

Chapter 1. Signal Transmission in the Auditory System

Academic and Research Staff

Professor Dennis M. Freeman, Professor William T. Peake, Professor Thomas F. Weiss, Dr. Bertrand Delgutte,¹ Dr. Donald K. Eddington,² Dr. Susan E. Voss,¹ Joseph Tierney²

Visiting Scientists and Research Affiliates

Dr. Ruth Y. Litovsky,¹ Dr. John J. Rosowski,¹ Michael Ravicz¹

Graduate Students

C. Cameron Abnet, Alexander J. Aranyosi, Bryan C. Bilyeu, Gregory T. Huang, Sridhar Kalluri, Courtney C. Lane, Christopher J. Long, Abraham R. McAllister, Martin F. McKinney, Christopher S. McNulty, Jekwan Ryu, Chandran V. Seshagiri, Jesse L. Wei

Undergraduate Students

Shelley M. Cazares, Ian Chen, Nasos D. Dousis, Richard Y. Huang

Technical and Support Staff

Janice L. Balzer

1.1 Middle and External Ear

Sponsors

National Institutes of Health
Grant R01 DC00194
Grant P01 DC 00119
National Science Foundation
Grant IBN 96-0462

Project Staff

Professor William T. Peake, Dr. John J. Rosowski, Dr. Susan E. Voss, Bryan C. Bilyeu, Gregory T. Huang, Michael Ravicz, Jekwan Ryu

1.1.1 Goals

The goal of the Auditory Mechanics group is to understand how the structures of the external and middle ear affect what we hear through measurements of normal function and structure in normal and pathological ears. We expect to determine the role each component of the ear plays in hearing. In pursuing this goal we make physiological and anatomical measurements in human ears and use the large patient population at the Massachusetts Eye and Ear Infirmary to test structure and function inferences.

We also take advantage of the wide variations in ear structure within the animal kingdom, measuring function and structure in a variety of animal ears.

1.1.2 Clinical Correlations of Structure and Function in Human Middle Ear

In conjunction with the clinical staff in the Department of Otolaryngology of the Massachusetts Eye and Ear Infirmary, we investigated the relationships of ear pathology and post-surgical structure to hearing level. These studies include a correlation analysis between pathological stapes structure and hearing level in patients with otosclerosis (a disease marked by the proliferation of bone and bony fixation of the stapes). The surprising conclusion is that pathological changes in the soft tissues that support the stapes are better correlated with hearing loss than the degree of bony fixation of the stapes. A second study demonstrated the prevalence and the degree of hearing loss after reconstructive surgery for otosclerosis.

1 Eaton Peabody Laboratory of Auditory Physiology, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts.

2 Cochlear Implant Research Laboratory, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts.

1.1.3 Analyses of Normal and Pathological Middle-Ear Function

Several series of middle-ear measurements come to functional conclusions regarding middle-ear pathology and post-surgical hearing levels. (1) Some preliminary computer-microvision measurements of three-dimensional stapes motion were performed to address the fundamental issue of whether the human stapes can be assumed to act as a translating piston. The present data set suggests that the piston assumption is valid below 1000 Hz but may not hold at higher frequencies. (2) A complete set of functional measurements and analyses of the effects of tympanic-membrane perforations on middle-ear function led to the first quantitative description of how ear-drum perforations of different sizes affect the frequency dependence and sensitivity of hearing function. (3) After making measurements of the functional effects of different middle-ear surgical techniques, we came to the conclusion that two common techniques for reconstructing the middle-ear air spaces after disease lead to similar function. (4) We continued our analyses of other middle-ear surgical techniques, contributing to papers that review various diagnostic and surgical procedures and make specific recommendations about surgical approaches and materials.

1.1.4 Measurement of Middle-Ear Mechanics in Intact Ears

Much of our existing knowledge of middle-ear mechanics comes from measurements in animals or human cadavers in which the external ear has been surgically removed. This removal is necessary to control the sound stimulus at the tympanic membrane. However, measurements in living humans can only be performed with the external ear intact. Also owners of exotic animals (e.g., zoos) might allow experimenters to make measurements in the intact ears of anesthetized animals. We have developed and tested a sound-delivery system that permits accurate measurements of middle-ear impedance from within the intact ear canal at frequencies up to 5 kHz. This system has been used to measure the impedance of eleven exotic cat species.

1.1.5 The Adaptive Significance of Differences in Middle-Ear Structure

Correlations made between the structure of the middle-ear in 36 species of cats (from tigers to house cats) and the climates they inhabit challenge the

common idea that large middle-ear air spaces are an adaptation for desert environments. While it was demonstrated that several cat species with relatively large middle-ears inhabit arid climates, one cat with a large middle-ear is a jungle dweller. Furthermore, the cat species with large ear cavities all come from different branches of the cat family, making it unlikely that the large middle-ear is an evolutionary leftover.

