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Contributions of the Lateral Intraparietal Cortical Area to
Smooth Pursuit Eye Movements

by

John O'Leary

DISSERTATION

Submitted in partial satisfaction of the requirements for the degree of

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Abstract

We use the information we receive through our senses to guide our movements. Our daily lives are full of far more sensations than we want to act upon, however, so it is essential that our brain can direct the right parts of our sensory experience to our motor systems. This thesis explores how the brain might control how strongly a visual input affects action in the context of smooth pursuit and saccades, which are the eye movements we use to keep a moving object in our high-resolution center of vision. I explored the hypothesis that area LIP is involved in the control of smooth pursuit by recording from the area while monkeys followed moving targets. I found that the trial-to-trial fluctuations of LIP firing rate and pursuit velocity were correlated. This “LIP-pursuit correlation” was present for pursuit both before and after the saccade. The correlation with postsaccadic pursuit velocity could not be explained away when metrics of the saccade were included as control variables. The LIP-pursuit correlation was not present when the target appeared outside the receptive field of the neuron under study. Variability in the strength of the LIP-pursuit correlation was predictable from the average firing rates at the end of the saccade. Meanwhile, one monkey performed another task in which the target did not move. In this task, there were nonetheless small postsaccadic eye movements known as “glissades”, and LIP activity was also correlated with these glissades. Taken together, these results suggest that LIP is involved in the guidance of pursuit eye movements. I conclude by discussing what sort of role LIP could be playing in the pursuit system, and speculate that it could be either encoding features of the motion

such as direction or speed or it could be setting a gain that determines how strongly visual motion at a spatial location is converted to an eye movement.

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Chapter 1: Introduction

Imagine standing at the corner of Market Street and Van Ness Avenue in San Francisco during a weekday rush hour. Most likely, you would be bombarded with sensory input. You'd probably catch smells from the nearby donut shop, hear conversations of passers by, and watch car after car head to or from US 101. Of all these sensations, you would probably only care about a small fraction. For example, you might follow the movements of a red car to determine if it is your friend coming to pick you up, while trying to “tune out” everything else you see. Our brains have the highly useful ability to prioritize sensory information. We don't have to treat all inputs equally, but rather can guide action with some, focus on others with attention, and ignore the rest. In this thesis, I explore the ability of the brain to flexibly use sensory data in the context of eye movements, with a particular focus on the lateral intraparietal cortical area and smooth pursuit movements.

Animals with foveae need to point their eyes at whatever they wish to see clearly. When that object of interest is moving, primates use two distinct classes of eye movement, smooth pursuit and saccades, to keep the target object in the high-resolution center of vision. Saccades are rapid jumps that are programmed based on the difference in the initial and desired positions of the eyes. Typical saccade latencies after an unexpected change in the position of the target are around 200 ms, and typical durations and peak eye velocities for moderate-sized (10°) saccades are 50 ms and $250^\circ/\text{s}$ (Leigh and Zee, 2006). Smooth pursuit, meanwhile, is a slower “tracking” eye movement that is driven by the velocity, rather than position, of the target (Rashbass, 1961). A shorter latency

movement, it typically begins about 100 ms after the onset of motion (Leigh and Zee, 2006). Unlike saccades, which are planned and then executed in a ballistic fashion, ongoing smooth pursuit is continuously modified based on visual feedback. While smooth pursuit responses have been found in response to motion of up to 150°/s, the gain of pursuit is generally highest for motions of 30°/s or less (Lisberger and Westbrook, 1985).

The dynamic transformations of visual motion into smooth pursuit

There is an ever-growing body of evidence that the smooth pursuit system does not simply transform visual motion into an eye movement in a fixed manner. Rather, it can make flexible use of the motion we see, turning identical visual stimuli into different pursuit commands depending on behavioral context. The system seems principally to execute such selective control over the transformations of vision into action by adjusting gains that determine how strongly a given motion stimulus drives pursuit. For example, evidence for one form of pursuit “gain control” was discovered by perturbing the motion of a target with brief pulses of motion while it moved at different baseline speeds (Schwartz and Lisberger, 1994). It was found that the gain of the monkey’s response to the same perturbation grew as a function of the underlying pursuit speed.

Another important line of research that is relevant to pursuit gain control has shown that saccades can modulate the strength of the visuomotor transformation for pursuit. When a moving target is relatively far from the fovea, the initial pursuit response is much slower

than the target velocity. Lisberger (1998) showed that when a monkey then makes a saccade to the target, the pursuit response after the saccade is much stronger, and in most cases matches the target velocity well (Figure 1-1). Since accurate pursuit began *immediately* after the saccade—rather than one latency of the pursuit system later—and pursuit was much weaker when a monkey did not make a saccade by a given time than when he did, the author argued that the visual motion that drives postsaccadic pursuit exists in the brain before the saccade, and that the saccade results in an increase in the gain on the transmission of that motion to the pursuit system. The understanding of how saccades influence pursuit gain was subsequently refined by experiments in which the target jumped to a new position while the saccade was in progress (Schoppik and Lisberger, 2006). These experiments demonstrated that target motion has progressively less influence on pursuit the farther it is from the endpoint of the saccade, suggesting that a “spotlight” of limited spatial scale follows the eyes around and increases pursuit gain only for visual motion that falls underneath it.

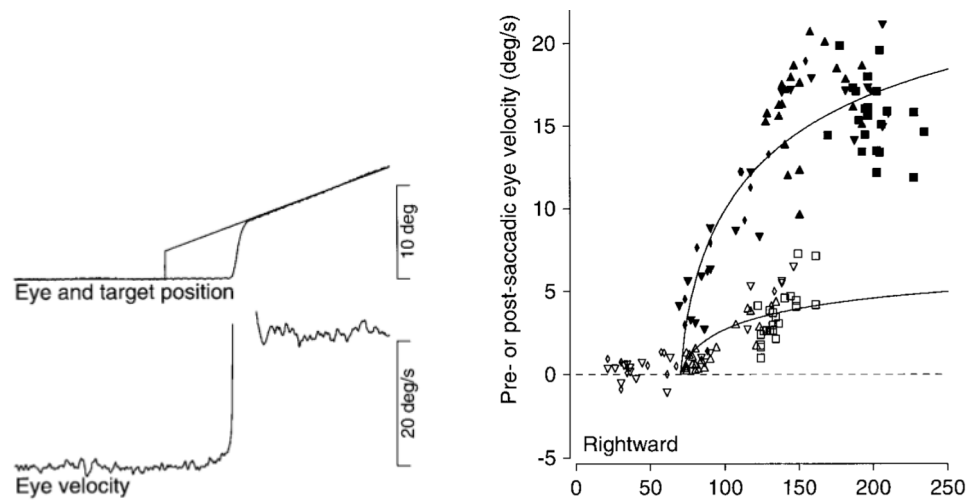


Figure 1-1

Evidence for the enhancement of pursuit by saccades. Left panel: eye and target position (top) and eye velocity (bottom) for one pursuit trial. The large sudden deflection in a the bottom panel represents a saccade. Right panel: Symbols represent the eye velocity on individual trials before (open) and after (filled) the monkey had made a saccade. Eye velocities are plotted as a function of how along after the onset of target motion the measurements were taken. (Adapted from Lisberger, 1998)

The pursuit system's flexibility in the face of visual motion has also been demonstrated in tasks where subjects choose between two moving targets. In experiments where both targets are identical and there is no instruction to follow a particular target, the initial pursuit response follows the average of motion vectors of the two targets (Lisberger and Ferrera, 1997; Gardner and Lisberger, 2001). By contrast, when a cue such as color or motion is used to indicate which target should be pursued, subjects can modulate their pursuit initiation so that it follows the motion of one target much more than the other (Ferrera and Lisberger, 1995; Garbutt and Lisberger, 2006; Shichinohe et al., 2009). In addition, it has been shown that saccades can act as a potent selection signal in these two

target pursuit tasks. In a study where monkeys were allowed to freely choose one of the targets, pursuit switched immediately after a saccade to the chosen target from the initial averaging mode to selectively being driven by the motion of that target (Gardner and Lisberger, 2001). The effect of the saccade on pursuit this task was very similar to that when only one target is present, and it is likely that saccades invoke use same mechanism of gain control in both situations.

Neural circuitry underlying basic sensorimotor transformations for pursuit

At the same time as the complexity of the smooth pursuit behavior has been uncovered, there has been a parallel expansion in the set of brain areas that are thought to play a role in pursuit. An early imagining of the “pursuit circuit” in monkeys included just a few brain areas and largely focused on the roles of those areas in the basic transformation of visual motion into pursuit motor commands (Lisberger et al., 1987). Since the skeleton laid out then remains in place in today’s view of pursuit anatomy (Figure 1-2), it should be reviewed. Smooth pursuit begins with vision, so the signals that drive pursuit first emerge from the retina. From there they pass through the lateral geniculate nucleus and striate cortex, and end up at the start of the traditional heart of the pursuit system, area MT. There is good reason to believe that MT is the main source of visual motion signals for pursuit: The firing of MT neurons is tuned to motion directions and speeds to which the pursuit system responds (Albright, 1984; Lisberger and Movshon, 1999), lesions of MT greatly impair pursuit (Newsome et al., 1985), and microstimulation in MT can elicit

and modify pursuit movements (Komatsu and Wurtz, 1989; Groh et al., 1997; Carey et al., 2005).

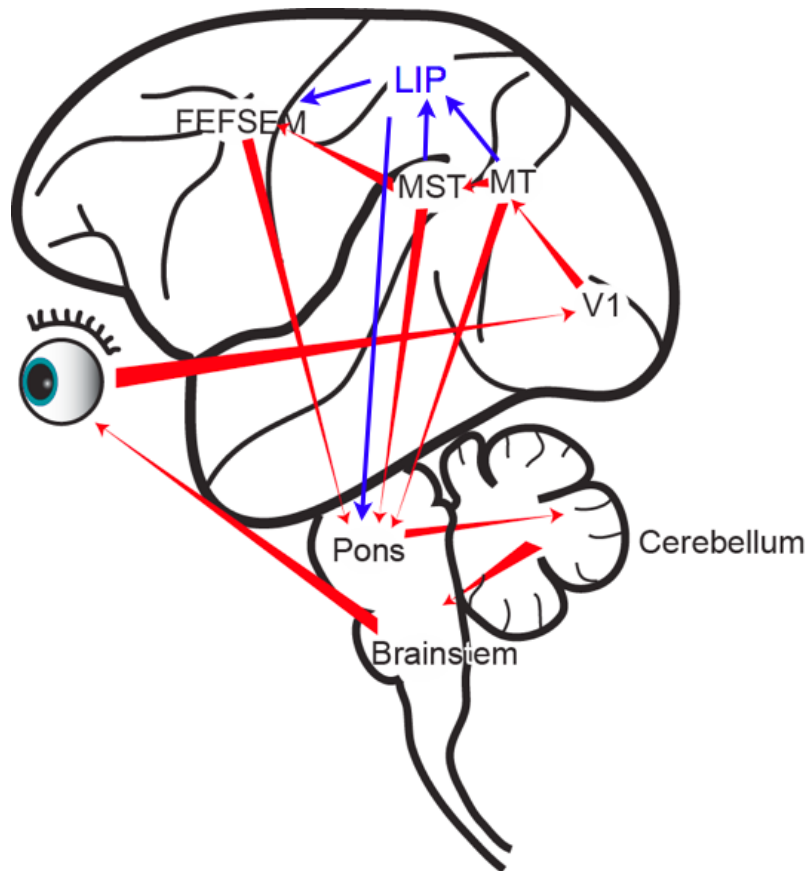


Figure 1-2

A diagram of part of the pursuit circuit. Areas which seem to play a fundamental role in the basic pursuit behavior are shown in black. Feed-forward connections between areas are depicted as arrows. Area LIP and its connections are also represented and colored blue. (Picture courtesy Jennifer Li)

The next stop on the classic pursuit pathway is area MST, which also contains an abundance of cells tuned to the direction of visual motion (Desimone and Ungerleider, 1986; Tanaka et al., 1986). The exact role of MST in pursuit has remained much less clear than that of MT, but it has been proposed that MST is more involved in the maintenance of ongoing pursuit, given that lesions (Dursteler and Wurtz, 1988) and

microstimulation (Komatsu and Wurtz, 1989) have greater effects after the initial phase of pursuit. Further support for this idea comes from MST recordings during pursuit maintenance: Unlike in area MT, many cells in this area maintain their firing when the pursuit target momentarily disappears, which suggests that their discharge can represent the pursuit movement itself (Newsome et al., 1988).

The visual motion signals from MT and MST are thought to next pass through the dorsolateral pontine nucleus (DLPN). Lesions of this nucleus cause deficits in both the initiation and maintenance of pursuit (May et al., 1988), and neurons located there respond in relation to a mix of visual motion and eye movement signals (Suzuki and Keller, 1984; Suzuki et al., 1990; Ono et al., 2005). After the DLPN, the pursuit command is developed further in the floccular complex of the cerebellum. By this stage, the responses of individual neurons encode the kinematics of the eye movement fairly reliably, suggesting that the nature of the upcoming movement is largely determined (Shidara et al., 1993; Medina and Lisberger, 2007). Finally, the output of the cerebellum travels to the brain stem, which generates the appropriate commands to the muscles that move the eyes.

Adding pieces to the pursuit puzzle: FEF and SC

In the years since this description of the pursuit circuit as a relay from parietal motion areas to the pons to the cerebellum, research has implicated several other brain areas in the control of pursuit. Notably, some of this work has suggested that these other areas

might underlie the different ways, discussed above, in which the pursuit system can make selective use of visual motion. First, neurons were found in the frontal eye fields (FEF), classically a saccadic structure, that discharged in relation to pursuit movement, and it was shown that microstimulation in some parts of FEF can elicit smooth eye movements (MacAvoy et al., 1991; Gottlieb et al., 1993; Gottlieb et al., 1994). (There has been some inconsistency in the nomenclature in discussion of this area; I will refer to the portion of FEF that is related to saccades as FEF_{SAC} and that which has been tied to pursuit as FEF_{SEM} .) Subsequently, Tanaka and Lisberger demonstrated that microstimulation in FEF_{SEM} during fixation dramatically increased the size of the pursuit movements monkeys made in response to pulses of visual motion (Tanaka and Lisberger, 2001, 2002). The authors argued that the FEF_{SEM} stimulation was increasing the same pursuit gain that varies with the speed of ongoing pursuit, and thus that one of the roles of FEF_{SEM} is to act as a gain controller for pursuit.

Meanwhile, Krauzlis and others have been gathering evidence that the superior colliculus (SC) is involved in smooth pursuit. Neurons in the rostral portion of the SC, which have been traditionally associated with fixation and small saccades, also discharge during smooth pursuit (Krauzlis et al., 1997, 2000). More interestingly, in a task where monkeys had to choose between two targets using pursuit, target choice was predictable in advance of movement from the activity of rostral SC neurons and could be biased by microstimulation below the threshold that evoked a saccade (Krauzlis and Dill, 2002; Carello and Krauzlis, 2004).

