Title
Temporal Constraints on Saccadic Eye Movements

Author
Parsons, Brent

Publication Date
2017

Peer reviewed|Thesis/dissertation

Temporal Constraints on Saccadic Eye Movements

by

Brent David Parsons

A dissertation submitted in satisfaction of the

requirements for the degree of

Doctor of Philosophy

in

Vision Science

in the

Graduate Division

of the

University of California, Berkeley

Committee in Charge:

Professor Bruno A. Olshausen, Ph.D. (Chair)
Professor Clifton M. Schor, Ph.D.
Professor Richard B. Ivry, Ph.D.

Spring 2017

Abstract

Temporal Constraints on Saccadic Eye Movements

by

Brent David Parsons

Doctor of Philosophy in Vision Science

University of California, Berkeley

Professor Bruno A. Olshausen, Chair

Although we are rarely aware of it, our ability to visually perceive and successfully interact with the world depends on a rapid and carefully orchestrated sequence of eye movements. Roughly three times a second, large high-velocity movements known as saccades drastically alter the spatial and temporal stream of visual input. To investigate the temporal constraints on saccadic eye movements and identify biases in oculomotor behavior, I developed a simple but novel task: rapid alternating saccades (RAS). Human participants are asked to make a series of eye movements back and forth between stationary targets as quickly as possible.

In Chapter 2, I investigate the characteristics of one of the most prominent and well-known biases in eye guidance, inhibition of return. Participants made RAS between two targets or following an “hourglass” pattern in which the same location is only sampled every fourth eye movement. The experiments revealed that both saccade dwell times and secondary saccade characteristics were dramatically altered when the eye returned directly to a previously viewed location. The effects depended on the direction of movement and the angular difference between subsequent saccades. The results further explicate the inhibition of return phenomenon and provide novel insight into motor and attentional constraints governing the rate of sequential eye movements.

Chapter 3 explores interactions between the eye and the hand. Findings indicate that the maximum rate of RAS increases when concurrent and directionally compatible hand movements accompany the eye movements. The increase is the result of shorter dwell times, higher saccade peak velocity, and a decrease in secondary saccade occurrence. The findings occur independently of changes in saccade amplitude or direction. Hand movements in the opposite direction of the eye result in longer dwell times and more frequent secondary saccades. The experiments illustrate the tight temporal coordination between saccades and arm motor systems during sequential movements.

Acknowledgements

I am deeply indebted and grateful to my advisor, Richard Ivry, whose unwavering support and dedicated guidance made this dissertation possible. Rich is an encouraging mentor, an inspiring scientist, and a kind and caring individual.

The dissertation has also benefited greatly from the support of my family, friends, colleagues, and the academic community at U.C. Berkeley.

Table of Contents

List of Figures

Chapter 2

Chapter 3

List of Tables

Chapter 2

Chapter 3

Chapter 1: Introduction

In order to survive we must continuously shift our gaze to bring prioritized regions of the world into high-resolution central vision, or what is called the foveal region of the retina. Saccadic eye movements, whether volitional or reflexively elicited, change the foveal input; as such, they impose a fundamental bottleneck on the extraction and processing of visual information. To understand and model vision we need to have some account of how gaze is controlled. To date, the majority of research on this topic has focused on the spatial rather than the temporal aspects of viewing behavior. Dominant models in the field, based on low-level spatial properties of external sensory input, make predictions about where to look in a scene but often fail to consider temporal properties and constraints on eye movements. Knowing when our gaze shifts and for how long it remains at a given position are crucial elements for any formal model of vision. Moreover, to date, there has been little work on the tight temporal coupling between vision and action, a phenomenon that is fundamental to natural behavior. The research undertaken in this dissertation is designed to address these gaps in knowledge and provide behavioral insight into the temporal constraints that guide the control of saccadic eye movements.

The experiments make use of a task originally described by Alfred Wilhelm Volkmann, a German anatomist, in 1846 (Westheimer 1989). Participants are asked to make sequential saccadic eye movements back and forth across the visual field to stationary targets as quickly as possible. These rapid alternating saccades (RAS) are used to investigate temporal constraints in eye movements and identify biases in oculomotor behavior. The task has several advantages over existing approaches. In contrast to a typical reaction time study, RAS consists of sequences of eye movements, more akin to natural viewing behavior. In addition, the data can be collected in roughly one fifth the time and provide a measure of ocular behavior that is free from the biases associated with exogenous or endogenous orienting. RAS provides a measure of oculomotor behavior that shares much in common with studies of visual scanning but still affords tight experimental control over saccade parameters. The task is amenable to the efficient collection of large data sets, can be applied in a range of contexts, and given its resemblance to natural eye movement patterns has the potential to be clinically applicable.

To understand the temporal aspects of saccadic eye movements, the studies consider a comprehensive set of oculomotor parameters. Saccades are differentiated from other movements made by the human body in that their dynamics are remarkably stereotyped and independent of cognitive control. There is a consistent relationship, known as the ‘main sequence,’ between the amplitude of a saccade and its duration and peak velocity. Consideration of the relation between these three variables across different conditions can yield important insight into how the brain controls movement kinematics. Closely related to these movement dynamics is the question of whether or not the initial

primary saccade lands at its target destination. To characterize saccade endpoints, the studies consider (1) the gain, the degree of saccade undershoot or overshoot, (2) the accuracy, the mean offset from the target, and (3) the precision, or scatter in the landing positions. Primary saccades are often followed by small secondary saccades which are thought to bring the eye closer to its intended destination. To understand the properties of secondary saccades the experiments analyze the frequency of their occurrence, their latency, and amplitude. Finally, following a saccade, distinct neural circuits are engaged to hold the eye in place at its targeted location. The duration of these dwell times reveal the essential interplay between motor programming and visual processing demands.

The first set of experiments (Chapter 2) address a well-established bias in attentional and motor programming, known as inhibition of return (IOR). Crucial to computational models of eye guidance, IOR describes a mechanism that leads us to explore the visual field and avoid returning to a previously viewed location. In contrast to reports from attentional IOR (2.3.1), the experiments show that saccadic IOR is present but has a reduced effect on vertical saccades and that inhibition for both horizontal and vertical saccades appears to decrease as amplitude becomes larger. A follow-up experiment (2.3.2) was devised to understand if these inhibitory effects depend on saccade amplitude, a constant zone around the target, or the angular differences between subsequent saccades. Pitting these hypotheses against each other, the experiments provide clear evidence that inhibition is independent of zone or amplitude but grows weaker as saccadic angular differences increase. The studies also demonstrate specificity for exact return locations, as small deviations in angle caused nonlinear dramatic changes in the inhibitory strength. This distinction for direct return locations was further supported by data showing that return locations were associated with greater secondary saccade frequency and smaller secondary amplitude. These changes occurred without any concomitant change in saccade kinematics or endpoint error.

The next set of studies (Chapter 3) investigated temporal coupling between hand movements and sequential saccades. They specifically addressed the question of whether manual action could have an influence on saccade programming. Participants made RAS in different directions either alone or accompanied by hand movements or contingent beeps. The first experiment (3.3.1) revealed that concurrent and directionally compatible pointing movements resulted in shorter dwell times, higher saccade peak velocity, and a reduction in the rate of secondary saccade occurrence. This effect was seen equally both in the presence and absence of saccadic inhibition of return. Hand movements in the opposite direction of the eye resulted in longer dwell times and a greater frequency of secondary saccades but had no effect on peak velocity. To control for potential confounds of arousal or attention, we included a condition in which each saccade was accompanied by a contingent beep. This failed to change dwell times or secondary saccades characteristics but did lead to an increase in

saccade peak velocity. A follow-up experiment (3.3.2) was undertaken to corroborate these results and test for an influence of saccade size or direction on the findings. We replicated the effect directionally compatible hand movements had on saccade dwell times, peak velocity, and secondary saccade occurrence and demonstrated that the results occurred equally for horizontal and vertical saccades of varying amplitudes.

The temporal constraints on saccadic control remains a relatively underexplored and underappreciated aspect of our visual exploration of the environment. To better understand this crucial issue, I have carried out a series of studies to characterize and elucidate the principles underlying oculomotor biases. I begin (Chapter 2) with a comprehensive investigation of one of the most well-known saccadic biases, inhibition of return, and demonstrate how spatial factors constrain the temporal features of this inhibition. I then look at hand-eye coordination (Chapter 3), and uncover novel ways in which manual actions influence saccade programming. My hope is that this work provides a foundation and an inspiration for further investigation into saccadic temporal constraints.

Chapter 2: Spatial constraints in saccadic inhibition of return

2.1 Introduction

Exploration of the visual environment requires serial shifts of attention that bring prioritized regions of space onto the central fovea. The efficiency of this exploration, it has been argued, is dependent on a mechanism that prevents gaze from continuously returning to the highest priority location. Computational accounts of active vision incorporate this bias as a fundamental feature of visual scanning (Itti & Koch, 2001), yet the behavioral underpinning and properties of such a bias remain controversial (Berlucchi, 2007; Bays & Husain, 2012; Wilming et al. 2013).

Evidence for the existence of a mechanism biasing attention away from previously viewed locations was originally discovered by Posner & Cohen (1984) and was subsequently labelled 'inhibition of return" (IOR), (Posner et al., 1985). The authors found that inserting a sufficient delay (> 225 ms) between the presentation of an exogenous cue and the delivery of a target stimulus resulted in prolonged reaction times to the target. This cue-target paradigm, requiring covert shifts of attention, has guided much of the subsequent research on the phenomenon and has led to an interpretation of IOR as being primarily sensory or attentional in nature (Posner et al., 1985; Tassinari et al., 1987; Spence & Driver, 1998; Bennett & Pratt, 2001; Dorris et al., 2002; Fecteau, Bell, & Munoz, 2004; Satel et al., 2011).

One influential account, however, makes a case for the importance of oculomotor programming in generating the observed effects (Rafal, Calabresi, & Brennan, 1989). Strong support for this view comes from a study by Hooge & Frens (2000) that demonstrated a form of IOR distinct to the oculomotor system, termed inhibition on saccadic return (ISR). Using rapid sequences of saccades, the fixation durations to return locations were found to be up to 40% longer than those to other regions of the scene. The effect size is much larger than that reported for cue-target IOR (typically < 10%), is limited to 4 degrees of visual angle rather than the entire visual field (Bennett & Pratt, 2001), and disappears after 180ms instead of lasting for up to two seconds (Posner et al., 1985). The studies that have followed up on this work have largely focused on visual scanning behavior in tasks such as free viewing or active search. Some of these experiments have provided evidence for ISR (Bays & Husain, 2012; Luke et al., 2014), while others have questioned its existence (Wilming et al., 2013). Few have considered more recent work on the canonical cue-target IOR effect and its relation to ISR.

The present study builds upon the Hooge & Frens (2000) findings to further investigate the properties underlying ISR using a larger subject pool and an expanded set of parameters. The task, voluntary rapid alternating saccades (RAS) between predefined points, combines the ecological validity of visual scanning with the tight experimental control typically observed in cue-target or

reaction time experiments. Participants made sequential saccades either returning to the same location or in an hourglass pattern between four points.

We use RAS to investigate the characteristics of ISR, testing five core questions. First, is ISR greater in the periphery relative to the perifoveal visual field. Recent studies using cue-target IOR have found greater inhibition as stimuli are presented at more distant eccentricities (Bao & Pöppel, 2007; Lei & Bao 2012; Bao et al., 2013). These findings have been linked to the spatial inhomogeneity of the visual field (Pöppel & Harvey, 1973) and the notion of two independent attentional processing modes (Pöppel, Cramon, & Backmund, 1975) for perifoveal and peripheral stimuli.

Second, is ISR weakened or is it eliminated when saccades are made along the vertical axis, as recently reported for IOR in monkeys (Tian & Hafed, 2015). Vertical stimuli activate lateralized visuo-motor structures (e.g. superior colliculus) simultaneously and may thus mediate the bilateral inhibition proposed to underlie the ISR phenomenon (Wang et al., 2011).

Third, does ISR exist as a phenomenon distinct from saccadic momentum, a linear increase in fixation duration accompanying changes in saccade angle (Smith & Henderson, 2009; Wilming et al., 2013). A nonlinear increase in inhibition when saccades return to a previously viewed location would provide evidence for an independent ISR mechanism (Luke et al., 2014).

Forth, is ISR best characterized as a constant zone around the target (Hooge & Frens, 2000; Bennett & Pratt, 2001) or might it instead depend on the angle between subsequent eye movements (Anderson, Yadav, & Carpenter, 2008; Smith & Henderson, 2009; Bays & Husain, 2012). A dependence on angle rather than zone would suggest ISR is likely driven more by motor than perceptual or attentional constraints.

Finally, what role, if any, do secondary fixational saccades play in generating the observed behavioral effects. Fixational, micro-saccadic oscillatory processes have recently been proposed as a mechanism underlying classical inhibitory effects in cue target IOR studies (Tian, Yoshida, & Hafed, 2016).

2.2 Materials and Methods

2.2.1 Participants

16 individuals participated in experiment 2a (two subject were excluded from analysis because of tracker loss), and 10 individuals participated in experiment 2b. Participants were undergraduates at the University of California at Berkeley and naive of the purpose of the experiment. They participated in the study in exchange for course credit. All participants had normal or corrected to normal vision.

