Monaural Spectral Contrast Mechanism for Neural Sensitivity to Sound Direction in the Medial Geniculate Body of the Cat

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Imig, Thomas J., Pierre Poirier, W. Andrew Irons, and Frank K. Samson. Monaural spectral contrast mechanism for neural sensitivity to sound direction in the medial geniculate body of the cat. J. Neurophysiol. 78: 2754–2771, 1997. Central auditory neurons vary in sound direction sensitivity. Insensitive cells discharge well to all sound source directions, whereas sensitive cells discharge well to certain directions and poorly to others. High-frequency neurons in the latter group are differentially sensitive to binaural and monaural directional cues present in broadband noise (BBN). Binaural directional (BD) cells require binaural stimulation for directional sensitivity; monaural directional (MD) cells are sensitive to the direction of monaural stimuli. A model of MD sensitivity was tested using single-unit responses. The model assumes that MD cells derive directional sensitivity from pinna-derived spectral cues (head related transfer function, HRTF). This assumption was supported by the similarity of effects that pinna orientation produces on locations of HRTF patterns and on locations of MD cell azimuth function peaks and nulls. According to the model, MD neurons derive directional sensitivity by use of excitatory/inhibitory antagonism to compare sound pressure in excitatory and inhibitory frequency domains, and a variety of observations are consistent with this idea. 1) Frequency response areas of MD cells consist of excitatory and inhibitory domains. MD cells exhibited a higher proportion of multiple excitatory domains and narrower excitatory frequency domains than BD cells, features that may reflect specialization for spectral-dependent directional sensitivity. 2) MD sensitivity requires sound pressure in excitatory and inhibitory frequency domains. Directional sensitivity was evaluated using stimuli with frequency components confined exclusively to excitatory domains (E-only stimuli) or distributed in both excitatory and inhibitory domains (E/I stimuli). Each of 13 MD cells that were tested exhibited higher directional sensitivity to E/I than to E-only stimuli; most MD cells exhibited relatively low directional sensitivity when frequency components were confined exclusively to excitatory domains. 3) MD sensitivity derives from excitatory/inhibitory antagonism (spectral inhibition). Comparison of responses to best frequency and E/I stimuli provided strong support for spectral inhibition. Although spectral facilitation conceivably could contribute to directional sensitivity with direction-dependent increases in response, the results did not show this to be a significant factor. 4) Direction-dependent decreases in responsiveness to BBN reflect increased sound pressure in inhibitory relative to excitatory frequency domains. This idea was tested using the strength of two-tone inhibition, which is a function of stimulus levels in inhibitory relative to excitatory frequency domains. The finding that two-tone inhibition was stronger at directions where BBN responses were minimal than at directions where they were maximal supports the model.

INTRODUCTION

Although azimuthal (horizontal) localization of tonal stimuli depends exclusively on binaural disparity cues (Middlebrooks and Green 1991; Yin and Chan 1988), pinna (or spectral) cues are also important for localization of broadband sounds (Blauert 1983). Distortion or elimination of pinna cues in humans causes a substantial decrease in accuracy of vertical localization and an increase in front/back reversals in the horizontal plane (Fisher and Freeman 1968; Gardner and Gardner 1973; Musicant and Butler 1984; Oldfield and Parker 1984).

Acoustical measurements in a variety of species (e.g., cats: Musicant et al. 1990; Rice et al. 1992; humans: Batteau 1967; Hebrank and Wright 1974b; Searle et al. 1975; Shaw 1974) demonstrate that diffraction of high-frequency sounds waves by the head and pinna produces a free field to tympanic membrane transformation in gain that is both frequency and direction dependent. The spectral transformation is referred to as the head-related transfer function (HRTF) (Wightman and Kistler 1989), and Fig. 1 shows examples that were obtained in a cat by Musicant et al. (1990). Surgical removal of a cat’s pinna completely changes the HRTF (Musicant et al. 1990) and HRTFs shift with respect to the head when pinna orientation changes (Young et al. 1996), showing that the HRTF is determined mainly by the pinna.

Unilaterally deaf humans can localize broadband high-frequency sounds but not tonal stimuli (Butler 1975; Häusler et al. 1983; Slattery and Middlebrooks 1994), showing that directional information can be derived from monaural spectral cues. Monaural localization also has been studied in normal hearing individuals in which unilateral deafness is simulated by unilateral ear occlusion. They localize all sounds toward the side of the functional ear regardless of actual location. Some residual localization capacity may remain (Butler 1986; Butler et al. 1990; Fisher and Freeman 1968; Hebrank and Wright 1974a; Oldfield and Parker 1986; Slattery and Middlebrooks 1994) although whether this is due to monaural mechanisms is controversial (Wightman and Kistler 1997). The capacity of other species to localize sound monaurally has not been extensively studied. Monaurally deafened cats can localize the elevation of noise bursts with normal accuracy (Sutherland 1991, 1994). By comparison, accuracy of azimuthal localization by monaurally deafened cats is better than chance but poor as compared with binaural localization (Jenkins and Masterton 1982; Neff and Casseday 1977).

Single units in the superior colliculus (SC) derive directionality in part from monaural cues. Spatially selective neurons form an auditory space map in the deep layers of the SC in a number of species including cat (Middlebrooks and Knudsen 1984), ferret (King and Hutchings 1987), guinea pig (Palmer and King 1985), and barn owl (Knudsen 1984).
In the guinea pig and ferret, both monaural spectral and binaural cues contribute to directional tuning. At stimulus levels within ~20 dB of a unit’s threshold, azimuth and elevation tuning to broadband noise-burst (BBN) stimulation is determined largely by monaural mechanisms; at higher levels, binaural mechanisms are most important (King et al. 1994; Moore et al. 1993; Palmer and King 1985).

Monaural and binaural mechanisms also contribute to neural directionality in the lemniscal auditory system of the cat. Azimuth sensitivity is a characteristic of many central auditory neurons, i.e., they respond well at some azimuths and poorly at others (azimuth function peaks and nulls, respectively). Responsiveness is poor regardless of sound pressure level (SPL) at null directions [auditory cortical field (AI); Imig et al. 1990; Rajan et al. 1990; medial geniculate body (MGB); Irons 1989; inferior colliculus (IC); Aitkin and Martin 1987; Aitkin et al. 1984; Moore et al. 1984]. Comparison of binaural and monaural (unilateral ear occlusion) responses to free-field BBN stimulation shows that high-frequency neurons may derive azimuth sensitivity from binaural disparity cues [binaural directional (BD) cells] and/or monaural spectral cues [monaural directional (MD) cells] at midbrain (IC; Poirier et al. 1996), thalamic (MGB; Irons 1989; Samson et al. 1996), and cortical levels (AI; Samson et al. 1993, 1994). Sensitivity to monaural spectral cues also contributes to elevation sensitivity. Preliminary reports suggest that MD cells in the IC, MGB, and AI are sensitive to elevation, whereas BD cells are more likely to be broadly tuned and/or insensitive (Imig et al. 1995; Poirier et al. 1995; Samson et al. 1991).

How do neurons derive directional sensitivity from monaural spectral cues? Antagonistic interactions between excitatory and inhibitory domains in frequency response areas may provide a spectral contrast mechanism for directional sensitivity (e.g., Neti and Young 1992; Rhode and Greenberg 1992, 1994; Shamma and Symmes 1985; Shamma et al. 1993; Young et al. 1988; Zakarauskas and Cynader 1993). The hypothetical operation of such a mechanism is shown in Fig. 1. HRTFs associated with two sound directions (0° and 36° elevation) (redrawn from Musicant et al. 1990) are represented by light and heavy lines. A single-unit frequency response area composed of excitatory (+) and inhibitory (−) domains also is shown. Given a broadband sound with a flat spectrum in the free field, the HRTFs will represent the spectral distribution of sound pressure at each direction. A stimulus presented at 0° would produce relatively greater pressure in the excitatory than in the inhibitory domain thus causing a net excitation and neural discharge. At 36°, pressure would be relatively greater in the inhibitory than in the excitatory domain, producing a net inhibition and silencing of the cell. Overall, neural responsiveness to different sound directions would reflect the net excitatory/inhibitory interactions resulting from the differential pressure distribution in excitatory and inhibitory frequency domains. Although this illustration depicts how elevation sensitivity might be derived, the same principle applies to azimuth sensitivity.

