Research Article

The Interaural Time Difference Pathway: a Comparison of Spectral Bandwidth and Correlation Sensitivity at Three Anatomical Levels

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ABSTRACT

Temporal differences between the two ears are critical for spatial hearing. They can be described along axes of interaural time difference (ITD) and interaural correlation, and their processing starts in the brainstem with the convergence of monaural pathways which are tuned in frequency and which carry temporal information. In previous studies, we examined the bandwidth (BW) of frequency tuning at two stages: the auditory nerve (AN) and inferior colliculus (IC), and showed that BW depends on characteristic frequency (CF) but that there is no difference in the mean BW of these two structures when measured in a binaural, temporal framework. This suggested that there is little frequency convergence in the ITD pathway between AN and IC and that frequency selectivity determined by the cochlear filter is preserved up to the IC. Unexpectedly, we found that AN and IC neurons can be similar in CF and BW, yet responses to changes in interaural correlation in the IC were different than expected from coincidence patterns (“pseudo-binaural” responses) in the AN. To better understand this, we here examine the responses of bushy cells, which provide monaural inputs to binaural neurons. Using broadband noise, we measured BW and correlation sensitivity in the cat trapezoid body (TB), which contains the axons of bushy cells. This allowed us to compare these two metrics at three stages in the ITD pathway. We found that BWs in the TB are similar to those in the AN and IC. However, TB neurons were found to be more

sensitive to changes in stimulus correlation than AN or IC neurons. This is consistent with findings that show that TB fibers are more temporally precise than AN fibers, but is surprising because it suggests that the temporal information available monaurally is not fully exploited binaurally.

Keywords: binaural, temporal, bandwidth, interaural time difference, bushy cell, cochlear nucleus

INTRODUCTION

An acute sensitivity to temporal differences between the sound waveforms to the two ears strongly contributes to our ability to localize sounds in azimuth and to extract signals in noise. These temporal differences can be described along axes of interaural time difference (ITD) and interaural correlation. Sensitivity to temporal differences first arises in the superior olivary complex (SOC) (Goldberg and Brown 1968; Yin and Chan 1990; Finlayson and Caspary 1991; Joris and Yin 1995; Joris 1996; Batra et al. 1997), but has been studied mainly at the level of the midbrain (reviewed by Palmer and Kuwada 2005). In both mammalian and barn owl pathways, changes in this sensitivity have been reported along the ascending neuraxis (Albeck and Konishi 1995; Fitzpatrick et al. 1997; Spitzer and Semple 1998).

To gain insight into the initial mechanisms underlying interaural temporal sensitivity, our laboratory has studied neurons even earlier in the neuraxis than

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the SOC: the auditory nerve (AN) (Joris 2003; Louage et al. 2004; Joris et al. 2008) and bushy cells in the cochlear nucleus (CN) (Louage et al. 2005; Louage et al. 2006; van der Heijden et al. 2011a). Spherical and globular bushy cells provide excitatory and (via the medial and lateral nucleus of the trapezoid body) inhibitory input to the SOC nuclei that are involved in the extraction of binaural temporal cues (Cant and Benson 2003). Their temporal coding can differ strikingly from their AN input, both in cat and in rodents (Joris et al. 1994b; Joris et al. 1994a; Kuenzel et al. 2011; Recio-Spinoso 2012). In previous work, our laboratory studied binaural responses to broadband noise manipulated in various interaural parameters and compared these to responses of the monaural input pathways. Of course, monaural neurons are not directly sensitive to these interaural parameters: we compute “pseudo-binaural” responses, which are simply counts of coincidences between monaural responses to these various broadband stimuli presented in succession. Using this approach, it was shown that the enhanced temporal coding in monaural pathways benefits sensitivity to binaural temporal differences, both in interaural correlation (Louage et al. 2006) and in ITD (Louage et al. 2005; van der Heijden et al. 2011a).

In two previous studies (Mc Laughlin et al. 2007; Mc Laughlin et al. 2008), the same approach was used to examine spectral bandwidth (BW) in AN and inferior colliculus (IC), because psychophysical studies suggested a wider BW binaurally than monaurally (for background: see “DISCUSSION”). The first study (Mc Laughlin et al. 2007) used a spectral technique, while a second study (Mc Laughlin et al. 2008) used a temporal technique. Both studies came to the same conclusion: for the same CF range, there was no mean difference between BWs in the AN and IC indicating that, in the ITD pathway, there is little frequency convergence between AN and IC. However, responses to changes in correlation were also measured, which revealed differences between IC and AN. While an IC neuron and an AN fiber may have the same BW and CF, responses to changes in interaural correlation in the IC tended to be qualitatively different than for pseudo-binaural responses in the AN. AN fibers almost always showed expansive responses to changes in correlation while IC neurons showed both expansive and compressive (particularly at low CFs) responses. The term expansive means that a neuron is more sensitive (large changes in firing rate) to changes in correlation when the sounds are highly correlated, than when they are uncorrelated or decorrelated; compressive means the opposite, i.e., that a neuron is less sensitive to changes in correlation for highly, than for poorly, correlated sounds. This was an unexpected result because psychophysical

studies show that humans are most sensitive to decorrelation when interaural correlation is high (Gabriel and Colburn 1981) and this sensitivity is thought to be crucial for spatial perception (Durlach and Colburn 1978). Also, it is counterintuitive that the potential for an expansive relationship, as found in the pseudo-binaural responses in the AN, is not fully exploited at the binaural level in the IC.

Several synaptic sites of integration are interposed between the AN and IC. To better understand the transformation along the ITD pathway, we here apply the analysis developed in Mc Laughlin et al. (2008) to recordings obtained in the TB and compare BW and correlation sensitivity at three anatomical stages (the AN, TB, and IC). We find that BWs in the TB are similar to those in the AN and IC and that TB neurons are even more expansively sensitive to changes in stimulus correlation than AN or IC neurons.

METHODS

We present responses from single cells in the AN, TB, and IC of the cat, consisting of both archival and new data. The TB recording procedures have been described previously in Louage et al. (2005) and are only briefly described here. We compare the TB data with AN and IC measurements previously published in Mc Laughlin et al. (2008), with the addition of AN data from 65 fibers from one animal (bringing the total to 150 AN fibers). The stimuli used and the analysis techniques for measuring BW and correlation sensitivity are identical to those used in Mc Laughlin et al. (2008).

