

## **Section 3    Auditory Physiology**

Chapter 1    Signal Transmission in the Auditory System



# Chapter 1. Signal Transmission in the Auditory System

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## 1.1 Introduction

### Sponsors

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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. Our long-term objective is to determine the anatomical structures and physiological mechanisms that underlie vertebrate hearing and to apply that knowledge to clinical problems. Studies of cochlear implants in humans are carried out at the MEEI Cochlear Implant Laboratory. The ultimate goal of these devices is to provide speech communication for the deaf through electric stimulation of 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

### 1.2.1 Structure-Function Relations in Middle Ears

#### Project Staff

Professor William T. Peake, Dr. John J. Rosowski

The goal of this project is to investigate and formulate rules which relate the structure of the external and middle ears of land-dwelling vertebrates to hearing function. This goal is being achieved by testing and refining acoustic and mechanical models of the auditory periphery with new measurements of external and middle structure and function. In the past year, we have advanced the applications of our external- and middle-ear modeling efforts into new areas. Our work on the structure of the ear in the earliest (250 million years old) mammals has resulted in two manuscripts accepted for publication<sup>1</sup> which derive predictions of auditory function of these mammals from their middle-ear structure. These

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<sup>1</sup> J.J. Rosowski and A. Graybeal, "What Did Morganucodon Hear?" *Zool. J. Linnean Soc.*, forthcoming; J.J. Rosowski, "Hearing in Transitional Mammals: Predictions from the Middle-ear Anatomy and Hearing Capabilities

predictions are consistent with the view that the suite of adaptations that define mammals (e.g., homeothermy, hair, soft palate and the mammalian jaw and ear) all evolved simultaneously, allowing these animals to develop a nocturnal life style.

We have also used our models of the auditory periphery to explain observations that the ear is most easily damaged by sounds with intense middle-frequency (1-10 kHz) spectral components.<sup>2</sup> Our investigations of the effects of the middle-ear cavity on auditory function continued; measurements were made of the cavities' contribution to the middle-ear input impedance in the gerbil,<sup>3</sup> an animal with a hypertrophied middle-ear air space. An expanded model of the effect of the middle-ear air space was also developed<sup>4</sup> in order to investigate the effect of direct acoustic stimulation of the cochlear windows by middle-ear sound pressure. We have also submitted a paper critiquing some common measures of the performance of the auditory periphery.<sup>5</sup>

## 1.2.2 Basic and Clinical Studies of the Auditory System: External and Middle Ears.

### Project Staff

Professor William T. Peake, Dr. John J. Rosowski

The goals of this project are to understand the workings of the normal and pathological human external and middle ear. The techniques used include the interaction of measurements of the acoustics and mechanics of the human auditory periphery with acoustic and mechanical models of ear performance.

The work on this project has proceeded on three fronts:

1. A manuscript indicating that temporal bones extracted from cadavers are valid models of the human middle ear was published.<sup>6</sup>
2. Additional work with temporal bones has addressed the issue of what are the modes of ossicular motion.<sup>7</sup> The results suggest that the malleus rotates at sound frequencies below 1 kHz. However, at higher frequencies, the malleus also translates and may bend.
3. Model investigations of the effects of direct acoustic stimulation of the cochlear windows<sup>8</sup> indicate that the residual hearing observed in many middle-ear pathologies may be completely explained by the action of sound on the cochlear windows. The resultant models allow quantitative predictions of the effects of various middle-ear reconstruction techniques on hearing.

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of Extant Mammals," in *The Evolutionary Biology of Hearing*, eds. A.N. Popper, R.R. Ray and D.B. Webster (New York: Springer-Verlag, forthcoming).

- 2 J.J. Rosowski, "The Effects of External- and Middle-ear Filtering on Auditory Threshold and Noise-induced Hearing Loss," *J. Acoust. Soc. Am.*, forthcoming.
- 3 M.E. Ravicz, J.J. Rosowski, and H.F. Voigt, "Acoustic Impedance Measurements in the Gerbil Ear," *J. Acoust. Soc. Am.* 87 (Suppl. 1): S101 (1990).
- 4 W.T. Peake, J.J. Rosowski, and T.J. Lynch III, "Acoustic Coupling to Cochlear Windows," Abstracts of the 15th Midwinter Meeting of the Association for Research in Otolaryngology, St. Petersburg, Florida, February 1991, forthcoming.
- 5 W.T. Peake and J.J. Rosowski, "Impedance Matching, Optimum Velocity and Ideal Middle Ears," *Hear. Res.*, forthcoming.
- 6 J.J. Rosowski, S.N. Merchant, P.J. Davis, K.M. Donahue, and M.D. Coltrera, "Cadaver Middle Ears as Models for Living Ears: Comparisons of Middle-ear Input Immittance," *J. Otol. Rhinol. Laryngol.* 99: 402-412 (1990).
- 7 K.M. Donahue, J.J. Rosowski, and W.T. Peake. "Can the Motion of the Human Malleus Be Described as Pure Rotation?," Abstracts of the Fifteenth Midwinter Meeting of the Association for Research in Otolaryngology, St. Petersburg, Florida, February 1991, forthcoming.
- 8 W.T. Peake, J.J. Rosowski, and T.J. Lynch III, "Acoustic Coupling to Cochlear Windows," Abstracts of the 15th Midwinter Meeting of the Association for Research in Otolaryngology, St. Petersburg, Florida, February 1991, forthcoming.