2.2.2 Visual Stimuli and Presentation

Visual stimuli were generated using Matlab Software and presented on a gamma-corrected 21' CRT monitor with a refresh rate of 100hz at a viewing distance of 57cm. The display resolution was set to 1,024 x 768. Experimental trials and communication with the eye tracker were controlled using Psychtoolbox in Matlab.

The visual saccade targets were black circles, with a diameter of 1º and a luminance of 7.4 cd/m^2, presented on a uniform gray background (72.2 cd/m^2). There were either two stimulus locations, for return saccades or four stimulus locations arranged in a rectangle, for the hourglass condition. The fixation target, a black cross, was presented at the center of the screen.

2.2.3 Task Design and Procedure

In each trial the task was to make 10 primary saccades as quickly as possible either back and forth between two targets or in an "hourglass pattern" between four stimulus locations arranged in a rectangle. Each trial terminated once 10 primary saccades were detected online.

Subjects were instructed to complete the sequence as quickly as possible. Each trial started with the subject fixating a black cross presented on a gray background in the center of the screen. After a randomly determined time (0.5-1.5s) the fixation target disappeared and the saccade targets were presented. If a blink was detected during the saccade sequence, subjects were asked to repeat the trial. Participants received auditory feedback (a short beep) at the end of a successful trial.

In experiment 2a the visual saccade targets were either 5º or 15º apart arranged vertically or horizontally. In the hourglass condition the separation between targets in the movement direction was 4º. The eight conditions, a 2x2x2 factorial design (5-0 H, 5-4 H, 15-0 H, 15-4 H, 5-0 V, 5-4 V, 15-0 V, 15-4 V), were selected randomly from a uniform distribution on each trial. Each block consisted of 40 trials. Participants completed 4 blocks of the experiment, yielding roughly 200 eye movements per condition in total.

In experiment 2b the visual saccade targets were either 5º, 10º, or 20º apart arranged horizontally. The separation between the targets in the movement direction was set at 0º, 0.5º, 1º, 2 º, 4º, or 8º. The fourteen conditions, a pseudo-factorial design structured to isolate the effect of both zone and angle (5-0, 5-0.5, 5-1, 5-2, 10-0, 10-0.5, 10-1, 10-2, 10-4, 20-0, 20-1, 20-2, 20-4, 20-8), were selected randomly from a uniform distribution on each trial. After 35 trials, participants were given a break. Each block consisted of 70 trials. They completed 4 blocks of the experiment, again yielding roughly 200 eye movements per condition in total.

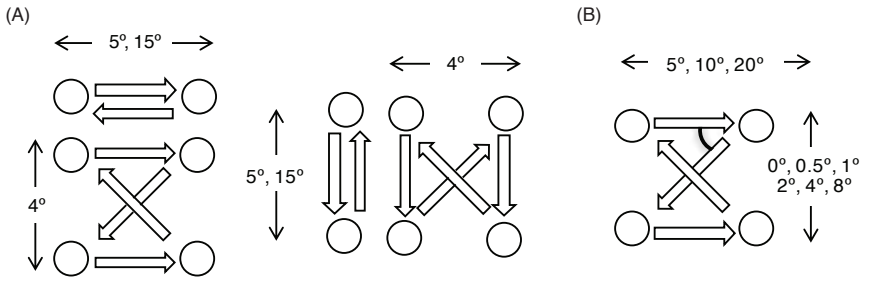

Figure 2.1 Experimental methodology and conditions. (A) In the first experiment subjects made rapid alternating saccades (RAS) of 5º or 15º in horizontal and vertical directions either returning between two points or in an hourglass pattern. The separation of the hourglass was held constant at 4º. (B) In the second experiment subjects made horizontal RAS of 5º, 10º, or 20º. The vertical separation of the hourglass varied between 0º and 8º. This allowed us to independently isolate the influence of the anglular difference between subsequent saccades across different amplitudes.

2.2.4 Eye Movement Recording and Analysis

Eye movements were recorded monocularly, using the right eye, on a desktop mounted SR Research Ltd. EyeLink 1000 eyetracker. Pupil position was sampled at 1000hz. To calibrate and validate gaze position tracking, two nine-point grids were presented to subjects at the beginning of the experiment. Velocity was computed using a 9-sample moving filter. Saccade onset was detected as the first time point at which both velocity exceeded 22 º/s and acceleration exceeded 4000 º/s. When velocity and acceleration fell below these thresholds, the end of the saccade was registered. Both primary and secondary saccades were detected in this way. The same smoothing procedure and saccade detection algorithm were used in both experiments. Further analysis of eye movements was undertaken offline using a custom written script in Matlab.

The average accuracy of the Eyelink 1000 system is 0.25-0.50º of visual angle. During calibration, we ensured that the average tracking error for all subjects was < 0.5º. Subjects viewed the stimuli binocularly and head position was stabilized with a combined head and chin rest. To avoid measurement noise, participants were asked to maintain a steady head position through the trials. We recorded with the "pupil-CR" (Corneal Reflection) mode to compensate for any small head movements. The centroid mode was used to track the center of the thresholded pupil. Recent studies have shown that changes in pupil size can lead to systematic deviations in the reported gaze position (Ivanov & Blanche, 2011; Hooge, Holmqvist, & Nyström, 2016; Nyström, Hooge, & Andersson, 2016). Although we did not correct for these pupil-size related artifacts we have no reason to expect differences in pupil dynamics across the different conditions. Video-based eye trackers are also known to be slightly less accurate at measuring large vertical eye movements because the pupil can be partly occluded by the eyelids and eyelashes. To guarantee the accuracy of our recordings, we used the exclusion criteria detailed below and visually inspected the saccade traces before further analysis was carried out.

Endpoint scatter, precision, was determined by calculating the covariance matrix for each subject and location. We used the sum of the variance in the two orthogonal directions, the mean squared distance from the mean (van Beers, Haggard, & Wolpert, 2004), as our measure of precision.

2.2.5 Exclusion Criteria

The first saccade in each trial was excluded from analysis. Outliers were removed from the data. Primary saccades with amplitudes < 3º, durations > 130ms, or dwell times < 50ms or > 800ms and outside of 3SDs for the individual subject were rejected. In addition, we also excluded saccades whose landing or starting position were greater than 3º away from the target and those that started or landed outside of the screen coordinates. This resulted in ~9% of all registered saccades being excluded in Exp. 2a and ~8% of registered saccades being excluded in Exp. 2b.

Secondary saccades were identified using the same velocity and acceleration criteria as primary saccades. Only those occurring > 20 ms after the primary saccade, with an amplitude < 20% of the target amplitude, and having a duration > 8ms but < 50ms were included. Only the first secondary saccade following a primary saccade was accepted for further analysis.

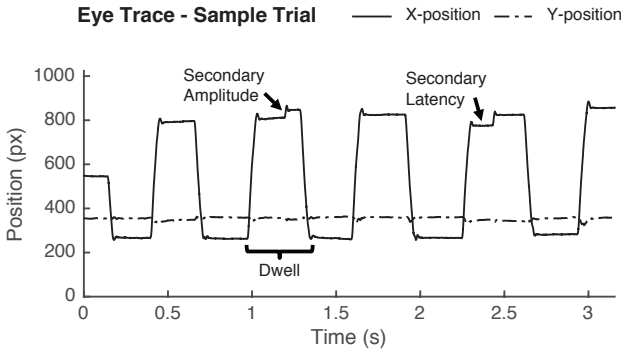

Figure 2.2 Saccade parameters. On each trial (10 saccades) we extracted the dwell times, endpoint precision, and the secondary saccade frequency, amplitude, and latency for further analsyis.

2.2.6 Statistical Analysis

Saccade parameters were compared statistically between conditions using a repeated measures ANOVA in SPSS. When the assumption of sphericity was violated, appropriate corrections were used. Post-hoc comparisons were made with Bonferoni corrected p-values.

2.3 Results

The experimental manipulations of saccadic inhibition of return yielded significant differences in both dwell times and in the properties of secondary saccades. Experiment 2a (2.3.1) describes how those changes depended on the direction and amplitude of the saccades. Experiment 3b (2.3.2) examines the influence of the zone around the target and the angular difference between subsequent saccades.

2.3.1 Exp. 2a: Amplitude and Direction

In Exp. 2a subjects made RAS of 5º or 15º between two points or in an hourglass pattern both horizontally and vertically. The width of the hourglass was set at 4º, the suggested zone of saccadic inhibition of return. Hooge & Frens (2000) found that separations between targets larger than 4º led to no additional reduction in saccade dwell times. A repeated measures factorial ANOVA was used to test for effects of amplitude (5,15), direction (horizontal, vertical), and condition (return, hourglass).

There was a main effect on dwell times for amplitude, with subjects taking longer to complete sequential saccades at 5º than at 15º ($F(1,13) = 69.07$, $p < .001$). Replicating the ISR effect, dwell times were significantly shorter in the hourglass condition than in the return condition, ($F(1,13) = 128.80$, $p < .001$). Notably the effect occurred for both the horizontal and vertical directions, although there was a significant interaction, ($F(1,13) = 7.66$, $p = .016$), with the magnitude of the ISR effect being greater for horizontal saccades. There was also a significant interaction for dwell times between amplitude and condition, ($F(1,13) = 10.56$, $p = .006$) indicating that the strength of ISR was larger for 5º saccades than for 15º saccades.

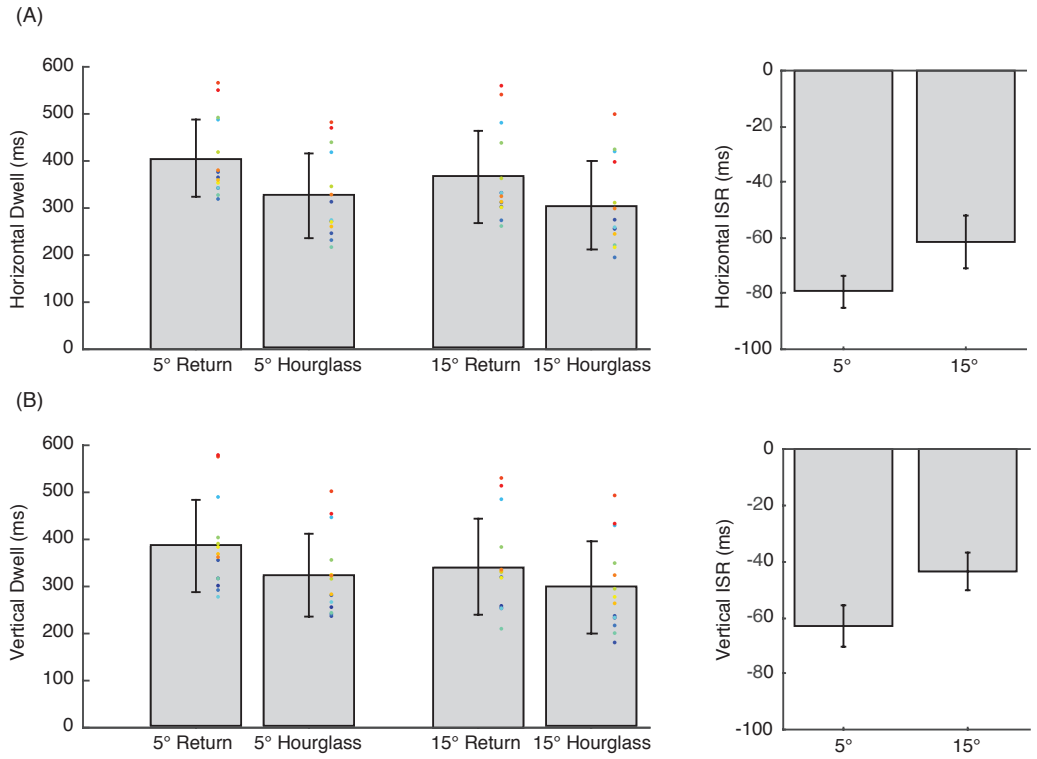

Figure 2.3 Mean dwell duration and magnitude of inhibition of saccadic return, ISR, in both the horizontal (A) and vertical (B) directions in Experiment 2a. Colored points represent individual subjects.

To understand the changes in dwell times, we also examined the characteristics of secondary saccades that followed the primary saccade. We found that secondary saccades were more common in the return than hourglass conditions, ($F(1,13) = 23.64$, $p < 0.001$). Secondary saccades were also more prevalent at the larger amplitude ($F(1,13) = 6.96$, $P = 0.020$), and there was a significant interaction term indicating that the decrease in secondary saccade frequency was greatest at the larger amplitudes ($F(1,13) = 6.36$, $p = 0.026$). Secondary saccade latency was unchanged between the return and hourglass conditions, but the amplitude was significantly larger for hourglass saccades ($F(1,13) = 21.93$, $p < 0.001$). The changes in secondary saccades between return and hourglass conditions occurred without a corresponding change in either the gain, accuracy, or precision of the movements.