Experiments were performed to test five predictions. 1) HRTFs are postulated to provide directional cues to which MD cells are sensitive. Changes in pinna orientation produce displacement of HRTF patterns that should cause similar displacements of MD cell azimuth function peaks and nulls. 2) MD cells should have frequency response areas that consist of excitatory and inhibitory domains. 3) MD sensitivity should require sound pressure in excitatory and inhibitory frequency domains. 4) MD sensitivity should reflect excitatory/inhibitory antagonism (spectral inhibition) that produces direction-dependent reductions in response. 5) Decreases in responsiveness to BBN should occur at directions where there is an increase in sound pressure in inhibitory relative to excitatory frequency domains. The results of these experiments are largely consistent with the predictions, suggesting that MD cells use antagonistic inputs from excitatory and inhibitory frequency domains to derive directional sensitivity from HRTF spectral cues. Some of these results have been reported in preliminary form (Imig et al. 1994; Irons 1989).

This work represents a part of the PhD research conducted by W. Andrew Irons.

METHODS

Eighteen healthy young-adult cats with clean external ears, translucent tympanic membranes, and low-threshold single-unit responses were used in the experiments. All husbandry and experimental procedures were carried out using protocols approved by the Institutional Animal Care and Use Committee of the Kansas University Medical Center. Chronic recording procedures were used in the MGB of 14 cats, and acute recording procedures were used for the remainder. Acute recording procedures have been described in detail elsewhere (Barone et al. 1996).

Surgical implant of a chronic recording chamber was carried out using inhalation anesthesia (0.8–1.5% isoflurane in O2) and standard aseptic procedures under veterinary supervision. Postoperative discomfort was ameliorated with analgesics. A stainless steel recording chamber was positioned stereotaxically over a cranio-
ometry and fastened to the skull with dental acrylic and stainless steel screws. A stainless steel tube, used to secure the animal’s head to the support frame during recording sessions, was attached to the chamber. The chamber was sealed with a stainless steel cap at times other than during recording sessions to protect the craniotomy from mechanical damage and infection. The dura mater was covered with a broad spectrum antibioticophthalmic ointment (bacitracin, neomycin, and polymyxin) before sealing the chamber.

Cats were allowed to recover fully from the surgery before the first recording session, and thereafter recording sessions were scheduled at 2-wk intervals. Animals were anesthetized during chronic recording sessions to prevent movements. Anesthesia was induced with isoflurane in O₂ and atropine (0.1 mg/kg im) was injected. Isoflurane was replaced with pentobarbital sodium (initial dose, 10 mg/kg iv), which was maintained throughout the recording session with an intravenous infusion pump at a rate sufficient to eliminate pinna reflexes and spontaneous movements (2–4 mg·kg⁻¹·h⁻¹). Dexamethasone (2 mg/kg iv) was injected to reduce the possibility of cerebral edema. Application of ophthalmic ointment prevented corneal drying. Tracheal intubation ensured a patent airway. Breathing and heart rates were monitored during the recording session, and temperature was maintained using a thermostatically controlled heating pad. After the recording session, animals were kept warm until they awakened from the anesthesia. Marking lesions were placed during terminal recording sessions for histological localization of recording sites. Each animal was given a lethal dose of anesthetic at the end of the terminal recording session and perfused through the heart with a 10% solution of formol saline. Histological processing has been described previously (Barone et al. 1996).

Single-unit recordings were carried out in an electrically shielded, anechoic, sound-isolation chamber. The anesthetized cat rested in a sling with its head rigidly fixed by clamping the head-support tube. The head was positioned with the horizontal Horsley-Clarke plane tilting forward and down at an angle of ~18° from horizontal, which approximates the head position of an alert cat looking forward. The ears were pulled to an upright position using strings that were attached to the outer surfaces of each pinna. Sterility was maintained within the recording chamber throughout the procedure. Single-unit activity was recorded using paralene-insulated, tungsten electrodes (Frederick Haer) with nominal impedances of 1–5 MΩ measured at 1 kHz in the brain. Details concerning single-unit recording, computer control of data collection, and data analysis have been described previously (Barone et al. 1996; Samson et al. 1993).

An array of loudspeakers with similar frequency response characteristics allowed the free-field presentation of sounds the directions of which could be varied in azimuth (direction in the horizontal plane passing through the interaural line) and elevation. Loudspeakers were aimed at the interaural midpoint and located at a distance of 0.79 m from it. An aluminum tubing frame supported loudspeakers along a vertical meridian (vertical array) of an imaginary sphere centered on the cat’s head. The vertical array consisted of seven loudspeakers spaced at 22.5° intervals (±67.5, ±45, ±22.5, and 0°). A horizontal array of 13 loudspeakers spaced at 15° intervals along a 180° arc of the equator was attached to the vertical support. Sound direction could be varied in elevation by presenting sound from different loudspeakers and could be varied in azimuth the same way or by rotating the frame about its vertical axis.

Auditory waveform synthesis, acoustic calibration, stimulus timing and sequencing, and data collection were controlled by a PDP 11/73 computer. Stimulus waveforms were generated at an output sample rate of 100 kHz using a 16-bit D/A converter (Boys Town National Research Hospital), low-pass filtered at 40 kHz (Kemo VBF/8, −180 dB/octave) to prevent aliasing, attenuated with computer controllable attenuators, and amplified. Each loudspeaker was calibrated by placing a microphone (B&K type 4133 1/2-in) at the center of the loudspeaker array, aiming it at the loudspeaker, and performing a fast Fourier transform (FFT) on the impulse response. Tables of maximum SPLs attainable at different frequencies were derived from FFT data and stored in a computer disk file for use during experiments. High-frequency drivers (Radio Shack 40–1310B) with a usable frequency range between 4 and 40 kHz were used for these studies. Output increased from 4 kHz to a peak at 8 kHz at 20 dB/octave, decreased by 5 dB/octave up to 35 kHz, and then decreased at 60 dB/octave. Loudspeakers with lower frequency output were also available for use to characterize frequency tuning <4 kHz.

A random number generator produced BBN waveforms with a flat spectrum (0–50 kHz) and random amplitude distribution. The actual spectrum of the BBN delivered to the animal was shaped by the sound system (mainly the loudspeaker). Band-pass stimuli were synthesized by summing together random-phase, equal-amplitude sine-waves in 5 Hz steps between the frequency limits of the band-pass. Band-pass stimuli with band limits of 1–40 kHz were sometimes used (also referred to as BBN). Although the fine structure of the two BBN stimuli differed, their effective bandwidths were similar, and there was no difference in responses of cells that were tested with both stimuli. Stimulus envelopes for all stimuli were 50 ms in duration and had linear rise/fall times of 5 ms.