The stimulation results of Carello and Krauzlis stand in contrast with similar attempts by Gardner and Lisberger (2002) to influence target choice with electrical stimulation in a two-target task. These authors found that suprathreshold stimulation in both the FEF_{SAC} and SC consistently resulted in the target at the endpoint of the evoked saccade being chosen for pursuit, solidifying the link between saccades and pursuit target choice. When they attempted to influence presaccadic target choice by stimulating below threshold in the FEF_{SAC}, however, they failed to find an effect. There were some differences between these studies that may explain different effects of subthreshold stimulation on presaccadic target choice were found: First, Gardner and Lisberger did not attempt subthreshold stimulation in the SC. Although the FEF_{SAC}, where they did stimulate, projects strongly to the SC (Leigh and Zee, 2006), these results taken together may have revealed differential roles for these two areas. Second, in the Carello and Krauzlis task, the monkeys had to identify the correct target based on a prior cue, while in the Gardner and Lisberger task the two targets were the same and the monkey's task was to freely choose between them. It may be that these structures only come into play when there is a visual search or discrimination component to the task. Finally, motion directions were always radial relative to the fixation point in the task where stimulation was ineffective, whereas the targets moved along the horizontal axis in the Carello and Krauzlis task. Ferrera (2000) found that monkeys could better modulate their presaccadic pursuit in two target tasks when motion was in that configuration instead of radial.

Is LIP also a part of the pursuit circuit?

Given that the FEF and SC, two areas traditionally associated with the control of saccades, have now been implicated in the control of pursuit as well, it is worth considering if any other saccadic areas also have a pursuit function. I thus decided to turn to the lateral intraparietal area (LIP), and ask whether it too is involved in pursuit control. Along with the FEF and the SC, area LIP is generally regarded as one of the main brain areas involved in the high-level control of saccadic eye movements (Tehovnik et al., 2000; Glimcher, 2003). Unlike in the adjacent area 7a, many neurons in LIP exhibit an increase in firing rate prior to the onset of saccades (Barash et al., 1991), and microstimulation in LIP can evoke saccades (Thier and Andersen, 1998). Anatomically, LIP is well-situated to play a role in pursuit and saccades, in that it receives input from many visual cortical areas (Andersen et al., 1990) and projects to the FEF and the SC (Lynch et al., 1985). Importantly for a possible role of the area in pursuit, the visual areas that project to LIP include MT and MST.

The exact function of LIP has been a subject of debate for many years. One group of researchers has held that it should be viewed foremost as a place where eye movement plans are developed (Andersen et al., 1997). Their position arose after studies of LIP cells during the memory saccade task. It was found that neurons exhibited activity that could be attributed to vision, memory, and saccade initiation; these different types of activity were interpreted as the stages of an “intention” to make a visually guided saccade (Gnadt and Andersen, 1988; Barash et al., 1991). A different line of research has focused on the

possible role of LIP in representing the salience of a visual stimulus and controlling spatial attention. When a monkey makes a saccade that brings a target into the visual RF of a neuron, its response depends on how recently that target appeared on the display (Gottlieb et al., 1998). A target that appeared recently, and is thus more salient, elicits a much larger response than a target that has been on the screen for a while. Bisley and Goldberg (2003, 2006) found that monkeys could more accurately perceive a low-contrast stimulus when the neurons that represented its location were firing most. Since spatial attention is operationally defined as an increase in contrast sensitivity, they concluded that an “attentional spotlight” follows the peak of LIP activity.

Another view of LIP has been promoted by Shadlen and colleagues, who have recorded extensively from the area while monkeys decide in which direction a noisy visual stimulus is moving and indicate their decision with a saccade. In this task, the firing rate of many LIP neurons gradually increases on trials when the monkey eventually decides to make a saccade into its RF, and decreases when the monkey is going to look away (Shadlen and Newsome, 2001; Churchland et al., 2008). When the difficulty of the decision is varied by adding noise to the stimulus, the firing rate increases more slowly for higher levels of noise. For all noise levels, however, the firing rate eventually reaches the same level by the time the saccade starts, as if the activity level needs to cross a threshold first (Roitman and Shadlen, 2002). The dominant interpretation of these results has been that LIP activity reflects an ongoing decision process, with neurons acting as integrators of evidence in favor of a choice that is made when the evidence exceeds a bound (Gold and Shadlen, 2007). Still another angle has been added by studies of LIP in

decision-making tasks where the size of the reward given to the monkey for making a saccade to a target is varied. When a monkey knows that making a saccade to a target will result in a relatively large reward, LIP firing rates during the decision are higher (Platt and Glimcher, 1999). Based on this finding, it was concluded that LIP represents the relative value of choices.

LIP has thus been ascribed multiple functions, and it seems increasingly unlikely that just one of the interpretations of its activity will turn out to be correct. Instead, LIP probably plays several roles in perception and behavior. Perhaps the main participants in the “intention vs. attention” recognize this, as they seem to have moderated their positions over the years. A recent review that argues for a primarily intentional function of LIP concedes that it probably has an attentional role as well (Andersen and Cui, 2009), and a review from those on the attention side proposes that LIP activity is a “priority map” that is used to guide either spatial attention or saccades (Bisley and Goldberg, 2010). Additionally, some of the different takes on LIP can be reconciled with each other with little difficulty. A decision as made in the task of Shadlen and others is ultimately the selection of a saccade plan. If a monkey knows that making a saccade to a target will yield a higher reward, he will likely place a higher attentional priority there.

Regardless of whether LIP activity is ultimately more about intention, attention or something else, the research done so far on the area has given us ample reason to suspect that it may have a role in controlling smooth pursuit. Connections can be made between nearly all of the proposed functions of LIP and some facet of pursuit behavior, which

raises the possibility that the pursuit system may make use of the area as well: Spatial attention is thought to be implemented in the brain as increases in the gain of neurons that represent sensory signals (Reynolds and Chelazzi, 2004). If LIP controls attention in perceptual tasks by increasing sensory gains, it may be also involved in regulating gain for pursuit. The proposal that LIP controls the intention to move also points toward a role in pursuit gain control, considering the tight relationship between saccades and how strongly visual motion affects pursuit. Finally, the decision view of the area provides reasons to investigate whether it has a pursuit function: Choices developed there may be carried out by either eye movement system.

Additionally, there is already some evidence that LIP contains neurons that respond during pursuit. Early studies of the inferior parietal lobule identified “tracking neurons” that increased their firing during pursuit movements (Lynch et al., 1977). However, since this work was done before the identification of the distinct areas that are today considered to make up this region, it is unclear which of these neurons were actually recorded in LIP rather than MST or area 7a. More recently, Bremmer and colleagues (1997) reported a moderate number of pursuit-responsive neurons that they anatomically verified to be in LIP. There have been no further reports of similar neurons in LIP or of failed attempts to find them. The study of Bremmer et al. left open the question of whether the pursuit responses they observed were truly related to the pursuit behavior or just to the visual or saccadic responses of the neurons they studied.

In light of the foregoing context, I decided the properties of LIP during smooth pursuit deserved further investigation. Chapters 2 and 3 document my main experiments, in which monkeys performed a combined saccadic and smooth pursuit task while I recorded their behavior and the responses of LIP neurons. I found that the neural responses I recorded were related to pursuit velocity on a trial-by-trial basis. In my conclusions, I propose that these results are the strongest evidence yet for an LIP-pursuit link and suggest avenues for future exploration of the issues raised in this thesis.

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Chapter 2: Linking LIP Activity to Smooth Pursuit

Introduction

We only use a small fraction of our sensory experience to guide our movements. When a quarterback in American football drops back for a pass, his visual system tracks the movements of 21 other players, the flashbulbs of the reporters, and the video on the JumboTron. Eventually, just one of those visual images will represent his intended receiver, and the quarterback must determine how to throw the ball based on the motion of that player alone, while ignoring the rest. If we are to understand sensorimotor integration, we need to understand this process: That is, we need to uncover how the brain selects a subset of sensory inputs to drive movement and modulates their transmission to motor systems.

These issues of selection and modulation are faced by the smooth pursuit eye movement system (Krauzlis, 2004; Lisberger, 2010). The pursuit system appears to have multiple mechanisms for regulating how strongly a given visual motion drives pursuit. Making a saccade to a moving target profoundly increases the responsiveness of the pursuit system to that target's motion, as if a gain has been turned up for a portion of visual space (Lisberger, 1998; Schoppik and Lisberger, 2006). When there are two targets on a video screen, subjects can either track either the average of their motion vectors (Lisberger and Ferrera, 1997; Gardner and Lisberger, 2001) or choose to favor one target over the other

(Carello and Krauzlis, 2004; Garbutt and Lisberger, 2006; Shichinohe et al., 2009). Additionally, what may be a separate gain on visual motion is set by the speed of the eyes during ongoing pursuit (Schwartz and Lisberger, 1994).

In this work, we sought to add to existing knowledge about the neural circuitry that enables the pursuit system to turn select visual motion inputs into movement. It is widely believed that monkey area MT provides the sensory representation that is used for pursuit (Newsome et al., 1985; Groh et al., 1997). When a saccade to a moving target is elicited by microstimulating in the saccadic portion of the frontal eye fields (FEF_{SAC}) or the superior colliculus (SC), subsequent pursuit is guided by the motion of the target (Gardner and Lisberger, 2002). Microstimulation in the smooth eye movement region of the FEF (FEF_{SEM}) increases the responsiveness of pursuit to pulses of motion (Tanaka and Lisberger, 2001). Meanwhile, in a task a monkey must choose between two targets, microstimulation in the SC below the threshold where saccades are evoked leads to the choice of the target in the movement field of the stimulation site for pursuit (Carello and Krauzlis, 2004), and the activity of single SC neurons predicts pursuit target choice (Krauzlis and Dill, 2002). A natural companion to these areas is the lateral intraparietal area (LIP). LIP is anatomically connected to MT, FEF_{SAC} , FEF_{SEM} and SC (Andersen et al., 1990; Tian and Lynch, 1996; Leigh and Zee, 2006), and has been implicated in the control of saccades (Barash et al., 1991), spatial attention (Bisley and Goldberg, 2006), and decision making (Shadlen and Newsome, 2001; Hanks et al., 2006)—three aspects of behavior that can be connected to the pursuit system’s ability to selectively use visual motion for movement guidance. LIP has been little studied in the context of pursuit eye

movements, but there is already some evidence that it could play a role in their guidance (Lynch et al., 1977; Bremmer et al., 1997).

We addressed the question of whether LIP is involved in smooth pursuit by recording the activity of neurons while monkeys performed a mixture of saccades and smooth pursuit. In our data, we found correlations between trial-by-trial fluctuations in the activity of single neurons and the pursuit response both before and after the saccade. On average, these correlations reached their peak for neural activity that came before the behavioral windows we studied. We conclude that area LIP likely is involved in the guidance of pursuit movements, and raise the possibility that its activity has a role in setting a gain in the system that determines how strongly visual motion drives pursuit.

Materials and Methods

We recorded eye movements and neural activity from two adult male rhesus monkeys (*Macaca mulatta*). Each monkey was instrumented for experiments with a socket for head restraint and a scleral search coil for monitoring eye movements using surgical procedures that have been described previously (Ramachandran and Lisberger, 2005). In a separate surgery, each animal was implanted with a titanium recording cylinder that was placed normal to the skull over a craniotomy centered at stereotaxic coordinates P5, L12. Prior to the experiments described here, the monkeys had been trained to sit in a primate chair with their heads restrained, and to fixate and track targets presented on a video display in exchange for liquid reinforcement. All procedures were approved in

advance by the Institutional Animal Care and Use Committee at UCSF and were in compliance with the National Institutes of Health *Guide for the Care and Use of Laboratory Animals*.

Behavioral procedures

The presentation of visual stimuli and the acquisition of behavioral data were controlled by a real-time application developed in our laboratory and known as “Maestro” (<http://keck.ucsf.edu/~sruffner/userguide/index.html>). The software ran on a PC under Windows XP and used the real-time kernel RTX (VentureCom). The Maestro PC sent commands for the display of the visual stimuli over an Ethernet link to another, display PC that ran Linux. The display PC controlled the monitor that presented the visual stimuli to the monkey. For monkey I, stimuli were presented on a 20-in., 1,280 X 1,024 resolution, CRT monitor that was positioned 38 cm from the monkey’s eyes, yielding a field of view of 56° X 43°. The monitor was replaced between monkeys. For monkey G, the resolution of the 22-in CRT was 2,304 X 1,440 pixels, the viewing distance was 41 cm, and the field of view of 60° X 40°.

The horizontal and vertical eye position signals generated by the scleral search coil were differentiated by analog circuits that rejected frequencies higher than 25 Hz with a roll-off of 20 dB per decade. These resulting velocity signals and the original were sampled at 1 kHz and stored to disk by the experimental control software.

Electrophysiological procedures

Up to five platinum/tungsten electrodes (impedance: 2-4 M Ω) at a time were lowered into the recording cylinder with a Mini Matrix microdrive (Thomas Recording, Giessen, Germany). Neural signals were amplified and filtered conventionally, and a real-time template-matching system was used to select waveforms of single units (Plexon, Inc., Dallas, TX). For most units, a raw spike waveform was digitized and isolation was checked and improved offline using custom software (<http://keck.ucsf.edu/~sruffner/jmwork/index.html>). For the remaining units, the Plexon offline sorter was used for this instead.

We classified units as being in area LIP using a passive receptive field mapping procedure and a memory saccade task. The RF mapping procedure was similar to that described by (Huang and Lisberger, 2009), only with static spots instead of patches of moving dots. The monkey fixated a dim red point while a bright white 1° spot was flashed throughout the visual field. In each behavioral trial, we presented 8 repetitions of a 200 ms appearance of a spot followed by a 500 ms interval between presentations. The mapping procedure involved 48 different stimulus locations in 6 different behavioral trials, each presented at least 6 times.

We counted the spikes from the neuron under study during each 200 ms stimulus period and computed a receptive field map online using MATLAB functions (Natick, MA). We averaged across the 6 or more stimulus presentations to obtain an average firing rate for

each stimulus location, and then used the *interp2* function to interpolate a smooth RF surface from the average firing rates. The peak of the RF surface was taken as the center of the RF. In general, we mapped the RF happened in two stages. First, a rough estimate of the RF map was determined with a coarse stimulus grid that covered much of the monitor. The resulting RF surface then was used to guide reduction of the spacing between the points on the grid and a shift in the center of the grid so that the entire responsive region of the visual field could be re-mapped at a higher resolution.

Once we had estimated the center of the neuron's RF, we measured the responses of the neuron during a standard memory-guided saccade task (Barash et al., 1991). Trials designed to study memory-guided saccades again began with fixation of a stationary spot at the center of the screen for 700 to 1200 ms. Then, the ultimate saccade target appeared for 200 ms. After a delay period of random duration between 800 and 1200 ms, the fixation spot disappeared and the monkey had 500 ms to respond with a saccade to the remembered location of the saccade target. For each neuron, we recorded the responses for memory-guided saccades for two target locations, in separate but interleaved trials. One target location was in the center of the RF, and the other location was in a portion of the visual field well outside the RF of the neuron under study.

Units were classified as being in area LIP if they had constrained visual receptive fields (Ben Hamed et al., 2001) and displayed the characteristic memory or saccadic period activity patterns of cells in that area during the memory saccade task (Barash et al.,

1991), or if they were found near an abundance of other cells that displayed those characteristic activities.

