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Smooth-pursuit and Saccadic eye movements: One clock or two?

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One clock or two?

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This thesis is submitted to the
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Abstract

It is commonly believed that saccadic and smooth-pursuit eye movements involve different neural and behavioural organization. However, the question of how these different movements are timed with respect to a pacing goal is less understood. In two experiments, we investigated the idea that repetitive saccadic and smooth pursuit eye movements might share the same clocking mechanisms or neural networks for timing. Eye movements exhibit predictive tracking (negative latencies) at fast frequencies and reactive (positive latencies) tracking at slow frequencies. In the first experiment, monotonic changes in pacing (speeding up and slowing down) were used to establish the point at which a transition occurs between reactive and predictive behaviours. The point of transition exhibited a strong hysteresis depending on the direction of the monotonic pacing. In subsequent trials, subjects were instructed to make smooth pursuit movements up to the point of transition after which they switched to making saccades. The saccade latencies were compared between saccade-only and switched trials. Although no uniform pattern was seen across individuals, some subjects were able to track nearly identically to baseline trials after the target switch. In the second experiment, subjects were instructed to continue making saccadic eye movements after being entrained to either a saccadic or smooth pursuit stimulus train using a synchronization-continuation design. The decomposed clock and motor variance measures and correlations at higher lags showed no differences between synchronizing conditions. Our results indicate that timing is represented globally without particular reference to the effector system for broad classes of repetitive oculomotor tasks.

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Chapter 1 - Introduction

1.1 Oculomotor Control

As the sensory organ that provides us with the most spatially detailed view of our environment, the eyes require control strategies that support many types of functions. The primary goal of controlling the eyes is to fixate and maintain fixation on relevant targets that surround us or with which we interact. The area of our eyes most sensitive to finite detail is the fovea, and actions that center important visual content on this area are referred to as foveating movements. Such movements are accomplished by a synergy between relatively simple reflexive networks as well as sensory and motor related brain areas that are dedicated to advanced processing of visual stimuli and the construction of according movements. On a subcortical level, some of these structures include the cerebellum, brain stem networks, collicular networks, and the basal ganglia. Input to these areas often originates from cortical areas, including the visual cortex where retinal images are processed, and the motor cortex's dedicated eye field areas where advanced movement planning occurs.

There are six extraocular muscles that contract and relax in synergy to accomplish the movements for each eye. The eyes rotate about three axes, allowing for vertical, horizontal and torsional motions. The degree to which an extraocular muscle contracts is proportional to the spiking rate of its respective motor neuron. Thus, maintaining gaze in a given direction requires a tonic rate of spiking activity in the motor neuron, whereas movement of the eyes occurs in accordance with a change in spiking rate.

1.1.1 Degrees of freedom

Specific interneuron pathways between sets of extraocular motor neurons reduce the degrees of freedom from six per eye to a total of two, ultimately requiring only azimuth, and elevation commands from the motor networks. Bruce and Friedman (2002) summarize these relationships as follows. The Descartes-Sherrington's law of reciprocal innervation asserts that the six muscles act as three agonist and antagonist pairs. In other words, when an agonist is contracted the antagonist is relaxed via inhibitory connections between the motor neurons.

Another set of constraints that is useful for mammals with forward directed binocular vision is Hering's law of motor correspondence. This law describes the conjugate movements between each eye. So, the muscles that drive vertical movements are coupled between the eyes, as well as the adducter of one eye with the abducter of the other.

Finally, Listing's and Donders' laws attribute a specific torsion to a given azimuth and elevation. Overall, the decrease in numbers of degrees of freedom allows for more simplistic control mechanisms that would be otherwise required.

1.1.2 The saccade system

Saccades are jumping movements of the eyes that are used to quickly foveate a new target. The eyes may accelerate up to a peak rotational velocity of approximately 800 degrees per second, and the duration of saccades is linearly proportional to their amplitude (Sparks, 2002). Although the durations of eye movements are extremely short, there are observations of mid-saccade changes to the flight path of the eye. An extremely low latency movement feedback mechanism must exist allowing for this online control. Since visual processing delays are longer than the duration of most saccades, and eliminating proprioception from extraocular muscles does not effect on line movement corrections, Guthrie et al. (1983) proposed that copies of motor commands, called corollary discharge, are the source of feedback.

