Neural Mechanisms for Auditory Perception

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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 and localize sounds in complex acoustic environments comprising reverberation and competing sound sources. In the past year, we focused on two research projects: (1) Directional sensitivity of low-frequency inferior colliculus neurons in reverberant environments (Aim 1); (2) Characterizing the response properties of neighboring neurons in the inferior colliculus using tetrode recordings.

Directional sensitivity of midbrain auditory neurons in reverberant environments

The disparate path lengths from a sound source to a listener's ears give rise to an interaural time difference (ITD), the most important cue for the localization of sounds that contain low-frequency energy. Previous neurophysiological studies of the sensitivity of auditory neurons to ITD have typically used anechoic stimulus conditions. This artificial situation is unlike that which humans encounter when listening in rooms, where the direct sound is followed by numerous acoustic reflections from boundary surfaces which lead to pronounced temporal fluctuations in ITD for sustained sounds. Despite such distortion, normal-hearing listeners are generally able to accurately localize sounds in reverberant environments. In an effort to address the neural mechanisms that mediate such robust perception, we investigated the effects of reverberation on the directional sensitivity of low-frequency, ITD-sensitive neurons in the inferior colliculus (IC).

We recorded from single units in the central nucleus of the IC of anesthetized cats. Stimuli were 400-ms bursts of exactly-reproducible Gaussian noise filtered with either anechoic or reverberant binaural room impulse responses (BRIR). The reverberant BRIRs were simulated for a typical classroom using the room-image method. The virtual spatial stimuli were presented from azimuths spanning the frontal hemifield (–90º to +90º) at several distances through a closed acoustic system.

In general, reverberation led to a demodulation of neural responses as a function of azimuth – peak firing rates were reduced and minimum firing rates were increased as compared to the anechoic condition. Reverberation also led to a decrease in the mutual information between stimulus azimuth and spike count. The degradation in azimuth sensitivity became more pronounced as the distance from the source to the listener increased, and therefore the ratio of direct to reverberant energy decreased.

To determine to what extent these degradations can be explained by current binaural models, we compared our physiological results to the predictions of a cross-correlator model of IC neurons (Hancock and Delgutte, *J. Neurosci.* 24:7110-7). The model accurately predicted the neural responses to anechoic virtual spatial stimuli but, in general, predicted a worse degradation of directional sensitivity in reverberation than actually observed. This result suggests that low-frequency ITD-sensitive neurons in the IC are to some extent

robust to reverberation, in that they perform better than predicted by current models of binaural processing. Future efforts will be directed at identifying the neural mechanisms responsible for this robustness.

Our finding that most IC neurons are more robust to the degradation in binaural cues caused by reverberation than predicted by current models of binaural processing suggests that there may exist neural mechanisms that

help listening in reverberant environments. Elucidating these mechanisms and incorporating them into binaural models may ultimately lead to processors for hearing aids and cochlear implants that perform better in reverberant rooms.

Response properties of neighboring neurons in the auditory midbrain

The inferior colliculus (IC), the primary nucleus in the mammalian auditory midbrain, occupies a central position in the ascending auditory pathway because nearly all ascending neural pathways converge and synapse in the central nucleus of the inferior colliculus. Further, the anatomical arrangement of axons and neurons in the IC suggests the existence of distinct functional regions which may play a role in organizing different types of physiological information. To investigate this organization, we characterized the response properties of neighboring neurons in the ICC.

To record reliably from neighboring neurons, we adopted a relatively new electrophysiological technique, *tetrode* recordings. Tetrodes have four closely spaced recording sites (<20μm) which record multi-unit activity from a small number of neighboring neurons. The recorded signals contain action potentials originating from more than one neuron. Based on action potential wave shape differences across the four channels, we reconstruct the contributions of individual neurons. Applying tetrode recordings to the ICC of anesthetized cats, we successfully reconstructed individual spike trains for 190 neurons at 52 recording sites. To quantify the advantage of using tetrodes, we compared results of spike sorting using all four channels of the tetrode with the results obtained using only one channel from the same recording. At best, only 32% of the single-unit spike trains obtained using tetrode sorting were correctly identified using single-channel recordings. Also, using single-channel spike sorting, 44% of the single-unit spike trains obtained from tetrode were indistinguishable from at least one other single-unit spike train. This suggests that sorting from a single channel can result in a high incidence of misclassifying multi-unit groups as single-units.

Using tetrodes, we characterized the pure tone responses of single-units in the ICC in terms of frequency selectivity, level dependence, temporal discharge patterns, and sensitivity to interaural time differences. We compared the response properties between every pair of neurons recorded at a single site. We found significant correlation in best frequency and pure tone threshold between neighboring pairs; however, we found large disparities in bandwidth, level dependence, temporal discharge patterns, and sensitivity to interaural time differences. These results suggest that neighboring neurons in ICC can greatly differ in membrane properties and/or their patterns of synaptic input from different brainstem nuclei and tonotopic regions.

