

Neural Coding and Auditory Perception

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Neural coding of sound in complex acoustic environments

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The long-term goal of this project 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) Physiological and psychophysical studies of sound localization in reverberant environments (Aim 1); (2) Spatio-temporal representation of pitch in the auditory nerve and cochlear nucleus (Aim 2).

Sound localization in reverberant environments: Relating neural responses to human perception

Reverberation, which is ubiquitous in everyday listening environments, poses a challenge to sound localization. In reverberant rooms, acoustic reflections interfere with the direct sound, leading to pronounced fluctuations in interaural differences in time (ITD) and level (ILD) over the course of a stimulus. These effects become more severe as the distance from sound source to listener increases, which causes the ratio of direct to reverberant energy (D/R) to decrease.

We conducted two parallel studies aimed at characterizing the influence of acoustic reflections occurring in typical classrooms on both the directional sensitivity of low-frequency ITD-sensitive neurons in the inferior colliculus (IC) of anesthetized cats and the localization performance of human listeners. These studies were conducted in collaboration with Dr. Barbara Shinn-Cunningham at Boston University. Our results demonstrate that (1) both neural discharge rates and human judgments of azimuth vary systematically with source azimuth in the presence of realistic reverberation and (2) both neural and behavioral sensitivities to azimuth degrade with increasing distance from the sound source, and therefore decreasing direct-to-reverberant energy ratio.

Recent theoretical studies of ITD processing in the auditory brainstem and midbrain [1] suggest that psychophysical performance may be more consistent with models that compare the total neural activity across a small number of broadly tuned spatial channels rather than with the classic “place code” for sound localization proposed by Jeffress. Inspired by these theoretical studies, we showed that our human behavioral results in reverberation are qualitatively consistent with a hemispheric difference model of sound localization, in which sound source location is

estimated by comparing the total activity in two broadly tuned spatial channels comprising the population of ITD-sensitive IC neurons on each side of the brain.

Our finding that a simple hemispheric difference model for sound localization accounts for trends in the psychophysical performance in reverberation has implications for understanding the effects of hearing impairment on sound localization. Because this model depends in the overall activity in two large populations of neurons, it may be more robust to central and peripheral lesions than the traditional place code, in which source location is represented by specific neurons.

Spatio-temporal representation of the pitch of complex tones in the auditory nerve and cochlear nucleus

Traditionally, models of pitch processing have relied either on a purely spatial representation based on the frequency-to-place mapping in the cochlea, or on a purely temporal representation dependent on neural phase locking. In recent physiological studies, we showed (1) that neither of these pitch representations accounts for all key psychophysical observations, and (2) that the auditory nerve (AN) contains spatio-temporal cues to resolved harmonics of a complex tone that might be used in pitch extraction. These cues require both phase locking and sharp cochlear frequency selectivity, and seem to be more consistent with psychophysical data than traditional place and temporal cues. We hypothesized that these spatio-temporal cues may be extracted by central neurons sensitive to the relative timing of spikes from AN inputs innervating neighboring regions of the cochlea, and tested this hypothesis by recording from single units in the cochlear nucleus (CN) of anesthetized cats.

To test the whether CN neurons are sensitive to the spatio-temporal pattern of their AN inputs, we adopted the method of Carney [2] using "Huffman sequences", which are complex acoustic stimuli with a flat magnitude spectrum and a rapid phase transition near the neuron's characteristic frequency (CF). By manipulating the steepness of the phase transition, we systematically varied the relative timing of spikes across the tonotopic array of fibers. Consistent with Carney's results, we find that the sensitivity of both AN fibers and CN neurons to the phase pattern of Huffman sequences depends strongly on stimulus level. With increasing level, rate responses of AN fibers increasingly favor stimuli with sharp phase transitions (which have a longer duration), suggesting that the peak discharge rates saturate. While the responses of most CN neurons follow the same trend, a minority showed greater sensitivity to the steepness of the phase transition than AN fibers, suggesting they are sensitive to the spatio-temporal pattern of their inputs. At present it remains unclear whether these phase-sensitive neurons correlate with unit types based on tone-burst response patterns.

