

The Postsaccadic Unreliability of Gain Fields Renders It Unlikely that the Motor System Can Use Them to Calculate Target Position in Space

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SUMMARY

Gain fields, the eye-position modulation of visual responses, are thought to provide a mechanism by which the motor system can accurately calculate target position in space despite a constantly moving eye. Current gain-field models assume that the modulation of visual responses by eye position is accurate at all times, even around the time of a saccade. Here, we show that for at least 150 ms after a saccade, gain fields in the lateral intraparietal area (LIP) are unreliable. The majority of LIP cells with steady-state gain fields reflect the presaccadic eye position. The remainder of the cells have responses that cannot be predicted by their steady-state gain fields. Nonetheless, a monkey's oculomotor performance is accurate during this time. These results suggest that current models built upon a simple gain-field algorithm cannot be used to calculate the position of a target in space that flashes briefly after a saccade.

INTRODUCTION

The eye is constantly in motion, with brief epochs of fixation alternating with saccades. Due to these eye movements, a single location in space can occupy many different retinal locations. Yet, despite a moving eye, the motor system is spatially accurate and generates appropriate movements to visual targets. The visual responses of parietal neurons often vary monotonically with increasingly eccentric orbital position (the “gain fields”) (Andersen et al., 1985, 1990; Andersen and Mountcastle, 1983). Gain fields provide an elegant way of combining two independent sensory signals (Dayan and Abbott, 2001), and the visual and eye position signals manifest in the activity of parietal

neurons provide the best neural example of them. A number of computational theories have used gain fields to solve the problem of spatial accuracy, such that gain fields have become a generally accepted mechanism by which the brain calculates target position in space (Andersen, 1997; Brotchie et al., 1995; Cassanello and Ferrera, 2007; Chang et al., 2009; Genovesio and Ferraina, 2004; Marzocchi et al., 2008; Pouget and Sejnowski, 1997; Salinas and Abbott, 1996; Snyder, 2000; Zipser and Andersen, 1988). However, in order for gain fields to be useful for localizing the targets of motor movements in supramaximal coordinates, they must accurately reflect eye position.

The source of the eye position signal that modulates visual responses in the parietal cortex is unknown, although there are two plausible candidates: a corollary discharge of the motor command that maintains steady-state eye position (Morris et al., 2012; Sylvestre et al., 2003) or a proprioceptive oculomotor signal that measures the veridical position of the eye in the orbit (Wang et al., 2007). An efference copy signal would be expected to occur simultaneously with or even precede the saccade. A proprioceptive signal would precede the change in eye position (Wang et al., 2007; Xu et al., 2011). Thus, the temporal dynamics of the gain fields should reveal the source of the eye position signal.

In order to shed light on the two alternatives, we studied the time course of the eye-position modulation of visual responses of neurons in the lateral intraparietal area (LIP). We measured the responses of neurons that had steady-state gain fields to stimuli flashed at various times after saccades that moved the eye from orbital positions associated with strong visual responses to orbital positions associated with weak visual responses, and vice versa. We found that 50 ms after these saccades, most neurons gave visual responses that reflected the presaccadic eye position. A second class of neurons gave visual responses that could not be predicted by the steady-state gain fields and whose relationship to the steady-state values varied with saccade direction. It was not until 250 ms after these saccades that the majority of visual responses accurately reflected the postsaccadic eye position. Although every gain field

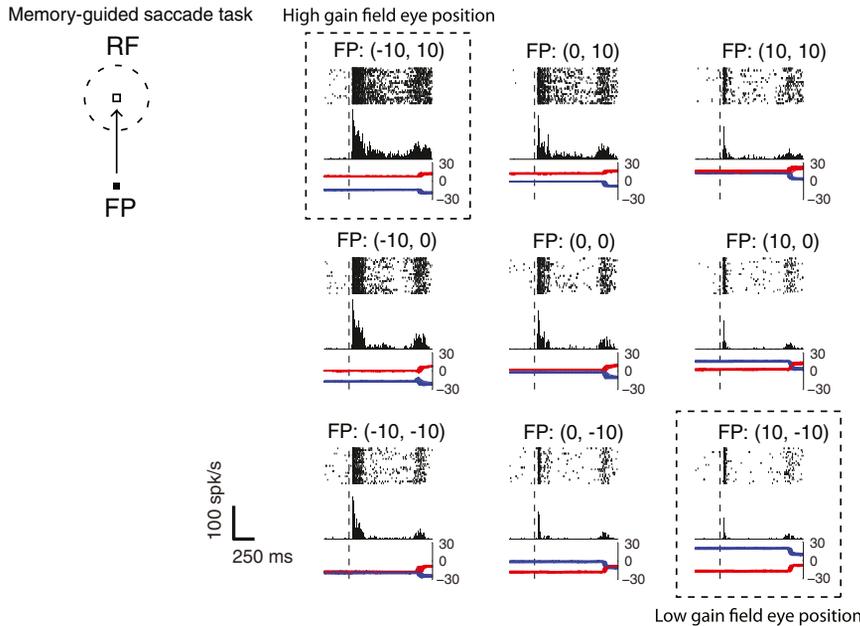


Figure 1. Steady-State Gain-Field Mapping Task and Example Visual Responses

In each trial, the animal performed a memory-guided saccade (arrow) from a fixation point (solid square) to a visual stimulus (empty square) flashed in the neuron's receptive field (dashed circle). Fixation points were located in one of nine possible orbital locations (coordinates), one at the center of the orbit (0, 0) and the others spaced 10° horizontally and/or vertically away from the center. The steady-state gain field response at each of the nine different fixation point locations is plotted for an example LIP neuron (right panel). Activity is aligned on saccade target presentation (dotted line). The histogram beneath each raster indicates the average activity of the corresponding raster, plotted with bin width of 20 ms and without smoothing. Eye positions for each trial are superimposed beneath each raster (horizontal, blue; vertical, red). The eye positions of greatest and least visual responses are marked (dotted boxes; high and low gain-field responses, respectively).

was grossly inaccurate 50 ms after a saccade, the monkeys' behavior was nonetheless spatially accurate to visual targets presented at this time.