1.1.6 Publications

Journal Articles

- Cherukupally, S.R., S.N. Merchant, and J.J. Rosowski. "Correlations between Stapes Pathology and Conductive Hearing Loss in Otosclerosis." *Ann. Otol. Rhinol. Laryngol.* 107: 319-26 (1998).
- Merchant, S.N., M.J. McKenna, and J.J. Rosowski. "Current Status and Future Challenges of Tympanoplasty." *European Arch. Oto-Rhino-Laryngol.* 255: 221-28 (1998).
- Merchant, S.N., M.E. Ravicz, S.E. Voss, W.T. Peake, and J.J. Rosowski. "Middle Ear Mechanics in Normal and Diseased and Reconstructed Ears." *J. Laryngol. Otol (UK)* 112: 715-31 (1998).
- Whittemore, K.R., S.N. Merchant, and J.J. Rosowski. "Acoustic Mechanisms: Canal Wall-up versus Canal Wall-down Mastoidectomy." *Otolaryngol., Head Neck Surgery* 118: 751-61 (1998).

Theses and Dissertations

- Bilyeu, B. *Computer-microvision Study of the Three-dimensional Motion of the Human Stapes*. M.Eng. thesis. Department of Electrical Engineering and Computer Science, MIT, 1997.
- Voss, S.E. *Effects of Tympanic-membrane Perforations on Middle-ear Sound Transmission: Measurements, Mechanisms and Models*. Ph.D. diss. Department of Electrical Engineering and Computer Science, MIT, 1997.

Meeting Papers

- Han, W.W., J.J. Rosowski, and S.N. Merchant. "Post-stapedotomy Air-bone Gap: A Clinical and Acoustico-mechanical Analysis." *Abstracts of the 21st Midwinter Meeting of the Association for Research in Otolaryngology*, St. Petersburg Beach, Florida, February 15-19, 1998, p. 66.
- Huang, G.T., J.J. Rosowski, S. Puria, and W.T. Peake. "Noninvasive Technique for Estimating Acoustic Impedance at the Tympanic Membrane (TM) in Ear Canals of Different Size." *Abstracts of the 21st Midwinter Meeting of the Association*

for *Research in Otolaryngology*, St. Petersburg Beach, Florida, February 15-19, 1998, p. 111.

Peake, W.T., and J.J. Rosowski. "Structural Variations in the Middle Ears of Species in the Cat Family: Habitat Correlations." *Abstracts of the 21st Midwinter Meeting of the Association for Research in Otolaryngology*, St. Petersburg Beach, Florida, February 15-19, 1998, p. 4.

Voss, S.E., J.J. Rosowski, S.N. Merchant, and W.T. Peake. "How Do Tympanic Membrane Perforations Cause Conductive Hearing Loss?" *Abstracts of the 21st Midwinter Meeting of the Association for Research in Otolaryngology*, St. Petersburg Beach, Florida, February 15-19, 1998, p. 66.

1.2 Cochlear Mechanics

Sponsors

W.M. Keck Foundation

Career Development Professorship

National Institutes of Health

Grant R01 DC00238

Thomas and Gerd Perkins Professorship

John F. and Virginia B. Taplin Health Sciences
and Technology Award

Project Staff

Professor Dennis M. Freeman, Professor Thomas F. Weiss, C. Cameron Abnet, Alexander J. Aranyosi, Bryan C. Bilyeu, Shelley M. Cazares, Ian Chen, Nasos D. Dousis, Richard Y. Huang, Abraham R. McAllister, Christopher S. McNulty, Jekwan Ryu, Jesse L. Wei

1.2.1 Electrical Properties of the Tectorial Membrane

The tectorial membrane (TM) is a gelatinous structure that overlies the mechanically sensitive hair bundles of sensory cells in the inner ear. This strategic position suggests that the TM plays a key role in cochlear micromechanics. However, little is known about the physicochemical properties of this tissue.

The TM is a polyelectrolytic gel. It is mostly water: 97% by weight. The rest of the gel is a network of protein and sugar macromolecules that have ionizable charge groups. This fixed charge is thought to contribute to the osmotic and mechanical properties of the TM.

The amount of fixed charge in the TM has been estimated by measuring the electrical potential of the TM with microelectrodes. However, it has been difficult to obtain stable and repeatable measurements using this method. During the past year, we have developed an entirely new approach for measuring the electrical potential of the TM.

The electrical potential of the TM results because fixed charge in the TM interacts with mobile carriers to develop a space charge layer at the interface between the TM and bathing solution. This space charge layer gives rise to a junction potential between the TM and bath. If the TM is positioned so that it is in contact with two baths, then the electrical potential between the baths is the difference between two junction potentials: one between the TM and bath 1, and one between the TM and bath 2. If the baths have identical solutions and if the TM is homogeneous, then the electrical potential between the baths will be zero. However, the junction potentials are very sensitive to the ionic compositions of the baths. For example, the magnitudes of the junction potentials decrease as the ionic strength of the baths increase. Thus, by using baths with different concentrations of KCl (the predominate salt in the solution that normally bathes the TM), a potential difference between the baths can be recorded. This potential difference can be used to estimate the fixed charge in the TM.

Figure 1 illustrates the design of our experimental chamber. The TM contacts the two baths at opposite ends of its long dimension. Thus the two baths are separated by more than 300 μm .

