

Signal Transmission in the Auditory System

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1 Middle and External Ear

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In mammals sound is coupled to the inner ear through a common set of structures, which vary in their configuration among species and individuals. Our goal is to understand the relationships between the structure and acoustic function of the ear. This knowledge can be applied (a) to suggest the evolutionary processes that produced these structural variations, (b) to interpret the effect of pathological processes on human hearing, and (c) to guide reconstruction of damaged human ears so as to restore useful hearing.

1.1 Comparative Structure and Function in Mammalian Ears

People commonly experience changes in their hearing sensitivity as a result of changes in atmospheric pressure, for instance in airplane landing or ascending a mountain. The effects on the middle ear's response to sound of static pressure across the tympanic membrane have been well described, but the roles of different structures on this hearing deficit are not known. The gerbil ear has been used to test the idea that the two components of the tympanic membrane behave differently in response to static pressure. Measurements of motion of the tympanic membrane in response to sound (Lee and Rosowski, 2001)¹ indicate that these components — *pars tensa* and *pars flaccida* — have similar reactions to pressure differences. Thus, if *pars flaccida* has evolved to reduce the effects of pressure differences on the acoustic response of the middle ear, in spite of its differences in structure, its mechanical properties do not indicate great specialization.

¹ C-Y Lee, and J.J. Rosowski, "Effects of middle-ear static pressure on *pars tensa* and *pars flaccida* of gerbil ears," *Hearing Research* 153:146-163 (2001).

Chinchillas are often used for research on inner-ear function, and their middle ears have unusual structural features. Recent measurements (Rosowski and Ravicz, 2001)² indicate that (unlike other species) the inner ear contributes significantly to features of the acoustic input admittance at very low frequencies. As a consequence, the admittance has non-linear properties and is not compliance-like. This is a step toward understanding how the special structural features of chinchilla middle ear affect hearing capabilities and how they might influence survival in this species.

1.2 Middle-ear Function in Human Ears

Cadaveric ears from humans provide material for acoustic measurements in human ears; previously published results have indicated that these ears have acousto-mechanical properties that are undistinguishable from life ears. New results (Ravicz et al., 2000)³ demonstrate that some mechanical features are affected by the way in which the cadaver ears are stored. These results are important to the growing community that uses these preparations for physiological work.

A group at Columbia University, including a researcher from Antwerp, Belgium, have developed a system for measuring 3-dimensional motion of ear structures in response to sound. Drs. Rosowski and Merchant have joined this group in making measurements on human cadaveric ears. So far, this cooperative effort has yielded a description of the three-dimensional motion and its variation among structures of the middle ear (Decraemer et al., 2001).⁴

Perforations of the tympanic membrane are a common pathology which produces an appreciable hearing loss. However, neither the features of this loss nor the physical mechanisms involved have been clearly determined. In fact, the clinical literature contains widely variant descriptions. Human cadaver ears have now been used to measure the effects of well controlled perforations (Voss et al., 2001).⁵ The measurements show that loss in response caused by the perforation is (a) largest at low frequencies, (b) decreases monotonically with frequency in the low frequency region, (c) increased with the size of the perforation, and (d) is independent of the location of the perforation. Extensive measurements aimed at determining the mechanisms are near publication. The base-line measurements in normal ears have been reported (Voss et al., 2000).⁶

Middle-ear disease and its treatment often lead to disease-free ears in which some of the structures have been destroyed. Surgeons have developed procedures for reconstructing these ears to provide useful hearing. Although these procedures sometimes provide hearing sensitivity that is close to normal, the surgical results vary considerably, often for reasons that are not clear. To understand the mechanisms involved, measurements in cadaveric human ear preparations have been used with control of aspects of one kind of surgical reconstruction (Mehta et al.,

² J.J. Rosowski, and M.E. Ravicz, "The middle-ear input admittance in chinchilla: Effect of middle-ear cavities and some low-frequency peculiarities," *Abstracts of the 24th Midwinter Meeting of the Association for Research in Otolaryngology*, St. Petersburg, Florida, February 4-8, 2001, p. 62.

³ M.E. Ravicz, S.M. Merchant, and J.J. Rosowski, "Effect of freezing and thawing on stapes-cochlear input impedance in human temporal bones," *Hearing Research* 150: 215-224 (2000).

⁴ W.F. Decraemer, S.M. Khanna, J.J. Rosowski, and S.N. Merchant, "Complete 3-dimensional motion of the ossicular chain in a human temporal bone," *Abstracts of the 24th Midwinter Meeting of the Association for Research in Otolaryngology*, St. Petersburg, Florida, February 4-8, 2001, p. 221.

⁵ S.E. Voss, J.J. Rosowski, S.N. Merchant, and W.T. Peake, "How do tympanic-membrane perforations affect human middle-ear sound transmission?" *Acta Otolaryngol.* 121:169-173 (2001).

⁶ S.E. Voss, J.J. Rosowski, S.N. Merchant, and W.T. Peake "Acoustic responses of the human middle ear," *Hearing Research* 150: 43-69 (2000).

2001).⁷ In the “Type III tympanoplasty” a graft replaces the tympanic membrane and two missing ossicles by making a connection directly to the remaining ossicle, the stapes. Experimental tests have demonstrated the importance of the graft material, the connection to the stapes, and the mobility of the stapes on the performance of the reconstruction. These observations provide guidance for changes in surgical procedures which should lead to more consistent surgical results. Measurements in live patients will be used to test understanding of this performance of the surgical construction.

