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Oblique Effect: A Neural Basis in the Visual Cortex

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Li, Baowang, Matthew R. Peterson, and Ralph D. Freeman. Oblique effect: a neural basis in the visual cortex. *J Neurophysiol* 90: 204–217, 2003. First published February 26, 2003; 10.1152/jn.00954.2002. The details of oriented visual stimuli are better resolved when they are horizontal or vertical rather than oblique. This "oblique effect" has been confirmed in numerous behavioral studies in humans and to some extent in animals. However, investigations of its neural basis have produced mixed and inconclusive results, presumably due in part to limited sample sizes. We have used a database to analyze a population of 4,418 cells in the cat's striate cortex to determine possible differences as a function of orientation. We find that both the numbers of cells and the widths of orientation tuning vary as a function of preferred orientation. Specifically, more cells prefer horizontal and vertical orientations compared with oblique angles. The largest population of cells is activated by orientations close to horizontal. In addition, orientation tuning widths are most narrow for cells preferring horizontal orientations. These findings are most prominent for simple cells tuned to high spatial frequencies. Complex cells and simple cells tuned to low spatial frequencies do not exhibit these anisotropies. For a subset of simple cells from our population (n = 104), we examined the relative contributions of linear and nonlinear mechanisms in shaping orientation tuning curves. We find that linear contributions alone do not account for the narrower tuning widths at horizontal orientations. By modeling simple cells as linear filters followed by static expansive nonlinearities, our analysis indicates that horizontally tuned cells have a greater nonlinear component than those tuned to other orientations. This suggests that intracortical mechanisms play a major role in shaping the oblique effect.

INTRODUCTION

Receptive field (RF) structure is altered dramatically in the transformation from LGN to visual cortex. Specifically, center-surround organization is replaced by elongated RFs with specific orientation preferences (Hubel and Wiesel 1962, 1974). Behaviorally, oriented detail is not uniformly resolvable. In particular, spatial detail with vertical and horizontal orientations is more finely resolved than that with oblique angles. This has been designated the "oblique effect" (Appelle 1972). The classical finding is that human subjects perform best on a spatial acuity test when the visual targets are oriented horizontally or vertically (Berkley et al. 1975; Campbell and Kulikowski 1966; Emsley 1925; Higgins and Stultz 1950; Jastrow 1893; Taylor 1963). The general finding applies to a variety of other measurements including contrast sensitivity (Campbell and Kulikowski 1966; Mitchell et al. 1967), orientation selectivity (Andrews 1965, 1967; Blake and Holopigian 1985; Campbell and Kulikowski 1966; Orban et al. 1984), orientation discrimination (Bouma and Andriessen 1968; Caelli et al. 1983; Coletta et al. 1993; Ferrera and Wilson 1990; Heeley and Buchanan-Smith 1992; Heeley and Timney 1988; Mustillo et al. 1988; Orban et al. 1984; Regan and Price 1986; Vogels et al. 1984; Westheimer and Beard 1998), Vernier acuity (Saarinen and Levi 1995; Westheimer and Beard 1998), motion discrimination (Ball and Sekuler 1980, 1982; Coletta et al. 1993; Gros et al. 1998; Matthews and Welch 1997), and reaction time (Attneave and Olson 1967; Essock 1980. For reviews of the literature, see Appelle 1972; Howard 1982; Howard and Templeton 1966.).

The oblique effect has also been studied in animal subjects. It has been demonstrated behaviorally in the cat (Orban and Kennedy 1979; Parriss 1964; Vandenbussche and Orban 1983), monkey (Bauer et al. 1979; Boltz et al. 1979; Nissen and McCulloch 1937) and other species (Appelle 1972). However, the oblique effect measured through animal psychophysics is not as consistent as in humans. Some cat behavioral studies have failed to find significant effects (Bisti and Maffei 1974; Blake and Holopigian 1985; De Weerd et al. 1990).

Early investigators attributed orientation anisotropies to physical properties of the visual system such as asymmetric optics, sparser photoreceptor packing in the retina along oblique angles, and frequent microsaccade eye movements along the Cartesian axes. However, experimental data demonstrate that these physical factors do not significantly contribute to the effect (Higgins and Stultz 1950; Nachmias 1960). It is clear that the anisotropies have a neural basis (Campbell and Kulikowski 1966; Maffei and Campbell 1970; Mitchell et al. 1967).

Some physiological single-cell studies in the primary visual cortex (V1) of the monkey (De Valois et al. 1982; Mansfield 1974; Poggio and Fischer 1977) and the cat (Bauer and Jordan 1993; Kalia and Whitteridge 1973; Kennedy and Orban 1979; Payne and Berman 1983; Pettigrew et al. 1968; Wilson and Sherman 1976) have reported that there are more cells tuned to horizontal and vertical than oblique. However, other investigations, also in monkeys and cats, failed to find significant differences in the numbers of cells tuned to different orientations (Campbell et al. 1968; Finlay et al. 1976; Henry et al. 1974; Hubel and Wiesel 1968; Noda et al. 1970; Poggio et al. 1977; Rose and Blakemore 1974; Wilson and Sherman 1976). Visual evoked potential (VEP) studies, in monkeys and cats,

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have also produced mixed results with some showing (Bonds 1982; Mansfield and Ronner 1978) and others failing to show (Campbell et al. 1973) orientation anisotropies.

The unequal distribution of orientation preference is just one characteristic that has been investigated. Differences in orientation tuning specificity have also been studied. Neurons in V1 with horizontal or vertical preferences have been reported to exhibit narrower orientation tuning widths (Kennedy and Orban 1979; Nelson et al. 1977; Orban and Kennedy 1981; Rose and Blakemore 1974). However, in other work, orientation-specific differences in tuning width were not observed (Finlay et al. 1976; Mansfield 1974; Wilson and Sherman 1976).

One possible explanation for why some physiological studies find an oblique effect whereas others do not could be that anisotropies are only exhibited in a subpopulation of neurons. For example, it has been reported that the orientation preference anisotropy is exclusively due to simple cells (Orban and Kennedy 1981; Orban et al. 1984). Orientation tuning width asymmetries have also been claimed to be limited to simple cells (Nelson et al. 1977; Orban et al. 1984; Rose and Blakemore 1974). On the other hand, other studies have found pronounced anisotropies in complex cells as well (Albus 1975; Henry et al. 1978; Payne and Berman 1983). Spatial characteristics might be another differentiating factor. Leventhal and Hirsch (1977) reported that only cells with small RF sizes exhibit orientation anisotropies. Other studies find the effect only in the foveal region and not in the periphery (Kennedy and Orban 1979; Mansfield 1974; Orban and Kennedy 1981). DeValois et al. (1982) suggested the RF size and fovea-parafovea distinctions are actually the result of spatial frequency differences, although they did not have a large enough sample size to substantiate this.

Several investigations have assumed that V1 is the site of origin for the oblique effect. Electroretinogram (ERG) measurements have been unable to find an effect at the retina level (Maffei and Campbell 1970). Single-unit studies in cats (Orban and Kennedy 1979, 1981) and monkeys (Levitt et al. 1994) have reported anisotropies in area 17 but not 18, and functional magnetic resonance imaging (fMRI) measurements in humans show an oblique effect only in V1 and not in other visual areas (Furmanski and Engel 2000). However, recent optical imaging studies of area 18 (Liu and Pettigrew 2003; Wang et al. 2003) and single-unit recordings from the inferior temporal cortex (Orban and Vogels 1998) demonstrate that orientation anisotropies can also be found outside of the primary visual cortex. Furthermore, a study of the small orientation biases in the cat lateral geniculate nucleus (LGN) has shown that a slight preference for horizontal and vertical orientations is evident in the thalamus (Vidyasagar and Urbas 1982). The preference remains even with areas 17 and 18 lesioned, suggesting that the feedforward connections from LGN neurons may play a significant role in shaping the selectivity and preference for cardinal orientations in the primary visual cortex.

Drawing solid conclusions from the existing research is difficult due to conflicting results. This is confounded by the fact that each study used different experimental techniques and analysis criteria. Furthermore, the number of cells sampled was typically less than 100. Several studies have attempted to get around the issue of limited sample size through imaging techniques. Orientation anisotropies have been observed with optical imaging (Chapman and Bonhoeffer 1998; Coppola et al. 1998b; Liu and Pettigrew 2003; Wang et al. 2003; Yu and Shou 2000), VEP recordings (Arakawa et al. 2000; Bonds 1982; Freeman 1975; Frost and Kaminer 1975; Maffei and Campbell 1970; Mansfield and Ronner 1978; Moskowitz and Sokol 1985; Nelson et al. 1984; Sokol et al. 1987), and fMRI (Furmanski and Engel 2000). However, these techniques do not provide a characterization of the response properties of individual neurons. It is also not clear if observed anisotropies are the result of differences in relative population size or differences in the response amplitudes of individual neurons.