We also recorded CN responses to equal-amplitude harmonic complex tones and compared these responses with spatio-temporal sensitivity assessed with Huffman sequences. The principle of local scaling invariance in cochlear mechanics was used to infer the spatio-temporal response pattern to a given complex tone from a set of temporal response patterns measured from a single neuron as a function of fundamental frequency. We find that some CN neurons are better able to maintain salient pitch cues in their rate responses compared to AN fibers at high stimulus levels. However at this point, we are uncertain whether these neurons are especially sensitive to the spatio-temporal pattern of their AN inputs, nor is it clear that they correspond to a specific cell type in the CN.

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Hancock KE. "A physiologically-based rate code for interaural time differences (ITD) predicts bandwidth-dependent lateralization". 30th Midwinter Meeting of the Association for Research in Otolaryngology, Denver, CO, February 2007.

Bilateral Cochlear Implants: Physiological and Psychophysical Studies

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Project Staff:

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Bilateral cochlear implantation is becoming increasingly common in the hope of restoring the functional benefits of binaural hearing, including accurate sound localization and improved speech reception in noise. While most wearers of bilateral cochlear implants benefit, these benefits seem to be due primarily to the ability to exploit the acoustic head shadow and utilize interaural level differences. In contrast, bilateral implantees show great variability in their ability to process interaural time differences (ITD), which confer the greatest binaural benefits in normal-hearing listeners, and even the best implanted subjects do not discriminate ITD as well as normal. The overall goal of this project is to give a detailed, quantitative characterization of sensitivity to ITD with bilateral cochlear implants by means of closely-integrated psychophysical, neurophysiological and modeling studies. We first describe the results of the neurophysiological, psychophysical and modeling studies separately, then draw general conclusions from a comparison of the three approaches.

Neurophysiology

ITD sensitivity for constant-amplitude pulse trains

We developed an animal model of bilateral cochlear implantation in order to study neural ITD sensitivity for bilateral electric stimulation of the cochlea [1]. Cats were deafened with ototoxic drugs, and the effectiveness of deafening was verified by measuring click auditory brainstem responses. At one week post deafening, cats were anesthetized and implanted bilaterally with 8-channel electrode arrays. We then recorded from single units in the inferior colliculus (IC) in response to trains of biphasic pulses delivered to a single electrode pair in each ear using a wide bipolar configuration. Because pulse trains evoke a temporally precise response in the auditory nerve, they are ideal to determine fundamental limitations on ITD processing in the brainstem.

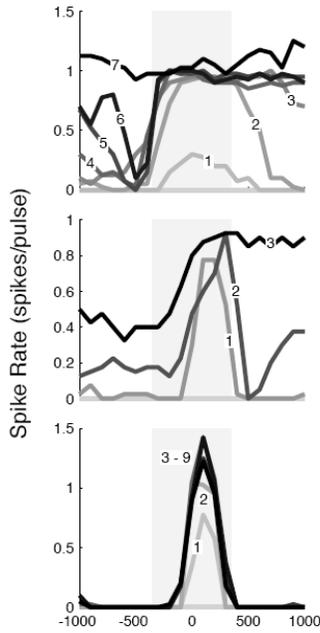


Fig. 2. Rate responses of 3 IC neurons as a function of ITD for 40-pps pulse trains. Numbers next to each curve show the stimulus level in dB re. threshold.

For low pulse rates, a vast majority of single units were sensitive to ITD at moderate intensities, and the electric ITD tuning was as sharp as found for acoustic stimulation with broadband noise in normal-hearing animals (Fig. 1). However, the sharpness and shape of ITD tuning often depended strongly on stimulus intensity (Fig. 2); some neurons had dynamic ranges of ITD sensitivity as low as 1 dB. Neural ITD discrimination thresholds (assessed with metrics from detection theory) were best at pulse rates below 100 pps and degraded with increasing pulse rate. At rates above 150 pps, most neurons only gave an onset response to the stimuli, consistent with results for monaural electric stimulation.

The sharp neural ITD sensitivity found with electric stimulation of appropriate intensity is encouraging for the prospect of restoring the functional benefits of binaural hearing in bilaterally-implanted human subjects. The comparable ITD sensitivities of individual IC neurons with acoustic and electric stimulation contrasts with the poorer psychophysical performance of implanted human subjects compared to normal hearing subjects in most tasks requiring ITD processing. This contrast suggests that neural plasticity resulting from deprivation of binaural experience may play a role in the poor ITD discrimination with current bilateral implants.

