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Los Angeles

Testing neural mechanisms
that may underlie spatiotopic processing
in area MT

A dissertation submitted in partial satisfaction of the
requirements for the degree Doctor of Philosophy
in Neuroscience

by

Wei Song Ong

2012

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ABSTRACT OF THE DISSERTATION

Testing neural mechanisms
that may underlie spatiotopic processing
in area MT

by

Wei Song Ong

Doctor of Philosophy in Neuroscience

University of California, Los Angeles, 2012

Professor James Bisley, Chair

It may be hard to fathom, but our eyes make 3-5 fixations every second, connected by short, rapid eye movements known as saccades. As a result of this motion, the target object changes retinal position even though it may remain in the same spatial position. As such, the image of the world that falls on our retina is constantly changing, but we perceive the world as stationary. It is important for us to be able to detect the moving objects in space and predict and judge their position and trajectory, for instance, a moving car. Here, we study the processing coordinate system of visual motion, to see if it is coded for in retinal (relative to the eye) or spatial (relative to the world) coordinates.

To do this, we used human psychophysics, which is a method used for quantitatively measuring performance of the perceptual system using stimuli that are systematically varied. We measured the ability of nine human subjects to discriminate the direction of two moving-dot stimuli that were separated temporally. In each trial, the subjects were required to make a leftward or rightward saccade after the presentation of the first stimulus. In doing so, the second stimulus could appear in the same spatial or retinal position as the first. Using this paradigm, we found that subjects were better at detecting the differences in direction when the two stimuli were placed in the same spatial location than when the two stimuli were placed in the same retinal location. This suggests that memory for motion is likely processed and stored in a region that is spatiotopic or that automatically accounts for saccades. Using a similar task, in which a saccade was not executed, we showed that as the two stimuli to be compared were spatially displaced from each other, the distance at which performance deteriorated increased at increasing eccentricities, in a fashion which best matched the receptive field sizes of area MT. From this first set of experiments, we conclude that area MT plays an important role in the memory for motion process, and that this is carried out in spatiotopic coordinates.

As it is well established that information about visual motion is processed in area MT/V5 in both monkeys and humans, the fact that this area contributes in a memory for motion task is not unexpected. What is surprising is that it appeared to do so in spatial coordinates; MT has been traditionally thought to be a retinotopic area. However, there has been recent debate as to whether it can process information in spatial coordinates. In the next two studies, we look

closely at how area MT may be able to perform spatiotopic processing by recording extracellularly from individual neurons in three animals.

The first of these experiments had the animals performing a simple saccade task in which a spatially stable moving dot stimulus was presented in either the pre-saccadic or post-saccadic receptive field of the neuron being recorded from. The MT neurons we recorded from responded as if their receptive fields were purely retinotopic, and did not respond to stimuli presented in the pre-saccadic receptive field after the saccade and did not respond to stimulus presented in the post-saccadic receptive field before the saccade. Furthermore, when a stimulus was presented in the post-saccadic receptive field, the neurons did not start responding to it until well after the end of the saccade, as if it had just appeared on the screen. This means that the receptive field of the neurons do not shift to their post-saccadic location before or during the saccade, a process termed anticipatory remapping, but remain linked to the retina.

There is a possibility that spatial processing could come from neural remapping within MT in a more subtle fashion that does not require the receptive fields to shift ahead of time. To look at this, we performed another set of experiments where a transiently presented stimulus is present in the future receptive field of the neuron, but is no longer present when the eye movement is made. If visual responses to the stimuli in the post-saccadic receptive field are transferred from one neuron to another at the same level of processing (within MT), we would see a remapped trace of the visual signal after the eye reaches the new fixation position. Using a black disc presented on a white background for 50ms, we find that MT neurons do not remap responses to

the stimulus when it is no longer present. Hence we conclude that MT neurons do not appear to have any form of remapping.

In conclusion, we have shown that motion perception involves some spatial processing, however area MT, the traditional motion processing area, has receptive fields which work strictly in retinal coordinates. These receptive fields do not shift preemptively to their post-saccadic location prior to the end of the saccade and the neurons in area MT do not appear to pass visual information to each other at the end of the saccade. We propose the presence of an automatic process which updates motion information to spatial coordinates, possibly through the transfer of information to an area which is spatiotopic or which has strong remapping activity, such as LIP or FEF. This would account for the optimal performance we see in the first experiment in spatiotopic locations, while also providing an explanation for the lack of spatial processing we see in area MT.

The dissertation of Wei Song Ong is approved.

Joaquin Fuster

Dario Ringach

Dean Buonomano

James Bisley, Committee Chair

University of California, Los Angeles

2012

For my parents

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VITA

April 21, 1984

Born, Kajang, Malaysia

2007

Biochemistry, BSc, First Class Honours;
Imperial College,
London, United Kingdom

PUBLICATIONS

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Chapter 1:

Introduction

Primates, human or not, rely heavily on their visual system. It is what that allows us to spot a lion in the savannah at 50 paces, or a loved one at a crowded airport. It is also a system which has common origins throughout the animal kingdom but subsequently evolved independently, giving rise to the distinctive insect compound eyes as well as the human simple eye, thus allowing us insight into its importance. Here we focus on the primate visual system, as this is the sense which sighted individuals use most for interaction with our environment.

Many think of the visual system as consisting only of our eyes – which I really prefer to think of as a periscope that allows the visual system concealed within the skull to peer out into the world. That is not to downplay their importance, for the eye is really a part of the brain that extends outwards. Light is allowed in through the window of the lens, and this light is then picked up by a mosaic of photosensitive rod and cone cells lying on the retina which in turn sends this information to the back of the brain where the visual areas reside.

The reception of this retinal image may seem like a one-off event where a snapshot is taken of a visual scene, and then decoded by the brain. However, scene viewing is more of a spatial-temporal event, as our efforts to take in the visual scene is carried out via a number of gaze shifts, resulting in the reception of drastically different retinal images over a short period of time.

The brain is then required to integrate this patchwork of views to form a coherent picture of the scene into a world-centric coordinate system.

In this work, I will answer the question of whether the processing of motion information occurs when the images taken are still present in its 'raw' retinal form, or if it happens after they have been integrated into spatial (i.e. head- or world-centric) coordinates. As the earlier visual areas (areas V1, MT, MST) that show motion processing do so in retinal coordinates, we also looked to see if there may be a mechanism present in these areas to transition the information to spatial coordinates.

In the next section (1.1), I will give an overview on visual stability and how we think that it can be brought about. I will describe the main mechanisms thought to underlie this process, with a particular focus on the mechanism of remapping, which will then be further illustrated in section 1.2. Within that section, I will describe studies which have shown evidence of remapping in multiple brain areas (section 1.2.1), and a brain signal which allows for the mechanism of remapping to be carried out efficiently and effectively (section 1.2.2 Corollary discharge). Next, we will delve into the middle temporal area (MT), a region of the brain where visual motion is processed (1.3) and that I have focused on in my studies. At the end of this chapter (section 1.4), I will describe the experimental aims and the key results of the studies.

1.1 Visual Stability

The world around us is mostly stable – that is, most of the objects do not change drastically in location or appearance from one minute to another. For example, your favorite chair by the window will stay there no matter how long you take to look around the room. However, your dog may not. It is important for us to be able to keep track of moving entities and at the same time, keep track of where the stable unchanging objects are while we move through the environment, which makes the visual input to our eyes constantly changing.

In addition to a shifting visual input every time the eye moves, we also only receive clear images when the eye is not moving. These fixations tend to last for only 100-150 ms (Yarbus, 1961; Viviani, 1990). These images are also separated from their actual locations in space and time, and connected by fuzzy, blurred images that are taken during a saccade. Our eyes also track objects, using a smooth pursuit movement, but here we focus only on what happens to the visual information during saccadic eye movements.

It is thought that there are a few possible mechanisms by which the brain allows us to perceive the world as being stable. The first thing that needs to be addressed is the suppression of the sweeping image change which moves up to 900 deg/sec during a saccade. The brain appears to ignore the visual input that comes through the eye during these movements – this is termed saccadic suppression.

The second and most idealized way is that the visual information is received and processed via world-centric coordinates, which would render its representation space invariant, hence,

insensitive to changes in the response field of the neuron. However, given that most visual areas use the retinal coordinate frame, it would seem an unlikely scenario. A second way is through the providence of a positional signal together with the visual information present in the receptive field of the neuron. This would allow the computation of a map which represents our visual world utilizing spatial coordinates within our brain. Such gain field neurons, which respond differently to the same object within its receptive field depending on eye position, have been found in V3A, V4, MT and MST (Galletti and Battaglini, 1989; Bremmer et al., 1997; Bremmer et al., 1999; Bremmer, 2000). These neurons could be able to pass this information to a higher up spatial map to update its percept of the visual world with each eye movement. (Zipser and Andersen, 1988; Morris et al., 2012)

Third, it is possible that we only maintain a snapshot of the world in retinal coordinates, and this map is updated with every eye movement we make. To maintain visual stability, a preparatory signal could be supplied to these brain areas, and allow them to shift their receptive field in anticipation of the upcoming eye movement. Conceptually, we know this as anticipatory remapping (further elaborated in the following section), as a way to allow for spatial updating of the retino-centric map as the visual image of the world is displaced. What this means is that shortly before a saccade, these neurons respond not only to what is in their classical receptive field, but also to the stimuli that are present in their future receptive field. A preparatory signal which originates from the motor area and known as the *corollary discharge*, (explained in section 1.2.3), supplies vector information regarding the upcoming ballistic eye movement and allows the target area to prepare for the imminent translocation of the visual signal.

Evidence that these prei-saccadic mechanisms play a role in creating the percept of a stable world comes from the bizarre mislocalization of briefly flashed stimuli around the time of a saccade. Under darkened conditions, this gives rise to a percept that the stimulus is shifted from its actual location in the direction of or opposite to the direction of the saccade. The former occurs when the flash is presented before the initiation of the saccade, while the latter occurs when the flash is presented after saccade onset. This effect is particularly strong when the experiment is carried out in a completely darkened room whereby the subject can only rely on the retinal signal from the flashed stimulus (Honda, 1993; Schlag and Schlag-Rey, 2002). On the other hand, under illuminated conditions, the perception of the mislocalized stimulus is consistently clustered around the saccade end-point. This is termed saccadic compression, and has been demonstrated to occur in the dimensions along and orthogonal to the saccade direction. (Ross et al., 1997; Lappe et al., 2006). Thus, these phenomena give us the insight that the mechanisms which the brain uses to maintain visual stability are likely to occur during saccades.

1.2 Remapping – A mechanism that could explain spatial stability

In this section, I define the terms and concepts related to remapping, the neural process that I will primarily be examining in this study.

The first report of a remapping signal was made in the lateral intraparietal area (LIP) in the posterior parietal cortex by Duhamel et al in 1992. The group showed that the neurons in this area were able to shift their receptive fields pre-emptively prior to the saccade to allow responses to the stimulus that would fall in the receptive field of the neuron at the next fixation point. This

neural mechanism is known as anticipatory remapping and the concept of spatial updating is what that allows for visual stability.

A neuron which is able to perform anticipatory remapping can have the unique ability to respond to stimuli placed in two distinct locations during time period right before a saccade is executed. First, it could continue providing information on the stimulus which is present in its presaccadic receptive field during the current fixation. Second, more crucially, is as the neuron receives the information about the impending saccade, it starts responding to the stimulus in the imminent receptive field even before the eye has moved from the current fixation. After the eye makes a saccade and achieves fixation at the new location, a subsequent increase in neuronal activity is seen- and this is the expected visual response. If we see this expected visual response without the prior anticipatory increase in activity, it must mean that the neuron is responding to the appearance of the stimulus in its environment and not via remapping during the saccade.

For example, in figure (1) shown below, the initial fixation point is represented by the point labeled FP1. This would be the location which falls on the fovea of a person whose eye is held steady at that point. RF1 is the associated receptive field of a given neuron. When a rightward saccade is made and the person moves his eye so that it lands at the second point (FP2), the neuron starts responding to its post-saccadic location – shown as RF2. The receptive fields (RFs) referred to in this example all correspond to the typical activity seen by all retinotopic neurons, which means that if a stimulus appears in the receptive field of the neuron, we see a burst of activity, while we do not observe any changes in activity when the same stimulus is presented outside of the receptive field.

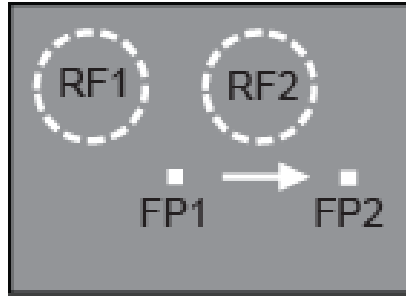


Figure1:

The positions of the initial fixation point (FP1), the saccade target (FP2), the pre-saccadic receptive field (RF1) and the post-saccadic receptive field (RF2) were set so that the classical receptive field at FP1 was RF1 and the receptive field at FP2 was RF2. The arrow indicates the direction of the saccade.

In theory, the maintenance of visual stability via remapping could occur in a couple of ways. First, a neuron could shift its receptive field to the post-saccadic location prior to or during the actual eye movement, allowing the taking in of visual information of the future field in a bottom up manner. Second, the neuron in question could receive input from other neurons at the similar level of processing after the saccade, a process which could transfer useful, identifying information from one region to another without it having to reprocess the visual information from the top.

When a neuron is able to remap its receptive field towards the region of space to which it would soon be responding, around the time of a saccade, we would expect to see it respond to the object which is present in RF2 *before* the eye is stabilized on FP2. This would be a response which anticipates the entry of a visual stimulus into its receptive field by the end of a saccade. This type of remapping can be observed by calculating the latency of the response; a neuron remaps in an anticipatory manner if it responds faster to an object which had already been present in RF2 after

a saccade, compared to its response when the object makes a sudden appearance in the receptive field.

If the receptive field has moved to the next location prior to the execution of a saccade, which is shown by responding preemptively to RF2, it follows that this cell would stop responding to RF1 before the eye leaves FP1. This has been demonstrated to be the case in a study by Nakamura (2002) who showed that the response to a stimulus in RF1 immediately preceding the saccade is attenuated compared to a response observed when the visual stimulus was presented well before the saccade in the same location.

Alternatively, neurons within the same area which have previously processed the visual information in a different retinal coordinate could transfer the information to the neurons who would soon respond to the same location. This can be illustrated using figure 1: while the eye is foveating FP1, the entire visual field would be subdivided into many many receptive fields, each watched over by a different neuronal population. So while we focus on the neuron whose receptive field is at RF1, there would be neurons which respond to RF2 while the eye is stable at FP1. When a saccade occurs, this second population of neurons could shunt the information that it already has about the visual information of that location in space over to the first neuron, making the overall process much more time efficient. This is because the visual information from the world is first detected by the photoreceptors on the retina, and this information is then sent up to the LGN, then V1, followed by the extrastriate areas and the parietal cortex. This process occurs via multiple synapses and takes time and energy to accomplish. At each level, this information undergoes processing and combines responses from both the dorsal (the 'where')

and ventral (the ‘what’) pathway, which then informs the later areas of its features, identity, and even its importance (for review, see(Farivar, 2009)). In contrast, the remapping of visual information would possibly allow for all this information to be attained through one short synaptic transference – so it makes sense for this process to occur. This can be seen through the use of a stimulus which was transiently present in RF2, but is then no longer present after the saccade is initiated.

