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Signals related to eye position are essential for visual perception and eye movements, and are powerful modulators of sensory responses in many regions of the visual and oculomotor systems. We show that visual and pre-saccadic responses of frontal eye field (FEF) neurons are modulated by initial eye position in a way suggestive of a multiplicative mechanism (gain field). Furthermore the slope of the eye position sensitivity tends to be negatively correlated with preferred retinal position across the population. A model with Gaussian visual receptive fields and linear-rectified eye position gain fields accounts for a large portion of the variance in the recorded data. Using physiologically derived parameters, this model is able to subtract the gaze shift from the vector representing the retinal location of the target. This computation might be used to maintain a memory of target location in space during ongoing eye movements. This updated spatial memory can be read directly from the locus of the peak of activity across the retinotopic map of FEF and it is the result of a vector subtraction between retinal target location when flashed and subsequent eye displacement in the dark.

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Spatial memory, movement planning and perceptual localization all require the integration of retinal and extra-retinal signals. The relationship between retinal and extraretinal signals across a population of neurons can offer clues to the computations performed by those neurons. For example, if retinal and eye position signals are spatially congruent, then the population can perform an addition of retinal target position and eye position vectors (Siegel, 1998). Vector addition can provide an approximation of target location in head-centred coordinates. On the other hand, there are cases in which it may be useful to subtract the effects of changes in eye position from a representation of retinal target position. This may occur when one needs a memory of target location in space that is stable across changes in eye position (Balan & Ferrera, 2003). Results from neural network simulations and analytical derivations suggest that vector subtraction can be computed by models in which specific parameters of the retinal and eye position signals are anti-correlated across the population (Xing & Andersen, 2000; Cassanello & Ferrera, 2007; Keith *et al.* 2007). These constraints for vector addition and subtraction can be derived by analysing computational models in which eye position and retinal inputs are represented in 2-D maps and are combined multiplicatively (Siegel, 1998; Xing & Andersen, 2000; Cassanello & Ferrera, 2007). Such models predict a systematic relationship (positive or negative correlation) between visual and eye position signals in networks of neurons specialized to perform one computation or the other. However, more general models can be constructed that perform both computations without relying on any systematic relationship between visual and eye position signals (Salinas & Abbott, 1995; Pouget & Sejnowski, 1997).

Eye position signals have previously been reported in macaque supplemental eye fields (Schlag *et al.* 1992) and dorsolateral prefrontal cortex (DLPFC; Funahashi & Takeda, 2002), but not specifically in frontal eye field (FEF). Studies that have looked at effects of eye position on activity in FEF have reported negative results (Goldberg & Bruce, 1990). No systematic relationship between eye position and visual signals has yet been reported in either DLPFC or FEF. To characterize the interaction of retinal and extraretinal signals in the FEF, we trained monkeys to perform a delayed visually guided saccade task in which both retinal target position (RTP) and initial eye position (IEP) eccentricity were varied systematically. We recorded from 150 neurons in the FEF and we tested their responses for statistical significance of IEP and RTP. We found very clear evidence of eye position modulation of the neuronal responses in this population. We then fitted the firing rates

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recorded from each cell to a simple model consisting of a Gaussian visual receptive field modulated multiplicatively by a linear-rectified function of the eye position. From these fittings we obtained the receptive field centres and the slopes of the eye position sensitivity function and studied the correlation of these parameters across the population. We first tested cells with a delayed memory-guided saccade task (MEM) to determine the receptive/movement field. Then, using the visually guided saccade task (VGS), we determined the IEP sensitivity and RTP sensitivity for neuronal responses during six fixed time intervals typical within each trial (see Methods). These sensitivities gave an estimate of the gain field parameters and the retinal receptive field of the neurons, respectively.

We found that over the population of neurons, slopes of the eye position gain fields and positions of the retinal receptive fields were negatively correlated in all the recorded intervals in which it was meaningful to map a receptive/movement field. This relationship can be exploited to compute a vector difference between the initial target location and a subsequent gaze shift. However, there was no evidence that eye position affected receptive/movement field location, consistent with the notion that FEF neurons represent visual stimuli and movements in retinal or oculocentric coordinates. The results are consistent with a model for computing vector subtraction which has the following features. (1) The computation is performed by a single layer of neurons. (2) The neurons code retinal target location and movements in retinal coordinates. (3) Visual responses are modulated by eye position multiplicatively. (4) Across the network, there is a systematic relationship between preferred retinal location and the slope of the eye position sensitivity function.

Methods

Experiments were performed on three juvenile male rhesus monkeys (*Macaca mulatta*) weighing between 5 and 8 kg. All methods were approved by the Institutional Animal Care and Use Committee (IACUC) at Columbia University and the New York State Psychiatric Institute (NYSPI). Monkeys were prepared for experiments by surgical implantation of a post used for head restraint, a monocular scleral search coil for eye position monitoring, and a recording chamber to give access to the cortex. All surgical procedures were performed using aseptic technique and general anaesthesia. Monkeys were trained to sit in a primate chair for the duration of the experiment with their heads restrained and perform the saccade tasks. Correct performance of the task was reinforced by liquid reward. Animals were not killed at the end of the experiment, but are participating in follow-up experiments under the same experimental protocol and subject to approval from Columbia University and NYSPI IACUC.

Surgical procedures

After premedication with ketamine 10 mg kg^{-1} and atropine 0.04 mg kg^{-1}, anaesthesia was induced with propofol 4 mg kg^{-1} I.V., and maintained with isoflurane 1–4% in oxygen, via an endotracheal tube. Pulse oximetry, inspired and end tidal concentrations of carbon dioxide and anaesthetic agent, ECG, blood pressure, core body temperature, and heart and respiratory rates were measured. Adequate anaesthesia was determined by a veterinary technician, specifically responsible for anaesthesia, by monitoring respiration rate, blood pressure, heart rate and inspired and expired isoflurane concentrations, using signs such as muscle tone, movement, response to skin pinch, and the palpebral reflex.

Surgical sites were clipped and depilated, and prepared with antiseptic solution (Nolvasan, betadine and isopropyl alcohol). Aseptic techniques were used during surgery. The animals were monitored continuously after surgery. Pain was treated with buprenorphine (0.03 mg kg^{-1} I.M.), twice daily or as needed for at least 48 h. Intravenous prophylactic penicillin or other broad spectrum antibiotics were given immediately after surgery, and other antibiotics, topical and systemic, were used as needed.

Visual stimulation

Visual stimuli were generated and controlled by a Cambridge Research Systems (Cambridge, UK) VSG2/3F video frame buffer. The output from the video board was displayed on a calibrated 94 cm colour monitor (Mitsubishi, Tokyo, Japan) with a 60 Hz non-interlaced vertical refresh and 64 kHz horizontal refresh rate. The monitor stood at a viewing distance of 61 cm so that the display area subtended roughly 40 deg horizontally by 30 deg vertically. The spatial resolution of the display was 1280 pixels by 1024 lines. Fixation targets were small (0.5 deg) red squares presented on a uniform black background. The luminance of the fixation target was 65.0 cd m^{-2}, whereas the background was close to 0 (below the photometer threshold of 0.01 cd m^{-2}) and was not detectable by human observers even after dark-adapting for 20 min. The frame buffer was programmed to send out digital pulses (frame sync) for timing purposes at the beginning of each video frame in which a target was turned on or off. These pulses were recorded by the computer using a hardware timer, and stored together with the neuronal and eye movement data.

Eye position recording

Eye position was measured using a monocular scleral search coil system (CNC Engineering, Seattle, WA, USA). Horizontal and vertical eye positions were sampled at

1 kHz per channel. Eye velocity was derived from position using a zero time delay digital differentiating filter.

Neuronal recording and electrical stimulation

Recording chambers (20 mm diameter) were implanted on the skull overlying the arcuate sulcus, positioned at stereotaxic coordinates 25A, 15L. At the start of each recording session, a hydraulic microdrive was mounted on the recording chamber. Recordings were made using platinum–iridium electrodes with impedances of 0.1–1 MΩ. Signals from the microelectrode were amplified, filtered and monitored on an oscilloscope and audio monitor. A time–amplitude window discriminator converted extracellular action potentials into digital pulses, which were sampled by the computer with 0.01 ms time resolution. Units were isolated on the basis of waveform. When a unit was isolated, stimulus parameters such as position and size were adjusted to optimize its response. Neuronal spike trains were collected and stored along with eye position and velocity records.

Electrical microstimulation was used to map the region of cortex from which neuronal recordings were obtained in each monkey. Sites in peri-arcuate cortex were stimulated through the same electrode used to record neuronal activity. The stimulation consisted of a train of 0.2 ms biphasic pulses at a rate of 350 pulses s^{-1} delivered by an optically isolated pulse stimulator (AM Systems, Seattle, WA, USA). The output of the stimulator was gated by a computer-generated voltage level so as to be synchronized with other trial events. The current threshold for evoking saccades was determined by stimulating during a fixation task (Opris *et al.* 2001). The threshold was defined as the current level at which involuntary saccades were evoked on about half the stimulation trials (Bruce *et al.* 1985). For all sites, electrically evoked saccades were almost always contraversive and showed a mediolateral gradation of amplitudes (Bruce & Goldberg, 1985). In addition, the evoked saccade direction rotated systematically as the depth of the electrode changed. These features of the saccade amplitude and direction map are characteristic of the FEF.

Behavioural protocols

Monkeys were trained to perform various oculomotor tasks during neuronal recording: a memory-saccade task (MEM, Fig. 1*A*), a visually guided saccade (VGS, Fig. 1*B* and *C*) with variable IEP and target location, and a two-target forced choice task with eccentric fixation points (VGCH, Fig. 1*D*). All tasks had a block-randomized design: the trial conditions were presented in random order with a block of trials comprising one instance of each condition. The monkey had to correctly complete one trial for each condition before moving on to the next block of trials. Incorrect trials were not used in any of the analyses.

