Phase sensitivities, excitatory summation fields, and silent suppressive receptive fields of single neurons in the parastriate cortex of the cat

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Romo PA, Wang C, Zeater N, Solomon SG, Dreher B. Phase sensitivities, excitatory summation fields, and silent suppressive receptive fields of single neurons in the parastriate cortex of the cat. J Neurophysiol 106: 1688–1712, 2011. First published June 29, 2011; doi:10.1152/jn.00894.2010.—We have recorded single-neuron activity from cytoarchitectonic area 18 of anesthetized (0.4–0.7% isoflurane in 65% N2O:35% O2 gaseous mixture) domestic cats. Neurons were identified as simple or complex on the basis of the ratios between the phase-variant (F1) component and the mean firing rate (F0) of spike responses to optimized (orientation, direction, spatial and temporal frequencies, size) high-contrast, luminance-modulated, sine-wave drifting gratings (simple: F1/F0 spike-response ratios > 1; complex: F1/F0 spike-response ratios < 1). The predominance (~80%) of simple cells among the neurons recorded from the principal thalamorecipient layers supports the idea that most simple cells in area 18 might constitute a putative early stage in the visual information processing. Apart from the “spike-generating” regions (the classical receptive fields, CRFs), the receptive fields of three-quarters of area 18 neurons contain silent, extraclassical suppressive regions (ECRFs). The spatial extent of summation areas of excitatory responses was negatively correlated with the strength of the ECRF-induced suppression of spike responses. Lowering the stimulus contrast resulted in an expansion of the summation areas of excitatory responses accompanied by a reduction in the strength of the ECRF-induced suppression. The spatial and temporal frequency and orientation tunings of the ECRFs were much broader than those of the CRFs. Hence, the ECRFs of area 18 neurons appear to be largely “inherited” from their dorsal thalamic inputs. In most area 18 cells, costimulation of CRFs and ECRFs resulted in significant increases in F1/F0 spike-response ratios, and thus there was a contextually modulated functional continuum between the simple and complex cells.

luminance-modulated gratings; simple and complex cells; spatial and temporal properties; classical and extraclassical receptive fields; primary visual cortex

Hubel and Wiesel (1965) postulated that in the domestic cat, the so-called parastriate cortex (cytoarchitectonic area 18 of Gurwitsch and Chatschaturian 1928; cf. Otsuka and Hässler 1962) constitutes a “higher order” visual cortical area (Fig. 1). Consistent with this postulate, area 18 of the cat receives numerically massive associational “feedback” input from the cells in the supragranular layers of ipsilateral striate cortex [cytoarchitectonic area 17 (area V1), Fig. 1, A and B]. Furthermore, reversible inactivation of ipsilateral area 17 abolishes or significantly reduces the magnitude of responses to visual stimuli of almost 30% of neurons in the visuotopically corresponding part of area 18 (Casanova et al. 1992; Sherk 1978). Also consistent with the postulate, several lines of evidence indicate that area 18 of eutherian carnivores, such as domestic cats, might be a homolog of area V2 of primates (e.g., Payne 1993). Thus, whereas in the cat the vertical meridian is represented at the border of cytoarchitectonic areas 17 and 18, in primates it is represented at the border of area 17 and area V2. Second, the visuotopic maps in area 18 of the cat (Albus and Beckmann 1980; Hubel and Wiesel 1965; Payne 1990; Tolbot 1942; Tusa et al. 1979) and areas V2 of primates (Gattass et al. 1981; Rosa 1997) approximate distorted “mirror images” of the visuotopic maps of the contralateral visual field in areas 17. Third, at any given retinal eccentricity, the so-called minimum response fields (Barlow et al. 1967) of single neurons in area 18 of the cat (Albus and Beckmann 1980; Dreher et al. 1980; Dreher 1986; Hubel and Wiesel 1965; Tretter et al. 1975; Tusa et al. 1979), like those of single neurons in area V2 of macaque monkeys (Foster et al. 1985; Gattass et al. 1981; Levitt et al. 1994; Orban et al. 1986), are on average two- to threefold larger than those of their area 17 counterparts.

On the other hand, there is substantial evidence indicating that area 18 of the cat is a part of the primary visual cortex. Thus many studies report a numerically large, direct input to area 18 from the dorsal lateral geniculate nucleus (LGNd; see for reviews Dreher 1986; Payne and Peters 2002; Stone et al. 1979). Furthermore, despite the fact that the magnitudes of responses to visual stimuli of almost 30% of cat area 18 neurons are strongly affected by inactivation of ipsilateral area 17 (see above), the receptive field properties of most neurons in this area appear to be only weakly affected by acute ablation (Dreher and Cottée 1975) or reversible inactivation (Sherk 1978; cf. also Casanova et al. 1992) of ipsilateral area 17.

Several issues relevant to the question of the serial (hierarchical) vs. parallel relationship between the striate (area 17) and parastriate (area 18) cortices of eutherian carnivores have not been examined. In virtually all studies of the principal part of cat primary visual cortex, area 17 (see for reviews Dreher 1986; Orban 1984; Payne and Berman 1983; Payne and Peters 2002; Stone et al. 1979), large proportions of neurons were identified as simple, that is, presumed “first-order” cortical cells, on the basis of qualitative criteria developed by Hubel and Wiesel (1962). Furthermore, in both cats and macaques there is an excellent correlation between identification of area 17 neurons as simple or complex based on the qualitative criteria and their identification based on the quantitative criteria of strength of phase sensitivity in their responses to sine-wave
luminance-modulated achromatic gratings (cf. Bardy et al. 2006; De Valois et al. 1982; Movshon et al. 1978a, 1978b; Skottun et al. 1991). By contrast, there is a degree of controversy concerning paucity (e.g., Hubel and Wiesel 1965) or otherwise (see for review Dreher 1986; Harvey 1980; Orban 1984; Payne and Peters 2002) of simple cells in area 18, and to our knowledge, there are no published records of the frequency distribution of strength of phase sensitivity of area 18 neurons to stimulation with luminance-modulated, sine-wave gratings.

Another issue that so far has not been a focus of detailed investigation concerns the so-called “silent suppressive surrounds” or extraclassical receptive fields (ECRFs) in the receptive fields of area 18 neurons. Although the presence of silent suppressive regions in the receptive fields of at least some of cat area 18 neurons is well established (Camarda 1979; Dreher et al. 1992; Hammond and Andrews 1978; Harvey 1980; Hubel and Wiesel 1965; Orban and Callens 1977), the amount of quantitative information about the properties of ECRFs of area 18 neurons is very limited.

In the present study we have found that 1) the majority of neurons in cat area 18 can be identified as simple, rather than complex, on the basis of both qualitative and quantitative criteria developed for area 17 neurons; 2) the receptive fields of most area 18 neurons contain strong suppressive ECRFs; 3) stimulation of ECRFs usually results in significant increases in the phase sensitivity and hence “simplification” (cf. Bardy et al. 2006) of the responses to stimuli presented in the classical receptive fields (CRFs); and 4) spatial and temporal frequency and orientation tunings of the suppressive ECRFs of parastriate neurons are remarkably similar to those of their presumed LGNd input neurons but much broader than those of their CRFs. Overall, the results support the primary visual cortex status of cat area 18 and suggest that the silent suppressive surrounds of area 18 neurons are, at least partially, “inherited” from their dorsal thalamic inputs. Some of the findings already have been presented in an abstract (Romo et al. 2009).

METHODS

Animals, anesthesia, and surgical procedures. Experiments were performed according to the guidelines of the National Health and Medical Research Council’s Code of Practice for the Care and Use of Animals for Scientific Purposes in Research in Australia and were approved by the Animal Care Ethics Committee of the University of Sydney. Eleven adult domestic cats (Felis catus) of either sex, weighing 2.5–5 kg, were supplied by Laboratory Animal Services of the University of Sydney.

The animals were initially anesthetized with a gaseous mixture of 2–4% isoflurane (Abbott Australasia, Kurnell, NSW, Australia) in 65% N2O-35%O2. Throughout the subsequent surgical procedures, the level of isoflurane in the mixture was maintained in the range 0.75–1.5%, that is, the levels at which the withdrawal reflexes to pinching the animal’s forelimb were just abolished.

Throughout the experiment the animal’s head was held firmly in a stereotaxic frame. The neuromuscular transmission to striated muscles was initially abolished with an intravenous infusion of a 2-ml bolus of gallamine triethiodide (40 mg/ml; Sigma-Aldrich, St. Louis, MO). This was followed throughout the recording sessions by a continuous intravenous infusion of gallamine (10 mg·kg−1·h−1). Potential residual eye movements were prevented by bilateral cervical sympathe-
tomy (Rodieck et al. 1967). The animals were artificially ventilated via a tracheal cannula. Peak expired alveolar CO₂ was maintained at 3.7–4.0% by adjusting stroke volume (range 30–50 ml) and/or rate (range 18–25 strokes/min) of the pulmonary pump. The body temperature was maintained at 37.5°C, monitored by a subcappular probe with an Animal Temperature Controller 1000 (World Precision Instruments, Sarasota, FL). The heart rate was monitored continuously and maintained in the range 180–230 beats/min (the smaller the animal, the higher the heart rate) by adjusting the isoflurane level in the gaseous mixture in the range 0.4–0.7%. The electroencephalogram (EEG), recorded with a metal screw touching the dura over the frontal cortex, was also monitored continuously. A “deep sleep” state, characterized by delta waves (0.5–4.0 Hz) in the EEG, was maintained by adjusting, when necessary, the level of isoflurane in the gaseous mixture.

A broad-spectrum antibiotic, 15 mg/kg amoxicillin trihydrate (150 mg, Betamox; Norbrook Laboratories, Tullamarine, Victoria, Australia) and 0.3 ml of atropine sulfate (0.6 mg; Apex Laboratories, Somersby, NSW, Australia) were administered intramuscularly daily. Application of aqueous solution of 1% atropine sulfate (Sigma Pharmaceuticals, Clayton, Victoria, Australia) and 0.1% phenylephrine hydrochloride (Isopto-Frin; Alcon, Frenchs Forest, NSW, Australia) on alternate days dilated the pupils, blocked accommodation, and retracted the nictitating membranes. The corneas were protected with zero-power, air-permeable contact lenses, which remained in place for the duration of the experiment. The eyes were focused on a tangent screen positioned 57 cm in front of the eyes, using appropriate (as assessed by streak retinoscopy) corrective lenses. Artificial pupils (3 mm in diameter) were positioned at the centers of the dilated pupils. With the use of a fiber-optic light source (Pettigrew et al. 1979), the optic discs of each eye were back-projected daily on the tangent screen positioned 57 cm in front of the eyes. Each grating was presented within a circular window, with the rest of the screen held at the mean luminance of ~50 cd/m². Optimal stimulus parameters were estimated online by quantitatively derived orientation and spatial and temporal frequency tuning curves. The orientation and spatial and temporal frequency tuning curves were determined at 100% Michelson contrast. Contrast was defined as \( \frac{L_{\text{max}} - L_{\text{min}}}{L_{\text{max}} + L_{\text{min}}} \), where \( L_{\text{max}} \) and \( L_{\text{min}} \) are, respectively, maximum and minimum luminances in the pattern. This was followed by quantitative assessment (using optimized grating patches) of the contrast sensitivity function of the cell. When assessing the size of the summation receptive field (sRF), the orientation, direction, and spatial and temporal frequencies were optimized while contrast was reduced to that which produced 80% of maximal response (usually 80–90% contrast). The diameter of the sRF was defined as the diameter of circular patch of optimized (orientation, direction, contrast, spatial and temporal frequencies) sine-wave luminance-modulated drifting grating that evoked the maximal response (spatial summation field, cf. Bringuier et al. 1999). For each cell, the diameters of grating patches used for final assessments of orientation and spatial and temporal tuning curves were 90–100% of the diameter of the sRFs. Increasing the size of a blank patch in the center of an annulus of drifting gratings centered on the discharge field allowed us to determine quite precisely the “boundary” of the excitatory sRF. The stimulation of the area surrounding the sRF, the ECRF itself, did not evoke discharges above the level of background (spontaneous) activity.

