Visual Spatial Summation in Macaque Geniculocortical Afferents

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INTRODUCTION

Studies of modulation from beyond the “classical” excitatory receptive field in macaque primary visual cortex (V1) (Allman et al. 1985; Levitt and Lund 1997; Maffei and Fiorentini 1976; Nelson and Frost 1978; Polat et al. 1998; Sceniak et al. 1999, 2001, 2002) inspired renewed interest in the spatial extent of the excitatory receptive field in V1 (Cavanaugh et al. 2002a,b; Jones et al. 2001; Kapadia et al. 1999; Levitt and Lund 2002; Sceniak et al. 1999, 2001, 2002). In turn, these studies led to further investigations into the spatial extent of the excitatory receptive field and nonclassical surround suppression within the lateral geniculate nucleus of the thalamus (LGN) and its impact on cortical processing (Jones et al. 2000; Solomon et al. 2002).

The spatial properties of LGN excitatory receptive fields have been studied extensively (Derrington and Fuchs 1979; Hicks et al. 1983; Kaplan and Shapley 1982; Rodieck and Stone 1965; So and Shapley 1979). It is well known that, like retinal ganglion cells, LGN neurons display antagonistic center-surround receptive fields. It has been known for some time that stimulation of the region beyond the excitatory LGN receptive field can produce a suppressive effect (Hubel and Wiesel 1961; Levick et al. 1972; Singer and Creutzfeldt 1970). LGN suppressive surrounds have been studied in cat (Cleland et al. 1983; Jones et al. 2000; Murphy and Sillito 1987; Sillito et al. 1993; Vidyasagar 1984) and New World monkeys (Solomon et al. 2002). We report in this paper an analysis of spatial summation and surround suppression in geniculocortical afferents in pharmacologically inactivated macaque visual cortex and relate the findings to afferents’ anatomical origin in the LGN as parvocellular (P), magnocellular (M), or koniocellular (K) cells.

Within the LGN of macaques, there is spatial overlap in the anatomical organization of the P, M, and K neurons (Hendry and Reid 2000; Hendry and Yoshioka 1994). It is known that M and P cells project predominantly to V1 layers 4Ca and 4Cb, respectively (Blasdel and Lund 1983; Hendrickson et al. 1978; Hubel and Wiesel 1972). K cells are also known to project predominantly to superficial layers (Hendry and Reid 2000). However, the spatial overlap of neurons within the layers of the LGN makes it difficult to precisely correlate receptive field properties with cell type and cortical projections.

Recent evidence suggests that K cells project specifically to superficial layers, whereas M and P cells specifically project to layer 4C within V1 (Chatterjee and Callaway 2003). Therefore by studying the visual spatial summation of geniculocortical afferents within muscimol-inactivated cortex, and by locating the recording positions within the V1 layers, we were able to characterize the visual spatial properties of the M, P, and K pathways. Previous reports of the spatial properties of LGN receptive fields in simian (Solomon et al. 1999) and prosimian primates (Irvin et al. 1993; Xu et al. 2001) suggested that there is overlap between K, M, and P cells. However, there has not been a systematic analysis of the macaque geniculocortical inputs that terminate directly within V1.

It has been shown that the spatial properties of primate V1 neurons are dependent on the stimulus contrast (Kapadia et al. 1999; Sceniak et al. 1999). Contrast-dependent area summation has been attributed largely to intracortical connections. Others reported contrast-dependent area summation in LGN and retinal responses (Kremers et al. 2001; Nolt et al. 2004; Solomon et al. 2002). Dissociating responses intrinsic to each stage of the visual processing stream is difficult in the intact system.
because there is substantial feedback from the primary visual cortex to the LGN (Felleman and Van Essen 1991; Murphy and Sillito 1987; Salin and Bullier 1995; Sherman and Guillery 1996; Sherman and Koch 1986; Van Horn et al. 2000). Therefore a major question of this study is whether visual spatial summation in geniculocortical afferents is dependent on the contrast of the visual stimulus.

By silencing the cortex, we were able to directly measure the response properties of the geniculocortical responses without the modulatory influences of corticogeniculate feedback. Using this approach, we found that excitatory spatial summation in the LGN input to the cortex is contrast invariant, as reported in the results. Like reports of others we find that there are substantial surround suppression signals originating in the LGN (Jones et al. 2000; Kremers et al. 2001; Nolt et al. 2004; Ozeki et al. 2004; Solomon et al. 2002; Webb et al. 2005) and these suppressive responses must be considered in models of cortical function.

METHODS

Standard electrophysiological recording techniques were used in acute preparation of macaque monkeys (Sceniak et al. 1999, 2001; Usrey et al. 2003). Extracellular action potentials were collected from isolated single geniculocortical afferent arborizations using extracellular microelectrodes. Spikes were analyzed both during experiments and off-line, using standard software packages and custom software written specifically for this purpose. Details of the procedures used in the experiments and the data analysis are given below.

