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Brightness Induction: Rate Enhancement and Neuronal Synchronization as Complementary Codes

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Summary

In cat visual cortex, we investigated with parallel recordings from multiple units the neuronal correlates of perceived brightness. The perceived brightness of a center grating was changed by varying the orientation or the relative spatial phase of a surrounding grating. Brightness enhancement by orientation contrast is associated with an increase of discharge rates of responses to the center grating but not with changes in spike synchronization. In contrast, if brightness enhancement is induced by phase offset, discharge rates are unchanged but synchronization increases between neurons responding to the center grating. The changes in synchronization correlate well with changes in perceived brightness that were assessed in parallel in human subjects using the same stimuli. These results indicate that in cerebral cortex the modulation of synchronicity of responses is used as a mechanism complementary to rate changes to enhance the saliency of neuronal responses.

Introduction

The perceived brightness and the contrast of visual stimuli are influenced by surrounding stimuli (Agostini and Galmonte, 2002; Cannon and Fullenkamp, 1991; Huang et al., 2002; Sillito and Jones, 1996; Yu et al., 2001). These interactions are often correlated with a modulation of the discharge rates of neurons in the visual cortex (Blakemore and Tobin, 1972; DeAngelis et al., 1994; Knierim and Van Essen, 1992; Nelson and Frost, 1978; Rossi and Paradiso, 1999; Sengpiel et al., 1997; Walker et al., 2000). For example, when a sinusoidal grating of high contrast is surrounded by another grating of high contrast, the perceived contrast of the center grating depends on the orientation of the surround. Perceived contrast is minimal with an iso-oriented and maximal with a cross-oriented surround, as the perceived brightness of the white bars of the grating increases with orientation offset (Cannon and Fullenkamp, 1991; Ejima and Takahashi, 1985; Solomon et al., 1993; Yu et al., 2001) (Figures 1B and 1C). This change in perception is closely correlated with changes of neuronal discharge rates in the primary visual cortex. An iso-oriented surround suppresses neuronal responses much more than a cross-oriented surround (Blakemore and Tobin, 1972; DeAngelis et al., 1994; Knierim and Van Essen, 1992; Nelson and Frost, 1978; Sengpiel et al., 1997; Walker et al., 2000).

There are cases, however, where changes in perceived brightness are not correlated with changes in neuronal firing rates. One example is the phase-dependent brightness-induction effect. Here, the enhancement in perceived contrast of the center grating is induced by phase offsets between the surround and the center grating (Cannon and Fullenkamp, 1991; Ejima and Takahashi, 1985; Yu et al., 2001) (Figure 1A). In this condition, the discharge rates of neurons in early visual areas do not correlate with perceived brightness because responses remain equally suppressed by the surround grating, irrespective of its phase-relation to the center grating (DeAngelis et al., 1994; Tanaka et al., 1987). Interestingly, however, this enhancement of perceived brightness by phase offset is associated with increased BOLD responses in human V1 (Williams et al., 2003). This suggests that the brightness enhancement caused by phase offset, even if not associated with rate increases in V1, is nevertheless due to mechanisms that operate in early visual areas. A mechanism that does not rely on rate modulation but can also modify the saliency of neuronal responses is the precise synchronization of discharges. Like an increase in discharge rate, it enhances the impact of neuronal responses by rendering them more efficient in driving receiving neurons (Usrey et al., 1998). As recent evidence indicates that BOLD responses correlate not only with neuronal discharge rates but also with synchronization (Niessing et al., 2005), we hypothesized that brightness induction by phase offset could be associated with increased synchronization of responses to the center stimuli.

In order to test this hypothesis, we investigated changes of neuronal discharge rates and synchrony in area 17 of anesthetized cats in response to center and surround gratings of different orientations and phase relations. Both center and surround gratings were sinusoidally modulated, had the same high contrast (0.83–0.97; mean luminance 31.4 cd m^{-2}), the same spatial frequency (0.5–1.2 cycles/°), and drifted with the same speed (1–3°/s). Thus, without introduction of a phase or orientation contrast, the two gratings merged into one large grating. In order to comply with psychophysical studies, we used large center stimuli (up to 11.4° of visual angle) that covered areas much larger than the sizes of individual receptive fields (RFs). To investigate neuronal responses, we recorded multiunit activity (MUA) and local field potentials (LFPs), either with multiple, individually

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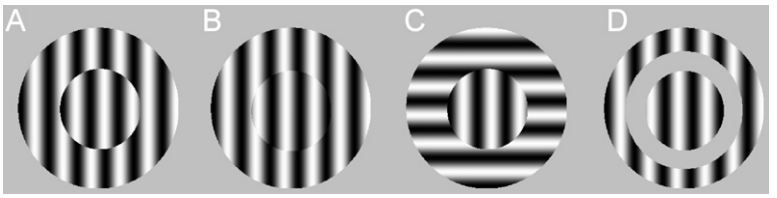

Figure 1. Stimulation Conditions that Lead to Changes in Perceived Contrast of the Center Grating

The center gratings in all four panels have identical physical contrasts in brightness. Nevertheless, when simultaneously viewing the center gratings in (A), (B), and (C), most observers perceive the least contrast (or sharpness) in the center grating surrounded by an iso-oriented grating that has a very small offset from or is fully in phase with the center (B). An increase in either phase offset (A) or orientation contrast (C) of the surround strongly increases the perceived contrast of the center. The phenomenon in (A) is known as the brightness induction effect. (D) If the surround is segregated from the center by a gray ring, the brightness induction effect disappears.

adjustable tungsten electrodes (up to four electrodes simultaneously, 162 recording sites in total) or with multisite silicon probes (16 channel Michigan probes, three separate recordings with up to two probes simultaneously, 68 recording sites in total). In all experiments, we recorded activity of neurons responding to the center grating, and, in one experiment, we also recorded responses to the surround grating. Discharge rates were assessed from peristimulus time histograms (PSTHs) that were averaged across 20 responses to identical stimulus conditions (trials), each stimulus presentation lasting for 2–4 s. Synchrony was assessed from cross-correlation functions (CCFs) computed between pairs of MUA or, in the case of long-distance synchrony, from the coherence functions between MUA and LFP signals (see Experimental Procedures). These correlation functions were computed from single-trial responses and subsequently averaged across 20 identical trials.

Results

Rate Changes

Confirming previous studies, the discharge rates of responses to the center grating were modulated by the presence of the surround. The surround produced the strongest rate suppression in the iso-orientation condition, and this suppression gradually decreased with increasing orientation difference between center and surround [96 recording sites, ANOVA with linear contrast, $F(1, 95) = 8.56$, $p = 0.004$] (Figures 2A and 2B). Thus, increasing the orientation contrast between the center and surround enhanced the neuronal responses to the center. The effect size between the two extreme conditions (0° and 90° orientation contrast) was in the medium range ($d = 0.46$), indicating a moderately strong modulation of response amplitudes relative to the variability of the responses (see Experimental Procedures). The absolute magnitude of the modulation (9%) corresponded well to the magnitude of contrast enhancement in psychophysical experiments (e.g., 6%–12% across subjects [Yu et al., 2001]) but was weaker than the reported modulation of single-unit responses to small center and closely spaced surround stimuli (Jones et al., 2001). The reason is that the center stimuli used in the present study exceeded the size of the classical RFs of the recorded neurons. This had two attenuating effects on surround suppression. First, the large center stimulus already induced some surround suppression itself. Second, on average, the distance between the surround stimulus and the classical RFs was increased. Hence, the surround stimuli suppressed center responses by no more than 50% (Figure 2B).