## Publications and Papers Presented

- Donahue, K.M., J.J. Rosowski, and W.T. Peake. "Can the Motion of the Human Malleus Be Described As Pure Rotation?" Abstracts of the 15th Midwinter Meeting of the Association for Research in Otolaryngology, St. Petersburg, Florida, February 1991. Forthcoming.
- Peake, W.T., J.J. Rosowski, and T.J. Lynch III. "Acoustic Coupling to Cochlear Windows." Abstracts of the 15th Midwinter Meeting of the Association for Research in Otolaryngology. St. Petersburg, Florida, February 1991. Forthcoming.
- Peake, W.T., and J.J. Rosowski. "Impedance Matching, Optimum Velocity and Ideal Middle Ears." *Hear. Res.* Forthcoming.
- Ravicz, M.E., J.J. Rosowski, and H.F. Voigt. "Acoustic Impedance Measurements in the Gerbil Ear." *J. Acoust. Soc. Am.* 87 (Suppl. 1): S101 (1990).
- Rosowski, J.J. "The Effects of External- and Middle-ear Filtering on Auditory Threshold and Noise-induced Hearing Loss." *J. Acoust. Soc. Am.* Forthcoming.
- Rosowski, J.J., "Hearing in Transitional Mammals: Predictions from the Middle-ear Anatomy and Hearing Capabilities of Extant Mammals." A talk presented at the Symposium on the Evolutionary Biology of Hearing, Sarasota, Florida, May 1990.
- Rosowski, J.J. "Hearing in Transitional Mammals: Predictions from the Middle-ear Anatomy and Hearing Capabilities of Extant Mammals." In *The Evolutionary Biology of Hearing*. Eds. A.N. Popper, R.R. Ray and D.B. Webster. New York: Springer-Verlag. Forthcoming.
- Rosowski, J.J., and A. Graybeal. "What Did Morganucodon Hear?" *Zool. J. Linnean Soc.* Forthcoming.
- Rosowski, J.J., S.N. Merchant, P.J. Davis, K.M. Donahue, and M.D. Coltrera. "Cadaver Middle Ears as Models for Living Ears: Comparisons of

Middle-ear Input Immittance." *Ann. Otol. Rhin. Laryngol.* 99: 402-412 (1990).

## 1.3 Cochlear Mechanisms

### Project Staff

Professor Thomas F. Weiss, Professor Lawrence S. Frishkopf, Dr. Dennis M. Freeman, Kristin J. Dana, Farzad Ehsani

The results of several studies, described in last year's Progress Report, have now been published.<sup>9</sup> The progress described below focuses primarily on newer projects.

Our longer-term goal is to investigate the micro-mechanical mechanisms by which vibrations of macroscopic inner ear structures are conveyed to the receptor (hair) cells. For this purpose, we have developed *in vitro* preparations to (1) place a dissected portion of an auditory receptor organ in a chamber on the stage of a compound microscope; (2) perfuse the tissue with artificial lymph solutions; (3) stimulate the organ hydrodynamically; and (4) measure displacements of inner ear structures in response to changes in solution composition and to audio frequency hydrodynamic stimulation. We have developed both an isolated preparation of the cochlear duct of the alligator lizard and isolated tectorial membrane (TM) preparations of the chick and alligator lizard cochlea.