In the MEM task (Fig. 1*A*), monkeys made saccades to the remembered location of a visual cue. The cue location varied among eight positions, equally spaced (45 deg) around the clock. At the beginning of each trial, the monkey fixated on a small red square. A peripheral cue was flashed for 300 ms followed by a variable

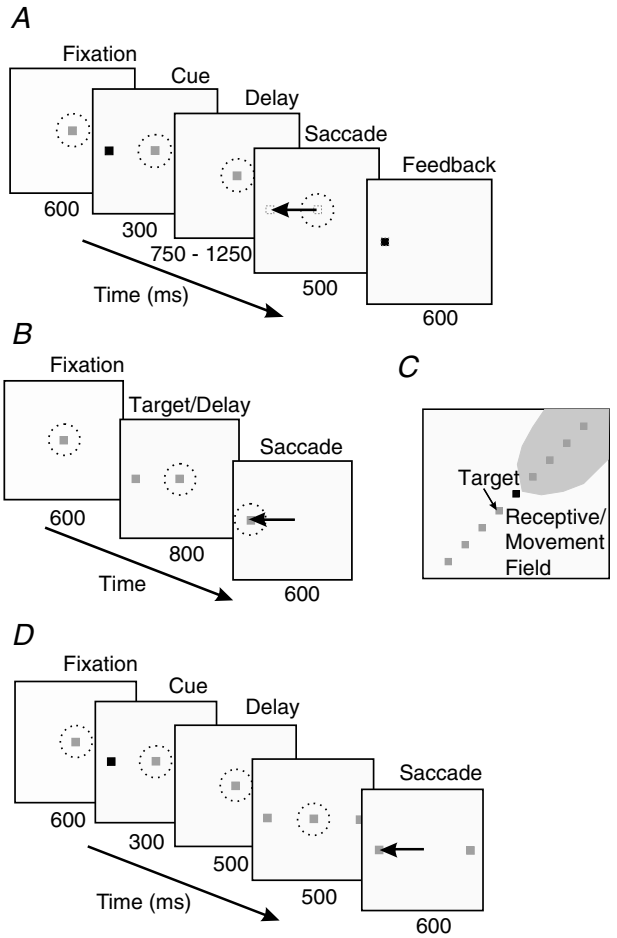

Figure 1. Behavioural tasks used in this study
A, temporal sequence of memory-saccade task (MEM). The monkey fixates a target in the centre of the display for 600 ms, then a peripheral cue is flashed for 300 ms. After a variable delay, the fixation target disappears, cueing the animal to make a saccade to the remembered location of the cue. After the saccade, the cue reapears to provide feedback about saccade accuracy. *B*, temporal sequence of the visually guided saccade task (VGS). After 600 ms fixation the target is turned on eccentrically for a delay interval of 800 ms. At fixation point extinction the monkey saccades to target. *C*, geometrical arrangement of the VGS task. Fixation points and targets are evenly spaced along the preferred direction of the cell including the centre of gaze and eight eccentric locations. *D*, visually guided choice task: the monkey must choose the target that has been cued. The monkey fixates at the centre of gaze and at two eccentric locations displaced by 10 deg to the left and right. The probability of making a saccade to the right or to the left of each fixation point is always exactly the same and all the saccade amplitudes are 10 deg.

delay (750–1250 ms) during which the fixation target remained on and the monkey maintained fixation within a 2 deg × 2 deg window. At the end of the delay, the fixation target disappeared and the monkey was allowed up to 600 ms to make a saccade to the remembered location of the cue. After the 600 ms saccade interval, and if the monkey's memory-saccade was within a 3 deg × 3 deg window centred on the cue location, the cue re-appeared to provide feedback to the monkey and corrective saccades were generally made at this time. Before commencing data collection, the eccentricity of the peripheral cue was varied to find the optimum eccentricity for each neuron. Data were then recorded with a fixed eccentricity.

In the VGS task (Fig. 1*B* and *C*), the monkey had to fixate on one of nine different eccentric locations positioned along a line running through the receptive/movement field. The fixation points were spaced from –16 to +16 deg, relative to the centre of the screen in intervals of 4 deg. A visual saccade target was presented at one of the remaining eight locations. The monkey had to hold fixation during a delay period in which both fixation point and saccade target were on. When the fixation point extinguished, the monkey performed a visually guided saccade to the visual target located at one of the remaining eight locations.

For analysis of neural activity, each trial of the VGS task was divided into six time epochs: (1) fixation interval, 600 ms; (2) visual interval, first 200 ms after the onset of the target; (3) delay interval, 200–800 ms after saccade target onset; (4) movement interval, time between the extinction of the fixation target and the trial end; (5) pre-saccadic interval, 100 ms prior to initiation of the saccade; (6) peri-saccadic interval, 200 ms window centred on saccade onset.

One potential confound of the VGS task is that eccentric eye position might be associated with a covert plan to make a re-centring saccade. Such a plan could result in a negative correlation between eye position and response field location. To address this, we employed a task in which monkeys were forced to plan saccades towards or away from the response field with equal probability for each eye position. The VGCH is a two-target forced choice task (Fig. 1*D*). The task has a fixation interval of 600 ms followed by a cue interval of 300 ms duration. The cue indicates the target the monkey should select to get rewarded. After the cue interval there is a delay period of 500 ms during which only the fixation point is lit. This delay period is followed by another 500 ms interval in which both targets and the fixation point are on. The 'go' signal is provided by extinguishing the fixation point, after which the monkey has up to 600 ms to choose and saccade to the cued target. Thus, within each trial there were seven recording intervals corresponding to fixation, cue, delay with fixation point only, delay with fixation point and target(s) on, movement, pre-saccadic and peri-saccadic intervals. The task had six stimulus conditions corresponding to two possible saccades from three different fixation points: the centre of gaze and two eccentric fixations 10 deg on each side of the centre of gaze. From each fixation point there was always the same probability of making a saccade to the right or to the left, and the amplitude of either saccade was always 10 deg at all fixation eccentricities.

Data analysis

The VGS (Fig. 1*B* and *C*) task had 72 different stimulus conditions arising from nine initial fixation point locations and eight target locations. The condition in which the target position and initial fixation position were the same was not presented. The other conditions were presented randomly within each block. For analysis, each trial was divided into the six recording intervals described above and the average firing rate was computed within that window. Each stimulus condition was repeated at least five times for each cell. The average number of repetitions was typically 10–12 with some units recorded over 20 complete blocks.

The analysis had two main objectives. The first objective was to test for the presence and significance of eye position modulation on the firing rate of FEF neurons. To test for significant modulations in firing rate, a two-way ANOVA was performed with IEP and RTP as the independent factors.

To determine linearity of response, firing rate during the fixation interval was plotted as a function of eye position and fitted with a second-order polynomial:

$$r(y) = a_1 + a_2 y + a_3 y^2 \quad (1)$$

where r is firing rate, y is eye position and a_1–a_3 are the fitted parameters. A slope for the dependence of firing rate during the fixation interval on eye position was obtained by taking a_2/a_1, the ratio of the eye position linear coefficient and the constant coefficient.

The second objective was to extract from the data estimates for the receptive/movement field (RF) location and the eye position gain field slope for each neuron, and investigate a possible correlation between these two parameters. This was necessary to determine whether the vector subtraction condition was obeyed and to test the validity of the model put forth in the Results. Once the receptive field centres and gain field slopes were extracted, we plotted gain field slope *versus* receptive field centres and computed a regression line. Based on this scatter plot, units within the first and third quadrants were classified as summation cells and units belonging to the second and fourth quadrant were termed subtraction cells (see Results). Simple regression over this scatter plot may not be appropriate for these cases because both variables show large variability. We tried robust estimation methods, which confirmed the results found with standard linear regression.

The extraction of the receptive/movement field centres and the gain field slopes was performed by fitting the model given by eqn (2) below to the data recorded during the visual, delay, pre- and peri-saccadic intervals.

$$R(x, y) = a_1 + a_2 \exp\left(-\frac{1}{2a_4^2}(x - a_3)^2\right)[1 + a_5 y]_+ \quad (2)$$

This equation is the product of a Gaussian receptive field and a linear-rectified eye position gain field. The square brackets indicates that this magnitude is either positive or zero. The two variables are retinal target position (x) and eye position (y). To extract the five parameters a_1 to a_5 we used the Matlab non-linear fitting routine nlinfit. Confidence intervals were computed for the extracted parameters using Matlab function nlparci. The parameters are background firing rate a_1, receptive field (RF) amplitude a_2, RF centre a_3, RF width a_4 and gain field slope a_5. For each task interval of each trial we computed the firing rate for that interval and provided the fitting routine, the set of measured firing rates with the corresponding target position and eye position coordinates. The target position coordinates were converted to retinal coordinates by taking the difference between the screen locations of the target and the screen locations of the fixation point. The fixation point locations ranged from −16 to +16 deg eccentricities in screen coordinates, in steps of 4 deg, which provides a range of retinal target locations between −32 and +32 deg. The conversion from screen coordinates to visual angle involves a linear approximation whose error grows as (1–cos(visual angle)). Hence, the maximum error was 15% for the largest visual angle (32 deg).

The choice task (VGCH, Fig. 1*D*), was a control experiment performed to test the hypothesis that the observed correlation between receptive/movement field centres and gain field slopes was not an artifact of saccade planning towards the receptive field centre (see Methods and Results). In this experiment there were two groups of six trials; all 12 stimulus conditions were presented randomly within each block. In six trials the monkey had to saccade to the cued location in a two-target forced choice option. The other six trials had only one saccade target at the cued location and were used as a control for the choice trials. In this experiment the firing rates were computed in seven trial epochs: (1) fixation interval, 600 ms; (2) cue interval, first 300 ms after the onset of the peripheral cue; (3) delay interval, 0–500 ms after cue offset; (4) second delay, 0–500 ms after onset of two-choice targets while monkey held fixation; (5) movement interval, 600 ms time interval from the extinction of the fixation target to the end of the trial; (6) pre-saccadic interval, 100 ms prior to initiation of the saccade; (7) peri-saccadic interval, 200 ms window centred on saccade onset.

