NEURAL CORRELATES OF SACCADE TARGET SELECTION AND PROGRAMMING IN SUPERIOR COLICULUS

by

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Abstract

Decision-making process involves sequential stages of sensory processing, perceptual selection of a target for the behavior, preparation of an action, and execution of that action. Superior colliculus is at the center of a network which integrates the sensory information into evidence towards decisions about whether, to where and when a saccade should be made, and is therefore a suitable model to explore different aspects of these stages. This work explores the dynamics of interactions of SC populations during a decision that involves selection of a particular stimulus among the alternative options as the target for a future saccade. I show that these interactions evolve in time along with the requirements of the task, and the patterns of this evolution are different among neurons from the same or different SC populations. I further explore the impact of correlations within the activity rates of these neurons on the efficiency of coding this decision variable. I show that while the variability in pairs of neurons seems to increase the available information about the encoded target for the saccade, they decrease the performance of two biologically plausible decoders over simulated large populations. Finally, I explore the role of neurons in intermediate layers of SC in saccade production in a task where the subjects anticipate the possibility of withholding a programmed saccade. I show that while an accumulation of evidence towards a decision to execute a saccade appears to happen in SC, this activity pattern cannot fully account for the behavior of the subject. SC should be mainly considered as the threshold unit that transfers this decision variable from an accumulation unit elsewhere in the brain, such as the frontal eye fields, to the execution unit in the brainstem. This work confirms previous findings on the role of SC in two perceptual and executive stages of a decision process and provides additional insights on the details of how these roles are implemented.
Co-Authorship

Martin Paré designed the experiments. Kelly Shen, Gregory S. Day, and Martin Paré collected the data. Kelly Shen and Martin Paré pre-processed the single cell datasets used in chapters 3 and 4. I and Martin Paré designed the analyses. I conducted the analyses. I wrote the manuscripts.
Statement of Originality

(Required only for Division IV Ph.D.)

I hereby certify that all of the work described within this thesis is the original work of the author. Any published (or unpublished) ideas and/or techniques from the work of others are fully acknowledged in accordance with the standard referencing practices.

(Saba Farbodkia)

(August, 2017)
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List of Abbreviations

Superior Colliculus (SC)
Frontal Eye Field (FEF)
Excitatory Burst Neurons (EBNs)
Inhibitory Burst Neurons (IBNs)
Omnipause Neurons (OPNs)
Cross-Correlograms (CCGs)
Post Stimulus Time Histogram (PSTH)
Joint Post Stimulus Time Histogram (JPOSTH)
Post Stimulus Time Coincidence Histograms (PSTCH)
Mutual Information (MI)
Fisher Information (FI)
Artificial Neural Networks (ANNs)
Support Vector Machines (SVMs)
Winner-Takes-All (WTA)
Reaction Times (RTs)
Response Fields (RFs)
Time of Onset of Growth of Activity (TOGA)
Discrimination Time (DT)
Discrimination Magnitude (DM)
Standard Error of Mean (SEM)
Chapter 1

Introduction

One of the main goals of cognitive neuroscience is to understand how decisions and actions are represented in the brain. Behavioral decisions can usually be thought of as sequences of two main stages: the “decision that”, which is the selection between two or more alternative goals or targets, and the “decision to”, which is whether and when to execute an action (Schall, 2001). Different networks of neurons are involved in different components of these stages: the perceptual component of decision-making requires the features of the stimuli to be first represented by the sensory neurons as inputs to the association cortices. The neurons in association cortices, in turn, calculate the decision variables from this input, representing a categorization of the stimuli, or evidence towards it (Gold & Shadlen, 2001; Schall, 2013). The decision signal is in turn passed to the movement-planning structures, where the executive component of the decision is made. A movement is believed to occur when the activity of neurons in these structures surpasses a biophysical threshold, which shifts the activity of these or the neurons downstream to them into a bursting mode, acting as the physical trigger that activates the motor neurons that innervate the muscles (Glimcher, 2003; Schall, 2013).

The two stages of perceptual and motor planning of the decisions are dissociated from each other (J.I. Gold & Shadlen, 2001; Schall, 2013). Target selection process can still be completed, even if no movements are produced or if the execution of movements is delayed (Bennur & Gold, 2011; Gold & Shadlen, 2001; Gregoriou, Gotts, & Desimone, 2012; Schall, 2013; Thompson, Biscoe, & Sato, 2005).

Superior colliculus is an excellent candidate for studying the different stages of decision processes. In primates, it has evolved to receive cortical inputs, enabling it to be involved in controlling more complex behavior. SC is composed of several layers of cells which are involved in visual processing, and
orientation of the saccadic eye movements (as well as maintaining fixation). It can be described as a location where various inputs from the cortex and basal ganglia converge and transform into outputs to the burst generator circuits in the reticular formation, for the control of eye movements (Hikosaka and Wurtz, 1983; Paré and Wurtz, 1997; Everling and Munoz, 2000; Munoz et al., 2000a; Preuss, 2007).

Anatomically, SC is located at the center of a network of sensory and motor structures. The neurons in its superficial layers receive their inputs from retina (Pollack and Hickey, 1979) and visual areas of cortex (Tigges and Tigges, 1981; Lui et al., 1995). The neurons in intermediate layers receive inputs from visual cortex area 19 (Lui et al., 1995), and auditory inputs from inferior colliculus (Kudo et al., 1984). The integration of the sensory information from these different sources makes SC an ideal location for controlling the saccadic eye behavior. SC sends its outputs to the oculomotor nuclei in the brainstem, where the saccadic burst generators are located (Gandhi and Keller, 1997; Rodgers et al., 2006). These are excitatory and inhibitory burst neurons (EBNs and IBNs) whose burst activities activate the contralateral and ipsilateral nuclei that contract or relax the eye muscles. In addition, the Omnipause neurons (OPNs) are also involved in controlling saccades. OPNs are inhibitory neurons that are active at the time of fixation and inhibit EBNs and IBNs. The rostral neurons of SC, which have a tonic activity during fixation, send excitatory inputs to the OPNs (Paré and Guitton, 1994; Gandhi and Keller, 1997; Everling et al., 1998; Büttner-Ennever et al., 1999). The caudal neurons send excitatory inputs to the contralateral EBNs and IBNs (Sugiuchi et al., 2005; Shinoda et al., 2011). Figure 1-1 summarizes these connections.

To initiate a saccade, EBNs and IBNs need to be activated, which is accomplished by the connections from caudal SC (Shinoda et al., 2011). Moreover, the OPNs activity needs to be suppressed which may happen as a result of suppression of the excitatory activity of the rostral neurons of SC (Munoz and Guitton, 1991; Paré and Guitton, 1994; Yoshida et al., 1999), as well as their disinhibition by the IBNs after activation of IBNs by excitatory inputs from caudal SC (Yoshida et al., 1999; Shinoda et al., 2011) along with their disinhibition through central mesencephalic reticular formation inhibitory pathways.
Figure 1-1: Neural circuits in SC and brainstem underlying controlling a rightward horizontal saccade. Solid lines are the pathways that are activated. Dashed lines are the pathways that are suppressed. Open circles indicate excitation, and filled circles depict inhibition. The figure is from Shinoda et al. (2011).
which are stimulated by SC (Wang et al., 2013). The inhibition that the OPNs exert on the burst neurons works as a gating mechanism that avoids the excitatory input from the caudal SC from generating a burst in these premotor neurons. Any threshold mechanism that transforms a decision signal into a planned eye movement needs to overcome this inhibition.

Neurons from different layers or within the same layer of SC interact with each other as well. Horizontal neurons or connections within superficial layer cause a decrease in the response of a neuron from this layer to a stimulus in its receptive field (RF), if another stimulus is presented simultaneously at a distant location not in its RF (Rizzolatti et al., 1974; Behan and Appell, 1992). Similar inhibitory connections are presumed to exist in the intermediate layer (Munoz and Istvan, 1998). Deep layers show horizontal inhibitory connections from the rostral parts of SC to the caudal parts, but less so in the reverse direction (Behan & Kime, 1996).

The role of SC as a motor map is well established. Its layers are organized in maps that represent the contralateral visual field. The rostral part of this map corresponds to the fovea, and moving toward the caudal parts, parts of space that fall closer to the margins of the visual fields get represented on the map. The neurons in intermediate layers can be seen as a map where the desired location in the visual space to be foveated is represented on them by the neurons which have a higher activity. When one is fixating on a particular target, the eyes are already foveating on the desired spot in the space. This means that the neurons which represent the fovea in the visual field must be active at this point, as found by (Munoz and Wurtz, 1993). This will signal that the desired spot to be the foveated is the same as the spot that is being foveated, that there is no error signal, and that no saccade is needed to be made in order to correct such error. When the neurons other than those in the rostral end of SC which correspond to fovea get activated, they signal that the desired spot in the space to be looked at is now different from where the eyes are actually foveated on. An error signal is generated which will drive a saccade to be made to the spot in the visual field which corresponds to the response field of the neurons in the map that have increased their
activity. Once the saccade is made, the fovea will be fixating on the desired target again, rostral neurons corresponding to fovea will start to fire, error will go back to zero, and no saccade will be generated until an error signal is generated again (Krauzlis et al., 1997; Hafed et al., 2009). Since there can be only one location that can be foveated at any time, once the neurons in the caudal parts of SC start to increase their activity to signal anew desired spot to be foveated, the neurons in rostral part of SC start to become silent, and remain so until the saccade is executed. If more than one potential target appears in the visual field, the activity of neurons representing the corresponding spatial locations on the map will increase, which would mean more than one error signal would be generated. In this case, a lateral inhibition process would cause the neurons of one of these locations to suppress the others and eventually represent the winning and only desired location in the field to make a saccade to (Munoz et al., 2000b; Munoz, 2002; Otero-Millan et al., 2011).

The activity of neurons on this motor map signals the amplitude and direction of saccades from the current fixation point (Sparks, 1975), and thus forms a topographic map similar to what the visual neurons in superficial areas present (Mays and Sparks, 1980; Sparks and Mays, 1990). This means that the motor and visual maps in superior colliculus’s different layers correspond to each other (May, 2006). This, along with the inter-laminar interactions between neurons in superficial layers and intermediate layer neurons that share the same receptive fields as them (Rhoades et al., 1989; Behan and Appell, 1992; Hall and Lee, 1993, 1997; Lee and Hall, 1995; May, 2006), can be seen as a basis to propose that the motor processing in SC happens partially through inputs from visual processing neurons in the corresponding part of superficial areas. These interactions can underlie the process of target selection for saccades, when the saccades are directed toward a visual goal. A group of SC neurons, visuomovement neurons, show both visual and saccade related activities (Wurtz and Goldberg, 1972). It is possible that these neurons work at the interface of visual and movement neurons, by integrating the responses of visual neurons into movement-related activity (May, 2006). The other possibility is that the visual responses of these visuomovement neurons are not causally dependent on the visual neurons within SC,
but rely on inputs from other areas that send projections to intermediate layers, such as prestriate cortex or superior temporal sulcus (Lui et al., 1995).

Sensorimotor integration in SC may be sufficient in target selection and saccade programming in natural contexts where the saccades are oriented toward a visual stimulus with salient features. However, interactions with other brain areas may be necessary for producing behavior that is more goal-directed. For these types of behavior, interactions outside SC, for example with basal ganglia, cerebellum, or cortex, for example, frontal eye fields and lateral intraparietal area (LIP) may be necessary. (Wurtz and Goldberg, 1972; Schiller et al., 1979; Lynch, 1992; Pierrot-Deseilligny, 1994; Hanes and Wurtz, 2001; Wardak et al., 2002; Takakusaki et al., 2004; de Weijer et al., 2010; Herweg et al., 2014). Superior colliculus receives and sends projections from and to many of these areas (Baizer et al., 1991; Schall et al., 1995; Hanes and Wurtz, 2001; Paré and Wurtz, 2001; Sommer and Wurtz, 2001, 2003; Wurtz et al., 2001; Berman et al., 2009a; Lyon et al., 2010; Baldwin and Kaas, 2012).

This work explores the mechanisms underlying two main functions of SC: target selection and movement programming.

SC activity during a visual search task has been characterized before (McPeek and Keller, 2002a, 2002b, Shen and Paré, 2007, 2011; Shen et al., 2011a). The early visual responses to targets and distracters are usually similar and non-discriminating. The activity closer to the time of saccade, however, discriminates between the goal of saccade and other locations, and also between the target and distracters regardless of where the saccade is made to (Shen et al., 2011a). SC, along with LIP and FEF, forms a visual salience map that guides the selection of the visual goal for a saccade. This can be thought of as a topographic map where the visual responses that are evoked by stimuli in response fields (RFs) of its neurons are integrated into a signal that represents the salience of the objects falling onto that map. The salience can be determined based on the features of the stimuli in a bottom-up manner, or by the behavioral goals of the subject in a top-down fashion (Wolfe, 1994; Itti and Koch, 2000; Gee et al., 2008). This signal can evolve
into a movement-related response that directs a saccade towards the location of the most salient object among the stimuli (McPeek and Keller, 2002a, 2002b; Thompson et al., 2004; Thompson and Bichot, 2005; Ipata et al., 2006; Thomas and Pare, 2007). The visual search task was first designed for studying mechanisms of visual attention in humans, and required them to report the presence of a particular stimulus, the target, among the other stimuli, the distracters, usually with a manual response (Paré et al., 2009). Several studies have focused on determining which attributes of the stimuli can guide the attention in an efficient way, and therefore, making the task easy to perform (Beck, 1966; Treisman and Souther, 1985; Treisman and Gormican, 1988; Duncan and Humphreys, 1989; Wolfe, 1992; Theeuwes and Kooi, 1994; Wolfe and Horowitz, 2004). Therefore, different versions of the task can be employed to study the search behavior. In one version of the task, these guiding features are used as the only distinguishing feature between the targets and distracters, and the search behavior is guided primarily by the stimulus-oriented attention. Other versions may use a conjunction of these features to distinguish between the target and distracters, making the search more difficult (Paré et al., 2009). The task has been utilized to study the neural mechanisms underlying these processes in monkeys (Bichot et al., 2001; Thompson et al., 2004, 2005; Shen and Paré, 2007; Shen et al., 2011b). Figure 1-2 depicts two versions of this task as adapted for monkeys.

While the characteristics of single neurons during this task are well characterized, less is known about the role of populations of neurons in selecting the target of the saccade. The neurons that respond to different stimuli and compete with each other for selection of one of them are expected to have inhibitory lateral connections that allow for the population with the largest response to suppress the activity of the other competing populations in a winner-takes-all fashion. Conversely, the neurons that share their response fields and respond to the same stimulus can be expected to have excitatory connections that mutually increase their activity. If so, we would expect to see a negative correlation in the spike rates of the former group, and a positive correlation in the spike rates of the latter group, both on average and on a trial-by-trial basis. Moreover, we would expect to see a tendency among the neurons in the latter group to spike
Figure 1-2: Visual Search Task adapted for monkeys. The task starts with a fixation period, and continues with presentation of multiple stimuli simultaneously, while the fixation signal disappears, allowing the subjects to execute a saccade to their selected target. The task can have different versions. In one possible version (A), the target is different from the distracters by a single feature, such as color. In another version (B), the target is different from the distracters through the conjunction of two features (such as shape and color), while distracters are different from each other by either of the two features. Figure is adapted from (Shen et al., 2010) with permission.

A  Feature Search

B  Conjunction Search
together in relatively close time intervals, while we expect one of the neurons in former group to become silent in close time intervals to when the other neuron spikes. The second chapter examines the interactions of neurons whose RFs either overlap, or are opposite of each other on the visual field, during a visual search task, at various time lags and intervals, as a function of the type of stimulus that falls in their RF. We explore two types of interactions: first the correlations in the average rates of activity over trials and the trial-by-trial variability in these rates; second, the temporal correlations in the spike times and the levels of spike synchronization. To examine how these interactions contribute to the evolution of the decision dictated by the neural activities of these neurons, we ask three main questions. First, do these interactions change from the time of processing of sensory information to the time that a decision about the location of a target for a future saccade is made? Second, are these interactions modulated by the stimulus condition, in a manner that could potentially contribute to encoding the decision outcome of each trial? Third, do these interactions show different patterns between the two groups of neuronal pairs with shared or opposite RFs, in a way that is in line with our expectations about the cooperation and competition among these neurons? Our hypothesis was that if the interactions in SC local populations and between those are important for the performance of this task, we would find positive trial-by-trial correlations in spike rates of neurons from the same local populations, but negative ones from the neurons in competing populations. Also, we hypothesized that if these interactions reflect the requirements of the task, they should become stronger from one behaviorally relevant epoch to another.

In the third chapter we focus on how well the activity rates of the neurons in SC can be used to predict the choice of the saccade goal by the subject. Specifically, we use the results of the second chapter to examine the impacts of correlations in trial-by-trial variability of neural responses on the coding capacity of small populations in SC, and how they, in combination with behavioral results, can be used to infer about coding mechanisms employed by SC. We expect that ignoring correlated variability can lead to an underestimation of the extent that the neural responses can predict the stimuli, due to the shaping of the response distributions, if correlations in variability of responses around their averages to each stimulus
and correlations in the tuning curves of the neurons have opposite signs (Pola et al., 2003; Averbeck et al., 2006; Hu et al., 2014), or if they have the same sign and are large in magnitude (Ecker et al., 2011; Hu et al., 2014). Ignoring correlated variability should lead to an overestimation, if the correlations in the variability and the tuning curves have similar sign and are small in magnitude (Pola et al., 2003; Averbeck et al., 2006; Hu et al., 2014), or if they point to the same direction as the multiplication of the derivatives of the tuning curves (Moreno-Bote et al., 2014). This chapter provides an example of individual neurons whose activities encode more information about the target of a behavior, than the behavior of the subjects indicates. In other words, an optimal decoder is able to infer the type of stimulus from the neural activities at a higher rate than the subjects did. In the context of this example, we explore whether the availability of this information changes when a population of neurons is taken into consideration, instead of well-isolated single neurons. Moreover, we explore how different decoding schemes can affect the availability of the information available from small populations of SC neurons, and which decoding scheme provides better predictions of the behavior. In this sense, SC provides an excellent model for exploring population codes, since it is a well-studied part of the oculomotor system that is involved in processing of both sensory and motor information necessary for regulating the well-studied saccadic behavior.

The fourth chapter explores the role of SC in decisions about the execution of a movement. About 20 ms before saccade onset, the SC neurons in intermediate layers show a bursting activity. This bursting activity is not observed on trials where a saccade is not generated (Sparks, 1978; Paré and Hanes, 2003). Given the discharge properties of its neurons, and its position within this network of connections between the cortex, basal ganglia, and brain stem, superior colliculus has a key role in determining the goal for saccade, as well as initiating the saccadic movement. Particularly, given the indirect connections from caudal SC to the OPNs in the brainstem, we expect that executing a decision to make a saccade should involve an activity rate in SC sufficiently large and lasting to suppress the OPNs, and overcome the inhibitions that they exert on the EBNs. In this chapter we use the data from singly-recorded neurons to
explore the time that it takes for the brain to program and execute a saccade, under the circumstances when it anticipates to be required to potentially withhold that saccade. We apply a rise-to-threshold model to the neural activity rates, the increase in which resembles the accumulation of evidence in favor of a decision to execute a saccade. These models mainly consist of an output unit that integrates evidence over time in favor of one or another option, until the accumulated evidence meets a criterion (Gold and Shadlen, 2007). This criterion can be defined as a threshold on the value for the accumulating variable, surpassing which triggers a response.

Physiologically, surpassing of such threshold could produce an all-or-none response in a downstream area, committing the corresponding output unit to execution of an action in accordance to the selected option. Therefore, surpassing the decision criterion or lack of it by an output unit would determine whether the decision option that the output unit controls will be selected or not. For example, decision processes with two different options to be selected can be seen as the process of the two output unit competing against each other in accumulating the evidence in favor of the option they each control. The option will be selected that is associated with whichever unit whose accumulated evidence reaches its threshold first. This can be true about tasks in which there are two possible targets where the subject needs to select one, such as a two (or more) -alternative forced-choice task, such as visual search task (Gold and Shadlen, 2001; Ratcliff et al., 2003; Purcell et al., 2012). An illustration of the processes underlying the decisions in such tasks can be found in top panels of Figure 1-3.

In the tasks where only one target exists, and the decision is about whether to execute a movement to that target or countermand that movement, the process can also be seen as the decision that is made by only one unit, which promotes movement: If the unit keeps accumulating evidence until it surpasses its threshold, the movement will be executed. Otherwise, no movement will be made. The inhibition of this unit can be seen as happening through a “stop” process which inhibits the accumulation process in the unit and avoids it from reaching its threshold (Logan et al., 1984; Boucher et al., 2007). A variant of a
Figure 1-3: Comparison of activity rates at the accumulation unit (top) and threshold unit (bottom) when the activity rate in accumulation unit surpasses its decision criterion (left) and when it doesn’t. The red line indicates the decision criterion. The gray vertical line is to signify the time when the activity rate in the accumulation unit surpasses the criterion in the left. The threshold unit is assumed to be the caudal SC, which sends excitatory inputs to IBNs and EBNs when the step-function produced a positive input. Figure adapted from (Simen, 2012)
particular group of raise-to-threshold models, the linear ballistic models (Brown and Heathcote, 2005), has been used to establish that the variability in linearly estimated rates of growth in FEF can account for the variability in reaction times (Hanes and Schall, 1996). Following the same model, we explore whether the rate of increase in the neural activity during a given trial can determine its reaction time. We also ask whether there is a fixed threshold in SC, surpassing which entails the execution of a movement. Using these two pieces of information we ask whether SC should be considered an accumulation unit in the decision process, an implementation of the threshold mechanism, or both. We distinguish between the accumulation process and the threshold implementation. The threshold mechanism involves a step-function transformation that turns the input from integrative accumulation function into an all-or-none output, as illustrated in Figure 1-3. It acts like a switch that has been turned on, activating the areas downstream and executing the saccade. For this to happen, the input from the accumulation unit needs to reach a critical value, corresponding to a decision criterion (Simen, 2012).

The accumulation unit and threshold may be both implemented in the same brain areas such as SC using different classes of neurons for implementing each, or with different phases of activity of the same neurons corresponding to each. Alternatively, it can be implemented in different brain areas, with, for example, the FEF corresponding to the accumulation unit and SC corresponding to the threshold mechanism.

In the fourth chapter, we ask three questions about the role of SC in accumulation of evidence and implementation of a threshold mechanism. First, does the activity during the bursting period of SC movement cells correspond to a threshold mechanism that can determine the behavioral outcome of each trial? Second, does the growth of activity in SC movement cells represent a process of the accumulation of evidence towards a decision to execute a saccade? Our hypothesis is that if this is true, then the changes in the rates of growth in SC cells should be able to account for the variability in observed reaction times, with the assumption of a fixed threshold. Third, do the activity rates at the onset of burst represent the decision criterion surpassing which starts the all-or-none response which implements the
threshold? This chapter uses the data from a Countermanding Task. The countermanding task involves two different types of trials: the trials in which a movement should be executed, and trials in which a movement is initially planned but is expected to be cancelled later in the trial. The latter group, which is also called STOP trials, is further divided in two more subcategories based on the outcome of the trial: the CANCELED trials, and non-CANCELED trials (errors). The task was first designed to study inhibitory control (Lappin and Eriksen, 1966). However, the task is also suitable for studying neural correlates of accumulator models of decision-making, as it creates two distinct sets of responses in one of which, the decision is executed, and in the other it is not. Moreover, the task generates an extended range of reaction times that would not be produced if the STOP trials did not exist (Rieger and Gauggel, 1999; Ozyurt et al., 2003; Åkerfelt et al., 2006; Mirabella et al., 2006; Stuphorn and Schall, 2006; Emeric et al., 2007), and this allows for investigating different versions of accumulator models of decision-making that can account for variability in response times. Figure 1-4 depicts the task.

