Modification of Response Functions of Cat Visual Cortical Cells by Spatially Congruent Perturbing Stimuli

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INTRODUCTION

The response properties of striate cortical neurons have often been analyzed on the basis of their responses to one-dimen-
sional sinusoidal gratings or simple bar or spot stimuli, under the presumption that their spatial integration and response functions to these stimuli are at least piecewise-linear. By this assumption, responses to a number of spectrally pure stimuli can be combined to produce a kernel (e.g., Movshon et al. 1978) that potentially predicts a cell’s approximate response to spectrally complex, real world stimuli. Measurements made with more complicated stimuli, such as multiple light bars (Bishop et al. 1973) and compound sinusoidal gratings (e.g., Bonds 1989; De Valois and Tootell 1983) use an overtly excitatory stimulus to drive the cell. The addition of a second (perturbing) stimulus that by itself does not excite the neuron reveals, by modulating the excitation from the first stimulus, both excitatory and inhibitory subliminal (nonlinear) influences that are not apparent from the use of a spectrally pure stimulus. Additionally, drifting bars presented outside the cor-
tical receptive field have been found to change the optimum orientation for bar stimuli inside the receptive field (Gilbert and Wiesel 1990). These results all challenge the assumption of approximate spatial linearity of the cortical receptive field.

Most experiments involving compound stimuli have involved systematic analyses of response suppression. Suppression of a cell’s response depends on, among other factors, the orientation of the perturbing stimulus (e.g., Bishop et al. 1973; Bonds 1989; Creutzfeldt et al. 1974; Morrone et al. 1982; Nelson and Frost 1978; Sillito 1975). Additionally, experiments using compound gratings show that the suppression of a cell’s response to a base sinusoidal grating (which drives the cell) can depend on the spatial frequency of the perturbing stimulus (Bauman and Bonds 1991; De Valois and Tootell 1983). These results imply that suppression is not merely a result of the integration of contrast energy (e.g., Heeger 1992), but also involves more sophisticated spatial interactions.

Here we develop this concept further by considering a hypothesis in which a cell’s response is a nonlinear function that is not merely suppressed, but rather completely transformed by the presence of an overlaid sinusoidal perturbing grating (PG) to which the cell does not respond when it is presented alone. We further hypothesize that the reorganization of the receptive field is not a static change, but is dependent on the relationship between the stimulus that drives the cell and the PG. To test these hypotheses we measured a cell’s response as a function of orientation or spatial frequency with a single sinusoidal grating. We then superimposed on the receptive field a second (perturbing) grating at an orientation or spatial frequency that does not by itself excite the cell and measured the response curves again. In nearly all tests the location of the peak as well as the entire response function shifted significantly in the presence of the PG. Because of these shifts, the usual measure of response suppression (measured by stimulation with a base grating that is spatially optimal when presented alone) overes-
etimates the actual amount of response suppression. We suggest that the modification of the response function resulting from the use of PGs can enhance the discrimination of orientation differences.

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METHODS

Preparation

We prepared 11 adult cats (2.0–4.0 kg) for single-unit electrophysiological recording following guidelines from the American Physiological Society, The Society for Neuroscience, The National Institutes of Health, and Vanderbilt University’s Animal Care and Use Committee. Each cat received an intramuscular injection of 0.2 mg atropine sulfate (Elkins-Sinn, Cherry Hill, NJ), to reduce secretions, and 5 mg acepromazine maleate (TechAmerica, Elwood, KS) to reduce anxiety. Approximately 30 min after these injections, the cat was anesthetized with a 5% mixture of halothane (Fluothane, Ayerst, Philadelphia, PA) in O₂. After venous cannulation, the halothane was discontinued, and surgical anesthesia was maintained by injections of 2.5% sodium thiopental (Surital, Park-Davis, Morris Plains, NJ). A tracheal cannula was inserted, the head was mounted in a stereotaxic apparatus, and a 2 × 4 × 4 mm hole was drilled over the area centralis representation in area 17, Horsley-Clarke coordinates P4–L2. The exposed dura was reflected, and an electrode was positioned over a cortical area free of blood vessels. The cortex was covered with Agar, and a hydraulic seal was formed using melted Tackiwax (Cenco, Chicago, IL). Electrocardiogram (EKG) electrodes were inserted to monitor the heartbeat, and electrodes were inserted over the lateral suprasylvian gyrus to monitor generalized brain activity.

To suppress eye movement the animal was paralyzed with a 1.0-ml intravenous injection of gallamine triethiodide (Flaxedil, American Cyanamid, Pearl River, NY). Paralysis was maintained with an intravenous delivery of 10 mg · kg⁻¹ · h⁻¹ of Flaxedil, and anesthesia was supplemented with 1 mg · kg⁻¹ · h⁻¹ of Surital. Artificial respiration was maintained at 30 strokes per minute with a mixture of 75% N₂O, 23.5% O₂, and 1.5% CO₂. End-tidal pCO₂ was maintained at 3.9% by adjusting the stroke volume. Rectal temperature was maintained at 37.5°C with a hot water blanket. The nictitating membranes were retracted with 10% phenylephrine hydrochloride and the pupils dilated with 1% atropine sulfate eye drops. Contact lenses with artificial 4-mm pupils were then fitted to the eyes (Robson and Enroth-Cugell 1978). Spectacle lenses were then fitted by refraction to focus on a tangent screen 57 cm from the cat. The retinal area centralis and the optic disk locations were plotted for each eye.