In this task it was not possible to fit the full model because there were only two retinal target positions for each of the three eye positions (see Behavioural protocols) located 10 deg to the left or to the right of the fovea. Therefore each cell was simply classified as having its receptive field to the left or right of the fovea based on which location gave the strongest visual response. The slope of the gain field was estimated by fitting a linear or second-order polynomial function of eye position to the recorded data and taking the ratio of the linear coefficient to the constant coefficient as an estimate of the slope. This procedure was applied to all intervals in this task.

Based on the responses during the various recording intervals the unit could be classified as visual, visuomovement or movement following the classification of Bruce & Goldberg (1985). We define a visuomovement index (VMI) based on the mean firing rate (FR) during the visual and the pre-saccadic interval of the VGS task:

$$\mathrm{VMI} = \frac{[\mathrm{FR(visual)} - \mathrm{FR(pre-saccadic)}]}{[\mathrm{FR(visual)} + \mathrm{FR(pre-saccadic)}]}. \quad (3)$$

The index varies from −1.0 for a cell that responds before the saccade but not before the onset of the visual target, to +1.0 for cells that respond to the visual target but not prior to the saccade. This index was used to establish three classes of cells: visual (index between 0.33 and 1.0), movement (index between −1.0 and −0.33) and visuomovement (index between −0.33 and 0.33). In a broader sense we can define the unit to be more visual if its VMI is larger than zero and more of the movement type if this index is negative. To investigate correlations between summation or subtraction cells and their visual or movement character this latter broader classification was used.

Results

We trained three macaque monkeys to perform a delayed VGS (Fig. 1*B* and *C*) to eccentrically located targets from a variety of eccentric fixation points. The purpose of this experiment was 2-fold: to test the presence of eye position-dependent modulation on the firing rate of FEF neurons and test the hypothesis that FEF may be involved in computing a vector subtraction between retinal position of a saccade target and the eye position at fixation before the saccade. We recorded 150 individual cells with a minimum of five repetitions of each trial condition; 49 from monkey C, 42 from monkey E and 59 from monkey F.

Once we had isolated a unit we determined the preferred direction of the cell by using the MEM task (Fig. 1*A*) with fixed eccentricity targets in eight different directions. We computed on-line the firing rate from the response to the MEM task for the seven recording intervals described in the Methods. We selected the direction that showed maximum response among the visual or pre-saccadic task intervals. Targets and fixation points for the VGS task were then aligned with the preferred direction of the neuron. Figure 2

shows the spike rasters and histograms for an example FEF visual neuron during the VGS task. The upper and lower rows of Fig. 2 show firing rate for a single retinal target location (−4 deg) and two different eye positions (upper row, 16 deg; lower row, −12 deg), during four trial epochs. The response in all trial intervals was stronger when the eyes were pointing to the right than to the left.

Figure 3 shows the response of the cell in Fig. 2 over the entire range of eye and target positions. Figure 3*A* shows firing rate as a function of eye position during the fixation interval. Even though there was no peripheral target during the fixation interval, trials were sorted according to the location where the target would appear later in the trial (grey dots). This accounts for the multiple data points at each eye position. The mean firing rates for each eye position are plotted as block dots and fitted with a bi-linear function. Figure 3*B* and *C* shows the initial visual response of the same neuron plotted either as a function of IEP (Fig. 3*B*) or RTP (Fig. 3*C*). The neuron shows clear retinal tuning of the visual receptive field between 4 and 8 deg to the left of the fovea (−6.5 deg). This unit showed a strong visual response and almost no movement response and was therefore classified as a visual cell (VMI, 0.78, eqn (3)) following Bruce & Goldberg (1985).

Figure 4 shows the activity of a visual-movement or build-up cell (VMI, − 0.33, eqn (3)). The saccade target was placed at +8 deg (on the right). The model fit (eqn (2)) accounted for 95% of the variability in firing rate during the visual interval ($r^2 = 0.949$; $P < 10^{-20}$). This cell was typical in that the eye position modulation was strongest during the fixation and visual intervals, but became weaker around the time of the movement.

Statistical significance of eye position and retinal position signals

A two-way ANOVA using IEP and RTP as descriptors was performed on the activity of each neuron within each trial epoch, as described in the Methods. Table 1 summarizes the ANOVA results for each recording interval. For each interval, the two rows show number of cells and the percentage of the total that displayed significant effect of

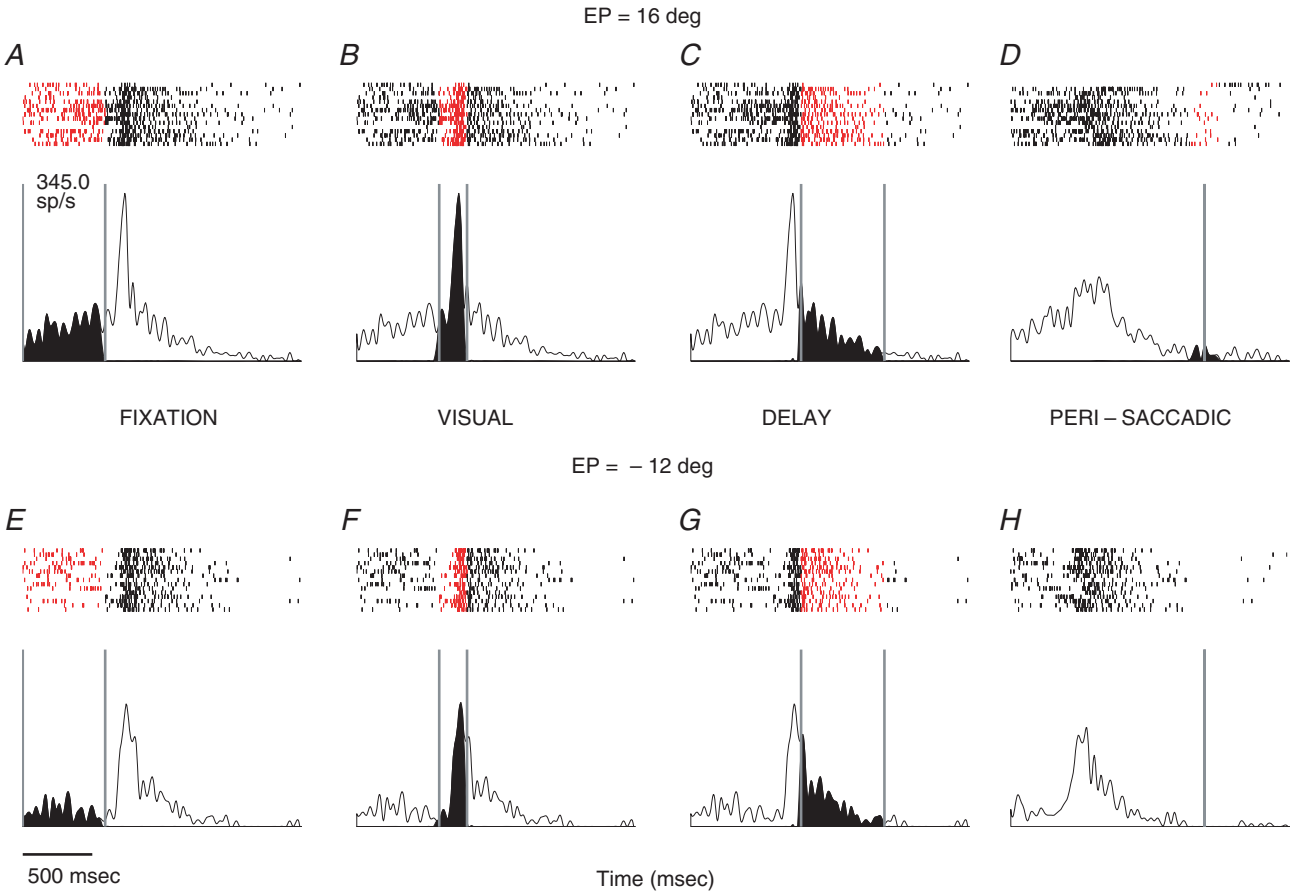

Figure 2. Spike rasters and histograms for a visual cell
The retinal target position was −4 deg for all subplots. Top row: eye position, 16 deg (right). Bottom row: eye position, −12 deg (left). Four different task epochs are shown: Fixation, Visual, Delay and Peri-saccadic. Spikes are aligned on visual target onset for the first three epochs, and on saccade onset for the last.

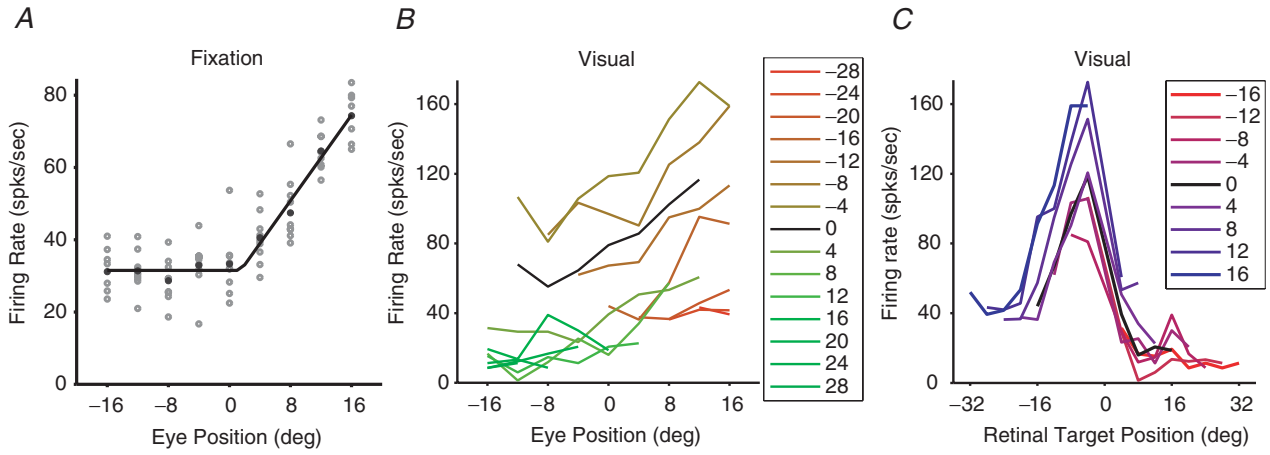

Figure 3. Responses of cell in Fig. 2
A, eye position sensitivity during fixation interval with no peripheral target. *B*, eye position sensitivity average firing rates plotted against eye position before the visually guided saccade. Each curve corresponds to a fixed retinal target position and therefore fixed saccade amplitude. *C*, retinal sensitivity: average firing rates plotted against target location in retinal coordinates. Each curve corresponds to a fixed eye position before the saccade. This cell clearly has a localized receptive field centred between 4 and 8 deg to the left of the fovea and a positive slope in its eye position sensitivity.

