Response facilitation from the “suppressive” receptive field surround of macaque V1 neurons

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Abbreviated Title: facilitation from the far surround

Number of pages: 45  Number of figures: 7  Number of Tables: 0
ABSTRACT

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 were 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 intra-cortical 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.
Key words: primary visual cortex, contextual effects, feedback, horizontal connections, top-down

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 (sRF\textsubscript{high} or sRF\textsubscript{low}), respectively, and to the region between these two sRF components as the “near” surround. We refer to the region beyond the sRF\textsubscript{low} as the “far” surround (Fig. 1A).

Figure 1 near here

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 sRF\textsubscript{low} (Angelucci et al. 2002b) (Fig. 1A). Polysynaptic chains of horizontal connections are also too slow (Bringuier et al. 1999; Girard et al. 2001; Grinvald 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 surround 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 1994, 1993). 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 at 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 1993, 1991; 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 · hr⁻¹) and paralyzed (vecuronium bromide, 0.1 µg · kg⁻¹ · hr⁻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 respirated with a 30:70 mixture of O₂ and N₂O. Electrocardiogram was continuously monitored, end tidal CO₂ was maintained between 30-33 mm Hg, 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 msec.

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 57cm (at which the screen subtended a visual angle of 28°). For each cell, we first determined the preferred orientation, 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 less than 90% of response saturation for the cell (typically between 50-80% 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 standard deviations greater than the spontaneous firing rate; typically between 4-30%; the cell in Fig. 2C was one exception). We then 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 0.1-14° and consisted of 11 radii (0.1°, 0.2°, 0.4°, 0.8°, 1.2°, 1.6°, 2.5°, 5°, 7.5°, 10°, 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 2s and a 2s 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 \( \mu \)A for 30 s, tip negative) were made along the length of each electrode penetration in order to assign laminar location to recorded V1 neurons. At the end of the recording session the animal was euthanized 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 \( \mu \)m on a freezing microtome. 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. Since far surround facilitation is the main response property that we wished to quantify in this study, and in order 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, 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 \( R_{\text{Exc}} \) in the following statistical model:

\[
U_{\text{Inh}} = W_{\text{Inh}} \int s(\mathbf{x}) \cdot w(\mathbf{x}) \, d\mathbf{x}
\]

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

\[
U_{\text{Exc}} = I_c - R_{\text{Inh}} + W_{\text{Exc}} \int s(\mathbf{x}) \cdot w(\mathbf{x}) \, d\mathbf{x}
\]

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

Here, the variables \( R_{\text{Exc}} \) and \( U_{\text{Exc}} \) and \( R_{\text{Inh}} \) and \( U_{\text{Inh}} \) 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

\[
w(\mathbf{x}) = w(||\mathbf{x}||) = \exp\left(-||\mathbf{x}||^2 / (2\sigma)^2\right)
\]

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), \( T_{\text{Inh}} \) (threshold for inhibition), \( W_{\text{Exc}} \) (weight of excitation), \( W_{\text{Inh}} \) (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 which 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.

**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 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. feedforward, feedback and horizontal connections). High levels of excitation generate suppression, while 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, while 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 towards 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. 2A-D left column). Confirming previous reports (Cavanaugh et al. 2002a; Sceniak et al. 1999; Sengpiel et al. 1997), for most cells (e.g. cells in Fig. 2A-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 towards larger stimuli. The cell in Fig. 2C did not show either phenomenon, while 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 stimulation. 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 $\geq$ 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 in the right panel of Fig. 2D). 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 the right panels of Figs. 2A,D,3); however, some cells (e.g. cells in the right panel of Fig. 2B-C) were only tested with two contrast conditions (HH and LH or LL).