1.2.1 Areas that demonstrate remapping

In order for a signal to be recognized as a remapping response, it needs to adhere to a few criteria. Firstly, it should not be a response which is explainable by the visual onset of a stimulus in the absence of a saccade plan. It should also be an observable elevation (or reduction) of neural activity that cannot be explained by the execution of a saccade by itself.

Given the hypothesized importance of remapping in the maintenance of visual stability during eye movements, it is not surprising that the brain areas which show the most robust remapping signals are places which have both visual and motor signals such as LIP, FEF (frontal eye field), and SC (superior colliculus).

In LIP, neurons are able to transfer their receptive fields ahead of the eye movement, showing an increase in activity that is independent of the saccade when an object is present in the post-saccadic receptive field of the neuron. Using a typical remapping paradigm which consisted of a transient stimulus, it was shown that LIP neurons are able to respond to a stimulus that was never

actually present in the classic retinotopic receptive field of the neuron (Duhamel et al., 1992a; Nakamura and Colby, 2002; Heiser and Colby, 2006; Berman et al., 2007). Furthermore, when a stable stimulus is present in the context of a search task, the neurons are able to demonstrate anticipatory remapping towards a stimulus which is entering its receptive field even before the saccade is initiated. Additionally, information about this upcoming object is present in this early signal which precedes the saccade, allowing the brain to differentiate between an object which potentially contains reward and one which does not (Mirpour & Bisley, 2012, under review).

Areas more associated with motor signals, FEF and SC have also been found to demonstrate remapping (Walker et al., 1995; Sommer and Wurtz, 2006; Churan et al., 2011). Together with the MD (mediodorsal) nucleus of the thalamus, these three areas form an interconnected system which receives motor commands from the cortex and generates corollary discharge signals. As corollary discharge signals are thought to be essential for remapping activity, it is unsurprising that FEF and SC have remapping activity, and the inactivation of the MD nucleus disrupts the ability of the subject to perform double step saccades accurately (Sommer and Wurtz, 2002). The double step saccade task is one in which two saccades are made by the subject, one after another, to two remembered locations in the dark. In subjects where remapping is disrupted, either through a unilateral stroke in the parietal region (Duhamel et al., 1992b; Heide et al., 1995; Heide and Kompf, 1998) or transaction of the corpus collusum (which allows communication between the left and right hemispheres) (Berman et al., 2005; Berman et al., 2007), subjects are able to make the first saccade, but have difficulty locating the second target accurately, as they are no longer able to update the new location information accurately to the spatial map. After the

eye makes the first saccade, the remembered retinal location of the second location no longer corresponds to that in world coordinates.

Areas V2, V3 and V3a are parts of the extrastriate cortex that also show remapping, though they lack the robust motor signal shown by the parietal and motor areas. As we move down the hierarchy from V3a to V3 then V2, the portion of neurons which demonstrates anticipatory remapping prior to saccade onset decreases (16%, 9% and 2% respectively), compared to 35% of LIP neurons. (Duhamel et al., 1992a; Nakamura and Colby, 2002). This suggests that remapping is not a bottom-up process.

1.2.2 Corollary discharge

Helmholtz referred to self-induced eye movements as an ‘effort of will’, which in turn informs the other brain regions of its motor intentions. The main idea behind this was that when we move our eyes and bodies, a signal which comes from the originating motor center imparts the precise vector and timing of this movement to the rest of the brain, thus helping us maintain a sort of anticipatory stability. In a total paralysis experiment from 1976 (Stevens et al., 1976), the subject reported that “when he attempted to move his eyes to the right, they [the eyes] felt paralysed, yet the visual world was [perceptually] spatially relocated to the right”. The observers reported that no actual eye movement was made by the subject’s eyes. This allows the conclusion that cortical motor areas ‘inform’ the visual areas that an eye movement is being attempted, and the perceptual areas adjust their notions accordingly, despite the movement not having been actually made. Two important points are made in this study – the first being that proprioception sensors

are not responsible for the feedback to the percepts, as the brain perceives the visual world to have moved based on the subject's effort to make an eye movement while neither the eye nor the world has. This is further substantiated by studies which directly stimulated the motor nuclei of the eye in the brainstem and found that the movement was not compensated for in the percept (Mays et al., 1987). The second point gleaned from this study is that communication with perceptual areas occur prior to the motor nuclei, and this transmission takes place heedless of the actual oculomotor response. This is the signal termed corollary discharge (Sperry, 1950).

The corollary discharge signal adheres to a few criteria. Firstly, it is a detectable signal which precedes the actual movement of the target muscle. This signal would originate from a motor area but travel away from the executing muscle group. This also assumes that if this signal is perturbed or ablated, it would not affect the executed motor action under conditions which it would not be needed, such as simple saccades. However, when this information is required, as that in a double-step saccade task where the subject makes eye movements to two remembered locations in total darkness, the corollary discharge signal becomes important as no visual feedback is available. The corollary discharge signal is what that allows us to adjust the precepts of the visual world by transforming retinal to spatial coordinates ahead of time to maintain visual stability.

1.3 Area MT

In this work, we will be collecting neuronal data from the middle temporal area (MT) in the brain. This is for two reasons: firstly, the neurons in this area are sensitive to moving visual stimuli and stimulation of this area changes the percepts of visual motion (Salzman et al., 1990;

Groh et al., 1997; Nichols and Newsome, 2002). Secondly, the results from our psychophysics study (see chapter 2) suggest that area MT participates in spatial processing in a memory for motion task.

Area MT lies on the floor of the superior temporal sulcus and was first described by Dubner and Zeki (Dubner and Zeki, 1971) in non-human primates to be preferentially tuned for the direction and speed of moving visual stimuli. The location of the corresponding human brain area (Huk et al., 2002) was detailed in a case study which involved a patient who complained of a loss of visual movement perception following a stroke (Zihl et al., 1983). For example, she was not able to stop pouring tea into a cup at the right time because she was unable to perceive the movement of the fluid in the cup when it rose as it appeared to be frozen. This impairment contributed to her inability to go out, as she was unable to judge the speed of cars. In her own words, “when I’m looking at the car first, it seems far away. But then, when I want to cross the road, suddenly the car is very near”, which made her unable to cross streets while being able to identify the car itself without difficulty. The patient appeared to have suffered bilateral lesions in the parietal region, clearly outside the borders of the primary visual cortex and analogous to the MT and MST regions in the monkey cortex (Zihl et al., 1983). This was one of the first clues which isolated the human brain region that allowed for perceived visual motion.

Area MT receives direct inputs primarily from area V1, and also from the LGN, areas V2 and V3. Neurons in area V1 form a retinotopic map of the contralateral half of the visual field and maintain the retinal topography, which means that areas adjacent to each other on the retina are represented by adjacent neuronal populations. This contributes to the general assumption that

area MT processes motion in retinal coordinates. Apart from that, experiments carried out using anesthetized animals have indicated that area MT has a highly ordered representation of the visual field (Gattass and Gross, 1981; Albright and Desimone, 1987) and differs from area V1 only in its cruder topography and larger receptive fields (Allman and Kaas, 1971b). However, recent studies have suggested that MT can operate in a spatiotopic coordinate system. Melcher and colleagues (2005) first showed that motion information can be integrated in a spatiotopic manner across a saccade; while Zhang and Li (2010) showed that perceptual learning for a motion-discrimination task can take place in a non-retinotopic location. In chapter 2, we show that memory for motion is carried out optimally in spatiotopic coordinates and that the process has a coordinate system most similar to area MT. The most direct evidence of human MT/V5 utilizing spatial coordinates came from an fMRI study by d'Avossa et al (d'Avossa et al.), which demonstrated an invariance of the BOLD signal in a head-centric reference frame.

Despite these findings, there have also been studies which reiterated the retinotopic nature of area MT. Gardner et al (Gardner et al.) produced fMRI evidence that human MT adhered to work in retinal coordinates, while Morris et al (Morris et al.) demonstrated that the advantage of motion integration across saccades in spatial coordinates disappears with temporal certainty and is not limited to stimuli which share a head-centric invariant location. As MT is thought to mediate the motion after-effect, experiments carried out by Knapen et al (Knapen et al.) to find adaptation in spatiotopic reference frames failed to appreciate this effect compared to that carried out in retinotopic coordinates. To this end, Crespi et al (2011) attempted to reproduce results from the d'Avossa (2007) and Gardner (2008) studies and concluded that the different BOLD signals were due to the assignment of covert attention to regions in the peripheral space. In the

second set of experiments that we carry out (see chapter 3), we recorded acutely from area MT of non-human primates to explicitly test if the neurons in this area responded to stimuli in retinal or spatial coordinates.

1.4 Experimental aims

In this study, we wanted to find out what the processing coordinates are in a memory for motion task and the brain area which is responsible for it. We then asked if the neural activity in area MT could give us insight into the spatial processing we see, and how is this process occurring. We address these questions using the following experiments.

1.4.1 Processing coordinates in a memory for motion task (Chapter 2)

Aim 1a: What are the coordinates for motion processing and short term memory?

It has been well established that visual motion is processed in area MT and does so in retinotopic coordinates. However, there has been psychophysical evidence from adaptation and integration studies which suggested that motion processing may use a reference space that is linked to locations in space (Melcher and Morrone, 2003; Melcher, 2005). In order to understand the processing coordinate of visual motion, we had human subjects perform a direction discrimination task where the stimuli to be compared appear sequentially in the same retinal or spatial location. The idea behind it is that the subject would be more sensitive in detecting the difference in motion when it is not compared in the same coordinates. Hence if motion processing occurs in retinal coordinates, we would expect performance to be better in that

condition compared to the condition utilizing the same spatial coordinates. Here, we show that the decoding and/or retention of visual motion occurs in spatial coordinates.

Aim 1b: Where is this process occurring?

In the task we use, a memory component is also present, and this involves an additional operation of information retention. The work of Fuster and colleagues (Fuster et al., 1981; Zhou and Fuster, 1996) has demonstrated that cortical areas involved in encoding the features of a particular stimulus would also maintain that information.

Using the known linear relationship between the receptive field size of a given visual area and its retinal eccentricity, we looked at the point at which the performance in the memory for motion task dropped off with a step function when the two stimuli to be compared were sufficiently far apart. This demonstrates that the neurons which processed the visual stimuli were of two independent populations. We found that the relationship best reflects that of area MT. Furthermore, the role of area MT in memory for motion tasks is supported by lesion, microstimulation, and psychophysical studies (Bisley and Pasternak, 2000; Bisley et al., 2001; Zaksas and Pasternak, 2006). Hence we concluded that area MT may have the ability to carry out processing in spatial coordinates.

1.4.2 To reconcile the psychophysical evidence for spatial processing in area MT with neural data (Chapter 3)

Aim 2a: Are MT neurons spatiotopic?

There are several different explanations for our previous result, which suggested that MT may process memory for motion information in spatial coordinates. The first, most idealized way, is that if some neurons are purely spatiotopic, i.e. their frames of reference were tied to a fixed reference point in the world, then the information they encode does not change when eye movements are made. To test this, we recorded MT neurons from animals while they performed a simple saccade task in which a spatially stable moving dot stimulus was presented for 500 ms in one of two locations, the pre-saccadic receptive field or the post-saccadic receptive field. Using this stimulus, we were able to demonstrate that MT neurons responded as if their receptive fields were purely retinotopic.

Aim 2b: Can neurons process information in spatial coordinates even when their receptive fields are retinal-centric?

In a process known as anticipatory remapping, neurons such as those in LIP, FEF and SC are able to shift their receptive fields ahead of time, before an eye movement is executed. The advantage of this is that visual stability is maintained by allowing prior knowledge of the stimulus that would fall in the receptive field of the neuron at the next fixation point. In order to test whether MT could process information in spatial coordinates using this mechanism, we looked to see if the neuron responds to the object in the post-saccadic receptive field earlier than what you would expect if it had just appeared. Using the moving dot stimulus, we did not find

the neurons responding faster to the object in the post-saccadic receptive field when it was present prior to the saccade. Hence we conclude that area MT neurons do not demonstrate anticipatory remapping with a spatially stable moving dot stimulus.

1.4.3 Is there any remapping in area MT? (Chapter 4)

Aim 3: Can MT neurons demonstrate remapping with a transient stimulus?

Given that we are unable to demonstrate anticipatory remapping in area MT, we asked if information can be passed from one neuron to another within the same cortical area before or during a rapid eye movement. To probe this, we used a transient stimulus, which was traditionally used in remapping experiments. This 50 ms flashed stimulus which would allow observation of the presence of the neural signal for an object that was never present in the typical (or retinotopic) receptive field of the neuron.

We recorded from MT neurons while the animal performed a saccade task, in which a flashed disc could appear in the post-saccadic receptive field of the neuron before or after the saccade. Even with this stimulus, we found no remapping in area MT. However, in doing these experiments, we found an apparent remapped response to white stimuli presented on black background - which turned out to be an artifact due to the long phosphor decay of the monitor.

1.5 Summary

Answering the questions posed above will give us a better understanding of how area MT may appear to process information in spatial coordinates while having retino-centric receptive fields.

This will allow us to better understand how we process visual information in space while we look around the world, inducing a temporal and spatial displacement of the image projected on the retina with each eye movement. It will also give us a better knowledge of the processing in MT, to recognize the extent of its communication and reliance with the other regions of the dorsal stream, and appreciate the mechanisms which it has and does not have access to.

Chapter 2:

Psychophysical evidence for spatiotopic processing in area MT in a short-term memory for motion task

Wei Song Ong, Nina Hooshvar, Mingsha Zhang and James W. Bisley

2.1 Abstract

Area MT has long been established as a cortical area involved in the encoding of motion information and has been thought to do so in retinotopic coordinates. Zaksas et al (2001) previously showed that memory for motion has a spatial component by demonstrating that subjects do significantly worse on a match-to-sample task when the stimuli to be compared were spatially separated. The distance at which performance deteriorated (the *critical spatial separation*) increased at increasing eccentricities, suggesting that area MT was involved in the process. In this study, we asked whether optimal performance occurred when the stimuli were in the same retinotopic or spatiotopic coordinates. We found that the performance was best when the stimuli appeared in the same location in space rather than the same retinal location, after an eye movement. We also found that the relationship between retinal eccentricity and the critical spatial separation approximated that of area MT, as found previously. We conclude that area MT plays an important role in the memory for motion process, and that this is carried out in spatiotopic coordinates. This conclusion supports the hypothesis that MT processing may have a spatiotopic component.

2.2 Introduction

It is well established that information about visual motion is processed in area MT/V5 in both monkeys (Dubner and Zeki, 1971; Maunsell and Van Essen, 1983; Britten et al., 1992; Salzman et al., 1992) and humans (Watson et al., 1993; Tootell et al., 1995; Huk et al., 2002). It has also been suggested that cortical areas that play a role in encoding the features about a particular stimulus could also be involved in the retention of that information (Fuster et al., 1981; Zhou and Fuster, 1996). This would suggest that MT could play a role in a memory for motion task. Indeed, this idea is supported by lesion (Bisley and Pasternak, 2000), microstimulation (Bisley et al., 2001) and psychophysical (Zaksas et al., 2001) data in non-human primates. In particular, Zaksas et al (2001) showed performance in a memory for motion task degrades slightly if the two stimuli to be compared are spatially separated by a critical distance. This distance increased as the eccentricity of the stimuli increased in a way that matched the receptive field sizes of neurons in area MT.

