Response Facilitation From the “Suppressive” Receptive Field Surround of Macaque V1 Neurons

Jennifer M. Ichida,1*,i Lars Schwabe,1,2*, Paul C. Bressloff,2 and Alessandra Angelucci1
1Departments of Ophthalmology, Moran Eye Center and 2Mathematics, University of Utah, Salt Lake City, Utah

Submitted 16 March 2007; accepted in final form 8 August 2007

Ichida JM, Schwabe L, Bressloff PC, Angelucci A. Response facilitation from the “suppressive” receptive field surround of macaque V1 neurons. J Neurophysiol 98: 2168–2181, 2007. First published August 8, 2007; doi:10.1152/jn.00298.2007. In primary visual cortex (V1), neuronal responses to optimally oriented stimuli in the receptive field (RF) center are usually suppressed by iso-oriented stimuli in the RF surround. The mechanisms and pathways giving rise to surround modulation, a possible neural correlate of perceptual figure-ground segregation, are not yet identified. We previously proposed that highly divergent and fast-conducting top-down feedback connections are the substrate for fast modulation arising from the more distant regions of the surround. We have recently implemented this idea into a recurrent network model (Schwabe et al. 2006). The purpose of this study was to test a crucial prediction of this feedback model, namely that the suppressive “far” surround of V1 neurons can be facilitatory under conditions that weakly activate neurons in the RF center. Using single-unit recordings in macaque V1, we found iso-orientation far-surround facilitation when the RF center was driven by a low-contrast stimulus and the far surround by a small annular stimulus. Suppression occurred when the center stimulus contrast or the size of the surround stimulus was increased. This suggests that center-surround interactions result from excitatory and inhibitory mechanisms of similar spatial extent, and that changes in the balance of local excitation and inhibition, induced by surround stimulation, determine whether facilitation or suppression occurs. In layer 4C, the main target of geniculocortical afferents, lacking long-range intracortical connections, far-surround facilitation was rare and large surround fields were absent. This strongly suggests that feedforward connections do not contribute to far-surround modulation and that the latter is generated by intra-cortical mechanisms, likely involving top-down feedback.

INTRODUCTION

In primary visual cortex (V1), neurons respond best to oriented stimuli of optimal size inside their receptive field (RF) and are usually suppressed by iso-oriented larger stimuli involving the extra-classical RF surround (Allman et al. 1985; Blakemore and Tobin 1972; DeAngelis et al. 1994; Gilbert and Wiesel 1990; Nelson and Frost 1978). The mechanisms and pathways giving rise to surround modulation in V1, a phenomenon that could underlie perceptual “figure-ground” segregation (Knierim and Van Essen 1992; Lamme 1995), are not yet identified and have recently been the focus of much debate. A V1 neuron’s optimal stimulus size is larger at low than at high contrast (Kapadia et al. 1999; Sceniak et al. 1999; Sengpiel et al. 1997). Here we refer to the radius of a high- or low-contrast stimulus evoking the largest response from a V1 neuron as the neuron’s high- or low-contrast summation RF (sRFhigh or sRFlow, respectively, and to the region between these two sRF components as the “near” surround. We refer to the region beyond the sRFlow as the “far” surround (Fig. 1A).

Previous studies have shown that iso-orientation surround suppression is fast (Bair et al. 2003) and long range (Cavanaugh et al. 2002a; Levitt and Lund 2002; Sceniak et al. 2001), arising far beyond the monosynaptic range of horizontal connections; the latter only extend as far as the size of a V1 cell’s sRFlow (Angelucci et al. 2002b) (Fig. 1A). Polysynaptic chains of horizontal connections are also too slow (Bringui`er et al. 1999; Girard et al. 2001; Grivvald et al. 1994; Slovin et al. 2002) to account for the fast onset of suppression from the far surround (Bair et al. 2003). Thus we recently proposed (Angelucci and Bressloff 2006; Angelucci and Bullier 2003) that highly divergent (Angelucci et al. 2002b) and fast-conducting (Girard et al. 2001) extrastriate feedback connections to V1 are the substrate of far-surround modulation (Fig. 1A). Recently we have implemented this idea into a recurrent network model (Schwabe et al. 2006). In this model, similar to a previous network model (Dragoi and Sur 2000; Somers et al. 1998), center-surround interactions result from cortical excitatory and inhibitory mechanisms of similar spatial extent and an asymmetry in the functional threshold and response gain between excitatory and inhibitory neurons. As a result of this asymmetry, inhibitory neurons are essentially silent for weak visual inputs, causing the surround to have a facilitatory effect; conversely, strong inputs cause the activity of inhibitory neurons to increase rapidly and surround suppression to occur. Unlike the model of Somers et al. (1998), in which surround modulation was generated solely by horizontal connections, our model assumed fast suppression from the far surround to occur via top-down feedback connections targeting excitatory neurons in the near surround and in the RF center sending monosynaptic horizontal connections to local inhibitors in the RF center (Fig. 1B). A central prediction of this feedback model is that the “suppressive” far surround of V1 neurons can be facilitatory when the RF center is driven by a low-contrast stimulus and the surround by a small annular stimulus. On the other hand, far-surround suppression is predicted under conditions that strongly activate neurons in the RF center, such as when the latter is driven by a high-contrast stimulus or the surround by a large stimulus.

Contrast-dependent iso-orientation facilitation from the far surround, as predicted by our model, has not been previously described experimentally. Physiologically, iso-orientation sur-
The receptive field (RF) center and surround of V1 neurons: presumptive anatomical substrates and mechanisms. A: diagram of the different components of the RF center and surround of a typical V1 neuron: 1) the high-contrast summation RF (sRF_high) or RF center (area inside dashed ring) is measured by presenting a high-contrast grating patch of increasing radius and defined as the stimulus radius at the neuron’s peak response; 2) the low-contrast summation RF (sRF_low; area inside solid ring) is measured and defined as the sRF_low but using a low-contrast grating patch of increasing radius; 3) the “near” surround (light gray area) is the region between the sRF_high and the sRF_low, in Schwabe et al. (2006), the RF center is defined as the minimum response field (mRF) of the neuron, and the near surround as the region between the mRF and the sRF_low.

