XX. COMMUNICATIONS BIOPHYSICS

A. Signal Transmission in the Auditory System

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RESEARCH OBJECTIVES AND SUMMARY OF RESEARCH

National Institutes of Health (Grants 1 RO1 NS10737-01, 1 RO1 NS10916-01 and 5 RO1 NS11000-02)

William M. Siebert, William T. Peake, Thomas F. Weiss

Research related to hearing has a long tradition in the Research Laboratory of Electronics. We shall report on those aspects of current projects that are concerned primarily with the physiological processes involved in the processing of acoustic signals in the ear and in the auditory nervous system. Our efforts have been concentrated on the more peripheral parts of the system from the middle ear to the brain stem nuclei.

Our physiological experiments are carried out in the Eaton-Peabody Laboratory which is operated jointly by M. I. T. and the Massachusetts Eye and Ear Infirmary. In August 1974 the laboratory moved from temporary quarters at M. I. T. to the new building at the Massachusetts Eye and Ear Infirmary, in Boston.

1. Middle Ear

The relation between acoustic input impedance and the transmission of sound through the human middle ear is the subject of the doctoral thesis research of W. M. Rabinowitz. He has developed a method of measuring the magnitude and angle of the input impedance as a function of frequency. A computer is used to control the stimulus tone and store the measurements so that they can be manipulated conveniently. A psychophysical method for measuring changes in middle-ear transmission had been developed previously. The goal now is to measure the changes in both of these characteristics which occur during an acoustic reflex (middle-ear muscle contractions) and static pressure changes. The results will extend our basic knowledge of the human middle ear and should provide a firmer basis for the interpretation of new diagnostic measurements now being obtained by "impedance audiometry" and "tympanometry."

The measurement of the load impedance of the middle ear, that is, the input impedance of the inner ear in the cat, is the topic of a Master's thesis[1] by T. J. Lynch III in which he measured the sound pressure on both sides of the stapes footplate and the velocity of the stapes. Current experiments are aimed at extending the range of some of these measurements. The result will be a description of the inner-ear input impedance in terms of two components, one resulting from the stapes and its ligament and the other from the cochlea.

2. Inner-Ear Mechanics

It is generally accepted that the mechanical properties of the cochlear partition play an important role in the frequency analysis performed by the inner ear. Recent analytical work by Siebert[2] points out important disagreements between experimental results and existing theories of cochlear mechanics, which indicate that further investigation of the mechanical properties is necessary. The sound pressure in the inner-ear fluids has been measured in the basal turn of cat cochlea by V. Nedzelnitsky,[3,4] who is now developing techniques to extend these measurements to higher turns of the cochlea, with support from the Research Fund of the American Otological Society.

3. Transduction in the Inner Ear

Inner-ear sensory processes are being studied in the lizard Gerrhonotus multicarinatus where it is possible to record electric responses of single hair cells and supporting cells. The anatomy of this organ has been studied by Mulroy[5] and the characteristics of the intracellular electric responses have been related with the anatomical cell type.[6,7] Responses have also been recorded from single auditory-nerve fibers[8] which indicate qualitatively different responses from the two ends of the organ. We are now developing microelectrode methods to allow intracellular recording for a longer time and measurement of basilar membrane motion using the Mössbauer effect.

4. Auditory Nerve

A Ph. D. thesis by D. H. Johnson[9] on the responses of single auditory-nerve fibers in the cat to single tones has been completed. Two measures of activity, synchrony and average discharge rate, are defined and applied to experimentally obtained data. A model generated to account for the responses to single tones is used to predict the synchronized responses of auditory-nerve fibers to two-tone stimuli (excluding combination tones).

A study of auditory-nerve responses in pathological ears by M. C. Liberman, E. C. Moxon, and N. Y. S. Kiang has been augmented by a cooperative arrangement with the Temporal Bone Laboratory at the Massachusetts Eye and Ear Infirmary. Thus far we have studied three cats injected with large doses of ototoxic drugs 1-3 years previously. Contrary to earlier findings in animals up to 6 months after the injections, there appears to be considerable loss in the number of nerve fibers that can be electrically excited. Temporal bone histology demonstrated an extensive loss of spiral ganglion cells. This result has implications for long-term cochlear implants. A few animals with surgical lesions in the cochlea have also been studied and the electrical responses were correlated with histological findings. Of interest also are some histopathological observations in animals whose thresholds to acoustic stimulation have dropped precipitously during acute experiments. In seven of these animals, five showed signs of "endolymphatic hydrops" and the other two showed collapse of Reissner's membrane.

The relationship between gross potentials and single-unit activity in the auditory nerve has been studied with a new method enabling the measurement of the average potential developed at the round window when a single neuron in the nerve discharges. The importance of this result is that theories that gross neural potentials are the summed action potentials of individual neurons may now be tested. A paper summarizing this work by Kiang, Moxon, and Kahn was presented at the First International Congress of Electrocochleography, New York, June 1974, and will be published in the symposium volume.

