Published in final edited form as:

Hear Res. 2012 June ; 288(0): 47–57. doi:10.1016/j.heares.2012.01.011.

Circuits for Processing Dynamic Interaural Intensity Disparities in the Inferior Colliculus

George D. Pollak

Section of Neurobiology, The University of Texas at Austin, Austin, TX USA 78712,
gpollak@mail.utexas.edu

Abstract

Interaural intensity disparities (IIDs), the cues all animals use to localize high frequency sounds, are initially processed in the lateral superior olive (LSO) by a subtractive process where inputs from one ear excite and inputs from the other ear inhibit LSO neurons. Such cells are called excitatory-inhibitory (EI) neurons and are prominent not only in the LSO but also in higher nuclei, which include the dorsal nucleus of the lateral lemniscus (DNLL) and inferior colliculus (IC). The IC is of particular interest since its EI cells receive diverse innervation patterns from a large number of lower nuclei, which include the DNLLs and LSOs, and thus comprise a population with diverse binaural properties. The first part of this review focuses on the circuits that create EI cells in the LSO, DNLL and IC. The second section then turns to the responses evoked by dynamic IIDs that change over time, as with multiple sounds that emanate from different regions of space or moving sound sources. I show that many EI neurons in the IC respond to dynamic IIDs in ways that are not predictable from their responses to static IIDs, IIDs presented one at a time. In the final section, results from in vivo whole cell recording in the IC are presented and address the connectional basis for the responsiveness to dynamic IIDs. The principal conclusion is that EI cells comprise a diverse population. The diversity is created by the particular set of inputs each EI type receives and is expressed in the differences in the responses to dynamic IIDs that are generated by those inputs. These results show that the construction of EI neurons in the IC imparts features that not only encode the location of an individual sound source, but also that allow animals to determine the direction of a moving sound and to focus and localize a single sound in midst of many sounds, as typically occurs in the daily lives of all animals.

Keywords

Inferior colliculus; dorsal nucleus of the lateral lemniscus; dynamic IIDs; inhibition; whole cell recordings

1.0 Introduction

The neural basis of sound localization has been one of the most, if not the most active area of research on the auditory system over the past 40 years. The reason that investigators have directed attention to localization is that it is one of the few auditory percepts for which the

© 2012 Elsevier B.V. All rights reserved.

Corresponding Author-George D. Pollak, Section of Neurobiology, 337 Patterson Laboratory Building, The University of Texas at Austin, Austin, Texas 78712, Tel: 1-512-471-4352; fax 1-512-471-9651, gpollak@mail.utexas.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

cues are well established as are the circuits that process those cues. This review deals with the circuits and mechanisms that underlie the processing of interaural intensity disparities (IIDs), the cues all animals use to localize high frequency sounds (Erulkar, 1972). The initial sections deal with the circuitry and the types of transformations in binaural properties that occur in the nuclei in the ascending binaural system, the lateral superior olive (LSO), the dorsal nucleus of the lateral lemniscus (DNLL) and the inferior colliculus (IC). The transformations were derived from extracellular recordings with single-barrel and multi-barrel electrodes that contained blockers of inhibitory receptors. Those studies showed that neurons at each level respond in a similar way to static IIDs, IIDs presented one at a time. The following sections then focus on the processing of dynamic IIDs, IIDs that change over time, as occurs, for example, with multiple sounds that emanate from different regions of space or moving sound sources. Focus is on the circuits in the DNLL and IC, and how those circuits confer new binaural properties that are expressed in selective responses to dynamic IIDs. The final section then turns to recent studies of *in vivo* whole cell recordings of IC neurons and why the information afforded by whole cell recordings revealed additional inputs to IC cells that were previously unsuspected, and why they provide additional insights into the ways that IC neurons respond differently to dynamic IIDs than they do to static IIDs.

1.1 IIDs are initially processed in the LSO and subsequently in the DNLL and IC

The intensities received at each ear are coded by auditory nerve fibers and by the bushy cells in the cochlear nucleus upon which the auditory nerve fibers synapse. The coded intensities at each ear are then processed by a subtractive mechanism in the LSO (Boudreau et al., 1968; Caird et al., 1983; Park et al., 1996; Tollin et al., 2008), where inputs from one cochlear nucleus excite their targets in the LSO while inputs from the cochlear nucleus on the other side inhibit the same LSO neurons (Fig. 1). The projections from the contralateral cochlear nucleus first synapse in the MNTB, which provides the inhibitory input to the same LSO cell that received an excitatory input from the ipsilateral cochlear nucleus (Cant et al., 1986; Moore et al., 1983). Such cells are called excitatory-inhibitory (EI) cells and virtually all LSO cells are EI.

In its simplest form, the subtractive process in the LSO is illustrated by an IID function (Fig. 1). IID functions are generated with static IIDs, where a sound is first presented to the excitatory (ipsilateral) ear and the spike count is obtained at some fixed intensity, usually at 5–20 dB above threshold. A sound is then presented simultaneously to the inhibitory (contralateral) ear, first at a low intensity and then at progressively higher intensities. Each combination of the fixed excitatory intensity and variable inhibitory intensity produces a different IID, and the spike-counts evoked by each IID are recorded. All LSO cells display progressive spike suppression with increasing intensity at the inhibitory ear, where discharges are reduced to a criterion degree, either complete or 50% spike suppression, at a particular IID.

In addition to the LSO, two other brainstem auditory nuclei have large populations of EI cells. The first is the DNLL (Brugge et al., 1970; Kelly et al., 1998; Pecka et al., 2007; Yang et al., 1994b). The DNLL is the pontine nucleus just caudal to the IC, whose high frequency cells are purely GABAergic (Adams et al., 1984; Oliver et al., 1989; Winer et al., 1995b) and have binaural properties that are predominately or even exclusively EI. The other is a subpopulation of high frequency cells in the IC, the auditory midbrain nucleus (Irvine et al., 1990; Li et al., 1992; Roth et al., 1978; Wenstrup et al., 1986). The EI cells in both the DNLL and IC receive strong excitatory projections from the LSO on the opposite side (Brunso-Bechtold et al., 1981; Casseday, 2002; Ross et al., 1989), and the EI properties in both nuclei are largely, but not entirely inherited from the LSO.