When executing saccades, bursts of spikes are transmitted to extraocular muscles via motor neurons from brainstem areas. Specific neurons called the excitatory, inhibitory, and omnipause burst neurons (EBN, IBN, and OPN) generate the spikes required in the control of saccades. Whereas EBNs fire to cause muscle activation, IBNs fire simultaneously to decrease activity in antagonists. Interestingly, spiking of the OPNs causes inhibition of EBNs and during saccades OPNs are not active (Curthoys et al., 1984). Since EBNs and IBNs are only active during movement, the increased motor neuron activity required to maintain a new gaze position requires other structures. A neural integrator receives the movement signals parallel to the motor neurons and integrates the commands, thus establishing a new tonic spiking rate after the saccade has ended via other neurons (Moschovakis, 1997).

The bursting activity from these brainstem neurons can be triggered by the superior colliculus. Arranged in a topographical fashion, each collicular neuron codes for a direction and amplitude (Stanford et al., 1996). Populations of these neurons are activated prior to a saccade, and the subsequent movement is an average of all the spatial characteristics coded by that population.

Visually guided saccades may be initiated through various networks. The superior colliculus receives strong input directly from the retina. This pathway is responsible for reflexive foveation. One the other hand, voluntary saccades are mediated by the frontal eye field (FEF), parietal eye field (PEF), and supplementary eye field (SEF), which are all specialized areas of the motor cortex (Hanes & Wurtz, 2001). While each of these project to the superior colliculus, other cortical networks connect the three eye-field areas together directly. Furthermore, the FEF also projects to the brainstem saccade generator, allowing for cortical mediation of collicular saccade control. Collectively these cortical areas are active during memory-guided saccades, antisaccades, spontaneous saccades, and purposive saccades such as those directed towards sounds (Sparks, 2002).

1.1.3 The smooth-pursuit system

Smooth-pursuit eye movements are those used to maintain foveation to objects in motion, or static objects while one's self is in motion. While peak velocity of the eyes during smooth-pursuit is nearly 100 degrees per second, tracking is optimal for velocities under 25 degrees per second. Establishing the velocity of a smooth-pursuit visual target depends on the retinal slip of the target over a period of time. The functions which drive smooth-pursuit are largely neocortical, yet the networks synapse on subcortical reflexive oculomotor structures to effect the intended movements.

First in the process of initiating smooth-pursuit, the visual cortex area V1 codes information about target motion. Downstream cortical areas include area V5, parietal area 7a and ventral intraparietal area, medial superior temporal area, middle temporal area, and a an area of the FEF specifically dedicated to smooth-pursuit, located just posterior to the FEF area responsible for saccadic functions. These are involved in the integration of the target motion, and target identification and discrimination. Subcortical areas also implicated in pursuit movements include the dorsolateral and medial pontine nuclei, nucleus reticularis tegmenti ponti. The cerebellum is also crucuial to smooth-pursuit, including the flocculus, paraflocculus, dorsal vermis, and fastigial nucleus.

Whereas the role of cortical structures is largely in identifying the target and its motion, and developing or initiating memory-guided movement plans, subcortical involvement is mostly efferent related. For effecting movement, these cortical networks project to the cerebellum's structures that support the smooth movement phases of the vestibulo-ocular reflex (VOR).

1.2 Temporal organization of movement

All voluntary movements have a temporal structure that is carefully constructed to ensure the successful completion of the intended goals of the motor action. Many levels of temporal organization exist. Some tasks, such as reaching towards and grasping an object, involve sequencing of muscle activation of agonist/antagonist pairs. Since grasping an object is not usually timed to an explicit pacing stimulus, this type of temporal organization is emergent based on the task constraints, and is referred to as implicit timing. On the contrary, motor tasks such as playing the piano must be temporally organized to be synchronous with an external pacing signal. For ongoing consistency, such tasks would require the generation of an internal timing representation of the periodic interval. Referred to as explicit timing, this type of temporal organization is thought to engage a central clock process (Zelaznik et al., 2002).