The responses to optimized sRF stimulation and to combined sRF and ECRF stimulation were tested with a series of visual stimuli: a 1-s “blank” to determine the mean background activity, followed by a grating drifting for 3 s and then separated from the next 3-s presentation of the grating with a 1-s blank interval. Each testing series comprised a segment at which a patch of drifting grating was centered on the discharge field and restricted to the sRF. This stimulus, referred to as “sRF stimulus,” was set to optimal orientation, direction, contrast, and spatial and temporal frequencies. The sRF stimulus was then combined with a series of surrounding sinusoidal drifting gratings (extending to a diameter of 28°) of the same spatial and temporal frequencies as the sRF. However, orientations of the surround stimuli varied in four distinct steps relative to orientation of stimuli covering the sRF (hence 0°, 45°, 90°, and 135°). The surround stimuli drifted in both directions orthogonally to their orientations (hence 180°, −45°, −90°, and −135°). To ensure that the stimulation of surround per se did not elicit spike activity, an “ECRF alone” stimulus (drifting grating confined to the surround) was run with each series. Each series of visual stimuli was repeated 10 times and presented in a pseudorandomized fashion.

Assessment of receptive field structure in relation to ON and OFF discharge regions. The excitatory discharge field is defined in the present study as the area within which, when those spatial stimuli evoked neuronal discharges at a rate exceeding that of the background (“spontaneous”) activity (as determined subjectively by monitoring the response over the loudspeaker; cf. minimum response field of Barlow et al. 1967). The minimum response or discharge fields of recorded neurons were plotted separately through the ipsilateral and contralateral eyes (with the other eye covered by a black occluder) using elongated light (generated by a hand-held ophthalmoscope) and hand-held dark bars. Neurons were identified as either simple (S-cells) or complex (C-cells) based on the spatial arrangement of their excitatory discharge regions as revealed by the stationary flashing (Hubel and Wiesel 1962) and/or the moving light and dark (Maske et al. 1985) optimally oriented bars. Cells with spatially separate discharge regions for the light (ON) and dark (OFF) bars were identified as simple, whereas cells with spatially overlapping light bar and dark bar discharge regions (overlapping ON and OFF discharge regions) were identified as complex (Burke et al. 1992; Gilbert 1977; Henry 1977). The ocular dominance class was determined by subjective auditory assessment of the relative magnitude of responses to the optimally oriented stimuli presented separately via each eye. For binocular cells, the excitatory discharge fields were plotted separately for each eye. The quantitative assessments of other features of the receptive fields of binocular neurons are based on the data obtained with the stimuli presented via the dominant eye.

Assessment of CRF properties and interactions between the centers and silent surrounds. Achromatic sine-wave contrast-modulated drifting gratings of variable size, orientation, and spatial and temporal frequency were generated by the visual stimulation system EXP0 (P. Lennie, University of Rochester, Rochester, NY) and presented on a calibrated cathode ray tube monitor (Barco, Kortrijk, Belgium) placed 57 cm in front of the cat’s eyes. Each grating was presented within a circular window, with the rest of the screen held at the mean luminance of ~50 cd/m². Optimal stimulus parameters were estimated online by quantitatively derived orientation and spatial and temporal frequency tuning curves. The orientation and spatial and temporal frequency tuning curves were determined at 100% Michelson contrast. Contrast was defined as \( \frac{L_{\text{max}} - L_{\text{min}}}{L_{\text{max}} + L_{\text{min}}} \), where \( L_{\text{max}} \) and \( L_{\text{min}} \) are, respectively, maximum and minimum luminances in the pattern. This was followed by quantitative assessment (using optimized grating patches) of the contrast sensitivity function of the cell. When assessing the size of the summation receptive field (sRF), the orientation, direction, and spatial and temporal frequencies were optimized while contrast was reduced to that which produced 80% of maximal response (usually 80–90% contrast). The diameter of the sRF was defined as the diameter of circular patch of optimized (orientation, direction, contrast, spatial and temporal frequencies) sine-wave luminance-modulated drifting grating that evoked the maximal response (spatial summation field, cf. Bringuier et al. 1999). For each cell, the diameters of grating patches used for final assessments of orientation and spatial and temporal tuning curves were 90–100% of the diameter of the sRFs. Increasing the size of a blank patch in the center of an annulus of drifting gratings centered on the discharge field allowed us to determine quite precisely the “boundary” of the excitatory sRF. The stimulation of the area surrounding the sRF, the ECRF itself, did not evoke discharges above the level of background (spontaneous) activity.

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The tuning of the ECRF for spatial and temporal frequencies was determined separately. The optimized sRF-confined stimulus was then combined with a series of surrounding sinusoidal drifting gratings (extending to a diameter of 28°) tuned to the orientation that resulted in the maximal suppression (as above). To determine the spatial and temporal tuning curves for the effect of ECRF stimulation on the sRF response, the spatial or temporal frequencies of the surround stimuli were varied individually.

Data analysis and statistics. The identification of cells as either simple or complex based on the spatial distribution of ON and OFF discharge regions (see above) was compared with identification based on the analysis of cell responses to optimized sRF-confined grating patches. Thus cells in which the phase-variant F1 component of the response to drifting sine-wave gratings was greater than the overall mean firing rate, F0 (F1/F0 spike-response ratio > 1), were identified as simple, whereas those in which F1/F0 spike-response ratio was <1, were identified as complex (cf. Bardy et al. 2006; Skottun et al. 1991).

In view of the very low background activities of most cells, the spontaneous activity was not subtracted from F0 used in data analysis. Hartigan’s dip test (Hartigan and Hartigan 1985) was used to assess the unimodality or otherwise of the frequency distribution of F1/F0 spike-response ratios of area 18 cells.

The direction selectivity index (DSI) of a given cell was calculated according to the following formula:

\[ \text{DSI} = \left[ \frac{R_p - R_{ap}}{R_p} \right] \times 100, \]

where \( R_p \) and \( R_{ap} \) are, respectively, the peak discharge rates for optimized sRF-confined stimulus moving in the preferred and anti-preferred directions along the axis perpendicular to the optimal orientation.

The strength of suppression was assessed quantitatively using the suppression index (SI), defined as

\[ \text{SI} = \left[ \frac{R_{\text{min}} - R_{\text{max}}}{R_{\text{max}}} \right] \times 100 \]

Many cells did not generate spikes when 1° (smallest size used in the present study) gratings were presented in the center of the discharge fields. In all cells, as the diameter of the optimized drifting grating patches increased above 1°, the magnitude of response (number of spikes) gradually increased until it reached a maximum (\( R_{\text{max}} \)). In different cells, the \( R_{\text{max}} \) was reached at different diameters of grating patches. Once the maximum magnitude of response was reached, further increases in the size of the grating patches resulted in \( J \) reduction in the magnitude of response (suppression), 2) response saturation, or 3) suppression followed by a “rebound” in the magnitude of response (“countersuppression”). \( R_{\text{min}} \) is defined in this study as the magnitude of response when the strength of suppression is greatest (see RESULTS, Impact of the stimulus size on magnitude of response of area 18 neurons). The DSIs and SIs of simple and complex cells were calculated on the basis of the magnitude of F1 component of the spike responses and the mean firing rate (F0) of the responses, respectively.

Statistical significance of the differences between sets of data was assessed using nonparametric tests: Mann-Whitney U-test, Wilcoxon matched-pairs signed-ranks test, and Spearman rank correlation coefficient test (Siegel 1956), referred to in this article as the Mann-Whitney test, Wilcoxon test, and Spearman correlation coefficient test, respectively. The Mann-Whitney test was used to assess significance of differences between two independent sets of data. The Wilcoxon test was used for paired-data comparisons. The statistical significance between the two sets of data was accepted if the associated probability (\( P \)) value was 0.05 or less at the two-tailed criterion, unless otherwise indicated. Values in the text are either means ± SD or means ± SE.

Localization of recording sites. At the end of each experiment, the animal was deeply anesthetized by intravenous injection of sodium pentobarbitone (120 mg/kg, Lethabar; Virbac, Australia). The animal was perfused transcardially with 500 ml of warm (37°C) saline followed by 1,000 ml of 4% paraformaldehyde in phosphate buffer (0.1 M at pH 7.4). The brain was extracted from the skull and maintained in 30% sucrose in phosphate buffer until it sank. The caudal third of the hemisphere of interest was coronally sectioned (at 50 μm) on a cryostat. Sections were mounted onto gelatinized slides, air-dried, and viewed using bright-field microscopy to locate the tracks made by electrodes coated with 1,1'-dioctadecyl-3,3,3',3'-tetramethyl indocarbocyanine perchlorate (DiI). The sections were counterstained for Nissl substance with cresyl violet. In most cases, DiI marked the entire length of the electrode track (cf. DiCarlo et al. 1996). Using computer-assisted drawing programs combined with information about the location of cells in relation to the cortical surface and electrolytic lesions, we were able to reconstruct laminar locations of the majority of the recorded cells.

RESULTS

The present sample consisted of 133 neurons, all of which responded consistently (with a peak discharge rate of at least 5 spikes/s) to optimized patches (optimal orientation, preferred direction, optimal spatial and temporal frequencies, optimal size) of drifting gratings presented through one eye (dominant in the case of binocular cells). About three-quarters of the neurons (102/133, 76.5%) were recorded in long, oblique penetrations through the part of area 18 located in the medial bank of the marginal sulcus (Fig. 1, A and C), with the rest (31/133) in shorter penetrations, radial to the lateral part of the marginal gyrus (Fig. 1A). The minimum response (discharge) fields (e.g., Barlow et al. 1967; Dreher et al. 1980) of the cells were located within 15° of area centrales and within 8° from the representation of zero horizontal meridian (cf. Tusa et al. 1979).

