TARGET PROFITABILITY IS REPRESENTED IN THE MONKEY SUPERIOR COLLICULUS DURING VISUOSACCADIC FORAGING

by

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Abstract

Behavioural choices of animals as they acquire resources in the wild are well characterized by foraging theory; however, the neural mechanisms underlying these behaviours are not well understood. The goal of this thesis is to understand the brain mechanisms involved in selecting and executing such foraging behaviours. To do so, rhesus monkeys performed a novel visuosaccadic foraging task while we recorded the activity of single neurons in the intermediate layers of the superior colliculus (SC_i). An important innovation of this task is that both target profitability – the measure of value in the simplest case of foraging theory – and saccade choice are measured separately. We hypothesized that target profitability is represented in the SC_i in addition to its well characterized role in saccade planning and preparation.

Visual Foraging Task: Monkeys harvested coloured dots representing prey items by fixating them for a pre-specified handling time. On each trial, multiple prey are presented, sharing identical physical attributes except that each was one of three colours. All prey of the same colour shared the same profitability [Profitability = reward magnitude (ml)/handling time (s)]. According to foraging theory, intake of reward is maximized if prey are selected in descending order of their profitability. Indeed, we found subjects gradually approached optimal efficiency. We computed an index of the relative subjective profitability of each prey colour, which compared the rank order with which monkeys chose prey of each colour.

This subjective index of profitability was then compared to concomitant SC activity attributed to the prey item in the neuron's response field (RF). First, we found that the amount of SC activity reflected the subjective profitability of the RF targets, and established that this effect was not simply a result of saccade goal planning. Second, profitability information remains dominant throughout the handling period until reward delivery, after which activity also became

selective for upcoming saccades. Together, our results highlight the prominent role of target profitability in shaping SC_i activity. We propose that profitability information in the SC_i may play an important role in resolving competition between numerous target representations to choose the next saccade goal.

Co-Authorship

Dr. Michael C. Dorris was the principal investigator for the studies described in this thesis. Both Dr. Dorris and I were involved in the planning and implementation of the experimental protocols. I was solely responsible for animal training, data collection, and analyses contained in this thesis. I produced the first draft of this thesis and subsequent drafts involved the editorial submissions of Dr. Dorris.

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I would also like to thank Dhushan Thevarajah, my work-til-2am and matlab-learning buddy. You are always the first person I look for to go through my thesis, rescue me when I lock myself out at night, or entertain me when I get bored at a party. I admit: you are the life of the lab. Now can I have my squash racquet back please? And my stuffed tuberculosis (whom you hid in the ceiling) wants an apology!

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Chapter 1

Introduction

Obtaining an adequate amount of resources in a limited amount of time is essential to the survival of all living organisms. Often, we must choose between several options that yield varying amount of reward given varying degree of time commitment. For instance, a squirrel searching for food in a forest may simultaneously encounter several options that it can eat. How does the squirrel decide which to choose first: the acorn, which has a large edible seed but takes significant time to crack open, or the sun flowers seeds, which are individually faster to open but give a smaller caloric reward? To study how animals extract resources in the wild, behavioural ecologists have developed foraging theory, which outlines critical variables and optimal behavioural strategies across a variety of environmental niches (for review see Stephens and Krebs 1986). While behaviour is well characterized by foraging theory in the natural environment, the neural mechanisms underlying the decision processes leading to these behaviours are poorly understood. Therefore, the goal of this thesis was to understand the brain mechanisms involved in selecting the simplest of such foraging behaviours: when there is a trade-off between two decision variables – time and reward.

1.1 VISUOSACCADIC SYSTEM AS A MODEL SYSTEM TO STUDY DECISION MAKING

We used a new visuosaccadic task to elicit foraging behaviour in monkey subjects. Investigations concerning the neural basis of decision-making have largely focused on the visuosaccadic system for a number of practical reasons. All primates have a specialized region on their retina known as the fovea, which offers the highest visual acuity (Leigh and Zee 2006). Primates extract detailed visual information from their surroundings by making ballistic eye-movements, called saccades, to align their foveae on different objects of interest throughout the visual field. Some have likened the pattern of saccades to foraging for visual information in our environment (Hutton, 2008, Chi et al., 2007). Moreover, deciding when and where to look is the most common overt choice that primates make, occurring approximately three times every second. These visuosaccadic decisions play a consequential role in everyday life. For example, a human driver must make many saccades to be able to watch the road ahead, identify the traffic light above, and read road signs off to the side accurately. It has been proposed that suboptimal decisions by novice drivers on where to look while driving may account for the high rate of vehicular accidents amongst this group compared to more experienced drivers (Fisher et. al., 2006; Underwood, 2007). In addition to obtaining information, gaze is also important for controlling other effectors, such as when manually moving an object from one location to another (Johansson et al., 2001).

The visuosaccadic system has a number of features that make it ideal for studying neural mechanisms involved in decision-making. First, saccades are simple movements.

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Their simplicity can be attributed to the spherical nature of the eyeball, a minimal amount of inertia, the lack of external load involved in eye movements, the stereotypical nature of saccades, and the fact that saccades are controlled exclusively by three pairs of antagonistic muscles (Wurtz and Goldberg, 1989). Second, the neural circuitry involved in processing visual input and those controlling motor output are some of the best-understood processes of the nervous system, making the visuosaccadic system a good candidate for studying the decision-making that links sensory input to motor output. Finally, eye-movements can be measured both accurately and non-invasively.

1.2 VISUAL AND NON-VISUAL VARIABLES INVOLVED IN VISUOSACCADIC DECISION MAKING

Two approaches for studying visuosaccadic decision-making based on sensory variables are the motion discrimination task and the visual search paradigms. In motion discrimination tasks, subjects are presented with a display of randomly moving dots. A subset of these dots moves coherently in one direction and subjects are rewarded for making a saccade towards one of two possible saccade targets contingent upon the dominant direction of dot movement. Various brain regions typically associated with saccade control show modulation of activity during the motion viewing epoch that is dependent upon the percentage of dot coherence (Lateral Intraparietal Area (LIP): Kiani and Shadlen, 2009; Roitman and Shadlen, 2002; Frontal Eye Fields (FEF): Kim and Shadlen 1999; Superior Colliculus (SC): Horwitz and Newsome, 1999; Horwitz and

Newsome 2001). These studies have been influential in establishing the model that a decision is made based on an accumulation of sensory evidence in visuosaccadic brain regions for one direction over the other. In support of this model, if a subject is unexpectedly given the chance to, for a smaller reward, opt out of making a decision, the subject is more likely to choose this opt-out option when typically ambiguous visual evidence fails to conclusively bias LIP activity one way or the other (Kiani and Shadlen, 2009).

A second approach to study visuosaccadic decision-making is visual search tasks. In a typical visual search task, multiple visual stimuli are simultaneously presented, one of which differs from the others by some physical attribute (e.g. green target among red distracters). The odd stimulus is the target to which subjects must make a saccade to obtain a reward, while all other stimuli are distractors to be ignored. Across a number of saccadic brain regions, neuronal activities have been shown to evolve over time to discriminate whether the stimulus in the neuron's receptive field is a target or a distractor (LIP: Ipata et al., 2006; Buschman and Miller, 2007; Thomas and Paré, 2007; FEF: Thompson et al., 1996; SC: McPeek and Keller, 2002; Keller et al., 2005; Shen and Paré, 2007). Neurons in these brain regions are believed to integrate information from different feature maps, each of which encodes a single feature dimension (e.g. colour, shape, etc). The result is saliency maps: topographically organized neurons whose activities represents the salience, or distinctiveness, of objects in the visual world independent of the particular feature that it possesses (for a review see: Fecteau and Munoz, 2006;

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Kusunoki et al., 2000; Thompson and Bichot, 2005). Potential targets compete on this saliency map in a winner-take-all type contest (Koch and Ullman, 1985; Standage et al., 2005) to guide attention and saccades (Thompson and Bichot, 2005).

Aside from the physical properties that distinguish targets from distractors, saliency can also be affected by non-visual variables based on the goals and prior knowledge of the viewer (but see: Fecteau and Munoz, 2006). Some common non-visual variables that can be easily manipulated in a laboratory setting include reward magnitude, reward probability, and the product of the two, known as expected value. These factors have been shown to affect behaviour, such as by biasing choices and error rates (Collier, 1982; Gmeindl et al., 2005; Koval et al., 2004; Milstein and Dorris, 2007; Takikawa et al., 2002b; Tolman, 1932). In the brain, these variables modulate baseline activities in a number of brain regions, such as the basal ganglia, posterior parietal cortex, prefrontal cortex, and superior colliculus (Barraclough et al., 2004; Dorris and Glimcher, 2004; Ikeda and Hikosaka, 2003; Inoue et al., 1985; Kobayashi et al., 2002; Leon and Shadlen, 1999; Platt and Glimcher, 1999; Sato and Hikosaka, 2002; Sugrue et al., 2004; Tehovnik et al., 1999; Watanabe, 1996; Watanabe et al., 2002).

Finally, timing also plays an important role in decision making. One prominent example is temporal discounting, the tendency to assign greater profitability to immediate rewards compared to later rewards, which has been observed both in humans (Crean et al., 2000; Kable and Glimcher, 2007; Kirby and Marakovic, 1996; Richards et al., 1999) and animals (Ainslie, 1974; Logue, 1995; Rachlin, 1995a; Rachlin and Green, 1972). In

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fact, activity in the FEF and LIP fire more strongly following a cue for a short delay to reward, in a manner similar to the increase in activity following a cue for a large reward (Louie and Glimcher, 2010; Roesch and Olson, 2005).

Neural correlates of time estimation are typically represented as a monotonic decrease or increase in activity during delay periods between stimuli presentations (for a review see: Durstewitz, 2004). The rate of increase or decrease adapts to changes in the length of delay (Thevarajah et al., 2009). Furthermore, this differential rate of change between short and long delays in the posterior parietal cortex during an interval time discrimination task is related to the monkey's ability to discriminate interval times (Leon and Shadlen, 2003).

Although numerous studies have examined how each of the non-sensory variables contributes to decision making, these variables are often only manipulated in isolation (but see Milstein and Dorris, 2007). In the real world, choices are often not this simple because they may involve multiple options with varying amount of reward and tradeoffs. Here, we used a foraging theory framework to examine how the brain combines information from two dimensions, reward magnitude and timing, to efficiently guide saccade choices.

1.3 THE ROLE OF THE SUPERIOR COLLICULUS IN SACCADE SELECTION

Specifically, this thesis focused on the neurons in the intermediate layers of the Superior Colliculus (SC_i) to study the combined effect of reward magnitude and timing.

The SC is a bipartite laminated structure located on either side of the midline in the dorsum of the midbrain, each layer topographically organized in a retinocentric map of the contralateral visual field (Robinson, 1972; Schiller and Stryker, 1972). The three superficial layers respond to targets presented in a specific part of the visual space relative to the fovea that defines their response field. Neurons in the four deeper layers tend to exhibit dual sensory and motor responses directed to their response field. As this thesis aims to examine how particular saccades (motor) are selected from multiple visual targets (sensory), we focused our analysis on the intermediate layers of the superior colliculus (SC_i).

Neurons of the SC_i receive many signals from upstream regions (Hikosaka, 1989; Paré and Wurtz, 1997; Segraves and Goldberg, 1987) that provide inputs related to visual, reward, probability, time, attention, memory, and other context-dependent factors (Fig. 1) (Brody et al., 2003; Buonomano and Karmarkar, 2002; Coe et al., 2002; Ding and Hikosaka, 2006; Durstewitz, 2004; Hikosaka et al., 2006; Kobayashi et al., 2002; Leon and Shadlen, 1999; Matell and Meck, 2004; Platt and Glimcher, 1999). Importantly for the purpose of our study, information of reward and time are also observed in neurons of the SC_i (Reward magnitude: Ikeda and Hikosaka, 2003; Time: Thevarajah et al., 2009), therefore giving the SC_i the necessary information for selecting appropriate saccade targets.

Increasing evidence has been found to suggest that neurons of the SC_i are involved in selecting saccade vectors, instead of simply relaying decisions made

upstream. Studies involving temporal inactivation and sub-threshold stimulation of the SC confirmed a role of the SC in target selection (McPeek and Keller, 2004; Thevarajah et al., 2009). The SC_i may then send saccade commands directly through its connection downstream to the burst generator located in the reticular formation (Rodgers et al., 2006), which subsequently activates oculomotor neurons. Alternatively, the SC_i may influence eye movement indirectly, through feedback connections to the frontal eye fields (Sommer and Wurtz, 2004a; 2004b) or basal ganglia (McHaffie et al., 2005). Therefore, the SC_i may be the last site along the visuosaccadic circuit where activity could represent selection processes without necessarily resulting in an eye movement (see omni-pause neuron in Fig. 1).

In summary, the wealth of input from upstream structures combined with the proximity to motor output makes the SC_i a good candidate for combining sensory, reward, and time information for choosing specific target from multiple options in a foraging environment.

