

Subthreshold facilitation and suppression in primary visual cortex revealed by intrinsic signal imaging

(area 17/cat/filling-in/extra-classical receptive field/optical imaging)

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ABSTRACT Neurons in primary visual cortex (area 17) respond vigorously to oriented stimuli within their receptive fields; however, stimuli presented outside the suprathreshold receptive field can also influence their responses. Here we describe a fundamental feature of the spatial interaction between suprathreshold center and subthreshold surround. By optical imaging of intrinsic signals in area 17 in response to a stimulus border, we show that a given stimulus generates activity primarily in iso-orientation domains, which extend for several millimeters across the cortical surface in a manner consistent with the architecture of long-range horizontal connections in area 17. By mapping the receptive fields of single neurons and imaging responses from the same cortex to stimuli that include or exclude the aggregate suprathreshold receptive field, we show that intrinsic signals strongly reveal the subthreshold surround contribution. Optical imaging and single-unit recording both demonstrate that the relative contrast of center and surround stimuli regulates whether surround interactions are facilitative or suppressive: the same surround stimulus facilitates responses when center contrast is low, but suppresses responses when center contrast is high. Such spatial interactions in area 17 are ideally suited to contribute to phenomena commonly regarded as part of “higher-level” visual processing, such as perceptual “pop-out” and “filling-in.”

A prominent feature of nearly every region of the mammalian cortex is a dense network of patchy, long-range horizontal connections within the superficial cortical layers (1). In primary visual cortex, these connections arise primarily as axonal branches of pyramidal cells in layers 2/3 (2, 3), and link neurons located at distances up to several millimeters away in the superficial cortical layers. Long-range horizontal connections make excitatory synapses on their target neurons (4), but those postsynaptic neurons can be excitatory (spiny stellate or pyramidal cells) or inhibitory (smooth stellate cells, see ref. 5).

Although these anatomical features of horizontal connections are by now well established, their physiological role remains only partially understood. Long-range connections in area 17 are clustered into regions with similar orientation preference (6), and form a likely substrate for mediating influences on neurons from outside their “classical” receptive field. (We define the classical receptive field as the region over which a stimulus can evoke a suprathreshold spike response from the cell.) These influences can include modulation of orientation specific responses in area 17 neurons (7, 8). Consistent with the anatomy of long-range connections, the effect of electrically stimulating lateral connections in cortical slices can be both excitatory and inhibitory, although the balance between the two can be modified (9). Reducing thalamocortical excitation, either in the long term by a retinal lesion (10) or in the short term by an artificial scotoma (11, 12),

causes changes in receptive field size and location that are likely mediated by enhanced horizontal excitation (13). In contrast, several studies indicate a range of inhibitory effects from stimulating receptive field surrounds, including iso-orientation suppression of center responses (14–17).

In this study, we demonstrate that the surround can either facilitate or suppress responses depending on the level of center stimulation. By combining single-unit recording with optical imaging of intrinsic signals (to record activity over an expanse of cortex), we find that the same surround stimulus, which by itself or in the presence of very weak center stimulation evokes an excitatory response, can suppress responses evoked by strong iso-orientation center stimulation. These data are highly consistent with recent theoretical proposals on how the receptive field surround interacts spatially with the center (18, 19).

MATERIALS AND METHODS

Surgery and Recording Chamber Placement. Female cats aged 10 weeks to adult were initially anesthetized with a mixture of ketamine (15 mg/kg) and xylazine (1.5 mg/kg, i.m.). Subsequently, anesthesia was maintained either by continuous infusion of sodium pentobarbital (1.5–2 mg/kg per hr, i.v.), or by isoflurane (0.5–1.5%) in a mixture of 70% N₂O/30% O₂. A tracheotomy was performed to facilitate artificial ventilation. The animal's heart rate and electroencephalogram were continuously monitored to ensure adequate levels of anesthesia. Expired CO₂ was maintained at 4% by adjusting the stroke volume and the rate of the respirator. The animal was placed on a heating blanket and the rectal temperature was maintained at 38°C. A mixture of 5% dextrose and lactated Ringers for fluid maintenance was given by continuous i.v. infusion. Craniotomy and durotomy were performed to expose cortex from Horsley–Clark AP0 to P7.0 mm and from the midline to roughly 4 mm lateral. To prevent eye movements, paralysis was initiated with gallamine triethiodide (10 mg/kg per hr) after completion of surgery. A stainless steel chamber (20 mm diameter) was cemented to the skull with dental acrylic and the inner margin was sealed with wax. To minimize cortical pulsations due to respiration and heart beat, the chamber was filled with silicone oil and sealed with a transparent quartz plate.