Recording

All procedures were approved by the K.U. Leuven Ethics Committee for Animal Experiments and were in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals. Adult cats with normal eardrums and middle ears were anesthetized with a mixture of acepromazine (0.2 mg/kg) and ketamine (20 mg/kg), administered via intramuscular injection. A venous cannula allowed infusion of Ringer's solution and sodium pentobarbital, which was titrated to maintain a deep anesthetic state as judged from clinical parameters (withdrawal reflex and heart and breathing rate). A tracheal cannula was placed and the basioccipital bone was exposed. The TB was exposed by drilling a longitudinal slit as close as possible to the medial wall of the bulla and about 3–5 mm rostral to the jugular foramen. A micromanipulator was used to support a hydraulic microdrive (Trent Wells, Coulterville, CA). Glass micropipettes, filled with 3 M NaCl or KCl, were positioned in the TB under visual control, just lateral or

medial to the rootlets of the abducens nerve. The angle of penetration ranged from 0 to 30 ° mediolaterally relative to the midsagittal plane. After placing the electrode in the TB, the basioccipital bone was covered with warm 3 % agar. Sounds were presented through dynamic speakers attached to earbars that were tightly inserted into the cut ear canals. From previous works (Spirou et al. 1990; Smith et al. 1991; Smith et al. 1993), it is known that TB responses as reported here are likely exclusively derived from spherical and globular bushy cells.

The stimuli were generated digitally using commercially available hardware (Tucker-Davis Technologies, Alachua, FL) and were compensated for the acoustic transfer function measured with a probe tube near the eardrum and a 12.7-mm condenser microphone (Brüel and Kjaer, Denmark). The neural signal was amplified, filtered, and displayed. Action potentials from individual fibers were discriminated and timed (1 μ s resolution).

Stimuli

When a single fiber was isolated, the excitatory ear was determined and the spontaneous rate (SR) was measured. A threshold tracking algorithm was used to determine the threshold curve characteristic frequency (CF_{thr}) and width of the threshold function 10 dB above the minimum threshold (horizontal dashed line and double arrow (BW_{thr})). The fiber's response to a number of frozen Gaussian broadband noises was then measured. All noise tokens used in this study had a bandwidth of 50–8,000 Hz, were 1,000 ms in duration, repeated 25–75 times (typically 35 repetitions) once every 1,200 ms. The first group of noise tokens was presented at 70 dB sound pressure level (SPL). We refer to the responses of such a group of noise tokens, at one SPL, as a dataset. If time allowed, datasets at other levels (between 30 and 80 dB SPL) were collected.

To compare the monaural TB responses with the AN and binaural IC responses, a coincidence analysis was used to calculate functions equivalent to noise delay functions (NDF) and interaural correlation functions (rICF). We refer to such functions as “pseudo-binaural” functions, but for simplicity, the adjective “pseudo-binaural” is not always included. For a detailed description of the reasoning behind the analysis, the reader is referred to Joris (2003), Louage et al. (2004), and Joris et al. (2006b). We count coincidences between pairs of responses to pairs of stimuli that would normally be delivered binaurally. Simple coincidence detection is generally thought to be the fundamental operation of neurons in the medial superior olive (MSO) (Goldberg and Brown 1969; Yin and Chan 1990; van der Heijden et al. 2013), which is the main source of ITD sensitivity for the frequencies and species (cat) reported here. A more

restricted sensitivity to ITDs is also present in low-frequency neurons in the lateral superior olive (LSO) (Finlayson and Caspary 1991; Joris and Yin 1995; Batra et al. 1997; Tollin and Yin 2005), but the focus in the present study is on the binaurally excited coincidence detectors in the MSO.

Noise delay functions

Responses to a noise token, referred to as the A + token, were first obtained from the fiber. Next, responses to the same noise token but with its polarity inverted (i.e., a phase shift across all frequencies of π radians), referred to as the A – noise token, was obtained from the same fiber. A pseudo-binaural NDF could then be calculated by counting the number of coincident spikes, within a chosen bin width (50 μ s), between two separate (sets of) spike trains recorded from the same monaural fiber, for different delays imposed between the two spike trains. Two types of pseudo-binaural NDF were obtained. The NDF to correlated noise is obtained by counting coincidences for all possible pairs of spike trains in response to the A + (or, separately, to the A –) stimulus. The number of coincidences is then summed and graphed as a function of delay. The same procedure is used to calculate the anticorrelated NDF, but now spike trains in response to the A + stimulus are paired with spike trains from the A – stimulus. Finally, the anticorrelated function is subtracted from the correlated NDF to yield the “difcor.” This subtraction is a simple means to linearize the responses and improves the extraction of BW and CF metrics described in the next section (Mc Laughlin et al. 2007).

Interaural correlation functions

To characterize correlation sensitivity, we studied the number of spikes (for binaural neurons) or the number of coincidences (for monaural neurons) as a function of stimulus correlation. Stimulus correlation was varied by creating noise tokens with different inter-token correlations from mixes of two independent tokens of broadband noise (Robinson and Jeffress 1963). Inter-token correlation values (1, 0.99, 0.96, 0.911, 0.844, 0.76, 0, –1) were spaced unequally in order to maximize the sampling close to an inter-token correlation of 1. For a more detailed description of this stimulus, see Louage et al. (2006). For the AN and TB fibers, we collected responses to these noise tokens with different inter-token correlations and then again used coincidence analysis to calculate a pseudo-binaural rICF. To maximize the number of different inter-token correlation values, all possible unique combinations of tokens were computed, 36 in total. This means that responses to each

token were compared to the responses to all other tokens, yielding a dense sampling of coincidence rate as a function of inter-token correlation value. For example an inter-token correlation of 0.96 is achieved using the 1 and 0.96 noise tokens, but an inter-token correlation of -0.96 can also be achieved by using the -1 and 0.96 noise tokens. Note that this differs from the analysis in our previous two papers (Mc Laughlin et al. 2007; Mc Laughlin et al. 2008), where only one token was used as the reference token and compared with the other tokens. The method used here (Louage et al. 2006) gives rICFs which are better fit by the power function (see below) but has a negligible effect on the bandwidth measurements. The pseudo-binaural rICFs for the AN presented here and also presented in Mc Laughlin et al. (2007, 2008) have been recalculated using the new method.

