Localization by interaural time difference (ITD): Effects of interaural frequency mismatch

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(Received 20 April 1998; revised 8 March 1999; accepted 19 March 1999)

A commonly accepted physiological model for lateralization of low-frequency sounds by interaural time delay (ITD) stipulates that binaural comparison neurons receive input from frequency-matched channels from each ear. Here, the effects of hypothetical interaural frequency mismatches on this model are reported. For this study, the cat's auditory system peripheral to the binaural comparison neurons was represented by a neurophysiologically derived model, and binaural comparison neurons were represented by cross-correlators. The results of the study indicate that, for binaural comparison neurons receiving input from one cochlear channel from each ear, interaural CF mismatches may serve to either augment or diminish the effective difference in ipsilateral and contralateral axonal time delays from the periphery to the binaural comparison neuron. The magnitude of this increase or decrease in the effective time delay difference can be up to 400 μs for CF mismatches of 0.2 octaves or less for binaural neurons with CFs between 250 Hz and 2.5 kHz. For binaural comparison neurons with nominal CFs near 500 Hz, the 25-μs effective time delay difference caused by a 0.012-octave CF mismatch is equal to the ITD previously shown to be behaviorally sufficient for the cat to lateralize a low-frequency sound source. © *1999 Acoustical Society of America.* [S0001-4966(99)05206-6]

PACS numbers: 43.64.Bt, 43.64.Qh, 43.66.Pn, 43.66.Qp [RDF]

INTRODUCTION

The familiar axonal propagation delay (APD) model (Jeffress, 1948) for localizing a sound source by interaural time difference (ITD) stipulates exact frequency matching between inputs from the two ears to each binaural coincidence neuron. If we interpret exact to mean originating from exactly symmetric, single hair cells, this exact match corresponds for the cat to an alignment precision of one part in 3000 (55 000 type I afferents, 20 afferents/inner hair cell). In the mammalian auditory system, binaural neurons first occur at the level of the superior olivary complex (SOC); thus the high degree of precision in the synaptic innervation to the binaural neurons must exist even after intermediate synaptic relays in the cochlear nuclei. Does a physiological or developmental mechanism exist that is capable of identifying such exact matches and ensuring that input to a given binaural neuron arises from hair cells at precisely symmetrical locations?

In this paper, we explore the effects of possible interaural frequency mismatches (nonsymmetric innervation) on the function of low-frequency binaural comparison neurons. In particular, we examine the degree of mismatch that can occur before the APD localization model breaks down, in effect determining the limits imposed on the peripheral innervation of a single-CF channel in the APD model. To do this, we have represented the auditory periphery up to the level of the binaural comparison neurons with a linear model based on the work of Carney and Yin (1988), and we have represented the binaural comparison neurons themselves as cross-correlators. We examine the response properties of model binaural comparison neurons that receive input arising from exactly one cochlear channel (i.e., hair cell) from each ear with slight (0.2 octave or less) characteristic frequency (CF) mismatches between the two ears. Specifically, we examine the responses of the model binaural neurons to narrow-band sounds (continuous tones) and to broadband sounds (sound pressure impulses). For both the narrow-band and broadband stimuli, we investigate the relationship of response magnitude to ITD. For the narrow-band stimuli, we also investigate the relationship of best interaural phase difference (IPD) to stimulus frequency, thereby deriving the characteristic phase (CP) and delay (CD) of each model binaural comparison neuron.

Several previous investigators have proposed that input to binaurally responsive neurons might originate from different places along the basilar membrane, but only one published work (Shamma *et al.*, 1989) has addressed the quantitative effect of such a CF mismatch upon binaural cell response properties. For example, while recording from a population of neurons near the SOC, Guinan *et al.* (1972) found about half of the neurons had ''approximately equal'' best frequencies for stimulation of the two ears; consequently, about half would have had two best frequencies that were unequal. A small proportion of the neurons they recorded from were localized to the medial superior olive—a structure often implicated in processing of ITDs. Other investigators have proposed that certain aspects of physiologi-

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cal data might be explained by CF mismatches. Yin and Kuwada (1983) suggested that the nonzero CP they observed of some binaural neurons in the IC could be a result of afferents originating in populations of spiral ganglion cells with different best frequencies (a CP precisely equal to zero is an obligatory characteristic of the APD model). While the IC is not generally considered to be the most peripheral stage of binaural interaction, binaural responses of IC neurons are likely to reflect interactions at more peripheral stages. Yin and Kuwada (1984) also noted that phase changes for small population differences are substantial. To date, however, no one has examined closely the physiological differences in tuning from the two ears to binaural comparison neurons and the relationship of those differences to best-ITD. Perhaps this is because, as we see here, the CF differences required to create substantial delay differences are small.

It has been suggested that the differential delays caused by binaural CF differences could be suitably used to create a system for ITD processing that required no tuned axonal delays. This idea was originally proposed by Schroeder (1977), and later implemented in a model for interaural difference processing by Shamma and colleagues (1989). The implementation described by Shamma, which used no differential axonal delays, was intended to be illustrative rather than explanatory; the authors noted that both cochlear and axonal delays would almost certainly be incorporated in the determination of best-ITD in any binaural neuron. Nevertheless, the cochlear-delay-only model was harshly criticized on the basis that CF differences required to create significant best-ITDs would be larger than CF differences observed physiologically. As we shall show, however, even small CF differences are sufficient to compensate for substantial ITDs. Shamma's particular implementation of binaural neuron afferents was based on a biophysical model of the gerbil cochlea. Here we present results from a model in which activity of afferents to binaural comparison neurons is based on physiologically measured eighth nerve responses in the cat. Thus in addition to identifying the quantitative relationship of small interaural CF mismatches to the responses of model binaural neurons, it also should be possible to compare the results presented here with physiological data available from binaural neurons in the cat brainstem.

Our results in summary are: For binaural comparison neurons receiving input from one cochlear (CF) channel from each ear, (1) interaural CF mismatches may serve to either augment or diminish the effective difference in ipsilateral and contralateral axonal time delays from the periphery to the binaural comparison neuron, (2) the magnitude of this increase or decrease in the effective time delay difference can be up to 400 μs for CF mismatches of 0.2 octaves or less for binaural neurons with CFs between 250 Hz and 2.5 kHz, (3) a 0.012-octave CF mismatch near 500 Hz will change the effective time delay difference by 25 μs—the ITD behaviorally shown to be sufficient for lateralization of a low-frequency sound source, and (4) a distinguishing effect of interaural frequency mismatch is to create nonlinearity in the nominally linear best-IPD versus frequency curve.

