

Investigation of spatial location coding in the lateral superior olive using virtual space stimulation

D. J. Tollin and T. C. T. Yin

*University of Wisconsin, Department of Physiology, Madison, Wisconsin, 53706 USA
tollin@physiology.wisc.edu*

1. Introduction

The ability to determine the spatial location of sounds is one of the most basic of perceptual abilities. There are three primary cues to sound location two of which arise because the two ears are separated in space by an acoustically opaque object (the head) so sounds arriving at the ears from different locations differ in both arrival time and sound level. The magnitude of these interaural differences in time (ITDs) and level (ILDs) vary systematically with location, particularly in the horizontal plane (Kuhn, 1987). The third, "spectral" cues, results from the frequency- and direction-dependent interaction of sound with the pinnae, head, and torso (Shaw, 1974). Psychoacoustical studies have determined that low-frequency sounds are localized based primarily on ITDs and high-frequency sounds based primarily on ILDs (Rayleigh, 1907; Stevens and Newman, 1936). Spectral cues are thought to be used to localize sounds in the median sagittal plane, where interaural cues are minimized.

The superior olivary complex (SOC) in the midbrain of mammals contains two nuclei, the lateral (LSO) and medial superior olive (MSO), which are the first major sites in the ascending auditory pathway to receive inputs from both ears. The importance of the SOC for sound localization is evident from lesion studies where section of its inputs dramatically disrupts localization (Masterton et al., 1967; Moore et al., 1974). The LSO and MSO are traditionally thought to separately extract ILD and ITD cues, respectively. The LSO has been hypothesized to play a central role in localization through the extraction of ILDs (Boudreau and Tsuchitani, 1968). ILD sensitivity results because LSO cells are inhibited (I) by sounds to the contralateral ear and excited (E) by sounds to the ipsilateral ear; we call these IE cells. In higher auditory nuclei, including inferior colliculus (IC), medial geniculate body, and auditory cortical areas, many cells are sensitive to changes in sound location (see Irvine, 1986). These nuclei likely derive their spatial sensitivity in part from LSO, which projects predominantly to the contralateral dorsal nucleus of the lateral lemniscus and IC (Glendenning and Masterton, 1983).

Despite the pivotal role the LSO is hypothesized to play in localization, there are no previous studies of the spatial-location coding ability of LSO, probably because of its inaccessibility. Investigation of location coding in general is also limited by additional difficulties such as placing the positions of the pinnae in a "normal" orientation, generating signals and controlling their direction over a wide range of space at high spatial resolution *and* knowing precisely the acoustic signals at the two ears. The latter is essential in order to relate the neuronal responses to the direction-dependent cues. With free-field sounds, it can also be difficult to separate sensitivity

due to the amplification effects of the pinna at any one ear from binaural influences (e.g., Semple et al., 1983).

To avoid these complications, previous studies presented tones or broadband noise over earphones, so the signals to the ears could be known precisely. Such studies show that LSO cells are sensitive to ILDs and to ITDs of the envelopes of high-frequency sounds when presented in isolation or in combination (Boudreau and Tsuchitani, 1968; Caird and Klinke, 1983; Batra et al., 1997; Joris and Yin, 1995). In free field, the cues also arrive in combination making it difficult to determine which cue (or cues) contributed to any measured neural response. Earphone delivery of signals affords independent control over ITD and ILD and has proven useful for studying neural mechanisms of localization, however, such studies have not addressed the contributions of spectral cues or natural combinations of cues. Clearly, neither traditional free-field nor earphone approaches allow a complete investigation of the role each cue plays under natural conditions. Here, we investigate spatial location coding in LSO using a hybrid approach that allows us to present precisely controlled spatial stimuli with natural combinations of localization cues over earphones. This is called the virtual acoustic space technique and it has been used to study location coding in auditory nerve (Poon and Brugge, 1993; Rice et al., 1995), inferior colliculus (Delgutte et al., 1999; Keller et al., 1998), and auditory cortex (Brugge et al., 1994; Nelken et al., 1997).

