The influence of surround suppression on adaptation effects in primary visual cortex

Stephanie C. Wissig1 and Adam Kohn1,2
1Dominick Purpura Department of Neuroscience, Albert Einstein College of Medicine, Bronx, New York; and 2Department of Ophthalmology and Visual Sciences, Albert Einstein College of Medicine, Bronx, New York

Submitted 19 August 2011; accepted in final form 12 March 2012

Wissig SC, Kohn A. The influence of surround suppression on adaptation effects in primary visual cortex. J Neurophysiol 107: 3370–3384, 2012. First published March 14, 2012; doi:10.1152/jn.00739.2011.—Adaptation, the prolonged presentation of stimuli, has been used to probe mechanisms of visual processing in physiological, imaging, and perceptual studies. Previous neurophysiological studies have measured adaptation effects by using stimuli tailored to evoke robust responses in individual neurons. This approach provides an incomplete view of how an adapter alters the representation of sensory stimuli by a population of neurons with diverse functional properties. We implanted microelectrode arrays in primary visual cortex (V1) of macaque monkeys and measured orientation tuning and contrast sensitivity in populations of neurons before and after prolonged adaptation. Whereas previous studies in V1 have reported that adaptation causes stimulus-specific suppression of responsivity and repulsive shifts in tuning preference, we have found that adaptation can also lead to response facilitation and shifts in tuning toward the adapter. To explain this range of effects, we have proposed and tested a simple model that employs stimulus-specific suppression in both the receptive field and the spatial surround. The predicted effects on tuning depend on the relative drive provided by the adapter to these two receptive field components. Our data reveal that adaptation can have a much richer repertoire of effects on neuronal responsivity and tuning than previously considered and suggest an intimate mechanistic relationship between spatial and temporal contextual effects.

orientation tuning; contrast sensitivity; spatial context; neurophysiology

MAINTAINED SENSORY STIMULATION, or adaptation, typically reduces the responsivity of sensory neurons. This was first thought to reflect simple fatigue, but it is now known that adaptation also alters tuning by suppressing responses to some stimuli more than others (for review, see Kohn 2007). In V1, suppression has been found to be strongest for stimuli matched to the adapter, causing repulsive shifts in preference after adaptation on the flank of the tuning curve (Dragoi et al. 2000, 2001, 2002; Movshon and Lennie 1979; Muller et al. 1999; Saul and Cynader 1989a, 1989b; but see Ghisovan et al. 2009). This has led to proposals that adaptation-induced changes in tuning serve to reduce representational redundancy (Barlow 1990; Muller et al. 1999) or to improve discriminability between stimuli (Muller et al. 1999). However, studies in area MT have found that adaptation causes tuning to shift toward the adapter (Kohn and Movshon 2004; Kremkberg et al. 2006b). This observation suggests that cortical areas may differ in the ways they adapt, affording distinct benefits of adaptation (Stevenson et al. 2010).

The effects of adaptation on neuronal responses are of interest, in part, because their strong perceptual consequences offer a powerful tool for understanding the physiological basis of perception (Jin et al. 2005; Kohn and Movshon 2003, 2004; Krekelberg et al. 2006b). In addition, adaptation is frequently used in imaging studies to probe the selectivity of cortical areas, making an understanding of its effects on neurons critical for relating these measurements to the underlying neurophysiology (Grill-Spector and Malach 2001; Krekelberg et al. 2006a). Finally, adaptation-induced changes in tuning represent an active adjustment of neuronal resources to the current environment, providing clues to the computational goals of these networks.

To understand the consequences of adaptation, it is crucial to know how it alters neuronal selectivity and responsivity, because these effects determine how neuronal resources are distributed to encode sensory information. Previous neurophysiological studies have characterized the effects of adaptation by recording sequentially from individual cells and assuming that the average observed effect is representative of how a broader population adapts. This assumption is problematic. First, if physiologists sample preferentially from more responsive units, the cells selected for study may represent a biased sample (Olshausen and Field 2005). More importantly, most previous neuronal adaptation studies have used stimuli tailored to provide robust drive to the selected neuron (Albrecht et al. 1984; Giaschi et al. 1993; Kohn and Movshon 2003, 2004; Movshon and Lennie 1979; Nelson 1991; Priebe et al. 2002; van Wezel and Britton 2002; Yang and Lisberger 2009). However, the population response evoked by any adapter will in fact consist mostly of cells that are driven well below their peak response. Because the most well-established mechanisms of adaptation are activity dependent (e.g., postsynaptic hyperpolarization and synaptic depression; Abbott et al. 1997; Carandini and Ferster 1997; Sanchez-Vives et al. 2000), weakly driven cells may adapt quite differently from strongly driven ones. The strategy of tailoring stimuli also limits suppressive influences, such as those from the receptive field surround (Cavanaugh 2002a, 2002b), which could modulate the consequences of adaptation.

To determine how stimulus history affects the neuronal population response in V1, we implanted microelectrode arrays and measured orientation tuning and contrast sensitivity before and after prolonged (40 s) adaptation. This approach provided large samples of cells and ensured the inclusion of cells with a broad range of response properties. We found that adaptation
can have a much broader range of effects in V1 than previously considered, including effects that have previously only been reported in area MT. We provide a simple model that can explain this diverse set of phenomena and that relies on a balance between stimulus-specific suppression and disinhibition. In addition to explaining differences in the effects of adaptation observed in V1 and area MT, our results have important implications for interpreting functional imaging results and, more broadly, suggest the need for a reevaluation of the purpose of adaptation-induced changes in neuronal responsiveness and tuning.

MATERIALS AND METHODS

General methods. Before surgery, monkeys (Macaca fascicularis) were premedicated with 0.05 mg/kg atropine and 1.5 mg/kg diazepam. Anesthesia was induced with ketamine (10 mg/kg). The animal was then intubated and placed on 1.0–2.5% isoflurane in a 98% O2-2% CO2 mixture. Surgery was performed to place intravenous catheters in the saphenous veins of both legs. The monkey was then placed in a stereotaxic frame, and a craniotomy and durotomy were made over the sphenoid sinuses of both sides of the brain. A microelectrode array (Blackrock Microsystems) was implanted, and the brain was covered with agar to prevent dessication. For the remainder of the experiment (typically 7 days), anesthesia was maintained with an infusion of sufentanil citrate (6–24 μg·kg⁻¹·h⁻¹; adjusted as needed for each animal) in an electrolyte solution. To minimize eye movements, the animal was paralyzed with vecuronium bromide (0.1 mg·kg⁻¹·h⁻¹). Blood pressure, ECG, EEG, end-tidal PCO2, temperature, and lung pressure were continuously monitored. The pupils were dilated with topical atropine, and the corneas were protected with clear gas-permeable hard contact lenses. Supplementary lenses were used to bring the retinal image into focus. All procedures were approved by the Institutional Animal Care and Use Committee of the Albert Einstein College of Medicine at Yeshiva University and were in compliance with the guidelines set forth in the United States Public Health Service Guide for the Care and Use of Laboratory Animals.