Measurement of the osmotic response of the receptor organ is one way to measure the viability of the organ. This measurement can give insight into mechanisms of ion transport in the cells of the organ. Measurement of the osmotic response of the TM to changes in solution composition can yield information about the physical-chemical properties of the TM. To investigate these osmotic responses, we have devised a video microscopy system that consists of a compound microscope, displacement detector, video camera, video digitizer, and personal computer. We can routinely measure the location of a microscopic object in three dimensions with respect to a reference location with this system. The height of the object along the optical axis of the microscope is measured by bringing the object into focus in the microscope and measuring the height of the

<sup>9</sup> D.M. Freeman and T.F. Weiss, "Superposition of Hydrodynamic Forces on a Hair Bundle," *Hear. Res.* 48: 1-16 (1990); D.M. Freeman and T.F. Weiss, "Hydrodynamic Forces on Hair Bundles at Low Frequencies," *Hear. Res.* 48: 17-30 (1990); D.M. Freeman and T.F. Weiss, "Hydrodynamic Forces on Hair Bundles at High Frequencies," *Hear. Res.* 48: 31-36 (1990); D.M. Freeman and T.F. Weiss, "Hydrodynamic Analysis of a Two-dimensional Model for Micromechanical Resonance of Free-standing Hair Bundles," *Hear. Res.* 48: 37-68 (1990); D.M. Freeman, "Anatomical Model of the Cochlea of the Alligator Lizard," *Hear. Res.* 49: 29-38 (1990); R.C. Kidd and T.F. Weiss, "Mechanisms that Degrade Timing Information in the Cochlea," *Hear. Res.* 49: 181-208 (1990).

microscope stage with a displacement detector. The location of the object in the plane perpendicular to the optical axis is measured by displaying the microscope field on a video terminal and using a mouse-controlled cursor that is superimposed on the video image. Clicking the mouse results in acquisition of all three coordinates of an object, which are then placed in a file along with the time of data acquisition. In addition, the video images can be acquired, image-processed, and saved in files. Software has been written that allows us to measure the locations of beads (microspheres 1 – 5  $\mu\text{m}$  in diameter) on cochlear structures and to acquire images during an experiment. Experimental results—absolute bead locations as a function of time, Euclidean distances between beads as a function of time, sequences of images—can be displayed during the experiment.

With the video microscopy system we have continued to examine the osmotic response of the isolated auditory receptor organ of the alligator lizard to perfusion with artificial lymph solutions. The principal finding of this study is that the cochlear duct of the alligator lizard swells in some iso-osmotic solutions but not in others. The duct swells in solutions that contain both potassium and chloride ions, but does not swell if either sodium is substituted for potassium or gluconate is substituted for chloride. A manuscript is being prepared which describes these results and their implications for mechanisms of ion transport in hair cells; the ototoxicity of endolymph, which may play a role in Ménière's disease; and the use of *in vitro* preparations.

In collaboration with Dr. Douglas A. Cotanche of the Anatomy Department at the Boston University Medical School, we have developed an isolated TM preparation for studying the physical-chemical properties of the TM. The intact TM is microdissected from the auditory receptor organ of either chick or alligator lizard and cemented onto the surface of an experimental chamber using a tissue adhesive. Beads are allowed to settle on the TM and the positions of each bead in three dimensions is measured with the video microscopy system as solutions of different composition are perfused through the chamber. Video images of the TM have also been obtained with the video microscopy system.

The isolated TM preparation has several advantages over preparations in which the TM is in place surmounting the receptor organ. In studies of shrinkage/swelling of the TM, using this method eliminates a possible ambiguity caused by shrinkage/swelling of the underlying tissue. Furthermore, structural features of the TM are more readily visualized when TM is isolated than when

it is in place in the receptor organ. Preliminary results from both chick and alligator lizard TMs reveal that both the dimensions and microstructure of the TM are critically dependent on the composition of the bathing solution. Changes in osmolarity and ionic strength produced very large (>500%), rapid changes in dimensions. Large (100%) changes in dimensions and microstructure were seen when the sodium, potassium, and calcium content of artificial lymph solutions were changed even though the solutions were iso-osmotic and had the same ionic strength.

## **Publications**

Freeman, D.M., and T.F. Weiss. "Superposition of Hydrodynamic Forces on a Hair Bundle." *Hear. Res.* 48: 1-16 (1990).

Freeman, D.M., and T.F. Weiss. "Hydrodynamic Forces on Hair Bundles at Low Frequencies." *Hear. Res.* 48: 17-30 (1990).

Freeman, D.M., and T.F. Weiss. "Hydrodynamic Forces on Hair Bundles at High Frequencies." *Hear. Res.* 48: 31-36 (1990).

Freeman, D.M., and T.F. Weiss. "Hydrodynamic Analysis of a Two-dimensional Model for Micromechanical Resonance of Free-standing Hair Bundles." *Hear. Res.* 48: 37-68 (1990).

Freeman, D.M. "Anatomical Model of the Cochlea of the Alligator Lizard." *Hear. Res.* 49: 29-38 (1990).

Kidd, R.C., and T.F. Weiss. "Mechanisms That Degrade Timing Information in the Cochlea." *Hear. Res.* 49: 181-208 (1990).