Area MT has generally been thought to operate in a reference frame linked to the retina (retinotopic) (Albright and Desimone, 1987; Gardner et al., 2008). Recently, however, d'Avossa et al (2007) showed that the responses in human MT have a processing component that uses a reference frame linked to locations in space (spatiotopic). This is supported by psychophysical evidence from adaptation and integration studies (Melcher and Morrone, 2003; Melcher, 2005), although not from the motion aftereffect (Knapen et al., 2009). As we rarely fixate on the same spot in the world for more than half a second at a time, one might expect that the processing of short-term memory for motion would occur in a spatiotopic reference frame rather than a retinotopic one. To test this, we asked whether the processing of memory for motion is better

when two motion stimuli to be compared are presented in the same retinal or spatial locations. We also asked whether people have a critical spatial separation that increases with eccentricity and whether this correlates best with the receptive field sizes of neurons in area MT or neurons in other related areas. We found that the process is optimal in spatiotopic coordinates and that critical spatial separation matched the receptive field size of MT neurons. This suggests that MT may process memory for motion information in a spatiotopic coordinate system.

2.3 Methods

Subjects

Nine (4 female) adult human subjects (including 3 of the authors) participated in the study. Subjects had either normal or corrected to normal vision. Psychophysical experiments were approved through the UCLA Institutional Review Board. Before collecting data, each subject performed a training session of approximately 100 trials to acclimatize them to the task and response buttons.

Behavioral Task

All the experiments were run using the REX system (Hays et al., 1982). Stimuli were presented on a 22" Viewsonic C225f monitor running at 100Hz with a resolution of 1024x768, which was placed 57 cm from the subjects' eyes. The subjects' eye positions were monitored by a SMI eye tracker and recorded at 1 kHz in REX. All subjects performed a variation of a match-to-sample task (Fig. 1) in which they were shown two random dot patterns, the *sample* and *test*, separated temporally by a 1350 ms delay. Their task was to indicate, by pressing one of two buttons, whether the directions of motion were the same or different. The subjects received feedback in

the form of an audible beep after a correct response. On each trial the sample moved in one of eight possible directions: the 4 cardinal directions and the 4 directions that are 45 deg from cardinal. On different trials, the test direction could differ from the sample direction by either a clockwise or counter-clockwise rotation. The stimuli were created using VEX software (Laboratory of Sensorimotor Research, NEI) and consisted of moving dots within a stationary circular aperture. The dots all moved in the same direction (100% coherence). The lifetime of an individual dot was equal to the duration of the stimulus presentation (500 ms). The dot density was kept constant at 21%. The white dots were presented on a dark background in a dimly lit room to prevent the use of scotopic vision.

The first variation of the task was aimed at testing whether better performance would be seen when the two stimuli were in the same retinal or spatial locations (Fig. 1). In this task, the subject had to fixate a small square point 5 deg to the right or left of the center of the screen for 750-1250 ms, after which the sample appeared at 7 deg eccentricity. The fixation point had a mark that pointed to the stimulus location so there was no spatial uncertainty and the subjects could optimize their attentional strategy. This stimulus was followed by a delay that ranged from 450 ms to 900 ms after which the fixation point jumped 10 deg to the other side of the screen. Subjects had 300 ms to execute a saccade to the new fixation point. The new fixation point had a mark that pointed to the test stimulus location, and the test appeared at this location 1350 ms after the sample stimulus disappeared. The test stayed on for 500 ms and was followed by a 250 ms delay after which the fixation point dimmed, signaling to the subject that it was time to respond. The test was always placed at the same eccentricity as the sample, but could appear at 2 possible locations on the screen: the same spatial location as the sample or the same retinal

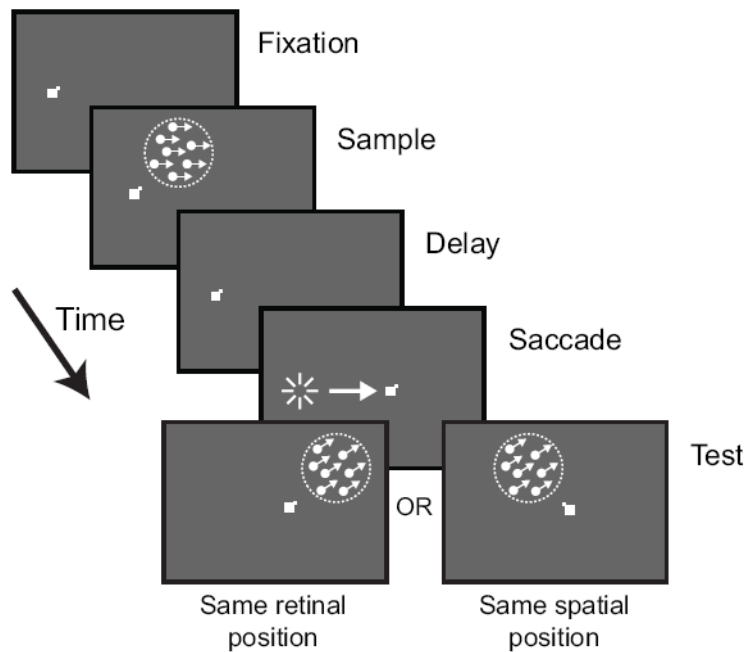


Figure 1.

The direction difference discrimination task. On each trial, the fixation spot could appear on either side of the screen and had a small mark that pointed towards the location where the stimulus would appear. The sample stimulus appeared for 500 ms and there was a 1350 ms delay before the test stimulus appeared. During the delay, the fixation point jumped to the opposite side of the screen. The test stimulus either appeared in the same retinal or spatial location as the sample. Subjects indicated whether the dots in the sample and test stimuli were moving in the same direction or not by a button press.

location as the sample (Fig. 1). Direction differences were assigned using the method of constant stimuli; on each trial the direction difference was pseudo-randomly chosen from a discrete set of 8 direction differences and the subjects could not predict whether it would be a 'same' trial, a difficult 'different' trial or an easy 'different' trial. For data analysis, performance from all sessions was pooled (usually 2-3 sessions and an average of 475 trials per subject). Thresholds

were defined as the smallest angle between sample and test directions that allowed for discrimination at the 75% correct level. These were calculated by fitting the data with a Weibull function, weighted by the number of trials at each point, using the maximum likelihood method (Quick, 1974; Zaksas et al., 2001).

The second variation of the task was aimed at testing whether subjects had a critical spatial separation similar to that seen in the monkey. This task was similar to the task described above and differed only in the following ways. Firstly, the fixation point was located at the center of the screen, so the subject was not required to make any saccades. Secondly, the stimuli could appear at 3, 7, or 14 deg eccentricity (although only one eccentricity was used in a block of trials). The aperture sizes and velocities were optimized for each condition (Table 1). Thirdly, while the sample was always placed in the same location within a block, the test could appear in any of 4 locations: the same location as the sample or one of 3 different locations with various stimulus separations (Table 1). Within a block, both the sample and test were always placed in the same visual hemifield at the same eccentricity. Thus, the sample and test appeared at locations around an imaginary circle, with separations measured directly between the center of the two stimuli. Fourthly, the fixation point did not have a mark that pointed to the stimulus location, so there was some uncertainty in where the test could appear. Finally, within a session, only two direction differences were tested. These were chosen to be close to the subject's threshold. Data were analyzed if, within a session, there was a step function in performance in which the better performance was in the condition in which there was no spatial separation. Generally, a difference in performance can only be seen along the sloping portion of the psychometric function (see difference between functions in Fig. 2a). Because we only sampled 2 points on the

function, we would sometimes get performance that was on the asymptotes. In these sessions we found no change in performance for any separation. Critical spatial separations were defined as the spatial separation of stimuli in the match-to-sample task that produced a decline in performance. These were calculated by fitting a sigmoid function to the performance data plotted as a function of the spatial separation and taking the midpoint of the function as the critical spatial separation.

| Eccentricity (°) | Stimulus separations (°) | Diameter of stimulus (°) | Speed of dots (°) |
|---------------------|-----------------------------|-----------------------------|----------------------|
| 3.5 | 0, 1.5, 2.5, 5.0 | 1.4 | 4 |
| 7 | 0, 3.0, 5.0, 10.0 | 3.0 | 8 |
| 14 | 0, 6.0, 10.0, 20.0 | 6.0 | 16 |

Table 1: The optimized stimuli conditions for each tested eccentricity

2.4 Results

2.4.1 Spatiotopic vs retinotopic

To ask whether optimal performance on a memory for motion task requires the sample and test to be in the same spatial or retinal locations, we recorded data from 8 human subjects performing a direction discrimination task. In the task, they compared the directions of motion of two coherently moving random-dot stimuli (*sample* and *test*) separated by a 1350 ms delay during which a 10 degree saccadic eye movement was made to the right or left. In this paradigm the test could appear either in the same retinal or spatial location as the sample (Fig. 1).

Subjects' performance was better when the sample and test were placed in the same spatial location than when they were placed in the same retinal location. Figure 2a shows the data from a single subject. The performance of the subject is plotted against the angle of direction difference between the sample and test stimuli. To calculate the threshold, the data in each condition were fitted with a Weibull function and the threshold was defined as the direction difference at which the subject could perform the discrimination at 75% correct. The data obtained in the retinotopic condition is shown by the black circles (fit shown by solid line, $R^2=0.919$) while the data from the spatiotopic condition is denoted by crosses (fit shown by dashed line, $R^2= 0.950$). The data demonstrates that the subject was able to discriminate smaller direction differences in the spatiotopic condition (threshold: 7.73 deg) than in the retinotopic condition (threshold: 10.03 deg). Indeed, at direction differences near to the threshold, the subject consistently performed better when the stimuli were in the same spatial positions.

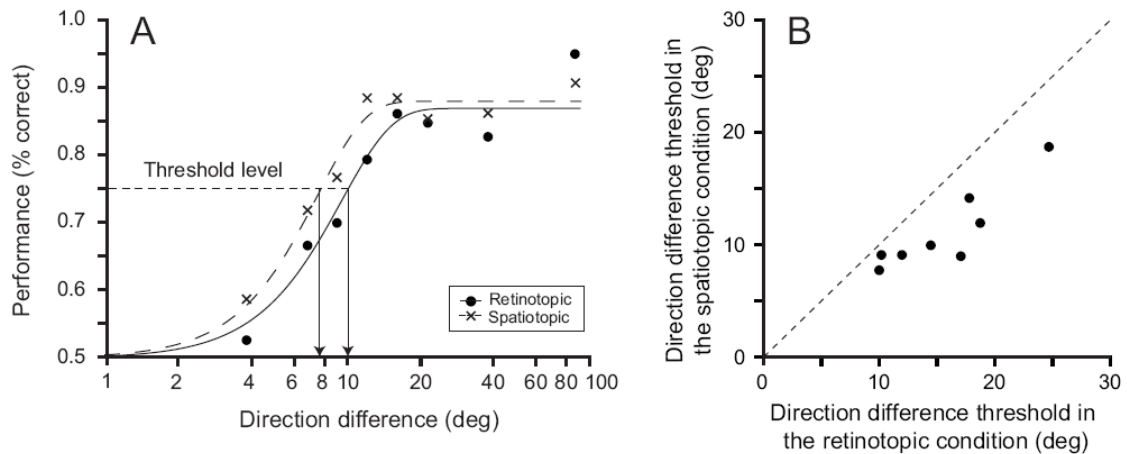


Figure 2.

Effect of test stimulus location on performance. (a) The performance of a single subject is plotted against the angle of direction difference between the sample and test stimuli. Black circles show the data obtained in the retinotopic condition. Solid line shows the best fitted Weibull function ($R^2=0.919$; Threshold: 10.03 deg); Crosses show the data obtained in the spatiotopic condition, fit shown with a dotted line ($R^2=0.950$; Threshold: 7.73 deg). (b) The thresholds of 8 subjects in the spatiotopic condition plotted as a function of the thresholds in the retinotopic condition. Each point represents the data from a single subject. Across the population, the thresholds in the spatiotopic condition were significantly better than in the retinotopic condition (paired t-test, $p=0.0001$).

All 8 subjects showed better performance when the sample and test were in the same spatial location than when they were in the same retinal location (Fig. 2b). Here we compare the thresholds from each individual under the two conditions. All of the points fall below the dashed unity line, showing that all subjects were able to distinguish smaller angle differences in the spatiotopic condition compared to the retinotopic condition. Thus, across the population, there was a significantly lower threshold in the spatiotopic condition compared to the retinotopic condition (paired t-test, $p=0.001$). Independent of performance, saccade metrics were the same under both conditions for all subjects.

Performance at an unrelated location was not significantly better than performance at the retinotopic location. To test whether the better performance at the spatiotopic location was due to a local deficit at the retinotopic location rather than an enhancement at the spatiotopic location, we tested the 5 subjects who participated in all experiments in a control task. In this task, the test could appear at the same retinal location or at a different control location. The control location was at equal eccentricity to the sample, was not in the spatiotopic location, and was counterbalanced so that no retinal location was tested more often than any other location in either condition. As in the main task, a small point on the fixation spot indicated the location of the test stimulus. We found that performance was similar in the retinotopic and control conditions ($p > 0.95$, paired t-test), with thresholds (mean \pm SEM) of 11.67 ± 1.32 deg and 11.64 ± 0.67 deg for the retinal and different conditions respectively. In addition, the mean performance in the control condition was significantly worse than in the spatiotopic condition when data from the same 5 subjects were compared ($p = 0.013$, 2-tailed t-test assuming unequal variance). These data show that the difference between thresholds at the spatiotopic and retinotopic conditions was due to enhanced performance at the spatiotopic location.

2.4.2 The relationship between retinal eccentricity and critical spatial separation

Having previously shown that the critical spatial separation correlated with the receptive field size of MT neurons in the monkey (Zaksas et al., 2001), and then finding that the optimal reference frame was in spatiotopic coordinates in humans, we asked what the relationship was between retinal eccentricity and critical spatial separation in the human. Given that area MT is traditionally thought to operate in retinotopic coordinates, we proposed 2 plausible reasons that

could explain the difference between our result and the previous animal result. First, humans may not use MT, in which case the critical spatial separation, representing the receptive field size, may be different in the two species. Second, the assumption that MT only operates in a retinotopic coordinate frame may be incorrect (d'Avossa et al., 2007), thus our results may still implicate area MT in this task. To test these two possibilities, 8 subjects performed a direction discrimination task in which the sample and test always appeared at the same eccentricity, but could be separated by varying degrees of visual angle. In any given block of trials, only one out of three eccentricities (3.5, 7, and 14 degrees) was tested and within the block the stimulus size, speed of the dots and separation distances were kept constant (Table 1).

As eccentricity increased, the distance between stimuli required to induce a drop in performance increased. For each eccentricity from each subject, a sigmoidal function was fitted to the data points and the midpoint of the function was taken as a measure of the critical spatial separation. For example, Figure 3 shows the performance from the same single subject as in Figure 2a plotted against the separation distance between the sample and test stimuli. The red circles and fit demonstrates the subject's performance at 3.5 degrees eccentricity, the blue at 7 degrees eccentricity, and the black at 14 degrees eccentricity.