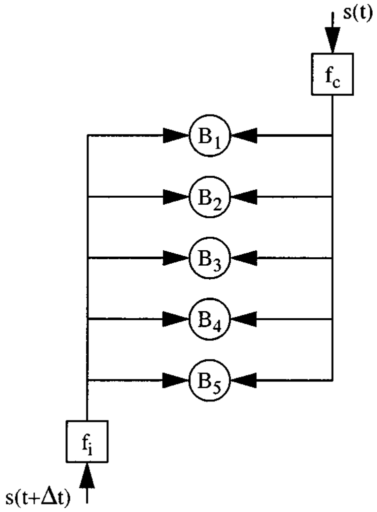

FIG. 1. Model used for analysis. Each model binaural comparison neuron (B_n) receives signals from ipsilateral and contralateral ears corresponding to sound ($s(t)$) processed through delayed gammatone filters (f_i and f_c) from ipsilateral and contralateral ears. In the absence of CF mismatches, the ladderlike afferent innervation causes binaural neurons 1–5 to be selective for different interaural time delays (Δt).

I. METHODS

To answer questions about the effect of interaural frequency mismatches on ITD localization, we constructed simple models of the auditory periphery (one each for ipsilateral and contralateral ears) and of a binaural comparison neuron. The model binaural neuron was innervated by a single channel from the ipsilateral ear and a single channel from the contralateral ear. The CFs from these two innervating channels were either identical or nearly identical; in the case where the two CFs were the same, the resulting innervation to the binaural neuron was consistent with the description of an APD model binaural neuron. Input to the model binaural neuron corresponded to sounds (narrow- or broadband) processed through the two periphery models. The response of the model binaural neuron was computed as the cross-correlation of the two inputs (see Fig. 1).

A. Auditory periphery model

The linear models of the auditory periphery were based on the time-delayed gammatone impulse responses functions described by Carney and Yin (1988; or see the Appendix), along with additional time delays corresponding to axonal propagation delays from the periphery to the binaural neurons.

The set of gammatone impulse responses were presented by Carney and Yin as a simple descriptive model (mathematical description) of the impulse responses computed by reverse-correlation (REVCOR) analysis of low-CF eighth nerve axons in the cat. Each impulse response relates sound pressure at the external ear canal to change in instantaneous spike rate in the eighth nerve axon (measured with respect to a background spike rate not correlated to the sound), and includes a CF-dependent time delay (representing the appropriate observed cochlear propagation time). The filters in our cochlear representations were graded with respect to CF;

and, through the Carney–Yin functions, they were also graded appropriately with respect to cochlear time delay (for the cat cochlea). The filter functions were normalized to yield unit energy in response to a unit impulse.

Every signal transmission path from the cochlea to the binaural comparison neurons in the SOC passes first through a synaptic relay in the cochlear nucleus. This synaptic relay is the secure synapse of the eighth nerve axons onto spherical bushy cells via the large endbulbs of Held (Rhode and Greenberg, 1992). We elected not to explicitly implement this relay synapse in our model; it would have been equivalent to adding an identical constant (synaptic) delay to every CF channel and would have had no effect on our computations.

The final element of our peripheral model corresponded to the axonal propagation delays from the cochleas to the binaural comparison neurons. For localization by ITD, it is the difference in axonal propagation delays from the ipsilateral and contralateral ears to the binaural comparison neuron that is critical, rather than the absolute time delays. To determine the range of these differences, we estimated the range of physiologically realizable differences that would be relevant for a cat. Based on an ear spacing of 10 cm, we estimated the maximum ITD, corresponding to a laterally located sound source, to be approximately 300 μs. This is the largest axonal propagation delay difference required by the APD model.

B. Binaural neuron model

In Jeffress' initial description of the APD model, the binaural neurons were described as spike coincidence detectors. Rather than modeling spike activity as point processes, we chose to base our computations on functions describing the time course of the instantaneous spike rate (or probability density). Over the course of our studies, we modeled the binaural neurons with the following candidate binaural comparison functions: cross-correlation of the filtered ipsilateral and contralateral sound pressure waveforms, cross-correlation of the rectified filtered sound pressure waveforms, peak coincidence of peaks of the filtered sound pressure waveforms, and maximum peak height of the sum of the ipsilateral and contralateral filtered sound pressure waveforms. Because cross-correlation is the binaural comparison function most commonly used in models of ITD computation (Colburn and Durlach, 1978), and because responses of neurons in the SOC and of IPD-sensitive neurons in the IC are accurately described by coincidence detection or cross-correlation (Goldberg and Brown, 1969; Yin *et al.*, 1987; Yin and Chan, 1990), we present the results we obtained with that function in this paper.

The binaural comparison function, cross-correlation, that we used here was:

$$p_{\text{bin}} = \int_{-\infty}^{\infty} p_i(t) p_c(t) dt, \qquad (1)$$

where p_{bin} is taken to be the instantaneous spike rate of the model binaural neuron, and $p_i(t)$ and $p_c(t)$ are the instantaneous spike rates of its ipsilateral and contralateral afferent inputs, respectively. The instantaneous spike rate on each afferent input is taken to be a delayed function of the sound pressure waveform at the source filtered by the appropriate model cochlear filter; e.g.,

$$p_i(t+\Delta t_p) = f_{i,CF}(t) * s_i(t-\Delta t_A). \qquad (2)$$

Here $p_i(t)$ is the instantaneous spike rate determined by convolving the appropriate cochlear filter function, $f_{i,CF}(t)$, with the modeled acoustic input, $s_i(t)$. Δt_A and Δt_P correspond to acoustic propagation delay from the sound source to the ear and axonal propagation delay from the ear to the binaural comparison neuron. For each model binaural neuron, the best-ITD for a particular class of signals (e.g., continuous tones, impulses) was taken to be the one that yielded the maximum value of p_{bin} for that class. Although the figures presented in this paper were based on the use of Eq. (1), the qualitative conclusions that we draw from them were not altered by the use of the other binaural comparison functions.

