Comparison of Bandwidths in the Inferior Colliculus and the Auditory Nerve. I. Measurement Using a Spectrally Manipulated Stimulus

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McLaughlin M, Van de Sande B, van der Heijden M, Joris PX. Comparison of bandwidths in the inferior colliculus and the auditory nerve. I. Measurement using a spectrally manipulated stimulus. J Neurophysiol 98: 2566–2579, 2007. First published September 19, 2007; doi:10.1152/jn.00595.2007. A defining feature of auditory systems across animal divisions is the ability to sort different frequency components of a sound into separate neural frequency channels. Narrowband filtering in the auditory periphery is of obvious advantage for the representation of sound spectrum and manifests itself pervasively in human psychophysical studies as the critical band. Peripheral filtering also alters coding of the temporal waveform, so that temporal responses in the auditory periphery reflect both the stimulus waveform and peripheral filtering. Temporal coding is essential for the measurement of the time delay between waveforms at the two ears—a critical component of sound localization. A number of human psychophysical studies have shown a wider effective critical bandwidth with binaural stimuli than with monaural stimuli, although other studies found no difference. Here we directly compare binaural and monaural bandwidths (BWs) in the anesthetized cat. We measure monaural BW in the auditory nerve (AN) and binaural BW in the inferior colliculus (IC) using spectrally manipulated broadband noise and response metrics that reflect spike timing. The stimulus was a pair of noise tokens that were interaurally in phase for all frequencies below a certain flip frequency (fflip) and that had an interaural phase difference of π above ffflip. The response was measured as a function of ffflip and, using a separate stimulus protocol, as a function of interaural correlation. We find that both AN and IC filter BW depend on characteristic frequency, but that there is no difference in mean interaural correlation. We find that both AN and IC filter BW depend on characteristic frequency, but that there is no difference in mean interaural correlation.

INTRODUCTION

Auditory spectral bandwidth (BW) is the measure of an ear or a neuron’s ability to integrate over adjacent spectral regions and is a determining factor in frequency resolution. Auditory bandwidth limits the effect of masking and is therefore key to our understanding of how humans perform everyday listening tasks such as detecting speech in a noisy environment. This has been studied extensively for monaural hearing, but the concept of bandwidth can be extended to binaural neural processing. In this case bandwidth is a measure of the range of frequencies to which a binaural neuron is sensitive to binaural differences. Although it is intuitive that the decomposition of a sound into different frequency channels is of fundamental value for monaural hearing, this is less obvious for binaural hearing.

In humans, azimuthal sound localization is a binaural process where the dominant cue is interaural time difference (ITD) (Macpherson and Middlebrooks 2002; Middlebrooks and Green 1990; Wightman and Kistler 1992). These ITDs are analyzed by the brain using a process similar to cross-correlation (Colburn 1977). For a narrowband filter the cross-correlation function would be more oscillatory than that for a broader filter, where the cross-correlation function would be more damped and the central lobe narrower. For some binaural tasks, such as the localization of a single source in an environment lacking significant reflections, the band-pass filtering in the cochlea thus seems disadvantageous because it broadens the cross-correlation functions. This could be offset by converging frequency channels in the CNS, allowing the brain to compare the signal at the two ears over a wide frequency range.

In line with this reasoning, a number of psychoacoustic studies in humans have reported wider bandwidths under binaural listening conditions than under monaural or diotic listening conditions, by a factor of 2 or 3 (Bourbon and Jeffress 1965; Sondhi and Guttmann 1966; Zurek and Durlach 1987). However, other studies report no difference between monaurally and binaurally measured BW (Hall et al. 1983; Kohlrausch 1988; van der Heijden and Trahiotis 1998, 1999).

Physiologically, spectral analysis starts in the cochlea and is further elaborated in the CNS, where both frequency sharpening and broadening have been described (Ehret and Merzenich 1988; Suga 1995). Another example at the level of the midbrain is found in the barn owl, which shows spectral convergence in ITD-sensitive neurons (Mazer 1998; Peña 2000; Peña et al. 2001; Takahashi and Konishi 1986).

In mammals with low-frequency hearing, it has been shown that sensitivity to ongoing ITDs changes in several respects between the superior olivary complex (SOC) and the midbrain (Fitzpatrick et al. 1997; Kuwada et al. 2006; McAlpine et al. 1998; Spitzer and Semple 1998). However, whether spectral tuning in ITD-sensitive neurons changes along the auditory pathway has not been studied explicitly. Also, monaural spectral tuning has not been systematically compared with binaural spectral tuning. Our first goal was to physiologically measure bandwidths in ITD-sensitive cells at the level of the midbrain, using a purely binaural stimulus paradigm. We adapted the paradigm used in the behavioral experiments of Kohlrausch (1988) and of Kollmeier and Holube (1992). Our second goal was to compare these bandwidths of ITD-sensitive neurons with the monaural auditory periphery. To enable us to measure a monaural BW, we first analyze the responses recorded in the auditory nerve (AN) using a coincidence-detection technique and then derive a bandwidth with the same analysis also used on ITD-sensitive neurons. By doing this, we effectively mea-

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sure the range of stimulus frequencies that affect the coding of temporal structure in the response of AN fibers. Henceforth, we simply refer to this range as the “monaural BW.” Because of our interest in mechanisms underlying ITD sensitivity, our measurements focus on neurons with low characteristic frequency (CF).

METHODS

Overview

In this study we measured BW in binaural cells in the inferior colliculus (IC) using a binaural broadband noise stimulus that was interaurally in phase below a certain frequency, \( f_{\text{flip}} \), and \( \pi \) radians out of phase above \( f_{\text{flip}} \) (Fig. 1A). We measured the spike rate of binaural cells to this stimulus configuration as a function of \( f_{\text{flip}} \) (Fig. 1E, expected response). We then used a curve-fitting method to extract a measure of BW and CF from this binaural response.

To obtain a comparable measure of BW in monaural cells we also recorded responses to these same stimuli in AN fibers. Here, the various ipsi- and contralateral stimulus components from the binaural experiment were presented sequentially and monaurally to a single ear, and the response of auditory nerve fibers was measured. Afterwards a coincidence analysis was used to calculate a “pseudobinaural” response from the monaural data (Fig. 2). The same curve-fitting method as used for the real binaural data was then used to estimate CF and BW for monaural cells.