The present results also confirm the finding that the phase offset of an iso-oriented surround does not modulate the amplitude of the responses to the center (DeAngelis et al., 1994; Tanaka et al., 1987). In the experiments with tungsten electrodes, the changes in rate responses were nonsignificant [123 recording sites, ANOVA, $F(3, 242) = 0.13$, $p = 0.94$; effect size, $d = 0.12$; Figure 2C] and the same was true for the experiments with Michigan probes [56 recording sites, ANOVA, $F(1, 55) = 0.117$, $p = 0.73$; $d = 0.02$] (Figures 2D and 2E, see raw PSTHs in Figure 2F).

We investigated separately the rate responses of simple cortical cells because these are highly sensitive to the phase of the gratings. They exhibit a sinusoidal modulation of their discharges (Skottun et al., 1991), which is sensitive to surround suppression (Xu et al., 2005). In order to determine whether this fast modulation is sensitive to the phase offset between center and surround, single units were extracted (DeAngelis et al., 1994, 1999) by spike-sorting techniques. We then fitted a sine function to each PSTH and used the amplitude of the fitted function as a measure of the sinusoidal rate modulation (see Figure 3A and Experimental Procedures for details).

The majority of the isolated neurons (13 out of 20) had response characteristics of complex cells, and their response amplitudes were modulated by fewer than four spikes/s for all four phase offsets: 0°, 60°, 120°, and 180°. The responses of the remaining seven cells exhibited a strong sinusoidal modulation but again showed neither a significant nor a systematic dependence on the phase offset of the surrounding grating [ANOVA, $F(3, 24) = 1.55$, $p = 0.23$; $d = 0.43$] (Figure 3B). This makes it unlikely that the changes in apparent brightness caused by phase offset are mediated by rate changes of simple cell responses, whose contribution might have been underestimated by the analysis of MUA.

In conclusion, our results agree with previous studies (Blakemore and Tobin, 1972; DeAngelis et al., 1994; Knierim and Van Essen, 1992; Nelson and Frost, 1978; Sengpiel et al., 1997; Tanaka et al., 1987; Walker et al., 2000), which indicated that firing rates are systematically affected by the orientation offset but not by the phase offset of surround gratings.

Changes in Synchrony

Remarkably different results were obtained for changes in synchrony. The synchronization between neurons responding to the center grating decreased in a step-like function as soon as an orientation contrast was introduced but did not increase further with increasing orientation contrast [124 pairs, ANOVA, $F(1, 123) = 5.7$,

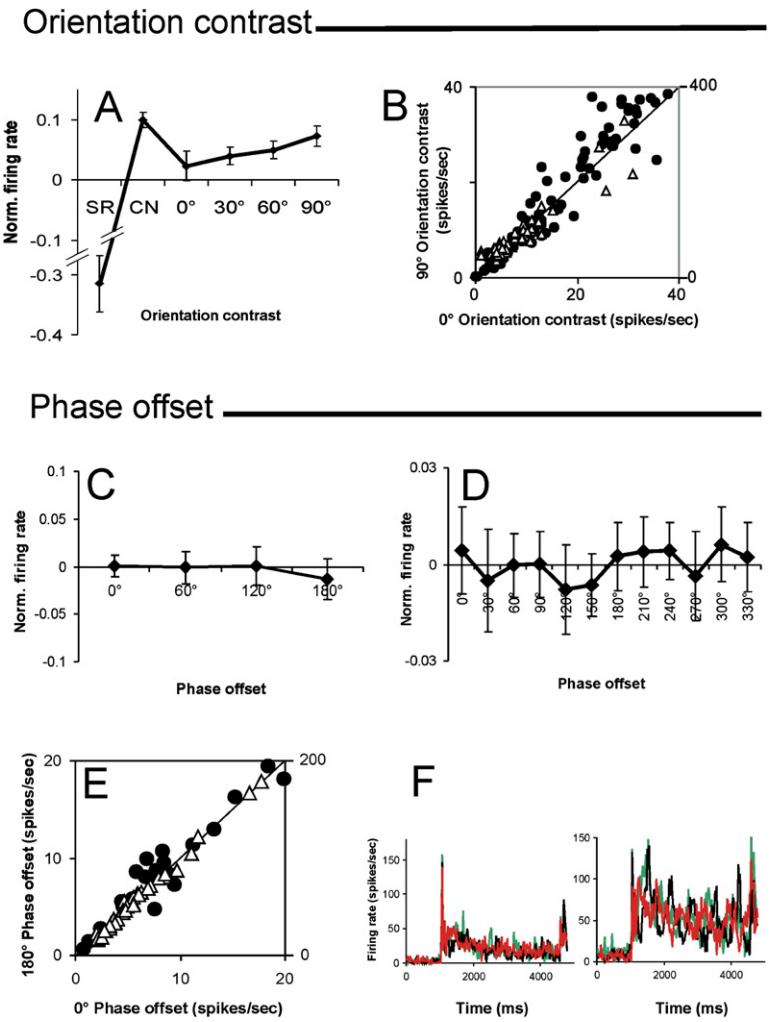

Figure 2. Firing-Rate Responses for Recording Sites Stimulated by the Center Grating and Modulated by Surround Gratings

Prior to averaging, the measures for firing rates were normalized (see Experimental Procedures). The values in the scatter plots are not normalized. (A) Population average of firing-rate responses to the surround presented alone (SR), center presented alone (CN) and with four different orientation contrasts between center and surround. (B) Firing rates for individual recording sites in response to 0° and 90° orientation contrasts. (C and D) Average firing-rate responses for different degrees of phase offset between center and surround obtained in the experiment with tungsten electrodes (C) and Michigan probes (D). (E) Firing rates for recording sites recorded with Michigan probes and for 0° and 180° phase offsets. The data in this graph and in (B) are shown at two scales due to the large variability in the number of neurons composing MUA. Circles, left y axis; triangles, right y axis. (F) Peristimulus time histograms (PSTHs) for the typical responses for which cross-correlation functions are shown in Figure 4F (black, green, and red: 0°, 90°, and 180° phase offset). Vertical bars: standard error of measurement.

p = 0.018]. This change in synchrony amounted to about 10%, with d = 0.38 (Figures 4A and 4B). Such changes would, according to our hypothesis, reduce, rather than enhance, apparent brightness and thus could not account for the perceptual changes associated with these stimuli.

In contrast to the effects of orientation offset, changing the phase relation between center and surround gratings produced much larger and highly significant effects on the strength of synchronization between the cells responding to the center grating. Response synchronization steadily increased with increasing phase offset. These changes in synchrony could be fitted well by a sinusoidal function and peaked at the maximum offset of 180° [Tungsten: 128 pairs; ANOVA, $F(3, 252) = 6.3$, $p < 0.001$; Michigan: 415 pairs; ANOVA with quadratic contrast, $F(1, 414) = 131.2$, $p = 0.0$] (Figures 4C–4E). The changes amounted to 20% and 26%, respectively, and were associated with effect sizes of 0.63 and 0.42. These changes in synchrony remained similar and highly significant even in the individual recordings (n = 3) performed with Michigan probes (ANOVAs, all F values > 41.4, all p values < 0.0001, d.f. within groups ranging between 56 and 207). Therefore, synchronization of neuronal responses is systematically affected by the phase offset of an iso-oriented surround grating, increasing smoothly with phase offset.

