AN ANALYTICAL STUDY OF ELECTRIC RESPONSES AT THE PERIPHERY OF THE AUDITORY SYSTEM

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Abstract

Acoustic stimuli, especially if they are impulsive in nature, give rise to well-defined neuroelectric events in the auditory nerve of many animal species. In this research, the summated action potentials of the cat's auditory nerve were recorded with gross electrodes from locations in the vicinity of the cochlea. This report is primarily concerned with the analytic study of the behavior of these neural potentials in relation to changes in stimulus parameters.

In order to investigate possible relations between the neural and the cochlear microphonic potentials, electrical activity was recorded in cats whose auditory nerve had degenerated. Characteristics of the microphonic response to clicks were determined. A "slow" potential that does not reverse with stimulus polarity as the microphonic does was discovered.

Neural responses to condensation and rarefaction clicks were observed over a wide range of stimulus intensity; it was found that the differences between the responses to the two-click polarities depend on the intensity. These differences can be interpreted in terms of two excitatory processes, one of which can be related to the microphonic potential, and the other seems to be related to the "slow" potential.

Neural responses to impulsive stimuli were studied as a function of stimulus repetition rate. For moderate intensities, the amplitude of the neural response begins to decrease for rates higher than 10/sec. Stimulus-locked neural activity can be detected in averaged responses up to rates of nearly 3000/sec. The effect of overlapping of response waveforms is described in terms of a mathematical model.

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I. INTRODUCTION

1.1 GENERAL PLAN OF THIS STUDY

In studying a communication system, one can take the point of view that he is interested only in input signals and output signals and the relations between them. This "black-box" approach may be fruitful in the study of systems in which the transfer function can be simply defined in mathematical terms. But often it is not advantageous when it is applied to biological communication systems. For most of these systems the stimulus-response relations are so complex that it is difficult to determine appropriate mathematical descriptions that apply over a wide range of conditions. In studying such a system, it is desirable to maintain close connection between the description of input-output relations and the physiological processes involved, so that knowledge of one can help to organize the study of the other. In the work described here, we are concerned with both input-output relations and physiological mechanisms.

In Section IV a mathematical model has been developed which merely describes changes in response waveforms. However, the usefulness of the model lies not only in this description, but also in its implications concerning the physiological processes. In Section III, on the other hand, a model of a physiological process is proposed that leads to an interpretation of some observed input-output relations.

The research reported here deals with the periphery of the auditory system. Input signals are acoustic stimuli; output signals are summated action potentials of the auditory nerve recorded with gross electrodes. Sections III and IV present the results of studies of the relationship of the neural output to the input for changes in two stimulus parameters. Emphasis is put upon the study of impulsive stimuli. In Section II, input-output relations are studied for electrical responses of the cochlea that are not neural. The results of Section II assist us in interpreting the results of Sections III and IV. Section I contains: (a) descriptions of those features of the anatomy and physiology of the ear that are pertinent to signal-transmission processes; (b) a discussion of results and interpretations of previous studies of electrophysiological responses; and (c) a description of the experimental procedures employed.

1.2 GENERAL ANATOMY AND PHYSIOLOGY OF THE AUDITORY SYSTEM

If the auditory system is thought of as a communication channel, the signal-transmission path can be quite well defined at the input end of the system (see Fig. 1). The acoustic signal produces a vibration of the ear drum, which is transmitted by the small bones of the middle ear to the oval window of the cochlea. At this point the vibration is transduced into a pressure variation in the cochlear fluid, which bends the cochlear partition near the oval window. This disturbance is then propagated along the cochlea in a wave motion on the cochlear partition. This motion, somehow, leads to the excitation of the nerve endings in the organ of Corti. The neural signals are then

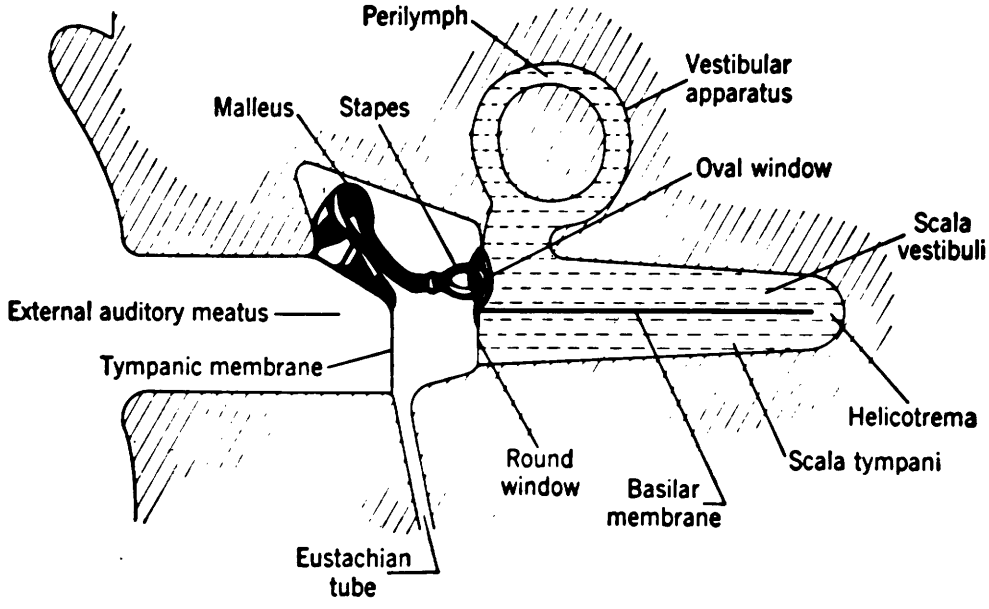


Fig. 1. Schematic drawing of the ear. (From von Békésy and Rosenblith (11).)

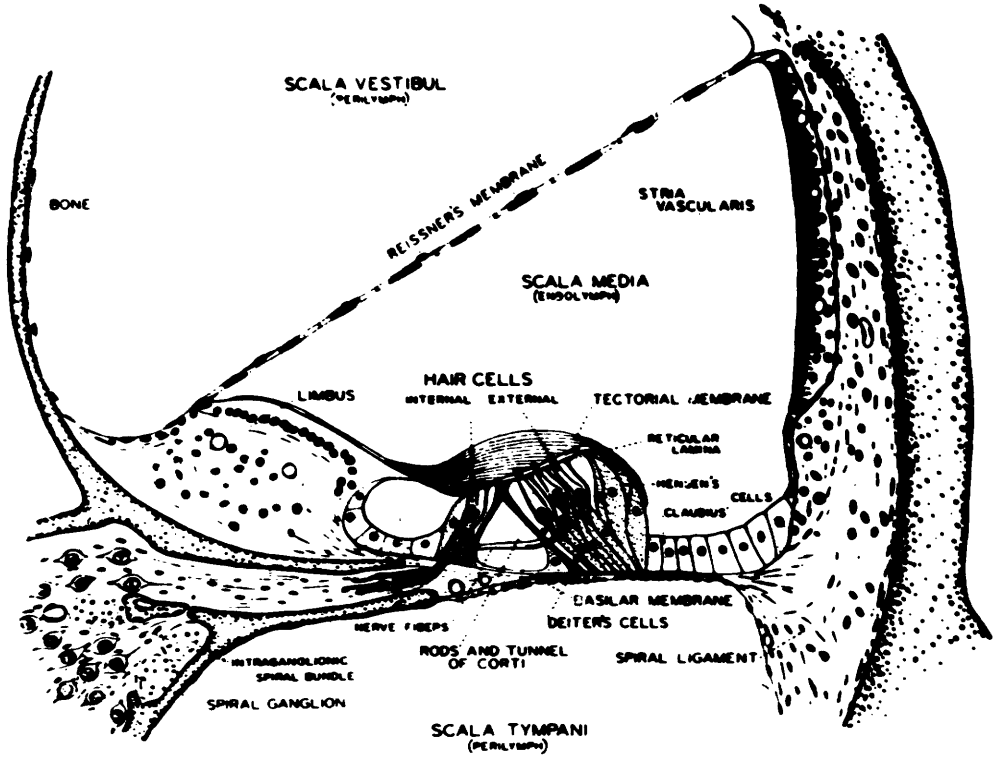


Fig. 2. Cross-section drawing of second turn of guinea pig cochlea. (From Davis and Associates (16).)

propagated along the nerve fibers of the auditory nerve into the medulla. From that point onward, the flow of the neural signals is not so well defined. Certain pathways have been identified, but they will not be discussed here because we are primarily interested in the peripheral part of the system. A fairly recent review discusses the "higher" centers of the auditory system (30). The signal transmission through the peripheral part of the auditory system may be affected by higher nervous centers. Two different processes have been studied: (a) Neural signals can produce changes in the tension of the muscles of the middle ear which alter the signal transmission through the middle ear (34, 79). (b) Efferent neuronal pathways may affect the transmission in the inner ear (31, 61). There also is some evidence that auditory nerve responses can be altered by stimulation of other sense modalities (60).

1.3 ANATOMY OF THE INNER EAR

The anatomy of the cochlea is rather well known. Figure 2 shows the structure of the cochlea in a cross section of one turn. The paths followed by the nerve endings to the hair cells have been determined in some detail (25), and the size and number of fibers in the nerve have been studied (52, 29). The dimensions of the cochlea have been determined accurately (26).

1.4 MECHANICAL PROPERTIES OF THE INNER EAR

Our knowledge of the mechanical properties of the cochlear membranes, and of the way in which they respond to various stimuli, results almost entirely from a long series of experiments performed by von Békésy (10, 11). Stated briefly, the mechanics of the cochlea is as follows: Vibration of the stapes produces a pressure difference in the cochlear fluid and a resulting vibration of the cochlear partition. The vibration can be described as a traveling wave moving from base to apex. For sinusoidal vibration of the stapes, the partition has a maximum amplitude of vibration at one position. The position depends on frequency, moving from the apex toward the base as the frequency is increased. The tuning is not sharp, however. Low-frequency sinusoids produce a point of maximum vibration near the apex, but the whole basilar membrane vibrates, and the change in amplitude with position is very gradual. High-frequency tones produce a maximum amplitude of vibration near the stapes, and the amplitude decreases rather rapidly to zero on the apical side of the maximum. Hence, the tuning curves (amplitude versus frequency) for a given point along the cochlea drop off faster above the peak frequency than below it.

This picture of the mechanical behavior of the cochlea is greatly simplified. Some of the complications that have been observed are: (a) the wavelength for the traveling wave is not uniform along the cochlea and depends on the stimulus intensity at high intensity (1); and (b) if the motion of the structures along the organ of Corti is observed during sinusoidal stimulation, the direction of motion changes from one position to another (8).

1.5 ELECTROPHYSIOLOGY OF THE COCHLEA

The physiology of the cochlea has been studied extensively by recording electric potentials from electrodes placed in or near the cochlea. These potentials have been classified in four classes by Davis (14): the endocochlear potential, the cochlear microphonic potential, the summating potential, and the action potentials of the auditory nerve. It is this neural response with which this report is primarily concerned. It is the signal that carries "information" about the acoustic stimulus into the central nervous system. The other potentials are thought to play a role in the excitation of the action potentials, but their significance in the signal-transmission process is not completely determined. Since these other potentials will be referred to later, we shall discuss them now in some detail.

a. Endocochlear Potential

If potential differences are measured between various points in the cochlea, in the absence of acoustic stimuli, various dc potential differences are observed (6, 73). The potential within each scala is nearly constant, but a voltage of 70-90 mv can be measured between the scala media and either the scala tympani or the scala vestibuli. The region within which this positive potential exists is shown in Fig. 3. Three studies, in each of which a different method was used, have indicated that the stria vascularis plays an important role in the production and maintenance of this dc potential (18, 56, 76). The functional significance of this dc potential is a matter of speculation. Under some

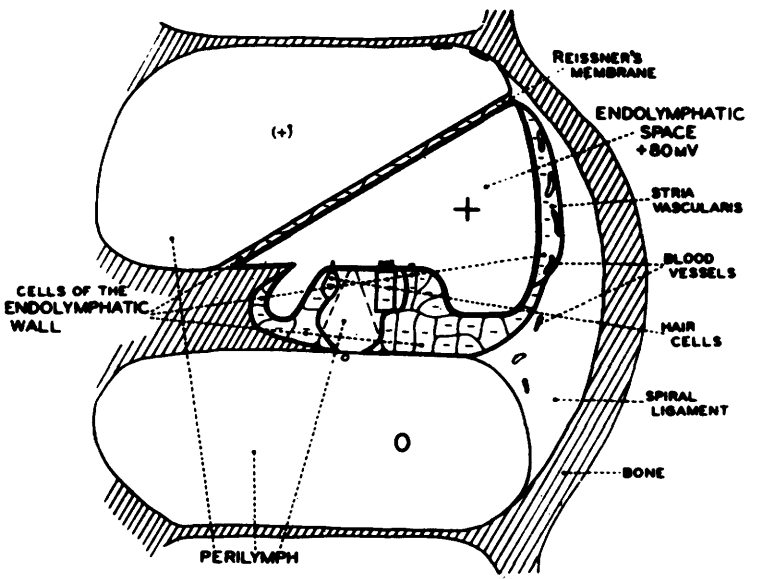


Fig. 3. Diagram of the distribution of the dc potentials: intracellular, negative; endocochlear, positive. Reference potential is perilymph of scala tympani. (From Tasaki, Davis, and Eldredge (73).)

conditions it appears to change in parallel with the microphonic potential (7), and to be distributed in space similarly to the microphonic potential (73). The endocochlear potential can also be increased or decreased by a steady displacement of the basilar membrane (6, 73). These observations have led to the suggestion that the endocochlear potential represents a source which is amplitude-modulated to produce the cochlear microphonic potential (6, 7, 14). However, Davis has also stated that "the D-C endocochlear potential is not necessary for the generation of CM. (It may, however, serve to make the CM response larger or more sensitive.)" (18). It has also been shown that the microphonic can be small or absent when the dc potential is normal (18, 76).

b. Cochlear Microphonic Potential

The electric response that has been studied most extensively is called by Davis (14) the cochlear microphonic (CM). The most striking characteristic of CM is its apparent linear dependence on the acoustic stimulus over a considerable range. For sinusoidal stimuli, CM is sinusoidal and its amplitude varies linearly with the amplitude of the stimulus up to moderate intensities (74).

The source of the cochlear microphonic is thought to lie in the organ of Corti, probably in the hair cells. The evidence for this is the observation that the polarity of the microphonic reverses when the electrode is moved through the organ of Corti (7, 73). It has also been shown that in cases in which the organ of Corti is damaged or missing, CM is reduced or missing (18, 76). The difference of polarity of CM in different locations has been used to produce records of auditory responses in which either the neural or microphonic component is emphasized (74).

It has been shown that the cochlear microphonic recorded by this technique is produced by small sections of the organ of Corti. The response recorded at one site is not altered when the response at another position is varied by obstructing the motion or by addition of chemicals (75). It has also been demonstrated (74) that the responses recorded from different turns of the cochlea may have quite different waveforms. By moving the basilar membrane with a fine vibrating needle, von Békésy showed that CM is proportional to the displacement of the membrane (4). Also, the variation of the microphonic with position along the cochlea has been observed to be covariant with the amplitude of vibration (74). When the stimulus intensity is increased sufficiently, the amplitude of CM increases more and more slowly until it levels off and even decreases with increasing intensity (74). An interesting feature of the departure from linearity is that the waveform of the response to sinusoidal stimulation remains nearly sinusoidal even in the nonlinear region for medium and high frequencies; some clipping, which has been ascribed to nonlinear transmission in the middle ear (14), can be observed at low frequencies.

When von Békésy (9) moved the organ of Corti with a vibrating electrode, he found that the greatest microphonic potential was produced by radial vibrations when the electrode was near the outer hair cells, and by longitudinal vibration when the electrode was

near the inner hair cells. (In both forms of vibration the electrode moves parallel to the basilar membrane: in the longitudinal mode it moves along the direction from oval window to helicotrema, and in the radial mode it moves perpendicularly to this direction, that is, transversely.) Von Békésy's observations (8, 9) suggest that, for sinusoidal stimuli, the inner and outer hair cells produce microphonics in response to different directions of motion at different positions along the cochlea.

Von Békésy has shown that the power dissipated by the microphonic potential is greater than that delivered by the acoustic stimulus (5). Hence, it seems that the microphonic potential represents the output of a "biological power amplifier" rather than just a transduction of the acoustic energy into electric energy. Possibly the dc endocochlear potential represents the source that is modulated by the acoustic signal (6).

Although the role of the microphonic in the signal-transmission process is not definitely established, it is often considered to act as a direct electrical stimulus on the nerve endings (14). It has also been suggested that some sensory nerve endings are not sensitive to electrical stimulation (39) and that, therefore, chemical excitation seems more reasonable (40).

c. Summating Potential

Less is known about the summating potential (SP) than about the endocochlear or the cochlear microphonic (CM) potentials. It was first described (20) in 1950, but it proved difficult to give a consistent description of its behavior. Recently, in several papers, Davis and his coworkers suggest a possible mechanism for the production of SP, and assign to it a role in the excitation of the nerve endings (15, 17, 18).

When cochlear responses to fairly long bursts of high-frequency tones are observed, the microphonic potential often appears to shift its base line during the burst (Fig. 4). This shift has been called the "summating potential." It can be thought of as resulting

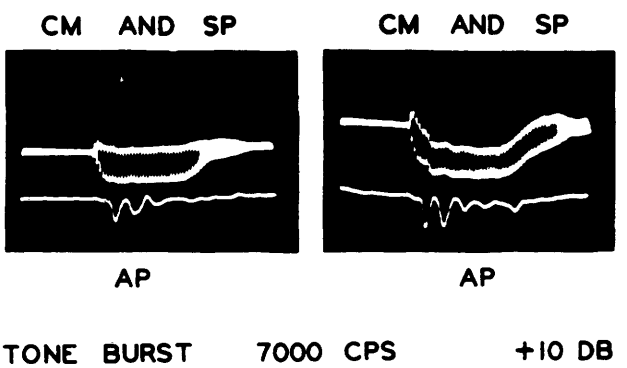


Fig. 4. Cochlear microphonic and summating potential (upper traces) and action potential (lower traces) from basal turn of guinea pig in response to 7000-cps tone burst. Duration of plateau of tone burst, 4 msec; rise time, 1 msec; stimulus is 10 db stronger for the responses on the right. (From Pestalozza and Davis (58).)

from a kind of detection or demodulation process that produces a signal having the waveform of the signal envelope if the carrier has a sufficiently high frequency. The process performing the detection can be thought of as rectification followed by integration (summation).

The difficulties connected with the study of this response arise largely from its variability from one preparation to another, and from time to time during an experiment. It sometimes has one polarity, and sometimes another, and it seems to be increased by anoxia and surgical trauma (17), which may indicate that it is not significant in a healthy preparation. Davis has dealt with these "vagaries of the summating potential" (15) by postulating two summating potentials of opposite polarity. However, the negative summating potential, SP_-, is the one that is most often observed, and has been placed in prominence by the theory that has been proposed (15). Davis also states that "the usual polarity is negative, ... under certain circumstances, particularly in fresh preparations and with weak stimuli, the polarity is positive" (17).