Experimental paradigm

After we completed the basic characterizations of the neuron under study, we ran one or more blocks of a smooth pursuit task. Each pursuit stimulus was presented as part of a separate behavioral trial, which began with a fixation point that the monkeys had to fixate within 2 degrees for a random duration of 800 to 1400 ms. The fixation point then extinguished and a moveable target appeared either inside or outside the receptive field of the neuron under study and immediately moved either leftward or rightward for 500 to 600 ms. To help improve the monkey's tracking performance throughout the stimulus motion, the target then jumped 1° further in the direction of motion and became a stationary fixation target for a random period of 500 to 600 ms. After the pursuit target appeared and started to move, the monkeys were given a grace period of 400 ms to bring their eyes within 3° (Monkey I) or 4° (Monkey G) of the moving target and keep them within the fixation window for the duration of the trial. The different fixation requirements were used for the two monkeys because Monkey G proved unable to perform the task at a high level of success when the smaller window was used.

In general, the exact positioning of the pursuit targets was either inside or outside the RF of the neuron under study, with the details based on its RF properties. For "In RF" trials, the initial position of the target was inside the RF of the neuron under study. The exact

target location for the “In RF” trials varied somewhat from neuron to neuron. In general the target was placed within a part of the RF that produced at least 50% of the maximum response. Control analyses revealed that the exact location of the target inside the RF did not influence the effects we report here, so we have elected to finesse the minor differences in target placement between the two monkeys and across neurons. For “Out RF” trials, the initial target position was outside the RF. The direction of target motion was always either leftward or rightward and was chosen to satisfy two constraints. First, direction was chosen with the aim of minimizing presaccadic smooth pursuit and maximizing the temporal reliability of the initial saccade used by the monkey to catch up to the target. In general, this constraint dictated using the motion direction that took the target “more away” from the position of fixation. Second, targets always moved toward the center of the RF, towards regions that produced larger responses in the RF testing block. Figure 2-1 gives an example of how target positions and motion directions would be chosen in a typical experiment.

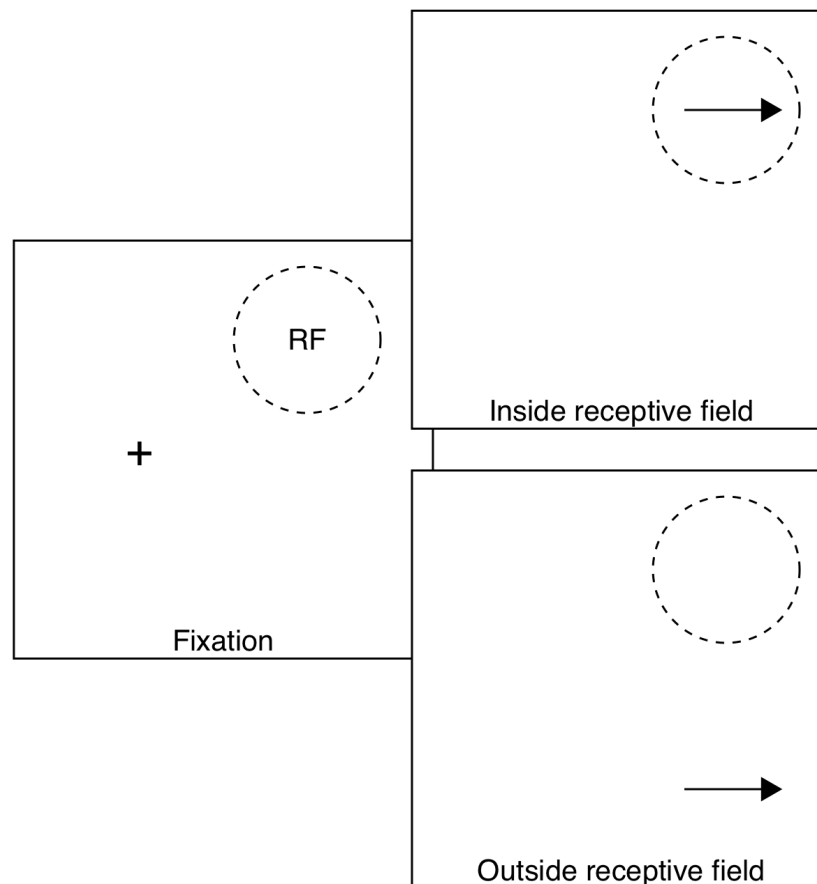


Figure 2-1

How stimuli were configured for experiments. The cross in the left panel represents the fixation point, and the dashed circle represents the receptive field (RF) of the neuron being studied. When the fixation point disappears, the target appears either inside the RF (upper right panel) or outside the RF (lower right panel). The arrow points in the direction of motion, which is chosen to be the direction along the horizontal axis that is away from the fixation point.

An experimental block consisted of one configuration of the “In RF” and “Out RF” initial target positions and movement directions. We typically recorded 200-250 trials in monkey I’s experiments and 300-450 trials for monkey G’s experiments. After a satisfactory number of trials were collected during the first block, one or two additional blocks of data were collected for a different initial target position or positions. Finally, for

some cells in Monkey G, we concluded a study of a neuron by collecting one or two blocks of data under a saccade-only task that had the same stimulus geometry and timing as the pursuit task, but with stationary rather than moving targets. Thus, the monkey's task was simply to make a saccade toward and then fixate the target.

Data analysis

Each trial in our database was inspected visually using custom software for purposes of marking the start and end times of saccades. For each trial, the software computed estimates of saccade onsets and offsets from the filtered eye velocity traces by finding intervals where the eye speed exceeded $50^\circ/\text{s}$. The software assigned provisional start and end times of the saccade by expanding these intervals on each side by fixed offsets. These estimates were viewed on top of the eye velocity traces and refined as necessary by the user. Some trials were discarded during the visual inspection phase of saccade marking due to the presence of slow eye movements indicative of sleepiness, or in the case of Monkey G, the lack of a clearly distinguishable end time for the first saccade after the onset of target motion. $5.6\% \pm 6.6\%$ (mean \pm std. dev.) of trials were rejected for each experimental block.

Analyses of the relationship between eye movements and LIP activity were performed in MATLAB. The bulk of our analyses involved Pearson correlation and partial correlation coefficients. Pearson's partial correlation coefficient $r_{xy.z}$ gives the strength of the linear relationship between two variables, x and y , after the effect of a set

\mathbf{Z} of additional variables has been removed. This quantity can be written in terms of the partial correlations of progressively smaller sets of variables:

$$r_{xy,\mathbf{Z}} = \frac{r_{xy,\mathbf{Z}\setminus\{z\}} - r_{xz,\mathbf{Z}\setminus\{z\}}r_{yz,\mathbf{Z}\setminus\{z\}}}{\sqrt{1 - r_{xz,\mathbf{Z}\setminus\{z\}}^2} \sqrt{1 - r_{yz,\mathbf{Z}\setminus\{z\}}^2}}$$

with $r_{xy,\emptyset} = r_{xy}$ when there are no more control variables left, so when z is one variable,

$$r_{xy,z} = \frac{r_{xy,\cdot} - r_{xz,\cdot}r_{yz,\cdot}}{\sqrt{1 - r_{xz,\cdot}^2} \sqrt{1 - r_{yz,\cdot}^2}}$$

Partial correlations can also be computed by correlating the residuals of the regression of x on \mathbf{Z} with those of the regression of y on \mathbf{Z} , which is what we did in practice, via the MATLAB function *partialcorr*. The following t-statistic is defined for a partial correlation coefficient:

$$t = r_{xy,\mathbf{Z}} \sqrt{\frac{n - 2 - k}{1 - r_{xy,\mathbf{Z}}^2}}$$

where k is the number of variables in \mathbf{Z} . If all the variables are normally distributed, this statistic is distributed as t_{n-2-k} under the null hypothesis of no relationship between x and y when \mathbf{Z} is controlled for. We used this t-statistic as an initial threshold when we tested for significant stretches of partial correlation coefficients, as is described in more detail below.

Results

We recorded eye movements and the activity of neurons in area of LIP of two monkeys (34 from monkey I, 46 from monkey G) while they performed a task that required them to make a saccade to and then pursue a target that moved through or outside of the RF of

the neuron under study. Prior research has shown that the smooth eye movement after a saccade is enhanced as a consequence of the execution of the saccade. Our goal was to ask whether LIP might be involved in this enhancement by analyzing the trial-by-trial correlations between the activity of LIP neurons and the amount of enhancement of eye velocity after the saccade.

Eye movements and responses of an LIP unit during a typical experiment

The target motions we used to record from LIP neurons comprised a change in target position from the point of fixation into the receptive field of the neuron under study, followed by a ramp motion at constant speed that took the target away from the position of fixation (Figure 2-2 A, dashed trace). The monkey fixated the target before it was displaced, then showed a latency of almost 200 ms before producing a saccade that took the eye quite close to the moving target. Immediately after the saccade, the eye moved smoothly and tracked the target quite closely. On average the eye position of tracking was very close to target position (Figure 2-2 A, thick black trace), but there was considerable trial-to-trial variation in the latency of the saccade and the amplitude, as shown by the multiple fine traces in Figure 2-2 A. Records of eye velocity for the same set of responses (Figure 2-2 C) illustrate the presence of only a very small change in eye velocity before the first saccade, a rapid and large deflection of eye velocity in relation to the saccade, and then considerable trial-to-trial variation in the post-saccadic smooth eye velocity.

LIP neurons responded during the smooth pursuit task in a manner that made sense given their receptive fields and peri-saccadic responses. When the pursuit target appeared inside the RF of the neuron under study and started to move (Figure 2-2 B), the cell fired an initial burst of spikes about 50 ms after target onset, and then paused briefly before emitting a longer period of spike that reach firing rates over 100 spikes/s. The neuron returned to a low level of activity soon after the onset of a saccade from the fixation point to the target, at the time of the red dots in the raster. Saccade latency averaged 164 ms in Figure 2-2 B. When the target appeared at a location outside the RF (Figure 2-2 D), the neuron displayed little or no increase in firing rate. Saccades to moving targets that appeared outside the receptive field led to a reduction in firing to below baseline.

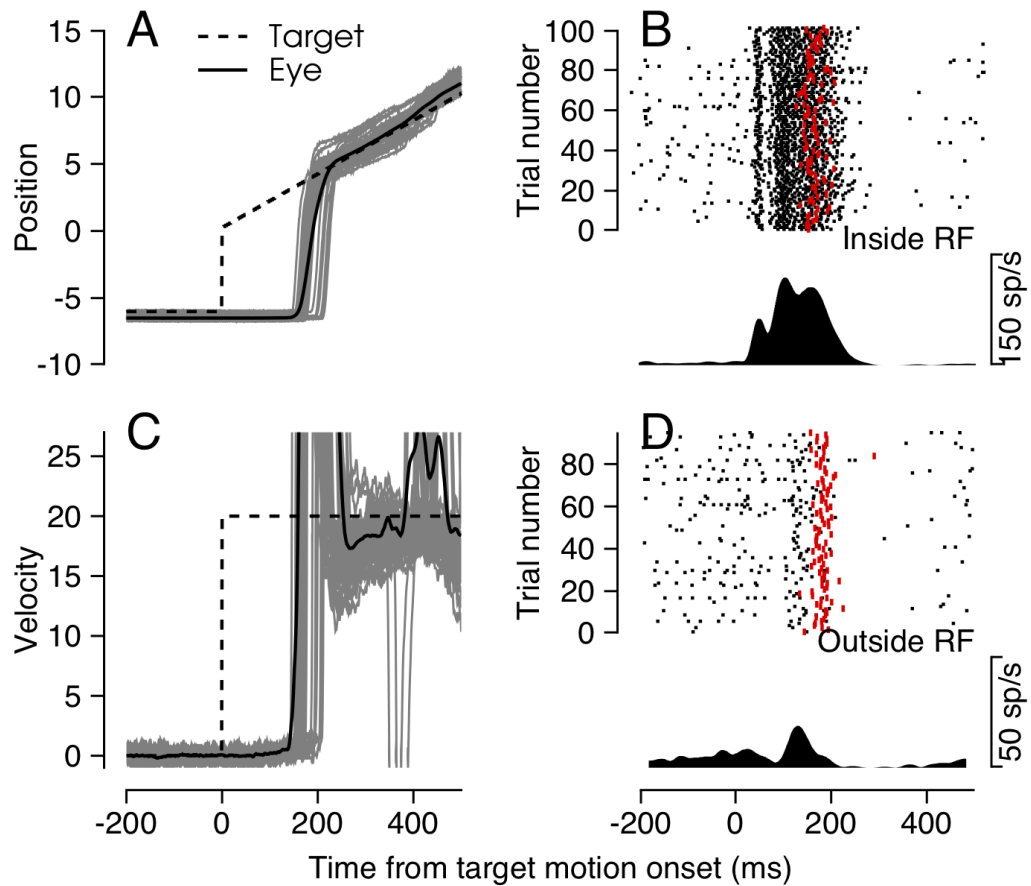


Figure 2-2

Eye movements and neural activity from a typical experiment. A: eye and target positions along the direction of target motion as a function of time relative to the start of target motion. The dashed line shows the target position. The thick solid trace gives the average eye position across trials, and each thin solid trace is the eye position on a single trial. C: same as A, but for eye target velocities. B: neural activity for the In RF trials. Each black dot on the raster is a spike, and each red dot is the start of a saccade. The PSTH below the raster depicts the average firing rate for these trials. D: same as B, but for the Out RF trials. Data are from monkey I.

We did not observe pursuit specific responses in LIP neurons, outside of the expected responses to the saccadic eye movements that were used to bring the eye to the moving tracking target. The average firing rate profiles for individual experimental blocks (Figure

2-3, grey curves) generally rose from baseline to a peak that was reached prior to the end of the saccade. In general, the firing rate curves for individual experiments resembled the average across trials (Figure 2-3, bold black curves). The trajectories of firing rate were similar for LIP neurons recorded in the two monkeys for moving targets that appeared in the receptive field (Figure 2-3 A,B), as well as for saccade targets that appeared in the receptive field and remained stationary for 21 neurons in monkey G (Figure 2-3 C). The bulk of the block-by-block variation in Figure 2-3 was a consequence of some cells being more active than others, but some resulted from our experimental design, which used different target positions within the receptive field in multiple blocks of trials for some neurons.