A method was developed to record extracellular potentials from spiral ganglion cell bodies. Although most of the results resembled those obtained by recording from the axons of the auditory nerve, there were a few differences that may be associated with local injury.[10]

5. Cochlear Nucleus

Two manuscripts on the posterior portions of the cochlear nucleus have been submitted for publication by Godfrey, Kiang, and Norris. A survey of single-unit responses from the anterior portions of the cochlear nucleus continues under T. R. Bourk and B. E. Norris. This study maps classified units onto a block model developed in a previous study (submitted for publication by Kiang, Godfrey, Norris, and Moxon) on the posterior regions of the cochlear nucleus. Some preliminary correlations between unit types and cell types can be made but it is still too early to ascertain the level of details for which conclusions can be drawn. Some studies using orthodromic and antidromic electric stimulation were initiated in order to verify hypotheses concerning the mechanisms that generate characteristic response patterns.

6. Dorsal and Intermediate Striae

An important output pathway for the posterior cochlear nucleus is the combined dorsal and intermediate striae. Dr. J. C. Adams studied the physiological responses recorded with microelectrodes in the striae and, in collaboration with W. B. Warr at Boston University Medical School, is using the horseradish peroxidase method to study the anatomical connections of the fibers in the striae. The findings indicate that the striae contain not only output fibers from the PVCN and DCN but also fibers that enter the cochlear nucleus from the VNLL and the periolivary nuclei of both sides, the contralateral cochlear nucleus, and possibly the cerebellum. A paper on this study was given at the Cajal Club, American Association of Anatomists, April 1974, and is being prepared for publication.

7. Auditory-Nerve Potentials

Two papers, entitled "Recording Auditory-Nerve Potentials as an Office Procedure"[11] and "Auditory-Nerve Potentials from the Ear Canals of Patients with Otologic Problems,"[12] were presented by P. B. Montandon and others at the Otoneurotology Meeting of the Triilogical Society in the Spring of 1974. Although the work on human subjects was entirely supported by a grant from the American Otological Society, the technical development of equipment and the animal work was done in the Eaton-Peabody Laboratory with private funds. Various members of the laboratory served in an advisory capacity on this project and participated in the preparation of manuscripts.

8. Middle-Ear Muscles

J. J. Guinan, Jr. is initiating work on the pathways involved in the acoustic reflex in the cat. His plans involve electrical stimulation combined with ablation of brain stem structures to determine which may be involved in acoustically evoked contractions of the tensor tympani and stapedius muscles.

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XX. 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 1 RO1 NS11153-01)

Louis D. Braida, Nathaniel I. Durlach, Jae S. Lim, Steven R. Purks, William M. Rabinowitz, Elliot Singer

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.[1-6] Aside from providing greater insight into basic phenomena of intensity perception and loudness, we expect the results 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 conducted further research on intensity resolution and begun to develop a general theory of loudness.

In one project we explored the matter of whether the deviations from Weber's law that are observed at high levels for low- and intermediate-frequency tones and have been ascribed to the presence of higher harmonics created within the auditory system[7] occur also for a tone of sufficiently high frequency (10 kHz) to ensure that the higher harmonics are inaudible.[8] The results of this study suggest that the deviations are reduced but not eliminated at higher frequencies.

In a second project we determined the ability of listeners to discriminate between two intensity ratios $r+\Delta r$ and $r-\Delta r$ as a function of the intensity ratio r.[9] The results of this experiment were roughly consistent with the function that is assumed in our perceptual-anchor model of context coding to describe the dependence of the accuracy with which the "distance" between a given intensity and a perceptual anchor is measured on the distance to be measured.[6]

In a third project we showed that the reduced response variability observed in identification experiments when the intensity presented in a given trial is the same (or close to) the intensity in the previous trial can be ascribed almost entirely to the effect of the previous trial on the placement of criteria rather than on sensitivity.[9] This result implies, among other things, that the listener does not use the previous trial as a simple anchor. If he did, sensitivity would be increased in the intensity region surrounding the intensity presented on the previous trial.

In a fourth project we explored the extent to which loudness matches obtained between a tone presented in quiet and the same tone presented in noise can be predicted from measurements of cumulative sensitivity in identification experiments with the same stimuli.[10] Although the identification results evidenced a dependence of the shape of the cumulative sensitivity function on the presence of noise that was not predicted by the theory of resolution, the masked and unmasked tone intensities required for equal loudness corresponded roughly, as expected, to equal values of cumulative sensitivity.

In a fifth project, we initiated a theoretical effort to extend our theory of resolution to a theory of equal-loudness matching that is applicable to a wide variety of situations (tone in quiet vs tone in noise, tone at one frequency vs tone at another frequency, tone in normal ear vs tone in recruiting ear, etc.) and is capable of predicting both points of subjective equality and response variability. Much of our work during the coming year will be directed to the development and evaluation of this theory.

