SPATIAL UPDATING IN THE LATERAL INTRAPARIETAL CORTEX

by

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Recent experiments in neurophysiology have begun to examine the active nature of our perceptual experience. One area of research focuses on the impact of eye movements on visual perception. With each eye movement, a new image is presented to the brain, yet our perception is that the world remains stable. This phenomenon, termed spatial constancy, depends on a convergence of information about our eye movements with sensory information from the visual system. Neurons in the lateral intraparietal cortex (LIP) contribute to the construction of an internal representation of space that is updated or "remapped" with each eye movement.

Although the basic phenomenon of remapping has been described, many questions remain unanswered. Here we describe two experiments designed to gain a greater understanding of spatial updating in the primate brain. First, we hypothesized that spatial updating would be equally robust throughout the visual field. We tested this by monitoring the activity of neurons in LIP while varying the direction over which a stimulus trace must be updated. We found that individual neurons remap stimulus traces in multiple directions, though the strength of the remapped response is variable. Across the population of LIP neurons, remapping is effectively independent of saccade direction. These findings indicate that the activity of LIP neurons can contribute to the maintenance of spatial constancy throughout the visual field.

Second, to begin to understand the circuitry underlying remapping, we studied a special case: when a stimulus must be updated from one visual hemifield to the other. We hypothesized that the forebrain commissures provide the primary route for this across-hemifield remapping. We tested this by comparing the signal related to within- and across-hemifield remapping. We predicted that in split-brain monkeys, across-hemifield remapping would be abolished while within-hemifield remapping would remain robust. Surprisingly, we found that in split-brain monkeys, LIP neurons can remap stimulus traces across hemifields, though this signal is weaker than that associated with within-hemifield remapping. This finding implies that while the forebrain commissures are likely to be the primary route for the interhemispheric transfer of visual information, they are not the only route available. This indicates that a distributed network of brain regions supports spatial updating.

Dedicated to William C. Heiser

A loving father who inspired my pursuit of knowledge

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1. Chapter 1: General Introduction

1.1. The ever stable world

We usually think of perception as leading to action. Sensory information is acquired and processed, a decision is made, and an action is generated. The relationship between perception and action can be considered a forward function in which sensory information influences the generation of movement. Also important to consider, however, is the reverse function in which action influences perception. One of the most striking illustrations of the influence of action on perception comes from our visual experience. We explore the visual world using the high-acuity region of the retina, the fovea. This exploration takes the form of rapid eye movements, or saccades, that re-direct the fovea toward locations of interest. Interestingly, the effect of these movements is potentially detrimental to perception. With each eye movement, a new image impinges on the retina. The result is that a given location in the world corresponds to a new location on the retina. If our visual perception of the world simply reflected the forward processing of sensory information, we would experience objects in the world jumping around with each eye movement. Instead, our movements go unnoticed and our perception is that the world remains stable. Our own experience, then, tells us that visual perception must be based on both the forward flow of sensory information and the reverse flow of motor information.

The idea that action influences perception is an old one. Over 100 years ago, Helmholtz postulated that the *Willensantrengung*, or "effort of will," was used to

compensate for the movement of the visual scene induced by a saccade (Helmholtz, 1866). He demonstrated this with a simple experiment: if the eye is displaced by pressing it gently with the finger, the world seems to jump. If this same movement is produced voluntarily with a saccade, the image of the world remains stable. The perceptual stability we experience reflects the fact that what we see is not a direct impression of the external world, but an internal representation of it that is actively constructed. This internal representation must be updated in conjunction with each eye movement. Recent physiological experiments have begun to explore the neural basis of perceptual stability. Specifically, it has been observed that neurons throughout the brain update visual information at the time of eye movements. This dynamic process, termed spatial updating, is the focus of the present experiments.

The ultimate goal of this research is to gain a better understanding of the neural mechanisms underlying spatial updating in the primate brain. Our experiments build on the existing knowledge of the characteristics and signals involved in spatial updating. The goal of this chapter is to review the relevant literature. In particular, we will focus on a neurophysiological phenomenon, termed remapping, and its relation to spatial constancy. Following this review, we will set forth the two experimental aims of the present study.

1.2. Signals that contribute to spatial constancy

With each eye movement, there are at least three sources of information the brain could use to create the percept of spatial constancy (Bridgeman et al., 1994; Wurtz, 2003). The first signal is visual. When the eyes move, the image of the visual field is

swept across the retina. This full-field motion could be used to indicate that the eye has moved, as long as the head and body remain stationary. This signal, however, requires a lighted contoured environment that may not always be present. The second signal is proprioceptive in nature. The stretch receptors in the eye muscles provide information about when and where the eyes move. Upon demonstrating the existence of the extraocular stretch receptors, Sherrington postulated that proprioceptive information could be used to achieve perceptual stability (Sherrington, 1898). Although the role of proprioceptors has subsequently been investigated, their exact role has yet to be determined (Donaldson, 2000).

We alluded to the final signal in the preceding section. The signal Helmholtz referred to as the 'effort of will' is, in modern neurophysiological terms, a corollary discharge signal. This is a copy of the eye movement command that is sent upstream to other brain areas, rather than downstream to activate the muscles and generate the movement. This information can be used to inform areas throughout the nervous system about the impending eye movement. The great advantage of the corollary discharge signal is that it is available before, during or after the eye movement is generated. In contrast, visual and proprioceptive signals are available to the brain only after the eye movement is underway. Because the corollary discharge signal is available even before the eyes begin to move, it is thought to be especially important for the generation of spatial constancy. Visual areas can use the corollary discharge signal to anticipate what the visual world will look like after the saccade is complete. This allows a visual representation of the world to be available immediately after the eyes reach the new location and without the delay associated with reafferent visual signals.

1.3. Neurons update stimulus locations

Neurophysiological studies have begun to uncover the neural mechanisms that contribute to spatial constancy. Single-unit recording studies in awake behaving monkeys have shown that neurons in parietal, frontal and extrastriate cortex, as well as the superior colliculus, update spatial locations at the time of an eye movement (Goldberg and Bruce, 1990; Duhamel et al., 1992a; Walker et al., 1995; Nakamura and Colby, 2002). These neurons respond to the memory trace of a stimulus location which has been updated in conjunction with the eye movement. The single step task was first used to observe the updating activity of neurons in the lateral intraparietal area (Duhamel et al., 1992a). The task is schematized in Figure 1. In this task, a stimulus is presented briefly outside of the receptive field of the neuron being recorded (panel A). The monkey makes an eye movement from one fixation point (FP1) to another (FP2). The eye movement will move the receptive field onto the location at which the stimulus previously appeared (panel B). The critical feature of the task is that the stimulus is presented briefly enough that it is extinguished even before the eyes began to move. That is, no stimulus was ever present in the receptive field. If the neuron responded as a simple photoreceptor, it would not respond in this task. Instead, it exhibits a brisk response around the time of the eye movement (panel C). Duhamel and colleagues chose the term "remapping" to describe the activity observed in the single step task. This term emphasizes that visual information is being shifted, or remapped, from the coordinates of the initial eye position to the coordinates of the new eye position. The effect of remapping is to maintain a representation of visual space in eye-centered coordinates (Goldberg and Bruce, 1990; Duhamel, et al., 1992a; Colby et al., 1995). That is, the location of a stimulus is always coded in terms of its distance and direction from the location of the fovea. This

information can subsequently be used by the oculomotor system to guide eye movements toward targets.

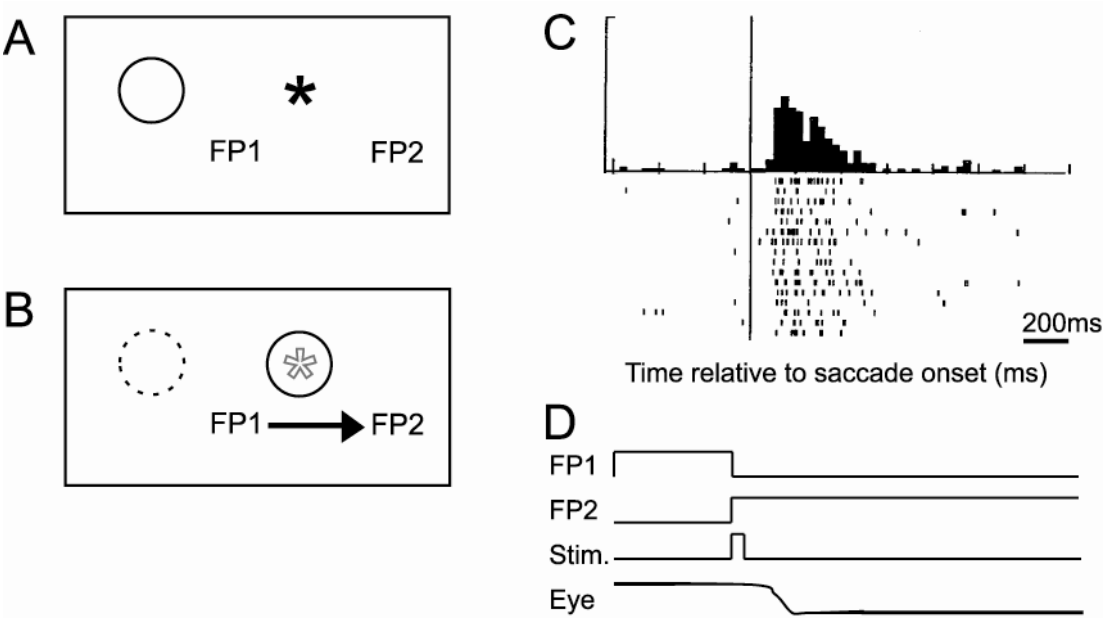

Figure 1. The single step task is used to observe updating activity.

A, B. Spatial configuration of the single step task. Circle represents the receptive field of the neuron. A. The monkey initiates the trial by fixating on an initial fixation point (FP1). Three sensory events take place simultaneously. FP1 disappears, a new fixation point appears (FP2), and a stimulus is flashed briefly in the upper right visual field (asterisk). B. The monkey makes a rightward saccade from FP1 to FP2, moving the receptive field onto the location where the stimulus had previously appeared. Critically, the stimulus has been extinguished by the time the monkey initiates the saccade to FP2. This means that there is no physical stimulus in the receptive field either before or after the saccade. C. The neuron responds with a strong burst of activity after the eye movement. The histogram is aligned on saccade onset, and represents the summed activity across all trials. The rasters below show activity on individual trials, where each tic mark represents a single action potential. Vertical scale bar indicates a firing rate of 100 spikes/sec. D. Timecourse of events. The timing diagram emphasizes that the stimulus is extinguished before the onset of the saccade. Modified from Duhamel, et al, 1992.

Can activity in the single step task be attributed to the stimulus or saccade alone? Control tasks demonstrate that it cannot (Figure 2). If the stimulus is presented while the monkey simply maintains fixation at FP1, the neuron does not respond (panel B). This is because the stimulus was placed in the opposite hemifield, well outside the bounds of the receptive field. Analogously, if the animal executes the saccade in the absence of the

stimulus flash, the neuron remains silent (panel C). This is not surprising because the saccade is directed away from the receptive field, and into the ipsiversive hemifield. The neuron responds only if the two events occur in conjunction with one another, as they do in the single step task (panel A). The critical factor is the location of the stimulus relative to the final eye position: it must appear at the retinotopic location of the receptive field following the eye movement. Because the stimulus and saccade alone do not generate any response, the activity in the single step task is interpreted as a response to the memory trace of the stimulus. In these early studies, researchers always used spatial configurations in which the stimulus and saccade alone did not activate the neuron. This is most easily achieved by placing the stimulus in the opposite visual hemifield, and by directing the saccade toward the opposite hemifield. The ipsiversive configuration, therefore, became the standard one in which to test spatial updating.

1.4. Updating supports spatially accurate behavior

The need for an updated visual representation can be assessed behaviorally with the double step task (Hallett and Lightstone, 1976; Goldberg and Bruce, 1990; Mays and Sparks, 1980). The task is deceptively simple. The subject is instructed to make sequential saccades to two briefly flashed targets. An important feature of the task is that the targets are presented so briefly that they are extinguished before the initiation of the first saccade. The first saccade can be correctly computed using retinal information alone. To compute the second saccade, however, the size and direction of the first saccade must be taken into account. If the sequence is computed using only retinal information, the second saccade would be incorrectly executed. Accurate performance,

then, requires that the location of the second target be updated in conjunction with the first saccade. Neurophysiological studies have demonstrated that performance of the double step task is impaired in patients with parietal lobe damage (Duhamel et al., 1992b; Heide et al., 1995). Similar observations have been made in monkeys with temporary lesions of LIP (Li and Andersen, 2001). In contrast, patients with lesions to frontal areas show only minor spatial impairments (Heide et al., 1995). Together, these findings indicate that parietal cortex is particularly important for generating updated representations that can be used to guide behavior.

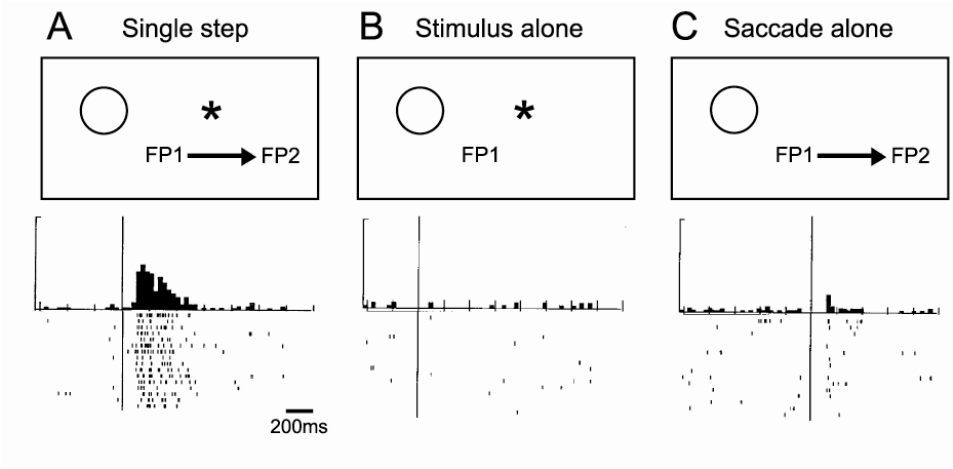

Figure 2. Remapping activity observed in a single LIP neuron during single-step and control tasks.

In each series, the upper panel represents the spatial configuration used during the task; lower panel represents data from a single neuron. A. Single step task. The monkey makes a single rightward saccade from FP1 to FP2, moving the neuron's receptive (open circle) onto the location where the stimulus had previously appeared. Critically, the stimulus has been extinguished by the time the monkey initiates the saccade to FP2. This means that there is no physical stimulus in the receptive field either before or after the saccade. The neuron responds with a strong burst of activity after the eye movement. B. Stimulus control task. The monkey's task is to maintain fixation at the intial fixation point (FP1) while the stimulus is presented. The neuron is not activated, indicating that the stimulus is outside the bounds of the classic receptive field. C. Saccade control task. The monkey makes the identical saccade to that used in the single step task, but the stimulus is not presented. Because the saccade is directed away from the response field, the saccade alone does not drive the neuron. The neuron is active only when the stimulus and saccade occur in conjunction with one another, as they do in the single step task. Histograms are aligned on saccade onset for the single-step and saccade-alone tasks, and on stimulus appearance for the stimulus-alone task. Rasters show activity on individual trials; each tic mark represents a single action potential. Vertical scale bar indicates a firing rate of 100 sp/s. Modified from Duhamel, et al, 1992.

1.5. Response properties in LIP

Neural activity in area LIP reflects multiple aspects of the monkey's environment and behavior (Andersen et al., 1997; Colby and Goldberg, 1999). Here we highlight the response properties most relevant to our experiments. Nearly all LIP neurons respond to simple visual stimuli presented in the receptive field (Colby et al., 1996; Robinson and Goldberg, 1978), and about half the population shows saccade-related activity that can occur before, during or after a saccade directed toward the response field (Barash et al., 1991b). These neurons also carry memory signals: they are active in the delay period between the flash of a target and the later initiation of a saccade toward the stimulus location (Gnadt and Andersen, 1988). The visual, memory and saccade response fields overlap in most neurons (Barash et al., 1991a). The receptive fields of LIP neurons are spatially restricted, though they vary considerably in size. On average, they are 12 deg across, but they can be as small as 2 deg or extend to cover an entire visual quadrant (Ben Hamed et al., 2001).

In addition to these sensory and motor properties, LIP neurons are also modulated by attention. Directing attention toward the location of the response field leads to an enhancement of visual responses (Robinson and Goldberg, 1978; Bushnell et al., 1981). This attentional enhancement is independent of motor-planning, as it occurs regardless of whether a saccade will be directed toward the response field (Colby et al., 1996). The activity of these neurons has been hypothesized to function as a 'salience map' in which only the most salient or behaviorally relevant visual stimuli are strongly represented (Gottlieb et al., 1998). Finally, and perhaps most importantly for our purposes, most LIP neurons (95%) update stimulus traces in conjunction with eye movements (Duhamel et al., 1992a).

1.6. Signals involved in spatial updating

How are updated stimulus representations generated? One model postulates that it relies on the combination of just two signals: a visual signal and a corollary discharge signal related to the generation of the saccade (Quaia et al., 1998). We have schematized a simplified version of this model in Figure 3. The essence of the model is that the corollary discharge induces a transfer of visual information from one group of neurons to another. Stepping through the model illustrates why this scenario seems likely. In this figure, the neuron under study is located in the right hemisphere; its receptive field is located in the left visual field. When the eyes are at the initial fixation position, the stimulus is in the right visual field. It is represented by neurons in the left hemisphere ("pre neurons"), and not by the neuron under study (panel A). After the eye movement, coding the location of the stimulus in terms of the coordinates of the initial fixation position is no longer valid, thus the "pre neurons" should no longer fire. The stimulus location must be coded in terms of the coordinates of the final fixation position. That is, a new group of neurons ("post neurons") must be activated. The visual information must be transferred from the "pre neurons" to the "post neurons" (panel B). The transfer of visual information cannot be haphazard, however, or both perception and behavior would be negatively impacted. The new coordinates of the stimulus are strictly defined by the size and direction of the eye movement. This information is contained in the corollary discharge. The corollary discharge signal, then, can be used to specify which neurons should be activated after the completion of the saccade. This signal is postulated to initiate the transfer of visual information from one group of neurons to another.

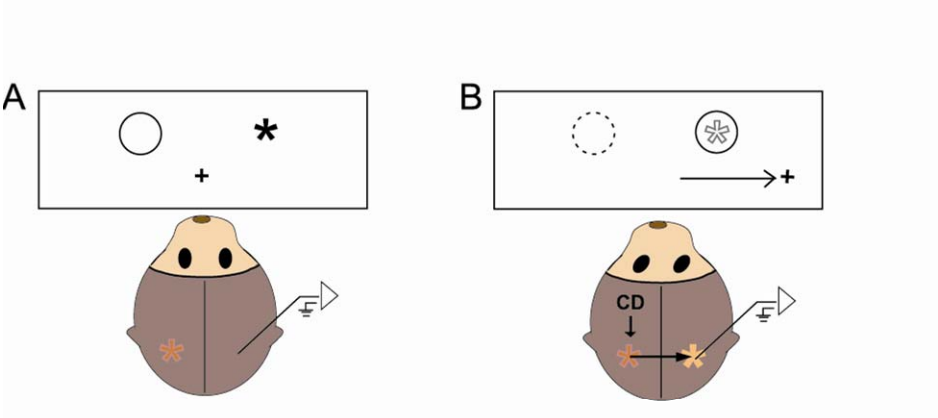

Figure 3. Model of the signals involved in remapping.

In this example, the neuron under study is located in the right hemisphere; it has a receptive field in the upper left visual field (open circle). Electrode indicates recording site. A. The initial representation of the stimulus. The monkey's gaze is directed toward an initial fixation point (central crosshair). The stimulus is presented in the right visual field. It is represented by neurons in the left hemisphere (orange star). B. Transfer of visual activity in conjunction with the saccade. The monkey makes a saccade to a new fixation point (arrow), moving the neuron's receptive field onto the previously stimulated location. The corollary discharge of the saccadic motor command (CD) initiates a transfer of visual activity from the neurons that encode the initial retinal location of the stimulus (orange asterisk in the left hemisphere) to the neurons that encode the retinal location when the eyes are at the new fixation position (yellow asterisk in right hemisphere). As a result, the neuron under study fires in response to the updated memory trace of the stimulus. This remapping provides a continued, retinotopic representation of the salient location where the stimulus appeared.

1.7. Cortical interactions mediating spatial updating

Parietal cortex, and in particular area LIP, has been implicated as the site for the generation of spatial updating signals (Colby and Goldberg, 1990; Heide, et al, 1995; Quaia, et al, 1998). In addition to LIP, remapping has been observed in the frontal eye fields (FEF; (Goldberg and Bruce, 1990; Umeno and Goldberg, 1997, 2001)) and superior colliculus (SC; (Walker et al., 1995)). Both of these areas play an important role in visual processing and saccade generation (Wurtz and Albano, 1980; Schall et al., 1995). Furthermore, through their reciprocal connections with each other and with LIP, they are likely involved in generating updated spatial representations. Here we highlight three key anatomical features.

First, both LIP and FEF project to the intermediate layers of the SC (Lynch et al., 1985; Andersen et al., 1990b; Schall et al., 1995). These pathways have been shown to carry a range of visual, memory and saccade-related signals (Pare and Wurtz, 1997, 2001; Sommer and Wurtz, 2001). Second, there are prominent reciprocal projections from the superior colliculus back to both of these cortical areas, though the SC source of these projections is different. The superficial visual layers of the SC project to LIP via the pulvinar nucleus of the thalamus (Hardy and Lynch, 1992; Clower et al., 2001). Neuronal responses in both the superficial SC (Wurtz et al., 1980) and pulvinar (Bender, 1981; Petersen et al., 1985) are predominantly visual in nature, thus it is likely that the projection from superficial SC to LIP conveys visual information. In contrast, most of the collicular projections to FEF originate from the intermediate layers of the SC (Lynch et al., 1994), where neurons exhibit both visual and saccade-related responses (Wurtz et al., 2001). Of particular interest is the recent finding that the pathway from SC to FEF via the medial dorsal nucleus of the thalamus carries corollary discharge signals (Lynch et al., 1994; Sommer and Wurtz, 2002). Third, LIP and FEF are reciprocally interconnected (Petrides and Pandya, 1984; Andersen et al., 1990a). This pathway may allow for the relay of corollary discharge signals from FEF to LIP. Together, these pathways provide a substrate by which remapped visual signals could be generated and relayed throughout the brain.

1.8. Goals

One of the most surprising facets of remapping is that, at the time of the eye movement, neurons are responsive to locations outside their classical receptive fields. An

important implication of this finding is that neurons have access to information from throughout the visual field. It should be possible to observe evidence of a remapped stimulus trace every time the receptive field lands on a previously stimulated location, regardless of the location of the stimulus. This access to visual information from beyond the boarders of the RF even extends to the opposite visual hemifield. Indeed, in the original demonstration of remapping in area LIP, stimulus representations were updated from one visual hemifield to another (Duhamel et al., 1992a). This across-hemifield updating must require a transfer of information between neurons in opposite hemispheres, because the representation of visual stimuli is highly lateralized (Trevarthen, 1990). Here we describe two experiments designed to gain a greater understanding of the factors that influence spatial updating in the primate brain.

The goal of the first experiment is to provide a deeper understanding of the factors that influence remapping by investigating the degree to which individual neurons have access to information from different portions of the visual field. We hypothesized that individual neurons would respond in the single step task regardless of the direction in which the stimulus trace is updated. We tested this systematically by varying a task in which spatial information is updated in conjunction with saccades of different directions. Additionally, we tested whether stimulus traces are updated equivalently within as compared to across hemifields. We expected that in an intact animal, remapping would be equally robust in each of these conditions.

The goal of the second experiment was to investigate the neural circuitry underlying across-hemifield remapping. We hypothesized that the forebrain commissures -- the corpus callosum and anterior commissure -- provide the primary path

for this updating, which is presumed to require an interhemispheric transfer of visual information. We tested this by recording from neurons in split-brain monkeys while they performed two versions of the single step task. In the within-hemifield version, the representation of the stimulus remains in the same hemifield before and after the eye movement. In contrast, the stimulus representation must be updated from one hemifield to the other in the across-hemifield version of the task. We expected that in the absence of the forebrain commissures, across-hemifield remapping would be compromised as compared to when the stimulus must be updated within a single hemifield.

2. Chapter 2: Accessing information throughout the visual field

2.1. Overview

In this chapter we present physiological experiments designed to gain a greater understanding of spatial updating in the lateral intraparietal cortex. Specifically, we were interested in whether remapping is independent of the direction over which a stimulus trace must be updated. We tested this systematically by varying the saccade direction in a spatial updating task. We addressed three primary experimental questions. 1) Does remapping vary with changes in saccade direction? 2) Does the direction of the saccade relative to the RF location affect remapping signals? 3) Is remapping equally robust for stimulus traces updated within and across hemifields? We expected that remapping would be independent of each of these factors.

2.2. Introduction

Neurons in the lateral intraparietal cortex (area LIP) remap the locations of salient stimuli when the eyes move (Goldberg and Bruce, 1990; Duhamel et al., 1992a; Gottlieb et al., 1998; Kusunoki et al., 2000). In addition to LIP, neurons in numerous cortical and subcortical regions remap stimulus locations in conjunction with eye movements (Mays and Sparks, 1980; Goldberg and Bruce, 1990; Duhamel et al., 1992a; Walker et al., 1995; Umeno and Goldberg, 1997, 2001). We focus our studies on LIP for two reasons. First, previous reports indicate that remapping is prevalent in area LIP, where nearly 95% of neurons exhibit this property (Duhamel et al., 1992a). Second, the behavioral correlates

of spatial updating have been found to rely on parietal cortex (Heide et al., 1995; Li and Andersen, 2001).

The neural circuit that generates remapping relies upon the integration of visual signals present in parietal cortex with oculomotor signals relayed to this area (Colby, 1998; Quaia et al., 1998). We asked whether the combination of incoming oculomotor and visual signals could lead to discrepancies in the strength of remapping. Three findings suggest that such discrepancies are unlikely. The first finding is related to the representation of visual signals in area LIP. No strong biases in the representation of the visual field have been demonstrated, suggesting that this area can encode information equally well for all regions of the visual field (Ben Hamed et al., 2001). This is important because we hypothesize that remapping requires a transfer of visual information between LIP neurons that encode the location of the stimulus before and after the saccade. The second finding is related to the representation of oculomotor signals. Previous studies have shown that both the frontal eye field and superior colliculus represent all directions and sizes of saccades (Wurtz and Albano, 1980; Bruce and Goldberg, 1985). These are the two regions most likely to be involved in generating and supplying a corollary discharge signal to LIP. The corollary discharge signal is critical for initiating the transfer of visual information. If remapping is independent of saccade parameters, LIP must receive corollary discharge information about all types of saccades. The third finding is related to the anatomical connections between LIP and FEF. The projections from FEF to LIP are not strictly topographic (Stanton et al., 1995). This finding implies that neurons representing stimuli in all portions of the visual field can have access to

information about all sizes and amplitudes of saccades. Altogether, these observations support the idea that updating will be robust regardless of the parameters of the saccade.

2.3. Experimental Aims

We hypothesized that individual LIP neurons would respond in the single step task regardless of the direction in which the stimulus trace is updated. We tested this by using a task in which spatial information is updated in conjunction with saccades of different directions. We addressed three experimental questions. First, we asked whether stimulus traces are remapped equally robustly in different directions. Second, we asked whether the direction of the saccade relative to the location of the RF has any bearing on signals related to remapping. Third, we asked whether stimulus traces are updated equivalently within a hemifield as compared to across hemifields. Our prediction was that remapping would be immune to all of these changes. We addressed these questions by assessing the response of individual neurons during four versions of the single step task. In each version, the stimulus must be updated in conjunction with a saccade of a different direction.

2.4. Methods

Experimental design

We used the single step task to assess the remapping of a stimulus trace across changes in saccade direction (Figure 4A). Each neuron was tested in four versions of the task. The saccade directions were along the horizontal and vertical meridians (right, left, up and down). Saccade amplitude (20 deg), stimulus location, and final eye position

were identical for all conditions (panel B). We were principally interested in neural activity generated immediately after the onset of the saccade. Using the same final eye position for all conditions avoided potential confounds with orbital position modulation during the peri-saccadic epoch.

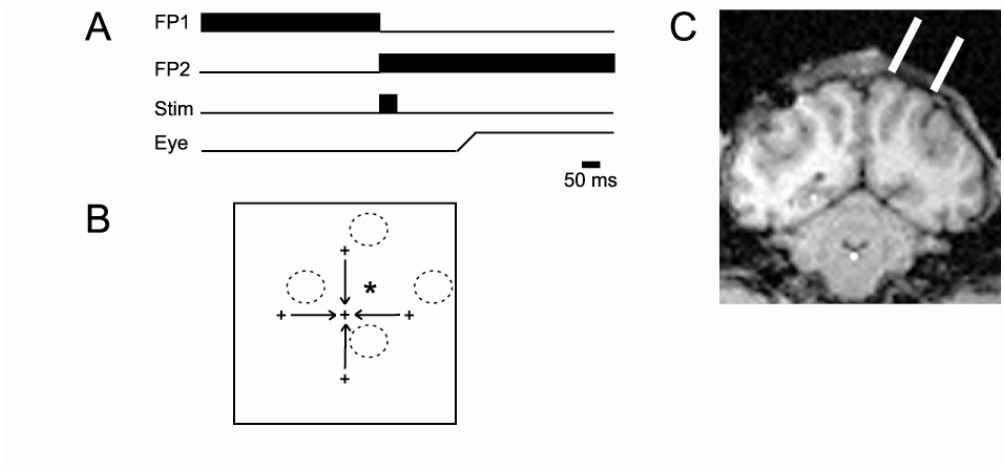

Figure 4. Paradigm used to assess spatial updating in different directions.

A. Timing of the Single Step Task. The monkey holds its gaze on fixation point FP1 300-500 ms. Three events then occur simultaneously. FP1 disappears, a new fixation point appears (FP2) and a stimulus is flashed for 50 ms. The monkey makes a visually guided saccade to FP2. The monkey maintains its gaze on FP2 for an additional 500-700 ms. B. Spatial configurations. The monkey begins each trial at one of four peripheral fixation locations and makes a saccade to the central fixation point. Each dashed circle represents the location of the receptive field (RF) when the monkey is fixating one of the peripheral fixation points. In this example, the RF is up and to the right. The arrows represent the 20 degree saccades. The saccade will move the RF onto the location of the flashed stimulus (star). The stimulus is in the same location for all conditions. C. Coronal magnetic resonance image showing the location of the recording chamber in Monkey OE. Neurons were recorded on the lateral bank of the intraparietal sulcus.

Two control tasks were used to assess whether activity observed in the single step task is attributable to visual or motor factors. In the stimulus control task, the stimulus was presented while the animal maintained fixation at the first fixation point. In the saccade control task, the saccade was executed, but in the absence of the stimulus. The complete data set for each neuron in this experiment is 3 tasks X 4 directions, for a total of 12 conditions. We collected 20 trials per condition.

Measuring remapping activity

Remapping activity in the single step task represents a response to a stimulus trace which has been updated in conjunction with the saccade. We measured activity in the single step task relative to each event of interest: the stimulus and the saccade. Previous experiments of spatial updating have reported that the onset of the remapped response can be quite variable, ranging from 50ms before to 250ms after the onset of the saccade (Umeno and Goldberg, 1997, 2001).

In order to have the most robust and unbiased measure of remapping to compare across the four test directions, we used standard analysis epochs. The saccade epoch was 0-300ms relative to saccade onset, and was used to compare activity in the single step and saccade control tasks. The stimulus epoch was 200-500ms relative to stimulus onset, and was used to compare activity in the single step and stimulus control tasks. These epochs are similar to those used in previous studies (Kusunoki and Goldberg, 2003). Additionally, these epochs correspond to the time when activity in the single step task diverges from activity in the control tasks.

2.5. Results

We recorded from 290 neurons in area LIP of two monkeys (Figure 4C). Of these, 281 (140 from Monkey O; 141 from Monkey F) were visually responsive and are included in the analyses described here. The locations of the receptive fields are schematized in Figure 5.

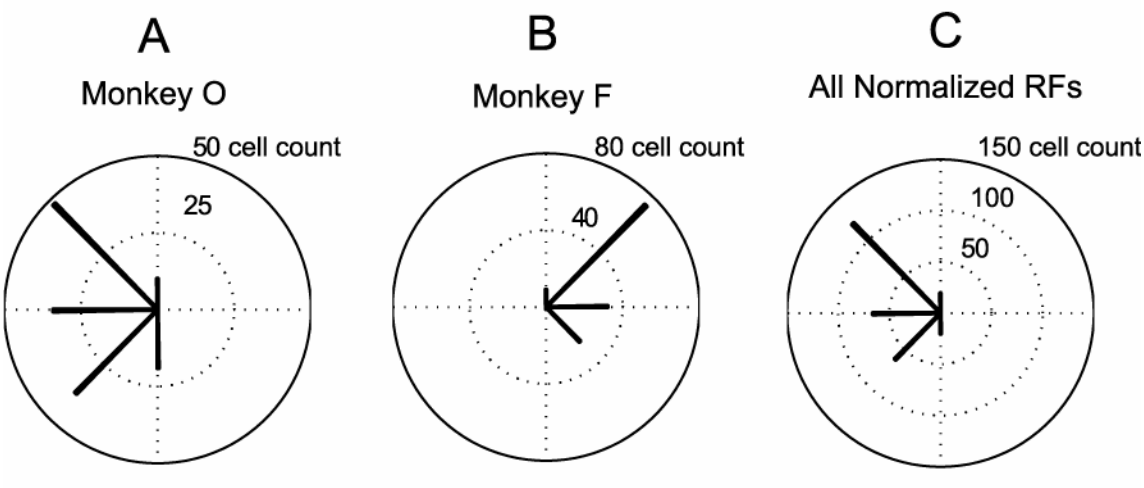

Figure 5. Location of receptive fields (RF) of neurons tested.

Each polar plot represents the number of neurons with RFs at a particular location relative to the fovea. RFs were mapped to one of 8 standard locations around the fovea, but at variable eccentricies. Only angular location is represented here. A. Monkey O. Neurons were recorded from the right hemisphere; RFs were located in the left visual field. n=141. B. Monkey F. Neurons were recorded from the left hemisphere; RFs were located in the right visual field. n=140. C. RF locations were standardized so that ipsiversive and contraversive saccades could be compared. RFs throughout the visual field were not equally represented; there were more receptive fields located in the upper field than in the lower field. n=281.

2.5.1. Results, Part 1: Canonical saccade directions

LIP neurons remap stimulus traces in multiple directions

Our primary finding is that individual neurons can remap stimulus traces in multiple directions (Figure 6). The neuron illustrated had robust remapping in conjunction with each saccade direction tested (top row). The control tasks, however, demonstrate that some of the activity observed in the single step task can be attributed to the presence of the stimulus (middle row) or generation of the saccade (bottom row). The ipsiversive condition (third column) was the single step configuration originally used to observe remapping in parietal cortex (Duhamel et al., 1992a). In this condition, the saccade is directed away from the RF and the stimulus is located in the opposite visual hemifield. Because neurons in LIP have a contralateral bias (Barash et al., 1991a), the saccade alone is unlikely to generate a motor-related response. Placing the stimulus in the opposite hemifield ensured that it was well outside the RF and would not drive the neuron. When neither the stimulus nor the saccade alone drive the neuron, all activity in the single step task can be attributed to remapping the stimulus trace. Because the control conditions are unlikely to activate the neuron, the ipsiversive condition became the standard configuration with which to test for remapping. Our goal was to determine whether neurons could remap stimulus traces in all directions, including those for which the control conditions generate responses.