In the present study, we examine our database of physiological data from thousands of cells to provide a more thorough analysis of the neural correlates of perceptual orientation asymmetries. We have examined selectivity, response characteristics, and the relative numbers of cells tuned to different orientations as a function of cell type and spatial frequency preference. We have also performed spatial and temporal analyses on a subset of cells for which we measured two-dimensional (2D) space-time RFs. To test the hypothesis that the orientation selectivity anisotropy found in V1 might be formed by the feedforward connections from LGN cells, we examined the linear and nonlinear contributions to the orientation tuning of simple cells through a spatial RF analysis (Gardner et al. 1999). This analysis makes use of a common model for simple cells consisting of a linear filter followed by a static expansive nonlinearity (Albrecht and Geisler 1991; Anzai et al. 1999; DeAngelis et al. 1993b; Emerson et al. 1989; Heeger 1992; Movshon et al. 1978; Tolhurst and Dean 1987). The linear filter is believed to be formed from afferent LGN connections as well as cortical contributions (Ferster 1988; Jagadeesh et al. 1997; Reid and Alonso 1995), while the expansive nonlinearity is assumed to arise solely through intracortical mechanisms (Anzai et al. 1999; Douglas et al. 1995; Gardner et al. 1999; Somers et al. 1995; Volgushev et al. 1996). If anisotropies in orientation tuning selectivity result from feedforward LGN connections, they should be evident in the linear RF analysis of simple cells.

METHODS

Physiological methods

Extracellular recordings are made from cells in the striate cortex of anesthetized and paralyzed cats. Recordings from well-isolated single units are obtained using multiple (2–4) tungsten-in-glass microelectrodes (Levick 1972) (or commercial models). Electrode penetrations are made along the medial bank of the postlateral gyrus, 4 mm posterior and 2 mm lateral from the Horsley-Clarke origin (Horsley and Clarke 1908) at an angle of 10° medial and 20° anterior. These penetrations produce tracks that pass through multiple layers and orientation columns within the central ±15° projection of the visual field (DeAngelis et al. 1993a). After a single unit is identified by the waveform of its response, the RF size, optimal spatial frequency, and orientation are measured quantitatively using sinusoidal gratings. Details of the surgical and experimental procedures are described elsewhere (Anzai et al. 1999; DeAngelis et al. 1993a).

Orientation tuning curves are measured using drifting gratings at the optimal size and spatial frequency for each cell. Gratings are drifted at a temporal frequency of 2 Hz and are presented monocularly to the dominant eye. Contrast is chosen to elicit a robust response. A minimum of five orientation samples are spaced in 5–15° steps around the optimal value to produce a well-defined tuning curve. A no-stimulus condition (i.e., a blank screen) is used to obtain an estimate

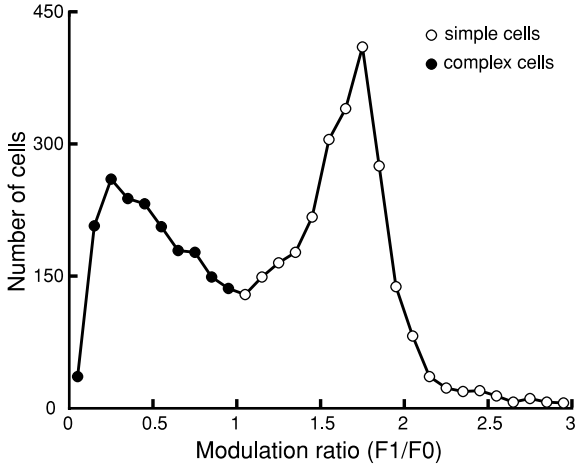

FIG. 1. Distribution of simple (○) and complex (●) cells. Cells with a modulation ratio (1st harmonic over the DC of the response) ≥1 are defined as simple; otherwise they are defined as complex.

of spontaneous activity. Conditions are presented in random order and displayed for a 4-s duration with a 2- to 4-s inter-stimulus interval. The condition set is repeated four to five times.

2D spatial RFs are mapped using a sparse-noise reverse correlation technique (DeBoer and Kuyper 1968; Eggermont et al. 1983; Jones and Palmer 1987; Sutter 1975). For details of the method as employed here, see DeAngelis et al. (1993a). Briefly, a rectangular stimulus patch is presented to the classical RF of the cell being recorded. The patch is oriented along the preferred orientation and divided into a 20×20 element grid. Individual bar stimuli of either high (32 cd/m^2) or low (2 cd/m^2) luminance are displayed one at a time on random grid locations for a 40-ms duration with a mean background luminance of 20 cd/m^2. Cross-correlating the stimulus with the response produces a linear approximation to the space-time RF profile.

Data analysis

Optimal orientation, response amplitude, and tuning width (full width at half height) are estimated from a Gaussian fit to the orientation tuning data [by use of a Levenberg-Marquardt least-squares fitting procedure (Press et al. 1992)]. For complex cells, fits are applied to the DC (mean firing rate minus the mean spontaneous firing rate) of the peri-stimulus time histogram (PSTH). For simple cells, fits are applied to the first harmonic (2 Hz) of the PSTH. Cells are classified as simple or complex based on the classical criteria (Hubel and Wiesel 1962) and also on the ratio (F1/F0) of the first harmonic to the DC of the PSTH with optimal stimulus parameters. Cells with an F1/F0 ratio ≥1 are classified as simple (Skottun et al. 1991; but see Mechler and Ringach 2002 for an alternative view of this classification system). The ratio of 1 is the approximate middle point of the bimodal distribution of F1/F0 ratios for our population of cells (Fig. 1).

A spatial analysis is performed on a cell's measured RF to estimate linear and nonlinear contributions to orientation selectivity using the method of Gardner et al. (1999). A summary of the method is as follows. We apply a discrete Fourier analysis to the 2D spatial RF (as illustrated in Fig. 11*A*) at the optimal correlation delay to obtain a 2D amplitude spectrum. The spectrum is then fit by a pair of 2D Gaussian functions that are symmetric about the origin (see Fig. 11*B*). The orientation tuning curve predicted by the 2D RF is obtained by sampling points in the spectrum at different angles at a fixed radius corresponding to the same spatial frequency used in the grating measurements (see Fig. 11*C*). The predicted tuning curve is then fit with a Gaussian function to obtain estimated tuning parameters. In general, the predicted tuning curve of simple cells is broader than that measured using drifting gratings (Gardner et al. 1999; Volgushev et al. 1996). The ratio of the measured and predicted tuning widths (as expressed by the variances of the Gaussian fits) is an estimate of the magnitude of the cell's expansive output nonlinearity (Gardner et al. 1999).

The χ^2 statistic is used when assessing the significance of anisotropies in the distribution of cells tuned to different orientations. The proportion *Z* test is applied when comparing the population sizes at two selected orientations. Otherwise, estimates of the significance of orientation anisotropies are obtained through the *F* test, one-way ANOVA.

RESULTS

The results reported here are derived from our laboratory database enabling us to perform analyses on large samples of cells that meet homogeneous selection criteria. To address the physiological basis of the oblique effect, we analyzed response amplitude, spatial frequency preference, orientation preference, orientation specificity, and spatial-temporal RF characteristics for area 17 neurons that were recorded using the same experimental setup and procedures. Data from cells are included in the analysis if they meet the following four significance criteria: *1*) the orientation tuning protocol must include at least four repetitions, *2*) spike rates at the preferred orientation must be greater than one SD over the spontaneous firing rate, *3*) the tuning curve must have a statistically significant peak (ANOVA, $P < 0.05$), and *4*) the tuning curve must be well fit by a Gaussian ($R^2 > 0.85$). (*R* is the multiple correlation coefficient.)

The dataset that meets these criteria consists of 4,418 cells. We binned these cells into 16 groups according to their preferred orientations. Each bin is 22.5° wide to cover the full 360° orientation space. In our coordinate system, 0 and 180° correspond to horizontal orientations drifting downward and upward, respectively. Ninety and 270° correspond to vertical orientations drifting to the left and to the right, respectively.

Figure 2 (▲) displays the numbers of cells from the total population tuned to each orientation bin. The plot has obvious

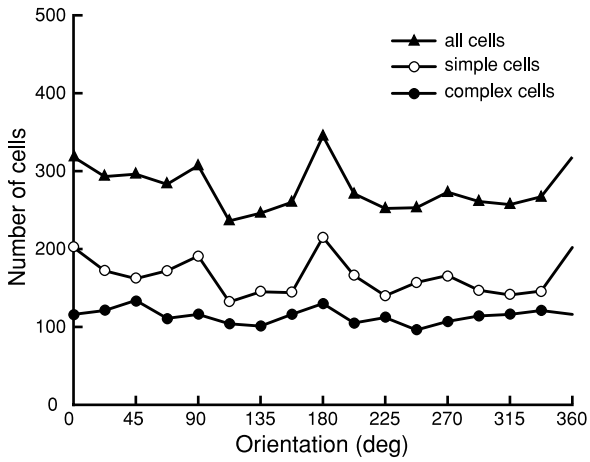

FIG. 2. Distribution of preferred orientation of cells in area 17. The full 360° of orientation space are divided into 16 bins and each bin is 22.5° wide. The top curve (▲) shows the distribution of preferred orientation for both simple and complex cells. Clear peaks are shown at horizontal and vertical orientations (0, 90, 180, 270°), with a higher predominance at horizontal (0 and 180°). Distributions are plotted separately for simple (○) and complex (●) cells. The distribution for simple cells resembles that of the overall population, but complex cells are more or less evenly distributed. Sample sizes for simple and complex cells are 2,598 and 1,820, respectively.