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2. Binaural Hearing

National Institutes of Health (Grant 1 RO1 NS10916-01)

H. Steven Colburn, Robert H. Domnitz, Nathaniel I. Durlach,
Phillipe Esquissaud, Neil T. Shepard, William M. Siebert,
Richard M. Stern, Jr., Yvonne M. Walkowski

The objective of this research continues to be the development of 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.

During the past year we completed three sets of experiments and two theoretical studies of binaural interaction. The experimental work is directed toward a fundamental property of binaural interaction, the interaction of interaural time difference and interaural level difference.[1] In the first set of experiments[2] sensitivity to interaural time delay of click stimuli as a function of interaural time difference with interaural amplitude difference as a parameter was measured. Results show that 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[3] also occurs when the stimulus is a click. These results are important because this asymmetry is a fundamental problem for all theories of binaural interaction[4] and the peripheral effects of stimulus level on the latency of responses are different for the two types of stimuli. In the second set of experiments, which is part of the doctoral thesis research of R. H. Domnitz, low-frequency tonal stimuli were used and the relation between the sensitivity to interaural differences and the subjective attributes of the binaural image space was examined. A common set of subjects was used for experiments on subjective image position matching, interaural time discrimination, and interaural amplitude discrimination; measurements were made in regions throughout the interaural amplitude-interaural time plane. Data analysis based on related theoretical work is under way to test the hypothesis that a single underlying dimension is sufficient to characterize results in both position-matching and discrimination experiments. In the third set of experiments[5] an experimental technique for measuring the shape and size of perceived sound images was developed and tested. The technique has been tested with sinusoidal and noise signals centered but with different interaural parameters, and the results are promising. In both cases the measured shape and size of the signal images corresponded to the observers' subjective descriptions of the images.

Two exclusively theoretical studies have been completed. The first[6] shows that the dependence of binaural detection thresholds on the interaural parameters of the target is predicted by almost any model based on interaural amplitude and/or phase differences and by wide classes of models based on interaural correlation. This includes almost every published binaural detection model and implies that the data for the dependence on interaural parameters of the target do not provide a significant test of the detailed mechanisms and the internal noise postulates of these models.

The second theoretical study[7] extended the model for binaural interaction based on auditory-nerve fibers[8] to include the discrimination of interaural time delay of signals whose energies are restricted to high frequencies. The same basic mechanism that had been used to describe interaural time discrimination of low-frequency tones and the detection of a tone in noise[9] was used to operate on firing patterns of fibers sensitive to high frequencies. These fibers do not respond to the detailed time structure of the stimulus but do respond to the envelope fluctuations. Predictions compare well with available data.

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3. Hearing Aids

[A portion of this work is being carried out in collaboration with the Harvard-M. I. T. Rehabilitation Engineering Center, with support from the U. S. Department of Health, Education, and Welfare, Grant 23-P-55854.]

Louis D. Braida, Nathaniel I. Durlach, Martin C. Schultz, Lawrence G. Bahler, Ian M. Beguesse, David H. Gluss, Bruce L. Hicks, Richard P. Lippmann, William M. Rabinowitz, Yvonne M. Walkowski

The goal of this program is to develop improved signal-processing schemes to match acoustical signals to residual sensory capacity in people with nonconductive hearing impairments.

During the past year considerable effort has been devoted to program planning and to the preparation of proposals. Projects have been initiated in three areas: signal enhancement and the reduction of interference, matching speech to residual auditory function, and tactile aids.

We are studying the feasibility of developing an antenna array system to improve the listener's ability to hear a signal from one direction in the presence of interfering signals from other directions, and a comb-filtering system to improve the listener's ability to hear a "target" speech signal in the presence of interfering signals that originate from the same point in space as the target signal.

Projects have been initiated on multiband amplitude compression (for listeners with reduced dynamic range) and on pitch-invariant frequency lowering (for listeners with residual hearing only at the lower frequencies). The instrumentation required for the study of multiband amplitude compression is essentially complete and future work will focus on measuring speech intelligibility in a variety of impaired listeners as a function of the values chosen for the various relevant parameters (e. g., number of frequency channels, gain and compression ratio in each channel, attack and release times, and so forth). The work on pitch-invariant frequency lowering has focused on computer processing of speech to obtain a variety of frequency-lowering transformations. Two such schemes are being implemented. In the simpler scheme a computer is used to dilate speech linearly in time-synchrony with voice pitch in real time. The more complex scheme involves off-line processing to achieve a variety of linear and nonlinear warpings of the amplitude spectra of pitch periods of speech.

We have started to develop a simple, wearable, vibrotactile aid to provide a totally deaf user with a general awareness of acoustical signals and with the gross amplitude and temporal characteristics of these signals, and a general-purpose, laboratory-based, computer-controlled, tactile-display system for research on more complex aids. The general-purpose system will be used to study the effectiveness of schemes designed to provide the user with an improved ability to detect and localize sound sources in complex acoustical environments, and of schemes designed specifically to facilitate speech communication. Among the speech-communication schemes that are being considered are a swept spectral-display scheme and a swept articulatory-feature scheme. As background for the design of the articulatory-feature scheme, we plan to conduct a detailed experimental study of the technique employed by certain deaf-blind people in which speech is perceived by placing a hand on the talker's face and neck (the "Vibration" or "Tadoma" method).