C. Analysis of model neurons

To examine the effects of CF mismatch, we initially constructed an array of model binaural neurons, each of which received input from identical CF channels from peripheral models corresponding to the ipsilateral and contralateral ears. Members of the array were distinguished by the difference in axon propagation delay of input from the two ears. Over the entire array, these differences spanned the range from 0 to 300 μs. This initially constructed array corresponded to an iso-CF population of binaural neurons described by the APD model, and formed a standard to which we could compare our later results.

For each model iso-CF binaural neuron in this array, the best-ITD was taken to be the ITD that maximized the left-hand term in Eq. (1). The best-ITD was computed both for broadband stimuli (sound pressure impulses) and for narrowband stimuli (continuous tones).

A model iso-CF neuron's response to sinusoidal sound as a function of ITD is given by the cross-correlation of the sinusoidal responses of the two peripheral filters; we computed each neuron's response for several frequencies in the passband of the peripheral filters (where the passband is defined as frequencies for which the response is within 40 dB of the maximum response).

The composite curve is another characterization commonly made for binaural neurons. It is the sum of response versus ITD for sinusoids of several frequencies. Because our peripheral models are linear and we use cross-correlation—also a linear function—the composite curve for the entire frequency continuum for the binaural neuron is exactly equal to the curve of response to broadband noise versus ITD (Yin *et al.*, 1986). In practice, a dense sampling of frequencies within the passband would be sufficient to construct an excellent approximation of the composite curve. Further, because all elements of the model are linear, the response of a binaural neuron to broadband noise as a function of ITD is identical to its response to a sound pressure impulse as a function of ITD (i.e., given by the cross-correlation of the impulse response functions of the two peripheral filters).

A further characterization of binaural neurons is derived from the graph of best interaural phase difference (IPD) versus stimulus frequency. When these data are fit with a straight line, the slope of this line is the characteristic delay (CD) of the binaural neuron and the *y*-intercept is the characteristic phase (CP) (Yin and Kuwada, 1983). While the physiological relevance of the CP and CD is not clear, these parameters do have value as descriptors; we computed values of CP and CD for the model binaural neurons. For our model, computation of best-IPD versus frequency is accomplished by taking the difference in the phase responses of the two peripheral channels.

After computing all these response parameters for the initially constructed iso-CF array, we modified the array by modest systematic perturbations of the cochlear origin (i.e., the CF) of the innervating contralateral input. In addition to modifying the frequency tuning of the contralateral input to the binaural neurons, this also modified the effective propagation delay to the binaural neurons from the contralateral ear by changing the CF-dependent cochlear delay and damping.

For each perturbation in the contralateral CF, we again computed the CP and CD for the model binaural neurons, as well as the best-ITDs for broadband and narrow-band stimuli. These binaural comparison neurons now had different CFs from the two ears, and so responses to binaurally presented tones were typically largest for tones at frequencies somewhere between the two CFs.

II. RESULTS

To provide a baseline for comparison, we first present the results of our analysis for an iso-CF binaural comparison neuron that has a 100 μs longer delay from the contralateral ear than from the ipsilateral ear, and receives input from peripheral channels with identical CFs of 800 Hz from both ears. This scheme describes a binaural neuron of the APD model that is tuned to a part of the contralateral auditory hemifield. The frequency response curve, corresponding to both ipsilateral and contralateral peripheral channels, is shown in Fig. 2. Figure 2(a) shows the impulse responses from the two ears (ipsi—solid line; contra—dashed line); the additional 100-μs contralateral axonal propagation delay (Δt_P) is clearly visible in the comparison of the contralateral and ipsilateral impulse responses. The additional delay is also apparent in comparison of the phase responses of the ipsilateral and contralateral channels shown in Fig. 2(c).

The response of the iso-CF model binaural neuron is characterized in Fig. 3. Responses to sinusoidal stimuli of several frequencies are shown in Fig. 3(a). Figure 3(b) shows the normalized responses to the same frequencies. For every stimulus frequency, the peak response occurs at 100 μs—an ITD determined by the difference in the axonal propagation delays from the peripheral filters. The composite curve shown in Fig. 3(c), formed from summing the sinusoidal response curves [Fig. 3(a)] for all frequencies, is identical to the wide-band response versus ITD curve, and also peaks at 100 μs.

In Fig. 3(d) we show the plot of best interaural phase difference (IPD) versus stimulus frequency for this iso-CF binaural neuron. We compute the CP and CD of this neuron by using a least-squared-error (LSE) method to find the best linear fit of phase as a function of frequency for the frequencies 200, 400, 600, 800, 1000, 1200, and 1400 Hz. These frequencies were chosen because the neuron's response to them is within 40 dB of its response to a best-frequency stimulus. For this model neuron, the only difference between the two peripheral channels is a time delay, and so the best-IPD versus frequency plot is exactly linear. While in this case the LSE fit is unnecessary, we include it here for comparison with other model neurons. The characteristic phase (*y*-intercept) of the neuron is 0, and the characteristic delay (slope) is 100 μs—the difference in propagation times from the ipsilateral and contralateral peripheral channels.

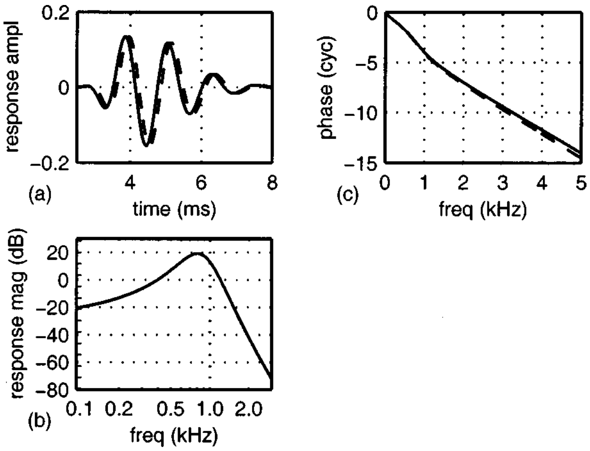

FIG. 2. Peripheral filter properties for the model binaural neuron with 100-μs contralateral delay and no CF mismatch: (a) Impulse responses, (b) frequency tuning curves, (c) phase tuning curves. Solid lines are for ipsilateral channel; dashed lines are for contralateral channel. Ipsilateral and contralateral frequency tuning curves are identical.