1.4 FORAGING THEORY

Foraging Theory was first proposed in 1966 to mathematically describe feeding behaviour in animals using the assumption that animals behave to maximize individual calorie intake per unit time (Emlen, 1966; Kamil et al., 1987; MacArthur and Pianka, 1966). Foraging theory models can be divided into two main classes (Stephens and
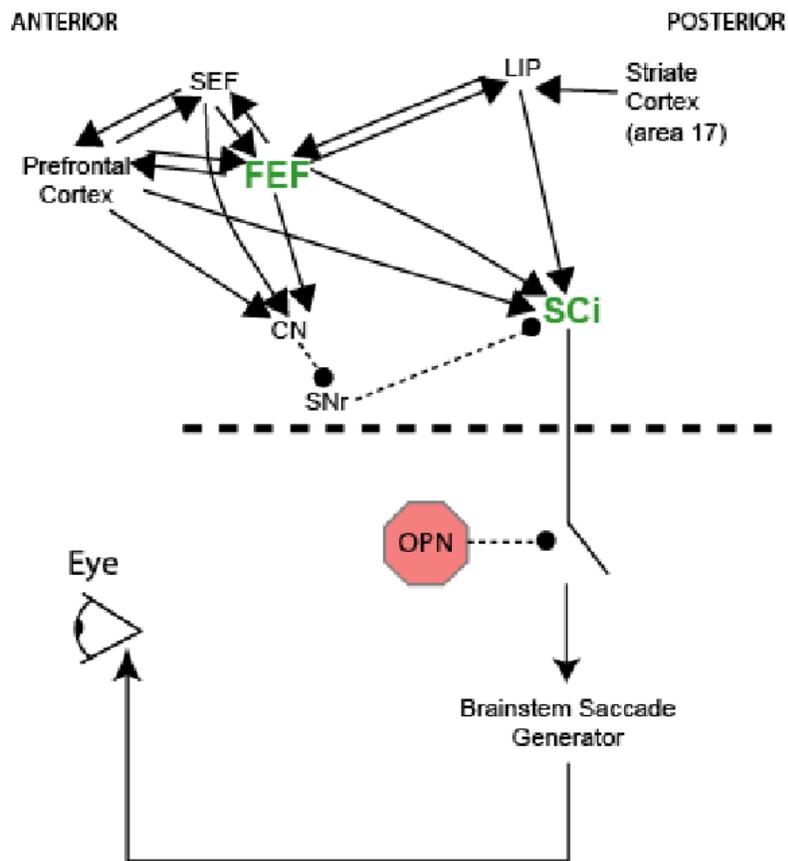
Figure 1 Schematic of major brain regions and connections involved in controlling saccadic eye movements.

Solid lines represent excitatory connections. Dashed lines represent inhibitory connections. The horizontal dashed line demarcates the transition to the saccade generating circuitry in the brainstem. The powerful inhibition exerted by the omnipause neurons (OPNs) prevents upstream premotor activity from triggering saccades. OPNs act as a saccadic gate so that the SC_i is potentially the last site within the saccadic circuit where profitability can modulate saccade selection and preparation without directly triggering saccades. CN – caudate nucleus; FEF – frontal eye fields; LIP – lateral intraparietal area; SCi – intermediate layers of superior colliculus; SEF – supplementary eye fields; SNr – substantia nigra; OPN – omnipause neurons. Figure adapted from Munoz et al., 2000.

Krebs, 1986). The patch model examines how long an animal should spend in a *patch* of resources, which gives diminishing amount of reward the longer that an animal spends in it because the resources are exhausted. Here the organism must decide when to leave a patch of diminishing resources (e.g. patch of strawberries) to search for a potentially better patch of resources. The risk involves not finding another patch, the wasted opportunity costs involved during searching, or finding a new patch whose resources are less than the abandoned patch. This class of models is largely concerned with the exploitation/exploration tradeoff (Stephens and Krebs, 1986).

The second class, which was the focus of this thesis, is the prey model. This class deals with how organisms should choose when faced with multiple items, known as *prey*. Here organisms must decide what prey types to harvest upon encounter to maximize reward intake at the lowest cost. Prey can be harvested into a predictable currency of reward (e.g. calories) but require a predictable handling time to harvest (e.g. average time required to crack open an acorn or chase after a rabbit). Therefore prey can be rank ordered in terms of their *profitability*, defined as reward magnitude divided by handling time. When prey is abundant, organisms maximize their rate of reward intake by choosing prey with the highest profitability. Insects (Marden and Waddington 1981), rodents (Phelan and Baker 1992), birds (Krebs et al. 1977), and humans (Hill et al. 1987; Keegan 1986), to name just a few, have all been shown to exhibit behavioural strategies that satisfy predictions of foraging theory.

Traditionally, prey models of foraging theory have been studied with food items being the prey and the main currency of reward being the difference between caloric gain and expenditure. However, the definition of prey and reward may extend to describe other currencies of reward. Recently, foraging theory has also been used to describe trends in humans gathering information on the internet (Pirolli and Card 1998) as well as shopping behaviours (Rajala and Hantula 2000). For ease and accuracy of delivery, we used different magnitudes of liquid reward delivered to thirsty monkeys.

In this thesis, we used a new foraging task adapted for recording neurons in the visuosaccadic system. In deciding which prey item to harvest, many factors can come into play, such as reward magnitude, handling time, risk of injury, rate of encounter, and rate of recognition. For simplicity, this thesis will focus on only two critical variables of *profitability*: reward magnitude and handling time. Subjects were presented with an array of coloured dots representing prey items, which they can harvest one at a time for a liquid reward by fixating on a visual prey for a pre-specified handling time. In keeping with the terminology of foraging theory, potential visual targets in the visual field will be referred to as prey items throughout. Visual prey can be one of three colours and all prey of the same colour shared the same reward magnitude and handling time, hence the same profitability. *Reward magnitude* is defined as the net volume of reward gained per prey. *Handling time* is the time between prey encounter and prey consumption, which includes the time required to catch a prey and consume it. Because we were using ballistic, high velocity and accurate saccades with tightly packed prey items, the time between prey

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encounter was almost, but not entirely, inconsequential, resulting in handling time being primarily controlled by consumption time. The end result of using this stripped down visuosaccadic foraging task was that the *profitability* of each visual prey can be controlled in the laboratory setting.

1.5 ADVANTAGES OF OUR FORAGING TASK

Using a foraging based task extends the visuosaccadic decision making field in three important ways. First, as mentioned previously, choices in real life usually involve more than one decision variables, unlike the typical visuosaccadic decision making tasks. We studied the variables of reward and time together by borrowing profitability from foraging theory, which has been observed to accurately describe animal behaviour in the wild. Second, the frequency that the subject chooses prey of each colour provided an overt index of relative subjective profitability of different coloured prey. This leads to the third and most important benefit. Our foraging task will help resolve the long-standing issue of the contribution of target profitability compared to saccade planning processes on premotor neural activity in the SC_i. The foundation of decision theory is that organisms choose options that they prefer (Samuelson, 1938). In visuosaccadic tasks where choice is indicated by saccades, that means saccades are planned to targets with the highest profitability, making it difficult to separate these two processes. Here, multiple prey share the same profitability, allowing us to compare between the neural activity when subjects

ultimately make a saccade to different locations in relation to the response field, while the profitability of the prey inside the response field is the same.

1.6 SCOPE OF STUDY

Our study examined the neuronal processes involved in selecting visual prey in a visuosaccadic foraging task. In a foraging environment, the subject is presented with multiple prey items with varying rewards for different time commitment trade-offs. Although the subject can obtain a reward from any of the prey items, ultimately it must select a single action to execute at a time. The first part of this thesis confirmed that our foraging task is appropriate for eliciting behaviour that reflects foraging theory predictions and can be used to index the subject's relative estimates of prey profitability. Our behavioural results demonstrated that monkeys choose prey based on prey profitability as determined by the prey's reward payoff (see RESULTS). Having established the validity of our task, we will test 2 hypotheses related to the role of SC_i neurons in transforming target profitability into specific actions.

Hypothesis 1: Prey profitability is represented in SC_i activity

I hypothesize that SC_i firing rate will be influenced by prey profitability so that the ranking of prey colour according to SC_i firing rate will be correlated to the ranking of prey colour according to behavioural choice patterns. This hypothesis was tested by comparing SC_i activity in response to the prey inside the neuron's RF with the behavioural estimate of prey profitability derived from the monkeys' choice patterns. To

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ensure that any effects are not simply the result of saccade preparation processes, SC_i firing rates was compared between when the prey item in the RF was selected versus when an extra-RF prey item was selected instead, while the colour of the prey item in the RF was the same.

Hypothesis 2: The evolution from prey profitability to saccade goals is reflected in SC_i activity

I hypothesize that SC_i activity will become increasingly selective for the next saccade goal as the end of the handling time approaches. This hypothesis was tested by comparing firing rates between three epochs: initially after a prey item is acquired, just before receipt of reward and prior to subsequent saccadic choice. A statistical interaction between prey profitability and evolution within the handling time would support this hypothesis.

Chapter 2

METHODS

We recorded the extracellular activity of single neurons in the intermediate layers of the SC of two male rhesus monkeys (*Macaca mulatta*) weighing 8 to 14.5kg each, while they performed a saccadic eye movement task for liquid reward. All procedures were approved by Queen's University Animal Care Committee in accordance with the guidelines of the Canadian Council on Animal Care. Animals were under the close supervision of the University veterinarian.

2.1 ANIMAL PREPARATION

Physiological recording techniques as well as surgical procedures were similar to those used by Munoz and Istvan (1998) and Thevarajah et al. (2009). Each monkey underwent two separate surgeries for attaching the head fixation post and the microelectrode chamber. Anesthesia was induced with an intramuscular injection of ketamine HCl (10 mg/kg) in order to insert the I.V. A bolus of Propofol (10mg/mL *i.v.*) was then administered and the animal was prepared for the surgery. The hair was shaved around the scalp, the monkey subject was intubated with an endotracheal tube, and a rectal probe was inserted to monitor temperature. Anesthesia was maintained throughout the duration of the surgery with 1%-2% isofluorane gas and heart rate, respiratory rate, and body temperature were monitored.

Both surgeries were done following similar procedures. For the positioning of the head fixation post, the monkey subject was secured in a stereotaxic frame, and a longitudinal incision was made along the midline of the scalp to expose the cranium. The cranium was cleaned and titanium screws were inserted into the bone to act as anchors for the dental acrylic implant to follow. The head fixation post was positioned atop the skull and embedded in dental cement. In the second surgery, a single craniotomy was made based on stereotaxic coordinates that allowed later access of microelectrodes to both the left and right Superior Colliculi (stereotaxic coordinates: centered on the midline and angled 38° posterior of vertical). A recording chamber was positioned over the craniotomy and embedded in dental acrylic.

Following each surgery, the monkeys were given injections of the anti-inflammatory drug Anafen (100mg/mL) once, the antibiotic Baytril (50mg/mL) for ten days, and the analgesic Bupenorphine (0.3mg/mL) for three to five days. The monkeys were monitored closely until they were fully conscious and mobile and were observed closely for the next 3 days to ensure there were no complications. Monkeys were given a minimum of six weeks for head post surgery and a minimum of one week for chamber surgery recovery before the start of behavioural training.

The monkeys were monitored, fed, and their pens cleaned by animal care personnel. Every second day the recording chamber and region surrounding the implant was cleaned with sterile saline, peroxide and Betadine to prevent infection. The day before an experimental session, the monkeys were placed on water control by removing

water bottles from the cages. During an experimental session, the monkeys were rewarded with water for the correct completion of the behavioural task and were allowed to work to satiation. The weight and health of the monkeys were carefully monitored to ensure that they were adequately hydrated. Supplemental fruit was given at the end of successfully completed experimental sessions.

2.2 EXPERIMENTAL PROCEDURES

Throughout the experiments, monkeys were seated in a primate chair with their heads firmly attached to the chair via the head-post in the implant. The monkeys faced a translucent white screen 57 cm away which spanned $\pm 42°$ of the central visual field. A sipper tube was placed in the monkey's mouth that allowed water rewards to be administered. The amount of water rewards is controlled by a solenoid valve. The position of the left eye was sampled at 250Hz by an EYELINK II infrared eye tracker (SR Research) secured to the primate chair. Behavioural paradigms, visual displays, delivery of liquid reward, and storage of both neuronal discharge and eye position data were under the control of a Pentium 4 personal computer running real-time data acquisition software (GRAMALKN, Ryklin Software). All data analyses were performed offline on a Pentium 4 personal computer running MATLAB version 7.0.4 (Mathworks Inc).

The activity of single neurons was recorded with tungsten microelectrodes (FHC Inc.), which were lowered with a microdrive (NAN Instruments) through 23 gauge, 41

mm long stainless steel guide tubes attached to the recording chamber. The guide tubes were situated within a delrin grid inside the recording chamber (Crist et al., 1988). Single-cell discharges were sampled at 1 kHz after passing through a digital window discriminator (Plexon Inc.) which excludes spikes which did not meet amplitude and time constraints.

