Processing of Interaural Intensity Differences in the LSO: Role of Interaural Threshold Differences

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Park, T. J., P. Monsivais, and G. D. Pollak. Processing of interaural intensity differences in the LSO: role of interaural threshold differences. J. Neurophysiol. 77: 2863–2878, 1997. Cells in the lateral superior olive (LSO) are known to be sensitive to interaural intensity differences (IIDs) in that they are excited by IIDs that favor the ipsilateral ear and inhibited by IIDs that favor the contralateral ear. For each LSO neuron there is a particular IID that causes a complete inhibition of discharges, and the IID of complete inhibition varies from neuron to neuron. This variability in IID sensitivity among LSO neurons is a key factor that allows for the coding of a variety of IIDs among the population of cells. A fundamental question concerning the coding of IIDs is: how does each cell in the LSO derive its particular IID sensitivity? Although there have been a large number of neurophysiological studies on the LSO, this question has received little attention. Indeed, the only reports that have directly addressed this question are those of Reed and Blum, who modeled the binaural properties of LSO neurons and proposed that the IID at which discharges are completely suppressed should correspond to the difference in threshold between the excitatory, ipsilateral and inhibitory, contralateral inputs that innervate each LSO cell. The main purpose of this study was to test the threshold difference hypothesis proposed by Reed and Blum by recording responses to monaural stimulation and to IIDs from single cells in the LSO of the mustache bat. Our results show that although the IID sensitivities of some LSO cells correspond to the difference in threshold between the excitatory and inhibitory ears, in the majority of cells the difference in thresholds did not correspond to the cell’s IID sensitivity. The results lead us to propose two models to account for IID sensitivities. One model is similar to that proposed by Reed and Blum and emphasizes differences in the thresholds of the excitatory and inhibitory inputs. This model accounts for the minority of cells in which the IID of complete inhibition corresponded to the difference in threshold of the inputs from the two ears. The other model, which accounts for the cells in which the IID of complete inhibition did not correspond to the difference in the thresholds of the inputs from the two ears (the majority of cells), places emphasis on differences in latencies of the excitatory and inhibitory inputs. The models incorporate features that are concordant with the known properties of the neurons that project to the LSO and together can account for the diversity of IID sensitivities among the population of LSO neurons.

INTRODUCTION

Interaural intensity differences (IIDs) are the binaural cues that animals use to localize high-frequency sounds (e.g., Erulkar 1972; Irvine 1986; Mills 1972). In mammals, IIDs are first coded by neurons in the lateral superior olive (LSO). The LSO receives its principal excitatory inputs from the ipsilateral ear and inhibitory inputs from the contralateral ear. The excitation is provided by the projections of spherical bushy cells in the ipsilateral cochlear nucleus, whereas the inhibition is from globular bushy cells in the contralateral cochlear nucleus (Cant 1991; Cant and Caseday 1986; Caspary and Finlayson 1991; Grothe et al. 1994; Kuwabara et al. 1991; Smith et al. 1991; Zook and DiCaprio 1988). The globular bushy cells do not directly inhibit LSO cells, but rather first synapse on principal cells in the medial nucleus of the trapezoid body, which then provide a powerful glycinergic inhibition to LSO neurons. These projections underlie the changes in the firing rates of LSO cells to different IIDs. Typically, the firing rate of an LSO cell declines as IIDs shift from favoring the excitatory ear to favoring the inhibitory ear until responses are completely inhibited (e.g., Boudreau and Tsuchitani 1968; Caird and Klinke 1983; Covey et al. 1991; Park et al. 1996; Sanes and Rubel 1988).

The decline in firing rate at the LSO with increasing contralateral intensity is thought to be due to two principal processes: 1) a progressive increase in the strength of inhibition at the LSO cell with intensity and 2) a shortening of the latencies of inhibitory inputs with intensity (Caird and Klinke 1983; Grothe and Park 1995; Haplea et al. 1994; Hirsh et al. 1985; Irvine and Gago 1990; Joris and Yin 1995; Park et al. 1996). Thus the contralateral intensity that produces complete spike suppression needs to evoke both an inhibitory strength that is at least equal to that of the excitation and an inhibition that is temporally coincident with the excitation. The particular IID that generates temporally coincident inputs of equal strength, and thereby produces complete suppression, varies from neuron to neuron (Park et al. 1996; Sanes and Rubel 1988). Some LSO neurons require IIDs that favor the ipsilateral ear; others require IIDs that favor the contralateral ear; and others are completely suppressed when the signals at the two ears are equally intense. This variability in IID sensitivity is a key factor that presumably allows the population of LSO cells to code for the particular IID received at the ears.

A fundamental question that has received little attention is how features arranged in the LSO endow each cell with its own particular IID sensitivity. Indeed, the only reports that directly address this question are those of Reed and Blum (Blum and Reed 1991; Reed and Blum 1990). They modeled the binaural properties of LSO neurons and proposed that the IID at which discharges are completely suppressed should correspond to the difference in threshold between the excitatory and inhibitory inputs that innervate each LSO cell. If, for example, the cell has excitatory and inhibitory inputs with equal thresholds, increasing the intensity to the excitatory ear should increase the strength of the excitatory input. In the same way, increasing the intensity to the inhibitory ear would increase the strength of the inhibitory input...
input. The hypothesis assumes that because both inputs have
the same threshold, when the intensity at both ears is equal,
the inputs from the two ears would generate equal synaptic
strengths in the target LSO cell. Implicit in the hypothesis
is that at the IID of complete inhibition, the inputs from
the two ears are coincident at the LSO target cell. Under these
conditions, the coincidence of an inhibitory strength that
exactly balances the excitatory strength would result in a
complete suppression of discharges in the LSO cell. The
same general effects should occur for a cell in which the
excitatory input has a lower threshold than the inhibitory
input. However, because the excitatory input has a lower
threshold, it would be stronger and arrive earlier than the
inhibitory input when the intensities at the two ears are equal.
Thus, to match the strengths and timing of the two inputs,
and achieve complete inhibition, the intensity at the inhibi-
tory ear would have to be greater than the intensity at the
excitatory ear. Furthermore, the IID that achieves complete
spike suppression should correspond to the difference in the
thresholds of the inputs from the two ears.