IEP and RTP, as well as those that showed significance of the interaction term (INT), at $P < 0.05$ significance level.

We found evidence for the presence of extra-retinal eye position signals in a majority of FEF neurons. The fixation interval, in which only the fixation spot was visible, was the single epoch with the highest number of units displaying significance for the IEP (113/150, 75%). The initial response to the saccade target was modulated by IEP

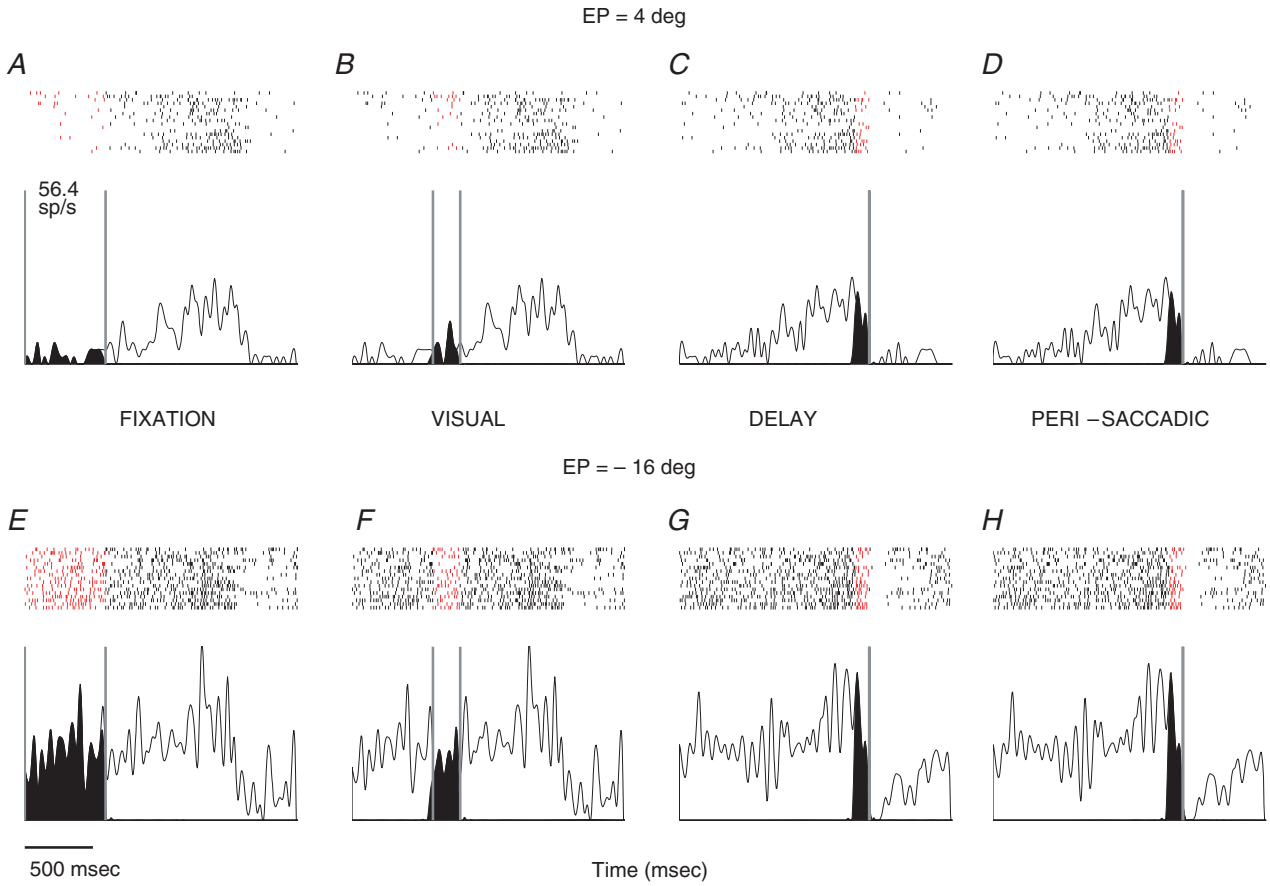

Figure 4. Spike rasters and histograms for a visual-movement cell
The format of this figure is identical to that of Fig. 2.

Table 1. Two-way ANOVA results showing the significance of initial eye position (IEP) and retinal target position (RTP) in the response of 150 cells tested with the VGS task

Fixation			Visual			Delay		
IEP	RTP	INT	IEP	RTP	INT	IEP	RTP	INT
113	NA	NA	99	95	10	104	141	25
75%	NA	NA	66%	63%	7%	69%	94%	17%
Post-saccadic			Pre-saccadic			Peri-saccadic		
IEP	RTP	INT	IEP	RTP	INT	IEP	RTP	INT
82	130	22	58	133	24	75	139	23
57%	87%	15%	39%	89%	16%	50%	93%	15%

The columns give the numbers corresponding to all six recording intervals. The rows of the table show the number of cells and percentage at the $P < 0.05$ significance level. The headings Fixation, Visual, Delay, Movement, Pre-saccadic and Peri-saccadic refer to the temporal epochs of the VGS task within which neural activity was averaged. IEP, initial eye position; RTP, retinal target position; INT, interaction term.

in 66% (99/150) of the cells whereas 39% (58/150) showed this type of modulation in their pre-saccadic responses. The results for the delay and peri-saccadic intervals were 69% (104/150) and 50% (75/150), respectively. Thus, the number of cells showing significant eye position effects was not constant across all trial epochs, but tended to decrease as the time for the saccade drew near.

The significance of RTP was maximal in the peri-saccadic as well as the delay intervals with 139/150 (93%) and 141/150 (94%) neurons showing rate modulation dependent on RTP, respectively. In addition 133/150 (89%) neurons showed significant effect of RTP in their pre-saccadic responses whereas only 95/150 (63%) showed this effect on their visual responses. This increase between the visual epoch and the delay, pre- and peri-saccadic intervals in the portion of neurons showing significant effect of the RTP (63% to between 89% and 94%) survived when the significance level was reduced to $P < 0.01$ (46% to 70% range).

In general, eye position effects were more likely to reach significance in the fixation, visual and delay intervals as compared to the pre-saccade, peri-saccade and movement intervals. This may indicate that eye position signals in FEF play more of a role in visual remapping than saccade programming.

We performed simulations to determine whether the ANOVA results were more consistent with a multiplicative or additive interaction between retinal and eye position inputs. In theory, if retinal and eye position inputs are multiplied, there should be a large interaction term in the ANOVA. In practice, the significance of interaction term might be reduced by noise. We simulated multiplicative and additive models which otherwise had the same parameters. We added random noise to the retinal and eye position signals in both models and calculated ANOVAs. For the multiplicative model, the retinal position was significant ($P < 0.05$) in 99/100 runs, the eye position modulation was significant in 89/100 runs and the interaction was significant in 26/100 runs. The interaction term reached significance less often because not only are the retinal and eye position inputs multiplied, but the independent noise associated with each input is also multiplied. For the additive model, retinal position and eye position were both significant in 100/100 runs, whereas the interaction was significant in only 8/100 runs. The proportion of significant interaction terms for the actual ANOVA results (Table 1) falls somewhere between the additive and multiplicative simulations. These results suggest that multiplying two noisy signals does not always result in a significant ANOVA interaction, and, hence, the lack of such interaction does not rule out a multiplicative model.

Table 2. Values of fitted coefficients for eqn (2)

Coefficient	Mean	S.D.	Range	Units
a_1	11.21	11.09	0 to 47.35	spikes s^{-1}
a_2	45.09	117.3	0 to 500	spikes s^{-1}
a_3	18.51	11.61	−56.68 to 47.84	deg
a_4	23.24	50.34	1.18 to 150	deg^2
a_5	0.0662	0.0935	−0.294 to 0.481	1 deg^{-1}

The coefficients for the receptive field centre (a_3) and eye position slope (a_5) were converted to absolute values before computing the mean and standard deviation.

Relationship between gain field slope and response field location in FEF

In this section we studied systematic dependences among the parameters of the retinal and eye position sensitivity functions. Because FEF cells vary in their degree of visual and movement-related activity, the term 'retinal' is used to denote a response coded in retinal coordinates, not necessarily a visual response. For example, many FEF cells in our sample had no response to the onset of the visual target, but responded robustly prior to the saccade and this presaccade activity was spatially tuned. There was no evidence that the preferred retinal target location in any task interval varied with IEP for any of these cells.

The most salient feature of the data was that the slope of the eye position sensitivity was negatively related to receptive field position across the population of neurons. To quantify this, we fitted the data recorded for each task interval to eqn (2) as detailed in the Methods. Of the five parameters a_1–a_5, the most important is the relationship between the receptive field centres a_3 and the gain field slopes a_5. The average value and range of these coefficients is given in Table 2. The fitting procedure allowed us to assign to each cell a unique receptive field centre and gain field slope for each recording interval except for the

fixation interval in which the receptive field centre cannot be sampled because the only RTP is always the fovea (see Methods).

We observed that many cells showed a tonic modulation of background firing with eye position before the saccade target was presented. In fact, eye position effects were statistically most robust during the fixation interval. Therefore, we used this background activity to estimate the eye position sensitivity in the absence of any retinal stimulus other than the fixation point. To obtain an estimate of the slope of the eye position sensitivity function for this background activity, we fitted the firing rates recorded during the fixation interval to a general second-order equation (eqn (1)). The average value and range of the fitted coefficients are given in Table 3.