Optical Recording. We used the technique of intrinsic signal imaging (20, 21). The cortical surface was illuminated with a bifurcated fiber optic light guide attached to a 100-W tungsten-halogen lamp source powered by a regulated power supply. The light was passed through an infrared cutoff filter and an orange (600 ± 10 nm) filter, and was adjusted for even illumination of the cortical surface at an intensity within the

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linear range of the camera's sensitivity. We used a slow-scan video camera (Bischke CCD-5024N, RS-170, 30 Hz, 60 dB s/n) fitted with a microscope (22) consisting of back-to-back camera lenses (50 and 55 mm, f1.2) allowing both a high numerical aperture and a shallow depth of field. Light of 540 nm was used to image the superficial cortical vasculature. To image activity dependent oximetric signals, the focal plane was adjusted 300 μm below the surface, and 600 nm (10 nm bandpass) light was used. Data collection was under the control of an imaging system (Imager 2001, Optical Imaging, Durham, NC) that performed analog subtraction of a stored reference image (collected during presentation of a neutral gray screen) from the stimulus image (collected during presentation of an oriented grating), such that the image could be digitized in real time while retaining the full signal-to-noise ratio of the camera.

Visual Stimulation. All visual stimuli were presented to the contralateral eye, with the ipsilateral eye covered. The animal's eyes were focused on the monitor by back-projecting the retinal vasculature pattern with a reversible ophthalmoscope and fitting the eyes with appropriate contact lenses. Constancy of eye position was verified before and after every experiment to within 0.4° using this vasculature pattern. Stimuli were generated by a 486 computer running STIM software (K. Christian, Rockefeller University) at a resolution of 640×480 pixels. The stimuli were shown at a 60-Hz frame rate on a 14-inch monitor (Sony Trinitron) positioned approximately 30 cm away from the animal. Individual frames were computed prior to the beginning of the experiment and shown under the timing control of the data-collection computer.

The stimulus set consisted of four center stimuli, four surround stimuli, four full-field stimuli (equivalent to center plus surround, no phase difference), and one neutral gray screen ("background"), presented in an interleaved manner. Four center stimuli were generated by presenting a small circular or square window against a neutral gray background within which a drifting square-wave grating (0.75 cycle per degree, 1.5 degrees/sec) was shown at one of four orientations (0° , 45° , 90° , 135°). Four surround stimuli were constructed in an identical manner, except that the grating was shown outside the window, and neutral gray was shown inside the window. Square windows were always oriented along the 0° and 90° directions. Typically, the topmost edge of the window was positioned to fall within the imaged area.

The timing of the stimulus was chosen to give the maximum optical signal, as determined in preliminary experiments. The oriented grating was shown in a stationary position for 5 sec, and then was drifted at a rate of 1.5 Hz. Camera frames at 30 Hz were summed into five larger time blocks of 900 msec each. The first and last frames were discarded for the purposes of analysis; thus, the data represent the summed signal from 1300 msec to 4600 msec after the start of stimulus motion. Data for each set of stimuli were typically collected over 3–5 hr.

Single-Unit Recording. Single units were recorded with tungsten microelectrodes of impedance 2–4 M Ω . The signal was amplified, filtered at 1–10 kHz, digitally windowed, and collected on a 486 computer using a 200-MHz A/D board (software written by L.J.T.). Receptive fields were first hand plotted, and subsequently quantified (see legend to Fig. 3 *A* and *B*). To examine center/surround interactions, stimuli identical to those in the imaging session were used, with grating orientations adjusted to the preferred orientation of the cell.