Stimulation and data acquisition

We mapped the receptive field location and size using a hand-driven light source backprojected onto the tangent screen. A cathode ray tube (CRT) display 57 cm from the cat was then centered on the receptive field. Stimulus patterns were displayed on a Tektronix 608 (P31 phosphor; mean luminance 110 cd/m²; 10° visual field) at 256 receptive field. Stimulus patterns were displayed on a Tektronix 608 ray tube (CRT) display 57 cm from the cat was then centered on the receptive field. Stimulus patterns were displayed on a Tektronix 608 ray tube (CRT) display 57 cm from the cat was then centered on the receptive field. Stimulus patterns were displayed on a Tektronix 608 ray tube (CRT) display 57 cm from the cat was then centered on the receptive field.

We calculated the mean response and the 95% confidence interval of the mean from the data collected for each stimulus. The 95% confidence interval is defined as the range within which the mean of an equal number of samples from the same distribution will lie 95% of the time. We claim that a PG affects significantly a response function if the mean of each datum from the PG presentation lies outside the 95% confidence interval of control stimuli measurements both preceding and succeeding the test. This conservative measure accounts for any drift in the cell’s response function not due to the PG.

The resolution of our measurement of shifts in the tuning curves depends on the sampling interval in the orientation or spatial frequency domains. To improve the estimate of the location of a response function’s actual peak, we linearly interpolated the response’s derivative around the measured peak. This method relied on three data points to estimate the peak location, providing better stability. This technique requires a smooth function with no inflections between the three points other than the peak, but this assumption is implicit when we sample the tuning curves at discrete intervals. We repeated the interpolation for each sample and calculated a 95% confidence interval on the measure.

Using only the sampling rate, the peak can be resolved to within one sample width. However, with repeated measures and interpolation, we can increase the resolution of the peak for the average response function. We can calculate the resolution of a single sample from the interpolated estimate as follows:

Let $n$ = number of stimuli

Let $SW$ = the spacing between sample

Let $|p_k|$ = the peak spike count measured (an integer)

Let $|p_{k+1}|$ and $|p_{k-1}|$ be the spike counts at the two neighboring measures

Let $p_{k_{est}}$ = the stimulus orientation generating the maximum number of spikes

The tuning function is the result of sampling, so the location of the actual peak of the response function ($p_k$) may be up to ± $SW/2$ distant from $p_{k_{est}}$. We calculate a likely estimate of the true peak by using the two neighboring data points $p_{k-1}$ and $p_{k+1}$

$$p_k = p_{k_{est}} - SW/2 \times \frac{|p_{k+1}| - |p_{k-1}|}{2|p_k| - |p_{k+1}| + |p_{k-1}|} (1)$$

Given $p_k$, we now wish to calculate how sensitive this estimate is to a change in the dependent variable (spikes):

Let $SR = \text{sample _ resolution} = \text{the allowable range of } p_k \text{ given constant spike counts}$. Then
data resulted in a typical sample resolution of 6. The amount of time spent collecting data at a given orientation or resolution is derived from repeated measures, so it is proportional to its two neighbors. For a given cell the confidence interval for the total number of spikes collected at the measured peak location and the triangles show a shift of peak in one direction and a shift of both the peak and the CoM shift the same amount. The diamonds show a change in CoM without a change in the function peak location, and the squares indicate a lateral shift where the center of mass (CoM). The squares correspond to the center of the neighborhood of orientations or spatial frequencies that cause the cell to fire most often. The CoM is the indicator of an entire curve’s location (Stewart 1991), as opposed to relying on some particular feature location, such as the peak. The CoM also seems relevant because in the natural environment a neuron is more likely to be presented with suboptimal stimuli within its tuning envelope. The location of a response function’s CoM corresponds to the center of the neighborhood of orientations or spatial frequencies that cause the cell to fire most often. Therefore we may wish to detect changes in the entire response function location since it impacts on the estimate of a cell’s response to all stimuli. The sample resolution of the CoM depends on the absolute number of spikes collected during an experimental trial.

Adopting Eq. 4 to our orientation response function data resulted in a typical sample resolution of 0.10°, which allowed us to identify peak location shifts of as little as ±0.20°. Decreasing the width between samples or increasing the number of times a stimulus is presented improves the resolution of the peak location by reducing the 95% confidence interval.

Figure 1 is a theoretical example of how an orientation response function peak is shifted dpk degrees by a PG located dOR degrees distant from the single grating optimum orientation. Additionally Fig. 1 shows the variety of relationships that we encountered between the response function peak, response function suppression, and shifts in the center of mass (CoM). The squares indicate a lateral shift where both the peak and the CoM shift the same amount. The diamonds show a change in CoM without a change in the function peak location, and the triangles show a shift of peak in one direction and a shift of CoM in the other direction.

