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Directional Sensitivity of Neurons in the Primary Auditory (AI) Cortex: Effects of Sound-Source Intensity Level

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Reale, Richard A., Rick L. Jenison, and John F. Brugge. Directional sensitivity of neurons in the primary auditory (AI) cortex: effects of sound-source intensity level. *J Neurophysiol* 89: 1024–1038, 2003; 10.1152/jn.00563.2002. Transient sounds were delivered from different directions in virtual acoustic space while recording from single neurons in primary auditory cortex (AI) of cats under general anesthesia. The intensity level of the sound source was varied parametrically to determine the operating characteristics of the spatial receptive field. The spatial receptive field was constructed from the onset latency of the response to a sound at each sampled direction. Spatial gradients of response latency composing a receptive field are due partially to a systematic co-dependence on sound-source direction and intensity level. Typically, at any given intensity level, the distribution of response latency within the receptive field was unimodal with a range of approximately 3–4 ms, although for some cells and some levels, the spread could be as much as 20 or as little as 2 ms. Response latency, averaged across directions, differed among neurons for the same intensity level, and also differed among intensity levels for the same neuron. Generally, increases in intensity level resulted in decreases in the mean and variance, which follows an inverse Gaussian distribution. Receptive field models, based on response latency, are developed using multiple parameters (azimuth, elevation, intensity), validated with Monte Carlo simulation, and their spatial filtering described using spherical harmonic analysis. Observations from an ensemble of modeled receptive fields are obtained by linking the inverse Gaussian density to the probabilistic inverse problem of estimating sound-source direction and intensity. Upper bounds on acuity is derived from the ensemble using Fisher information, and the predicted patterns of estimation errors are related to psychophysical performance.

INTRODUCTION

Animals must localize the source of transient sound under a wide range of conditions in the natural world. This localization ability is tied to the functional integrity of primary auditory (AI) cortex (Jenkins and Merzenich 1984) and, presumably, to those AI neurons sensitive to sound source direction (Barone et al. 1996; Benson et al. 1981; Brugge et al. 1994, 1996; Eggermont and Mossop 1998; Eisenman 1974; Imig et al. 1990; Middlebrooks and Pettigrew 1981; Rajan et al. 1990; Samson et al. 1993, 1994; Soviarvi and Hyvarinen 1974) and to the major cues that the animal uses in localizing sound on the horizontal plane (Brugge et al. 1969, 1973; Irvine et al. 1996; Phillips and Irvine 1981, 1983; Reale and Brugge 1990; Reale and Kettner 1986; Semple and Kitzes 1993a,b).

Directional sensitivity and selectivity of an AI neuron are embodied in the auditory spatial receptive field, which is defined by those sound-source directions in azimuth and elevation from which a sound systematically affects the response of the cell (Brugge et al. 1994, 1996). Auditory spatial receptive fields are not static—they change in size and shape when competing sound is introduced into the acoustic environment (Brugge et al. 1998; Reale et al. 2000) and when the intensity of the sound source varies (Brugge et al. 1996). Typically, when there are no competing sounds and the intensity level of the source is at or very near the threshold, an AI spatial receptive field is confined to a small portion of acoustic space (Brugge et al. 1994, 1996, 1998; Eisenman 1974; Middlebrooks and Pettigrew 1981; Rajan et al. 1990). With few exceptions (see Imig et al. 1990; Rajan et al. 1990; Samson et al. 1993, 1994), increasing the stimulus strength by no more than 10 dB over a wide range (40–80 dB) of suprathreshold intensities results in marked increase in receptive field size whether measured along the azimuth, along the elevation, or along both (Brugge et al. 1994, 1996, 1998; Imig et al. 1990; Middlebrooks and Pettigrew 1981; Rajan et al. 1990). This attribute of AI spatial tuning is observed in other auditory cortical fields as well (Middlebrooks et al. 1994, 1998). Thus rather than providing a highly restricted view of auditory space, spatial tuning at the cortical level affords a nearly complete view of possible sound-source directions. In this setting, detailed information on sound-source direction must be encoded by a receptive field metric (e.g., discharge rate or latency or pattern) that has an orderly relationship to direction (Brugge et al. 1996; Jenison 1998; Middlebrooks et al. 1994, 1998; Furukawa and Middlebrooks 2002).

Previous studies from our laboratory showed that the first-spike latency of most AI cells was tightly locked to the onset of a transient directional stimulus and that for a sizeable proportion of these cells this latency metric was distributed in an orderly way across the spatial receptive field (Brugge et al. 1996, 1998; Reale et al. 2000). We hypothesized that directional information was derived from these spatial gradients. To examine this possibility in a more rigorous way and to relate the findings to extant psychophysical data, we first developed functional approximations to auditory spatial receptive fields. These approximations employed only directional dimensions of azimuth and elevation (Jenison 1998), although we later

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extended that approach to space-time (Jenison et al. 2001b). We then used maximum likelihood estimation methods to demonstrate that an ensemble of AI neurons with receptive fields having gradients of response latency contained sufficient information to account for auditory spatial acuity of both cat and human (Jenison 1998; Jenison et al. 1998). In an extension to this theoretical observer approach, we showed how a relative timing referent could be derived from the ensemble response and thereby obviate the apparent lack of a temporal marker for the onset of the stimulus (Jenison 2001a).

Systematic spatial gradients of response latency were often evident in AI spatial receptive fields over a wide range of intensity level of the sound source and hence the size of the field. We argued that this preservation of a functional gradient may account for a listener's ability to localized sound under changing intensity conditions (Brugge et al. 1996). Under most natural common listening conditions the intensity of the sound changes and is *unknown* to the listener. In our initial receptive field analyses, however, the intensity level of the sound source was assumed to be *known* to the theoretical observer and hence was ignored in the functional approximation. We have now extended our functional modeling approach to include, along with directional parameters, the intensity level of the sound source as an *unknown* parameter to be estimated by the theoretical observer.

In this paper we describe the changes in the AI spatial receptive field that typically occurs with changes in intensity of the source. We show that the resultant systematic changes of response latency within the receptive field are faithfully modeled using functional approximation techniques that include intensity as an *unknown* parameter. We then introduce the use of spherical harmonic analysis to quantify concomitant changes in receptive field shape. We go on to develop a probability density function that links the receptive field model with an inverse Gaussian distribution for response latency, which we then use in an information theoretic analyses of a simulated ensemble of AI neurons to derive estimation errors in azimuth and elevation when the intensity level of the sound source was assumed to be *unknown*. The modeled results are in agreement with psychophysical findings. Preliminary reports have been presented (Jenison 2001b; Jenison et al. 2001a).

METHODS

Adult cats, with no sign of external or middle ear infection, were premedicated with Acepromazine (maleate) (0.2 mg/kg, im) and Ketamine (hydrochloride) (20 mg/kg, im). A catheter was inserted into the femoral vein for iv drug administration and fluid replacement. Atropine sulfate (0.1 mg/kg, sc), dexamethasone sodium (0.2 mg/kg, iv), and procaine penicillin (300,000 units, im) were also administered before the animal was deeply anesthetized either with sodium pentobarbital (11 cats) or with halothane (4 cats). Pentobarbital sodium was administered intravenously (40 mg/kg, iv). Halothane (0.8–1.8%) was administered with a carrier-gas mixture of oxygen (33%) and nitrous oxide (66%) through an endotracheal tube using a scavenged VerniTrol vaporizer system and an anesthesia ventilator. Samples of inspiratory and expiratory air were drawn continuously from within the endotracheal tube and a respiratory gas analyzer (Ohmeda 5250) used to measure pulse rate, oxygen saturation, airway pressure, and concentrations of O₂, CO₂, N₂O, and halothane, on a breath-by-breath basis. When halothane was employed a muscle relaxant (pancuronium bromide, 0.15 mg/kg, iv) was administered just before recordings began, if spontaneous respiration was irregular or otherwise compro-

mised. Paralysis could be maintained throughout the experiment by supplemental doses of pancuronium. Muscle relaxation under halothane anesthesia, combined with careful monitoring of inspired and expired gases and vital signs, provided a highly stable long-term recording environment. Experimental protocols were approved by the University of Wisconsin Institutional Animal Care and Use Committee.