We recorded activity using 10 × 10 arrays of microelectrodes (400-μm spacing, 1-mm length). Waveform segments that exceeded a threshold (a multiple of the RMS noise on each channel) were digitized (30 kHz) and sorted off-line. Waveforms were separated into units with the use of principal component analysis and a clustering algorithm (Shoham et al. 2003) and were then further refined by hand sorting. We quantified sort quality by a simple signal-to-noise (SNR) algorithm (Shoham et al. 2003) and were then further refined by hand. Each microelectrode array consisted of 100 sites (2.2-mm spacing, 1-mm length). Waveform segments that exceeded a threshold (a multiple of the RMS noise on each channel) were digitized (30 kHz) and sorted off-line. Waveforms were separated into units with the use of principal component analysis and a clustering algorithm (Shoham et al. 2003) and were then further refined by hand sorting. We quantified sort quality by a simple signal-to-noise (SNR) algorithm (Shoham et al. 2003) and were then further refined by hand. We also calculated each neuron’s orientation selectivity index (OSI) as

\[ \text{OSI} = \frac{\sum_{n=1}^{M} R_n e^{\log_2(i/2j)}}{\sum_{n=1}^{M} R_n} \]  

(1)

where \( R_n \) is the response to stimulus drifting in the direction \( \theta_n \). Units with an OSI < 0.2 were deemed untuned and binned together regardless of offset. For the remaining units, we averaged responses to gratings of the same orientation, but drifting in opposite directions.

Data were fit with a von Mises function, defined as

\[ r_p(\theta) = m + ae^{\cos(\theta - \theta_{\text{pref}} - 1)} \]  

(2)

where \( r_p(\theta) \) is the predicted response, \( m \) is an offset, \( a \) determines the height of the tuning curve, \( \theta \) determines the tuning bandwidth (quantified as the width of tuning halfway between the minimum and maximum evoked response), \( \theta_{\text{pref}} \) is the preferred orientation, and \( \theta \) is the stimulus orientation. Note that the optimal fit could involve a negative baseline, but responses were half-rectified and thus could not be negative.

The function was fit by maximizing the log likelihood of observing the measured data given the predicted response. Under the assumption of Poisson spiking statistics, the log likelihood can be written as

\[ \log L = \sum_{i=1}^{N} \log \left( \frac{r_p^n e^{-r_p}}{r_m!} \right) \]  

(3)

where \( r_m \) and \( r_p \) are the measured and predicted responses, respectively, and the sum is over stimulus conditions (El-Shamayleh and Movshon 2011). We obtained similar results with nonweighted least-squares fitting, but this does not take into account that neuronal response variance is proportional to its strength.

For each cell, we quantified fit quality as a normalized log likelihood for which the upper bound was based on an “omniscient model” that used the measured responses as the prediction (a value of 1) and the lower bound was the likelihood of a model with predicted responses equal to the average measured response across all conditions (a value of 0; El-Shamayleh and Movshon 2011; Stocker and Simoncelli 2006). After removing visually unresponsive units (peak evoked response <1 SD above the mean spontaneous activity), we excluded cells on the basis of the following criteria, applied in the order indicated: 1) cells for which the normalized likelihood was < 0.5 (13–25% of cases; on average, the normalized likelihoods were 0.87 in the remaining cells); 2) cells for which the pre- or postadaptation responses measured tuning before adaptation with 25 repetitions of each stimulus, presented in block randomized order with a uniform gray screen randomly interleaved to provide a measure of spontaneous activity. We discarded the first repetition of each stimulus because we observed a strong onset transient at the beginning of the stimulus sequence. Tuning after adaptation was measured with 15 presentations of each test stimulus; 5 s of top-up adaptation were provided between test stimuli. A similar adaptation protocol was used for the contrast adaptation experiments but with test stimuli of fixed orientation. Contrasts ranged from 1.6 to 100% in octave steps; the adapting stimulus was shown at full contrast. All adaptation conditions were randomly interleaved with a recovery period of at least 10 min between conditions.

Data analysis. For analysis of gratings responses, we used either the F1 component of the response or the mean firing rate, depending on which was larger (Skottun et al. 1991). For compound stimuli, responses were measured using mean firing rate. All reported firing rates are evoked rates (those in excess of the firing rate to a uniform gray screen). To bin cells for population tuning curves, we determined the offset of each neuron from the adapter by calculating its preferred orientation as the vector sum of its responses to the test stimuli. We also calculated each neuron’s orientation selectivity index (OSI) as...
were <22.5° in bandwidth (8–18% of remaining cases), since this was the spacing of our test stimuli and we were thus not confident of our measurements in these cases; and 3) cells whose preference shifted by >30° from the average effect seen in the population (8–13% of the remaining cells), since previous studies indicated that shifts larger than this likely occurred because isolation was lost and the pre- and postadaptation responses were from different cells (Dragoi et al. 2000; Kohn and Movshon 2004).

To analyze the contrast data, we calculated the area under the half-wave rectified, logarithmic contrast-response functions, before and after adaptation. We excluded cells that did not respond after adaptation (area of 0, <5% of cases for large stimuli and ~10% of cases for small stimuli), because we could not distinguish whether the absence of response was due to complete suppression or loss of isolation.

All statistical evaluation used t-tests; ratios were log-transformed before evaluating. All indications of variation in the graphs and text are standard error of the mean (SE), unless otherwise noted.

Model. To provide a direct illustration of how stimulus-specific adaptation in the center and surround could generate the range of effects we observed, we implemented a simple model. We defined a set of neurons whose responses were determined by tuned drive to the classical receptive field (CRF) divided by the activation of a more broadly tuned surround. Specifically, the response of the CRF of each cell, \( r_{\text{CRF}}(\theta) \), was defined by a von Mises function (Eq. 2; \( b = 3; a = 1–1.3 \) for weak to strong CRF input, respectively). Cells had preferred orientations \( \theta_{\text{pref}} \) evenly spaced in the range 0–90°. The surround was defined similarly but with broader tuning \( (b = 2.5; \text{Cavanaugh et al. 2002a}) \) and ranged from weakly to strongly suppressive \( (a \text{ set to } 0.4–0.9) \). The peak value \( (0.9) \) provides suppression of roughly 50%, consistent with the average suppression recruited in V1 by large gratings (Cavanaugh et al. 2002a). The net input to the cell was defined as

\[
 r_{\text{input}}(\theta) = \frac{r_{\text{CRF}}(\theta)}{1 + r_{\text{surround}}(\theta)}
\]

The spiking response, \( r_{\text{sp}} \), was defined by passing the input through a nonlinearity:

\[
r_{\text{sp}}(\theta) = k [ r_{\text{input}}(\theta) - V_{\text{th}} ]^+ \]

where \( k \) is a scaling factor, \( V_{\text{th}} \) is the threshold, the subscript + indicates half-wave rectification, and \( n \) is an exponent. We used \( k = 0.03, V_{\text{th}} = 6, \) and \( n = 3 \) (Priebe and Ferster 2006). The inclusion of an adaptive threshold was important for providing a mechanism for nonspecific (universal) changes in responsivity.

