## Spatial Sensitivity in the Dorsal Zone (Area DZ) of Cat Auditory Cortex

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Stecker, G. Christopher, Ian A. Harrington, Ewan A. Macpherson, and John C. Middlebrooks. Spatial sensitivity in the dorsal zone (area DZ) of cat auditory cortex. J Neurophysiol 94: 1267-1280, 2005. First published April 27, 2005; doi:10.1152/jn.00104.2005. We compared the spatial sensitivity of neural responses in three areas of cat auditory cortex: primary auditory cortex (A1), the posterior auditory field (PAF), and the dorsal zone (DZ). Stimuli were 80-ms pure tones or broadband noise bursts varying in free-field azimuth (in the horizontal plane) or elevation (in the vertical median plane), presented at levels 20-40 dB above units' thresholds. We recorded extracellular spike activity simultaneously from 16 to 32 sites in one or two areas of  $\alpha$ -chloralose-anesthetized cats. We examined the dependence of spike counts and response latencies on stimulus location as well as the information transmission by neural spike patterns. Compared with units in A1, DZ units exhibited more complex frequency tuning, longer-latency responses, increased prevalence and degree of nonmonotonic rate-level functions, and weaker responses to noise than to tonal stimulation. DZ responses also showed sharper tuning for stimulus azimuth, stronger azimuthal modulation of first-spike latency, and enhanced spatial information transmission by spike patterns, compared with A1. Each of these findings was similar to differences observed between PAF and A1. Compared with PAF, DZ responses were of shorter overall latency, and more DZ units preferred stimulation from ipsilateral azimuths, but the majority of analyses suggest strong similarity between PAF and DZ responses. These results suggest that DZ and A1 are physiologically distinct cortical fields and that fields like PAF and DZ might constitute a "belt" region of auditory cortex exhibiting enhanced spatial sensitivity and temporal coding of stimulus features.

## INTRODUCTION

The auditory cortex plays a critical role in the soundlocalization behavior of many species as evidenced by the behavioral deficits that follow from its ablation or inactivation (Jenkins and Masterton 1982; Malhotra et al. 2004a; Thompson and Cortez 1983). Whether this role is to compute or merely pass along spatial information, the lesion results clearly imply that sound-source locations are encoded in the activity of cortical neurons. The nature of spatial representation in the auditory cortex, however, remains poorly understood despite numerous studies of spatial sensitivity. By analogy with the visual cortex, or with auditory-visual representation in the superior colliculus, one might reasonably expect to find a topographic map of auditory space in the cortex, yet physiological studies have failed to demonstrate any such map (Imig et al. 1990; Middlebrooks and Pettigrew 1981; Rajan et al. 1990a). As an alternative, we have argued that sound-source locations are represented in a distributed fashion by large populations of cortical neurons, each of which responds panoramically, transmitting information about sound sources located throughout the entire acoustic field (Middlebrooks et al. 1998).

It is also not clear whether particular regions of the cortex are specialized for the processing of auditory spatial information. A recently popularized view of monkey auditory cortex proposes (by analogy with monkey visual cortex) the existence of separate processing "streams" specialized for the processing of spatial and spectral information (Rauschecker 1998). That view is partly supported by physiological data that reveal some between-area differences in selectivity for the spatial locations or spectro-temporal content of acoustic stimuli (Recanzone et al. 2000; Tian et al. 2001). Studies of cortical neurophysiology in the cat, however, have revealed only minor differences in spatial sensitivity between various cortical areas. Rather, it appears that neurons throughout the auditory cortex are able to represent sound-source locations with similar accuracy. Furthermore, the responses of neurons in most areas of auditory cortex are modulated by stimulus location in similar ways, exhibiting broad spatial tuning that affects both the magnitude (spike count) and latency of neural responses (Imig et al. 1990; Middlebrooks and Pettigrew 1981; Rajan et al. 1990b). The emerging view has been that the auditory cortex is equipotent in terms of spatial coding. That view is consistent with the general notion of broadly distributed spatial representations, but an alternative possibility is that specialization for the processing of auditory space exists in regions of the cortex in which spatial sensitivity has not yet been studied.

In an effort to address the potential for spatial specialization in unstudied regions of the auditory cortex, we have begun to describe the spatial sensitivity of neurons in fields beyond primary auditory cortex (A1) in the cat, most recently the posterior auditory field (PAF) (Stecker et al. 2003). There we identified a number of important features of PAF responses suggestive of a role in spatial processing. Compared with neurons in A1, those in PAF are more sharply tuned for sound-source locations, their spatial tuning is less affected by increases in stimulus level, their preferred locations sample space more uniformly, and their spike patterns are more informative about stimulus location. Perhaps most significantly, response latencies of PAF neurons (which are longer than those of A1 neurons by tens of milliseconds) are strongly modulated by stimulus location, providing a robust temporal code for auditory space. Overall, these differences suggest that PAF is a strong candidate for a site of spatial processing. Aside from the differences in response latency, however, the effects appear as quantitative differences between neural populations that each exhibit significant variation between individual neurons.

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As such, one cannot conclude from physiological results alone that PAF is specialized or even necessary for the processing of auditory space, although recent behavioral evidence from cortical inactivation studies has suggested a critical role of PAF, along with A1 and the field of the anterior ectosylvian sulcus (fAES), in sound localization (Malhotra et al. 2004a).

Another promising region of cat auditory cortex, in terms of spatial sensitivity, is the "dorsal zone" (DZ) of auditory cortex (He and Hashikawa 1998; Middlebrooks and Zook 1983; Sutter and Schreiner 1991), which shares a number of physiological attributes with PAF. DZ extends dorsally from A1 into the ventral bank of the suprasylvian sulcus (SSS). Neurons in DZ can be distinguished from those in neighboring A1 on the basis of spectral tuning and response latency, and DZ is further set apart by a distinctive set of thalamocortical projections. Whereas A1 receives its strongest input from the ventral division of the medial geniculate (MGv), DZ receives projections mainly from the dorsal division (MGd), the dorsal cap of MGv, and the posterior group (PO) of thalamic nuclei (He and Hashikawa 1998; Huang and Winer 2000; Middlebrooks and Zook 1983). A number of features of DZ responses are suggestive of a role in spatial processing. First, as in PAF, many DZ neurons exhibit complex frequency tuning-often extending to high frequencies (>12 kHz)-that involves multiple excitatory and inhibitory domains (Sutter and Schreiner 1991). As we have argued previously, such tuning might play a role in the processing of monaural spectral cues to sound-source location (particularly in elevation). Second, initial investigations of DZ (Middlebrooks and Zook 1983) revealed a large number of "predominantly binaural" neurons that showed no response to monaural stimulation in contrast to the neurons more common to A1 that responded well to contralateral monaural stimulation and were either facilitated or inhibited by simultaneous ipsilateral stimulation. This pattern of binaural sensitivity suggests that DZ might contain a wider variety of spatial tuning beyond the forms commonly observed in regions of the cortex more strongly dominated by contralateral input (e.g., A1 and PAF). Third, DZ neurons have been shown to exhibit long response latencies (He et al. 1997; Mendelson et al. 1997). By analogy with the responses of PAF neurons, this raises the possibility that DZ units might exhibit spatial modulation of response timing as a robust form of spatial coding.