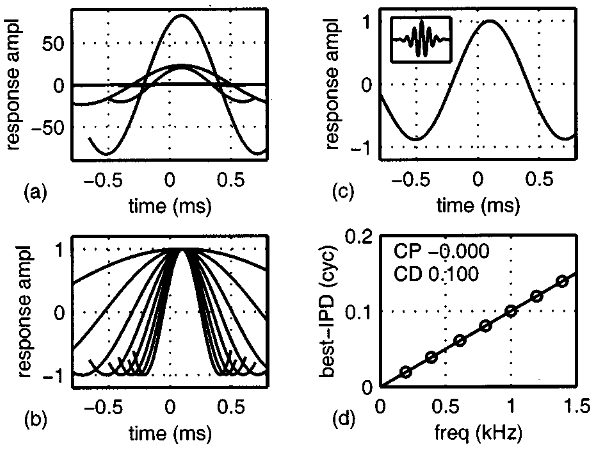

FIG. 3. Response properties of model binaural neuron with 100-μs contralateral delay and no CF mismatch: (a) Response to narrow-band stimuli (pure tones) as a function of ITD, (b) normalized curves from (a), (c) response to wide-band stimuli (sound pressure impulses) as a function of ITD—equal to the composite curve—peaks at 100 μs; inset shows response for ITDs from −5 to 5 ms, (d) best-IPD as a function of stimulus frequency.

As can be seen from analysis of the model iso-CF neuron we described, the incorporation of an additional time delay has no effect on frequency tuning of the peripheral channel, but does affect the phase response by adding to it a

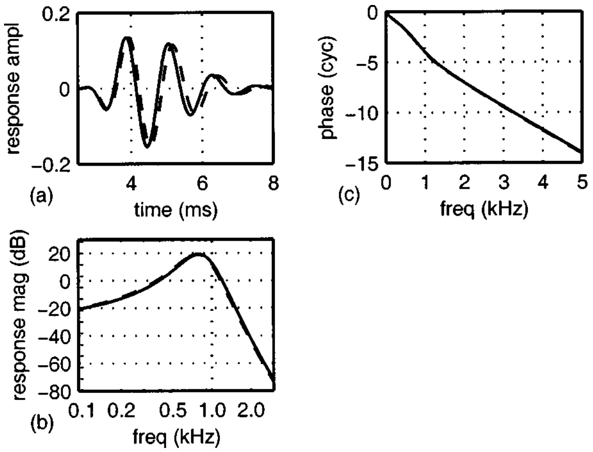

FIG. 4. Peripheral filter properties for the model binaural neuron with no time delay and 0.05-octave CF mismatch: Impulse responses (a), frequency tuning curves (b), and phase tuning curves (c). Solid lines are for ipsilateral channel; dashed lines are for contralateral channel.

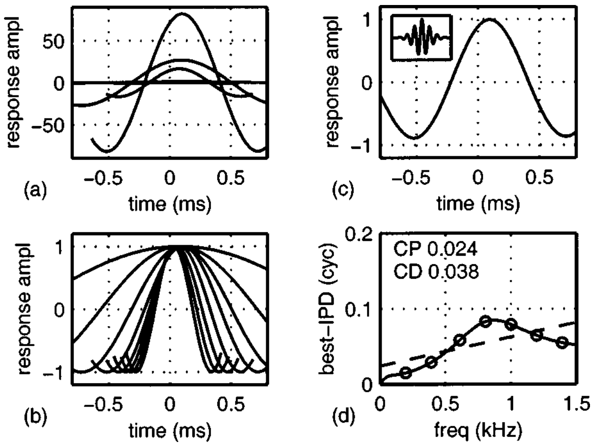

FIG. 5. Response properties of the model binaural neuron with no time delay and 0.05-octave CF mismatch (contralateral CF lower): (a) Response to narrow-band stimuli (pure tones) as a function of ITD. (b) Normalized curves from (a). (c) Response to wide-band stimuli (sound pressure impulses) as a function of ITD (equal to the composite curve) peaks at 95 μs; inset shows response from -5 to 5 ms. (d) Best-IPD as a function of stimulus frequency.

linear component whose slope corresponds to the added delay time. The added strict time delay has analogous effects on the response properties of the binaural neuron, simply shifting the best ITD by the added delay time, and adding a linear component to the best-IPD versus frequency plot.

To clearly distinguish the effects of time delay from CF mismatches, we next describe the results of our analysis for an iso-delay binaural neuron with identical propagation time delays from the two ears, but different CFs. The binaural neuron we use for this receives input from the 800-Hz ipsilateral channel, and input from the 721-Hz contralateral channel (corresponding to an 0.05-octave mismatch in CF).

Figure 4 shows the frequency tuning curves for the ipsilateral and contralateral peripheral channels of the iso-delay neuron, along with their corresponding impulse response functions and phase tuning curves. In comparing the peaks of the impulse response functions, there appears to be an effective difference in time delay from the ipsilateral and contralateral peripheral channels; this apparent delay is the manifestation of differences in the ''strict'' cochlear propagation delay (T_d) and cochlear damping time constant (T_a) in the two peripheral models (see the Appendix).

The response of this iso-delay binaural neuron is characterized in Fig. 5. Responses to sinusoidal stimuli as a function of ITD are shown in Fig. 5(a). In contrast to responses of the iso-CF neuron, these responses peak at different ITDs. Figure 5(c) shows the composite curve for the iso-delay binaural neuron; the composite curve has a maximum for an ITD of 95 μs. The wide-band response curve again exactly matches the composite curve. Thus this neuron is tuned to a part of the contralateral hemifield.