Ear plugging was used to infer the responses of single neurons to monaural stimulation. Unilateral ear occlusion was effected by injecting a viscous liquid ear mold compound (Ear Mold Impression Material, All American Mold Lab) into the concha and ear canal. Attenuations produced by ear plugs varied between 32 and 70 dB in the range of 4–32 kHz, between 35 and 55 dB at 2 kHz, and 25 dB at 1 kHz (Samson et al. 1993). Data sets consisting of single-unit responses to BBN bursts that varied in azimuth and SPL were compared statistically to determine whether ear plugging had a significant effect on the cell’s response. Nonparametric statistics were used because cells discharged a small number of spikes and therefore spike counts are not normally distributed. One of two methods was used depending on whether or not repeat data sets were obtained using one treatment condition. If replications were available, an analysis of variance (ANOVA) was used on the ranked responses. Otherwise, a χ² test or a Fisher exact probability test was used (Samson et al. 1993, 1994; Siegel 1956). Elevation data were treated in the same manner.

**RESULTS**

These findings are based on recordings from well-isolated single units in two tonotopic subdivisions of the MGB (ventral nucleus, VN, and lateral part of the posterior group of thalamic nuclei, PO) (Imig and Morel 1985a,b) with supplemental data from one unit in cortical field AI. The search for single-unit responses was carried out using BBN bursts that were presented sequentially from loudspeakers spaced at 30° intervals along the horizontal array throughout the frontal field. At each location, SPL was varied from 0 to 80 dB in 20-dB steps before changing to the next loudspeaker. Single and multiunit low-threshold frequency selectivity was assessed regularly to ensure that the electrode was located in a high-frequency (>4 kHz) representation.

Once a single unit was encountered, a data set was obtained to assess azimuth sensitivity. This consisted of responses to 10–20 repetitions of BBN bursts that were typically presented at 30° intervals throughout the frontal field and between 0 and 80 dB SPL in 20-dB steps at each azimuth. If a unit responded well at some azimuths and poorly
at others (i.e., was azimuth sensitive), it was studied further to characterize its sensitivity to monaural and binaural directional cues. Additional data sets were obtained using monaural stimulation of the contralateral ear, monaural stimulation of the ipsilateral ear, and finally repeating binaural stimulation to assess response stability (i.e., contra- and ipsilateral with respect to the recording site in the left MGB). Monaural stimulation was simulated by the use of unilateral ear plugging, which attenuated sound reaching one ear. Rather complete response profiles to monaural and binaural stimulation were obtained for 103 azimuth-sensitive cells in the MGB (Samson et al. 1996). Best frequencies (BFs, center frequency of excitatory response domains) of the sample ranged between 4.2 and 37 kHz.

The role of monaural and binaural mechanisms in determining a unit’s directional sensitivity was inferred by comparison of responses to monaural and binaural BBN stimulation as described by Samson et al. (1993, 1994). Units were classified as BD ($n = 69$) if they were azimuth sensitive to binaurally presented BBN but were insensitive to monaural stimulation, i.e., responded well at each direction, were unresponsive to monaural stimulation, or exhibited completely different response borders (defined by adjacent peaks and nulls) under binaural and monaural conditions. Units were classified as MD ($n = 30$) if they were sensitive to the azimuth of monaural BBN stimulation and exhibited some or all of the same response borders under monaural and binaural conditions. MD cells are estimated to represent $\sim 17\%$ of the high-frequency neurons in VN and PO based on a previous report that 57% of the units in VN and PO were azimuth sensitive (Burone et al. 1996) and on the proportion of MD cells (29%, 30/103) in the azimuth-sensitive sample used for this report. All MD cells exhibited short-latency onset responses (minimum 1st spike latencies ranged between 6.7 and 32.7 ms, mean 10.2 ms), and these are the responses described in detail below. Additionally, some units (4/30) also exhibited long-latency responses in the range of 43–200 ms. These usually occurred at higher levels, although the long-latency response of one unit was related reciprocally to its short-latency response over a wide range of SPL.

**Monaural directional sensitivity**

Figure 2 compares the monaural and binaural responses of a MD cell. Its responses to monaural contralateral BBN stimulation (CS) are displayed in the form of an azimuth-level response area (ALRA), a normalized iso-response contour plot (Fig. 2A). The cell was most responsive at 45 and 60° of azimuth and was completely unresponsive at 90° regardless of SPL. These data are replotted as an azimuth function (CS, Fig. 2C) in which responses are averaged over SPL and normalized. Responses are near optimal at the function peak (45 and 60°) and minimal at the null (90°). The terms “peak” and “null” are used rather loosely throughout this report to refer to peaks and valleys in azimuth and elevation functions. Cells were classified as azimuth sensitive if azimuth function modulation was $\geq 75\%$ (in this case, modulation was 100%). There was no significant statistical difference between monaural contralateral and binaural azimuth functions (CS and BS, respectively, Fig. 2C) indicating that directional tuning was determined entirely by monaural input. The cell was unresponsive to ipsilateral monaural BBN stimulation. Thus this cell was classified as MD-E0, MD indicating that it derived azimuth sensitivity from monaural stimulation and E0 indicating that it received excitatory (E) input from one ear and that stimulation of the other was ineffective (0).

This cell was also sensitive to the elevation of monaural contralateral BBN stimuli (CS, Fig. 2D). The elevation-level response area (ELRA) represents the cell’s responses at elevations distributed along the vertical meridian passing through a peak azimuth (45°). The unit was most responsive at 0° elevation and less responsive above and below the horizontal plane. It was entirely unresponsive at 45° elevation regardless of SPL. There was no significant statistical difference between monaural and binaural elevation functions (CS, BS, Fig. 2F). This is consistent with the previous results and shows that directional tuning was determined entirely by monaural input.

Unlike MD-E0 cells that are strictly monaural, MD-EI cells receive binaural inhibition and an example of such a cell is shown in Fig. 14B. The binaural azimuth function (BS) shows a peak located in the contralateral rear quadrant. The peak is defined by nulls at 30 and 180°, and these features also were seen in response to monaural contralateral BBN stimulation (CS), thus earning the cell a MD classification. Compared with the binaural function, the contralateral monaural function revealed increased responsiveness on the ipsilateral side of the head, leading to the conclusion that the cell received inhibition from the ipsilateral ear. Although they differ with respect to binaural inhibition, both MD-E0 and MD-EI cells derive directional sensitivity from monaural spectral cues, and thus their monaural responses are treated together in the remainder of the report.

MD cells are sensitive to the direction of monaural BBN stimuli but are insensitive to the direction of monaural tonal stimuli (and also to binaural tonal stimuli in the case of MD-E0 cells). This characteristic is illustrated by the MD-E0 cell in Fig. 2. An ALRA was obtained to binaural stimulation with 20-kHz BF tone bursts (Fig. 2B). Unlike its response to noise stimulation, the neuron responded well to tone bursts at each azimuth from which they were presented. The azimuth function (BS 20 kHz, Fig. 2C) shows that discharge rate, averaged over SPL, varies to some degree as a function of sound direction but it exhibits less modulation (42%) than the BBN functions and does not meet the 75% criterion for azimuth sensitivity. Similar differences in elevation sensitivity are seen in response to BBN and 20-kHz BF tones (Fig. 2D–F). These findings suggest that azimuth and elevation sensitivity depend on monaural cues that are present in BBN but not in tone bursts. According to the model, these monaural cues are pinna spectral cues, and MD cells derive directional sensitivity from them by use of excitatory/inhibitory antagonism to compare sound pressure in excitatory and inhibitory frequency domains. The remainder of this report describes the results of experiments designed to test the validity of this model.

