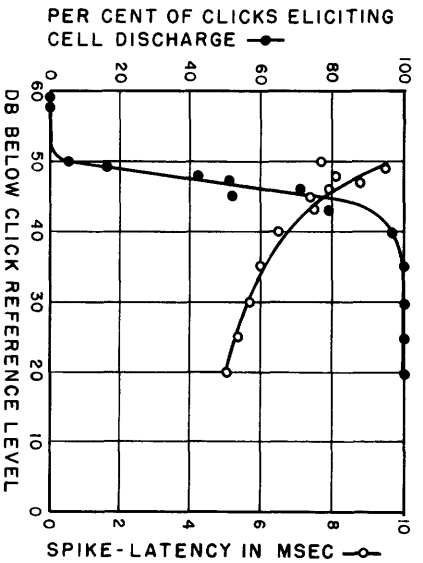

Fig. 25. Percentage of clicks eliciting a response from a single element in the cochlear nucleus of the cat, as a function of click intensity. Each point is based on ten to forty click presentations. (From Rosenblith, Proceedings of the Symposium on Information Networks, Polytechnic Institute of Brooklyn, 1954.)

individual elements and of aggregates of elements, which they attribute to threshold fluctuations.

In all of these experiments, the stimulus range over which response is uncertain is orders of magnitude greater than the uncontrollable variations in the stimulus. These, then, represent the direct evidence for threshold fluctuations; both the Rosenblith and Pecher studies point to a similar sort of threshold distribution function, possibly normal, certainly single-peaked. We must realize, however, that these distributions are to be understood in very different stimulus contexts, and it is therefore necessary to be cautious in making any comparisons.

McGill and Rosenblith (67, 68) used a model in which threshold has a probability character to account for the amplitude of the N_1 response to the second of a pair of clicks as a function of the first click intensity and of the time interval between the two clicks (see Section II-9 and Fig. 13). On the basis of a one-population model, to whose postulates the present model is indebted, they were able to predict the response to a second click as a function of first click intensity, the interval between clicks and the second click intensity being held constant. The existence of a more sensitive population is also suggested by certain discrepancies in their results.

The present model extends the one that McGill and Rosenblith formulated. The experiments described in the following sections were explicitly designed, as will become evident, for testing the hypothesis of fluctuating thresholds and for studying the population structure in the peripheral auditory system.

VI. VARIABILITY OF THE N_1 RESPONSE

It was recognized from the first that a model in which threshold is a random variable would have interesting statistical properties. We ask this question: If a system of neural units is repeatedly presented with the same stimulus, what statistical character would the set of responses be expected to have? The mean response amplitude, discussed in the last section, led to the intensity function. Another parameter of interest is the standard deviation of the set of response amplitudes. This is a measure of the variability or spread of the response amplitudes about their mean.

1. Theoretical Development

(a) Variability characteristics of a single population. The probability that a unit will respond to a stimulus S is given by Eq. 5.4:

$$p(S) = \int_{-\infty}^{S} D(s)\, ds$$

The probability that the unit will fail to respond is evidently (1 - p(S)). In the present case the value of the parameter p depends on the intensity of the stimulus, and takes on values from zero to 1.

For the moment, to conform with the more familiar treatments of the binomial problem, we drop the explicit dependence on S and let p(S) = p, and (1 - p(S)) = q. We now ask for the probability that, of a population N, n units will respond. Since the units are independent, we have at once

$$P(n) = \binom{N}{n} p^n q^{N-n} \tag{6.1}$$

If we define

$$\bar{n} = \sum_{n=0}^{N} nP(n) \tag{6.2}$$

$$\sigma_n^2 = \overline{(n-\bar{n})^2} = \sum_{n=0}^{N} (n-\bar{n})^2 P(n) \tag{6.3}$$

it is readily shown (75) that

$$\bar{n} = pN \tag{6.4}$$

$$\sigma_n^2 = Npq \tag{6.5}$$

The first result is intuitively clear, and we made use of it in the previous section. We turn our attention to the second of these equations.

$$\sigma_n^2 = Npq = Np(1-p) = \frac{N}{4} - N\left(p - \frac{1}{2}\right)^2 \tag{6.6}$$

We note that σ_n^2, regarded as a function of p, is a parabola opening down, vanishing at p = 0 and at p = 1, and having its maximum value, N/4, at p = 1/2. These results are readily interpreted at the end points. When p = 0, no unit can ever fire, leading always to zero response and therefore to zero variability; at p = 1, all units must always fire, and thus variability is again zero.

Thus far we have computed the variance in the number of responding units as a function of the probability of a single unit response. To obtain the variance in amplitude from this is a trivial step. By definition:

$$\sigma_A^2 = \overline{(A-\bar{A})^2}$$

But A = rn. Therefore

$$\sigma_A^2 = r^2\overline{(n-\bar{n})^2} = r^2 \cdot \sigma_n^2 = r^2 Np(1-p) \tag{6.7}$$

We reintroduce the dependence of p on S. Thus

$$\sigma_A(S) = r\left\{Np(S)\,(1 - p(S))\right\}^{1/2} \tag{6.8}$$

We demonstrated in Section V that the intensity function is related to the response probability p(S) by the equation

$$\bar{A}(S) = rNp(S) = A_{max}\, p(S) \tag{6.9}$$

Substituting in Eq. 6.8, we obtain

$$\sigma_A(S) = \frac{A_{max}}{\sqrt{N}}\left\{\frac{\bar{A}(S)}{A_{max}}\left(1 - \frac{\bar{A}(S)}{A_{max}}\right)\right\}^{1/2} \tag{6.10}$$

Thus we see that from the intensity function the form of the variability function is determined to within a multiplicative constant.

The values of $\bar{A}$ and σ_A at a single point allow us to determine the size of the population. For p = 1/2 (S = $S_{1/2}$), we have

$$\sigma_A(S_{1/2}) = \frac{A_{max}}{2\sqrt{N}} = \frac{\bar{A}(S_{1/2})}{\sqrt{N}} \tag{6.11}$$

Thus

$$N = \left(\frac{\bar{A}(S_{1/2})}{\sigma_A(S_{1/2})}\right)^2 \tag{6.12}$$

$S_{1/2}$ is determined from the condition $\bar{A}(S_{1/2}) = \frac{1}{2} A_{max}$. The choice of the point $S_{1/2}$ is quite arbitrary from a theoretical point of view. It is easily shown (Appendix 1) that the choice p = m/n leads to the result

$$N = \frac{n - m}{m} \left(\frac{\bar{A}(S_{m/n})}{\sigma_A(S_{m/n})} \right)^2 \tag{6.13}$$

where $S_{m/n}$ is determined from the condition $\bar{A}(S_{m/n}) = m/n\, A_{max}$.

(b) Variability characteristics of several independent populations. When more than one population is involved, the results obtained above are readily generalized. Suppose that we have k populations. The response amplitude to a stimulus S is given by

$$A = \sum_{i=1}^{k} r_i n_i = \sum_{i=1}^{k} A_i \tag{6.14}$$

where r_i is the response of a single unit of the i^{th} population, and n_i is the number of responding units of that population. Averaging, we have

$$\bar{A}(S) = \sum_{i=1}^{k} r_i \bar{n}_i = \sum_{i=1}^{k} r_i N_i p_i(S) = \sum_{i=1}^{k} \bar{A}_i(S) \tag{6.15}$$

$$\sigma_A^2(S) = \overline{(A-\bar{A})^2} = \overline{\left(\sum_{i=1}^{k} (A_i - \bar{A}_i) \right)^2} = \sum_{i=1}^{k} \sum_{j=1}^{k} \overline{(A_i - \bar{A}_i)(A_j - \bar{A}_j)} \tag{6.16}$$

In the case of independent populations, the terms in which $i \neq j$ all vanish, so that

$$\sigma_A^2(S) = \sum_{i=1}^{k} \overline{(A_i - \bar{A}_i)^2} = \sum_{i=1}^{k} \sigma_{A_i}^2(S) \tag{6.17}$$

As shown in the last section:

$$\sigma_{A_i}^2(S) = \frac{A_{i\,max}^2}{N_i} \left(\frac{\bar{A}_i(S)}{A_{i\,max}} \right) \left(1 - \frac{\bar{A}_i(S)}{A_{i\,max}} \right) \tag{6.10a}$$

If the intensity functions $\bar{A}_i(S)$ and the parameters N_i are known (i = 1, . . . , k), the function $\sigma_A^2(S)$ can be calculated from Eqs. 6.17 and 6.10a. Starting just from the intensity function $\bar{A}(S)$, it is not possible to separate out the component functions $\bar{A}_i(S)$ except in the case of disjoint populations (Section V-3b). In general, then, we cannot predict $\sigma_A(S)$ from $\bar{A}(S)$.