To quantify the relationship between inter-token correlation and spike rate, we fitted a power function (Shackleton et al. 2005) to the rICFs,

$$R(\rho) = a + b((1 + \rho)/2)^p \quad (1)$$

where R is the number of coincidences, ρ is the inter-token correlation, and a , b , and p are free parameters. In the fitting procedure, b and p could have any positive value but could not be negative. This means that the curvature of the rICF (both for expansive and compressive functions) is completely expressed by one parameter, namely p .

Extracting BW and CF metrics—curve fitting method

A curve fitting method was used to obtain a measure of CF and BW from the difcor (Mc Laughlin et al. 2008), further referred to as CF_{ND} and BW_{ND} to distinguish them from the measures based on the frequency threshold curve (CF_{thr} and BW_{thr}). The study of Mc Laughlin et al. (2008) contains a complete description of the method. The basic conceptual and methodical steps are briefly outlined here. Conceptually, a NDF can be viewed as the autocorrelation of filtered broadband noise: the correlation of the monaural output from one filter with the monaural output of another identical filter. We assumed that this filter had a Gaussian shape, determined by a mean and standard deviation. For initial values, we take a mean equal to the CF_{thr} and a standard deviation equal to half of BW_{thr} . The inverse Fourier transformation of this filter gives the cross-correlation function, in terms of correlation and delay, expected for a binaural neuron with that given CF_{thr} and BW_{thr} . The cross-correlation function is then converted to an estimated NDF using the rICF data measured on the

same neuron, i.e., the rICF data are used to convert correlation into spike rate. After comparison of this estimated NDF and the actual NDF, the filter parameters (mean and standard deviation) are adjusted and the procedure is repeated.

Figure 1 illustrates the six-step iterative procedure that was used to find the CF and BW. Step 1: An initial estimate of CF and BW was obtained from the threshold curve. Step 2: Using this estimate of CF and BW, a simple filter model was used to calculate a correlation-delay function (i.e., a cross-correlation function, for both correlated and anti-correlated stimuli). Step 3: The rICF data was used to convert the correlation-delay function to an estimated NDF (again both correlated and anti-correlated). Step 4: The estimated difcor was calculated by subtracting the estimated correlated NDF from the estimated anti-correlated NDF. Step 5: The sum of the squared differences was calculated between measured and estimated difcor. Step 6: A minimization method was used to improve the CF and BW estimate. Steps 2–6 were repeated until the best estimate of CF and BW was found. As in Mc Laughlin et al. (2008), a measure of the quality of fit (Q), based on the amount of variance accounted for by the curve fitting, was defined

FIG. 1. Schematic diagram of curve fitting method for estimating CF and BW using a correlation model based on a Gaussian filter. Measured data are shown in boxes with thick lines and curve fitting steps are shown in boxes with thin lines. Step 1: Initial CF and BW estimate from threshold curve. Step 2: Model estimates a correlation-delay function. Step 3: Correlation data is used to convert this to an estimated noise delay function (NDF). Step 4: Calculate the difcor. Step 5: Calculated sum of the squared differences (SSD) between measured and estimated difcor. Step 6: Use a minimization method to improve the CF and BW estimate. Repeat steps 2–6 until best estimate of CF and BW is found.

$$Q = 1 - \frac{\sum_k (Y_{fit_k} - Y_{data_k})^2}{\sigma^2} \quad (2)$$

where Y_{fit} is the estimated difcor, Y_{data} is the measured difcor, and σ_{data}^2 is the variance of the measured difcor. Fits with Q less than 70 % were excluded from the analysis.

Coincidence model

A coincidence model was developed to better understand the differences between TB and IC. We applied a simple coincidence operation to the responses of one TB fiber, mimicking the convergence of multiple monaural inputs from each ear onto a single coincidence detector with binaural excitatory inputs. Importantly, this model distinguished between “monaural coincidences” (simultaneous spikes from the same ear) and “binaural coincidences” (simultaneous spikes from different ears) by assigning different thresholds (number of coincident input spikes needed to trigger an output spike) to these two types of coincidences. Complex biophysical models have been used to investigate the effects of morphology and ion channel properties (Agmon-Snir et al. 1998; Zhou et al. 2005; Day and Semple 2011) on MSO processing (reviewed by Jennings and Colburn 2009). Our approach is different and simpler and is not intended to fully model the physiology of MSO neurons, but rather to explore the effect of several parameters on the rate of spike coincidences and its dependence on ITD and correlation. As inputs, we used responses recorded from a TB fiber with CF of 230 Hz, for which spike trains to 50 repetitions of the eight noise tokens with different interaural token correlations were available. Parameters of the model were the number of unilateral inputs, the monaural and binaural threshold (thr_{mon} and thr_{bin} , explained below), and the length of the coincidence window. First a number of spike trains, equal to the specified number of inputs, were randomly selected from the 50 available repetitions (all in response to the same noise token). One group of spike trains was selected as ipsilateral inputs and one group as contralateral inputs. A given spike train could never be simultaneously present ipsi- and contralaterally. For example, if the model is set to three inputs from each side, we randomly selected three spike trains as contralateral input and 3 different spike trains as ipsilateral input. Since all spike trains were from the same TB fiber, our procedure makes the implicit assumption that all inputs to the coincidence detector were identical in their properties. The spike trains were rebinned with a bin width equal to the coincidence window (50 or 250 μ s) and were, for each side, summed as in a PST histogram. The two PST histograms were

then fed into the coincidence detector. To simulate a NDF, the PST histograms were delayed relative to each other in steps equaling the coincidence window. To simulate a rICF, we combined noise responses corresponding to different combinations of interaural token correlations on opposite sides at 0 μ s ITD. For each value of ITD or interaural correlation, we counted the number of coincident spikes per coincidence window, both monaurally and binaurally. An effective *monaural* coincidence was defined as an occurrence of a number of spikes in one bin on one side that was $\geq thr_{mon}$. The number of monaural coincidences was constant for a given sample of spike trains and was not dependent on ITD or interaural correlation. An effective *binaural* coincidence was defined as an occurrence, within a coincidence window, of a number of spikes $\geq thr_{bin}$ with each side contributing at least one spike. For each binaural value (of ITD or interaural correlation), the bins resulting in effective monaural or binaural coincidences were counted as output spikes, with the restriction that only a single “output spike” could be generated for each bin. Thus, if in a given time bin, both thr_{mon} and thr_{bin} were exceeded, the output for that time bin was still only one spike. Finally, an absolute refractory period of 1 ms was applied, and the resulting spike count converted to spike rate. Each simulation condition was calculated 50 times using different random selection of spike trains and the resulting ITD and rICF functions were averaged.

