Binaural Interaction Revisited in the Cat Primary Auditory Cortex

Jiping Zhang, Kyle T. Nakamoto, and Leonard M. Kitzes. Binaural interaction revisited in the cat primary auditory cortex. J Neurophysiol 91: 101–117, 2004. First published September 24, 2003; 10.1152/jn.00166.2003. The binaural interactions of neurons were studied in the primary auditory cortex (AI) of barbiturate-anesthetized cats with a matrix of binaural tonal stimuli varying in both interaural level differences (ILD) and average binaural level (ABL). The purpose of this study was to determine: 1) the distribution of preferred binaural combinations (PBCs) of a large population of neurons and its relationships with binaural interactions and binaural monotonicity; 2) whether monaural responses are predictive of binaural responses; and 3) whether there is a restricted set of representative binaural stimulus configurations that could effectively classify the binaural interactions. Binaural interactions were often diverse in the matrix and dependent on both ABL and ILD. Compared with previous studies, a higher proportion of mixed binaural interaction type and a lower proportion of EO/I type were found. No monaural neurons were found. Binaural responses often differed from monaural responses in the number of spikes and/or the form of the response functions. The PBCs of the majority of EO and PB neurons were in the contralateral field and midline, respectively. However, the PBCs of EE units were evenly distributed across the contralateral and ipsilateral fields. The majority of the nonmonotonic neurons responded most strongly to lower ABLs, whereas the majority of monotonic neurons responded most strongly to higher ABLs. This study demonstrated that in AI a restricted set of binaural stimulus configurations is not sufficient to reveal the binaural responses properties. Also, monaural responses are not predictive of binaural responses.

INTRODUCTION

Binaural interactions of neurons in auditory cortex (AC) have been investigated in numerous studies with dichotic and free-field stimuli in various species, such as cat (Imig and Adrián 1977; Imig et al. 1990; Irvine et al. 1996; Middlebrooks et al. 1980; Phillips and Irvine 1979, 1983; Reale and Kettner 1986; Samson et al. 1993, 1994; Schreiner and Cynader 1984; Semple and Kitzes 1993a,b), ferret (Kelly and Judge 1994), rat (Kelly and Sally 1988), chinchilla (Benson and Teas 1976), bat (Liu and Suga 1997; Manabe et al. 1978; Razak and Fuzessery 2000, 2002; Shen et al. 1997), monkey (Brugge and Merzenich 1973; Recanzone et al. 1999), and guinea pig (Rutkowski et al. 2000). In dichotic studies, binaural interaction was invariably defined by comparing responses to binaural stimuli with responses to monaural stimuli. Imig and Adrián (1977) classified binaural interactions as summation, suppression, occlusion, and monaural. Mixed binaural interactions, consisting of combinations of these basic categories, were subsequently added to this scheme (Reale and Kettner 1986; Semple and Kitzes 1993a,b). A second scheme, originally proposed by Goldberg and Brown (1969), explicitly linked binaural interactions to monaural responses. Responses to monaural stimulation of the contralateral and ipsilateral ears are typically classified separately as excitatory or no response (e.g., EE or EO). The binaural interactions of EE neurons were further classified as summation, occlusion, and facilitation according to the comparison between binaural response and the sum of the monaural responses. For EO neurons, inhibitory influence was assessed by an inhibitory ratio (i.e., binaural response divided by the response of the excitatory ear). It was typically designated as an inhibitory binaural interaction if the response to stimulation of the excitatory ear was diminished by stimulation of the other ear. According to this classification scheme, many studies in the auditory cortex used a 2-letter code to designate the monaural response types followed by the specification of the binaural interaction type.

These schemes were often used to determine the topography of binaural interactions in the auditory cortex. Neurons of different binaural interaction classes were reported to be topographically segregated in bands that are oriented orthogonally to iso-frequency contours (Imig and Adrián 1977; Middlebrooks et al. 1980). Neurons with common binaural response properties were also reported to be organized in a columnar fashion (Imig and Adrián 1977). Later studies demonstrated that neurons with similar binaural interactions aggregate in clusters rather than in continuous bands (Kelly and Judge 1994; Kelly and Sally 1988; Razak and Fuzessery 2000, 2002; Reale and Kettner 1986; Rutkowski et al. 2000; Shen et al. 1997). In these studies, the binaural interactions of neurons were often classified by testing the stimuli over a narrow range of levels (e.g., near threshold) (Middlebrooks et al. 1980), rather than over the wide variety of binaural stimulus configurations that is likely to occur in a normal sound environment. Because these mapping studies required the sampling of as many single or multiunits as possible within each animal, the assumption was often made, explicitly or implicitly, that binaural interactions observed at one or a very few stimulus levels would typify the interactions that occur at any level. However, mixed, often complex binaural interactions have been observed when a sufficient matrix of binaural stimuli was employed (Irvine et al. 1996; Semple and Kitzes 1993a,b). Such results raise the possibility that previous mapping studies examined a subset of responses that did not necessarily reflect the diversity of binaural interactions that cortical neurons could exhibit. Thus one purpose of this study was to examine the binaural responses of a large population of cortical neurons to a wide range of
binaural stimulus configurations to determine whether there might be a restricted set of representative configurations that could be used efficiently and effectively in mapping studies.

Previous studies have shown an orderly spatial organization of various neuronal parameters related to the encoding of monaural contralateral sound intensity in cat AI, such as minimum threshold, dynamic range, best sound pressure level (SPL), and nonmonotonicity of intensity functions (Heil et al. 1994; Schreiner et al. 1992). Other response parameters such as the sharpness of frequency tuning and minimum contralateral latency were also found to be nonrandomly distributed across the isofrequency axis (Mendelson et al. 1997; Schreiner and Sutter 1992). If binaural responses can be predicted from monaural responses, then the monaural maps can be used to predict the topography of responses to binaural stimuli. Thus another aim of this study was to determine whether monaural responses are good predictors of binaural responses.

Dichotic studies using characteristic frequency (CF) tones varied over wide ranges of interaural level differences (ILD) and average binaural levels (ABL) have provided examples of preferred binaural combinations (PBC; i.e., the binaural combinations that elicited the highest range of response strength) located in representations of contralateral, ipsilateral, and midline acoustic space (Irvine et al. 1996; Semple and Kitzes 1993a,b). Very similar foci appear in the series of excellent papers by Imig and colleagues (Clarey et al. 1994; Imig et al. 1990; Samson et al. 1993, 1994). In these studies, noise bursts were presented from speaker positions arranged around the animal. Response preference was assessed by varying stimulus level and azimuth. Examples shown from both types of study indicate foci of activity across the range of stimulus level, from very low to the highest used in the 2 types of paradigms. Thus both free-field and dichotic studies have demonstrated preferences for specific areas of acoustic space. The third purpose of the present study was to examine the distribution of the PBCs of a large number of units to determine the manner and extent to which the population covers the frontal acoustic field, and the relationship between PBCs and both binaural interactions and binaural monotonicity.