The case of particular interest to us, since it provides the simplest interpretation of the observed intensity function (Section V-4), is that of two disjoint or nearly disjoint

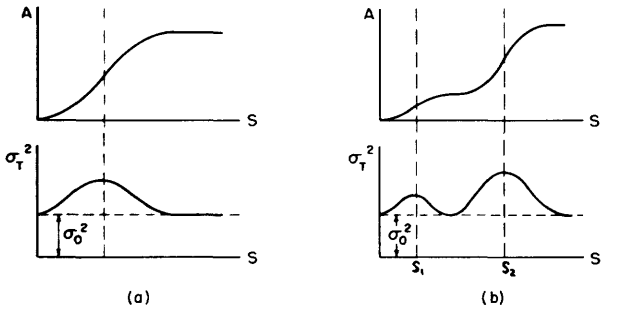

Fig. 26. Intensity function, and the corresponding type of variability function predicted by the model: (a) for one population, (b) for two disjoint populations. σ_o was chosen arbitrarily. Note that a peak of the σ-function occurs at the stimulus value at which an intensity function component reaches half its maximum amplitude.

populations. The variability function predicted by the model in this case consists of the two peaked functions obtained by treating the two populations separately, over the appropriate (disjoint) ranges (see Fig. 26). The peaks occur at S_1 and S_2, where $p_1(S_1) = 1/2$, $p_2(S_2) = 1/2$.

(c) Other sources of variability. In recording from any system, we encounter response variability from a variety of sources external to the system under study. Amplifier noise, biological noise,* and stimulus fluctuation – all contribute to the variability of the observed response. Let A_T be the total observed amplitude, A the neural contribution to A_T that would be produced by a constant stimulus, and A_o that part of A_T attributable to external sources. Then $A_T = A + A_o$. Assuming that A_o takes on positive and negative values with equal probability, and averaging, we obtain $\overline{A}_T = \overline{A}$, so that results obtained for the intensity function without considering external sources remain valid. We assume also that A and A_o are statistically independent. By the same reasoning that led to Eq. 6.17, we obtain

$$\sigma_T^2 = \sigma_A^2 + \sigma_o^2 \tag{6.18}$$

where σ_T^2 is the measured variance, σ_A^2 the variance of the neural component that would be observed in the case of a constant stimulus, and σ_o^2 the variance resulting from the combined effect of all external sources. For independent sources, σ_o^2 is again a sum of squares. We assume finally that σ_o is stimulus-independent, a reasonable assumption for amplifier noise and for biological noise, though not for variability having the stimulus as its source. In Appendix 2 we show, however, that the contribution from stimulus variability is very small. Introducing the dependence on S and substituting from Eq. 6.8, we have

*Here would be considered fluctuations of the electric potential arising in the biological medium that separates the source from the electrode.

$$\sigma_T^2(S) = \sigma_A^2(S) + \sigma_o^2 = r^2 N p(S)\,(1 - p(S)) + \sigma_o^2 \qquad (6.19)$$

In Fig. 26, we have plotted σ_T^2 versus S for one- and two-population cases; σ_o was chosen arbitrarily.

2. The Data

Extensive variability studies were carried out on three animals (C-333, C-341, C-349). The results of these studies are shown in Figs. 27-32. Each point is based on the responses to about 100 identical clicks, presented at a fixed rate of either one per second or 0.4 per second* (all clicks presented to a single cat were at one rate). The click intensity was systematically increased in equal steps over the range indicated in the figures. The size of the intensity step was 10 db in C-333, 4 db in C-341, and 5 db in C-349. In C-333 there are a few 5-db steps; in C-349, a few 10-db steps.

The peak-to-peak amplitudes of the N_1 responses to clicks were measured, and the mean and standard deviation computed at each intensity. These results are plotted together as functions of stimulus intensity in the figures noted above. The mean yields the intensity (or I-) function, $\bar{A}(S)$; the standard deviation yields what we shall hereafter call the σ-function, $\sigma(S)$. Two σ-functions are plotted on each graph. One, like the intensity function, is based on 100 responses at each intensity; the other is determined from the first 50 of these responses. This is done in order to indicate the degree of stability of σ within each sequence.

In C-333 responses were recorded simultaneously from two locations. Thus, in sequences 40 to 50 we have simultaneous data from locations 1 and 2 (Fig. 27); similarly, in sequences 56 to 71, from locations 3 and 4 (Fig. 28). The degree of stability of σ-functions and I-functions among different sequences and at different locations is indicated by a comparison of these figures.

In C-341 two electrode locations were used, labeled 2 and 3. At location 2, signal-to-noise ratio was very favorable, allowing detection of responses at -98 db; but the microphonic content of the responses recorded there at intensities greater than -50 db rendered N_1 analysis difficult. Thus in Fig. 29 only the data below -50 db are presented (sequences 23 to 35). At location 3, the microphonic was negligible over a 90-db range, but the comparatively low signal-to-noise ratio made difficult the detection of responses below -90 db. Data from this location are presented over the range from -88 to 0 db. These data consist of two parts: sequences 40 to 58, from -88 to -28 db (Fig. 30) and sequences 59 to 74, from -60 to 0 db (Fig. 31).

In C-349, all data were recorded at a single location and at a single gain (Fig. 32). The intensity function above -30 db is not too reliable; microphonic contaminates the N_1 response over that range.

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*Such a series of responses to a fixed stimulus will be called a "sequence." In the course of an experiment, successive sequences are numbered consecutively.

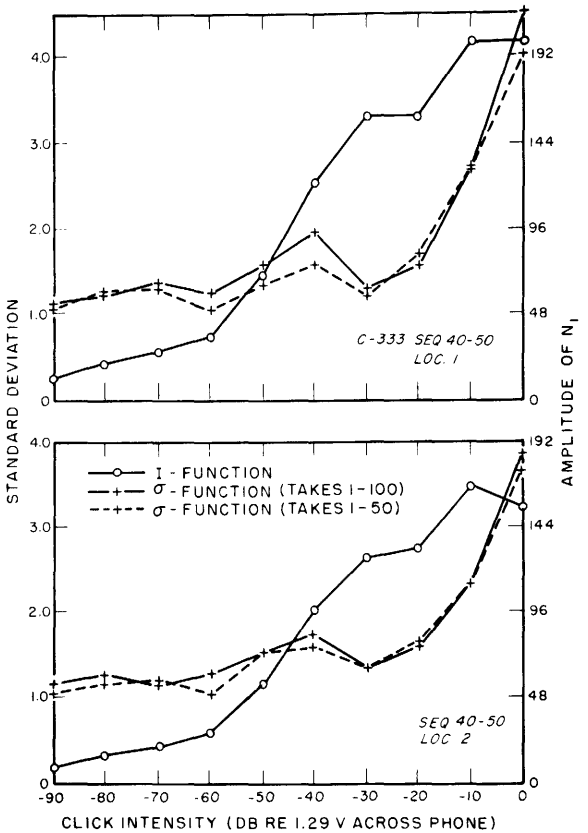

Fig. 27. I-functions and σ-functions, C-333, recording simultaneously from two locations (locations 1 and 2).