Amplitude (Condition)	Mean (SD) of Parameters			
	Dwell (ms)	Secondary Frequency (%)	Secondary Latency (ms)	Secondary Amplitude (º)
Horizontal				
5º (Return)	404 (83)	16 (7)	219 (46)	0.95 (0.32)
5º (Hourglass)	325 (91)	12 (9)	194 (39)	1.55 (0.69)
15º (Return)	365 (98)	25 (13)	191 (35)	1.20 (0.30)
15º (Hourglass)	304 (93)	15 (15)	202 (67)	1.35 (0.56)
Vertical				
5º (Return)	385 (97)	21 (11)	180 (46)	0.91 (0.20)
5º (Hourglass)	322 (86)	12 (9)	182 (32)	1.32 (0.55)
15º (Return)	340 (102)	28 (6)	162 (30)	1.21 (0.28)
15º (Hourglass)	296 (96)	16 (12)	172 (38)	1.32 (0.41)

Table 2.1 Average dwell times and secondary saccade frequency, latency, and amplitude for saccades made horizontally or vertically either in the return or hourglass condition in Experiment 2a.

To investigate further the effect of secondary saccades on dwell times we extracted the dwell durations both before and after a saccade that was accompanied by a secondary movement. Previous studies have suggested that secondary saccade occurrence can lead to significant prolongation of saccade dwell times (Wu, Kwon, & Kowler, 2010). We replicated these results and found that dwell times were longer both in the fixations before ($M = +18ms$, $SD = 17$), ($t(13) = 3.93$, $P = 0.002$), and during ($M = +104ms$, $SD = 33.8ms$), ($t(13) = 11.46$, $p < 0.001$), secondary saccade occurrence. The influence of secondary saccades in prolonging dwell times following a primary saccade was greater, however, in the hourglass condition ($F(1,13) = 18.32$, $p = 0.001$). Because of the decreased frequency of secondary saccades in the hourglass condition, this did not translate into a meaningful effect on the overall mean dwell times between conditions. In fact, despite differences in frequency and amplitude, the contribution of secondary saccades to dwell times was nearly equal across all conditions tested.

Amplitude (Condition)	Mean (SD) of Parameters			
	Dwell Before (ms)	Dwell After (ms)	Dwell Before Contribution (ms)	Dwell After Contribution (ms)
Horizontal				
5º (Return)	+ 5 (37)	+ 89 (83)	+ 1 (6)	+ 15 (9)
5º (Hourglass)	+ 26 (69)	+ 157 (91)	+ 4 (8)	+ 18 (13)
15º (Return)	+ 21 (38)	+ 97 (98)	+ 4 (9)	+ 22 (10)
15º (Hourglass)	+ 60 (76)	+ 124 (93)	+ 7 (8)	+ 18 (15)
Vertical				
5º (Return)	+ 4 (27)	+ 62 (97)	+ 2 (7)	+ 14 (13)
5º (Hourglass)	- 8 (39)	+ 127 (86)	- 1 (4)	+ 15 (10)
15º (Return)	+ 21 (18)	+ 75 (102)	+ 6 (6)	+ 22 (19)
15º (Hourglass)	+ 16 (45)	+ 98 (96)	+ 2 (7)	+ 14 (10)

Table 2.2 Change in dwell durations for fixations either preceding or during the occurrence of secondary saccades in Experiment 2a. Contribution represents change in overall dwell duration as a result of secondary saccade fixations.

2.3.2 Exp. 2b: Zone vs. Angle

Exp. 2a showed that the strength of ISR was stronger for 5º saccades than it was for 15º saccades. This runs counter to many experiments showing that inhibition of return, IOR, is actually larger at more distant eccentricities (Bao & Pöppel, 2007; Bao et al., 2013). ISR, as introduced by Hooge & Frens (2000), has been characterized as a constant zone around the target. Although the zone was a constant 4º for both 5º and 15º saccades in Exp. 2a, the angular difference between subsequent movements was larger for 5º saccades (39º vs.15º) (Fig. 2.3 A,B). To uncover whether the ISR effect depends eccentricity, zone, and/or the angular difference between successive saccades (Smith & Henderson, 2009; Bays & Husain, 2012), we systematically varied horizontal hourglass length and height in Exp. 2b. Participants made saccades either at 5º, 10º, or 20º amplitude with the height of the hourglass either 0.5º, 1º, 2º, 4º, or 8º (Fig. 2.4 A,B)

We used a one-way repeated measures ANOVA (zone, angle) to test for main effects of either angle or zone on dwell times. When the angle of saccades across the three amplitudes were equated, we found differences in dwell only when the angle changed ($F(2,18) = 26.50$, $p < 0.001$) and not when the zone changed ($F(2,18) = 0.75$, $p = 0.488$). When equivalent zones were tested, a significant effect occurred again for changes in angle ($F(1,9) = 26.29$, $p = 0.001$) but not for changes in zones ($F(2,18) = 2.01$, $p = 0.164$).

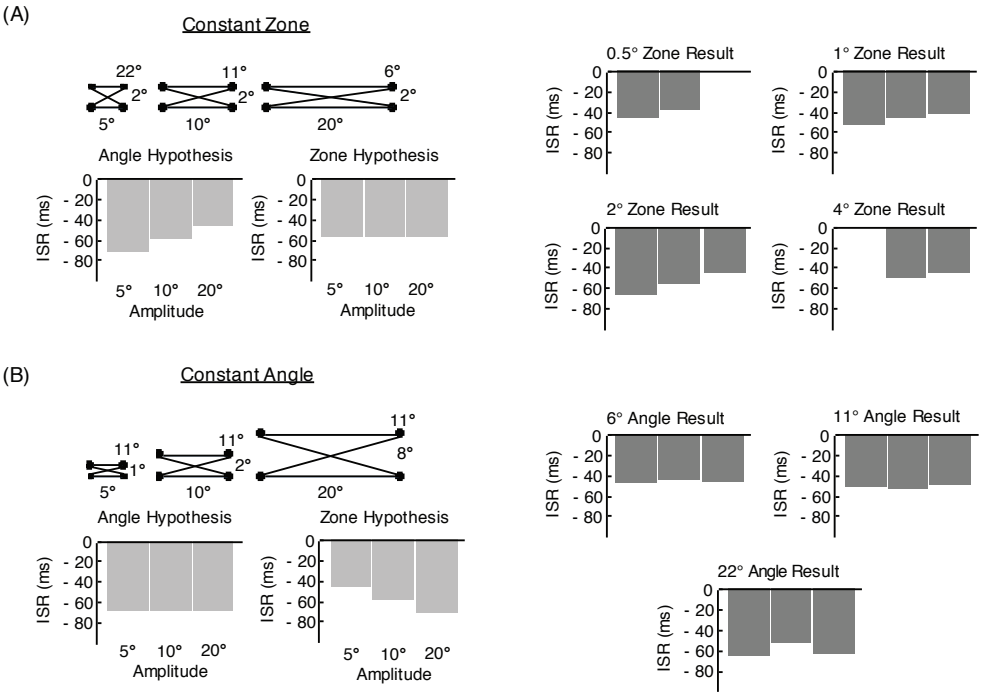

Figure 2.4 Experiment 2b methodology and results. (A) If inhibition of saccadic return, ISR, is modulated by the distance separating the targets than when that zone is held constant, ISR should also remain constant. (B) If, on the other hand, ISR depends on the angle between subsequent saccades holding the angle constant should result in equivalent measures of ISR. The results favor the angle hypothesis.

The features of secondary saccades on the other hand, depended primarily on the amplitude of the saccade and did not show differences depending on equivalent zones or angles. Table 2.3 shows the percentage occurrence of secondary saccades at the three amplitudes either in the return condition or in the hourglass conditions. We averaged the secondary saccade characteristics in the hourglass saccades and used a two way repeated measures ANOVA (amplitude, condition) for analysis. There was a main effect of frequency for both amplitude ($F(2,18) = 41.19$, $p < .001$) and condition ($F(2,18) = 11.71$, $p = 0.008$), with no significant interaction. Secondary saccade latency dropped with larger amplitude saccades ($F(2,18) = 20.26$, $p < 0.001$) but showed no differences between return and hourglass conditions ($F(2,18) = 0.56$, $p = 0.457$). Secondary saccade amplitude was greater for larger amplitude saccades ($F(2,18) = 30.55$, $p < 0.001$) and in the hourglass condition ($F(2,18) = 5.38$, $p = 0.046$).

Amplitude / Zone / Angle	Mean (SD) of Parameters			
	Dwell (ms)	Secondary Frequency (%)	Secondary Latency (ms)	Secondary Amplitude (º)
5º / 0º / 0º	420 (76)	25 (15)	201 (22)	0.78 (0.20)
5º / 0.5º / 6º	375 (91)	23 (16)	205 (21)	0.91 (0.34)
5º / 1º / 11º	369 (87)	18 (13)	208 (25)	0.98 (0.40)
5º / 2º / 22	356 (91)	18 (14)	203 (28)	1.09 (0.46)
10º / 0º / 0º	395 (69)	33 (13)	199 (25)	0.84 (0.18)
10º / 0.5º / 3º	356 (90)	26 (20)	193 (17)	0.83 (0.21)
10º / 1º / 6º	353 (93)	25 (17)	197 (24)	0.86 (0.21)
10º / 2º / 11º	343 (98)	25 (21)	199 (32)	0.94 (0.26)
10º / 4º / 22º	342 (99)	25 (20)	190 (29)	0.94 (0.28)
20º / 0º / 0º	381 (65)	47 (16)	181 (27)	1.11 (0.17)
20º / 1º / 3º	338 (87)	37 (24)	177 (29)	1.13 (0.21)
20º / 2º / 6º	338 (88)	38 (24)	174 (28)	1.14 (0.19)
20º / 4º / 11º	330 (88)	36 (26)	171 (30)	1.21 (0.24)
20º / 8º / 22º	319 (92)	37 (25)	164 (28)	1.29 (0.25)

Table 2.3 Average dwell times and secondary saccade frequency, latency, and amplitude for horizontal saccades of different amplitudes and separations in Experiment 2b.

2.4 Discussion

The two experiments revealed that the strength of inhibition of saccadic return, ISR, is determined by three factors: whether the eye movements are made primarily along the horizontal or vertical axis, the size of the angular change between subsequent eye movements, and whether or not the saccade returns exactly to the previously viewed location. Experiment 2a demonstrated that a constant zone of 4º around the targets produced ISR for both horizontal and vertical saccades but that the effect size was larger for horizontal saccades (~ 22% vs ~17%). When the zone around the targets was held constant, ISR appeared to decrease with larger amplitude saccades.

Experiment 2b allowed us to ask if inhibition over different saccade amplitudes was modulated by a constant zone around the targets, as suggested by 2a, or if inhibition instead changes depending on the angular difference between subsequent saccades. We found that ISR was equivalent across different saccade amplitudes when the angles were equated. This dependence on angle held despite the fact that dwell times themselves were inversely correlated with saccade amplitude. Finally, the difference in dwell times between return and hourglass saccades was much larger than the changes caused by increases in angle alone. The specificity for exact return locations, a roughly

700% increase over angle changes at non-return locations, provides evidence for a non-linear influence of ISR on dwell times.

The experiments also illustrated important constraints on the production of secondary saccades. The frequency of secondary saccade occurrence was much greater following return saccades than it was in the hourglass conditions, but those return secondary saccades tended to have a smaller overall amplitude. Larger amplitude saccades are accompanied by more frequent, lower latency, and larger amplitude secondary saccades. Several lines of evidence suggest that secondary saccade occurrence, while perhaps related to ISR, was not a principle driver of the observed effects on dwell times. First, secondary saccades in the hourglass conditions tended to prolong dwell times at a much greater level than in the return conditions. This fact meant that the overall contribution of secondary saccades to dwell times was roughly equal between return and hourglass saccades (Table 2.2). Second, despite a greater frequency of secondary saccades at larger amplitudes, dwell times were conversely much shorter as target amplitude increased (Table 2.3). This suggests that independent mechanisms may contribute to determination of dwell times and secondary saccade occurrence.

2.4.1 Specificity for Return Saccades

The most striking aspect of our results were the significant changes that occurred when saccades were made directly to the previously viewed target locations, the return condition. A separation between return targets as small as 0.5º or a change in return angle of 6º (Table 2.3) resulted in significant reductions in dwell times (~40ms). The idea that return saccades matched precisely in amplitude and location are unique accords with the original study of Hooge & Frens, (2000) and a more recent study by Luke et al., (2014) but stands in contrast to other studies of visual scanning (Tatler & Vincent, 2008; Smith & Henderson, 2009; Bays & Husain, 2012; Wilming et al., 2013). These authors describe either a roughly linear inhibitory effect dependent upon angle (Smith & Henderson, 2009; Bays & Husain, 2012) or fail to find any significant differences for saccades within 50º of the return location (Tatler & Vincent, 2008; Wilming et al., 2013). Some have argued that ISR can be fully accounted for by saccadic momentum, a tendency for the eye to continue in the same direction, and the addition of an amplitude effect in which subsequent saccades of the same amplitude are delayed (Smith & Henderson, 2009; Wilming et al., 2013). Our results contradict this hypothesis as amplitude differences in hourglass saccades of less than 1% still resulted in dramatic reductions in dwell time. This specificity for precise return locations also provides a challenge for any attempt to explain ISR in terms of residual activation in the superior colliculus (Wang et al. 2011).

Several factors may account for the difference in results between the present study and past experiments on visual scanning. Because of the nature of visual scanning, past studies have binned saccades angles, typically with 30º or

more, and so lack the specificity used in our experiment. The occurrence of saccades which are precisely matched in amplitude and angle may be relatively rare in such experimental designs. The presence and interaction between other bottom-up (e.g. luminance, contrast, complexity) and top-down factors (e.g. center-bias, task demands, search strategy, attention) known to influence dwell durations in such visual scanning paradigms may lead to additional confounds. Because the RAS task allows us to ensure that incoming and outgoing saccades are matched in both amplitude and angle and is free from these other confounds, we believe it provides a more direct and bias-free measure of the underlying ISR phenomenon.