The great majority (105/129, 81.5%) of neurons in which we tested responsiveness to stimuli presented separately via each eye were identified as binocular, since they generated spike responses to appropriate visual stimuli presented via either eye (with the other eye covered; cf. Dreher et al. 1992; Harvey 1980). Although consistent with Harvey’s (1980) report, the proportion of thus-identified binocular neurons among presumptive simple cells (F1/F0 spike-response ratios > 1; see below) was lower (69/88, 78.5%) than that (36/41, 88%) among presumptive complex cells (F1/F0 spike-response ratios < 1; see below), the difference between the two groups was not significant (0.2 < \( P < 0.3; df = 1; \chi^2 \) test, 1-tailed criterion).

Phase Variance of Area 18 Neurons

Figure 2A shows the peristimulus time histogram (PSTH) of spike responses of strongly phase-variant area 18 cells to optimized sine-wave luminance-modulated grating patch. Note that the magnitude of the grating phase-variant, first-Fourier harmonic (F1) component of responses was much greater than the mean firing rate (F0), and hence the F1/F0 spike-response ratio of the cell was >1. However, in a substantial proportion of neurons (see below), the phase-variant F1 component of the spike response was smaller than the mean firing rate (F0), and hence the F1/F0 spike-response ratio was <1 (see PSTH in Fig. 2B).

The frequency distribution of F1/F0 spike-response ratios of the present sample of area 18 neurons (Fig. 2C) is strongly skewed in favor of presumed simple cells. Thus cells with
F1/F0 spike-response ratios > 1 constituted over two-thirds (90/133, 67.5%) of the present sample. Note also that there are two clear peaks in the frequency histogram: the larger one, constituted by presumptive simple cells with F1/F0 response ratios of 1.6–1.8, and a smaller one, constituted by presumptive complex cells with low F1/F0 spike-response ratios of 0.2–0.5. Indeed, unlike the frequency distribution of F1/F0 spike-response ratios of a sample of cells recorded by us from area 17 (Bardy et al. 2006; cf. Dean and Tolhurst 1983), the frequency distribution of F1/F0 spike-response ratios of the present sample of cells is significantly (dip value 0.0443; P = 0.045; boot strapping 1,000; Hartigan’s dip unimodality test) different from a unimodal distribution.

**F1/F0 Vs. Spatial Separation of ON and OFF Discharge Fields Within Receptive Fields**

Over two-thirds of area 18 cells (62/90, 69%; Fig. 2 C) with F1/F0 spike-response ratios > 1, like their presumed counterparts in area 17 (Bardy et al. 2006; cf. also Dean and Tolhurst 1983), the frequency distribution of F1/F0 spike-response ratios of a sample of cells recorded by us from area 17 (Bardy et al. 2006; cf. also Dean and Tolhurst 1983), the frequency distribution of F1/F0 spike-response ratios of the present sample of cells is significantly (dip value 0.0443; P = 0.045; boot strapping 1,000; Hartigan’s dip unimodality test) different from a unimodal distribution.

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simple rather than complex cells. Furthermore, one cell with F1/F0 spike-response ratio > 1 (thus presumed to be simple) had overlapping ON and OFF discharge regions in its minimum discharge field.

Over one-quarter of neurons in the present sample (39/133, 29.5%) were not identifiable as simple or complex on the basis of criterion of spatial separation vs. spatial overlap of ON and OFF discharge regions in their receptive fields. Most commonly (29/133, 22%), we were unable to reveal ON and/or OFF discharge regions in their receptive fields when using stationary, flashing, optimally oriented light bars, and these cells generated spike responses only when stimulated with moving, optimally oriented bars, darker than the background. In a smaller proportion (10/133, 7.5%) of cells, not only were we unable to reveal OFF and/or ON discharge regions in their receptive fields when using stationary, flashing, optimally oriented light bars, but these cells generated spike responses only when moving, optimally oriented bars brighter than the background were used.

Two-thirds of the cells (26/39, 65%) that we were unable to identify as simple or complex using one of Hubel and Wiesel’s principal criteria exhibited an “intermediate” F1/F0 spike-response ratio (range 0.5–1.5; Fig. 2C). Furthermore, those cells constituted a clear majority (26/43, 60.5%) of cells that exhibited intermediate F1/F0 spike-response ratios.

**Laminar Location: Simple Vs. Complex Cells**

We reconstructed the laminar location of almost 80% of cells (105/133) in our sample. In most cases, our electrode did not reach the infragranular layers 5 and 6, and hence very few (5/105) neurons were sampled from these layers.

As indicated in Fig. 2D, nearly three-quarters (57/77, 74%) of the cells with F1/F0 spike-response ratios > 1 were located in either the principal geniculocortical layer 4 (granular layer) or the geniculocortical lower half of layer 3, layer 3b (cf. Freund et al. 1985; Humphrey et al. 1985). The remaining simple cells were recorded from the superficial layers 1 and 2 and from the upper part of layer 3, layer 3a (18/77, 23.5%), or from the infragranular layer 6 (2/77, 2.5%).

The majority of cells with F1/F0 spike-response ratios < 1 (16/28, 57%) were also located in the geniculocortical layers 4 and 3b (Fig. 2D). Of the remainder, most (9/28, 32%) were recorded from the nongeniculocortical supragranular layers 2 and 3a, and only very few were recorded from the infragranular layers 5 (2 cells) and 6 (1 cell).

Overall, presumed simple cells (F1/F0 spike-response ratios > 1) constituted over three-quarters (57/73, 78%) of neurons recorded from the thalamocortical layers 4 and 3b. Although the preponderance of simple cells was less pronounced among neurons recorded from the supragranular layers 1, 2, and 3a, they still constituted two-thirds (18/27, 66.5%) of the patch recorded from these layers.

**Impact of Grating Patch Size on Magnitude of Responses of Area 18 Neurons**

In all area 18 neurons, as the diameter of the high-contrast (80–100%) patches of gratings of optimal spatial and temporal frequencies and optimal orientation increased above 1°, the magnitude of spike responses (number of spikes) also increased (Fig. 3, A and B). In the majority of both simple and complex cells (78/133, 58.5%; 55 simple, 23 complex), the magnitude of response reached maximum at a particular diameter of grating patch (excitatory sRFs), and further increases in the patch’s diameter resulted in gradual substantial reductions in the magnitude of their spike responses (cf. “type 2” cells in cat area 17 in Sengpiel et al. 1997). Indeed, in almost one-third of this group of neurons (24/78, 30.5%; 16 simple, 8 complex), the spike responses were completely or almost completely (>90%) suppressed when the grating patches reached maximal (28°) diameter (e.g., F1 component of response of simple cell 1 in Fig. 3A or F0 of response of complex cell 1 in Fig. 3B).

In over 15% (22/133, 16.5%; 13 simple, 9 complex) of sampled neurons, although further (beyond the optimal) increases in the diameter of the optimally oriented high-contrast grating patches resulted in gradual and substantial reductions in the magnitude of response, extending the stimuli into the distal part of the receptive field resulted in “countersuppression;” that is, reduction of the magnitude of response was less when presented grating patches were larger (see DeAngelis et al. 1994; Li and Li 1994; Sadakane et al. 2006; Walker et al. 2000; Wang et al. 2009 for a similar phenomenon in area 17).

Finally, in one-quarter of the sample (33/133, 25%; 22 simple, 11 complex), the magnitude of response plateaued at a particular diameter of the grating patches and further increases in the size of the patches did not produce significant changes in the magnitude of responses (response saturation, e.g., F1 component of response of simple cell 3 in Fig. 3A or F0 of response of complex cell 3 in Fig. 3B; cf. “type 1” cells in cat area 17 in Sengpiel et al. 1997).

The peak magnitudes of responses of simple cells to sRF-confined optimized gratings (mean 35.9 spikes/s, SD ±30.2 spikes/s; range 5.4–139.2 spikes/s) were slightly but not significantly (P > 0.486; Mann-Whitney test, 1-tailed criterion) higher than those (mean 33.35 spikes/s, SD ±25.25 spikes/s; range 5.1–118.0 spikes/s) of complex cells (cf. Fig. 3C). The peak magnitudes of responses of simple cells (mean 20.15 spikes/s, SD ±25.95 spikes/s; range 0.0–121.8 spikes/s) to high-contrast optimized grating patches producing maximal reduction of the responses were slightly but not significantly (P > 0.255; Mann-Whitney test, 1-tailed criterion) lower than those (mean 20.8 spikes/s, SD ±22.1 spikes/s; range 0.0–97.7 spikes/s) of complex cells (Fig. 3C).

**Size of sRFs and Minimum Discharge Fields Vs. Magnitude of Suppressive Indexes**

When high-contrast (80–100%) patches of gratings were used, there was almost a complete overlap in the sRF diameters of simple and complex cells (Fig. 3D). Indeed, the mean diameter of sRF of simple cells (10.07°, SE ±0.65°) was not significantly smaller (P < 0.129; Mann-Whitney test, 1-tailed criterion) than that (11.92°, SE ±1.09°) of complex cells. It is also apparent from Fig. 3D that there was a negative correlation between the diameters of sRF and the strength of suppression (SI; see METHODS). The negative correlation is clearly discernable for both simple and complex cells (see Fig. 3D; Spearman correlation coefficient test).

The diameters of sRFs of simple cells in which the SIs were by 10.220.32.247 on June 28, 2017 http://jn.physiology.org/ Downloaded from
those (mean 5.85°, SE ± 0.70°; n = 25) of simple cells in which SIs were ≥75% (top histogram in Fig. 3E). Similarly, the diameters of the sRFs of complex cells with SIs ≤25% were substantially (mean 16.95°, SE ± 2.35°; n = 13) and significantly (P < 0.0005; Mann-Whitney test) larger than those (mean 6.6°, SE ± 1.1°; n = 11) of complex cells in which SIs were ≥75% (top histogram in Fig. 3E).

It is unlikely that the negative correlation between the diameters of sRF and the SI is a side effect of the limited maximal size (28° diameter) of grating patches used to test the strength of suppression. Thus, in the case of complex cells, and to a lesser extent, simple cells, there was also a negative correlation between the diameters (along the axis of optimal orientation) of minimum discharge fields revealed by stimuli presented via the dominant eye and the magnitudes of their SIs (bottom histogram in Fig. 3E). In particular, the minimum discharge fields of complex cells (mean 4.82°, SE ± 0.51°; range 2.6–7.8°; n = 9) whose SIs were ≤25% were highly
rates to optimized gratings confined to the sRFs were substantially higher (mean 26.65 spikes/s, SD ± 16.45 spikes/s; n = 25) for simple cells with SI ≥75%. Similarly, for complex cells with SI ≥25%, the peak discharge rates to optimized gratings confined to the sRFs were substantially (mean 42.4 spikes/s, SD ± 31.0 spikes/s; n = 13) and significantly (P < 0.005; Mann-Whitney test) higher than those (mean 22.8 spikes/s, SD ± 27.0 spikes/s; n = 11) for complex cells with SI ≥75%. The inverse relationship between the SIs and the peak discharge rates to optimized stimuli confined to sRFs suggests that silent suppressive regions spatially overlap (at least partially) with the spike-generating regions, CRFs.

