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

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. Cochlear implants electrically stimulate intracochlear electrodes to elicit patterns of auditory nerve fiber activity that the brain can learn to interpret. The ultimate goal for these devices is to provide speech communication for the profoundly deaf.

1.2 Signal Transmission through the External and Middle Ear

The goal of our work is generate and test physical rules that relate specific external and middle-ear structures to the overall function of the external and middle ear.

1.2.1 Structure-Function Relations in Middle Ears

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Dr. John J. Rosowski, Professor William T. Peake, Janice L. Balzer, Greg T. Huang, Michael E. Ravicz, David A. Steffens, Su W. Teoh, Susan E. Voss

The external and middle ear transform environmental sound from airborne atmospheric vibrations to sound pressures and vibrations in the fluid-filled inner ear. This transformation results from the action of specific structures including (1) the funnel-like shape of the external ear tube, (2) the pressure-transformer mechanism of the tympanic membrane and the stapes footplate, and (3) the lever mechanism of the ossicles. The transformation is greatly influenced by the acoustical and mechanical properties of the ear's structures. Our aim last year was to elucidate the function of three important structural features.

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The Cochlear Windows

We continued our efforts to test and refine the classic assumption that the cochlea responds to the pressure difference between the cochlear windows within the middle ear. Cats were prepared so that we could independently control the sound pressure magnitudes and angles of stimuli presented to the two windows. Measurements of cochlear responses to these stimuli were analyzed using linear systems theory to determine the common-mode and difference-mode gain of the inner ear. These measurements suggest that the common-mode gain is 20-40 dB smaller than the difference mode gain. This work is included in a master's thesis submitted to the Department of Electrical Engineering and Computer Science on January 20, 1995.[2]

Middle-Ear Size

We have also investigated the effect of ear size on middle-ear function by examining middle-ear structure and its acoustic function in members of the cat family. Three different kinds of measurements were made: (1) Anatomical measurements of skull and bony ear size were made from more than 100 museum specimens that included 32 of the 36 living species of cat. Middle-ear volume was demonstrated to be proportional to the square of skull length, while the cross-sectional area of bony ear canal and tympanic ring grows as the square-root of skull length. This dichotomy suggests changes in function with animal size. (2) The middle-ear air spaces of a deceased domestic cat and a lion were serially reconstructed from anatomical and CT scanned sections. These data were consistent with the museum data in that while the volume of the lion middle-ear air spaces was nearly 20 times that of the domestic cat, the area of the lion's tympanic membrane is only three times larger. (3) Acoustic measurements of middle-ear function were made in the deceased lion which suggest rules that relate impedance to size in this family. This work is the

subject of a poster at the Association for Research in Otolaryngology meeting.[3]

Pars Flaccida of the Tympanic Membrane

We are also investigating the contribution of the *pars flaccida* of the tympanic membrane to middle-ear mechanics. The tympanic membrane of many mammals is composed to two parts. The *pars tensa* is stiff and is attached to the ossicles, while the compliant *pars flaccida* is generally small and distant from the ossicular attachment. Most treatments of middle-ear mechanics ignore the flaccida. We have investigated the role of *pars flaccida* in the gerbil ear where the *flaccida* takes up about 20 percent of the total membrane area. Measurements of middle-ear input impedance, middle-ear pressure and middle-ear transmission made with normal, stiffened and absent *flaccida* have demonstrated that the *flaccida* has a significant effect on middle-ear mechanics especially at low frequencies. Improved middle-ear models that include *pars flaccida* effects are being investigated. Part of this work is the subject of S.W. Teoh's master's thesis.[4]

1.2.2 Basic and Clinical Studies of Middle-Ear Function

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Dr. John J. Rosowski, Professor William T. Peake, Janice L. Balzer, Dr. Sunil Puria, Michael E. Ravicz, David A. Steffens

We have spent the last year testing and revising our models of human middle-ear function. New model analyses of the effects of middle-ear reconstructive procedures were prepared and published.[5]

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2 S.E. Voss, *Is the Pressure Difference Between the Oval and Round Window the Effective Acoustic Stimulus to the Inner Ear*, S.M. thesis, Dept. of Electr. Eng. and Comput. Sci., MIT, 1995.

3 J.J. Rosowski, W. T. Peake, G. T. Huang, and D. T. Flandermeyer, "Middle-ear Structure and Function in Felidae," *Abstracts of the 18th Midwinter Meeting of the Association for Research in Otolaryngology*, forthcoming.

4 S.W. Teoh, "Effects of Pars Flaccida in Middle-Ear Acoustic Transmission", S.M. thesis, Dept. of Electr. Eng. and Comput. Sci., MIT, forthcoming.

These analyses made predictions about the effect of variations in ossicular prosthetic shapes and implantation procedures. The predictions of outcome for one class of surgical procedures (Type IV Tympanoplasty for severely diseased middle ears) were demonstrated to compare well with real surgical cases[6] and point out the importance of considering the acoustic effects of the surgical procedure on hearing outcome. Empirical tests of the Type IV model were also performed using a cadaveric human temporal-bone preparation. Measurements were made of the stapes motion in a mock Type-IV preparation that allows manipulation of middle-ear volume and tympanic-graft stiffness. The results of these tests were consistent with model predictions.

1.2.3 Publications

Journal Articles

Merchant, S.N., J.J. Rosowski and M.E. Ravicz. "Mechanics of Type IV and V Tympanoplasty. II. Clinical Analysis and Surgical Implications." *Am. J. Otol.* Forthcoming.