2.4.2 Zone vs. Angle

Hooge & Frens (2000) proposed that an inhibitory region of approximately 4º around the target is generated after each saccade. More recent studies on visual scanning have supported the existence of a zone (Luke et al., 2014) or have suggested that changes in the angle between subsequent movements drive inhibition (Tatler & Vincent, 2008; Smith & Henderson, 2009; Bays & Husain, 2012; Wilming et al., 2013). To adjudicate between these two hypotheses, we devised conditions with matching angles and zones across different amplitudes. Our results provide clear evidence, at least for horizontally-oriented saccades, that ISR is dependent on the angle and not the zone around targets. Moreover, the independence of the strength of ISR from changes in amplitude also further distinguishes IOR (Bao & Pöppel, 2007) from ISR and provides an additional constraint for any neural models of the effect (Wang et al., 2011). The study was limited in that we did not test zones larger than 8º or angular differences in saccades greater than 22º. As such, we cannot address whether or not a sharp change in the strength of inhibition occurs when the angular difference surpasses 62º (Wilming et al., 2013). Our paradigm also does not allow us to isolate the influence of saccadic momentum (Smith & Henderson, 2009) as all saccades within a condition were of roughly the same amplitude. Future studies investigating the effect of saccadic momentum for saccades of different amplitudes might help to further disentangle the two phenomena.

2.4.2 Horizontal Vertical Differences

Shorter dwell durations for vertical RAS in comparison to horizontal RAS was first reported in the original experiment of Hooge & Frens (2000). Differences in the strength of ISR for vertical saccades however was not addressed and has not been shown in any subsequent study of ISR. Our results replicated the differences between horizontal and vertical dwell times but also found that the strength of ISR is reduced for vertical saccades. This finding appears to contradict the hypothesis that ISR is strictly governed by the angle between subsequent eye movements and adds an additional constraint on any

interpretation of the phenomenon. One possibility is that the directional changes in the strength of ISR arise from neurophysiological differences between horizontal and vertical eye movements. Vertical saccades are initiated by distinct pulse generators, premotor neurons, and oculomotor muscles (Sparks, 2002). Vertical eye movements also activate lateralized visuo-motor structures bilaterally and at the same time. This fact has been used to explain the decrease in inhibition that vertical eye movements show for distracting objects (Van der Stigchel & Theeuwes, 2008). Alternatively, the lower inhibition along the vertical axis may have a more functional explanation and relate to the statistical distribution of saccades across the visual field. Across a variety of tasks, human observers have been shown to make disproportionally more horizontal than vertical eye movements (Tatler & Vincent, 2009; Bays & Husain, 2012). Decreased behavioral relevance for saccades along the vertical axis may limit the strength and importance of inhibiting return saccades.

2.4.3 Changes in Secondary Saccades

We investigated secondary saccades properties based on the hypothesis that they may have had a causal influence on dwell times and the ISR phenomenon. Previous studies have provided evidence that the occurrence of a secondary saccade prolongs dwell times (Wu, Kwon, & Kowler, 2010) and that IOR in cue-target paradigms can be explained through the modulation of small fixational eye movements, known as micro-saccades (Tian, Yoshida, & Hafed, 2016). Our analysis revealed a clear increase in the rate of secondary saccade occurrence and a decrease in amplitude when the eye returned to the previously viewed location. This difference, even at the smallest target separations, is surprising given the potential distracting effect of nearby targets in the hourglass condition. The increase in frequency and the smaller overall amplitude also occurred despite equal levels of endpoint accuracy and precision between return and hourglass saccades. Secondary saccades have been assumed to function primarily as an error correcting mechanism (Becker & Fuchs, 1969; Tian, Ying, & Zee, 2013), hence their traditional label as corrective saccades. Recent work, however, has shown that multiple factors, independent of the distance between saccade endpoint and the target, can influence secondary saccade occurrence (Lemij & Collewijn, 1989; Ohl, Brandt, & Kliegl, 2011; 2013; Schut et al., 2017). Our study adds to this evidence and illustrates that ISR can exert a significant influence on secondary saccade programming.

The present study replicates previous work showing that the occurrence of secondary saccades prolongs dwell times (Wu, Kwon, & Kowler, 2010). We found longer dwell times with secondary saccades both in the presence and absence of ISR. Remarkably, eye movements to return locations led to a greater production of secondary saccades, but they did not directly prolong overall return dwell times. Because dwell durations for return saccades containing a secondary saccade were approximately 40ms shorter than corresponding hourglass

saccades, the contribution between the two conditions ended up being equivalent. The longer duration for larger amplitude secondary saccades in the hourglass condition only contributed +3ms to this difference. The latency of these secondary saccades was also equivalent between the two conditions. This puzzling finding appears to suggest that the occurrence of a secondary saccade in the return condition led to a release of inhibition and allowed the eye to more rapidly shift to the subsequent target location. The result has parallels with the literature on micro-saccades (Rolfs, Laubrock, & Kliegl, 2006; Tian, Yoshida, & Hafed, 2016) and may provide a basis for linking the literature between the two fields.

2.5 Conclusion

We investigated how the properties of inhibition of saccadic return (ISR) are influenced by changes in target amplitude, direction, zone or angle of separation. Our results provide clear evidence for the existence of ISR independent of other ocular-motor biases, such as saccadic momentum, and demonstrate that changes in saccade dwell time are primarily driven by angular differences between subsequent saccades and not a constant zone around the target. The independence of ISR from eccentricity and an asymmetry between horizontal and vertical saccades further distinguishes ISR from traditional measures of IOR and constrain any neural implementations of the phenomenon. We also uncovered a novel role for ISR in the programming of secondary saccades that occurs independently from any error correcting mechanism. Our study provides a relatively bias-free baseline measure of ISR that can be used to inform modern computational accounts of visual behavior.

Chapter 3: Hand pointing affects rate, peak velocity, and secondary saccade frequency of rapidly alternating saccades

3.1 Introduction

The majority of our interaction with the world requires a tight temporal coupling between eye movements and manual actions. Reaching for a glass of water, playing the piano, or climbing a tree requires constant rapid communication between the eye and the hand. In fact, it is rare for the two movements to be made in isolation and our survival often depends on fast and simultaneous activation of both saccadic and manual motor programs. Excellence in high-speed hand-eye coordination, whether in basketball or video games, is praised and richly rewarded in our society. The Olympic sport of table tennis provides an astounding example of the potential and limitations of the two systems. Players are able to carry on a game while hitting the ball nearly four times a second. This implies that gaze is able to shift back and forth across the table with pauses, or dwell times, of only 200ms. The gaze shifts occur while concurrently processing the visual information, planning compatible return actions, and carrying out the movements.

Despite the ubiquity of hand-eye coordination in natural behavior, the study of eye movements and manual action have largely progressed independently. The small selection of experiments that have looked at the relationship between concurrent manual and ocular movements have tended to focus on the influence that gaze has on subsequent arm movements (Prablanc et al., 1979; Johansson et al., 2001; Crawford, 2004; Jackson et al., 2005). Because of their short reaction time and duration, saccades in a cued laboratory experiment are typically completed before reaching movements have even begun. Under such conditions, preceding saccades have been shown to influence the both the metrics and kinematics of arm movements (van Donkelaar, 1997; van Donkelaar & Staub, 2000; Crawford, 2004; Niechwiej-Szwedo et al., 2004; Richardson et al., 2013; Lee et al.,2013). This emphasis on the use of visual feedback from the eyes in guiding hand trajectory has dominated theoretical and experimental work in the field.

The reverse influence of manual movements on saccadic performance, perhaps just as common in continuous naturalistic behavior, remains relatively unexplored. One of the most prominent findings of studies that have considered the effect the hand has on the eye is a delay in the onset of cued saccades when concurrent arm movements are planned (Mather & Fisk, 1985; Fisk & Goodale, 1985; Bekkering et al. 1994; Lee et al., 2013; Thura, Boussaoud, & Meunier, 2008; Lee et al., 2013; Armstrong et al., 2013, but see Lünenburger, Kutz, & Hoffmann, 2000; Snyder et al., 2002). Studies in monkeys (Snyder et al., 2002) and in human participants (Armstrong et al., 2013; Epelboim et al., 1997) have provided evidence that reaching movements also increase the peak velocity of saccades, although the effect may disappear when trials are presented in a block

design (Armstrong et al., 2013). Other studies have observed decreases (Lee et al., 2013) in saccade peak velocity or changes only when hand movements are made in the opposite direction (Gorbet & Sergio, 2009). Conflicting evidence also exists for the effect of arm movements on the frequency of secondary saccade occurrence (Epelboim et al., 1997; Lünenburger et al., 2000). Despite these differences, it is clear from these studies that the commands for planned manual actions are available to the saccadic system and may provide an additional temporal constraint in their functioning.

Taking inspiration from the sport of table tennis, we have devised a task, rapid alternating saccades (RAS), in which subjects were required to sequentially shift their gaze back and forth across the visual field as quickly as possible either with or without concurrent hand movements. We've chosen self-guided pointing movements outside of the subject's field of gaze in order to overcome the greater inertia, longer latency, and longer duration of reaching movements and to isolate motor programming from visual and proprioceptive guidance. The experiments attempt to resolve controversies in the field and consider whether concurrent pointing movements influence sequential saccade metrics, specifically dwell times, peak velocity, and the frequency of secondary saccade occurrence. We further test whether the observed behavior depends on the amplitude and direction of the movements and if it occurs above and beyond simple attentional orienting.

3.2 Materials and Methods

3.2.1 Participants

12 individuals participated in experiment 3A and 10 participated in experiment 3B. Participants were undergraduates at the University of California at Berkeley and naive of the purpose of the experiment. They participated in the study in exchange for course credit. All participants had normal or corrected to normal vision.

3.2.2 Visual Stimuli and Presentation

Visual stimuli were generated using Matlab Software and presented on a gamma-corrected 21' CRT monitor with a refresh rate of 100hz at a viewing distance of 57cm. The display resolution was set to 1,024 x 768. Experimental trials and communication with the eye tracker were controlled using Psychtoolbox in Matlab.

The visual saccade targets were black circles, with a diameter of 1º and a luminance of 7 cd/m^2, presented on a uniform gray background (72.2 cd/m^2) either 5º, 10º, or 20º apart arranged either horizontally or vertically. There were either two stimulus locations, for return saccades, or four stimulus locations

arranged in a rectangle, for the hourglass condition. The fixation target, a black cross, was presented at the center of the screen.

3.2.3 Task Design and Procedure

In each trial the task was to make 10 primary saccades as quickly and as accurately as possible either back and forth between two targets or in an "hourglass pattern" between four stimulus locations arranged in a rectangle. In conditions requiring hand movements, observers were instructed to point their index finger concurrently with their saccades either in compatible or incompatible directions. Each trial terminated once 10 primary saccades were detected online.

A trial started with the subject fixating a black cross presented on a gray background in the center of the screen. After a randomly determined time (0.5-1.5s), the fixation target disappeared and the saccade targets were presented. If a blink was detected during the saccade sequence, subjects were asked to repeat the trial. Participants received auditory feedback (a short beep) at the end of a successful trial.

In experiment 3a the visual saccade targets were arranged symmetrically on the screen with a horizontal separation of 10º of visual angle. The vertical height of the rectangle in the hourglass condition was set at 4º, the suggested zone of saccadic inhibition of return (Hooge & Frens, 2000). Six conditions were presented. Observers made back and forth, return saccades, either alone or accompanied by directionally compatible pointing movements, directionally reversed pointing movements, or contingent auditory tones presented 50ms after the saccade. The contingent auditory condition was used to control for potential influences of attention or arousal. The other two conditions consisted of hourglass saccades either alone or accompanied by directionally compatible pointing movements. The conditions were presented in six separate blocks with the order selected from a random distribution. Subjects were allowed to rest between blocks. Each block consisted of 30 trials, yielding roughly 300 eye movements per condition in total.

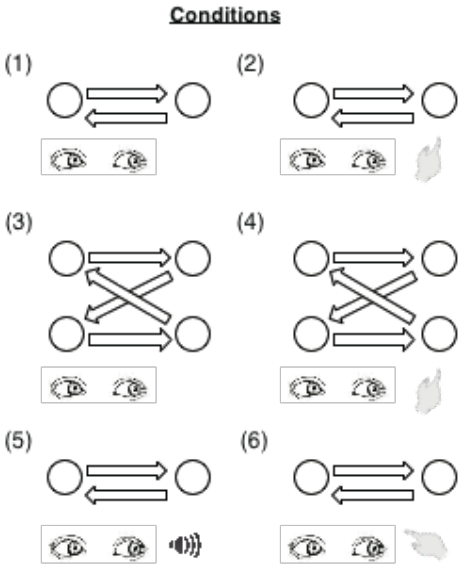

Figure 3.1 Experiment 3a methodology and conditions. Subjects made rapid alternating saccades (RAS) horizontally returning or in an hourglass pattern either independently or accompanied by directionally compatible pointing movements, directionally incompatible pointing movements, or contingent beeps. Saccadic gain, precision, peak velocity, duration; secondary saccade frequency, amplitude, and latency; and dwell duration were extracted and considered for further analysis.

