Primate area V1: largest response gain for receptive fields in the straight-ahead direction

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Although neuronal responses in behaving monkeys are typically studied while the monkey fixates straight ahead, it is known that eye position modulates responses of visual neurons. The modulation has been found to enhance neuronal responses when the receptive field is placed in the straight-ahead position for neurons receiving input from the peripheral but not the central retina. We studied the effect of eye position on the responses of V1 complex cells receiving input from the central retina (1.1–5.7° eccentricity) while minimizing the effect of fixational eye movements. Contrast response functions were obtained separately with drifting light and dark bars. Data were fit with the Naka–Rushton equation: $r(c) = R_{max} \times c^n/(c^n + c_{50}{}^n) + s$, where $r(c)$ is mean spike rate at contrast c, R_{max} is the maximum response, c_{50} is the contrast that elicits half of R_{max}, and s is the spontaneous activity. Contrast sensitivity as measured by c_{50} was not affected by eye position. For dark bars, there was a statistically significant decline in the normalized R_{max} with increasing deviation from straight ahead. Data for bright bars showed a similar trend with a less rapid decline. Our results indicate that neurons representing the central retina show a bias for the straight-ahead position resulting from modulation of the response gain without an accompanying modulation of contrast sensitivity. The modulation is especially obvious for dark stimuli, which might be useful for directing attention to hazardous situations such as dark holes or shadows concealing important objects (Supplement 1: Video Abstract, Supplemental digital content 1, *http://links.lww.com/WNR/A295*). *NeuroReport* 25:1109–1115 © 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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Introduction

In the primary visual cortex of primates (V1), complex attributes of visual stimuli, such as orientation and related direction of movement, are coded in neural activity [1]. In addition to the spatiotemporal parameters of visual stimuli, V1 responses are also influenced by the position of the eye in the orbit [2–5]. As the initial results displayed a diversity of effects, a systematic pattern was recognized only recently by Durand *et al.* [6]. They demonstrated that eccentric eye position resulted in enhanced responses when receptive fields of V1 cells receiving input from the peripheral retina (median eccentricity 14.8°) were placed in the straight-ahead direction. They described this as 'privileged processing of the straight-ahead direction' and suggested that it could be important during navigation of cluttered natural environments. Durand and colleagues did not detect a preference for the straight-ahead location in a heterogeneous sample of neurons receiving input from the central retina, where effects would be expected to be smaller.

To improve sensitivity for detecting smaller effects, we focused on complex cells that are not direction-selective, which comprise a large fraction of our neuronal samples from V1 [7,8]. In previous experiments on primates, unspecified, heterogeneous samples of neurons have been analyzed.

Because of its visual importance, we have also analyzed the interaction of stimulus contrast with eye position by measuring contrast response functions separately for bright and for dark stimuli. Responses were described by a hyperbolic ratio function [9], also known as the Naka–Rushton equation:

$$r(c) = R_{\max} \times c^n / \left(c^n + c_{50}^n\right) + s, \qquad (1)$$

where $r(c)$ is cell firing response at contrast c, $R_{\max}$ is the maximum response, c_{50} is the contrast sensitivity, the contrast that elicits the half of $R_{\max}$, n is nonlinearity, s is spontaneous (ongoing) activity. This approach has the advantage that specific model predictions are possible: in a contrast gain model, the contrast response function is shifted horizontally, which is related only to c_{50} changes; in a response gain model, $R_{\max}$ is changed, which is related to a multiplicative effect on the contrast response function; and in a nonlinearity change model only the

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constant n is changed [10]. Our results are consistent with a change in response gain as a function of eye position but not a change in contrast gain or contrast sensitivity.

Although many studies of visual neurons have used gratings that combine positive and negative contrasts, 'darks' occur more frequently than 'brights' in natural scenes and 'darks' and 'brights' are treated differently by the visual system [11]. In this paper, we present the first measurements of the effects of eye position that separately analyze responses to bright and to dark stimuli.

Materials and methods

Data were collected from a female rhesus monkey (M46) prepared for electrophysiological recording and trained to fixate as previously described [12]. This monkey was one of a group of four macaques used to study effects of eye movements [13] and response properties of complex cells in V1. Data from M46 are similar to data from the three other monkeys in the following ways: (a) proportion of simple and complex cells, relative modulation, and spatial frequency selectivity (Kagan I, Gur M, Snodderly DM, in preparation); (b) visual and extraretinal effects of saccadic eye movements [13]; and (c) direction selectivity, orientation selectivity, and spontaneous activity [14]. Although we were limited for logistical reasons from varying eye position with the other animals, comparisons of neuronal activity among the four animals with the fixation target straight ahead indicate that the visual physiology of M46 is representative of the group. All procedures complied with the NIH guidelines.

