30 Beyond the Classical Receptive Field: Surround Modulation in Primary Visual Cortex

ALESSANDRA ANGELUCCI AND S. SHUSHRUTH

The concept of the classical receptive field (RF) (Barlow, 1953; Hubel & Wiesel, 1959) and hierarchical feedforward models of the visual system (Hubel & Wiesel, 1962; Riesenhuber & Poggio, 2003) have provided a foundation for theories of the neural representation of visual objects. These theories view cells as "filters" or "feature detectors" and visual information as ascending through a hierarchy of cortical areas (Van Essen & Maunsell, 1983), with RFs in higher areas processing information from increasingly larger regions of visual space and coding for increasingly more complex aspects of visual stimuli. These models are feedforward in that the increasingly complex and invariant representation of objects is built by integrating convergent feedforward inputs from lower levels.

In recent years, anatomical, computational and physiological evidence has challenged these theories. Anatomically, in addition to feedforward projections between cortical areas, there is a massive system of feedback connections that is unaccounted for by purely feedforward models. Computationally, feedforward models can perform object recognition in simple environments but not in cluttered environments such as natural scenes. This is because local information processed by neuronal RFs in natural scenes is ambiguous, and the computation of object boundaries requires knowledge about the global properties of a scene for disambiguation. Physiologically, there is evidence that in the visual system global-to-local computations occur even at the lowest level of processing, that is, in the primary visual cortex (V1), where neuronal responses to local features within their RFs are affected by the perceptual organization of the scene as a whole. A fundamental example of such computations is surround modulation—the ability of neurons in V1 (and other areas) to change their response to stimuli within their classical RF depending on visual context, i.e., the stimuli presented in the RF surround (Allman, Miezin, & Mc Guinness, 1985; Blakemore & Tobin, 1972; Maffei & Fiorentini, 1976; Nelson & Frost, 1978). This phenomenon implies integration of signals across distant visual field locations, well beyond the classical RF of single V1 neurons, and thus cannot be easily explained by feedforward mechanisms and classical RF concepts.

In the present chapter we first review the phenomenology of surround modulation in V1, then examine the circuitry and mechanisms that may generate it, and finally discuss its role in visual processing and perception.

PHENOMENOLOGY OF SURROUND MODULATION

Hubel and Wiesel (1965) first described a class of cells in areas 18 and 19 of the cat visual cortex that were selective for the length of a bar, in that their response was suppressed by stimuli extending beyond a critical length. They named these cells "hypercomplex," believing they were generated by converging feedforward afferents from area 17 complex cells. However, later studies found that even simple and complex cells throughout area 17 showed length tuning and that increasing the width of a stimulus had a similar effect (Gilbert, 1977; Maffei & Fiorentini, 1976; Nelson & Frost, 1978). The terms "end stopping" and "side inhibition" or surround suppression came to replace the term hypercomplex. These early reports suggested that the notion of the classical RF was insufficient to understand the neural substrates of visual perception. However, the concept of a non-classical RF (or surround) did not become established until the mid-1980s (Allman, Miezin, & Mc Guinness, 1985). A series of studies followed in which surround modulation was characterized quantitatively using circular or annular gratings and varying systematically the stimulation parameters. Overall, these studies indicated that surround

modulation is a property of most V1 cells: 56–86% of cells in cat V1 (Sengpiel, Sen, & Blakemore, 1997; Walker, Ohzawa, & Freeman, 2000) and 60–100% in macaque V1 (Cavanaugh, Bair, & Movshon, 2002a; Sceniak, Hawken, & Shapley, 2001; Shushruth et al., 2009). They also showed that the predominant surround effect is *suppression* of the spiking response to RF stimulation, and that this suppression is sensitive to surround stimulus parameters (such as orientation, spatial frequency, speed, and contrast), that is, the suppression is reduced or turns to *facilitation* for specific stimulation parameters. Below we review these studies.

Spatial Properties of Surround Modulation: Defining the Receptive Field and the Surround

The surround is defined as the region outside the RF where presentation of stimuli does not cause the cell to spike but can modulate its response to stimuli inside the RF. Therefore, any study of surround modulation requires defining the limits of the RF. This is not simple because RF size varies depending on how it is measured. A common approach to map the RF has been to use a small stimulus (a light or dark bar or small grating) at the appropriate orientation for the cell to delimit the visual field area that elicits spikes from the cell, a measure of RF size termed *minimum response field* (mRF) or *classical RF* (Barlow, Blakemore, & Pettigrew, 1967; Hubel & Wiesel, 1962). However, intracellular recordings in cat area 17 (Bringuier et al., 1999) have demonstrated that the mRF is surrounded by a larger subthreshold depolarizing field incapable of driving the cell when stimulated alone but capable of increasing the cell's response when stimulated with the mRF. With extracellular recordings, this subthreshold region of the RF can be revealed by measuring the cell's response to a circular grating of increasing radius centered on the mRF. A typical V1 cell increases its response with grating size up to a peak and is suppressed for further increases in size (figure 30.1, black curve). The RF size thus corresponds to the grating's radius at the cell's peak response. In macaque V1 at parafoveal eccentricities, RF dimensions based on these areal summation measurements using high-contrast gratings are two to three times larger than the mRF of the same cells (Angelucci et al., 2002). Furthermore, when this measure of RF is performed using gratings of low contrast, the stimulus area over which summation occurs increases by about twofold compared to the summation area measured with high-contrast gratings (figure 30.1, gray curve) (Sceniak et al., 1999; Sengpiel, Sen, & Blakemore, 1997). In this chapter we refer to the RF size based on these summation measurements at high or low stimulus contrast, as the cell's high- or low-contrast summation RF (sRF_{high} and sRF_{low}, respectively) (figure 30.1).

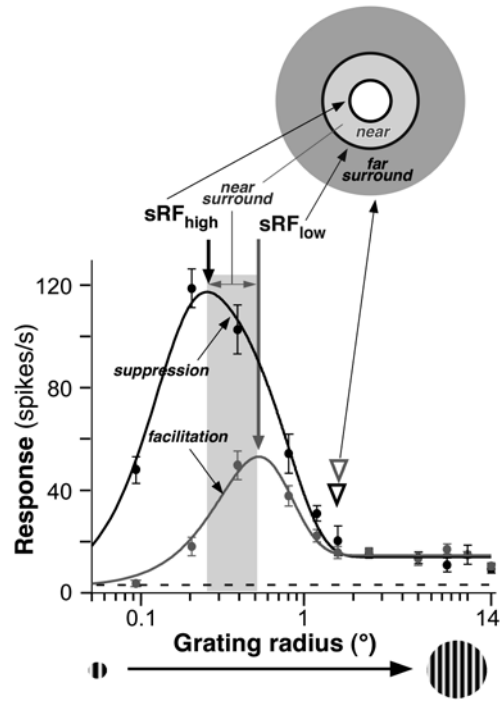

FIGURE 30.1 Size tuning curve of an example cell in macaque V1. Black and gray curves show responses to a grating of high (70% contrast) and low (12%) contrast, respectively. Dashed line shows mean spontaneous firing rate. Thick arrows indicate the radii of the sRF_{high} (black; 0.26°) and sRF_{low} (gray; 0.54°). Gray shaded column indicates the near surround. Arrowheads point at surround radius at high (black; 1.41°) and low (gray; 1.41°) contrast. Cartoon illustrates schematics of the different components of the RF and surround of a V1 cell: white area, RF; gray area, surround, consisting of a near and a far region. (Modified from Shushruth et al., 2009.)

FACILITATORY MODULATIONS: STUDIES WITH DISCRETE STIMULI A consequence of the contrast dependence of the sRF size is that stimuli presented in the region between the sRF_{high} and the sRF_{low} (gray column in figure 30.1) can exert facilitatory or suppressive effects, depending on stimulus contrast. Whether this region should be considered part of the surround or part of the RF has been a matter of debate. In particular there is still disagreement as to whether surround effects can be facilitatory under specific stimulation conditions. Several studies have shown that facilitatory modulations occur predominantly when discrete stimuli (bars or Gabor patches) are presented at the end zones of the mRF collinearly aligned in visual space with the orientation of the stimulus inside the mRF (figure 30.2A) (Chisum, Mooser, & Fitzpatrick, 2003; Kapadia et al.,

1995; Maffei & Fiorentini, 1976; Nelson & Frost, 1985; Polat et al., 1998). This facilitation dominates when the stimulus in the mRF is presented at low contrast, and can turn to suppression when it is presented at high contrast (Kapadia, Westheimer, & Gilbert, 2000; Mizobe et al., 2001; Polat et al., 1998). This phenomenon, known as *collinear facilitation*, is thought to be the neural correlate of perceptual contour integration (Hess & Field, 1999; Kapadia, Westheimer, & Gilbert, 2000) (discussed below). If one regards the sRF_{low} of a cell as part of the cell's RF, then these facilitatory effects can be viewed as simply occurring within the RF (figure 30.2A), and therefore, one would conclude that there are no facilitatory surround effects (Angelucci & Bullier, 2003; DeAngelis, Freeman, & Ohzawa, 1994; Fitzpatrick, 2000; Walker, Ohzawa, & Freeman, 1999). Collinear facilitation and increased spatial summation at low stimulus contrast would thus simply share similar mechanisms. Consistent with this interpretation, the strength of collinear facilitation decreases with increasing spatial separation of the stimuli inside and outside the mRF (figure 30.2A, bottom). However, because the region between the sRF_{high} and sRF_{low} can be suppressive at high contrast (figure 30.1, black curve), it can also be viewed as part of the surround. This observation together with anatomical studies (discussed below) suggesting a distinctive circuitry for this region have led some (Angelucci & Bressloff, 2006) to refer to it as the *near surround* and to the region beyond the sRF_{low} as the *far surround* (figure 30.1). Moreover, not all facilitatory surround effects can be attributed to stimulation of the RF by a surround stimulus, because facilitatory inputs can arise 12° away from the RF center in both cat (Mizobe et al., 2001) and macaque V1 (Ichida et al., 2007; Shushruth et al., 2012).

A more comprehensive explanation of surround effects, instead, is that the sign of surround modulation depends on the strength of activation of both the RF and its surround. When the RF is strongly activated (e.g., by an optimally oriented high-contrast stimulus fitted to the cell's sRF_{high}), weak or strong surround stimulation evokes predominantly suppression (Cavanaugh, Bair, & Movshon, 2002a; DeAngelis, Freeman, & Ohzawa, 1994; Ichida et al., 2007; Levitt & Lund, 1997; Sceniak, Hawken, & Shapley, 2001; Sengpiel et al., 1998; Shushruth et al., 2009). Instead, surround facilitation is more frequently observed for weak stimulation of both the RF and the surround. For example, it occurs in 34–38% of V1 cells when the RF and surround are stimulated with discrete elements (of optimal orientation for the cell) (Chen et al., 2001; Polat et al., 1998) (figure 30.2A), especially if the element in the RF is at low contrast. It is also frequently observed (~60% of macaque V1 cells) when the sRF_{low} is stimulated by an optimally oriented grating near the cell's contrast threshold and the surround by an iso-oriented thin annular grating; lowering the contrast of this surround stimulus increases the strength of facilitation, whereas increasing the width of the annular grating turns the facilitation into suppression (Ichida et al., 2007) (figure 30.2B). Similarly, surround facilitation emerges in many cells (~35% in macaque) when both the RF and surround are weakly stimulated with high-contrast gratings of suboptimal orientation for the recorded cell (Shushruth et al., 2012). Importantly, the threshold for suppression versus facilitation is cell specific, so that there is no single contrast level or surround stimulus size that causes facilitation across the entire cell population.

SUPPRESSIVE MODULATIONS: STUDIES WITH LARGE GRATINGS In most other studies surround modulation was investigated using a central grating fitted to the cell's sRF_{high} surrounded by a large annular grating involving the near and far surround, while varying the center and surround grating parameters (e.g., their relative orientation, spatial frequency and contrast). These studies found that when the sRF_{high} is stimulated by a grating of optimal orientation for the cell, a large iso-oriented surround grating predominantly *suppresses* the cell response (Cavanaugh, Bair, & Movshon, 2002a; DeAngelis, Freeman, & Ohzawa, 1994; Levitt & Lund, 1997, 2002; Sceniak, Hawken, & Shapley, 2001; Sengpiel, Sen, & Blakemore, 1997; Walker, Ohzawa, & Freeman, 2000), even when the center grating contrast is lowered (Cavanaugh, Bair, & Movshon, 2002a; DeAngelis, Freeman, & Ohzawa, 1994; Levitt & Lund, 1997). Suppression is reduced or abolished, occasionally turning to facilitation, as surround stimulus parameters increasingly differ from those of the center grating. Facilitation was rarely observed in these studies because of the strong surround stimulation exerted by large surround annuli.

Furthermore, the surround is not always organized in a concentric and symmetric fashion, as suppression can arise from a single modulatory zone (Walker, Ohzawa, & Freeman, 1999), from only the end or side zones of the sRF, and is often stronger at the end zones (Cavanaugh, Bair, & Movshon, 2002b; DeAngelis, Freeman, & Ohzawa, 1994; Sceniak, Hawken, & Shapley, 2001). Moreover, suppression is stronger in the near than in the far surround.