In the present study, we tested the threshold difference
hypothesis proposed by Reed and Blum by recording re-
sponses to monaural stimulation and to IIDs from single
cells in the LSO of the mustache bat. We chose the mustache
bat because it has a well-developed LSO and because it was
the subject in our previous studies of IID processing in the
dorsal nucleus of the lateral lemniscus and inferior colliculus
(e.g., Klug et al. 1995; Yang and Pollak 1994), which are
two of the principal targets of LSO projections. Here we
present evidence that suggests that although the IID sensitivi-
ties of some LSO cells correspond to the difference in thresh-
old between the excitatory and inhibitory ears, in the major-
ity of cells the difference in thresholds between the two ears
did not predict the cell’s IID sensitivity. The results lead us
to propose a model similar to the one proposed by Reed and
Blum to account for some cells, as well as additional models
to account for the majority of cells. The models incorporate
a few additional features that are concordant with the known
properties of the neurons that project to the LSO and together
can account for the diversity of IID sensitivities among the
population of LSO neurons.

Methods
Surgical and recording procedures

Fifteen Jamaican mustache bats, *Pteronotus parnellii parnellii*,
were experimental subjects. Before surgery, animals were anesthe-
tized with methoxyflurane inhalation (Metrone, Pitman-Moore)
and pentobarbital sodium (10 mg/kg ip). The hair on the bat’s
head was removed with a depilatory, and the head was secured in
a head holder with a bite bar. The muscles and skin overlying the
skull were reflected and lidocaine (Elkins-Sinn) was applied
topically to all open wounds. The surface of the skull was cleared
of tissue and a ground electrode was placed just beneath the skull
and electrode placement was based on stereotaxic coordinates.
Subsequently, the electrode was advanced from outside of the
experimental chamber with a piezoelectric microdrive (Burleigh
712 IW).

At the end of each experiment, the locations of recording sites
were confirmed by a small isomophoretic injection of horseradish
peroxidase. The animal was deeply anesthetized and perfused
through the heart with buffered saline and 4% glutaraldehyde. The
brain was dissected out, frozen, and cut into 40-μm sections that
were then processed for horseradish peroxidase reaction product.

Acoustic stimuli, data acquisition, and processing

A custom-made electronic switch shaped sine waves from a
Wavetek oscillator (Model 136) to 20-ms tone bursts having 0.5-m rise-fall times. During data acquisition, the sound intensity
of the bursts was selected pseudorandomly by a Macintosh Ici
computer that controlled an electronic attenuator (Wilsonics,
model PATT) via a 24-bit digital interface (Metabyte MAC
PIO-24) and a Digital Distributor (Restek Model 99). The output
of the attenuator went to two earphones (Panasonic ultrasonic ce-
ramic loudspeaker, EFR-OTB40K2), each fitted with a plastic
probe tube (5 mm diam), that were placed in the funnel of each
pinna. Maximum sound intensity was 85 dB SPL measured 0.5
cm from the opening of the probe tubes. Sound pressure and the
frequency response of each earphone were measured with a 1/4-in.
Bruel & Kjaer microphone (type 4135) and a Brue &
Kjaer measuring amplifier (type 2608). Each earphone showed
less than ±3 dB variability for the frequency range used (55–65
kHz) and intensities between the earphones did not vary more than
±2 dB at any of those frequencies. Tone bursts were presented at
a rate of four per second. Acoustic isolation between the ears was
40–50 dB, and was determined empirically by testing monaural
units during the course of the experiments as described previously
(Park and Pollak 1993).

Spikes were fed to a window discriminator and the output of
the discriminator was fed to the computer. When a unit was encoun-
tered, its characteristic frequency (the frequency to which the neu-
ron was most sensitive) and absolute threshold were audiovisually
determined to set stimulus parameters subsequently controlled by
the computer. The characteristic frequency was defined as the fre-
cency that elicited responses at the lowest sound intensity to
which the unit was sensitive. Binaural stimuli set at the unit’s
characteristic frequency were then presented to determine whether
the unit was monaural or binaural, and if it was binaural, whether
it was inhibitory/excitatory (IE) or excitatory/excitatory. Units
were classified as IE if sound at the contralateral (inhibitory) ear
suppressed the responses evoked by stimulation of the ipsilateral
(excitatory) ear. For each IE unit, sounds at various intensities
were presented monaurally to the contralateral ear and the influence
of this stimulation was monitored audiovisually. Only cells in
which monaural stimulation of the contralateral ear did not evoke
discharges were classified as IE (in fact, none of the cells we
encountered in the LSO discharged to monaural stimulation of the
contralateral ear).
Rate-intensity and IID functions were generated for each unit. Rate-intensity functions were generated with tone bursts at the unit’s characteristic frequency presented to the ipsilateral (excitatory) ear at intensities from 10 dB below to 40 dB above threshold. The values for these intensities were estimated audiovisually before data acquisition and we defined the threshold of the excitatory input as the intensity just below the intensity that first evoked responses. Each intensity was presented 20 times, or in a few units 10 times, and the order of presentation was varied pseudorandomly. IID functions were generated with sound intensity at the ipsilateral (excitatory) ear fixed at 10–40 dB above threshold, and the intensity at the contralateral (inhibitory) ear varied pseudorandomly from ~20 dB below to 40 dB above the intensity at the excitatory ear. Because the intensity values presented to the inhibitory ear were locked to the excitatory intensity value, and not predetermined audiovisually, there may have been some degree of error (<10 dB) in estimates of the inhibitory threshold. Data were displayed on the computer screen for inspection during the experiments and stored on hard disk for later analysis.