**MD receptive field location follows changes in pinna orientation**

Changing pinna orientation from sideways to forward facing causes a corresponding movement in prominent features
FIG. 2. MD cells are sensitive to the direction of monaurally presented broadband noise (BBN) bursts and insensitive to the direction of best frequency (BF) tone bursts (8815-12). A: azimuth-level response area shows the cell’s response to monaural contralateral BBN stimulation (CS). Iso-response contour lines and shading represent 5, 25, 50, and 75% of maximum (maxima are indicated by large diamonds). Cell responded optimally at 45° azimuth, and it was unresponsive at 90°. B: azimuth-level response area shows the cell’s response to binaural BF (BS 20 kHz) tone bursts. Cell responds well at each azimuth. C: azimuth functions were obtained by averaging responses over sound pressure level (SPL) and normalizing. Responses obtained using contralateral monaural (CS) and binaural (BS) BBN stimulation were statistically indistinguishable. In both cases, functions exhibited 100% modulation (i.e., high azimuth sensitivity). In response to BF tone bursts presented binaurally (BS 20 kHz), the cell exhibited 42% modulation (lower azimuth sensitivity). D: elevation-level response area shows the cell’s response to monaural contralateral BBN stimulation (CS). Data in panels D–F were obtained at 45° azimuth. E: elevation-level response area shows the cell’s response to binaural BF (20 kHz) tone bursts. Cell responds well at each elevation. F: elevation functions were obtained by averaging responses over SPL and normalizing. Those obtained using monaural (CS) and binaural (BS) BBN stimulation were statistically indistinguishable. In both cases, they exhibited 99% modulation (high elevation sensitivity). In response to BF tone bursts presented binaurally (BS 20 kHz), the cell exhibited much lower modulation (39%). Recording site was located in the lateral part of the posterior group of thalamic nuclei.

of the HRTF with respect to the head (Young et al. 1996). If MD directional tuning depends on pinna-derived spectral cues, then the locations of azimuth-function peaks and nulls should follow changes in pinna orientation on the side of the ear that provides excitatory input to the cell.

Pinna orientation was controlled by use of positioning strings that were glued to the medial and lateral margins of each pinna close to the scalp. Adjustment of the tension on the strings allowed independent positioning of each pinna. By placing knots in the strings and using a slotted holder to
engage the knots, different orientations could be reliably reproduced. Figure 3 shows both pinnae in the forward and side positions. Pinna orientation can be described roughly by reference to an imaginary line oriented perpendicular to the plane defined by the free margins of the pinna. In both forward and side positions, this line projected nearly horizontally. In the forward position, it formed an angle of ~25° with midsaggital plane; in the side position it formed an angle of ~40–45°. Thus pinna orientation in these two positions differed by 20–25° of angular rotation.

By independently changing the position of each pinna, it was possible to show that the location of peaks and nulls in a MD cell’s azimuth function followed changes in orientation of the pinna on the side of the excitatory ear. The responses of a thalamic MD-E0 unit that received contralateral excitatory input are illustrated in Fig. 4A. Azimuth functions are identified according to pinnae orientations (e.g., IsCf, Ipsi side Contra forward) and are grouped according to the orientation of the contralateral pinna. Those plotted with continuous lines were obtained with the contralateral pinna in the forward position (Cf); those plotted with interrupted lines were obtained with the contralateral pinna in the side position (Cs). Azimuth function peaks in the contralateral pinna forward group are displaced toward the left of those in the contralateral pinna side group. The mean best azimuth (midpoint of the 75% range) for the two Cf functions was 16.5°, the mean for the five Cs functions was 37.4°, a difference of ~21° which corresponds closely with the estimated angular rotation of the pinna.

There was no systematic relationship between ipsilateral pinna orientation and best azimuth. With the contralateral pinna in the forward position, similar best azimuths were found for forward and side orientations of the ipsilateral pinna (IsCf, 16°, IfCf, 17°). With the contralateral pinna oriented to the side, there was greater variation in best azimuth (34–43°), but there was no systematic relationship to ipsilateral pinna orientation. Average best azimuths for Is (38.5°) and If functions (36.7°) were similar.

Although the effect of pinna orientation was tested using only one thalamic MD cell, confirming observations also were obtained from a MD-E0 cell located in cortical field AI. Figure 4B shows eight azimuth functions that were obtained using different pinna orientations. As was the case with the thalamic cell, azimuth function peaks in the contralateral pinna forward group are displaced toward the left of those in the contralateral pinna side group. In neither the contra forward or contra side group does ipsilateral pinna orientation bear a systematic relationship to any features of the azimuth function. In both MD units, directional tuning followed the orientation of the pinna on the side of the ear that provided excitatory drive and was unaffected by the orientation of the other pinna. Although these data are limited to the responses of two MD cells, the results are unambiguous and consistent with the hypothesis that HRTFs provide the monaural spectral cues from which MD cells derive directional sensitivity.

**Frequency response areas of MD cells exhibit excitatory and inhibitory domains**

The model predicts that MD cells receive excitatory and inhibitory inputs from different frequency domains. Frequency response areas of MD cells were mapped to determine if they exhibited this property. Excitatory frequency domains were determined by presenting tone bursts at a peak...
shows a cell’s responses to tone-burst stimulation as a joint function of probability test, tested SPL. Inhibitory domains were identified using a two- of excitatory domains for MD cells averaged 0.52 octaves, in the lateral part of the posterior group of thalamic nuclei. from 1.45 to 2.5. The average ratio was 1.82 and was slightly

contour is indicated by a bold line. Domains are indicated by regions of lighter shading. The 50% response domain was measured at 30 dB above its lowest threshold.

frequency and SPL. Iso-response contour lines and shading represent 5, 25, There was not any obvious harmonic relationship between 50, and 75% of maximum ( maximum is indicated by a large diamond ) . Inhibitory domains had thresholds within 20 dB of each

20 dB steps from near threshold to 80 dB SPL ) . Monaural stimulation was used to ensure that binaural inhibition, if present, did not influence the observations. Responses were plotted as iso-response contours ( e.g., Fig. 5A ). In this case, the contours delimited two, narrow, low-threshold, excitatory domains that were separated from each other by a region in which tone bursts did not excite the cell at any tested SPL. Inhibitory domains were identified using a two-
tone stimulation paradigm. Two-tone stimuli consisted of constant ( F1 ) and variable ( F2 ) frequency components that were presented simultaneously. F1 was centered in an excitatory domain ~15 dB above threshold. F2 was presented at different frequencies and SPLs. If the two-tone response was smaller than the F1 response, this was taken as evidence that the F2 stimulus was inhibitory. Figure 5B shows the two-tone response area that delimits regions of two-tone inhibition. The 50% iso-response contour was used to indicate the approximate locations of inhibitory domains and was combined with the excitatory response ( Fig. 5A ) to show both inhibitory ( “-” and stippled ) and excitatory frequency domains in a frequency response area ( FRA, Fig. 5C ).

FRAs consisting of flanking excitatory and inhibitory domains were characteristic of all MD cells that were tested using two-tone stimulation. FRAs consisting of one ( Fig. 6, A and B ) or two low-threshold excitatory domains ( Figs. 5C, 6C, and 14A ) were encountered commonly. Figures 6D and 11A show examples with three excitatory domains. The cell in Fig. 6D was lost before the existence of inhibitory domains could be verified. The finding that FRAs of MD cells exhibit distinct excitatory and inhibitory domains is consistent with the spectral contrast model.

Detailed excitatory FRAs were available for a sample of 65 BD and MD cells. FRAs for BD cells that exhibited binaural inhibition were obtained using monaural stimulation. FRAs for the remaining BD cells were obtained using binaural stimulation because they exhibited binaural facilitation and were less responsive to monaural stimulation. The combined MD/BD sample included 15 units that exhibited two or more excitatory frequency domains. In each FRA, excitatory domains had thresholds within 20 dB of each other and were separated by a frequency range throughout which the cell was not excited by tones at intensities <60 dB above threshold ( Figs. 5C, 6C, D, 11A, and 14A ). Some cells in both the MD and BD samples exhibited multiple excitatory domains, but this feature was more common in the MD ( 9 / 24, 37% ) than in the BD ( 6 / 41, 15% ) sample. These proportions were significantly different ( Fisher exact probability test, P < 0.037 ) ( Siegel 1956 ).