1 Note that, whereas in Fig. 1A the RF center is the sRF_high and the near surround the region between the sRF_high and the sRF_low, in Schwabe et al. (2006), the RF center is defined as the minimum response field (mRF) of the neuron, and the near surround as the region between the mRF and the sRF_low.

round facilitation has previously been shown to occur only following stimulation of surround regions near the RF center, especially with low-contrast stimuli (Kapadia et al. 1995, 1999; Polat et al. 1998; Sadakane et al. 2006; Sceniak et al. 1999). Similarly, psychophysically surround “facilitation” has commonly been observed in experiments where contrast detection thresholds were measured in the presence or absence of collinear iso-oriented flanks near the central grating (Kapadia et al. 1995; Polat and Sagi 1993, 1994). Instead, iso-oriented stimuli in the RF center and far surround have typically been shown to be suppressive, even at low contrast (Cavanaugh et al. 2002b; DeAngelis et al. 1994; Levitt and Lund 1997; Sengpiel et al. 1998). Perceptually, subjects have been shown to judge the apparent contrast of a central grating embedded in an iso-oriented surround grating to be lower than in the absence of the surround. In other words, when psychophysical experiments have been performed suprathreshold, the most commonly observed effect of an iso-oriented surround grating has been “suppression,” even when the central grating was of lower contrast than the surround (Cannon and Fullenkamp 1991, 1993; Ejima and Takahashi 1985; Xing and Heeger 2001). These previous studies may have failed to observe far-surround facilitation because they used large stimuli involving both the near and far surround, a stimulus that in our model, like in the experimental data, generates suppression (see legend of Fig. 1B). In particular, because the strength of surround suppression has been shown to be highest in the near than in the far surround (Levitt and Lund 2002; Walker et al. 1999), in those previous studies, stimulation of the region of maximal surround strength may have masked the modulatory influences of the weaker far surround.

In this study, using a visual stimulus designed to minimize afferent stimulation of neurons in the near surround and to isolate the modulatory signals from the far surround, we observed far-surround facilitation or suppression under conditions of weak or strong activation of the RF center, respectively. These results, consistent with the predictions of the model proposed by Schwabe et al. (2006), suggest that center-
surround interactions in V1 result from excitatory and inhibitory mechanisms of similar spatial extent and that changes in their balance determine whether the interactions are suppressive or facilitatory.

**METHODS**

**Surgical preparation and recording**

We recorded extracellularly in V1 of 5 anesthetized (sufentanil citrate, 4–12 μg·kg⁻¹·h⁻¹) and paralyzed (vecuronium bromide, 0.1 μg·kg⁻¹·h⁻¹) macaque monkeys (*Macaca fascicularis*). All procedures conformed to the guidelines of the University of Utah Institutional Animal Care and Use Committee. Animals were artificially resiredated with a 30:70 mixture of O₂ and N₂O. Electrocardiogram was continuously monitored, end tidal CO₂ was maintained between 30 and 33 mmHg, rectal temperature near 37°C, and blood oxygenation near 100%. Single-unit recordings were made with glass-coated tungsten microelectrodes (4–6 MΩ; FHC, Bowdoin, ME) in the opercular region of V1. Spikes were conventionally amplified, filtered, and sampled at 22 kHz by a dual processor G5 Power Macintosh computer running a custom software (EXPO) written and kindly donated to us by Dr. Peter Lennie. Spikes were displayed on a monitor, and templates for discriminating spikes were constructed by averaging multiple traces. The timing of waveforms that matched the templates was recorded with an accuracy of 0.1 ms.

**Visual stimuli**

Sinusoidal gratings of the same mean luminance as the background were generated by the same software and computer that recorded spikes and were displayed on a calibrated monitor (Sony GDM-C520K) refreshed at 100 Hz of mean luminance ~45.7 cd/m², at a viewing distance of 57 cm (at which the screen subtended a visual angle of 28°). For each cell, we first determined the preferred orientation and spatial and temporal frequency. Then the size and center of the minimum response field (mRF) were carefully located quantitatively using a grating patch of 0.1° radius. Using a grating patch matched to the cell’s mRF size, we generated a contrast response function for each cell and used the individual cell responses to tailor the contrast values for the remaining stimuli. High-contrast values were chosen to be <90% of response saturation for the cell (typically between 50 and 80% contrast); low-contrast values were generally chosen to be those eliciting ≤50% of the maximum response in the contrast-response function but still eliciting a reliable response (at least >2 SDs greater than the spontaneous firing rate; typically between 4 and 30%; the cell in Fig. 2C was one exception). Then we performed spatial summation measurements at two contrast levels using circular patches of drifting gratings of increasing radius centered over the cell’s mRF. The patch radius ranged from 0.1 to 14° and consisted of 11 radii (0.1, 0.2, 0.4, 0.8, 1.2, 1.6, 2.5, 5, 7.5, 10, and 14°). We refer to this experimental protocol as the “patch-size experiment.” From these patch-size tuning curves at high and low contrast, we extracted for each cell the patch radius at peak response (i.e., the size of the sRF<sub>high</sub> and sRF<sub>low</sub>; see Fig. 1A). The latter were then used to create the center and far-surround stimuli used in the “annulus-size experiment.” In the latter experimental protocol, visual stimuli consisted of a center grating the size of the cell’s sRF<sub>high</sub> surrounded by an annular grating with a fixed outer radius (14°) and an inner radius of decreasing size, from 14° to a size no smaller than the radius of the cell’s sRF<sub>low</sub>, often larger (we used 9 annulus inner radii). Thus there was always a blank annulus (covering the near surround), of the same luminance as the background interposed between the center grating patch and the surround annular grating. For this stimulus, we used the same two contrast values, high and low, as used for the patch-size experiment, with the contrast of the center and surround grating being controlled independently. Control conditions included a blank screen (same luminance as the background) for a measure of spontaneous activity, a center-alone condition for a baseline response and a surround annulus-alone condition to ensure that the surround stimulus alone did not drive a response. Stimuli were presented randomly in a block-wise fashion with a duration of 2 s and a 2-s inter-stimulus interval. Each block was repeated 10 times, and the responses across blocks were averaged to calculate the mean firing rate.

**Histology and track reconstruction**

Electrolytic lesions (1 μA for 30 s, tip negative) were made along the length of each electrode penetration to assign laminar location to recorded V1 neurons. At the end of the recording session, the animal was killed with sodium pentobarbital and perfused transcardially with saline, followed by 4% paraformaldehyde. Tissue blocks containing the electrode penetrations were cryoprotected and then sectioned at 40 μm on a freezingmicrotome. Alternate sections were stained for Nissl or cytochrome oxidase.

Electrode tracks were reconstructed by drawing lesions on each individual section using a camera lucida attached to a light microscope, and individual sections were aligned using vascular landmarks and section outlines as fiducial marks.