In this study, we recorded primarily from locations in the ventral bank of SSS, varying the caudorostral position of penetrations to sample posterior (dorsal to tip of the posterior ectosylvial sulcus (PES), near PAF, and the dorso-posterior field EPd), middle (dorsal to central A1), and anterior [dorsal to tip of the anterior ectosylvial sulcus (AES), near the anterior auditory field (AAF)] regions of DZ. We delineated the posterior, anterior, and dorsal borders of DZ based on sulcal pattern and its ventral border based on marked differences between DZ and A1 responses. It should be noted that the boundaries of DZ are not well characterized in the literature. Sutter and Schreiner (1991) reported no physiological border between dorsal and ventral auditory fields, whereas He and Hashikawa (1998) reported clear physiological differences between DZ and A1. It also is possible that our DZ recording sites strayed into neighboring fields. Posterior penetrations may have involved units that could be alternatively labeled as EPd or dorsal PAF. Similarly, anterior penetrations could have extended into AAF. In addition, DZ itself might contain dis-

TABLE 1. Summary of animals used and units recorded in each cortical unit

	Gender	A1	PAF	DZ	Border
Cat0101	Q*	15/1	50/8	_	
Cat0102	5	24/3	19/3		_
Cat0103	3		10/2	8/1	_
Cat0105	Q*	15/1	50/4		_
Cat0201	3		59/4		_
Cat0202	ð	63/8	79/10		_
Cat0203	ð	89/6	10/2	67/7	_
Cat0204	ð	16/1	99/8	75/5	_
Cat0302	ð		60/5	85/7	_
Cat0303	ð	3/1	36/3	26/4	_
Cat0305	Ŷ	29/2		16/1	
Cat0306	Ý*	15/1		15/1	
Cat0307	ģ*	_			32/2
Cat0402	3	_			53/4
Cat0404	Q*	14/1		14/2	
Cat0405	ð	36/3		31/2	10/1
FOTAL		319/28	472/49	337/30	95/7

Each cell of the table indicates the number of units recorded and number of penetrations, as a ratio, in each cortical field (A1, PAF, or DZ) and cat. *Far right column* indicates recordings made in the vicinity of the A1/DZ border and not included in A1 or DZ population analyses. Data from *cat0101–cat0202* were included in the samples of A1 and PAF units reported by Stecker *et al.* (2003). Data from *cat0203–cat0405* are new to this report. Female cats indicated by \*were previously used in a chronic recording experiment in which they were trained to detect trains of acoustic clicks among task-irrelevant noise bursts that varied in location. Cats were not trained to localize or discriminate the spatial positions of acoustic stimuli.

crete subregions. Without clear physiological markers for field borders (e.g., tonotopic reversal), their identification is difficult. We attempted to address these concerns in two ways. First, recordings in DZ were largely confined to the ventral bank of SSS, well away from the presumed border with A1 and/or PAF, while anterior recordings were monitored for indications (e.g., short-latency responses) of contamination by AAF units. Second, a series of recordings were made in the border region between A1 and DZ to characterize the sharpness of the transition of response properties between A1 and DZ.

### METHODS

Aside from the region of cortex recorded, all procedures of animal preparation, stimulus generation and presentation, unit recording, and data analysis were essentially identical to those of Stecker et al. (2003), and complied with the guidelines of the University of Michigan Committee on Use and Care of Animals. A brief discussion of methods follows; for a more detailed discussion, see Stecker et al. (2003).

#### Animal preparation

Sixteen purpose-bred male (10) and female (6) cats, weighing between 2.8 and 7.0 kg were used in this study. Five of the female cats were previously trained to detect acoustic stimuli in a chronic behavioral study. The remaining cats participated only in the acute experiments. Data from six of the cats were included in the samples of A1 and PAF units reported by Stecker et al. (2003). The DZ data from those cats and all data from the remaining 10 cats are new to this report (see Table 1). Surgical anesthesia was induced and maintained with isofluorane (2–3%) in nitrous oxide (2 l/min) and oxygen (1 l/min). After surgery, cats were transferred to intravenous  $\alpha$ -chloralose (1.5 mg/ml) in Ringer solution for unit recording. Dosage was  $\sim 3$  mg  $\cdot$  kg<sup>-1</sup>  $\cdot$  h<sup>-1</sup> and adjusted to maintain an areflexive state. Atropine

sulfate (0.1–0.2 ml im) was administered at regular intervals throughout the experiment to suppress mucosal secretions. After partial removal of the scalp and right temporalis muscle, a craniotomy of 1-cm diam exposed the right middle ectosylvian gyrus, PES, and SSS. The animal was positioned in the center of a sound chamber with its head held by a bar attached to a skull fixture and its body suspended in a fabric sling. Thin wire supports maintained symmetric pinna placement throughout the experiment. A warm-water heating pad maintained body temperature at 37°C. Core temperature was monitored using an electronic esophageal or rectal thermometer. Heart and respiration rates were monitored using an electronic stethoscope placed in the esophagus or under the fore-limb. Experiments lasted from 2 to 5 days, after which the cats were killed. The right cortical hemisphere was then removed and immersed in buffered formalin for later visual confirmation of the region of cortex recorded.

#### Experimental apparatus and stimulus generation

Recordings were made in a  $2.6 \times 2.6 \times 2.5$ -m sound-attenuating chamber, the surfaces of which were lined with sound-absorbing foam (Illbruck) to suppress reflections. Sounds were presented one at a time from calibrated loudspeakers located 1.2 m from the cat's head and spaced 20° apart in the ear-level horizontal plane (for assessment of azimuth sensitivity) or in the vertical median plane (for assessment of elevation sensitivity). Loudspeaker locations are expressed in degrees azimuth or elevation, relative to the loudspeaker directly in front of the cat  $(0^{\circ})$ . Positive azimuths correspond to the cat's right side (ipsilateral to the recording site); positive elevations increase upward and to the rear (90° is directly overhead). The loudspeaker placed directly behind the cat corresponds to 180° (azimuth or elevation). Loudspeakers were placed at all 20° multiples of azimuth including  $0^{\circ}$ , and all  $20^{\circ}$  multiples of elevation from  $-60^{\circ}$  ( $60^{\circ}$  below the frontal horizon) to  $+200^{\circ}$  (20° below the rear horizon). Experiments were controlled by a personal computer, and acoustic stimuli were synthesized digitally using equipment from Tucker-Davis Technologies (TDT; Gainesville, FL). All stimuli were generated with 16- or 24-bit precision at a 100-kHz sampling rate. A computer-controlled multiplexer permitted any one loudspeaker to be activated at a time. Stimuli were either 80-ms Gaussian noise bursts with abrupt onsets and offsets or 80-ms pure tones with 5-ms raised-cosine onset/offset ramps.

#### Data acquisition and spike sorting

Extracellular unit activity was recorded using multi-site siliconsubstrate microprobes. These probes, provided by the University of Michigan Center for Neural Communication Technology (Anderson et al. 1989), permitted simultaneous recording from  $\leq 16$  cortical sites, and are fabricated in several formats. The data presented here were obtained using primarily single-shanked probes with linear arrays of either 16 recording sites spaced every 100 or 150 µm or (less commonly) 8 sites spaced every 200  $\mu$ m. Impedances were between 1 and 4 M $\Omega$  on 16-site linear probes (site area: 177  $\mu$ m<sup>2</sup>) and 340–360 k $\Omega$  on 8-site probes (site area: 1,250  $\mu$ m<sup>2</sup>). Seven penetrations spanned the presumed border between A1 and DZ; of these, three used 16-site single-shank probes penetrating the cortical surface tangentially and four used 4-shank probes oriented orthogonally to the cortical surface (see Fig. 12). Four-shank probes contained four 1,250- $\mu$ m<sup>2</sup> recording sites, spaced by 200  $\mu$ m, on each of four parallel shanks 3.75 mm long and separated by 200µm. Impedances on four-shank probes ranged from 300 to 400 k $\Omega$ . In general, two probes were placed simultaneously in different cortical areas (DZ, PAF, and/or A1), and we recorded from up to a total of 32 sites. Activity at each site was amplified, digitized (TDT RA16, 25-kHz sampling rate), band-pass filtered (0.2-4 kHz), resampled at 12.5 kHz, and stored on a computer disk for off-line analysis. On-line monitoring of spikes allowed estimation of thresholds and frequency tuning prior to the collection of spatial data.

Off-line spike sorting involved the following three steps: first, multi-site "denoising" reduced correlated noise across the recording array (Bierer and Anderson 1999). Second, candidate spikes were identified by thresholding relative to the (prestimulus) background RMS level. Third, candidate spike waveforms were clustered, by hand or by statistical cluster analysis, based on their projection onto principal components. Poststimulus times of spikes accepted in the clustering procedure were stored with  $20-\mu s$  resolution.