Qualitatively, the changes in synchrony between responses to the center grating were similar irrespective of whether the distance between recording site pairs was short (overlapping RFs of the same Michigan probe, 200 μm to 1 mm) or long (between two Michigan probes, at least 2 mm) (Figure 4D). However, the short-distance synchrony was modulated more strongly than long-distance synchrony (the respective averages were 18% and 12% with effects sizes of 0.60 and 0.24). The changes in synchrony between the two most extreme stimulation conditions (0° and 180° phase offset) for individual pairs of recording sites are shown in a scatter plot (Figure 4E). The magnitude of these changes in synchrony corresponds very well to the magnitude of changes in the perceived contrast that was assessed with similar stimuli in psychophysical experiments (8%–24% across subjects; Yu et al., 2001) and also to the increase of the BOLD response in human V1 (~25% change; Williams et al., 2003). To illustrate the temporal properties of the observed spike synchrony between pairs of MUAs, we show examples of CCFs that either do or do not include the stimulus-locked component of the synchronization (i.e., shift-predictors)

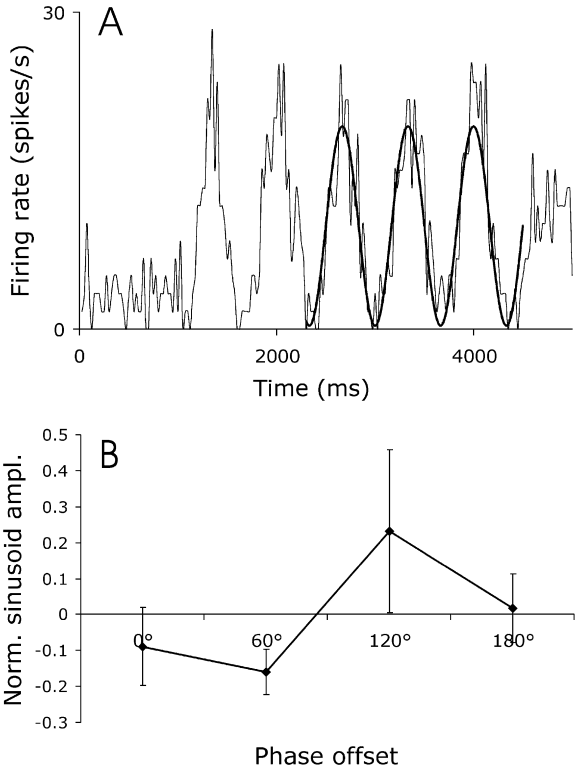

Figure 3. Amplitudes of Sinusoidal Fits to PSTHs as a Function of the Phase Offset between Center and Surround

(A) Single-unit PSTH accumulated over 20 repetitions of one stimulus condition (phase offset = 0°). Thick black line: fitted sine wave with a frequency of 1.5 Hz (the grating frequency). The amplitude of the sine wave is used as a measure of response modulation. (B) Mean amplitudes of response modulation for six single units as a function of phase offset. Vertical bars: standard error of measurement.

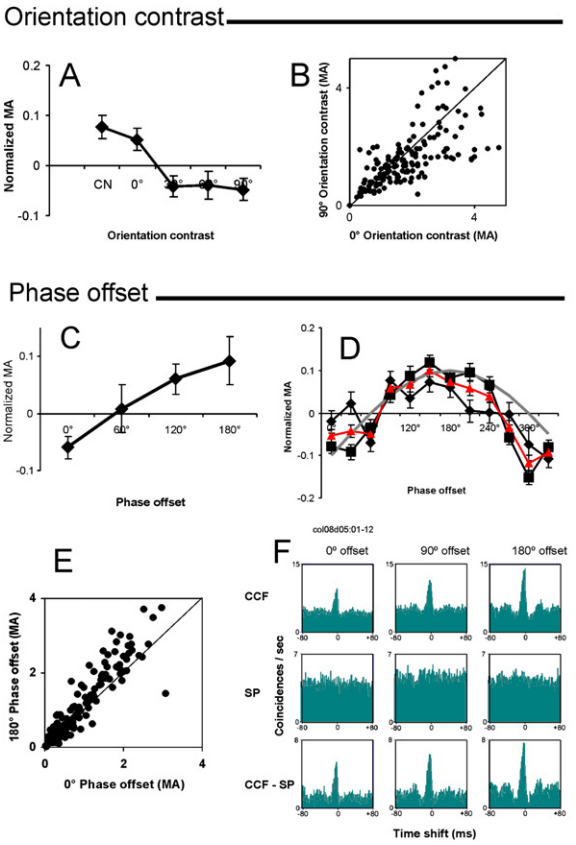

Figure 4. Strength of Synchrony between the Recording Sites Whose Rate Responses Are Shown in Figure 2

Prior to averaging, the measures of synchronization (measured by modulation amplitude, MA) were normalized, while the values in the scatter plots were not normalized (see Experimental Procedures). (A) Average strength of synchronization between the sites investigated in Figure 2A. (B) Strength of synchrony between individual pairs of recording sites for the same stimulation conditions as in Figure 2B. (C and D) Strength of synchronization for the same sites and same stimulation conditions as in Figures 2C and 2D, respectively. The three different lines show the grand average (red triangles), and the short- (diamonds) and long-distance synchrony (squares) between sites belonging to the same or to two different Michigan probes. The solid gray line indicates the fitted sine function: $(0.2\,sin(\theta/2)) - 0.1$. (E) Strength of synchrony between pairs of recording sites for the same responses as shown in Figure 2E. (F) Example of raw cross-correlation functions (CCF), shift predictors (SP), and the cross-correlation with subtracted shift predictors (CCF − SP). Examples are shown for three different levels of phase offset (0°, 90°, and 180°). Vertical bars: standard error of measurement.

(Figure 4F). The strength of the effect exerted by the phase offset is illustrated by showing CCFs for different offset magnitudes.

Psychophysical Measurements

The phase-offset-dependent decoupling between the center and surround has been proposed to reflect the mechanism of perceptual segregation (Gail et al., 2000; Singer, 1999). Accordingly, it is not immediately clear whether the increase in the synchrony of the responses to the center grating reflects the process of figure-ground segregation rather than the changes in perceived contrast. To distinguish between these possibilities, we correlated the physiological measures with the corresponding psychophysical functions. As the perception of phase-offset gratings has been investigated only for the extreme cases (0° and 180° offset; Yu et al., 2001), we conducted an additional psychophysical experiment, in which we investigated in human subjects the detailed psychophysical functions associated with the detectability and the perceived contrast of the figure, respectively (see Experimental Procedures).

