Neural Coding and Auditory Perception

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1. Neural coding of sound in complex acoustic environments

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The long-term goal of this research is to understand the neural mechanisms that mediate the ability of normal-hearing people to understand speech and localize sounds in everyday acoustic environments comprising reverberation and competing sound sources. Our research has been primarily focused in three areas: (1) Effect of reverberation on the directional sensitivity and coding of amplitude envelope in inferior colliculus (IC) neurons; (2) Neural coding of the pitch of harmonic complex tones in the auditory nerve (AN) and cochlear nucleus (CN); (3) Adaptive mechanisms for the coding of sound intensity in auditory neurons.

1.1 Effect of reverberation on directional and modulation sensitivity of IC neurons

Normal-hearing listeners have little difficulty localizing sounds and understanding speech in most reverberant settings, despite the distortion of the sound localization cues and temporal envelope cues important for speech reception. To determine whether there exist neural mechanisms providing robust coding in reverberation, we recorded responses of IC neurons to simulated reverberant stimuli with characteristics appropriate for typical classrooms. Initially, these studies were conducted in anesthetized cat. Subsequently, we introduced an unanesthetized rabbit preparation for single-unit recording in IC, based upon the preparation pioneered by Kuwada [13]. This development was motivated in part by reports that the time course of neural echo suppression differs in awake and anesthetized animals [24]. Nevertheless, the effects of realistic reverberation on directional properties of IC neurons were found to be similar in the two preparations.

1.1.1 Effect of reverberation on azimuth sensitivity of low-frequency, ITD-sensitive neurons

In both anesthetized cat and awake rabbit, we found that reverberation degrades the directional sensitivity of low-frequency IC neurons sensitive to interaural differences (ITD) by decreasing the range of firing rates across azimuths for broadband noise, as expected from the decorrelation between the two ear input signals. However, the degradation is not uniform throughout the stimulus duration. Because reverberant energy builds up over time, the source location is represented relatively faithfully during the early portion of a sound, but this representation becomes increasingly degraded later in the stimulus. The directional sensitivity of IC neurons follows a similar time course: responses are more robust to reverberation in the early portion of the stimulus than

later on. Moreover, the degradation is not as large as predicted by a binaural processing model [9] based upon the average interaural cross-correlation over the entire stimulus duration. Neurons whose temporal response patterns are most onset-dominated tend to have the most robust responses in reverberation, when compared to model predictions. These results suggest that neural adaptation provides a simple mechanism for improving directional sensitivity in reverberation.

In parallel human psychophysical experiments, we found that the range of perceived azimuths is compressed in reverberation, an effect that resembles the compression of the range of firing rates in IC neurons. Human lateralization judgments were consistent with predictions from a population rate model for decoding the measured IC responses, suggesting a subcortical origin for robust sound localization in reverberant environments. The best match between psychophysical data and model predictions was obtained when neural activity was integrated over a 50-100 ms time window. This neural estimate of binaural integration time is consistent with that derived from psychophysically data [8].

1.1.2 Effect of reverberation on azimuth sensitivity throughout the tonotopic axis

While human listeners rely primarily on low-frequency ITD cues for localizing a broadband sound source in an anechoic environment [14], they are likely to use whatever cues are the most robust in challenging listening conditions. Rakerd and Hartmann [17] have argued for the importance of high-frequency interaural level differences (ILD) for sound localization in reverberation. In some circumstances, listeners may also use ITD cues available in the amplitude envelopes of high-frequency sounds.

To address these questions, we characterized the effect of reverberation on the directional sensitivity of IC neurons in unanesthetized rabbit across a wide span of the tonotopic axis. We used two types of virtual space, broadband noise stimuli: "ITD-only" in which ITD varies with azimuth while ILD is nearly 0 dB for all azimuths, and "ITD+ILD", where both cues vary with azimuth according to a spherical head model.