1.3 Unpaced explicit timing tasks and related timing models

Research into explicit timing tasks began by observing response variability during repetitive finger tapping (Stevens, 1886). These experiments were developed to include both paced and unpaced conditions, with the former being commonly used to examine predictive and reactive behaviour, and the latter to observe open-loop timing processes.

The most common paradigm for examining unpaced tapping is the synchronization-continuation design. In this two-phase procedure, subjects begin by making motor responses with a pacing stimulus for a predetermined number of intervals. Following this entrainment phase, the pacing stimulus-train is extinguished and the subjects are instructed to keep responding at the same rate. The first segment is referred to as the synchronization phase, and the second is called the continuation phase. The analytical measure during such tasks is the response variability and autocorrelations within the series of continuation intervals.

1.3.1 Weber's Law

Through the analysis of response variability in unpaced timing tasks, researchers have noted that the variance of response intervals varies linearly with the square of the length of the target interval. Coined as Weber's Law, this trend is observed in explicitly timed movement tasks such as repetitive finger tapping, saccadic eye movements, as well as perceptual tasks such as interval duration discrimination (Collins et al., 1998; Hazeltine et al., 1997). This relationship is a result of the cumulative error of a central clocking process, and that an increasing number of errors over longer intervals has a greater cumulative effect.

Continuous repetitive movement tasks like circle drawing lack a discrete event structure and the temporal organization is not driven by a central clocking process. Variability in such tasks does not change with respect to pacing in the same manner as explicitly timed tasks and the implicit temporal structure does not adhere to Weber's Law (Zelaznik et al., 2005).

1.3.2 Wing and Kristofferson model of timing

When examining data from unpaced periodic finger tapping tasks, variability between successive response intervals is relatively high while the accuracy of timing persists over time with little drift in the mean interval duration. Explanation for these observations is accounted for with a model that describes two independent sources of variability that are jointly involved in the execution of timed movements (Wing & Kristofferson, 1973). Named after the authors who proposed the model, the Wing and Kristofferson (WK) model involves separate clock and motor components (Figure 1).

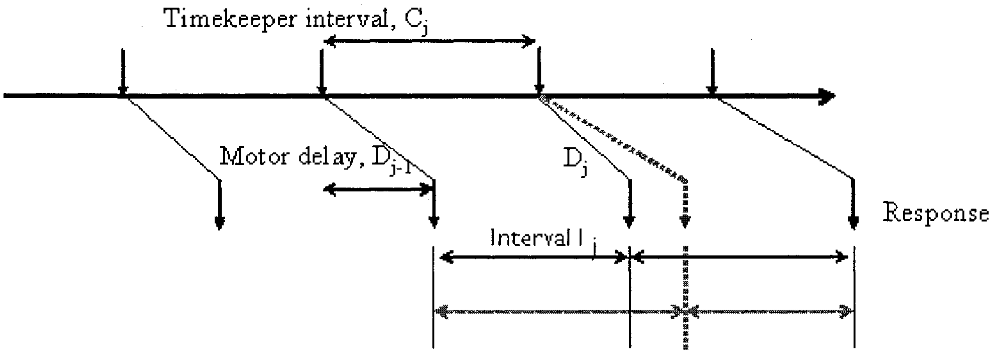


Figure 1. Graphical representation of the Wing and Kristofferson model of timing. The illustration represents the stream of processing from top to bottom, leading from the timekeeper to subsequent motor areas, and a final motor response. Accordingly, inter-response interval Ij is influenced by the clock interval Cj, and motor delay components from the current interval Dj and from the previous interval Dj-1. Adapted from Balasubramaniam, 2006.

In order of occurrence, the clocking component first provides explicit signals in the form of ticks. Each clock signal is assumed to be independent from the next, implying no active error correction process in the fundamental timekeeper. Thus, errors in the clock component are cumulative and account for the drift in timing responses. Second, the motor component describes the neural processes downstream from the clock component, which uses the clock signal to initiate a motor response. These motor pathways, which include networks ascending to motor cortices and subsequent descending motor commands, are more variable due to processing delays. Since the model assumes independence between the clock and motor components, even with increased variability in the motor system, the clock provides unhindered signals for subsequent responses.