Our results with acutely deafened animals also indicate significant differences from normal animals in the relationship between the distribution of neurons' best ITDs and their best frequencies (BF). Specifically, neither best ITD nor width of tuning varies with electrode depth in penetrations parallel to the tonotopic axis of the IC. This finding suggests that the inverse correlation between best ITD and BF seen in normal-hearing animals [2-4] depends on the integrity of cochlear tuning, and provides some support for "stereausis" models of binaural processing in which interaural delays are created through interaural disparities in the cochlear

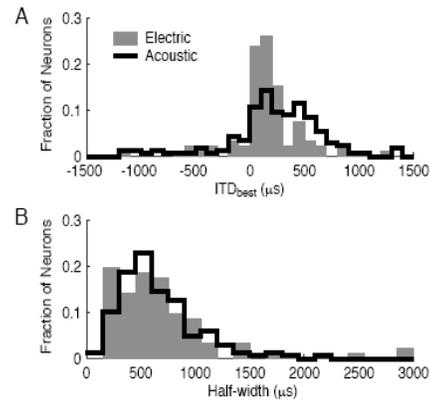


Fig. 1. Distribution of best ITD (A) and half width of ITD tuning (B) in the IC for bilateral electric stimulation with 40-pps pulse trains and for acoustic stimulation with broadband noise. While the best ITD distributions differ somewhat, the half-width distributions are similar.

places of origins (and therefore traveling wave delays) of the inputs to the binaural coincidence detectors [5,4].

ITD sensitivity for amplitude-modulated pulse trains

Today's processors for cochlear implants typically encode sound in each spectral channel by amplitude modulating (AM) a fixed-rate pulse train. Thus, current bilateral implants only deliver ITD information in the envelope (modulations), even though results from normal hearing suggest that ITDs in the fine structure of low-frequency sounds is a more potent directional cue than envelope ITD. We therefore investigated the ITD sensitivity of IC neurons with sinusoidally AM pulse trains [6]. ITD was introduced independently to the modulator and/or the carrier pulses in order to determine the relative efficacy of envelope and fine structure for delivering ITD information.

We found that many IC cells are sensitive to ITD in both the envelope (ITD_{Env}) and fine structure (ITD_{FS}) for appropriate modulation frequency and carrier rate. ITD_{Env} sensitivity generally improved with increasing modulation frequency up to the maximum modulation frequency that elicited a sustained response in a neuron, and was nearly independent of carrier rate (1000 vs. 5000 pps). Neural ITD_{Env} discrimination thresholds (based on signal detection theory) were nearly constant when expressed relative to the width of each AM cycle over the range of modulation frequencies tested. Because IC neurons rarely have sustained responses to AM pulse trains at modulation frequencies above 200-300 Hz, we expect neural ITD sensitivity to degrade at higher modulation frequencies, consistent with the degradation seen psychophysically [7].

While a 1000-pps constant-amplitude pulse train only produces onset responses in IC neurons, low-frequency (40-Hz) amplitude modulation restored both sustained responses and ITD_{FS} sensitivity in many neurons. ITD_{FS} sensitivity was relatively sharp for a 1000 pps pulse train but non-existent at 5000 pps. This is similar to acoustic stimulation where sensitivity to ITD_{FS} in IC neurons drops rapidly above 1500 Hz [8-9]. Overall, the best ITD sensitivity was found for ITD contained in the fine structure of a moderate rate (1000 pps) modulated pulse train.

Our results suggest that a bilateral cochlear implant strategy that successfully conveys ITD cues should control the timing of current pulses based on the fine time structure of the sound sources at each ear. Further benefit from improved sensitivity to envelope ITD might be achieved by temporally sharpening the amplitude envelope as with "transposed stimuli" [10-11], albeit with the possible side effect of distorting speech information contained in the envelope.