There was not any obvious harmonic relationship between center frequencies of the excitatory domains in the multipeaked FRAs. The center frequency of an excitatory domain was measured at 30 dB above its lowest threshold. Only adjacent peak spacing was determined in the case of FRAs with three peaks. The ratio of the center frequencies of the higher frequency peak divided by the lower ranged are stippled and identified by circled minus signs. Recording site was located in the lateral part of the posterior group of thalamic nuclei.

azimuth. Tones varied in frequency ( one-quarter or one-eighth octave steps between 4 and 40 kHz ) and SPL ( 10–20 dB steps from near threshold to 80 dB SPL ). Monaural stimulation was used to ensure that binaural inhibition, if present, did not influence the observations. Responses were plotted as iso-response contours ( e.g., Fig. 5A ). In this case, the contours delimited two, narrow, low-threshold, excitatory domains that were separated from each other by a region in which tone bursts did not excite the cell at any tested SPL. Inhibitory domains were identified using a two-
FIG. 6. Examples of frequency response areas of MD cells showing excitatory and inhibitory frequency domains. Cell in D was lost before the existence of inhibitory areas could be tested. A: 9314-2, recording site located in the lateral part of the posterior group of thalamic nuclei. B: 9317-7, recording site in the ventral nucleus. C: 9314-5, recording site in the ventral nucleus. D: 9314-10, recording site was located in the lateral part of the posterior group of thalamic nuclei.

whereas for BD cells averaged 1.20 octaves ($t = -5.73$, $df = 51$, $P < 0.0001$).

MD sensitivity usually requires stimulation of both excitatory and inhibitory frequency domains

The model hypothesizes that directional sensitivity results from comparison of sound pressure in excitatory and inhibitory frequency domains. If this is true, then MD cells should exhibit directional sensitivity to stimuli with spectral components that engage both excitatory and inhibitory domains (E/I stimuli) and should be insensitive to the direction of stimuli with spectral components limited only to excitatory domains (E-only stimuli). To test the prediction, azimuth and elevation function modulation was measured for E-only and E/I stimuli. Useful data were obtained from 13 MD cells (BF range: 6–37 kHz). In all cases, excitatory and inhibitory frequency domains initially were delimited as described above.

The elevation sensitivity of the MD cell the FRA of which appears in Fig. 6C was tested using a variety of stimulus spectra. Its excitatory and inhibitory domains are represented in Fig. 8A (bottom). Data were obtained using the E-only and E/I stimuli the spectral compositions of which are shown in Fig. 8A, top ($\rightarrow$, 1 or 2 frequency components; ––––, indicate BBN or band-pass stimuli). ELRAs obtained using E/I stimuli exhibited narrow elevation tuning (e.g., Fig. 8C); those obtained using E-only stimuli exhibited insensitive responses (e.g., Fig. 8D). Elevation function modulation bears a systematic relationship to stimulus type (Fig. 8B). Relatively low modulation (<45%) occurred in response to E-only stimuli that consisted of one frequency component (22.2 kHz), two frequency components that were located in different excitatory domains (15.5 + 22.2 kHz), or many hundreds of frequency components in a single excitatory domain [band-pass (BP) 22–24 kHz, BP 22–
FIG. 8. Elevation sensitivity of a MD-E0 cell (9314-5; see text for definition) requires stimulation of both excitatory and inhibitory frequency domains. **A**: spectral composition of test stimuli is shown in relationship to excitatory and inhibitory frequency domains. **Bottom**: location of excitatory and inhibitory domains (from data in Fig. 6C). —— cell’s response to tone-burst stimulation averaged over SPL and represents the location of the excitatory domains. Location of the inhibitory domain is indicated (— — — and — →). Spectral composition of stimuli used to test elevation sensitivity is shown (top): —— individual frequency components; —— band-pass stimuli composed of discrete frequency components spaced in 5-Hz intervals. Stimuli are divided into 2 groups: those with energy confined only to excitatory domains (E-only stimuli) and those with energy in both excitatory and inhibitory domains (E/I stimuli). **B**: elevation functions (responses averaged over SPL) exhibited higher modulations for E/I stimuli (——) than for E-only stimuli (— — —). **C**: example of an elevation-level response area (ELRA) obtained using an E/I stimulus (BBN). **D**: example of an ELRA obtained using an E-only stimulus (22.2 kHz).

Relatively high modulation (>90%) was obtained from E/I stimuli that consisted of two frequency components (20 + 22.2 kHz) or many frequency components (BP 13–24 kHz, BBN). The cell was tested with an additional E/I stimulus (BP 13–20 kHz) but showed no short-latency response so no elevation function appears for this stimulus in Fig. 8B. Lack of a response to this stimulus is discussed later.

Similar results were obtained for azimuth function modulation. One example is shown for the MD cell the FRA of which appears in Fig. 6A. Spectral compositions of test stimuli are shown in relationship to the cell’s excitatory and inhibitory frequency domains in Fig. 9A. In response to a broadband E/I stimulus, the cell showed a focal response in the contralateral rear quadrant (Fig. 9C). It was insensitive to the location of a narrow band E-only stimulus (Fig. 9D). Azimuth functions (Fig. 9B) reveal relatively little modulation in response to E-only stimuli and greater modulation to E/I stimuli.

These examples support the hypothesis that directional sensitivity of MD cells requires frequency components in both excitatory and inhibitory frequency domains. Individual MD units each showed greater modulation to E/I stimuli than to any E-only stimulus. Data for the sample are summarized in Fig. 10, which shows the distribution of elevation and azimuth function modulations for E-only and E/I stimuli. The distribution is bimodal. The high modulation mode is composed mainly of modulations for E/I stimuli that ranged from 64 to 100%. The low modulation mode is composed exclusively of modulations for E-only stimuli that ranged from 21 to 79%. Overall, the mean modulations for the two types of stimuli were significantly different (EI, 91.4%; E-only, 37.9%, t = 17.7, df = 58, corrected for heterogeneous variance, P < 0.0001).

Stimuli were classified according to number of frequency components, i.e., one, two, or hundreds in the case of bandpass stimuli and BBN. Modulations for most E-only stimuli were lower than those for any E/I stimulus regardless of whether the E-only stimulus was a single frequency (E, mean 35%), two frequency components located in different excitatory domains (E + E, mean 49%), or hundreds of frequency components confined to a single excitatory domain.
FIG. 9. Azimuth sensitivity of an MD-E0 cell (9314-2) requires stimulation of both excitatory and inhibitory frequency domains. A: spectral composition of test stimuli in relationship to excitatory and inhibitory frequency domains. Bottom: location of excitatory and inhibitory domains (from data in Fig. 6A). See Fig. 8 legend for details. B: azimuth functions (responses averaged over SPL) exhibited higher modulations for E/I stimuli (—) than for E-only stimuli (– – –). Some azimuth functions are averages of several azimuth-level response area (ALRA) data sets: BBN (n = 3), band-pass (BP) 1–15.5 (n = 2), BP 13–40 (n = 4), BP 13–15.5 (n = 2). C: example of an ALRA obtained using an E/I stimulus (BBN). D: example of an ALRA obtained using an E-only stimulus (BP 13–15.5 kHz).

FIG. 10. Directional response modulation is greater to E/I than to E-only stimuli. This graph shows the azimuth and elevation function modulations obtained to all E/I and E-only stimuli that were used in the sample of 13 MD cells. Each cell was tested with several stimuli, and for each individual cell, modulations were greater to E/I stimuli than to E-only stimuli. For the sample, modulation was significantly greater to E/I than to E-only stimuli. BP EI, band-pass stimulus that included both excitatory and inhibitory domains; E + I, 2 frequency components, one of which was located in an excitatory domain, the other in an inhibitory domain; E, a single frequency component located in an excitatory domain; BP E, a band-pass stimulus that was limited to an excitatory domain; E + E, 2 frequency components located in different excitatory domains.