METHODS

Animal preparation

Four healthy adult cats, free from external and middle ear infection, were used in this study. The cats were anesthetized with pentobarbital sodium (40 mg/kg intraperitoneally). Anesthesia was maintained throughout surgery and the physiological recording by intravenous injections of pentobarbital sodium through a cannula in the radial vein. Body fluid level was maintained by intravenous administration of 5% dextrose in lactated Ringer solution throughout the experiment. Atropine sulfate (0.048 mg) and Dexamethasone sodium phosphate (0.044 mg) were injected at the beginning of surgery and at 24-h intervals to reduce bronchial secretions and cerebral edema, respectively. Body temperature was monitored by a rectal probe and maintained at 38°C by a feedback-controlled heating blanket. A tracheotomy was performed to allow unobstructed breathing and to reduce respiration noise. A metal rod was attached to the exposed dorsal surface of the skull with small screws and dental cement. The cat was then secured to a stereotaxic-like recording frame by the metal rod. The pinnae were resected and earpieces inserted and acoustically sealed within the transected external auditory canals. A small hole was made through the skull, and a small incision was made in the dura to expose part of the primary auditory cortex. Warm saline or mineral oil was applied to the cortex during the experiment to prevent drying.

Acoustic stimuli

Tonal stimuli were 50 ms in duration with a 6-ms rise–decay time, presented at 800-ms intervals, and repeated 40 times at each SPL. Tone pips were generated digitally by a MALab system (Kaiser Instruments) controlled by a Macintosh computer. Stimuli were transduced by STAX earphones that were housed in metal canisters. The canisters were coupled directly to the earpieces. Tympanic SPL (re 20 μP) was calibrated at each ear from 100 Hz to 30 kHz under computer control with a calibrated probe tube and a 0.5-in. condenser microphone (Brüel and Kjær). The calibrations were stored in the computer for use in controlling attenuators to obtain desired SPLs.

Recording system

Responses of single neurons were recorded with parylene-insulated tungsten microelectrodes (1–3 MΩ impedance). Electrodes were oriented orthogonally to the pial surface. The electrode signal was amplified (×1,000), filtered (0.3–3.0 kHz), and then sent to a digital oscilloscope for display. Data were analyzed both on- and off-line by the MALab system. Recording was conducted in a double-wall, sound-insulated chamber. Electrode advancement was controlled from outside the sound-insulated chamber.

Data collection procedure

Neurons were recorded from the middle layer (mainly III and IV) within a single isofrequency contour of primary auditory cortex of each cat. Whereas the companion paper (Nakamoto et al. 2004) focuses on the topography of binaural interactions within an isofrequency contour, the data presented in this paper are pooled across animals. Once a single neuron was isolated, its CF (i.e., the frequency to which the neuron was most sensitive) and threshold at CF were determined. For each animal, the CF of the first neuron was selected as the stimulus frequency to be used for the study of subsequently isolated neurons in that animal (fixed-stimulus frequency). If the CF of the isolated neuron was within ±0.15 octave of the fixed-stimulus frequency, the neuron was further analyzed; otherwise the neuron was discarded. The fixed-stimulus frequency for the 4 animals was between 8 and 15.6 kHz. For each neuron, the rate/level function of responses to monaural contralateral stimuli was collected; an ipsilateral rate/level function was collected if the unit was responsive to monaural ipsilateral stimuli. A matrix of binaural stimuli was then presented in which the ILD and ABL were varied systematically. ILD was varied from −20 to +20 in 10-dB steps: negative ILDs indicate that ipsilateral stimulation was greater than contralateral stimulation. ABL was defined as the sum, in dB, of the contralateral and ipsilateral stimuli divided by 2. At each ILD, ABL varied from 20 to 70 in 10-dB steps. A binaural stimulus can be described in terms of its ILD and ABL or in terms of level at the contralateral and ipsilateral ears. While bearing this equivalency in mind, we shall more frequently use the derived terms ILD and ABL because they more simply describe a trajectory of stimuli at some interaural relation.

Data were collected from each stimulus point in the binaural matrix. The contralateral and ipsilateral monaural rate/level functions were repeated at the end of the data collection of each neuron to assess response stability.

Data analysis and binaural interaction classification

Neurons in the auditory cortex were first classified as EE, EO, OE, and PB according to their monaural response properties. Neurons were classified as EE if they responded to stimulation of either ear;
EO if they responded to stimulation of the contralateral ear but not to stimulation of the ipsilateral ear; and OE if they responded to stimulation of the ipsilateral ear but not to stimulation of the contralateral ear. Neurons that did not respond to stimulation of either ear, or only very weakly, but responded strongly to binaural stimulation were designated PB (predominantly binaural).

Neurons within each group were further classified according to their binaural interaction behavior within the stimulus matrix. Because of the low number of spikes sometimes evoked in auditory cortex cells, we used an arbitrary criterion of a 20% change in response to delimit a category of binaural interaction (Fig. 1). Binaural interactions were assessed for each binaural combination in the stimulus matrix. If both the binaural and the monaural response at the corresponding stimulus level were <10 spikes, this binaural combination was excluded from the binaural interaction classification analysis. For EE neurons (Fig. 1A), a binaural interaction that produced a response to a binaural stimulus that was >120% of the sum of the monaural responses at corresponding stimulus levels was classified as facilitation (F). It was classified as inhibition (I) if the binaural response was <80% of the response to stimulation of the dominant ear. If the binaural response was between 80% of the sum of the monaural responses and 80% of the response to stimulation of the dominant ear, the binaural interaction was classified as occlusion (O). A binaural response that was within ±20% of the sum of the respective monaural responses was considered to be the result of random fluctuations or very weak binaural interactions, and therefore indicative of no significant binaural interaction (N). For EO or OE neurons (Fig. 1B), a binaural interaction that produced a response to a binaural stimulus that was 20% greater than the monaural response to stimulation of the dominant ear at the corresponding stimulus level was classified as facilitation (F). The dominant ear was either contralateral or ipsilateral for EO neurons or ipsilateral for OE neurons. If the binaural response was <80% of the response to stimulation of the dominant ear, the binaural interaction was considered to be indicative of inhibition (I). If the response was within ±20% of the response to stimulation of the dominant ear, the binaural interaction was considered indicative of no interaction (N). The binaural interaction of PB units was invariably facilitative because the response of these units to monaural stimuli is either zero or a very small fraction of their response to binaural stimuli.