**Data analysis and statistical model fitting**

The spatial summation data of V1 cells are typically fit with the difference (or the ratio) of the integral of two Gaussians (DOG or ROG models) (Cavanaugh et al. 2002a; Sceniak et al. 2001): a center excitatory Gaussian representing the RF center and an overlapping but spatially broader inhibitory Gaussian representing the suppressive surround. In these models, the spatially broader inhibition dominates outside the excitatory RF center, and thus they could not capture the far-surround facilitation observed in our annulus-size experiments. Because far-surround facilitation is the main response property that we wished to quantify in this study and to extract more robust measures of patch radius, annulus width, or inner radius at suppression and facilitation onset, needed for our quantitative analysis, we fit the summation data from both the patch-size and annulus-size experiments with a “thresholded” (t)-DOG model (see Figs. 2 and 4). This statistical model describes excitation and inhibition as two Gaussians of identical spatial scales, with the inhibition becoming effective after a threshold is crossed. Specifically, the responses to a stimulus s in the patch-size and annulus-size experiments were fitted with the variable R<sub>Exc</sub> in the following statistical model

\[
U_{th} = W_{th} \int s(x) \cdot w(x) \, dx
\]

\[
R_{th} = \max(0, U_{th} - T_{th})
\]

\[
U_{Exc} = I_{s} - R_{th} + W_{Exc} \int s(x) \cdot w(x) \, dx
\]

\[
R_{Exc} = \max(0, U_{Exc})
\]

Here, the variables R<sub>Exc</sub> and U<sub>Exc</sub> and R<sub>th</sub> and U<sub>th</sub> correspond to the firing rate and inputs of a center excitatory and inhibitory neuron, respectively. The weight function used to model the spatial integration is given as

\[
w(x) = w(|x|) = \exp(-|x|^2/(2\sigma^2))
\]

where \(\sigma\) determines the scale of the spatial integration, which was performed in two dimensions. This weight function depends only on the distance, and is the same for both the integration of the center...
excitatory and inhibitory neuron. Five free model parameters were used to fit the data: $I_C$ (size-independent additive input to the center excitatory neuron), $T_{inh}$ (threshold for inhibition), $W_{exc}$ (weight of excitation), $W_{inh}$ (weight of inhibition), and $\sigma$ (scale of the spatial integration). The values of these free-model parameters were optimized to provide the best least-square fit to the data. In this model, the threshold for inhibition was the main determinant of the optimal patch radius and annulus width for spatial summation. Analysis was performed on both the raw data and the model fits that yielded similar results. In the RESULTS, we report the analysis based on the statistical model fits unless otherwise specified. Statistical tests used to determine statistical significance are reported in the RESULTS.

FIG. 2. Patch-size and surround annulus-size tuning curves for 4 representative V1 neurons showing far-surround facilitation. A–D, left: responses (mean firing rate) of 4 V1 complex cells as a function of the radius of a circular optimal grating patch (stimulus shown in D). Black and gray curves, responses to a high- and low-contrast stimulus, respectively (contrast is indicated in each panel). Here and in the right-hand graphs, the dashed horizontal lines indicate the cell’s mean spontaneous firing rate, the solid lines represent fit to the data (dots) using the statistical thresholded difference of Gaussian (t-DOG) model (see METHODS), and error bars are SE. Arrows, stimulus radius at the peak (maximum) response at high (black, sRF$_{high}$) and low (gray, sRF$_{low}$) contrast. Icons at the top of A are as in Fig. 1A with orange areas indicating RF and surround components that are activated at the indicated point (arrows) in the size-tuning curves. Near-surround facilitation strength (see Fig. 5A for a definition) for each cell was: A, 122%; B, 174%; C, 0%; D, 17%. Right: responses of the same 4 cells as a function of the width of the surround annular grating (stimulus shown in D). Black, red, and gray curves, responses to a high-contrast center and surround stimulus (HH), a low-contrast center and high-contrast surround stimulus (LH), and to a low-contrast center and surround stimulus (LL), respectively. High- and low-contrast values used were the same as indicated for the respective patch-size tuning curves to the left. Arrowheads, annulus width at suppression onset (i.e., at 10% reduction of the cell’s response to center-only stimulation) in each contrast condition. Triangles, responses to center-only stimulation. Blue squares, response to the surround stimulus of smallest inner diameter presented alone. For the cells in B and C, we only measured responses in the HH and LL conditions. The cells in B and D showed <10% suppression in the LL condition. For the cell in C, the mean firing rate in response to a 100 or 4% contrast center grating was similar, but the lower-contrast grating evoked far-surround facilitation. A: far-surround facilitation strength (see Fig. 5B for a definition): 0% (HH), 71% (LH), 82% (LL); center grating radius: 0.1°; smallest gap radius: 0.4°. B: facilitation strength: 0% (HH), 35% (LL; note that in the raw data the facilitation strength = 48%); center grating: 0.2°; smallest gap radius: 0.7°. C: facilitation strength: 0% (HH), 24% (LL); center grating: 0.2°; smallest gap radius: 1.5°. D: facilitation strength: 0% (HH), 0% (LH; in the raw data the facilitation strength = 29%); 20% (LL); center grating: 0.2°; smallest gap radius: 0.4°.
RESULTS

The goal of this study was to test the central mechanism that in our network model determines the sign (i.e., facilitation or suppression) of the modulatory effect of the surround, and a specific prediction that stems from such a mechanism. Specifically, in the model, the surround modulates the balance of local excitation/inhibition in a manner that reflects the total amount of excitation reaching the center excitatory and inhibitory neurons from different sources (i.e., feedback, feedforward, and horizontal connections). High levels of excitation generate suppression, whereas low levels of excitation generate facilitation. A model’s prediction that stems from this mechanism is that when the RF center is stimulated with a low-contrast (i.e., weak) grating, a small (i.e., weak) iso-oriented grating in the surround generates facilitation, whereas a large (i.e., strong) surround grating generates suppression. On the other hand, the same small surround grating that facilitates the response to a low-contrast center grating will instead suppress the response to a high contrast center grating; this is because the latter stimulus is sufficiently strong to activate the local inhibitory neurons (Fig. 1B). It also follows that larger (i.e., strong) gratings in the surround are required to suppress the response to lower-contrast gratings in the RF center. Contrast-dependent iso-orientation surround facilitation and shift in the onset of suppression toward larger stimuli have previously been shown to occur for the near-surround region (Sceniak et al. 1999). In this study, we have tested the model’s prediction that both phenomena can also be induced by stimuli in the far surround. Furthermore, as in the model far-surround modulation occurs via inter-areal feedback connections, we designed a center-annular surround stimulus that allowed us to isolate the feedback contribution to far-surround modulation.