The amplitude of SP increases with intensity, but it is also difficult to obtain consistent measurements. In some cases the polarity of SP changes from plus to minus as the intensity of the stimulus is increased (17), so that one is not quite sure what he is measuring. It does seem to be quite well established that the amplitude of SP continues to increase for the high intensity levels at which CM is decreasing (17).

The summating potential seems to have its largest value when it is measured between an electrode in scala media and an indifferent electrode (neck, scala tympani). Its spatial distribution across the cochlea differs from that of the microphonic potential. However, this does not necessarily indicate that SP and CM arise from different structures, since the impedance of the membrane and fluids differ for the CM and the SP that have different frequency compositions (17). The variation of the amplitude of the summating potential along the cochlea is also quite different from the microphonic. Although the actual data have not been published in detail, it is stated that "SP response is associated more closely with the position of maximum amplitude of displacement ... apparently the SP response is associated particularly with the part of the resonance pattern where amplitude is large but the wave length of the traveling wave is becoming short" (17). That is, SP seems to have a maximum in the region of the cochlea in which the amplitude of vibration is decreasing from its maximum (2).

Although the source of the summating potential is not well established, evidence has been cited which suggests that the internal hair cells may be the source of the negative component, SP_- (18). This suggestion, together with several others, has been woven into a comprehensive theory by Davis (15) who assumes that SP_- is produced by the internal hair cells in much the same way as the microphonic potential is produced by the external hair cells. The rectification and integration are presumed to result from mechanical action, in which a constant shift of the tectorial membrane relative to the hair cells introduces a constant bending with resulting dc potential. This shift is assumed to occur in the longitudinal direction (along the cochlear duct). The possibility of having this kind

of motion is indicated by von Békésy's observation of eddies (2) in the perilymph in the same region where SP, presumably, is largest. Also, von Békésy has shown that longitudinal vibration of the tectorial membrane is most efficient in producing CM when the vibration occurs near the internal hair cells (7). In Davis's theory, the microphonic and summating potentials are then assumed to act as electric stimuli on the nerve endings that terminate on the external and internal hair cells, respectively. The microphonic, since it follows the fast vibration of the membrane, tends to excite the nerve fibers in synchrony with the stimulus frequency; this provides a mechanism that codes the stimulus frequency into frequency of neural response. The summating potential will tend to excite neurons in a more localized area because it is more closely associated with the point of maximum deflection. Hence, SP seems suited to code stimulus frequency in terms of place along the cochlea. The nerve fibers that end on the internal hair cells are more discrete along the cochlea (25), and hence seem to be better adapted to efficient "place" coding. This theory thus offers two possibilities for frequency coding, since "place" and "period" (50, 21) are represented in the cochlea by separate mechanisms. Davis also suggests that SP is the more important process at high intensities because it is still increasing when CM is decreasing. Hence, SP extends the dynamic range of the cochlea. These are the important points of a theory that encompasses many known phenomena, although many of the specific mechanisms are still to be verified.

1.6 AUDITORY NERVE POTENTIALS

The summated action potentials of the auditory nerve fibers can be recorded from wire electrodes placed almost anywhere near the cochlea (67). Certain electrode arrangements provide action potentials ("neurals") with a minimum of microphonic potential (23, 67, 74). The potential recorded by these large ("gross") electrodes represents some kind of summation of the action spikes of the individual axons in the auditory nerve.

The shape of the neural in response to an acoustic click, as recorded from a cat, is shown in Fig. 5. Click responses of similar waveform have been recorded from several other animals (43, 45, 46, 60, 64, 66, 71). The two negative deflections have been designated (63) by the symbols N_1 and N_2.

When one looks for neural responses with gross electrodes, it is easiest to find well-defined responses when the stimuli are impulsive. A great deal of work has been done on determining characteristics of the "click response." (Generally, the click has been generated by applying a short (0.1-msec) rectangular voltage pulse to an earphone.) A neural response of similar shape is produced at the onset of noise or high-frequency (above 5 kc) tone, if the stimulus is turned on rapidly enough. If the tone or noise is turned on gradually, no neural response of this type (N_1) is observed (37). This fact can be explained if we consider the gross electrode response as an indication of synchronous "firing" of a large number of neural units. When the stimulus changes rapidly, many units are stimulated at the same time, and their responses are summated at the electrode to give a large deflection. During maintained stimulation, however, the units

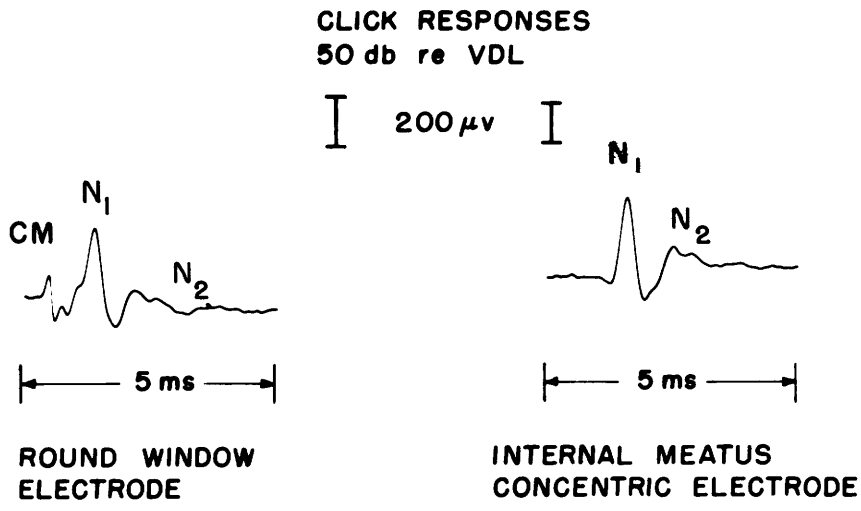


Fig. 5. Click responses recorded simultaneously between an electrode near the round window (left trace) and reference electrode, and between concentric electrodes in the internal auditory meatus (right). In all records, upward deflection indicates negativity of the round-window electrode with respect to the reference electrode, or negativity of the core electrode with respect to the sleeve for the concentric electrode. Note that the microphonic potential is not visible in the response from the concentric electrode. (C-504.)

do not necessarily fire synchronously, and no synchronized response of the N_1 type is observed with the gross electrode.

For low-frequency stimuli (lower than 2000 cps), a neural response can be detected for each cycle of the stimulus, in addition to a larger response at the stimulus onset (23). If the frequency of the stimulus is sufficiently low that the responses in each cycle do not overlap, the shape of the neural is similar to that of the click response (68). After a low-frequency tone has been turned on, the amplitude of the neural response decreases steadily for several minutes (23). In order to avoid this adaptation phenomenon when studying the effect of other stimulus parameters, many workers have preferred to use clicks and short bursts of tone at a repetition rate that is low enough (1/sec) to avoid adaptation. Under these conditions, the amplitudes of the click responses seem to be independent of each other (27). Changes in response with repetition rate will be described in Section IV.

By using stimuli of this type, the changes in the response with stimulus intensity have been studied (28, 18). In general, the amplitudes of N_1 and N_2 increase with intensity. This is interpreted as an indication that more and more neural units respond as the stimulus strength is increased. Frishkopf describes this behavior mathematically in terms of a probability model (27, 28). He found that, for low intensities, the data can be represented in terms of a uniform population of identical neural units with randomly varying thresholds. The question of how many populations are needed to represent the dynamic range has not been studied in detail, but it has been suggested that there are three populations (18).

It is also observed that the latency of the "neurals" decreases as the stimulus intensity is increased. The mechanisms involved in this latency change have not been investigated, but a similar change is found when peripheral nerve is excited electrically (24). It has been suggested that this decrease in latency is attributable to the fact that with stronger excitation the "triggering level" is reached earlier (22).

One of the most striking properties of the neural response is observed when impulsive stimuli are presented against a background of noise. A very low level of noise (that is, one that cannot be detected in the microphonic component) reduces the neurals appreciably (63). This phenomenon can also be interpreted in terms of a desynchronizing of the action potentials. The noise stimulates the neural units continuously, and some of them respond at any given instant. Hence, when the click occurs, some of the recent responders are refractory and unable to respond. This interpretation is supported by the observation that acoustic noise can mask responses to electric stimulation of the auditory nerve (49). The masking phenomenon was also treated by Frishkopf in terms of a probabilistic model (27). The results supported the single-population model for low-intensity stimuli.

Observations have also been made of the effects of previous stimuli on neural responses to impulsive stimuli. McGill and Rosenblith (53, 54) found that the response to the second of two clicks was reduced if the two clicks were separated by less than approximately 100 msec. The response to the second click decreases if the interval between clicks decreases, and if the intensity of the first click is increased. The response to the second click is never supernormal. Neural responses to clicks can be affected for longer periods by bursts of high-intensity sound (48, 42, 65). Following exposure to noise and high-frequency tones, the amplitude of the neural response recovers monotonically to its pre-exposure level. For exposures at low frequencies (200-500 cps) there is a period of supernormal response (65, 44). It is interesting to note that for most reversible recoveries after exposure to intense sound, CM remains nearly unchanged (42, 48, 65).

In this section we have emphasized the main characteristics of the neural response for various stimulus patterns. We did not attempt to present all of the work that has been done; studies of the effects of drugs, temperature, surgical interference, and so forth, have not been mentioned. An extensive bibliography of this work has been given by Davis (14).

Some important observations of the response of single auditory nerve fibers have been made by means of microelectrodes (71, 72, 47). In general, it can be stated that the results are compatible with the model which considers the N_1 deflection of the gross electrode response to be a summation of single-unit action-potential spikes from the auditory nerve fibers. Tasaki's results indicate that the auditory nerve fibers quite often respond with two spikes to an impulsive stimulus, and he suggested that the second neural component (N_2) may be a result of this (71). Other data (67) indicate, however, that this interpretation may be only partially correct. In the presence of continued

stimulation by high-frequency tones single units exhibit a decrease in the rate of firing after an initial burst (32, 33, 71). They continue, however, to fire at a rate that exceeds the rate of spontaneous activity. The decrease in number of firing units together with a desynchronization of those that fire makes it more difficult to detect the existing neural activity with gross electrodes.

Although it is desirable to draw parallels between electrophysiological and behavioral data, very little work has been done on collecting both kinds of data from the same animals. In one study it was found that the threshold for observation of the click response in pigeons was very close to the behavioral threshold (43).

1.7 EXPERIMENTAL PROCEDURES

In general, the techniques used in all of the work reported here are similar to those used by other workers (e.g., Frishkopf (27), and Goldstein, Kiang, and Brown (38)). A cat is anesthetized with Dial (75 mg/kg) injected into the peritoneal cavity. After a tracheal canula has been inserted, the bulla of one ear is exposed and the bone opened so that the round window of the cochlea becomes accessible. A wire electrode is placed in contact with the bone near the round window. Responses are recorded between this electrode and a reference lead attached to the headholder. In some experiments, a section of the skull and a portion of the cerebellum were removed to expose the eighth nerve at the point where it enters the medulla from the internal auditory meatus. Responses were then recorded from a concentric electrode placed in the nerve.

In all experiments, the stimuli were generated by a Permoflux PDR-10 earphone connected to a plastic tube that was tied into the external auditory meatus.

The animal was placed in a soundproof, electrically shielded room. Various stimulus waveforms were generated electronically (38) and fed into the room to the earphone. The potentials obtained from the electrodes were amplified (amplifier passband, 8-7000 cps) and observed on an oscilloscope, recorded on magnetic tape, and/or processed by an average response computer (13).

During the experiment, the condition of the animal was maintained as constant as possible. The temperature of the room was regulated at approximately 25°C. Rectal temperature was monitored and maintained between 35-37°C by using a heating pad. If there were indications that the effect of anesthesia was wearing off, an additional dose of 0.25-0.5 cc was given.

At the beginning of each experiment the animal's threshold for neural responses was determined by reducing the stimulus intensity to a level that produced responses that were visually detectable on the oscilloscope screen approximately 50 per cent of the time. This "threshold" is called VDL (visual detection level). This level was determined at the beginning of the experiment and the measurement was repeated several times during the experiment, in order to check the stability of the preparation. Furthermore, the size of an averaged response to a moderately intense stimulus (20-30 db re VDL) was measured at least once every hour, and after periods of intense stimulation, which might

be expected to cause long-lasting aftereffects. If the response amplitude differed by more than 10 per cent from the "standard" value, all acoustic stimulation ceased until the response had returned to the 10 per cent limit. For all of the animals studied, the VDL for "clicks" produced by applying 0.1-msec rectangular pulses to the earphone at a rate of 1/sec was between -95 db and -105 db re 4 volts.

II. ELECTRIC RESPONSES FROM DENERVATED COCHLEAS

We now present results from experiments performed on cats with unilateral degeneration of the eighth nerve. The purpose of these experiments was to study the behavior of non-neural electric responses that can be recorded from electrodes near the round window. The results of these experiments are involved in the interpretation of the behavior of neural responses (Secs. III and IV).

2.1 SPECIAL TECHNIQUE

The surgery required to obtain the denervated preparations was performed by Dr. N. Y-S. Kiang at the Eaton Peabody Laboratory of Auditory Physiology, of the Massachusetts Eye and Ear Infirmary. The eighth cranial nerve was sectioned at the point where it enters the medulla from the internal auditory meatus. In order to expose the nerve at this point, a portion of the skull was removed and the cerebellum was pushed aside above the nerve. After the nerve had been sectioned, the wound was closed and the animal allowed to recover from the surgery. After sectioning, a time of approximately five weeks was allowed for degeneration of the nerve cells. After this period, the animals were prepared as described in Section I, and the remaining electric responses were observed with electrodes near the round window. Histological preparation of the studied cochleas is still being carried out at the Eaton Peabody Laboratory. Since it is difficult to section the nerve completely without injuring the blood supply to the cochlea, the extent of the degeneration will not be known completely until the histology has been completed.

This technique has been used previously to observe CM responses to clicks (62, 69). The shapes of the CM responses to short rectangular pulses which we obtained (Fig. 6) are reasonably similar to those obtained by other workers who used similar acoustic systems (69, 27). (Another technique (74) for observing microphonic potentials that are relatively free from "neurals," without damaging the nerve, has been used extensively in guinea pigs.)

The CM responses to clicks as observed with a round-window electrode are "contaminated" in several ways:

(a) The shape of the microphonic response is determined by the entire mechanical system, consisting of the earphone, connecting tube, outer and middle ear cavities (including the eardrum and ossicles), and the relevant portions of the cochlea. Since we did not monitor the signal at any point between the earphone input and the round-window electrode, we do not know in what way the various parts of the system contribute to the CM response. The best indicator of the acoustic pressure response to the rectangular pulse is that measured by Frishkopf (27) with the same type of earphone operating into a 1-cc cavity.

(b) The CM recorded at the round window is a weighted sum of the microphonic potentials produced all along the basilar membrane, and hence will probably not represent the motion of any one region. Probably, only the basal turn contributes significantly

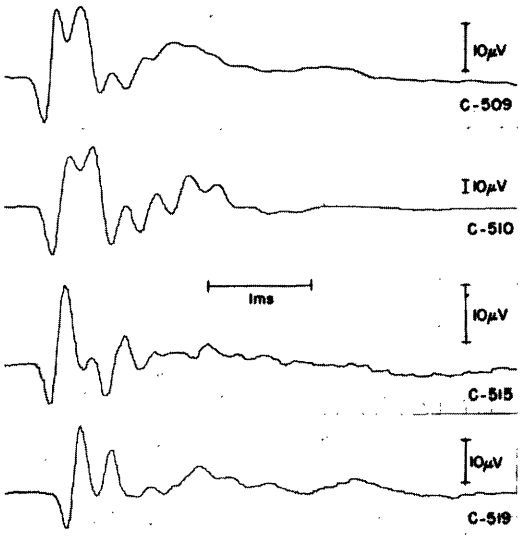


Fig. 6. Microphonic potentials in response to rarefaction clicks from 4 animals with denervated cochleas. Clicks were produced by applying rectangular pulses of 0.1-msec duration to PDR-10 earphone. Intensity, -60 db re 4 volts. Traces were obtained by averaging 64 responses recorded from electrode near round window.

to CM at the round window (3, 75), and there is evidence that a large part of the basal turn vibrates in phase (1, 74). Hence, as a first approximation, the shape of the CM recorded from the round window can be assumed to represent the motion of the membrane in the basal turn. The validity of this approximation depends upon the frequency composition of the acoustic stimulus.

(c) The extent to which the potentials recorded at the round window contain components other than CM may depend upon the success of the nerve-sectioning procedure, the physiological condition of the animal, and so on.

2.2 IMPULSE RESPONSE

In Section I evidence indicating that the microphonic potential can be considered as the response of a linear system for low and medium intensity stimuli was cited. If this is true, the system can be characterized by its "impulse response," h(t). In particular, the response $e_o(t)$ to any stimulus waveform $e_i(t)$ (within the linear range) can be found by convolving the stimulus with the impulse response. Thus

$$e_o(t) = \int_{-\infty}^{\infty} e_i(\tau)\, h(t-\tau)\, d\tau \qquad (1)$$

Also, the Fourier or Laplace transform of the impulse response is the transfer function of the system (35). In order to determine the impulse response of the system (earphone, tube, ear), a rectangular pulse was applied to the earphone and the microphonic response

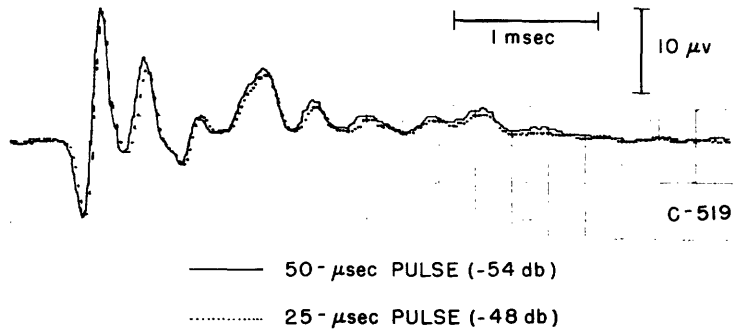


Fig. 7. Averaged microphonic responses to rarefaction clicks produced by 25-μsec and 50-μsec pulses of equal area.

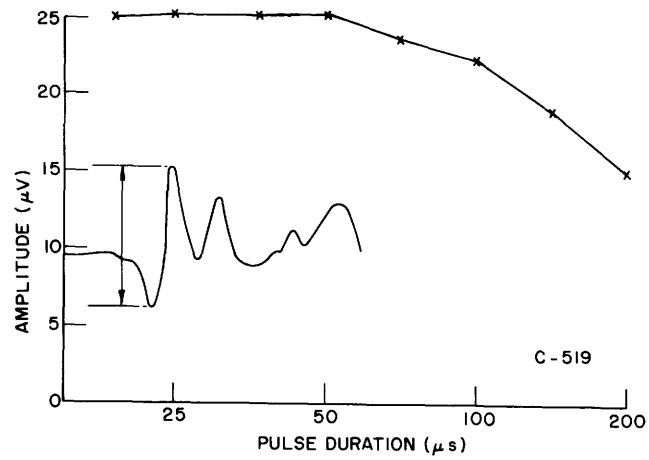


Fig. 8. Peak-to-peak amplitude of the microphonic in response to rarefaction clicks as a function of pulse duration. The area under the pulse is kept constant. Inset indicates the amplitude that was measured. Intensity of 100-μsec pulse, -60 db re 4 volts.

was observed. The duration of the pulse was then decreased and its amplitude increased so that the area under the pulse remained constant. If the pulse is short compared with the impulse response, it will effectively be an impulse for the system. For this condition, changing the pulse duration and keeping the area constant should not change the response. In Fig. 7, CM responses for 25- and 50-μsec pulse durations are superimposed to show that the difference is negligible in that range. In Fig. 8, peak-to-peak amplitude of the CM is plotted against pulse duration; a pulse of approximately 50 μsec, or less, is effectively an impulse. Since 100-μsec pulses had been used extensively by previous workers and the departure from the impulse response is slight, we have continued to use this length. The data indicate that the CM responses to the "clicks" can indeed be considered to be the "impulse response" of the system at moderate intensities.