Based on the relationships between each of the model's components, predictions can be made about the series of response intervals in an unpaced periodic motor task. In accordance with the labeling of components in figure 1:

Inter-response interval $I_j = C_j + D_j - D_{j-1}$ [1]

The model predicts a negative autocorrelation function at lag 1, expecting a value less than zero and greater than negative one-half when. These values are calculated by normalizing the lag 1 autocovariance function by the lag 0 autocovariance function. This prediction is due to the influence of D_{j-1} on the I_j. Thus, an estimation of the variance in motor delay, var(D), within in a series of *n* response intervals from I_j to I_{j+n}, is equal to the negative of the autocovariance function at lag 1:

$\mathrm{var}(D) = -\ \mathrm{acov}(I(1))$ [2]

Furthermore, because the WK model has no consideration for active error correction processes, it is expected that autocorrelation function at lags greater than one are equal to zero. The nature of interactions between all of the model's proposed components ultimately leads to the following equation, attributing clock and motor related variances to total variance:

$$\mathrm{var}(I) = \mathrm{var}(C) + 2\mathrm{var}(D) \qquad [3]$$

Equations 1 through 3 are adopted from Wing et al. (1984).

However, a common observation in these timing tasks is that violations of the WK model's predictions occur frequently. This calls into question the assumptions that underlie the WK model. Major debates include the closed-loop versus open-loop nature of the central clock, and the relationship between clock and motor components of the WK model. It has been suggested that revision of the WK model may be necessary to include error correction processes. Presumably, these error correction mechanisms would take advantage of movement feedback from two likely sources, the higher-latency proprioceptive feedback and lower-latency corollary discharge from executed motor commands (Wing, 1977a; 1977b).

Although the WK model was initially conceived by observing response intervals in a finger tapping tasks, the model was later applied to periodic movements of many other effectors. In such tasks, it was noted that estimated motor delay varies with effector, while clock variability stays constant according to the target interval. Additionally, the frequency of trials which violate the WK predictions also varies with effector (Wing, 1977a; 1977b).

1.4 Timekeeping processes and related neurophysiology

1.4.1 Pacemaker-accumulator model

The pacemaker-accumulator model is based on an information processing approach to timekeeping. Initially proposed by Gibbon et al. (1984) and later revised by Meck (1996), this model outlines multiple components, including a stochastic periodic pacing signal and a counter. Because the model specifies that discrete output, i.e. a clock tick, is generated when a threshold of fundamental ticks has accumulated, a pacemaker-accumulator is very compatible with the previously mentioned WK model for timing variability. Behavioural data strengthens the pacemaker-accumulator model in that response variability likely arises from these multiple components, promoting the suggestion for dissociation between the motor and timekeeping functions.

This model proposes the substantia nigra, which is located in the basal ganglia, as the source of the continual repetitive pulses. Downstream, this signal passes through the striatum to the globus pallidus internus, which tracks the number of pulses it receives and acts as an accumulator. The accumulator activation grows until a threshold level has been reached leading to the output of a clock tick and to resetting the activation level for another interval. Clock ticks are passed to the thalamus and cortex for comparison with stored representations of learned task-specific durations.

The term *information processing* is used to describe this view on timekeeping because it involves the contribution of multiple systems, some of which are not autonomous and are mediated by high-level functions. Figure 2 illustrates the proposed processing stream of the pacemaker-accumulator model. Although the stochastic signal from the pacemaker is likely low on processing demands, this signal is gated by attention factors through a switch. Subsequently, memory functions evaluate the accumulated pulses to an expected value in a comparator, leading to downstream activity when the intended threshold is attained.