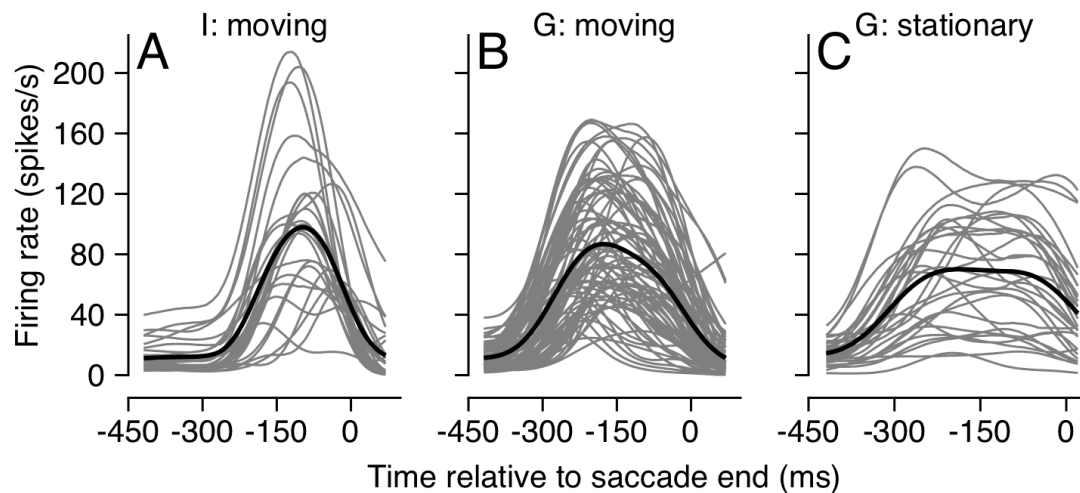


Figure 2-3

The diversity in average firing rates observed across experiments. Each thin trace is the PSTH from a single experimental block. The thick trace is the average of the thin traces in each panel. A and B are constructed from neural activity recorded during the pursuit task for monkey I (A) and G (B). C contains data from the stationary task that was run on monkey G. All traces are constructed by aligning the single trial data on the end of the saccade.

LIP-pursuit correlations for post-saccadic eye velocity

Our analysis capitalizes on the trial-by-trial variation in both the neural activity and the eye movements recorded in each block of trials. The extent of the variation can be seen in the eye velocity traces of Figure 2-2 C and the rasters of Figure 2-2 B, and raises the question of whether LIP firing rate and post-saccadic smooth eye velocity covary on a trial-by-trial basis.

To evaluate the trial-by-trial covariation between neural activity and pursuit speed we computed partial correlation coefficients between LIP and pursuit, while controlling for several saccade metrics simultaneously: latency, amplitude, duration, and peak perisaccadic speed. We will denote these partial correlation coefficients as $r'_{LIP(t_n),pur(t_p)}$, where $LIP(t_n)$ is a smooth, time-varying estimate of firing rate created by convolving single trial spike trains with a Gaussian of $\sigma=40$ ms and $pur(t_p)$ is the pursuit speed at time t_p . The value of $r'_{LIP(t_n),pur(t_p)}$ that emerges from the partial correlation analysis represents the linear relationship that remains between $LIP(t_n)$ and $pur(t_p)$ when the effects of the other movement variables have been removed. All partial correlations were computed with spike trains and behavioral data aligned with respect to the end of the saccade, as illustrated in Figure 2-4 A.

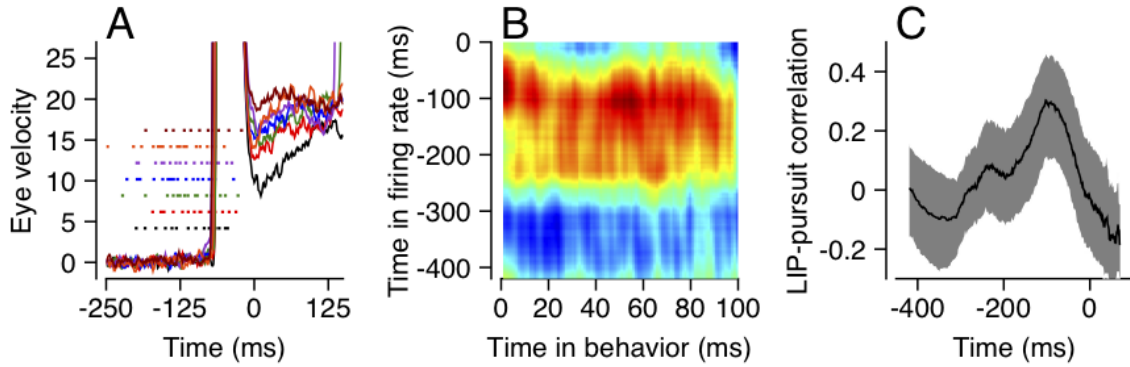


Figure 2-4

Correlation of postsaccadic pursuit with LIP activity for the example experiment. A: Traces are the eye velocities and dots are the spike times for several trials that span the range of postsaccadic eye velocities in the experiment. Neural activity and behavior that come from the same trials are colored the same. B: partial correlation of eye velocity with firing rate. The color of each point in the heat map gives the LIP-pursuit correlation for firing rate and eye velocity at a different pair of times relative to the end of the saccade. Dark red colors represent the highest correlation coefficients and dark blue colors represent the lowest correlations. C: the black trace is the correlation between neural activity and the average postsaccadic pursuit speed from 20-60 ms after the end of the saccade as a function of the time of the neural activity used to compute the correlation. The surrounding gray ribbon shows the bootstrapped 95% confidence on this correlation for each time.

In the example of Figure 4B, each pixel shows $r'_{LIP(t_n),pur(t_p)}$ computed for a different pair of times t_n and t_p during the firing rate and the eye movement for saccades to a moving target presented within the receptive field of on LIP neuron. The color surface has a red stripe that appears for most pixels representing firing rate at times between 50 and 225 ms before the end of the saccade, and for the range of pixels representing smooth eye velocity from 0 to 100 ms after the end of the saccade. The red pixels indicate pairs of times when a higher firing rate in the LIP neuron was correlated with a higher postsaccadic eye velocity in the associated tracking behavior. Because $r'_{LIP(t_n),pur(t_p)}$ did not change much with t_p , we chose to reduce postsaccadic eye speed to a single value for

subsequent analyses by averaging the eye speed on each trial between 20 and 60 ms to create a quantity that will be denoted \overline{pur} . In subsequent analyses, however, we computed the correlation of this one measure of eye velocity with firing rate at each time over a range of times up to the time of the saccade. We will refer to the partial correlation between \overline{pur} and neural activity as $r'_{LIP(t_n),\overline{pur}}$, or the “LIP-pursuit correlation”. For this example neuron, the LIP-pursuit correlation rose to a positive peak of approximately 0.26 that occurred when neural activity at around 100 ms before the end of the saccade was correlated with the mean eye velocity 20-60 ms after the end of the saccade (Figure 4C, bold curve). The lower bounds of bootstrapped 95% confidence intervals for the LIP-pursuit partial correlations (gray ribbon) exceed 0 for firing rates from about ~150 to ~50 ms before the end of the saccade.

Population data for LIP-pursuit correlations

We recorded a positive LIP-pursuit correlation in many neurons and found that it persisted clearly at the population level. We computed $r'_{LIP(t_n),\overline{pur}}$ for each dataset and then averaged the correlation time courses across datasets for each monkey. Notably, the resulting averages (Figure 2-5 A) had similar shapes in the two monkeys and overlapped throughout the time interval we analyzed. Recall that time on the x-axis indicates the time during the firing rate trace and that the correlation for each time was between firing rate at that time and the eye velocity in the fixed interval from 20 to 60 ms after the end of the saccade. The traces peaked at a correlation value of ~0.06 that occurred for neural activity ~50 ms prior to the end of the saccade. The standard errors (gray ribbons)

remained well from zero for about 50 ms on each side of the peak correlation, indicating that the average LIP-pursuit correlation at these times was reliable. We also found that the broad positive peak in $r'_{LIP(t_n),pur}$ for neural activity before the end of the saccade was only present when the target appeared inside the RF. For both monkeys (Figure 2-5 C,D), there was a positive peak about 50 ms before the end of the saccade in the average $r'_{LIP(t_n),pur}$ for targets that started inside the receptive field, but not for targets that started outside the receptive field.

The average time courses of $r'_{LIP(t_n),pur}$ reveal an important trend, but also mask considerable variation in correlation strength across experimental blocks. The distributions in Figure 5B illustrate the variation in the peak LIP-pursuit correlations in the individual blocks. The firing of some neurons was much more strongly correlated with postsaccadic pursuit than that of others. We sought to determine the fraction of our experiments for which there was evidence of a statistically significant relationship between LIP activity and postsaccadic pursuit.

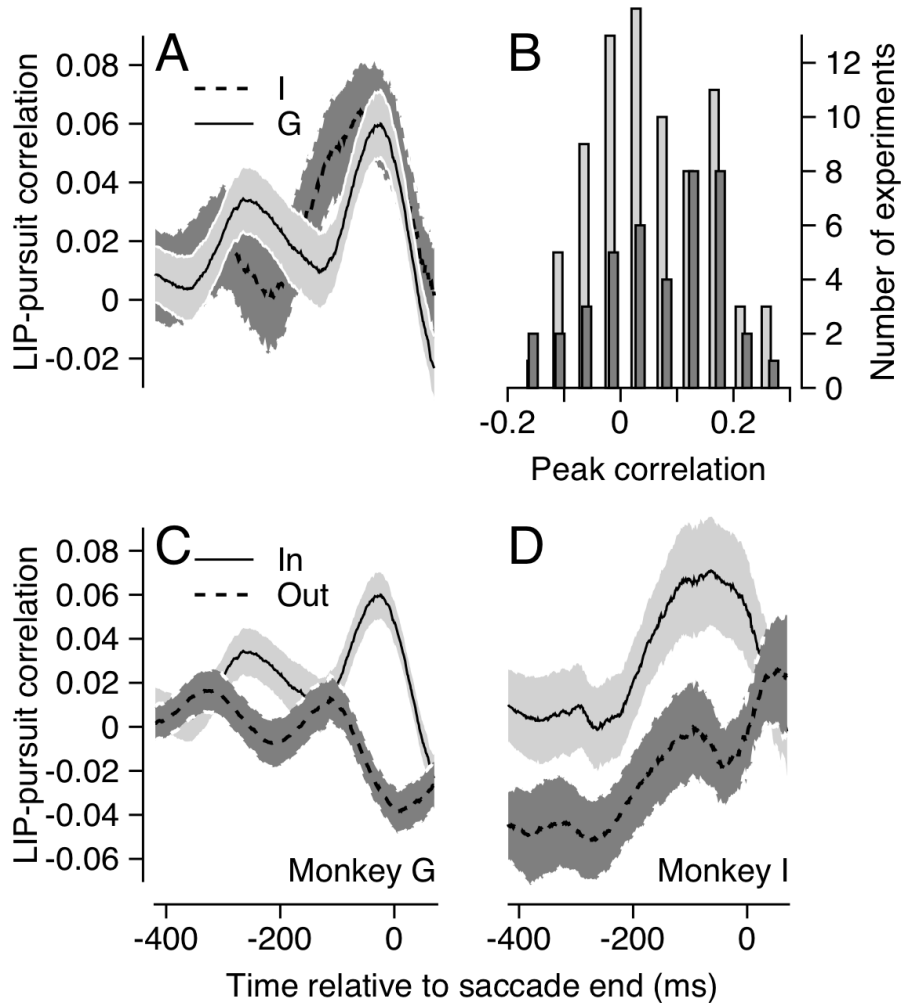


Figure 2-5

LIP-pursuit correlations for all experiments. A: the average LIP-pursuit correlations for each monkey as a function of the time of the neural activity. Monkey G is represented by the solid line and monkey I is represented by the dashed line. B: the distribution of correlation coefficients is shown at the time of the peak of the average correlation traces in A. The distributions are colored by monkey as in A. C: Average LIP-pursuit correlations for monkey G for In RF (solid lines) versus Out RF (dashed lines) trials. D: Same as C, but for monkey I. The In RF trace in this panel differs from the corresponding trace in A because for some experiments, there were no Out RF data, and thus these were excluded from this average. All error ribbons represent the standard error of the mean.

We tested whether the In RF trials from each experiment gave rise to any LIP-pursuit correlation coefficients that were significantly larger than zero by means of a suprathreshold cluster test (Nichols and Holmes, 2002), which tests whether there were

longer stretches of “high” correlation in the data than would be expected if there were no genuine relationship between neural activity and behavior. Such a test handles the multiple testing problem that arises when the significance of several hundred correlation coefficients needs to be evaluated simultaneously, as is the case for each of our experiments, by controlling the familywise error rate. For each block of data, the test proceeded as follows: First, we converted $r'_{LIP(t_n),\overline{pur}}$ at every time point to its corresponding t -statistic. We then identified the longest “cluster” of contiguous time points for which the t -statistic of all the points was greater than a threshold, which we set to be 2. We refer to the length of this “maximum cluster” as L_{max} . The cumulative distribution of L_{max} for each monkey (Figure 6A) reveals that monkey G’s experimental blocks generally produced maximum clusters that were longer than those found in monkey I’s blocks. About 42% of monkey G’s blocks contained clusters of greater than 50 ms, while around 24% of monkey I’s blocks contained a cluster of at least that length.

Next, we determined the distribution of L_{max} under the null hypothesis by randomly permuting the relationship between the single-trial postsaccadic velocities and firing rate profiles 1000 times and storing the L_{max} statistic for each synthetic dataset. Experimental blocks were deemed to have yielded significantly positive LIP-pursuit correlations if less than 5% of the synthetic datasets yielded above threshold clusters that were as long or longer than the true L_{max} . The results of this process are shown for one dataset in Figure 6B, with the actual L_{max} (dashed line) in that case being greater than 99.7% of the synthetic L_{max} values (solid line). Figure 2-6 C provides a sense of where the maximum cluster length from all experimental blocks fell on the corresponding null distributions.

Here, the length of the maximum cluster at the 95% percentile of the permutation distribution is plotted as a function of the length of L_{max} for the actual data. Points to the right of the line of slope 1 (dashed line) had actual maximum cluster lengths that reached statistical significance by the permutation analysis, amounting to ~31% of monkey G's and ~20% of monkey I's datasets.

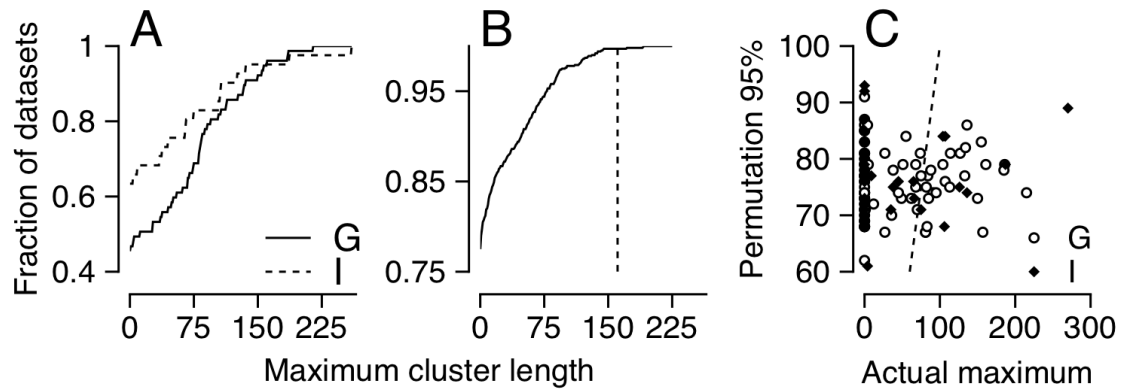


Figure 2-6

Significance of correlation coefficients for individual experiments, as assessed by the length of clusters of high correlations and a permutation test. A: The cumulative distribution of “maximum cluster lengths”, or the lengths of the longest clusters of contiguous time points where the LIP-pursuit correlations was higher than a threshold. A separate distribution is shown for each monkey. B: The solid line gives the cumulative distribution of maximum cluster lengths for the permutation datasets generated from a single experiment’s data. The dashed line shows where the true maximum cluster length for that dataset fell on the permutation distribution. C: The actual maximum cluster length of each experiment is plotted against the cluster length at the 95th percentile of the corresponding permutation distribution. Open circles are for monkey G, and filled circles are for monkey I. The actual and 95th percentile cluster lengths are equal along the dashed line.