2.3 BEHAVIOURAL PARADIGM

Prior to this experiment, both monkeys were trained on other visuosaccadic tasks, and thus, were familiar with the association between fixating on visual stimuli presented on a screen for water rewards. For this thesis, the monkeys were trained to perform two additional tasks: the *delayed task,* and the *foraging task.*

The delayed task was used to map out receptive fields (RF) of neurons and characterize their visual, delay, and motor properties. In this task (Fig 2), a visual stimulus (4.2cd/m^2 luminance, 0.25° visual radius, CIE x - 0.64, y - 0.35), referred to as the fixation point (FP), was back-projected onto the centre of the translucent screen. The monkey had 600ms in which to align the fovea with the FP ($\pm$3°) and maintain fixation for 500-1000ms. A target stimulus (T), identical to the FP, then appeared in the periphery. Both the FP and the T were visible for 600-2000ms, termed the delay period, after which the FP disappeared. A liquid reward was given if the monkey maintained steady fixation on the FP for the duration of FP presentation and then made a saccade to the T within 100-500ms of FP disappearance. For each neuron, the T was presented in a

A Delayed Task

Time

Delayed Period
(600 - 2000 ms)

Target-directed
Correct Saccade

B Foraging Task

Time

Trial
(~15 s)

Inter-trial Interval
(4 s)

Subsequent Trial
(~15 s)

C Small Central Response Field   Large Eccentric Response Field

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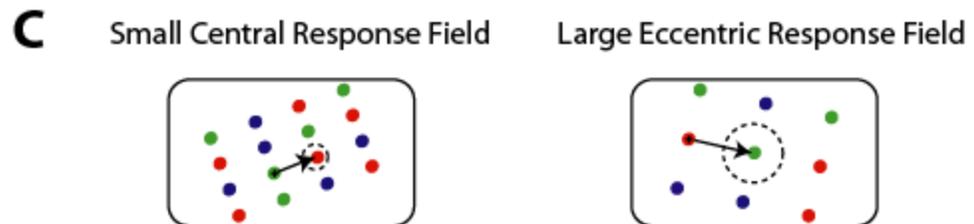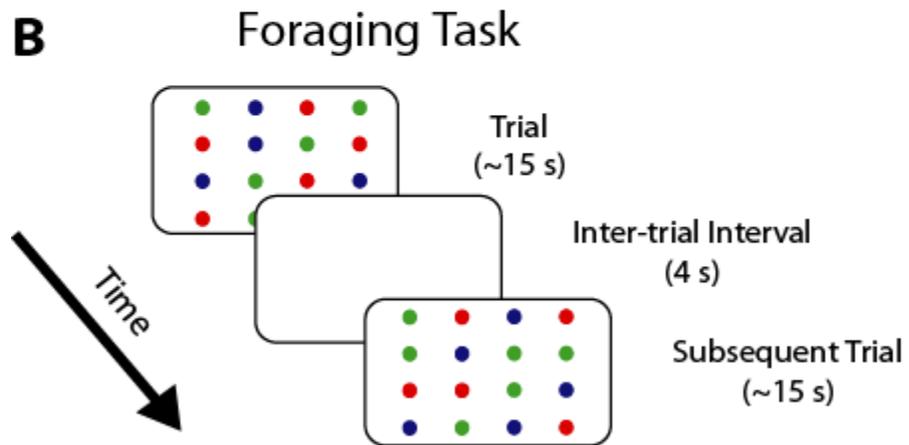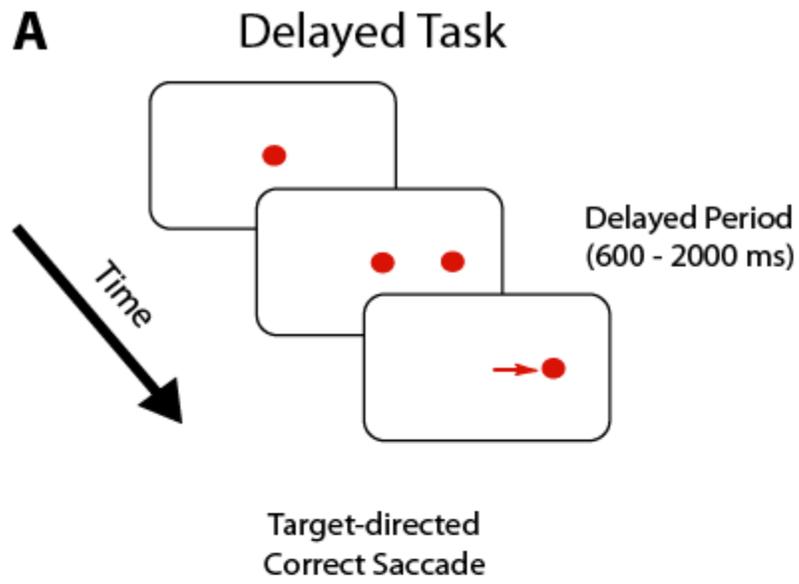
Figure 2 Schematic of behavioural paradigms.

Each panel denotes a successive display on a computer monitor. A) Delayed task: Subjects received a liquid reward for trials in which they made a correct saccade to red targets (red arrow), after the center fixation point disappears. Targets were presented in a variety of locations throughout the visual field to locate the response field (RF) of each neuron. B) Foraging task: Subjects received a liquid reward for every fixation on an unharvested prey for the assigned handling time. Each colour of prey is associated with a different objective profitability, defined as reward magnitude divided by handling time. Note that between trials the associations between colour and profitability remain constant but the spatial distribution of the prey types change. C) Examples of how the grid of prey in the foraging task can be modified to accommodate neuronal response fields that are small and centrally located (left panel) or large and eccentrically located (right panel). The goal is to have the prey adjacent to the current fixation position located in the neuron's response field. The cross-hairs represent the current fixation position. The black arrow and dashed circle approximate the optimal saccade vector and size of response field, respectively, for the neurons under study.

variety of locations throughout the visual field over 30-130 trials to delineate the RF. Once the target location that elicited the most activity had been determined, an additional 5-20 trials with the T presented in the centre of the response field was used to determine the visual, delay, and motor properties (Fig 3).

In the foraging task (Fig 2), each trial began with the display of an array of circular stimuli (visual prey) on the screen in front of the subject. All visual prey were identical in terms of luminance and size ($4.20cd/m^2$ luminance, $0.25°$ visual radius) but each prey could be one of three colours (Red: CIE x - 0.64, y - 0.35; Green: CIE x - 0.34, y - 0.54; and Blue: CIE x - 0.15, y - 0.08). In each trial, all three colours were presented in equal proportions, randomly distributed, and arranged in a rectangular grid. Monkeys were free to fixate any of the prey, in whichever order they choose. Each prey colour was associated with a specific amount of liquid reward known as *reward magnitude*. To harvest this reward, each prey colour had to be fixated for a predetermined time known as *handling time.* Therefore, each prey colour had a specific *profitability*, which is the ratio of reward magnitude and handling time. Once harvested, the prey's colour turned into an equilu minant grey ($4.20cd/m^2$ luminance; CIE x - 0.354, y - 0.401) and was no longer associated with any reward. This prevented subjects from obtaining repeated rewards from the same target.

The duration of the trial was determined independently for each block so that the monkey could only harvest approximately 65-80% of the visual prey during each trial. For most blocks, multiplying the average handling time by the number of prey gave a
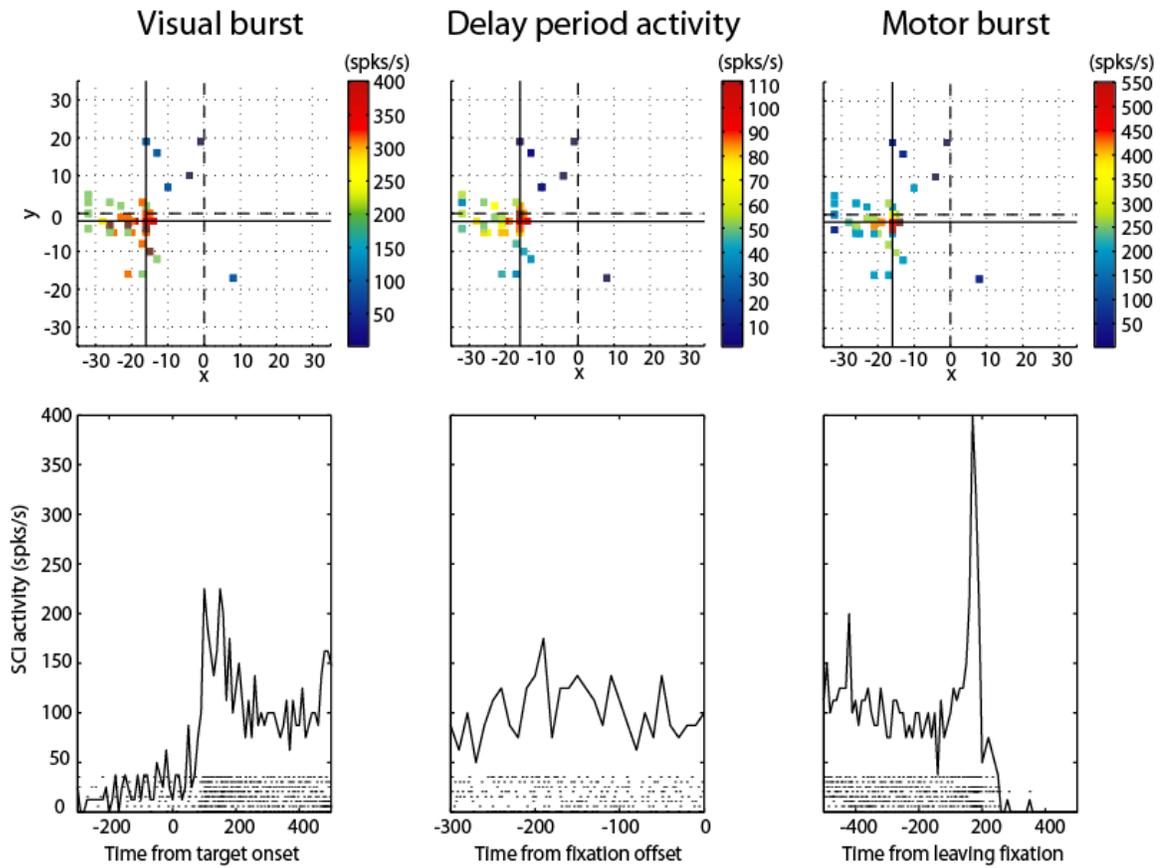
Figure 3 SC$_i$ activity from a representative neuron during the delayed task.

Top panels: Neuron's peak activity distribution on the visual field during each of the major events of a delayed task (target onset – visual burst, delayed period, movement onset – motor burst). Solid crosshair indicates the location of the defined response field used for the foraging task. Bottom panels: Rasters (dots) and peri-stimulus time histogram (solid line) showing average activity at each of major events of a delayed task. Each raster marks the time of an action potential while each line of the raster represents one trial. Only trials corresponding to the defined RF are shown in the bottom panels (n = 8). The neuron presented here possesses all three characteristics: visual burst, delayed activity, and motor burst. To increase statistical power, neurons were used if they showed at least one of these characteristics and had a defined RF (See Table 2).

good estimate for an appropriate trial length, as there is a relatively minimal amount of time used in reaction time and saccade duration. This prevented monkeys from harvesting 100% of the targets. Because there was not enough time to harvest all of the rewards, there was an incentive to be selective in their choices of prey to maximize intake of reward. Specifically, foraging theory indicates that they would maximize their intake of reward over time by harvesting prey colours in decreasing order of their profitability.

Throughout a block of trials, visual prey that share the same colour were associated with the same reward magnitude and handling time, and hence a common profitability. The possible reward magnitudes associated with prey types were 0.04mL, 0.08mL, 0.12mL, 0.16mL, and 0.20mL (resulting in the solenoid valve being opened for 23ms to 159ms, depending on reward magnitude), while handling times were chosen from 500ms, 1000ms, 1500ms, 2000ms, and 2500ms (Table 1). Both reward magnitude and handling times were selected randomly without replacement for each block. Based on these profitabilities, monkeys would work for about 3 hours before being satiated. In some cases, multiple blocks of data, featuring different combinations of profitability-colour associations, were collected while recording from a single neuron during a single experimental session. The location of prey items of a particular colour were shuffled from trial to trial, but prey of the same colour always shared the same profitabilities throughout a block.

During behavioural training, 16 visual prey were used on each trial. During neuronal recording, the number of prey items was reduced to 6 – 12 to accommodate the

Table 1 List of reward magnitude and fixation times used in the foraging task.

