

## XIX. COMMUNICATIONS BIOPHYSICS

### A. Signal Transmission in the Auditory System

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### RESEARCH OBJECTIVES AND SUMMARY OF RESEARCH

National Institutes of Health (Grants 5 PO1 GM14940-07 and 1 RO1 NS11000-01)

W. T. Peake, T. F. Weiss

Research aimed at understanding the reception and processing of acoustic signals by the auditory system has continued in the Eaton-Peabody Laboratory, which is operated jointly by M. I. T. and the Massachusetts Eye and Ear Infirmary. The Laboratory is operating in temporary quarters at M. I. T.; the move to the new building at the M. E. E. I., in Boston, is planned for sometime next year.

Our approach has been to make quantitative experimental measurements of responses at the various stages of the system and from these measurements to develop models that relate response variables to the input signals and to the underlying physiological mechanisms. Most of our experimental work has been carried out on cats, but we have used a species of lizard that has convenient and interesting anatomical features for studying inner-ear transduction mechanisms. We continue to concentrate our efforts on the more peripheral parts of the system, including the middle and inner ear, the auditory nerve, and the brainstem nuclei.

Although some of the general properties of signal transmission in the mechanical systems of the middle and inner ear are fairly well determined, the roles that the various anatomical components play in producing these properties are still poorly understood. For example, evidence indicates that the basilar membrane in the inner ear behaves as a mechanical frequency analyzer, but the mechanical properties of the basilar membrane have not been determined, and the forces that produce basilar membrane motion have never been measured. V. Nedzelnitsky is now completing a doctoral thesis<sup>1</sup> in which he measured sound pressure in the basal end of the cochlea of anesthetized cats. His measurements demonstrate that over a wide range of frequencies and sound-pressure levels the sound pressures in the fluid in scala vestibuli and scala tympani are linearly related to sound pressure at the tympanic membrane. The magnitude of the sound pressure in scala vestibuli exceeds that in scala tympani by at least 15 dB from approximately 100 Hz to at least 5,000 Hz (Fig. XIX-1). Consequently, the pressure difference across the cochlear partition, which produces the motion of the sensory organ, is approximately equal to the sound pressure in scala vestibuli. This pressure can exceed the pressure at the tympanic membrane by as much as 30 dB, thereby indicating that the middle ear provides pressure gain at some frequencies. T. J. Lynch is now beginning experiments to determine the components of the input impedance of the cochlea, by delivering the sound stimulus

(XIX. COMMUNICATIONS BIOPHYSICS)

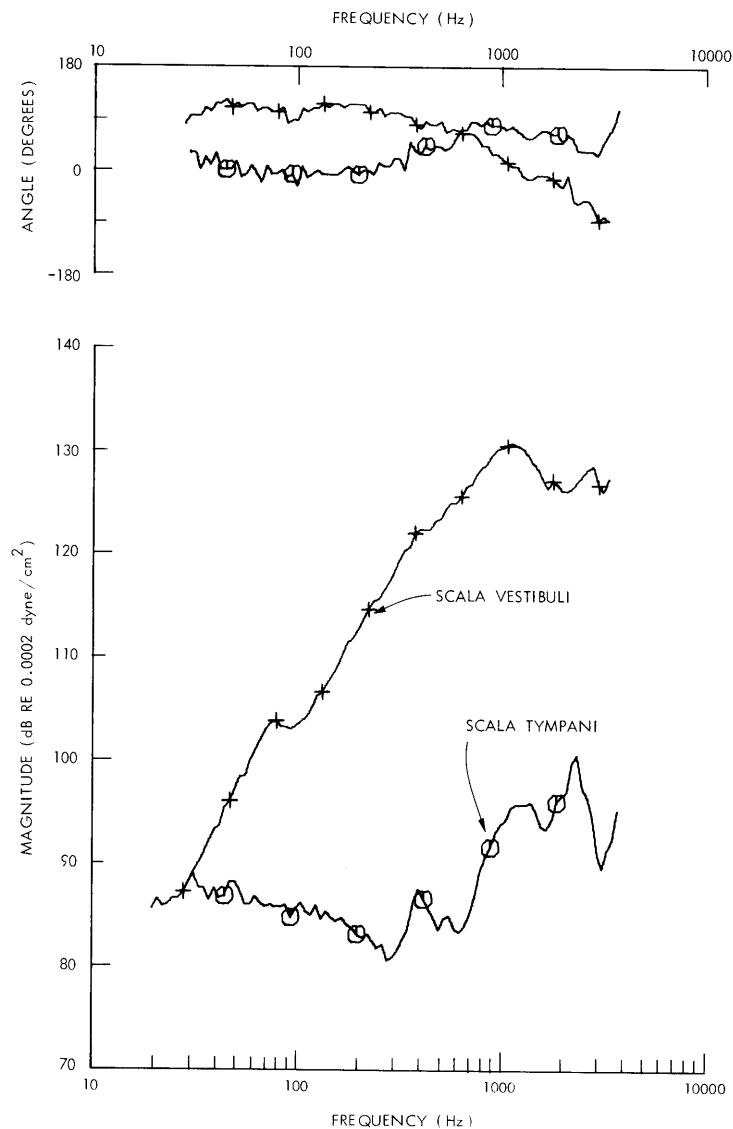


Fig. XIX-1. Sound pressures measured in scala vestibuli and scala tympani of the basal turn of a cat cochlea in response to tones at a sound pressure of 105 dB re .0002 dyn/cm<sup>2</sup> at the tympanic membrane. Phase angle is expressed relative to that of the sound pressure at the tympanic membrane; a negative phase indicates phase lag. Symbols on curves are for identification only and do not indicate data points, which were evenly spaced on the logarithmic scale with 40 points/decade.

directly to the oval window and measuring stapes velocity with the Mössbauer method. Sound pressure will be measured in the air outside the stapes footplate and in the inner ear fluid on the medial side of the footplate.