The binaural interaction type of a neuron was classified according to the kinds of binaural interactions it exhibited within the stimulus matrix. Thus the binaural interaction type of a neuron was considered to be F, I, O (for EE neurons), or N if it demonstrated predominantly facilitative, inhibitory, occlusive, or no binaural interaction in the stimulus matrix. The binaural response type was classified as mixed if more than one type of interaction occurred within the binaural matrix [e.g., inhibition and facilitation (IF); facilitation and occlusion (FO); inhibition and occlusion (IO); and inhibition, occlusion, and facilitation (IOF)]. The criterion for the inclusion of more than one type of interaction was that the type of interaction occurred at ≥3 contiguous stimulus points within the binaural matrix. To reduce the number of neuron categories, designation of no interaction (N) was not included in the classification scheme even if it occurred at ≥3 contiguous stimulus points unless no other type of binaural interaction occurred.

The monotonicity of the response function with the increase of ABL at each ILD was evaluated separately. A criterion of 30% reduction in the number of evoked spikes, relative to the peak response, was used to distinguish monotonic from nonmonotonic response functions. If the maximum response at a particular ILD was <10 spikes, the response function at this ILD was excluded from the analysis. A neuron was classified as binaurally nonmonotonic (NM) if the majority of the ABL response functions were nonmonotonic; and it was classified as binaurally monotonic (M) if the majority of functions were monotonic; otherwise, it was classified as other.

RESULTS

Complete monaural and binaural data were obtained from 113 single neurons in primary auditory cortex (AI). According to their monaural response properties, 32 were classified as EE, 57 as EO, 6 as OE, and 18 as PB neurons. According to our criteria, 34 neurons (30.09%) demonstrated a single type of binaural interaction within the stimulus matrix, i.e., not more than 2 contiguous stimulus points showing other binaural interaction type within the matrix (Fig. 2, A-4 and B-4; Fig. 4A-3; Fig. 5A-3; Fig. 7A-3; Fig. 8, A-2, B-2, and C-2). The binaural interaction type of these units was independent of ABL and ILD. However, the degree of inhibition or facilitation was strongly dependent on ABL and ILD. Because any combination of ABL and ILD can be specified in terms of stimulus level at each ear, the degree of inhibition and facilitation can be understood as being dependent on the stimulus level at the 2 ears.

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**FIG. 1.** Classification of binaural interactions of neurons. Rate level functions shown in A and B are hypothetical. A: classification of EE neuron’s binaural interaction at ILD 0 and ABL 70. C+I: sum of the contralateral (C) and ipsilateral (I) monaural responses at the corresponding sound pressure levels (SPLs). Dominant: stronger monaural responses. B: classification of EO and OE neurons’ binaural interaction at 80 dB SPL. Dominant: contralateral for EO neurons or ipsilateral for OE neurons. F, N, O, and I: facilitation, no interaction, occlusion, and inhibition, respectively. See text for description of binaural interaction designations.

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Binaural interaction of EE neurons

EE neurons exhibited a variety of binaural interactions within the stimulus matrix. Figure 2 shows the binaural interactions of 3 EE neurons. The panels in the 1st column show the monaural rate level functions of 3 EE neurons. The panels in the 2nd column show binaural response functions at different ILDs and ABLs, plotted as a function of SPL at the dominant ear. For comparison, the dominant monaural response function is included (dashed line). Numbers on the right of the symbols refer to ILD. Positive ILDs favor the contralateral ear and negative ILDs favor the ipsilateral ear. The panels in the 3rd column show the response contours of activity plotted at different contralateral and ipsilateral levels of the matrix. Filled squares indicate the stimulus points. Legend within A-3 illustrates the ILD and ABL values, and demonstrates that the stimuli can be designated in terms of these parameters or the SPL at each ear. Gray scale indicates the magnitude of the response in 20% divisions, as shown on the right. White * indicates the stimulus that evoked the largest response within the stimulus matrix, i.e., the best binaural combination (BBC). Darkest response areas show the neurons' preferred binaural combinations (PBCs) that elicited ≥80% maximal response within the stimulus matrix. The panels in the 4th column show the binaural interaction behaviors within the stimulus matrix for each neuron.

The monaural responses of unit 00K015.011 increased monotonically with SPL (Fig. 2A-1). In contrast to the monaural response functions, binaural responses increased when the level of the contralateral stimulus was <60 dB but then decreased at higher contralateral levels (Fig. 2A-2). Except for ABL 70 of ILD +10 and ILD +20, at each ILD, the binaural responses at ABLs between 30 and 70 were >120% of the sum of the monaural responses evoked at corresponding SPLs (Fig. 2A-4). Accordingly, this neuron was classified EE/F. The best binaural combination (BBC) of this neuron was at ABL 60, ILD −10 (i.e., contralateral 55, ipsilateral 65 dB). The interpolated contour of the binaural combinations that evoked ≥80% of the response at the BBC (shown in black) is defined as the neuron's preferred binaural combinations (PBC). It is evident in this data format that the PBC of this neuron is predominantly at ipsilateral and midline ILDs above 40 ABL.
Unit 00K015.030 responded similarly to monaural contralateral and ipsilateral stimuli (Fig. 2B-1). Both monaural and binaural responses changed nonmonotonically with SPL (Fig. 2B-1 and B-2). This neuron was classified as EE/O because its binaural responses were \( >80\% \) of the sum of the monaural responses (Fig. 2B-4) and were \( >80\% \) of the contralateral monaural responses. As can be seen in Fig. 2B-3, the BBC of this neuron was at ABL 30 and ILD 20, and its PBC was mainly distributed at ipsilateral ILDs below ABL 35. The monaural responses of unit 01K003.007 were contralateral dominant (Fig. 2C-1). Its binaural responses changed nonmonotonically, with increasing ABL at each ILD (Fig. 2C-2 and C-3). The binaural interaction of this unit varied greatly within the stimulus matrix, from facilitation at lower and middle ABLs around 0 ILD to no interaction or occlusion at other combinations of ABL and ILD (Fig. 2C-4). The classification of this unit was therefore EE/FO.

Figure 3 shows 2 examples of EE neurons that exhibited inhibitory binaural interactions at contiguous combinations of ABL and ILD. For neuron 01K004.022, the ipsilateral monaural response function changed nonmonotonically, whereas the contralateral monaural response function changed monotonically with SPL (Fig. 3A-1). The binaural responses of this neuron increased monotonically with ABL at ILDs from –10 to +20 (Fig. 3, A-2 and A-3). Relative to the dominant ipsilateral response function, with increasing ABL, the binaural interaction progressed from inhibition to occlusion or no interaction (Fig. 3A-4). Unit 01K003.038 responded more strongly to monaural contralateral stimulation than to monaural ipsilateral stimulation (Fig. 3B-1). The binaural responses of this unit, however, were either occlusive or inhibitory (Fig. 3, B-2, B-3, and B-4). Thus, whereas ipsilateral stimulation was excitatory when presented alone, it was clearly inhibitory when presented as a component of a binaural stimulus that favored ipsilateral and some midline ILDs. These 2 neurons were classified as EE/IO neurons.