The distributions of E/I and E-only modulations were nonoverlapping except for the responses of two cells that exhibited relatively high modulation to E-only stimuli. One unit contributed modulations of 52% (BF tone) and 66% (narrow band-pass) for two E-only stimuli. Its responses were somewhat variable between data set repetitions so we don’t attribute much significance to these relatively high modulations. But the other cell was more interesting because it exhibited very consistent responses and a high modulation to the azimuth of a two-tone stimulus in which both components were located in excitatory domains. Its frequency re-
response area (Fig. 11A) consisted of three excitatory domains centered at 6, 10, and 18 kHz. There was an inhibitory domain between the 6- and 10-kHz excitatory domains, but the remainder of the frequency range was not explored using the two-tone paradigm. This MD-E0 cell responded only to stimulus of the contralateral ear. Figure 11B shows azimuth functions in which responses are plotted as spikes / stimulus (averaged over SPL) rather than normalized responses as was done in previous figures. In response to BBN stimulation, the peak response occurred behind the head (180°) with nulls at −30 and −60°. Considering only the ±90° azimuth range over which measurements were obtained for E-only and E/I stimuli, modulation was greatest to BBN (93%). Relatively low modulation was obtained for 6-kHz (37%) and 10-kHz tones (43%), consistent with the responses of most other MD cells to tonal stimuli. Higher modulation (79%) occurred in response to a two-tone stimulus consisting of 6- and 10-kHz components. This was the highest modulation seen to any two-tone E-only stimulus in our sample.

Directional sensitivity to the two-tone stimulus appears to reflect suppression of the 10-kHz response by the 6-kHz response. One interpretation is that the tone-evoked excitatory response was followed by a period of decreased responsiveness. At −30 and −60° where the two-tone response shows a null, the first spike latency to the 6-kHz tone was shorter than that to the 10-kHz tone for equal SPL stimuli. At these azimuths, the magnitude of response to the two-tone stimulus was similar to that of the 6-kHz tone. Decreased responsiveness after the 6-kHz excitation could eliminate the excitatory response to the 10-kHz tone. At directions where the two-tone response was near maximal (e.g., 0–90°), the response to 10-kHz stimulation occurred at shorter latency than the response to 6-kHz stimulation for equal SPL stimuli, and the response to the two-tone stimulus was similar in magnitude to that of the 10-kHz stimulus.

Azimuth-dependent differences in first spike latencies to the two tones are understandable because of threshold differences; at −30 and −60°, threshold was considerably higher for 10-kHz than for 6-kHz tones, whereas thresholds for 6- and 10-kHz tones were more nearly equal at other azimuths. At each azimuth, first spike latencies showed monotonic decreases with increasing SPL reaching asymptotic minima of 11 ms (10 kHz) and 20 ms (6 kHz). At different azimuths, threshold differences shifted the 6- and 10-kHz latency functions with respect to each other along the SPL axis, causing the 6-kHz response to occur earlier at some azimuths, and the 10-kHz response to occur earlier at others.

**Directional sensitivity derives predominantly from direction-dependent strength of spectral inhibition**

The model postulates that antagonistic excitatory-inhibitory spectral interaction (spectral inhibition) causes discharge rate modulation. Alternatively, facilitatory interactions also could produce modulation. The relative contributions of spectral facilitation and spectral inhibition to directional sensitivity was evaluated. Spectral facilitation and inhibition can be assessed by comparing a unit’s responsiveness to a multifrequency stimulus with its responsiveness to a tonal BF stimulus. Greater responsiveness to a multifrequency stimulus indicates facilitation; less responsiveness indicates inhibition. Figure 12A shows a unit’s discharge rate (DR, averaged over SPL) plotted as a function of azimuth for BF tones and three different E/I stimuli. At each azimuth, the DRs to E/I stimuli were smaller than those to the BF stimulus, suggesting that E/I stimuli produced a net inhibition at each direction. Figure 12B shows another unit’s DR elevation functions for a BF stimulus and a variety of E/I stimuli. DRs for E/I stimuli (interrupted lines) were considerably smaller than those to the BF stimulus (continuous lines) at all directions except −45°. Here, the responses to BBN and the BF tone were approximately equal. These data are typical of the sample in showing that DRs to E/I stimuli were less than or equal to those to BF stimuli. This shows that spectral inhibition is a major contributor to the directional tuning of MD cells in response to E/I stimuli.

Although responses to E/I stimuli revealed only spectral inhibition, this does not completely rule out the possible existence of spectral facilitation. The above-mentioned results are based on DRs that were averaged over SPL. Facilitation could be present at certain SPLs but not be evident in the averaged response because of a predominance of inhibition at other SPLs. An analysis was performed to determine whether facilitation was present to any stimulus within a data set. This entailed selecting the maximum spike count...
response from each data set, regardless of stimulus direction or SPL (in those cases in which replicated data sets were available, maximum responses were averaged). Maximum response values were obtained from data sets for E/I stimuli ($R_{EI}$) and BF stimuli ($R_{BF}$), and these were used to express maximum responsiveness to an E/I stimulus as a percentage of the maximum responsiveness to the BF stimulus ($100 \times R_{EI}/R_{BF}$). Figure 13 shows the ratios that were obtained from the MD sample. If facilitation occurred in response to a particular stimulus in an E/I data set, then the value of the ratio should be $>100\%$. In most cases, the ratio was $\approx 100\%$. In only a few cases was it larger, and in these cases, the relative response difference between E/I and BF stimuli was small. Thus if there is a net facilitation of maximal responses to E/I stimuli, it occurs only in a small proportion of the cases and it is of relatively small magnitude.

Although negligible net facilitation appears to be present in the responses of MD cells to E/I stimuli, it is possible that MD cells may exhibit a net facilitation to E-only stimuli. Responses to 14 multicomponent E-only stimuli were obtained from eight MD cells. Responsiveness ratios to multiple-component E-only stimuli varied from 38 to 147\%, but on average were nearly identical to that for BF stimuli ($100 \pm 25.7\%$, SD). Whether this variability represents experimental error (e.g., uncontrolled changes in unit responsiveness), a mixture of spectral inhibition and facilitation that differs among units to E-only stimuli or other effects (e.g., Fig. 11) cannot be determined from these data.

**Effect of sound direction on strength of two-tone inhibition**

The model postulates that directional variation of responsiveness to BBN is a result of changes in the level of sound pressure in inhibitory relative to excitatory domains. This idea was tested using two-tone stimuli. The strength of two-tone inhibition is a function of the relative stimulus levels in excitatory and inhibitory frequency domains; e.g., increased level in an inhibitory domain relative to an excitatory domain causes stronger two-tone inhibition. According to the model, two-tone inhibition should be relatively strong at a BBN response null and relatively weak at a response peak.

Four MD cells were tested with monaural, two-tone stimulation presented from peak and null directions. The responses of a MD-EI cell are illustrated in Fig. 14. Azimuth functions were obtained for the full 360° circle around the head using binaural and monaural contralateral BBN stimulation (BS and CS, respectively, Fig. 14B). The cell’s monaural FRA exhibited two excitatory domains and flanking inhibitory domains (Fig. 14A). Figure 14C shows normalized responses to monaurally presented two-tone stimuli that consisted of a constant frequency F1 (15.5 kHz, centered in the lower excitatory domain) and a variable frequency F2. The amplitudes of F1 and F2 in each two-tone stimulus were adjusted so that they were identical in SPL (in the free field). Two-tone responses were obtained at a null direction (30° azimuth) using four different SPLs (continuous lines). At each SPL, the two-tone stimuli produced strong inhibition when F2 was located within frequency ranges adjacent to F1. Two-tone inhibition was minimal at a peak direction (120° azimuth, interrupted lines). These results are consistent with the hypothesis. At a null direction, increased sound pressure within inhibitory domains relative to the 15-kHz
excitatory domain could account for decreased responsiveness to BBN stimulation. At a peak direction, stimulus levels were too low in inhibitory relative to excitatory domains to suppress the cell’s response.