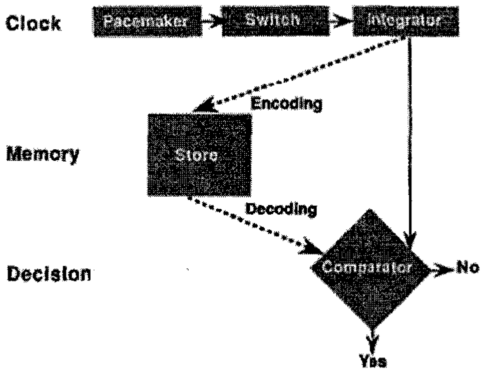


Figure 2. Proposed information processing flow according to the pacemaker-accumulator model of timekeeping. Adapted from Meck et al. (2001).

1.4.2 Dynamical systems

Schöner (2001) discusses how self-organized timekeeping systems can be established from the dynamics of multiple neural networks, where no single component has dedicated clock-like properties. Contrasting the pacemaker-accumulator model, the information processing demands of self-organized systems are minimal. Schöner posits that limit-cycle attractors could be driving a closed trajectory oscillator between activation and inhibition characteristics of the system. The oscillator would be self-sustaining, yet acted on by stiffness and damping from sensory feedback, effector kinematics, signal processing delays, and noise. Thus it is expected that the state of all the neural networks involved in a task contribute to the internal representation of a temporal structure. In Schöner's view (2001), a system with self-organizing temporal properties is able to provide a timekeeping reference without many of the complex information processing networks required for establishing a temporal goal, storing it in memory, generating movement, then comparing actual movement with that which was intended and generating error corrections. In a dynamical timing network, error corrections are thought to be achieved via positive or negative damping from internally generated feedforward state estimates, low latency efference copies, and actual performance measures from sensory feedback (Balasubramaniam, 2006).

In relation to behavioural data, if specific conditions are met, the dynamical systems approach is compatible with the negative lag-1 autocorrelation function between successive response intervals as predicted and observed using the WK model. The requirements to be compliant are that noise must be introduced from more than one source, or that a second oscillator exists with mutual coupling to the first. Accordingly, it has been shown that a single autonomous limit-cycle attractor cannot self-regulate with respect to time (Daffertshofer, 1998), supporting the notion of multiple oscillators in the timing network.

Interestingly, there are hypothetical advantages for models of timing networks that have multiple clocking structures. Helmuth and Ivry (1996) noted that response variability was decreased in a two-hand tapping task as compared with the unimanual equivalent. In theory, this effect can be explained by the dynamics of coupled clocking mechanisms, whether multiple stochastic accumulating clocks, such as a pacemaker-accumulator system, or multiple self-sustaining limit-cycle oscillators. If we consider two stochastic accumulator clocks that each generate increasing activity until an activation threshold is reached, one can define the relative timing relationship between each clock passing threshold. The relative timing results in event output based on an activation level average between both accumulator clocks, accounting for reduced variability in event timing when coupled. In this situation, true mutual coupling is the result of the event output generated based on average activation resetting both clocks simultaneously.

On the other hand, if we consider two self-sustaining limit-cycle oscillators comprised of all task-related networks, the relative timing between the oscillators is defined by their phase relationship. When such oscillators are mutually coupled, they eventually become phase locked with each matching the other's frequency and activation trajectory. A coupled relationship between oscillators exists when the dynamic variables of one timer contribute to the dynamic equations of the other. When such a coupled system is perturbed away from a stable phase locked state, the dynamics of each drives the other back towards a state of aligned trajectories.

There has been recent evidence supporting that such dynamics are fundamental in the timekeeping systems. For example, within series of predictive saccades, the latencies of the responses correlate over a span of two seconds, and the sequence of responses forms a fractional Brownian series (Shelhamer, 2005a; 2005b). In consideration of all relevant studies, it is most plausible that a multi-component representation of timekeeping exists, which exploits the computationally simplistic qualities of a self-organizing dynamical system and is supported by other related networks.

1.4.3 The cerebellum in timing tasks

Deficits in timing tasks may arise due to many types of neurological pathologies. Lesions of the cerebellum result in distinctive changes to timed response performance as a function of the locus of pathology. Ivry et al. (1988) observed cerebellar patients during timing tasks and measured response variability according to the WK decomposition. The authors documented increased central clock variability in patients with lesions to the lateral cerebellum, and increased motor variability concurrent with lesions of the medial cerebellum. In addition to impairing performance in timing tasks, cerebellar lesions also impair the performance in a duration discrimination task (Ivry & Keele, 1989) and velocity perception (Ivry & Diener, 1991). As these deficits are noted in both performance and perception timing tasks, the generalized loss of timing ability supports the likelihood of globally represented timekeeping networks that are called upon for multiple functions.