Among 32 EE neurons, 5 were classified EE/F, 6 were EE/FO, 6 were EE/IOF, 11 were EE/IO, 1 was EE/I, and 3 were EE/O (Table 1). The type of binaural interaction exhibited by the great majority of EE neurons varied within the stimulus matrix and thus was a joint function of ABL and ILD. The location and overall size of the PBC varied greatly across the set of EE units. In Fig. 2, for example, unit 00K015.011 preferred ipsilateral and midline stimuli at high ABLs, unit 00K015.030 preferred ipsilateral stimuli at low ABLs, and unit

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<tr>
<th>Binaural Interaction</th>
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<th>Proportion (%)</th>
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<tr>
<td>EE</td>
<td>32</td>
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<tr>
<td>EE/F</td>
<td>5</td>
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<tr>
<td>EE/I</td>
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<td>0.89</td>
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<tr>
<td>EE/IOF</td>
<td>6</td>
<td>5.31</td>
</tr>
<tr>
<td>EE/FO</td>
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<tr>
<td>EE/IO</td>
<td>11</td>
<td>9.73</td>
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<tr>
<td>EE/O</td>
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<td>2.66</td>
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<tr>
<td>EO</td>
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<tr>
<td>EO/I</td>
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<tr>
<td>PB</td>
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<td>15.93</td>
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01K003.007 preferred near-midline stimuli at low and intermediate ABLs. The examples shown in Figs. 2 and 3 illustrate a general characteristic of EE units: the form of the monaural functions is typically a very poor predictor of the topography of their binaural interactions.

### Binaural Interaction of EO Neurons

Fifty-seven neurons responded to monaural contralateral stimulation and did not respond to monaural ipsilateral stimulation, and thus were designated EO neurons. Among these neurons, 20 had predominately binaural inhibitory interactions and were classified as EO/I neurons (Table 1). Six neurons had predominately facilitative binaural interactions and were designated EO/F. The other 31 neurons showed mixed inhibitory and facilitative binaural interactions, and were classified EO/IF. No monaural EO (i.e., EO/N) neurons were found.

Figure 4 shows 2 examples of EO/F neurons whose binaural responses were greater than their responses to monaural contralateral stimulation at the corresponding contralateral stimulus level. Ipsilateral monaural stimulation evoked no spikes when presented alone, but facilitated responses to contralateral stimulation. The responses of unit 01K004.011 to contralateral monaural stimulation increased modestly to 70 dB and then declined at 80 dB (Fig. 4A-1). Its binaural responses changed nonmonotonically at ILD 0, +10, and +20 but monotonically at ILD −10 and −20 with increasing ABL (Fig. 4A-2). When the contralateral stimulus level was between 40 and 60 dB, the facilitation at midline and contralateral ILDs resulted in responses that were 2 to 4 times greater than the monaural responses. The binaural facilitation resulted in a PBC focus of enhanced activity at middle ABLs favoring the contralateral ear. As can be seen in Fig. 4A-3, this neuron showed facilitatory interactions at the great majority of binaural combinations with the exception of ABL70 at ILD 0 and ABL 50 at ILD −20 within the stimulus matrix. Both monaural and binaural responses of unit 01K004.010 changed monotonically with increasing contralateral SPL (Fig. 4B-1). Except for the lower ABLs at ILD +20 and the higher ABLs at ILD −20, the response to each stimulus with contralateral levels >20 dB was facilitated (Fig. 4B-3). The monotonicity and facilitation resulted in a PBC focus at high ABLs favoring the midline and contralateral ear (Fig. 4B-2). Neither of the monaural responses of these 2 units, which happened to be somewhat similar, were predictive of the shape or magnitude of their binaural responses, and therefore of the location of their respective PBCs.

The responsiveness of the 20 EO/I units to the levels of contralateral and ipsilateral stimulation within the stimulus matrix varied greatly. When contralateral stimulation was fixed, the responses of 17 neurons decreased systematically as the ipsilateral stimulus level was increased (i.e., as ILD changed from favoring the contralateral ear to favoring the ipsilateral ear). Among these neurons, 10 demonstrated almost purely binaural inhibitory interactions; the binaural responses of 6 of these neurons were completely inhibited at ILD −10 and −20. The responses of unit 01K004.035 exemplify this behavior (Fig. 5, A-1, A-2, and A-3). No spikes were evoked at ILD −20 and −10. At other ILDs, the degree of inhibition increased with the level of ipsilateral stimulation (Fig. 5, A-1 and A-2). Seven of the 17 neurons exhibited predominantly...
inhibitory interactions, with no binaural interaction at some combinations of ABL and ILD. The binaural behavior of the other 3 neurons was more complicated. For example, the binaural inhibition of neuron 01K004.008 was greater at the more contralateral and ipsilateral ILDs (Fig. 5, B-1 and B-3), resulting in a broad PBC located at middle and high ABLs around midline (Fig. 5B-2). A “trough” EO neuron was found that responded strongly at ILD -20 and +20 and was inhibited at midline ILDs.

The type of binaural interaction exhibited by the majority of EO neurons (31 of 57) varied with ABL and ILD. These units exhibited binaural inhibition, facilitation, and no interaction within the stimulus matrix and consequently were classified as EO/IF. Examples of this behavior are shown in Fig. 6. The contralateral monaural responses of unit 00K015.001 changed monotonically with increasing SPL (Fig. 6A-1). Its binaural responses at ILD 0, +10, and +20 changed nonmonotonically with increasing ABL, but monotonically at ILD -10 and -20. When the contralateral stimuli were fixed at middle levels, low levels of the ipsilateral stimuli facilitated the binaural responses, whereas high ipsilateral levels inhibited the binaural responses. This resulted in a PBC focused at lower and middle ABL levels at ILD 20. Units 01K003.029 and 00K015.019 responded nonmonotonically to increasing levels of contralateral monaural stimulation but monotonically to the increasing ABL of binaural stimulation within each ILD (Fig. 6, B and C). Thus in contrast to unit 00K015.001 (Fig. 6A), binaural stimulation of these units overcame the inhibition that caused the monaural nonmonotonicity. The response of unit 01K003.029 to the binaural matrix was, in a sense, the inverse of the response of unit 00K015.001 in that over most of the range of contralateral stimulus levels, the binaural responses of this unit were facilitated at midline and ipsilateral ILDs and inhibited at contralateral ILDs. Thus ipsilateral stimuli produced no response when presented alone but when accompanied by a wide range of contralateral stimuli, they evoked responses that were appreciably larger than those evoked by monaural contralateral stimuli and by binaural stimuli favoring the contralateral ear. This behavior produced a PBC that was focused at the higher ABLs, at ILDs favoring the ipsilateral ear. This location of the PBC is, of course, unexpected for a unit defined monaurally as an EO unit. In contrast to the binaural behavior of units 00K015.001 and 01K003.029, the binaural responses of unit 00K015.019 were similar in form across ILD. With the exception of ILD 20, all of the binaural responses of this unit were inhibited when the level of the contralateral stimulus was <40 dB and all were facilitated when the level of the contralateral stimulus was >60 dB. From the complex binaural interaction of the 3 neurons shown in Fig. 6, it is clear that units within a single binaural classification category can have remarkably divergent response patterns. This is particularly apparent in the column of panels on the right, which indicate the pattern of response facilitation and inhibition within the stimulus matrix.