1.3 Middle-ear Function in Cats

1.3.1 The family *Felidae*

We have focused on the cat family to search for structural and functional variations in the middle ear that might be related to ecological and ethological adaptation of the species. One approach has been to measure acoustic properties (input admittance) in ears of a selection of the 37 species in the family. We were able to get access to these exotic cat ears, when the animals were anesthetized for purposes of the owners of the animals (e.g. zoos). We developed non-invasive measurement methods that did not injure the ear in any way and tested these methods in domestic cat ears (Huang et al., 2000)⁸. Measurements were made in 17 ears of 11 species ranging in size from tiger to sand cat (Huang et al., 2000).⁹ The results show that two features of the input admittance vary with size of the animal: the low-frequency admittance-amplitude increases with size. A sharp dip in admittance magnitude decreases in frequency as size increases. These results are interpreted in terms of possible evolutionary pressures that may be involved. In addition, one species, the sand cat, did not show evidence of the sharp dip, which was evident in all other species. Further measurements in sand-cat ears have agreed in the lack of this feature. The existence of unique acoustic and structural features for the ears of this species invite speculation about how they might provide adaptation to the desert habitat of this species.

1.3.2 Developing cat ears

We have joined with a group at the Boys Town Research Hospital in Omaha, in a study of structural and functional changes in the middle ears of immature domestic cats. Using the Boys Town collection of kitten skulls of known age, we have described the structural changes with age and determined the acoustical consequences of the large variations in the middle ear cavities (Peake et al., 2001).¹⁰ The changes in the configuration of the ossicular chain will form the second leg of this work.

⁷ R.P. Mehta, M.E. Ravicz, J.J. Rosowski, and S.N. Merchant, “A temporal bone preparation to investigate mechanisms of Type III tympanoplasty,” *Abstracts of the 24th Midwinter Meeting of the Association for Research in Otolaryngology*, St. Petersburg, Florida, February 4-8, 2001, p. 104.

⁸ G.T. Huang, J.J. Rosowski, and W.T. Peake, “A noninvasive method for estimating acoustic admittance at the tympanic membrane,” *J. Acoust. Soc. Am.* 108:1128-1146 (2000).

⁹ G.T. Huang, J.J. Rosowski, and W.T. Peake, “Relating middle-ear acoustic performance to body size in the cat family: measurements and models,” *J. Comp. Physiol. A.* 186:447-465 (2000).

¹⁰ W.T. Peake, J.J. Rosowski, C.C. Shen, E.J. Walsh, and J.D. McGee, “Developmental variations in structure of kitten middle ear: acoustic consequences,” *Abstracts of the 24th Midwinter Meeting of the Association for Research in Otolaryngology*, St. Petersburg, Florida, February 4-8, 2001, p. 61.

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Journal Articles Published

Huang, G.T., J.J. Rosowski, and W.T. Peake, "Relating middle-ear acoustic performance to body size in the cat family: measurements and models," *J. Comp. Physiol. A*. 186:447-465 (2000).

Huang, G.T., J.J. Rosowski, and W.T. Peake, "A noninvasive method for estimating acoustic admittance at the tympanic membrane," *J. Acoust. Soc. Am.* 108:1128-1146 (2000).

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Lee, C-Y and J.J. Rosowski, "Effects of middle-ear static pressure on *pars tensa* and *pars flaccida* of gerbil ears," *Hearing Research* 153:146-163 (2001).

Ravicz, M. E. , S.M. Merchant, and J.J. Rosowski, "Effect of freezing and thawing on stapes-cochlear input impedance in human temporal bones," *Hearing Research* 150: 215-224 (2000).

Voss, S.E., J.J. Rosowski, S.N. Merchant, and W.T. Peake, "How do tympanic-membrane perforations affect human middle-ear sound transmission?" *Acta Otolaryngol.* 121:169-173 (2001).

Voss, S.E., J.J. Rosowski, S.N. Merchant, and W.T. Peake "Acoustic responses of the human middle ear," *Hearing Research* 150: 43-69 (2000).

Theses

O'Connor, K. N. *Analysis of exotic cat vocalizations and middle-ear properties*, MEng. thesis, Massachusetts Institute of Technology, Jan. 2001.

Meeting Papers Published

Peake, W.T. , J.J. Rosowski, C.C. Shen, E.J. Walsh, and J.D. McGee, "Developmental variations in structure of kitten middle ear: acoustic consequences," *Abstracts of the 24th Midwinter Meeting of the Association for Research in Otolaryngology*, St. Petersburg, Florida, February 4-8, 2001, p. 61.

Rosowski, J.J. and M.E. Ravicz, "The middle-ear input admittance in chinchilla: Effect of middle-ear cavities and some low-frequency peculiarities," *Abstracts of the 24th Midwinter Meeting of the Association for Research in Otolaryngology*, St. Petersburg, Florida, February 4-8, 2001, p. 62.

Mehta, R. P. , M.E. Ravicz, J.J. Rosowski, and S.N. Merchant, "A temporal bone preparation to investigate mechanisms of Type III tympanoplasty," *Abstracts of the 24th Midwinter Meeting of the Association for Research in Otolaryngology*, St. Petersburg, Florida, February 4-8, 2001, p. 104.

Decraemer, W.F. , S.M. Khanna, J.J. Rosowski, and S.N. Merchant, "Complete 3-dimensional motion of the ossicular chain in a human temporal bone," *Abstracts of the 24th Midwinter Meeting of the Association for Research in Otolaryngology*, St. Petersburg, Florida, February 4-8, 2001, p. 221.

2 Cochlear Mechanics

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2.1 Properties of the Tectorial Membrane

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Project Staff

Amy Englehart, Kinuko Masaki, Betty Tsai, Jesse Wei, Professor Dennis M. Freeman, Professor Thomas F. Weiss

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 its mechanical behavior.

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. The interaction of water with the matrix of macromolecules gives the TM viscoelastic mechanical properties. The fixed charges on the macromolecules attract mobile counter-ions which cause the TM to take up water. Thus the electrical, osmotic, and mechanical properties of the TM are interwoven.