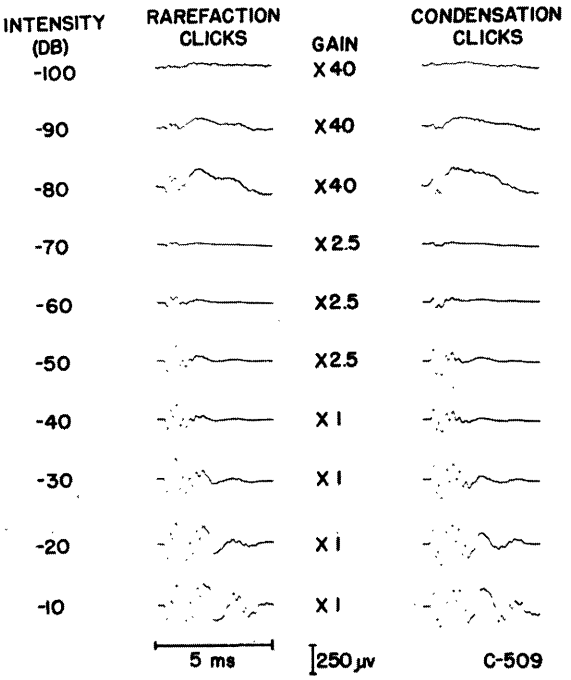


Fig. 9. Averaged responses to condensation and rarefaction clicks (0.1 msec) from a denervated cochlea. Threshold for visual detection of the microphonic in single traces lies at approximately -70 db! Click repetition rate 10/sec up to -30 db, 1/sec above -30 db. Click reference level, 3.8 volts. Number of responses averaged: 512 at -100 and -90 db; 256 at -80 and -70 db; 128 from -60 to -30 db; 32 at -20 db; 16 at -10 db.

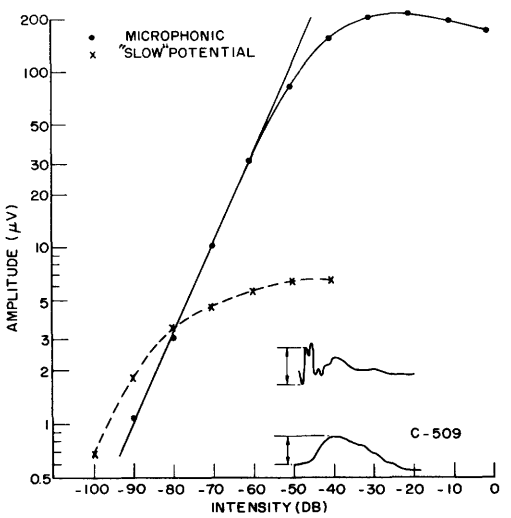


Fig. 10. Amplitudes of CM and "slow" potentials versus intensity from data of Figs. 9 and 12. The amplitudes measured are indicated in the insets. The "slow" potential cannot be measured at high stimulus intensities because a faster component overrides it in the records. The straight line indicates the linear growth of CM in the low-intensity range; that is, the amplitude increases by a factor of 10 for a 20-db rise in stimulus intensity.

2.3 CHANGES WITH STIMULUS INTENSITY

Figure 9 shows averages of cochlear responses of a denervated ear to short pulses of both polarities over a range of 90 db. It appears that the waveform of the "early" CM response does not change appreciably over the low-intensity range (-100 to -50 db). The amplitude of this CM response is plotted against intensity in Fig. 10. The linear increase of amplitude with waveform over the low-intensity range supports the conclusions of others (for example, Tasaki, Davis, and Legouix (74)) that the CM can be considered as the response of a linear system over this range. The departure from linearity at high intensities (Fig. 10) is similar to that in CM curves obtained for pure tones in normal preparations (70, 74, 79). In the high-intensity range, the most striking change in the waveform of the response is the appearance of large potentials at relatively long latencies.

2.4 REVERSAL OF RESPONSE WITH STIMULUS POLARITY CHANGE: THE SLOW POTENTIAL

One of the characteristics of CM that has been used to distinguish it from other potentials is its reversal of polarity with a change in stimulus polarity (63). Inspection of the records of Fig. 9, however, shows that the electric response from the denervated ear does not reverse completely when the polarity of the stimulus pulse is changed. In Fig. 11 averaged responses to condensation and rarefaction pulses are superimposed to demonstrate this lack of total reversal. Figure 12 shows the waveforms that are obtained when we add an equal number of responses to condensation and rarefaction clicks. The resulting waveforms represent mathematically the component in the two types of responses that does not reverse. This "common" component appears to have a relatively constant shape in the low-intensity range. Figure 13 shows this for two different animals. This common component starts at a significantly longer latency than the CM. This indicates that it is not merely the result of imperfect cancellation resulting from variability in the response or the preparation. For low intensities, cancellation is complete during the first quarter or half millisecond after the onset of CM. The amplitude of the slow wave is plotted against intensity in Fig. 10. At intensities above -50 db the common component changes in character because it then includes faster waves. This may indicate that when the process that gives rise to CM becomes nonlinear, it becomes asymmetrical, so that the CM responses cease to cancel perfectly. These faster potentials might also be partly summating potential, since SP becomes more prominent at high intensities (17). Because SP has only been studied for tone bursts, it is difficult to determine what it might look like in a click response.

Since the slow common potential at low intensities is primarily negative and has about the same latency as N_1, it might represent the response of some nerve fibers that have remained functional after the surgery. In order to determine whether this response has the properties of a neural response, a series of responses to condensation and

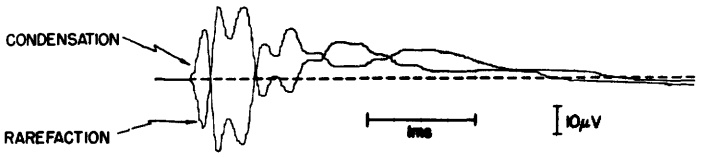


Fig. 11. Superimposed averaged responses to condensation and rarefaction clicks. (Same data as for Fig. 9.) Note asymmetry with respect to base line. (C-509.)

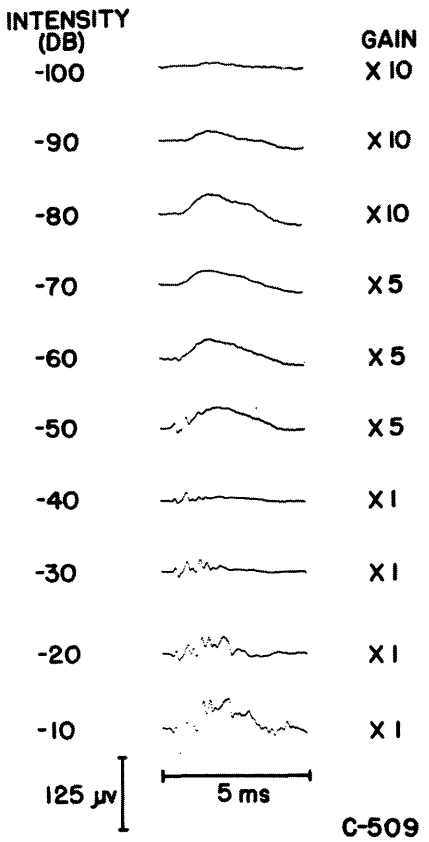


Fig. 12. Responses from a denervated cochlea obtained by adding equal numbers of responses to condensation and rarefaction clicks. Total number of responses added in each trace: 1024 at -100 and -90 db; 512 at -80 and -70 db; 256 from -60 to -30 db; 64 at -20 db; 32 at -10 db.

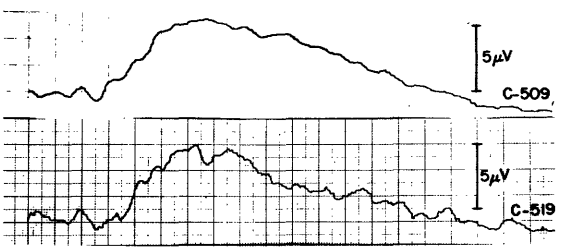


Fig. 13. Sums of responses to condensation and rarefaction clicks from two preparations with sectioned eighth nerves. Intensity, -60 db re 4 volts; click repetition rate, 10/sec. Number of responses averaged, 128.

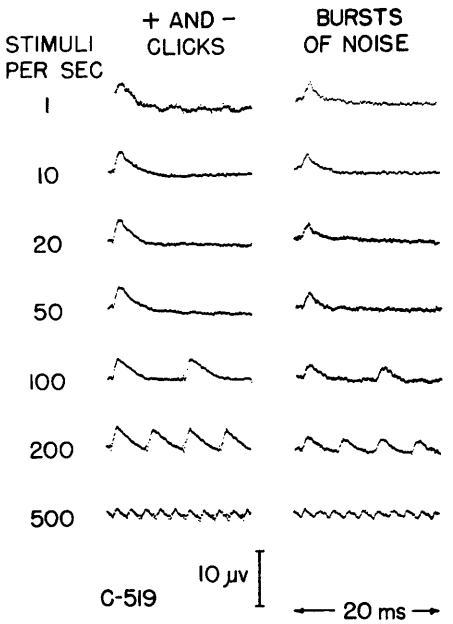


Fig. 14. Averaged responses from a denervated cochlea as a function of stimulus repetition rate. Left-hand column was computed by adding equal numbers of condensation (−) and rarefaction (+) click responses. Right-hand column is averaged responses to 0.1-msec bursts of wideband noise. Number of responses averaged: Left column, 1/sec, 64; other rates, 512. Right column, 1/sec, 128; other rates, 256. Click intensity, −60 db re 4 volts; noise-burst intensity, −60 db re 1 volt rms.

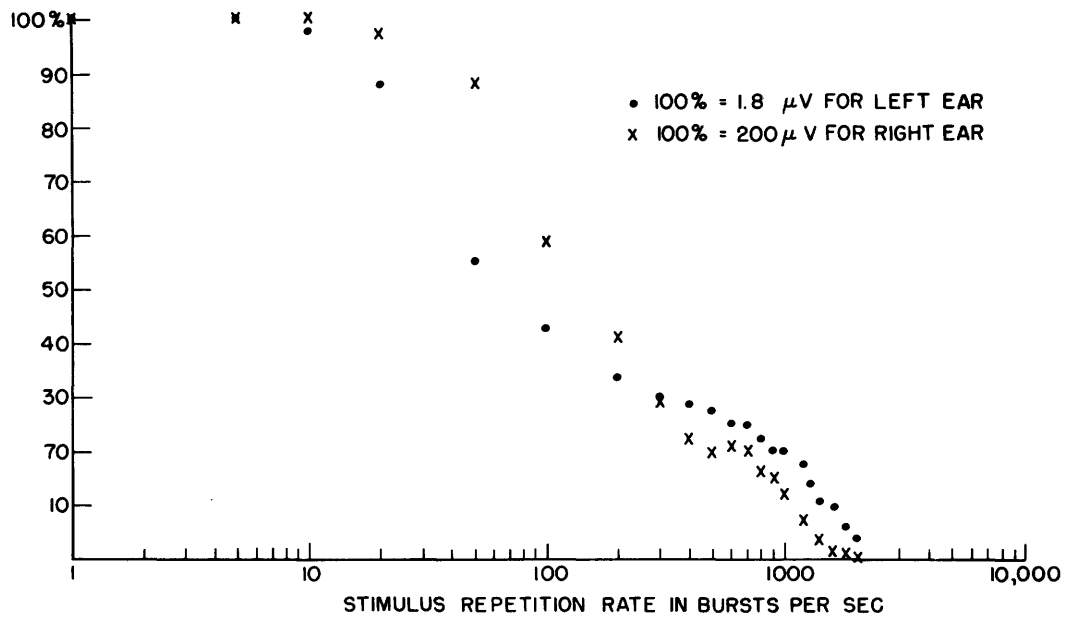


Fig. 15. Normalized response amplitude versus repetition rate. Stimuli were 0.1-msec noise bursts with an intensity of −65 db re 1 volt. The left eighth nerve was sectioned; right ear, normal. (C-510.)

rarefaction clicks was recorded at several repetition rates. The CM response does not change in shape or amplitude for click rates up to 800/sec (see Fig. 48). At this rate the responses overlap each other, so that it is impossible to measure the individual responses directly. The common potential computed from the sum of responses to condensation and rarefaction clicks also remains constant for repetition rates below those at which overlapping occurs (see Fig. 14). This constancy with repetition rate is not observed with neural responses from normal ears at moderate stimulus intensities (see Sec. IV). In this sense, this "slow" response appears to be non-neural. In one of the sectioned preparations (C-510) a small component potential was observed that decreased with rate in nearly the same way as the neural potential in a normal ear. Figure 15 indicates that in this preparation some of the nerve cells remained responsive after the surgery.

2.5 RESPONSES TO NOISE BURSTS

If short (0.1 msec) noise bursts are used as stimuli, the microphonic potentials have waveforms similar to that obtained with rectangular pulses, but the amplitude of CM varies; sometimes it has the polarity that results from a rarefaction click, sometimes the polarity that results from a condensation click (Fig. 16). This result can be predicted from the linear system model for CM. If the noise burst has a duration, δ, then the superposition integral can be written.

$$e_o(t) = \int_0^{\delta} e_i(\tau)\, h(t-\tau)\, d\tau \qquad (2)$$

If the noise burst is very brief compared with the variations in the impulse response,

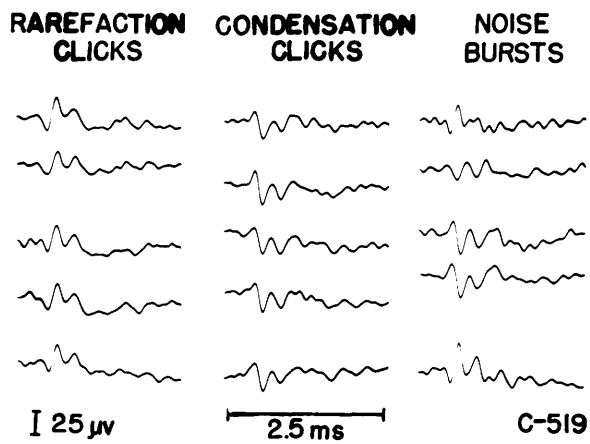


Fig. 16. Microphonic responses to clicks (0.1-msec), and 0.1-msec noise bursts. Click intensity, -60 db re 4 volts; noise-burst intensity, -40 db re 1 volt rms.

the integral can be simplified:

$$e_o(t) = h(t) \int_0^{\delta} e_i(\tau)\, d\tau \qquad (3)$$

This indicates that the CM response to a short burst of noise, has the wave shape of the impulse response and an amplitude that is a random variable equal to the integral of the input voltage during the burst. If the noise is symmetrical about zero voltage, then the mean amplitude of the CM response to noise bursts will be zero. Hence, if a large number of responses to noise bursts is averaged, CM should tend to be very small (13). However, when responses to noise bursts are averaged a slow potential remains, which resembles that obtained when responses to condensation and rarefaction clicks are summed. This potential changes with noise-burst intensity as shown in Fig. 17, and with repetition rate as shown in Fig. 15. This potential seems to be the same as the previously discussed "slow" potential. The presence of this potential in both averaged responses to noise bursts and in sums of responses to condensation and rarefaction clicks is compatible with a model in which the response is the sum of a linear-system response plus a "slow" potential of invariant polarity.

The invariant polarity of the "slow" potential might suggest that we are dealing with the summating potential. Most summating potentials have been recorded in responses to high-frequency tone pips whose duration is several milliseconds. For click stimuli, the presence of SP is difficult to establish. However, noise bursts can be increased in length and if our "slow" potential is SP, its duration should be equal to the duration of the stimulus. Figure 18 shows averaged responses to noise bursts of different length. The slow potential increases in duration with increasing burst length. In this respect it is similar to SP. However, there are several characteristics of this slow potential that distinguish it from SP_- as Davis and his associates (17) describe it: (a) The slow potential is more prominent at low intensities, whereas the threshold for detection of the SP_- is normally at least 20 db above the "threshold" for CM. Our electrode placements differ from those used by Davis' s group, so that such comparisons may not be meaningful. (b) The growth of the slow potential with intensity seems to level off in the middle-intensity range (Fig. 10), whereas SP_- continues to increase with intensity up to levels of cochlear injury (15). (c) The onset of the "slow" potential is approximately 0.4 msec later than the onset of CM to clicks, whereas for tone pips SP_- starts essentially simultaneously with CM (58).

We have also found that the slow potential may have a different polarity from SP when the two are observed in the same ear. Figure 19 shows responses to tone bursts from a denervated and a normal ear in the same cat. In both instances the asymmetrical displacement of the base line (SP) is positive. However, the "slow" potential for this same ear was, as in all our preparations, negative. The positive polarity for SP in Fig. 19 (as observed at the round window) is the same polarity reported by other workers (58), and corresponds to negative summating potential SP_-.

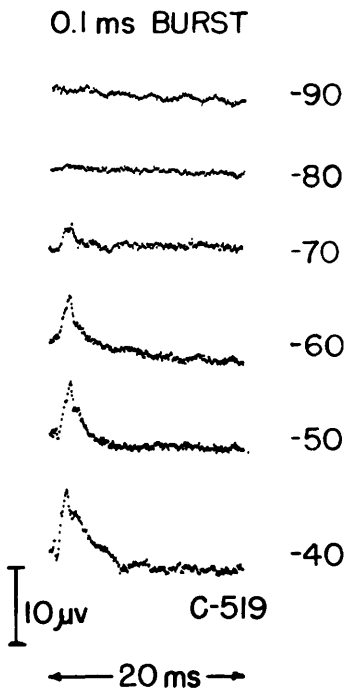


Fig. 17. Averaged responses to noise bursts of 0.1-msec duration. Intensity re 1 volt rms. Number of responses averaged: 512 at -90 and -80 db; 256 at other intensities.

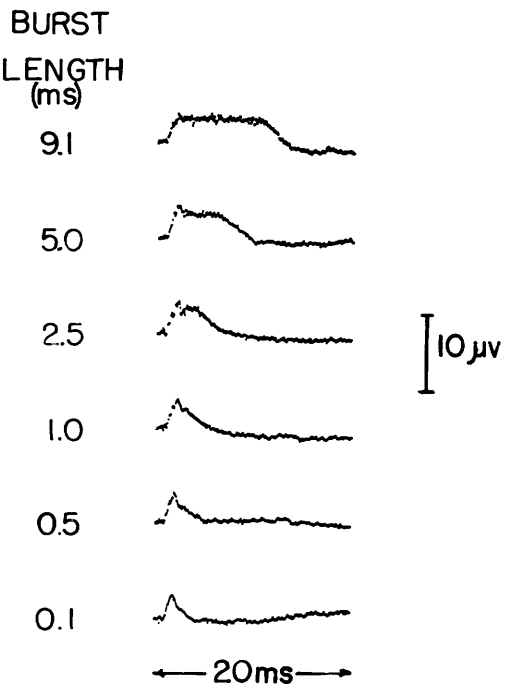


Fig. 18. Averaged response to noise bursts for different burst lengths. Intensity, -60 db re 1 volt rms. Number of responses averaged, 256. (C-519.)