In experiment 3b the visual saccade targets were arranged symmetrically, either horizontally or vertically, with separation of either 5º or 20º. Observers made back and forth, return saccades, either alone or accompanied by directionally compatible pointing movements in the different directions and amplitudes. Eight conditions were presented, yielding a 2x2x2 factorial design (amplitude x direction x condition). The eight conditions were presented in separate blocks with the order selected from a random distribution. Subjects were allowed to rest between blocks. Each block consisted of 20 trials, yielding roughly 200 eye movements per condition in total.

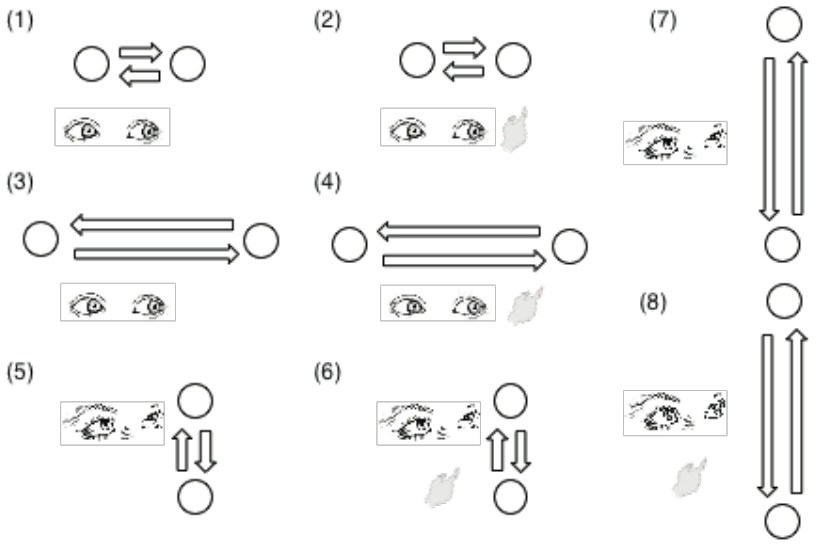

Figure 3.2 Experiment 3b methodology and conditions. Subjects made rapid alternating saccades of 5°or 20° either horizontally or vertically and either with or without directionally compatiable pointing movements.

3.2.4 Hand Movement Recording and Analysis

Hand pointing movements were recorded using a combination of Matlab Software and Makey-Makey hardware, a single board microcontroller that allows for low latency, precise, easily-adjustable, noise-free user input (Schubert, D'Ausilio, & Canto, 2013). Participants used the index finger of their dominant hand to make pointing movements between two response boards set up on the desk at approximately waist level. The response boards were thin metal sheets covered in modeling clay. The width between the two boards scaled with the target amplitude of the saccade with separations of either 3 cm, 5 cm, or 8 cm. The boards were arranged either horizontally or vertically depending upon the condition. Responses were registered when the subject's index finger made contact with the response board.

3.2.5 Eye Movement Recording and Analysis

Eye movements were recorded monocularly, using the right eye, on a desktop mounted SR Research Ltd. EyeLink 1000 eyetracker. Pupil position was sampled at 1000hz. To calibrate and validate gaze position tracking, two nine-point grids were presented to subjects at the beginning of the experiment. Velocity was computed using a 9-sample moving filter. Saccade onset was detected as the first time point at which both velocity exceeded 22 º/s and acceleration exceeded 4000 º/s. When velocity and acceleration fell below these thresholds, the end of the saccade was registered. Both primary and secondary saccades were detected in this way. The same smoothing procedure and saccade detection algorithm was used in both experiments. Further analysis of eye movements was undertaken offline using a custom written script in Matlab.

The average accuracy of the Eyelink 1000 system is 0.25-0.50º of visual angle. During calibration, we ensured that the average tracking error for all subjects was < 0.5º. Subject viewed the stimuli binocularly and head position was stabilized with a combined head and chin rest. To avoid measurement noise, participants were asked to maintain a steady head position throughout the trials. We recorded with the "pupil-CR" (Corneal Reflection) mode to compensate for any small head movements. The centroid mode was used to track the center of the thresholded pupil. Recent studies have shown that changes in pupil size can lead to systematic deviations in the reported gaze position (Ivanov & Blanche, 2011; Hooge et al., 2016; Nyström et al., 2016). Although we did not correct for these pupil-size related artifacts, we have no reason to expect differences in pupil dynamics across the different conditions. Video-based eye trackers are also known to be slightly less accurate at measuring large vertical eye movements because the pupil can be partly occluded by the eyelids and eyelashes. To guarantee the accuracy of our recordings we used the exclusion criteria detailed

below, and visually inspected the saccade traces before further analysis was carried out.

To analyze endpoint error, accuracy, we calculated the mean positional offset from the target for each subject and location. Endpoint scatter, precision, was determined by calculating the covariance matrix for each subject and location. We used the sum of the variance in the two orthogonal directions, the mean squared distance from the mean (van Beers, Haggard, & Wolpert, 2004), as our measure of precision.

3.2.6 Exclusion Criteria

The first saccade in each trial was excluded from analysis. Outliers were removed from the data. Primary saccades with amplitudes < 60% of the target amplitude, durations more than 3SD from the individual mean, or dwell times < 50ms or > 800ms and outside of 3SDs for the individual subject were rejected. In addition, we also excluded saccades whose landing or starting position were off the screen or greater than 3º away from the target for 5º saccades, 4º away for 10º saccades, and 5º away for 20º saccades. This resulted in ~5% of all registered saccades being excluded in Experiment 3a and ~10% being excluded in Experiment 3b.

Secondary saccades were identified using the same velocity and acceleration criteria as primary saccades. Only those occurring > 20 ms after the primary saccade, with an amplitude < 40% of the target amplitude, and having a duration > 8ms but < 40ms were included. Only the first secondary saccade following a primary saccade was accepted for further analysis.

3.2.6 Statistical Analysis

Saccade parameters were compared statistically between conditions using a repeated measures ANOVA in SPSS. When the assumption of sphericity was violated appropriate corrections were used. Post-hoc comparisons were made with Bonferoni corrected p-values.

3.3 Results

Experiment 3a (3.3.1) describes how concurrent hand movements influence saccade metrics. Experiment 3b (3.3.2) examines how the effect generalizes to saccades of different amplitudes and directions.

3.3.1 Exp. 3a

To isolate and characterize the effect of pointing movements on eye movements, six conditions were included in the first experiment. Subjects made 10º rapid alternating saccades (RAS) either returning or in an hourglass pattern

and either alone or accompanied by concurrent and directionally compatible pointing movements (Conditions 1-4). To identify the role that attention or arousal might have played participants also made saccades in the return pattern with accompanying contingent short beeps (Condition 5) or directionally incompatible pointing movements (Condition 6). The first four conditions were analyzed with a repeated measures ANOVA with two levels: pattern (return, hourglass) and movement type (eye, eye/hand). Individual statistical tests comparing Condition 1 to Condition 5 or 6 were conducted using paired-sample student t-tests.

Concurrent and directionally compatible pointing movements led to significant reductions in dwell times ($F(1,11) = 18.81$, $p = 0.001$). As observed in previous studies (Chapter 2), dwell times were also shorter in the hourglass compared to return conditions ($F(1,11) = 6.38$, $p = 0.025$). There was no interaction between movement type and condition, suggesting that hand movements affected dwell times equally, both in the presence and the absence of saccadic inhibition of return (Hooge & Frens 2000).

Compatible pointing movements additionally lead to higher saccade peak velocities ($F(1,11) = 26.76$, $p < 0.001$) and fewer secondary saccadic movements ($F(1,11) = 7.13$, $p = 0.022$). There were no corresponding changes in saccade gain, precision, or duration. The large reductions in dwell times (~ 35ms) could not be explained merely by the lower frequency of secondary saccades (Table 3.2) as the change in mean dwell time due to secondary saccades amounted to only +3ms in the return condition and +2 ms in the hourglass condition.

Return RAS dwell times made with contingent beeps were not significantly different from those made without beeps, ($t(11) = 1.63$, $p = 0.13$). Peak velocity however, was slightly higher in the auditory condition, ($t(11) = 2.30$, $p = 0.042$). Changes were not observed in any of the other saccade metrics.

Pointing subjects index fingers in the opposite direction of the saccadic eye movements led to significantly longer dwell times ($M = +71$ms, $SD = 60$ms) than when saccades were unaccompanied by hand movements ($t(11) = 5.68$, $p < 0.001$). The manipulation also led to a greater likelihood of secondary saccades ($t(11) = 2.69$, $p = 0.021$). Saccade gain, precision, duration, and peak velocity were unaffected.

Condition (Pattern)	Mean (SD) of Parameters		
	Dwell (ms)	Peak Velocity (°/s)	Secondary Frequency (%)
1. Eye (Return)	276 (65)	362 (49)	18 (11)
2. Eye/Hand Same (Return)	241 (50)	380 (55)	14 (12)
3. Eye (Hourglass)	239 (63)	373 (52)	15 (20)
4. Eye/Hand Same (Hourglass)	205 (44)	385 (46)	9 (14)
5. Eye/Beep (Return)	259 (60)	374 (54)	18 (16)
6. Eye/Hand Different (Return)	361 (92)	369 (56)	29 (21)

Table 3.1 Average dwell time, peak velocity, and secondary saccade frequency across conditions in Experiment 3a.

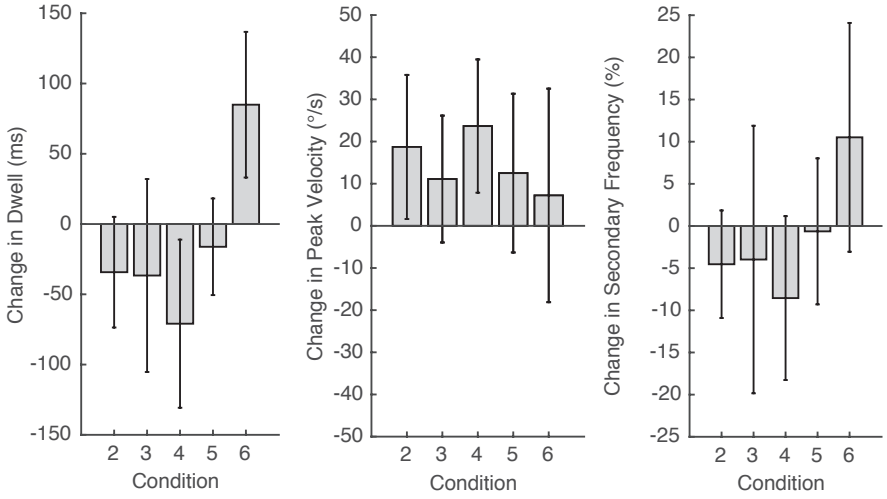

Figure 3.3 Results from Experiment 3a. Changes in dwell, peak velocity, and secondary saccade frequency for Conditions 2-6 (see Table 3.1) when compared to Condition 1, Eye (Return).

Amplitude (Condition)	Mean (SD) of Parameters			
	Dwell Before (ms)	Dwell After (ms)	Dwell Before Contribution (ms)	Dwell After Contribution (ms)
1. Eye (Return)	- 7 (15)	+ 90 (34)	- 1 (4)	+ 15 (9)
2. Eye/Hand Same (Return)	- 10 (37)	+ 87 (38)	- 2 (4)	+ 12 (10)
3. Eye (Hourglass)	- 2 (29)	+ 114 (62)	+ 1 (4)	+ 12 (10)
4. Eye/Hand Same (Hourglass)	- 7 (28)	+ 111 (65)	0 (4)	+ 10 (9)
5. Eye/Beep (Return)	0 (28)	+ 93 (42)	0 (4)	+ 14 (11)
6. Eye/Hand Different (Return)	+ 10 (31)	+ 84 (37)	+ 5 (12)	+ 19 (11)

Table 3.2 Experiment 3a change in dwell for fixations either preceding or during the occurence of secondary saccades. Contribution represents change in overall dwell duration as a result of secondary saccade fixations.

3.3.2 Exp. 3b

Experiment 3a illustrated that concurrent and complementary pointing movements affect dwell times, peak velocity, and secondary saccade occurrence. In Experiment 3b, we sought to corroborate these findings and understand how these effects depend on the size and direction of the movements. A repeated measures factorial ANOVA was used to test for effects of amplitude (5º or 20º), direction (horizontal, vertical), and condition (eye, eye/hand).

Confirming the results from Experiment 3a, subjects dwell times were significantly shorter when accompanied by concurrent pointing movements ($F(1,9) = 9.31$, $p = 0.014$). Although the size of the effect appears to be larger for horizontal and smaller amplitude saccades (Figure 3.4), the interaction terms were not significant. Replicating previous studies (Chapter 2), dwell times were significantly shorter for larger amplitude saccades ($F(1,9) = 58.97$, $p < 0.001$).

Concurrent and complementary pointing movements did not have a significant effect on the gain, precision, or duration of saccades but again resulted in significantly higher peak velocity ($F(1,9) = 8.73$, $p = 0.016$) and a reduction in the frequency of secondary saccades ($F(1,9) = 5.45$, $p = 0.044$).