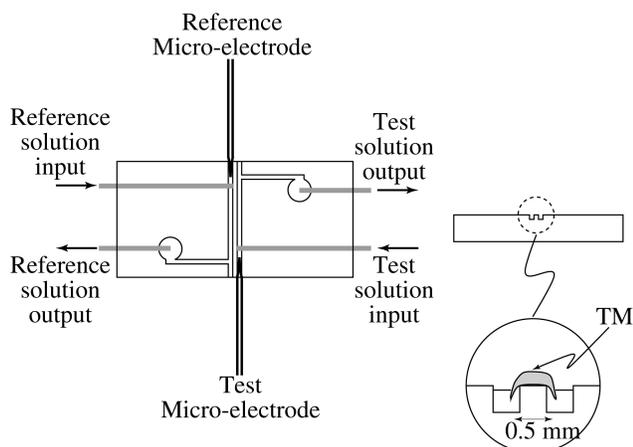


Figure 1. Schematic of test chamber. Two parallel troughs are arranged so that they are perfused by test and reference solutions, respectively. The potential between the troughs is measured with a pair of microelectrodes. The TM is placed so that it creates a bridge between the troughs, as shown in the cross-sectional view on the right.

This separation far exceeds the maximum separation that is possible with a micropipette, which is limited by the smallest dimension of the TM. Furthermore, the square corners of the troughs tightly entrain the bath solutions by capillarity, and excess fluid between the troughs is quickly drawn into the troughs. Thus unintentional saline shorts between the troughs are rare.

Results from a typical experiment are shown in Figure 2. It can be seen that the measured potentials were stable to within a millivolt over periods of ten minutes. Other experiments demonstrate equal stability and repeatability to within 2 mV. Such periods of stability were never obtained using previous methods for measuring TM potential.

The results in Figure 2 were analyzed using an isotropic polyelectrolytic gel model. The analysis suggests that the fixed charge concentration is -232 mmol/L. This estimate is a factor of 8 to 10 times greater than previous estimates. However, because of the stability and repeatability of the method, these results cannot be easily dismissed.

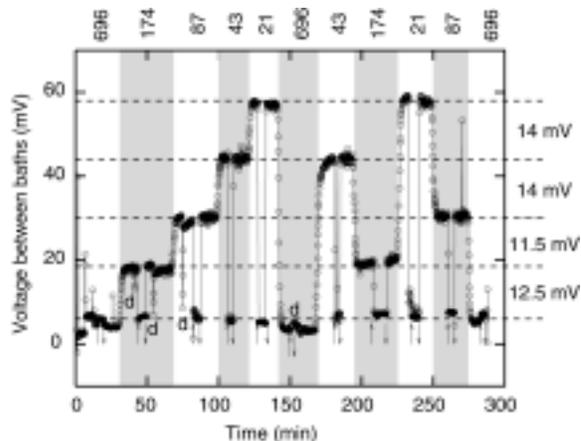


Figure 2. Results from a typical experiment. Circles indicate the voltage between the baths, measured as a function of time. Shading indicates times when different concentrations of KCl (given at the top of the figure) were present in the test solution. The reference solution is 696 mmol/L KCl throughout. Up and down arrows surround times when a salt bridge was positioned to “short” the potential between the baths. The letter “d” indicates times when a drop of saline was intentionally placed on the TM to create a saline bridge between the baths. Dashed lines indicate an average voltage for each test solution. Differences between the average voltages are indicated on the right.

1.2.2 Blebs

Blebs are outward herniations of cell membranes that form when cells are exposed to adverse conditions. Sensory cells in the inner ear form blebs on their apical surfaces in response to various forms of trauma, including acoustic overstimulation, application of ototoxic drugs, and ischemia. To understand the conditions that promote blebbing in hair cells, we have examined blebs in an *in vitro* preparation of the alligator lizard cochlea. We place the cochlea in an experimental chamber that simulates the normal fluid environment, in which different fluids bathe the apical and basal parts of the cochlea. We then apply test solutions to the apical and basal parts of the cochlea and observe effects of the test solutions using a microscope.

Blebs formed in all our experiments in which both the apical and basal parts of the cochlea were exposed to a standard culture medium during dissection. In approximately half of those experiments, the blebs shrank and disappeared after the cochleae were placed in the experimental chamber and the perfusates were changed so that (1) the apical solution was high in potassium and (2) the basal solution was high in sodium, as occurs naturally.

Blebs did not form when cochleae were dissected in a culture medium in which the cations were replaced with NMDG^+ , a large cation that cannot readily enter cells. Blebs also did not form when cochleae were dissected in a culture medium in which the anions were replaced with glutamate $^-$, a large anion. These results suggest that permeant extracellular ions are necessary for bleb growth.

Figure 3 shows the image of a cochlea that was dissected and then bathed in a culture medium containing 1 mmol/L Gd^{+3} , which is known to block transduction channels and stretch-activated channels. There are no blebs on these cells, presumably because the Gd^{+3} blocked bleb formation. Figure 4 shows the same cochlea after the bathing media were changed so that the apical solution was high in potassium and the basal solution was high in sodium, as occurs naturally. In this image, large blebs are visible on the hair cells. Removal of the Gd^{+3} appears to have allowed blebs to start growing.

These results demonstrate our ability to alter the course of bleb development in hair cells through changes in extracellular media. Under appropriate conditions the growth of blebs can be blocked or reversed. Through such manipulations we hope to develop a better understanding of the process of bleb formation.