Contrast-dependent spatial summation and iso-orientation facilitation from the near and far surround: example responses

We measured area-summation curves for 80 cells in macaque parafoveal V1 (2–8° eccentricities) by stimulating each cell with circular patches of drifting sinusoidal gratings of increasing radius at high and low contrast and measuring the cell’s response as a function of the patch radius (the “patch-size experiment”). As previously reported, cells increased their response with increasing patch radius up to a peak and then showed response suppression or asymptoted at the peak for further increases in patch radius (Fig. 2, A–D, left). Confirming previous reports (Cavanaugh et al. 2002a; Sceniak et al. 1999; Sengpiel et al. 1997), for most cells (e.g., cells in Fig. 2, A and B) the patch radius at peak response (or sRF, black and gray arrows in Fig. 2), was larger at low than at high stimulus contrast. In other words, at low stimulus contrast, most patch-size tuning curves showed iso-orientation near-surround facilitation, and a shift in the onset of suppression toward larger stimuli. The cell in Fig. 2C did not show either phenomenon, whereas the cell in Fig. 2D showed both phenomena in the raw data, but the t-DOG model fit did not capture the facilitation.

We asked whether a similar contrast-dependent increase in spatial summation could be induced by stimuli in the far surround. For 70 neurons from which we had obtained patch-size tuning curves, we tested the effects of far-surround stimuli. Our far-surround stimuli were designed to minimize afferent stimulation of neurons in the near surround (i.e., of neurons sending horizontal connections to the center neuron) and to isolate the modulatory signals from the far surround (presumed to be mediated by feedback connections, see Fig. 1A). These stimuli consisted of a center circular grating patch the size of the neuron’s sRF_{high} and an annular surround grating. The outer radius of this annulus was fixed at 14°, and the inner radius was systematically decreased from 14° to a size ≳ sRF_{low} of the cell (decreasing the inner radius of the annulus corresponds to increasing the annulus width), so that there was always a blank gap between the center and surround gratings (stimulus shown Fig. 2D, right). We refer to this stimulus configuration as the “annulus-size experiment.” Note that to generate this center-annular surround stimulus in the course of the experiment, we used sRF sizes derived from the raw patch-size tuning data not from the t-DOG fits to these data. We used three different contrast conditions for this center-annular surround stimulus: high contrast center and surround (HH), low-contrast center and high contrast surround (LH), and low-contrast center and surround (LL). High- and low-contrast values were the same as used to measure patch-size tuning curves for the same neurons. Whenever possible we recorded the cell’s response to all three contrast conditions (e.g., cells in Figs. 2, A and D, and 4, right); however, some cells (e.g., cells in Fig. 2, B and C) were only tested with two contrast conditions (HH and LH or LL).

As with the patch-size experiments, in the annulus-size experiments at low stimulus contrast (LH and/or LL conditions) many cells showed iso-orientation far-surround facilitation, and a shift in the onset of suppression toward larger surround stimuli. Figure 2, A–D (right) shows annulus-size tuning curves for four example cells which in the low-contrast conditions (red and gray curves), but not in the high-contrast condition (black curve), showed response facilitation followed, in most cases, by suppression as the surround annulus width was progressively increased. Reflecting the variability in the strength of response facilitation seen in the population (and quantified in the next section of RESULTS), cells in Fig. 2, A and B, showed stronger facilitation than those in C and D. A few cells (9%) showed far-surround facilitation at low contrast but no far-surround suppression in any contrast condition (not shown). Peristimulus time histograms (PSTHs) for the example cells from Fig. 2 show that the facilitation happens early in the response (orange curve in Fig. 3, right) and is sustained past the response to the center-only stimulus (black curve in Fig. 3, right). No facilitation is seen in the PSTH in response to a high contrast center stimulus presented together with a high contrast surround stimulus (orange curve in Fig. 3, left) of a size that evoked facilitation at low contrast.

Far-surround facilitation originated well outside the RF center as the surround annulus of smallest inner diameter was always outside the neuron’s sRF_{low} and when presented alone, did not evoke any response from the cell (Fig. 2, blue squares). For example, the radius of the sRF_{high} and sRF_{low} for the cell in Fig. 2A measured 0.1 and 0.4°, respectively; far-surround facilitation for this cell occurred 6.2° away from the RF center, i.e., 5.8°, outside the sRF_{low} of the cell. Similarly, the sRF_{low} for the cells shown in Fig. 2, B–D, measured 0.2 or 0.4°, and far-surround facilitation occurred 11.4–12° away from the RF center, i.e., >10° outside the cells’ sRF_{low}. Furthermore, if facilitation were caused by direct stimulation of the RF center by the sur-
round grating, one would expect it to occur closer to the RF than suppression. To the contrary, we found that for all cells showing both far-surround facilitation and suppression, the facilitation occurred farther from the RF center than the suppression (e.g., Fig. 2, A–D, right; this observation is quantified in the next section of RESULTS and in Fig. 5D). Thus we are confident that far-surround facilitation was not due to stimulation of the RF center by the surround grating.

In addition to iso-orientation far-surround facilitation, most cells (up to 83% see following text) in the lower contrast conditions also showed a shift in the onset of
suppression toward larger surround widths. In other words, larger stimuli in the surround were needed in the lower contrast condition than in the higher-contrast condition to evoke suppression (compare black, red and gray arrowheads in Fig. 2, A and D); for some cells, even the largest surround stimulus was not sufficient to evoke significant suppression at low contrast (e.g., Fig. 2, B and D). The cell in Fig. 2C was 1 of 11 cells in our sample for which there was no contrast-dependent shift in the onset of far-surround suppression or the shift occurred in the opposite direction. This cell also showed no shift in the patch-size experiment (see Fig. 2C, left). In Fig. 2 and in the remainder of our analysis, we defined onset of suppression as a 10% reduction in the cell’s response to center-only stimulation. However, we performed the same analysis also using as definition of suppression onset a 10% reduction in the cell’s largest response (whereas for most cells in the HH condition, the largest response and the center-only response coincided, this was not the case in the low-contrast conditions that evoked facilitation). Using the latter definition of suppression onset abolished the shift effect only in a few cells, but at the population level we found the same result, i.e., a shift of suppression onset toward larger surround widths at low contrast (see following text). About 40% of cells showed no far-surround facilitation in either low-contrast conditions, but showed a contrast-dependent shift in the onset of suppression toward larger annulus widths (Fig. 4).