Animal preparation

Acute experiments were performed on adult Old World monkeys (Macaca mulatta and Macaca radiata) in strict compliance with the guidelines for humane care and use of laboratory animals published by National Institutes of Health and PHS. All procedures conformed to the guidelines approved by The Salk Institute Animal Care and Use Committee and the details of the procedure are identical to those published by Chatterjee and Callaway (2002). A total of 11 animals were used for the study with about 12 isolated single units recorded per animal.

Briefly, each animal was initially tranquilized with ketamine, trepho-tomized, and placed in a stereotaxic apparatus. Geniculocortical afferents were recorded extracellularly in the primary visual cortex of anesthetized (sufentanil citrate: 6–12 μg · kg⁻¹ · h⁻¹) and paralyzed (pancuronium bromide: 0.1–0.2 mg · kg⁻¹ · h⁻¹) adult macaque monkeys. The monkey’s eyes were protected with clear plastic contact lenses. The fovea was visualized with an ophthalmoscope to determine its projection to the stimulus screen. The receptive fields of the recorded afferents were within 5° of the fovea, as expected from the locations of recording sites on the opercular cortical surface.

Cortical activity was eliminated through superfusion of a large region of cortex posterior to the lunate sulcus (about 8 × 5 mm) with the γ-aminobutyric acid type A (GABA_A) agonist muscimol (50 mM, Sigma–Aldrich, St. Louis, MO). After removing the dura, we placed Gelfoam on the pial surface with an opening for recording electrodes in the center of the Gelfoam. Tubing that delivered the muscimol solution (50 mM in 0.9% sterile saline, 0.1–0.2 mL/h) was secured near the skull opening with bone wax to allow it to drain into the Gelfoam. After electrode insertion, the opening and Gelfoam were covered with agar to seal the brain.

Inactivation of the cortex was verified by recording extracellularly in the primary visual cortex before to application of muscimol and determining that the neuronal responses diminished after the application of muscimol (about 1 h after initiation). The electrode was then advanced until visually evoked neuronal activity was detected. Afferent action potentials could be distinguished based on their characteristic small amplitude and short spike duration (methods described in detail by Chapman et al. 1991).

Extracellular recording and histology

Action potentials were recorded extracellularly using tungsten microelectrodes (tips 5–15 μm). The amplified extracellular signal was input into an A/D converter in an SGI O2 computer. Single units were discriminated on the SGI computer using custom window-discrimination software designed specifically for this task. Strict criteria for single-unit recording included fixed shape of the action potential and the absence of spikes during the absolute refractory period. Small electrolytic lesions (2–3 μA for 2–3 s) were made along the length of each penetration.

After each experiment animals were killed (Nembutal) and perfused through the heart (0.9% saline followed by 4% paraformaldehyde 10 and 20% sucrose) to allow for a histological reconstruction of the electrode-recording track. After blocking and cutting the fixed cortical tissue, thin sections (50 μm) were stained for cytochrome oxidase and counterstained with thionin (Chatterjee and Callaway 2002).

Visual stimulation

The visual stimuli were generated on a Silicon Graphics O2 computer and displayed on a Sony color monitor operating at 100-Hz frame refresh and 600 × 800-pixel resolution. The mean luminance of the display was 56 cd/m². The screen measured 24 × 34 cm (height × width) and was placed at a viewing distance of 100 cm (covering 14 × 19° of visual angle, respectively). Responses to afferent inputs were measured by stimulating visually with drifting sine-wave gratings. Each drifting sine-wave grating patch was presented on a gray background (56 cd/m² mean luminance with screen size) for 4 s with an interstimulus interval of 4 s. The interstimulus blank period was used to determine the spontaneous firing rate.

Optimal drifting sinusoidal gratings

Each cell was stimulated monocularly through the dominant eye with the nondo maninant eye occluded. Corrective lenses were used and obtained the optimal optical correction by isolating an initial unit and listening for the response to a series of gratings of increasing spatial frequency, as different corrective lenses were placed in front of the eye. Receptive fields were located at eccentricities between 2 and 5°.

Initially, the approximate location of the center of each receptive field was found by using a mapping stimulus, a small (0.2° diameter) circular grating patch (mean luminance 53–56 cd/m²). The grating patch was systematically moved around the computer screen under mouse control until a maximal firing rate was heard from an audio monitor. Once the receptive field was located, the spatial frequency and temporal frequency were varied under mouse control to elicit a maximal response.