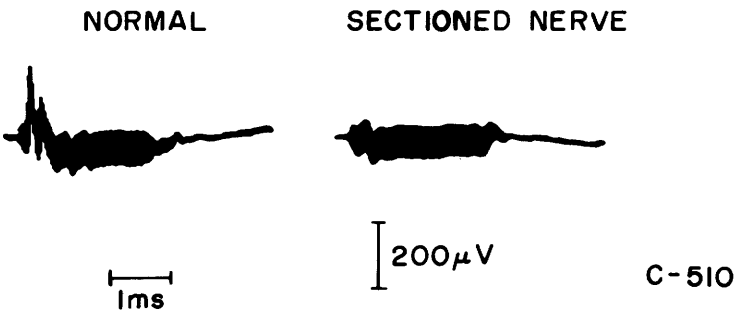


Fig. 19. Responses from a normal and denervated cochlea in the same cat to a 7-kc tone burst (10-msec duration; 1-msec rise-fall time; intensity, -20 db re 1 volt rms). Note asymmetrical deflections with respect to base line.

It would be desirable to determine the distribution of the "slow" potential inside the cochlea, in order to obtain some knowledge of its origin. We would also like to know how it varies with distance along the basilar membrane.

III. CHANGES IN AUDITORY-NERVE RESPONSES AS A FUNCTION OF STIMULUS INTENSITY

3.2 INTRODUCTION

The dependence of the auditory-nerve response on stimulus intensity has been described by many workers (28, 18). Frishkopf (27) has presented click-response data covering a wide intensity range. Davis's (18) "input-output curves" plot the amplitude of neural responses against the intensity for high-frequency tone pips. In all the published data, the amplitude of the neural response increases rather smoothly with increasing intensity (although there is sometimes a plateau) (27), while both onset and peak latency decrease with increasing intensity. The latency decreases fairly rapidly (20 μsec/db) near threshold, and is almost constant for high intensities (27).

3.2 RESULTS

In studying click responses recorded from the vicinity of the round window, several workers have noted differences between the responses to rarefaction and condensation clicks at certain intensities (19, 43, 63). However, it is difficult to be sure that these differences involve just the neurals because of the possible contribution of the CM component in records obtained from electrodes near the round window. It has been shown that auditory-nerve responses relatively free from CM can be obtained from a concentric electrode placed in the internal auditory meatus (23). Figure 5 illustrates the relation between the two types of record.

Figure 20 shows single responses to condensation and rarefaction clicks recorded by such a concentric-electrode configuration for an intensity range of 100 db. In Fig. 21 average peak-to-peak amplitude and N_1-peak latency are plotted against intensity for the data of Fig. 20. These results can be described as follows: (a) At low intensities the neural responses to the two polarities are nearly equal in amplitude and latency. (b) At high intensities the amplitudes are nearly equal, but the latency of the response to the rarefaction click is consistently shorter by approximately 0.2 msec. (c) At -60 db and -50 db the neurals differ strikingly; for condensation clicks the amplitude increases monotonically with intensity, while the response to rarefaction clicks changes shape and becomes smaller (in some sense) in this range. At -60 db (rarefaction click) a new "bump" (arrow) appears at the front end of N_1; this bump grows, and at -50 db is larger than the second deflection. Since we measure latency to the largest negative peak, a large change in latency occurs between -60 db and -50 db.

Figure 22 shows superimposed averaged responses to condensation and rarefaction clicks in another preparation. This display shows clearly that the two response waveforms are nearly the same for both low and high intensities, but a definite latency difference appears at high intensities. Amplitude and latency of the averaged responses are plotted in Fig. 23 as a function of intensity.

Figure 24 shows averaged responses to noise bursts of short (0.1-msec) duration

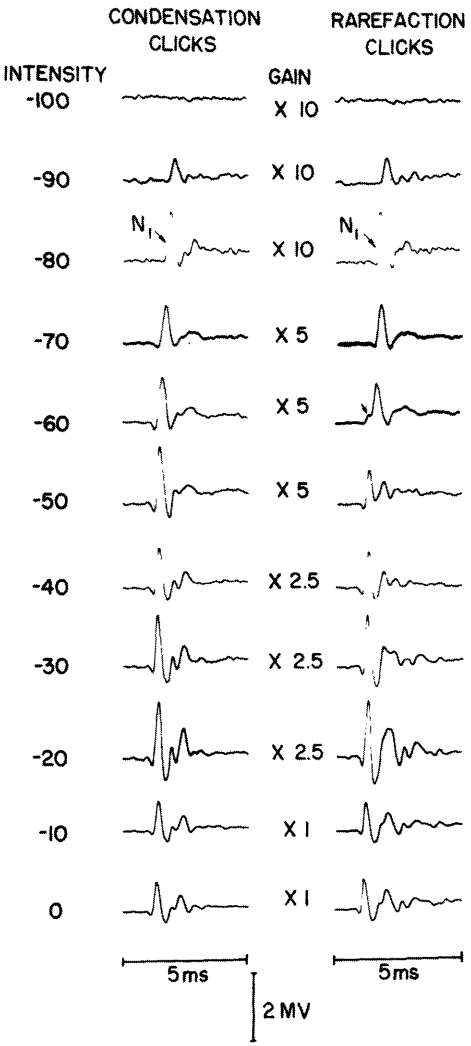


Fig. 20. Single responses to condensation and rarefaction clicks recorded from concentric electrodes in the internal meatus. Downward deflection indicates positivity of the center electrode relative to the sleeve. Click repetition rate, 1/sec; click reference level, 2.5 volts. (C-503.)

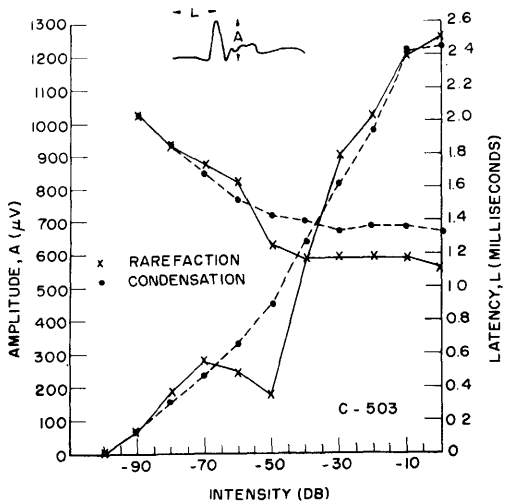


Fig. 21. Amplitude and latency of N_1 responses to condensation and rarefaction clicks (data of Fig. 20). Measurements were made as indicated in inset. When two negative peaks occurred in the response (-60 and -50 db), measurements were made to the larger of the two peaks. Latencies were measured from the time of application of the voltage pulse to the phone; they include approximately 0.3 msec of sound propagation time.

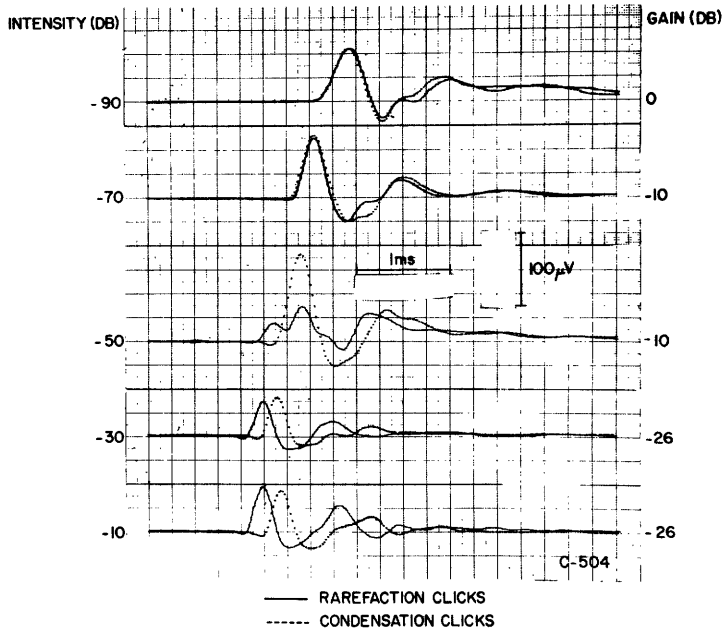


Fig. 22. Averaged responses to condensation and rarefaction clicks (C-504). Conditions are the same as for Fig. 20, except that clicks were presented at a rate of 5/sec. Click reference level, 2.8 volts. Number of responses averaged: at -90 db, 128; at -70 db, 64; at -50 db, 64; at -30 db, 16; at -10 db, 16.

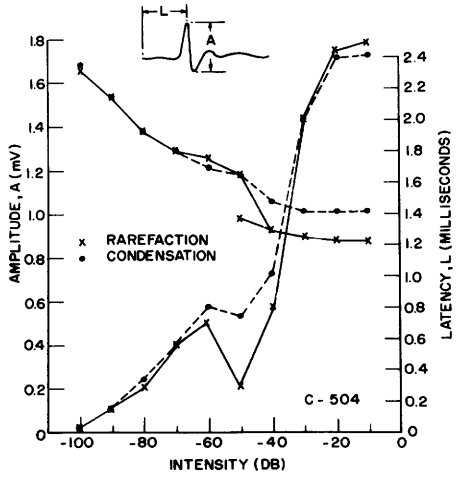


Fig. 23. Amplitude and latency versus intensity for C-504. Measurements made in the same way as those plotted in Fig. 21. At -50 db, the latencies of both negative peaks in the rarefaction click response are indicated.

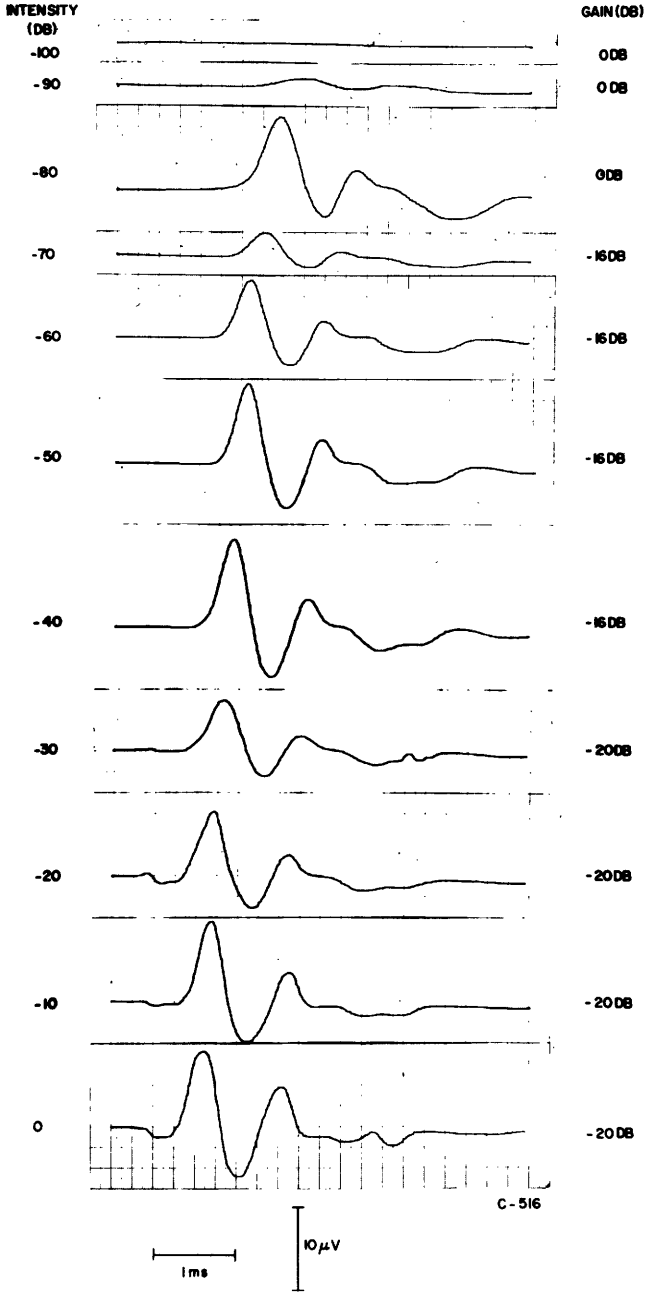


Fig. 24. Averaged neural responses to noise bursts as a function of intensity. (0 db = 1 volt rms to earphone.) Number of responses averaged: 256 at -100 and -90 db; 128 at -80 db; 64 from -70 to 0 db.

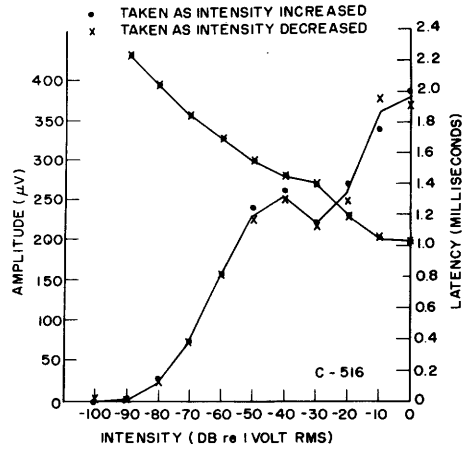


Fig. 25. Amplitude and latency of averaged responses to noise bursts (Fig. 24) versus intensity. Stimulus intensity was raised from -100 db to 0 db, and decreased to -100 db. The dip in the amplitude curve at -30 db might be the result of putting a large number of rarefaction click responses similar to those at -50 db in Figs. 20 and 22 into the average. (Note that intensity levels for noise bursts and clicks cannot be compared directly.) A rather sudden change in latency appears after the dip in the amplitude curve.

recorded from electrodes near the round window. Figure 25 is a plot of amplitude and latency as a function of intensity for these neurals. We have seen that these short noise bursts yield CM responses that resemble CM responses to clicks (see Fig. 16); we might therefore expect that the averaged neural responses to noise bursts would be comparable to neural responses to clicks. Figure 25 shows in some detail that the data on neural responses to noise bursts appear to be consistent with our data on condensation and rarefaction clicks.

3.3 INTERPRETATION

In order to interpret the differences in the behavior of neural responses to condensation and rarefaction clicks, we would like to know the mechanisms that underlie the neural responses. Although these mechanisms are not known, many experimental results are helpful in thinking about the process of excitation of neurals. In particular, we can think in terms of the excitation of neural units by a wave that travels along the cochlear partition from base to apex (11). The form of this wave for our stimuli is not known, but it has been shown that CM recorded inside the cochlea is proportional to the displacement of the membrane (4, 74). There is also evidence that displacement in one direction only excites the neural response (20, 68). We would like to interpret the condensation and rarefaction click responses in terms of the waveform of the CM response to the clicks. Since we do not have data on the form of the CM along the whole cochlea, we must make the approximation that the CM observed near the round window is an adequate representation of the motion of a large part of the basal turn.

Davis has stated that rarefaction at the eardrum leads to neural excitation (20). This

statement is in agreement with the data of Figs. 21 and 23. These figures show that at high intensities the neural response to the rarefaction click has a shorter latency than the condensation click neural response. Rosenblith and Rosenzweig (68) have found that with low-frequency tones the neural responses occur during the positive portion of the microphonic potential recorded from electrodes near the round window. This suggests that the positive microphonic potential represents the rarefaction phase of displacement. The data in Fig. 9 agree with this interpretation, since the initial microphonic deflection for the rarefaction click is positive.

If we consider that positive deflection of the microphonic is associated with excitation, and assume that the neural response is triggered when the microphonic potential reaches a certain level, then a latency difference would be expected between the neural responses to condensation and rarefaction clicks. (The existence of a trigger level associated with a generator potential has been established for the nerve endings in Pacinian corpuscles (51).) This latency difference should be approximately 0.2 msec, since the first positive microphonic deflection in response to a condensation click is approximately 0.2 msec later than the first positive deflection for a rarefaction click. Since the microphonic waveform changes rapidly in time, a change in amplitude would produce little change in the time at which the triggering level is reached. Therefore, we would expect very little change in latency to occur with increasing intensity. These expectations agree quite well with the latency data in the high-intensity range (-40 db to 0 db), and thus support the hypothesis that CM represents the excitatory process for neurals in this intensity range. However, at low intensities, this picture does not seem to fit, since the latency of neural responses for both click polarities is nearly the same, and this common latency changes rather rapidly with intensity. Perhaps another excitatory process (other than the process represented by the microphonic) predominates in the low-intensity range. This excitatory process should be indifferent to changes in click polarity. The "slow" potential described in Section II has several characteristics that make it a candidate for such a process: (a) This "slow" potential is the same for both click polarities. (b) It has a relatively gradual slope so that the instant at which the trigger level is reached will change with stimulus intensity; hence there will be latency changes with intensity similar to those actually observed. (c) At low intensities it is more prominent than CM. (See Fig. 10.)

The striking difference between the condensation and rarefaction click responses in the intermediate intensity region can now be considered in terms of these two excitatory processes. In this range we can assume that both processes are effective, and that excitation by CM becomes predominant as the intensity increases from -60 to -40 db. If we consider the instants at which these processes reach the assumed trigger levels (see Fig. 26), it appears that the positive swing of the condensation-click CM reaches its peak just ahead (0.1 msec) of the onset of the "slow" potential. Hence, as one process takes over from the other, a smooth change in neural latency takes place. However, the first positive deflection of the rarefaction-click CM has its peak earlier (0.3 msec)

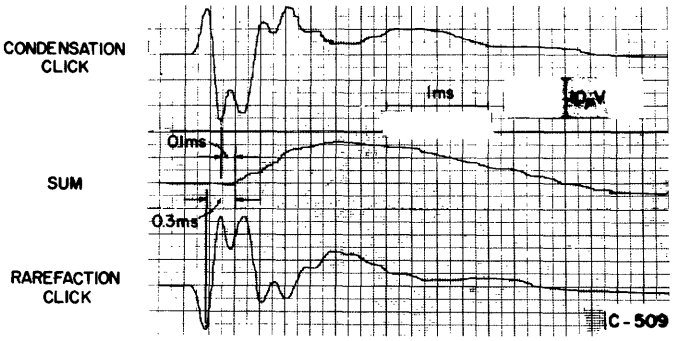


Fig. 26. Averaged responses to condensation and rarefaction clicks and their sum from a denervated cochlea. (Same data as Figs. 9 and 12.) Stimulus intensity, -60 db; positive potential at round window electrode indicated by downward deflection.