### **1.3.1 Regeneration of Primary-auditory Neurons in vitro**

#### **Project Staff**

Dr. Robin L. Davis

To determine whether intrinsically-regulated growth features contribute to the precise quality of regeneration observed in the lower vertebrate auditory system, neurite regeneration was studied from individual goldfish primary-auditory neurons placed in the homogenous conditions of tissue culture. We observed stereotyped morphology and timing of neurite outgrowth *in vitro* and the properties observed from these same neurons *in vivo*. These findings suggest that some morphological properties of neurite regeneration, as well as the way in which the growth was attained, may be

important endogenously-determined features in adult regenerating primary-auditory neurons.

### **Publications**

Davis, R.L. "Conditioning Lesions Promote Primary-auditory Neurite Regeneration *in vitro*." *Abstr. Assoc. Res. Otolaryngol.* 13: 316-317 (1990).

Davis, R.L., and W.F. Sewell. "Neurite Regeneration from Single Primary-auditory Neurons *in vitro*." Submitted to *J. Neurosci*.

Davis, R.L. "Specificity of VIII<sup>th</sup> Nerve Regeneration in Lower Vertebrates." *J. Exp. Zool.* (mini-review from a neurosciences symposium, Molecular and Cellular Events in Development and Regeneration, submitted for review).

### **1.3.2 Stimulus Coding in the Auditory Nerve and Cochlear Nucleus**

#### **Project Staff**

Dr. Bertrand Delgutte, Dr. Peter A. Cariani

The goal of our research is to understand neural mechanisms for processing of complex acoustic stimuli at the level of the auditory nerve and cochlear nucleus. Our modeling work on nonlinear responses of auditory-nerve fibers to complex stimuli has progressed. A particular focus of this model is on suppression phenomena, which play a key role in masking and speech processing.

We have investigated how this model might be used to develop improved analysis-synthesis systems for telecommunications.<sup>10</sup> This work is based on the premise that auditory models only respond to features of the acoustic signal that are perceptually relevant. Indeed, the model response to speech processed by a high-quality speech coding system resembled more the response to natural speech than the response to a poor-quality coder. We further showed that nonlinear processing in the model helps to predict the relative salience of selected spectral manipulations for speech-like stimuli.

We have analyzed data on the responses of auditory-nerve fibers at very low sound levels.<sup>11</sup> These kinds of data are important for understanding physiological substrates of behavioral thresholds and may shed light on cochlear mechanisms in a range where nonlinear phenomena are likely to be less prominent. Results show that the growth of driven discharge rate with sound pressure for tones at the characteristic frequency (CF) is well approximated by a power function. The exponent of this function is greater for fibers with low spontaneous rates (SR) of discharge than for high-SR fibers. The detection-theoretic measure  $d'$  also shows a power-law behavior as a function of sound pressure, but the mean exponent was about the same for all fibers. Thresholds based on  $d'$  were lower for high-SR fibers than for low-SR fibers, suggesting that high-SR fibers are most appropriate for signal detection. Rate-level functions for tones at frequencies other than the CF also showed a power-law behavior. The exponent was larger for tones below the CF than for tones above the CF. This frequency dependence is probably of mechanical origin because the growth of basilar-membrane motion shows a similar dependence.

We are beginning to investigate possible neural mechanisms for the representation of periodicities of complex waveforms in the auditory nerve and the cochlear nucleus. We are conducting a series of experiments on the responses of auditory-nerve fibers to speech-like, single-formant stimuli with fundamental frequency that is systematically varied. Specifically, we are investigating whether auditory nerve fibers show an enhanced response when their CF is a small multiple of the fundamental frequency, which is predicted by rate-place models of auditory processing. Preliminary results suggest that these enhanced responses are most prominent for low-CF fibers and high fundamental frequencies; this is consistent with filter-bank models of cochlear processing.

Neurons with "chopper" response patterns in the cochlear nucleus show enhanced synchronization to the fundamental frequency of amplitude modulated tones when this modulation frequency is close to the "intrinsic oscillation" or "chopping" frequency of the cell.<sup>12</sup> We are developing a simple neuron model to ascertain whether threshold

<sup>10</sup> B. Delgutte, "Physiological Models of Masking and Speech Processing," *J. Acoust. Soc. Am.* 87: S13 (1990).

<sup>11</sup> B. Delgutte, "Power-law Behavior of the Discharge Rates of Auditory-nerve Fibers at Low Sound Levels," Fifteenth Midwinter Meeting, Association of Research in Otolaryngology, St. Petersburg, Florida, February 1991, forthcoming.

<sup>12</sup> D.O. Kim, J.G. Sirianni, and S.O. Chang, "Responses of DCN-PVCN Neurons and Auditory Nerve Fibers in



accommodation can account for this behavior and whether these kinds of neurons could play a role in periodicity detection. We plan to utilize complex waveforms, periodic and aperiodic click trains, noise, and speech-like sounds to investigate the temporal responses of chopper neurons.