4. Musical Pitch

National Institutes of Health (Grant 1 RO1 NS11680-01)

Peter D. Besen, Howard L. Golub, K. Uno Ingard, Adrian J. M. Houtsma

The objective of this project is to obtain a deeper understanding of the auditory processes that underlie the transformation of a complex sound containing more than one tone into a sensation of musical pitch.

a. Pitch Ambiguities of Harmonic Two-tone Complexes

Experiments are being conducted in which the pitch confusions of two-tone harmonic stimuli are measured as a function of harmonic number. These data are used to test and evaluate a general stochastic model of pitch perception which had been developed earlier.[1] Computer programs to control the experiments were rewritten from PDP-4 machine language to PSYCBL.

b. Loudness of Harmonic and Inharmonic Two-tone Complexes

Harmonic and inharmonic test sounds comprising two tones were aurally matched for both harmonic (frequency ratio 3/2) and inharmonic (frequency ratio 277/265) two-tone standards.[2] Both diotic (both tones in both ears) and dichotic (one tone in each ear) stimuli were used. Preliminary results show a general 1-2 dB drop in apparent loudness when the test sound is harmonic, regardless of the frequency ratio of the standard. We think that this phenomenon is significant and must have a central origin, since the effect of combination tones has been ruled out by the results from the dichotic paradigm. Experimentation continues.

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5. Musical Acoustics

Norlin Music, Inc.

Adrian J. M. Houtsma, William L. Henke, Mark D. Chow,
Robert P. Boland, John S. Allen, John C. Willett

The objective of this project is to develop a systematic approach to the design and construction of musical instruments. Thus far the project has been limited to stringed instruments. Acoustical performance criteria are developed by carefully comparing subjective evaluations of an instrument by professional musicians with physical performance data measured in the laboratory. Experimental methods are developed to provide understanding and control of relevant physical parameters that determine acoustical performance. This should enable an instrument maker to have an instrument meet certain performance criteria consistently.

a. Comparison Study of Acoustic Guitars

Evaluations by musicians of different makes of acoustic guitar were compared with the top frequency-response of these guitars. It was found that such a response, which is the sound output of an instrument measured in an anechoic chamber with microphones all around for a constant sinusoidal driving force at the bridge, provides a unique and sufficient description or "sound print" of the instrument. The comparisons enabled us to derive some criteria for making a good instrument.

Work has begun on attaining a descriptive model of the acoustic guitar.[1, 2] Starting with an ideal string model, we transform the displacement of the string into a force function at the bridge. This can be transformed in turn into sound output through experimentally determined frequency-response curves. The model is evaluated by comparing its output with actual data obtained from harmonic analysis of plucked guitar tones. The simple assumption that the force transformation at the bridge is linear yields results that agree qualitatively. Present investigations recognize a nonlinear square-law transformation for the force component in the direction of the string, and a linear transformation for the force component that is normal for the string.

A prototype of a new acoustic steel-string guitar has been developed and built (U. S. Patent applied for through the M.I.T. Innovation Center Cooperative). The traditional compromise between acoustical and structural requirements was resolved by putting countertorque on the bridge rather than reinforcing the entire sound board with heavy braces. Tests showed a considerably stronger and more evenly distributed frequency response compared with that of other available instruments.

b. Comparison Study of Electric Guitars

Outputs of electric basses and six-string guitars of different makes were subjected to a harmonic analysis of open string tones. Characteristic differences were related to physical characteristics of the instrument, e.g., string suspension, body sturdiness, pickup location, and pickup details.[3] It was found that besides the well-understood effects of pickup location, the details of the pickup's magnetic circuitry were of great importance to its tone. In general, if we know the effective portion of the string that establishes the variable reluctance in the magnetic circuit, we may assume that no frequencies will be picked up whose string wavelengths are comparable to or smaller than the effective string portion. This phenomenon, together with the relatively high inductance of the pickup coil and significant loading effects of passive circuitry on most electric guitars, makes such instruments severely limited in the high-frequency regions.

c. Design of Wound Strings

A new method has been developed to determine the proper gauges for wound strings in fretted instruments. It results in a set of strings with identical gauges for the steel core, and the appropriate amount of wrapping to ensure equal tension for all strings when they are tuned to the proper pitch. Such strings not only guarantee a uniform "feel" in playing and provide a uniform load on the instrument's bridge but also result in uniform tension changes when the strings are fretted so that if the fret positions are properly calculated the instrument plays exactly in tune over its entire range.

d. Studies of Other Instruments

Studies on the acoustically relevant parameters of several other instruments (cello, banjo) are in progress.