Adaptation was implemented by scaling the synaptic input \( (r_{\text{CRF}}, r_{\text{surround}}) \) and changing the threshold \( (V_{\text{th}}) \). The adaptation effect at each orientation was determined by a scaling factor, \( a_{\text{CRF}}(\theta) \), which was strongest at the adapted orientation and depended on the drive to the center \( (a) \) as follows:

\[
a_{\text{CRF}}(\theta) = 1 - k_{\text{adapt}} e^{b[\cos(\theta - \theta_{\text{adapt}})]} - 1\]

where \( k_{\text{adapt}} \) was a constant that sets the overall strength of adaptation. For the CRF, \( k_{\text{adapt}} = 0.15 \) and \( b = 5 \); the surround was defined similarly, but with \( k_{\text{adapt}} = 0.6 \) and \( b = 4.2 \). These factors were chosen to provide adaptation effects that were slightly more orientation-specific than the tuning width of the center and surround \( (r_{\text{CRF}}, r_{\text{surround}}) \), generating changes in tuning consistent with those observed in the data. The response of the CRF after adaptation was defined as

\[
r_{\text{CRF-adapted}}(\theta) = a_{\text{CRF}}(\theta) r_{\text{CRF}}(\theta),
\]

the threshold after adaptation was defined as

\[
V_{\text{th-adapted}} = V_{\text{th}} + r_{\text{sp}}(\theta_{\text{adapt}})[k_{1} - k_{2}(\theta_{\text{pref}} - \theta_{\text{adapt}})]
\]

where \( k_{1} \) and \( k_{2} \) are constants (set to 0.028 and 0.0007, respectively, arbitrary values chosen to match the range of effects seen in our data). This rule results in an increase in threshold (i.e., a hyperpolarization) that is largest for strongly driven cells adapted at their preferred orientation \( (\theta_{\text{pref}} = \theta_{\text{adapt}}) \) and a decrease in threshold for cells adapted far from their preferred orientation \( (\theta_{\text{pref}} - \theta_{\text{adapt}} = 90°) \). A conceptually similar model has been proposed to explain color and contrast adaptation effects in V1, but with an emphasis on the interaction between the excitatory and suppressive mechanisms within the CRF (Dhruv et al. 2011; Taibly et al. 2008).

Fitting a reduced model to each cell. We fit a reduced version of the model described above to each cell. This model consisted of four parameters to describe the tuning before adaptation \( (\theta_{\text{pref}}, Eq. 2) \). The postadaptation tuning was a transformed version of the preadaptation tuning. It was computed by multiplying the preadaptation tuning by a difference-of-circular-Gaussian functions consisting of tuned disinhibition and suppression:

\[
r_{\text{post}}(\theta) = r_{\text{pre}}(\theta) \left[ 1 - k_{\text{supp}} e^{d_{\text{supp}}[\cos(\theta - \theta_{\text{adapt}})]} + k_{\text{disinhib.}} e^{d_{\text{disinhib.}}[\cos(\theta - \theta_{\text{adapt}})]} \right]
\]

where \( k \) and \( b \) determine the strength and tuning width, respectively, of the adaptation-induced suppression and disinhibition. Pre- and postadaptation responses were passed through a nonlinearity to generate the measured responses \( (Eq. 5) \), with free parameters \( n \) and \( V_{\text{th-post}} \) \( (V_{\text{th-pre}} \) was set to zero). We fit by maximizing the log likelihood, as described above) this equation to the raw responses of each cell, to determine the optimal values of \( k_{\text{supp}}, b_{\text{supp}}, k_{\text{disinhib.}}, n, \) and \( V_{\text{th-post}} \).

We fit to the responses of each cell a set of nested models \( (n = 62) \), in which we explored all possible combinations of free and constrained parameters for the adaptation effect \( (k \) and \( b \) for the adaptation-induced suppression and disinhibition and \( n \) and \( V_{\text{th-post}} \) for the nonlinearity); the preadaptation data were always fit with four parameters. When a parameter was fixed, its value was set to its average value in the full model across all cells and conditions. We evaluated the relative goodness of fit of these models by using a corrected Akaike information (AICc) criterion (Turkheimer et al. 2003). This exercise allowed us to determine the relative importance of adaptation-induced suppression and disinhibition and changes in threshold in generating the effects on tuning, across stimulus conditions.

RESULTS

We implanted microelectrode arrays in V1 of anesthetized, paralyzed monkeys (17 array implants in 12 monkeys) and recorded from single units and small multiunit clusters. The arrays were inserted roughly 600 μm into cortex, providing recordings primarily from layer 2/3 neurons, whose axons provide the major output to higher cortex (Felleman and Van Essen 1991). Neuronal RFs were located in the lower visual field, at an eccentricity of 2–3°.

To measure orientation tuning, we presented drifting sinusoidal gratings that were 7.4° in diameter, sufficiently large to cover comfortably the RFs of all of the recorded neurons. Gratings had a spatial (1.0 cpd) and temporal frequency (6.25 Hz) appropriate for most parafoveal V1 cells (Foster et al. 1985) but were not tailored to the preference of any particular cell. To minimize selection bias, we analyzed responses from all visually responsive units, defined as those whose peak evoked response was at least 1 SD above the spontaneous firing rate. Gratings evoked modest peak firing rates, with a mean increase of 15.2 ± 0.4 spikes/s relative to the spontaneous firing rate (Fig. 1A; \( n = 1,372 \); median 10.9 spikes/s). This is roughly three times lower than measurements made with gratings tailored to match the properties of V1 RFs \( (47.2 ± 2.0 \text{ spikes/s}, n = 196; \text{Kohn and Smith 2005}) \) and emphasizes that our visual stimuli provide relatively weak drive to most neurons.
Although responses were weak, cells were well tuned. We quantified tuning quality with an OSI (see MATERIALS AND METHODS) whose value is 1 if the cell responds to a single orientation and 0 if it is unselective. The mean OSI was 0.40 ± 0.006 (Fig. 1B), comparable to previous measures in primate V1 obtained with optimized gratings in well-isolated single units (~0.50; Ringach et al. 2002). Because the OSI conflates tuning width with the strength of nonselective responses, we also quantified tuning quality as the ratio of the response at the orthogonal orientation (90° offset from the preferred) to the preferred orientation (Fig. 1C). The median value of this metric was 0.14; the mean was 0.21 ± 0.007.

In addition, we separately analyzed the responses and tuning of single units in our data set (n = 361; open bars in Fig. 1, A–C; see MATERIALS AND METHODS for criterion). The firing rates (mean peak rate 12.7 ± 0.7 spikes/s) were slightly lower, and tuning quality was slightly better (OSI of 0.47 ± 0.007 and median and mean orthogonal-to-preferred ratio of 0.06 and 0.13 ± 0.01, respectively) than for the data set as a whole, but there were no striking differences. Because adaptation effects also were not dependent on isolation quality (see Table 1, discussed below), we pooled units in the majority of our analyses.

Effects of adaptation with gratings. To determine the effects of adaptation, we measured tuning with a continuous, pseudorandom sequence of drifting gratings (1-s presentation) before and after one of the gratings was presented for 40 s. We used top-up stimuli (5 s) between postadaptation tests to maintain the effects of adaptation. Only the adaptation direction varied across implants so that we could combine measurements across populations.

The effects of adaptation on several example neurons are shown in Fig. 2. When the orientation of the adapter was matched to the neuron’s preference (Fig. 2A), adaptation frequently caused a weak reduction in responsivity and a decrease in tuning bandwidth (left panel, thin compared with thick lines after adaptation); in roughly 40% of preferred adapted cells, responsivity was enhanced after adaptation (cell data shown at right). Contrary to previous V1 studies, when the adapter was slightly offset from the cell’s preference, tuning shifted toward the adapting orientation (Fig. 2B). This was due to a stronger reduction in responsivity to test stimuli different from the adapter than to those similar to the adapter. Finally, adaptation of neurons whose preference was nearly orthogonal to the adapter (Fig. 2C) resulted in a facilitation of responsivity and broadening of tuning.