Figures 2-3 near here
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 towards larger surround stimuli. **Figure 2A-D** (right column) 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 the Results), cells in **Fig. 2A-B** showed stronger facilitation than those in **Fig. 2C-D**. A few cells (9%) showed far surround facilitation at low contrast but no far surround suppression in any contrast condition (not shown). Peri-stimulus 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 column) and is sustained past the response to the center-only stimulus (black curve in **Fig. 3** right column). 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 column) 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<sub>low</sub>, and when presented alone did not evoke any response from the cell (blue squares in **Fig. 2**). For example, the radius of the sRF<sub>high</sub> and sRF<sub>low</sub> 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<sub>low</sub> of the cell. Similarly, the sRF<sub>low</sub> for the cells shown in **Fig. 2B-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<sub>low</sub>. Furthermore, if facilitation were caused by direct
stimulation of the RF center by the surround 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. 2A-D right column; this observation is quantified in the next section of the 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 below) in the lower contrast conditions also showed a shift in the onset of suppression towards 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. 2A,D); for some cells even the largest surround stimulus was not sufficient to evoke significant suppression at low contrast (e.g. Fig. 2B,D). The cell in Fig. 2C was one 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 left panel of Fig. 2C). 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 (while 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 towards larger surround widths at low contrast (see below). 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 towards 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, while 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 inset of Fig. 5A) as

\[
\left(\frac{R_{\text{Peak}} - R_{\text{Cir}}}{R_{\text{Cir}}}\right) \times 100
\]
where $R_{Peak}$ is the maximum response at low contrast and $R_{Ct}$ is the response to a low contrast stimulus the size of the cell’s sRF$_{high}$. A facilitation strength = 0 indicates no facilitation. The strength of far surround facilitation was calculated from the annulus-size tuning curve (see inset of Fig. 5B) as indicated above for near surround facilitation, but here $R_{Peak}$ was the maximum response in a given contrast condition and $R_{Ct}$ 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, while 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. **Fig. 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 $3^\circ$ and a second peak around $10^\circ$ (population mean=$6.2^\circ\pm0.56$), and could range up to $12^\circ$. 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 $7.7^\circ\pm0.8$ and $3.2^\circ\pm0.43$ 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 $8.8^\circ\pm0.63$ and $4.4^\circ\pm0.4$ 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 the Results), we also quantified and compared the contrast-dependent shift in spatial summation from the near (Fig. 6A-B) and far surround (Fig. 6C-D). For each cell we determined the radius of the sRF at high and low contrast (Fig. 6A), and calculated the $sRF_{low}/sRF_{high}$ ratio for each cell as a measure of the contrast-dependent shift in near spatial summation (Fig. 6B). For most cells (68.8% for analysis based on raw data, 76.3% based on the model’s fits) the $sRF_{low}$ was larger than the $sRF_{high}$, 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 $sRF_{low}/sRF_{high}$ 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 to the higher contrast condition. Specifically, when compared to the HH condition, 76.2% of cells showed a shift in suppression onset to a wider surround annulus in the LH condition (red dots in Fig. 6C), and 83.3% in the LL condition (circles). The mean annulus width at suppression onset in the lower contrast conditions (LH and LL) was highly significantly different from the mean in the high contrast condition (HH); specifically, for mean HH (8.7±0.35) vs. mean LH (10.6±0.46) p=0.0016 (Student’s t-test), and for mean HH (8.5±0.35) vs. 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<sub>high</sub> 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, and normalized it to the radius of the cell’s sRF<sub>high</sub>. A ratio >1 (or <1) indicates that the stimulus in the far surround at onset of suppression was larger (or smaller) than the cell’s sRF<sub>high</sub>. This is a measure of how much larger than the sRF<sub>high</sub> a stimulus in the far surround needed to be in order to evoke suppression at low contrast, and thus can be directly compared to the sRF<sub>low</sub>/sRF<sub>high</sub> ratio. The population average (13.7±1.4 for the LH, 15.4±1.4 for the LL conditions; Fig. 6D) was well above 2, i.e. well above the mean sRF<sub>low</sub>/sRF<sub>high</sub> ratio for the
population, indicating that a much larger stimulus was needed in the far surround than in the near surround to evoke suppression at low contrast. This finding also indicates that suppression is stronger from the near than from the far surround, as suggested previously (Levitt and Lund 2002). Thus, near and far surround suppression both showed a shift towards larger surround stimuli at low contrast, but the far surround shift was much larger than the near shift, indicating that the near surround has a much stronger suppressive influence than the far surround. About 87% of cells showing a contrast-dependent shift in spatial summation from the near surround (defined as a $sRF_{low}/sRF_{high}$ ratio > 1) also showed a shift in spatial summation from the far surround at low contrast (defined as > 1 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 vs. 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 above 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 4C\(\alpha\), which has intra-laminar horizontal connections – Lund et al., 2003). Specifically, only one cell in 4C\(\beta\) and one or two cells in upper-4C\(\alpha\) (one of these two cells was at the layer 4B/upper-4C\(\alpha\) 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, 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 geniculo-cortical 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 geniculo-cortical 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, 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 has 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-4Cα that had a larger (6.6°) far surround radius (neurons in upper-4Cα, 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, 7C) and demonstrate that facilitation can also arise from similarly distant
surround regions (Figs. 5C-D, 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. While 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°. **Fig. 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° x 2.4) for the sRF\textsubscript{low}, with most cells having sRF\textsubscript{low} radii <3.8°. **Fig. 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 were 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_{low} of V1 neurons, and thus well beyond the extent of monosynaptic horizontal connections.