RESULTS

We evaluated the optical imaging data based on responses to 40–70 presentations of interleaved center/surround stimuli per experiment in 12 animals.

Optical Imaging Reveals Center and Surround Activation. Fig. 1 shows representative plots of the cortical activity gen-

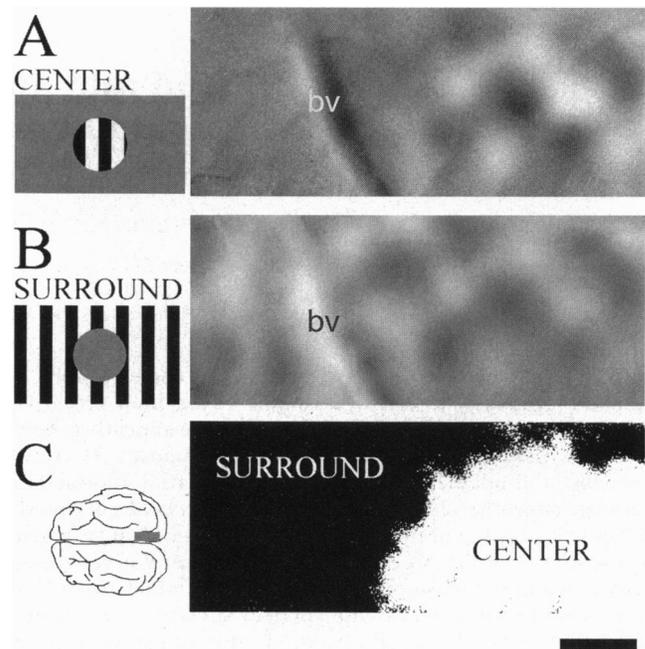


FIG. 1. Cortical responses to *A* (center) and *B* (surround stimuli). Stimuli are shown schematically at the left. Each map represents the response, summed over 56 presentations, to vertical grating stimuli divided by the response to horizontal grating stimuli. *bv*, an artifact from a large superficial blood vessel. (*C*) The activity border, calculated from single-condition maps, obtained in response to center and surround gratings each presented at four discrete orientations. White regions are points where maximal activity was elicited by one of the center stimuli and black regions are points where maximal activity was elicited by one of the surround stimuli. Note that although the border runs approximately through the image center, surround activity extends throughout the entire cortical region. Similarly, faint center activity is just detectable anterior of "bv." The overhead view of the cat's brain (Fig. 1*C*, left) shows the location and orientation of the imaged cortex. (Bar = 1 mm.)

erated from center (Fig. 1*A*) and surround stimuli (Fig. 1*B*). The spatial location of activity for the center stimulus is in agreement with standard maps of retinotopy in cat area 17, because the top edge of the spot is positioned 3° below the area centralis and on the vertical meridian [for example, Tusa *et al.* (23) report coordinates of P4.0 for the representation of area centralis in most cats, and show examples of visual fields between 0 and -5° elevation located between P3.0 and A0.6]. However, two other features appear in this image apart from this retinotopic correspondence. First, the clear edge that appears in the stimulus does not exist in the cortical map. Many orientation domains are strongly activated by both center and surround stimuli (Fig. 1). This fuzziness is not entirely unexpected, as a particular point of the retinal image is known to be capable of directly activating a whole population of cortical cells, with a spatial spread of up to a few millimeters (13, 24). The second feature to note, however, is that the magnitude of activity varies across the cortical surface, such that by comparing the center and surround maps, a reasonable approximation of the edge location can be made. To quantify this location, we compared the magnitude of the center and surround maps at each pixel in the image. Fig. 1*C* shows the result of this comparison. Regions that gave a greater response to the center stimulus are shown in white, whereas regions that gave greater response to the surround stimulus are shown in black. We define the border thus obtained as the cortical location of the stimulus edge.