Statistics

To compare BW and power fits in the TB with BW and power fits in the AN and IC data, trend lines were calculated using a loess approach (Cleveland and Devlin 1988). This was applied using the loess option in the “smooth” function in Matlab (Mathworks, Natwick, MA) with the span set to cover 50 % of the data. The data were bootstrapped (1,000 samples) using the “bootstrap” function in Matlab (Mathworks, Natwick, MA) to calculate the 95 % confidence intervals. Statistically significant differences were defined as regions where confidence intervals did not overlap. Linear regression (regress function, Matlab) was used to compare BW_{thr} with BW_{ND} measurements, and CF_{thr} with CF_{ND} measurements; $p < 0.01$ was considered statistically significant.

RESULTS

We present measurements from a total of 62 datasets recorded from 36 TB fibers in seven cats. Because of our interest in ITD sensitivity to fine-structure, we restrict our sample to fibers that show phase locking to fine-structure: the 36 fibers presented all had CFs

<2.7 kHz. Six datasets were excluded because of a poor agreement between the curve fitting method and the NDF (Q less than 70 %). First, we present some examples of BW measurements for individual TB fibers. Then the rICF data and BW measurements from the TB are compared with those in the AN and IC at a population level. We also compare the shape of the rICFs in the AN, IC, and TB and look at the effects of stimulus level on BW. Finally, we explore possible mechanisms with a simple model.

Individual datasets

Figure 2 shows results for a representative TB fiber. The pseudo-binaural NDFs to correlated noise (thick line) and anticorrelated noise (thin line) are shown in Figure 2A. The threshold curve is shown in Figure 2B and CF_{thr} was measured as the frequency at minimum threshold (vertical dashed line). Threshold curve bandwidth (BW_{thr}), i.e., the width of the threshold function 10 dB above the minimum threshold, is indicated with the horizontal dashed line and double arrow. This example illustrates that measuring BW from the threshold curve is noisy; measuring BW only a few decibels higher would give a much wider measure of BW. Figure 2E shows the fiber's expansive

rICF (solid line), which is well described by the power function fit (dashed line; $p = 5.45$). The rICF shows extreme rectification: anticorrelated stimuli result in low coincidence rates that are rather independent of the degree of anticorrelation, while correlated stimuli result in high coincidence rates that are steeply dependent on the degree of correlation. The extreme rectification is also reflected in the strong floor effect in the NDFs (Fig. 2A). The difcor, shown as the solid line in Figure 2C, was calculated by subtracting the anticorrelated NDF from the correlated NDF and normalizing that difference to its maximum. The estimated difcor which has been fitted to the measured difcor (see "METHODS," Fig. 1) is shown as the dashed line on Figure 2C. This estimate, based on both the tuning curve and rICF data, agrees relatively well with the measured difcor, and the corresponding filter shape is shown in Figure 2D ($CF_{ND} = 622$ Hz, $BW_{ND} = 299$ Hz, $Q = 86$ %). The threshold curve measures of BW and CF ($CF_{thr} = 559$ Hz, $BW_{thr} = 228$ Hz) roughly agree with those obtained from the curve fitting method.

Figure 3 shows another example of a TB dataset, this one collected from a fiber with a higher CF. Again, there is clear rectification in the NDFs to correlated and anticorrelated noise (Fig. 3A). The rICF (Fig. 3E) is well described by the power fit (dashed line, $p = 2.31$). In the

FIG. 2. Typical NDF and rICF for responses of a TB fiber. **A** NDF calculated from TB data. *Thick line*, response to correlated noise; *thin line*, response to anticorrelated noise. Peak ratio (PR) is calculated by dividing the height of the second peak (SP) by the height of the central peak (CP). **B** Characteristic frequency (CF_{thr}) is measured at the minimum on the curve. Bandwidth (BW_{thr}) is measured as the width of the curve 10 dB above threshold. **C** *Solid line*, difcor calculated by subtracting the anticorrelated NDF from the correlated NDF; *dashed line*, difcor estimated by the curve fitting method. **D** Filter shape estimated by the curve fitting method and the corresponding characteristic frequency (CF_{ND}) and bandwidth (BW_{ND}). **E** rICF (*solid line*) with fitted power fit (*dashed line*). p gives the power of the fit (see Eq. 1).

FIG. 3. Same analysis as in Figure 2 but for a TB fiber with higher CF. For the explanation, see the corresponding panels in Figure 2.

previous example (Fig. 2A, E), the coincidence rate to uncorrelated noise is very low so that there is little room for a further decrease in coincidence rate for inter-token correlations < 0 . This is not the case for the example of Figure 3, where the coincidence rate is high for uncorrelated noise (Fig. 3A, C), yet the rICF is still expansive. Calculation of the difcor (Fig. 3C, solid line) removes most of the rectification from the response and there is a good fit with the estimated difcor (Fig. 3C, dashed line). The resulting estimated filter shape and BW and CF estimate are shown in Figure 3D ($CF_{ND} = 2,416$ Hz, $BW_{ND} = 504$ Hz, $Q = 88$ %). Again, there is reasonable agreement between the threshold curve measurements ($CF_{thr} = 2,639$ Hz, $BW_{thr} = 626$ Hz) and the curve fitting measurements.

Population analysis

Curve fitting method versus threshold curve. The BW_{thr} measure used above is the traditional threshold tuning curve bandwidth at 10 dB above threshold. There are a number of issues associated with this measure. It is noisy as it relies on only three data points (the minimal threshold and two points at 10 dB above it); the points on the threshold curve are collected at different SPLs, and SPL can in itself affect bandwidth; and the 10 dB level, though

standardly used, is arbitrary. However, given its widespread use, we feel it is useful to compare the BW_{thr} with our BW_{ND} measure.

In the IC, there was considerable variation between BW estimated by the curve fitting method and BW measured on the threshold curve (Fig. 4A). There is a positive correlation between the two measures, but the range of BW_{ND} values is compressed compared to the BW_{thr} values. The dashed line shows the line of equality and the solid line shows the line of best fit found using linear regression (slope = 0.42, intercept = 90, $p = 1.5e - 10$, $r^2 = 0.53$). Similar relationships are found in both the AN and TB (Fig. 4C: slope = 0.39, intercept = 151, $p = 2.8e - 34$, $r^2 = 0.48$; and Fig. 4E: slope = 0.35, intercept = 211, $p = 5.7e - 5$, $r^2 = 0.3$, respectively); again the curve fitting method tended to estimate a narrower BW than that measured on the threshold curve.