Effect of Contrast on Size of sRF and Strength of Suppression

Generally, optimized grating patches of a given size but of lower contrasts evoke weaker responses (fewer spikes) than the grating patches of the same size but of higher contrasts (Fig. 4, A–C). When medium-contrast (30–45%) stimuli were used, the sizes of sRFs of many simple (Fig. 4A) and complex cells (Fig. 4C) were larger than those of the same cells when the high-contrast (80–90%) stimuli were used. Indeed, this was the case in over two-thirds (7/10, 70%) of complex cells and nearly one-half (9/19, 47.5%) of simple cells (Fig. 4D). All cells included in the sample responded vigorously (peak discharge rate at least 15 spikes/s) to high-contrast optimized gratings. At high contrast, the mean diameters of sRFs of both simple (11.6°, SD ± 7.25°; n = 19) and complex cells (12.95°, SD ± 7.85°; n = 10) were very similar to those in the whole sample (see Size of sRFs and Minimum Discharge Fields Vs. Magnitude of Suppressive Indexes) but substantially smaller than those (simple: 14.0°, SD ± 9.3°; complex: 15.0°, SD ± 8.25°) when the medium-contrast (30–45%) gratings were used.

Although the sRF sizes of simple and complex cells at medium contrasts were not significantly (in both cases P > 0.05; Wilcoxon test, 1-tailed criterion) different from those at high contrast, the relative strength of suppression induced by stimulation of silent surround tended to be substantially less (e.g., Fig. 4, A and B). Indeed, as indicated in Fig. 4E, at medium contrasts the mean SIs of both complex (40.6%, SE ± 11.2%) and simple (48.9%, SE ± 7.5%) sRFs were substantially higher (mean 26.65 spikes/s, SD ± 16.45 spikes/s; n = 25) for simple cells with SI ≥75%. Similarly, for complex cells with SI ≥25%, the peak discharge rates to optimized gratings confined to the sRFs were substantially (mean 42.4 spikes/s, SD ± 31.0 spikes/s; n = 13) and significantly (P < 0.005; Mann-Whitney test) higher than those (mean 22.8 spikes/s, SD ± 27.0 spikes/s; n = 11) for complex cells with SI ≥75%. The inverse relationship between the SIs and the peak discharge rates to optimized stimuli confined to sRFs suggests that silent suppressive regions spatially overlap (at least partially) with the spike-generating regions, CRFs.

Fig. 3. sRFs and peak discharge rates vs. suppression indexes (SI) of area 18 neurons. A and B: examples of the relationships between the magnitude of responses and the diameter of optimized grating patches for simple and complex cells. The magnitude of responses plotted for simple cells represents the magnitude of F1 components of responses, whereas the magnitude of responses for complex cells represents the mean firing rates, F0. Insets: PSTHs of responses to grating patches of particular diameters at a and b in A and at c and d in B. In most cells, the magnitude of response reached a maximum (Rmax) at a particular size of the grating patch (excitatory sRFs), and further increases in the diameter of the patch resulted in gradual substantial reduction (Rmin) in the magnitude (number of spikes/s) of responses (cells 1 in A and B). However, a subset of neurons that exhibited suppression when grating patches larger than optimal were presented exhibited a “rebound” (or “countersuppression”) in the strength of the response when even larger stimuli were presented (cells 2 in A and B). Finally, some cells did not exhibit a significant reduction in the magnitude of responses when stimuli larger than excitatory summation area were presented (cells 3 in A and B). Error bars in A and B indicate SE. C: the magnitudes of the Rmax responses of area 18 cells to optimized high-contrast, sine-wave, luminance-modulated drifting grating patches vs. the magnitude of the Rmin responses to orientation- and to spatial and temporal frequency (but not size)-optimized grating patches. Filled arrows indicate mean magnitudes of the F1 component of response of simple cells; open arrows indicate mean magnitudes of the F0 of spike responses of complex cells. Note that in about three-quarters of both simple (68/90) and complex cells (32/43), the magnitude of the Rmin responses was significantly (P < 0.05; Wilcoxon test) lower than that of the Rmax responses. D: plot of sRF sizes vs. magnitude of SIs of simple and complex cells in the present sample. The numbers next to the particular points in the plot indicate the number of cells in which the diameters of the sRF and the SIs were the same. Note that there is a negative correlation between the size of sRF and the magnitude of SIs: cells with lower SIs tended to have larger sRFs (solid line, regression line for simple cells; dashed line, regression line for complex cells; Spearman’s correlation coefficient test for both). E, top histogram: relation between the mean diameters of sRFs and the magnitude of SIs. Note that both simple and complex cells with strong SIs (≥75%) had substantially and significantly (P < 0.002; Mann-Whitney test) smaller sRFs than those with weak SIs (<25%). Bottom histogram: relation between the mean minimum discharge fields and the magnitude of SIs. F: relation between the mean background (“spontaneous”) spike activity and the magnitude of SIs. Error bars in E and F indicate SE. G: inverse relation between the peak discharge rates to sRF-confined optimized stimuli and the magnitude of SIs. Note that a proportion of simple and complex cells with lower SIs (<50%) tended to respond more strongly to optimized sRF-confined stimuli (solid line, simple cells; dashed line, complex cells; Spearman’s correlation coefficient test).
7.5%) cells were substantially lower than those (complex: 50.6%, SE 10.1%; simple: 56.45%, SE 7.0%) at high contrast. Furthermore, for the whole sample (simple and complex cells combined), the mean SI at medium contrasts (46.05%, SE 6.2%) was significantly \((P < 0.0064; \text{Wilcoxon test})\) lower than that (54.45%, SE 5.7%) at high contrasts.

**Spatial Frequency Tuning of sRFs**

Consistent with earlier reports (cf. Movshon et al. 1978c), at high contrasts (80–100%) the sRFs of most area 18 neurons were spatial frequency tuned; that is, their spike responses could be evoked by a fairly narrow range of spatial frequen-
cies, and unlike the spatial frequency low-pass cells (Fig. 5A), they tended poorly to the lowest spatial frequency tested (Fig. 5, B–D). The spatial frequency tuning of both the F1 component and mean firing rate F0 of spike responses was apparent in both simple (Fig. 5B) and complex cells (Fig. 5, C and D). In the great majority (72/90, 80%) of simple and a majority (25/43, 58%) of complex neurons, the spatial frequencies producing the maximal F1 and F0 of spike responses were identical (e.g., spatial frequency-tuned simple cell in Fig. 5B and spatial frequency-tuned complex cell in Fig. 5D).

However, in a small proportion (18/90, 20%) of simple and a large proportion (18/43, 42%) of complex cells, the spatial frequencies resulting in maximal F1 were quite different from those resulting in maximal F0. In the case of complex cells, the spatial frequencies resulting in maximal F1 were almost invariably (17/18) lower than those resulting in maximal F0 (e.g., spatial frequency-tuned complex cell in Fig. 5C).

The spatial frequency-tuned cells constituted over two-thirds of both simple (62/90, 69%) and complex cells (31/43, 72%). The diameters of optimally oriented grating patches, which were used to establish spatial frequency-tuning curves of CRF of each cell, were 90–100% of the diameters of their sRFs. The mean sRF diameters (10.25°, SD ± 6.2°) of spatial frequency-tuned simple cells were slightly and not significantly (Mann-Whitney test) larger than those (9.65°, SD ± 6.25°) of low-pass simple cells. Furthermore, the diameters of sRFs of almost three-quarters (44/62, 71%) of spatial frequency-tuned simple cells and almost three-quarters (20/28, 71.5%) of low-pass simple cells were >6°. On the other hand, the diameters of sRFs of almost all (11/12, 91.5%) low-pass complex cells were >8°, whereas the sRF diameters of a large proportion (12/31, 38.5%) of spatial frequency-tuned complex cells were <8°. The mean diameters (11.3°, SD ± 7.6°) of the sRFs of spatial frequency-tuned complex cells were only slightly smaller than those (13.55°, SD ± 5.95°) of low-pass complex cells. Overall, thus, there was no discernable correlation between the sRF diameters of cells (and hence the diameters of the grating patches used to assess the spatial frequency tuning) and the pattern of spatial frequency tuning (spatial frequency tuned vs. low pass) of the cells.

**Optimal Spatial Frequencies**

As indicated in Fig. 6A, there was almost a complete overlap in the optimal (preferred) spatial frequencies of sRFs of simple and complex cells. However, the spatial frequencies optimal for complex cells (mean 0.26 cycle/deg, SD ± 0.17 cycle/deg) tended to be somewhat higher than those (mean 0.21 cycle/deg, SD ± 0.14 cycle/deg) for simple cells.

The optimal spatial frequencies of spatial frequency-tuned simple cells (mean 0.23 cycle/deg, SD ± 0.11 cycle/deg) were highly significantly (P < 0.0006; Mann-Whitney test) higher than those (mean 0.12 cycle/deg, SD ± 0.13 cycle/deg) of low-pass simple cells. Similarly, the optimal spatial frequencies of frequency-tuned complex cells (mean 0.31 cycle/deg, SD ± 0.15 cycle/deg) were highly significantly (P < 0.0001; Mann-Whitney test) higher than those (mean 0.1 cycle/deg, SD ± 0.07 cycle/deg) of low-pass complex cells (cf. Fig. 6A). The same trends were apparent among cells recorded from the principal geniculocortical layer, layer 4 (Fig. 6B). Thus the mean optimal spatial frequencies of layer 4 low-pass simple (F1 component) and low-pass complex cells (mean firing rate, F0) were, respectively, 0.08 (SD ± 0.05) and 0.16 (SD ± 0.04) cycle/deg. The mean optimal spatial frequencies of layer 4 spatial frequency-tuned simple and complex cells were higher: 0.23 (SD ± 0.11) and 0.36 (SD ± 0.16) cycle/deg, respectively. Again, the differences between the spatial frequency low-pass simple and complex cells vs. spatial frequency-tuned simple and complex cells were significant (P < 0.05, Mann-Whitney test, for both simple and complex cells).