The hair cells of the cochlea are the receptor cells for hearing. They are stimulated mechanically and, in turn, they stimulate the endings of auditory-nerve fibers. The

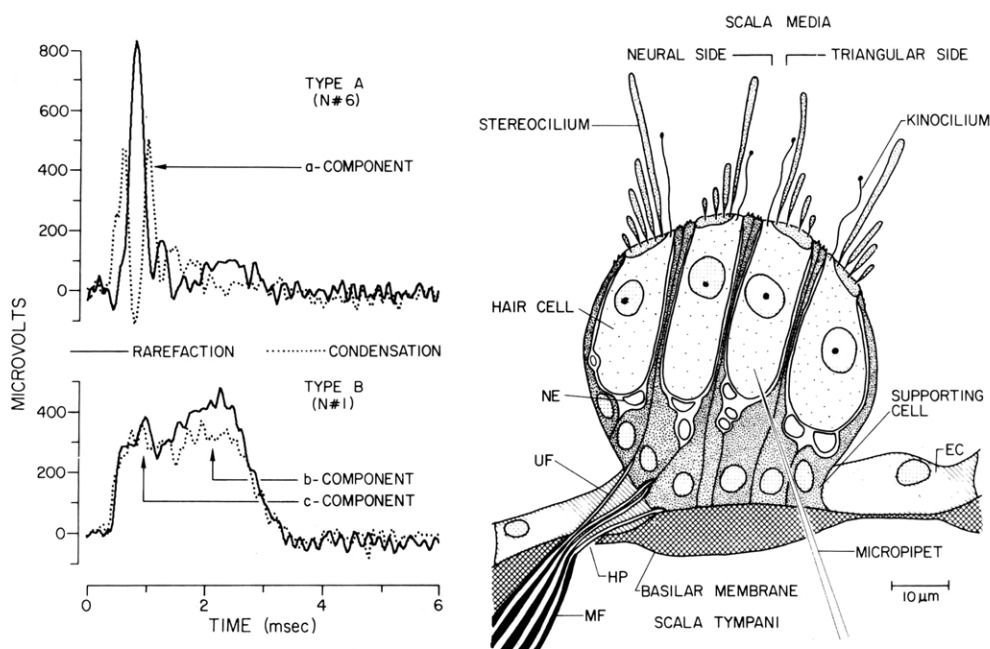


Fig. XIX-2. The right side shows a drawing of a transverse section through the papilla. The tip of a micropipet is shown schematically in a hair cell. EC, hyaline epithelial cells; HP, habenula perforata; MF, myelinated portion of a nerve fiber; NE, nerve ending; UF, unmyelinated nerve fiber. The left side shows averaged electric responses to acoustic clicks (both condensation and rarefaction polarities) recorded in two cells. As the micropipet was advanced into the papilla the lower (type B) responses were recorded in the first cell (N#1). After advancing the micropipet deeper into the papilla, the upper (type A) responses were recorded (N#6). After recording the click response in N#6, dye was ejected from the micropipet and found in a single hair cell. Averaged responses to clicks (with a 40/s repetition rate and a peak pressure of roughly 100 dB SPL) were computed from approximately 1000 individual responses sampled at 40- $\mu$ s intervals.

processes by which these specialized cells carry out this transducer action are not understood. Because mechanical stimulation of hair cells produces an electric response, it has been postulated that the electrical properties of these cells play a role in the transducer action. Previous attempts to record intracellular electric responses in the cochlea have produced few results. We have now been able to measure intracellular electrical responses from individual hair cells and supporting cells with micropipets in the basilar (auditory) papilla of the inner ear of the alligator lizard. Quantitative results have been obtained for continuous tones, tone bursts, and acoustic-click stimuli. The recording site has been inferred by injecting dye from the recording pipet, and locating the dye in single cells in the papilla. Some preliminary results<sup>2</sup> have been presented and others<sup>3</sup> will be published. Our principal findings are that electrical responses to sound occur in both hair cells and supporting cells, response waveforms to clicks are different in these two cell types (see Fig. XIX-2), and intracellular response characteristics reflect frequency selectivity in the papilla of the lizard and are related to hair-cell morphology. Our results also suggest that these intracellular

(XIX. COMMUNICATIONS BIOPHYSICS)

potentials may be sources of such extracellular potentials as cochlear microphonic and summing potentials, neighboring hair cells and supporting cells may be electrically coupled, and intracellular potentials in hair cells may be a causal step in the generation of action potentials in auditory-nerve fibers. We have suggested<sup>3</sup> a model of the transduction process in hair cells.