Next, spatial frequency, temporal frequency, and contrast response were measured under computer control with drifting sine-wave gratings (square apertures, 4 × 4° of visual angle) positioned at the locations estimated from hand mapping. All parameters were optimized over a complete range of responsiveness. If no clear peak response was observed in plotted results, the temporal frequency or spatial frequency-tuning curves were repeated using a greater range of values. These optimal values for spatial frequency and temporal frequency were used in subsequent characterizations. The sine-wave grating orientation was fixed throughout and randomly chosen across cells.

After determining the optimal grating spatial and temporal frequency, the center of the receptive field was confirmed. This was done...
with the tuning-curve–optimized values for spatial and temporal frequency using the 0.2° test grating (circular aperture with drifting sine wave) under mouse control. Small perturbations in location were tested to determine whether the center position produced a maximal response based on the audio monitor. The size of the test patch was also either increased or decreased to confirm these values for center position.

Responses to cone-isolating stimuli were also collected to identify achromatic, blue-yellow cone-opponent, and red-green opponent neurons. Cone-isolating stimuli were modulations around the white point, which was the same as for achromatic stimuli discussed above. Drifting sine-wave grating patches (1–4° square aperture) were presented for each cone-isolating color map (l-cone, m-cone, and s-cone). Each cone-isolating stimulus was presented 10 times at the spatial frequency and temporal frequency optimized from the achromatic stimuli described above. Cone-isolating stimuli were presented at the maximum cone contrast achievable with our monitor (13, 15, and 24% for L-, M-, and S-cone isolating stimuli, respectively). Cone-isolating stimuli were modulations around the white point, which was the same as for achromatic stimuli discussed above. Cone-isolating stimuli were presented at the maximum cone contrast achievable with our monitor (13, 15, and 24% for L-, M-, and S-cone isolating stimuli, respectively). Responses were measured as either the first harmonic amplitude and phase of the cell’s response to a drifting sine-wave grating stimulus or the mean response amplitude.

A contrast response function was obtained for each neuron. Ten different luminance contrasts were tested ranging from 2 to 99% in logarithmic steps. Stimulus contrasts were tested in sequential order from low (2%) to high (99%) contrast with two repeats. This was done to avoid effects of hysteresis. Contrast was defined as: \( (L_{\text{max}} - L_{\text{min}})/(2L_{\text{mean}}) \).

**Spatial summation**

Circular patches of drifting sinusoidal gratings were presented, centered over the receptive field center. The patch sizes were presented in a random order. The radius ranged from 0.1 to 5° of visual angle in logarithmic steps. Each summation curve consisted of 10 radii with two repeats at each size. Stimulus centering was confirmed by determining whether there was a monotonic increase in response for suboptimal stimulus patch sizes.

This procedure was performed at two contrast levels. The contrast levels chosen were taken from the linear region of the contrast response function of each cell. Therefore the contrast levels were chosen based on the cell’s response. Low contrasts were chosen such that they were near the low end of the linear range of the contrast response function (20–50% of maximum response), but elicited responses that were significantly greater than the spontaneous firing rate (≥2 SDs). High contrasts were selected to elicit responses that were between 80 and 90% of the maximum response for each cell.

**Data analysis**

All spatial frequency-tuning responses and most area-summation tuning curves were analyzed using the first harmonic of the cell’s response to the drifting sine-wave gratings. In cases where the mean response was greater than the first harmonic (20% of cells), the mean responses were used for analysis of the area-summation experiment.

Each summation curve was fitted using the following empirical function

\[
R(s) = R_0 + K_c \int \int e^{-i\theta}drd\theta - K_i \int \int e^{-i\theta}drd\theta
\]

Here, \( R_0 \) is the spontaneous rate and each integral represents the relative contribution from excitatory and inhibitory components, respectively. Values of the excitatory gain \( K_c \), the excitatory space constant \( a \), the inhibitory gain \( K_i \), and the inhibitory space constant \( b \) were optimized to provide the best MSE (mean squared error) fit to the data. Excitatory space constant measures are taken as the parameter \( a \) from the fitted curves. A suppression index (SI) measure was also estimated from the fitted curves. This measure is the ratio of the area under the inhibitory Gaussian divided by that of the excitatory Gaussian (SI = \( K_i / K_c a \)). The ratio of the area under the two components captures the strength of excitation and suppression by including the spatial spread as well as the gain, unlike the ratio of peak to minimum response, which compares only the response gain.

Spatial frequency response functions were fitted with a difference-of-Gaussians (DOG) model (Rodieck and Stone 1965) of the following form

\[
R = R_0 + R_c - R_s
\]

where \( R_0 \) represents the spontaneous baseline activity and \( R_c \) and \( R_s \) represent the spatial weighting functions of the center and surround Gaussians, respectively. Each Gaussian component is of the following form

\[
R' = C \cdot K[1 - e^{-i(\theta^2 + \theta^2)}]
\]

where \( R' \) is the Gaussian spatial weighting function of either the center \( R_c \) or surround \( R_s \). Each Gaussian is composed of a parameter for stimulus contrast \( C \), peak sensitivity \( K \), spatial frequency \( f \), and the space constant \( \sigma \) (radius of Gaussian at 1/e of peak).