Recording

We recorded from the IC and the AN in separate experiments. IC data were obtained from eight animals and AN data were obtained from six animals. Our methods of single-unit recording in the IC and the AN have been described before (Joris 2003; Louage et al. 2004). 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. Cats with clear eardrums were induced with an intramuscular injection of a 1:3 mixture of acepromazine (0.2 mg/kg) and ketamine (20 mg/kg). Anesthesia for surgical preparation and recording was maintained with sodium pentobarbital infused through a femoral vein, to eliminate the withdrawal reflex to toe pinch. The animals were placed on a heating pad in a double-walled soundproof chamber.

FIG. 1. Flip-frequency (\( f_{\text{flip}} \)), noise delay (ND), and correlation stimulus configurations and resulting responses. A and B: spectral representation of the 2 \( f_{\text{flip}} \) stimulus configurations, where \( A^- \) (black block) is \( \pi \) radians out of phase with \( A^+ \) (open block). \( f_{\text{flip}} \) is varied systematically. C and D: representation of the frequency selectivity of the binaural response. Effective binaural interaural correlation (\( \rho \)) within the filter as a result of the stimulus configuration is shown at the top of the figure (\( \rho = +1 \) or \( \rho = -1 \)). Thick lines: broadband filter; thin line: narrowband filter. E and F: expected rate curves showing the total response from the neuron as \( f_{\text{flip}} \) moves through the filter. Small blocks under the frequency axis show the particular stimulus configuration at that frequency. Thick lines: response from broadband filter; thin line: response from narrowband filter. G: interaural time delay (ITD) is varied between the 2 ears by delaying interaurally correlated or anticonrelated noise. H: ND functions. Thick line: expected response to correlated noise; thin line: expected response to anticonrelated noise. I: interaural correlation between 0 and 1 is achieved by presenting a mixture of independent noise token 1 (Ind 1: open block) and independent noise token 2 (Ind 2: shaded block) in one ear while presenting Ind 1 in the other. An interaural correlation of 0 results from all Ind 2 in one ear and Ind 1 in the other. A mixture of the phase inverted Ind1 (Inv Ind1: black block) and Ind2 in one ear and Ind 1 in the other gives an interaural correlation between 0 and -1. J: representation of a typical nonlinear rate vs. interaural correlation function (rICF); response rate increases with increasing interaural correlation.
attenuated chamber (Industrial Acoustics, Niederkruiten, Germany). The bullae were vented with a polyethylene tube.

The IC was exposed anterior to the tentorium; some tentorium was removed in cases where it severely limited access to the IC. Neurons were isolated with glass-insulated tungsten or indium electrodes. The dorsal border of the central nucleus of the IC was defined physiologically by the presence of background discharges phase-locked to binaural beats of low-frequency pure tones (Kuwada et al. 1979) and the IC was histologically processed to confirm the site of recording.

The AN was exposed through a posterior fossa approach, involving the removal of a small area of cerebellum. Single AN fibers were isolated with glass micropipettes filled with 3 M NaCl, inserted into the nerve trunk under visual guidance.

**IC stimuli**

**NOISE DELAY AND THRESHOLD CURVE.** We first tested the neuron’s sensitivity to interaural time delays (ITDs) by collecting noise delay (ND) functions (Yin et al. 1986). The stimulus consisted of a pair of corre!ated (A+ A−) or antecorrelated (A− A+) pseudorandom broadband noise tokens (lower cutoff 50 or 100 Hz; upper cutoff between 8 and 10 kHz), where A+ represents the original noise token and A− is the same noise token with inverted waveform, which corresponds to a π phase shift at all frequencies. The ITD was systematically varied while measuring the average firing rate. Based on a quick preliminary assessment, the range of ITDs and step increment were chosen to appropriately characterize the shape of the ND functions. Typical stimulus parameters [(duration/repetition interval) × number of presentations] were 1/1.5 s × 10 or 20, or 5/6 s × 3. Figure 1G shows a schematic of the stimuli and Fig. 1H shows the corresponding responses. In the subsequent stimulus protocols we will examine the effect of changes in the stimulus fine structure on the response of the neuron. Therefore we wanted to find the delay at which the neuron was most sensitive to changes in fine structure. The “best delay” (BD) of the neuron was defined as the ITD at which the difference between the correlated and anticorrelated responses is maximal. This is typically, but not always (see RESULTS; Figs. 6 and 7), also the ITD at which the response to correlated noise is maximal. All subsequent binaural stimuli were presented with an ITD equal to the neuron’s BD.

The spontaneous rate (SR) was measured and a threshold-tracking algorithm with ipsilateral, contralateral, and/or binaural stimulation (using an ITD equal to the BD) was used to determine the characteristic frequency (CFthr). The binaural threshold curve was used in further analyses. However, it was not always possible to obtain a binaural threshold curve and in these cases the ipsilateral or contralateral threshold curve was used. The threshold curve bandwidth (BWthr) was measured at 10 dB above the CF threshold.

**SPECTRAL DATA.** Next we measured the BW and CF of the neuron using a spectrally manipulated stimulus (BW and CF) similar to that used by Kohlrausch (1988) and Kollmeier and Holube (1992). This stimulus closely resembles the binaural edge pitch stimulus (Klein and Hartmann 1985). Both ears were stimulated by Gaussian broadband noise tokens (lower cutoff 50 or 100 Hz; upper cutoff 8 or 10 kHz) that differed only in their interaural properties. In one ear a reference token (A+) was presented, whereas in the other ear the same noise token was presented but now with a phase shift of π radians for all frequency components above a given frequency, ftyp (Fig. 1A). We denote this mixed polarity noise as A+ A−, where the A indicates that it was the same noise token as the reference token and the “+ +/−” refers to the phase shift of π radians above a certain ftyp. The pair of noise tokens is referred to as A+ A−. To evaluate the importance of different frequency components in determining the binaural responses ftyp was then systematically varied over a frequency range estimated from the threshold tuning curve. The ftyp range over which an increase in spike rate occurs reflects the frequency selectivity of the binaural response (illustrated schematically in Fig. 1C), which reflects the “binaural bandwidth.” This is illustrated by the following example. For a cell with a narrow bandwidth (Fig. 1C, thin line) only a narrow band of frequencies around CF affects the response of the cell. When ftyp is increased from its lowest value, the spike rate is not affected until ftyp enters this narrow region. On increasing ftyp further, it quickly moves out of this frequency band. The resulting growth function (spike rate as a function of ftyp) is thus steep (Fig. 1E, thin line). Conversely, when the bandwidth is large (Fig. 1C, thick line), a wider region of frequencies shapes the binaural response and the function grows more gradually (Fig. 1E, thick line).