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\[ pk \pm SR = pk - SW/2 \times \frac{|pk_i| - |pk_j|}{2|pk| + |pk_i| + |pk_j|} \]  

(2)

Since we are interested only in the magnitude of the resolution, we subtract \( pk \) from each side and take the absolute value

\[ SR = \frac{|pk - pk - 2*SW/2 \times \frac{1}{2|pk| - |pk_i| - |pk_j|}}{2|pk| - |pk_i| - |pk_j|} \]  

(3)

or

\[ \text{sample_resolution} = \frac{SW}{2|pk| - |pk_i| - |pk_j|} \]  

(4)

Resolving the peak location thus depends on the difference between the total number of spikes collected at the measured peak location and its two neighbors. For a given cell the confidence interval for the resolution is derived from repeated measures, so it is proportional to the amount of time spent collecting data at a given orientation or spatial frequency. Applying Eq. 4 to our orientation response function data resulted in a typical sample resolution of \( \pm 0.005^\circ \), much higher than the resolution of the peak, allowing the detection of very small changes in the response function location. As with the peak measure, to support the claim of a shift, we calculated the mean and 95% confidence interval of the CoM. Note that, when the response function peak and CoM shift in opposite directions (Fig. 1), the response function becomes skewed in the direction of the peak shift.

Suppression, as usually reported in the literature (e.g., Bishop et al. 1973; Bonds 1989; DeAngelis et al. 1992; Morrone et al. 1982; Nelson and Frost 1978), is measured as the difference (defined here as \( |dsg_{\text{pk}}| \)) between the response rate found with a spatially optimal (single-grating) stimulus and the response rate generated by that same stimulus with the addition of a PG. However, if the response function peak shifts, then suppression measured between the peak of the control measurement and the peak of the test measurement (\( \text{dpk} \)) yields a different value of suppression.

We defined response function bandwidth measurements by calculating the half-height (HH) of the peak and on both sides of the peak interpolated around the measured points closest to the HH value, to give us the full-width (FW) response bandwidth at HH. Orientation bandwidth is measured in degrees and spatial frequency bandwidth in log units. The sample resolution on each side of the bandwidth estimate is \( SW/D \), where \( D \) is the difference in the total number of spikes between the first interpolation point and the second. FWHH resolution for the data presented here is typically \( \pm 1^\circ \). Bandwidth measures implicitly depend on the measured firing rate and shifts in both the response function peak and CoM. Figure 1 shows an example in which the response function peak is stationary and the CoM shifts, effectively increasing the response function bandwidth. Changes in a response function’s measured bandwidth can result from peak and CoM shifts in opposite directions, CoM shifts with no peak shift and even peak and CoM shifts by varying amounts in the same direction.

**RESULTS**

**Reshaping response functions**

![Figure 1: Theoretical changes in response functions. A response function may have multiple characteristics changing simultaneously. The original response function (solid line) can have a shifted center of mass (CoM) and peak (dotted line), a shifted CoM with no peak shift (long dash line) and a peak that shifts in one direction with a CoM that shifts in the opposite (short dash line). Each of these shifts can be accompanied by response facilitation or suppression. The change in the response function peak of the 1st curve and the CoM of the 3rd curve are indicated along with the dOR value of a hypothetical perturbing grating (PG) orientation. We generated these curves by calculating a new peak and CoM location for the original response function. We found that the bandwidth changed because of these manipulations.](http://jn.physiology.org/)

In previous studies involving interaction between two stimuli (e.g., Bishop et al. 1973; Bonds 1989; DeAngelis et al. 1992; Morrone et al. 1982) influences on excitation were usually measured with a base (excitation) stimulus positioned...
at the cell’s optimum orientation. If a PG changes the orientation or SF yielding the peak response, the suppression measured at the location of the single stimulus optimum must be greater than the suppression measured between the peaks of the perturbed and unperturbed response functions. Figure 2 shows the orientation response function for a single grating from simple (A) and complex (B) cells. Each datum indicates the average response from 10 trials with the corresponding limits showing the 95% confidence interval of the mean. The dashed and dotted response functions in each figure shows the cell’s response in the presence of two different PGs. In each case, the average values of the perturbed response functions lie outside the 95% confidence intervals of the single stimulus curve. In the remainder of the paper (unless otherwise specified), described changes exceeded the 95% confidence interval of the control measurements.

In Fig. 2A, a PG oriented at 105° changes the optimum value of the base grating orientation from 55 to 45°, while a PG at 5° moves the location of the base grating response peak to 65°. The location of the response function peak for the complex cell shifts from 65 to 45° with the addition of a grating oriented at 95° and shifts to 75° with a PG oriented at 45° (Fig. 2B).

Usually the response function CoM is implicitly assumed to be the same as the peak location. However, shifts in location of the response function peak reshape the filter function, resulting in a shift of the CoM. The PG oriented at 105° causes the simple cell response function CoM to shift from 55.7 to 52.3°, while a PG oriented at 5° moves the CoM to 58.3°. The CoM of the complex cell response function shifts from 69.3° either to 62.9 or 71.2° with PGs oriented at 95 and 45°, respectively. Here the shift of the CoM is repulsive, moving away from the orientation of the PG.

Changes in the optimum orientation for the simple cell shown in Fig. 2A might be explained by selective response suppression near the orientation of the PG. However, the complex cell shift in Fig. 2B also demonstrates response facilitation at orientations away from that of the PG. Displacements of the response function peak and CoM locations can thus

**FIG. 2.** Perturbed orientation response functions. A: a simple cell’s orientation response function (solid line) and the function after the addition of spatially congruent gratings oriented at 5° (long dash) and 105° (short dash). B: a complex cell’s orientation response function (solid) and the function with perturbing stimuli at 45° (long dash) and 95° (short dash). Changes in the peak response location by perturbing stimuli lead to a measure of response suppression between the peaks in addition to the measure at the orientation generating the single grating peak response.
result from suppression and facilitation that is asymmetric about the base grating response function peak or CoM location. Due to these complexities, no single analytic model (e.g., a Gaussian function) could be applied and capture the salience of the broad variety of the changes seen. However, response function peak and CoM shifts are convenient descriptions that reduce this complicated operation into simple metrics.