Although overall the optimal spatial frequencies of cells with larger sRFs tended to be lower, the trend was weak. Thus, in the case of complex cells, the mean optimal spatial frequencies of cells with sRFs ≥12.5° (mean 0.22 cycle/deg, SD ± 0.196 cycle/deg) were barely significantly (P < 0.05; Mann-Whitney test, 1-tailed criterion) lower than those (mean 0.33 cycle/deg, SD ± 0.145 cycle/deg) of complex cells with sRFs <6.5° (Fig. 6C). Furthermore, the mean optimal spatial frequencies of simple cells with sRFs ≥12.5° (mean 0.166 cycle/deg, SD ± 0.112 cycle/deg) were not significantly (0.113 < P < 0.115; Mann-Whitney test, 1-tailed criterion) lower than those (mean 0.212 cycle/deg, SD ± 0.139 cycle/deg) of simple cells with sRFs ≤6.5° (Fig. 6C).

**High Cutoff Spatial Frequencies and Spatial Frequency Bandwidth**

The high cutoff frequencies or “visual acuities” (cf. Maffei and Fiorentini 1973; Movshon et al. 1978c) of low-pass simple cells (mean 0.32 cycle/deg, SD ± 0.14 cycle/deg) were substantially and highly significantly (P < 0.00006, Mann-Whitney test) lower than those (mean 0.59 cycle/deg, SD ± 0.28 cycle/deg) of spatial frequency-tuned simple cells. Similarly, the high cutoff frequencies of low-pass complex cells (mean 0.41 cycle/deg, SD ± 0.19 cycle/deg) were substantially and highly significantly (P < 0.005 Mann-Whitney test) lower than those (mean 0.88 cycle/deg, SD ± 0.62 cycle/deg) of spatial frequency-tuned complex cells. The overall spatial frequency tuning widths or “bandwidths” of sRFs of spatial frequency-tuned complex cells (mean 2.0 octaves, SD ± 0.55 octaves; range 0.8–2.8 octaves; n = 31) and simple cells (mean 2.01 octaves, SD ± 0.68 octaves; range 0.8–2.8 octaves; n = 62) were virtually identical.

**Spatial Frequency Tuning of Suppressive ECRFs**

We tested the spatial frequency tuning of ECRFs of 49 cells. All cells included in the subsample responded quite vigorously to high-contrast optimized gratings confined to their sRFs (peak discharge rate > 10 spikes/s). The frequency distribution of F1/F0 spike-response ratios of these cells to sRF-confined optimized stimuli was very similar to that for the whole sample (cf. Fig. 5E vs. Fig. 2C). Many aspects of the spatial frequency tunings of suppressive ECRFs were very similar to the spatial frequency tunings of the excitatory responses evoked by stimuli confined to the sRFs. Thus J) in most cases, cells with low-pass sRFs exhibited strong ECRF-induced suppression only at low spatial frequencies (Fig. 5A); 2) in many cells whose sRFs were sharply tuned for spatial frequencies, the ECRFs were also tuned (albeit quite broadly) for spatial frequencies (Fig. 5, B and D); and 3) for many cells there was a good correspondence between the spatial frequencies evoking the strongest spike responses from the sRFs and the spatial frequencies evoking the strongest suppression from the ECRFs (Fig. 5F). However, there were also quite substantial differences in the spatial frequency tunings of sRFs and ECRFs.
Thus, in virtually all cells with low-pass sRFs, a substantial (occasionally even maximal) suppression of sRF-induced discharges was apparent when ECRFs were stimulated with gratings of the spatial frequencies higher than the high cutoff frequencies of excitatory responses evoked by stimuli confined to the sRFs (Fig. 5A); 2) overall, especially in the case of simple cells, the spatial frequencies evoking the strongest suppression from the ECRFs tended to be higher than those evoking the strongest discharges from the sRFs (e.g., Fig. 5, A and B); 3) in most cells, low-spatial frequency stimuli confined to the ECRF evoked a significant suppression of sRF-induced excitatory responses (Fig. 5, A and D); and 4) the suppressive ECRFs of low-pass sRF cells tended to be tuned to lower spatial frequencies than those of cells with spatial frequency-tuned sRFs.

The ECRF-induced suppression of excitatory responses to sRF-confined stimuli frequently affected F1 components and mean discharge rates (F0) of spike responses to a different degree. In the case of simple cells, the F1/F0 spike-response ratios were either increased (Fig. 5A) or slightly reduced (Fig. 5B) when the ECRF-induced suppression was at its maximum. On the other hand, in the case of complex cells, the ECRF-induced reduction in the magnitude of spike responses resulted invariably in the greater reduction of magnitude of F0 and hence an increase in F1/F0 spike-response ratios (Fig. 5, C and D).

Spatial Frequency Bandwidth

Overall, the spatial frequency tunings of ECRFs were broader than those of sRFs (Fig. 5, A, C, and D). Spatial frequency tunings of ECRFs of some cells were broader than those of any of the sRFs (cf. Fig. 6F vs. Fig. 6E). Indeed, the bandwidths of spatial frequency tuning of ECRFs of simple (mean 2.35 octaves, SD ±0.588 octaves; range 1.5–3.5 octaves; n = 21) and complex cells (mean 2.41 octaves, SD ±0.754 octaves; range 1.2–3.6 octaves; n = 12) were substantially broader than those of sRFs of tuned simple and complex cells (Fig. 6F vs. Fig. 6E).

Temporal Frequency Tuning of sRFs

The sRFs of most area 18 cells were temporal frequency tuned (see Fig. 7, A, B, and E; cf. band-pass area 18 cells of Movshon et al. 1978c). Whereas in the simple cells the magnitudes of both F1 and F0 were strongly temporal frequency tuned (Fig. 7A), in the complex cells only F0 was tuned to temporal frequencies (Fig. 7B). The excitatory responses of a minority of simple (Fig. 7, C and E) and a minority of complex cells (Fig. 7, D and E) induced by sRF-confined (optimally oriented and optimal spatial frequency) grating patches were largely low pass in respect to the temporal frequencies. However, in both simple (Fig. 7C) and complex low-pass cells (Fig. 7D), there were significant spike responses at the highest temporal frequencies tested (15 Hz).

As indicated in Fig. 7E, there was virtually a complete overlap between the optimal temporal frequencies of simple cells (F1 component of spike responses) and those of complex cells (mean firing rate, F0). Furthermore, although the mean optimal temporal frequency of simple cells (3.48 Hz, SD ±2.54 Hz; range 0.5–9.4 Hz, n = 90) was slightly lower than the mean optimal temporal frequency of complex cells (3.8 Hz, SD ±2.6 Hz; range 0.5–11.5 Hz, n = 43), the difference between the two populations was not significant (0.2776 < P < 0.2810; Mann-Whitney test; 1-tailed criterion).

About two-thirds of simple (59/90, 65.5%) and complex cells (27/43, 63%) were temporal frequency tuned (Fig. 7E). Although in our sample, the proportion of temporal frequency low-pass cells (47/133, 35.5%; Fig. 7E) is similar to that of spatial frequency low-pass cells (40/133, 30%), only minorities of temporal frequency low-pass simple (13/31, 42%) and low-pass complex cells (4/16, 25%) were also spatial frequency low pass.

The optimal temporal frequencies of tuned simple cells (mean 4.8 Hz, SD ±2.91 Hz; range 0.7–9.4 Hz; n = 59) were highly significantly (P < 0.00006; Mann-Whitney test) higher than those (mean 1.51 Hz, SD ±1.04 Hz; range 0.5–5.0 Hz; n = 31) of low-pass simple cells (Fig. 7E). Similarly, the optimal temporal frequencies of tuned complex cells (mean 4.83 Hz, SD ±2.6 Hz; range 0.7–11.5 Hz, n = 27) were highly significantly (P < 0.00022; Mann-Whitney test) higher than those (mean 1.89 Hz, SD ±0.96 Hz; range 0.5–3.4 Hz; n = 16) of low-pass complex cells (Fig. 7E). On the other hand, the high cutoff temporal frequencies of tuned cells and low-pass
cells, either simple or complex, were not significantly different from each other (Fig. 7F).

Clear majorities of both simple (27/42, 64.5%) and complex cells (9/15, 60%) recorded from the granular layer (layer 4) were temporal frequency tuned. Overall, the optimal temporal frequencies of simple cells (tuned and low pass combined) recorded from layer 4 were slightly higher (mean 4.1 Hz, SD ± 3.1 Hz; range 0.5–10.7 Hz; n = 42) than those (mean 3.6 Hz, SD ± 3.1 Hz; range 0.5–11.5 Hz; n = 15) of complex cells (tuned and low pass combined) recorded from this layer. Again, the difference between the two populations was not significant (0.1539 < P < 0.1562; Mann-Whitney test; 1-tailed criterion).

Fig. 6. Spatial frequency tuning: sRFs and suppressive ECRFs. A: frequency histogram of optimal spatial frequencies for the present sample of area 18 neurons when the stimuli were confined to sRFs. Note that the optimal spatial frequencies of low-pass simple and complex cells tended to be lower than those of their frequency-tuned counterparts. B: frequency histogram of optimal spatial frequencies of sRFs of simple and complex cells located in layer 4 of area 18. Note the same trends that are apparent in A. C: relation between the diameters of sRFs and optimal spatial frequencies. Both simple and complex cells with sRFs ≤ 6.5° tended to prefer higher spatial frequencies than those preferred by their counterparts with sRFs ≥ 12.5°. In the case of complex cells, the difference is marginally significant (P < 0.05; Mann-Whitney test, 1-tailed criterion). Error bars in C indicate SE. D: frequency histogram of spatial frequency high cutoffs of sRFs of the present sample of area 18 cells. The mean spatial frequency high cutoffs of low-pass and spatial frequency-tuned simple cells tended to be lower than those of low-pass and spatial frequency-tuned complex cells. E: frequency histogram of spatial frequency bandwidth of sRFs of area 18 neurons. The mean spatial frequency band for simple cells at 2.0 ± 0.68 octaves (mean ± SD) was virtually identical to that of complex cells (2.0 ± 0.55 octaves). F: frequency histogram of spatial frequency bandwidth of suppressive ECRFs of area 18 neurons. The mean spatial frequency band of suppressive ECRFs for simple cells at 2.35 ± 0.59 octaves was very similar to that of complex cells (2.4 ± 0.75 octaves) but substantially greater than that of excitatory responses when the patches were confined to sRFs (see E).
**Temporal Frequency Tuning of Suppressive ECRFs**

In virtually all simple cells (Fig. 7, A and C), as well as in most complex cells (Fig. 7D), the magnitudes of both the F1 component of spike responses and the mean firing rate (F0) were only weakly modulated by the changes in the temporal frequencies of ECRF-confined stimuli. However, in temporal frequency-tuned complex cells, only the mean firing rates (F0), but not the phase-variant F1 components of spike responses, were dependent on the temporal frequency of the gratings in the ECRFs (Fig. 7B). In almost three-quarters of the cells tested (27/37; 16/23 simple, 11/14 complex) there was a substantial (range 25–80%) and significant \( P < 0.05 \) (Wilcoxon test) suppression of sRF-induced responses even when the temporal frequency of ECRF-confined stimuli was 15 Hz (cf. Fig. 7, B–D). Cells whose sRFs were temporal frequency low pass constituted almost one-third (8/27, 29.5%; 3 simple, 5 complex) of these cells. By contrast, the sRFs of all but one (9/10) cell in which the ECRF-confined stimuli did not produce a significant suppression at 15 Hz (Fig. 7A) were temporal frequency tuned.