RESULTS

Here we report on 73 neurons recorded from the mustache bat LSO. The characteristic frequencies ranged from 29 to 113 kHz. The 73 neurons were all IE in that they were excited by stimulation of the ipsilateral ear and inhibited by stimulation of the contralateral ear. Because the influence of stimulation to each ear was similar among the LSO population, we hereafter refer to the ipsilateral ear as the excitatory ear and the contralateral ear as the inhibitory ear. Rate-intensity and IID functions were measured for each cell. Rate-intensity functions were obtained by presenting intensities to the excitatory ear that ranged from 10 dB below to 40 dB above threshold in 10-dB steps. IID functions were obtained by driving the neuron with a fixed intensity at the excitatory ear and then documenting the suppressive influence of increasing intensities at the inhibitory ear. Because the intensity at the excitatory ear was fixed, each intensity at the inhibitory ear generated a different IID. By convention, positive IIDs indicate that the sound was more intense at the excitatory ear than at the inhibitory ear, whereas negative IIDs indicate that the sound was more intense at the inhibitory ear. Below we first describe the characteristics of the IID functions that we measured, focusing on the sensitivity of these cells to particular IIDs. We then describe the thresholds for the excitatory and inhibitory inputs to the LSO cells and how those thresholds relate to IID sensitivity. Twelve monaural cells that were also located in the LSO were not included in the following analyses.

IID functions

The IID function in Fig. 1 illustrates how LSO cells responded to different IIDs. In this example, the intensity presented to the excitatory ear was held constant at 40 dB SPL, whereas the intensity to the inhibitory ear was varied from 0 to 60 dB SPL. The greatest spike counts were evoked by IIDs with low intensities at the inhibitory ear. Indeed, the spike counts evoked with low intensities at the inhibitory ear (0–10 dB SPL) were similar to the counts evoked when the 40-dB SPL signal at the excitatory ear was presented alone or monaurally (not shown). Increasing the intensity at the inhibitory ear caused a gradual decline in the spike count and eventually a complete inhibition of spike activity. We hereafter refer to the smallest IID capable of complete spike suppression as the IID of complete inhibition. For this cell, the discharges evoked by the 40-dB SPL signal at the excitatory ear were first completely inhibited when the signal at the inhibitory ear was 50 dB SPL, and thus the neuron’s IID of complete inhibition was −10 dB (Fig. 1, asterisk).

IID of complete inhibition as a descriptor of IID sensitivity

Here we show why we chose to focus on the IID of complete inhibition as an indicator of a cell’s IID sensitivity,
and not other points on the IID function, such as the IID that produced a 50% reduction in response rate. One of the problems encountered when studying IE neurons concerns the choice of a feature that uniquely describes the unit’s sensitivity to IIDs. Spike count is an unstable index because the spike count depends on factors other than the IID, such as stimulus duration and absolute intensity. Thus a given spike count can be evoked by a variety of IIDs, and one IID can evoke a range of spike counts when different absolute intensities and/or different stimulus durations are used. The only point on the function that apparently does not vary with other stimulus features is the IID of complete inhibition: binaural signals that have IIDs more positive than the IID of complete inhibition generate discharges, whereas binaural signals with more negative IID values result in complete spike suppression and these results obtain over a 30- to 40-dB range of absolute intensities and a wide range of tone burst durations.

These features are illustrated by the cells in Figs. 2 and 3. Figure 2 shows IID functions from an LSO cell obtained with tone bursts that had different durations. Because this LSO cell, as well as the majority of others, responded with a sustained discharge pattern to ipsilateral tone bursts (as in Fig. 1), tones with longer durations elicited higher spike counts than did tone bursts of shorter durations. Nevertheless, the IID of complete inhibition obtained with 30-ms tone bursts had the same value as that obtained with tone bursts of shorter durations.

The LSO cell in Fig. 3 illustrates that the IID of complete inhibition is invariant over a 30-dB range of absolute intensities. Each of the three IID functions in Fig. 3, right, was measured with a different intensity at the excitatory ear. For the IID function in Fig. 3, top, the intensity at the excitatory ear was 27 dB SPL and complete inhibition occurred when the signal at the inhibitory ear was also 27 dB SPL at an IID of 0 dB. The IID functions in Fig. 3, middle and bottom, were measured with signals that were 10 and 20 dB more intense at the excitatory ear. For each 10-dB increase in the intensity at the excitatory ear, a corresponding increase in intensity at the inhibitory ear was required to achieve complete spike suppression. In other words, so long as the intensity at the excitatory ear was on the linear portion of the rate-intensity function, the IID of complete inhibition remained constant and was always 0 dB for this LSO neuron.

In contrast to the invariance observed for the IID of complete inhibition, IIDs that evoked a certain spike count along the IID function changed depending on the intensity presented to the excitatory ear. For example, the IID corresponding to a 50% decline from the peak spike count was different for each of the curves in Fig. 3. In Fig. 3, top, the 50% point of the function occurred at an IID of 9.5 dB (ipsilateral = 27 dB, contralateral = 17.5 dB). Increasing the intensity to the excitatory ear by 10 dB caused the 50% point to shift to an IID of 16.5 dB (Fig. 3, middle). When the intensity at the excitatory ear was raised by an additional 10 dB, the IID of the 50% point changed again to 25 dB (Fig. 3, bottom).

The observations described above were consistent for the population of LSO cells. On average, the 50% point changed by 7.0 dB for each 10-dB increase at the excitatory ear. On the other hand, the IID of complete inhibition changed by an average of only 1.1 dB for each 10-dB increase at the excitatory ear. A paired t-test comparing the change in the 50% point and the change in the IID of complete inhibition with absolute intensity for each cell showed that the IID of complete inhibition was significantly less variable than the 50% point (df = 72, t = 16.25, P < 0.0001).