Nerve spike and eye position recording

Single units were recorded extracellularly with quartz-insulated platinum-tungsten alloy electrodes (Thomas Recording Giessen, Germany) with impedance at 1 kHz of 1–5 MΩ. Signals were amplified and band-pass filtered (300–5000 Hz) by TDT hardware (Tucker-Davis Technologies Alachua, Florida, USA) and processed with the BrainWare (TDT, Matlab, MathWork, Natics, Massachusetts, USA) software package and custom software written in Matlab. Position of the dominant eye was monitored by a scleral search coil [15], whose signal was amplified (Remmel Labs EM7 Katy, Texas, USA) sampled at 200 Hz and recorded along with spike arrival times (0.1 ms time resolution) and spike shapes collected at 20–25 kHz. The trial initiated when the monkey correctly pressed a lever in response to illumination of the fixation LED and continued for 5 s provided that the gaze remained within a predefined fixation window, usually about ± 1.0° Saccades were automatically detected using a stability criterion combined with a velocity threshold of 10 deg./s [16], and responses occurring within ~100 ms of a saccade were excluded during data analysis so that data were collected only during intersaccadic drift periods. Using this approach enabled us to accurately and reliably map receptive fields [7,12,16,17].

Stimulus presentation

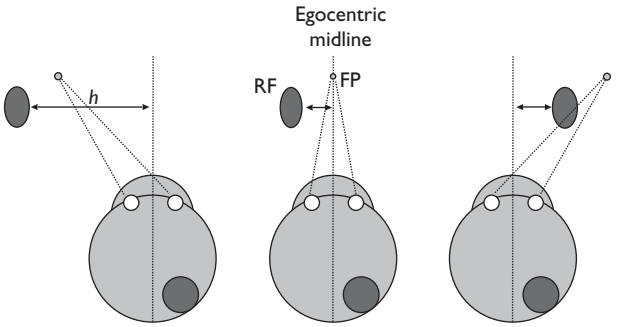
Stimuli were presented at a 160 Hz refresh rate (not-interlaced) on a 21 inch CRT monitor (Sony, 500 PS) with the fixation LED attached, viewed binocularly at a distance of 115–172 cm. The LED was positioned so that the receptive field of the neuron was approximately centered on the screen. To collect data at different eye positions, the monitor and LED were moved together to different horizontal positions: 0 (straight ahead), 10° left, and 10° right (Fig. 1).

Visual stimuli were drifting bars that were optimized for orientation, length, velocity, and color (green or red). Incremental (bright) bars and decremental (dark) bars were presented on the same background, either a color produced by activation of a single gun of the monitor or a neutral gray background of the same luminance [12]. We found no noticeable difference between receptive fields mapped with luminance increments and decrements presented on a color or a gray background.

Receptive field mapping

The width and location of receptive field activating regions (ARs) was estimated with increment and decrement bars (bar width 2–16 minarc, mean 7 ± 3 minarc) swept forward and back at 1.5–7 deg./s across the receptive field in a direction orthogonal to the optimal orientation axis [7]. Bars were 0.3 log unit brighter or darker than the background; bright bars were 10 cd/m^2, dark were 2.5 cd/m^2, and background was 5 cd/m^2. Average peristimulus time histograms of responses were constructed, and the AR width was measured as 95% of the region of increased firing (see Fig. 1 of Kagan *et al.* [7]).

Fig. 1



Schematic of three different eye positions in the orbit (10° left, straight ahead, 10° right) illustrating the relationship between hypothetical receptive field (RF) and the absolute horizontal distance from the egocentric midline (h). For RFs located in the left visual field, the distance h is largest for fixation to the left, smaller for fixation to the right, and minimal for fixation straight ahead, at the range of RF eccentricities (< 5°) and 10° eye position shifts used in our dataset, FP = fixation point.