During the past year, two previously-submitted manuscripts have been published.<sup>13</sup>

### 1.3.3 Electrical Stimulation of the Auditory Nerve

#### Project Staff

Dr. Bertrand Delgutte, Scott B.C. Dynes

This research aims at understanding physiological mechanisms of electrical stimulation to help design improved cochlear implants. We are recording the responses of auditory-nerve fibers to electric currents applied through electrodes inserted into the cochlea. In one series of experiments, the threshold of auditory-nerve fibers is measured as a function of the duration of brief rectangular current pulses. These very basic experiments are important for understanding not only stimulation of the auditory nerve, but also stimulation of myelinated fibers in general. Preliminary results suggest that the threshold for long pulses was about 10-dB lower for cathodal currents than for anodal currents, consistent with the predictions of a biophysical model of myelinated nerve fibers.<sup>14</sup> Time constants describing the decrease in threshold with pulse duration were lower for anodal currents than for cathodal currents, contrary to model predictions. In another series of experiments, the threshold of auditory-nerve fibers for stimulation through one intracochlear electrode is measured while a subthreshold current is applied through another electrode. These experiments study "electrode interactions" that are likely to limit the performance of certain multiple-channel cochlear implants. Preliminary results suggest that the threshold current varies linearly with the subthreshold current; this is consistent with the notion that these electrode interactions are due to linear summation of the electric fields produced by stimulation of each electrode.

### Publications and Papers Presented

Delgutte, B. "Physiological Mechanisms of Psychophysical Masking: Observations from Auditory-nerve Fibers." *J. Acoust. Soc. Am.* 87: 791-809 (1990).

Delgutte, B. "Two-tone Suppression in Auditory-nerve Fibers: Dependence on Suppressor Frequency and Level." *Hear. Res.* 49: 225-246 (1990).

Delgutte, B. "Physiological Models of Masking and Speech Processing." *J. Acoust. Soc. Am.* 87: S13 (1990).

Delgutte, B. "Power-law Behavior of the Discharge Rates of Auditory-nerve Fibers at Low Sound Levels." Paper presented at the 15th Midwinter Meeting, Association for Research in Otolaryngology, St. Petersburg, Florida, February 1991. Forthcoming.

## 1.4 Middle-Ear Muscle Reflex

#### Project Staff

Dr. John J. Guinan, Jr., Dr. James B. Kobler, Michael P. McCue

Our aim is to determine the structural and functional basis of the acoustically elicited middle-ear muscle reflexes.

Our previous work has shown that stapedius motoneurons can be divided into categories based on the laterality of their response to sound and that these categories are partly spatially segregated in the brainstem. Stapedius motoneurons which respond to contralateral sound have their cell bodies in one location, those which respond to sound in either ear in another location, and so forth. During the past year, we have attacked the question of whether there is also spatial segregation in the organization of stapedius motor fibers as they enter the stapedius muscle. In other muscle systems which show central segregation, there is also peripheral segregation.

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Unanesthetized Decerebrate Cats to AM and Pure Tones: Analysis with Autocorrelation/Power-spectrum," *Hear. Res.* 45: 95-113 (1990).

<sup>13</sup> B. Delgutte, "Physiological Mechanisms of Psychophysical Masking: Observations from Auditory-nerve Fibers," *J. Acoust. Soc. Am.* 87: 791-809 (1990); B. Delgutte, "Two-tone Suppression in Auditory-nerve Fibers: Dependence on Suppressor Frequency and Level," *Hear. Res.* 49: 225-246 (1990).

<sup>14</sup> J.T. Rubinstein, "Analytical Theory for Extracellular Stimulation of Nerve with Focal Electrodes. II. Passive Myelinated Axon," *Biophys. J.*, forthcoming.



We have attacked this question by two methods. First, we have examined the locations of labeled cells following injections of single fascicles of the stapedius nerve with HRP and compared these patterns with those produced by injections of the whole stapedius muscle. All of the individual fascicles received innervation from all four brainstem regions which have stapedius motoneurons. This pattern rules out strict segregation within individual fascicles, but considering that the proportions of labeled cell bodies in each region varied from one case to the next, there may be some weak segregation.

Our second method was to analyze the distribution of unit types obtained in recordings from individual fascicles. There were fascicles which contained stapedius motoneurons in each of the four laterality types, fascicles which contained stapedius motoneurons of only one type, and everything in between. A statistical analysis of these data suggests that the distribution could not have been produced by a random selection of unit types from a large pool. This is consistent with some segregation of stapedius motoneurons present at the level of the fascicles entering the stapedius. The function of this segregation for the stapedius is not clear. The general principal of the presence of peripheral segregation if there is central segregation is upheld, but the degree of segregation peripherally may be less than it is centrally.