The receptive field centre parameter was estimated by fitting eqn (2) to activity in the visual, delay or presaccade interval, depending on which interval had the strongest response. Figure 5*A* shows the correlation of the slope of the eye position sensitivity function with the location of the receptive field. An eye position slope of 0.1 corresponds to a 100% modulation of firing rate for a gaze shift of 10 deg. The overall slope of the regression line relating gain field slope to RF centre was of the order of -1×10^{-3}. The same parameter for the numerical simulations in Fig. 7 was of the order of -9×10^{-4} (see below (Gain field model and vector subtraction)). Hence, the strength of eye position input to FEF was adequate to account for accurate spatial updating in the model.

The eye position slopes were again plotted against the receptive field centre in Fig. 5*B*. However, in this case, the two parameters were both estimated from activity during the visual epoch of the task. The results are generally in agreement with those of Fig. 5*A*, in which the eye position slope was derived from activity during the initial fixation interval, except that there is more scatter. (Note that the y-axis scale is different in the two panels of Fig. 5) The differences are due to various factors. Typically, cells that were not strongly modulated by eye position during the fixation interval became much more strongly modulated after the saccade target was presented. The converse was also observed – cells that were strongly modulated during fixation became weakly modulated when the target was presented. In other words, the visual or movement activity overcame the eye position effect. Nevertheless, across the population there was a significant negative correlation between eye position slope and response field location.

To determine whether the relationship between retinal and eye position sensitivity was simply due to a contralateral visual bias coupled with an ipsilateral eye position bias, we examined the responses of neurons that had receptive fields centred on the vertical meridian. We recorded 18 such neurons. We found that for these neurons, the negative relationship between receptive field location and eye position sensitivity still held. For example, a cell whose receptive field was on the upper vertical meridian tended to increase its firing rate when gaze shifted downwards. For these 18 neurons, the correlation between RF centre and EP slope for activity during the fixation interval was significant ($r^2 = 0.38$; $P = 0.006$) and had a negative slope (-0.0014). For activity during the visual interval, the correlation was not significant, but the slope was still negative (-0.0066).

Table 3. Values of fitted coefficients for eqn (1)

Coefficient	Mean	S.D.	Range	Units
a_1	14.90	14.96	0 to 76	spikes s^{-1}
a_2	0.239	0.384	−1.09 to 3.54	spikes s^{-1} deg
a_3	0.012	0.013	−0.06 to 0.075	spikes s^{-1} deg^2
a_3/a_2	0.177	0.361	−2.367 to 0.944	1 deg^{-1}
a_2/a_1	0.027	0.036	−0.13 to 0.188	1 deg^{-1}

The coefficients for the linear (a_2) and quadratic (a_3) terms were converted to absolute values before computing the mean and standard deviation.

Quality of fit

We assessed the quality of the fittings of the parameters in the following way. For each recorded cell we used the parameters fitted with eqn (2) – background, amplitude, receptive field centre, receptive field size and gain field slope — to compute a predicted response for each stimulus condition. There were a total of 72 stimulus conditions comprising nine initial fixation points and eight target locations. Equation (2) is the joint tuning curve for retinal and eye position sensitivity and predicts the mean firing rate for each stimulus condition given the five fitted parameters. Therefore the predicted responses were compared to the mean firing rate for each condition averaged over trial repetitions. The fittings were done for activity during the visual, delay, pre-saccadic and peri-saccadic intervals.

We plotted average firing rates against predicted responses and computed the correlation coefficient for these plots. The r^2 coefficient gives an estimate of the percentage of the variance accounted by the model for that particular cell. This procedure is equivalent to taking the ratio of the variance of all predicted responses and the variance of the mean firing rates over the stimulus conditions. Typical values ranged from 0.4 to 0.98 per cell. The smaller values correspond to units with a small range of firing rates across stimulus conditions; either units with high background firing with low modulation due to visual stimulus or eye movement, or units with low firing rates overall. The best fittings correspond to units with very sharply defined receptive and/or movement fields and those that are very responsive to either visual stimulus or saccade preparation.

When we consider the entire population, the scatter plot of the mean firing rates over stimulus conditions

versus predicted responses during the visual interval, the accounted variance was 94.78% ($P < 10^{-10}$). Similar figures were obtained for delay, pre and peri-saccadic recording intervals, suggesting that eqn (2) gives a very good description of the mean responses of these neurons across the population. The distribution of mean firing rates is rather uniformly distributed in a single cluster cloud along the identity line ranging from 0 to 120 spike s^{-1}. Other methods (regression based on the first principal component and robust regression) confirmed the goodness of fit of the model.

Saccade planning

It is possible that the observed spatial modulation of firing rates may be an artifact of saccade planning. When the subject is fixating eccentrically it is possible that the oculomotor system may be planning a saccade towards the centre of gaze. This is a natural assumption because the centre of gaze is the natural relaxed position of the eyes. This saccade preparation could be towards or away from the receptive field of the neuron depending on its location. When gaze is shifted in the direction opposite the RF, a saccade towards the centre of gaze will also be in the preferred direction of the cell and therefore likely to result in elevated activity before the saccade. Conversely, if gaze is shifted towards the receptive field, a re-centring saccade will be away from the RF and is likely to be accompanied by a reduction in activity. Thus, a default plan to re-centre the eyes may result in an apparent negative correlation between IEP and RF location.

To test this hypothesis we trained two of the monkeys on a spatial matching target selection task in which the probability of a saccade towards or away from the RF was equal for all IEPs. This task is illustrated in Fig. 1*D*. The monkey first fixated to initiate the trial. In the basic configuration, the position of the initial fixation target was straight ahead, 10 deg left, or 10 deg right. The monkey was then cued to a position 10 deg to the left or right of fixation. After a delay, either one or two targets appeared and the monkey made a saccade to the one that matched the position of the cue. The entire display was rotated so

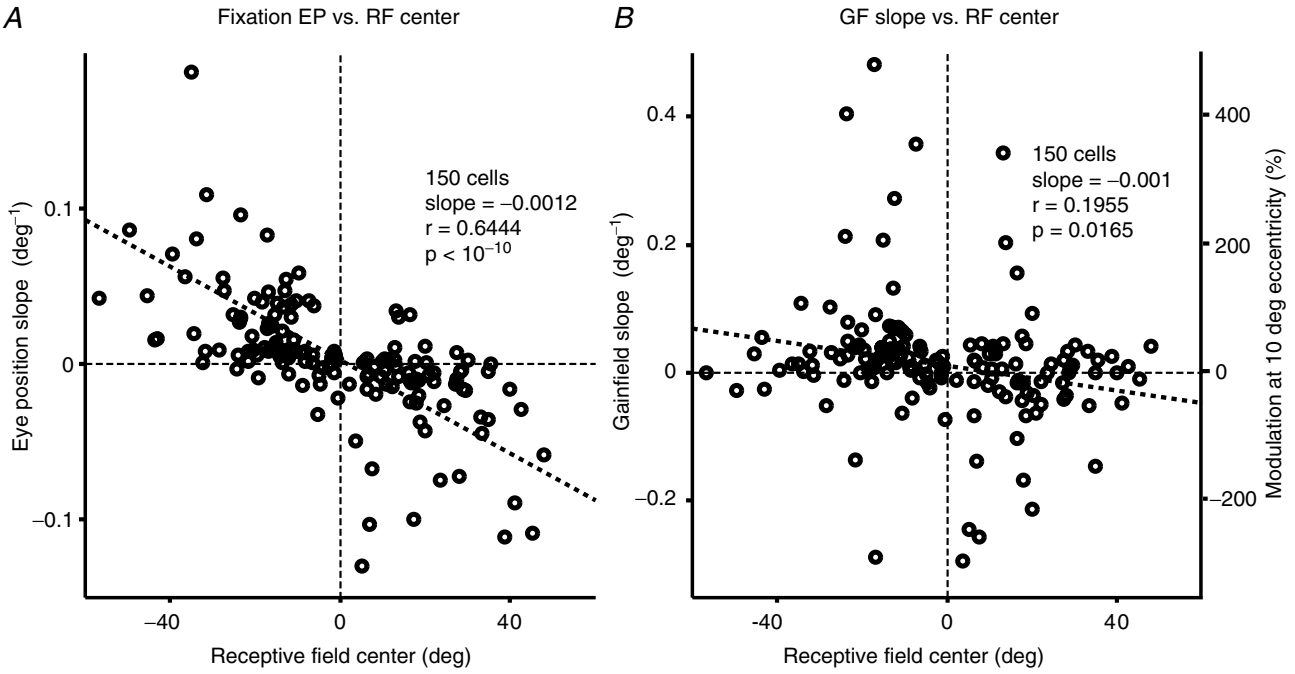

Figure 5. Scatter plot of the eye position sensitivity slopes *versus* the receptive field centres fitted to the recorded data ($n = 150$ cells)

A, eye position dependence of the responses during fixation. This is the change in the background response due to the change in position of the eye. A polynomial was fitted (eqn (1)) to the response during fixation using eye position as a variable and the linear coefficient (a_2) has been divided by the constant coefficient (a_1) to estimate the slope. No receptive field centre can be fitted during this interval because there is no target. The receptive field centres have been extracted from the response during the visual interval (parameter a_3 from eqn (2)). From the group of 85 neurons with larger slopes, cells deep into the upper left and lower right quadrant are subtraction cells (77/85) because their gain field slopes have a sign opposite to their receptive field centres. Cells deep into the upper right and lower left quadrant (8/85) are summation cells. Cells near the origin with small receptive field eccentricities and shallow gain field slopes can behave as either subtraction or summation cells. *B*, scatter plot of gain field slopes *versus* receptive field centres fitted to the responses recorded during the visual interval. The abscissa is parameter a_3 and the ordinate is parameter a_5 from eqn (2).

that the target positions were aligned with the RF of each individual cell.