When the animal reached a surgical plane of anesthesia, the pinnae and other soft tissue were removed from the head. Hollow earpieces were inserted into the truncated ear canals, sealed in place, and connected to specially designed earphones. The transfer characteristics of the left- and right-ear sound delivery systems were measured in vivo near the tympanic membrane. A chamber was cemented to the skull over the exposed left auditory cortex, filled with warm silicone oil, and hydraulically sealed with a glass plate on which a Davies-type microdrive was mounted. Action potentials were recorded extracellularly with tungsten-in-glass microelectrodes in cortical area AI; their times-of-occurrence were measured with respect to stimulus onset within a window extending from 5 to 100 ms either by using a 1- μ s resolution and storing for off-line analyses or by digitizing their waveforms at 25 kHz and using BrainWare software (TDT, Gainesville, FL) on-line and off-line to sort action potentials among single units. Tone burst stimuli delivered monaurally or binaurally were used to estimate the best frequency (BF) of a neuron and some response area features related to binaural interactions as described previously (Brugge et al. 1996). The partial tonotopic map obtained by repeated electrode penetrations made during the course of an experiment confirmed that the recordings were obtained from neurons in AI.

Sound-source stimuli were impulsive transients (either 6.4 or 10 ms duration) delivered in virtual acoustic space, as described previously (Brugge et al. 1994; Reale et al. 1996). In later experiments this stimulus presentation was accomplished with a TDT System II (TDT). A veridical model of virtual acoustic space (Chen et al. 1995; Wu et al. 1997) was used to synthesize, in quasi-real-time, transient signals for sound-source directions positioned in a spherical coordinate system (-180° to $+180^\circ$ azimuth, -36° to $+90^\circ$ elevation) and centered on the cat's interaural axis. The virtual acoustic space used was derived from HRTFs measured in a single cat and hence not tailored to each of our experimental animals. Acoustic calibration, performed in-ear on each animal, was used to provide a common intensity reference among animals; namely, the maximum intensity for a particular sound-source stimulus that occurs in the virtual acoustic space. Intensity level is expressed as decibels of attenuation (dBA) from this maximum. The spatial receptive field of a neuron, for a sound source of a particular intensity level, was mapped using a virtual acoustic space composed of either 1,650 directions on a Cartesian graticule (approximately 4.5° azimuth by 9° elevation spacing, Brugge et al. 1996) or 524 directions arranged along a spiral path (approximately 9° separation) to provide uniform spherical sampling (Jenison et al. 2001b). In either case, the spatial receptive field is rendered (on paper) using the quartic-azimuthal equal area projection, which minimizes distortion in the frontal hemisphere and includes all of auditory space around the cat.

RESULTS

Our results were derived from 244 single AI neurons from which spatial receptive fields were obtained at different intensity levels. The BFs of these neurons ranged from 5.9 to 29.1 kHz. Typically, AI neurons in our sample exhibited little or no spontaneous activity and responded to an effective spatial stimulus with a single spike or a short burst of spikes for up to tens of hundreds of closely spaced directions. At each effective direction, we measured the latency to the first spike evoked by that stimulus. There were several observations common to all neurons studied, as described in detail in a previous report (Brugge et al. 1996). At any given intensity, response latency often varied within the receptive field by approximately 3–4

ms, although for some cells the spread could be as much as 20 ms. The distribution of response latency within the receptive field at any given intensity was typically unimodal. The mean of the distribution differed among neurons for the same intensity level, and most often also differed among intensity levels for the same neuron. Increases in intensity typically resulted in decreases in the mean of the distribution. Response latency, averaged across directions, was longest for an intensity level near threshold for the cell, and decreased rapidly at intensity levels approximately 20–30 dB above this threshold. Further increases in intensity could evoke either asymptotic or non-monotonic behaviors. Over a range of 10–50 dB, the mean latency across a receptive field would typically shorten by at least approximately 1–5 ms. Figure 1 illustrates several of these response attributes for one neuron. The left-hand column shows quartic-authalic maps of response latency (color coded) at each of six intensity levels with highest intensity at the top. Here the empirically measured response latency, averaged across all effective directions, increased from 12.5 to 32.7 ms over the 45-dB range of intensity studied (right-hand column, open symbols). Similarly the SD of the distribution increased from 2.2 to 27.2 ms. This empirical SD (dashed horizontal lines) contains both the *unsystematic* and the *systematic* components of the response variability. The systematic component at any given intensity is due to the dependence of response latency on the direction of the sound source.

Functional approximation of the auditory spatial receptive field under changes in sound source intensity

Initially we developed a receptive field model that accounted for the systematic variability in response latency that depended on sound-source direction, and partitioned out the unsystematic variability (Jenison 1998). Here we illustrate the behavior of this model, which has now been extended to account for the systematic variability that depends also on sound-source intensity (for a theoretical treatment, see Jenison 2001b; Jenison et al. 2001a). This extended functional approximation method was applied to all 244 single units in our sample. No systematic differences were seen in the modeled data that could be attributed to the anesthetic used.

Our prior functional approximation work on spatial receptive fields used spherical basis functions with free parameters (w_{ij} , κ_{ij} , β_{ij} , and α_{ij}) for fitting the basis functions. The free parameters serve only to mathematically approximate the receptive field, where α and β specify the placement of each basis function on the sphere, κ specifies each width, and w specifies each weight. The current extension of this approximation now includes an exponential dependence on the intensity level, η , of the sound source defined as

$$rf_i(\theta, \phi, \eta) = \sum_{j=1}^M w_{ij} \exp\{\ln(\eta) \kappa_{ij} (\sin \phi \sin \beta_{ij} \cos(\theta - \alpha_{ij}) + \cos \phi \cos \beta_{ij})\} + \exp\{\xi_{ij} \eta\} \quad (1)$$

and a corresponding free fitting parameter ξ . The nonlinear dependence on η was introduced to modulate the width parameter κ of the spherical basis functions and allow for the shape of the receptive field to depend on sound intensity. Similarly, the nonlinear dependence of mean latency on intensity is provided by introduction of the final term $\exp\{\xi_{ij} \eta\}$ in

Eq. 1. Constrained optimization techniques were used to fit the parameters w_{ij} , β_{ij} , α_{ij} , and ξ_{ij} of the M basis functions defined by Eq. 1 to the dependent neural response of interest—which in this case was response latency. The details of the approximation techniques can be found in Jenison (1998, 2001b).

The *middle column* of Fig. 1 shows the results of applying this extended model to the empirical data (*left column*) from the same neuron. Although the latency data occupies a spherical coordinate system, the model approximation is simply a form of regression through a scatter of data where the predicted latency corresponds to the systematic mean value for any given direction and intensity. Thus the model captures the mean latency as a function of direction (*middle column*) as well as the increase in response latency, averaged across directions, as a function of decreasing intensity (*right column*, filled symbols). The modeled receptive fields also exhibit an increasing RMS residual error with decreasing intensity (*right column*, solid horizontal lines). Since this RMS residual error estimates the unsystematic component of response variability, it is seen to be smaller than the total variability (i.e., corresponding dashed horizontal lines). We note here features of these receptive fields that we return to in the DISCUSSION. At highest stimulus intensities, the receptive field is very large and the latency distribution is very narrow. Under this condition, the spatial latency gradients are shallow and variance in response latency is small. At the other end of the dynamic range, the receptive fields are relatively small with latency gradients that are steep and latency variance that is high.

The relationship between modeled and empirical data are further exemplified using data from six additional neurons in Fig. 2. For each neuron, the spatial receptive field was sampled at between four and six intensity levels separated by 5, 10, or 20 dB. The lowest level was usually chosen to be within 20 dB of the minimum threshold for that cell. For many cells, this lowest level produced a mean (and SD) of response latency that measured in tens of milliseconds. Furthermore, increasing the intensity level resulted in significantly reduced mean values and SD that typically asymptote to <5 ms. For other cells, like those in the lower right of Fig. 2, the magnitude of change observed across all sampled intensity levels was <10 ms. Regardless of these idiosyncrasies, the modeling process is clearly faithful to the specifics of each neuron's "latency versus intensity" profile. For each neuron modeled, the input set consists of all measured response latencies (1,003–4,334 for these 6 units) together with their corresponding sound-source direction and intensity level.