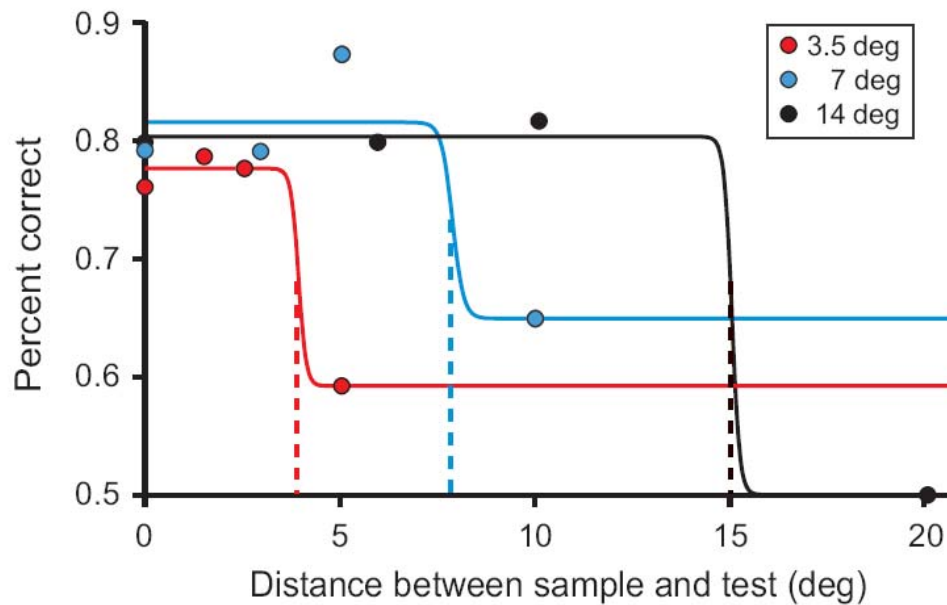


Figure 3.

Performance as a function of stimulus separation for 3 eccentricities. The performance of a single subject (same as in Fig. 2a) is plotted against the separation distance between the sample and test stimuli for 3 eccentricities (27 ± 1.9 trials per point). Red circles show data from 3.5 deg eccentricity (midpoint of fit: 3.94); Blue circles from 7 deg eccentricity (midpoint: 7.90); Black circles from 14 deg eccentricity (midpoint: 15.07).

The relationship between critical spatial separation and retinal eccentricity was consistent among all the subjects; there was an increase in critical spatial separation as eccentricity increased. The average critical spatial separations for the 8 subjects are plotted in Figure 4 as a function of eccentricity (black circles). The critical separation for locations closer to the fovea were smaller, and increased with distance, consistent with the relationship between eccentricities and receptive field sizes in various visual areas in the monkey (solid black lines). More importantly, the critical spatial separations in the human are similar to those found in the monkey (triangles; { }) and most consistent with the receptive field sizes for MT neurons. When a linear fit was made through the raw critical spatial separations from our data, the confidence intervals for slope and offset

included the slope and offset calculated from the MT data (Albright and Desimone, 1987) but for none of the other cortical areas.

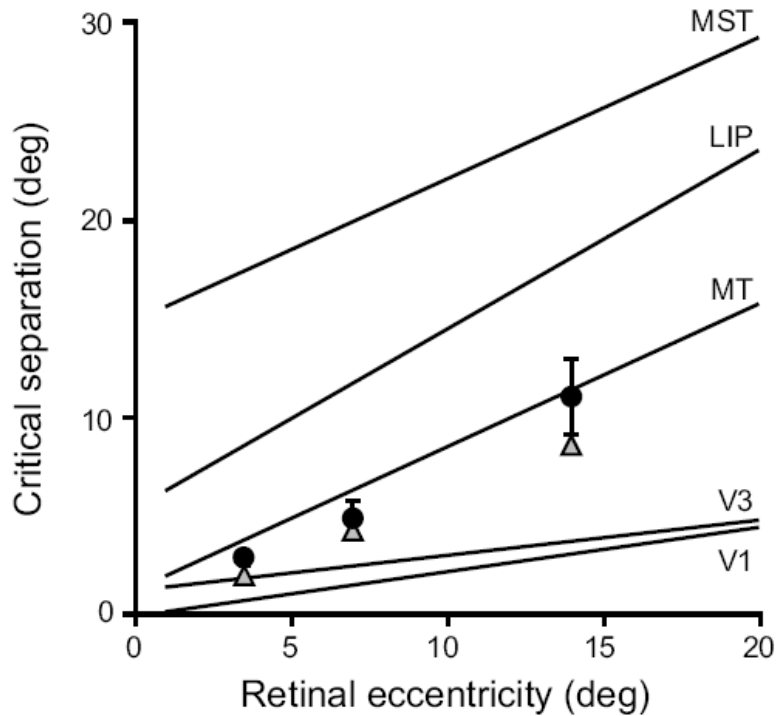


Figure 4.

Effect of eccentricity on critical spatial separation. Black circles show the mean critical spatial separations measured from 8 subjects as a function of eccentricity. The lines of best fit from data comparing receptive field sizes of neurons in cortical areas V1, V3, MT, LIP, and MST with eccentricity (Dow et al., 1981; Desimone and Ungerleider, 1986; Albright and Desimone, 1987; Felleman and Van Essen, 1987; Ben Hamed et al., 2001) are plotted for comparison. Grey triangles show the critical spatial separations recorded from monkeys in a similar task (Zaksas et al., 2001). The variation of the critical spatial separation with eccentricity measured is similar to the monkey and most consistent with the receptive field sizes for MT neurons.

2.5 Discussion

We have shown that thresholds for direction discrimination in a memory for motion task are better when the sample and test stimulus are placed in the same spatial locations compared to when they are placed in the same retinal location or in a control location following a saccade.

This is perhaps unsurprising given our experience in everyday conditions – the motion information we use in short-term memory comes from motion in space rather than motion that is tied to the retina. More surprising was the finding that the critical spatial separation that induces the behavioral differences in performance best approximated the size of receptive fields in MT – an area generally thought to process information in an exclusively retinotopic coordinate frame.

Our interpretation of these data rest on the assumption that the task will be performed optimally when the same processing unit is involved at critical junctures within the trial. By moving a stimulus to a new location, a new unit with the appropriate spatial receptive field will be recruited, and the transfer of information from one unit to another will introduce noise. We observe this noise as a slight decrease in performance. Thus, our interpretation of the data is that the areas involved in the storage and comparison of this information must have a spatiotopic reference frame, because performance was reduced when the test stimulus was placed in the same retinal location or a control location following a saccade. The simplest explanation for our finding is that information is automatically transferred to the appropriate processing unit during a saccade. This could occur via a remapping mechanism similar to that seen in the lateral intraparietal area (Duhamel et al., 1992a; Kusunoki and Goldberg, 2003), the frontal eye fields (Umeno and Goldberg, 1997), the superior colliculus (Walker et al., 1995) and a number of visual areas (Nakamura and Colby, 2002). In this case, by placing the test in the same retinal

location after a saccade, the decrease in performance results from shifting the information back to the original unit, which had just had the information shifted away by the remapping mechanism.

We think it unlikely that the dim lighting in the room biased performance towards a spatiotopic coordinate frame. Our reason for this is that in studying the motion aftereffect in a dimly lit room, Knapen et al (2009) found the effect in the retinotopic location rather than a spatiotopic location. Suggesting that the presence of light does not automatically set all motion processing to a spatiotopic reference frame. Conversely, using slightly different stimuli in a dark room, Ezzati et al (2008) found a weak motion aftereffect in the spatiotopic location in addition to that in the retinotopic location. This suggests that light is not necessary for spatiotopic processing.

It is also possible that the better performance in the spatiotopic condition does not represent improved performance at the spatiotopic location, rather it is due to a local deficit in performance at the retinotopic location due to adaptation or some other low level process. This is unlikely to be due to adaptation, given that adaptation causes the repulsion of directions of motion near to the adapting stimulus, which would predict better performance at the retinotopic location than the spatiotopic location (Wenderoth and Wiese, 2008). Our sample stimulus was only 500 ms and the directions changed on each trial, so it is unlikely that adaptation played a major role in this task. In line with this, we found no difference in performance between the control condition and the retinotopic condition, but we did find a significant difference between the control condition and the spatiotopic condition. This suggests that the better performance at the

spatiotopic location implies a benefit at this location, rather than a deficit at the retinotopic location.

Having found that there is a spatial component involved in processing memory for motion in the monkey, Zaksas et al (2001) showed that the critical spatial separation changed with eccentricity in a way that matched the receptive field sizes in area MT. In our study, we looked to see whether this would also be seen with humans. Our logic is that the critical spatial separation gives an indication of the region of space covered by the processing unit. Since the most basic processing unit in cortex is the neuron, we interpret this to mean the receptive field sizes of the neurons within the brain area involved in this process. The theory is that if the two stimuli are separated but still close enough that they would both fall within the neurons' receptive fields, then no decrement would be seen because the processing would remain within the set of neurons (ie. the processing unit). Conversely, if the two stimuli are separated by more than a receptive field diameter, then information would have to be transferred from one set of neurons to another. In this case, noise would be introduced and performance would suffer. In Figure 4, we superimposed the mean critical spatial separations of our data (circles) on the plotted receptive field sizes of neurons in cortical areas V1, V3, MT, LIP, and MST as taken from the literature (Dow et al., 1981; Desimone and Ungerleider, 1986; Albright and Desimone, 1987; Felleman and Van Essen, 1987; Ben Hamed et al., 2001). On its own, the data from our study appear to best correspond to the receptive field to retinal eccentricity relationship of area MT; when taken together with the monkey data, the association only becomes stronger. It should be noted that the critical spatial separation measurements in this study should be viewed as rough approximations of the actual values. This task was imperfect in the sense that we neither collected full

psychometric functions for each separation, nor did we test enough separations to get an accurate representation of when the performance begins to drop. However, the data are still clear enough to show that the performance drop occurred at greater distances at greater eccentricities and the estimates of the critical spatial separations are similar to the previous estimates in the monkey. We should also note that the only evidence linking the spatiotopic effects with MT is the relationship between the critical separation and eccentricity. While psychophysics can never link, with 100% certainty, the role of a cortical area with the process being studied, ours does so as convincingly as possible. Given that MT is the only cortical area with a receptive field profile that matches our critical separation measures and is also involved in processing motion and memory for motion information – we can think of no other plausible explanation for our results.

Area MT has been well studied in the monkey and is traditionally thought of as a retinotopic area. Recently, it has been suggested that MT may be involved in spatiotopic processing. Evidence for this comes from a psychophysical study that showed that the integration of motion information over time can be performed in spatiotopic coordinates (Melcher and Morrone, 2003) and from an fMRI study that showed spatiotopic BOLD information in MT (d'Avossa et al., 2007). However, a more recent study found no evidence for spatiotopic processing in the BOLD response (Gardner et al., 2008) and results from psychophysical studies on motion or direction aftereffects, both thought to involve MT, have predominantly found evidence for retinotopic processing with weak if any evidence for spatiotopic processing (Ezzati et al., 2008; Wenderoth and Wiese, 2008; Knapen et al., 2009). Interestingly, apart from the presence of gain fields (Bremmer et al., 1997), there is no electrophysiological evidence to support the idea of MT as processing spatiotopic information, although one study, examining a codebook readout of a

population of neurons, did not find evidence of pure spatiotopic processing (Krekelberg et al., 2003). Our data appear to strongly support the hypothesis that MT in the human can process visual motion information in a spatiotopic coordinate frame. Indeed, our data would suggest that it is a default mechanism, since there was a significant difference in performance under the two conditions and the subjects were always aware of where the stimuli would appear. Whether this is unique to the human or whether MT neurons in the monkey will be shown to have spatiotopic properties, such as peri-saccadic remapping, is yet to be shown.

Chapter 3:

A lack of anticipatory remapping of retinotopic receptive fields in area MT

Wei Song Ong and James W. Bisley

3.1 Abstract

Area MT has traditionally been thought to be a retinotopic area. However, recent fMRI and psychophysical evidence have suggested that human MT may have some spatiotopic processing. To gain an understanding of the neural mechanisms underlying this process, we recorded neurons from area MT in awake behaving animals performing a simple saccade task in which a spatially stable moving dot stimulus was presented for 500 ms in one of two locations: the pre-saccadic receptive field or the post-saccadic receptive field. MT neurons responded as if their receptive fields were purely retinotopic. When the stimulus was placed in the pre-saccadic receptive field, the response was elevated until the saccade took the stimulus out of the receptive field. When the stimulus was placed in the post-saccadic receptive field, the neuron only began its response after the end of the saccade. No evidence of pre-saccadic or anticipatory remapping was found. We conclude that gain fields are most likely to be responsible for the spatiotopic signal seen in area MT.

3.2 Introduction

When staring at a point in space, the region of a scene represented in detail is small. We make multiple fast movements with our eyes to various points in space to obtain a more comprehensive picture of the world. As this occurs, the image incident on our retina is constantly changing, but we perceive the world as stationary (Wurtz, 2008). One way that this stability is thought to occur is via the passing of information from neuron to neuron within a cortical area before or during the time of a saccade (Duhamel et al., 1992a). This ‘remapping’ removes the smear of visual information racing across the retina and provides a more stable map of the visual field. A second possibility is that a signal from the eyes (Wang et al., 2007) or from areas driving the eyes (Sommer and Wurtz, 2002) giving information about their position can be combined with the visual information to calculate the locations of objects in a spatial reference frame (Zipser and Andersen, 1988). Such a signal is thought to be present in a number of visual areas in the form of gain fields (Andersen and Mountcastle, 1983; Bremmer et al., 1997; Bremmer, 2000). A third and more idealized way to accomplish this stability would be if some neurons were spatiotopic, i.e. their frames of reference are tied to a fixed reference point in the world, and the information they encode doesn’t change when eye movements are made (Galletti et al., 1993). However, neurons in most visual areas are thought to be strictly retinotopic, i.e. their frames of reference are tied to a fixed point on the retina, so every eye movement brings new stimuli into the receptive field.

The medial temporal (MT) area is thought to be very important in the perception of motion and it was generally accepted that it carried out its tasks in retinotopic coordinates (Albright and Desimone, 1987; Krekelberg et al., 2003; Gardner et al., 2008). However, a recent fMRI study

suggested that human MT has a spatiotopic processing component (d'Avossa et al., 2007) and psychophysical evidence from adaptation, perceptual learning and integration studies appear to support this ((Melcher and Morrone, 2003; Melcher, 2005; Zhang and Li, 2010) but see (Morris et al., 2010)). Recently, we conducted a psychophysical study on humans which used a short-term memory for motion task that appeared to corroborate the possibility of spatiotopic processing in area MT (Ong et al., 2009). While MT neurons are known to have gain fields (Bremmer et al., 1997), it is not clear whether such activity explains the apparent spatiotopic BOLD signal in human MT (d'Avossa et al., 2007). In this study, we asked if the activity of MT neurons can explain the spatiotopic processing seen in these studies via pre-saccadic remapping or by the presence of spatiotopic receptive fields. We found that MT neurons processed information in a retinotopic coordinate frame and did not appear to exhibit preparatory remapping with a spatially and temporally stable stimulus.

3.3 Materials and Methods

Subjects

All experiments were approved by the Chancellor's Animal Research Committee at UCLA as complying with the guidelines established in the Public Health Service Guide for the Care and Use of Laboratory Animals. Two male rhesus monkeys (8-10kg) were implanted with head posts, scleral search coils, and recording cylinders during sterile surgery under general anesthesia; animals were initially anesthetized with ketamine and dexdomitor and maintained with isoflurane. For details see Mirpour et al. (2009).