Together, these chapters examine different aspects of two types of decision processes in SC. The role of interactions of neurons in different populations during perceptual decision making, and the impacts of these interactions on the efficiency of the neural code are explored in the second and third chapters. The process of accumulation of evidence and implementation of a threshold for an executive decision in the activities of individual cells is the topic of the fourth chapter. The process of accumulation of evidence and implementation of the decision criterion for the perceptual decision, as well as the impacts of interactions of neurons on the variability of the accumulation rates and behaviorally observed reaction times for either of the decision types are not covered in this work. Future work can address these questions.
Figure 1-4: The countermanding task. In the GO trials, the subjects are expected to respond to the appearance of the target, as the fixation point disappears. On some interleaved trials (STOP trials, right), the fixation point reappeared after a variable delay and instructs the subjects to withhold the execution of the response. If the subject cannot successfully withhold the response, the trial will be considered as an error. Figure is adapted from (Paré and Hanes, 2003)
Chapter 2

Neural Interactions in SC during Saccade Target Selection

2.1 Abstract

The role of superior colliculus in saccade target selection is well established, however, the interactions of populations of SC neurons with each other during this process are not characterized. Exploring these interactions can be informative about the role of populations in decision making. Here we investigate the dynamical changes in temporal correlations in spiking activity of pairs of neurons during a visual search task as well as the correlations in the averages and variabilities of spike rates between pairs of neurons. We examine these interactions between two groups of neurons. First, those whose response fields overlap and therefore represent the same stimulus, which we expect to synchronize their activities with each other to select a target and show positive correlations in their spike rates. Second, those whose response fields are across from each other in the visual field, and we expect their activities to compete with each other to select the target in a winner-takes-all fashion. We explore how these correlations can be modulated by different stimulus conditions, that is, target vs. distracters, in behaviorally relevant time epochs of the task in each group of neurons. We find that both correlations in trial-by-trial variability of spikes rates and temporal correlations of spikes are modulated by the stimulus condition in pairs with opposite RFs, and that this modulation gradually progresses with the behavioral events in the task. In neighboring pairs which share their RFs, variability correlations increase during the discrimination epoch for both stimulus conditions, but in saccadic epoch they decrease for target trials. This stimulus-dependent modulation in saccadic epoch is smaller in comparison to what observed in pairs with opposite RFs. The temporal correlations in neighboring pairs are significantly different from zero in all epochs, except for target trials in saccade epochs. This implies that the role of competition among the neurons that represent different stimuli in SC’s saccade target selection is stronger than the role of collaboration among neurons that
represent the same stimuli. Further, the collaboration among the latter neurons is more pronounced during the discrimination phase than in execution of the saccade.

### 2.2 Introduction

Various studies, recordings from activities of single neurons, have established a role for SC in saccade target selection (Sparks, 1999, 1990; Glimcher and Sparks, 1992; Ratcliff et al., 1992, 2003, 2007; Shen and Paré, 2006; Paré et al., 2009; Shen et al., 2011a, 2011b; Shen and Pare, 2014). However, given the broad response fields of neurons in SC, it is believed that the decisions about the target for a saccade should be made by a population of neurons. Little is known about the interactions of the neurons during this perceptual decision making process. Previous work has characterized the temporal synchronies between the spikes of pairs of neurons in SC of non-primate mammalians and birds while they were not actively engaged in a task. Interlaminar synchronous spontaneous depolarizations have been observed in slices of rat SC where the signal is transmitted from the deeper layers to superficial ones (Saito and Isa, 2005). Significant synchronizations have been reported at 50% or more of recordings that were less than 1 mm apart in SC of awake cats observing coherent motions, but not incoherent ones (Brecht et al., 2001; Pauluis et al., 2001) and in 29% of the neuronal pairs from anesthetized cats (Brecht et al., 1999). Groups of cells separated by less than 3 mm in superficial and deep layers of avian tectum have also been reported to show strong synchronizations (Neuenschwander et al., 1996). Here, we examine the interactions of neurons within or between different populations of the primate SC which respond to different stimuli, while the subject is engaged in a decision-making task.

Two different aspects of interactions among neurons, which allow for them to act together, are of particular interest to us. The first aspect is the temporal correlations between spikes of different neurons. Temporal synchronies allow the functional relevance of neurons to be decided dynamically in the task by determining which functional network they belong to at a time. They also facilitate generating a response in downstream neurons, for example, if they are summed supra-linearly (Singer, 1993; Singer and Gray, 1995; Jermakowicz and Casagrande, 2007). Spike Synchrony can also serve as an aspect of the neural
code. For instance, the presence of temporal correlations in SC can impact the decoding mechanisms used in determination of saccade metrics (Brecht et al., 2004b). The second aspect is the correlations in the spike rates of different neurons. Correlations in the average spike rates of neurons over several trials can limit their coding capacity as a population, while correlations in the variability of the spikes rates from one trial to another can either enhance or limit that capacity. Briefly, if the correlations in variability of activity rates of neurons change from one stimulus to another, they can be used to carry information about the stimuli as well (Pola et al., 2003; Averbeck et al., 2006). Many empirical studies have found evidence for the contribution of correlated variability to the capacity of the neuronal ensemble in discriminating the stimuli (Averbeck and Lee, 2003; Golledge et al., 2003; Rolls et al., 2004; Pillow et al., 2008; Meytlis et al., 2012), although many of them found that this contribution is small (<10%).

We investigate the structure of correlations in spike rates and timings during the visual search task, and examine how they dynamically change with the task demands. We explore how the correlations in trial to trial variability of rate of activities of pairs of neurons, as well as their temporal synchronies, can be modulated by different stimuli, and how this modulation changes dynamically from one behavioral epoch of the task to another. Particularly we examine whether the interactions among the neurons increase from chance levels during the visual processing epoch, the epoch where the saccade target is selected, or the epoch where the saccade is executed. We examine this over two groups of neural pairs, those that shared their Response Fields (RFs) and those whose RFs were opposite of each other in the visual field, to gain an insight on how these interactions change as a result of decision-making among neurons that are collaborating towards selection of a target, compared to neurons that are competing against each other for that purpose (Cohen et al., 2010). Our hypothesis was that if the neurons in SC cooperate or compete with each other based on whether they are responding to the same or different stimuli, then we should expect that the interactions between neurons show different patterns between pairs of these two groups. Moreover, if neural interactions are important for the process of decision making in SC, we would expect
to see stronger correlations during epochs that are more relevant for the decision, than those which are more concerned with the sensory or motor processing.

2.3 Methods

2.3.1 Animal Preparation

Three female monkeys (*Macaca mullatta* 4-7 kg, 9-12 years old) were trained and tested according to the protocols developed based on guidelines by Canadian Council on Animal Care (CCAC) and approved by Queen’s University animal care Committee. Before the training and testing started, during a one-time surgical operation on each animal, scleral search coils were placed into each eye subjunctively and a dental acrylic implant was anchored into the animal’s skull. The implant also included a plastic head-holding device, which was used to fix the animal’s head during the experiments. A plastic recording cylinder was placed in the implant centered on the midline with its top tilted 40 degrees towards posterior (Shen and Paré, 2007). The details of these procedures are explained elsewhere (Shen and Paré, 2006).

2.3.2 Behavioral task

During each recording session, monkeys were seated in a primate chair with their eyes at a distance of 57 cm from the screen. The stimuli were generated by a display program using MATLAB and were presented on a 37in computer monitor (Mitsubishi XC-3730C Megaview Pro 37, 60-Hz noninterlaced, 800 × 600 or 1,024 × 768 resolution, 16- or 32-bit color depth).

The subjects were presented with an array of objects, one of which was a designated target. A saccade was required to be made to the target. The target was defined as the only object that is different from all other objects in the array by means of one feature (color). Since the SC neurons are mostly reported not to be feature selective, the color for the targets and distracters were changed randomly on different trials to account for the response being driven by the difference in the colors, rather than being specific to a particular color.
Each trial began with the appearance of a stimulus in the center of the screen, which the subject was required to look at within 1,000 ms of its appearance and foveate it for 500–800 ms. Positions of the stimuli were equidistant from the fixation stimulus and each other. The total number of distracters was kept constant at 7. The subjects had to foveate the target within 500ms after presentation of the stimuli and remain so for about 200 ms (Shen and Paré, 2006).

Throughout this document the terms “target trials” and “distracter trials” would refer to trials where the target or distracters have appeared in the response field of the neuron being recorded, correspondingly.

2.3.3 Electrophysiology

Neurons extracellular potential was recorded from the intermediate layers of superior colliculus (approximately 1-3 mm deep in SC) using Tungsten microelectrodes (1-2mOhms at 1 kHz) which were inserted using guide tubes placed in a grid system in the recording cylinder. Neurons from opposite colliculi were recorded simultaneously by inserting two guide tubes. Neighboring neurons were recorded simultaneously, either using two electrodes with different diameters in the same guide tube (number of pairs: 21), or using the same electrode (number of pairs: 23).

The recorded signal was amplified and low-pass and high-pass filtered using the Multichannel Acquisition Processor of the Plexon Neurotechnology Research System (Plexon Inc.) Plexon Offline Sorter was used to isolate the waveforms into distinct units based on the principal components of the waveform shapes, using characteristics such as the height of the peaks and depth of the valleys. The probability of the waveforms coming from the two different units being marked as belonging to the same units was held at 0.05, or less (Multi-variate ANOVA, conducted by the Offline Sorter software, Plexon Inc). We further visually inspected the waveforms in time, on a 1-10 ms scale, to ensure the quality of the segregation of the waveforms, based on the shapes of the waveforms and their distances in a multi-dimensional space.

2.3.4 Data analysis
The response fields of neurons were determined during a delayed-saccade task (Shen and Paré, 2007). Only visuomovement neurons were considered for further analysis. They showed visual activity that was not specific to the type of the stimulus in their receptive field within 100 ms of the stimulus presentation in their receptive field.

Correct trials were considered as those where fixation was maintained until a signal cued the subject to make a saccade, after which a single saccade was made to a target and maintained there for at least 200 ms. For pairs with shared Response Fields (RFs), we considered the trials during which the target was in the receptive field, as “target trials”. From the remaining trials, we picked the “distracter trials” as those in which the target had appeared in locations that were at least 135 degrees away from the screen location corresponding to neuron’s receptive field (See Figure 2-1). For pairs from the opposite hemispheres, the target trials for one cell constitute the distracter trials with the target being the furthest from the RF for the other cell. Therefore, the distracters trials were considered as the trials that were not target trials for either or the neurons in the pair. This could include trials were the target was away from the RFs of both cells less than 90 degrees, depending on the size of RFs (See Figure 2-2). We included only the pairs that had at least 10 trials of each type, with reaction times (RTs) that were in an overlapping range between the two trial types. That is, we sorted the correct trials of each type based on their reaction time, and selected the larger value between the lower bound of the ranges of the RTs for both trial types, and the smaller value between the upper bounds of the two ranges. Some cells were recorded in small ensembles, so each individual cell might have been used in more than one pair.

Rasters of neural responses were transformed into continuous spike density functions (SDFs) by convolving spike trains with a Gaussian kernel when analyzing the saccade related activity, or a post-synaptic potential function with a combination of a 1-ms time constant for growth and a 20-ms time constant for decay, for analysis of visual response. The SDFs were aligned on either the time of onset of stimulus presentation or the onset of the saccade.
Figure 2-1: Example of rasterplots for a neuron that was included in the analysis. Each black dot represents a spike. The pink vertical line indicates the onset of the saccade. The red circles indicate the time of onset of stimuli relative to the saccade onset for each trial. The pink curve shows the average SDF over all trials in each panel. The schematic graph at the center depicts what we considered the target (top square) and distracter trials (3 bottom squares) for each neuron. The target is shown as a dark circle. The pink area indicated the RF of the cell. In the three examples of distracter trials on the bottom, the target is at the three furthest locations from the RF.
Figure 2-2: A schematic depiction of target and distracter trials for pairs with opposite RFs. The pink shades depict response fields of one of the neuron in the pair. The black circle depicts the target.

**Target trials**

![Target trials diagram]

**Distracter trials**

![Distracter trials diagram]
The saccade activity was defined as the peak of SDF over within ±25 ms from the onset of saccade. The baseline was defined as the average of SDF over a 100 ms window before the onset of stimuli. The visual activity was initially defined as the average of SDF over a 100ms window after the onset of stimuli, for comparison with previous work (Shen et al., 2011a). For the rest of analysis, the 25 ms epoch after the onset of visual response was used. The time of onset of visual response was determined by first creating a postsynaptic potential (PSP) spike density function over all the trials visual responses, and then finding the time when the SDF became larger than the average baseline by 5 standard deviations (the baseline was set to 5 Hz, if it was equal to 0) and stayed so for at least 10 ms. The visuo-Movement Index (VMI) was calculated as the difference between the visual-related activity and movement-related activity for each cell, divided by the sum of those values.

For each neuron, a Receiver Operating Characteristics (ROC) analysis was implemented on the two sets of target and distracter trials with overlapping reaction time ranges. Pairs in which both cells showed a consistent gradual increase in their area under the curve value, in time, moving from target presentation to saccade generation, were selected. Discrimination magnitude (DM) was defined as the upper limit of the area under the ROC curve distinguishing between the stimulus conditions on stimulus aligned responses. Discrimination time was defined as the time when the DM reaches a 0.75 level for each cell. To estimate the DT for shorter and longer reaction times separately, we used the median of the reaction times on the trial set with smaller number of trials to divide its reaction times in two groups of short and long ones. Then from the reaction times from the other set, we found matching trials whose reaction times were in ranges overlapping with each group. We then calculated the DTs for each group of short and long trials separately.

For the pairs which had different DTs, the median of the two was used. Similarly, for the pairs which had different VMIs, the median of the two was used as well.

**Correlations in spike rates averages and variability**
The activities from these selected neuronal pairs were then used to characterize the structure of correlations in the dataset. The correlation coefficients were determined for signal correlations (correlation in average responses to each stimulus), and noise correlations (correlations in variability of responses around those averages).

The Pearson correlation coefficient is obtained by

\[
    r = \frac{\sum_{i=1}^{n}(x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_{i=1}^{n}(x_i - \bar{x})^2 \sum_{i=1}^{n}(y_i - \bar{y})^2}}
\]

where \( n \) is the number of data points, and bars indicated averages over the sample.

Implementing this for our purpose would mean taking \( n \) as the number of stimulus types for signal correlations, or the number of trials for variability correlations, taking \( x \) as responses of one neuron in the pair, and \( y \) as the response of the other.

For signal correlations, one needs to insert average responses for each stimulus type for \( x_i \) and \( y_i \), for each \( i \). This would give us:

\[
    \text{Signal Correlation}_{12} = \frac{\langle (m_{1s} - \langle m_{1s} \rangle_s)(m_{2s} - \langle m_{2s} \rangle_s) \rangle_s}{\sqrt{\langle (m_{1s} - \langle m_{1s} \rangle_s)^2 \rangle_s \langle (m_{2s} - \langle m_{2s} \rangle_s)^2 \rangle_s}}
\]

as derived by Averbeck & Lee (2004), for signal correlations between neuron 1 and 2, where \( \langle \rangle \) indicates averaging and \( m_{is} \) indicates the mean response of neuron \( i \) to stimulus \( s \).

For noise correlations, the trial by trial covariability is important, so one needs to insert individual trials and their differences from the averages. Averbeck & Lee (2004) derive such equation for neurons 1 and 2, as

\[
    \text{Variability Correlations}_{12} = \frac{\langle (r_{1sn} r_{2sn})_N - m_{1s} m_{2s} \rangle_s}{\sqrt{\langle (r_{1sn} - m_{1s})^2 \rangle_N \langle (r_{2sn} - m_{2s})^2 \rangle_N}}
\]

where \( r_{ian} \) is the response of neuron \( i \) to stimulus \( s \) for trial \( n \); and \( m_{is} \) is the mean response of neuron \( i \) to stimulus \( s \). Variability correlations are sometimes called noise correlations in the literature, because the trial-by-trial variability in responses of a neuron to the same stimulus is considered to be noise. However,
since these correlations can sometimes be informative about the stimulus type, we use the less ambiguous nomenclature “Variability correlations”.

**Temporal correlations**

Crosscorrelograms are calculated to measure spike synchrony or the temporal correlations of two neurons by counting the number of times that two neurons spike with a specified lag time between their spikes, as follows:

\[
CCG_{12}(\tau) = \frac{1}{N} \sum_{n=1}^{N} \sum_{t=1}^{T} r_{1}^{n}(t)r_{2}^{n}(t + \tau)
\]

where \(CCG_{12}(\tau)\) is the cross-correlation between neurons 1 and 2 and the time lag \(\tau\), \(N\) indicates number of trails, \(T\) indicates the number of time bins in each trial, and \(r_{i}^{n}(t)\) indicates the response of neuron \(i\) at trial \(n\) at time bin \(t\), which can be either 1 or 0, if the neuron has spiked at that time bin on that trial or not, respectively (Brody, 1999).

A shift-predictor was calculated as follows (Aertsen et al., 1989), and was subtracted from the CCG, to account for the component of CCG caused by increases in responses of neuron due to the stimulus.

\[
ShP_{12}(\tau) = \sum_{t=1}^{T} PSTH_{1}(t)PSTH_{2}(t + \tau)
\]

using the following:

\[
PSTH_{i}(t) = \frac{1}{N} \sum_{n=1}^{N} r_{i}^{n}(t)
\]

where \(PSTH_{i}(t)\) is the value of Post-stimulus Time histogram for neuron \(i\) at time bin \(t\), \(N\) is the number of trials, \(r_{i}^{n}(t)\) is the response of neuron \(i\) on trial \(n\) at time bin \(t\), which can be either 0 or 1, depending on whether the neuron has had a spike or not (Brody, 1999). It is an estimate of the average firing rate of an individual cell as a function of time over many trials, and it has two components. One is related to the
firing rate of the cell in general, and produces a relatively constant rate over all time bins. The other
reflects the changes in the firing rate over specific time intervals, for example as a result of the
modulation of the firing rate by responding to a stimulus or encoding for a movement (Perkel et al.,
1967). $ShP_{12}(\tau)$ is the value of shift-predictor at time lag $\tau$ between the neurons 1 and 2, and $T$ is the
number of time bins in the trial. It corrects for changes in the CCG shape that are a result of correlated
changes in firing rates of the two cells, for example, as a result of co-modulation by a stimulus that both
cells respond to, while leaving unaffected the changes in CCG that are a result of effects of the stimulus
on the functional connectivity of the two cells (Perkel et al., 1967). The shift predictor for each stimulus
condition and epoch was made using the activity rates in the corresponding trials and time windows. The
chance levels were estimated by assuming a Poisson process for the firing rates and by taking 2 standard
development away from the mean, as obtained from the PSTHs.

The Joint Post-Stimulus Time Histograms (JPSTHs) were calculated as

$$JPSTH_{12}(t_1, t_2) = \langle r_{1n}(t_1) r_{2n}(t_2) \rangle$$

where the $\langle x \rangle$ implies the average of $x$ over different trials (Aertsen et al., 1989; Brody, 1999; Cohen et
al., 2010), to visualize the cross-correlations along time, relative to the task events. The shift-predictor
was calculated as the cross multiplication of the two cells’ PSTH vectors and the resulting matrix was
subtracted from the JPSTH matrix. To normalize, the result was divided by the result of cross
multiplication of standard deviations of the PSTH function of the cells.

Coincidence Histograms were formed by averaging the JPSTH matrix values for each time point in the
trial on the anti-diagonal and its 10 surrounding diagonals on each side (corresponding to lags -10 to 10),
in order to highlight the synchrony of spikes over the shortest lags, along time with regard to task events
(Aertsen et al., 1989; Brody, 1999; Cohen et al., 2010).

2.4 Results

2.4.1 Description of Dataset
We report the results from 44 pairs in the same hemisphere, and 15 pairs from the opposite hemispheres. Among the pairs recorded from the same hemisphere, 23 were recorded on the same electrode.

The fixation period activity of the 63 individual cells in these 59 pairs averaged 6 ± 9 Hz (range: 0-38 Hz). The average of their visual activity was 36 ± 24 Hz (range: 4-110 Hz) and their saccadic activity averaged 217 ± 109 Hz (range: 74-447 Hz) for target trials in the search task. The saccadic activity of the cells during the search task was not significantly different from their saccadic activity during the delayed-saccade tasks (paired t-test, p=0.23). Following Shen et al. (2011) discrimination magnitude (DM) was defined as the upper limit of the area under the ROC curve distinguishing between the stimulus conditions on stimulus aligned responses, and averaged 0.96 ± 0.04 (range: 0.83-1). Discrimination time was defined as the time when the DM reaches a 0.75 level and averaged at 131 ± 12 ms (range: 111-161) after the onset of stimulus and -49 ± 21 ms (range: -85 to -11) before saccade onset time. A Visual-Movement index was defined as the difference between the mean discharge rate over the first 100 ms following stimulus presentation and the peak discharge rate within 25 ms of saccade onset divided by the sum of the two, and averaged -0.70 ± 18 (range: -18 to -98). All cells showed visual activity to any stimulus (target or distracter) that appeared in their receptive field, but their saccade activity was always greater. These results are summarized in Figure 2-3. The median DTs (stimulus-aligned) averaged 130 ± 9 ms (range: 111-152) for neighboring pairs and 136 ± 9 (range: 121-157) for the pairs with opposite RFs. The differences between the DTs in each pair averaged 12 ± 9 ms (range: 1-34) for neighboring pairs and 19 ± 11 (range: 5-48).

The average of peak saccadic activities, discrimination times, and discrimination magnitudes for all the selected cells were compared to the corresponding average values from the former dataset recorded from this lab (Shen et al., 2011), to ensure comparability. None of these values were significantly different from previously reported results from this other dataset (one-sample t-test, p=0.8, p=0.07 and p=0.07 respectively ).
Figure 2-3: Two indicators of each neuron’s ability to discriminate target, discrimination magnitude and discrimination time in ms, calculated on neural activities aligned on stimulus onset (first two columns on the left) or saccade (right column) as a function of neuron’s visual response (top row), maximum saccade related activity (middle row), and visuomovement index (bottom row).
2.4.2 Correlations in Average and Variability of Response Rates

The tuning curves of two sample pairs are shown in Figure2-4 (A and B). For the pairs which share their RFs (Figure2-4A), the tuning curves show a positive correlation (r= 0.99). Their average responses to different stimuli decrease or increase together, with a reasonably similar pattern. For the pair from opposite hemispheres (Figure2-4B), the tuning curves have a weaker negative correlation (r= -0.46). The average of responses for the stimulus that produces the maximum average response in one neuron is at its minimum value in the other neuron. Figure2-4C and D, show the variability correlations among two pairs with shared and opposite RFs respectively. The responses to each individual trial are standardized by subtracting the average responses for each stimulus type and dividing by the standard deviation, and are then plotted for each neuron in a pair, against the responses of the other neuron in that pair.

Correlations in each pair’s activities were first calculated over all eight different conditions, using a 100 ms time window before the onset of saccade. We selected this length of window, because smaller windows can underestimate the correlations (Averbeck and Lee, 2004; Cohen and Kohn, 2011a). However, the shortest reaction times that we included in our analysis were only slightly larger than 100 ms (112 ms), limiting the maximum length of the window that we could use. To calculate the correlations in the tuning of neurons to the spatial location of target (Signal correlations), the average of activities for each condition was taken into consideration, and the correlation coefficient was calculated. The average signal correlation for the 44 neighboring pairs was 0.90 ± 0.14 (range: 0.41-0.99) and statistically significant from 0 (t-test, p<0.05). All neighboring pairs had positive signal correlation as expected. For the 15 pairs from the opposite hemispheres, the average Signal correlation calculated for eight different conditions, was -0.36 ± 0.18 (range: -0.68 to 0.08) and statistically significant from 0 (t-test, p<0.05). All pairs but one had negative signal correlations. The distribution of these values is shown as the abscissas in Figure2-4E.