		Handling Times (ms)				
	Profitability (mL/s)	**500**	**1000**	**1500**	**2000**	**2500**
Reward Magnitude (mL)	**0.04**	0.08	0.04	0.027	0.02	0.016
	0.08	0.16	0.08	0.053	0.04	0.032
	0.12	0.24	0.12	0.08	0.06	0.048
	0.16	0.32	0.16	0.11	0.08	0.064
	0.2	0.4	0.2	0.13	0.1	0.08

response field vectors of the neurons under study. The prey were arranged in an evenly distributed 4 by 4, 2 by 3, 3 by 3, or 3 by 4 grid spanning up to $\pm 25°$ horizontal and $\pm 25°$ vertical of the subject's central visual field. The eccentricity and orientation of the array was adjusted for each neuron being recorded so that the distance between prey was equal to the eccentricity of the RF from the fovea (Fig 2C). This ensured that a prey item was always in the RF except in the case when subjects fixate on targets on the outer edge of the grid, causing the RF to extend beyond the grid.

2.4 NEURONAL CLASSIFICATION

We recorded the activity from saccade-related neurons located between 1.0 and 3.0 mm below the surface of the SC. The center of each neuron's response field was defined as the location relative to central fixation that was associated with the most vigorous activity during target-directed saccades in a delayed task (Fig 2). To be included in our analysis, neurons had to meet at least one of the following requirements (Fig 3), (1) *visual burst,* a transient burst of activity that was time-locked to onset of the preferred saccadic target and was at least 50 spikes/s above the mean fixation activity (500-200ms before target presentation) (Dorris et al., 2002), 2) *delayed activity*, neural activity during the delayed period that was significantly greater than the mean fixation activity (paired t-test, $p<0.01$) (Wurtz et al., 2001) or 3) *motor burst,* a transient burst of activity that was

time-locked to saccade onset that was higher than fixation and delayed activity (Wurtz et al., 2001)(Table 2).

2.5 DATA ANALYSIS

2.5.1 Behavioural Data

Within a given block, each colour, red, green and blue, has a unique profitability associated with it. This profitability was defined as the reward magnitude available from the chosen prey divided by the handling time (Stephens and Krebs, 1986):

$$P_C = \frac{R_C}{T_C} \tag{1}$$

Where P_C denotes profitability of the colour C, R_C denotes the magnitude of water reward (ml) associated with the colour C, and T_C denotes the handling time (ms) associated with the colour C. C can be either R, G, or B, indicating red, green, and blue, respectively.

Profitability was associated with each choice (i) that a subject makes in a given trial, which is equal to the profitability of the colour of the prey that was chosen:

$$P_i = P_{Ci} \tag{2}$$

Where P_i represents the profitability of choice i and P_{Ci} refers to the profitability of the colour C of the prey being harvested at choice i.

Table 2 Neuronal classification.

Neuron Firing Characteristic	Number of Neurons
Visual Burst Only	0
Delayed Activity Only	0
Motor Burst Only	6
Visual Burst + Delayed Activity	7
Delayed Activity + Motor Burst	1
Visual Burst + Motor Burst	0
Visual Burst + Delayed Activity + Motor Burst	12
Total	26

We define the *efficiency,* E_i, of each choice as a comparison of the profitability chosen for each choice versus the maximum profitability that was available within the array at that time. This can be calculated by dividing the profitability associated with that choice, P_i, by the highest available profitability present at the time that the choice was made, P_{Hi}:

$$E_i = \frac{P_i}{P_{Hi}} \tag{3}$$

Therefore, if a prey item associated with the highest profitability available was selected the efficiency score would be 1.

The *foraging efficiency* associated with each trial was defined as the sum of the efficiencies of all the choices made in that trial, divided by the number of choices made or, in other words, the average efficiency of the trial:

$$E_{trial} = \frac{\sum_{i=1}^{n} E_i}{n} \tag{4}$$

Where E_{trial} denotes the foraging efficiency of the trial, E_i denotes the efficiency of the *i*th choice, and *n* denotes the number of choices made in the trial.

The foraging efficiency was plotted for each trial to observe how well the subjects were learning the associations. To better visualize trends across trials, a five-trial running average centered on the current trial (i.e., the average efficiency from trial-2 to trial+2) was calculated and plotted (see Fig 4C and F).

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To examine if subjects' efficiency is significantly different from choosing randomly, *chance efficiency* was computed for each block by simulating 10,000 trials of random target selection. The procedure above for calculating efficiency was used on these 10,000 simulated trials and then averaged to give the chance efficiency. A t-test was performed between chance efficiencies and average foraging efficiencies.

The *relative subjective profitability* of each colour was quantified based on the nonparametric Kruskal-Wallis test (Freund, 2004). The first chosen stimulus in a given trial was given a ranking of *N*, where *N* is the total number of prey items initially present in the grid. The next chosen stimulus was given a ranking of *N*-1 and rankings decreased by 1 each time until the last choice:

$$R_i = N - (i - 1) \tag{5}$$

Where R_i is the ranking of the *i*th choice target.

All prey that were not selected by the end of the trial were assumed to tie for last place; hence each was assigned the mean of the ranks that they jointly occupy, namely, ranks 1 to the rank below the last rank harvested:

$$R_{i>n} = \frac{\sum_{j=1}^{N-n} j}{N - n} \tag{6}$$

Where $R_{i>n}$ is the ranking of each target that was not selected by the end of the trial and *j* is each of the remaining rankings.

The prey were then grouped by colour and their ranking added together to give the subjective profitability of that colour, for that particular trial:

$$SP_C = \sum R_C \tag{7}$$

Where SP_C is the subjective profitability of each colour, the subscript C having a value of R, G, or B, and R_C represents the ranking of each prey that features the colour C.

The relative subjective profitability (RSP_C) of a colour C is SP_C normalized by dividing by the sum of all possible ranks:

$$RSP_C = \frac{SP_C}{SP_R + SP_G + SP_B} \tag{8}$$

Similar to the foraging efficiency, a running average of RSP_C was presented as the running average over five trials.

The *time to behavioural acquisition* was defined as the first trial in which the RSP significantly differed (Kruskal-Wallis test, $p<0.01$) across the 3 prey colours and remained significantly different for at least 5 consecutive trials. Note that for some experiments, particularly those with similar profitabilities, time to behavioural acquisition was never reached because no consistent preference between prey colours was reached. This measure was useful for defining the beginning of steady-state behaviour as well as providing an estimate of learning rate.

To observe how differences between prey profitabilities affected learning rate, we used the chance efficiency described above as the measure of differences between prey profitabilities. Large differences in profitabilities are associated with low chance efficiency as there is a larger penalty for not choosing the best option exclusively. Time

to behavioural acquisition is plotted against chance efficiency to see any correlation between these two measures.

2.5.2 Neuronal Data

A total of 52 neurons were recorded, 26 of which are used in the remaining analysis. This discrepancy is due to blocks of trials being excluded because 1) the subject never reached behavioural significance or 2) there were not enough neuronal data for one or more of the prey type – saccade direction combination (e.g. less than five saccades into the RF when a prey of low profitability is in the RF).

Rasters of neuronal discharge were categorized based on the colour of the prey inside the RF, rather than the prey that was aligned with the fovea. *Neuronal profitability* (NP) was estimated by averaging firing rate for each colour in a 200ms window during the handling time. As the shortest handling time used was 500ms, 200ms was a reasonable time frame that allowed us to differentiate between the beginning, middle, and end of the handling time (see Temporal Encoding), while obtaining a sufficient sampling of action potentials for an accurate estimate of the firing rate.

Trials in which a certain colour was never in the response field were excluded from the calculation of the running average (see discontinuities in Fig 7).

2.5.3 Representation of Prey Profitability in SC_i Activity

Analyses were limited to the relatively steady state after behavioural acquisition. To prevent any situation from being under-represented (e.g. not enough instances where a prey of the preferred colour is in the RF but the subject chose not to saccade into the RF), blocks were only used if they contain at least five instances of each of the six RF prey colour and saccade direction combinations. That is, each block must contain at least ten fixations with each of the prey types in the RF, five while preparing a saccade into the RF and five while preparing a saccade out of the RF. In total, 28 experimental blocks fulfilled these criteria, recorded from 26 neurons.

Our first hypothesis was that behavioural index of prey profitability will match neuronal index of prey profitability. This hypothesis was tested by comparing neuronal and behavioural rankings of the prey colours. For each block, the behavioural ranking of the colours was first determined by finding the average RSP for each colour after the time to behavioural acquisition. The colour with the highest average RSP was considered the 1st ranked colour for a given block, so that:

$$\overline{RSP}_{C1} > \overline{RSP}_{C2} > \overline{RSP}_{C3} \qquad (9)$$

Where $\overline{RSP}$ is the average RSP for a certain colour and the subscripts *C1, C2, C3* indicates the colour and ranking to which the $\overline{RSP}$ belongs. Each colour is therefore associated with a behavioural ranking *b* for a given block.

The neuronal ranking of each colour was then determined by finding the average NP associated with each colour after the time to behavioural acquisition. NP, as noted above, is simply the trial-by-trial average firing rate of the SC_i neuron when a certain

colour is in its response field. For the purpose of testing hypothesis one, only NP recorded from the middle of the handling period (200-0ms before delivery of reward) was included. This epoch allowed the maximum amount of time for neuronal activity to accumulate during the handling period, while minimizing effects of eye movement and any artifact from the reward delivery system. Similar to behavioural ranking, the colour with the highest average NP was considered the 1st ranked colour for a given block, so that:

$$\overline{NP}_{C1} > \overline{NP}_{C2} > \overline{NP}_{C3} \tag{1}$$

Where $\overline{NP}$ is the average NP for a certain colour and the subscripts *C1, C2, C3* indicates the colour and ranking to which the $\overline{NP}$ belongs. Each colour is therefore associated with a neuronal ranking *s* for a given block.

The behavioural and neuronal ranking of each colour for the 28 blocks were recorded in a 3 by 3 contingency table. This table was used in a chi-square test of independence to determine if neuronal ranking is affected by behavioural ranking.

As a control to separate any effects of prey profitability from effects of saccade goals, neuronal data was further categorized by the monkey's subsequent action: saccade into the RF and saccade to a location other than the RF. The discharges of all 26 neurons were combined into a population response by grouping neuronal waveforms from each neuron according to the behavioural ranking of the colour in the RF, as indicated by the relative subjective profitability index. For each behavioural rank, only blocks where the neuronal rank for that colour matched the behavioural rank were used for this analysis.

The average firing rates of different ranking and subsequent actions were compared in a 2-way ANOVA.

2.5.4 Evolution from Target Profitability to Saccade Goals

Our second hypothesis was that neuronal activity evolves during the handling period from primarily encoding the profitability of the prey in the RF to increasingly encoding the next particular saccade that will be made. To quantify the change in discharge of each neuron during the handling period, we collected neuronal data from three separate 200ms epochs: the early epoch was defined as 0-200ms after the monkey's gaze entered the invisible window surrounding the prey to be fixated, the middle epoch was defined as the 200ms immediately prior to reward being given, and the late epoch was defined as 300-100ms before the monkey's gaze left the invisible window surrounding the prey. These epochs were designed to encompass pre-saccadic processing without capturing transient visual or motor-related bursts of activity. Average latency from reward delivery to gaze leaving the invisible window surrounding the prey were between 606ms and 867ms (722.95ms, 606.32ms, 717.36ms, 821.90ms, and 866.25ms for each of the handling times from 500ms to 2500ms, respectively). The epoch between the early and middle epochs vary in length due to different handling times, and therefore were not used in the analysis.

Lastly, a 3-way analysis of variance was used to determine any interaction effects of timing epochs, profitability ranking, and subsequent saccade choice.

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Chapter 3

RESULTS

The results will be presented in four sections. The first section investigates how prey profitability influences choices using two behavioural indices. A foraging efficiency index provides a global metric that indicates whether subjects base their choices on prey profitability. A relative subjective profitability measures the rank order in which prey colours are preferred. This subjective profitability index provided a psychometric function of estimated profitability.

In the second section, we developed a neuronal profitability index as a neurometric function of estimated profitability. The neuronal profitability index is based on the firing rate associated with the colour of prey in the response field.

In the third section, we tested our main hypothesis that prey profitability is represented in SC_i activity by comparing the ranking of prey types according to the neuronal and behavioural profitability indices.

The fourth section addressed our second hypothesis that the neurometric function evolves over time to increasingly represent saccade choice. A 3-way ANOVA examining the effects of profitability ranking, subsequent saccade goal, and timing epoch summarized our findings.

3.1 PSYCHOMETRIC FUNCTIONS OF CHOICE EFFICIENCY AND PREY PROFITABILITY

During most blocks of trials, subjects developed a prey colour preference (Fig 4).

Early in most blocks, before the association between colour and profitability was

established, subjects chose prey colour in a relatively random manner (Fig 4A – left

panel). With experience, the subject eventually chose prey colours in descending order of

their objective profitability (Fig 4A – right panel). Note that, occasionally, subjects

glanced briefly at targets without maintaining fixation long enough to harvest the rewards

(Fig 4A non-numbered fixations). These brief fixations were not included in our analysis.