How do we assess remapping activity given the presence of activity generated by the stimulus or saccade alone? We devised an analytical method to determine which

single step conditions showed significant remapping. We defined remapping as activity that cannot be accounted for by either the stimulus or the saccade alone. To assess

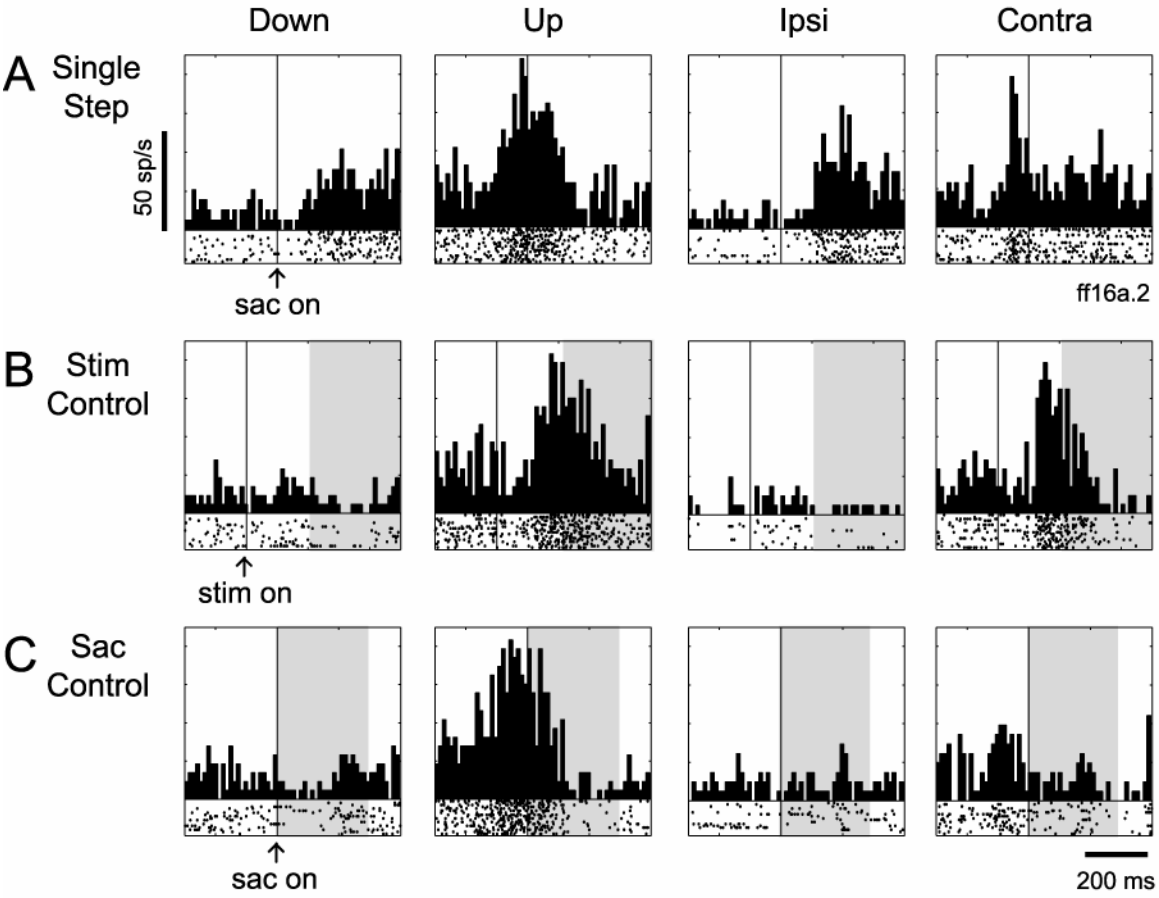

Figure 6. Example of a neuron that remaps stimulus traces in multiple directions.

Each column represents data from one saccade direction (downward, upward, ipsiversive or contraversive). A. Single Step Task. Data are aligned on the onset of the saccade. The lower portion of each panel shows rasters from single trials: each row represents a single trial; each dot represents an action potential. The histograms above are the average activity of the neuron (in 10ms bins) over 16-20 trials. For all directions, there is robust activity during the single step task. B. Stimulus control task. Data are aligned on the onset of the stimulus. The grey shaded region represents the epoch during which activity in the stimulus control task is compared to activity in the single step task (200-500ms after the onset of the stimulus). The amount of activity varies across the conditions. C. Saccade control task. Data are aligned on the onset of the saccade. Conventions as in A and B. The epoch of interest (shaded region) is 0-300ms after the onset of the saccade. As in the stimulus control task, the saccade alone generates variable amounts of activity across the four conditions. The ipsiversive condition is the configuration originally used to test remapping. If no activity is generated in either control task, then all activity present in the single step task can be attributed to the remapped stimulus trace. In our paradigm, the control conditions generated variable amounts of activity, creating the need for new analysis methods that could take into account activity generated by the stimulus or saccade alone. If activity in the single step task is greater than the activity generated in both the stimulus and saccade control tasks (t-test, $p > 0.025$), remapping is considered significant. This neuron showed significant remapping for downward, ipsiversive and contraversive saccades.

significance, we used a t-test (alpha = 0.025) to make two comparisons. First, we compared single step activity to stimulus control activity. Second, we compared single step activity to saccade control activity. Remapping is considered statistically significant if activity in the single step task is greater than activity in each of the control tasks. Using these statistical criteria, we found that the example neuron in Figure 6 shows significant remapping for three of the saccade directions tested (downward, ipsiversive and contraversive). Across the population of neurons that had significant remapping in at least one direction, over half (56%, 91/162) showed significant remapping activity for more than one saccade direction (Figure 7). This indicates that most remapping neurons in LIP can access information from multiple regions well-beyond the classically defined receptive field.

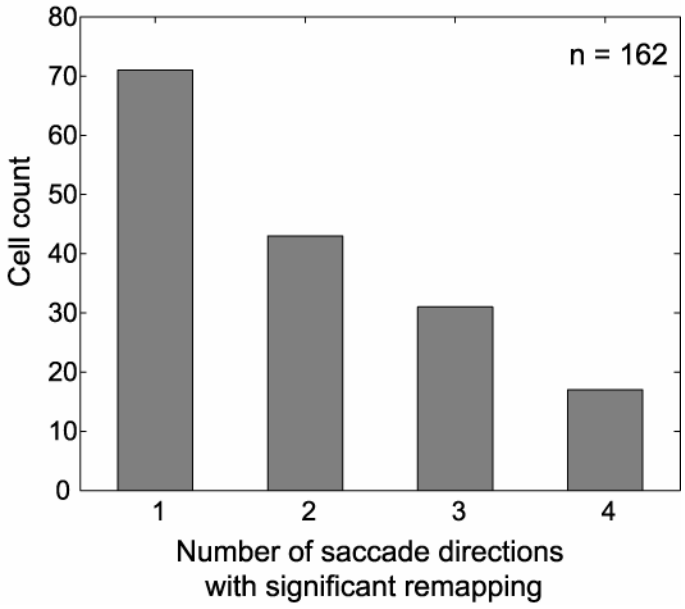

Figure 7. Many LIP neurons remap stimulus traces in multiple directions.

Bars represent the number of neurons with significant remapping for 1, 2, 3 or 4 saccade directions. Remapping was considered significant if activity in the single step task was greater than that in each of the control tasks (t-test, alpha = 0.025).

Quantifying the magnitude of remapping

Having found that individual neurons could remap stimulus traces in multiple directions, we were next interested in directly comparing the strength of remapping in each direction. To be certain that we were comparing only updating activity across the four directions, it was critical to account for activity generated in the control conditions. We use the data from the neuron in Figure 6 to illustrate this three-step procedure

First, we compared the activity generated in each direction of the single step task to that generated in each of the two corresponding control conditions. We computed two indices: a Stimulus Index and a Saccade Index. $Index = (A - B)/(A + B)$, where A is the mean firing rate in the single step task and B is the firing rate in either the stimulus control task or the saccade control task. Index values scale from -1 to +1, where positive values indicate that single step activity is greater than control activity. Negative values indicate that control task activity is greater. These indices also normalize for absolute firing rate, which allows all neurons to contribute equally.

Second, we assessed the strength of remapping in each direction by comparing the Stimulus and Saccade Indices for each direction. In Figure 8 (panel A), each dot represents data from one of the test directions. A neuron is considered to remap for a particular direction if both indices are positive. That is, if activity in the single step task is greater than that observed in each of the control tasks. These samples fall into the upper right shaded quadrant. Samples where either the Stimulus or the Saccade Index is negative fall into one of the other three quadrants. These samples are considered non-remapping samples. In agreement with our statistical assessment, we found that this particular neuron remaps for 3 of the 4 test directions.

Third, we assessed the magnitude of remapping by computing a Remap Index. It is computed by calculating the distance of the point from the origin. For non-remapping samples (i.e., those that do not fall into the shaded quadrant), the Remap Index is set to 0. The Remap Index (RI) ranges from 0 to 1.4, where 0 indicates no detectable remapping and 1.4 indicates robust remapping. For the example neuron described here, the most robust remapping is for ipsiversive saccades (RI = 0.98); contraversive and downward saccades show nearly equal remapping (contra = 0.55; down = 0.51). There is no detectable remapping for upward (RI = 0). With this analysis, we now have a method to compare the strength of remapping in different directions while simultaneously accounting for activity generated in both of the control conditions.

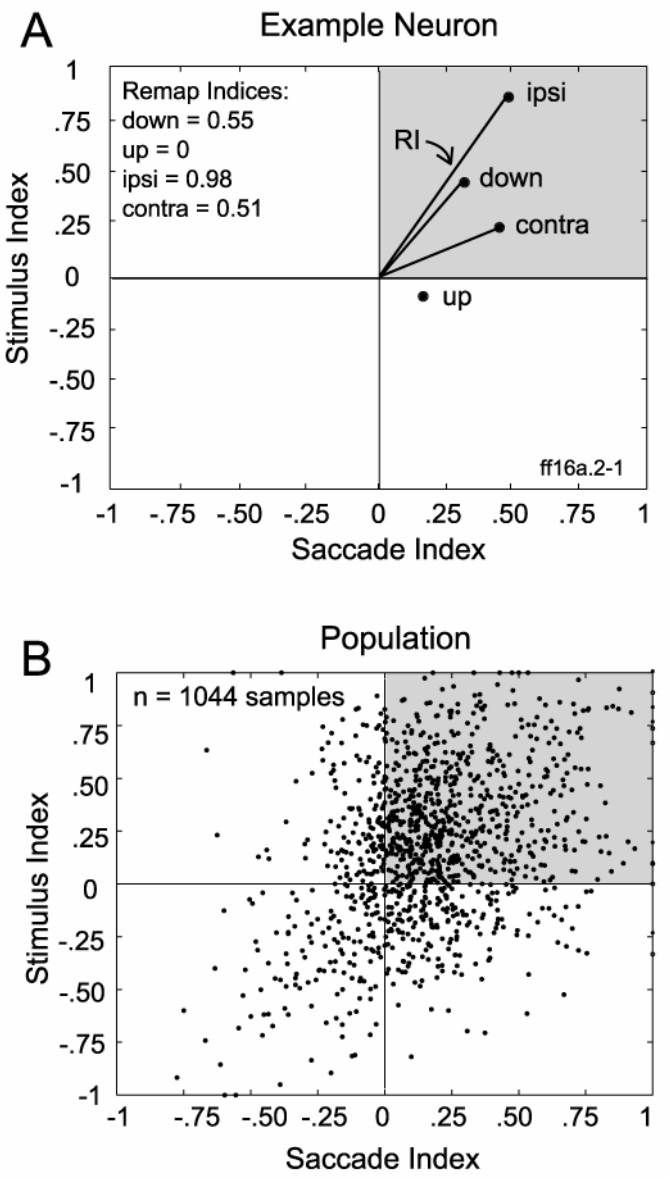

Figure 8. Method used to calculate the Remap Index.

A. Data from the example neuron in Figure 6. Each dot represents data from a single test condition. If single step activity is greater than that observed in each control condition, the Stimulus and Saccade Indices are both positive. These samples fall into the upper right (shaded) quadrant and are considered to show remapping. The Remap Index for these conditions is computed by calculating the distance of the point from the origin. Conditions that fall into one of the other three quadrants have no detectable remapping; their Remap Index is set to 0. The Remap Index ranges 0 to 1.4, where 0 indicates no detectable remapping and 1.4 indicates robust remapping. For this neuron, the neuron showed detectable remapping for 3 of the 4 test conditions; the most robust remapping was for ipsiversive saccades. The neuron showed no detectable remapping for upward saccades. B. Population data. Each dot represents data from a single neuron during a test of remapping in one direction. Each neuron was tested in four directions and therefore contributes four datapoints to the plot. Remapping was detectable for 57% of the samples.

We used the Remap Index to assess the strength of remapping for the entire population of samples. If the points were equally distributed on the plot, we would expect only 25% of the samples (281 neurons X 4 test directions) to fall into the upper right 'remapping' quadrant. Instead, we observed that 57% of the samples are in the remapping quadrant (Figure 8B). This proportion was statistically significant (Chi square, $p < 0.01$). With this analysis method, remapping is detectable in most samples.

Our definition of remapping depends upon detecting an increase in neural activity above what may be generated by the stimulus or saccade alone. If a neuron is already robustly activated by either the stimulus or saccade alone, it will be difficult to detect a remapping signal above these other signals. We were therefore interested in exploring the relationship between the Remap Index and neural activity in the different tasks (Figure 9). We tested two predictions. The first prediction was that the strength of remapping would be related to the amount of activity in the single step task. That is, if single step activity is a direct reflection of the strength of remapping, we would expect to find a positive correlation between single step activity and the Remap Index. The second prediction was that when activity in the control conditions is high, remapping would be less detectable (i.e., the Remap Index would be small). If this were the case, we would expect to find a negative correlation between activity in the control tasks and the Remap Index. To test these predictions, we compared activity observed in the three tasks to the Remap Index. In panel A, we plot activity in the single step task against the Remap Index for each condition. Each dot represents data from one direction tested in one neuron. There was no significant relationship between the Remap Index and strength of activity in the single step task (linear regression, $r = 0.035$, $F =$

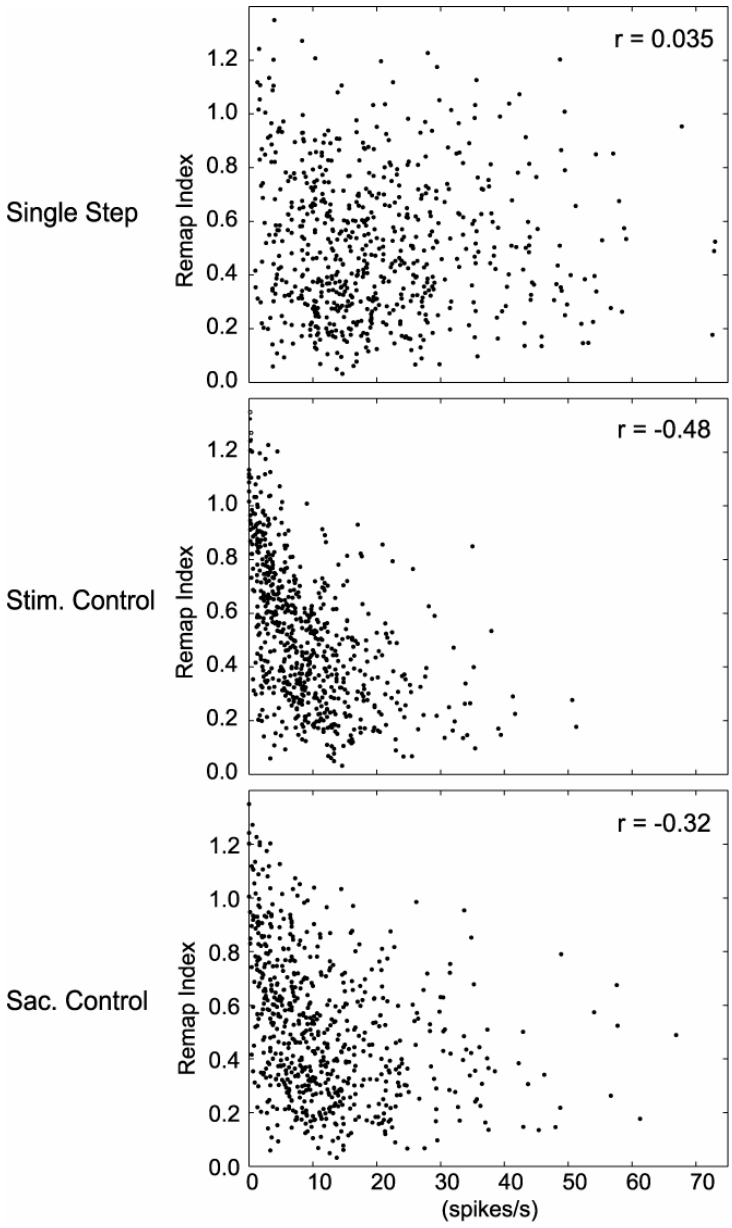

Figure 9. Relationship between the strength of remapping and firing rate in the three tasks.

Each dot represents data from one sample (ie, a test of remapping for a single neuron in one direction, n = 655). Only samples with positive Remap Indices are included. A. Comparison of the Remap Index and neural activity in the single step task. Firing rate is calculated in the epoch 0-300ms relative to saccade onset. There is no significant relationship between single step activity and the Remap Index. This indicates that neural activity observed in the single step task is not a direct reflection of updating activity. B, C. Comparison of the Remap Index and activity observed in the control tasks. B. Stimulus control task. Stimulus control activity is measure in the epoch 200-500ms relative to stimulus onset. There is a significant negative correlation between the Remap Index and stimulus control activity. C. Saccade control task. Activity in the saccade control task is measured in the epoch 0-300ms relative to the onset of the saccade. There is a significant negative correlation between saccade control activity and the strength of remapping. These negative correlations indicate that if the stimulus or saccade alone robustly drive the neuron, the strength of the neural signal attributable to updating will be small. Conversely, when activity related to pure visual or motor factors is not present, remapping is likely to be robustly detected.

0.791, $p > 0.3$). This indicates that the strength of remapping cannot be predicted simply by measuring activity in the single step task. On the other hand, we found a significant negative correlation between the strength of the Remap Index and activity in each of the control conditions (Panels B and C). This indicates that if the stimulus or saccade alone robustly drive the neuron, remapping is likely to be small in magnitude. The correlation between stimulus control activity and Remap Index (linear regression, $r = -0.48$, $F = 201.31$, $p < 0.0001$) was larger than that between the saccade control and the Remap Index (linear regression, $r = -0.32$, $F = 75.22$ $p < 0.0001$). Altogether, the interpretation of these results is that the strength of remapping cannot be predicted by activity in the single step task alone. We conclude that the strength of remapping is largely affected by other signals the neuron may be carrying during a particular epoch.

In individual neurons, the strength of remapping varies with direction

We used the Remap Index to compare, in individual neurons, the magnitude of the remapping signal in the four test directions. Each of the polar plots in Figure 10 represents data from a single neuron. Along the cardinal axes, we plot the Remap Index for the different saccade directions. Some neurons remap equally robustly for all saccade directions (left panel). Other neurons are highly selective (right panel) and effectively remap for only a single direction. To quantify the strength of remapping in the four test directions, we computed a Selectivity Index for each neuron. This is the normalized vector sum of the Remap Indices from the four directions (see Figure 11). We calculate the Selectivity Index by first normalizing the Remap Index for each direction by the sum of the Remap Indices for all directions. If the normalized

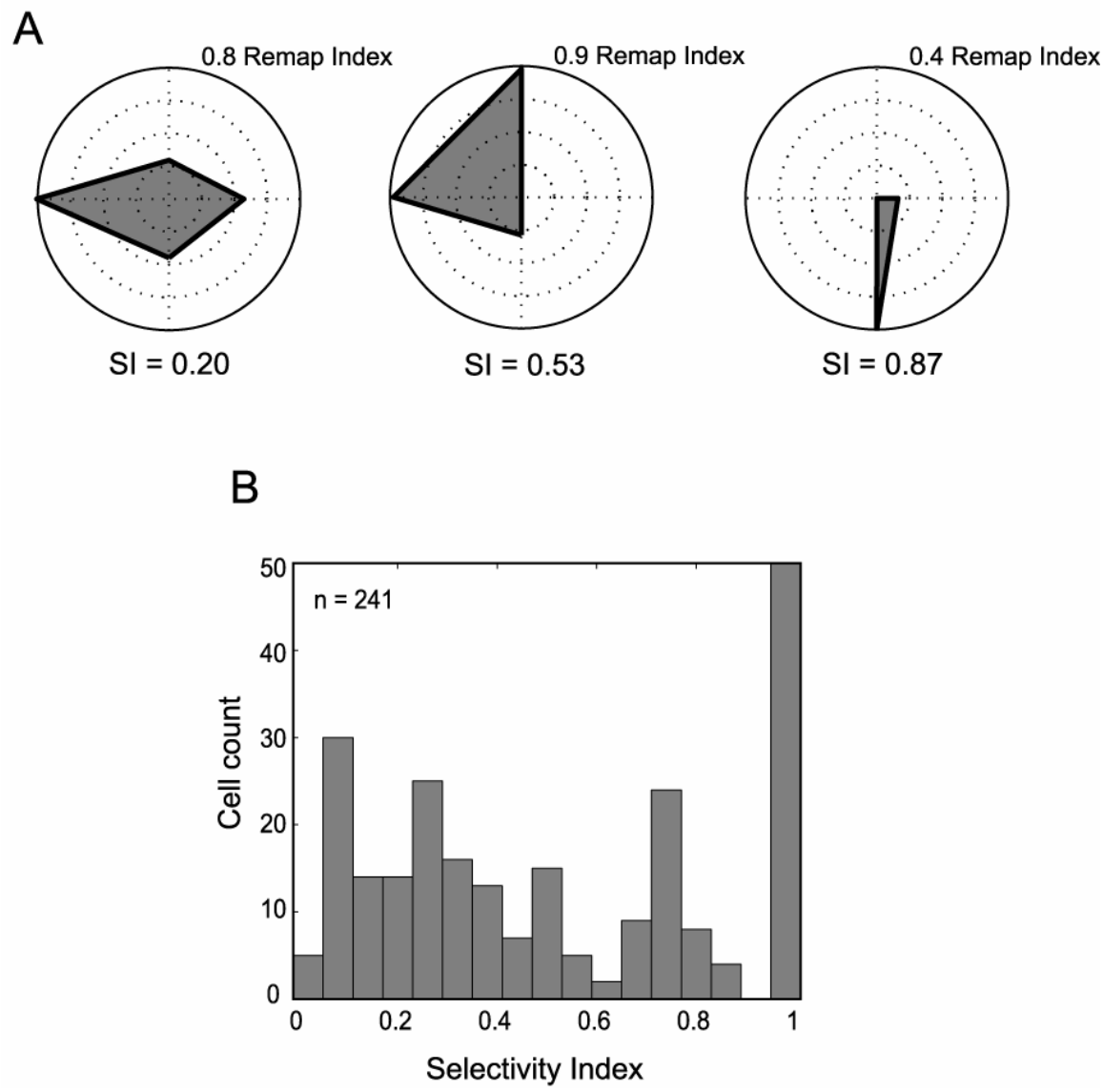

Figure 10. Comparison of the variability of remapping in individual neurons.

A. Each polar plot represents data from a single neuron. The Remap Index for the four test directions is plotted along the cardinal axes. Some neurons remapped stimulus traces robustly in all four saccade directions (left panel). Others were more selective (right panel). Polar plots were quantified with a Selectivity Index (SI): values near 0 indicate that the neuron remapped stimulus traces equally robustly for all directions tested. Values near 1 indicate that the neuron remapped stimulus traces for only one saccade direction. See Figure 11 for details. B. Distribution of Selectivity Indices. Neurons showed a broad range of selectivities (mean = 0.51, s.d. = 0.33).

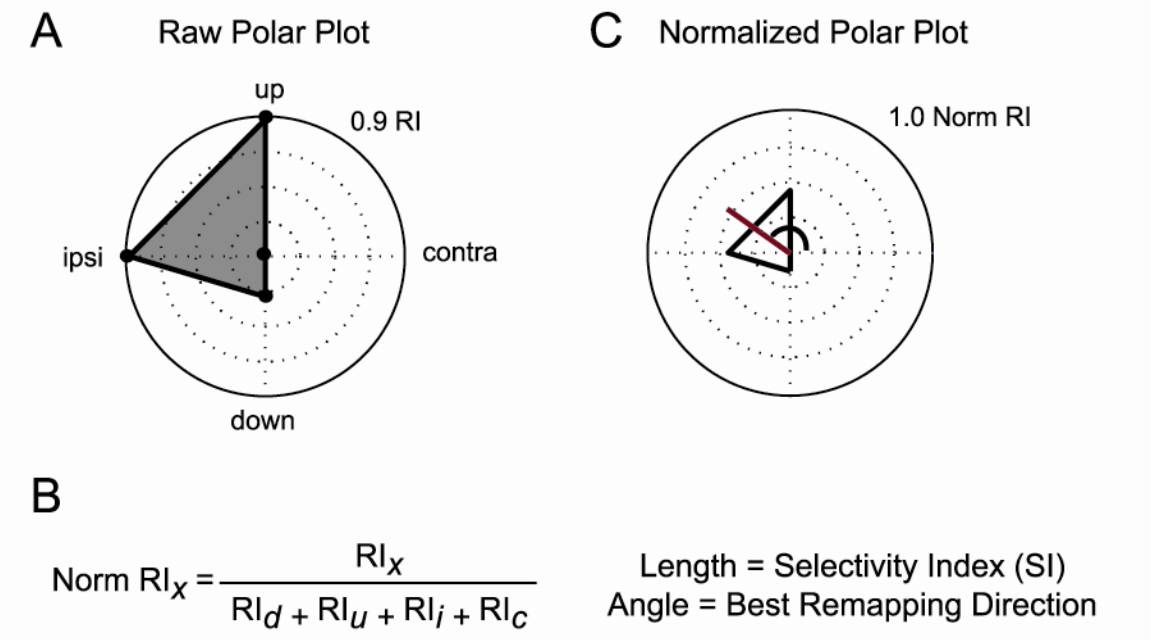

Figure 11. Method used to calculate the selectivity of remapping and best remapping direction in individual neurons.

A. Polar plot comparing the strength of remapping in each of the test directions. The Remap Indices (RI) for each direction are plotted along the cardinal axes (black dots). Ipsiversive saccades are represented to the left; contraversive saccades to the right. The maximum possible RI is 1.4. For this particular neuron, the maximum RI was 0.90. This neuron remapped stimulus traces for upward, downward and ipsiversive saccades. It had no detectable remapping for contraversive saccades. B. Formula used to normalize the RIs. The RI for each direction (RIx) is normalized by the sum of the Remap Indices from all 4 test directions. This normalization method has two important features. First, it puts all neurons on the same scale, so that the population can be compared. Second, it can be used to determine how well-distributed the remapping activity is. If the neuron remapped equally robustly in the four conditions, the normalized RIs would all be 0.25. C. Normalized polar plot. The normalized RIs are plotted along the cardinal axes. The shape of the plot is identical to that in A; it differs only in magnitude. The normalized polar plots are used to compute the Selectivity Index and best remapping direction. The normalized RIs are summed as vectors, where the direction of the vector points in the direction of the saccade (ie, up-down, ipsi-contra). This yields a single vector that represents the RIs of all four conditions (red line). The length of this vector is a measure of how selectively the neuron remaps stimulus traces across the four directions. This value is termed the Selectivity Index (SI). If the neuron remapped equally robustly in all four conditions, the vectors would sum to 0. This would indicate perfectly universal remapping. The direction in which the vector points (arc) is taken to represent the best remapping direction for the neuron. Method is adapted from Cook and Maunsell (2002).

Remap Indices are summed as vectors, with each vector pointing in the direction of the saccade, the result is a single vector. The length of this vector is a measure of the neuron's selectivity and is referred to as the Selectivity Index. If a neuron remaps equally robustly for all directions, the Selectivity Index = 0. Conversely, if a neuron remaps stimulus traces for only a single direction, the Selectivity Index = 1. The distribution of Selectivity Indices for the population is shown in panel B of Figure 10. The large bar at 1 represents those neurons that remap for only a single direction (n = 50). Overall, the distribution of Selectivity Indices is quite broad, indicating that neurons show a variable range of tuning (mean = 0.51, s.d. = 0.33). The interpretation of this result is that for many neurons in LIP, remapping is effectively universal, while for others this signal is restricted to only a single saccade direction.

We were intrigued by the finding that a relatively large subset of the population remapped stimulus traces for only a single saccade direction. We explored this finding further by asking whether selectivity and strength of remapping are related (Figure 12). Specifically, we compared the Remap Indices for the uni-directional neurons to those observed for the multi-directional neurons. Uni-directional neurons have positive Remap Indices for only a single direction (Selectivity Index = 1, n = 50) whereas multi-directional neurons have positive Remap Indices for more than one direction (Selectivity Index < 1, n = 191). For each neuron, we used the maximum Remap Index to represent its ability to update stimulus traces. On average, multi-directional neurons carried a more robust remapping signal than did the uni-directional neurons (t-test, $p < 0.0001$). This indicates that neurons that remap in multiple directions tend to remap more robustly than neurons that remap in only a single direction.

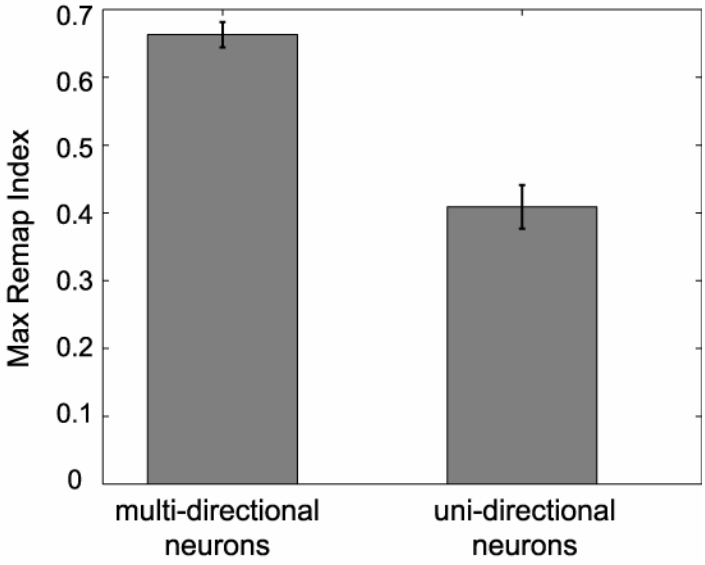

Figure 12. Comparison of remapping strength and selectivity.

The bars represent the average maximum Remap Index for neurons that remapped stimulus traces in multiple directions (left bar, n = 191) and for neurons that remapped stimulus traces in only one direction (right bar, n = 50). Error bars represent the standard error of the mean. Neurons that remapped in multiple directions carried significantly stronger signals associated with spatial updating (t-test, $p < .0001$)

There is no overall bias toward remapping for particular saccade directions

Is there any bias in which saccade directions show remapping? For instance, do neurons remap more strongly in the classic ipsiversive condition? This seems likely because this configuration often yields control conditions with the smallest amount of activity. We addressed the issue of directional bias in three ways. First, we determined the number of neurons that showed significant remapping for each of the four test directions (Figure 13A). The bars in this figure represent the number of neurons with significant remapping for saccades downward, upward, ipsiversive or contraversive. We tested all neurons in each of these directions, so the maximum value for each bar is equal to the number of neurons in the dataset (n = 281). We found no significant differences between the number of samples with significant remapping for each of the four test

directions (Chi-square test, $\chi^2 = 0.14$, d.f. = 3, $p > 0.50$). Thus, although the ipsiversive condition may frequently yield controls with little activity, remapping occurs with near equal frequency for all four test directions.

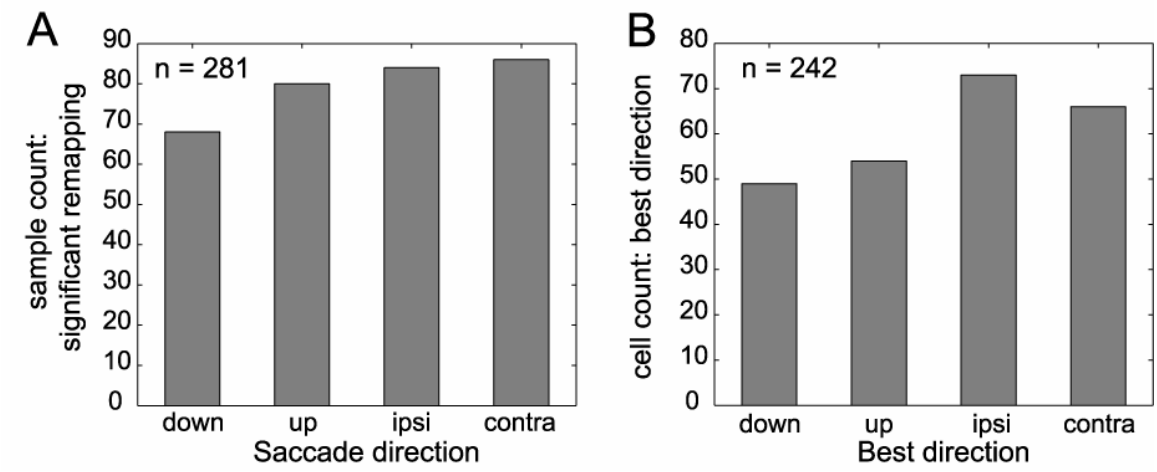

Figure 13. Assessment of bias in remapping direction.

A. Number of neurons with significant remapping for saccades downward, upward, ipsiversive or contraversive. Each neuron was tested in each saccade direction, so the maximum value for each direction is equal to the number of neurons in the population. There was no trend toward remapping to occur more frequently for one particular saccade direction. B. Number of neurons with the best remapping for saccades downward, upward, ipsiversive or contraversive. Best direction is defined as the saccade direction with the largest Remap Index. Only those neurons with a positive Remap Index for at least one direction are included. There is no significant bias toward the population showing the most robust remapping for one particular saccade direction.

The second way we addressed the issue of directional bias was to analyze which of the four saccade directions yielded the largest Remap Index for each neuron. That is, do neurons tend to carry their most robust remapping signal for one particular direction? As described above, our prediction was that the best remapping occurs for ipsiversive saccades. These data are plotted in Panel B of Figure 13. We included only those neurons that remapped (i.e., Remap Index > 0) for at least one direction (n = 242/281). The null hypothesis is that across the population of neurons, the four saccade directions are equally preferred. Although there is a slight bias toward the most robust remapping

for ipsiversive saccades, there was no significant difference between the number of neurons that preferred each of the test directions (Chi-Square test, $\chi^2 = 6.033$, $p > 0.10$). We conclude that there is no strong bias toward the population of neurons remapping most robustly for one particular direction.

Third, we used the polar plots to determine the direction with the most robust remapping for each neuron (see Figure 11 for details). We can analyze the polar plots to interpolate between the actual saccade directions we tested and make inferences about saccades of all directions. In Figure 14A, we show the best remap direction for the population of remapping neurons (n = 241/281). All directions are represented, though there is an apparent over-representation of directions along the horizontal and vertical meridians. These are the saccade directions we tested, so the population of neurons that remap stimulus traces in only a single direction necessarily have best directions along the meridians. In the lower panels, we separately plot neurons that remapped stimulus traces in only a single direction (panel B, n = 50) and those that remapped stimulus traces in multiple directions (panel C, n = 191). When the data are plotted this way, it becomes clear that for multi-directional neurons, all saccade directions are represented. For both the multi-directional and uni-directional neurons, the distribution of preferred directions is uniform (Rayleigh's test, both comparisons, $p > .05$). Based upon the three findings described here, we conclude that memory traces are remapped in conjunction with saccades of all directions. Furthermore, across the population, there is no bias toward a preference to remap stimulus traces in any particular direction. These results support the hypothesis that remapping is independent of saccade direction.

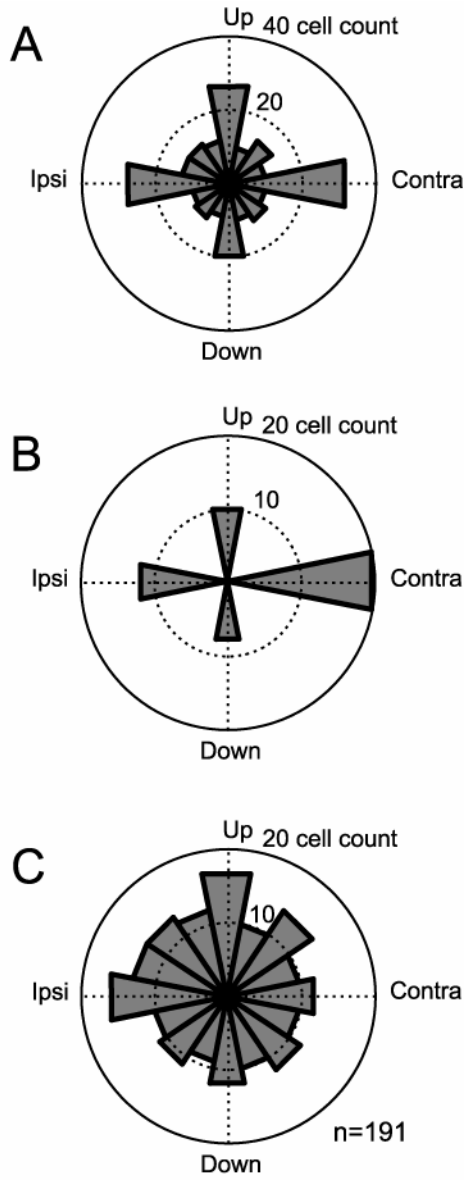

Figure 14. Across the population of neurons, there is no bias in the preferred direction of remapping.

The method used to calculate best remapping direction is described in 9. A. All neurons. Each bin represents a count of the number of neurons with best remapping direction for a particular region of the visual field. Contraversive saccades are represented to the right; ipsiversive saccades are represented to the left. Directions throughout the visual field are represented, though there is an apparent over-representation of saccade directions along the horizontal and vertical meridians. These locations represent the four saccade directions tested (n = 241). B. Uni-directional neurons. Neurons that remap stimulus traces in only a single direction must have best directions along the meridians, the saccade directions we tested. There is no significant tendency for uni-directional neurons to prefer one particular saccade direction (n = 50, Rayleigh's test, $p > 0.05$). Conventions as in A. C. Multi-directional neurons. For neurons that remap in multiple directions, the best remapping directions are uniformly distributed throughout the visual field (n = 191, Rayleigh's test, $p > 0.05$). Conventions as in A.