This sequence was repeated with the same reference token (A+) in the same ear but the mixed polarity tokens now with a phase shift of π radians below, rather than above, a given ftyp (Fig. 1B). This mixed polarity token is referred to as A− A+, where the −/+ indicates that

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**FIG. 2.** Construction of pseudobinaural response from auditory nerve (AN) data. A: stimulus configurations are presented sequentially to the same ear. Coincidence detection (within a 50-µs time window) between the relevant spike trains (B) results in ftyp functions (C). D: relevant combinations of stimulus pairs for each frequency that result in the ftyp functions. Open block: A+; black block: A−. **J Neurophysiol • VOL 98 • NOVEMBER 2007 • www.jn.org**
there was a phase shift of $\pi$ below $f_{\text{rip}}$. This stimulus configuration resulted in a response that decreased with $f_{\text{rip}}$ (Fig. 1F). We refer to the responses, shown in Fig. 1, E and F, as $f_{\text{rip}}$ functions.

The noise tokens were 1,000 ms in duration with a repetition interval of 1,200 ms, which corresponds to a pause of 200 ms between noise tokens. The sound level was usually 60 or 70 dB overall SPL and additional levels were collected if time allowed. The $f_{\text{rip}}$ range did not usually cover the entire bandwidth of the stimulus, but was set wider than the BW from the threshold curve to obtain asymptotic firing rates near the upper and lower limits. In initial experiments the data were collected using a large number of repetitions (typically 10) at a limited number of $f_{\text{rip}}$ values (steps of 25–200 Hz depending on CF) presented in sequential order. Because the data sometimes suggested drifts in responsivity, in subsequent experiments we randomized the presentation order. Due to hardware limitations we could randomize only the order of each $f_{\text{rip}}$ step and not each individual repetition. We therefore resorted to finer $f_{\text{rip}}$ steps (2–25 Hz depending on CF) in a random presentation order but with fewer repetitions (typically two).

**CORRELATION SENSITIVITY.** The rationale behind the $f_{\text{rip}}$ stimulus is that the output of the neuron depends on the effective correlation between the stimuli at the two ears. The effective interaural correlation of the $f_{\text{rip}}$ stimulus is the interaural correlation after monaural filtering by the auditory system. It differs from the interaural correlation of the original stimulus because correlated and anticorrelated parts of the stimulus are spectrally segregated and are weighted by the band-pass filtering in the monaural pathways. By systematically changing $f_{\text{rip}}$ we change the interaural correlation of the original stimulus. The resulting change in spike rate, which depends on the effective interaural correlation, will reflect the BW of the filters. However, the spike rate of binaural neurons is not necessarily linearly related to the effective interaural correlation. To derive a binaural BW measurement from the $f_{\text{rip}}$ functions we need to take the dependence of spike rate on interaural correlation into account. This can be achieved by using a stimulus in which interaural correlation is varied but is not spectrally segregated into correlated and anticorrelated parts, as described in the next paragraph. The resulting graphs of spike rate as a function of interaural correlation are referred to as rICF, following other authors (Albeck and Konishi 1995; Coffey et al. 2006; Saberi et al. 1998; Shackleton and Palmer 2003; Shackleton et al. 2005; Yin et al. 1987). In contrast to the $f_{\text{rip}}$ function, the shape of the rICF is not affected by spectral filtering by the auditory system. Thus we can use these rICFs as a calibration stimulus.

To measure rICF, the interaural correlation of the stimulus was varied by combining different sources of broadband noise (Robinson and Jeffress 1963). The stimulus is illustrated schematically in Fig. 1, I and J and a more detailed description can be found in Louage et al. (2006). Two independent tokens of Gaussian broadband noise (lower cutoff 50 or 100 Hz; upper cutoff between 8 and 10 kHz) were either presented unmixed as reference tokens or combined to produce different mixed tokens. However, in contrast to the $f_{\text{rip}}$ stimulus the mixture was across the entire stimulus bandwidth (Fig. 1F). To achieve an interaural correlation of between 0 and 1 a reference token was presented in one ear, whereas a mixed token was presented in the other ear. This mixed token was a combination of the reference token and the second independent noise token, and the interaural correlation was varied by adjusting the relative amounts of each token contributing to the mixed token. To achieve an interaural correlation of between 0 and −1 the same reference token was presented to the same ear but now the mixed token was a combination of the phase-inverted reference token and the second independent noise token.

Interaural correlation values were changed in evenly spaced steps. This step size was kept constant within a data set but could change between data sets from 0.02 to 0.1. (A data set refers to a set of responses recorded for one set of stimulus conditions, such as the responses recorded for a range of $f_{\text{rip}}$ values or the responses recorded for a range of interaural correlation values.) Stimulus duration, repetition interval, and SPL were the same as for the $f_{\text{rip}}$ stimulus. The number of repetitions was between 15 and 60 (typically 20), depending on response rate and SR. A schematic of a typical rICF is shown in Fig. 1J.

To quantify the relationship between interaural correlation and spike rate we fitted a positive or a negative power function (Eqs. 1a and 1b, respectively) to the rICF

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

(1a)

$$R(\rho) = a + b(1 - \rho)^2$$

(1b)

where $R$ is the response rate; $\rho$ is the interaural correlation; and $a, b,$ and $p$ are parameters of the fit. Shackleton et al. (2005) previously showed that these power functions best describe the rICFs measured in the guinea pig. The positive power function was fitted to monotonic rICFs, which showed an increasing response rate with increasing correlation (Fig. 4C), whereas the negative power function was fitted to monotonic rICFs, which showed a decreasing response rate with increasing correlation (Fig. 6C). For the correlation responses that were nonmonotonic we first fitted Eq. 1a to the rICF and then separately fitted Eq. 1b to the same rICF. We then found the intersection of these two fits ($p_0$). A convex nonmonotonic rICF could then be described by the positive power fit from $p = -1$ to $p = p_0$ and by a negative power fit from $p = p_0$ to $p = +1$ (Fig. 7E). For a concave nonmonotonic rICF this order was reversed.