Instead, the next harvested prey was considered the next saccade goal.

To quantify how foraging strategies were influenced by profitability, we measured

efficiency by comparing the reward received by the subject against the reward predicted

by foraging theory (Fig 4C). Foraging theory predicts that subjects would rank prey

according to their objective profitability and harvest all prey of the highest available

profitability first before moving on to prey with the next highest profitability. For most

blocks, there was a gradual increase in foraging efficiency until it approached optimal

efficiency, resulting in observed efficiency ($\bar{x} = 0.90$, $\sigma = 0.11$) that is consistently higher

than chance efficiency ($\bar{x} = 0.62$ $\sigma = 0.097$) (t-test p<0.0001) if prey types were chosen at

random.

The relative subjective profitability, derived from the monkey's choice patterns,

provided a trial-by-trial estimate of each prey type's subjective profitability (Fig 4B).

This index measured only the relative preference between prey colours and not their
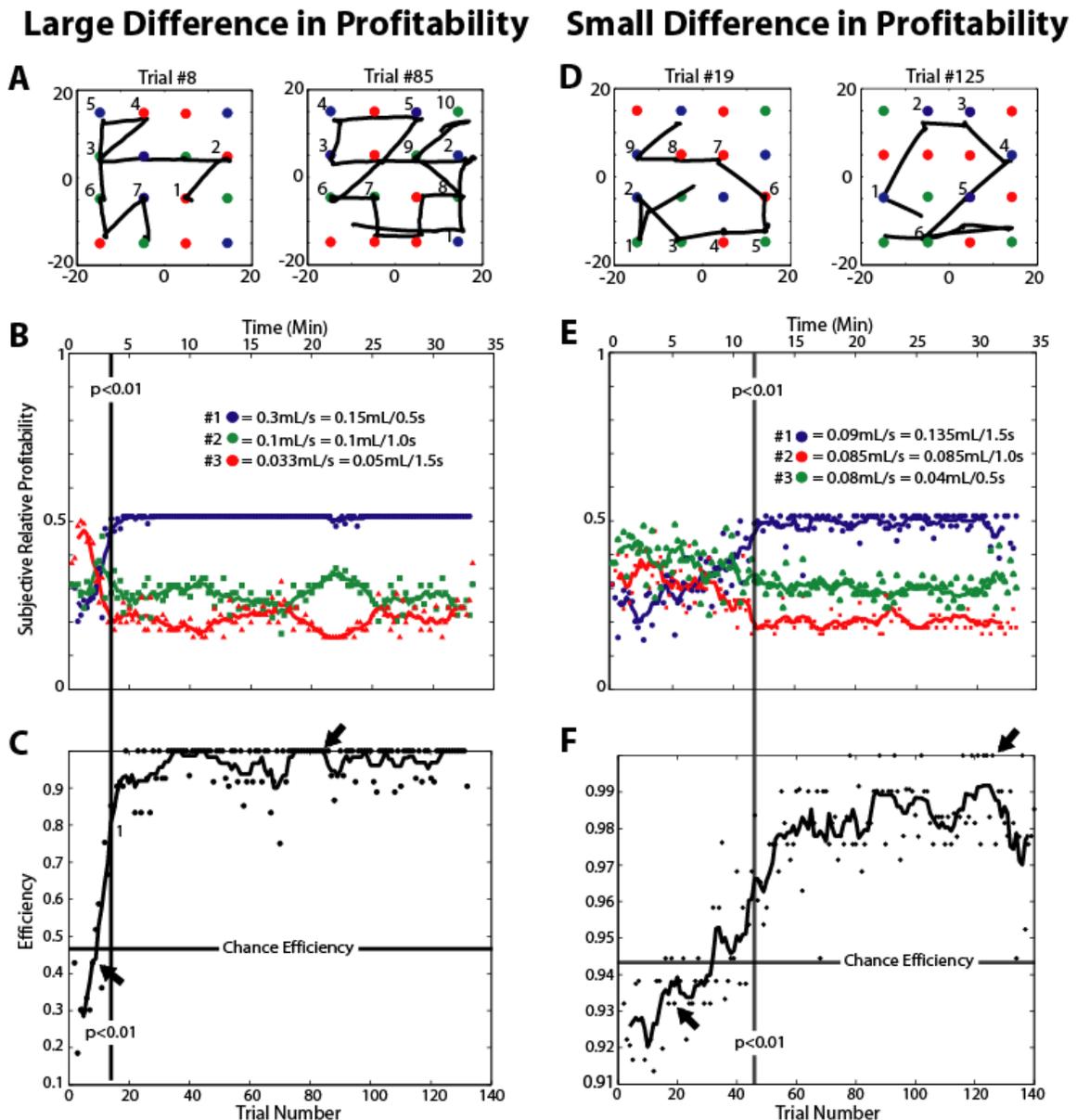
Figure 4 Behaviour during two blocks of the foraging task.

Both blocks were obtained early in training and therefore contain only behavioural data and profitabilities are different from those used in neuronal recording (see Table 1). The difference in profitability between the three types of prey was large for the block represented on the left and small for the block represented on the right. **Top panels** – The scan-paths during representative trials early in each block before the association between prey colour and profitabiltiy was established and late in the block after this association was established. **Middle panels** – The relative profitability indexes for prey of each colour were calculated by summing the ranks

associated with each colour (see text for details). Each data point represents a single trial and the solid line represents the running average of the behavioural relative profitability index over 5 trials. The vertical line represents the time to behavioural acquisition (Kruskal-Wallis ANOVA on ranks, $p<0.01$, see text for details) across the 3 target colours and remained significantly different for at least 5 consecutive trials. **Bottom panels** – The global efficiency of saccade choices for harvesting reward. Each dot represents the efficiency on a single trial and the black line represents a running average of efficiency over 5 trials. Black arrows indicate the trial from which scan-paths in the top panels were taken.

exact profitabilities. That is, this index indicated the rank order of prey preference but not the degree to which prey types are preferred over others. Initially, subjects chose prey randomly, as indicated by a relative profitability of approximately 0.33 for all colours. Over time, subjective profitabilities of the three colours separated from each other, indicating that subjects were choosing prey types with different priorities. In this block, the rank orders of the prey colours were consistent with the predictions of foraging theory.

To obtain an objective behavioural time when prey preferences were established, termed the *time to acquisition*, we used the trial at which the relative subjective profitabilities of the prey colours are significantly different from each other (Krauskal Wallis $p<0.05$) and remain so for five trials or more. In the sample block in Figure 4B, the behavioural time to acquisition was reached at trial 14, or approximately 3.5 minutes of foraging. All subsequent neuronal analyses were performed after the time to acquisition, when behaviour has reached a steady state.

For comparison, a block with small differences in profitability is shown in Figure 4D, E and F. The relative profitability of each colour again began near 0.33 and eventually separated out (Fig. 3E). However, it took 43 trials –approximately 10.75 minutes – to reach the behavioural time to acquisition.

In certain cases, generally those involving two or more prey types with similar profitabilities, subjects' ranking of prey colours violated the foraging theory prediction (e.g. #2 and #3 ranked target in Fig 4E). This demonstrates that this index measures

subjective, not objective, profitability. This is important because the SC_i is close to the motor output end of the visuosaccadic process; hence we expect SC_i activity to be correlated to subjective, not objective, profitability. For comparison with neuronal measures, we used the subjective measure of profitability.

To quantify the effect of the differences in prey profitability on the time to acquisition, we needed a measure of the differences in prey profitability. Chance efficiency is inversely proportional to the differences in prey profitability since there would be a greater penalty for choosing sub-optimally when the difference between the profitability of the suboptimal and optimal prey is large. Chance efficiency was computed for each block by simulating 10,000 trials of random target selection, which is then plotted against the time to acquisition for that block (Fig 5). When the differences in profitabilities was large between prey colours, chance efficiency was low and learning rate was fast (Fig 4C). On the other hand, when the differences in profitabilities were small, chance efficiency was large and learning tended to be slow (Fig 4F). A positive correlation between chance efficiency and time to behavioural acquisition suggests that relative profitabilities is a factor in learning how to allocate choices within our foraging task (Fig 5 – $r^2 = 0.11$, $p = 0.03$).

The left and right panels of Figure 4, together with Figure 5, show that blocks in which the difference between prey profitabilities was large are characterized by fast acquisitions and subjective profitabilities that follow foraging theory predictions. In contrast, when the difference between prey profitabilities is small, blocks are

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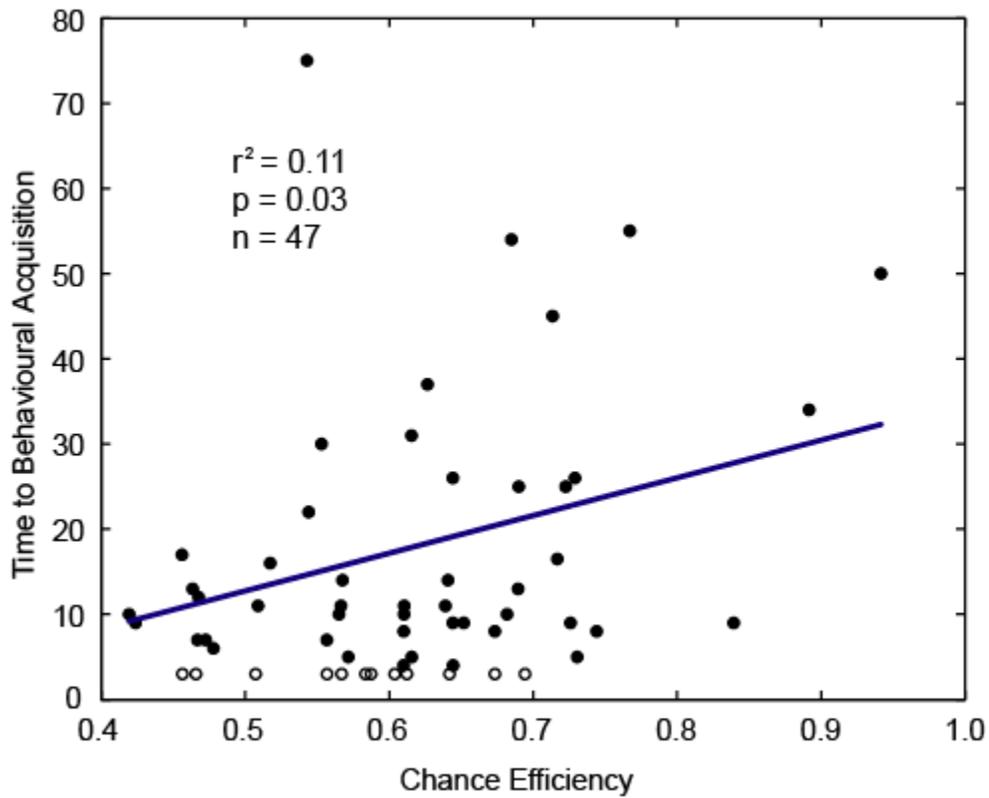
Figure 5 Linear regression analysis comparing difference in profitability and learning rate.

Difference in profitability is estimated using chance efficiency while learning rate is estimated by the time to behavioural acquisition (see text for details). On some blocks, subjects significantly differentiated between colours from the beginning, perhaps due to biases from a previous block, and maintained the same order of preference throughout the block. These blocks are omitted from this analysis (hollow circles).

characterized by slow acquisitions and occasional violations of foraging theory predictions. In summary, foraging efficiency demonstrates that our monkey subjects understand the visuosaccadic foraging task. In addition, we have coarse experimental control over the rate of acquisition through differences in objective profitabilities. Finally, behavioural choices provide a measure of relative subjective profitability, from which we can determine the rank order of prey type preference and the behavioural time to acquisition.

3.2 ESTABLISHING A NEUROMETRIC FUNCTION OF PREY PROFITABILITY

To determine if neuronal activity is ranked by prey profitability we compared neuronal activity to the subjective profitability index. SC_i activity was categorized based on the prey colour within the response field (Fig 6B shaded backgrounds). The representative trial in Figure 6A and B shows that activity changes based on prey profitability in the RF, generally increasing going from a profitability of 0 in the response field (no target – black shaded area) to highest subjective profitability in the response field (green targets – green shaded area).