Physiological recordings

We recorded extracellular single-unit activity from area MT using tungsten microelectrodes guided by coordinates from magnetic resonance imaging (MRI) images. Recorded neurons were considered to be in MT if they were found on the floor of the superior temporal sulcus, showed robust directionally selective responses to moving dot stimuli and had receptive field sizes consistent with those found in previous studies (Desimone and Ungerleider, 1986; Albright and Desimone, 1987). After isolating the response of a single neuron, the size and position of the receptive field was mapped. The preferred direction was calculated by recording the response of the neuron to 8 standard directions of motion (0, 45, 90, 135, 180, 225, 270, and 315 deg from vertical) using a random dot stimulus (100% coherence), and fitting the data with a Gaussian. The preferred direction was taken as the peak of the Gaussian fit. We discriminated action potentials during the recording epoch using the MEX pattern spike sorter (monkey E) or SortClient using the Plexon system (monkey D). The experiments were run using the REX system (Hays et al., 1982) and visual stimuli were presented on a CRT using the associated VEX software. Eye positions were monitored using the DNI coil system and signals were collected at 1kHz.

Behavioral Task

Stimuli were presented on a Samsung SyncMaster 1100DF CRT running at 100Hz situated in a dark room. The temporal precision of stimulus onset and offset was captured by a photoprobe on the corner of the monitor. To begin a trial (Fig. 1), the monkeys had to fixate a spot on the screen (FP1); they were required to maintain fixation as long as the spot was on. In most trials, the

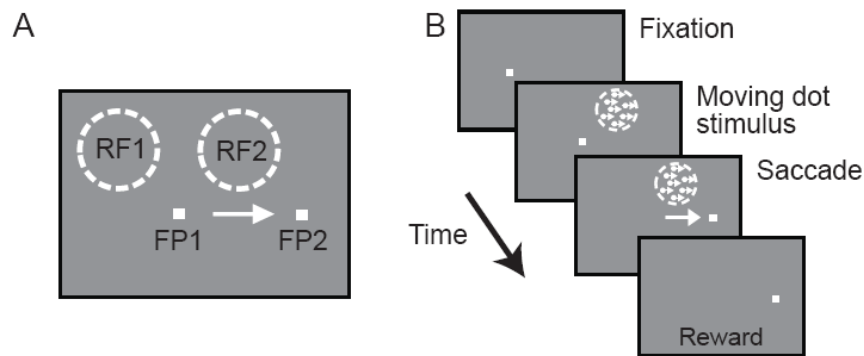


Figure 1.

Task. **A**, In a given session, the positions of the initial fixation point (FP1), the saccade target (FP2), the pre-saccadic receptive field (RF1) and the post-saccadic receptive field (RF2) were set so that the classical retinotopic receptive field at FP1 was RF1 and the receptive field at FP2 was RF2. **B**, In the stable moving dot stimulus task, a 500 ms coherently moving dot stimulus appeared in the receptive field 50 ms before FP1 was extinguished. This was typically about 308 ms prior to saccadic onset.

initial fixation point was extinguished after 300-800 ms and a new fixation point (FP2), to which the animals had to make a saccade, appeared simultaneously. The position of FP2 was chosen so that it was not in the receptive field when the animal was fixating FP1 and that its onset never produced a significant response. Once set, the positions of these two points were kept constant throughout the session (Fig 1A). In all cases, the animals had to maintain fixation within a 3.5 deg square window. In most of the trials, a task irrelevant moving dot stimulus (100% coherence) was presented at the pre-saccadic (RF1) or post-saccadic (RF2) receptive field location for 500 ms. The stimulus was composed of 5.5 dots per deg² moving at 8 deg/sec in the preferred direction. The stimulus appeared 50 ms before the initial fixation point was extinguished (Fig 1B). Given a mean saccadic latency of 258.7 ± 56.7 , this resulted in the stimulus

being presented on average for 308 ms prior to the saccade. In the remaining trials, the animal made a saccade, but no moving dot stimuli were presented.

Neural data analysis

Data were recorded from 73 MT neurons. We analyzed neural activity from all correctly performed trials. Data were aligned by stimulus onset, the beginning of the saccade, and the end of the saccade. Spike density functions were calculated, by convolving spike trains with a Gaussian kernel with a 10 ms sigma. Data were normalized by the value of the half-height of the visual response.

To compute the latency of the neural response, we used the Poisson method described previously (Maunsell and Gibson, 1992; Bisley et al., 2004). Briefly, a Poisson distribution of the background activity was taken from the 100 ms prior to stimulus onset. The latency was taken as the first bin of three consecutive bins after the stimulus onset to have a response that was significantly greater ($p < 0.01$) than that found in the background distribution. For stimulus onset, bin sizes were 2 ms, but for the post-saccadic responses, which were sometimes less consistent, bin sizes of 4-6 ms were occasionally used. The response off time was defined as the time at which the spike density function first dropped below a value that was half way between the pre-saccadic response and the response well after the saccade.

3.4 Results:

3.4.1 Absence of spatiotopic receptive fields in area MT

To test whether neurons in area MT have spatiotopic or retinotopic receptive fields, we trained 2 monkeys to perform a saccade task during which a 100% coherent moving dot stimulus was presented for 500 ms in one of two locations. Within a session, the two fixation points (and hence the direction of the saccade) were kept constant, as were the locations of the stimuli (RF1 and RF2; Fig. 1A). These trials were randomly interleaved with trials in which a flash could occur briefly around the time of the saccade; the results of which are described below. Prior to running this task, the direction tuning of the isolated neuron was recorded so that the dots in the saccade task moved in the neuron's preferred direction. We recorded the activity of 73 single MT neurons (30 from Monkey D; 43 from Monkey E) in this task.

All 73 neurons had retinotopic receptive fields. Figure 2A (black trace) shows the recorded response of a single neuron when the stimulus was presented in RF1, while the monkey was fixating FP1. The grey bar on the abscissa represents the interval in which the stimulus was present. When a saccade from FP1 to FP2 occurred and the stimulus was placed in RF1, the neuronal response fell off (green trace), as would be expected of a neuron with a retinotopic receptive field. Likewise, when the stimulus was presented in RF2, the main increase in visual activity occurred after the saccade had been made (blue trace), also consistent with a retinotopic receptive field. In this neuron there was a small initial response that occurred at a slightly longer latency when the stimulus was placed in RF2 compared to RF1. This occurred in approximately 10% of the neurons and is consistent with the activity of MT neurons to remote stimuli (Zaksas and Pasternak, 2005).

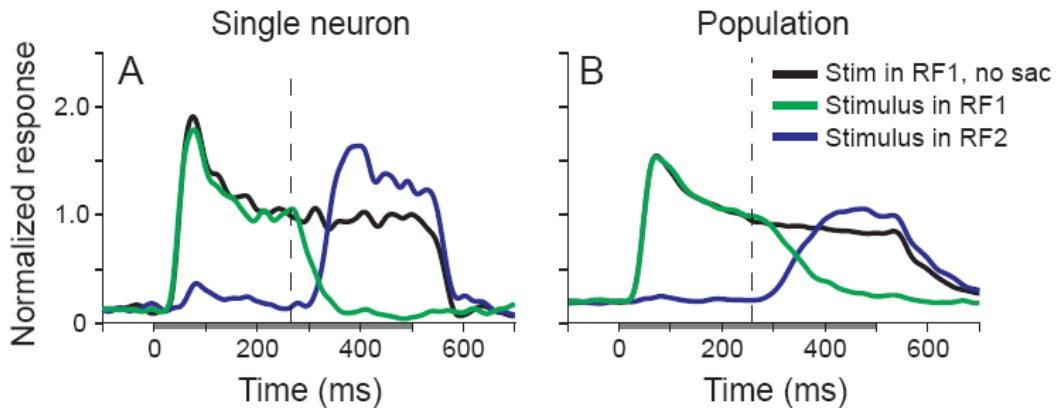


Figure 2.

Mean normalized responses of MT neurons to the stable moving dot stimulus. **A**, An example MT neuron. **B**, The mean normalized response from 73 MT neurons from two monkeys. The grey bar under the abscissa represents the interval during which the stimulus was present. The black trace shows the response when the stimulus was presented in the receptive field of the neuron in the condition where the animal did not make a saccade. The green trace shows the response when the stimulus was presented in the pre-saccadic receptive field of the neuron and a saccade was made; the blue trace shows the same, but with the stimulus presented in the post-saccadic receptive field. The vertical dashed line indicates the mean time of saccadic onset.

Similar retinotopic responses were seen in all of the neurons we examined; no single neuron showed evidence of a true spatiotopic receptive field. Thus, the mean normalized population response shows a clear transition in response from RF1 to RF2 across the saccade (Fig. 2B). There was also a noticeable increase in activity as the stimulus in RF2 was brought into the receptive field (blue trace), compared to the response when the monkey was fixating RF1 and the stimulus was present in RF1 (black trace). This is probably because the response of the neuron to the stimulus in RF1 had adapted after approximately 300 ms of presentation, so the initial response to a stimulus brought into the receptive field of an unadapted neuron by a saccade

appears greater. However, this response was not as strong as the initial visual transient seen when the stimulus appeared in RF1.

3.4.2 Absence of perisaccadic remapping of a stable stimulus

Although the receptive fields were clearly retinotopic, we asked whether spatiotopic processing could occur via pre-saccadic or anticipatory remapping (Duhamel et al., 1992a). To do this, we analyzed the latencies of the neural responses under conditions in which the stimulus was presented in the receptive field and under conditions in which the stimulus was brought into the receptive field by a saccade. We found that the latency of the response to a stimulus brought into the receptive field by a saccade when aligned by the saccade offset (blue trace, Fig. 3A) was similar to the response latency when the stimulus was first presented in the receptive field (black trace). To quantify this, we calculated the latency of the visual on-response from individual neurons and compared it to the latency of the response aligned by saccade onset (green trace, Fig. 3A) and by saccade offset (blue trace). The differences between the latencies for all neurons in which latencies could be quantified are shown in the histograms in Figs. 4A & B. It is clear that when aligned by saccade onset (Fig. 4A), the latencies of the post-saccadic responses were significantly longer than the on-response latencies ($p < 0.001$, t-test comparing mean with 0), with a mean difference in latency of 31.5 ± 1.8 ms. Only one neuron had a response latency aligned by saccade onset that was shorter than the visual latency. Thus, we can conclude that MT neurons do not show significant pre-saccadic remapping to a spatially stable moving stimulus. Furthermore, there was no significant difference in response latencies between the post-saccadic response aligned by saccade offset and the on-response latencies ($p = 0.635$; Fig. 4B). From this

we interpret that there is not even a quickening of the latency, which would indicate anticipatory remapping.

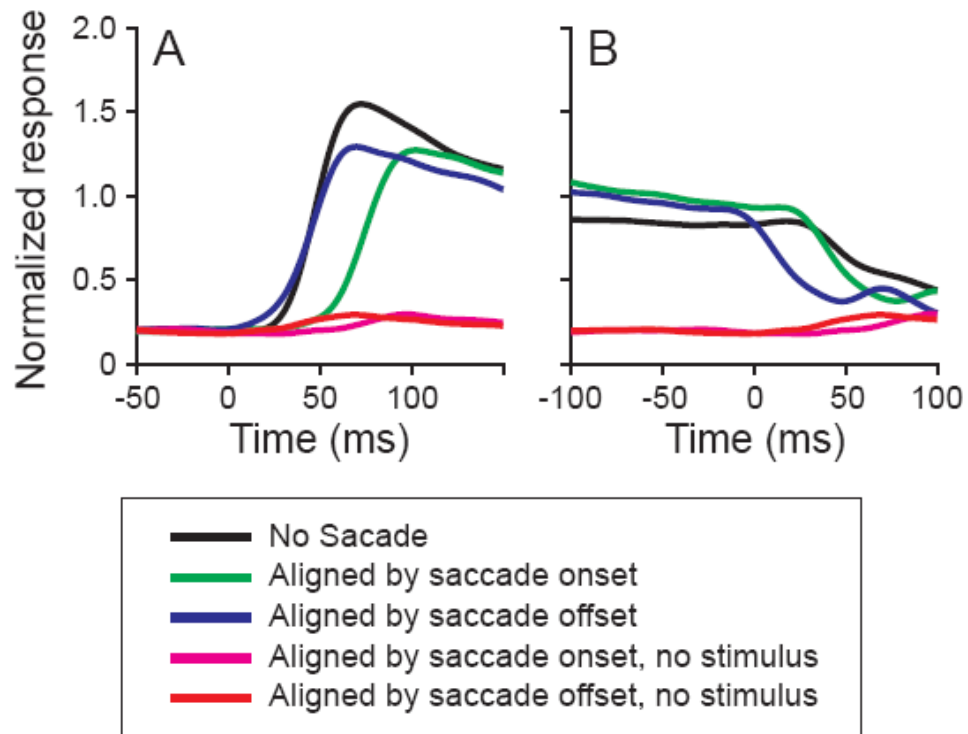


Figure 3.

Mean latencies of responses as a function of stimulus onset, saccadic onset or saccadic offset. **A**, The mean normalized on-responses from 73 neurons. When no saccade was made, the on-response represents the initial visual response (black trace). When a saccade was made, the on-response represents the response to the stimulus brought into the receptive field by a saccade (blue & green traces). The no stimulus traces show the responses when a saccade was made, but no stimulus was presented. **B**, Mean normalized off-responses from the same 73 neurons under the same 5 conditions.

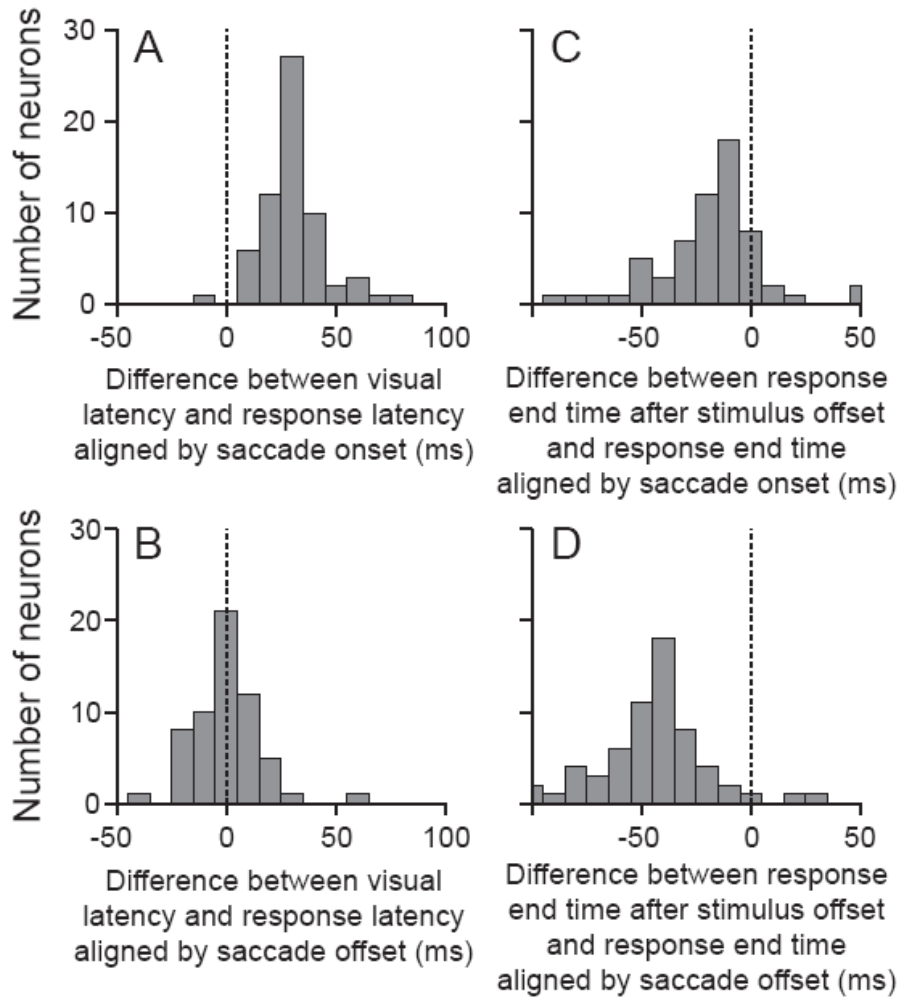


Figure 4.

