

## 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 in the External and Middle Ear

The goal of our work is to understand the relationship between the structures of the external and middle ear and their functions.

## 1.2.1 Structure-Function Relations in Middle Ears

### Sponsor

National Institutes of Health  
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### Project Staff

Dr. John J. Rosowski, Professor William T. Peake, Michael E. Ravicz, David A. Steffens

The middle-ear is a key link in the hearing process. In normal hearing, sound signals are delivered to the inner ear by the middle ear. Disease, age, and injury can degrade the performance of the middle ear. In part of our work, we investigate the relationship between the structures of the middle-ear air space and tympanic-membrane and the function of the middle ear. We are making joint anatomical and physiological measurements in a series of rodent and cat species with different tympanic membrane and middle-ear air-space morphologies. We will also use similar methods in cats to investigate whether the response of the cochlea is completely determined by the difference in pressure across the two cochlear windows.

In the last year, we have moved towards our goal in the following ways:

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<sup>1</sup> Research Affiliate, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts.

1. We have analyzed our measurements on middle-ear cavity and tympanic membrane function and incorporated the results into a paper presenting new measurements of the middle-ear input impedance in cats<sup>2</sup> and into a model of the mammalian external and middle ear.<sup>3</sup> These analyses support the theory that the primary effect of middle-ear cavities is consistent with a "series" model. The cavities impede the volume-velocity of sound at the tympanic membrane but have little effect on how the membrane and ossicles respond for a given volume velocity. An additional analysis of anatomical and physiological measurements, made on many mammalian species, points out that different species have greatly different middle-ear cavity impedances and that the relative magnitudes of the impedance of the cavity and the impedance of the rest of the ear varies widely among mammals.<sup>4</sup>
2. We have taken the "series" model and our data a step further and analyzed the effect of variations in middle-ear volume on auditory thresholds in a desert rodent (the Mongolian gerbil).<sup>5</sup> This analysis suggests that the middle-ear cavity in a gerbil plays a large role in limiting low-frequency auditory thresholds even though the cavity has a volume larger than the brain case. This conclusion is contrary to the suggestion that the large middle-ear cavities of these and other specialized desert rodents have evolved to permit maximum sensitivity to low-frequency sound.
3. A series of new measurements tested the "classic" assumption that the inner ear responds to the sound-pressure difference between the oval and round window.<sup>6</sup> The external and middle ears of cats were prepared so that we could independently control the magnitude and phase of the sound pressure at the two cochlear windows. The cochlear

potential, measured with a round-window electrode, was our indicator of cochlear response. The potential was determined with sound stimuli presented at both or either cochlear window. The results indicate that the difference in sound pressure at the windows is clearly the primary stimulus to the cochlear potential.

The results of our work have direct significance to our understanding of human disease, animal ethology, and the basic hearing process. Chronic and acute otitis media are very common causes of hearing dysfunction. One significant effect of these diseases is a reduction in the air volume of the middle ear. This reduction can be transiently caused by the accumulation of fluid or more permanently produced by the accumulation of debris within the middle ear or actual alterations in the bony walls of the cavity. Our work will enable a clearer understanding of the role of the middle-ear air spaces in both normal and diseased ears.

The ethological issues we are testing concern the role of enlarged middle-ear air spaces. Our work on a number of rodent species and a wide selection of cat species will test the popular idea that large middle-ear air spaces represent an adaptation to arid environments.

Our work on specification of the effective stimulus to the inner ear also has direct clinical consequences in that surgeons routinely manipulate the pressure difference between the cochlear windows when they reconstruct severely diseased middle ears. Our new measurements support the efficacy of such procedures. Furthermore, the results of our measurements have implications for our fundamental understanding of inner ear mechanisms. Any indication that the cochlea is sensitive to stimuli other than the difference in sound pressure at the cochlear windows will require basic changes in cochlear theories.

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<sup>2</sup> T.J. Lynch III, W.T. Peake, and J.J. Rosowski, "Measurements of the Acoustic Input Impedance of Cat Ears: 10 Hz to 20 kHz," *J. Acoust. Soc. Am.*, forthcoming.

<sup>3</sup> J.J. Rosowski, "Models of External and Middle-Ear Function," in *The Springer Handbook on Auditory Research*, Volume 6: Auditory Computation, eds. H.L. Hawkins, T.A. McMullen, A.N. Popper, and R.R. Fay (New York: Springer-Verlag, forthcoming).

<sup>4</sup> J.J. Rosowski, "Outer and Inner Ear," in *The Springer Handbook on Auditory Research*, Volume 4: Comparative Mammalian Hearing, eds. A.N. Popper, and R.R. Fay (New York: Springer-Verlag, forthcoming).

<sup>5</sup> M.E. Ravicz and J.J. Rosowski, "The Effect of Middle-Ear Cavity Size on Acoustic Power Flow in the Ear of the Mongolian Gerbil," in *Abstracts of the Seventeenth Midwinter Meeting of the Association for Research in Otolaryngology*, February 6-10, 1994, p. 145.

<sup>6</sup> S.E. Voss, J.J. Rosowski, and W.T. Peake, "Is the Pressure Difference Between the Oval and Round Windows the Stimulus for Cochlear Responses?" in *Abstracts of the Seventeenth Midwinter Meeting of the Association for Research in Otolaryngology*, February 6-10, 1994, p. 87.



## 1.2.2 Basic and Clinical Studies of Middle-Ear Function

### Sponsor

National Institutes of Health  
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### Project Staff

Dr. John J. Rosowski, Professor William T. Peake,  
Dr. Sunil Puria, Michael E. Ravicz

Our goal of understanding the relationship between the structure and function of the auditory periphery includes defining the effect of middle and external ear pathologies on auditory function. To help achieve this goal, we have continued measurements of function in human ears using temporal-bones donated at the time of death, and we have applied the models we determined from our animal work to questions concerning middle-ear pathologies and treatments.

Dr. Puria has led a project to measure the pressure transfer function of the human middle ear.<sup>7</sup> The excised temporal bones were prepared to allow reproducible placement of a calibrated sound source and microphone in the ear canal together with a miniature hydrophone in the cochlear vestibule. The preparation procedure included the placement of "flush" tubes—one near the round window, the other in the vestibular canals—to keep the cochlea fluid filled. These measurements suggest that the human middle ear acts as a band-pass pressure amplifier with a maximum gain of about 20 dB between 1 and 5 kHz. At lower frequencies, the gain is roughly proportional to frequency; at higher frequencies the gain decreases as frequency increases.