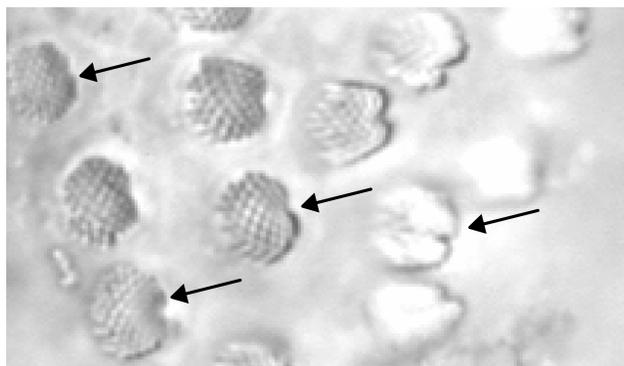


Figure 3. Image of a portion of the lizard cochlea. The arrows point to some of the hair bundles.

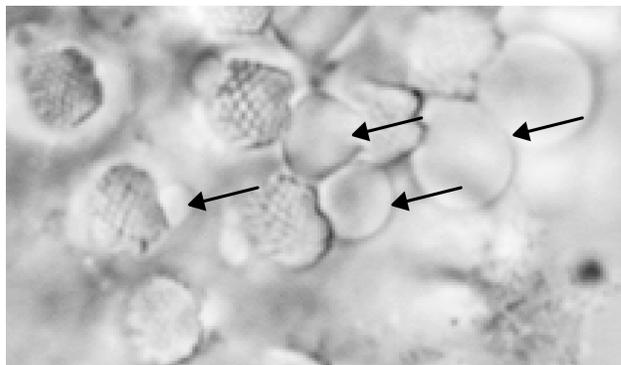


Figure 4. Image of cochlea shown in Figure 3 after blebs have formed. The arrows point to some of the blebs.

1.2.3 Publications

Journal Articles

Davis, C.Q., and D.M. Freeman. "Statistics of Sub-pixel Registration Algorithms Based on Spatiotemporal Gradients or Block Matching." *Opt. Eng.* 37: 1290-98 (1998).

Davis, C.Q., and D.M. Freeman. "Using a Light Microscope to Measure Motions with Nanometer Accuracy." *Opt. Eng.* 37: 1299-304 (1998).

Meeting Papers

Abnet, C.C., and D.M. Freeman. "Deformations of the Isolated Mouse Tectorial Membrane Produced by Calibrated Oscillatory Forces." *Abstracts of the 21st Midwinter Research Meeting of the Association for Research in Otolaryngology*, St. Petersburg Beach, Florida, February 15-19, 1998, p. 183.

Aranyosi, A.J., C.Q. Davis, and D.M. Freeman. "Experimental Measurements of Micromechanical Transfer Functions in the Alligator Lizard." *Abstracts of the 21st Midwinter Research Meeting of the Association for Research in Otolaryngology*, St. Petersburg Beach, Florida, February 15-19, 1998, p. 183.

Theses and Dissertations

Abnet, C.C. *Measuring Mechanical Properties of the Tectorial Membrane with a Magnetizable Bead*. Ph.D. diss. Department of Electrical Engineering and Computer Science, MIT, 1998.

Bilyeu, B.C. *Computer Microvision Measurements of Stapedial Motion in Human Temporal Bone*. S.M. thesis. Department of Electrical Engineering and Computer Science, MIT, 1998.

Cazares, S.M. *Osmotic Response of the Mouse Tectorial Membrane to Changes in Predominant Alkali Ion*. B.S. thesis. Department of Electrical Engineering and Computer Science, MIT, 1998.

1.3 Auditory Neural Coding of Speech

Sponsor

National Institutes of Health/National Institute
for Deafness and Communicative Disorders
Grant DC02258
Grant DC00038

Project Staff

Dr. Bertrand Delgutte, Sridhar Kalluri, Martin F. McKinney, Chandran V. Seshagiri

The long-term goal of this project is to understand neural mechanisms for the processing of speech and other biologically-significant sounds. Efforts during the past year have focused on three different areas: (1) neural representation of musical pitch, (2) neural correlates of auditory masking, and (3) a mathematical model of onset neurons in the cochlear nucleus.

1.3.1 Neural Representation of Pitch

We have continued investigating correlates of the subjective octave in auditory-nerve (AN) fiber responses. We had previously shown that a temporal model of pitch based on interspike intervals from AN fibers successfully predicts the octave enlargement effect, the tendency of listeners to prefer frequency ratios slightly greater than 2:1.³ Recent focus has been on detailed analyses of interspike interval (ISI) deviations that give rise to the octave enlargement effect in the model. Specifically, we compared neural ISIs with predictions of a point-process model of AN discharges that simulates a wide variety of physiological data.⁴ This "multiplicative" model states that the instantaneous probability of discharge is the product of a component representing excitation by the stimulus and a component representing the refractory properties of the neuron.

AN ISIs systematically deviate from multiples of the stimulus period for pure-tone stimuli. Two separate mechanisms are responsible for the ISI deviations: for low-frequency (< 400 Hz) tones, ISIs are slightly

smaller than stimulus-period multiples while, for mid-frequency (400-3000 Hz) tones, they are larger than stimulus-period multiples. The low-frequency effect is due to the phase-locking of AN fibers: When the fiber discharges twice during a stimulus period, the following interval must be slightly shorter than a stimulus period in order to maintain the average interval length imposed by phase-locking. This effect is predicted by the multiplicative model for AN activity.

The mid-frequency effect reflects the fact that a spike closely following another one occurs at a later phase than average within the stimulus cycle. This effect, which is possibly due to a decrease in conduction velocity during the relative refractory period, is poorly predicted by the multiplicative model. We are currently investigating whether the Hodgkin-Huxley model for electrically-excitable membranes predicts the effect.