In contrast to previous studies (e.g., Furukawa and Middlebrooks 2002), we chose to record from as many sites as possible per penetration rather than to obtain recordings from clearly isolated single neurons. The spike-sorting procedure described in the preceding text was used to obtain the best possible isolation of neural signals; in general, however, we conservatively consider the recordings to be from multi-unit clusters rather than single isolated neurons. In past studies—including that of Stecker et al. (2003), whose procedures were identical to those of the current study—we have not observed significant differences between tuning properties estimated from such recordings and those that could be reliably identified as single isolated neurons. Thus we do not distinguish between them in this report; the term "unit" is used in reference to both.

Units that responded with <1 spike per trial, on average, to their most effective stimulus were rejected from further analysis as were units the average response of which across all stimuli varied by more than a factor of two between the first and second halves of blocks of trials in a recording session. This screening procedure was carried out independently for responses to stimuli varying in azimuth and elevation (see *Experimental procedure*). A number of PAF and A1 units included in this analysis were included in the sample of Stecker et al. (2003). Table 1 indicates the number of units in each area that appeared in that sample or are new to the current study.

#### Experimental procedure

Recordings in this study focused on cortical areas DZ, PAF, and A1, which were identified initially by the cortical sulcal pattern and secondarily by their responsiveness to pure-tone stimulation, tonotopic organization, and response latencies. Penetrations in DZ proceeded in the lateromedial direction into the ventral bank of the SSS. Penetrations in area PAF proceeded in the dorsoventral or lateromedial direction along the caudal bank of the PES. These cortical regions were additionally confirmed by examination of response latencies (median latencies were 22 ms in DZ, 29 ms in PAF, and 17 ms in A1) and the identification of broad or complex (multi-peaked) tuning to pure-tone frequency. Penetrations in A1 passed obliquely into the middle ectosylvian gyrus, generally proceeding in a rostrocaudal direction. Search stimuli, consisting of broadband noise bursts and 0.5- to 30-kHz pure tones, were presented from loudspeakers located at 0 or  $-40^{\circ}$  azimuth in the horizontal plane or  $+80^{\circ}$  elevation in the median plane (10° forward of overhead). Penetration depths were adjusted to maximize the number of active recording sites, with typically 10–14 sites per probe showing unit responses.

Study of the units in each penetration began with estimates of their thresholds to noise bursts, tested in 5-dB increments of SPL. The stimuli were presented from a location at which units responded reliably, most often from loudspeakers at azimuths of 0 or  $-40^{\circ}$  in the horizontal plane or in the mid-sagittal plane at  $+80^{\circ}$  elevation. Typically, unit thresholds varied by <10 dB across sites in a single penetration, and the modal threshold was adopted as the representative threshold for the penetration. Responses to pure-tone stimuli were tested using tone frequencies varying in 1/3- or 1/6-octave steps from 1 to 30 kHz; tone levels varied in 10-dB steps, typically from 0 to 50 dB SPL. Pure tones were always presented from  $80^{\circ}$  elevation; this overhead location was chosen because the spectrum of the cats' directional transfer function tended to be flattest there, minimizing the

Symbol	Description			
$\Delta C_{}$	Modulation of spike count by azimuth			
$\Delta L_{}$	Modulation of response latency by azimuth			
$\Delta C_{z}$	Modulation of spike count by elevation			
$\Delta L_{-l}$	Modulation of response latency by elevation			
W	Width of count-based azimuth tuning			
W <sub>L</sub> ==	Width of latency-based azimuth tuning			
W <sub>C</sub> at	Width of count-based elevation tuning			
W	Width of latency-based elevation tuning			
ξ <sub>C</sub>	Centroid of count-based azimuth tuning			
$\xi_{I} = \xi_{I}$	Centroid of latency-based azimuth tuning			
E al	Centroid of count-based elevation tuning			
50,el	Centroid of latency-based elevation tuning			
TSR	Spatial information transmitted by spike pattern			
$TSR_{a}$	Spatial information transmitted by spike count			
TSRL	Spatial information transmitted by response latency			

 TABLE 2.
 Statistics of spatial sensitivity

effects of filtering by the pinna on the units' responses (Xu and Middlebrooks 2000). Next, we measured the units' spatial sensitivities using 80-ms noise bursts 20, 30, and 40 dB above threshold, presented from 18 locations in the horizontal plane (-180 to  $+160^{\circ}$  in  $20^{\circ}$ steps) and 14 locations in the mid-sagittal plane (-60 to  $+200^{\circ}$ ). Stimuli were presented in pseudorandom order such that each combination of SPL and location was presented once before all combinations were repeated in a different random order; 40 repetitions were completed for each penetration. Neural activity was recorded from 20-50 ms before to 80-200 ms after the stimulus onset. Measurement of spatial sensitivity was often followed by presentations of additional stimuli related to other research questions, so that study at each penetration or pair of penetrations lasted from 2 to 14 h. Experiments yielded data from 2 to 18 (median = 5.5) penetrations per animal in A1, PAF, and DZ. In some cases, additional penetrations were made outside these areas; those recordings are not included in this report.

### Data analysis

SPATIAL SENSITIVITY ASSESSED BY ANALYSIS OF SPIKE COUNT AND RESPONSE LATENCY. After spike sorting, spike times were stored as latencies relative to the onset of sound at the loudspeaker. Arrival of sound at the cat's head followed a delay of  $\sim 3.5$  ms due to acoustical travel time. Spatial sensitivity was assessed by analyzing spike rates, response latencies, and the amount of stimulus-related information conveyed by spike patterns. From these, we computed statistics of response modulation, spatial tuning width, and preferred location. These are summarized in Table 2 and briefly described in the following text; for mathematical definitions, see (Stecker et al. 2003).

DEPTH OF RESPONSE MODULATION BY LOCATION ( $\Delta$ ). The depth (or range) of response modulation characterized the degree to which response latencies or spike counts varied across space. It was computed as the range of geometric mean latency or arithmetic mean spike count (normalized to 1 at max count) across location.  $\Delta L$  has units of milliseconds and  $\Delta C$  is a proportion of maximum spike count, ranging from 0 (no modulation) to 1 (100% modulation).

SPATIAL TUNING WIDTH (*W*). Spatial tuning width characterized the range of locations that were effective in eliciting a strong or rapid response from a given unit. Tuning width  $W_{\rm C}$  or  $W_{\rm L}$  was defined as the range of locations (not necessarily contiguous) associated with spike counts of  $\geq 50\%$  of maximum or latencies within the shortest 25% of the latency range across location. *W* has units of degrees.

SPATIAL CENTROID ( $\xi$ ). Following Middlebrooks et al. (1998), we characterized the preferred stimulus locations of individual units by calculating the spatial centroid, or spatial center of mass of the units'

peak responses. The peak was defined as the contiguous set of locations eliciting responses within 25% of maximum spike count or within the shortest 25% of the latency range and including the location eliciting the maximum (or shortest latency) response overall. We then computed a vector sum of angles to stimulus locations included in the peak, each weighted by spike count or inverse latency; the angle of the resultant vector gave the spatial centroid  $\xi_{\rm C}$  or  $\xi_{\rm L}$ .

SPATIAL INFORMATION TRANSMITTED BY SPIKE PATTERNS (TSR). As in previous work (Furukawa and Middlebrooks 2002; Furukawa et al. 2000; Mickey and Middlebrooks 2003; Middlebrooks et al. 1998; Stecker et al. 2003), we estimated the spatial information transmitted by temporal patterns of neural response using a statistical pattern-recognition algorithm implemented using a customized version of the MATLAB Neural Network Toolbox (The Mathworks, Natick MA). The approach used here was described in detail by Stecker et al. (2003). Briefly, it involved the classification of neural spike patterns by the stimulus locations most likely to have elicited them. For this analysis, different types of spike patterns were computed in each of three separate conditions. In the first, single-unit spike patterns were compiled by computing bootstrapped spikedensity functions (SDFs) for each unit. These were spike times recorded on eight randomly selected (with replacement, see Efron and Tibshirani 1991) trials corresponding to a particular stimulus location (stimulus levels 20-40 dB above threshold were included), convolved with a Gaussian impulse ( $\sigma = 1$  ms) and resampled to produce a histogram of spike count per 2-ms bin. The motivation for bootstrapping in this case was to obtain reliable estimates of stimulus-related spike patterns while also preserving a measure of trial-by-trial variability in patterns. Because bootstrapped SDFs pool data across trials, however, transmitted-information estimates based on them cannot be interpreted in terms of information per trial. In the other two conditions, we assessed the specific information-bearing features of neural responses in each cortical area by generating "reduced" spike patterns that contained only normalized spike count or response latency averaged across the set of eight selected trials and expressed as a scalar value.