With the help of our clinical associates at the Massachusetts Eye and Ear Infirmary, we have expanded our analysis of previous models of diseased and reconstructed middle ears. The results of these analyses were presented at two conferences<sup>8</sup> where we suggested that small modifications in current surgical procedures could lead to

improved hearing results. These modifications included: stapes prostheses with larger areas, maintaining a volume of at least 0.5 cc for the reconstructed middle-ear cavity, and stiffer grafts for isolating the round window from sound.

## 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, Henry E. Chung, C. Quentin Davis, Lisa F. Shatz

Our goal is to study the mechanisms by which the 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.

Previously, we have measured osmotic responses to isosmotic solutions of different sodium, potassium, and calcium concentration in the isolated chick tectorial membrane. That work has been submitted for publication.<sup>9</sup> However, the structure and biochemical composition of the tectorial membrane shows considerable diversity across species. Therefore, during the past year we have investigated the physicochemical properties of tectorial membranes isolated from the lizard and mouse cochlea using the same techniques. Basically, in this procedure we dissect the tectorial membrane from the cochlea, place it in a chamber through which solutions of known composition are perfused. The tectorial membrane is decorated with microscopic latex beads whose three-dimensional motions in response to solution changes are meas-

<sup>7</sup> S. Puria, J.J. Rosowski, and W.T. Peake, "Middle-Ear Pressure Gain in Humans," in *Biophysics of Hair Cell Sensory Systems*, eds. H. Duifhuis, J.W. Horst, P. van Dijk, and S. van Netten (River Edge, New Jersey: World Scientific Publishing Co., 1993).

<sup>8</sup> S.N. Merchant, J.J. Rosowski, and M.E. Ravicz, "Acoustical Aspects of Type IV and V Tympanoplasty," paper presented at the Meeting of the American Academy of Otolaryngology, Head and Neck Surgery, Minneapolis, Minnesota, October 3-8, 1993; J.J. Rosowski, "Analyses of Middle-Ear Reconstructive Techniques," paper presented at the Meeting of the American Oto-Neurologic Society, Minneapolis, Minnesota, October 2, 1993.

<sup>9</sup> 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<sup>+</sup>, K<sup>+</sup>, and Ca<sup>2+</sup> Concentration," submitted to *Hear. Res.*

ured automatically with a system consisting of a compound microscope, CCD camera, video digitizer, and workstation. Results for all three species (chick, lizard, and mouse) show that increasing calcium concentration from the low values (20  $\mu\text{mol/L}$ ) typical for the solution that bathes the tectorial membrane *in situ* (endolymph) to the higher concentrations (2  $\text{mmol/L}$ ) found in normal extracellular fluids causes the tectorial membrane to shrink with a time course of about five minutes. The shrinkage is largely reversed when calcium concentration is lowered but with a slower time course (tens of minutes).

Tectorial membranes from all three species also swell when isosmotic, high-sodium solutions are substituted for high-potassium solutions. However, the magnitude of this response is much greater for the chick (mean of 135 percent) than for either the mouse (mean of 14 percent) or the lizard (mean of 10 percent). Swelling in high-sodium solutions is at least partially reversed on return to high-potassium solutions. However, irreversible changes result during long-duration (60-minutes) exposures to high-sodium solutions that give rise to large swelling responses.

Our results are consistent with the simple hypothesis that the tectorial membrane is a polyelectrolyte gel with fixed ionizable charge groups that can bind ions differentially. This picture of the tectorial membrane is similar to that for other connective tissues: the binding of ions modulates the fixed charge density which changes the concentration of counter ions in the tissue and hence its water content.

The shrinkage and swelling of the tectorial membrane in response to changes in ion concentration may have implications for hearing. For example, a number of factors are known to change ion composition of the lymph including acoustic overstimulation, anoxia, systemic administration of ethacrynic acid, or perfusion of the cochlea with ouabain, etc. Our results show that changes in the ionic composition of the bath can lead to changes in the structure of the tectorial membrane. Changes in its structure are likely to cause changes in the delivery of the mechanical stimulus to the hair cells and hence to affect hearing.

### 1.3.1 Publication

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  $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{Ca}^{2+}$  Concentration." Submitted to *Hear. Res.*

## 1.4 Stimulus Coding in the Auditory Nerve and Cochlear Nucleus

### Sponsor

National Institutes of Health  
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### Project Staff

Dr. Bertrand Delgutte, Dr. Peter A. Cariani

We are investigating the neural mechanisms underlying auditory perception at the level of the auditory nerve and cochlear nucleus. In the past year, we have focused on temporal patterns of neural discharge that convey pitch and speech information. These temporal patterns are analyzed by recording the responses of auditory nerve fibers and cochlear nucleus neurons in anesthetized cats. All-order interspike interval distributions (autocorrelation histograms) are computed and the properties of these distributions are compared with psychophysical data.

Our previous results had shown that the pitch of a complex tone corresponds to the most frequent interspike interval in the auditory nerve for a wide variety of stimuli. Responses of cochlear nucleus units to the same stimuli were recorded to determine whether pitch might also be represented by interspike interval patterns there. Virtually all single units in the cochlear nucleus that responded to the stimuli showed pitch-related intervals, and these were usually the most frequent in the distribution. Thus, cochlear nucleus units might convey pitch information to more central auditory stations through an interspike interval code.

We have continued our investigation of the neural mechanisms underlying the perceptual segregation of concurrently-presented vowels. Human listeners identify pairs of concurrent vowels better when they differ in fundamental frequency ( $F_0$ ) than when they have the same  $F_0$ . Previously we had found that the constituents of a vowel pair could be identified from the aggregate interspike interval distributions of the auditory nerve with an accuracy comparable to human perceptual judgements. During the past year, we sought to explain how vowel identification might be improved for pairs with different  $F_0$ s without requiring an explicit determination of  $F_0$ . We found that differences in  $F_0$  create changing alignments in the onsets of vowel periods, and that these changing alignments create transient changes in interspike interval distributions of auditory-nerve fibers. One possibility is that these changes allow

the auditory system to perform a spectral analysis over relatively short (5-10 ms) time windows and integrate these analyses over time to identify the vowel constituents. Along these lines, we developed a new algorithm for identifying the constituents of a double vowel from running interspike interval distributions. This algorithm is consistent with human perceptual data showing effects of period asynchronies on the identification of concurrent vowels.