RESULTS

The Temporal Dynamics of the Gain Fields after a Saccade

After we isolated and mapped out the receptive field of each LIP neuron, we evaluated its steady-state gain field using a simple memory-guided saccade task (Hikosaka and Wurtz, 1983) with 9 fixation points (Andersen and Mountcastle, 1983), one at the center of the orbit and the others spaced 10° horizontally and/or vertically away from the center. Each trial began with the monkey fixating a stable point of light for at least 500 ms before the saccade target appeared. We determined the eye positions associated with the greatest and least visual responses, defining these as the "high" and "low" gain field eye positions, respectively (Figure 1). We then asked how a prior saccade (the "conditioning saccade") from the high to low or the low to high gain field eye position affected the neuron's response to a visual probe stimulus flashed in the most effective portion of its receptive field at various times after the saccade.

We recorded a total of 89 LIP neurons with steady-state visual gain fields in two monkeys. No cell responded to a stimulus flashed in its receptive field 50 ms after a conditioning saccade in the way predicted by the steady-state gain field. For 47 cells, we flashed the probe for 50 ms at various times (50, 100, 150, 250, 350, 450, 650 ms) after the end of the conditioning saccade; 400 to 1,000 ms after the flash, the monkey made a memory-guided delayed saccade to the spatial location of the now vanished probe (Figure 2A; two-saccade task). For 42 cells, we flashed the probe for 75 ms with delays of 50, 550, or 1,050 ms after the end of the saccade. The probe then served

as the second target in a double-step paradigm (Figure 5A; three-saccade task). The probe was behaviorally relevant in both tasks, and the monkey did not receive a reward when he failed to make a saccade to its spatial location. Neuronal responses to probes flashed 50 ms after first saccades were similar in both tasks and for both monkeys, and we pooled these results for the purpose of analysis.

Fifty milliseconds after the end of the conditioning saccade, the gain fields were universally inaccurate. Sixty-one of the eighty-nine neurons with steady-state gain fields (69%) responded to the probe with the intensity expected from the presaccadic eye position, as if the eyes had not moved. This modulation consistently reflected the presaccadic orbital position for saccades in both high-to-low (Figure 2B) and low-to-high (Figure 2C) gain field directions. We refer to these neurons as "consistent cells." The visual responses of the remaining 28 cells (31%) had various properties, none of which could be predicted by their steady-state gain field responses. We refer to these neurons as "inconsistent cells." For some of these cells, the 50 ms postsaccadic response was higher than the expected steady-state gain field response for both high-to-low (Figure 3A) and low-to-high (Figure 3B) gain field saccades; for others, the 50 ms postsaccadic response was lower (Figure 3C, high-to-low; Figure 3D, low-to-high).

In order to quantify the relationship between the responses to probes flashed after the conditioning saccade and the responses expected from the steady-state gain field, we calculated a gain field index:

$$GFI(t) = \frac{(V_{\text{probe}(t)} - V_{\text{post(steady)}})}{(V_{\text{pre(steady)}} - V_{\text{post(steady)}})}$$

where $GFI(t)$ is the gain field index at postsaccadic time t , $V_{\text{probe}(t)}$ is the visual response to the probe flashed at postsaccadic time t , $V_{\text{pre(steady)}}$ is the steady-state visual response at the

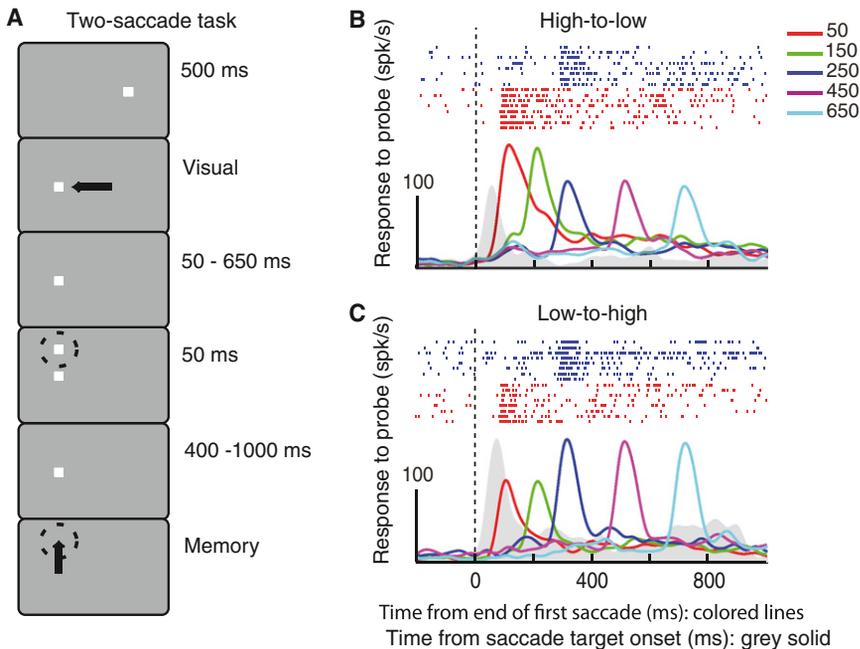


Figure 2. Gain-Field Modulated Visual Responses of LIP Neurons in the Two-Saccade Task