Orientation Specificity of Cortical Activation. Fig. 2 shows maps of orientation preference constructed from the imaging data. Preferred orientation at each cortical point (computed by

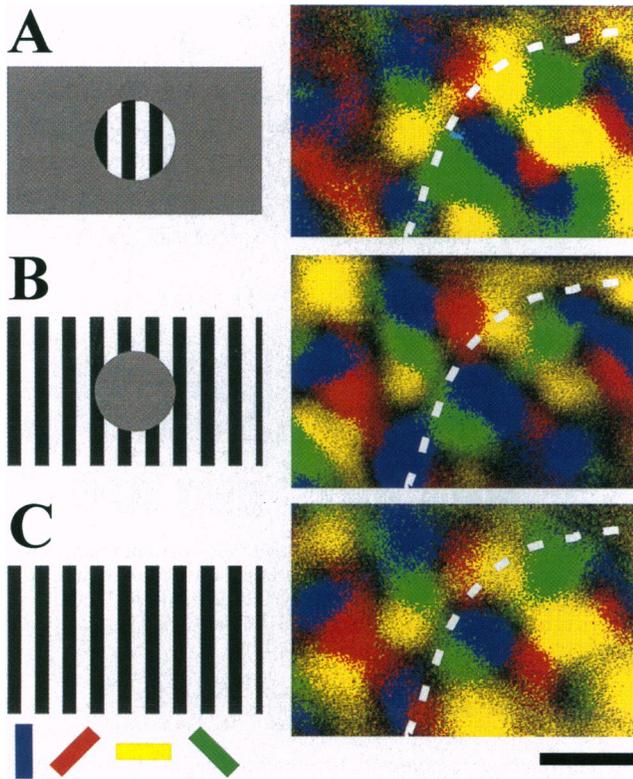


FIG. 2. Maps of the summed orientation vector for (A) center, (B) surround, and (C) full-field stimuli. Vector angle, coding orientation preference at each pixel, is shown by color, and vector magnitude, coding strength of orientation-specific signal, is shown by intensity. Brightest intensities are one standard deviation above the image mean and are approximately equal for all three maps. The dotted white line denotes the stimulus border (see Fig. 1C). Although the center stimulus evokes a stronger (brighter) response within the center representation (right of the border), the center stimulus continues to elicit strong, orientation-specific signals outside the center representation (left of the border). Similarly, the surround stimulus elicits strong signals within the center representation, filling-in the map of orientation preference. The good correspondence of preferred orientation angle across all three maps indicates that the "filled-in" regions receive iso-orientation activation. (Bar = 1 mm.)

taking the angle of the vector averaged response to all orientations at each pixel) is shown by the color code and strength of orientation preference (magnitude of the vector average) is shown by intensity (black coding for weakest orientation preferences). Fig. 2A shows the cortical response to the center stimulus (the dotted white line showing the location of the stimulus edge, obtained as in Fig. 1). Strong magnitudes are observed over the center representation (right, posterior side of image), whereas weaker magnitudes occur over areas that are not directly stimulated (left, anterior side of image). The map of orientation preference agrees well with the map obtained from a full-field stimulus (Fig. 2C). Similarly, the cortical response to the surround stimulus (Fig. 2B) shows strong magnitudes over the region of direct activation (left, anterior side), and a significant, though weaker response over the center representation (right, posterior side). Again, the map of orientation preference corresponds well with that obtained during full-field stimulation. Distant cortical points, including pixels well inside (for surround stimuli) and well outside (for center stimuli) the center representation, show activity exclusively in iso-orientation domains.