SPATIAL EXTENT AND STRENGTH OF SURROUND MODULATION Two different stimulus protocols have been used to measure the extent and strength of

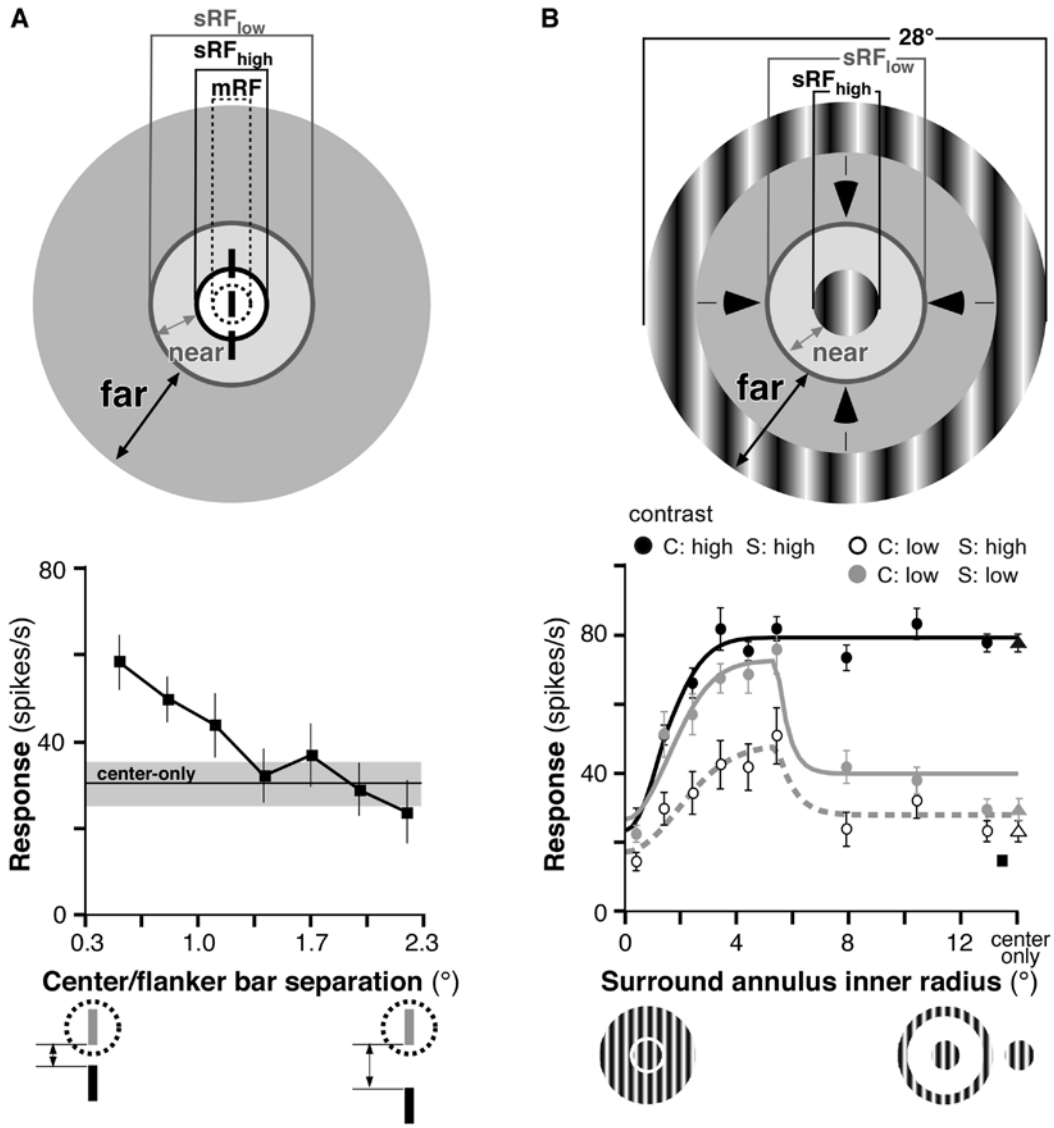

FIGURE 30.2
Center and surround stimuli that can evoke facilitatory modulations. (A) Collinear facilitation. (Top) cartoon indicates different RF and surround components and the bar stimuli used to evoke collinear facilitation. (Bottom) Response of a V1 cell in awake macaque as a function of the spatial separation of the bar stimuli inside and outside the mRF. Horizontal line marks the cell's response to the center bar alone (presented at low contrast). Gray area represents 1 SEM of the center-only response. Iso-oriented and co-aligned discrete stimuli inside and outside the mRF, but within the sRF_{low}, can evoke facilitation. (Bottom modified from Kapadia et al., 1995, reproduced with permission from Cell Press.) (B) Facilitation from the far surround. (Top) RF and surround components and the grating stimuli used to evoke far-surround facilitation. The center grating is matched to the size of the sRF_{high}, and the inner radius of the annular grating in the surround is decreased (arrows) from 13° to the size of the cell's sRF_{low}, thus stimulating only the far surround. (Bottom) Response of a V1 cell in an anesthetized macaque as a function of the inner radius of the surround annular grating. Dashed and solid curves indicate responses to different combinations of center (C) and surround (S) stimulus contrast as follows: 70%/70% (black), 20%/70% (dashed gray), 20%/20% (solid gray). The triangles are responses to center-only stimulation. The square indicates response to a surround stimulus of smallest inner radius presented alone. At high center contrast, surround stimulation always evokes suppression. When the center grating is at low contrast, a small annular stimulus in the far surround evokes facilitation, followed by suppression as more of the surround is stimulated. Thus, large surround stimuli of any contrast evoke suppression. (Modified from Ichida et al., 2007, reproduced with permission from the American Physiological Society.)

surround modulation: the expanding patch (figure 30.1) and expanding annulus (figure 30.2B) methods. The former activates both the near and far surround, but it predominantly reveals the stronger suppressive effects from the near surround. The latter, by masking out the near surround, reveals the weaker modulations from the far surround. In macaque V1 at parafoveal eccentricities, the average surround radius measured with the expanding patch method is ~1.6°, that is, five to six times larger than the sRF_{high} of V1 cells, and can extend up to ~3° (Cavanaugh, Bair, & Movshon, 2002a; Levitt & Lund, 2002; Sceniak, Hawken, & Shapley, 2001; Shushruth et al., 2009). Surround radius measured with the expanding annulus method is larger, averaging 5.5° and extending up to 12.5° (Shushruth et al., 2009).

Near-surround suppression is strong; about 50% of V1 cells in macaque are suppressed by 60% or more (mean 58%, ranging up to 87%) (Sceniak, Hawken, & Shapley, 2001; Shushruth et al., 2009), and ~40% in cat are suppressed by more than 40% (Walker, Ohzawa, & Freeman, 2000). Far-surround suppression (mean 25%, ranging up to 61%) is weaker than near-surround suppression (Shushruth et al., 2009). Surround facilitation has a similar spatial extent as suppression, that is, it can arise up to 12° away from the RF center, and near-surround facilitation is stronger (mean 64%) than far-surround facilitation (mean 32%) (Ichida et al., 2007).

Surround modulation occurs in all V1 layers (Levitt & Lund, 2002; Sceniak, Hawken, & Shapley, 2001; Walker, Ohzawa, & Freeman, 2000). However, subtle laminar differences exist that may reflect laminar differences in connectivity. For example, in macaque V1 larger surrounds are absent in geniculocortical recipient layer 4C (Ichida et al., 2007; Shushruth et al., 2009), a layer lacking long-range intracortical connections. This suggests that the larger far surrounds in other V1 layers are generated by long-range intracortical connections within these layers. Moreover, near- and far-surround suppression in macaque V1 are both stronger in the supragranular layers (4B and above) (Sceniak, Hawken, & Shapley, 2001; Shushruth et al., 2009).

Tuning of Surround Modulation

THE EFFECTS OF CHANGING THE ORIENTATION OF THE SURROUND STIMULUS By stimulating the RF with gratings of optimal parameters for the recorded cell while varying the parameters of the grating in the surround, previous studies concluded that surround modulation is selective for surround stimulus orientation and spatial and temporal frequency and that this selectivity is similar to, but broader than that of the same cells' RF (Cavanaugh, Bair, & Movshon, 2002b; DeAngelis, Freeman, & Ohzawa, 1994; Li & Li, 1994; Webb et al., 2005). Typically, suppression is maximal when the center and surround gratings have the same orientation, spatial frequency, drift direction (Cavanaugh, Bair, & Movshon, 2002b; DeAngelis, Freeman, & Ohzawa, 1994; Levitt & Lund, 1997; Muller et al., 2003; Sengpiel, Sen, & Blakemore, 1997; Walker, Ohzawa, & Freeman, 1999) and speed (Li & Li, 1994). Suppression is reduced or disappears, sometimes turning to facilitation, as the difference in orientation (or other parameters) between the center and surround stimuli is increased. Instead, suppression is insensitive to the relative spatial phase of the stimuli in the RF and surround (DeAngelis, Freeman, & Ohzawa, 1994; Levitt & Lund, 1997) or to chromatic contrast (Solomon, Peirce, & Lennie, 2004). The orientation tuning of surround modulation also depends on a cell's position in the orientation map, with suppression being more sharply tuned at orientation domains than at pinwheel centers (Hashemi-Nezhad & Lyon, 2011), likely reflecting differences in the orientation specificity of the local and long-range connectivity at these different map locations.

Most previous studies used gratings that stimulated both the near and far surround. Recently, however, Shushruth et al. (2013), using annular gratings confined to the near or far surround, found that near suppression is more sharply tuned than far suppression (figure 30.3). Using similar stimuli and a contrast-matching task, these authors obtained a similar result for near- and far-surround suppression of perceived contrast in human observers. In both V1 cells and human perception, broader tuning of far-surround suppression was due to nonoptimal stimulus orientations exerting stronger suppression in the far than in the near surround. These results suggest different orientation specificities of the circuits underlying near- and far-surround suppression and point to an important relationship between surround suppression in V1 and in human perception. The same study also found laminar differences in the orientation tuning of both near- and far-surround suppression, suggesting laminar differences in the orientation specificity of their underlying circuitry (see below). Specifically, near suppression is most sharply tuned in layers 3B, 4B and 4Cα, and far suppression in layer 4B. Below we discuss the idea that the different tuning of near- and far-surround suppression may reflect a statistical bias in the distribution of oriented elements in natural images.

THE EFFECTS OF CHANGING THE ORIENTATION OF THE CENTER STIMULUS Few studies have examined how the orientation tuning of surround modulation is affected by changing the orientation of stimuli inside the RF.

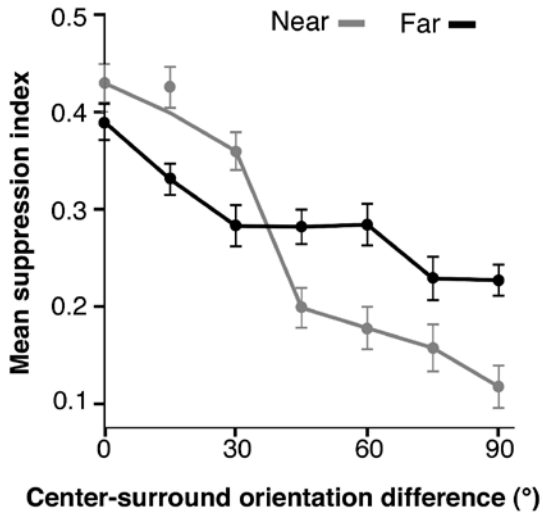

FIGURE 30.3 Orientation tuning of near- and far-surround suppression. Mean suppression index (SI) for a population of macaque V1 cells (n = 68), caused by near-(gray) or far-surround (black) stimulation. Far-surround stimulation was achieved using the stimulus in figure 30.2B, with a center grating of 75% contrast at the optimal orientation and a surround grating of 2° inner radius varied in orientation. For near-surround stimulation the surround grating had a 2° outer radius and was separated from the center grating by a 0.25° gap. Thus, complementary surround regions were stimulated in the two conditions. SI = 1 – (R_{CS}/R_C), where R_{CS} is the response to the center + surround stimulus and R_C the response to the center-only stimulus. A larger SI indicates stronger suppression. (Modified from Shushruth et al., 2013.)