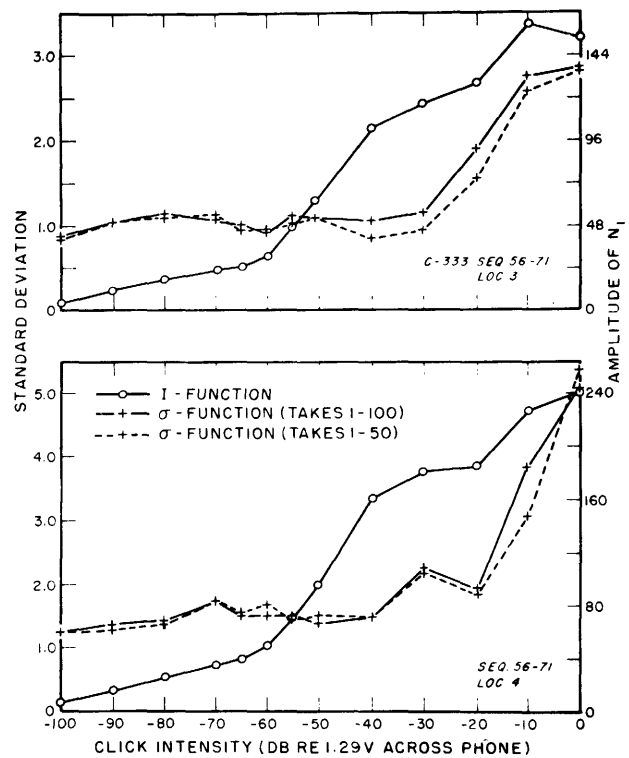

Fig. 28. I-functions and σ-functions, C-333, recording simultaneously from two locations (locations 3 and 4).

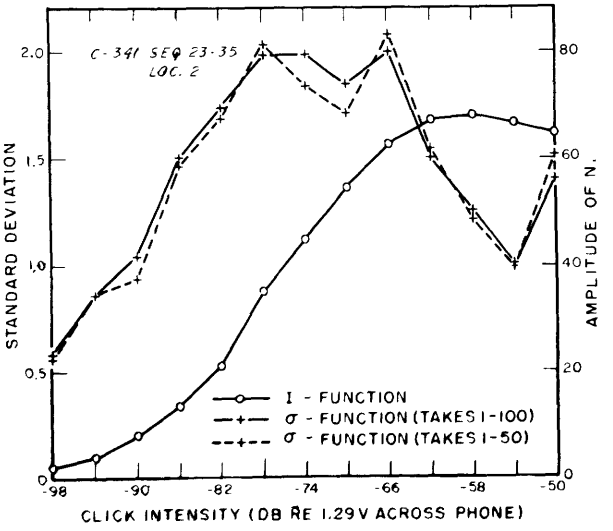

Fig. 29. I-function and σ-function, C-341, location 2; range, -98 to -50 db.

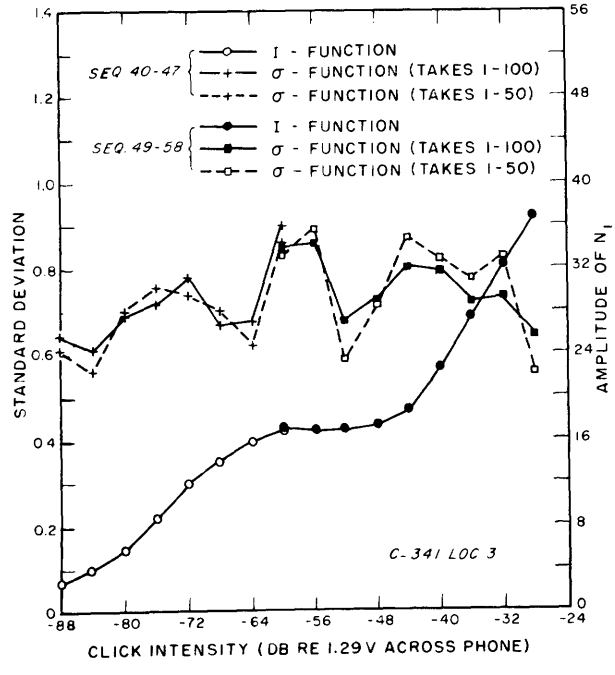

Fig. 30. I-function and σ-function, C-341, location 3; range -88 to -24 db.

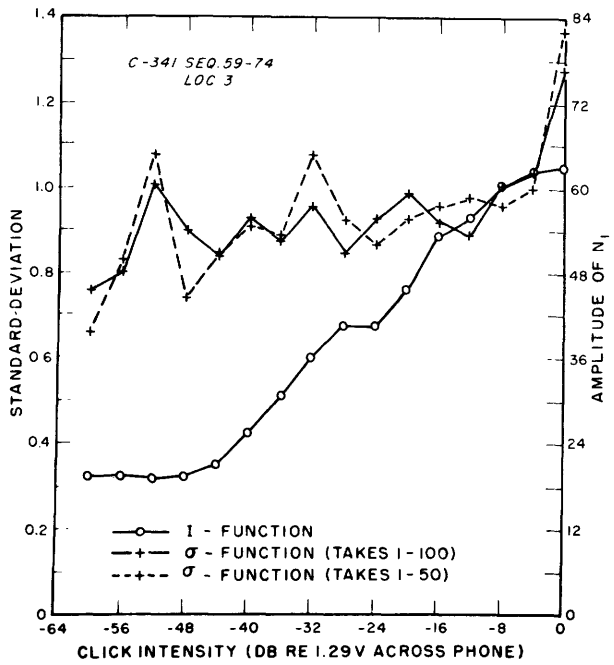

Fig. 31. I-function and σ-function, C-341, location 3; range, -60 to 0 db.

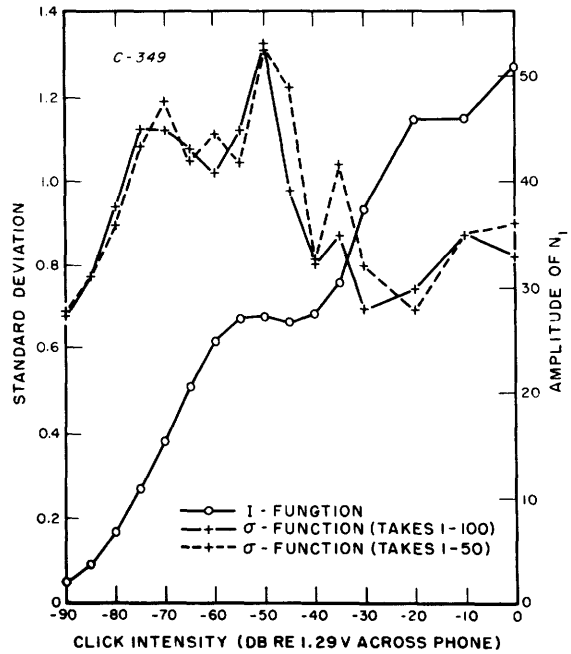

Fig. 32. I-function and σ-function, C-349, location 1; range, -90 to 0 db.

3. Comparison of the Data with the Predictions of the Model

The model predicts for a single population a σ-function of the form of Eq. 6.19 (Fig. 26a). This function peaks at p = 1/2. An examination of Figs. 27-30 and Fig. 32 shows that all of the experimentally obtained σ-functions increase monotonically for the first 20-30 db above threshold, and then decrease over an additional 10-20 db interval, reaching a minimum near -60 db. Over the same range, the intensity function exhibits the first stage of growth (discussed in Section IV), ending at approximately -60 db in either a plateau (C-341 and C-349), or a much accelerated growth function (C-333). The peak of the variability data over this interval occurs at approximately, or somewhat above, the half-growth point of this component of the intensity function.

In Figs. 33-36 we have replotted the intensity and σ-function data over the range of this initial stage of growth. The intensity function was interpolated by a smooth curve, which we tentatively assume represents the amplitude growth of a single population of neural units.