The perceived contrast of the center grating increased monotonically with the phase offset and peaked at the maximum of 180° [ANOVA, $F(11, 48) = 11.7$, $p < 0.0001$] (Figure 5A). The resulting psychophysical function matched closely the changes in the strength of synchronization in cat area 17 and could be fitted well by a sinusoid. In contrast, figure-ground segregation, measured by the accuracy with which subjects distinguished between two center gratings of different sizes, did not correspond to the changes in synchrony. Subjects performed 100% correctly already with phase shifts as small as 5°, the "just noticeable difference" (JND) being estimated for phase offsets of about 2.4° of phase angle (Figure 5B). The time needed to identify the size of the center grating also saturated at low values of phase offsets (~10°) (Figure 5C). This suggests that any increase in the phase offset beyond about 10° does not contribute to the ability to segregate the foreground from the

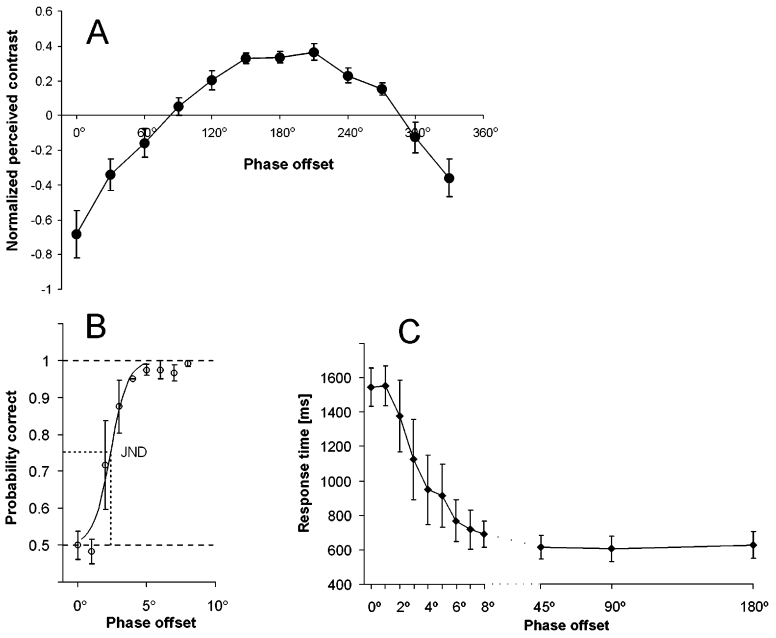

Figure 5. Psychophysical Judgments of Perceived Contrast and Detection Accuracy of the Center Stimulus as a Function of Phase Offset between the Center and Surround

(A) Normalized changes in the perceived contrast of the center grating averaged over five subjects. (B) Probability to correctly identify whether a large or small center grating was presented as a function of phase offset (average over three subjects). Chance level, 0.5; JND, "just-noticeable difference." (C) Latency of responses in (B). Vertical bars: standard error of measurement.

background stimulus. Therefore, the changes in the strength of synchronization correlate closely only with the perceived contrast of the center stimuli and do not correlate with the segregation of the center from the surround.

Spatial Segregation between Center and Surround

The brightness induction phenomenon disappears if the surround is segregated from the center grating by a gray ring (Figure 1D) (Ejima and Takahashi, 1985; Yu et al., 2001), suggesting that the border between the center and the surround plays an important role for the induction of perceived brightness. If changes in perceived brightness are due to changes in synchrony between cells responding to the center, then the introduction of a ring should reduce the effects of phase offsets on response synchronization.

We investigated this prediction in a separate experiment (11 recording sites with appropriate orientation preferences, 36 pairs, two Michigan probes inserted), where gray rings of different sizes (0°, 0.5°, and 1° of visual angle) were introduced between the center and surround gratings (see Experimental Procedures for detail). The introduction of the ring did not significantly affect the average firing rates of the cells' responses to the center grating. The main factors of gap [$F(3, 120) = 1.60$; $p = 0.19$] and offset [$F(2, 120) = 0.50$; $p = 0.61$] were not significant, and the significance of the interaction was only marginal [$F(6, 120) = 2.09$; $p = 0.06$] (Figure 6A).

In contrast, synchrony decreased drastically with the introduction of the ring (Figure 6B), and the changes were highly significant [$F(2, 420) = 136.7$; $p < 0.0001$]. The effect of the gap was, by all indicators, the most prominent effect in the entire study: the effect sizes ranged between 1.5 and 2.3. The scatter plot in Figure 6C and the typical correlograms in Figure 6D illustrate these strong effects. Although the changes in synchrony matched most closely the psychophysical function in the conditions without a gap, the above mentioned sine-like relationship between phase offsets and synchrony did not replicate exactly in this experiment (Figure 6B). We attribute this to the relatively small sample size. This effect of phase offset was still detectable but primarily in the significant interaction [$F(6, 420) = 3.04$; $p = 0.006$], while the significance of the main effect was marginal [$F(3, 420) = 2.49$; $p = 0.06$].

In conclusion, the introduction of a gap between center and surround—a manipulation that destroys the effect of phase offset on apparent brightness—strongly reduced the synchronicity between cells responding to the center. This must also reduce strongly any perceptual effect that relies on response synchronization.

Synchrony across the Contour Boundary

In order to investigate whether the observed changes in synchrony with phase offset were global or confined only to responses to the center grating, we measured synchrony between pairs of sites activated by the center and surround gratings, respectively. In addition, we investigated the changes in the strength of synchrony between the sites activated exclusively by the surround grating. To this end, we inserted two Michigan probes in area 17 such that the RFs of the respective recording sites did not overlap and were completely covered either by the center or by the surround grating. To study these long-range interactions, we selected recording-site pairs whose RFs shared the same orientation and were aligned collinearly. We assessed this long-distance synchrony by determining the spike-field coherence (SFC). This is a more sensitive measure than the CCF computed from neuronal discharges. It assesses the extent to which the discharges of a cell are synchronized with the activity of larger cell populations by quantifying the precision of the correlation between action potentials at one site with fluctuations of the local field potential at another site (Fries et al., 1997) (see Experimental Procedures).

As expected, the firing rates of the neurons responding to the surround were not affected by phase offsets [n = 11 MUA signals; ANOVA, $F(11, 120) = 0.01$, $p = 0.9$;