Rosowski, J.J., S.N. Merchant and M.E. Ravicz. "Mechanics of Type IV and V Tympanoplasty. I. Model Analysis and Predictions." *Am. J. Otol.* Forthcoming.

Rosowski, J.J. and S.N. Merchant. "Mechanical and Acoustical Analyses of Middle-ear Reconstruction." *Am. J. Otol.* Forthcoming.

Meeting Paper

Rosowski, J.J., W. T. Peake, G, T. Huang and D. T. Flandermeyer. "Middle-ear Structure and Function in Felidae." *Abstracts of the Eighteenth Midwinter Meeting of the Association for Research in Otolaryngology,* St. Petersburg, Florida, February 5-9, 1995. Forthcoming.

Theses

Teoh, S.W. *Effects of Pars Flaccida in Middle-Ear Acoustic Transmission.* M.S. thesis. Dept. of Electr. Eng. and Comput. Sci., MIT. Forthcoming.

Voss, S.E. *Is the Pressure Difference between the Oval and Round Window the Effective Acoustic Stimulus to the Inner Ear.* M.S. thesis. Dept. of Electr. Eng. and Comput. Sci., MIT, 1995.

1.3 Cochlear Mechanisms

Sponsor

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Project Staff

Professor Thomas F. Weiss, Dr. Dennis M. Freeman, Dr. Devang M. Shah, C. Cameron Abnet, Alexander J. Aranyosi, C. Quentin Davis, Zoher Z. Karu, Lisa F. Shatz

Our goal is to study the cochlear mechanisms by which motions of macroscopic structures in the inner ear produce discharges in nerve fibers that innervate the hair cells.

1.3.1 Osmotic Responses of the Tectorial Membrane in the Mouse, Chick, and Alligator Lizard

We completed studies of osmotic responses of the isolated tectorial membrane (TM) in response to changes in bath ion composition in the chick[7] and the mouse cochlea.[8] We have also presented a comparative study of the osmotic responses in

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5 J.J. Rosowski and S.N. Merchant, "Mechanical and Acoustical Analyses of Middle-ear Reconstruction," *Am. J. Otol.,* forthcoming; J.J. Rosowski, S.N. Merchant and M.E. Ravicz, "Mechanics of Type IV and V Tympanoplasty. I. Model Analysis and Predictions," *Am. J. Otol.,* forthcoming.

6 S.N. Merchant, J.J. Rosowski and M.E. Ravicz "Mechanics of Type IV and V Tympanoplasty. II. Clinical Analysis and Surgical Implications," *Am. J. Otol.,* forthcoming.

7 D.M. Freeman, D.A. Cotanche, F. Ehsani, and T.F. Weiss, "The Osmotic Response of the Isolated Tectorial Membrane of the Chick to Isosmotic Solutions: Effect of Na , K , and Ca^2 Concentration," *Hear. Res.* 79: 197-215 (1994).

8 D.M. Shah, D.M. Freeman, and T.F. Weiss, "The Osmotic Response of the Isolated, Unfixed Mouse Tectorial Membrane to Isosmotic Solutions: Effect of Na , K , and Ca^2 Concentration," submitted to *Hear. Res.* 1995; D.M. Shah, D.M. Freeman, and T.F. Weiss, "The

three species—mouse, chick, and alligator lizard.[9] TMs from all three species show qualitatively similar osmotic responses. In all three species, increasing the calcium concentration from the low values typical for endolymph to the higher concentrations found in perilymph causes the TM to shrink reversibly. In all three species, for solutions with low calcium concentrations, the TM swells when isosmotic, high-sodium solutions are substituted for high-potassium solutions. These qualitative similarities suggest that common mechanisms are at work in all three species. However, the magnitudes of osmotic responses of the chick TM are much greater than are those of either the mouse or lizard TM. Furthermore, the spatial pattern of swelling differs across these three species. Osmotic responses for the mouse are primarily changes in thickness with little change in the orthogonal directions. For the chick, radial displacements are often larger than thickness changes. Osmotic responses of the lizard are largely isotropic. These differences in response patterns suggest that there are intrinsic differences in the TMs of these three species. The differences may well be related to differences in ultrastructure and biochemical composition that have been described.

Our measurements of osmotic responses of the tectorial membranes are consistent with simple gel models that are similar to those used to describe other connective tissues. Biochemical studies have shown that the TM contains fixed (nondiffusible), ionizable charge groups that can bind ions differentially. The binding of ions (1) modulates the fixed charge density, (2) changes the concentration of mobile counterions in the tissue, and (3) causes water to flow into or out of the tissue. Thus, the tissue can shrink and swell in response to changes in bath composition, even those that are isosmotic.

In principle, the state of ionization of any of the fixed, ionizable groups in the TM that can bind hydrogen ions will depend upon pH. Thus, we might expect a change in pH to result in shrinking or swelling of the TM. In other connective tissues, it has been possible to infer important properties, such as the charge density of the fixed charges, from measurements of hydration (shrinking/swelling) as a function of pH. Therefore, we have initiated a study of the effect of pH on the isolated mouse TM. Preliminary results have shown that changes in pH in the range 3-11 cause large, rapid osmotic responses. In general, the TM swells for both low and high pH, but is independent of pH for pH in the range 6-8.