We found good correlation between CF_{ND} and CF_{thr} in both the IC (slope = 0.90, intercept = 63, $p = 2.7e - 26$, $r^2 = 0.86$), the AN (slope = 0.89, intercept = 79, $p < 6.8e - 168$, $r^2 = 0.96$) and the TB (slope = 0.88, intercept = 123, $p = 3.3e - 43$, $r^2 = 0.98$) (Fig. 4B, D, and F, solid line is line of best fit). There appears to be little difference between the CF measured using the curve fitting method and that measured on the threshold curve. In general, the curve fitting method gave an excellent fit to the data

FIG. 4. Relationship between NDF and threshold curve estimates of BW and CF. **A** Relationship between NDF bandwidth (BW_{ND}) and threshold curve bandwidth (BW_{thr}) in the IC. **B** Relationship between NDF center frequency (CF_{ND}) and threshold curve center frequency (CF_{thr}) in the IC. **C**, **D** Same relationships in the AN. **E**, **F** Same relationships in the TB. In all panels, *solid lines* show line of best fit (linear regression), *text insets* report regression coefficients, and *dashed lines* show the line of equality.

with a mean Q of 92 % (5 % standard deviation) for all the AN data, a mean Q of 90 % (7 % standard deviation) for all the TB data, and a mean Q of 88 % (7 % standard deviation) for all the IC data.

Noise delay functions: bandwidth. Figure 5A shows the BW_{ND} as a function of CF_{ND} for all the TB fibers (red plusses). The BW_{ND} measurements from the AN and IC, previously reported in Mc Laughlin et al. (2008), are shown as triangles and circles, respectively. BW_{ND} measured in the TB, AN, and IC shows considerable overlap across the entire range of CFs with no clear separation between BW estimates from any of the three anatomical levels. The box centered around 500 Hz shows the range of binaural critical bands in humans estimated by a number of psychoacoustic studies using broadband stimuli (Kohlauch 1988; Kollmeier and

Holube 1992; van der Heijden and Trahiotis 1999) and is commented on in the “DISCUSSION.”

Figure 5B shows the trend lines for BW_{ND} as a function of CF_{ND} calculated using a loess fitting approach for the TB (red line), the AN (black line), and the IC (green line). The 95 % confidence intervals for each group are indicated with dashed lines. The confidence intervals for the TB, the AN, and the IC overlap across the entire CF_{ND} range, indicating that the BW_{ND} measurements are not statistically significantly different.

Because peripheral BW increases with SPL (Rhode 1971; Evans 1977; De Boer and de Jongh 1978; Carney and Yin 1988), we examined the effect of SPL in a limited number of fibers. Figure 6 shows BW_{ND} estimates for all TB fibers with datasets at two or more SPLs. Each symbol represents one animal and datasets from the same cell are joined by a line. There

FIG. 5. Relationship between BW and CF estimated from the NDFs. **A** Comparison of BW between AN (275 datasets), TB (62 datasets), and IC (71 datasets). Green circles represent the IC data, black triangles represent the AN data, and TB data are represented with a red plus sign. The box centered at a CF of 500 Hz indicates the range of critical bands measured in humans using wide band stimuli. **B** Trend lines for data shown in **A**. The thick line shows the trend line and dashed lines indicate 95 % confidence intervals. The green lines show the IC data, the black lines show the AN data, and the red lines the TB data. No statistically significant differences were found between the BW_{ND} measurements for AN, TB, or IC.

was a tendency for BW to increase with increasing SPL, but it was not statistically significant. This is in line with the results in IC and AN (Mc Laughlin et al. 2008), where a clear increase with SPL was also absent.

Noise delay functions: damping. NDFs of low CF neurons show a damped oscillatory pattern, as illustrated in Figures 2A and 3A. In a linear system, damping of a filter's impulse response is inversely proportional to its bandwidth (i.e., a narrow band system has a very oscillatory response). In a nonlinear system, the damping of the impulse response will still be influenced by the system's bandwidth. However, the degree of nonlinearity will also shape the impulse response, with the result that damping is no longer inversely

FIG. 6. Relationship between BW_{ND} and SPL in the TB. Data points from the same cell are joined by a line. Different symbols indicate data from different animals.

proportional to bandwidth. Since the auditory system is nonlinear, measurements of damping in NDFs are influenced by both BW and the degree of nonlinearity. Measuring $rICF$ is a way of quantifying the systems' nonlinearities. By taking the $rICF$ into account, the curve fitting method can separate how these nonlinearities shape the NDF from how BW shapes the NDF.

In previous studies from this laboratory, the damping of NDFs in the AN and IC was quantified (Joris et al. 2005, 2008). It was shown that there is a marked difference in damping between the two levels and that this difference is CF dependent. At the lowest CF s (<500 Hz), NDFs in the IC are more oscillatory than pseudo-binaural NDFs in the AN, while the opposite is true for CF s >500 Hz. In a linear system, this would suggest BW differences between the AN and IC. However, the present results (Fig. 5) and our previous studies (Mc Laughlin et al. 2007; Mc Laughlin et al. 2008), which take account of each neuron's nonlinearities, show that the BW distribution is very similar in the AN, TB, and IC. This suggests that the damping differences are due to differences in the nonlinearities present in the AN, TB, and IC. In this and the following section, we examine the relationship between damping and correlation sensitivity in these structures to elucidate any differences.