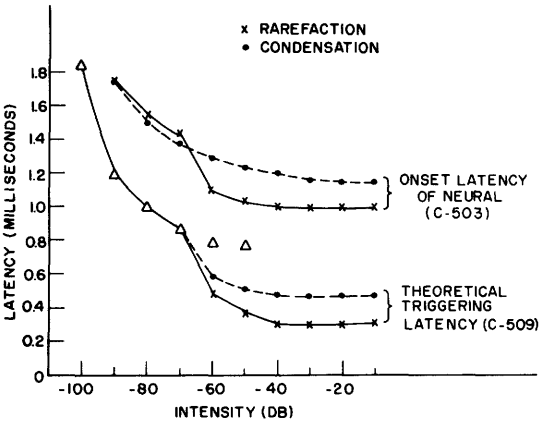


Fig. 27. Neural latency versus intensity. Top curves show onset latency of rarefaction and condensation click responses (C-503, Fig. 20). Lower curves show the latency at which the trigger level is first reached by the assumed excitatory process. Triangles indicate the time at which the "slow" potential (C-509, Fig. 12) reaches its trigger level. The trigger level was chosen arbitrarily as the peak value of the slow potential at -100 db, which is near threshold for the neural response. Dots and x's on the lower curves indicate the time at which the trigger level is reached by CM for condensation and rarefaction clicks (C-509, Fig. 9). Trigger level was taken as the value of the first positive peak of the rarefaction click response at -60 db, since that is the intensity at which the early "bump" is first observed.

than the onset of the "slow" potential. Hence, it is possible that the two processes excite separate neural responses. The appearance of the small early bump (at -60 db, Fig. 20) points to a change-over in effective excitatory mechanism which may result in a jump in latency of the largest negative peak (Fig. 21). Neural units that have fired in response to the CM mechanism may be refractory when the "slow" potential reaches the normal trigger level. Hence, the decrease in the peak-to-peak amplitude of the most prominent neural with increasing intensity (rarefaction clicks, -50 to -60 db); it was this neural that

at lower intensities was excited by the "slow" potential. This explanation implies that the two processes act, at least in part, on the same population of neural units. Using this model and choosing arbitrary trigger levels for the "slow" and microphonic potentials, we plot in Fig. 27 the instant of triggering against intensity, together with the onset latencies measured from the neural responses of Fig. 20. The results indicate that the model does predict latency changes of the order found. The (relatively constant) difference between the experimental and theoretical curves can be interpreted as a result of the time consumed by the excitatory process plus the time taken up by conduction from the point of initiation of the action potential (presumably in the organ of Corti) to the point in the internal meatus at which the neural response was recorded.

3.4 DISCUSSION

This model of excitation of neural responses is quite speculative. It provides an interpretation for the changes in responses to condensation and rarefaction clicks, and seems to describe the data rather well. It has not yet been applied to responses to tone pips. In contrast, Davis's (15, 18) model, which also involves two excitatory mechanisms (see Sec. I), is based largely on neural responses to tone pips. It is possible that the two models of neural excitation are compatible, and that further research will establish the ranges within which they are valid. For instance, our model would predict that the neural responses to high-frequency tone bursts would have latencies dependent on the polarity of the burst at high intensities. It has been reported that this does not occur, and it has been suggested that the summating potential represents the excitatory process in this case (19). Perhaps SP_- is an important process for high-intensity tone bursts, but not for high-intensity clicks for which there is little to "summate." These problems can only be resolved by further experimentation.

Several experiments can be mentioned that would test our proposed model. One of them involves the production of a unidirectional pulse of CM. Since we know the form of the microphonic response to a click, and that it seems to represent, for moderate intensities, the response of a linear system, it should be possible to insert a compensating network between the pulse generator and the earphone so as to produce a unidirectional microphonic response. Such a stimulus could then be used to investigate the various hypotheses of the model concerning the polarity of the microphonic potential that is effective in neural excitation, the intensity range in which CM is important, and the concept of excitation at a fixed trigger level.

Another experiment involves the study of both CM and neural responses to noise bursts. Equation 3 indicates that the amplitude of CM to short noise bursts should be a random variable with zero mean. If the CM alone is the effective stimulus, this situation should lead to some very small neural responses – even for noise bursts of quite high intensity. This does not seem to be a desirable property for an auditory system because it might leave some large short sounds undetected. However, a nonlinear process (the "slow" potential in our model and SP_- in Davis's model) would

detect these stimuli. An experiment for investigating the correlation between the amplitude of neural responses and the amplitude of CM in response to short noise bursts would constitute another test.

The experiments suggested above are intended to test the hypothesis of two excitation processes. This concept is the important aspect of our model. An assumed fixed trigger level may poorly approximate the actual mechanism. Our neglect of the effect of travel time along the cochlea may also be significant. At this stage, however, we must hazard gross approximations in order to establish a workable model.

[It has recently been reported (41) that large neural responses have been obtained in a cat in which the CM was apparently absent as the result of the administration of kanamycin. These results are compatible with the picture proposed above. Presumably, the low-intensity mechanism is still active in this preparation, so that the absence of CM does not lead to the absence of neurals.]

IV. CHANGES IN AUDITORY-NERVE RESPONSES AS A FUNCTION OF STIMULUS REPETITION RATE

4.1 INTRODUCTION

The way in which neural responses in the auditory system vary with repetition rate is of interest for several reasons: (a) Changes with rate of stimulation are important in understanding any sensory system because they reveal something about the physiological mechanisms that underlie the responses. (b) Neural representation of rate is of particular interest in the auditory system because of its possible relation to mechanisms of pitch perception. (c) Rate is a stimulus parameter that must be considered in any experiment. In order to decide what particular rate is optimal for a given experimental problem, one must know how the responses that are being studied depend on rate.

In 1930, Wever and Bray (78) suggested that a bundle of nerve fibers could respond synchronously to much higher frequencies than each individual fiber could, by responding in "volleys." When "volleying" in response to high-frequency tones, individual auditory neurons might respond only to every second, third or fourth cycle, but the summated action potential of the whole nerve would contain a representative event for each cycle. Derbyshire and Davis (23), in their studies of neurals at the onset of tones, interpreted their results in terms of volleying. Galambos and Davis (32, 33), and Tasaki (71), in working with microelectrodes at peripheral locations of the auditory system, observed that, although single neurons tended to respond during a particular portion of each cycle, they did not respond to every cycle. But the neurons that they observed did not seem to respond regularly to every n^{th} cycle either; rather, they responded in a probabilistic way. Their work indicated that some form of statistical "volleying" might actually occur in the auditory system. We were interested in seeing in what way the neurals recorded by gross electrodes reflect this volleying behavior.

Synchronous neural responses have also been considered as a mechanism underlying pitch perception. It has been shown that for low repetition rates, subjects can make pitch judgments which indicate that the repetition rate of the signal envelope is the "signal dimension" being judged, rather than the frequency spectrum of the signal. (See Goldstein and Kiang (37) for a discussion of this work and for other references.) Miller and Taylor (55) found that subjects could match the repetition rate of interrupted noise (which is the stimulus that we have used) to the frequency of pure tones for rates up to approximately 250/sec. A possible neural representation of stimulus repetition rate might consist in having the neurals time-locked (or synchronized) with the stimulus; hence the range of rates for which the nerve produces such synchronized responses would indicate the range for which this method of coding is possible.

4.2 TECHNIQUES

In recording potentials from the cochlea, one is always faced with the problem of separating and identifying the various component potentials. In particular, it is often

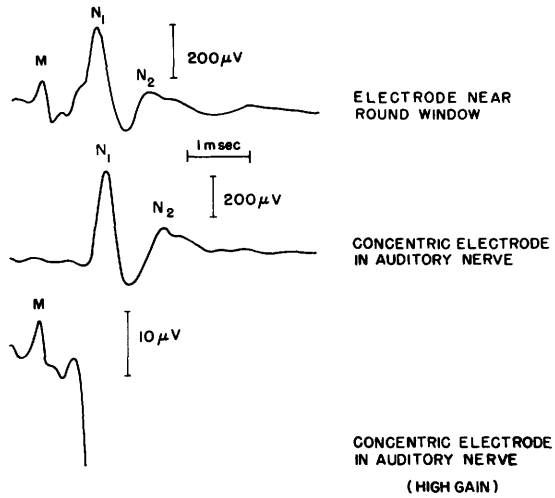


Fig. 28. Averaged click responses recorded simultaneously from two electrode pairs. The microphonic component is indicated by M. Top trace was recorded between an electrode near the round window and a reference lead on the headholder. Positivity of the round window electrode with respect to the reference electrode is indicated by downward deflection. Middle and lower traces were recorded between concentric electrodes placed inside the internal auditory meatus. Downward deflection indicates that the center electrode is positive with respect to the sleeve. The two lower traces represent the same averaged data; the greatly amplified bottom trace is not complete, since it goes off scale beginning with the initial positive deflection of the neural response. Number of responses averaged, 512; stimulus intensity, -50 db re 2.8 volts; condensation click, C-504.

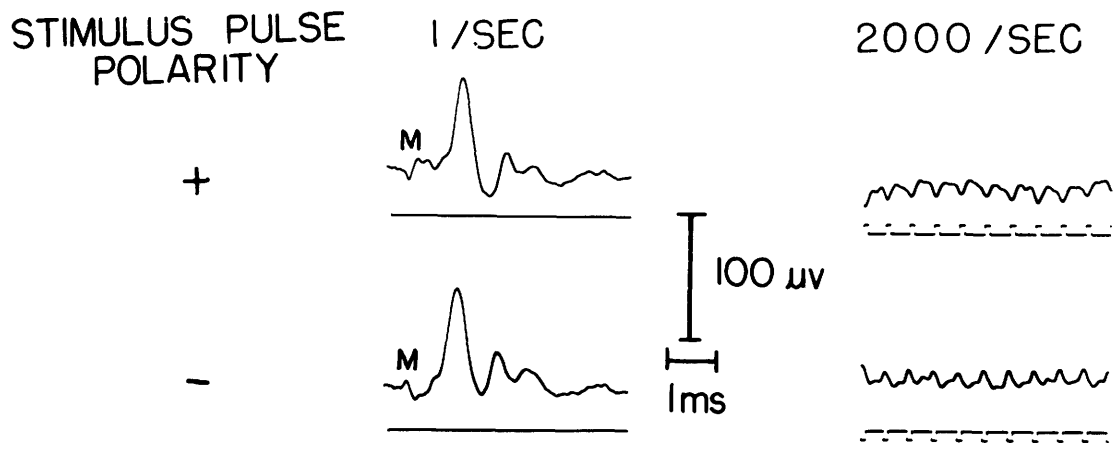


Fig. 29. Rarefaction and condensation click responses at click repetition rates of 1/sec and 2000/sec. Electrode located near the round window. Note that only the microphonic, M, reverses with reversal of stimulus polarity at 1/sec, whereas practically the whole pattern reverses at 2000 clicks/sec. Intensity, 35 db re VDL (13).

difficult to measure the neurals because of their overlap with CM. One method of separating these two components, which has been extensively used in guinea pigs (74), requires that electrodes can be conveniently introduced into the appropriate cochlear scalae. Derbyshire and Davis (23) minimized the CM content of their records from cats, by using concentric electrodes placed in the auditory nerve. We have used this type of electrode also, and find that the ratio of neurals to CM is indeed much higher than it is in records taken between an electrode near the round window and an indifferent location on the headholder. However, some CM is recorded even from a concentric electrode in the internal meatus (Fig. 28). For low-intensity clicks, CM and neurals are clearly separated in the resulting responses. However, this separation is maintained only at low and medium intensities and, in particular, only at low stimulus repetition rates. Figure 29 illustrates that for 2000 clicks per second, the response recorded from an electrode near the round window reverses almost completely, and hence seems to be largely CM. Thus it is difficult to study neural responses to clicks at high repetition rates by means of round-window electrodes.

Since the CM reverses when the polarity of the stimulus is reversed, it can be canceled by adding the response to a rarefaction click to that of a condensation click (27). Figure 30 illustrates the results (13) of carrying out this process with the aid of the special purpose digital computer ARC-1. This method of processing can be used to reduce the microphonic content of the records, and it enables the detection of neural components at high rates.

Another difficulty is encountered when clicks are used as stimuli in rate studies. It

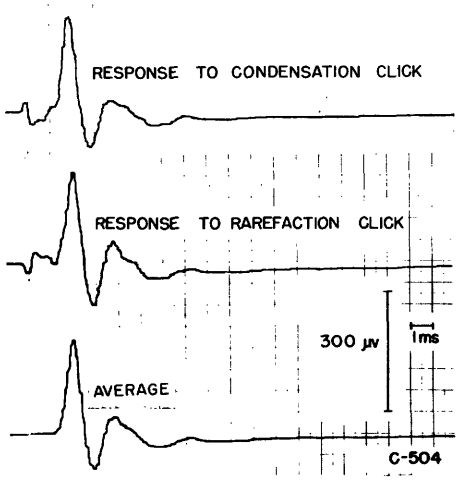


Fig. 30. Averaged responses to condensation and rarefaction clicks (two top traces) compared with the average that results when equal numbers of condensation and rarefaction click responses are added. Recording from a round-window electrode. Stimulus intensity, -50 db re 2.8 volts. Number of responses averaged: 64 for top and middle traces, and 128 in bottom trace.

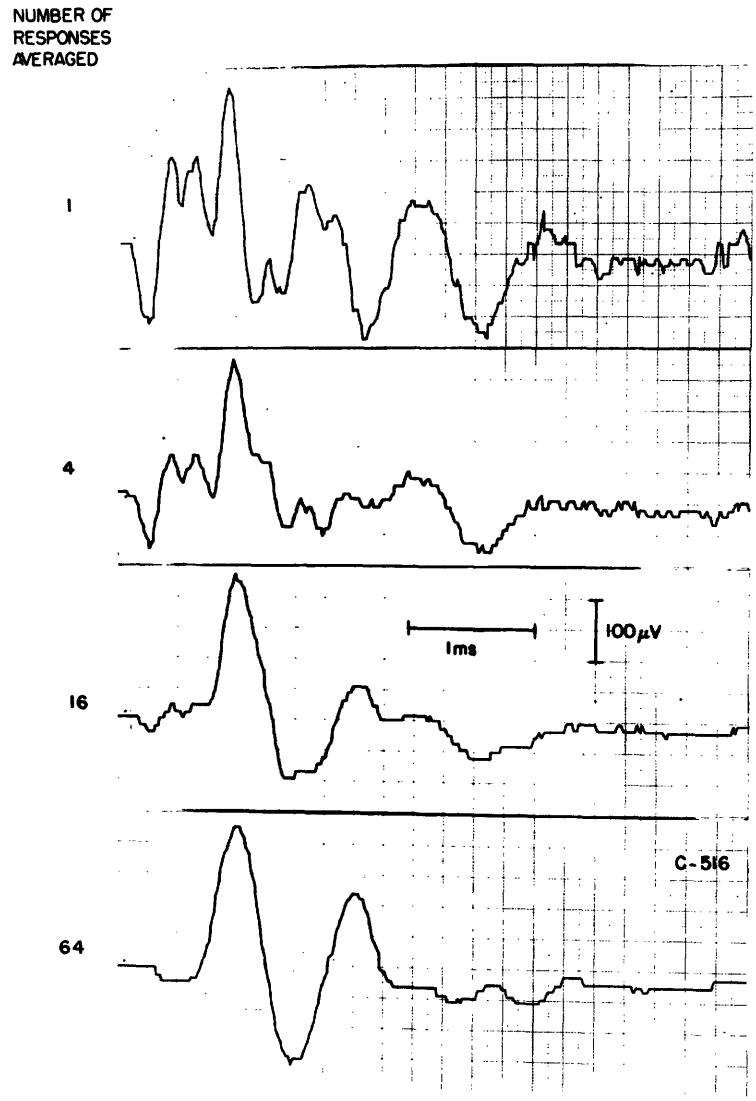


Fig. 31. Averaged responses to 0.1-msec noise bursts showing effect of the number of responses that are averaged. Intensity, -10 db re 1 volt rms. (C-516.)

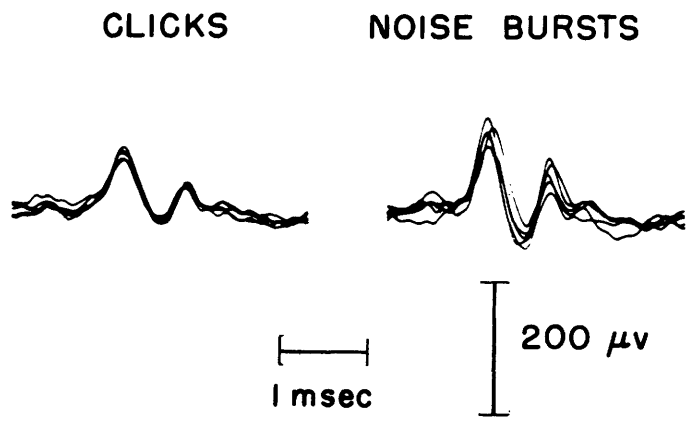


Fig. 32. Responses to clicks (0.1 msec) and to noise bursts (0.1 msec) recorded from near the round window. Each picture shows superimposed responses to 5 consecutive stimuli presented at a rate of 1/sec. Click intensity, -70 db re 4.4 volts; noise burst intensity, -55 db re 1 volt rms. Note greater variability of amplitude and latency for responses to noise bursts. (C-512.)

is possible that the frequency characteristic of the acoustic system tends to emphasize certain stimulus repetition rates. In order to overcome this difficulty, we usually used short (0.1 msec) bursts of noise as stimuli and computed averages of the resulting responses. Noise bursts have the property that over a certain range their frequency spectrum is not changed when the burst repetition rate is changed. Each noise burst produces a microphonic potential similar to that produced by a short rectangular pulse (Fig. 16), but the amplitude varies randomly about a zero mean. Hence, if a large number of responses to noise bursts is averaged, the microphonic potentials tend to approach the average value of zero. This is illustrated in Fig. 31.

Short noise bursts sound like clicks at low repetition rates, except that the loudness varies appreciably from one click to another. Both the amplitude and latency of the neurals are more variable for short noise bursts than for clicks (Fig. 32). Hence, the averaged neural responses cannot be regarded as typical responses in the sense that they probably do not look like any one response. At higher rates, the chopped noise sounds like continuous noise. At rates higher than approximately 2000/sec listeners are unable to distinguish it from continuous noise (55).

The stimulus equipment used in this study was identical to that previously reported (38), except that a General Radio Type 1390 A noise generator with a frequency range of 0-20,000 cps was used. Responses were often averaged "on-line" (13) during the experiment. If more than one electrode combination was used, the data were recorded on FM magnetic tape at a speed of 30 in/sec, which gives the recording system a frequency range of 8-5000 cps. In all but one experiment, the cats were anesthetized with CIBA Dial (75 mg/kg) by injecting it into the peritoneal cavity. In other respects the experimental apparatus and procedure were the same as those reported

by Goldstein, Kiang and Brown (38).

We have usually recorded between a wire electrode placed on the bone near the round window and a reference lead on the headholder. This electrode placement requires very little surgery, and the preparations remain stable over long periods of time.

In most of our experiments, the stimulus intensity was fixed at a moderate level of approximately 35 db above VDL. The VDL "thresholds" to 0.1-msec noise bursts for the cats used in this study lay in the range -90 db to -105 db re 1 volt rms to the earphone. (The reference level of the noise was set at 1 volt rms, when the noise was passed through a lowpass filter (8 kc, 18 db/octave). The filter was inserted to approximate the lowpass characteristics of the earphone.)