Although extensive measurements have been made of response characteristics of single auditory-nerve fibers, most of these records have been obtained from the central end of these fibers where they leave the ear and enter the brain. The nature of the responses at more peripheral locations has been a matter of speculation. During his stay with our group as a postdoctoral fellow, L. U. E. Kohllöffel was successful in recording single-unit responses from the region of the spiral ganglion. Kohllöffel is now at the Physiological Institute of the University of Erlangen, West Germany, and his results are being prepared for publication. Recording of action potentials in the alligator lizard has also been carried out in the more peripheral parts of primary auditory neurons. Electric stimulation has been used as a method of exciting auditory-nerve fibers, a method which bypasses the receptor mechanisms. E. C. Moxon has demonstrated that electric stimulation of the cochlea can produce auditory-nerve fiber responses resulting from a mechanical response in the cochlea, as well as from direct electric stimulation of the nerve.<sup>4</sup>

Work on the coding of acoustic stimuli into action potential patterns in auditory-nerve fibers has been concentrated on responses to more complex stimuli. D. H. Johnson has been seeking a quantitative description of response patterns in response to two-tone stimuli. Responses to speech sounds have also been recorded; Kiang and Moxon<sup>5</sup> have discussed possible implications for speech coding in normal and pathological ears.

The recording of electric responses of the auditory nerve in humans has been demonstrated by many groups in the past several years; this technique is of interest as a possible clinical diagnostic procedure. Dr. P. B. Montandon of the Massachusetts Eye and Ear Infirmary has been investigating this technique with the assistance of N. T. Shepard, using instruments (an acoustic stimulator and an electronic averager) which were designed by N. D. Megill. The problem of interpreting the measurements of action potentials in patients in terms of the location and nature of the pathology is quite complicated. No adequate model exists for relating the potentials recorded (with a large electrode) at a distance from the nerve to the responses of single nerve fibers recorded with micropipets. One aspect of this problem is concerned with the spatial distribution of the potentials. N. D. Megill is pursuing experiments in cats to determine the conduction pathways by which potentials spread from the inside of the cochlea to other locations. The question of how these potentials are changed by experimental procedures (e. g., ototoxic drugs) and by naturally occurring abnormalities is being studied in cat cochlea by M. C. Liberman. This work should help to define the diagnostic possibilities of such recordings in humans.

We continue our efforts to relate response characteristics of single nerve cells in the brain stem to cell and synapse morphology. Three papers concerned with the posteroventral and dorsal cochlear nuclei are nearly completed. T. R. Bourk is working on cells in the anterior ventral cochlear nucleus. A Master's thesis by Paul Hochfeld<sup>6</sup> demonstrated that some cells in the cochlear nucleus respond to stimuli to both ears, and that a substantial fraction of this group is located in the fusiform-cell layer in the dorsal cochlear nucleus.

J. J. Guinan is now spending a second year in the Department of Biophysics, University College, London. He will return during the coming year to continue his work on the central nervous system. J. C. Adams, a postdoctoral fellow, has started work with both anatomical and physiological techniques on the dorsal acoustic stria, one of the pathways connecting the cochlear nucleus with other nuclei.

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## XIX. COMMUNICATIONS BIOPHYSICS

### B. Auditory Psychophysics

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### RESEARCH OBJECTIVES AND SUMMARY OF RESEARCH

#### 1. Intensity Perception and Loudness

National Institutes of Health (Grant 5 PO1 GM14940-07)

L. D. Braida, N. I. Durlach

This research is oriented toward the creation of a coherent, quantitative, and unified theory of intensity perception and loudness, and involves the construction and integration of models of decision making, sensory processes, short-term memory, and perceptual context effects, as well as extensive psychophysical experimentation.<sup>1-4</sup> Aside from providing greater insight into basic phenomena of intensity perception and loudness, we expect the results of this work to be of value in the study of equivalent problems involving other stimulus dimensions and subjective attributes (and other senses), in the study of memory processes involving more complex stimuli or more complex tasks, and in various applications (such as the evaluation of annoyance in the study of noise pollution and the interpretation of abnormal intensity perception and loudness in subjects with hearing impairments).

During the past year, we have completed an experiment to determine the effects of variations in the payoff matrix on resolution and bias in the absolute identification of sound intensity. The results indicate that resolution is left unchanged by such variations, and that the variations in bias are roughly the same as those that would occur with an ideal receiver.<sup>5</sup> We have also completed an extensive series of experiments on roving-level discrimination and absolute identification designed to explore the dependence of resolution and bias on the position of stimulus intensity within the range of intensities to which the listener must attend in the experiment (the resolution and bias "edge effects"). Also, a new model has been developed for context-coding based on the notion of perceptual anchors and subjective "distance" measurements between the intensity to be coded and the anchors. This model, which assumes that the extremes of the stimulus range constitute natural anchors, has been found to be roughly consistent with the resolution edge effect in both roving-level discrimination and absolute identification, and with the effect on resolution of presenting an objective anchor in absolute identification.<sup>6</sup>

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## 2. Binaural Interaction

National Institutes of Health (Grant 5 PO1 GM14940-07)

H. S. Colburn, N. I. Durlach

The objective of this research is to obtain a unified quantitative theory of binaural interaction that is applicable to a wide variety of binaural phenomena and is consistent with neurophysiological data on the auditory system. Binaural interaction is an important topic for study because it is of great functional significance (playing an important role in both detection and localization), provides the auditory scientist with a powerful tool for exploring various properties of both normal and impaired auditory systems, and, despite the large amount of attention it has received, is still not well understood.