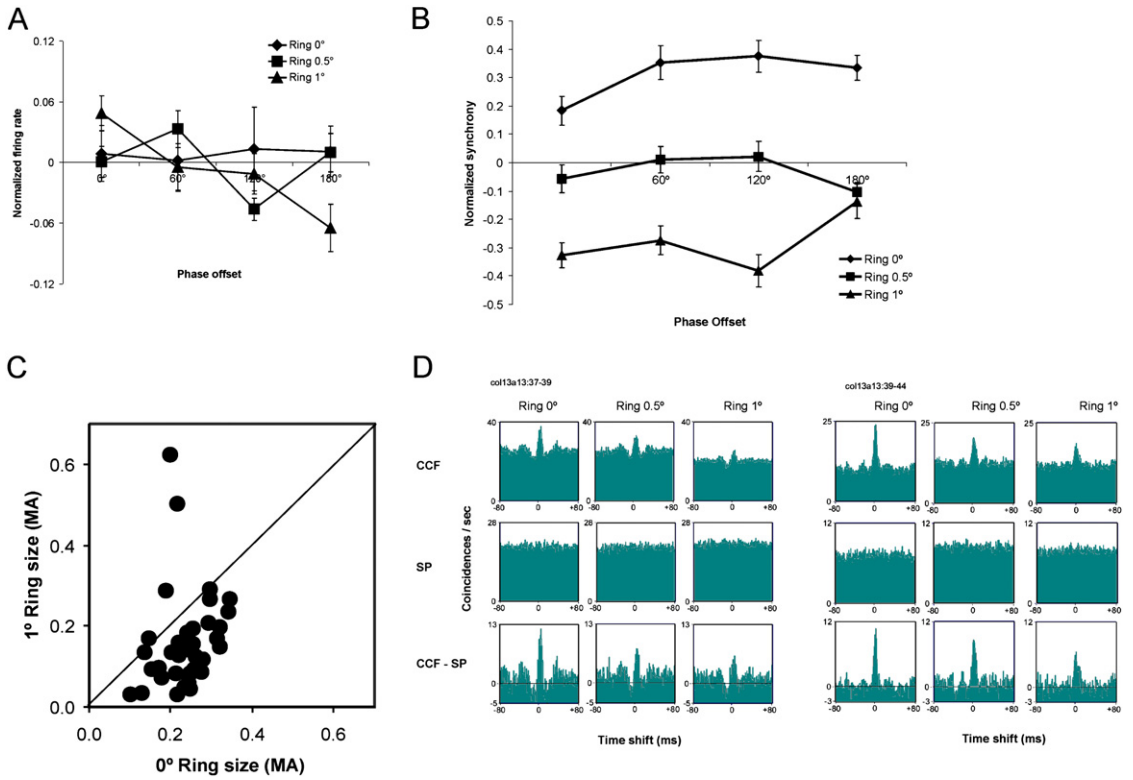

Figure 6. Effects of Gaps and Phase Offsets between Center and Surround on Firing Rate and Synchrony of Responses to the Center Grating (Figure 1D)

The width of the gap was 0°, 0.5°, or 1° of visual angle. (A) Population changes of rate responses. (B) Population changes of the strength of synchrony (all normalized). (C) Change in synchrony for all 36 pairs shown as a scatter plot between minimum and maximum ring size and for 0° phase offset. (D) Typical cross-correlation functions (CCF), shift predictors (SP), and their difference (CCF − SP) for two pairs of units. Vertical bars: standard error of measurement.

Figure 7A]. Consistent with previous reports (Engel et al., 1990), the short-distance SFCs between the responses evoked either by the center or the surround, which were recorded from the same Michigan probe, were about five times stronger than the long-distance SFCs between the two probes (~0.01 versus ~0.002, respectively). Nevertheless, the long-distance coherence between the pairs of sites, responding respectively to the center and the surround gratings, was sensitive to stimulation conditions and changed significantly as a function of phase offset [frequency range 20–80 Hz; 2 MUA sites; 11 LFP sites, 22 pairs, 20 trials/condition; ANOVA, $F(11, 252) = 14.5$, $p < 0.0001$]. SFC decreased continuously with increasing phase offset and reached minimal values with the maximum offset of 180° (Figure 7C). These changes in SFC occurred mostly in two γ-frequency bands (31–60 Hz and 61–80 Hz) and were highly consistent and associated with large effect sizes (2.03 and 1.7, respectively). The changes in coherence in the β range (20–30 Hz) were much less systematic and associated with a much lower effect size ($d = 0.3$) (Figure 7D). A similar decrease in γ-band synchrony across the border of two phase-offset gratings has been observed in V1 of awake monkeys (Gail et al., 2000). Thus, phase offset also affects long-distance synchrony across the center-surround border but the synchrony changes in the direction opposite to that between neurons stimulated by the center grating. Therefore, the phase-offset-dependent increase in synchrony of responses to the center grating is not global but is restricted to responses evoked by the center stimulus.

Phase offset also induced significant changes in SFC between responses to the surround grating [11 sites and 55 pairs; ANOVA, $F(11, 339) = 22.2$, $p < 0.0001$]. However, these changes were not systematically related to the degree of phase offset (Figure 7B) and were of considerably smaller effect size ($d = 0.3$) than the changes of SFC across the center-surround border.

Discussion

The present findings indicate that surround stimuli modulate not only the rate of responses to center stimuli but also their synchronization. These two variables are sensitive to different properties of the stimuli. Rates are modulated by changes in the orientation of the surround, implying the involvement of orientation-selective inhibitory mechanisms. By contrast, synchronization is modulated by other stimulus properties, such as the phase offset and the separation between center and surround, implying the involvement of mechanisms that are sensitive to the continuity of contours. Traditionally, in experiments on simultaneous contrast, changes in firing rate have been considered to be the only candidate mechanism to explain changes of perceived brightness. Our findings suggest that synchronization could have a

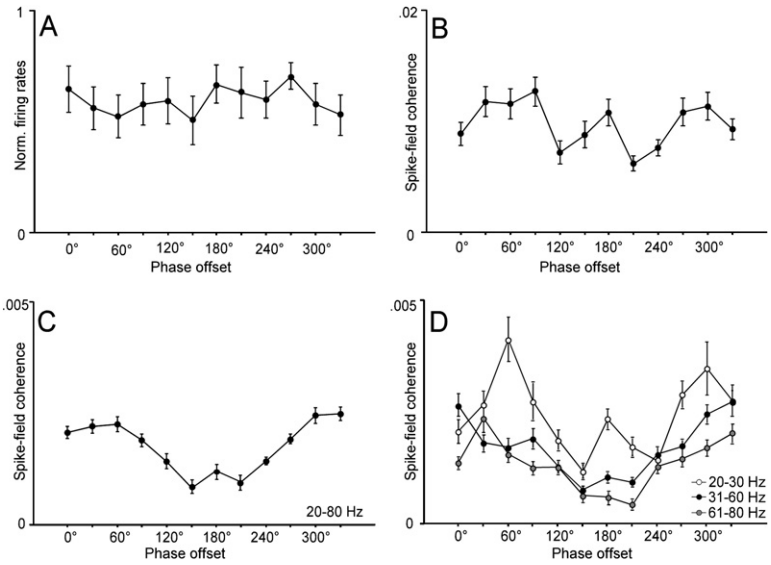

Figure 7. Responses to the Surround and Spike-Field Coherence (SFC) between the Responses to the Center Stimulus and the Surround as a Function of Phase Offset

(A) Normalized average rate responses at recording sites whose RFs were covered by surround stimuli. (B) SFC between responses to surround stimuli. (C) SFC between pairs of sites stimulated by center and surround, respectively. (D) Same data as in (C) decomposed into three frequency ranges. Vertical bars: standard error of measurement.

similar function, in particular, because, as we have shown, it correlates well with perception in conditions in which discharge rates remain unchanged. Evidence indicates that cortical neurons act as coincidence detectors and are sensitive to increases of synchronous firing (Konig et al., 1995; Usrey et al., 1998). Thus, an increase in synchronization should produce an effect on the saliency of neuronal responses equivalent to that of an increase in discharge rate (Abeles, 1982; Konig et al., 1996). This suggests the possibility that modulation of discharge rates and synchrony are complementary in adjusting the saliency of neuronal signals. This interpretation is consistent with the finding that phase offsets enhance BOLD responses to the center stimulus without significantly enhancing firing rate (Williams et al., 2003) because recent evidence indicates that hemodynamic responses increase not only with increases in discharge rates but also with increases in response synchronization (Niessing et al., 2005).