Effect of the Surround on Center Responses. Having shown that distant regions of cortex are activated by a localized stimulus in an orientation-specific manner, we wished to establish the source of the distant activation. We reasoned that

by measuring receptive field sizes at known locations relative to the stimulus edge representation, we could determine whether these optical signals represented activity arising inside or outside of the classical receptive field. In four cats, micro-electrode recordings were made in both the center and surround representations in imaged cortex. Data from two of

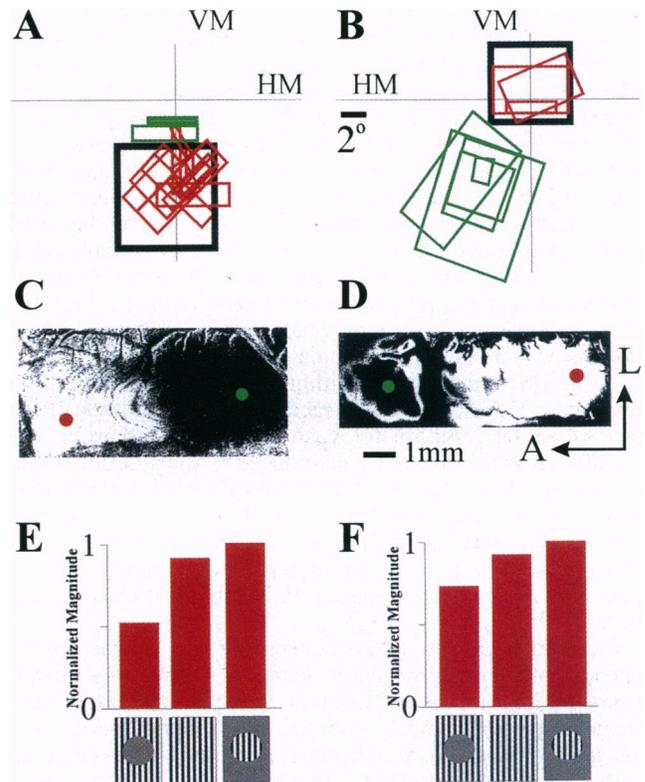


FIG. 3. Positioning of subthreshold (surround) and suprathreshold (center) receptive fields relative to the intrinsic signal map. (A and B) Single-unit receptive fields recorded from center (red) and surround (green) areas of cortex in two animals. The border of the center stimulus (which was square for these experiments) is shown in black. Figures are drawn to the same scale. Receptive fields were determined quantitatively by collecting responses to 10 repetitions each of 16 directions of high-contrast bars of optimal length, width, and velocity under computer control. The stimulus positions for which responses differed significantly from background levels were corrected for a 100-msec latency, verified by comparison with the position of the offset response to stimuli of reverse direction, and diagrammed with an outer rectangle, slightly overestimating the measured receptive field area. (C and D) Locations of the electrode penetrations from which the data in A and B, respectively, were obtained superimposed on a map of the imaged center/surround border calculated by the same methods as in Fig. 1C. White represents center dominated regions, black represents surround dominated regions. Red receptive fields in A were recorded from the red position in C, etc. Receptive field locations show a clear positional separation with nearly all receptive fields contained entirely within the appropriate stimulus region. Figures are shown at the same scale. (E and F) Magnitude of the optically imaged response for each of the stimuli from two animals in which the highest signal-to-noise ratio was obtained. Magnitudes were calculated from 100- μm^2 regions of the optical map where single-unit receptive fields lay entirely within the area of the center stimulus. Responses were normalized; the activity present during the background stimulus is represented as 0 and the response to a high-contrast center stimulus as 1. The chosen region is large enough that the standard error between pixels is less than 1% of the signal magnitude. In both cases, the surround stimulus generated an optical signal with over one-half the magnitude of the center-only signal (52% in E and 72% in F; compare with Fig. 4A). Surround suppression was also observed in that the full-field stimulus (center + surround) generated a smaller optical signal (92% in E, 91% in F; compare with Fig. 4B) than center only stimulation. VM, vertical meridian; HM, horizontal meridian; A, anterior; L, lateral.