### 1.4.1 Publication

Delgutte B., P. Cariani and M.J. Tramo, "Neurophysiological Correlates of the Pitch of Complex Tones." *J. Acoust. Soc. Am.* 93: 2293 (1993).

### 1.4.2 Binaural Interactions in Auditory Brainstem Neurons

#### Sponsor

National Institutes of Health  
Grant P01-DC00119

#### Project Staff

Dr. Bertrand Delgutte, Dr. John J. Guinan, Jr., Dr. John J. Rosowski

Several acoustic cues are important for sound localization, including interaural time (ITD), interaural level (ILD) differences, and spectral shape. In collaboration with Dr. T.C.T. Yin and his colleagues at the University of Wisconsin in Madison, we are studying the relative contribution of these cues to the directional sensitivity of neurons in the inferior colliculus (IC). The activity of single units was recorded in anesthetized cats in response to "virtual space" (VS) stimuli delivered through closed acoustic systems. These stimuli were generated by passing broadband noise through digital filters constructed from head-related transfer functions measured in one cat. We focused on high-CF (> 5 kHz) units, which are likely to be sensitive to spectral features.

The sensitivity of neurons to stimuli whose virtual position varied along the horizontal and vertical planes generally resembled that found in previous free-field studies. For most units, responses to monaural VS stimuli were less directional than those for binaural stimuli, suggesting that binaural interactions were important for the directional response of these neurons. The type of binaural interactions (e.g., EE, EI, or mixed) determined with VS stimuli was consistent with that found for broadband noise.

We also generated modified VS stimuli in which one or more of the localization cues (ITD, ILD, or spectrum) were set constant for all locations. For example, "0-ITD" stimuli were constructed by delaying the waveform in the leading ear to set the ITD to zero for every azimuth. "Delta-ITD" stimuli were created by taking the waveforms for the position directly in front, then introducing the appropriate ITD for each azimuth. Results suggest that, for most of these high-CF units, ILD is the most potent cue, followed by spectral shape, then by ITD. These results are consistent with human psychophysical experiments showing the dominance of ILD cues for high-frequency stimuli. At a more general level, our results demonstrate the usefulness of virtual-space techniques for bridging the gap between free-field studies of the directional sensitivity of neurons and dichotic studies of ITD and ILD sensitivity.

### 1.4.3 Publication

Delgutte, B., P.X. Joris, R.Y. Litovsky, and T.C.T. Yin. "Different Acoustic Cues Contribute to the Directional Sensitivity of Inferior-Colliculus Neurons as Studied with Virtual-Space Stimuli." *Abstracts of the 17th Midwinter Research Meeting of the Association for Research in Otolaryngology*, St. Petersburg, Florida, February 6-10, 1994.

### 1.4.4 Electrical Stimulation of the Auditory Nerve

#### Sponsor

National Institutes of Health  
Grant P01-DC00361

#### Project Staff

Dr. Bertrand Delgutte, Scott B.C. Dynes

We are studying physiological mechanisms of electrical stimulation of the cochlea because this information will help design improved processing schemes for multiple-channel cochlear implants. During the past year, we have studied auditory-nerve fiber correlates of interactions observed psychophysically when pulsatile electric stimuli are applied in rapid succession. We measured the responses of auditory-nerve fibers in anesthetized cats for pairs of monophasic pulses separated by short intervals. Results show that neural interactions between successive current pulses occur on three different time scales:

1. The shortest interactions occur when the first pulse in a pair is subthreshold. For cathodic first pulses, the threshold for following cathodic pulses was decreased, while anodic first pulses increased the threshold of following cathodic pulses. These results are qualitatively consistent with viewing the first pulse as leaving a residual charge on the neural membrane. The time constant of these capacitive effects is 100-200 usec. These subthreshold interactions are likely to play an important role in continuous interleaved sampling (CIS) processors for cochlear implants because most pulses are probably subthreshold in this situation, so that elicitation of a spike would require interaction over multiple pulses. Particularly interesting is the result that subthreshold interactions for biphasic pulses similar to those used in CIS processors cannot be predicted from simple ideas about charge integration by the neural membrane. On the other hand, these interactions are consistent with psychophysical data showing sensitization for biphasic pulses preceded by either anodic/cathodic or cathodic/anodic pulses. Thus, the neural and psychophysical data are consistent with each other, but both are at variance with current theoretical conceptions of neural excitation.
2. When the first pulse was suprathreshold, the threshold for the second pulse was found to decrease with increasing interpulse delay, as expected from the refractory properties of nerve fibers. The decrease was such that at 2 msec interpulse delay, the threshold for the second pulse averaged about 5 dB greater than the threshold for a single pulse. Thus, these interactions due to suprathreshold pulses last longer than subthreshold interactions. These suprathreshold interactions may not severely limit the performance of CIS processors providing that there is a sufficient pool of nerve fibers that discharge at different times (volley principle).
3. In addition to interactions between two successive pulses, further results provide evidence for the existence of long-term interactions occurring cumulatively over multiple pulses. Because these multipulse interactions have not been systematically characterized, it is difficult at this point to assess their significance for CIS

processors. We plan to examine these interactions in more detail during the next year.

#### 1.4.5 Publications

Dynes, S.B.C., and B. Delgutte. "Neural Response to Nonsimultaneous Electrical Stimuli: Physiological Results." Conference on Implantable Auditory Prostheses, Smithfield, Rhode Island, July, 1993.

Dynes, S.B.C., and B. Delgutte. "Temporal Mechanisms of Auditory-Nerve Response to Multiple Electric Pulses." *Abstracts of the 17th Midwinter Research Meeting of the Association for Research in Otolaryngology*, St. Petersburg, Florida, February 6-10, 1994.

Rubinstein, J.T., and S.B.C. Dynes. "Latency, Polarity, and Refractory Characteristics of Electrical Stimulation: Models and Single-Unit Data." *Abstracts of the 16th Midwinter Research Meeting of the Association for Research in Otolaryngology*, St. Petersburg, Florida, February 6-11, 1993, p. 76.