Monte Carlo simulation

The veracity of the model in estimating the systematic component of response variability is limited by the inherent variability (noise) introduced by the modeling process itself. This model noise is the result of the data dependence on the constrained optimization techniques that were used to fit parameters to the basis functions that served to model the response latency (see Jenison 1998, 2001b). There is no true solution of the model for a particular neuron given a finite input set consisting of measured response latencies together with their corresponding sound-source directions and intensity levels. Therefore the estimates of systematic variability shown in Figs. 1 and 2 need to be compared with this inherent noise to

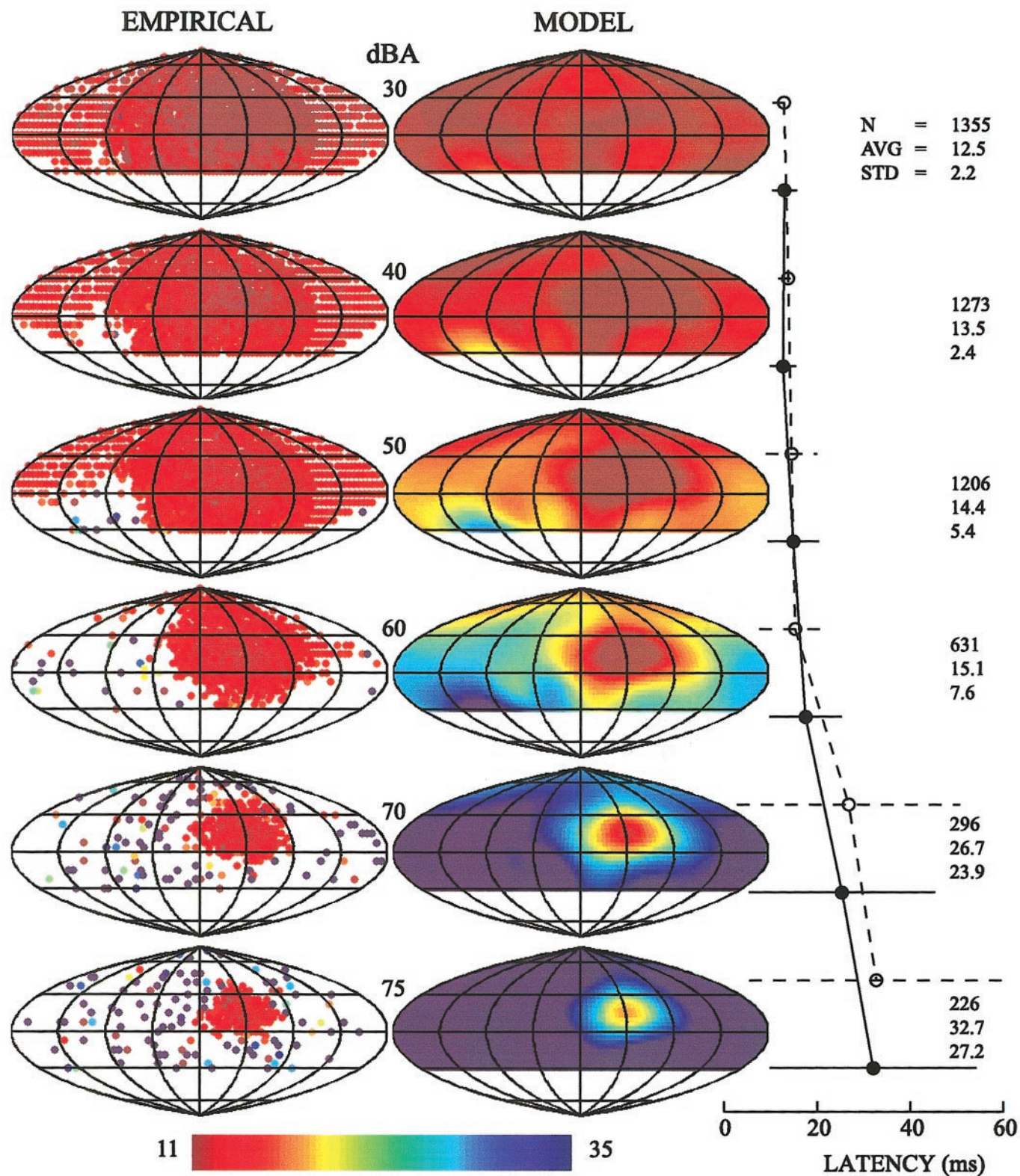


FIG. 1. Auditory space receptive field based on 1st-spike latency from 1 AI neuron obtained at 6 different intensities. Intensity in dBA shown above each row. Color bar annotations denote response latency limits (ms). *Left column*: maps of empirical values of response latency (color coded) using a quartic-azimuthal projection. Central meridian corresponds to 0° azimuth and is directly in front of the head; meridians forming edges (left edge = -180° and right edge = +180°) of the projection are behind the head. Central parallel corresponds to 0° elevation and is coincident with interaural axis. *Middle column*: map projection of spherically modeled response latency. *Right column*: graphs of response latency, averaged across directions, of empirical data (open symbols) and modeled data (filled symbols) as a function of intensity. The 2 graphs are displaced vertically for clarity of presentation. Values for number of observations (N), average (AVG), and SD (STD) are annotated for each empirical map at each intensity.

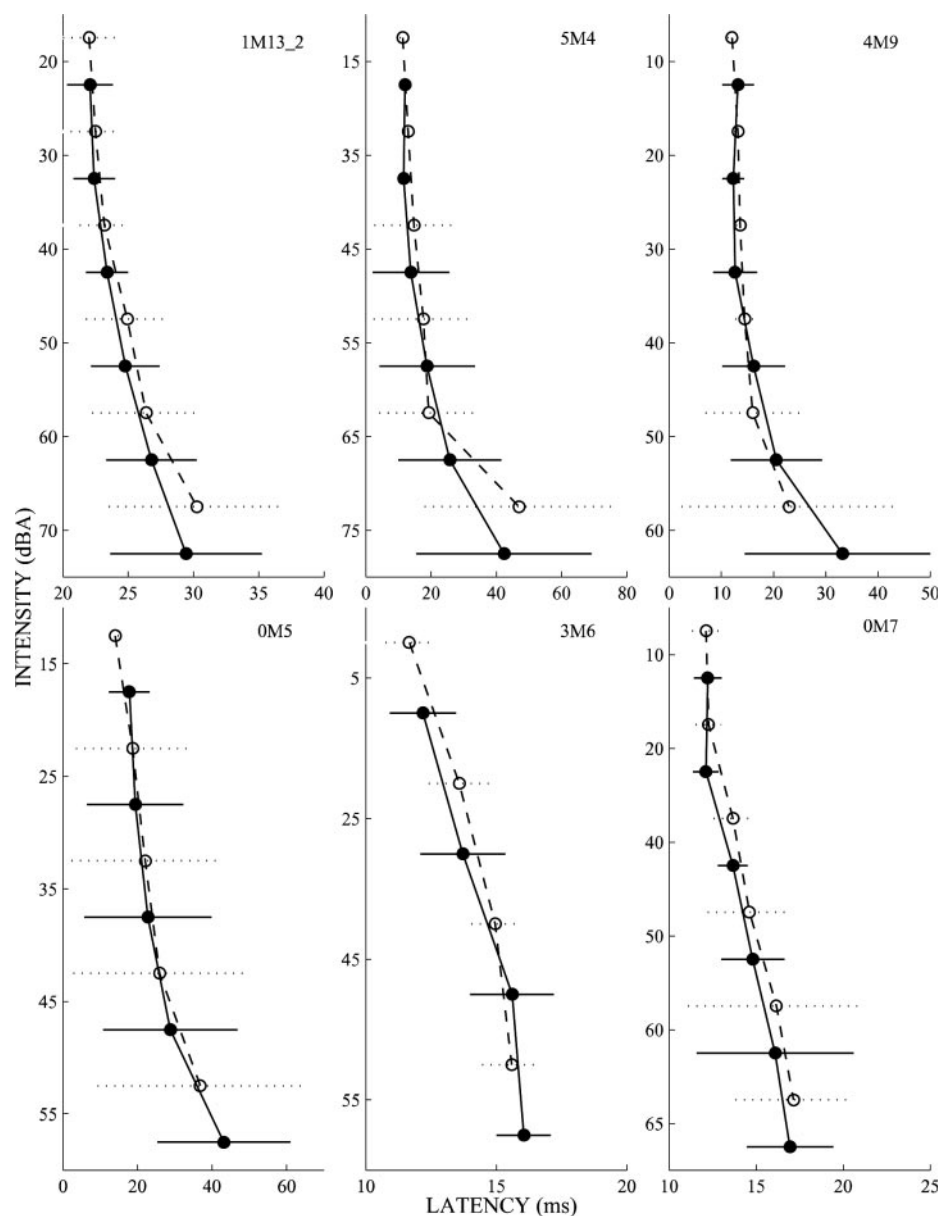


FIG. 2. Response latency, averaged across directions, as a function of intensity level. Six panels obtained from different neurons. Empirical data use open symbols for means and dashed horizontal lines for SD. Modeled data use filled symbols for means and solid horizontal lines for residual (RMS) error. The residual error lines for the modeled receptive fields are naturally shorter, because they estimate just the unsystematic variability. By comparison, empirically measured SD reflects both systematic and unsystematic variation.

judge their validity. The method we employed to measure the model's noise used Monte Carlo simulations. Figure 3 illustrates the results of this analysis using the same neuron that was depicted in Fig. 1. The total number of measured response latencies composing the input set for this cell was 4,987. In the Monte Carlo approach, one-half of these potential inputs are chosen at random (with replacement) and that sub-set was used to model the cell's spatial receptive field. The sample and model process was repeated 40 times as prescribed by Efron and Tibshirani (1993). The *left column* maps the receptive fields for each intensity level using the mean value at each direction obtained from the Monte Carlo simulation. The *middle column* maps the receptive fields using the SD at each direction. In general, regions with the shortest response latencies are also the regions that map to the smallest SD. The *right column* reproduces the function (model) from Fig. 1 that showed the systematic increases in response latency and RMS error (from 2.6 to 22.1), collapsed across directions (filled circles, solid horizontal lines). In addition, the function that

results from Monte Carlo simulation plots the mean response latency (filled squares) and its RMS error (i.e., model noise), collapsed across directions, for direct comparison. At each intensity level, the model noise is seen to be significantly less than its paired value. These findings suggest that the model approximations to the receptive fields shown in Figs. 1 and 2 were indeed valid estimates of systematic variability in response latency that is due to both the dependence of latency on the direction of the sound source and to the intensity level of the source.