The average of responses to each stimulus does not tell us about the outcome of each individual trial. The variability in individual responses to each stimulus is an important factor in predictability of the outcome.
Figure 2-4: A, B: Tuning curves of a pair of neurons which share their receptive fields (A), and a pair which do not (B). C, D: Correlations between the responses of two neuronal sample pairs on individual trials. E: Correlated variability for each trial group, as a function of signal correlations for each pair (therefore each pair which shares their RF is represented by two data points, and each opposite pair is represented by three). Signal correlations are calculated over the whole length of tuning curve, that is, with 8 positions. “Tar” and “Dis” stand for target and distracter trials, respectively. “Opp” stands for pairs whose RFs are opposite of each other on the screen. The large circles and the crosses inside them indicate the averages for each group and their standard deviations for the signal and variability correlations.
based on the neural response. The correlations between neurons in variability of their responses to one stimulus can impact how this variability may or may not be canceled out at the population level. These correlations can be illustrated by looking at all the responses from a pair of neuron to the same stimulus, on different trials.

The correlation in variability of the responses changed from one stimulus condition to another. For the neighboring pairs the correlated variability was calculated for two stimulus conditions: when the target is in the shared RFs of pairs (see Figure 2-1, top schematic panel), and when the distracter is in their RFs (see Figure 2-1, 3 bottom schematic panels). The variability correlations for target trials over this 100 ms window averaged on 0.02 ± 0.32 (range: -0.62 to 0.74) or the 44 pairs which shared their RF, and were significantly different (paired t-test, p<0.05) from those on trials where the distracters were in the shared RF, which averaged at 0.26 ± 0.22 (range: -0.40 to 0.73). For the 15 pairs whose RFs were opposite of each other the variability correlations on trials where the target was at least in one of the RFs (see Figure 2-2, top) averaged -0.01 ± 0.22 (range: -0.24 to 0.42, n=30) and were not significantly different (unpaired t-test, p=0.8) from trials where a distracter was in both RFs (Figure 2-2, bottom), averaged at 0.00 ± 0.12 (range: -0.18 to 0.24). These results are summarized in Figure2-4E.

The changes in correlations from one task epoch to another can tell us about the role of interactions among the neurons in the processes underlying perceptual or executive decision-making in SC. To investigate the changes in variability correlations of each pair as a result of behaviorally relevant events as the task progresses in time, we selected four 25ms windows and measured the variability correlations for target or distracter trials over these windows for each pair. The windows are as follows: 25ms after the onset of visual response, 25ms before the discrimination time (obtained with responses aligned on stimulus, median DT used for pairs with different DTs), 25ms after the discrimination time, and 25ms before saccade onset.
For the neighboring pairs, a two-way ANOVA showed that changes in variability correlations were significant from one behavioral epoch to another (p<0.05), and that impact of the stimulus conditions on variability correlations regardless of the behavioral epoch and the interaction of the two factors were also significant (p<0.05 for both).

Figure 2-5 summarizes these results. Over the first three epochs, the variability correlations between the two stimulus conditions are not significantly different from each other (two-tailed paired t-tests, p= 0.59, p= 0.50, and p=0.19 for each epoch correspondingly). The averages for target trials over the 44 pairs, for the three epochs were 0.07 ± 0.21, 0.19 ± 0.25, and 0.13 ± 0.25 correspondingly. Averages for distracter trials for the three epochs were 0.09 ± 0.18, 0.16 ± 0.19, and 0.19 ± 0.20. However, they are significantly different over the last epoch, where the target trials had an average of -0.03 ± 0.26 for their variability correlations over the 44 pairs, and distracter trials had an average of 0.11 ± 0.17 (two-tailed t-test, p<0.05). Therefore, a modulation of variability correlations that may contribute to discrimination of the stimuli is not observed during the stimulus epoch where the variability correlations are positive (significantly different from 0, one-sample t-test, p<0.05) on average regardless of the stimulus, but it is present during the saccade epoch when the variability correlations become close to 0 for target trials on average (one-sample t-test, not significantly different from 0, p= 0.19), but not for distracters (one-sample t-test, significantly different from 0, p< 0.05).

Figure 2-6 shows how the variability correlations change from one epoch to another for each neighboring pair, for each stimulus condition. The saccade epoch shows the lowest for target trials but not for distractors, and the discrimination epochs show the highest variability correlations. The DT for this analysis was estimated using neural activity aligned on stimulus onset, and because the DT is shown to be more variable with stimulus onset time than with saccade onset time (Ratcliff et al., 2003; Shen and Paré, 2011). Similar results were found for our dataset as well. When aligned on saccade onset, DTs showed less variability than when aligned on stimulus onset and this difference was significantly different.
Figure 2-5: Changes in variability correlation from target to distracter trials, for neighboring pairs, for two stimulus conditions, over four behaviorally relevant epochs: 25 ms after the onset of visual response, 25 ms before the time of target discrimination (DT), 25 ms after the time of target discrimination, and 25 ms before saccade onset. Each blue line represents a pair. Bars and the errors represent the average and standard error of mean over the population. Target trials are those when the target is in the shared RF, and distracter trials are those when a distracter is in the shared RF. The lines and stars indicate different significance levels (n.s for not significant, * for p<= 0.05, ** for p<= 0.01, and *** for p<=0.001). The markers on top of the line indicate whether the difference between the two groups is significant. The markers at the bottom end of each line indicate whether that group is significantly different from 0.
Figure 2-6: Changes in variability correlations in neighboring pairs from one behavioral epoch to another for the four specified epochs, for each of the stimulus condition. Bars and the errors represent the average and standard error of mean (SEM) over the population.
(average slopes: 0.27 ± 0.60 for saccade aligned, and 0.72 ± 0.84 for stimulus aligned; two-sample t-test, p<0.05). We wondered if repeating the analysis with DTs estimated with neural responses aligned on saccade onset would eliminate some of the response variability in DT period due to the misalignment of trials in time, and will therefore create a better estimate of the variability correlations. The variability correlations in the 25 ms window before DT (estimated using saccade-aligned responses) were 0.12 ± 0.21 for target trials and 0.17 ± 0.20 for distracter trials, and they were both significantly different from 0 (one-sampled t-test, p<0.05). This is consistent with the results obtained from the estimates of DT based on stimulus onset. However, for the 25-ms window after DT the results were more similar to what was obtained for saccade epoch. The variability correlations in this window were 0.03 ± 0.27 for target trials and they were not significantly different from 0 (one-sampled t-test, p=0.5). They were 0.18 ± 0.16 for distracter trials, and they were significantly different from 0 (t-test, p<0.05).

For the pairs from opposite hemispheres, the target trials are considered as those when the target falls into the RF of one of the two cells in the pair. The distracter trials are those when the target doesn’t fall into either RF. A two-way ANOVA (for four different time epochs and two different trial types) showed that the effects of both time and trial types as well as their interaction are significant for this group of pairs as well (p<0.05).

Figure 2-8 summarizes these results. The difference between variability correlations between the two stimulus conditions failed to reach significance over the first epoch (target trials: -0.03 ± 0.11; distracter trials: 0.02 ± 0.07; paired t-test, p=0.06). However, they were significantly different from each other over the last three epochs (two-tailed t-test, p<0.05 for all three epochs), where the averages for target trials for the three epochs were -0.18 ± 13, -0.37 ± 0.12, and -0.54 ± 0.15 correspondingly, and 0.01 ± 0.16, 0.0 ± 0.9, and -0.04 ± 0.12 for distracter trials. For all epochs, the variability correlations for distracter trials failed to reach significance (one-sample t-test, p=0.12, p=0.73, p=0.82, and p=0.14). For target trials, the
Figure 2-7: Changes in DTs for slow and fast reaction times. Top: DTs for each cell as obtained by aligning the trials on saccade onset. For each group of short and long reaction times, a DT is obtained separately, and its time before saccade onset is plotted against the average reaction time in that group. Bottom: Same as the top, except that the alignments are on stimulus onset.
Figure 2-8: Changes in variability correlation from target to distracter trials, for opposite pairs, for two stimulus conditions, over four behaviorally relevant epochs: 25 ms after the onset of visual response, 25 ms before the time of target discrimination (DT), 25 ms after the time of target discrimination, and 25 ms before saccade onset. Each blue line represents a pair. Bars and the errors represent the average and standard error of mean (SEM) over the population. Target trials are those when the target is in one of the RFs, and distracter trials are those when the target is in none of the RFs. The lines and stars indicate different significance levels (n.s for not significant, * for p<= 0.05, ** for p<= 0.01, and *** for p<=0.001). The markers on top of the line indicate whether the difference between the two groups is significant. The markers at the bottom end of each line indicate whether that group is significantly different from 0.
visual epoch did not have variability correlations that were significantly different from 0 (one-sample t-test, p=0.30), but the final three epochs did (one-sample t-test, p<0.05).

Figure 2-11 highlights the changes in values of variability correlations from one epoch to another for each pair with opposite RFs, for each stimulus condition. It shows a consistent decrease in variability correlations in trials where the target is in one of the RFs, from visual epoch towards saccade epoch. For trials where a distracter is in both RFs, the variability correlations do not significantly change across the behavioral epochs.

### 2.4.3 Changes in Correlations in Different Groups of Cells

All cells in our dataset showed both visual and movement related activity and therefore can be considered as potential units that integrate a sensory variable into a decision variable to guide a movement. We tested whether the strength of variability correlations changed as a function of the proportion of strength of sensory-related activity to that of movement related activity. For each pair, we measured the levels of variability correlations as a function of the median of VMIs of the cells in each pair. A negative correlation was observed between the VMI and the variability correlations for pairs with shared RFs, in all four behavioral epochs for target trials, indicating that cells with stronger movement-related activity showed stronger positive correlations. These correlations became significant over the last three behavioral epochs (t-statistics, p=0.06 for visual epoch, p<0.05 for the three others). For the pairs with opposite RFs, positive correlations were observed between the variability correlations and the VMIs for target trials, indicating that neurons with stronger movement-related responses, showed stronger negative variability correlations. Only the correlation over the target trials for saccade epoch reached significance for these pairs (t-statistic, p<0.05 for saccade epoch; P=0.2, p=0.6, and p=0.4 for the three other epochs). The correlations over the distracter trials did not reach significance for any of the behavioral epochs or the group of pairs (p>0.15 for all). For neighboring pairs, we found that both the temporal and variability correlations were at their highest around the pair’s median discrimination time. We were interested to see
if the changes in correlations around this time could be linked to changes in reaction times. We therefore repeated the above analysis.

Figure 2-9 shows these results.

The observation that cells with stronger movement-related activities show stronger positive variability correlations for pairs from the same populations, and stronger negative variability correlations for the pairs from different populations indicates that the variability correlations can have a bigger impact on the process of target selection as the goal for a future movement, than on processing the sensory aspect of the stimuli. This is in line with the observation that these variability correlations were not significantly different from each other for different stimulus conditions and generally small during the visual epoch.

**2.4.4 Changes in Correlations in Trials with Different Reaction Times**

We asked whether the variability correlations in each condition would change with the behavioral outcome. We looked at the changes in the variability correlations with reaction times to answer this question. We divided the trials for each pair into two groups of short and long trials for each stimulus condition. Then, we investigated whether the variability correlations were different over the slow and fast RT conditions, for each stimulus condition.

For pairs with shared RFs, the variability correlations over a 25 ms window before saccade averaged -0.05 ± 0.34 and -0.11 ± 0.30 for fast and slow RT target trials, respectively. They averaged at 0.10 ± 0.24 and 0.09 ± 0.24 for fast and slow RT distracter trials, respectively. None of these differences reached significance (two samples t-tests, p=0.40 and p=0.90). For the pairs with opposite RFs, the variability correlations over a 25 ms window before saccade averaged -0.48 ± 0.21 and -0.56 ± 0.15 for fast and slow RT target trials, respectively, and the difference between the two was not significantly different (two-sampled t-test, p=0.25). They averaged at -0.06 ± 0.22 and -0.04 ± 0.11 for fast and slow RT distracter trials, respectively, and their difference did not reach significance as well (two-sampled t-test, p=0.75).
For neighboring pairs, we found that both the temporal and variability correlations were at their highest around the pair’s median discrimination time. We were interested to see if the changes in correlations around this time could be linked to changes in reaction times. We therefore repeated the above analysis.

**Figure 2-9:** Changes in magnitude of variability correlations as a function of the median of VMIs of the individual cells in each pair. Upper row shows the pairs with shared RFs. Bottom row shows the pairs with opposite RFs. Correlation coefficient for each trial type is indicated in the same color. A star at the top of the Pearson correlation coefficient indicates significance level of $p<0.05$ for difference from 0.
for an epoch of 50 ms around median DT times for each pair, after re-estimating the DTs for short and long RT trials (aligned on saccade).

Figure 2-10 shows the results of this analysis. The variability correlations over this 50 ms window were not significantly different between the short and long RTs, for target trials for either of the pair groups (pairs with shared RFs: 0.05 ± 0.32 for fast RTs, 0.08 ± 0.30 for slow RTs, two-sample t-test: p=0.51; pairs with opposite RFs: -0.26 ± 0.15 for fast RTs, -0.33 ± 0.10 for slow trials, two-sample t-test: p=0.10). There was a significant change in variability correlations between the short and long RT distracter trials for pairs with shared RFs, with the correlations being stronger for the slower reaction times (0.12 ± 0.30 for fast RT trials, 0.29 ± 0.33 for slow RTs, two-sample t-test: p=0.01). But this was not observed in pairs with opposite RFs (-0.06 ± 0.27 for fast RTs, 0.00 ± 0.17 for slow RTs, two-sample t-test: p=0.43).

Generally, we found that while the variability correlations are not significantly different from each other in groups of trials with different reaction times, they are slightly smaller in the fast trials. Therefore, it can be suggested that if the variability correlations have any impact on improving the performance of the subjects, that impact should happen through a decorrelation process.
Figure 2-10: Comparison of rate variability and temporal correlations between the slow and fast trials, for each stimulus condition and group of pairs. (***) indicates significant difference with p<0.05. Lack of stars indicates lack of significant difference.
2.4.5 Synchrony and Correlations in Spike Timing

Variability correlations describe the levels of correlations in spike counts of the trial-by-trial responses of two neurons. We are also interested to know whether there are any correlations in timings of the spikes of one neuron in reference to the timings of the spike of the other, to infer about the role of spike synchrony in the process of decision-making in SC as well as any potential causal interactions among local populations in SC. In order to visualize the changes in synchrony in the activity of a pair with regard to time of the behavioral events, I created JPSTH plots that captured from 50 ms before onset of stimulus to a time point that included the time of onset of saccade in 90% of the trials. Figure 2-12 and Figure 2-13 show the JPSTH diagrams, along with PSTCH and CCGs for target and distracter trials during this time window for samples from neighboring pairs, and pairs with opposite RFs, respectively. The correlations in timing of the spikes regardless of when in the behavioral task they happen are measured as crosscorrelograms (CCGs). For each pair with shared or opposite RFs, I calculated the CCGs over the same four different time epochs defined in previous section, for two stimulus conditions: trials where the target was in the shared RF of the neighboring pairs or at least one RF of the opposite pairs, and trials were the target was in the RF of neither of the cells.

Figure 2-14 shows an example of a pair with shared their RF that the synchronous activity decreases for the target trials during the saccade epoch. Figure 2-15 shows an example of CCGs for a sample pair with opposite RFs. The difference between CCGs of target trials during the saccadic epoch and the rest of epochs and stimulus conditions in this pair is representative of the rest of the population.

To summarize the results of the CCGs we assessed whether the values of cross-correlation at each time lag of CCGs are significantly different from the value they would have by chance, and if so, by how much. I used the sum of the area under the 5 central lags in the CCG, to compare the ratios of the cross-correlation values to the 95% confidence intervals of the chance level. Figure 2-16 and Figure 2-17 show the distribution of the ratios for individual pairs for two stimulus conditions for each group of pairs and epoch.
Figure 2-11: Changes in variability correlations in opposite pairs from one behavioral epoch to another for the four specified epochs, for each of the stimulus condition. Bars and the errors represent the average and standard error of mean (SEM) over the population.
Figure 2-12: JPSTH diagram for a sample pair along with the corresponding PSTH from each cell in the pair. The coincidence histogram (B) shows the average of JPSTH values at each time point on the anti-diagonal (corresponding to lag 0) and the next 10 diagonals on each side of it (-10 to +10 ms lag times). The CCG (C) is different from what show in Figure 8, because it is measured over a different time window. The blue lines around the CCG indicate the chance levels. The vertical and horizontal black lines on the JPSTH and the vertical black line on the Coincidence histogram plot show the discrimination time (stimulus-aligned). The red lines on JPSTH plot show the onset of the stimuli. Three top panels are for trials when a target is in the shared RF, and the three bottom ones are for distracter trials. A boxplot of the reaction times for the correct target and distracter trials is shown at the bottom.
Figure 2-13: Same as previous figure, for a sample of opposite pairs. Target trials are those in which the target is in one of the RFs, and distracter trials are those in which the target is in none of the RFs.
Figure 2-14: CCGs for a sample neighboring pair. Each plot corresponds to a behaviorally relevant epoch: 25 ms after the onset of visual response, 25 ms before the time of target discrimination (DT), 25 ms after the time of target discrimination, and 25 ms before saccade onset. Each lag is 1ms long. Red lines indicate 95% confidence intervals from chance levels. This pair is recorded from two separated electrodes. Target trials are those when the target is in the shared RF, and distracter trials are those when a distracter is in the shared RF.
Figure 2-15: CCGs for a sample pair with opposite RFs. Conventions are the same as Figure 2-12.
For neighboring pairs, these ratios were significantly different from 0 for all behavioral epochs except the saccadic epoch (one-sampled t-test, p=0.7 for target trials at saccadic epoch, p<0.05 for the rest). Neither the stimulus condition nor the behavioral epochs had a significant effect over the ratios of the cross-correlation values to their chance levels (two-way ANOVA, stimulus condition: p=0.17, behavioral epochs: p=0.18, and their interaction: p=0.52). The ratios averaged over the 44 pairs for the target trials were 0.16 ± 0.31, 0.20 ± 0.37, 0.17 ± 0.44, and -0.02 ± 0.40 for the four epochs of after visual response, before DT, after DT, and before saccade, correspondingly. For distracter trials, these averages were 0.16 ± 0.44, 0.24 ± 0.52, 0.20 ± 0.47, and 0.17 ± 0.49, correspondingly.

For the 15 opposite pairs, these ratios were significantly different from 0 for target trials for all behavioral epochs except the visual epoch (one-sampled t-test, p=0.4 in visual epoch, p<0.05 for the three other epochs). They failed to reach significance for distracter trials over all four epochs (one-sampled t-test, p=0.4, p=0.2, p=0.17, and p=0.13 respectively). A two-way ANOVA showed that both stimulus conditions and the behavioral epochs had a significant effect on modulation of the ratios of the sum of cross-correlation values at the 5 central lags to sum of their chance levels for the pairs with opposite RFs (p<0.05, for both variables and their interaction). The averages of these ratios for the target trials were 0.03 ± 0.19, -0.33 ± 0.38, -0.75 ± 0.54, and -1.89 ± 1.43. For distracter trials, these averages were 0.04 ± 0.26, -0.08 ± 0.25, -0.06 ± 0.16, and -0.11 ± 0.27.

These ratios were significantly different between the two groups of pairs for the last three epochs (two-sampled t-test, p<0.05) but not for the visual epoch (two-sampled t-test, p=0.07).

Among the pairs that shared their RF, some were recorded on the same electrode which could hide the spikes that were generated at the same time for one of the neurons in the pair, therefore underestimating the level of synchrony. We tested whether there was a difference in the synchronies for pairs with shared RF which were recorded on the same electrode and those which were recorded on different electrodes. The pairs which were recorded on different electrodes showed higher levels of synchrony on average than
the other group during the saccadic epoch, with their ratios of cross-correlation values to chance-level showing an average of $0.05 \pm 0.38$ for target trials over the saccadic epoch (which was not significantly different from 0, 1-sampled t-test, $p=0.46$), compared to $-0.13 \pm 0.34$ for the same epoch and stimulus condition in pairs which were recorded on the same electrode. This difference was significant (one-tailed t-test, $p<0.05$), indicating that the amount of asynchrony in the saccadic epoch is overestimated in half of our neighboring sample pairs. On the other hand, for the post-DT epoch for target trials and the pre-DT epoch for distracter trials, the level of synchrony was significantly smaller in pairs recorded on the same electrode, than those which were not (one-tailed unpaired t-test, $p<0.05$). This difference underestimated the amount of synchrony for these epochs and stimulus conditions from $0.22 \pm 0.43$ and $0.32 \pm 0.57$ for pairs recorded on different electrodes (both significantly different from 0, 1-sampled t-test, $p<0.05$) to $0.02 \pm 0.20$ and $0.09 \pm 0.28$ for pairs recorded on same electrodes, respectively (neither significantly different from 0, 1-sampled t-test, $p=0.6$ and $p=0.15$, respectively).

All the neighboring pairs showed a significant cross-correlation value on at least one of the 10 central time lags, in at least one of the behavioral epochs during either of stimulus conditions. 33 (75%) of them showed at least one significant cross-correlation value in either one of the discrimination epochs or the saccade epoch for the target trials. Of these 33, 17 were recorded on the same electrode. 38 pairs showed a significant cross-correlation value on at least one of the 5 central time lags, in at least one of the behavioral epochs during either of stimulus conditions. 17 pairs showed at least one significant cross-correlation value in one of the discrimination epochs or the saccade epoch for the target trials. Of these 17, 7 were recorded on the same electrodes. 19 pairs (43%) showed at least two consecutive significant peaks for at least one of the two stimulus conditions, among the 11 central lags, when the CCGs were calculated for the whole length of trial up to the 90th percentile reaction time.
Figure 2-16: Distribution of ratios of the sum of CCG peaks to the sum of their chance 95% confidence interval levels, for the five central lags (-2 to 2, each lag being 1 ms) for neighboring pairs as a function of the stimulus condition. Target trials are those when the target is in the shared RF, and distracter trials are those when a distracter is in the shared RF. Each plot corresponds to one of the 4 behaviorally relevant epochs: 25 ms after the onset of visual response, 25 ms before the time of target discrimination (DT), 25 ms after the time of target discrimination, and 25 ms before saccade onset. Each line represents one pair. The bars represent the ratios of these averages of these sums over the population of 44 pairs.
Figure 2-17: Distribution of ratios of the sum of CCG peaks to the sum of their chance 95% confidence interval levels, for the five central lags (-2 to 2, each lag being 1 ms) for opposite pairs as a function of the stimulus condition. Target trials are those when the target is in one of the RFs, and distracter trials are those when the target is in none of the RFs. Each plot corresponds to one of the 4 behaviorally relevant epochs: 25 ms after the onset of visual response, 25 ms before the time of target discrimination (DT), 25 ms after the time of target discrimination, and 25 ms before saccade onset. Each line represents one pair. The bars represent the ratios of the averages of these sums over the population of 15 pairs.
The middle plots in Figure 2-12 and Figure 2-13, the Coincidence Histogram, provides a summary of the JPSTH diagram at its center along the anti-diagonal. This diagonal of the JPSTH corresponds to the lag 0 in CCG, but is spread over the length of the trial. Large values on this diagonal indicate high levels of synchrony between the two neurons in the pair, at the corresponding times during the trial. The coincidence histogram averages the value of JPSTH at each time point over the 21 central diagonals (corresponding to lags -10 to 10).