The finding that individual neurons have preferred remapping directions led us to ask about the factors that determine the best direction. In particular, we were interested in knowing whether the best direction is related to the location of the receptive field. We addressed this by calculating the difference between the best remapping direction (as determined by the polar plots) and the location of the receptive field (Figure 15A). We computed the smallest angle, so the data range from 0 to 180 degrees. If the best remapping direction were aligned with RF location, we would expect many neurons to show small angular offsets. Alternatively, if the best remapping direction were frequently opposite the RF, we would expect the majority of neurons to have large angular offsets. In the bar graph in panel B, we divided the data into 5 groups binned into increments of 36 degrees. Overall, the distribution is relatively flat, indicating that there is no systematic relationship between RF location and best remap direction. This was confirmed statistically (Chi-square test of proportions, $\chi^2 = 4.1475$, $p > 0.05$). This observation indicates that the preferred remapping direction is not determined by the direction of the saccade relative to the location of the RF.

The population remaps stimulus traces for all saccade directions

The analyses above demonstrate that individual neurons can remap stimulus traces in all saccade directions. We next extend our analyses to the population level. Of particular interest is whether, at the population level, stimulus traces are updated in conjunction with all saccade directions. The analyses described here parallel those used for the analysis of single neurons. Specifically, we compared activity in the single step task to that from each of the corresponding control tasks. Here we treat each direction

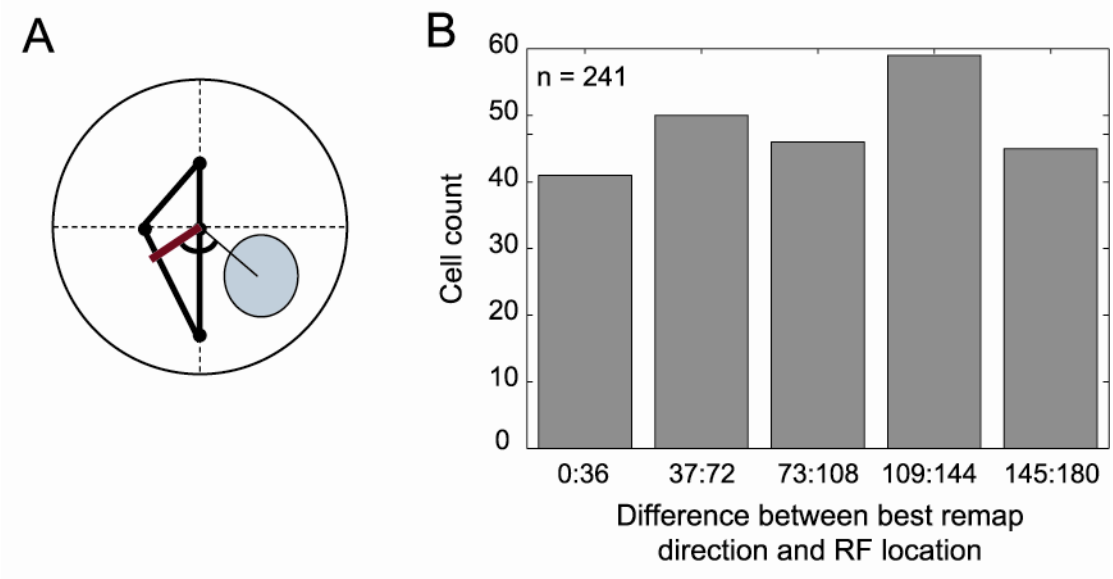

Figure 15. Difference between the best remapping direction and receptive field location.

A. Method used to calculate the difference between best direction and RF location. Polar plots described in Figure 11. Red line indicates the best remapping direction. Grey circle indicates the location of the RF. Arc indicates the smallest angular difference between these. B. Distribution of differences. Data are binned by increments of 36 degrees. There are no significant differences between the number of neurons in the different bins. This indicates that there is no significant relationship between location of the receptive field and best remapping direction.

tested in each neuron as a separate sample. With this analysis we can assess whether the *population of neurons* shows universal remapping as opposed to whether *individual neurons* do so. If activity in the single step task is significantly greater than that generated in each of the control conditions (t-test, alpha = 0.025, Bonferroni correction), we conclude that the population remaps stimulus traces for that particular direction. In Figure 16, we plot activity in the single step task against that generated in the corresponding control conditions for each sample. Each row of panels represents data from one of the test directions: the left panels compare single step activity to stimulus control activity; the right-hand panels compare activity from the single step and saccade control tasks. The red asterisk indicates conditions in which activity in the single step

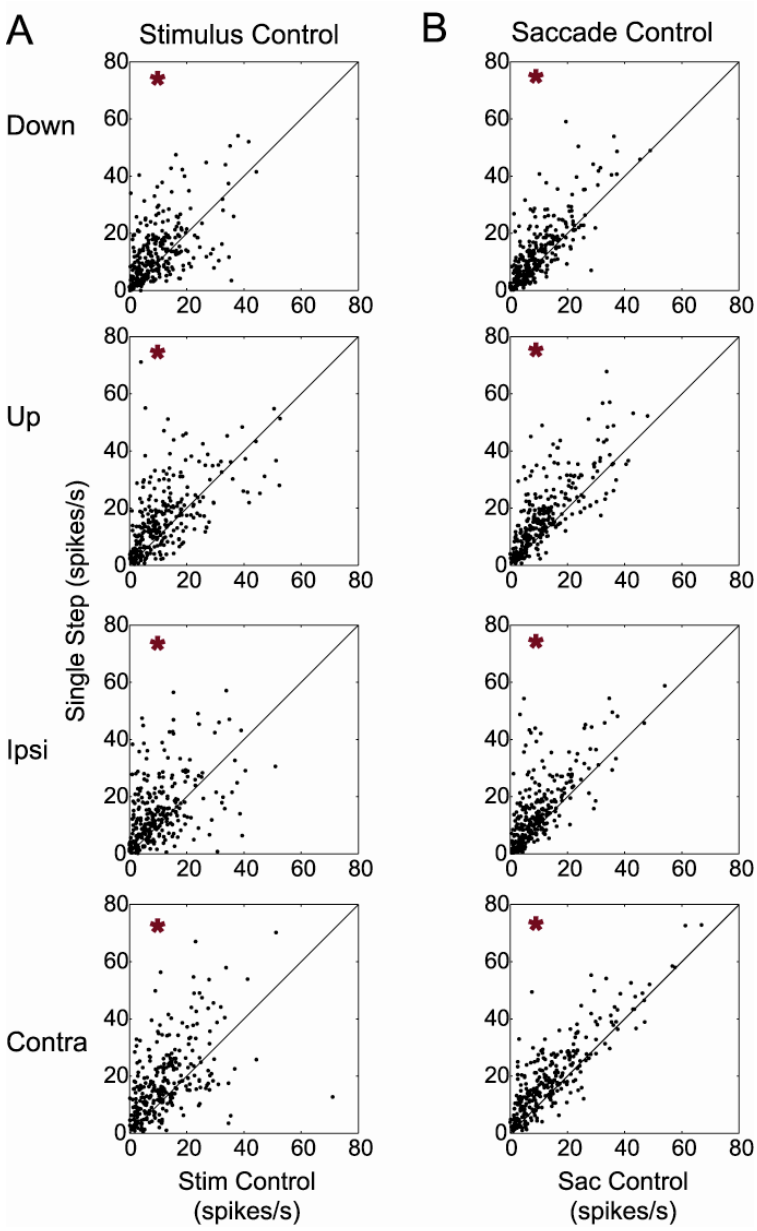

Figure 16. At the population level, stimulus traces are remapped in conjunction with all saccade directions.

Each row of panels represents data from one saccade direction. A. Comparison of single step activity and stimulus control activity. Each dot represents the activity of a single neuron in the single step task plotted against its activity in the stimulus control task. Mean firing rate is computed in the epoch 200-500 ms relative to stimulus onset. Red asterisk indicates that activity in the single step task is significantly greater than that observed in the stimulus control task (t-test, $p < 0.025$). For all directions, single step activity is greater than stimulus control activity. B. Comparison of single step and saccade control activity. Mean firing rate is computed in the epoch 0-300 ms relative to the onset of the sacade. For all directions, single step activity is significantly greater than saccade control activity. Conventions as in A. If single step activity is greater than activity in both control tasks, the population is considered to remap remap stimulus traces for that direction. This criterion is met by all directions ($n = 281$).

task is greater than that in the control tasks. For all directions, activity in the single step task is significantly greater than that generated by either the stimulus or saccade alone (t-test, all comparisons, $p < 0.0001$). We conclude that at the population level, stimulus traces are remapped in conjunction with all saccade directions tested.

The evidence that the population remaps stimulus traces in all directions prompted us to compare directly the strength of remapping across the different directions. We quantified the strength of remapping with the Stimulus and Saccade Indices described in the preceding section. Here we use these indices to compare the strength of remapping for the different saccade directions (Figure 17). These distributions can be used to make two points. First, they can provide further evidence that remapping is significant for each saccade direction. If, for a particular direction, both distributions are significantly skewed toward positive values (t-test, alpha = 0.025, Bonferroni correction), we conclude that remapping is significant. We found that all distributions are significantly skewed toward positive values ($p < .00001$), confirming the finding that the population remaps stimulus traces for saccades in all four directions.

The second issue we addressed with the Stimulus and Saccade Indices was to ask whether, at the population level, the strength of remapping varies with changes in saccade direction. We tested this separately for each set of indices. We used a repeated measures ANOVA to compare the indices obtained for each of the four directions. A repeated-measures test takes into account systematic differences between neurons, making it a more sensitive test than a one-way ANOVA. The repeated measures test provides a better chance of detecting differences, should they exist. We found that there is no significant main effect of direction for either the Stimulus Index (d.f. = 3, F = 1.86, p >

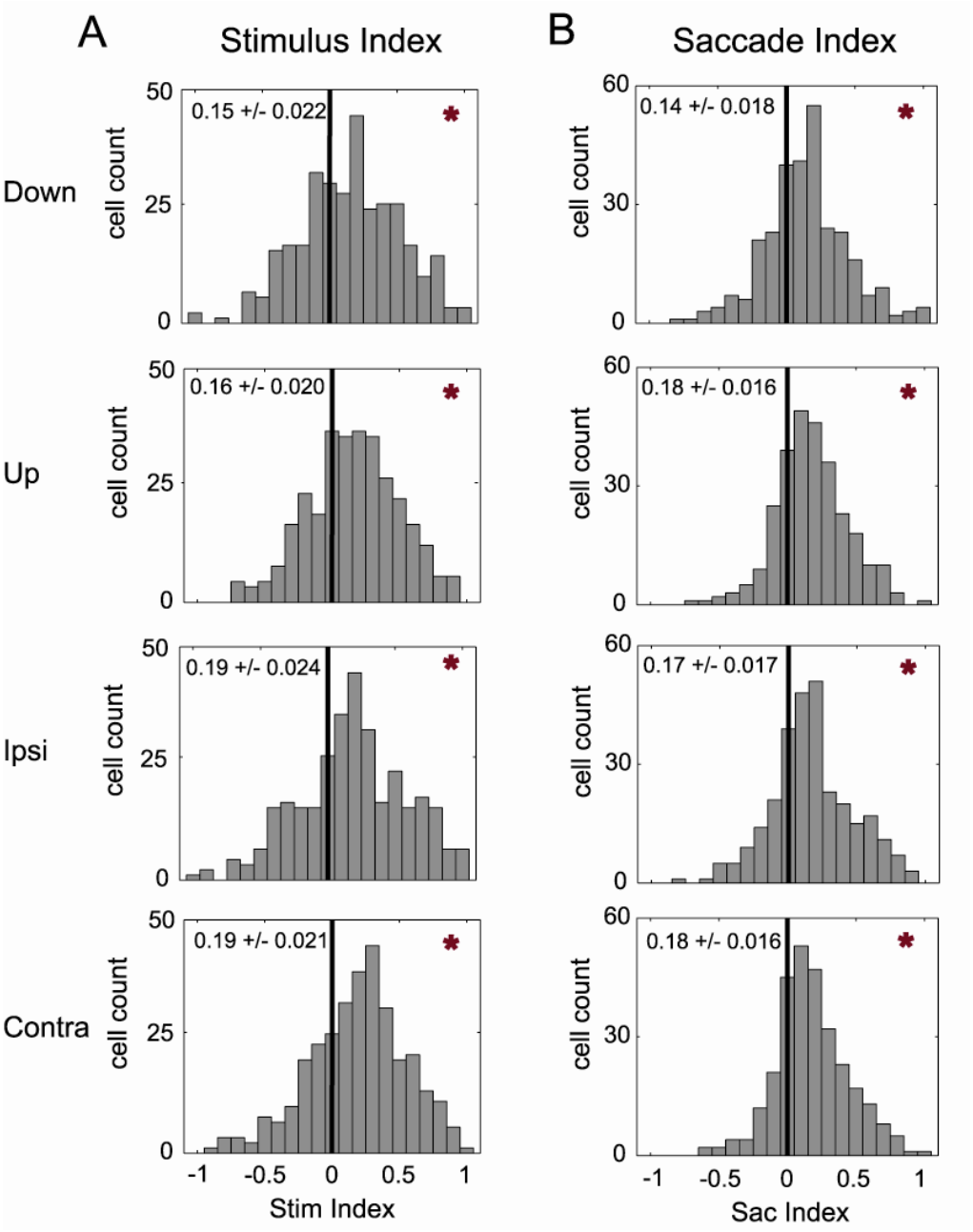

Figure 17. Comparison of the strength of remapping as a function of saccade direction.

Indices are calculated using the following formula: Index = (A-B)/(A+B), where A represents firing rate measured in the single step task and B represents firing rate measured in one of the control tasks. Positive values indicate that activity in the single step task is greater than that observed in the control task. Numbers in the upper lefthand corner of each panel represent mean +/- s.e.m.. Red asterisk indicates that the distribution is significantly skewed toward positive values (t-test, alpha = 0.025). A. Stimulus Indices. B. Saccade Indices. For all directions, both sets of distributions are significantly skewed toward positive values. This provides evidence that at the population level, stimulus traces are remapped in each test direction. Additionally, there are no differences across either set of indices. This indicates that the strength of remapping does not vary across the test conditions (n = 281).

0.14) or the Saccade Index (d.f. = 3, F = 1.50, p > 0.20). We conclude that at the population level, the strength of remapping does not vary with changes in saccade direction.

Of critical importance is whether there are differences in the strength of remapping when activity in the two control conditions is accounted for simultaneously. We used the Remap Indices to compare three features of remapping: 1) the average remapping signal carried in each direction; 2) the frequency of remapping; and 3) the magnitude of the remapping signal carried by remapping neurons.

To address the first issue of differences in the average remapping signal, we analyzed the entire population of Remap Indices (Figure 18A). That is, we include both samples with and without detectable remapping (i.e., Remap Index > 0 and Remap Index = 0). This informs us of whether, across the entire population of samples, there are any differences in the average remapping signal carried in each direction. In the left column, each distribution represents data from one direction. Qualitatively, the distributions look very similar. The most striking feature they share is that they are all heavily weighted toward zero; these are the samples where there was no detectable remapping. To compare the distributions, we used a non-parametric Kruskall-Wallis repeated-measures ANOVA with direction as the factor of interest. There were no differences between the magnitude of the Remap Index for any of the test conditions (d.f. = 3, χ^2 = 4.84, p > 0.18). This indicates that the magnitude of the remapping signal does not vary with changes in saccade direction.

The second question of interest was whether remapping occurs with equal frequency for all directions. To answer this question, we analyzed the number of positive

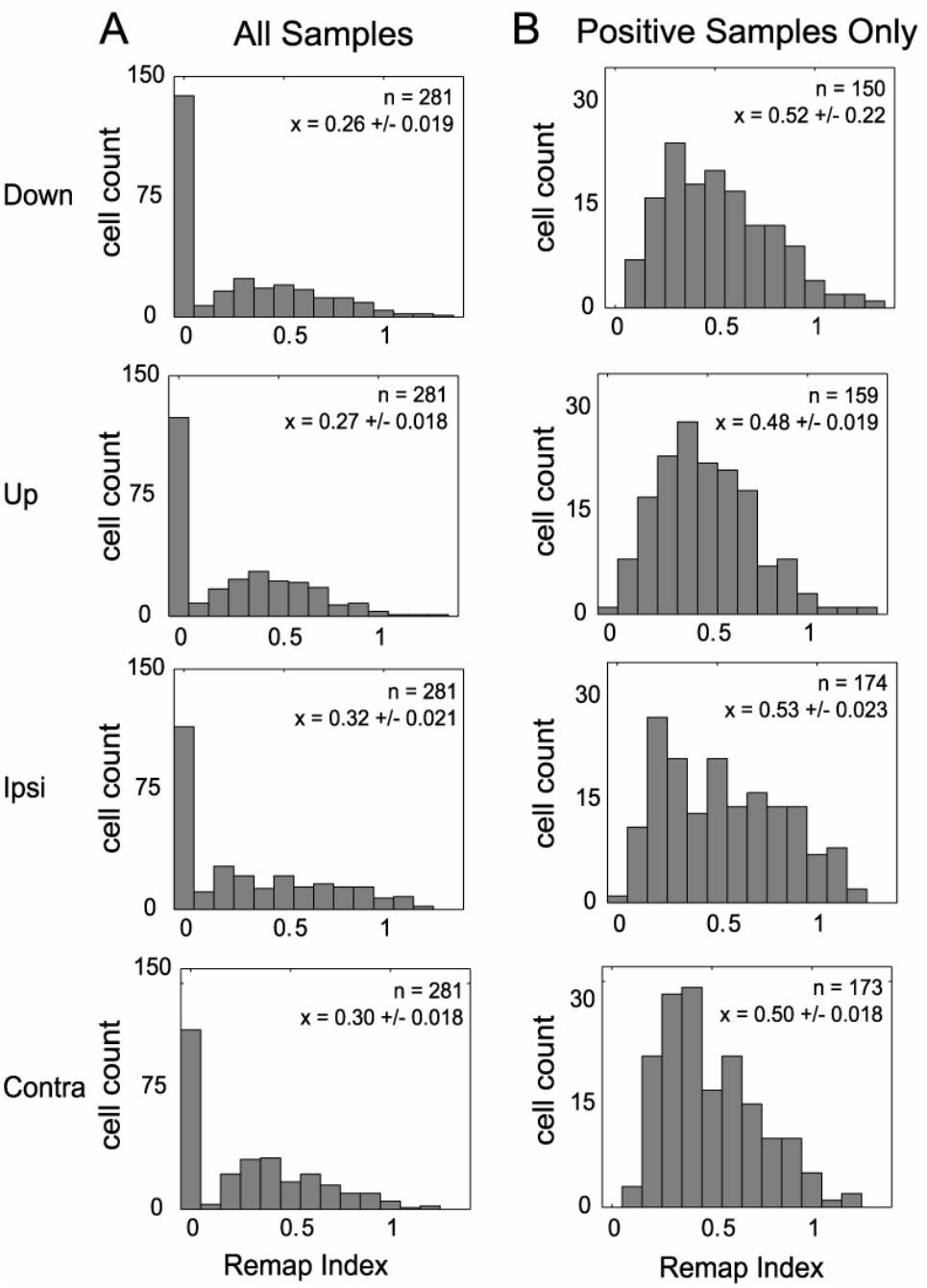

Figure 18. Comparison of the distribution of Remap Indices for the four test directions.

The Remap Index is a measure of how robustly a neuron remaps stimulus traces for saccades of a particular direction. Positive values indicate that there was remapping; values of zero indicate that remapping was not detectable. A. All samples. For each direction, the distribution of indices is broad, with a large proportion of samples at 0. There were no significant differences between any of the distributions. Numbers in the upper righthand corner are the means +/- s.e.m.. B. Positive samples only. Each histogram represents the distribution of positive Remap Indices, the samples with detectable remapping. There were no differences between any of the distributions. These results indicate that stimulus traces are remapped equally robustly across the four test directions.

Remap Indices observed for each direction (Figure 19). A positive Remap Index indicates remapping. We used a Chi-square test of proportions to compare the frequency of remapping in each direction. We found that there were no significant differences between the proportions of neurons that remapped for each of the test conditions (Chi-Square test, $\chi^2 = 0.051$, $p > 0.60$). We conclude that remapping occurs with equal frequency for the four directions.

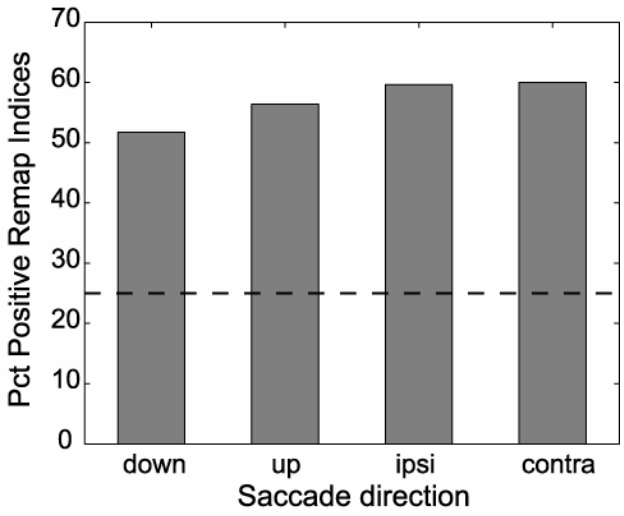

Figure 19. Comparison of the percentage of positive Remap Indices for the four test directions.

The dotted line indicates the number of positive samples expected by chance (25%). For all directions, there is a significantly greater proportion of positive samples than expected by chance. Additionally, there are no significant differences between the number of positive samples observed across the test conditions.

Finally, for remapping neurons, does the magnitude of the signal they carry vary with changes in direction? To answer this question, we compared only the positive samples for each direction (Figure 18B). We used a one-way ANOVA to assess whether there were any differences between the four directions. In agreement with earlier findings, we found no significant differences between any of the directions when the data

were analyzed this way (d.f. = 3, χ^2 = 1.44, p > 0.70). Together, the results of our analyses of the Remap Index reveal that at the population level, the frequency and strength of remapping is independent of saccade direction.

Remapping latency does not vary across saccade directions

When do neurons in LIP first respond to the updated stimulus trace? We were interested in whether there were any differences in the latency of remapping in the four conditions. Previous experiments focused on the latency of remapping relative to the onset of the saccade. Accordingly, that will be our focus here. We analyzed response latency at both the single cell and population levels.

As discussed in previous sections, it is often the case that some of the activity we observe in the single step task is attributable to pure visual or motor factors, rather than to updating. We therefore had to devise a method to determine when remapping begins, even if other signals are present in the neural response. We did this in the following way. First, we limited this analysis to those samples where the stimulus alone did not drive the neuron. This reduced the number of required comparisons from 2 (single step vs. stimulus AND single step vs. saccade) to 1 (single step vs. saccade), while still maintaining a relatively large population of samples to analyze for each direction (sample sizes: down = 104, up = 83, ipsi = 117, contra = 76). Second, we determined the onset of remapping by calculating the time at which activity in the single step task first exceeded that in the saccade control task (see Figure 20A). We call this timepoint the Divergence Time because it reflects the time at which single step and saccade activity diverge. In Panel B, each row represents one of the test conditions, and each dot represents the

Divergence Time for a single neuron during that condition. For each direction, there is a wide range of times, indicating that the onset of remapping can be quite variable. This finding is similar to those reported previously (Umeno and Goldberg, 1997). Critically, we found no difference between divergence time for the different test conditions (One-way ANOVA, $\chi^2 = 4.02$, $p > 0.26$). This result provides evidence that the time it takes to compute the updated location of a stimulus traces does not vary with changes in saccade direction.

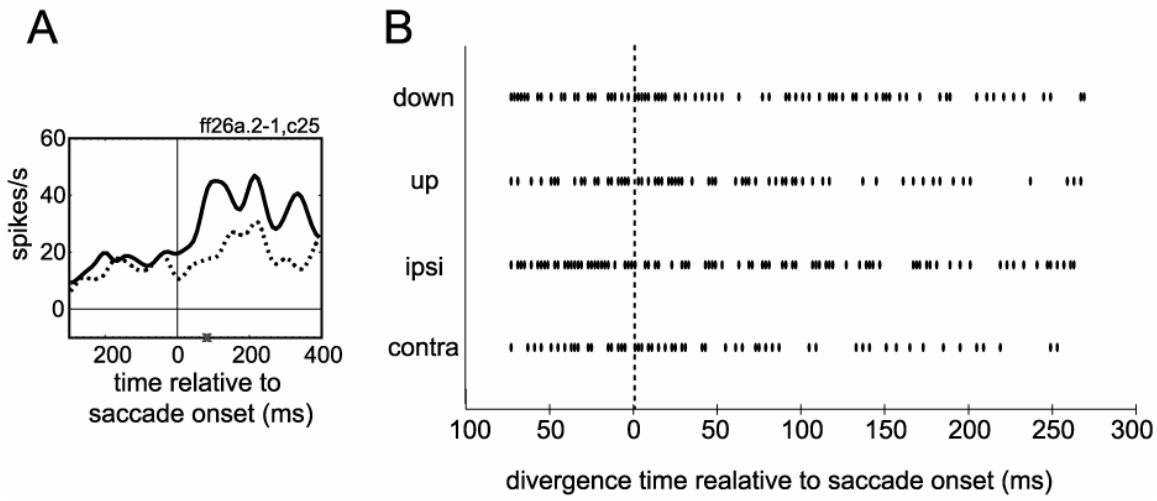

Figure 20. Comparison of the onset of updating activity in individual neurons.

A. Activity of a single neuron for a test of remapping in one direction. Solid line represents single step activity. Dotted line represents saccade alone activity. Data are aligned on the onset of the saccade. Red marker along the x-axis indicates the time at which activity in the single step task is first significantly greater than activity in the saccade control task (80ms). This time-point is called the Divergence Time. B. Comparison of divergence time across the four test directions. Each row represents data from one test direction. Each black dot represents data from a single neuron during a test of remapping in one direction. Only conditions where there was no significant activity in the stimulus control task are included. The onset time for remapping varies widely, but does not vary systematically with changes in saccade direction.

We next compared the latency and timecourse of remapping at the population level. We constructed histograms using only those samples where neither the stimulus nor the saccade generated a response in the visual or motor epoch (see Appendix). In part A of Figure 21, each panel represents data from the single step (solid lines) and saccade control tasks (dotted lines) for one of the test directions. The data are aligned on the onset of the saccade. This figure can be used to make two main points. First, for all directions, activity in the single step task is greater than activity in the saccade control task. Second, activity in the single step task begins to exceed saccade control activity before the beginning of the saccade, and remains elevated until well after the saccade is completed.

We quantified the onset of remapping by calculating the Divergence Time for each population histogram. This time is indicated by the red markers along the x-axis. Across the four test directions, there is little variability in when signals associated with spatial updating first become available (mean -10 ms, range -25 ms to +5 ms). We conclude that across the four test conditions, the time at which information about updated stimulus locations becomes available is effectively the same.

The temporal dynamics of the single step activity are influenced by activity present in the saccade control task, particularly in the epoch 100-200ms after the onset of the saccade. In this experiment, it is the *difference* between activity in the single step and saccade control tasks that is of particular interest. This is the activity we attribute to remapping the stimulus trace. In panel B, we highlight the difference between activity in the single step and control tasks. Each histogram represents the difference signal for one of the test conditions; they are constructed by subtracting the saccade task PSTH from the

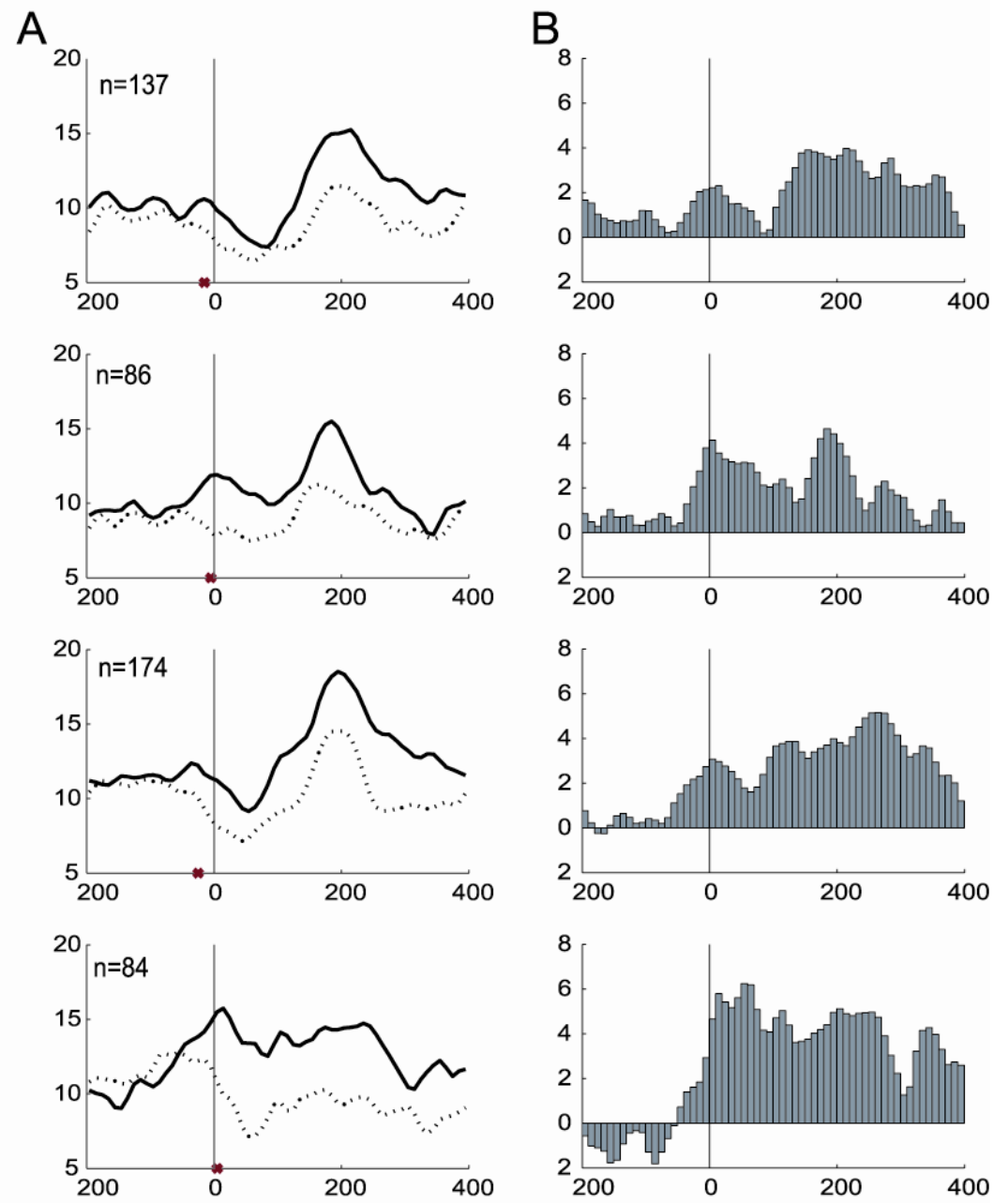

Figure 21. Comparison of the timecourse of remapping across the four test directions.

A. Population Histograms. Data from single step (solid lines) and saccade control (dotted lines) tasks are shown aligned on the onset of the eye movement. Only conditions with no significant response in the visual or saccade epoch of the control tasks are included. For all directions, activity in the single step task first exceeds the saccade control activity before the start of the eye movement. Red marker along the x-axis indicates the time at which activity in the SS task is first significantly greater than saccade control activity. Updating activity persists until after the saccade is completed. The post-saccadic phase of the single step response are influenced by activity present in the saccade control task. B. Data from A are replotted as difference histograms. Each histogram represents the difference between activity in the single step and saccade control tasks. This difference represents activity attributable to remapping the stimulus trace. This signal is similar across the four test conditions: it begins before the onset of the saccade and persists until after it is completed. Bin size = 10 ms.

single step PSTH. The difference histograms show the observations described above: first, remapping activity begins just before the onset of the saccade for all directions; second, this activity persists until well after the saccade is completed for all directions.

Remapping is independent of RF eccentricity

We were interested in whether the magnitude or selectivity of remapping varies as a function of the distance of the receptive field from the fovea. For instance, do neurons with more foveal RFs have greater access to remapped visual traces? To address this issue, we divided the population into three groups: neurons with receptive fields located within 10 degrees of the fovea were considered central, and those with those with receptive fields greater than 20 degrees from the fovea were considered peripheral. Neurons with RFs between these were put in a middle category. With these categories, we had a reasonable population of neurons in each group (Central = 84, Middle = 110, Peripheral = 47). In Figure 22, we show the distributions of Selectivity Indices for the three groups of neurons. We found no differences between any of the groups of neurons (K-S test, $p > 0.5$ for all comparisons). This indicates that regardless of eccentricity, neurons show equally selective remapping responses. We compare the strength of remapping for these groups of neurons in panel D. Each bar represents the average Remap Index for each group of neurons. We found that the strength of remapping does not vary with changes in RF eccentricity (Wilcoxon ranksum, all comparisons, $p > 0.5$). Taken together, these results indicate that neurons with receptive fields located throughout the visual field carry equally selective and robust spatial updating signals.

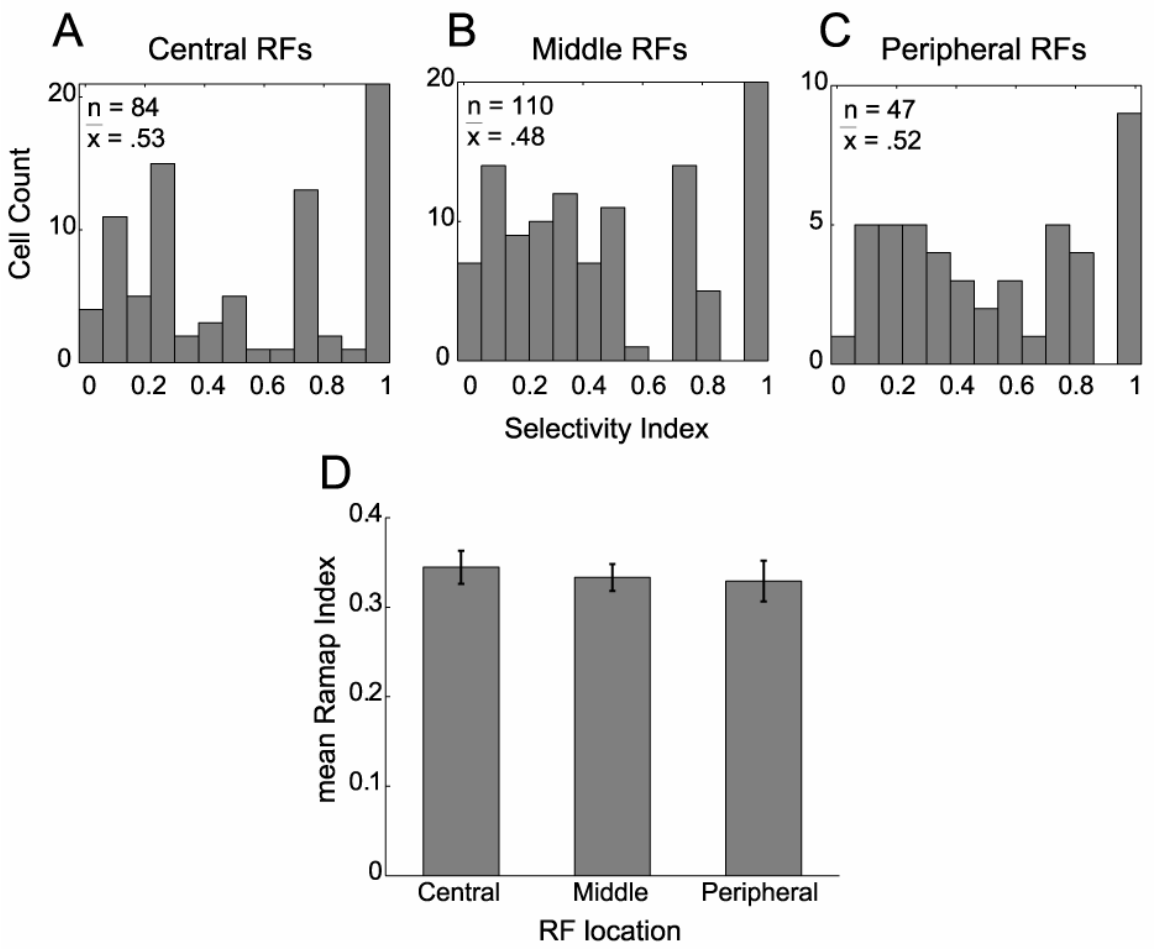

Figure 22. Comparison of remapping properties for neurons with RFs in the central, middle and peripheral visual field.

A, B, C. Comparison of Selectivity Indices. There was no difference in the universality of remapping for neurons with RFs in different regions of the visual field D. Comparison of the strength of remapping. Bars represent the average Remap Index for each group of neurons. There are no differences in the strength of remapping for any of the groups.

2.5.2. Results, Part 2: Normalized saccade direction

In the original remapping paradigm, the stimulus was always placed in the hemifield opposite from the RF and the saccade was always directed away from the RF. The rationale behind this approach was that with this spatial configuration, neither the stimulus nor the saccade alone would drive the neuron. In the present experiment, we tested the same four saccade directions, regardless of the location of the RF. Thus, for any given neuron, some saccades are directed toward the RF while others are directed away from it. We anticipated that there might be systematic differences in responses according to whether the saccade was directed toward or away from the RF. Specifically, if the saccade is directed toward the RF, it usually will drive the neuron. Likewise, the stimulus alone frequently drives the neuron for saccades directed toward the RF. This is because the outer edge of the RF is often unbounded (Figure 23A). On the other hand, if the saccade is directed away from the RF, it is unlikely that there will be activity present in either control task (panel B). As established in previous sections, the presence of activity in the control tasks influences the detectability of remapping. We therefore developed a normalization procedure that would allow us to determine whether there was any relationship between remapping and the direction of the saccade relative to the RF.