In evaluating the frequency of statistical significance that we observed, it is important to remember that the t -statistic we used when identifying clusters of positive correlations depends on the number of trials used in the dataset. In general, monkey G’s experimental blocks included more trials than did monkey I’s; this may explain why we found

statistical significance more often in monkey G's experiments, and why the number of significant experiments was not higher for both monkeys. For example, a partial correlation of 0.1 when 4 variables are controlled for yields a t -statistic of greater than 2 when there are more than 402 trials. The number of usable trials for the two monkeys was 382 ± 79 for G and 226 ± 60 (mean \pm std. dev.) for I. Given the size of the correlation coefficients that we measured, we would have typically needed to collect more trials to attain significance in a larger percentage of our experiments. Our results were also likely affected by the somewhat arbitrary choice of 2 as the t threshold for the identification of clusters. The need to choose an arbitrary cluster-forming threshold is an acknowledged problem in suprathreshold cluster tests (Nichols and Holmes, 2002). Note, however, that tests like our have been shown to give highly reliable control over the familywise error rate for a variety of cluster thresholds (Hayasaka and Nichols, 2003), so our results are unlikely to be an overestimate the percentage of experiments with significant positive correlations in our data.

What predicts the strength of the LIP-pursuit correlation?

We next asked whether any of several variables that characterized the responses of LIP neurons were related to the magnitude of the LIP-pursuit correlation, and found that the firing rate of the cell at the end of the saccade was a good predictor of $r'_{LIP(t_n), \overline{pur}}$. Recall that the average firing rate varied across considerably neurons (Figure 2-3). To determine whether $r'_{LIP(t_n), \overline{pur}}$ was positively related to the average firing rate at the end of the saccade divided experimental blocks into 3 groups depending on the average firing rate

from 25 ms before to 25 ms after saccade end. We then averaged the time-varying neuron-pursuit correlations for the experiments in the top and bottom thirds of the distribution of firing rate. For both monkey G (Figure 2-7 A) and monkey I (Figure 2-7 B), the average $r'_{LIP(t_n),pur}$ time course was higher and had a clearer peak for the high-firing rate experiments (black curves and light gray ribbons) versus the low-firing rate experiments (dashed curves and dark gray ribbons). Further, a scatter plot revealed a significant correlation between the average LIP-pursuit correlation over interval and the mean firing rate, both measured from 25 ms before to 25 ms after the end of the saccade (Figure 2-7 C). The average firing rate around the end of the saccade explained 13.6% of the variance in average neuron-pursuit correlation for monkey G, and 14% of the corresponding variance for monkey I.

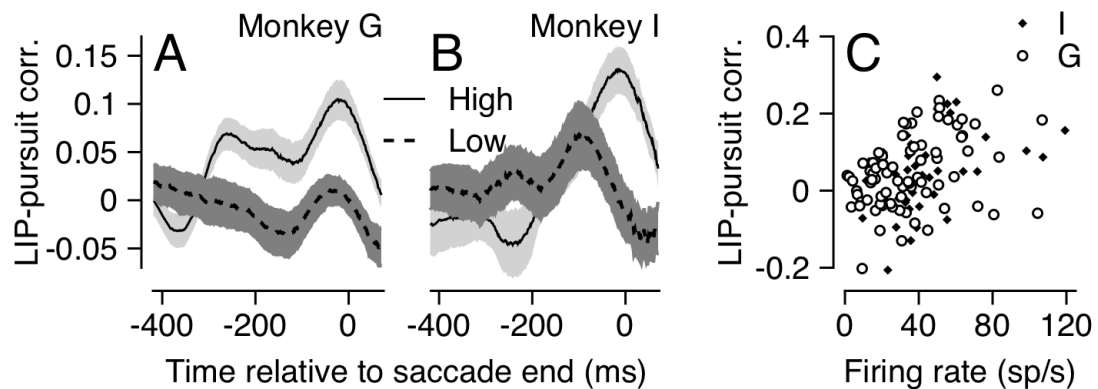


Figure 2-7

Dependence of the LIP-pursuit correlation on the firing rate of the neuron around the end of the saccade. A: The solid line and light grey error ribbon depicts the average (\pm s.e.m.) correlation for experiments in the top third of monkey G's distribution of firing rates around the end of the saccade. The dashed line and dark grey ribbon correspond to the lower third of the distribution. B: Same as A, but for monkey I. C: The average firing rate over the peri-saccade end interval is plotted against the correlation for over the same interval for each dataset of monkey G (open circles) and monkey I (filled circles).

We attempted to predict $r'_{LIP(t_n),pur}$ in the same manner from the position of the target relative to the center of the RF and from a classification of cells based on their activity in the memory saccade task, but we found that neither of these variables predicted the strength of the neuron-pursuit association as well as did the average firing rate around the end of the saccade.

LIP-behavior correlations for a stationary target

In Monkey G we often recorded LIP responses during a block of saccades to stationary targets, creating a dataset for analyzing the trial-by-trial correlation between LIP firing rate and the smooth eye velocity of the post-saccadic drifts, or glissades, emitted by this monkey (Figure 2-8 A, arrow). The post-saccadic smooth eye velocities had magnitudes that ranged from 1 to 5 deg/s, measured over the interval from 20 to 60 ms after the end of the saccade (Figure 2-8 B).

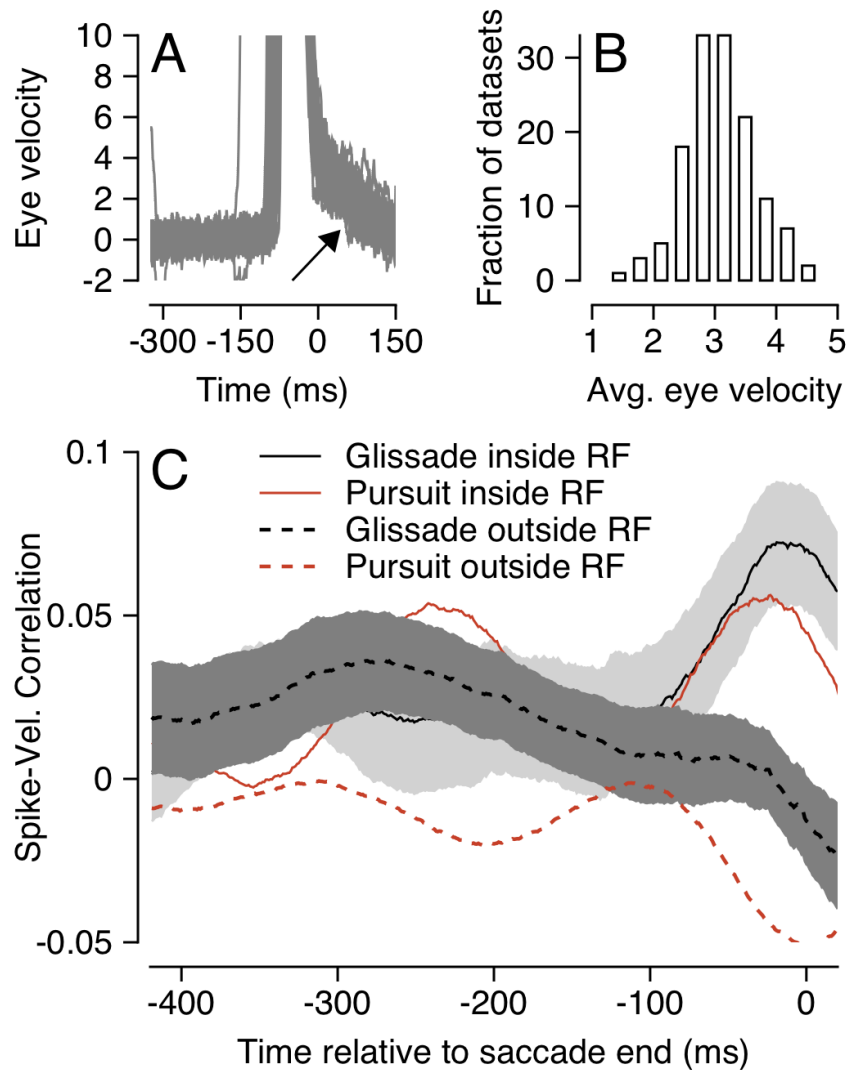


Figure 2-8

Eye velocity during the stationary target task and LIP-glissade correlations for monkey G. A: Single trial eye traces from one stationary task dataset are displayed on top of each other as a function of time from the end of the saccade. The arrow points to the rough location of the time interval used for the measurement of the postsaccadic eye velocity on each trial, the distribution of which is shown in B. C: The average (\pm s.e.m.) LIP-glissade correlations are depicted for Inside RF trials by the solid lines and light grey ribbons and the outside RF correlations are shown with dashed lines and dark grey ribbons. The corresponding LIP-pursuit correlations for the subset of datasets with stationary task data are given in red.

We found a consistent correlation between the firing of LIP neurons and the smooth eye velocity after saccades to stationary targets. As before, we chose a single measure of the

post-saccadic eye velocity in the interval from 20-60 ms after the end of the saccade, and computed the trial-by-trial correlation of that one measure with firing rate as a function of time. For saccades to targets within the receptive field of the neuron under study, the LIP glissade correlation (Figure 2-8 C, continuous curve and light gray ribbon) peaked when firing rate was taken just before the end of the saccade. As before, there was not a consistent LIP-glissade correlation when the saccade target was outside the receptive field of the neuron under study (dashed curve and dark gray ribbon). trial-by-trial basis with LIP activity. The time course of the LIP-glissade correlation in Figure 2-8 C was very similar to that of the LIP-pursuit correlation for the same monkey in Figure 2-5 C.

LIP-behavior correlations for presaccadic smooth pursuit

Although we designed our experiments with the aim of minimizing presaccadic pursuit, we nonetheless frequently observed small smooth eye movements before the saccade in monkey G's tracking of moving targets (Figure 2-9 A, solid lines). On average eye speed exceeded 0.5 deg/s by 143 ms after the onset of target motion. Such small pursuit movements are common in monkeys when the target moves away from the fovea (Lisberger and Westbrook, 1985). By contrast, monkey G's eye velocity did not change on average during the presaccadic interval when the task required only saccades to stationary targets (Figure 2-9 A, dashed lines). As expected, the neurons increased their firing well above baseline for both tasks during this period (Figure 2-9 B). Given that saccade amplitudes and metrics were somewhat different in response to moving versus

stationary targets, the difference in the amplitude of the firing rate responses in Figure 2-9 B probably is not related to the presence or absence of small smooth eye velocities.

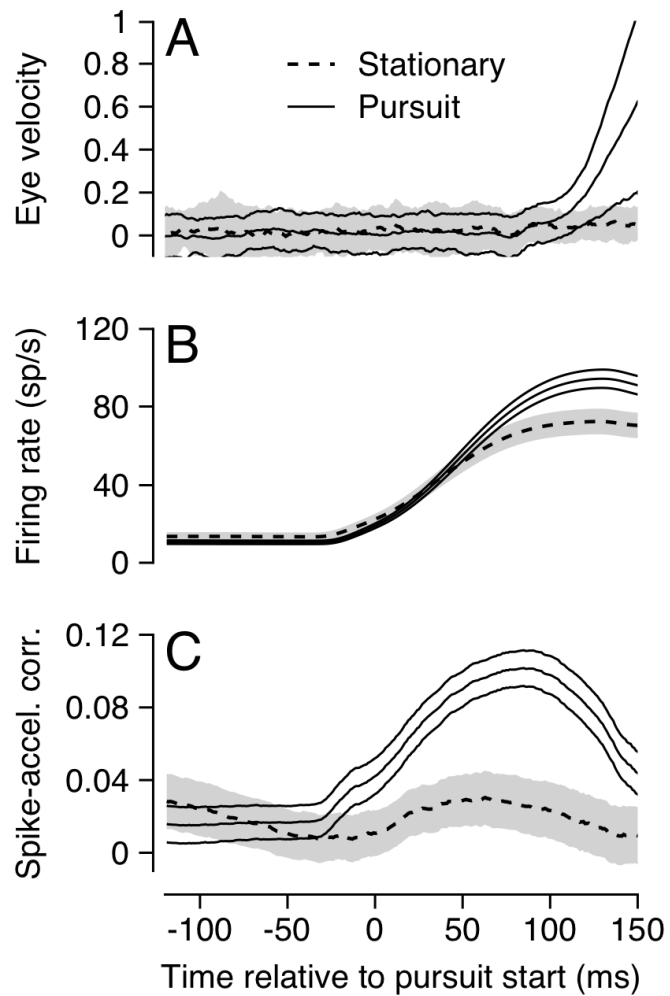


Figure 2-9

LIP-pursuit correlations for presaccadic pursuit for monkey G. Solid lines give the average (\pm s.e.m.) eye velocity (A), firing rate (B), and correlation of firing rate at different times with eye acceleration from 100-150 ms. All times are relative to the onset of the target. Dashed lines and grey ribbons show the same quantities for the stationary task.

Using an approach similar to that used for the analysis of postsaccadic pursuit, we found that presaccadic neural activity was correlated with the small presaccadic smooth pursuit we observed. We quantified pursuit strength on each trial as the change in eye velocity from 100 ms to 150 ms after the start of target motion and then computed the correlation between this measure and the smoothed firing rate at different times. We discarded the small number of trials on which the saccade began sooner than 150 ms after the onset of target motion. Figure 2-9 C shows that the “LIP-presaccadic-eye-velocity correlation” rose after the onset of target motion to a positive peak of ~ 0.1 that occurred when eye velocity was correlated with firing rate 80 ms after the onset of target motion. The positive correlation was present for the pursuit task (solid curves showing mean ± 1 standard error) but not for the stationary task (dashed curve with light gray ribbon).

Correlations of trial-by-trial saccade metrics with neural activity

To place our findings of correlations between LIP activity and pursuit eye movements in a broader context, we also studied the trial-by-trial correlations between neural activity and metrics of the targeting saccade that came during the initiation of pursuit. The LIP-saccade correlations between firing rate and saccade latency, amplitude, and peak velocity were generally less consistent across monkeys and tasks than were the LIP-pursuit correlations. As before, we chose a single measure for each saccade parameter and correlated firing rate over a range of times with the saccade measures. For the correlation with saccade latency, we aligned firing rates with respect to the onset of target motion. For the correlations with saccade amplitude and peak velocity, we aligned firing

rates on the end of the saccade. For these two variables, we computed partial correlation coefficients, using as control variables the remaining variables from the set of saccade metrics used in the computation of $r'_{LIP(t_n), \overline{pur}}$.