We obtained the area under of the coincidence histograms as the sum of the values of the JPSTH for the 20 central lags, over the same four epochs that we used for the analysis of variability correlations (25ms after onset of visual response, 25ms before discrimination time, 25ms after discrimination time, and 25ms before saccade onset) and contrasted them between the stimulus conditions. The results are shown in Figure 2-18 for neighboring pairs and Figure 2-19 for opposite pairs. For neighboring pairs, neither the behavioral epochs, nor stimulus conditions significantly affected the sums of the coincidence histogram values (two-way ANOVA, p=0.54 and p=0.22, respectively). However, their interaction did (p<0.05). The stimulus conditions in none of the four analyzed epochs had a significant effect on the sums of coincidence histograms (two-tailed paired t-test, p=0.8, p=0.18, and p=0.54), except for the pre-DT epoch (two-tailed paired t-test, p<0.05). For pairs with opposite RFs, both the behavioral epochs and stimulus conditions significantly and their interaction affected the sums of the coincidence histogram values (two-way ANOVA, p<0.05). The sums of these values were significantly different across the two stimulus conditions for discrimination and saccadic epoch (an average of 0.00 ± 0.07, -0.27 ± 0.24, -0.56 ± 0.32, and -1.54 ± 1.11 for target trials and 0.05 ± 0.12, -0.3 ± 0.18, 0.00 ± 0.06, and -0.06 ± 0.17 for distracter trials) but not for the visual epoch. Changes over the four behavioral epochs were significant both for the target trials (one-way ANOVA, p<0.05), and distracter trials (one-way ANOVA, p<0.05) for neighboring pairs, but only significant for target trials in pairs with opposite RFs (one-way ANOVA, p<0.05).
Figure 2-18: Comparison of areas under the coincidence histogram from trials when that target is in the shared RF, with those when the distracter is, over the 4 behaviorally relevant time epochs, for pairs with a shared response field. Each line represents one pair. The bars represent the averages and SEMs over the population.
Figure 2-19: Comparison of areas under the coincidence histogram from trials when the target is one of the RFs with those when a distracter is in both RFs, over the 4 behaviorally relevant time epochs, for pairs with opposite response fields. Each line represents one pair. The bars represent the averages and SEMs over the population.
2.5 Discussion

We explored signal, trial-by-trial rate variability, and temporal correlations between neurons in SC during a visual search task. We found that the pairs with shared RFs show strong signal correlations, but the signal correlations for pairs whose RFs are opposite of each other are not as strong. We found that for neighboring pairs, variability correlations and coincidence histograms can show positive values which are significantly different from 0 in all epochs, except the saccadic epoch for target trials. The only modulation by stimulus conditions for these pairs happened for variability correlations in saccade epoch. While for pairs with opposite RFs, both variability and temporal correlations are mostly negative, and they are stimulus-modulated in all epochs except the visual epoch, and that this stimulus-dependent modulation gradually progresses with the behavioral events in the task.

The accuracy of all our analysis in this chapter is dependent on a reliable estimate of correlations. Calculating correlations in short windows can lead to lower correlations (Averbeck and Lee, 2004; Cohen and Kohn, 2011b). We used a window of 100 ms to measure our correlations in spike rates, which is close to the longest that our task design would allow. But we also used smaller windows to be able to track how the correlations magnitude changes along time as the behavioral task progresses. The use of smaller windows can mask some of the correlations that result from slower frequencies of synchrony among the neurons. This should be kept in mind, when interpreting these results. A possible source of overestimations of correlations is to mistakenly categorize the activity of several cells into one unit (Cohen and Kohn, 2011b). We minimized this type of mistakes by carefully taking the shape of spike waveforms into consideration, examining the change of shapes of spike waveforms in time, and monitoring the spike patterns and rates over the whole recording session. The biggest limitation of this work is that here, we measured the correlations between simultaneously recorded pairs of neurons, but not larger populations. It is not clear how generalizable the results from the pairs will be to larger populations. Some studies suggest that the presence of weak pairwise correlations can imply stronger correlations at the network level (Averbeck et al., 2006; Schneidman et al., 2006). Others have suggested that making
inferences about correlations at the population level from observations on pairwise correlations leads to mis-stimation of their impacts (Roudi et al., 2009). For example, making assumptions about the relationship between pairwise variability correlations and tuning curve distances in order to fill in the covariance matrix by interpolation, can mask information-limiting correlations (Moreno-Bote et al., 2014). Lastly, about half of our neighboring samples were recorded on the same electrode which affects the detection of spikes which are exactly synchronized between a pair. We verified that general pattern of our observations is maintained when considering only the pairs that are recorded from separate electrodes. That is, the stimulus condition did not have a significant effect on the level of synchrony in any of the behavioral epochs on this group of neighboring pairs, the highest levels of synchrony were observed during the discrimination epoch, and the pairs de-synchronized during the saccadic epoch.

Previous studies that have explored variability correlations have found different patterns of correlations between different pairs of neurons, depending on their RFs locations, preferred stimulus, and the differences between these between the two cells in a pair, as well as the type of stimulus they were presented with. For example, one study found that FEF pairs with a shared RF recorded from a during a visual search task showed larger variability correlations when the target was in their shared RF, and smaller variability correlations when the target was away from their RF (Cohen et al., 2010). Some studies have reported no significant change in magnitudes of variability correlations from pairs recorded from different columns of barrel cortex of rat (Petersen et al., 2001), as a result of changing the stimulus type (Golledge et al., 2003), or as a result of differences in preferred orientation of individual cells in each pair (Montijn et al., 2014). Others have reported a change in magnitudes of variability correlations as a function of differences between preferred stimuli between the individual cells in each pair in primate medial temporal lobe (MT) (Bair et al., 1996; Cohen and Newsome, 2008), or changes in the behavioral context of the task (Cohen and Newsome, 2008). Similar to our findings here, Ponce-Alvarez, Thiele, Albright, Stoner, & Deco (2013) found that the magnitude of variability correlations in MT is on average smaller for when the preferred stimulus of a pair with shared RF is presented at their RFs.
The dynamic changes in variability correlations as a result of changes in stimulus conditions or task behavioral epochs can have functional implications for the behavioral performance. For example, a reduction in correlated variability in activities of the neurons in area V4 has been associated with attention (Mitchell et al., 2009). Attention has been shown to increase performance by decreasing the correlations in response fluctuations in area V4 four times more than by increasing the response rates (Cohen and Maunsell, 2009). This is in line with our observations that variability correlations for target trials significantly decreased during the saccadic epoch compared to distracter trials, and also the observation that in faster trials, the variability correlations were smaller than in slower trials. On the other hand, attention increases communication among neurons in two different brain areas by increasing the correlations between the two. For example, attention increased the trial-by-trial variability in neural responses which was shared between the primary visual cortex and middle temporal lobe (Ruff and Cohen, 2016). It has also been shown to increase correlations in the spike trains of anterior cingulate and prefrontal cortices, suggesting a mechanism for integration of the relevant information for selection of a target, across different areas (Oemisch et al., 2015).

Correlations in timing and rates of neural responses can have a role in the way that neurons encode stimuli or behavior (Niremberg et al., 2001; Schneidman et al., 2003; Averbeck and Lee, 2004; Latham and Nirenberg, 2005; Josić et al., 2009). If correlations in the variability of response rates vary from one stimulus condition to another, they may carry extra information, in addition to what is carried by the rate modulation of responses in different stimulus conditions (Pola et al., 2003). In our samples, both neighboring and opposite pairs showed a modulation in their levels of correlated variability as a result of having the target in their RF, in a way that was not observed in trials were the distracters were in the RFs of both neurons in the pair, at least during the saccadic epoch.

One of the ways that correlated variability is suggested to impact the discriminability of one stimulus condition from another is how it shapes the distribution of responses to each stimulus condition within the
response space, through its interaction with the correlations in tuning curves of the neurons (Pola et al., 2003; Averbeck et al., 2006; Josić et al., 2009). This could happen, for example, when the direction of the longest axis of distribution of the responses to each stimulus is in the same direction as that of the distribution of averages of responses to each stimulus, which can increase the overlap between the responses from different stimuli. Conversely, if these directions are orthogonal to each other, they can reduce such overlap. In our data, the directions between the spread of these distributions are neither completely parallel (or in line) nor orthogonal. Therefore, it is difficult to predict the shaping effects of correlated variability on the discriminability capacity of our pairs. A break-down of the information content of responses of each pair about the stimuli can determine the type and extent of any shaping effects by correlated variability.

Temporal correlations can also increase the discriminability of a stimulus, because the synchronous activity between two neurons can be used as an additional third channel of information (Meister, 1996; Dan et al., 1998). For example, it’s been shown that the dynamic changes in neural synchronies in premotor cortex can distinguish between two behavioral outcomes, while the responses of individual neurons, whether in terms of spike rates or spike timings, cannot discriminate between those behavioral conditions (Vaadia et al., 1995b; for more discussion, see Friston, 1995; Vaadia et al., 1995a).

Isolated significant cross-correlation values in CCGs were observed in 75% of our neighboring pairs. This pattern is comparable with what has been reported in the past in SC of cats, where significant synchronizations were observed for 70% of the neuronal pairs in anesthetized animals (Pauluis et al., 2001).

The synchrony between the neurons in our neighboring pairs did not increase during the discrimination or saccadic epochs of the target trials as much as it decreased between the neurons in those pairs the RFs of which were located opposite of each other in the visual field. This could have an interesting interpretation with regard to the levels of contribution of collaboration vs. competition among neurons in SC in
selecting the target of a saccade (Cohen et al., 2010). Previously, it has been shown that individual visuomovement neurons in SC have a strong capacity to discriminate between the target and distracters (Shen & Paré, 2007; Shen et al., 2011). Sparse codes are suggested to benefit from synchronizing the responses of the few neurons that participate in them at any given time, in order to strengthen the response magnitude. It is an interesting observation that if there is any sparse coding mechanism at work in SC, it may not be as strongly supported by the synchrony of the neurons which are responding to the same target as much as it is supported by the competition between the neurons which are competing for its selection. The de-synchronization of spike times between pairs whose RFs were opposite of each other in the visual space can indicate the presence of a winner-takes-all mechanism in the selection of target.

On the other hand, the highest levels of synchrony among the neighboring pairs were observed during the discrimination time, and the lowest levels of it were observed during saccadic period. This may highlight a role for the collaborative interactions of neurons in the process of discrimination of the target from distracters, as opposed to the execution of the saccade. It is noteworthy that neither the synchronies, nor the variability correlations in either of the pre- and post-discrimination epochs were stimulus-modulated. This indicates that while the temporal correlations might facilitate the process of discrimination through the coordination of responses of individual neurons, they may not be directly part of the neural code.

How do these interactions arise in SC? Are they the result of local connections, or are they driven from shared input from other areas? Lateral connections have been identified in intermediate layers of SC (Moschovakis et al., 1988; Munoz and Istvan, 1998). Evidence has been found that gap junctions, or gap-like junctions may also exist in SC/tectum (Sinués Porta et al., 1988; Liu et al., 2016). On the other hand, SC receives both excitatory and inhibitory inputs from many other brain areas that are involved in visual processing and saccade target selection, such as FEF (Komatsu and Suzuki, 1985; Sommer and Wurtz, 2001; Inoue et al., 2015), LIP (Paré and Wurtz, 1997; Ferraina et al., 2002), PFC (Everling and Johnston, 2013; Savage et al., 2017), and basal ganglia (Fujiyama, 2009). One can use the shape of the CCGs to
make inferences about the sources of synchrony among neurons. In our sample, the pairs with shared RFs showed mostly flat CCGs with the significant peaks spanning over only a few lags. The peaks did not consistently occur over a specific range of lags, and were therefore, not helpful in locating the source of synchrony. For the pairs with opposite pairs on the other hand, the peaks were wider and more symmetric, although for a few pairs, some asymmetry was observed as well. The symmetry in CCGs generally suggest a shared input as the source of synchrony, whereas the asymmetric CCGs can suggest a direct connection between the two cells (Nowak and Bullier, 2000). Therefore, it can be suggested that the synchrony in SC during a visual search task may be mainly driven from shared input from other areas. If so, to observe the patterns of synchrony in our pairs with opposite RFs, this common input should be excitatory to one cell, and inhibitory to the other. Contralateral projections may be non-existent from cortical areas other than FEF, and even in FEF, they are generally weak (Distel and Fries, 1982). FEF has been found to send both excitatory and inhibitory projections to the neurons on the same side. However, in the contralateral SC, only one of the 36 recorded neurons was modulated by optical stimulation from FEF and the average activity was left unaffected (Inoue et al., 2015). On the other hand, correlations among FEF neurons from opposite hemispheres may compensate for the absence of shared input from the same hemisphere. Such correlations have been observed during a visual search task in FEF neurons with non-overlapping RFs (Cohen et al., 2010). Interestingly, such side-specific projections to both ipsi- and contralateral SC have been observed from brainstem (Wang et al., 2010). If the asynchrony observed in SC pairs from opposite hemispheres is the result of common inputs from the brainstem, it may be appropriate to consider them mainly as the effects of the target selection in SC, rather than a contributing factor to it.

Making inferences about the shape of a CCG knowing the interactions of neurons is a straightforward problem. However, it should be noted that the inverse problem, which we have tried to tackle in here, has no unique solutions, and many different scenarios can be conceived to result in the same CCG general shape (Aertsen et al., 1989; Nowak and Bullier, 2000).
Chapter 3

Insights on Superior Colliculus Populations Encoding the Target of a Saccade

3.1 Abstract
Correlations in average and trial-by-trial variability of activity rates in neural populations impact the amount of information that they carry about the stimuli or behavior. Here, we investigate the impacts of these correlations on the capacity of the visuomovement neurons from intermediate layers of SC to instantiate a decision about the target of a saccade during a visual search task. Previous research has shown that the activity rates in these neurons outperform the behavior of the subject in selection of the saccade target. We examined whether these correlations could have a limiting impact on the growth of information in simultaneously recorded pairs or simulated populations of neurons, which are either collaborating with each other to select a stimulus that falls into their overlapping response field as a target or competing against each other to select different stimuli which fall into their non-overlapping RFs. We found that correlated variability increased the information in our recorded neuronal pairs, regardless of whether these pairs shared their RF or not. However, the impact of correlated variability on the performance of simulated populations using two different decoding schemes was different. Positive values of correlated variability among the cells of simulated larger populations with shared RFs decreased their performance. A similar result was observed for negative values of correlated variability among the cells of simulated larger populations with opposite RFs. This shows that while additional information from correlated variability is available at the level of pairs, the decoders may not be able to extract it.

3.2 Introduction
One of the most important questions facing cognitive neuroscience is how activities of populations of neurons account for specific decisions and actions. The role of superior colliculus in target selection and execution of saccadic eye movements is well established, and therefore it provides a great model to study population coding. Most studies of population coding in SC have focused on decoding the motor
commands of SC using the spike rates of neurons, without considering the impacts of correlations in the variability of activity rates from trial to trial (Kutz et al., 1997; Brecht et al., 2004b; Gandhi and Katnani, 2011; Katnani et al., 2012).

Correlations in the tuning curves of neurons, which we call signal correlations, always limit the capacity of the overall population to distinguish between different stimuli (Pola et al., 2003; Schneidman et al., 2003), because they introduce some level of redundancy to the range of stimuli that can be encoded by those neurons. However, the impact of correlations between the variabilities of spikes rates of neurons from one trial to another to the same stimulus, which we call variability correlations, on the capacity of the ensemble to distinguish among the stimuli cannot always be predicted. For example, correlated variability may avoid noise from being averaged out over the population, and thus reduce discrimination capacity of the ensemble (Zohary et al., 1994). On the other hand, if correlated variability is different from one stimulus to another, it may provide additional discriminability between the stimuli (Pola et al., 2003). Finally, the relationship between the correlated variability and the correlation in tuning curves can affect the distribution of responses belonging to different stimuli and help to either increase or decrease the overlaps between them in the response space, as depicted in (Pola et al., 2003; Averbeck et al., 2006). An illustration of how the shaping impacts of these interactions is provided in Figure 3-1. Many empirical studies have found evidence for the contribution of correlated variability to the capacity of the neuronal ensemble in discriminating the stimuli (Averbeck and Lee, 2003; Golledge et al., 2003; Rolls et al., 2004; Pillow et al., 2008; Meytlis et al., 2012), although many of them found that this contribution is small (<10%).

Regardless of the amount of the information available in the population, it is possible that not all of it might be used by neural substrates downstream to the SC, depending on what decoding mechanism they use. For example, it is possible that the decoder is not optimal, and cannot approximate the true probabilities of the possible outcomes. Or that it is biased, and while it is adjusted to capture a reasonably
close approximation of probability distribution of possible outcomes, it assigns the probabilities wrongly to the outcomes (Schneidman et al., 2003).

Here we first compare the amount of information that individual neurons and simultaneously recorded pairs in intermediate layers of SC carry about the stimuli from their visual responses to saccade-related activity during a visual search task. We also examine the impacts of correlated variability on the amount of information that each pair carries. Because we had observed similar signs for signal and variability correlations, we hypothesize there should be a reduction in information due to the stimulus-independent component. Because the variability correlations changed from one stimulus to another, we hypothesized there must some increase in the information due to stimulus-dependent component. To investigate whether the impacts of correlated variability augment with the size of the population (Schneidman et al., 2003; Ince et al., 2013), we simulate larger populations using sampled pair-wise correlations.

Next, we explore how much of the available information in this network can be used by the neurons downstream. We test two biologically plausible decoding schemes and examine how their performance changes in time, with the size of population and different levels of variability correlations. The first is a suboptimal winner-take-all model (Shamir, 2006), applied to pools of neurons corresponding to one option competing with other pools of neurons corresponding to other options. The pool that shows the highest rate of activity suppresses the other pools, for example via lateral inhibition, and wins the competition (Koch and Ullman, 1985; Shadlen et al., 1996; Cave, 1999). The second, a more optimized decoding scheme, is an artificial neural network, in which the responses of neurons that show a higher discrimination capacity will be assigned higher weights in the final decision, as a result of learning (Bishop, 2006). We explore how the performance of these decoders is impacted negatively by correlated variability among neurons with shared RFs and neurons with opposite RFs. We also explore the impact of introducing cells with weak discriminability capacity on the performance of these decoders to account for less optimal populations.
Figure 3-1: Effects of interactions of signal and variability correlations on shaping the distribution of responses to each stimulus, and increasing or decreasing the overlap between them. Each ellipse in a panel represents the responses to a different stimulus. Figure is adapted from (Pola et al., 2003).
3.3 Methods

3.3.1 Behavioral task, physiology, description of dataset

The data for simultaneously recorded neuronal pairs were collected from three female monkeys (*Macaca mulatta*, 4.5-6.0 kg, 8-10 years) according to the protocols developed based on guidelines by Canadian Council on Animal Care (CCAC) and approved by Queen’s University animal care Committee. The details of these procedures are explained in chapter 2 and elsewhere (Shen and Paré, 2006).

The search task during which these pairs were recorded involved presentation of an array of objects, one of which was a designated target. A saccade was required to be made to the target. The target was defined as the only object that is different from all other objects in the array by means of one feature (color). Throughout this document the terms “target trials” and “distracter trials” would refer to trials where the target or distracters have appeared in the response field of the neuron being recorded, correspondingly.

Neurons extracellular potential was recorded from the intermediate layers of superior colliculus (approximately 1-3 mm deep in SC) using Tungsten microelectrodes which were inserted using guide tubes placed in a grid system in the recording cylinder. Neurons from opposite colliculi were recorded simultaneously by inserting two guide tubes. Neighboring neurons were recorded simultaneously, either using two electrodes with different diameters in the same guide tube (number of pairs: 21), or using the same electrode (number of pairs: 23). The recorded signal was amplified and low-pass filtered at 8 kHz and high-pass filtered at 80 kHz. Plexon Offline Sorter was used to isolate the waveforms into distinct units based on the principal components of the waveform shapes.

The data from singly-recorded neurons were taken from a dataset previously collected in this lab (Shen et al., 2011) as described before in details elsewhere. This allowed us to conduct the simulations on two versions of the task with varying degrees of difficulty. In 44 sessions, the search target was different from the distracters in only one feature (color). In 43 sessions, it was different from the distracters as a result of the conjunction of two features (shape and color).
3.3.2 Analysis of information in neuronal pairs

We use information theory to assess the potential capacity of neurons responses in discriminating between the target and distracters, regardless of what decoding mechanisms are employed. Information theory is based on the concept of uncertainty about a variable $x$, and how knowledge of another variable may reduce the uncertainties about it. Uncertainty is expressed in the form of “Entropy”, which is defined as

\begin{equation}
H(x) = - \sum_{i=1}^{N} p(x_i) \log p(x_i)
\end{equation}

where $x_1, x_2, \ldots, x_N$ are the different values that $x$ takes. As can be seen, the entropy does not depend on the value of the $x$, but on the distribution of the probabilities with which $x$ takes different values.

One can also write the entropy of $x$ given that the value of another variable, $y$, is known

\begin{equation}
H(x|y) = - \sum_{j=1}^{M} p(y_j) \sum_{i=1}^{N} p(x_i|y_j) \log p(x_i|y_j)
\end{equation}

which is the amount of uncertainty left about $x$, after one gets to know about $y$. Here $N$ is the number of unique values that $x$ takes, and $M$ is the number of unique values that $y$ takes. If one deduces this entropy of $x$ conditional on $y$, from the entropy of $x$, the result would tell how $y$ is informative about $x$. This is called the “mutual information” between $x$ and $y$, as it is symmetric and holds for $x$ being informative about $y$ as well (Dayan and Abbott, 2001).

\begin{equation}
I(x,y) = H(x) - H(x|y) = H(y) - H(y|x)
\end{equation}

The maximum value that mutual information between $x$ and $y$ can take is either the entropy of $x$, or entropy of $y$, whichever smaller.

The first step in applying information theory in order to quantify the information that neural responses carry about the stimulus type is to calculate the probabilities of each stimulus type occurring, as well as the probabilities of each response occurring. In this analysis, neural responses are considered as the number of spikes over a specified window.
For our analysis, the stimulus is either a target or a distracter and the probability of it being each can be stated by counting the number of trials each has been presented to the response field of recorded neuron, and dividing it by the total number of trials. These probabilities are set during the experiment.

The neural responses on the other hand, can be more various and take different values. The simplest way to quantify the marginal probabilities of each response is to count the number of occurrence of each element of the response set, and divide that by the total number of trials. However, if the number of trials is not large enough, not all possible responses would get a chance to occur during that experiment session, and the ones that do occur might not occur in numbers that represent their true probability. Because of that, in datasets with small numbers of trials a bias can be introduced to the probabilities that are calculated in this way. In case of a neuronal pair, the responses will have two dimensions. This would mean the possible responses of the pair will be a combination of the possible responses for each individual cell in the pair -subjected to the effects of correlations- so one would need an even larger number of trials.

To calculate the information, we also need the probabilities of each neural response given each stimulus type. To obtain the conditional probability of each unique response given each stimulus condition, we once count the number of times that the response has happened when a target was presented and divide it by the total number of target trials. We then repeat the process for distracter trials.

Using these probabilities and using the equations (1-3), we can quantify the information in the responses of the neuronal pairs, \( r \), about the stimulus type, \( s \), as

\[
I(R,S) = - \sum_{i=1}^{N} p(r_i) \log p(r_i) - \left( - \sum_{j=1}^{M} p(s_j) \sum_{i=1}^{N} p(r_i|s_j) \log p(r_i|s_j) \right)
\]

\[
= \sum_{j=1}^{M} p(s_j) \sum_{i=1}^{N} p(r_i|s_j) \log p(r_i|s_j) - \sum_{i=1}^{N} p(r_i) \log p(r_i)
\]
where \( N \) is the number of unique responses, and \( M \) is the number of stimulus types.

If the number of neurons is more than one, \( r \) will be a vector of responses with its number of elements equal to the number of neurons, and its probability will be the joint probability of the individual responses in it.

To address the effects of variability correlations on the information that the neuronal pairs carry about the type of stimulus, we needed to quantify the information also under the condition of absence of noise correlations. This is not directly possible using the recorded responses, because the responses are representing the correlations that existed during the time of recording. One needs to de-correlate the recorded responses. The simplest way to do this can be by assuming that the responses of each cell in the pair occur independent of those of the other, that is, the joint probabilities of their responses is equal to the multiplication of probabilities of corresponding individual responses (Latham and Nirenberg, 2005).

\[
p(x_1, \ldots, x_N) = \prod_{i=1}^{N} x_i
\]

where \( x_i \) is the response of neuron \( i \). For this analysis, \( N=2 \). Shuffling the trials many times and averaging over them will have the same effect.

One can make such “de-correlated” joint probability distributions of cell responses both for the marginal and conditional (on stimuli) probabilities and quantify the information using them. The difference between the mutual information obtained from these de-correlated joint probability distributions, and the ones obtained from the observed distributions will tell us the amount of loss or gain on the information as an effect of noise correlations.

All the information quantities calculated in this chapter where normalized to their maximum possible value, which is the entropy of the stimulus.
The spikes that occurred in a time window of specific width around a certain point of time with regard to saccade were counted and this integer number of spikes was used as the values that the response could take, for each cell in the pair. The responses of the neuronal pair on each trial, therefore, were vectors with two entries, each corresponding to one cell in the pair, and representing the number of spikes which that cell had generated during that time window. Different widths for the window were tried, and the epoch time with regard to saccade was moved in time until 60 ms before the saccade.