Presentation of a PG also resulted in significant changes in the orientation tuning bandwidth. The simple cell’s full-width half-height (FWHH) response bandwidth to a PG oriented at 105° expands from 33.0° (single grating) to 49.4°, and to 37.7° with a PG oriented at 5°. The complex cell’s FWHH bandwidth of 34.3° (single grating) contracted slightly to 33.5° and expanded to 42.4° with PGs oriented at 95 and 45°, respectively.

Because PGs can shift the location of the response function peak, the degree of response suppression differed when assed at the orientation that generated a peak response with a single grating (\(d_{sg_p k}\)) and between the response function peaks found with single and double gratings (\(d_{dp k}\)). In the case of the simple cell and PG oriented at 105° (Fig. 2A), the suppression measured between response function peaks is 66% as opposed to 71% measured between the two functions at the location of the single grating optimum orientation. Similarly, for the complex cell and the PG oriented at 45°, the suppression between peaks is 35% as opposed to 38% measured at the location of single grating optimum orientation (Fig. 2B).

Because response suppression can also depend on a second grating’s spatial frequency (Bauman and Bonds 1991; DeValois and Tootell 1983), we measured the cell’s response function when exposed to PGs that were of the same orientation as the base grating but had spatial frequencies outside the cell’s response range. Figure 3 shows spatial frequency response functions for a simple cell (A) and a complex cell (B). The addition of a PG with a spatial frequency of 0.4 c/deg shifted the simple cell’s optimum spatial frequency from 1.00 c/deg (single grating) to 0.80 c/deg (Fig. 3A). A PG with a spatial frequency 0.8 c/deg added to the base grating shifted the location of the complex cell’s response peak from 0.38 to 0.29

FIG. 3. Perturbed spatial frequency response functions. A: a simple cell’s spatial frequency response function (solid line) and the function after the addition of a spatially congruent stimulus at 0.4 c/deg (dashed line). B: a complex cell’s spatial frequency response function (solid line) and its response in the presence of a 0.8 c/deg perturbing stimulus (dashed line). Similar to orientation response functions, the response function peak location shifts. The response suppression measured at the spatial frequency generating the single grating peak response is greater than the suppression measured between the 2 peaks.
c/deg (Fig. 3B). The 0.4 c/deg PG shifts the simple cell’s CoM from 0.97 to 0.95 c/deg. The 0.8 c/deg PG caused the complex cell’s CoM to shift from 0.38 to 0.35 c/deg. Neither the simple cell’s 1.54-octave bandwidth nor the complex cell’s 2.25-octave bandwidth changed significantly.

The shift in the peak response as a function of base grating spatial frequency from PGs of differing spatial frequency also results in greater apparent response suppression at the location of the single grating optimum spatial frequency. The simple cell in Fig. 3A shows a response drop of 38% at the location of the single grating stimulus optimum spatial frequency but only 29% between the two peaks. Similarly, the complex cell’s suppression is measured as 49.3% at the location of the single grating peak response, but only 31.8% between the two peaks (Fig. 3B), again demonstrating that the usual measure of response suppression overestimates the actual response suppression.

**Orientation response function suppression across a population of neurons**

Across a population with PGs of different orientations, we generally found that a cell shows response suppression that is proportional to the angle between the PG orientation and the single grating optimum orientation (dOR), at least within the range of dOR that we explored (30°–90°). In some cases, usually those in which the PG was oriented nearer to the preferred orientation, facilitation was found. This presumably indicates encroachment of the PG into a range of excitatory orientations that was subthreshold with a single stimulus. Figure 4 displays a typical pattern in one cell of response suppression as a function of dOR. The difference in responsiveness is shown measured at the optimal orientation ($d_{sg\_pk}$), diamonds and that between the peaks of the unperturbed and perturbed perturbed response functions ($dpk$, circles; see e.g., Fig. 2). We assumed that because of the symmetry of orientation tuning functions the suppression magnitude was a function of the magnitude (but not necessarily the sign) of dOR (e.g., Bishop et al. 1973), and separated the data along the dOR = 0° axis. Linear regressions on each half of the divided data represent an approximation of the dependence of the cell’s response on dOR, irrespective of whether the neuron’s response was generally suppressed or, in some cases, facilitated. In Fig. 4, the linear regression on data generated using negative dOR values has a slope of $-4.75$ and intercept $-260$, and a slope of $2.05$ and intercept $-94$ for positive dOR values. The signs of the slopes show that suppression on both sides of dOR = 0° increases with the angle between the PG and the orientation generating the single grating peak response, at least as far as an orientation difference of about 70°. Although dOR intercept values are the traditional representation of a linear regression, they may be interpreted accurately only over the range of measured values; thus they indicate the dOR value at which a trend reverses. In this case the negative values for intercepts indicate facilitation occurring at smaller measured dOR values, changing to suppression for larger values.