Non-invasive method for interaural electrode matches with bilateral implants

Psychophysical data suggest that a key issue for the successful implementation of a binaural prosthesis is the ability to match the cochlear positions of stimulation channels in each ear [12-13]. We used our cat model of bilateral cochlear implants with 8-electrode arrays implanted in each cochlea to develop and test a noninvasive method based on evoked potentials for matching interaural electrodes [14]. The arrays allowed the cochlear location of stimulation to be independently varied in each ear. The binaural interaction component (BIC) of the electrical auditory brainstem response (EABR) was used as an assay of binaural processing. BIC amplitude peaked for interaural electrode pairs at the same relative cochlear position and dropped with increasing cochlear separation in either direction (Fig. 3). This orderly decrease in BIC amplitude suggests that the BIC reflects binaural interactions occurring between

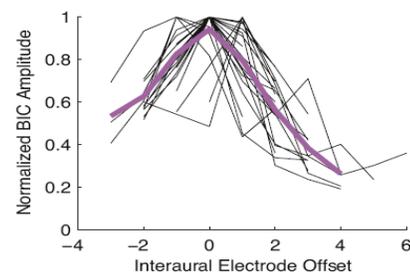


Fig. 3. Amplitude of the binaural interaction component (BIC) of the EABR as a function of interaural electrode separations for 25 measurements in 7 animals. Thick purple line shows the mean. For each measurement, the stimulating electrode was fixed in one ear and varied in the opposite ear. For 22/25 measurements, BIC peaks when the stimulating electrodes are at the same cochlear location in both ears, and the offset never exceeds the distance between two adjacent electrodes (0.75mm).

specific cochleotopic channels.

To directly test the hypothesis that BIC amplitude peaks when electrodes in the two ears activate maximally overlapping neural populations, we measured multi-unit neural activity along the tonotopic axis of the IC with 16-channel recording probes and determined the spatial pattern of IC activation for each stimulating electrode. We found that the interaural electrode pairings that produced the best aligned activation patterns in the IC were also those that yielded maximum BIC amplitude.

These results suggest that EABR measurements may provide a non-invasive method for assigning frequency-channel mappings in bilateral implant recipients, such as pediatric patients, for which psychophysical measures of pitch ranking or binaural fusion are unavailable. A BIC is detectable in over half of normal-hearing newborns tested with acoustic clicks [15], suggesting that the required binaural brainstem circuits are in place at birth and that BIC might also be measurable in bilaterally implanted infants (9-12 months).

Psychophysics

ITD sensitivity for constant-amplitude pulse trains

ITD sensitivity for constant-amplitude pulse trains was studied in detail for four subjects with adult-onset deafness implanted bilaterally with Advanced Bionics CII systems [16]. Fig. 4 shows ITD JNDs for low-rate pulse trains as a function of time since the start of binaural processor use for the 4 subjects. During the period between implantation of the second ear and beginning use of their second processor, the subjects continued monaural listening with their first-ear sound processor. The subjects fall into two groups depending on whether they developed ITD sensitivity before or after they began using their second processor or not, and the subjects who developed ITD sensitivity early were those who had experienced the shortest period of binaural deprivation. Subjects C109 and C120 (red and magenta) developed ITD sensitivity very early in their testing, well before beginning daily use of their second sound processor. In contrast, ITD sensitivity for C105 and C128 (blue and cyan) did not develop until well into their daily experience with bilateral listening. ITD JNDs for subjects C105, C109 and C128 improved over several months after ITD sensitivity was first observed. Due to C120's restricted availability, we could not track his ITD sensitivity.

The mean (across four subjects) normalized ITD JND are shown as a function of number of pulses for 50-pps (red circles) and 800-pps (magenta triangles) trains in Fig. 5. The solid lines are linear regressions to the data on double logarithmic coordinates. The blue and cyan lines show regression functions computed from ITD JNDs measured in normal-hearing subjects for high-pass click trains [17]. The dashed line with a slope of -0.5 represents the inverse square root dependence predicted for an ideal observer able to optimally integrate independent ITD information across clicks/pulses [18].

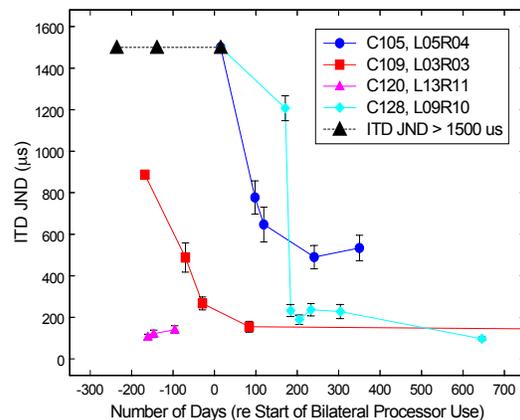


Fig. 4. ITD JND vs. time since start of binaural processor use for constant-amplitude, biphasic pulse trains (300-ms duration) with the repetition rate identified in the legend. The black triangles mark sessions when a subject's ITD was too large to be measured. Error bars represent the standard error of the mean.