These interactions have been incorporated into a polyelectrolyte gel model. The important parameters of this model are the amount of fixed charge and the elasticity of the matrix. To determine these properties and to test the validity of the gel model, we have measured the osmotic and mechanical properties of the TM.

2.1.1 Osmotic properties of the tectorial membrane

Dependence on ionic strength

To determine the osmotic properties of the TM, the TM was isolated and bathed in media of several ionic strengths (varied by changing the KCl concentration). The thickness of the TM was measured by tracking beads placed on the surface. Consistent with the gel model, decreasing the KCl concentration of the bath caused the TM to swell. Figure 1 shows swelling in response to changes in KCl concentration with the bath adjusted to a pH of 10. We obtained similar results with the bath adjusted to a pH of 7.3.

Figure 2 shows pooled measurements from several experiments at pH 7.3. As the ionic strength was reduced, the thickness of the TM increased. These measurements were compared to predictions of the polyelectrolyte gel model for several fixed charge concentrations. The best fit had a fixed charge concentration of 10.7 mM. At pH 10, the best fit had a fixed charge concentration of ~20 mM.

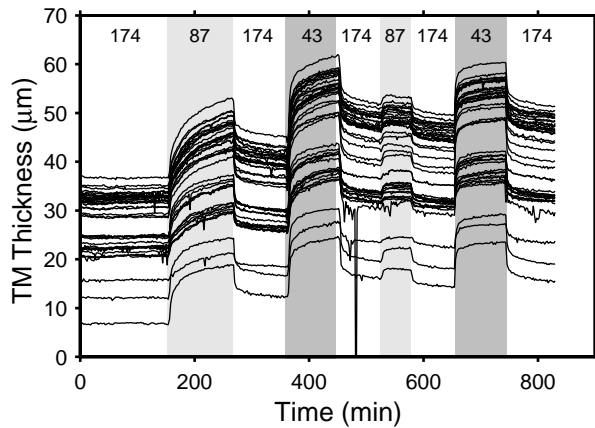


Figure 1: Swelling of the TM in different ionic bath concentrations at pH 10. This is an example of a typical ionic strength experiment. Different shadings represent time intervals in which each bath solution was perfused. The numbers across the top indicate the KCl concentration. Each line represents the thickness of the TM at one location. The TM swelled when exposed to a medium with a lower ionic strength, and shrank again when exposed to media with a higher ionic strength.

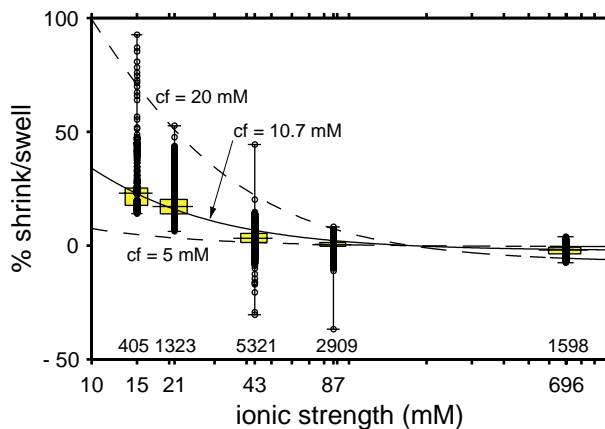


Figure 2: TM swelling in different ionic bath concentrations at pH 7.3. This plot shows the amount of swelling as a function of bath ionic strength for several experiments. Each dot represents the percent change in thickness measured at a single location. The number of measurements is indicated at the bottom. The horizontal lines are the median, the boxes represent the interquartile range, and the vertical lines are the full range at each ionic strength. The solid line is the least squares fit of the gel model, which gives an estimate of 10.7 ± 4.0 mM fixed charge concentration (cf). The dashed lines are predictions of the gel model for fixed charge concentrations of 5 and 20 mM.

The gel model predicts that non-ionic solutes to which the TM is permeant should have no osmotic effect on the TM. Consistent with this prediction, adding glucose to the bath had no effect on TM thickness. However, adding PEG, a non-ionic solute with a molecular weight of 20,000, caused the TM to shrink. We conclude that large non-ionic solutes are excluded from the TM, and thus exert osmotic effects.

Dependence on ionic species

Previous studies have shown that replacing K^+ with Na^+ in the bathing medium causes the TM to swell. Since both ions carry the same charge, the change should not exert any electro-osmotic effects; the response is most likely due to direct binding of ions to the matrix. To determine which ions bind, we measured changes in TM thickness as K^+ was replaced with ions of various column I metals.

Figure 3 shows pooled measurements of 25 locations on two TMs. As had been shown previously, replacing K^+ with Na^+ caused the TM to swell. Subsequently perfusing the K^+ bath caused the TM to shrink. Replacing K^+ with Li^+ caused the TM to shrink slightly, although this change was not significant. Replacing K^+ with Rb^+ or Cs^+ caused no significant effect. Swelling in Na^+ was repeatable at the end of the experiment. Thus the swelling response is specific to Na^+ .

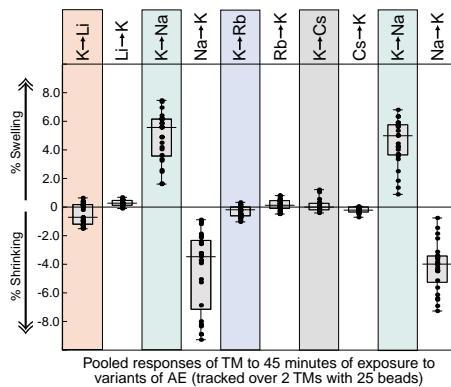


Figure 3: Changes in TM thickness in various baths. This plot shows the measured thickness change for 25 locations on two TMs as the dominant cation in the bath was changed. The top axis shows the bath changes; the left axis shows the percent change in thickness. Dots are individual data points, wide horizontal lines represent the median, boxes represent the interquartile range.