**Binaural interaction of OE neurons**

Six neurons responded to ipsilateral monaural stimuli but not to contralateral monaural stimuli and were consequently classified as OE. Among these neurons, 4 showed predominant contralateral inhibition (OE/I), one showed predominant contralateral facilitation (OE/F), and the other one showed mixed contralateral inhibition and facilitation (OE/IF). No monaural OE (i.e., OE/N) neurons were found. Figure 7 shows 3 examples of OE neurons. Neuron 01K004.031 was inhibited strongly by contralateral stimulation, its response being confined to the most ipsilateral ILD (Fig. 7, A-1, A-2, and A-3). The binaural responses of unit 01K004.002 were strongly and broadly facilitated by contralateral stimulation (Fig. 7, B-J,
B-2, and B-3). Perhaps paradoxically, the PBC was near midline and ILD +10 rather than at ILD +20, where the contralateral stimulus was at its highest level (Fig. 7B-2). The ipsilateral monaural and binaural responses of unit 00K015.032 changed nonmonotonically with increasing SPL and ABL, respectively (Fig. 7C-1 and C-2). When the level of the ipsilateral component of the binaural stimuli was ≤40 dB, responses to stimuli at all ILDs were greater than the respective monaural responses. At higher levels of the ipsilateral stimulus, responses to ipsilateral ILDs were facilitated, inhibited, or not significantly affected, whereas responses to contralateral ILDs were inhibited. The pattern of mixed binaural facilitation and inhibition in the stimulus matrix resulted in a PBC that was located at middle ABL levels, expanding to the ipsilateral limit of the stimulus matrix. As was the case with EE and EO units, it is clear that the PBCs and zones of binaural facilitation and inhibition of OE units are broadly divergent.

Binaural interactions of PB neurons

Eighteen neurons responded either minimally or not at all to monaural stimulation of either ear, but did respond reliably to binaural stimulation. They were consequently classified PB neurons. Consistent with previous findings (Irvine et al. 1996; Kitzes et al. 1980; Semple and Kitzes 1993a), the PBC of most (12 of 18) PB neurons was restricted near midline (i.e., at ILD 0, −10, and +10). Figure 8 shows the binaural responses of 3 PB neurons. Unit 01K004.003 is typical of this class of neurons in that the greatest facilitation occurred when the level of stimulation was equal at the 2 ears (Fig. 8A-1 and A-2). Unit 01K001.005 exhibits two-way intensity network tuning (Semple and Kitzes 1993b), in that its fully circumscribed PBC, focused at ILD 0, is determined by joint nonmonotonic tuning to the SPLs at the 2 ears (Fig. 8B-1 and B-2). Unit 01K003.017 demonstrates that occasionally the PBCs of these units can be most responsive to stimuli at lateral ILDs.

PBC location within the binaural stimulus matrix

The interpolated shapes of PBCs of neurons often depended on differences of a few spikes evoked by contiguous stimuli within the binaural matrix. Therefore we have emphasized the general location of PBCs rather than the details of their topog-
raphy. It is valuable, nevertheless, to gain an appreciation of the size of the PBCs across combinations of ILDs and ABLs, particularly with respect to the binaural classification of cortical units. Two measures of the PBC were determined for each unit. The 1st measure is an estimate of the width of the PBC—the largest ILD range within the PBC. The 2nd measure was the center of the PBC (CPBC), defined as the arithmetic mean, in dB, of the stimulus points within the PBC. These measures of the PBCs of our entire sample of 113 neurons are shown in Fig. 9, A and B. In these figures, each row represents one neuron. The number in each box is the ABL of the CPBC, and each box is centered at the ILD of the CPBC. The lines associated with each box represent the greatest width of the PBC between stimuli in the matrix. The PBCs of most (34 of 57, 59.7%) EO neurons were confined to contralateral ILDs (Fig. 9A). For EO/I neurons, the PBCs of 16 of 20 (80.0%) neurons were ≤10 ILD and confined to contralateral ILDs, with 10 of these 20 (50.0%) confined to ILD +20. The PBCs of EO/IF neurons were more broadly distributed: 17 of 31 (54.8%) were confined to contralateral ILDs, with 5 of 31 (16.1%) confined to ILD +20. In contrast to the typically narrow PBCs of the EO/I units, the PBCs of 8 EO/IF spanned a range of 20 ILD and one spanned a range of 30 ILD. Although our sample of EO/F neurons is small, the PBCs of this class of neuron appear to be more broadly distributed across ILD than that of EO/I neurons. The PBC widths of these units ranged between a small range of ILD to a full 30 ILD. The ABL values in Fig. 9A also indicated that EO units with narrow PBCs (<20 ILD range) covered the entire range of tested ABLs, whereas EO units with broad PBCs (≥20 ILD range) tended (10 of 15 units) to occur in the upper half of the ABL range (i.e., ≥45 ABL).

The locations of the CPBCs of the EO units in the binaural stimulus matrix are shown in Fig. 10, A-1 and A-2. The CPBCs of EO neurons were significantly biased toward contralateral ILDs [Fig. 10, A-1 and A-2; chi square test, degrees of freedom (df) = 1, $\chi^2 = 32.67, P < 0.001$; the trough neuron was not included]. This bias toward contralateral ILDs results from the
large percentage of EO units that were inhibited by ipsilateral stimulation. However, the ABLs at the CPBCs of these neurons varied across the entire ABL range tested (i.e., between 20 and 70 ABL) regardless of the type of binaural interactions (Figs. 9A and 10A-1). The majority (20 of 24, 83.3%) of the binaural nonmonotonic neurons contributed the lower half of the ABL range (<45 ABL); the CPBCs of the majority (27 of 29, 93.1%) of the binaural monotonic neurons were located in the upper half ABL range (Fig. 10A-2). The ABLs of CPBCs of binaural nonmonotonic EO neurons are significantly lower than that of binaural monotonic EO neurons (nonparametric Mann–Whitney U-test, \( n_{NM} = 24, n_{M} = 29, U = 44.5, P < 0.01 \)). Moreover, 83.3% (20 of 24) of the CPBCs located in the lower half of the ABL range derived from binaurally nonmonotonic EO units, and 84.4% (27 of 32) of the CPBCs located in the upper half of the ABL range derived from binaurally monotonic EO units.