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6. Localization and Signal Separation

Clarence J. LeBel Fund

Campbell L. Searle, David R. Cuddy, Mark F. Davis,
Dennis M. Freeman, Michael A. Krasner

Work has been completed on an auditory localization study which was undertaken two years ago. We are able to show by physical measurements of the transfer function from a free-field sound source to a microphone in a subject's ear canal that two independent localization cues are generated by the pinna. For sound sources in the vertical median plane there is a systematic change in the frequency response as a function of elevation angle and a disparity between the left-ear and right-ear responses that also changes systematically with elevation angle. Independent psychophysical measurements indicate that these pinna cues are detectable by subjects, and both are used by subjects in vertical localization tasks. A paper on this research will appear in the Journal of the Acoustical Society of America.

Work on the computer-controlled audio processing system has also been completed. This system is a high-quality adaptive filter under the control of a PDP-12 computer. The computer analyzes the input signal and adjusts the frequency response of the filter according to some desired algorithm. This work is reported in an S. M. thesis by D. R. Cuddy, entitled "A Computer-Controlled Audio Processing System," submitted to the Department of Electrical Engineering, M. I. T., August 1974.

C. Transduction Mechanisms in Lateral Line and Vestibular Organs

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RESEARCH OBJECTIVES AND SUMMARY OF RESEARCH

1. Studies of Receptor Potentials in Lateral Line Hair Cells

National Institutes of Health (Grant 1 RO1 NS11080-01A1)

Lawrence S. Frishkopf, Charles M. Oman, Keld Baden-Kristensen

Our major goal continues to be the clarification of mechanisms of transduction in hair cells. In the coming year we plan to investigate possible changes in ionic permeability of the hair cell associated with intracellular potential changes that result from stimulation.[1-3]

In the past year considerable effort has been spent in obtaining and setting up the apparatus required to record and analyze intracellular potentials from hair cells in lateral line organs. Major items of equipment have recently been acquired, including a small digital computer (DEC Lab 8/E), a stepping micromanipulator, and high-resolution stereo optics. These components are now being tested and interfaced.

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2. Studies of Transduction in the Semicircular Canals of Fish

National Institutes of Health (Grant 1 RO1 NS11080-01A1)

M. I. T. Health Sciences Fund

Charles M. Oman, Lawrence S. Frishkopf

During the past summer, we collaborated with Professor M. H. Goldstein of Johns Hopkins University at the Marine Biological Laboratory, Woods Hole, Mass. The goal of this work was to study the relationship between cupular motion and neural output in the semicircular canals of the skate, Raja erinacea.[1] This project was initially conceived as another approach to the problem (addressed earlier in the lateral line[2]) of analyzing the mechanics of cupular motion and relating the dynamics of this motion to neural adaptation. Our first attempts to open the canal and drive the cupula hydraulically were not successful. We found that the cupula was frequently traumatized by this procedure and that, with available formulations of artificial perilymph[3] and endolymph,[4] we were unable to maintain spontaneous activity and sensitivity in the ampullary nerve of the isolated labyrinth. An improved skate Ringer's solution was developed in which the spontaneous activity of the system could be maintained for up to 24 hours. Small changes in Ca^{++} and Mg^{++} concentrations in the Ringer's solution proved critical, a finding which has implications for our understanding of hair cell synaptic mechanisms.[5] Refined procedures for cutting the canal were developed which caused minimal changes in sensitivity. Artificial endolymph injected into the canal dramatically decreased the sensitivity of the system. The effect was reversible. We concluded that the artificial endolymph that we were using was not adequate as a physiological medium.

We also examined the dynamics associated with the unopened semicircular canals by applying caloric stimuli. We found that the small density differences thus produced in the canal endolymph stimulated afferent units in a quite repeatable way. There appear to be differences in the dynamics of the response of individual units to long-term constant caloric stimulation. Tonic units were sometimes found, while other units in the same preparation often appeared more phasic. On the basis of limited data, the dynamics appear consistent with those observed by other investigators[6,7] in response to angular acceleration in the semicircular canals of the skate and monkey.

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3. Development of a Quantitative Vestibular/Neurological Test Battery

National Institutes of Health (Grant 5 TO1 GM01555-08)

John R. Tole

Our main interest is the problem of making objective clinical measurements on patients with equilibrium disorders. In this study we are concentrating on the development of a quantitatively related battery of tests for use in the diagnosis and prognosis of peripheral vestibular disorders (e.g., Menière's disease and acoustic neuromas without brainstem involvement), using eye movements as the sole measure of system response. Such a quantitative test battery offers the possibility of making the pattern-recognition processes in neurological diagnosis and prognosis more standardized and objective, and also makes it easier to assess the relative value of individual test procedures. The development and evaluation of this test battery constitutes a major portion of the doctoral thesis of John R. Tole. The work is being conducted at M. I. T. and in the Otoneurology Clinic at the Massachusetts Eye and Ear Infirmary in association with Alfred Weiss, M. D.