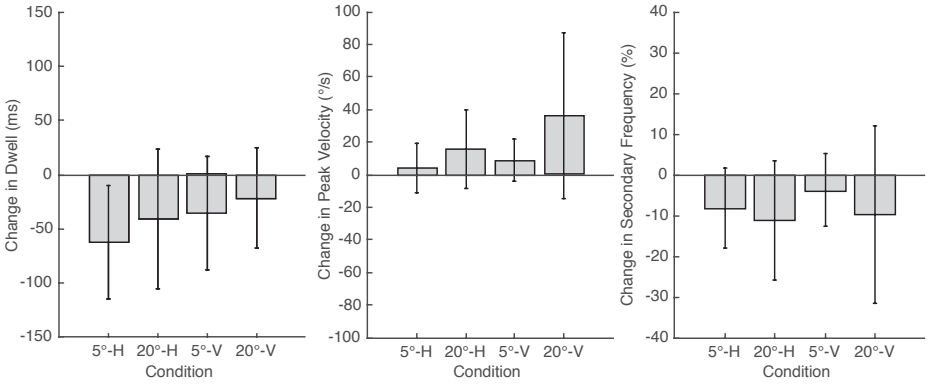

Figure 3.4 Results from Experiment 3b. Changes in dwell, peak velocity, and secondary saccade frequency when saccades of the corresponding direction (H - Horizontal, V - Vertical) and amplitude (5°, 20°) were accompanied by directionally compatible hand movements.

Condition (Amplitude)	Mean (SD) of Parameters		
	Dwell (ms)	Peak Velocity (°/s)	Secondary Frequency (%)
Horizontal			
Eye (5º)	333 (90)	244 (47)	20 (15)
Eye/Hand (5º)	271 (49)	248 (51)	12 (7)
Eye (20º)	282 (100)	471 (84)	31 (27)
Eye/Hand (20º)	242 (55)	487 (74)	20 (16)
Vertical			
Eye (5º)	339 (93)	196 (40)	24 (16)
Eye/Hand (5º)	303 (69)	205 (46)	20 (12)
Eye (20º)	257 (80)	442 (93)	30 (25)
Eye/Hand (20º)	236 (62)	478 (86)	20 (13)

Table 3.3 Average dwell, peak velocity, and secondary saccade frequency across conditions in Experiment 3b.

3.4 Discussion

The study demonstrates a clear influence of manual action on the characteristics and kinematics of sequential eye movements. Both Experiment 3a and 3b showed that directionally compatible pointing movements led observers to make saccadic eye movements with shorter dwell times, higher peak velocity, and a reduced rate of secondary saccade occurrence. These changes were robust and present both in the presence and the absence of inhibition of saccadic return (3a) and when saccades were made at different amplitudes and in different directions (3b). The saccadic facilitation from pointing movements requires that the two actions are directionally compatible. Moving the hand in the opposite direction of the eye led to significantly prolonged dwell times, a greater likelihood of secondary saccades, and had no effect on saccade peak velocity. To control for the effects of attention and arousal, we included a condition in which auditory beeps accompanied the sequential saccades. This led to higher peak velocity but had no effect on saccade dwell times or secondary saccade occurrence. These results provide novel insight into the temporal coordination between saccade and manual motor systems during sequential movements.

3.4.1 Changes in Dwell

In contrast to the majority of studies in the field, which have shown a delay in the onset of a saccade during coordinated hand movements (Mather & Fisk, 1985; Fisk & Goodale, 1985; Bekkering et al., 1994; Lee et al., 2013; Thura, Boussaoud, & Meunier, 2008; Lee et al., 2013; Armstrong et al., 2013) we observed a significant reduction in saccade dwell times. The previous studies have largely required reactions to the abrupt onset of an unpredictable cue. The longer reaction times in such conditions might be explained by the longer time needed by arm movement planning and reflect a purposeful delay to keep the internal representation of the visual target steady until the hand movement is fully specified (Henriques & Crawford, 2000). Indeed, Bekkering et al. (1994) showed that saccadic reaction times were not delayed when subject were merely asked to make a button press. In our study, subjects made continuous pointing movements and voluntarily moved their eyes between predictable static cues. The reduction in dwell times for coordinated manual movements suggests that advance planning of hand motor commands is available and interacts with the saccade gaze holding system. When pointing movements have sufficient time to be planned in advance, they can facilitate rather than delay saccade initiation. Inclusion of a control condition, in which saccades were accompanied by contingent beeps, rules out any explanation of the effect merely in terms of increased attention or arousal.

The yoking between the saccade and hand motor systems is further demonstrated by the prolonged saccadic dwell times we observed when saccades and pointing movements were made in opposite directions. The study supports the notion of shared attentional resources between the two systems (Khan, Song, & McPeek, 2011), but stands in contrast to a study by Jonikaitis & Deubel (2011) showing that manual movements could be prepared without a concurrent effect on saccade performance. We instead found mandatory interference when hand movements were made in the opposite direction of the saccades. This result also accords with several studies showing delayed saccade reaction times to hand movements made in opposite directions (Lünenburger, Kutz, & Hoffmann, 2000; Snyder et al., 2002; Niechwiej-Szwedo et al., 2004; Gorbet & Sergio, 2009), and with a recent paper by Armstrong et al. (2013), showing delayed saccade RT when subjects made coordinated hand movements under a visuo-motor reversal. In contrast to those studies, our experiment involved consecutive movements and cannot be explained merely by an anchoring of the saccade to fixation until hand motor programming is sufficiently planned. Subjects knew and could plan well in advance for both the hand and ocular movements. Rather, we propose that saccades and hand movements, which have both been shown to be represented in gaze-centered frames of reference (Batista, Buneo, Snyder, & Andersen, 1999; Buneo, Jarvis, Batista, & Andersen, 2002; Medendorp, Goltz, Vilis, & Crawford, 2003) share planning resources and that spatial incompatibility between the two movements

delayed both of their onsets.

It is interesting to consider our findings of reduced dwell durations in light of a number of recent studies that have shown an influence of manual action on our perception of time. Yokosaka et al., (2015) have shown that hand movements compress the time interval between visual events and that this effect increases with the velocity of the hand movements. Tomassini & Morrone (2016) demonstrated that the effect is dependent on the location of the hand and the direction of the hand movement. Other studies have suggested that subjective duration is expanded both before (Hagura, Kanai, Orgs, & Haggard, 2012) and after (Park, Schlag-Rey, & Schlag, 2003) manual action. While experiments have reported distortions of time around singular saccadic eye movements (Yarrow, Haggard, Heal, Brown, & Rothwell, 2001; Burr, Morrone, & Ross, 2005) nothing is known about the relationship between dwell times and duration perception. The RAS paradigm and the effects reported here may provide a way of linking these two fields.

3.4.1 Changes in Peak Velocity

Our study provides supporting evidence that concurrent hand movements can affect the kinematics, or main sequence, of saccadic eye movements. We found higher peak velocity for sequential saccades accompanied by concurrent and directionally compatible pointing movements. Epelboim et al. (1997) suggested that the peak velocity increase they observed in a head-free condition may have been caused by a change in eye-head coordination, or VOR gain. Follow-up studies have indeed shown that changes in head movement amplitude and velocity influence saccade peak velocity (Freedman, 2008). Our replication of the effect, when subjects' heads were fixed, suggests that the hand-eye interaction is independent of changes in head position. In line with the Snyder et al., (2002) experiment on exogenous orienting in monkeys and the Armstrong et al., (2013) study in humans, the increase in saccade peak velocity was eliminated when the hand movements were made in the opposite direction of the eye. In contrast to Armstrong et al., (2013) we also observed the effect when trials were presented in a block design, possibly due to differences in task demands. We failed to find a difference in peak velocity when hand movements were made in the opposite direction of the saccade (Gorbet & Sergio, 2009). The conflicting results presented by Lee et al. (2013), in which reaching movements led to decreases in the peak velocity of saccades, may have been caused by differences in saccadic amplitude between the different conditions. The present study controls for saccade amplitude and is not subject to such confounds. Our study not only confirms previous findings but also demonstrates that simple pointing movements, rather than reaches, are sufficient for manual action to affect saccade kinematics.

Recent theoretical discussions have linked the vigor or peak velocity of a saccade to reward processing (Shadmehr, Orban de Xivry, Xu-Wilson, & Shih,

2010). Saccades in monkeys to targets that predict a juice reward (Takikawa et al., 2002), or the presentation of a stimulus with greater intrinsic value, such as a face, result in higher saccadic peak velocities (Xu-Wilson, Zee, & Shadmehr, 2009). Change in the inter-trial interval, causing an assumed change in the reward rate prediction error, can lead to increases or decreases in saccade peak velocity (Haith, Reppert, & Shadmehr, 2012). As Shadmehr, et al. (2010) suggest, increases in peak velocity with coordinated reaching movements might also be explained within this reward framework. Our findings that both contingent auditory tones and coordinated pointing movements increase saccade peak velocity generalize and provide additional support for this viewpoint.

3.4.1 Changes in Secondary Saccades

We observed a robust effect of manual action on the frequency of secondary saccade occurrence across different saccade amplitudes and directions. Compatible pointing movements led to a reduction in secondary saccade occurrence while movements made in the opposite direction elevated secondary frequency. While this data supports the findings of Lünenburger et al., (2000) they stand in contrast to the results of Epelboim et al., (1997). The Epelboim et al., (1997) study allowed subjects to freely move their heads and thus may have led to different eye-head coordination strategies when reaching movements were used. Further studies are needed to elucidate the effect that head movements, independent of primary saccade amplitude and error, have on secondary saccade programming.

One of the traditional assumptions of secondary saccades is that they are produced and driven strictly by the retinal error between the target position and the saccade landing position. Our finding that secondary saccade occurrence was influenced by concurrent manual action independent of changes in saccade accuracy or precision challenges that assumption. Manual actions, perhaps due to spatial properties of the efference command, appear to either raise or lower the threshold the brain uses to assess the relevance of retinal error. Notably this change occurs without a concurrent change in the latency or amplitude of these secondary movements. Hand movements in the same direction as a concurrently programmed primary saccade seem to override secondary saccade programming, while those in an opposite direction induce conflicting signals that elevate their occurrence. This finding adds to a growing body of literature that suggests non-error correcting factors contribute to secondary saccade programming (Lemij & Collewijn, 1989; Ohl et al., 2011; 2013; Schut et al., 2017).

3.4.1 Neural Implementation

Several regions of the brain have been implicated in hand-eye coordination and may underpin the interactions reported in this study. As with the behavioral experiments, the majority of these studies have focused on the ways in which gaze influences arm- or hand-related neural activity, typically in either

the motor or posterior parietal cortex (Mushiake, Tanatsugu, & Tanji, 1997; Baker, Donoghue, & Sanes, 1999; Batista et al., 1999; Falciati, Gianesini, & Maioli, 2013; Yttri, Liu, & Snyder, 2013; Hiraoka et al., 2014; Hwang et al., 2014). One notable finding from these studies is that inactivation of the parietal reach region (PRR) can also affect saccade amplitudes, but only when they are made with concurrent reaching movements Hwang et al., (2014). The normally independent eye movement pathways receive motor planning information during coordinated eye hand movements.

Supporting this finding, neuronal changes caused by concurrent hand movements have also been reported in the typically ocular-motor regions of the cortex. Thura et al. (2008) demonstrated that merely having the hand in the vicinity of the saccade target was sufficient to modulate firing patters in the frontal eye fields (FEF). Dean, Hagan, & Pesaran (2012) went further and showed that a subpopulation of lateral intraparietal cortex (LIP) neurons, firing coherently at a 15 Hz beta-frequency, were able to reliably predict the reaction times of concurrently planned reaches and saccades, but not of saccades made alone. They argue that this illustrates a sharing of motor programming in the LIP between saccades and reaches that can be used to speed up or slow down their initiation. Future studies will be needed to determine if this inter-pathway communication between the PRR and LIP/FEF also affects saccade peak velocity or secondary saccade occurrence.

Downstream of these cortical areas, neural changes related to eye-hand coordination have been seen in both the superior colliculus (SC) and the cerebellum. Reyes-Puerta et al., found that neuronal firing in the SC is elevated (2010) and begins sooner (2011) during combined eye-hand movements. There was no relationship was between SC neural activity and saccade peak velocity. The finding illustrates that the motor planning that originates cortically is passed onto the SC and does not bypass the SC through direct pathways to the brainstem saccade generators (Schiller, True, & Conway, 1980). The cerebellum is also reciprocally connected with cortical regions such as the posterior parietal cortex (Prevosto, Graf, & Ugolini, 2010) and has been shown to have differential activation during hand-eye coordination (Miall, 2001; Nitschke, Arp, Stavrou, Erdmann, & Heide, 2005). Notably, cerebellar activity has been implicated in control of saccade kinematics (Takagi, Zee, & Tamargo, 1998; Herzfeld et al., 2015) and secondary saccade occurrence (Herzfeld & Shadmehr, 2016; Sun et al., 2016) and may serve to mediate the effects reported in our study.

3.5 Conclusion

Coordination between the hands and eyes is essential for successful goal-directed behavior. While the effect of vision and eye movements on manual action has received attention, much less is known about how hand movements influence the operation of the eye. Previous studies in the field have also generally relied on isolated movements triggered by an exogenous cue. Here we

provide evidence, during sequential movements voluntarily initiated, that hand pointing modulates saccade dwell times, peak velocity, and secondary saccade occurrence. These effects are independent of general arousal or attention, depend on directional compatibility between the hand and the eye, and generalize to different amplitudes and directions of movement.