Receptive field shape changes with intensity level

We showed above that average response latency data from the functionally modeled receptive fields in our study typically followed their empirically derived counterparts, whether the nonlinear growth in latency as a function of intensity was expansive or compressive. We have also observed that in extending the model from its original form there appears to be

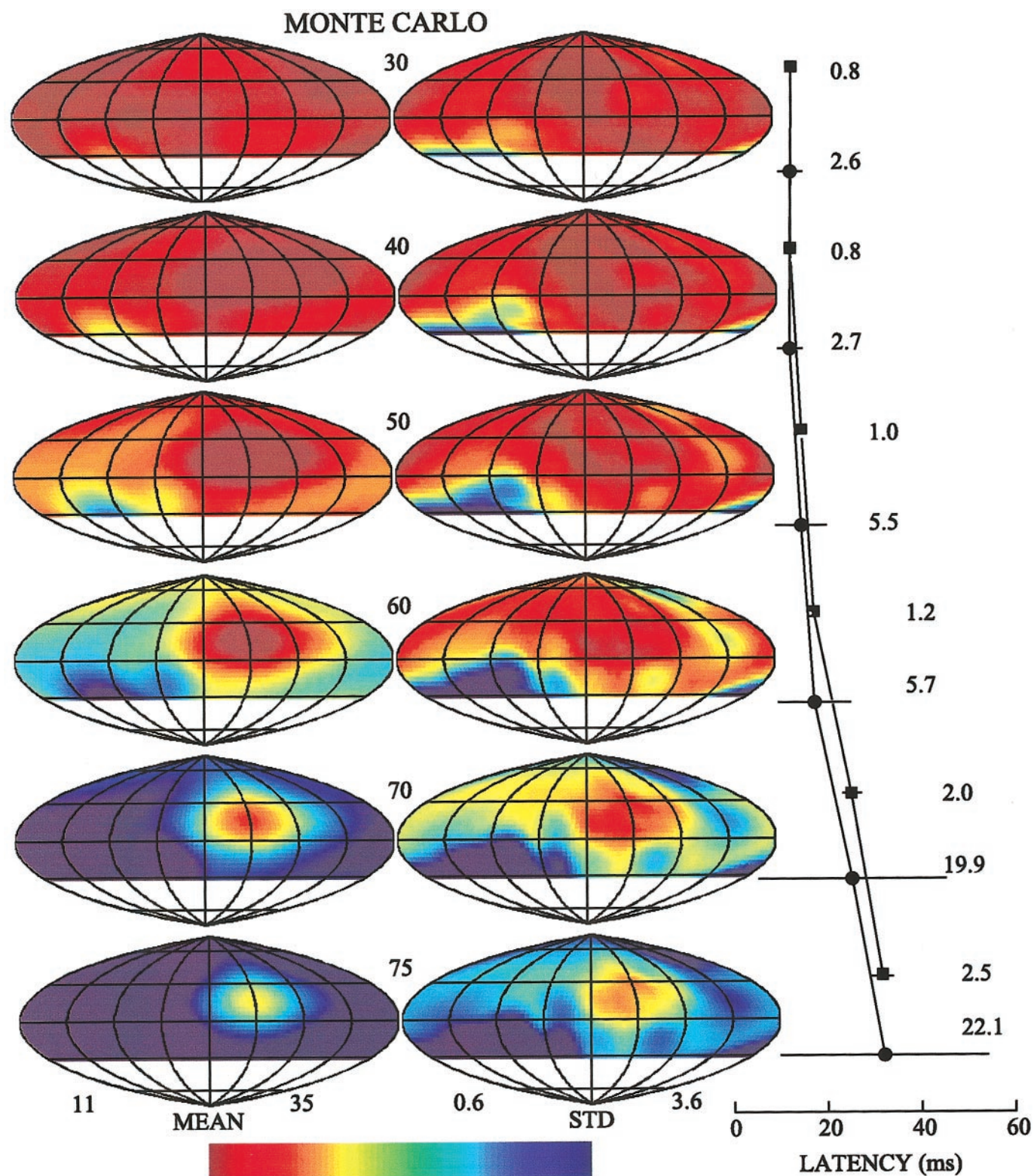


FIG. 3. Auditory space receptive field based on response latency from 1 AI neuron using Monte Carlo simulation of spherically modeled data. Intensity in dBA shown above each row. *Left column*: map projection of mean response latency obtained from 40 invocations of spherical modeling process. *Middle column*: map projection of SD of modeling process. Color bar annotations below each columns denote response latency and SD limits, respectively. *Right column*: graphs of mean latency, collapsed across directions, of single-invocation modeled data (●) and Monte Carlo modeled data (■) as a function of intensity. Values for residual (RMS) error are annotated for both functions at each intensity. See Fig. 1 for further details.

sufficient degrees of freedom to capture the potential changes in shape of the receptive field that typically attend intensity level changes. One visualization of these shape changes is provided by iso-response contours, as shown by solid white lines on the spatial receptive fields of three neurons illustrated in Fig. 4. Because the approximation encompasses both the dependence on spatial direction and on intensity level, a spatial receptive field can be examined at any chosen intensity level and on any graticule. Here we chose intensities varying from 10 (*top*) to 60 dBA (*bottom*) and a graticule with 9° spacing. At

a near-threshold intensity level, a particular response contour is typically confined to only a quadrant of acoustic space, most often contralateral to the cerebral location of the cell under study. For these exemplar cells, and for most others in our sample, raising the intensity level produced concomitant changes in size and location of the contours. Here, for example, the iso-response-latency contours for 1 unit (*left column*) is seen to change in size, location, and orientation as intensity is increased from 50 to 10 dBA. Neither contour is present in this unit's receptive field determined at 60 dBA. In other neurons,