1.3.2 Measurement of Sound-Induced Motion of Cochlear Structures

We have developed a system to measure the sound-induced motion of key structures in the cochlea of the alligator lizard, including the basilar and tectorial membranes, the hair bundles of hair cells, and even individual stereocilia. The capabilities of the system have been examined in preliminary experiments. The basic idea is to obtain images of the receptor organ under stroboscopic illumination synchronized with the hydrodynamic stimulus to the organ. Motion information is calculated from pairs of images obtained at different phases of the motion. The methods for extracting motion estimates from the images are described in a manuscript[10] and preliminary results have been presented.[11]

1.3.3 Publications

Journal Articles

Davis, C.Q., and D.M. Freeman. "Statistics of Sub-Pixel Motion Estimates Based on Optical Flow." Submitted to *IEEE Trans. Pattern Anal. Mach. Intellig.*

Freeman, D.M., D.A. Cotanche, F. Ehsani, and T.F. Weiss. "The Osmotic Response of the Isolated Tectorial Membrane of the Chick to Isosmotic Solutions: Effect of Na^+, K^+, and Ca^{2+} Concentration." *Hear. Res.* 79: 197-215 (1994).

Osmotic Response of the Isolated, Unfixed Mouse Tectorial Membrane: Effect of Na^+, K^+, and Ca^{2+} Concentration," presented at the 18th Midwinter Research Meeting of the Association for Research in Otolaryngology, St. Petersburg, Florida, February 5-9, 1995.

9 D.M. Freeman and T.F. Weiss, "Species Dependence of Osmotic Responses of the Tectorial Membrane: Implications of Structure and Biochemical Composition," presented at the 18th Midwinter Research Meeting of the Association for Research in Otolaryngology, St. Petersburg, Florida, February 5-9, 1995.

10 C.Q. Davis and D.M. Freeman, "Statistics of Sub-Pixel Motion Estimates Based on Optical Flow," submitted to *IEEE Trans. Pattern Anal. Mach. Intellig.*

11 C.Q. Davis and D.M. Freeman, "Direct Observations of Sound-Induced Motions of the Reticular Lamina, Tectorial Membrane, Hair Bundles, and Individual Stereocilia," presented at the 18th Midwinter Research Meeting of the Association for Research in Otolaryngology, St. Petersburg, Florida, February 5-9, 1995.

Shah, D.M., D.M. Freeman, and T.F. Weiss. "The Osmotic Response of the Isolated, Unfixed Mouse Tectorial Membrane to Isosmotic Solutions: Effect of Na^+, K^+, and Ca^{2+} Concentration." Submitted to *Hear. Res.*

Meeting Papers

Davis, C.Q., and D.M. Freeman. "Direct Observations of Sound-Induced Motions of the Reticular Lamina, Tectorial Membrane, Hair Bundles, and Individual Stereocilia." Presented at the 18th Midwinter Research Meeting of the Association for Research in Otolaryngology, St. Petersburg, Florida, February 5-9, 1995.

Freeman, D.M., and T.F. Weiss. "Species Dependence of Osmotic Responses of the Tectorial Membrane: Implications of Structure and Biochemical Composition." Presented at the 18th Midwinter Research Meeting of the Association for Research in Otolaryngology, St. Petersburg, Florida, February 5-9, 1995.

Shah, D.M., D.M. Freeman, and T.F. Weiss. "The Osmotic Response of the Isolated, Unfixed Mouse Tectorial Membrane: Effect of Na^+, K^+, and Ca^{2+} Concentration." Presented at the 18th Midwinter Research Meeting of the Association for Research in Otolaryngology, St. Petersburg, Florida, February 5-9, 1995.

1.4 Stimulus Coding in the Auditory Nerve and Cochlear Nucleus

Sponsor

Project Staff

Dr. Bertrand Delgutte, Dr. Peter Cariani, Martin F. McKinney

This research investigates neural mechanisms underlying auditory perception at the level of the auditory nerve and cochlear nucleus. In the past year, we have focused on two projects: (1) correlates of the "stretched octave" in interspike intervals of auditory-nerve fibers, and (2) representation of vowels in the auditory nerve. We have also written a review of models[12] that predict performance in basic psychophysical tasks based on the activity of auditory-nerve fibers.

When listeners are asked to adjust the frequencies of two pure tones so that they sound one octave apart, they choose frequency ratios slightly greater than 2:1. In order to investigate possible correlates of this "octave stretch" phenomenon in the temporal patterns of neural discharges, we recorded the activity of auditory-nerve fibers in anesthetized cats for low-frequency pure-tone stimuli, taking particular care to obtain very precise measurements of spike times. As is well known, interspike intervals for low-frequency (< 4-5 kHz) tones occur approximately at the stimulus period and its multiples. Our results show that the earlier modes of interspike interval histograms (ISIH) actually occur slightly, but systematically later than the times expected from the stimulus period. These mode offsets are consistent with the refractory properties of neurons: they are significant for interspike intervals smaller than 5 msec, and decrease monotonically with increasing length of the interspike interval.

Two models were investigated for their ability to predict an octave stretch based on the offsets of modes of ISIHs. The first model matches modes of the ISIH for the lower-frequency tone with even-ordered modes of the ISIH for the higher-frequency tone. Subjective octave corresponds to the frequency ratio giving the best match. This model predicts no octave stretch because mode offsets depend primarily on the length of the interspike interval regardless of stimulus frequency. The second model scales the time scale of the higher-frequency ISIH by a factor of two before matching its modes with corresponding modes for the lower-frequency ISIH. This model was found to predict an octave stretch consistent with psychophysical data. In particular, the trend of increasing stretch with increasing frequency was correctly predicted. These results provide support for temporal models of pitch perception.