To characterize effects across our population of cells, we calculated population tuning curves by binning cells by the offset between their preferred orientation and that of the adapter, normalizing the data from each cell by its peak response, and then averaging. This method allowed us to characterize effects in all neurons (n = 1,372), even those with poor tuning. In contrast to previous reports of strong suppression after adaptation in V1 (~50%; Giaschi et al. 1993; Nelson 1991), we found neurons adapted near their preferred orientation (Fig. 3A, top row; 0–15° offset) had only slightly weaker responses after adaptation (thick) compared with before (thin). The average peak response was reduced by 3%. Moreover, responsivity was consistently facilitated in cells whose preference was nearly orthogonal to the adapter (9% enhancement for cells offset by 75–90°, third row). Again, in contrast to previous findings that V1 tuning shifts away from the adapter, we observed attractive shifts in preference (e.g., ~19° in cells offset by 30–45°, negative shift indicating toward the adapter; second row). In untuned cells (OSI < 0.2), adaptation had little effect on responsivity (Fig. 3A, bottom row).

We then focused on cells with well-tuned responses (n = 769), which we fit with a circular Gaussian function. We extracted from these fits the preferred orientation, peak responsivity, and tuning bandwidth of each cell before and after adaptation. We applied moderately strict criteria for fit quality (see MATERIALS AND METHODS), discarding data from roughly 45% of units. This approach thus provides a complementary view to the population tuning curves, which included all responsive cells. Figure 4A shows the peak response after compared with before adaptation (top), arranged by the offset of the cell’s preference from the adapter. Responsivity was only suppressed in cells adapted near their preferred orientation (within 15°). Even in these cells, suppression was weak (geometric mean ratio of 0.92; P = 0.09 for difference from 1). For cells with greater offsets, adaptation led to facilitation; for instance, for cells adapted nearly orthogonal to their preferred
Table 1. Effects of adaptation on tuning parameters for adaptation with small and large gratings and small and large compound stimuli

<table>
<thead>
<tr>
<th>Table 1. Effects of adaptation on tuning parameters for adaptation with small and large gratings and small and large compound stimuli</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preferred</strong></td>
</tr>
<tr>
<td><strong>Response ratio</strong></td>
</tr>
<tr>
<td>Preferred</td>
</tr>
<tr>
<td>SNR &gt; 3.5</td>
</tr>
<tr>
<td>Flank</td>
</tr>
<tr>
<td>SNR &gt; 2.75</td>
</tr>
<tr>
<td>SNR &gt; 3.5</td>
</tr>
<tr>
<td>Orthogonal</td>
</tr>
<tr>
<td>SNR &gt; 2.75</td>
</tr>
<tr>
<td>SNR &gt; 3.5</td>
</tr>
</tbody>
</table>

The top row for each parameter indicates the effects observed in the full data set. The bottom row (signal-to-noise ratio SNR > 3.5) indicates the effects in well-isolated single units. Because the number of such units was low for some conditions, we also considered a more lax criterion (SNR > 2.75; middle row). Effects were qualitatively similar for the whole data set (consisting primarily of multi-unit activity) and for well-isolated single units.

orientation (offsets of 60–90°), the mean response ratio was 1.21 (P < 0.001). Adaptation also caused significant attractive shifts in preference (Fig. 4A, middle), which were maximal at offsets of 15–30° (mean shift of 3.72 for cells with offset of 15–45°, P < 0.001). Finally, adaptation resulted in a decrease in tuning bandwidth for cells adapted near their preferred orientation (Fig. 4A, bottom; mean ratio of 0.92, P = 0.008) and a slight increase in those adapted orthogonally (offsets of 60–90°, mean ratio of 1.08, P < 0.001).

The effects of adaptation showed a clear dependence on the relationship between the adaptation and the cells’ preferences. It is thus unlikely that these effects arose from instability in the recordings (e.g., drift in anesthesia). Nevertheless, we quantified the fluctuations in tuning and responsivity that arose during extended recordings, in the absence of adaptation. We used responses to gratings similar to those used in our adaptation experiments (1 cdp, drift rate of 6 Hz, size ≥4°). We compared tuning at the start of the recording period with that measured roughly 2 h later (n = 297 cells matching the criteria used for Fig. 4). The mean response ratio of the tuning curves in these two epochs was 0.98 (95% confidence interval of 0.98–1.03), the mean shift was 0.2 ± 0.3°, and the mean bandwidth ratio was 0.99 (confidence interval of 0.94–1.02). The changes in tuning following adaptation are thus much larger than those that would be expected from fluctuations in the recordings.

Role of stimulus size. Our stimuli were substantially larger (7.4°) than those used in most previous V1 adaptation studies and also larger than the RFs of individual V1 neurons. V1 cells are inhibited by stimuli in the “surround,” outside the CRF (for review, see Angelucci and Bressloff 2006). Adaptation with annular stimuli can reduce the efficacy of the surround (Cavanaugh et al. 2002a; Durand et al. 2007; Webb et al. 2005).

We wondered whether the weak suppression and attractive shifts in preference, notably different results from those of previous V1 studies, could be related to our inclusion of responses from all cells rather than only the most responsive. We therefore investigated whether the most responsive cells adapted more similarly to those described in previous studies. For preferred adapted cells, we found that changes in responsivity were indeed correlated with preadaptation response strength (Fig. 5A, r = −0.23, P = 0.02); strongly driven cells tended to suppress more strongly. In weakly responsive cells, we frequently observed response facilitation. However, for flank adapted cells, there was no relationship between shifts in preference and response strength (Fig. 5B, r = −0.03, P = 0.65): attractive shifts in preference occurred even in cells with strong responses. Thus, although weak stimulus drive partially explains the weak suppression we observed in preferred adapted cells, both the response facilitation and the attractive shifts in orientation preference of flank adapted cells suggest a distinct mechanism involving disinhibition.

**Role of stimulus size.** Our stimuli were substantially larger (7.4°) than those used in most previous V1 adaptation studies and also larger than the RFs of individual V1 neurons. V1 cells are inhibited by stimuli in the “surround,” outside the CRF (for review, see Angelucci and Bressloff 2006). Adaptation with annular stimuli can reduce the efficacy of the surround (Cavanaugh et al. 2002a; Durand et al. 2007; Webb et al. 2005).
We hypothesized that the surround inhibition recruited by our stimuli was weakened after adaptation and that this disinhibition played a role in the tuning effects we observed. To test this, we adapted V1 neurons with small gratings (1° in diameter), the typical size of V1 RFs at the eccentricity of our recordings (Cavanaugh et al. 2002a). We placed these stimuli in the center of the aggregate RF and analyzed responses from cells whose RF center fell within 0.5° of the stimulus center (n = 489 cells). This criterion selects cells for which the influence of the surround is reduced but not eliminated. Correspondingly, the peak firing rate in these neurons was 20.8 ± 0.9 spikes/s on average, roughly 33% higher than that evoked by large gratings.

We found that adaptation with small gratings caused more substantial response suppression in preferred adapted cells, with a mean response ratio of 0.75 (P < 0.001; P = 0.01 for comparison with large gratings; Fig. 4B). Most strikingly, in flank adapted cells, adaptation with small gratings led to significant repulsive shifts in preference (maximal for cells offset by 15–30°, 2.52°, P = 0.01), opposite to those seen after exposure to large adapters (P < 0.001). This is consistent with orientation-specific reductions of responsivity near the adapter, an effect that is also visible in the average response of untuned units (Fig. 3B, bottom). Other effects of adaptation were not noticeably different for large and small stimuli: responsivity was facilitated in orthogonally adapted neurons (1.19; P < 0.001; P > 0.1 for comparison with large gratings), and changes in bandwidth were negligible for both preferred (0.93; P = 0.09) and orthogonally adapted cells (1.04; P = 0.11). Further comparisons between effects seen with large and small stimuli are provided in Table 1, as is a comparison of effects in multiunit activity and well-isolated single-unit activity.