Due to the circuits that innervate the EI cells in both the DNLL and IC, the EI cells in those nuclei respond differently to dynamic IIDs than they do to static IIDs. More specifically, the IID that evokes a criterion suppression is constant with static IIDs. However, when dynamic IIDs are subsequently presented, in DNLL cells (Pecka et al., 2007; Yang et al., 1994a; Yang et al., 1994b) and in many IC cells (Burger et al., 2001; Dahmen et al., 2010; Sanes et al., 1998), there is a dramatic shift in the way the IC neuron responds to the same static IIDs that were previously presented (there is a change in the IID that evokes the criterion inhibition). Such changes in IID sensitivity following exposure to dynamic IIDs have been demonstrated using a variety of dynamically varying IID configurations, and in a variety of mammals. In two studies, temporally separated binaural signals that emanated from different regions of space were presented (Burger et al., 2001; Pecka et al., 2007), a stimulus configuration used in psychophysical studies of the precedence effect (Pecka et al., 2007; Wallach et al., 1949; Zurek, 1987). Another study presented a long (1–2 sec) binaural stimulus at a fixed IID and then changed the IID, which then evoked a response that differed from the same IID presented statically (Sanes et al., 1998). Yet another study presented noise binaurally for 1–4 sec in which the IIDs randomly fluctuated around a certain average range and then showed that the static IID to which the neuron was previously most sensitive shifted in the direction of the mean IIDs of the noise (Dahmen et al., 2010).

Importantly, the responses of both DNLL and IC cells to the dynamic stimuli used in several of the previous studies closely predict the behavioral responses of humans when presented with the same stimuli (Dahmen et al., 2010; Pecka et al., 2007). Thus, both the responses to static and dynamic stimuli observed in the DNLL and IC of animals appear to be critically important for acoustic perception. Below I turn first to the circuits that project to the DNLL and the response transformations that cause the changes in the responses to dynamic IIDs in DNLL cells, followed by a similar description of the even more complex circuitry and response transformations that occur in the IC.

1.2 Processing of dynamic IIDs in the DNLL

High frequency DNLL neurons are EI, as they receive excitatory inputs from the contralateral ear and inhibitory inputs from the ipsilateral ear. The contralaterally evoked excitation is provided by excitatory projections from the contralateral LSO (Fig. 2) (Glendenning et al., 1981; Oliver, 2000; Yang et al., 1994c; Yang et al., 1996). The ipsilaterally evoked inhibition comes from two sources; a glycinergic projection from the ipsilateral LSO and a GABAergic projection from the opposite DNLL via the commissure of Probst (Fig. 2) (Chen et al., 1999; Oliver et al., 1989; Yang et al., 1996). As shown in Fig. 2B, the ipsilaterally evoked inhibition was revealed by iontophoretically applying glutamate to the DNLL neuron thereby generating a carpet of background activity. A tone presented to the ipsilateral ear evokes a gap in the background activity (Fig. 2C) that can only be caused by inhibition at the DNLL neuron. Of particular importance is that the inhibition evoked by ipsilateral stimulation has a unique feature; the inhibition outlasts the duration of the signal that evoked it for periods of 10 to 80 ms (Fig. 2C) (Burger et al., 2001; Pecka et al., 2007; Yang et al., 1994a; Yang et al., 1994b). The inhibition that lasts for a period beyond the duration of the stimulus that evoked it is called “persistent inhibition”. As shown in Fig. 2D, blocking glycinergic inhibition with strychnine only eliminates the early inhibition, the inhibition that occurs for the duration of the tone. However, when both glycinergic and GABAergic inhibition are blocked, as in Fig. 2D, all the inhibition is eliminated, showing that the persistent inhibition is caused by the GABAergic innervation that presumably originates in the opposite DNLL.

Persistent inhibition has been obtained from the DNLLs in two species of bats and from the DNLL of gerbils, and appears to be a universal feature of the DNLL in mammals. The persistence, in essence, endows DNLL cells with a short-term memory of the inhibitory

stimulus. Thus by presenting an initial binaural signal that is more intense at the ipsilateral ear, the DNLL on that side is persistently inhibited and thereby deprives its targets, in the opposite DNLL and in the IC, of their inhibitory innervation for the duration of the persistence, a feature that I return to below.

Persistent inhibition is not evident in IID functions obtained with an individual binaural signal, a static IID, but rather its influence is evident with temporally separated multiple sound sources that emanate from different regions of space, which have IIDs that change over time and thus are dynamic (Pecka et al., 2007; Yang et al., 1994a; Yang et al., 1994b). The way persistent inhibition influences binaural processing is illustrated in Fig. 3. The stimuli in Fig. 3A were three, equally intense tones presented to the contralateral (excitatory) ear at different inter-pulse intervals. The first tone was binaural with an IID that produced a complete suppression of spikes, whereas the two following tones were monaural, and each evoked a strong discharge when presented alone. When the first binaural tone was followed 10 ms later by a second monaural tone, and 10 ms after that by the third monaural tone, not only were the spikes to the first tone completely suppressed, but the initial binaural tone also caused nearly a complete suppression of spikes to the second tone (Fig. 3A, middle panel). There was little or no suppression of responses evoked by the third tone. The suppression of responses to the second was due to the persistent inhibition generated by the strong ipsilateral stimulus of the first binaural tone, and the persistent inhibition was over when the third tone was presented, thereby allowing the third tone to evoke a strong discharge. That the suppression of responses to the second tone was due to persistent inhibition evoked by the first binaural signal was confirmed with weaker ipsilateral signals (Fig. 3B). When the ipsilateral intensity of the first binaural tone was weak, the weak ipsilateral signal did not produce a persistent inhibition and thus failed to suppress discharges to the second, monaural tone.

The point is that when the initial binaural signal had a stronger ipsilateral than contralateral intensity, the initial binaural signal generated a persistent inhibition that changed the responses to trailing sounds. Since the DNLL provides strong, bilateral inhibitory projections to the IC (Grothe et al., 1994; Li et al., 1992; Ross et al., 1989; Shneiderman et al., 1989; Shneiderman et al., 1988; Zhang et al., 1998), the changes in the responses to trailing sounds should be reflected in the responses of EI cells in the IC to the same dynamic stimuli.

1.3 The projections to the IC create a population with highly diverse response properties

The IC is the common target of the projections from the majority of lower auditory nuclei and thus is a nexus in the ascending auditory pathway (Fig. 4) (Casseday, 2002; Oliver, 1992; Pollak et al., 1986; Winer et al., 1995a). Some of the projections are from lower binaural nuclei, such as the LSOs and DNLLs, while others are from monaural nuclei, such as the cochlear nucleus, ventral nucleus of the lateral lemniscus and superior paraolivary nucleus among others. Moreover, some of the projections are excitatory, e.g., from the contralateral LSO, while an equally larger number are inhibitory (e.g., from the two DNLLs), where some of the inhibitory projections are GABAergic and others are glycinergic.

The projections to the IC are organized in two major ways. The first is tonotopic, whereby the projections representing a particular frequency in each of lower nucleus converge upon a sheet of cells in the IC that represents the same frequency (Casseday, 2002; Loftus et al., 2010; Oliver, 1992). The second is “nucleotopic”, in that many lower nuclei project to only restricted regions of each isofrequency sheet in the IC and not to other regions in the sheet (Casseday, 2002; Loftus et al., 2010; Ross et al., 1989). The projections of other nuclei are more widespread. Due to the regional or nucleotopic projections, the IC is a nucleus

composed of cells groups that differ substantially in the complement of excitatory and inhibitory inputs they receive from lower nuclei. The different innervation patterns, in turn, create a heterogeneous population in each isofrequency sheet, where the response properties of subgroups of IC cells evoked by both simple and complex acoustic stimuli differ substantially from the response properties expressed by other subgroups tuned to the same frequency (Klug et al., 2002; Pollak et al., 2003; Xie et al., 2005; Xie et al., 2007).