We find that IC neurons low with low characteristic frequencies (CF <2 kHz) are sensitive to ITD in the fine structure of the stimulus waveform, while high-CF neurons are sensitive to ITD in the amplitude envelope. In anechoic conditions, the rate responses of both groups of neurons provide comparable directional information with ITD-only stimuli. However, reverberation causes a greater degradation in directional sensitivity for high-CF neurons than for low-CF neurons with ITD-only stimuli. When ILD cues are introduced, directional responses of low-CF neurons are largely unchanged, while those of high-CF neurons are enhanced, and the enhancement is particularly pronounced in the reverberant condition. As a result, directional sensitivity in reverberation is comparable throughout the tonotopic axis of the IC with ITD+ILD stimuli. This result suggests that, at high frequencies, ILDs provide better directional information than envelope ITDs in reverberation, consistent with psychophysical data [18]. The lack of robustness of envelope ITD cues in reverberation may explain why they receive low perceptual weight in human localization judgments [14].

To determine the extent to which the frequency-dependent effects of reverberation observed in the IC are of peripheral origin, we measured responses of auditory-nerve (AN) fibers in anesthetized cats to the same ITD-only stimuli as used in the IC experiments. The spike trains were analyzed by the shuffled correlation technique [12], which simulates processing by a bank of ideal coincidence detectors receiving inputs from left and right AN fibers. Consistent with the IC results, we find that the directional information in AN fibers (as measured by the peak shuffled correlation) is degraded in reverberation. The degradation is more severe in high-CF fibers than in low-CF fibers, suggesting that peripheral and acoustic factors play an important role in our IC results with ITD-only stimuli. This finding is consistent with the observation of a greater degradation in the representation of envelope pitch cues compared to temporal fine-structure cues by cochlear nucleus neurons in reverberation [21].

1.1.3 Effect of reverberation on coding of envelope modulations

Speech reception depends critically on temporal modulations in the amplitude envelope of the speech signal. Reverberation encountered in everyday environments can substantially attenuate these modulations [10]. To assess the effect of reverberation on the neural coding of amplitude envelope, we recorded from single units in the IC of awake rabbit using 100% sinusoidally amplitude modulated broadband noise stimuli presented in simulated anechoic and reverberant environments. The modulation frequency was typically varied from 4 to 256 Hz.

Phase locking to modulation frequency was consistently weaker in the reverberant condition than in the anechoic condition, indicating that reverberation degrades temporal coding, as expected. However, phase locking was on average better for reverberant stimuli than for anechoic stimuli whose modulation depth was matched to the average modulation depth of the reverberant stimulus. This suggests that the envelope representation is more robust for realistic, dynamic reverberant stimuli, than for static, anechoic stimuli, when controlling for average modulation depth. We tested the hypothesis that this dynamic coding advantage results from firing rate adaptation boosting the early response when reverberant energy is lowest. We did not find a significant correlation across neurons between the dynamic coding advantage and the amount of adaptation, suggesting that that firing rate adaptation cannot fully explain the dynamic coding advantage.

We compared the time course of the neural responses to the time course of the modulations in the stimulus envelope. In some neurons, phase locking to each modulation cycle of a reverberant stimulus sharply degraded during the first 100 ms of the stimulus before stabilizing, paralleling the evolution of modulation depth in the stimulus as reverberant energy builds up. However, in other neurons, phase locking was stable or even slowly increased over time, despite the decrease in stimulus modulation depth. We measured in the same neurons the nonlinear transformation from stimulus modulation depth to neural phase locking, using static SAM broadband noises with modulation depths ranging from 0 to 1. We used this input-output function to predict the time course of the reverberant response from the time course of the modulation depth in the reverberant stimulus. In most neurons, the measured neural phase locking in reverberation was greater than the prediction from the input-output function, even in later portions of the stimulus, suggesting that this input-output function is not static, and may depend dynamically on preceding stimulation history.

To test this hypothesis, we presented long continuous dynamic SAM broadband stimuli whose modulation depth is drawn every 250 ms from a non-uniform distribution of modulation depths. In the "anechoic-like" distribution, high modulation depths (above 0.8) have a high probability, similar to an anechoic environment in which natural sounds are typically highly modulated. In the "reverberant-like" distribution, low modulation depths (below 0.25) have a high probability, similar to reverberant environments in which modulations are reduced. In several neurons phase locking of neural responses to the stimulus envelope was larger in the "reverberant-like" condition than in the "anechoic-like" condition. These findings suggest that the nonlinear transformation from stimulus modulation depth to neural phase locking adapts to the modulation depth statistics of the stimulus to improve neural coding of amplitude modulation in low-modulation depths environments, such as noisy or reverberant settings.