In summary, we found that adaptation with large gratings led to a weak reduction in responsivity and attractive shifts in tuning preference. This differs qualitatively from previous reports in V1, which emphasize that tuning shifts away from the adapter, as a consequence of stimulus specific suppression.

**Adaptation with compound gratings.** Reducing stimulus size allowed us to minimize the influence of surround suppression. We next sought a manipulation that would increase the drive to the surround relative to that of the CRF. We reasoned that if the influence of stimulus size on the effects of adaptation was due to an influence of weakened surround suppression offsetting adaptation effects within the CRF, these effects should be particularly prominent for stimuli that provided strong drive to
the surround and weak drive to the CRF. To test this, we measured responses to large compound gratings, constructed by reducing the contrast of our standard grating and superimposing two additional gratings of equal contrast but with spatial frequencies one octave higher and lower. Because V1 neurons are narrowly tuned for spatial frequency (De Valois et al. 1982), distributing contrast across frequency components should reduce the drive each cell receives (Fig. 6A). The surround, on the other hand, is broadly tuned for spatial frequency (Webb et al. 2005) and should thus remain well-tuned.

Compound gratings evoked weaker responses than similarly sized gratings (mean $10.3 \pm 0.4$ spikes/s; $n = 992$), but responses remained well-tuned (mean OSI $0.40 \pm 0.007$). Adaptation with compound gratings resulted in significant response facilitation (Fig. 6B; $n = 560$ cells). Remarkably, even cells adapted in their preferred direction responded more strongly after adaptation than before (mean ratio of $1.15, P = 0.01$; for cells offset by $60–90^\circ$, mean ratio of $1.15, P < 0.001$). As with large gratings, large compound stimuli produced attractive shifts in tuning preference (for flank adapted cells, $-4.10^\circ, P < 0.001$) and had weak effects on tuning bandwidth, causing a slight narrowing for preferred adapted cells (mean ratio of $0.89, P = 0.04$).

We were concerned that these adaptation effects could involve alternative mechanisms, arising from the altered frequency content of the compound grating (e.g., lower spatial frequency components which may recruit inhibition; Bredfeldt and Ringach 2002), the lower contrast of the component gratings, or interactions between those components (e.g., normalization; Carandini et al. 1997). To test whether the surround was indeed the critical factor, we adapted neurons with small compound stimuli ($n = 447$; Fig. 6C). Adaptation with these stimuli led to response suppression in preferred adapted cells (mean ratio of $0.86, P < 0.001$) and repulsive shifts in preference for flank adapted ones ($+2.06^\circ, P < 0.001$). That is, facilitation and attractive shifts could be reversed to suppression and repulsive shifts, respectively, by reducing stimulus size. Further quantification of the effects of compound adapters is provided in Table 1.

**Influence of the adaptation protocol.** Whereas changes in stimulus size affected the consequences of adaptation for preferred and flank adapted cells, the effects in orthogonally adapted cells did not depend on stimulus size or type. In these cells, we observed a consistent facilitation of responsivity and a weaker but often significant increase in tuning bandwidth. These effects can be explained by a decrease in threshold after adaptation. Why would this occur? We suspected that it was related to the adaptation protocol that we and others have used, in which tuning before adaptation was measured with a continuous stimulus sequence (e.g., Dragoi et al., 2002; Kohn and Movshon 2003, 2004; Ohzawa et al. 1985). Orthogonally adapted cells responded more strongly to this sequence ($6.3 \pm 0.1$ spikes/s on average) than to the adapter ($2.6 \pm 0.3$ spikes/s, $P < 0.001$), which by definition evoked a minimal response. As a result, these cells would be expected to recover during

![Fig. 4. Effects of adaptation on tuning parameters. A, top: peak response after adaptation divided by the peak response before adaptation. Data represent the geometric mean of the ratios, binned by the cell’s offset from the adapter, in increments of $15^\circ$. Error bars represent 95% confidence intervals calculated as bootstrap estimates of the mean. Middle: same as in A, for shifts in preferred orientation. Data represent the arithmetic mean of the difference between the preferred orientation after adaptation and before. Negative values indicate shifts toward the adapter. Bottom: same conventions for the bandwidth ratio. Data represent the width of the tuning curve at half-maximal responsivity after adaptation divided by that before. The mean bandwidth was $53.5 \pm 0.6^\circ$ for the data set as a whole and $55.2 \pm 3.8^\circ$ for single-unit activity. B: same as in A, for adaptation with small gratings.](http://jn.physiology.org/)

![Fig. 5. Relationship between firing rate and changes in responsivity and preference. A: response ratio as a function of the preadaptation firing rate for preferred adapted cells (offsets within $15^\circ$ of the adapter). B: the shift in preferred orientation following adaptation, as a function of the preadaptation firing rate for flank adapted cells (offsets between $15^\circ$ and $45^\circ$ from the adapter).](http://jn.physiology.org/)
adaptation from a hyperpolarization induced by the preadaptation test stimulus sequence.

To test this, we adapted cells with large gratings but placed a 5-s interstimulus interval (gray screen) between the preadaptation test stimuli (Fig. 7A; n = 428 well-fit cells of 890 responsive cells). Although visual stimuli rarely appear in such temporal isolation (see Wolfson and Graham 2009 for a related discussion on perceptual effects), this protocol ensures that cells receive less frequent drive and thus should hyperpolarize less during the preadaptation period. We found no response facilitation in orthogonally adapted cells with this modified protocol (Fig. 7A, middle). The mean response ratio was 0.85 (n = 136) compared with 1.21 (n = 262) for our standard protocol (Fig. 7, A and B, middle panels; P < 0.001 for difference). Similarly, the small but significant increase in tuning bandwidth we observed after orthogonal adaptation with
the standard protocol (1.08, Figs. 4 and 7B, right) was eliminated (mean ratio of 0.99; Fig. 7A, right; P = 0.004 for difference). Results were otherwise consistent with our previous findings. Response suppression was stronger after preferred adaptation (0.85; P = 0.01) than that observed with the standard protocol (P = 0.24), and flank adapted cells shifted toward the adapter (−4.5°, P < 0.001). To be sure that the modulation of adaptation effects by surround suppression was not affected by the adaptation protocol we used, we collected additional data with our modified protocol using small gratings. In this case, adaptation led to repulsive shifts for flank adapted cells (2.1°, n = 70, P < 0.001 for difference with large stimuli) and stronger suppression for preferred adapted cells (0.53, n = 24, P < 0.001 for difference with large stimuli), consistent with our previous results.

We conclude that the facilitation of responsivity and increase in bandwidth in orthogonally adapted cells reflects a recovery from a reduced responsiveness induced by the preadaptation test stimuli.

Contrast adaptation. Our measurements of tuning were conducted with high-contrast stimuli. Because surround effects are weak at low contrast (Cavanaugh et al. 2002a, Sceniak et al. 1999), the effects involving disinhibition from a weakened surround may only occur at high contrast. We therefore investigated how adaptation affects responses to stimuli of varying contrast by measuring responses to gratings and compound stimuli of fixed orientation before and after adaptation at full contrast.

We analyzed data from all cells whose responses were modulated by stimulus contrast, defined as a response at maximal contrast that was at least twice that at low contrast. We did not measure the orientation preference of these cells, but this criterion likely means that the presented orientation fell on the neuron’s tuning curve flank or peak.