Chapter 4: Conclusion

The goal of this dissertation was to better understand temporal constraints on saccadic eye movements. The experiments and data presented make significant contribution to this underexplored yet critical aspect of our daily life. We developed a novel task, with wide applicability, and used it to elucidate constraints and biases in oculomotor control. The findings can be summarized in terms of three key aspects of saccadic behavior: dynamics, secondary saccade characteristics, and dwell durations.

The dynamic features of saccadic eye movements are thought to be stereotyped and well understood. The experiments replicated the 'main sequence' relationship between saccade amplitude, duration, and peak velocity but also indicated important departures from the established wisdom. Chapter 3 revealed influences on saccade peak velocity that occurred independent of changes in amplitude or duration. Both directionally compatible pointing movements and contingent auditory tones led to higher saccade peak velocity. This finding accords with recent theoretical work linking changes in peak velocity to reward processing.

Secondary saccades have traditionally been thought to function largely as a way to correct for primary saccade landing error. The different studies provide novel evidence that non-error correcting signals influence secondary saccade programming and characteristics (e.g. frequency, latency, amplitude). Chapter 2 revealed that saccades that return to an immediately viewed target location are accompanied by a greater percentage of secondary saccades than targets to other locations. This occurred despite equivalent gain and precision between the movements. Secondary saccades at this return location also seem to release the system from inhibition and contribute to shorter relative dwell times. Chapter 3 indicated that concurrent manual actions can influence secondary saccade programming, again independent from changes in endpoint error. Directionally compatible pointing movements reduced secondary saccade occurrence while pointing movements in the opposite direction of the primary saccade elevated their occurrence. Although we replicated results showing that the occurrence of a secondary saccade can prolong dwell times, we found that the relative infrequency of secondary saccade occurrence meant they had little influence on overall dwell times across the different experiments.

Dwell durations, however, did show significant differences based on other experimental manipulations. Chapter 2 & 3 indicated that dwell times were inversely correlated with saccade amplitude across all directions tested. Chapter 2 provided convincing evidence that dwell times are modulated by the angular difference between subsequent saccades and are dramatically prolonged for saccades that return precisely to a previously viewed location. This inhibition on dwell times for saccades that return to a previous location was also found to be greater along the horizontal than the vertical axis. Chapter 3 showed that

concurrent and directionally compatible hand movements could reduce dwell times while hand movements in the opposite direction of the saccade prolonged dwell times. These findings provide important constraints on recent attempts to model saccade generation as resulting from an autonomous timer with a mean timer value.

Using the RAS task, the studies in this dissertation were able to provide support for a number of previously recognized oculomotor biases. The experiments also uncovered novel biases and detailed the conditions under which these were observed. Taken together, the results challenge many of the assumed and established principles underlying saccadic behavior and provide a strong foundation for further investigations and experiments in the field.

References

Anderson, A. J., Yadav, H., & Carpenter, R. H. S. (2008). Directional Prediction by the Saccadic System. *Current Biology*, *18*(8), 614–618. http://doi.org/10.1016/j.cub.2008.03.057

Armstrong, I., Judson, M., Munoz, D., Johansson, R., & Flanagan, R. (2013). Waiting for a hand: saccadic reaction time increases in proportion to hand reaction time when reaching under a visuomotor reversal. *Frontiers in Human Neuroscience*, *7*. http://doi.org/10.3389/fnhum.2013.00319

Baker, J. T., Donoghue, J. P., & Sanes, J. N. (1999). Gaze Direction Modulates Finger Movement Activation Patterns in Human Cerebral Cortex. *The Journal of Neuroscience*, *19*(22), 10044–10052.

Bao, Y., & Pöppel, E. (2007). Two spatially separated attention systems in the visual field: evidence from inhibition of return. *Cognitive Processing*, *8*(1), 37–44. http://doi.org/10.1007/s10339-006-0151-x

Bao, Y., Wang, Z., Liang, W., Wang, Y., Pöppel, E., & Li, H. (2013). Inhibition of return at different eccentricities in the visual field share the same temporal window. *Neuroscience Letters*, *534*, 7–11. http://doi.org/10.1016/j.neulet.2012.11.046

Batista, A. P., Buneo, C. A., Snyder, L. H., & Andersen, R. A. (1999). Reach Plans in Eye-Centered Coordinates. *Science (New York, N.Y.)*, *285*(5425), 257–260. http://doi.org/10.2307/2898696?ref=search-gateway:d3eb93d0ce9c03d649dc40bb23579bc5

Bays, P. M., & Husain, M. (2012). Active inhibition and memory promote exploration and search of natural scenes. *Journal of Vision*, *12*(8), 8–8. http://doi.org/10.1167/12.8.8

Becker, W., & Fuchs, A. F. (1969). Further properties of the human saccadic system: Eye movements and correction saccades with and without visual fixation points. *Vision Research*, *9*(10), 1247–1258. http://doi.org/10.1016/0042-6989(69)90112-6

Bekkering, H., Adam, J. J., Kingma, H., Huson, A., & Whiting, H. T. A. (1994). Reaction time latencies of eye and hand movements in single- and dual-task conditions. *Experimental Brain Research*, *97*(3), 471–476. http://doi.org/10.1007/BF00241541

Bennett, P. J., & Pratt, J. (2001). The Spatial Distribution of Inhibition of Return. *Psychological Science*, *12*(1), 76–80. http://doi.org/10.1111/1467-9280.00313

Berlucchi, G. (2007). Inhibition of return: A phenomenon in search of a mechanism and a better name. *Cognitive Neuropsychology*, *23*(7), 1065–1074. http://doi.org/10.1080/02643290600588426

Buneo, C. A., Jarvis, M. R., Batista, A. P., & Andersen, R. A. (2002). Direct visuomotor transformations for reaching. *Nature*, *416*(6881), 632–636. http://doi.org/10.1038/416632a

Burr, D. C., Morrone, C., & Ross, J. (2005). Saccadic eye-movements cause relativistic compression of time as well as space. *Journal of Vision*, *5*(8), 918–

918. http://doi.org/10.1167/5.8.918
Crawford, J. D. (2004). Spatial Transformations for Eye-Hand Coordination. *Journal of Neurophysiology*, *92*(1), 10–19. http://doi.org/10.1152/jn.00117.2004
Dean, H. L., Hagan, M. A., & Pesaran, B. (2012). Only Coherent Spiking in Posterior Parietal Cortex Coordinates Looking and Reaching. *Neuron*, *73*(4), 829–841. http://doi.org/10.1016/j.neuron.2011.12.035
Dorris, M. C., Klein, R. M., Everling, S., & Munoz, D. P. (2002). Contribution of the Primate Superior Colliculus to Inhibition of Return. *Journal of Cognitive Neuroscience*, *14*(8), 1256–1263. http://doi.org/10.1162/089892902760807249
Epelboim, J., Steinman, R. M., Kowler, E., Pizlo, Z., Erkelens, C. J., & Collewijn, H. (1997). Gaze-shift dynamics in two kinds of sequential looking tasks. *Vision Research*, *37*(18), 2597–2607. http://doi.org/10.1016/S0042-6989(97)00075-8
Falciati, L., Gianesini, T., & Maioli, C. (2013). Covert oculo-manual coupling induced by visually guided saccades. *Frontiers in Human Neuroscience*, *7*. http://doi.org/10.3389/fnhum.2013.00664
Fecteau, J. H., Bell, A. H., & Munoz, D. P. (2004). Neural correlates of the automatic and goal-driven biases in orienting spatial attention. *Journal of Neurophysiology*.
Fisk, J. D., & Goodale, M. A. (1985). The organization of eye and limb movements during unrestricted reaching to targets in contralateral and ipsilateral visual space. *Experimental Brain Research*, *60*(1), 159–178. http://doi.org/10.1007/BF00237028
Freedman, E. G. (2008). Coupling Between Horizontal and Vertical Components of Saccadic Eye Movements During Constant Amplitude and Direction Gaze Shifts in the Rhesus Monkey. *Journal of Neurophysiology*, *100*(6), 3375–3393. http://doi.org/10.1152/jn.90669.2008
Gorbet, D. J., & Sergio, L. E. (2009). The behavioural consequences of dissociating the spatial directions of eye and arm movements. *Brain Research*, *1284*, 77–88. http://doi.org/10.1016/j.brainres.2009.05.057
Hagura, N., Kanai, R., Orgs, G., & Haggard, P. (2012). Ready steady slow: action preparation slows the subjective passage of time.
Haith, A. M., Reppert, T. R., & Shadmehr, R. (2012). Evidence for Hyperbolic Temporal Discounting of Reward in Control of Movements. *The Journal of Neuroscience*, *32*(34), 11727–11736. http://doi.org/10.1523/JNEUROSCI.0424-12.2012
Henriques, D. Y. P., & Crawford, J. D. (2000). Direction-dependent distortions of retinocentric space in the visuomotor transformation for pointing. *Experimental Brain Research*, *132*(2), 179–194. http://doi.org/10.1007/s002210000340
Herzfeld, D. J., & Shadmehr, R. (2016). Cerebellar output encodes a corrective saccadic command (Commentary on Sun et al.). *European Journal of*

Neuroscience, *44*(8), 2528–2530. http://doi.org/10.1111/ejn.13345
Herzfeld, D. J., Kojima, Y., Soetedjo, R., & Shadmehr, R. (2015). Encoding of action by the Purkinje cells of the cerebellum. *Nature*, *526*(7573), 439–442. http://doi.org/10.1038/nature15693
Hiraoka, K., Kurata, N., Sakaguchi, M., Nonaka, K., & Matsumoto, N. (2014). Interaction between the premotor processes of eye and hand movements: Possible mechanism underlying eye–hand coordination. *Somatosensory & Motor Research*, *31*(1), 49–55. http://doi.org/10.3109/08990220.2013.838553
Hooge, I. T. C., & Frens, M. A. (2000). Inhibition of saccade return (ISR): spatio-temporal properties of saccade programming. *Vision Research*, *40*(24), 3415–3426. http://doi.org/10.1016/S0042-6989(00)00184-X
Hooge, I., Holmqvist, K., & Nyström, M. (2016). The pupil is faster than the corneal reflection (CR): Are video based pupil-CR eye trackers suitable for studying detailed dynamics of eye movements? *Vision Research*, *128*, 6–18. http://doi.org/10.1016/j.visres.2016.09.002
Hwang, E. J., Hauschild, M., Wilke, M., & Andersen, R. A. (2014). Spatial and Temporal Eye–Hand Coordination Relies on the Parietal Reach Region. *The Journal of Neuroscience*, *34*(38), 12884–12892. http://doi.org/10.1523/JNEUROSCI.3719-13.2014
Itti, L., & Koch, C. (2001). Computational modelling of visual attention. *Nature Reviews. Neuroscience*, *2*(3), 194–203. http://doi.org/10.1038/35058500
Ivanov, P., & Blanche, T. (2011). Improving gaze accuracy and predicting fixation onset with video based eye trackers. *Journal of Vision*, 11(11), 505.
Jackson, S. R., Newport, R., Mort, D., & Husain, M. (2005). Where the Eye Looks, the Hand Follows. *Current Biology*, *15*(1), 42–46. http://doi.org/10.1016/j.cub.2004.12.063
Johansson, R. S., Westling, G., Bäckström, A., & Flanagan, J. R. (2001). Eye–Hand Coordination in Object Manipulation. *The Journal of Neuroscience*, *21*(17), 6917–6932. http://doi.org/10.1146/annurev.neuro.20.1.303
Jonikaitis, D., & Deubel, H. (2011). Independent Allocation of Attention to Eye and Hand Targets in Coordinated Eye-Hand Movements. *Psychological Science*, *22*(3), 339–347. http://doi.org/10.1177/0956797610397666
Khan, A. Z., Song, J. H., & McPeek, R. M. (2011). The eye dominates in guiding attention during simultaneous eye and hand movements. *Journal of Vision*, *11*(1), 9–9. http://doi.org/10.1167/11.1.9
Lee, D., Poizner, H., Corcos, D. M., & Henriques, D. Y. (2013). Unconstrained reaching modulates eye–hand coupling. *Experimental Brain Research*, *232*(1), 211–223. http://doi.org/10.1007/s00221-013-3732-9
Lei, Q., & Bao, Y. (2012). The Eccentricity Effect of Inhibition of Return Is Independent of Cortical Magnification. *Journal of Vision*, *12*(9), 674–674. http://doi.org/10.1167/12.9.674
Lemij, H. G., & Collewijn, H. (1989). Differences in accuracy of human saccades between stationary and jumping targets. *Vision Research*, *29*(12), 1737–1748. http://doi.org/10.1016/0042-6989(89)90156-9

Luke, S. G., Smith, T. J., Schmidt, J., & Henderson, J. M. (2014). Dissociating temporal inhibition of return and saccadic momentum across multiple eye-movement tasks. *Journal of Vision*, *14*(14), 9–9. http://doi.org/10.1167/14.14.9

Lünenburger, L., Kutz, D. F., & Hoffmann, K. P. (2000). Influence of arm movements on saccades in humans. *European Journal of Neuroscience*, *12*(11), 4107–4116. http://doi.org/10.1046/j.1460-9568.2000.00298.x