All 21 complex and 20 simple cells tested with PGs of various orientations (across a total of 177 trials) had at least one case in which the perturbed response function differed significantly from responses to at least one control preceding and one control succeeding the test. To find whether the suppression patterns found in simple and complex cells represent either a common or two different distributions (Morrone et al. 1982), we calculated the mean of the response suppression for simple and complex cells independently. Here and except where noted, the means for simple cells (26.15%, conf 95% = ±8.9%) and complex cells (19.25% conf 95% = ±7.7%) were not significantly different, so the results from the two sets of cells were combined.

Across all cells tested using PGs with negative (counterclockwise) dOR values, the maximum suppression found was 90.57%, and the maximum negative suppression (i.e., facilitation) was −81.54%. The overall average was 20.26% (conf 95% = ±1.38%). Measurements made using PGs with positive (clockwise) dOR values show suppression extremes of 89.8 and −105.8%, with a 22.8% (conf 95% = ±1.33%) average, indicating an approximate symmetry of the effect across the direction of the orientation difference.

To determine whether suppression in all cells followed a common underlying pattern, we calculated linear regressions (similar to Fig. 4) on data from each cell individually and then combined the results. The distribution of slope values produced by these regressions is summarized in Fig. 5. The top half of the figure shows data resulting from trials using PGs with negative dOR values; the bottom half of the figure shows results for positive dOR trials. In both cases, the majority (62%) of the cells show response suppression increasing with
increasing dOR magnitude. PGs with negative dOR values result in an average slope of $-0.93\%/\text{deg}$ with an average intercept at $-23.86\%$, and PGs with positive dOR values result in regressions with an average slope of $1.14\%/\text{deg}$ and intercept at $-23.22\%$. An average neuron thus shows increased response suppression with increasing dOR magnitude regardless of its sign. Additionally, the negative values for the intercepts indicate that an average neuron shows facilitation for smaller dOR values, and only larger dOR values actually suppress the response. In 11/19 cases, the last point of the curve at dOR values of 50–80° does not appear to fall on the fit curve, suggesting a breakdown of this trend for the largest dOR values. On average, the intercepts and slopes were uniformly distributed with an average value of zero. Although in individual cells suppression measured between response function peaks can strongly depend on the SF of a PG, there is no common trend over the population. We also measured response perturbation at the SF that produced the peak response for a single grating ($dsg_{\text{pk}}$) as a function of dSF. Again, individual cells could show large changes, but linear regressions result in slopes and intercepts with an average of zero for both positive and negative dSF values. This measure of response suppression overestimates the actual suppression by a factor of about 1.6.

**Shifts in orientation response function location**

To determine the dependence of peak response dislocations on the PG orientation across a population, we measured shifts in the location of both the response function peak and the CoM. The location of the perturbed peak was compared with the average value for the control response function measured both preceding and after the test. All 41 cells tested with PGs of varied orientation showed significant peak shifts. The displacements tended to be repulsive for PGs with orientations close to ($\pm 50\%$) the orientation generating the single grating optimal orientation (dOR). The regression calculated on the data with negative dOR values in Fig. 6 has a slope of 0.14 deg/deg (i.e., degrees displacement per degree dOR) and an intercept of 6.19°. The regression on positive dOR values produced a slope of 0.11 deg/deg and an intercept of $-8.37\%$. The negative intercept for positive dOR values and the positive intercept for negative dOR values shows that the PG causes the orientation for peak response to shift away from the orientation of the PG, as also reported by Gilbert and Wiesel (1990) for perturbing line patterns.
positive slope for both negative and positive dOR values shows that the repulsion is strongest for nearby PGs, and that it decreases as dOR increases.

To test for a common trend across the population, we calculated linear regressions on peak shift versus dOR values from each cell. Figure 7 shows the distributions of slopes from these regressions, with separation of positive and negative dOR values. Tests using PGs with negative dOR values yielded an average slope of 0.14 deg/deg (conf95% = ±0.096), and the average slope for PGs with positive dOR values is 0.17 deg/deg (conf95% = ±0.064). As dOR increases, the peak shift is reduced then changes to attraction as dOR approaches about 50° distance from the optimum orientation for a single grating.

The population distribution of the peak shift is shown in Fig. 8A, which indicates the maximum significant displacement of the orientation tuning peak found for each cell (n = 41) in degrees, with negative displacements (n = 26) indicating repulsion by the PG and positive values (n = 15) attraction. Maximum shift values ranged from 1° to over 20° across the population. The mean maximum displacement for repulsion in a given cell was −7.61°, and the median was −6.29°. Of the fewer cells that showed attraction, the mean and median maximum values were 3.87 and 5.91°, respectively.

Because the shape of the tuning curve changed, often irregularly, in the presence of a PG, the CoM was considered a more characteristic indicator of the overall behavior of the function. We found significant CoM displacement in 19/20 simple and 20/21 complex (95% total) cells. The diamonds in Fig. 6 show typical changes in CoM location (dCoM) as a function of dOR for a single cell. Across the population (Fig. 8B), PGs resulted in 32 repulsive (negative) maximum CoM displacements and 9 attractive maximum displacements. The mean repulsive CoM displacement was −3.61°, with a median of −2.99°. For attraction, the mean dCoM was 3.42°, and the median was 2.32°. Like the peak dislocations, the CoM of a response function is, on average, repulsed by the PGs. Likewise, increasing dOR decreases the magnitude of the CoM shift, which changes from repulsion to attraction with dOR values around ±60°. Similar overall results are reported by Dragoi et al. (2000), who found using optical imaging that adaptation to gratings on the flank of a tuning curve caused shifts away from the adapting orientation, whereas adaptation to orthogonal gratings resulted in no shift.