The solid line is the theoretical σ-function predicted by the model for one population (Eq. 6.19):

$$\sigma_T^2(S) = \frac{A_{max}^2}{N} p(S)\,(1 - p(S)) + \sigma_o^2 \qquad (6.19a)$$

Here we have made use of the fact that $A_{max} = rN$. In this expression, only σ_o and N are free parameters; p(S) is obtained from the intensity function: $p(S) = \overline{A}(S)/A_{max}$ (Eq. 6.9). The points $S_{1/10}, S_{2/10}, \ldots, S_{9/10}$, obtained in this way, are represented by vertical lines in the figures. A_{max} is determined from the amplitude of the plateau whenever possible (Figs. 34, 35, 36). For C-333 (Fig. 33), where there is no definite plateau, we have attempted to extend the intensity function in a smooth way to determine A_{max}; there is of course a certain arbitrariness in such a choice. We can also estimate σ_o experimentally. At p = 0, $\sigma_o^2 = \sigma_T^2$, this condition is certainly fulfilled in the absence of a stimulus. We have made use of this fact to determine σ_o, measuring the difference of amplitude between fixed baseline points of the signal detected in the absence of a stimulus and computing the variance of a large number of such values. The interval between these baseline points is chosen approximately equal to the interval that separates the positive and negative peaks of the N_1 response. This interval is seen in Fig. 21 to be relatively constant over the entire stimulus range. The values thereby determined have been used as a guide in choosing the parameter σ_o of the model. If by departing somewhat from the measured value of σ_o a better fit to the data could be obtained, the value providing the better fit was used. In general, however, the two sets of values agree within 20 per cent. A comparison is shown in the table below.

The value of N was chosen in each case to match the theoretical curve to the experimental value of σ_T at the point $S_{1/2}$ (p = 1/2):

$$N = \frac{\bar{A}^2(S_{1/2})}{\sigma_T^2(S_{1/2}) - \sigma_o^2} \qquad (6.12a)$$

In C-341, where several sets of data are available over the sensitive range, the value of N determined from the one set (Fig. 34) has been used to fix its value for the other (Fig. 35). In the latter case, the theoretical σ-function is almost entirely determined without reference to the variability data. One still has some freedom in σ_o, since it may change from one electrode location to another. In the case in question, the experimental values of σ_o turned out to be nearly identical at the two locations (0.59 and 0.60); consequently, a single value of σ_o was used in the theoretical functions for both.

	C-333	C-341	C-349
σ_o (expt'l)	0.88	0.60	0.45
σ_o (model)	0.86	0.53	0.45
N	360	320	175

The dashed lines surrounding the σ-function of the model represent a 70 per cent confidence interval for n = 100. That is to say, in a system exactly described by the model, a determination of σ_T based on 100 amplitude measurements would lie within the interval with probability 0.7 (Appendix 3).

The data points do not lie within the interval with this frequency, but the discrepancy is pronounced only above -65 db. In fact, below this value, approximately 70 per cent of the data points do lie in the confidence interval. In general, the deviations from the model are systematic and essentially the same in all cases: the peak of the experimental variance always occurs to the right of the peak of the theoretical curve; the data points to the left of the theoretical peak lie under the curve; the points to the right lie over it. A shift to the right in the theoretical function of 2-4 db would tend to correct both of these difficulties. There is, at present, no justification for such a shift; it is possible, however, that the interpretation according to which the number of units firing, and therefore p(S), is proportional to the N_1 amplitude, requires small corrections; these corrections could bring about such a shift or an equivalent change. This is only a guess and would require independent verification.

Above -65 db, just before and in the region of the plateau (C-341 and C-349), the data points deviate widely from the theoretical curve and tend to peak again; within the framework of the model this has no simple explanation, since one would expect decreasing or constant variance in such an interval.

In the second interval of amplitude growth, extending from -60 db or -50 db to 0 db,

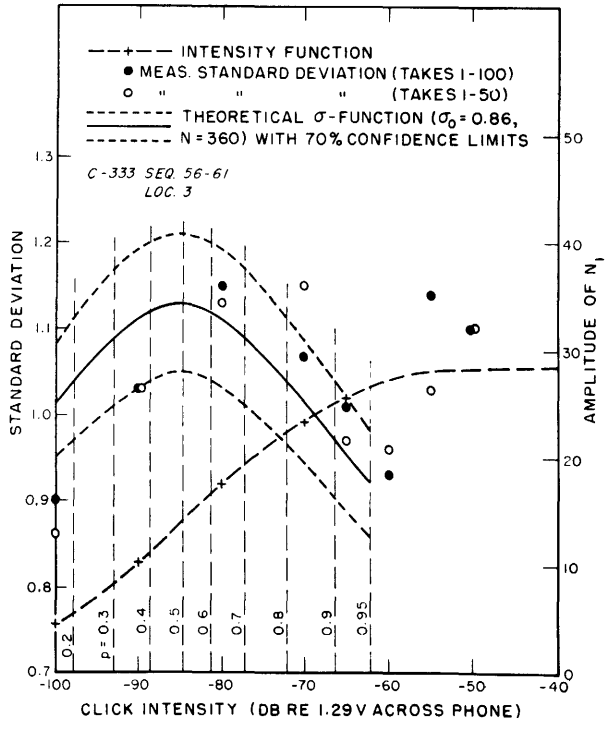

Fig. 33. Comparison of the theoretical variability function (with 70 per cent confidence limits) and the measured values of σ, over the range of initial growth of the intensity function; C-333, location 3.

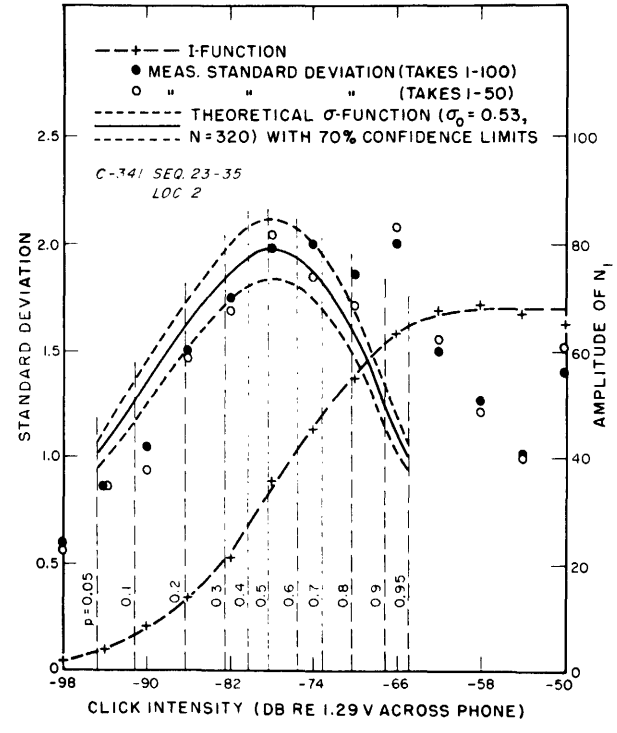

Fig. 34. Comparison of the theoretical variability function (with 70 per cent confidence limits) and the measured values of σ, over the range of initial growth of the intensity function; C-341, location 2.

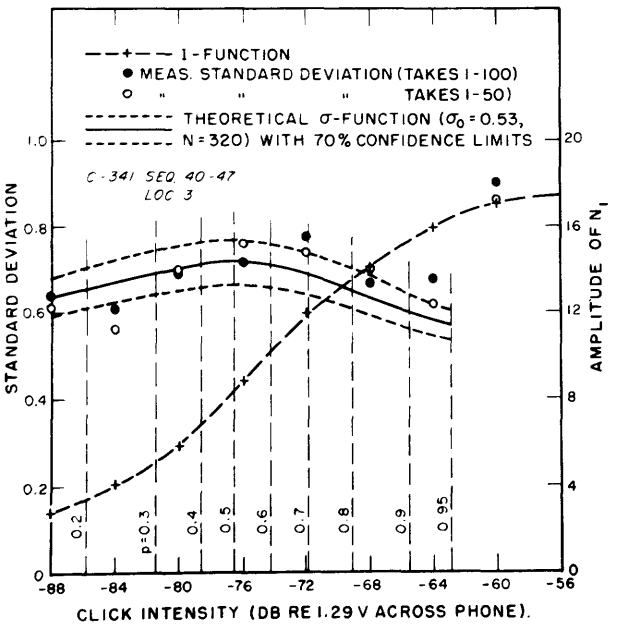

Fig. 35. Comparison of the theoretical variability function (with 70 per cent confidence limits) and the measured values of σ, over the range of initial growth of the intensity function; C-341, location 3.