Previous measurements have shown that replacing K^+ with Na^+ has no effect when either Ca^{+2} is removed from the bath with EGTA or when the Ca^{+2} concentration is above 2 mM (Freeman et al, 1994; Shah et al, 1995). In addition, switching from a bath with 2 mM Ca^{+2} to an EGTA-buffered bath causes a large swelling response of the TM. In light of these results, we propose that Na^+ and Ca^{+2} bind competitively to sites within the TM. Binding of Ca^{+2} increases tension on the matrix, causing the TM to shrink; binding of Na^+ releases this tension, allowing the TM to swell.

2.1.2 Mechanical properties of the tectorial membrane

Because of the small size of the tectorial membrane (<50 μm thick), its mechanical properties are challenging to measure directly. We have developed a new technique that uses an atomic force cantilever to determine the transverse mechanical impedance of the isolated TM. A noise-like mechanical stimulus (10 Hz to 20 kHz) was applied to the chamber containing the TM (figure 4). A cantilever of known impedance was placed on the surface of the TM, and the motion of this cantilever was measured to determine TM transverse impedance. These measurements were repeated at several static indentations of the cantilever to determine if the TM impedance is linear.

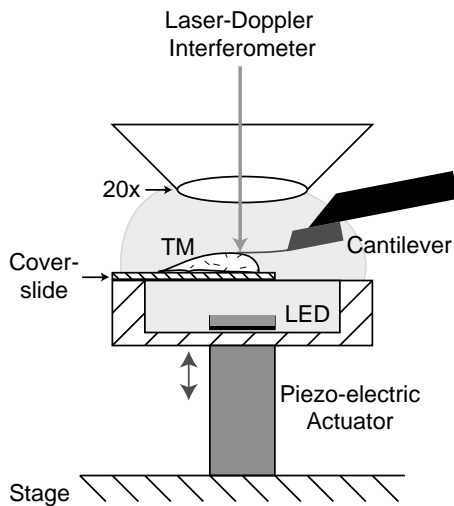


Figure 4: Experiment Setup. The TM sits on a coverslide on an experiment chamber and is bathed in artificial endolymph. The TM is brought towards an atomic force cantilever by elevating the microscope stage, and a piezo-electric actuator mechanically drives the chamber containing the TM. The TM exerts a force on the cantilever, whose velocity is measured by a laser-Doppler interferometer.

Results (figure 5) show that the magnitude of the TM impedance decreases with increasing frequency with an average slope of -4.8 dB/octave, suggesting that the TM impedance has both viscous and elastic properties over a wide frequency range. This conclusion is supported by the phase of the impedance, which remains constant between -45 and -90 degrees over the frequency range measured. Most mechanical models of the cochlea represent the TM by a small number of discrete elements. Such models cannot accurately describe the mechanical properties of the isolated TM. In addition, we see no evidence of a mechanical resonance of the isolated TM, although

such resonance has been proposed as a frequency-tuning mechanism *in vivo*.

Measurements at various static indentations of the cantilever show that the TM impedance grows faster than linearly with compression. This nonlinear impedance may contribute to the compressive nonlinearity of the cochlea. Curiously, the slope and phase of the response remain constant with compression, meaning that the viscous and elastic components of impedance increase proportionally.

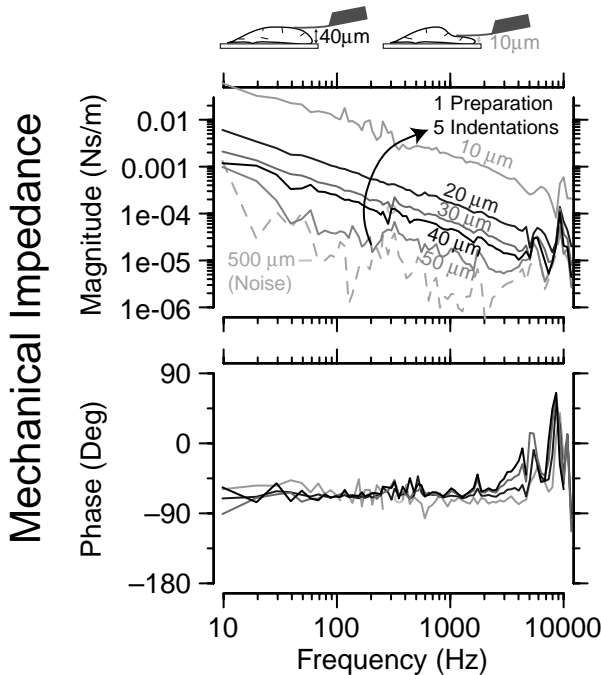


Figure 5: TM impedance at various static indentations of the cantilever. The figure at the top illustrates two static indentations. The numbers represent the distance between the coverslide of the chamber and the underside of the cantilever. Therefore, for values of $40 \mu\text{m}$ and less, they represent the thickness of the TM. Solid lines show the impedance over the frequency range for which measurements were taken, while the dotted line represents the noise floor. The magnitude of the impedance drops with frequency with a median slope of -4.8 dB/octave . The phase remains constant between -45° and -90° .

2.2 Sound-induced Motions of Cochlear Structures

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Project Staff

Alexander Aranyosi, David Chen, Professor Dennis M. Freeman, Professor Thomas F. Weiss

Mechanical vibrations caused by sound are detected by hair cells in the cochlea. The organization of hair cells and supporting cells into a tissue determines the mechanical properties of the cochlea. To better understand the mechanics of hearing, we are studying the motions of the cochlea and its component structures in response to sound stimulation. To this end, our group has developed an *in vitro* preparation for studying cochlear mechanics. The cochlea of an alligator lizard is clamped in an experiment chamber so that it can be viewed with a light microscope while it is stimulated with sound. By using stroboscopic illumination and the optical sectioning property of the light microscope, we obtain slow-motion, three-dimensional images of micromechanical structures during sound stimulation. We have developed image processing algorithms to make quantitative measurements of motion directly from these images with nanometer precision.