Construction of “binaural” responses from AN data

To allow comparison between monaural and binaural responses we used exactly the same stimuli in AN and IC experiments. However, in the AN experiments the stimuli were not presented binaurally but were played monaurally, one after the other, to the same ear. We then used a coincidence analysis (described in this section) to allow comparison between the monaural and binaural responses. In the AN it was not necessary to collect the ND curve because there is no ITD sensitivity. In fact in the AN analysis there are no interaural parameters, only intertoken parameters.

In the AN, as in the IC experiments, SR was measured and CF and threshold were determined using a threshold-tracking algorithm. We then sequentially presented the same spectrally manipulated stimuli also used in IC experiments. The sequence started with an A− noise token followed by an A+− noise token with a very low $f_{\text{rip}}$. The sequence continued with A−− noise tokens with increasing $f_{\text{rip}}$, and ended with an A−− noise token. Noise bandwidth, duration, repetition interval, and SPL were all the same as for the IC. However, more repetitions were needed to accumulate enough spikes for coincidence analysis (between 15 and 40 depending on the $f_{\text{rip}}$ increment). Noise tokens such as those used to measure rICFs in the IC were also presented while recording from the AN. Again, noise bandwidth, duration, repetition interval, and SPL were all the same as for the IC but the number of repetitions was higher (15 to 60, typically 40). Interaural correlation values were either evenly spaced, as in the IC experiments, or spaced unequally to maximize the sampling close to an interaural correlation of 1 (i.e., 0.99, 0.96, 0.91, 0.84, 0.76, −0.1) (Louage et al. 2006).

The rationale behind the coincidence analysis is provided in Joris (2003) and Joris et al. (2006b). As in a previous study (Joris et al. 2006c) analysis consists of counting the number of coincident spikes, within a particular bin width (50 μs), between two separate responses from the same auditory nerve fiber (e.g., the response to noise token A+ and the response to noise token A+−). We calculated the $f_{\text{rip}}$ function in the AN by counting the number of coincidences between the response to each repetition of the reference stimulus A+ with the response to each repetition of the A+− noise tokens, at each flip frequency (see Fig. 2). The second $f_{\text{rip}}$ function was calculated by using the response to the A− noise token as the reference stimulus.
and then counting all the coincidences with the response to each $A^{+/−}$ noise tokens. Although more repetitions were needed to have enough spike trains in the AN, being able to switch reference tokens meant that data collection was in a sense more efficient.

The rICF function for the AN was also calculated using the coincidence analysis technique. The response to a reference token was compared with the response to a mixed token giving varying interaural correlation values between −1 and 1. As in the IC the relationship between interaural correlation and spike rate was quantified by fitting either Eq. 1a or Eq. 1b to the measured correlation function.

Henceforth the terms $f_{\text{flip}}$ function and rICF refer to the respective rate curves from either the AN after coincidence analysis or the IC.

**Extracting BW and CF metrics**

**CURVE-FITTING METHOD.** Earlier, in IC stimuli, SPECTRAL DATA, it was described how the frequency selectivity of the monaural inputs to the binaural processor was expected to affect the shape of the $f_{\text{flip}}$ function—i.e., the narrower the bandwidth, the steeper the curves. We quantified this relationship as follows. We assumed that the filter had a Gaussian shape with a mean corresponding to the CF of the filter and SD value corresponding to half the BW. The normalized cumulative power $P(f)$ is the integral of the power transfer of the filter. For the Gaussian filter shape

$$P(f) = \frac{1}{2} \left[ 1 + \text{erf} \left( \frac{\sqrt{2}(f - \text{CF})}{BW} \right) \right]$$

where erf is the error function. The filter transfer function and its power are therefore completely determined by the two parameters, CF and BW.

The next step in the curve-fitting technique is to relate the normalized power of the filter to the response rate of the neuron. We have measured the relationship between interaural correlation and spike rate (see IC stimuli, CORRELATION SENSITIVITY). Therefore if we relate power to interaural correlation we can use the measured rICF to fit Eq. 2 to the $f_{\text{flip}}$ functions. The power of the filter can be related to the interaural correlation using the following equation from van der Heijden and Trahiotis (1997)

$$\rho(f) = \frac{P_p(f) - P_n(f)}{P_p + P_n}$$

where $P_p$ is the power of the section of the filter stimulated by the correlated part of the stimulus and $P_n$ is the power of the section of the filter stimulated by the anticorrelated part of the stimulus. In the present case, $P_p$ and $P_n$ correspond to the power of the portions of noise spectrum below and above $f_{\text{flip}}$ and their dependence on $f_{\text{flip}}$ CF, and BW is described by Eq. 2. $P_p$ is equal to $P_p + P_n$, which is the total power of the filter and is therefore constant. Equation 3 is derived by dividing Eq. A1a from van der Heijden and Trahiotis (1997) by Eq. A1b. Equations 2 and 3, along with the rICF, now allow us to estimate a $f_{\text{flip}}$ function that could be fitted to the measured $f_{\text{flip}}$ function to derive an estimate of the two filter parameters BW and CF (see following text).

**APPLICATION.** The first step in the curve-fitting analysis was to estimate an initial BW and CF based on the threshold curve (Fig. 3, step 1). Using these starting values Eqs. 2 and 3 were used to compute two normalized interaural correlation versus flip-frequency functions corresponding to the $A^{+/−}$ and $A^{−/+}$ cases (Fig. 3, step 2). Next, the rICF was used to convert the estimated interaural correlation versus flip-frequency functions into estimated spike rate versus flip-frequency functions (Fig. 3, step 3). Then the sum of the squared differences (SSDs) was calculated between the estimated and measured $f_{\text{flip}}$ functions (Fig. 3, step 4). Finally a minimization method, implemented in Matlab (The MathWorks, Natick, MA) using standard built-in functions, was used to adjust CF and BW (Fig. 3, step 5). Steps 2 to 5 were repeated until a minimum SSD was reached, giving the final estimated CF and BW.