**Orientation and Direction Selectivities of Suppressive ECRFs**

As in the case of cat area 17 cells (e.g., Akasaki et al. 2002; Bardy et al. 2006, 2009; Naito et al. 2007; Sadakane et al. 2006; Sengpiel et al. 1997; see for review Seriès et al. 2003), in all area 18 cells, the relative strength of reduction of the magnitude of response to optimized sRF-confined stimuli was to some extent dependent on the relative orientation of gratings in the large (28° outer diameter) annuli in the silent suppressive ECRF (Fig. 8, A and C).

Almost one-third of the sample (simple: 26/90, 29%; complex: 14/43, 32.5%) exhibited a very high degree of direction selectivity (DSI > 90%) to stimuli confined to sRFs. Thus they responded well to the optimally oriented, sRF-confined, high-contrast gratings drifting in one so-called preferred direction along the axis perpendicular to the optimal orientation (see PSTHs in Fig. 8, Aa–Ca) but only weakly or hardly at all (see PSTHs in Fig. 8, Ab–Cb) to the motion of the same stimuli in the opposite, that is, antipreferred, direction. In some strongly direction-selective cells, the strength of ECRF-induced suppression was greater when the large (28° outer diameter) ECRF-confined annuli moved in the antipreferred, rather than preferred, direction (Fig. 8, Cd vs. Ce). In others, however, the strength of ECRF-induced suppression was greater when the large stimuli moved in the preferred, rather than antipreferred, direction (Fig. 8, Ad and Bd vs. Fig. 8, Ae and Be). Overall, as in the case of cells recorded from cat area 17 (cf. Peterson et al. 2004), cells exhibiting a substantial degree of direction selectivity (DSI > 50%) constituted large majorities of both simple (73/90, 81%) and complex cells (30/43, 70%).

In high proportions of simple and complex cells, the significant reductions in magnitude of response of cells when both sRFs and ECRFs were stimulated simultaneously were accompanied by significant \( P < 0.05 \) (Wilcoxon test) increases in F1/F0 spike-response ratios (Fig. 8, A and C; see Effect of Simultaneous Stimulation of sRFs and ECRFs on Phase Sensitivity of Area 18 Cells). In Fig. 9A, we have plotted the magnitude (in spikes/s) of cells’ responses to stimulation of sRFs with optimized (optimal orientations, preferred direction of movement, optimal spatial and temporal frequencies, and optimal size) high-contrast gratings against the magnitude of their responses to sRF-confined optimized grating patches plus “suppressively most effective” annuli of optimized gratings, whose internal diameter corresponded to the sRF while external diameter was 28°. Whereas the spatial and temporal frequencies and contrast of the gratings in ECRF annuli were the same as those of gratings confined to the sRFs, their orientation varied. For each cell, the magnitudes of responses plotted are for those orientations of ECRF-confined annuli which produced the greatest reduction in magnitude, that is, the strongest suppression of sRF-driven responses. We have excluded from the plot I the cells (4/97) in which stimulation of ECRFs with gratings of any orientation did not produce significant \( P < 0.05 \) (Wilcoxon test) reduction or increase in the magnitude of responses to optimized sRF-confined stimuli and 2) the cells (14/97) in which stimulation of ECRFs with gratings of some orientations produced significant \( P < 0.05 \) (Wilcoxon test) increases in the magnitude of responses to optimized sRF-confined stimuli.

In almost two-thirds of the cells in which we tested the orientation tuning of significant, purely suppressive ECRFs (51/79, 64.5%), the ECRF gratings that were the most effective “suppressors” of the sRF-induced excitatory responses were iso-oriented in respect to the sRF-confined gratings (Fig. 9B).

In Fig. 9C we have plotted the mean widths of orientation tuning curves of excitatory responses for all our area 18 cells, expressed as the relative magnitude of responses to different orientations in relation to the optimal orientation. The sRFs of all cells were tuned for orientation (see insets in Fig. 5, A–D), and the mean width at half-height of orientation tuning curves of sRF-induced excitatory responses of the entire sample \( n = 133 \) was 40.45° (SD ± 11.4°). Furthermore, the mean width at half-height of orientation tuning curves for the sRF-induced excitatory responses of the simple cells \( n = 90 \) was virtually identical to that \( n = 43 \) of complex cells.

In both the iso-orientation-tuned suppressive ECRFs and non-iso-orientation-tuned suppressive ECRFs groups, the orientation tunings of the silent suppressive ECRFs were much broader than the orientation tunings of sRF-alone-induced excitatory responses (Fig. 9C). Cells with iso-orientation-tuned suppressive ECRFs constituted over two-thirds (28/41, 68%) of cells recorded from layer 4, and the orientation tuning of suppressive ECRFs of cells recorded from layer 4 was also very broad (Fig. 9D).

In cells exhibiting a low degree of direction selectivity (DSI > 50%) to stimuli restricted to sRFs, the relative strength of ECRF-induced suppression tended to be less than that in cells with DSI > 90% (Fig. 9E). However, in both groups, the mean relative strengths of suppression when the ECRF-confined annuli moved in the antipreferred direction (180°) were not significantly different (in both cases \( P > 0.5 \); Mann-Whitney test, 1-tailed criterion) from those when the ECRF annuli moved in the preferred direction (0°).

In both simple and complex cells, suppression induced by the ECRF stimuli iso-oriented with sRF stimuli or by the ECRF stimuli oriented ±45° to sRF-confined stimuli tended to be stronger than suppression induced by the ECRF stimuli of other relative orientations (Fig. 9F).
Effect of Simultaneous Stimulation of sRFs and ECRFs on Phase Sensitivity of Area 18 Cells

In many complex (Figs. 5C, 5D, 8B, and 8C) and simple cells (Fig. 5A), simultaneous stimulation of sRFs and ECRFs resulted in substantial and significant increases in their phase sensitivity, that is, substantial and significant ($P < 0.05$; Wilcoxon test) increases in their $F_1/F_0$ spike-response ratios (cf. Bardy et al. 2006 for similar “simplification” of responses of area 17 cells).

In Fig. 10, we have plotted the relation between changes in the magnitude of responses to stimulation of sRF due to costimulation of suppressive ECRFs (with 28° outer diameter optimized gratings) on the phase sensitivities of responses of a subpopulation of area 18 neurons (see Orientation and Direction Selectivities of Suppressive ECRFs). It
is apparent that although in many cells significant reductions in the magnitude of responses resulted in significant increases in F1/F0 spike-response ratios, with very few exceptions, the large significant increases in F1/F0 ratios occurred only when the magnitude of responses was reduced by at least 60% (Fig. 10A).

In Fig. 10B, we have plotted the magnitude of changes in F1/F0 spike-response ratios during the most effective stimulation of suppressive ECRFs in relation to the “original” F1/F0 spike-response ratios to optimized stimuli confined to the sRF. Significant changes (all but 1 increased) in F1/F0 spike-response ratios accompanying the reduction in the magnitude of responses were not confined to cells exhibiting particular phase sensitivities. Indeed, significant increases in F1/F0 spike-response ratios were about equally common in cells identified as simple (31/54, 57.5%) or complex (14/25, 56%) on the basis of F1/F0 spike-response ratios to optimized high-contrast grating patches confined to the sRFs. However, the proportions of cells in which stimulation of the suppressive ECRF resulted in significant increases in F1/F0 spike-response ratios were much greater among the simple (16/20, 80%) and complex (8/11, 72.3%; cf. Fig. 8B) cells that exhibited “intermediate” phase sensitivities (F1/F0 spike-response ratios in the range 0.5–1.5) than in simple cells (15/34, 44%) exhibiting very high phase sensitivities (F1/F0 spike-response ratio > 1.5) or complex cells (6/14, 43%) exhibiting very low phase sensitivities (F1/F0 spike-response ratio < 0.5).

The differences in proportions of cells in which stimulation of the suppressive ECRF resulted in significant increases in F1/F0 spike-response ratios might be related to the fact that, as indicated in Fig. 10C, SIs of both simple (F1/F0 spike-response ratios 1–1.5; mean SI 64.5%, SE ±6.4%) and complex cells (F1/F0 spike-response ratios 0.5–1.0; mean SI 63.9%, SE ±9.6%) with intermediate phase sensitivities were substantially and significantly (in both cases P < 0.02; Mann-Whitney test) higher than those (mean SI 36.2%, SE ±4.9%) of complex cells with low phase sensitivities (F1/F0 spike-response ratio ≤ 0.5).

DISCUSSION

Frequency Distribution of F1/F0 Spike-Response Ratios of Area 18 Neurons

In over two-thirds of the present sample, the F1 components of their spike responses to optimized high-contrast, sine-wave luminance-modulated grating patches drifting through their receptive fields were greater than the mean firing rate, F0; that is, their F1/F0 spike-response ratios were >1.

It has been reported in the past that the frequency distributions of F1/F0 spike-response ratios (to optimized grating patches) of neurons recorded from areas V1 of anesthetized domestic cats (Li et al. 2003; Movshon et al. 1978a, 1978b; Skottun et al. 1991), macaques (De Valois et al. 1982; Ringach et al. 2002; Skottun et al. 1991), laboratory rats (Girman et al. 1999), house mice (Niell and Stryker 2008), and tammar wallabies (Ibbotson et al. 2005) are not unimodal, with frequency “dip” at the intermediate F1/F0 ratios of 0.7–1.3, that is, close to the ratio of 1. The apparent bimodality of frequency distribution of F1/F0 spike-response ratios has been invoked in support of the argument that in area V1, at least, cells with F1/F0 ratios >1 and these with ratios <1 represent two distinct groups of neurons.

The frequency distribution of F1/F0 spike-response ratios of the present sample is similar to that of the sample of neurons recorded by us (Bardy et al. 2006) from area 17 of anesthetized cats. Thus, in both samples, about two-thirds of cells exhibited F1/F0 spike-response ratios >1, and most of these (41/54, 76% of area 17 cells vs. 63/90, 70% of area 18 cells) were highly phase sensitive (F1/F0 response ratios >1.5). Despite the fact that the proportion of area 18 cells recorded from the thalamorecipient layers (~80%) was much higher than that (~55%) in our area 17 sample, the proportions of cells with F1/F0 spike-response ratios >1 were similar (32.5% in area 18 vs. 37% in area 17). However, the proportion of cells exhibiting very low phase sensitivities was substantially greater in the area 18 sample.