We used the following procedure to normalize the four standard test directions relative to the receptive field location (Figure 24). During data collection, we mapped the RF to one of 8 angles (of varying eccentricities) around the fovea. This produced two classes of neurons: Oblique neurons have RFs along one of the oblique axes (n = 185);

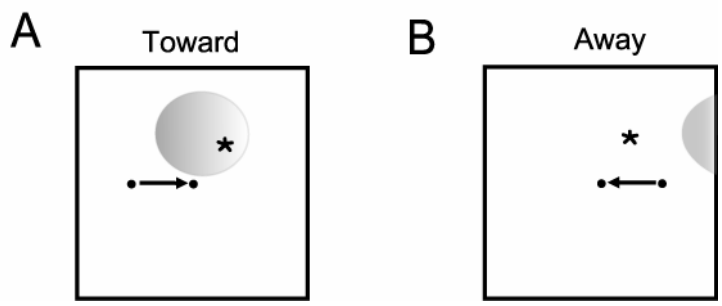

Figure 23. Schematic representation to show why activity in the control tasks varies as a function of saccade direction relative to RF location.

In each panel, arrow represents saccade tested in the single step task. Asterisk represents location of the to-be-updated stimulus. Grey circle represents the location of the RF when the eyes are at the initial peripheral fixation location. The outer edge of the RF is often unbounded. A. For saccades directed toward the RF, both the saccade and the stimulus are likely to be encompassed by the RF. They will likely generate a response in the control tasks. B. For saccades directed away from the RF, it is unlikely that the stimulus or saccade alone will be in the RF.

Cardinal neurons have RFs on one of the cardinal axes (n = 96). We then computed the angular offset (dotted lines) between the saccade direction and angle of the receptive field. This angular offset is the normalized saccade direction, and represents the direction of the saccade relative to the RF location. After normalization, the saccade directions for Oblique neurons become 45, 135, 225 and 315. The saccade directions for Cardinal neurons become 0, 90, 180 and 270. We refer to the normalized saccade directions as "saccade categories." Some of the categories are complementary: 45/315; 135/225 and 90/270. For these cases, the more ipsiversive saccade is ascribed to the larger angle. We chose this convention because an ipsiversive saccade is less likely to drive the neuron than a contraversive saccade. This normalization procedure allowed us to address three issues: whether remapping is observable for all saccade categories; whether the magnitude of remapping varies across saccade categories; and whether the latency of remapping varies with changes in saccade category.

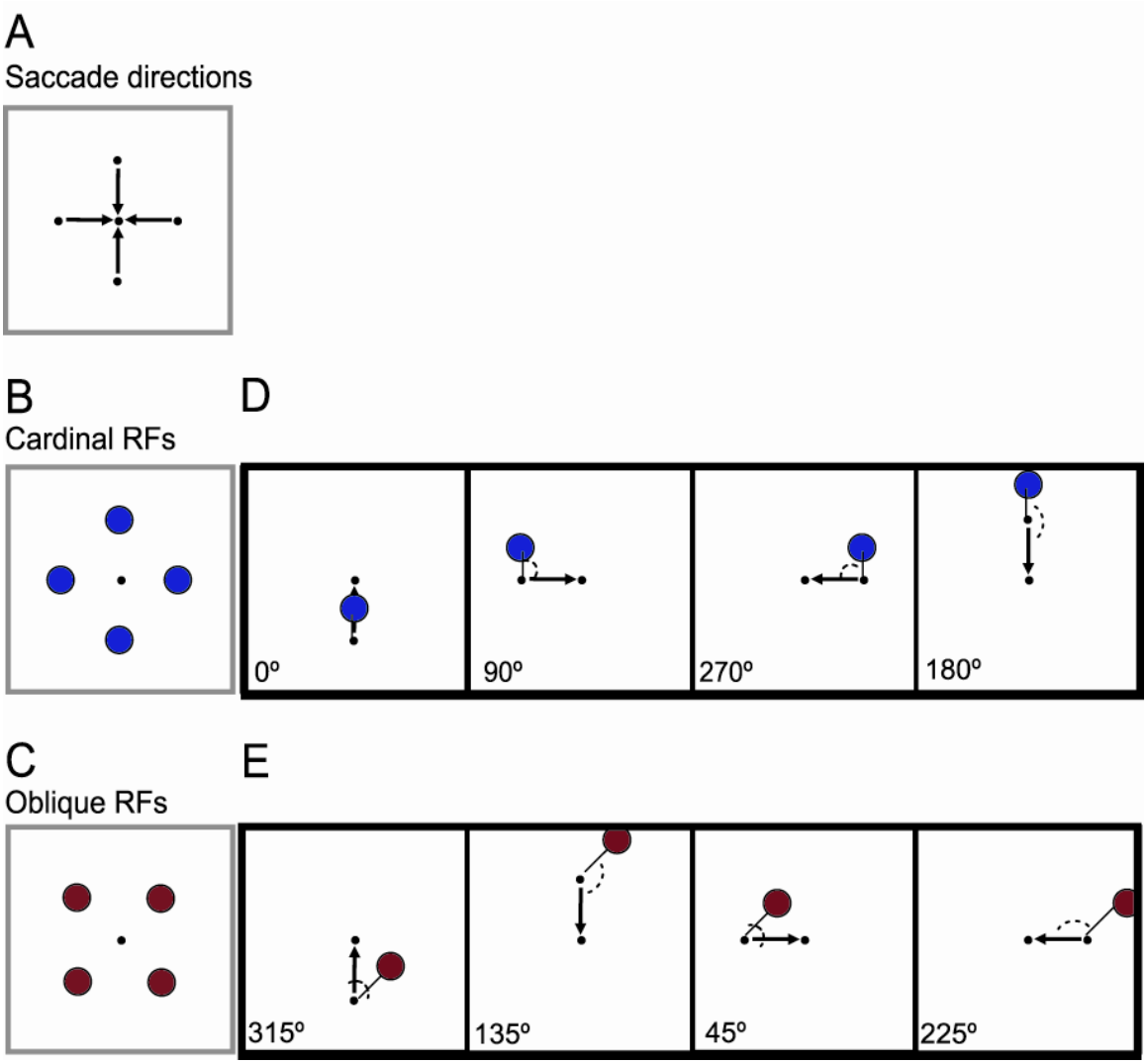

Figure 24. Method used to normalize saccade direction relative to RF location.

A. The same standard saccade directions were used for all neurons. The four outer dots represent the four starting locations. Arrows represent the direction of the saccade. Central dot represents the final fixation location for all conditions. B, C. Receptive fields (RFs, filled circles) are mapped to one of 8 locations around the fovea. These locations fall along one of the cardinal (B) or oblique (C) axes. In these examples, the recording hemisphere is left; rightward saccades are therefore contraversive and leftward saccades are ipsiversive. D. Example of normalized saccade directions for a neuron with RF on one of the cardinal axes. In this example, the RF is located straight up from the fovea. The blue circle represents the location of the RF when the eyes are at the first fixation point. The upward saccade is directly toward the location of the RF; the normalized saccade direction is 0 degrees. The rightward and leftward saccades are complementary: they are both offset by 90 degrees. For complementary pairs, the more contraversive saccade is assigned to the smaller category. For this example, the rightward saccade is contraversive and is categorized as 90 degrees while the ipsiversive leftward saccade is categorized as 270 degrees. The downward saccade is directly opposite the RF; it is categorized as 180 degrees. In this configuration, the RF frequently lands on the location of the first fixation point. E. The same process is used to normalize the saccade directions for neurons with RFs (red circle) on the oblique axes. In this example, the RF is located up and to the right. The saccades are categorized as 45, 135, 225 and 315. These form two complementary pairs of categories: 45/315 and 135/225.

Individual neurons can remap for all saccade categories

The first question was whether neurons remap stimulus traces for all saccade categories. As described in the previous sections, remapping is considered significant if activity in the single step task is significantly greater than activity in each of the control tasks (t-test, alpha = 0.025). Single neurons showed significant remapping for all saccade categories (Figure 25). We separately compare the saccade categories from each class of cells: data from Cardinal cells (0, 90, 180, 270 degree categories) are shown in A; data from Oblique cells (45, 135, 225, 315 degree categories) are shown in B. Statistically, there were no differences in the proportions of neurons that showed significant remapping for either class of cells (Chi-square test, $p > 0.05$ for both cell classes). This analysis, however, reveals an interesting trend in the data from the Cardinal cells: fewer neurons remap for the 180 degree category than for the other three categories. These findings indicate that neurons in LIP exhibit significant remapping for all saccade directions relative to the RF, though fewer neurons carry this signal when the saccade is directly opposite the RF.

Having observed significant remapping for all categories, we wanted to examine in more detail the signal carried by the population of neurons. We addressed this by comparing activity in the single step task to that from each of the corresponding control tasks (t-test, alpha = 0.025). Data from the eight saccade categories are represented in Figure 26: Cardinal cells are on the left; Oblique cells are on the right. For all eight saccade categories, activity in the single step task is significantly greater ($p < 0.025$) than activity in the stimulus control task (Panels A and C). Significance is denoted by the red asterisk. We also found that activity in the single step task was significantly greater ($p <$

0.025) than saccade control activity for all categories *except* the 180 degree category (Panels B and D). Remapping is considered significant only if single step activity is significantly greater than both stimulus control and saccade control activity. With this analysis, we found that remapping is significant for all saccade categories except the 180 degree category. We conclude that at the population level, stimulus traces are remapped for nearly all saccade directions relative to the RF. This signal is obscured when the saccade is directly opposite the RF.

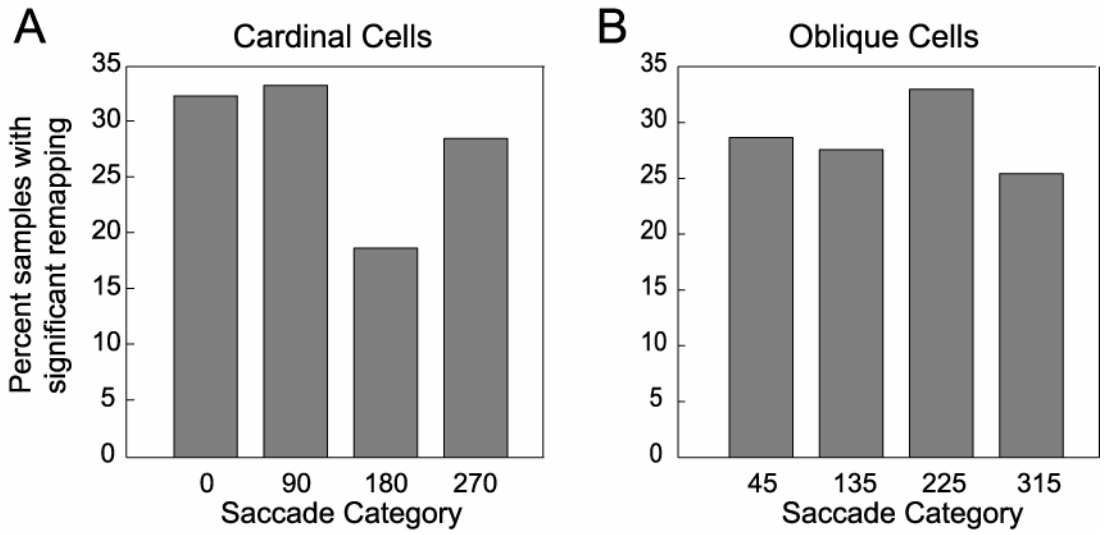

Figure 25. Comparison of the number of samples with significant remapping for each saccade category.

Each neuron from each class of cells contribues 4 samples. Significant remapping is defined as single step activity that is significantly greater than activity in each of the corresponding control conditions (t-test, alpha < 0.025). A. Cardinal Cells. Cells with receptive fields along one of the cardinal axes. The 180 degree category has a lower percentage of samples with significant remapping. In this condition, the saccade alone often generates activity during the remapping epoch because the RF is moved onto the location of the initial fixation point. Even though this fixation point is extinguished well before the saccade, the FP itself is a salient stimulus and is remapped (see Figure 27). The 90 and 270 categories are complementary; a similar percentage of the samples remap for these categories. B. Oblique Cells. Cells with receptive fields along one of the oblique axes. Remapping occurs at nearly equal frequencies for the four categories. The complementary pairs are 45/315 and 135/225. Except for the 180 degree category, the range is narrow, indicating that remapping occurs at nearly the same frequency for all saccade categories.

The finding that remapping did not reach statistical significance for the 180 degree category prompted us to explore this condition further. The example neuron in Figure 27 illustrates why it is often difficult to detect remapping for the 180 degree saccade category: the saccade alone generates a robust response during our analysis epoch (0-300 ms relative to saccade onset). This response is likely attributable to remapping the location of the first fixation point. As schematized in the left-hand panels, if the saccade is directly opposite the RF, it will move the RF onto the location of the initial fixation point. Because the fixation point is a salient visual stimulus, it can, and often is, remapped. The analysis of remapping as a function of normalized saccade direction reveals a pattern in the data that was previously undetectable. Furthermore, it provides insight into why remapping is sometimes not detectable, namely that this signal can be obscured by activity related to remapping the fixation point.

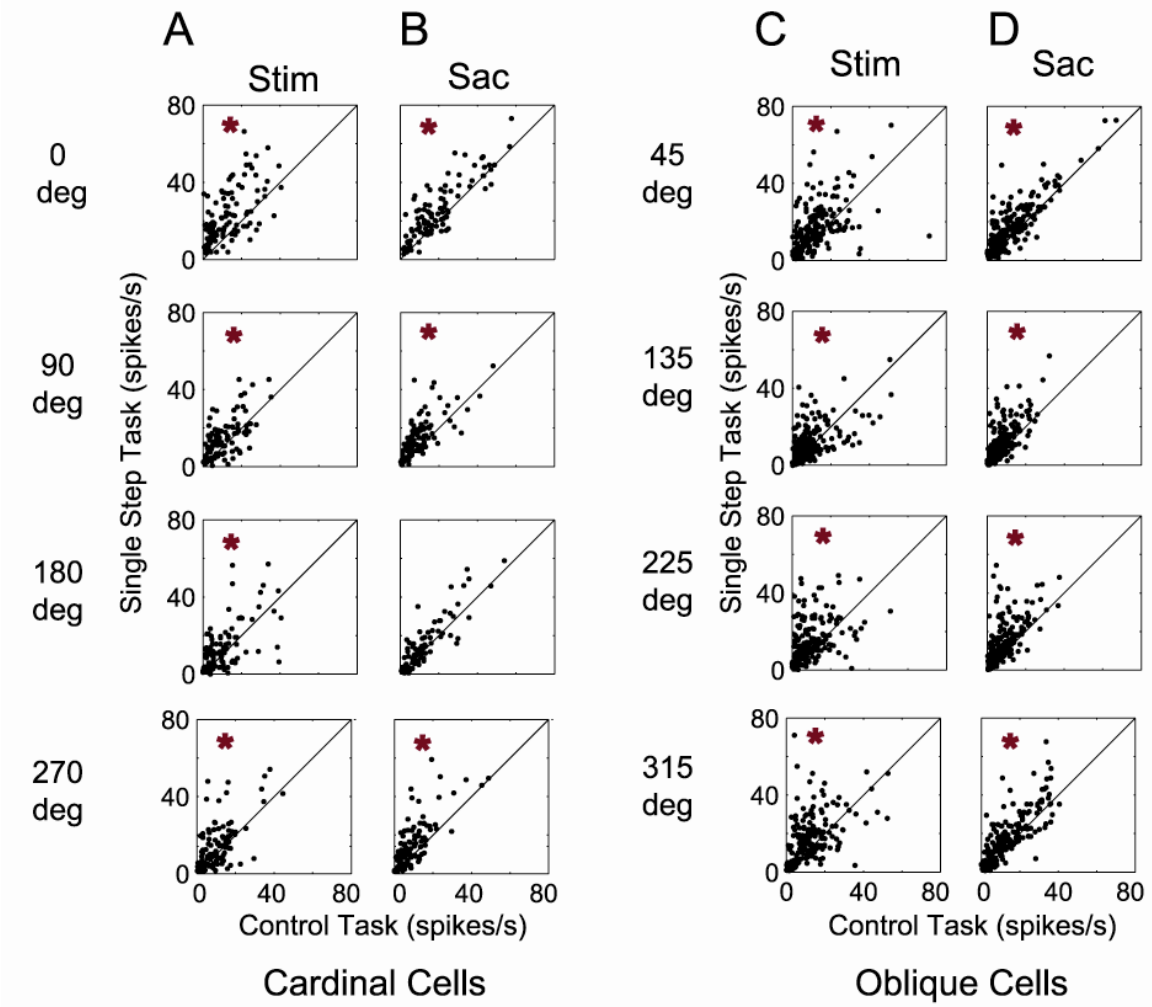

Figure 26. Population level assessment of remapping for the 8 saccade categories.

Saccade category represents saccade direction relative to the location of the receptive field. All samples from all neurons are included in this analysis, regardless of the amount of activity in the control tasks. Remapping is considered significant if activity in the single step task is significantly greater than activity observed in each of the control tasks. Data from Cardinal cells (n = 96) plotted in A and B; Data from Oblique cells (n = 185) plotted in C and D. A, C. Single step task compared to stimulus control task. Each dot represents the activity of a single neuron during the single step task plotted against the activity observed when the stimulus is presented alone. Firing rate represents the mean activity in the epoch 200-500ms after presentation of the stimulus. For all saccade categories of both classes of cells, activity in the single step task is significantly greater than that observed in the stimulus control task (t-test, $p < 0.025$). Significance is indicated by the red star. Axes are identical on all plots (0-80 spikes/s); labels have been removed for clarity. B, D. Activity in the single step task compared to saccade control activity. Mean activity is calculated in the epoch 0-300ms relative to saccade onset. Conventions as in A and C. For all saccade categories except the 180 degree category, activity in the single step task is significantly greater than activity in the saccade control task. Together, these results indicate that the population shows significant remapping for all saccade directions relative to the RF location except for saccades directly opposite the RF.

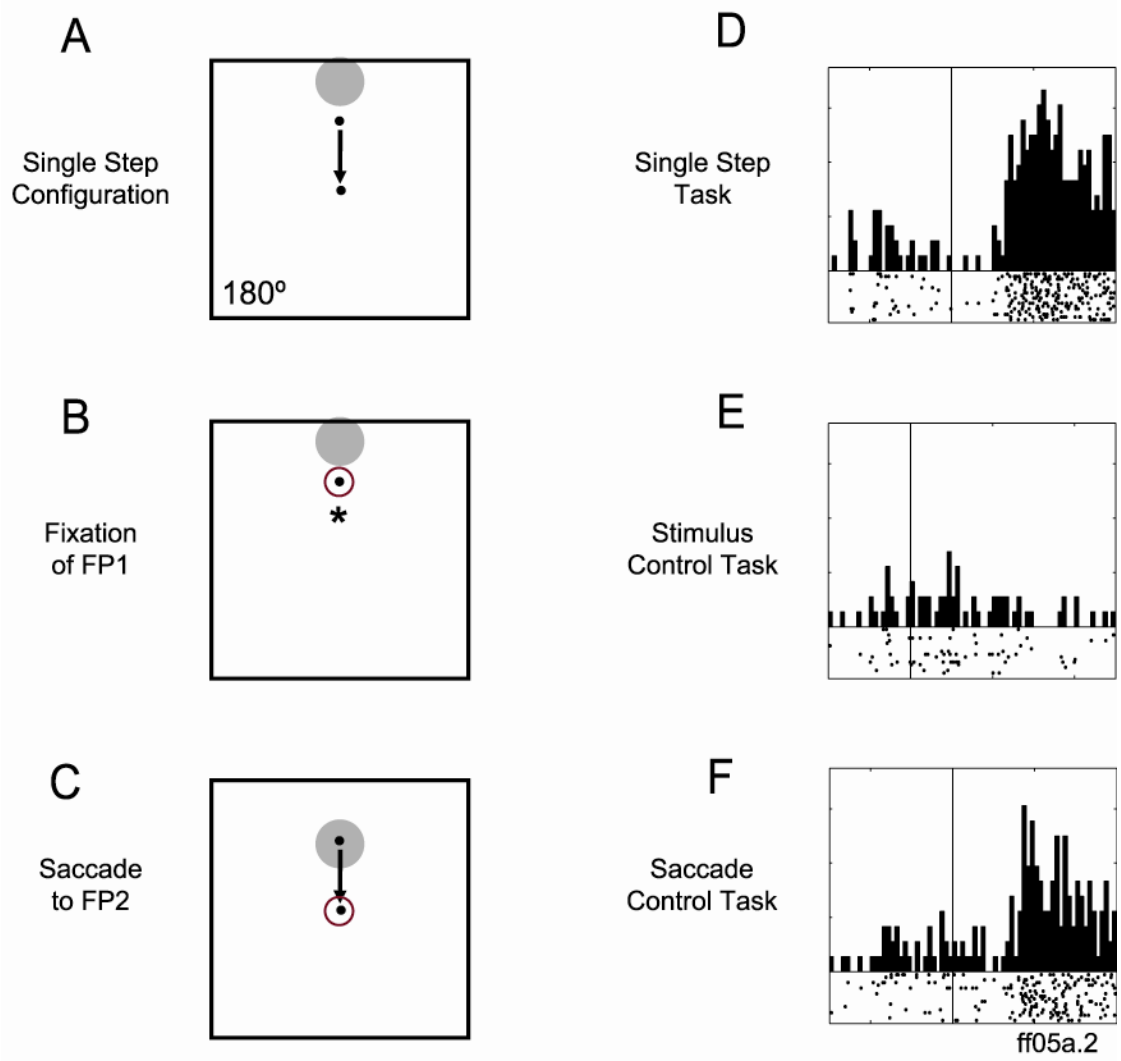

Figure 27. Example of a neuron that remaps the fixation point.

Remapping of the fixation point during is prevelant for the 180 degree saccade category. The 180 degree saccade category represents a saccade directly opposite the location of the RF. A. Spatial configuration of the single step task. Grey circle represents the receptive field (RF). Dots represent FP1 (upper) and FP2 (lower). Arrow represents the saccade from FP1 to FP2. B. Location of the RF during fixation of FP1. Star represents the to-be-updated stimulus. Red circle represents where the monkey is looking. C. Saccade to FP2. The saccade moves the RF onto the location where FP1 appeared. Because the fixation point is a salient visual stimulus, it can be remapped. D-F. Example of a neuron that remapped the location of the fixation point. D. Activity during the single step task. Data are aligned on the onset of the saccade. The neuron exihibits a robust response around the time of the eye movement. E. Saccade control task. The neuron responds in conjunction with the execution of the saccade, even when the stimulus was not presented. This response occurs with nearly the same latency as the response in the single step task. This activity cannot be considered pure motor-related activity because the eye movement is not in the direction of the response field. We attribute this response to remapping the location of the fixation point. This type of activity was common in our paradigm. F. Stimulus control task. The stimulus alone did not drive the neuron. Conventions for histograms as in Figure 6.

Comparison of the magnitude of remapping across saccade categories

The analyses above revealed differences between the eight saccade categories. We were therefore interested in directly comparing the strength of the remapping signal associated with each saccade category. Here, we focus on separate analyses of the two groups of neurons. We can exploit the fact that each neuron is tested in four of the saccade categories and, when appropriate, use repeated measures statistics to determine whether there are any differences between the categories. The central issue here is to assess whether the strength of remapping varies with changes in saccade direction relative to RF location. We analyzed the Remap Indices from each saccade category to compare three features of remapping: 1) the average remapping signal; 2) the frequency of remapping; and 3) the magnitude of the signal carried by remapping neurons.

The first issue is whether the strength of remapping varies as a function of saccade category. We used a repeated measures ANOVA to compare the mean Remap Index for each saccade category of the two groups of neurons (Figure 28). For the Cardinal cells (Panel A), we found that the strength of remapping for the 180 degree category is significantly diminished as compared to the other groups ($p < 0.05$, Tukey's HSD). There were no differences between any of the other groups. Together, these results indicate that if the saccade is directed toward the RF, or is only partially offset from it, the magnitude of the remapping signal carried by the population is invariant. If the saccade is directly offset from the RF, however, the strength of remapping is diminished. This finding parallels the observations reported in the previous section: remapping is reduced in magnitude for saccades directly opposite the RF.

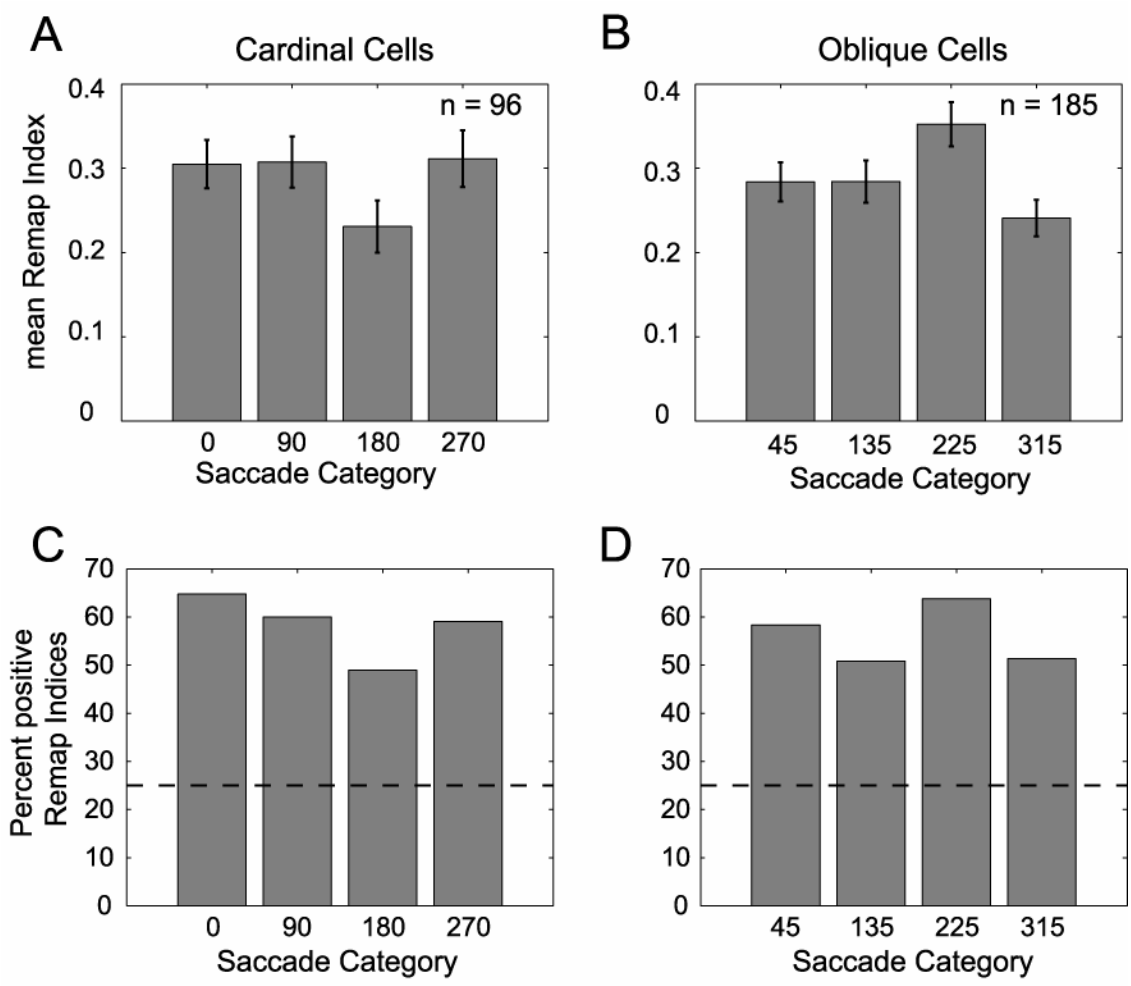

Figure 28. Analysis of the strength of remapping as a function of saccade category.

A and B. Comparison of the mean Remap Index (RI) for each saccade category. Both remapping and non-remapping samples are included. Error bars represent standard error of the mean. A. Cardinal cells. The 180 degree RI is significantly smaller than the other three categories. There is no difference in the mean RIs for the other groups. B. Oblique cells. The 225 degree saccade category has significantly greater remapping than the other three categories. C, D. Comparison of the number of positive remapping samples for each category. All categories had a significant proportion of samples with positive remap indices (Chi-Square test, $p < 0.05$). There were no differences in the number of samples with positive remap indices for either population of neurons (Chi-square test of proportions, $p > 0.05$).

This analysis also revealed some differences across saccade categories of the Oblique cells (Panel B). We found that the Remap Index for the 225 degree saccade category was significantly *greater* than for the other three categories ($p < 0.05$, Tukey's HSD). These saccades are well-offset from the RF and often have a slight ipsiversive component (see Figure 24). There were no differences between any of the other groups. These results suggest that the strength of remapping can be modulated by the direction of the saccade in relation to the location of the RF.

The second question was whether the frequency of remapping varies across the different saccade categories. That is, how do the percentages of neurons with positive Remap Indices (i.e., those with any detectable remapping) compare across the saccade categories of each cell class? These data are shown in Panels C and D of Figure 28. There were no differences in the frequency of remapping for any categories (Chi-Square test, $p > 0.05$ for Cardinal and Oblique cells). Qualitatively, the results of this analysis are similar to those achieved in assessment of the frequency of statistically significant remapping (see Figure 25). We conclude that the proportion of neurons that carry a detectable remapping signal does not vary across saccade categories.

Finally, for those neurons that remap stimulus traces for each saccade category, does the magnitude of the remapping signal vary? For this analysis, we compare only the positive Remap Indices for each saccade category (Figure 29). The number of positive Remap Indices varies between the categories, so the sample sizes are not identical. We used a one-way ANOVA to compare the average positive Remap Index for each saccade category within each group of neurons. There were no significant differences between the saccade categories of either group of neurons ($p > 0.05$). This demonstrates that for

neurons where remapping is detectable, the strength of this signal does not vary as a function of saccade category.

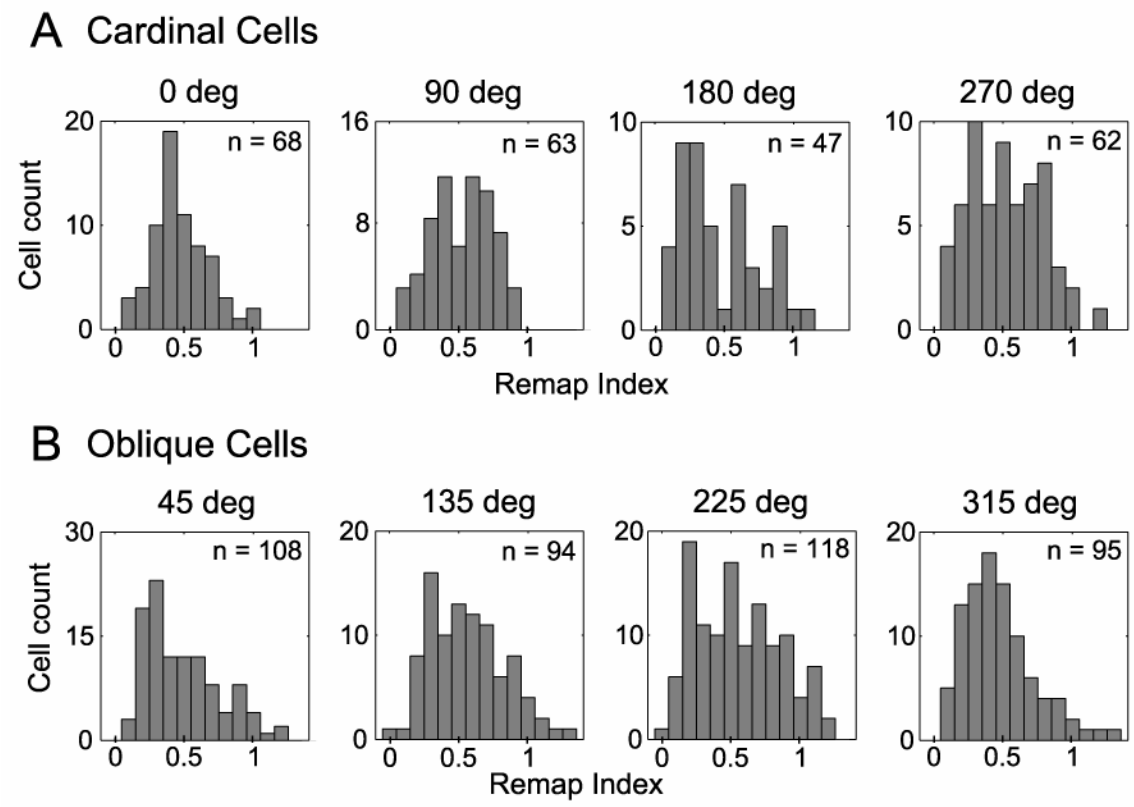

Figure 29. Comparison of positive Remap Indices for the different saccade categories.

Neurons with positive Remap Indices are those where remapping was detectable. The number of positive samples varies across the groups. There were no differences between saccade categories of within either group of cells. Additionally, there were no differences across the 8 categories. For neurons that remap, the strength of this signal does not vary across normalized saccade direction.

We wanted to compare the magnitude of remapping across all 8 saccade groups, so we re-plotted the positive Remap Index for each saccade category. The categories are displayed according to how far the saccade was from the RF (Figure 30). The 0 degree bar, on the left, is data for conditions in which the saccade was directly into the RF. Bars to the right are for saccades more distant from the RF. The 180 degree bar represents data from conditions in which the saccade was directly opposite the RF. Bars beyond it

represent saccades that were progressively closer to the RF. Although there are no significant differences between any of the groups (ANOVA, $p > 0.05$), there are some noteworthy trends. The magnitude of the remapping signal increases as the angular distance from the RF increases. This signal drops off suddenly for saccades directly opposite the RF (180 degree category). The remapping signal then increases for the 225 degree category and gradually decreases again as the saccade moves closer to the location of the RF. For neurons where remapping is detectable, there is evidence that the magnitude of this signal varies as a function of the saccade direction relative to the RF location. There are two reasons for this. First, as the direction of the saccade becomes more offset from the RF, the stimulus and saccade alone are less likely to drive the neuron. This allows the remapping signal to be more detectable (Figure 9). Second, for the 180 deg category, activity related to remapping the fixation point obscures the remapping signal of interest.

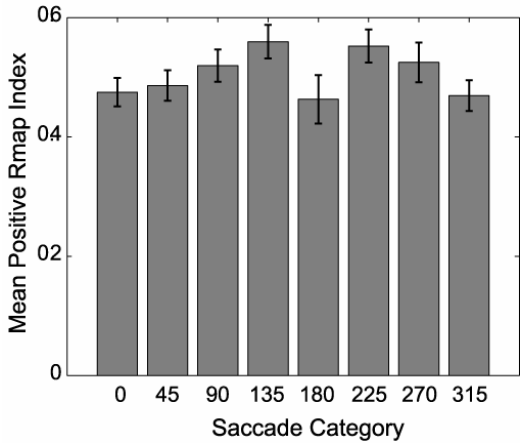

Figure 30. Comparison of the strength of remapping across all 8 saccade categories.

Bars represent the average positive Remap Index for a particular saccade category. This is the signal carried by the population of remapping neurons for each direction. Error bars represent the standard error of the mean. There are no significant differences between any of the groups, but there is a tendency for the strength of remapping to increase for saccades farther from the RF. As angular distance from the RF increases, the stimulus and saccade alone are less likely to drive the neuron. Remapping is therefore more detectable. The Remap Index drops off sharply for saccades directly opposite the RF.

Timecourse analysis of normalized saccade direction

Normalizing saccade direction revealed interesting variabilities in the magnitude of remapping. Will it reveal any variability in the timecourse of remapping? We addressed this question at both the single cell and population levels. As described in previous sections, our method for analyzing the onset of remapping requires that we use only the subset of data where there is no response in the stimulus control task. This requirement reduces the number of samples available for analysis. To ensure that we had a large enough dataset from which to draw inferences, we collapsed across the complementary saccade categories. That is, we combined data from complementary saccade categories (i.e., 45 and 315; 90 and 270; and 135 and 225). This approach yielded 5 groups of samples with angular offsets from the RF of 0, 45, 90, 135 and 180. We were able to do this because in the analyses of magnitude, we found few differences between the complementary saccade categories.

Does the onset time of remapping vary across the 5 groups? We first addressed this question by computing the Divergence Time for individual neurons (Figure 31). This is the time at which activity in the single step task first exceeds activity in the saccade control task. We found no differences in the onset of remapping for the different saccade categories (Kruskall-Wallis one-way ANOVA, d.f. = 4, $\chi^2 = 2.28$, $p > 0.68$). This indicates that the time at which information about an updated stimulus trace first becomes available is independent of where the saccade is directed relative to the RF location.