1. Methods

1.1 The Virtual Acoustic Space technique

It is possible to simulate over earphones the sounds that would be produced in the ears by free-field sounds (Wightman and Kistler, 1989a;b) allowing the creation of a virtual auditory space (VAS). A VAS is created by first measuring the acoustical responses to broadband stimuli presented from many spatial locations using a probe microphone placed near each eardrum. After the spectral characteristics of the acoustic delivery and recording system are removed from the recordings, only the frequency- and direction-dependent free-field-to-eardrum spectral transformations, the Head Related Transfer Function (HRTF), remain. For a given location, a left- and right-ear pair of HRTFs embodies all localization cues for that location.

In this report, sound location was manipulated by filtering a single token of broadband noise (200 ms) through a left- and right-ear HRTF corresponding to desired locations in azimuth and then delivering these conditioned signals via earphones. The HRTFs were from one cat from the measurements of Musicant et al. (1990). The VAS approach offers many significant advantages over traditional earphone or free-field delivery. First, human studies show that VAS stimuli are externalized and localized to approximately the same locations in the free-field where the HRTFs were measured (Wightman and Kistler, 1989b). Second, each of the localization cues can be manipulated independently by digitally altering the HRTFs. Finally, we can study the effect of each ear independently by comparing responses to monaural and binaural signals, which is difficult to do using traditional free-field techniques.

Responses of well-isolated LSO cells to VAS stimuli were recorded in pentobarbital-anesthetized cats. Both pinnae were removed and custom tight-fitting hollow earbars were inserted into the external auditory meati, allowing a closed and calibrated acoustical system for each ear. The LSO was approached ventrally and

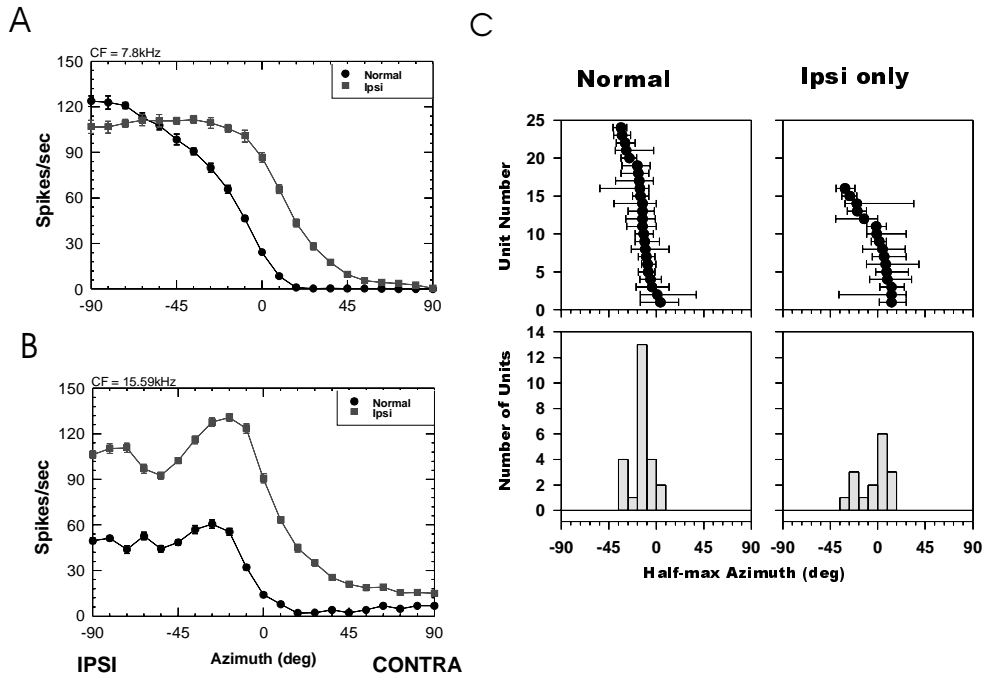


Figure 1. Mean discharge rate as a function of azimuth for the Normal (circles) and Ipsi-only (squares) conditions for 2 LSO cells (A-B). The Normal binaural condition reflects the IE interaction; cells respond to stimuli in the ipsilateral field and the contralateral inhibition reduces the response to the stimuli to the ipsilateral ear in isolation. C. Half-max azimuths and 25-75% ranges for the Normal and Ipsi-only conditions.

neural activity from single cells was recorded extracellularly, amplified, and discriminated. Penetrations through LSO were verified histologically.