Contrast-dependent iso-orientation facilitation from the near and far surround: population statistics

Near- and far-surround facilitation at low contrast in our network model are generated by a common mechanism, i.e., surround modulation of the local excitation/inhibition balance (Schwabe et al. 2006). However, in the model, the anatomical circuits generating near- and far-surround facilitation are different. This is also suggested by previous experimental data. Specifically, although near-surround facilitation has been proposed to be mediated by feedforward (Kremers et al. 2001; Nolt et al. 2004; Solomon et al. 2002) and/or horizontal (Schwabe et al. 2006; Somers et al. 1998) connections, far-surround facilitation is thought to be generated by intracortical mechanisms involving feedback and possibly horizontal connections (Schwabe et al. 2006). To gain some insights into whether similar or different mechanisms and substrates underlie near- and far-surround facilitation, we first quantified and compared the distributions of the strength of near- and far-surround facilitation for a population of 70 cells.

The strength of near-surround facilitation was calculated from the low-contrast patch-size tuning curve (see Fig. 5A, inset) as

\[
\frac{(R_{\text{peak}} - R_{\text{ctr}})}{R_{\text{ctr}}} \times 100
\]

where \( R_{\text{peak}} \) is the maximum response at low contrast and \( R_{\text{ctr}} \) is the response to a low-contrast stimulus the size of the
cell’s sRF\textsubscript{high}. A facilitation strength = 0 indicates no facilitation. The strength of far-surround facilitation was calculated from the annulus-size tuning curve (Fig. 5B, inset) as indicated in the preceding text for near-surround facilitation, but here $R_{\text{Peak}}$ was the maximum response in a given contrast condition and $R_{\text{Ctr}}$ was the response to center-only stimulation in the same contrast condition. The analysis for far-surround facilitation was performed on the t-DOG fits to the annulus-size data. The analysis for near-surround facilitation, instead, was performed on the raw data rather than on the model’s fits because the t-DOG model, although it accurately captured the annulus-size tuning curves, tended to overestimate the strength of facilitation from the near surround. About 60% of the cells for which we had both annulus-size and patch-size data ($n = 70$) showed >10% response facilitation from the near surround at low contrast (Fig. 5A; 54% of cells showed >15% facilitation). Similarly, we observed >10% far-surround facilitation in 61% of cells at low contrast (Fig. 5B; 50% of cells showed >15% far-surround facilitation), but little far-surround facilitation was seen at high contrast (4% of cells showed >15% facilitation in the HH condition). However, facilitation from the near surround was stronger (mean for cells with near facilitation strength >15% = 63.9 ± 8.3%) than from the far surround (mean for cells with far facilitation strength >15% = 31.8 ± 2.25%). The t-DOG model slightly underestimated far facilitation strength; in the raw data 57% of cells showed far facilitation strength >15% with a mean value of 43.2 ± 4.2%, and ranging up to 158%. Thus near- and far-surround facilitation showed similar distributions but differed in strength. However, only a fraction of cells that showed near-surround facilitation also showed far-surround facilitation and vice versa. Specifically, 51% of cells showing near facilitation strength >15% also showed far facilitation strength >15%, and only 57% of cells showing far facilitation showed near facilitation. Furthermore we found no significant correlation between the strength of near- and far-surround facilitation on a cell-by-cell analysis ($r = -0.02$; Pearson’s correlation). Overall, these findings suggest that near- and far-surround facilitation are mediated by different pathways.
To demonstrate that far-surround facilitation did not depend on direct stimulation of the sRF_low of the cells by the far-surround grating, we determined for each cell the distance from the RF center at which facilitation took place. Figure 5C shows that the surround annulus inner radius at the cell’s peak response across the population had a bimodal distribution, showing one peak around 3° and a second peak around 10° (population mean = 6.2 ± 0.56°) and could range up to 12°. For each cell, we also normalized the annulus inner radius at peak response to the radius of the cell sRF_high. Facilitation set in at distances 5–200 times the radius of the cells’ sRF_high (mean = 45 ± 12.86, median = 20.7). Thus far-surround facilitation was induced by annular stimuli located at distances in the surround well beyond the size of the cells’ sRF_low, i.e., well outside the RF center and beyond the monosynaptic range of horizontal connections. This point is further emphasized in Fig. 5D, which additionally shows that for all cells the onset of facilitation (defined as 10% increase in the cell’s response to center-only stimulation) took place farther from the RF center than the onset of suppression (defined as 10% reduction in the cell’s response to center-only stimulation, circles in the figure, or as 10% reduction in the cell’s peak response, dots in the figure). For cells showing >10% far-surround facilitation and suppression, the mean annulus inner radius at facilitation and suppression onset were 7.7 ± 0.8 and 3.2 ± 0.43° for suppression measured from center-only response (the difference between these means was highly significant, P = 2.3 −0.05, Student’s t-test) or 8.8 ± 0.63 and 4.4 ± 0.4° for suppression measured from peak response (the difference between these means was also highly significant, P = 1.68 −0.07).

Contrast-dependent shifts in the onset of suppression from the near and far surround: population statistics

Based on the same rationale that induced us to compare near- and far-surround facilitation (see previous section of results), we also quantified and compared the contrast-dependent shift in spatial summation from the near (Fig. 6, A and B) and far surround (C and D). For each cell, we determined the radius of the sRF at high and low contrast (Fig. 6A and B) and calculated the sRF_low/sRF_high ratio for each cell as a measure of the contrast-dependent shift in near spatial summation (Fig. 6C and D). For these cells, annulus width at suppression onset was taken to be the largest width tested (i.e., 14°). For cells showing >10% far-surround facilitation and suppression, the mean annulus inner radius at facilitation and suppression onset were 7.7 ± 0.8 and 3.2 ± 0.43° for suppression measured from center-only response (the difference between these means was highly significant, P = 2.3 −0.05, Student’s t-test) or 8.8 ± 0.63 and 4.4 ± 0.4° for suppression measured from peak response (the difference between these means was also highly significant, P = 1.68 −0.07).
For most cells (68.8% for analysis based on raw data, 76.3% based on the model’s fits), the sRF\text{low} was larger than the sRF\text{high}, indicating that larger stimuli in the near surround were needed to induce suppression at low stimulus contrast. Consistent with previous results (Cavanaugh et al. 2002a; Sceniak et al. 1999), the population average for the sRF\text{low}/sRF\text{high} ratio was 2.1 ± 0.14 (the mean ratio computed from the t-DOG model’s fits was slightly smaller, 1.8 ± 0.15). Thus on average V1 neurons increased their response over a region of space about twice as large at low than at high stimulus contrast before becoming suppressed.