Near and far surround facilitation

While 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 towards larger stimulus sizes in the patch-size tuning curve (i.e. have a sRF_{low}/sRF_{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_{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. Third the 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 while 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. 7B-C), whose sizes 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 whose RFs 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 about 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**

Supported by the National Science Foundation (grants IBN0344569 to A.A. and DMS0515725 to P.C.B.), the National Eye Institute (grants EY015262 to A.A., and EY015609 to J.I.), the Wellcome
Trust (061113), the University of Utah Research Foundation (to A.A.), and by a grant from Research to Prevent Blindness, Inc., to the Department of Ophthalmology, University of Utah.

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References


FIGURE LEGENDS

**Figure 1.** 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$_{high}$, but using a low contrast grating patch of increasing radius; 3) the “near” surround (*light gray area*) is the region over which presentation of gratings at the same orientation as the center grating suppresses or facilitates the cell’s response to an optimal grating in the center, depending on the grating’s contrast; 4) the far surround (*dark gray area*) is the region outside the sRF$_{low}$ over which presentation of gratings at the same orientation as the center grating suppresses the cell’s response to an optimal high contrast grating in the center. Feedforward connections (*green*) to V1 from the lateral geniculate nucleus (*LGN*) are commensurate with the sRF$_{high}$ of V1 neurons (Angelucci and Sainsbury 2006). Intra-areal V1 horizontal connections (*red*) are commensurate with the sRF$_{low}$ of their V1 neurons of origin, while extrastriate feedback connections (*blue*) to V1 are commensurate with the full spatial scale of the center and surround field of V1 neurons (Angelucci et al. 2002b). (B): Basic architecture of the recurrent network model of center-surround interactions proposed by Schwabe et al. (2006). Only the major afferent pathways that more directly affect the response of the center excitatory and inhibitory neurons are
shown. For the full network architecture see Schwabe et al. (2006). Different connection types are indicated as color-coded arrows (according to legends in A and B). Dashed boxes: populations of excitatory (Exc) or inhibitory (Inh) V1 neurons in the RF center; filled gray boxes: population of excitatory neurons with RF centers positioned in the near and far surround of the center neurons. \( E_{FF} \): excitatory neurons in other V1 layers sending feedforward afferents to the Exc neurons in V1 layers 2/3. \( E_{FB} \): excitatory neurons in extrastriate cortex sending feedback projections (blue arrows) to Exc neurons in V1. Icons at the bottom: different components of the RF center and surround (as in A), with orange areas indicating the components that are activated when each respective network submodule is active. Stimulation of the near surround modulates the response to a center stimulus via horizontal connections (red arrows) targeting both excitatory and inhibitory neurons in the center. The interneurons are assumed to have higher threshold and gain than the local excitatory neurons, and thus only generate suppression under sufficiently high levels of local excitation (e.g. a high contrast stimulus in the RF center). If the center stimulus is of low contrast, instead, the Inh neurons are inactive and stimulation of the near surround generates facilitation, as demonstrated experimentally (Polat et al. 1998; Sceniak et al. 1999). In the model, fast suppression from the far surround occurs via feedback connections targeting excitatory, but not inhibitory, neurons in the near surround and in the RF center, which in turn via horizontal connections, excite the local Inh neurons. This is based on the anatomical finding that feedback axons contact almost exclusively excitatory neurons in V1 (Johnson and Burkhalter 1996). It follows that if the local interneurons are inactive (as for a low contrast stimulus in the RF center), a small stimulus in the far