As a measure of the quality of fit, we calculated the Pearson chi-squared value (Sokal and Rohlf 1997)

$$\chi^2 = \sum \frac{(Y_{\text{data}} - Y_{\text{fit}})^2}{Y_{\text{fit}}}$$

where $Y_{\text{fit}}$ is the estimated $f_{\text{flip}}$ function and $Y_{\text{data}}$ is the measured $f_{\text{flip}}$ function. A $P$ value was calculated using the chi-squared value and the number of degrees of freedom. Only data sets with $P < 0.05$ were used in the analysis.

**Data sets without rICFs**

rICFs were not available for every neuron. In these cases we removed some of the rectifying nonlinearities from the $f_{\text{flip}}$ functions by subtracting responses to stimuli of opposite polarity—an approach for response linearization used by others (Goblick and Pfeiffer 1969; Joris 2003; Möller 1977). We obtained a “diffflip” by subtracting the response to $A^{−/+}$ from the response to $A^{+/−}$. Also, an estimated diffflip function was calculated directly from the estimated interaural correlation versus flip-frequency functions shown in Fig. 3, step 3. Then the SSD was calculated between the estimated and measured diffflip functions. The rest of the steps in the curve-fitting method were the same as for normal $f_{\text{flip}}$ functions. As a measure of the quality of fit a chi-squared value was calculated using Eq. 4, where $Y_{\text{fit}}$ is the estimated diffflip and $Y_{\text{data}}$ is the measured diffflip. Data sets with $P < 0.05$ were excluded from the analysis.

We tested the validity of the diffflip approach versus the rICF approach as follows. We first calculated BWs for all data sets for which an rICF was available, using the standard curve-fitting method. We then obtained a second measure of BW by applying the same
curve-fitting method, but now skipping the step that uses the rICFs to convert interaural correlation into spike rate. This meant that we fitted Eqs. 2 and 3 directly to the measured \( f_{\text{flip}} \) functions. We then used linear regression analysis to compare the original measure of BW (including the rICF) with the second measure of BW (not using the rICF) (data not shown). In the IC we found a slope of 0.86 with a y-intercept of −19 Hz (\( P < 0.001, r^2 = 0.96 \)). In the AN a slope of 0.86 with a y-intercept of −18 Hz was found (\( P < 0.001, r^2 = 0.94 \)). This analysis shows that not including rICF in our standard curve-fitting procedure leads to an overestimation of BW.

Next, we obtained a third measurement of BW by applying the dflip curve-fitting method to the same data sets (i.e., all data sets for which an rICF was available). We then used linear regression analysis to compare the original measure of BW (including the rICF) with this third measure of BW (obtained using the dflip and no rICF; data not shown). In the IC we found a slope of 0.99 with a y-intercept of −19 Hz (\( P < 0.001, r^2 = 0.96 \)). This y-intercept value was well within the SD of the IC BW measurements in every CF group (see next section and Fig. 9C, inset). In the AN a slope of 0.99 with a y-intercept of −18 Hz was found (\( P < 0.001, r^2 = 0.94 \)). Again, this y-intercept value was well within the SD of the AN BW measurements in every CF group. This shows that when no rICF is available, fitting to the dflip gives a more accurate estimate of BW than simply fitting directly to the \( f_{\text{flip}} \) functions.

We were satisfied that using the dflip curve-fitting method gave a reasonable estimate of BW. Therefore the standard curve-fitting method was used when rICFs were available and, when not available, the dflip curve-fitting method was used. In the following analysis we make no distinction between the two methods; the resulting values are both reported as BWs. We will denote measures derived from the spectral curve-fitting method by the subscript "sm" (CFs, BWs).

Statistics

In both the IC and AN we grouped the data based on CF. Four groups with CF ranges spanning one octave (187.5 < G1 ≤ 375 Hz; 375 < G2 ≤ 750 Hz; 750 < G3 ≤ 1,500 Hz; 1,500 < G4 ≤ 3,000 Hz) were chosen. This grouping was chosen to strike a balance between accurately parameterizing the data based on CF while ensuring that there were adequate numbers of data sets in each group. We then used a two-way ANOVA to test for differences between the mean BW measurements in IC and AN across each CF group. We compared the variances of each CF group using an F-test corrected for multiple comparisons. \( P < 0.01 \) was considered statistically significant.

RESULTS

Useful data were obtained from 39 IC neurons and 49 AN fibers. From the 39 IC neurons we collected 81 data sets, 8 of which were excluded because of a poor-quality fit (\( P > 0.05 \), from Eq. 4). Of the remaining 73 data sets rICFs were available in 42. From the 49 AN fibers we collected 77 data sets and 9 were excluded because of a poor-quality fit (\( P > 0.05 \), from Eq. 4). Of the remaining 68 data sets rICFs were available in 44. We first present the results of the \( f_{\text{flip}} \) stimulus for individual neurons in the IC and then in the AN. We then present the results on a population level and compare the IC with the AN.

Inferior colliculus

Data for a first IC neuron are shown in Fig. 4. ND curves (Fig. 4B) were collected first to determine the neuron’s BD, which here was 600 μs. Figure 4D shows the binaural thresh-
old curve obtained using a tracking algorithm, showing a CF of 518 Hz and BW of 305 Hz. Figure 4A shows the f functions. By manipulating the spectral parameters of the stimulus (f) while keeping the temporal parameters (ITD) fixed at the neuron’s BD, the stimulus contained varying mixtures of correlated and anticorrelated frequency bands. By increasing f in the A+/- condition, the firing rate of the cell grew from a low to a high value (Fig. 4A, thin line). For the A+/- stimulus, at low f the neuron was responding to a completely correlated stimulus and therefore responded maximally, whereas at high f the neuron was responding to a completely anticorrelated stimulus and responded minimally. For the A+/- stimulus, at low f the neuron was responding to a completely anticorrelated stimulus and therefore responded maximally. The f functions cross somewhere around 550 Hz, which agrees well with the CF of the neuron. Both f functions are relatively flat from 100 to about 400 Hz, at which point the A+/- response starts to increase and the A+/- response starts to decrease. These trends continue to around 650 Hz at which point both f functions start to level out. This range of 250 Hz, over which the neuron was sensitive to changes in the interaural correlation of the stimulus, gives a rough indication of the BW of the neuron. Note that, in theory, the maximal firing rates to the A+/- and A+/- f functions should be identical because the stimuli are identical at opposite extreme values of f. However, in some neurons these responses were unequal and all f function pairs were therefore normalized independently by fitting them with arctan functions.