**IID of complete inhibition varies among the LSO population**

Although the IID of complete inhibition was constant for an individual neuron, it varied considerably from cell to cell. Figure 4, top, shows IID functions from eight representative LSO cells. Some cells were completely inhibited when the intensity at the inhibitory ear was equal to the intensity at the excitatory ear (an IID of 0 dB). Other cells were completely inhibited at negative IIDs, when the intensity at the inhibitory ear was higher than the intensity at the excitatory ear. A few cells were completely inhibited at positive IIDs, when the intensity at the excitatory ear was higher. Notice that the general shape of the functions was similar among cells: each cell showed a decline in spike count as IIDs were changed from more intense at the excitatory ear to more intense at the inhibitory ear.

The histogram in Fig. 4 shows the distribution for the IIDs of complete inhibition for the 73 cells tested. The IID of complete inhibition ranged from +10 dB (excitatory ear more intense) to −40 dB (inhibitory ear more intense). The peak of the distribution occurred at an IID of −10 dB, where the stimulus to the inhibitory ear was 10 dB more intense than the stimulus to the excitatory ear.

**Thresholds of the excitatory inputs and the inhibitory inputs to LSO cells**

The question that we address below is whether the IID of complete inhibition is determined by the difference between...
The thresholds of inputs from the excitatory and inhibitory ears. To make this determination, we first show how we estimated the thresholds of excitatory inputs and the thresholds of inhibitory inputs. We then consider the extent to which the thresholds of the inputs from the two ears differed among the population of LSO cells. In the final section we turn to the issue of whether differences in thresholds could account for the cells’ IID of complete inhibition.

The threshold of the excitatory input was obtained from the neuron’s rate-intensity function, under the assumption that spike count in the LSO cell increases directly with input strength. Thus we defined the threshold of the excitatory input as the intensity just below the intensity that first evoked responses. By this definition, the excitatory threshold of the cell in Fig. 3 was 7 dB SPL (left). The threshold of the inhibitory input to a cell was estimated from the cell’s IID functions. It is defined as the intensity just below the intensity that first inhibited the discharges evoked by stimulation of the excitatory ear. For the cell in Fig. 3, the threshold of the inhibitory input was also 7 dB SPL (right). It should be noted that the threshold of the inhibitory inputs was independent of the intensity at the excitatory ear, at least for intensities that were in the dynamic range of the neuron’s rate-intensity function. In Fig. 3, for example, the threshold of the inhibitory inputs remained constant at 7 dB SPL when the intensity at the excitatory ear was 27, 37, or 47 dB SPL (top, middle, and bottom IID functions). The thresholds of inhibitory inputs were constant and were independent of the intensity at the excitatory ear in 66 of 73 cells that we studied. The small variations in threshold measures observed for the other seven cells were not systematically correlated with changes in the intensity at the excitatory ear and may reflect minor variations from one sampling to another. For these seven cells, the median threshold measure was taken to be the cell’s inhibitory threshold.

For the 73 cells studied, the distribution of thresholds for the excitatory input was very similar to the distribution of thresholds for the inhibitory input. The histograms in Fig. 3.
with the inhibitory ear to reach complete inhibition. Following this line of reasoning, a neuron with a negative IID of complete inhibition should have an excitatory threshold that

FIG. 4. Representative IID functions and distribution of IIDs of complete inhibition for 73 LSO neurons tested. Top: IID functions from 8 cells illustrate how IID sensitivity varied among population from which we recorded. Bottom: distribution of IIDs of complete inhibition for 50 cells tested. Stimuli were 20-ms tones presented at each unit’s characteristic frequency. Intensity to ipsilateral (excitatory) ear was fixed at 20 dB above threshold while intensity to contralateral (inhibitory) ear was varied.

If the difference in thresholds from the two ears is indeed the explanation for a neuron’s particular IID sensitivity, then a wide range of threshold differences among the population would seemingly be necessary to generate the various IIDs of complete inhibition shown in Fig. 4. Each neuron’s IID of complete inhibition would result from the particular combination of thresholds for its excitatory and inhibitory inputs. For example, a neuron with a positive IID of complete inhibition should have an excitatory threshold that is proportionally higher than its inhibitory threshold. Thus this cell would require a greater intensity at the excitatory ear compared

FIG. 5. Distributions of excitatory thresholds (A), inhibitory thresholds (B), and difference between excitatory and inhibitory thresholds for each LSO cell (C).
is lower than its inhibitory threshold, whereas the two thresholds should be the same for a cell whose IID of complete inhibition is 0 dB.

To evaluate whether the difference between the excitatory and inhibitory input thresholds corresponded to each neuron's IID of complete inhibition, we first subtracted the threshold of the inhibitory input from the threshold of the excitatory input, and in the section below we compare the threshold differences with the IID of complete inhibition. A difference of 0 dB obtains when the excitatory and inhibitory thresholds were matched, as they were for the cell shown in Fig. 3. For cells with a threshold of excitation that was higher than the threshold of inhibition, the difference was positive. On the other hand, for cells with a threshold of excitation that was lower than the threshold of inhibition, the difference was negative. Consistent with the hypothesis of Reed and Blum, there was a wide distribution of excitatory and inhibitory threshold differences among the population of LSO neurons. As shown in Fig. 5C, threshold differences ranged from −20 dB (the threshold of the inhibitory input was 20 dB higher than the threshold of the excitatory input) to +30 dB (the threshold of the inhibitory input was 30 dB lower than the threshold of the excitatory input). Almost half of the cells showed no difference between the thresholds of the excitatory and inhibitory inputs. Thus the distribution peaked at 0 dB.

**Correspondence between the IID of complete inhibition and the difference in excitatory and inhibitory thresholds**

We turn next to the central question of this study: the degree to which a neuron's IID of complete inhibition is determined by the difference between the thresholds of its excitatory and inhibitory inputs. Recall that the prediction of the Reed and Blum hypothesis is that the difference between the thresholds of the inputs from the two ears should correspond to the IID of complete inhibition.