It is not clear how the changes in rate responses interact with the changes in synchronization when the orientation contrast between center and surround is manipulated. In this case, perception is correlated with rates and not with synchrony. One possibility is that the interaction is nonlinear and that, at the level of perception, the changes in rates have precedence over those in synchrony.

The mechanisms that underlie the observed changes in synchronization are not clear. Response synchronization depends on both the excitatory and inhibitory tangential connections (Engel et al., 1991; Schillen and Konig, 1994; Traub et al., 2001), reflects the anisotropy of these connections (Schmidt et al., 1997), and is, in addition, highly susceptible to modulation by stimulus configuration (for review see Singer, 1999). Synchronization is particularly strong among neurons responding to continuous or collinear contours (Gray et al., 1989). This dependence on continuity accounts well for the decrease of synchronicity across the center-surround border when the phase offset increases. Changes in phase offset are also likely to modulate the rate responses of the cells straddling the border between the center and surround (Gilbert, 1977; von der Heydt et al., 1984). However, the present results do not allow us to determine whether and how these border effects are translated into enhanced synchrony that propagates across all neurons responding to the center stimulus. The finding that phase offsets and gaps between center and surround had opposite effects on synchrony excludes involvement of a mechanism that is solely sensitive to continuity. The fact that the effects are present despite anesthesia excludes the participation of higher attention-dependent cognitive functions and favors the involvement of low-level computations.

Interestingly, changes in the synchronization of responses to the center grating do not correlate with the ability to perceptually segregate the center from the surround. Perceptual segregation is already complete with phase offsets that are too small to produce noticeable changes in apparent brightness and detectable changes in synchrony. Hence, neither the modifications in rate nor in synchrony of the responses to the segregated surfaces seem to be involved in the segmentation process proper. This suggests the possibility that the primary cues for figure-ground segregation are the illusory lines that are induced at the border between the center and surround and that are detected by specialized neurons (von der Heydt et al., 1984).

In conclusion, the present results demonstrate for the first time (to our knowledge) a close correlation between a psychophysical function and corresponding changes in the strength of neuronal synchrony. In addition, the data indicate that similar perceptual effects can correlate either with changes in discharge rate or changes in synchrony. This leads us to conclude that, in cortical processing, increases in discharge rate and spike synchronization can be used as equivalent and complementary mechanisms to raise the saliency of neuronal responses and to generate similar perceptual effects.

Experimental Procedures

Preparation

Anesthesia was induced with ketamine (Ketanest, Parke-Davis, 10 mg kg^{-1}, intramuscular) and xylazine (Rompun, Bayer, 2 mg kg^{-1}, intramuscular) and maintained with a mixture of 70% N_2O and

30% O_2 supplemented with halothane (0.5%–1.0%). After tracheotomy, the animals were placed in a stereotactic frame. A craniotomy was performed, and the skull was cemented to a metal rod. After completion of all surgical procedures, the ear and eye bars were removed, and the halothane level was reduced to 0.4%–0.6%. After assuring that the level of anesthesia was stable and sufficiently deep to prevent any vegetative reactions to somatic stimulation, the animals were paralyzed with pancuronium bromide (Pancuronium, Organon, 0.15 mg kg^{-1} h^{-1}). Glucose and electrolytes were supplemented intravenously and through a gastric catheter. The end-tidal CO_2 and rectal temperature were kept in the range of 3%–4% and 37°C–38°C, respectively.

Visual Stimulation

Anesthetized Preparation

Stimuli were presented binocularly on a 21 inch computer screen (HITACHI CM813ET) with 100 Hz refresh rate. To obtain binocular fusion, the optical axes of the two eyes were first determined by mapping the borders of the respective RFs and then aligned on the computer screen with adjustable prisms placed in front of one eye. The software for visual stimulation was a combination of custom-made programs and a stimulation tool, ActiveSTIM (www.ActiveSTIM.com). In order to obtain orientation tuning curves, we presented sinusoidal gratings moving in 12 directions with steps of 30°.

In about one-half of the recordings with tungsten electrodes, in which we investigated surround modulation by orientation contrast, we included two control stimulus conditions. These control conditions consisted of the figure presented alone and the background together with a gray patch in place of the figure. The latter stimulus was used to ensure that the background did not directly activate the neurons under investigation. Orientation and direction of movement, as well as spatial frequency and stimulus velocity of the center grating, were adjusted to activate a maximal number of cells and were kept constant in each recording.

In the experiments with tungsten electrodes, the size of the center grating was chosen such that it covered all of the receptive fields (RFs) (size ranging between 2° and 10° of visual angle), and the diameter of the background was adjusted to double that of the center grating, thus covering an area about four times as large. The gratings were of rectangular shape and the average luminance of the gratings matched that of the background.

All the investigations of surround effects with Michigan probes were made with gratings of circular shape (0.7 cycles/° spatial frequency, 2.2°/s drifting speed). Surround gratings always subtended 15.4° of visual angle. The size of the center was always adjusted to match the sizes of the RF clusters, subtending either 11.4° for recording the responses to the center only or 9.2° for simultaneous recording of the responses to center and surround.

In recordings with tungsten electrodes, phase offsets were varied randomly within the range between 0° and 180° and were subsequently sorted into the following four groups: 0°, 1°–60°, 61°–120°, and 121°–180°. With Michigan probes, the phase offsets ranged from 0° to 330° and were shifted in steps of 30°, resulting in 12 different stimulus conditions. To investigate the effect of a ring segregating center from surround, only four phase offsets were used (0°, 60°, 120°, and 180°) but with three levels of separation between center and surround: ring widths of 0°, 0.5°, and 1° of visual angle. The ring had the neutral gray color of the screen background. Different stimulation conditions were always presented in a randomized order.

Psychophysics with Human Subjects

Seven subjects (age 24–48 years) with normal or corrected-to-normal vision participated in the study. To investigate the changes in the perceived contrast, five subjects were asked to make simultaneous comparisons between the contrasts of center gratings of two stimuli, in which one always had zero offset relative to the surround, while the offset in the other stimulus varied randomly between 0° and 330° in steps of 30° (12 stimulation conditions). The gratings were always oriented vertically and identical to those used in the physiological study with Michigan probes (size, contrast, and spatial frequency), with the exception that the gratings were not drifting but were presented still. In addition, we added a narrow but clearly perceivable gray ring that separated center from surround. This ring indicated the area within which the contrast needed to be judged and was particularly helpful in the conditions with zero phase offset.

The two stimuli were in each trial presented for 3000 ms, with their respective positions assigned randomly either to the left or the right side of the screen. Subjects first reported the stimulus that appeared to have stronger contrast (i.e., "left" or "right") and then judged the relative contrast of that stimulus. Subjects were instructed to use a scale at which zero indicates equal contrast and to freely choose the upper limit of the scale. The five subjects participating in this experiment used the following maximum values in their contrast judgments: 3, 4, 5, 6, and 7. Prior to averaging the responses from different subjects, we normalized individual responses by the procedure described in the section titled "Normalization."