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1 Note that, while in Fig. 1B the RF center is the sRF\textsubscript{high} and the near surround the region between the sRF\textsubscript{high} and the sRF\textsubscript{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\textsubscript{low}.
surround is facilitatory, while it is suppressive when the local interneurons are active (as for a high contrast stimulus in the RF center). Large stimuli in the far surround are predicted to suppress the response to high or low contrast center stimuli, as the large amount of feedback input to the center neurons is now sufficient to activate the center interneurons.

**Figure 2.** Patch-size and surround annulus-size tuning curves for four representative V1 neurons showing far surround facilitation. **(A-D) Left column:** Responses (mean firing rate) of four 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* indicates the cell’s mean spontaneous firing rate, the *solid lines* represent fit to the data (*dots*) using the statistical t-DOG model (see Methods), and error bars are s.e.m. *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 **Figure 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%. **(A-D) Right column:** Responses of the same four 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°.

**Figure 3.** PSTHs for the cells shown in Fig. 2. *Left column*: response in the HH condition; *right column*: response in the LL condition. *Black curves*: response to a center-only stimulus of high contrast in the left column and of low contrast in the right column. *Orange curves*: response to a center stimulus presented together with a surround grating of a width that generated peak facilitation in the LL condition. The surround annulus width at peak response for each cell is indicated at the top right corner of each right panel. Note that the two panels in D are not plotted at the same scale.

**Figure 4.** Patch-size and surround annulus-size tuning curves for two representative V1 neurons showing contrast-dependent shifts in the onset of suppression, but no far surround facilitation. (A-B) *Left column*: Patch-size tuning curves. Near surround
strength for each cell was: (A) 175%, (B) 8.9%. \textbf{(A-D) Right column:} Annulus-size tuning
curves for the same two cells. \textbf{(A):} Facilitation strength: 0% (HH), 12% (LH), 9% (LL);
center grating: 0.2°; smallest gap radius: 0.5°. \textbf{(B):} Facilitation strength: 0% (HH), 0% (LH),
0% (LL); center grating: 0.4°; smallest gap radius: 0.4°. Conventions are as in \textbf{Fig. 2}.

\textbf{Figure 5.} Contrast-dependent iso-orientation facilitation from the near and far surround:
population data. \textbf{(A):} Strength of near surround facilitation seen at low stimulus contrast in
the patch-size experiment in a population of 70 cells (same cells as in B). \textit{Arrow:} median
(51.2%) for cells showing >15 facilitation strength. In the \textit{inset} we show how we computed
the strength of near surround facilitation on a representative V1 neuron patch-size tuning
curve measured at high (\textit{black curve}) and low (\textit{gray curve}) contrast. \textbf{(B):} Strength of far
surround facilitation in the HH condition (\textit{black}), and in the low contrast condition (usually
LL) evoking the strongest facilitation (\textit{gray}) in the annulus-size experiments. \textit{Arrow:}
median (28.7%) based on model (39% based on the raw data) for cells showing >15%
facilitation strength at low contrast. In the \textit{inset} we show how we computed the strength of
far surround facilitation on a representative V1 neuron annulus-size tuning curve measured
in the HH (\textit{black curve}) and LL (\textit{gray curve}) conditions (same cell as in \textbf{Fig. 2A}). \textbf{(C):}
Distribution of the annulus inner radius at the cell’s peak (maximum) response in the low
contrast condition that evoked the strongest facilitation. This is a measure of how far from
the RF center facilitation set in. \textit{Arrow:} median (6.7°). \textbf{(D):} Scatter plot of annulus inner
radius at suppression vs at facilitation onset. All points are above the diagonal indicating
that the annulus inner radius at facilitation onset was larger than at suppression onset.