4.3 RESULTS

a. Neural Responses at the Onset of Stimulation

Figure 33 shows averaged responses to the onset of tone bursts of several frequencies. Since the tone burst is turned on rapidly, a transient response occurs at the onset and is superimposed on the sinusoid. The first response is complicated by the interaction of these two components of the stimulus. The later response amplitudes decrease steadily throughout the record. Derbyshire and Davis (23) observed that the amplitude

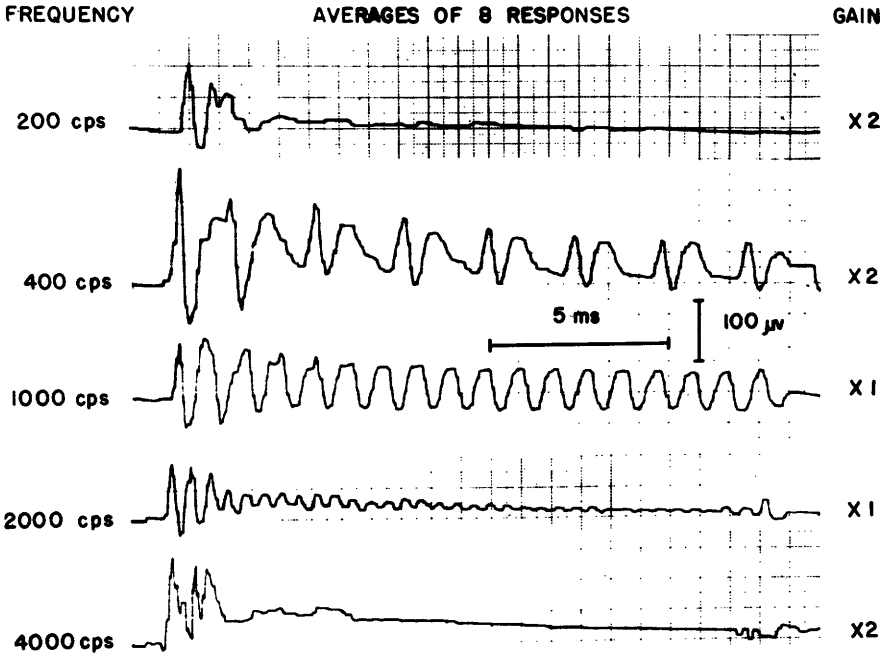


Fig. 33. Averaged responses to the onset of tone bursts. Tones were turned on in "sine phase" with fast (10-μsec) rise time. Burst length, 19 msec; bursts repeated at rate of 1/sec; stimulus intensity, -40 db re 1 volt rms. Concentric electrode in internal auditory meatus. (C-502.)

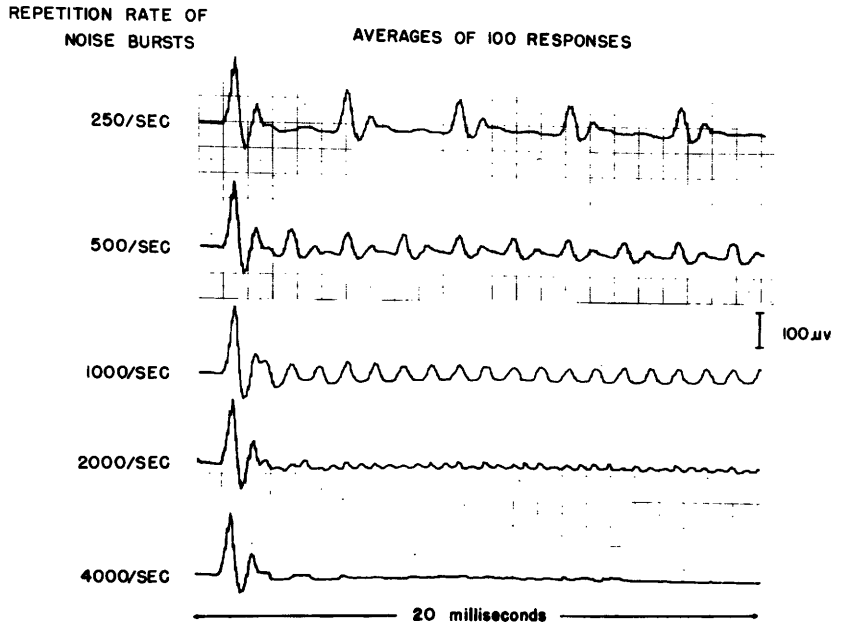


Fig. 34. Averaged neural responses at the onset of trains of noise bursts for several burst rates. Burst length, 0.1 msec; duration of "trains," 20 msec; "train" repetition rate, 1 in 4 seconds; electrode near round window; stimulus intensity, -50 db re 1 volt rms; VDL, -90 db re 1 volt. Note that the neurals are largest in response to the first burst, and continue to decrease throughout the trains. Electrode near round window. (C-500.)

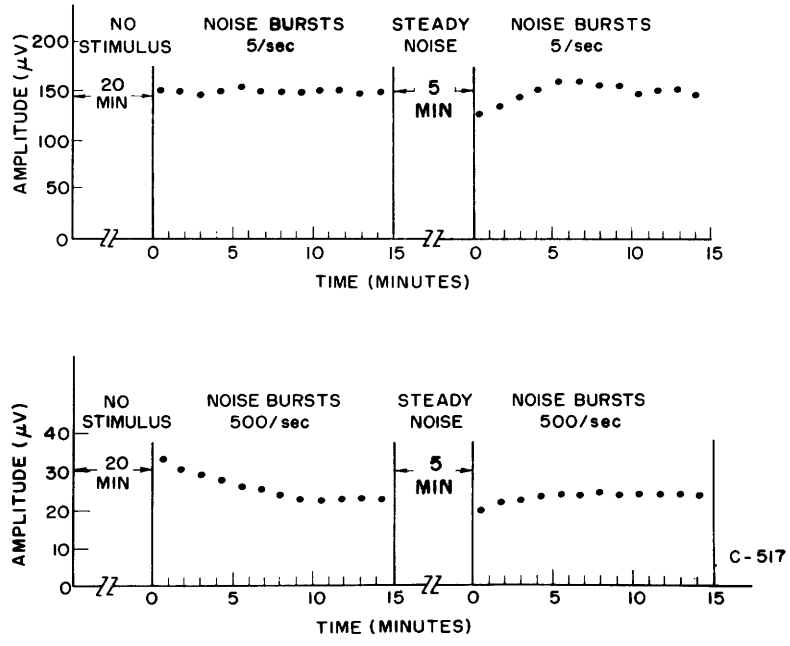


Fig. 35. Amplitude of averaged neural responses to 0.1-msec bursts of noise for two repetition rates. The stimulus was turned on and off as indicated. The level of the steady noise was equal to the "burst-level" (59) of each noise burst (-60 db re 1 volt rms). Each point is the average of 128 responses. Note the difference in voltage scale for the two rates of stimulation.

of the neurals continues to decrease for 7-10 minutes, and finally stabilizes.

The synchronized responses tend to disappear at high frequencies, a fact that Derbyshire and Davis (23) also observed. For the stimulus intensity that we used, the synchronized responses also disappear at low frequencies, but this phenomenon represents a combination of effects: (a) The slow rise of the low-frequency stimulus is less effective in producing synchronized action potentials (37). (b) The earphone attenuates the low frequencies (200/cps) more than the higher ones (such as 1000 cps). (c) The sensitivity of the cat to pure tones as measured in behavioral experiments is approximately 20 db less at 200 cps than at 1000 cps (57). In view of these difficulties and of the additional problem of separating neural responses from CM, we have not studied responses to sinusoidal stimulation extensively.

Averaged responses at the onset of trains of noise bursts are illustrated in Fig. 34. In order to further investigate the time course of what might be called "adaptation" of these neural responses, we performed the experiment depicted in Fig. 35. After an initial 20-min period of silence, the noise bursts were delivered at a rate of 5/sec, and the amplitude of averaged responses was measured every minute. Figure 35 shows that at a rate of 5/sec there is little change in amplitude with prolonged stimulation. After 5 minutes of steady noise, the amplitude of the neural responses to a noise burst is decreased; but it returns to its earlier level within approximately 5 minutes. After another 20 minutes of silence, the same pattern of stimulation was carried out for a burst of 500/sec. The results show that there is an appreciable decrease in the amplitude of the response during the first 10 minutes. After 5 minutes of steady noise, the average response is again reduced and recovers again to its earlier level. Figure 36 illustrates that prolonged stimulation at a rate of 500/sec can produce an aftereffect on neural responses to bursts delivered at the rate of 5/sec. These data indicate that a "steady state" is reached, in the sense that the amplitude of the neural responses stabilizes after the stimuli have been "on" long enough. The way in which this steady state is reached depends on previous stimulation.

Figure 35 shows that adaptation to bursts at 5/sec and at 500/sec differs because of the difference in power that is delivered in these two instances. The duration of the bursts was kept constant at 0.1 msec. Figure 37 shows that if, on the other hand, we stimulate with noise bursts having a constant sound-time function (STF), no appreciable adaptation in the size of neurals occurs after changes in repetition rate because the power delivered is constant.

b. Neural Responses in the Steady State

In order to describe changes in amplitude as a function of repetition rate, we averaged responses to noise bursts after the responses had reached a steady state. In most of the cases we have used a constant burst length of 0.1 msec. Generally, the stimulus was left on at a fixed "burst level" (59) during the experiment, and its repetition rate was changed step by step from low to high rates. After the repetition rate had been

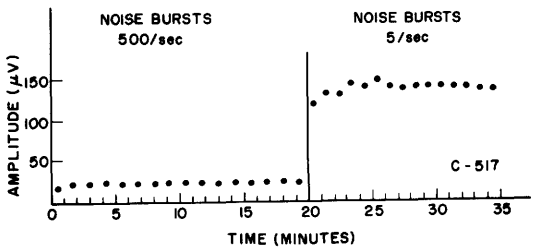


Fig. 36. Effect upon amplitude of neural responses to noise bursts at rate of 5/sec of prolonged stimulation by noise bursts at rate of 500/sec. (Same conditions as in Fig. 35.)

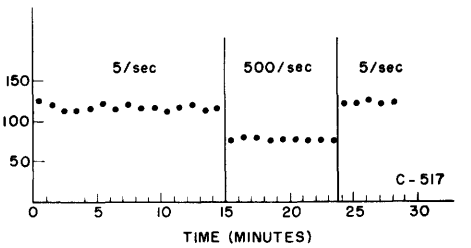


Fig. 37. Amplitude of averaged responses to noise bursts with sound-time fraction kept constant at 1/5. (Other conditions are the same as in Figs. 35 and 36.)

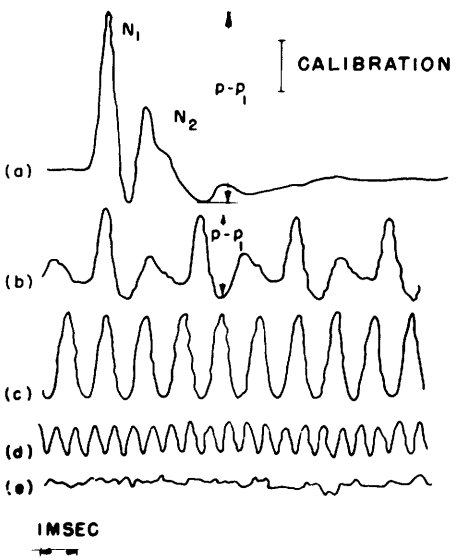


Fig. 38. Averaged responses to 0.1-msec bursts of noise at repetition rates of: (a) 10, (b) 400, (c) 1000, (d) 2000, and (e) 3000/sec. Electrode near the round window. The amplitude that was measured and plotted in the following traces is indicated by $P - P_1$. (a) Average of 500 responses at 10/sec; calibration line, 100 volts. (b) Average of 500 responses at 400/sec; calibration line, 50 volts. (c) Average of 4000 responses at 1000/sec; calibration line, 50 volts. (d) Average of 4000 responses at 2000/sec; calibration line, 25 volts. (e) Average of 4000 responses at 3000/sec; calibration line, 12.5 volts. (C-480.)

changed to a higher value, we waited a few seconds before having the ARC-1 compute the average of responses. The stability of the average was checked. For moderate stimulus intensities, results could be replicated within 10 per cent during the time interval required for obtaining a complete amplitude-versus-rate curve. (See, for instance, Fig. 39.) We found that if we left the bursts of noise "on" continuously, we eliminated slow changes in response amplitude that would have occurred had the stimulus been

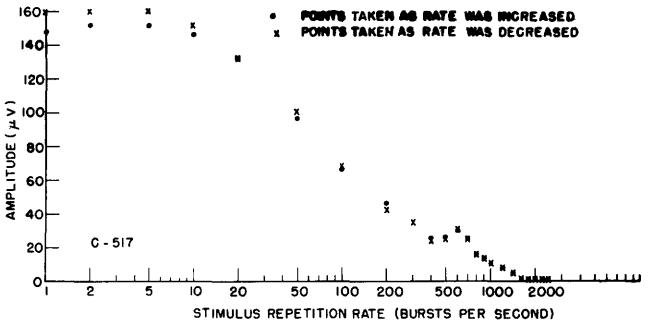


Fig. 39. Peak-to-peak amplitude of averaged responses to 0.1-msec noise bursts as a function of repetition rate. Repetition rate was first increased from 1/sec to 2400/sec, and then decreased to 1/sec. Noise-burst level, -60 db re 1 volt rms.

turned on after a period of no stimulation.

Figure 38 shows a typical set of averaged responses for several stimulus repetition rates. Peak-to-peak amplitudes of averaged responses are plotted as a function of rate in Fig. 39. These are typical of those obtained from approximately 15 cats. In all animals, the features of the amplitude-rate curve are: (a) For the moderate intensity used, the amplitude of the response remains constant for rates up to approximately 10/sec. (b) A small peak occurs around the rate 600-700 per sec. (c) A synchronized neural response cannot be detected by our methods for rates higher than approximately 3000/sec.

Figure 40 shows averaged responses from two electrode locations (round window and internal meatus) in the same preparation. Figure 41 shows peak-to-peak amplitude versus rate for these two locations. As might be expected, since the responses of first-order auditory neurons are being recorded at both locations, the two amplitude-versus-rate curves behave in about the same way, at least, up to rates of 500/sec. The differences observed for higher rates will be discussed in section 4.4 in terms of a mathematical model that takes account of overlapping responses.

c. Effect of Anesthesia

In order to determine whether the change in neural responses with rate is affected by anesthesia, we obtained rate functions before and after administration of Dial. In such an experiment a cat is first anesthetized with ether and then immobilized by a spinal section at the C2 level. The ear tube and the round-window electrode are put into place and the ether is allowed to "blow off." In this state, the round-window electrode records large muscle potentials, but these are minimized by the averaging process. After a rate function has been obtained, Dial (75 mg/kg) is injected intraperitoneally, and one hour later the experiment is repeated on the anesthetized animal. The results are plotted in Fig. 42. It is clear that the anesthesia has little effect on the average amplitude of

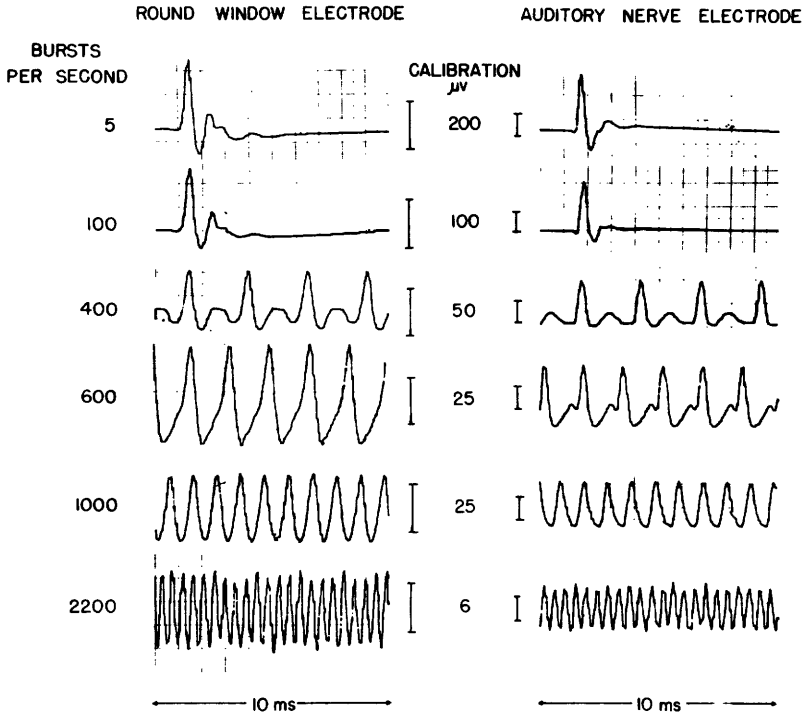


Fig. 40. Averaged responses to 0.1-msec noise bursts from two electrode locations. Stimulus intensity, -60 db re 1 volt rms. Number of responses averaged, 1024. (C-504.)

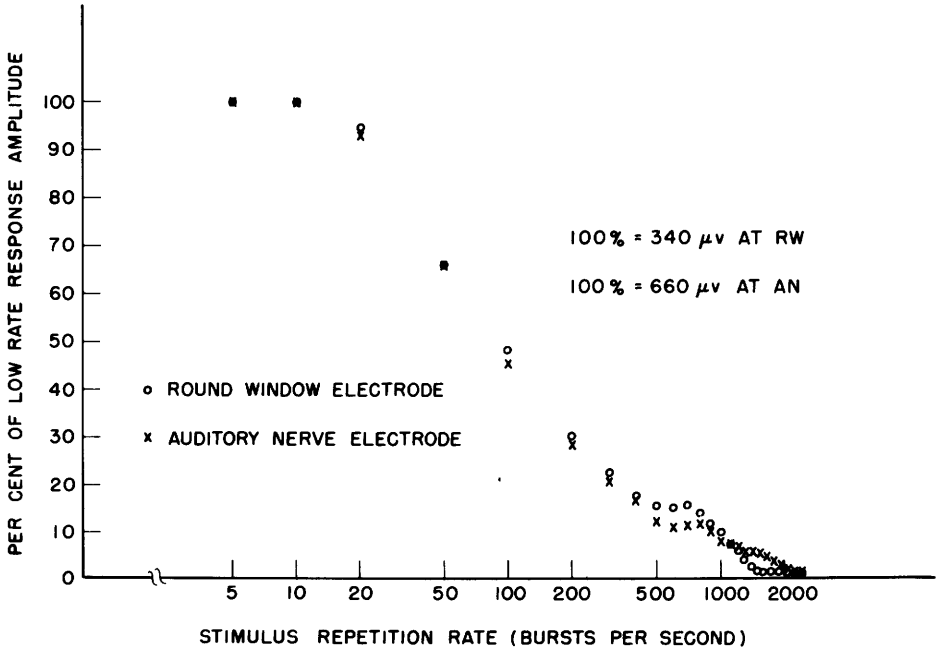


Fig. 41. Peak-to-peak amplitude of averaged responses to 0.1-msec noise bursts from two electrode locations. (Same conditions as in Fig. 40.) (C-504.)