In 10 of the 73 cells (14%), the difference between the excitatory and inhibitory thresholds corresponded to the IID of complete inhibition. Two examples are shown in Figs. 3 and 6. The cell shown in Fig. 3 had an excitatory threshold of 7 dB and an inhibitory threshold of 7 dB (the difference between the thresholds was 0 dB). The IID of complete inhibition for this cell was also 0 dB: the cell was completely inhibited when the intensity at the inhibitory ear was equal to the intensity at the excitatory ear at each of the three intensities that we presented to the excitatory ear. The cell shown in Fig. 6 differs from the previous example in that the thresholds of its excitatory and inhibitory inputs were different. For this cell, the threshold of the excitatory input was 10 dB SPL and the threshold of the inhibitory input was 30 dB SPL, a difference of −20 dB. The IID functions show that its IID of complete inhibition was also −20 dB (inhibitory ear more intense) at each excitatory intensity tested (Fig. 6, top, middle, and bottom IID functions). As in the previous example, the disparity in thresholds corresponded to the IID of complete inhibition. For these cells, it would appear that IID sensitivity was determined primarily by the difference between excitatory and inhibitory thresholds.

In the majority of cells (63 of 73) the difference between the thresholds of the excitatory and inhibitory inputs did not correspond to the neuron's IID of complete inhibition. In all but two of these cells, the IID of complete inhibition occurred at a more negative IID (favoring the inhibitory ear) than would be predicted from the thresholds of their inputs. On average, the observed IID of complete inhibition was 12 dB more negative than the IID expected from the threshold difference. Three examples are shown in Figs. 7–9. For the cells shown in Figs. 7 and 8, the excitatory and inhibitory thresholds were equal, which was the case for 30 of the cells. Thus the difference between the excitatory and inhibitory thresholds was 0 dB for these cells. However, for the cell shown in Fig. 7, the IID of complete inhibition was −10 dB (inhibitory ear more intense), and it was −20 dB (inhibitory ear more intense) for the cell in Fig. 8.

The cell in Fig. 9 differed from the units in Figs. 7 and 8 in that the thresholds for the excitatory and inhibitory inputs were not the same, which was the case for 33 of the cells. The excitatory threshold of the unit in Fig. 9 was 20 dB SPL, whereas the inhibitory threshold was 0 dB SPL. Despite the 20-dB difference in thresholds, the IID of complete inhibition was 0 dB. Thus this cell, like the previous two examples, did not show an exact correspondence between the thresholds of the excitatory and inhibitory inputs and the IID of complete inhibition.

The graph in Fig. 10 shows the distribution of threshold differences and IIDs of complete inhibition for the 73 cells. Even though the majority of cells did not show an exact correspondence between threshold differences and IID of complete inhibition, with few exceptions the IID of complete inhibition was more negative than predicted from threshold differences. Consequently, the threshold differences and IIDs of complete inhibition were positively correlated for our sample of 73 cells ($r^2 = 0.449$; the correlation coefficient was 0.532 when only the 63 cells that did not show an exact correspondence were evaluated). Thus the thresholds of the inputs to LSO cells were associated with ~45% of the variance in the observed distribution of IIDs of complete inhibition.

**Relation of latencies and strengths of excitation and inhibition to IID of complete inhibition**

As discussed previously, the Reed and Blum hypothesis deals explicitly with threshold differences, but it also implicitly assumes that at the IID of complete inhibition latencies of excitation and inhibition are coincident and equally strong. Although it was not our main objective to evaluate latencies, some insights about latency correspondence can be obtained from examination of the spike trains evoked as the intensity at the inhibitory ear was increased. The spike trains of cells in which threshold differences corresponded to the IID of complete inhibition were consistent with the idea that equal inhibitory and excitatory strengths first occurred with coincident inputs. This is illustrated in Fig. 11A for the same cell shown in Fig. 3. Recall that in this cell the excitatory threshold was equal to the inhibitory threshold and the IID of complete inhibition was 0 dB. In this example the ipsilateral (excitatory) intensity was fixed at 27 dB SPL, 20 dB above threshold. When the contralateral intensity was increased from 7 to 17 dB SPL, the spike count declined from 84 to
45 spikes. An additional 10-dB increment at the inhibitory ear resulted in a complete inhibition. There are two significant features in the raster displays that pertain to the strengths and latencies of the inputs from the two ears. The first feature is that when the contralateral intensity was 17 dB SPL (IID of +10 dB), the initial spikes were unaffected (Fig. 11A, \), whereas the subsequent spikes were partially suppressed. This implies that 1) the inhibition was not as strong as the excitation, thereby allowing for a reduced number of discharges, and 2) the inhibition arrived slightly later than the excitation, thereby allowing for the unhindered expression of the first spikes. The second significant feature is that an additional contralateral intensity increment of 10 dB (IID of 0 dB) caused a complete inhibition. This suggests that at an IID of 0 dB, the inhibitory strength equaled the excitatory strength and that due to a shortening of inhibitory latency with intensity, a well-documented feature of auditory neurons (Caird and Klinke 1983; Grothe and Park 1995; Harnischfeger et al. 1985; Park et al. 1996; Pollak 1988; Yin et al. 1985), the two events became temporally coincident.