To distinguish between complex and simple cells, an overlap index (OI) was calculated as:

$$\mathrm{OI} = \frac{0.5\,(W_{\mathrm{INS}}+W_{\mathrm{DEC}})-\mathrm{sep}}{0.5\,(W_{\mathrm{INC}}+W_{\mathrm{DEC}})+\mathrm{sep}}, \qquad (2)$$

where W_{INC} and W_{DEC} denote the widths of increment and decrement ARs and sep denotes the separation between AR centers [7]. This index ranged from negative values for spatially separated INC ('on') and DEC ('off') ARs to 1 for complete and symmetric overlap. Cells with OI greater than 0.5 were considered complex. The total extent of INC ('on') and DEC ('off') ARs was considered the classical receptive field. Only complex cells with two ARs are included in the present sample. We restricted our analysis to this cell class for three reasons: (a) complex cells with two ARs are the most frequent cell type we encounter in V1 [7,8]; (b) small effects are easier to detect in a uniform sample; and (c) both light and dark stimuli could easily be tested under identical spatial conditions on the same cells.

With the eye looking straight ahead, receptive fields in this sample were in the lower left visual field between 1.1 and 5.7° eccentricity (0.2 and 5.25° horizontal eccentricity).

Contrast response measurements

Once the receptive field had been mapped, complete contrast response functions were obtained with a drifting light bar for 17 cells and with a dark bar for 11 of the same cells. A contrast of 1 was defined as twice the background luminance for the bright bars and one-half the background luminance for the dark bars. The contrast series (nine values) typically consisted of the following multiples of the maximum contrast for light and dark bars (0, 0.01, 0.02, 0.04, 0.08, 0.16, 0.32, 0.64, 1). A complete contrast series at all three eye positions was collected for all except one cell, for which data were collected for two eye positions.

The extent of the sweep was adjusted so that the motion of the bar covered an area slightly larger than the receptive field and the bar was swept across the field several times during the trial. The average number of spikes fired during each sweep (combining both directions of motion accumulated across multiple behavioral trials) was computed and converted to an average spike frequency by dividing by the duration of the sweep. This frequency was slightly lower than average spike frequency based on the precise width of the classical receptive field, but the extent of the sweep was constant across conditions; hence, it did not bias the results. Utilizing a longer sweep had the advantage of minimizing the effects of small errors of positioning and measurement. Even with this slight underestimate, the spike frequency ranges recorded were similar to the ranges recorded in earlier studies (fig. 7 of Albrecht and colleagues [9,18]).

Data analysis

The average spike frequency data were fit with the hyperbolic ratio (Naka–Rushton) equation (Introduction) using the curve-fitting tool in Matlab to estimate parameters and to calculate the 95% confidence intervals for the curve fits at different eye positions. Statistics reported for the parameters $R_{\max}$, the maximum response, and c_{50}, the contrast evoking half the maximum response, are mean ± SE. *T*-tests for group comparisons and *F* statistics for the coefficients of linear regressions were computed with the Matlab statistical toolbox.

Results

Effects of eye position

The contrast response functions of V1 neurons were well fit by the hyperbolic ratio equation for all experimental conditions. Figure 2 shows an example of contrast response functions for bright and dark bars where the maximum response occurred at different eye positions. Similar to earlier authors, we found that eye position had varied effects on the responses of V1 neurons [2–5]. In many cases, there was a clear preference for the straight-ahead eye position, illustrated in the top row, but there were also examples of the converse, illustrated in the bottom row. To confirm the reliability of the measurements, the contrast response in the straight-ahead position was remeasured on seven occasions, and the mean absolute difference in $R_{\max}$ was only 9.3%. An example of repeat measurement of a full contrast response curve is illustrated in the upper right panel of Fig. 2 (*cf.* squares and circles).