The basic framework of our approach allows for the possibility of investigating several side issues of some interest. The first is whether the eyes move in conjugate fashion during all types of vestibular stimulation. This has usually been taken for granted in clinical tests, but there have been several contradictory findings.[1, 2] We plan to investigate to find out whether certain stimulus modalities (for example, combinations of body tilt and caloric stimulation) elicit disconjugate ocular responses and whether such responses might improve the selectivity or sensitivity of clinical measurements.

It is anticipated that the clinical data obtained in this study also may be of value in mathematical modeling of vestibular function. Such modeling has been successful in predicting both subjective and ocular responses to vestibular stimulation[3] in research applications, but has not been of great value in clinical work. The last situation may be due to the lack of good bilateral models of the system which, for example, would describe the system response when unilateral labyrinthectomy is performed. Should the data that are taken warrant it, an attempt will be made to construct such a model. Such an undertaking might help to organize the findings of the study in a theoretical framework and perhaps suggest further experimental procedures.

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RESEARCH OBJECTIVES AND SUMMARY OF RESEARCH

Our activities center on clinical instrumentation, cardiovascular physiology, and health-care delivery. Some of these projects involve close collaboration with medical investigators, and make use of our hospital-based laboratory facility. This laboratory is being moved from the Boston City Hospital to Beth Israel Hospital, along with the Harvard Medical School Unit. In this report we summarize aspects of the specific projects: cardiac muscle mechanics, cardiac electrophysiology, and a portable arrhythmia monitor.

1. A Contraction Sequence Controller for Isolated Cardiac Muscle Experiments

National Institutes of Health (Grant 5 TOl GM01555-08)

Allen W. Wiegner

A device has been constructed to provide controlled contraction-relaxation sequences for isolated cardiac muscle experiments. It is used in conjunction with a feedback control system for isolated cardiac muscle experiments designed by David L. Sulman as part of his doctoral thesis research program.

Isolated cardiac muscle preparations are widely used for measuring the mechanical properties of cardiac muscle tissue and the effect on the myocardium of various drugs and physiological states such as hypoxia. A typical preparation is a papillary or trabecular muscle from the ventricle of a small mammal such as rat, guinea pig, or cat. The muscle is suspended in an oxygenated Krebs-Henseleit solution containing glucose. When regularly stimulated by parallel-plate electrodes, such a preparation remains stable for hours.

Sulman's system, the Cardiac Muscle Load Controller, allows control of either the length ("length control") or force ("force control") of a muscle under test. It was designed to be controlled by a small general-purpose computer (DGC Nova 800) with appropriate analog interfaces.[1] The Contraction Sequence Controller (CSC) described here replaces the NOVA computer for basic isolated muscle experiments.

Five different contraction sequences, or modes of contraction, may be programmed by the CSC. They are isometric, isotonic, "nonphysiological" (the equivalent of the afterloaded isotonic contractions of conventional weight-and-lever apparatus), and two types of physiological ("normal") contractions.

Isometric: The muscle remains in length control, with length held at resting length, and does not shorten.

Isotonic: The muscle remains in force control, with force held at the resting force, or preload. There is no afterload, and the muscle shortens only against preload.

Nonphysiological: In the resting state, the CSC controls length. After stimulation, the system remains in length control while force rises until it equals a preset load (preload and afterload). At this point force control begins and the muscle is held at constant force during shortening and subsequent lengthening back to the resting length. Length control returns and force is allowed to decrease to preload. Thus the sequence is isometric contraction, isotonic shortening, isotonic lengthening, isometric relaxation.

Physiological (Normal): The sequence is isometric contraction, isotonic shortening, isometric relaxation, isotonic lengthening. The experimenter has the option of constraining either length or force in the resting state. (The four corresponding phases in the intact ventricle are isovolumic contraction, systolic ejection, isovolumic relaxation, and diastolic filling.)

It can be seen that the physiological sequence simulates the situation in the intact ventricle more closely than the nonphysiological, since in the former sequence isometric relaxation precedes isotonic lengthening and external work is performed by the muscle.

At the heart of the CSC is a logical network, a finite-state machine (FSM), with five states. The state of the machine determines which parameter (length or force) is controlled at what value. The input signals to the FSM come from a stimulus pulse, three comparators, and a peak detector (which detects minimum length). The output signals of the machine are length/force, which indicates which of those two is controlled, and gate controls for two analog switches. The analog switches allow either rest length or peak (minimum) length, and preload or total load to be sent to the Load Controller.

Preload, afterload, and length of the muscle are precisely controlled by the CSC to within 0.01 gm and 0.005 mm, respectively, with an accuracy of 0.25% over the appropriate ranges. Loads and lengths can be quickly and conveniently readjusted between contractions, another significant improvement over the weight-and-lever apparatus.

Physiological contractions were conceived in order to simulate the situation in the intact ventricle. Evidence from preliminary experiments indicates that physiological sequencing does indeed strengthen papillary muscle preparations. At identical preload, afterload, and resting length, a muscle contracting physiologically shortens to a greater extent than it does when undergoing afterloaded isotonic contractions.