During the past year, we have completed an experiment on the ability to discriminate interaural time delay for tone complexes whose frequency spectrum lies well above the critical frequency (1500 Hz) at which the auditory system is insensitive to delay for simple tones. This experiment was conducted in order to determine the extent to which the sensitivity to delay that has been observed previously for high-frequency signals of significant bandwidth is based on the use of envelope information transmitted on high-frequency fibers in the auditory nerve or of carrier information transmitted on low-frequency fibers resulting from combination tones generated within the ear. The results of this experiment, which employed low-frequency noise to mask the combination tones, indicate that the former hypothesis is correct.<sup>1</sup>

In addition to this experimental work, significant progress has been made in the preparation of previous results for publication,<sup>2-6</sup> and in the initiation of new research. One of the new projects is directed toward a more rigorous examination of the relation between interaural sensitivity and the subjective attributes of the binaural image space. A second project is concerned with evaluating the extent to which the asymmetry in the function describing the dependence of interaural time sensitivity on interaural time that occurs when an interaural amplitude difference exists and when the stimulus is a low-frequency tone<sup>2</sup> also occurs when the stimulus is a click. At present, this asymmetry constitutes a fundamental problem for all theories of binaural interaction.<sup>6</sup>

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(XIX. COMMUNICATIONS BIOPHYSICS)

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3. Hearing Aids

National Institutes of Health (Grant 5 PO1 GM14940-07)

Clarence J. LeBel Fund

L. D. Braida, H. S. Colburn, N. I. Durlach, C. L. Searle

The goal of this program is to develop improved signal-processing schemes to compensate for nonconductive hearing losses.

During the past year, we have outlined a program involving the development and use of a new master hearing aid facility. The facility will be highly flexible and capable of providing a much wider variety of signal transformations than is available in present hearing aids or than has been explored by other "master aids." The facility will be used to study the perceptual manifestations of impairments, to determine signal transformations appropriate for particular impairments, to train impaired listeners in the use of specific transformations, to simulate currently available aids, and to mimic the perceptual effects of impairments for listeners with normal hearing. In order to combine the advantages of a laboratory facility with those of a wearable aid, the system will make use of a wearable array of microphones and earphones, a computer controlled signal-processing facility, and a radio link to transmit the signals received by the microphones to the signal-processing equipment and the processed signals back to the earphones. The computer will be able to alter the processing performed on signals in real time on the basis of the characteristics of the signals, the responses of the listeners in psychophysical tests, and control commands issued by the experimenter and the user of the aid. The processing will be oriented toward improved control of angular directivity patterns and improved matching of speech signals to residual auditory function. The directivity processing will make use of phased-array antenna techniques, be adaptive, and be capable of providing a number of different patterns simultaneously. The signal that results from this directivity processing will be analyzed into short-term spectral components, and these components will be transformed and resynthesized for transmission to listeners. The transformation elements will include linear filtering, time delays, amplitude compression, and frequency compression.



4. Localization and Signal Separation

Clarence J. LeBel Fund

C. L. Searle

We are pursuing two main areas of research in signal separation:

1. What cues and signal-processing methods are used by humans to localize sound in the vertical median plane?

2. What signal processing is needed to imitate the signal-separation accomplished by humans in recognizing one musical instrument or one voice among many?

Physical measurements of pinna frequency response have been made and are now being processed by computer. These measurements must then be correlated with psychophysical measurements to complete our research on vertical localization. To imitate the recognition task, we must complete a hardware-software system for independently processing signals in 10 or more  $1/3$  octave audio channels.

## XIX. COMMUNICATIONS BIOPHYSICS

### C. Aural Combination Tones: Pure and Applied

#### Academic Research Staff

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#### RESEARCH OBJECTIVES AND SUMMARY OF RESEARCH

National Institutes of Health (Grant 1 RO1 NS10737-01)

J. L. Goldstein, W. T. Peake, W. M. Rabinowitz

A quantitative theory was formulated for the determination of the pitch of complex tones in psychophysical measurements with human subjects. This work has been accepted for publication.<sup>1</sup> In September 1973, Professor Goldstein went to Israel to become a member of the Engineering Faculty at Tel Aviv University.

An experimental study is under way in which psychophysical measurements of combination tones will be combined with measurements of acoustic input impedance of the human middle ear. Both kinds of measurement will be used to assess the changes in middle-ear transmission that result from contractions of middle-ear muscles (the acoustic reflex) and from static air-pressure differences across the tympanic membrane. Preliminary results obtained with the combination tone method have been presented.<sup>2</sup> This method allows determination of changes in middle-ear transmission based entirely on measurements of the sound-pressure levels necessary for generating and cancelling the combination tone sensation. A system for measuring acoustic impedance is now being developed so that the two measures can be combined to give a more complete description of the effects of the acoustic reflex and static pressure differences.