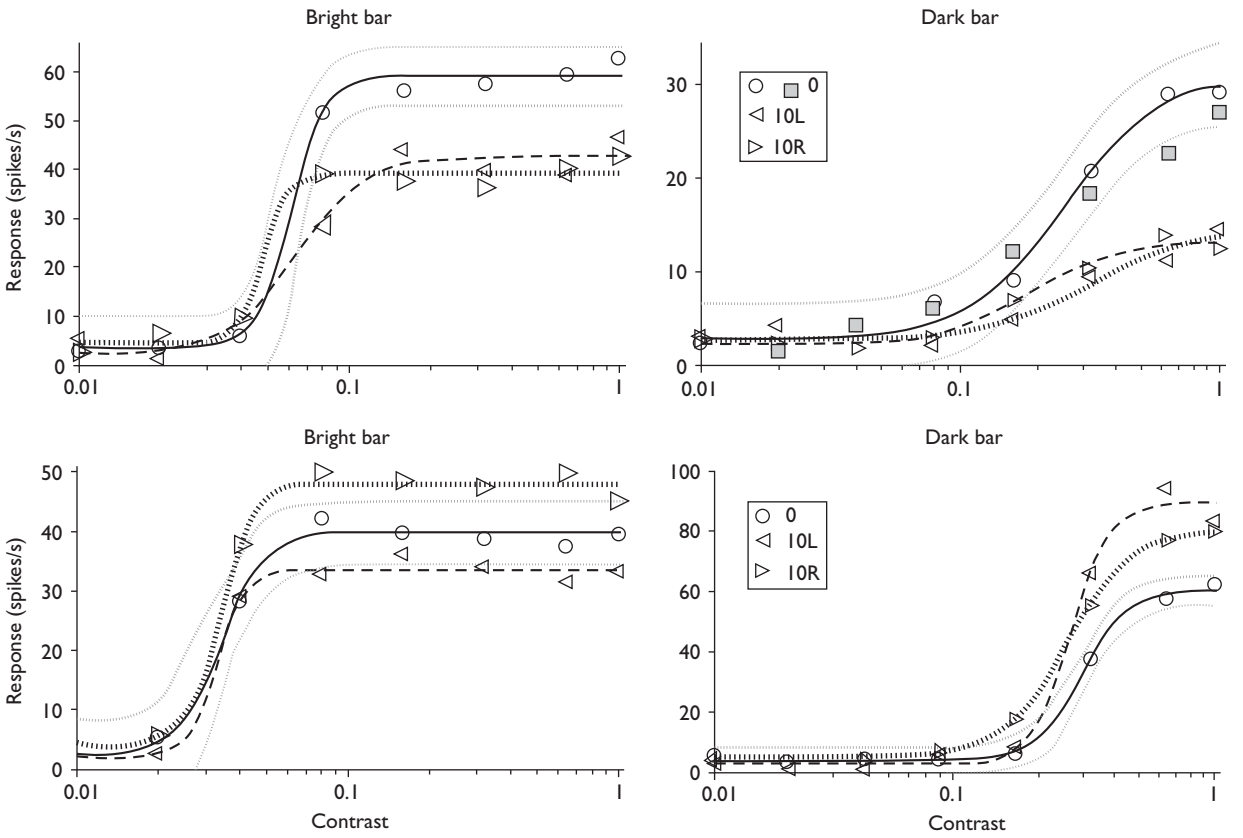
To summarize the overall effect of eye position across cells, the $R_{\max}$ values were normalized by dividing the $R_{\max}$ for each eye position by the mean of the $R_{\max}$ values across all three eye positions for each cell. Bright bar and dark bar responses were analyzed separately. The normalized $R_{\max}$ values for all cells are plotted at their respective horizontal receptive field positions for the three eye positions in Fig. 3.

When eye position was straight ahead (EP0), receptive fields were scattered in the lower left visual field as determined by the topographic map in the cortex. As the monkey fixated eccentrically, receptive fields moved with the eye to different horizontal positions in space [18]. For bright bars, there were no significant differences in mean responses at different eye positions, and for dark bars only the difference between responses in the left eye position and the straight-ahead position was significant ($P < 0.01$ by *t*-test, two tailed).

Effect of receptive field position

Durand *et al.* [6] found that the responses of V1 neurons receiving input from the peripheral retina were modulated by eye position such that the strongest response

Fig. 2



Example of contrast response functions of V1 complex cells measured at three different eye positions and fit with the hyperbolic ratio equation: straight ahead (EP0, thick line, open circles); 10° horizontally to the left (EP10L, heavy dashed line, left-pointing triangles); or 10° horizontally to the right (EP10R, finer dashed line, right-pointing triangles). Dotted, thin lines represent the 95% confidence interval around the curve fit to responses in the straight-ahead (EP0) position. As a measure of goodness of fit, mean r values for the three curve fits for each cell ranged from 0.986–0.994. Upper row left: cell 30b2, right: cell 0913_dec, responses were the largest at EP0, but in the bottom row left: cell 0302, right: cell 23_b2_dec responses were larger at other eye positions. Filled squares in the top right panel represent repeat measurements performed at EP0 after measures at EP10L and EP10R.

