XXIII. COMMUNICATIONS BIOPHYSICS[*]

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RESEARCH OBJECTIVES AND SUMMARY OF RESEARCH

The principal scientific research objective of the Communications Biophysics Group is to obtain a better understanding of sensorineural processes. Our approach combines both electrophysiological and behavioral experimental techniques with machine data processing and analytical methods of communication theory. While our principal objectives are scientific, we are interested in applications of our research results and of new technological developments to clinical medicine.

Members of our group have ties with several hospitals and with the Harvard Medical School. In particular, we have a close working relationship, including sharing of facilities and joint staff appointments, with the Eaton-Peabody Laboratory of Auditory Physiology, which is operated jointly by the Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, and M. I. T. Another example is the recent establishment of a Bioengineering Laboratory as a joint Harvard-M. I. T. endeavor at the Thorndike Memorial Laboratory of Boston City Hospital.

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Our research program can be divided into five major areas: Auditory Physiology, Auditory Psychophysics, Neuroelectric Correlates of Behavior, General Neurophysiological Research, and Biomedical Engineering. The programs for each will be discussed individually.

A. Auditory Physiology

The primary objective of this work is the improvement of understanding of signal transmission and coding of sound stimuli in the auditory system. A large portion of the experimental work is carried out in the Eaton-Peabody Laboratory of Auditory Physiology. New construction at the Eye and Ear Infirmary required the demolition of the Eaton-Peabody Facility in the spring of 1970. The laboratory is now in temporary quarters provided by M. I. T. in Cambridge near the M. I. T. campus. Experimental work in the new location started in October 1970 after a six-month hiatus required for renovating the space and installing the facilities. The new laboratory space includes two experimental chambers and associated electronic equipment, an operating room, histological laboratory, electronics shop, animal quarters, darkroom, data processing rooms, and an office in contiguous space.

1. Mechanical Signals in the Middle and Inner Ear

a. Measurement of velocity by means of the Mössbauer effect

Our system of obtaining velocity waveforms from synchronous detection of γ-ray discharges will be improved to provide automatic calibration of the velocity signal. A system has also been planned in which a sinusoidal acoustic stimulus will be controlled by a digital computer so that velocity magnitude and phase can be measured as frequency is swept through the range of interest.

W. T. Peake, G. K. Lewis

b. Measurements of sound pressure in the inner ear fluid

The small pressure probe that was developed for this purpose has been tested in two calibration devices and was found to be adequate for measuring sound pressure in fluid. A few preliminary experiments in cats indicated that the sensitivity of the probe in conjunction with other electronic equipment is enough to give accurate measurements in the basal turn of the cat cochlea. Such measurements have not been reported previously and they will contribute substantially to our understanding of the mechanics of the inner ear.

T. F. Weiss, V. Nedzelnitsky

c. Mechanical responses of the inner ear to electric stimulation

Experiments during the past year have clearly demonstrated that a mechanical response can be produced in the inner ear by electric stimulation. The relation of the electric stimulus to "equivalent" acoustic stimuli has been determined for certain kinds of stimuli. These results can be related to previous observations of human "hearing" produced by electric stimulation. A doctoral thesis is being completed on this topic.

E. C. Moxon, W. T. Peake, N. Y. S. Kiang

2. Transduction Mechanisms in Hair-Cell Systems

a. Electric potentials in the inner ear of the cat

Intracochlear measurement of electric responses to acoustic stimuli have determined the distribution of these potentials in a transverse plane in the cochlea. Three papers which present and interpret these results have been submitted for publication.

T. F. Weiss, W. T. Peake

b. Electric potential in the inner ear of lizards

An experimental program of measurements in the lizard was undertaken (in collaboration with Dr. Michael J. Mulroy) because the relative simplicity of the inner-ear anatomy seems to provide considerable advantage in performing experiments. This project will try to associate specific cells in the inner-ear receptor with patterns of electric response. At present, micropipettes filled with two different kinds of dye are being used in an attempt to mark individual cells.

T. F. Weiss, D. W. Altmann, R. G. Turner, Jr.

c. Transduction in hair cells of the lateral line organ

We are attempting to obtain intracellular recordings of receptor potentials from hair cells of the lateral line organ of the mudpuppy, Necturus maculosus. In a preliminary study of this organ,[1] such potentials have been found. It is our intention to study these responses more quantitatively by determining the shape of the response to sinusoidal stimuli and the response amplitude as a function of stimulus intensity and frequency. We also intend to try to determine whether or not changes occur in the resistance of the hair-cell membrane as a result of stimulation.

L. S. Frishkopf, A. J. Liff

d. Organization and medullary projections of branches of the VIIIth nerve of the bullfrog

We continue our effort to determine the anatomical relationships and central connections of branches of the eighth nerve of the bullfrog that innervate separate peripheral organs. On the basis of our recent finding[2] that the branches of the posterior rannus of the eighth nerve remain separate through the ganglion to the medulla, we expect that selective lesions in the ganglion will enable us to locate the projections of these branches in the medulla.

L. S. Frishkopf

3. Stimulus Coding in Auditory Nerve Fibers

a. Simultaneous recordings from two auditory-nerve fibers

Analysis has been carried out on responses recorded simultaneously from pairs of auditory-nerve fibers in anesthetized cats. Tests of independence of action potential patterns for conditions of (i) stimulation with tones, and (ii) no acoustic stimulation (spontaneous activity) are consistent with the hypothesis that the variability in the firing patterns of auditory-nerve fibers results from statistically independent random processes.[3] This work is being prepared for publication.

N. Y. S. Kiang, D. H. Johnson, T. F. Weiss

b. Auditory-Nerve responses to high-level tones

This project has demonstrated that dramatic reductions in spike rate occur when the level of a tone is increased at certain levels. Large changes in the phase of the response also occur with the same increase in level. These results are contrary to the usual description of receptor properties. The results are being systematized and will be prepared for publication.

N. Y. S. Kiang, T. Baer

c. Efferent system to the cochlea

Two papers have recently been published[4,5] which report the work on electric stimulation of the crossed olivocochlear bundle.

N. Y. S. Kiang, W. T. Peake

d. Responses of single auditory-nerve fibers in cochleas damaged by drugs

A manuscript will be prepared on the previous experimental work on this project in which the normal function of the cochlea is altered by the administration of an antibiotic, kanamycin. Further experimental work is planned.

N. Y. S. Kiang, E. C. Moxon

4. Single cells in the cochlear nucleus

The auditory-nerve fibers terminate in the brain stem in the cochlear nucleus. Electric responses from cells in this nucleus are being studied in an effort to relate response properties to morphology of the cells. This work combines physiological experiments with anatomical investigations being carried out in the laboratory of Dr. D. K. Morest in the Department of Anatomy, Harvard Medical School.

N. Y. S. Kiang, T. R. Bourk

5. Signal transformation in brainstem nuclei

Certain brainstem auditory neurons (in the medial nucleus of the trapezoid body) receive a single very large presynaptic ending. In the vicinity of these, unusual "double-unit" waveforms can be recorded. We have recently shown that the first part of the "double-unit" waveform is due to the firing of the large presynaptic ending, and the second part is due to the firing of the postsynaptic cell.[6] Usually each firing of the large presynaptic ending causes the postsynaptic cell to fire; however, in some cases the postsynaptic cell does not fire. It appears possible that there is an inhibitory synaptic input to these cells which is able to "gate" the effect of the presynaptic ending. We intend to explore this possibility in further experiments along with other properties of the "double-unit" waveforms. We shall continue to develop methods for recording intracellularly from these cells.

J. J. Guinan, Jr., R. Y-S. Li

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B. Auditory Psychophysics

The general goal of this research is to determine and understand the performance of the auditory system, and to apply this understanding to problems in the perception of speech and music, the transmission of information by means of artificial auditory displays, and the diagnosis and treatment of hearing disorders.

In some of our studies, the observed performance appears to be explainable in terms of the physiology of the peripheral auditory system, and there is considerable interaction between the psychophysical and physiological research. In others, the performance appears to depend strongly on portions of the nervous system about which knowledge is still relatively limited, and our models cannot yet be related to the underlying physiology.

At present, the program in auditory psychophysics is undergoing a transition that results from our newly acquired interest in hearing impairments and our new requirements for more precise specification and control of the acoustic stimulus. As a result of these new elements, a significant portion of our work during the past year has been devoted to preliminary planning, familiarization with past research, crude exploratory experiments, and further development of our computer-controlled laboratory facilities. We hope that this preparatory work will be completed during the coming year, and that specific new research projects in these areas will be well under way in 1972.

1. Intensity Perception

During the past year, our efforts to develop a general theory of intensity perception[1] have focused on theoretical modifications of the memory model, further processing of data from previous experiments, further experiments to examine deviations from Weber's law, the design of new experiments to further guide the development of our theory, the examination of deviations from Weber's law for sound intensity, and the preparation of previous results for publication.

The theoretical modifications have been motivated by our previous experimental results which indicate that when the intensity range of the stimulus set is appreciably greater than the difference limen, performance depends on the position of the stimulus within the range. Thus, for example, in one-interval identification and

and category-scaling experiments, and in two-interval, roving-level, discrimination experiments, resolution is appreciably better at the extremes of the intensity range than in the middle. Similarly, in two-interval, roving-level, discrimination experiments, the bias is much greater at the extremes than in the middle, and of opposite sign at the two extremes. These features of the data indicate that our memory model is inadequate and needs to be revised. Furthermore, our initial work on this problem suggests that resolution and bias are strongly interdependent, that both involve common underlying memory processes, that one cannot hope to fully understand resolution without simultaneously understanding certain elements of bias, and that experimenter-subject feedback decreases resolution (as well as bias) in two-interval, roving-level, discrimination. The new experiments that have been designed to guide future development of the theory include additional two-interval, roving-level, discrimination experiments, identification experiments with a standard and with asymmetric payoff matrices, and intensity-ratio discrimination experiments. The examination of deviations from Weber's law has been motivated by our experimental results on one-interval identification and category scaling, and two-interval, roving-level discrimination, which suggest that Weber's law is not sufficiently accurate to be used as a postulate in our theory of intensity perception. Although it is well known that Weber's law is inaccurate at low intensities, it is often assumed that it provides an accurate description of intensity discrimination at medium and high intensities. According to a number of recent studies (which have measured intensity discrimination with increased precision) Weber's law is inaccurate at high, as well as at low, intensities, and the intensity region over which the law provides an accurate description is relatively small. According to our own recent experiments,[2, 3] in which the ability to discriminate intensity in a two-interval, fixed-level paradigm was measured as a function of intensity for frequencies 1000 Hz and 250 Hz, resolution is essentially constant (i.e., Weber's law is valid) only between roughly 15 and 50 dB SL. Below 15 dB SL resolution deteriorates rapidly, and above 50 dB SL it improves uniformly with intensity. The preparation of previous results for publication has resulted in two papers summarizing our results thus far on resolution in one-interval paradigms.[4, 5]

During the coming year, we hope to continue our theoretical explorations, perform further two-interval, roving-level discrimination experiments (as well as some of the other recently designed experiments), and continue to prepare articles summarizing previous work.