In practice, the value of information found to be carried about the stimuli can be higher than 0 even for some randomly generated neural responses. For example, even the neural data from the fixation period where no stimulus is present may show some positive values of information about the stimuli. To correct for this overestimation of the true information by the data due to randomness, we permutated the trials in each session so the target and distractor trials were randomly interleaved, and calculated the information carried by this set of randomly assigned neural responses to either of the two categories. We repeated this process for 1000 times. Then, using a one-sampled t-test, we tested whether the observed value of information for the true distribution of responses between the two categories was significantly different from the distribution of 1000 information values generated in this way.

Another source of upward bias in the calculated information is the small number of trials which makes it impossible to measure the true probability distributions of individual responses. To correct for this bias, we used a toolbox developed by (Magri et al., 2009) which uses a method suggested by (Pola et al., 2003), where the bias is calculated as

\[ \text{Bias} = \frac{1}{2N \ln 2} \left\{ \sum_s (R_s - 1) - (R - 1) \right\} \]

where \( N \) is the number of trials (in total over all stimuli), \( s \) is the stimulus, \( R \) is the number of different unique responses, and \( R_s \) is the number of different unique responses for each stimulus.
The breakdown of information contribution by the stimulus-independent and stimulus-dependent components of the variability correlations was implemented using a toolbox from Magri et al. (2009). The stimulus-independent component is calculated as

\[ I = - \sum_r p(r) \log p_{\text{ind}}(r) - \sum_{r,s} p(s)p_{\text{ind}}(r|s) \log p_{\text{ind}}(r|s) \]

where \( p_{\text{ind}}(r) \) and \( p_{\text{ind}}(r|s) \) stand for the de-correlated joint probabilities for the marginal and conditional probabilities of responses of pairs, respectively.

The stimulus-dependent component is calculated as

\[ I = H(r) - H(r|s) + \sum_r p(r) \log p_{\text{ind}}(r) - \sum_r p_{\text{ind}}(r|s) \log p_{\text{ind}}(r|s) \]

where \( H \) stands for entropy.

### 3.3.3 Analysis of simulated populations

The analysis of responses of neural pairs and the impacts of variability correlations on their information content may not be representative of larger populations. To assess the effects of noise correlations on performance of SC population in telling apart the two types of trials, it was first necessary to simulate a population response built from singly recorded neurons responses. Using such simulated population responses, two different schemes were used to tell the target and distractor trials apart. I will first describe how the population responses were generated. Then, I will describe the classification/decision schemes.

**Simulations of Populations Responses** For all the population simulations in this chapter, the simulation of the task was simplified by reducing the number of stimuli to two, one target and one distracter. For each of these locations, a population of a certain size was simulated by randomly picking a number of neurons, equal to the desired size for the populations, from a singly-recorded dataset (described in Shen, Valero, Day, & Paré, 2011).
To generate the responses of each population, a multivariate normal distribution was made, using the average and variances from responses of each neuron in that population to all of its trials with the relevant stimulus type, where each dimension of the distribution corresponded to a neuron. This means that if for example the population was meant to represent having a target in the response fields of its neurons, only recorded responses from target trials for the corresponding randomly picked neurons were used to generate the multivariate normal distribution. From this distribution, every random pick of response vectors would be considered a simulated “target trial” for that population. The randomly generated negative responses were either replaced by 0, or removed by adding the absolute value of the smallest negative number to the whole vector.

When a trial is generated by picking such a random vector, the amount of correlation among the elements in the vector can be controlled by modifying the covariance matrix that is used to build the multivariate normal distribution. Each entry in the covariance matrix is the multiplication of variances of the two neurons, multiplied by a correlation coefficient to determine the amount of correlation among neurons in that population. The value for this coefficient was drawn from a standard normal distribution plus a fixed value for the average, in every simulation. I systematically changed this added fixed value to determine the effects of noise correlations on the population’s performance. For the case of assessing the effects of no correlations, instead of using the normal distribution, the value of correlation coefficient was deterministically set to be 0.

When generating such randomly drawn matrices, not every combination of correlation coefficients in the overall matrix is possible. This is because if, for example, neurons n1 and n2 have a correlation coefficient of 1, while neurons n1 and n3 have a correlation coefficient of 1 as well, the correlation coefficient between n2 and n3 cannot be set randomly at 0 anymore, because both n2 and n3 have strong correlations with n1, so it rather should be set at 1, too. In order to make sure my randomly selected combination met this requirement, I checked if the resulting covariance matrix was positive semi-definite.
Figure 3-2: A summary of the process for simulating the decision outcome of two pools of neurons the RF of which are opposite of each other on the screen, through a winner-takes-all mechanism. $n$ is the number of neurons in each pool, $R_{stim}^{i}$ is the response of neuron $i$ to stimulus $stim$, and the decisions are made by implementing a sum over the responses from all neurons in each pool with equal weights.
Figure 3.3: The process for determining the outcome of the decision using a trained network of neurons, whose weight is determined based on previous performance during a training phase.
It can be shown that the attribute of positive semi-definiteness can guarantee such consistency among the elements of the overall matrix (personal communication, Mike Roth, Queen’s University).

For each simulation for the purpose of analysis of information at the population level, only one spatial population response was generated, which would respond to a number of target or distracter trials with proportions similar to what had been done in the experiments.

For every different condition of analysis (magnitude and sign of variability correlations), n random picks of neurons (n=2, 10, 50 or 100) were used to generate a population. For every randomly selected population, 50, 100, or 500 random picks of response vectors were generated, with each response vector corresponding to the simulation of a behavioral “trial”. The performance of the population (or the information that it carried about the stimuli) were measured over these trials. This process was repeated 50 times, aimed to simulate 50 behavioral sessions when distinct populations are recorded. Each of these is called an “iteration” from now on. The performance over these 50 iterations was averaged and reported for each different condition of analysis (Shadlen et al., 1996; Astrand et al., 2014).

The information that the population carried about the stimulus type was quantified in the same way as for pairs, except that now the neural responses had larger dimensions to them. For the “de-correlated” condition, however, the large number of neurons would not allow for quantification of information by calculating a fake distribution of joint probabilities, without investing large amounts of technical resources, because instead of an outer product of two vectors, this now requires a Kronecker product on large-dimension matrices. The “de-correlated” condition for the simulated populations was simply generated by inserting no noise correlations among the population’s neurons, by setting the correlation coefficient to 0.

For the purpose of analysis of performance of the pooled and ANN model, the populations were simulated in the same way that is explained in above, except that two populations are simulated.
Whenever this was the case, the two vectors of averages of relevant activities of randomly picked neurons for each population were put together and a corresponding covariance matrix was built for all the neurons in the two populations, to build one multivariate normal distribution from which both target and distracter trials were generated for their corresponding populations. This allowed me to insert correlations between the two populations as well as within them. All the trials from all iterations were put together before training and testing the classifier. This process was repeated 30 times (called a run), to generate reliable averages and standard deviations for each analysis.

During all the analyses of decoder performances on simulated populations in this chapter, the recorded neural responses were convolved with a Gaussian kernel to generate spike density functions (Hanes et al., 1998). The averages of the spike density function values over a specified window of time, over all trials of the same type, were then used to generate the average and variances for each neuron in the multivariate normal distributions. All the responses were aligned on saccades. Different epochs before the saccade onset, and different widths of window over which the activity was averaged were tried.

In one analysis, the correlation coefficients were selected in a way that would more closely replicate the values obtained from SC. In one form of this analysis, the correlation coefficients were randomly selected from the observed correlation coefficients in our pairs: correlation coefficients from pairs with shared RFs during trials with the target in RF, correlation coefficients from pairs with shared RFs during trials with the distracter in RF, and correlation coefficients from pairs with opposite RFs during trials with the target in at least one of the RFs. In another form, the correlation coefficients were randomly drawn from a normal distribution with the average and standard deviations of sampled values in our pairs, for each of these three categories.

Decoding /Decision-making schemes Once the populations’ responses with desired inserted noise correlations are generated, one needs to define how the downstream areas would be driven by these responses.
One simple physiologically plausible scenario is that responses from each population simply compete with each other in magnitude, and whichever that is bigger silences the other through inhibitory inputs, and wins the competition in sending a message to downstream populations, so a saccade is made towards their corresponding physical space. The simplest way this can be modeled is by averaging the responses of each population, and selecting whichever was larger as the saccade goal. If the selected response belongs to the population whose response was generated from target trials, then the target has been selected as the saccade goal, and one can mark that as a correct trial. The performance of the model can be defined as the percentage of such correct trials over all the generated trials (Zohary et al., 1994; Cohen and Newsome, 2009). One can compare these performance rates for different magnitudes of noise correlations, to assess the effects of noise correlations on the populations’ performance in the task.

This model simplifies the decision-making process by making the assumption that all the neurons in the population have equal contribution to the decision-making process. It doesn’t explain how the connections among the neurons within or between the populations have been modified as a result of being trained on the task, to be able to generate such results.

Because we don’t know what decision-making/decoding scheme the brain actually uses, it is sensible to try more than one to see if the effects of noise correlations on populations’ performance would be consistent, regardless of the decoding scheme. The other decoding method that I chose for this analysis is Artificial Neural networks (ANNs).

A neural network is a computational system or a mathematical function that maps a vector of inputs to one of a set of outputs. This can be done adaptively, that is the network can learn based on “experience” (exposure to new data). For example, for each input data, a class label can be assigned which will be compared by the output of the network. The difference between this label and the output that the network has generated is called an error. The error will be used to modify the network in a way that the error becomes smaller. The structure of network will be kept as final when the error is minimized.
The transformation usually happens as a series of functions organized in sequential “layers”. In a simple form of a neural network, the first layer, referred to as “input layer” receives the multi-dimensional data and generates outputs in the form of

\[ a_j = f \left( \sum_{i=1}^{I} w_{ji}^{(1)} x_i \right) \]

Where I is the number of nodes in the input layer, and \( j=1, 2, \ldots, H \), while \( H \) is the number of nodes in output layer. \( w_{ji}^{(1)} \) are weights and what get modified during learning. \( f(x) \) is called an activation (transfer) function and is usually a differentiable nonlinear function the role of which is to limit the range of values that the units in intermediate layer can get. For example, in a biologically plausible network, this can be set to a saturating linear function which generates outputs of 0 or 1, only, which can correspond to a neuron firing or not.

The output vector will be compared to the desired labels, or “targets”, that the network is provided with beforehand, during a supervised learning. The difference between the two can be expressed in the form of an error as a function of network’s parameters, or weights, \( E(w) \). The goal of the network is to find the vectors \( W \) such that the \( E(w) \) is minimized. This is done through iterative numerical solutions where \( W \) gets updated at each iteration, and \( E(w) \) is evaluated, until the minimum is achieved. To know if the minimum is achieved, one needs to check if the gradient of error functions equals to 0. (Bishop, 2006).

ANNs are a good choice of a decoding method for this purpose for several reasons. First, their architecture is flexible and can be designed to meet physiologically plausible scenarios. Second, they are efficient classifiers that can learn to classify almost any patterns of data. Third, they are adaptive, that is, they can learn which also is a main feature of biological neural networks. As a result of such feature, I expect that the ANN model performance not to be reduced after introduction of non-informative cells to the simulated populations, because the contribution of these cells should become small after training. On
the other hand, the performance of the pooled WTA model should be severely impacted by the introduction of non-informative cells to the populations.

Neural Networks Toolbox from MATLAB ® (MathWorks Inc.) was used to implement the ANN. Supervised learning was used to train the ANN. Every input node corresponded to one neuron in the populations. That is, the input layer would be fed with the response vector generated as explained in previous section. There is one unit in the hidden layer, which was determined after a preliminary analysis, trying different numbers of hidden units between 1 and 20. The transfer functions were set to linear, but other transfer functions were also tried. The number of free parameters was between 3 and 201, and was always smaller than the size of samples in the training set (2500-5000 trials), avoiding overfitting. The method of training is Levenberg-Marquardt backpropogation. There is one single node in the output layer that makes a binary decision corresponding to one of the two conditions, when the target is presented in the population on the right, or when it is presented to the population on the left. Physiologically, this can be interpreted as a downstream area corresponding to one of the two populations, generating a burst if the target is in the response field of its corresponding population, and not generating a burst if the target is in the response field of the other population. A second output node can correspond to the other population, but for the sake of simplicity I just adhere to one.

For each iteration, 100 or 200 trials were generated. In half of them, the target was presented to the population on the right matrix, and in the other half, the target population was on the left. All trials from all iterations were put together, 50% of them were used for training the network, 5% for validating, and 45% for testing.

I tried another decoding method, Support Vector Machines (SVMs), in my preliminary analysis. The time that it took for an SVM to classify the simulated trials was substantially larger than the time for ANNs. Moreover, there is no known physiologically described mechanism in brain areas that imitates an SVM. Therefore, I discarded the SVM from the rest of analysis for its lack of time efficiency and biological
plausibility. Other methods of decoding, such as Bayesian classifiers, were not tried because they have been shown to be outperformed by ANNs and SVMs (Astrand et al., 2014).

3.4 Results

3.4.1 Information in sample neuronal pairs

We measured the amount of information that the activities each of the 44 neighboring pairs and 15 pairs with opposite RFs described in chapter 1 carried about the stimulus in a 100 ms-window before the onset of saccade. An example of these pairs is shown in Figure 3-4. The neurons in this pair share their RF. They also have positive signal correlations, meaning that they have similar tuning curves and both increase and decrease their responses to the same stimulus conditions, on average. However, on a trial-by-trial basis, when a neuron increases its response, the other usually decreases its responses, indicating that they have negative variability correlations. The responses of the neurons to two stimulus conditions are well-separated for most part, and there is only a small overlap between the two trials types. Part of this is due to the way that signal and variability correlations have shaped the distribution of responses. When the variability correlations between the two neurons are ignored, the distribution of responses to each stimulus condition expands (the circles) and the amount of overlap between the responses of the two trial types increases. The difference in the signs of the signal correlation and variability correlations is expected to increase the information that the pair carries about the stimuli, compared to a de-correlated state where variability correlations are ignored. This amount is represented by the top stacked bar on the right (Stim Ind) in the bottom plot of Figure 3-4. The variability correlations between the two neurons slightly change in the magnitude from one stimulus to another. This stimulus-specific change could also contain some information about the stimulus type. This amount is represented by the middle stacked bar on the right (Stim Dep). The signal correlations between the two neurons introduce some redundancy to the amount of information that they carry about the stimuli together. The linear sum of the information that each individual neuron carries about the stimuli (the bar on the left) is higher than what the pair
Figure 3-4: An example of a pair where variability correlations add to the amount of information that the pair responses carry about the stimuli. The neurons in the pair share their RF. Left: The red data points represent the responses of the pair on trials where a distracter was in their shared RF. The back data points represent the responses to trials where the target was in the pair’s shared RF. The rectangles show the possible range of responses if their pair’s responses were not correlated at all. The pair has positive signal correlations (the correlation over the centers of the red and black circles), but negative variability correlations over both stimulus conditions, represented by the r values of the same color and the linear fit through the corresponding set of data points. Right: Comparison of information values carried by each cell in the pair and the linear sum of it (left bar), and the overall information carried by the pair (the whole bar on the right), and its overall decomposition into the information carried by the pair responses in the de-correlated state (lowest stacked bar on the right), and contribution of the variability correlations from stimulus-dependent (middle stacked bar on the right) and stimulus-independent components (top stacked bar on the right).
together carry without the contribution from the variability correlations (the lower stacked bar at right), or even the total information that the pair carry together (the whole bar on right).

For each pair, we measured eight different quantities: 1) the amount of information that the pair carry together about the stimulus; 2 and 3) the amount of information that the activity of each individual cell in the pair carries about the stimulus when considered in isolation from the other cell; 4) the amount of information that the activities of pair would carry about the stimulus, if the variabilities in activities of cells in the pair were not correlated from trial to trial (de-correlated state); 5) the difference between the actual amount of information that the pair carries about the stimulus and this de-correlated state; 6) the difference between the actual amount of the information that the pair carries and the amount that the most informative cell in the pair would carry individually; 7) the amount of information that would be gained due to stimulus-modulated variability correlations; and 8) the amount of information that could be either gained or lost due to the overall shaping effects of variability correlations.

Figure 3-5 show the distribution of these 8 values over the 44 neighboring pairs. The pairs carried 0.98 ± 0.06 of the maximum possible amount of MI about the stimulus. This was on average 1.10 times more than what the more informative cell in each pair carried, which implies that information carried by the two cells in each pair are not completely redundant. The pairs in de-correlated state carried slightly smaller amounts of information about the stimulus, which indicated that the correlations had a slight increasing impact on the information content of the pairs (an average of 2% of the maximum possible information).

Two other lengths of window were tried as well: 70 ms before saccade and 10 ms before saccade. The information carried by the activities over the 10 ms before the saccade had an average of 0.88 ± 0.12 and was significantly smaller than that carried by the activity over 100 ms before saccade onset (p<0.001), but the activity over the last 70ms window before saccade carried about the same amount as 100 ms before it (0.98 ± 0.06).
Figure 3-5: Distribution of information content in the activities of neighboring pairs in different conditions and differences between them, over a window of 100ms before the onset of saccade, normalized by the entropy of the stimulus (maximum possible value for the mutual information). Each boxplot shows the distribution of information over the 46 pairs for the following: Pair: actual amounts of information in each pair; Cell 1: information content of the less informative cells in each pair; Cell 2: information content of the more informative cell in each pair; De-correlated: information content of the pair, if there were no correlations; Actual – De-correlated: difference between the first and fourth value for each pair, signifying the amount of information that is gained or lost due to overall effects of variability correlations; Pair – Cell 2: The difference between information that each pair carries and what the more informative cell in that pair carries, implying the level of redundancy between the cells in each pair, when compared to information content of cell 2. Icorr_I: The information amount that could be lost or gained due to the shaping effects of the variability correlations on the distribution of responses and their overlaps. Icorr-D: The information amount that could be gained due to modulation of variability correlations from one stimulus to another. Red crosses indicate outliers.
Figure 3-6 shows the distribution of the same 8 values calculated over a 100 ms window before saccade onset for the 15 pairs with opposite RFs. The results were similar for opposite pairs. The activity over 100 ms and 70 ms window before saccade carried $0.95 \pm 0.08$ of the maximum possible information, on average. This decreased to $0.83 \pm 0.22$ for a 10 ms window before saccade. Correlations increased the information by about 4%.

A major motivation for us to measure the correlations in variability of responses between neuronal pairs in chapter 2 was to explore their impacts on the amount of information that the neurons in SC carry about the stimulus at different points of time. There, based on the analysis of similar cases from the literature, we made three predictions about the potential impacts of correlated variability on our pairs’ information content: First, because the correlations magnitude seem to change from one stimulus condition to another at least at some time epochs for some pairs, we predicted that some amount of information should be added because of these stimulus-modulated correlations to what would be expected to be carried by the pair otherwise. Moreover, as the relationship between the sign of signal correlations and variability correlations has an effect on the shaping of each pair’s response distribution to each stimuli and the amount of overlap between the these distributions, we predicted that for pairs that signal and variability correlations have opposite signs, such as the one in Figure 3-4, the amount of information should increase. Figure 3-7 shows the overall difference between the information that the pair carries and that in the de-correlated state on the y axis, for each neighboring and opposite pair. The pairs with same signs of variability and signal correlations are expected to have negative values for the difference in information content between the correlated and de-correlated states due to the shaping effects of the correlations on the response distributions, as shown in Figure 3-1. However, they can have positive values of information difference due to the stimulus-dependent component of contribution of variability correlations to the information. The pairs with opposite signs of variability and signal correlations are expected to show only an increase in the information as a result of correlations, whether due to the shaping effects of the correlations or due to the stimulus-dependent component of the contribution.
Figure 3-6: Same as previous figure, for opposite pairs.
Figure 3-7: The overall gain or loss of information due to impacts of variability correlations. Variability correlations are shown for each stimulus condition separately. Top panel shows the pairs with shared RF which all have positive signal correlations. Bottom shows those pairs with opposite RFs which have negative signal correlations.
All the three time windows tested above ended on saccade onset, and therefore, while they show the impact of the length of window on the amount of information, they do not highlight how the information is built up throughout time. We therefore quantified the actual amount of information carried by the pairs over four behaviorally relevant epochs of the same length: 25 ms after the onset of visual response, 25 ms before the discrimination time for the pair (median of the discrimination times for individual cells in each pair determined with responses aligned on stimulus), 25 ms after the discrimination time, and 25 ms before saccade onset. We then compared these values to the amount of information the de-correlated pair as well as each of the individual cells in the pair carried about the stimuli in the same behavioral epochs.

Figure 3-8 shows the results of this analysis for neighboring pairs, and Figure 3-9 for pairs with opposite RFs. The most prominent result is that the build-up of information along time and effects of correlations and redundancy of cells on it is similar for both groups of pairs. In both groups, the mutual information has its highest value at the closest time to saccade. A one-way ANOVA over the four different time epochs showed significant changes in amount of information in pairs and individual neurons of both groups (pairs with shared and opposite RFs) over time (p<0.0001). For both groups, de-correlation has a negligible decreasing impact on the amount of information that the pair carries around this time. In both groups, the more informative cell in each pair, individually, carries most of the information that the pair carries, which means the second cell’s information is mostly redundant.

The above results on the information content of our sample pairs are over-estimated for two reasons: first, because they are calculated over correct trials only and therefore do not replicate the behavioral performance of the subjects. An average of 80% of all trials over all sessions when neighboring pairs were recorded was correct. Repeating the analysis with all the trials revealed that including only the correct trials had over-estimated the information in the complete response distributions of our sampled neighboring pairs by only 7% at the point with maximum information in the epoch of 25 ms before saccade, possibly, because of the number of incorrect trials having been small overall. The rest of analysis in this chapter is conducted on both correct and incorrect trials in each stimulus condition.
Figure 3-8: The dynamics of information build-up in neighboring pairs as the time progresses in the task. The information content are compared for pairs in their actual correlated state and the hypothetical de-correlated state where variability correlations are ignored (top panel), and for pairs in their actual state to the information content of each individual cells in the pair (middle and bottom panels) over 4 behaviorally relevant epochs: 25 ms after the onset of visual response, 25 ms before the discrimination time (before DT), 35 ms after the discrimination time (after DT), and 25 ms before saccade onset. Blue lines indicate the pairs for which information content is significantly different from chance levels. Grey lines indicate chance levels for each condition.
Figure 3-9: The dynamics of information build-up in opposite pairs as the time progresses in the task. The information content are compared for pairs in their actual correlated state and the hypothetical de-correlated state where variability correlations are ignored (top panel), and for pairs in their actual state to the information content of each individual cells in the pair (middle and bottom panels) over 4 behaviorally relevant epochs: 25 ms after the onset of visual response, 25 ms before the discrimination time (before DT), 35 ms after the discrimination time (after DT), and 25 ms before saccade onset. Blue lines indicate the pairs for which information content is significantly different from chance levels. Grey lines indicate chance levels for each condition.
Second, because the number of trials over which the content of information in our neuronal pairs’ activities is calculated is limited, this is expected to introduce an upward bias in measuring the information (Panzeri et al., 2007). The amount of information carried by neighboring pairs in both correct and incorrect trials, after it is corrected for the bias, was decreased by about 3% at the point with maximum information (average of pairs’ information over 25ms before saccade). We therefore chose to continue our analysis without correcting for bias in the rest of this chapter.

Finally we measured whether the information carried by each pair during each epoch is significantly different from their corresponding chance level values. The information carried by all the individual cells and pairs was significantly different from chance in saccade epoch. In the visual response epoch, the information carried by none of the individual cells and pairs was significantly different from chance (p>0.01). Generally, the pairs and individual cells showed a gradual progression of a significant information growth over time.