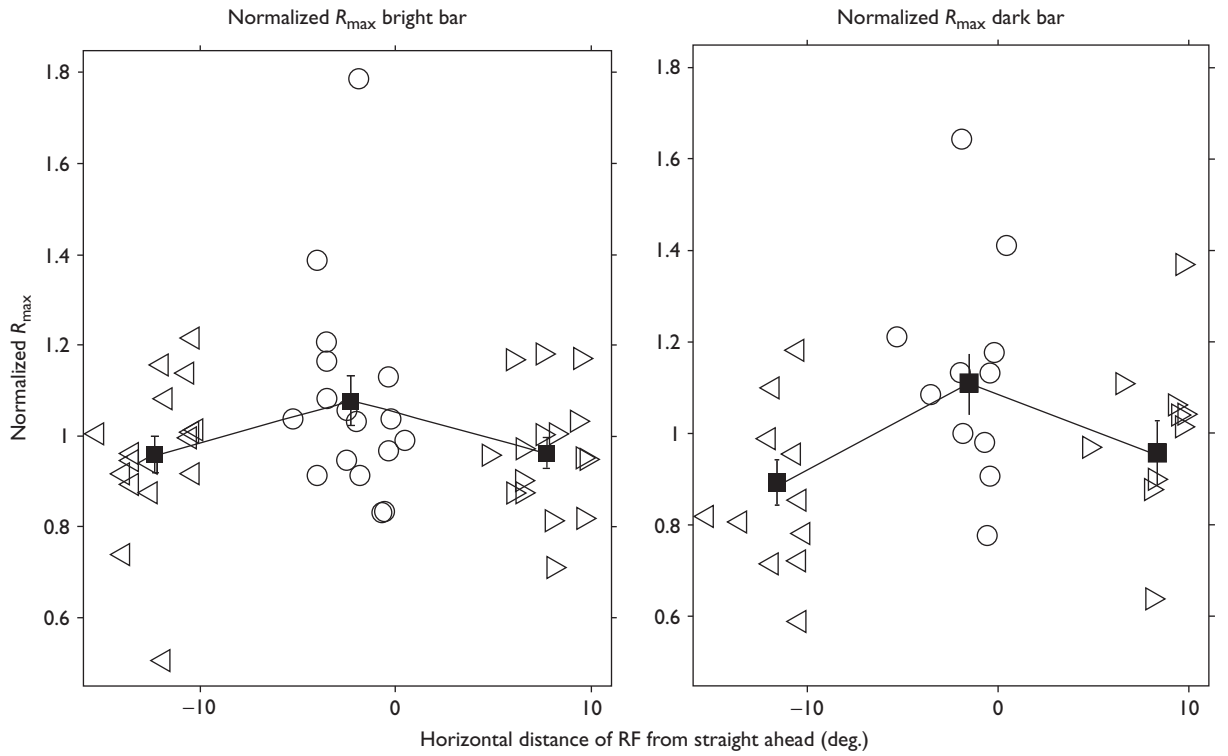
occurred when the gaze position placed the receptive field in the straight-ahead position, although the gaze was directed to one side. We have examined whether this principle also applies to our sample of complex cells that received input from the central retina. We treated horizontal receptive field location as an absolute distance from straight ahead and combined data for the right and left eye positions (Fig. 4).

For dark bars (right panel), higher responses were elicited when the receptive field was nearer to the straight-ahead direction ($n = 11$, $P < 0.02$ for slope; double-sided test). This outcome is consistent with the idea of privileged processing of the straight-ahead direction, and it indicates that the privilege extends to neurons receiving from the central retina. For bright bars (left panel), the effect of the egocentric direction of the receptive field was harder to demonstrate ($n = 17$, $P = 0.07$, double sided for slope), although we had a larger sample with bright bars. The effects of the receptive field position for dark and bright bars were not significantly different [t-test with variance of residuals $P > 0.1$; one-way analysis of covariance: mean slope, 0.098 confidence interval (-0.097 to 0.0292)], and there was no statistically significant difference in R_{max} at the central gaze position ($R_{max} = 36.4$ for dark bars, 33.3 for light bars). We note that Durand and colleagues did not use any dark stimuli for their measurements, which may have made it more difficult to detect the small effects of eye position on cells receiving from the central retina.