To quantify damping, we measured the "peak ratio" of the correlated NDFs (Yin et al. 1986; Joris et al. 2005). We defined the central peak (CP) as the largest peak in the NDF and the secondary peaks (SP) as the next two closest peaks (Figs. 2A and 3A). The peak ratio was then calculated as the mean height of the secondary peaks to that of the central peak: strong damping results in small peak ratios. Note that we did not use the BW measure developed by Joris et al. (2005) based on the envelope of the NDFs calculated with the Hilbert transform because the pseudo-

binaural NDFs in the TB are frequently too “peaked” or rectified (e.g., Fig. 2A) to define a meaningful envelope with that method. In Figure 7A, we examine the relationship between the degree of expansion/compression in the rICF data (i.e., the nonlinearities), using the power fit variable p (ordinate), and the degree of damping in the NDFs, measured with the

FIG. 7. Population plots of power fit variable p . AN fibers are represented by triangles, open black triangles represent high SR fibers (SR > 18 spikes/s), and filled gray triangles are for low SR fibers (SR < 18 spikes/s). IC cells are represented by green circles. TB fibers are represented by a red plus. **A** The power fit variable p is plotted against the peak ratio—a measure of damping of the NDF. **B** Measured and estimated power fit variable p against characteristic frequency for the IC, AN, and TB populations. **C** Trend lines and 95 % confidence intervals for the data shown in **B**.

peak ratio (abscissa). Plusses are the values for the TB data. Values for the AN and IC data previously reported in Mc Laughlin et al. (2008) are shown on the same plot as triangles and circles, respectively. For the AN data, low SR (<18 spikes/s) fibers are shown as gray triangles and high SR fibers as empty triangles. The TB data overlap with the data from the AN and IC. There is a negative correlation between the peak ratio of the NDFs and the expansiveness of the rICF, i.e., NDFs that are heavily damped (small peak ratios) tend to have an expansive rICF (high p). Combined with Figure 5, i.e., with the similarity in BW between the three groups of neurons, this indicates that much of the damping present in NDFs is not related to the BW of the neuron but rather to the neuron’s sensitivity to changes in correlation. An exception to this trend is TB and AN fibers with higher CFs (>2,400 Hz). This is not unexpected since the responses of that population of fibers (indicated by the dashed box in Fig. 7A) contains an envelope component (Louage et al. 2005; Louage et al. 2006), which alters the relationship between peak ratio and rICF expansiveness.

Correlation functions. Figure 7B shows the power fit variable p as a function of CF for our AN, TB, and IC data. Figure 7C shows the trend lines and 95 % confidence intervals for the same data. When compared to the AN and IC, the expansiveness of the TB rICFs is striking. In the AN, p tends to be around 2. As we move along the ITD processing pathway to the TB, we see a much wider range of values for p , with lowest values around 2 and some extremely expansive rICFs ($p > 10$), which are not seen in the AN (note that the ordinate in Fig. 7A is logarithmic). The non-overlapping AN and TB confidence intervals, across much of the CF_{ND} range (Fig. 7C), show that these difference are statistically significant. Thus, the TB provides the binaural system with input spike trains of such temporal precision that the number of coincidences steeply depends on interaural correlation, especially for values near perfect interaural correlation. However, in the IC, such extremely expansive rICFs are not encountered. In fact, we find a fair number of compressive rICFs in the IC ($p < 1$), particularly at lower CFs, which are not seen in the AN or TB. For much of the low CF range (<1,000 Hz), the IC confidence intervals do not overlap with the AN and TB confidence intervals (Fig. 7C), indicating that these difference are statistically significant. This explains why Joris et al. (2005, 2008) found differences in NDF damping between the IC and AN, while Mc Laughlin et al. (2008) found no differences in BW.

We see two possible reasons why the potential for extreme correlation sensitivity present in the TB is not apparent at the level of the IC. One possibility is that

the extreme correlation sensitivity is present in the MSO but is somehow lost or degraded by the level of the IC. This possibility seems unlikely. Visual comparison of NDFs in MSO (Yin and Chan 1990; Bremen and Joris 2013) and IC suggest more overlap between MSO and IC than between MSO and TB. Coffey et al. (2006) also found no difference in the expansiveness of IC neurons versus subcollicular (presumably SOC) neurons. A more likely possibility is that the extreme correlation sensitivity in the TB is not fully exploited by the system, which would imply that our simple scheme of coincidence detection does not adequately capture the actual process in the MSO. In the final section, we explore a number of ways in which this process may differ from our simple coincidence counts used to generate the pseudo-binaural functions and examine the effects on sensitivity to delay and correlation.

Possible sources of binaural compression

We refer to the difference in expansivity between monaural neurons (AN and TB fibers) and binaural (IC) neurons as “binaural compression.” In short, it refers to the observation that the spike rate of binaural neurons, even when measured at their optimal ITD (“best delay”), grows less with increasing correlation than the rate of coincidences in monaural neurons. In this final section, we use a simple model to examine factors that could contribute to such compression. Our goal is not to be exhaustive or to attain physiological realism, but rather to give an indication of the kind of factors that might be considered. A wide range of parameter values was explored (Franken and Joris 2012) and will be separately reported, but for the purposes of the present paper, only a single, representative example is illustrated. As input to the model, we use the response of a TB fiber with CF of 230 Hz, which was near the extreme in terms of spike timing as quantified with the different measures used in previous studies. Its maximum vector strength to a short CF tone was 0.99 and was 0.96 to a long (1 s) tone at 200 Hz; spontaneous activity was 1.2 spikes/s; correlation index to broadband noise (Joris et al. 2006a) was 22. The top panels of Figure 8 show the NDF (Fig. 8A) and rICF (Fig. 8B) using only a single input on each side, with a high monaural threshold ($\text{thr}_{\text{mon}} = 6$) and a low binaural threshold ($\text{thr}_{\text{bin}} = 2$). With these parameters, only binaural coincidences occur, at a low rate. The resulting NDF and rICF are nearly identical to the simple coincidence counts used in this paper, such as illustrated in Figures 2A, E and 3A, E. The rICF is extremely expansive ($p = 9.1$).

The first—and in a sense most fundamental—issue that we examined is the effect of convergence of multiple

FIG. 8. NDFs (left column) and rICF (right column) for different simulation parameters, using spike trains from one TB fiber as input. The dashed line in the right panels shows power fit. **A, B** Convergence of a single ipsi- and contralateral input. Monaural threshold (thr_{mon}) was 6, binaural threshold (thr_{bin}) was 2, coincidence window was 50 μs . **C, D** Convergence of 10 ipsi- and 10 contralateral inputs, drawn from the same TB fiber, with $\text{thr}_{\text{mon}}=6$ and $\text{thr}_{\text{bin}}=2$. **E, F** As in **A** and **B** but jitter was randomly added to spike trains (see text) before counting coincidences. **G, H** As in **A** and **B**, but using a coincidence window of 250 μs .