Sillito et al. (1995) showed in a few V1 cells that maximal suppression occurred when the stimuli in the RF and surround were of the same orientation, irrespective of whether they were presented at the cell's preferred orientation. This result was replicated in a small population of broadly orientation-tuned cells in macaque V1 (Cavanaugh, Bair, & Movshon, 2002b), but the prevalence of this tuning behavior in V1 cells remained unclear. Furthermore, Sillito et al. (1995) reported that any orientation discontinuity in the RF and surround evoked facilitation, even when the RF was stimulated with an orientation orthogonal to that preferred by the cell, which did not activate the cell in the absence of surround stimulation. Others (Cavanaugh, Bair, & Movshon, 2002b; Walker, Ohzawa, & Freeman, 1999) could not replicate this result and attributed it to encroachment of the surround stimuli onto the RF. Recently, Shushruth et al. (2012) reexamined this issue by recording the response of a large population of cells in macaque V1 to high-contrast gratings of changing orientation in the RF and surround; they used the stimulus shown in figure 30.2B, growing the far-surround grating toward the RF without stimulating the near surround. They found that for the majority of V1 cells (including sharply orientation-tuned cells) the orientation specificity of surround modulation is independent of the stimulus orientation preferred by the RF, but changes with the orientation presented to the RF. Strongest suppression occurs when the stimuli in the RF and surround are of the same orientation (figure 30.4A, B), and strongest facilitation occurs when the stimuli are cross-oriented (figure 30.4C), even when the stimulus in the RF is not at the cell's preferred orientation, but provided that this stimulus reliably activates the cell when presented without a surround stimulus. Thus, surround stimulation had no effect when the RF was stimulated by orientations orthogonal to optimal. Unlike previous studies, Shushruth et al. (2012) found that facilitation emerged in many (35%) cells when the RF and surround were both weakly activated, the RF by stimuli of suboptimal orientation for the recorded cell, the surround by small annular gratings. Thus, previous studies failed to observe facilitation likely because they used stimuli that strongly activated the surround and/or the RF. To explain the tuning behavior of surround modulation, Shushruth et al. (2012) proposed a computational model that is discussed below.

Contrast Dependence of Surround Modulation

The contrast of the stimuli in the RF and surround affects the spatial extent, tuning and strength of surround modulation. Surround sizes are larger when measured with low-contrast gratings (Shushruth et al., 2009). The orientation selectivity of surround modulation is reduced when the contrast of the stimulus in the RF is reduced (Cavanaugh, Bair, & Movshon, 2002b; Hashemi-Nezhad & Lyon, 2011), and (as discussed above) surround orientations that typically evoke suppression can facilitate the cell's response when center stimulus contrast is reduced (e.g., figure 30.2B). When the RF and surround are stimulated at low contrast, the strength of surround suppression is reduced (Cavanaugh, Bair, & Movshon, 2002a; Sadakane et al., 2006; Schwabe et al., 2010), and many cells show facilitatory surround effects (Ichida et al., 2007). For any given center stimulus contrast, suppression strength increases as surround stimulus contrast increases. However, there have been variable reports on the effects of changing center stimulus contrast on the strength of surround suppression. In some studies a high-contrast surround stimulus suppressed more strongly the response to a lower-contrast than to a higher-contrast center stimulus (Cavanaugh, Bair, & Movshon, 2002a; Levitt & Lund, 1997). Schwabe et al. (2010), instead, observed weaker surround suppression for lower-contrast than for

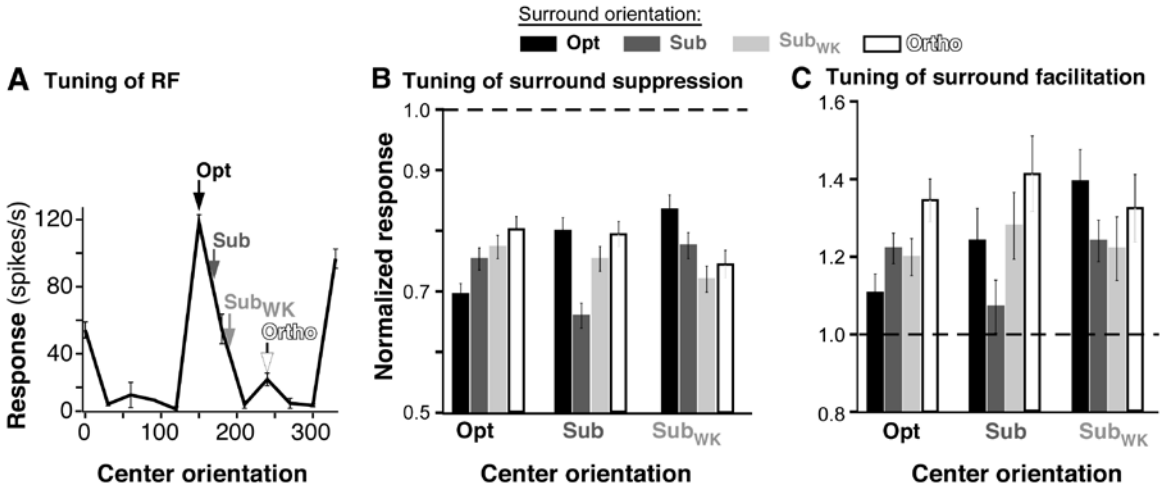

FIGURE 30.4 Orientation tuning of surround suppression and facilitation. (A) Orientation-tuning curve of the RF response for a V1 cell. The arrows indicate four orientations chosen for this cell to characterize the orientation specificity of surround modulation. Opt, optimal orientation; Sub, Sub_{WK}, suboptimal orientations evoking weaker responses from the cell, with Sub_{WK} evoking a weaker response than Sub; Ortho, orthogonal. For each cell four orientations were similarly chosen on the basis of the cell's RF tuning curve. (B) Mean normalized population responses to each of three center grating orientations (indicated on the *x* axis) presented together with one of four surround grating orientations (bars of different gray levels). Each center + surround response was measured at the largest surround grating size used and normalized to each respective center-only response. For any center orientation, suppression is maximal for iso-oriented center-surround stimuli. (C) Mean normalized population responses for cells showing surround facilitation. Responses were measured at the surround grating size that evoked maximal facilitation for each cell. Facilitation is weakest in the iso-orientation condition and is strongest at the surround orientation nearest to orthogonal to that presented in the RF. (A–C, modified from Shushruth et al., 2012, reproduced with permission from the Society for Neuroscience.)

higher-contrast center stimuli. Using model simulations, Schwabe et al. (2010) were able to reconcile these discrepancies by demonstrating opposite effects on surround suppression strength depending on both the size and the contrast level of the stimulus presented to the RF. In particular, weaker suppression of lower-contrast than higher-contrast center stimuli is observed when the center stimulus is near the cell's contrast threshold.

Surround stimulation also changes the contrast response function of a V1 cell in a manner that is best described by a change in response gain, that is, a divisive suppression that scales responses equally at all contrasts (Cavanaugh, Bair, & Movshon, 2002a).

Timing and Dynamics of Surround Modulation

Using a variety of stimuli and methodological approaches, several studies have shown that the onset of orientation-specific surround suppression is delayed by 15–60 ms relative to the RF response (Hupé et al., 2001; Knierim & Van Essen, 1992; Lamme, 1995; Lamme, Rodriguez-Rodriguez, & Spekreijse, 1999; Nothdurft, Gallant, & Van Essen, 1999, 2000). Bair, Cavanaugh, and Movshon (2003) measured the onset latency of surround suppression using dynamic center-surround stimuli (160 ms duration), with the center fixed at the preferred orientation for the cell and the surround orientation changed from preferred to orthogonal to preferred. They measured the timing of response change when the surround stimulus transitioned from a nonsuppressive to a suppressive orientation, and therefore effectively measured the onset timing of orientation-tuned suppression. The average suppression latency relative to the stimulus transition was 60 ms (range 25–110 ms), with suppression being delayed on average by 9 ms relative to the onset of the RF response. This delay was about 30 ms longer for weakly than for strongly suppressed cells. Moreover, by moving the surround grating progressively farther from the RF, they found that the latency of suppression induced by stimuli in the far surround was similar to that induced by stimuli in the near surround (figure 30.5). These results point to an underlying circuit with fast conduction velocity and high spatial divergence and convergence. As discussed below, interareal feedback connections to V1 show both properties.

Xing et al. (2005) looked at the time course of orientation tuning based on reverse correlation analysis of stimuli two to five times larger than the radius of the neuron's sRF_{high}. They found that suppression consists

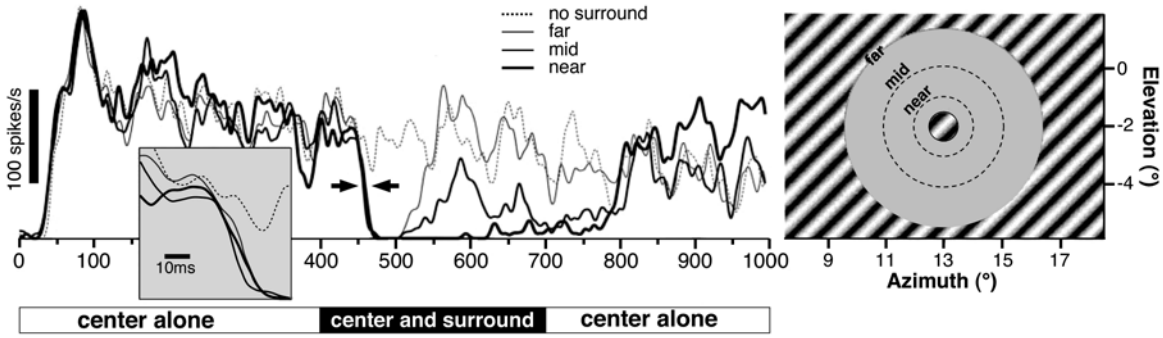

FIGURE 30.5 Time course of surround suppression for stimuli at different distances from the RF. (Left) mean firing rates of an example cell in response to a center-only stimulus, or a center + surround stimulus involving the near, mid, or far surround (lines of different thickness). (Gray inset) Blowup of the curves around the time of suppression onset. For this cell the onset of the RF response was 48 ms, and the onset of near suppression was 65 ms. (Right) The stimulus used consisted of a center grating fitted to the sRF_{high} and a grating in the surround whose inner radius was moved away from the RF, from near to far (dashed circles). The center stimulus appeared first (at $t = 0$) and lasted for 1 s, and the surround stimulus appeared at $t = 400$ ms and lasted for 300 ms. (Modified from Bair, Cavanaugh, & Movshon, 2003; reproduced with permission from the Society for Neuroscience.)

of an early component, which is orientation *un*tuned and peaks at virtually the same time as the stimulus-driven excitation, and a late component, which is orientation tuned and peaks about 17 ms after the peak of excitation. The untuned component was also seen when the stimulus was confined to the sRF_{high} of the neuron, suggesting that it arises from suppression of the feedforward input itself, perhaps as a result of surround suppression of geniculocortical afferents (see below).

ANATOMICAL CIRCUITS FOR SURROUND MODULATION

Feedforward connections to V1 from the lateral geniculate nucleus (LGN), long-range intra-V1 horizontal connections, and feedback connections from extrastriate cortex to V1 have all been implicated in surround modulation.

The Role of Feedforward Connections

V1 receives driving feedforward inputs from the LGN, with afferents from the magnocellular and parvocellular channels terminating primarily in layer 4Cα and 4Cβ, respectively (Lund, 1988). These connections are spatially restricted, that is, they connect corresponding regions of visual field representation in LGN and V1 (Perkel, Bullier, & Kennedy, 1986), and are thought to contribute to the spatial and tuning properties of V1 cells' RFs (Bauer et al., 1999; Hubel & Wiesel, 1962; Reid & Usrey, 2004). However, several lines of evidence indicate that geniculocortical afferents also contribute to V1 surrounds. First, in addition to their classical center-surround RF, LGN cells have an extraclassical, nonlinear surround that overlaps and extends beyond the classical RF and that can strongly suppress LGN responses (Alitto & Usrey, 2008; Bonin, Mante, & Carandini, 2005; Felisberti & Derrington, 1999; Levick, Cleland, & Dubin, 1972; Sceniak, Chatterjee, & Callaway, 2006; Solomon, White, & Martin, 2002). Median surround radius in macaque LGN at parafoveal eccentricities is 0.8° (up to ~5°, but <2.5° for most cells) (Sceniak, Chatterjee, & Callaway, 2006), thus significantly smaller than surrounds in V1. There is strong evidence that surround suppression in the LGN originates subcortically (Alitto & Usrey, 2008), and therefore, it must influence V1 responses to large stimuli. Second, blockade of intracortical inhibition in cat V1 does not abolish near-surround suppression (Ozeki et al., 2004). Third, two mechanisms contribute to surround suppression in V1, one having broad spatiotemporal tuning (likely originating in the LGN), the other being sharply tuned for orientation, spatial and temporal frequency (likely generated intracortically) (Webb et al., 2005).

However, LGN surround suppression cannot fully account for V1 surrounds. First, the orientation tuning of surround modulation in V1 points to intracortical mechanisms for its generation. Although some have argued that surround suppression in cat LGN is orientation tuned (Naito et al., 2007; Sillito, Cudeiro, & Murphy, 1993), others have disagreed (Bonin, Mante, & Carandini, 2005), and yet others have shown that geniculate surround suppression is substantially less orientation tuned than in V1 (Ozeki et al., 2009). LGN

surrounds in primates, instead, are untuned for orientation (Solomon, White, & Martin, 2002; Webb et al., 2002). Therefore, the LGN is unlikely to be the source of strong orientation-selective surround suppression in V1. Second, LGN surrounds are significantly smaller than V1 surrounds. In macaque the narrow visuotopic spread of geniculocortical axons added to the size of the LGN surrounds can account for the size of V1 cells' near surround, but not for their far surround (Angelucci & Sainsbury, 2006). The different RF sizes of LGN and V1 cells further argue that a stimulus of optimal size for a V1 cell is suppressive for most LGN cells. Thus, V1 cells at the peak of their size-tuning curve summate inputs from partly suppressed LGN afferents, indicating that suppression in the LGN does not necessarily lead to surround suppression in V1. In summary, the spatial scale of geniculate afferents to V1 can contribute to the V1 cell's sRF_{high} and to near-surround, but not far-surround, suppression in V1. The absence of far surrounds in V1 layer 4C (Ichida et al., 2007) is also consistent with this notion.