During the past year, we have used the system to investigate the mechanical properties of the basilar papilla. Models of the alligator lizard cochlea assume that the basilar papilla undergoes a simple rocking motion in response to sound stimulation. However, previous observations of the motion of the basilar papilla (Frishkopf and DeRosier, 1983; Holton and Hudspeth, 1983) suggest

that this simple model may not be entirely accurate; rather, the motion of the basilar papilla was observed to increase at the basal end for frequencies above 3 kHz. To better understand the mechanical properties of the basilar papilla, we have quantitatively measured its motion as a function of frequency and position.

Figure 6 shows the motion of the basilar papilla at four locations in one lateral cross-section in response to a 120 dB SPL (in fluid), 5 kHz tone. This cross-section is near the basal end, where hair cells are most sensitive to stimuli near 3–4 kHz. A cross-sectional image of the basilar papilla has been placed in the background to show the measurement locations. Circles show the positions at each of eight evenly-spaced stimulus phases. The scale bars indicate the scale of the anatomy; motions have been scaled up by a factor of five for visibility. At each location, the papilla moves in an elliptical fashion. The shape of the ellipse changes with lateral position. These elliptical trajectories can be described as the sum of a translational and a rotational component of motion. The solid lines in figure 6 show the least-squares fit of this two-component model to the measurements.

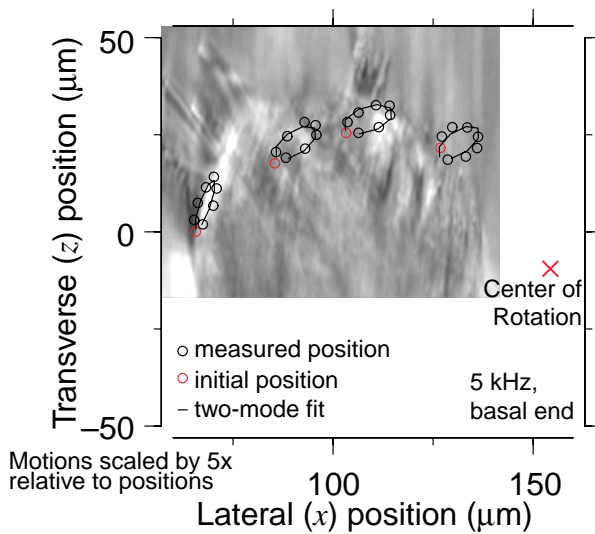


Figure 6: Trajectories of motion of the basilar papilla. The background shows an xz cross section of the basilar papilla. Circles show the motion of four points on the basilar papilla in response to a 120 dB SPL (in fluid), 5 kHz tone. The elliptical motions are exaggerated by a factor of 5 for clarity. Lines represent the least-squares fit of a two-mode model of motion, with $1.77 \mu\text{m}$ translation and 1.96° rotation about the point marked with an \times . The rms error of the fit was $0.175 \mu\text{m}$.

At the neural edge (right-hand side of image), motions due to translation and rotation are nearly orthogonal. Thus we can estimate the frequency dependence of the translational and rotational modes from the motion of the neural edge. Figure 7 shows these estimates as a function of frequency near the basal end (solid lines), center (short-dash lines) and apical end (long-dash lines) of the free-standing region of the basilar papilla. The rotational component has a peak near 5 kHz; this peak is largest at the basal end of the basilar papilla. The translational component is roughly independent of frequency and position. These differences in the frequency dependence of each component demonstrate that the basilar papilla has two modes of motion.

Both modes contribute to the excitation of hair cells. The translational mode maximally excites hair cells on the neural and abneural edges of the papilla, and minimally excites hair cells in the center of the papilla. The rotational mode maximally excites hair cells on the abneural edge, and minimally excites hair cells near the neural edge. Consequently either mode, taken alone, introduces a sharp minimum of sensitivity at some lateral position. Because these minima occur at different positions, however, the combination of modes allows all hair bundles to have similar sensitivities. The peak in rotation near 5 kHz at the basal end of the papilla increases the sensitivity of hair cells located there, compensating for a reduction in sensitivity due to their shorter hair bundles. Thus the multi-modal motion of the basilar papilla ensures that the sensitivity of the cochlea is similar for all hair cells.

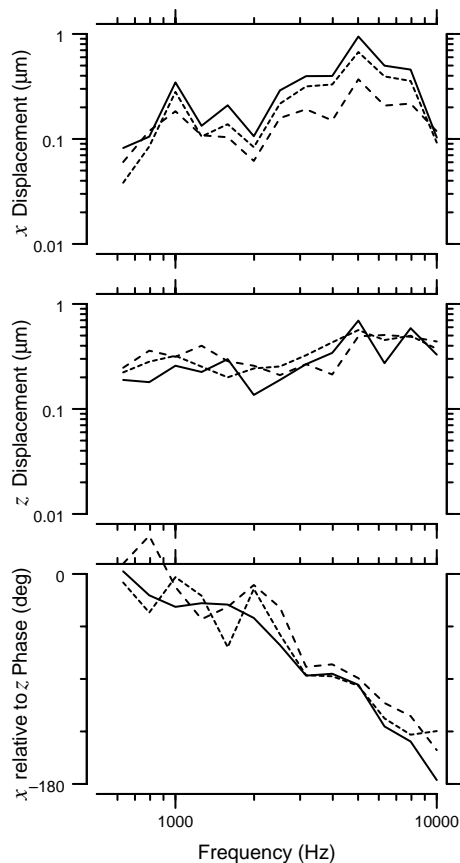


Figure 7: Lateral (x) and transverse (z) motion vs. frequency. The top plot shows the lateral component of motion of the abneural side of the basilar papilla as a function of frequency at three longitudinal positions (basal end: solid; center of papilla: short dash; apical end: long dash). The center plot shows the transverse component of motion at these same locations. The bottom plot shows the phase of the lateral component relative to the transverse component. Note that the lateral component has a peak near 5 kHz, and that this peak is largest at the basal end, where hair cells have best frequencies near 4 kHz. The transverse component shows no significant peak. The phase of lateral motion lags that of transverse motion by an amount that increases with frequency.