In general, the LIP-saccade correlations were less consistent than the LIP-pursuit or LIP-glissade correlations. In accord with other studies of the relationship of LIP to behavior (Janssen and Shadlen, 2005; Churchland et al., 2008; Kiani et al., 2008), higher presaccadic firing rates were on average associated with lower saccade latencies (Figure 2-10 A), for both monkeys and for both saccade and pursuit tasks. During the pursuit task the average LIP-saccade amplitude correlation rose to just over 0.05 prior to the end of the saccade (Figure 2-10 B), reaching its peak earlier for monkey G than for monkey I. In the stationary task, the neuron-amplitude correlation oscillated around zero but did not show a decisive trend. The correlation with peak eye speed also failed to show a consistent trajectory across monkeys and tasks, although both monkeys showed a positive correlation that peaked before the end of the saccade during the pursuit task (Figure 2-10 C). This finding of a correlation between saccadic eye speed and perisaccadic LIP activity stands contrasts with an earlier failure to find such a relationship (Powell and Goldberg, 2000).

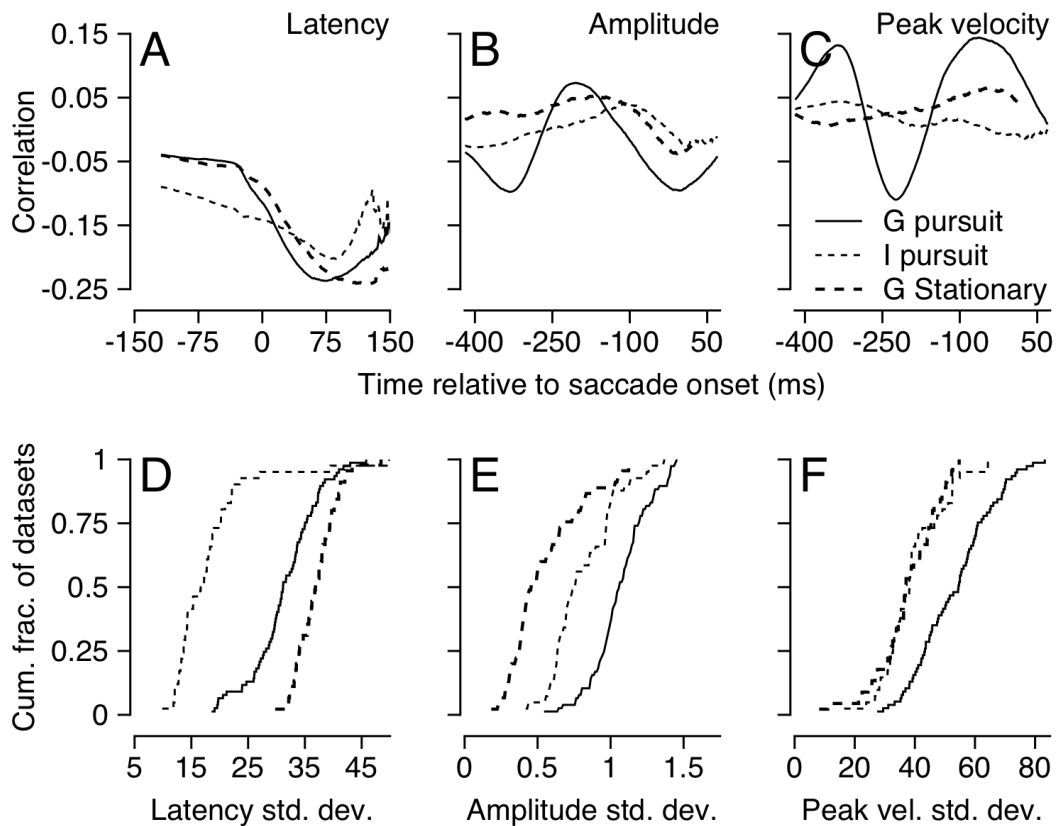


Figure 2-10

Trial-by-trial relationships of saccade parameters with neural activity and characterization of behavioral variation. In each panel, the data are plotted separately for the pursuit task for each monkey and for the stationary task for monkey G. A: average correlation of saccade latency with firing rate at different times relative to the appearance of the target. B,C: correlation of saccade amplitude (B) and peak saccade velocity (C) with firing rate aligned relative the end of the saccade. D-F: cumulative distributions of the standard deviation of saccade latency, amplitude, and peak velocity for each dataset.

In general, monkey G made more variable and slower saccades than monkey I. The bottom row of graphs in Figure 2-10 plot cumulative distributions of the standard deviation of each saccade metric for each block (Figure 2-10 D-F) For the pursuit data, the standard deviations for the saccade metrics were generally higher for monkey G than for monkey I. The greater variability in behavior may explain why the pursuit task firing

explained more of the variance in behavior for monkey G than for monkey I, as neurons generally encode larger differences in behavior more reliably.

Discussion

Our work has identified multiple novel relationships between trial-by-trial variation of LIP activity and smooth pursuit. We found that neural activity in this area was positively correlated with pursuit speed when a target appeared inside the neuron's RF, and was uncorrelated with pursuit when the target appeared outside the RF. There was such a correlation between neural activity and behavior for both presaccadic and postsaccadic pursuit movements. We also found that cells with higher firing rates were better correlated with pursuit. Importantly, the peak LIP-pursuit correlations in the population came for neural activity that preceded pursuit, which is consistent with this neural activity causing behavior. We thus suspect that LIP plays a role in the generation of smooth pursuit eye movements. In the following, we connect our findings to knowledge of how the pursuit system selects a target to follow and consider a role for LIP in driving variation in the pursuit behavior.

Comparison with previous studies of LIP and pursuit

Some previous work has suggested that LIP may be involved in the control of pursuit movements. Lynch et al. (1977) identified "visual tracking neurons" in the inferior parietal lobule that increased their firing during pursuit but not during fixation. However,

as this work was done before the IPL was thought of as comprising distinct areas, no attempt was made to classify the neurons in this study as belonging to LIP versus 7a or MST. We thus do not know which, if any, of the tracking neurons they reported finding were located in LIP. Later, Bremmer et al. (Bremmer et al., 1997) identified neurons in LIP that discharged for certain directions of pursuit. These researchers found that a surprisingly high percentage (39%) of the LIP neurons they studied discharged in a directionally tuned manner during pursuit. Given that there are neurons in LIP that respond to visual stimuli presented in the central visual field (Ben Hamed et al., 2001), it is possible that the responses during pursuit that Bremmer et al. observed reflected visual and/or delay activity of neurons with visual receptive fields near the fovea. We believe our work provides stronger evidence for a causal role of LIP in generating pursuit because we have gone beyond averages to show correlations between single-trial fluctuations in neural activity and behavior. Now that we have identified the time intervals and circumstances under which LIP activity may drive pursuit, microstimulation there could provide further evidence for a causal link between activity in the area and pursuit.

How might LIP fit into the circuit?

Since there can be many different moving objects in our visual field at one time, and we generally don't want to track all of them, it is important that we have the ability to select which motion drives smooth pursuit. The primate brain meets this requirement by adjusting gains that control how strongly the pursuit system responds to motion. Saccades

are one of the most dramatic ways to increase the gain on motion for pursuit. We have reproduced (Figure 2) the finding of many that the smooth pursuit response goes from weak to strong after saccade. The study of this phenomenon in depth has led to the conclusion that saccades “turn up the gain” on motion that is already in the brain (Lisberger, 1998; Gardner and Lisberger, 2001, 2002), and that the pursuit gain is only increased for motion in a restricted spatial window around the endpoint of the saccade (Schoppik and Lisberger, 2006).

One interpretation of our results is that LIP neurons are part of the network that determines how strongly visual motion at a spatial location is transmitted to the pursuit system. In this understanding, higher firing rates in LIP are associated with faster pursuit speeds because the higher firing rates reflect elevated gain for the motion in the neuron’s receptive field. Such an interpretation is compatible with our finding that the positive LIP-pursuit correlation is not present when the target is outside the RF. We see similarities between a view of LIP as setting the gain on visual motion for pursuit and the proposal of some researchers that LIP activity reflects the locus of spatial attention (Bisley and Goldberg, 2010): An increase in the effectiveness of a visual signal in driving behavior can be fairly likened to the improvements in perception that accompany shifts in visual attention.

In interpreting our results, it is important to keep in mind that neuron-pursuit correlations were present both before and after the saccade. This finding makes it seem unlikely LIP activity is specifying the size of the large gain change that is characteristic of the

postsaccadic enhancement of pursuit, as one might expect only postsaccadic pursuit to be correlated with LIP in that case. It is possible that LIP is involved in setting some form of gain for pursuit, but is not itself responsible for the large perisaccadic gain changes. Our finding also casts doubt on the hypothesis of Wilmer and Nakayama (Wilmer and Nakayama, 2007) that areas like LIP, which have been implicated in high-level motion processing, would only become involved in the control of pursuit after the saccade. On the other hand, many studies of attention have made a distinction between bottom-up and top-down forms of spatial attention, with the former typically being held to operate on a faster timescale than the latter. If we view the LIP-pursuit correlations as reflecting the area's role in setting an attention-like gain on visual motion, the finding of correlations for both presaccadic and postsaccadic pursuit could be seen as consistent with the idea that LIP activity reflects both forms of attention, since it seems likely that the early activity in our task is largely determined by the pop-out effect of the suddenly appearing stimulus and the later activity is more determined by top-down processes.

There are explanations for our results other than a role for LIP in setting the gain on visual motion for pursuit. It may be that the firing of neurons we recorded represents the speed of visual motion in a rate coded fashion. Some neurons in LIP have been shown to be tuned to the direction of a passively viewed visual stimulus (Fanini and Assad, 2009); it would be interesting to determine speed tuning can be found under similar circumstances that is of a high enough resolution to support the observed accuracy and precision of pursuit. Another important line of work has argued that LIP neurons accumulate evidence in favor of a decision to move in particular direction, with the

movement happening when the population activity reaches a particular level (Shadlen and Newsome, 2001; Roitman and Shadlen, 2002; Gold and Shadlen, 2007). One could place our results in this framework by considering the LIP-pursuit correlation a reflection of a “decision to pursue”. It is worth noting, however, that while the “decision” view of LIP has typically held that neurons in the area are responsible for a binary outcome for the spatial location they represent (whether or not to go there), our results suggest that LIP can also be involved in determining the nature of a continuously varying response to a stimulus at a location (how fast to pursue what is there). Thus, to the extent that the pursuit correlations that we have uncovered reflect a decision to pursue, it would be a different sort of decision. Finally, another prominent proposal for the role of LIP is that it represents the intention to make a saccade to a particular location (Gnadt and Andersen, 1988; Andersen and Cui, 2009). We do not feel that our results rule out this possibility. It may be that LIP serves multiple functions in orienting and deciding, and we have uncovered an additional one that is layered on top of the others.

LIP neuron-pursuit correlations as “gain noise”?

Our laboratory has been interested in why our behavior varies from trial-to-trial, even when we are trying to make the same movement. Evidence is converging that much, but not all, of the variation in eye speed during the initiation of pursuit originates in the visual system (Osborne et al., 2005; Medina and Lisberger, 2007; Schoppik et al., 2008), and is perhaps a consequence of the variable responses of MT neurons. The present results raise the possibility that an additional source of variation in pursuit responses is neural

variation in area LIP. If, as proposed above, LIP variation represents variation in a gain that interacts with the visual motion representation, we might consider the link between LIP fluctuations and behavior to be a reflection of the role of “gain noise” in determining the motor output. That is, motor variation could arise from variation in both the sensory representation and from variation in additional factors like motivation, attention, and reward anticipation. The variation in these other factors could result be manifested in LIP variation, which could in turn result in a variable gain that is applied to a neural representation of motion that emerges from cortical areas less susceptible to “extraretinal” influences, such as area MT.

The neuron-pursuit correlations we have observed are certainly small in magnitude on average, but not atypically so for neurons that in sensory and parietal cortices. Studies of area LIP in decision-making tasks have found that trial-by-trial variation in firing rate or the rate of increase in firing is inversely correlated with saccade latency (-0.09-.3 on average) (Janssen and Shadlen, 2005; Churchland et al., 2008; Kiani et al., 2008). By contrast, neuron-pursuit correlations for cells in the flocculus of the cerebellum (Medina and Lisberger, 2007) and the smooth pursuit region of the FEF (Schoppik et al., 2008) are much higher. In addition, it is important to remember our finding that the magnitude of the LIP-pursuit correlations increases with firing rate. This means that the correlations we measured for some experimental blocks likely would have been higher had we configured the stimulus in those cases to pass closer to the RF center during the postsaccadic interval. We note that our finding that neurons with higher average firing rates are more correlated with pursuit makes sense, as it has been shown that under some reasonable

pooling assumptions, noise correlations between neural activity and behavior are larger when neurons are more correlated with each other (Zohary et al., 1994), and it has also been found that the noise correlation between neurons increases with firing rate (de la Rocha et al., 2007).

We have thus provided the strongest evidence yet that LIP is involved in the control of smooth pursuit eye movements, and suggested possible ways in which this area could be interacting with the pursuit circuit. Our results add a new behavior to the toolkit that has been used to investigate the function of this area, one whose distinctive property of a continuously varying output may help answer persistent questions about the significance of its activity and how it is “read out” by other parts of the brain.

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Chapter 3: Supplementary results

This chapter serves as a supplement to the results presented in the Chapter 2. The data I present in the figures here is the same data that was collected in the experiments described in the Methods section of that chapter. I report here on more of the basic characteristics of my dataset that may be of interest to specialists and on some extra analyses of that data that shed further light on the relationship between LIP and smooth pursuit.

Memory saccade responses and receptive fields

As is typical for recordings in area LIP (Barash et al., 1991), we found neurons that exhibited a variety of response patterns during the memory saccade task. Some of this diversity can be seen in the responses of four neurons during trials where the target appeared in the RF (Figure 3-1). All neurons increased their firing rates above baseline after the onset of the stimulus (time 0, left panel). In the version of the memory saccade task I used, the target was extinguished after 200 ms. Importantly, some of the neurons maintain their firing rates above baseline well after that time. This is the “memory” or “delay period” activity that is one characteristic of area LIP. Also important is the rapid increase in firing rate before the start of the saccade (time 0, right panel) that some of these neurons exhibit. Neurons in the surrounding area, 7a, lack this presaccadic activity (Barash et al., 1991)

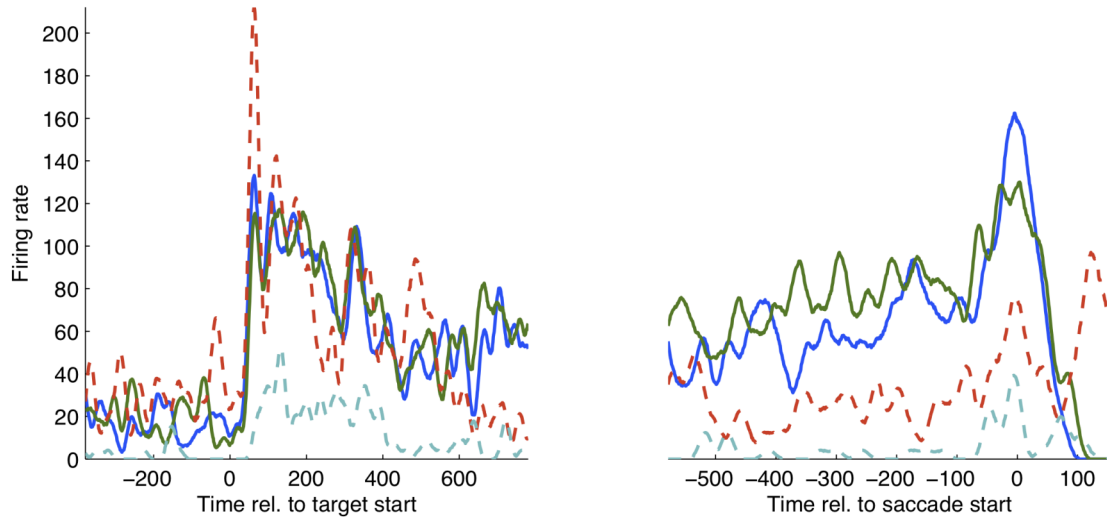


Figure 3-1

Sample neural responses during the memory saccade task. Each trace depicts the average firing rate as a function of time for one neuron. Dashed lines plot the activity of neurons that were statistically classified as having presaccadic activity. Plot is divided in two because of the random length of the delay period and the desire to clearly reveal visual and saccade locked activity.