### 1.5 Interactions of Middle-Ear Muscles and Olivocochlear Efferents

#### Sponsor

National Institutes of Health  
Contract PO1 DC00119

#### Project Staff

Dr. John J. Guinan, Jr.

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

During the past year, we have analyzed data and prepared for publication our results on the innervation of the stapedius muscle.<sup>10</sup> In a previous study using intracellular labeling of physiologically identified stapedius motoneurons, we showed that there is functional spatial segregation in the stapedius motoneuron pool.<sup>11</sup> In the same animals, we have now traced each sufficiently labeled axon

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<sup>10</sup> S.R. Wiener-Vacher, J.J. Guinan, Jr., J.B. Kobler, and B.E. Norris, "Motoneuron Axon Distribution in the Stapedius Muscle of the Cat: An Intracellular Labeling Study", submitted to *J. Comp. Neurol.*

<sup>11</sup> S.R. Vacher, J.J. Guinan, Jr., and J.B. Kobler, "Intracellularly Labeled Stapedius-Motoneuron Cell Bodies in the Cat Are Spatially Organized According to Their Physiologic Responses," *J. Comp. Neurol.* 289: 401-415 (1989).

into the stapedius muscle to determine whether a similar functional spatial segregation is present within the muscle. Ten labeled axons of physiologically identified stapedius motoneurons were visible in the facial nerve and five could be traced to endplates within the stapedius muscle. In one case, a stapedius motoneuron innervated only a single muscle fiber; we think that this is the first documented case of such remarkably fine-grained motor innervation. Overall, there were 39 observed branches from the five axons (we may have missed others). This indicates an average innervation ratio ( $\geq 7.8$ ) which is much higher than that obtained from present estimates of the numbers of stapedius motoneurons and muscle fibers. Muscle fibers innervated by a single axon were spread over a wide area in the muscle, suggesting that spatial segregation in the stapedius muscle is unlikely. Thus, the reasons for the central functional spatial segregation in the stapedius motoneuron pool are more likely related to organizing factors which originate in the brain rather than to organizing factors which originate in the muscle.

### 1.5.1 Publication

Wiener-Vacher, S.R., J.J. Guinan, Jr., J.B. Kobler, and B.E. Norris. "Motoneuron Axon Distribution in the Stapedius Muscle of the Cat: An Intracellular Labeling Study." Submitted to *J. Comp. Neurol.*

## 1.6 Cochlear Efferent System

### Sponsor

National Institutes of Health  
Grant 2R01 DC00235

### Project Staff

Michael P. McCue, 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, we have analyzed data and prepared for publication results on our newly-discovered class of vestibular primary afferent neurons, fibers which respond to sounds at moderately high sound levels.<sup>12</sup> Like their cochlear homologues, these vestibular afferent fibers receive efferent projections from brain-stem neurons. We have explored efferent influences on the background activity and tone-burst responses of the acoustically-responsive vestibular afferents. Shock-burst stimulation of efferents excited acoustically-responsive vestibular afferents; no inhibition was seen. A fast excitatory component built up within 100-200 ms of shock-burst onset and decayed with a similar time course at the end of each shock burst. During repeated 400 ms shock bursts at 1.5 s intervals, a slow excitatory component grew over 20-40 s and then decayed, even though the shock bursts continued. Efferent stimulation excited acoustically-responsive vestibular afferents without appreciably affecting their sound-evoked responses. This provides strong evidence that the excitation is due to efferent synapses on afferent fibers instead of efferent synapses on hair cells. Efferent stimulation enhanced the tone-induced within-cycle modulation of discharge rate (i.e., increased the a.c. gain) without changing the degree of phase locking to low frequency tones as measured by the synchronization index; i.e., there was little or no improvement in the bidirectionality (linearity) of nerve fiber output. The acoustically-responsive vestibular afferents provide a mammalian model for studying purely excitatory efferent effects in a hair cell system. Anatomically, these vestibular efferent synapses resemble lateral olivocochlear efferent synapses on cochlear nerve fibers, which suggests that lateral efferents may have an excitatory effect. A paper describing these results has been submitted.<sup>13</sup>

During the past year, we have begun work on a project to compare efferent-evoked effects on auditory-nerve fibers with different spontaneous rates. We have implemented and done preliminary experiments with a paradigm in which auditory-nerve-fiber rate versus sound level functions with and without efferent excitation are obtained with randomized presentation of both the sound level and the presence of efferent stimulation.

<sup>12</sup> M.P. McCue, and J.J. Guinan, Jr., "Acoustic Responses from Primary Afferent Neurons of the Mammalian Sacculus,." *Assoc. Res. Otolaryngol. Abstr.* 16: 33 (1993).

<sup>13</sup> M.P. McCue, and J.J. Guinan, Jr., "Influence Of Efferent Stimulation On Acoustically-Responsive Vestibular Afferents in the Cat," submitted to *J. Neurosci.*



### 1.6.1 Publications

McCue, M.P., and J.J. Guinan, Jr. "Acoustic Responses from Primary Afferent Neurons of the Mammalian Sacculus." *Assoc. Res. Otolaryngol. Abstr.* 16: 33 (1993).

McCue, M.P., and J.J. Guinan, Jr. "Acoustically-Responsive Fibers in the Vestibular Nerve of the Cat." Submitted to *J. Neurosci.*

McCue, M.P., and J.J. Guinan, Jr. "Influence Of Efferent Stimulation On Acoustically-Responsive Vestibular Afferents in the Cat." Submitted to *J. Neurosci.*

## 1.7 Cochlear Implants

### Sponsor

National Institutes of Health  
Grant PO1-DC00361  
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### Project Staff

Dr. Donald K. Eddington, Dr. William M. Rabinowitz, Dr. 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