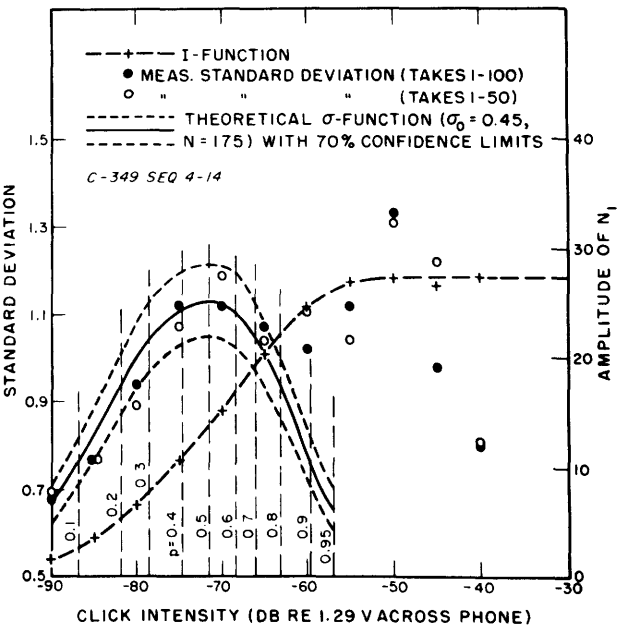

Fig. 36. Comparison of the theoretical variability function (with 70 per cent confidence limits) and the measured values of σ, over the range of initial growth of the intensity function; C-349, location 1.

the variance data obtained are not consistent with the assumption of a single insensitive population, of the kind postulated in the model. No pattern emerges which we can say is characteristic of σ-functions over this range. Smaller intervals between successive stimulus levels and more takes per level may be required before we can resolve the detailed population structure in this interval. If there are many overlapping populations, the present approach is not likely to succeed.

VII. THE EFFECT OF BACKGROUND NOISE UPON THE AMPLITUDE OF N_1

1. The Data

As we noted in Section II-7, the response to a click in the presence of a continuing background of noise is smaller than the response to the same click presented alone. The explanation of this "masking" phenomenon lies in the fact that auditory neurons are continually being excited by the noise; when a click is presented, some fibers which would ordinarily have responded are refractory, in threshold or in amplitude, and thus are unable to respond or respond fully. The responses evoked by the noise background are asynchronous and therefore not readily detected.

We have determined masked and unmasked intensity functions (that is, intensity functions obtained with and without noise background) in three cats, using unfiltered noise (Sec. III-2). The unmasked intensity functions for all three of these animals (C-305, C-306, C-307) show a two-stage growth of the sort described in Section IV. Figures 38-40 show the masked and unmasked intensity functions obtained. In Fig. 37 responses to masked and unmasked clicks are shown side by side over a 60-db range; these responses were obtained from C-307, at a noise level of -82 db. (The 12-db correction required for unfiltered noise (Sec. III-2) was included in the values given here and below.)

The intensity functions here have the same significance as those discussed in Section IV. Each point represents the average N_1 amplitude of about ten responses to identical clicks. In a typical experiment, the noise level is at, let us say, -80 db. The click intensity is set at -90 db; ten clicks are delivered without noise background and then ten more with the noise turned on. The click intensity is then changed to -80 db and the procedure repeated. This is continued to 0 db. The noise level can now be changed and the intensity functions run again.

The relation between the noise level and the click intensity was discussed in Section III. The 0-db noise level is chosen so that its rms amplitude is equal to the amplitude of a 0-db click. We regard the noise and click thus calibrated as being approximately equivalent levels of stimulation,* the one continuous and the other impulsive. The objection raised – that the noise contains peaks of amplitude much greater than the amplitude of the click – has been met by comparing the masking effect of wide-band noise with that of the same noise, peak-clipped to its rms amplitude. We find that the amount of masking produced by these two methods does not differ significantly. It appears from this that the masking effect of the large but relatively infrequent peaks in the unclipped noise is small.

*This postulated equivalence is to be understood in the probability sense defined in the model; i.e., the threshold of a unit in the resting state will, with equal probability, be found to lie below noise and click levels of numerically equal intensity.

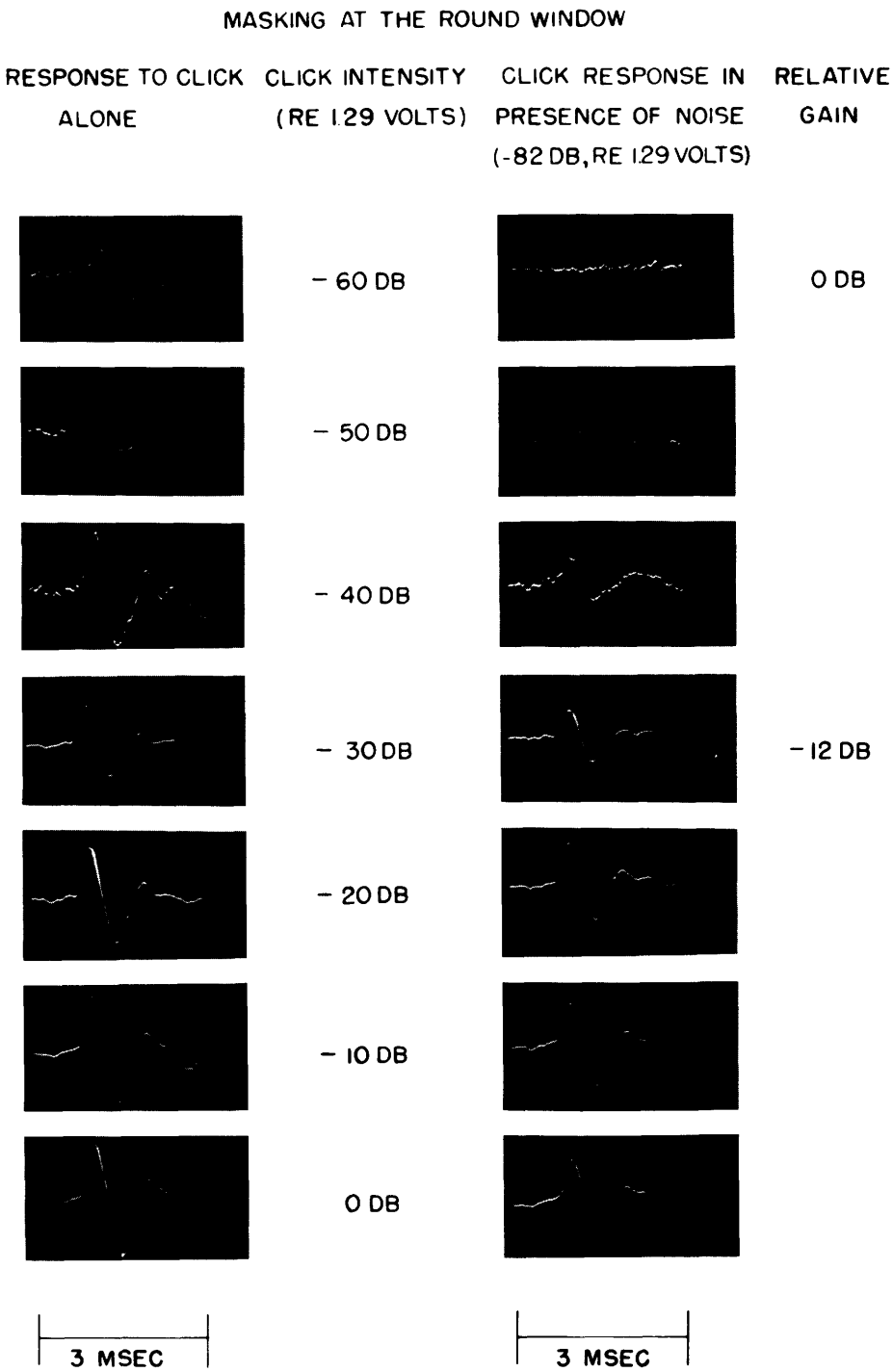

Fig. 37. Responses to clicks over a 60-db range, with and without background noise; noise level -82 db, unfiltered. C-307. Note that the voltage gain of the recording equipment was reduced by 12 db (factor of 1/4) at S = -30 db.