Figure 9B shows the distributions of the CPBCs of EE, PB, and EO neurons. The CPBCs of EE neurons were broadly distributed across ILD (Figs. 9B and 10B-1). The numbers of units at contralateral and ipsilateral ILDs were not significantly different (chi square test, \( df = 1, \chi^2 = 0.037, P > 0.05 \)). The small number of units in each binaural interaction category of EE units precludes generalizations about the distribution of CPBCs of each category across ILD. Nevertheless, there are a few suggestions of ILD preferences among these units. The CPBCs of 6 EE/IO units occurred at contralateral ILDs, whereas one occurred at ipsilateral ILDs, 2 occurred at 0 ILD, and one occurred at near 0 ILD. The CPBCs of 2 EE/FO units occurred at ipsilateral ILDs, whereas one occurred at contralateral ILDs and 3 occurred at 0 ILD or near 0 ILD. The CPBCs of 3 EE/F units occurred at ipsilateral ILDs, whereas one occurred at contralateral ILDs and one occurred near 0 ILD. Similar to the CPBCs of EO neurons, the CPBCs of the EE population covered the entire range of tested ABLs (Fig. 10B-1). The CPBCs of 83.3% (10 of 12) of binaural nonmonotonic EE neurons were located in the lower half of the ABL range, and those of 80% (12 of 15) of binaural monotonic EE neurons
BINAURAL INTERACTION REVISITED IN AI

A

ILD (dB)

-20
-10
0
10
20

B

ILD (dB)

-20
-10
0
10
20

OE

PB

EE/O

EE/OF

EE/FO

EO/F

EO/F

EO/F

EO/F
were located in the upper half of the ABL range (Fig. 10B-2). The ABLs of CPBCs of binaural nonmonotonic EE neurons are significantly lower than that of binaural monotonic EE neurons (nonparametric Mann–Whitney U-test, \( n_{NM} = 12, n_{M} = 16, U = 15, P < 0.01 \)). Moreover, 66.7% (10 of 15) of the CPBCs located in the lower half of the ABL range derived from binaurally nonmonotonic EE units, and 81.2% (13 of 16) of the CPBCs located in the upper half of the ABL range derived from binaurally monotonic EE units.

The CPBCs of the majority of PB neurons were within ±10 ILD (Figs. 9B and 10C-1). In contrast to EO and EE units, the CPBCs of PB units did not span the range of tested ABLs. None occurred below 37 ABL and 13 (72.2%) of them occurred at ≥50 ABL. Nevertheless, the differential distribution of CPBCs derived from binaurally monotonic and nonmonotonic EO and EE units across ABL is apparent in the data obtained from PB units: the ABLs of the CPBCs of the majority of binaural nonmonotonic neurons were lower than those of the majority of the binaural monotonic neurons (Fig. 10C-2).

Figure 11 is a summary of the distribution of PBCs of EO, EE, and PB units at the ILDs tested. Each column in Fig. 11A is a tally of the number of units of each type whose PBC included the indicated ILD. Thus units with broad PBCs contributed to more than one column. The number of EO neurons increased monotonically as ILD changed from ipsilateral to contralateral. The PBCs of EE neurons were distributed almost equally across the tested ILDs and PB neurons clearly preferred near-midline ILDs.

The height of each of the 3 components of each column in Fig. 11A is determined by both the width of the PBCs of the respective types of units and the number of each type of unit in our data base. To the extent that our sample of these binaural response types is an accurate reflection of their actual proportions in auditory cortex, this representation of our data accurately indicates the relative numbers of maximally activated units of each binaural response type at each ILD. Because the proportions of units in our sample might differ from the actual proportions in auditory cortex, the data in Fig. 11A were plotted in Fig. 11B as proportions of the number of units in each category. This normalization emphasizes the contribution of PBC width in determining the sensitivity of the units to ILD. As ILD changed from ipsilateral to contralateral, the proportion of maximally activated EO units increased monotonically. At ILD +10, 61.4% of these units were maximally excited and at ILD +20 fully 80.7% of them were maximally excited. The distribution of maximally excited EE units across ±20 ILD was rather flat, varying between 37.5 and 59.4%. The distribution of maximally excited PB units showed a clear peak at 0 ILD (i.e., 72.2%), diminishing to 22.2% at −20 ILD and 11.1% at +20 ILD.

**Fig. 10.** Distributions of the arithmetic CPBCs of AI neurons within the EO, EE, and PB groups. Top panels: relationship between CPBCs and the binaural interaction types. Bottom panels: relationship between CPBCs and binaural monotonicity. Diagonal dashed lines represent 0 ILD and the dashed rectangles represent the range of the stimulus matrix. Trough neurons are not included in these plots. Note that there is an overrepresentation of CPBCs at contralateral ILDs for EO neurons (A) and at near midline ILDs for PB neurons (C). The CPBCs of EE neurons are distributed evenly at contralateral and ipsilateral ILDs (B). Also note that, regardless of the binaural interaction types, the CPBCs of the majority of the nonmonotonic neurons were located in the lower ABL range (<45 ABL), and the CPBCs of the majority of the monotonic neurons were located in the higher ABL range (≥45 ABL). M, monotonic; NM, nonmonotonic.
DISCUSSION

By analyzing monaural responses and binaural responses to a large stimulus matrix, the present study demonstrated the following. 1) The type and strength of the binaural interactions of AI neurons often depend on the level of the stimulus at each ear. Consequently, they are often diverse across a range of binaural stimulus configurations. Thus a small set of binaural stimuli is often insufficient to reveal the binaural responses properties of AI neurons. 2) The binaural input, binaural interactions, and binaural monotonicity determine the location of the PBC of AI neurons. The CPBCs of binaurally monotonic EO, EE, and PB units are located in the higher range of ABLs, whereas those of binaurally nonmonotonic units are located in the lower range of ABLs. 3) Monaural responses are poor predictors of binaural responses. These observations are discussed in the following sections.

Binaural interaction classification in the auditory cortex

Much of the research on binaural interactions throughout the auditory system derived from analyses of responses to a small set of binaural stimuli. Stimuli were often delivered by fixing the level at one ear while varying the level at the other or by fixing ABL and varying ILD. Often, only one or 2 levels of the constant-level stimulus or ABL were examined. Although such sampling allows rapid testing of each neuron, it can oversimplify the binaural behavior of neurons. This effect is evident in the comparison of the proportions of various categories of binaural interaction found in the present and previous studies (Tables 2 and 3). When monaural responses were specified (Table 2), the proportions of the major categories of binaural interaction are similar. The exceptions are the proportions of EE and PB units found in the study of the guinea pig and the proportion of PB units reported by Irvine et al. (1996). When monaural responses were incompletely or not specified (Table 3), the proportions of the major categories of binaural interaction are more variable. The major differences between the present study and the previous studies included in the two tables are 1) a higher proportion of units exhibiting mixed binaural interactions was found in the present study and 2) no monaural neurons were found in the present study. These differences can possibly be attributed to differences in the criteria of binaural interaction classification, stimulus configuration, species, and single-unit and multiunit responses.