Regardless of the type of spike pattern, 20 patterns per stimulus type were generated from one half of trials (the "training" set) and used to construct a pattern-recognition template for each stimulus location. Twenty additional spike patterns were generated from the remaining trials (the "test" set), and each of these was classified according to the most similar (smallest vector Euclidean distance) template obtained in the previous step, thus estimating the most likely stimulus location given the observed neural response. Estimates of stimulus locations were expressed as joint stimulus-response probability matrices (confusion matrices, see Fig. 1), from which we calculated total stimulus-related (TSR) transmitted information (the average of partial information across stimuli; Furukawa and Middlebrooks 2002). Transmitted information (mutual information) reflects the reduction in uncertainty about stimulus location given the network responses, and has units of bits. One bit of transmitted information implies perfect discrimination of two regions of space (e.g., left vs. right) or more continuous discrimination with some error. Perfect identification of 18 locations corresponds to 4.17 bits. For the present study, we calculated the transmitted information from classifications based on single-unit spike patterns (TSR<sub>s</sub>) and reduced spike patterns consisting of only spike counts (TSR<sub>C</sub>) or response latencies (TSR<sub>L</sub>) obtained from single-unit responses.

It should be noted that the interpretation of TSR information rates is subject to the effects of bias caused by sample-size limitations resulting in nonuniformity of the confusion matrices. This effect positively biases the information rate, but the amount of such bias is limited. By re-analyzing randomly-permuted data, Stecker et al. (2003) estimated the bias to be less than +0.06 bits in recordings of PAF and A1 units. A second potential source of bias arises when relatively distinctive SDFs occur infrequently in the data set (e.g.,



FIG. 1. Examples of neural responses in dorsal zone (area DZ; *top 4 rows*), posterior auditory field (PAF; 2 *middle rows*), and primary auditory cortex (A1; 2 *bottom rows*). Each row summarizes the response of a single neural unit. *Left*: frequency-response area (FRA) plots mean spike count in response to pure-tone stimulation varying in frequency (x axis) and intensity (y axis). *Middle left*: rasters of spike times (x axis) elicited by noise stimuli varing in azimuth (y axis, levels roved 20–40 dB above unit threshold). Blue shading indicates stimulus duration. *Middle right*: rate-azimuth function plots mean spike count plotted against stimulus azimuth at levels 20 (blue) and 40 (red) dB above unit threshold. *Right*: joint stimulus-response probability matrix (confusion matrix) depicts the ability of neural responses (single-unit spike-patterns) to encode stimulus azimuth. The area of each circle indicates the proportion of responses to stimuli at a given target azimuth (x axis) classified—based on likelihood—at a particular response azimuth (y axis). *TSR* information rates computed from each confusion matrix are given along the left axis.

when recording from a sharply tuned neuron that responds on a minority of trials). Such distinctive SDFs produce dependence in the confusion matrix even when they reflect random occurrences, and because mutual information is unaffected by "incorrect" classifications, TSR information rates can thus be overestimated. This problem is further exacerbated by bootstrapping, and examination of units in our data suggests that this bias-though highly variable across unitscould exceed 0.5 bits in some cases. However, because distinctive SDFs reflect both random and deterministic aspects of the neural data, it is difficult to distinguish bias of this type from real sensitivity to stimulus parameters. A systematic analysis of the sources and magnitudes of bias, however, is beyond the scope of this paper. Instead, we have attempted to constrain the effects of bias by comparing information rates computed identically across studies of different neural populations. There is no reason to expect increased bias in the present data relative to prior reports (e.g., Stecker and Middlebrooks 2003; Stecker et al. 2003), and so we will not consider these effects further.

The linear Euclidean distance metric of the pattern-recognition algorithm raises another consideration: the algorithm cannot recognize disjunctions in the input space (e.g., as would occur if a single stimulus elicited two different types of neural responses each dissimilar to their combined mean) and thus may not have detected information in spike patterns optimally. The frequency and degree of such effects could not be known without pursuing more complex information-theoretic analyses, but visual inspection of spike patterns did not reveal any obvious examples of such effects. Following Stecker et al. (2003), we consider the current TSR estimates to represent lower bounds on transmitted information in the case where complex or context-dependent responses might appear. Most importantly, our focus in this report is on comparing information rates between cortical fields rather than accurately estimating them in absolute terms. Because all information estimates were based on the same set of methods, and assuming that neither bias nor algorithm performance differed between the neural populations being compared, these effects should have no effect on the interpretation of the current results.

IDENTIFICATION OF FREQUENCY-TUNING PEAKS FROM FREQUENCY RESPONSE AREAS. Pure-tone responses were analyzed by computing the frequency response area (FRA, a contour plot of spike count as a function of pure-tone frequency and level: Fig. 1, *left*) for each unit. Characteristic frequency (CF) for each unit was defined as the frequency of the lowest-level stimulus that elicited a response exceeding the (averaged prestimulus) spontaneous rate by  $\geq 40\%$  of maximum spike rate (measured across stimuli). The CF also defined the primary frequency-tuning "peak." Secondary frequency-tuning peaks, when present, were defined similarly, but only where the FRA indicated a reduction of  $\geq 50\%$  in response at frequencies intermediate of adjacent peaks.

TESTS OF STATISTICAL HYPOTHESES. Following Stecker et al. (2003), we used nonparametric permutation tests to compare distributions of spatial statistics between cortical fields, stimulus levels, etc. Tests recomputed sampling distributions of interest (generally the difference between medians) under 5,000 different permutations of variable labels. The proportion exceeding (or falling below) the actual computed value gives the probability of type I error, or "P value." Unless otherwise noted, P values given in the text refer to this method. They are stated with one significant digit, although we adopted a fixed criterion for statistical significance of P < 0.05. Note that the sensitivity of a 5,000-permutation test is limited to 0.0002, so "P <0.0002" indicates a difference more extreme than any obtained by random permutation. Other standard statistical tests (e.g., linear regression) used the MATLAB Statistics Toolbox (The Mathworks). Except as otherwise noted, tests between cortical areas compared the full population of units recorded in each area, i.e., 319 units in A1, 472 units in PAF, and 337 units in DZ, as given in Table 1.



FIG. 2. Frequency response areas of DZ units are more often multipeaked than are those of A1 units. *Left:* histograms of number of peaks in A1, DZ, and PAF frequency response ares (FRAs). Symbols plot median values in each area. *Right:* distributions of characteristic frequency (CF). For multi-peaked neurons, CF was defined as the frequency of the most sensitive peak. *y* axis values give proportion of units per bin of 0.5 octaves on the *x* axis. Symbols plot median CF in each field.

### RESULTS

## Frequency tuning in DZ and PAF is more complex than in A1

General observations suggest broad similarities between DZ physiology and the responses of units in PAF, which together differed from A1 in the complexity of their frequency tuning, latency of their responses, prevalence of nonmonotonic ratelevel functions, and general preference for stimulation by pure tones rather than by broadband noise. Figure 1 summarizes the physiological responses of example units recorded in DZ, PAF, and A1. Note the prevalence, among DZ units, of multi-peaked and complex (nonmonotonic and patchy) frequency tuning. Typically, A1 units exhibited sharp tuning to a single welldefined characteristic frequency at low levels that broadened with increasing stimulus intensity. In contrast, PAF units often exhibited complex multi-peaked frequency tuning. As depicted by the examples (which are typical), units in DZ resembled PAF units in this respect. Figure 2 (left) plots distributions of FRA complexity (described by the number of frequency-tuning peaks in each unit's FRA) in all three fields. The majority of A1 units exhibited a single, well-defined peak of frequency response, whereas the majority of DZ units exhibited multipeaked ( $\geq 2$ ) frequency tuning. PAF, noted for complex tuning (Loftus and Sutter 2001), was intermediate. These results are consistent with those of Sutter and Schreiner (1991), who reported larger numbers of multipeaked neurons in dorsal than in ventral regions of auditory cortex.