All quantifications are expressed as the median or mean ± SE, unless otherwise stated. Statistical tests were performed using a one-way Tukey–Kramer ANOVA test for significance (Matlab or S-plus). Nonparametric comparisons were performed with the Wilcoxon ranked-sum test.

**RESULTS**

**Area-summation responses**

The spatial summation properties of the classical receptive field (CRF) of each geniculocortical afferent and its suppressive nonclassical surround were determined by stimulating with drifting sine-wave gratings confined to circular apertures. The stimulus for these area-summation experiments was a drifting sine-wave grating of spatial frequency that produced the largest evoked response. The optimal spatial frequency value maximally stimulated the classical receptive field center while poorly stimulating the classical surround. Therefore the optimal spatial frequency provides estimates of the excitatory classical receptive field center while minimizing interactions between the classical and nonclassical surrounds. Area-summation responses were used to determine the spatial extent of the CRF center and the nonclassical surround. As stimulus size increased, responses showed increasing summation that either plateaued or peaked depending on the presence of a nonclassical suppressive surround (Fig. 1A).

Area-summation responses were well fitted with a DOG model. The CRF was modeled as a single Gaussian fitted to the extent of the CRF ON–OFF subunits (Fig. 1B; also see Methods). Nonclassical surrounds were fitted with a second Gaussian that was linearly summed with the CRF center Gaussian (DeAngelis et al. 1994; Sceniak et al. 1999; cf. Rodieck and Stone 1965). The spatial extents of CRFs and nonclassical surrounds were estimated as the excitatory space constant \( a \) and the inhibitory space constant \( b \), respectively. A suppression index (SI) was used to quantify the strength of the nonclassical suppressive surrounds. The SI was estimated as the ratio of the area under the CRF Gaussian to the area under the nonclassical surround Gaussian. SI therefore ranges from 0 to 1, with complete surround suppression corresponding to 1.0 and an absence of surround suppression to 0.
Spatial characterization of geniculocortical afferents

Histological reconstructions of electrode penetrations after each experiment allowed us to determine the anatomical laminar position of the geniculocortical responses (see METHODS). For the afferent recordings that histological data could be recovered \((n = 70\) out of \(136\)), the anatomical origin of these responses was tracked to the input layers 4A, 4C\(\alpha\), and 4C\(\beta\) (Fig. 2). The spatial extent of the CRF center appeared smallest in layer 4A (median = 0.22°, Fig. 2, A and C), but not significantly smaller than in layer 4C\(\alpha\) or layer 4C\(\beta\) \((P > 0.05,\) one-way Tukey–Kramer ANOVA test). Spatial extent was smaller in layer 4C\(\beta\) (median = 0.46°) than in layer 4C\(\alpha\) (median = 0.51°), but this trend was also not statistically significant \((P > 0.05,\) one-way Tukey–Kramer ANOVA test). There were also no apparent sublaminal trends for excitatory spatial extent within layer 4C\(\alpha\) or layer 4C\(\beta\).

Variability of CRF center spatial extent estimates \((a,\) excitatory space constant) showed differences based on anatomical layering. Layer 4A contained the least variability of CRF center size for all input layers \((0.28\) and \(0.15,\) 95% confidence limits, \(n = 17\); Fig. 2C). Within layer 4C, the excitatory space constants were more variable in layer 4C\(\alpha\) \((0.65\) and \(0.34°,\) 95% confidence limits, \(n = 35\)) than in layer 4C\(\beta\) \((0.76\) and \(0.17°,\) 95% confidence limits, \(n = 13\)). This variability results from a greater number of large RFs in layer 4C\(\alpha\) than in layer 4C\(\beta\). Spatial summation responses were measured at a range of eccentricities \((2\) and \(5°\) parafoveal) and therefore not at identical eccentricities. However, because of our estimations of eccentricity it was not possible to determine trends in spatial summation with eccentricity. The proportion of afferent responses at each depth varied between penetrations and eccentricity varied both between and within penetrations.