Our research on the auditory representation of vowels is carried out in collaboration with Dr. Tatsuya Hirahara from the NTT Basic Research Laboratory in Tokyo. Dr. Hirahara's psychophysical experiments suggest that the identity of front vowels depends primarily on the amplitude ratio of two harmonics of the fundamental frequency in the vicinity of the first formant. Our experiments aimed at

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[12] B. Delgutte, "Physiological Models for Basic Auditory Percepts," in *Auditory Computation*, eds. H. Hawkins and T. McMullen (New York: Springer-Verlag, forthcoming).

determining how these "crucial" harmonics are encoded in both the average discharges rates and the temporal discharge patterns of auditory-nerve fibers. Preliminary results using vowel stimuli with a wide range of fundamental frequencies suggest that profiles of average rates against CF show broad local maxima near the frequencies of the crucial harmonics and that the relative amplitude of these peaks varies in an orderly fashion with formant frequency. These results generally support the concept of crucial harmonics as a possible basis for vowel distinctions and suggest that the auditory nerve may convey more rate-place information than previously thought about voice pitch and vowel identity.

Publications

Cariani, P.A., and B. Delgutte. "Transient Changes in Neural Discharge Patterns may Enhance the Separation of Concurrent Vowels with Different Fundamental Frequencies." *J. Acoust. Soc. Am.* 95: 2842 (1994).

Delgutte, B. "Physiological Models for Basic Auditory Percepts." In *Auditory Computation.* Eds. H. Hawkins and T. McMullen. New York: Springer-Verlag. Forthcoming.

Delgutte, B. "Neural Correlates of Basic Psychophysical Functions." *Abstracts of the 18th Midwinter Meeting of the Association for Research in Otolaryngology,* St. Petersburg, Florida, February 5-9, 1995.

McKinney, M.F., and B. Delgutte. "Physiological Correlates of the Stretched Octave in Interspike Intervals of Auditory-Nerve Fibers." *Abstracts of the 18th Midwinter Meeting of the Association for Research in Otolaryngology,* St. Petersburg, Florida, February 5-9, 1995.

1.4.1 Binaural Interactions in Auditory Brainstem Neurons

Sponsor

National Institutes of Health
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Project Staff

Dr. Bertrand Delgutte, Dr. Ruth Y. Litovsky

We are studying neural mechanisms for sound localization in the auditory midbrain in collaboration with Dr. T.C.T. Yin and his colleagues at the University of Wisconsin in Madison. Our specific aim is to determine which of many acoustic cues for sound localization, including interaural time (ITD), interaural level (ILD) differences, and spectral shape, are most important for the directional sensitivity of cells in the central nucleus of the inferior colliculus (IC). We use "virtual-space" (VS) stimuli that use closed acoustic systems to mimic the sound pressure waveforms that are produced in the ear canals for free-field stimuli. VS stimuli are ideally suited for our aims because they are realistic and rich in localization cues, and they provide precise control over each individual cue. We have previously reported that for IC neurons with high characteristic frequencies (> 5 kHz), ILD is generally the most potent cue, followed by spectral shape, and by ITD. In the past year, we wrote a brief report of these findings,[13] and extended our work in two directions: (1) comparing the response of IC neurons to VS stimuli with responses to simpler stimuli, and (2) investigating the response to stimuli that produce a precedence effect.

Central auditory neurons can be classified into binaural types by comparing their responses to monaural stimuli with responses to binaural stimuli. For example, binaural interactions for IC neurons are classified as being either inhibitory or facilitatory depending on whether the response to binaural stimuli is smaller or larger than the response to the most effective monaural stimulus (usually the contralateral one). We found that binaural interactions measured with VS stimuli were consistent with those determined from responses to broadband noise. The most common type of interaction was mixed, with the ipsilateral ear being inhibitory for ILDs favoring the ipsilateral side, and facilitatory for ILDs favoring the contralateral ear. The effect of such mixed interactions is to enhance the directional sensitivity of IC neurons because the response to stimuli located on the contralateral side is enhanced while the response to ipsilateral stimuli is suppressed. A more quantitative attempt to predict responses to VS stimuli from responses to broadband noise was made by (1) measuring discharge rate versus ILD for broadband noise, and (2) transforming these rate-ILD functions into rate-

[13] B. Delgutte, P.X. Joris, R.Y. Litovsky, and T.C.T. Yin, "Relative Importance of Different Acoustic Cues to the Directional Sensitivity of Inferior-Colliculus Neurons," in *Advances in Hearing Research,* G.A. Manley, G.M. Klump, C. Kppl, H. Fastl and H. Oeckinghaus, eds., (Singapore: World Scientific, forthcoming).

azimuth functions using head-related transfer functions for frequencies near the CF. Predicted rate-azimuth functions were in good agreement with responses to VS stimuli for about half of the cells tested. We are currently investigating whether predictions can be improved by an appropriate choice of the linear filter representing the frequency selectivity of each neuron.

The precedence effect is an auditory illusion important for accurate sound localization in echoic environment. Drs. Yin and Litovsky have previously reported correlates of the precedence effect in the responses of IC neurons: When two brief binaural stimuli are presented in succession, the response to the lagging stimulus (which simulates an echo) is suppressed for a majority of neurons. Such echo suppression is found for both free-field and dichotic stimuli, and has a time course ranging from 1 msec to 100 msec. Recent pilot experiments show that echo suppression also occurs with VS stimuli, and that the time course of suppression is similar to that observed for free-field and traditional dichotic stimuli. Our data further suggest that echo suppression is largest for leading VS stimuli that produce the largest response, consistent with free-field results. These pilot experiments show the feasibility of using VS stimuli for studying which localization cues are the most important for the precedence effect.