Finally, the curve of best-IPD versus stimulus frequency for the iso-delay neuron is shown in Fig. 5(d). In this case, the difference in the phase responses is not exactly linear, but exhibits a bump near the CF of the binaural neuron. For a gammatone filter, the phase response changes most rapidly near the CF of the filter; the bump in the curve of best-IPD versus stimulus frequency reflects the fact that the phase is rapidly changing at a lower frequency for the filter with the lower CF (i.e., the contralateral filter). This bump near the CF is characteristic of the model binaural neurons that have CF mismatches. From the LSE fit to the phase sample frequencies, the CP of this neuron is 0.024 cycles, and the CD is 38 μs. Curves of best-IPD versus frequency are shown in Fig. 6 for iso-delay model binaural neurons with ipsilateral CF of 800 Hz and contralateral CF mismatches of up to 0.2 octaves.

The effect of CF mismatch on a model neuron that has a specific nonzero propagation time-delay difference is described in Figs. 7 and 8. In this case, the binaural neuron receives contralateral input with axonal propagation delay 200 μs longer than the ipsilateral input. In the absence of any CF mismatch, this neuron would therefore have a best-ITD of 200 μs. Like the earlier two model neurons, for this neuron the ipsilateral input arises from the 800-Hz channel. The contralateral input to this model binaural neuron is from the 888-Hz channel—a -0.05-octave mismatch.

In Figs. 7 and 8 it can be seen that the responses to

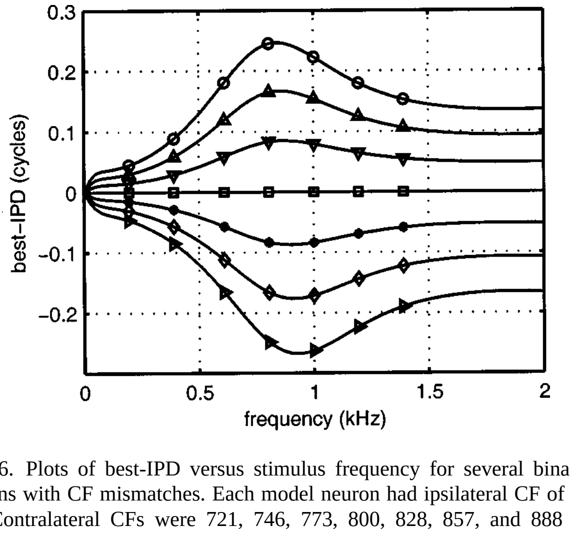

FIG. 6. Plots of best-IPD versus stimulus frequency for several binaural neurons with CF mismatches. Each model neuron had ipsilateral CF of 800 Hz. Contralateral CFs were 721, 746, 773, 800, 828, 857, and 888 Hz, corresponding to CF differences of -0.15, -0.10, -0.05, 0.0, 0.05, 0.10, and 0.15 octaves (bottom to top).

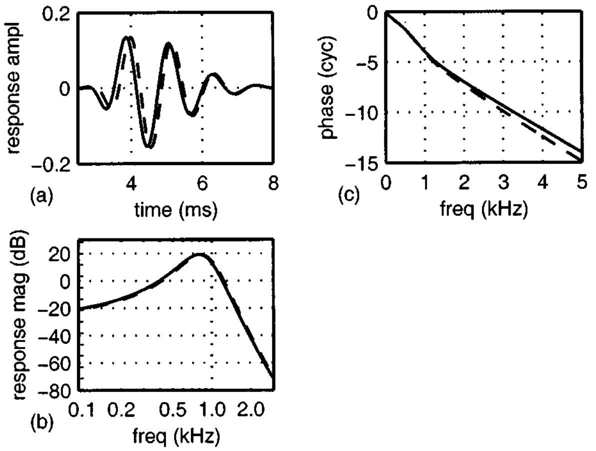

FIG. 7. Peripheral filter properties for the model binaural neuron with 200-μs time delay and -0.05-octave CF mismatch: Impulse responses (a), frequency tuning curves (b), and phase tuning curves (c). Solid lines are for ipsilateral channel; dashed lines are for contralateral channel.

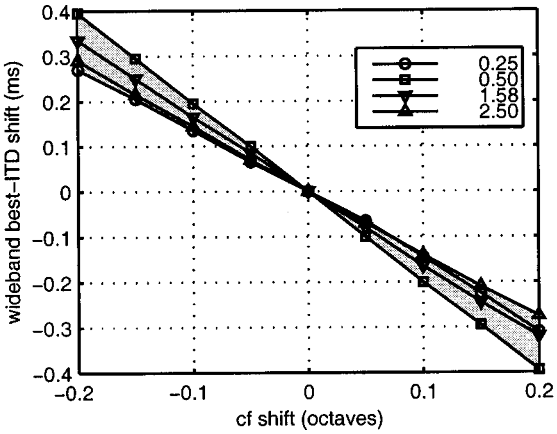

FIG. 9. Change in best-ITD due to CF mismatches up to 0.2 octaves in model neurons. Shaded area shows empirically determined upper and lower bounds for model binaural neurons with nominal CFs between 0.25 and 2.50 octaves. Also shown are curves for four specific binaural neurons with nominal CFs equal to 0.25, 0.50, 1.58, and 2.50 kHz.

sinusoids peak at different times. The composite curve for this neuron, again the same as its wide-band response versus ITD curve, peaks at 105 μs. The plot of best-IPD versus frequency once again displays the bump near the CFs characteristic of CF mismatch. For this model neuron there is also a linear component in the plot of best-IPD versus frequency that is due to the difference in axonal propagation times. From the best-IPD versus frequency plot, the LSE fit shows the CP of this neuron to be -0.022 cycles and the CD to be 157 μs.

As can be seen from the two non-iso-CF examples, an important effect of CF mismatch for these model binaural neurons is a change in the effective time delay for arrival of signals from the two ears, in effect modifying the best-ITD and hence spatial tuning of the neuron. For wide-band sounds, the range of shift in best-ITD due to CF mismatches is shown in Fig. 9 for model binaural neurons with nominal CFs between 0.25 and 2.5 kHz. It can be seen from the figure that the change in best-ITD is between 100 and 200 μs for a CF mismatch of 0.1 octaves, and increases for larger mismatches.

