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**TUTORIAL**

# Neural mechanisms of binaural hearing

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**Abstract:** Humans, and other mammals, make use of three cues to localise sound sources. Two of these are binaural, involving a comparison of the level and/or timing of the sound at each ear. For high frequencies, level differences result from shadowing by the head. For low-frequencies, localisation relies on the time differences between the signals at the ears that result from different sound paths to the ears. The third cue depends on sensitivity to the elevation-dependent pattern of spectral peaks and troughs that result from multiple sound waves interfering at the tympanic membrane. Different physiological mechanisms process these different localisation cues. Neurons in the dorsal cochlear nucleus are selectively sensitive to the spectral notches that result from interference between sound waves at the ear. Interaural level differences are initially processed in the lateral superior olive by neurons receiving inhibition from one ear and excitation from the other. Interaural time differences are converted into discharge rate by neurons in the medial superior olive with excitatory inputs from both ears and that only fire when their inputs are coincident. The contribution of such coincidence detectors to sound-source localisation is discussed in the light of recent observations.

**Keywords:** Binaural hearing, Interaural differences

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## 1. CUES FOR LOCALISATION

The cues used to localise a sound source derive from having two ears separated by an acoustically opaque medium. Sounds arriving at the ears can be characterised by an interaural time delay (ITD) caused by a longer sound path to one ear and, depending on the frequency, an interaural level difference (ILD) resulting from the shadowing effect of the head. Head shadowing effects are minimal for low-frequencies for which the wavelength is longer than the head width, whilst for high-frequencies with wavelength shorter than half the width of the head, interaural phase differences (IPDs) that result from the ITD present an ambiguous cue. For high-frequency or complex sounds, the time delay generates a difference in the time of arrival of the first wave-front and an on-going delay of the envelope. In addition to these cues, interaction of sound waves with the outer ear results in frequency-dependent spectral colouring of broadband sounds.

Psychophysically it has been shown that low-frequency sounds can be localised using IPDs alone, and high-frequency sounds by their ILDs e.g. [1,2]. For complex sounds the envelope delay may also be used [3]. Spectral cues permit accurate monaural sound localisation of complex sounds and provide cues for sound elevation e.g. [4,5].

Evidence in both mammals and birds suggests that ITD, ILD and pinna cues are processed in anatomically-distinct auditory pathways see [6–8]. These pathways begin with the projection of discrete neural populations in the ventral cochlear nucleus (VCN) to the sub-nuclei of the superior olivary complex (SOC), the primary site of binaural integration. Above the SOC responses to binaural stimulation largely reflect this first processing step, but with additional elaboration and convergence. Detailed reviews of the neural coding of interaural cues for localisation are available [6,7,9,10].

## 2. PINNA SPECTRAL EFFECTS

Young and his colleagues have investigated the neural representation of spectral filtering in the cat which has substantial pinna-generated spectral notches. They hypothesised a role for several of the principal neuron types of the dorsal cochlear nucleus (DCN) in detecting spectral notches. Type IV cells are extremely sensitive to changes in the frequency of high-frequency, pinna-generated, spectral notches [11], and are profoundly inhibited by spectrally-complex sounds with notches at their best

frequency because of a combination of inhibition and excitation from Type II neurons and the auditory-nerve respectively. Such sensitivity could provide a neural substrate for the ability to localise in elevation. Additionally, somatosensory input to the DCN potentially provides feedback concerning pinna position for integration with localisation cues within the DCN [12]. DCN principal cells project directly to the contralateral inferior colliculus (IC, [13]), the principal target nucleus of the brainstem binaural neurons. However, it remains unknown how pinna-based cues for localisation are incorporated there with other binaural cues. Deficits in localising elevated sound sources after section of the DCN output pathway provide support for a role for the DCN in sound-source localisation [14,15].