Published papers

Journal Articles Published

Abnet, C.C. and Freeman, D.M. "Deformations of the isolated mouse tectorial membrane produced by oscillatory forces." *Hearing Research* 144: 29-46 (2000).

Meeting Papers Published

Aranyosi, A.J. and Freeman, D.M., "Mechanical properties of the basilar papilla of alligator lizard." *Abstracts of the Twenty Fourth Midwinter Research Meeting of the Association for Research in Otolaryngology*, St. Petersburg, FL, February 2001.

Wei, J.L. and Freeman, D.M., "Osmotic responses of the isolated mouse tectorial membrane to column I metal ions." *Abstracts of the Twenty Fourth Midwinter Research Meeting of the Association for Research in Otolaryngology*, St. Petersburg, FL, February 2001.

Theses

Wei, J.L., "Osmotic and electrical responses of the isolated mouse tectorial membrane." M.D. Thesis, Harvard/MIT Division of Health Sciences and Technology, June 2001.

3 Auditory Neural Coding of Speech

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Project Staff

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The long-term goal of our research is to understand the neural mechanisms that mediate the ability of normal-hearing people to understand speech in the presence of competing sounds and how these mechanisms are degraded in the hearing-impaired. In the past year, we made progress toward testing the physiological basis of the notched noise method for estimating auditory filter shapes. We have also continued effort on 3 projects initiated previously: (1) Neural correlates of musical dissonance in the inferior colliculus, (2) Mathematical model of onset neurons in the cochlear nucleus, and (3) Studies of electrical stimulation of the auditory nerve aimed at improving speech processors for cochlear implants.

3.1 Frequency selectivity of auditory-nerve fibers studied with the notched-noise method

The aim of this study is to test if the Notched Noise Method, a widely-used psychophysical technique for estimating auditory filters shapes from masking data, can be applied to physiological data from auditory-nerve fibers. In particular, we hypothesize that suppression plays a significant role in masking by band-reject noise, contrary to the power spectrum model of masking.

For this purpose, we recorded from auditory-nerve fibers in anesthetized cats in response to pure tones in band-reject noise. Pure tones were at or near the characteristic frequency (CF), 10-20 dB above threshold. Noise rejection bands were either placed symmetrically around the tone frequency or centered at frequencies 10% above or 10% below the signal frequency. The noise level was adjusted until it just masked the tone. Results indicate that Patterson's Rounded Exponential (Roex) filter model produces good fits to masked threshold curves from single fibers. Auditory filters 20-dB bandwidths and center frequencies are in good agreement with the values of bandwidth and CF for pure-tone tuning curves.

Masked threshold were also measured for nonsimultaneous presentation of the tone and the masker. Because suppression only occurs for stimuli that overlap in time, comparison of this nonsimultaneous condition with simultaneous masking estimates the effect of suppression on auditory filters. For almost all neurons, bandwidths of auditory filters in nonsimultaneous masking were narrower than those obtained in the simultaneous case.

These findings suggest that suppression plays a role in the masking of auditory-nerve fibers by band-reject noise and that the psychophysical notched-noise method may overestimate the bandwidths of human auditory filters. Such an overestimation may have profound implications for models of auditory processing based on these filters.

3.2 Neural correlates of musical dissonance in the inferior colliculus

Roughness, the percept associated with temporal envelope modulations in the 20-200 Hz range, is a key determinant of musical dissonance. Because most neurons in the inferior colliculus (IC) preferentially respond to envelope modulations in this frequency range, the dissonance of musical intervals is likely to be coded in their responses.

To test this hypothesis, we recorded from single units in the IC of anesthetized cats in response to dissonant and consonant musical intervals, and compared various neural response metrics to perceived dissonance ratings. Stimuli consisted of two sets of musical intervals composed of a) two pure-tones and b) two six-harmonic complex tones. We found that intervals judged to be more dissonant elicited greater fluctuations in discharge rate for most IC neurons. These fluctuations occurred at beat frequencies of neighboring partials. In addition, for onset neurons, more dissonant intervals evoked higher average discharge rates. We previously found correlates of dissonance in the auditory nerve by processing their responses to extract rate fluctuations in the 20-200 Hz range. That such processing is not necessary in the IC suggests that a form of bandpass filtering occurs centrally at or below the IC.

These results are consistent with the idea that musical dissonance is coded in specific temporal discharge patterns and, more generally, that neural processing in the auditory periphery and brainstem can shape musical percepts. A preliminary report of this work has been presented at the 12th International Hearing Symposium in the Netherlands (McKinney et al., 2001).¹¹

3.3 Mathematic model of onset neurons in the cochlear nucleus

The cochlear nucleus (CN) receives the terminals of all auditory-nerve (AN) fibers from the cochlea and gives rise to parallel pathways that convey selected information about acoustic stimuli to different parts of the brain. Onset neurons in the CN are characterized by a prominent response at the onset of sounds followed by little or no response in the steady-state. Onset neurons are interesting because they contrast sharply with both their AN inputs and other CN neurons, which respond vigorously throughout stimuli, and because onset transients are important in speech and music perception and sound localization.

We used mathematical models to study the neural mechanisms underlying the signal transformations that lead to Onset responses. Our strategy was to focus on 3 key response properties of Onset neurons: 1) Onset response patterns for high-frequency tone bursts, 2) entrainment to low-frequency tones (firing 1 spike per cycle), and 3) growth of discharge rate with stimulus level for tones and broadband noise.