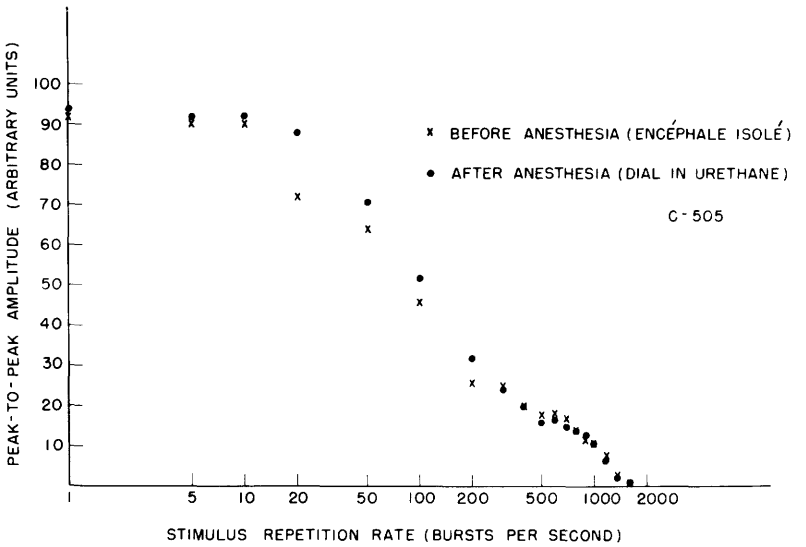


Fig. 42. Peak-to-peak amplitude of averaged responses to 0.1-msec noise bursts before and after anesthesia. Amplitude of low rate of response was approximately 150μv; intensity, 35 db re VDL.

these responses. The plotted data were taken over a period of several hours. They give indication of the stability of the amplitude-versus-rate curves.

d. Effect of Burst Length and Burst Pattern on Neural Responses

If we examine the effects of these variables upon the amplitude-versus-rate curve, we are faced with the fact that practically none of the parameters can be manipulated independently. By changing the duration of bursts, we also change the power level, the duty cycle, and the time between bursts (that is, off-time). To make a thorough analysis it is necessary that families of parametric curves be obtained. We do not pretend that our data constitute such an ambitious investigation. Rather, we have attempted to assess some of the effects of each of the above-mentioned variables.

Figure 43 shows averaged responses to noise bursts of several durations. The differences in waveforms of the neurals can be interpreted in terms of a "slow" negative potential with an onset latency of approximately 1.5 msec. This potential appears to last longer in response to longer noise bursts. One effect of the addition of this slow potential is a decrease in the peak-to-peak amplitude of N_1 when the burst length is increased from 0.1 msec to 1.0 msec. In Fig. 44 the amplitude is plotted against repetition rate for these two burst lengths. At low rates the smaller amplitude of N_1 for the longer burst results from the phenomenon illustrated in Fig. 43. The more sizable differences in amplitude at higher rates are attributable to the effect of the higher average power that the longer bursts deliver.

In Fig. 45 an amplitude-versus-rate curve for responses to a constant power stimulus (STF = 1/5) is compared with a curve for noise bursts of constant duration. The differences between the two curves can be interpreted as follows:

At high rates (1000-2000/sec) the two stimulus conditions are quite similar (as a

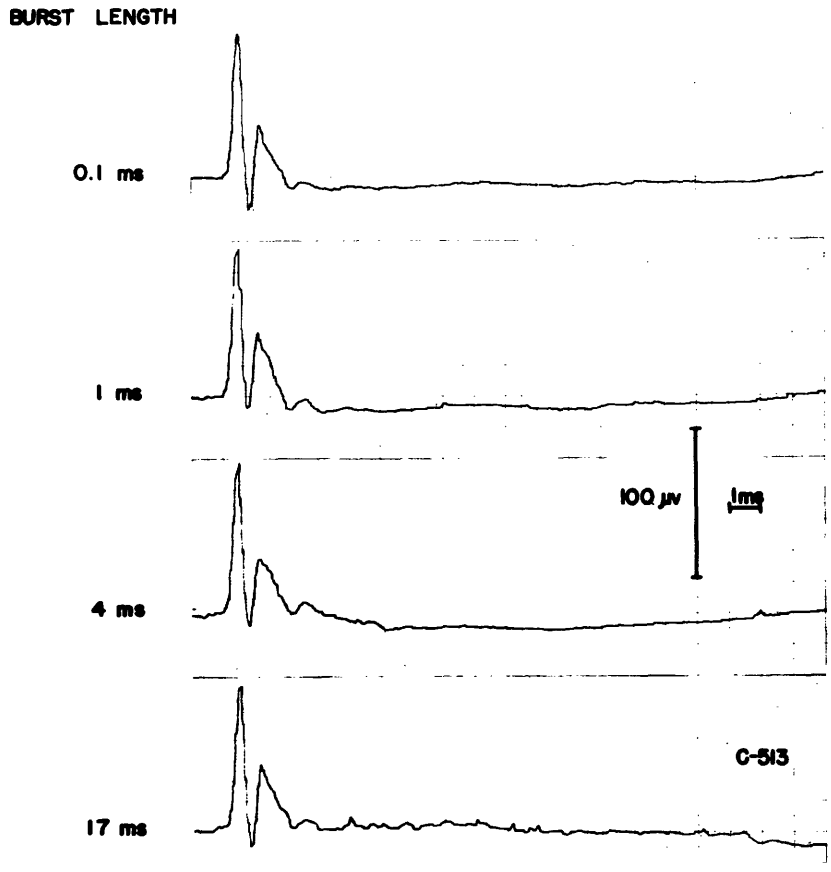


Fig. 43. Averaged responses to noise bursts of several durations. Burst level, -60 db re 1 volt rms; number of responses averaged, 64. Note that the positive (downward) N_1 deflections move upward as the duration increases from 0.1 msec to 1.0 msec.

matter of fact at 2000/sec they are identical), hence the amplitudes are nearly equal in this range. In the middle range the higher power level of the stimulus pattern that delivers the constant power produces greater adaptation, and hence a smaller steady-state response. At the lowest rates the small difference between the two curves is probably the result of the slow component that we have discussed (Fig. 43). The higher power level does not give rise to a great reduction in amplitude at the low rates, since the time between stimuli (1.6 sec at a rate of 0.5/sec) is long enough to allow the system to recover after each burst. It appears that the differences cannot be explained entirely on the basis of different off-times, since, as Fig. 44 illustrates, large differences in amplitude exist at 10/sec between responses to noise bursts of 0.1-msec and 1.0-msec duration. For these two sets of stimuli, the average powers differ by a factor of 10, although the off-times, at low rates (e.g., 10/sec) are very nearly the same.

In order to test this interpretation, we have used the stimulus pattern shown in

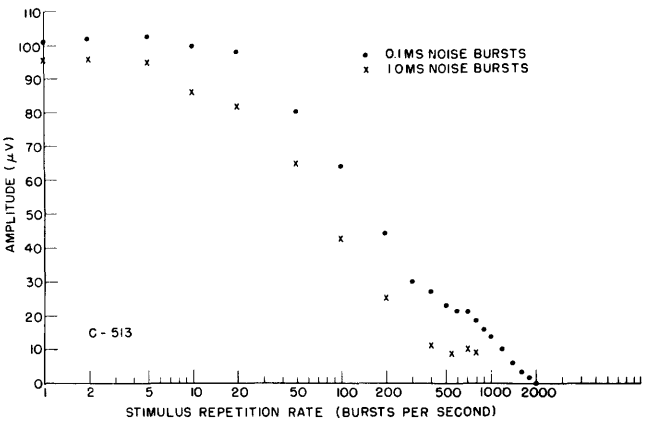


Fig. 44. Amplitude of averaged responses to noise bursts versus repetition rate for burst lengths of 0.1 and 1.0 msec. Burst level, -60 db re 1 volt rms. (See Fig. 43.)

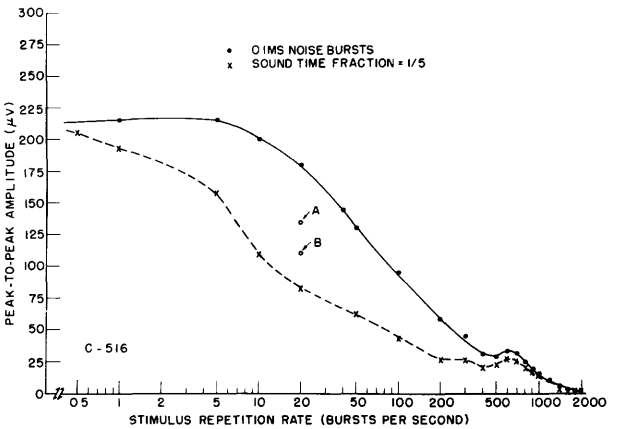


Fig. 45. Amplitude of responses to noise bursts versus rate for bursts of 0.1-msec duration, and bursts of constant sound-time fraction (1/5). Burst level, -60 db re 1 volt rms. Electrode near round window.

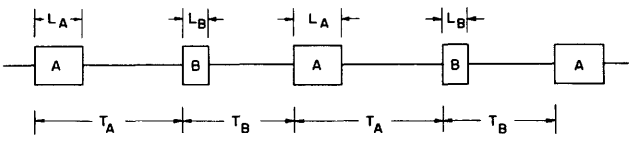


Fig. 46. Stimulus pattern consisting of alternating noise bursts of different duration (L_A and L_B), and different intervals (T_A and T_B) between onsets of bursts.

Fig. 46. The responses to the long bursts, A, and to the short bursts, B, were averaged separately. If L_A = 9.9 msec, L_B = 0.1 msec; and if $T_A = T_B$ = 50 msec, we find that the neural response to burst A is larger than that to burst B. The averaged amplitudes are shown in Fig. 45 as points A and B. For the rate of 20/sec and an STF of 1/5, the burst duration of 10 msec approximates very closely the value of 9.9 msec used in the pattern of Fig. 46. The average power for these values of parameters is, however, only about half of that given by the constant STF signal, and, on the other hand, is 50 times as large as the power delivered by the 0.1-msec bursts at the same rate of 20/sec. These data emphasize the importance of the off-time, since the short (0.1-msec) bursts now give rise to smaller responses than the longer (9.9-msec) ones.

In order to test this interpretation further, the burst lengths L_A = 9.9 msec and L_B = 0.1 msec were kept constant and the time interval T_A was varied. The sum of T_A and T_B was maintained at 100 msec. The results are plotted in Fig. 47. The results

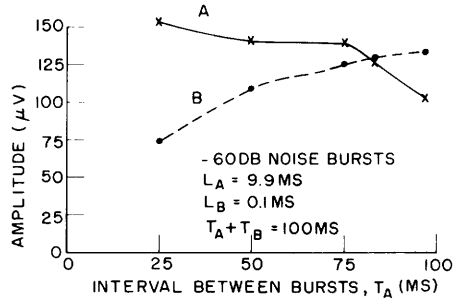


Fig. 47. Amplitude of averaged responses to noise bursts for stimulus pattern shown in Fig. 46. Burst level, -60 db re 1 volt rms. Curve A depicts the amplitude of the neural responses in response to the longer bursts. (C-516.)

show again that while off-time is a factor in determining the size of the response, the average power level is also important. If T_A = 97 msec – a situation in which the short burst occurs just 3 msec before the long one – the peak-to-peak amplitude of the average response to the short bursts for the same rate (20/sec) is still smaller than that obtained when all bursts are 0.1 msec long (Fig. 45). However, the off-time is 87.1 msec for the mixed stimulus pattern, and only 49.9 msec when all bursts are 0.1-msec long.

We have not fully investigated the characteristics of these various types of adaptation phenomena. The sample results presented here show that, in general, the shape of the rate curve does not change drastically as the burst length is changed, or as we change from a signal of constant burst length to a signal of constant sound-time fraction.

e. Changes in Microphonic Potential with Rate

Pictures of microphonic potentials in response to clicks are shown for different repetition rates in Fig. 48. The responses were recorded by an electrode situated in the

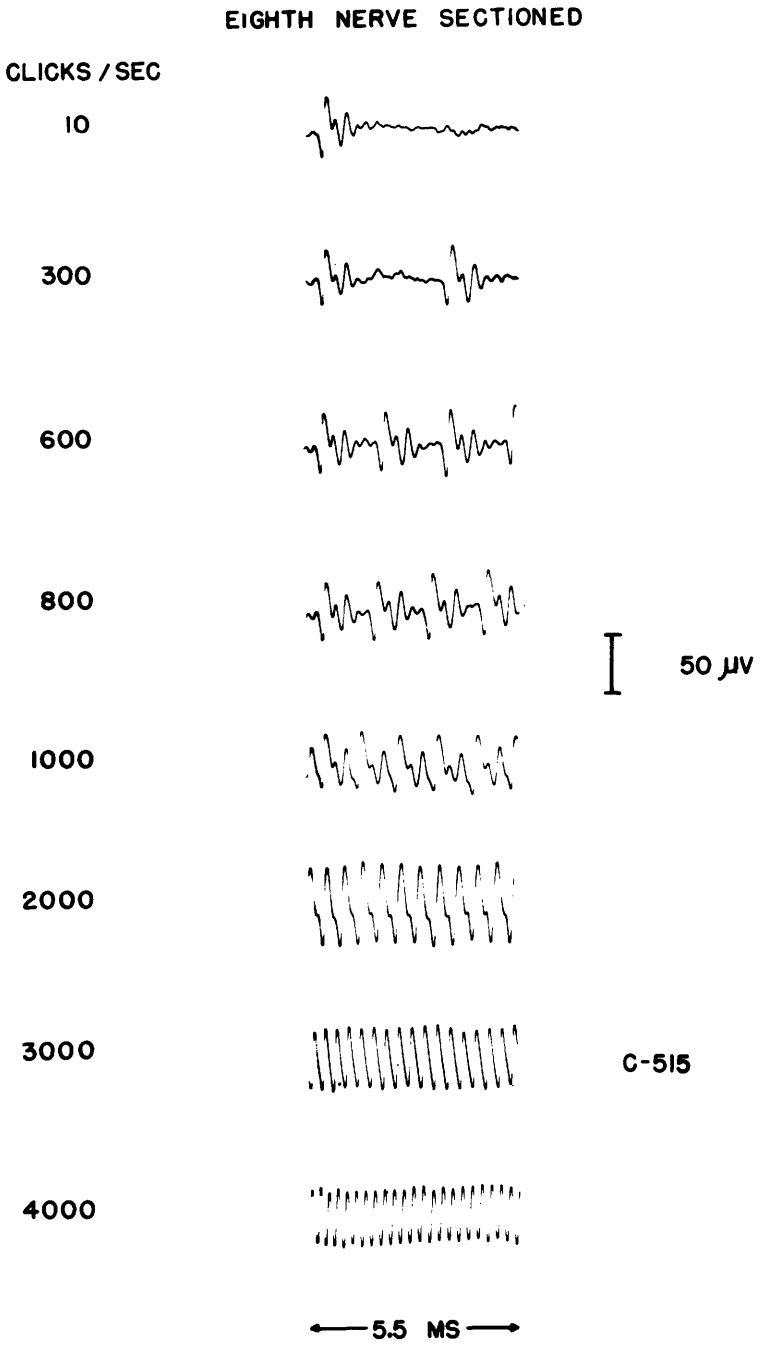


Fig. 48. CM in response to clicks as recorded from the round window of a denervated cochlea. Click intensity, -50 db re 3 volts.

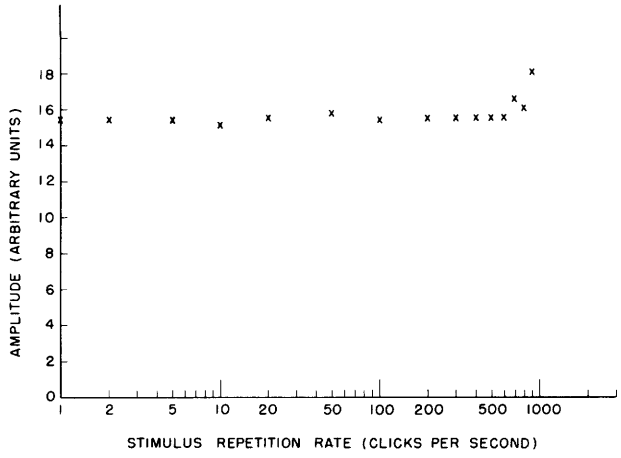


Fig. 49. Amplitude of CM responses to clicks as a function of repetition rate. Click intensity, -65 db re 3 volts; amplitude, approximately 50 volts. (C-510.)

vicinity of the round window of a cat whose eighth nerve had been sectioned approximately 5 weeks before the experiment. No neural response is apparent in this cat. It is clear from Fig. 48 that the amplitude of the microphonic potential does not change appreciably until the responses to individual clicks begin to overlap. This fact is in agreement with previous observations for two clicks separated by short time intervals (53, 69). The peak-to-peak amplitude of CM is plotted as a function of rate in Fig. 49 for another cat. A constant amplitude for CM would have been predicted as long as CM is considered to be the response of a linear system. Of course, this model has been suggested by previous studies.

4.4 A MODEL DEALING WITH OVERLAPPING OF NEURAL RESPONSES

We have examined the possibility that some of the rate data might be interpreted in terms of a simple overlapping of response waveforms. We first tried this approach in an attempt to explain the "bump" in the amplitude-versus-rate curve near 600/sec. In some cats the "bump" occurred at the rate at which the large negative deflection (N_1) coincides in time with N_{22} in the response to the previous burst (see Fig. 50). The prominence of the N_{22} peak varies considerably from one preparation to another.

Underlying the notion that responses add when they overlap is the assumption that the waveform of the neural response changes little with repetition rate. This assumption can be tested quite easily for rates up to 300/sec or 400/sec because at these low rates each response waveform is completed before the next one starts. Figure 51 shows superposed averaged responses at several low rates; the amplitudes have been normalized to make the N_1 peaks equal. The response waveforms stay nearly identical for 1, 10, 20, and 50 bursts/sec so that they cannot be drawn separately. At 100 bursts/sec the latency of the N_2 deflections is increased. This phenomenon occurs consistently. Figure 52 plots latency of the negative peaks of the neural response as a

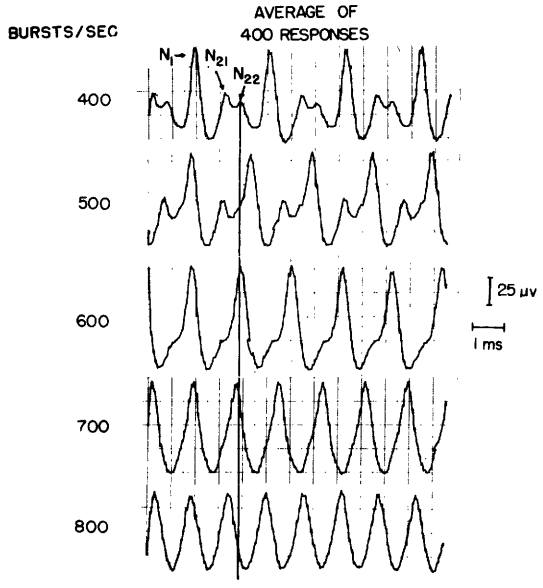


Fig. 50. Averaged neural responses to 0.1-msec bursts for several rates. The vertical line drawn through peak labeled N_{22} (in the response to 400/sec bursts) intersects the N_1 peak to the "next" burst in the averaged response to 600 bursts/sec. The peak in the amplitude-versus-rate curve at 600/sec (see Fig. 54) suggests that N_1 and N_{22} add when they overlap at this rate. Numbers of responses averaged, 400. (C-498.)

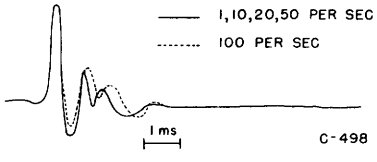


Fig. 51

Normalized averaged responses to noise bursts at several repetition rates. Amplitudes have been normalized, since the N_1 at 50/sec is only 70 per cent of N_1 at 1/sec. Stimuli, 0.1-msec noise bursts; intensity, 30 db re VDL = -65 db re 1 volt rms.