Publications

Delgutte, B., P.X. Joris, R.Y. Litovsky, and T.C.T. Yin. "Relative Importance of Different Acoustic Cues to the Directional Sensitivity of Inferior-Colliculus Neurons." In *Advances in Hearing Research*. Eds. G.A. Manley, G.M. Klump, C. Kppl, H. Fastl and H. Oeckinghaus. Singapore: World Scientific. Forthcoming.

Delgutte, B., P.X. Joris, R.Y. Litovsky, and T.C.T. Yin. "Different Acoustic Cues Contribute to the Directional Sensitivity of Inferior-Colliculus Seurons as Studied with Virtual-Space Stimuli." *Abstr. Assoc. Res. Otolaryngol.* 17: 86 (1994).

1.4.2 Electrical Stimulation of the Auditory Nerve

Sponsor

Project Staff

Dr. Bertrand Delgutte, Scott B.C. Dynes

We are studying physiological mechanisms of electrical stimulation of the cochlea in the hope that such information will help design improved speech processing schemes for cochlear implants. During the past year, we have investigated auditory-nerve fiber correlates of interactions observed psychophysically when pulsatile electric stimuli are applied in rapid succession. Specifically, experiments consisted in modifying the state of an auditory-nerve fiber using one or more monophasic current pulses, and then probing the threshold characteristics of this modified state using a single monophasic pulse. The probe pulse is used to measure the threshold and the dynamic range of the neural response for several intervals following the conditioning stimulus.

For single subthreshold cathodic conditioning pulses, the probe threshold was decreased for short ($<$ 600 *sec) probe delays. Following this, the probe threshold increased above its resting threshold about 1 dB for delays between 1 and 4 msec, after which it relaxed to its resting value. For anodic conditioners followed by a cathodic probe, the probe threshold was increased for short probe delays, followed by a short period when the threshold decreased below its resting value. For both anodic and cathodic conditioners, the initial phases are qualitatively consistent with a passive model in which the threshold change is due to a residual charge left by the conditioner on the neural membrane. However, the "overshoot" phases cannot be explained by a first-order passive model. Modeling studies suggest that this behavior can be reproduced using active models of nerve membranes that show large potassium currents (Hodgkin-Huxley, Rothman-Young-Manis) but not by models in which potassium currents are smaller (Frankenhaeuser-Huxley, Chiu et al., Schwarz-Eikhof).

Our results with subthreshold conditioners contrast with those of similar studies in other (nonauditory) systems. These studies show a monotonic relaxation of probe threshold to the resting value, contrary to the multiple-phase effects that we observe. Thus, the auditory nerve may well be specialized in its ability to respond to pulses presented in rapid succession. In support of this interpretation, the most successful model in predicting our data was originally developed for bushy cells in the cochlear nucleus. Bushy cells are thought to be specialized for fine timing. The finding that classic mammalian node models do not predict auditory nerve behavior as well as the bushy-cell model will impact the development of future models of the response of auditory neurons to electrical stimulation.

The relative spread of threshold (RS) is a measure of the variability in the neural threshold. It can also

been considered as a measure of the dynamic range of nerve fibers. Analysis of the RS of auditory-nerve fibers as a function of probe delay shows an increase in the RS for short probe delays for subthreshold conditioners, but not for suprathreshold conditioners. This result means that a subthreshold conditioning pulse effectively increases the dynamic range of the fiber for a brief period of time. This finding may partly explain why cochlear-implant patients show improved speech reception when the pulse rate of continuous-interleaved sampling processors is increased. The increase in the dynamic range may allow a more precise encoding of stimulus intensity and may create a more natural pattern of neural activity than that created by a slower pulse rate.

Publication

Dynes, S.B.C., and B. Delgutte. "Temporal Mechanisms of Auditory-Nerve Fiber Response to Multiple Electric Pulses." *Abstr. Assoc. Res. Otolaryngol.* 17: 163 (1994).

1.5 Interactions of Middle-Ear Muscles and Olivocochlear Efferents

Sponsor

National Institutes of Health
    Grant PO1-DC00119

Project Staff

Dr. John J. Guinan, Jr.

Our aim is to determine the actions and interactions of the acoustically elicited middle-ear muscle reflexes and the olivocochlear efferent reflexes.

During the past year, we have continued work to measure and understand the effects of medial efferent-inhibition in the cochlea on sound activation of the middle-ear muscle reflexes. We activate medial efferents by electrical stimulation with an electrode at the midline of the floor of the fourth ventricle and monitor middle-ear-muscle (MEM) acoustic reflexes by measurements of the reflex-induced changes in ear-canal sound pressure level. Our results to date show relatively small changes in

MEM reflex thresholds and level-function growth due to activation of medial efferents. This contrasts with reductions of 20 dB or more in the responses of auditory-nerve fibers with low spontaneous rates (SRs) at sound levels near the MEM reflex threshold and with the same activation of medial efferents. Our results contradict the hypothesis that low-SR fibers activate the MEM reflexes.

1.6 Cochlear Efferent System

Sponsor

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Project Staff

Dr. John. J. Guinan, Jr., Dr. Christopher A. Shera, Konstantina Stankovic

Our aim is to understand the physiological effects produced by efferents in the mammalian inner ear including medial olivocochlear efferents, which terminate on outer hair cells, and lateral efferents, which terminate on auditory-nerve fibers.