### 3.4.2 Information in simulated populations

The total effects of correlated variability on the information content of our sampled pairs were small. We asked if this could be due to small number of neurons (n=2) over which we analyzed the correlations and their effects, and whether the results would change at all, if we had recorded from a larger ensemble of neurons, rather than just a pair. To answer this question, using the responses from a dataset of singly recorded neurons, we simulated a population response where the activity of each neuron on each trial was randomly picked from a multivariate normal distribution the averages for which was a vector of average responses from randomly picked neurons for that population, and the covariance matrix was made using the variances of the individual neurons in the population and a correlation coefficient which represented the amount of variability correlation. We did this for neurons recorded in two conditions of the task: Feature visual search, and Conjunction visual search. Since Conjunction task is more difficult, we expected the information carried by populations of same size and correlations level to be lower for this
task, unless when the population size is large enough for the information to reach at its maximum possible level.

We systematically changed the value for the correlation coefficient from 0 to 0.2 and compared the information that the population carried about the stimulus in each condition. The information was calculated over two different lengths of window and 3 different population sizes. With a window length of 20ms, the information quickly reached to its maximum possible value (entropy of the stimuli) as the number of neurons increased from 2 to 5, and 10. By a population size of 10 the differences between different conditions were effectively absent. At a population size of 5, correlated variability seemed to decrease the amount of information for the more difficult task, but this effect was small and not consistent across all epochs. The biggest change was around 5% decrease for a population size of 5. This pattern was not observed over the other task, or population sizes. Figure 3-10 shows these results.

3.4.3 Performance of a simulated population optimized on the task
While from the results of the last population simulation it seems that correlated variability may be able to decrease the amount of information that a population carries, the reduction that we observed is neither large enough to account for the low performance of our subjects in the task, nor shows a consistent pattern over all time epochs. Moreover, it is only observed at a small ensemble size of 5 neurons. Lastly, it contradicts the results from the pairs’ analysis, where correlations seemed to have increased information.

Given the possibility that not all of available information in SC might be used by neural substrates downstream to it, depending on what decoding mechanism they employ, we tested a few different decoding mechanisms which could demonstrate a larger loss of information from SC to the downstream areas. We expected this to give us a chance to explore the impacts of correlations in larger populations, without the performance saturating at its maximum with only a few neurons.
Figure 3-10: Information carried by small ensembles of neurons with shared RFs in 20ms of their activities, as a function of time before saccade and magnitude of correlated variability.
**Pooled winner-takes all Model:** Two populations of neurons are simulated by randomly picking from activities of neurons in a dataset of single recorded units (described in Shen & Paré (2011)). One population’s cell activities are picked from a normal distribution made from the trials where the target has been in the receptive field of cells, with the average and standard deviation of the distribution corresponding to those of neural responses during our sampled trials. The cell activities of the other population are picked from a normal distribution made from trials where a distracter has been in the receptive field of the cells. For each trial, the activities of the neurons in each population are averaged, and whichever that is larger, will be taken as the “target” population. If the activities of the same population were indeed taken from the target trials, the trial will be considered to be correct.

For each different combination of randomly selected neurons, 500 trials were tried. And 50 different combinations of neuron picks were tried, for each condition (referred to, as iterations, from this point on). Different epochs before the saccade onset, and different widths of window over which the activity was averaged were tried. Also, correlated variability of different magnitude was added to the two populations and their effects on the model’s performance were quantified.

Using the activities in a 20 ms wide window, centered on 20 ms before the onset of saccade, with no correlated variability within or between populations, the average performance of the model is as follows: 97.11 ± 7.66, and 94.70 ± 9.63, for feature and conjunction tasks, respectively, with one neuron in each population; 100 ± 0.00 and 98.20 ± 2.45, for 10 neurons in each population, and 100.00 ± 0.00 and 100.00 ± 0.00, for 50 or 100 neurons in each population.

For populations of size 10, 50, or 100 neurons, adding correlated variability with an average correlation coefficient of 0, 0.05, 0.1, 0.15 and 0.2 among the neurons within or between each population did not change performance of the model for either of the tasks for more than 0.1% (decreasing effects by within-population variability correlations, increasing effect by between-population variability correlations).
Keeping the average magnitude of variability correlations among neurons with shared RF fixed at 0.2, we systematically changed the variability correlation for neurons with opposite RFs from 0 to -0.2 as well, and observed the changes in model’s performance as a function of it. The changes in model’s performance during the feature task were absent (for n=50 and n=100 in both tasks, and n=10 in feature task), inconsistent (for n=1, for both tasks), or negligible (0.5%, for n=10 in conjunction task).

Figure 3-11 summarize these results for positive, and negative values of variability correlations between the populations of neurons whose RFs are opposite from each other (Top and middle panels), and positive values of variability correlations among neurons in each population, which share their RFs (bottom panel).

We also compared the performance of network under the effect of different magnitudes of correlated variability, in different epochs of time relative to saccade. For a fixed population size of 50, we moved a 20-ms wide window from 10 to 60 ms before saccade, for every 5 ms, and plotted the performance of the model under the effect of different magnitudes of correlated variability, either within or between populations. Figure 3-12 show the results of these simulations. As we moved further from saccade onset, the effects of correlated variability became more pronounced, and the patterns became more consistent. Larger values of correlated variability among neurons of the opposite populations increased the performance of network for a maximum change of about 13% in both tasks, while those among neurons in the same population decreased it for about a maximum change of 9% in the feature task, and 10% in conjunction task.

**Neural Network Model:** Our model in previous section is based on the assumption that each SC population does a simple average over the responses of all neurons in it, and whichever population that has a greater activity gets selected as it suppresses the activity of others, and will determine the final behavior’s target. This is an obvious oversimplification. For example, all neurons in our model have the same weights for their input to the population activity. In reality, it is reasonable to expect that in a
Figure 3-11: Performance of a pooled winner-takes-all model as a function of population size, for different values of variability correlations among neurons with shared RFs. The activity of neurons is averaged over a 20ms window before saccade. Black represents performance of the model on Feature search task, and red represents its performance on Conjunction search task. Top: There is no correlated variability between neurons with opposite RFs. Middle and bottom: The average variability correlation for neurons with shared RF is fixed at 0.2.
Figure 3-12: Pooled Winner-Takes-all Model's performance as a function of time and average variability correlations magnitude among neurons with shared RFs. Length of the time window is 20 ms, and there are 50 neurons in each population. Top: The average magnitude of variability correlations among neurons with opposite RFs is 0. Middle and bottom: The average variability correlation for neurons with shared RFs is fixed at 0.2.
network that is well-trained on the task, the neurons that are better at the task gain stronger weights. To address this, we tried another decoding scheme where a linear supervised neural network was used as a classifier to separate different types of trials. Each input node in this decoder corresponded to one neuron in our population.

We simulated two spatial populations with the same neurons for each run. Half of the input nodes in the network belonged to the spatial population A, and the other half to the population B. In half of the trials that the network was trained with, neurons in population A were fed with target trial activities, while population B neurons received distracter trial activities, and in the other half, this was reversed. That is, the two trial types that the network was trained with were” target in A” trials vs. the “target in B” trials. We tested the network on trials that were not formerly presented to it, and measured the performance of the network as the percentage of the trials it classified correctly. Each time, the network was run with trials from 50 different combinations of neurons (50 trials for each combination, a total trial number of 2500 for each time the network was run). The network was run 30 times for each time epoch, and the performance was averaged over these 30 runs.

The positive variability correlations among the neurons with shared RFs decreased the performance of the network by about 14% in the conjunction task, and about 10% in the feature task, in a population size of 100 neurons. With smaller population sizes this effect was reduced (Figure 3-13).

The two-population set-up allowed us to test the effects of between-population correlated variability. Negative correlated variability between the two populations decreased the performance of the model, especially on the input from epochs further from saccade, similar to the effects observed in the pooled WTA model. However, this effect was slightly smaller and never exceeded 8% of change for either of the tasks. As with our first model, the effects were not persistent for the smaller population size of 2. shows the results of this analysis.
Figure 3-13: Performance of a neural network trained and tested on the neural activities from 20ms sliding windows, as a function of time from saccade, and average variability correlations among neurons with shared RFs.
Positive correlated variability between the two populations could increase the performance by up to 18%, in the conjunction task when the population size was 100 neurons in each population.

The impacts of correlated variability, whether decreasing or increasing the information, were consistently more pronounced in larger populations and in epochs further from the saccade.

Figure 3-14 and Figure 3-15 summarize these results.

**Replicating a Population in SC with Correlations from Our Sampled Pairs** The neurons in populations simulated in above have their correlation coefficients inserted among them based on a systematically increasing or decreasing average value. These values were capped at -0.2 and 0.2, because for large populations, the number of valid combination of values that produce a positive semi-definite matrix decreases substantially, making it difficult to find a valid covariance matrix that can have large values of correlation coefficients for our simulations. The same problem occurred when we tried to insert correlations coefficients from our sampled pairs from the following categories: trials where the target was at least in one of the RFs of pairs with opposite RFs, where the variability correlations averaged on 0.02 ± 0.23; Target trials from neurons with shared RFs, where variability correlations averaged on 0.02 ± 0.25; and Distracter trials from pairs with shared RFs, where the variability correlations averaged on 0.3 ± 0.22.

### 3.4.4 Performance of a simulated random (suboptimal) population on the task

The results of our models performances are largely higher than the behavioral performance of our subjects. This is partially because when recording neurons is done selectively and only neurons that are well responsive to the task are recorded. Not all neurons in the SC populations that contribute to target selection are as responsive as those in our sample. It can be hypothesized that the neurons with better performance must gain larger weights in the process of making a decision, as a result of learning and plasticity, and that the input of neurons whose responses are not highly informative about the task will be ignored. Our results in previous chapters have been based on this assumption. However, it is possible that this assumption is not completely correct. Here, we tried to compose populations that have different
Figure 3-14: Performance of a neural network model as a function of time and variability correlations among neurons with opposite RFs. The average of variability correlations among neurons with shared RF is fixed at 0.2. Length of window is 20ms.
Figure 3-15: Performance of a neural network model as a function of time and variability correlations among neurons with opposite RFs. The average of variability correlations among neurons with shared RF is fixed at 0.2. Length of window is 20ms.
proportions of informative and non-informative cells with regard to our task. We made these populations by randomly selecting different number of neurons in our populations and decreasing their selectivity for the target. This can be done by reducing their responses to target, as the main difference between the responses to target and distractors is their magnitudes. The closest performances to behavioral ones (about 84% correct for feature task, and 68% for the Conjunction task) were observed for a proportion of about 80% of non-informative cells for both the pooling model and the neural network, for the Feature task, with a population size of 10 neurons. For Conjunction task, the proportion of uninformative cells could bring the performance of both models low enough to replicate the behavioral performance of the subjects was about 70-75%, as shown in Figure 3-16 (top).

We expected that introducing uninformative cells to the pool decreases the performance for the pooling model, where all neurons have equal weights in the decision process, but not for the neural network, where the weights of contribution of neurons are adjusted through learning. To our surprise, including non-informative or less informative cells decreased the performance for both models, albeit less so for the neural networks. This could imply the less informative cells are assigned smaller weights in the decision-making than the more informative cells, but not 0 weights. Our analysis confirms this prediction, showing that the weights for the uninformative cells over our trained networks are significantly smaller than those assigned to informative cells.

Increasing the population size to 50, 100, and 1000 neurons, increased the performance of model, for the same proportions of non-informative cells, but this increase was not a linear function of the number of cells. In the case of a 50-cell population, none of the tested proportions of the non-informative cells can bring the results closer to our observations for the feature task, with the ANN model. With the pooled model, a proportion of about 80% could replicate the subjects’ behavior. For Conjunction task, a proportion of about 80% of uninformative cells is required to replicate the subjects’ performance, with an ANN model, and a proportion of about 75% with the pooled model. With a population of 100 neurons,
Figure 3-16: Performance of a pooled winner-takes-all and a neural-network model compared on Feature-Search and Conjunction tasks, as a function of proportion of non-informative cells in the simulated population. Activities are averaged over a 20 ms window centered on 10 ms before saccade. The responses to target were decreases to 10% of their original values, in the non-informative cells. Top: Population size is 10. Bottom: Population size is 50.
the behavioral performance was achieved when about 90% of the pool constituted uninformative cells for the feature task, and about 80% for conjunction. With a population of 1000 neurons, these proportions were about 95% for the feature task and 85% for the conjunction task, using a pool model.

3.5 Discussion

We found that the individual visuomovement cells in intermediate layers of SC don’t encode significant amounts of information about the stimulus in their visual response rates, but that the amount of information encoded in their activity rates increases with time and is maximized around the time of saccade. We found that for most pairs that we recorded, the majority of information that one cell carried about the stimulus type was redundant, and carried also by the other cell. We also found that correlated variability increased the information in our neuronal pairs, regardless of whether these pairs shared their RF or not. However, its positive values among the cells of larger populations with shared RFs, and its negative values among the cells of larger populations with opposite RFs decreased the performance of the two decoders that we used.

The fact that SC cells carry significant amounts of information about the stimulus during different behavioral epochs does not tell us whether this information has emerged in SC or is a reflection of information represented in other areas, passively passed onto it. A comparison of the information content of the individual cells in SC with individual cells in upstream brain areas can give us an idea about this. If SC cells integrate the information available from cells in other areas to make new inferences about the stimulus that is not available from what carried by the individual cells in those areas, then the information content of individual cells in SC must be higher than the individual cells in those areas. On the other hand, if the cells in SC are merely reflecting the information passed onto them, they should at most carry the same amount of information as the upstream area’s individual cells. Assuming that in the process of transferring the signal some noise will be introduced to the passed signal, the information content of the SC cells must be less than the upstream area. We can make such comparison with the reports from FEF (Bichot et al., 2001). While it takes around 7-10 FEF cells to predict the outcome of a trial with an
accuracy of 95% or higher in feature task up to an estimated 40 ms before saccade time, in SC it only takes 2 cells with the same mechanism of decoding (pooled WTA). This indicates that some information emerges in SC that is not directly available in FEF cells. Whether this additional information is obtained by integrating the signal from different cells in FEF or cells from other areas, such as the superficial layers of SC or LIP, cannot be determined from this analysis.

The effects of correlated variability can be different from one brain population to another, depending on the structure of correlations, and the structure of population (Abbott and Dayan, 1999; Averbeck et al., 2006; Ecker et al., 2011). For example, while it has been shown that positive correlations can decrease information in homogeneous populations (Zohary et al., 1994; Sompolinsky et al., 2001), it has been shown that negative correlations can increase the information (Sompolinsky et al., 2001). It has been concluded by Shamir & Sompolinsky (2006) and Abbott & Dayan (1999) that uniform variability correlations cannot limit the growth of information in homogenously tuned populations. While in our population simulations, the variability correlations are randomly selected from a Gaussian distribution with a mean close to what observed our samples, the distribution doesn’t follow the functional distance of the neurons, similar to what these studies have used. Instead, it uses averages of physiologically obtained values for inside and between the two populations corresponding to two different response fields. Therefore, it assumes that the functional distance between the neurons inside a population is not significant. Shamir & Sompolinsky (2006) found out that even non-uniform variability correlations the magnitude of which is dependent on functional similarity of neurons cannot limit the information growth, unless the neuronal population is homogeneous in all of their response properties except their preferred stimulus. Since our sampled neurons have tuning curves of different width or different response magnitudes, this could be a reason why correlated variability did not have a consistent and large limiting factor on our simulated populations.

Generally, the growth of information will be limited if the noise in the system is structured in a way that it can grow linearly with the signal, to keep the signal-to-noise ratio constant, and the signal and noise keep
being overlapped (Shamir, 2014). Moreno-Bote et al. (2014) proposed that the distribution of noise will be overlapping with the signal, if the variability correlations are proportional to the product of derivatives of the tuning curves of the neurons in the population, so whenever that the noise shifts the neural responses in the response space, the shift will happen along the tuning curve, which will make the response to get overlapped with responses to other stimuli. This will happen if the product of derivatives of the tuning curves points in the direction of the larger eigenvectors of the covariance matrix. Our work in chapter 2 explored the signal and variability correlations between the neurons in each pair, with the idea that the directions of the signs of the two will tell us about the impact of variability correlations on the information content of the pair. This can be related to the idea posed above. If the neurons have positive variability correlations for the stimulus range between the two peaks of their tuning curves, the correlations shouldn’t be information limiting. For a pair with opposite RFs, this range covers the whole stimulus range that both neurons respond to, so positive variability correlations should not limit the information for such pair. For a pair with closely similar tuning curves, this covers only a small range of stimuli that both neurons respond to, so for most stimuli the positive variability correlation will be information limiting. Stimulus-modulated correlations with patterns like this seem to be an emergent property of bump attractor models, where the variability correlations for the stimuli within the range between the two preferred stimuli of neurons is different from the variability correlations of the neurons for the stimuli that are either to the left or the right of both preferred stimuli (Pouget et al., 1998). Recently, similar correlations have been found in vivo in PFC (Wimmer et al., 2014). However, the sign of these correlations was not the same as the product of derivatives, most of the time. The pattern observed among our neighboring pairs is similar to this pattern: the variability correlations for the stimuli at the peak of tuning curve (target) are the smallest and often have a negative value in our sample set. The variability correlations for the distracters have positive values. Accordingly, the correlations in our sample set can be expected to reduce the information. However, this was not what we found in our pairs. This analysis only takes into account the effects of shaping of the distribution of noise and signal due to
interactions of correlated variabilities with correlations in tuning curves. It does not consider the stimulus-
specific effects that could arise if the correlated variabilities differ from one stimulus to another. In
chapter 2, we found that correlated variabilities can be different from target trials to distracter trials, and
this could increase the information of the pair.

It has been suggested that the limiting effects of correlated variability on growth of information can be
larger in larger populations (Quiroga and Panzeri, 2009; Ince et al., 2013). Our results found some
limiting effects of correlated variability in the decoding performance of simulated populations, although
these effects were not large enough to account for the behavioral performance of the subjects. A major
limitation of this analysis was that the covariance matrix was not measured over a simultaneously
recorded population, but over pairs, and it was these pair-wise values that were used to simulate a
covariance matrix over a larger population (Roudi et al., 2009).

The use of a decoder has been suggested to be the best way to assess whether the information saturates or
not, even though this comes with the pitfall that the limitation of performance of the decoder can be due
to its sub-optimality (Moreno-Bote et al., 2014; Panzeri et al., 2015). The pooling mechanism in the
pooled WTA model where the less and well informative cells all have equal weights to the final input,
seems to be a plausible mechanism to be at work for our data. Similar results have been obtained in other
works, after adding cells that were less informative about the task (Ince et al., 2013). The ANN that we
have applied here has a binary output unit which could correspond to a downstream area making a binary
decision. This can be an oversimplification if the activity in the downstream area is coarse and not
represented by a binary state (Pouget et al., 1998).

One of the limitations of this work is that we haven’t examined the noise from other areas that are
involved in determining the final behavior, including the areas downstream to SC. This could potentially
account for the low number of neurons required to account for the target choice. Recordings from FEF
during a visual search show that FEF cells activities are also highly informative about the location of a
target, and only a few cells from FEF are needed to fully predict the behavior (Bichot et al., 2001). On the other hand, the receptive fields in both FEF and SC are broad, and the determination of the final location of the goal for saccade on the salience map requires a precision that cannot be afforded by the borders of response field of one neuron. Here, we did not determine the exact coordinates of the saccade goal on the map, and this could have increased the number of required neurons for higher performance rates. Vector summation, winner-takes-all, and Bayesian models have been applied to SC activity to predict the saccade choice, or its metric properties (Van Gisbergen et al., 1987; McIlwain, 1991; Brecht et al., 2004b; Kim and Basso, 2010), however, these studies did not explore the correlations in variability of spike rates of the neurons with each other.

Here, we focused on the spike rates, and not temporal codes. This should not be a big limitation, since the spike rates usually carry the majority of information in a code, and here, the amount of information in the rate codes of an individual cell alone was already higher than the behavioral performance of the subjects.

Finally, we used Shannon information in our analysis, here. Some of the previous works which we have discussed in here have used Fisher information. It has been shown that Fisher information gives a reliable estimate of Mutual information in the populations larger than 200, but not for small populations of a size up to a few tens (Yarrow et al., 2012). We used Mutual Information to analyze our data. It is not clear to us how generalizable is the conclusions of an analytic study based on Fisher information and in the limit of large population sizes, to our study of small ensemble, using Shannon Information.
Chapter 4

Evidence Accumulator or Threshold: the Role of Superior Colliculus in Saccade Executive Decision making

4.1 Abstract
The evidence accumulation models explain the process of decision-making by accumulation of evidence in favor of a decision until the accumulated evidence reaches a certain decision criterion. The stop-signal paradigm requires the inhibition of an already planned movement in a subset of its trials (STOP trials), and the execution of the movement on others (GO trials). It allows for studying the neural processes underlying preparation and execution of a movement. Previous work in FEF has shown that variability in linearly estimated rates of accumulation of evidence in favor of executing an eye movement can explain the variability in reaction times in the GO trials of a stop-signal task, while the decision criterion remains fixed regardless of the reaction times. Here, examining the patterns of activity of superior colliculus (SC) throughout and at the end of the accumulation phase, we show that the variability in linearly estimated rates of accumulation cannot predict the reaction times of the control trials in this task. However, we show that the activity rates at the end of activity growth period of these cells resemble a threshold that can predict the execution of a saccade, and that this threshold is fixed regardless of the reaction times. We conclude that while FEF could be considered as the accumulation unit for the preparation of a movement, SC should be seen as the implementation of a threshold unit that reads the output of the accumulation by FEF and transforms it into an “all or none” response, resembling a step-function transformation that can open a “gate” for execution of the saccade.

4.2 Introduction
Accumulation models assume that decisions are made by noisy accumulation of evidence in favor of one of the alternative choices, until the accumulated evidence reaches a criterion, defined as the amount of evidence needed to generate a response (Glimcher, 2003; Brown and Heathcote, 2005, 2008; Shadlen and
Kiani, 2013; Smith and Ratcliff, 2015; Forstmann et al., 2016). They have had great success in explaining decision making behaviors and their underlying neural processes, since in many brain areas, such as SC, LIP, and FEF, neurons have been found that increase their activity during the decision time in various tasks, until their activity reaches a fixed threshold. Most of these studies have interpreted the increase in the activity of neurons as the accumulation of evidence in favor of deciding for a particular choice, and the surpassing of activity rates from a fixed value as a threshold representing the commitment to that decision (Hanes and Schall, 1996; Horwitz and Newsome, 1999; Kim and Shadlen, 1999; Roitman and Shadlen, 2002; Ratcliff et al., 2003, 2007; Ferrera et al., 2009; Ding and Gold, 2012; Smith and Ratcliff, 2015). While this fixed value has been considered as the threshold for commitment to a decision, it should not be considered as the process for execution of the decision, but as a criterion passing which should be further detected by the downstream areas and passed to motor areas, similar to opening a “gate” that leads to the execution of the decision (Lo and Wang, 2006). Physiologically, a threshold circuit should implement a non-linear transformation of the accumulated evidence that generates an “All or none” response, similar to a step function (Simen, 2012). On the other hand, the assumption of linear growth of activity rates has been suggested to simplify the evidence accumulation models, without impairing the predictions of the model about the behavioral reaction times (Brown and Heathcote, 2005, 2008; Heathcote and Love, 2012). Here, we explore the SC activity during a stop-signal task, with regard to these two attributes.

The stop-signal paradigm involves inhibition of an already planned movement and provides an excellent framework for studying the dissociation between the neural processes underlying the preparation of a movement from those associated with its execution. The uncertainty about whether the stop signal would appear on a given trial or not creates a range of reaction times which are typically longer than the reaction times generated during a task with similar target but without the stop, in both humans (Ozyurt et al., 2003; Åkerfelt et al., 2006) and non-human primates (Stuphorn and Schall, 2006). Therefore, as the subjects perform the task, it provides a range of behavioral measures that can be used to verify the models.
suggested to explain the observed patterns of neural activity in different brain areas. One such successful model is a race model in which a GO process, representing the neural processes underlying the execution of a movement, competes with a STOP process, representing the neural processes underlying the inhibition of response (Logan and Cowan, 1984). This race model can be considered a form of an evidence accumulation model.