During the past year, data analysis and writing have been done to prepare for publication our results on the responses to sound and axon conduction velocities of stapedius motoneurons (These data provide the basis for the division of stapedius motoneurons into response-type groups.)

We have begun work on a project to measure the overall change in transmission,  $\Delta T$ , produced by middle-ear muscles to determine whether the maximum  $\Delta T$  is substantially different for crossed, uncrossed and binaurally-evoked stapedius reflexes. To measure  $\Delta T$ , we have assembled acoustic systems which have two sound sources and a microphone in each ear canal and have built a suitable computer-controlled signal analysis system. We are now beginning work on measurement techniques for determining the mechanical output of the middle ear.

## 1.5 Cochlear Efferent System

### Project Staff

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

Our aim is to understand the physiological effects produced by medial olivocochlear (MOC) efferents which terminate on outer hair cells in the mammalian cochlea. It has been proposed that (1) a major role of medial olivocochlear efferents is to control the cochlear amplifier and (2) the mechanical output of the cochlear amplifier produces traveling waves in both directions along the cochlea with the backward waves producing stimulus frequency otoacoustic emissions (SFEs).

To test these hypotheses, the effect of efferents on SFEs was determined by measuring changes in the ear canal sound pressure,  $\Delta P$ , produced by stimulation of medial efferents.<sup>15</sup> For most probe tones,  $\Delta P$  amplitude was a few dB lower than the amplitude of the SFE and  $\Delta P$  phase was opposite that of the SFE. These data indicate that efferent stimulation inhibits the SFE. In addition, the efferent-induced change in the compound action potential of the auditory nerve ( $\Delta N1$ ) was compared to  $\Delta P$  using tone pips (for  $\Delta N1$ ) and tones (for  $\Delta P$ ) of the same frequency and level. As the amplitude of the efferent effect was varied by changing efferent shock rate or amplitude,  $\Delta N1$  was approximately proportional to  $\Delta P$ . These data are consistent with the hypothesis that efferents control the gain of an amplifier which is responsible for the sensitivity of the cochlea. In contrast to previous work which has shown that efferents affect emissions generated by cochlear nonlinearities, the present work demonstrates that an efferent effect on an emission may be generated primarily by linear processes and may directly reflect efferent effects on the cochlear amplifier.

Efferent activity and two-tone suppression might affect the cochlear amplifier at different sites and produce similar effects. Their effect on stimulus-frequency otoacoustic emissions (SFEs) in cats was compared by measuring the vector change in ear-canal sound pressure. The results indicate that contributions to the SFE originate along a large fraction of the length of the cochlea and that SFEs may provide a "window" into the action of the cochlear amplifier.<sup>16</sup>

<sup>15</sup> J.J. Guinan, Jr., "Inhibition of Stimulus Frequency Emissions by Medial Olivocochlear Efferent Neurons in Cats," Association for Research in Otolaryngology, Abstracts 14, forthcoming.

<sup>16</sup> J.J. Guinan, Jr., "Changes in Stimulus Frequency Otoacoustic Emissions Produced by Two-tone Suppression and

We have published a paper which shows the signal processing properties of a group of brainstem auditory neurons.<sup>17</sup>

Work has begun on a project to determine the correspondence between the number of medial efferents that fire and the effects produced. Our intention is to evoke activity in medial efferents with brainstem shocks and determine the percentage of them which fire by analyzing recordings from single medial efferent fibers. The effects of this efferent activity will be assessed by measuring changes in N1. The results are intended to determine the size of the effect of a single efferent fiber on auditory-nerve responses, and how these effects summate (i.e., linearly, or with saturation, etc).

### **Publications**

Guinan, J.J., Jr. "Inhibition of Stimulus Frequency Emissions by Medial Olivocochlear Efferent Neurons in Cats." Association for Research in Otolaryngology, Abstracts 14. Forthcoming.

Guinan, J.J., Jr. "Changes in Stimulus Frequency Otoacoustic Emissions Produced by Two-tone Suppression and Efferent Stimulation in Cats." *Proceedings of the 1990 Conference on the Mechanics and Biophysics of Hearing*. Forthcoming.

Guinan, J.J., Jr., and R.Y.S. Li. "Signal Processing in Brainstem Auditory Neurons which Receive Giant Endings (Calyces of Held) in the Medial Nucleus of the Trapezoid Body of the Cat." *Hear. Res.* 49: 321-334 (1990).