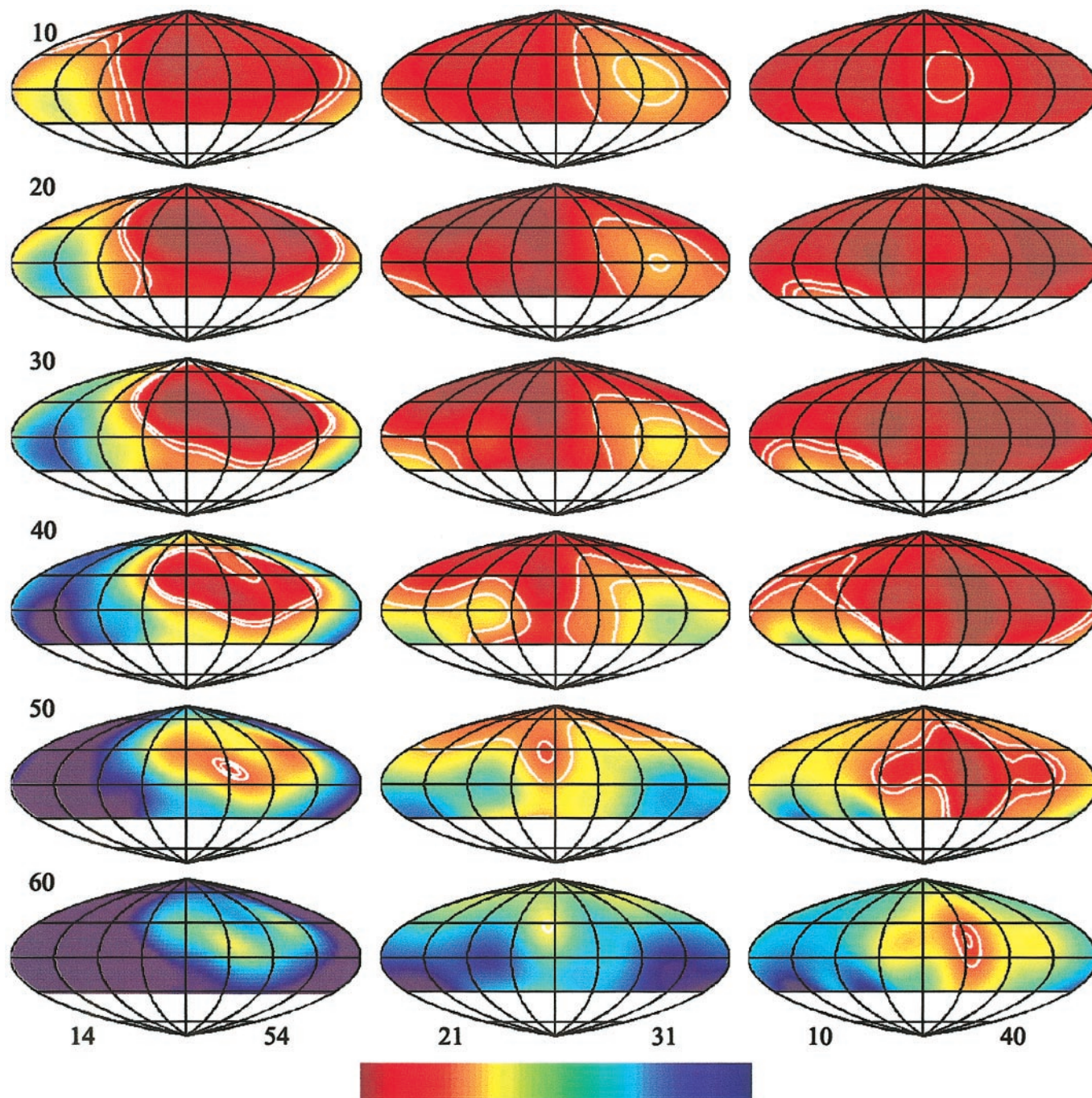


FIG. 4. Auditory space receptive field based on response latency using spherical model for 3 AI neurons. Columns correspond to different single units. Color bar annotations, below each column, denote response latency limits (ms). Intensity in dBA shown above each row. Solid white lines map isolatency contours (1-ms separation). See Fig. 1 for further details.

still more complicated changes are seen due to a nonmonotonic relationship between response latency and intensity level. To capture these changes quantitatively, and thereby study systematically intensity related changes in spatial receptive field shape, we turned to spherical harmonic analysis.

Spherical harmonic analysis

Spherical harmonics provide a complete orthonormal basis for expressing a function defined on a sphere (Hobson 1965), and the spatial receptive field is a natural spherical function. They play a role similar to that of cosines and sines in the Fourier transform. Spherical harmonics vary according to their so-called spatial frequency, l , ranging from 0 to ∞ , and their moment, m , which ranges from $-l$ to $+l$. The complex spherical harmonics themselves are defined in terms of the associated Legendre functions as follows

$$Y_l^m(\theta, \phi) = (-1)^m \sqrt{\frac{2l+1}{4\pi} \frac{(l-m)!}{(l+m)!}} P_l^m(\cos \theta) e^{im\phi}$$

The periodic nature of the spherical harmonic is separated into elevational (θ) dependence via the Legendre function, and

azimuthal (ϕ) dependence via the moment parameter m in the complex exponential function.

Since spherical harmonics form a complete orthonormal basis, it allows an arbitrary function, in our case, $rf(\theta, \phi, \eta)$, to be expanded in terms of complex spherical harmonics such that

$$rf(\theta, \phi, \eta) = \sum_{l=0}^{L_{\max}} \sum_{m=-l}^l a_l^m Y_l^m(\theta, \phi)$$

The transform is carried out for the frequencies l only up to some finite frequency $L_{\max}$. The absolute value of the moment m is bounded by l . Spherical harmonics are illustrated in Fig. 5 using one spatial receptive field from a token single unit. When the moment m equals 0, the harmonics are referred to as zonal harmonics, and vary only in elevation and not in azimuth. In these cases, there will be l cycles observed along any meridian on the sphere. When the moments m equal the frequency (l), the harmonics are known as sectorial, and periodic variation is observed as a function of azimuth, dividing the sphere into longitudinal sectors. Any other configurations of m and l are referred to as tesseral harmonics, which reflect a checker board pattern on the sphere. The analysis on the sphere

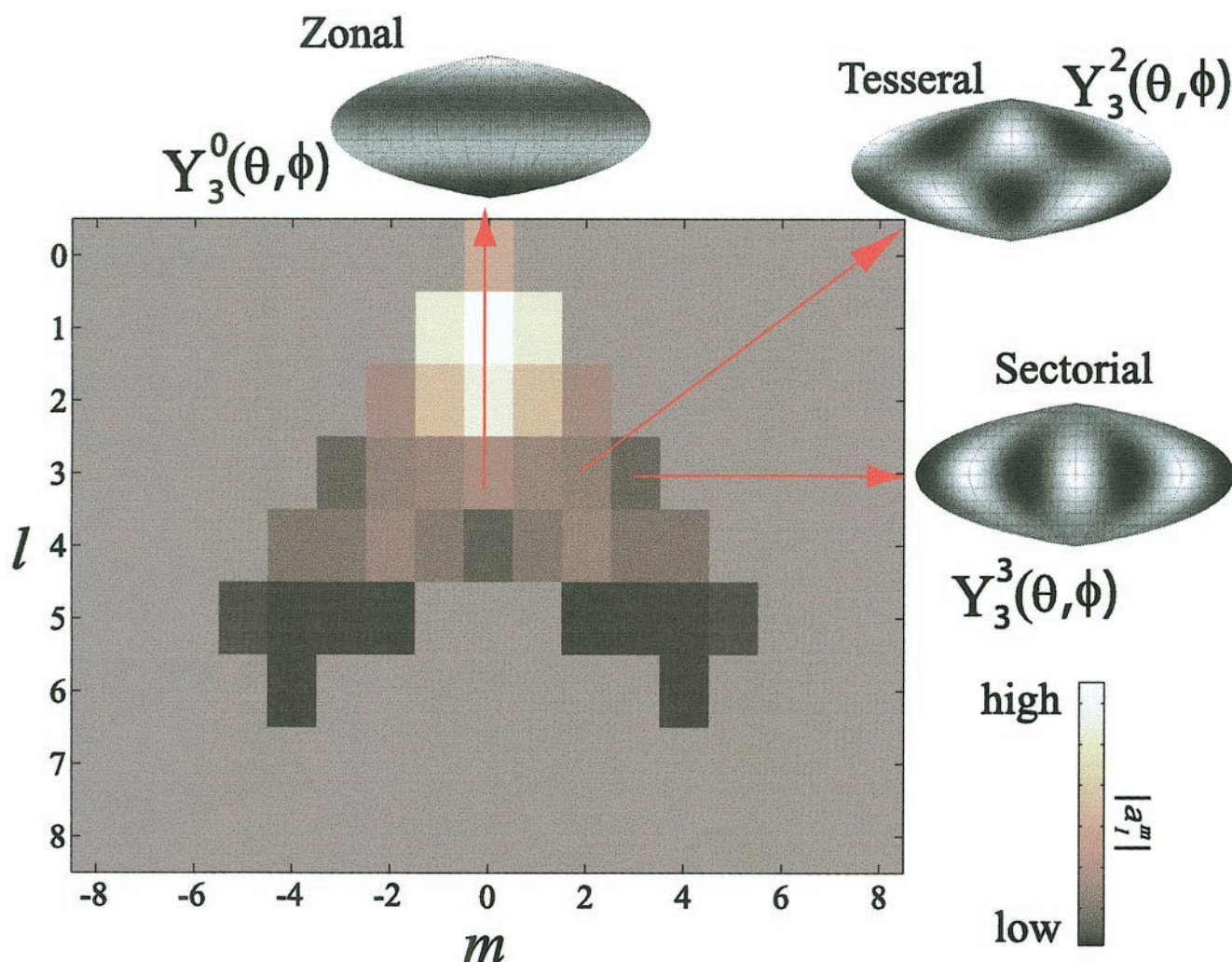


FIG. 5. Spherical harmonic magnitude spectrum for an auditory space receptive field. Spherical harmonics vary according to their frequency, l , ranging from 0 to ∞ , and their moment, m , which ranges from $-l$ to $+l$. Magnitude coefficients $|a_l^m|$ are color coded and form a pyramid ranging from $[l, m] = 0, 0$ to $[l, m] = L_{\max}, \pm L_{\max}$. Examples of zonal, sectorial, and tesseral harmonics are shown as map projections and connected by arrows to their corresponding elements in the magnitude spectrum.