The heterogeneity of response properties is well illustrated by EI cells in the IC (Park et al., 1994). All EI cells display the same response property to static IIDs, in that they all display a progressive spike suppression with higher ipsilateral intensities, and thus express IID functions similar to LSO and DNLL cells. However, as discussed below, EI cells in the IC are constructed in a variety of ways and thus constitute a diverse subpopulation and almost express different response properties to dynamic stimuli.

1.4 The IC has at least four types of EI cells

Most EI cells have one of four principal connectional patterns that were deduced from previous extracellular and connectional studies. The first type is the simplest since these cells inherit their EI properties entirely from the contra LSO and receive no direct innervation from the ipsilateral ear (Fig. 5-1). In these cells, blocking inhibition with bicuculline or strychnine causes no change in the ipsilaterally evoked spike suppression, and thus no change in their IID functions (Park et al., 1994; Pollak et al., 2002). The failure to eliminate the ipsilaterally evoked spike suppression suggests that the inhibition evoked by ipsilateral stimulation occurred in a lower nucleus, presumably the LSO. The absence of ipsilaterally evoked inhibition in some IC cells was confirmed in a recent intracellular study (Li et al., 2010) where, in several IC cells, the contralaterally evoked discharges were completely suppressed by ipsilateral stimulation, yet ipsilateral stimulation alone evoked no IPSPs in the IC cell at any intensity (not shown).

In marked contrast to the EI cells that inherit their EI property from the LSO, the second type of EI property is formed *de novo* in the IC. The construction is from an excitatory, monaural projection of unknown origin driven by the contralateral ear and an inhibitory projection from the DNLL on the opposite side, a nucleus driven by the ear ipsilateral to the IC (Fig. 5-2), thereby creating the EI property in the IC. In these cells, either blocking GABAergic inhibition at the IC or reversibly inactivating the contralateral DNLL eliminates the ipsilaterally evoked inhibition and converts these EI cells into monaural cells (Burger et al., 2001; Faingold et al., 1993; Li et al., 1992). Additional support for the *de novo* formation of EI properties came from a recent study that employed intracellular recordings. In a few EI cells recorded in that study, contralateral signals evoked large EPSPs and discharges while ipsilateral signals evoked only IPSPs with amplitudes that increased with stimulus intensity (Li et al., 2010). When binaural signals were presented, the contralaterally evoked responses were progressively reduced in amplitude with increasing ipsilateral intensities. With ipsilateral intensities 20–30 dB more intense than the contralateral signal, the binaural response was nearly a flat line, showing that the ipsilaterally evoked inhibition suppressed the contralaterally evoked excitation and that the inhibition occurred in the IC cell.

The third EI type is a “hybrid”, in that these cells are innervated by both the LSO and the contralateral DNLL (Fig. 5-3). In these cells, blocking inhibition at the IC does not eliminate the EI property, but rather shifts the IID function to the right (Park et al., 1993; Park et al., 1994). Thus, the EI feature in these cells is apparently formed in the LSO, but due to the input from the DNLL, a lower intensity at the ipsilateral ear now generates the criterion degree of inhibition, i.e., either complete or 50% spike suppression. When the inhibition from the DNLL is blocked by iontophoretic application of bicuculline at the IC or by

reversibly inactivating the DNLL, a stronger ipsilateral signal is required to generate the criterion degree of spike suppression, thereby producing a rightward shift in the IID function (Burger et al., 2001; Faingold et al., 1993; Li et al., 1992).

A fourth EI type also derives its EI property from LSO projections but these cells receive inhibitory inputs from both the contralateral and ipsilateral DNLL (Fig. 5-4). The influence of the projections from the contralateral DNLL is the same as that described for the third, hybrid, type, which is a shift in the IID that produces the criterion spike suppression. The projection from the ipsilateral DNLL seems not to influence the IID function but rather shapes the rate level function, by reducing the spike-counts evoked by stimulation of the contralateral ear and transforming the rate-level function from one that was monotonic, due to LSO inputs, into one that is non-monotonic due to the inhibition evoked by the DNLL on the same side as the IC.

1.5 The projections from the DNLL to the IC confer new response properties for responding to dynamic IIDs

The feature that links three of the four types of EI neurons presented above is innervation from the DNLLs. As described above, the DNLL plays a special role in at least some forms of differential responsiveness to dynamic compared to static binaural stimuli. It is noteworthy that the only type of IC cell that has been shown to process dynamic IIDs differently than static IIDs are IC cells whose EI properties are formed *de novo* in the IC, from a monaural excitatory input driven by the ear contra to the IC and by an inhibitory projection from the DNLL contra to the IC (Burger et al., 2001). It is also noteworthy that the same study found that cells that inherit their EI property from the LSO respond the same way to dynamic and static IIDs and thus their binaural responses are not changed by dynamic IIDs.

The dynamic stimuli presented to *de novo* EI cells were two sounds that were separated in time and had different IIDs, simulating two sounds that emanate from different regions of space (Fig. 6). This stimulus configuration simulates the stimuli used in psychophysical experiments on the precedence effect. The IID of the first sound favored (was more intense in) the excitatory (contralateral) ear and thus simulated a sound in the hemifield contralateral to the IC. Since the sound was louder in the excitatory than the inhibitory ear, it not only drove the IC cell but it also produced a persistent inhibition in the DNLL on that side. The IID of the trailing sound favored the inhibitory (ipsilateral) ear and simulated a sound source that emanated from a location in the sound field ipsilateral to the IC. When the trailing sound was presented alone, it failed to evoke discharges due to activation of the DNLL that inhibited the IC cell. However, when the first sound was followed by the trailing sound, the neurons responded to both the first and trailing sounds, even though the same neuron failed to respond to the trailing sound when it was presented alone. In other words, the reception of the initial signal at the excitatory (contralateral) ear reconfigured the circuit by generating a persistent inhibition in the DNLL, which deprived the IC cell of its ipsilaterally evoked inhibition for the duration of the persistent inhibition, and thereby allowed the IC cell to respond to the trailing sound.

While the cells described above showed some of functional consequences of projections from the contralateral DNLL, there have been no studies that have directly shown the impact of projections from the ipsilateral DNLL, the DNLL on the same side as the IC. The ipsilateral DNLL also sends strong projections to the IC and the persistence of inhibition in all DNLL cells suggests that both the ipsilateral and contralateral DNLLs play important roles in generating selective responses to dynamic IIDs. Recent studies that used *in vivo* whole cell recordings of EI cells in the IC of awake bats (Li et al., 2010) suggest that projections from the ipsilateral DNLL do indeed have a profound influence on the

responsiveness of some IC neurons to dynamic IIDs, and, for reasons explained below, these cells are probably far more prevalent in the IC than was previously supposed.

