Section 3  Auditory Physiology

Chapter 1  Signal Transmission in the Auditory System
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1.1 Introduction
Research on the auditory system is carried out in cooperation with two laboratories at the Massachusetts Eye and Ear Infirmary (MEEI). Investigations of signal transmission in the auditory system involve the Eaton-Peabody Laboratory for Auditory Physiology, whose long-term objective is to determine the anatomical structures and physiological mechanisms that underlie vertebrate hearing and to apply this knowledge to clinical problems. Studies of cochlear implants in humans are carried out at the MEEI Cochlear Implant Research Laboratory. The ultimate goal for these devices is to provide speech communication for the deaf. Cochlear implants electrically stimulate intracochlear electrodes to elicit patterns of auditory nerve fiber activity that the brain can learn to interpret.

1.2 Signal Transmission in the External and Middle Ear
The goal of this work is to understand the relationship between the structure and function of the external and middle ear.

1.2.1 Structure-Function Relations in Middle Ears

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Project Staff
Dr. John J. Rosowski, Professor William T. Peake, David A. Steffens

In this project, we have determined how structural variations in the middle- and external ears of various vertebrate species contribute to differences in auditory function. Our work in this area has taken two interrelated paths. One path has been to make acoustic measurements of middle- and external-ear function in the gerbil, a small mammal with a highly specialized middle-ear air space and life style. Measurements of middle-ear input impedance were made before and after manipulations of the middle-ear air space (figure 1). The impedance measured with the air spaces sealed, vented, partially opened and widely opened are all consistent with a model in which the impedance of...
the middle-ear air spaces is in series with the rest of the middle-ear (figure 2). Furthermore, the data and model analysis indicate that the air-space impedance is primarily reactive except at the lowest frequencies. When extrapolated to human ears, these results can be used to predict the effects of certain middle-ear pathologies.

The second method we use to investigate middle-ear structure and function is comparison of the dimensions of various middle-ear structures in mammals with known auditory capabilities. The results of this analysis illustrate that mammals with good hearing sensitivity at frequencies less than 1 kHz tend to have larger middle-ear dimensions while those species with sensitive hearing restricted to the high and ultrasonic frequencies (f > 10 kHz) have smaller middle-ear dimensions. The results of this analysis have been used to predict the auditory capabilities of very early fossil mammals. These predictions suggest that the small shrew-like mammals that existed at the reptile-mammal transition 200 million years ago were not sensitive to low-frequency sounds as modern reptiles are but, like modern shrews and rats, were most sensitive to high-frequency sounds.

1.2.2 Basic and Clinical Studies of Middle-Ear Function

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Project Staff
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Our goal is to understand the relationship between the structure and function of auditory periphery including definition of the effect of middle- and external-ear pathologies on auditory function. To help achieve this goal, we are measuring function in human ears using temporal-bones donated at the time of death, and we have applied models from our animal work to questions concerning middle-ear pathologies and treatments.

\[ \text{Figure 1. Measurements of middle-ear input impedance in a gerbil ear before and after various manipulations of the middle-ear air spaces: sealed, the air spaces are closed; vented, a long-narrow tube is placed through the bony walls of the air space, the tube vents any excess pressure in the air space to the atmosphere; hole open, a small 2 mm diameter, hole is made in the air space walls; wide open, the bony walls of the air space are widely opened.} \]

In conjunction with Dr. Saumil Merchant, a physician member of the Otolaryngology Department at the Massachusetts Eye and Ear Infirmary, measurements were made of the cochlear input impedance (the acoustic load on the middle ear) in seven fresh and thawed temporal-bone specimens. Preliminary results of these measurements\(^3\) suggest that the cochlear impedance is loosely approximated by a series combination of a cochlear resistance and the stiffness of the oval window membrane (annular ligament) at the entrance to the inner ear, which has been observed in animal ears. However, these measurements also indicate a resistive component to the annular-ligament impedance which has not been seen in animal work. This work is being expanded to include measurements of the


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Figure 2. (a) The series model of the middle ear, relating the middle-ear input impedance $Z_T$ to the impedance of the air spaces $Z_{MEC}$, and the rest of the middle ear $Z_{TOC}$. (b) Model interpretations of the effect of sealing the air spaces. Moving the switch on the right to each of the four possible positions models: a sealed middle-ear air space $S$, venting $V$, opening a small hole $H$, and widely opening $O$. $Z_V$ is the impedance of the vent tube and the series combination of $M_H$ and $R_H$ is the acoustic impedance of the small hole.

middle-ear transfer function in isolated temporal bones.