2. Perception of Musical Pitch

Most of the experimental work in the first phase of the project on musical pitch perception was completed during the past year. Extensive psychophysical experiments were conducted to test the ability of musically sophisticated listeners to identify musical intervals defined by stimuli containing no fundamental energy. The experiments were designed to test critically, under conditions that closely simulate musical perception, the place-frequency detection theory[6] and the temporal-periodicity detection theory.[7] Both theories were conclusively shown to be inadequate by our experimental finding that pitch perception with the complex tones that we employed as stimuli is essentially independent of whether the full spectrum of the complex tone is presented to one ear or whether it is divided between a subject's two ears. A detailed description of this work and experimental results that are typical for subjects with adequate training has been published.[8]

The basic experimental stimuli used to define musical notes were half-second samples of periodic sounds which were two successive harmonics of the fundamental frequency. The choice of the lower harmonic number used in any presentation of a note was made at random from a successive range of three. This procedure effectively prevented identification of intervals defined by a pair of notes on the basis of information in only one of the two harmonics. Subjects' ability to correctly identify (percent correct) 8 familiar musical intervals distributed over a half-octave range was examined as a function of various stimulus conditions, including (i) stimulus amplitude, (ii) average lower harmonic number, (iii) absolute frequency, and (iv) monotic (complete spectrum in one ear) and dichotic (spectrum divided between ears) stimuli. The major findings are the following. First, interval-identification data with monotic and dichotic stimuli are very similar, except for differences at higher intensities that are well accounted for by combination tones.[9] Second, interval identification deteriorates monotonically with increasing harmonic number, and is random for harmonic numbers exceeding approximately 10. Third, and finally, all monotic stimuli for which identification performance was better than random consisted in either behaviorally resolvable tones or generated such tones as combination tones (where a behaviorally resolvable tone is defined as a partial of a complex tone that can be aurally matched to a simple tone of similar frequency as the partial).

In the coming year we shall continue with current theoretical work to characterize the confusions that subjects make in identifying intervals in terms of a statistical decision model. The precise nature of these confusions could provide evidence on the relative importance of spatial or temporal cues in the central mechanisms (postcochlea) that are responsible for musical pitch perception. In the second phase of this project additional experiments are planned to investigate the binaural integration properties of the pitch processor, and it is expected that the theoretical work of the first phase will indicate still other experiments.

3. Binaural Hearing

Work continues on a general theory of binaural hearing[10] based on auditory-nerve data. Observations from auditory-nerve activity are used to determine a mathematical description of the peripheral transduction from pressure waves to auditory-nerve patterns. The limitations on binaural performance are then separated into two components: those that are due to information loss in the peripheral encoding, and those that are due to the restricted processing capabilities of the central nervous system.

Theoretical work has proceeded both on the peripheral encoding model and on the restrictions of the central system. In the first area, we have started to determine, using both analytic and simulation techniques, the effects of refractory behavior in the auditory-nerve patterns on predictions made from a model without refractoriness. Also, some earlier work related to models of peripheral encoding has been published.[11] In the second area, recent work has been focused on symmetry properties with respect to simultaneous variation in interaural amplitude ratio and interaural time delay. A major defect of the theory has been predictions of symmetry that are contradicted by experiments on discrimination of interaural time delay. Two modifications of the theory were considered: one predicts asymmetry in binaural detection experiments and has been rejected on the basis of recent experimental results (see below), and one requires additional study of auditory-nerve patterns and is still being pursued.

Several experiments were performed in connection with the theoretical analysis. The investigation of some symmetry properties of binaural masked detection thresholds[12] resulted in rejection of a proposed modification of the theory and support for the model as originally formulated. An exploratory experiment on the binaural detection of tones in a background of pseudo-random noise supports the conclusion from the theoretical analysis that the random character of the stimulus is less important than the random nature of the peripheral encoding. A second exploratory experiment on the ability to use fine time structure binaurally also supported the predictions of the theory. Neither of the exploratory experiments was sufficiently extensive to merit publication, and both should be repeated.

During the coming year, first priority will be given to preparing the backlog of past work for publication. We also plan to complete the study of refractory effects and to carry out an experiment related to a basic assumption of the model – that binaural comparisons of the detailed time structure of the auditory-nerve patterns can be made only among fibers with approximately the same best frequencies.

4. Aural Combination Tones

Work continues in our comparative physiological and psychophysical study of aural combination tones. Psychophysical and physiological combination tone phenomena are both describable as effects equivalent to tones added to the stimulus.[9] The amplitudes of this equivalent tone are similar for the psychophysical and physiological data, but the phases are not. The phase of the psychophysical combination tone depends strongly upon the amplitude of the primary stimulus (typically, it decreases 10° per 1 dB increase in stimulus amplitude), while the phase of the physiological combination tone is not dependent upon stimulus amplitude. This gross difference in the phase behavior in otherwise highly correlated behavioral and physiological data motivated work during the past year to test further the adequacy of the "equivalent stimulus tone" descriptions of the combination tone phenomena. This work, which we outline below, confirmed and extended the range of validity of the earlier descriptions and has provided a basis for further work.

In a physiological experiment similar to those reported previously,[13] additional data were gathered that showed little or no effect of stimulus amplitude upon combination-tone phase measured either in cancellation tests or in the phase coherence of the auditory-nerve spikes. We also tested the contention of de Boer, et al.[14] that simple transducer nonlinearity contributes significantly to some of the combination-tone data that we previously reported and described as effects equivalent to tones in the stimulus. A simple transducer nonlinearity will produce the strongest combination-tone effects when it is driven equally by the two stimulus tones. In fact, little or no combination-tone effect was found in nerve fibers driven by two-tone stimuli with equal amplitude and frequencies near the characteristic frequency so that the tones were about equally effective in exciting the fiber. (The frequency interval of the two tones was 10% or less.) While these data provide no basis for attributing any of the combination phenomena previously reported to transducer nonlinearity, there is experimental support for transducer nonlinearity as the generator of neural phase locking to the higher frequency stimulus tone (f_2) in some of the data previously reported.

Theoretical work has been done in examining the combination-tone effects generated by exponential transducer models that have been found to give excellent descriptions of neural responses to simple stimuli.[11] This model was extended to tone complexes and was used to simulate PST histograms. We found that at stimulus frequencies above ~1 kHz the transducer generates combination-tone phase locking that is small compared with the experimental findings. The model transducer must be driven with a stimulus containing the combination tone to simulate the experimental data.

Two new psychophysical experiments were performed to further examine the phase of the behavioral combination tone. In one of these experiments, concerned with the binaural lateralization of the aurally generated combination tone, the following procedure was used. We first generated a combination tone of frequency $2f_1-f_2 = 500$ Hz in one ear, by stimulating it with a complex tone of frequencies f_1 and f_2. Next, we measured the amplitude and phase of the externally generated 500-Hz tone that precisely cancelled the combination tone, as a function of the level of the primary two-tone stimulus. Finally, we shifted the externally generated cancellation tone to the contralateral ear and examined the lateralization of the image produced by the binaural interaction of this externally generated tone and the aurally generated combination tone, as a function of the phase of the external tone. In general, we found that the image followed the level-dependent cancellation phase: The image was approximately in the center when the phase of the external tone was opposite to the cancellation phase, and it was off to one side, or split, when the phase of the external tone was equal to the cancellation phase. These results show that the "equivalent tone in stimulus" description of the behavioral combination tone is consistent with binaural lateralization phenomena and with current models of binaural interaction.[10] Moreover, independently of models, the experiment shows that the phase of the $2f_1-f_2$ timing information within some neurons beyond the auditory nerve carries the information of the level-dependent cancellation phase.

In a second experiment we extended our previous work on cancellation of combination tones by measuring level dependence at high frequencies.[15] The amplitude and phase of the cancellation tone for $2f_1-f_2$ were measured as a function of primary stimulus level with $f_1 = 8$ kHz and $f_2 = 9.6$ kHz. The phase of the cancellation tone varied grossly with primary stimulus level in a similar manner to that found with much lower stimulus frequencies. Because it is known that neural time locking to tonal stimuli deteriorates with increasing stimulus frequency, this result gives evidence that the temporal information that generates a level-dependent cancellation phase exists within the cochlea. Thus, for low stimulus frequencies, the auditory nerve should contain the information of cancellation phase in temporal form.

In general, the gross difference in the phase properties of the psychophysical and physiological combination tones appears to be a real one and to imply one of the following: (a) the psychophysical and physiological operations for measuring combination tones are different (i.e., cancellation of tonal sensations and cancellation of neural coherence are not concurrent operations); (b) the operations are concurrent in awake subjects, but the concurrence disappears when the physiological measurements are made on subjects under anesthesia; (c) the operations are concurrent, independently of anesthesia, in a population of auditory-nerve fibers that was systematically missed in the physiological experiment.

According to available physiological data, the first hypothesis implies that the behavioral phase information is not carried on either a single auditory-nerve fiber or on a group of such fibers with neighboring characteristic frequency. Therefore, the physiological data would give the correct measure of the cochlear combination tone, while the psychophysical measure would reveal some aspects of how central mechanisms process the whole auditory-nerve pattern to produce tonal sensation. Since this hypothesis would force us to reject all existing conceptions of monaural and binaural processing of complex tones, we plan to pursue it only if the two remaining hypotheses fail. In future work we plan to investigate the second hypothesis first, by studying the effects of anesthesia upon the timing of auditory-nerve spike responses to tonal stimuli. If necessary, the third hypothesis will be investigated by making a survey of the spatial pattern of auditory-nerve responses to a fixed two-tone stimulus. The consequences of either of the last two hypotheses being correct are also nontrivial. According to the second hypothesis, some efferent mechanism might, in the unanesthetized subject, greatly influence the timing of auditory-nerve spikes, at least for complex stimuli. According to the third hypothesis, a particular group of peripheral nerve fibers are responsible for tonal sensation and tonal lateralization, and this group would have been systematically missed in the samples of earlier experiments.

5. Hearing Impairments

Our ultimate goals in studying hearing impairments are to gain an increased understanding of auditory function, improved audiometric techniques, and improved hearing aids. During the past year, we have continued work that we believe is relevant to the development of a research program on hearing impairments. This work can be divided roughly into four areas: familiarization with previous research, development of appropriate laboratory facilities and test procedures, preliminary experiments on listeners with impaired hearing, and a search for appropriate research strategies.

In the preliminary experiments, we performed a variety of psychoacoustic tests on three listeners, each of whom was diagnosed as having a different type of sensorineural impairment. These experiments helped to acquaint us firsthand with some important phenomena related to hearing impairments (e.g., recruitment and abnormal tone decay), to provide us with preliminary data on the relative stability of measurements made on listeners with hearing impairments, to sharpen our concern about the necessity of developing a truly flexible test facility and improved means for specifying the stimulus at various points in the peripheral auditory system, and to reinforce the idea that psychoacoustic research on hearing impairments could be vastly improved if the experimenter were able to experience the same sounds as those experienced by the subject whom he is studying (and be cognizant of the similarity).

In conjunction with these experiments, computer programs were developed for the PDP-4 computer to simulate standard audiometers and to provide adaptive versions of conventional psychoacoustic tests for the determination of absolute and differential thresholds and of points of subjective equality (matching experiments). The preliminary results that have been analyzed suggest that our specific adaptive technique provides relatively stable estimates of the absolute threshold and of the differential threshold for intensity, but is unsatisfactory for estimates of the differential threshold for frequency. Also, the technique employed for matching experiments (which was modelled after the adaptive procedure that was used for threshold measurements in order to minimize training problems) proved cumbersome and of little use in cases with pronounced distortion. In general, attempts to characterize the impairment were limited by the large effort required to develop specialized tests for each listener, despite the fact that the development of these tests involved only new software and was much easier than it would have been if new hardware were required. This problem points out the need for powerful, but flexible, problem-oriented software languages if the flexibility of the computer is to be fully realized in diagnostic tests.