During the past year, two papers were published describing a new class of vestibular primary afferent neurons which respond to sound at moderately high sound levels.[14] These papers show responses of these fibers to clicks and tones, how these responses change with efferent stimulation, and demonstrate that the fibers originate in the saccule.

Tuning curves and other properties of acoustically-responsive vestibular afferents are described in a third paper.[15] Acoustically-responsive vestibular afferents in the cat have broad tuning curves centered at 800 Hz. At their best frequencies (BFs), the minimum thresholds for rate increases are 90 dB SPL or higher. At levels 10-15 dB lower than the rate thresholds, responses of these fibers synchronize to low-frequency tones. There was a slight tendency for fibers with higher BFs to have higher thresholds and wider tuning curves. With two sound sources, one tightly coupled to the skull and one loosely coupled, almost identical tuning curves were obtained. This is consistent with the adequate stimulus for acoustically responsive vestibular afferents being the sound conducted

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[14] McCue, M.P., and J.J. Guinan, Jr., "Acoustically-Responsive Fibers in the Vestibular Nerve of the Cat," *J. Neurosci.* 14: 6058-6070 (1994); McCue, M.P., and J.J. Guinan, Jr., "Influence Of Efferent Stimulation On Acoustically-Responsive Vestibular Afferents in the Cat," *J. Neurosci.* 14: 6071-6083 (1994).

[15] McCue, M.P., and J.J. Guinan, Jr., "Spontaneous Activity and Frequency Selectivity of Acoustically Responsive Vestibular Afferents in the Cat," submitted to *J. Neurophysiol.*

through the tympanic membrane and ossicles, rather than vibration from bone conduction. Sensitivity of the saccule to sound has a long phylogenetic history in vertebrates and our data show that this sensitivity is present in the cat.

We also studied the statistical properties of the spontaneous activity of these acoustically responsive vestibular afferents. Acoustically responsive vestibular afferents have spike interval distributions which are similar to those of the irregular vestibular neurons reported by Walsh et al.[16] Also, acoustically responsive vestibular afferents are virtually indistinguishable from the irregular vestibular afferents of Walsh et al. in plots of coefficient of variation versus skew from interval histograms. A detailed examination of the statistical properties of these fibers shows that their firing patterns can be closely modeled by probability density functions from the Erlang family. Although there are many possible explanations for the generation of such functions, one simple one is worth stating: The inter-spike intervals from acoustically responsive vestibular afferents are equivalent to those of a unit which, after it fires becomes unresponsive for about 9 ms, and then at the arrival of the second of two events from a Poisson event generator, it fires again. How this relates to the actual spike generation mechanism is not known. Since there is a strong correlation between threshold and spontaneous rate in cochlear auditory-nerve fibers, we looked for such a correlation in acoustically responsive vestibular afferents. We found no obvious relationship. There was, however, a slight tendency for more irregular fibers to have lower thresholds. These data are described by McCue and Guinan.[15]

During the past year, we have completed a project and submitted a paper comparing efferent effects measured by compound action potentials versus by ear-canal distortion products.[17] This work was done so that we could understand the reasons why measurements of efferent responses in humans show lower values than measurements of efferent responses in cats. Efferents were activated by sound in the contralateral ear in cats in which the middle-ear muscles had been cut, or in which middle-ear muscle reflexes were abolished by barbiturate anesthesia. Cochlear mechanical effects were monitored by measuring the distortion product otoacoustic emission (DPOAE) evoked by

two-tone stimuli (frequency: f1 < f2) in the external ear. Cochlear neural effects were monitored by measuring the compound action potential of the auditory nerve in response to tone pips at the f2 frequency of the DPOAE measurement. Contralateral sound suppressions of CAPs and DPOAEs were qualitatively similar in all animals, but suppression of CAPs was always as large, or larger, than suppression of DPOAEs. Thus, the reported differences in efferent reflex strength between human work (which used DPOAEs) and animal work (which used CAPs) may arise from inherent differences between the CAP and the DPOAE tests, rather than from a species difference in efferent effects.

During the past year, we have worked on a project to compare efferent-evoked effects on auditory-nerve fibers with different spontaneous rates and to compare the time course of efferent effects. An abstract by Guinan and Stankovic has been submitted describing this work.

1.6.1 Publications

Guinan J.J., Jr., K.M. Stankovic. "Medial Olivocochlear Efferent Inhibition of Auditory-Nerve Firing Mediated by Changes in Endocochlear Potential." *Abstr. Assoc. Res. Otolaryngol.* 18: 172 (1995).

McCue, M.P., and J.J. Guinan, Jr. "Acoustically-Responsive Fibers in the Vestibular Nerve of the Cat." *J. Neurosci.* 14: 6058-6070 (1994).

McCue, M.P., and J.J. Guinan, Jr. "Influence Of Efferent Stimulation On Acoustically-Responsive Vestibular Afferents in the Cat." *J. Neurosci.* 14: 6071-6083 (1994).

McCue, M.P., and J.J. Guinan, Jr. "Spontaneous Activity and Frequency Selectivity of Acoustically Responsive Vestibular Afferents in the Cat." Submitted to *J. Neurophysiol.*

Puria, S., J.J. Guinan, Jr., and M.C. Liberman. "Olivocochlear Reflex Assays: Effects of Contralateral Sound on Compound Action Potentials vs. Ear-Canal Distortion Products." Submitted to *J. Acoust. Soc. Am.*

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[16] B.T. Walsh, J.G. Miller, R.R. Gacek, and N.Y.S. Kiang, "Spontaneous Activity in the Eight Cranial Nerve of the Cat," *Intern. J. Neurosci.* 3: 221-236 (1972).