By contrast, in area V2 of macaque monkeys (with its miniscule direct projection from the LGNd; e.g., Bullier and Kennedy 1983; Yukie and Iwai 1981), complex cells (F1/F0 spike-response ratios <1) constitute the great majority (100/137, 73%) of neurons (Levitt et al. 1994; cf. also Foster et al. 1985). Furthermore, the majority of the complex cells in area V2 of macaques exhibit very low phase sensitivities (F1/F0 ratios ≤0.5), less than one-half of the simple cells exhibit high phase sensitivities (F1/F0 ratios >1.5; Levitt et al. 1994), and the overall frequency distribution of F1/F0 spike-response ratios appears to be unimodal (Levitt et al. 1994).

F1/F0 Spike-Response Ratios vs. Spatial Overlap of ON and OFF Discharge Regions in the Receptive Fields of Area 18 Neurons

Almost 95% of cells in cat area 17 identified as simple or complex on the basis F1/F0 spike-response ratios were also...
identified as simple or complex on the basis of spatial distinctness vs. spatial overlap of their ON and OFF discharge regions (Bardy et al. 2006; cf. Skottun et al. 1991).

The idea that in area 18, like in area 17, F1/F0 spike-response ratios around 1 separate simple from complex neurons is supported by a good correlation between 1) the cell F1/F0 spike-response ratios of >1 and the presence of spatially distinct ON (light bar) and OFF (dark bar) discharge regions in their receptive fields and 2) the cell F1/F0 spike-response ratios of <1 and the presence of spatially overlapping ON (light bar) and OFF (dark bar) discharge regions in their receptive fields. However, in nearly one-third of the present sample, we were unable to identify cells as simple or complex using the criterion of spatial separation vs. spatial overlap of ON and OFF discharge regions.

**A Simple cell**

- F1/F0: 1.81
- sRF: 8°

**B Complex (intermediate) cell**

- F1/F0: 0.92
- sRF: 4°

**C Complex cell**

- F1/F0: 0.32
- sRF: 4.4°

**a) sRF preferred direction**

- DSI: 95%

**b) sRF anti-preferred direction**

- DSI: 97%

**c) ECRF alone**

- DSI: 98%

**d) sRF + ECRF (anti-preferred direction)**

- F1/F0: 1.88

**e) sRF + ECRF (preferred direction)**

- F1/F0: 1.87

**f) orientation/direction tuning plots of ECRFs**

- 250ms
discharge regions. In turn, three-quarters of these cells, when stimulated with optimized grating patches, exhibited intermediate F1/F0 spike-response ratios (range 0.5–1.5).

Overall, the proportion of area 18 cells that exhibited F1/F0 spike-response ratios to optimized gratings >1 (67.5%) is only slightly higher than the proportion (~61%) of area 18 cells identified ("spatially separate light edge and/or dark edge response regions when tested with moving edges") as S (simple) or S1H (end-stopped simple cells) in a much larger sample of cells recorded in long, oblique penetrations through the part of area 18 located in the medial bank of the marginal sulcus (Harvey 1980; cf. Orban and Kennedy 1981). Similarly, the proportion of area 18 cells that exhibited F1/F0 spike-response ratios <1 when optimized gratings were used (32%) is only slightly lower than the combined proportion (~39%) of area 18 cells identified as C (or C1H) and B (or BH) cells by Harvey (1980). According to Harvey (1980), “both C and B cells have spatially coincident light and dark edge response regions and give mixed ON and OFF discharges when tested with stationary flashing stimuli.” Our complex cells with high (>75%) SIs are not only characterized by relatively small sRFs, but like B cells of Harvey (cf. Henry 1977; Henry et al. 1983 for C and B cells in area 17; Orban and Kennedy 1981 for C and B cells in areas 17 and 18), they have relatively small minimum discharge fields and very low background spike activities (cf. also “type 1” complex cells in area 17, Sillito 1977).

**Relationship Between Simple and Complex Neurons in Areas 17 and 18**

There is an ongoing debate about the relation between the simple and complex cells. Thus, on one hand, Hubel and Wiesel proposed that at least in the striate cortices, the relationship is hierarchical; that is, simple cells receiving direct excitatory input from the geniculate neurons constitute the first-order cortical neurons, whereas complex cells receiving their excitatory visual input via the simple cells constitute the higher order neurons. On the other hand, there is substantial evidence indicating that a substantial proportion of complex cells in area 17, like virtually all layer 4 simple cells in this area, receive direct excitatory input from the LGNd (see for review Reid et al. 2002) and thus also qualify for the status of first-order neurons. Similarly, although most area 18 neurons receiving monosynaptic input from the LGNd appear to be simple cells, a substantial proportion of area 18 cells identified as complex also receive monosynaptic inputs from the LGNd (Harvey 1980; Stone and Dreher 1973; Tretter et al. 1975; cf. for review Stone et al. 1979).

Spatially opponent ON and OFF excitation in discharge fields of simple cells in cat area 17 is invariably accompanied by spatially opponent intracortical inhibition (e.g., Ferster 1988). In some cases at least, the distinction between the “simplicity” and “complexity” appears to be based on the strength of intracortical inhibition rather than a cell’s presumed hierarchical status in the feedforward visual information-processing stream. Thus, in many simple neurons in area 17 (Borg-Graham et al. 1998; Eysel and Shevelev 1994; Sillito 1975) or simple cells located in supragranular (nonthalamorecipient) layers 2 and 3 in area 18 (Pernberg et al. 1998), the local iontophoretic blockade of GABA_A-mediated intracortical inhibition results not only in substantial increases in the magnitude of responses and background spike activity but also in enlargement of spatially distinct ON and OFF discharge regions. These enlargements result in complete or at least partial spatial overlaps of ON and OFF discharge regions and hence conversion (at least by applying classic Hubel and Wiesel’s criteria) of simple cells into complex cells.

**Changes in Phase Sensitivity During Costimulation of sRFs and Suppressive ECRFs**

In over three-quarters of cells that exhibited intermediate phase sensitivities (F1/F0 spike-response ratios in the range 0.5–1.5), ECRF-induced reduction in the response magnitude was accompanied by significant and often substantial increases in the phase sensitivity (F1/F0 spike-response ratios) of their responses to optimized gratings.

By contrast, only in about 40% of cells with either very high (simple cells with F1/F0 ratios >1.5) or very low (complex cells with F1/F0 ratios <0.5) phase sensitivities, ECRF-induced reductions in response magnitude were accompanied by significant increases in F1/F0 spike-response ratios. Since the F1/F0 ratio is theoretically bounded from above, one would expect virtual paucity of cells in which ECRF stimulation produces large changes in F1/F0 ratios among simple cells with high F1/F0 ratios. Indeed, this is the case in both area 17 (Bardy et al. 2006) and area 18 (the present study).

Overall, in area 18, cells with intermediate phase sensitivities appear to represent a sort of “bridging” group between simple cells with very high phase sensitivities and complex cells with very low phase sensitivities (cf. intermediate simple and complex categories in area 17; Bardy et al. 2006).

**Spatial Frequency Tuning of sRFs of Area 18 Neurons vs. That of LGNd Neurons**

The optimal spatial frequencies of area 18 neurons, when the stimuli are restricted to sRFs, are remarkably similar to the optimal spatial frequencies of linear responses (F1 component) of their presumed input Y-type LGNd neurons but substantially lower than those of X-type LGNd neurons (Berardi et al. 1982; Bisti et al. 1985; Derrington and Fuchs 1979; Ferster and Jagadeesh 1991; Friend and Baker 1993; Lemkuhle et al. 1980; Maffei and Fiorentini 1973; Movshon et al. 1978c; So and Shapley 1979, 1981; Troy 1983). On the other hand, whereas the...
sRFs of most area 18 neurons are spatial frequency tuned (present study; cf. also Movshon et al. 1978c), linear responses of most Y-type LGNd cells appear to be spatial frequency low pass, and their spatial frequency tuning tends to be substantially broader (Derrington and Fuchs 1979; Lehmkuehle et al. 1980; So and Shapley 1981, 1979) than that of area 18 neurons. Similarly, the spatial frequency tuning of neurons in areas 17 of both cats (cf. Bauman and Bonds 1991; Campbell et al. 1969; Frazor et al. ...
Temporal Frequency Tunings of sRFs of Area 18 Neurons Vs. Those of LGNd Neurons

Overall, the optimal temporal frequencies of most area 18 neurons (both simple and complex) appear to be substantially lower than those of Y-type or even X-type LGNd neurons (present study vs. Derrington and Fuchs 1979; Lehmkuhle et al. 1980; cf. Movshon et al. 1978c). The difference is especially pronounced in the case of low-pass neurons (cf. Derrington and Fuchs 1979). However, the optimal temporal frequencies of substantial minorities of temporal frequency-tuned simple (11/59, 18.5%) and temporal frequency-tuned complex cells (6/27, 22%) were in the same range (>7 Hz) as the optimal temporal frequencies of Y-type LGNd cells (cf. Derrington and Fuchs 1979).

It is not clear at this stage to what extent the tuning of cat area 18 neurons to low temporal frequencies is a result of their intrinsic properties and/or the reflection of slow temporal integration of the cortical network. The attenuation of response at low temporal frequencies that characterizes temporal frequency-tuned area 18 cells (present study; cf. also Movshon et al. 1978c) appears to be induced by GABA-mediated intracortical inhibition (Vidyasagar and Heide 1986). In macaque monkeys, the optimal temporal frequencies of V1 neurons also tend to be substantially lower than those of the LGNd neurons (e.g., Hawken et al. 1996), and again, the intracortical inhibition is likely to be involved.

Size of Excitatory Receptive Fields Vs. Strength of Suppression

The sizes of sRFs of area 18 neurons and the magnitudes of SIs appear to be negatively correlated (cf. similar trend in cat area 17, Bardy et al. 2006). Furthermore, in the case of cat area 2004; Maffei and Fiorentini 1973) and macaque monkeys (cf. Bredfeldt and Ringach 2002; Frazor et al. 2004; see for general earlier review see Shapley and Lennie 1985) is also substantially narrower than the spatial frequency tuning of the LGNd neurons.

Temporal Frequency Tunings of sRFs of Area 18 Neurons Vs. Those of LGNd Neurons

Overall, the optimal temporal frequencies of most area 18 neurons (both simple and complex) appear to be substantially lower than those of Y-type or even X-type LGNd neurons (present study vs. Derrington and Fuchs 1979; Lehmkuhle et al. 1980; cf. Movshon et al. 1978c). The difference is especially pronounced in the case of low-pass neurons (cf. Derrington and Fuchs 1979). However, the optimal temporal frequencies of substantial minorities of temporal frequency-tuned simple (11/59, 18.5%) and temporal frequency-tuned complex cells (6/27, 22%) were in the same range (>7 Hz) as the optimal temporal frequencies of Y-type LGNd cells (cf. Derrington and Fuchs 1979).
18 (present study) as well as in the case of cat area 17 (Sadakane et al. 2006; Sengpiel et al. 1997, 1998; Song and Li 2008; Tailby et al. 2007; Wang et al. 2009) and areas V1 (Cavanaugh et al. 2002; Ichida et al. 2007; Kapadia et al. 1999; Sceniak et al. 1999; Sceniak et al. 2001; Shushruth et al. 2009) and V2 (Shushruth et al. 2009) of macaque monkeys, the low-contrast-induced increases in the sizes of sRF were usually accompanied by significant decreases in the strength of suppressive surrounds. It has been argued that the low-contrast increases in the size of sRFs of cells in the primary visual cortices might be partially attributable to the accompanying strengthening of coupling of excitatory corticocortical synapses (Sceniak et al. 1999) and/or inherited from the contrast-dependent size tuning of the LGNd neurons (cf. Ozeki et al. 2004; Solomon et al. 2002; Tailby et al. 2007; see however, Sceniak et al. 2006).