1.6 Whole cell recordings in the IC show that most EI cells receive an ipsilaterally evoked subthreshold, excitatory input

As mentioned previously, a recent study used in vivo whole cell recordings in the IC and found a number of cells whose responses, in terms of both their inputs, as revealed by sound evoked post-synaptic potentials (PSPs), and their outputs, sound evoked spikes, were entirely consistent with either an inherited EI property or with EI properties formed *de novo* in the IC (Li et al., 2010). These cells, however, represented a small minority of the sample of 28 cells that were recorded. In the majority of cells, the inputs seen with whole cell recordings were more complex than those suggested by discharge patterns in extracellular recordings, and thus the circuitry of the various EI types in Fig. 5 is not incorrect, but is incomplete.

With whole cell recordings, subthreshold excitatory post-synaptic potentials (EPSPs) evoked by ipsilateral stimulation were seen in the majority of EI cells that were recorded (20/28). A representative example is shown in Fig. 7. The ipsilaterally evoked EPSPs were surprising, since the results from extracellular studies gave no hint of such a projection. The reason is that the ipsilaterally evoked EPSPs were always subthreshold. Thus, ipsilateral stimulation would not have evoked discharges even when inhibition was blocked at the IC making the EPSPs invisible with extracellular recordings.

The ipsilaterally evoked EPSPs had another surprising feature; their behavior with increasing sound intensity is paradoxical. The paradox is that EPSP amplitudes increased with intensity, even though the same ipsilateral intensities, when presented binaurally, reduced EPSP amplitudes and suppressed contralaterally evoked spikes (Fig. 7A). Indeed, the EPSPs evoked by ipsilateral signals at the same intensity that caused complete spike suppression when presented binaurally were identical (Fig. 7B&C). In other words, with IIDs that completely suppressed discharges, the cell behaved as if the contralateral signal was not even present, even though that contralateral signal, when presented alone, evoked a suprathreshold EPSP and discharges. Such response features raise two inter-related questions: First, what circuit could account for these features? Second, although the subthreshold, ipsilaterally evoked EPSPs are not a factor in the generation of static IIDs, what functional impact might they have on the responses to dynamic IIDs?

Turning first to circuitry, two projections could account for the EPSPs and their behavior to both monaural and binaural stimulation: 1) an excitatory projection from the contra LSO; and 2) an excitatory projection, of unknown origin, evoked by ipsilateral stimulation (Fig. 7D). The explanation is that with binaural signals, increasing ipsilateral intensity increases the strength of the subthreshold ipsilateral excitation while causing an even larger *decrease* in the strength of the excitatory input from the LSO (due to inhibition from the MNTB). An IID is reached at which the input from the LSO is completely suppressed while the ipsilateral excitatory input is still present and is unattenuated. At that IID, the binaural signal will evoke an ipsilateral EPSP, which is the same EPSP that is evoked only by ipsilateral stimulation at that ipsilateral intensity (Fig. 7B&C). But even though the addition of an ipsilateral excitation, as in Fig. 7D, can fully account for the EPSPs and discharges evoked by monaural and static IIDs, when the conductances that underlie each response were computed, the conductances showed that these cells received an even more complex set of projections than indicated by the EPSPs and spikes.

1.7 Conductances reveal additional inputs

A PSP is the net change in membrane potential generated by some underlying combination of sound evoked excitatory and inhibitory innervation. The conductances, on the other hand, show the relative magnitude and timing of the excitation and inhibition that evoked the PSP, and thereby reveal a more detailed view of the inputs that generated the response than suggested by the EPSP alone. The conductances were computed from current clamp records as described in previous studies (Gittelman et al.; Gittelman, 2009; Priebe et al., 2005). The conductances computed for an EI cell that expressed ipsilaterally evoked EPSPs are shown in Fig. 8. The conductances show that contralateral stimulation evoked both an excitatory and an inhibitory conductance, and that ipsilateral stimulation also evoked both an excitatory and inhibitory conductance. Most importantly, the binaural excitatory conductance and the binaural inhibitory conductance were both *smaller* than the excitatory and inhibitory conductances evoked by monaural stimulation of the contra ear (Fig. 8A). In other words, a contralateral signal evoked a large inhibitory conductance, but when an ipsilateral signal was presented together with the contralateral signal, the inhibitory conductance was substantially reduced. Exactly the same results were obtained for the excitatory conductances. It follows that both the excitatory and inhibitory inputs that generated those conductances must have originated, at least in part, from lower binaural nuclei that are themselves EI.

The excitatory binaural nucleus is most likely the LSO, as this is the principal lower binaural nucleus where EI properties are initially formed and it sends strong excitatory projections to the opposite IC. The inhibitory binaural nucleus is most likely the ipsilateral DNLL, since this is the only lower nucleus that; 1) provides inhibitory projections to the IC; 2) is binaural (EI); and 3) is driven by stimulation to the ear contralateral to it. The origins of the other ipsilateral evoked excitatory and inhibitory conductances are unknown.

1.8 Conductances suggest selective responses to dynamic binaural stimuli

The circuitry revealed by the conductances is shown in Fig. 8B. The circuit suggests that these neurons should respond differently to dynamic IIDs than would be predicted from their responses to static IIDs, and that the differential responses to dynamic IIDs should be unique to EI cells formed by that circuit. The selectivity for dynamic IIDs in these cells is a consequence of both the ipsilaterally evoked EPSPs and the putative projection from the ipsilateral DNLL. I illustrate the differential responsiveness for dynamic IIDs in Figs. 9–10 for cells of the type shown in Figs. 7–8. The prediction is that these cells should respond differentially to the direction and velocity of sounds moving across space, and those responses should be different than the responses of the same cells to static IIDs. In addition, these cells should respond differently to two, temporally separated binaural sounds presented from different regions of space than they do to the same stimuli presented alone.

The differential responses evoked by dynamic IIDs that are predicted from the circuit in Fig. 8 and are illustrated in Figs. 9 and 10. The responses predicted for dynamic IIDs were derived in two ways. The first way simply added the EPSPs that were actually evoked when tones were presented to each ear. The EPSPs were added with a temporal delay that simulated a sound moving from the ipsilateral into the contralateral sound field or from the contralateral into the ipsilateral sound field, as in Fig. 9C and D. The second way was to compute the PSP that would be evoked by a signal when the inhibitory inputs from the DNLL were persistently inhibited. The EPSP was computed from the conductance evoked by contralateral stimulation, as shown in Fig. 8. Only the excitatory conductance was used to compute the predicted response (e.g., blue trace in Fig. 9C) since the inhibitory input from the DNLL is assumed to be persistently inhibited.