We propose that V1 cells inherit a spatially restricted orientation-untuned component of suppression from the LGN (Webb et al., 2005; Xing et al., 2005) whose spatial scale is determined by the visuotopic spread of geniculocortical afferents and LGN surround sizes. However, intracortical mechanisms must contribute a spatially broader and strongly orientation-tuned component to V1 surround suppression.

The Role of Horizontal Connections

In macaque V1, excitatory neurons in layers 2/3, 4B/upper 4Cα and 5/6 send intralaminar projections linking regions over several millimeters (Rockland & Lund, 1983). Similar projections have been described in V1 layers 2/3 of many other species, for example, tree shrew (Rockland & Lund, 1982) and cat (Gilbert & Wiesel, 1983). Horizontal connections in layers 2/3 were first proposed to generate surround modulation in V1 (Gilbert et al., 1996) because many of their features are well suited to explain many properties of surround modulation. In particular, these connections in layers 2/3 link preferentially neurons of similar orientation preference (Malach et al., 1993) with RFs aligned along an axis in visual space collinear with the orientation preference of the connected neurons (Bosking et al., 1997; Schmidt et al., 1997; Sincich & Blasdel, 2001) (see figure 30.1; chapter 44 by Field, Golden, and Hayes). This property could generate the orientation tuning of surround modulation and collinear facilitation. Instead, horizontal connections in different V1 layers do not appear to link cortical domains of similar functional property (eye dominance) (Li et al., 2003; Lund, Angelucci, & Bressloff, 2003), a feature that may explain the weaker orientation tuning of surround modulation in the infragranular V1 layers (see above; Shushruth et al., 2013). Moreover, horizontal connections, at least in layers 2/3, contact both excitatory (80%) and inhibitory neurons (McGuire et al., 1991), a property that is useful to generate both long-range suppression and facilitation. Finally, these connections only elicit subthreshold responses (Hirsch & Gilbert, 1991; Yoshimura et al., 2000) and thus do not drive, but only modulate, the response of their target cells.

However, studies in macaque in which the spatial dimensions of V1 neurons' RFs and surrounds were quantitatively compared with the visuotopic extent of horizontal and feedback connections to the same V1 sites have led to new hypotheses on the role of these connections (Angelucci et al., 2002). By combining neuronal tracer injections with electrophysiological characterization at and around the injected V1 site, these studies demonstrated that the monosynaptic spread of V1 horizontal connections is commensurate with the size of the sRF_{low}, or near surround, of V1 cells. Thus, these connections cannot monosynaptically account for the extent of V1 cells' far surrounds.

Polysynaptic chains of horizontal connections are also unlikely to underlie far-surround modulation because of the slow conduction velocity of horizontal axons. A variety of methods have estimated the speed of signal propagation within V1 to be 0.1–0.3 m/s (Bringuier et al., 1999; Grinvald et al., 1994; Slovin et al., 2002), but 0.1 m/s for most horizontal axons (Girard, Hupé, & Bullier, 2001). As discussed above, surround signals in V1 can arise 12.5° from the RF center. In parafoveal V1 this corresponds to a cortical distance of approximately 29 mm (using a magnification factor of 2.3 mm/° at 5° eccentricity) (Van Essen, Newsome, & Maunsell, 1984). Signals traveling at 0.1 m/s along horizontal axons would take 290 ms to reach the RF (97 ms for horizontal axons conducting at 0.3 m/s). Polysynaptic chains of horizontal connections would further add integration times of about 5–20 ms at each synaptic relay. Thus, clearly horizontal connections are too slow to account for the fast onset of far-surround suppression (9–60 ms, see above). These connections, however, could mediate near-surround suppression, as they can relay signals to the RF from a distance of 3 mm (average radius of horizontal connections in macaque V1) (Angelucci et al., 2002) in about 10–30 ms, which is compatible with the onset delay of near-surround suppression.

Thus, the spatiotemporal properties and synaptic physiology of horizontal connections are well suited to

underlie near-surround modulation in V1. This includes facilitatory effects from the near surround, such as increased spatial summation at low stimulus contrast (figure 30.1A) (Kapadia, Westheimer, & Gilbert, 1999; Sceniak et al., 1999) and collinear facilitation (figure 30.2A), but also near-surround suppression (e.g., size tuning at high contrast; figure 30.1). In principle, both facilitatory and suppressive effects associated with size tuning and its contrast dependence can be accounted for by the interaction of the horizontal networks with local GABAergic neurons (Schwabe et al., 2006; Somers et al., 1998). Recordings from cortical slices have shown that weak electrical stimulation of horizontal circuits elicits purely EPSPs, whereas stronger stimulation elicits EPSPs followed by strong IPSPs (Hirsch & Gilbert, 1991). Therefore, low level of activity in the network, as may be evoked by low-contrast stimuli, results in summation; instead, high-contrast or large-size stimuli would lead to higher level of activity in the horizontal network and subsequent recruitment of inhibition, resulting in suppression. In summary, horizontal connections are likely to contribute to near-surround modulation, its contrast dependence and orientation tuning, but they are unlikely to generate far-surround modulation.

The Role of Feedback Connections

V1 sends feedforward projections to several extrastriate areas, including V2, V3 and V5/MT, which in turn send a dense network of feedback projections to V1. These projections arise from excitatory neurons in layers 2/3A and 5/6 of extrastriate cortex, target both excitatory and inhibitory neurons (Anderson & Martin, 2009; Gonchar & Burkhalter, 2003), and terminate in V1 layer 1 and in the same layers (2/3, 4B and 6) that give rise to feedforward projections from V1. Functionally, feedback connections do not drive V1 cells but enhance their responses to stimulation of their RF (Hupé et al., 1998, 2001; Mignard & Malpeli, 1991; Sandell & Schiller, 1982).

Recent studies on the spatiotemporal properties and functional organization of feedback connections have led to suggest that they underlie far-surround modulation in V1 (Angelucci & Bressloff, 2006; Angelucci & Bullier, 2003). First, feedback connections to V1 have the appropriate spatial extent to underlie far-surround modulation (Angelucci et al., 2002). Feedback connections from V2, V3 and MT convey information to V1 from regions of visual space that are about 5, 10 and 25 times, respectively, the size of the V1 cell's sRF_{high}. Second, inactivation of area MT in macaque (Hupé et al., 1998) and of posterotemporal visual cortex in cat (presumed homologue of primate inferotemporal cortex) (Bardy et al., 2009) by cooling reduces surround suppression in V1. In contrast, inactivation of area V2 loci by GABA does not affect the modulation of V1 responses generated by static texture patterns in the surround (Hupé et al., 2001). This result, however, does not rule out involvement of feedback connections from other extrastriate areas. Furthermore, the stimulus used by Hupé et al. (2001) was confined to the near surround, thus likely recruiting, in addition to feedback, horizontal connections, which were unperturbed in this study. Third, feedback connections have the appropriate conduction velocities to account for the fast onset of surround modulation. Electrical stimulation studies between macaque areas V1 and V2 have shown that both feedforward and feedback connections conduct at 2–6 m/s, which is about 10 times faster than the conduction velocity of V1 horizontal connections (Girard, Hupé, & Bullier, 2001). Fast and highly divergent feedback connections also explain how the onset latency of surround suppression is almost independent of cortical distance (Bair, Cavanaugh, & Movshon, 2003) (figure 30.5). If chains of horizontal V1 connections mediated far-surround suppression, one would expect the latency of suppression to increase with distance from the RF center, a prediction that was not confirmed by Bair, Cavanaugh, and Movshon (2003). In summary, on the basis of propagation speed and spatial extent, feedback connections are the most likely substrate for far-surround modulation in V1.

Data on the patterning and functional organization of feedback connections relative to the orientation map in V1 is controversial, with reports of both anatomically widespread (Maunsell & Van Essen, 1983; Rockland & Pandya, 1979; Ungerleider & Desimone, 1986) and orientation-unspecific (Stettler et al., 2002) V2-to-V1 feedback connections, and "patchy" and orientation-specific V2-to-V1 feedback connections (Angelucci & Bressloff, 2006; Angelucci et al., 2002; Shmuel et al., 2005) in primates. One hypothesis is that there are multiple feedback systems with differing functional specificities, possibly terminating in different V1 layers (Angelucci & Bressloff, 2006). In particular, the broader orientation tuning of far-surround suppression compared to near-surround suppression (Shushruth et al., 2013) (figure 30.3) suggests that feedback connections are more broadly orientation biased than horizontal connections. Furthermore, sharper tuning of far-surround modulation in V1 layer 4B suggests greater orientation specificity of feedback to this layer.

In summary, it is likely that the RF center and surround of V1 neurons result from integration of signals from feedforward, horizontal and feedback

connections operating at different spatiotemporal scales (figure 30.6). The sRF_{high} of V1 neurons is generated by converging feedforward inputs from the classical RF of LGN cells whose response is partially suppressed by stimuli of optimal size for the V1 cell (light green arrows in figure 30.6). Near surround-modulation is generated by all three sets of connections: feedforward inputs from the extraclassical RF of LGN cells (dark green arrows) strongly suppressed by large stimuli, horizontal (red arrows), and feedback (blue arrows) connections. Instead, far-surround modulation is mediated exclusively by feedback.

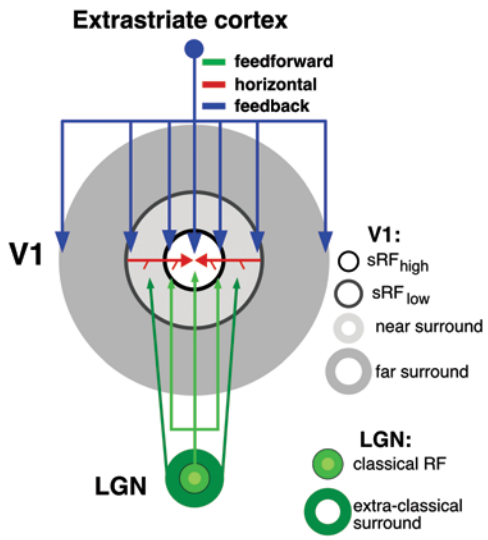

FIGURE 30.6 Circuits for surround modulation. Anatomical circuits (arrows) postulated to generate the RF center (white area) and surround (gray areas) of V1 neurons.

MECHANISMS FOR SURROUND MODULATION

Synaptic Mechanisms

Based on the model in figure 30.6, surround suppression in V1 likely results from multiple mechanisms. Surround suppression of LGN afferents would cause withdrawal of feedforward excitation and therefore fast untuned suppression of V1 cells; increased inhibition via horizontal and feedback connections acting through local inhibitory neurons would then cause slower tuned suppression. In vivo intracellular recordings have provided evidence for both reduced excitation and increased inhibition in the steady-state response of cat V1 cells to stimuli of intermediate length (8°) (Anderson et al., 2001). However, reduction in both excitatory and inhibitory conductances was observed for shorter (4°) and longer stimuli (12° length or 20° diameter) (Anderson et al., 2001; Ozeki et al., 2009). Importantly, this steady-state decrease in excitation and inhibition was temporally preceded by a transient increase in inhibition and could not be fully explained by suppression of inputs from the LGN. Similar stimuli as used in cortex did not evoke strong enough or sufficiently orientation-tuned suppression in LGN to account for suppression in V1, which therefore requires additional intracortical mechanisms. Ozeki et al. (2009) proposed that a steady-state decrease in excitatory and inhibitory conductances can be explained if V1 operates as an inhibition-stabilized network in which strong recurrent excitation is balanced by strong recurrent inhibition (figure 30.7). Within such a network, an increase in external excitatory input (via the surround pathways) to a local inhibitory neuron leads to a transient increase

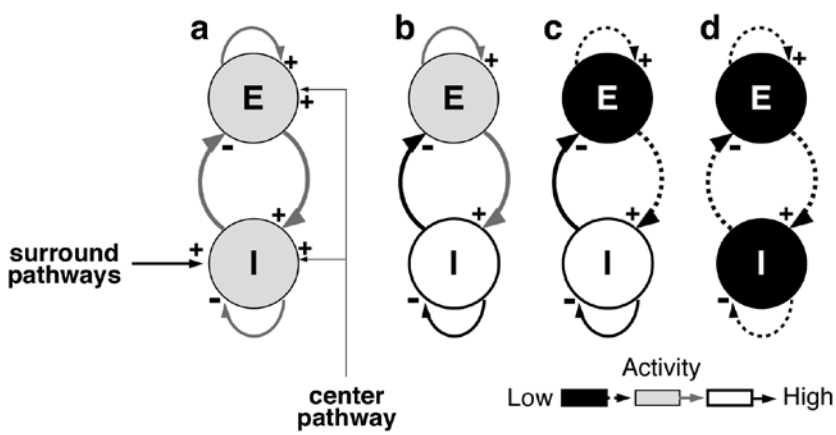

FIGURE 30.7 Inhibition-stabilized network model. Excitatory (E) and inhibitory (I) neurons making recurrent and reciprocal connections receive excitatory (+) feedforward inputs driven by RF stimulation, and lateral excitatory inputs driven by surround stimulation. (**a–d**) Sequence of events occurring when a surround stimulus is added to a preexisting center stimulus. Gray scale codes activity level. (Modified from Ozeki et al., 2009, with permission.)

in inhibition (figure 30.7b, c), which in turn leads to a withdrawal of recurrent excitation and inhibition at steady state (figure 30.7d).