To directly compare subjective profitability index to SC_i activity, a similar neurometric function of prey profitability was needed. This neuronal profitability index was created by averaging together the activity for each handling period with the same colour in the response field. Similar to behavioural measures, neuronal activity evolved
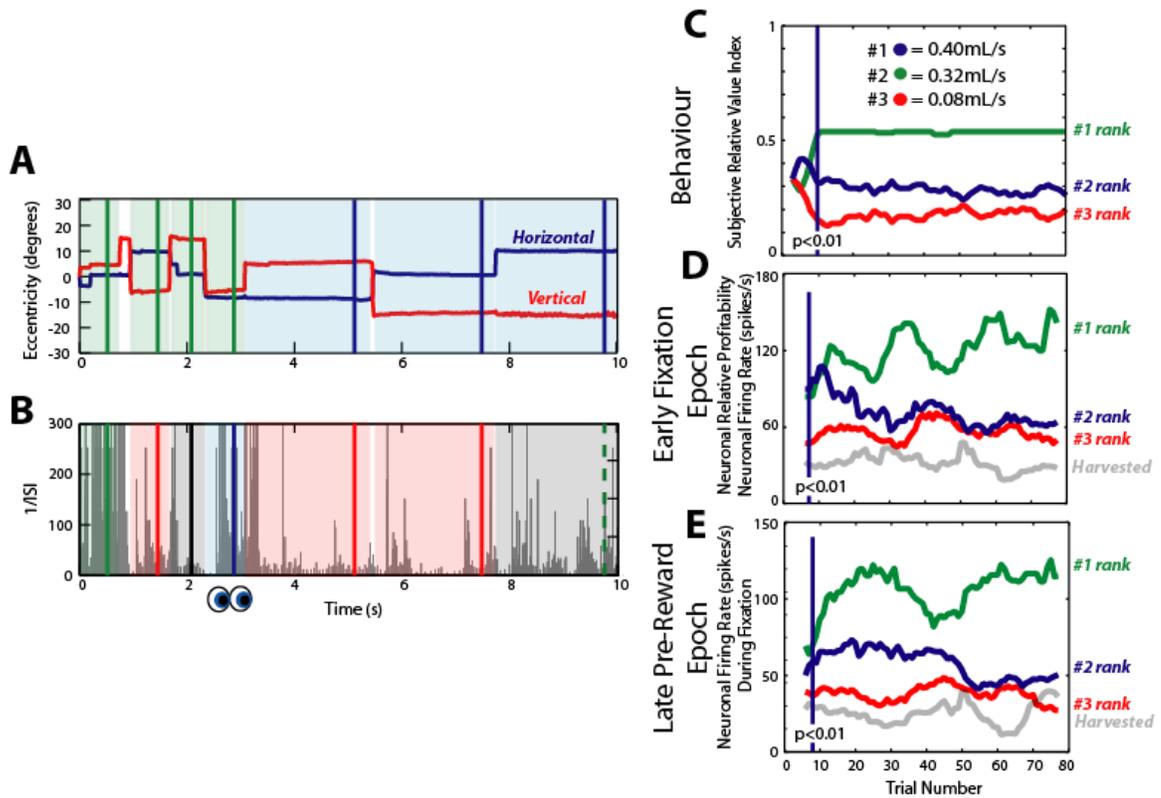
Figure 6 Behaviour and neuronal activity during individual blocks of trials of the foraging task.

Left panel – Data from a representative trial within the block. Eye position (A) and instantaneous spike rates (B) are plotted against time. Vertical lines indicates the time at which subject received a reward. On the eye position plot, the colour of the vertical lines and the shaded background indicates the prey colour that is being fixated; the width of the shaded background indicates the time of this fixation. The colour of the vertical lines and shaded background in the spike rate plot indicates the prey colour inside the neuron's response field at that time. Aside from the three prey colours, a black shaded background indicates instances when there is no prey in the neuron's response field. This can be due to either the subject looking at the edge of the screen (black solid vertical lines) or because the prey has already been harvested (coloured dashed lines). The eyeballs indicate handling times followed by a saccade into the response field. **Right panel** – Psychometric (C) and neurometric (D and E) functions of prey profitability throughout the block. Grey neurometric functions represent neuronal activity when a previously harvested prey is in the RF. As subjects cannot harvest a previously harvested prey, psychometric measure of profitability cannot be obtained in these instances. Vertical lines indicate the times to acquisition according to the Kruskal Wallis rank sum test (psychometric function) or ANOVA (neurometric function). All subsequent analyses uses only data obtained after the *psychometric function* reaches the time to acquisition.

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throughout a block to differentiate prey types (Fig 6). Neuronal activity changed over time to become statistically different based on colour (ANOVA *p<0.01*). A neuronal rank order of prey colours and time to acquisition can be obtained from this neuronal profitability index and compared to their behavioural equivalent. In the sample block in Figure 6, both the behavioural and neuronal profitability indices ranked green as the most profitable, followed by blue and then red (Fig 6C, D, E). The times to acquisition are also qualitatively similar (Fig 6C, D, E – vertical lines).

This differentiation in neuronal activities was related to profitabilities, not to an inherent colour preference of neurons. This is illustrated when the same neuron was recorded from in two consecutive blocks in which the mappings between prey colour and profitability was changed (Fig 7). The neuronal activity first evolved to reflect the first profitabilities; when the profitabilities changed, the neuronal activity associated with each colour also changed. All further analyses will be conducted on the relatively steady state period after the time to behavioural acquisition was reached.

3.3 REPRESENTATION OF PREY PROFITABILITY IN SC_i ACTIVITY

Our first hypothesis was that neuronal activity in the SC_i contains profitability information that could be used to guide behaviour during the visuosaccadic foraging task. We tested this hypothesis by comparing the rank order of colours according to the behavioural and neuronal profitability indices.

Behavioural and neuronal ranking of each prey type were collected in a contingency table. A bar graph representation of the contingency table (Fig 8) showed that the cases in which

A

#1 ● = 0.24mL/s   #1 ● = 0.16mL/s
#2 ● = 0.08mL/s   #2 ● = 0.11mL/s
#3 ● = 0.02mL/s   #3 ● = 0.06mL/s

B

C

Trial Number

45
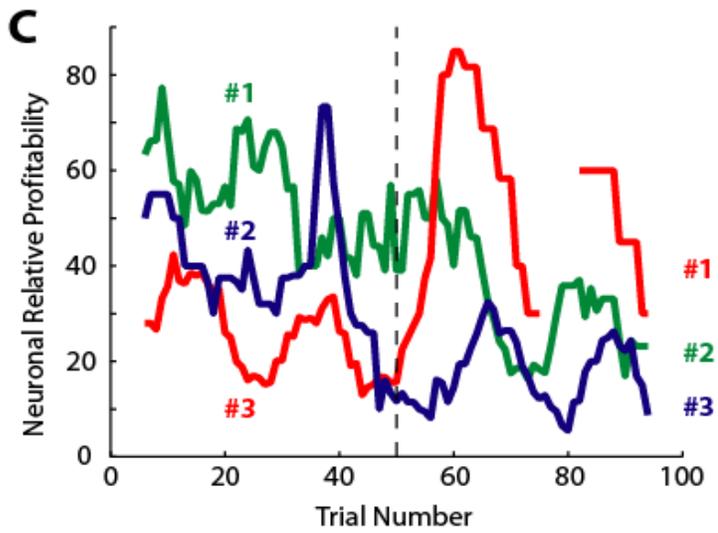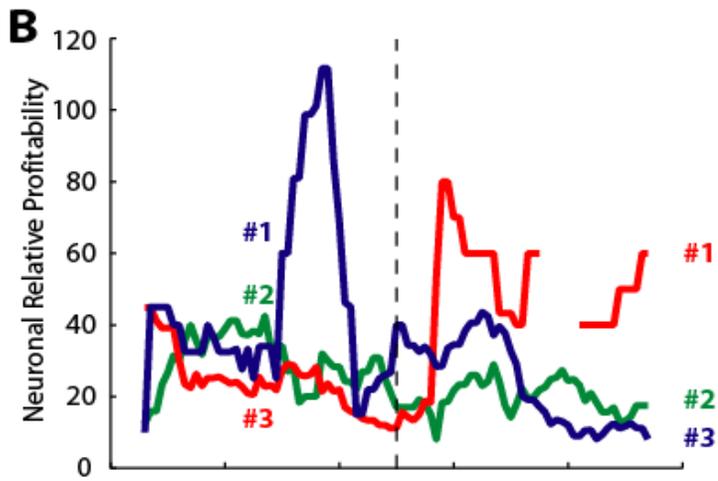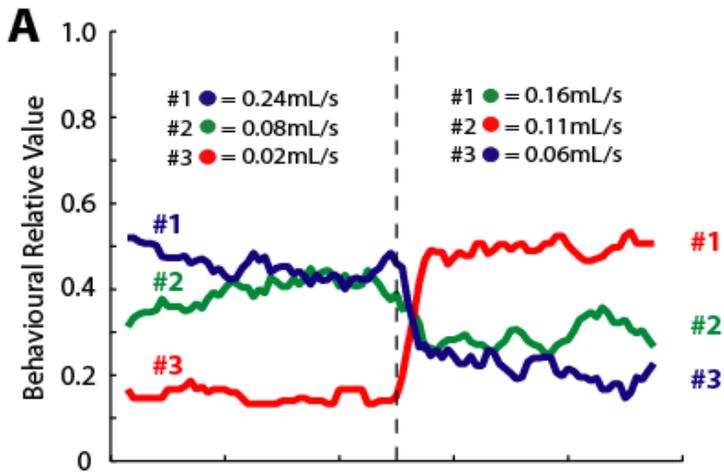
Figure 7 Psychometric (A) and neurometric (B and C) indexes of prey profitability for two consecutive blocks of the same neuron.

Neurometric function was computed using two separate epochs during the fixation period: early (B) and middle (C) (see text for details). Gaps in neurometric function graphs represent trials in which the response field did not land on that colour. Vertical dashed lines denote the trial at which one block ends and another one begins.
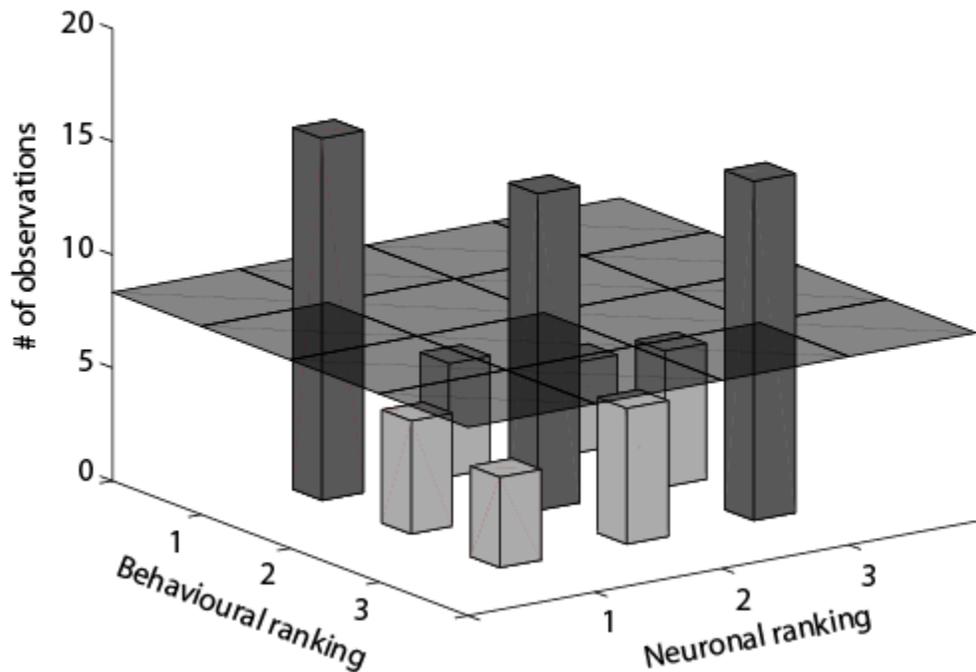
Figure 8 Comparison of psychometric and neurometric functions.

Each bar represents the frequency in a cell of a 3 by 3 contingency table with behavioural ranking on the y axis and neuronal ranking on the x axis. Dark grey bars are instances where behavioural ranking matched neuronal ranking, which would be consistent with our first hypothesis that neuronal activity represents subjective profitability. The grey plane depicts the predicted frequency if neuronal ranking is unaffected by behavioural ranking. The middle epoch was used for this analysis (see text).

the behavioural ranking of a prey type matched its neuronal ranking (dark grey bars) is more frequent than would be expected by chance (grey plane). A chi-square test using this contingency table revealed an interaction between behavioural ranking and neuronal ranking (q = 24.72, p = 0.00, df = 4).

The neuronal ranking of the 2nd behavioural ranking colour is complicated by changes in available prey during a trial. For example, after all of the 1st ranked prey items have been harvested, the 2nd ranked prey items now becomes the theoretically most profitable prey for driving action, and this shift in relative profitability may be reflected in neuronal activity. Separating data of the 2nd ranked colour into before and after the 1st ranked colour has been all harvested reveals a trend for higher activity in the after condition (Into RF: p = 0.26; Out of RF: p = 0.37, not shown). More data is needed to adequately evaluate this effect.

While neuronal ranking of the colours co-varied with behaviour, it is still possible that neuronal activity was not reflecting the profitability of the prey itself. Instead, the heightened neuronal activity at highly profitable prey may be due to the execution of saccades into the response field. That is, saccades are more likely to be directed into the response field when a high profitability prey is in the response field and neuronal rankings simply reflect saccade selection and/or preparation processes. An advantage of our foraging task is that each trial contains multiple prey of the same type, allowing us to control for the effect of saccade goal by comparing between saccades being directed into versus away from the RF while the prey colour within the RF is kept constant.