To better characterize the population we recorded, I used criteria based on those of Sommer and Wurtz (2000) to classify cells as having visual, memory, and presaccadic activity. In brief, I defined a several time epochs and used a t-test with an alpha of 0.05 to compare the mean activity between periods. Cells were classified as having visual or memory if the mean activity in those epochs was higher than the activity in the baseline epoch. Cells were classified as having presaccadic activity if the activity in the presaccadic epoch was greater than the activity in the memory epoch. All cells had visual activity, which is in concert with some previous results (Bisley and Goldberg, 2006). A high percentage of cells in both monkeys had memory activity (84% for monkey G, 71% for monkey I). About the same percentage of monkey I's cells (68%) and fewer of monkey G's cells (45%) had presaccadic activity (Figure 3-2).

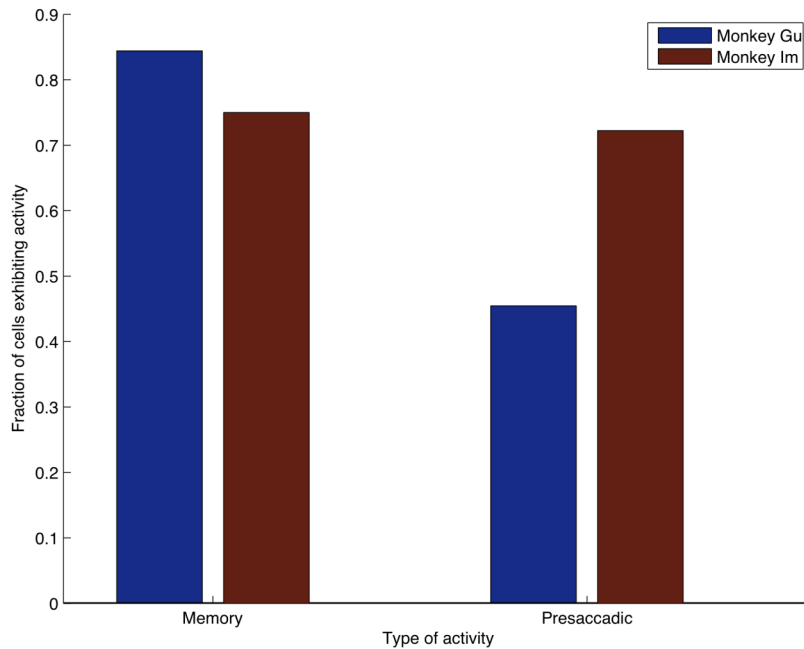


Figure 3-2

Fraction of cells having memory (left bars) and presaccadic (right bars) activity during the memory saccadic task.

The neurons I recorded displayed a diversity of visual receptive fields that is characteristic of LIP (Ben Hamed et al., 2001). Nine example RF maps from monkey G are shown in Figure 3-3. No quantitative analysis of RF structure was done. It appeared, however, that neurons that were closer to the fovea (second row, first and second column) had more regularly shaped and smaller RFs, while neurons that were more in the periphery were larger and probably sometimes extended off the monitor (top right).

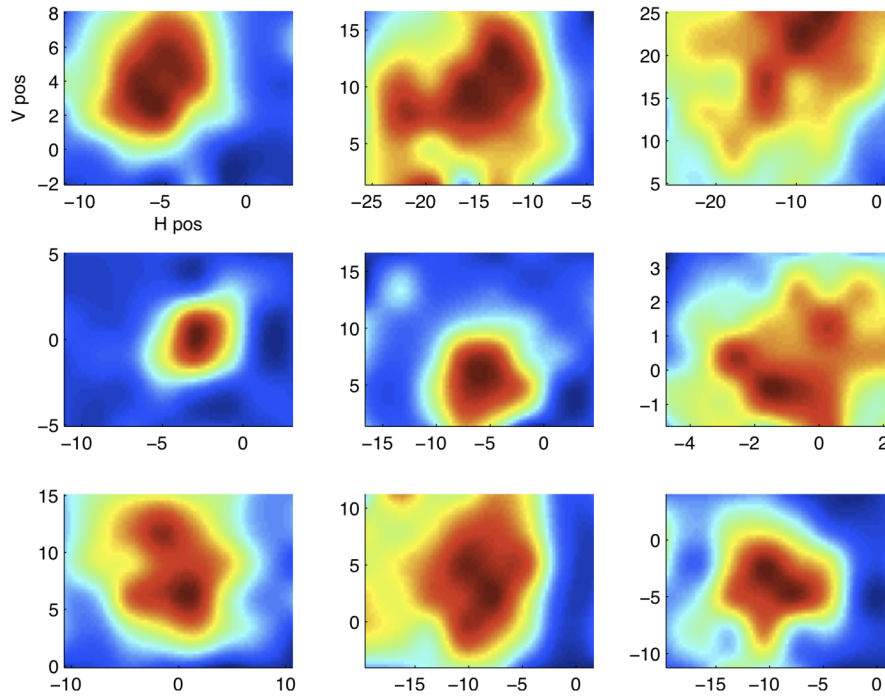


Figure 3-3

Example visual RFs from monkey G. Each panel displays the visual RF from a different neuron, as obtained from a passive mapping task. Dark red in each heat map corresponds to the highest level of firing observed and dark blue corresponds to the lowest activity level. The full color map is used for each panel, so the same color in two different heat maps does not necessarily represent the same firing rate.

Deconstructing the LIP-pursuit correlations

Recall that the LIP-pursuit correlations for that I described in Chapter 2 are actually partial correlation coefficients with several control variables that I wanted to ensure could not explain away the apparent correlation between LIP and postsaccadic pursuit. To help readers better understand the effects of the different control variables on the LIP-pursuit correlation, I will show some of the intermediate stages of my analysis of the relationship between postsaccadic pursuit and LIP activity.

First, consider the equation for the partial correlation between x and y while controlling for one variable z :

$$r_{xy.z} = \frac{r_{xy} - r_{xz}r_{yz}}{\sqrt{1 - r_{xz}^2} \sqrt{1 - r_{yz}^2}}$$

Clearly, $r_{xy.z}$ is only going to be less than r_{xy} if z is correlated with both x and y . Thus, if a second behavioral variable is going to explain away a correlation between LIP activity and postsaccadic pursuit speed, it has to be correlated with both pursuit speed and LIP. By considering which other behavioral variables are correlated with pursuit speed, then, we can see which ones have a chance of explaining an LIP-pursuit correlation. The distribution of these correlations for each monkey is shown along the top row of Figure 3-4. In this and subsequent figures, *psvel* refers to the measure of postsaccadic pursuit speed that was analyzed through the bulk of this thesis, *lats* refers to saccade latency, *ampl2* is saccade amplitude, *peakv2* is peak eye speed during the saccade, and *durs* represents saccade duration. The relationships between the other variables and *psvel* appear to be generally stronger for monkey G (blue lines) than for monkey I (green lines).

Also included in this figure are the relationships between each of the control variables and each other (panels in remaining rows of figure). These reveal a strong covariance, especially for monkey G, between saccade latency and amplitude, that has been observed before (Guan et al., 2005). Note that the expected “main sequence” relationships between saccade amplitude, peak eye speed, and saccade duration show up to varying degrees in the lower panels (de Brouwer et al., 2002). For monkey I, as expected, amplitude and peak speed are positively correlated, as are amplitude saccade duration. For monkey G,

amplitude and peak velocity are more often negatively correlated. When the partial correlation between the two variables, controlling for duration, is computed instead, the expected positive relationship is revealed (van Beers, 2007). The negative correlation between peak speed and saccade duration (lowest panel) has been seen previously in humans (van Beers, 2007).

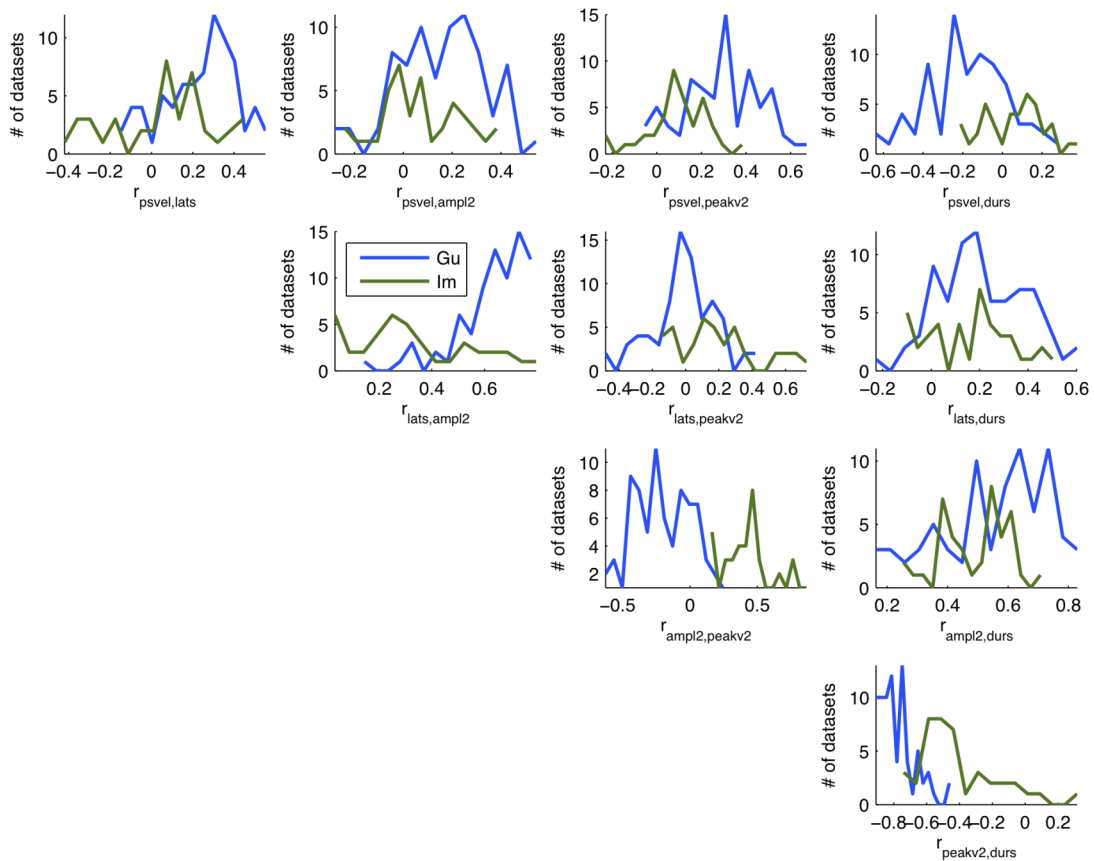


Figure 3-4

Correlations between postsaccadic pursuit speed and the other variables considered in the LIP-pursuit correlations. In each panel, the distribution of correlation coefficients between two variables is plotted separately for each monkey. One variable in the correlation is the same going down each row and column

The population average unadjusted correlation between postsaccadic pursuit speed and LIP firing rate (Figure 3-5) largely resembles the average partial correlation for these

variables (Figure 2-5). Both peak between 0.05 and 0.1 shortly before the end of the saccade. A noticeable difference between the two is the more prominent early peak in the unadjusted correlation for monkey Gu. The effects of including just one control variable in the partial correlation are varied (Figure 3-6). For monkey I, the partial correlations for none of the control variables (thin green lines) differs much from the unadjusted correlation (thick green lines). Meanwhile, each control variable has a noticeable effect for monkey G. Including latency or amplitude (upper panels) results in a higher peak correlation for activity near the end of the saccade than in the unadjusted case. The results of controlling for peak speed or duration (lower panels) are very similar to each other, as might be expected given the strong negative correlation between those two variables if each was also related to LIP activity in an opposite way (Figure 3-4, lowest panel). In both cases, the early peak is increased in size and the late peak is reduced to around zero.

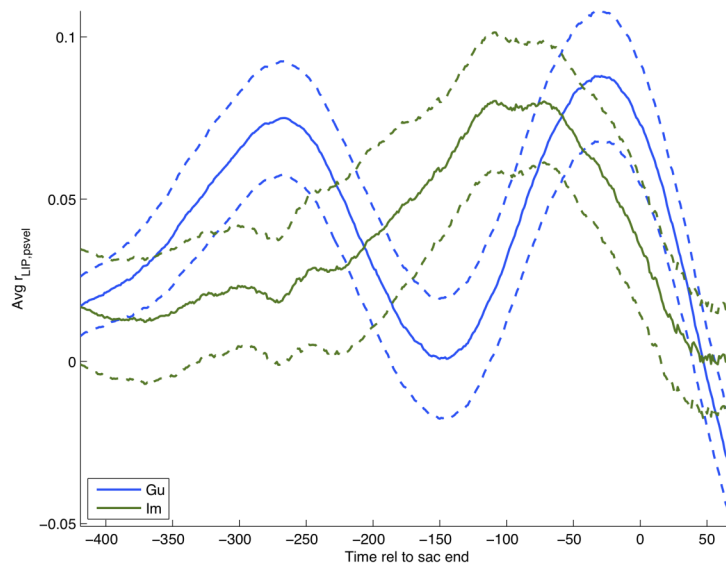


Figure 3-5

Average unadjusted correlation between postsaccadic pursuit speed and LIP activity. Each line shows the population average Pearson correlation coefficient between firing rate and postsaccadic pursuit speed for one monkey as a function of the time of the neural activity that was used to compute the correlation. Dashed lines represent standard errors of the mean.