Overall, our results point to an important role of dynamic neural processes for robust stimulus coding in reverberation.

***1.2 Coding of pitch in the auditory nerve and cochlear nucleus***

1.2.1 Spatio-temporal representation of pitch in the auditory nerve

The pitch of harmonic complex tones plays an important role in speech and music perception and the analysis of auditory scenes, yet traditional neural codes provide only an incomplete description of the psychophysical data [5]. Studies of the AN and CN have primarily focused on temporal pitch cues available in interspike interval distributions [1, 11, 16, 19, 26]. While this neural re-

presentation accounts for many pitch phenomena, it has trouble explaining the greater pitch salience for stimuli containing resolved harmonics compared to stimuli consisting entirely of unresolved harmonics [3]. On the other hand, the rate-place representation of pitch is degraded at higher stimulus levels [20] and fails to account for the upper frequency limit to musical pitch at ~4000 Hz. The failures of traditional rate-place and interval-based representations motivates a search for neural pitch codes that would combine spatial and temporal information.

We tested physiologically a spatio-temporal representation of pitch proposed by Shamma [22] which is based on phase cues created by the cochlear traveling wave. We measured responses of AN fibers in anesthetized cat to harmonic complex tones with missing fundamentals and equal-amplitude harmonics. We used the principle of scaling invariance in cochlear mechanics [28] to infer the spatiotemporal response patterns to a given stimulus from the responses of a single fiber to a series of complex tones as a function of their fundamental frequency (F0). Scaling invariance implies that the spatio-temporal response pattern is entirely determined by the ratio of fiber CF to stimulus F0.

The left panels in Fig. 1 show the temporal response patterns of an AN fiber to a series of harmonic complex tones for three different stimulus levels. The ordinate is the "neural harmonic number" CF/F0, and time on the horizontal axis is also expressed in dimensionless units (txF0). Consistent with the cochlear traveling wave, the response patterns show more pronounced latency changes when the CF coincides with a resolved harmonic (integer CF/F0) than when it falls between two harmonics. To extract these spatio-temporal cues, we compute the spatial derivative of the response pattern, then integrate the absolute value of the derivative over time. The resulting "mean absolute spatial derivative" (MASD) shows local maxima at the frequencies of Harmonics 2-4, while corresponding peaks in the average discharge rate are only found at the lower stimulus level (Fig. 1, right and middle panels). Thus, spatio-temporal pitch cues persist at levels at which the rate-place representation fails due to rate saturation.
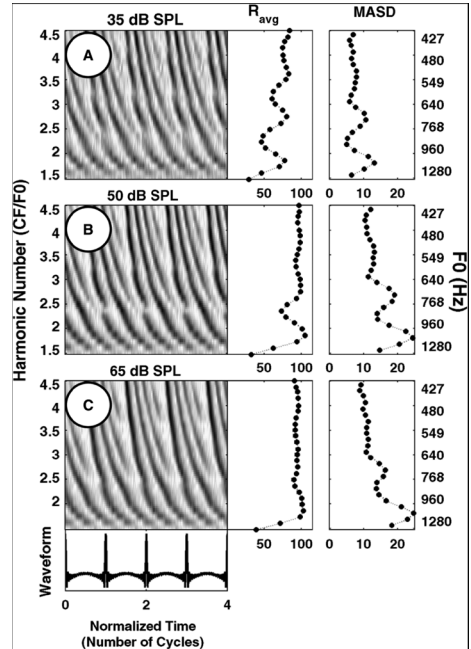
Fig. 1. Spatio-temporal response pattern of an AN fiber (CF=1920 Hz) to a series of harmonic complex tones at 3 different stimulus levels. Threshold at CF was 25 dB SPL.