Interestingly, two-tone stimulation using a F1 centered in the upper excitatory range (26.3 kHz, Fig. 14D) showed strong and more or less equivalent inhibition at both null and peak directions. This suggests that the excitatory drive produced by the upper excitatory domain was suppressed at both peak and null locations and thus may not have contributed much, if any, to the cell’s BBN response. Although this is only speculation in the case of this unit because it was not tested using an E/I stimulus that included only the high-frequency excitatory domain, there is other evidence that suggests that excitatory drive from one of a cell’s multiple excitatory domains can be suppressed completely at both peak and null locations. The unit shown in Fig. 8 was unresponsive to an E/I stimulus (BP 13–20 kHz) that included one of two excitatory domains.

Figure 15 shows the responses of another MD cell to two-tone stimulation presented from null and peak elevations. This cell was classified as MD-EI because it received excitatory input from the ipsilateral ear and inhibitory input from the contralateral ear. All responses shown here were obtained using ipsilateral monaural stimulation. Figure 15A shows an elevation function (averaged over SPL) that was obtained using BBN stimulation. The unit was most responsive at elevations of 0 and 22.5° and least responsive at directions below the horizontal plane. Tone burst stimulation shows an excitatory domain centered at 20 kHz (Fig. 15B).

Responses to two-tone stimulation are displayed in Fig. 15C. These are averages of responses that were obtained at six different levels over a 50-dB range beginning ~10 dB above F1 threshold. The response to the F1 stimulus alone was nearly identical at the two locations. The two-tone function for the null (−22.5%) shows prominent inhibitory troughs on both the high- and low-frequency sides of the 20-kHz F1 frequency. The two-tone function for a peak elevation (22.5%) shows little evidence for inhibition on the high-frequency side. There is a trough on the low-frequency side, but it is not as deep as that obtained at the null elevation. Thus two-tone inhibition appears to be present at both peak and null directions, but it is more prominent at the null. Comparable two-tone data also were obtained on two other MD cells in which two-tone inhibition was stronger at null than at peak directions. These data suggest that MD sensitivity is a result of changes in the level of sound pressure in inhibitory relative to excitatory frequency domains.

**Directional tuning varies with pattern of E/I stimulation**

FRAs of MD cells typically exhibit multiple excitatory domains, multiple inhibitory domains, or both multiple excit-
stimulation of the excitatory domain and the low-frequency inhibitory domain (BP 1–15.5 kHz) resulted in a response null at 180°. Because response nulls presumably occur at directions where spectral inhibition is strongest, this suggests that different inhibitory domains produce different directional patterns of spectral inhibition.

Different local minima in the BBN azimuth function may be the result of spectral inhibition produced by different inhibitory domains. A null in the BBN function at 30° corresponds to the null in the BP 13–40 kHz function but not in the BP 1–15.5 kHz function. A null in the BBN function at 180° corresponds to the minimum of the BP 1–15.5 kHz function but not one in the BP 13–40 kHz function. A more systematic analysis of this problem must await additional data.

**DISCUSSION**

MD cells in the MGB derive directional sensitivity from monaural cues that are present in BBN but not tone bursts, as is the case for MD cells in cortical field AI of the cat (Clarey et al. 1995; Samson et al. 1993). Our results suggest that MD neurons derive directional sensitivity from monaural HRTF cues using antagonistic excitatory/inhibitory interactions to compare sound pressure in excitatory and inhibitory frequency domains.

**Monaural spectral cues**

MD cells were distinguished from other cells in the MGB by virtue of their directional sensitivity to monaurally presented BBN bursts. Although we made no attempt to measure the acoustic cues from which MD cells derived directional sensitivity, we assume that they were high-frequency spectral cues as described by the HRTF (Musicant et al. 1990; Rice et al. 1992). A critical reader might question this interpretation, however, because the use of multiple loudspeakers to present sounds from different azimuths introduces a potential source of error. Loudspeakers had similar but slightly different frequency response characteristics, and these introduce loudspeaker-dependent variations in noise spectra in addition to the HRTF-dependent spectral variation. Nevertheless, it seems very unlikely that frequency-response differences among loudspeakers accounted for anything more than a minor component of differences in unit responsiveness that we interpreted as direction dependent. The azimuth tuning of a few MD cells was studied using only a single moveable loudspeaker (Figs. 2 and 4A). In these cases, there can be no question that response modulation was azimuth dependent not loudspeaker dependent. In a previous study of MD cells in cortical field AI (Samson et al. 1993), azimuth functions for a given MD cell were found to be similar whether they were obtained using a single moveable loudspeaker or a multiloudspeaker array. Furthermore, similar azimuth functions were obtained with the array rotated to different positions so that different loudspeakers were used to present sound from the same direction. These observations show that neural responsiveness of MD cells depends on azimuth and are not the result of differences in loudspeaker characteristics. Thus the HRTF spectral cues seem to be the main determinant of neural responsiveness to different sound directions.
Effect of pinna orientation

Young et al. (1996) measured HRTFs for pinna orientations similar to those used in the present study. They found that the spatial distribution of spectral notches shifted in location with respect to the head but maintained a constant relationship to the pinna. Thus although movement of the pinna does produce some changes in HRTFs, movement may not introduce sufficient distortion of spectral cues as to greatly change MD cell directional sensitivity.

The directional preference of single units has been shown to be dependent on pinna position in a number of different species with mobile pinnae. A unit’s directional preference may be shaped by monaural mechanisms for sounds presented at near threshold levels (Middlebrooks and Pettigrew 1981; Sun and Jen 1987). In such cases, a unit’s receptive field follows the pinna’s acoustic axis (direction of maximum amplification). For stimuli presented at higher levels that might reasonably be assumed to produce suprathreshold stimulation at both ears, the influence of pinna position on neuronal directional preference has been interpreted as resulting from changes in monaural acoustic axis and binaural disparity cues (Aitkin et al. 1984; Middlebrooks and Knudsen 1987). As is the case in previous studies, the present findings show that directional preference of MD cells closely follows the position of the pinna on the side of the head from which it receives excitatory input. Nevertheless, the mechanism responsible for this is different from those that have been described previously because it is monaural but not strictly dependent on changes in directional amplification. Changes in directional amplification might correlate closely with changes in location of a response peak, as has been demonstrated in the cat’s superior colliculus (Middlebrooks and Knudsen 1987), but this does not account for the corresponding movement of response nulls on both sides of the azimuth function peak. Spectral patterns present in the HRTF produce response nulls by a mechanism of spectral inhibition.

Central versus peripheral mechanisms

Mechanisms by which pinna-derived spectral cues are represented in neural discharge rates appear to differ in central and in peripheral auditory neurons. Poon and Brugge (1993) studied the responses of auditory eighth nerve fibers to synthetic spectral notches in filtered noise bursts that mimic naturally occurring spectral notches. They concluded that the responses of eighth nerve fibers reflect the amount of sound pressure within their excitatory response areas. This conclusion is also consistent with the findings of Rice et al. (1995), who studied the responses of auditory eighth nerve fibers to noise bursts that were filtered to mimic the HRTF in the cat. Although two-tone suppression can be demonstrated in the responses of eighth nerve fibers (Sachs and Kiang 1968), Poon and Brugge (1993) concluded that energy outside the excitatory response area does not appear to play a major role in a fiber’s response to the notch stimuli. In contrast to eighth nerve fibers, the azimuth and elevation sensitivity of MD cells to monaural BBN stimulation appears critically dependent on integration of input from excitatory and inhibitory frequency domains. Directional sensitivity is low in response to stimuli with frequency components limited to excitatory frequency domains but high in response to stimuli with frequency components that are distributed in both excitatory and inhibitory frequency domains.