## **1.5.1 The Generators of the Brainstem Auditory Evoked Potential**

### **Project Staff**

Professor Nelson Y.S. Kiang, Professor William T. Peake, Dr. Barbara C. Fullerton, Jennifer R. Melcher

When a punctate sound is presented to the ear, a time-varying potential can be recorded from electrode pairs on the surface of the head. The potential waveform at short latencies (< 10 msec following the stimulus) is distinguished from the potential at longer latencies by a

characteristic series of deflections, each about one msec in duration. Similar waveforms have been measured in every mammalian species in which recordings have been attempted. It is believed that the short-latency potential is generated by cells in the auditory nerve and brainstem. Thus, this potential is called the brainstem auditory evoked potential (BAEP).

The goal of Melcher's thesis is to better understand which cells generate the different components of the BAEP. In previous years progress has been made along two lines: (1) a series of lesion experiments were begun, and (2) a model for BAEP generation was developed. The model relates the activity of individual cells in the auditory pathway to the BAEP and has served as a guide for designing and interpreting the experiments. The lesion experiments involve injecting a neurotoxin into different parts of the cat brainstem and correlating the resulting cell loss with changes in the BAEP.

The lesion experiments and a preliminary analysis of the cell loss in each case were completed during the last year. We have determined that two of the BAEP components are generated by cells in separate pathways within the auditory system. A more refined assessment of cell loss is in progress.

### **Publication**

Melcher, J.R., B.C. Fullerton, J.J. Guinan, N.Y.S. Kiang, and I.M. Knudson. "Cellular Generators of the Brainstem Auditory Evoked Potential in Cat." Poster presentation at the 20th Annual Meeting of the Society for Neuroscience, St. Louis, Missouri, October 28-November 2, 1990.

## **1.6 Cochlear Implants**

### **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

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Efferent Stimulation in Cats," *Proceedings of the 1990 Conference on the Mechanics and Biophysics of Hearing*, forthcoming.

<sup>17</sup> J.J. Guinan, Jr., and R.Y.S. Li, "Signal Processing in Brainstem Auditory Neurons Which Receive Giant Endings (Calyces of Held) in the Medial Nucleus of the Trapezoid Body of the Cat," *Hearing Res.* 49: 321-334 (1990).

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: (1) the complex, electrically heterogeneous structure of the cochlea; (2) the geometry and placement of the stimulating electrodes, (3) the stimulus waveform, and (4) 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 interpreting the results of experiments involving intracochlear stimulation of animal and human subjects. As a first step towards understanding this interaction, 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 to use these potential distributions as inputs that drive models of auditory nerve fibers.

Last year, we continued the development of the three-dimensional, finite element model of the human cochlea for prediction of the potential distribution produced in this structure by electrical stimulation of model electrodes of arbitrary position and geometry. We have begun (1) investigating different numerical techniques that will allow us to specify anisotropic media and (2) porting the model to a Thinking Machine computer to reduce computational time. Continued measurements of potential at unstimulated electrodes made in ten subjects implanted with intracochlear electrodes confirmed the asymmetric potential distributions predicted by the model. Psychophysical measures of the interaction between two electrodes stimulated simultaneously also exhibited the predicted asymmetries in the 13 subjects measured to date.

We have also begun work on the development of linear and nonlinear models of extracellular excitation of myelinated and unmyelinated nerve fibers. Psychophysical measures have confirmed model predictions that an electrical stimulus composed of a single, biphasic pulse of subthreshold amplitude produces a residual membrane depolarization that can reduce the threshold of a second pulse when it follows the first within several hundred microseconds. The 100  $\mu$ s time constant of this sensitization effect as measured psychophysically is consistent with the time constant of the residual depolarization predicted by the model.

## ***Publications***

Eddington, D.K. "An Electroanatomical Model of Intracochlear Electrical Stimulation." Paper presented at the Second International Cochlear Implant Symposium, Iowa City, Iowa, June 4-8, 1990.

Rubinstein, J.T. "An Analytical Model for Electrical Stimulation of Nerve 2: Passive Myelinated Axon." *Biophys. J.* Forthcoming.

## ***Project B: Psychophysical Measures and their Correlation with Speech Reception***

### **Project Staff**

Dr. Donald K. Eddington

One striking aspect of speech reception measurements made with subjects using cochlear implants is the wide range of performance. This project is designed to identify basic psychophysical measures that correlate with the subject's speech reception ability. These correlations should help us to both identify basic performance deficits that might be overcome with alternative processing schemes and to relate correlations found between pathology and psychophysical measures in experimental animals to their potential effect on speech reception.

We have reported correlations of speech reception with two psychophysical measures [threshold ( $r = -0.78$ ) and interaction ( $r = -0.86$ )] in 16 subjects. These correlations are consistent with an interpretation that the density of excitable fibers that remain in each subject is one underlying factor important for speech reception.