We also found a preponderance of high-frequency sensitivity in DZ compared with A1, consistent with the results of Middlebrooks and Zook (1983), who reported an abrupt upward shift in CF at the transition from A1 to DZ. Figure 2 (*right*) plots distributions of characteristic frequency (CF, the frequency of the most sensitive peak) in A1, DZ, and PAF. A clearly significant proportion of units in all three fields had CFs in the range 4–30 kHz. DZ—and to a lesser extent, PAF—contained relatively few neurons with CF <4 kHz, whereas a large number of A1 units had CFs 2–4 kHz. Lower-frequency A1 units were undersampled because we did not routinely record in the rostral bank of PES. Therefore the high-frequency bias of DZ compared with A1 was likely greater than Fig. 2 indicates. Overall, median CF was higher in DZ (10.1 kHz) than in PAF (7.1 kHz) or A1 (7.5 kHz).

## Long, stimulus-sensitive response latency in PAF and DZ

A second feature of PAF responses shared by DZ units was long and stimulus-dependent response latency. Rasters of spike



FIG. 3. Distributions of response latency in DZ (black line), PAF (gray line), and A1 (shaded region). *Left*: distributions of overall latency (median of 1st-spike latencies computed for each stimulus azimuth). *Right*: distributions of spatial modulation of response latency (range of 1st-spike latency across azimuth  $\Delta L_{az}$ ). In each panel, values on the *y* axis give the proportion of units per bin of 5 ms on the *x* axis, and symbols plot median values across the population in each cortical area.

times recorded for noise stimuli varying in azimuth are plotted in Fig. 1, *middle left*. Whereas A1 units overwhelmingly responded with short latency (<20 ms) that was relatively insensitive to changes in stimulus azimuth, PAF units responded with longer latency (>20 ms) that was strongly modulated by location. DZ units generally exhibited latency modulation similar to PAF units although their latencies were intermediate between those of PAF and A1 units. Median overall latency in DZ (22.04 ms) was significantly longer than that in A1 (17.64 ms, P < 0.0002) and shorter than that in PAF (28.75 ms, P < 0.0002). This difference is quantified across neural populations in Fig. 3, which reveals significant differences in both the overall latency (left) and range of latency modulation (right) observed among PAF and A1 units. Although latencies were generally shorter in DZ than PAF, a number of units in DZ responded with latencies of  $\geq 60$  ms, consistent with previous reports of very long-latency responses in the area (He and Hashikawa 1998). Like those of PAF units, the response latencies of DZ units were strongly modulated by sound-source location. The range of latency across azimuth was significantly smaller in A1 (median: 3.11 ms) than in either PAF (10.62 ms, P < 0.0002) or DZ (8.38 ms, P <0.0002), which did not differ significantly from one another. It is interesting to note that latencies of many DZ units appeared to follow a different pattern than those of PAF units. The DZ units responded with one fixed latency across a wide range of contiguous azimuths, shifting to a different fixed latency at other locations. Latency shifts often occurred near 0 and 180°. The pattern of abrupt latency shift across azimuth is seen clearly for three DZ neurons in Fig. 1 and can be contrasted with the more gradual latency modulation of the depicted PAF units.

## Many DZ and PAF units respond nonmonotonically to increasing sound level

We calculated the monotonicity ratio, defined as the ratio of the response at the highest level tested to the maximum observed response (Sutter and Schreiner 1991), for each unit. A monotonicity ratio near 1 indicates that a unit's spike count increased monotonically with stimulus level, 0 indicates a complete failure to respond at the highest tested level, and intermediate values indicate weakened responses to high-level stimuli. We adopted a criterion value of 0.5 to define units with nonmonotonic rate-level functions. The proportion of these was significantly greater in DZ (69/337 = 20%) than in A1 (36/319 = 11%, P < 0.0002) and less than in PAF (134/472 = 28%, P < 0.0002). Median monotonicity ratios were significantly lower in DZ (0.780) than in A1 (0.839, P < 0.01) and higher than in PAF (0.688, P < 0.005), consistent with past results showing stronger nonmonotonicity in dorsal than in ventral auditory cortex (Sutter and Schreiner 1995). Figure 4 plots distributions of monotonicity ratio across cortical fields. Distributions in all three fields (*left*) were clearly nonunimodal. Rather modes were observed at values of 0 (completely nonmonotonic), 1 (completely monotonic), and at some intermediate values. Within the intermediate region, distributions did not differ greatly between fields except for a slight elevation in the proportion of moderately nonmonotonic DZ and PAF units with ratios <0.3. The largest differences between areas were instead found in the proportions of units with ratios near 0 and 1 (*right*).

## DZ and PAF units respond more strongly to tones than noise

A fourth similarity between units in DZ and PAF was their preference for tonal stimulation over noise. For units whose tone responses were recorded, we computed the ratio of best noise response (across all tested stimulus locations and levels) to best tone response (across all tested frequencies and levels). The results indicate that 258/337 (77%) of DZ units preferred tones to noises (noise/tone ratio <1), compared with 59% (188/319) of A1 units and 74% (351/472) of PAF units. Mean noise/tone ratios were 0.781 in PAF, 0.724 in DZ, and 0.986 in A1. Consistent with results in PAF (Stecker et al. 2003), noise/tone ratios were significantly correlated with monotonicity ratios in PAF (r = 0.2073, P < 0.0001) and DZ (r =0.2938, P < 0.0001) but not in A1 (r = 0.0272, P < 0.7). That is, on average, units in DZ and PAF that were nonmonotonic were somewhat more likely to prefer tones than were monotonic units. While similar to results obtained in PAF (Phillips et al. 1995; Stecker et al. 2003), DZ units' preference for tones over noise runs counter to reports that neurons exhibiting multi-peaked FRAs (which are more prevalent in DZ than A1) respond more strongly to noise than to tonal stimulation (Sutter and Schreiner 1991).

## Preferred locations of DZ units sample contralateral and ipsilateral space more completely than those of PAF or A1 units

Figure 5 plots distributions of preferred azimuths and elevations in A1, PAF, and DZ. Overall, the majority of units in



FIG. 4. Cortical areas differ in the proportion of units responding nonmonotonically to changes in sound level. Monotonicity ratio (the ratio of spike count at highest stimulus level to maximum spike count across level) ranges from 0 (highly nonmonotonic) to 1 (purely monotonic). *Left*: distributions of monotonicity ratio in PAF (gray line), DZ (black line), and A1 (shaded region). Values on the y axis are proportions of units per bin of 0.1 on the x axis. Symbols plot median monotonicity ratio in each area. *Right*: bars indicate proportions of units in each area with extreme (near 0 or 1) or moderate monotonicity ratios.



FIG. 5. Preferred locations by cortical area. Top: distributions of azimuth centroids  $\xi_{C,az}$  in A1 (left), PAF (middle), and DZ (right). Each panel is presented as a top-down view, with 0° (plotted upward on the page) indicating the rostral orientation of the cat's head and the radius of the curve indicating the relative proportion of units with centroids at each location. "NC" values indicate the proportion of units in each area that were too broadly tuned for the computation of a spatial centroid. Negative azimuths (plotted to the left) indicate locations contralateral to the recording site; positive azimuths correspond to ipsilateral locations. Especially in A1 and PAF, the majority of units prefer contralateral stimulation. DZ, in contrast, features a large minority of ipsilaterally tuned units. Bottom: distribution of elevation centroids  $\xi_{C,el}$  by cortical area. Each panel is formatted as a side-on view from the cat's right side, with 0° (plotted to the right) again indicating the rostral pole. Among tuned units, many-regardless of cortical area-prefer stimulus locations 20-60° above the frontal horizon, consistent with the acoustic axis of the pinnae. DZ and PAF additionally contain significant numbers of units preferring stimulation from low frontal and rearward locations, possibly related to the increased prevalence of nonmonotonic rate-level functions in these areas.

all three fields preferred contralateral (negative azimuths) over ipsilateral (positive azimuths) stimulation. DZ, however, contained a higher proportion of units preferring ipsilateral azimuths than A1 or PAF. Omitting untuned units and those with centroids that fell within 10° of the interaural midline, significantly more DZ units (26%) possessed ipsilateral centroids than did PAF units (15%, P < 0.0002) or A1 units (10%, P < 0.0002) 0.0002). In terms of elevation, the majority of tuned units in all three areas preferred stimulus locations aligned with the acoustic axis of the pinnae,  $20-60^{\circ}$  above the frontal horizon. A number of units in PAF and DZ, however, preferred low or rearward elevations. This may reflect the increased numbers of nonmonotonic units in PAF and DZ; such units may have responded most strongly when stimuli were subject to acoustic attenuation (e.g., due to interference by the cat's body) that occurred when stimuli were presented from the rear.