As a consequence of integration of excitatory and inhibitory inputs from different frequency domains, MD cells exhibit greater response modulation to HRTF spectral cues than would be expected from auditory eighth nerve fibers. It is not uncommon for MD cells to be completely unresponsive to certain directions regardless of SPL. Eighth nerve fibers reveal the presence of spectral notches as increased thresholds and decrements in responsiveness (Poon and Brugge 1993a,b) but would be expected to respond to any sound direction (or any HRTF spectrum) given a sufficiently high SPL. Thus for responses averaged over a broad range of SPLs, MD cells show greater direction-dependent response modulation (i.e., greater directional sensitivity) than eighth nerve fibers.

Some MD cells exhibit focal directional selectivity to monaural stimulation, a pattern of response to HRTF spectra that does not appear to be present in peripheral auditory neurons. Spectral notches may be represented as response minima in receptive fields of eighth nerve fibers (Poon and Brugge 1993a,b; Rice et al. 1995). Thus in response to a broad range of SPLs, eighth nerve fibers would be expected to respond well at all directions with a local minima in discharge rate reflecting the presence of a spectral notch. In contrast, a spectral notch in theory could produce either a response null or peak in a MD cell. A MD cell with an appropriate configuration of excitatory and inhibitory domains might respond to all directions except those at which a spectral notch center frequency corresponds with the CF of the excitatory domain because only at this location does spectral inhibition reach a sufficient level to cancel excitatory drive. The monaural azimuth function of the cell illustrated in Fig. 14B shows some of these characteristics in that it is responsive to a broad range of azimuths. This pattern is somewhat similar to that expected from eighth nerve fibers, although the decrement in discharge rate at the null location is more pronounced. On the other hand, a MD cell might receive more powerful and/or lower threshold inhibitory input than excitatory input, such that at most directions spectral inhibition predominates and the cell does not respond. Only when a spectral notch is centered on an inhibitory frequency domain does the excitatory drive predominate and the cell respond. In this case, azimuth and elevation functions would appear as focal response peaks surrounded by response nulls and a number of examples are illustrated here (e.g., Figs. 2, 4, 8, and 9).

Frequency response areas of MD cells

All MD cells that were tested exhibited frequency response areas that consisted of excitatory and inhibitory domains. FRAs of MD and BD cells show some differences that might be related to a specialization for responding to HRTF spectra. First, excitatory domains of MD cells were, on average, narrower than those of BD cells. This could be a result of flanking inhibitory domains that restrict the width of excitatory domains. Second, response areas consisting of multiple excitatory domains were more common in the MD
than the BD sample, suggesting that this may reflect a mechanism for recognition of HRTF spectra. The pattern of multiple excitatory and inhibitory domains is reminiscent of frequency response areas generated by a three-layer neural network model that was designed to transform spectral representation of pinna filtered stimuli into a space-mapped representation of sound direction at the output (Neti and Young 1992). Under conditions of monaural input, many of the neurons in both the hidden and output layers had FRAs that consisted of interdigitated excitatory and inhibitory frequency domains. In some cases, the excitatory-inhibitory–excitatory domain architecture could be interpreted as a spectral notch detector with the center frequency of the notch corresponding to the center frequency of the inhibitory domain, although in other cases, such a simple interpretation was not possible.

Single units with multiple excitatory and interleaving inhibitory domains have been found in cortical field AI of the cat. Sutter and Schreiner (1991) discovered that neurons with multiple excitatory frequency domains were limited almost entirely to the dorsal third of the field. Whether or not neurons with multipeaked response areas in dorsal AI usually have MD properties is unknown, although one example of an AI MD cell with two excitatory domains has been documented (Samson et al. 1993). The finding that multipeaked response areas are present in parts of the MGB that project to AI (ventral nucleus and the lateral part of the posterior group of thalamic nuclei) (Morel and Imig 1987) leaves open the possibility that such cortical response areas may reflect subcortical processes.

Relationship of spectral inhibition and facilitation to directional sensitivity

Our results suggest that direction-dependent strength differences in spectral inhibition produce MD sensitivity. Responses to E/I stimuli clearly reveal a net spectral inhibition; there is little evidence for a net spectral facilitation in these responses. On the other hand, these data do not rule out the possibility that spectral facilitation may play some role in the responses of these cells. It is possible that responses to E/I stimuli represent a sum of spectral facilitation and spectral inhibition to all frequency components of the stimulus, but that spectral inhibition is the dominant interaction so that the result is a net spectral inhibition. Our findings certainly leave open the possibility that spectral facilitation may be present in the responses to E-only stimuli. Spectral facilitation has been demonstrated in the responses of cortical neurons in the cat (Nelken et al. 1994; Sutter and Schreiner 1991). Nevertheless, even if spectral facilitation is present in the responses of some MD cells, most are insensitive to the direction of E-only stimuli, suggesting that by itself spectral facilitation does not play a major role in their directional sensitivity.

Whereas direction-dependent variation in spectral inhibition seems to be an important mechanism of MD sensitivity, another mechanism was encountered that was capable of producing directional sensitivity to monaural stimulation. Interactions between frequency components in excitatory frequency domains may contribute to MD sensitivity in some cells (e.g., Fig. 11) by virtue of differences in responsiveness, threshold, and latency of responses in the different domains. Postexcitatory decrement in responsiveness may play a role in the directional sensitivity of this cell, but the mechanism responsible for the decrement is unknown. Significant differences in the minimum latency in different excitatory domains of multipeaked cortical neurons have been reported by Sutter and Schreiner (1991). In most cases, the high-frequency domain exhibited a longer latency than the low-frequency domain, but in other cases, the opposite was true as was the case of one cell that is included in the present report (i.e., Fig. 11).

Spectral cues and sound localization

Cats derive different types of directional information from spectral cues in different frequency ranges. HRTFs show a single spectral notch that systematically changes in frequency between 5 and 18 kHz as a function of azimuth and elevation, and a more complex pattern of peaks and notches at higher frequencies (18–50 kHz) (Rice et al. 1992). Accuracy of vertical and horizontal orientation in the frontal field is nearly the same to BBN and 5–18 kHz band-pass noise, and orientation accuracy to high-pass noise (>18 kHz) is poor, suggesting that spectral information in the 18–50 kHz range is irrelevant for this task (Huang and May 1996). In contrast, removal of high-frequency components has little effect on minimal audible angles in the horizontal plane but causes an increase in minimum audible angles at positive and negative elevations in the median plane (May and Huang 1996). Many MD cells have excitatory and inhibitory frequency domains that span both the 5- to 18-kHz and 18- to 50-kHz frequency ranges. Thus their directional sensitivity has a potential role in both of these behavioral tasks.

We thank C. Bailey for careful preparation of histological materials, data analysis, and preparation of illustrations and H. Cheng for computer programming.

Support for this work was provided by the National Institute on Deafness and Other Communicative Disorders (DC-00173); BRSG S07 RR 05373 and 554855 awarded by the Biomedical Research Support Grant Program, Division of Research Resources, National Institutes of Health; Fonds de la Recherche en Santé du Québec (P. Poirier); and Fonds pour la Formation de Chercheurs et l’Aide à la Recherche (P. Poirier).

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Received 7 March 1997; accepted in final form 7 July 1997.

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