If the firing rate modulation was a consequence of the eye movement preparation alone we would not expect any dependence of firing rate on the initial fixation point, and only an overall larger response to the target located nearer to the receptive field of the neuron. Therefore we would expect to find no significant effect of the IEP on the firing rates of the units tested. Figure 6*A* shows activity of a typical FEF neuron during two-target (choice) trials. The cell responded more strongly preceding rightward saccades (bottom row), but the response was clearly modulated by IEP. The best eye position was 10 deg to the left, opposite to the RF location. The slope of the eye position sensitivity had the same sign regardless of whether the monkey made leftward or rightward saccades.

Table 4 summarizes the results of a two-way ANOVA conducted on the recorded firing rates using as descriptors the IEP and RTP. As in the VGS task there is a large number of units displaying significant modulation of their firing rates by the IEP. The percentages are similar to the numbers shown in Table 1 for the VGS task. Notably the highest numbers of units displaying eye position modulation in their rates is achieved again during the fixation interval (66%) and in the part of the delay period that has only the fixation point lit (75%). Once again the number of units displaying significance for IEP decreases over time during the trial as movement approaches.

Figure 6*B* shows the same analysis for the original VGS task across the population of cells tested with the choice task. The plot shows average gain field slope (± S.E.M.) against preferred target location over the population of neurons recorded with the target selection task. However, in the experimental design there are only two possible retinal target locations and therefore it was not possible to estimate the RF position. Hence the results are expressed in terms of preferred target location.

There were small but non-significant differences in mean eye position slope between trials with saccades towards or away from the RF. When pooled over saccade direction, the eye position gains were significantly different from zero (t test; $P \leq 0.05$; $n = 56$). The average eye position slope corresponds to a firing rate modulation of approximately 10% over a gaze shift of 10 deg. Although saccade direction did not have a significant effect on the average slope, it is interesting that there was a small tendency for the absolute value of the eye position slope to be larger on trials where the saccade was away from the RF. Hence, the eye position effect does not appear to depend on planning a saccade towards the RF.

Table 4. Two-way ANOVA results showing the significance of initial eye position (IEP) and retinal target position (RTP) in the response of 56 cells tested with the choice task

Fixation			Cue			Delay FP only		
IEP	RTP	INT	IEP	RTP	INT	IEP	RTP	INT
37	5	7	36	33	16	42	41	18
66%	9%	12%	64%	59%	29%	75%	73%	32%
Delay 2 targets			Pre-saccadic			Peri-saccadic		
IEP	RTP	INT	IEP	RTP	INT	IEP	RTP	INT
30	46	20	21	41	17	27	45	21
54%	82%	36%	38%	73%	30%	48%	80%	38%

The columns give the numbers corresponding to all six recording intervals. The rows of the table show the number of cells and percentage at the $P < 0.05$ significance level. All definitions as Table 1. If the slope of eye position sensitivity function were zero ANOVA should show no significance of IEP. These results allow us to reject the saccade planning hypothesis to explain the correlation between eye position and neuronal receptive field location.

Subtraction-summation *versus* visual-movement

Based on the relationship between receptive field position and gain field slope, units can be classified as 'subtraction cells' (negative relationship; upper left and lower right quadrants of Fig. 5) or 'summation cells' (positive relationship; upper right and lower left quadrants of Fig. 5). Neurons can also be classified along a visual–movement dimension based on responses recorded during the visual and pre-saccadic task intervals (Bruce & Goldberg, 1985). We used the VMI defined in eqn (3) to classify the neurons broadly into visual when VMI was positive and movement-related when VMI was negative. Here we address two questions. (1) Are cells with responses showing significant effect of IEP mostly visual or movement cells? (2) Are subtraction cells preferably visual, movement or visuo-movement cells?

Roughly two-thirds of the cells were classified as movement related (94/150, 63%) and one-third visual (56/150, 37%). Of the visual cells, 46/56 (82%) were classified as subtraction cells based on activity during the fixation interval, whereas 10/56 (18%) were summation cells. For movement cells, 76/94 (81%) showed the subtraction pattern, whereas 18/94 (19%) were summation cells. Thus, the proportion of cells in each class (subtraction/summation) was similar for visual and movement-related neurons. These proportions remained constant even when more stringent criteria were used to classify the cells (i.e. we repeated the analysis using only cells with absolute values of VMI > 0.1, 0.2 and 0.3).

Gain field model and vector subtraction

A simple quantitative model was developed to show that a gain field-like model can accurately compute vector subtraction using parameters derived from the

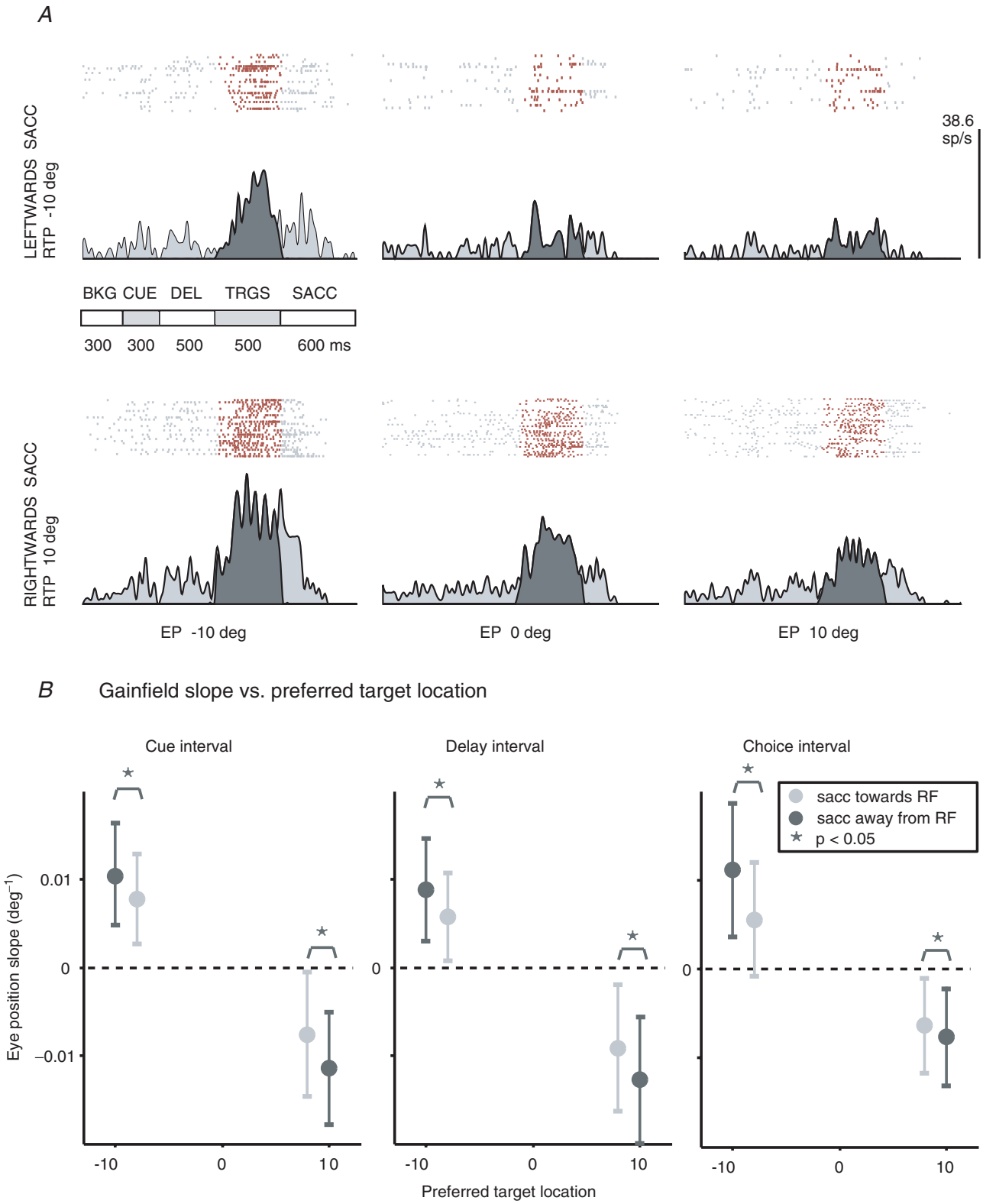

Figure 6. The VGCH task

A, response of a typical cell to the task. The interval in which the two targets between which the monkey has to choose are turned on, has been darkened. The upper row shows all leftward saccades with RTP at −10 deg. The columns correspond to IEP fixations to the left (−10 deg), at (0 deg) and to the right (+10 deg), respectively. This unit has a receptive field to the right of the fovea as its response is consistently higher in the lower row. The response is clearly modulated by the EP with a negative slope; this is negatively correlated with the receptive field

physiological data. The model is based on the idea that FEF neurons integrate retinal and extraretinal eye position signals taking advantage of a multiplicative modulation of the retinal response function by a gain field dependent on the eye position. The term 'retinal' is meant to denote a function whose argument is retinal position. It does not imply anything about the source of the signal, or whether the signal is visual or movement-related. The model applies equally to any population of neurons with response fields that are fixed in retinal/oculocentric coordinates regardless of whether they have visual or saccade-related activities. It is intended to illustrate, in principle, how the brain might take advantage of the observed negative correlation between eye position and retinal signals. Numerical simulations show that the model can perform accurate vector subtraction using key parameters derived from the physiological results.

It is important to specify clearly what computation the model is meant to achieve. The goal is to update across eye movements the position, in retinal coordinates, of a remembered target whose location is fixed in head-centred space. Assume that a subject is holding gaze at a fixation point (instantaneous origin of the retinotopic map) and a light cue is flashed at a position x. The retinal target position (x) is given by the vector defined between the fovea (O) and the target location T at the time it was last seen, $x = OT$. This x is measured from the fovea in the same (retinal) coordinate system in which the receptive field centres (ρ) of the neurons in the population are measured. The cue extinguishes after a brief interval and a second fixation point FP2 comes on at eccentricity y (measured from the original FP1). Subsequently the animal shifts gaze to FP2. The eye position variable is the difference between two successive fixations (FP1 and FP2), thus $y =$ FP2–FP1. It is important to note that the sensory stimulation comes first and the eye movement subsequently occurs in darkness. This model computes in a single step the vector difference x–y. A longer theoretical discussion of the model can be found elsewhere (Cassanello & Ferrera, 2007).