Distributions of response latencies as a function of stimulus onset and saccadic onset or saccadic offset. **A & B**, Histograms showing the difference in response latencies between the visual latency and the latency of the response aligned by saccade onset (**A**) or offset (**B**). **C & D**, Histograms showing the difference in the response end time between the end of the response caused by the stimulus being extinguished and the end of the response caused by the stimulus being removed from the receptive field by a saccade, aligned by saccade onset (**C**) or saccade offset (**D**).

To test whether the variation in alignments shown in Figs. 4A & B were due to the distance between receptive fields, we asked whether there was any correlation between this distance and the latency. We were unable to find any correlations between the length of the saccade or the

distance between the edges of the moving dot stimulus and the alignment of neural latencies ($p > 0.47$). Together these data suggest that the responses of MT neurons are driven by light hitting the relevant photoreceptors on the retina, whether by stimulus onset or by being brought on to them by a saccade.

Another way that neural responses could produce a spatiotopic BOLD response is by maintaining information about a stimulus after a saccade has taken the stimulus out of the receptive field. To test this we compared the drop off in activity when a stimulus was taken out of the receptive field by a saccade to the drop off in activity when the stimulus was turned off. The off time was defined as the time at which the spike density function first dropped below a value that was half way between the pre-saccadic response and the response well after the saccade. In all cases the neural response decreased (Fig 3B), however this did not occur immediately. The mean off times were 23.2 ± 2.8 ms, 49.6 ± 3.0 ms and 66.6 ± 3.8 ms when aligned by saccade offset (blue trace), saccade onset (green trace) and stimulus offset (black trace) respectively. The differences between the off times under the two saccade alignments and the off time from stimulus offset are shown in Figs. 4C & D. There was a small but significant difference in off response between the drop off when the stimulus was extinguished and when the saccade data were aligned by saccade onset ($p < 0.001$). Consistent with this, we found a greater difference when the saccade data were aligned by saccade offset ($p \ll 0.001$). Interestingly, in both cases the off times occurred earlier when a saccade took the stimulus out of the receptive field than when the stimulus disappeared. This is the opposite to what would be predicted if spatiotopic processing was occurring and may be consistent with a weak effect of saccadic suppression (Bremmer et al., 2009).

3.5 Discussion

Area MT has historically thought to be an area that has retinotopic receptive fields and processes information in retinotopic coordinates; however, recent studies have suggested that it may contain some spatiotopic processing (Melcher and Morrone, 2003; d'Avossa et al., 2007; Ong et al., 2009). We looked at the response of neurons in area MT to stable moving dot stimuli and found that MT neurons responded as if they had purely retinotopic receptive fields and did not show pre-saccadic or anticipatory remapping.

In the 40 years in which the responses of MT neurons have been recorded (Allman and Kaas, 1971a), no studies have explicitly tested whether the receptive fields of MT neurons were retinotopic or spatiotopic by having animals make a saccade while a stimulus was presented in neurons' receptive fields. This is most likely because of the robust retinotopic receptive fields seen under typical recording conditions and the fact that receptive fields appeared to be retinotopically stable when gaze was set at different locations to study gain field activity (Bremmer et al., 1997). However, given the recent suggestion that human MT has some spatiotopic selectivity (d'Avossa et al., 2007) and the psychophysical result that some processing in a memory for motion task was optimal in a spatiotopic coordinate system with MT-like receptive field sizes (Ong et al., 2009), we asked whether single unit activity in MT had any spatiotopic processing. Consistent with our expectations, we found that receptive fields in MT were clearly retinotopic. Further, we found that the timing of the activity around the time of a saccade was consistent with a visual on-response to a stable moving dot stimulus. Similar conclusions have recently been reached by a study that used a general linear model to extract

receptive field information from a random noise stimulus during the slow phase of the optokinetic nystagmus and during fixation (Hartmann et al., 2011).

It is possible that the spatiotopic processing seen in the functional imaging was not due to spatiotopic receptive fields, but was due to retinotopic information being passed from one neuron to another before or at the time of a saccade. Averaged out over the hemodynamic response, this may appear as a spatiotopic signal. Such remapping is found in many neurons in later cortical and subcortical areas (Duhamel et al., 1992a; Walker et al., 1995; Umeno and Goldberg, 1997) and, to briefly flashed stimuli, in a number of earlier visual areas (Nakamura and Colby, 2000, , 2002). We asked whether MT neurons show this remapping by comparing the onset of the visual response to the onset of the response to the stimulus as it was brought into the receptive field by a saccade. We found that almost all of the neurons showed no evidence of pre-saccadic remapping. Furthermore, the mean latency for the post-saccadic response aligned by saccadic offset was not different to the visual latency, suggesting that MT does not respond to a stimulus brought into its receptive field until the eye stops moving. Finally, we showed that the response to a stimulus does not linger once it has been moved out of the receptive field by a saccade. Taken together, we interpret these data as suggesting that there is no remapped response in MT that can explain the spatiotopic signal seen in the fMRI study.

Given that MT neurons appear to have purely retinotopic receptive fields (Hartmann et al., 2011) and no pre-saccadic or anticipatory remapping one may ask: what is the genesis of the spatiotopic signal that has been seen in human area MT (d'Avossa et al., 2007)? One possible difference is the species, however Gardner et al (2008) have shown retinotopic processing in

human MT in a task involving focused attention at the fovea. This has led to the hypothesis that the spatiotopic signal may require peripheral attention (Burr et al., 2010). In our study, the animal was neither required to carry out a task at the fovea nor the periphery, but we expect that the absence of an attention-demanding task at the fovea would appropriate sufficient attentional resources to a sudden onset stimulus in the periphery (Jonides and Irwin, 1981), giving us a response that would be similar to that in the study identifying spatiotopic processing in human MT (d'Avossa et al., 2007). This leaves the possibility that gain fields, seen in single MT neurons (Bremmer et al., 1997), may be the best explanation of the spatiotopic BOLD signal in human MT.

Chapter 4:

Area MT does not demonstrate remapping with a flashed stimulus

Wei Song Ong and James W. Bisley

4.1 Abstract

The middle temporal area (MT) is a mid-level visual area, which has traditionally been thought to process motion information in a retinocentric coordinate frame. However, a number of psychophysical and fMRI studies carried out in humans have suggested that there is some spatiotopic processing in MT. In this study, we test the hypothesis that the spatial processing could come from neural remapping within MT. Previously, we found that MT neurons do not appear to predictively remap activity to a spatially stable moving dot stimulus. Given that neurons in a number of earlier visual areas remap responses to a transiently flashed stimulus, we asked whether MT neurons remap activity under these stimulus conditions. In this study, we presented a circular stimulus for 50 ms in the pre-saccadic or post-saccadic receptive fields of MT neurons around the times of a saccade. Using a black stimulus on a white background, we found that MT neurons do not remap responses to briefly flashed stimuli. However, we found that the persistence of a white image on a black background in the dark room created a neural artifact that could be mistaken as a remapped signal. During stable fixation, the black stimulus and white stimulus produced similar responses. We conclude that spatiotopic processing in MT cannot be explained by remapped responses within MT.

4.2 Introduction

It is important for us to detect the trajectory of moving objects in the world around us. For instance, while trying to cross the street it is important to know the location, speed and direction of any cars that may be near you. However, as our eyes make 3-5 fixations every minute, objects of interest change their retinal position even though they may remain in similar spatial locations. Yet, despite the fact that the image of the world that falls on our retina is constantly changing, we perceive the world as stationary and are able to predict and judge the position and velocity of the moving cars even as we move our eyes. One might expect that an area which decodes this motion does so either in spatial coordinates or is able to update the retinotopic map using a mechanism which provides a preparatory signal, such as that of corollary discharge (Sperry, 1950; Sommer and Wurtz, 2002), allowing a shift of the receptive field in anticipation of the upcoming eye movement.

Much of the decoding of visual motion is carried out by area MT (the middle temporal area; (Albright and Desimone, 1987; Newsome et al., 1988; Salzman et al., 1990; Britten et al., 1992). Neurons in MT have traditionally been thought to code information about motion in a retinocentric coordinate frame and this has been explicitly tested and confirmed in non-human primates (Hartmann et al., 2011; Ong and Bisley, 2011) and in humans (Gardner et al., 2008). However, there have been a number of human studies suggesting that area MT has the capacity to process information in spatial coordinates. Under certain conditions (d'Avossa et al., 2007; Crespi et al., 2011), the BOLD signal in human MT responds similarly to a motion stimulus presented in the center of the screen regardless of whether or not the stimulus is in the ipsi- or contra-lateral visual field. In addition, psychophysical studies have shown that the integration of

motion can occur across a saccade when the stimuli are presented in the same spatial, but not retinal, location (Melcher and Morrone, 2003) and that memory for motion is best processed in a spatial coordinate frame similar to the receptive field sizes of neurons in area MT (Ong et al., 2009).

A number of studies have attempted to elucidate how neural activity in MT could explain the psychophysical and BOLD results suggesting spatial processing within MT. These studies have focused on three possibilities. First, it is possible that the motion processing could be carried out in a spatial coordinate system, either head- or world- centered, instead of using a retino-centric reference frame. Two recent studies found no evidence of spatial processing at the neural level in MT (Hartmann et al., 2011; Ong and Bisley, 2011). Second, activity from cells that respond differentially based on the position of the eye (Bremmer et al., 1997), could be used to calculate the true position in space (Zipser and Andersen, 1988; Morris et al., 2012), however it is unclear how this could produce a spatiotopic BOLD response. Lastly, it is possible that a visual map of the world is maintained in retinal coordinates, but that it accounts for eye movements by updating information about what will appear in the receptive field. This remapping has been demonstrated in a number of areas within the brain, including parietal cortex (Duhamel et al., 1992a), frontal cortex (Umeno and Goldberg, 1997), the superior colliculus (Walker et al., 1995) and a number of earlier visual areas (Nakamura and Colby, 2002).

Remapping has traditionally been tested in two main ways. The first utilizes a stimulus briefly flashed in the post-saccadic receptive field before an eye movement is made. Neurons that exhibit remapped responses will respond to the stimulus, even though it is never presented in the

classical receptive field (Duhamel et al., 1992a; Nakamura and Colby, 2002). The second utilizes a spatially stable stimulus that is present well before and well after the eye movement. Neurons with predictive remapping begin to respond to the stable stimulus before the response could get there via the standard visual pathway (Duhamel et al., 1992a; Mirpour and Bisley, Submitted). We previously showed that neurons in MT do not exhibit predictive remapping using a spatially stable moving dot stimulus (Ong and Bisley, 2011). However, it is possible that MT neurons remap information, but do not do so predictively. If this were the case, then remapping should be seen using a flashed stimulus. In addition, some neurons in earlier visual areas, which project to MT, have been shown to exhibit remapped responses when tested with a flashed stimulus (Nakamura and Colby, 2002). Therefore, in this study we tested the hypothesis that MT neurons exhibit peri-saccadic remapping by presenting a brief stimulus in the post-saccadic receptive fields of MT neurons before the onset of a saccade.

4.3 Materials and Methods

Subjects

All experiments were approved by the Chancellor's Animal Research Committee at UCLA as complying with the guidelines established in the Public Health Service Guide for the Care and Use of Laboratory Animals. Three male rhesus monkeys (8-16kg) were implanted with head posts, scleral search coils, and recording cylinders during sterile surgery under general anesthesia; animals were initially anesthetized with ketamine and dexdomitor and maintained with isofluorane. For details see Mirpour et al. (2009).

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Behavioral Task

Stimuli were presented on a Samsung SyncMaster 1100DF CRT running at 100Hz in a dark room. The temporal precision of stimulus onset and offset was captured by a photoprobe on the corner of the monitor. To begin a trial (Fig. 1), the monkeys had to fixate a spot on the screen (FP1); they were required to maintain fixation as long as the spot was on. In most trials, the initial fixation point was extinguished after 300-800 ms and a new fixation point (FP2), to which

the animals had to make a saccade, appeared simultaneously. The position of FP2 was chosen so that it was not in the receptive field when the animal was fixating FP1. The onset of FP2 and the execution of a saccade to it by the animal never produced a significant response. Once set, the positions of these two points were kept constant throughout the session (Fig 1A). In all cases, the animals had to maintain fixation within a 3.5 deg square window. In most of the trials, a moving dot stimulus or a luminance matched disc was presented at the pre-saccadic (RF1) or post-saccadic (RF2) receptive field location. In the remaining trials, no stimuli were presented. These stimuli were always task irrelevant and were either black on a white background or white on a black background. In this study, we analyzed the responses to the flashed stimulus and not to the moving dot stimulus. It was flashed for 50 ms in the pre- or post-saccadic receptive field. In saccade trials, the stimulus onset could occur between 150 ms before to 300 ms after the time the first fixation point was extinguished. This allowed us to examine the response as a function of when it appeared relative to when the monkey made the saccade.

Neural data analysis

Data were recorded from 137 MT neurons (black on white condition only: 23 neurons from monkey D; white on black condition only: 24 neurons from monkey D, 41 neurons from monkey E; both conditions: 27 neurons from monkey D, 22 neurons from monkey H). Neural activity was analyzed from correctly performed trials. In each analysis, neurons were only included if they had at least 5 trials in each condition being compared. Spike density functions were calculated for visualization only, by convolving spike trains with a Gaussian kernel with a 5 ms sigma. Data were normalized by the maximum response to the moving dot stimulus moving in the preferred direction. Quantitative analyses were based on actual spike rates within three time

windows: a 150 ms window starting 25 ms after the stimulus onset (visual response); a 150 ms window starting 175ms after the moving dot stimulus onset (late visual response); and a 150 ms window starting 25 ms after saccade offset (post-saccadic response)

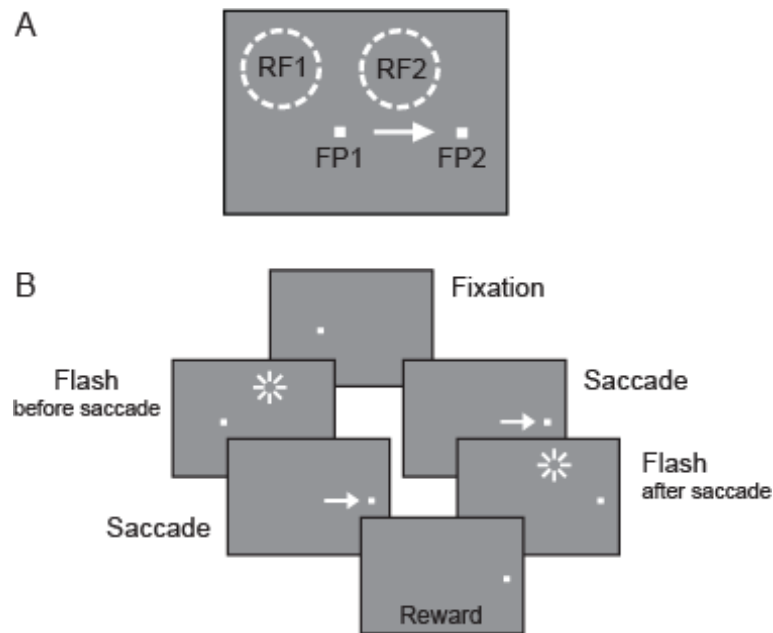


Figure 1:

Task. **A**, In a given session, the positions of the initial fixation point (FP1), the saccade target (FP2), the pre-saccadic receptive field (RF1) and the post-saccadic receptive field (RF2) were set so that the classical receptive field at FP1 was RF1 and the receptive field at FP2 was RF2. **B**, In the task, a 50 ms stimulus could appear between 150 ms before to 300 ms after the time the first fixation point was extinguished. Given a mean saccadic latency of 259 ± 57 ms, it could be presented in either receptive field prior to, after, or during the saccade.