Measurements and models from our animal work were used to produce a model (figure 3) of the effect of direct acoustic stimulation of the cochlear windows, which bypass the tympanic membrane and ossicles in normal and pathological human ears. Analysis of the model demonstrates that the alternate "acoustic" pathway for sound entry to the inner ear is not important in normal auditory function but may be a major component of that function in pathological ears in which the normal conduction mechanism is interrupted. Comparisons of the model's predictions of hearing function in pathological cases with patient audiograms support the hypothesized role of direct-acoustic stimulation in pathological ears (figure 4).

1.3 Cochlear Mechanisms

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Project Staff
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Our goal is to study the mechanisms by which motions of macroscopic structures in the inner ear produce motions of the mechanically sensitive hair bundles of sensory receptor (hair) cells. Because of its strategic location, the tectorial membrane must play an important role in the mechanical stimulation of hair bundles. However, there have been few direct observations of the tectorial membrane, and its critical properties remain obscure. During the past year, we have continued our efforts to measure the physicochemical properties of the tectorial membrane.

Changes in the ionic composition of the bath induce changes in the volume of the isolated tectorial

\[ Z_T = \frac{P_T}{U_T} = Z_{TOC} + Z_{MEC} \]
when the original bath composition is restored, permanent changes in the structure of the tectorial membrane can result from long exposures to high-sodium, low-calcium solutions.

During the past year, we have studied the effects of brief (15 minute) exposures to test solutions. We have found (1) that responses to brief exposures are consistent with those for long exposures and (2) that the effects of brief exposures are more nearly reversible. Therefore, we have been able to measure responses to brief exposures of as many as 20 different ionic solutions in a single preparation. Results show that even very low levels of calcium (< 10 μmol/L) significantly change the structure of the tectorial membrane.

Because of the considerable diversity in tectorial membrane structure across species, it is important to compare results obtained for chick tectorial membrane with results from other species. During the past year, we have initiated studies of physicochemical properties of the tectorial membrane of the alligator lizard—a species in which the importance of mechanical processes at the level of individual hair bundles has been directly demonstrated. Initial results suggest that the tectorial membrane of the lizard (1) swells when high-potassium, low-calcium solutions are replaced by high-sodium, low-calcium solutions and (2) shrinks when calcium is increased from μmol/L to mmol/L concentrations. These results are qualitatively similar to results with chick tectorial membrane.

**Publications**


1.3.1 Stimulus Coding in the Auditory Nerve and Cochlear Nucleus

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Project Staff

Dr. Bertrand Delgutte, Dr. Peter A. Cariani

We have been investigating the correspondence between human auditory psychophysics and neural activity patterns at the level of the auditory nerve and the cochlear nucleus. We want to gain insight into what kinds of information the auditory system uses to represent complex acoustic stimuli. We have recorded from representative samples of auditory nerve fibers in anesthetized cats and computed autocorrelation histograms to estimate the aggregate interspike interval distribution over the entire auditory nerve. Our results for a wide range of complex stimuli suggest that the pitch heard by human listeners corresponds to the most frequent interspike interval in the auditory nerve.

In the past year, we ran a physiological analog of a classical psychophysical experiment in which all three components of a harmonic complex are shifted in frequency by the same amount, resulting in a shift in perceived pitch. Our results showed that the pitch shifts estimated from the interspike interval distributions closely followed those observed in psychophysical studies. We also carried out a physiological analog of a pitch dominance experiment in which two harmonic complexes (harmonics 3-5 versus harmonics 6-12) with slightly different fundamental frequencies (FO) were presented together. At FOs above 150 Hz, the most frequent interspike interval in the auditory nerve always corresponded to the pitch associated with harmonics 3-5 rather than the pitch of harmonics 6-12, consistent with human psychophysical data. These results show that models of pitch perception based on aggregate interspike interval distributions can account for classical experimental results for pitch shift and pitch dominance.