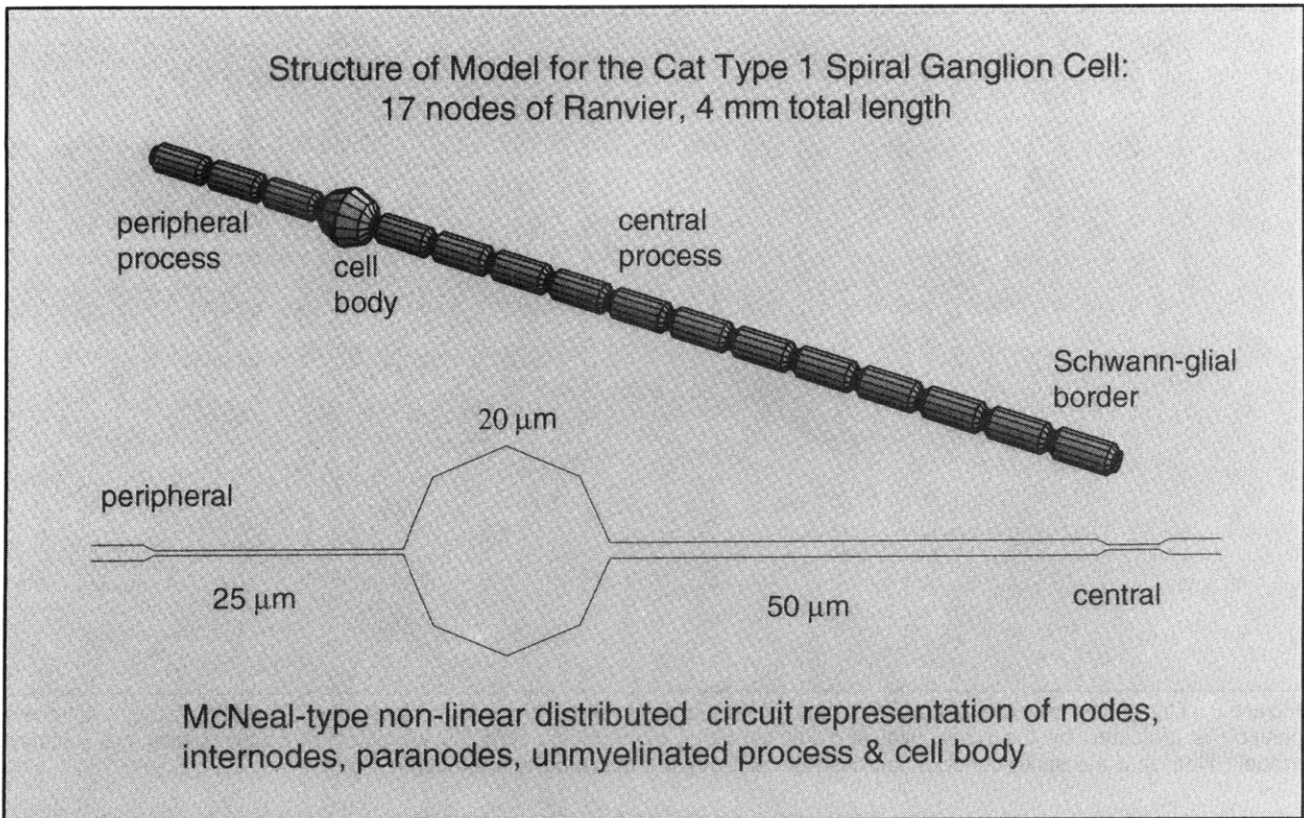
Dr. Donald K. Eddington, Dr. Jay T. Rubinstein

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 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, geometry and placement of the stimulating electrodes, stimulus waveform, and distribution of excitable auditory nerve fibers. An understanding of how these factors interact to determine the activity patterns is

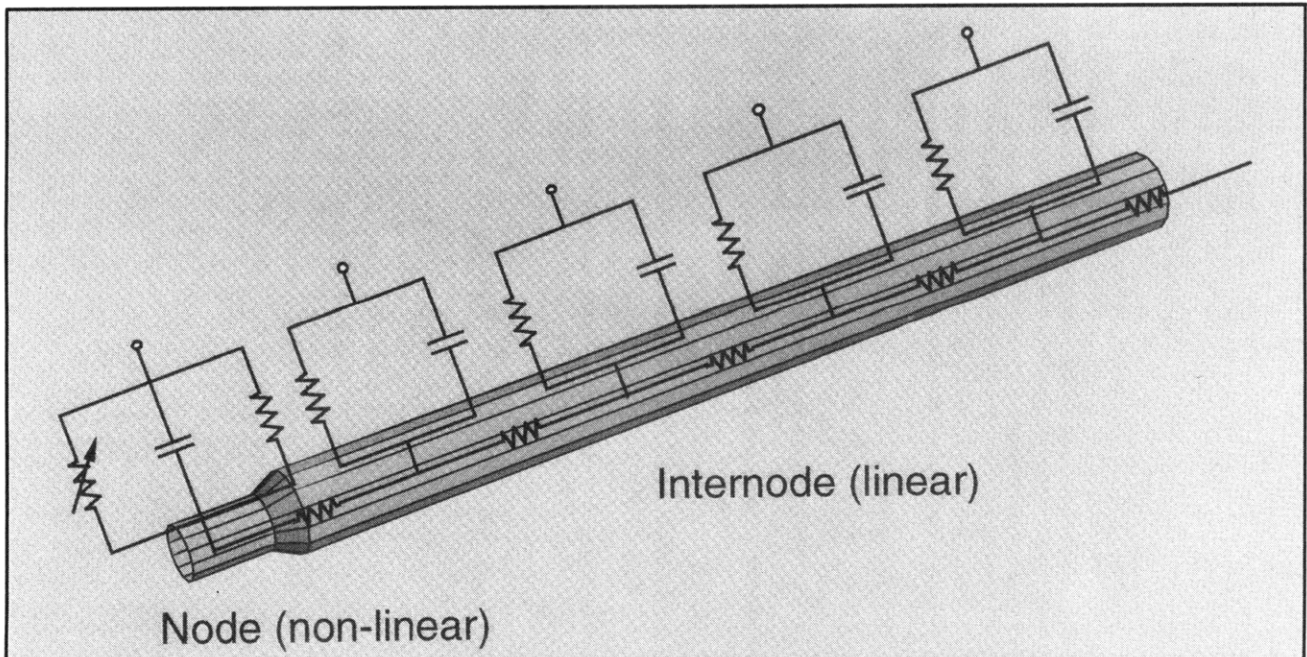
fundamental to designing better devices and interpreting the results of experiments involving intracochlear stimulation of animal and human subjects. As a first step toward this understanding, the goal of this project is to (1) construct a software model of the cochlea that predicts the distribution of potential produced by the stimulation of arbitrarily placed, intracochlear electrodes and (2) use these potential distributions as inputs that drive models of auditory nerve fibers.