We normalized the data from each cell by the response at full contrast and averaged across cells to compute population contrast-response functions. Adaptation with large gratings (Fig. 8A) caused a reduction in responses evoked by low-contrast but not high-contrast stimuli (thin line before compared with thick line after adaptation). Compound grating adapters caused similar but weaker effects (Fig. 8B) as expected given the weaker CRF drive these provide.

To quantify these effects, we calculated for each neuron the ratio of the area under the contrast-response function after adaptation compared with before. We chose this metric because the response functions showed little saturation, and as a result, the fits of the commonly used hyperbolic ratio function were not well constrained. Adaptation with gratings resulted in a geometric mean area ratio of 0.54 (P < 0.001 for difference from 1); compound gratings resulted in a weaker ratio of 0.82 (P < 0.001; difference between stimuli, P < 0.001). We conducted similar measurements with small (1°) stimuli to reduce the influence of the surround (Fig. 8, C and D). In this case, adaptation caused strong response suppression of test stimuli at all contrasts, for both grating (mean ratio of 0.11, P < 0.001, Fig. 8C) and compound stimuli (mean ratio of 0.55, P < 0.001, Fig. 8D, P < 0.001 for differences between stimuli). The ratios were significantly lower for small stimuli compared with large, for both types of stimuli (P < 0.001 for gratings; P < 0.001 for compound gratings).

A simple model to account for V1 adaptation effects. To provide a more formal account of how surround suppression can influence adaptation-induced changes in tuning, we created a simple model. The parameters of this simulation (see MATER-

Fig. 8. Effects of adaptation on contrast sensitivity. A: population contrast-response functions for large gratings before (thin) and after (thick) adaptation. B: same as in A, for compound stimuli. C: same as in A, for small gratings. D: same as in A, for small compound stimuli.
IALS AND METHODS) were arbitrary but were chosen to provide a range of effects similar to those observed in our recordings. Each neuron received orientation-tuned synaptic input, which was divisively suppressed by a similarly but more broadly tuned surround (Cavanaugh et al. 2002b; Webb et al. 2005). The net drive (CRF divided by surround activation) was passed through a threshold nonlinearity to generate the measured response.

The effects of adaptation were implemented with two mechanisms. First, adaptation led to stimulus-specific suppression (i.e., strongest near the adapter) of synaptic input. This occurred for both the CRF and the surround and was in proportion to the drive provided (i.e., strong activation led to stronger effects). This mechanism is motivated by the observation that adaptation can cause synaptic depression (Abbott et al. 1997; Markram and Tsodyks 1997; but see Boudreau and Ferster 2005) and the hyperpolarization of responsive neurons (Cardin and Ferster 1997, Sanchez-Vives et al. 2000). If this were to occur in tuned presynaptic cells, it would result in stimulus-specific suppression. Second, adaptation altered the effective response threshold of the neuron, reflecting the activation of an intrinsic hyperpolarizing conductance. In our model, this occurred in proportion to the cell’s response to the adapter (see MATERIALS AND METHODS for further details).

Figure 9A illustrates the effects of adaptation in a model neuron for a stimulus that provided robust drive to the CRF and weak recruitment of the surround (e.g., a small stimulus that encroaches minimally on the surround). The stimulus-specific reduction in synaptic input led to repulsive shifts in the tuning of both the CRF and the surround (Fig. 9A, left). Because the cell received strong drive, adaptation also caused a substantial hyperpolarization (implemented as a rightward shift of the nonlinearity; Fig. 9A, middle). The net effect on tuning was a repulsive shift in preference and reduction in responsivity (Fig. 9A, right).

Figure 9B: same as in A, for stimulus drive that strongly activates the RF surround. C: peak response ratio (left), shift (middle), and bandwidth ratio (right) for model neurons with preferred orientations offset from 0 to 90° from the adapter. Each line represents a different stimulus condition. Line style indicates the strength of CRF drive. Gray scale indicates the strength of surround drive.

Fig. 9. A simple model of adaptation in V1. A: example of the effects of adaptation on a model neuron receiving strong drive within the CRF and weak drive to the surround. Left: effect of adaptation on synaptic inputs (dotted compared with solid line) and tuning (thin line before compared with thick line after adaptation) of the center (top) and surround (bottom) drive. Middle: effect on the response nonlinearity. Right: net effect on tuning. Arrowhead represents the orientation of the adapter
9A, right), as we observed after adapting to small drifting gratings. Figure 9B illustrates the consequences of adapting with a stimulus that provided weak input to the CRF but strong drive to the surround (e.g., a large stimulus that only partially overlapped the CRF). The effects on synaptic input were similar in nature to those shown in Fig. 9A, but the effects on the surround were much stronger than those within the CRF. Because surround suppression was stronger, responsivity was weaker and the neuron thus hyperpolarized only slightly. The net effect was an attractive shift in preference and a facilitation of responsivity, as we observed after adapting with large compound gratings. This occurred because disinhibition from adapting the surround outweighed the reduced synaptic input to the CRF and the small increase in response threshold.

Adaptation could have a wide range of effects depending on the relative drive to these two RF components (Fig. 9C). Stimuli that provided robust drive to the CRF (dotted lines) and minimal drive to the surround (gray lines) resulted in stronger response suppression and repulsive shift in preference. Stimuli that provided strong input to the surround (black lines), particularly when paired with weak drive to the CRF (thick solid lines), resulted in facilitation after adaptation and attractive shifts in preference.

The model presented in Fig. 9 provides a qualitative match to the range of adaptation effects we observed across stimulus conditions. To provide a more quantitative evaluation of the importance of these mechanisms, we fit a reduced model that captures the key elements to the data of each cell. We considered responses evoked by small and large gratings (n = 1,547 cells) presented either with (Fig. 7A) or without (Fig. 4) an interstimulus interval. We considered a set of nested models (62 in total; see MATERIALS AND METHODS for further details), which we fit to the data of each cell. Every variant of the model included four parameters to describe the tuning before adaptation. The full model contained an additional six parameters to capture the effects of adaptation: the strength and tuning of adaptation-induced suppression (2 parameters) and disinhibition (2 parameters), and the response nonlinearity (2 parameters). The remaining 61 variants of the model fit to each cell were based on allowing all possible combinations of free and fixed adaptation parameters (e.g., only allowing the strength of disinhibition to vary across cells, or only its tuning, or the combination of these, etc.). When parameters were fixed, they were set at the average values across all cells.

Because we measured responses to a limited number of test stimuli in each cell, the full model (6 free parameters to describe the effects of adaptation) was overspecified. In fact, the best model, based on a relative goodness-of-fit criterion that penalized extra parameters (see MATERIALS AND METHODS), contained only a single parameter: the change in response threshold. Although this model could capture changes in overall responsiveness across stimulus conditions and adapter offsets, it could not explain the size-dependent effects of adaptation on preference (Fig. 4, middle row).

The next best model contained two free parameters: the strength of disinhibition and the change in threshold. In this model, the strength and tuning of adaptation-induced suppression were thus similar across conditions, as was the tuning of the disinhibition. The fit of this model was 0.88 in normalized log-likelihood units, where a value of 1 corresponds to a model consisting of the data itself and 0 to a model that predicts the same mean response to each stimulus (Stocker and Simoncelli 2006). That the strength of disinhibition could vary across cells and conditions allowed for both repulsive and attractive shifts in preference.