Intracellular recordings in cat V1 found that natural visual stimulation of the RF and surround compared to stimulation of the RF alone caused an increase in membrane hyperpolarization (stronger IPSPs) and an increase in trial-to-trial reliability of EPSPs and spikes in pyramidal neurons (Haider et al., 2010). Instead, fast-spiking inhibitory neurons increased their firing rates during RF and surround stimulation, possibly causing increased IPSP amplitude in pyramidal cells.

Models

PHENOMENOLOGICAL MODELS Phenomenological models have focused on understanding the computation underlying surround modulation. They describe surround modulation as resulting from two overlapping Gaussian mechanisms, an excitatory mechanism (representing the RF) and a spatially broader inhibitory one (representing the surround), interacting either subtractively (DoG model) or divisively (RoG model) (Cavanaugh, Bair, & Movshon, 2002a; Sceniak et al., 1999). Both models can satisfactorily fit spatial summation curves measured experimentally. They also accurately describe the contrast dependence of the sRF, either as a contrast-induced change in the size of the center excitatory Gaussian (DoG model) or as a change in the gains of both the center and surround Gaussians (RoG model). In contrast to some mechanistic models (Schwabe et al., 2006; Somers et al., 1998) (see below), the DoG model predicts the strength of surround suppression to be insensitive to stimulus contrast (Sceniak et al., 1999; Schwabe et al., 2010). However, when strength of suppression is calculated directly from neuronal responses rather than from DoG model parameters, it does show a clear contrast dependence, with weaker suppression occurring at low contrast (Schwabe et al., 2010).

Phenomenological models, however, by virtue of their design, do not have the same explanatory and predictive power of mechanistic neuronal network models.

MECHANISTIC MODELS This second group of models have attempted to understand how cortical circuits generate surround modulation. The models of Stemmler, Usher, and Niebur (1995) and Somers et al. (1998) have focused on understanding how facilitation at low contrast and suppression at high contrast can occur using fixed cortical connections. These models consist of a lattice of orientation hypercolumns, each comprising several orientation columns with two populations of neurons (excitatory, E, and local inhibitory, I) reciprocally and recurrently connected within each column. Different hypercolumns interact via orientation-specific horizontal connections targeting both local E and I neurons. Both models make the crucial assumption that there is an asymmetry in the response of the E and I neurons, such that for weak visual inputs (e.g., low-contrast stimuli) I neurons are silent, and inputs from the surround increase the E neuron response (causing facilitation). Instead, for strong inputs (e.g., high-contrast stimuli) the I neuron response increases, and surround inputs thus cause suppression. In the model of Stemmler, Usher, and Niebur (1995), the E–I asymmetry is implemented as a lower spontaneous input to the I than to the E neurons, whereas in the model of Somers et al. (1998), it is implemented as I neurons having higher threshold and gain than E neurons, as originally proposed by Lund et al. (1995). This mechanism can also reproduce the contrast dependence of sRF size. This is because at low contrast only the E neurons are active, and as stimulus size is increased, more and more of the horizontal network gets recruited, leading to an increase in the E neuron activity, which saturates at stimulus sizes corresponding to the length of horizontal connections. Instead, at high contrast I neurons are active, and increases in stimulus size recruit horizontal inputs that bring the I neurons to threshold; thus, suppression occurs at smaller stimulus sizes. A similar mechanism was used in the model of Schwabe et al. (2006). The latter, however, extended these previous models, introducing interareal feedback connections to V1 to account for the fast onset and large extent of surround suppression, and using realistic spatial scales and conduction velocities for horizontal and feedback circuits. This model can account for a wider range of physiological data compared to its two predecessor models, including (1) suppression and facilitation from the far surround using annular surround gratings such as those in figure 30.2B (Ichida et al., 2007; Levitt & Lund, 2002; Shushruth et al., 2009), (2) the effects of inactivating feedback connections on RF center and surround responses (Hupé et al., 1998), (3) the timing and dynamics of surround suppression (Bair, Cavanaugh, & Movshon, 2003), and (4) the contrast dependence of suppression strength (Cavanaugh, Bair, & Movshon, 2002a; Levitt & Lund, 1997; Schwabe et al., 2010). With respect to the last point, in fact, this model provided an explanation for apparently contradictory data on the effects on suppression strength of lowering center stimulus contrast (see above).

Recently, there has been theoretical (Bressloff & Cowan, 2002; van Vreeswijk & Sompolinsky, 1996) and experimental (Mariño et al., 2005; Stimberg et al., 2009) support for the idea that the cortex operates in

a regime of strong but balanced recurrent excitation and inhibition. Ozeki et al. (2009) have shown that only an inhibition-stabilized network can explain the synaptic physiology of surround modulation (see above, figure 30.7). Shushruth et al. (2012) extended the model of Schwabe et al. (2006) by incorporating orientation tuning and strong local recurrent connections between orientation columns (figure 30.8A). This model could explain the stimulus-dependent orientation specificity of surround modulation (Shushruth et al., 2012) (figure 30.4). In the model this tuning behavior results from the interaction of orientation-specific surround inputs with strong and poorly orientation-specific local recurrent connections. The mechanism is shown in figure 30.8B. When the stimulus in the RF is at the optimal orientation (0°; figure 30.8B, a–c), the E1 cells receive strongest feedforward activation and, thus, provide the strongest recurrent excitation within the center hypercolumn; because of the strong recurrency, the whole hypercolumn becomes strongly activated. Iso-oriented surround stimuli thus suppress the strongest source of recurrent excitation within the hypercolumn, i.e. the E1 cells: recurrent excitation is withdrawn, and the whole hypercolumn becomes suppressed. This withdrawal of excitation is greater when the E1 cells are strongly suppressed by an optimally oriented (0°) surround stimulus (figure 30.8B, c) than when they are weakly suppressed by a nonoptimal one (–22.5°; figure 30.8B, b). When the RF center is stimulated by a suboptimal orientation for the E1cells (–22.5°; figure 30.8B, d–f) instead, these cells receive weaker feedforward excitation and thus contribute weaker recurrent excitation within the hypercolumn. Suppression of the E1 cells by an optimal (0°) stimulus now has little effect on the hypercolumn activity (figure 30.8B, e). Instead, the E2 cells, which are maximally activated by a stimulus of –22.5° orientation, provide the strongest recurrent excitation to the hypercolumn, and suppressing them results in strongest suppression of the whole hypercolumn (figure 30.8B, f). In summary, recurrent excitation is weakest when center and surround stimuli are at the same orientation; because of the strong recurrent regime, the level of recurrent excitation in the hypercolumn has a greater effect on the E1 neuron responses than the direct inhibition from the surround pathways.

ROLE OF SURROUND MODULATION IN VISION

Role in Visual Information Processing

It has been suggested that surround suppression could reflect two important computations performed by sensory neurons—gain control and/or redundancy reduction.

Neurons in V1 maintain their orientation tuning even at high stimulus contrasts, which saturate their response. This property, and many nonlinearities of V1 RF responses, can be explained by a normalization model, according to which the activity of each neuron is divided by the responses of a pool of neighboring neurons (Carandini & Heeger, 1994; Carandini, Heeger, & Movshon, 1997). Recently, this model has been extended by suggesting that for larger stimuli the activated cells in the surround sharing similar functional properties to those of the RF also contribute to the normalization pool (Schwartz & Simoncelli, 2001). Contrast normalization is a desirable computation that allows V1 neurons to handle the range of contrasts in natural scenes because single neurons lack the dynamic range needed for this task (Heeger, 1992).

A second hypothesis is that surround suppression serves to reduce redundancies in visual inputs. Theoretically, the "efficient coding" hypothesis (Barlow, 1961) states that sensory neurons are tuned to the statistics of natural images (Geisler, 2008; Simoncelli & Olshausen, 2001) and that their role is to reduce redundancies in sensory inputs by maintaining statistical independence in their responses. Because natural scenes contain strong spatial correlations, with neighboring locations being highly similar, it has been suggested that surround suppression serves to reduce information redundancy in natural images by maximizing statistical independence in the response of neurons representing such correlated inputs. Schwartz and Simoncelli (2001) examined the response of oriented filters (as models of V1 RFs) to natural images and found strong dependency between the responses of spatially separated filters. They implemented a form of divisive normalization wherein each filter's response was divided by a weighted sum of the responses of other filters, with the weights derived to maximize the independence of filter responses to an ensemble of natural images. The filter responses to grating stimuli now showed properties similar to those seen in V1 neurons, such as contrast-dependent spatial summation, thus supporting the theory.

The idea that surround modulation subserves a form of efficient coding is also supported by experimental evidence. Stimulation of the RF surround of V1 neurons in awake macaques with natural images increases the selectivity of individual neurons, reduces the correlations between the responses of neuron pairs, and increases the sparseness of neuronal responses (Vinje & Gallant, 2000, 2002). Sparseness is a nonparametric measure of neuronal selectivity. A neuron with increased

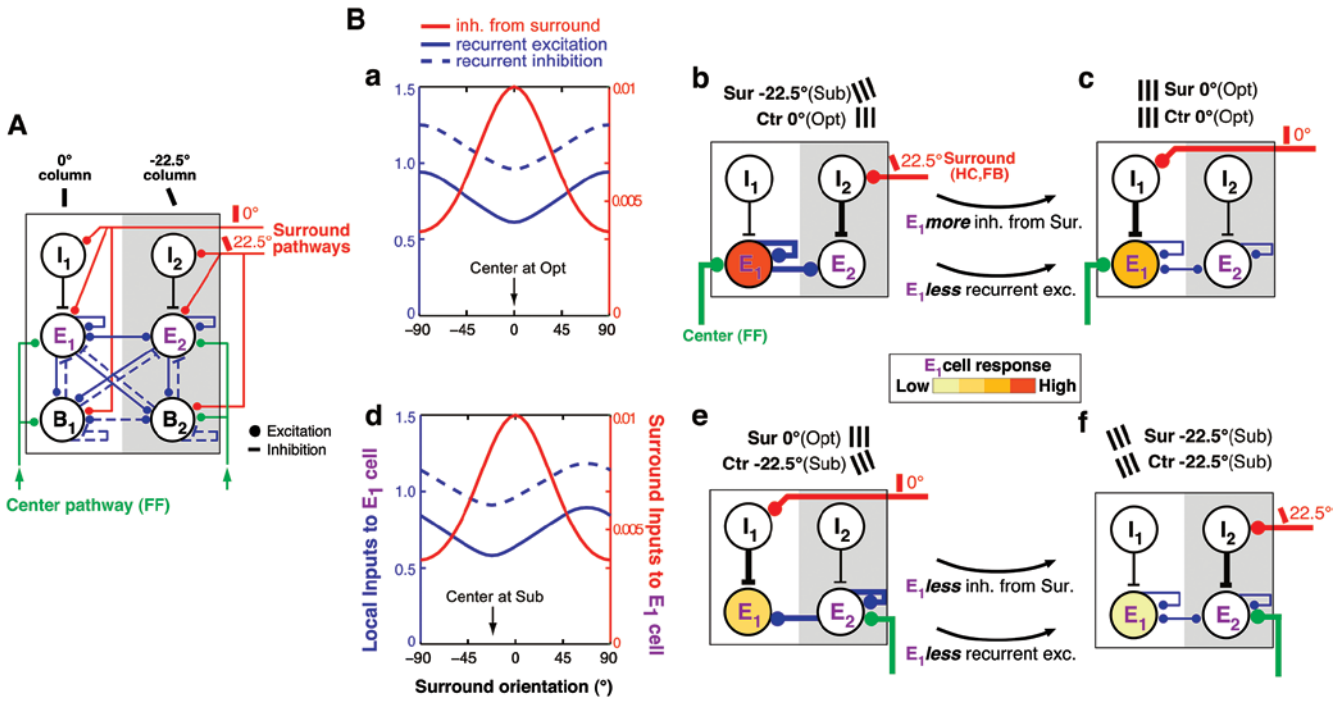

FIGURE 30.8 Network model of V1 with strong recurrent connections. (A) The network architecture consists of one hypercolumn of 32 recurrently connected orientation columns, of which only two (preferring 0° and –22.5° orientation) are shown for simplicity. Each column consists of an excitatory neuron (E) and two kinds of inhibitory neurons, high-threshold inhibitory neurons (I), which receive surround modulation from outside the hypercolumn, and basket neurons (B), which support local recurrent connections within the hypercolumn. The surround modulatory inputs (red) are orientation specific, the local recurrent connections (blue) are not. (B) The mechanism underlying stimulus-dependent orientation tuning of surround suppression. (a, d) Inputs to the E1 cell preferring 0° orientation for varying surround orientations, when the center is stimulated at the neuron's preferred orientation (a) or at a suboptimal, nonpreferred orientation (d). The solid blue curve indicates the local recurrent inputs from E neurons in other orientation columns; the dashed blue curve indicates the local recurrent inputs (negative) from B neurons in the same and other orientation columns; the red curve is the input (negative) from the surround. Note that the surround input (red *y*-axis) is much smaller than the local recurrent inputs (blue *y*-axis). (b, c) Diagrams showing the inputs that most affect the E1 cell response for a center stimulus at the optimal orientation (0°) for cell E1, and a surround stimulus at –22.5° (Sub) (b) or at 0° (Opt) (c) orientations. Only the relevant cells and connections are depicted. Line thickness indicates input strength. White and gray shading indicate 0° and –22.5° orientation columns, respectively. Changing the surround orientation from Sub (b) to the iso-orientation condition (c) leads to increased inhibition of the E1 cell via the surround inputs and to less recurrent excitation. (e, f) Same as in b and c, but for a center orientation of –22.5° and surround orientations of 0° (e) or –22.5° (f). This leads to reduced inhibition of the E1 cell via the surround pathways, but also to less recurrent excitation; the latter causes stronger suppression at iso-orientation. (Modified from Shushruth et al., 2012; reproduced with permission from the Society for Neuroscience.)

sparseness responds to a more restricted set of stimuli and therefore is more selective (Olshausen & Field, 2004), and this mechanism has been suggested to increase the efficiency of information transmission about a visual stimulus (Vinje & Gallant, 2002).