(A) The two-saccade task. Dashed circle represents the receptive field of the neuron under study and arrows represent directions of saccades. (B and C) Single-cell responses to probes flashed at different times after a conditioning saccade in the high-to-low (B) and low-to-high (C) directions. Activity immediately following the conditioning saccade consistently indicates the presaccadic eye position. Activity is aligned on the end of the first saccade (dotted line), averaged across trials, and convolved with a 20 ms Gaussian filter. Colors indicate different timings of the probe (100 and 350 ms not shown). Rasters show spikes in the 50 (bottom) and 250 (top) ms probe delay conditions. The solid curve (gray) shows the steady-state visual response at the postsaccadic orbital position during a memory-guided saccade task; for this curve, 0 on the abscissa is the time of appearance of the saccade target. See also Figure S2.

presaccadic orbital position, and $V_{\text{post(steady)}}$ is the steady-state visual response at the postsaccadic orbital position. An index value of 1 meant that the response to the probe reflected the presaccadic eye position; an index value of 0 meant that the response to the probe reflected the postsaccadic eye position. In the 50 ms postsaccadic case, the consistent cells, whose 50 ms postsaccadic response resembled the presaccadic visual response, had mean gain field indices of 0.98 ± 0.42 (median = 0.92) for high-to-low saccades and 1.02 ± 0.44 (median = 0.94) for low-to-high saccades. These values are not different from each other or from 1 ($p = 0.48$ by Mann-Whitney U test), indicating that saccade direction had little effect on the index (Figure 4A, detailed view; see Figure S1 available online; all consistent cells). The inconsistent cells, whose 50 ms postsaccadic responses could not be predicted by the steady-state values, had on average positive gain field indices for saccades in the high-to-low direction (mean = 0.85 ± 1.72 , median = 0.79) and negative gain field indices for saccades in the low-to-high direction (mean = -1.01 ± 1.35 , median = -0.88). In contrast to the index values of the consistent cells, these values differed significantly for saccades in opposite directions ($p < 0.01$ by Mann-Whitney U test). These data show that the consistent cells comprise a rather homogeneous population of cells whose activity is dependent on eye position and the inconsistent cells an inhomogeneous population whose activity in the immediate postsaccadic period varies with saccade direction.

No cells exhibited the steady-state postsaccadic gain field at 50 ms (Figure 4A, two- and three-saccade cells) or 150 ms (Figure 4B, two-saccade cells) after conditioning saccades in either direction. After 250 ms, however, the majority of cells ($n = 40$, 85%) accurately reflected the response values predicted by the steady-state gain fields (Figure 4C, two-saccade cells). The remainder of the cells ($n = 7$, 15%) did so by 350 ms (Figure 4D,

two-saccade cells). The median values of the gain field indices had a similar time course (Figure 4E). We also calculated the time point of transition from nonveridical to veridical eye position information (see Experimental Procedures; Figure 4F). 43 of the 47 cells (91%) reported the steady-state values in the same stimulus interval for saccades in both directions.

We recorded 13 cells that had no eye-position modulation of visual responses to test if the spatial inaccuracy of immediate postsaccadic visual responses were simply the result of flashing stimuli around the time of a saccade. For these cells, responses to visual probes were not statistically different ($p > 0.05$ by KS test) regardless of the probe delay and the direction of the first saccade (Figure S2).

Behavioral Performance during the Period of Gain-Field Inaccuracy

Although the gain fields among the population of neurons reflect eye position inaccurately immediately after the first saccade in the two-saccade task, there is a potential shortcoming to using this task to assess the monkey's behavioral performance during this period. In the two-saccade task, the retinal location of the second target and the vector of the saccade necessary to acquire it are coincident. Therefore, it could be argued that the task does not depend on the accuracy of the gain fields since it can be solved without employing a suparetinal mechanism. The double-step task has been used to show that the oculomotor system can compensate for an intervening saccade and accurately acquire a target even when there is a dissonance between the retinal location of a target and the vector of the saccade necessary to acquire it (Hallett and Lightstone, 1976). If the brain used a gain-field mechanism to solve the double-step task, the position of targets flashed immediately after a saccade would be calculated as if the eyes had not moved.