Future work on hearing impairments will continue to be oriented toward the development of a strategy and program for research, and the improvement of facilities, devices and measurement techniques (see Sections 6 and 7). In addition, aside from performing further preliminary experiments on listeners with impaired hearing, we intend to explore three areas for possible research projects. The first area involves the phenomenon of recruitment and is concerned with the extent to which the loudness function in a recruiting ear can be predicted from the ear's dynamic range (where the upper limit is defined by the loudness discomfort level or a more precise equivalent), and the extent to which the differential threshold for intensity in a recruiting ear is approximately the same as in a normal ear (provided the intensity level is measured in SPL rather than SL and is not too close to the absolute threshold in the recruiting ear). These questions are of interest to us because of the apparent confusion in publications on these questions and because of their relation to the theory of intensity perception that we are developing (see Section A). The second area, which we intend to explore in collaboration with the Speech Communication Group of the Research Laboratory of Electronics, involves general background research for improved hearing aids and is concerned with the development of improved methods for characterizing speech-perception difficulties and for determining transformations of the speech-signal space that are well matched to the impaired system's residual sensitivity (not only in terms of detection, but also in terms of resolution in time, amplitude, and frequency) and for which the speech signals in the transformed space can be understood without excessive training. Despite the large amount of previous research in this area, we are not convinced that this research has been adequate. Thus, for example, we plan to explore the possibility that certain impairments in which the ability to understand speech is much worse than would be expected merely on the basis of the audiogram (and therefore tend to be diagnosed in terms of central disabilities and to be viewed as untreatable by hearing aids) are the result of relatively peripheral auditory disorders that degrade features of the signal other than amplitude (e.g., phase or timing) and consequently might be treatable with new types of hearing aids that focus on these other features. Similarly, we plan to explore whether it is possible to construct improved schemes for lowering the frequency content of speech signals by applying recent advances in the understanding of speech perception and speech production. For example, we hope to determine the usefulness of a transformation of speech-signal space that simulates the speech signals that would be produced by a human speaker with an abnormally large vocal tract (and therefore lowers the frequency region of the spectrum envelope of the speech signals in a manner that capitalizes on the ability to understand speech over a wide variety of vocal-tract sizes). The third area relates to the problem of enabling the experimenter to more fully appreciate the signal distortions experienced by the listener with impaired hearing. In general, we believe that a better appreciation of these distortions would lead to a greatly improved understanding of the impairment and a greatly improved capability for the design of a hearing aid. Aside from considering the possibility of trying to include people with hearing impairments on our own research staff, we intend to explore a variety of methods for simulating the distorted signal produced by an impaired ear with a predistorted signal fed to a good ear (and a variety of methods for evaluating the success of such a simulation). Although there are undoubtedly certain types of impairments for which no satisfactory predistortion exists, we do not yet know their relative importance. Moreover, to the extent that such a predistortion exists and can be determined, it is likely to provide a very useful guide in the design of an appropriate aid.

6. Stimulus Specification and Acoustic Transducers

At present, psychophysical studies of both normal and impaired auditory systems are limited by inadequate acoustic transducers and inadequate knowledge and techniques for specifying and/or controlling the stimulus at various points of the system peripheral to the auditory nerve. Examples of these inadequacies are apparent in (i) the relatively poor fidelity of bone-conduction stimulators (relative to the fidelity of the equipment that is available for producing the electrical signal at the input to these transducers); (ii) the uncontrolled variability of the stimulus delivered through earphones or bone-conduction stimulators at the input to the auditory nerve (caused by uncontrolled variations in the coupling between the transducer and the head, and in various internal structures such as the middle-ear muscles and the jaw muscles); and (iii) the problems related to comparisons between the minimum audible field and the minimum audible pressure (the "missing 6-dB problem") and to the occlusion effect in bone-conduction experiments.

In an attempt to eliminate some of these inadequacies, we hope to initiate a variety of new projects concerned with acoustic transducers, measurement of middle-ear function, and signal-calibration techniques. In particular, we intend to develop a probe-tube system for measuring the acoustic signal at the ear drum, a bone-conduction stimulation system for bypassing the most peripheral portions of the auditory system, and a system for measuring the acoustic impedance of the middle ear. We also plan to examine the extent to which a bone-conducted signal can be calibrated relative to an air-conducted signal (or vice versa) by cancellation, to develop a new method for determining changes in the intensity of signals at the input to the cochlea by measuring the associated changes in the phase of combination tones, and to explore the possibility of constructing an earphone with very low impedance. Brief comments on each of these three projects will be made.

a. Calibration by air-bone cancellation

It is well known that, under certain conditions, it is possible to cancel a bone-conducted sound with an air-conducted sound. Thus, in principle, if either stimulus can be properly calibrated, the other can be calibrated by cancellation. Very little is known, however, about the range of parameter values for which cancellation is possible, or the precise extent to which cancellation can be achieved for a fixed set of values. Moreover, since the relative properties of the two signals depend strongly on the state of various muscles in the head (e.g., those controlling the jaw) and on the extent to which the ear is occluded (e.g., by the earphone used to produce the air-conducted sound), further research is required in order to determine whether such a scheme can be made practical for routine calibration purposes.

b. Calibration by cancellation of combination tones

When two tones of different frequency ($f_1 < f_2$) are presented to the ear (and the values of various parameters are chosen properly), it is possible to hear a combination tone of frequency $2f_1-f_2$. This combination tone, which appears to be generated in the cochlea, can be cancelled (and therefore measured) very precisely by an externally introduced tone of frequency $2f_1-f_2$ and appropriate amplitude and phase. Previous research (see Section B) has shown that (a) the amplitude of the cancellation tone grows almost linearly with the amplitude of the two-tone stimulus, while the phase decreases at typically 10° per dB; (b) for primary stimulus tones (f_1 and f_2) with roughly equal amplitudes, the cancellation adjustment is relatively insensitive to changes in the amplitude of the higher frequency (f_2) tone; and (c) the cancellation phase is invariant to arbitrary linear-plus-constant phase transformations of the stimulus. These combination-tone phenomena, together with the cancellation-measurement technique, appear to provide an excellent means for determining changes in the amplitude of the lower frequency (f_1) tone at the input to the cochlea, and thus for monitoring signal amplitude. Further research is required, however, in order to develop this technique.

c. Low-impedance earphone

All existing earphones are relatively "hard" acoustic structures (i.e., of high acoustic impedance). This characteristic not only leads to a variety of differences between earphone listening and free-field listening, but is a primary cause of the uncontrolled variability of the signal produced by earphones at the eardrum. Thus, at low frequencies, the signal at the eardrum is critically dependent upon the seal of the earphone around the ear, and minor leaks in the seal cause major changes in the effective input to the ear. Similarly, at frequencies greater than roughly 2 kHz, small differences in earphone characteristics appear to have such large influences on the effective input to the ear that most results at these frequencies must be regarded with considerable skepticism.

If an earphone could be designed that "looks like free space to the ear," many of these problems would disappear, since the pressure-velocity relations in the ear canal would then be determined primarily by the input impedance to the ear. In principle, it should be possible to build such an earphone by appropriate use of feedback. Furthermore, the availability of such a system might permit a significant improvement in ear protectors by cancellation of some components of the bone-conducted sound and/or the sound that is attenuated (but not eliminated) by the passive shields that constitute the conventional protectors. The actual design of such a system, however, presents a variety of theoretical and practical problems requiring considerable further research.

7. General Facilities and Instrumentation

In order to support a wide range of psychoacoustic research on normal and impaired auditory systems, we are continuing to develop general-purpose facilities for stimulus generation and control, response monitoring, and data processing. During the past year, we have concentrated on the development of an integrated hardware-software system for experiment control. To facilitate the use of the computer, we are attempting to develop powerful, flexible, and easy to learn problem-oriented languages. The first of these is an interpretive language modified for experiment control that is suitable for small computers (PDP-8/12) with 8000 words of core memory, and retains many powerful computational features. We have also designed inexpensive timing, synchronizing, and analog-to-digital conversion circuitry for the PDP-8L computer, new circuitry for sharing a high-capacity disk memory, and appropriate software modifications that permit a variety of system programs to take advantage of this memory. This effort complements previous efforts to develop circuitry for sharing relatively expensive peripheral devices. In addition to developments related to the computer facility, we have designed an inexpensive improved four-quadrant multiplier for analog signals which provides greater suppression of distortion components.

Future work will be concerned with completing the computer-controlled psychoacoustics facility. We intend to achieve improved control performance by developing a compiler to supplement the interpretive language, and to develop an automated system for studying speech confusions, using the PDP-12 computer for stimulus generation and the disk memory for waveform storage. We also plan to design new improved electronically controllable attenuators of high quality for this facility. Substantial instrumentation development will also be associated with the projects on stimulus specification, bone-conduction and impedance measurements, and acoustic transducers (Section 6).

J. E. Berliner, L. D. Braida, D. J. Callahan, H. S. Colburn, N. I. Durlach,
J. L. Goldstein, A. J. M. Houtsma, W. F. Kelly,
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C. Neuroelectric Correlates of Behavior

Eyelid responses in the rat continue to be the main concern of this research. Our interest in conditioning and its neural substrate led to this subject, but it is clear that questions about conditioning must to a considerable degree wait upon answers to more fundamental problems. Be that as it may, it has been necessary at this stage of our inquiry to make sure that control of the eyelids in the rat (our subject of choice) through various conditioning procedures is feasible, and our behavioral work thus far has been directed largely toward that problem.

Recent experiments have been successful in conditioning the corneal reflex by classical procedures that are very much like those used in eyelid conditioning studies with human subjects and, more recently, with rabbits. Our earlier failures can be attributed largely to the use of unconditional stimuli, air puffs, that were too weak. They were strong enough to elicit full vigorous blinks, but it appears that the occurrence of a strong response following appropriate CS-UCS pairings is not in itself sufficient for conditioning. This is best understood, perhaps, through Spence's[1] view of the unconditional stimulus which sees a dual role for the UCS; not only does it elicit the unconditioned response, but it has motivational, drive properties that are necessary for the occurrence of a conditioned one. It has also been possible to establish a conditioned eyelid response with a shock UCS delivered to the snout through subcutaneous electrodes. Alternative procedures for conditioning may provide some necessary flexibility in the analysis of the conditioned blink. Classical conditioning studies planned for the coming year are parametric in nature and, we hope, will serve two purposes: (i) to determine the optimum conditions for establishing simple and discriminative conditioned eyelid responses in the rat, and (ii) to determine how similar eyelid conditioning in this species is to that in other species.

Operant control of the eyelids using positive reinforcement has been more difficult to achieve. Rats can learn to close their eyes when the response is followed by food reinforcement, but under all of the procedures that have been tried thus far the training is very difficult. Our problem, then, is to determine whether this task is inherently difficult for the rat, and if so why, or whether our procedures have been at fault. We had hoped to find in the literature on human eyelid conditioning some clues to the solution of this problem, but the positive reinforcement procedures used with human subjects have not been really comparable to those employed with animals. Plans for the coming year include studies of the human eyelid response under operant conditioning procedures that will permit direct comparisons with the nonhuman animal work.

The behavioral work has also been concerned with the nature of the electromyogram (EMG) recorded from the eyelid. A preliminary study of the eyelid EMG in rat was described by Donald M. Edwards[2] in an undergraduate thesis in electrical engineering, and this has been followed up with additional work in the unanesthetized animal, including some conditioning experiments now in progress. If the EMG turns out to be a practicable measure of eyelid responses in the classical conditioning situation, it will expedite the parametric conditioning studies that are contemplated because our present technique for measuring eyelid responses (measuring eyelid position by means of the light reflected from the orbital region) is rather difficult and time-consuming. It is of interest that the rat's eyelid EMG resembles that described for human subjects; it too has a brief, short-latency component (approximately 12 ms) which is followed after a pause of variable duration (30-100 ms) by a more prolonged discharge. The nature of the early response is still in question, and we hope that it may be more amenable to analysis in the rat, wherein the choice of experimental procedures is greater, than it has been in the human.

Both components of the eyelid response have been seen in the activity of single eyelid motoneurons recorded by micropipette electrodes in the facial nucleus of lightly anesthetized rats. The discharge patterns of eyelid motoneurons in response to air puffs (like those used in the conditioning experiments) will be described in a preliminary study of these cells that is nearing completion.

Representation of the eyelids in sensorimotor cortex of the rat remains elusive. Earlier maps of "somatosensory" and "motor" areas of rat cortex have not been of much help; and, in fact, it has been necessary to reevaluate those maps. Electrical stimulation below the cortical surface through "semi-microelectrodes" has yielded a map of the motor area that occupies much less cortex than the motor area described by Woolsey,[3] especially in its anterior and lateral extents. The smaller area found in our work may simply reflect the refinement in stimulation techniques, i.e., the smaller electrodes and smaller currents needed to evoke movements. A study is just beginning in which some independent criterion for distinguishing our motor area is being sought; an attempt will be made first to determine if there is a preferential antidromic response from this cortical region to stimulation of the pyramidal tract.