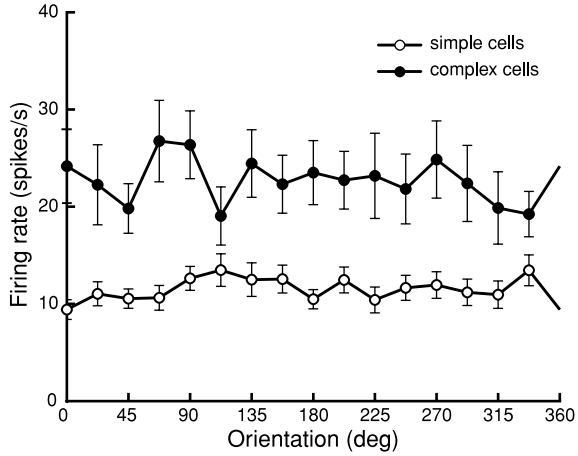

FIG. 3. Mean response amplitude as a function of preferred orientation. Only cells with orientation runs conducted at 50% contrast are included (n = 1,848). Neither simple (○, P = 0.102, F test) nor complex (●, P = 0.591, F test) cells show significant orientation specific variations of response amplitude. Bars represent ±1 SE.

peaks at horizontal and vertical orientations (0, 90, 180, and 270°) that are highly significant ($P < 0.001$, χ^2 test); 15.1% of the cells are tuned to horizontal orientations, whereas a flat distribution would produce only 12.5%. A smaller number, 13%, were tuned to vertical orientations, which is significantly less than that for horizontal ($P < 0.01$, Z test). The oblique orientations had the fewest numbers of cells with only 11% for 135 and 315°. These percentages are comparable with distributions of preferred orientation across the cortical surface of area 17 as measured through optical imaging (Chapman and Bonhoeffer 1998; Coppola et al. 1998b; Liu and Pettigrew 2003; Wang et al. 2003; Yu and Shou 2000). Figure 2 also shows the orientation distributions separately for simple cells (○) and complex cells (●). From the figure, it is clear that most of the anisotropy comes from simple cells. Complex cells are distributed more or less equally across all orientations (P = 0.584, χ^2 test). This is consistent with previous results, which indicate that the oblique effect, in terms of orientation distribution, is limited to simple cells (Nelson et al. 1977; Orban and Kennedy 1981; Pettigrew et al. 1968). Nevertheless, the effect is still evident when analyzing simple and complex cells together. This result is consistent with VEP measurements, optical imaging, and fMRI studies that show an effect when pooling over large populations of cells (Arakawa et al. 2000; Bonds 1982; Campbell and Kulikowski 1966; Chapman and Bonhoeffer 1998; Coppola et al. 1998b; Frost and Kaminer 1975; Furmanski and Engel 2000; Liu and Pettigrew 2003; Mansfield and Ronner 1978; Moskowitz and Sokol 1985; Sokol et al. 1987; Wang et al. 2003; Yu and Shou 2000).

Because VEP and imaging techniques are presumably not only sensitive to numbers of neurons but also to the level of neural activity, we performed an analysis on the response amplitudes at different orientations to determine if this is a contributing factor. This analysis was performed on the subset of cells recorded with gratings of 50% contrast (n = 1848) to avoid variations in response amplitude due to stimulus strength. Figure 3 plots the mean firing rate versus orientation for simple (○) and complex (●) cells. Complex cells tend to exhibit larger response rates than simple cells (mean of 22.8 vs. 11.5 spikes/s), but we observe no significant variation across orientation for either cell type. This result is consistent with previous reports from single-cell recordings in the cat (Rose and Blakemore 1974). This suggests that VEP and optical imaging studies reporting an oblique effect (Arakawa et al. 2000; Chapman and Bonhoeffer 1998; Coppola et al. 1998b; Frost and Kaminer 1975; Liu and Pettigrew 2003; Moskowitz and Sokol 1985; Wang et al. 2003; Yu and Shou 2000) are likely to be measuring differences in population sizes and not alterations in the response amplitudes of individual cells.

Heightened orientation selectivity and discrimination at horizontal and vertical orientations measured psychophysically in humans (Campbell and Kulikowski 1966; Furmanski and Engel 2000; Heeley et al. 1997; Maffei and Campbell 1970; Mustillo et al. 1988; Orban et al. 1984; Taylor 1963) and cats (Orban and Kennedy 1979; Parriss 1964; Vandenbussche and Orban 1983) might be accounted for, at least in part, by the predominance of cells tuned to these orientations. To determine if variations in the shape of orientation tuning curves are also involved, we analyzed the width (full width at half height) and maximum absolute slope of the curves as a function of orientation.

Figure 4 plots the mean tuning width for simple (○) and complex (●) cells as a function of preferred orientation. Overall, tuning widths are comparable to values from previous studies (e.g., Gizzi et al. 1990). Here we show that simple cells have significantly narrower tuning at horizontal compared with other orientations ($P < 0.00001$, F test). The mean tuning width for simple cells preferring horizontal is 28° compared with 35° for other orientations. Complex cells have wider tuning widths (mean = 40°) with insignificant narrowing at horizontal orientations (P = 0.179, F test). This finding supports the view that an unequal distribution of tuning widths plays a role in heightened orientation selectivity. As with the anisotropies in numbers of cells, tuning width anisotropies are limited to simple cells.

Heightened orientation discrimination at cardinal angles can also potentially arise from anisotropies in the shape of orientation tuning curves. The equivalent of orientation discrimination for a single cell is optimal at orientations where the slope of the orientation tuning curve is steepest (Bradley et al. 1987; Geisler and Albrecht 1997; Vogels and Orban 1990). We

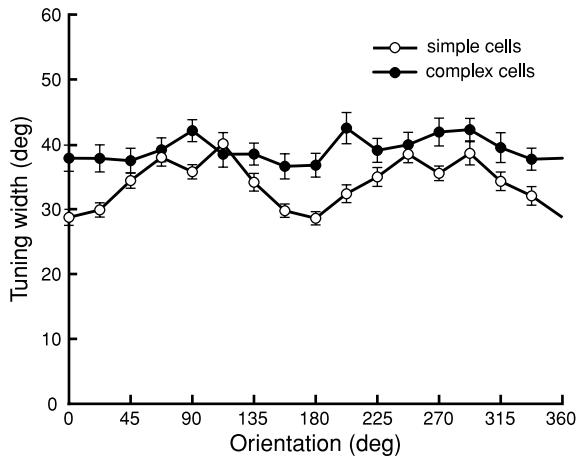

FIG. 4. Orientation tuning width as a function of preferred orientation. Simple cells (○) show a significant ($P < 0.00001$) narrowing of orientation tuning at horizontal orientations (0 and 180°). Complex cells (●) show no significant variations ($P > 0.1$).

calculate these orientations by finding the peaks in the absolute value of the derivative ($dG/d\theta$) of the Gaussian fits to the orientation tuning curves, $G(\theta)$. The distribution of orientations at which the steepest slope occurs (Fig. 5*A*) shows similar anisotropies to the distribution of preferred orientations (Fig. 2). A disproportionate number of cells exhibit a maximum slope at horizontal and vertical orientations ($P < 0.00000001$). This anisotropy is more prominent in simple cells (Fig. 5*A*, ○) than complex cells (●). Because the derivative of a Gaussian curve is characterized by two peaks, each cell is represented twice in Fig. 5. Figure 5*B* plots the mean absolute value of the peak slope as a function of orientation. On average, cells in the striate cortex exhibit a peak change in response of 0.91 spikes · s^{-1} · $°^{-1}$ change in stimulus orientation. Slopes tend to be steepest at horizontal orientations (1.04 spikes · s^{-1} · $°^{-1}$).