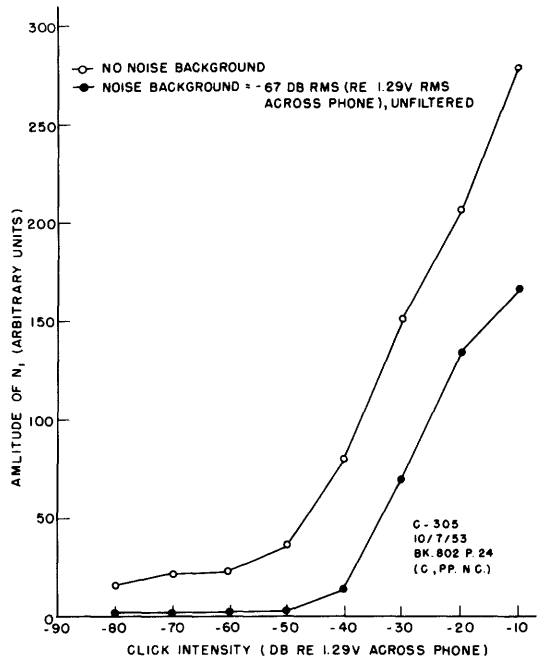

Fig. 38. Intensity functions for clicks, with and without noise background; noise level -67 db, unfiltered. C-305. Each point represents the average N_1 amplitude of ten responses to identical stimuli.

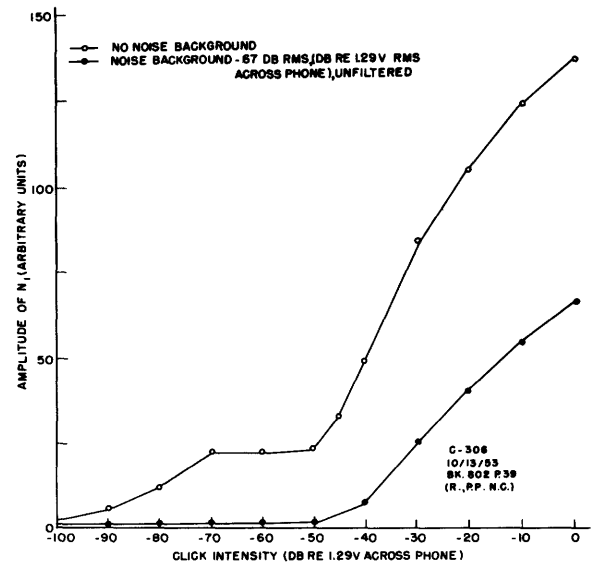

Fig. 39. Intensity functions for clicks, with and without noise background; noise level -67 db, unfiltered. C-306. Each point represents the average N_1 amplitude of ten responses to identical stimuli.

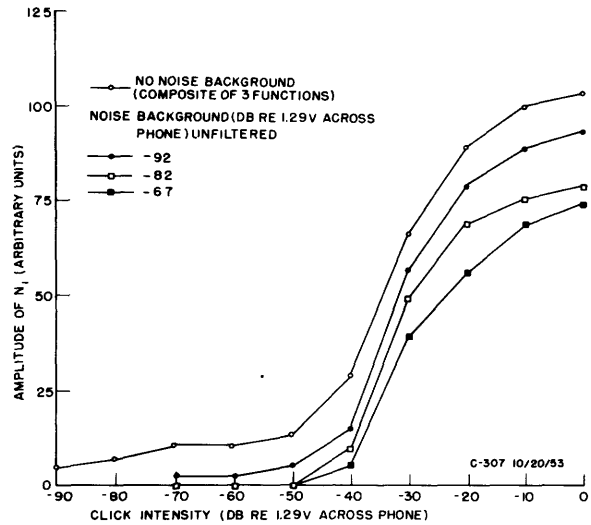

Fig. 40. Intensity functions for clicks, with and without noise background; noise levels -92, -82, and -67 db, unfiltered. C-307. Each point of the masked functions represents the average N_1 amplitude of ten responses to identical stimuli. The upper curve was obtained by averaging the three unmasked functions which correspond to the masked functions shown; thus each point represents the average N_1 amplitude of thirty responses to identical stimuli.

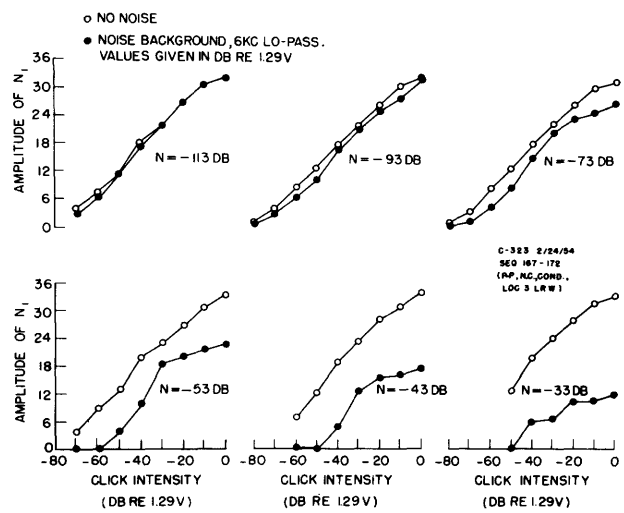

Fig. 41. Intensity functions for clicks, with and without noise background; noise levels -113, -93, -73, -53, -43, and -33 db, filtered 6-kc low-pass. C-323. Each point represents the average N_1 amplitude of ten responses to identical stimuli.

In C-305 and C-306 only one noise level was used, -67 db. In C-307, masked and unmasked intensity functions were obtained at three levels (-92, -82, and -67 db).

We also ran masking functions on C-323, using filtered noise (6-kc low-pass); the results of this experiment are shown in Fig. 41, for six levels of noise (-113, -93, -73, -53, -43, -33 db). The N_1 threshold in this animal was rather high (about -70 db), and the intensity function shows only a single stage of growth; it appears as if no sensitive population were present.

2. Predictions of the Model

Let us imagine that a population of neural units, having the properties postulated in Section V, is presented with a continuous constant-level stimulus ("noise"), whose intensity lies within the range of threshold fluctuations of the units. Whenever the threshold of a unit drops below the "noise" level, the unit fires, is rendered refractory, and recovers; at some later time the unit's threshold again drops below the noise level, and the unit fires again. We make the assumption that, at the time we are considering, the system has reached an equilibrium in which, in equal intervals of time, approximately equal numbers of units fire.

Now a click of intensity S is presented to the system. To predict the amplitude of the resulting N_1 response would require much more information than we have at present. In particular, it would be necessary to know the threshold probability distribution of a unit as a function of the time after the unit fires, and as a function of the stimulus that caused it to fire. Then also, one would have to know approximately how fast threshold fluctuations occur, that is, the characteristic rate of such fluctuations. A higher rate implies a smaller response to the click; for, in a short interval preceding the click, more units would have dropped below the noise level and fired.