Although crucial for accurate timekeeping, the precise neurophysiological role of the cerebellum is not clear. However, random inter-spike intervals were recorded from the the spiking patterns in the Purkinje cells of the inferior olive nucleus. These findings suggest that cerebellar functions are not pacemaker, nor oscillator related.

1.5 Eye movements in timing tasks

Eye movements have some advantages as a means to investigate underlying timing mechanisms. Whereas the movement of limbs and digits has much imprecision, the eyes are much more precisely controlled effectors. This can partially be attributed to the physical properties of the eyes. As the eyes' geometry is spherical and rotational movements occur within a lubricated cavity, the system is very consistent and predictable. Furthermore, the eyes are guided by extremely accurate spatial information. Because of this, the eyes are able to hold very precise fixations. It is thus easy to reliably determine accurate timing for movement onset. This has led to the finite discriminations between predictive and reactive movements, and the precision required for finding long-term correlations. Also, the eyes are controlled via cranial nerves that offer much shorter signal transduction times than spinal nerves. Other advantages pertaining to movement feedback of eye movements will also be outlined in the following section.

1.5.1 WK model applied to periodic eye movements

Collins et al. (1998) tested the applicability of the WK model to a periodic saccadic task. The authors hypothesized that the same clocking mechanisms which drive movement execution in finger tapping tasks are also used in producing periodic saccades, and that similar data would be recorded using saccades. Expanding on previous research, the authors also made predictions that fewer violations of the WK model would be observed. As previously mentioned, violations of WK model might be the result of movement related error correction processes. Proprioceptive feedback from the effectors which move our limbs is necessary for ensuring both accurate and finite control. However, the remarkably precise control of eye movements relies much less on the proprioceptive feedback from the extraocular muscles. Again, this is because proprioception is very high latency and eye movements are of short duration. Thus, the authors expected that the decreased role of proprioception from the extraocular muscles in oculomotor control would lead to fewer attempts at error correction, and subsequently fewer violations. Results confirmed that the WK model is equally applicable to periodic saccades as compared with conventional finger tapping paradigms. Also, they confirmed that fewer violations occurred when using eye movements as compared with other effectors.

Smooth-pursuit eye movements are incompatible with a traditional synchronization-continuation paradigm. As pursuit tracking is necessarily driven by a moving stimulus, the continuation phase is impossible to construct since it implies removing the pacing stimulus.

1.5.2 Paced visual tracking, and predictive versus reactive behaviours

When tracking a periodic jumping target, one would make saccades which exhibit a reactive or predictive behaviour. The elicited behaviour depends on the frequency of the target motion. Fast frequencies, approximately 0.5Hz period and faster, evoke predictive behaviour and the eyes anticipate target motion (negative latency) whereas slow frequencies, usually less than 0.5Hz evoke a reactive mode of tracking and the target leads the eyes (positive latency) (Becker, 1991). The latency of the eye movements in relation to a target quantifies the time differential, usually in milliseconds, between the initiation of the eye movement and the onset of target movement.

Typical saccade reaction time to a randomly displayed visual target is approximately 200ms, yet some stimuli can evoke reactive saccades, called express saccades, with latency as low as 80ms (Bruce & Friedman, 2002). Since a positive latency of 80ms is the absolute minimal time required for a sensory driven reaction to occur, the definition of a predictive saccade includes saccades with up to a positive 80ms latency as the initiation must have been generated via internal anticipatory mechanisms.

1.5.3 Dissociation of reactive and predictive visual tracking

Although the control of both reactive and predictive saccades involve some common neural pathways, there is a distinct change in overall neural activity when switching to and maintaining a predictive mode of tracking. Concordant with establishing a predictive mode is an increase in activity in the basal ganglia, specifically the striatum and substantia nigra pars reticulata (Simó et al., 2005). Other research has implicated the basal ganglia in the internal representation of time (Rao et al., 1997) suggesting that a predictive mode of tracking relies on an internal clock.