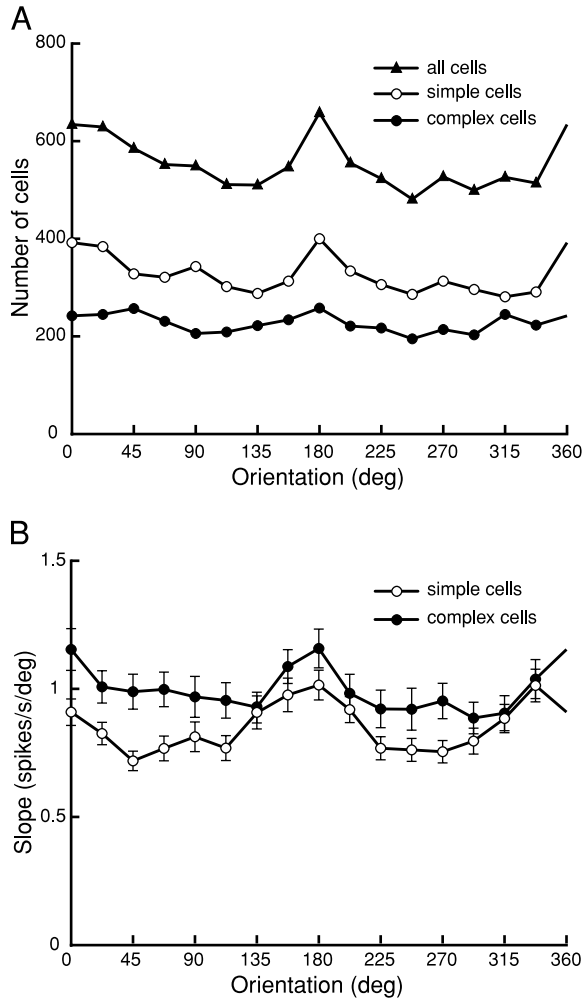

FIG. 5. Distribution of the peak slope of the orientation tuning curve (change in response per degree change in orientation). *A*: the numbers of cells exhibiting peak absolute slopes at different orientations. Because the derivative of a Gaussian curve is characterized by 2 peaks, each cell is represented twice. For simple cells (○), a significantly disproportionate number of cells exhibit the steepest part of their orientation tuning curve at horizontal orientations ($P < 0.0000001$). The anisotropy is also significant when considering simple and complex cells together (▲, $P < 0.0000001$) but not significant for complex cells alone (●, $P > 0.05$). *B*: slope of the orientation tuning curve as a function of the orientation producing the peek change in response per unit change in orientation. Both simple (○) and complex (○) cells show significantly ($P < 0.005$) steeper slopes at horizontal orientations (0 and 180°).

Simple and complex cells show similar distributions of slope values as a function of orientation.

Physiological and behavioral studies have suggested a variety of conditions under which the oblique effect is observed. Some indicate that the effect is limited to cells with RFs in the foveal region (De Valois et al. 1982; Mansfield 1974; Orban and Kennedy 1981; Wilson and Sherman 1976). Others suggest that only cells with small RF size (Leventhal and Hirsch 1977, 1978) or high spatial frequency preferences (Appelle 1972; Campbell and Kulikowski 1966; Kupersmith et al. 1984) are involved. Because all of our recordings are from a fairly circumscribed region around the area centralis, we are not able to analyze the effects of eccentricity. However, we are able to examine the effects of spatial frequency (SF). To do this, we sorted the simple and complex cells based on optimal SF, and categorized the top 25% and bottom 25% of each type as high and low SF cells, respectively. Figure 6*A* shows the distribution of preferred orientation for high SF simple cells (SF >0.593 cycles/°; $n = 637$). These cells exhibit the same distribution features as the overall population of simple cells with significant peaks at horizontal and vertical orientations ($P < 0.005$, χ^2 test). The orientation distribution for low SF simple cells (Fig. 6*B;* SF <0.25 cycles/°; $n = 637$) doesn't exhibit statistically significant structure ($P > 0.05$, χ^2 test). Neither high (Fig. 6*C;* SF >0.65 cycles/°, $n = 512$) nor low (Fig. 6*D;* SF <0.268 cycles/°, $n = 511$) SF complex cells show significant variations from a flat distribution with Poisson variance ($P > 0.05$, χ^2 test).

The narrower selectivity for horizontal orientations is also most pronounced for high SF simple cells. Figure 7*A* shows tuning width distributions for high (—) and low (- - -) SF simple cells. Only the high SF simple cells show significantly narrower tuning at 0 and 180° ($P < 0.0001$, *F* test). Low SF simple cells (Fig. 7*A*, - - -) and complex cells (Fig. 7*B*) don't show significant narrowing ($P > 0.2$, *F* test). Another relevant measurement is the slope of the orientation tuning curve. Analysis of this parameter shows that only cells tuned to high SF exhibit significant anisotropies. This is most significant for simple cells (Fig. 8*A; P* < 0.02), but complex cells also exhibit this in a significant way (Fig. 8*B; P* < 0.05). These findings demonstrate that within the central visual field, the oblique effect is limited to high SF.

To further characterize these orientation anisotropies, we analyzed the linear 2D RF maps for 104 simple cells. These cells all had preferred spatial frequencies >0.25 cycles/° and display the same anisotropies as the larger population, as shown in Fig. 9. The top bar plot (Fig. 9*A*) shows the numbers of cells tuned to horizontal, vertical and the two oblique orientations. The distribution is similar to the larger population with a disproportionate number of cells preferring horizontal and vertical compared with oblique ($P < 0.003$, *Z* test). Here we used coarser binning due to the smaller sample size (45 vs. 22.5°). Because the larger population of simple cells reveals no directional asymmetries, the forward and reverse directions are combined. For example, the horizontal category is comprised of both 0 and 180° orientations. Figure 9*B* shows the orientation tuning width for horizontal, vertical, and oblique orientations measured using drifting gratings. Here the two oblique orientations are combined into one group because of limited numbers. As is the case in the larger population, cells prefer-

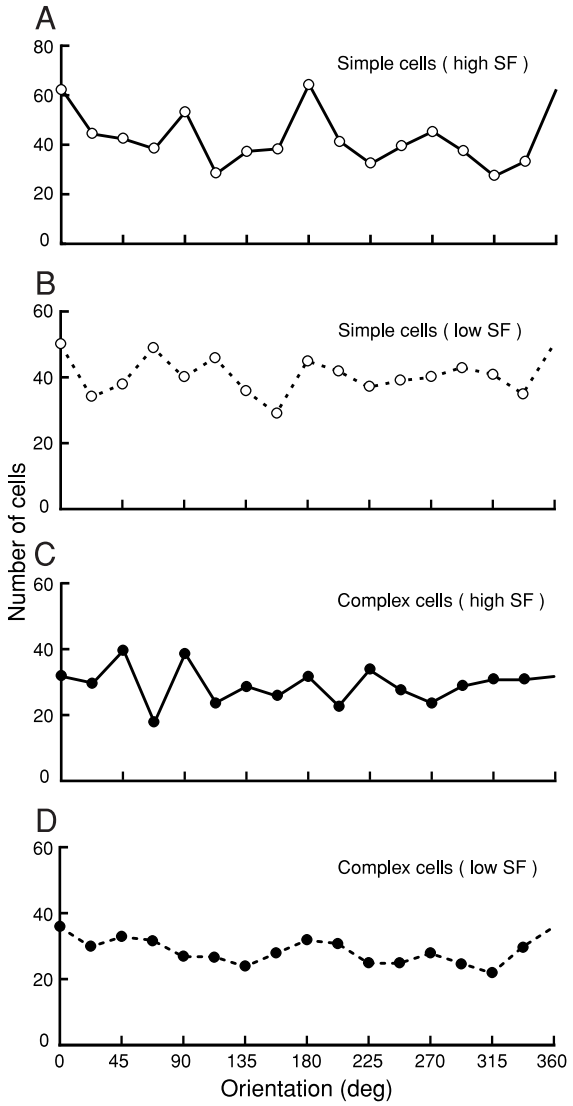

FIG. 6. Distribution of preferred orientation for cells tuned to high and low spatial frequency (SF). *A*: the number of cells is plotted as a function of preferred orientation for high SF simple cells. Significant peaks ($P = 0.0002$ χ^2 test) in the numbers of cells are observed at horizontal and vertical orientations. Low SF simple cells (*B*) don't show significant variations ($P = 0.71$, χ^2 test). For complex cells, neither high SF (*C*, $P = 0.31$, χ^2 test) nor low SF (*D*, $P = 0.94$, χ^2 test) tuned cells show significant variations with preferred orientation.

ring horizontal orientations have significantly narrower tuning widths ($P < 0.05$, F test). In this analysis, oblique tuning widths are slightly narrower than those for vertical orientations, but the difference is not significant [$P > 0.3$, Tukey test (Hochberg and Tamhane 1987)].

We performed a temporal analysis on this subset of cells with measured space-time RFs to address psychophysical (Essock 1980; Olson and Attneave 1970) and VEP (Essock 1980; Moskowitz and Sokol 1985; Olson and Attneave 1970; Skrandies 1984; Sokol et al. 1987) reports of longer response latencies at oblique compared with horizontal and vertical orientations. Response latency was determined by measuring the time delay of the maximum response in the cell's spatial-temporal RF. Mean peak response latencies for cells preferring horizontal, vertical and oblique orientations are shown in Fig. 10. No significant differences in latency are observed for these orientations ($P = 0.6$, F test).