Across the AN fiber population, spatio-temporal cues to resolved harmonics were available for F0s between about 350 Hz and 1.2 kHz. The lower F0-limit is determined by the frequency selectivity of the cochlea, while the upper limit is caused by the degradation of phase-locking to the stimulus fine structure at high frequencies. The spatio-temporal representation correctly predicts the existence of an upper F0 limit to the perception of the pitch of complex tones with missing fundamentals, and its effectiveness does not depend on the relative phases between resolved harmonics. Because there is no cochlear traveling wave with electric stimulation, the spatio-temporal representation is also consistent with the poor pitch perception with cochlear implants [2]. The spatio-temporal representation thus accounts for key trends in psychophysical pitch phenomena.

1.2.2 Extraction of spatio-temporal cues in the cochlear nucleus

An obvious question is whether the spatio-temporal pitch cues available in the AN are actually extracted in the central auditory system. The spatio-temporal pattern of AN activity also contains cues to other perceptual features of sounds, such as loudness and timbre. In principle, these spatio-temporal cues can be extracted by central neurons sensitive to the relative timing of spikes from AN inputs innervating neighboring regions of the cochlea. One such mechanism is cross-

frequency coincidence detection (XFCD), where a central neuron would fire more when its AN inputs with different CF discharge in synchrony [4]. To evaluate whether such coincidence detection occurs in the cochlear nucleus (CN), we recorded from AN fibers and CN neurons in anesthetized cat using stimuli designed to systematically manipulate the spatio-temporal pattern of AN activity. We compared AN fiber responses to those of a peripheral auditory model [27], and CN responses to those of a XFCD model operating on AN inputs.

We used Huffman sequences, transient stimuli with a flat magnitude spectrum and a 2π phase transition around a specific frequency FT. By manipulating the steepness of the phase transition, we systematically varied the relative timing of spikes across the tonotopic array of fibers without changing the firing rates [4]. The stimulus with a sharp phase transition excited actual and model fibers more coincidentally across CF in the late portion of the response (Fig. 2, left). XFCD model neurons transformed the differences in the degree of coincidence across AN fibers into differences in temporal patterns: Their responses showed later peaks for sharp transition stimuli and earlier peaks for broad transition stimuli (Fig. 2, middle). CN primary-like-with-notch (Pri-N) and some primary-like units had responses consistent with the model (Fig. 2, right), suggesting these units may behave as XFCDs.

Our results suggest that the firing patterns of some CN neurons are consistent with a XFCD mechanism operating on AN activity. In ongoing work, we are investigating whether the CN neurons sensitive to spatio-temporal cues better code the pitch of harmonic complex tones in their rate responses than do insensitive neurons.
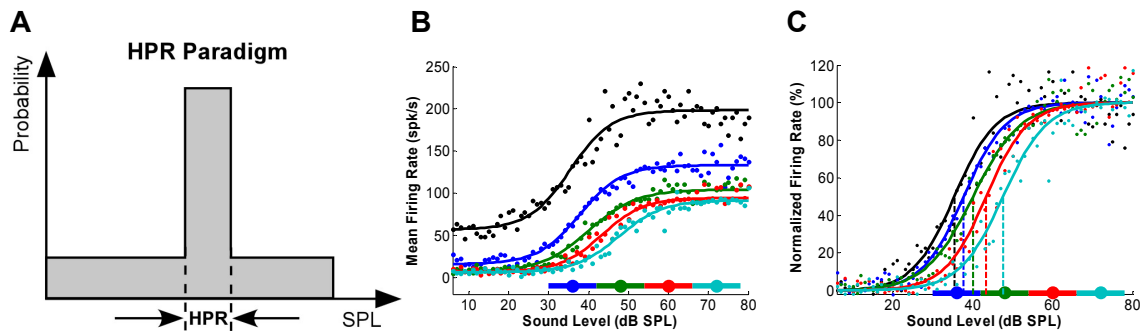
1.3 Dynamic range adaptation in the auditory nerve