In contrast to cells in which threshold differences corresponded to their IIDs of complete inhibition, the raster displays of cells in which threshold differences did not correspond to their IIDs of complete inhibition were different. In these cells the strengths of excitation and inhibition appeared to be equated at an IID that did not produce coincidence of inputs from the two ears. An example is shown in Fig. 11B, which displays rasters from the cell in Fig. 7. In this cell the thresholds of the excitatory and inhibitory ears were the same (both were 10 dB SPL), although the IID of complete inhibition was not 0 dB but rather −10 dB (inhibitory ear more intense). Here the ipsilateral (excitatory) intensity was fixed at 40 dB SPL. When the contralateral intensity was increased from 20 to 30 dB SPL, the spike count decreased from 145 to 67. This intensity increment did not affect the initial spikes but caused a partial suppression of subsequent spikes. An additional 10-dB increment at the contralateral ear (IID of 0 dB) completely suppressed later discharges, suggesting that the strengths of inhibition and excitation were now matched, but left a substantial portion
of the initial discharges (Fig. 11B, *). The presence of the initial discharges suggests that the inhibition was not completely coincident with the excitation, although the strengths of the two inputs appeared to be equal during the latter, sustained portion of the discharge train. Increasing the contralateral intensity by another 10 dB (so the IID was –10 dB) appeared to shorten the latency of the inhibition and thereby suppress not only the later spikes but the initial discharges as well. A similar pattern of spike suppression with increasing intensity at the contralateral (inhibitory ear) is also apparent for the neuron in Fig. 1. Although it was not mentioned previously, this unit, like the unit in Fig. 11B, had an IID of complete inhibition (–10 dB) that did not correspond to the threshold difference of the two ears (10 dB SPL for the contralateral ear and 10 dB SPL for the ipsilateral ear). In short, cells in which the threshold differences corresponded exactly to the IID of complete inhibition appeared to have latencies of excitation and inhibition that were closely matched, whereas cells in which threshold differences did not correspond to their IIDs of complete inhibition appeared to have inhibitory latencies that were longer than excitatory latencies.

**DISCUSSION**

In this report we evaluate the degree to which interaural threshold differences determined the observed IIDs of complete inhibition for LSO cells. The two main findings were 1) that only a minority of the cells demonstrated a correspondence between the IID of complete inhibition and the difference in thresholds of the excitatory and inhibitory inputs and 2) that for most LSO cells, the observed IID of complete inhibition occurred at a more negative IID (requiring a greater intensity at the inhibitory ear compared with the excitatory ear) than would be expected from their threshold differences. These findings suggest that for the majority of cells modifications to the Reed and Blum threshold model are required. In the sections below, we propose models that could account both for cells whose IIDs of complete inhibition agreed with the difference between the thresholds of...
their excitatory and inhibitory inputs and for those cells in which the threshold differences did not correspond to the IID of complete inhibition. The working hypotheses on which the models are based are that intensity disparities create differences in response magnitude, latency, and the recruitment of different numbers of cochlear nucleus neurons from the two sides. The IID of complete inhibition occurs when spike trains from the two ears have equal efficacies and coincide in time at the target LSO cell.

Efficacy-intensity functions are another way of relating the thresholds of excitation and inhibition to the IID of complete inhibition

Before describing the models, we digress for a moment to introduce efficacy-intensity functions. We do this because the reasoning that led to the models can be more readily visualized from these functions than from the rate-intensity and IID functions presented in Figs. 3 and 6–9. These functions plot the thresholds as well as the “efficacy” or strength of the excitatory and inhibitory inputs as a function of intensity. In RESULTS, we defined “thresholds” as those intensities that either just evoked discharges or that just began to suppress discharges at the LSO cell. Although this is clearly not a direct measurement of the thresholds of the input fibers, we assume there is some minimal input activity level that produces a noticeable change in the discharge of the postsynaptic LSO cell. Thus we use the term “input thresholds” operationally, as an index of the lowest level of activity that influences the LSO target cell. Similar considerations apply to the way that we estimated the “strengths” of excitation and inhibition. The only requirement for equal strengths is that the conductance change caused by the inhibitory inputs be sufficiently large to prevent the excitation from reaching a threshold level. Because we could not measure conductances or changes in conductance with extracellular electrodes, we estimated the strengths of excitation from the spike counts evoked by sounds presented to the ipsilateral ear. The assumption here is that the ipsilaterally evoked spike counts of the LSO cell increase in direct proportion
to the strength or efficacy of the excitatory inputs. We then assumed that the contralateral sound intensity that completely suppressed discharges evoked by a particular ipsilateral intensity generated an inhibition whose strength was equal to the excitation.

Examples of efficacy-intensity functions from LSO cells in which the threshold difference between the excitatory and inhibitory inputs predicted the IID of complete inhibition are shown in Fig. 12, A–C. Efficacy-intensity functions of cells in which the threshold differences did not correspond to the IID of complete inhibition are shown in Fig. 12, D–F.

To illustrate how these functions were obtained, we consider the efficacy-intensity function in Fig. 12C. The efficacy curve for the excitatory input shows the threshold for evoking spikes (•) and the increases in the efficacy or strength of the excitatory input as the intensity is increased. Because we assume spike count increases directly with input strength, the excitatory efficacy curve is a stylized replot of the rate-intensity function shown in Fig. 6. The efficacy curve for the inhibitory input shows the threshold of inhibitory inputs (•), which is simply the threshold for inhibition taken from the IID curves in Fig. 6. The three points on the function show the contralateral intensities necessary to completely inhibit the spikes evoked by each of the three excitatory intensities used to generate IID functions in Fig. 6 (note that the inhibitory efficacy curve is therefore not a replot of a single IID function). As described above, the inhibitory efficacy function was derived under the assumption that when both the strength and arrival time of the inhibitory inputs match those of the excitatory inputs, the cell is completely inhibited. Thus the excitatory efficacy at a given intensity above threshold (estimated from the rate-intensity function) is shown as an open circle, and the intensity that evoked a matching efficacy from the inhibitory ear, which completely inhibited discharges, is shown as the filled circle directly across from the open circle. The double headed arrow indicates the intensity difference required to produce equal efficacies from the two inputs and corresponds to the IID of complete inhibition. These matched efficacies are then plotted for the different absolute intensities presented to the

FIG. 9. Rate-intensity and IID functions obtained from an LSO cell whose IID of complete inhibition (0 dB) did not correspond to difference in its excitatory and inhibitory thresholds (20 dB). Other details as in Fig. 6.
was 0 dB. The thresholds and latencies of input fibers are shown diagramatically with arrows. The threshold of each fiber is indicated by its position relative to the target LSO cell: fibers with low thresholds are at the top and fibers with progressively higher thresholds are below. The latency of the input is indicated by the distance of each fiber from the target LSO cell. We postulate that this LSO neuron receives excitatory and inhibitory fibers that are matched for absolute threshold, threshold range, and latency: the thresholds of the excitatory and inhibitory inputs are equal and the efficacies of the inputs are matched at equal intensities. These features generate excitatory and inhibitory input efficacies that are parallel and overlap (Fig. 13, Cell A, right). Because the thresholds and efficacies of the excitatory and inhibitory inputs are matched when the intensities at the two ears are equal and generate an IID of 0 dB, the arrival time and strength of the excitatory drive is canceled by the inhibitory drive that has the same strength as the excitation.