\textit{Circles:} suppression onset defined as 10% reduction in the cell’s center-only response.
\textit{Dots:} suppression onset defined as 10% reduction in the cell’s peak response. \textit{Light}
circles/dots: cells showing no far surround suppression in the low contrast condition that evoked facilitation. Arrowheads: means (see Results for values). Stimulus icons in A-D are as in Figs. 1-2.

**Figure 6. Contrast-dependent shifts in the onset of suppression from the near and far surround: population data.** (A): Scatter plot of the sRF radius at high (sRF\textsubscript{high}) and low (sRF\textsubscript{low}) contrast measured from the patch-size tuning curves (n=80 cells). Empty and filled circles: values obtained from the t-DOG model’s fits to the size-tuning data or from the raw data, respectively. Note that many filled circles are superimposed onto each other. There are 61 empty circles and 55 filled circles above the diagonal, indicating larger sRF\textsubscript{low} than sRF\textsubscript{high} for a majority of cells. Filled and empty arrowheads: means of raw data (sRF\textsubscript{high} radius 0.35°±0.018, sRF\textsubscript{low} radius 1.03°±0.2) or of t-DOG model’s fits to the data (sRF\textsubscript{high} radius 0.3°±0.018, sRF\textsubscript{low} radius 1.13°±0.3), respectively. (B): Histogram of the entire population in (A), showing the distribution of the sRF\textsubscript{low}/sRF\textsubscript{high} ratio computed on a cell-by-cell basis. A ratio >1 indicates that the sRF is larger at low contrast. White and black bars: ratio computed based on the t-DOG model fits, and the raw data, respectively. Here and in (C-D), arrowheads are population means (see Results for values). (C): Scatter plot of the annulus width at suppression onset in the HH vs LH (red dots) and HH vs LL (circles) conditions, measured from the annulus-size tuning curves. Suppression onset here and in all remaining figures is defined as a 10% reduction in the response to center-only stimulation. Most points fell above the diagonal, indicating that suppression set in at larger annulus widths in the lower contrast conditions compared to the high contrast condition. Points at the very top of the scatter plot indicate cells that showed < 10% suppression in the LH and/or LL conditions (e.g. cells in Fig. 2B,D). For these cells, annulus width at
suppression onset was taken to be the largest width tested (i.e. 14°). **(D):** Distribution of the equivalent radius of the annular surround grating that evoked suppression in the LH (*red*) and LL (*gray*) conditions normalized to the radius of the sRF$_{\text{high}}$.

**Figure 7.** Laminar distribution of near and far surround facilitation and far surround suppression. **(A):** Distribution of facilitation strength versus relative cortical depth for all cells for which we could recover histologically the laminar information (n=68). *Red circles:* strength of far surround facilitation (measured as in Fig. 5B); *black circles:* strength of near surround facilitation (measured as in Fig. 5A). Here and in (B-C), the *solid lines* indicate median values calculated at intervals of 10% of total cortical depth; *numbers on the right of each plot* indicate cortical layers (layer 4C is *shaded*). **(B):** Laminar distribution of the annulus inner radius at onset of facilitation (*red circles*; contrast condition that gave the largest facilitation) and of suppression (*gray circles*; HH condition) measured in the annulus-size experiment for all cells that showed >15% strength far surround facilitation in panel (A). Gray circles on the Y axis indicate cells with <15% far surround suppression strength; these cells were not included in the computation of the median values. **(C):** Distribution of the annulus inner radius at suppression onset versus cortical depth for all cells that showed >15% far surround suppression strength in the annulus-size experiment in the HH condition.