inputs. Coincidence detection is akin to an “AND” operation and has the disadvantage that the output rate is always lower than that of its inputs, since input spikes that are not coincident do not result in an output. The

output rates of our coincidence analyses are therefore always unphysiologically low (e.g., Figs. 2A and 3A, compare with spike rates in Yin and Chan 1990). The output rate can be increased by increasing the number of converging inputs, but there is an inherent source of “compression” in coincidence detection: no matter how many coincident input spikes occur within a coincidence window, only one output spike can be generated. Perhaps this accounts for the binaural compression observed in the previous sections. The convergence ratio to MSO neurons is unknown, but indirect estimates suggest that it is rather low (Couchman et al. 2010; Franken and Joris 2012; Franken et al. 2013; van der Heijden et al. 2013). Figure 8C, D shows the output for 10 inputs on each side, using the same firing thresholds as before ($\text{thr}_{\text{mon}} = 6$ and $\text{thr}_{\text{bin}} = 2$). As expected, the higher number of input fibers increases the output rate of the coincidence detector (to ~ 180 spikes/s). It also broadens the central peak of the noise delay function and compresses the rICF function ($p = 4.2$). These changes make the output indeed more akin to responses observed in MSO and IC, but the expansivity of the rICF is still at the upper range observed in IC for that CF (Fig. 7B). Note also that monaural coincidences cause a baseline response level at unfavorable ITDs.

Another parameter that would be expected to soften sharp peaks in NDFs and steep expansion in rICF is temporal jitter across the inputs. Some jitter must unavoidably be present, for example consequent to differences in axon parameters for the different inputs from one side (length, diameter, intermodal distance) (Beckius et al. 1999; Karino et al. 2011). Adding a random amount of jitter to each input (chosen from a Gaussian distribution with mean 0 ms and standard deviation of 0.2 ms) causes again broadening of the central peak of the noise delay function (Fig. 8E) and compression of the rICF function (Fig. 8F; note that only two inputs are used for panels E–H). The effects are similar to those in Figure 8C, D except that there is no elevation of base response rate due to monaural coincidences, since there is only a single input on each side. Similar but much more limited changes occur when the coincidence window is lengthened to 250 μs (instead of 50 μs). This fivefold increase affects the overall spike rate (which peaks at ~ 75 spikes/s), but the change in shape of the NDF and rICF is surprisingly small.

DISCUSSION

In a series of previous reports (Joris et al. 2005; Mc Laughlin et al. 2007; Joris et al. 2008; Mc Laughlin et al. 2008), we contrasted binaural IC responses with pseudo-binaural responses from AN fibers, to gain insight into the mechanisms underlying ITD sensitivity. We studied NDFs obtained in the IC, i.e., ITD

functions to broadband noise, and their monaural equivalents in the AN, i.e., coincidence counts as a function of delay between monaural responses. At low CFs, both sets of functions have a damped oscillatory shape. These studies revealed that the damping of NDFs is dependent on both spectral BW and sensitivity to interaural correlation: AN and IC neurons from a similar CF range do not differ in BW but do show differences in NDF damping and in sensitivity to interaural correlation, with more expansive correlation functions corresponding to more strongly damped NDFs. Also, these studies showed, surprisingly, that binaural neurons in the IC do not show the steep dependence on ITD or interaural correlation predicted from a simple coincidence operation on AN spike trains. In this report, we build on this approach by focusing on a higher monaural stage in the ITD processing pathway, namely the TB. We recorded responses in the TB using the same broadband noise stimuli used in the previous reports and applied the same analysis techniques, allowing us to compare three different stages in the ITD processing pathway.

Bandwidth measurements

We used a curve fitting method to extract spectral BW from binaural NDFs collected from IC neurons. Using the same curve fitting method, we extracted BW measurements from pseudo-binaural NDFs calculated from responses recorded in the AN and TB using a coincidence analysis. At all three levels, we saw an increase in BW with increasing CF, consistent with previous studies that measured BWs in AN fibers using tones or clicks (Kiang et al. 1965; Pfeiffer and Kim 1972; Liberman 1978; Rhode and Smith 1985) or noise (Ruggero 1973; Evans 1977; De Boer and de Jongh 1978; Carney and Yin 1988; Joris et al. 2005).

We calculated trend lines and confidence intervals for BW_{ND} as a function of CF_{ND} and found no differences in BW between the three anatomical levels (Fig. 5). Some psychophysical studies suggest that binaural critical bands are two or three times broader than monaural critical bands (Bourbon and Jeffress 1965; Sondhi and Guttman 1966; Zurek and Durlach 1987). However, other psychophysical studies show that they are the same (Hall et al. 1983; Kohlrausch 1988; van der Heijden and Trahiotis 1998, 1999). Our results suggest that convergence of frequency channels along the ITD processing pathway, up to the level of the IC, is such that there is no measurable broadening in the range of frequencies affecting ITD sensitivity. The BW determined by cochlear filtering and measured in the AN is preserved in the TB, is presumably preserved during the coincidence detection process in the MSO, and is still preserved in the IC. Note that our definition of BW is restrictive: It

is the range of stimulus frequencies that affects coincidence patterns in AN or TB fibers, or ITD sensitivity in binaural neurons. The similarity of BW in AN, TB, and IC does not preclude that neurons at these levels differ in the extent of convergence of frequency channels in a way that does not affect coincidence patterns or ITD sensitivity. For example, an IC neuron could receive a monaural, nonphase-locked, wideband input that affects overall response rate and the frequency threshold curve, but that would not affect the shape of the NDF.

The BW values measured here are broad compared to published behavioral values for human (Fig. 5A, box). This is in line with behavioral measurements in cats, which show a smaller binaural masking level difference (BMLD) (Hoppe and Langford 1974; Wakeford and Robinson 1974; Geesa and Langford 1976) and a wider BW than humans in monaural conditions (Watson 1963; Pickles 1979). Similar conclusions seem to apply to the guinea pig (Palmer et al. 2000) and gerbil (Lingner et al. 2012). Physiological measurements of monaural frequency tuning on primates, including humans, also point in the same direction (Joris et al. 2011; Verschooten et al. 2012), i.e., their peripheral frequency tuning being sharper than in cats, though admittedly the differences are clearest at frequencies above a few kilohertz.

Relationship between SPL and bandwidth

We reported previously that BW measured using a spectrally manipulated stimulus (Mc Laughlin et al. 2007) increases slightly with increasing SPL in both the IC and AN. Mc Laughlin et al. (2008) measured BW from NDFs and also found a slight increase in BW with increasing SPL (IC 1.0 Hz/dB, AN 3.5 Hz/dB). Using a different metric, Joris et al. (2005, 2008) also reported an increase in temporal damping with increasing SPL in both the IC and the AN, consistent with an increase in BW. For the TB fibers in this study, the SPL dependence of BW appeared to be more varied among TB fibers than in the AN or IC with some TB fibers showing very large increases in BW and others showing small but consistent decreases.