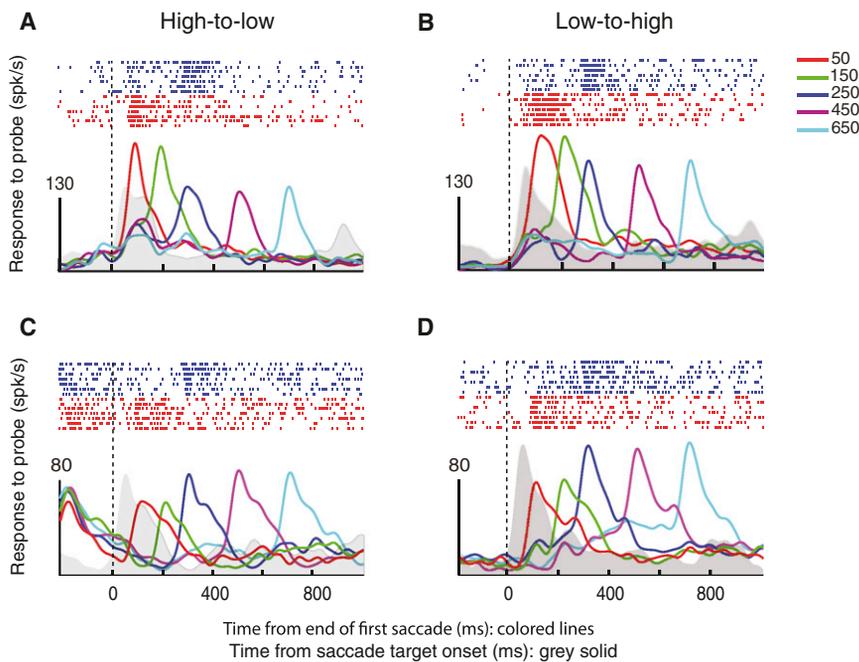


Figure 3. Visual Responses of Inconsistent Cells in the Two-Saccade Task

(A and B) Visual responses of single inconsistent LIP neuron that shows high-to-low modulation for saccades in both the high-to-low (A) and low-to-high (B) gain field directions. Activity immediately following the conditioning saccade inconsistently indicates the presaccadic eye position. Conventions same as in Figure 2B. Rasters show spikes in the 50 (bottom) and 250 (top) ms probe delay conditions.

(C and D) Visual responses of single inconsistent LIP neuron that shows low-to-high modulation for saccades in both the high-to-low (C) and low-to-high (D) gain field directions. See also Figure S2.

We used the three-saccade task (Figure 5A), which cannot be solved without employing a suparetinal mechanism, to test if the inaccuracy of the gain fields immediately after a conditioning saccade was reflected in the monkeys' behavior. In this task, the monkey performed a traditional double-step task following a conditioning saccade in the high-to-low or low-to-high gain field direction. Two targets, one blue and one red (the probe), appeared simultaneously 50, 550, or 1,050 ms after the end of the first saccade. The red probe flashed in the cell's receptive field for 75 ms and disappeared. The blue target appeared outside the cell's receptive field and remained on until the monkey made a visually guided saccade to its location, after which the monkey immediately made a memory-guided saccade to the spatial location of the red probe. In order to acquire the red target accurately, the monkey had to compensate for the change in eye position caused by the saccade to the blue target—there was now a dissonance between the retinal location at which the target had appeared and the vector of the saccade needed to acquire the target. As expected, the cells gave inaccurate responses 50 ms after the saccade and accurate responses 550 ms and 1,050 ms after the conditioning saccade (Figure 5B, high-to-low conditioning saccade; Figure 5C, low-to-high conditioning saccade).

Despite the inaccuracy of the gain fields immediately after the conditioning saccade in the three-saccade task, third saccades were largely accurate regardless of when the probe was flashed (Figure 6A). There were small mislocalizations of third-saccade endpoints in the early compared to the late probe condition (50 and 1,050 ms delay, respectively) for both monkeys (2.89° maximum, $0.90 \pm 0.52^\circ$ mean), but these inaccuracies depended upon the direction of the preceding (second) rather than the conditioning (first) saccade (Jeffries et al., 2007). When we analyzed the mislocalization vectors after reorienting the conditioning saccades in the rightward horizontal direction, there was

no net mislocalization effect (Figure 6B, mean $x = 0.05 \pm 0.68^\circ$, $p > 0.05$ by KS test; mean $y = -0.05 \pm 0.79^\circ$, $p > 0.05$ by KS test). When we analyzed the mislocalization vectors after reorienting the second saccades in the rightward horizontal direction, however, a small but

significant effect emerged (Figure 6C; $x = -0.47 \pm 0.69^\circ$, $p < 0.05$ by KS test; $y = -0.01 \pm 0.64^\circ$, $p > 0.05$ by KS test).

DISCUSSION

In these experiments, we investigated the temporal dynamics of visual gain fields in LIP and the accuracy of eye movements to visual targets presented after the end of a saccade. We found that for the first 150 ms after a saccade, visual responses either reflected the presaccadic eye position or were unrelated to the responses predicted by the steady-state gain fields. Nonetheless, the unreliability of the eye position signal had no effect on the monkey's oculomotor behavior. Here, we discuss two theories that have been promoted to explain spatial accuracy despite a constantly moving eye and the implication of our results on the identity of the eye position signal that modulates visual responses in LIP.

Two Theories of Spatial Accuracy

Two theories have been advanced to explain how the brain achieves a spatially accurate representation of visual space for action and perception despite a moving eye. The first, originated by Ewald Hering, is that the brain uses eye position to calculate target position in space, which would render intervening saccades irrelevant (Pouget and Sejnowski, 1997; Pouget and Snyder, 2000; Salinas and Abbott, 1996; Zipser and Andersen, 1988). The gain-field theory is the modern descendant of Hering's conjecture and is exceptionally tractable computationally. According to this theory, eye-position modulated visual responses serve as the fixed weights in a network that transforms the spatial location of visual stimuli presented in retinotopic coordinates into head-centered coordinates. A critical aspect of the network model is that the fixed weights of the eye position modulation are always reliable, so that the