Figure 10 shows the average values of the two fit parameters, as a function of stimulus condition (line style and color) and of the cells’ offset from the adapter. The strength of disinhibition was only weakly dependent on the offset of the cell’s preferred orientation from the adapter (Fig. 10A; 3-factor ANOVA: F = 4.5, P = 0.03) but was stronger for large (black lines) than small stimuli (gray lines; F = 49.7, P < 0.001). The adaptation protocol had no influence (dotted vs. solid lines; F = 1.4, P = 0.24). This is consistent with our observation of opposite shifts in preference after adaptation with large (stronger disinhibition) and small (weaker disinhibition) gratings independent of adaptation protocol.

The changes in response threshold displayed a different behavior (Fig. 10B). There was a strong dependence of this parameter on the offset of the neuron’s preference from the adapter (F = 287.3, P < 0.001) and on the adaptation protocol (F = 600.0, P < 0.001) but only a weak influence of stimulus size (F = 4.2, P = 0.04). The change in threshold for the standard adaptation protocol involved a small hyperpolarization for cells adapted near their preferred orientation and a depolarization for offset neurons. For the modified adaptation protocol, adaptation only led to hyperpolarization, which was strongest for preferred adapted cells.

In summary, a quantitative comparison of a set of nested models showed that the key mechanisms for explaining the range of V1 adaptation effects we observed are 1) adaptation-induced response suppression, which is orientation specific and similar across stimulus sizes and adaptation protocols; 2) the

Fig. 10. Parameters of a reduced model fit to neuronal responses. A: the strength of disinhibition for model neurons with preferred orientations offset 0 to 90° from the adapter. Each line represents a different stimulus condition. Line style indicates the adaptation protocol; line shading indicates stimulus size. B: same as in A, for the change in effective threshold.

J Neurophysiol • doi:10.1152/jn.00739.2011 • www.jn.org
strength of tuned adaptation-induced disinhibition, which is strongest for larger stimuli; and 3) changes in effective threshold, which depend on the offset of the neuron’s preference and the strength of drive in the preadaptation period.

DISCUSSION

Previous adaptation studies have focused on studying effects using stimuli that are tailored to the preferences of individual neurons and have assumed that the observed effects are representative of those in a broader population. We used microelectrode arrays to record from population of neurons, which were adapted with a single stimulus, not tailored to the preference of any particular cell. Using this technique, we found a broader range of adaptation effects in V1 than previously reported: adaptation could cause response suppression or facilitation, as well as repulsive or attractive shifts in orientation preference. These diverse effects could be accounted for by a simple model in which stimulus-specific suppression occurs in both the CRF and surround, with the net effect on tuning depending on the relative drive to these two RF components.

Comparison with previous studies. Our data obtained with small gratings are consistent with previous findings that adaptation leads to stimulus-specific suppression of responsivity (Dragoi et al. 2000, 2001, 2002; Giaschi et al. 1993; Muller et al. 1999; Nelson, 1991; Saul and Cynader 1989a, 1989b). For adapting with large stimuli, however, our results diverge substantially from previous findings. First, response suppression after adaptation was weaker than with small stimuli, particularly at high contrast, when surround suppression is strongest. Second, adaptation with large gratings caused attractive shifts in orientation preference. Both effects were particularly striking for compound gratings; adaptation with these stimuli resulted in enhanced responsivity even in cells adapted in their preferred direction. Previous qualitative reports have noted a lack of response suppression in V1 after adaptation with large complex stimuli (Hammond and MacKay 1977; Hammond et al. 1988). However, to our knowledge, ours is the first demonstration, in any cortical area, that adaptation with a stimulus that evokes robust, well-tuned responses leads exclusively to response facilitation (i.e., in all cells, regardless of offset from the adapter). It is important to note that these size-dependent facilitatory effects are distinct from those described by Dragoi and colleagues in cat V1 (Dragoi et al. 2000, 2001), which involved enhanced responsivity on the tuning curve flank opposite to the adapter (i.e., stronger repulsive shifts) and required adaptation of at least 2-min duration.

Across stimulus conditions, we found that adaptation caused changes in tuning bandwidth of 10% or less. This contrasts with the findings of Dragoi et al. (2001, 2002), who found sharper tuning after both preferred and orthogonal adaptation. This discrepancy could reflect differences in experimental approach, noted above, but likely reflects different metrics of tuning quality. Our measurement of bandwidth emphasizes the sharpness of tuning around the preferred orientation; Dragoi et al. (2001, 2002) used an index that provides a more global measure of tuning quality and depends on responses to all orientations (Ringach et al. 2002). Because orthogonal adaptation leads to local (stimulus specific) suppression, the value of the OSI can increase without altering the shape of the tuning curve around its peak.

Attractive shifts in tuning preference have been previously observed in area MT (Kohn and Movshon 2004; Krekelberg et al. 2006b). Two potential explanations have been offered to reconcile these findings with those in V1: either cortical areas adapt differently, or adapted feedforward input from lower cortex gives rise to novel effects downstream due to the influence of recurrent circuitry within MT (Compte and Wang 2006; Kohn and Movshon 2004). The data presented here provide a simpler explanation. MT RFs are substantially larger than those in V1 at the same eccentricity (Albright and Desimone 1987; Van Essen et al. 1984), so adapting MT cells with optimized stimuli would recruit substantial surround suppression in V1, causing attractive shifts in V1 tuning. As a result, attractive shifts in MT may simply be inherited from V1 (Kohn and Movshon 2003). In any case, our results show clearly that there is currently no evidence for a qualitatively different strategy in how V1 and MT adapt to persistent visual stimuli.

This explanation does not imply that effects in MT necessarily reflect those in V1. For instance, our model suggests that adaptation with large-bandwidth stimuli (e.g., coherent random dot kinematograms) would result in facilitation in V1. However, the effect this would have in MT would also depend on whether these stimuli directly adapted MT cells. Unlike the spatial specificity of prolonged gratings adaptation within the RFs of individual MT neurons (suggesting inheritance from V1; Kohn and Movshon 2003), the effects of brief adaptation with dot fields transfers between subregions, suggesting a direct effect on MT cells (Priebe et al. 2002). This may explain why previous studies have found a reduction in MT responsivity after adaptation with coherent dots (Krekelberg et al. 2006b; Van Wezel and Britten 2002; Yang and Lisberger 2009; see also discussion in Kohn and Movshon 2004). The effects of adaptation in MT (and other extrastriate areas) are likely to reflect a combination of local and inherited effects, depending on stimulus size, composition, and perhaps duration.

Our suggestion that adaptation can cause both response reduction and facilitation is consistent with several recent studies. Dhruv et al. (2011) measured the effects of adaptation on contrast sensitivity in macaque V1 and showed that adaptation can lead to response facilitation when it reduces the strength of a normalization signal. Unlike our study, however, the mechanism explored was entirely within the RF and the effects were not orientation specific; the attractive shifts we observed required a tuned disinhibition and only occurred for stimuli that extended beyond the CRF. Camp et al. (2009) showed that the influence of the suppressive extra-CRF in the lateral geniculate nucleus of the marmoset can be reduced by prolonged adaptation. These effects were spatially specific but not tuned for stimulus orientation or spatiotemporal frequency and were attributed to retinal mechanisms. Finally, Tailby et al. (2008) showed that adaptation with chromatically modulated stimuli can alter the color preference of V1 neurons, resulting in shifts in preference toward or away from the adapter, much like the effects we observed for orientation tuning. Each of these studies targets a distinct type of normalization signal with unique features and possibly a distinct origin. A unifying theme, however, is that adaptation 1) can reduce both excitatory drive to the RF and the suppressive influence of a normalization signal (see Freeman et al. 2002 for a contrary finding); and 2) the effects of adaptation will depend critically on the balance between its effects on these two inputs. This
suggests that the type of effects these studies describe likely represents a basic operating principle of sensory neurons and circuits.