The model is a point neuron with excitatory, independent AN inputs spanning a range of characteristic frequencies (CF: the frequency to which an AN fiber is most sensitive). To predict Onset response patterns, the model must have a short time constant and many weak synapses, so as to act as a coincidence detector. Moreover, the AN inputs must span a relatively wide range of CFs (> 1 octave). Variations in the number of inputs, the CF distribution of inputs, and refractory characteristics can predict the diversity of Onset neurons. Specifically, Onset response patterns with short interspike intervals for high-frequency tone bursts (chopping) are produced when the model has a constant refractory period. On the other hand, Onset response patterns with no chopping are produced by a more complex membrane model where the refractory period depends on the membrane voltage. By varying the number of AN inputs, this model with variable refractoriness can produce either response patterns to tones with no late activity or patterns with moderate late activity. The model also predicts inter-relationships, which depend on the CF

¹¹ M.F. McKinney, M.J. Tramo, and B. Delgutte, "Neural correlates of the dissonance of musical intervals in the inferior colliculus," In *Physiological and Psychophysical Bases of Auditory Function*, eds. D.J. Breebaart, A.J.M. Houtsma, A. Kohlrausch, V.F. Prijs, and R. Schoonhoven. (Maastricht: Shaker, 2001).

range spanned by the AN inputs, between the ability to entrain over a broad frequency range and how discharge rate grows with stimulus level for tones and noise.

These results demonstrate that a wide variety of response properties of Onset neurons can be understood in terms of relatively simple principles such as enhancement of temporal patterns by coincidence detection and tradeoffs between the ability to entrain to rapidly fluctuating stimuli and the ability to code stimulus amplitude in a graded manner. Similar principles may operate in other neurons in the nervous system. Two papers reporting this work have been submitted to the *Journal of Computational Neuroscience* (Kalluri and Delgutte, submitted).^{12,13}

3.4 Physiological experiments aimed at improved stimulus coding for cochlear implants

Many modern cochlear implants stimulate the cochlea with modulated pulse trains based on amplitude modulations in the input sounds. Rubinstein et al.¹⁴ suggested that the neural representation of the modulation waveform might be improved by introducing a sustained, high-rate, desynchronizing pulse train (DPT), which would randomize and desynchronize neural responses in a manner similar to spontaneous activity in a healthy ear.

To test this hypothesis, we recorded responses of auditory-nerve fibers in acutely-deafened, anesthetized cats elicited by electric pulse trains (5 kp/s) delivered via an intracochlear electrode. Our stimuli were 10 min long and consisted of biphasic pulses (cathodic/anodic, 20 μ sec/phase) at 0-7 dB above threshold. Responses to pulse trains showed adaptation during the first 2 min, followed by a sustained response for the remainder of the stimulus. Steady-state rates ranged from 0 to 150 spikes/sec, comparable to rates of spontaneous activity in a healthy ear. For almost half of the fibers, the interval histogram (IH) for responses in the steady-state portion had a prominent mode near 5 msec and an exponentially-decaying tail. This 5-msec mode is not found for spontaneous activity in a healthy cochlea.

We also recorded responses to pulse trains that contained sinusoidally amplitude-modulated segments (depth 0.2). Most neurons responded better to modulated segments than to unmodulated ones. Responses to these low modulation depths resembled responses to tones in a healthy ear in terms of period and interval histograms.

These results provide support for Rubinstein's idea that, by creating neural activity similar to spontaneous activity in a healthy auditory nerve, a high-rate pulse train may lead to more natural coding of the modulation waveform in the temporal discharge patterns. Clearly, more work is needed to determine whether the improvement in temporal coding seen with sinusoidal modulators extends to the complex waveforms produced by cochlear implant processors with speech stimulation. A report of this research was accepted by the *Journal of the Acoustical Society of America* (Litvak et al., in press).¹⁵

¹² S. Kalluri, and B. Delgutte, "Mathematical models of cochlear nucleus onset neurons. I. Point neuron with many weak synaptic inputs," Submitted to *J. Comput. Neurosci.*

¹³ S. Kalluri, and B. Delgutte, "Mathematical models of cochlear nucleus onset neurons. II. Model with dynamic spike-blocking state," Submitted to *J. Comput. Neurosci.*

¹⁴ J.T. Rubinstein, B.S. Wilson, C.C. Finley, and P.J. Abbas, "Pseudospontaneous activity: stochastic independence of auditory nerve fibers with electrical stimulation," *Hearing Research*, 127:108-118 (1999).

¹⁵ L.M. Litvak, B. Delgutte, and D.K. Eddington, "Auditory nerve fiber responses to electric stimulation: modulated and unmodulated pulse trains," *J. Acoust. Soc. Am.*, Forthcoming.

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Journal Article, Accepted for Publication

Litvak, L.M., B. Delgutte, and D.K. Eddington, "Auditory nerve fiber responses to electric stimulation: modulated and unmodulated pulse trains," *J. Acoust. Soc. Am.*, Forthcoming.

Journal Articles, Submitted for Publication

Kalluri, S. and B. Delgutte, "Mathematical models of cochlear nucleus onset neurons. I. Point neuron with many weak synaptic inputs," Submitted to *J. Comput. Neurosci.*

Kalluri, S. and B. Delgutte, "Mathematical models of cochlear nucleus onset neurons. II. Model with dynamic spike-blocking state," Submitted to *J. Comput. Neurosci.*

Book Chapter Published

McKinney, M.F., M.J. Tramo, and B. Delgutte, "Neural correlates of the dissonance of musical intervals in the inferior colliculus," In *Physiological and Psychophysical Bases of Auditory Function*, eds. D.J. Breebaart, A.J.M. Houtsma, A. Kohlrausch, V.F. Prijs, and R. Schoonhoven. (Maastricht: Shaker, 2001).