Publications

Journal Articles, Published or in press

Cedolin L. and Delgutte B. Pitch of complex tones: Rate-place and interspike-interval representations in the auditory nerve. *J. Neurophysiol.* 94: 347–362 (2005).

Lane C.C. and Delgutte B. Neural correlates and mechanisms of spatial release from masking: Single-unit and population responses in the inferior colliculus. *J. Neurophysiol.* 94: 1180-1198 (2005).

Dreyer A. and Delgutte B. Phase locking of auditory-nerve fibers to the envelopes of high-frequency sounds: Implications for sound localization. *J. Neurophysiol.,* in press.

Meeting Papers

Cedolin L. and Delgutte B. Spatio-temporal representation of the pitch of complex tones in the auditory nerve. To be presented at *14th Intern. Sympos. on Hearing,* Cloppenburg, Germany, August 2006.

Devore S. and Delgutte B. Robustness to reverberation of directionally-sensitive neurons in the inferior colliculus. *Comput. and Systems Neurosci. 2006*, Salt Lake City, UT, March 2006.

Devore S., Ihlefeld B., Shinn-Cunningham B. and Delgutte B. Neural and behavioral sensitivities to azimuth degrade with distance in reverberant environments. To be presented at *14th Intern. Sympos. on Hearing,* Cloppenburg, Germany, August 2006.

Theses

Cedolin, L. *Neural Representations of Pitch: Role of Peripheral Frequency Selectivity.* Doctoral Dissertation, Harvard-MIT Division of Health Sciences and Technology, 2006.

Seshagiri, CV. *Response Properties of Neighboring Neurons in the Auditory Midbrain.* Doctoral Dissertation, Harvard-MIT Division of Health Sciences and Technology, 2006.

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Bilateral Cochlear Implants: Physiological and Psychophysical Studies

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The long-term goal of our research is to identify the best stimulus configurations for effectively delivering binaural information with bilateral cochlear implants using closely-integrated neurophysiological, psychophysical and theoretical studies. Studies in the past year have focused on measuring sensitivity to interaural time differences (ITD) of bilaterally implanted human subjects and neurons in the auditory midbrain of implanted cats. We have also studied how ITD tuning depends on electric stimulation parameters for mathematical models of binaural neurons.

Psychophysics
We measured ITD sensitivity in bilaterally-implanted human listeners as a function of stimulation parameters. We focused on the effect of the number of pulses and the stimulation rate of unmodulated pulse trains delivered to a single interaural electrode pair.

At low pulse rates (50 pps), data from three subjects show that the just-noticeable difference (JND) in ITD for a single pulse is significantly larger than that for a train of pulses. For one subject (C109), the ITD JND decreases from 254 μs to 80 μs as the number of pulses increases from 1 to 15. Another subject's (C120) JND decreases from 290 μs to 99 μs. The third subject's (C128) ITD JND for a single pulse is outside of the physiological range (>700 μs), but his JND for a train of 15 pulses is 241 μs.

Surprisingly, we find that, at higher pulse rates such as 800 and 1450 pps (the carrier rate for the processing strategy used by the subjects), ITD sensitivity degrades with increasing number of pulses. For example, C109's ITD JND increases from 293 μs to 594 μs when the number of pulses increases from 30 to 240. For C120, the JND increases from 323 μs to >700 μs when the number of pulses increases from 8 to 17. For Subject C128, the JND was unmeasurable for high-rate pulse trains.

Our data indicate that both the stimulation rate and the number of pulses affect the subjects' ITD sensitivity for unmodulated pulse trains. According to the optimal integration model of signal detection theory, the threshold should vary inversely to the square root of the number of pulses. The improvement in performance observed at low rates with increasing number of pulses is qualitatively consistent with this prediction (and similar to results from normal-hearing subjects for click trains), but quantitatively smaller than predicted. For high-rate pulse trains, however, subjects seem to be mainly using ITD information in the first few pulses, and increasing the number of pulses actually degrades subjects' ITD sensitivity, suggesting that information from the later pulses fails to be properly integrated.

Neurophysiology
We recorded from single-units in the inferior colliculus (IC) of acutely deafened, anesthetized cats in response to electric stimulation delivered through bilaterally-implanted intracochlear electrodes. We focused on the neural coding of ITD with sinusoidally amplitude modulated (SAM) pulse trains, since most implant processors encode sound in each channel by amplitude modulations of a carrier pulse train. ITD was introduced independently to the modulation and carrier in order to assess their relative efficacy in delivering ITD information.