[17] Puria, S., J.J. Guinan, Jr., and M.C. Liberman, "Olivocochlear Reflex Assays: Effects of Contralateral Sound on Compound Action Potentials vs. Ear-Canal Distortion Products," submitted to *J. Acoust. Soc. Am.*

1.7 Cochlear Implants

Sponsor

Project Staff

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

Most people who suffer profound hearing impairment have lost the ability to translate the acoustic energy of sound into electrical signals carried to the brain by the auditory nerve. Cochlear implants are electronic devices designed to bypass the external and middle ears and reintroduce these signals by exciting the auditory nerve directly. These devices include a microphone connected to a belt-worn package of electronics (called a sound processor) that translates acoustic signals to electric stimuli. When these stimuli are directed to auditory nerve fibers using an array of electrodes implanted in the deaf patient's cochlea (inner ear), they elicit patterns of nerve activity that the brain interprets as sound.
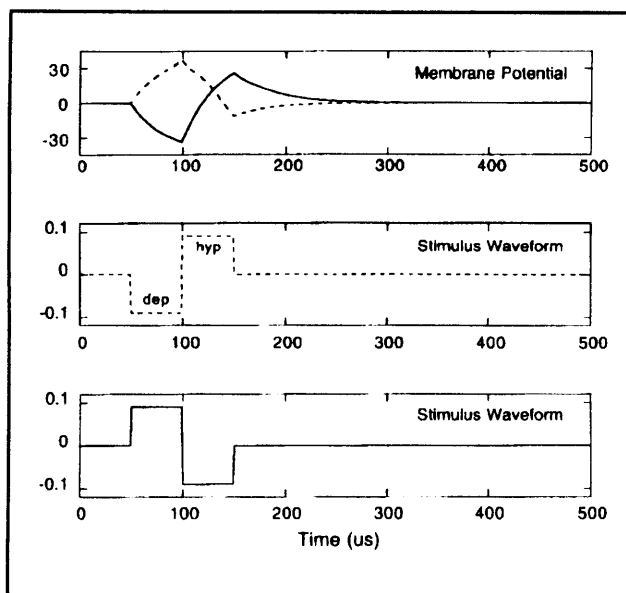

Figure 1. The top panel shows the responses of the membrane potential predicted by a model "nerve fiber" to the two, subthreshold biphasic stimuli (50 μs/phase) plotted in the lower two panels. Each of the 15 nodes of the myelinated axon model consist of a variable, nonlinear conductance (based on the characteristics of voltage dependent sodium channels) and a linear membrane resistance and capacitance. The nodal parameters were derived from measurements in mammal at 37°C and the internodal parameters are from frog (with C_m adjusted to give an appropriate conduction velocity).

Our work is directed at understanding the fundamental mechanisms underlying the sound sensations produced by electrical stimulation of the auditory system and using that information to develop cochlear implant systems that improve speech reception. One of our ongoing efforts is directed at reducing the interference between electrical stimuli that can occur when they are presented close together in time.

In figure 1, the top panel shows the predicted response of a model axon's membrane potential for the two biphasic stimuli (50 μs/phase) plotted in the lower two panels. Note that at t = 150 μs, when the biphasic pulses are completed, the membrane potential is nonzero and takes 150 to 200 μs to return to its resting state. Thus, when the cathodic (depolarizing) phase is last, the membrane remains partially depolarized (solid line of top panel) and will tend to reduce the threshold of subsequent stimuli delivered within this "sensitized" period.

This effect is seen in figure 2 where probe threshold (in dB relative to the nonmasked probe threshold) is plotted as a function of the delay between the onset of the subthreshold masker stimulus and the onset of the probe stimulus. In this case, the stimuli are directed to the most apical electrode of a subject's Ineraid electrode array (return electrode in the temporalis muscle) and an adaptive, forced-choice procedure is used to measure psychophysical threshold.
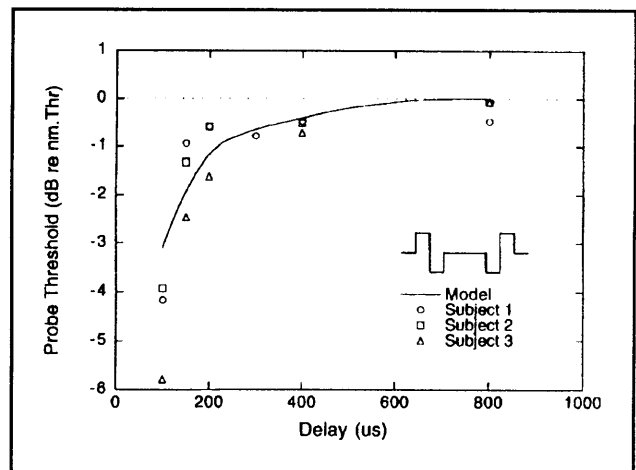

Figure 2. Forward masking results for a subthreshold, anodic-phase-first biphasic masker followed by a cathodic-phase-first, biphasic probe. Probe threshold is plotted in dB relative to the nonmasked threshold and as a function of the delay between the onset of the masker and the onset of the probe. The masker is presented 2 dB below its nonmasked threshold. Subject results are represented by symbols and the model axon predictions by the solid line.