## 3. INTERAURAL LEVEL DIFFERENCES

The initial processing of ILDs occurs in the lateral superior olive (LSO) where high-frequency neurons are relatively over-represented. The small spherical bushy cells of the ipsilateral VCN form excitatory synapses on LSO principal neurons [16–18]. Additionally, LSO neurons receive inhibitory inputs from neurons in the ipsilateral medial nucleus of the trapezoid body (MNTB) which in turn receive excitatory input from the globular bushy cells of the contralateral cochlear nucleus [17–20]. The pathway from VCN to MNTB is characterised by synapses producing secure, short-latency responses and, therefore, near coincident arrival at the LSO of the ipsilateral excitation and the contralateral inhibition. Neurons in the LSO are sensitive to the balance of intensity at the ears because the excitation due to ipsilateral sounds is reduced by increasing levels of contralateral sounds [21–24]. The discharge rate varies sigmoidally as a function of ILD, varying from the response to the ipsilateral sound alone to complete inhibition by the contralateral sound as in Fig. 1.

The high-frequency limb of the LSO projects *contralaterally* to the IC [25] such that sensitivity to ILDs of neurons from the IC onwards is the mirror image of that in LSO [26–29]. The slope of the ILD function and the ILD at which the inhibition takes effect varies across the different cells in the IC even for stimulation with best frequency tones (Fig. 1B). Similar sensitivities to ILDs are found in the primary auditory cortex (review [10]).

Investigations at the level of the LSO, IC and auditory cortex, demonstrate that high-frequency cells sensitive to ILDs are also sensitive to onset time differences and to the delays of the envelope of complex sounds [23,30–35] presumably mediating our abilities to localise high-frequency sounds on the basis of the time delay of their envelopes.

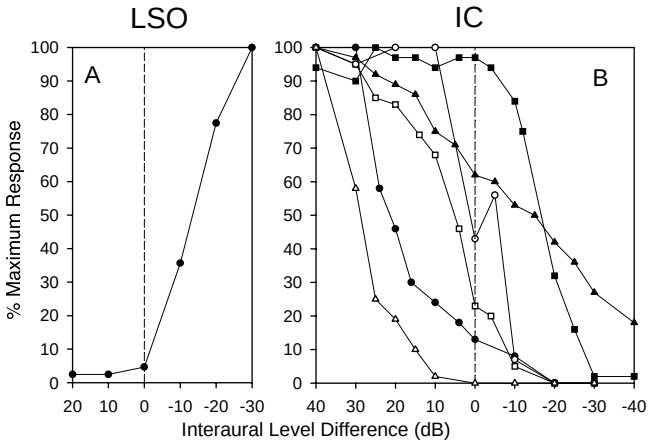


**Fig. 1** Discharge rates as a function of the ILD for A. a single LSO neuron [24] and B. 6 IC neurons [6].

## 4. INTERAURAL TIME DIFFERENCES

For many terrestrial mammals (particularly humans), localisation of sound sources in the horizontal plane is achieved by an exquisite sensitivity to differences in the fine-time structure of low-frequency ($<1,500$ Hz) components between the two ears [36]. Consistent with this, neurons sensitive to ITDs of low-frequency signals have been recorded from auditory nuclei in a wide range of species [37–40].

However, the exact means by which ITD-sensitive neurons contribute to localising a sound source remains to be determined. Figure 2 shows the dominant model of the organisation of the neural circuitry for processing ITDs postulated by Jeffress [41] to explain contemporary psychophysical data. The model consists of an array of neurons in the brain that respond when inputs from the two ears arrive coincidentally. Each neuron is characterised by

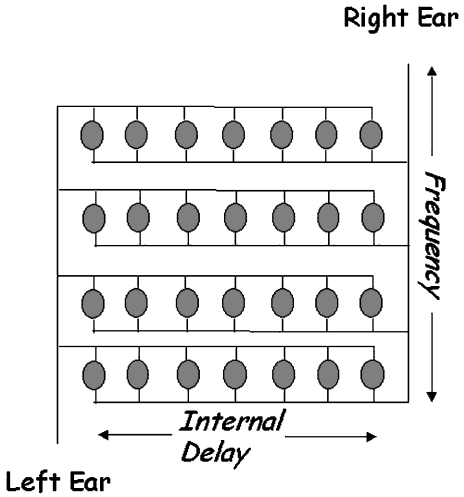


**Fig. 2** An array of coincidence detecting cells fed by delay lines from each ear. It is assumed that at each frequency there is a full representation of internal delays, covering the physiological range of azimuthal positions.

a different transmission delay from the two ears. When the interaural delay that results from the azimuthal position of the sound source exactly compensates for the extra conduction time from one ear, the inputs are coincident and the firing of the neuron indicates the azimuthal position. The model assumes a systematic arrangement of axonal delays across the array of coincidence detectors, creating a topographic representation of ITDs and, thus, a map of sound-source positions in the azimuthal plane. In the following we examine the degree to which these component parts of the model are supported by physiological data.