3. Results

3.1 Spatial Receptive Fields

Our results are based on 27 high characteristic frequency (CF > 3 kHz) LSO cells. All units were modulated by changes in spatial location. Figure 1A-B shows the two general shapes of azimuthal spatial receptive fields (SRFs) for 2 LSO cells. Each panel shows for two conditions the mean discharge rate computed over the 200-ms duration of the stimulus as a function of azimuth and ± 1 standard error of the mean for 20 presentations. In the “Normal” condition, the stimuli were presented binaurally with the full complement of localization cues, as would occur for free-field stimulation. In the “Ipsi-only” condition, the stimuli were presented only to the ipsilateral (ipsi) ear while the contralateral (contra) earphone was silent. For all units, the stimulus level was approximately 15-20 dB above the threshold level for the noise stimulus presented to the ipsi ear alone at $(0^\circ, 0^\circ)$. Each unit in Fig. 1 is clearly modulated by sound location, with high discharge rates for sounds in the ipsi sound field, a segment near the midline of rapidly declining rates, and low rates for contra sounds. The data show that at these sound levels, the monaural ipsi-only SRFs were similar in shape to the binaural SRF measured in the same cell. But consistent with IE interaction, the binaural responses at most azimuths in the frontal hemisphere were inhibited relative to the monaural responses at the same azimuth, particularly for sounds in the contra sound field where the contra sound is more intense. At these

sound levels, the Normal SRFs were generally either sigmoidal shaped (Fig. 1A) or contained a single peak in the ipsi sound field (Fig. 1B).

The properties of the SRFs were summarized by calculating the azimuth at which the discharge rate fell to 50% of maximal - the half-max azimuth (e.g., Delgutte et al., 1998) - and also the range of azimuths corresponding to 25-75% of the maximum rate. The half-max azimuth indicates the location of the rising, steepest portion of the SRF in azimuth while the 25-75% range gives information about the steepness of the shoulders of the SRFs. Figure 1C shows the population of half-max azimuths for the Normal condition, which are located primarily in the ipsi sound field (median=-13°), and the Ipsi-only condition, which are located more towards the contra field (median=3°). Median ranges for the Normal and Ipsi-only conditions were 25.7° and 31.5°, respectively. Consistent with IE interaction, the distribution of half-max azimuths for 13 cells for which both Normal and Ipsi-only SRFs were measured was significantly different [$t(12)=6.97$, $p<0.0005$]. For the same 13 cells, differences in steepness were also significant [$t(12)=7.06$, $p<0.0005$].

3.2 Effect of localization cue manipulation on receptive fields

As sound source azimuth is changed, the three main localization cues also change and the extent to which the cell is sensitive to each cue determines how the response of the cell is modulated with azimuth. If the azimuthal sensitivity of LSO cells is determined primarily by their ILD sensitivity, then we predict that the cells should respond over a large range of azimuths in the ipsi field but be inhibited for azimuths in the contra field. But given the full complement of cues, what cue or cues does the LSO really encode? To answer this question, the HRTFs were digitally manipulated by independently varying (or holding constant) in azimuth each of the three localization cues in isolation while holding constant (or varying) the others. This “titration” method of manipulating the cues will allow us to identify the determinants of the Normal SRFs of each LSO cell. When a cue was held constant, we fixed them at the values at the position (0°,0°).

ITD was manipulated in two ways. For the “0-ITD” case, the HRTFs were manipulated so that at each azimuth the ITD was 0 μ s. This was done by delaying the leading HRTFs in time and advancing the lagging HRTFs for each location until the delay corresponding to the maximum in the cross-correlation function between the left- and right-ear HRTFs equaled 0 μ s. For the “ Δ -ITD” case, ITD was manipulated in isolation by first taking the HRTFs for the (0°,0°) position, which initially has zero interaural delay, and introducing the ITD appropriate for each azimuth. ILD and spectral cues for the left- and right-ear were held constant at those for the location (0°,0°) as azimuth was varied.