Subjects made ten practice trials to familiarize themselves with the task and to establish the scale that they would use for the judgments. Each subject performed 15 experimental trials per condition, resulting in a total of 180 trials. Subjects freely adjusted the viewing distance from the screen, which was usually about 1 meter. All experiments were performed in a dimmed room, and the experimental procedure lasted about 20 min.

The ability to detect the segregation of the center from the surround grating by phase shift was investigated with three subjects, one of them participating also in the perceived contrast experiment. We presented a single stimulus with randomly varying phase offsets between center and surround, which had either one of the nine smaller values: (0°–8° in steps of 1°) or one of the three larger values (45°, 90°, and 180°) and the size of the center grating was either the same as for the investigation of the perceived contrast or had a 30% smaller diameter, the two sizes being clearly distinguishable. There was no gray ring to help the segregation between the center and surround.

Subjects needed to identify the size of the center grating by pressing the response button held in the right hand if the center was large and the button held in the left hand if the center was small. This resulted in a total of 24 experimental conditions. The stimulus remained on the screen until the subjects pressed one of the buttons. Subjects were instructed to emphasize accuracy but also to respond as quickly as possible. Subjects were also instructed to guess if they were uncertain about the size of the center stimulus. In addition to accuracy, we also measured the response times. After ten practice trials, each subject performed 20 trials per condition, resulting in a total of 480 experimental trials. The experimental procedure lasted about 20 min. For the data analysis, responses to the small and large center gratings were pooled together.

Recordings

Data were recorded from 12 adult cats. In ten cats, multiunit activity (MUA) was recorded with multiple varnish-coated tungsten electrodes (1.0–2.0 MΩ impedance at 1000 Hz) from a region of area 17 corresponding to the central part of the visual field (0°–12° eccentricity). Signals were amplified 10,000× and band-pass filtered between 300 Hz and 3 kHz. In two cats, MUA was recorded with multiple SI-based multielectrode probes (16 channels per electrode) supplied by the Center for Neural Communication Technology at the University of Michigan (Michigan probes). Each probe consisted of four 3 mm long shanks that were separated by 200 μm and contained four electrode contacts each (1250 μm^2 area, 0.3–0.5 MΩ impedance at 1000 Hz, intercontact distance 200 μm). In these experiments, signals were filtered between 500 Hz and 3.5 kHz and between 1 and 100 Hz for extracting MUA and local field potentials, respectively. The signals were then sent to an analog-to-digital converter and, after the detection of spikes, stored in computer memory. In some of the recordings, the waveforms of detected spikes were recorded for a duration of 1.2 ms, which allowed the later application of offline spike-sorting techniques. The borders of MUA RFs were mapped from responses to moving single bars and monitored through a loudspeaker and an oscilloscope.

The electrodes and probes were positioned such that they would enter the cortex approximately perpendicular to the surface. By advancing the tungsten electrodes in steps of about 50 μm, we sampled responses from all cortical layers. However, no lesions were made to determine precisely the layers from which the respective recordings were made.

Michigan probes allowed simultaneous recording from neurons with overlapping RFs at different cortical depths and along an axis tangential to the cortical surface, spanning a distance of about

700 μm in both directions. To investigate modulation of the responses to the center grating, we recorded simultaneously from two probes inserted in proximity to each other and repeated such recording sessions by withdrawing the probes and reinserting them at another position in the same hemisphere. In addition, we made one single-probe recording by advancing one of the probes deeper in the cortex (400 μm). This last probe was later combined with another distantly inserted probe for simultaneous recording of responses to surround and center. The depths at which the probes were inserted into the cortex varied between 1 and 1.8 mm. Therefore, as in the experiments with tungsten electrodes, responses had probably been sampled from all layers.

As all comparisons of stimulus-related response changes were confined to recordings obtained from fixed sites, sampling from different layers cannot have mimicked the observed stimulus dependencies. If the described surround effects are restricted to certain layers, pooling recordings from different layers attenuates the effects and, hence, is unlikely to generate false positive results. We can also exclude that some of the multiple recording sites picked up activity from the same cells because we computed cross-correlation functions between all sites (see below). If such stereo recordings had happened, the cross-correlograms should have shown the sharp center peak that is characteristic of auto-correlograms but, due to the sufficiently large spatial separation of recording sites (minimum 200 μm), this was never the case.

Analysis

Measures of Firing Rates

Peristimulus time histograms (PSTH) and cross-correlation functions (CCFs) were computed for response epochs of 1.9–3.9 s, excluding the initial responses to stimulus onset.

To investigate rate modulation dependent on the relative grating position, i.e., sinusoidal modulation of rate responses, it was necessary to extract single-unit activity (SUA), otherwise the PSTHs are smoothed due to the varying phase relations in multiunit activity (DeAngelis et al., 1994). SUAs were isolated by an offline spike-sorting technique in which the spike waveforms were first subjected to principal component analysis (PCA). A single unit was isolated if, in the 3D PCA space, we found a distinctive cluster of waveforms that was clearly segregated from all the remaining waveforms. To minimize contamination with spikes from another unit, we adopted highly conservative criteria for isolating a single unit, which resulted in a relatively small number of SUAs. In one experiment with 12 levels of phase offset (0°–330°, 30° steps) and 16 simultaneously recorded MUAs, we obtained 4 SUAs and another set of 16 units for which we suspected contamination from other single units. We refer to the latter ones as postsorting MUA, or pMUA. In another experiment with four levels of phase offset (0°–180°, 60° steps), we sorted waveforms from 11 recording channels and obtained 36 units: $N_{SUA} = 16$ and $N_{pMUA} = 20$. For further analysis, the data from these two experiments were pooled, and only the stimulation conditions with overlapping parameters were analyzed (i.e., 60° steps in phase offsets).

The average firing rate with which the extracted SUAs responded to the stimuli ranged from 2.2 to 30.1 spikes/s, with an average of 10.1 spikes/s. To estimate the strength of sinusoidal rate modulation, a sine function was fitted to a PSTH averaged over 20 presentations (trials). The fitting required minimizing the errors of the sinusoid's amplitude, phase, and vertical offset. The frequency of the sinusoid was fixed at 1.5 Hz, which was the temporal frequency of the grating stimulus. To ensure that only sustained responses were fitted, the sine fits were confined to response epoch starting 1300 ms after the stimulus onset and lasting 3200 ms. A common measure for response modulation is the ratio between the fitted amplitude and the change in the mean firing rate (Skottun et al., 1991). As a simplification, we used the fitted amplitudes directly as measures of rate modulation, which was sufficient for the present purposes. Analysis of variance (ANOVA) was applied to fitted amplitudes, which were first normalized for each unit individually (as discussed in the section titled "Normalization") across four stimulus conditions: 0°, 60°, 120°, and 180° phase offset. A strongly modulated unit had a rate response of at least 4 spikes/s in at least one of the four stimulation conditions.