Turning first to moving sounds, the circuitry in Figs. 8 should generate responses selective for both the direction of movement and for the rate of movement. The rationale, as shown in Fig. 9B, is that a sound source moving from the ipsilateral to the contralateral sound field would first evoke a subthreshold EPSP from the ipsilateral ear, which should summate with the EPSP from the LSO evoked when the sound moves into the contralateral sound field, thereby enhancing the EPSP (PSP evoked with inhibition at IC in Fig. 9C). That response, however, should be further amplified because when the sound was initially in the ipsilateral sound field, the sound should not only evoke an EPSP (from the monaural, ipsilateral excitatory input) but the sound should also persistently inhibit the ipsilateral DNLL (Fig. 9C). Thus, when the sound moves into the contralateral field, it should evoke a large excitation from the LSO, but that excitation is not attenuated by inhibition from the DNLL because of the persistent inhibition at the DNLL. The unbuffered excitation from the LSO then summates with the subthreshold excitation evoked previously by the ipsilateral ear (Fig. 9Aa' and blue line in 9C), generating a very strong excitation. As mentioned previously, the amplitude and time course of the EPSP that should be evoked only by the excitation was calculated from the contralaterally evoked excitatory conductance, and is shown as the blue trace in Fig. 9C.

If the movement of the sound is slowed, such that the period of persistent inhibition in the DNLL is over when the sound enters the contralateral sound field, the amplification due to the absence of inhibition from the DNLL is lost (Fig. 9Ab'). Additionally, the ipsilateral evoked EPSP will have decayed, and now when the sound moves into the contralateral field, the sound should evoke the same response as it did when presented monaurally to the contralateral ear (Fig. 9Ab').

Conversely, sounds moving from the contra into the ipsilateral sound field should evoke different responses, as shown in Fig. 9Aa,b & 9D. Now the initial contralateral sound should evoke a large excitation (and spikes) and when the sound enters the ipsilateral field, it should evoke a subthreshold EPSP that summates with the contralaterally evoked response to generate a larger response than was evoked by the monaural contra signal alone, but not as large as the response evoked by movement from the ipsi- to the contralateral sound field because the DNLL was inhibited by that movement. With slower movements, the contra-evoked excitation would be over and thus there should be no summation of excitatory responses (Fig. 9Ab, b'). In this case, the moving sound should simply evoke the same responses as the responses evoked by each monaural signal. Thus the prediction for a cell with this circuitry is that this type of EI cell should respond selectively to the direction of the movement and the speed of movement of a sound source across space.

1.9 EI cells with ipsilaterally evoked EPSPs should also respond differently to multiple sounds

The same logic applied to moving sound sources also applies to two sequential sounds that emanate from different locations in space. As one example, consider a situation in which the first sound occurs in the contralateral (excitatory) sound field with a trailing sound in the ipsilateral (inhibitory) sound field (Fig. 10A). Under these conditions, the responses to the first sound should evoke a subthreshold EPSP but if the second (trailing) sound follows before the EPSP has decayed, the EPSP evoked by the trailing sound should sum with the EPSP generated by the first sound, thereby driving the EPSP evoked by the second sound to a suprathreshold level. Thus, the cell should fire to the second sound, even though the response to second sound is subthreshold if presented alone. Notice that this is the same stimulus configuration that was presented in Fig. 6 to a cell whose EI properties were created *de novo* in the IC. Although the cell in Fig. 10 is innervated by the ipsilateral DNLL, and not the contralateral DNLL, the net effects on the trailing sounds are similar for both types of cells, but for different reasons. Both fire to the trail sounds but only if there is an

initial sound in the contralateral sound field. The reason that the cell in Fig. 6 fires to the trailing sound is because the initial sound persistently inhibits the contralateral DNLL and thereby eliminates the inhibition that would normally be evoked by the trailing sound. For cells with an ipsilaterally evoked EPSP (the cell in Fig. 10) the firing evoked by the trailing sound is due to the summation of the excitation evoked by the first sound and the EPSP evoked by the trailing sound, which would have been subthreshold if the trailing sound were presented alone. It also follows that if the trailing sound occurred at a later time, after the initial EPSP had decayed, the trailing sound would only evoke the same subthreshold response that it did when presented alone (Fig. 10).

Next consider the more interesting condition, where the first sound is presented in the ipsilateral (inhibitory) hemifield followed by a sound in the contralateral (excitatory) hemifield (Fig. 10B). In this case, the ipsilateral DNLL plays the major role. The first sound in the ipsilateral field evokes a subthreshold EPSP, as it does when presented alone. However, it also generates a persistent inhibition in the ipsilateral DNLL. If the trailing sound in the contralateral hemifield follows shortly thereafter, before the persistent inhibition has decayed, the EPSP evoked by the LSO projection is not reduced by inhibition from the DNLL, and would be larger than the EPSP evoked if the contralateral signal were presented alone. The net result is that the trailing signal should summate with the tail end of the EPSP evoked by the first signal, but the summated response is much larger than would be evoked if the DNLL were not persistently inhibited. This is the same argument advanced above for a sound source moving from the ipsi- into the contralateral sound field, but in this case it is for two discrete sounds rather than one continuous sound. If the trailing signal is presented after the persistence in the DNLL has decayed, the trailing signal should evoke the same response that it would evoke if presented alone.

2.0 Concluding Comments and Discussion

The IID functions first expressed by LSO neurons are also expressed in a similar form in each higher order binaural nucleus, such as the DNLL and IC, and the response features of IID functions should be more or less sufficient to encode the location of a sound source, as has been proposed by several investigators (Pollak et al., 2003; Tollin et al., 2008; Wenstrup et al., 1988). If the basic IID functions are already fully expressed in the LSO and if they are sufficient to code for the location of a sound source, then what advantages accrue to the additional projections that innervate EI neurons in nuclei above the LSO? The principal theme advanced here is that the richness of the circuits that innervate each nucleus in the ascending auditory pathway adds correspondingly to the variability and plasticity of the responses of their neuronal population to binaural stimuli more complex than static IIDs. This variability culminates in the IC, as the IC receives the convergent projections from the majority of lower auditory nuclei.

One important feature that distinguishes lower nuclei from the IC is that the inputs that innervate the neurons in each lower nucleus are more or less stereotyped, whereas the inputs that innervate IC cells differ markedly among the IC population. All LSO cells, for example, receive excitation from the ipsilateral cochlear nucleus and inhibition from the contralateral cochlear nucleus via the MNTB. Similarly, most if not all high frequency DNLL cells receive excitatory innervation from the opposite LSO and inhibition from the ipsilateral LSO and the opposite DNLL. The difference in innervation between the LSO and DNLL endows DNLL neurons with more variability in their responses to multiple sounds than occurs in the LSO, as illustrated in Fig. 3. The point, however, is that all DNLL neurons respond in a similar manner to multiple sounds because they all receive the same complement of excitatory and inhibitory inputs. In contrast, the population of EI cells in the

IC receives vastly different patterns of innervation. Each projection pattern, in turn, must confer new and unique response features to each of the EI types in the IC.