Measurement of Phosphor Decay

To quantify the phosphor decay, a photodiode (OP955; Optek Technologies) was fixed to the CRT and the disc stimulus was presented 95 times under the same conditions used to perform the experiment. The photodiode was connected to the A to D input in REX and the resulting voltages recorded at 1 kHz. The signals from 95 presentations were averaged, normalized and rectified, so that the peak signal to the stimulus was 1 and the background was 0.

4.4 Results

4.4.1 Absence of perisaccadic remapping using a briefly presented stimulus

Although we did not see evidence of remapping when using stable visual stimulus (Ong and Bisley, 2011), others have found responses to briefly flashed stimuli in a range of earlier extrastriate areas (Nakamura and Colby, 2002). To see whether MT neurons also show remapping to such a stimulus, we trained 3 monkeys to perform a saccade task during which a circular disc was presented briefly (50 ms) in the pre- (RF1) or post- (RF2) saccadic receptive fields (Fig 1A). Within a session, the two fixation points (and hence the direction of the saccade) were kept constant, as were the locations of the stimuli (RF1 and RF2). These trials were randomly interleaved with trials in which a 100% coherent moving dot stimulus were used instead of the black circular disk. In this first section, we will describe the responses when a black stimulus was presented on a white background (black-on-white).

When presented well before or after the saccade, the flashed stimulus drove the responses of MT neurons when presented within the classical receptive field. When the disc was presented in the post-saccadic receptive field after the saccade (stimulus onset 125-350 ms after saccade onset;

average saccade duration 29 ± 3 ms), MT neurons responded with a strong visual burst. This is illustrated in Figs 2a and 2b, in which the black traces show the mean response to the flashed black stimulus in a single example neuron (Fig 2a) and in the population of neurons (Fig 2b).

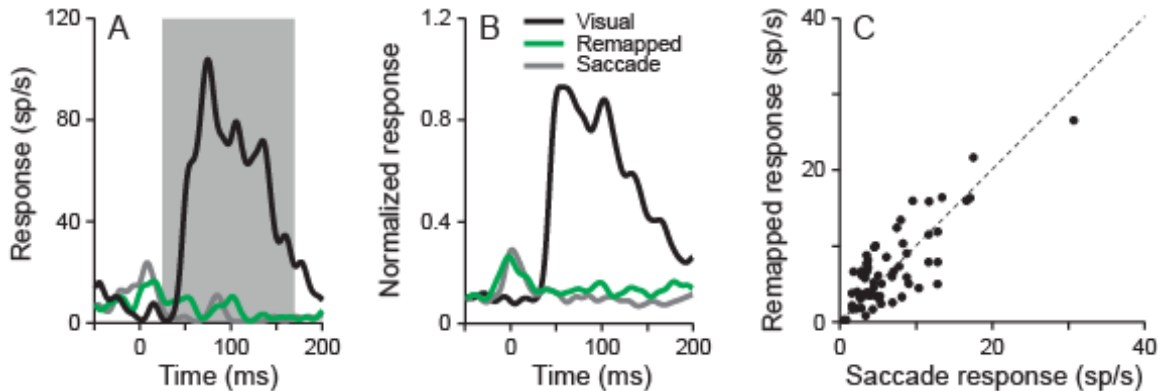


Figure 2:

Responses to the black disc presented on a white background for 50 ms. **A-B**, The black traces show the neural responses from a single neuron (**A**) or from a population of 60 neurons (**B**) when the stimulus was presented in the post-saccadic receptive field 125-350 ms after the saccade onset, aligned by stimulus onset. The green traces show the neural responses when the stimulus onset occurred 55-80 ms before saccade onset, aligned by saccade offset. The grey traces show the responses to the saccade when no stimulus was presented, aligned by saccade offset. **C**, Mean responses of the 60 neurons from a 150 ms window starting 25 ms after the saccade offset as represented by the grey box in **A**. Each point represents the response of a single cell when a saccade was made and no stimulus was presented (abscissa) and when the stimulus was presented in the post-saccadic receptive field 55-80 ms before saccade onset (ordinate).

No neurons responded to the black disc when it was presented in the post-saccadic receptive field just before the saccade began. A neuron exhibiting remapping would be expected to respond to a stimulus flashed in the post-saccadic receptive field just before the saccade

(Duhamel et al., 1992a; Nakamura and Colby, 2002). The green traces show the responses of the single neuron (Fig 2a) and the population (Fig 2b) to a stimulus flashed in the post-saccadic receptive field 55 – 80 ms prior to saccade onset, aligned by the end of the saccade. Because the stimulus was flashed for 50 ms, the stimulus had been off the screen for 5-30 ms prior to the start of the saccade. It is clear that in both cases, there is no obvious remapped response. To test whether there was a significant remapped response, we compared the activity in the remapped condition to the response aligned by the end of the saccade when no stimulus was presented (gray lines, Figs 2a & b). Using a 150ms window that started 25 ms after the end of the saccade (indicated by the shaded region of Fig 2b), we compared the activity between the remapped response and the saccade response and found no significant difference in the population (Fig 2c, $p = 0.27$, Wilcoxon Sign Rank test). These data are consistent with our previous finding that MT neurons do not remap (Ong and Bisley, 2011).

4.4.2 Response of MT neurons to a transient white stimulus on a black background

Most studies that have identified remapped responses have utilized white stimuli flashed on a black background. We found that the response to a white stimulus flashed in the classical receptive field of an MT neuron produced a similarly vigorous response. The black traces in Figs 3a & b show this response for the same neuron illustrated in Fig 2a (Fig 3a) and the population of 102 neurons (Fig 3b) aligned by stimulus onset, which occurred 125 – 350 ms after the end of the saccade.

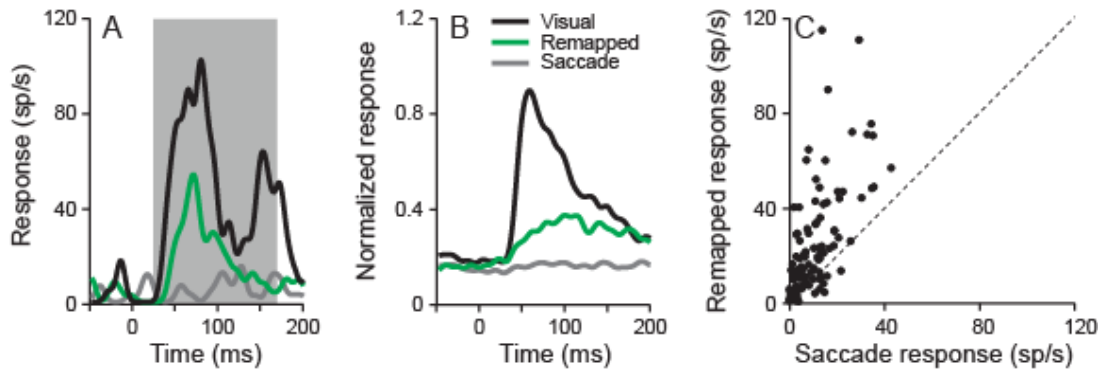


Figure 3:

Responses to the white disc presented on a black background for 50ms. **A**, Response of a single example. **B**, Normalized responses of 102 neurons. **C**, Mean responses of the 102 MT neurons to a stimulus flashed in the post-saccadic receptive field 55-80 ms before the saccade onset are plotted against the mean responses of the same neurons when a saccade was made without the flashed stimulus. Data are from a 150ms window starting 25 ms after the saccade offset as represented by the grey box in **A**. All other conventions as in Fig 2..

Using a white stimulus on a black background, we found an apparent remapped response, however, as we will show below, this was an artifact. Unlike the response to the black stimulus on a white background, the response to the white stimulus appeared to remap. The green traces in the single neuron (Fig 3a) and population response (Fig 3b) show the activity when the white stimulus appeared in the post-saccadic receptive field 55-80ms before saccade onset. These responses were substantially greater than the responses in the saccade alone condition (gray traces, Figs 3a & 3b). When we compared the responses across a 150 ms window starting 25 ms after the end of the saccade, we found that the remapped response was significantly greater than the response in the saccade only condition in 62 individual neurons and in the population as a whole (Fig 3c, $p < 0.001$, Wilcoxon Sign Rank test).

We found apparent remapping when a white stimulus was presented on a black background, but not when a black stimulus was presented on a white background, even in many individual neurons (eg. compare green traces, Figs 2a & 3a). In the following sections, we start by testing whether this difference is due to differential responses to the different foreground-background conditions, then conclude that it appears to be an artifact due to the slow phosphor decay of the CRT screen in the white-on-black condition.

4.4.3 Visual responses of MT neurons are similar to white-on-black and black-on-white stimuli

Given the puzzling discrepancies in neural responses obtained in the remapping study, we collected data from 46 neurons under both black-on-white and white-on-black stimulus conditions. From these neurons, we examined the responses of neurons to the 50 ms flash in the post-saccadic receptive field 125-350ms after the end of the saccade. We found that the neural responses were similar in the black-on-white and the white-on-black conditions. Figure 4a shows the mean normalized responses of the 46 neurons plotted as a function of time. Although there was a trend for a slightly more robust response to the black stimulus, we found that the visual responses in a 150 ms window, starting 25 after stimulus onset (shaded region Fig 4a) were not significantly different from each other (Fig 4b, $p=0.35$, Wilcoxon Sign Rank test). These results are not surprising given the properties of the V1 cells that predominately project to MT (Movshon and Newsome, 1996). These data suggest that the difference in the remapped responses were not due to an intrinsic property of the cells.

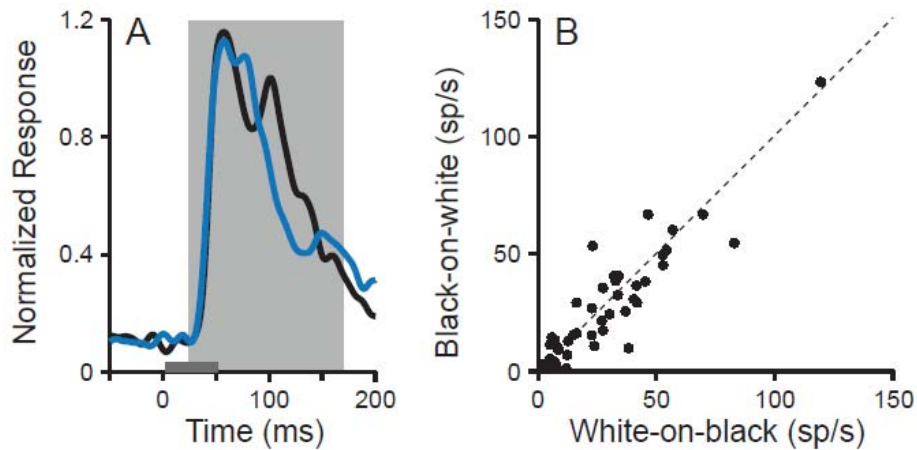


Figure 4:

Comparison of visual responses to the black and white flashed stimuli. **A**, The mean normalised responses of the 46 neurons from which data were collected in both conditions when the stimulus was presented in the post-saccadic receptive field 125-350 ms after the onset of the saccade. The black trace shows the neural response when a black disc was presented on a white background (black-on-white) and the blue trace shows the corresponding response when a white disc was presented on a black background (white-on-black). The dark grey bar on the abscissa represents the duration which the stimulus was present **B**, Mean responses of the 46 neurons from a 150 ms window starting 25 ms after the stimulus onset, as represented by the grey box in **A**. Each point represents the response of a single cell to the 50 ms flashed disc when it was presented in the white-on-black condition (abscissa) and when it was presented in the black-on-white condition (ordinate).

4.4.4 An explanation for the apparent remapped response seen in the white-on-black condition

Although it is possible that MT neurons remap responses to a white stimulus and not to a black stimulus, we believe this is unlikely because they respond to the stimuli in the same way during stable fixation. Thus, we asked whether the apparent remapped response in the white-on-black condition could be due to another factor. A clue to the cause of this activity can be seen in Fig 3b. The ‘remapped’ response (green trace) began to grow substantially around the same time as the visual latency (black trace). We have previously shown that when a spatially stable moving

dot stimulus is brought into the receptive field by a saccade, MT neurons begin to respond at the same time as the visual latency (Ong and Bisley, 2011). In addition, the remapped response is also attenuated compared to the visual response (Fig 4b), akin to a response to a lower contrast version of the previous stimulus (Sclar et al., 1990; O'Keefe and Movshon, 1998; Heuer and Britten, 2002). Thus, the response is similar to what would be expected if a low contrast stimulus was brought into the receptive field by a saccade. We believe that this is occurring due to the slow phosphor decay of the CRT.

To test our hypothesis that the apparent remapped response to a flashed white stimulus is due to slow phosphor decay, we measured the luminance of the flashed stimulus as a function of time under conditions identical to those used to record the neural data. The mean rectified normalized luminance traces to the black and white flashed discs aligned by stimulus offset are shown in Fig 5. The 100 Hz pulsing of the beam passing the photodiode is averaged out by recording across 95 presentations, but can be seen as a small pulse in the background when the black stimulus was used (black trace) and in the stimulus response when the white stimulus was presented (blue trace). Following the offset of the stimulus, the drop off in mean rectified normalized luminance in both traces was steeper than an exponential decay, so we quantified the drop off by identifying the time at which the trace passed an absolute normalized luminance of 0.5, 0.33 and 0.1 after stimulus offset. When the white disc was presented on the black background, the mean rectified normalized luminance reached 0.5 in approximately 30 ms, 0.33 in approximately 44 ms and 0.1 in approximately 85 ms. When the black disc was presented on the white background, the mean rectified normalized luminance reached 0.5 in approximately 7 ms and 0.1 in approximately 10 ms. Thus, although the white stimulus was extinguished 5-30 ms prior to saccade onset for the

data presented in Fig 3, by the time the saccade ended, the relative absolute luminance of the stimulus would have still been at least around 0.2 – the value at 60 ms after stimulus offset, assuming an average saccadic duration of 30 ms and an offset 30 ms prior to saccade onset. Given that MT neurons are sensitive to low contrast stimuli (Sclar et al., 1990), that the apparent remapped response in Fig 3b is similar to that expected if a dim stimulus was brought into the receptive field by a saccade, that the white stimulus persisted on the screen during the duration of the saccade and the absence of any response when the black stimulus, which did not persist, was presented, we conclude that the apparent remapping in Fig 3a & b is an artifact due to the slow decay of the white stimulus.