Figure 2A shows an example of the effects of manipulating ITD information on the SRF. When ITD was varied naturally with azimuth, but ILD and spectral cues set constant at those corresponding to the (0°,0°) position, response was not modulated with azimuth (Δ -ITD, Fig. 2A). This finding suggests that ITD contributes very little to the SRF (at least based on discharge rate computed over the duration of the stimuli). Consistent with this finding, holding ITD constant at 0 μ s for all azimuths while naturally varying the ILD and spectral cues results in a SRF that is nearly identical to the Normal SRF (0-ITD, Fig. 2A).

ILD was also manipulated. For the 0-ILD condition, the amplitudes of the HRTFs were adjusted so that at each azimuth, the ILD, as computed through a 1/3-octave bandpass filter centered on the CF of the cell under study, was 0 dB. All

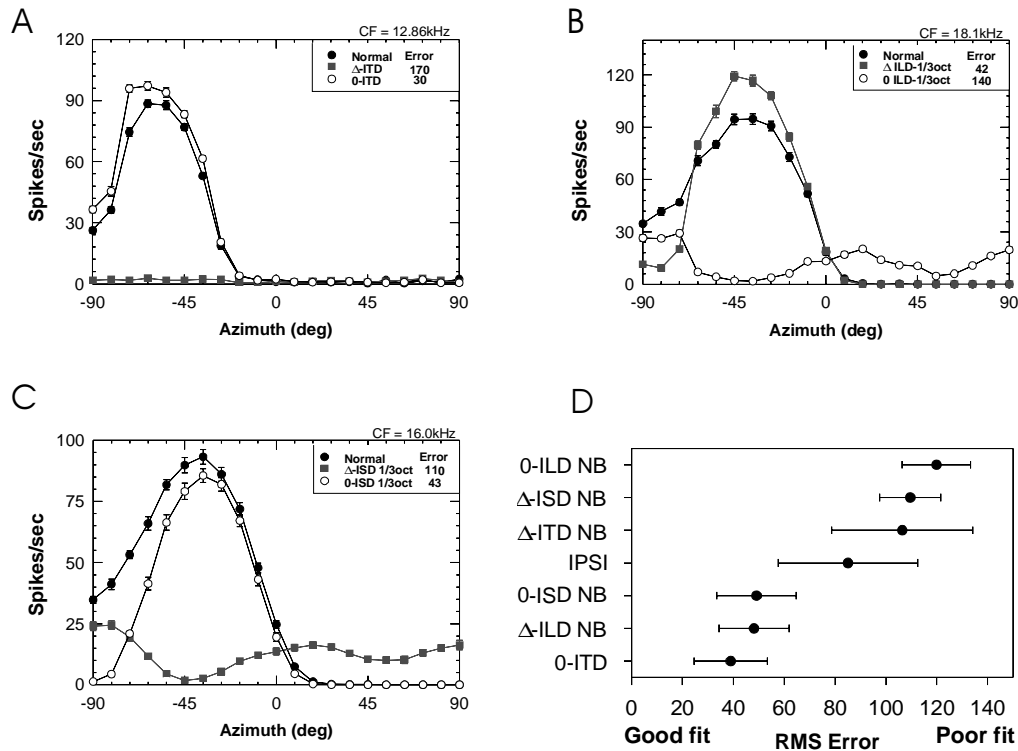


Figure 2. Effects of ITD (A), ILD (B), and spectral (C) cue manipulations on azimuthal sensitivity. The values in the upper right-hand corner of each panel are the normalized RMS error of the difference between the Normal and manipulated receptive fields. D. Population means and 95% confidence intervals for the RMS error computed for each of the localization cue manipulations.

other aspects of the signals to the two ears as a function of azimuth were not changed; that is, ITD and the monaural spectral cues still changed naturally. ILD was also varied naturally with azimuth, the Δ -ILD condition, while ITD was held constant at 0 μ s and the spectral cues held constant at those for the location (0°,0°).

Figure 2B shows an example of the effects of manipulating ILD. Responses were greatly modulated by natural changes in only ILD and the resulting SRF was similar to the Normal SRF (Δ -ILD, Fig. 2B). The close correspondence between the Normal and the Δ -ILD condition suggests that ILD plays a large role in the formation of the Normal SRF. The 0-ILD condition confirms this hypothesis – holding ILD constant at 0 dB but varying ITD and spectral cues naturally with azimuth has a large detrimental effect on the SRF.