The present study designated the binaural interaction type of a neuron by comparing its binaural response at each stimulus point in the stimulus matrix with its monaural response at the corresponding stimulus level. Previous studies (Table 2) in cat evaluated binaural interactions by comparing responses at 0 ILD with the monaural responses of the dominant ear (Phillips and Irvine 1983) or by comparing binaural responses in the ILD function obtained at one or 2 base intensities with monaural responses (Irvine et al. 1996). In guinea pig, binaural responses in average ILD functions were compared with responses to stimulation of the dominant ear (Rutkowski et al. 2000). Other studies (Table 3) classified binaural interactions by comparing binaural responses with the responses to stimulation of the dominant ear. In these studies, binaural responses

<table>
<thead>
<tr>
<th>Binaural Interaction</th>
<th>A: Cat Single Unit</th>
<th>B: Cat Single Unit</th>
<th>C: Cat Single Unit</th>
<th>D: Guinea Pig Single and Multiunit</th>
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</thead>
<tbody>
<tr>
<td>EE</td>
<td>28.32</td>
<td>28.30</td>
<td>39.00</td>
<td>57.90</td>
</tr>
<tr>
<td>EE/F</td>
<td>4.42</td>
<td>5.80</td>
<td>19.10</td>
<td>10.80</td>
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<tr>
<td>EE/I</td>
<td>0.89</td>
<td>10.30</td>
<td>23.40</td>
<td></td>
</tr>
<tr>
<td>EE/O</td>
<td>2.66</td>
<td>16.80</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EE/M</td>
<td>20.35</td>
<td>5.80</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EE/N</td>
<td>0.00</td>
<td></td>
<td>9.60</td>
<td>12.90</td>
</tr>
<tr>
<td>EO</td>
<td>50.44</td>
<td>52.80</td>
<td>49.30*</td>
<td>41.10</td>
</tr>
<tr>
<td>EO/F</td>
<td>5.31</td>
<td>5.50</td>
<td>18.80*</td>
<td>4.10</td>
</tr>
<tr>
<td>EO/I</td>
<td>17.70</td>
<td>31.60</td>
<td>24.10*</td>
<td>20.30</td>
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<tr>
<td>EO/M</td>
<td>27.43</td>
<td>11.30</td>
<td></td>
<td>7.30</td>
</tr>
<tr>
<td>EO/N</td>
<td>0.00</td>
<td>4.40</td>
<td>6.40*</td>
<td>9.40</td>
</tr>
<tr>
<td>OE</td>
<td>5.31</td>
<td>12.60</td>
<td></td>
<td>0.35</td>
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<tr>
<td>OE/F</td>
<td>0.89</td>
<td>3.00</td>
<td></td>
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<td>3.30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OE/N</td>
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<td>1.10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PB</td>
<td>15.93</td>
<td>6.30</td>
<td>11.70</td>
<td>0.35</td>
</tr>
</tbody>
</table>

Values are percentages. A: present study; EE/M, EO/M, and OE/M are from EE/IOF, EE/IO, and EE/OF, EO/IF, and OE/IF in Table 1, respectively; B: Irvine et al. 1986; C: Phillips and Irvine 1983; D: Rutkowski et al. 2000. * Including both EO and OE neurons.
were examined by holding the sound level at the dominant ear at a certain value while changing the sound level delivered to the other ear. The sound level held at the dominant ear differed across studies. Because binaural interaction type and strength vary with level, as demonstrated in the present study, differences in the reported proportions of various types of binaural interactions are readily predictable.

Another contribution to the different proportions within each binaural interaction category shown in Tables 2 and 3 is the stimulus configurations used to classify the binaural interaction type. In most of the previous studies, these stimulus configurations are from EML (excitatory monaural level)-constant method or ABL (average binaural level)-constant method, and they are often only a slice or two in the stimulus matrix used in the present study. As shown in this study, in agreement with Semple and Kitzes (1993b), the binaural interaction of most neurons in AI is not invariant across ILD and ABL. The nonmonotonic monaural response functions of unit 00K015.011 (Fig. 2A) increased by 10.220.33.5 on October 28, 2016 http://jn.physiology.org/ Downloaded from

Prediction of binaural responses from monaural responses in the auditory cortex

The location of the PBC within the binaural stimulus matrix and the magnitude of the binaural response are difficult to predict from monaural response functions or from a simple summation of these functions. For example, the monaural response functions of unit 00K015.011 (Fig. 2A) increased monotonically with SPL, its response to contralateral stimulation being about twice the amplitude of its responses to ipsilateral stimulation. Yet its PBC was clearly biased toward ipsilateral ILDs. The nonmonotonic monaural response functions of unit 00K015.030 (Fig. 2B) were essentially identical, both in magnitude and shape. Whereas such nonmonotonicity could predict that its PBC would be located at lower ABLs, the functions offer no hint that its PBC would be located at ipsilateral ILDs or that its CPBC would occur near the ipsilateral limit within the stimulus matrix. Similarly, the monaural response functions of the 2 EO/IF units illustrated in Fig. 6, A and B were similar in form yet the binaural response functions differed greatly. The responses of one unit to stimuli at contralateral ILDs were facilitated and those at ipsilateral ILDs inhibited, whereas the responses of the other unit to the same stimuli were facilitated and inhibited in the opposite direction. The PBC of the former unit was located at midlevel ABLs at the contralateral edge of the stimulus matrix, whereas the PBC of the latter unit was at higher ABLs at ipsilateral ILDs. The extreme example of the inability to predict binaural responses from monaural responses, of course, is PB neurons because most PB neurons do not respond to monaural stimuli but respond strongly to binaural stimuli.

For the majority of AI neurons in cat, azimuth tuning in the
free field depends on binaural stimulation (BD neurons; Samson et al. 1994). Similar to our results, they found that lateral-field neurons, including those with similar monaural and binaural thresholds, often exhibited differently shaped monaural and binaural functions. Binaural-level functions reflected level-dependent binaural interactions. They also found that binaural and monaural level tuning was not comparable for all midline responses. They also found that binaural aural thresholds, often exhibited differently shaped monaural field neurons, including those with similar monaural and bin-son et al. 1994). Similar to our results, they found that lateral-free field studies are consistent in demonstrating that monaural kamoto et al. 2004). Thus the present dichotic study and free-field studies are consistent in demonstrating that monaural responses are not good predictors of binaural responses for the great majority of AI neurons.

These considerations raise 2 issues. The first issue pertains to the representation of a stimulus across a population of responsive units. For EO and OE neurons, the representation of highly lateralized, low-level stimuli should depend mostly on monaural responses, given that these stimuli should not be effective at the distant ear. However, the representation of moderate level signals is likely to depend on a mixture of monaural and binaural responses, whereas the representation of high level signals should depend to a large extent on the result of binaural interactions. Thus as the level of a stimulus increases, the system must be able to track the increasing con-tribution of binaural interactions, despite the apparent lack of predictable continuity from lower-level monaural responses to higher-level binaural responses. The second issue pertains to the relevance of the topography of monaural functions to the topography of binaural responses in auditory cortex. Monaural functions have been shown to be organized spatially in AI and the parameters of some of these functions (e.g., tuning and threshold) are closely related to each other (Schreiner and Mendelson 1990; Schreiner and Sutter 1992; Schreiner et al. 1992). However, given the considerations outlined above, although such monaural maps may apply very well to cortical activation by low level stimuli, it is very likely that they differ significantly from the topography of activity evoked by moderate- and high-level stimuli that result from binaural interac-tions. Furthermore, because our sample of 113 units contained no monaural cells, the cortical activity evoked by these levels of stimulation could result entirely from binaural interactions.