A long standing issue in hearing research is the "dynamic range problem" [25], the discrepancy between the vast range of sound levels (100-120 dB) over which the auditory system responds behaviorally with fine acuity, and the limited range (20-40 dB) over which the firing rates of most auditory neurons vary with stimulus level. In a search for neural mechanisms that would alleviate the dynamic range problem, we investigated whether dynamic range adaptation, a phenomenon first observed in the IC [6], already occurs in primary auditory neurons.
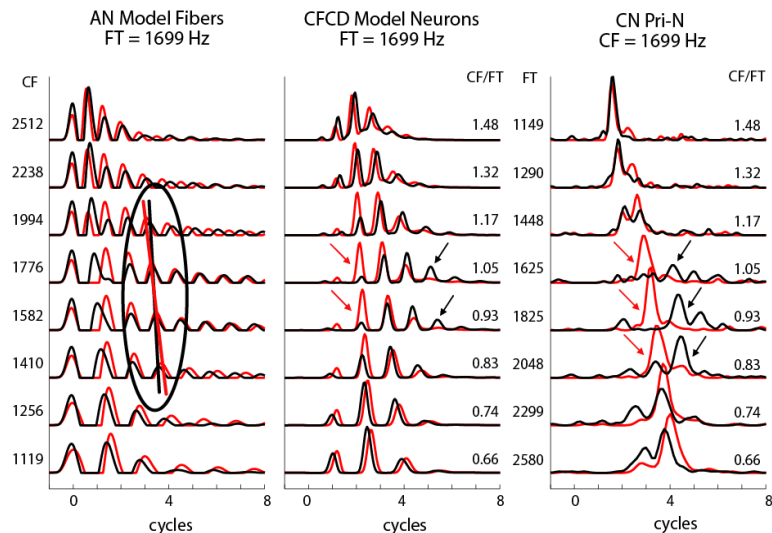
Fig. 2. Left: Spatio-temporal response pattern of the AN model to Huffman stimuli with FT at 1669 Hz. Red and black lines show responses to stimuli with broad and sharp phase transitions, respectively. Middle: Response pattern of an array of XFCD model neurons receiving inputs from model AN fibers. Right: Responses of a CN Pri-N unit to a series of Huffman stimuli with varying FT.

We measured rate-level functions of AN fibers in anesthetized cat using continuous, dynamic stimuli with a level distribution containing a high-probability region (HPR, Fig. 3A). We found that, when the HPR center level is changed, the dynamic range of AN fibers shifts systematically toward the most probable levels (Fig. 3B-C). This dynamic range adaptation is distinct from classic firing rate adaptation, which is characterized by a decrease in firing rate without a change in sensitivity or operating point [23]. Such decreases in firing rates are also apparent with the HPR stimuli in Fig. 3B, i.e. AN fibers show mixed adaptation.

Fig. 3. *Dynamic range adaptation in the AN. A. Distribution of sound levels in a dynamic stimulus with high-probability region (HPR). B. Rate-level functions of an AN fiber to CF tones for four stimuli with different HPRs. Dots: Data; lines: Fitted curves. Black: Responses to stimuli with uniform probability level distribution. Colors code each HPR condition; HPR center level and range are shown by solid circle and horizontal bar. C. Rate-level functions normalized to their minimum and maximum highlight dynamic range adaptation.*

To assess the functional significance of dynamic range adaptation, we computed the Fisher information for level discrimination based on the rate responses of the AN fiber population to broadband noise. Fisher information is a quantitative measure of coding precision of a stimulus parameter (here, sound level). We found that the peak Fisher information shifts systematically toward the HPR, consistent with rate-level function shifts observed in single fibers, thereby improving the precision of level coding within the HPR. However, this benefit is partially offset by a decrease in the peak Fisher information, which reflects a decrease in maximum firing rates due to firing rate adaptation.

In order to determine the time course of dynamic range adaptation we used HPR stimuli in which the mean sound level alternates between two values every 5 s [7]. We found that dynamic range adaptation occurs within a second, but is significantly slower than the time course of firing rate adaptation. We further found that dynamic range adaptation is weaker in the AN than in the IC data of Dean et al. [6, 7]; however the time course of adaptation is similar at the two sites.

Our findings suggest that rapid adaptive processing to changes in the sound level distribution first occurs in the auditory periphery and is enhanced along the auditory pathway. While the adaptive dynamic range shifts in the AN are too small to account for psychophysical performance in intensity discrimination over a wide level range, they are likely to contribute significantly to the stronger dynamic range adaptation observed in the IC.