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## XIX. COMMUNICATIONS BIOPHYSICS

### D. Transduction Mechanisms in Lateral Line Organs

#### Academic Research Staff

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Prof. C. M. Oman

#### RESEARCH OBJECTIVES AND SUMMARY OF RESEARCH

National Institutes of Health (Grant 5 PO1 GM14940-07)

L. S. Frishkopf, C. M. Oman

##### 1. Research Objectives

The lateral line system is closely related morphologically, embryologically, and phylogenetically to the auditory and vestibular systems. Because of their similar structure and common origin, these organs are sometimes collectively referred to as the acoustico-lateralis system. The goal of our research is to add to our understanding of transduction mechanisms in sensory hair cells of the acoustico-lateralis organs through physiological and anatomical studies of free-standing lateral line neuromasts. We propose to study the specific mechanisms associated with mechanoelectric transduction and afferent impulse generation in these organs. Specifically, we propose to investigate the dynamic relationships between water flow field, cupula motion, intracellular events, such as receptor potential and membrane conductance changes, synaptic processes, and afferent nerve activity. We also propose to test directly in these organs the postulated relationship between the morphological orientation and directional sensitivity of hair cells. We plan to develop methods to permit more precise control of cupula displacement. Established electrode techniques will be employed in recording from and staining hair cells intracellularly and in recording nerve impulse activity. Conductance changes will be determined by standard bridge circuitry or by voltage-clamp methods. Synaptic activation in the absence of mechanical stimulation will be produced by galvanic current. We propose to control stimuli, analyze receptor potentials, and reduce nerve spike data by means of a small on-line computer. We anticipate that information regarding transduction mechanisms obtained from the study of this relatively simple and accessible organ will also aid us in understanding these processes in the auditory and vestibular organs.

##### 2. Summary of Research

#### Hair-Cell Receptor Potentials

Present theories of hair-cell transduction attempt to relate the morphological orientation of the hair cells to the externally recorded potential changes and the neural activity observed in response to stimulation.<sup>1</sup> A consistent interpretation has been outlined which adequately accounts for data obtained from lateral line, vestibular, and auditory organs in a variety of vertebrate species. This interpretation is based, however, on two assumptions: First, that a hair-cell membrane potential change (receptor potential) at the stimulus frequency underlies the observed microphonic responses; second, that hair cells of opposite orientation respond in opposite phase. It is clearly important to a unified theory of hair-cell operation that these assumptions be validated.

Our recent studies involving intracellular recording from hair cells in free-standing

## (XIX. COMMUNICATIONS BIOPHYSICS)

lateral line neuromasts of Necturus<sup>2</sup> and studies in canal neuromasts of Lota<sup>3</sup> have directly demonstrated the occurrence of receptor potentials that are consistent with the known morphological orientation of hair cells in these organs. In both species intracellular potentials that follow the stimulus in frequency are found. By means of a dye injection technique, these potential changes have been shown to originate only in hair cells. Moreover, in cells of the same organ subject to the same stimulus conditions, responses of opposite phase have been found. We believe that such responses are from oppositely oriented hair cells, so that cupula displacements depolarizing cells of one orientation hyperpolarize neighboring cells that are oppositely oriented. Unfortunately, we have not been able to obtain direct histological evidence of the opposite morphology of these cells because of the difficulty of finding and following particular stained cells with the electron microscope. In Necturus, the responses of the hair cells and associated nerve fibers are rapidly abolished by application of 0.1% methylene blue, although the dc potential is unaffected. We have observed that methylene blue is taken up by the cupula; at the moment that the cupula becomes visible the response disappears, and subsequently the hair cells stain. As the dye disappears, first the receptor potential and then the nerve response returns. We take this as evidence that the potential has a physiological, rather than mechanical or other artifactual origin.

In summary, the observed responses are believed to be receptor potentials for three reasons: First, they are found only in hair cells; second, responses of opposite phase are found, in agreement with the known orientation properties of the hair cells; third, both hair-cell and nerve responses are rapidly and reversibly abolished by methylene blue.

We have identified this response as a receptor potential in the sense that it is a stimulus-related response of physiological origin found only in the hair cells. Thus far, however, there is no solid evidence that the response activates the synaptic mechanism postulated earlier by Davis.<sup>4</sup> At least, the sequence in which receptor potential and nerve response return following inactivation with methylene blue is consistent with such a function. If the nerve response returned first, the receptor potential could hardly play a causal role. One difficulty in ascribing such a role to the receptor potential is its small size. Maximum response amplitudes seen in hair cells of Necturus were  $\sim 0.8$  mV and in Lota, 1.5 mV. But as Flock<sup>3</sup> has pointed out, extremely small currents are required to excite electroreceptor organs (see Bennett<sup>5</sup>), a system closely related phylogenetically to the lateral line organs. Perhaps, therefore, the small size of the receptor potential is not inconsistent with a synaptic activating function.

### Cupula Structure and Dynamics

Our inability to specify accurately the stimulus proved to be a considerable weakness in studying receptor potentials and neural responses in Necturus. That is, although the motion of the driver was known, the phase and amplitude response of the cupula was not. In order to provide a more precise description of various stimulus situations, we found it useful to study the anatomy of the cupula and its dynamic behavior in response to flows produced by an oscillating sphere near the organ.<sup>6</sup> We found that the cupula consists of a central ribbon surrounded by a cylindrical gelatinous sheath. These two components appear distinct in their mechanical, morphological, and staining characteristics. They appear respectively to overlie hair-cell and supporting-cell regions. Cupula growth rate was measured as approximately 10  $\mu\text{m}/\text{hour}$ . Since the cupulae extend into the surrounding water, they are readily available for observation if they are made visible by staining or outlined by depositing ink particles. A stroboscopic technique was developed to observe directly amplitude and phase of cupula motion to sinusoidal stimulation. Measurements were obtained of phase vs frequency of the cupula, which seemed in reasonable