Mather, J. A., & Fisk, J. D. (1985). Orienting to targets by looking and pointing: Parallels and interactions in ocular and manual performance. *The Quarterly Journal of Experimental Psychology*, *37*(3), 315–338. http://doi.org/10.1080/14640748508400938

Medendorp, W. P., Goltz, H. C., Vilis, T., & Crawford, J. D. (2003). Gaze-Centered Updating of Visual Space in Human Parietal Cortex. *The Journal of Neuroscience*, *23*(15), 6209–6214. http://doi.org/10.1126/science.4048942

Miall, R. C. (2001). Cerebellar activation and eye-hand motor coordination. *Neuroimage*, *13*(6), 1227. http://doi.org/10.1016/S1053-8119(01)92541-8

Mushiake, H., Tanatsugu, Y., & Tanji, J. (1997). Neuronal Activity in the Ventral Part of Premotor Cortex During Target-Reach Movement is Modulated by Direction of Gaze. *Journal of Neurophysiology*, *78*(1), 567–571. http://doi.org/10.1152/jn.00575.2016

Niechwiej-Szwedo, E., McIlroy, W. E., Green, R., & Verrier, M. C. (2004). The effect of directional compatibility on the response latencies of ocular and manual movements. *Experimental Brain Research*, *162*(2), 220–229. http://doi.org/10.1007/s00221-004-2146-0

Nitschke, M. F., Arp, T., Stavrou, G., Erdmann, C., & Heide, W. (2005). The cerebellum in the cerebro-cerebellar network for the control of eye and hand movements — an fMRI study. In *Creating coordination in the cerebellum* (Vol. 148, pp. 151–164). Elsevier. http://doi.org/10.1016/S0079-6123(04)48013-3

Nyström, M., Hooge, I., & Andersson, R. (2016). Pupil size influences the eye-tracker signal during saccades. *Vision Research*, *121*, 95–103. http://doi.org/10.1016/j.visres.2016.01.009

Ohl, S., Brandt, S. A., & Kliegl, R. (2011). Secondary (micro-)saccades: The influence of primary saccade end point and target eccentricity on the process of postsaccadic fixation. *Vision Research*, *51*(23-24), 2340–2347. http://doi.org/10.1016/j.visres.2011.09.005

Ohl, S., Brandt, S. A., & Kliegl, R. (2013). The generation of secondary saccades without postsaccadic visual feedback. *Journal of Vision*, *13*(5), 11–11. http://doi.org/10.1167/13.5.11

Park, J., Schlag-Rey, M., & Schlag, J. (2003). Voluntary action expands perceived duration of its sensory consequence. *Experimental Brain Research*, *149*(4), 527–529. http://doi.org/10.1007/s00221-003-1376-x

Posner, M. I., & Cohen, Y. (1984). Components of visual orienting. *Attention and performance X: Control of language processes*, *32*, 531-556.

Posner, M. I., Rafal, R. D., Choate, L. S., & Vaughan, J. (1985). Inhibition of return: Neural basis and function. *Cognitive Neuropsychology*, *2*(3), 211–228. http://doi.org/10.1080/02643298508252866
Pöppel, E., & Harvey, L. O. (1973). Light-difference threshold and subjective brightness in the periphery of the visual field. *Psychological Research*.
Pöppel, E., Cramon, von, D., & Backmund, H. (1975). Eccentricity-specific dissociation of visual functions in patients with lesions of the central visual pathways. *Nature*.
Prablanc, C., Echallier, J. F., Komilis, E., & Jeannerod, M. (1979). Optimal response of eye and hand motor systems in pointing at a visual target. *Biological Cybernetics*, *35*(2), 113–124. http://doi.org/10.1007/BF00337436
Prevosto, V., Graf, W., & Ugolini, G. (2010). Cerebellar Inputs to Intraparietal Cortex Areas LIP and MIP: Functional Frameworks for Adaptive Control of Eye Movements, Reaching, and Arm/Eye/Head Movement Coordination. *Cerebral Cortex*, *20*(1), 214–228. http://doi.org/10.1093/cercor/bhp091
Rafal, R. D., Calabresi, P. A., & Brennan, C. W. (1989). Saccade preparation inhibits reorienting to recently attended locations. *Journal of Experimental Psychology: Human Perception and Performance*, *15*(4), 673.
Reyes-Puerta, V., Philipp, R., Lindner, W., & Hoffmann, K.-P. (2010). Role of the Rostral Superior Colliculus in Gaze Anchoring During Reach Movements. *Journal of Neurophysiology*, *103*(6), 3153–3166. http://doi.org/10.1152/jn.00989.2009
Reyes-Puerta, V., Philipp, R., Lindner, W., & Hoffmann, K.-P. (2011). Neuronal activity in the superior colliculus related to saccade initiation during coordinated gaze–reach movements. *European Journal of Neuroscience*, *34*(12), 1966–1982. http://doi.org/10.1111/j.1460-9568.2011.07911.x
Richardson, B. A., Cluff, T., Lyons, J., & Balasubramaniam, R. (2013). An eye-to-hand magnet effect reveals distinct spatial interference in motor planning and execution. *Experimental Brain Research*, *225*(3), 443–454. http://doi.org/10.1007/s00221-012-3384-1
Rolfs, M., Laubrock, J., & Kliegl, R. (2006). Shortening and prolongation of saccade latencies following microsaccades. *Experimental Brain Research*, *169*(3), 369–376. http://doi.org/10.1007/s00221-005-0148-1
Satel, J., Wang, Z., Trappenberg, T. P., & Klein, R. M. (2011). Modeling inhibition of return as short-term depression of early sensory input to the superior colliculus. *Vision Research*.
Schiller, P. H., True, S. D., & Conway, J. L. (1980). Deficits in eye movements following frontal eye-field and superior colliculus ablations. *Journal of Neurophysiology*, *44*(6), 1175–1189. http://doi.org/10.1152/jn.00575.2016
Schubert, T. W., D'Ausilio, A., & Canto, R. (2013). Using Arduino microcontroller boards to measure response latencies. *Behavior Research Methods*, *45*(4), 1332–1346. http://doi.org/10.3758/s13428-013-0336-z
Schut, M. J., Fabius, J. H., Van der Stoep, N., & Van der Stigchel, S. (2017).

Object files across eye movements: Previous fixations affect the latencies of corrective saccades. *Attention, Perception & Psychophysics*, *79*(1), 138–153. http://doi.org/10.3758/s13414-016-1220-6

Shadmehr, R., Orban de Xivry, J. J., Xu-Wilson, M., & Shih, T.-Y. (2010). Temporal discounting of reward and the cost of time in motor control. *The Journal of Neuroscience : the Official Journal of the Society for Neuroscience*, *30*(31), 10507–10516. http://doi.org/10.1523/JNEUROSCI.1343-10.2010

Smith, T. J., & Henderson, J. M. (2009). Facilitation of return during scene viewing. *Visual Cognition*, *17*(6-7), 1083–1108. http://doi.org/10.1080/13506280802678557

Snyder, L. H., Calton, J. L., Dickinson, A. R., & Lawrence, B. M. (2002). Eye-Hand Coordination: Saccades Are Faster When Accompanied by a Coordinated Arm Movement. *Journal of Neurophysiology*, *87*(5), 2279–2286. http://doi.org/10.1152/jn.00854.2001

Sparks, D. L. (2002). The brainstem control of saccadic eye movements. *Nature Reviews. Neuroscience*. *3*(12), 952-964.

Spence, C., & Driver, J. (1998). Inhibition of return following an auditory cue The role of central reorienting events. *Experimental Brain Research*, *118*(3), 352 360.

Sun, Z., Junker, M., Dicke, P. W., & Thier, P. (2016). Individual neurons in the caudal fastigial oculomotor region convey information on both macro- and microsaccades. *European Journal of Neuroscience*, *44*(8), 2531–2542. http://doi.org/10.1111/ejn.13289

Takagi, M., Zee, D. S., & Tamargo, R. J. (1998). Effects of Lesions of the Oculomotor Vermis on Eye Movements in Primate: Saccades. *Journal of Neurophysiology*, *80*(4), 1911–1931. http://doi.org/10.1016/0014-4886(71)90056-2

Takikawa, Y., Kawagoe, R., Itoh, H., Nakahara, H., & Hikosaka, O. (2002). Modulation of saccadic eye movements by predicted reward outcome. *Experimental Brain Research*, *142*(2), 284–291. http://doi.org/10.1007/s00221-001-0928-1

Tassinari, G., Aglioti, S., Chelazzi, L., Marzi, C. A., & Berlucchi, G. (1987). Distribution in the visual field of the costs of voluntarily allocated attention and of the inhibitory after-effects of covert orienting. *Neuropsychologia*, *25*(1), 55–71. http://doi.org/10.1016/0028-3932(87)90043-1

Tatler, B. W., & Vincent, B. T. (2008). Systematic tendencies in scene viewing. *Journal of Eye Movement Research*, *2*(2). http://doi.org/10.16910/jemr.2.2.5

Tatler, B. W., & Vincent, B. T. (2009). The prominence of behavioural biases in eye guidance. *Visual Cognition*, *17*(6-7), 1029–1054. http://doi.org/10.1080/13506280902764539

Thura, D., Boussaoud, D., & Meunier, M. (2008). Hand Position Affects Saccadic Reaction Times in Monkeys and Humans. *Journal of Neurophysiology*, *99*(5), 2194–2202. http://doi.org/10.1152/jn.01271.2007

Tian, J., Ying, H. S., & Zee, D. S. (2013). Revisiting corrective saccades: role of visual feedback. *Vision Research*.
Tian, X., & Hafed, Z. (2015). Testing for inhibition of return with purely vertical cues: implications for models of covert visual attention. *Journal of Vision*, *15*(12), 70–70. http://doi.org/10.1167/15.12.70
Tian, X., Yoshida, M., & Hafed, Z. M. (2016). A Microsaccadic Account of Attentional Capture and Inhibition of Return in Posner Cueing. *Frontiers in Systems Neuroscience*, *10*. http://doi.org/10.3389/fnsys.2016.00023
Tomassini, A., & Morrone, M. C. (2016). Perceived visual time depends on motor preparation and direction of hand movements. *Scientific Reports*, *6*, 27947. http://doi.org/10.1038/srep27947
van Beers, R. J., Haggard, P., & Wolpert, D. M. (2004). The Role of Execution Noise in Movement Variability. *Journal of Neurophysiology*, *91*(2), 1050–1063. http://doi.org/10.1152/jn.00652.2003
Van der Stigchel, S., & Theeuwes, J. (2008). Differences in distractor-induced deviation between horizontal and vertical saccade trajectories. *Neuroreport*, *19*(2), 251–254. http://doi.org/10.1097/WNR.0b013e3282f49b3f
van Donkelaar, P., & Staub, J. (2000). Eye-hand coordination to visual versus remembered targets. *Experimental Brain Research*, *133*(3), 414–418. http://doi.org/10.1007/s002210000422
van Donkelaar, P. V. (1997). Eye–hand interactions during goal-directed pointing movements. *Neuroreport*, *8*(9), 2139.
Wang, Z., Satel, J., Trappenberg, T. P., & Klein, R. M. (2011). Aftereffects of Saccades Explored in a Dynamic Neural Field Model of the Superior Colliculus. *Journal of Eye Movement Research*, *4*(2).
Westheimer, G. (1989) History and methodology. In Wurtz, R. H. Wurtz & M. E. Goldberg (Eds.), *The neurobiology of saccadic eye movements* (Vol. 3). Elsevier Science Limited.
Wilming, N., Harst, S., Schmidt, N., & König, P. (2013). Saccadic Momentum and Facilitation of Return Saccades Contribute to an Optimal Foraging Strategy. *PLoS Computational Biology*, *9*(1), e1002871. http://doi.org/10.1371/journal.pcbi.1002871
Wu, C.-C., Kwon, O.-S., & Kowler, E. (2010). Fitts's Law and speed/accuracy trade-offs during sequences of saccades: Implications for strategies of saccadic planning. *Vision Research*, *50*(21), 2142–2157. http://doi.org/10.1016/j.visres.2010.08.008
Xu-Wilson, M., Zee, D. S., & Shadmehr, R. (2009). The intrinsic value of visual information affects saccade velocities. *Experimental Brain Research*, *196*(4), 475–481. http://doi.org/10.1007/s00221-009-1879-1
Yarrow, K., Haggard, P., Heal, R., Brown, P., & Rothwell, J. C. (2001). Illusory perceptions of space and time preserve cross-saccadic perceptual continuity. *Nature*, *414*(6861), 302–305. http://doi.org/10.1038/35104551
Yokosaka, T., Kuroki, S., Nishida, S., & Watanabe, J. (2015). Apparent Time Interval of Visual Stimuli Is Compressed during Fast Hand Movement. *Plos*

One, *10*(4), e0124901. http://doi.org/10.1371/journal.pone.0124901
Yttri, E. A., Liu, Y., & Snyder, L. H. (2013). Lesions of cortical area LIP affect reach onset only when the reach is accompanied by a saccade, revealing an active eye-hand coordination circuit. *Proceedings of the National Academy of Sciences*, *110*(6), 2371–2376. http://doi.org/10.1073/pnas.1220508110