Previous research in FEF has shown an increase in neural activity during the control trials of the stop-signal task, representing the GO process in the race model, until the activity reaches a fixed threshold. The variable rates of increase of activity have been used to explain the variability in reaction times, assuming that time of onset for growth is fixed for all trials, and the growth is linear (Hanes and Schall, 1996). The assumption of linearity of the accumulation rate in FEF is in line with the linear ballistic accumulation models (Brown and Heathcote, 2008).

Little is known about how variabilities in linear accumulation rates in neurons of other brain areas can predict the variability in reaction times during this task. Here, we investigate whether the same model can be applied to Superior colliculus (SC). Anatomically and physiologically, SC is a suitable candidate for implementing the threshold mechanisms for commitment to execution of a saccade has been previously suggested to have an activity threshold, surpassing which would generate a saccade. Moreover, it has neurons that increase their activity in a way that resembles the accumulation of evidence (Munoz and Wurtz, 1995; Paré and Hanes, 2003; Ratcliff et al., 2003). Anatomically, it is at the center of a network of connections from the cortex to brainstem (Munoz et al., 2000b; Shinoda et al., 2011), which could enable the transition from the planning of a movement to its execution. Here, we investigate whether the variability of linearly estimated rates of activity growth in SC can explain the changes in reaction times distributions. We further examine whether the patterns of activity in SC resemble the accumulation of evidence in favor of a decision or the “all or none” pattern expected from a threshold unit which transfers the decision variable to the execution unit.
4.3 Methods

4.3.1 Data collection
The data for this work were collected from two male rhesus monkeys (Macaca mulatta; 7-10 kg) received a single surgical procedure, in accordance with the Institute of Animal Care and Use Committee and the Canadian Council on Animal Care, and has been previously described in details elsewhere (Paré and Hanes, 2003).

4.3.2 Behavioral task
The behavioral task is also described in details in Paré & Hanes, 2003. Briefly, 66% of trials (GO trials), after the initial fixation period, the fixation point disappeared with the target appearing at the same time, and the monkey was rewarded for making a saccade toward the target. In the remaining 33% (non-canceled STOP trials), after a delay of a variable length following the disappearance of fixation point, the fixation point would re-appear, instructing the monkey to inhibit the saccade. The monkey was rewarded for keeping fixation for 600 ms after the re-appearance of fixation point (canceled STOP trials).

4.3.3 Data Analysis
Onset of saccade was defined as the time when the eyes velocity was ≥ 20°/s. Trials with more than one saccade were excluded.

Spike trains were convolved with a Gaussian kernel (SD= 10) function to generate Spike Density Functions (SDFs). Threshold was initially defined for each neuron as its average activity over all GO trials at 10-20 ms before saccades onset for comparison with the ROC analysis, and was later modified based on the findings of the ideal criterion from the ROC analysis.

Using a signal detection theory approach, the ideal criterion was evaluated based on the peak of activities for GO trials vs. canceled STOP trials by maximizing the area under ROC curve which represents the probability of dissociating between the two, increasing the rates of true positives and decreasing the rates of false positive, while keeping specificity and sensitivity equal. This ideal criterion was later used to find
the time of threshold, by finding the time point where the difference between the average activity of all
the sampled cells and this value was minimized using a least square method. The ROC analysis was also
repeated by comparing the peaks of STOP trials against values of threshold from the GO trials.

To compare the thresholds and growth rates across trials, the trials were grouped by first sorting them
based on their reaction times and then having each group contain 10 different closest reaction times.
Other binning mechanisms were tried as well, for example, grouping every 11 consecutive trials
regardless of them having the same reaction time or not, after having them sorted based on their reaction
times. However, the different groupings of trials did not substantially change the results. The activity was
averaged in each group along time, after being aligned on saccade onset.

The threshold for each group was initially defined as the average of activity over all the trials in that
group at the 10-20 ms time window before the saccade, and was later modified to a window of 8-18 ms
before saccade onset, based on the results from the ROC analysis. The thresholds calculated for each
group were used to calculate the correlations of threshold and reaction times.

The measure that we used to mark the beginning of the activity growth interval was the time of onset of
growth of activity (TOGA). The simplest approximation for this measure was 110 ms after the onset of
the stimuli, for all cells, based on the observations on when the activity starts the increase the first time,
after the visual activity had dropped in case of visuo-movement cells. In an alternative approach, the time
of onset of activity growth was determined according to (Pouget et al., 2011) using a sliding window
approach, and was defined as the first time point before the peak of activity where the average SDF did
not increase significantly according to a Spearman Rank’s correlation over a 10 ms time window. This
measure was used on the average SDF over all GO trials and was fixed for each cell. The general patterns
of the results did not change between these two alternative approaches.
For the analysis of rates of growth and prediction of reaction times, only activities from GO trials were used. The linear rate of growth was defined as the slope of the linear regression fitting activity rate as the function of time on an interval between the start point of growth of movement-related activity and 18 ms before the saccade. Two estimates of this value were made, once by regressing average of SDFs for each group of trials along all the time points in that interval, and one more time along 10 equally spaced points along the interval. The RT simulation results for these two different approaches were not notably different.

The rates of growth for the bi-linear model were calculated as the slopes of two separate linear fits over two distinct intervals over the activity rates. For each grouped trial, the previous interval was divided into two parts at the point where the 1st derivative of the SDF often suddenly increase, which we call it the “transition point”. The transition point was most clear on the longest trials where the growth of the activity seemed to start with a slow and inconsistent rate, and would suddenly change into a faster rate. The first interval started at the time of onset of growth movement-related activity and ended at the transition point. The second interval started at the transition point and ended at the beginning of previously defined threshold window (18 ms before saccade).

Four different methods were used to find the transition point. Here we just describe one, and present the results for this method. In this method, a hypothetical line was considered that would connect the endpoint of the growth interval (the beginning of the threshold window, 18 ms before saccade onset) to the beginning of the growth interval, that is, to TOGA. The point on the SDF that had the maximum distance from its corresponding point on this line was considered as the transition point. Figure 4-1 shows the averaged SDFs for grouped trials for an example cell, with transition points found by the algorithm described in above.

For each cell, the reaction times were generated by the linear model by dividing the difference between the value of threshold and the value of the SDF at TOGA by the rate of growth, and then adding the
Figure 4-1: The activities of an example neuron in grouped trials aligned on saccade. The red stars indicate the transitions points, where the convexity of SDF on the growth intervals becomes maximal.
TOGA and difference between the threshold time window and the onset of saccade (18 ms). The rate of growth was the only factor that varied from one trial to another, and it was selected from a normal distribution whose mean and standard deviation corresponded to the mean and standard deviation of observed rates of growth for the neuron. The generated reaction times that were negative were omitted. The process was repeated until the number of generated reaction times was equal to the number of behavioral trials for that session. Then the reaction times were sorted. This was called one simulation. For every cell 1000 simulations were generated. For each cell, the results of corresponding reaction times from all 1000 simulations were averaged together, and these averages were reported as the final reaction times predicted by the model.

For simulations of reaction times using the bi-linear model, the time and value of threshold was replaced by those from the transition point, and a fixed period of bursting, calculated as the average time between the transition point and the previously defined threshold window, was added to the reaction time.

A Kolmogorov-Smirnov test was used to test whether the simulated reaction times and the observed behavioral ones belonged to the same distribution for each session. It was also used to test whether the distribution of threshold values for a given cell followed a normal distribution.

To assess the goodness of linear fits, the coefficient of determination ($R^2$) was used, defined as the proportion of the variance in the dependent variable that can be predicted from the independent variable to the total variation in the dependent variable, measured as sum of squares of differences between the predicted data by the model and the mean of observed data divided by sum of squares of differences in the observed data and their mean.

To test whether the slope of a linear regression was significantly different from 0, a t-statistic was used, defined as the slope of regression divided by the standard error of the slope, measured as standard
deviation of the dependent variable divided by the degrees of freedom, divided by the standard deviation of independent variable.

All these past three measures were calculated using a MATLAB Statistical Toolbox (Mathworks Inc.)

**4.4 Results**

We studied the responses of 32 neurons with movement-related activity in SC. Some cells showed a transient burst of activity started earlier than 100 ms after the presentation of the target (averaged at 60.89 ± 12; range: 51-93 ms) estimated as the first point in time after the stimulus onset when the SDF becomes 5 times larger than the non-zero baseline and remains so for at least 10 ms. A rise in activity started after this transient activity, which gradually, although not always consistently, increased over time, followed by a bursting period at 31 ± 8.46 ms before the onset of saccade on average (range: 16-55 ms), estimated using the average of SDFs on the longest 20% of trials and finding a point of time where the 2nd derivative of the SDF becomes an extremum. An example neuron which shows a transient burst of visual activity is shown in Figure 4-1.

As previously shown (Paré & Hanes, 2003), this movement-related activity increased in non-canceled STOP trials and GO trials until a saccade was made. In canceled STOP trials, it increased in the beginning, but was modulated following the STOP signal, so that the maximum activity in these trials is always less than that of GO trials.

For most neurons, the increase in the movement-related activity during the GO trials was consistent over time for short reaction time trials, but not for longer ones. This poses the question whether the rate of growth in activity should be calculated over the whole interval from the first point in time when the movement-related activity starts to increase until the saccade happens.

**4.4.1 Estimating the threshold (validation of threshold estimate by neural activity)**
Assuming there is a threshold that dictates the final behavior, we sought to show that the maximum activity of canceled STOP trials also always falls below the threshold. Physiological evidences (Hanes and Schall, 1996; Pouget et al., 2011) suggest the threshold must be met around 10-20 ms before saccade given that microstimulation of SC can generate saccades with a latency of 8 or 20 ms (Robinson, 1972; Miyashita and Hikosaka, 1996). Moreover, a fixed time of about 10 ms is necessary for the burst neurons in the brainstem to generate a saccade (Scudder et al., 2002), and the OPNs need to pause around 10 ms before the onset of a saccade (Everling et al., 1998).

Paré and Hanes (2003) compared the peaks of activity rates on GO trials with those from STOP trials, to establish a neural basis for distinguishing between the two types of the trials. We averaged the activity of all GO trials of each cell on the 10-20 ms interval before the onset of saccade, and compared this with the maximum activity of canceled STOP trials for that cell. For all cells but one, the average peak of canceled trials remained below threshold (Figure 4-3, Top-left), indicating that the value of threshold may be able to distinguish between the two types of trials as well.

These results were restricted by the fact that our estimate of the threshold was based only on inferred evidences. In order to validate this estimate, we took an additional approach to determine the threshold and then compared the result with this estimate. We used a receiver Operator Characteristics (ROC) analysis to find a criterion to tell the trials apart, and then used this criterion to estimate the threshold.

To estimate the ideal criterion, for each neuron, we found the lowest discharge rate that minimized the number of GO trials with their peak of activity being below that rate, and the number of stopped trials with their peak being above it. For some cells, due to the lack of overlap in the range of values that the peak activity rates of these two trial types could take (see an example in Figure 4-2, bottom panel), a range of such ideal criterions are generated. In these cases we selected the median of this range as the ideal criterion. We then compared the value of this ideal criterion to the threshold that we had estimated.
Figure 4-2: Comparison of distributions of peak of activities from two sample neurons on STOP trials (dark histograms) and GO trials (light grey histograms), and the amount of the overlap between the two groups. For the neuron in the top panel, due to the overlap from the two groups the ideal criterion from the ROC analysis (dark red) cannot distinguish between the two trial types with 100% accuracy. For the neuron in the lower panel, due to complete separation of the responses from the two groups, a range of values for the ROC ideal criterion are possible. We pick the lowest of such values for further analysis (dark red). The value of threshold for each cell, defined as the activity rate on a 11 ms time window centered 15 ms before the onset of saccade on the average of all GO trials is marked by a bright red vertical line.
Figure 4-3: Top-left: Comparison of the average of peaks of activity rates on the STOP trials with values of threshold from each cell. Top-right: Area under the Receiver Operator Characteristics (ROC) curve, distinguishing between the peaks of activities in canceled STOP trials and threshold values on single trials. Bottom-left: Comparison of each cell’s threshold value with the ROC ideal criterion obtained by comparing the peaks of Go and canceled STOP trials. For cells where the two groups of trials are not overlapping at all, a range of ideal criterions are obtained marked by the horizontal line. Bottom-right: The time window (relative to saccade) when the ideal criterion for each neuron becomes equal to its threshold value.
based on physiological evidence (Figure 4-3, Lower left). There was a strong correlation between the two estimates (Pearson Correlation coefficient, r>0.9).

Next, we determined the time that the average activity of the cell on its GO trials reaches this criterion, with regard to saccade onset. For 21 cells, this time happened between 10-20 ms before the onset of saccade, as suggested by physiological evidences. The average activity on GO trials of the other cells reached their ROC criterions at reasonable close time points varying between 25 to 5 ms before saccade onset. The average of these times over the 32 cells was -13.44 ± 5.19 (range: -22 to -6), as shown in Figure 4-3, bottom right panel.

Finally, we tested whether an ROC analysis could dissociate between the average values of SDF at 10-20 ms and the peaks of NOGO trials. The goodness of this discrimination capacity is represented by the value of area under an ROC curve (Figure 4-3, Top right). For 16 cells, this value was larger than 0.95, and for all cells except one, it was larger than 0.75 (average: 0.93 ± 0.07; range: 0.76-1.00). For all the analysis after this section, we excluded this cell.

These observations suggest that for most of these cells a threshold value can be expected to exist which would dictate the execution of a saccade in about 25 ms or less. We next explore whether the change in the average activity of each neuron over this window strongly correlates with the changes in reaction times.

4.4.2 Change of threshold with reaction time
Given the results from the previous section, we redefined the threshold as an 11 ms window centered on 13 ms before the onset of saccade (18-8 ms before saccade onset).

For each neuron, we grouped the trials with each group containing 10 successive reaction times and averaged their activities together along time, with the activities aligned on the time of saccade onset. We then calculated the average activity over a window of 18-8 ms before the saccade for each group and
plotted it against the average of reaction times of trials in that group. One such graph for an example neuron is shown in Figure 4-4 (top panel). The slope of regression line is 0.03 and is not significantly different from zero (t-statistic=0.46, p=0.6), implying that the threshold does not change across different reaction times. For 16 cells, the slope or reaction times with the threshold value was significantly different from 0 (t-statistic, p<0.05). The correlation between reaction times and threshold values was generally weak and the average of the slopes over all neurons was -0.05 (Figure 4-4, middle panel), and was not significantly different from 0 (1-sampled t-test, p=0.4). We examined the distribution of the threshold values to assess whether they followed a normal distribution, indicating a lack of relationship between the reaction times and the threshold values (Kolmogorov-Smirnov test, p>0.5). The distribution of probabilities for this test is shown in Figure 4-4, bottom panel.

We tested whether the slight negativity in the correlation between RTs and thresholds over the population resulted from the fact that the threshold values can be adaptively decreased to decrease the cost of decision-making when the RTs become too long (Drugowitsch et al., 2012; Forstmann et al., 2016). We reasoned that if that is the case, we should observe more negative correlations between threshold and reaction times in sessions where the reactions times are longer on average. Figure 4-5 does not confirm the existence of such relationship. Repeating the analysis with the average reaction times instead of the median for the bottom plot did not change the results.

We tried different centers and lengths of time windows within the 20-5 ms window before that onset of saccade, but this didn’t substantially change the observed pattern in the results.

The lack of a consistent relationship between the reaction times and threshold activity suggests a fixed threshold over the population. We then looked at whether this difference can be explained by the changes in the rate with which the movement-related activity increases over time to reach the threshold.
Figure 4-4: Top: Threshold values for each trial group for a sample neuron (averaged activity on 18-8 ms before saccade onset), as a function of their reaction times. Middle: slopes of changes of threshold with reaction times over the trials groups, for each neuron. Bottom: Probability of a Kolomogorov-Smirnov test for the distribution of the threshold values following a normal distribution.
Figure 4-5: Top: Linear regressions between reaction times and threshold values for all sessions. Red dots indicate the threshold values for the minimum and maximum reaction times in each session. Pink circles indicate the median of thresholds and median reaction times for each session. Bottom: slopes of the regressions of the top panel compared against the mean reaction time in each session.
4.4.3 Change of rates of growth with reaction time

We tested if the changes in growth rate are correlated with the changes in reaction times. We defined the growth rate as the slope of the linear regression fit to the neural activity as a function of time between the onset of growth of movement-related activity and the threshold window. Again we grouped the trials based on their reaction times and analyzed the average activities.

Figure 4-6 (top panel) shows the rate of growth of activity changes for different reaction times for a sample neuron. The slope of regression line over this distribution is negative, indicating that with a decrease in growth rate the reaction time increases. This is in line with a model where the threshold is fixed and the rate of growth determines the reaction time: the slower the rate of the growth of the activity, the longer it takes for the activity to reach the threshold.

The bottom panel shows that there is a strong negative correlation between the linearly estimated rates of growth and reaction times for all 32 neurons (average of Spearman’s rank correlation coefficient: $-0.97 \pm 0.05$; range: -0.8 to -1).

4.4.4 Predicting reaction time from neural data

In order to validate whether a model of fixed threshold and variable rate of growth explains our data, we simulated reaction times for each cell, by first subtracting the activity rate at the time of onset of growth of movement-related activity for each trial from the average threshold, and then, dividing it by a growth rate which was randomly selected from a normal distribution of growth rates with a mean and standard deviation equal to the mean and standard deviation of growth rates of that cell. For each session, we generated the same number of reaction times as the number of trials that were correctly completed in the behavioral task. We repeated this process 1,000 times for each session, and tested if the distribution of averaged simulated reaction times was significantly different from that of actual reaction times.

For most cells the shape of distribution of simulated reaction times looked similar to that of the actual reaction times within that session for more than 80% of the simulated RTs. However, for most cells there
Figure 4-6: Top: Rates of growth for each trial group for sample neuron (the slope of a linear regression over the activity rates of the neuron along time, on an interval between the time of onset of growth of activity and the threshold window), as a function of their reaction times. Bottom: Spearman’s rank correlation coefficient for the reaction times and linear rates of activity growth, for each neuron.
were a few trials that had extremely large reaction times that made the simulated RT distribution to significantly deviate from the actual RT distribution. An example of a cell with a distribution that contains more of simulated RTs that don’t match our behavioral data is shown in Figure 4-7.

Figure 4-8 compares the average predicted reaction times from the model with those observed behaviorally for each session. The reaction times from each distribution are averaged all together for each session and contrasted against each other in the top left panel. The three next panels contrast the two distributions over the 10% shortest (bottom left), 10% longest (bottom right), and the median (top right) of RTs from each distribution. It is clear that the largest deviations between the two distributions are caused by the longest reaction times, as they show the smallest correlation among the three groups (Pearson’s correlation coefficient, r=0.33, compared to r=0.71 for the short and median RTs). Since it was these longest simulated reaction times that created the largest deviation from the behaviorally observed distribution of reaction times, we used their proportion as a measure to determine the failure of the simulation. The percentage of simulated RTs that were longer than 500ms, the maximum accepted value in our behavioral sessions averaged 0.09 ± 0.07 (range: 0-0.3) over the population, as is shown in the following histogram for all cells (Figure 4-9, middle). The proportion of RTs longer than 500 ms was larger than 5% for 21 cells (68%). The proportion of these long RTs was large enough to objectively deviate the distribution of predicted RTs from the distribution of behaviorally observed ones, since a Kolmogorov-Smirnov test showed that the probability of the two distributions being drawn from the same was only 0.04 ± 0.11 on average (range: 0.00- 0.42). Only for four cells, this probability was larger than 0.05. Although the longest 10% of reaction times were responsible for the largest deviations in the simulations, it should be noted that some deviation also happened for the shorter and medium-length reaction times, as is clear from the correlation coefficient value of 0.7 for these groups. Figure 4-9 (bottom) shows the correlation coefficients for every 10 percentile of the reaction times. Since the longest and shortest reaction times are extreme and happen with least frequency, we examined whether the effect remains after omitting them. Omitting the first and last 10 percentiles of simulated and behaviorally
Figure 4-7: Example of a neuron for which the fixed-threshold model with variable rates of growth estimated from linear fits over the activity produces long reaction times (longer than 500 ms allowed by the behavioral limits).
Figure 4-8: Comparison of simulated reaction times from a fixed-threshold model with linearly estimated variable rates of growth and the behaviorally observed reaction times. Each data point represents the (average) RTs for one neuron’s for the specified range of RTs: Top-left: all reaction times for each session are averaged together and represented by a single data point. Top-right: Only median values of RTs from the two distributions are compared. Bottom-left: each data point represents the average of the 10% shortest RTs from each distribution (actual vs. simulated) for each session. Bottom-Right: each data point represents the average of the 90% shortest RTs from each distribution (actual vs. simulated) for each session.
Figure 4-9: Top: Probability of the behaviorally observed RT distribution being the same as the simulated RT distribution. Middle: Proportion of reaction times generated by the model that are longer than 500 ms, for each session. Bottom: Correlation Coefficients obtained for each 10 percentiles of the RTs, as described for Figure 4-8.
observed reaction times from the analysis changed the results only for three cells, as for 24 cells a Kolmogorov-Smirnov test showed that the simulated and observed RTs still belong to distinct distributions.

These results indicate that the fixed threshold model with a variable rate of growth approximated by a linear fit cannot completely replicate the behavioral results obtained from experiments. We examined whether this was because the linear model was not suitable to estimate the rates of growth. The linear estimate produces good fits for the shorter reaction times, but not for the longest reaction times in most cells. For each cell, the goodness of the fit for each trial group was determined by the $R^2$ measure, and then, the correlation between the coefficients of determination ($R^2$) for each grouped trial with its reaction times was examined. Figure 4-10 (top panel), shows an examples of a neuron where the linear fits do not well capture the changes in the rates of growth for longer grouped trials. The bottom panel shows that for all cells, $R^2$ decreased with reaction times, which indicates the linear fits were getting worse for trials with longer reaction times.

After establishing that the linear fit does not provide a good approximation of rates of growth, we were interested in finding another simple approximation. We noticed that the increase in the cell’s activity in the longer trials is not monotonic, but includes an initial slower phase, when the activity sometimes even decreases and then starts to increase again, and a second fast-growth phase when a burst in the activity generates a rate of growth closer to what observed in the short trials. We refer to the point of time when the rate of growth drastically changes as “transition point” from now on (See Figure 4-1 for these points on the grouped activities of an example neuron).

The rise-to-threshold model that we have used here is inadequate, at least partially because its parameters are not estimated properly. We specifically needed to find a better estimate of the rate of growth. We next tried a different estimate of the rate of growth.
Figure 4-10: Top: Example of a neuron where linear regression does not provide good fits to the activity rates for longer grouped trials. Bottom: Spearman’s rank correlation coefficient for the reaction times and goodness of linear fits over the activity rates of grouped trials, for each neuron. Negative values indicate that goodness of linear fits decreased with RTs.
Bi-linear Growth

Based on the observations about the changes in activity growth rate over the time, a model can be proposed in which the activity increases in two phases with two different rates: the first phase has a slower rate of growth, and the second phase includes a period of bursting activity with a high rate of growth. The second phase resembles an “all or none” response, a simple neural implementation of a step function, which could represent the threshold mechanism which determines commitment to execution of a movement. The increase in the activity in the first phase could correspond to accumulation of evidence in favor of the decision towards making a movement.

We have previously shown that the rate of activity at the end of the bursting phase, that is, during the threshold window which we defined before, is fixed and can distinguish between the trials in which a movement was executed and those where the movement was countermanded, and therefore, we can suggest that it corresponds to a state in neural activity that opens a “gate” downstream.

We are now interested to investigate whether slow phase of activity growth in SC corresponds to accumulation of evidence in favor of a decision to execute a saccade, which if surpasses a certain criterion can turn on the switch by initiating a burst process. We therefore asked three questions with regard to the first phase of growth: first, whether the activity rate at the end of the first phase will be able to distinguish between the trials with and without an executed movement. Second, whether the activity rate at the end of this point is going to be fixed across trials with different reaction times. Third, whether the changes in the linearly estimated rates of growth of activity during the first phase would be able to account for the variability in reaction times.