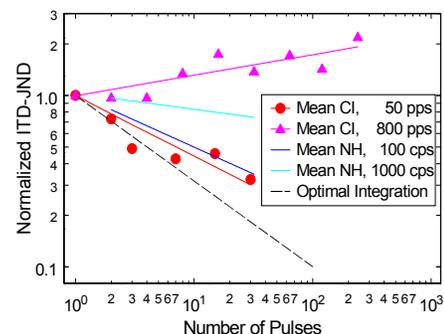


Fig. 5. ITD JND normalized re. JND for single pulse a function of the number of pulses or clicks in a train.

The regression slopes for the 50-pps CI results (solid red) and normal-hearing 100-cps results (blue) indicate a substantial integration of ongoing ITD information to a similar degree, although not quite optimal.

For the normal-hearing subjects, increasing the click rate to 1000 cps greatly reduced the integration of the ongoing ITD information (cyan). The CI results for 800 pps (magenta) show ITD sensitivity *decreasing* as a function of pulse number, indicating that the pulses beyond the first few pulses in a train may compromise the saliency of the onset information.

Responses of single units in the cat IC to bilateral electric stimulation with 40-pps pulse trains show neural ITD JNDs improving with the number of pulses at a rate close the inverse square-root law predicted for the ideal observer [1]. This result parallels both the normal-hearing and CI results for low-rate clicks/pulses. With increasing pulse rate, the neural ITD JNDs became dominated by information in the onset response because the ongoing response decreased and was negligible by 320 pps. This does not account for our higher-rate (800-pps) results showing an actual degradation in ITD JND with increasing duration, suggesting the degradation may occur beyond the IC.

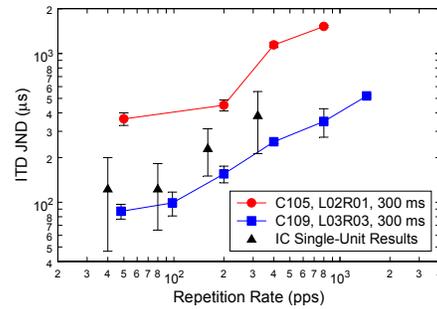


Fig. 6. Mean behavioral and neural ITD JNDs plotted vs. the repetition rate of pulse trains. Error bars represent standard deviations.

Fig. 6 compares ITD JND as a function of pulse rate for two CI subjects with single-neurons ITD JNDs from the cat IC. Subject C105 has relatively poor ITD sensitivity while C109 has good sensitivity. The effect of rate is similar for the neural data and the behavioral data from C109. The single-neuron ITD JNDs fall within the range of JNDs measured for the two CI users.

ITD sensitivity as a function of interaural disparities in cochlear stimulation sites

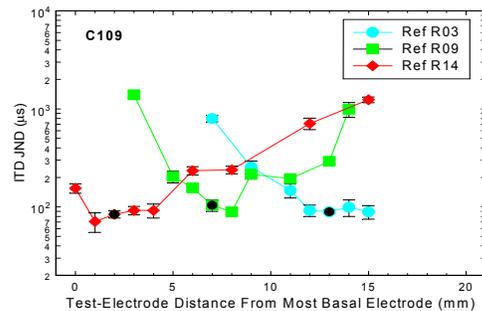


Fig. 7. ITD JND for 300-ms pulse trains (50 pps, 27 μs/phase) plotted as a function of the position of the left test electrode paired with the right reference electrode identified in the legend. Black dots mark the test electrode paired with the reference electrode in the subject's sound processor.