Interaural correlation

In the IC, we measured the response of binaural neurons to changes in interaural correlation. Using the same stimuli, we collected responses from monaural fibers in the AN and TB and computed pseudo-binaural responses to changes in correlation using a coincidence analysis. We could then quantify the compressiveness or expansiveness of the rICFs by fitting them with a power function (Shackleton et al. 2005) and compare correlation responses at three levels in the ITD processing pathway. In

the AN, all but one fiber showed an expansive rICF. This means that if the auditory system processed the spike timings in the AN with a simple coincidence detector, having two identical excitatory inputs, the output firing rate would be very sensitive to changes in interaural correlation. The rICFs in the TB are even more expansive suggesting that a binaural system with a simple coincidence detector based on TB spike timing would be even more sensitive to changes in correlation, as was indeed shown by Louage et al. (2006) using signal detection analysis. However, at the level of the IC, we do not observe this extreme correlation sensitivity—a phenomenon we refer to here as binaural compression.

There are several possible explanations for the reduced correlation sensitivity in the IC relative to the TB. First, the phenomenon of binaural compression perhaps arises at the level of the IC rather than at the level of the MSO. A number of pieces of evidence suggest that this is unlikely: (1) NDFs of MSO neurons (Yin and Chan 1990; Bremen and Joris 2013) look rather “IC-like”, and (2) a study by Coffey et al. (2006) found no differences in correlation sensitivity between IC and subcollicular (presumably SOC) neurons. Of course, additional data may reveal systematic differences. A second possibility is that our TB recordings are not from fibers that give input to the MSO. For reasons discussed earlier (Louage et al. 2005; Joris and Smith 2008), we are confident that the vast majority of fibers recorded here are from spherical and globular bushy cells and feed into the ITD pathway. However, there is likely a recording bias (e.g., based on fiber diameter or location), and the ratio of recordings from the two cell types is uncertain, so it is difficult to judge how representative our recordings are for the entire bushy cell population. Since spherical bushy cells are excitatory to the MSO and globular bushy cells inhibitory (via the medial and lateral nucleus of the trapezoid body), and because these two cell types may differ in their responses to noise, there is also uncertainty regarding the temporal properties of the excitatory and inhibitory inputs converging on the MSO. Third, we have only looked at the number of coincidences, not at the variability in the number of coincidences. Perhaps response variance is decreased in the IC responses, so that IC neurons perform equally well on binaural tasks as TB neurons, notwithstanding the differences in shape of rICFs and NDFs in the two populations. Arguing against this possibility is the observation that decorrelation thresholds are lower in TB fibers than in IC neurons (Shackleton et al. 2005; Louage et al. 2006). Finally, our scheme of coincidence analysis is only a crude approximation of the actual process occurring in MSO neurons. We illustrated a few factors that give more realism to the coincidence counts, without resorting to a full-fledged MSO model (Fig. 8). Most importantly, we wanted to check for the inherent compression expected from converging inputs (see “RESULTS,” section “Possible Sources of Binaural Compression”: the fact that only a

single output spike can be generated within a stimulus cycle, no matter how many input spikes). A mere increase in the number of convergent inputs indeed causes changes consistent with the effect of binaural compression, but overall these changes are surprisingly modest (Fig. 8C, D). Introduction of jitter among the inputs (Fig. 8E, F) or broadening of the coincidence interval (Fig. 8G, H) also gave some binaural compression and broadening of peaks in the NDF, but again the effects are modest. One factor not tested here is the convergence of fibers of different CF. A preliminary exploration (not shown) suggests that such convergence can cause strong binaural compression and broadening of peaks in the NDF. Similar effects are seen for NDFs at the level of the AN (Joris et al. 2006c). Unfortunately, we do not have enough TB recordings from individual animals at closely spaced CFs to evaluate the plausibility of that factor. Finally, one factor which is difficult to assess with the data available but which we think must be important is that it is unlikely to have two SBC fibers within an animal (and, even more unlikely, that would converge on the same MSO neuron) that give responses to broadband noise that are as similar to each other as two spike trains from the same fiber. The AN input to SBCs is dominated by only a couple of endbulbs of Held (Ryugo and Sento 1991), and each AN fiber forms only one large endbulb (Rouiller et al. 1986; Sento and Ryugo 1989), so that the mix of dominant inputs and their exact timing pattern must be unique for each SBC. A parametric study of the effects of these diverse factors is needed to better understand their relative roles in generating binaural compression.

The finding of weaker binaural sensitivity than expected from the acute temporal coding in the input pathways does not alter our view of the AN-to-TB transformation as a preprocessing step for improved binaural interaction. It points to the importance of a better characterization of what “coincidence detection” actually means. Ideally, the MSO output should only depend on binaural, spatial sound parameters. ITD sensitivity in IC is fairly robust against variations in SPL and behaves surprisingly linear with spectral changes (Yin et al. 1986; Joris et al. 2005), in fact more so than expected from AN responses (Joris et al. 2008). Likewise, it is less vulnerable to degradation by reflections in reverberant environments than predicted from a simple crosscorrelation model (Devore et al. 2009). Compared to AN fibers, responses of bushy cells are more temporally precise and reproducible and have higher sensitivity, over a wider range of SPLs, for (pseudo-binaural) changes in correlation and ITD (Louage et al. 2006; van der Heijden et al. 2011a). However, the output spike rate of a coincidence detector receiving only two identical inputs is unphysiologically low. To achieve higher output spike rates, convergence of multiple afferents from each side onto the coincidence detector is needed, which

creates two new issues. Convergence unavoidably introduces some degree of decorrelation between inputs, because of monaural and binaural differences in CF and differences in exact timing patterns even for neurons with identical CF. It also introduces a base level of monaural coincidences which do not convey binaural information. In line with previous work from this laboratory, the finding here of similar spectral bandwidth but more expansive correlation sensitivity in bushy cells, compared to AN and IC neurons, suggests the hypothesis that enhanced response features of bushy cells enable the combination of invariant binaural temporal sensitivity and high output spike rates. Perhaps the enhanced response features of bushy cells enable the circuit to better deal with the often conflicting demands of a biological implementation of coincidence detection such as a short coincidence window and high output rates in the face of constraints such as variability of neural response and limitations in the precision of wiring.

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