The rICF function is shown in Fig. 4C (solid line) with its positive power fit superimposed (dashed line). In this case the rICF is rather linear. The curve-fitting method now used this rICF to fit Eq. 2 to the f functions. The fit is shown in Fig. 4A as dashed lines and the corresponding predicted filter shape is shown in Fig. 4E. The CF measured on the f function is in good agreement with the threshold curve (CF = 543 Hz, CF = 518 Hz). However, the BW measured on the f function is smaller than that measured on the threshold curve (BW = 152 Hz, BW = 305 Hz). Note that the 10-dB level is standardly used to measure BW, although its choice is somewhat arbitrary. We will return to this issue in the final sections of RESULTS and DISCUSSION.

FIG. 5. Inferior colliculus (IC) data set with expansive correlation function. For the explanation of A and C see Fig. 4, A and C; for B and D see Fig. 4, D and E.

FIG. 6. IC neuron with a trough-type ND function. For the explanation of A–C see Fig. 4, A–C; for D see Fig. 4E.
Figure 5 is an example of a cell tuned to a higher frequency. The threshold curve (Fig. 5B) shows that CFthr is 1,597 Hz. The normalized response to the A⁺A⁻/ stimulus (Fig. 5A, thin line) is constant up to a fflip of around 1,700 Hz. The fflip function then increases steeply until 2,000 Hz and reaches a plateau. The inverse of this response pattern is seen in the response to the A⁺A⁻/ stimulus (thick line). The fflip function then increases steeply until 2,000 Hz and reaches a plateau. The inverse of this response pattern is seen in the response to the A⁺A⁻/ stimulus (thick line). The rICF for this neuron (Fig. 5C, solid line) is nonlinear and is well described by the positive power fit (dashed line). The curve-fitting method now used the fflip functions and the rICF function to estimate the filter shape shown in Fig. 5D. For this cell there was relatively good agreement between CF derived from the fflip and threshold curves (CFs 1,722 Hz, CFthr = 1,597 Hz) but the BW was considerably smaller for the fflip function than for the threshold curve (BWs = 620 Hz, BWthr = 810 Hz).

In most IC cells, the main feature of the ND function is the large peak at the best delay, which is usually the peak nearest zero ITD (Yin et al. 1986). However, in a minority of neurons the main feature is a deep trough near 0 ITD (McAlpine et al. 2001; Shackleton et al. 2005; Yin et al. 1986) and the maximal response is actually obtained to anticorrelated noise. In this series of experiments we encountered four such cells; an example is shown in Fig. 6. Here, the ND curve shows a maximal response to anticorrelated noise (thin line, Fig. 6B) and a minimal response to correlated noise (thick line). We were unable to collect a threshold curve for this cell. The normalized fflip function (Fig. 6A) shows that the cell responds maximally to the A⁺A⁻/ stimulus at low fflips and maximally to the A⁺A⁻/ stimulus at high fflips. In both cases the maximum response occurs where the stimulus is almost all A⁺A⁻. This is also shown in the rICF (Fig. 6C) where the maximum spike rate occurs at a correlation of −1. No special adaptations were needed to apply our curve-fitting method to this type of cell.

The final example shows ND curves (Fig. 7B) that are almost identical for correlated (thick line) and anticorrelated noise (thin line). Neurons with such responses have been called “polarity-tolerant” (Joris 2003); their ITD sensitivity is dominated by envelope components. For the example shown in Fig. 7 the maximal difference between the correlated and anticorrelated ND curves (i.e., the best delay) was at 100 μs. For this polarity-tolerant cell our standard A⁺A⁻/ stimulus resulted in nonmonotonic fflip curves, as expected (data not shown). To obtain monotonic fflip functions, we adapted the fflip stimulus by replacing the phase-inverted portion of the noise (“A⁻” in Fig. 1A) by an independent noise token (“B” in Fig. 7A). The resulting fflip functions in Fig. 7C are now monotonic and can be analyzed with our standard curve-fitting method. The rICF of this cell, shown in Fig. 7E, includes negative correlation values and is therefore nonmonotonic. We used the part of the rICF between interaural correlations of 0 and +1 to convert interaural correlation to spike rate in the curve-fitting method. Only two polarity-tolerant cells were studied in the IC and with this slightly adapted stimulus we were able to estimate their filter BW.

**Auditory nerve**

The reader is reminded that the fflip functions and rICFs shown in this section are pseudobinaural responses that have
been calculated from the monaural response of the AN using coincidence analysis (Fig. 8A, top). The AN responses do not show differences in average rate to the various noise tokens used (neither to the tokens with differences in fflip nor to those with differences in interaural correlation); only the temporal discharge patterns differ. These temporal differences will become clear only after coincidence analysis. Figure 8 shows a typical AN data set and Fig. 8B shows the monaural threshold curve for this fiber. The fflip functions shown here (Fig. 8A) were constructed using the coincidence analysis outlined in METHODS. The shape of the AN fflip functions was similar to that in the IC and we were able to apply the same curve-fitting method, without any modifications, to these data.

The rICF (solid line) and its positive power fit (dashed line) are shown in Fig. 8C. As in the IC, the curve-fitting method now used this rICF to fit Eq. 2 to the fflip functions. The fit is shown in Fig. 8A as dashed lines and the corresponding estimated filter shape is shown in Fig. 8D. The BW estimations from the fflip function and the threshold curve are quite similar (BWthr = 236 Hz, BWs = 227 Hz) as are the CF estimates (CFthr = 707 Hz, CFs = 651 Hz).

Population comparisons

**Fflip function CF versus BW.** In the following population plots AN data are shown as filled triangles and IC data as open circles. Data sets recorded from the same cell are joined by a line. Figure 9, A and B shows that BWs increases with CFs in both the AN and the IC. In Fig. 9C, the same data from Fig. 9, A and B are now shown together on the same plot but on log axes. There was no clear separation, but rather considerable overlap, between the range of BWs measured in the IC compared with the range measured in the AN. There was an even spread of BWs within each animal and there was no one animal that individually influences the spread of data in either the IC or the AN (data not shown). The inset in Fig. 9C shows the data divided into four CFs groupings (see METHODS). The IC is shown as a dashed line and the AN as a solid line. The mean BWs is plotted at the geometric mean CFs of the group and the error bars show the SD of each group. Using a two-way ANOVA we did not find any statistically significant differences between the mean BW measurements for IC and AN across each CF group. However, comparing the variances between the AN and IC, we found that the IC group centered at 551 Hz had a significantly greater variance than the corresponding AN group (F-test, P < 0.01). The differences in variance between the other AN and IC groups were not significant.