Previous results from a few CI users suggested that optimization of ITD sensitivity may require a precise match of the cochlear stimulation sites across the two ears [12-13]. To assess the importance of such matching in our subjects, we measured the dependence of ITD sensitivity on interaural electrode separation. A “reference” electrode was held constant in one ear, and the ITD JND was measured as a function of the position of the “test” electrode in the other ear. Fig. 7 shows results from C109 for 3 reference electrodes in the left ear. The electrode pairings (black dots) chosen for the processor based on measures of fusion, pitch and ITD sensitivity gave the best ITD JNDs in only four of the 10 reference conditions across the 4 subjects. The offset between the processor-paired test electrode and the one giving the best ITD sensitivity was typically just one electrode, suggesting that small adjustments in the processor channel-to-electrode mappings could give moderate improvements in overall ITD sensitivity when listening through the processor.

For each reference electrode, we measured the range (“half-width”) along the electrode array over which the ITD JND was no more than twice the best JND. We also estimated the mean half-width for the binaural interaction component (BIC) of the EABR measured as a function of interaural electrode separation in cat [14]. The mean half width for the cat BIC (4.5 mm) was well

within the range of ITD JND half-widths in the human subjects (mean: 3.7 mm; range: 0.8-6.75 mm). These half-widths for electric stimulation are substantially larger than the 0.7 mm estimated from measurements of ITD JND in normal-hearing listeners using sinusoidally amplitude-modulated high-frequency tones with different carrier frequencies in the two ears [19]. Thus, binaural measures based on EABR and ITD JNDs concur with monaural measures of electrode interactions [20] in showing that electric stimulation excites a wider extent of the cochleotopic axis than acoustic stimulation.

Neural Modeling

Our work during the past year has included computational modeling of the activity of auditory nerve fibers and binaural brainstem neurons in response to electric stimulation. Models of brainstem neurons include the medial and lateral superior olives (MSO and LSO) as well as IC, although most effort has been focused on the MSO as the key nucleus for ITD sensitivity. In all of these areas, our goal is to understand the basis of the observed behaviors, including neurophysiological and psychophysical observations.

Several distinctive aspects of the physiological data from bilaterally implanted animals are predicted by the models. First, the narrow range of stimulus levels for which IC neurons are ITD sensitive [1] is expected from the narrow dynamic range of auditory-nerve responses to electric stimulation [21-24] and the lack of ITD sensitivity in the MSO cell when there are substantial responses to monaural inputs. This narrow dynamic range is consistent with the absence of spontaneous activity, the high synchronization of firings (both to the stimulus and across the fiber population), the high degree of entrainment and, generally, the greatly reduced randomness of discharge patterns compared to acoustic stimulation. To date, we have modeled the peripheral activity descriptively, by specifying the input to the MSO model neuron in terms of probabilities of events and their timing for each stimulus pulse.

This lack of sensitivity to ITD when monaural inputs are strong and highly-synchronized is illustrated in Fig. 8 for an MSO model neuron based on the same biophysical descriptions of the ion channels as in Zhou et al. [25]; however, the model was simplified to have a single compartment containing all synapses and no inhibition. Fig. 8 shows that, when the inputs to the model MSO cell have large firing rates appropriate for electric stimulation, increases in the synchronization

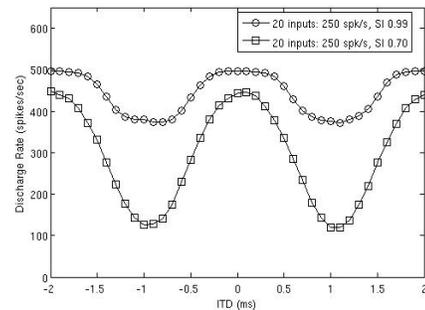


Fig. 8. Rate-ITD functions for model MSO cell with 20 inputs from each side for 500-pps pulse train stimulus. The legend shows the average firing rate and synchronization index SI of the inputs. Note minimal modulation depth of the rate-ITD function for the larger SI.