We then quantified the contrast-dependent shift in the onset of suppression seen in the annulus-size experiments. For each cell, we determined the surround annulus width at suppression onset in each contrast condition (Fig. 6C). For most cells, larger surround stimuli were required to induce suppression in the lower contrast conditions compared with the higher contrast condition. Specifically, when compared with the HH condition, 76.2% of cells showed a shift in suppression onset to a wider surround annulus in the LH condition (Fig. 6C, red dots), and 83.3% in the LL condition (circles). The mean annulus width at suppression onset in the lower contrast conditions (LH and LL) was significantly different from the mean in the high contrast condition (HH); specifically, for mean HH (8.7 ± 0.35) versus mean LH (10.6 ± 0.46) P = 0.0016 (Student’s t-test) and for mean HH (8.5 ± 0.35) versus mean LL (11.5 ± 0.44) P = 6.62 × 0.07. Using a different definition of suppression onset (i.e., 10% reduction in the largest response) still produced a statistically significant result, i.e., P = 0.04 (for HH vs. LH), and P = 4.02 × 0.05 (for HH vs. LL). To directly compare the amount of the shift in spatial summation from the far surround with that from the near surround, we normalized to the sRF\text{high} of the cell, the equivalent radius of the annular surround grating that evoked suppression in the low-contrast conditions (Fig. 6D). The equivalent radius of the surround grating evoking suppression was estimated as follows. First we determined the area of the annular surround grating at onset of suppression in each low-contrast condition (LH and LL); the outer and inner borders of this annular grating were the points of suppression onset in the HH condition and in the LH (or LL) condition, respectively. Then we calculated an equivalent radius for this annulus area by dividing the area of the annulus by \pi \text{radius}^2. Comparing the sRF\text{high} ratio of the annulus inner radius at suppression onset in the HH condition/ in the LL condition. Similarly, 98% of cells showing a far-surround shift also showed a near-surround shift in spatial summation at low contrast. Thus most cells showed contrast-dependent shifts in spatial summation from both the near and far surround. However, we found no significant correlation between the amount of near versus far shift in spatial summation (r = 0.03; Pearson’s correlation), suggesting that at least the magnitude of the contrast-dependent shift from the near and far surround is determined by different factors.

Response properties and laminar distribution of cells with far facilitatory surrounds

To further characterize the cells showing far-surround facilitation, for each cell, we determined whether the strength of far-surround facilitation correlated with any of the following variables: orientation selectivity index of the RF center response (r = 0.03, P = 0.81; Pearson’s correlation), direction selectivity index of the RF center response (r = 0.06; P = 0.68), optimal spatial (r = 0.026, P = 0.83) and temporal (r = 0.16, P = 0.21) frequency, and RF center size (sRF\text{high}; r = 0.1, P = 0.39; sRF\text{low}; r = 0.005, P = 0.969). There was no significant correlation between far-surround facilitation strength and any of the preceding variables. Most cells in our sample had complex RFs. The spontaneous activity of the cell (response to the blank) and its response strength (maximum response-spontaneous activity), measured in the same contrast condition that evoked facilitation in the annulus-size experiment, were also uncorrelated with far facilitation strength (r = 0.098, P = 0.45, and r = 0.129, P = 0.32, respectively). These results suggest that the cells showing far-surround facilitation are not a unique population of neurons at least with respect to the variables we have examined.

However, far-surround facilitation was virtually absent in layer 4C, i.e., the main target layer of geniculocortical connections, and a layer that lacks long-range intra- and inter-areal connections (except for upper-layer 4Ca, which has intra-laminar horizontal connections) (Lund et al. 2003). Specifically, only one cell in 4CB and one or two cells in upper-4Ca (1 of these 2 cells was at the layer 4B/upper-4Ca border) showed far-surround facilitation strength >15%, even though 24% of cells in our population were recorded in layer 4C (Fig. 7A, red circles). Cells with strong far-surround facilitation (>30%) were located in layers 2/3, 4B, 5, and 6, i.e., layers that unlike 4C are targeted by inter-areal feedback connections and within which pyramidal cells make intra-areal horizontal connections (see Angelucci and Bressloff 2006; for a review). In contrast, the strength of near-surround facilitation showed a complementary distribution across the V1 layers: it was strongest in the input layers of V1 (4C, 3B/4A, and 6) and weakest in 2-3A and 4B and at the 5/6 border (Fig. 7A, black circles). Statistical analysis showed significantly stronger near facilitation than far facilitation in layers 3B/4A and 4C (P = 0.019; Kruskal-Wallis test). This laminar distribution of near- and far-surround facilitation strengths suggests that geniculocortical feedforward connections may contribute to near- but not far-surround facilitation, perhaps because of the restricted spatial
spread of these connections (see DISCUSSION). In Fig. 7B, for all cells showing >15% far-surround facilitation, we plot as a measure of surround size the surround annulus inner radius at the onset of facilitation (red circles) or suppression (in the HH condition, gray circles) versus cortical depth. Consistent with the hypothesis that spatially restricted geniculocortical feedforward connections do not contribute to the generation of the large far-surround fields of V1 cells, the largest facilitatory surrounds were seen outside layer 4C, in layers 2/3 and 4B and at the layer 5/6 border. The largest suppressive surrounds of these cells were also outside layer 4C, mainly in the upper V1 layers. The few cells showing far-surround facilitation in 4C (n = 2–3) had facilitatory and suppressive surround sizes (3–4.6° radius) coextensive with the largest suppressive surrounds previously reported for the macaque lateral geniculate nucleus (LGN) (Sceniak et al. 2006); the latter may thus contribute to these smaller “far” surrounds in 4C (see DISCUSSION). The results shown in Fig. 7B were not specific to the population of cells showing far-surround facilitation. In Fig. 7C, we plot the laminar distribution of annulus inner radius at suppression onset (in the HH condition) for all neurons that showed >15% far-surround suppression strength (regardless of whether they showed far-surround facilitation). Again, the largest suppressive surrounds were outside layer 4C, and the upper layer cells had surround sizes that were significantly larger than cells in all other layers (P = 0.025, Kruskal-Wallis test). The cells in 4C had surround sizes coextensive with the largest LGN surrounds; perhaps one exception was a cell in upper-4Ca that had a larger (6.6°) far-surround radius (neurons in upper-4Ca, however, make horizontal connections).