### ***Publication***

Eddington, D.K. "Psychophysical Correlates of Speech Reception in Subjects Using Multi-channel Cochlear Implants." Paper presented at the Second International Cochlear Implant Symposium, Iowa City, Iowa, June 4-8, 1990.

## ***Project C: Cues Used by the Brain to Assign Pitch Based on Electrode Position***

### **Project Staff**

Dr. Donald K. Eddington

Subjects with intracochlear electrodes provide a unique opportunity to elicit activity patterns in the array of auditory nerve fibers that cannot be elic-

ited in normal hearing individuals using acoustic stimuli. This opportunity to present novel inputs to the brain and to determine how human subjects perceive them provides a powerful tool for probing the processing mechanisms of the "central processor." We have been using this tool to identify cues that the brain uses to determine the relative pitch of perceptions produced by two electrical stimuli that are temporally but not spatially equivalent. Preliminary results in three subjects indicate that the subjects use the apical boundary of excitation when assigning relative pitch to these stimuli.

### ***Project D: 3D Reconstruction and Display of Data Obtained from Computerized Tomography (CT) of the Temporal Bone***

#### **Project Staff**

Meng Y. Zhu

The goal of this project is to construct 3D computer representations of the inner ear structures by reconstructing the x-ray attenuation data from a sequence of parallel slices obtained during CT scanning. In order to optimize the resolution of the representation, raw CT data are used in the reconstruction rather than the image data derived from a down-sampling process. One use of these 3D representations is to compute intracochlear electrode positions in individual human subjects. These positions are helpful in interpreting the results of psychophysical measures such as electrode interaction and can be used to customize our models of current spread for individual subjects. Considerable effort has also been invested in designing software for the display of these 3D structures.

## **1.7 Anatomical Basis for the Relationships Between Binaural Hearing and Brainstem Auditory Evoked Potentials in Humans**

#### **Project Staff**

Dr. Jill C. Gardner, Dr. Robert A. Levine, Dr. Barbara C. Fullerton, Ellen Carlisle, Steven M. Stufflebeam

In ongoing studies, we have been making behavioral and physiological measurements on patients with multiple sclerosis (MS) who show specific losses in auditory functions. We are investigating

whether these functions, which involve using cues to determine the lateral position of sounds (auditory lateralization), depend on the integrity of the brainstem auditory pathway. We are using nuclear magnetic resonance (nmr) imaging to localize lesions, which occur in multiple sclerosis, with respect to the nuclei and fiber tracts of the auditory pathway in the brainstem.

We have had good initial success correlating the sites of brainstem lesions to the performance of the MS patients on a variety of tasks. Over 50% of the patients we have examined showed deficits in auditory lateralization although their hearing appeared to be otherwise normal. In the nmr scans, some of the abnormalities were focal and clearly defined, typical of what has been described in MS, while others were diffuse, and in some cases covered a considerable extent of the brainstem. All of the subjects with lesions in the brainstem auditory pathway performed abnormally on some aspect of the lateralization tasks. The subjects with diffuse lesions showed deficits far more severe than the MS group as a whole.

Previous studies, which for the most part focused on abnormalities in the cerebral cortex, have found little relationship between nmr "lesions" and the symptoms of MS patients. Our initial analysis of the data indicates that there are clear correlations between the extent of lesions, the psychoacoustics and a physiological measure, and the brainstem auditory evoked potential, which is widely used clinically. Our data suggest that we may be seeing a variety of abnormalities in the nmr scans that have not been previously described. Our efforts at the present are directed toward developing methodologies for characterizing the normal brainstem and defining and quantifying MS related abnormalities in magnetic resonance scans.

#### ***Publications***

Furst, M., J.C. Gardner, R.A. Levine, B. Fullerton, and P. Cuneo. "Localizing the Brainstem Auditory Pathway in Human Magnetic Resonance Images: An Algorithm Matching MR Scans to a Computerized Anatomic Atlas." Paper presented at the Association for Research in Otolaryngology, 14th Midwinter Meeting, St. Petersburg, Florida, February 1990.

Gardner, J.C., M. Furst, R.A. Levine, B. Fullerton, and B.R. Rosen. "An Anatomic Atlas and Mapping Algorithm for Localizing the Brainstem Auditory Pathway on Magnetic Resonance Scans." Paper presented at the Society of Magnetic Resonance in Medicine, Ninth Annual Meeting, New York, 1990.



*From left, graduate student Donna K. Hendrix, Professor Lawrence S. Frishkopf, Professor Thomas F. Weiss, and Research Scientist Dr. Dennis M. Freeman are shown with plastic models of the inner ear of a lizard (magnified 50 times).*