The focus in this review was on the influences of the DNLLs, and how their properties could be translated into reconfiguring the responses of their targets in the IC for dynamic IIDs, such as trailing sounds or for sound sources that move across space. It should be noted, however, that the projections from lower centers could have other influences as well. For example, Tsai et al., (2010) suggest that mirror image inputs from inhibitory binaural nuclei, such as the ipsilateral LSO or contralateral DNLL, could act to subtract the excitation from contralateral LSO and thereby stabilize the discharge rates of IC cells to binaural signals at different intensities. The subtraction would endow IC cells the ability to effectively encode small changes in IIDs, regardless of absolute intensity.

While the DNLL inputs undoubtedly play a major role in creating the response transformations in IC neurons, there are a myriad of other inputs that play upon IC neurons about which little is known. What all of this suggests is that IC neurons are even more diverse and express even more varied response properties to dynamic and other complex stimuli than we currently know or even suspect.

Acknowledgments

supported by NIH grant DC007856

Abbreviations

EPSP	excitatory postsynaptic potential
DNLL	dorsal nucleus of the lateral lemniscus
EI	neurons that are excited by stimulation of one ear and inhibited by stimulation of the other ear.
FM	frequency modulation
IC	inferior colliculus
IID	interaural intensity disparity
IPSP	inhibitory postsynaptic potential
LSO	lateral superior olivary nucleus
PSP	postsynaptic potential

References Cited

- Adams JC, Mugnaini E. Dorsal nucleus of the lateral lemniscus: A nucleus of GABAergic projection neurons. *Brain Research Bulletin*. 1984; 14:585–590. [PubMed: 6098348]
- Boudreau JC, Tsuchitani C. Binaural interaction in the cat superior olive S segment. *J Neurophysiol*. 1968; 31:442–454. [PubMed: 5687764]
- Brugge JF, Anderson DJ, Aitkin LM. Responses of neurons in the dorsal nucleus of the lateral lemniscus of cat to binaural tonal stimulation. *J Neurophysiol*. 1970; 33:441–458. [PubMed: 4314734]
- Brunso-Bechtold JK, Thompson GC, Masterton RB. HRP study of the organization of auditory afferents ascending to central nucleus of inferior colliculus in cat. *J Comp Neurol*. 1981; 197:705–722. [PubMed: 7229134]

- Burger RM, Pollak GD. Reversible inactivation of the dorsal nucleus of the lateral lemniscus reveals its role in the processing of multiple sound sources in the inferior colliculus of bats. *J Neurosci.* 2001; 21:4830–4843. [PubMed: 11425910]
- Caird D, Klinke R. Processing of binaural stimuli by cat superior olivary S-segment. *Exp Brain Res.* 1983; 52:385–399. [PubMed: 6653700]
- Cant NB, Casseday JH. Projections from the anteroventral cochlear nucleus to the lateral and medial superior olivary nuclei. *J Comp Neurol.* 1986; 247:457–476. [PubMed: 3722446]
- Casseday, JH.; Fremouw, T.; Covey, E. The inferior colliculus: A hub for the central auditory system. In: Oertel, D.; Popper, AN.; Fay, RR., editors. *Integrative Functions in the Mammalian Auditory Pathway.* Vol. Vol 15. New York: Springer-Verlag; 2002. p. 238-318.
- Chen L, Kelly JB, Wu SH. The commissure of probst as a source of GABAergic inhibition. *Hear Res.* 1999; 138:106–114. [PubMed: 10575119]
- Dahmen JC, Keating P, Nodal FR, Schulz AL, King AJ. Adaptation to stimulus statistics in the perception and neural representation of auditory space. *Neuron.* 2010; 66:937–948. [PubMed: 20620878]
- Erulkar SD. Comparative aspects of spatial localization of sounds. *Physiological Reveiws.* 1972; 52:237–360.
- Faingold CL, Anderson CA, Randall ME. Stimulation or blockade of the dorsal nucleus of the lateral lemniscus alters binaural and tonic inhibition in contralateral inferior colliculus neurons. *Hear Res.* 1993; 69:98–106. [PubMed: 8226354]
- Gittelman JX, Pollak GD. It's about time: how input timing is used and not used to create emergent properties in the auditory system. *J Neurosci.* 31:2576–2583. [PubMed: 21325525]
- Gittelman JX, Li N, Pollak GD. Mechanisms underlying directional selectivity for frequency modulated sweeps in the inferior colliculus revealed by in vivo whole-cell recordings. *J Neurosci.* 2009; 29:13030–13041. [PubMed: 19828816]
- Glendenning KK, Brunso-Bechtold JK, Thompson GC, Masterton RB. Ascending auditory afferents to the nuclei of the lateral lemniscus. *J Comp Neurol.* 1981; 197:673–703. [PubMed: 7229133]
- Grothe B, Schweizer H, Pollak GD, Schuller G, Rosemann C. Anatomy and projection patterns of the superior olivary complex in the Mexican free-tailed bat, *Tadarida brasiliensis mexicana*. *J Comp Neurol.* 1994; 343:630–646. [PubMed: 8034792]
- Irvine DR, Gago G. Binaural interaction in high frequency neurons in the inferior colliculus of he cat: effects of variation in sound pressure level on sensitivity to interaural intensity disparities. *Journal of Neurophysiology.* 1990; 63:570–591. [PubMed: 2329362]
- Kelly JB, Buckthought AD, Kidd SA. Monaural and binaural response properties of single neurons in the rat's dorsal nucleus of the lateral lemniscus. *Hear Res.* 1998; 122:25–40. [PubMed: 9714572]
- Klug A, Bauer EE, Hanson JT, Hurley L, Meitzen J, Pollak GD. Response selectivity for species-specific calls in the inferior colliculus of Mexican free-tailed bats is generated by inhibition. *J Neurophysiol.* 2002; 88:1941–1954. [PubMed: 12364520]
- Li L, Kelly JB. Inhibitory influence of the dorsal nucleus of the lateral lemniscus on binaural responses in the rat's inferior colliculus. *J Neurosci.* 1992; 12:4530–4539. [PubMed: 1432109]
- Li N, Gittelman JX, Pollak GD. Intracellular recordings reveal novel features of neurons that code interaural intensity disparities in the inferior colliculus. *J Neurosci.* 2010; 30:14573–14584. [PubMed: 20980615]
- Loftus WC, Bishop DC, Oliver DL. Differential patterns of inputs create functional zones in central nucleus of inferior colliculus. *J Neurosci.* 2010; 30:13396–13408. [PubMed: 20926666]
- Moore MJ, Caspary DM. Strychnine blocks binaural inhibition in lateral superior olivary neurons. *J Neurosci.* 1983; 3:237–242. [PubMed: 6822858]
- Oliver DL. Ascending efferent projections of the superior olivary complex. *Microsc Res Tech.* 2000; 51:355–363. [PubMed: 11071719]
- Oliver DL, Shneiderman A. An EM study of the dorsal nucleus of the lateral lemniscus: inhibitory, commissural, synaptic connections between ascending auditory pathways. *J Neurosci.* 1989; 9:967–982. [PubMed: 2926487]