The phase of isometric relaxation is also under study at this time. In the past relaxation has been studied, for the most part, in the context of purely isometric twitches. Present experiments concerning the effect of various drugs and physiological states on isometric relaxation should have more direct relevance to the in vivo heart. Data collected from these experiments should also enable us to extend work on models of cardiac muscle contraction to include the relaxation phase of a twitch.

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2. Cardiac Electrophysiology

National Institutes of Health (Grant 5 TO1 GM01555-08)

M. I. T. Health Sciences Fund

Chester H. Conrad

In collaboration with Dr. John Temte and Dr. Bernard Lown at the Harvard School of Public Health, work continues in electrophysiological experiments aimed at elucidating mechanisms of ventricular ectopic beats.

An array of bipolar suction electrodes, described in Quarterly Progress Report No. 114 (pp. 243-248), has been used to record monophasic action potentials (MAP's) and unipolar electrograms from the epicardial surface of normal and acutely ischemic dog hearts. Localized ischemia was induced by occlusion of the left anterior descending branch of the left coronary artery.

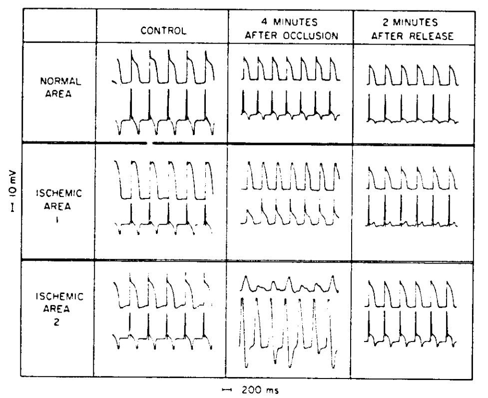


Fig. XX-1.

Monophasic Action Potentials (MAP's).
Upper trace: Attenuated intracellular potential (MAP).
Lower trace: Unipolar electrogram. Very slight ischemic changes are evident in "normal area" electrograms.

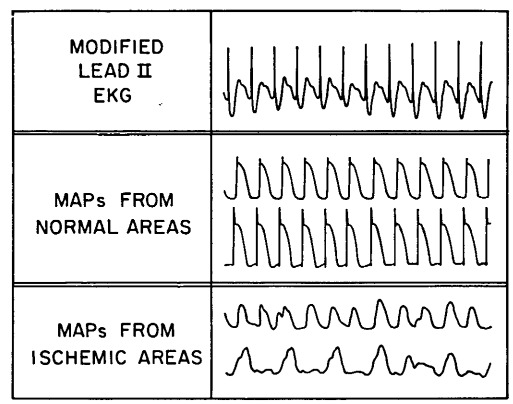


Fig. XX-2.

EKG and MAP's from normal and ischemic areas. Note 2:1 block in one MAP recording from ischemic area (lowest trace).

Figure XX-1 shows typical MAP's and electrograms recorded during such an experiment (control, occlusion, release). In the normal (nonischemic) area we see only the decrease in amplitude with time characteristic of the MAP recorded with these suction electrodes and small changes in the electrogram. In some ischemic areas (ischemic area 1) the electrogram shows S-T segment elevation, and the MAP usually shows a marked decrease in amplitude. In other ischemic areas, however (ischemic area 2), the electrogram exhibits tall R waves, often with a rounded peak, smooth downstrokes, and intermittent negative "afterpotentials." The MAP's associated with this type of electrogram may show greatly slowed upstrokes (depolarization phase), lasting as long as 120 ms. Occasionally alternation or periodic variation in amplitude is observed. In such cases, the larger MAP complexes usually correspond to the electrogram complex with the negative "afterpotentials." Figure XX-2 shows an example of a 2:1 conduction block in the ischemic area relative to the normal area.

3. An Arrhythmia Analysis System for Ambulatory Subjects

Boston City Hospital Purchase Order 1176-05-21335-C4

Joseph B. Walters, Jr.

Our objective is to develop a portable EKG rhythm monitoring system suitable for ambulatory subjects. The instrument will examine each QRS complex, catagorize it by morphology and timing, and provide a summary of cardiac rhythm for a 24 hour period. Other statistics such as rate extremes and trends will also be provided. The unit will be battery operated and may be carried by the subject during normal daily activities.