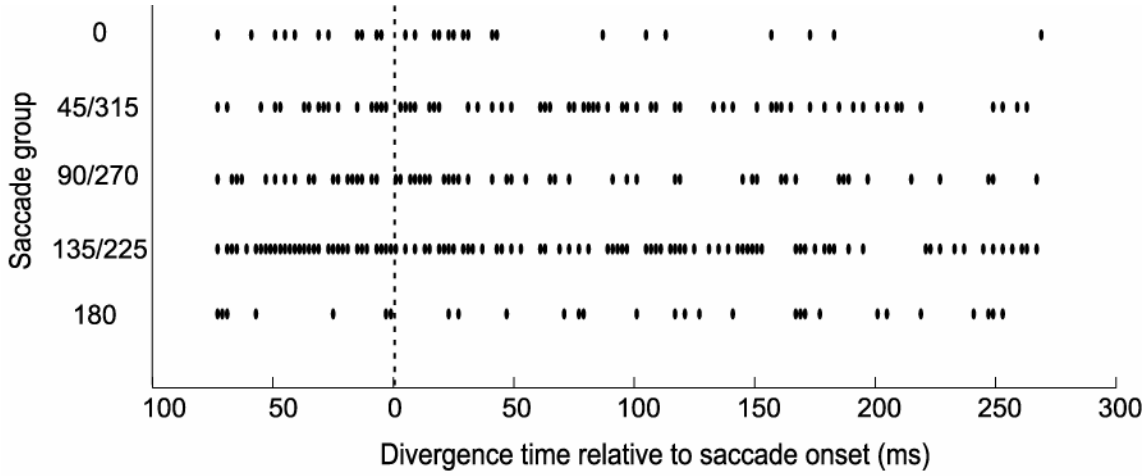

Figure 31. Comparison of the onset of updating activity for the different saccade groups.

Divergence time represents the time when activity in the single step task first became significantly greater than saccade control activity. This is the time at which information about the remapped stimulus trace is first available. Only neurons with no significant visual response in the stimulus control task are included in this analysis. Data from complementary saccade categories were collapsed, yielding 5 groups instead of 8. Each row represents data from one of these groups. Each dot represents the divergence time of a single neuron. Neurons exhibit a broad range of times, indicating that the onset of remapping can be quite variable. There were no significant differences between the divergence times of any groups.

We were interested in whether the timecourse of the population response varied across the groups. In order to isolate the remapping response, we constructed population histograms using only those samples where there was no significant activity in the visual or saccade epoch of either control task (see Appendix). For analysis of the saccade control task, this was the 200ms epoch beginning 100ms before the onset of the saccade. In contrast, the remapping epoch is the 300ms epoch beginning at the onset of the saccade (Figure 32). Activity in the single step task (solid line) is greater than that generated by the saccade alone (dotted line) for each combined saccade category. Single step activity begins to exceed activity in the saccade control task before the onset of the eye movement for all combined saccade categories. We wanted to know if there is any variability in the time at which the onset of remapping occurs, so we determined the Divergence Time for the set of population histograms. These time-points are marked by

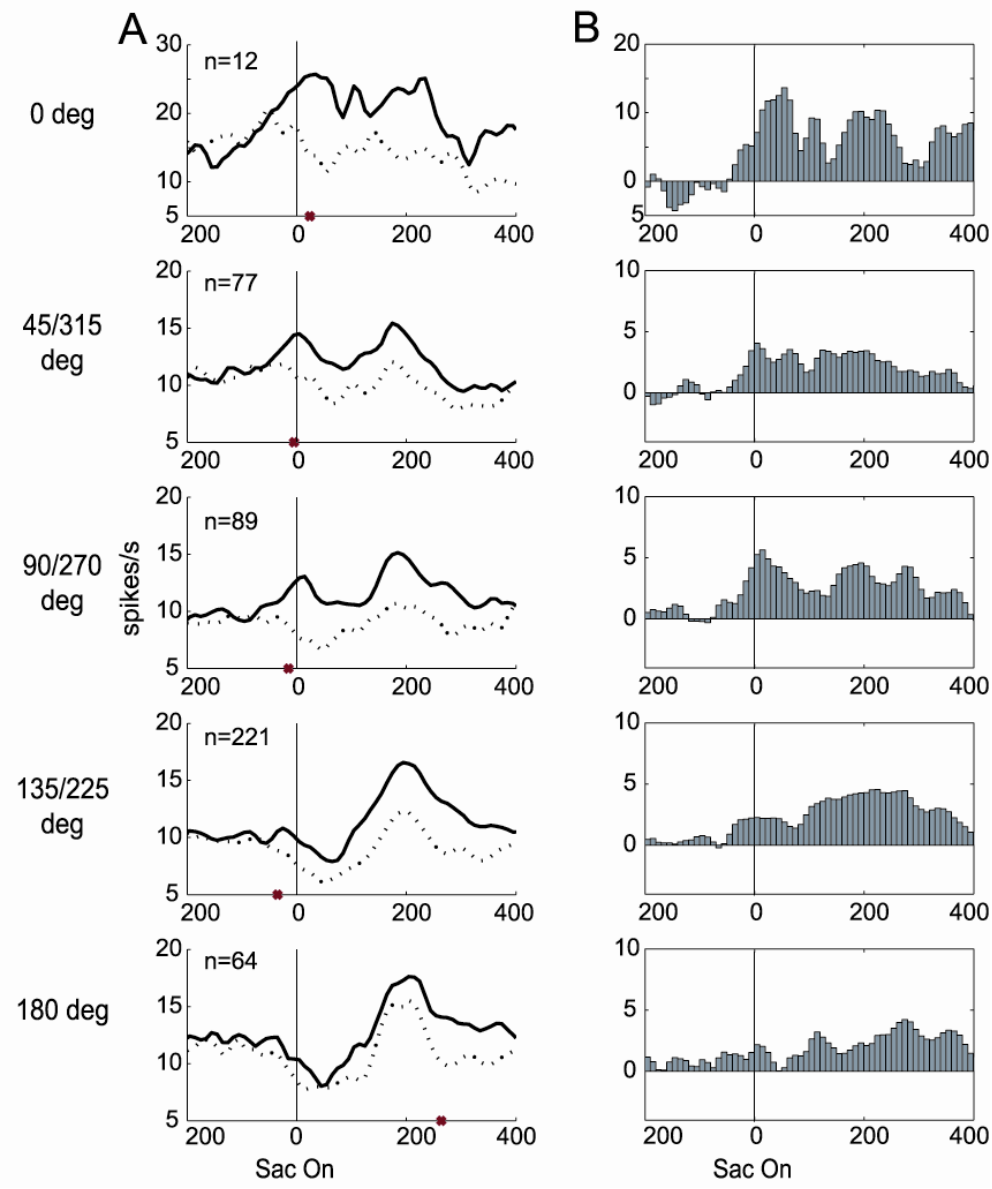

Figure 32. Comparison of the timecourse of remapping for the different saccade categories.

Data from complementary saccade categories were combined to yield 5 groups instead of 8. A. Population Histograms. Data are aligned on the onset of the saccade. Solid line represents activity in the single step task; dotted line represents activity during the saccade control task. Only neurons with no significant activity in the visual epoch of the stimulus control task, or motor epoch of the saccade control task are included (see Methods). Red marker along the x-axis represents the time when activity in the single step task was first significantly greater than saccade control activity. For most conditions, this occurs before the onset of the saccade. Activity in the saccade control activity during the post-saccadic epoch varies across the groups. Saccade control activity present during this epoch is attributed to remapping the fixation point, a phenomenon most likely to occur for the 180 deg group. Activity that cannot be accounted for by the generation of the saccade is attributed to remapping the stimulus trace. B. Difference Histograms. These are constructed by subtracting the saccade control PSTH from the single step PSTH. For all groups except 180, activity related to updating is clearly present even before the onset of the saccade.

the red ‘x’ along the x-axis of each figure. For most groups, the Divergence Time is tightly coupled to the onset of the eye movement. The exception to this is for the 180 degree group. Because there is so much activity present in the post-saccadic remapping epoch of the saccade control task, Divergence Time does not occur until well after the saccade is completed (264 ms).

The amount of activity in the saccade control task varies across the groups: for angles more distant from the RF, saccade alone activity is higher during the post-saccadic epoch. This activity is attributable to remapping the FP, a phenomenon more likely to occur for saccades directed opposite the RF than for any other saccade group. In these population histograms, remapping activity is defined as single step activity that cannot be accounted for by the generation of the eye movement. We re-plot the population histograms as difference histograms to highlight the similarities in remapping across the groups (column B). The difference histograms make it clear that for most groups, remapping begins around the time of saccade initiation and persists until well after it is completed. Based on these analyses of the timecourse of remapping for the different groups, we conclude that there is little variability in the time at which information about the updated stimulus trace becomes available. The exception to this is that for saccades directly opposite the RF, this information may not become available until well after the onset of the saccade.

2.5.3. Results, Part 3: Remapping within vs. across hemifields

In the previous sections, we established that stimulus traces can be updated in conjunction with saccades of all directions. Our paradigm also allowed us to determine

the influence of other important variables. Specifically, the experimental design also included variations in whether the stimulus was updated within a single hemifield or from one hemifield to the other. In within-hemifield updating, the representation of the stimulus remains within the same hemifield both before and after the saccade (Figure 33A). In contrast, for across-hemifield updating, the representation of the stimulus is moved from one hemifield to the other (panel B). We reasoned that these two conditions must require different circuitry. Specifically, across-hemifield remapping must involve a transfer of information from one hemisphere to the other. When the stimulus remains in the same hemifield, however, the information transfer can occur between neurons in a single hemisphere.

Does this *mode of transfer* affect remapping signals? We addressed this question by directly comparing within- and across-hemifield conditions. For this analysis, we compared just two of the four test conditions of our paradigm for each neuron, one for across and one for within. For across-hemifield remapping, we always used the ipsiversive condition: a horizontal saccade moved the representation of the stimulus from one hemifield to the other. For within-hemifield remapping, we used one of the vertical saccade conditions. With a vertical saccade, the representation of the stimulus always remains in the same hemifield. When the RF was located in the upper visual field, we used the downward saccade as the representative within-hemifield condition. We used the upward saccade when the RF was located in the lower visual field. Choosing the within-hemifield condition based on the RF location yielded control conditions with minimal activity, therefore providing the best chance of detecting differences related to

remapping. From our original dataset, we selected 159 neurons to include in this analysis; more detailed selection criteria are described in the Appendix.

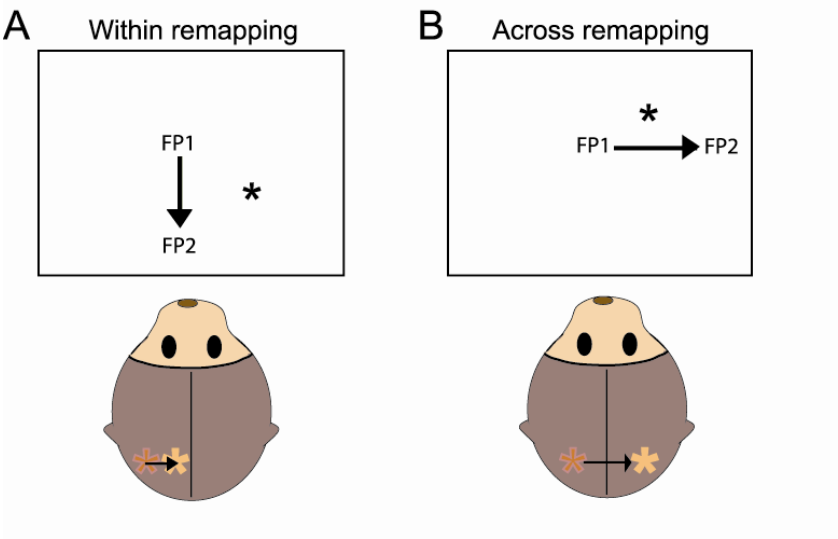

Figure 33. Schematic representation of within and across hemifield updating.

A. Within-hemifield updating. The stimulus is located in the right visual field when the eyes are at FP1. Its retinal location is represented by neurons in the left hemisphere (orange asterisk). When the eyes reach FP2, the location where the stimulus appeared is still in the right visual field, and therefore represented by neurons still within the left hemisphere (yellow asterisk). Updating in this condition involves a transfer of visual signals between sets of neurons located within the same cortical hemisphere. B. Across-hemifield updating. The stimulus is located in the right visual field when the eyes are at FP1, and therefore represented by neurons in the left hemisphere (orange asterisk). When the eyes reach FP2, however, the location where the stimulus appeared is now in the left visual field. This retinal location is represented by neurons in the right hemisphere (yellow asterisk). Consequently, updating in this condition represents a transfer of visual information between sets of neurons in opposite cortical hemispheres.

Comparison of remapping magnitude for within and across updating

The first question was whether neurons that remap stimulus traces within and across hemifields occur with equal frequency. In Figure 34, we compare the frequency of neurons that showed significant remapping for within-hemifield only, for across-hemifield only, and for both types of remapping. We found that most neurons with significant updating activity remapped stimulus traces in both the within and across hemifield conditions (53%). A nearly equal proportion showed significant remapping for within only and for across only (within = 22%, across = 24%). We conclude that although the circuitry underlying these two conditions may differ, neurons with the capability of remapping within and across occur in equal frequency.

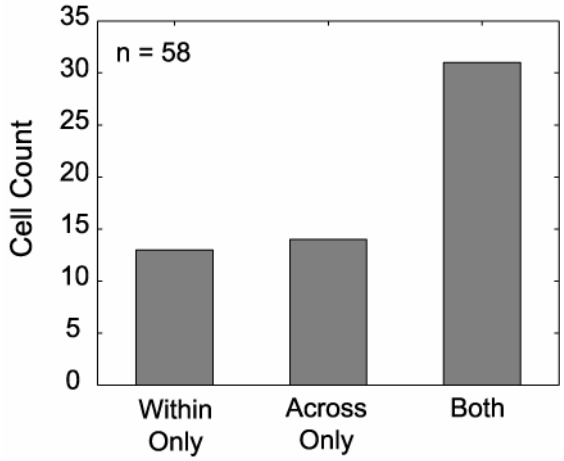

Figure 34. Comparison of number of neurons that remap stimulus traces within and across hemifields.

Bars represent the number of neurons that show significant remapping for within-hemifield updating, across-hemifield updating, or both types of updating. Nearly equal numbers of neurons showed significant remapping during only one of these conditions. Most showed significant remapping for both conditions.

Individual neurons update stimulus traces both within and across hemifields, but does the population show significant remapping for both conditions? We addressed this issue by comparing, for each condition, single step activity to that of the corresponding controls (Figure 35). In panels A and B, we compare single step activity to that generated by the stimulus alone. In panels C and D, we compare activity in the single step and saccade control tasks. For both conditions, we found that single step activity is significantly greater than activity in either control task (t-test, $p < 0.001$, all comparisons). Based on these results, we conclude that at the population level, stimulus traces are robustly updated both within and across hemifields.

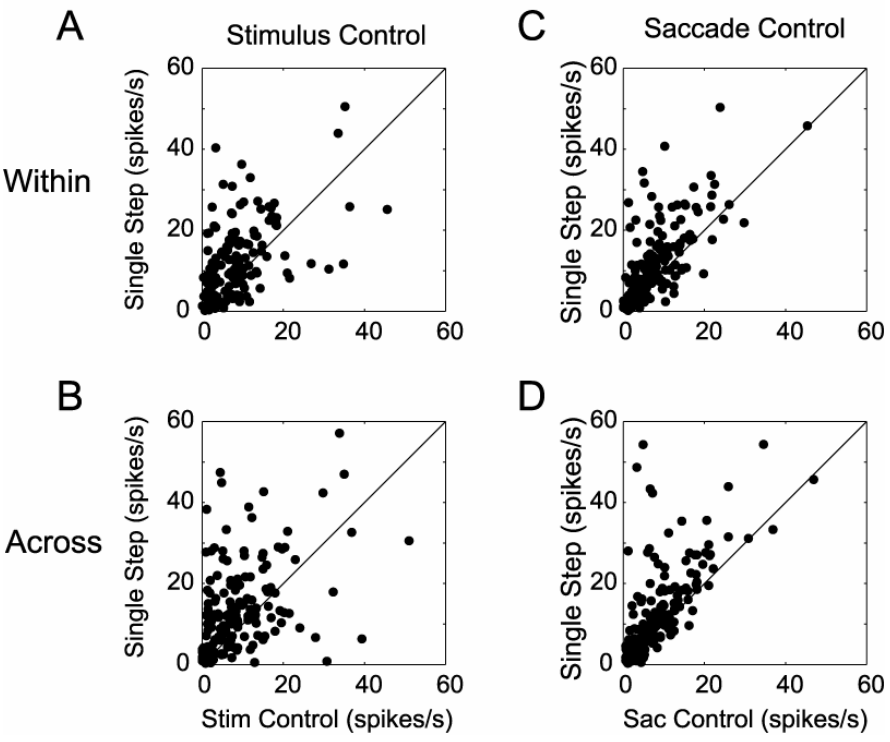

Figure 35. Comparison of single step and control activity for within- and across-hemifield updating.

A and B. Comparison of single step and stimulus control activity. For both within (A) and across (B) hemifield updating, single step activity is significantly greater than stimulus control activity (t-test, $p < .001$, both comparisons). C and D. Comparison of single step and saccade control activity for within (C) and across (D) hemifield updating. For both types of remapping, activity in the single step task is greater than that generated by the saccade alone ($p < 0.001$, both comparisons). Activity in the single step tasks is greater than that of both corresponding control indicating that the population shows significant updating activity for within- and across-hemifield conditions. $n = 159$.

We were interested in whether the strength or frequency of remapping is affected by the mode of transfer. We addressed this by analyzing the Remap Indices (Figure 36). The upper panels show the distributions of all remap indices for within and across hemifield remapping. As discussed previously, the Remap Index is positive for samples in which activity in the single step task is greater than that of both control tasks. If these criteria are not met, the Remap Index is set to 0. We found that there is no difference in the magnitude of the Remap Index for these two conditions (within = 0.31 +/- 0.027 s.e.m.; across = 0.34 +/- 0.029 s.e.m.; Wilcoxon matched test, $p > 0.80$). Additionally, remapping occurs with equal frequency for within and across conditions (Panel E). For neurons with detectable remapping, what is the magnitude of the signal they carry? We addressed this question by comparing just those samples with positive Remap Indices (Panels C and D). We found that the distributions of positive Remap Index for these two conditions are not different (within = 0.55 +/- 0.029 s.e.m.; across = 0.55 +/- 0.032 s.e.m.; K-S test, $p > 0.70$). These results demonstrate that neurons in LIP remap stimulus traces within and across hemifields with equal frequency and strength.

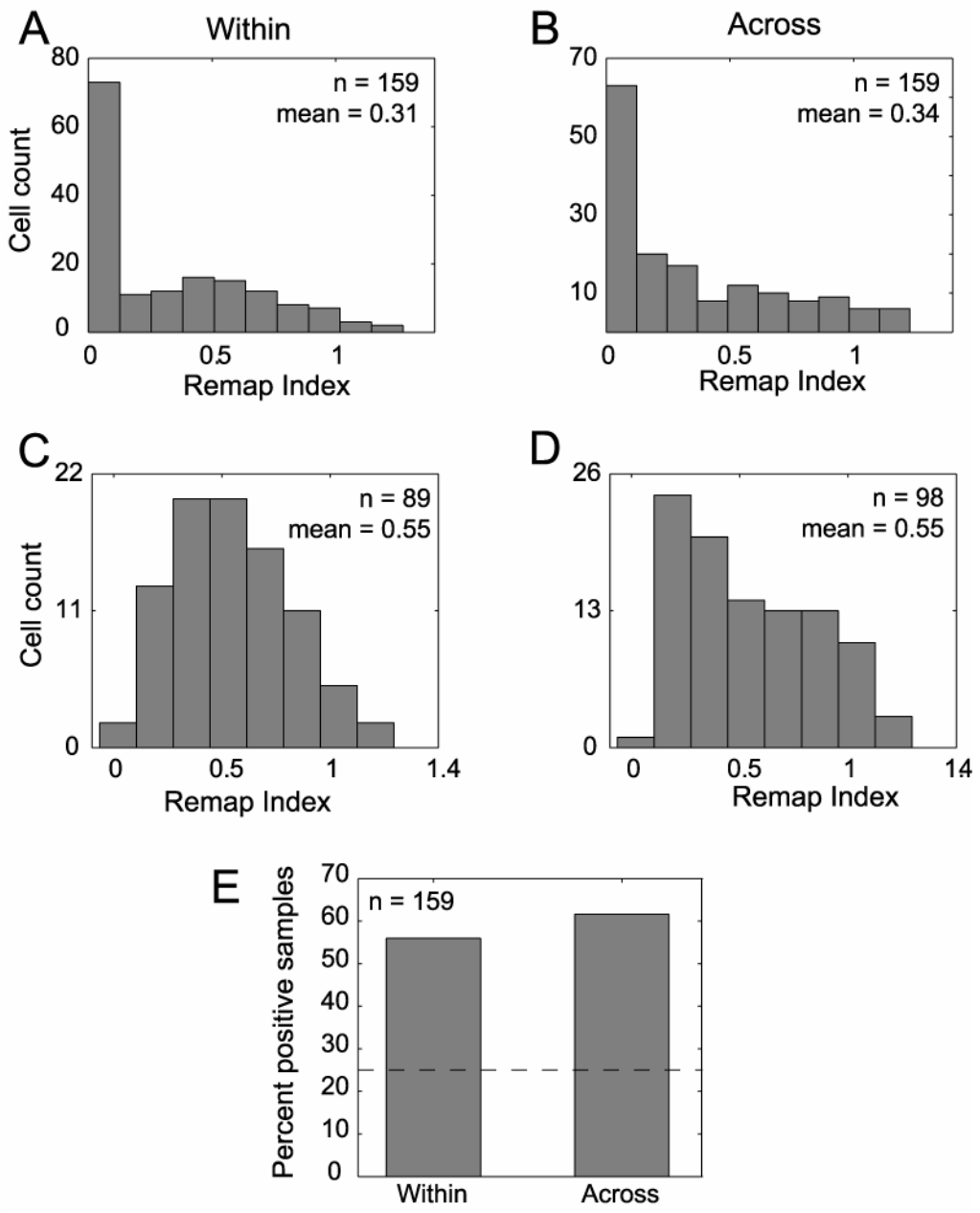

Figure 36. The magnitude and frequency of remapping does not vary between within and across conditions.

A and B. Distribution of all Remap Indices (RI) for within (A) and across (B) hemifield remapping. There is no difference between the two conditions. C and D. Comprison of positive RIs for within (C) and across (D) conditions. Samples with positive RIs are those that show remapping. For these neurons, there is no difference in the magnitude of remapping for the two conditions. E. Percentage of samples with positive RIs. For both conditions, a significant proportion of samples show remapping (chance = 25%), and the frequency does not differ between the two conditions.

Comparison of timecourse for within and across updating

Is the time at which remapping occurs affected by whether the stimulus must be updated within or across hemifields? We used the Divergence Time measure to assess the onset time of remapping in individual neurons (Figure 37). As described in previous sections, Divergence Time represents the time at which activity in the single step task first exceeds activity in the saccade control task. We found no differences between the two conditions (signrank, $p > 0.40$). This indicates that regardless of whether individual neurons must access information from within the same hemifield, or from the opposite hemifield, this information is available at the same time.

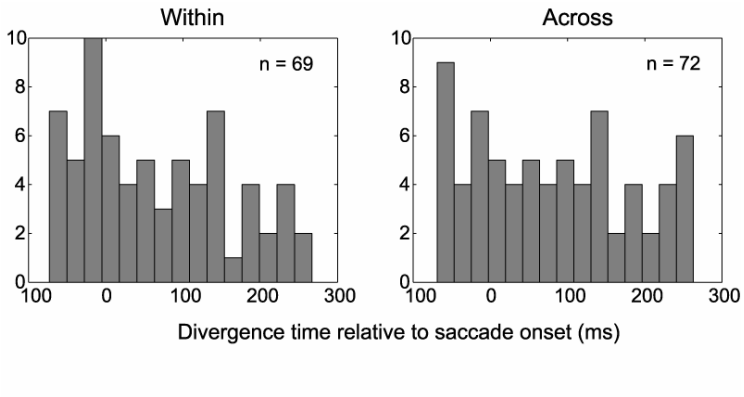

Figure 37. Comparison of the onset of remapping activity for within and across hemifield updating conditions.

Divergence time represents the time at which activity in the single step task first exceeds that of the saccade control task. Only neurons with no significant response in the stimulus control task are included. There is no difference in divergence time for within and across hemifields conditions (signrank $p > 0.40$).

We constructed population histograms using only those neurons with no activity in any control task (see Appendix for details). In other words, if a neuron is included in this analysis, it contributed to both the within and across population histograms (Figure 38). The population activity reflects the two basic findings described above. Namely, the magnitude and latency of remapping do not vary between within and across hemifield conditions. For both within and across updating, activity in the single step task (solid line) begins to rise above activity in the saccade control task (dotted line) even before the onset of the saccade. Updating activity persists for many hundreds of milliseconds after the completion of the saccade.

Activity in the saccade control affects the temporal dynamics of the single step task. We can isolate the signal related to updating by subtracting saccade control activity from single step activity (panels C, D). These difference histograms can be used to summarize the observations described above: 1) neurons in LIP carry robust signals related to updating stimulus traces both within and across hemifields; 2) remapping activity begins before the onset of the saccade for both conditions; 3) updating signals persist until well after the saccade is completed. Based on the findings described here, we conclude that signals related to updating stimulus traces within and across hemifields are effectively identical.

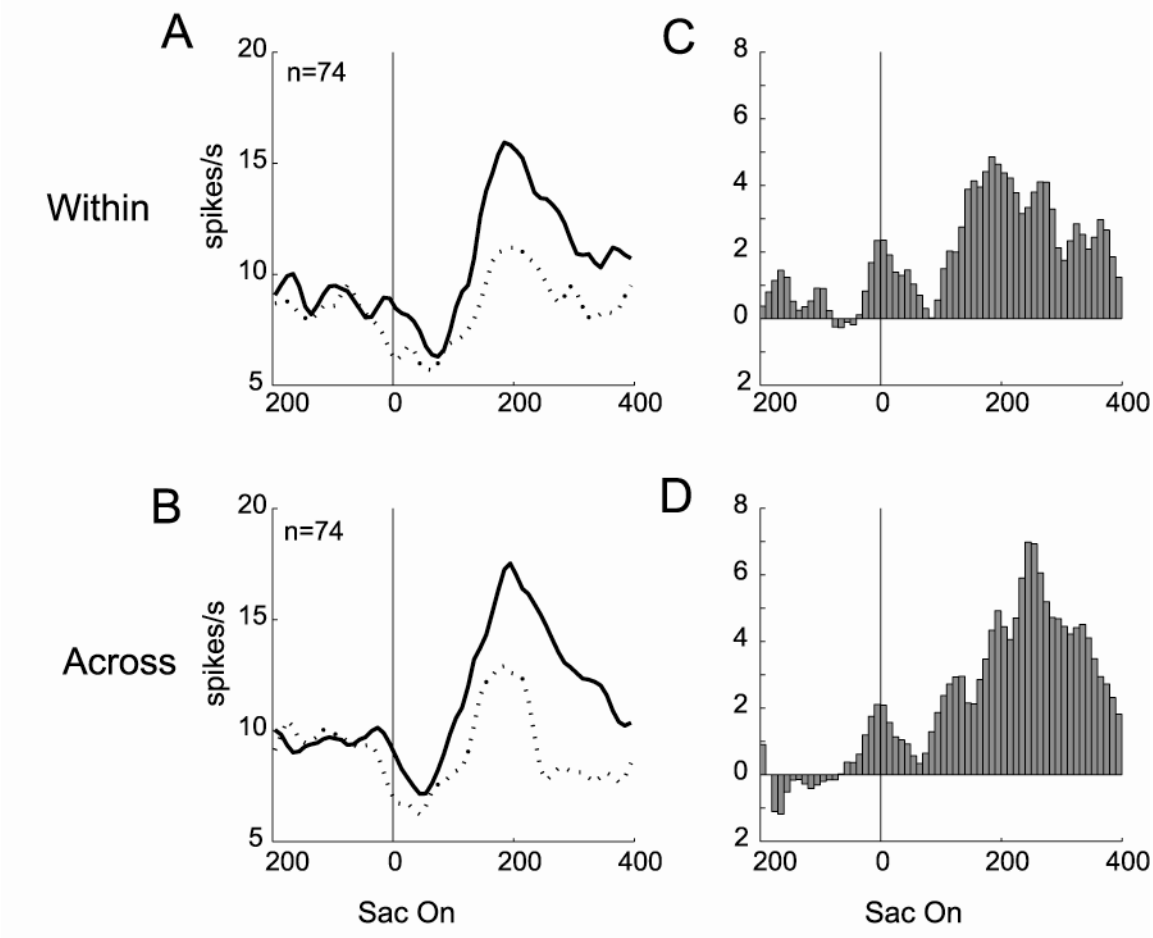

Figure 38. Comparison of the timecourse of remapping for within and across hemifield remapping.

(A,B) Population Histograms. Data from single step (solid lines) and saccade control tasks (dotted lines) are aligned on the onset of the saccade. Only neurons where there was no significant activity in the stimulus or saccade epoch of the control tasks are included. For both within and across conditions, activity in the single step task begins to rise above saccade control activity before the onset of the saccade. This activity persists until well after the saccade has been completed. Single step activity that cannot be accounted for by the eye movement alone is attributed to updating the location of the stimulus. (C,D) Difference Histograms. Data from A and B are re-plotted to emphasize the similarities between the two conditions. Difference histograms are constructed by subtracting saccade control activity from single step activity. The timecourses for remapping stimulus traces within- and across-hemifields are quite similar.

2.6. Discussion

Overview

The goal of this experiment was to gain a greater understanding of the factors that influence spatial updating signals in lateral intraparietal cortex. Specifically, we were interested in whether updating would be affected by changes in the direction over which a stimulus must be updated. We found that individual neurons can update spatial locations in conjunction with saccades of multiple directions, although the strength of this signal often varies with direction. There were indications that the strength of remapping is related to the amount of activity attributable to the stimulus or saccade alone. At the population level, remapping was effectively independent of saccade direction. Here we discuss the implications of our findings.

LIP subserves spatially accurate behavior for all saccade directions

Our experience informs us that there are no perceptual differences associated with making eye movements toward objects located in different regions of the visual field. Behavioral experiments indicate that this is indeed the case: spatial locations are updated in conjunction with all saccade directions (Hallett and Lightstone, 1976; Baizer and Bender, 1989). This is measured behaviorally with the double step task. In this task, two sequentially flashed targets must be acquired by two consecutive saccades. The critical factor in this task is that the targets are presented so briefly that they are extinguished before the eye movements begin. The first saccade can be easily coded using retinal

coordinates. The second saccade, however, can only be performed correctly if the target displacement brought about by the first saccade is taken into account. Experiments in both monkeys and humans indicate that the double step task is accurately performed for saccades of varying directions, including horizontal, vertical and oblique.

What are the neural underpinnings of this ability? Remapping the memory trace of the second target accomplishes the necessary transformation: the memory trace can be shifted from the coordinates of the initial eye position to the coordinates of the new eye position. If remapping subserves spatially accurate behavior, lesions to areas responsible for generating this signal should impair the ability to perform the double step task. This prediction was verified in studies of patients with unilateral parietal lobe lesions (Duhamel et al., 1992b; Heide et al., 1995). These patients performed both saccades accurately when the first was directed into the spared (ipsilesional) hemifield. The second saccade was inaccurate only when the first was directed into the contralesional hemifield. These subjects could perform accurate visually guided saccades into the contralesional hemifield, indicating that they could both see the target and generate contraversive saccades. They failed on the double step task because they could not calculate the change in target location brought about by the first eye movement. In contrast, patients with damage limited to the frontal cortex show only minor spatial errors. More recently, the finding that parietal cortex is critical for spatial updating was observed in monkeys: performance of the double step task is impaired following temporary lesions to LIP (Li and Andersen, 2001). In sum, these findings indicate that parietal cortex is important for updating.

The remapped representation generated in LIP could be used to guide accurate eye movements. LIP is strongly interconnected with both the superior colliculus (Lynch et al., 1985; Clower et al., 2001) and frontal eye fields (Cavada and Goldman-Rakic, 1989a; Schall et al., 1995; Stanton et al., 1995), and both of these areas are intimately involved in saccade generation (Wurtz and Albano, 1980; Schall, 1997). Through these connections, the updating activity in LIP could be used to generate accurate eye movements toward targets of interest. Our finding that stimulus traces are robustly updated with all saccade directions indicates that the population activity of LIP could guide spatially accurate behavior in conjunction with all saccade directions. The first step in characterizing this relationship would be to simultaneously monitor neural activity and behavioral performance on multiple directions of the double step task. With this paradigm, we could determine if behavior and activity are correlated. Further experiments of this kind are necessary for gaining an understanding of the specific contributions of parietal cortex to spatial behavior.

LIP neurons can access information from throughout the visual field

We found that across the population of neurons, stimulus traces can be updated in conjunction with saccades of all directions relative to the receptive field (RF) location. We demonstrated this by normalizing the direction of the saccade relative to the location of the RF. The classically defined RFs in LIP are restricted in extent: they average ~12 deg across and are primarily confined to the contralateral hemifield (Barash et al., 1991a; Ben Hamed et al., 2001). When an eye movement is executed, these neurons must receive information that allows them to respond to visual stimuli presented virtually anywhere in the visual field. This responsiveness, however, is limited, in that it is

contingent upon the saccade moving the receptive field onto the location of the previously flashed stimulus. If the metrics of the saccade are such that the RF is not moved onto the stimulus location, the neuron does not respond (Kusunoki and Goldberg, 2003). We found that the visual responsiveness of neurons can be shifted in any direction relative to the RF location. This implies that any given LIP neuron must be interconnected with other neurons with RFs distributed throughout the visual field.

While on the whole, neurons could remap stimulus traces for all normalized saccade directions, there were indications that the magnitude of this signal varies. For example, it was often difficult to detect remapping in conjunction with a saccade directly opposite the RF (the 180 deg category). In this configuration, the saccade moved the receptive field onto the location of the initial fixation point (FP1), a salient visual stimulus that had been extinguished just before the saccade. During the saccade alone task, many neurons remapped the location of the fixation point, and consequently exhibited a robust response. Thus, for this configuration, we often could not detect a single step response that was significantly greater than the saccade alone task. As we discuss next, early experiments on spatial updating shed light on this observation.

One of the first remapping studies used spatial configurations similar to our 180 deg category (Goldberg and Bruce, 1990). In this experiment, Bruce and Goldberg measured activity during the double step task, rather than the single step task. The interpretation of the response in the single and double step tasks is identical: activity reflects a response to the updated memory trace of the second saccade target. The configuration of interest is the 'back-and-forth' version of the double step task that used just two stimuli, FP1 and FP2. The monkey's task was to make a saccade to FP2 and

then back to FP1. The location of FP2 was chosen so that the saccade would move the RF onto the location of FP1. That is, FP2 was directly opposite the RF, as it is in our 180 deg configuration. Neurons in FEF responded robustly just after the onset of the first eye movement that moves the RF onto the location of the previously extinguished FP1. In other words, neurons updated the location of FP1 in conjunction with the first saccade. This lends credence to our conclusion that the activity we observed in the saccade alone task for the 180 degree condition can be attributed to remapping the location of FP1. In sum, we found that activity related to remapping the fixation point likely contributes to the differences in the strength of remapping for different directions.

Temporal dynamics of saccade-related activity affect remapping signals

The analysis of normalized saccade direction also revealed some interesting temporal dynamics related to the generation of the saccade itself. In the population histograms (see Figure 32), we observed a suppression in the saccade-alone activity that began just before the onset of the eye movement and lasted for ~100ms. This suppression increased as the direction of the saccade moved away from the RF, and was maximal for a saccade directly opposite the RF. Such inhibitory activity has been documented in many saccade-related areas, including LIP (Barash et al., 1991a) and SC (Munoz and Istvan, 1998), as well as in primary motor cortex (Georgopoulos et al., 1982). Excitatory activity for movements in one direction combined with inhibitory activity for movements in the opposite direction are thought to act as a push-pull mechanism that facilitates movement generation (Munoz and Fecteau, 2002). Thus, while the post-saccadic dip in activity is not directly related to remapping, the dynamics of this

saccade-related activity influence the overall shape of the response during the single step task.

Validation of a remapping model

A mechanism by which neurons in LIP could remap stimulus traces has been put forth by Goldberg and colleagues (Colby, 1998; Quaia et al., 1998). Here we describe the essential elements of the model and discuss the consistencies and inconsistencies between the predictions of the model and our results. The logic behind the model is simple. During the single step task, the to-be-updated stimulus activates a set of neurons that encode its location when the monkey's eyes are at the initial fixation point. At the time of the eye movement, this activity is shifted from the first group of neurons to a new set of neurons whose receptive fields will encompass the stimulated location once the eyes are at the new fixation point.

A simplified version of the model is schematized in Figure 39. The basic claim of the model is that neurons should remap every time a saccade moves the receptive field onto a previously stimulated location in the visual field. The critical feature of the model is that it works as a coincidence detector: remapping happens if and only if a neuron receives both corollary discharge (CD) and visual (VIS) signals. The origin of the CD signal is unknown, and could originate from one, or several, oculomotor structures. In the Goldberg model, the CD signal is hypothesized to be transferred to LIP from FEF. The VIS signal is transferred between neurons within LIP.

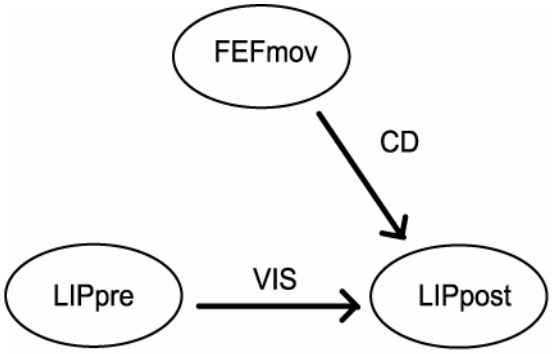

Figure 39. Simplified description of the Quaia remapping model.