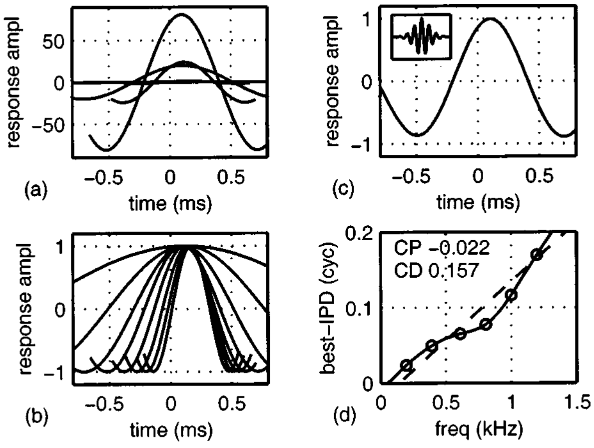

FIG. 8. Response properties of the model binaural neuron with 200-μs time delay and -0.05-octave CF mismatch (contralateral CF higher): (a) Response to narrow-band stimuli (pure tones) as a function of ITD. (b) Normalized curves from (a). (c) Response to wide-band stimuli (sound pressure impulses) as a function of ITD (equal to the composite curve) peaks at 105 μs; inset shows response from -5 to 5 ms. (d) Best-IPD as a function of stimulus frequency.

From Fig. 9, we can deduce what must comprise a ''single-CF channel'' for the APD model for localization by ITD. The specific question we ask is how accurate must interaural frequency matching be in order for a cat to localize sounds based only on ITD? Wakeford and Robinson (1974) showed that cats are able to lateralize 0.5- and 1.0-kHz tone bursts with ITDs of approximately 25 μs (lateralization performance is substantially poorer for 2.0-kHz tones). From our computations (cf. Fig. 9), for a binaural comparison neuron with a nominal CF near 500 Hz, 25 μs corresponds to an interaural frequency mismatch of approximately 0.012 octaves. So, we conclude that in the context of the APD model, a single-CF channel near 500 Hz should be interpreted as signals arising within a frequency band with a width of 0.012 octaves. If we assume that the inner hair cells are equally distributed per octave, this frequency band corresponds to a range of four hair cells.

III. DISCUSSION

A. Overview

The set of Carney–Yin delayed gammatone impulse responses (Carney and Yin, 1988) provides a family of functions—one function for each CF below approximately 3 kHz—that describe the filter properties of cat cochlear channels over that frequency range. We know that the descriptions are imperfect and incomplete. They do not include the nonlinearities that we know exist in cochlear dynamics: not the memory nonlinearity of adaptation (Lewis and Henry, 1995), nor the static nonlinearities such as synchrony suppression and stochastic resonance effects imposed by the spike threshold (Javel, 1981; Greenwood, 1986; Lewis and Henry, 1995), nor the nonlinearity of two-tone suppression (Nomoto *et al.*, 1964; Sachs and Kiang, 1968), nor the dependence that we know exists between REVCOR-derived impulse responses and the ambient sound amplitude (Carney and Yin, 1988; Lewis and Henry, 1994). Nevertheless, we know that even without incorporating any of these nonlinear properties, single-level REVCOR-derived impulse responses, upon which Carney and Yin's functions are based, can provide fairly faithful predictions of the input–output properties of cochlear channels; e.g., they can predict fairly accurately the temporal pattern of instantaneous spike rate in response to an acoustic stimulus waveform of arbitrary complexity (de Boer and de Jongh, 1978; Carney and Yin, 1988; Wolodkin *et al.*, 1996).

In the studies reported in this paper, we have explicitly excluded from our peripheral model two other cochlear channel nonlinearities—a soft-onset threshold nonlinearity (or half-wave rectification) of the filtered sound pressure waveform, and spontaneous background activity—however, we have not ignored them. The effect of including the background activity in our computations would simply have been to shift the response amplitude curves upward; and we observed from our studies that the effect of including half-wave rectification was primarily the elimination of below-zero response amplitudes. Because our computations concerned primarily time-to-peak values, inclusion of these nonlinearities does not alter our conclusions.

For the results we have presented here, we have used cross-correlation as the comparison mechanism of the model binaural neurons. We have chosen to use this comparison mechanism for several reasons. First, for sinusoidal stimuli, the computed best-ITDs (or best-IPDs) using either summation or peak coincidence of ipsilateral and contralateral inputs as the binaural comparison function are mathematically identical to those using cross-correlation as the comparison function. Second, while a similar mathematical equivalence does not hold for impulse and noise stimuli, the qualitative observations we made from our studies using summation and peak coincidence as the binaural comparison function are the same as those we present using cross-correlation. Third, comparison of binaural responses of cat medial superior olive neurons with monaural responses indicates that those neurons are accurately described as coincidence detectors (Yin and Chan, 1990). Fourth, while it is unlikely that strict cross-correlation *per se* is carried out by the biological analogues of our mathematical constructs, physiological evidence indicates that the response of real binaural IC neurons to noise and tone stimuli can be accurately described by a cross-correlation function (Yin *et al.*, 1987). While the IC itself is unlikely to be the locus of interaural time difference interaction—most IPD-sensitive neurons in the IC do not phase lock to monaural stimuli (Yin and Kuwada, 1984)—it is the predominant target of central projections from the MSO (Adams, 1979). Consequently, it is likely that the responses of IPD-sensitive neurons in the IC reflect interactions that occur at the more peripheral level of the MSO.

In the studies reported in this paper, we elected to use the delayed gammatone impulse response functions as descriptive models of the cochlear channels. Our descriptive model of binaural interaction in a brainstem neuron (our binaural comparison function) was cross-correlation. We synthesized models of binaural ITD computation by combining these descriptive models (delayed gammatone impulse responses for two CFs, plus cross-correlation). Having done so, we examined the properties that emerged from these synthetic models. The conclusions that we draw are based on those properties and therefore, ultimately, on our synthesis and the descriptive models that we incorporated into it. In today's reductionist environment in biology, one might be tempted to employ synthetic models of the cochlea (e.g., based on hair cell and basilar membrane micromechanics, the dynamics of the hair cell/cochlear axon synapse, and the dynamics of the cochlear axon spike trigger) and synthetic models of the binaural brainstem neuron. The modeling traditions of engineering lead us to believe that such an approach is far less than optimal. For the elements of our synthetic models we much prefer descriptive models, with well-defined properties and easily assessable fidelity, to synthetic models whose emergent properties and fidelity are uncertain at best.