Psychophysical experiments show that listeners can identify better both constituents of a pair of simultaneously-presented vowels if the pitches of the two vowels are slightly different. In a physiological experiment motivated by this result, we have found that (1) each single vowel evokes a characteristic aggregate interspike interval distribution, (2) one single vowel constituent of a double vowel pair can always be identified from correlations between the double vowel pattern and the various single vowel patterns, (3) the second single vowel constituent can often be identified if the first correctly identified vowel is "subtracted" from the double vowel pattern (via partial correlation), and (4) vowel identification through this method improves when the voice pitches are made slightly different. These results suggest that vowels can be discriminated using aggregate temporal information alone and that explicit pitch identification may not be necessary to account for improved identification of constituent vowels with increasing voice pitch differences.

When two sounds with different pitches are played simultaneously, certain pitch ratios appear to be pleasant or consonant, while others appear harsh or dissonant. In order to investigate neural correlates of these phenomena, we have recorded the responses of auditory-nerve to stimuli associated with different degrees of consonance and dissonance. Response patterns to pairs of pure tones forming dissonant intervals showed beating for all responding fibers. No beating patterns were found for pure-tone consonant intervals. Beating patterns were also found for dissonant pairs of complex tones, but were restricted to fibers whose characteristic frequencies were close to two partials of the complex tones. These beating patterns in the frequency range 20-200 Hz are thought to be physiological correlates of roughness. A quantitative model that sums the physiologic roughness across the array of auditory-nerve fibers can predict the relative dissonances of the different musical intervals. These results suggest that certain aspects of harmony perception are encoded in the temporal patterns of discharge of auditory-nerve fibers.

Publications


1.4 Electrical Stimulation of the Auditory Nerve

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Project Staff
Dr. Bertrand Delgutte, Scott B.C. Dynes

The goal of these studies is to understand the mechanisms of electrical stimulation of the auditory nerve to design better cochlear implants. For this purpose, we record from auditory-nerve fibers in anesthetized cats in response to electric stimuli applied through electrodes similar to those used in humans. In the past year, we have measured the responses to pairs of brief monophasic pulses separated by short intervals. This stimulus is the simplest configuration that can show some of the interpulse interactions that are likely to occur in interleaved sampling speech processors. For suprathreshold first pulses, the threshold for the second pulse was found to decrease with increasing interpulse delay, as expected from the refractory properties of nerve fibers. Interpulse delays at thresholds were consistently shorter for a cathodal first pulse than for an anodal first pulse with the same amplitude. (The second pulse was always anodal.) This latency difference can be interpreted as the spike conduction time from a peripherally-located cathodal site of excitation to the more central anodal site of excitation. Consistent with this interpretation, the difference in latencies between cathodal and anodal single pulses was approximately equal to the conduction time estimated from the two-pulse experiment. We plan to pursue these experiments to identify the different sites of nerve excitation for various stimulus conditions.

Another series of experiments examined whether responses to two-pulse stimuli can be used to predict responses for more complex stimulus conditions. Three pulses of equal amplitude were presented in rapid succession. The pulse amplitude was chosen so that each pulse would, by itself, be well above threshold. The delay between Pulses 1 and 2 was adjusted so that Pulse 2 would just produce a spike with high probability, and the delay between Pulses 2 and 3 was adjusted so that Pulse 3 would meet the same criterion. The delay between Pulses 2 and 3 was found to be consistently longer than the delay between Pulses 1 and 2. This result shows that the refractory period cannot be seen as a fixed characteristic of a neuron because it depends on past history of stimulation. Model simulations show that the magnitude of the changes in refractory period are severely underestimated by classical Hodgkin-Huxley dynamics. This result has implications for the design of interleaved sampling speech processors in which one attempts to minimize interactions between successive pulses.

1.5 Interactions of Middle-Ear Muscles and Olivocochlear Efferents

Sponsor
National Institutes of Health
Contract P01-DC00119

Project Staff
John J. Guinan, Jr.