using complex spherical harmonics is fundamentally similar to how we analyze an acoustic waveform (signal) as a function of time using similar complex exponentials. To determine the coefficients of the spherical transform, we integrate the product of each spherical harmonic and a modeled spatial receptive field $rf(\theta, \phi, \eta)$ over θ and ϕ

$$a_l^m = \int_0^{2\pi} \int_0^\pi \bar{Y}_l^m(\theta, \phi) rf(\theta, \phi, \eta) \sin \phi d\phi d\theta$$

where $\bar{Y}_l^m(\theta, \phi)$ is the complex conjugate. The spherical magnitude coefficients $|a_l^m|$ form a pyramid with the apex corresponding to $[l, m] = 0, 0$ and a base ranging from $[l, m] = L_{\max}, -L_{\max}$ to $[l, m] = L_{\max}, +L_{\max}$. The magnitude weight of each harmonic is colored coded. $L_{\max}$ can be as large as necessary to account for the highest spatial frequency in the receptive field, although in our analyses it has been conservatively set to 20. Examples of zonal, sectorial, and tesseral harmonics are shown for their corresponding element in this spherical magnitude spectrum. Since the coefficients a_l^m are complex, there is a corresponding phase spectrum, just as in the case of Fourier analysis, which reflects the degree of harmonic shift. To the degree that the receptive field is spatially low-pass, the spectral matrix will be dominated by the apical region of the spectrum pyramid. In this example the magnitude of the coefficients are negligible for $l > 6$. The spectrum matrix is useful for capturing the orthogonal contributions of the different types of spherical harmonics. For example, a spectrum dominated by the edge of the pyramid would reflect primarily sectorial harmonics.

We have used spherical harmonic analysis to study shape changes in our sample population. Figure 6 illustrates an example of that analysis using the data from the three units in Fig. 4. As sound intensity was decreased (*top to bottom*), there was a general trend for the receptive field to become more spatially high-pass, as signaled by the increased magnitudes of the coefficients toward the base of the spectrum pyramid. The unit's spectra shown in the right panel tends to be composed primarily of sectorial harmonics relative to zonal harmonics, in contrast with the other two units. All include the more complex tesseral harmonics. To quantify these changes across intensity we derived distributions using the ratio of averaged magnitude coefficients from 165 units with appropriately sampled intensity levels. Specifically, the log ratio of average sectorial ($l = m$) magnitude coefficients to average zonal ($m = 0$) magnitude

coefficients $\log_{10} \frac{|\bar{a}_m^m|}{|\bar{a}_l^0|}$ provides a measure of the relative strength of each class for each receptive field. Figure 7 presents the resulting distributions (*left column*) obtained at a low intensity level (generally within 10 dB of threshold) and at a high-intensity level (generally 25 dB greater). At both levels, the mode of the histogram favors the zonal harmonics as reflected by the increased area below a log ratio of zero in both distributions. Thus it appears that across our population, spatial receptive fields do not evidence a marked preference for periodic variation as a function of azimuth in the manner exemplified by the predominance of sectorial harmonics for one unit in Fig. 6. Rather, elevational dependence, in addition to azimuthal, is a common attribute in AI spatial receptive fields. Furthermore, our analysis indicated that this elevational dependence was expressed in a given cell's receptive field across

intensity levels. A scatter diagram of the two intensity conditions used in this analysis illustrates that a unit's log ratio remains relatively constant over intensity levels ($r = 0.80$). Finally, the general low-pass nature of spatial receptive fields, discussed informally earlier, is here shown quantified as decibel magnitude spectra, averaged across the sample of 165 units, as a function of frequency l . The curve pertaining to the high-intensity calculation (solid line) is uniformly lower than that corresponding to the low intensity sample (dashed line), indicating the additional spectrum shift to lower spatial frequencies at higher intensity levels.

Information theoretic analysis of sound-source direction from ensemble responses

Information provided by a single neuron is not likely to be sufficient to localize the direction of a sound source due to both the broadness of the spatial receptive field and to the ambiguity between a given response and the direction and/or intensity of the source eliciting that response. This can be appreciated by inspecting the iso-response contours within a receptive field (e.g., Fig. 4). Rather, we hypothesize that sound direction is encoded by a population of neurons having different but overlapping spatial receptive fields (Jenison 1998, 2001a,b; Jenison et al. 2001a). In this approach, the neural responses (in our case response latency) are considered as random variables, and each neuron has a probability density function that links the receptive field model to statistical behavior of the random variable. A population of such cells can then be investigated analytically using *Fisher information* to show how directional acuity is enhanced or degraded as a consequence of neural response variability and the structure of the receptive field.

Most analytical derivations for Fisher information are based on the assumption of a multivariate Gaussian distribution of error. However we have recently argued that the inverse Gaussian (IG) density also performs well in capturing the dependence of response-latency variance as a function of the mean latency (Jenison 2001b; Jenison et al. 2001a). Previously, we had only considered a linear model of variance growth. The inverse Gaussian density, with the linked receptive field model, $rf_i(\theta, \phi, \eta)$, is

$$p_{IG}(x_i | \theta, \phi, \eta) = \sqrt{\frac{\lambda}{2\pi[x_i + \gamma]}} \exp \left[\frac{-\lambda[x_i + \gamma - rf_i(\theta, \phi, \eta)]^2}{2[x_i + \gamma]rf_i(\theta, \phi, \eta)^2} \right] \quad (2)$$

The mean corresponds to the receptive field $rf_i(\theta, \phi, \eta)$ and the variance is $\frac{rf_i(\theta, \phi, \eta)^3}{\lambda}$ for the i th neuron in the population ensemble. The important characteristic of the IG is that, like the Poisson, the variance depends on the magnitude of the mean. The IG has a more direct relationship to the Gaussian and has been employed for analyzing inter-spike intervals by Tuckwell (1988), Levine (1991), and Iyengar and Liao (1997). The IG is a more accurate model of spike latency compared with the standard Gaussian employed in Jenison (1998, 2000). The parameter γ has typically been used as an additional degree of freedom for purposes of improving the fit of univariate models. The Fisher information derivation for the IG distribution can be found in Jenison (2001b). There the full Fisher information matrix was constructed as a 3×3 matrix whose diagonal corresponds to information for each parameter,