**DISCUSSION**

We have shown that the suppressive far surround of V1 neurons is not always suppressive but can facilitate a V1 neuron’s response to an optimal stimulus in its RF center when the latter is driven by a low-contrast stimulus and the surround by an iso-oriented small annular stimulus. Facilitation turns into suppression when the center stimulus contrast or the size of the surround stimulus is increased. These results are consistent with a recent network model of center-surround interactions proposed by Schwabe et al. (2006) and suggest that the surround of V1 neurons acts by modulating the balance of local excitation and inhibition and that center-surround interactions result from excitatory and inhibitory mechanisms of similar spatial extent. We have also shown that far-surround facilitation is rare and weakest in layer 4C and that large far-surround fields are absent in this V1 layer, suggesting that feedforward connections do not contribute to far-surround modulation and that the latter is instead generated intracortically.

**Contrast-dependent shifts in spatial summation and iso-orientation facilitation from the far surround**

Shifts in spatial summation at low stimulus contrast (Kapadia et al. 1999; Sceniak et al. 1999; Sengpiel et al. 1997) and iso-orientation surround facilitation (Kapadia et al. 1995; Polat et al. 1998) have previously been shown to occur only from surround regions near the RF center. Results from psychophysical experiments have generally paralleled those from physiological experiments, so much so that often they have been interpreted as they perceptual correlate of center-surround interactions in V1 (for a review, see Series et al. 2003). However, in this study, we observed an increase in spatial summation when low-contrast stimuli in the RF center were presented together with high- or low-contrast small annular stimuli in the far surround, i.e., well outside the RF center. Specifically, in >50% of the cells, as the width of the annular grating in the far surround was increased, the cell’s response to a low-contrast stimulus in the RF center was first facilitated and then suppressed. In addition, when the contrast of the center stimulus was lowered, for most cells (~83%) larger stimuli in the surround were needed to suppress the cell’s response than when the center stimulus contrast was higher.
Previous studies have shown iso-oriented stimuli in the far surround to typically suppress the response of V1 neurons to optimally oriented gratings in their RF center, even when the latter were presented at low contrast (Cavanaugh et al. 2002b; DeAngelis et al. 1994; Levitt and Lund 1997; Sengpiel et al. 1998). Surround suppression has also been the most commonly observed effect in psychophysical studies performed at suprathreshold (see INTRODUCTION). Our results indicate that these previous studies failed to observe far-surround facilitation because they used large surround stimuli involving both the near and the far surround. In particular, stimulation of the stronger near surround may have masked the facilitatory influences from the far surround. In our annulus-size experiment, the near surround was not stimulated, and facilitation occurred at far-surround annulus widths that were specific for each cell with larger widths most often evoking suppression. Thus our results are not inconsistent with previous data and suggest that the size of the surround stimulus, in addition to its orientation and contrast, is an important determinant of the sign (i.e., facilitation or suppression) of the modulatory surround effect. Consistent with our results, a recent psychophysical study, using a center-annular surround stimulus similar to the one used in this study, demonstrated facilitatory interactions in suprathreshold contrast perception induced by surround stimuli 7.5° from the target center grating (Nurminen and Laurinen 2006).

Previous studies have reported that suppression can arise from regions of the surround up to 13–16° in diameter (Cavanaugh et al. 2002a; Levitt and Lund 2002; Sceniak et al. 2001). Here we report even larger suppressive surround fields (up to ~26° in diameter; Figs. 6C and 7C) and demonstrate that facilitation can also arise from similarly distant surround regions (Figs. 5, C and D, and 7B). Our results indicate that center-surround interactions in V1 result from excitatory and inhibitory mechanisms of similar spatial extent and that it is the change in the balance of local excitation/inhibition induced by surround stimulation that determines the sign of the modulation. However, center-surround interactions in V1 have previously been described as the difference or ratio of the integral of two Gaussian functions having different spatial scales: an excitatory Gaussian representing the RF center and an overlapping, spatially broader inhibitory Gaussian, representing the suppressive surround (DOG or ROG models) (Cavanaugh et al. 2002a; Sceniak et al. 1999). These statistical models, although good descriptors of many properties of center-surround interactions, are inconsistent with far-surround facilitation because in these models, the spatially broader inhibition dominates outside the excitatory RF center mechanism. In contrast, iso-orientation far-surround facilitation was predicted and thus is consistent with, our recently proposed recurrent network model (Schwabe et al. 2006) (Fig. 1B) in which excitation and inhibition have similar spatial extent. Although our data provide support for our model by reporting the basic predicted phenomenon, i.e., facilitation from the far surround at low contrast for small but not large surround annulus widths, further experimentation is under way in our laboratory to fully characterize the facilitation.

Could the facilitation seen in our study have resulted from direct stimulation of the RF center by the surround grating? For example, could we have underestimated the size of the cells sRF\textsubscript{low}? The mean radius of the sRF\textsubscript{low} across our neuronal sample was 1°, and most (93%) cells had sRF\textsubscript{low} sizes <1.6°. Based on our stimulus sampling between these radii (see METHODS), we could have underestimated the size of the sRF\textsubscript{low} by 0.3° for 83% cells, by 0.8° for 9% of cells, and by 2.4° for 7.5% of the cells. Introducing these errors to our estimates of the sRF\textsubscript{low} for the entire population yielded a mean sRF\textsubscript{low} radius of 1.45°, with most cells having sRF\textsubscript{low} radii <2.4°. Figure 5C demonstrates that in >70% of cells, far-surround facilitation occurred at distances >2.4°. However, it could be argued that the location of the peak response in the low-contrast patch-size tuning curve is an underestimate of true RF center size as this results from center-surround antagonism. Previous studies have used as a measure of RF center size the space constant of the center Gaussian, derived from the DOG fits to the patch-size tuning curve (e.g., Sceniak et al. 1999). In a previous study (Angelucci et al. 2002b), we estimated that the space constant of the center excitatory Gaussian was on average 2.4 times larger than the peak of the size tuning curve measured directly from the data. In the present study, this would correspond to a mean population radius of 2.4° (1 × 2.4°) for the sRF\textsubscript{low} with most cells having sRF\textsubscript{low} radii <3.8°. Figure 5C again shows that in at least 60% of cells far-surround facilitation occurred at distances >3.8°. Thus even if we had underestimated the size of the RF for every cell, for most cells, facilitation still arose from regions of the surround well outside the “corrected” RF center size. But perhaps the strongest evidence against the argument that far-surround facilitation resulted from direct stimulation of the RF center by the surround grating is the observation that in all annulus-size tuning curves facilitation occurred farther away from the RF center than suppression (Fig. 5D). If facilitation was due to stimulation of the RF center by the surround grating, one would expect it to occur closer to the RF than suppression. We conclude that facilitation in our data occurred from surround regions well outside the sRF\textsubscript{low} of V1 neurons and thus well beyond the extent of monosynaptic horizontal connections.