We show here the analytical derivation of the differential equation for the gain field function, $g(y|\rho)$, which expresses how eye position sensitivity varies with receptive field location such that changes in eye position will shift the peak of the population response in the manner required for spatial updating via vector subtraction. We start with an explicit Gaussian form for the retinal sensitivity part of the response while leaving the eye position sensitivity part unspecified,

$$\begin{aligned} R(x, y, \rho) &\equiv f(x, \rho) g(y, \rho) \\ &\equiv A \exp\left(-\frac{1}{2\sigma^2}(x-\rho)^2\right) g(y, \rho) \end{aligned} \tag{4}$$

Note that eqn (4) looks like eqn (2); with the coefficient a_1 set to zero, $a_2 = A$, $a_3 = \rho$ and $a_4 = \sigma$. We looked for the conditions to get a maximum value for the response R over an array of neurons labelled by their cortical location ρ (which will become the fitting parameter a_3 in eqn (2)) when the saccade amplitude is given by the difference between the RTP and the IEP. We computed a constrained maximization over the receptive field locations in order to determine the peak of the population response. To do this we differentiated with respect to the position in the map (i.e. receptive field centre) ρ and find that the gain field function g, must obey the following differential equation:

$$\begin{aligned} \frac{\partial}{\partial \rho} \log g|_y &= -\frac{\partial}{\partial \rho} \log f|_x \\ &= -\frac{1}{\sigma^2}(x-\rho) \equiv -\frac{1}{\sigma^2} y, \end{aligned} \tag{5}$$

where in the right hand side of eqn (5), one enforces the constraint $\rho = x - y$ in order to obtain an eye position sensitivity function that depends only on the variables y and ρ. This is the vector subtraction condition. Assuming that f is a Gaussian, and employing the constraint $\rho = x - y$, we obtain the last identity, which can be integrated over ρ to solve for g. The solution has the form of an exponential function of $-\frac{\rho}{\sigma^2} y$ with the linear rectified approximation, valid for sufficiently large values of σ, giving the form of the model in eqn (2). The key result is that the parameter that modulates the eye position sensitivity function ($-\rho/\sigma^2$) is inversely related to that which specifies the peak of the retinal sensitivity function (ρ).

To test the validity of the analytical result, we performed numerical simulations. The simulations comprised an array of neurons each of which takes as inputs the retinal target position (x) and eye position (y). The output is remembered target location in retinal coordinates which is read-out from the location of the peak of the population activity in the retinal map. The output is updated each time the eye position changes and is computed in a single iteration.

eccentricity. This EP dependence is evident for eye movements both towards and away from the receptive field of the unit. *B*, population data from the VGCH task; correlation between eye position sensitivity slope and receptive field location. The plot shows the average and S.E.M. of the gain field slope over the population of units recorded with the choice task segregated according to whether the saccade was towards or away from the receptive field. If the null hypothesis that the correlation between gain field slope and receptive field location were true, the eye position sensitivity slope should not be significantly different from zero.

The full model comprised 81 neurons with Gaussian retinal tuning and linear-rectified eye position sensitivity functions. The retinal position sensitivities of a subset of these neurons are shown in Fig. 7*A*. The corresponding eye position sensitivities are shown in Fig. 7*B*. The gain field function is rectified whenever the eye position drives the sensitivity below zero to prevent negative values of the firing rate. Notice the negative correlation between the slope of the eye position sensitivity and the preferred retinal location across the population of neurons. Other models (Pouget & Sejnowski, 1997) have used sigmoidal eye position functions. However, we found that a

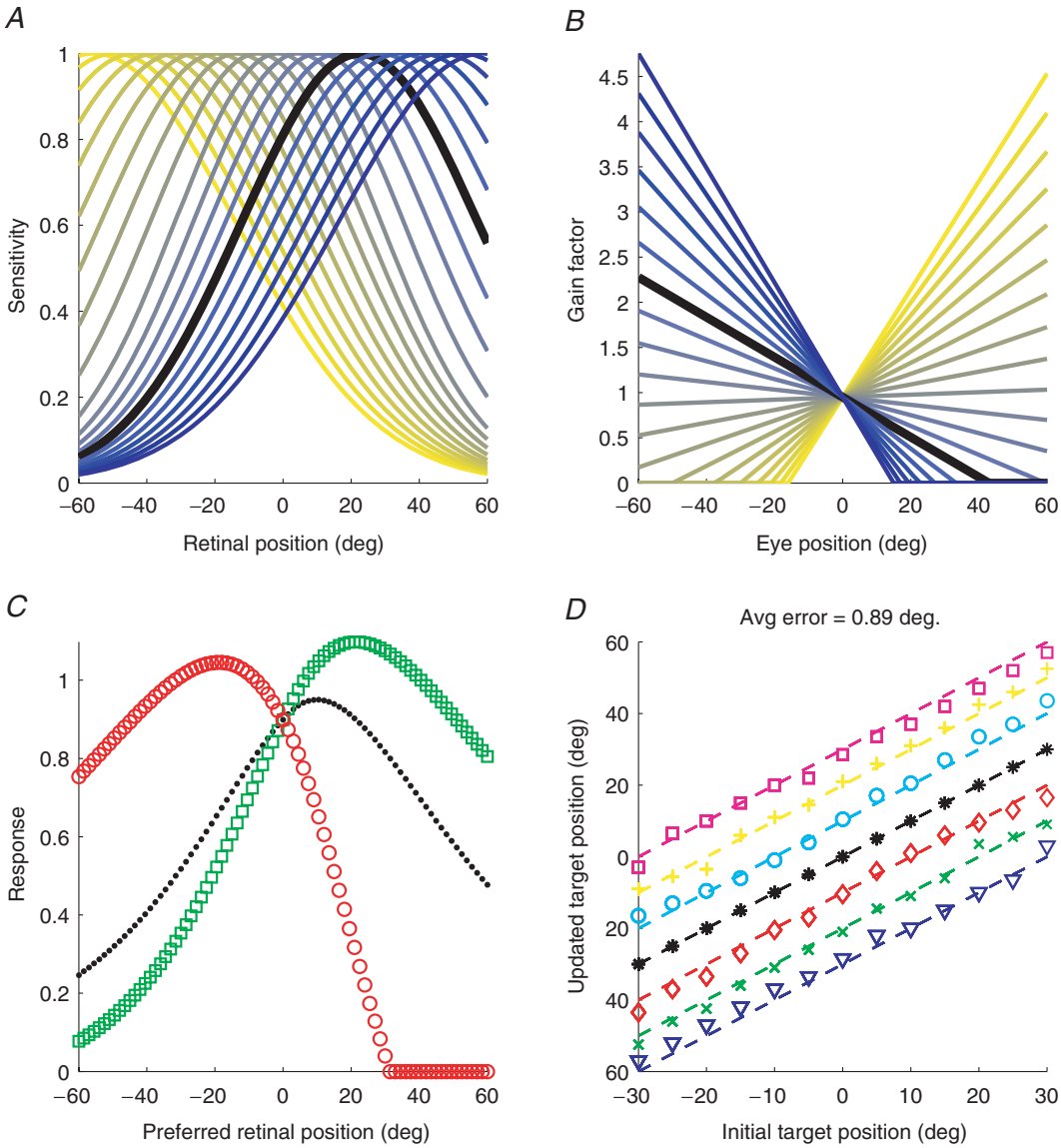

Figure 7. One-dimensional model used in simulating the firing rate of FEF neurons during double-step saccades

A, retinal sensitivity functions for a subset of 20 model neurons. *B*, eye position sensitivity functions. The colour of each curve matches the corresponding retinal sensitivity function in *A*. *C*, population response. The response of each model unit is plotted as a function of the preferred retinal position of that unit. The black dots are the population response for a 10 deg rightward target when fixation is straight ahead. The green squares are the population response to the same initial retinal target location after gaze has shifted 10 deg to the left, thus requiring a 20 deg rightward saccade. The red circles are the population response to the same 10 deg rightward target following a 30 deg rightward gaze shift, thus requiring a 20 deg leftward saccade. *D*, predicted saccade amplitude as a function of initial retinal target position following gaze shifts of −30 (□), −20 (+), −10 (○), 0 (*), +10 (◇), +20 (×) and +30 (▽) deg. The error was computed as the difference between the exact vector difference between target and fixation point and the saccade vector estimated from the peak of the population response.

linear-rectified function suffices. It may be that the response saturation of the sigmoid is not essential to the performance of the model.

The response of a model FEF neuron follows the form given in eqn (2) where, for simplicity, we set the background a_1 to be zero and the amplitude of the visual response a_2 to be normalized to unity. The receptive field centres a_3 were spaced evenly every 2.5 deg from −100 to +100 deg. The receptive field sizes a_4 were chosen to follow the equation $a_4 = 30\ \text{deg} + 0.3 \times a_3$. Therefore the sizes of the receptive fields increase with eccentricity (Bruce & Goldberg, 1985). This feature, while not essential to the model, improved its performance. Finally the gain field slopes follow the relation $a_5 = -0.001 \times a_3$. The proportionality constant was taken directly from the data of Fig. 5. Notice that the gain factors are small. The average slope is of the order of 0.03 deg^{-1}. This corresponds to a 3% change in firing rate for every degree of change in eye position. Over the entire primate oculomotor range of ±50 deg, the average model neuron shows a firing rate modulation due to eye position of about 200%. The absolute magnitude of the gain field slopes is not a critical feature of the model. Rather, the accuracy of the predictions depends on the relative variation in gain field slope across the population. Hence, the model could perform accurately if the eye position sensitivity were increased. The model shows that the typical magnitude of the eye position effects measured physiologically is adequate for accurate vector subtraction.