Unlike the effects on R_{max}, the contrast sensitivity, c_{50}, was not detectably affected by eye position or by the direction of the receptive field relative to straight ahead (Fig. 5). The c_{50} for bright bars was consistently lower than c_{50} for dark bars at all receptive field directions, and there was no significant trend for either bright or dark stimuli.

The mean spontaneous activity s (measured with contrast 0, $n = 17$) ranged from 4.1 to 5.2 spikes/s and was not

Fig. 3



Normalized maximum response, R_{max}, of the contrast response functions of V1 complex cells as a function of horizontal distance of the receptive field from the straight-ahead position. Circles and triangles indicate the eye positions (straight ahead, 10° right, and 10° left) that produced the particular receptive field locations. For these analyses, R_{max} has been normalized by dividing the values for each eye position by the mean of the R_{max} values across all eye positions for each cell. Left panel: normalized R_{max} measured with bright bars ($n = 17$ cells). Right panel: normalized R_{max} measured with dark bars ($n = 11$ cells). Filled squares indicate the mean R_{max} value at each eye position and error bars show SEs. RF, receptive field.

influenced by eye position (one-way analysis of variance, $P = 0.83$).

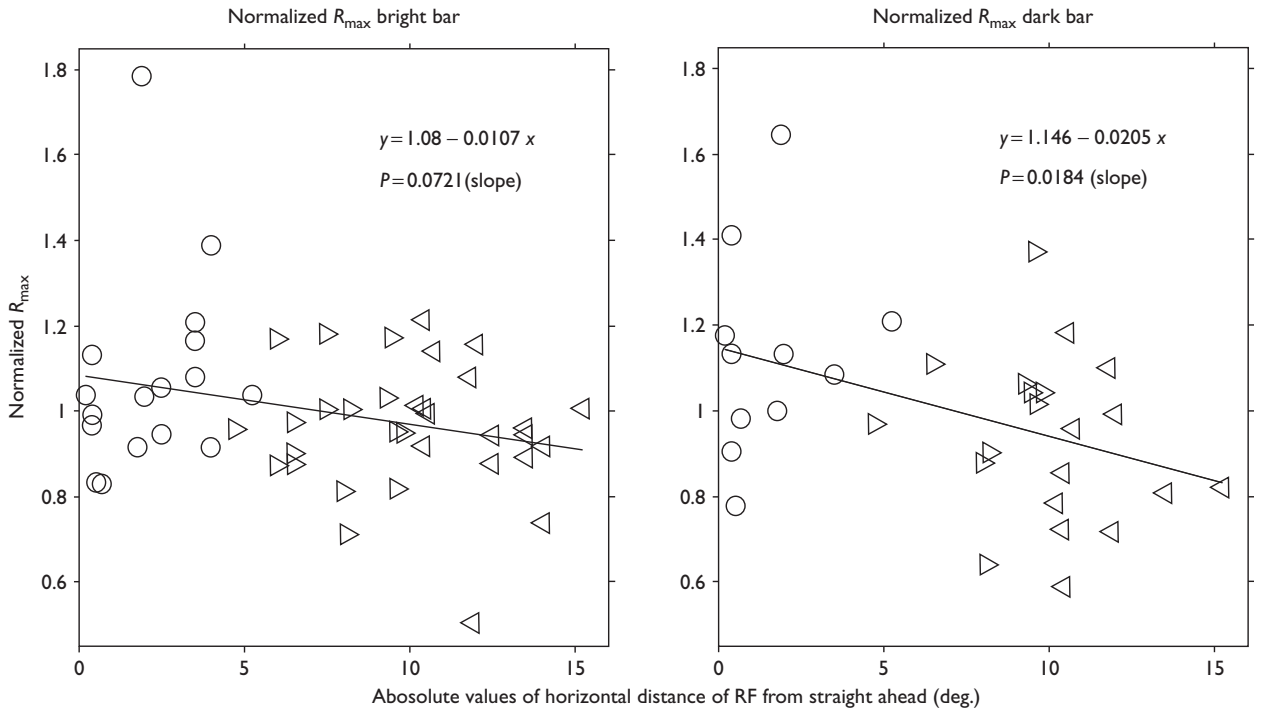
Discussion

Gaze position modulates neurons in many brain regions, and it has generally been thought to facilitate the localization and manipulation of objects in extrapersonal space [19]. The modulatory influence on cortical neurons can be described as a gain field that tunes the neuron to a particular direction in space [19]. If all directions in space were equally important, one could reasonably expect that all spatial directions would be equally represented in cortical populations. However, Durand *et al.* [6] discovered that gaze modulation of V1 neurons receiving input from the peripheral retina is directionally biased; neuronal responses are strongest when the gaze directs the receptive fields of the neurons in the straight-ahead direction.