1.5.1 Basic and Clinical Studies of the Auditory System

Our aim is to determine the actions and interactions of the acoustically elicited middle-ear muscle reflexes and the olivocochlear efferent reflexes. As a first step in our project to measure the sound-level dependence of the middle-ear acoustic reflexes with and without activation of medial olivocochlear (MOC) efferents, we have begun studying MOC effects on brain stem evoked potentials (BAEPs). In anesthetized cats, we measured BAEPs at the vertex in response to clicks at a variety of sound levels, with and without activation of MOC efferents and before and after the efferents were cut near the vestibulo-cochlear anastomosis. This cut severs the axons to the cochlea but leaves the collaterals to the cochlear nucleus intact.

Before the cuts, stimulation of MOC efferents with an electrode at the midline of the floor of the fourth ventricle shifted the BAEP responses to higher sound levels by approximately the same amount as auditory-nerve responses (N1) were shifted to higher sound levels. After the cuts, no changes in BAEPs were produced by MOC stimulation. Thus, from experiments to date, the effects of efferent stimulation on BAEPs appear to be due solely to MOC inhibition of cochlear responses with no effect attributable to the MOC collaterals to the cochlear musculature.

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7 This project is the direct successor of the 1991 project: Middle-Ear Muscle Reflex.
nucleus. The lack of effect of MOC collaterals to the cochlear nucleus on BAEPs is consistent with these collaterals not innervating bushy cells in the cochlear nucleus\(^8\) and the hypothesis that bushy cells are the dominant cochlear-nucleus cell type involved in producing BAEPs.\(^9\) Additionally, the absence of changes in BAEPs due to severing efferents near the vestibulo-cochlear anastomosis means that measurements of BAEPs can serve as a good control for the integrity of the auditory brainstem in experiments on middle-ear muscle reflexes involving such efferent cuts.

During the past year, final manuscript revision was done for publication of our results on the sound-frequency selectivity of single stapedius motoneurons in cats which has now appeared in the *Journal of Neurophysiology*.\(^{10}\)

**Publications**


### 1.6 Cochlear Efferent System

**Sponsor**

National Institutes of Health
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**Project Staff**

John J. Guinan, Jr., Michael P. McCue

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version of this work will be presented early in 1993.13

Publications


1.7 Cochlear Implants

Sponsor

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Project Staff

Donald K. Eddington, William M. Rabinowitz, Jay T. Rubinstein, Joseph Tierney, Marc A. Zissman

1.7.1 Project A: Models of Current Spread and Nerve Excitation During Intracochlear Stimulation

Project Staff

Dr. Donald K. Eddington, Dr. Jay T. Rubinstein

The basic function of a cochlear prosthesis is to elicit patterns of activity on the array of surviving auditory nerve fibers by stimulating electrodes that are placed in and/or around the cochlea. By modulating these patterns of neural activity, these devices attempt to present information that the implanted subject can learn to interpret. The spike activity patterns elicited by electrical stimulation depend on several factors: the complex, electrically heterogeneous structure of the cochlea, the geometry and placement of the stimulating electrodes, the stimulus waveform, and the distribution of excitable auditory nerve fibers. An understanding of how these factors interact to determine the activity patterns is fundamental to designing better devices and to interpreting the results of experiments involving intracochlear stimulation of animal and human subjects. As a first step towards this understanding, the goal of this project is to construct a software model of the cochlea that predicts the distribution of potential produced by the stimulation of arbitrarily placed, intracochlear electrodes and use these potential distributions as inputs that drive models of auditory nerve fibers.

This year we continued the development of the three-dimensional, finite difference model of the human cochlea that predicts the potential distribution produced in this structure by electrical stimulation using model electrodes of arbitrary position and geometry. In order to make the use of this model more practical by reducing the time to compute a solution, the model was implemented on a SUN SPARCstation-2 where solutions are computed in twenty minutes rather than the eight hours required by the original VAX-750 system.

A series of solutions were computed to test the model's sensitivity to variations in the resistivity of the major cochlear components (e.g., perilymph, endolymph, bone, nerve and basilar membrane). These solutions documented the stability of the model and confirmed our intuition that the asymmetric potential distributions predicted by the model and reported in previous years reflect the basic, three-dimensional anatomy of this structure.