The spatial extent of nonclassical surround suppression was also examined with respect to anatomical organization \((n = 70,\) Fig. 2B). On average, surround suppression within layer 4C\(\alpha\) showed greater spatial extent than that within layer 4C\(\beta\) \((median = 0.62\) and \(0.51°,\) respectively). However, this difference between the nonclassical surround extent of layers 4C\(\alpha\) and 4C\(\beta\) was not statistically significant \((P > 0.05,\) one-way Tukey–Kramer ANOVA test). The median extent of surround suppression for layer 4A was \(0.5°\) and was also not significantly different from layers 4C\(\alpha\) and 4C\(\beta\) \((P > 0.05,\) one-way Tukey–Kramer ANOVA test). The local regression smoothing (smooth curve in Fig. 2B) suggested a sublaminal trend toward greater extent of surround suppression in lower than in upper layer 4C\(\alpha\). Variability in the estimates of the extent of surround suppression was least in layer 4A \((0.7\) and \(0.3°,\) 95% confidence limits; Fig. 2C). Within layer 4C, variability in the extent of surround suppression was greater in layer 4C\(\alpha\) \((0.9\) and \(0.3°,\) 95% confidence limits) than in layer 4C\(\beta\) \((0.85\) and \(0.15°,\) 95% confidence limits) and this was attributed to the larger range of surround sizes seen in 4C\(\alpha\) (see Fig. 2C).

Overall, the median spatial extent of the excitatory CRF center and the nonclassical surround for the geniculocortical afferents tested were \(0.46\) and \(0.80°,\) respectively \((Fig. 2, D and E, mean = 0.58 ± 0.04\) and \(1.30 ± 1.90°,\) respectively, \(n = 136\)). These estimates are slightly larger than those for the population shown with anatomical reconstructions \((Fig. 2, A\) and \(B)\). However, the differences between estimates are within the variability of the two sample populations. On average, the space constant ratio \((\text{inhibitory/excitatory or } b/a)\) had a median value of \(1.5\) \((Fig. 2F, mean = 2.93 ± 0.3)\). Therefore the suppressive surrounds were 1.5-fold the size of the CRF centers.

The strength of the suppressive nonclassical surrounds appeared to be bimodal \((Fig. 3, A–C)\). Most area-summation response functions showed either strong surround suppression \((SI > 0.80)\) or no surround suppression \((SI = 0)\). Across the entire population of geniculocortical responses \((n = 136)\), the median SI for responses with any surround suppression \((SI > 0.1)\) was \(0.83\) \((mean = 0.85 ± 0.22)\). Over 80% of the afferent responses showed strong surround suppression \((n = 109, SI > 0.5)\), whereas 20% showed weak to no surround suppression.

For those responses with surround suppression \((SI > 0.5)\), all input layers showed high median surround suppression \((0.91, 0.90,\) and \(0.99\) for layers 4A, 4C\(\alpha\), and 4C\(\beta\), respectively; \(Fig. 3A)\). Responses with no surround suppression \((SI = 0)\) were also found in all input layers \((4A, 4C\alpha,\) and \(4C\beta)\). For responses with surround suppression \((SI > 0.1)\), variability of surround strength was lowest in layer 4C\(\beta\) \((1.0\) and \(0.97,\) 95% confidence limits) and greater in layers 4A \((1.1\) and \(0.73,\) 95% confidence limits) and 4C\(\alpha\) \((0.96\) and \(0.84,\) 95% confidence limits; \(Fig. 3B)\).
Across the population of isolated geniculocortical responses tested, receptive field spatial properties tended to be contrast invariant (Fig. 4A). CRF center size, as estimated from the excitatory space constant of the DOG model, showed no significant difference \((P > 0.05,\) Wilcoxon ranked-sum test) between estimates at high and low contrast (mean = 6 ± 19\%, \(n = 48,\) Fig. 4, B and C). However, the spatial extent of the suppressive nonclassical surround \((b_{low} \text{ vs. } b_{high})\) was significantly greater at low contrast than at high contrast \((P < 0.01,\) Wilcoxon ranked-sum test, mean % difference (low to high contrast) = 20 ± 42\%, \(n = 48;\) Fig. 4, D and E).

Overall, the strength of the nonclassical surrounds tended to be high at both low- and high-contrast levels. In addition, there was a significant \((P < 0.01,\) Wilcoxon ranked-sum test) difference between the strength of nonclassical suppressive surrounds estimated at high and low contrast [mean % difference (low to high contrast) = −13 ± 31\%, \(n = 48,\) Fig. 4, F and G]. The nonclassical surround strength was, on average, greater at higher contrasts than at lower contrasts.

The spatial extent of the excitatory classical receptive field was contrast invariant, whereas the strength and spatial extent of the nonclassical surround did appear to be dependent on the contrast used to measure each parameter. The extent of the nonclassical surround was larger at low contrast compared with estimates at high contrast and the strength of the suppression was greater at higher contrast levels. Albeit significant, the contrast-dependent changes in both the extent and strength of the suppressive surrounds are relatively small (20 and 13\%, respectively).