Intracellular recordings from cat V1 have shown that for excitatory cells, natural stimulation of the surround increases the sparseness of the spiking response and the trial-to-trial reliability of membrane potential responses (see above) (Haider et al., 2010). An increase in spike reliability allows neurons with sparse responses to overcome trial-to-trial response variability and, thus, to transmit reliable information to downstream neurons.

In natural images there is a statistical relation between edge orientation and distance between edges, such that nearby edges have a higher probability than distant edges of being co-oriented and cocircular and of belonging to the same physical contour (Geisler et al., 2001). The different orientation tuning of near- and far-surround suppression observed in macaque V1 (Shushruth et al., 2013; see above) may reflect this statistical bias; accordingly, suppression should be narrowly tuned for nearby edges and more broadly tuned for distant edges. Sharply orientation-tuned near-surround suppression may serve to detect small orientation differences in nearby edges, whereas broadly tuned

far-surround suppression may serve to direct saccades/attention to salient distant locations.

Another class of computational models of vision considers visual processing a form of statistical inference (Yuille & Kersten, 2006). One approach of this class of models is the predictive coding theory, which posits that higher visual areas learn the statistical regularities of natural images and feed back to lower areas predictions based on such regularities. The activity in lower areas reflects deviations from these predictions, that is, from these regularities (Rao & Ballard, 1999); thus, only nonmatched predictions are signaled to higher areas. In these models neurons respond higher to unpredictable elements of the visual scene, such as pop-out stimuli and edges. Spratling (2010) has proposed an alternative implementation of predictive coding wherein horizontal connections within V1 take the role ascribed by other models to feedback input.

Role in Visual Perception

Above, we have discussed how surround modulation could serve visual information processing. Although such computations could ultimately serve visual perception, surround modulation in V1 has also been proposed to be the direct neural correlate of some perceptual contextual effects.

The observation that, compared to similar stimuli, dissimilar stimuli in the RF and surround result in higher neuronal responses led to the suggestion that surround modulation in V1 plays a role in visual saliency and pop-out perceptual phenomena (Knierim & Van Essen, 1992; Nothdurft, Gallant, & Van Essen, 1999). More generally, surround modulation enhances neuronal responses in regions of orientation discontinuities, which typically occur at object boundaries (Nothdurft, Gallant, & Van Essen, 2000). This property has been hypothesized to underlie the perceptual ability of delineating figures from background—a process termed "figure–ground segregation." Lamme (1995) and Zipser, Lamme, and Schiller (1996) recorded from V1 while presenting figure–ground stimuli defined by differently oriented line segments (figure 30.9). They reported that neuronal responses were higher when the RF was located on the figural part of the stimulus than when it was on the background, although the local stimulus in the RF was the same in both conditions. The larger response to the figure persisted even when the diameter of the figure was increased to 8°. These results suggested that V1 represents figure–ground relationships in visual scenes. However, using similar stimuli, Rossi, Desimone, and Ungerleider (2001) failed to find any difference in response to the figure versus the background, except when the boundaries of the figure were within 1° of the cells' mRF border and thus likely within their sRF. This suggested that V1 neurons respond to local figure boundaries rather than to the figure per se. Alternatively, given the large size of V1 surrounds, the differential responses of V1 cells to figure and background could simply reflect different strengths of surround suppression evoked by different amounts of surround stimulation in the two conditions. Specifically, compared to the figure condition, in the background condition a larger fraction of the surround is activated by a stimulus of the same orientation as that in the RF, causing stronger suppression. In conclusion, additional studies are needed to determine whether these phenomena are just manifestations of surround modulations or responses to texture boundaries, as opposed to true figure–ground analysis in V1. However, the longer latency of figure–ground signals (30–70 ms after RF response onset) (Lamme, 1995; Zipser, Lamme, & Schiller, 1996), compared to that of surround modulation (9 ms) (Bair, Cavanaugh, & Movshon, 2003) suggests that these may be two separate phenomena and that the latter is at a processing stage prior to figure–ground analysis.

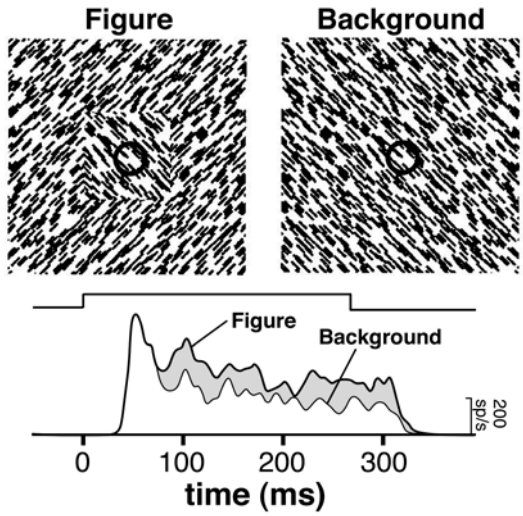

FIGURE 30.9 Figure–ground segregation. (Top) Figure and background stimuli used to stimulate the RF (circles) of V1 cells. (Bottom) V1 cell response to the two stimuli at the top. The response is higher when the RF overlays the figure than when it overlays the background. (Modified from Zipser et al., 1996; reprinted with permission from the Society for Neuroscience.)

Collinear facilitation in V1 cells (figure 30.2A) is thought to be the neural correlate of perceptual "contour integration," which is the visual system's ability to segregate into a contour collinear line segments from a background of randomly oriented elements (see

figure 30.2; chapter 44 by Field, Golden, and Hayes). Psychophysical studies have demonstrated that individual contour elements can be grouped with other elements based on the Gestalt principles of good continuation (Hess & Field, 1999). Contour integration is the topic of chapter 44 by Field, Golden, and Hayes in this volume and therefore is only briefly discussed here. Kapadia et al. (1995) conducted parallel psychophysical studies in humans and electrophysiological recordings in macaque V1 on the effect of collinearly placed flankers on the perception of target line elements. They reported that the flankers enhanced the detectability of the target in human observers as well as the response of V1 neurons to an iso-oriented line segment inside the RF (figure 30.2A). Li, Piech, and Gilbert (2006) further demonstrated a close correlation among the perceptual saliency of a contour, the animal performance on a contour detection task, and V1 responses. We refer the reader to chapter 70 of this volume by Li and Gilbert for details on these studies.

In summary, surround modulation enhances neuronal responses to perceptually salient aspects of a visual scene such as contours, figure boundaries and texture borders. Accordingly, it has been proposed that V1 serves as a preattentive map of visual saliency in which higher neuronal responses correspond to the perceptual salience of the image location they represent (Li, 2002). This map serves to direct visual attention to the most salient locations in a scene.

CONCLUSIONS AND FUTURE DIRECTIONS

Models of V1 based purely on classical RF concepts and feedforward interactions are insufficient to understand the neuronal basis of visual perception. These models have portrayed a view of V1 neurons as localized and functionally independent windows over the visual world. Studies of surround modulation have, instead, demonstrated that the responses of V1 neurons even to simple visual stimuli reflect integration of signals from distant cortical regions. This process engages a complex network of feedforward, local recurrent, and long-distance horizontal and feedback circuits. The selective properties of surround modulation and the precise connectivity of V1 may serve to provide a meaningful representation of the image structure that goes beyond the computation of contrast gain control and redundancy reduction.

Surround modulation has so far been extensively characterized using highly simplified stimuli and by recording from one neuron at a time. A challenge for future research is to understand how V1 neurons respond to the kind of contextual information that is present in natural scenes, and how the response of individual neurons relates to the large-scale population activity in cortical networks. Multielectrode array recording of V1 neuronal population responses to natural visual stimuli can provide the next step in understanding the role of context in natural vision. Furthermore, causal relationships among neuronal circuits, surround modulation, and visual perception need to be established. Recent advances in the ability to perturb specific neural circuits using viral technology and molecular genetic techniques (Han et al., 2009; Luo, Callaway, & Svoboda, 2008; Osakada et al., 2011), even in nonhuman primates, will open new avenues for addressing this challenge.

REFERENCES

Alitto, H. J., & Usrey, W. M. (2008). Origin and dynamics of extraclassical suppression in the lateral geniculate nucleus of the macaque monkey. *Neuron*, *57*, 135–146. doi:10.1016/j.neuron.2007.11.019.

Allman, J., Miezin, F., & McGuinness, E. (1985). Stimulus specific responses from beyond the classical receptive field: Neurophysiological mechanisms for local-global comparisons in visual neurons. *Annual Review of Neuroscience*, *8*, 407–430. doi:10.1146/annurev.ne.08.030185.002203.

Anderson, J. C., & Martin, K. A. C. (2009). The synaptic connections between cortical areas V1 and V2 in macaque monkey. *Journal of Neuroscience*, *29*, 11283–11293.

Anderson, J. S., Lampl, I., Gillespie, D. C., & Ferster, D. (2001). Membrane potential and conductance changes underlying length tuning of cells in cat primary visual cortex. *Journal of Neuroscience*, *21*, 2104–2112.

Angelucci, A., & Bressloff, P. C. (2006). The contribution of feedforward, lateral and feedback connections to the classical receptive field center and extra-classical receptive field surround of primate V1 neurons. *Progress in Brain Research*, *154*, 93–121.

Angelucci, A., & Bullier, J. (2003). Reaching beyond the classical receptive field of V1 neurons: Horizontal or feedback axons? *Journal of Physiology, Paris*, *97*, 141–154. doi:10.1016/j.jphysparis.2003.09.001.

Angelucci, A., Levitt, J. B., Walton, E., Hupé, J. M., Bullier, J., & Lund, J. S. (2002). Circuits for local and global signal integration in primary visual cortex. *Journal of Neuroscience*, *22*, 8633–8646.

Angelucci, A., & Sainsbury, K. (2006). Contribution of feedforward thalamic afferents and corticogeniculate feedback to the spatial summation area of macaque V1 and LGN. *Journal of Comparative Neurology*, *498*, 330–351. doi:10.1002/cne.21060.

Bair, W., Cavanaugh, J. R., & Movshon, J. A. (2003). Time course and time–distance relationships for surround suppression in macaque V1 neurons. *Journal of Neuroscience*, *23*, 7690–7701.

Bardy, C., Huang, J. Y., Wang, C., Fitzgibbon, T., & Dreher, B. (2009). "Top-down" influences of ispilateral or contralateral postero-temporal visual cortices on the extra-classical receptive fields of neurons in cat's striate cortex. *Neuroscience*, *158*, 951–968. doi:10.1016/j.neuroscience.2008.09.057.

Barlow, H. B. (1953). Summation and inhibition in the frog's retina. *Journal of Physiology*, *119*, 69–88.

Barlow, H. B. (1961). Possible principles underlying the transformation of sensory messages. In W. A. Rosenblith (Ed.), *Sensory communication* (pp. 217–234). Cambridge, MA: MIT Press.

Barlow, H. B., Blakemore, C., & Pettigrew, J. D. (1967). The neural mechanisms of binocular depth discrimination. *Journal of Physiology*, *193*, 327–342.

Bauer, U., Scholz, M., Levitt, J. B., Lund, J. S., & Obermayer, K. (1999). A model for the depth dependence of receptive field size and contrast sensitivity of cells in layer 4C of macaque striate cortex. *Vision Research*, *39*, 613–629.

Blakemore, C., & Tobin, E. A. (1972). Lateral inhibition between orientation detectors in the cat's visual cortex. *Experimental Brain Research*, *15*, 439–440. doi:10.1007/BF00234129.

Bonin, V., Mante, V., & Carandini, M. (2005). The suppressive field of neurons in lateral geniculate nucleus. *Journal of Neuroscience*, *25*, 10844–10856.