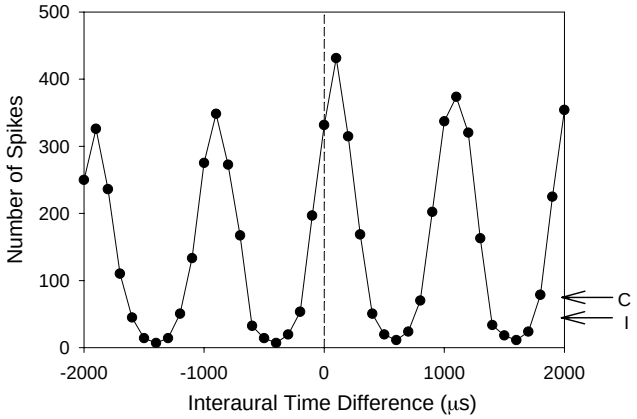


**Fig. 3** Discharge rate as a function of the interaural delay of a 1,000 Hz tone. C represents the response to contralateral tones and I to ipsilateral tones. Modified from [7].

### 4.1. Coincidence Detection

The existence of coincidence detecting neurons is the least contentious element of the Jeffress model. Evidence for coincidence detection as the mechanism by which time differences are converted to neural responses has been obtained at the level of the SOC, and at all subsequent stages in the auditory pathway. The initial processing of interaural timing cues occurs in the medial superior olive (MSO) in which neurons tuned for low-frequency sounds are relatively over-represented. MSO neurons receive excitatory input from the large spherical bushy cells of each VCN [16,42,43] which preserve, and even enhance [44], the timing accuracy seen in the auditory nerve providing exquisitely-timed inputs. Unfortunately, due to difficulties in recording activity of single MSO neurons, our knowledge of their responses is based on only a relatively small number of recordings [34,40], Other studies have reported neural responses from recording sites which may not have been verified as within the boundaries of the MSO (e.g. [45–49], reviews [7,50]). Nevertheless, all evidence suggests that MSO neurons perform an operation of coincidence detection between excitatory inputs from the two ears as originally proposed in the Jeffress model. MSO neurons are largely *insensitive* to interaural level differences or to onset delays in the absence of ongoing delays.

The response of a neuron in the MSO as a function of the interaural delay of a best-frequency tone is illustrated in Fig. 3. The response to monaural stimulation of either ear alone, indicated by the arrows marked 'C' for contralateral and 'I' for ipsilateral, is small compared with the maximum response attained binaurally at favourable ITDs. Also, the response varies greatly as a function of the interaural delay between the tones at each ear, falling below monaural response levels at unfavourable ITDs. Finally, the response cycles at the period of the stimulus (1,000 Hz), indicating that the sensitivity is to the relative phase between the two ears, not simply onset ITD. The coincidence detection hypothesis predicts that the maximum output of a MSO neuron occurs when the externally-imposed ITD results in simultaneous arrival of phase-locked activity from each ear. Predicted and measured interaural phase delays producing maximum facilitation are usually in good agreement [34,45,48,49]. MSO neurons also receive inhibition, possibly arising in the MNTB [51,52] which may be vital in establishing the characteristic delay [53]. The major target nucleus of the MSO is the ipsilateral IC, and it is from recordings in the IC that much of our detailed knowledge of the processing of ITDs is derived. Further evidence from the responses of IC and MSO neurons to filtered noise or noise with different degrees of interaural correlation confirms that ITD-sensitivity results from a process of coincidence detection following peripheral filtering [7,34,54,55].