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2. Bilateral Cochlear Implants: Physiological, Psychophysical and Computational Studies

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The goal of this project is to identify the best stimulus configurations for effectively delivering binaural information with bilateral cochlear implants (BiCI) by means of complementary neurophysiological, psychophysical and theoretical studies. This year, physiological studies focused on characterizing the effect of auditory experience on sensitivity to interaural time differences (ITD) in midbrain auditory neurons. Psychophysical studies tested whether encoding ITD in amplitude-modulated pulse trains with synchronized carriers can improve ITD discrimination.   We also continued developing models of responses of auditory brainstem neurons to stimulation through BiCIs.

Neurophysiology

Human BiCI users do poorly on tasks involving ITD, a cue which provides important benefits to normal–hearing listeners, especially in challenging acoustic environments. Yet the precision of neural ITD coding in acutely-deafened, bilaterally-implanted cats is essentially normal ([3]. One possible explanation for this discrepancy is that neural plasticity induced by the extended periods of binaural deprivation typically experienced by cochlear implant users may degrade neural ITD sensitivity. To test this hypothesis, we recorded from single units in the inferior colliculus (IC) of two groups of bilaterally-implanted, anesthetized cats that maximally differ in binaural experience: acutely-deafened cats, which had normal binaural hearing until experimentation, and congenitally deaf white cats, which received no auditory inputs until the experiment.

Rate responses of only half as many neurons showed significant ITD sensitivity to low-rate pulse trains in congenitally deaf cats compared to acutely-deafened cats. Poor ITD sensitivity in congenitally deaf cats was often associated with increased spontaneous activity and poorly timed, long latency spike responses to stimulus pulses. For neurons that were ITD sensitive, ITD tuning was broader and best ITDs were more widely distributed in congenitally deaf cats. Thus, while some neurons in congenitally deaf cats show a rudimentary form of ITD sensitivity, ITD tuning properties for the population as whole clearly differ from those in animals with normal auditory experience, with many neurons showing broad tuning poorly adapted to the ITDs encountered in the acoustic environment.

In order to quantitatively evaluate the functional implications of the degraded ITD coding observed in congenitally deaf cats, a neural population model that predicts psychophysical ITD discrimination in normal hearing [2] was modified to fit IC physiology in deaf animals. Modeling results support the idea that the changes in ITD coding resulting from deprivation of binaural experience substantially contribute to the poor psychophysical performance by human BiCI users.

Our finding of abnormal ITD coding in congenitally deaf cats are germane with studies in human BiCI subjects showing effects of the age at onset of deafness and duration of deafness on psychophysical ITD sensitivity and binaural auditory brainstem responses. An important question is whether the negative effects of auditory deprivation on neural ITD coding can be reversed by electric stimulation and, if so, whether there is a critical period for reversal to occur.

Behavioral and neural ITD sensitivities with electric pulse trains are poor for the high pulse rates used in today's cochlear implant processors. Laback and Majdak [1] have shown that ITD discrimination at high-rate pulse rates can be improved by introducing binaurally-coherent jitter in the pulse train stimuli. To examine the neural mechanisms underlying this finding, we studied the effect of jitter on ITD sensitivity of IC neurons for both BiCI stimulation in deaf animals and acoustic stimulation in normal-hearing animals. For pulse rates above ~300 pps, jitter increased

the firing rates in about one-third of IC neurons and gave these neurons ITD sensitivity comparable to that observed for low-rate periodic pulse trains. Thus, jitter appears to unmask neural ITD sensitivity by restoring sustained firing in IC neurons. Preliminary modeling studies suggest that jitter acts by introducing coherent fluctuations in neural responses at the input to the binaural coincidence detectors. This work may lead to new processing strategies that harness the effect of jitter to improve sound localization and speech reception in noise with BiCI.