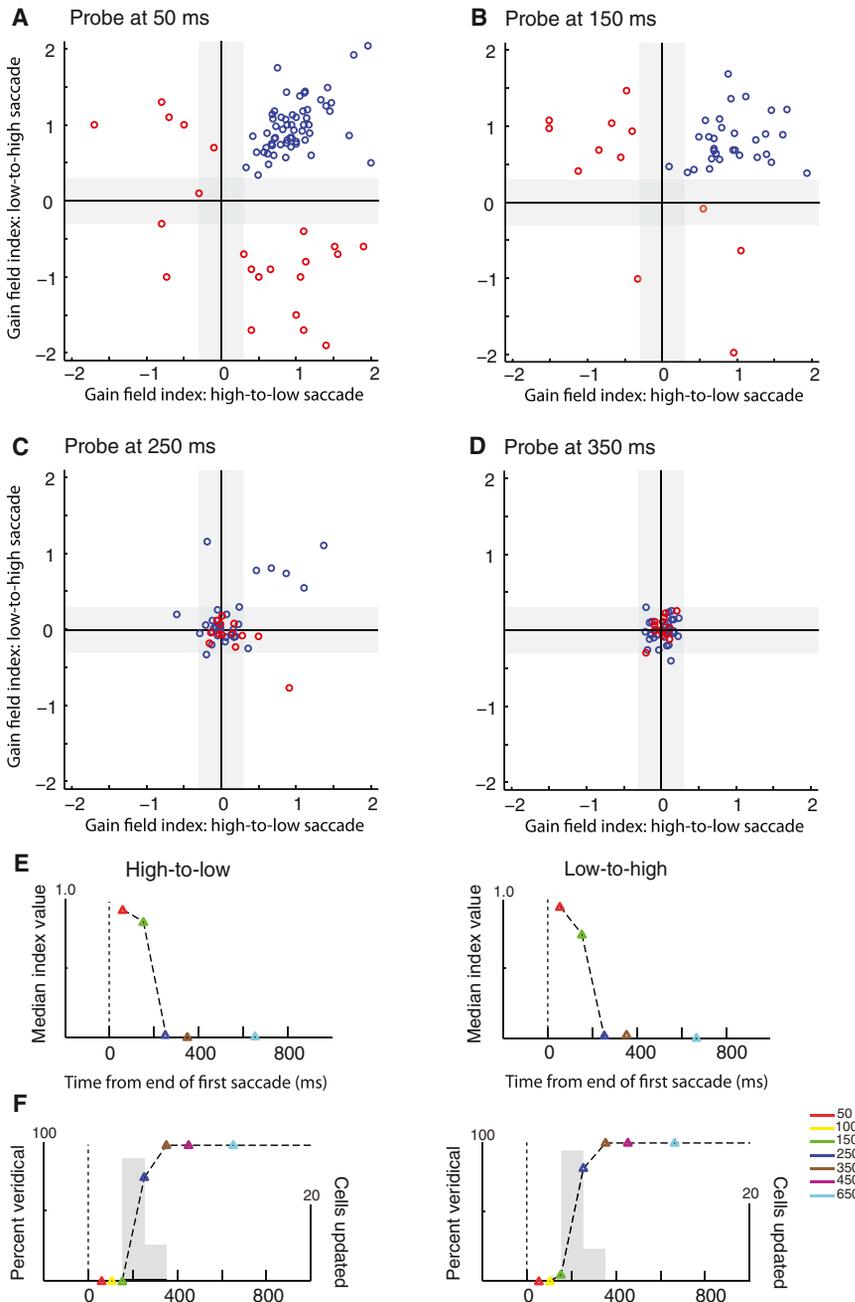


Figure 4. Population Gain Field Indices and Development of Veridical Responses for LIP Neurons

(A) Detailed view of the majority of gain field indices in the 50 ms probe delay condition during the two- and three-saccade tasks. Indices for conditioning saccades in the low-to-high direction (ordinate) plotted against indices for conditioning saccades in the high-to-low direction (abscissa). Gain field indices for individual consistent cells (blue circles) were strongly predictive of the presaccadic eye position (mean $x = 0.98 \pm 0.42$, median $x = 0.92$; mean $y = 1.02 \pm 0.44$, median $y = 0.94$). Gain field indices for individual inconsistent cells (red circles) showed no predictive value for the pre- or post-saccadic eye positions (mean $x = 0.85 \pm 1.72$, median $x = 0.78$; mean $y = -1.01 \pm 1.35$, median $y = -0.88$). Gray bars encompass index values within 30% of the expected steady-state gain field responses. See also Figure S1.

(B to D) Gain field indices for visual gain field modulation in the 150 (B), 250 (C), and 350 (D) ms postsaccadic cases during the two-saccade task. (E) Median gain field index values from (A)–(D) for conditioning saccades in the high-to-low (left) and low-to-high (right) directions plotted against time after saccade.

(F) Development of veridical gain field response after high-to-low (left) and low-to-high (right) conditioning saccades. Percentage of cells exhibiting the veridical gain field response after conditioning saccade (ordinate, left axis) plotted against time after saccade (abscissa). Triangles represent probe presentation times. Cumulative histogram shows time of first veridical gain field response after high-to-low conditioning saccades, across population of cells in the double-saccade task ($n = 47$). Grey bars represent number of cells updated in each probe interval (ordinate, right axis).

Nonetheless, monkeys make accurate saccades to stimuli flashed immediately after a conditioning saccade, even when there is a dissonance between the retinal location of the stimulus and the saccade necessary to acquire it. We cannot exclude that the immediate postsaccadic responses of the inconsistent cells reflects an alternate set of gain fields that is accurate but different from the

transformation of the visual responses occurs accurately at all times.