Multiple-unit and single-unit responses to tactile stimulation in the curarized rat have been used to determine the cortical region serving somesthetic functions. The responsive region is again less extensive than earlier maps indicate, although the orientation of the various parts of the body seems to agree well with the earlier work. A more intensive search will now be undertaken for cortical responses to stimulation of either the cornea or the eyelid. It may well be that the cells responsive to such stimulation are few in number and occupy only a very small cortical region. A similar situation may hold for the representation of the eyelid in the motor area, and a more exhaustive search must also be undertaken for a site where electrical stimulation gives rise to movements of the eyelid.

During the coming year an attempt will be made to delineate the macropotentials in the brainstem associated with the corneal reflex. Of particular interest will be any slow potentials related to cellular activity in the facial nucleus. If there is a characteristic slow potential in the facial nucleus when the rat blinks in response to corneal stimulation, it could prove beneficial on at least two counts. First, it could aid in the placement of microelectrodes, especially in chronic animals prepared for both behavioral and electrophysiological study. Second, it might in itself provide a useful monitor of the activity in the eyelid motoneuron pool, depending, of course, upon its relationship to the cellular activity.

Our plans to investigate the trigeminal afferents involved in the corneal reflex were not realized during the past year, but we hope to begin this study in the coming one. In particular, an effort will be made to determine the location, the response properties, and the receptive fields of second-order afferents in the spinal trigeminal complex that respond to corneal stimulation.

R. D. Hall, E. P. Lindholm, B. L. Hicks

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D. General Neurophysiological Research

In addition to the physiological work previously described, research in our laboratory has included and will continue to include various other studies of the nervous system. These studies are generally of the kind that we feel will profit from our interest in analytical and computer techniques. One current objective is the following.

1. Electrical Properties of Nerve Membrane

We are continuing to study the dependence of ion conductances on ion concentration in voltage-clamped lobster axons, using the sucrose-gap technique. Attention has been focused recently on the "instantaneous linearity" property of nerve membrane.

T. F. Weiss, P. Demko, Jr.

E. Biomedical Engineering

In broadest terms our objective is to apply engineering technology to practical problems in patient care, health delivery systems, and clinical research. Our activities are not restricted to particular organ systems, although we have a strong interest in the cardiovascular system. Our research interest goes beyond the level of bioinstrumentation development into the clinical applications and medical research problems themselves. A well-equipped bioengineering laboratory has been established as a joint Harvard-M.I.T. endeavor at the Thorndike Memorial Laboratory of Boston City Hospital. This facility serves as a base of operations for engineering activities within the medical community. Graduate students often pursue thesis projects at the hospital – frequently in cooperative projects with physicians. Furthermore, the laboratory serves as a point of contact for members of the medical community who desire engineering consultation. The laboratory facility at R.L.E. and the hospital facility complement each other. Complex instrumentation and/or computer software are pursued most intensively at M.I.T. and are later transferred to the hospital laboratory for clinical application. Studies involving clinical data, animal experimentation, etc. are centered at the hospital, as well as a moderate amount of bioinstrumentation development.

Several on-going research projects are listed below.

1. Ectopic Beat Detection

Continuing interest centers around the problem of reliably detecting and categorizing ectopic cardiac activity from EKG recordings. During the past year we developed an ectopic-beat detector based on a simple pulse-duration criterion. This device estimates the duration of the widest component in the EKG complex, compares it with a stored reference based on an observably normal beat, and declares abnormal morphology on the basis of exceeding a specified fraction of this reference. Preliminary evaluations suggest that this system works as well as an earlier system which compared the duration of the individual beat with a running average of the previous four normal beats. Our ultimate objective is to devise practical methods for monitoring ectopic activity in both ambulatory and hospitalized patients.

2. EKG Characterization Techniques

a. Apparatus has been constructed which characterizes the electrocardiographic waveforms as a series of straight-line segments. An error criterion is established and new line segments are added to the characterization only as often as is needed to remain within the established error. The apparatus is implemented with 8 linear-integrated circuits and gives promise of economical preprocessing that yields approximately a ten-to-one reduction in data rate.

b. A short-term memory incorporating MOS shift registers and using delta modulation has been designed. Such techniques as matched-filtering and temporal pattern recognition can be easily implemented by using such multiple access delay-line memories. These possibilities will be further exploited, although the 200-ms memory was designed principally to allow observation of the P-wave of electrocardiograms while using the much larger QRS complex for purposes of detection.

3. Display Techniques

A resettable sweep system and a continuous position controller have been added to our three-dimensional oscilloscope. This addition allows photographic superposition of many electrocardiographic complexes lasting over periods up to 50 min long. Waveforms of abnormal morphology are clearly visible when displayed in this manner. Records from hospitalized patients have been scanned for ectopic activity with greater success than is obtainable with human evaluators.

4. EEG Correlates of Metabolic Encephalopathy

Patients with uremia experience significant alterations in CNS functions. This is manifested clinically by CNS irritability with twitches or seizures, and changes in level of consciousness which may vary from slight drowsiness to deep coma. Changes in the EEG have been described in these patients, and some workers argue that the EEG may provide a sensitive indicant of CNS state in these patients. This project proposes to monitor EEG's of uremic patients being dialyzed at Boston City Hospital. The EEG will be analyzed using averaged evoked potentials, spectral analysis, and autocorrelation techniques. The objective of the study is to determine if systematic changes in EEG data are of predictive value in managing uremic patients.

5. Noninvasive Blood-Pressure Monitoring in Ambulatory Patients

This project aims at developing an instrument to monitor blood pressure by measuring pulse wave velocity in the arterial system. An approximately linear relationship has been demonstrated between diastolic blood pressure and the velocity of pulse wave propagation in the major elastic arteries. Work is under way to develop reliable means of detecting pulse wave arrivals using ultrasonic techniques.

6. Dynamic Monitoring of Physiological Variables in Ambulatory Patients

The objective of this effort is to develop a miniature portable data recorder that will permit the acquisition of heart rate, number of ectopic beats per minute, and possibly blood pressure over a 24-hour period in ambulatory patients. This instrument would have wide applicability to the study of cardiovascular disease.

7. Magnetic Tape Recording System

A data recording-reproduction system capable of multiplexing 3 low-frequency data channels on a single-voice bandwidth magnetic tape channel has been designed and constructed. The basic algorithm involves time-multiplexing the three signals in the form of relative pulse positions. While it does not produce truly periodic sampling, the code developed by the device does have a perfectly periodic frame rate and thus allows correction for variations caused by irregularities in tape speed.

8. Analog Interface

The design of an analog input-output interface for our digital data processor has been completed. This interface can accommodate 16 analog output channels; two of the output channels will be used as horizontal and vertical signals to a display, and the remaining will be used for waveform simulation. The interface includes multiple buffering and a timing system that permits period sampling, irrespective of the activity of the central processor. At present, it is being implemented in terms of medium-scale integrated (MSI) circuitry.

9. Pacemaker Evaluation Techniques

The hospital group has recently initiated a Cardine pacemaker follow-up clinic. As a part of this activity, studies are being conducted on the amplitude-duration threshold curve, and instrumentation is being designed to facilitate remote pacemaker analysis via telephone lines.

S. K. Burns, R. G. Mark

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A. "PARADOXICAL" WAVES, BONE CONDUCTION, AND COCHLEAR MODELS

In the course of his extensive studies of cochlear function, Békésy showed in a number of ways that the pattern of vibrations in the cochlea is quasi-independent of the mode of cochlear stimulation. Perhaps the most important of these demonstrations were his observations that "a tone presented by bone conduction can be completely cancelled by a tone transmitted to the ear by air conduction, so that nothing at all is heard"[1] and that the wave motion in the cochlea is "paradoxical,"[2] in that the direction of wave propagation is from base to apex independently of whether the source is at the oval window or in the apical turn. Corroborating evidence for these phenomena was provided by Wever and Lawrence[3] and by Tasaki, Davis, and Legouix[4] who showed that the cochlear microphonic produced by various artificial forms of mechanical stimulation could be cancelled by an appropriate vibration of the stapes.

No comprehensive analysis of these phenomena has ever been presented. Qualitatively, the most commonly accepted explanation[5-8] is that a disturbance of the cochlear fluids at any point produces a compressional wave that travels at high velocity and creates a pressure difference between the oval and round windows. This pressure difference in turn sets up a more slowly traveling wave in the cochlear partition starting at the base and progressing toward the apex. The details of this two-step process, however, have never been made clear. Indeed, there seems to have been at least a vague feeling[3, 6, 8] that one-dimensional long-wave models of the type first proposed by Zwislocki[9,10] and later considered by many authors[11-14] cannot account for the observed effects without modification (e.g., distribution of the effective source along the partition). In fact, however, phenomena similar to paradoxical propagation and bone-conduction cancellation are fundamental properties of <u>all</u> cochlear models of the long-wave type, provided only that certain boundary and symmetry conditions are met.

The argument is similar in style to one suggested by Zwislocki,[5] but differs significantly in details. We begin with the usual[10] long-wave one-dimensional sinusoidal steady-state equations in the form

$$p = p_1 - p_2 = vZ \qquad \text{(membrane dynamics)} \tag{1}$$

$$\frac{dv_1}{dx} = \frac{dv_2}{dx} = -v \qquad \text{(continuity)} \tag{2}$$

$$\left.\begin{aligned} j\omega\rho v_1 &= -\frac{d(S_1p_1)}{dx} \qquad (3) \\ j\omega\rho v_2 &= -\frac{d(S_2p_2)}{dx} \qquad (4) \end{aligned}\right\} \quad \text{(inertial effects in scalae)}$$

where

(a) p_1, p_2, v_1, v_2 are the (complex) pressures and volume velocities in the x-direction in scala vestibuli (1) and scala tympani (2).

(b) v = (complex) volume velocity per unit length of the cochlear partition

(c) ρ = density of perilymph; ω = radian frequency

(d) S_1, S_2 = areas of scala vestibuli and scala tympani, respectively.

(e) Z = (complex) acoustic impedance of a point on the partition.

In general, all of these (except ρ and ω) may be functions of the distance x along the partition from the oval window.

To complete the specification of the model, it is necessary to describe the boundary conditions at the oval and round windows and at the helicotrema. These are indicated schematically in Fig. XXIII-1. Z_1 and Z_2 represent the acoustic impedances that are seen looking out from the oval and round windows, respectively. P is the pressure resulting from "air-conducted" sound that would be measured at the stapes if it were blocked. (In fact, because of the air in the middle-ear cavity, there is a degree of coupling between the oval and round windows in the normal ear, but the effect is small and will be ignored. A more careful analysis would not alter the essential character of our conclusions.) V corresponds to a volume velocity source artificially introduced at the apex. We shall also assume, for the moment, that the helicotrema and/or the membrane near the apex is a short circuit between the two scalae at the frequencies of interest.

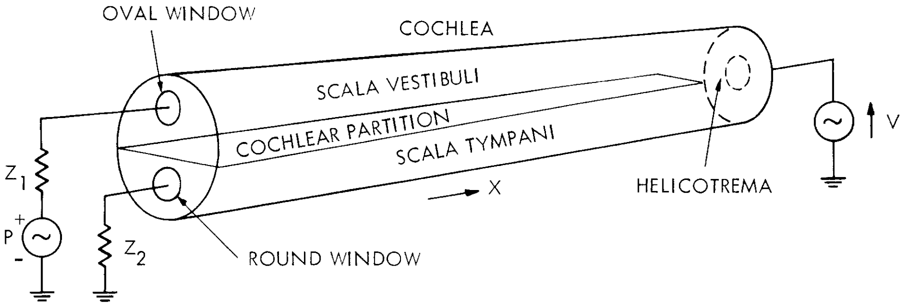

Fig. XXIII-1. Boundary conditions.