We performed a spatial analysis on the RFs to explore the relative roles of linear and nonlinear mechanisms in shaping the narrower orientation tuning width at horizontal orientations. The orientation tuning characteristics of simple cells have been shown to be a result of both linear and nonlinear mechanisms. A widely used model consists of a linear filter followed by a static expansive nonlinearity (Albrecht and Geisler 1991; Anzai et al. 1999; DeAngelis et al. 1993a; Heeger 1992; Movshon et al. 1978; Tolhurst and Dean 1987). The linear filter is composed mainly of feed-forward LGN connections (Jagadeesh et al. 1997; Reid and Alonso 1995) but is also shaped by cortical circuitry (Ferster 1988; Pollen and Ronner 1982; Troyer et al. 1998). The expansive nonlinearity is assumed to be solely a result of cortical factors such as spiking mechanisms and intercellular circuits. It has been shown (Gardner et al. 1999; Volgushev et al. 1996) that nonlinear mechanisms play a major roll in sharpening the orientation tuning of simple cells. Here, we ask if the narrower tuning at

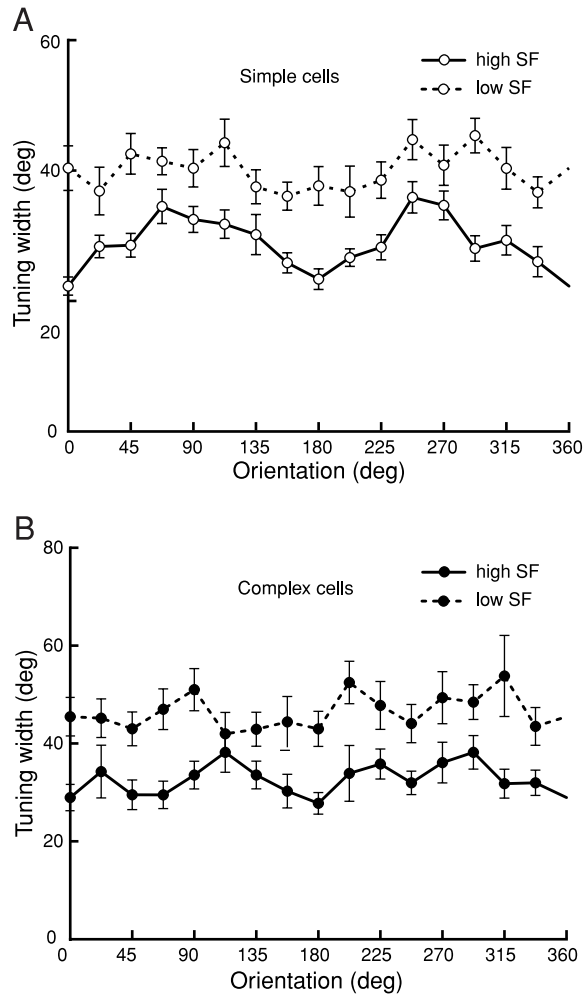

FIG. 7. Orientation tuning width asymmetries for cells tuned to high and low SF. *A*: simple cells tuned to horizontal and vertical show significantly ($P < 0.0000001$, F test) narrower tuning widths at high spatial frequencies (—) but not low spatial frequencies (- - -, $P = 0.2$, F test). *B*: neither high (—, $P = 0.37$, F test) nor low (- - -, $P = 0.87$, F test) complex cells exhibit significant variations in tuning width.

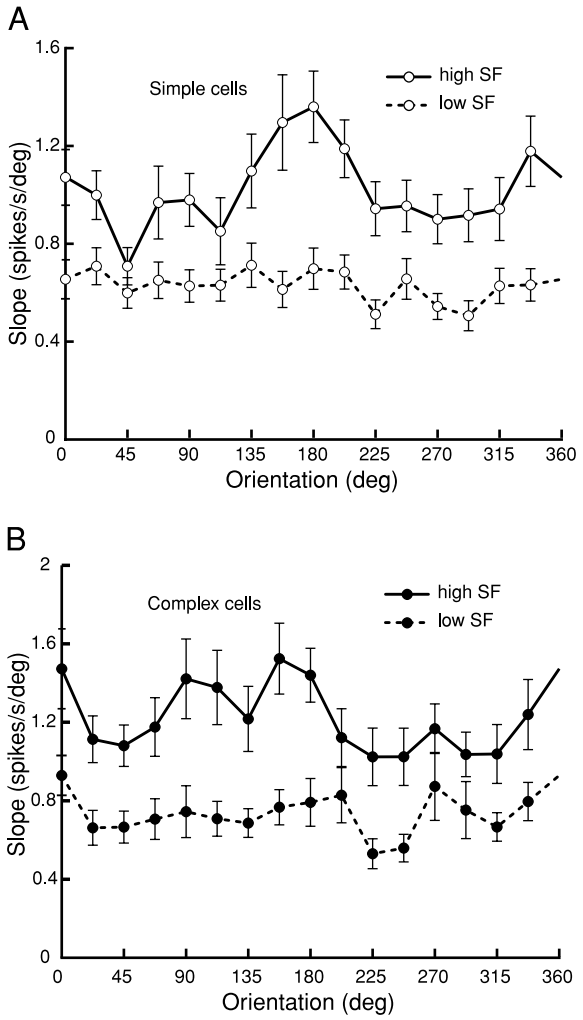

FIG. 8. Peak slope asymmetries for cells tuned to high and low SF. *A*: simple cells tuned to horizontal show significantly steeper peak orientation tuning slopes at high SF (—, $P < 0.05$, *F* test) but not at low SF (- - -, $P > 0.5$, *F* test). *B*: like simple cells, complex cells tuned to horizontal also show significantly steeper peak slopes at high SF (—, $P < 0.05$, *F* test) but not at low SF (- - -, $P > 0.05$, *F* test).

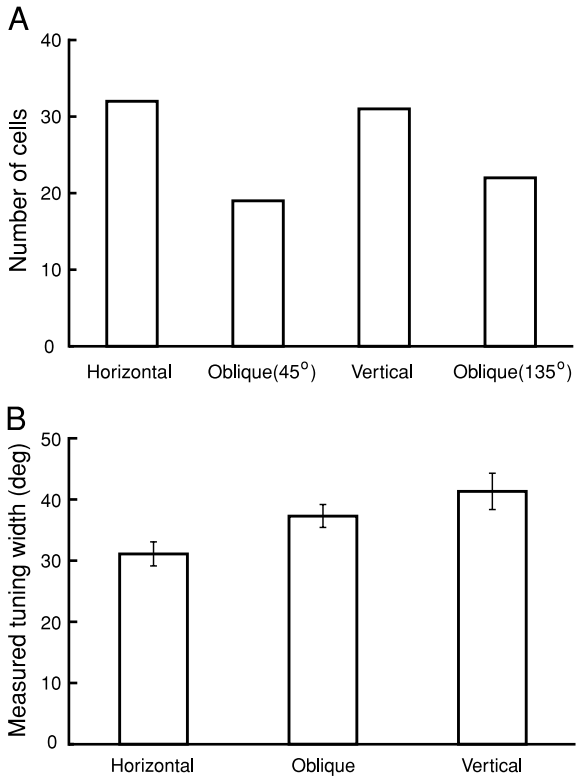

FIG. 9. Preferred orientation (*A*) and tuning width (*B*) anisotropies for the 104 medium to high SF simple cells for which there are 2D RF data. *A*: this subpopulation has the same distribution as the larger population of high SF simple cells with increased numbers of cells tuned to horizontal and vertical. The numbers of cells preferring horizontal, vertical, and 2 the oblique orientations are 32, 31, 19, and 22 respectively. *B*: compared with vertical and oblique orientations, cells tuned to horizontal orientation show sharper tuning widths ($P = 0.011$, *F* test).

horizontal orientations exhibited by simple cells is the result of linear or nonlinear mechanisms.

An example analysis is shown in Fig. 11. Figure 11*A* shows the measured 2D spatial RF at optimal correlation delay for a cell tuned near horizontal (−18°). We fit the frequency domain of this RF with two 2D Gaussian functions (Fig. 11*B*). We extracted points from the frequency domain fit as shown by the semicircle in Fig. 11*B*, and the resulting function is plotted in Fig. 11*C*. This was then fit by a Gaussian curve to obtain the predicted tuning width. Figure 11*D* shows the tuning curve measured using drifting gratings (—) and the Gaussian fit (- - -). For this cell, the predicted tuning width is ~22% wider than the measured tuning width (42.5 vs. 34.7°). This difference is within the range found in our previous study (Gardner et al. 1999).