Visual neurons in LIP encode the location of the stimulus before the saccade (LIPpre). The LIPpre neurons are functionally connected to other neurons in LIP that will encode the location of the stimlus after the saccade (LIPpost). Visual information (VIS) is transferred between these two groups of neurons. FEF movement cells (FEFmov) send a corollary discharge signal (CD) about the impending eye movement to LIPpost neurons. This circuit acts as a coincidence detector: remapping occurs if and only if the LIPpost neurons receive both a CD and VIS input (Modified from Quaia, et al, 1998).

Our data can speak to two predictions of the model. The first prediction is that individual neurons in LIP should remap stimulus traces regardless of saccade direction. Consistent with this prediction, we observed that individual neurons can remap stimulus traces in conjunction with saccades of multiple directions. We also found, however, that many neurons showed significant remapping for only a subset of the test directions. Based on this observation, we conclude that there must be additional factors, not accounted for by the model, that contribute to remapping.

The second prediction of the model is that remapping should occur for stimuli located anywhere in the visual field. In the single step task, the location of the stimulus is determined by the location of the RF, thus our analysis of neurons with RFs at different eccentricities can speak to the issue of stimulus location. We found that neurons at all eccentricities show robust remapping. This indicates that there is no preference for neurons at a particular location in the visual field to prefer to remap in conjunction with a

20 degree saccade. Instead, neurons with RFs located throughout the visual field have equal access to information brought into the RF with a 20 degree eye movement. In sum, our findings are generally consistent with the model, though some of our observations cannot be accounted for by the model. In the next section, we will discuss two factors that may be important to consider in future models of spatial updating.

In individual neurons, remapping varies with saccade direction

Our expectation was that remapping would be equally robust for all saccade directions in all neurons. Instead, we found that in *individual neurons*, the strength of remapping often varied with changes in saccade direction. In particular, we found that many neurons showed significant remapping for only a subset of the test directions. Additionally, the magnitude of the signal associated with the test directions was quite variable. Here we discuss two possible sources of this variability.

The first source of variability is related to detectability. In our paradigm, the amount of activity generated in the control conditions varied considerably. Thus, for some saccade directions, remapping was difficult to detect because this signal co-occurred with robust stimulus or saccade-related activity (see Figure 9). This issue is reminiscent of that encountered with the visually guided saccade task: the presence of a stimulus and generation of a motor response co-occur. As a result, neural activity cannot be definitively attributed to either. This problem prompted Hikosaka and Wurtz to develop the delayed saccade task in order to separate in time the neural signals attributable to sensory or motor activity (Hikosaka and Wurtz, 1983). More recently, studies of V4 neurons found that attentional modulation of visual signals can be

effectively revealed only if the stimulus itself does not drive the neuron to its maximal firing rate (Reynolds et al., 2000). Thus, the difficulty in detecting one neural signal in the presence of others has been observed in other paradigms. The problem has been solved by separating events in time or by reducing the magnitude of signals that are not of primary interest. Another way to address the issue of universality of remapping would be to record in other areas that have remapping, but also have smaller receptive fields. With smaller receptive fields, the stimulus and saccade alone would be less likely to drive the neuron in the control tasks, allowing remapping to be more easily detectable for more test directions. One region of particular interest is V3A, a visual area that has both remapping (Nakamura and Colby, 2002) and smaller RFs (Galletti and Battaglini, 1989; Nakamura and Colby, 2000).

Second, spatial updating relies on the convergence of visual and corollary discharge signals. If either of these signals varies across the test directions, the resultant remapping signal could vary as well. Visual signals in LIP can be modified by orbital position (Andersen et al., 1990c). In our paradigm, we attempted to minimize orbital modulation effects that would influence our measures of remapping. Specifically, we chose the same neutral position as the final endpoint for all saccade directions tested. This necessitates that the starting location varies. It is possible that the visual signals related to encoding the location of the stimulus vary when the eyes are at different starting points. Individual neurons in LIP are preferentially active in conjunction with different orbital positions, but across the population, all positions are equally represented (Andersen et al., 1990c). This is similar to our finding that while individual neurons

showed the strongest remapping for particular directions, across the population, all directions were represented.

2.7. Summary

The goal of this experiment was to determine whether neurons in the lateral intraparietal cortex (LIP) have access to visual information throughout the visual field. We addressed this by asking whether neurons in LIP update stimulus traces equally robustly in conjunction with saccades of different directions. Here we discuss four main conclusions that emerge from our experimental findings. First, individual neurons have access to visual information from multiple regions beyond their classically defined receptive fields. This conclusion is supported by our observation that single cells in LIP can remap stimulus traces in multiple directions. A second, parallel conclusion is that spatial updating in LIP is effectively independent of saccade direction: at the population level, stimulus traces are updated in conjunction with all saccade directions, even when we consider direction as a function of receptive field location. Third, despite these findings that remapping is virtually universal, we obtained evidence that the detectability of updating signals can vary. We observed this variability both at the level of single neurons and in the population, and found that it was attributable to the strength of activity in the stimulus and saccade control tasks. Our final conclusion is that neurons in LIP have equal access to visual information, whether it originates in the same or opposite hemifield. Specifically, we compared the updating of stimulus traces within- and across-hemifields. We found no differences in the magnitude or timing of remapping in these two conditions. Taken together, our findings support the hypothesis that the activity of

LIP neurons can contribute to the maintenance of spatial constancy throughout the visual field.

3. Chapter 3: Remapping in the split-brain monkey

3.1. Overview

In this chapter we present data from experiments designed to assess the neural circuitry supporting spatial updating. Specifically, we investigated the role of the forebrain commissures when remapping requires the interhemispheric transfer of visual information. We recorded from individual neurons in the lateral intraparietal cortex of both split-brain and intact monkeys during two conditions of the single step task. In the within-hemifield condition, the location of the stimulus must be updated within a single hemifield; in the across-hemifield condition, the stimulus must be updated from one hemifield to the other.

3.2. Introduction

In the original demonstration of remapping in the lateral intraparietal cortex (area LIP), it was observed that stimulus representations could be updated from one visual hemifield to another (Duhamel et al., 1992a). In the experiments described in Chapter 2, we confirmed and extended these observations. We found that stimulus traces are robustly updated both within and across hemifields. Furthermore, we found no difference in the strength or timecourse of these signals. This indicates that neurons in LIP have equal access to visual information from both visual hemifields. In the case of across-hemifield remapping, what is the neural circuitry supporting this access? Remapping involves a transfer of visual information from neurons representing the stimulus location before the eyes move, to those representing the stimulus location after the eyes have

moved. In the case of across-hemifield updating, the representation of the stimulus is moved from one visual hemifield to the other. We presume that this requires an interhemispheric transfer of visual information, as the representation of visual stimuli is highly lateralized (Trevarthen, 1990). We hypothesized that the corpus callosum is the primary pathway for across-hemifield remapping.

Previous studies have demonstrated that the corpus callosum is the most prominent route for interhemispheric communication in the primate brain (LaMantia and Rakic, 1990; Houzel et al., 2002). While it was initially assumed that in visual areas the primary function of these fibers is to knit together representations of the midline, it is now clear that these connections are quite elaborate and extend to regions of the visual field that are far from the midline (Van Essen et al., 1982; Maunsell and Van Essen, 1983a). Of particular interest is that the parietal cortex has extensive callosal connections linking both homotopic and heterotopic areas (Pandya and Vignolo, 1969; Seltzer and Pandya, 1983). Neuropsychological studies have demonstrated that the corpus callosum mediates interhemispheric communication in several visual domains, including color perception, association of visual form information, and visuomotor association (Holtzman, 1984; Gazzaniga, 1987; Trevarthen, 1990; Corballis, 1995). Based upon these observations, we expect that these fibers are involved in updating visual information from one hemisphere to the other.

3.3. Experimental Aim

Our experimental aim was to determine whether the forebrain commissures are necessary for updating visual information from one hemisphere to the other. We

addressed this aim by recording from LIP neurons in two split-brain monkeys while they performed two versions of the single step task. In the within-hemifield version, the stimulus trace is updated within the same visual hemifield. In contrast, it must be updated from one hemifield to the other in the across-hemifield version of the task (Figure 40). Our prediction was that in the absence of the forebrain commissures, across-hemifield remapping would be compromised as compared to remapping within a single hemifield.

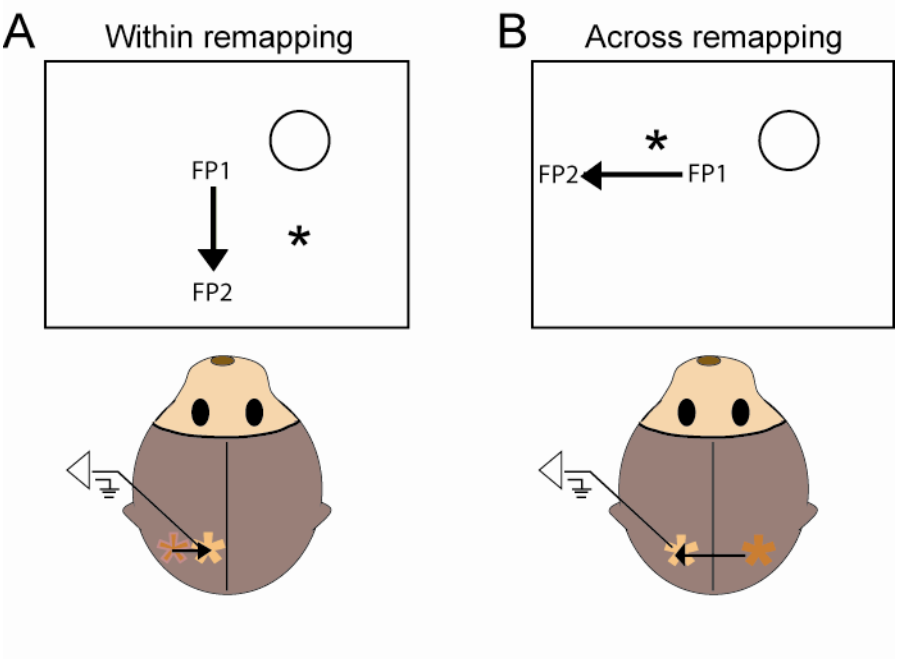

Figure 40. Spatial configurations used to compare within- and across-hemifield remapping.

The exact configuration is determined by the location of the receptive field. The hypothetical neuron under study is located in the left hemisphere (yellow asterisk); it has a receptive field (circle) in the upper right visual field. A. Within condition. The stimulus appears in the right visual field when the eyes are at FP1. Its retinal location is represented by neurons in the left hemisphere (orange asterisk). After the monkey makes a downward saccade to FP2, the location where the stimulus previously appeared is still in the right visual field, and therefore represented by neurons still within the left hemisphere, including the neuron under study. Visual signals are transferred within the same (left) hemisphere. B. Across condition. The stimulus is located in the left visual field when the eyes are at FP1, and therefore represented by neurons in the right hemisphere (orange asterisk). When the eyes reach FP2, the location where the stimulus appeared is now in the right visual field, represented by neurons in the left hemisphere. Updating in this condition involves a transfer of visual information between sets of neurons in opposite cortical hemispheres. We expected that in the absence of the forebrain commissures, across remapping would be less robust than within remapping.

3.4. Methods

Animals

Four rhesus monkeys (*Macaca mulatta*) were used in this study. Monkeys CH and EM underwent a complete transection of the corpus callosum and anterior commissure (Figure 41). A description of the commissurotomy can be found in the Appendix. Monkeys OE and FF, with commissures intact, served as controls.

Experimental design

We tested each neuron in two conditions of the single step task (Figure 42A). The exact geometry of the two conditions was tailored for each neuron, based on the location of the receptive field (see Figure 40). By definition, different spatial configurations are required for remapping stimulus traces within and across hemifields. We held saccade amplitude constant and varied the saccade direction for each condition of the task. With a vertical saccade, the representation of the stimulus remains within the same hemifield before and after the eye movement. In contrast, a horizontal ipsiversive saccade moves the representation of the stimulus from one hemifield to the other. We used these configurations for most neurons. For the remaining neurons, we used diagonal saccades for one or both conditions. Average saccade amplitude was 24.5 deg (± 5.3 s.d.). For each condition of the single step task, we recorded neural activity during the corresponding control tasks. A complete data set for each neuron consisted of 6 types of trials: 3 tasks (stimulus control, saccade control, single step) x 2 conditions (within, across).

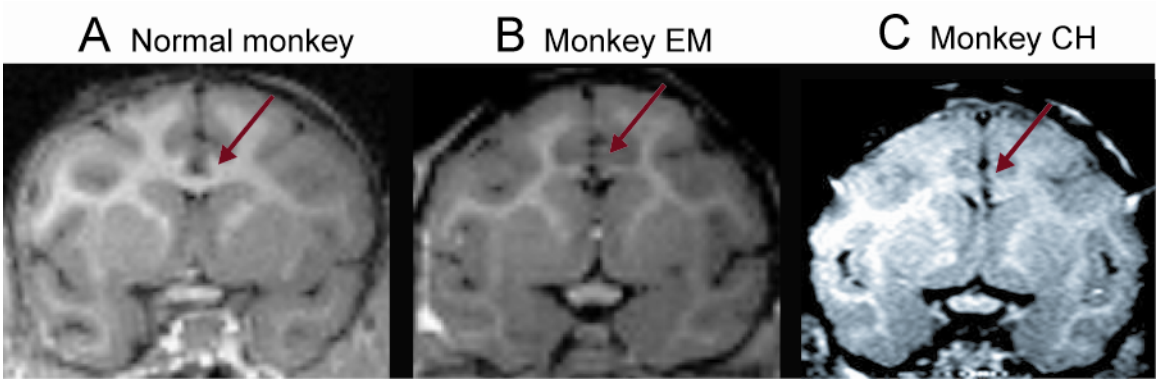

Figure 41. Coronal MR images.

Coronal MR images from a normal monkey (panel A) and from the two split-brain monkeys studied in the present experiment: monkey EM (panel B) and monkey CH (panel C). Arrows point to the location of the corpus callosum (A) or its absence (B,C).

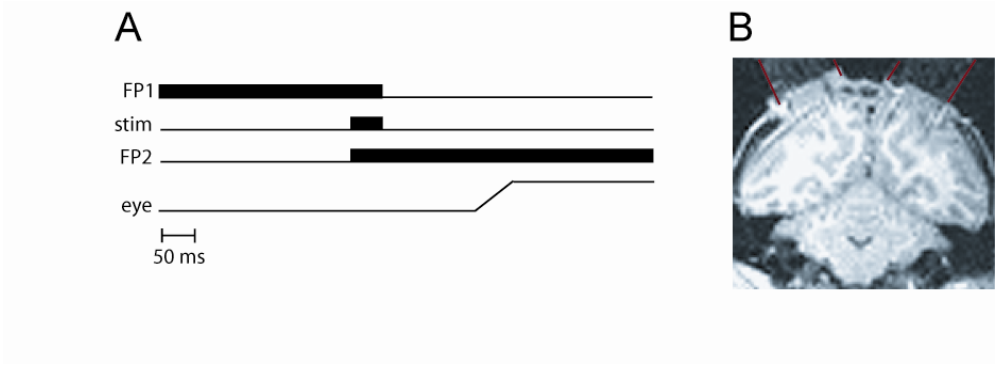

Figure 42. Behavioral paradigms and locations of recording locations for assessment of spatial updating in the split-brain monkey.

A. Timing of the single step task. The monkey holds its gaze on fixation point FP1 300-500 ms. Two events then occur simultaneously: a peripheral stimulus flashes for 50 ms and a new fixation point (FP2) is illuminated. The offset of the stimulus is concident with the offset of FP1. This was the monkey's cue to make a visually guided saccade to FP2. The monkey maintains its gaze on FP2 for an additional 500-700 ms. B. Coronal magnetic resonance image showing the locations of the recording chambers in monkey CH (red lines). Neurons were recorded from the lateral bank of the intraparietal sulcus in both hemispheres.

Selecting neurons for analysis.

The nature of our experimental question required that we test two conditions of the single step task for each neuron. Because neurons in LIP have relatively large response fields, it was often the case that the stimulus alone would drive the neuron in one or both stimulus control tasks. During recording sessions, we attempted to use spatial configurations for which the to-be-remapped stimulus was well outside of the receptive field when the monkey was at the first fixation point. To be certain that the response in the single step task could not be attributed to the presence of the stimulus alone, we analyzed the activity in the stimulus control tasks. We omitted neurons from further analysis if they had a significant visual response in either stimulus control task. We assessed this with a t-test ($p < .05$), comparing activity in a visual epoch (50-250 ms after stimulus onset) to baseline activity (200-300 ms after fix attain).

Measuring remapping activity.

We used a standard epoch to analyze activity in the single step tasks: 0-200ms relative to saccade onset. Using a standard epoch gives us an unbiased way to compare remapping activity between the two test conditions. This epoch is similar to that used in other remapping studies (Kusunoki and Goldberg, 2003), and captures the peak response observed in the population histograms. To be certain that the activity observed in the single step task could not be attributed simply to generating the saccade, we measured activity in the same 200ms epoch of the saccade control tasks. Single step activity exceeding that observed in the saccade control task was considered remapping activity.

We used a simple subtraction to quantify the updating response: Remapping = Single step activity – Saccade control activity.

3.5. Results

General Results

We recorded from 306 visually responsive LIP neurons in three hemispheres of two split-brain monkeys (Figure 42B). Of these, 223 met our criterion of no significant response in either of the stimulus control conditions, and were included for further analysis. We recorded from 74 visually responsive LIP neurons in two hemispheres of two intact monkeys. Of these, 55 met our criteria and were included in the analyses described here.

LIP neurons can remap stimulus traces across-hemifields in the split-brain monkey

Our primary finding is that individual neurons in LIP update visual signals both within and across hemifields in the split-brain monkey. An example neuron is shown in Figure 43. The response to within-hemifield updating is shown in panel C. The neuron began to fire before the onset of the saccade, and its activity persisted well after the saccade was completed. This same neuron also responded when the stimulus was updated across hemifields (panel D). Thus, even after the major pathway connecting the cerebral hemispheres has been removed, neurons in LIP still have access to information about visual signals from the opposite hemifield. The control tasks demonstrate that this response cannot be attributed to visual or motor responses.

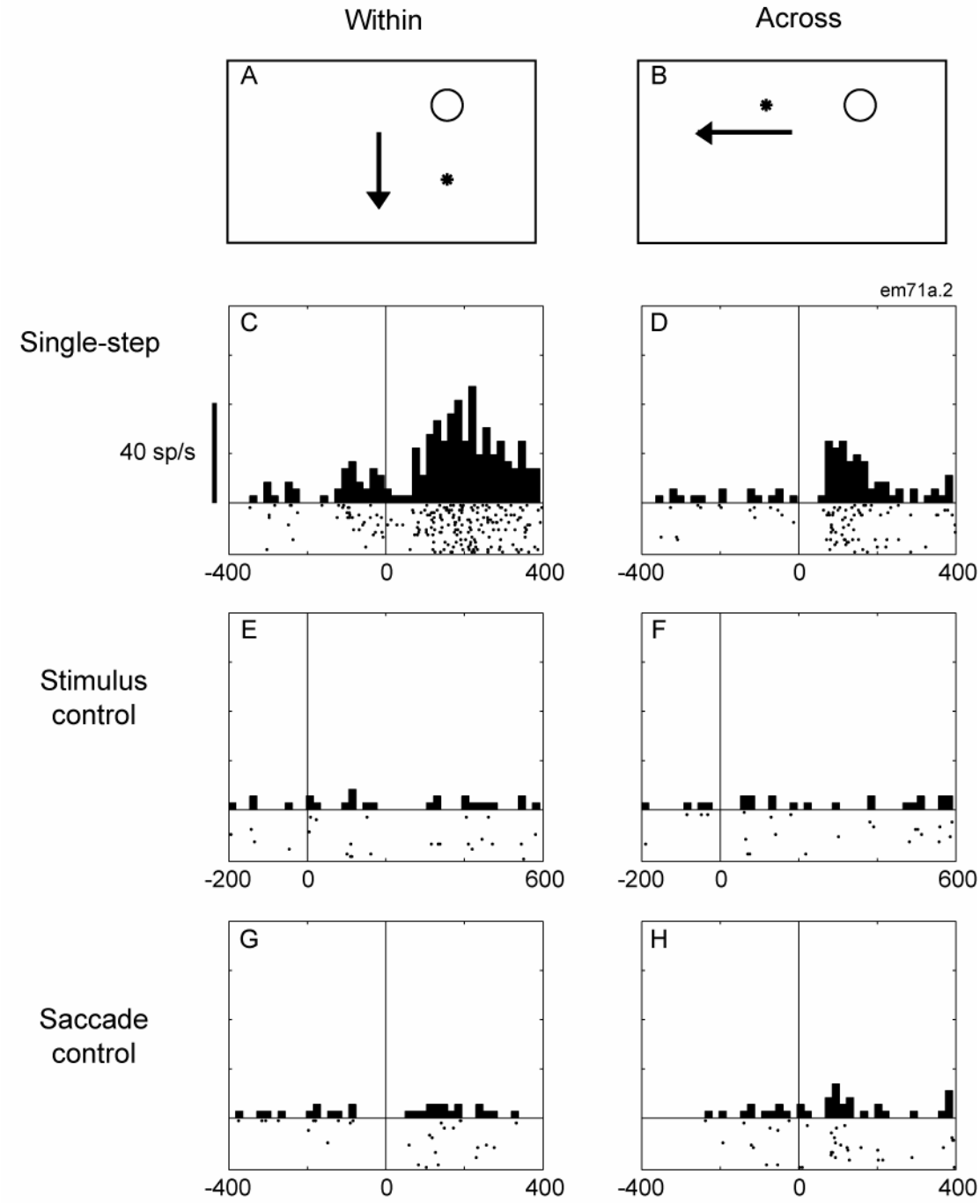

Figure 43. Example of a neuron that remaps stimulus traces both within and across hemifields in the split-brain monkey.

A, B. Spatial configurations for within and across conditions. In the lower panels, the histogram represents average firing rate. Rasters represent individual trials and tic marks represent action potentials. C, D. Within and across single step conditions. Data are aligned on saccade onset. The neuron fired briskly for both conditions. E, F. Stimulus controls. Data are aligned on stimulus onset. G, H. Saccade controls. Data are aligned on saccade onset. For both within and across conditions, remapping activity is significantly greater than that elicited by the stimulus or saccade alone.

The neuron does not respond when the stimulus is presented in the absence of the saccade (panels E, F). Similarly, the responses in the saccade control conditions were negligible (panels G, H). It is only when the stimulus and saccade occur in conjunction with one another, as they do in the single step task, that the neuron responded. Closer inspection of the activity elicited in the two single step conditions reveals that the remapped response differs in two key ways. First, the magnitude of the response was attenuated in the across condition as compared to the within condition. Second, the onset of the response was later for across than for within hemifield remapping. Thus, transection of the FC leads to changes in the strength and timing of signals related to updating spatial locations across hemifields.

For this neuron, the response in the saccade control task varies between the within and across conditions. In particular, for the across condition, the saccade alone elicits a small response that occurs at nearly the same latency as the updating response observed in the single step task. For this condition, the saccade moves the outer edge of the receptive field onto the location of the initial fixation point, FP1. The fixation point is a salient visual stimulus and therefore can be remapped; we attribute this post-saccadic response to remapping the location of the fixation point. For the particular configurations we used, this activity was more common in the across than the within version of the task. Our analysis methods were designed to account for the disparity in activity generated in the saccade control tasks.

We assessed whether individual neurons showed statistically significant remapping in both conditions. Remapping was considered statistically significant if activity in the single step task was significantly greater than that observed in the saccade

control task (t-test, $p < .05$). This method differs from that used in the parametric study of spatial updating described in the preceding chapter. In the current experiment, we eliminated neurons where the stimulus could contribute to the response observed in the single step task. We therefore have only one comparison to make when assessing significant remapping activity. Namely, we compare single step and saccade control activity.

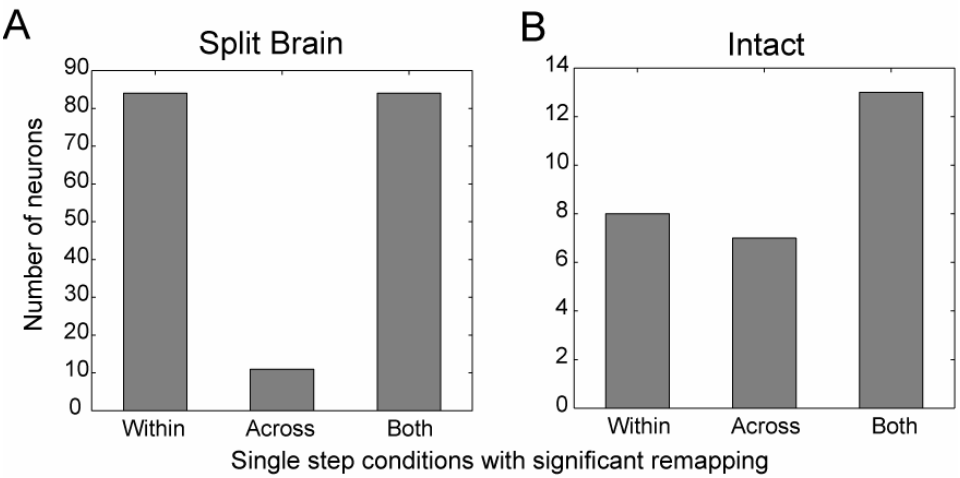

Figure 44. Number of neurons that show significant remapping for within-hemifield updating only, across-hemifield updating only, or both types of updating.

Significance was assessed with a t-test comparing single step activity to saccade control activity in the epoch 0-200ms relative to saccade onset (alpha = 0.05). A. Split-brain monkey. An equal proportion of neurons show significant remapping for within only and for both types of remapping (within only = 47%, both = 47%). A small number show significant remapping for the across condition only (6%). B. Intact monkey. In the intact monkey, most neurons with signficant remapping show this activity for both conditions (46%). Nearly equal proportions show significant remapping in only one condition (within only = 28%, across only = 25%).

In the split-brain monkeys, most neurons (179/223) showed statistically significant remapping in at least one condition of the single step task (Figure 44A). Almost half of the population remapped stimulus traces only within the same hemifield (46%). An example of such a neuron is shown in Figure 45. An equal number (46%), however, remapped stimulus traces both within and across hemifields. A small number

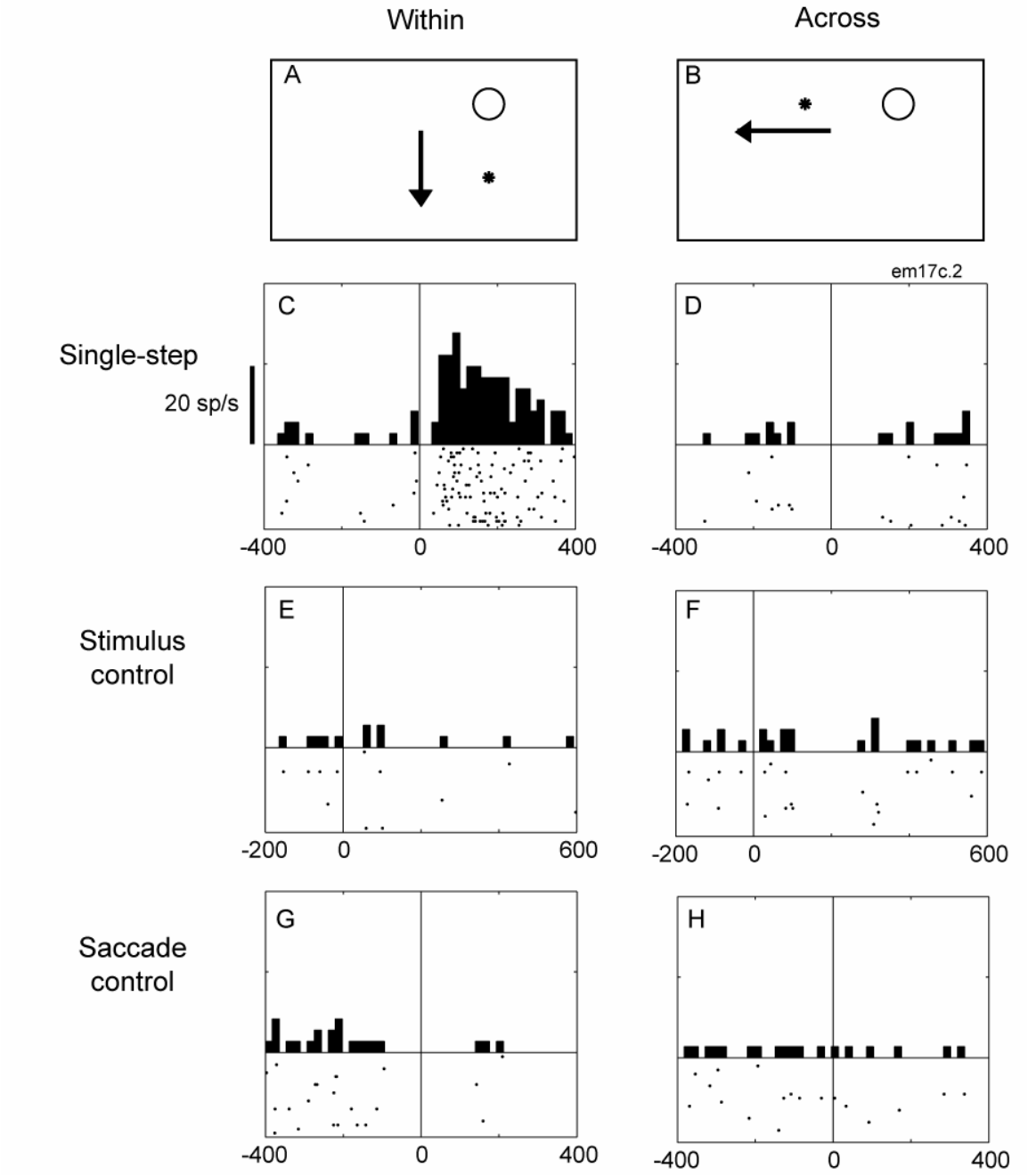

Figure 45. Example of a neuron that remaps stimulus traces within but not across hemifields in the split-brain monkey.

A, B. Spatial configurations. C, D. Single step task. E, F. Stimulus controls. G, H. Saccade controls. Conventions as in Figure 43.

of neurons (6%) showed remapping only in the across condition. These findings indicate that even in the absence of the forebrain commissures, many neurons update stimulus traces across hemifields. Across-updating neurons, however, are fewer in number than those that update within-hemifield. In contrast to these findings in the split-brain monkey, we found that in the intact monkey, the majority of neurons with significant updating activity remap for both conditions (46%, Figure 44B). The remaining neurons are nearly equally divided between those that remap within only (28%) and those that remap across only (25%). These results indicate that the reduction in across-hemifield remapping observed in the split-brain monkey results from transection of the forebrain commissures.

Why do some neurons remap stimulus traces for only the within or across configuration while others remap for both conditions? We were interested in whether they could be distinguished by the sensory, motor or cognitive signals they carry. We analyzed activity generated in the memory-guided saccade task to determine whether individual neurons carried memory or motor signals; neurons were selected for analysis based on their visual response in this task, so all carry visual signals. The memory epoch was 250 to 350 ms after stimulus onset; the saccade epoch was -100 to +100 ms relative to the onset of the saccade. For both epochs, activity was compared to baseline with a t-test (alpha = 0.05). We compared response properties for the groups of neurons that remapped within only, across only, or both within and across (Table 1). In the split-brain monkey, most neurons that exhibited statistically significant remapping activity had both memory- and saccade-related activity, in addition to their visual activity. This trend was the same for all three groups of neurons. Based on these findings, we conclude that the

ability to remap stimulus traces within or across hemifields is independent of the types of signals a neuron carries.

Table 1. Visual, memory and saccade characteristics of neurons with statistically significant remapping activity.

	Any remapping	Within only	Across only	Within and Across
Split-brain monkey				
vis only	41 (18%)	15 (17%)	2 (20%)	3 (4%)
vis-mem	8 (4%)	3 (3%)	1 (10%)	0
vis-sac	39 (18%)	18 (21%)	5 (50%)	7 (9%)
vis-mem-sac	134 (60%)	51 (59%)	2 (20%)	64 (86%)
Intact monkey				
vis only	6 (21%)	3 (37%)	1 (14%)	2 (15%)
vis-mem	2 (7%)	0	1 (14%)	1 (8%)
vis-sac	12 (43%)	3 (37%)	3 (43%)	6 (46%)
vis-mem-sac	8 (29%)	2 (25%)	2 (29%)	4 (31%)

Remapping across hemifields is attenuated

How does the magnitude of the remapping signal compare for the within- and across-hemifield conditions? The experiment was designed such that the within hemifield condition served as a control measure of how robustly a given neuron responds to remapped stimulus traces. We predicted that if updating were to occur across hemifields, it would be less robust than when the stimulus is updated within a single hemifield. To test this, we directly compared the remapping activity generated in the two single-step conditions (Figure 46A). The magnitude of the remapped response was greater for within- than across-hemifield updating (Wilcoxon matched pairs test, $p < .0001$). This finding confirms our prediction that in the absence of the forebrain

commissures, the ability to remap stimulus traces across hemifields is compromised. The counterpart to our prediction about remapping in the split-brain monkey is that we expected to see no difference in the strength of remapping when the commissures are left intact (Figure 46B). This is, indeed, what we found: when the commissures are intact, there is no difference in the strength of remapping within- as compared to across-hemifields. This indicates that normally there is no cost associated with updating stimulus traces from one hemifield to the other.

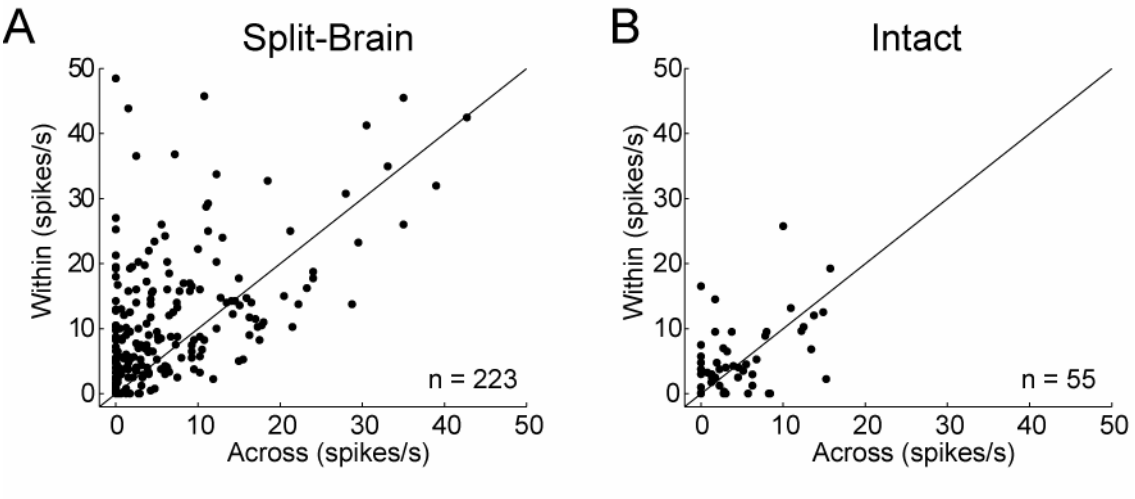

Figure 46. Magnitude of updating activity for within and across conditions.

Each point represents data from a single neuron. Activity is measured in the epoch 0-200 ms relative to saccade onset. A. In the split-brain monkey, activity was significantly greater for within than for across hemifield remapping (Wilcoxon paired-sample test, $p < .0001$). B. In the intact monkey, there is no difference in the magnitude of remapping within and across hemifields (Wilcoxon paired-sample test, $p > 0.30$).

In order to compare quantitatively the results from the split-brain and intact monkeys, we computed a Within-Across Remapping Index (WA Index) for each neuron. With this index, we can assess how robustly neurons remap stimulus traces across hemifields as compared to within a single hemifield. Remapping activity is single step activity that cannot be accounted for by the stimulus or saccade. In this experiment, we included in analysis only those neurons where the stimulus alone did not produce a response in either condition (see Methods). This eliminated the need to compare single step activity to stimulus control activity. Instead, the comparison of single step and saccade control activity is sufficient. The WA index normalizes remapping activity observed in the single step tasks to the total activity observed in the single step and saccade control tasks.

$$\text{WA Index} = \frac{(SSw - SACw) - (SSa - SACa)}{(SSw + SACw) + (SSa + SACa)}$$

Where *SSw* and *SSa* are the firing rates measured in the within and across versions of the single step task, and *SACw* and *SACa* are the firing rates measured in the corresponding saccade control tasks. Positive values indicate that updating was more robust for within hemifield than for across hemifield updating. Negative values indicate that updating in the across-hemifield condition was more robust than updating in the within-hemifield condition. If there is no difference in the magnitude of remapping within and across hemifields, the WA Index is 0.