Mathematically these boundary conditions can be described by Eqs. 5-7.

$$P - Z_1 v_1(0) = p_1(0) \tag{5}$$

$$-Z_2 v_2(0) = p_2(0) \tag{6}$$

$$v_1(\ell) + v_2(\ell) + V = 0, \tag{7}$$

where ℓ is the length of the cochlea.

Our principal result can then be stated as the following theorem.

Theorem 1

If $S_1 = kS_2$ (where k is a constant independent of x), then for any choice of V a value of P can be found such that the velocity, v, of the partition is zero for all x. The value of P that cancels the motion is given by

$$P = \frac{V}{1+k}[Z_2 - kZ_1]. \tag{8}$$

The proof of the theorem is immediate on observing that the following choices for the variables satisfy (1)-(7) if P is given by (8):

$$v = 0; \qquad v_1 = \frac{-k}{1+k} V; \qquad v_2 = \frac{-1}{1+k} V \tag{9}$$

$$p_1 = p_2 = \frac{Z_2 v S_2(0)}{(1+k)S_2} + \left[\frac{j\omega\rho V}{(1+k)S_2}\right]x. \qquad (10)$$

It is noteworthy that Theorem 1 does not depend at all on any assumptions about the nature of the membrane impedance, Z. In fact, since the membrane is motionless under the conditions of this theorem, it would still be valid for much more elaborate membrane models (including, for example, longitudinal stiffness) than those described by (1). For the same reason, the theorem should be applicable to the cochlea over a much wider range of frequencies than those for which the long-wave assumptions leading to (1)-(4) are justified.

The essence of the theorem is that precise cancellation of the effects of the two sources depends upon the symmetry condition $S_1 = kS_2$. Insight into the reason for this condition, as well as further understanding of other conditions under which cancellation of stimuli will occur in the cochlea can be gained from a study of the electrical equivalent circuit for (1)-(7) shown in Fig. XXIII-2 (voltage ~ pressure, current ~ volume velocity). Here the condition $S_1 = kS_2$ is reflected in a proportionality between the upper and lower series impedances, z_i and kz_i. Making $v_1 = kv_2$ then guarantees no voltages or currents in the shunt branches, since the voltage drops across the upper and lower series impedances will be equal, and the structure starts with a shunt short at the helicotrema. Finally, to satisfy Kirchhoff's voltage law around the left-hand mesh, it is necessary and sufficient to choose P as in (8). Evidently, if the upper and lower series impedances were <u>not</u> proportional, it would not be possible by adjustment of P alone to cancel the currents resulting from $V \neq 0$ in all the shunt branches simultaneously.

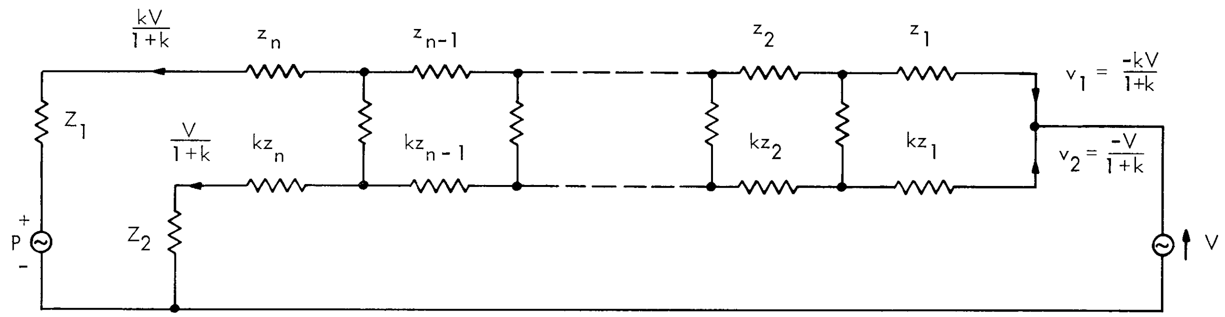

Fig. XXIII-2. $P = \frac{V}{1+k}(Z_2 - kZ_1)$.

It is easy to see in Fig. XXIII-3 that the addition of other velocity sources at various places along the cochlea does not destroy the possibility of cancelling all of the shunt currents by a single choice of P, provided that each source in the

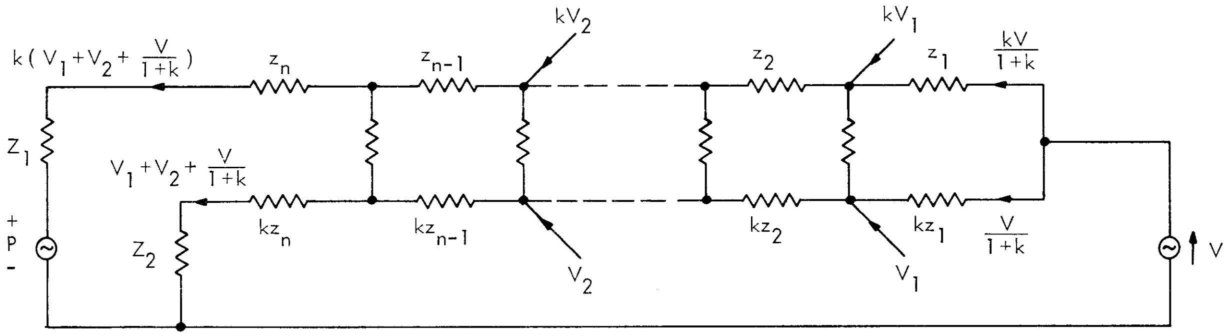

Fig. XXIII-3. $P = \left(V_1+V_2+\frac{V}{1+k}\right)(Z_2-kZ_1)$.

scala tympani is balanced by a source k times larger in the scala vestibuli. We may also introduce continuous source volume velocities per unit length $V_1(x)$ and $V_2(x)$, in place of or in addition to V. Equation 2 is then replaced by

$$\frac{dv_1}{dx} = V_1 + v \tag{11}$$

and

$$\frac{dv_2}{dx} = V_2 - v \tag{12}$$

and we may prove the following theorem.

Theorem 2

If $S_1 = kS_2$, then for any choice of distributed sources V_1 and V_2 such that $V_1 = kV_2$ a value of P can be found such that the velocity, v, of the partition is zero for all x. The value of P which cancels the motion is given by

$$P = \int_0^\ell V_2(x)\, dx\, [Z_2-kZ_1]. \tag{13}$$

Again the proof is immediate on choosing

$$v_1 = kv_2 = -k \int_x^\ell V_2(x)\, dx. \tag{14}$$

If we accept that $S_1 \approx kS_2$ in the cochlea, then Theorems 1 and 2 provide rather simple possible explanations of Békésy's observations. There is nothing in any of our arguments to suggest in which direction the wave resulting from stapes vibration will appear to progress — the direction depends upon the form of Z. Theorem 1 implies, however, that if it appears to move in one direction with stapes stimulation (e.g., from base to apex), then it must appear to propagate in the same direction (from base to apex) when driven artificially at the apex. (Otherwise complete cancellation could not be produced by the superposition of both stimuli.) This is the essence of Békésy's "paradoxical" motion. On the other hand, Theorem 2 explains Békésy's bone-conduction cancellation result if we assume that the principal effect of bone conduction directly on the cochlea is to produce a more or less uniform compression of the temporal bone, and if we further assume that such a compression is equivalent to a distributed volume velocity source per unit length in each scala proportional to the area; that is, $V_i \sim S_i$ which implies $V_1 \approx kV_2$.

Physically, our explanation of Békésy's observations is not inconsistent with the current qualitative explanation of a rapidly propagated compression wave establishing a pressure distribution which in turn produces displacement of the partition. In fact, since we represented the perilymph as incompressible, we in effect permitted "compression waves" of infinite velocity. But the proposed theory differs from the usual explanation in its emphasis on the importance of the symmetry condition $S_1 = kS_2$ and on balanced excitation $V_1 = kV_2$. Presumably, for example, the usual theory would imply that an isolated velocity source in one scala at the middle of the cochlea would be as easy to cancel as an isolated source at the apex. But the new theory states that an isolated unbalanced central source could not be cancelled by stapes displacement (at least for frequencies that would normally produce significant motions of the partition at the point where the source is applied – see below). No doubt experiments to test this point could be set up using, perhaps, the cochlear microphonic procedure of Tasaki, et al.[4]

There are very little available data on cochlear dimensions against which to test the hypothesis $S_1 = kS_2$. Some data of Wever[15] are shown in Fig. XXIII-4; whether these support or refute the assumption depends on the precision thought to be necessary. Certainly proportionality breaks down for small x. In this regard, it is perhaps worthwhile to make three points.

1. Paradoxical motion is a qualitative phenomenon; it is implied by the cancellation property of Theorem 1, but precise cancellation is certainly not required.

2. Under normal circumstances a sinusoid produces substantial motion only in a limited region, say, 30% of the partition. For cancellation to be effective, it is sufficient that $S_1 \approx kS_2$ and $V_1 \approx kV_2$ over just this region. (This conclusion is not entirely independent of Z; in fact, it requires that Z be such that $p = p_1 - p_2 \approx 0$ on the apical side of the active region under normal conditions of stimulation. The observation that in the cochlea v is very small above the active region does not require that ρ be small because, in principle at least, Z could be large. But it does not seem likely that this is the case for the cochlea. Incidentally, if we accept

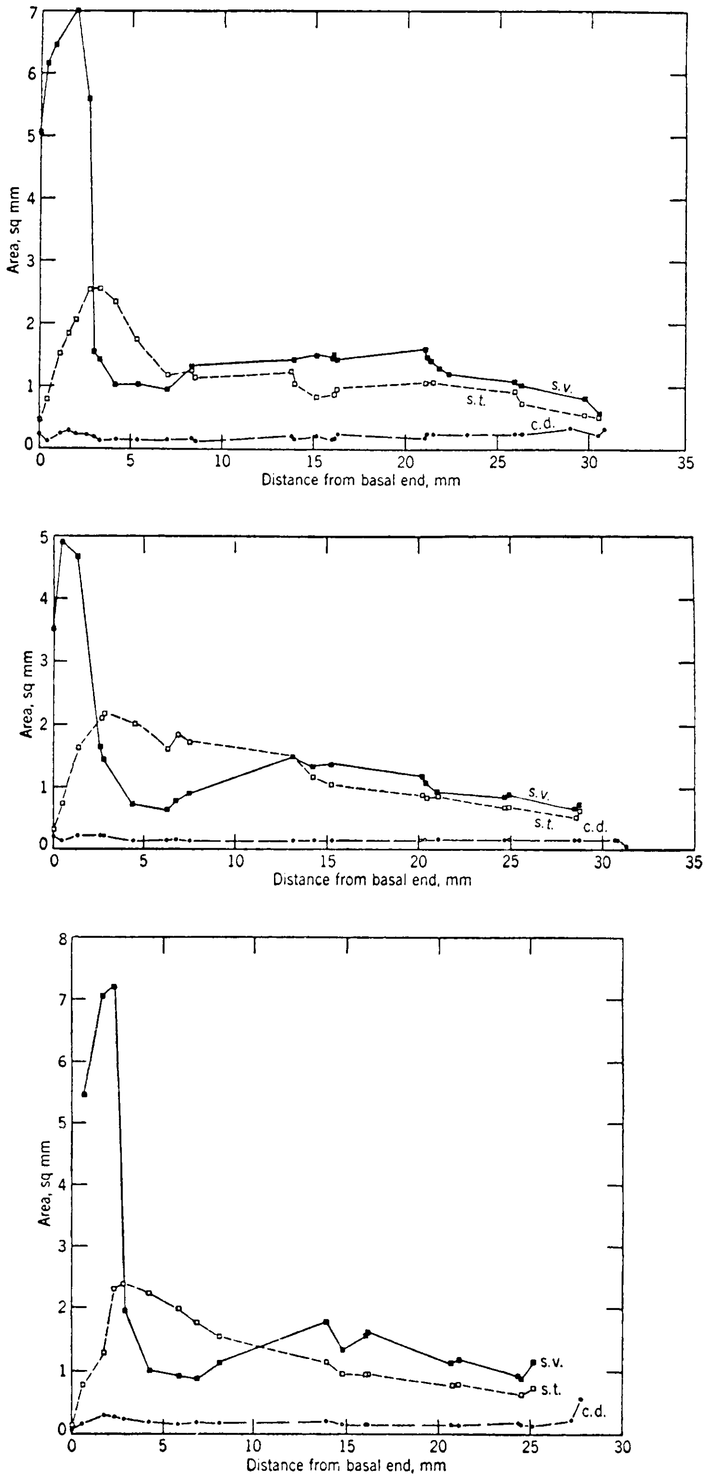

Fig. XXIII-4. Cross-sectional areas of the cochlear passages. Three different human ears. (s.v., scala vestibuli; s.t., scala tympani; c.d., cochlear duct.) (Reproduced from E. G. Wever.[15])

the assumption that p is very small above the active region, then it is not necessary to assume, as we did earlier, that the helicotrema and/or apical portion of the membrane is a short circuit at moderate and high frequencies.)