### 4.2. Characteristic Delays

The Jeffress model proposes a fixed internal delay to each coincidence-detector neuron. This means that an ITD should exist that evokes maximal neural output independent of the stimulating frequency. In their pioneering IC study, Rose *et al.* [56] found that neurons did actually respond equally to different stimulus frequencies only at a particular ITD. This delay, which they termed the 'characteristic delay' (CD), was presumed to reflect the fixed, axonal conduction delay of the input from one ear with respect to the other. Subsequently, Yin and Kuwada [29,37,57] measured the interaural phase evoking discharge maxima, for a range of tonal frequencies, and determined the CD from the slope of the plot of mean best interaural phase angle versus tone frequency. These data extended the observations of Rose *et al.* and demonstrated that, in the anaesthetised cat, the CD was not restricted to the peak or the trough of the delay function, but could occur also at ITDs intermediate between peaks and troughs. The position of some CDs on the flanks of delay functions led Yin and

Kuwada to propose that, rather than the CD, a parameter such as the peak of the delay curve for a wideband stimulus was more likely to be functionally relevant.

Although CDs removed from either a peak or a trough in the delay function are inconsistent with the Jeffress model, a number of plausible explanations for their appearance, particularly at levels above the MSO, have been posited. These include convergent input of MSO neurons onto single IC neurons [58,59], and the action of ITD-sensitive inhibition in sculpting responses of ITD-sensitive neurons [60].

Earlier recordings of ITD sensitivity at the level of the auditory thalamus and primary auditory cortex, although less extensive than for the IC, suggested relatively little transformation of the responses of neurons at the lower levels as the pathway is ascended [61,62]. However, studies in unanaesthetised preparations have suggested a number of significant differences likely as a result of convergence and excitatory/inhibitory interactions (see [63]).

### 4.3. Delay Lines, Labelled Line or Population Codes for ITD

The orderly arrangement of the neural delay lines in the Jeffress model results in a spatial mapping of ITD. There is some evidence for this in the MSO (confounded by small samples [34]) with neurons with peak discharges near zero delay in rostral MSO locations and those with peaks at progressively longer ipsilateral delays in more caudal positions. Additional evidence for this proposition comes from studies in *nucleus laminaris*, the avian ITD comparator (see [8,64,65]), but the evidence in mammals for a systematic arrangement of delay-lines feeding the coincidence detectors remains equivocal [66,67].

In the Jeffress model, lateral position is signalled by the position of the maximal discharge in an array of neurons. This means that all delays, in an ordered delay-line, are required. Models of binaural hearing e.g. [68] assume a distribution of characteristic delays which is centred around midline and declines as ITD increases. Although early data from the cat suggested this was so [29,37,57] later studies show that the peaks of ITD functions on a single side of the mammalian brainstem and midbrain are distributed around a mean of $+200$ to $+300\,\mu$s, [38–40,69] outside the physical limits of many small mammals, and well away from the midline where spatial acuity appears to be greatest [70]. In fact, the distribution of peak ITDs appears to be an invariant function of head-size across a range of mammalian species [39].

McAlpine *et al.* [71] measured the responses of a large sample of low best-frequency neurons in the guinea pig IC to interaurally delayed noise. The full range of possible interaural delays was not represented within each frequency region, but varied systematically along the main frequency axis (Fig. 4A). Peak output of the lowest best-frequency neurons occurred at relatively long interaural delays, and peak output of the highest best frequency neurons occurred at short interaural delays, such that the peak ITD expressed in terms of phase was approximately 45°, or 1/8 of a cycle of interaural phase, independent of best frequency.

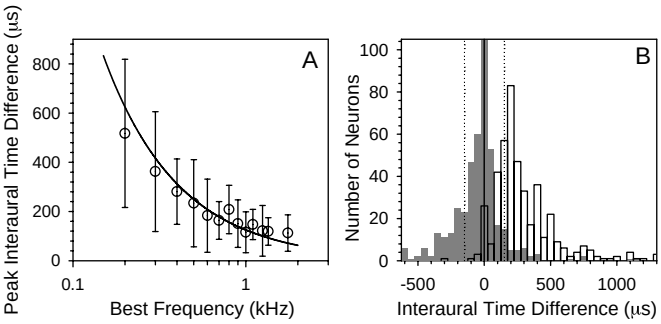


**Fig. 4** A. The mean best delay to interaurally delayed noise and the standard deviation of the mean as a function of neuron best-frequency. The curve indicates the value of the ITD equivalent to 1/8 cycle of IPD across the frequency range over which ITD-sensitivity is observed. B. Distribution of peak ITDs (open bars) and maximum slopes of ITD functions (filled bars) for the neurons contributing to part A. The dashed line is the animals physiological range of interaural delays. Modified from [71].