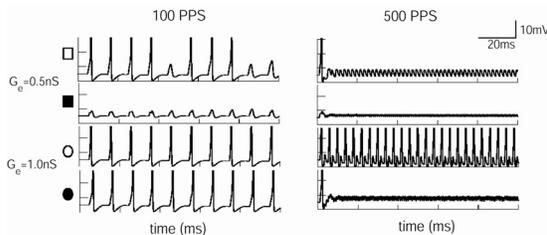


Fig. 9. Membrane voltage (with action potentials) of MSO cell model for different values of synaptic strength G_e and different pulse rates. The 4 curves are: 0-ms ITD and $G_e=0.5$ nS, 1-ms ITD and $G_e=0.5$ nS, 0-ms ITD and $G_e=1$ nS, 1-ms ITD and $G_e=1$ nS. Left column functions are for 100 pps and right column functions are for 500 pps. Note the lack of ongoing responses for the lower G_e .

index of these inputs actually lead to a degradation in ITD sensitivity of the MSO cell. In fact, for stimulation with low-rate pulse trains, firing rates of the MSO model can be larger when the inputs from the two sides are out of phase than when they are in phase; one obtains, for example, two MSO output spikes for each binaural current pulse, as observed in some physiological data at higher levels with large ITDs (both with electric stimuli [1] and with acoustic clicks [26]).

Another important observation in our brainstem models and in the physiological data is the lack of ongoing responses to

suprathreshold, constant-amplitude pulse trains at higher pulse rates. Fig. 9 shows the membrane potential of the model MSO cell in response to electric pulse trains for two pulse rates and two different strengths of the excitatory synaptic conductances. For the lower synaptic strength (top two curves), the model shows no ongoing response to 500 pps, in contrast to the vigorous response to 100 pps. Increasing the synaptic strength can overcome the refractory/adaptation behavior

and allow strong responses at 500 pps (bottom two panels). It is clear that, even at the level of the MSO (as represented by a relatively simple model), several factors interact to determine ITD sensitivity. In general, the matching of the input profile (including numbers, firing rates, and degree of synchronization of the inputs) to the cell parameters (including channel dynamics as well as synaptic strengths) determines the ITD sensitivity of the neuron.

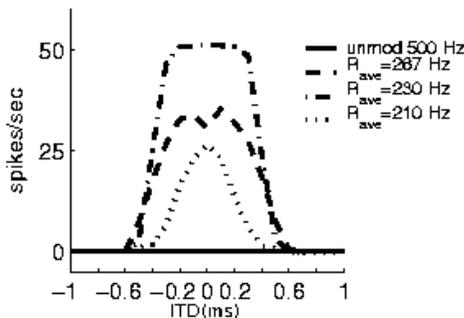


Fig. 10. Rate-ITD functions of MSO model cell for 500-pps pulse train. Curves (see legend) show the unmodulated case (solid curve) and three cases with 50-Hz amplitude modulation with different firing rates of the inputs.

responses by AM is obtained in a model with no inhibition, even though and interplay of excitation and inhibition with different time courses is often invoked as an explanation for such phenomena [27-28].

Parallels between the three approaches

We summarize here the close parallels found between our neurophysiological, psychophysical, and modeling studies:

1. ITD tuning in both IC neurons and brainstem model neurons is as sharp with bilateral electric stimulation as with acoustic stimulation for stimulus levels near threshold. At those intensities, the mean neural ITD JNDs based on rate responses of single neurons fall within the range of the psychophysical JNDs. However, ITD tuning in most IC neurons is restricted to a narrow range of stimulus levels, and ITD sensitivity in model neurons requires a close match between the input parameters (firing rate and synchrony) and the intrinsic cell parameters.
2. For low pulse rates (<100 pps) both the neural and behavioral ITD JNDs improve as the number of pulses in the stimulus train increases.
3. For higher pulse rates, both IC and model neurons give primarily an onset response to a pulse train, with little ongoing response. Psychophysical data from implanted subjects show a parallel degradation of ITD JNDs with increasing pulse rate, and at the higher rates, subjects are only able to use ITD information in the first few pulses.
4. Spatial patterns of BIC amplitude as a function of interaural electrode separation in cats parallel the dependence of psychophysical ITD sensitivity in human subjects.

These parallels between neural and psychophysical results suggest that the binaural system may operate basically normally in the bilaterally implanted subjects, despite prolonged periods of binaural deprivation in some subjects. However, the patterns of activity evoked in the population of ITD sensitive IC neurons clearly differ between normal acoustic stimulation and bilateral electric stimulation, and these differences may be even more pronounced in long-term deaf animals. Future studies will examine the effects of long-term binaural deprivation on neural ITD sensitivity with bilateral cochlear implants.

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