Our results show that the eye-position modulation of visual responses is not always reliable. For at least 150 ms after a saccade, visual responses of LIP neurons either reflect the presaccadic orbital position (the consistent cells) or are unrelated to their steady-state gain fields (the inconsistent cells). A simple calculation that uses the steady-state ensemble of visual responses as a set of basis functions or the hidden layer of a neural network at all times would be grossly inaccurate in this epoch.

Therefore, it is possible that the brain could calculate target position from this temporary set of gain fields using an algorithm that ignores the consistent cells, decodes the immediate postsaccadic responses of the inconsistent cells, and gradually changes as the ensemble of responses revert to their steady-state values at a collection of different times.

No formulation of the gain-field model has ever made an exception for stimuli flashed immediately after a saccade. For example, Pouget and Sejnowski emphasize the reliability of the gain field values: “Choosing the hidden units in advance greatly simplifies optimization since the input weights are fixed and only

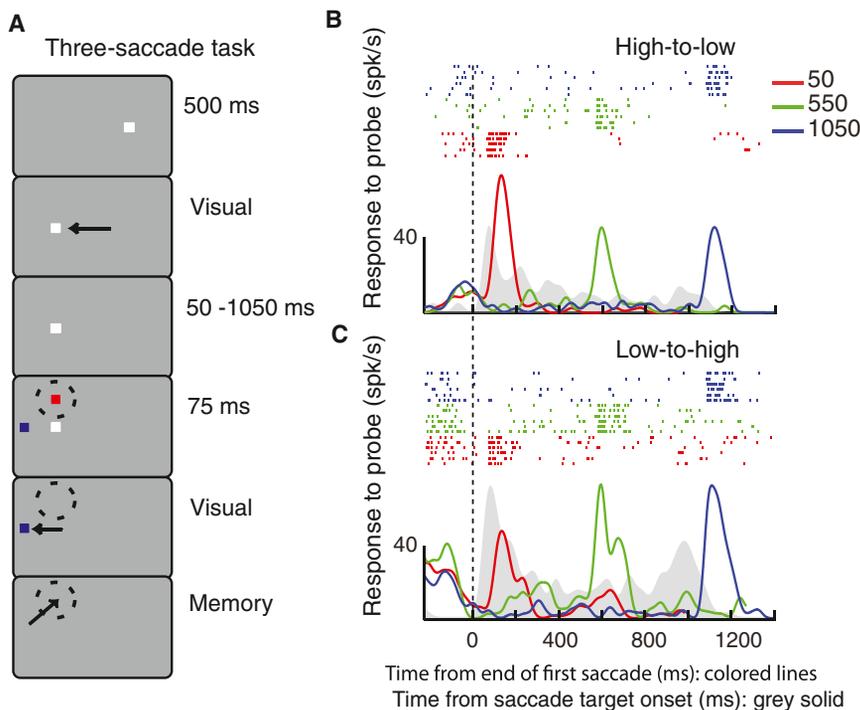


Figure 5. Gain-Field Modulated Visual Responses of LIP Neurons in the Three-Saccade Task

(A) The three-saccade task. Dashed circle represents the receptive field of the neuron under study after the monkey has performed the first (conditioning) saccade, and arrows represent directions of saccades. Note that the target of the third saccade is in the neuron's receptive field when it appears (after the conditioning saccade), but its spatial location is not in the neuron's receptive field after the second saccade, when the monkey must acquire its spatial location with the third saccade. (B) Responses to probes flashed at different times after a conditioning saccade in the high-to-low direction. Conventions same as in Figure 2B. Rasters show spikes in the 50 (bottom) and 550 (top) ms probe delay conditions. (C) Activity of the same neuron as in b after a low-to-high conditioning saccade.

the weights from the hidden to the output units need to be determined" (Pouget and Sejnowski, 1994). In light of our results, if the model is to choose the hidden units in advance, it must now factor in the timing of the most recent saccade in order to decide whether to use the steady-state values for all gain-modulated neurons or the immediate postsaccadic values of the inconsistent cells.

The second theory, originated by Hermann von Helmholtz, is that rather than using eye position, the brain calculates a spatially accurate saccadic vector, using a corollary discharge of the intervening saccade to adjust the sensory representation of target position. The modern descendent of this theory is the phenomenon of receptive field remapping: this process remaps the receptive fields of visual neurons so that a stimulus that will be brought into the receptive field by a saccade, or that flashes and disappears before a saccade, will drive the cell. The oculomotor system effectively performs a vector subtraction to recalculate the saccade trajectory needed to acquire the target (Goldberg and Bruce, 1990), without the need to calculate the target's position in suparetinal coordinates. The remapping phenomenon demonstrates the necessary temporal properties for monkeys to solve the double step task (Batista et al., 1999; Colby et al., 1996; Duhamel et al., 1992; Kusunoki and Goldberg, 2003; Sommer and Wurtz, 2006). Receptive field remapping must be driven by a corollary discharge of the motor command because it can occur before the eye movement. It therefore avoids the perisaccadic errors that would arise if the brain used a gain-field mechanism to calculate target position. That the brain depends upon a corollary discharge of the first saccade to perform the double-step saccade is shown by two studies: (1) the corollary discharge signal that shifts receptive fields in the frontal eye field around the time of a saccade arises from the

superior colliculus via the medial dorsal nucleus of the thalamus. Reversible lesions in the medial dorsal nucleus of the thalamus impair the monkeys' performance in the double-step task (Sommer and Wurtz, 2002). (2) Humans with parietal lesions cannot perform the double-step task accurately because they cannot compensate when the first saccade is made in the direction contralateral to the lesion (Wardak et al., 2002). These findings demonstrate the important role of corollary discharge and receptive field remapping in maintaining the spatial accuracy of saccade targets across eye movements.