This year, we refined our nonlinear, single-unit model to include a passive, myelinated cell body (see figures 1 and 2). Varying the membrane capacitance and resistance to simulate variations in the myelination of the cell body produces profound effects on conduction. Without myelination, spikes will not propagate across the cell body unless voltage-sensitive sodium channels are present in the soma. With increasing myelination, spikes conduct in the orthograde direction but not retrograde (see figures 3 and 4). A model cell body with myelin thickness comparable to that of the internode propagates spikes in both directions. These simulations demonstrate the biophysical feasibility of physiologically observed, somatic spike rectification and implicate the anatomic asymmetry of the nodes of Ranvier adjacent to the soma as a possible mechanism.

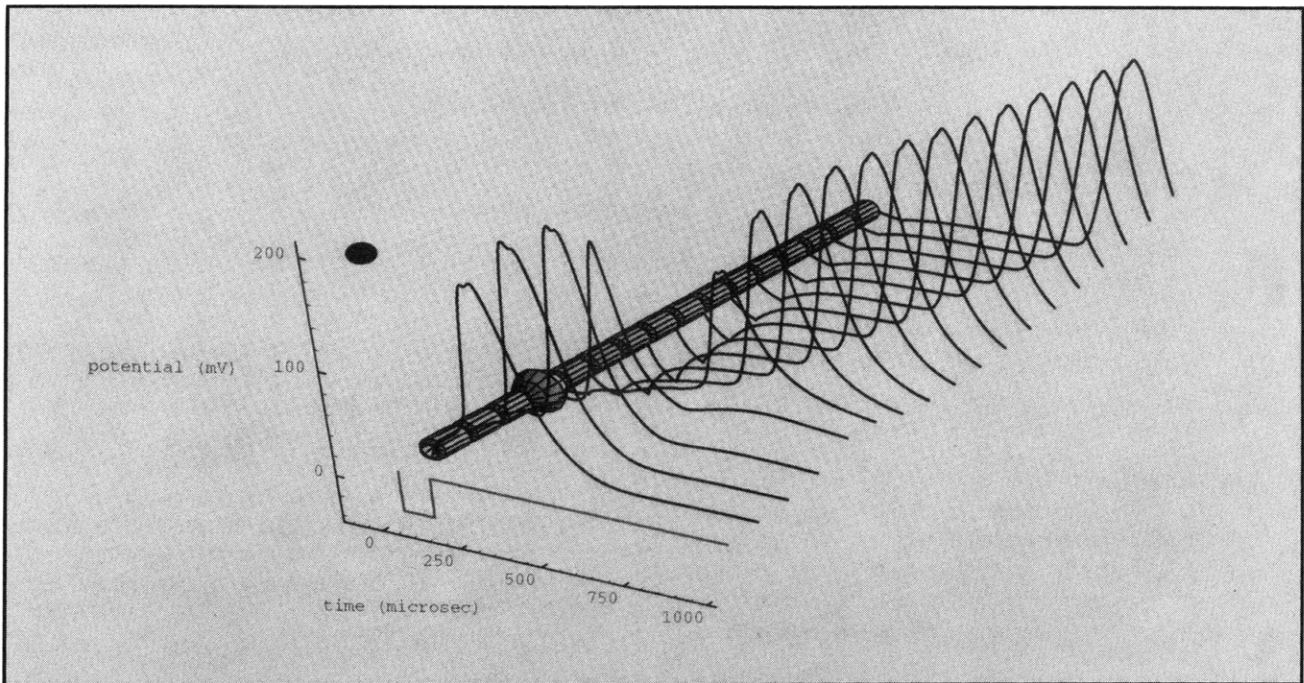
A multichannel stochastic model of the mammalian node of Ranvier has also been developed. This model represents N sodium channels in parallel with a membrane capacitance and leakage resistance. Each channel consists of a single-channel conductance obtained from the patch-clamp and fluctuation literature and a gate controlled by three m (activation) particles and one h (inactivation) particle. Particle open and closed times are random (exponential distribution) with mean obtained from the reciprocal of the particle's rate constant. Thus the open/closed time probability density functions are time-varying. The model has been tested by substituting Frankenhauser-Huxley kinetics and membrane parameters for the mammalian data and comparing the relative spread of threshold (RS) predicted by the model with that measured for peripheral amphibian nodes. The experimental data are very closely approximated by the simulations. This is the first direct numerical verification that the microscopic sodium channel fluctuations are sufficient to account for the macroscopic fluctuations of threshold to electrical stimulation.



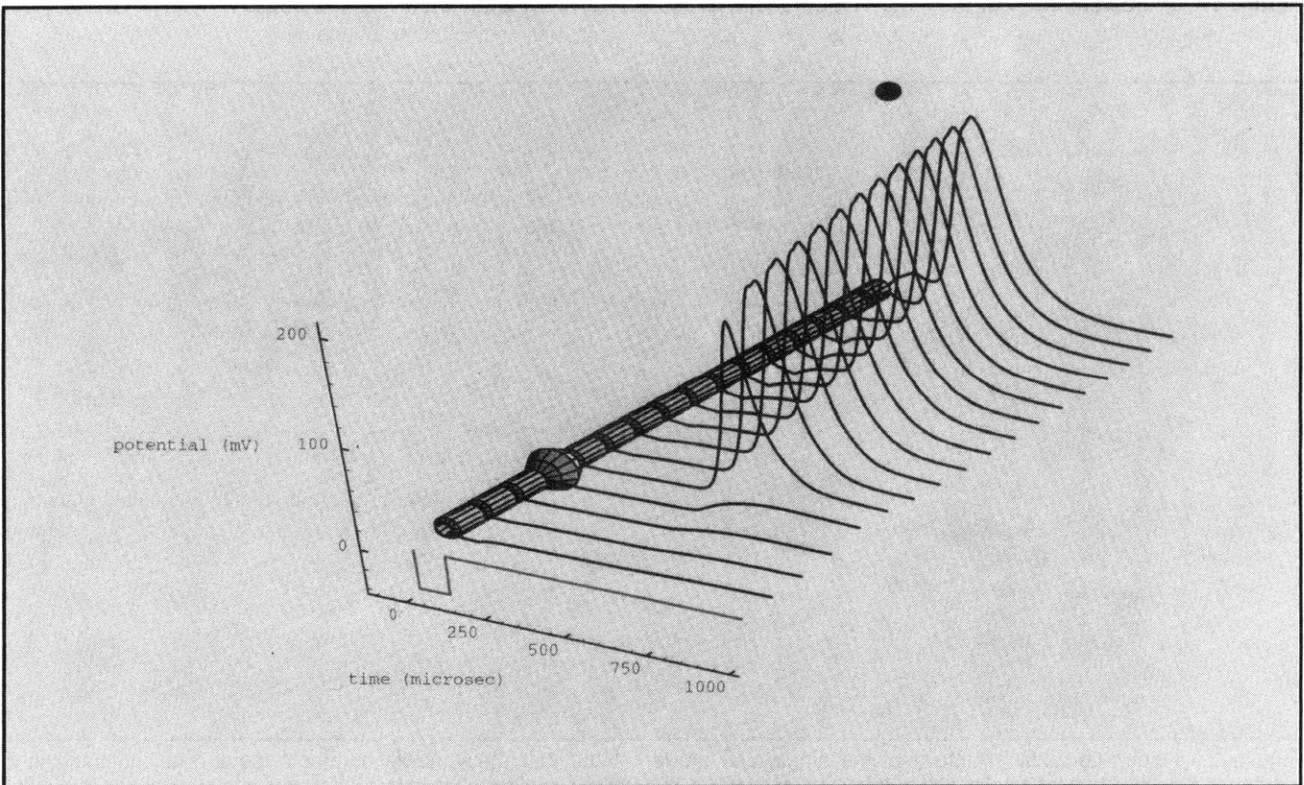
**Figure 1.** Overall structure of the single-unit model that includes a representation of the cell body.