3. Békésy's celebrated observation that bone-conducted sound could be "completely" cancelled by air-conducted sound is not in fact all that convincing. "Complete" cancellation was, in reality, only achieved at 400 Hz. At 100 Hz the sensation was confused by a tactile effect, whereas at 800 Hz no complete cancellation could be obtained. Békésy blames this failure on the influence of middle-ear resonances – but he does not explain why such resonances should cause difficulties.

It seems possible, then, that the degree of proportionality between the scalae areas observed anatomically is adequate to explain the degree of cancellation observed behaviorally. But more evidence of both kinds would obviously be welcome.

W. M. Siebert

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B. REDUCTION OF MUSCLE NOISE IN THE ELECTROCARDIOGRAM

Coronary patient monitoring devices often fail to function properly when muscle noise (accompanying self-movement of the patient) superimposed on the EKG is significant as compared with the amplitudes of the various waves of the EKG. Since this problem has been more or less[1] ignored, the author, under the supervision of Professor Stephen K. Burns and Dr. Roger G. Mark, undertook a research project to evaluate several possible methods for reducing muscle artifacts at the output of the EKG preamplifier.[2]

Characterization of muscle noise and of EKG's in terms of frequency spectra,[3-7] correlation functions,[7, 8] and amplitude distributions[9] indicated that it would be virtually impossible to reduce muscle artifacts without considerably distorting the underlying EKG. The QRS wave generally has a large amplitude, however, and is commonly used as a triggering signal for monitoring devices. We decided to evaluate various noise-reduction techniques by observing the ability of each to produce a reliable triggering signal for monitoring devices.

Simultaneous recordings were made from two different EKG leads (denoted hereafter as W_1 and W_2) for which the EKG morphologies were similar. A dual preamplifier designed by Burns and an Ampex FM tape recorder were used to record from the two leads while the subject flexed the muscles underlying the recording electrodes. Figure XXIII-5a and 5b shows recorded segments in which the muscle noise completely obscures the underlying EKG. The same segments are used to demonstrate the effectiveness of the various noise-reduction techniques.

The techniques evaluated are the spatial average (W_1+W_2), the square (W_1W_1), the sum of squares $\left(W_1^2+W_2^2\right)$, the product (W_1W_2), the integral of the square ($\int W_1W_1\,dt$), the integral of the sum of squares $\left(\int W_1^2+W_2^2\,dt\right)$, the integral of the product ($\int W_1W_2\,dt$), 6 dB/octave lowpass filtering, and 24 dB/octave lowpass filtering. Multiplication was accomplished by using an analog voltage multiplier, and integration by using a 0.2 Hz lowpass filter.

The results for spatial averaging, squaring, the sum of squares, and the product are shown in Fig. XXIII-5. None of these methods reduced the noise sufficiently to provide an adequate triggering signal. The effects of the integration techniques (see Fig. XXIII-6) give considerable improvement over those of the previous methods. Nevertheless, these techniques are also inadequate for producing a reliable triggering signal. Note that the integral of the product ($\int W_1W_2\,dt$) is analogous to the signal-detection technique of matched filtering and may be useful when the noise in the two leads is uncorrelated.

The method showing the most promise is lowpass filtering. Figures XXIII-7 and XXIII-8 show the effects of lowpass filtering at 6 dB/octave and at 24 dB/octave using

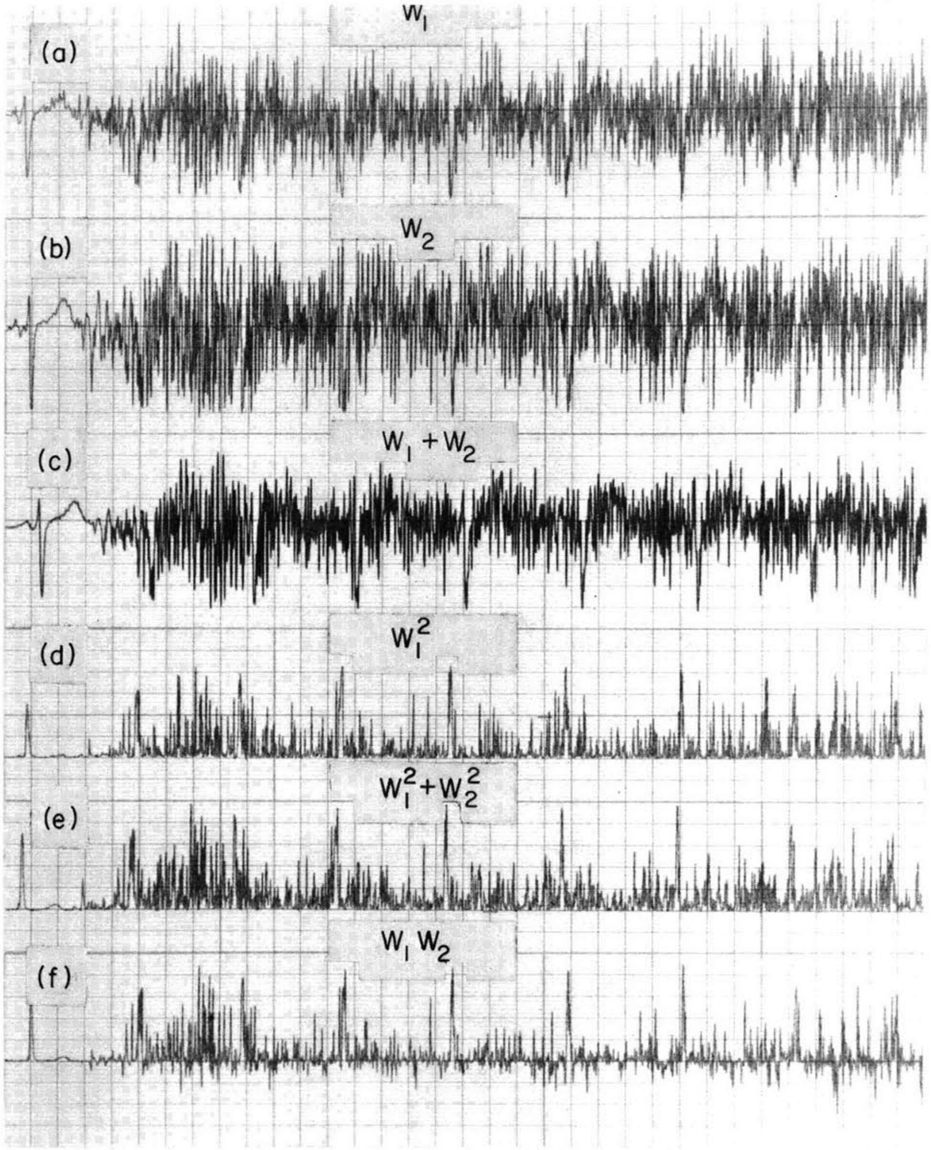

Fig. XXIII-5. Effects of noise reduction techniques on extremely noisy EKG's. The results of applying the noise-reduction techniques discussed in this report to the simultaneously recorded EKG's in (a) and (b) are illustrated in (c) through (f). The noise in leads W_1 and W_2 was produced as the subject flexed both pectoralis muscles. All traces can be aligned properly by using the first (and only recognizable) QRS wave in each trace as a time origin.

(a) W_1 (EKG obscured by muscle noise); 200 ms/div.
(b) W_2 (EKG obscured by muscle noise); 200 ms/div.
(c) $W_1 + W_2$ (spatial average).
(d) $W_1 W_1$ (square).
(e) $W_1 W_1 + W_2 W_2$ (sum of squares).
(f) $W_1 W_2$ (product).

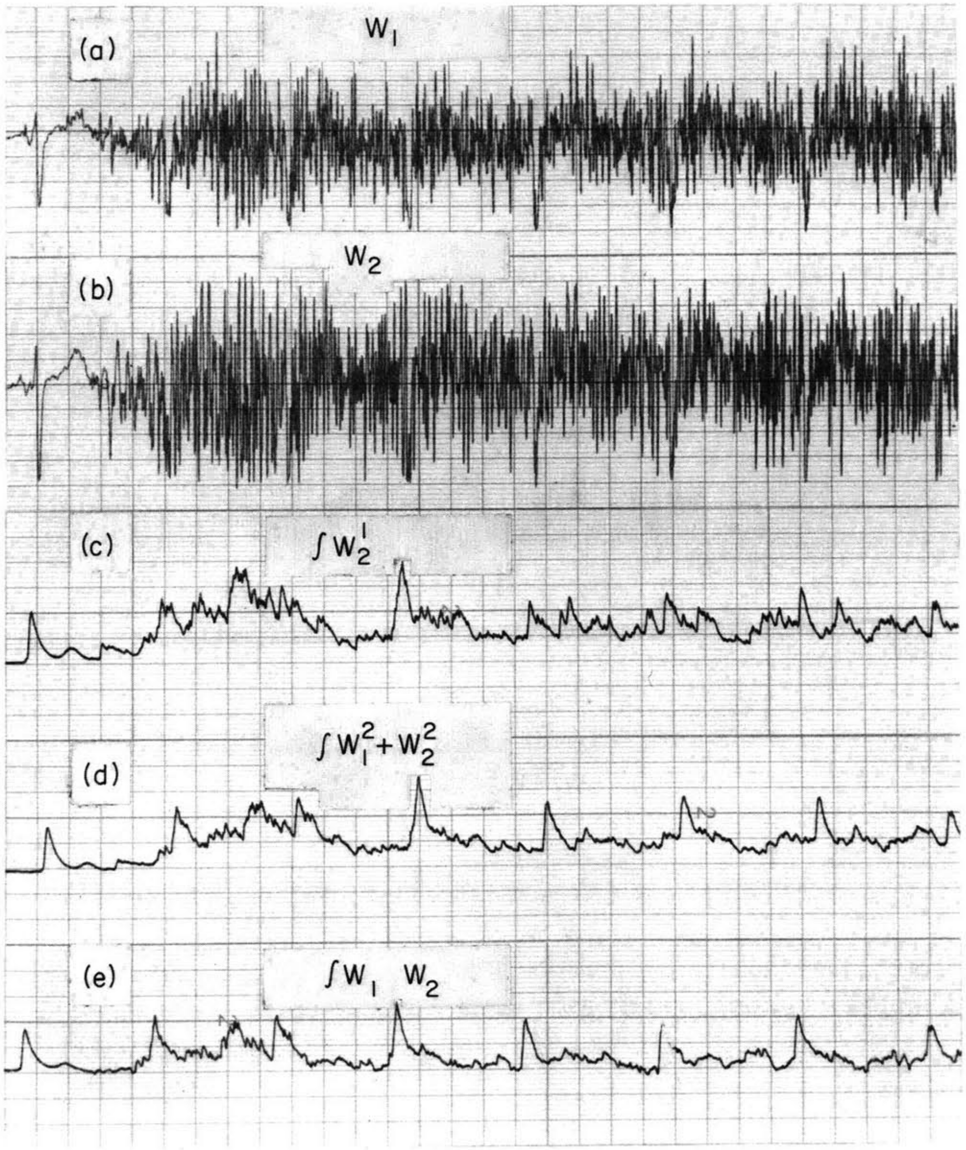

Fig. XXIII-6. Integration of the square, the sum of squares, and the product. The segments of W_1 and W_2 shown in (a) and (b) are the same segments illustrated in Fig. XXIII-5a and 5b. The integrals of the square, the sum of squares, and the product were approximated by filtering each with a 0.2 Hz lowpass filter. All traces can be aligned properly by using the first QRS wave in each trace as a time origin (the sharp rise in the integral corresponds to the RS segment of the EKG).