We found that the distribution of WA Indices from the split-brain monkeys (Figure 47A) is significantly skewed toward positive values (one-tailed t-test, $p < 0.0001$). This indicates a preference toward remapping within-hemifield as compared to across-hemifields. This finding was statistically significant in both split-brain monkeys (one-tailed t-test, $p < 0.0001$, both monkeys). In contrast, there is no significant shift

away from 0 in the distribution of WA Indices in the intact animals (one-tailed t-test, $p > 0.60$). These data are plotted in Figure 47B. This result provides more evidence that, in the normal monkey, there is no difference in the magnitude of the signal associated with these two conditions. The critical question is whether there is any difference in the distributions from the two groups of animals. The average Index value from each group of monkeys was different (split-brain: mean = 0.11, s.e.m. = 0.012; intact: mean = 0.019, s.e.m. = 0.018). This finding was statistically significant (KS test, $p < 0.001$). Together these findings indicate that while there is normally no difference between remapping within and across hemifields, transection of the forebrain commissures compromises the signal associated with updating stimulus traces across hemifields.

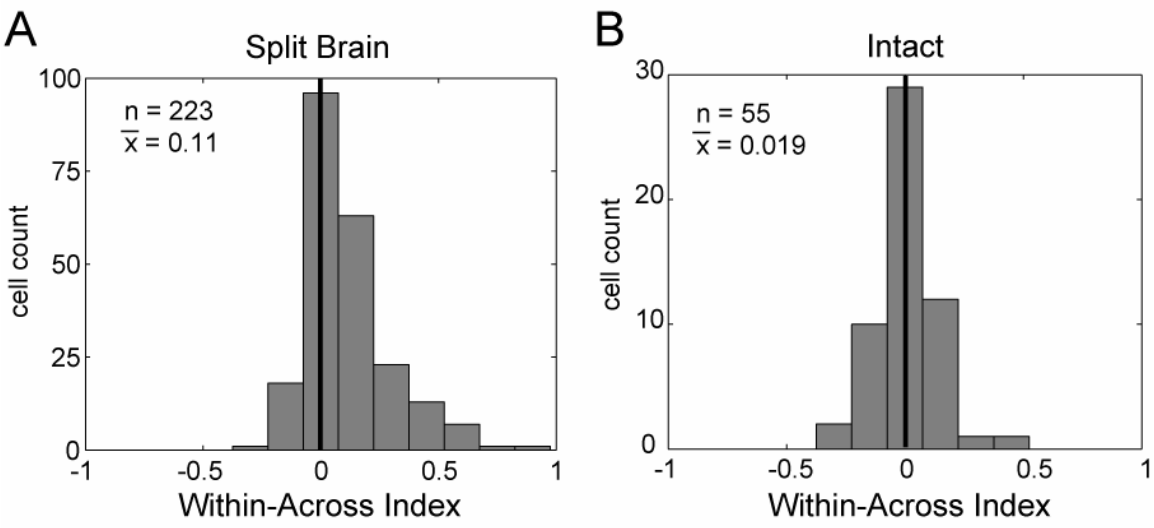

Figure 47. Strength of remapping for within and across conditions.

A. Split-brain monkey. The distribution is significantly skewed toward positive values (one-tailed t-test, $p < 0.00001$), indicating more robust remapping for within than across hemifield conditions. B. Intact monkey. The distribution is not significantly different from 0 (one-tailed t-test, $p > 0.60$), indicating that normally there is no difference in the strength of remapping stimulus traces within and across hemifields. Importantly, the distibutions are significantly different from one another (Kolmogorov-Smirnov test, $p < 0.05$).

Remapping across hemifields occurs later

We asked whether the timecourse of across-hemifield remapping was affected by disconnecting the cerebral hemispheres. In the previous sections, we analyzed spike counts in a fixed epoch. Here we are interested in when an appreciable change in updating activity first occurs. For each neuron, we defined the latency of the neural response in each of the remapping conditions relative to the beginning of the saccade (see Appendix for details). Specifically, we wanted to know if, in individual neurons, remapping begins at the same time for the within and across conditions. In this analysis, we include only those cells where the latency was definable for both conditions (split-brain: $n = 74$; intact: $n = 37$). For each neuron, we plotted the latency of within-hemifield remapping against across-hemifield remapping (Figure 48A). Points that fall along the unity line represent neurons with remapping activity that began at the same time for the two conditions. For the split-brain monkey, we found that most points fall below the line, indicating that remapping across-hemifields is delayed relative to remapping within-hemifields. This finding was statistically significant (Wilcoxon signrank test, $p < .01$). In the intact monkey (Figure 48B), there was no difference in latency for across-hemifield remapping as compared to within-hemifield remapping (Wilcoxon signrank test, $p > 0.60$). We conclude that in individual neurons, there is normally no difference in the time at which neural signals associated with remapping within and across hemifields become available. In the absence of the forebrain commissures, however, the information related to across-hemifield remapping is delayed.

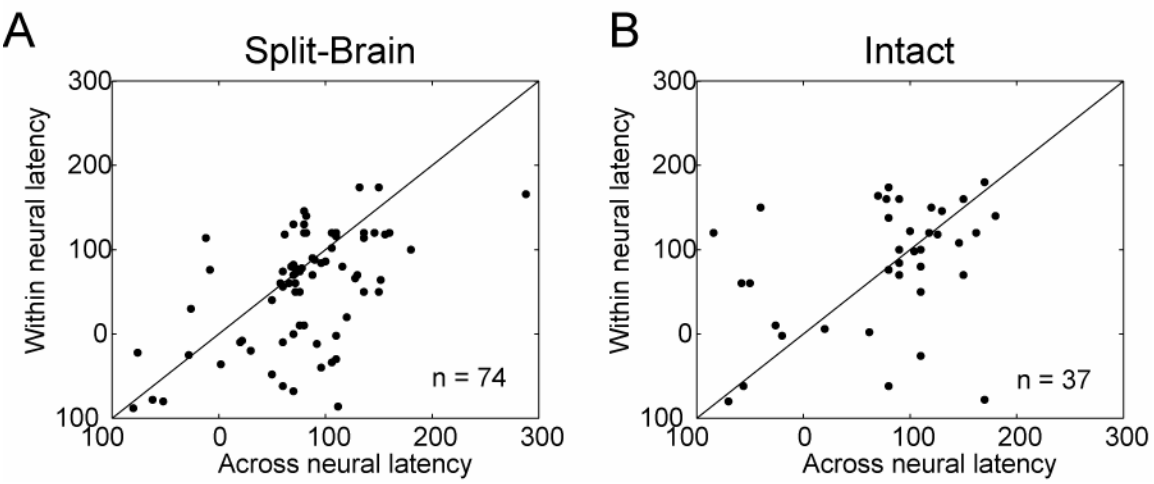

Figure 48. Response latencies for within and across hemifield remapping.

Latency is defined relative to the onset of the saccade. A. Split-brain monkey. Each dot represents the latency observed in the within condition plotted against latency observed in the across condition. Most of the dots fall below the unity line, indicating that there was a tendency for the remapped response to occur later for the across-hemifield condition. This finding was statistically significant (Wilcoxon signrank test, $p < 0.01$). B. Intact monkey. There was no tendency for remapping to occur later for the across-hemifield condition (Wilcoxon signrank test, $p > 0.60$).

We performed a second analysis to assess latency differences between the two conditions. In the first analysis described above, we were limited to using the subset of data where both the within and across conditions had a definable neural latency. In this second analysis, we included all latencies, regardless of whether they were matched between the two conditions (Figure 49). Our findings here parallel those described above. In the split-brain monkeys (panels A and B), remapping occurs earlier for within-hemifield updating (n = 169, mean = 54.50 ms, s.e.m. = 5.34 ms) than for across-hemifield updating (n = 117, mean = 76.39 ms, s.e.m. = 5.70 ms). This finding is statistically significant (Wilcoxon rank sum test, $p < 0.01$). In contrast, there is no difference in the latency of remapping in the intact monkey (panels C and D). Here, remapping latencies averaged 67.55 ms (+/- 11.72 ms s.e.m.) for the within condition and 65.84 ms (+/- 11.12 ms s.e.m.) for the across condition (Wilcoxon rank sum test, $p >$

0.05). Together, these findings indicate that the interhemispheric commissures normally provide a pathway by which visual information can be rapidly transferred from one hemisphere to the other.

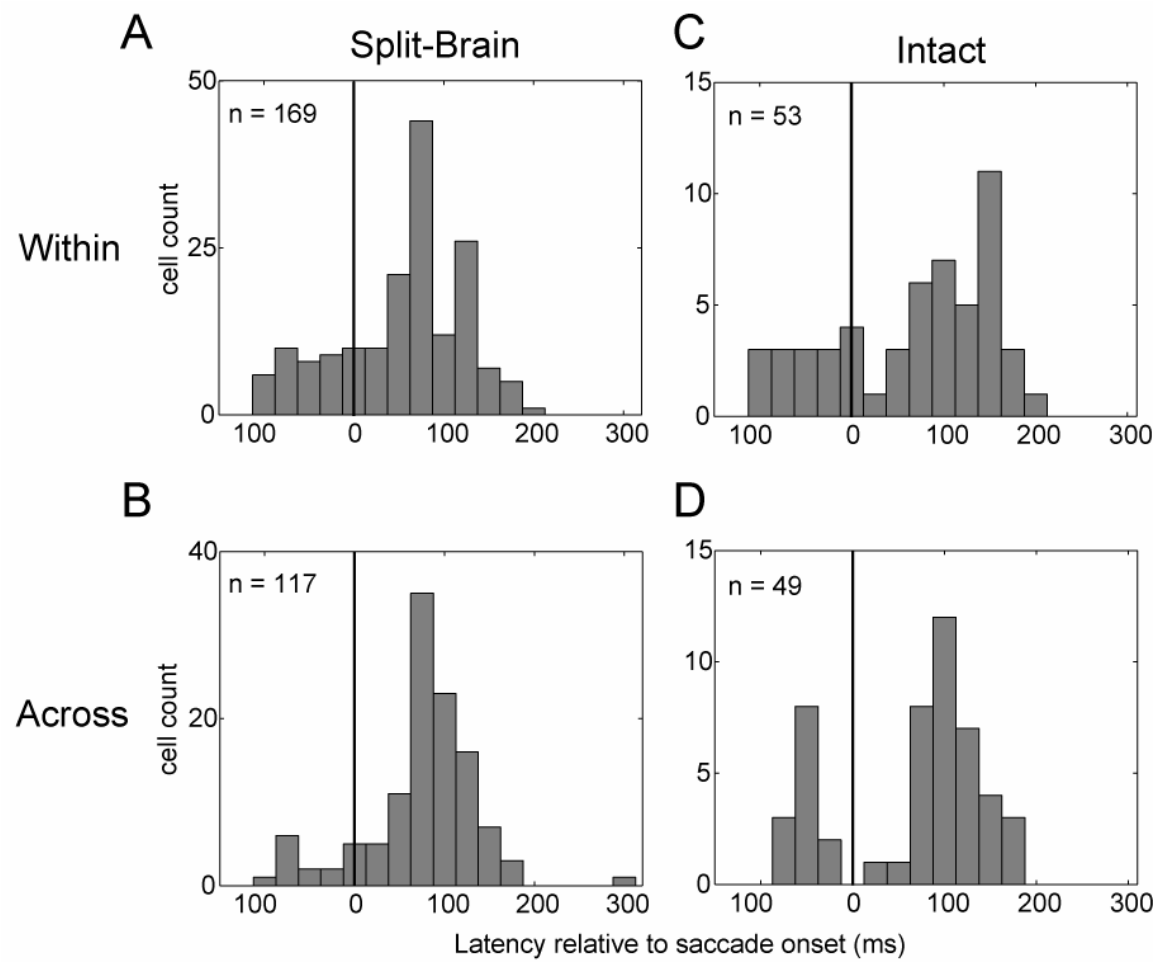

Figure 49. Comparison of the latency of remapping within and across-hemifields.

Latency is defined relative to saccade onset. Vertical line indicates the onset of the saccade. A, B. Split-brain monkey. In the absence of the forebrain commissures, latency is earlier for within hemifield updating (mean 54.50 ms) than for across hemifield updating (mean 76.39 ms). This difference was statistically significant (Wilcoxon rank sum test, $p < 0.01$). C, D. Intact monkey. Normally, there is no difference in the latency for remapping within and across hemifields (within mean = 67.55 ms; across mean = 65.84 ms; Wilcoxon rank sum test, $p > 0.05$).

In both conditions, and in both groups of animals, we observed considerable variability in the latency of remapping (see Figure 49). These results are similar to previous studies in which a wide range of latencies were observed for remapping (Umeno and Goldberg, 1997). One striking observation is that remapping can occur quite early. In particular, some neurons respond in the single step task at a time that precedes the expected visual latency of the neuron (Goldberg and Bruce, 1990; Duhamel et al., 1992a; Walker et al., 1995; Umeno and Goldberg, 1997). These predictive signals provide an updated representation that is available before reafferent visual signals are available. Remapping is considered predictive in nature if the onset of the response in the single step task is earlier than the visual latency observed in the memory guided response task. The mean visual latency we observed in the memory guided saccade task was 98.65 ms (+/- 1.09 ms s.e.m.); thus, on average, remapping latencies earlier than this can be considered predictive in nature. To determine whether remapping latencies were predictive, we directly compared the observed visual latency to the observed remapping latency for each neuron. For some predictive neurons, the response in the single step task begins even before the onset of the saccade. Thus, for these neurons, the location of the receptive field seems to shift well before the eyes begin to move. These *presaccadic* latencies are a subset of the *predictive* latencies.

We were interested in whether neurons in the split-brain monkey could still exhibit predictive remapping. In particular, we were curious about whether the proportions of predictive and presaccadic latencies were similar between the within and across conditions. We observed a nearly equal proportion of predictive responses for within- and across-hemifield updating in the split-brain monkey (within 63% (107/169),

across 58% (68/117)). We observed a similar proportion of predictive responses in the intact monkey (within 62% (33/53), across 61% (30/49)). Thus, even if the primary route for the interhemispheric transfer of information is abolished, signals related to spatial updating are still transferred between hemispheres with remarkable speed.

What about the frequency of *presaccadic* latencies? That is, is there any difference in the frequency of neurons showing the earliest predictive latencies? In contrast to our findings about the overall frequency of predictive neurons, we found that in the split-brain monkey there were twice as many neurons with presaccadic latencies for the within condition as for the across condition (within 22% (38/169), across 11% (13/117)). In the intact monkey, presaccadic latencies occurred in nearly equal frequency for the two conditions (within 25% (13/53), across 27% (13/49)). Similar proportions of predictive and presaccadic neurons were observed in the subset of neurons used in the paired analysis (Figure 48). Thus, while across-hemifield remapping still does occur quite rapidly in the split-brain animal, fewer neurons exhibit presaccadic latencies than in the within-hemifield condition. This implies that the absence of the forebrain commissures impairs the very earliest signals when across-hemifield remapping is required.

The timecourse of across-hemifield remapping is altered

The analyses above focused on the signals carried in individual neurons. We next consider the signals carried by the population of neurons in area LIP during within and across hemifield remapping. We constructed population histograms (Figure 50) using the subset of neurons that showed no significant activity in the saccade control task (A, split-

brain n = 91; B, intact n = 46). We limited this analysis to this subset of neurons in order to attain an accurate measure of remapping in the two conditions. The population histograms confirm three key findings regarding the magnitude of the neural signal associated with spatial updating. First, in the split-brain monkey (panel A), there is a pronounced increase in activity associated with remapping stimulus traces both within (green line) and across hemifields (red line). This indicates that even in the absence of the forebrain commissures, stimulus traces are updated across hemifields. Second, remapping is more robust for the within than for the across-hemifield condition. Thus, while signals associated with across hemifield remapping are still present, they are compromised relative to within-hemifield signals. Third, when the commissures are intact (panel B), we find, as expected, that remapping is equally robust for both within and across-hemifield conditions. This demonstrates that in the normal monkey, there is no tendency for remapping to be stronger when it occurs within a single hemifield.

The population histograms also point to a difference in the timecourse of these signals. Specifically, in the split-brain animal, the signal associated with within-hemifield remapping begins even before the onset of the saccade. In the across condition, remapping does not begin until after the start of the eye movement. In contrast, there is little difference between the timecourse of the two conditions when the commissures are intact. We compared the timecourse of remapping in these two conditions by calculating the WA index over time on the entire population of neurons (Figure 51). We computed the WA index in a 50 ms window beginning 300 ms before the onset of the saccade. This window was then shifted forward by 10 ms and the WA Index was recomputed in the next 50 ms window. We repeated this procedure until 500 ms after the start of the

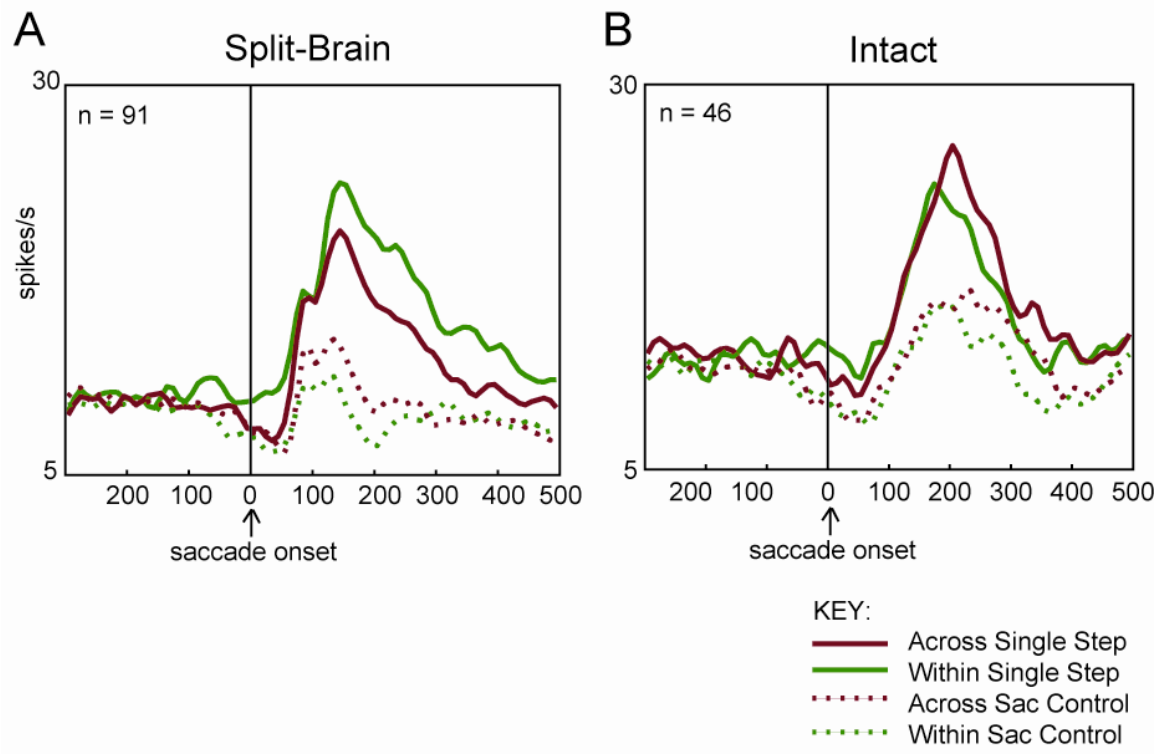

Figure 50. Population histograms for remapping within and across hemifields. Data are aligned on the onset of the saccade.

Only neurons with no significant stimulus or saccade-related activity are included. A. Split-brain monkey. For both the within and across hemifield single step tasks, there is an increase in activity shortly after saccade onset. This increase is greater and occurs earlier for within (green) as compared to across (red) hemifield remapping. The saccade alone (dotted lines) elicits a small response for both conditions. B. Intact monkey. In the intact monkey, there is no bias toward greater activity for within-hemifield remapping.

saccade. We found that in the absence of the forebrain commissures, the WA Index first reached significance 110 ms before the onset of the saccade, and remained significant throughout the duration of the test period (500 ms after saccade onset). The index reached its maximum 190 ms after saccade onset. Thus, well before the initiation of the saccade, there is a difference in the neural signal associated with updating stimulus traces within as compared to across hemifields, and this difference persists for many hundreds of milliseconds after the saccade is completed. In contrast, in the intact animal, the WA

Index remains near 0 throughout the duration of the analysis epoch. This indicates that there is normally no difference in the timecourse of signals associated with updating stimulus traces within and across hemifields.

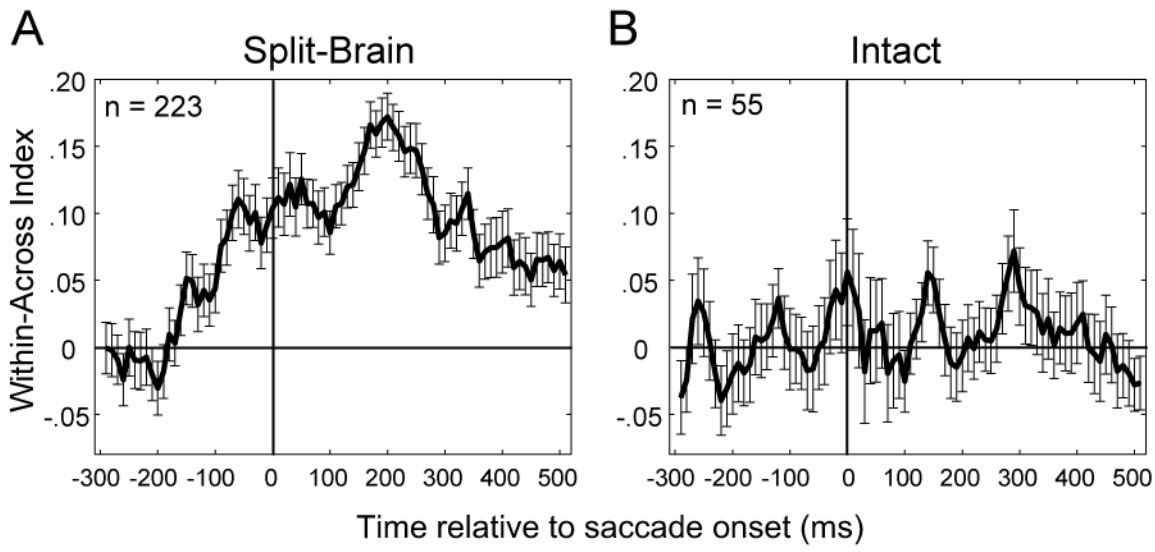

Figure 51. Analysis of the timecourse of remapping within and across hemifields.

Each plot shows the Within-Across Index computed as a function of time. Positive values indicate that remapping is more robust for the within than the across condtion. Values near 0 (horizontal line) indicate that remapping is equal for the two condtions. The index is computed in 50ms epochs, beginning 300ms before the onset of the saccade. The epoch is moved up by 10ms, and the index is re-computed. This procedure is repeated for all timepoints until 500ms after the onset of the saccade. Error bars represent standard error of the mean. A t-test (alpha = 0.05) is used to assess significance at each timepoint. A. Split-brain monkey. The Within-Across Index first becomes significantly positive beginning 110ms before the onset of the saccade. It remains significant throughout the duration of the analysis epoch. This indicates that the difference in updating is present before the eye movement is generated and lasts well beyond its completion. B. Intact monkey. The Within-Across Index remains near 0 throughout most of the test period. This indicates that normally there is no difference in the timecourse of updating for these two conditions.

Remapping across hemifields is independent of receptive field location

In the normal monkey, the representation in LIP extends ~5 degrees into the ipsilateral visual field (Ben Hamed et al., 2001). We were interested in whether those neurons with receptive fields (RFs) located close to the midline had differential access to information from the opposite hemifield, as compared to those neurons with more peripheral RFs. We asked two questions regarding the impact of RF location on the properties of across-hemifield remapping in the split-brain. First, is the strength of across-hemifield remapping related to the RF location? We addressed this question by comparing the RF eccentricity of each neuron to its WA index (Figure 52). Linear regression revealed that there was no significant relationship between RF location and ability to remap stimulus traces across hemifields ($p > 0.3$). Thus, the strength of across-hemifield remapping, as compared to within-hemifield remapping, is independent of RF location. This implies that neurons in LIP have equal access to stimuli in the opposite hemifield, regardless of whether they have proximal or peripheral receptive fields.

Second, is the latency of remapping related to the RF location? Specifically, we wanted to know if neurons with receptive fields located close to the midline have earlier access to information about stimulus traces remapped across hemifields. In Figure 53, we plot neural latency against receptive field eccentricity for each neuron. There was no significant relationship between remapping latency and receptive field eccentricity (linear regression, within $p > 0.20$, across $p > 0.50$). From this, we can infer that there is no difference in the time required to compute the updated location of a visual stimulus, regardless of how far across the vertical meridian the signal must be transferred.

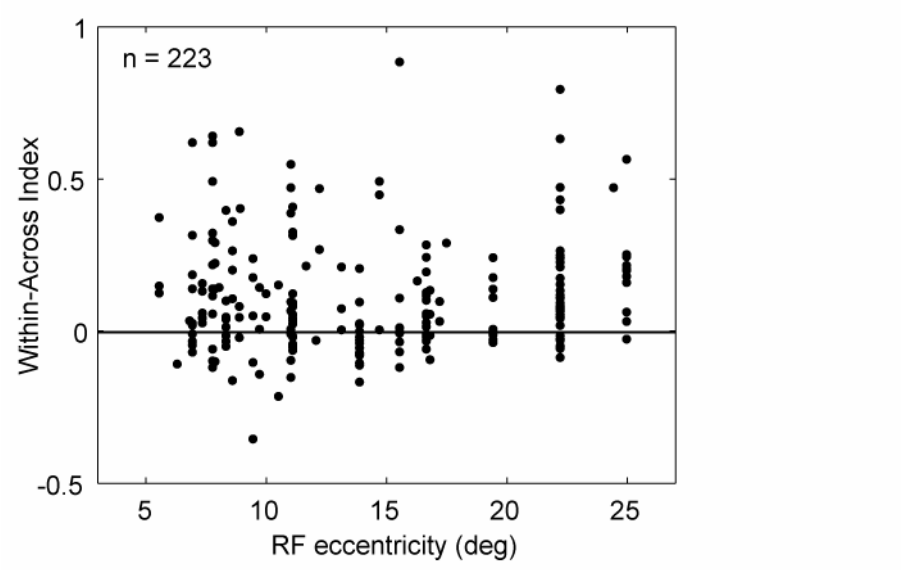

Figure 52. Comparison of receptive field eccentricity and strength of remapping in the split-brain monkey.

For each neuron, absolute receptive field eccentricity was estimated using the memory guided saccade task. A Within-Across Index of 0 indicates equivalent remapping in each version of the task. There was no significant relationship between receptive field location and Within-Across Index (linear regression, $p > 0.3$).

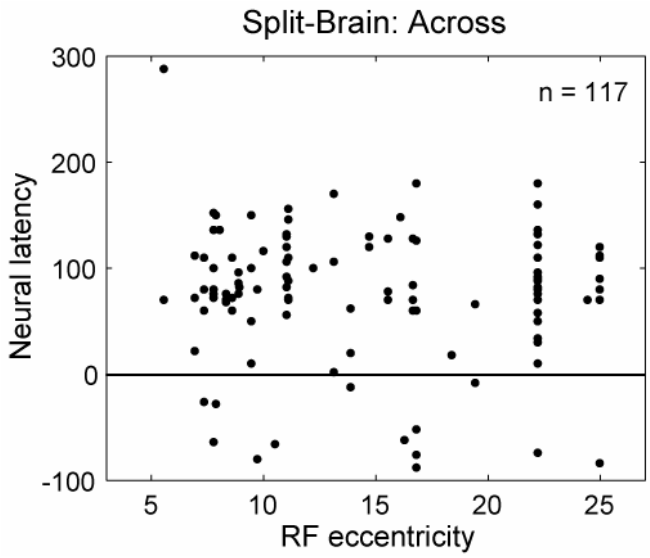

Figure 53. Remapping latency in the across-hemifield condition in the split-brain monkey.

Receptive field eccentricity is plotted against neural latency relative to saccade onset. There was no relationship between neural latency and receptive field eccentricity (linear regression, $p > 0.5$).

3.6. Discussion

Overview

The goal of this experiment was to gain insight into the neural circuitry underlying spatial updating. In the original studies of spatial updating, the stimulus had to be remapped from one hemifield to the other. We presume that across-hemifield updating requires a transfer of information between neurons in opposite hemispheres because the representation of the visual field is lateralized (Trevarthen, 1990). We hypothesized that the forebrain commissures would be required for across-hemifield remapping. Our essential finding is that, even in the absence of the forebrain commissures, neurons in the lateral intraparietal area can update stimulus traces across hemifields. This indicates that alternative pathways must be available to subserve this function. The results obtained from this special case provide insight into the circuitry required for across-hemifield remapping. Here we discuss the implications of our observations on spatial updating in the split-brain monkey.

Signals related to across-hemifield remapping exist, but are modified

Our observations of across-hemifield remapping in the split-brain monkey can be viewed as two sides of the same coin: information about stimulus traces can be transferred interhemispherically, but this transfer is limited. Our principle finding is that remapping across-hemifields occurs even in the absence of the forebrain commissures. A substantial proportion of neurons show significant remapping for the across-hemifield

condition. Furthermore, we found that at the population level, stimulus traces can still be robustly updated across-hemifields. This indicates that the forebrain commissures are not required for the interhemispheric transfer of visual information; alternative pathways are sufficient. Our second main finding is that across hemifield remapping is compromised in the absence of the forebrain commissures. Specifically, we found that it is both diminished in magnitude and delayed in onset. Considering that the corpus callosum alone is composed of over a half-billion axons (Lamantia and Rakic, 1990), it is not surprising that we observed these changes. The reduction in magnitude may be explained by the fact that in the split-brain monkey, subcortical structures, such as the superior colliculus, are required to compute the updated location of the stimulus. It is possible that this computation yields a signal that is less robust than that generated by the connected cortical hemispheres. The delayed onset could be due to a circuitous route required for the remapped signal to reach LIP. In sum, our findings indicate that while compensatory pathways do exist, these pathways may be limited in their function.

Our findings are consistent with previous studies in split-brain humans and animals, showing that visual information can be transferred interhemispherically but that this transfer is often compromised (Gazzaniga, 1987; Corballis, 1995; Gazzaniga, 1995). In all cases, subcortical structures were implicated in this transfer. Interestingly, not all visual information has equal access to subcortical routes. For example, there is little transfer of color or form information (Hughes et al., 1992; Corballis, 1995; Forster and Corballis, 2000). The finding that color information is not transferred is especially intriguing considering that neurons in the superior colliculus show little color sensitivity (Kadoya et al., 1971). This suggests a way to address the question of whether the

superior colliculus is responsible for across-hemifield remapping in the split-brain monkey. Specifically, we could ask whether equiluminant visual stimuli are remapped across hemifields. If they are not remapped, it would suggest that the superior colliculus is indeed involved in remapping stimulus traces interhemispherically. Our findings indicate that the disconnected cerebral hemispheres have remarkable access to information present throughout the visual field.

Subcortical pathways can be used to guide behavior

What are the behavioral ramifications of disconnecting the cerebral hemispheres? We have discussed the changes in neural activity, but do these changes have behavioral consequences? We addressed this issue by assessing performance of the split-brain monkeys on the double step task. In this task, the animal must make sequential saccades to two remembered target locations. Accurate performance of the second saccade requires that the spatial representation of the second target be updated. We compared two conditions of the double-step task, analogous to those tested physiologically with the single step task. Within-hemifield sequences required that the second target be updated within the same hemifield, whereas across-hemifield sequences required that the second target be updated from one visual field to the other.

Initially, both animals were impaired on across-hemifield, but not within-hemifield, sequences. With experience, performance of across-hemifield sequences improved substantially. Interestingly, we found that the deficit could be reinstated by changing the locations of the targets. Correct performance does not generalize to all targets, but can develop through experience. This indicates that the neural circuitry

required for across-hemifield updating is available, but may not be recruited until needed. Despite the significant improvement, performance of across-hemifield sequences was less accurate than for within-hemifield sequences, even after many months (> 20 mos) of experience. This impairment corresponds to our finding that the neural signal associated with across-hemifield remapping is less robust than within-hemifield remapping. These parallel findings suggest that the remapping we observed could be used to guide behavior.

Experimenters studying split-brain humans have also found that the disconnected hemispheres can transfer information required to guide behavior. The information required to guide both eye movements (Holtzman, 1984; Corballis, 1995) and manual responses (Berlucchi et al., 1995) is transferred interhemispherically in the absence of the forebrain commissures. Our findings, along with those described here, indicate that subcortical pathways are sufficient to subserve many kinds of behavior.

Post-lesion recovery of function

Reorganization of neural circuits and recovery of function following lesions to structures throughout the neuraxis are well-documented phenomena (Gilbert, 1998). The timecourse and nature of recovery can vary considerably, however. Following some lesions, recovery of function is rapid and spontaneous, whereas following others, extensive behavioral training is required. A striking example of spontaneous recovery of function occurs following lesions of either the superior colliculus or frontal eye fields (Schiller et al., 1979). Lesions to either structure alone induce transient deficits in the generation of eye movements. Within a matter of weeks, and without explicit behavioral

training, the ability to generate accurate eye movements recovers. This indicates that neural reorganization can be quite rapid and spontaneous. On the other hand, training-dependent recovery of function has been documented in both monkeys and cats following lesions of extrastriate areas dedicated to motion detection (Rudolph and Pasternak, 1999; Huxlin and Pasternak, 2004). In these animals, the ability to discriminate visual motion is initially impaired following the lesion. This ability recovers after extensive behavioral training on motion detection tasks. It is interesting that recovery was retinotopic: only stimuli placed in trained regions of the visual field were discriminable. This is similar to our observation that new sequences of the double-step task required additional training before they could be performed correctly. These findings indicate that reorganization is not always spontaneous, but can occur with training.

In our split-brain animals, recordings of neural activity were conducted many months (~15 mos) after the commissurotomy, and only after the animals had been trained on the double-step task. It is not clear if the remapping we observed in the across-hemifield condition is spontaneous or if it is related to the behavioral training. That is, we may have observed across-hemifield remapping because the animals had been trained on a task that required them to use this information. It is possible that we would not have observed across-hemifield remapping in LIP if the animals had not been trained on the double step task. Findings in intact animals argue against this, as remapping is observed in animals that were never trained on the double step task (Walker et al., 1995). We observed this as well: the animals we used in the experiments of Chapter 2 were never trained on the double step task. It is not clear, however, if the same would be true of

across-hemifield updating following a lesion to the forebrain commissures. To address this issue, recordings in naïve split-brain animals would have to be conducted.

Alternative circuits for across-hemifield remapping

Contrary to our expectation, we found evidence that remapping across-hemifields occurs even in the absence of the forebrain commissures. This observation implies that alternative pathways are used to transfer information from one hemifield to the other. Here we describe a circuit that could be used for across-hemifield remapping in the absence of the forebrain commissures. We believe that the superior colliculus is vital for this transfer. Remapping has been observed in the intermediate layers of the SC (Walker et al., 1995). While it is not clear where this signal originates, we hypothesize that in the split-brain monkey, the SC is capable of computing the across-hemifield signal. Its functional properties support this possibility. Neurons in the intermediate layers of the SC exhibit both visual and saccade-related activity, and they are modulated by cognitive factors such as attention and memory (Schiller and Koerner, 1971; Goldberg and Wurtz, 1972; Wurtz et al., 2001). Both the sensorimotor and cognitive signals carried by neurons in the SC are essential elements of remapping (Quaia et al., 1998). It therefore seems likely that this structure could independently compute the updated location of visual stimuli.

Critically, though, could neurons in the SC do *across-hemifield* remapping? In the superior colliculus, there is a topographic representation of the contralateral visual field (Cynader and Berman, 1972). Neurons in all layers (i.e., superficial, intermediate, deep) of the SC are linked via the intertectal commissures (Moschovakis et al., 1988a, b),

and the intertectal commissures connect the SC through its entire rostrocaudal extent (Olivier et al., 1998; Munoz and Istvan, 1998). Thus, neurons that encode locations throughout the visual field are interconnected. Additionally, neurons in all layers are interconnected with one another (Moschovakis et al., 1988a, b), indicating that if remapping is restricted to a single layer of the SC, this signal could be transmitted to other layers. These findings suggest that the circuitry required for across-hemifield remapping exists in the SC.

An important issue is whether there are any anatomical pathways by which remapped signals generated in the SC could reach LIP. The superficial layers of the SC send a prominent projection to LIP through the pulvinar nucleus of the thalamus (Clower et al., 2001). These second-order subcortical projections to cortex were determined using transneuronal herpes virus tracers. These tracers are effective for two reasons (Ugolini et al., 1989). First, they are selectively transported at synapses. Second, the virus is replicated within the recipient neuron, which amplifies the signal at each point of transfer. They have proven to be a powerful tool for elucidating neural circuits. The ascending pathway from pulvinar to cortex has been referred to as a second visual pathway (Diamond and Hall, 1969), as it is carries primarily visual information, and provides an alternate route by which visual information can reach cortex.

In support of the argument that remapped visual information could be transmitted along this path is the observation that neurons in the pulvinar have visual responses that are modified by eye movements (Robinson and Petersen, 1985). This was determined by measuring the responses of pulvinar neurons to the external motion of a stimulus, as compared to motion caused by a saccade. These neurons respond robustly to external

motion, but are unresponsive if the same motion is caused by an eye movement. This indicates that the visual responses of pulvinar neurons are modified by extra-retinal signals. One likely candidate signal is corollary discharge, though a proprioceptive signal has not been ruled out. Altogether, there is a wealth of evidence supporting the hypothesis that the SC could remap stimulus traces across-hemifields, and that this signal could be transmitted to LIP via the pulvinar.