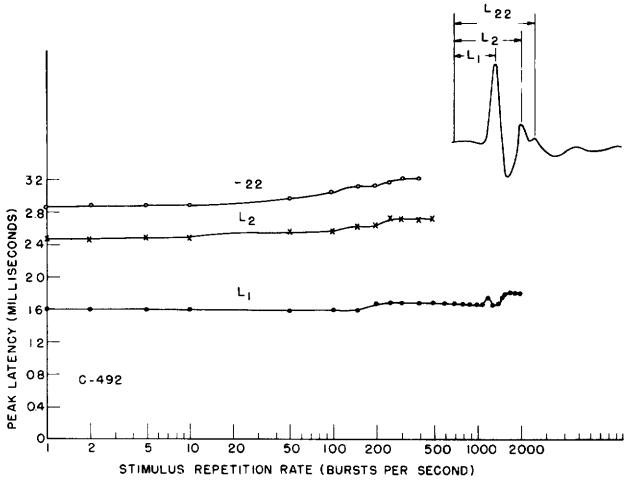


Fig. 52

Peak latencies of averaged responses to noise bursts versus repetition rate. Latencies were measured in steps of 80 μsec, which accounts for the discontinuities in the curves. Stimuli, 0.1-msec noise bursts; intensity, -65 db.

function of repetition rate for another preparation. It, too, indicates that the later peaks shift slightly with respect to the earlier N_1 deflection. However, Figs. 51 and 52, together, show that the waveforms of the neurals change little at rates for which there is no overlap between responses.

In order to test whether at high rates the waveforms can be synthesized from the waveform observed at 100/sec, we computed some waveforms that would result from adding the "standard" waveform to itself with appropriate shifts in time. Figure 53 compares the computed and experimental waveforms. The differences between the recorded data and the synthesized waveforms would be reduced if the model for overlapping responses included the experimentally observed latency shift of Fig. 52. For instance, the computed waveforms at 400/sec would match the experimental response much better if the small peak (arrow) were moved slightly to the right. The increase in the latency of this peak in the experimental data is not included in the model. The same latency shift explains the disappearance of the small peak in the experimental response at 600/sec, a peak that shows clearly in the computed response.

However, the computed waveforms resemble their experimental counterparts sufficiently to justify further investigation of this model for overlapping responses. Although the changes in response waveforms with rate are reproduced fairly well, the change in neural amplitude is not. Figure 54 shows a curve of peak-to-peak amplitude versus rate for the waveforms computed by overlapping. The mathematical model that is suggested by this can be formalized mathematically as

$$\overline{G(t, f)} = w(f) \sum_{n=-\infty}^{n=\infty} \overline{G}(t-n/f, f_\ell); \qquad n = 0, \pm 1, \pm 2, \pm 3, \ldots$$

in which

$\overline{G(t, f)}$ = the average response as a function of time, t, and stimulus repetition rate, f.

$\sum_{n=-\infty}^{\infty} \overline{G}(t-n/f, f_\ell)$ = the response computed by adding a low rate (f_ℓ) average response, $\overline{G}(t, f_\ell)$, to itself with a shift in time appropriate to the rate, f, that is of interest.

w(f) = a function depending on rate only, which represents an amplitude-versus-rate curve with the effects of overlapping removed.

This model has also been applied to cortical responses to repetitive stimuli (36).

Figure 53 indicates that the model fits reasonably well, as far as the time variable (waveform) is concerned. The inclusion of the function w(f) aims at fitting the amplitude changes to rate; it can be calculated as the quotient of the two functions plotted in Fig. 54. The result is given in Fig. 55. This curve represents the change in response amplitude as a function of rate; the effects of overlap present in both curves of Fig. 54 do not enter into the determination of w(f).

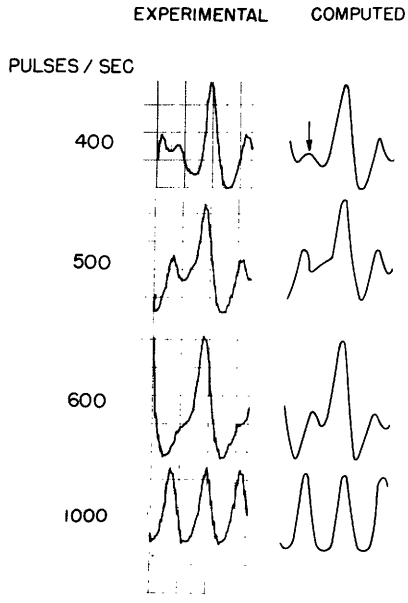


Fig. 53. Comparison of averaged responses to 0.1-msec bursts of noise with computed waveforms. Note that the amplitudes of the computed waveforms have been chosen to make them appear approximately the same size as those of the experimental data. (C-498.)

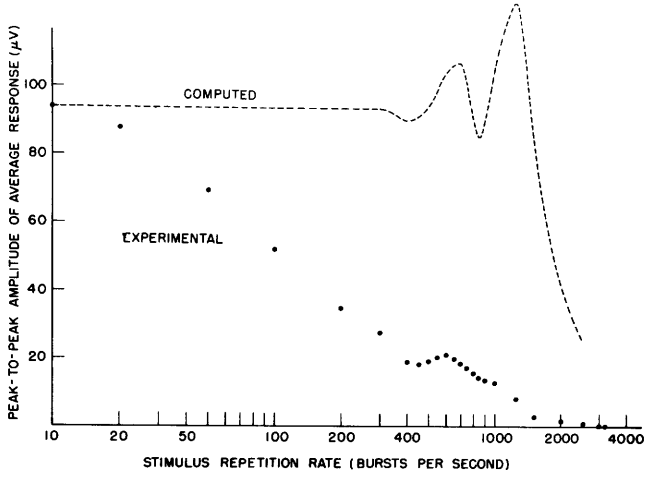


Fig. 54. Peak-to-peak amplitude of neural responses versus repetition rate for the averaged responses, and for waveforms computed on the basis of the model for overlapping responses.

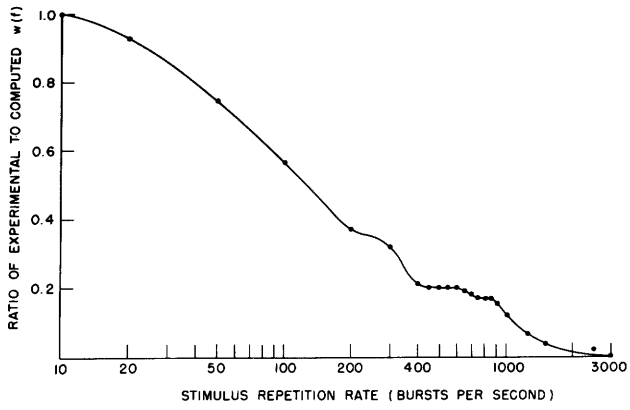


Fig. 55. The weighting function, w(f), computed as the ratio of the two curves of Fig. 54.

The curves in Fig. 41 can also be interpreted in terms of this model for overlap. It was pointed out that the response amplitude for the two electrode locations decreases similarly up to rates of approximately 400/sec. Above this rate, the round-window response becomes somewhat larger relative to the response from the auditory nerve. The range in which the round-window response is larger corresponds approximately to that in which the N_1 and N_2 component overlaps. Since in this cat the N_2 component is much smaller in the responses recorded in the nerve (Fig. 40), one would expect less effect of overlap at this location. Figure 56 shows the computed and experimental rate curves for the two locations. The weighting functions derived from these curves are plotted in Fig. 57. This figure shows that these weighting functions differ in the same range of rates as the experimental data of Fig. 41, although perhaps less so. The model for overlap works in the right direction without, however, being able to account for all the effects in detail.

In synthesizing high-rate responses we made use of the Fourier transform of the "standard" low-rate response. If we consider the response to a stimulus of rate, f, as a periodic function, it can be written as a complex Fourier series:

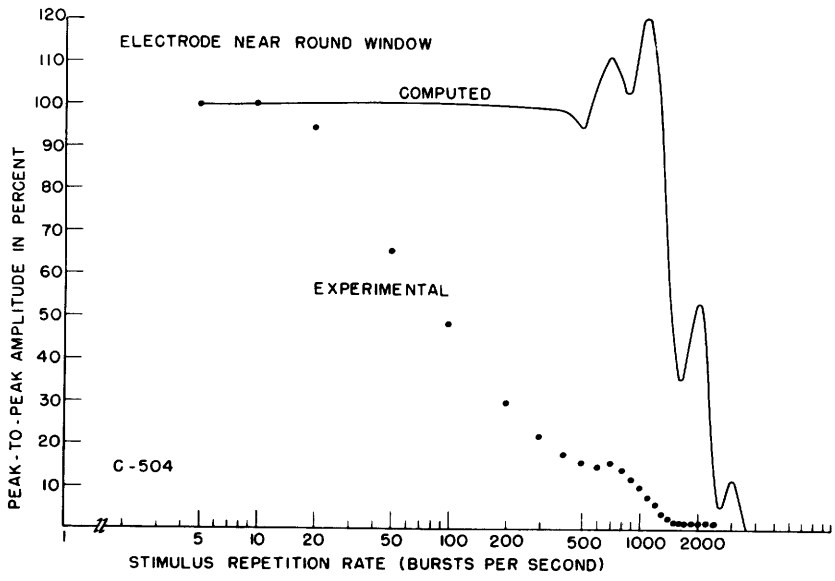
$$\text{Synthetic response} = \sum_{k=-\infty}^{\infty} a_k e^{j2\pi f_o t}$$

The coefficients, a_k, of this Fourier series are related to the Fourier transform, F(f), of the low-rate response, f(t), by the equation

$$a_k = 2f_o F(kf_o)$$

in which the Fourier transform and time function are related by

$$F(f) = \int_{-\infty}^{\infty} f(t)\, e^{-j2\pi ft}\, dt$$



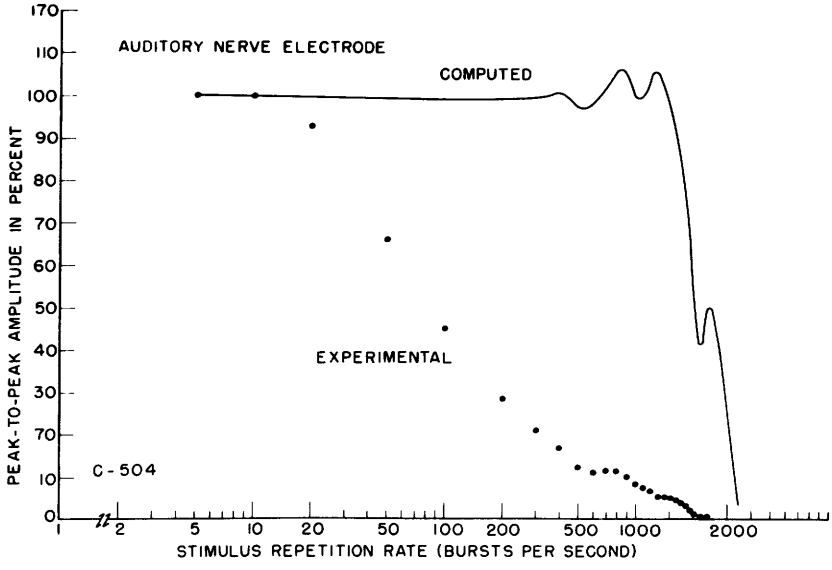


Fig. 56. Peak-to-peak amplitudes of averaged responses, and of responses computed on basis of the model for overlapping responses for two electrode locations.

$$f(t) = \int_{-\infty}^{\infty} F(f)\, e^{j2\pi ft}\, df$$

At moderately low rates for which only two or three responses overlap, it is simpler to compute the synthetic response by adding the waveforms in time. For higher rates, it is easier to add the harmonic Fourier components as given by the equation for synthetic

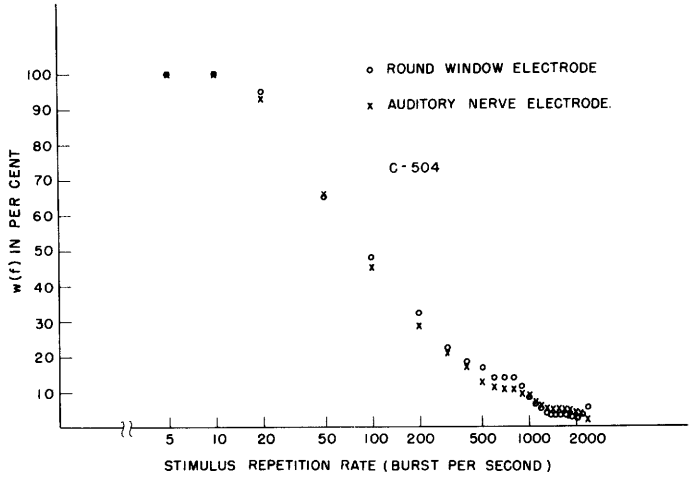


Fig. 57. The function w(f) for responses from the two electrode locations of Fig. 56.

response. Since the Fourier transform drops off quite rapidly at rates above 1500 cps, the higher harmonics are negligible compared with the fundamental for rates higher than approximately 750/sec. Hence the model predicts nearly sinusoidal waveforms for repetition rates higher than this frequency. This prediction seems to be bourne out by the data.

4.5 DISCUSSION

In section 4.4 we discussed the changes that occur in the neural responses in terms of a model in which these responses overlap. The model was reasonably successful in describing certain aspects of the data. One might feel that if N_2 represents a repetitive firing of the same fibers that produce N_1, as proposed by Tasaki (71), that it would not be rational to have these two peaks overlap. However, if the auditory nerve fibers respond in a probabilistic way, as Tasaki also observed (71), then it is entirely possible for neurals from the same fiber population to overlap. In the steady state there exists for the population of units a certain probability of responding to each individual burst. Hence, at higher rates, although no one unit is responding to every burst, there will be some units responding to each burst. If it is assumed that the electrode adds the unitary responses, the summated responses can exhibit overlap. In terms of this model, the

N_1 response can also overlap itself.

The model of overlapping responses leads to several conclusions:

(a) The peak in the amplitude-versus-rate curves near 600/sec can be interpreted as the result of overlapping of the N_1 and N_{22} peaks.

(b) Once we have accounted for the effects of overlap, the remaining decrease in neural amplitude with rate takes place in a rather gradual manner; it begins at approximately 10/sec and continues up to rates at which synchronized neurals can no longer be detected. Hence, if the decrease in response size results partly from "volleying" of single fiber responses, the changes in the volleying mode (for example, from once every two cycles to once every three cycles) must take place rather gradually as the rate is changed. Stated in terms of a probabilistic model, the probability of a unit responding to a stimulus burst does not change abruptly as the repetition rate is changed.

(c) We have been able to detect synchronized activity up to a rate of approximately 3000/sec. This figure agrees fairly well with the results of other workers (23, 71, 77). However, this figure is likely to be a limitation of our method rather than a limit of synchronous firing. This conclusion is based on the following reasoning: (i) If enough responses are averaged, we always find some small activity synchronized with the stimulus frequency. For rates higher than 3000/sec, this activity seemed an artefact of one kind or another. However, it may be that some synchronized neural response is still present, but it is "swamped" by the artefact that builds up with averaging. (ii) Experiments on animals with denervated cochleas indicate that small responses are present in the average response to noise bursts which seem to be neither ordinary neurals, nor microphonics (see Sec. II). These small responses cannot, by our methods, be separated from the neurals because they are equally small at high rates. (iii) The Fourier transform of the gross-electrode response drops very rapidly with frequency above 1500 cps. The model of overlapping responses predicts that at rates of 2000/sec or 3000/sec the synchronized response would become very small because of overlap, even if the elemental response remained constant in size. Therefore, from the point of view of the model for overlap, the gross-electrode response is a poor way to look at "the limit of synchrony."

The physiological mechanisms responsible for the gradual decrease in response amplitude of the neural responses with rate have not been examined in this study. A few suggestions can, however, be made. It has been shown that some peripheral sensory nerve fibers in cats recover their full "responsiveness" following a strong electric stimulus within 4-6 msec (12). If this figure is correct for the auditory nerve fibers, the drop in response amplitude starting at 10/sec must result from a decrease in responsiveness of some other link in the system. The McGill and Rosenblith (54) data, which showed that the neural response to the second of two clicks remains below its control value for click separation of more than 100 msec, point in the same direction. This figure is compatible with the drop-off at rates of 10/sec. The chain of events to be examined includes the following links: the middle ear, the cochlear partition with its

end organ; the "end organ neural junction," the dendritic terminals of the auditory neurons, the cells of the spiral ganglion, and finally the nerve fibers in the internal meatus. The question is: Where does this prolonged decrease in responsiveness occur, if not in the nerve fibers? We can only make the following observations. The microphonic potential in response to clicks does not decrease with increasing repetition rate (see Figs. 48 and 49), or when two clicks occur very close together (54). It has also been observed that when fairly intense stimuli are used to produce an aftereffect that reduces the neural response considerably, the microphonic is not reduced appreciably (42, 48, 65). If the microphonic potential can be considered to be an indication of the response of the end organ, it would appear that the system up to that point does not decrease in responsiveness for any of these situations. This suggests that the drop-off in responsiveness that starts at 10/sec, as well as the other effects, must be the result of events that occur at one or several locations beyond the locus of generation of CM (42, 48, 54, 65). Rate functions for the auditory-nerve responses to direct electrical stimulation might assist us in parceling out these effects. The role that these various electrical components play in limiting the responsiveness of the peripheral auditory system to high-rate stimulation deserves to be fully elucidated, especially in view of the role that time plays in auditory information transmission.

V. CONCLUDING REMARKS

It is hoped that the work reported here increases our understanding of the electrical events at the periphery of the auditory system. We have been able to collect and process a relatively large amount of reliable data in a short time because of the availability of modern electronic equipment; particularly important was the magnetic-tape recording system, and the special purpose digital computer ARC-1.

The data presented here show how microphonic and neural responses to impulsive stimuli vary with stimulus intensity and repetition rate. We were not interested in collecting data for its own sake, however. We have committed ourselves to certain interpretations that suggest possible underlying physiological mechanisms for the coding of acoustic stimuli into auditory nerve responses. In particular, we have suggested an interpretation for responses to condensation and rarefaction clicks in terms of two excitatory mechanisms that are themselves related to non-neural cochlear potentials. The proposed model describes certain aspects of the data fairly well and suggests further experiments to test the range of the model's validity. The postulated mechanisms will gain by being studied with techniques that provide data of a much finer grain.

The rate curves have led us to speculate about the activity of neural units in response to high rates of stimulation. Although "volleying" occurs, this does not necessarily imply that the neural units change suddenly in their mode of responding when stimulus rate is changed; rather, a gradual change may take place in the probability of firing to each stimulus. Our methods indicate that 3000/sec is an upper frequency limit at which synchronized responses can be detected. The model for overlapping responses leads us to question whether our data from gross electrodes imply that the same upper limit applies also to the synchronized activity of single units. Here, as elsewhere, microelectrode studies will help to resolve this problem, provided that the neural populations involved can be adequately sampled, and that the difficulties of quantifying the spike patterns will not prove overwhelming.

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