**Shifts in spatial frequency response functions**

To determine whether the location of the spatial frequency peak response depends on dSF, we measured dislocations on the same set of data used for SF-dependent response suppression. Nineteen of the 23 cells (83%) had significantly shifted peaks. However, unlike the orientation response function shifts, these displacements did not predictably depend on the difference between the PG spatial frequency and the optimal spatial frequency.

**FIG. 6.** Response function location dependence on dOR. The circles represent dislocations of the cell’s peak response location (dpk). Diamonds represent changes in the response function center of mass (dCoM). We plotted the data as a function of the angle between the perturbing stimuli and the single grating peak response location (dOR).

**FIG. 7.** Distribution of slopes from linear regressions on shifts in the peak location. The distribution of the slopes from linear regressions showing the correlation between shifts in the optimum base grating orientation and dOR for negative dOR values (white bars) and positive dOR values (black bars).
This analysis is based on a combined set of 9 simple and 14 complex cells over a total of 78 trials. PGs with negative dSF values produced maximal shifts of $-0.123$ and $0.292$ c/deg. Positive dSF valued trials produced shifts ranging from $-0.122$ to $0.172$ c/deg. Figure 9A shows the population distribution of the maximum shifts encountered in the 19 cells with significant shifts, plotted as positive (toward the spatial frequency of the PG) and negative values. The mean for eight positive maximum values (attraction toward the PG spatial frequency) was $0.088$ c/deg with a median of $0.101$ c/deg. The mean for 11 repulsive values was $-0.079$ c/deg with a median of $-0.055$ c/deg. While it would appear from Fig. 9A that for maximum shifts there was a greater tendency for repulsion, the average shift over all data are zero, and regressions applied to data from individual cells yielded on average positive intercepts and slopes. The positive intercept values show that, on average, PGs with orientations near the optimum orientation for a single grating broaden the response function, and the slope values show that this broadening decreases in magnitude with increasing dOR and changes to compression at approximately $dOR = \pm 55^\circ$.

**Orientation response function bandwidth**

To measure changes in the bandwidth of a response function, we calculated the FWHH bandwidth. The full-width measure was required because PGs often disrupted the symmetry of the response function. With PGs, all 41 cells yielded at least 1 bandwidth measure that showed significant change. Collectively, orientation response function bandwidths tended to broaden with low dOR values.

Analysis is based on 20 simple and 21 complex cells over a total of 177 trials. Change in bandwidth from PGs with negative dOR values ranged from $128.0$ to $-40.3\%$, averaging $25.9\%$ (conf\(_{95\%}\) = $\pm 7.98\%$), with a positive change indicating a broadening of the response function. Change from trials with positive dOR values ranged from $98.0$ to $-52.7\%$, averaging $23.7\%$ (conf\(_{95\%}\) = $\pm 6.45\%$). Linear regressions formed on the data from individual cells yielded on average positive intercepts and slopes. The positive intercept values show that, on average, PGs with orientations near the optimum orientation for a single grating broaden the response function, and the slope values show that this broadening decreases in magnitude with increasing dOR and changes to compression at approximately $dOR = \pm 55^\circ$. 

![Figure 8](http://jn.physiology.org/)

**FIG. 8.** Distribution of the maximum $dpk$ (A) and dCoM (B) values generated by PGs. The distribution of peak shifts is maximum at approximately $6^\circ$ for both the positive (attractive) and negative (repulsive) $dpk$ values. The distribution of dCoM values similarly peaks at approximately $3^\circ$ for both positive and negative dCoM values. For further statistics see text.

This analysis is based on a combined set of 9 simple and 14 complex cells over a total of 78 trials. PGs with negative dSF values produced maximal shifts of $-0.123$ and $0.292$ c/deg. Positive dSF valued trials produced shifts ranging from $-0.122$ to $0.172$ c/deg. Figure 9A shows the population distribution of the maximum shifts encountered in the 19 cells with significant shifts, plotted as positive (toward the spatial frequency of the PG) and negative values. The mean for eight positive maximum values (attraction toward the PG spatial frequency) was $0.088$ c/deg with a median of $0.101$ c/deg. The mean for 11 repulsive values was $-0.079$ c/deg with a median of $-0.055$ c/deg. While it would appear from Fig. 9A that for maximum shifts there was a greater tendency for repulsion, the average shift over all data are zero, and regressions applied to data from individual cells result in average slopes and intercepts that are also zero. Although a PG can usually change a cell’s optimum spatial frequency, the new location of the response function peak has no apparent relationship to the spatial frequency of the PG.

We also measured changes in a response function’s CoM as a function of dSF. All 23 cells showed at least one significant CoM shift. PGs with negative dSF values (Fig. 9B) dislocated the CoM up to $0.10$ and $-0.048$ c/deg away from the optimum measured with a single grating. Positive dSF-valued trials result in shifts ranging from $-0.05$ to $0.11$ c/deg. As with peak shifts, the size and direction of the CoM shifts were evenly distributed over all spatial frequencies, and the average CoM shift was zero.