Average activity was found for each of the saccade and rank combination and plotted in a bar graph (Fig 9).Only blocks for which neuronal and behavioural rankings are the same are shown, leaving 18, 14, and 16 blocks for each of the behavioural rankings 1, 2, 3, respectively.

48
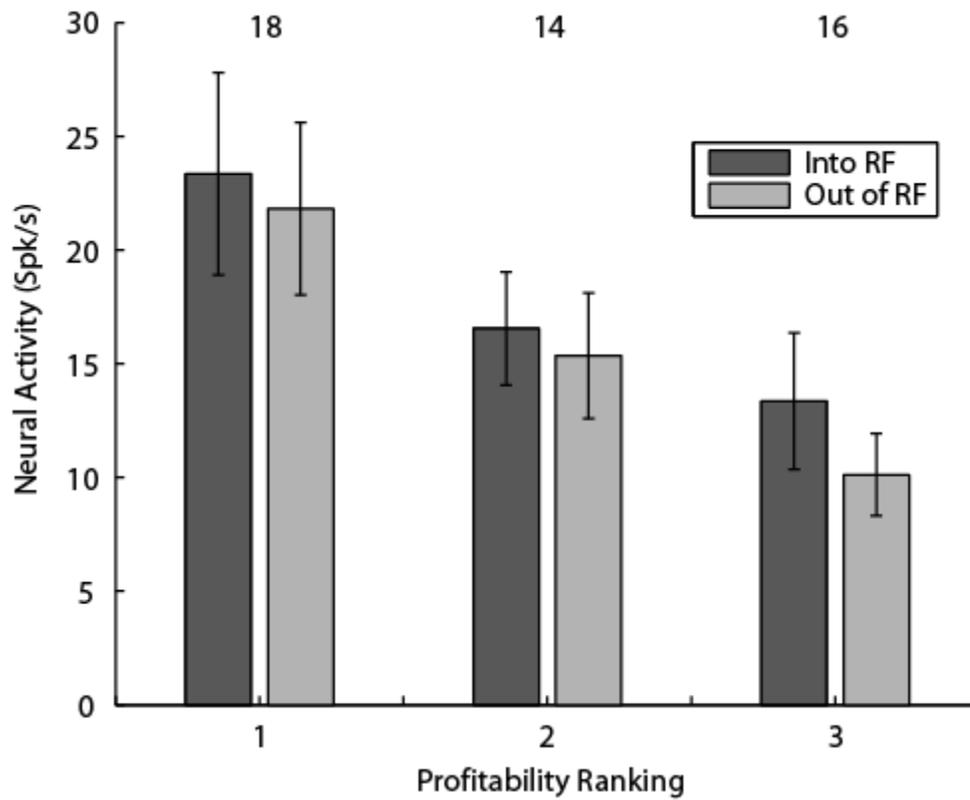
Figure 9 Average neuronal activity separated by behavioural ranking and subsequent saccade direction.

Only blocks for which neuronal and behavioural rankings are the same are shown and numbers above each group indicate the number of blocks that were included. The middle epoch was used in this analysis (see text).

Activity was only slightly higher when subjects were preparing a saccade into the response field (Fig 9), and this effect was not significant (Table 3), suggesting that the effect of profitability we observed was not solely due to preparing saccades towards prey items in the RF.

3.4 EVOLUTION OF SC$_i$ ACTIVITY

Hypothesis 2 was that SC$_i$ activity evolves throughout the handling period from representing prey profitability to saccade goals. The individual and combination effects of these three factors – profitability ranking, saccade goal, and timing epoch – were summarized using a 3-way ANOVA. The effects of profitability and timing on neural activity were significant, as was the interaction between them (Table 4). Somewhat surprisingly, although there is a trend of higher activity preceding saccades into the RF (Fig 9), this difference did not reach significance on its own. However, when saccade goal is considered in conjunction with timing epochs, the interaction effect becomes significant (Fig 10).

Table 3 2-way ANOVA analysis examining the effects of profitability ranking and saccade goal on neuronal activity during the middle epoch.

Source	Sum Sq.	D.f.	Mean Sq.	F	Prob>F
Ranking	14947.8	2	7473.88	17.98	< 0.0001
Saccades	521.8	1	521.8	1.26	0.2625
Ranking x Saccades	1353.6	2	676.8	1.63	0.1963
Error	3134117.8	7541	415.61		
Total	3184422.3	7546			

Table 4 3-way ANOVA analysis examining the effects of profitability ranking, saccade goal, and timing epoch on neuronal activity.

Source	Sum Sq.	D.f.	Mean Sq.	F	Prob>F
Ranking	81010.9	2	40505.4	64.49	< 0.0001
Saccades	1357.4	1	1357.4	2.16	0.1415
Timing	311997	2	155998.5	248.39	< 0.0001
Ranking x Saccades	458.6	2	274.3	0.44	0.6461
Ranking x Timing	31385.9	4	7846.5	12.49	< 0.0001
Saccades x Timing	21502.7	2	10751.4	17.12	< 0.0001
Error	14132953.4	22503	628		
Total	14877897.3	22516			
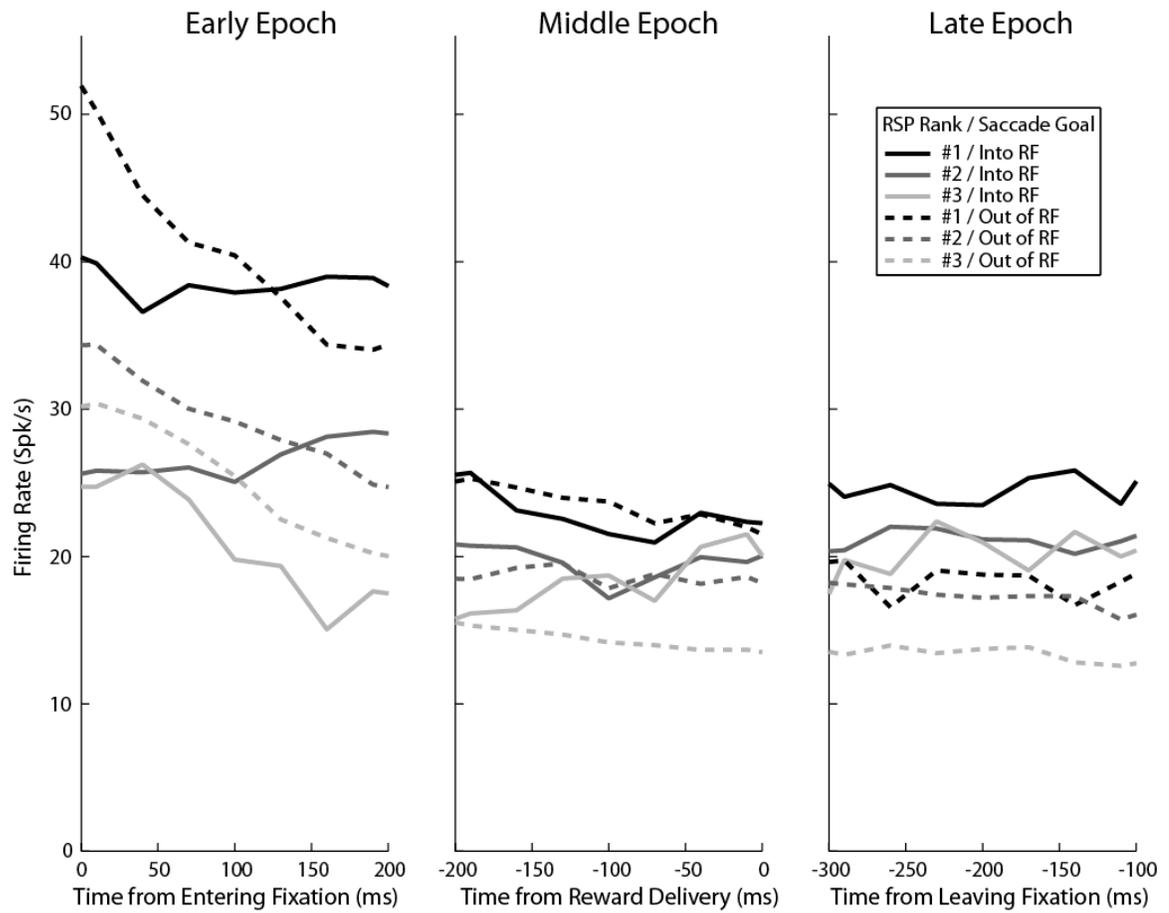
Figure 10 Evolution of neural activity as a function of time.

Average activities across each epoch were used in the calculation of the ANOVA in Table 3.

Chapter 4

DISCUSSION

This thesis examined how prey profitability affected SC_i activity during visual foraging. We developed a novel visuosaccadic foraging task and demonstrated that this task is appropriate for eliciting, from monkey subjects, behaviour that is contingent upon profitability (Fig 4). This is supported by subjects' efficiency in obtaining rewards, which evolves to approach optimal efficiency (Fig 4C and F). A relative subjective profitability index was calculated using the monkey's choice patterns, from which behavioural ranking of prey colours was obtained and compared to concomitant SC_i activity. Overall, we conclude that information about learned profitability is reflected in SC_i activity throughout the handling period, but evolve to reflect saccade goals just before eye movement. This is supported by two pieces of evidence, corresponding to our two tested hypotheses. Our first hypothesis was that prey profitability is represented in SC_i activity. A correlation between behavioural ranking and neuronal ranking (Fig 6, 9) provided support for the first hypothesis. This correlation was not merely a result of saccade preparation as activity was recorded well in advance of eye movement and SC_i activity did not differ whether a saccade was directed to the prey of a given colour in the RF or not (Fig 9, Table 3). Our second hypothesis was that the evolution from profitability information to saccade goals is reflected in SC_i activity. In support of this, we found that profitability ranking and timing each had a significant effect on SC_i activity. Although the effect of saccade direction on its own failed to reach significance, there is an

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interaction between timing and saccade goal as well as an interaction between timing and profitability ranking (Table 4). This demonstrates that prey profitability affects SC_i activity during the handling period in our task while the effect of saccade goal only becomes significant as the time of saccade approached (Fig 10).

4.1 PSYCHOMETRIC ESTIMATES OF PREY PROFITABILITY

The foraging task used in this study has several advantages for studying the neural mechanism underlying decision making. First, the scene is largely static for the duration of the trial, minimizing the large transient visual bursts that results from suddenly appearing stimuli in other tasks that may obscure analysis. In addition, static stimuli are more naturalistic in that stimuli rarely pop into existence in the real world. Second, this is a free-viewing task: rather than explicit instructions directing saccades, subjects are free to fixate any of the prey at any time during a trial to receive the corresponding amount of reward, a paradigm that is associated with more volitional decision-making. Third, the cost and reward of prey types are under strict experimental control. Finally, and most importantly, multiple prey items sharing the same cost and reward allow preparation for saccade to be dissociated from the profitability of prey.

Given the constraints of our task, foraging theory predicts that subjects will choose prey that has a higher profitability first (Stephens and Krebs, 1986). To establish that this was the case, we analyzed two aspects of choice behaviour: efficiency and ranked profitability. We needed to establish that animals selected prey based on profitability before SC activity could be compared to profitability and selection of prey in this task.

Using the amount of reward that the subject would receive according to this prediction as a measure of optimal efficiency, we found that indeed subjects tailored their choice behaviour so

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that they approached optimal efficiency (Fig 4C and F). This resulted in average foraging efficiencies that are significantly higher than if the subject had chosen prey randomly.

While efficiency provided information about the overall reward obtained for a trial and suggested that this laboratory version of foraging was suitable and understood by the monkey, a different index is needed to measure the relative subjective profitability of each individual colour so that it can be compared with concomitant SC_i activity. For this purpose, we developed the relative subjective profitability index based on the order in which colours were chosen throughout a trial (Fig 4B and E). Relative subjective profitability evolved throughout most blocks to reflect the objective profitabilities of the colours. Furthermore, when profitability changed abruptly, relative subjective profitability also changed to reflect the newly assigned profitability, providing evidence that behaviour is, in fact, related to perceived profitability and not to the physical attributes of stimuli themselves (Fig 7A). Importantly, this index only provides information on the relative profitability between colours, not the exact profitabilities. That is, this index indicates the rank order of prey type preference but not the degree to which one prey type is preferred over others.

Two examples illustrate the subjective nature of this index. First, in some cases (Fig 4E-D), ranking of prey colours, as indicated by the relative subjective profitability index, is inconsistent with predictions of the foraging theory. This incongruity rarely occurred, and usually when prey colours had similar profitabilities. Second (Fig 7), if prey profitability was switched abruptly after behaviour had stabilized, soon after the switch, the monkey continued to base its choices on the previous profitabilities (Fig 7A). As the animal learned the new associations, the monkey's choices changed to reflect the new perceived profitability. Importantly, because the SC

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is a structure close to the motor output, we expected that SC activity will reflect the relative

subjective profitability index, not objective profitability.