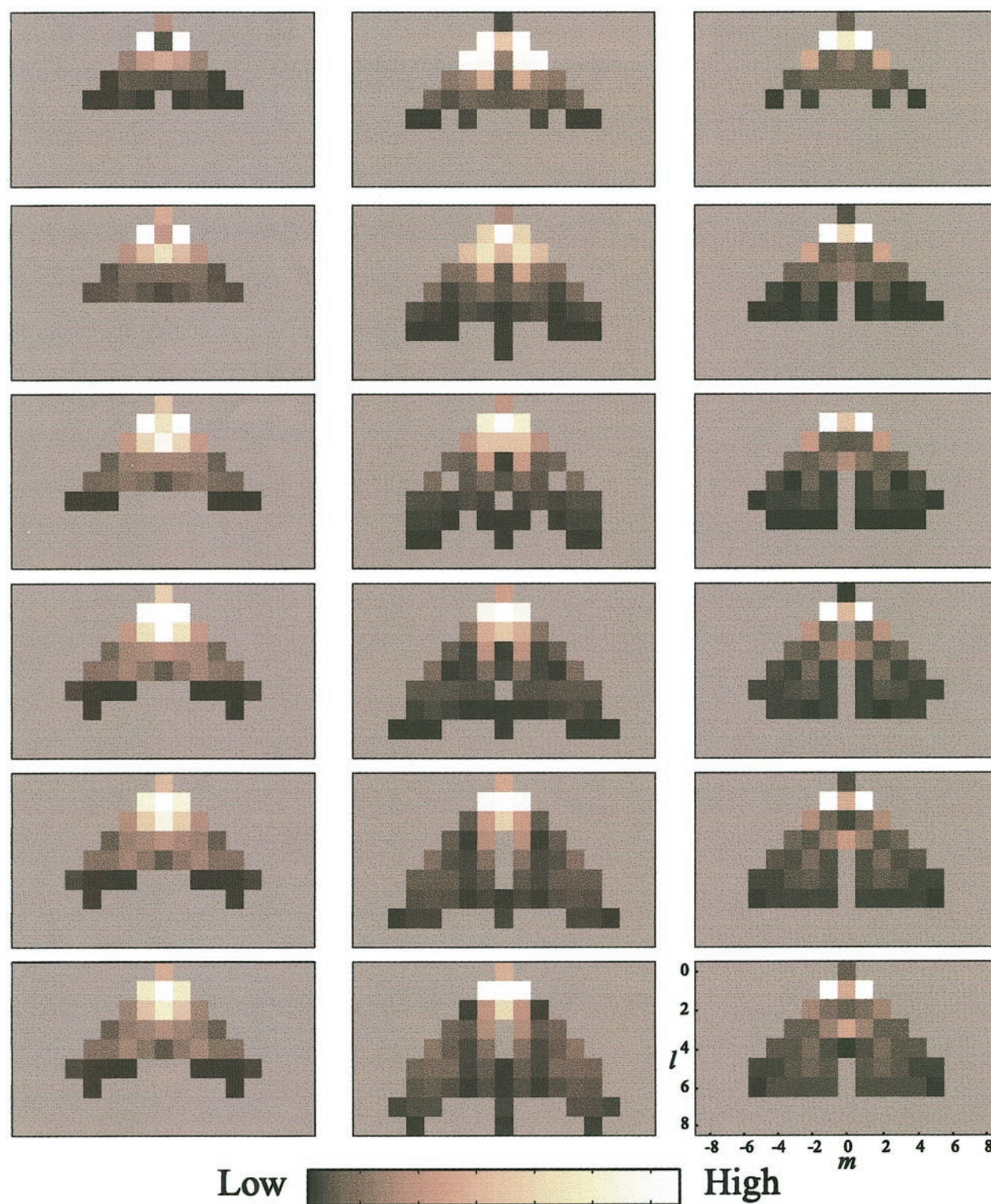


FIG. 6. Spherical harmonic magnitude spectra for auditory space receptive fields using spherical model for 3 AI neurons. Columns correspond to the same 3 units shown in Fig. 4. Intensity level decreases from top to bottom. See Fig. 4 for further details.

the two directional parameters θ and ϕ , and the intensity parameter η . The off-diagonal cells correspond to the cross-information. Inverting the Fisher information matrix results in a covariance matrix containing the individual Cramer-Rao lower bounds on estimation variance for each parameter and the covariance in the off-diagonals.

Consideration of only one parameter in the Fisher information matrix leads to the following construction with respect to the azimuth direction parameter θ for a population of N neurons

$$E \left\{ \frac{\partial}{\partial \theta} \log L(\theta, \phi, \eta) \right\}^2 = \lambda \sum_{i=1}^N \frac{[\partial r f_i(\theta, \phi, \eta) / \partial \theta]^2}{r f_i(\theta, \phi, \eta)^3} \quad (3)$$

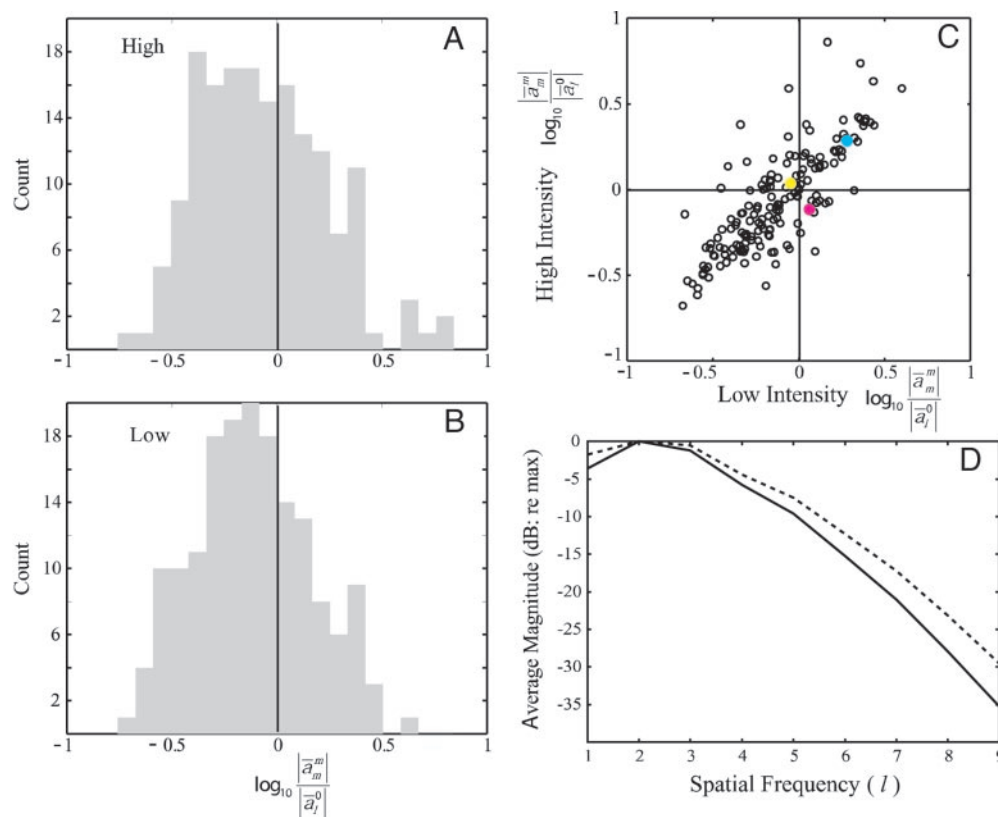


FIG. 7. The log ratio of average-sectorial magnitude coefficients to average-zonal magnitude coefficients for (A) high and (B) low intensity. $n = 165$ units. C: scatter diagram of log ratio of average coefficients for high and low intensities. Three color symbols derived from the 3 columns in Fig. 6: *left* (yellow), *middle* (magenta), and *right* (cyan). D: average receptive field spatial filtering, based on spherical harmonic analysis, as a function of spatial frequency (l) collapsed across moments (m). Solid line corresponds to high intensity and dashed line corresponds to low intensity.

This construction illustrates the deflation of information as the cube of the mean response latency; a consequence of the direct relationship between variance and mean for the IG. Figure 8 uses Fisher information to show how the lower bound on the standard error (SE) for azimuth depends on intensity level at three azimuth directions (*top*), and also how elevation error (*bottom*) depends on intensity for a population of 26 AI modeled units. We chose this subset of neurons because it represents the most complete sampling we have of receptive fields over a wide range of intensity. The model predictions of the remaining neurons is good, but the number and range of intensity was limited such that an attempt to extrapolate to over a 50-dB range would probably not accurately reflect the structures of their receptive fields. There are several trends in the population estimation error. First, the best acuity, reflected in the smallest SE, is for directions near the midline (0° azimuth). Second, improvement in acuity (smaller error) occurs as intensity is initially increased (i.e., moving from right-to-left along the dBA axis) from the lowest value (60 dBA), but only for azimuths off the midline. This dichotomy is perhaps not unexpected since it is well known that acuity is best at the midline, and therefore, is going to be most robust to very low intensities. Further increases in intensity always resulted ultimately in decreases in acuity (larger errors). Analysis of elevation errors (Fig. 8, *bottom*) reveals similar behavior for elevation estimates as a function of intensity. It follows, that there is an optimal intensity level for direction acuity that appears to be around 40 dBA for this population of units.

DISCUSSION

Characterizing auditory spatial receptive fields is not a single-factor (i.e., sound-source direction) problem since under

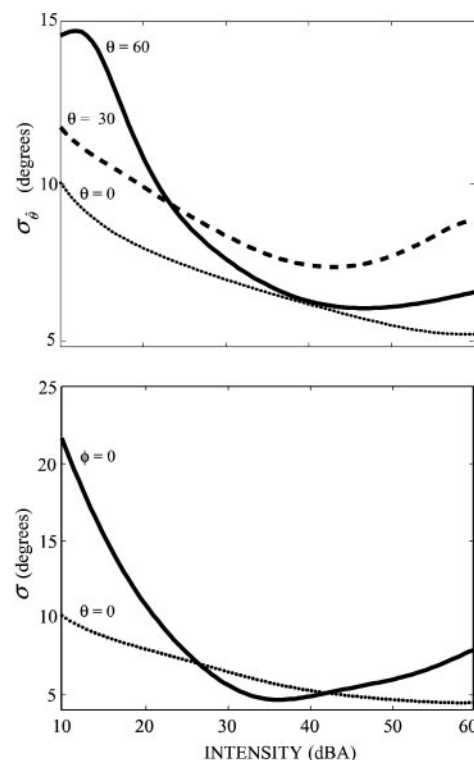


FIG. 8. Minimum directional estimation error by an ensemble of AI neurons as a function of sound-source intensity level. *Top*: error in azimuthal direction (σ_θ) for 3 simulations with sound-source azimuths of 60° , 30° , and 0° , respectively. Elevation fixed at 0° . *Bottom*: error in azimuthal direction (dotted line) and elevational direction (solid line) for simulations with sound-source azimuth of 0° and elevation of 0° .

natural conditions listeners localize sounds under varying behavioral conditions that include environments where sound sources vary in intensity over a wide range. These nondirectional variables can be reasonably hypothesized or experimentally demonstrated to be important in determining the operating characteristics of a cell's spatial receptive field (Benson et al. 1981; Brugge et al. 1998; Furukawa and Middlebrooks 2001; Reale et al. 2000; Recanzone et al. 1998, 2000; Su and Recanzone 2001), which in turn could confound localization ability.