agreement with a theoretical model based on estimates of cupula inertia and damping and experimental measurements of cupula stiffness that were made with the use of a fiberglass microspring. The dynamics of cupula movement in response to relatively uniform motion of the water surrounding the organ appear to be those of an over-damped second-order system with respect to velocity. The time constants of the response were expected to be heavily influenced by cupula length. But the model only relates cupula motion to local water flow velocity, and does not account for the complex nature of the oscillating boundary layer that is present in experimental situations in which a sinusoidal stimulus is applied at some distance from the animal. Further theoretical and experimental work, including microscopic flow visualization studies, is required before the phase relationship between an oscillating ball driver and cupula motion can be accurately predicted.

### Afferent Response

One way to quantify the stimulus to a particular neuromast more exactly is to stimulate the cupula directly by mechanical means, thereby minimizing the effect of cupula hydrodynamics. Such a technique, however, introduces other possibilities for stimulus artifact which must be carefully evaluated.<sup>7, 8</sup> In recent experiments<sup>9</sup> in which cupulae of individual organs were directly stimulated with a very small wire hook, it was found that lateral line nerve afferents in the tail of Necturus were directionally sensitive, and appeared to respond in a manner proportional to cupula velocity. Instantaneous frequency averaged over periods of constant cupula velocity appeared to be a linear function of velocity in this Flaxedilized preparation. Subsequent experiments in an isolated tail preparation suggest a lead/lag describing function relating cupula position to afferent instantaneous frequency. Efferent activity was observed in the intact preparation, but did not appear to play an active role in rendering the organ sensitive to cupula velocity. Rate-sensitive units have been observed in other acoustico-lateralis systems (e. g. , Goldberg and Fernandez,<sup>10</sup> and Precht, Llinas, and Clarke<sup>11</sup>) but have not previously been reported in lateral line.

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(XIX. COMMUNICATIONS BIOPHYSICS)

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## XIX. COMMUNICATIONS BIOPHYSICS

### E. Models of Cochlear Mechanisms

#### Academic Research Staff

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### RESEARCH OBJECTIVES AND SUMMARY OF RESEARCH

National Institutes of Health (Grant 5 PO1 GM14940-07)

W. M. Siebert, J. L. Davis

The usual long-wave theories of cochlear mechanics lead to a second-order inhomogeneous differential equation that (except for a few special cases) must be solved numerically. Parameter values can be chosen so that the predicted performance agrees well with experimental studies in most respects. The predicted performance is, however, more sensitive to certain parameters – particularly the depth of the scalae – than the experimental evidence implies. The data also suggest that the basic long-wave assumption is at best marginally satisfied and only for a limited range of frequencies and locations.

Recently,<sup>1</sup> we have been studying a short-wave model similar to one proposed more than 20 years ago by O. Ranke.<sup>2</sup> This theory avoids some of the deficiencies of the long-wave models; moreover, since it leads to a first-order equation, the results can be given in virtually closed form. The predicted phase characteristics, however, deviate sharply from those observed.

There are two ways in which the deficiencies of these models can be accounted for. The simplest explanation assumes they are a consequence of mathematical approximations (i. e., the long- or short-wave assumption). The numerical method of Lesser and Berkley<sup>3</sup> avoids either of these assumptions and thus provides a way to check this explanation. Computer studies are now in progress. If, as we have reason to suspect is likely, these studies show that the effects of mathematical approximations cannot entirely account for the difficulties, then it will be necessary to investigate the validity of some of the physical assumptions on which virtually all existing theories are based.

#### References

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2. O. F. Ranke, "Theory of Operation of the Cochlea: A Contribution to the Hydrodynamics of the Cochlea," *J. Acoust. Soc. Am.* 22, 772-777 (1950).
3. M. B. Lesser and D. A. Berkley, "Fluid Mechanics of the Cochlea, Part 1," *J. Fluid Mech.* 51(3), 497-512 (1972).

## XIX. COMMUNICATIONS BIOPHYSICS

### F. Biomedical Engineering

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### RESEARCH OBJECTIVES AND SUMMARY OF RESEARCH

National Aeronautics and Space Administration (Grant NGL 22-009-304)

Boston City Hospital Purchase Order 1176-21335

B-D Electrodyne Division, Becton Dickinson and Company (Grant)

S. K. Burns, R. G. Mark

Our broad research objective is the application of electrical engineering technology to clinically significant problems. Our activities are carried out in laboratories at the Research Laboratory of Electronics, in Cambridge, and also at the Biomedical Engineering Division of the Thorndike Memorial Laboratory of Boston City Hospital, in Boston. The hospital laboratory represents a joint M.I.T.-Harvard Medical School endeavor, providing a viable base of operations within an active medical community.

Research projects fall into three areas: (i) electronic instrumentation for patient care and physiological research, (ii) development and application of minicomputer and microcomputer systems, and (iii) experimental telemedicine systems. A few representative ongoing projects are briefly outlined below.