To explore these questions we first needed to quantitatively define the transition point, the point in time where the rate of growth changes from the first phase into the second. We used a few different methods and we show the results for one of the methods that defined the transition point as the point of the
maximal convexity of the SDF. More precisely, we consider a hypothetical line that connects the SDF value at the beginning of the growth interval to the SDF value at the endpoint of this interval. The transition point is defined as the point in time where the distance of this line from its corresponding value on the SDF becomes maximal.

After determining the transition point for each grouped trial, we tested whether the activity rates at the transition points could be considered as a physiological criterion surpassing which would predict the execution of a movement. A comparison of the activity rates at the transition points and the average of peaks of activity rates at STOP trials reveals an amount of overlap between the two (Figure 4-11, top panel), implying that these values cannot be considered as a fixed criterion which can always discriminate between the two types of decisions. To confirm this conclusion, we conducted an ROC analysis between these values and found that an ideal observer will not be able to tell apart these activity rates with probabilities higher than 0.75, for more than 4 cells (average: 0.57 ± 0.16; range: 0.31-0.88; Figure 4-11, bottom panel).

Moreover, we linearly regressed the activity rates for each grouped trial at their transition points with their corresponding reaction times, to test whether these values are fixed for all reaction times. The activity rate at the transition point decreased on trials with longer reaction times for most cells, and unlike what we suggested earlier for the threshold analysis, the changes in these values with reaction times have a negative average of -0.51 which is significantly different from 0 (1-sampled t-test, p<0.001). We examined whether this effect was due to the lower number of trials in the longer reaction time groups, which gives more weight to the contribution from these trials. Repeating the regressions while accounting for the number of trials in each trial group change the negative average of changes to -0.48, and this value was significantly different from 0, too (1-sampled t-test, p<0.001).

We also tested whether the variability in the rates of growth in the first phase could account for the variability in the reaction times. Using a fixed threshold at the transition point and a variable rate of
Figure 4-11: Top: Comparison of the activity rates at the points of transition (threshold*), with peaks of activities in STOP trials. Bottom: Area under the ROC curve for peaks of NOGO trials vs. activity rates at transition points for grouped trials.
growth from the onset of movement-related activity up to that point, and a fixed bursting period, we predicted a distribution of reaction times, and compared them with our previous simulation using the a linear estimate of rates of growth. The results of these simulations were not improved. The proportion of predicted reaction times that were out of the range of behavioral ones was still higher than 5% for 24 (74%) of the cells (average: 0.16 ± 0.18), and the probability of the predicted and observed reaction times belonging to the same distribution, reduced to 0.03 ± 0.14. The assumption of the fixed threshold at the transition point was clearly not valid, since these values decreased with reaction times. We therefore, tested another model where both the threshold and linearly estimated rates of growth in the first phase of growth were variable (with their covariability inferred from the data), and the duration of a burst period was fixed. This model did not improve the results either.

Other methods of finding the transition points did not change the general outcomes of the model with a bi-linear estimate of rates of growth, as well. We explored why this bi-linear model of activity growth did not produce reaction times similar to what found from behavioral experiments. We examined whether a linear fit can capture all the changes in the non-monotonic growth in the first phase. Figure 4-12 shows an example of a neuron for which the goodness of linear fits over the first phase of growth dropped with reaction times. The bottom panel shows that such negative correlation between the goodness of linear fit and reaction times is present for 28 (90% of) cells. Over all sessions, a drop in values of $R^2$ can be observed for the reaction time longer than 250 ms.

4.5 Discussion

We found a fixed threshold over our sampled population and variables rates of activity growth with RTs. However, we also found that linear estimates of rates of activity growth cannot capture the pattern of activity growth in the longer trials, and therefore fail to predict the distribution of RTs generated in the task. We also found that the activity levels at the transition point do not represent a threshold level that predicts execution of a saccadic movement. Over the population of our sample neurons, we found that the
Figure 4-12: Example of a neuron where linear regression over the first phase does not provide good fits to the activity rates for longer grouped trials. Distribution of regression values for $R^2$ values for the linear estimate of rate of growth over the first phase of growth for grouped trials with their reaction times, for each cell. Values of $R^2$ for goodness of linear fits as a function of reaction times, for all sessions together.
activity rate over the threshold window does not vary significantly with reaction times, confirming previous reports from this lab (Paré & Hanes, 2003).

We found that the linear estimates of the rates of growth of neural activity show a decreasing pattern with reaction times. For a few cells (12%), this linear account of changes in the rates of growth could explain the variability in the reaction times. Not all neurons from SC intermediate layers project to the brainstem, and some may show a more linear, rather than burst-like activity growth, similar to what reported in FEF. However, for most cells, the variability of the linearly estimated rates of growth cannot adequately account for the variability in the reaction times and the average reactions times predicted using these estimates are much longer than those observed behaviorally. This is because the patterns of activity growth in our sample are highly non-linear. We observed that the growth period for the longer trials can be considered as the sum of two phases: an initial slow and inconsistent growth period and a second period of bursting activity.

We first assumed that the first slow phase of ramping up activity represents a slow accumulation of a decision variable towards preparing a movement, and the second phase of bursting activity represents a non-linear mechanism for implementing a threshold for movement programming, by producing an “all or none” response (Glimcher, 2003; Lo and Wang, 2006; Simen, 2012). Our expectation was that once the accumulated evidence, represented by the increase in activity rate of the neuron, reaches a certain level, a bursting period is started that represents the same qualities expected from a “threshold step-function” as suggested by Simen, (2012).

We therefore tested another plausible method to estimate more realistic rates of growth of activity, by assuming an early decision criterion before the onset of the bursting activity, and by limiting the estimates of rates of growth of activity to the first, slow phase of accumulation. However, we found that that the values of this newly defined decision criterion cannot distinguish between the trials in which a movement was made and those where the movement was countermanded for most cells. Therefore, the values of neural activity at the end of the slow phase in about half of our SC sample neurons cannot account for the
level of accumulated evidence necessary to trigger a step-function transformation of neural responses in the threshold unit (Simen, 2012). This can be explained if we consider the FEF (Hanes and Schall, 1996), or another brain area, as the accumulator unit, the ramped-up activity of which causes the threshold latch to switch on, after it reaches a certain level (Glimcher, 2003; Lo and Wang, 2006). If so, the FEF activity should reach this critical level at a time before the bursting starts in SC. While a previous fixed threshold has been reported in FEF, it’s been characterized as happening around 20-10 ms before the onset of saccade (Hanes and Schall, 1996), however, in that study earlier times were not tested. In this scenario, the pseudo-ramp-up activity observed in SC should be considered as an incomplete reflection of the accumulation process in FEF resulting from the excitatory connection from FEF to SC, which is not a linear function of the ramping-up activity in FEF and therefore, doesn’t always follow its pattern of increase, particularly in the longest trials.

This could happen assuming the ramping activity in SC is a result of integration of ramping activity from FEF through a post-synaptic spike summation. If the pre-synaptic activity rate is high enough that the time distance between consecutive pre-synaptic spikes is shorter than the time constant for the post-synaptic receptors, such as it could be in the shortest trials, the integration could cause the post-synaptic activity resemble the pre-synaptic one. However, if the pre-synaptic activity rate is not high enough, such as it could be on the longest reaction times, the post-synaptic potential could fall back to its resting levels, before the next spikes arrive, and therefore no substantial integration would happen (Wong and Wang, 2006; Standage et al., 2014). Despite the initial absence of a perfect integration of FEF activity, the bursting activity in SC intermediate layers can still happen when the SC neurons are released from local and higher order GABAergic inhibitory signals. Once released from such inhibitions, the local excitatory networks and the NMDA receptor activation will be sufficient to generate bursting activity in SC intermediate layers (Saito and Isa, 2003). For example, a model replicating a reaction-time version of the motion-direction task, used burst neurons in SC to account for the threshold mechanism for the read-out of the decision variable. In this model the SC neurons received excitatory input from cortex and inhibitory
input from basal ganglia. The excitatory neurons in SC also sent excitatory recurrent connections to themselves and slow excitatory connections to SC inhibitory neurons, from which, they received inhibitory connections in return. The excitatory neurons in SC only produced a burst when their cortical input exceeded a certain threshold. Shorter reaction times were generated by inputs higher than threshold level, which affected the latency of the burst, but not its shape or amplitude. The slow connections from these neurons to inhibitory neurons in SC would ensure their activation in a fixed time after the onset of burst, which ended the burst in a stereotypical fashion (Lo and Wang, 2006). This model is not dependent on the build-up activity of the SC neurons in order to generate the burst, and therefore suits our results. Other variations of the same excitatory-inhibitory interactions have been applied to model the bursting activity in SC as well. For example, another model has used both the cholinergic input from build-up neurons and input from NMDA-type synapses, along with inhibition from mesencephalic reticular formation and inhibitory neurons in SC to generate the burst (Morén et al., 2013).

The fact that a release from the inhibitory input is necessary for the beginning of the bursting activity is in line with the observation that the first phase of the growth period in the longest trials sometimes includes short intervals where the growth is negative. Such negative growth intervals could be the result of inhibition from higher order areas, as predicted by the blocked input model (Logan et al., 2015), reflecting the inhibition that the brain can exert to bias the race between the go and stop processes, in order to lengthen a trial in anticipation of stop signal, during a block of trials where the probability of appearance of stop signal is not zero. Empirical studies have identified a network of supplementary motor area in non-human primates (Stuphorn and Schall, 2006), and premotor cortex, inferior frontal cortex, and basal ganglia such as striatum in humans to be involved in inhibiting the go process in trials where the response was stopped successfully (Ridderinkhof et al., 2004; Aron et al., 2007; Swick et al., 2011; Jahfari et al., 2012; Zandbelt et al., 2013a, 2013b). Some of these areas are also involved in proactive inhibition of the GO process in blocks of trials where the probability of appearance of the stop-signal is larger than zero (Chen, Scangos, & Stuphorn, 2010; Jahfari, Stinear, Claffey, Verbruggen, & Aron, 2010; Zandbelt,
Bloemendaal, Neggers, et al., (2013). Since SC receives inputs from many of these areas, the periods of negative growth in its activity rate may be explained by the inhibitory inputs from them. This explains the finding that our approach to estimate the linear rates of growth only over the first phase of growth did not improve the distribution of predicted reaction times. In fact, the proportion of the predicted reaction times longer than 500 ms slightly increased, when we calculated the rate of growth only over the first phase. The reason for this could be that the ramping up of activity is not completely linear even in the first phase of growth, at least in longer trials, but it includes intervals of negative growth.

We also found that the activity rates of most cells at the transition points decrease with reaction times. Over those cells for which these values are larger than the average of peaks of activities on STOP trials (that is, those cells for which these values can be assumed to be the criterion for the decision) the decrease was even more prominent on average over the population. Therefore, even if the activity rates can be considered the decision criterion in some cells, they do not represent a fixed criterion which surpassing which could open a gate to execute a movement, regardless of the reaction time. Dynamic thresholds have been observed before in which the decision threshold decreases with decision time, as an urgency signal arises for the brain to take an action (Rapoport and Burkheimer, 1971; Busemeyer and Rapoport, 1988; Ratcliff et al., 2003; Ditterich, 2006; Drugowitsch et al., 2012; Shadlen and Kiani, 2013; Forstmann et al., 2016). If the activity rates at the transition points could be considered as the decision criterions, a similar phenomenon could explain why they dynamically decrease with the reaction times.

The fact that the activity rates in SC cells at the onset of the burst cannot predict the behavioral outcome on a trial-by-trial basis, along with the fact that patterns of activity growth in the period before the burst on the longest trials does not consistently reflect an accumulation process for the evidence towards a saccade execution decision, questions the role of SC as an evidence accumulator for an executive decision, at least during a task that requires some level of proactive inhibitory control. On the other hand, the activity growth rates can predict the shortest reaction times with great accuracy. This may suggest a role for SC as an accumulation unit in the context of simpler tasks where no proactive inhibition is
required. Future work can compare the predictability of reaction times from the rates of activity growth in SC during two tasks that do and do not include proactive inhibitory control to answer this question.

The fact that the activity rates during the burst period at a fixed window time before the onset of saccade can predict the outcome of individual trials with reliable accuracy suggests the role of a threshold mechanism for SC. How can one determine that SC is a threshold unit? After all, the FEF also shows a burst like activity which has been taken as an evidence towards the FEF being the threshold unit (Simen, 2012). However, the transitions from the low to high activity rates are much slower than SC, and do not completely resemble the transient step-function-like changes in activity that should be expected from a threshold unit. Moreover, if there are feedback connections from the threshold unit back to the accumulator unit, the accumulator unit will show a burst-like activity as well (Simen, 2012). Ascending pathways from SC to FEF have been reported (Sommer and Wurtz, 2002, 2003, 2004), although they have been reported to decrease rather than increase the pre-saccadic activity in FEF (Berman et al., 2009). Due to these feedback connections and the general complexity of the network, the exact roles of SC and FEF might not be able to be completely disentangled. However, the role of SC in reading out the decision variable and passing that to the brainstem is certain. In non-ablated animals where the inactivation of SC has not found a chance to be compensated through post-lesion neural plasticity, FEF does not seem to be able to bypass the SC for creating accurate saccades (Hanes and Wurtz, 2001).

Our model uses data from single cells to replicate a behavior that is most probably generated by coordinated activity of a population of cells. In this model, we assumed that the threshold and the activity level at the time of onset of growth do not correlate with reaction time. However, for half of our sample, the assumption of a fixed threshold was an oversimplification, which we justified by an additional assumption of cancellation of threshold variability over the population. Therefore, it would have been more appropriate for our model to be implemented at the population level, instead. However, using a population’s data introduces other assumptions about the decision rule in the population, and the rates of correlation among the neurons activities (Zandbelt, Purcell, Palmeri, Logan, & Schall, 2014), which one
cannot address without simultaneous recordings from the population. Moreover, previous work shows that models that use data from ensembles of neurons can be reduced to a one-dimensional model similar to a diffusion model (Roxin et al., 2008; Forstmann et al., 2016). Therefore, the use of single neurons for implementing the decision model is not unjustified.
Chapter 5
General Discussion

Behavioral decisions constitute sequential stages of sensory processing, perceptual decisions about categorizations of stimuli based on their features and the goals of the task, preparation of a movement, and execution of the movement. Superior Colliculus has a role in guiding the saccadic behavior. During a task with multiple stimuli and one potential target, SC populations which respond to different stimuli engage in a process of decision making about the goal for a future saccade. During a task with one stimulus and a possibility for a need to cancel a saccade, SC populations responding to that stimulus engage in a process of decision making about the execution of the saccade. Many details of each of these processes have been uncovered in the previous works. Here, I examined novel aspects of involvement of SC in each of these stages.

In chapter 2 I replicated previous work which has established the role of individual neurons in SC in selection of a target for a saccade. Additionally, I looked at how the interactions between pairs of neurons in SC contribute to this process of target selection. I showed that the variability correlations between the neurons with shared response field cannot distinguish between a target and the distractors during the epoch of visual processing, but they do so when the movement is about to be executed. On the other hand, the variability correlations between the neurons which are competing against each other in order to generate a movement towards a stimulus in their response fields can distinguish when the target is in the RF of one of the neurons from when the target is in RF of neither of them, much earlier in time. This finding, that a competition between neurons with opposite RFs in SC can have a larger and earlier role in target selection than the collaboration between neurons with shared RFs does, was further confirmed by examining the cross-correlations between neurons spike timings across different time lags.
In chapter 3, I examined how the information that each individual cell carries about the stimulus in its RF changes along time. Individual cells in SC did not carry significant amounts of information about the stimulus during the visual epoch, implying that they don’t have a major role in sensory processing stage of the decision. However, the information in individual neurons or pairs of them quickly increases with time, confirming the role of SC neurons in target selection for the purpose of saccade planning. I explored what mechanisms of decoding could be employed by SC populations to replicate the behavioral outcomes by the subjects in the task. I also investigated the effects of variability correlations, and inclusion of non-informative cells in the process of target-selection on performance of the populations, and how these effects change as the size of the population increased.

In chapter 4, I explored the involvement of SC in the last stage of the decision process. I showed that SC implements a biophysical threshold mechanism, surpassing which triggers a movement to occur, through the activation of motor neurons downstream to it, and that the values of this threshold is fixed over the population regardless of the reaction times. I also showed that a linear account of accumulation of evidence cannot explain the behavioral results observed in the task, and therefore, suggested that SC should be observed as the circuit where a step-like transformation of accumulated evidence into a threshold switch is implemented. Further, I suggested that it should not necessarily be considered as the area where the accumulation of evidence itself happens, at least in a block of trials where the probability of stop-signal appearance is not zero, and therefore, at least some level of proactive inhibition exists.

This conclusion may first seem paradoxical to my conclusion from chapter 2 and 3, given that in there, I suggested a role for SC individual neurons and the interactions among them in accumulation of evidence that prefers selection of a particular stimulus as the target for a saccade. The key point in resolving this is the distinction that we made earlier between the processes underlying the “decision to” execute an action, and those about “decision that” which particular stimulus should be selected. While chapters 2 and 3 suggest a role for SC in accumulation of evidence for decisions of the latter type, our findings in chapter 3
casted some doubt on the role of SC as an accumulation unit for decisions of the former category. Future work needs to examine whether the patterns of accumulation in SC reflect both the target selection process and the GO process, during a stop-signal paradigm with multiple alternative targets.

In chapter 4, I suggest that a possible reason for the lack of a perfect integration of FEF accumulative activity in SC may be the inter-spike time intervals in FEF spike trains being larger than the time constant for the post-synaptic receptors in trials with longer reaction times. Additionally, I suggest the inhibition from higher order areas as another explanation for the lack of such perfect accumulation in SC. During our version of visual search task, the requirement of cancelling an already planned movement does not exist, and therefore, the inhibitory inputs from higher order brain areas will not necessarily exist in a RT-dependent manner. Moreover, the accumulation of evidence in SC about target selection may be the result of input from SC sensory areas, and therefore, not fully dependent on integration of the evidence accumulation process in FEF. Therefore, the lack of perfect integration of activity in SC during the longest trials of the countermanding task does not directly imply that a similar observation should be expected during the longest trials of a visual search task.

A distinction between an accumulation unit and a threshold mechanism needs to be made clear. In most of the literature, an assumption has been made that once the accumulated evidence reaches a particular value, that is a particular threshold, a decision is made. However, explicit mechanisms for reading this threshold are rarely offered. A threshold mechanism needs to be able to turn a linear function of accumulation into a step function with two states of on or off, which can stop or trigger motor neurons from generating a movement, or to do it, correspondingly. When the accumulation of the evidence is still going on, that is, while the preparation and planning for the movement is still happening, the switch needs to remain off. It should go on, only when a commitment to a decision is made. The implementation of this switch, in the neural circuits, can happen through a bursting mechanism that increases the activity level to a much higher, fixed rate of activity, in an infinitesimally short period of time, similar to what a step
function does. What triggers the switch to turn on is the activity level at the accumulation unit crossing a criterion. But for this to happen, the accumulation unit does not have to be located in the same circuit as the switch is implemented, although this is a possibility (Lo and Wang, 2006; Simen, 2012).

Whether due to accumulation of evidence in favor of the execution of the movement beyond a particular criterion in SC or another area such as FEF, when the switch in SC is turned on by the bursting activity, it will disinhibit the omnipause neurons in the brainstem, while activating excitatory burst neurons, which send their inputs to motor neurons in nuclei such as abducens (Sugiuchi et al., 2005; Shinoda et al., 2011). We suggest that a long lasting bursting activity in SC is required to overcome the inhibitions that the OPNs exert on the EBNs, and therefore a short, transitory rise in the activity to the rates equal to or higher than maximum activity rate at the threshold does not suffice for triggering the movement. This may explain why in some tasks, the visual activity can be higher than the saccadic activity, without triggering a movement (Jantz et al., 2012).

Our work in chapter 2 and 3 involved a task which included a decision about the selection of a target, followed by the execution of an action in most trials. We did not explore whether the time of discrimination between the stimuli by the SC neurons activities could predict the reaction times of the subjects, or whether the activity levels at these times were fixed for all reaction times. Experiments in SC with other two-alternative tasks suggest that this could be the case (Ratcliff et al., 2007). In FEF, the reaction times during a similar task could be accounted for by the activity of visually responsive neurons, only if the onset of accumulation is gated by a mechanism which avoids the activity during the visual processing phase from accumulating as part of the evidence towards a decision (Schall, Purcell, Heitz, Logan, & Palmeri, 2011).

In chapter 2, we used the shape of CCGs to make inferences about the source of observed temporal correlations in our data. Modelling work can provide further insight into the possible mechanisms underlying the emergence of the correlations. For example, On the other hand, some works have
suggested that with increasing the firing rate and variability of the input layer, without changing the input correlations, the correlations in the output layer increase (de la Rocha et al., 2007; Shea-Brown et al., 2008). Our findings do not support this scenario, because during the saccade epoch for target trials, when the firing rate is at its highest, the correlations decreased for our pairs with shared RFs. This might indicate that the inputs that give rise to these correlations in SC are not correlated themselves. One work suggests that coarse coding in networks with recurrent connections gives rise to correlations in the output layer that have a specific distribution as a function of stimulus condition and the distance between the preferred stimulus of the neuronal pairs. The patterns observed for these correlations are independent from the strength of the recurrent connections (Pouget et al., 1998). The results of this work resemble our observations for the pairs with shared RFs responding to the target trials, where the rate variability and temporal correlations both decrease. A possible mechanism for this is suggested to be the dynamic changes in synaptic strength which change the ratio of excitatory and inhibitory inputs. Inhibitory inputs are suggested to control the integration time window for the excitatory input in the post-synaptic neuron, and regulate spike timing, which can lead to synchrony. Removing the inhibition can change the ratio and interaction between these inhibitory and excitatory inputs and reduce the synchrony (Renart et al., 2010; Sippy and Yuste, 2013; Treviño, 2016). This scenario can more plausible be applied to our observations since the changes in inhibitory and excitatory inputs can also explain the generation of the bursting activity during this epoch.

We did not investigate the interactions of SC neurons during the process of making a decision about executing a saccade. However, we found that the interactions among neurons in the same population which respond to the same stimulus are generally weak both during the process of selection of the target and execution of the saccade. Since the interactions among neurons belonging to the same pool were weaker than those among to competing pools, one may suggest that the selection process most likely relies on inhibitory processes that suppress the activity of neurons in competing populations. However, after the selection of target, the competing pools are silenced and do not participate in the decision
process. Therefore, the execution of saccade will be left to be completed by a number of neurons which did not show strong interactions in previous stage. It remains to investigate what is the necessary number of neurons in SC to open the gate at the brainstem, and the extent of the role that spike synchrony may play in this.

Single neuron activities in many brain areas have been shown to be able to initiate a movement or change a network’s behavior. For example, in somatosensory and motor cortex, single neurons have been shown to trigger behavioral responses (Brecht et al., 2004a; Houweling and Brecht, 2008). Single neuron activity in visual or somatosensory cortices has been shown to be able to change the cortical states from slow-wave to rapid-eye-movement sleep and vice versa (Li et al., 2009). A single spike by a single neuron in rat barrel cortex can emit 28 spikes in postsynaptic neurons and change the behavior of the local network (London et al., 2010). In SC, studies that stimulate a single cell to measure the changes in behavior are still to be done, however, micro-stimulation studies have been done frequently. For caudal neurons it has been found that a 500 ms train of 0.3 ms pulses with a rate of 300 pulses/s and a current strength of 15-20 µA, can trigger eye movements in head restraint animals, on 50% of trials (Paré et al., 1994). While it is not straightforward to estimate the number of neurons stimulated by these currents, it has been estimated that the number should be of the order of 10s or 100, and it can be safely assumed that it is more than one, as it is estimated that these currents cover a range of 1 to 2 mm (Paré and Guitton, 1994; Tehovnik et al., 2006).

The number of neurons required to encode the maximum possible information about the location of the target could be as low as 2 around the saccade time, as estimated in chapter 3. Our additional analyses (not reported in that chapter) showed that even for an 8-stimulus model, less than 5 neurons in each corresponding population were required to predict the location of the target among the 8 possible locations. However, this number simply reflected the number of neurons necessary to instantiate the perceptual decision variable, and not the number required to execute the decision, or to encode the metrics.
and kinematics of the saccade. Additional work needs to address the required number of neurons for these processes.
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