In this paper, we have confirmed the basic concept of a bias in favor of the straight-ahead direction, and we found that it also applies to V1 neurons receiving input from the central retina. We believe that methodological refinements in our study improved our ability to detect these small effects, and they account for the differences between our results and those of Durand and colleagues. These refinements included the following: (a) we optimized stimulus parameters for each cell, including size, orientation, color, and speed of motion and (b) effects of fixational eye movements were minimized by removing data segments affected by saccades and by compensating for slow drift movements. Both refinements 1 and 2 should have a larger impact on responses elicited from neurons with small receptive fields in the central retina than responses from neurons with larger receptive fields in the periphery. Optimizing stimulus parameters elicits stronger responses, and minimizing effects of eye movements reduces variability in the data, leading to improved sensitivity to detect the effects of eye position in our experiments. Finally, focusing our analyses on a relatively uniform group of directionally unselective complex cells may have contributed to reduced variability of the results.

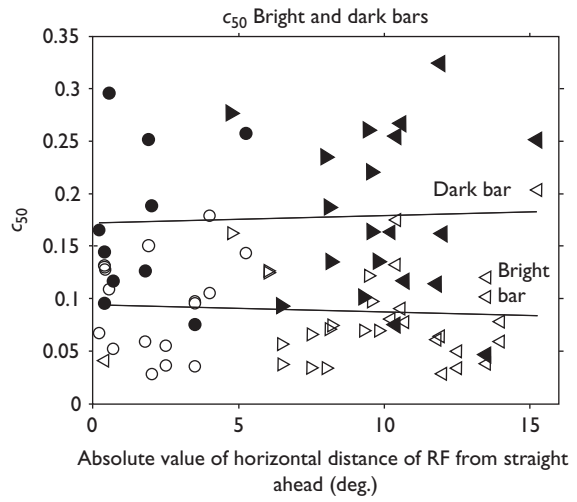
Another unique aspect of our experiments was the separate presentation of bright and dark stimuli. In addition, we constructed entire contrast response curves and showed that the gaze modulation affected the

Fig. 4



R_{max} of the contrast response functions of V1 complex cells as a function of the absolute horizontal deviation of the receptive field position from straight ahead. Same data and symbol conventions used for Fig. 3. Least squares regression lines, the corresponding equations, and the probability that the slope does not differ from zero (double sided) are indicated. RF, receptive field.

Fig. 5



Contrast sensitivity (c_{50}) of the same cells illustrated in Fig. 4 (not normalized) measured with dark bars (filled symbols) and light bars (open symbols) as a function of absolute deviation of the receptive field from straight ahead. Regression lines for both dark bar (upper line) and bright bar (lower line) data had slopes that did not differ from zero. RF, receptive field.

maximum response, R_{max}, but not the contrast sensitivity, c_{50}. In this respect, gaze modulation is similar to some other modulations of the contrast response, such as state of alertness [10] and feedback influence from area V1 to LGN [20].

Our results do not address the possible mechanisms contributing to gaze modulation of V1 responses, such as inputs from the extraocular muscles or top-down influences from higher cortical areas. Nevertheless, our results and those of Durand and colleagues show that the strength of modulation by eye position must be systematically matched to the topography of visual inputs to the cortex. To give privileged status to the straight-ahead direction, the gain fields [19] of V1 neurons must have their peak values at fixation locations that are mirror images of the spatial locations of their receptive fields when the eye is looking straight ahead. Future research will need to discover how this is accomplished.

A growing theme of recent research is an asymmetry in the way that the visual system treats lights and darks, beginning in the retina and continuing through to the cortex [11,21–23]. Our results add another aspect to this research area, suggesting that the contributions of eye movements may also be more readily apparent for dark stimuli. In a natural context, dark features such as shadows or holes may more strongly modulate V1 responses during navigation to avoid particularly dangerous situations [24].

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Conflicts of interest

There are no conflicts of interest.

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