Finally, the spectral cues were also manipulated. For the 0-ISD case, spectral cues were held constant as a function of azimuth by restricting them to those from the (0°,0°) position. ITD and ILD, as computed above, varied naturally with changes in azimuth. For the Δ -ISD condition, the spectral cues at each ear varied naturally with azimuth, but ITD and ILD were held constant at 0 μ s and 0 dB, respectively.

Figure 2C shows an example of the effects of manipulating just the spectral cues. When spectral cues were varied naturally with azimuth, but ITD and ILD held constant, the response was weakly modulated with changes in azimuth, but the modulation was not consistent with the Normal SRF (Δ -ISD, Fig. 2C). This suggests that spectral cues have only a marginal effect on the SRF. Confirming this, when

spectral cues were held constant as a function of azimuth, the resultant SRF was very similar to the Normal SRF (0-ISD, Fig. 2C).

To quantify the effect of the various localization cue manipulations on the SRFs, we computed a normalized RMS error of the difference between the Normal SRF and the manipulated SRF, where the normalization factor was the mean discharge rate computed across all azimuths for the Normal condition. The RMS error is indicated for each of the manipulated cues in Figs. 2A-C. Figure 2D shows the population means and 95% confidence intervals for RMS error computed for each of the localization cue manipulations. The examples in Figure 2 A-C were selected to have errors near the median error for the population for the given manipulation. Small errors indicate a close correspondence between the Normal SRF and the SRF measured with the cue manipulation.

When ITD was held constant in the 0-ITD condition, small errors arise indicating that across the population of cells ITD plays little role in shaping the spatial location sensitivity of LSO neurons. This notion is supported in the Δ -ITD condition where large errors are observed. This leaves open the possibility that the ILD and/or spectral cues contribute most. Holding the spectral cues constant with azimuth, the 0-ISD case, leads to small errors while varying spectral cues alone, the Δ -ISD case, yields large errors suggesting that spectral cues alone do not contribute greatly to the receptive fields. But when ILD in a 1/3-octave band centered on the CFs of each cell tested was varied in the Δ -ILD condition, small errors are present indicating that ILD plays a substantial role in determining the spatial SRF. Confirming this, holding ILD constant, the 0-ILD condition, gives large errors. Finally, the Ipsi-only condition generally yields large errors, but not the largest, indicating that at least some azimuthal sensitivity is retained by monaural stimulation.

4. Discussion

These are the first measurements of the sensitivity of LSO cells to changes in sound-source location in any species. The data provide two major conclusions. First, the form of the spatial receptive fields of most LSO cells are in accordance with their IE binaural interaction that has been described in earlier studies using earphones. Second, they demonstrate that the shape of the SRFs is largely due to the ILD sensitivity of the LSO cells. In sum, our results support the hypothesis that LSO cells compute a correlate of ILD from free field sounds.

All of the SRFs in the LSO had larger responses in the ipsi sound field and a poor response in the contra field in accordance with the contra-inhibitory, ipsi-excitatory responses described in earlier studies (Boudreau and Tsuchitani, 1968). Using the VAS technique we could easily compare the normal binaural response with the response to monaural stimulation of the ipsi ear. The monaural Ipsi-only SRFs were similar in shape to the binaural ones, as expected, since the stimulus level to the ipsi ear is higher for sounds in the ipsi sound field than in the contra. The effect of the inhibitory input from the contra ear is seen by the greater suppression in the contra sound field and the movement of the half-maximal azimuth toward the contra sound field under binaural stimulation.

By manipulating the HRTFs, we employed a titration method to determine which localization cues contributed to the spatial selectivity of the cell. By systematically setting each of the three cues to a constant while letting the others vary naturally in azimuth, we could compare the relative contribution of each cue. In all cases, ILD was the major determinant shaping the SRFs in azimuth. Despite the

demonstrated sensitivity of LSO cells to ITDs of the envelope of amplitude modulated signals (Joris and Yin, 1995), ITD of these noise stimuli had a weak effect in all cells and to a lesser degree the spectral cues were also largely ineffective.

5. Acknowledgements

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6. References

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