![Figure 9](http://jn.physiology.org/)

**FIG. 9.** Distribution of maximum spatial frequency tuning shifts for $dpk$ (A) and dCoM (B) found with PGs of differing spatial frequencies. While some individual cells showed substantial shifts, across all shifts there was a balance of repulsion and attraction, resulting in a population average of zero shift. Further statistics are presented in the text.
Spatial frequency response function bandwidth

In the spatial frequency domain, PGs resulted in significant bandwidth changes in all 14 complex cells, but in only 4/9 (44%) simple cells. Here we separate the data from simple and complex cells.

Complex cells perturbed using gratings with negative dSF values displayed bandwidth compression ranging from 100 to $-25\%$, averaging 41.8% ($\text{conf}_{95\%} \pm 4.65\%$). Bandwidth compression for complex cells exposed to PGs with positive dSF values ranges from 60 to $-53.8\%$, averaging 11.6% ($\text{conf}_{95\%} = \pm 3.01\%$). Linear regressions on data from individual cells perturbed with negative dSF-valued stimuli have an average slope of 107.1%/c-deg$^{-1}$ and intercept of 78%. The average slope for linear regressions on data from complex cells perturbed with positive dSF gratings is $-66.86%/c$-deg$^{-1}$ with an average intercept of 41.44%.

Simple cell bandwidth expansion caused by PGs with negative dSF values ranged from 25 to $-50\%$, averaging $-3.79\%$ ($\text{conf}_{95\%} = \pm 2.81\%$). Changes in the bandwidth of the base grating response function ranged from 140 to $-63.6\%$, averaging 5.51% ($\text{conf}_{95\%} = \pm 2.11\%$) for gratings with positive dSF values. Linear regressions on the data from simple cells result in an average slope and intercept equal to zero. While complex cell spatial frequency response function bandwidths are systematically changed by PGs, simple cell bandwidths are only affected minimally.

DISCUSSION

PGs modify a cell’s response to a base grating by 1) suppressing or facilitating response rates, 2) displacing response function peak and center of mass locations, and 3) compressing or expanding the bandwidth of the response function. The change in amplitude seen between the response function peaks demonstrates facilitation by PGs when measured with orientations close to ($\approx 50^\circ$) the orientation that generated the single grating peak response, with suppression occurring and increasing for PGs farther away from that orientation. The method of measuring suppression is important because the usual measure applied to response functions (at the single-stimulus peak) overestimates the amount of actual suppression due to the tuning peak shifts. In the orientation domain, the base grating peak and CoM shifts are usually repulsive in nature, decreasing in magnitude with increasing angles between the perturbing orientation and the optimum single grating orientation and changing to attraction at about 50°. The peak and CoM shifts were greatest with PGs nearest to the orientation generating the single grating peak response. Since the shifts were repulsive, when the shift was greater, the measured suppression at points between the original response function peak and the PG orientation was greater. Overall, PGs slightly broaden the orientation tuning function of all neurons and the spatial frequency response function of complex cells, but simple cell spatial frequency functions usually show little or no bandwidth change. Considering the complex nature of the interactions explored so far, we do not claim to have uncovered all possible influences from PGs. However, the responses that we have found would appear to be sufficiently well-organized to support the improvement of discrimination between the orientations of two simultaneously presented stimuli by an ensemble of neurons.

Response function suppression

Trends in the data presented here predict decreasing suppression for decreasing dOR values, with a maximum facilitation at dOR = 0°. The prediction of maximum suppression of the base grating by PGs with orientations orthogonal to the single stimulus optimum orientation is consistent with suggestions from previous studies (e.g., Bishop et al. 1973; Morrone et al. 1982). However, since we generally did not make measurements with PGs at the orthogonal orientation, we cannot confirm this projection. In some cases we saw reduction of suppression when the PG approached the orthogonal orientation, which is consistent with the observation in some cases of the greatest response suppression being found near the excitatory bandwidth limits of the single grating orientation response function (Bonds 1989).

These results are collectively consonant with the model of lateral inhibition in the orientation domain, first described psychophysically by Andrews (1967) and elaborated by Blake et al. (1970), Benevento et al. (1972), Bishop et al. (1973), and Carpenter and Blakemore (1973). In this model, orientation detectors consist of an excitatory orientation tuning function in combination with a more broadly tuned inhibitory orientation tuning function contributed by nearby detectors. Both tuning functions peak at about the same angle, but the relatively stronger contribution from the inhibitory mechanism as one moves away from the peak results in narrowing of the observed tuning function. The greatest impact of suppression can occur near the flanks of the excitatory tuning function or at the orthogonal, depending on the breadth of the overall inhibitory contribution. This result is likewise suggested by the dynamic tuning curves measured by Ringach et al. (1997). One pathway for this inhibitory input arises from the more broadly tuned inhibitory cells of lower layer 5 and upper 6 (Kisvarday et al. 1987) impinging on cells in layers 2/3 (Allison and Bonds 1994).