Binaural interaction and the location of preferred binaural combinations

PBC location varied broadly across the binaural stimulus matrix. In general, more PBCs occurred at contralateral and midline ILDs than at ipsilateral ILDs. The binaural input, binaural interactions, and binaural monotonicity determined PBC location. EO/I neurons were excited by stimulation of the contralateral ear and inhibited by stimulation of the ipsilateral ear, resulting in their PBCs being mainly located at contralat-eral ILDs. Responses of the great majority of EO/IF neurons were inhibited at ipsilateral ILDs but were facilitated at contralateral ILDs, resulting in the PBCs of these neurons also being distributed at contralateral ILDs. The binaural facilita-tion that activated PB neurons was most intense at or near midline ILDs. We do not have enough OE neurons to permit generalizations about the binaural interactions that influence the location of their PBCs, but their PBCs tended to be at ipsilateral ILDs rather than at contralateral ILDs. The PBCs of EE neurons had no clear ILD preference; that is, they were equally distributed at contralateral, midline, and ipsilateral ILDs.

As can be seen in Figs. 9 and 10, the CPBCs of EO and EE units varied across the entire tested range of ABL. This is consistent with the free-field studies of azimuth-level response areas (ALRAs) in that preferred SPL range varied across all sound levels tested (Clarey et al. 1994; Imig et al. 1990). The CPBCs of the majority of binaurally monotonic neurons are located in the upper range of ABL (±45 ABL) and the CPBCs of the majority of binaurally nonmonotonic neurons are located in the lower range of ABL. The net effect of this differential distribution of monotonicity is that the entire range of ABL is represented in the activity of the population of cortical cells. Moreover, it is apparent that maximal neuronal activity is likely to shift from binaurally nonmonotonic neurons to binaurally monotonic neurons as the sound level increases from low to high ABL. There is a spatial aspect to this shift in activity because binaurally monotonic and nonmonotonic units in an isofrequency contour in auditory cortex are spatially segregated into small, closely juxtaposed patches (companion paper: Nakamoto et al. 2004).

Following the classic papers by Goldberg and Brown (1969), it is generally held that EI units are sensitive to azimuth, whereas EE units are sensitive to ABL. As the azimuth of a stimulus changes from one side of the head to the other, the reduced stimulus level at one ear is presumably accompa-nied by an increased level at the other ear. Thus there is no or minimal net change in the average level of excitation imping-ing on the EE unit. Consequently, EE units would be insensitive to azimuth and exquisitely sensitive to ABL. If, as this scheme implies, EE units were equally sensitive to stimulation of either ear, the CPBC of EE units would be at 0 dB ILD and the width of their PBCs would extend over an appreciable range of azimuth. However, the distribution of CPBCs of EE units shown in Fig. 9B demonstrates that this is not the case in the AI of the cat. They are broadly distributed across the entire range of tested ILDs, varying from the most contralateral to the most ipsilateral ILD in the binaural stimulus matrix. Although some of the variation in the location of the CPBCs is undoubtedly attributed to unequal sensitivity to contralateral and ipsilateral stimulation, the data presented in Figs. 2 and 3 demon-strate that this is not the only source of variation. Rather than resulting from a summation, whether equal or unequal, of their monaural sources of excitation, as predicted from the classic proposal, these data demonstrate that level-dependent facilita-tion and inhibition often determine the location of an EE unit’s PBC.

To the extent that the stimuli used in this study to construct the ILD dimension actually are representative of stimulus azimuth, it does appear that the range of azimuths to which an EE cell is most responsive varies greatly from neuron to neuron. The maximal responsiveness of EE cells varied from a small range of ILD to the full range of tested ILDs. This range of sensitivity is evident in the widest dimension of the PBCs of these neurons shown in the lower half of Fig. 9B. There is no obvious relation between the ABL at the CPBC and the width of the PBC. The PBCs of EE cells with the same or very similar best ABLs vary in width from a small range to ±20 ILD. In addition, as is evident in the lower half of Fig. 9B and
in Fig. 10, B-1 and B-2, the location of the centers of the PBCs (i.e., the CPBCs) vary broadly across ILD and ABL. Taken together, these data suggest that a stimulus occurring at some ABL and ILD in contralateral, ipsilateral, or midline space, or, equivalently and perhaps more fundamentally, at a particular contralateral and ipsilateral level, will maximally excite a subpopulation of EE units with widely varying ranges and centers of azimuthal sensitivity.

These considerations do not seem to apply to EO units. Their CPBCs are significantly more prevalent at contralateral ILDs and the maximal width of their PBCs tend to be more narrow than that of EE units (Fig. 9). The maximal PBC width for 73.6% of EO units was ≈10 ILD, whereas this was true for 62.5% of EE units. The maximal PBC width for 35.1% of EO units was <10 dB ILD, whereas this was true for only 21.9% of EE units. The maximal PBC width of only 2 of the 20 EO/I units was >10 dB ILD. Thus in contrast to the considerations outlined above about the population of responsive EE units, the stimulus that would excite the largest subpopulation of EO units would occur at contralateral ILDs and this subpopulation would tend to respond maximally over comparatively narrow ranges of ILD.

A population of cells in auditory cortex has been described that are selective for stimuli delivered in the free field near the midline (Samson et al. 1994). They either failed to respond to lateralized noise bursts or responded weakly when either ear was plugged. The top 25% of ALRAs of these cells were at or near midline. Similar to these midline cells, PB units respond strongly to binaural tonal stimulation but not to monaural stimulation. They are distinguishable from EO/F units because the latter cells commonly respond strongly to monaural stimulation and therefore increased the ability to observe systematic cortical organization. Of course, the data collected in the awake animal reflect responses in more natural conditions, but the disadvantage is that the responses could be affected by uncontrollable factors (e.g., attention or motivation).

Although pentobarbital decreases the response rate of AI neurons to acoustical stimuli, in our study, it should decrease the response rate for both monaural and binaural conditions. As we compared the binaural response with the monaural response to determine the binaural interaction type, this possible effect should not have greatly influenced our analyses. Whitefield and Purser (1972) commented that although anesthesia altered the range of different discharge patterns observed in the MGB, it did not appear to alter the “range of effective stimuli” to which neurons were responsive. If that is also true in the primary auditory cortex, the conclusions we made about the PBC distribution should not vary greatly from what occurs in the awake animal.

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