4.2 NEUROMETRIC FUNCTION OF PREY PROFITABILITY

Next, we needed to develop a neurometric measure of prey profitability in order to

directly compare it with the psychometric measure of prey profitability. For this purpose, we used

the firing rate of SC_i neurons during the handling period, grouped according to the prey colour

inside the RF of the recorded neuron. On a trial-by-trial basis, SC_i activity changed between

fixations (Fig 6A and B). By grouping activity by colour of the prey in the response field, the

average firing rate provided a neurometric equivalent of the relative subjective profitability index.

Similar to the behavioural index, SC_i activity evolved over a block to differentiate between

colours (Fig 7C and D). All subsequent neuronal analyses were based on relatively steady-state

conditions after the time to behavioural acquisition. The ranking of colours by firing rate was

compared with the ranking of colours by the relative subjective profitability index to test the first

hypothesis.

4.3 SC_i ACTIVITY REFLECTS SUBJECTIVE PROFITABILITY

The first hypothesis we tested was that SC_i activity reflected the subjective profitability

of prey. SC_i neurons in general fire at a higher rate when a prey item of high subjective

profitability was presented inside its response field. Similar to the behavioural ranking, switching

the profitability associations causes the neuronal ranking to change (Fig 7), suggesting that the

ranking is based on profitability and not colour. A chi-square test of independence confirms that

there is an interaction between behavioural ranking and neuronal ranking (Table 3), with the

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majority of neuronal ranking corresponding to the relative subjective profitability index (Fig 8), in support of our hypothesis.

This result is consistent with previous research showing that SC_i activity reflects expectation of reward (Ikeda and Hikosaka, 2003; Ikeda and Hikosaka, 2007) and timing (Thevarajah et al., 2009) and expands on them by showing that SC neurons can also reflect relative profitability when more than one prey is rewarded. In a manner akin to visual discrimination tasks (Glimcher and Sparks, 1992; Horwitz and Newsome, 1999; Horwitz and Newsome, 2001; Paré and Wurtz, 2001; McPeek and Keller, 2002), our result further demonstrates that profitability information in the SC_i is not tied to any specific location, but tagged to prey types through learnt colour-profitability associations.

A potential confound often attributed to visual saccade tasks is the intimate relationship between profitability and saccade goal. Ultimately, animals are most likely to choose options of the highest profitability as the saccade goal, leading to the possibility that the increase in SC activity is primarily reflecting movement preparation and not prey profitability. Although Ikeda and Hikosaka (2003) showed that SC neurons sometimes exhibit anticipatory activity to high reward locations even if the target may not be there, it may still be argued that the anticipatory activity is only demonstrating that the monkey is preparing a movement to the preferred location prior to cue presentation. Indeed, Isoda and Hikosaka (2008) suggested that reward related activity in the SC that is incongruent with target location may delay saccadic reaction time, presumably because subjects need to change saccade plans.

To control for any effects of saccade preparation processes, we separated neuronal data by subsequent saccade direction to examine if the effect of subjective profitability remains. Although neuronal activity preceding a saccade into the response field was higher than activity

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preceding a saccade outside the response field, this effect was small (Fig 9) and not statistically significant (Table 3). On the other hand, the effect of subjective profitability was clear both preceding a saccade into the response field and preceding a saccade out of the response field.

For the purpose of this thesis, all saccades leading to the harvest of a prey not within the center of the neuron's RF is considered to be a saccade directed out of the RF. This inclusive method was necessary to obtain enough data for each prey profitability; however, some of the saccades categorized as directed out of the RF may in fact be directed towards prey at the edge of the RF, thus potentially influencing neuronal activity. This potential confound can be addressed in the future by obtaining more data so that the "out of RF" category can be limited to saccades directed to the hemifield opposite the RF. That being said, we feel any potential effects of surrounding prey will likely be small given the distribution of prey items are randomized on each trial.

The minimal effect of saccade goal during the middle epoch of the handling period examined above is somewhat surprising. The intermediate layers of the SC have long been considered integral to saccade selection and production. Anatomically, it is close to the motor output, projecting directly to the burst generator circuit in the reticular formation (Munoz et al., 2000). Functionally, many cells in the SC_i display pre-saccadic activity related to saccade selection and/or a transient burst aligned with the saccade (Munoz et al., 2000; Wurtz and Albano, 1980).

One possible explanation is that SC activity only initially reflects profitability information but evolves to reflect saccade goal. Recordings from our own lab have suggested that saccade selection in the SC is built up gradually throughout the fixation period. This build-up is especially slow when potential saccades are supposedly equal in profitability (Thevarajah et al.,

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2009). To test this hypothesis, we compared the neuronal activity between three epochs throughout the handling period: at the beginning of fixation, immediately before reward delivery, and shortly before leaving fixation.

4.4 TEMPORAL EVOLUTION

The second hypothesis that we tested was whether or not SC_i activity evolves from initially representing profitability to increasingly representing saccade selection. Consistent with our previous analyses, profitability had a significant effect on neuronal response but the effect of saccade direction was not significant on its own. Importantly for our third hypothesis, the main effect of timing, the interaction between timing and profitability, and the interaction between timing and saccade goal were all highly significant. Therefore, our results suggest that SC_i activity reflects profitability information throughout the handling time leading up to reward delivery, but evolve to reflect saccade goals as the time of saccade approaches.

No study to date has compared specifically the effects of profitability and saccade direction; however, Horwitz and Newsome (2001) performed a similar comparison but using a gradient of coherence in a motion discrimination task instead of profitability. Although many cells in the SC display activity that is correlated with coherence, they are moreover predictive of upcoming saccade, even when coherence is 0% (i.e. there is no real difference between either option).

A possible explanation to reconcile our results with those found by Horwitz and Newsome is the difference in reward distribution between our tasks. In their task, only one target is rewarded at a time. In addition, only a minority of the trials are 0% coherence and these trials are randomly interleaved between trials where one target can be perceptually distinguished as the

better option. This arrangement makes it more likely that, even on trials of 0% coherence, the chosen target is perceived as the "better" option, similar to being the most profitable. If this is true, then the heightened effect of saccade choice on SC activity observed by Horwitz and Newsome may be due in part to the effect of profitability that we observed in the present study. Our observations therefore do not contradict those observed by Horwitz and Newsome but simply suggest that the part played by profitability can also be quite significant.

Nevertheless, profitability information playing a dominant role over saccade goals throughout the handling time prior to reward delivery in affecting SC_i activity is surprising. Several reasons may have caused this unexpected result. First, the abundance of prey in our foraging task may have the effect of dampening the difference in neuronal activity between options as multiple saccade goals compete to be executed. Basso and Wurtz (1997; 1998) found that delay period activity in certain neurons of the SC_i decreases as the number of possible saccade options increases. The difference in neuronal activity between saccade goals and non-saccade goals may therefore be present, just reduced and therefore does not reach statistical significance on a single neuron basis with the amount of data presented here.

Second, the variability of harvest times may have delayed saccade selection processes. In addition to the five possible harvest times, prey that have been the target of the brief saccades described above would have a shorter than expected harvest time when the subject finally commits to harvesting it. If too much saccade preparatory activity is present during the handling time, the subject risks leaving a prey prematurely, before a reward can be given. With the uncertainty of when the next saccade should be initiated, the subjects may have waited for reward delivery as a signal before completing saccade selection. Profitability information and specific prey options may have been represented by only subtle differences in SC_i activity, which is

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amplified once reward is given. Data from our own lab shows that the rate of saccade selection in the SC is tailored to predictable timing of saccades (Thevarajah et al., 2009). This is supported by the greatest (Fig 10) and only significant (Table 4) effect of saccade direction in the latest epoch, after reward delivery.

Third, different cell types may represent different parts of the decision process. To increase statistical power, all cells that showed strong RF specific activity were analyzed together. In reality, during the delayed task, some cells displayed mostly a motor transient while others displayed different combinations of visual transient, motor transient, or sustained activity during the delayed period. With more data, different cell types should be analyzed separately to see if they represent each of the components of visualsaccadic foraging decisions – profitability, saccade vector, and timing – differently.

More data is needed to distinguish between these possibilities. Regardless of which of the above reasons is behind the minimal effect of saccade goal we observed, our results clearly show that SC_i activity strongly reflects prey profitability.

4.5 ORIGIN OF PROFITABILITY SIGNALS

It is important to note, however, that although our results suggest that SC_i activity reflects information about subjective profitability, it does not imply that these signals originated in the SC_i. The superior colliculus receive input from a variety of higher level areas such as the frontal eye fields (FEF), supplementary eye fields (SEF), lateral intraparietal area (LIP), and basal ganglia (Hikosaka, 1989; McHaffie et al, 2005; Paré and Wurtz, 1997; Segraves and Goldberg, 1987) that have been shown to encode each of the variables (e.g. reward or time) that determine profitability (Brody et al., 2003; Buonomano and Karmarkar, 2002; Coe et al., 2002;

Ding and Hikosaka, 2006; Durstewitz, 2004; Hikosaka et al., 2006; Kobayashi et al., 2002; Leon and Shadlen, 1999; Matell and Meck, 2004; Platt and Glimcher, 1999). Instead of relaying pre-determined saccade command to the SC, individual neurons in these areas may pass on information along a particular dimension and the SC_i integrates this information from across the saccadic network to compute profitability. The SC_i can in turn pass on this profitability information for further processing through feedback connections to the frontal eye field (Sommer and Wurtz, 2004a; 2004b) or basal ganglia (McHaffie, et al., 2005). The SC_i may also actively enhance the profitability signal into a final saccade decision through a combination of local recurrent excitation and lateral inhibition within the SC_i (Munoz and Istvan, 1998; Dorris et al., 2007). It is not clear in our study which of these mechanism is at work, however, it is clear that SC_i activity reflects the prey profitability that is necessary for selecting saccades.

4.6 FUTURE DIRECTIONS

This study borrowed from behavioural ecology to develop a novel visuosaccadic foraging task, opening a variety of research questions that this thesis was not able to cover. Some of these analyses can be performed using the visuosaccadic foraging task outlined in this thesis, some will require modifications to the task.

The current data set can be used for further analysis, although more experiments will be needed to obtain enough data for statistical power. For example, although we have shown that SC activity represents profitability of prey items, it is not clear to what extent this only represents relative profitability instead of absolute profitability. According to foraging theory, once the prey item with the highest profitability has been depleted, the animal should change strategy to forage for the prey item of the next highest profitability. This behaviour would predict that it is more

important to encode the relative profitability of prey items rather than the absolute profitability. To examine this, the current neuronal data attributed to the second ranking prey can be further divided into those that occurred while there are first ranked prey available and when all of the first ranked prey have been harvested, leaving the second ranked prey as most preferable. SC activity reflecting relative rather than absolute profitability would predict an increase in firing rate when the second ranked prey items become the currently preferred targets. Since dividing neuronal data into more specific categories will greatly decrease the sample size in each category, more data is needed to do this analysis.

The demonstration that SC activity represents some sort of information about prey profitability, relative or otherwise, makes it possible that the SC has an active role in selecting saccade vectors; however, it may still be only passively reflecting signals from other brain regions along the visuosaccadic pathway. Stimulation experiments is one way to distinguish between these two possibilities. An active role, such as by a race-to-threshold mechanism, would suggest that if we can artificially alter profitability signals in the SC, we can bias choice. To examine this, we can apply sub-threshold stimulation to the SC early in the handling period to see if the next saccade will be biased towards the prey inside the response field in particular, even if there are other prey items of the same colour elsewhere on the grid.

In the real world, foraging is often accomplished with other modalities, such as capturing prey with the hands. By adapting this task for the hand, where prey items are harvested by accurate arm movements towards the prey instead of saccadic eye movements, more questions can be addressed. Compared to saccadic eye movements, arm movements are slow and less accurate; how will this affect how each of the variables – reward magnitude and timing – affect subjective profitability? Will distance between targets become a significant variable to be

examined? In highly visual animals such as humans and other primates, how will saccadic decisions be made when they are not necessary for the completion of the task? In the brain, it will be interesting to see if the SC will continue to encode subjective profitability of prey when saccadic decisions are not necessarily based on prey profitability.

4.7 CONCLUSION

In this thesis, we first used foraging theory to elicit behaviour as a tool for analyzing relative profitability. We demonstrated that monkeys adjusted colour preference in a foraging task according to prey profitability in a manner that approaches optimal behaviour as predicted by foraging theory. Deviations from optimal suggest that the index derived from this behaviour reflects subjective, not objective profitability. The superior colliculus, a structure close to the motor output of the saccadic system, displays activity that predicts the subjective profitability. In addition, the relationship between SC activity and subjective profitability is not based solely upon saccade direction encoding, suggesting that SC_i activity represents not simply pre-determined saccade plans, but estimated profitability of targets that can be used to generate saccade plans. Only after the reward had been given did the SCi activity reflect the particular prey item that would be selected for the next saccade.

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