Suppression and/or shift of a cell’s spatial frequency response function is another example of spatial nonlinearity. The most significant difference between PG influences on orientation and SF response functions is that on average the latter show only a small amount of suppression and no shift, even though individual cells can show large changes. The lack of organized dependence on the perturbing SF may reflect the lack of an orderly physiological substrate for SF, unlike the clear pattern of orientation columns. Use of 2-deoxyglucose (Tootell et al. 1981) shows a columnar organization for SF in the cat visual cortex but does not reveal how the columns are related to one another. Similarly, analysis of electrode penetrations indicates a tendency for cells preferring similar spatial frequencies to be grouped, but there is no smooth transition between groupings, and adjacent cells can often have quite dissimilar spatial frequency preferences (Tolhurst and Thompson 1982). Optical imaging of neural activity reveals the presence of two more or less distinct groups of clusters, one selective to low spatial frequencies and high speeds and the other to high spatial frequencies and low speeds (Shoham et al. 1997). This can result in abrupt transitions at cluster borders and is thus consistent with the findings of Tolhurst and Thompson (1982). If local interactions were based on lateral inhibition in the spatial frequency domain, one might therefore expect at least some cells to have clearly demonstrable inhibitory flanks.
(Bauman and Bonds 1991; Ringach et al. 2000), with concomitant shifts of spatial frequency preference in the presence of PGs, while other cells might show little effect. This is also consistent with the apparently random organization of repulsion and attraction of spatial frequency peaks that we observed.

Mechanism for response function shifts

A change in the location of the peak of an orientation response function in the presence of a PG is consistent with lateral inhibition in the orientation domain. In many cases this shift was manifested not merely as a dislocation of the maximum but also as a displacement of the entire curve (e.g., Fig. 2). This result, together with suppression, can arise from a combination of inhibition for angles that are closer to the PG and disinhibition for angles that are further away (on the opposite side of the response function). This can occur by invoking a restriction of the range of effectiveness of the lateral inhibition, similar to that seen in the spatial domain (Hartline and Ratliffe 1957). Locally, the PG causes inhibition of adjacent orientations, but by decreasing the activity of these cells, their inhibitory impact on cells tuned to further orientations is decreased. The disinhibition that results in supragranular cells from inactivation of subgranular cells (Allison and Bonds 1994) is appropriate both in position (relative to the orientation peak) and magnitude to support this effect.

Psychophysical correlations

A consequence of shifting response functions is that the presence of one or more PG changes the grating orientation to which a neuron is most sensitive. Since the population of neurons exhibits a common trend, if higher cortical areas determine orientation from an ensemble input, confusion will occur by the differential activity within an ensemble (as opposed to strict excitation), perceived angle expansion will occur. This is because, as proposed above, the preferred orientations near to the base stimulus and slightly closer to the perturbing stimulus will be more densely packed than orientations further away, so that higher centers respond as if the angle between base and perturbing orientations is greater than its actual value. Consider a simplified example in which five cells are tuned to orientation ranges of 85, 88, 90, 92, and 95°. When driven by a stimulus oriented at 90°, the expected response from each might be {15, 18, 20, 18, 15} spikes/s. Adding a PG at 50° results in tuning peak shifts (due to repulsion) to {89, 90, 92, 94, 96} deg, with responses (from the 90° stimulus) now estimated to be {19, 20, 19, 18, 14} spikes/s. The simplified model assumes no change in the tuning bandwidths of the cells, merely a displacement of the tuning curve.

Here we presume that orientation is signaled by relative activity, which is calculated simply as the difference between the response of a given cell and the average response of its two neighbors. With a single grating at 90° the differential coding results in figures of {0.5, 2, 0.5} for the central three orientations of {88, 90, 92} deg, and thus the perceived orientation will be 90°. The PG yields relative responses of {1.0, 0, 1.5} for these same three cells and the perceived orientation will be 92°. Reciprocal activity patterns from cells tuned near to the orientation of the PG results in similar apparent displacement in the other direction, yielding a total angle expansion of 4°. Note that in this example the five cells initially spanning 10° of orientation (2.0° per cell) now span 7° of orientation (1.4° per cell). Such a coding scheme has the benefit that it results in increased discrimination.

If instead one relies on strict interpretation of the concept of labeled lines and detection by absolute, rather than relative, response levels, analysis of the repulsive shift of orientation response functions could also paradoxically predict compression of the perceived angle. Consider a cell A with a normal tuning peak at 90°, being stimulated at that orientation. Now, add a second grating at 60°, which is outside the excitatory passband of cell A. Through lateral inhibition, this second grating will depress the signal from cell A as well as shift the preferred orientation of cell A to, say, 95°. By the same mechanism some other cell B, which has a normal peak for orientation at 85°, will also have its peak moved by the second grating, in this case to 90°. A grating oriented at 90° will thus drive cell B more efficiently than it drives cell A. On the basis of this proposition, the perception of the grating will be one of 85°, which is a contraction, rather than expansion of the relative angle. The observation that perception tends to exaggerate narrow angles would discourage this interpretation, but this kind of influence may have some mitigating effect on the expansion discussed above.

The evidence presented here shows that the spatial organization of neurons in the primary visual cortex can be modified in real time, and that changes are dependent on context of the visual scene. Many cells show modification that is predictably dependent on the orientation and spatial frequency of second-order stimuli that do not excite the cell. Because of this behavior we can no longer consider a cell’s response to be a stationary linear or quasi-linear independent combination of the cell’s responses to individual orientations and spatial frequencies. We must now consider the response of a striate cortical neuron to be dependent on the relationship between all of the orientations and spatial frequencies present.

REFERENCES


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