#### 1. Instrumentation

a. Pulse Counter for Ambulatory Subjects. Some evidence suggests a relation between average (human) heart rate and the development of coronary artery disease. Average heart rate during normal daily activities is also related to the state of cardiovascular conditioning. The accurate recording of the number of heart beats in 24 hours would permit the testing of these hypotheses and could also prove a useful clinical device. A small battery-operated instrument has been developed to count the total number of pulses over any arbitrary period. It uses the EKG as input. When artifact or noise obscures the EKG, the device switches to an internal phase-locked loop to estimate pulse rate on the basis of the rate just prior to the noise period. Preliminary evaluation of the prototype appears very promising.

b. Telemetry System for Mouse EKG. An animal model for myocarditis is available in mice, who often die suddenly. It is felt that cardiac arrhythmia is the most likely cause of death. Long-term EKG monitoring from awake, unrestrained animals is required. A miniature low-power (5  $\mu$ A) EKG telemetry transmitter is under development which may be implanted in the animals and operate 6-8 months. Hybrid circuit techniques will be used to minimize size.



c. Optical EKG Reader. EKG and VCG data are usually recorded and often stored in the form of the chart recorder output. It is often desirable to enter such data in computers for analysis or display. A system is under development to scan the paper records optically and load them into the computer. The system will thus permit processing of data gathered with standard EKG equipment.

d. Transtelephonic Pacemaker Evaluation System. Both pacemaker impulse rate and EKG are necessary data to determine the functional status of implanted cardiac pacemakers. At least three different frontal leads are desirable to provide complete confidence. A transtelephonic EKG transmitter has been developed which incorporates automatic cycling through EKG leads I, II, and III and also signals the patient to apply his magnet to the pacer. The device has been proved in clinical trials and is ready for manufacture.

e. R-R Interval Histogram Display. In studying ambulatory patients with various cardiac arrhythmias, 12- or 24-hour portable EKG tape-recording systems are widely used. As an aid to the processing of these EKG tapes, a system has been developed which measures consecutive R-R intervals and displays the data in histogram format. In this way, rhythm data, spanning many hours, or even days, can be conveniently summarized.

## 2. Computer Applications

a. Load-Control System for Isolated Cardiac Muscle Experiments. An electromechanical system under the control of the NOVA Computer has been developed which permits simulation of physiologic loading for isolated cardiac muscle. In contrast to conventional loading techniques, where relaxation occurs at the same load as shortening, the new system allows isometric relaxation at peak shortening prior to isotonic relaxation at reduced load. The system can also present arbitrary nonphysiologic loading sequences, measure length and tension, and display the data.

b. Multiple Electrode Multiplexing and Display System. Investigation of the mechanisms of cardiac arrhythmia generation requires measurement of the temporal and spatial sequence of depolarization in the ventricle. Arrays of suction electrodes and intramural electrodes may be used to sample a number of points simultaneously. The NOVA computer system will function as the multiplexer and display system for the data.

c. Microprocessor Development. The availability of microprocessors such as the Intel 8008 makes the development of portable sophisticated physiologic data-processing devices feasible. For example, beat-by-beat EKG interpretation makes possible rather good arrhythmia detection that can be performed at the point of initial data collection (i.e., on the patient). We have completed feasibility studies and initial development of a portable computer system, capable of beat-to-beat analysis and storage of summarizing statistics. This system will be small enough that it may be carried on the patient's person over a 24-hour interval. When interrogated by another computer, this personal computer will provide statistics of significant events in the patient's EKG.

## 3. Telemedicine Systems

An experimental nursing-home "telemedicine" project is under way at Boston City Hospital to explore the advantages of providing medical care in nursing homes visited by geriatric nurse practitioners, with remote physician consultative support provided by telephone and facsimile equipment. It is hoped that such a system will allow nursing-home patients to receive close follow-up care in the nursing homes and eliminate risks, costs, and inconveniences of treating acute illnesses only in the hospital on an emergency basis.

(XIX. COMMUNICATIONS BIOPHYSICS)

A research program has begun that will attempt to develop a methodology for designing telemedicine systems for nursing homes throughout the country.

Questions to be addressed include:

- a. What patient load can be assigned to each nurse practitioner?
- b. How many consultant physicians are required to supervise a given number of nurse practitioners?
- c. What skills should nurse practitioners have?
- d. How can nursing-home patients be classified in terms of their medical needs?
- e. How can the mix of patient types alter workload assignments?
- f. What is the proper mix of communication and transportation facilities?
- g. What noneconomic performance measures are obtainable, reliable, and meaningful in a nursing-home context?

## XIX. COMMUNICATIONS BIOPHYSICS

### G. Neural Mechanisms of Eyelid Behavior

#### Academic and Research Staff

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### RESEARCH OBJECTIVES AND SUMMARY OF RESEARCH

National Institutes of Health (Grant 5 PO1 GM14940-07)

R. D. Hall

The long-term objective of this research is to contribute to the understanding of neural mechanisms of learning. Emphasis in our short-term research, however, is on more fundamental aspects of the behavior that we have chosen as a model for the study of conditioning, that is, eyelid responses in the rat.