Bosking, W. H., Zhang, Y., Schofield, B., & Fitzpatrick, D. (1997). Orientation selectivity and the arrangement of horizontal connections in tree shrew striate cortex. *Journal of Neuroscience*, *17*, 2112–2127.

Bressloff, P. C., & Cowan, J. D. (2002). An amplitude equation approach to contextual effects in visual cortex. *Neural Computation*, *14*, 493–525. doi:10.1162/089976602317250870.

Bringuier, V., Chavane, F., Glaeser, L., & Frégnac, Y. (1999). Horizontal propagation of visual activity in the synaptic integration field of area 17 neurons. *Science*, *283*, 695–699.

Carandini, M., & Heeger, D. J. (1994). Summation and division by neurons in primate visual cortex. *Science*, *264*, 1333–1336. doi:10.1126/science.8191289.

Carandini, M., Heeger, D. J., & Movshon, J. A. (1997). Linearity and normalization in simple cells of the macaque primary visual cortex. *Journal of Neuroscience*, *17*, 8621–8644.

Cavanaugh, J. R., Bair, W., & Movshon, J. A. (2002a). Nature and interaction of signals from the receptive field center and surround in macaque V1 neurons. *Journal of Neurophysiology*, *88*, 2530–2546.

Cavanaugh, J. R., Bair, W., & Movshon, J. A. (2002b). Selectivity and spatial distribution of signals from the receptive field surround in macaque V1 neurons. *Journal of Neurophysiology*, *88*, 2547–2556.

Chen, C., Kasamatsu, T., Polat, U., & Norcia, A. M. (2001). Contrast response characteristics of long-range lateral interactions in cat striate cortex. *Neuroreport*, *12*, 655–661.

Chisum, H. J., Mooser, F., & Fitzpatrick, D. (2003). Emergent properties of layer 2/3 neurons reflect the collinear arrangement of horizontal connections in tree shrew visual cortex. *Journal of Neuroscience*, *23*, 2947–2960.

DeAngelis, G. C., Freeman, R. D., & Ohzawa, I. (1994). Length and width tuning of neurons in the cat's primary visual cortex. *Journal of Neurophysiology*, *71*, 347–374.

Felisberti, F., & Derrington, A. M. (1999). Long-range interactions modulate the contrast gain in the lateral geniculate nucleus of cats. *Visual Neuroscience*, *16*, 943–956. doi:10.1017/S0952523899165143.

Fitzpatrick, D. (2000). Seeing beyond the receptive field in primary visual cortex. *Current Opinion in Neurobiology*, *10*, 438–443. doi:10.1016/S0959-4388(00)00113-6.

Geisler, W. S. (2008). Visual perception and the statistical properties of natural scenes. *Annual Review of Psychology*, *59*, 167–192. doi:10.1146/annurev.psych/58/110405.085632.

Geisler, W. S., Perry, J. S., Super, B. J., & Gallogly, D. P. (2001). Edge co-occurrence in natural images predicts contour grouping performance. *Vision Research*, *41*, 711–724. doi:10.1016/S0042-6989(00)00277-7.

Gilbert, C. D. (1977). Laminar differences in receptive field properties of cells in cat primary visual cortex. *Journal of Physiology*, *268*, 391–421.

Gilbert, C. D., Das, A., Ito, M., Kapadia, M., & Westheimer, G. (1996). Spatial integration and cortical dynamics. *Proceedings of the National Academy of Sciences of the United States of America*, *93*, 615–622. doi:10.1073/pnas.93.2.615.

Gilbert, C. D., & Wiesel, T. N. (1983). Clustered intrinsic connections in cat visual cortex. *Journal of Neuroscience*, *3*, 1116–1133.

Girard, P., Hupé, J. M., & Bullier, J. (2001). Feedforward and feedback connections between areas V1 and V2 of the monkey have similar rapid conduction velocities. *Journal of Neurophysiology*, *85*, 1328–1331.

Gonchar, Y., & Burkhalter, A. (2003). Distinct GABAergic targets of feedforward and feedback connections between lower and higher areas of rat visual cortex. *Journal of Neuroscience*, *23*, 10904–10912.

Grinvald, A., Lieke, E. E., Frostig, R. D., & Hildesheim, R. (1994). Cortical point-spread function and long-range lateral interactions revealed by real-time optical imaging of macaque monkey primary visual cortex. *Journal of Neuroscience*, *14*, 2545–2568.

Haider, B., Krause, M. R., Duque, A., Yu, Y., Touryan, J., Mazer, J. A., et al. (2010). Synaptic and network mechanisms of sparse and reliable visual cortical activity during nonclassical receptive field stimulation. *Neuron*, *65*, 107–121.

Han, X., Qian, X. G., Bernstein, J. G., Zhou, H. H., Franzesi, G. T., Stern, P., et al. (2009). Millisecond-timescale optical control of neural dynamics in the nonhuman primate brain. *Neuron*, *62*, 191–198. doi:10.1016/j.neuron.2009.03.011.

Hashemi-Nezhad, M., & Lyon, D. C. (2011). Orientation tuning of the suppressive extraclassical surround depends on intrinsic organization of V1. *Cerebral Cortex*, *22*, 308–326.

Heeger, D. J. (1992). Normalization of cell responses in cat striate cortex. *Vision Research*, *9*, 181–198.

Hess, R., & Field, D. (1999). Integration of contours: new insights. *Trends in Cognitive Sciences*, *3*, 480–486. doi:10.1016/S1364-6613(99)01410-2.

Hirsch, J. A., & Gilbert, C. D. (1991). Synaptic physiology of horizontal connections in the cat's visual cortex. *Journal of Neuroscience*, *11*, 1800–1809.

Hubel, D. H., & Wiesel, T. N. (1959). Receptive fields of single neurones in the cat's striate cortex. *Journal of Physiology*, *148*, 574–591.

Hubel, D. H., & Wiesel, T. N. (1962). Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. *Journal of Physiology*, *160*, 106–154.

Hubel, D. H., & Wiesel, T. N. (1965). Receptive fields and functional architecture in two nonstriate visual areas (18 and 19) of the cat. *Journal of Neurophysiology*, *28*, 229–289.

Hupé, J. M., James, A. C., Girard, P., & Bullier, J. (2001). Response modulations by static texture surround in area V1 of the macaque monkey do not depend on feedback connections from V2. *Journal of Neurophysiology*, *85*, 146–163.

Hupé, J. M., James, A. C., Payne, B. R., Lomber, S. G., Girard, P., & Bullier, J. (1998). Cortical feedback improves discrimination between figure and background by V1, V2 and V3 neurons. *Nature*, *394*, 784–787. doi:10.1038/29537.

Ichida, J. M., Schwabe, L., Bressloff, P. C., & Angelucci, A. (2007). Response facilitation from the "suppressive" receptive field surround of macaque V1 neurons. *Journal of Neurophysiology*, *98*, 2168–2181.

Kapadia, M. K., Ito, M., Gilbert, C. D., & Westheimer, G. (1995). Improvement in visual sensitivity by changes in local context: Parallel studies in human observers and in V1 of alert monkeys. *Neuron*, *15*, 843–856. doi:10.1016/0896-6273(95)90175-2.

Kapadia, M. K., Westheimer, G., & Gilbert, C. D. (1999). Dynamics of spatial summation in primary visual cortex of alert monkeys. *Proceedings of the National Academy of Sciences of the United States of America*, *96*, 12073–12078. doi:10.1073/pnas.96.21.12073.

Kapadia, M. K., Westheimer, G., & Gilbert, C. D. (2000). Spatial distribution of contextual interactions in primary visual cortex and in visual perception. *Journal of Neurophysiology*, *84*, 2048–2062.

Knierim, J. J., & Van Essen, D. (1992). Neuronal responses to static texture patterns in area V1 of the alert macaque monkey. *Journal of Neurophysiology*, *67*, 961–980.

Lamme, V. A. F. (1995). The neurophysiology of figure-ground segregation in primary visual cortex. *Journal of Neuroscience*, *15*, 1605–1615.

Lamme, V. A. F., Rodriguez-Rodriguez, V., & Spekreijse, H. (1999). Separate processing dynamics for texture elements, boundaries and surfaces in primary visual cortex of the macaque monkey. *Cerebral Cortex*, *9*, 406–413. doi:10.1093/cercor/9.4.406.

Levick, W. R., Cleland, B. G., & Dubin, M. W. (1972). Lateral geniculate neurons of the cat: Retinal inputs and physiology. *Investigative Ophthalmology*, *11*, 302–311.

Levitt, J. B., & Lund, J. S. (1997). Contrast dependence of contextual effects in primate visual cortex. *Nature*, *387*, 73–76. doi:10.1038/387073a0.

Levitt, J. B., & Lund, J. S. (2002). The spatial extent over which neurons in macaque striate cortex pool visual signals. *Visual Neuroscience*, *19*, 439–452. doi:10.1017/S0952523802194065.

Li, C., & Li, W. (1994). Extensive integration field beyond the classical receptive field of cat's striate cortical neurons: Classification and tuning properties. *Vision Research*, *34*, 2337–2355. doi:10.1016/0042-6989(94)90280-1.

Li, H., Fukuda, M., Tanifuji, M., & Rockland, K. S. (2003). Intrinsic collaterals of layer 6 Meynert cells and functional columns in primate V1. *Neuroscience*, *120*, 1061–1069. doi:10.1016/S0306-4522(03)00429-9.

Li, W., Piech, V., & Gilbert, C. D. (2006). Contour saliency in primary visual cortex. *Neuron*, *50*, 951–962. doi:10.1016/j.neuron.2006.04.035.

Li, Z. (2002). A saliency map in primary visual cortex. *Trends in Cognitive Sciences*, *6*, 9–16. doi:10.1016/S1364-6613(00)01817-9.

Lund, J. S. (1988). Anatomical organization of macaque monkey striate visual cortex. *Annual Review of Neuroscience*, *11*, 253–288. doi:10.1146/annurev.ne.11.0301188.001345.

Lund, J. S., Angelucci, A., & Bressloff, P. C. (2003). Anatomical substrates for functional columns in macaque monkey primary visual cortex. *Cerebral Cortex*, *13*, 15–24. doi:10.1093/cercor/13.1.15.

Lund, J. S., Wu, Q., Hadingham, P. T., & Levitt, J. B. (1995). Cells and circuits contributing to functional properties in area V1 of macaque monkey cerebral cortex: Bases for neuroanatomically realistic models. *Journal of Anatomy*, *187*, 563–581.

Luo, L., Callaway, E. M., & Svoboda, K. (2008). Genetic dissection of neural circuits. *Neuron*, *57*, 634–660. doi:10.1016/j.neuron.2008.01.002.

Maffei, L., & Fiorentini, L. (1976). The unresponsive regions of visual cortical receptive fields. *Vision Research*, *16*, 1131–1139.

Malach, R., Amir, Y., Harel, M., & Grinvald, A. (1993). Relationship between intrinsic connections and functional architecture revealed by optical imaging and in vivo targeted biocytin injections in primate striate cortex. *Proceedings of the National Academy of Sciences of the United States of America*, *90*, 10469–10473. doi:10.1073/pnas.90.22.10469.

Mariño, J., Schummers, J., Lyon, D. C., Schwabe, L., Beck, O., Wiesing, P., et al. (2005). Invariant computations in local cortical networks with balanced excitation and inhibition. *Nature Neuroscience*, *8*, 194–201. doi:10.1038/nn1391.

Maunsell, J. H. R., & Van Essen, D. C. (1983). The connections of the middle temporal visual area (MT) and their relationship to a cortical hierarchy in the macaque monkey. *Journal of Neuroscience*, *3*, 2563–2586.

McGuire, B. A., Gilbert, C. D., Rivlin, P. K., & Wiesel, T. N. (1991). Targets of horizontal connections in macaque primary visual cortex. *Journal of Comparative Neurology*, *305*, 370–392. doi:10.1002/cne.903050303.

Mignard, M., & Malpeli, J. G. (1991). Paths of information flow through visual cortex. *Science*, *251*, 1249–1251. doi:10.1126/science.1848727.

Mizobe, K., Polat, U., Pettet, M. W., & Kasamatsu, T. (2001). Facilitation and suppression of single striate-cell activity by spatially discrete pattern stimuli presented beyond the receptive field. *Visual Neuroscience*, *18*, 377–391. doi:10.1017/S0952523801183045.

Muller, J. R., Metha, A. B., Krauskopf, J., & Lennie, P. (2003). Local signals from beyond the receptive fields of striate cortical neurons. *Journal of Neurophysiology*, *90*, 822–831.

Naito, T., Sadakane, O., Okamoto, M., & Sato, H. (2007). Orientation tuning of surround suppression in lateral geniculate nucleus and primary visual cortex of cat. *Neuroscience*, *149*, 962–975. doi:10.1016/j.neuroscience.2007.08.001.

Nelson, J. I., & Frost, B. (1978). Orientation selective inhibition from beyond the classical visual receptive field. *Brain Research*, *139*, 359–365. doi:10.1016/0006-8993(78)90937-X.

Nelson, J. I., & Frost, B. (1985). Intracortical facilitation among co-oriented, co-axially aligned simple cells in cat striate cortex. *Experimental Brain Research*, *61*, 54–61.