## Spatial tuning of DZ units is similar to that of PAF units: sharper, more deeply modulated, and less sensitive to variation in stimulus level, than that of A1 units

More units in PAF and DZ were tuned to sound-source location than in A1, as evidenced by the relatively lower proportions of units (indicated by "NC" in Fig. 5) for which no centroid could be computed. That pattern is reiterated in the spatial tuning widths plotted in Fig. 6. Azimuth tuning widths were consistently and significantly narrower in DZ (median  $W_{C,az}$ : 205.2°) than in A1 (259.0°, P < 0.0002) or PAF (238.6°, P < 0.03) when stimuli were presented 20 dB above unit threshold. At higher stimulus levels (40 dB above unit threshold), a large number of units in each cortical area responded throughout 360° of azimuth, although the level-dependent increase in tuning width was less in PAF (21.0°)



FIG. 6. Distributions of spatial tuning width  $W_{C,az}$  and  $W_{C,el}$  in each cortical area. *Left:* distributions of azimuth tuning width  $W_{C,az}$  at levels 20 (*bottom left*) and 40 (*top left*) dB above unit threshold are plotted for areas DZ (black lines), PAF (dark gray lines), and A1 (light gray region). Symbols above each curve indicate the median value for each distribution. *Right:* distributions of elevation tuning width  $W_{C,el}$  in the 3 areas, formatted identically to azimuth plots.

than in A1 (36.0°, P < 0.008). The tuning of DZ units broadened by an intermediate amount that did not differ significantly from PAF or A1 (28.6°, P < 0.1). As a result of this broadening, median tuning widths measured at the higher level (340.6° in A1, 301.4° in PAF, and 306.3° in DZ) remained larger in A1 than in DZ (P < 0.0004) or PAF (P < 0.0002) but became similar between DZ and PAF (P < 0.4), suggesting that DZ units were not as level-independent as PAF units (Stecker et al. 2003). Figure 6, *right*, plots distributions of elevation tuning width  $W_{C,el}$  in each cortical area. Elevation tuning was very broad overall, and did not differ significantly between areas (P > 0.05).

Figure 7 plots distributions of spike-count modulation across space  $\Delta C$  in the three areas. Spike-count modulation by azimuth was similar in the three areas for low-level sounds (median  $\Delta C_{\rm az} = 0.73$ , 0.73, 0.75 in A1, PAF, and DZ, respectively), but was significantly weaker in A1 (median  $\Delta C_{\rm az} = 0.55$ ) than in PAF (0.63, P < 0.0002) or DZ (0.61, P < 0.0002) for stimuli 40 dB above unit threshold. Similarly, modulation by elevation  $\Delta C_{\rm el}$  was significantly stronger in PAF and DZ (median  $\Delta C_{\rm el} = 0.50$  in both) than in A1 (0.43, P < 0.0002) at 40 dB, but similar across areas at 20 dB above



FIG. 7. Distributions of spike-count modulation depth DC. Left: distributions modulation by azimuth  $\Delta C_{az}$  at levels 20 (*bottom left*) and 40 (*top left*) dB above unit threshold. *Right*: distributions of modulation by elevation  $\Delta C_{el}$ . Formatting follows Fig. 6.



FIG. 8. Distributions of spatial information (TSR<sub>s</sub>) transmitted by neural responses in each area. Stimuli varied in azimuth (*left*) or elevation (*right*) as well as in level. A pattern-recognition algorithm classified each spike pattern to one of the possible stimulus locations, and the resulting confusion matrices were used to compute the transmitted (mutual) information for each unit. Values on the ordinate are proportions of units per 0.1 bits on the abscissa. Black line, results for DZ units; gray line, results for PAF units; shaded region, results for A1 units. Symbols give median TSR<sub>s</sub> for each distribution.

threshold (median  $\Delta C_{el} = 0.68$ , 0.62, 0.64 in A1, PAF, and DZ).

## Spike patterns of DZ units are similar to those of PAF units in the amount of spatial information they transmit

We used statistical pattern recognition to assess the ability of changes in neural response patterns to signal changes in stimulus location. Summarized as bits of stimulus-related information TSR<sub>S</sub>, distributions of algorithm performance are plotted in Fig. 8. Spike patterns of DZ and PAF units transmitted a median TSR<sub>s</sub> of 0.68 and 0.70 bits, respectively, and did not differ significantly (P < 0.3). Both transmitted significantly greater azimuth-related information than did spike patterns of A1 units (median TSR<sub>s</sub>: 0.62 bits vs. DZ, P < 0.004; vs. PAF, P < 0.002). The proportion of units transmitting >1 bit, however, was greater in DZ (20.0%) than in either A1 (10.5%), P < 0.0002) or PAF (14.8%, P < 0.0002), suggesting a sizeable population of more-informative units there. This proportion also differed significantly between PAF and A1 (P <0.04). Elevation-related information rates were more similar between the areas, slightly higher in DZ and PAF (with medians of 0.44 and 0.46 bits, respectively) than in A1 (0.42 bits). Note, however, that elevation sensitivity was tested on the vertical median plane, where interaural differences are minimized. Testing at each unit's best azimuth might have revealed different (better) elevation sensitivity for many units (e.g., those with circumscribed spatial receptive fields).

## DZ units encode sound-source locations effectively using both spike count and latency of responses

Because area DZ, like PAF, encoded sound-source locations more accurately than primary auditory cortex and contained a large number of neurons whose response latencies were strongly modulated by changes in stimulus location, we hypothesized that—like PAF units (Stecker et al. 2003)—DZ units would be more effective at encoding space by response latency than spike counts. Here, we examined the relative contribution of response latency and spike count by assessing classification performance based on "reduced" spike patterns containing only latency or count information (see METHODS). Distributions of the resulting count and latency transmittedinformation estimates,  $TSR_C$  and  $TSR_L$ , are plotted in Fig. 9. As expected, spatial information transmitted by latency was



FIG. 9. Efficiency of azimuth coding by spike count and response latency. Distributions of spatial information are plotted as in Fig. 8. Here, algorithmic classification was based on normalized spike counts ( $TSR_C$ , *left*) or 1st-spike latencies ( $TSR_L$ , *right*) as described in METHODS.

greater in DZ (median TSR<sub>L</sub>: 0.36 bits) and PAF (0.38 bits) than A1 (0.33 bits, P < 0.02), but did not significantly differ between DZ and PAF (P < 0.1). Information carried by spike count, however, was greater in DZ (median TSR<sub>C</sub>: 0.29 bits) and A1 (0.28 bits)—which did not differ significantly (P < 0.3)—than in PAF (0.24 bits, P < 0.03).