**Chromatic classification of geniculocortical afferents**

Afferent geniculocortical inputs were further classified according to their likely LGN origins (magno-, parvo-, and koniocellular) as determined from responses to cone-isolating drifting-grating stimuli (L-cone, M-cone, S-cone) and to achromatic stimuli (Fig. 5). Responses showed a clear bimodal distribution for preference to L/M cone-isolating stimuli versus S-cone isolating drifting sine-wave gratings (Fig. 5A). The L/M cone-dominated group was sorted further by considering first-harmonic response phase differences between L- and M-cone isolating gratings \((\theta_{L−M})\). Within the L/M cone-dominated group, \(\theta_{L−M}\) was bimodally distributed between phases clustered near 0° (no cone opponency) and 180° (cone opponent; Fig. 5B). Therefore responses were sorted by first-harmonic response phase according to their preference to red/green opponent stimuli \((\theta_{L−M} > 90°)\) or achromatic stimuli \((\theta_{L−M} < 90°)\). Achromatic-dominated responses correspond to magno inputs from the LGN, whereas red/green opponent inputs correspond to parvo inputs and S-cone-dominated responses correspond to konio inputs. They are encountered only in superficial layers 4A and 3B (Chatterjee and Callaway 2003).

Across the population of geniculocortical afferent responses \((n = 117,\) 46\% of the responses were classified as magno, 29\% were parvo, and 25\% were konio (S-cone–dominated) LGN inputs (Fig. 6). There was a trend toward the konio inputs showing smaller spatial extent of summation (median = 0.41°) compared with either magno (median = 0.50°) or parvo (median = 0.53°) inputs. However, these trends were not statistically significant \((P > 0.05,\) one-way Tukey–Kramer test). The size of the nonclassical suppressive surround also
tended to be smaller in konio than in either magno or parvo inputs but was not statistically significant (0.60, 0.76, and 1.0° for konio, magno, and parvo, respectively; \( P < 0.05 \), one-way Tukey–Kramer ANOVA test).

Similar to the trends observed for the afferent responses shown in Fig. 3 that included histological data, the strength of surround suppression was bimodally distributed within all three populations (magno, parvo, and konio) with responses showing either strong (SI > 0.8) or negligible (SI < 0.5) surround suppression (Fig. 6). For responses with surround suppression (SI > 0.1), all three groups showed similar surround strength (median = 0.92, 0.84, and 0.89 for magno, parvo, and konio, respectively) and similar variability for either magno (0.97 and 0.87, 95% confidence limits), parvo (0.94 and 0.74, 95% confidence limits), or konio (0.95 and 0.82, 95% confidence limits; see bottom of Fig. 6) cell groups.

**Geniculocortical afferent CRF spatial structure**

The CRF spatial structure of the geniculocortical afferent responses was analyzed through the spatial frequency-response function (see METHODS). Each response function was fitted with a DOG model. Estimates of the spatial extent of the excitatory CRF center were similar when measured with the spatial frequency-tuning curve (mean = 0.54 ± 0.04°) or the integrated DOG model used with the area-summation data.

**FIG. 3.** Population distribution of surround suppression strength within geniculocortical afferents. A: SI estimates are shown distributed across cortical layers for cells with known laminar positions (n = 70). Responses were bimodal in all input layers (4A, 4Cα, and 4Cβ) with one population showing strong surround suppression (SI > 0.5) and another with no surround suppression (SI = 0). B: statistical box plot shows median SI values (with first through third quartiles) within each layer for those responses with SI > 0.2. C: distribution of SI estimates for the entire population (n = 136). Vertical closed arrow indicates the median SI value for responses with surround suppression (SI > 0.2). Open arrow indicates the response with no surround suppression (SI = 0).

**FIG. 4.** Contrast-invariant area summation in geniculocortical afferents. A: area-summation responses are shown plotted at 2 contrast levels. Mean firing rate responses (spikes/s) are plotted as a function of stimulus radius (degree of visual angle). High-contrast responses (60%) are shown as filled circles and low-contrast responses (20%) are shown as open circles. Solid and dashed curves are the integral DOG model fitted to high- and low-contrast data, respectively. Horizontal dashed lines indicate measures 2 SDs above and below mean spontaneous level. Representative response function showed contrast-invariant peak area-summation responses and typical surround suppression. B and C: excitatory space constant estimates are shown plotted for high- vs. low-contrast stimulation conditions. Majority of points fall along the unity ratio line. Population histogram indicates that, on average, there is no difference in estimates of excitatory space constant between the 2 contrast levels (low to high contrast). Vertical arrow indicates the mean percentage change (6 ± 19%). D and E: inhibitory space constant estimates shown plotted at high vs. low contrast. Across the population, inhibitory space constants were contrast invariant. Vertical arrow indicates the mean percentage change in the spatial extent of nonclassical surround suppression with contrast (20 ± 42%). F and G: SI estimates are shown plotted at high vs. low contrast. Population histogram is shown for the percentage change in the SI with contrast (low to high contrast). Vertical arrow indicates the mean percentage change in SI values with contrast (−13 ± 28%).
model (Fig. 7). CRFs with a single mechanism produced SC ratios of 0, whereas those with strong CRF center-surround antagonism produced SC ratios near 1. The magno-, parvo-, and koniocellular geniculocortical afferent populations each contained CRF responses with strong (SC ratio $>0.5$) CRF center-surround antagonism (63, 68, and 65% of subpopulation for magno, parvo, and konio, respectively; Fig. 7, A–C). CRFs with only weak surround mechanisms (SC ratio $<0.2$) were also found in all groups; however, the percentage of RFs lacking CRF surrounds was twice as great for konio inputs (21%) as for magno (11%) or parvo (12%) inputs (Fig. 7, A–C). Furthermore, cells completely lacking on–off antagonism were found only in the S-cone–dominated konio population (Fig. 8).