The model and subject data of figure 2 show that the overall influence of the masker is to reduce the probe's threshold. When compared to the dynamic range of electrical stimulation (4 to 20 dB), the maximum threshold shifts of 4 to 6 dB are relatively large, and it is clear that unintended deviations in fiber sensitivity of even 1 dB could have significant perceptual consequences.
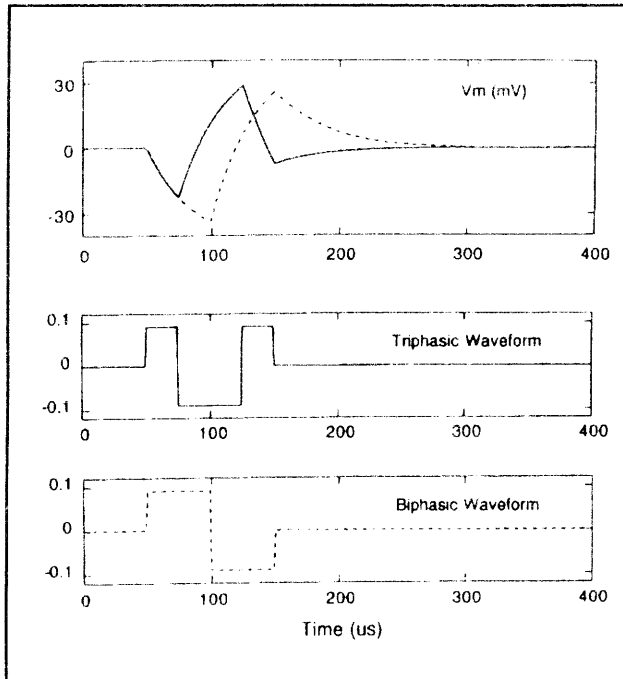

Figure 3. The top panel shows the membrane potential responses predicted by the same model axon of figure 1 to the subthreshold, triphasic and biphasic stimuli plotted in the lower two panels.

One approach to reduce these nonsimultaneous interactions uses triphasic stimulus waveforms. In the top panel of figure 3, the membrane potential of the model axon is plotted for two different waveforms, each presented at levels 2 dB below their respective unmasked thresholds. The broken line shows the model's response to the anodic-first biphasic waveform plotted in the bottom panel and the solid line represents the response to the triphasic waveform shown in the middle panel. Note that at t = 150 μs, the predicted deviation from the resting potential is considerably less for the triphasic than for the biphasic waveform. This suggests that a triphasic waveform may reduce the forward masking demonstrated in the results of figure 2.

The results of an initial test of this idea are shown in figure 4 where the effect of the triphasic masker on the probe's threshold is plotted as a function of masker's first phase duration. Although these data are preliminary, they show a significant null in
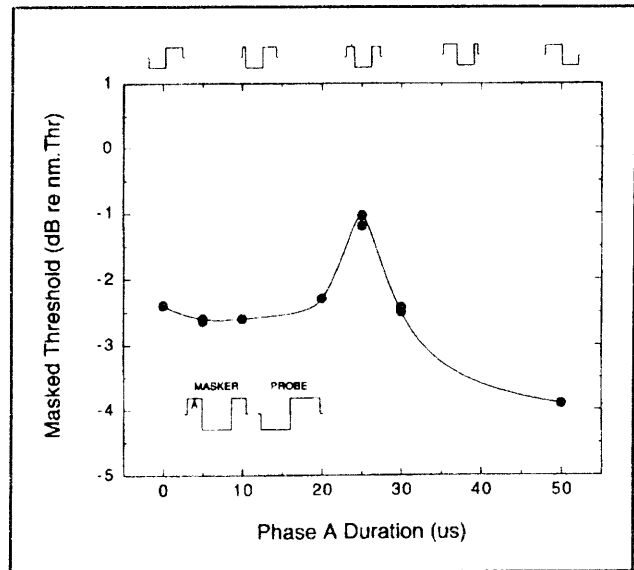

Figure 4. Forward masking results from a single Ineraid subject for the subthreshold, triphasic masker followed by a cathodic-phase-first, biphasic probe (50 μs/phase) shown as an inset in the lower left corner of the figure. The masker was composed of three phases (A,B,C) and constrained as follows: (1) charge-balanced, (2) total duration of 100 μs, (3) 2nd phase (B) cathodic and 50 μs in duration, and (4) level = 2 dB below the unmasked waveform's threshold. Because of these masker constraints, as the duration of the first phase (A) was varied from zero to 50 μs, the masker waveform changed from a cathodic-first, biphasic stimulus (A = 0 μs, B = C = 50 μs) to a symmetric triphasic stimulus (A = C = 25 μs, B = 50 μs) to an anodic-first biphasic stimulus (A = B = 50 μs, C = 0) as shown by the masker waveforms plotted along the top abscissa of the figure. Probe threshold is plotted in dB relative to the nonmasked threshold and as a function of the duration of the "A" phase of the triphasic masker.

forward masking for the balanced triphasic waveform and suggest that manipulation of the stimulating waveform can substantially reduce distortions caused by these nonsimultaneous interactions.

1.7.1 Publications

Eddington, D.K. "Recent Developments in Sound Processing." British Society of Audiology Annual Conference, Bathe, England, September 15-17, 1993.

Eddington, D.K. "Forward Masking During Intracochlear Electrical Stimulation: Models, Physiology and Psychophysics." *J. Acoust. Soc. Am.* 95: 2904 (1994).

Rabinowitz, W.M., and D.K. Eddington. "Effects of Channel-to-Electrode Mappings on Speech

Reception with the Ineraid Cochlear Implant."
Submitted to *Ear Hear.*