Investigation of the corneal reflex has continued with further attempts to characterize cells in the brainstem of the rat that respond to stimulation of the cornea. Nagano<sup>1</sup> has found such cells in a region on the ventromedial border of the trigeminal nuclei extending from the principal sensory nucleus to the nucleus caudalis of the spinal complex. This region includes adjacent areas of the reticular formation, especially the lateral reticular nucleus. The cells in this region were in two groups that were distinguished mainly by their thresholds to tactile and electrical stimuli, cells in one group having low thresholds for both kinds of stimulation, cells in the other relatively high thresholds. The two types of cells were not found to be differentially distributed among the various nuclei of the trigeminal complex or reticular formation. A second and independent division of the same cells was possible on the basis of their minimum response latencies to electrical stimulation of the cornea. Cells in one group had minimum latencies of 5-8 ms, and a second distinctive group was characterized by minimum latencies of 9-12 ms. Representation of the cornea along the ventromedial border of the trigeminal nuclei has recently been confirmed by Myers.<sup>2</sup> Myers also found other cells responsive to corneal stimulation. These were widely scattered throughout the reticular formation, sufficiently distant from the reticular units in the trigeminal border region to be considered a separate population. The distinctions between high- and low-threshold units and between long- and short-latency units described by Nagano were also confirmed by Myers.

In a preliminary attempt to identify interneurons of the corneal reflex Myers also measured thresholds and latencies of eyelid muscle responses evoked by electrical stimulation at sites where units responsive to corneal stimulation were isolated. The unit's response to corneal stimulation was also compared with the reflexive response of the muscle to the same stimulus. Cells in one class, for the most part in the trigeminal border region, seemed to be good candidates for a role in the corneal reflex, having short-latency responses that often, though not always, preceded orbicularis oculi responses to corneal stimulation. Muscle responses with low thresholds ( $\leq 3 \mu\text{A}$ ) and short latencies ( $\leq 4 \text{ ms}$ ) were elicited by stimulation at the recording sites. Cells in another class, all in the reticular formation, responded too late to play a role in the corneal reflex, and eyelid responses evoked by electrical stimulation at these sites had relatively high thresholds and long latencies. But other cells had mixed properties,

## (XIX. COMMUNICATIONS BIOPHYSICS)

some suggesting involvement in the reflex while others did not. It will be our task in the months ahead to find additional or more decisive indices for the identification of units serving the corneal reflex, and to determine in what capacity they serve it.

In remapping somatosensory and motor areas of the rat's cerebral cortex, Hall and Lindholm<sup>3</sup> have noted a conspicuous absence of a corneal representation in the primary sensory area. Why the cornea should differ in this respect from other tissues with cutaneous sensibility is not clear, but a genuine difference of this kind would seem to have significance for theories of perception, as well as theories of conditioning. The search for a corneal representation in primary somatosensory cortex has continued with both single-unit and evoked-potential recording techniques, and the findings continue to be negative. A more extensive search is now in progress to determine whether stimulation of the cornea leads to responses anywhere in the rat's cerebral cortex.

During the past year we have searched for an eyelid reflex that does not have the disadvantages associated with the corneal reflex. We have sought a reflex whose afferent limb is in a peripheral nerve that is more accessible than the ciliary nerve which innervates the cornea. This would permit the use of electrical stimulation, which is relatively easy to control and to measure in both acute and chronic preparations. It might also allow us to monitor the input to the central nervous system, which has obvious advantages for the analysis of central activity leading to eyelid responses. Eyelid responses elicited by electrical stimulation of the infratrochlear nerve appear to be very nearly what we have been looking for. Preliminary data from a few animals have been most encouraging for two reasons: the reflex is much more readily conditioned in our laboratory than the corneal reflex, and the conditioned response appears to involve no other muscular activity than that of the eyelid. It remains to be seen whether stimulation of the nerve through implanted electrodes can be made simple and reliable and whether the evoked impulse traffic in the infratrochlear nerve can be monitored.

Another study was initiated this year to determine whether it is possible to condition responses of orbicularis oculi motoneurons in the curarized rat. Success in this venture would provide us with all of the advantages that an immobilized preparation offers for the study of conditioning at the neuronal level, mainly through the use of conventional stereotaxic apparatus for the placement of microelectrodes. In our initial attempts we have made use of permanently implanted electrodes in the facial nucleus, a procedure that has proved to be more difficult than we anticipated. Although conditioning experiments are now under way, it is too early to report success.

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2. J. A. Myers, "Single-Unit Activity in the Rat's Brainstem during the Corneal Reflex," S.M. Thesis, Department of Electrical Engineering, M.I.T., 1973.
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## XIX. COMMUNICATIONS BIOPHYSICS

### H. Musical Acoustics Research

#### Academic and Research Staff

Dr. A. J. M. Houtsma

#### RESEARCH OBJECTIVES AND SUMMARY OF RESEARCH

Chicago Musical Instrument Company (Grant)

A. J. M. Houtsma

The development of musical instruments through the ages has been a long process of trial, error, survival, and extinction, and even today the best and most expensive handmade instruments are usually more a product of traditional apprenticeship than an organized scientific approach. Our work, which is focused primarily on stringed instruments, is an attempt to develop a systematic procedure that matches the design of a stringed instrument with the usually unpredictable properties of the material of which it is made. Because scientific research in this area has not produced significant numbers of new superior instruments and, at the same time, is out of touch with traditional craftsmen, an educational effort is being undertaken to teach the acoustical approach and the artistic handcraft skills to a group of interested students with the hope of encouraging a new kind of instrument maker. Ignacio Garabieta, Technical Instructor in the Department of Architecture, M. I. T., is collaborating on this project.