- Oliver, DL.; Huerta, MF. Inferior and Superior Colliculi. In: Webster, DB.; Popper, AN.; Fay, RR., editors. *The Mammalian Auditory System: Neuroanatomy*. New York: Springer-Verlag; 1992. p. 168-221.
- Park TJ, Pollak GD. GABA shapes sensitivity to interaural intensity disparities in the mustache bat's inferior colliculus: implications for encoding sound location. *J Neurosci*. 1993; 13:2050–2067. [PubMed: 8478690]
- Park TJ, Pollak GD. Azimuthal receptive fields are shaped by GABAergic inhibition in the inferior colliculus of the mustache bat. *J Neurophysiol*. 1994; 72:1080–1102. [PubMed: 7807197]
- Park TJ, Monsivais P, Pollak GD. Processing of interaural intensity differences in the LSO: role of interaural threshold differences. *J Neurophysiol*. 1997; 77:2863–2878. [PubMed: 9212244]
- Park TJ, Grothe B, Pollak GD, Schuller G, Koch U. Neural delays shape selectivity to interaural intensity differences in the lateral superior olive. *J Neurosci*. 1996; 16:6554–6566. [PubMed: 8815932]
- Pecka M, Zahn TP, Saunier-Rebori B, Siveke I, Felmy F, Wiegube L, Klug A, Pollak GD, Grothe B. Inhibiting the inhibition: a neuronal network for sound localization in reverberant environments. *J Neurosci*. 2007; 27:1782–1790. [PubMed: 17301185]
- Pollak, GD.; Casseday, JH. *The neural basis of echolocation in bats*. New York: Springer-Verlag; 1986.
- Pollak GD, Burger RM, Klug A. Dissecting the circuitry of the auditory system. *Trends Neurosci*. 2003; 26:33–39. [PubMed: 12495861]
- Pollak GD, Burger RM, Park TJ, Klug A, Bauer EE. Roles of inhibition for transforming binaural properties in the brainstem auditory system. *Hear Res*. 2002; 168:60–78. [PubMed: 12117510]
- Priebe NJ, Ferster D. Direction selectivity of excitation and inhibition in simple cells of the cat primary visual cortex. *Neuron*. 2005; 45:133–145. [PubMed: 15629708]
- Ross LS, Pollak GD. Differential ascending projections to aural regions in the 60 kHz contour of the mustache bat's inferior colliculus. *J Neurosci*. 1989; 9:2819–2834. [PubMed: 2549219]
- Roth GL, Aitkin LM, Andersen RA, Merzenich MM. Some features of the spatial organization of the central nucleus of the inferior colliculus of the cat. *J Comp Neurol*. 1978; 182:661–680. [PubMed: 721973]
- Sanes DH, Malone BJ, Semple MN. Role of synaptic inhibition in processing of dynamic binaural level stimuli. *J Neurosci*. 1998; 18:794–803. [PubMed: 9425020]
- Shneiderman A, Oliver DL. EM autoradiographic study of the projections from the dorsal nucleus of the lateral lemniscus: a possible source of inhibitory inputs to the inferior colliculus. *J Comp Neurol*. 1989; 286:28–47. [PubMed: 2768557]
- Shneiderman A, Oliver DL, Henkel CK. Connections of the dorsal nucleus of the lateral lemniscus: an inhibitory parallel pathway in the ascending auditory system? *J Comp Neurol*. 1988; 276:188–208. [PubMed: 3220980]
- Tollin DJ, Koka K, Tsai JJ. Interaural level difference discrimination thresholds for single neurons in the lateral superior olive. *J Neurosci*. 2008; 28:4848–4860. [PubMed: 18463238]
- Wallach H, Newman EB, Rosenzweig MR. The precedence effect in sound localization. *American Journal of Psychology*. 1949; 52:315–336. [PubMed: 18134356]
- Wenstrup JJ, Ross LS, Pollak GD. Binaural response organization within a frequency-band representation of the inferior colliculus: implications for sound localization. *J Neurosci*. 1986; 6:962–973. [PubMed: 3701417]
- Wenstrup JJ, Fuzessery ZM, Pollak GD. Binaural neurons in the mustache bat's inferior colliculus. II. Determinants of spatial responses among 60-kHz EI units. *J Neurophysiol*. 1988; 60:1384–1404. [PubMed: 3193163]
- Winer JA, Larue DT, Pollak GD. GABA and glycine in the central auditory system of the mustache bat: structural substrates for inhibitory neuronal organization. *J Comp Neurol*. 1995a; 355:317–353. [PubMed: 7636017]
- Winer JA, Larue DT, Pollak GD. GABA and glycine in the central auditory system of the mustache bat: structural substrates for inhibitory neuronal organization. *J Comp Neurol*. 1995b; 355:317–353. [PubMed: 7636017]

- Xie R, Meitzen J, Pollak GD. Differing roles of inhibition in hierarchical processing of species-specific calls in auditory brainstem nuclei. *J Neurophysiol.* 2005; 94:4019–4037. [PubMed: 16135548]
- Xie R, Gittelman JX, Pollak GD. Rethinking tuning: in vivo whole-cell recordings of the inferior colliculus in awake bats. *J Neurosci.* 2007; 27:9469–9481. [PubMed: 17728460]
- Yang L, Pollak GD. Binaural inhibition in the dorsal nucleus of the lateral lemniscus of the mustache bat affects responses for multiple signals. *Auditory Neuroscience.* 1994a; 1:1–17.
- Yang L, Pollak GD. The roles of GABAergic and glycinergic inhibition on binaural processing in the dorsal nucleus of the lateral lemniscus of the mustache bat. *J Neurophysiol.* 1994b; 71:1999–2013. [PubMed: 7931498]
- Yang L, Pollak GD. GABA and glycine have different effects on monaural response properties in the dorsal nucleus of the lateral lemniscus of the mustache bat. *J Neurophysiol.* 1994c; 71:2014–2024. [PubMed: 7931499]
- Yang L, Liu Q, Pollak GD. Afferent connections to the dorsal nucleus of the lateral lemniscus of the mustache bat: evidence for two functional subdivisions. *J Comp Neurol.* 1996; 373:575–592. [PubMed: 8889945]
- Zhang DX, Li L, Kelly JB, Wu SH. GABAergic projections from the lateral lemniscus to the inferior colliculus of the rat. *Hear Res.* 1998; 117:1–12. [PubMed: 9557973]
- Zurek, PM. The precedence effect. In: Yost, WA.; Gourevitch, G., editors. *Directional Hearing.* New York: Springer Verlag; 1987. p. 85-105.