The quantitative problem is seen to be quite involved and is beyond the scope of this report. However, some interesting qualitative and semiquantitative observations can be made. Let us assume, as in Section V, that a unit is absolutely refractory for 2 msec after firing; no stimulus, however strong, will cause it to fire in that interval. We also assume that the effect of firing is, in a general sense, to shift the threshold probability distribution to higher values, and thereby to decrease the probability of firing to any stimulus. We also postulate a simple model for threshold fluctuation, whereby a threshold state persists for an interval τ and then shifts abruptly to another value, in which it remains again for time τ. Successive threshold values are assumed to be uncorrelated. The rate of threshold fluctuation is then $1/\tau$. We assume that such fluctuations occur also in the absolute refractory interval, regarding that interval as one in which the available response amplitude is zero, while threshold remains a valid, if elevated, parameter.

We can then say the following: If the noise level lies in the interval of threshold

fluctuation, the population response to a maximal (or submaximal) click* may be reduced to any desired value simply by choosing the rate of threshold fluctuation sufficiently high. For if, in the two milliseconds preceding the click, a large fraction, let us say 95 per cent, of all units drops below the noise level and fires, then the response of the population to even a maximal click will be correspondingly small — 5 per cent of the unmasked response in the instance cited. Thus we get the interesting possibility that, in a model in which threshold is a fluctuating parameter, a relatively weak continuous stimulus can almost totally mask the response to a maximal click, provided that the rate of threshold fluctuation is sufficiently high. If, on the other hand, the threshold of each unit were fixed, we would expect a rather different result. In that case, noise of intensity N would totally mask responses to clicks for $S \leq N$; for $S > N$, however, the click response would be $\overline{A}(S) - \overline{A}(N)$, where $\overline{A}(S)$ is the unmasked intensity function.

Let us now consider the case of two disjoint populations of neural units, termed sensitive and insensitive (Sec. V). A constant level stimulus which lies entirely below the insensitive distribution can have no effect on it. Therefore, in the case in which the fluctuations are sufficiently rapid (previously cited), a weak noise will produce a masked intensity function that is nearly zero over the range of the sensitive population, and over the remaining range is smaller than the unmasked function by a constant amount. A constant-level stimulus that lies in the insensitive range should entirely mask the sensitive population; the masking problem over the insensitive range reduces again to that of one population, which we discussed above.

3. Comparison of the Data with the Predictions of the Model

The results obtained from the masking studies tend to support the hypothesis of an approximately disjoint population of sensitive units, with thresholds that fluctuate rapidly in time. In C-307 the amplitude growth of the unmasked function occurs in two stages, from -100 to -70 db, and from -60 to 0 db (Fig. 40). The average unmasked response amplitudes to clicks at -92 and -82 db are about 1/3 and 3/5, respectively, of that at -60 db; yet noise at -92 db reduces the response to a -60 db click to less than 1/4 of its unmasked amplitude (compared to 2/3 predicted by a fixed-threshold theory), and noise at -82 db reduces the same response to less than 1/10 of its unmasked value (compared to 2/5 from a fixed-threshold theory). The general tendency, then, is for low levels of noise to mask rather completely the responses to clicks of comparatively high intensity.

We can, moreover, use these data in order to estimate the fluctuation parameter, τ. Recall that if a unit has fired in the two milliseconds preceding a click, it cannot respond to the click. If a unit has not fired in these two milliseconds, we shall assume that it always fires to a supramaximal click, such as that at -60 db. Denote

*We define a maximal stimulus as one that evokes a response from every unit of a population when that population is in the resting state; i.e., S is maximal if $p(S) = 1$.

by p^* the probability that the threshold of a given unit lies below the noise level N, and by P the probability that a unit will fire to a supramaximal click in the presence of a continuous noise level N. In time T = 2 msec, the unit occupies T/τ threshold states. P is then the probability that a unit's threshold fails to fall below the value N in T/τ independent transitions. That is

$$P = (1 - p^*)^{T/\tau} \tag{7.1}$$

P can be determined from the data, being simply the ratio of the masked to the unmasked response for a supramaximal stimulus; T is 2 msec; p^* is a function of the noise level and of the way in which the threshold distribution recovers in time. We know, however, that $p^*(N) < p(N)$, where p is the probability of response of a unit in the resting state. The latter value can be obtained from the unmasked intensity function for clicks: $p(N) = \overline{A}(N)/A_{max}$. Substituting p for p^* in Eq. 7.1 establishes an upper bound for τ. In the table below we have tabulated the values of p, P, and τ_{max} for N = -92 db. Here we regard S = -60 db as a maximal stimulus over the sensitive range. The magnitude of τ_{max} implies a minimum rate of threshold fluctuation of about 2000 states per second.

C-307	p	P	τ_{max} (msec)
N = -92 db	~1/3	~1/4	~1/2

For N = -92 db, the masked and unmasked intensity functions differ by very nearly a constant amount over the insensitive range (Fig. 40), as the model predicts. At N = -82 db, some masking of insensitive units is observed, becoming pronounced at N = -67 db (Figs. 38 and 39). The data of C-323 (Fig. 41) make doubtful the hypothesis of a single insensitive population with rapidly fluctuating thresholds. Masking of a 0-db click is 63 per cent complete at N = -33 db. The comparable noise level, probability-wise, in the sensitive range occurs at -80 db, at which value the masking of a -60 db click is more than 95 per cent complete. Comparisons at other values of N and S show that masking in the insensitive range is less effective than in the sensitive range. These results suggest either a lower rate of threshold fluctuation or a multiple population structure. In view of the results given in Section VI, the latter interpretation is preferred.

VIII. CONCLUSIONS

The experiments concerning the variability and masking of the N_1 amplitude, which we have discussed in the two previous sections, constitute very different approaches to the problem of testing the model. Both approaches, however, have led to similar conclusions concerning the model's validity. These conclusions may be summarized as follows:

(1) It seems probable that a fairly homogeneous population of neural units, characterized by rapidly fluctuating thresholds, is responsible for the initial component of growth of the intensity function in the range from -100 db to -60 db. Present estimates of the size of this population vary from 150 to 400 units.

(2) Over the remaining range of the intensity function (from -60 db to 0 db), a single-population hypothesis does not appear capable of successfully accounting for the data within the framework of the model.

Let us briefly summarize the evidence on which these conclusions are based. First, the variability data show consistent peaking behavior over the interval of initial amplitude growth as the model predicts for a homogeneous population of units characterized by fluctuating thresholds; over the remaining intensity interval, no such simple behavior is exhibited. Second, we have seen from the masking data that a low-level noise is capable of differentially affecting the two components of amplitude growth; the results obtained are consistent with the predictions of the model over the range of the sensitive population.*

Even over the sensitive range we have seen that the model is not able to account for certain details of the observed data. As pointed out in Section VI, there exist small systematic discrepancies between the predicted and observed variability functions. However, in view of the fact that these departures are small and that over the sensitive range the masking data independently support the main premises of the model, we conclude that in that interval the model is valid in its essentials.

The approximate features of the model responsible for the observed discrepancies may lie in any one of several directions. First, as suggested in Section VI, the interpretation of the N_1 amplitude as a direct measure of the number of active units probably requires modification. Some measure which would take into account the degree of

*The apparent identification of a homogeneous population of sensitive units, characterized by fluctuating thresholds, and of a second, presumably heterogeneous, group of relatively insensitive units, leads to a number of general speculative questions. First, is it possible to relate these groups of hypothetical units to specific anatomical structures or groups of structures in the peripheral auditory system? Second, is it possible to discover psychophysical phenomena which exhibit a structure similar to that which appears, on the basis of electrophysiological data, to exist at a peripheral level in the cat? Third, do corresponding electrophysiological phenomena exist in species other than cat; in particular, do similar phenomena occur at the peripheral level in man? A demonstration of the latter would open to us a wide range of valid comparison between physiological and psychophysical data.

synchrony of firing, as well as the amplitude of response, would better reflect the amount of activity. Such a parameter might be the area of the N_1 resonse, or the area under the integral of that response. More information is needed regarding the nature of the transformation on the neural response which N_1 represents.