There were no strong correlations between the CRF center-surround structure and the presence of nonclassical surround suppression (Fig. 8). Nonclassical surround suppression was found coupled to CRF centers with either strong or weak CRF surround=center ratios. There was also no strong correlation between chromatic preference and spatial organization. However, konio afferents without any detectable classical on–off antagonism invariably had strong suppression from beyond the CRF.

**DISCUSSION**

We reported here that the spatial extent of excitatory CRF centers was contrast invariant in isolated geniculocortical afferent responses. However, the strength and spatial extent of the nonclassical suppressive surround varied with contrast by a small amount (13 and 20%, respectively). The spatial extent of the suppressive surround was greater at lower contrast levels and the strength of the surround was greater at higher contrast levels. Although our results differ from studies that reported contrast-dependent area-summation responses in the LGN and retina of other species (Nolt et al. 2004; Solomon et al. 2002), our preparation is functionally more reduced than that reported in other studies. By pharmacologically inactivating cortical neuronal responses, we eliminated corticogeniculate feedback influences. Corticogeniculate feedback was previously shown to significantly modulate LGN neuronal response gain (Przybyszewski et al. 2000) and may contribute to spatial summation changes observed in LGN. Also some of the effects of surround changes could have been interpreted as changes in the excitatory CRF (Nolt et al. 2004; Solomon et al. 2002).

Recent studies reported contrast-dependent area summation in the LGN of marmosets (Solomon et al. 2002) and cats (Nolt et al. 2004). Solomon et al. (2002) reported a 31% increase in the extent of summation at low contrast compared with high contrast and Nolt et al. (2004) reported a 75% increase. These reports of contrast-dependent area summation are substantially lower than those reported in primary visual cortex of macaque monkeys (Kapadia et al. 1999; Sceniak et al. 1999). The spatial extent of excitatory receptive fields was reported to be greater at low contrast than at high contrast by 2.3-fold (Sceniak et al. 1999) in anesthetized animals and by fourfold (Kapadia et al. 1999) in awake-behaving animals. The geniculocortical afferent inputs of macaque monkeys do not show contrast-dependent changes in the extent of excitatory spatial summation when

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**FIG. 5.** Chromatic classification of geniculocortical afferents. Cells were classified based on their response to cone-isolating drifting gratings. A: first-harmonic response for S-cone isolating drifting-grating stimuli vs. L-cone or M-cone stimuli was used to determine the relative contribution of S cones to L- or M-cone inputs (n = 117). All stimuli were presented at maximum achievable cone contrasts. First harmonic L, M, and S cone responses were normalized to unity ($L'$, $M'$, and $S'$ responses) and the normalized L' and M' responses are plotted against each other. Blue/yellow, red/green, and achromatic responses are shown as blue triangles, red circles, and open circles, respectively. $S'$ responses are implicit in their distance from the dashed line (such that $M' + L' \leq 0.5$). Histogram below the scatterplot illustrates the $S'$ responses. There is a clear bimodal distribution separating the S-cone–dominated (blue/yellow; blue bars) responses from the L/M-cone–dominated (red/green and achromatic; red and black bars, respectively) responses. B: L/M responses were subdivided into red/green or achromatic response based on the relative response phases to L-cone and M-cone isolating stimuli ($\theta_{L-M}$). Responses were classified as achromatic or red/green based on whether the phase differences $\theta_{L-M}$ clustered near 0° (<90°) or 180° (>90°) (in phase or antiphase, respectively).

(mean = 0.53 ± 0.06°). The classical surround, as measured with the DOG model fitted to the spatial frequency-tuning curves, was similar in size (mean = 1.4 ± 0.14°, n = 76) to the nonclassical surround size (mean = 1.3 ± 0.26°, n = 76), as measured with the expanding-aperture area-summation experiment.

The relative strength of center to surround mechanisms within the CRF was estimated as the ratio of the area under the surround to center Gaussians (SC ratio) from the DOG
pharmacologically isolated. However, these effects might be observed in the LGN of animals with normal unaltered visual systems by means of corticogeniculate feedback.