The predicted tuning widths for all 104 cells are summarized in Fig. 12. In Fig. 12*A*, the mean ± SE are plotted for the same horizontal, vertical, and oblique groups used in Fig. 9*B*. This figure indicates that the predicted tuning widths from the linear RFs are equal for all orientations ($P > 0.3$) and thus do not show the oblique anisotropies exhibited by tuning widths measured with drifting gratings (Fig. 9*B*). Figure 12*B* shows a scatter plot comparing predicted and measured tuning widths for each cell. Cells with horizontal, vertical, and oblique orientation preferences are plotted with ○, ×, and ●, respectively. Most cells fall below the diagonal line of slope 1. Cells preferring horizontal orientations (○) have clusters farthest below the line. The ratio between the predicted and measured tuning widths is an estimate of the exponent of the expansive nonlinearity exhibited at the output stage of simple cells (Gardner et al. 1999). The distribution of exponents estimated from our analysis is plotted in Fig. 13. The average exponent for all

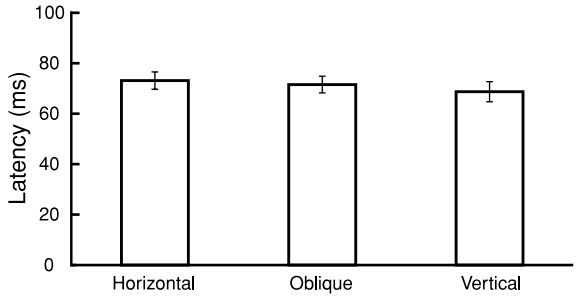

FIG. 10. Latency to peak measured for 104 simple cells. Response latencies show no significant variations with preferred orientation. The mean latencies for horizontal, oblique, and vertical orientations are 73.1, 71.5, and 68.7 ms, respectively. The latencies do not vary significantly across these orientations ($P > 0.5$, *F* test).

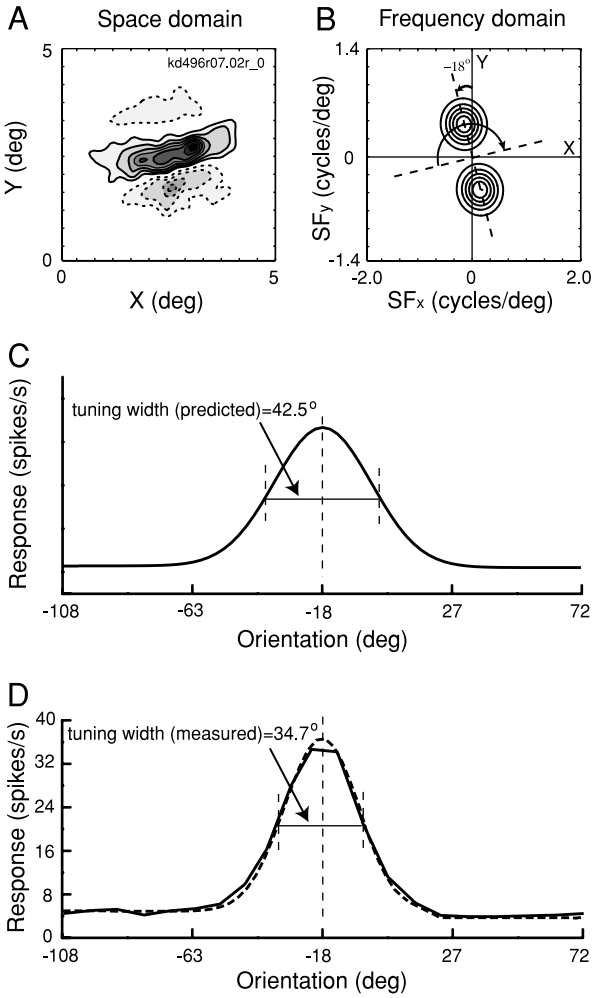

FIG. 11. Example of linear/nonlinear spatial analysis for a single cell. *A*: a contour plot of the 2D spatial RF. *B*: the frequency domain of the RF fit with a pair of 2D Gaussian functions. *C*: the orientation tuning curve predicted from the linear 2D RF. *D*: the orientation tuning curve measured using drifting gratings.

cells (geometric mean) is 2.17, which indicates a value approximated by a squaring nonlinearity. Cells preferring horizontal orientations (Fig. 13*A*) have a mean exponent of 3.17, which is significantly higher ($P < 0.01$, F test) than for vertical and oblique orientations (1.85 and 1.72, respectively). This suggests that the narrower tuning widths of cells preferring horizontal is the result of a larger expansive nonlinearity and thus cannot be accounted for by linear processes such as the feedforward connections from LGN to visual cortex. In other words, the neural origin of the oblique effect is likely to be based primarily on differences in intracortical connections.

DISCUSSION

Behaviorally, the oblique effect is robust and has been demonstrated in human subjects using a wide variety of experimental methodologies. Physiological investigations of the effect have not been as consistent. It is possible that a central problem with studies in which single cell populations are evaluated is sample size. Most results have been obtained from datasets with <100 cells. Some of the studies that have reported no differences in the numbers of cells tuned to different orientations actually show strong trends. However, because of limited cell counts, differences fall within sampling error. For instance, Rose and Blakemore (1974) reported that "there is no clear tendency for one major axis to be represented by a greater number of cells in the visual cortex." However, examination of their data shows clearly that twice as many simple cells were tuned to horizontal than to vertical or diagonal. This didn't reach statistical significance because they only recorded from 39 simple cells. Other studies found similarly strong trends that didn't reach statistical significance due to limited sample sizes (De Valois et al. 1982; Finlay et al. 1976; Noda et al. 1970).

A second reason why some physiological studies may have failed to observe significant anisotropies is that they didn't analyze separately different classes of cells. Our data show that only simple cells tuned to relatively high spatial frequencies exhibit significant meridional variations in cell count and tuning width. Several studies that observed orientation based

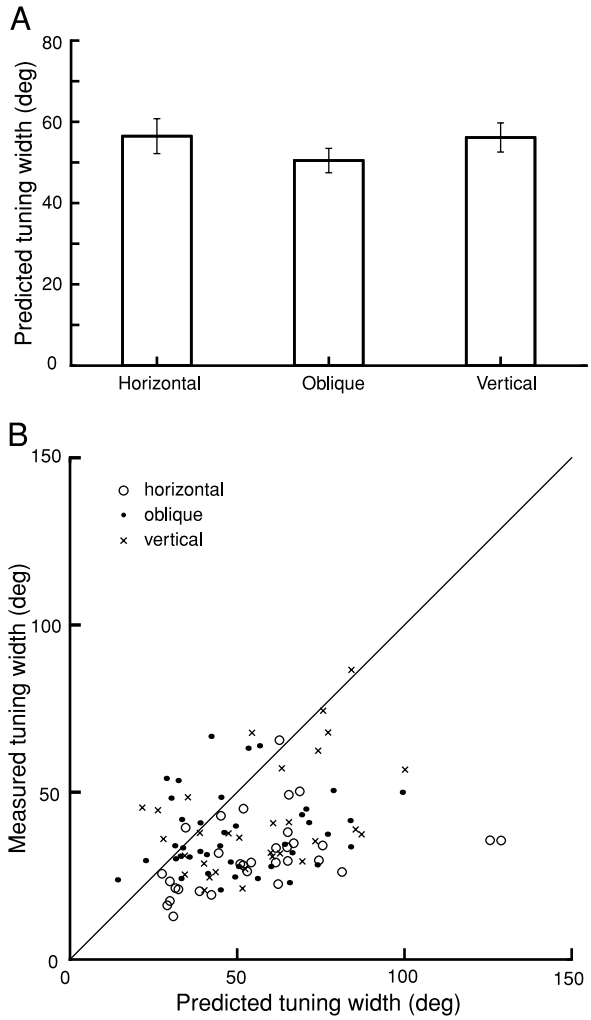

FIG. 12. Summary figure of predicted orientation tuning width data. *A*: the predicted orientation tuning widths calculated from the linear 2D RF of simple cells do not show the same narrowing at horizontal as seen when measured with drifting gratings. The mean tuning width of horizontal, oblique and vertical are 56.5, 50.5, and 56.1, respectively. *B*: a scatter plot of predicted vs. measured orientation tuning widths for cells preferring horizontal (○), vertical (×), and oblique (●) orientations. Cells falling on the diagonal line have the same measured and predicted tuning widths. Cells, especially those preferring horizontal orientations, tend to be below the line indicating a more narrow measured tuning width than that predicted from the linear RF.