A similar oversimplification is reflected in the model, where it has been assumed that all units fire simultaneously. Preliminary measurements indicate that the responses to a fixed stimulus, presented repetitively, show nonnegligible variations in the peak-to-peak duration of the response. On the basis of this result, it might be worthwhile to extend the model by regarding the latency of a unit's response as another statistical parameter. Interesting correlational properties between amplitude and duration of the response would come out of such a theory – properties which could be tested experimentally.

Still other postulates of the model have restricted applicability. The assumption of statistical independence of neural units and of populations of such units is, for peripheral neurons, a workable approximation which, in the central nervous system, probably breaks down completely. Attempts to extend the model centrally would have to take account of interactions between units. The concept of a homogeneous population of neural units also has limitations; even in the most uniform tracts of the nervous system, there exist in axon diameters small variations that would presumably give rise to variations in the amplitude of unit response and in threshold properties. A modification of the model, in which populations are discretely or continuously distributed over the insensitive range, might be useful in resolving the difficulties that we have encountered thus far in that interval.

There are a number of research problems, experimental and theoretical, that are suggested by the model we have developed. The time course of recovery of the threshold distribution function of a unit after firing can be directly investigated by using pairs of clicks; successive distributions are obtained at once from the intensity functions for the second click at successive separation times, when a maximal first click is used. If an arbitrary first click is used, a few simple considerations allow us to deduce the distributions from the data. An attempt to predict from the two-click data the response to a third click would provide a test of the superposability of the recovery effects involved. Also, with threshold distribution functions during the recovery interval available, quantitative predictions of the results of masking would be possible.

The central concept of the model, that of a fluctuating threshold, is very likely to have application to areas other than the peripheral auditory nervous system. In fact, the basic single-cell data obtained by Rosenblith (71) and by Pecher (72) were derived not from that system, but from second-order auditory cells and from frog sciatic nerve fibers, respectively. Macy (77) used this property in a model which accounts with considerable success for the recovery in time of response amplitudes at the auditory cortex, following stimulation by one or two conditioning clicks. If the concept of a fluctuating threshold should prove to be a general one, it would constitute an important addition to the classical all-or-nothing principle.

APPENDIX 1

$$\begin{cases} \sigma_A^2 = r^2\, Np(1-p) \\ \overline{A} = rNp \end{cases}$$

For $p = \frac{m}{n}$ $\qquad (S = S_{m/n})$

$$\sigma_A^2(S_{m/n}) = r^2\, N\left(\frac{m}{n}\right)\left(1 - \frac{m}{n}\right)$$

and

$$\overline{A}(S_{m/n}) = rN\left(\frac{m}{n}\right)$$

Therefore

$$\sigma_A^2(S_{m/n}) = \frac{1}{N}\left\{\overline{A}(S_{m/n})\right\}^2\left(\frac{n}{m}\right)\left(1 - \frac{m}{n}\right)$$

$$= \frac{1}{N}\left(\frac{n-m}{m}\right)\left(\overline{A}(S_{m/n})\right)^2$$

$$N = \left(\frac{n-m}{m}\right)\left(\frac{\overline{A}(S_{m/n})}{\sigma_A(S_{m/n})}\right)^2$$

APPENDIX 2

In a fixed-threshold system, with units so distributed along the threshold axis as to yield the observed intensity function, a stimulus variability of constant magnitude would give rise to a σ-function similar in shape to that predicted by the model. For it is readily seen that the response variability obtained in this way is proportional at every point to $d\bar{A}(S)/dS$; the latter peaks at the point of maximum slope of the intensity function, a point which, over the sensitive range, is nearly coincidental with the point $S_{1/2}$, at which the model predicts a maximum.

Measurements, however, show that the amplitude variability of the acoustic click is far too small to account for the magnitude of the response variability. The standard deviation of the click amplitudes is less than 0.025 db. Interpolating the intensity function near the point of maximum slope, we obtain a corresponding ratio of σ_A to $\bar{A}$ of less than 0.0016. The measured ratio at this point is about 0.05. Thus the stimulus variability can account for no more than 3 per cent of the response variability, and is therefore ruled out as a significant factor.

APPENDIX 3

The variance, s_T^2, of a sample of n amplitudes, drawn from a system which is exactly described by the model, is a random variable, whose expectation value is given by

$$\sigma_T^2 = r^2 Np(1-p) + \sigma_o^2$$

In the notation defined in Section VI-1c, $A_T = A + A_o$. A is binomially distributed (Eq. 6.1); for large N this approaches a normal distribution (75). A_o is assumed also to be a normal variable. Finally, recall that A and A_o were assumed to be independent. Therefore A_T, the sum of independent normal random variables, is itself normal (75). This result is readily extended to include several independent populations:

$$A_T = \sum_{i=1}^{k} A_i + A_o$$

Let x be a normal variable with variance σ_x^2, from which a sample $x_1 \ldots x_n$ is drawn. Then the variable

$$\frac{ns_x^2}{\sigma_x^2} = \left(\frac{1}{\sigma_x^2}\right) \cdot \sum_{i=1}^{n} (x_i - \bar{x})^2$$

is χ^2 distributed with (n-1) degrees of freedom (76). The moment generating function of the χ^2 distribution with m degrees of freedom is (76)

$$M_{\chi^2}(a) = (1 - 2a)^{-m/2}$$

Therefore

$$M_{\left(ns_x^2/\sigma_x^2\right)}(a) = (1 - 2a)^{-(n-1)/2}$$

The population variance of a random variable x, with moment generating function $M_x(a)$ is (76)

$$\sigma_x^2 = \left.\frac{\partial^2 M_x}{\partial a^2}\right|_{a=0} - \left.\left(\frac{\partial M_x}{\partial a}\right)^2\right|_{a=0}$$

Therefore

$$\sigma_{\chi^2}^2 = m(m+2) - m^2 = 2m$$

and

$$\sigma^2_{\left(ns_x^2/\sigma_x^2\right)} = \frac{n^2}{\sigma_x^4} \cdot \sigma^2_{\left(s_x^2\right)} = 2(n-1)$$

So finally

$$\sigma^2_{\left(s_x^2\right)} = \frac{2(n-1)}{n^2}\,\sigma_x^4 \approx \frac{2}{n}\sigma_x^4$$

$\sigma^2_{\left(s_x^2\right)}$ is the variance of the variable s_x^2. For large n, the χ^2 distribution is sufficient close to the normal distribution that the σ-interval about the mean may be interpreted as a 68 per cent confidence interval. Therefore s_x^2 lies in the interval

$$\left\{\sigma_x^2 - \sigma_{\left(s_x^2\right)}\right\} = \sigma_x^2\left\{1 - \sqrt{\frac{2}{n}}\right\}$$

to

$$\left\{\sigma_x^2 + \sigma_{\left(s_x^2\right)}\right\} = \sigma_x^2\left\{1 + \sqrt{\frac{2}{n}}\right\}$$

with probability of about 70 per cent. Or s_x lies in the interval

$$\sigma_x\sqrt{1 - \sqrt{\frac{2}{n}}} \quad \text{to} \quad \sigma_x\sqrt{1 + \sqrt{\frac{2}{n}}}$$

with probability 70 per cent. For n = 100, as in the experiments of Section VI, the 70 per cent confidence limits are therefore defined by the interval 0.93 $\sigma_T(S)$ to 1.07 $\sigma_T(S)$. These limits are plotted in the figures of Section VI.

Acknowledgment

I wish to express my thanks to Professor Walter A. Rosenblith for his encouragement of this work from its beginning, for many rewarding discussions during its progress, and for his helpful criticisms of the manuscript while it was in preparation. I would also like to thank Mr. Robert M. Brown for technical assistance, and Dr. David H. Raab and Dr. John R. Hughes for their help in the preparation of the animals. I am indebted to Mrs. Margaret Freeman of the M. I. T. Joint Computing Group for her help in analyzing the data.

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