**Size of Excitatory Receptive Fields of Primary Visual Cortex Neurons: Relation to the Sizes of Excitatory Receptive Fields of LGNd Neurons**

When the high-contrast optimized grating patches are used, the diameters of excitatory sRFs of simple and complex area 18 cells are ~2.5- to 3.5-fold larger than those of their visuotopic counterparts in area 17 (present study vs. Bardy et al. 2006; DeAngelis et al. 1992; Jones et al. 2000; Maffei and Fiorentini 1976; Sengpiel et al. 1997). Consistent with this, the optimal spatial frequencies of high-contrast gratings for exciting simple (mean, 0.26 ± 0.17 cycle/deg) and complex area 18 neurons (mean, 0.21 ± 0.14 cycle/deg) are ~2- to 3.5-fold lower than those for exciting their visuotopic counterparts (simple: mean 0.5 ± 0.3 cycle/deg; complex: mean, 0.7 ± 0.4 cycle/deg) in area 17 (cf. Bardy et al. 2006; Berardi et al. 1982; Bisti et al. 1985; Movshon et al. 1978a, 1978b, 1978c).

It remains unclear to what extent the difference between the sizes of the sRFs of area 17 neurons vs. those of area 18 neurons is related to the paucity of direct X-type LGNd inputs to area 18 (see Freund et al. 1985; Humphrey et al. 1985; Stone and Dreher 1973; for review see Payne and Peters 2002). Thus, although at high contrast, at least, the sRFs of Y-type LGNd neurons are only slightly larger than those of X-type LGNd neurons (e.g., Jones et al. 2000), the sRFs of area 17 neurons measured with high-contrast circular patches are on average approximately threefold larger than those of LGNd neurons with receptive fields at corresponding eccentricities (Bardy et al. 2006; Jones et al. 2000), whereas the sRFs of area 18 neurons identified as simple and located in the principal thalamorecipient layer 4 (and thus likely to receive monosynaptic inputs from the LGNd) are approximately eightfold larger than those of Y-type LGNd neurons with receptive fields at corresponding eccentricities (present study vs. Jones et al. 2000).

At both low- and high-contrast conditions, the sRFs of macaque V2 neurons are also approximately twofold larger than these of V1 neurons with receptive fields at corresponding eccentricities (e.g., Shushruth et al. 2009; see for review Sincich and Horton 2005). This consistent with this, the spatial frequencies optimal for exciting area V2 neurons, are approximately two- to threefold lower (mean, 1.4 cycle/deg; range <0.1–7 cycle/deg) than those (mean 3–4 cycle/deg; range up to 15 cycle/deg) for exciting area V1 neurons (area V1: De Valois et al. 1982; Foster et al. 1985; Levitt et al. 1994). Although the sizes of sRFs of V2 neurons located in different compartments (thick, thin, and pale cytochrome oxidase “stripes”; see for review Sincich and Horton 2005) are not significantly different from each other, the sRFs of neurons in the compartments that receive (indirectly) the input from the LGNd cells with larger receptive fields (magnocellular cells) tend to be substantially larger (Shushruth et al. 2009).

**Properties of ECRFs of Area 18 Neurons Vs. Those of Excitatory Receptive Fields of LGNd Neurons**

The spatial frequency tunings of the ECRFs of both simple and complex area 18 neurons are very comparable to the spatial frequency tunings of the excitatory receptive fields of LGNd neurons (cf. Derrington and Fuchs 1979; Lehmkule et al. 1980; Maffei and Fiorentini 1973; So and Shapley 1981). Similarly, the ECRFs of most area 18 neurons exhibited a degree of orientation tuning very comparable to that of the orientation tuning of Y-type LGNd neurons (e.g., Shou and Leventhal 1989). However, a lack of temporal frequency dependency of strength of suppression induced by the ECRF stimulation contrasts sharply with clear temporal frequency tuning of excitatory receptive fields of LGNd neurons (cf. Derrington and Fuchs 1979). To our knowledge, very little is known about the temporal frequency tuning of the suppressive surrounds of LGNd neurons (cf. Ishikawa et al. 2010). It is possible that the ECRFs of LGNd neurons are also characterized by poor temporal frequency tuning (see ECRFs of Neurons in Cat Primary Visual Cortex: “Inheritance” From the Feedforward Input).

**Properties of ECRFs vs. Those of sRFs of Neurons in Cat Primary Visual Cortex**

**Spatial frequency tuning.** In the case of cat area 17 neurons, the optimal spatial frequencies of suppressively most effective ECRF stimuli tend to be close to the spatial frequencies of gratings evoking the strongest excitatory responses from the sRFs, but the spatial frequency tunings of the ECRFs tend to be broader than those of the sRFs (e.g., DeAngelis et al. 1994; Li and Li 1994; cf. also Ishikawa et al. 2010). Similarly, in the case of area 18 neurons (present study), the spatial frequencies of ECRF gratings, which produced the strongest suppressive effects, were in most cases very close to the spatial frequencies of sRF-confined gratings, which produced maximal excitatory responses. Whereas cells with low-pass sRFs exhibited strong ECRF-induced suppression at low spatial frequencies, the spatial frequency tunings of the ECRFs of both simple and complex area 18 neurons were substantially broader than those of their excitatory sRFs. In some cases, the ECRF stimuli of spatial frequency exceeding spatial frequency high cutoff of stimuli evoking excitation from sRF were very effective suppressors of the sRF-induced responses.

The spatial frequency tuning of suppression evoked by stimulation of CRFs of area 17 neurons with stimuli oriented perpendicularly to the stimuli evoking maximal excitatory responses (so-called “cross-orientation suppression”) also tends to be much broader than that of the excitatory responses evoked by stimuli confined to the CRFs (e.g., Buman and Bonds 1991; Bonds 1989; DeAngelis et al. 1992; Morrone et al. 1982). Furthermore, in the case of cross-
oriented stimuli confined to CRFs, quite often substantial or even maximal suppression is evoked by stimuli whose spatial frequency exceeds the high cutoffs of stimuli evoking excitatory responses (Bauman and Bonds 1991; De Valois and Tootell 1983).

**Temporal frequency tuning.** In sharp contrast to clear temporal frequency tuning of sRFs, there was a virtual lack of temporal frequency dependency (at least over the range of temporal frequencies studied) of the strength of suppression tuning induced by the ECRF stimulation of most area 18 neurons. It is worth noting that the temporal frequency tuning of cross-orientation suppression evoked by stimulation of the CRFs of area 17 neurons is also much broader than that of the excitatory responses evoked by stimuli confined to the CRFs (e.g., Morrone et al. 1982), and the peak suppression occurs at temporal frequencies substantially higher than those evoking maximum excitation (Allison et al. 2001). Indeed, the temporal frequency tuning and the temporal frequencies evoking peak cross-orientation suppression in area 17 cells (Allison et al. 2001) are very similar to those evoking peak ECRF suppression in area 18 cells (present study).

**Orientation tuning.** The ECRFs of most area 17 (Akasaki et al. 2002; Bardy et al. 2006, 2009; Naito et al. 2007; Nelson and Frost 1978; Sengpiel et al. 1997; Sun et al. 2004; see for review Seriès et al. 2003) and area 18 neurons (present study) exhibited some degree of orientation tuning, and in most of those, the suppression of the sRF-induced spike responses was strongest when the gratings in the sRF and ECRF were iso-oriented. However, orientation tunings of ECRFs of areas 17 (Akasaki et al. 2002; Bardy et al. 2006, 2009; Naito et al. 2007; Sengpiel et al. 1997; see for reviews Seríes et al. 2003) and area 18 neurons (present study; cf. Sun et al. 2004) are invariably substantially broader than those of their sRFs.

**ECRFs of Neurons in Cat Primary Visual Cortex:**

**“Inheritance” From the Feedforward Input**

Putative mechanisms underlying the silent surround suppression in area 17 neurons of cats and macaques include 1) intrinsic intracortical excitation and inhibition and 2) intrinsic inhibition driven by the feedback from the “higher order” extrastriate areas, as well as 3) a reduction in the strength of feedforward excitatory drive from the LGNd (see for reviews Angelucci and Bressloff 2006; Bardy et al. 2009; Ishikawa et al. 2010; Seriès et al. 2003; Walker et al. 2000; Webb et al. 2005).

It has been suggested in the past that relative broadness of the spatial frequency tuning and broadness of orientation tunings of the silent suppressive regions of area 17 neurons indicate the excitatory convergence of many cortical neurons on the intrinsic inhibitory interneurons (e.g., DeAngelis et al. 1994; Heeger 1992). Indeed, until recently it was believed that intrinsic intracortical inhibition is the principal mediator of the silent surround suppression in the primary visual cortices. However, the local iontophoretic blockade of GABA$_A$-mediated intracortical inhibition reduces, but does not abolish, the silent suppression in cat area 17 (Ozeki et al. 2004).

Although there is substantial evidence indicating that the intracortical inhibition contributes to suppressive ECRFs of area 17 neurons (e.g., Ozeki et al. 2009), several lines of evidence are consistent with idea that suppressive ECRFs of neurons in areas 17 and 18 might be at least partially “inherited” from their LGNd inputs. Thus silent suppressive ECRFs are present in the receptive fields of the majority of cat (e.g., Bonin et al. 2005; Cleland et al. 1983; Dreher and Sanderson 1973; Girardin et al. 2002; Hubel and Wiesel 1961; Levick et al. 1972; Sadakane et al. 2006; Singer and Creutzfeldt 1970) and macaque LGNd neurons (see for review Alitto and Usrey 2008), and they exhibit a substantial degree of orientation selectivity (Naito et al. 2007; Sun et al. 2004). The majority of cat LGNd neurons (including the majority of Y-type LGNd neurons) have large silent suppressive receptive fields when the stimuli are presented via the nondominant eye (Sanderson et al. 1969; Singer 1970; see for review Wang et al. 1994). Furthermore, as mentioned earlier, the spatial frequency and orientation tunings of the ECRFs of area 17 and 18 neurons are substantially broader than those of their excitatory sRFs but very similar to those of their presumed LGNd input cells.

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**DISCLOSURES**

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