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Kalluri, S., and B. Delgutte, "Models for the diversity of response properties of cochlear-nucleus onset neurons," *Abstracts of the 23rd Midwinter Meeting of the Association for Research in Otolaryngology*, St. Petersburg, Florida, February 20-24, 2000, p. 184.

Tramo, M.J., P.A. Cariani, M.F. McKinney, and B. Delgutte, "Neural coding of tonal consonance and dissonance," *Abstracts of the 23rd Midwinter Meeting of the Association for Research in Otolaryngology*, St. Petersburg, Florida, February 20-24, 2000, p. 275.

Delgutte, B., Z.M. Smith, and A. Oxenham, "Auditory chimeras," *Abstracts of the 24th Midwinter Meeting of the Association for Research in Otolaryngology*, St. Petersburg, Florida, February 4-8, 2001, p.175.

Litvak, L.M., B. Delgutte, and D.K. Eddington, "Responses of auditory nerve fibers to sustained electric stimulation with high frequency pulse trains," *Abstracts of the 24th Midwinter Meeting of the Association for Research in Otolaryngology*, St. Petersburg, Florida, February 4-8, 2001, p. 254.

McKinney, M.F., M.J. Tramo, and B. Delgutte, "Neural correlates of the dissonance of musical intervals in the inferior colliculus," *Abstracts of the 24th Midwinter Meeting of the Association for Research in Otolaryngology*, St. Petersburg, Florida, February 4-8, 2001, p. 54.

4 Neural mechanisms of spatial hearing

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The long-term goal of our research is to understand the neural mechanisms of directional hearing in complex acoustic environments that include multiple sound sources and reverberation. Specific aims are to study neural correlates of (1) the precedence effect (PE), and (2) spatial release from masking (SRM) in the inferior colliculus. Our efforts in the past year have focused on making further experimental progress in the SRM study. A joint preliminary report of both studies was presented at an International Hearing Symposium (Litovsky et al., 2000).¹⁶

4.1 Neural correlates of spatial release from masking

Spatial release from masking is the improvement in signal detection obtained when a signal is separated in space from a masker. To look for correlates of this phenomenon, we record from single units in the inferior colliculus (IC) of anesthetized cats. Our stimuli are chosen to match psychophysical experiments—a broadband signal (100-Hz click train or 40-Hz chirp train) in a continuous broadband noise masker. Stimulus azimuth is simulated using head-related transfer functions.

We measured each unit's masked threshold for several signal and masker azimuths. Masked threshold is defined as the level of the masker at which the signal could be detected for 75% of the trials. For almost all neurons, masked threshold changed as a function of *noise* azimuth, indicating that release from masking did occur. However, for most neurons, the shape of the masked threshold curve remained the same as the *signal* azimuth varied. These neurons were not demonstrating a direct correlate of SRM in that the most effective masker azimuth did not depend on the separation between the signal and the noise. However, masked threshold in a minority of units did depend on signal azimuth. Even though individual neurons do not show a correlate of SRM, a population of neurons could show a correlate because the masked threshold curves are different for individual units. Therefore, we are continuing to collect data so that we can examine the population response of these neurons.

In order to understand the neural mechanisms underlying the neural responses, we have examined the masked threshold curves produced by a simple neuron model. The model depends only on the energy transmitted to the neuron through the head-related transfer functions and a simple model of the auditory periphery. This model is able to predict some of the masked threshold curves that do not depend on signal azimuth, but cannot predict the threshold curves that change shape with signal azimuth.

¹⁶ R.Y. Litovsky, C.C. Lane, C. Atencio, and B. Delgutte, "Physiological measures of the precedence effect and spatial release from masking in the cat inferior colliculus." In *Physiological and Psychophysical Bases of Auditory Function*, eds. by D.J. Breebaart, A.J.M Houtsma, A. Kohlrausch, V.F. Prijs, and R. Schoonhoven. (Maastricht: Shaker, 2001).

4.2 Significance for neural coding in complex acoustic environments

In SRM experiments, we study how the neural response to a sustained signal is masked by continuous noise. In our earlier studies of the precedence effect (PE), we examined how the response to a brief click is suppressed by a leading click. Despite the differences in these paradigms, results are similar in many respects. Both the PE and SRM are psychophysical phenomena likely to play a role when listening in complex acoustic environments, and both of these phenomena depend on the relative directions of the two stimuli. Our results show that IC neurons have directional patterns of masking and suppression that broadly correlate with these phenomena. Furthermore IC neurons exhibit a great deal of diversity in their responses to PE and SRM stimuli.

For some neurons, sound locations evoking the greatest neural response also produce the most masking and the most suppression of the lagging sound. For these neurons, masking and suppression tend to not directly depend on the separation between the signal and the masker, but rather on each of the two sound locations independently. For neurons of this type, correlates of PE and SRM should be sought in the responses of a population of neurons tuned to different spatial locations.

We also found neurons for which the directional pattern of masking or suppression could not be predicted from the response to the masker or direct sound. That the directional patterns of excitation and suppression are distinct suggest a complex neural circuitry possibly involving excitatory and inhibitory inputs from different subcollicular nuclei. These complex directional patterns may provide, in some neurons, a direct correlate of the PE and SRM.

Clearly, a complete understanding of the PE and SRM will require a better description of the underlying neural circuitry as well as quantitative models of masking and suppression in different populations of neurons.

Publication

Book Chapter Published

Litovsky, R.Y., C.C. Lane, C. Atencio, and B. Delgutte, "Physiological measures of the precedence effect and spatial release from masking in the cat inferior colliculus." In *Physiological and Psychophysical Bases of Auditory Function*, eds. by D.J. Breebaart, A.J.M. Houtsma, A. Kohlrausch, V.F. Prijs, and R. Schoonhoven. (Maastricht: Shaker, 2001).