Most cells in the central nucleus of the IC (>80%) were sensitive to ITD with low-rate (<100 pps) unmodulated pulse trains, and their ITD selectivity was similar to that found in the IC for normal-hearing animals. When single-neuron discrimination thresholds were calculated using detection theory, mean and best ITD JNDs were about 100 μs and 30 μs respectively for pulse rates below 100 pps. Neural ITD JNDs increased with increasing pulse rate as responses were increasingly restricted to the stimulus onset.

Amplitude modulation restored responsiveness and ITD sensitivity in many neurons at high pulse rates (1000 pps). Modulation ITD tuning was studied for modulation frequencies between 20 and 160 Hz and was generally broad at the lowest modulation frequencies but sharpened with increasing modulation frequency.

However, ITD tuning width was nearly constant when expressed in terms of interaural modulation phase, suggesting that the shape of the modulation waveform is directly related to ITD tuning. While fewer neurons showed sensitivity to

ITD in the carrier than in the modulation, tuning to carrier ITD, when present, was significantly sharper than that to modulation ITD. The mean neural ITD JND was ~100 μs for carrier ITD and 300 μs for modulation ITD at 160 Hz.

Neurocomputation
We are exploring the effects of stimulus parameters on ITD sensitivity of a model coincidence detector cell in the medial superior olive (MSO) for pulse-train stimuli with and without sinusoidal amplitude modulation (SAM). Our goal is to find input-parameter combinations that optimize tuning to carrier ITD. We found that (1) ITD tuning for unmodulated pulse trains (500 or 1000 pps) is highly sensitive to the model's synaptic strengths; (2) introducing amplitude modulation at 50-400 Hz can either improve or degrade ITD tuning; (3) ITD tuning to SAM pulse trains depends strongly on stimulus parameters, particularly overall amplitude.

In our simulations, ITD tuning depends on the interplay between the model's relative refractory period (RRP) and the synaptic and/or input parameters. For high-rate unmodulated pulse trains (with inter-pulse intervals shorter than the RRP), good ITD tuning occurs when the input amplitude exceeds the refractory threshold for interaurally in-phase inputs, but not for out-of-phase inputs. On the other hand, poor ITD tuning occurs when strengths of neither in-phase nor out-of-phase inputs exceed the refractory threshold, even if in-phase inputs are above rest threshold. Amplitude modulating the inputs reduces synaptic strength (and therefore neural firing) during half of each modulation cycle, thereby minimizing the effects of refractoriness on subsequent inputs. As a result, ITD sensitivity can be restored if AM releases the neuron from refractoriness for the in-phase condition.

Significance
Several common themes emerge by comparing our psychophysical, neurophysiological, and computational results. One is the degradation in both neural and psychophysical ITD sensitivity with increasing pulse rate for unmodulated pulse trains. In particular, the observation that neural responses are largely limited to stimulus onset for high-rate pulse trains may explain why psychophysical ITD JNDs do not improve with increasing number of pulses for these stimuli.

Another common theme is the strong effect of both overall amplitude and amplitude modulation on ITD sensitivity for high-rate pulse trains in both real and model neurons. Introducing amplitude modulation can improve ITD sensitivity of both model and actual neurons and, in the model, this is due in part to the interaction between the stimulus envelope and the dynamics of intrinsic neural membrane properties. The effect of AM in the neural and model data makes testing behavioral ITD sensitivity with AM pulse trains all the more important, and we plan to do so in the coming year.

Our physiological results with SAM pulse trains suggest that the carrier pulses rather than waveform modulation hold the greater potential for conveying useful ITD information. We therefore propose a processing strategy that uses the fine timing of the acoustic signal at each ear to determine the timing of delivered current pulses.

Publications

Meeting Papers

Eddington DK, Poon BB, and Noel V. Changes in fusion and localization performance when transitioning from monolateral to bilateral listening. Invited presentation, Conference on Implantable Auditory Prostheses, Pacific Grove, CA, July 2005.

Smith, Z.M., and Delgutte, B. What to do with the “where”: A physiologically inspired strategy for delivering interaural timing cues with bilateral cochlear implants. Invited presentation, Conference on Implantable Auditory Prostheses, Pacific Grove, CA, July 2005.

Smith, ZM, and Delgutte, B. Using ABR to match interaural electrode pairs with bilateral cochlear implants. 29th Midwinter Meeting of the Association for Research in Otolaryngology, Baltimore, MD, February 2006.

Theses

Poon, B.B. Sound localization and interaural time sensitivity with bilateral cochlear implants. Doctoral Dissertation, Harvard-MIT Division of Health Sciences and Technology, 2006.

Smith, Z.M.. *Binaural interactions in the auditory midbrain with bilateral electric stimulation of the cochlea.* Doctoral Dissertation, Harvard-MIT Division of Health Sciences and Technology, 2006.

Key words:
Binaural hearing, cochlear implants, neural coding, inferior colliculus