**Fig. 10.** Distribution of threshold differences and IDIs of complete inhibition for 73 LSO cells.

In this case, the threshold difference was −20 dB (higher threshold for the inhibitory ear) and the IID of complete inhibition was also −20 dB and was invariant with the intensities covering the linear portion of the rate-intensity function.

**Simple model can potentially account for the cells in which the difference in excitatory and inhibitory thresholds corresponded to the IID of complete inhibition.**

In this section we describe a model for cells whose threshold differences correspond to the IID of complete inhibition, and in the next section we present models for cells whose threshold differences did not correspond to the IID of complete inhibition. With regard to cells whose threshold differences predict their IID of complete inhibition, the significant feature of their efficacy-intensity functions is that the excitatory and inhibitory input efficacies are parallel. In other words, for each 10-dB increment at the excitatory ear, the increased excitatory drive was canceled by a corresponding 10-dB increment at the inhibitory ear. This is significant because it suggests that the strengths of excitation and inhibition increase with intensity on a one-to-one basis, a fundamental assumption of the threshold model.

A simple model, essentially the same as the one proposed by Reed and Blum, can potentially account for features displayed by these cells (Fig. 13). As explained below, the model assumes that the absolute thresholds of the excitatory and the inhibitory fibers are matched in some cells but are different in other cells. It also assumes that there is a close matching of latencies of the excitatory and inhibitory fibers, an assumption consistent with the latencies estimated from the raster displays in Fig. 11A.

We explain this model by considering the efficacy-intensity function of Fig. 13, Cell A, whose IID of complete inhibition was 0 dB. The thresholds and latencies of input fibers are shown diagramatically with arrows. The threshold of each fiber is indicated by its position relative to the target LSO cell: fibers with low thresholds are at the top and fibers with progressively higher thresholds are below. The latency of the input is indicated by the distance of each fiber from the target LSO cell. We postulate that this LSO neuron receives excitatory and inhibitory fibers that are matched for absolute threshold, threshold range, and latency: the thresholds of the excitatory and inhibitory inputs are equal and the efficacies of the inputs are matched at equal intensities. These features generate excitatory and inhibitory input efficacies that are parallel and overlap (Fig. 13, Cell A, right). Because the thresholds and efficacies of the excitatory and inhibitory inputs are matched when the intensities at the two ears are equal and generate an IID of 0 dB, the arrival time and strength of the excitatory drive is canceled by the inhibitory drive that has the same strength as the excitation.

**Fig. 11.** Dot raster displays taken from IID functions of 2 cells. A: rasters from cell presented in Fig. 3, a cell whose threshold difference equaled its IID of complete inhibition. Note that initial spikes (\(\ast\)) and later spikes are completely inhibited at same IID (\(\ast\)), suggesting both that inhibition was strong enough to completely inhibit excitation and that it arrived coincidentally with excitation. B: rasters from cell presented in Fig. 7, a cell whose threshold difference was 0 dB but whose IID of complete inhibition was −10 dB. Note that, at an IID of 0 dB, later spikes were completely inhibited, whereas a substantial portion of initial spikes persisted, suggesting that inhibition was strong enough to completely inhibit excitation but that it arrived slightly later, allowing earliest spikes to be expressed.
and arrives simultaneously with it. As a consequence of these events, the cell’s IID of complete inhibition is 0 dB regardless of the absolute intensity.

With a minor adjustment, this model can also account for cells whose IIDs of complete inhibition have values other than 0 dB. For these LSO cells we need only assume that the absolute thresholds of the fibers from the inhibitory ear are higher than those from the excitatory ear, although the range of thresholds of the fibers from the two ears are the same (Fig. 13, Cells B and C). The difference in absolute threshold for the excitatory and inhibitory ears corresponds to the IID of complete inhibition. For Fig. 13, Cell B, the lowest threshold of the inhibitory fibers is 10 dB higher than that of the excitatory fibers. Such an arrangement results in parallel input efficacies that do not overlap, but rather are separated by 10 dB. In this case, the arrival time and strength of the excitatory drive evoked by a particular intensity at the excitatory ear is matched when the intensity at the inhibitory ear is 10 dB higher than the intensity at the excitatory ear. In short, the excitatory strength at the LSO cell is canceled by an equally strong inhibition at an IID of −10 dB. Moreover, because each intensity increment causes the same change in excitatory and inhibitory efficacies or strengths, the 10-dB intensity disparity necessary for complete inhibition is maintained at all absolute intensities. The same arguments hold for Fig. 13, Cell C. In this cell, however, the separation between the excitatory and inhibitory efficacy curves is 20 dB and the IID of complete inhibition is −20 dB, regardless of absolute intensity. This model, then, is essentially the same as the Reed and Blum hypothesis in that it relies primarily on the difference (or absence of any difference) in thresholds of the excitatory and inhibitory inputs.

In the majority of LSO cells the difference in excitatory and inhibitory thresholds did not correspond exactly to the IID of complete inhibition and these cells had slightly different efficacy-intensity functions

We next turn to the cells whose IID of complete inhibition did not correspond to the difference in their excitatory and inhibitory thresholds. For intensities 10–20 dB above threshold and greater, the excitatory and inhibitory efficacy curves were parallel, like those of the cells described in the previous section. However, the curves partially or completely converged at their thresholds. Thus the efficacy-intensity curves at and around threshold appear to have different slopes and are not parallel. This effect is illustrated in the stylized efficacy-intensity functions presented in Fig. 12, D–F, where dashed lines are used to emphasis the apparent change in slope.