Highlights

- The IC has a diverse population due to its innervation from most lower nuclei.
- The circuits to the inferior colliculus confer selective responses to dynamic IIDs.
- Responding to dynamic IIDs in the IC are determined by inputs from the DNLL.

Fig. 1. IID function of an LSO cell. Discharges evoked by 20 ms tones are shown in the upper right panel. Each successive panel shows the discharge suppression due to increasing intensities at the contralateral (inhibitory) ear. The IID functions plot the spike counts as a function of the IID of the binaural stimulus. Adapted from Park et al., 1997.

Fig. 2.

Projections to the DNLL and their influences. A: A Monaural tone at the contralateral ear evokes a sustained discharge that lasts for the duration of the tone burst. The circuit activated is shown at top left. B: Background discharges evoked by the iontophoretic application of a glutamate/aspartate cocktail. C: A monaural tone at the ipsilateral ear evokes an inhibition that outlasts the duration of the tone that evoked it by 60 ms. The inhibition is expressed by the gap in the background activity. D: Iontophoretic application of the glycine receptor antagonist, strychnine, blocks the inhibition for the duration of the tone burst but does not block the persistent inhibition. E: Iontophoretic application of the GABA receptor antagonist, bicuculline, together with strychnine, eliminates all of the sound evoked inhibition.

Fig. 3.

Suppression of responses to trailing sounds in a DNLL neuron. Three tones were presented in succession. The first tone was always binaural while the trailing tones were monaural and were presented only to the contralateral (excitatory) ear. **A:** The IID of the first binaural sound was held constant at -30 dB (inhibitory ear more intense) while the second and third sounds were monaural and suprathreshold. In the top panel the inter-pulse interval (IPI) was only 2 ms. The persistent inhibition generated by the first binaural tone completely inhibited the responses to the second, trailing sound and partially suppressed responses to the third, trailing sound. As the IPI was lengthened to 10 ms, the second, trailing sound was still very strongly suppressed but the persistent inhibition was largely over when the third sound was presented, allowing the neuron to respond to every presentation of the third sound. The responses to the second sounds were still slightly suppressed even when the IPI was lengthened to 20 ms, although the responses to the third sounds were unaffected. **B:** Increasing the intensity at the inhibitory ear caused a progressive inhibition of responses to the second trailing sound when the IPI was held constant at 10 ms. Adapted from Pecka et al., 2009.

Fig. 4.

Some of the major projections to inferior colliculus (IC). Excitatory projections are shown as black lines, GABAergic projections are shown as red lines and glycinergic projections as orange lines. Solid lines are projections from binaural nuclei while dashed lines are from monaural nuclei. DNLL, INLL and VNLL are the dorsal, intermediate and ventral nuclei of the lateral lemniscus, LSO is lateral superior olivary nucleus, MNTB is medial nucleus of the trapezoid body, SPN is superior paraolivary nucleus. Not all projections are shown.

Fig. 5.

Four ways that EI properties have been proposed to be formed in the IC based on extracellular studies. See section 1.4 in the text for further explanation

Fig. 6.

Schematic illustration of why responses to trailing sounds are changed by reception of an initial sound in IC cells in which the EI property is created de novo by an excitatory projection from a lower monaural nucleus and an inhibitory projection from the contralateral DNLL. A: The cell fails to fire to a binaural signal in the ipsilateral sound field because the intensity at the inhibitory (left) ear is greater than the sound intensity at the excitatory (right) ear. The response failure at the IC is due to the strong inhibition from the contralateral DNLL. B: The same binaural signal as in panel A is preceded by an initial signal in the contralateral (left) sound field. The initial signal not only drives the IC cell, but also generates a persistent inhibition in the DNLL (indicated by change in shading from dark grey in A to light grey in B). When the second, or trailing signal, is presented, the trailing signal now evokes discharges because the IC cell is deprived of its inhibitory innervation from the DNLL due to the persistent inhibition evoked by the first signal. Hence the IC cell now fires to both the first and trailing signals, although it would not fire to the trailing signal when that signal was presented alone (as in A).

Fig. 7.

A: Monaural and binaural responses recorded with a patch electrode from an IC that had subthreshold EPSPs evoked by ipsilateral tones. Spike counts are shown to the right of each contra and binaural recording. **B:** Graph showing that amplitudes of binaural EPSPs decreased with ipsi intensity while amplitudes of EPSPs evoked by monaural ipsi signals increased. **C:** Ipsi EPSP at 50 dB and binaural EPSP when ipsi intensity was 50 dB were virtually the same. **D:** circuit proposed to account for responses. Data adapted from Li, et al., 2010.

A

Excitatory Conductances

Inhibitory Conductances

B

Circuit from spiking + PSP + conductances

C

Predicted PSPs computed with both excitatory and inhibitory conductances

Fig. 8.

A: Excitatory and inhibitory conductances computed for both monaural and binaural stimulation in a cell with ipsilaterally evoked EPSPs. All stimuli were best frequency tone bursts. The binaural tones were presented as static IIDs. B: The proposed circuit that underlies the conductances. C: The responses predicted from conductances are shown as dashed lines and the responses evoked by monaural and binaural tones are shown as solid lines. The predicted and sound evoked responses are in close agreement. Unpublished data.

Fig. 9.

Predicted responses from an EI cell with ipsilaterally evoked EPSPs whose conductances are shown in Fig. 8. A: Predicted responses to sounds moving fast and slow in the counter- or clock-wise directions. B: Predicted responses evoked by monaural sounds together with the circuits activated. C: Predicted responses evoked by sound moving in clockwise direction and the circuits activated. Note that when sound is initially in the ipsilateral sound field, the sound evokes a persistent inhibition in the ipsilateral DNLL. The ipsilaterally evoked EPSP sums with the contralaterally evoked EPSP computed from only the excitatory conductance (blue line). D: Responses evoked by a sound moving counter-clockwise.

Fig. 10.

Responses predicted for an EI neuron with ipsilaterally evoked EPSPs to multiple sounds. A: Responses predicted for an initial sound in the contralateral sound field followed by second sound in the ipsilateral sound field. If the second sound follows at short temporal interval that would allow the EPSP evoked by the first sound to summate with the EPSP evoked by the second sound, the EPSP evoked by the second sound would be boosted to a suprathreshold level. With longer intervals, the excitation evoked by the first sound would have decayed, causing the second sound to only evoke only a subthreshold EPSP, as it would if the second sound were presented alone. B: In this case the first sound is presented in the ipsilateral sound field and only evokes a subthreshold EPSP. However, since it is more intense at the ipsilateral than the contralateral ear, it also persistently inhibits the DNLL. A second sound in the contralateral sound field that follows shortly thereafter, will not only partially summate with the depolarization evoked by the first sound, but the second sound will evoke a larger than expected response because the second sound evokes only excitation. The inhibition normally evoked in the ipsilateral DNLL by the second sound is eliminated due to the persistent inhibition evoked by the first sound.