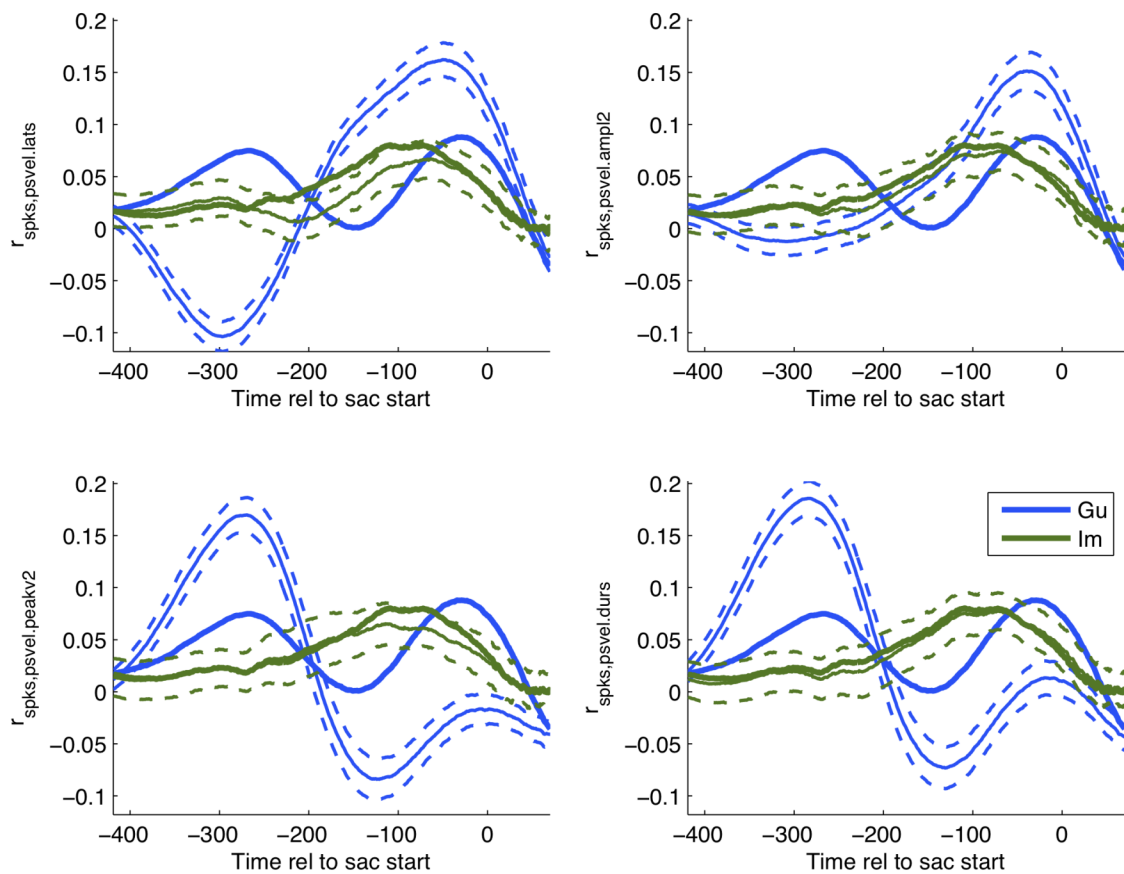


Figure 3-6

Partial correlations between LIP activity and postsaccadic pursuit velocity controlling for single variables. Each panel displays the average correlation (\pm s.e.m.) between LIP and pursuit while controlling for a different third variable as a function of the time of the neural activity used (thin lines). The significance of the variables names is given in the text. Also shown for comparison purposes is the unadjusted correlation between LIP and pursuit (thick lines).

LIP-pursuit correlations when the target is always inside the RF

For a subset of experiments done on monkey I, the target always appeared inside the RF. There were again two trial types in these experiments, but on one the target moved to the right after appearing, and on the other target moved to the left. I again computed the partial correlation between LIP activity and pursuit velocity in the same window as used

in previous postsaccadic pursuit analyses, while controlling for the full set of control variables used before (Figure 3-7). The average LIP-pursuit correlation for the rightward trials (blue lines) and the leftward trials (green lines) reaches a positive peak near the end of the saccade. The average LIP-pursuit correlations for the two motion directions are similar throughout.

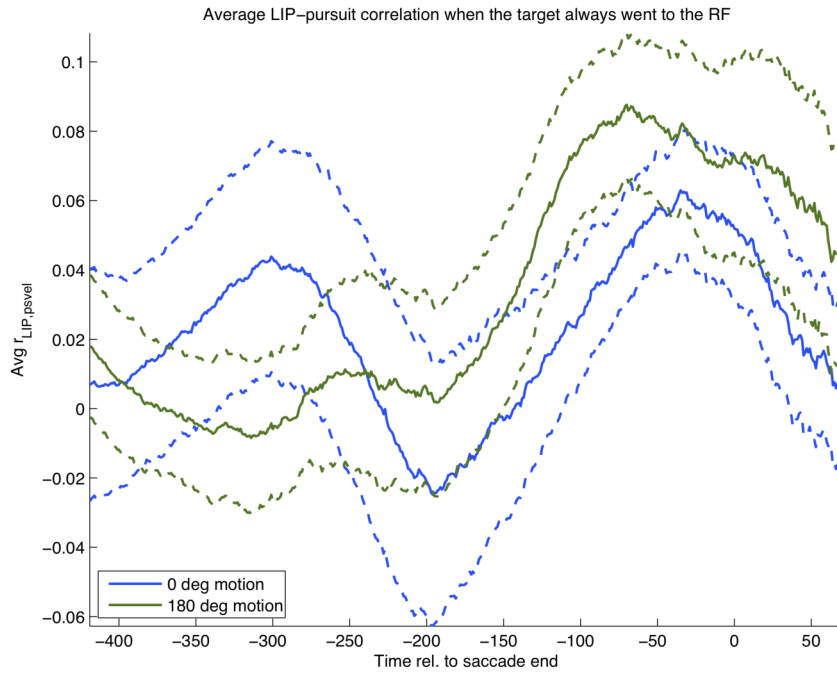


Figure 3-7

LIP-pursuit correlation when the target always appeared inside the RF. Solid lines show the average LIP-pursuit correlation (dashed lines, +/- s.e.m.) for experiments where the target always jumped to the RF of the neuron. The two traces represent different movement directions.

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Conclusions

In this thesis I have described experiments that examined the role of area LIP in guiding smooth pursuit eye movements. Using the naturally occurring variation in neural and behavioral responses as a window into the neural function, I tested for trial-by-trial correlations between firing rate in the area and pursuit behavior. I found that LIP activity was correlated with both presaccadic and postsaccadic pursuit speed. Correlations between LIP and saccade parameters could not explain the postsaccadic LIP-pursuit correlations. The variability of the LIP-pursuit correlations was large, so I attempted to determine what predicted its variability. I found that neurons that high firing rates at a window around the time of the saccade predicted high postsaccadic LIP-pursuit correlations. Finally, I also found in one monkey that when a target appeared but did not move, there were correlations between LIP activity and the speed of postsaccadic “glissades”.

Better evidence for an LIP-pursuit link

The fundamental contribution of this thesis is the strongest evidence yet for a role of LIP in pursuit guidance. Early in the modern exploration of parietal cortex, neurons that responded to pursuit were reported (Lynch et al., 1977). This study was conducted before the broad recognition of LIP as a functionally distinct area, however, so it is unclear how many of the reported neurons were located there. More recently, Bremmer et al. (1997) described pursuit responses in neurons that they histologically tied to LIP. My work adds

to the existing knowledge by revisiting this topic, which has received scant study, and shows for the first time that single-trial fluctuations in LIP activity are associated with fluctuations in pursuit. I believe this trial-by-trial link is stronger evidence for a pursuit function for the area than the examination of averages that was done by previous researchers. My results remain correlational as well, however, and causal experiments will have to follow.

It is worth noting that I observed few, if any, neurons that displayed the tonic discharge during pursuit that was characteristic of the sample neurons shown in the work of Bremmer et al. This may be due to a difference between where they and I were recording. The neurons I recorded much more resembled “classic” LIP neurons (Barash et al., 1991), yet they were nonetheless correlated with pursuit.

What exactly is its job during pursuit?

As described more fully in the first chapter of this thesis, the pursuit system has flexibility in how it uses visual motion. Depending on behavioral context, the same visual input can lead to smooth pursuit movements of varying speed, as if the pursuit system contains modifiable “gains” that determine how strongly visual motion drives pursuit. For instance, during on going pursuit, small perturbations in target speed lead to perturbations in eye speed. The higher the ongoing pursuit speed, the larger the pursuit system’s response to the perturbation (Schwartz and Lisberger, 1994). Similarly, when a saccade is

made to a distant target, postsaccadic pursuit is much stronger than presaccadic pursuit, as if the saccade is turning up the gain on the target's motion (Lisberger, 1998).

These experiments were motivated in part by a desire to understand the neural underpinnings of the pursuit system's ability to do things like control gain and select a target for pursuit. Since MT and MST neurons represent target motion the same whether the target is used for pursuit or not (Recanzone and Wurtz, 2000), it seems likely that these aspects of pursuit are controlled after those areas in the pursuit circuit. Our results are consistent with LIP being involved in the regulation of pursuit gain. In such an interpretation, the higher the firing rate of an LIP neuron, the higher the gain that is applied to the motion in that neuron's RF. When considering this possibility, it is important to keep in mind that we found an LIP-pursuit correlation for both presaccadic and postsaccadic pursuit. This means that if LIP is controlling a gain, it is not controlling one that is exclusively tied to the saccade. Therefore, any role for LIP in gain control for pursuit is not limited to specifying the size of the gain change that accompanies the saccade.

Another possibility is that LIP is acting more like MT and MST and encoding the nature of the motion rather than the gain that should be applied a motion representation that is generated someplace else in the brain. Indeed, some LIP neurons are tuned to the direction of visual motion (Fanini and Assad, 2009), and LIP activity has been tied to motion perception (Williams et al., 2003). I have found no reports in the literature of motion speed tuning in LIP, but some degree of tuning seems likely, given the robust

inputs to the area from MT and MST. Therefore, LIP may be representing the speed and direction of visual motion, and the pursuit system may be reading this representation out in the same way that it is thought to read from MT and MST.

These two possibilities need not be in opposition. It may be most appropriate to think about LIP as controlling *both* a gain and representing motion direction and speed. Far fewer neurons in LIP are directionally tuned than in MT or MST, and the directional tuning that is present is very broad. Even when motion is in their antipreferred direction, LIP neurons often still fire fairly vigorously (Fanini and Assad, 2009). This remaining activity may be an underlying spatial signal that is always present and can still influence pursuit, even when the neuron has not detected its preferred motion.

Placing these results in context

It is important to consider how these results might—or might not—be reconciled with existing approaches to the function of LIP. In doing so, a unifying observation may be that while many paradigms view LIP neurons as determining binary outcomes about the region of space they represent, my work suggests the involvement of neurons in the area in determining a continuously valued outcome for space. For example, the “intention” and “decision” takes on the region (Gold and Shadlen, 2007; Andersen and Cui, 2009) seem to assume that each neuron is voting on the question “Saccade here or don’t saccade here?”. Similarly, the proposals that LIP controls spatial attention appear to hold that neurons deciding whether to put the “attentional spotlight” at their RF or not. For

example, the work of Bisley and Goldberg (Bisley and Goldberg, 2006, 2010) proposes that the spotlight is at spatial location corresponding to the peak of LIP activity, and seems to regard the absolute height of that peak as irrelevant to behavior.

By contrast, my work suggests the involvement of LIP in a continuously varying outcome for a fixed spatial location. Each neuron seems to be saying *how strongly* to act based on what is in its RF, rather simply whether to act or not. A connection should probably be drawn, then, between these results and the finding that LIP encodes the relative value of targets (Platt and Glimcher, 1999). In the case of that work as well, the neurons are proposed to be making continuous judgments about space.

When trying to relate my results to existing conceptual frameworks for the area, my finding of LIP-pursuit correlations for both presaccadic and postsaccadic pursuit is again important. In both the decision and the intention view, the activity that leads up to the saccade is not directly tied to a behavior, but rather only has direct consequences if a decision is made or a saccade is executed. In my results, by contrast, presaccadic activity is associated with a motor behavior; it is directly tied to action rather only being related to the possibility of an action. In this sense, the priority map interpretation of LIP (Bisley and Goldberg, 2010) may fit better with the correlations I found, as it allows for LIP activity to be put to use even without a saccade.

Future directions

Many different experiments could be done to follow up on the work in this thesis. An obvious first step would be to see if microstimulation can modulate pursuit, as this would provide causal evidence for the involvement of LIP in pursuit. The basic experiment would be to simply microstimulate below the threshold needed to evoke a saccade while a target moves through the RF of the multiunit activity near the electrode. The prediction would be that presaccadic and postsaccadic pursuit are faster on stimulation trials than on controls.

It would also be interesting to apply microstimulation to two target tasks. In such a task, Gardner and Lisberger (2002) successfully affected postsaccadic pursuit choice by stimulating above the saccadic threshold in the SC and FEF, but failed to modulate presaccadic pursuit by stimulating below threshold in FEF (they did not try subthreshold stimulation in the SC). I would be very surprised if stimulating above the saccadic threshold in LIP did not result in pursuit target choice after the saccade. More interesting would be the results of subthreshold stimulation there. If stimulation biased presaccadic target choice, it would suggest different roles for LIP in FEF in oculomotor behavior. If it did not, then it would be worth trying subthreshold stimulation during a task more like that of Carello and Krauzlis (2004), which required a luminance discrimination prior to movement. These researchers found that stimulation in SC could influence pursuit, which suggests that stimulation in the upstream area LIP would have the same effects. If subthreshold stimulation in LIP affected pursuit during the Carello and Krauzlis task but

not the Gardner and Lisberger task, this would be suggest that LIP's involvement is contingent on the discrimination aspect of the Carello task. If area LIP is increasing gain of a stimulus by increasing its effective contrast (Reynolds and Chelazzi, 2004), stimulation effects may not be present due to ceiling effects if the contrast of the targets is already too high.

There are more single unit recording experiments to be done. For one, it is worth going after the question I described of whether LIP's role in pursuit is better understood as gain modulation or the representation of visual motion. A first and straightforward approach to this question would be a systematic investigation of the speed tuning of LIP neurons. These results would give an idea of the ability to LIP neurons to encode speed changes. This could be followed up with a study in which the direction tuning of neurons is measured, and LIP-pursuit correlations are then obtained for target motions at different points along the direction tuning curve. If the correlation disappears when motion is in the antipreferred direction, this would suggest that the pursuit system is using the information LIP provides about the specifics of the target motion.

Finally, when I began my experiments, I did not expect that studying relationships between LIP and presaccadic pursuit would be an option, as I knew that any presaccadic pursuit I observed would be small for all but the few neurons I would likely record with RFs near the fovea. I therefore set up my experiments so that presaccadic pursuit would be minimized, with the thought that I would focus on postsaccadic pursuit instead. I was surprised, then, that there were a correlation between LIP activity and the presaccadic

pursuit movements that I did measure, which were very small on average. It thus now seems like studying LIP's relationship presaccadic pursuit would not be an unusual technical challenge. Thus, it would be not exceptionally difficult to conduct more thorough studies of LIP-pursuit correlations for presaccadic pursuit. If the stimulus moves directly toward the fovea, the presaccadic pursuit response would be maximized and the number of complicating saccades would be minimized, as was observed long ago (Rashbass, 1961; Lisberger and Westbrook, 1985).

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