These results suggest that existing stochastic models of AN activity fail to simulate features of temporal discharge patterns that may be important for the octave enlargement effect. If so, computational theories of pitch will need to be revised to account for these phenomena.

1.3.2 Neural Correlates of Masking in the Inferior Colliculus

We have begun an investigation of neural correlates of auditory masking in inferior-colliculus (IC) neurons. Masking is important for understanding the neural coding of speech because most speech communications occur in noise backgrounds. Moreover, masking has played a key role in auditory theory since the work of Fletcher in the 1930s, and masking techniques used in psychophysics may be useful for studying the processing of acoustic stimuli by the nervous system as well.

In one series of experiments, we studied the responses of single IC units in anesthetized cats to broadband signals (click train or FM glides) in additive noise having the same long-term average power spectrum as the signal. Responses were collected as a function of noise masker level, and the masked threshold for which the signal was just detectable was measured. Neural masking could take either of two forms. For some neurons, the noise, by itself,

3 M.F. McKinney and B. Delgutte, "A Possible Neurophysiological Basis of the Octave Enlargement Effect," submitted to *J. Acoust. Soc. Am.*

4 Johnson and Swami, *J. Acoust. Soc. Am.* 74: 493-501 (1983).

produced no discharges, yet it was able to completely suppress the neural response to the signal (suppressive masking). In other neurons, masking occurred when the response to the noise exceeded the response to the signal without suppressing it (excitatory masking). Most neurons showed a combination of excitatory and suppressive masking. These results differ from the situation in the AN, where suppressive masking only occurs when the signal and the masker occupy different frequency regions.

A related series of experiments aimed at testing the hypothesis that a signal in noise might be detected via correlated temporal patterns of discharge in multiple neurons rather than from the activity of any single neuron. We obtained simultaneous recordings from multiple IC cells using “stereotrodes” with two closely-spaced (100 μ m) contacts. Single units were isolated based on the coincidence of waveform features recorded from the two electrodes. For the small sample of neuronal pairs that were analyzed, we found no correlation in discharge patterns other than what would be expected for two independent cells responding to the same stimulus. In the future, we plan to use multiple-contact electrode arrays in order to increase the data yield in these experiments.

These preliminary results suggest that mechanisms of masking may be different in the auditory midbrain than in the periphery, even in conditions when binaural interactions play a minimum role. This finding challenges the widely-held conception that masking is primarily due to peripheral mechanisms such as cochlear frequency selectivity. Ultimately, a better understanding of neural mechanisms of masking may help design hearing aids and implantable prostheses that perform better in noise.

1.3.3 Mathematical Model of Onset Neurons in the Cochlear Nucleus

Onset (On) units in the ventral cochlear nucleus (VCN) are characterized by phasic responses to high-frequency tone bursts, entrainment to low-frequency tones, and similar thresholds for tones and broadband noise. To better understand the cellular basis for these response properties, we are using our

previously-developed model to study how synaptic and electrical properties determine On unit responses to sound.⁵

Our model for On units is a point neuron with integrate-to-threshold membrane dynamics and excitatory synaptic inputs from model auditory-nerve (AN) fibers. Parameter values for membrane dynamics are constrained using voltage responses to current injections in octopus cells.⁶ Synaptic and input parameters are based on On-unit responses to acoustic tones and noise.

To match the current injection data, the membrane dynamics must have at least two processes: a fast lowpass process (e.g., leaky integration by membrane capacitance) with a time constant near 0.4 ms, and a slower highpass process (e.g., time-varying threshold) with a time constant near 0.7 ms. To explain temporal discharge patterns to tones, the model must have many (> 50) independent AN inputs and weak synapses. Further, to match the relative tone and noise thresholds observed in On units, the AN inputs in the model must span an approximately one-octave range of characteristic frequencies. These constraints on model inputs are consistent with connectivity patterns derived from anatomical studies. In general, we have determined that all the electrical, synaptic, and input features listed above acting together are needed for the model to have response properties of Onset units.

Our model provides important constraints on biophysical mechanisms for generating onset responses. By understanding which neuronal features determine On unit responses, we are in a position to explain the diversity of On-unit responses and their relation to VCN cell types.

1.3.4 Publications

Chapters in Books

Delgutte, B., B.M. Hammond, and P.A. Cariani. “Neural Coding of the Temporal Envelope of Speech: Relation to Modulation Transfer Functions.” In *Psychophysical and Physiological Advances in Hearing*. A.R. Palmer, A. Reese, A.Q. Summerfield, and R. Meddis, eds. London: Whurr, 1998, 595-603.

5 S. Kalluri and B. Delgutte, “Characteristics of Cochlear Nucleus Onset Units Studied using a Model,” In *Computational Models of Auditory Function*, S.G. Greenburg and M.L. Slaney, eds. (Amsterdam: IOS Press, forthcoming).

6 N.L. Golding, M.J. Ferragamo, and D. Oertel, “Octopus Cells: Fastest Cells in the Brain?” *Abstracts of the 20th Midwinter Meeting of the Association for Research in Otolaryngology*, 1997, p. 116.

Kalluri, S., and B. Delgutte. "Characteristics of Cochlear Nucleus Onset Units Studied using a Model." In *Computational Models of Auditory Function*. S.G. Greenberg and M.L. Slaney, eds. Amsterdam: IOS Press. Forthcoming.