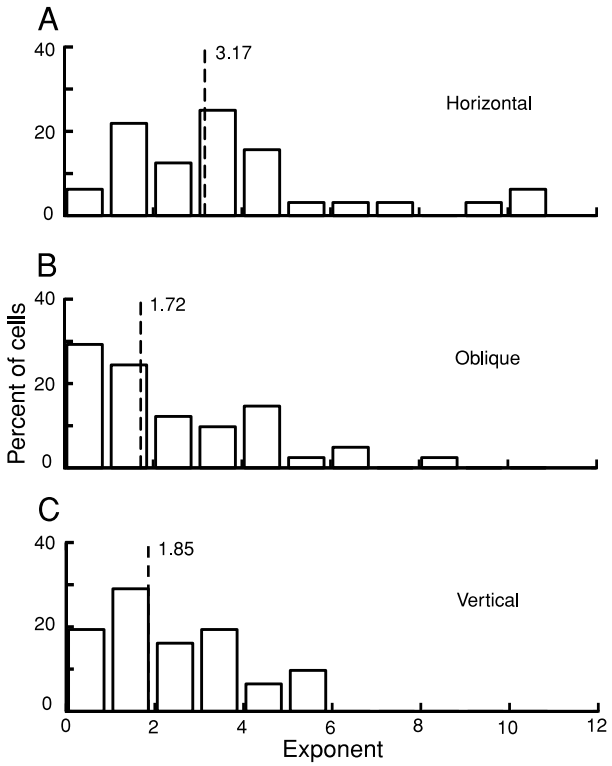

FIG. 13. Distribution of estimated exponents for simple cells preferring horizontal (*A*), oblique (*B*), and vertical (*C*) orientations. - - -, geometric mean values. The exponents for cells preferring oblique and vertical have mean values near 2, approximating a squaring output nonlinearity. The mean exponent values for cells preferring horizontal are significantly greater ($P = 0.0067$, *F* test), near 3, indicating that nonlinear mechanisms play a larger role in sharpening the tuning curves at horizontal orientations.

effects provided separate analyses for simple and complex cells (Kennedy and Orban 1979; Nelson et al. 1977; Orban and Kennedy 1981; Pettigrew et al. 1968; Rose and Blakemore 1974) or for foveal versus parafoveal cells (Mansfield 1974) or for small versus large RF sizes (Leventhal and Hirsch 1977; Payne and Berman 1983). Many of the studies that did not show an effect didn't differentiate between simple and complex cells or between high and low spatial frequency preference (Campbell et al. 1968; Henry et al. 1974; Wilson and Sherman 1976).

A third factor in previous examinations of meridional anisotropies is the broad definition of cardinal and oblique angles. For example, many studies do not differentiate between vertical and horizontal orientations. The early behavioral oblique effect studies proposed that the visual system processes both horizontal and vertical with a higher sensitivity than oblique. But our current results indicate that there is a strong bias for mainly horizontal orientations for which cells are both more numerous and more narrowly tuned. Cells preferring vertical orientations have similar tuning widths as those preferring oblique angles. Some studies that failed to show variations in tuning width, grouped vertical and horizontal data together (Finlay et al. 1976; Mansfield 1974), and this could have averaged out the effects seen exclusively at horizontal orientations. Furthermore, most studies used 45–90° bin sizes for categorizing orientations. The data reported here (using 22.5° bins) indicate that the magnitude of the oblique effect already begins to decline by 11.25° away from cardinal and oblique angles.

The finding that orientation anisotropy is mostly a horizontal effect is somewhat surprising. Contours of vertical orientations are used to process horizontal disparity and this may be expected to be finely tuned to assist in stereopsis. However, some previous results are compatible with those we present here. Mustillo et al. (1988) reported that orientation discrimination thresholds in humans are significantly lower for horizontal than for all other orientations including vertical. This effect applies to both crossed and uncrossed disparities. Orban et al. (1984) and Vandenbussche et al. (1986) also noted that orientation discrimination in humans is significantly better at horizontal than at other orientations. Heeley and Buchanan-Smith (1990) demonstrated that human orientation detection thresholds are significantly lower for horizontal than vertical. Spatial resolution (Coletta et al. 1993) and contrast sensitivity (Mitchell et al. 1967) are also reportedly better at horizontal orientations. In terms of the distributions of preferred orientations, the literature also suggests a higher proportion of cells tuned to horizontal than vertical. Leventhal and Hirsch (1980) reported that cells with small RF sizes in area 17 of the cat had a disproportional preference for horizontal and vertical orientations. But examination of their summary figure (Fig. 11*A*) shows clearly that most of this bias is toward horizontal orientations. They found ~25% more cells tuned to horizontal than to vertical, which appears to be significant ($P < 0.05$, *Z* test). Optical imaging measurements from the primary visual cortex of the cat (Liu and Pettigrew 2003; Yu and Shou 2000) and the ferret (Chapman and Bonhoeffer 1998; Coppola et al. 1998b) reveal that a larger area of cortical surface responds to horizontal compared with vertical. fMRI recordings in humans also show greater discrimination at horizontal than at vertical or oblique (Furmanski and Engel 2000).

The functional reason for superior visual performance at horizontal orientations is not clear. It could possibly play a role in postural stability relative to the horizon, but we know of no behavioral evidence for this. There is evidence that the orientation preference of cells in the visual cortex can be influenced by the visual environment. In humans, it is clear that uncorrected astigmatism can result in lasting meridional amblyopia (Freeman 1975; Freeman et al. 1972; Mitchell et al. 1973). Cats reared with visual stimuli of only one orientation tend to have cortical orientation preferences of the same orientation (Blakemore and Cooper 1970; Freeman and Pettigrew 1973; Hirsch and Spinelli 1970; Muir and Mitchell 1973). However, neurons selective to horizontal and vertical orientations tend to be less affected by environmental factors than oblique (Freeman and Pettigrew 1973; Leventhal and Hirsch 1975). And because an oblique effect is also found in the early development periods of kittens (Fregnac and Imbert 1978), ferrets (Chapman and Bonhoeffer 1998), and dark-reared animals (Leventhal and Hirsch 1980), it is unlikely that the oblique effect measured in adults is solely the result of the disproportionate energy distribution at the cardinal orientations characteristic of natural and "carpentered" scenes (Annis and Frost 1973; Coppola et al. 1998a; Keil and Cristobal 2000; Switkes et al. 1978; Timney and Muir 1976).

An important step in explaining the origin and implications of the oblique effect is determining where in the visual system the anisotropies are formed. The evidence is clear that neither

the optics of the eye nor the retina's photoreceptor mosaic contribute to the oblique effect (Campbell and Kulikowski 1966; Maffei and Campbell 1970; Mitchell et al. 1967). Eye movements have also been shown to make no contribution (Higgins and Stultz 1950; Nachmias 1960). This indicates that the oblique effect originates within the visual cortex or as a result of feedforward LGN connections or both. There is anatomical evidence suggesting that the unequal distribution of preferred orientations in V1 results from anisotropies in the retino-cortical projections (Colonnier 1964; Young 1960). However, the narrower orientation tuning at horizontal orientations might be shaped through intracortical mechanisms. A study of the small orientation biases in the cat LGN has reported a preference for horizontal, and to a lesser extent vertical orientations (Vidyasagar and Urbas 1982). The effect remains even after lesioning areas 17 and 18. The report suggests that the biases of LGN neurons might explain the higher selectivity for horizontal and vertical orientations found in V1. Our current findings suggest that this is not the case. The tuning curves predicted from the linear 2D RFs of simple cells cannot account for the observed sharpening of tuning at horizontal orientations. The data reported here indicate that cells preferring horizontal orientations exhibit superior selectivity due to a larger expansive nonlinearity. This strongly suggests nonlinear intracortical mechanisms rather than linear feedforward factors from LGN.

The finding that meridional anisotropies are found only in V1 simple cells but not complex cells has some interesting implications for the classical model of hierarchical visual processing where simple cells feed into complex cells which in turn supply the input to higher stages of the visual system (Hubel and Wiesel 1962, 1968). The clear implication is that a substantial proportion of simple cells must have direct input to a population of neurons in higher centers. It implies that all simple cells don't feed into complex cells in a manner that preserves the distribution of simple cell tuning characteristics. Furthermore, if perceptual measurements of the oblique effect are indeed the result of unequal distributions of orientation preference and selectivity, then the output of simple cells might comprise a substantial proportion of the input to visual processing areas mediating perception.

There have been different reports about the spatial conditions under which the oblique effect is observed. It has been suggested that the effect is primarily in the foveal region, and not found in the periphery (Berkley et al. 1975; Zoli 1973), and there is physiological support for this (Kennedy and Orban 1979; Mansfield 1974; Orban and Kennedy 1981). Leventhal and Hirsch (1977) suggested that the effect is only found for cells with small receptive fields. DeValois et al. (1982) hypothesized that the differentiating factor is spatial frequency. The data presented here are consistent with the spatial frequency hypothesis. In our data set, only cells with relatively high spatial frequency tuning are found to exhibit orientation anisotropies. Because all of our cells were recorded from within the region around the area centralis representation (central 15°), it is clear that spatial frequency plays a significant role in limiting the oblique effect. This is consistent with psychophysical (Coletta et al. 1993; Pointer 1996; Westheimer 2003) and physiological (Kalia and Whitteridge 1973; Wilson and Sherman 1976) evidence that the oblique effect exists in the periphery at relatively high spatial frequencies and is absent in the fovea at low spatial frequencies (Campbell and Kulikowski 1966). This, of course, doesn't rule out effects of eccentricity on the oblique effect (Rovamo et al. 1982; Westheimer 2003).