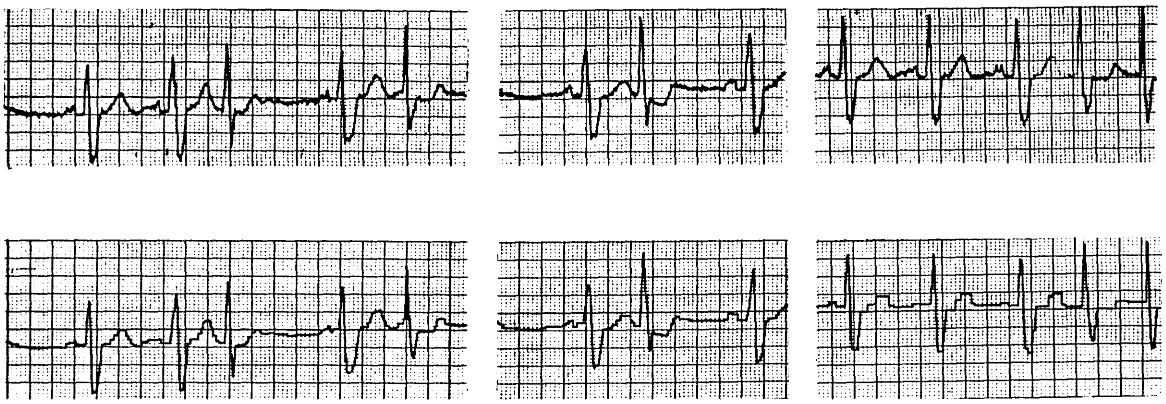
The system will use an INTEL 8080 microprocessor which has 8-bit arithmetic operations, interrupt capability, and a hardware stack facility. A nonportable 8080 processor system has been constructed and tested, and is being used for software development. An assembler that executes on the NOVA line of minicomputers has been developed for the 8080, which permits a major portion of the software development to be done on established systems. The assembler (ASM80) is a two-pass assembler implemented in NOVA Assembly language. ASM80 accepts assembly language statements as input and produces absolute binary as output. The assembler allows direct access to the full order code of the 8080. In addition to machine instructions, the assembler will accept various pseudo instructions to direct its operation.

The core of the monitoring system is the arrhythmia analysis routine executed by the processor. The algorithm will be similar to that described by Nolle and Clark.[1] At present, the algorithm is being implemented in ALGOL on a NOVA system.[2] After debugging and evaluation, the final algorithm will be written in 8080 assembly language for the portable processor system.

A significant fraction of the processor time required for EDG analysis in this algorithm is devoted to preprocessing the data. This preprocessing algorithm has been implemented and tested on the microprocessor system. The algorithm implemented is a Zero Order Interpolator (ZOI). A ZOI represents a waveform as a series of fixed amplitude but variable length segments. The output of this algorithm is a concise description of the EKG that is adequate for further processing to perform arrhythmia analysis. This algorithm was chosen because it is similar to the AZTEC algorithm developed by Cox,[3] and because of our practical experience with the algorithm.[4, 5]

The algorithm tracks the minimum and maximum values of the input signal. When the signal excursion has exceeded a specified maximum aperture a new segment of output is created to represent the previous signal data points. The amplitude of the segment is the average of the maximum and minimum values of the input, while the length is specified by the elapsed time since the last segment was output. As each output segment is produced, the maximum and minimum tracking is reset to the current sample value. Fifty-six machine instructions are required to execute this algorithm, taking approximately 0.2 ms to execute.

The algorithm represents the signal within a specified error tolerance. Thus with a rapidly changing signal (as the QRS complex) the output segments become shorter until limited by the sampling period. If a signal is not changing rapidly (as the baseline between QRS complexes), the output segments become longer until they limit at the specified maximum allowed length. Unlike conventional sampled representations, the ZOI adjusts its output rate to fit the actual changes in the input data. In the case of the EKG, the ZOI will produce a burst of segments every QRS complex, then produce very few segments in the interval between complexes. The expectation, verified by measurements,[5] is that in an EKG cycle the average output of data is from 5 to 10 times less



(a) (b) (c)

Fig. XX-3. Examples of Zero Order Interpolator (ZOI) representation produced by microprocessor. All data samples at 250 Hz.
(a) Aperture: 8 (~2.3% of peak-to-peak QRS value).
(b) Aperture: 12 (~3.5% of peak-to-peak QRS value).
(c) Aperture: 16 (~4.7% of peak-to-peak QRS value).

than in conventional sampling. In practice, this reduction in data rate is useful only if the analysis program is capable of handling the segment data as easily as if it were sampled data. Practical experience indicates that this is the case.[4]

Figure XX-3 presents a sampled EKG and the ZOI representation. The full range of the sampled data in the 8080 is 8 bits or 256 levels. In Fig. XX-3a the aperture constant was set at 8 or approximately 2.3% of the peak-to-peak range of the QRS complex (3.1% of full scale). With this aperture constant the comparison with the sampled data is very good. Note that in most cases the P wave is easily recognizable in the ZOI representation. As the aperture constant is increased (Fig. XX-3b and XX-3c) the fine structure of the EKG disappears in the ZOI representation. With an aperture constant of 16, or approximately 4.7% of the peak-to-peak value of the QRS, the P wave is not reliably represented in the ZOI representation. The representation would be adequate, however, for arrhythmia analysis and to classify QRS complexes by morphology.

The ZOI algorithm implemented in the 8080 averages less than 3.2% of the processing capability of the system, and hence leaves large reserves of computational power for analysis.

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