(a) W_1 (EKG obscured by muscle noise); 200 ms/div.

(b) W_2 (EKG obscured by muscle noise); 200 ms/div.

(c) Integral of W_1W_1.

(d) Integral of $W_1W_1 + W_2W_2$.

(e) Integral of W_1W_2.

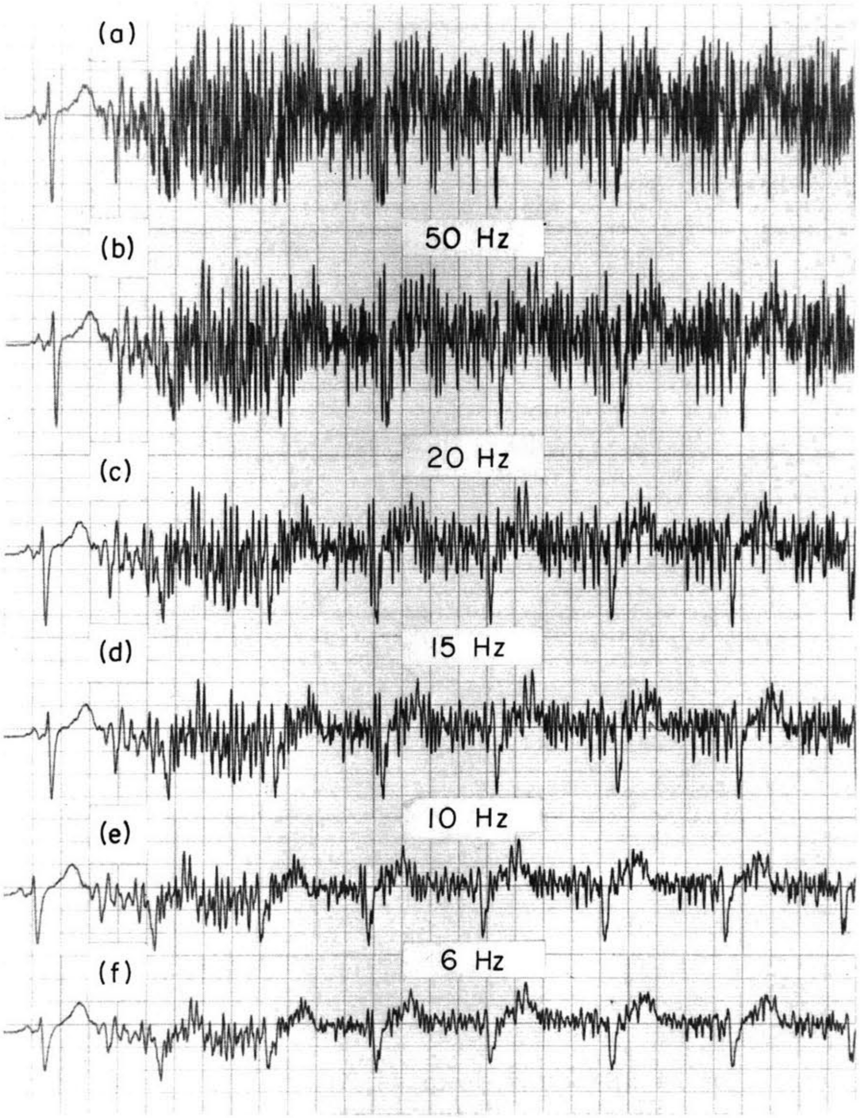

Fig. XXIII-7. Effects of 6 dB/octave lowpass filtering of an excessively noisy EKG. The record illustrated in (a), which is the same segment of W_2 illustrated in Fig. XXIII-5b, was filtered at 5 different cutoff frequencies using a 6 dB/octave lowpass filter. The results are shown in (b) through (f). All traces can be aligned properly by using the first QRS wave of each trace as a time origin.

(a) W_2 (EKG obscured by excessive muscle noise); 200 ms/div.

(b) W_2 filtered at 50 Hz.

(c) W_2 filtered at 20 Hz.

(d) W_2 filtered at 15 Hz.

(e) W_2 filtered at 10 Hz.

(f) W_2 filtered at 6 Hz.

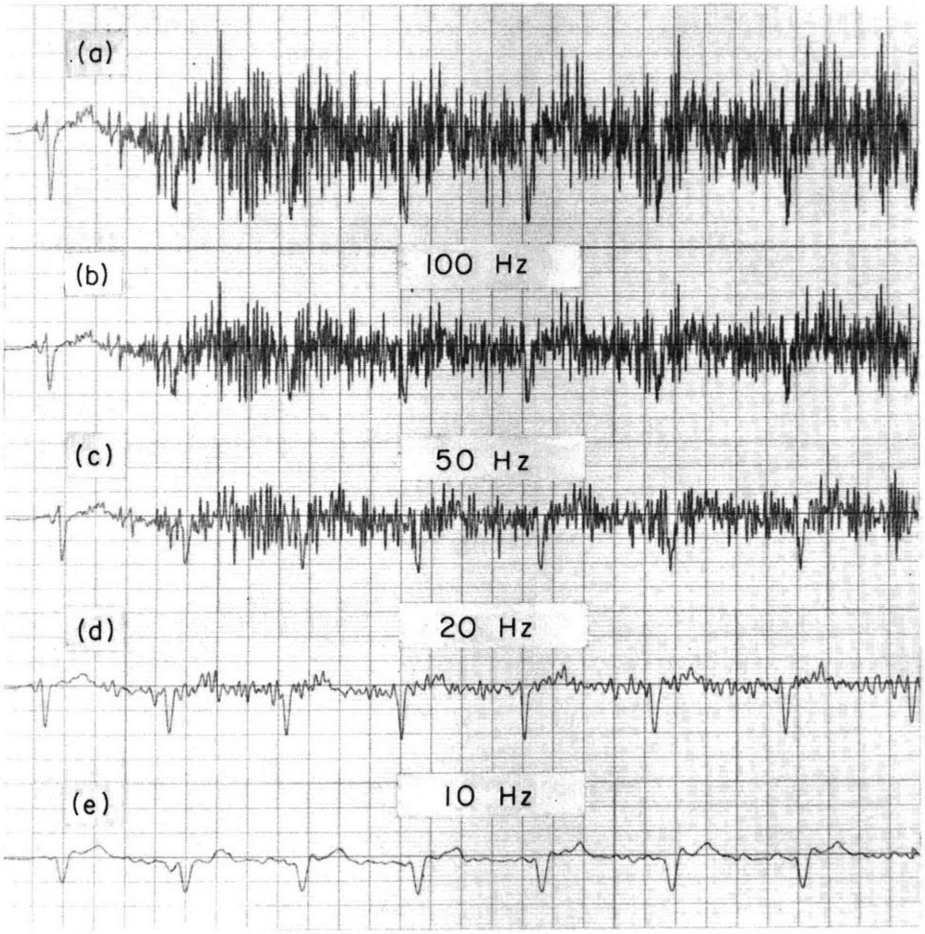

Fig. XXIII-8. Effects of 24 dB/octave lowpass filtering of an excessively noisy EKG. The record illustrated in (a), which is the same segment of W_1 illustrated in Fig. XXIII-5a, was filtered at 4 cutoff frequencies using a 24 dB/octave lowpass filter. The results are illustrated in (b) through (e). All traces can be aligned properly by using the first QRS wave of each trace as a time origin.
(a) W_1 (EKG obscured by muscle noise); 200 ms/div.
(b) W_1 filtered at 100 Hz.
(c) W_1 filtered at 50 Hz.
(d) W_1 filtered at 20 Hz.
(e) W_1 filtered at 10 Hz.

various cutoff frequencies. Although 6 dB/octave filtering (Fig. XXIII-7) is inadequate for producing a triggering signal, the results of 24 dB/octave lowpass filtering with a 20-Hz cutoff frequency (Fig. XXIII-8d) indicate that this technique will allow reliable detection of the QRS in the presence of excessive muscle noise.

In order to generalize these results, a more thorough investigation should be made to determine the optimal rolloff rate and cutoff frequency for use over a wide range of subjects and EKG leads.

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C. ANTIDROMIC AND ORTHODROMIC STIMULATION OF NEURONS RECEIVING CALYCES OF HELD

In certain parts of the auditory system where there are cells receiving very large presynaptic endings, all-or-none wave shapes picked up by an extracellular electrode are distinctly different from those found elsewhere.[1-3] Typically these wave shapes consist of an initial component that is usually positive (the P-component), followed roughly 0.4 ms later by another component that is often mostly negative (the N-component). (See Fig. XXIII-9.)

Evidence has been presented indicating that the P-component is due to the firing of the large presynaptic ending and the N-component is due to the firing of its postsynaptic cell.[1,2] We have attempted to test this hypothesis for neurons in the cat's medial nucleus of the trapezoid body (MNTB). These neurons receive very large presynaptic endings called calyces of Held.[4,5] If the hypothesis is true, then the N-component should be excitable antidromically and the P-component should not be (electronmicroscopy of these junctions indicates that their anatomy is typical of a chemical synapse[6,7]).

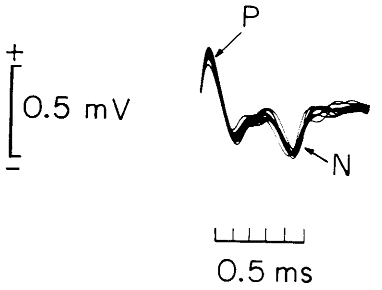

Fig. XXIII-9. Superimposed traces of all-or-none spike potentials recorded extracellularly in the medial nucleus of the trapezoid body.

Figure XXIII-10 is a schematic diagram of our stimulating and recording arrangement. The electrodes and the stimulus and recording apparatus have been described elsewhere.[8] In order to accurately control the time of occurrence of the orthodromic response, we found it convenient to orthodromically excite the neurons to be studied by means of electrical stimuli applied to the contralateral trapezoid body. Anatomical data indicate that the axons giving rise to the calyces of Held pass through this region[9,10] (see Fig. XXIII-10). If a unit responded to orthodromic electrical stimulation it also responded to acoustic stimulation with the same wave shape whenever we tested for this response.

We attempted to antidromically stimulate these neurons by means of an electrode in various parts of the brainstem auditory system and were successful when the electrode was in or near the lateral superior olive as shown in Fig. XXIII-10, and, in one case, near the dorso-medial periolivary nucleus. Anatomical studies have indicated that MNTB neurons send axons to both of these places.[5,11]

Both the antidromic response and the P-component of the orthodromic response of these neurons were elicited by stimuli above distinct thresholds, had very short latencies, usually 0.1-0.3 ms, (Figs. XXIII-11, XXIII-12, and XXIII-13), and responded after every stimulus for stimuli with repetition rates of several hundred per second. On the basis of these tests we conclude that our electrodes directly stimulated the neurons that produced the antidromic response, and the P-component of the orthodromic response; that is, there were no intervening synapses between the point of stimulation and the point at which the response was recorded.