Spike counts and response latencies generally show an inverse correlation, such that effective stimuli produce strong, short-latency responses. Consistent with the enhanced spatial coding and spatial modulation of response latency observed among PAF units, Stecker et al. (2003) found latency and count to be less correlated across stimuli in PAF than in A1. Here, we observed a similar pattern in DZ. Figure 10 plots distributions of latency/count correlations across units in the three fields. Approximately 55% of PAF units and 57% of DZ units had latency/count correlations between -0.5 and -1, compared with 62% of A1 units. The lower dependence of latency and count among units in PAF and DZ suggests that units might use the two features as independent coding dimensions. We used stepwise regression to predict across-unit variance in fullpattern spatial coding TSRs based on variance across units' coding by count (TSR<sub>C</sub>) and latency (TSR<sub>L</sub>). As previously reported (Stecker et al. 2003), the bulk of TSR<sub>S</sub> variance across PAF units (78%) was related to variance in TSR<sub>1</sub>-either alone (20%) or in conjunction with  $TSR_{C}$  (58%)—while very little (8%) could be predicted by  $\ensuremath{\mathsf{TSR}}_{\ensuremath{\mathsf{C}}}$  alone. Roughly the opposite was true of A1 units (23% of TSRs variance explained by  $\text{TSR}_{\text{C}}$ , 11% by  $\text{TSR}_{\text{L}}$ , 50% by either). The results can be interpreted to show that, among PAF units, accurate spatial coders made use of latency coding (whether or not they also used count coding), whereas those accurate spatial coders among A1 units encoded spatial location in their spike counts.



FIG. 10. Correlation between azimuth-dependent latency and spike count. The Pearson correlation of response latency and spike count across azimuth was computed for each unit. Distributions of the resulting correlation coefficient are plotted in proportion of units per rectangular bin of 0.16 on the x axis. Symbols plot median values of each area's distribution.

The pattern in DZ did not favor either predictor overall (15% by  $TSR_C$ , 11% by  $TSR_L$ , 56% by either), consistent with the better spatial coding by both count and latency among DZ units. Note that the proportion of variance explained redundantly by the two predictors combined was not vastly different in DZ than the other fields. DZ thus appears to contain a mixture of units that code space by count, latency, or both.

An important limitation of spatial coding by response timing is that absolute spike latencies are not directly represented in the brain. Because no independent reference of the stimulus time is available, latencies must be decoded from the responses themselves, possibly from the relative spike times of two or more neurons (Jenison 2001). Along these lines, Stecker and Middlebrooks (2003) found that relative spike times computed from simultaneously recorded A1 and PAF units (i.e., from one unit in each field) produced TSR information rates comparable to those based on absolute spike times. In that case, response latencies of A1 units (because they were weakly modulated by sound-source location) provided a reference for the more strongly modulated latencies of PAF units. Because DZ units in the current study exhibited similar patterns of response latency to PAF units, we suggest that DZ latencies could (in principle) be decoded through similar means.

#### Arrangement of spatial tuning across the cortex

As in previous studies (e.g., Furukawa and Middlebrooks 2002; Stecker et al. 2003), we commonly observed that units recorded from nearby sites on a single recording probe exhibited similar response properties. When probes were oriented lateral-to-medial within the ventral bank of SSS (ventral-todorsal along the cortical surface), we observed groups of similarly tuned units (i.e., units that preferred contralateral or ipsilateral azimuths) that were demarcated by one or more units with an opposite lateral preference. Five such sequences are illustrated in Fig. 11. Such groups covered between four and nine adjacent recording sites, corresponding to patches 450-1,200  $\mu$ m in width. We hypothesize that these patches correspond to a dorsal extension of the system of "binaural bands" (2-3 rostrocaudally elongated regions of units with similar binaural sensitivities, interdigitating with regions of different sensitivity) described in A1 (Imig and Adrian 1977; Middlebrooks et al. 1980; Nakamoto et al. 2004). In A1, binaural bands appear to correlate with regions of commissural input from contralateral auditory cortex (Imig and Brugge 1978). Similar patches of contralateral input occur within the ventral bank of SSS, consistent with the present observation of patchy spatial tuning in DZ.

# *Response patterns change abruptly near the expected A1/DZ border*

The preceding results indicate a clear distinction between the physiology of A1 and DZ neurons, in terms of complexity of frequency-tuning, latency of response, and pattern of spatial sensitivity. Nevertheless, DZ has been considered a subfield of A1 in some previous studies (Middlebrooks and Zook 1983), raising the question of whether a definitive boundary can be detected between the fields. In the current study, most DZ recordings were confined to dorsal regions of DZ (within the ventral bank of SSS), presumably well dorsal of any such



Centroid Azimuth (Contra⇔lpsi)

FIG. 11. Spatial tuning across recording probes in 5 DZ penetrations. In each panel,  $\leq 16$  lines plot normalized rate-azimuth functions for units recorded at separate sites during a single penetration (identified at *top right*) into the ventral bank of the suprasylvian sulcus (SSS). In each case, orientation of the single-shank probe was lateral to medial, approaching the middle cortical layers tangentially. Separate lines are arranged vertically by the relative location of each recording site; those near the tip of the probe (*top*) are deepest within the sulcus while those near the probe base (*bottom*) are more superficial. On an unfolded cortex, tip-to-base corresponds to dorsal-to-ventral. Symbols indicate the azimuth centroid  $\xi_{C,az}$  of each unit, if computable. Dotted lines indicate 0° and 180°, such that contralateral locations are found in the left half—and ipsilateral location in the right half—of each panel. In some cases, (23E1, 13e); in others, less variation in spatial tuning is apparent (32E).

border. To describe the physiology of units surrounding the border, we made penetrations using four-shank probes (see METHODS) in the expected vicinity of the A1/DZ border. These revealed separate groups of units with DZ-like and A1-like responses in close proximity. Figure 12 illustrates one such recording, made with two four-shank electrodes. Rasters and frequency response areas show temporally compact and sharply tuned responses, respectively, of units recorded on the ventral shanks of both probes. Such responses are consistent with A1 physiology, whereas the responses of units recorded on the dorsal shanks demonstrated DZ-like features including complex frequency tuning and late patterned temporal responses. The transition between response types across the cortical surface was abrupt (narrower than the spacing between shanks, which was 200  $\mu$ m) rather than gradual.

### DISCUSSION

#### Is DZ a distinct cortical field?

In summary, the current results reveal a distinct pattern of physiological response in DZ than in A1. The differences include, in DZ, more complex frequency tuning, longer-latency responses, increased prevalence and degree of nonmonotonic rate-level functions, and a weaker response to broadband relative to tonal stimulation. Each of these factors is consistent with a larger role for inhibition in shaping DZ responses than A1 responses (Sutter and Loftus 2003). With respect to spatial sensitivity (and perhaps partly reflecting such inhibitory processes), DZ units are more sharply tuned to free-field azimuth and their response latencies are more strongly modulated by stimulus location than are units in A1. As a result, the spike patterns of DZ units are generally more informative of soundsource locations than those of A1 units. Furthermore, the population of DZ units samples space more uniformly than A1



FIG. 12. Illustration of the A1–DZ border in 1 set of recordings (penetrations 37Ha and 37Hb). We recorded simultaneously from 2 4-shanked probes inserted perpendicular to the cortical surface (i.e., approximately parallel to the radial cell columns) and placed in the vicinity of the A1–DZ border. *Center*: the location and orientation of recording sites (black circles) relative to sulcal landmarks (SSS; PES: posterior ectosylvian sulcus; AES: anterior ectosylvian sulcus) and the location of the A1–DZ border (thin line) estimated from physiological responses. *Left* and *right groups* of panels plot rasters of spike times across azimuth (*left panel* in each pair) and frequency response areas (*right panel* in each pair, see Fig. 1) for one representative unit recorded on each shank of the posterior (*left panels*) probes. Shanks were arranged roughly dorsoventrally, such that upper panels indicate dorsal units, while lower panels indicate more ventral units. On both probes, a distinction is observed between A1-like responses (with single frequency-tuning peaks and relatively constant latency across azimuth) on the ventral shanks and DZ-like response (multipeaked frequency tuning and azimuth-sensitive spike timing) on the dorsal shanks. The transition between response types appears to be narrower than the inter-shank spacing, which was 200 µm.

in that it contains significant numbers of units preferring ipsilateral stimulation. Although several of these differences seem relatively clear (e.g., latency modulation and complex frequency tuning), many are more subtle despite their statistical significance (e.g., differences in spatial tuning width and transmitted information). While such minor differences can be useful in distinguishing cortical fields on the basis of physiological characteristics, their functional relevance may be questionable at best. Indeed, the paucity of clear (qualitative) physiological differences among cortical fields seems to argue against a strong view of functional specialization in the auditory cortex. Nevertheless, the overall pattern of results suggests that DZ is physiologically distinct from A1, and moreover that it might play an important role in sound-localization behavior.