**Near- and far-surround facilitation**

Although this is the first physiological study reporting contrast-dependent increase in spatial summation and iso-orientation facilitation from the far surround, previous studies have reported similar phenomena from the near surround. In particular, Sceniak et al. (1999) demonstrated that ~70% of V1 cells at low stimulus contrast show a shift in the peak response toward larger stimulus sizes in the patch-size tuning curve (i.e., have a sRF\textsubscript{low}/sRF\textsubscript{high} ratio >1). In our population, 71% of cells showed a similar shift of the peak response at low contrast, but in only 54% of the cells did the stimulus in the near surround actually facilitate the response to the stimulus in the sRF\textsubscript{high}. Similarly we found that 83% of cells showed a contrast-dependent shift in spatial summation from the far surround, but in only 50% of cells did the stimulus in the far surround facilitate the response to the center-stimulus alone. The similarity of these two phenomena raises the issue of whether near- and far-surround facilitation are generated by a common mechanism. Several lines of evidence suggest that this may not be the case. First, there was no correlation between the strength of near- and far-surround facilitation. Second about half of the cells that showed one type of facilitation did not show the other type. The third strength of near-
and far-surround facilitation showed significantly different and indeed complementary distributions across the cortical layers. While near-surround facilitation was strongest in layer 4C and other layers of V1 that receive direct LGN input (Blasdel and Lund 1983; Chatterjee and Callaway 2003; Hendrickson et al. 1978; Hendry and Reid 2000; Hubel and Wiesel 1972), far-surround facilitation was virtually absent in layer 4C; the latter instead was strongest in layers that, unlike 4C, are targeted by inter-areal feedback connections and within which pyramidal cells make intra-areal horizontal connections (reviewed in: Angelucci and Bressloff 2006). Furthermore, large facilitatory and suppressive surround fields were absent in layer 4C but predominated in layers (2/3 and 5/6) that have long-range intra-cortical connections. These results suggest that although feedforward connections may contribute to near-surround facilitation, they do not contribute to far-surround facilitation or suppression. The restricted spatial spread of geniculocortical axons (Angelucci and Sainsbury 2006) as well as the small size of LGN surrounds (Sceniak et al. 2006) are likely to be the main factors limiting the contribution of feedforward connections to the near surround. It is noteworthy that we did see some cells in layer 4C with “smaller” far surrounds (predominantly suppressive; Fig. 7, B and C), the sizes of which, however, matched the largest suppressive surround sizes previously reported for macaque LGN afferents (Sceniak et al. 2006). It is possible that these unusually large surround fields in the LGN contribute to the generation of the “smaller” far-surround fields we have observed in layer 4C. Previous studies in macaque did not report laminar differences in the strength or size of surround suppression measured in patch-size experiments (Levitt and Lund 2002; Sceniak et al. 2001). However, unlike our annular stimulus, the stimulus used in these previous studies did not isolate the contribution of intracortical mechanisms as it involved both the near and the far surround. Levitt and Lund (2002), however, in a smaller fraction of their V1 neuron population also measured surround sizes using an annular stimulus similar to the one used in the present study and still did not observe significant laminar differences. However, their largest surround stimuli were half the diameter of our largest stimuli, and they only recorded from 3 neurons in layer 4C. Consistent with our results, instead, a previous study in tree shrew reported marked differences in length tuning between cells in layers 2/3 and those in layer 4, reflecting differences in the connectivity of these two layers (Chisum et al. 2003).

Although our results suggest that feedforward connections do not contribute to far-surround modulation in V1, there is evidence that they contribute to near-surround modulation. First, primate LGN cells show extra-classical surround suppression and facilitation (Kremers et al. 2001; Sceniak et al. 2006; Solomon et al. 2002) [Sceniak et al. (2006), however, did not observe contrast-dependent near-surround facilitation in LGN afferents with corticogeniculate feedback inactivated]. Second, blocking intracortical inhibition in cat V1 does not abolish surround suppression in V1 in patch-size experiments (Ozeki et al. 2004). Third, it has been shown that two mechanisms contribute to surround suppression in macaque V1, one showing very broad spatio-temporal tuning, thus likely originating in the LGN, the other one showing sharp orientation and spatio-temporal tuning, and thus likely generated intracortically (Webb et al. 2005). However, the lack of orientation-tuned surrounds in the primate LGN (Solomon et al. 2002) suggests that feedforward mechanisms must interact with intracortical mechanisms (possibly horizontal and feedback connections) to generate orientation-tuned surrounds in V1, even those in the near surround.

**Origin of the far surround**

If far-surround modulation is not generated by feedforward mechanisms, what could then be its underlying anatomical substrate? We previously proposed that top-down feedback connections underlie the far surround (Angelucci and Bressloff 2006; Angelucci and Bullier 2003; Angelucci et al. 2002a). The annular stimulus used in this study was tailored to the spatial scales of horizontal and feedback connections. Specifically, in the annulus-size experiment the far-surround grating stimulated regions beyond the extent of monosynaptic horizontal connections with about less than half their extent being stimulated by the center grating. Because of the purely modulatory effect of horizontal connections (Hirsch and Gilbert 1991), neurons the RFs of which lay in the visual field position of the blank were most likely unable to propagate signals horizontally in the absence of concomitant afferent drive. It is highly unlikely that neurons with larger RFs in the blank region straddling the center and surround grating could have mediated these effects. This is because the largest sRF_{low} radii in our neuronal population measured 1.6° (see Fig. 6A), and far-surround facilitation in ~70% of cells occurred at distances >3.2° from the RF center (i.e., twice the radius of the largest sRF_{low}; Fig. 5C). In fact, for about half of the cells that showed far-surround facilitation, the facilitation took place at distances >7° from the RF center. The slow conduction velocity of horizontal axons argues against cascading horizontal connections mediating fast-occurring far-surround modulation (see Introduction). We conclude that far-surround modulation in our annulus-size experiments was most likely mediated by top-down feedback connections.

**ACKNOWLEDGMENTS**

Present address of L. Schwabe: Laboratory of Cognitive Neuroscience, Brain Mind Institute, Swiss Federal Institute of Technology, 1015 Lausanne, Switzerland.

**GRANTS**

This work was supported by National Science Foundation Grants IBN0344569 to A. Angelucci and DMS0515725 to P. C. Bressloff, National Eye Institute Grants EY-015262 to A. Angelucci and EY-015609 to J. Ichida, Wellcome Trust Grant 061113, the University of Utah Research Foundation funding to A. Angelucci, and a grant from Research to Prevent Blindness to the Department of Ophthalmology, University of Utah.

**REFERENCES**