Journal Articles

McKinney, M.F., and B. Delgutte. "A Possible Neurophysiological Basis of the Octave Enlargement effect." Submitted to *J. Acoust. Soc. Am.*

Tsai, E.J., and B. Delgutte. "Neural Mechanisms Underlying Intensity Discrimination: Responses of Auditory-nerve Fibers to Pure Tones in Band-reject Noise." Submitted to *J. Neurophysiol.*

Meeting Papers

Delgutte, B. "Temporal Interactions for Speech and Nonspeech Stimuli in the Inferior Colliculus." *Abstracts of the 21st Midwinter Meeting of the Association for Research in Otolaryngology*, St. Petersburg Beach, Florida, February 15-19, 1998, p. 205.

Kalluri, S., and B. Delgutte. "A Model of Ventral Cochlear Nucleus Onset Units." *Abstracts of the NATO Advanced Study Institute on Computational Hearing*, Lucca, Italy, July 1998.

Kalluri, S., and B. Delgutte. "Cellular Properties of Ventral Cochlear Nucleus Onset Units Studied using a Mathematical Model." *Abstracts of the 22nd Midwinter Meeting of the Association for Research in Otolaryngology*, St. Petersburg Beach, Florida, February 13-18, 1999, p. 144.

McKinney, M.F., and B. Delgutte. "Correlates of the Subjective Octave in Auditory-nerve Fiber Responses: Effect of Phase-locking and Refractoriness." *Abstracts of the 21st Midwinter Meeting of the Association for Research in Otolaryngology*, St. Petersburg Beach, Florida, February 15-19, 1998, p. 138.

1.4 Neural Mechanisms of Spatial Hearing

Sponsor

National Institutes of Health/National Institute
for Deafness and Communicative Disorders
Grant DC00119
Grant DC00038

Project Staff

Dr. Bertrand Delgutte, Dr. Ruth Y. Litovsky, Courtney C. Lane

The long-term goal of this project is to understand the neural mechanisms for sound localization in noisy and reverberant environments. Our efforts in the past year have focused on neural correlates of the release from masking that occurs when a signal and a noise masker are spatially segregated. Such spatial release from masking is likely to contribute to the "cocktail party effect," whereby normal hearing listeners can attend to a single voice and understand its message among a large number of speakers.

We recorded single-unit activity in the inferior colliculus (IC) of anesthetized cats in response to a broadband signal (100-Hz click train or 40-Hz chirp train) in continuous broadband noise. Stimulus azimuth was simulated using a virtual space (VS) technique: the signal in each ear was filtered through a head-related transfer function (HRTF) for the particular azimuth. Such VS stimuli possess three localization cues as in free field: interaural time (ITD) and level (ILD) differences, and spectral cues. The signal was always positioned at the midline (0° azimuth), while the noise azimuth was systematically in the frontal hemifield. Masked threshold was defined as the masker level for which the signal produced an in-average discharge rate over the masker response in 75% of the trials.

For most IC neurons, masked thresholds depended systematically on noise azimuth. Some neurons showed directionally-dependent changes in masked thresholds of 15-20 dB, comparable to the spatial release from masking observed psychophysically for broadband signals.

We also measured responses to modified VS stimuli for which some localization cues in the masker were held constant while the others varied with azimuth as in free field. The signal's localization cues were always appropriate for 0° azimuth. For some cells, the directionality of the masking effect could be almost entirely accounted for by changes in masker ILD. However, for some low-frequency cells, the masking effect depended on a combination of ITD and ILD.

These preliminary results are encouraging in that some IC cells show spatially-dependent changes in masking comparable in magnitude to psychophysical release from masking. Results of cue manipulations further suggest that the effect depends on multiple localization cues and neural mechanisms. In the future, we will determine whether the spatial pattern

of release from masking found psychophysically can be accounted for by changes in masked thresholds for a population of IC neurons.

1.4.1 Publications

Journal Article

Delgutte, B., P.X. Joris, R.Y. Litovsky, and T.C.T. Yin. "Receptive Fields and Binaural Interactions for Virtual-space Stimuli in the Cat Inferior Colliculus." *J. Neurophysiol.* Forthcoming.

Meeting Paper

Litovsky, R.Y., B.R. Cranston, and B. Delgutte. "Neural Correlates of the Precedence Effect in the Inferior Colliculus: Effect of Localization Cues." *Abstracts of the 21st Midwinter Meeting of the Association for Research in Otolaryngology*, St. Petersburg Beach, Florida, February 15-19, 1998, p. 40.

1.5 Cochlear Implants

Sponsors

W.M. Keck Foundation
National Institutes of Health
Grant P01-DC00361
Contract N01-DC-6-2100

Project Staff

Dr. Donald K. Eddington, Dr. Joseph Tierney, Christopher J. Long

1.5.1 Introduction

The basic function of a cochlear prosthesis is to provide a measure of hearing to the deaf by using stimulating electrodes implanted in or around the cochlea to elicit patterns of spike activity on the array of surviving auditory-nerve fibers. By modulating the patterns of neural activity, these devices attempt to present information about the acoustic environment that the implanted patient can learn to interpret. The overall goal of our work is twofold: (1) to understand the mechanisms responsible for the neural activity patterns elicited by electric stimulation, and (2) to use this understanding to design wearable sound processors that translate acoustic signals into electric stimuli that produce sound sensations deaf subjects can interpret.