**Fflip function BW versus SPL.** It is well known that cochlear bandwidth increases with SPL (Carney and Yin 1988; De Boer and de Jongh 1978; Evans 1977; Rhode 1971). Figure 10A shows BWs estimates for all IC neurons with data at two or more SPLs. Figure 10B shows the same data for the AN. Each symbol represents one animal and data sets from the same cell are joined by a line. In the AN most fibers showed an increase in BWs with increasing SPL, but this dependence was not strong and not all cells followed this trend. Using linear regression, we fit a straight line through the data points for each fiber in Fig. 10B and then used its slope as a measure of the change in BW. The average slope for all fibers was 2 Hz per 1-dB increase in stimulus level. In the IC most neurons also showed a moderate increase in BWs with increasing SPL. Here the average slope was 3.4 Hz/dB.

**Threshold curve BW versus Fflip function BW.** In the IC there was considerable difference between BWthr and BWs, with the latter being generally lower (Fig. 11A). The line of best fit, determined using linear regression, is shown as a solid line ($r^2 = 0.61, P < 0.01$), and the dashed line shows the line of equality. The BWthr shown here is the traditional value measured at 10 dB above threshold. This measure is arbitrary and noisy because it relies on only three data points (the minimal threshold and two points at 10 dB above it). A better measure, which takes into account all the data points, is the equivalent rectangular bandwidth (ERB), which is defined as the BW of a rectangular filter that has the same integrated area.

**FIG. 8.** AN data set with expansive interaural correlation function. A, top: schematic representation of the autocorrelation analysis used to build up a pseudobinaural response from the monaural data. For the explanation of **A** and **C** see Fig. 4, **A** and **C**; for **B** and **D** see Fig. 4, **D** and E.
measurements are not shown but the dotted line shows the line of best fit. Its slope is closer to 1 (slope_{ERB} = 0.88) than for the fit to BW_{th} and BW_s (slope_{BW} = 0.48).

In the AN we also see poor agreement between BW_{th} and BW_s (Fig. 11B). Excluding the three data points with BW_s > 1,000 Hz, the trend is similar to that in the IC, with BW_s being generally lower. The solid and dotted lines again give the linear regressions for all data points, as in Fig. 11A, for the BW_{th} and BW_s measurements ($r^2 = 0.51, P < 0.01$, slope_{BW} = 0.86) and the ERB measurements ($r^2 = 0.74, P < 0.01$, slope_{ERB} = 1.38), respectively.

**THRESHOLD CURVE CF VERSUS f_{flip} FUNCTION CF.** CF estimated from the $f_{\text{flip}}$ function was in good agreement with threshold curve CF in both the IC and AN (Fig. 11, C and D). There are more data points at CFs > 1.6 kHz for the AN than for the IC. This simply reflects our focus on binaural processing of fine structure, and the fact that the transition from fine structure to envelope occurs at higher CFs in the AN than in the IC (Joris 2003; Louage et al. 2004).

**DISCUSSION**

The main finding of this study is that spectral bandwidths, as manifest in temporal response properties, are not wider at the level of the IC than in the AN. There is considerable overlap between the range of BWs seen in the AN and IC (Fig. 9C). If anything, the binaural BWs tended to be smaller than the...
monaural ones, in contrast to psychophysical data concluding the opposite, as discussed in the following text. When the data were grouped based on CF we did not find any statistically significant differences in BW, except that the variance in the IC group centered at 551 Hz was significantly greater than the variance in the corresponding AN group. The differences in variance between the other CF groups were not statistically significant.

Curve-fitting method

The advantage of the method used in our study is that it gives a purely binaural measure of bandwidth, but it may seem overly complex so we pause here to restate the underlying rationale. In our description of the binaural system we made two assumptions. First, we assumed that the inputs from both ears were filtered by identical Gaussian filters. Second, we assumed that the output of a binaural cell was completely determined by the interaural correlation of the stimuli after this filtering. The f_{flip} stimuli were designed such that the shape of the auditory filter, along with the f_{flip} value, determined the effective interaural correlation of the stimulus (i.e., the interaural correlation after filtering). By changing f_{flip} we changed the effective interaural correlation in a frequency-specific way and the resulting changes in spike rate reflected the shape of the auditory filter. However, these changes in spike rate were not necessarily linearly related to the effective interaural correlation of the stimulus. Therefore to derive a meaningful measure of BW from the f_{flip} function we needed to quantify the relationship between interaural correlation and spike rate. To do this we used the rICFs, which were obtained to stimuli generated by mixing independent wideband noise sources. Filtering of such stimuli affects both the correlated and anticorrelated contributions equally, so that the interaural correlation of this stimulus is not affected by filtering in the auditory system. Thus the rICF provides the relation between interaural correlation and spike rate in the general case.

Consider the auditory filter as a power transfer function. The area under the curve restricted to frequencies below f_{flip} is proportional to the power of the interaurally correlated portion of the stimulus (P_p). Likewise the area under the curve with frequencies >f_{flip} is proportional to the power of the interaurally anticorrelated portion of the stimulus (P_n). We were able to calculate these powers for a given f_{flip} value using Eq. 2 and were then able to relate these powers to an interaural correlation value using Eq. 3. We could then obtain the predicted spike rate for that interaural correlation value from the measured rICF. This gave us an estimated f_{flip} function that could be fit to the measured f_{flip} function to obtain measurements of BW and CF.