The unequal distribution of preferred orientations in V1 can account, at least qualitatively, for many of the perceptual phenomena that make up the oblique effect. The classical effect is that spatial acuity is higher at horizontal and vertical orientations (Appelle 1972; Campbell and Kulikowski 1966). This agrees with the finding that there is a disproportionate number of cells tuned to horizontal and vertical at high spatial frequencies. Simple mathematical models of population coding predict that the observed unequal distribution of preferred orientation can account for heightened sensitivity, selectivity, and detection at cardinal orientations (Green and Swets 1966; Peterson et al. 1954; Zhang and Sejnowski 1999). These heightened characteristics can also be observed in the properties of single neurons. This is particularly true at horizontal orientations where cells tend to be more narrowly tuned and have steeper orientation response slopes. Furthermore, contrast sensitivity data replotted from Anzai et al. (1995) in terms of preferred orientation (Fig. 14) indicate that cells preferring horizontal and vertical have lower contrast thresholds than cells preferring oblique angles.

The steeper slopes in the orientation tuning curves found at horizontal angles can partially explain the superior orientation discrimination found behaviorally at the cardinal orientations. However, our data predict better performance only at horizontal orientations. Although some studies do report that human horizontal discrimination is superior to vertical (Mustillo et al. 1988; Orban et al. 1984; Vandenbussche et al. 1986), others indicate that vertical is better than oblique (Campbell and Kulikowski 1966; Heeley et al. 1997; Sokol et al. 1987). Our results indicate that there is no significant difference in the peak slopes of orientation tuning curves centered at vertical and oblique orientations. Perhaps the larger number of cells with peak tuning slopes at vertical orientations compared with oblique can account for the differences in psychophysically measured discrimination performance.

The observed physiological characteristics of V1 are also quantitatively in good agreement with psychophysical measurements of the oblique effect. Orientation selectivity measured in humans is between 17 and 25% broader at oblique compared with cardinal orientations (Blake and Holopigian 1985; Campbell and Kulikowski 1966). The data presented

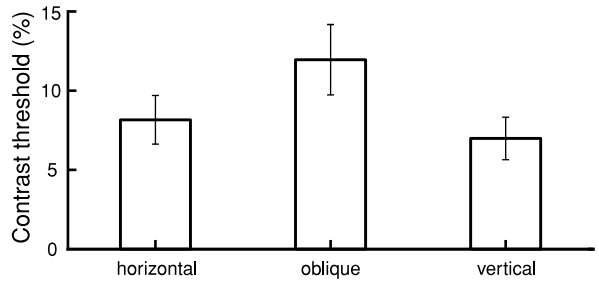

FIG. 14. Contrast threshold data from 55 simple cells replotted with permission from Anzai et al. (1995) to show the differences in contrast threshold for cells preferring horizontal, vertical, and oblique orientations. Simple cells tuned to horizontal and vertical orientations have lower contrast thresholds than those tuned to oblique orientations ($P < 0.05$). All cells had preferred spatial frequencies >0.25 cycles/°.

here show that cells preferring oblique orientations have a 17.8% broader tuning width compared with horizontal orientations (34.4° for oblique vs. 29.2° for oblique, Fig. 4). Similarly, orientation discrimination thresholds measured psychophysically in humans and cats is between 1.5 and 4 times as high at oblique compared with cardinal angles (Caelli et al. 1983; Heeley and Buchanan-Smith 1992; Mustillo et al. 1988; Orban et al. 1984; Vandenbussche and Orban 1983; Vandenbussche et al. 1986; Westheimer and Beard 1998). Assuming orientation discrimination threshold is inversely related to the slope of the orientation tuning curve, the present simple cell data predicts oblique discrimination thresholds 1.48 times as high as at horizontal orientations (Fig. 8*A*).

Reaction time is another measure of the oblique effect (Bauer et al. 1979; Essock 1980). While we observe no significant differences in response latencies, it is not clear that this would be expected. The reported reaction time difference for cardinal versus oblique orientations is ~200 ms (Essock 1980). The mean and SD of peak response latency found in the cat visual cortex at a luminance of 20 cd/m^2 is only 75 ± 24 ms (unpublished data). There isn't enough variance to account for 200 ms at least not in the cat. Furthermore, VEP measurements of cardinal and oblique response latencies in humans only find a difference of between 2 and 5 ms (Arakawa et al. 2000; Moskowitz and Sokol 1985; Skrandies 1984). It is difficult to resolve such small time differences in our data due to the limited number of measured RFs. However, what is known about the changes in reaction time with orientation suggests that there isn't a strong low-level physiological correlate. Unlike acuity, detection, and discrimination measurements, reaction time is sometimes categorized as a "class two" effect (Essock 1980). This is because reaction time measurements depend on the orientation of the head with respect to gravity (Attneave and Olson 1967), and the magnitude of the effect is greatly diminished with practice (Nakatani 1983). Other measurements, such as acuity, contrast sensitivity, and orientation discrimination, don't vary under these situations (Banks and Stolarz 1975; Corwin et al. 1977; Lennie 1974; Nakatani 1983).

Through a spatial analysis of the linear and nonlinear contributions to orientation tuning widths at different orientations, we conclude that the narrower orientation tuning of cells preferring horizontal orientations is the result of nonlinear intracortical factors rather than linear mechanisms, such as feedforward connections from LGN. We model the static output nonlinearity of simple cells as an exponent. Alternatively, the difference in tuning widths could potentially result from differences in spiking threshold. Higher spiking thresholds can result in narrower tuning through an iceberg effect. However, raised spiking thresholds would also be expected to result in lowered spontaneous firing rates. We don't find significant differences in spontaneous activity for simple cells tuned to horizontal orientations and high spatial frequencies (Fig. 15; $P > 0.2$). If anything, cells preferring horizontal orientations tend to have higher spontaneous firing rates. Thus spiking thresholds don't appear to be a contributing factor.

By analyzing a large population of cells, we have obtained a clear characterization of the orientation anisotropies found in the central representation of the primary visual cortex. We find a predominance of cells tuned to horizontal and vertical orientations. This is most evident for simple cells preferring relatively high spatial frequencies. Among this group, cells tuned to horizontal orientations are the most numerous and also the most selective. A linear/nonlinear analysis indicates that the narrowed tuning of such cells results from a greater expansive nonlinearity at the output stage of simple cells, and cannot be accounted for by the linear feedforward connections from LGN. This means that the narrower orientation tuning is due to intracortical mechanisms. The characterizations of neural anisotropies that we have found are generally in close agreement with measurements of perceptual anisotropies in humans.

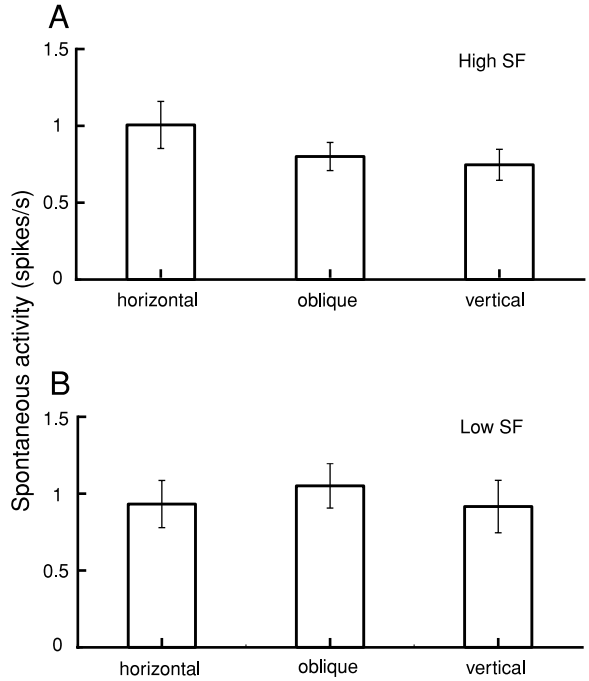

FIG. 15. Simple cells don't show significant variations in spontaneous activity as a function of preferred orientation. This is true for cells tuned to both high SF (*A*, $P = 0.28$, SF >0.593 cycles/°) and low SF (*B*, $P = 0.79$, SF <0.25 cycles/°).

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NOTE ADDED IN PROOF

A new study suggests an advantage for oblique stimuli when viewed in a naturalistic environment (Essock et al. 2003).

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