It is possible that receptive field remapping contributed to the inaccuracy of perisaccadic modulation of visual responses by eye position. We mapped the receptive fields carefully at the center of gaze, but placed the probe only at the most effective stimulus location in the two- and three-saccade tasks. If receptive field geometry changed as a function of the conditioning saccade, the probe might stimulate a less effective portion of the receptive field and appear to evoke a gain-field effect. This is, however, unlikely to explain the observed patterns of immediate postsaccadic responses for two reasons. The first is that although perisaccadic remapping can modulate receptive field shapes immediately after the saccade (Kusunoki and Goldberg, 2003), this effect is over by 150 ms, a time at which all consistent and inconsistent cells still exhibit spatially inaccurate visual responses. V4, which has a robust projection to LIP (Baizer et al., 1991), exhibits similar perisaccadic receptive field shifts, but these too resolve by 150 ms after the saccade (Tolias et al., 2001). The second is that the majority of cells gave *increased* responses immediately after conditioning saccades in at least one direction. Receptive field shifts could evoke this consistent high-to-low response pattern only if we erroneously mapped the receptive fields of most cells, missing their most effective locations. It is therefore unlikely that perisaccadic receptive field shifts are responsible for the immediate postsaccadic patterns of activity observed among the consistent and inconsistent cells.

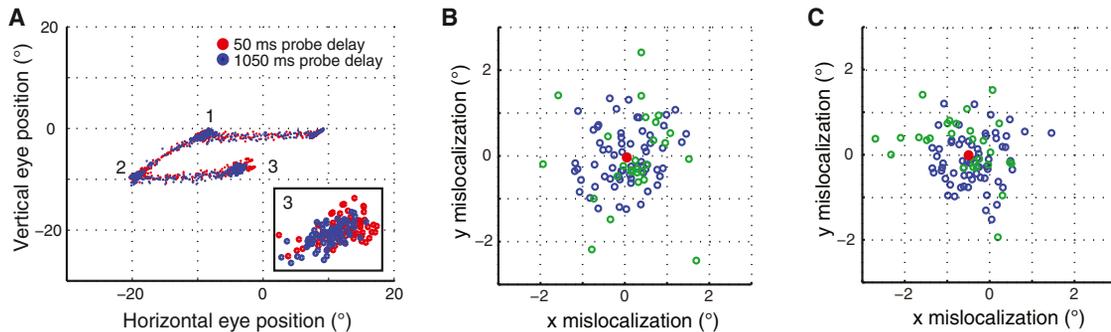


Figure 6. Saccadic Accuracy in the Three-Saccade Task

(A) Eye traces from all trials in one experimental block are shown for first saccades in one direction (monkey G). Comparison of behavior when the probe is presented early (50 ms, red) and late (1,050 ms, blue). Numbers (1, 2, 3) indicate order of saccades. Third saccade endpoint distributions for both delay conditions are shown (inset).

(B) Plot of third saccade mislocalization vectors in monkey G (blue) and W (green) normalized to first saccade vectors aligned in the rightward horizontal direction (mean $x = 0.05^\circ \pm 0.68^\circ$, mean $y = -0.05^\circ \pm 0.79^\circ$; KS test, $p > 0.05$). Mean mislocalization shows no net effect (red dot).

(C) Plot of third saccade mislocalization vectors when reoriented according to second saccade vectors normalized to the rightward horizontal direction. (mean $x = -0.47^\circ \pm 0.69^\circ$, KS test, $p < 0.05$; mean $y = -0.01^\circ \pm 0.64^\circ$, KS test, $p > 0.05$). Mean mislocalization corresponds to the direction opposite that of the second saccade (red dot).

The Source of Eye Position Information that Modulates Visual Gain Fields in LIP

The source of the eye position signal that modulates visual responses to create the gain fields is unknown. The steady-state responses and the immediate postsaccadic responses of the consistent cells could arise from a corollary discharge, but the slow time course is more consistent with that of the proprioceptive eye position signal in area 3a of somatosensory cortex, which lags eye position by an average of 60 ms (Xu et al., 2011). Oculomotor proprioception could provide visual gain fields in LIP with eye position information, just as neck proprioception likely provides head gain fields in LIP with head-on-body information (Snyder et al., 1998). It is important to note, however, that lesions in the proprioceptive pathway have no noticeable effect on monkeys' performance in the double-step task (Guthrie et al., 1983). It is more likely that the proprioceptive signal is used for calibration of the oculomotor system than for moment-to-moment control of saccades (Lewis et al., 1994).

Another possible source of the eye position signal could be the calculated signal described by Morris et al. (2012). These authors measured the activity of neurons in LIP when the monkey made a saccade to a position outside the neurons' receptive fields, without flashing a second target elsewhere. They noted that this baseline activity increased in one direction of saccades and decreased in the other direction. By subtracting the off-activity from the on-activity and comparing this to the steady-state eye position signal, the authors were able to calculate an eye position signal that nicely resembled the actual eye position. In LIP, this calculated signal lagged the eye position by approximately 200 ms, which closely approximates the temporal delay of the gain fields observed in our study.