3.7. Summary

The aim of this experiment was to determine whether the forebrain commissures are necessary for updating spatial representations across the vertical meridian. We addressed this aim by recording from neurons in the lateral intraparietal cortex (LIP) of split-brain monkeys while they performed two conditions of the single step task. In the within-hemifield condition, the stimulus trace is updated within the same visual hemifield. In the across-hemifield condition, the stimulus must be updated from one hemifield to the other. We expected that remapping in the across-hemifield condition, which requires an interhemispheric transfer of visual information, would be abolished in the split-brain monkey. The principal, and unexpected, finding of this experiment is that even in the absence of the forebrain commissures, LIP neurons can update stimulus traces from one hemifield to the other. This signal is modified in two important ways, however. It is both delayed in onset and reduced in magnitude as compared to when the stimulus is updated within a single hemifield. These differences are not present when the forebrain commissures are intact. Altogether, our findings support two main conclusions. First, in

the absence of the forebrain commissures, interhemispheric transfer of information still occurs. The forebrain commissures, while likely the primary route for interhemispheric transfer, are not the only route. Subcortical structures, especially the superior colliculus, are likely involved in this interhemispheric transfer. Second, as indicated by our observations that remapping is less robust in the absence of the forebrain commissures, these alternative pathways may be less effective. These conclusions are consistent with the idea that spatial updating is supported by a flexible network of cortical and subcortical structures.

4. Chapter 4: General Discussion

4.1. Overview

The objective of these investigations was to use single unit recording to gain a greater understanding of the phenomenon of spatial updating. We studied the activity of neurons in the lateral intraparietal cortex of awake monkeys. The experiments in Chapter 2 were designed to determine whether remapping is independent of the direction over which a stimulus trace must be updated. We observed that individual neurons could update stimulus traces in multiple directions. Furthermore, across the population remapping was equally robust for all saccade directions. This signifies that neurons in the lateral intraparietal cortex have access to visual information presented throughout the visual field. In Chapter 3, our goal was to identify the neural circuitry supporting spatial updating. We focused on a special case of updating: when the stimulus trace must be updated from one hemifield to the other. Specifically, we asked whether the forebrain commissures are required for the interhemispheric transfer of visual signals. We found that stimulus traces could indeed be transferred interhemispherically in the absence of the forebrain commissures, albeit with a reduction in strength. These results demonstrate a previously unrealized redundancy in the neural circuitry supporting spatial updating in the primate brain.

The purpose of this chapter is to place these results in the framework of the existing literature. We discuss three issues. First, we discuss the neural circuitry supporting remapping. Second, we discuss the ways in which remapping affects

perception. Finally, we discuss our observations in relation to updating in conjunction with movements other than saccades.

4.2. Circuitry for remapping in split-brain and intact animals

In this section, we describe the neural circuits that could support remapping during our experimental conditions. Spatial updating relies on two neural signals: a visual response and a corollary discharge. The visual signal must encode the stimulus and maintain this representation even after the stimulus is gone. In order for the stimulus trace to be remapped, a second signal is required to initiate the process. The second signal is a corollary discharge of the eye movement command, which informs the brain of the impending eye movement. The conjunction of information about the eye movement and the location of the visual stimulus leads to the generation of a remapped stimulus trace. What is the neural circuitry that supports remapping during the experimental conditions described in the preceding chapters? Behavioral experiments indicate that updating relies heavily on parietal cortex: both humans and monkeys with parietal lesions are impaired on tasks that require spatial updating (Heide et al., 1995; Li and Andersen, 2001). Accordingly, we focus our discussion of circuitry on parietal cortex, specifically area LIP. We begin by describing the specific circuitry for the three experimental conditions: within-hemifield remapping; across-hemifield remapping with the forebrain commissures intact; and across-hemifield remapping in the absence of the forebrain commissures. Following that, we consider in more general terms the interactions between the brain areas involved in spatial updating.

Within-hemifield updating does not require an interhemispheric transfer of visual information, so the same circuit can be used in intact and split-brain animals (Figure 54A). Neurons in LIP encode the location of a visual stimulus in the coordinates of the initial eye position (LIPpre neurons). LIP receives a corollary discharge (CD) of the saccade command. The conjunction of visual information and CD information leads to a shift of the visual signal to another group of neurons (LIPpost neurons) that will encode the location of the visual stimulus when the eyes reach their new position (Quaia et al., 1998; Colby and Goldberg, 1999). LIPpre and LIPpost neurons are in the same hemisphere, so the simplest circuit uses a transfer of visual information within a single LIP. Where does the CD signal originate? Neurons in the intermediate layers of the SC transmit corollary discharge signals to FEF via the medial dorsal thalamus (Sommer and Wurtz, 2002). LIP and FEF are strongly interconnected, offering a pathway by which the corollary discharge signal in FEF could be transmitted to LIP (Petrides and Pandya, 1984; Andersen et al., 1990a). Alternatively, the superior colliculus could transmit a CD signal directly to LIP. Either, or both, of these areas could provide the CD information LIP needs to compute the remapped location.

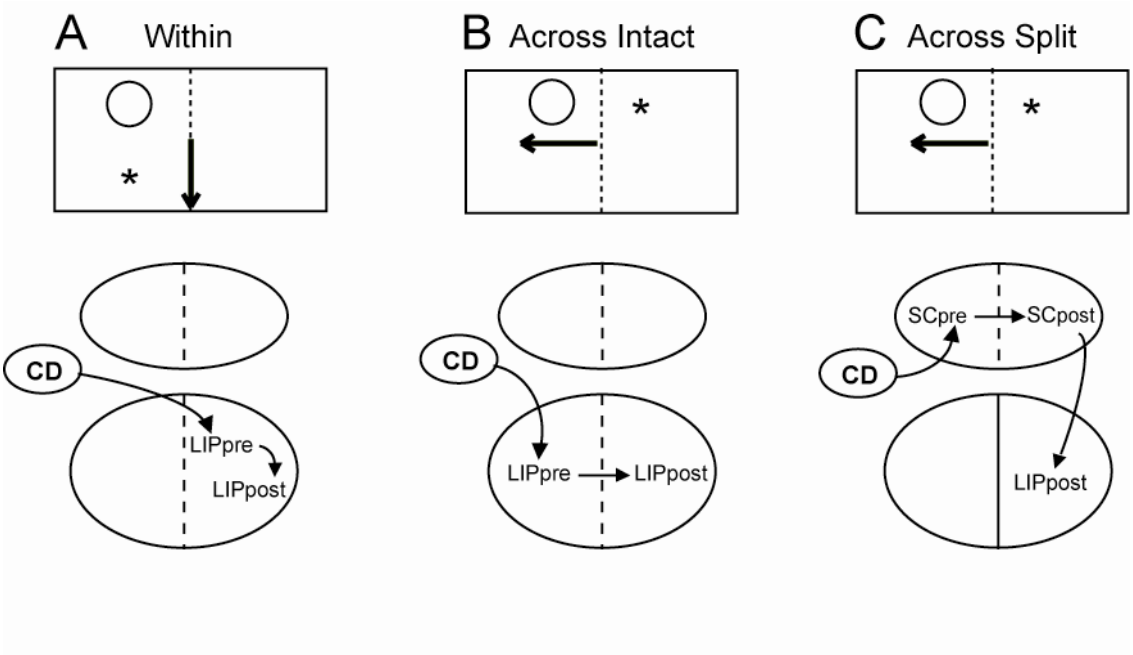

Figure 54. Model circuits for spatial updating in the three experimental conditions.

The circuits show how a neuron in the right hemisphere of LIP (LIPpost) could respond to a remapped stimulus trace. The upper panel in each series shows the spatial configurations used to test remapping. The saccade (arrow) moves the receptive field (circle) onto the location of the flashed stimulus (star). The lower portions in each series represent the superior colliculus (small oval) and area LIP (large oval). At the time of the eye movement, a corollary discharge signal (CD) initiates remapping. This leads to a transfer of visual information from "pre neurons" that represent the stimulus when the eyes are at the initial fixation location to "post neurons" that represent the stimulus when the eyes are at the final fixation location. A. Within-hemifield updating. The stimulus remains in the same hemifield before and after the eye movement. The transfer of visual information occurs between LIP neurons in a single hemisphere. This circuit does not require the forebrain commissures. It is the same for intact and split-brain monkeys. B. Across-hemifield updating in the intact monkey. The stimulus is updated from one hemifield to the other. Visual information is transferred from LIPpre in the left hemisphere to LIPpost in the right hemisphere. This transfer occurs via the forebrain commissures. C. Across-hemifield updating in the split-brain monkey. The forebrain commissures are not available for the transfer of visual information. Remapping occurs in the superior colliculus. Neurons in the left colliculus code the location of the stimulus when the eyes are at the initial fixation location (SCpre). In conjunction with the eye movement, visual information is transferred to neurons in the right colliculus (SCpost) via the intertectal commissures. The remapped visual trace is subsequently transferred to LIPpost.

For across-hemifield remapping in the intact animal, the scenario is very similar (Figure 54B). The only difference is in the transfer of visual information. A CD signal impinges on LIPpre in one hemisphere, which leads to a transfer of visual information to LIPpost in the other hemisphere. Our observations that across-hemifield remapping is compromised in split-brain monkeys supports the idea that normally the transfer of visual signals relies on the forebrain commissures that link up the entire rostrocaudal extent of the cortex (Pandya and Vignolo, 1969; Seltzer and Pandya, 1983; Schwartz and Goldman-Rakic, 1984; Hedreen and Yin, 1981). Thus, in the most parsimonious circuit, the transfer of visual signals in across-hemifield remapping occurs via the forebrain commissures.

Finally, we consider the case of across-hemifield remapping in the absence of the forebrain commissures (Figure 54C). We observed that visual information could be transferred interhemispherically in the split-brain monkeys, indicating that subcortical routes must be able to support this transfer of information. As detailed in the Chapter 3 Discussion, we hypothesize that in the split-brain monkey, the superior colliculus supports across-hemifield updating. Visual neurons in the superior colliculus encode the location of the stimulus when the eyes are at the initial eye position (SCpre). With the impending eye movement, a CD signal induces a remapping of visual information to neurons that will encode the location of the stimulus when the eyes reach the new fixation location (SCpost). This transfer of visual information is supported by the intertectal commissures that link up the rostrocaudal extent of the SC (Olivier et al., 1998; Munoz and Istvan, 1998). The remapped visual signal can subsequently be transferred to LIP via the pulvinar nucleus of the thalamus (Clower et al., 2001). The CD

observed in the SC (Sommer and Wurtz, 2002) can be used to generate the remapping signal in the SC.

It is useful to conceptualize the three conditions of remapping as three separate situations, each with its own neural circuit. In reality, however, it is likely that these circuits operate simultaneously. All of the areas in which remapping has been observed must be participating all the time. In addition to LIP and SC, remapping has also been observed in FEF (Goldberg and Bruce, 1990; Umeno and Goldberg, 1997, 2001) and extrastriate visual areas (Nakamura and Colby, 2002). The percentage of neurons that remap varies by area. Previous reports indicate that LIP has the greatest number (95%) of neurons with remapping (Duhamel et al., 1992a). In contrast, approximately 60% of FEF neurons remap and in SC 30% of neurons show this activity (Walker et al., 1995; Umeno and Goldberg, 2001). Interestingly, in extrastriate visual areas, the percentage of remapping neurons increases at each stage of the hierarchy: 11% in V2, 35% in V3 and 53% in V3A (Nakamura and Colby, 2002). The existence of remapping in regions distributed throughout the brain leads to the question of where the signal originates. Does the signal originate from a single locus, or is the computation distributed throughout multiple brain areas? There is evidence in support of both possibilities.

If remapping is computed at a single site, the most likely area is parietal cortex. There are three lines of evidence in support of this idea. First, remapping is most prevalent in LIP neurons as compared to the other areas. Second, lesions to parietal cortex lead to gross spatial impairments on the double step task, whereas lesions to frontal cortex do not (Heide et al., 1995; Li and Andersen, 2001). These lesion results suggest that parietal cortex is critically involved in spatial updating. It is worth noting,

however, that the comparable studies have not been conducted in subjects with lesions to all of the other areas described above. Third, LIP projects to all of the areas that show remapping (Petrides and Pandya, 1984; Lynch et al., 1985; Andersen et al., 1990a; Cavada and Goldman-Rakic, 1989b). Antidromic studies have revealed that much of the information transferred from LIP to FEF and SC is visual in nature (Ferraina et al., 2002). Together, these findings indicate that LIP could remap stimulus traces and subsequently export this information to other areas.

Alternatively, remapping may be independently computed at multiple sites. The first line of evidence in support of this possibility comes from the anatomical connections of the areas in which remapping has been observed. Neurons in all of these areas carry both visual and saccade-related signals, or have access to them via anatomical connections (Schall et al., 1995; Wurtz et al., 2001; Stanton et al., 1995). These are the two signals required for remapping. The second line of evidence comes from our observations on remapping. In the split-brain monkey, we observed across-hemifield remapping in LIP. The disconnected cortical hemispheres do not have direct access to visual information presented in the opposite hemifield. The most likely explanation for our observation, therefore, is that remapping is computed in the SC and this information is subsequently transferred to LIP.

Remapping is thought to be critical not only for guiding accurate behavior, but also for creating stable visual representations at the time of saccades (Goldberg and Bruce, 1990; Duhamel et al., 1992a; Ross et al., 1997; Colby and Goldberg, 1999). Functions of such importance are rarely the responsibility of a single area, but instead are distributed throughout multiple regions. For example, lesions to the SC or FEF induce

deficits in saccadic eye movements, but these deficits are quite transient unless both structures are removed (Schiller et al., 1979, 1980). These findings have been interpreted as evidence of parallel pathways (Schiller et al., 1980; Schiller et al., 1987). It may be the case that the circuitry supporting spatial updating lies somewhere between the two alternatives described here. Remapping may be distributed among multiple regions, but parietal cortex may have the greatest responsibility for this function.

4.3. Remapping influences action and perception

The ability of humans (Hallett and Lightstone, 1976) and monkeys (Mays and Sparks, 1980; Goldberg and Bruce, 1990) to perform the double step task indicates that the saccadic system has access to a dynamically updated representation of visual stimuli. Furthermore, this representation can be used to guide accurate behavior. Access to an updated representation is not limited to the oculomotor system, however, as these targets can also be accurately acquired manually (Hansen and Skavenski, 1985). Together, these findings indicate that the skeletomotor system has access to an accurate representation of target locations that can be used to guide many types of movements. In contrast, the *perceived* location of targets presented around the time of a saccade is often not veridical. If subjects are asked to report verbally the location of a target flashed around the time of a saccade, the perceived location is often inaccurate (Matin, 1965). These conflicting results suggest a dissociation between the perceptual report of target location and the ability to direct an action toward it.

The dissociation between action and perception was later demonstrated in a single experiment (Goodale et al., 1986). Subjects were asked to report, both verbally and

motorically, the location of a target that was displaced during the eye movement. Subjects failed to report the change in target position, as though they did not perceive it, even though both eye and arm movements toward the target location were accurate. Results such as these led to a new hypothesis of the visual system. In contrast to the hypothesis of separate processing streams dedicated to form and motion (Ungerleider, 1982), it was hypothesized that there is, instead, a specialization for action and perception (Goodale and Milner, 1992). Remapping contributes to accurate behavior, but, as we will discuss below, this may be at the expense of accurate perception (Ross et al., 2001; Kusunoki and Goldberg, 2003).

How accurately are targets perceived around the time of saccades? Studies in which subjects are asked to verbally report their perceptions offer mixed results. Targets presented in the 200ms time period beginning before the onset of the saccade appear to be displaced from their actual locations (Honda, 1991; Ross et al., 1997). There are conflicting reports regarding the direction in which targets are mislocalized, however. Some have found that targets presented anywhere in the visual field are mislocalized in the direction of the saccade (Matin, 1965; Cai et al., 1997), as if the entire visual field shifts in the direction of the saccade. Others have found that targets are mislocalized toward the saccade target (Ross et al., 1997). That is, targets presented either proximal or distal to the saccade endpoint appear to be compressed toward the endpoint location. A more recent experiment provides insight into the basis of these differences. Lappe and colleagues studied mislocalization errors under various conditions (Lappe et al., 2000). They found that in total darkness, all mislocalization errors are in the direction of the saccade. In contrast, if visual references are available, there is a compression toward the

saccade endpoint. These findings indicate that multiple signals can contribute to the localization of targets around the time of an eye movement.

Two of our observations on remapping are particularly relevant to the hypothesis that remapping contributes to perceptual mislocalizations around the time of saccades. First, we observed that for some neurons, remapping begins before the onset of the saccade. These neurons can respond at the location where the RF will be after the completion of the saccade ('new RF location'). Other remapping studies indicate that some of these neurons continue to respond at the original RF location ('old RF location') as well (Nakamura and Colby, 2002; Kusunoki and Goldberg, 2003). Around the time of the saccade, then, some neurons show dual responsiveness: they can respond to stimuli at both the old and new RF locations. This dual responsiveness likely contributes to perisaccadic mislocalizations (Kusunoki and Goldberg, 2003).

Second, for some neurons, remapping does not begin until after the onset of the saccade. Across the population of neurons, the remapping latency is quite variable. For many neurons there is a delay associated with computing the updated location of the stimulus. There was evidence of this delay in the population histograms as well. These histograms show that the response to the remapped stimulus trace begins before saccade onset, but the most robust response does not begin until ~100ms after this event. Although the eyes have begun to move to the new target location, the population does not yet respond robustly at the new location. If remapping were instantaneous with the onset of the saccade, we would expect no mislocalization errors. Instead, it takes some time to compute the remapped location, and during this interval, mislocalizations occur.

Psychophysical observations on the timecourse of mislocalizations are similar for both horizontal and vertical saccades (Honda, 1991; Ross et al., 1997). This is consistent with our observations that the timecourse and magnitude of remapping is equivalent across the four cardinal saccade directions, and further supports the idea that remapping contributes to these psychophysical effects. While the primary function of remapping may be to ensure an accurate representation of *stable* objects after saccades, this may come at the expense of perceptual mislocalizations of stimuli flashed only very briefly. Experiments in which perceptual reports and neural activity are monitored simultaneously may shed light on this apparent discrepancy. The major benefit to remapping is that it provides an updated representation of visual stimuli that is available immediately after the saccade, without the delay required if the brain had to rely only on a reafferent visual signal.

4.4. The brain must account for all types of movements

The need to keep track of movements is not limited to saccades. The brain must keep track of all movements generated. There is a large body of literature on saccadic updating. In comparison, relatively little is known about updating for other types of movements. Below we will discuss two other types of movements: gaze shifts (i.e., movements of both the eye and head) and smooth pursuit eye movements. When the head is free to move, eye and head movements are often coordinated. That eye and head movements are tightly coupled is illustrated by fact that if the superior colliculus is stimulated in an animal free to move its head (termed 'head-free'), movements of both the eye and head are induced (cat: (Roucoux et al., 1980); monkey: (Freedman et al.,

1996)). To date, most experiments exploring the neural basis of updating have studied saccades in animals whose heads are restrained. We will discuss some additional signals that will be important to consider when studying gaze updating. The second type of movement we will consider is smooth pursuit. This is the movement required to track a moving object. As with saccades, it is critical for both perception and behavior that the locations of visual targets are updated in conjunction with these movements.

Gaze shifts

Behavioral studies indicate that visual locations are updated during gaze shifts. If a target is flashed before a gaze shift, subjects can accurately acquire the target with a saccade or a reach (Henriques et al., 2002; Herter and Guitton, 1998; Smith and Crawford, 2001). How are gaze shifts updated? There are at least two neural signals that may be especially important to consider during gaze updating: vestibular and orbital modulation signals.

Behavioral and physiological studies provide evidence that updating can be based on vestibular signals. Humans and monkeys can update spatial locations following passive rotations of the body (Israel et al., 1999; Baker, 2002; Baker et al., 2003; Klier, 2004). In these experiments, the eyes and head remained fixed. The fixation point moves with the animal, so the vestibulo-ocular reflex is suppressed. Corollary discharge and neck proprioceptive signals are also unavailable, so subjects must rely on vestibular information to compute the updated location. Spatial updating is quite accurate in these conditions, indicating that vestibular information alone can be used to compute the updated location of visual stimuli (Israel et al., 1999). Physiological studies indicate that

LIP is involved. Neurons in LIP can use vestibular information to update spatial locations during passive rotations of the body (Powell, 1997; Baker et al., 2003). The ability to update during both components of a gaze shift suggests that LIP may have a particularly important role in gaze updating.

Neurons in various cortical areas, including LIP, have visual responses that are modulated by eye position (Andersen and Mountcastle, 1983; Andersen et al., 1985; Galletti and Battaglini, 1989; Andersen et al., 1990c; Galletti et al., 1991). That is, the strength of the visual response is dependent on where the animal is fixating. For example, a neuron may have a receptive field (RF) located 10 deg above the fovea. When the animal is fixating centrally, the neuron fires 5 spikes/s when a visual stimulus is placed in its RF. If the animal fixates at an eccentric location, say 20 deg to the right, the visual response may be twice as large, or 10 spikes/s. Thus, the visual response is modulated by the position of the eye in the orbit. Orbital modulation is defined as a 'gain field' because it can be described by multiplying the retinal visual response by eye position (Andersen et al., 1985).

This eye position signal can be combined with retinal information to code the locations of visual stimuli relative to the head. It is possible, then, that this signal will be important for updating target locations in conjunction with gaze shifts. Interestingly, some neurons in LIP have gain fields that are aligned with the retinal receptive field, while others have gain fields that are opposite the receptive field (Andersen et al., 1990c). Recent modeling experiments suggest that those with aligned fields may be particularly important for coding the locations of targets in head-centered coordinates (Xing and Andersen, 2000). Studying the activity of these neurons in conjunction with gaze shifts

may provide insight into the neural basis of updating target locations in conjunction with head movements.

We expect that in LIP, remapping will be robust following any change in gaze. This claim is based on three findings. First, locations can be accurately updated following head movements in any plane (Smith and Crawford, 2001; Medendorp et al., 2002). Second, across the population of neurons in LIP, there is no bias in the direction of gain fields (Andersen et al., 1990c). Third, we found no anisotropies for saccadic updating. Because saccades are a critical component of gaze shifts, a comparison of saccadic and gaze remapping would be especially informative. This comparison would allow for a dissociation of signals related to eye and head movements.

Smooth pursuit

Monkeys can make accurate saccades to targets flashed briefly during both horizontal and vertical pursuit movements (Schlag et al., 1990; Baker et al., 2003). Thus, the displacement of the eye during smooth pursuit can be taken into account in order to acquire a visual target of interest. Studies in LIP indicate that in addition to its role in saccadic updating, it is also important for updating in conjunction with smooth pursuit (Powell, 1997; Baker et al., 2003). We predict that in LIP, updating in conjunction with both vertical and horizontal smooth pursuit eye movements should be equally robust. This is based on two observations. First, we observed no anisotropies associated with saccadic updating. Second, behavioral studies show that locations are updated in conjunction with both vertical and horizontal smooth pursuit movements (Baker, 2002; Baker et al., 2003). A comparison of remapping activity during smooth pursuit and

saccades revealed that in LIP, remapping is less robust during smooth pursuit than during saccades (Baker et al., 2003). This suggests that the neural circuitry involved in updating during these two situations is different. As we will discuss below, areas MST and VIP may also be involved in smooth pursuit updating. Both areas are situated in the dorsal visual stream and interconnected with LIP (Lewis and Van Essen, 2000).

MST is active in conjunction with smooth pursuit eye movements (Newsome et al., 1988) and is involved in visual motion processing (Komatsu and Wurtz, 1988). Thus, although MST has not yet been studied during smooth pursuit updating, we suggest it may play a role. Furthermore, the pursuit response relies on extra-retinal input: these neurons continue to respond during pursuit even if the visual target is extinguished (Newsome et al., 1988). The extra-retinal input may be either a corollary discharge or a proprioceptive signal related to the generation of the smooth pursuit movement. The combination of visual and extra-retinal signals in MST could be used to provide information about the spatial relationships between the subject and the environment (Newsome et al., 1988). Interestingly, in most MST neurons (75%), the preferred directions for visual motion and pursuit are in opposing directions (Komatsu and Wurtz, 1988). This information may be useful for discriminating between motion of an object in the visual scene and self-induced motion. Together these observations indicate that MST may be involved in updating spatial locations during smooth pursuit eye movements.

A second area that may contribute to updating during pursuit is the ventral intraparietal area (VIP), located at the fundus of the intraparietal sulcus. Like MST neurons, VIP neurons also respond to visual motion and smooth pursuit (Colby et al., 1993b). Information about visual motion is likely conveyed to VIP through connections

with area MT (Maunsell and Van Essen, 1983b). All pursuit directions are equally represented, and, as in MST, this pursuit activity is provided by extra-retinal signals (Gabel et al., 2002; Schlack et al., 2003). In VIP, the relationship between preferred direction for smooth pursuit and visual motion is less precise than in MST (Schlack et al., 2003). One interesting property of VIP neurons is that they code the locations of targets in head-centered coordinates (Duhamel et al., 1997). That is, stimulus location is coded independently of the direction in which the eyes are looking. VIP has available the signals necessary to create a stable representation of target location relative to the head. Specifically, a stable representation could be created by subtracting the motion signal caused by the eye movement from the signal generated by the target (Schlack et al., 2003). It is worth noting that the head-centered representation in VIP stands in contrast to the eye-centered representation found in LIP (Colby, 1998).

Although the response properties in MST and VIP are similar, they may play different roles in updating in conjunction with smooth pursuit movements. In particular, MST may update a representation of the stimulus location in eye-centered coordinates while VIP updates in head-centered coordinates. The availability of an updated representation in each coordinate frame is useful for guiding different types of movements. An eye-centered coordinate frame is useful for guiding subsequent eye movements while a head-centered coordinate frame could be used for guiding movements of the head or mouth toward a target of interest (Colby, 1998).

4.5. Conclusions

The results of our experiments lead to two broad implications about spatial updating in the primate brain. First, our finding that spatial updating in parietal cortex is effectively independent of saccade direction implies that remapping can contribute to the maintenance of spatial constancy throughout the visual field. Second, our finding that across-hemifield remapping does not require the forebrain commissures indicates that a distributed network of regions supports spatial updating. The involvement of multiple redundant circuits reinforces the idea that updating is an important neural mechanism for generating stable spatial representations.

APPENDIX A

General Methods

General Procedures

Subjects

Subjects were four adult rhesus macaques, three male and one female, weighing 6.5-7.5 kg. All experimental protocols were approved by the University of Pittsburgh Institutional Animal Care and Use Committee, and were certified to be in compliance with guidelines set forth in the Public Health Service Guide for the Care and Use of Laboratory Animals.

Surgical Procedures: commissurotomy

For the animals used to assess spatial updating in the absence of the forebrain commissures (Chapter 3), a commissurotomy was performed at the outset of the experiment (Vogels et al., 1994). The monkeys were prepared for this surgery with dexamethasone, and anesthesia was induced with ketamine and maintained with isoflurane. Mannitol was administered throughout the surgery to minimize tissue swelling. During the following two weeks, analgesics were given to control postsurgical pain, and antibiotics were administered daily to prevent infection. Additionally, the monkey's health and behavior were closely monitored for signs of epileptiform activity or subdural swelling, and additional drugs were administered as needed to counteract these effects. The animals recovered fully before undergoing surgical preparation for behavioral training and subsequent recording.

Surgical Procedures: preparation for physiological recording

All animals underwent two surgeries to prepare them for chronic recording. In the first surgery, scleral search coils were implanted for monitoring eye position, and head restraint bars were affixed for the purpose of holding the monkey's head stable during testing sessions. Following completion of behavioral training, monkeys underwent second surgery to install a chamber for recording from area LIP. For the split-brain animals, recording began 14-21 months after the commissurotomy. The placement of the recording chamber was determined using 1) the standard stereotaxic locations for area LIP (5mm posterior and 12mm lateral in Horsley Clarke coordinates) and 2) anatomical information from structural magnetic resonance images. Surgical procedures are described in Nakamura and Colby, 2002.

Stimuli

During recording sessions, the monkey sat in a darkened room with its head fixed in a primate chair, facing a tangent screen 25 cm away. The screen subtended 100 deg horizontally and 75 deg vertically. Visual stimuli were back-projected on the tangent screen using a LCD projector. Stimulus presentation was under the control of two computers running a C-based program, CORTEX, made available by Robert Desimone at the National Institutes of Mental Health.

Measurement of stimulus decay

It these experiments, was critical that the to-be-updated stimulus had disappeared before the monkey initiated the saccade away from central fixation. We measured the phospho-persistence of the stimulus and determined the psychophysical threshold for each monkey, in order to ensure that the stimulus was perceptible only when the eyes were at central fixation. The stimulus did not vanish instantaneously when it was turned off, but decayed with a measurable time constant. We calculated the luminance threshold for each monkey in the memory guided saccade task, using a staircased design. We determined that the stimulus used in the remapping tasks was below perceptual threshold within 40ms of its offset for all monkeys. The monkeys typically initiated the saccade with a latency of 183ms (+/- 12 ms s.d.). Taken together, these observations show that the stimulus could not drive the response in the single step task.

Saccade data

Eye position was monitored using scleral search coils (Judge, 1980). Eye position was sampled at 250 Hz (initial behavioral testing of monkey EM; physiological testing of both monkeys) or 100 Hz (initial behavioral testing of monkey CH). Eye data were stored for offline analysis, along with CORTEX event markers, which indicated when stimuli appeared and were extinguished.

For all experiments, saccades were identified on the basis of velocity criteria, using a custom-written MATLAB program. The beginning of the saccade was defined as the timepoint when velocity exceeded 50°/sec. The end of the saccade was defined as the timepoint when velocity fell below 20°/sec. The program used additional spatial and temporal criteria to ensure that each saccade was identified correctly. The accuracy of saccade identification was verified by the experimenter. Saccade latency was defined as the difference between the time of the beginning of the saccade, relative to the time when central fixation was extinguished.

Behavioral paradigms

Memory guided saccade task. We used the memory guided saccade task (MGS) to search for neurons and assess their visual, memory and saccade-related response properties. In this task, the monkey initially maintained fixation on a central fixation point. After a random delay of 300-500 ms, a stimulus flashed in the receptive field for 50 ms. After a second delay of 400-800 ms, the fixation point was extinguished, cueing the monkey to make a saccade to the location of the flashed stimulus. After the saccade, the stimulus re-appeared and the monkey maintained fixation on it for an additional 300-500 ms.

To determine the location of a neuron's receptive field, we tested various stimulus locations and defined the location of the receptive field as that which gave the strongest visual response. For initial mapping of the receptive field, MGS targets were presented in eight canonical directions, in three concentric rings of increasing amplitude. For example, if the 'base amplitude' was set to 10º, targets appeared in each direction at distances of 10º, 20º, and 30º, yielding 24 targets total. We adjusted the base amplitude as needed in order to identify the location of best responsiveness. In general, we focused the initial mapping in the contralateral hemifield, using a base amplitude of 8 º.

Saccade control task. This task was used to demonstrate that activity in the single step task could not be attributed to the generation of the saccade. The timing of the task was identical to the single step task, except that no peripheral stimulus was presented. The monkey maintained fixation of the initial FP1 for 300-500 ms, after which T1 was illuminated. 50 ms later, FP1 was extinguished, cuing the monkey to make a saccade to T1. The monkey was required to fixate T1 for 500-700 ms.

Stimulus control task. The stimulus control task was used to ensure that the stimulus location used in the single step task was outside of the receptive field and did not drive the neuron. In this task, the monkey maintained central fixation for 300-500 ms. The peripheral stimulus was flashed for 50 ms, and the monkey was required to maintain fixation for an additional 1200-1500 ms. The trial was aborted if the monkey broke fixation at any time.

We collected 12-20 trials for each trial type. The different tasks were run in separate blocks of trials, and always in the same order: stimulus control, saccade control and single step. We collected data in this order because previous experiments have demonstrated that long-term inter-trial memory responses can persist after experience with the single step task (Umeno and Goldberg, 2001). Of critical importance is that the conditions of interest (four saccade directions in Chapter 2; within and across conditions in Chapter 3) were always randomly interleaved in each block of tasks.

Physiological recording

Neural activity was recorded using tungsten microelectrodes (FHC) introduced into the cortex through stainless steel guide tubes placed flush with the dura. The guide tubes were stabilized by a nylon grid (Crist Instruments) held rigidly in the recording chamber. Action potentials were amplified and filtered with a band-pass of 500 Hz to 5 kHz, and digitally sampled using template matching at 20 kHz. The template matching system was SPS-8701 (Signal Processing Systems).

Identifying area LIP

We used the following procedure to identify recording sites within the lateral bank of the intraparietal sulcus. In initial recording sessions, we mapped the location of the intraparietal sulcus within the chamber. We systematically recorded from the anterior-most to the posterior-most part of the chamber. We localized the sulcus as the transition from somatosensory responses on the medial bank, to visual responses on the lateral bank. Within the lateral bank, the response properties of neighboring areas 7a and VIP provided additional landmarks for the identification of area LIP. Area 7a is located superficially, and neurons here exhibit broad visual responsiveness and post-saccadic firing (Barash et al., 1991a, b). Area VIP is located in the fundus of the sulcus, and

neurons here exhibit striking selectivity for directional motion (Colby et al., 1993a). Area LIP is located between these two functionally distinctive areas. We identified LIP neurons according to the conjunction of two criteria. First, the depth of the recorded neuron had to be at least 2mm below the cortical surface. Second, the neuron had to respond selectively to contralateral visual stimuli.

Selecting neurons for analysis. Only neurons with a significant visual response in this task were included for analysis. We used the memory guided saccade task to assess the visual responsiveness of neurons. We used a t-test ($p < 0.05$) to compare activity in the 100 ms epoch beginning at the onset of the visual response to baseline activity (100 to 300 ms after achievement of fixation).

Methods specific to the parametric experiment, Chapter 2

Method to determine if the stimulus or saccade alone elicit a significant response

We used the following method to determine if the stimulus or saccade alone elicited a significant response. We used a t-test (one-tailed, $p < 0.05$) to compare activity in a response epoch of the control task to baseline activity (150 to 350 ms after fixation attainment). For the stimulus control task, the response epoch was 100 to 200 ms after the onset of the stimulus. For the saccade control task, the response epoch was -100 to +100 ms relative to the onset of the saccade.

Calculation of divergence time

The response in the single step task can represent activity attributable to three signals: the stimulus, the saccade and the remapped stimulus trace. In order to determine the onset time of the remapped response, we devised a method to disentangle these three signals. We limited our analysis to those samples where the stimulus alone did not produce a significant response. We constructed histograms of the single step and saccade control activity aligned on the onset of the saccade. We determined the onset of the remapped response by computing the time at which activity in the single step task first became significantly greater than (i.e., *diverged from*) that in the saccade control task. To determine this timepoint, we measured the response during a 50ms response window beginning 100ms before the start of the saccade (i.e., -100ms to -50ms relative to saccade onset). We used a t-test ($p < 0.05$) to determine if activity in the single step task was significantly greater than activity in the saccade control task. If there was no significant difference, the response window was shifted up by 10ms and the procedure was repeated until a significant difference was obtained. The midpoint of the first significant bin was considered the Divergence Time. We also used this method to calculate the Divergence Time for the population histograms.

Selection of neurons for analysis of within and across conditions

We put two restrictions on the neurons included in this analysis to ensure that the spatial configuration in the across-hemifield condition required an interhemispheric transfer of visual information. The first requirement was that the stimulus must initially be encoded by neurons in only a single hemisphere. LIP has RFs that can extend ~5 degrees into the ipsilateral visual field (Ben Hamed et al., 2001). Therefore to meet this requirement, the stimulus must be flashed > 5 deg from the midline when the monkey is at the initial

fixation point. We excluded neurons for which this criterion was not met. The second requirement was that the representation of the visual stimulus be moved from one hemifield well into the opposite hemifield (i.e., > 5 deg from the midline). Because we always used a 20 deg saccade, this led to the requirement that the RF be within 15 degrees of the fovea. From our dataset, 159 neurons met these criteria and were included in the analysis.

Methods specific to the split-brain experiment, Chapter 3

Measuring neural latency

We used the method of Nakamura and Colby (2000) to measure neural latency in individual neurons. For the single step task, we were interested in the latency of the remapped response to saccade onset, so we constructed histograms of neural activity aligned on saccade onset. Remapping latencies range from 50 ms before to 250 ms after the onset of the saccade (Umeno and Goldberg, 1997). Therefore, when defining the latency of the remapped response in individual neurons, we looked for the onset of the neural response in the time window from 100ms before saccade onset to 300 ms after saccade onset. To detect when the firing rate first began to differ significantly from baseline firing rate (200-300 ms after attainment of fixation), we measured activity in a 20ms response window beginning 100 ms before saccade onset. A t-test ($p < 0.05$) was used to asses whether activity in the response window differed significantly from baseline activity. If there was no significant difference, the window was shifted up by 2 ms, and the procedure was repeated until the activity in the response window was significantly greater than baseline activity. In order to avoid spurious results, we defined latency based on the time of occurrence of the first of two consecutive bins that achieved significance. The midpoint of the first bin was considered the onset of the neural response. If this criterion was not met by any bins up to 300 ms after saccade onset, we concluded there was no response associated with remapping the stimulus trace. In all cases, the calculated latency was verified by inspection. Neural latency can only be reliably defined with this method if we are certain that all of the activity present in the single step task is attributable to remapping the stimulus. Therefore, if there was any significant activity in the saccade control associated with a particular single step condition, we excluded that condition from this particular analysis. We used an analogous method to determine the visual response latency in the memory guided saccade task.

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