Nothdurft, H. C., Gallant, J. L., & Van Essen, D. C. (1999). Response modulation by texture surround in primate area V1: Correlates of "popout" under anesthesia. *Visual Neuroscience*, *16*, 15–34.

Nothdurft, H. C., Gallant, J. L., & Van Essen, D. C. (2000). Response profiles to texture border patterns in area V1. *Visual Neuroscience*, *17*, 421–436. doi:10.1017/S0952523800173092.

Olshausen, B. A., & Field, D. J. (2004). Sparse coding of sensory inputs. *Current Opinion in Neurobiology*, *14*, 481–487. doi:10.1016/j.conb.2004.07.007.

Osakada, F., Mori, T., Cetin, A. H., Marshel, J. H., Virgen, B., & Callaway, E. M. (2011). New rabies virus variants for monitoring and manipulating activity and gene expression in defined neural circuits. *Neuron*, *71*, 617–631. doi:10.1016/j.neuron.2011.07.005.

Ozeki, H., Finn, I. M., Schaffer, E. S., Miller, K. D., & Ferster, D. (2009). Inhibitory stabilization of the cortical network underlies visual surround suppression. *Neuron*, *62*, 578–592. doi:10.1016/j.neuron.2009.03.028.

Ozeki, H., Sadakane, O., Akasaki, T., Naito, T., Shimegi, S., & Sato, H. (2004). Relationship between excitation and inhibition underlying size tuning and contextual response modulation in the cat primary visual cortex. *Journal of Neuroscience*, *24*, 1428–1438.

Perkel, D. J., Bullier, J., & Kennedy, H. (1986). Topography of the afferent connectivity of area 17 in the macaque monkey: A double-labelling study. *Journal of Comparative Neurology*, *253*, 374–402. doi:10.1002/cne.902530307.

Polat, U., Mizobe, K., Pettet, M. W., Kasamatsu, T., & Norcia, A. M. (1998). Collinear stimuli regulate visual responses depending on cell's contrast threshold. *Nature*, *391*, 580–584. doi:10.1038/35372.

Rao, R. P., & Ballard, D. H. (1999). Predictive coding in the visual cortex: A functional interpretation of some extra-classical receptive-field effects. *Nature Neuroscience*, *2*, 79–87. doi:10.1038/4580.

Reid, R. C., & Usrey, W. M. (2004). Functional connectivity in the pathway from retina to striate cortex. In L. M. Chalupa & J. S. Werner (Eds.), *The visual neurosciences* (Vol. 1, pp. 673–679). Cambridge, MA: MIT Press.

Riesenhuber, M., & Poggio, T. (2003). How the visual cortex recognizes objects: The tale of the standard model. In L. M. Chalupa & J. S. Werner (Eds.), *The visual neurosciences* (Vol. 2, pp. 1640–1653). Cambridge, MA: MIT Press.

Rockland, K. S., & Lund, J. S. (1982). Widespread periodic intrinsic connections in the tree shrew visual cortex. *Science*, *215*, 1532–1534. doi:10.1126/science.7063863.

Rockland, K. S., & Lund, J. S. (1983). Intrinsic laminar lattice connections in primate visual cortex. *Journal of Comparative Neurology*, *216*, 303–318. doi:10.1002/cne.902160307.

Rockland, K. S., & Pandya, D. N. (1979). Laminar origins and terminations of cortical connections of the occcipital lobe in the Rhesus monkey. *Brain Research*, *179*, 3–20. doi:10.1016/0006-8993(79)90485-2.

Rossi, A. F., Desimone, R., & Ungerleider, L. G. (2001). Contextual modulation in primary visual cortex of macaques. *Journal of Neuroscience*, *21*, 1698–1709.

Sadakane, O., Ozeki, H., Naito, T., Akasaki, T., Kasamatsu, T., & Sato, H. (2006). Contrast-dependent, contextual response modulation in primary visual cortex and lateral geniculate nucleus of the cat. *European Journal of Neuroscience*, *23*, 1633–1642.

Sandell, J. H., & Schiller, P. H. (1982). Effect of cooling area 18 on striate cortex cells in the squirrel monkey. *Journal of Neurophysiology*, *48*, 38–48.

Sceniak, M. P., Chatterjee, S., & Callaway, E. M. (2006). Visual spatial summation in macaque geniculocortical afferents. *Journal of Neurophysiology*, *96*, 3474–3484.

Sceniak, M. P., Hawken, M. J., & Shapley, R. M. (2001). Visual spatial characterization of macaque V1 neurons. *Journal of Neurophysiology*, *85*, 1873–1887.

Sceniak, M. P., Ringach, D. L., Hawken, M. J., & Shapley, R. (1999). Contrast's effect on spatial summation by macaque V1 neurons. *Nature Neuroscience*, *2*, 733–739. doi:10.1038/11197.

Schmidt, K. E., Goebel, R., Löwell, S., & Singer, W. (1997). The perceptual grouping criterion of colinearity is reflected by anisotropies of connections in the primary visual cortex. *European Journal of Neuroscience*, *9*, 1083–1089.

Schwabe, L., Ichida, J. M., Shushruth, S., Mangapathy, P., & Angelucci, A. (2010). Contrast-dependence of surround suppression in macaque V1: Experimental testing of a recurrent network model. *NeuroImage*, *52*, 777–792. doi:10.1016/j.neuroimage.2010.01.032.

Schwabe, L., Obermayer, K., Angelucci, A., & Bressloff, P. C. (2006). The role of feedback in shaping the extra-classical receptive field of cortical neurons: A recurrent network model. *Journal of Neuroscience*, *26*, 9117–9129.

Schwartz, O., & Simoncelli, E. P. (2001). Natural signal statistics and sensory gain control. *Nature Neuroscience*, *4*, 819–825. doi:10.1038/90526.

Sengpiel, F., Baddley, R. J., Freeman, T. C. B., Harrad, R., & Blakemore, C. (1998). Different mechanisms underlie three inhibitory phenomena in cat area 17. *Vision Research*, *38*, 2067–2080. doi:10.1016/S0042-6989(97)00413-6.

Sengpiel, F., Sen, A., & Blakemore, C. (1997). Characteristics of surround inhibition in cat area 17. *Experimental Brain Research*, *116*, 216–228. doi:10.1007/PL00005751.

Shmuel, A., Korman, M., Sterkin, A., Harel, M., Ullman, S., Malach, R., et al. (2005). Retinotopic axis specificity and selective clustering of feedback projections from V2 to V1 in the owl monkey. *Journal of Neuroscience*, *25*, 2117–2131.

Shushruth, S., Ichida, J. M., Levitt, J. B., & Angelucci, A. (2009). Comparison of spatial summation properties of neurons in macaque V1 and V2. *Journal of Neurophysiology*, *102*, 2069–2083.

Shushruth, S., Mangapathy, P., Ichida, J. M., Bressloff, P. C., Schwabe, L., & Angelucci, A. (2012). Strong recurrent networks compute the orientation-tuning of surround modulation in primate primary visual cortex. *Journal of Neuroscience*, *4*, 308–321.

Shushruth, S., Nurminen, L., Bijanzadeh, M., Ichida, J. M., Vanni, S., & Angelucci, A. (2013). Different orientation-tuning of near and far surround suppression in macaque primary visual cortex mirrors their tuning in human visual perception. *Journal of Neuroscience*, *33*.

Sillito, A. M., Cudeiro, J., & Murphy, P. C. (1993). Orientation sensitive elements in the corticofugal influence on centre-surround interactions in the dorsal lateral geniculate nucleus. *Experimental Brain Research*, *93*, 6–16.

Sillito, A. M., Grieve, K. L., Jones, H. E., Cudeiro, J., & Davis, J. (1995). Visual cortical mechanisms detecting focal orientation discontinuities. *Nature*, *378*, 492–496.

Simoncelli, E. P., & Olshausen, B. A. (2001). Natural image statistics and neural representation. *Annual Review of Neuroscience*, *24*, 1193–1216. doi:10.1146/annurev.neuro.24.1.1193.

Sincich, L. C., & Blasdel, G. G. (2001). Oriented axon projections in primary visual cortex of the monkey. *Journal of Neuroscience*, *21*, 4416–4426.

Slovin, H., Arieli, A., Hildesheim, R., & Grinvald, A. (2002). Long-term voltage-sensitive dye imaging reveals cortical dynamics in behaving monkeys. *Journal of Neurophysiology*, *88*, 3421–3438.

Solomon, S. G., Peirce, J. W., & Lennie, P. (2004). The impact of suppressive surrounds on chromatic properties of cortical neurons. *Journal of Neuroscience*, *24*, 148–160.

Solomon, S. G., White, A. J. R., & Martin, P. R. (2002). Extraclassical receptive field properties of parvocellular, magnocellular, and koniocellular cells in the primate lateral geniculate nucleus. *Journal of Neuroscience*, *22*, 338–349.

Somers, D. C., Todorov, E. V., Siapas, A. G., Toth, L. J., Kim, D. S., & Sur, M. (1998). A local circuit approach to understanding integration of long-range inputs in primary visual cortex. *Cerebral Cortex*, *8*, 204–217. doi:10.1093/cercor/8.3.204.

Spratling, M. W. (2010). Predictive coding as a model of response properties in cortical area V1. *Journal of Neuroscience*, *30*, 3531–3543.

Stemmler, M., Usher, M., & Niebur, E. (1995). Lateral interactions in primary visual cortex: a model bridging physiology and psychophysics. *Science*, *269*, 1877–1880. doi:10.1126/science.7569930.

Stettler, D. D., Das, A., Bennett, J., & Gilbert, C. D. (2002). Lateral connectivity and contextual interactions in macaque primary visual cortex. *Neuron*, *36*, 739–750. doi:10.1016/S0896-6273(02)01029-2.

Stimberg, M., Wimmer, K., Martin, R., Schwabe, L., Marino, J., Schummers, J., et al. (2009). The operating regime of local computations in primary visual cortex. *Cerebral Cortex*, *19*, 2166–2180. doi:10.1093/cercor/bhn240.

Ungerleider, L. G., & Desimone, R. (1986). Cortical connections of visual area MT in the macaque. *Journal of Comparative Neurology*, *248*, 190–222. doi:10.1002/cne.902480204.

Van Essen, D. C., & Maunsell, J. H. R. (1983). Hierarchical organization and functional streams in the visual cortex. *Trends in Neurosciences*, *6*, 370–375. doi:10.1016/0166-2236(83)90167-4.

Van Essen, D. C., Newsome, W. T., & Maunsell, J. H. (1984). The visual field representation in striate cortex of the macaque monkey: Asymmetries, anisotropies, and individual variability. *Vision Research*, *24*, 429–448. doi:10.1016/0042-6989(84)90041-5.

van Vreeswijk, C., & Sompolinsky, H. (1996). Chaos in neuronal networks with balanced excitatory and inhibitory activity. *Science*, *274*, 1724–1726. doi:10.1126/science.274.5293.1724.

Vinje, W. E., & Gallant, J. L. (2000). Sparse coding and decorrelation in primary visual cortex during natural vision. *Science*, *287*, 1273–1276. doi:10.1126/science.287.5456.1273.

Vinje, W. E., & Gallant, J. L. (2002). Natural stimulation of the nonclassical receptive field increases information transmission efficiency in V1. *Journal of Neuroscience*, *22*, 2904–2915.

Walker, G. A., Ohzawa, I., & Freeman, R. D. (1999). Asymmetric suppression outside the classical receptive field of the visual cortex. *Journal of Neuroscience*, *19*, 10536–10553.

Walker, G. A., Ohzawa, I., & Freeman, R. D. (2000). Suppression outside the classical cortical receptive field. *Visual Neuroscience*, *17*, 369–379. doi:10.1017/S0952523800173055.

Webb, B. S., Dhruv, N. T., Solomon, S. G., Taliby, C., & Lennie, P. (2005). Early and late mechanisms of surround suppression in striate cortex of macaque. *Journal of Neuroscience*, *25*, 11666–11675.

Webb, B. S., Tinsley, C. J., Barraclough, N. E., Easton, A., Parker, A., & Derrington, A. M. (2002). Feedback from V1 and inhibition from beyond the classical receptive field modulates the responses of neurons in the primate lateral geniculate nucleus. *Visual Neuroscience*, *19*, 583–592.

Xing, D., Shapley, R. M., Hawken, M. J., & Ringach, D. L. (2005). Effect of stimulus size on the dynamics of orientation selectivity in macaque V1. *Journal of Neurophysiology*, *94*, 799–812.

Yoshimura, Y., Sato, H., Imamura, K., & Watanabe, Y. (2000). Properties of horizontal and vertical inputs to pyramidal cells in the superficial layers of the cat visual cortex. *Journal of Neuroscience*, *20*, 1931–1940.

Yuille, A., & Kersten, D. (2006). Vision as Bayesian inference: Analysis by synthesis? *Trends in Cognitive Sciences*, *10*, 301–308. doi:10.1016/j.tics.2006.05.002.

Zipser, K., Lamme, V. A., & Schiller, P. H. (1996). Contextual modulation in primary visual cortex. *Journal of Neuroscience*, *16*, 7376–7389.