The response modulation of individual units exhibited some dependence on the phase offset of the surround grating. However, in none of the single neurons did this modulation match the psychophysical function of perceived brightness (Figure 5A in the main text), nor did we, as reported in the main text and Figure 3B, observe a match for the averaged response. The same result was obtained for another set of 11 pMUAs. The fitted response amplitudes of these units also failed to exhibit a significant dependence on phase offsets [$F(3,40) = 1.61$, $p = 0.20$], the effect size was smaller than that of the SUAs ($d = 0.27$), and the trends did not suggest any similarity to the psychophysical function. In an attempt to improve the test power, we pooled the SUA and the pMUAs into a single analysis, resulting in a sample size of $n = 18$, but the results remained the same [$F(3,68) = 0.99$, $p = 0.36$, $d = 0.31$]. Also, the outcome of this analysis did not change when we lowered the threshold for detecting a simple cell from 4 to 1 spikes/s [$n = 11$ cells; $F(3, 40) = 1.46$, $p = 0.24$; $d = 0.70$] or when we analyzed the 11 pMUAs separately [$F(3, 40) = 1.61$, $p = 0.20$; $d = 0.26$].

Cross-Correlation Analysis

CCFs were computed with a resolution of 1.0 ms and for time shifts of ±80 ms. One concern is synchronized covariation of rate responses, which can boost the size of the center peaks in CCF and which could be then incorrectly attributed to the changes in precise temporal synchronicity of neuronal discharges (Brody, 1999). Our detailed analysis of sinusoidal rate modulation (section titled "Measures of Firing Rates") indicated that such rate covariation is unlikely to have affected our results to any significant degree. Only about one-third of the units showed sinusoidal rate modulation, and the strength of rate modulation in these units did not depend on the phase offset. We, nevertheless, investigated further the possibility that rate covariation contributed to our CCFs by computing the CCFs across randomly shuffled experimental trials, also known as shift predictors. Flat shift predictors indicate that the CCFs do not contain stimulus-locked temporal structures on the timescale investigated, and in our experiments, all shift predictors were flat (as illustrated in Figures 4F and 6D). This is expected because the grating drifting speed of 1.5 Hz corresponds to a much longer oscillation period (667 ms) than the timescale of CCFs. Thus, irrespective of whether we based our analyses on raw CCFs or on the CCFs with subtracted shift predictors, the analyses yielded the same results.

The strength of neuronal synchronization was quantified from the height of the center peak (P) relative to the height of the baseline (B) of the CCF. These values were obtained by fitting a damped Gabor function to each CCF by the Marquardt-Levenberg algorithm (for details see Konig, 1994). The strength of synchrony was then expressed as the modulation amplitude (MA) by using the following equation: $MA = P/(P + B)$. This procedure also allows one to test the significance of P, which was tested with α set to 0.05.

Selection of Recording Sites

Tungsten Electrodes. A recording site was included into analysis if it was sufficiently selective for one of 12 stimulus directions and if it synchronized its response with at least one other recording site in at least one direction. From a total sample of 181 recording sites, 96 (53%) were investigated further. This resulted in a total of 124 pairs for the investigation of surround effects on synchrony. The effects of orientation contrast on rate responses and synchrony were investigated with repeated-measure ANOVA and linear trends were tested by appropriate ANOVA contrasts. Effects of phase offsets were investigated at 123 sites and for 128 pairs. Each recording site (pair) was tested at zero phase offset (0°) and one condition of phase offset. For the four groups of different phase offsets (0°, 1°–60°, 61°–120°, and 121°–180°), the numbers of investigated sites were 123, 33, 46, and 44, and the numbers of pairs were 128, 30, 55, and 43, respectively. Thus, we performed a one-way analysis of variance with unequal sample sizes across stimulus conditions (i.e., nonorthogonal ANOVA).

Michigan Probes. Each recording site that was responsive and orientation selective was also synchronized strongly with at least one other site. Thus, no sites had to be excluded based on the synchronization criterion. From a total of 128 sites (8 × 16 channels), 68 well-responding and orientation-selective sites were used in the study. Of those, 54 served for the investigation of the responses to the center stimulus (23, 19, and 12 sites in the three separate recordings) and 13 for the investigation of responses to both the center and the surround. For correlation analysis, pairs of sites had to be preselected on the basis of the synchronization criterion. A pair was included into analysis only if the respective recording sites

synchronized strongly in at least two of the twelve different phase conditions. This resulted in equal sample sizes for all phase conditions allowing application of repeated-measure ANOVAs. Out of 545 possible pairs for the investigation of the responses to the center, 418 passed the synchronization criterion (176, 149, and 57 pairs for the three separate recordings and 36 for the investigation of the ring effect). No preselection was made for the investigation of spike-field coherence.

Normalization

Prior to analyzing average responses for the investigated populations of neurons, the measures of firing rates and MA were, for each particular site (pair), normalized relative to the mean value computed across all the stimulation conditions used in the analysis, i.e., (*response* − *mean*)/*mean*. Therefore, all measures were transformed to the scale centered on zero, positive values indicating that the measurements were above average and negative values that the measurements were smaller than average. Normalized values of firing rates and MA were used in all analyses except for the spike-field coherence. For the present data set, the overall firing-rate responses were on average 69.9 spikes/s (sd = 46.6, range 0.2–214 spikes/s) and the MA was on average 0.76 (sd = 0.87, range 0.1–12). All statistical tests were based on two-tailed p values for rejecting null hypotheses.

Effect Sizes

In order to compare the degree of surround modulation for firing rates and synchronization, we computed effect sizes. Effect size provides information that is different from the information provided by statistical significance. Significance indicates the probability that two populations differ in their means, and this probability depends on the sample size. In contrast, effect size is independent of the sample size and indicates the degree to which an independent variable affects the dependant variable relative to the variability in the population. Effect size provides information similar to the Pearson's correlation coefficient. We used a measure for effect size known as Cohen's *d* (Cohen, 1988). According to Cohen, the effect can be considered large if *d* is larger than 0.8 and should be considered small if *d* is smaller than 0.2. When applicable, we also corrected the effect sizes for the correlation between the variables in the repeated-measure designs because these dependencies can artificially boost the effect size. This correction was made by computing Cohen's *d* from the unpaired t test even in the experimental designs that were based on repeated measures. To compute Cohen's *d* from the t values, we used the following formula if the two groups had the same sample sizes:

$$d = \frac{2t}{\sqrt{df}}$$

and in the cases in which two groups had different sample sizes we used:

$$d = \frac{t(n_1 + n_2)}{\sqrt{df}\sqrt{n_1 n_2}}$$

where n_1 and n_2 are the sample sizes of each group, *df* represent the degrees of freedom, and *t* is the t value of a Student's test. Unless otherwise noted, the effect size was computed for the most extreme conditions: in the case of orientation difference for 0° and 90° and in the case of offset for 0° and 180°.

Spike-Field Coherence

In a first step of this analysis we computed the spike-triggered averages (STA) by using the spikes from one site as triggers for the averaging of the local field potential (LFP) recorded from another site (Gray and Singer, 1989). The STAs were computed with the same parameters as the cross-correlation functions. In order to obtain a measure of spike-field synchronization that was independent of the power of the LFP, we calculated the spike-field coherence (SFC). For each of the LFP segments used for the computation of the STA, the power spectrum was calculated and subsequently averaged to obtain the spike-triggered power spectrum. The SFC was then computed as the ratio between the power spectrum of the STA and the spike-triggered power spectrum of the LFP segments. For more details on this measure see Fries et al. (1997). This analysis gave qualitatively identical results irrespective of which site in a pair was taken as source of spikes and which site served as the source of the LFP signal.

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