these animals are shown in Fig. 3. Fig. 3*A* and *B* show receptive fields recorded at sites chosen to be well within the center and surround representations. The position of the recording sites relative to the cortical representation of the stimulus edge (calculated as in Fig. 1*C*) is shown in Fig. 3*C* and *D*. The location of the center stimulus (square, in these cases) is superimposed in black on the receptive fields recorded within the center representation. Note that in the first case (Fig. 3*A* and *C*) the center spot is below the area centralis, and thus the top edge is being imaged, whereas in the second case (Fig. 3*C* and *D*) the center spot covers area centralis, so the bottom edge is being imaged. (In our experiments, the imaged stimulus edge was consistently located between 3° and 5° below area centralis.) Clearly, for neurons at the location within the center representation marked in red, the surround stimulus excluded the suprathreshold center and engaged primarily the subthreshold receptive field surround. We determined (see, for example Fig. 3*C* and *D*) that at distances of >2 mm from the center/surround border, classical receptive fields are nonoverlapping. This distance is consistent with a previous report on receptive field progression, size and scatter within cat area 17 (24).

At the discrete locations within the center representation (red dots in Fig. 3*C* and *D*) we measured the magnitude of the intrinsic signal response for each stimulus to ascertain the modulation of the optical signal induced by the addition of the surround (Fig. 3*E* and *F*). A high-contrast surround stimulus causes an increase in cortical activation compared with a neutral gray (background) stimulus. However, a full-field stimulus (i.e., a high-contrast center plus surround) causes a reduction in activity compared with a high-contrast center stimulus alone.

We note here two issues concerning the use of optical imaging data to measure center/surround interactions. First, it is possible that the center location where activity levels were evaluated (Fig. 3*C* and *D*) contains two cell populations, one activated by the center and the other activated by the surround, so that the measured effects are actually due to responses of two independent cell populations. If so, one should expect the response to the full-field stimulus to equal the sum of the center and surround responses. This is clearly not the case: the full-field response is consistently less than the summed response (Fig. 3*E* and *F*), arguing that the facilitation and suppression effects involve the same cells. Second, optical recording does not distinguish between the activity of excitatory or inhibitory neurons, raising the issue of whether the largely subthreshold, iso-orientation activity generated in the center representation by the surround stimulus could be inhibitory in nature. Again, the fact that the full-field response is not a linear combination of the center and surround responses argues against such a possibility. That is, one would expect inhibitory activity present during surround stimulation to add to, not subtract from, the signal during full-field stimulation, because both inhibitory and excitatory activity would cause an increase in the strength of the optical signal. These issues are addressed more clearly, however, by recording the responses of single units to the same stimuli.

Single-Unit Recordings Demonstrate Biphasic Surround Effects. The data presented above indicate that the optically imaged spread of cortical activation cannot simply be due to spiking activity, and that it may include subthreshold components. We therefore examined whether suprathreshold single-unit responses (spikes) also show the same biphasic pattern of subthreshold, surround modulation observed with optical imaging. We recorded single-unit responses ($n = 30$ cells) to the identical stimuli used for optical imaging: a neutral gray screen without any stimulus contrast, a high-contrast center grating covering the receptive field center, a surround grating complementary to the center grating, and a full-field grating covering both center and surround. We adjusted the grating orientations to be optimal for each cell studied. For each cell,

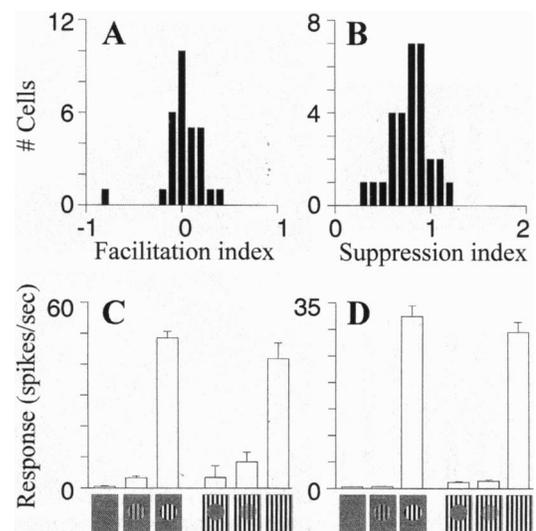


FIG. 4. Interactions between receptive field surround and center revealed by single-unit recordings. (A) Population histogram for the amount of spiking response elicited by the surround for neurons in center regions (such as red dots in Fig. 3*C* and *D*). The facilitation index, plotted on the x-axis, is calculated by:

$$\text{facilitation index} = \frac{R_{\text{surround}} - R_{\text{background}}}{R_{\text{center}} - R_{\text{background}}}$$