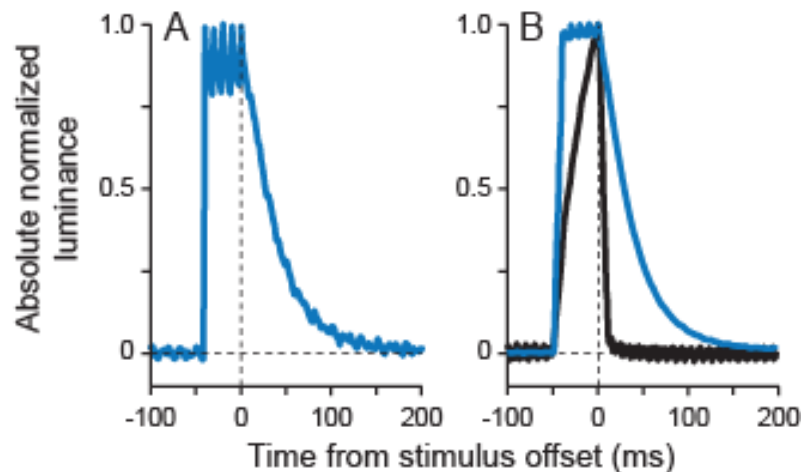


Figure 5:

Measured persistence of the stimuli on the CRT monitor. **A, B**, The blue trace shows the absolute normalized luminance from a single trial (**A**) and the mean absolute normalized luminance from 95 trials (**B**) when the white stimulus was presented on a black background. The black trace shows the mean absolute normalized luminance from 95 trials when the black disc was presented on a white background.

4.5 Discussion

In recent years, several studies have suggested that MT may perform some motion processing in a spatiotopic coordinate system (Melcher and Morrone, 2003; d'Avossa et al., 2007; Ong et al., 2009; Crespi et al., 2011). In this study, we attempted to identify a neural mechanism that might explain these results in the form of remapping. Using a stimulus briefly flashed around the time of a saccade, we found no evidence of remapping in any MT neurons. When taken together with data from previous studies (Hartmann et al., 2011; Ong and Bisley, 2011), we conclude that the spatiotopic processing of information in MT cannot be due to any form of remapping or to the presence of neurons with spatiotopic receptive fields.

Direct evidence for spatiotopic processing in MT has been limited to two fMRI studies that have found a spatiotopic BOLD signal in human MT under conditions in which attention is not restricted to the fovea (d'Avossa et al., 2007; Crespi et al., 2011). As in our previous study (Ong and Bisley, 2011), the stimuli present in the receptive field of the neuron are behaviorally irrelevant, but as the sudden onset of the stimulus is expected to draw attention (Jonides and Irwin, 1981; Yantis and Jonides, 1984; Theeuwes, 1991) and is not coupled with an attention demanding task at the fovea, we expect that the animal would attend to it. Hence it is unlikely that we do not see remapping or spatiotopic receptive fields in area MT in the non-human primate brain due to a lack of attentional allocation. So if MT neurons do not have spatiotopic receptive fields, what could be the genesis of the spatiotopic BOLD signal? One possibility is that gain fields, known to be present in MT (Bremmer et al., 1997), may affect the BOLD signal enough to produce an apparent spatiotopic response. Another possibility, which is not mutually exclusive, is that the BOLD signal may be overemphasizing top-down biases (Yoshor et al.,

2007). In this case, it could be due to attention, gain field effects or some other signal that could affect spatial processing.

Results from psychophysics alone (Melcher and Morrone, 2003; Ong et al., 2009) only provide indirect evidence that MT processes motion information in a spatiotopic coordinate system. These results could be explained by gain field modulation of activity (Bremmer et al., 1997), but also could be explained by the interactions of MT neurons with higher cortical areas to which they project, such as posterior parietal or prefrontal cortices.

An absence of remapping in MT

Traditionally, remapping studies have been carried out using transient stimuli flashed in the post-saccadic receptive fields of the neurons being probed perisaccadically (Duhamel et al., 1992a; Umeno and Goldberg, 1997; Kusunoki and Goldberg, 2003; Sommer and Wurtz, 2006; Berman et al., 2007). By exploiting its short lifetime, the response within the visual system persists beyond its actual presence, allowing us to trace the signal of an object which is no longer there. This technique gives us a little more sensitivity compared to the use of a spatially stable moving dot stimulus, in which only anticipatory responses can be identified (Duhamel et al., 1992a; Walker et al., 1995; Mirpour and Bisley, Submitted). Nevertheless, we continued to find no evidence of remapping in area MT, consistent with studies using spatially stable stimuli (Ong and Bisley, 2011) and one dimensional random noise stimuli (Hartmann et al., 2011).

The total absence of remapping in MT may seem to be unexpected based on the finding of remapping in areas that MT receives signals from (Nakamura and Colby, 2002) and projects to

(Duhamel et al., 1992a) and the relative ubiquity of other extra-retinal signals, such as attention (Treue and Maunsell, 1999; Reynolds et al., 2000; Khayat et al., 2006) and gain fields (Andersen et al., 1990; Bremmer et al., 1997; Bremmer et al., 1999; Bremmer, 2000). We believe that these results are consistent with the hypothesis that remapping plays a role in maintaining the stability of visual space by remapping signals in areas thought to act as priority or saliency maps (Thompson and Bichot, 2005; Fecteau and Munoz, 2006; Gottlieb et al., 2009; Bisley and Goldberg, 2010). In areas with responses more representative of stimulus importance, the imprecise timing of remapped responses (Umeno and Goldberg, 1997; Kusunoki and Goldberg, 2003) will primarily affect the perceived spatial and temporal stability of the stimulus around a saccade. This could easily explain peri-saccadic mislocalization or compression (Honda, 1989; Ross et al., 1997; Jeffries et al., 2007). However, the addition of extra activity in lower level processing areas could strongly influence the extraction of information about stimuli, leading to errors in judgment, which would be a distinct evolutionary disadvantage.

The confound of phosphor persistence

The standard P22 phosphor that is used in most color monitors decays to 10% peak emission in 6 ms or less (Sherr, 1993). However, the visual persistence of a bright stimulus presented on a black background in a dark room feels to the observer to be much longer; Britten and colleagues (1992) estimated it to be approximately 100 ms. We found that the output from a photodiode on our CRT under the conditions used for recording the neural data showed a decay which lasted many 10s of milliseconds. Given the sensitivity of MT neurons to low contrast stimuli (Sclar et al., 1990; O'Keefe and Movshon, 1998; Heuer and Britten, 2002), it is not surprising that we

perceive this persistence nor that this activity could trigger a response when brought into the receptive field via a saccade.

While the results we found using a white stimulus on a black background serve as a cautionary tail, we do not believe they negate previous reports of remapping. Many of the studies utilized LEDs reflected onto a tangent screen (Duhamel et al., 1992a; Walker et al., 1995; Umeno and Goldberg, 1997) or LCD projectors (Heiser et al., 2005; Sommer and Wurtz, 2006; Berman et al., 2007), which, are unlikely to have the same level of persistence that is inherent in a CRT display. In addition, many of these studies identified anticipatory remapping; neurons responded to the stimulus before a response could be expected via the visual system. These anticipatory responses cannot be explained by stimulus persistence and were also absent in MT (Ong and Bisley, 2011). However, our data clearly show that the best way to exclude persistence as a possible variable is to present dark stimuli on a bright background.

Chapter 5:

General Discussion

5.1 Summary

The aim of these experiments was to look at the processing coordinates of visual motion. As visual stability is an essential important feature of our lives, we proposed that motion processing occurs in spatial coordinates.

In the experiments conducted, we have shown that, while area MT appeared to play an important role in the memory for motion task, processing the information in spatiotopic coordinates, the spiking activity of the neurons in this area do not demonstrate coding for information in spatial (or head-centric) coordinates.

In the first project (Chapter 2), we utilized human psychophysics to show that performance is optimal in a memory for motion task when the two stimuli to be compared are presented in the same spatial location. This suggests that the coordinate system used in this process was not automatically tied to the retina. In section 2.4.2, we show that, when the two stimuli to be compared are displaced from each other, the critical separation at which the performance is compromised best matched that of the receptive field sizes of area MT. As MT neurons show preferential tuning of speed and direction of visual stimuli, the fact that it participates in the

memory for motion task is unsurprising; what is surprising is its apparent processing in spatial coordinates, as area MT has been long thought to work solely in retinal coordinates.

In the next two studies, we set out to test how MT neurons, which have been thought to receive and process visual information in retinal coordinates, can have spatiotopic processing.

In Chapter 3, where we performed the first set of experiments recording from area MT neurons in awake behaving primates, we found that these neurons did indeed process visual information in retinal coordinates and did not respond to a stable moving dot stimulus which was presented outside its retino-centric receptive field (section 3.4.1). We also followed it up with a set of analyses which showed that the receptive fields of MT neurons did not shift preemptively towards its post-saccadic location (section 3.4.2). Given that neurons in a number of earlier visual areas remap responses, we suggest the possibility that MT neurons do remap, but do not do so predictively. This means that the receptive fields of the neurons do not shift to their post-saccadic location before or during the saccade, a process termed anticipatory remapping, but remain linked to the retina.

There is a possibility that MT does carry out remapping, not in an anticipatory way but in a manner which does not require the receptive fields to shift ahead of time. In order to reveal this mechanism, we performed another set of experiments where a transiently presented stimulus is present in the future receptive field of the neuron, but is no longer present when the eye movement is made (Chapter 4). The hypothesis is that if visual responses to the stimuli in the future receptive field are transferred from one neuron to another at the same level of processing

in the brain, we would see a trace of the visual signal appear after the eye reaches the new fixation position – that is, the signal is remapped. Using a black disc presented on a white background for 50ms, we find the MT neurons do not remap responses to the stimulus when it is no longer present (section 4.4.1). Hence we conclude that MT neurons do not appear to have any form of remapping.

5.2 So, how do you explain the spatial processing in the memory for motion task?

The aim of the original experiment was to look at spatial processing in motion perception. We unexpectedly found that the candidate area for this process was a part of the brain which was known to primarily work in retinal coordinates, and we set out to test how this might be possible, either through having neurons with spatiotopic receptive fields or through being able to receive remapped signals from other neurons.

Other studies which utilized human psychophysics have established that area MT has a processing component that uses a reference frame linked to locations in space. This includes a study which showed that the integration, of motion occurs across a saccade when the stimuli are presented in the same spatial, but not retinal location (Melcher and Morrone, 2003), as well as the gaze invariance of a perceptual learning effect (Zhang and Li, 2010).

However, our results from Chapters 3 and 4 show that neurons in area MT are not spatiotopic, nor do they demonstrate anticipatory remapping or delayed transfer of information within the

same cortical area. These results were corroborated by Hartmann (2011) who, using one dimensional random noise stimuli, showed that receptive fields of area MT are strictly retinotopic.

We suggest that the visual motion is processed by MT neurons, but the information gleaned from that is handed to a different area of the brain, where it is stored or further processed. This brain area is likely to be one which works in spatial coordinates or which automatically remaps signals across saccade. This would perform the comparison best when it is coming from the same spatial location as opposed to when it is coming from the same retinal but different spatial location.

Candidate areas for this processing area include LIP and FEF, both of which demonstrate anticipatory processing, and the prefrontal cortex, which does not have receptive fields tied to retinal coordinates per se, but instead has a preference towards the contralateral visual field. LIP is an area which receives direct projections from area MT, and it exhibits anticipatory remapping in its neuronal activity (Duhamel et al., 1992a). LIP neurons also demonstrate the ability to hold the memory of a particular location in space, as well as the category of an object that had previously appeared in it (Freedman and Assad, 2009). A candidate area for the storage and retrieval of this motion information would be LIP. Another potential is FEF, which has remapping activity (Umeno and Goldberg, 1997; Crapse and Sommer, 2009) and responds during motion tasks (Ding and Gold, 2012).

The neurons in PFC could also perform this function – its neurons do not have receptive fields tied to retinal coordinates. It also has strong, task relevant memory and categorization signals,

which have to come from a more specialized area (Freedman et al., 2001; Roy et al., 2010), such as MT during a direction categorization task or the temporal lobe for object recognition.

Still, this does not completely explain the results of d'Avossa et al. (2007) who showed a spatiotopic BOLD signal in human area MT while Gardner et al. (2008) claimed that it is strictly retinotopic. A recent study suggested that the effects of attention dictated this observation i.e. when attention was not restricted to the fovea, the BOLD signal is spatiotopic, but when attention is restricted to the fovea, the BOLD signal is not spatiotopic (Crespi et al., 2011). Since our stimuli were inherently salient in the absence of an attention demanding task at the fovea (Chapter 3), we expected a response that would be similar to that in the study which showed spatial processing in human MT. However, we do not see this spatial processing in any shape or form with extracellular recordings.

It has been suggested that the BOLD signal obtained from fMRI studies is more closely correlated to that of local field potentials than that of single cell activity (Logothetis, 2008), especially under the conditions where top down modulation is present. In fact, under conditions of attention and awareness, fMRI signals are more strongly affected than what is predicted by the firing rates of neurons (Saenz et al., 2002). Keeping this in mind, it is possible that a spatiotopic BOLD signal can exist even when we do not see spatial processing in single neurons, as the BOLD signal is occurring much later and pooling the minute changes in the hemodynamic signal over a much longer period of time, which could give rise to a more sensitive measure of top-down influences (Yoshor et al., 2007).

5.3 Future studies

As we have proposed above, LIP appears to be a good candidate area for the storage of motion information in the memory for motion task. From the literature, we know that inactivation of MT disrupts the encoding for motion memory (Bisley and Pasternak, 2000) which is unsurprising given that the absence of this processing module prevents even the detection of motion (Newsome and Pare, 1988)

If LIP is the area of the brain which stores the motion information for later comparison, we would be able to observe that with recordings from LIP. To test this hypothesis, we would have the animal perform a motion task that needs a memory component. Such a task would require it to remember the motion direction of an initial moving dot stimulus and then indicate a match when one appears. If our hypothesis is true, we will be able to see the representation of the remembered motion direction during the delay period.

Another way to test this hypothesis is by using an inactivation experiment. It predicts that inactivation of LIP would result in a much decreased ability to remember motion direction, with no compromise of motion discrimination. I would have the animals perform a task that would need a memory component, such as our memory for motion direction discrimination task, and another which does not require working memory, for example having the animal indicate the direction of a moving-dot stimuli without requiring a retention of that memory. If LIP does store this information, we would expect the animal's performance to be much worse in the memory for

motion task, and no change in performance for the task which did not require a memory component.

As we have previously mentioned, the BOLD response recorded during fMRI sessions could overemphasize the top-down influence of attention. If this is the cause of the apparent spatiotopic processing in MT, we would predict that the BOLD signal in the monkey should show spatiotopic processing using a similar task to that used in the human studies (d'Avossa et al., 2007; Crespi et al., 2011). To test this hypothesis, we propose collecting BOLD data while having the animals perform the visually guided saccade task with the moving-dot stimuli in the periphery with and without an attention demanding task in the fovea. We predict that no difference between the species would be observed.

Chapter 6

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