We are in the final stages of the morphological work on one rat ear that will represent the anatomical component of the electro-anatomical model for this animal. From registered serial sections of the cochlea, we are currently generating the database through which the tissues and their electrical resistances are represented in the three-dimensional model. Using the rat, we will be able to make alterations in the anatomy of the cochlea and make measurements that would be impossible in our human subjects. This will provide an important tool in the future testing and refinement of this electroanatomical model.

Continued development of a single-fiber computer model of myelinated excitation by electrical stimulation has led us to model formulations that more accurately predict the following measurements in the cat: (1) strength-duration time constants for cathodal stimulation of 260 us instead of the 80 us predicted by the classical model, (2) anodal/cathodal threshold ratios between 1 and 4 instead of the 4.9 predicted by the classical model, (3) conduction velocity 4-6 m/sec/micron that are greater than found in the classical model, and (4) refractory periods that are three times shorter than predicted by the classical model. The anodal/cathodal threshold predictions have also been confirmed qualitatively by measurements made in the rat.

1.7.2 Project B: New Sound Processors for Auditory Prostheses

Project Staff
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Our collaboration with colleagues at Duke University and the Research Triangle Institute in the development of new processing algorithms to improve the speech reception of cochlear implant users has resulted in laboratory-based systems that increase the average single-syllable word recognition scores by 20 percentage points for the seven subjects tested.\(^4\) In addition to increasing the number of stimulating channels from four to six and implementing a different compression technique, the new algorithms were designed to reduce interference assumed to be caused by simultaneously activating intracochlear electrodes.

As a first step in our investigation to determine which of the differences between the new and old sound processing systems contributed to increased performance, we compared a subject's speech reception ability using three sound processing schemes. These schemes were: (1) the current commercial processor that uses four bandpass filters to segment the frequency spectrum from approximately 100 Hz to 4,000 Hz and presents the analogue outputs of these filters as simultaneous current waveforms to four of the implanted electrodes, (2) a 4-channel processor in which the envelopes of the four bandpass filter outputs are used to modulate biphasic pulse trains that are presented as interleaved stimuli to four of the implanted electrodes, and (3) a 6-channel version of processor (2). The 4-channel and 6-channel interleaved systems shared an amplitude compression scheme in which the top 60 dB of the envelope output range was logarithmically mapped into the subject's dynamic range. The commercial, 4-channel analogue system uses an automatic gain control that acts on the signal before processing by the bandpass filters.

One subject's ability to identify closed sets of consonants (24 consonants presented in a /aCa/ context) and vowels (8 vowels presented in a /bVt/ context) has been measured for these three processing schemes. Scores for consonant recognition using the analogue and interleaved, 4-channel processors were 87 percent and 89 percent respectively. While the difference in consonant recognition is not significant for the 4-channel processors, these scores are significantly different from the 96 percent scored with the 6-channel, interleaved processor. This implies that for consonant identification, differences in performance were due to increasing the number of channels but differences in compression and interleaving were probably not significant. The vowel scores were 79 percent and 87 percent for the 4-channel systems (analogue and interleaved respectively) and 98 percent for the 6-channel, interleaved system. Differences in the two 4-channel system scores suggest that differences in compression and/or interleaving may contribute to better vowel recognition. As with the consonant scores, increasing the number of channels also contributes to better vowel scores.

Two different psychophysical tests conducted with implanted subjects this year are leading to the design of new speech processors that will be tested next year. Loudness scaling experiments using electrical stimulation of the subjects' intracochlear electrodes show that the shape of the loudness growth function varies across electrodes. These results suggest customizing the function used to map channel energy to stimulus amplitude for each electrode rather than using the same function as is currently done. Psychophysical measures of interaction during electrical stimulation of nonsimultaneous stimuli at the same or different electrodes have revealed complex patterns of masking and unmasking that depend on the amplitude of the masker and the separation of the masker and test stimuli in both time and space. These measures of nonsimultaneous interactions have suggested new stimulus waveforms that may reduce these interactions. These waveforms are being tested in our single-unit models and, in the next year, will be tested as part of a 6-channel, interleaved sound processor.