B. Single-CF afferent channels

As originally proposed, the APD model specifies that each binaural comparison neuron receives input from only one channel from each ear, and that those channels have identical CFs. Monaural response properties (e.g., response threshold, Q10, etc.) of neurons throughout the SOC are similar to those in the auditory nerve (Goldberg, 1975), and so it is conceivable that binaural neurons are in fact innervated by a single channel from each ear. Innervation by a single channel is not a critical element of the model, as long as exact functional symmetry between the two ears is maintained. However, if we assume that there is innervation from only a single channel, the work we have presented here in part addresses the definition of ''identical CF'' or ''exact functional symmetry'' in this context of ITD localization: We find that the CFs of the innervating channels should lie within approximately 0.012 octaves of one another, depending upon the CF.

In a study of binaural neurons in the cat MSO, Yin and Chan (1990) observed that 72% (13/18) of observed interaural CF differences were within 0.2 octaves, and 77% were within 50 Hz. Conversely, 28% would have had CF differences larger than 0.2 octaves, and 22% would have had interaural CF differences larger than 50 Hz; at least some neurons in the cat MSO are not properly described as receiving input from the same CF channel from each ear. In fact, the mismatched CPDs resulting from the interaural CF differences observed by Yin and Chan would provide substantial errors in a localization system which relied upon exact interaural CF matches. To date, there have been no physiological data published that describe the relationship of best-ITD to interaural CF difference.

Anatomical and physiological studies of the nucleus laminaris (NL) in the chicken (Young and Rubel, 1983) and barn owl (Carr and Konishi, 1990), and the MSO in the cat (Smith *et al.*, 1993) have shown that these structures are possible substrates for neural implementation of the APD model. In particular, physiological and anatomical data in these studies suggest the existence of ladderlike afferent innervation of binaural neurons (Fig. 1) in the nucleus laminaris or medial superior olive, and a trend for binaural neurons with successively larger best-ITDs to lie successively further along the neural substrate. Unfortunately those studies do not report on the magnitude of interaural CF differences in the neurons studied. Consequently those studies do not address the question we have chosen for the focus of this manuscript—the possibility that interaural CF mismatches contribute significantly to ITD selectivity.

C. Best-ITD of model binaural neurons

The curves of response versus ITD for the model neurons we have described resemble similar curves for neurons in the IC (Yin and Kuwada, 1983) and MSO (Yin and Chan, 1990). The curves of response versus ITD for sinusoidal stimuli [Figs. 3(a), (b), 5(a), (b), and 8(a), (b)] are periodic with respect to ITD, and for the model neurons described in the figures, the normalized response curves approximately intersect near the response peaks—typical of the ‘‘peak-type’’ neurons observed by Yin colleagues in the MSO and IC. Curves of response versus ITD for model neurons with larger CF mismatches (not shown) do not intersect at a point; this type of response is similar to other neurons observed by Yin and Chan in the IC. The composite curve, constructed by adding the response versus ITD curves for several sinusoidal stimuli, was shown by Yin and colleagues to be a good first order predictor of the wide-band noise response versus ITD curve in both the IC and MSO. The response curves for wide-band stimuli (i.e., the composite curves) for the three model neurons we have described [Figs. 3(c), 5(c), and 8(c)] resemble the composite curves and response curves for wide-band noise as a function of ITD from neurons in the IC and MSO.

In the APD model, if the animal is presented with simultaneous identical stimuli to the two ears, every binaural comparison neuron receives input from the left ear that differs from the input it receives from the right ear only by its absolute time of arrival. If the response amplitude of each binaural neuron is determined either by coincidence or by cross-correlation of the inputs from the two ears, the difference in the times of arrival is the best-ITD of the neuron; and that best-ITD will be independent of the stimulus waveform. Thus for every binaural comparison neuron, the best-ITD for wide-band stimuli will be exactly the same as its best-ITD for any narrow-band stimulus.

In our implementation of the APD model, small CF mismatches resulted in best-ITDs for narrow-band stimuli that were dependent upon the stimulus frequency. These variations in best-ITD were small for small CF mismatches, and became larger as CF mismatch was increased. Because best-ITD for narrow-band stimuli were a function of stimulus frequency, the best-ITD for wide-band stimuli was necessarily different from most of these.

In most models of sound source localization by ITD, axonal propagation delay differences from the left and right ears determines the best-ITD of a binaural comparison neuron. We have presented specific analyses of three model binaural comparison neurons in this paper. Innervation from the ipsilateral ear to all three neurons is identical; each receives input in the 800-Hz CF channel. The cochlear origin of innervation from the contralateral ear to all three neurons is nearly identical; each receives input from within 0.05 octaves of the 800-Hz CF channel. The best-ITD of all three of these binaural comparison neurons is approximately 100 μs. However, as we have modeled them, the axonal propagation delay differences from left and right ears for these model neurons varies from 0 to 200 μs; the best-ITD for these binaural comparison neurons is not determined solely by the axonal propagation time difference!

D. Can cochlear propagation delay alone be used for ITD localization?

A theory of ITD localization in which cochlear propagation delay (CPD), rather than axonal propagation delay, is used to compensate for ITD has been proposed by Schroeder (1977). Criticism of this CPD theory has historically been based on the unproven assumption that if CPD *alone* were used to compensate for ITD, interaural CF differences larger than those found in physiological data would be needed in order to compensate for the largest physiologically relevant ITDs. Shamma and colleagues (1989) incorporated the CPD theory in a model for binaural processing in which CPD alone was used to compensate for ITD. The peripheral filters of that model were implemented through a biophysical model of the gerbil cochlea. At that time, no information was available regarding ITD selectivity of cells in the gerbil superior olivary complex, and so that model was unable to address directly the criticism that CF differences required for localization were in excess of those observed physiologically. [Spitzer and Semple (1995) have recently published data describing responses of gerbil MSO neurons.] Nevertheless, Shamma and colleagues did provide an estimate of the maximum CF difference required for the cat which is in accord with our computations.