There are a number of perceptual results consistent with our finding that surround suppression modulates the effects of adaptation. For instance, stronger motion aftereffects are observed after adaptation with smaller stimuli (Murakami and Shimojo 1995; Sachter and Zaidi 1993; Tadin et al. 2003). Similarly, the strength of the motion aftereffect induced by an adapter of constant size increases with eccentricity, consistent with the weaker surround suppression that such stimuli would recruit in larger peripheral RFs (Johnston and Wright 1983; Murakami and Shimojo 1995; Tadin et al. 2003). Finally, aftereffects induced by adaptation with a grating can be reduced by superimposing another grating of differing spatial frequency (Klein and Stromeyer 1980; Nachmias et al. 1973; Stecher et al. 1973; Tolhurst 1972), consistent with our results using compound stimuli. Although these perceptual effects support an interaction between surround suppression and adaptation, it is important to note that effects in V1 need not be mirrored in other cortical areas or in perception, because of the possibility of additional effects in higher cortical areas.

Methodological considerations. We performed our experiments in anesthetized, paralyzed animals because studying the effects of prolonged adaptation requires maintained visual fixation. It is unlikely that anesthesia significantly influenced our results. First, previous studies of brief adaptation have found little discrepancy between effects in anesthetized (Dragoi et al. 2000, 2001; Muller et al. 1999; Pribe et al. 2002) and awake animals (Dragoi et al. 2002, Pribe et al. 2002). Second, V1 response properties recorded under opiate anesthesia are remarkably consistent with those recorded in awake animals (Constantinople and Bruno 2011; Movshon et al. 2003). Third, our results strongly implicate surround suppression as a mechanism determining the effects of adaptation, and this suppression is robust in awake V1 (e.g., Roberts et al. 2007). Finally, adaptation in human subjects has strong perceptual aftereffects, even when the adapter is not perceived (e.g., He and Macleod 2001). Visual awareness is thus not a requirement for adaptation to be effective.

We recorded activity with multielectrode arrays, which led us to study how populations of neurons, with a diverse range of preferences, are affected by prolonged exposure to an adapter. A similar approach could, of course, be implemented using single electrode recordings, if a common set of stimuli were used across cells. In our analysis, we included effects in all cells, regardless of response strength, to preclude a bias toward the most responsive units. It is important to note, however, that our recordings also likely introduced some biases. First, the low impedance of our electrodes likely means that we sampled primarily from larger (pyramidal) neurons. Second, we implanted the arrays in the superficial layers of cortex, to a nominal depth of 600 μm below the cortical surface and never more than 1 mm (the length of the electrodes). We cannot rule out the possibility that neurons in other layers may adapt differently. Finally, our recordings included a mix of multunit and single-unit recordings. However, we found little difference between these types of recordings, in terms of tuning, responsiveness, or effects of adaptation.

Implications. Repeated presentations of a stimulus have been shown to cause a stimulus-specific decrease in the blood oxygen level-dependent (BOLD) response (Grill-Spector and Malach 2001). This reduction has been widely used to infer selectivity in a particular region of human cortex to some aspect of the adapter. Our results suggest a need for caution with this interpretation (see also Krekelberg et al. 2006a). The stimuli used in functional MRI experiments are typically large relative to the RF size of neurons in early visual cortex and thus recruit significant surround suppression in those areas. Therefore, a lack of BOLD response suppression in early cortex after adaptation may simply reflect disinhibition of the surround. For example, Fang et al. (2005) showed that adaptation with gratings (2–3° in diameter) causes an orientation-specific reduction in response strength, which increases in magnitude from V1 to V4. Because RFs increase in size in higher cortical areas, this result and others like it may simply reflect a reduced influence of surround suppression in higher cortex (for stimuli of constant size) rather than differences in selectivity, responsiveness, or susceptibility to adaptation.

Our data call into question a number of existing proposals concerning the functional role of adaptation-induced plasticity. First, the suggestion that adaptation provides metabolic savings (see Kohn 2007) seems inconsistent with the robust facilitation we saw after adaptation with large compound stimuli and the weak suppression we observed with other stimuli. Our finding of opposite shifts in preference for large and small adapters undermines the argument that adaptation reduces representational redundancy by decorrelating neural responses (Barlow 1990; Muller et al. 1999). Such an argument requires similar effects after adapting with any stimulus that evokes tuned responses. Proposals relating to improvements in discriminability afforded by shifts in preference (Muller et al. 1999) are problematic for the same reason.

What then is the functional benefit suggested by our findings? We believe it may be closely related to the role of surround suppression itself. Surround suppression highlights features that differ from their spatial context, giving rise to figure-ground segregation and determining salience (Series et al. 2003). Similarly, the effects of adaptation may serve to enhance the salience of features differing from their temporal context. This suggestion is not entirely new (Hosoya et al. 2005; Schwartz et al. 2007; Sharpee et al. 2006), but unlike previous studies, our data suggest an intimate mechanistic link between spatial and temporal contextual effects. For instance, stimuli that are different from their background will evoke robust responses, because they will not recruit surround suppression. In this case, adaptation will lead to weaker responses, by both reducing peak responsivity and repelling tuning. Homogeneous portions of the visual field, on the other hand, will elicit weaker responses, and adaptation can lead to response facilitation. Because of the reduced efficacy of the surround at such locations, the subsequent appearance of novel stimuli might be expected to elicit particularly strong responses, a sort of sensitization. In this sense, spatial and temporal contextual modulation may work hand in hand to control and define salience. Interestingly, recent work has proposed that attention may also involve surround suppression (Reynolds and Heeger 2009). If so, our results offer a concrete mechanism for the perceptual interaction between adaptation and attention (Chaudhuri 1990; Pestilli et al. 2007; Rezec et al. 2004; but see Morgan 2011) and suggest a shared mechanism for establishing spatial, temporal, and attentional context.
ACKNOWLEDGMENTS

We thank Amin Zandvakili, Xiaoxuan Jia, and Carlyn Patterson for assistance with data collection and Odella Schwartz, Matthew Smith, Sam Solomon, Bart Krekelberg, Franco Pestilli, and members of the laboratory for helpful comments and discussions.

GRANTS

This work was supported by National Eye Institute (Grant EY016774), National Institute of Child Health and Human Development (Grant 1P30-HD-O71593), and Research to Prevent Blindness.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

Author contributions: S.C.W. and A.K. performed experiments; S.C.W. and A.K. analyzed data; S.C.W. and A.K. prepared figures; S.C.W. and A.K. drafted manuscript; S.C.W. and A.K. edited and revised manuscript; S.C.W. and A.K. approved final version of manuscript; A.K. conception and design of draft manuscript; S.C.W. and A.K. edited and revised manuscript; S.C.W. and A.K. analyzed data; S.C.W. and A.K. prepared figures; S.C.W. and A.K. contributed to the writing and revision of the manuscript; S.C.W. and A.K. helped to write the manuscript.

REFERENCES


Morgan MJ. Wohlgemuth was right: distracting attention from the adapting stimulus does not decrease the motion after-effect. Vision Res 51: 2169–2175, 2011.