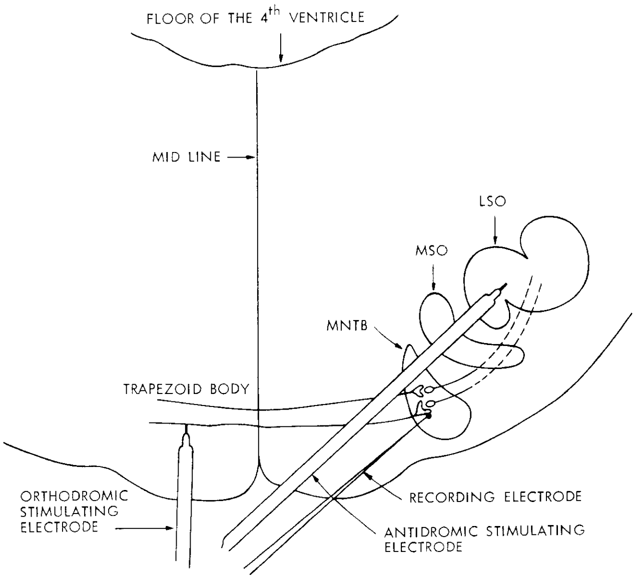

Fig. XXIII-10. Schematic transverse section through the brainstem of a cat showing the approximate locations of our electrodes. Two cells receiving calyces of Held are shown in the MNTB. Dotted lines indicate the presumed course of axons from neurons receiving calyces of Held.

MNTB = medial nucleus of the trapezoid body.
MSO = medial superior olivary nucleus.
LSO = lateral superior olivary nucleus.

The antidromic response and the N-component of the orthodromic response had similar wave shapes in a given neuron but the antidromic response in almost all cases lasted longer and was larger in amplitude than the N-component of the orthodromic response (Figs. XXIII-11, XXIII-12, and XXIII-13). Because of this, we deemed it necessary to show that they were indeed responses from the same neuron. We did this by showing that when one occurred the other did not occur for a short period of time because the neuron was refractory.

Figure XXIII-11 shows a demonstration of this from one neuron. The electrical stimuli were set to be near threshold so that a response did not appear every time. Although neither response appeared following 77 stimulus pairs, in none of the 439 total trials did both appear (in 218 only the orthodromic response was present, and in 144 only the antidromic response was present). These statistics indicate that there is an interaction taking place so that when the orthodromic response is present, the antidromic response is not. We have data similar to this from 11 different neurons.

Figure XXIII-12 shows data from an experiment in which the interval, T,

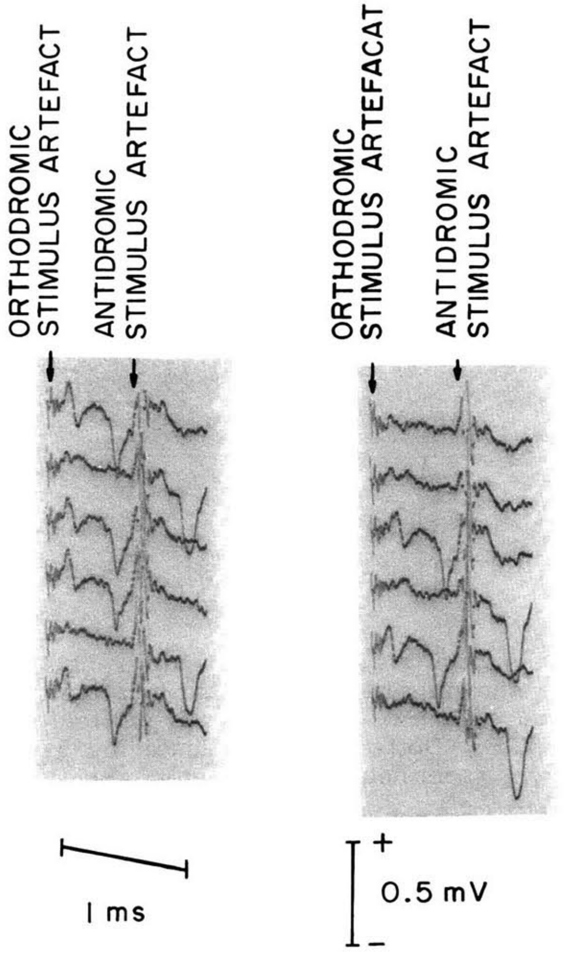

Fig. XXIII-11. Sequential traces each showing the response to an orthodromic electrical stimulation followed by an antidromic electrical stimulation. Time axes are skewed because the traces were recorded on moving film. Time interval between successive traces in a sequence is 2.5 ms. Sequences of 6 pairs of stimuli were presented at the rate of 4/sec.

between the orthodromic stimulus and the antidromic stimulus, has been varied. The orthodromic stimulus level was set so that an orthodromic response was produced in almost every trial and the antidromic stimulus level was set so that an antidromic response was produced in every trial (in the absence of previous orthodromic stimuli). As can be seen from Fig. XXIII-12c when T was 0.9 ms (the interval between the N-component of the orthodromic response and the normal time of the occurrence of the antidromic response was approximately 0.5 ms) an antidromic response occurred only when there was no previous orthodromic response. For longer T there were antidromic responses on some traces,

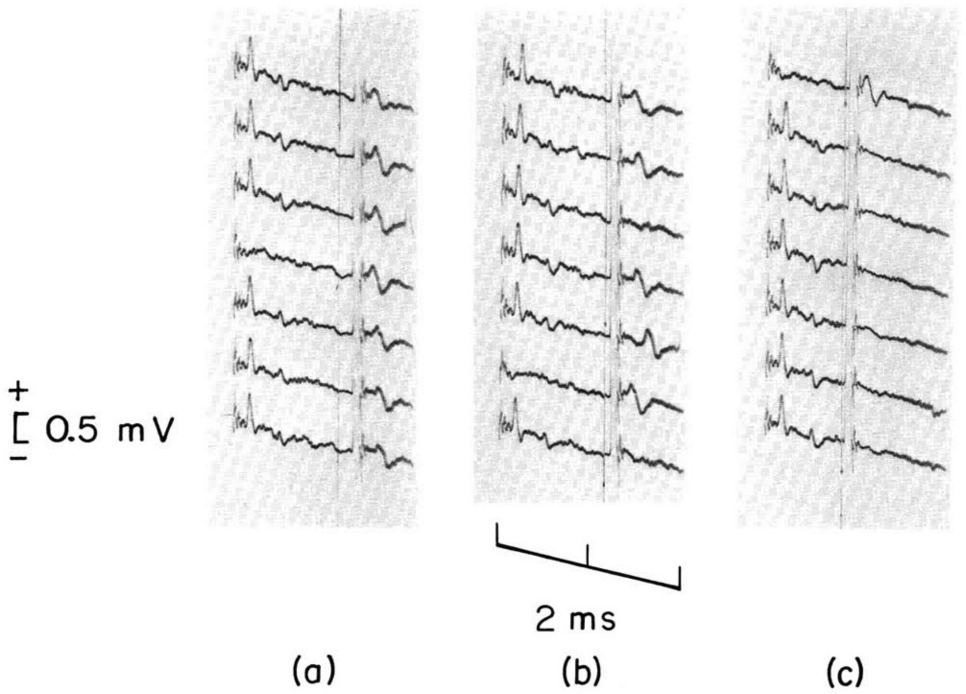

Fig. XXIII-12. Sequential traces each showing the response to an orthodromic electrical stimulation followed by an antidromic electrical stimulation. Time between the orthodromic stimulus and the antidromic stimulus has been successively shortened from (a) to (c). Time axes are skewed because the traces were recorded on moving film. Time interval between successive traces in a sequence is 2.5 ms. Sequences of 7 pairs of stimuli were presented at a rate of 4/sec.

and for T = 1.4 ms (Fig. XXIII-12a) the antidromic response occurred every time.

We have attempted to perform experiments similar to those shown in Fig. XXIII-11 and XXIII-12 with the stimulus timing set so that the antidromic response preceded the N-component of the orthodromic response. These experiments are difficult to interpret because the artifact from the orthodromic stimulus obscures the antidromic response. We have been able to obtain the desired type of data, however, by carefully examining recordings of experiments in which a neuron that had a high rate of spontaneous activity was antidromically stimulated (these spontaneous discharges had the same wave shapes as orthodromic electrical responses or sound-evoked responses, and we presume them to be orthodromic responses). We looked carefully at those cases in which a spontaneous orthodromic response occurred at various times relative to an antidromic response. A series of such cases is presented in Fig. XXIII-13. From them we see that the N-component of the spontaneous response did not occur whenever the antidromic response preceded the usual time of occurrence of the N-component

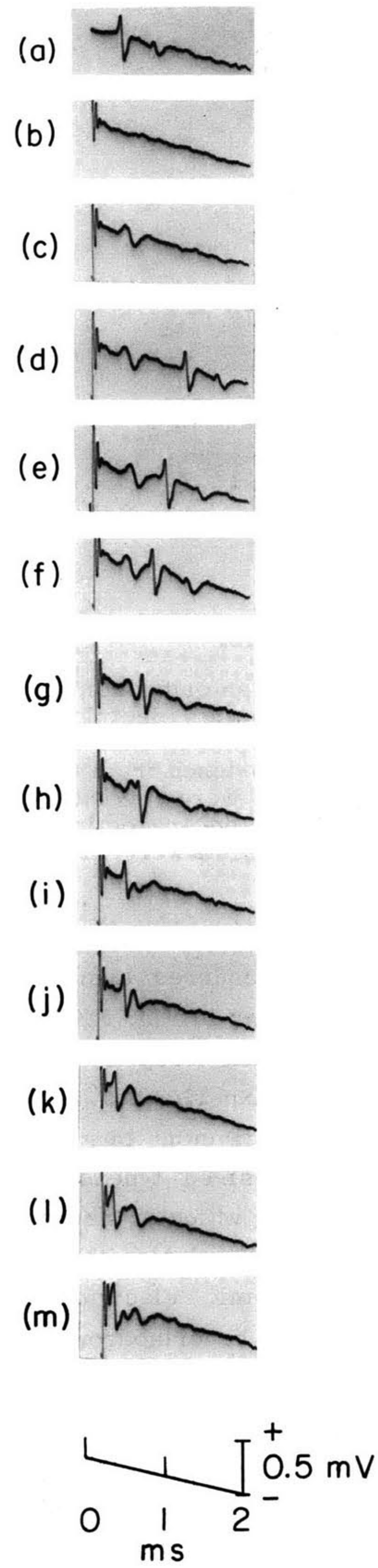

Fig. XXIII-13.

Trace (a) shows a spontaneous orthodromic discharge. Traces (b)-(m) show responses to near threshold antidromic stimulation. In trace (b) there is no antidromic response; in traces (c)-(m) there is an antidromic response in each record. In traces (d)-(m) there is also an orthodromic spontaneous discharge. Traces have been chosen and arranged to show the orthodromic spontaneous discharge at various times relative to the antidromic response. Time axes are skewed because the traces were recorded on moving film. Antidromic stimuli were presented in bursts of 12 stimuli with 4 ms between successive stimuli and at a repetition rate of 4/sec.

(relative to the P-component) by less than 0.3 or 0.4 ms.

We interpret these data as showing that the antidromic response and the N-component of the orthodromic response are from the same neuron. We have already concluded that the neurons producing the antidromic response and the P-component of the orthodromic response are being directly stimulated in our experiments. We conclude that the P and N components of the orthodromic response are due to different neurons because the antidromic response is not followed by a P-component, or any even crudely similar response, and in an orthodromic response the N-component follows the P-component in a time that is never less than ~0.4 ms. Furthermore, since the N-component follows the P-component, and the time between them is reasonable for a synaptic delay,[7] we conclude that the N-component is a postsynaptic response, and the P-component is a presynaptic response. This shows that what we have been calling the antidromic response is indeed an antidromic response.

Since the P-component is due to a presynaptic event that is picked up by an extracellular electrode, and is only seen in regions where there are large presynaptic endings,[1-3] we conclude that it is due to a large presynaptic ending. Since the only large presynaptic endings in the MNTB are the calyces of Held,[5] we conclude that the P-components are due to calyces of Held, and the N-components are due to the cells on which they synapse. This confirms the hypothesis that we set out to test.

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