The dependence of the position of peak ITD on neuronal best frequency has the consequence that the steepest slopes of delay functions are positioned within the physiological range, and often maximal around zero ITD (Fig. 4B). This suggests that for mammalian localisation the position of the peaks of ITD functions may be unimportant compared with the position of greatest sensitivity to the change in ITD. Consistent with this, Skottun *et al.* [72] have shown that, taking into account the discharge variability, single neurons have sensitivities that are comparable with the astonishing resolution observed psychophysically.

Fitzpatrick *et al.* [63] demonstrated that combination of the various binaural response types (peak, trough and intermediate) with both carrier and envelope ITD sensitivity over different frequency ranges provides an array of neurons with peaks over a wide range of interaural delay. They suggest that this represents an extension to the classical model, since this continuum assumes that the peak of firing is the important coding parameter. In support of this they have demonstrated an apparent sharpening of ITD tuning at least up to the level of the medial geniculate body and a frequency independence of the ITD tuning of many neurons [73]. However, since many of these delays fall outside the physiologically plausible range it is suggested

that they might be involved in detecting interaural correlation. The longest delays are created by trough neurons that can be thought of responding when there is an absence of short ITDs, ''Extending the representation to large ITDs may therefore create a continuous representation of the binaural correlation''.

### 4.4. An Alternative to the Jeffress Model

As an alternative model to a labelled line code, in which a particular neuron firing maximally indicates the azimuthal position of the source, McAlpine *et al.* [71] suggested that azimuth could be encoded in the form of a rate code mediated by broadly-tuned spatial channels. Within such a framework, azimuthal position of a sound source could be computed from the overall discharge rate within the broadly-tuned ITD channel on one side of the brain. Thus, for a sound moving away from the midline, activity increases in the contralateral hemisphere, towards the peak of the ITD functions, indicating that the sound source is shifting to a more lateral position. An inherent ambiguity in this model arises, however, because changes in stimulus level also alter the overall activity within these broad channels. This potential ambiguity can be resolved by computing azimuthal position from a comparison of activity on either side of the brain [74–76], or from comparison between binaural and monaural activity within the same hemispheric channel. In the two-channel model, an increase in activity due to a change in azimuthal position in one channel is accompanied by a decrease in activity in the other hemispheric channel. Alternatively, binaural activity in each hemisphere could be compared with monaural activity. The sound-level-mediated component of the monaural activity will be negligibly affected by changes in azimuth. These models remain untested.

## 5. MAPS OF AUDITORY SPACE

In the barn owl a topographic representation or ''map'' of auditory space is found in the optic tectum and external nucleus of the IC e.g. [77]: neurons respond only when the sound is within a relatively small three-dimensional space. This demonstration renewed interest in the use of free-field sound presentation, however much of the subsequent work has revealed little which could not be deduced from neuronal sensitivities to the individual binaural and spectral features alone. No map of auditory space appears to exist in the IC or auditory cortex, but such a map has been found in the external nucleus of the IC and in the deep layers of the superior colliculus [78–81].

## 6. CONCLUSION

Three anatomically separate pathways have evolved to exploit the monaural and binaural cues for the localisation of sound. The analysis of pinna cues likely involves a pathway from the DCN to the IC in which information about pinna position is also integrated. ILDs due to head shadowing are analysed first in the LSO. ITDs are analysed in the MSO. The Jeffress model for the neural circuitry underlying ITD accounts for many aspects of the psychophysics, and several of its tenets such as coincidence detection and characteristic delay are supported by physiological data. However, the model needs to be extended to account for peak, trough and intermediate type responses that provide a wide range of delays, possibly underpinning sensitivity to interaural correlation. Further, all possible delays may not be available within all frequency channels and the midline slope may be an important feature of the neuronal response. If such is the case, an alternative to the labelled line code for azimuthal position, represented by discharge maxima at discrete ITDs, suggests two broad hemispheric spatial channels whose activity level is directly modulated by azimuthal position.

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