In a recent study Ozeki et al. (2004) suggested that surround suppression found in V1 could be inherited from a spatially specific reduction in excitation driving the cortical response arising from the surround suppression found in LGN responses. Their conclusion was based on the finding that iontophoretic application of the GABAA-receptor antagonist, bicuculline methiodide (BMI), to neurons recorded in the visual cortex of anesthetized cats did not change the size-tuning curves. As others have suggested (Roberts et al. 2005; Webb et al. 2005), application of BMI presents various problems of interpretation. For example, BMI does not block excitatory intracortical synaptic transmission. Roberts et al. (2005) found that application of acetylcholine elevated excitation and inhibition and produced results that argued for intracortical effects of size-tuning changes. Here we find that there is a trend toward increased strength of surround suppression at high compared with low contrast (Fig. 4G). However, there is strong surround suppression at both contrasts unlike in cat (Ozeki et al. 2004). Although surround suppression originating in the LGN likely shapes the spatial tuning of V1 response, contrast independence of surround suppression strength (Sce

niam et al. 1999) and orientation tuning of the surround (Bonin et al. 2005; Jones et al. 2000; Solomon et al. 2002; Webb et al. 2005; Xu et al. 2002b) suggest that there are additional intracortical mechanisms of cortical surround suppression.

The afferent inputs of layers 4Ca, 4Cb, and 4A in macaque visual cortex were previously shown to originate in magnoc-, parvo-, and koniocellular layers of the LGN, respectively (Chatterjee and Callaway 2003). Afferent input responses were found only in layers 4Ca, 4Cb, and 4A (and bottom 3B). Previous reports suggest that K cells are spatially heterogeneous and display properties that are intermediate between M and P cells (Solomon et al. 1999, 2002; Xu et al. 2002a). Our results are consistent with these findings in that there is considerable overlap in the spatial properties of M, P, and K cells.

Across all geniculocortical afferent responses (n = 136), the spatial extent of excitatory summation was roughly half (mean = 0.5°) of that observed for primary visual cortical neurons (mean = 1.0°) (Cavanaugh et al. 2002a,b; Jones et al. 2001; Levitt and Lund 2002; Sceniak et al. 2001). On average, there was no statistical difference between the size of the excitatory summation zone as determined from empirical fits with the DOG equation for any of the input layers (4A, 4Ca, and 4Cb). However, the extent of excitation was smallest in...
layer 4A and largest in 4Cβ based on median values. Layer 4Cβ also displayed the greatest degree of variability in the spatial extent of the CRF.

The spatial extent of suppressive nonclassical surrounds was roughly half the size (1.0°) of that observed for neurons within primary visual cortex (2.2°) at similar eccentricities (2–5°) (Cavanaugh et al. 2002a,b; Jones et al. 2001; Levitt and Lund 2002; Sceniak et al. 2001). Suppressive nonclassical surrounds were smallest in layer 4Cβ (0.58°) and largest in layer 4Cα (1.1°). Layer 4Cα produced the greatest variability in the spatial extent of the suppressive surround. Within the afferent population, the spatial extent of the suppressive nonclassical surround was roughly 1.5-fold greater than the excitatory CRF center as estimated from the parameters of the DOG model fits. However, the classical surrounds were similar in size to the nonclassical surrounds, on average.

Surround suppression strength, as quantified by the suppression index (SI), was similar across the entire population of geniculocortical afferents (mean = 0.65, n = 136) to that observed for neurons in primary visual cortex (0.63; Sceniak et al. 2001). SI values were bimodally distributed in all input layers (4A, 4Cα, and 4Cβ, n = 70). Surround suppression was stronger, on average, for the afferent input responses within these layers than for the neurons of the same layers (see Sceniak et al. 2002). Responses with no surround suppression are found among magno, parvo, and konio inputs. It will be interesting to determine a possible functional role of these distinct response properties.

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Similar to reports of the spatial properties for marmosets (Solomon et al. 2002; White et al. 2001) and prosimians (Irvin et al. 1986; Norton and Casagrande 1982; Norton et al. 1988; Xu et al. 2002a) the spatial extent of the CRF was similar for M, P, and K cells in the macaque afferent responses. Although it is difficult to compare estimates of receptive field size across species, for similar eccentricities (2–5°) our estimates in macaques are similar to those reported in prosimians (Xu et al. 2002a).

Overall, there is substantial surround suppression in the afferent inputs, even in the absence of corticogeniculate feedback, for the M, P, and K pathways. Although the spatial extent of the excitatory CRF is contrast invariant, there is a small contrast dependency of the nonclassical surround. It is likely that this contrast dependency originates in the retina or through lateral inhibition originating in the LGN. These mechanisms likely contribute to improved signal-to-noise ratios or improved spatial localization of the retinal inputs.

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