Middlebrooks and Zook (1983) treated DZ, conservatively, as a region of primary auditory cortex (A1), albeit a region receiving a unique pattern of thalamocortical input. He and Hashikawa (1998), in contrast, found a distinct pattern of neuronal physiology in DZ inconsistent with the primary-like responses observed in A1. The results of the present study corroborate that observation and lend support to the view that A1 and DZ represent physiologically distinct cortical fields. Additional support comes from the observation that the ventral-to-dorsal transition of response properties is not gradual (as expected if these differences reflect continuous variation within a field), but abrupt (consistent with an inter-field border). The existence of a border between A1 and DZ is further supported by anatomical studies using SMI-32 antibody staining as a marker of areal divisions in cortex (Mellott et al. 2005). The border-like transition observed in our physiological results, however, might also coincide with transitions between binaural bands (Middlebrooks et al. 1980) in A1 and/or DZ. It is not currently understood whether these bands represent subfields within one or more functionally homogeneous cortical fields, interdigitating extensions of two or more distinct fields or individually distinct cortical fields. This question confuses the relationship of A1 with its neighboring fields, and must be addressed in the future by high-resolution physiological mapping of auditory cortex.

The argument that DZ is distinct from A1 is based on large differences between the behavior of neurons in the two fields. While the characteristics of DZ neurons set them apart from A1 neurons, they are-in nearly every respect-shared with PAF neurons. In both fields, as compared with A1, we observe sharper spatial tuning, enhanced coding of sound-source locations, complex frequency tuning, nonmonotonic rate-level functions, stronger responses to tones than to broadband noise, and elongated temporal responses with spatially modulated first-spike latency. The differences between DZ and PAF are fewer than the similarities but include overall shorter first-spike latencies in DZ (values are intermediate between PAF and A1), better coding of sound-source locations by spike counts in absence of temporal information in DZ, and larger numbers of ipsilaterally tuned neurons in DZ (possibly related to the appearance of "binaural bands"). One might argue, based on the results, that PAF and DZ correspond to a system of "belt" fields-characterized by complex, nonlinear, and long-latency responses-that surrounds the primary "core" fields of A1 and AAF (Harrington et al. 2005), which are characterized by simpler, linear, short-latency responses. We note, however,

that there are prominent anatomical differences between DZ and PAF; anatomical tracer injections in DZ produce retrograde label in compact clusters of cells in the dorsal cap of the lateral part of the lateral division of the MGB (Middlebrooks and Zook 1983) whereas that label has not been demonstrated following PAF injections.

## Are fields like DZ and PAF specialized for spatial processing?

As discussed in our report on spatial sensitivity in PAF (Stecker et al. 2003), the physiological characteristics of neurons in that field are better suited for encoding information about sound-source location than are neurons in A1. To the extent that such characteristics are shared by DZ neurons, a similar argument holds for DZ. The differences between fields, however, are quantitative (e.g., sharper spatial tuning, stronger modulation of spike count or latency); there are no clear qualitative differences in the manner of spatial coding between fields. Furthermore, our pattern-recognition analyses suggest that localization based on the responses of A1 neurons, although inferior to that based on PAF or DZ responses, should be reasonably accurate. We have argued that in the absence of qualitative differences between spatial sensitivity in various cortical fields, identification of each field's functional role in sound localization requires behavioral evidence (e.g., from lesion studies). Such evidence, however, has not provided a simple answer to this question. Chronic lesion studies in monkeys, for example, have demonstrated severe contralesional sound-localization deficits following extensive lesions of auditory cortex, but only minimal effects following restricted lesions of various regions within auditory cortex (Harrington and Heffner 2002; Heffner 2005). Studies employing temporary "inactivation" of auditory cortex (e.g., by cooling cortical tissue), however, have revealed profound deficits following inactivation of particular restricted regions-notably cat A1 (including DZ), PAF, and fAES-but not others (e.g., cat AAF and A2). Inactivation of either DZ or ventral A1 alone produces only partial deficits, suggesting that the two fields make up a single functional unit for sound localization (Malhotra et al. 2004b).

How are we to make sense of these cortical-inactivation results? Although PAF and DZ appear (in physiological terms) about equally specialized for spatial processing, inactivation of one (PAF) results in profound localization deficits, whereas inactivation of the other (DZ) results in only partial deficits. Further, with the exception of A1, surgical removal of other auditory fields in the cat results in only partial localization deficits, if any, regardless of the fields removed (Strominger 1969). One possibility is that between-field differences are not tied to specific functions and thus that cortical fields are not functionally discrete modules for specialized processing. Neural responses in various cortical fields differ in their sensitivity to various aspects of auditory stimuli (e.g., frequency, location, intensity) by amounts that affect their ability to convey useful information to subsequent processing and behavior. Given the emerging evidence for substantial potential for plasticity in developing and adult auditory cortex (Gilbert et al. 2001), it seems reasonable to assume that regions of cortex involved in spatiomotor processing might receive input from various regions of auditory cortex and that such inputs would be modified through development. If so, the most informative inputs to spatial processing might be derived from fields-like PAF or DZ-that accentuate spatial aspects of stimuli in their responses. In the absence of input from these fields (e.g., following focal lesions), mechanisms of plasticity might act to strengthen input from other fields (A1, AAF) that are less optimal, but nevertheless suitable, for spatial processing. As a result of cortical plasticity, the effects of chronic lesions only become severe when all potential input sources (i.e., all of auditory cortex) are removed. That is not to say that, in the normal state, all of auditory cortex is involved in spatial processing; merely that all of auditory cortex is capable, by degrees, of subserving it. Acute focal lesions (as caused by cooling), on the other hand, can produce catastrophic deficits by interrupting the input to spatial processing before plastic reorganization can take place.

#### How is space represented in the auditory cortex?

A reasonable expectation of much past research on spatial sensitivity in auditory cortex has been the existence of a topographic space map or local code for space (Stecker and Middlebrooks 2003). At this point, we have sampled a majority of fields in cat auditory cortex in search of the hallmarks of such a representation: sharp spatial tuning that is maintained at low and high intensities, uniform—or at minimum complete sampling of auditory space and orderly progression of best locations across the cortical surface. We have found no good evidence for a "space map" in any of the studied fields. Cortical neurons exhibit broad spatial tuning that broadens further for intense stimuli, and their best locations sample space in a decidedly nonuniform manner: the great majority prefer lateral locations and have rate-azimuth functions that are abruptly modulated near the interaural midline (Stecker et al. 2005).

We have argued previously for a distributed representation of auditory space in which individual neurons respond panoramically, encoding information about sound-source locations away from their peak response (Middlebrooks et al. 1994; Stecker and Middlebrooks 2003). Most recently, we have amended that view to reflect the nonuniform sampling of space by cortical neurons. Despite apparent "tuning" for locations far from the interaural midline, neurons encode midline locations best due to the steep slopes of their rate-azimuth functions (RAFs) in that region. McAlpine and colleagues have argued that low-frequency neurons in the auditory brain stem and midbrain similarly utilize the slopes of their tuning functions to encode interaural time differences (Brand et al. 2002; Harper and McAlpine 2004; McAlpine et al. 2001) across a limited number of ITD-sensitive channels (Marquardt and McAlpine 2001). Following that work, and based on the similarity of many cortical neurons' RAFs, Stecker et al. (2005) argued that the cortical population in each hemisphere is composed of two broad spatial "channels" responsive to contralateral and ipsilateral stimulation. Sound-source locations could be encoded by the difference in response between these channels (cf. von Békésy 1930; van Bergeijk 1962) in a manner that is not biased by changes in stimulus level. It is worth considering—based on the current results-that DZ contains a higher proportion of ipsilaterally tuned units than seen in A1 or PAF and that such units may be grouped in binaural bands interdigitating with

groups of contralaterally tuned units. If the opponent-channel theory of spatial coding in the auditory cortex (Stecker et al. 2005) is correct, this alternating pattern might be the closest equivalent of an auditory space map in the mammalian cortex.

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