R is the summed response to 10 presentations of the subscripted stimulus. A value of zero indicates no surround response. Values less than zero are possible when the response to the surround is less than the response to the background. The average index value is 0.0682, indicating that the surround alone caused a very weak spiking response across the population. (B) Similar population histogram of the suppression index in the same neurons for the addition of surround stimulation to center stimulation. The suppression index, plotted on the x-axis, is calculated by:

$$\text{suppression index} = \frac{R_{\text{full field}} - R_{\text{background}}}{R_{\text{center}} - R_{\text{background}}}$$

Values less than 1 indicate suppression, greater than 1 indicate facilitation. The average index value is 0.843, indicating that adding surround stimulation generally inhibited responses. (C and D) Facilitatory and suppressive effects of a high-contrast surround in two representative cells. The average response to 10 stimulus presentations is plotted versus the stimulus type. Stimuli are permutations of zero, low- and high-contrast centers with zero and high-contrast surrounds: (i) neutral gray center and surround, taken as background; (ii) low-contrast center grating, neutral surround; (iii) high-contrast center, neutral surround; (iv) neutral gray center, high-contrast surround; (v) low-contrast center, high-contrast surround; (vi) high-contrast center and surround. Notice that in both cells, the surround facilitates the response to the low-contrast center (compare second and fifth bars), but suppresses the response to the high-contrast center (compare third and sixth bars).

we calculated two normalized indices as a measure of surround facilitation or suppression, mimicking the calculation used for evaluating intrinsic signal activity (see the legend to Fig. 4). The "facilitation index" (Fig. 4*A*) represents surround-induced response above baseline levels expressed as a percentage of the center response; positive values imply that the surround grating caused an increase in responses relative to background (in effect representing a summation of subthreshold responses to cause increased firing). The "suppression index" (Fig. 4*B*) represents the ratio of the full-field response to the center response; values less than 1 indicate suppression of the center response by concurrent stimulation of center and surround.

To better demonstrate the facilitatory effect of the surround on single-unit responses, we added two new stimuli: (i) a center

stimulus of low contrast and neutral surround and (ii) a center stimulus of low contrast with a high-contrast surround. These stimuli were presented to a total of 17 cells, the low-contrast value being set independently near threshold for each cell. Responses to the full set of stimuli from two representative cells are shown in Fig. 4 *C* and *D*. In cells that also demonstrated the suppressive effect of the high-contrast surround on a high-contrast center, we observed small but present facilitatory effects of the same high-contrast surround on a low-contrast center, when the contrast was close to threshold for that cell. We conclude that the surround can have both facilitatory and suppressive effects, depending on the stimulus contrast. Because a high-contrast surround facilitates a low-contrast iso-orientation center response, we suggest that the center activation, via surround stimulation observed in optical recordings, is therefore likely to be excitatory in nature.

How Much of the Intrinsic Signal Is Subthreshold? Although Fig. 4*A* establishes that the suprathreshold single-unit response to the surround stimulus alone is very small (6.8% of the center response) optical signals from similar locations are quite strong (Fig. 1*B*). We plotted the intrinsic signal magnitude for each stimulus at the points shown in red in Fig. 3. Surround activation in these experiments was between 50 and 75% that of the center. Graphically, this means that all but 6.8% of the activity in the spot region of a surround intrinsic signal map (such as Fig. 1*B*) is subthreshold in origin, and that subthreshold activity may therefore represent one-half to three-fourths of the maximum obtainable intrinsic signal activity in that region.