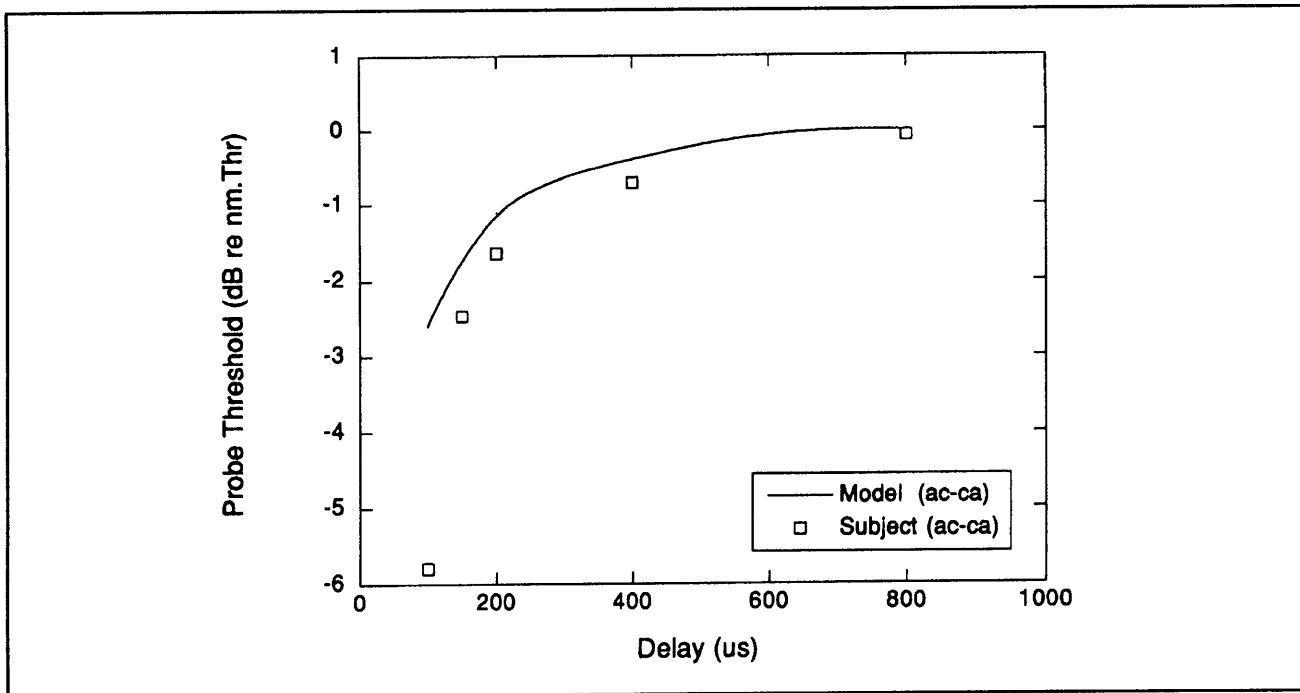
**Figure 2.** Node/internode structure of the single-unit model. Note that the variable conductance at the internode is a nonlinear function based on the characteristics of voltage dependent sodium channels.



**Figure 3.** Computed membrane potential as a function of time for the pictured model nodes. The stimulating electrode's position is indicated by the black oval and the cathodic, monophasic stimulus waveform is shown below the pictured model. Note that the spike conducts across the cell body in the orthograde direction.



**Figure 4.** Computed membrane potential as a function of time for the pictured model nodes. The stimulating electrode's position is indicated by the black oval and the cathodic, monophasic stimulus waveform is shown below the pictured model. Note that even though the model parameters are the same used in the model of figure 3, retrograde conduction is blocked at the cell body.



**Figure 5.** Forward masking results for an anodic-phase-first, biphasic masker followed by a cathodic-phase-first, biphasic probe (ac-ca). Probe threshold is plotted in dB relative to the nonmasked threshold and as a function of the delay between the masker and the probe. The subject results are represented by the symbols and the single-unit model predictions by the solid line.