This year's report concentrates on graduate student Christopher Long's work to determine (1) whether binaural advantages (e.g., sound-source localization and better speech reception in noise) can be realized by implantees with a pair of cochlear implants and (2) if it can be realized how this might occur. We report on experiments Mr. Long conducted with a bilaterally implanted subject which measured the binaural sensitivity to interaural time differences (ITDs) and interaural level differences (ILDs).

1.5.2 Methods

The subject was a 72-year-old woman with an Ineraid implant (right cochlea) and a Clarion implant (left cochlea) who has been under the care of the Warren Otologic Group of Warren, Ohio. She remembers hearing normally until age 25 when she noticed the onset of a bilateral hearing loss that progressed bilaterally until she became deaf at age 44. At age 59, she received the Ineraid cochlear implant and used that system on a daily basis until age 70, when she received the Clarion implant in an effort to improve her hearing using the new technology. Since then, she has been a full-time user of the Clarion implant alone. When she first received the Clarion implant, she attempted to use both the Clarion and Ineraid implants simultaneously—with unmatched processors and electrode pairs—for a brief period, but found the sensations confusing.

The stimulus trains (300 ms duration) used in these experiments consisted of fixed-amplitude, cathodic-first biphasic pulses (76.9 μ sec phase duration) delivered at 100 pps (813 pps in the pitch ordering test). Electrodes were stimulated in a monopolar configuration. The monopolar configuration of the 7th medial Clarion electrode and its far-field ground is denoted by "7MC." The second Ineraid electrode with its far-field ground is denoted by "2I." For both devices, electrode 1 represents the most apical electrode.

A pitch ordering test was used to rank order the electrodes by the pitch sensations they produced. We assumed that electrodes eliciting similar pitch sensations (across ears) were located at similar cochleotopic positions. Based on the results of this test, cochleotopically matched (or mismatched) electrode pairs were selected for further study in binaural psychophysical experiments.

A centering test was conducted with simultaneous, bilateral stimulation (100 pps; ITD = 0 μ sec) for electrode pairs in which such stimuli resulted in a fused percept (typically pitch-matched electrodes). The

amplitude of the Clarion stimulus was held constant at a comfortable level and the Ineraid stimulation amplitude was adjusted in order to produce a centered sensation. A one-interval, two-alternative, forced-choice (one-up, one-down, adaptive) procedure was employed. The result was used to determine the center of the range of Ineraid stimulus amplitudes to be used in the lateralization test. For an electrode pair in which the stimuli were not perceptually fused, the stimulus presentation method described above was used, but the subject was instructed to balance loudnesses of the two simultaneous sound sensations.

A limitation associated with the stimulation hardware used for these preliminary experiments restricted testing to ITDs ≥ 0 (for positive ITDs, the stimulus delivered to the Ineraid electrode is delayed relative to that delivered to the Clarion electrode). When measuring the sensitivity to ITD and ILD, the Clarion stimulus amplitude was held constant at a comfortable loudness level. In these experiments, ILD refers to the Ineraid amplitude deviation from the Ineraid amplitude that produces a centered, fused (unitary) percept (for ITD equal to zero). In cases where a fused percept was not obtained, the ILD refers to a deviation from the Ineraid amplitude that produced a sensation equal in loudness to that of the Clarion comfortable stimulus level (with ITD equal to zero).

The lateralization test was designed to measure the perceived location of sensations produced by a set of electric stimuli (that included a range of ILDs and ITDs) delivered to a particular electrode pair. For each presentation, the subject assigned a number from a lateralization scale that ranged from 1 to 7 (where 1 represented a sound sensation at the left ear, 4 a centered sound sensation, 7 a sound sensation at the right ear). A "none of the above" (NA) response was allowed if the subject could not assign a (single) number to the perceived location (e.g., if she heard more than one sound sensation during a single presentation). The stimulus set was made up of 15 bilateral stimuli (with five ILDs and three ITDs). The ILDs were selected to elicit sensations at locations covering the range from the far left to the far right and were determined from the informal tests. The ITDs (0 μ sec, 300 μ sec, and 600 μ sec) were chosen to span the range of ITDs relevant in real

world situations. On two days of testing with electrode pair 7MC/2I, a total of 33 of the randomized stimulus sets were presented.

1.5.3 Results

Measurements of the perceived lateral position as a function of ILD and ITD for the pitch-matched electrode pair 7MC/2I are shown in Figure 5. For ITD = 0 μ sec, increases in the right electrode stimulus amplitude cause the mean lateral position of the sensation to move clearly toward the right. That is, lateral position is sensitive to ILD.

These results also show lateral position sensitivity to ITD. For electrode 2I stimulated at 616 μ App, the mean lateral position of the elicited sensations shifts left as the right electrode stimulus is delayed. Similarly, the sensations produced by stimulating electrode 2I at 605 μ App (centered amplitude), tend to shift left as the right electrode stimulus is delayed. These shifts are significant ($\alpha < 0.01$ on a t-test) and demonstrate ITD sensitivity for these amplitudes. These results are consistent with normal hearing ITD effects on lateralization and are evidence of binaural sensitivity.