Figure 7*C* shows the population response for three example eye movements. Each point is the normalized response of a single neuron plotted as a function of its preferred retinal location. In all three cases, the initial target position is 10 deg to the right of fixation. The black dots show the population response when gaze is straight ahead. The green squares show the response when gaze has shifted 10 deg to the left so that the updated retinal target position becomes 20 deg to the right. The red circles are the response when gaze is shifted 30 deg to the right so that the position of the remembered target in retinal coordinates shifts to 20 deg to the left of the vertical meridian. Note that the population response is unimodal in all cases. Thus the most active cells in the population are those with receptive field eccentricity corresponding to the vector difference *x–y*.

Figure 7*D* shows the error between the updated retinal target position predicted by the model and the veridical position for a variety of eye positions and target positions. The black circles correspond to zero gaze shift so that the initial and updated target positions are the same. This verifies that the model encodes target position veridically in the default case of no eye movement. The dashed lines indicate constant intervening eye positions shifts ranging from 30 deg to the left of the centre of gaze for the uppermost curve (rightwards saccades) to 30 deg to the right for the lowermost curve (leftwards saccades) in steps of 10 deg. The average updated target position error was calculated by averaging the absolute difference between the observed and ideal updated target positions. This error averaged less than 1 deg over a range of 120 deg.

Discussion

Most FEF neurons recorded in this study showed clear evidence of eye position signals modulating their background, visual and movement-related activity. Across the population, there was a systematic relationship between the slope of the eye position sensitivity and receptive field position. A control experiment showed that the effect of eccentric gaze position was not likely to be due to covert planning of a saccade back towards the centre of gaze.

The relationship between eye position sensitivity and response field location is predicted by some models in which vector subtraction is computed using eye position gain fields (Xing & Andersen, 2000). The simple model presented here shows that the eye position gain field can be semi-linear and have a slope negatively proportional to the visual receptive field eccentricity. One implication of this model is that the locus of activity in the FEF moves to a different part of the retinal map whenever there is shift in gaze. However, the response fields of individual neurons remain fixed. The model therefore predicts that microstimulation of the FEF should produce saccades of fixed amplitude and direction regardless of IEP. This has been shown repeatedly in FEF (Robinson & Fuchs, 1969; Russo & Bruce, 1993; Fujii *et al.* 1998; Mushiake *et al.* 1999). This is also consistent with the view that many oculomotor structures encode saccades as a displacement from a given eye position, rather than as a final location (Dassonville *et al.* 1995; Dominey *et al.* 1997). Of course, one must take care in predicting neural response properties based on stimulation results; electrically evoked movements do not always match the receptive/movement fields of neurons at the stimulation site (Blohm, Keith & Crawford, 2006). Hence, results showing that saccades evoked by stimulation of FEF are independent of IEP are not inconsistent with the observation that neural responses in FEF are modulated by eye position.

Recently Campos *et al.* (2006) reported effects of saccade vector and eye position on the activity of neurons in the deep layers of monkey superior colliculus. Van Opstal *et al.* (1995) reported eye position modulation of saccadic activity in the colliculus similar to eye position gain fields found in the posterior parietal cortex (PPC). By contrast, we found that most of the neurons recorded in FEF have opposite eye position and saccade vector tuning. An alignment between eye position and retinal fields favours the computation of vector addition, thus resulting in an estimation of target location in head-centred coordinates. While it is possible that a subpopulation of neurons in the FEF may be involved with such a computation, the majority of the cells did not appear to have that function

at least when eye position at fixation and retinal location during the visual stimulation intervals are considered. Another difference with the colliculus is that we find strong eye position modulation in units having visual responses whereas the eye position modulation became weaker in cells with stronger activity around the time of the saccade.

Our experiments do not provide information about the origin of eye position signals in FEF, which may arise from proprioception, or from a copy of the eye movement command. Bizzi (1968) and Bizzi & Schiller (1970) argued against a proprioceptive origin of the eye position signals in the units that were active during saccades, because if the stretch applied to the antagonistic muscle during the saccade were responsible for the discharge, these same cells should fire during pursuit and the slow phase of nystagmus.

Receptive field remapping and spatial reference frames

The present experiments were not designed to determine whether neurons in FEF have shifting or morphing receptive fields in general (Bruce & Goldberg, 1985; Duhamel *et al.* 1992; Umeno & Goldberg, 1997). Shifting receptive fields are a phenomenon observed in visual neurons in LIP (Lateral Intraparietal Cortex) and FEF within a small window of time around a saccade. The eye position signals on which we based the analysis reported here were static or slowly varying signals recorded while the eye was stationary, and were found in all classes of neuron. The response fields of the neurons recorded in this study remained fixed in retinal coordinates. We found no evidence for supra-retinal reference frames in FEF. The model advanced here does not assume nor can it generate shifting receptive fields. The model works by shifting the locus of the peak of activity within a retinotopic map each time the eye moves. The receptive fields of the neurons in the map do not move. The eye position-related effects in this study may be unrelated to shifting receptive fields, except in the sense that they may represent a parallel mechanism for updating target location in working memory.

It is possible to extend the present model to give responses consistent with encoding visual targets in intermediate reference frames ranging through a continuum between purely eye-centred and purely head-centred, as has been reported in several cortical areas (VIP (Ventral Intraparietal Cortex), Duhamel *et al.* 1997; Schlack *et al.* 2005; PO/V6, Fattori *et al.* 1992; Galletti *et al.* 1993, 1995; PPC, Andersen *et al.* 1985; Batista *et al.* 1999; Bremmer *et al.* 1998; Mullette-Gillman *et al.* 2005). Dean & Platt (2006) have recently reported non-retinocentric and allocentric encoding by neurons in the posterior cingulate cortex. In order to encode in an allocentric reference frame, the model presented here needs to be extended to include gain fields related to head and body position. From our study we cannot rule out the presence of head position or head movement signals in coordination with eye position signals, but the framework provided by the model allows extensions to take into account integration of such signals.

Relation to other models

In posterior parietal cortex, Andersen & Mountcastle (1983) showed the effect of gaze direction on the excitability of neurons, and further characterized the nature of eye position signals and their relation to spatial encoding (Andersen *et al.* 1985, 1990). Droulez & Berthoz (1991), Zipser & Andersen (1988), Xing & Andersen (2000), Siegel (1998), Salinas & Abbott (1995), and Pouget & Sejnowski (1997) have presented detailed models involving sensory receptive fields and eye position-dependent multiplicative modulating interactions, either assuming those interactions explicitly or showing they get generated in the learning process of neural networks. Droulez & Berthoz (1991) presented a neural network capable of accounting for displacement of activity across a retinotopic map. Their model generated a saccade coded in spatial coordinates, although the whole process used strictly retinotopic inputs and updating of the eye position using eye velocity inputs. White & Snyder (2004) found that a neural network could accomplish spatial updating using gaze position, displacement or velocity signals.

Xing & Andersen (2000) developed a neural network that performed spatial updating in a double-step saccade task using retinal and eye position inputs. After training the network, they found two groups of hidden units, the first with receptive and gain fields aligned which was in charge of holding memory of the target location in head-centred coordinates. The second group had anti-aligned receptive and gain fields and its task was to compute the metric of the second saccade. Keith *et al.* (2007) found a similar relationship in a network in which the output was a 3-D rotational representation of eye orientation. These properties arose through training, whereas we found that such properties can be mathematically derived given a small number of assumptions. Xing & Andersen (2000) concluded that in solving a double-step saccade task, an explicit head-centred representation of target locations (Robinson, 1975; Sparks & Mays, 1983) was not necessary, nor was it necessary to compute a change in eye position due to the first saccade to then subtract this vector from the originally stored retinal target location (the vector subtraction hypothesis; Bruce & Goldberg, 1985; Quaia *et al.* 1998). Our present model also does not require an explicit head-centred representation as the receptive fields remain fixed relative to the retina. This is consistent with our data.

Our analysis and experiments assume that eye position is represented in 2-D maps in the FEF which represent

horizontal (h) and vertical (v) eye position, and that vector subtraction in this 2-D space is an appropriate mechanism for visual remapping. In reality, movements of the retinal image are caused by 3-D rotations of the eye, which can be described in terms of horizontal and vertical position, plus torsion (τ). The geometry of 3D rotations has important consequences for oculomotor control and visual remapping (Tweed & Vilis, 1987, 1990; Smith & Crawford, 2001; Angelaki & Hess, 2004). However, theoretical approaches have shown that it is possible to deal separately with the 2D translational and 3D non-linear aspects of remapping (Quaia & Optican, 1998; Keith *et al.* 2007). Neurophysiological experiments have shown that the transformation from 2-D (h,v) to 3-D (h,v,τ) coordinates may occur downstream of the superior colliculus (Van Opstal *et al.* 1991) and perhaps of the abducens nucleus (Klier *et al.* 2006). These observations would imply that the transformation is also downstream of FEF.

Whereas our model is specifically concerned with updating a remembered target location via vector subtraction, Salinas & Abbott (1995) and Pouget & Sejnowski (1997) developed models to deal with general sensorimotor transformations and include vector subtraction as a special case. These models neither require nor predict a systematic relationship between visual receptive fields and eye position gain fields such as that found in the current data. Salinas & Abbott (1995) described shifting receptive fields in the output layer of a neural network. They showed that if the inputs are translational invariant encodings of target and eye position, then these signals are integrated accurately to generate a command to acquire the target. Pouget & Sejnowski (1997) put forth the concept of basis functions, which are products of Gaussians encoding visual stimulus and sigmoids encoding eye position. Any non-linear function of these variables can be expanded as a linear combination of the basis functions. The sigmoids encoding eye position had uniform slope and centres evenly spaced across the eye position domain. By contrast, the model presented here has eye position functions that vary in slope but all have the same intercept at $\Delta y = 0$ (instantaneous fixation point). This model replaces the need of an evenly distributed encoding of the eye position with the variable, eccentricity-dependent slope of the gain field. This particular implementation generates a saccade map very consistent with recordings in microstimulation experiments in the FEF and with the data fitted here.

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