The question raised by these functions is: how do the excitatory and inhibitory efficacies, which diverge at low intensities, become parallel at higher intensities? The simplest model that could account for these efficacy-intensity functions invokes a mismatch in the latencies of the fibers from the excitatory and inhibitory ears (Fig. 14). This model, like the model in Fig. 13, assumes innervation by a small number of excitatory fibers and a small number of inhibitory fibers. For the hypothetical cells in Fig. 14, both populations of fibers have the same absolute thresholds and the same range of thresholds. The principal difference between the models in Figs. 13 and 14 is that the model in Fig. 14 incorporates differences in the latencies of the inhibitory inputs. For Fig. 14, Cells B and C, the latencies of the fibers from the excitatory ear are shorter than the latencies of the fibers from the inhibitory ear. In these examples, the thresholds for evoking excitation and inhibition are equal in these cells and the model predicts that when a particular intensity is presented to the excitatory ear, and evokes a certain excitatory drive, an equal intensity at the inhibitory ear will evoke the same strength from the inhibitory fibers. However, the inhibition will not completely cancel the excitation because the inhibition arrives slightly later than the excitation. To achieve a complete inhibition, an additional intensity increment at the inhibitory ear is required. The increased intensity increases the strength and shortens the latency of the inhibitory inputs, as seen in the raster displays in Fig. 11B. The shortened latency of inhibition brings the excitatory and in-
The efficacy-intensity functions of the neurons in Fig. 14, however, could also be explained by one or more alternative models that incorporate differences in the absolute thresholds, range of thresholds, and/or range of latencies for the fibers from the two ears. An example of an alternative model is shown in Fig. 15, *Cell B*. In this model, one or a few fibers are equally matched for the lowest absolute threshold, but the distribution of thresholds differs for the two inputs.

![Diagram](image)

**Fig. 13.** Model that can account for efficacy-intensity functions of LSO cells whose difference in excitatory and inhibitory thresholds corresponds to IID of complete inhibition. Filled arrows: excitatory fibers from ipsilateral ear. Open arrows: inhibitory fibers from contralateral ear. Threshold of each fiber is indicated by its position; fibers with low thresholds are above and fibers with progressively higher thresholds are below. *Cell A*: LSO cell that receives excitatory and inhibitory fibers that are matched for absolute threshold, threshold range, and latency. IID of complete inhibition in this cell should be 0 dB and should have efficacy-intensity function shown at right. *Cells B* and *C*: 2 LSO cells that receive similar innervation to *Cell A*, except that absolute thresholds of fibers from inhibitory ear are higher than those from excitatory ear. For these cells, difference in thresholds for excitatory and inhibitory ears corresponds to IIDs of complete inhibition. Predicted efficacy-intensity functions are shown at right. This model is essentially same as the Reed and Blum model.

Support for the idea of a latency mismatch is suggested by the latencies estimated from the raster displays in Fig. 11B. It is further supported by a recent study of the LSO in Mexican free-tailed bats in which interaural time disparities were manipulated to more directly address this issue (Park et al. 1996). In that study, the authors estimated that the latency of inhibition shortened by an average of 410 μs per 10-dB increase in intensity at the inhibitory ear along the dynamic portion of the rate-level and IID functions (the range was 100–1,500 μs per 10 dB), which is consistent with the latency effects suggested by the rasters presented here.

The efficacy-intensity functions of the neurons in Fig. 14, however, could also be explained by one or more alternative models that incorporate differences in the absolute thresholds, range of thresholds, and/or range of latencies for the fibers from the two ears. An example of an alternative model is shown in Fig. 15, *Cell B*. In this model, one or a few fibers are equally matched for the lowest absolute threshold, but the distribution of thresholds differs for the two inputs.
The distribution for the excitatory ear is continuous, whereas the thresholds of the majority of fibers from the inhibitory ear are higher than those from the excitatory ear. In this case, the thresholds for excitation and inhibition are equal. When the intensity at the excitatory ear is increased to 10–15 dB above threshold, an equivalent intensity increase at the inhibitory ear has less of an effect because it only increases discharge rate of inhibitory fibers with lowest thresholds without recruiting new fibers. A larger increase is needed at inhibitory ear to recruit new fibers and thereby increase inhibitory efficacy, which then cancels enhanced excitatory drive. Additional intensity increments at excitatory ear are then offset by equal intensity increments at inhibitory ear, because each intensity increment recruits a similar number of new fibers from each ear.

For the addition of one or a few inhibitory fibers whose thresholds are matched to the lowest threshold of the fiber(s) from the excitatory ear. However, the prediction of this model is that the thresholds of excitation and inhibition are equal, but the IID of complete inhibition has a value that is not 0 dB. We wish to point out that the models presented here are based on the data we collected and that we used relatively low to moderate overall intensities. Although we did not use extremely high intensities in our experiments, we would expect high intensities to compromise both the threshold hypothesis and the latency hypothesis, because both the rate-level-function and intensity-induced latency changes tend to saturate at high intensities.

In conclusion, the results we report here suggest that although interaural threshold disparities are the major factor in determining the IID of complete inhibition in a minority of LSO cells, in most of the LSO population interaural latency disparities also play a principal role. Our current information, however, does not allow us to conclude that IIDs of complete inhibition are due only to threshold differences in some cells and to latency differences in other cells, or whether there is a continuum along which the IID sensitivity of some LSO cells is more heavily weighted in terms of threshold disparities, whereas in others latency disparities are emphasized.

We should be able to clarify at least some of the uncertainties about the mechanisms underlying each cell’s IID of complete inhibition in future studies by evaluating, in each cell, excitatory and inhibitory thresholds and how those features relate to the way in which electronic time shifts and changes in absolute intensity affect the cell’s IID of complete inhibition.

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