At some Ineraid amplitudes, a significant ITD effect is not observed; these results can be understood in light of research with normal hearing listeners. For electrode 2I at 580 μ App, the ILD alone causes the percept to be lateralized to the left ear, leaving no room for an additional leftward shift with non-zero ITD. For electrode 2I stimulated at 627 μ App and 650 μ App, the lack of a significant ITD effect is consistent with results in normal hearing (for click stimuli) where large ILDs can greatly reduce the effect of ITDs on lateral position.⁷

The subject answered "none of the above" (NA) in 12.2% of her responses. While we did not routinely ask for detailed descriptions of the sensations eliciting NA responses, it is our impression that a significant number of the NA responses indicated the presence of two images.

Electrode pair 3MC/2I was chosen as a pair that was cochleotopically mismatched based on the pitch-ordering test. We hypothesized that if the ITD sensitivity observed with 7MC/2I were truly based on bin-

⁷ N.I. Durlach and H.S. Colburn, "Binaural Phenomena," In *Handbook of Perception*, vol. 4, E. Carterette and M. Friedman, eds. (New York: Academic Press, 1978); J. Blauert, *Spatial Hearing. The Psychophysics of Human Sound Localization*. Rev. ed. (Cambridge: MIT Press, 1997).

aural mechanisms, this pair (3MC/2I) should not be sensitive to ITD. Qualitatively, the sensations produced by bilateral stimulation of this electrode pair were very different than those produced with 7MC/2I. Rather than a single, fused sensation, the subject heard two separate sound sensations with different pitches. Because the subject could not perform the lateralization test with this electrode pair, we substituted a relative loudness scale (1 to 7; where: 1 indicated a left ear sensation much louder than the right, 4 indicated sensation levels match across the two ears, and 7 indicated a left ear sensation much softer than the right) to test for the presence of an ITD effect. The results of these tests are shown in Figure 6. As expected, there is a clear trend with ILD: as the right electrode amplitude increased, the right ear stimulus was judged as louder than the left on average. There is no significant, nor consistent, ITD effect. This is consistent with results from normal hearing subjects in which ITD sensitivity disappears when the cochleotopic positions of excitation are significantly mismatched. The clear lack of sensitivity to ITD and the lack of fusion leads us to conclude that the brain's binaural processing capability was not engaged by stimulation of these spatially mismatched electrodes.

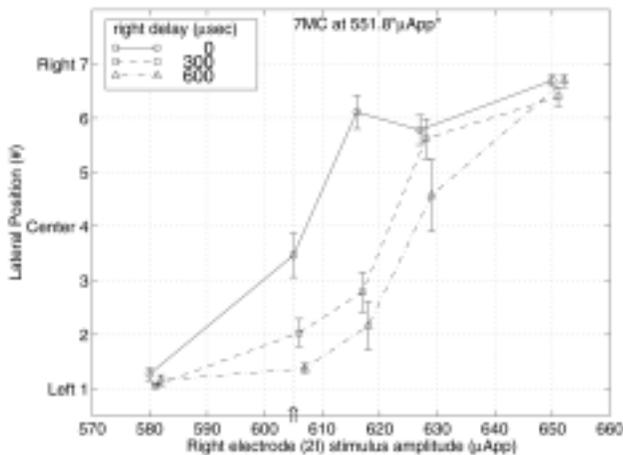


Figure 5. Mean lateral position (\pm standard error) as a function of ITD and ILD for stimuli delivered to Clarion electrode 7MC (level held constant at 551.8 μ App) and Ineraid electrode 2I. The arrow indicates the 2I stimulus amplitude that produces a centered sensation when stimulated simultaneously with 7MC at 551.8 μ App (ITD=0). Non-zero ITD data are shown slightly offset in amplitude for easier visual comparison.

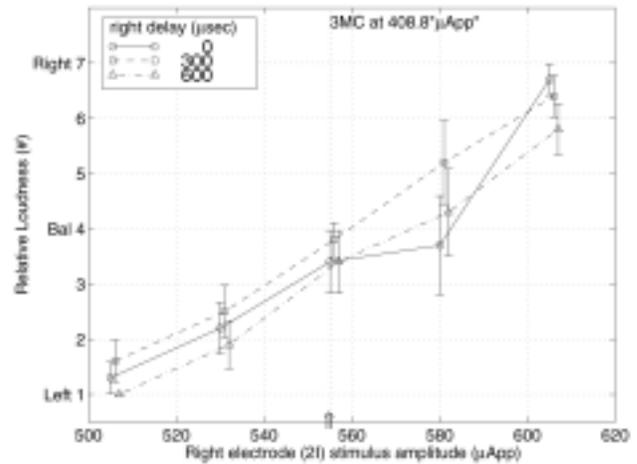


Figure 6. Mean relative loudness (\pm standard error) as a function of ITD and ILD for stimuli delivered to Clarion electrode 3MC (level held constant at 408.8 μ App) and Ineraid electrode 2I. The arrow indicates the 2I stimulus amplitude that produces a loudness balance sensation when stimulated simultaneously with 3MC at 551.8 μ App (ITD=0). Non-zero ITD data are shown slightly offset in amplitude for easier visual comparison.

1.5.4 Conclusion

The results of these experiments provide evidence that with proper coordination of the stimuli across ears, it may be possible to provide binaural advantages to cochlear implant users. Sound processing systems designed for bilateral stimulation will need to control the interaural parameters of level, phase and place of stimulation.