The REVCOR-derived peripheral filters in the model we have used here were designed with the constraint that both frequency and phase responses be similar to those of cat eighth nerve fibers, and so we are able to address the question of whether CF mismatches required by the CPD model fall within the range of observed CF differences in the cat. According to our computations, an interaural CF mismatch of 0.2 octaves or less—corresponding to 72% of the neurons examined by Yin and Chan (1990)—is sufficient to create ITD-shifts of 270 μs or more for CFs from 0.25 to 2.5 kHz. Based on Fig. 17 of the paper by Yin and Chan, approximately half of the binaural MSO neurons they studied had CFs lower than 500 Hz and approximately half had CFs between 500 and 1000 Hz. From our computations, an interaural CF mismatch of 50 Hz—corresponding to 77% of the neurons examined by Yin and Chan—is sufficient to create ITD-shifts of up to 300 μs for cells with CFs between 250 and 500 Hz, and ITD-shifts of 130 μs or more for cells with CFs between 500 and 1000 Hz; thus CF mismatches smaller than 50 Hz could create appropriate ITD-shifts in a large proportion of binaural neurons with CFs less than 1000 Hz. Neurons which have interaural CF differences greater than 50 Hz or 0.2 octaves (23% and 28% of the neurons studied by Yin and Chan) would potentially have even larger ITD-shifts caused by mismatched CPDs. We conclude from these data that the CPD theory is consistent with the interaural CF differences which have been reported. However, both axonal propagation delay differences and CF mismatches must be considered in determining the source of ITD sensitivity of a binaural neuron.

E. Characteristic phase and delay of the model neurons

The best-ITD of binaural neurons with CF mismatches is dependent both upon differential axonal propagation delays from the two ears and CF mismatch. For binaural neurons with no CF mismatch, the best-IPD versus frequency plot is exactly a straight line passing through the origin ($\mathrm{CP}=0$) and having a slope (CD) precisely equal to the best-ITD, which is in turn equal to the differential axonal delay. In the absence of any differential axonal delay, the dependence of phase response to frequency response allows computation of a definitive relationship of best-IPD to stimulus frequency; in the cat, this relationship is described through the gammatone filter equations. For a binaural neuron with large CF mismatch, this computation results in a graph that cannot be fit well by a straight line (cf. Fig. 6). Other filter equations appropriate for modeling peripheral responses of other species would result in definite, but different, relationships of best-IPD to stimulus frequency.

Linearity in the relationship of best-IPD to frequency is dependent upon both species and brainstem nucleus. Yin and Kuwada (1983) developed a system for classifying best-IPD versus frequency curves as linear or nonlinear. Their system compared the mean square differences of data points from the best fit line to the expected mean square differences obtained from random Monte Carlo simulations. Using this method to classify binaural neurons in the IC, they found that binaural neurons could have either linear or nonlinear plots of best-IPD versus frequency. Using the same system to classify MSO neurons in the cat, Yin and Chan (1990) reported that plots of best-IPD versus frequency were approximately linear. More sensitive tests of nonlinearity show that neurons in the rabbit IC (Kuwada *et al.*, 1987—chi-squared test) and SOC (Batra *et al.*, 1997—one-sample runs test) may have either linear or nonlinear best-IPD versus frequency plots.

We applied Yin and Kuwada's linearity test to the best-IPD versus frequency curves shown in Fig. 6, using the sample frequencies indicated by points in the figure. For model binaural neurons with ipsilateral CF of 800 Hz and contralateral CF mismatches of 0, ±0.5, and ±0.10 octaves, the plots of best-IPD versus frequency were classified as linear; plots from the binaural neurons with CF mismatches of +/−0.15 octaves were classified as nonlinear. Similar plots from neurons with CF mismatches of ±0.125 octaves are also classified as linear by this test; this CF mismatch corresponds to an ITD shift of more than ±200 μs. Consequently, even a binaural neuron that has a nearly linear best-IPD versus frequency curve may have a significant ITD shift caused by CF mismatch. We also applied a more sensitive runs test (Davis, 1986) of linearity similar to that described in Batra *et al.* (1997) using the points shown in Fig. 6 and six additional points spaced midway between them. To perform the runs test, we recorded the sequence of signs of deviations of samples from the best fit line, and then checked to see whether the number of runs in this sequence was greater or less than statistically expected. All the best-IPD versus frequency curves corresponding to nonzero CF mismatches contained exactly three runs and so were classified as nonlinear at the $\alpha=0.05$ level of significance. We observe that this in part reflects the noise-free nature of the computations; application of the runs test is inappropriate in this situation. Were we to include sufficient measurement noise in our model samples, the statistical test would not reject the hypothesis that these curves are linear.

Although we conclude that precise matching of ipsilateral and contralateral CFs is not necessary for binaural processing based on the APD model, we nonetheless conclude that the allowable range of mismatch is extremely narrow. Is it reasonable to expect the developmental processes for binaural neural circuitry to lead to CF matching as precise as 0.012 octaves? In a companion paper, we explore the possibility that the required precision of interaural CF matching might be reduced by appropriate intraaural CF mismatch.

ACKNOWLEDGMENTS

A preliminary version of this work was presented in 1994 at the International Hearing Symposium in Irsee, Germany. This work was funded by the Office of Naval Research (FD-N00014-91-J-1333), the National Institute for Deafness and Communication Disorders (DC00112), and the Institute for Scientific Computing Research at Lawrence Livermore National Laboratories (89-07 and 90-05).

APPENDIX: COCHLEAR FILTER MODEL

Our model cochleas were based on linear properties of low-CF eighth nerve afferents reported by Carney and Yin (1988). In the model, the response of the eighth nerve afferent with CF of f to an impulse of sound pressure is given by the set of equations:

$$T_a=1.3\left(\frac{f}{0.456}+0.8\right)^{-2.585}+0.4\left(\frac{f}{0.456}+0.8\right)^{-0.3447}, \quad \text{(A1)}$$

$$T_d=8.13\left(\frac{f}{0.456}+0.8\right)^{-0.7966}-\frac{1.25}{f}, \quad \text{(A2)}$$

$$h_f(t)=\begin{cases}(t-T_d)^5 e^{-(t-T_d)/T_a}\sin(2\pi f(t-T_d)), & t\geqslant T_d\\ 0, \quad t<T_d\end{cases} \quad \text{(A3)}$$

(frequency is in kHz, time in ms).

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