The signal that modulates the visual responses of the inconsistent cells during the immediate postsaccadic period is more difficult to understand. The most likely possibility is that the activity arises from differences in saccade trajectory rather than eye position, although our experiments were not designed

to test this hypothesis explicitly. Alternatively, the postsaccadic modulation could come from a different source than the one used during the steady state. LIP neurons have a steady-state eye position signal that lags the actual eye position (Andersen et al., 1990; Barash et al., 1991; Pouget and Sejnowski, 1994), but this signal is inaccurate 50 ms after a saccade (Bremmer et al., 2009). It could come from a motor eye position signal, but such a signal has never been seen in the cortex. It could also come from the postsaccadic movement cells in the frontal eye field, some of which begin to discharge immediately at the end of the saccade (Bizzi, 1968; Bruce et al., 1985).

Although our results are limited to the programming of saccades, we think it is unlikely that the skeletal motor system has access to a reliable gain-field system when LIP, the parietal area most tightly linked to the oculomotor system, does not. We suggest instead that gain fields provide feedback to recalibrate the efference copy signal after an eye movement or update a forward model to drive subsequent movements, but that current gain-field models cannot explain how the brain calculates the spatial location of movement targets at all times. Furthermore, we believe additional work studying the time course of eye-position modulated responses in other parietal areas, such as the parietal reach region, is warranted at this time.

EXPERIMENTAL PROCEDURES

General

We recorded from one hemisphere in each of two adult male Rhesus monkeys (*Macacca mulatta*). All monkey procedures were approved by the New York State Psychiatric Institute and Columbia University Medical Center Institutional Animal Care and Use Committees and were in compliance with the NIH Guidelines for the Care and Use of Experimental Animals. We prepared monkeys for recording by implanting a chamber positioned above LIP, located by T1 MRI. We recorded single unit activity extracellularly using 1 M Ω glass-coated tungsten microelectrodes (Alpha-Omega). Eye position was continuously monitored using subconjunctivally implanted scleral search coils. We used the REX system running under the ANX real-time operating system on a Dell Optiplex PC to control behavior

and collect unit and eye position information for online and subsequent offline analysis (Hays et al., 1982). The waveforms of single units were sorted and digitized by the MEX system, which is freely available for download from the website of the Laboratory of Sensorimotor Research at the National Eye Institute.

Visual stimuli were generated by a Hitachi CPX275 projector running at 60 Hz under control of the VEX visual display system. We used a photocell to monitor the actual appearance of stimuli on the screen and insure that the stimulus presentations were timed accurately. The stimuli were 440 cd/m² on a screen background of 1.5 cd/m² and decayed to background luminance within one ms of stimulus offset. Fixation and saccade windows in all tasks measured $\pm 3^\circ$ and 5° , respectively.

After each putative LIP neuron was isolated, the memory-guided saccade task was used to map out its receptive field. The fixation point was held at the center of the screen and a joystick was used to vary the retinotopic location of the visual probe until it elicited a maximal visual response, which indicated the center of the receptive field. Subsequent recordings in the gain field mapping, two-saccade and three-saccade tasks were all performed with the probe at the center of the receptive field.

In each two-saccade task block, normal probe trials were randomly interleaved with trials in which probes appeared outside the RF or not at all to ensure the monkey attended to the probe's location. Similarly, in the three-saccade task, the red probe randomly appeared inside or outside of the RF, but always far away ($>20^\circ$ degrees) from the blue target, which appeared outside of the RF.

Data Analysis

Steady-state gain field responses were defined as responses to stimuli flashed at least 600 ms after the beginning of a fixation. In order to be characterized as a gain field neuron, the cell had to have steady-state gain field responses in the interval from 0 to 160 ms after the probe presentation that differed significantly at two orbital positions 20° apart (two-sample t test, $p > 0.05$). Additionally, the high gain field peak response had to differ from the low gain field peak response by at least 15% of the mean of the two responses.

Gain field update times were calculated by fitting a sigmoid curve to the peak visual responses of all probe delays for saccades in one gain field direction using the `nlinfit` Matlab function. All fits yielded an R-squared value greater than 0.7, and 85% of the fits yield an R-squared value greater than 0.9. The gain field update time, or the time point of transition from nonveridical to veridical eye position information, was defined as the probe delay subsequent to the inflection point of the sigmoid fit. The response of cells without gain fields to the two-saccade task could not be fitted with sigmoids.

Behavioral data were reoriented so that the first or the second saccade vector pointed in the horizontal, rightward direction:

$$x' = x * \cos\left(\frac{(360 - \theta) * \pi}{180}\right) - y * \sin\left(\frac{(360 - \theta) * \pi}{180}\right)$$

$$y' = x * \sin\left(\frac{(360 - \theta) * \pi}{180}\right) + y * \cos\left(\frac{(360 - \theta) * \pi}{180}\right)$$

x and y represent the original saccade vector in real space, θ the angle of rotation, and x' and y' the reoriented saccade vector. Consequently, corresponding saccade mislocalization vectors for each trial block, defined as (mean endpoint of saccades to early probe – mean endpoint of saccades to late probe) were also reoriented.

SUPPLEMENTAL INFORMATION

Supplemental Information includes two figures and can be found with this article online at <http://dx.doi.org/10.1016/j.neuron.2012.10.034>.

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