## 1.7.2 Project B: Psychophysics of Intracochlear Electrical Stimulation

### Project Staff

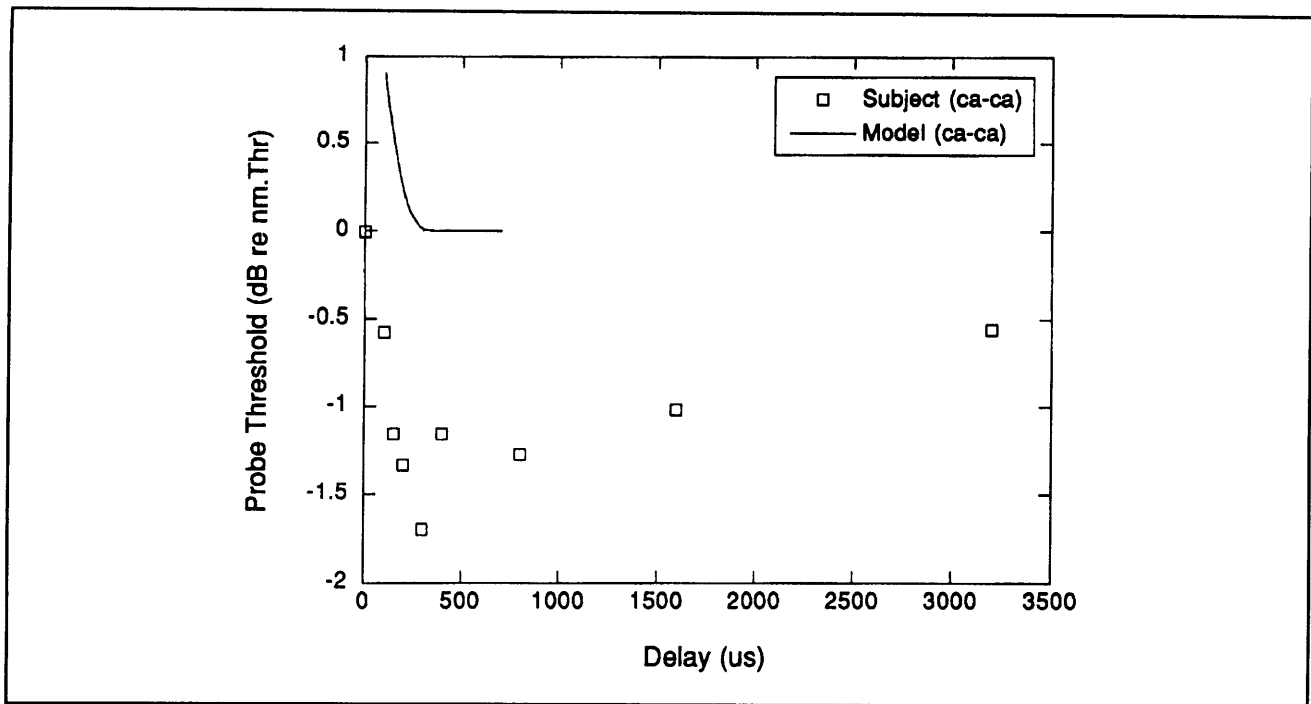
Dr. Donald K. Eddington

One goal of our psychophysical studies is to provide insight into the mechanisms that limit device effectiveness. Using a masking paradigm, we demonstrated in previous years that electrical stimuli delivered simultaneously by two intracochlear electrodes produce strong interactions and that the strength of these interactions across subjects is negatively correlated ( $r=-0.8$ ) with their speech reception scores. Processing systems that interleave stimuli in time reduce these interactions and produce improved speech reception in many subjects. This year, we focused on measures of forward masking to investigate the strength of nonsimultaneous interactions.

The electrical stimuli used in the forward masking experiments were single, charge-balanced biphasic pulses (phase duration 50us) presented to the same intracochlear electrode. The masker ampli-

tude was constant at  $-2$  dB below the unmasked threshold with the anodic phase first and cathodic phase second (ac). The following probe stimulus was presented with cathodic phase first (ca), and its amplitude was varied using a two-down, one-up adaptive procedure in a three alternative, forced choice context to measure threshold. For this ac-ca masker-probe condition, the single-unit model predictions are consistent with the subject data (figure 5). The subthreshold masker reduces threshold by as much as 6 dB for a 100 us masker/probe delay. This effect diminishes with increased delay and is negligible for delays longer than 800 us.

The data plotted in figure 6 are from the same subject using a cathodic-phase-first, anodic-phase-second masker. In this condition (ca-ca), the masker tends to decrease threshold less than the ac-ca case and its effect lasts longer than 3 ms. Note that the single-unit model's prediction for the ca-ca case is not consistent with the psychophysical results. This inconsistency will be explored in future single-unit studies in a cat. Because the nonsimultaneous interactions are significant, we are beginning to explore stimulation strategies that will minimize their impact.



**Figure 6.** Forward masking results for an cathodic-phase-first, biphasic masker followed by a cathodic-phase-first, biphasic probe (ca-ca). Probe threshold is plotted in dB relative to the nonmasked threshold and as a function of the delay between the masker and the probe. The subject results are represented by the symbols and the single-unit model predictions by the solid line.

### 1.7.3 Project C: New Sound Processors for Auditory Prostheses

#### Project Staff

Dr. Donald K. Eddington, Dr. William M. Rabinowitz, Joseph Tierney, Marc A. Zissman

This project is directed at the design, development, and evaluation of speech processors for use with implanted auditory prostheses in deaf humans. Work this year has focused in three areas: (1) developing a programmable, real-time, speech processing facility that can implement processor/stimulator algorithms for two independent eight-channel implants, (2) using the laboratory system to explore new sound processing algorithms in interactive test sessions with implanted subjects, and (3) designing and fabricating a programmable, wearable speech processor/stimulator that will allow subjects full-time use of processor algorithms developed and tested in our laboratory setting.

One focus of this year's testing of subjects was the exploration of input automatic-gain control. The area of signal level control/compression is important in cochlear implant systems because the wide dynamic range of acoustic signals (~100 dB) must be compressed to the relatively small dynamic range of electrical stimulation (~25 dB).

Using a real-time digital simulation of the subjects' commercial processor, the effects of systematic modifications of the AGC's dynamic characteristics were studied. Certain AGC manipulations have produced substantial increases in consonant identification. For example, on the identification of 16 intervocalic consonants (/a-C-/a/ tokens from the Iowa videodisc), one subject moved from 32 percent correct with the standard commercial processor to 52 percent correct when the AGC release time was decreased from 250 to 50 us. A second subject improved from 35 to 68 percent correct. A third subject, who is an excellent performer with his standard processor, was tested with 24 consonants; his score increased from 82 to 92 percent correct. One practical reason these results are important is because they suggest relatively simple changes in the subjects' commercial processor that may lead to significant improvements in speech reception.

#### 1.7.4 Publication

Wilson, B.S., C.C. Finley, D.T. Lawson, R.D. Wolford, D.K. Eddington and W.M. Rabinowitz. "Better Speech Recognition with Cochlear Implants." *Nature* 352: 236-238 (1991).