The dependence of AI spatial receptive field properties on sound-source intensity level is also indicated by dichotic stimulation studies that employed the two major interaural cues for directional hearing (i.e., interaural time and level differences). In these experiments, the exact relationship between neural response and an interaural cue was often critically dependent on the intensity level of the source (Brugge et al. 1969, 1973; Irvine et al. 1996; Phillips and Irvine 1981, 1983; Reale and Brugge 1990; Reale and Kettner 1986; Semple and Kitzes 1993a,b). Thus for most AI cells, uncertainty in the intensity level of the source introduces an inherent ambiguity between a given response and the interaural difference cue that maps onto the azimuthal direction of that source.

We have extended the nonparametric functional modeling of auditory space receptive fields to include the dimension of sound-source intensity. This new construction of the functional model is an important extension because it characterizes formally the covariation of response latency between two stimulus dimensions. Thus the model captured the systematic response variability due to the interplay of sound-source direction and sound-source intensity with negligible modeling error as demonstrated by cross-validation (i.e., Monte Carlo simulation).

Spherical harmonics

One interpretation of the spatial receptive field is that it reveals the spatial filtering characteristics of the neuron. The neuron, however, responds in both a linear, as well as nonlinear fashion, as a function of space, time, and intensity (Jenison et al. 2001b). A linear systems analysis analogous to Fourier analysis was used to expand the spatial function into characteristic patterns of spherical harmonics on the sphere. The composition of the receptive field may be dominated by a particular class of spherical harmonics. Although the tesseral harmonics are difficult to interpret in terms of patterns of directional sensitivity, the zonal harmonics reflect elevational spatial periodicity, and the sectorial harmonics reflect azimuthal periodicity. The azimuthal sensitivity of spatial receptive fields obtained from high-frequency neurons in other auditory cortical and subcortical areas appears determined largely by the pattern of interaural intensity differences (IID) caused by separation of the ears on the head (Delgutte et al. 1995; Fuzessery et al. 1990; Nelken et al. 1998; Tollin and Yin 2002b; Wenstrup et al. 1988). However, across these frequencies, the IID-azimuth relationship in the cat varies with spherical elevation (Martin and Webster 1989; Musicant et al. 1990). Taken together, these relationships predict that spatial receptive fields should be characterized by neither a predominance of solely zonal nor sectorial harmonics. Our data (Fig. 7) are consistent with this prediction in that the population distribution characterizing the range from zonal to sectorial was not peaked at either extreme, but rather in the middle.

Analytic formulation of the spatial receptive field

All cortical response metrics that have been studied as *neural-code* candidates for directional hearing suffer from some form of ambiguity between stimulus dimensions and unique response measurement. For example, in our AI sample, it is common for a cell to produce the same discharge rate or response latency for an array of sound-source directions (i.e., iso-response contour) in acoustic space; even when all other stimulus variables are held constant (Brugge et al. 1996, 1997; Jenison 1998). This ambiguity is easily compounded when additional stimulus dimensions (e.g., background noise or competing sound) are investigated (Brugge et al. 1998; Reale and Brugge 2000). The intensity level of the sound source is particularly notable in this regard (Heil et al. 1994; Phillips et al. 1994; Schreiner 1998). For example, most high-BF neurons in cat AI cortex are reported to exhibit an azimuthal sensitivity that is dependent on the intensity level of a free-field stimulus (Clarey et al. 1994; Imig et al. 1990; Rajan et al. 1990; Samson et al. 1993, 1994). A similar result is inferred when cat AI neurons are studied for the affect of intensity level on their interaural intensity difference sensitivity (Irvine et al. 1996; Semple and Kitzes 1993a,b); a major cue for the azimuthal direction of high-frequency sound sources. These intensity level effects are also common in other auditory cortical areas (Middlebrooks et al. 1998) and in lower levels of the mammalian central auditory system using both free-field or dichotic stimulus delivery (Boudreau and Tsuchitani 1968; Fuzessery et al. 1990; Irvine and Gago 1990; Semple and Kitzes 1987; Tollin and Yin 2002a; Wenstrup et al. 1988).

In most of the studies cited above, a small proportion of neurons has been identified with spatial receptive field characteristics that can be classified as intensity invariant. One reasonable suggestion, therefore, is that a neural code for sound-source direction is carried by this sub-population using one of the hypothesized receptive field characteristics (e.g., maximal response). In our studies, however, we have investigated an alternative proposal. Namely, that within an ensemble of AI cortical neurons with spatial receptive fields that are typically large and exhibit multiple co-variations among stimulus dimensions, there is sufficient information (in a statistical sense) to code for sound-source direction (Jenison 1998, 2000, 2001a; Jenison et al. 2001a). This information theoretic approach benefits greatly from the analytic formulation of the spatial receptive field and the application of standard quantitative tools for parameter estimation.

Fisher information

We, as well as others, have investigated the consequences of broad receptive fields on population coding using Fisher information and the Cramer-Rao lower bound (CRLB) under the assumption of independent noise (Jenison 1998; Paradiso 1988; Seung and Sompolinsky 1993), and correlated noise (Abbott and Dayan 1999; Gruner and Johnson 1999; Jenison 2000; Sompolinsky et al. 2001). The CRLB is a lower bound on the variance, or the SE, of any unbiased estimator, and is derived from Fisher information with respect to a family of parametric probability distributions. The CRLB is inversely related to Fisher information mathematically and intuitively. As the magnitude of Fisher information increases, we expect

the estimated SE to diminish. If the CRLB can be derived analytically, it can be used to compute the minimum possible variance about any value estimated by a theoretical ideal observer. Under the assumption of independence, even very broad and nonuniform spatial receptive fields in auditory cortex can demonstrate psychophysical localization acuity with as few as 10 cells in the population (Jenison 1998, 2000).

Most analytical derivations for Fisher information are based on the assumption of a multivariate Gaussian distribution of error; however, deviation from the standard Gaussian assumption requires alternative constructions for Fisher. By examining the residual error from the current model, we ascertained the magnitude of response-latency variance and modeled that variability using an alternative to the Gaussian distribution, that of the IG, whose variance depends on the mean latency and allows formal evaluation of the growth in variance using Fisher information. This relationship may prove useful beyond field AI, since response latency metrics have recently been shown to carry a significant proportion of the directional information in nonprimary auditory cortical areas (Furukawa and Middlebrooks 2002), and in visual (Gawne et al. 1996; Heller et al. 1995; Wiener and Richmond 1999) and somesthetic (Petersen et al. 2001) sensory representations.

The normal and Poisson densities are well known. The Poisson and its variants have been used extensively as point-process and rate models. Less familiar Tweedie densities include the inverse Gaussian and gamma. Most recently Barbieri et al. (2001) have modeled spike trains using these densities to address deficiencies in their earlier Poisson models (Brown et al. 1998). Tweedie densities are characterized by an index p where $E[x] = \mu$ and $\text{var}[x] = \lambda\mu^p$. The indices $p = [0, 1, 2, 3]$ correspond to the normal, Poisson, gamma, and IG, respectively (Jorgenson 1987, 1999). The IG distribution has a history dating back to 1915 when Schrodinger presented derivations of the density of the first passage time distribution of Brownian motion with motion drift (Chhikara and Folks 1989; Seshadri 1999). Tweedie (1941) coined the term inverse Gaussian based on his observation that the cumulant generating function of IG is the inverse of the cumulant generating function for the Gaussian. We have analyzed the goodness-of-fit of the IG (Jenison 2001b; Jenison et al. 2001a), and found it to be a reasonable model of increasing variability as a function of mean first-spike latency.

In this study, we employed the Fisher information derivation for the IG distribution that was recently suggested as a viable alternative to the standard Gaussian (Jenison 2001b; Jenison et al. 2001a). When a small ensemble of AI cells was studied in this way, the influence of sound-source intensity was manifested as a nonmonotonic relationship with acuity. Except near the midline (i.e., 0 azimuth), acuity was best at an intensity between the minimum and maximum level tested. These results have some support in the psychophysical literature at high-intensity levels (MacPherson and Middlebrooks 2000) and at low intensity levels (Su and Recanzone 2001). The nonmonotonic behavior can be explained in terms of the competing contributions to population coding. As the sound intensity increases the general trend for the population is to broaden and flatten the receptive fields that results in a general decrease in spatial gradients (see Figs. 1 and 6). However, it is also the

case that as the intensity decreases the mean first-spike latency increases together with an increase in variance (see Figs. 1 and 2). These two characteristics contribute to the increase in the standard error at high and low intensities.

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