Binaural bandwidth in psychoacoustics

The psychoacoustic studies that originally gave rise to the concept of a broader binaural bandwidth were based on a binaural version of Fletcher’s classic (Fletcher 1940) bandwidthing experiments. In Fletcher’s original experiments monaural BW was measured by masking a tone with a wideband
masker. The bandwidth of the masker was decreased while keeping the spectrum level constant and the detection threshold of the tone was measured. Detection thresholds stayed constant for wideband maskers but as the bandwidth of the masker became narrower detection thresholds started to decrease. The point at which thresholds started to decrease was defined as the critical band. Binaural versions of this paradigm use a tone presented to both ears with an interaural phase difference of 180° masked by a diotic noise masker. The binaural thresholds are different in two respects from Fletcher’s monaural data (Bourbon and Jeffress 1965; Hall et al. 1983; Sever and Small 1979; Zurek and Durlach 1987). First, thresholds are generally lower, indicating an overall binaural advantage. Second, when widening the noise masker, binaural thresholds keep rising beyond the monaural critical band, suggesting an effective bandwidth of binaural processing that is wider than its monaural counterpart.

This straightforward interpretation in terms of a wider binaural band, however, was contradicted by subsequent studies using masking paradigms different from Fletcher’s band-widening scheme: notched noise (Hall et al. 1983) and wideband maskers with frequency-dependent binaural properties (Kohlrausch 1988; Kollmeier and Holube 1992; Sondhi and Guttman 1966). These studies generally yielded narrower binaural bandwidths that are comparable with monaural bandwidths. It was subsequently shown by van der Heijden and Trahiotis (1998) that even binaural band-widening experiments can yield narrower bandwidths, provided that the correlation of the noise is slightly reduced from a perfect value of one. The authors argued that, rather than having a wider bandwidth, the accuracy or “signal-to-noise ratio” of the binaural system seems to deteriorate with stimulus bandwidth. Potential mechanisms behind this bandwidth dependence include limits in temporal acuity (Granatham and Wightman 1978), left–right asymmetries in peripheral filtering (Joris et al. 2005a; Schroeder 1977; Shamma 1989), and integration of binaural information across frequency channels (van de Par and Kohlrausch 1999).

The findings of the present study (Fig. 9) show that, at the level of the IC, the effective bandwidth of binaural responses is not systematically wider than the bandwidth at the level of the AN. In that respect, our physiological data do not justify the assumption of a wider “binaural bandwidth” found in the psychoacoustic literature (Bourbon and Jeffress 1965). If the apparent wider bandwidth of binaural detection is caused by a convergence of frequency channels, this convergence must take place at a stage beyond the IC. Because the stage of interaural interaction (coincidence detection) precedes the IC, the present study indicates that, at least at a population level, the interaural interaction is consistent with the peripheral, cochlear bandwidth. It is also of note that the \( f_{\text{flip}} \) functions in the IC were simple and sigmoidal in shape and resembled those measured in the AN.

Finally, human psychoacoustic studies using broadband stimuli measured binaural critical bands, centered at 500 Hz, of between 80 and 120 Hz (Kohlrausch 1988; Kollmeier and Holube 1992). Similar measurements of monaural critical bands centered at 500 Hz have been reported (Bourbon and Jeffress 1965; Fletcher 1940). This range is marked by a box centered at a CF of 500 Hz on Fig. 9C. This range of human critical bands is within the lower range of the BWs measured in cat IC cells with CFs around 500 Hz. It is also lower than any BWs measured in the cat AN fibers with CFs around 500 Hz. This seems consistent with a recent report on sharper frequency selectivity in humans compared with laboratory animals (Shera et al. 2002), but it should be cautioned that there are many difficulties in relating physiological data from animals to psychophysical data from humans.

Relationship with CF

The data presented here show a clear increase in measured BW with increasing CF (Fig. 9), both in the AN and the IC. This finding is in agreement with earlier studies undertaken in the AN using clicks or tones (Kiang et al. 1965; Liberman 1978; Pfeiffer and Kim 1972; Rhode and Smith 1985). Other studies in the AN using broadband noise and reverse correlation techniques also reveal a similar relationship (Carney and Yin 1988; De Boer and de Jongh 1978; Evans 1977; Ruggero 1973). This relationship is also consistent with binaural measurements of temporal damping taken from ND curves in the cat IC (Joris et al. 2005).

Relationship with SPL

For most neurons encountered in the IC an increase in SPL led to a small increase in BW. However, some neurons showed a small decrease in BW at higher stimulus levels or followed a nonmonotonic pattern. In the IC study using broadband stimuli, undertaken by Joris et al. (2005), the data follow a similar pattern. In general temporal damping shows a small decrease (i.e., a BW increase) with increasing SPL, but some neurons show an increase or a nonmonotonic pattern.

Most AN fibers encountered in this study also show an increase in BW with increasing SPL but smaller than that seen in the IC. Measurements obtained in the AN using the reverse-correlation technique (which uses broadband stimuli) (Carney and Yin 1988; De Boer and de Jongh 1978) also report an increase in BW with increasing SPL but they do not report specific values for BW increase on a population level. Using data reported from one fiber in Fig. 9 in Carney and Yin (1988) (CF = 525 Hz) we calculated a BW increase of 1.8 Hz/dB SPL. This is certainly within the range of BW increases that we have measured in the AN using our \( f_{\text{flip}} \) function curve-fitting approach (average increase of 2 Hz/dB).

Relationship with 10-dB threshold curve BW

We compared BWs measured with the \( f_{\text{flip}} \) stimulus to BWs measured with tonal thresholds—i.e., the bandwidth at 10 dB above threshold (Fig. 11). This comparison is one of apples and oranges, but it is a useful one given the common use of the latter measure. A common misconception generated by threshold tuning curves is that there is a tremendous increase in BW as SPL is increased. The frequency range over which pure tones are suprathreshold indeed increases with SPL, but this says little about the relative weighting of frequency components when they are present simultaneously. This weighting can be studied with methods using broadband stimuli (De Boer 1967; Recio-Spinoso et al. 2005; van der Heijden and Joris 2003) and, for the range of CFs and SPLs considered here, these methods reveal a rather modest increase in bandwidth with level, consistent with our findings (Fig. 10).
In conclusion, from our data and considering the psychophysical data, we conclude that at the site of binaural interaction the temporal comparisons are on average constrained to bandwidths also found in the monaural periphery. The physiological binaural BW shows somewhat larger variability than the monaural BW in the octave centered at 551 Hz, but there is certainly not an overall two- or threefold difference in mean BW, as suggested by some psychophysical studies (Gabriel and Colburn 1981; Trahiotis and Stern 1994), indicates effects of sound bandwidth that cannot be modeled by simple linear band-pass filters. The identification of underlying mechanisms remains a challenge for future physiological studies.

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REFERENCES