DISCUSSION

Subthreshold Stimulation. The fact that single-unit receptive fields are nonoverlapping between spot and surround regions more than 2–3 mm apart (Fig. 3*A* and *B*) suggests that any effects of the surround stimulus on the response of neurons located in the center region (and *vice versa*) are subthreshold in nature. The lack of significant single-unit responses during stimulation with the surround grating (Fig. 4*A*) confirms this observation. These observations, taken together, are strong evidence that spiking activity alone is not sufficient to account for the strength of the optical signal present. We suggest that the contribution of subthreshold signals, possibly resulting from metabolic activity in dendrites or at synapses, accounts for much of the observed intrinsic signal activity. Evidence suggests that the majority of subthreshold visual inputs, both excitatory and inhibitory, to a given area 17 neuron are specific to iso-orientations (25, 26). Thus, the balance of subthreshold activity to any given column may be expected to provide a well-localized signal that varies smoothly across the cortex in the manner of intrinsic signal activity maps (such as Fig. 1*A* and *B*).

Point Spread in Cortex. The question of the amount of cortex capable of responding to a given point in the visual field involves both the anatomical spread of thalamocortical and intracortical connections and the physiological effect of these connections. Previous studies suggest that thalamocortical afferents arborize over a maximum area of 1.8 mm² (27) or a maximum lateral distance of 1.0–1.5 mm. Similarly, single-unit studies of the point spread distance from retina to cortex have suggested values on the order of 1–2 mm (13, 24, 28, 29). These values are clearly too small to account for the amount of signal spread that we (up to 6 mm) and others [Grinvald *et al.* (17), up to 10 mm; Das and Gilbert (13), 3.2–5.2 mm] observe optically, suggesting that the lateral activity is mediated by intracortical connections and likely involves subthreshold influences. Within area 17, superficial layer pyramidal cells can have lateral axonal spreads of up to 6–8 mm (2, 3). Long-range horizontal connections are large enough to connect areas of completely separate receptive fields (30). It seems likely that

a combination of thalamocortical excitation, horizontal connections, and subthreshold activation (discussed above) is responsible for the large point spread areas observed with optical recording.

Relation to Visual Processing. Filling-in refers to the percept that occurs in normal monocular vision in the region of the blind spot, and in the vision of patients with focal lesions of the early visual system. The color and texture of the surrounding region is perceived in the region devoid of input. Ramachandran and Gregory (31) demonstrated that the same effect could be caused artificially by stimuli containing flickering random noise in a retinally stable region of the visual field. A possible mechanism behind the filling-in percept may be the dynamic expansion of cortical receptive fields (11, 12). Although our single-unit studies (Fig. 4*A*) fail to provide evidence that neurons in the center region expand their receptive fields enough to be significantly driven by the surround stimulus, our optical data suggest that cells in the center region have access to enough information that they could generate the filling-in percept under the right conditions. The optical signals could also represent feedback information from other visual areas that could generate filling-in by similar mechanisms (32).

Our finding that the level of center contrast regulates whether the surround modulation is facilitatory or suppressive is novel in cat visual cortex. Knierim and Van Essen (16) and Fries *et al.* (33) have observed the suppressive effect of an oriented surround in monkey V1, and have suggested that the maximal effect occurs at similar orientations of center and surround. Other kinds of surround effects have been observed, including an effect of the orientation of the surround on center responses in single cells (8). By lowering the detection threshold for iso-orientation stimuli, surround excitation is an appropriate mechanism for mediating the perceptual completion of occluded objects. Similarly, inhibition of center responses by the surround may mediate perceptual pop-out (34, 35), although in our experiments changing the phase of the center grating relative to the surround to create a pop-out center target resulted in an activity pattern not measurably different from that induced by the full-field condition (data not shown). Perceptual pop-out has many features and may also rely on temporally coded responses that cannot be detected with the intrinsic signal technique. Our finding that the same surround stimulus can have either a facilitatory or suppressive effect is also supported strongly by recent theoretical proposals and computational models of long-range connections in visual cortex (18, 19). Together, they demonstrate that even area 17 contains the physiological substrate to mediate phenomena associated with “higher level” vision, or at least can contribute significantly to the ability of a later area to do so.

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