Psychophysics

Most BiCI users wear speech processors with a stimulation strategy optimized for monaural speech understanding: envelopes extracted from filtered speech signals are used to modulate pulse trains of roughly 1000 pps. Because the commercial speech processors of BiCI users are unsynchronized between the two ears, the ITD encoded by the carrier pulse trains is not controlled. Smith and Delgutte [3] showed that, for neurons in cat IC, ITD sensitivity to unmodulated pulse trains was good at 40 pps, but became very poor at 1000 pps where response was limited to the onset. The same authors [4] also found that if the 1000-pps signal was amplitude modulated, ITD sensitivity to the carrier could be as good as the sensitivity to low rate pulse trains. This result suggested that synchronizing the carriers of BiCI processors and representing ITD in the carriers might improve ITD sensitivity for BiCI users.

We tested whether encoding ITD in amplitude-modulated pulse trains with synchronized carriers improves the psychophysical sensitivity to ITD in human subjects with BiCIs. A 1000-pps carrier modulated by a 50-Hz sinusoid was used to measure ITD sensitivity in three human BiCI subjects for three conditions: (1) ITD represented only in the envelope (carrier ITD fixed at zero), (2) ITD represented only in the carrier (envelope ITD fixed at zero), and (3) ITD in both the carrier and envelope (whole waveform delayed interaurally). The subject's implants were controlled by custom research hardware to achieve bilaterally-synchronized stimulation. None of the subjects showed sensitivity to ITD encoded only in the carrier (ITD JNDs were always above 200 μs for this condition). Moreover, encoding ITD only in the envelope was always as good as or better than when ITD was represented in both the envelope and carrier. These results suggest that BiCI subjects were unable to use ITD information available in the 1000 pps carrier.

Unlike physiological results from the cat IC, the results from human psychophysical tests show no advantage to encoding ITD in carriers of amplitude-modulated pulse trains. Either the human subjects are unable to utilize carrier ITD information available in midbrain auditory neurons or neural responses differ in major ways between deaf humans and acutely-deafened cats. In any case our psychophysical results provide no evidence that developing bilateral cochlear implants that represent ITD in synchronized carrier pulse trains across ears will result in better binaural performance, at least for carrier rates used in present processors.

Neurocomputation

Our computational modeling work is focused on understanding neural responses to cochlear implant stimulation. This year, we have refined our descriptions of neural responses at all brainstem levels, including auditory-nerve (AN) fibers, cochlear nucleus (CN) neurons, medial superior olive (MSO) neurons, and IC neurons. Although physiological data with electric stimulation are available primarily from AN and IC neurons, the modeling of neural activity in the intermediate nuclei is important for uncovering the mechanisms underlying the sensitivity of the IC response patterns.

In one study, the consequences of instability in the non-linear dynamics of nerve membrane were explored for pulse-train stimulation. We found that the exquisite sensitivity to amplitude modulation for pulse-train stimuli observed in AN responses is only obtained when dynamical instability is present in the model.

A further study focused on the characteristics observed in neurons sensitive to ITD in acutely deafened animal models for BiCI. In particular, the work addresses 1) pulse-rate-limitations for

ITD sensitivity to constant-amplitude pulse trains, 2) the intensity dependence of ITD sensitivity, and 3) the effects of amplitude modulation on ITD sensitivity with high-rate stimulation. We found that ITD sensitivity is highly dependent on specific configurations of membrane and synaptic parameters for different input stimulation rates. Specifically, stronger excitatory synaptic inputs and faster membrane responses are required for the model neurons to be ITD-sensitive at high stimulation rates, both in electric and acoustic stimulation. This raises the possibility of differences in neural mechanisms of binaural processing along the tonotopic axis so that some limitations in ITD sensitivity may be due to the mismatch between stimulation rate and cell parameters in ITD-sensitive neurons. In general, the high spike rates and strong phase-locking of AN fibers in response to electric stimulation result in changes in rate-ITD tuning curves in the IC. Amplitude modulation of the high-rate stimulation restores the ongoing ITD sensitivity through short-time reductions in the spike rate at the AN level. ITD sensitivity to temporal fine-structure is restored with amplitude-modulated high-rate stimulation in the model as in physiology.

These results suggest that there may not be a major difference between in the effects of electric vs. acoustic stimulation on binaural processing in the brainstem providing there is a good match between the parameters of the stimulation and those of the binaural circuits. The results offer hope that fine-structure ITD can be delivered to BiCI users with proper processing strategies.

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