Joiner & Shelhamer (2006a) furthered this notion and concluded that an internal clocking reference actively drives initiation of predictive but not reactive saccades. The authors provided evidence by observing saccade tracking behaviour following a transient perturbation to the timed stimulus. Through series of reactive saccades, behaviour following a perturbation was dependent on the characteristics of the perturbation. This supports the role of sensory functions initiating reactive saccades. Contrarily, following a perturbation during a series of predictive saccades, behaviour continued for a short period with no hindrance. The persistence of accurately timed responses in this scenario despite the perturbation supports that the timing of predictive saccades is generated internally.

1.5.4 Transition between reactive and predictive modes of visual tracking

Although conditions which evoke predictive and reactive behaviour have been tested extensively, it was only recently that the transition between tracking modes has been investigated. Shelhamer & Joiner (2003) presented subjects with saccadic tracking targets at frequencies between 0.2Hz and 1.0Hz. During these trials, pacing of the target was changed monotonically, increasing in frequency during one condition, and decreasing in frequency in the other.

Results indicate that switching between reactive and predictive modes of saccadic tracking occurs in an abrupt, not gradual manner. The authors label the behavioural switch as a phase transition, implying a bistable system. As a consequence of this bistability, when nearing the point of transition between behaviours, response latency distributions showed two separate groupings of high and low latencies. This bimodal behaviour is a typical property of a bistable physical system and is known as critical fluctuations.

Furthermore, the saccadic system exhibits a hysteresis. When one state of the system is established it will persist despite some temporal perturbations. Experimentally, this was observed as the behavioural transition occurred at a lower frequency during decreasing frequency trials as compared with increasing frequency trials. In other words, when subjects track a target as the pacing was gradually increasing, they generally showed critical fluctuations around 0.7Hz and reliably tracked in a predictive manner at frequencies higher than this. However, in trials where the target decreased in frequency, the subjects tracked predicatively until 0.5Hz when critical fluctuations began to occur, switching to a reactive behaviour thereafter.

Joiner & Shelhamer (2006b) replicated these observations with similar pacing rates in a smooth-pursuit tracking task. This research suggests that although the neural pathways related to the motor control of both types of eye movements are neurophysiologically separate, the timed initiation of either is likely reliant on a shared subsystem.

1.6 Current study

The purpose our study is to research characteristics of the neural timing mechanisms which are a popular topic of debate in current literature. Firstly, it is not yet known if the timing of short periodic intervals is represented globally, or if there are modality-specific limitations that may depend on the method of entraining the clocking networks. Even though it is commonly understood that the transfer of timing between effectors is possible, we seek to investigate the accuracy of this transfer. Secondly, it is not known with certainty whether the networks involved in timekeeping are isolated to a single structure, or if these processes are distributed among various areas of the brain. Furthermore, if the process of timekeeping is indeed distributed between multiple brain regions, there is growing evidence that the self-organizing dynamics between all of the task-related networks contribute to the emergence of a temporal structure.

The central idea to constructing the timing tasks used in our experiments is that the saccade and smooth-pursuit motor systems are largely segregated. We expect that when entraining the clock with timed responses with one type of eye movement, and when performing subsequent responses with the other type of eye movement, that any shared timekeeping processes will be distinguishable from those that are dependent on entrainment with separate motor pathways.

In the present study, we have run two complimentary experiments. Our first experiment was set up to analyze reactive and predictive behaviours during a paced tracking task. Tthis paradigm involved replicating and then expanding on the previous findings of Shelhamer & Joiner (2003) and Joiner & Shelhamer (2006b). Whereas these studies characterized the transition between reactive and predictive modes of tracking for both saccadic and smooth-pursuit targets, the authors did not include a paradigm to look at the transfer of timing entrainment from one type of tracking target to the other.

Using a similar procedure to the previous studies, we presented subjects a target with monotonically increasing or decreasing pacing rates. We then modified the task to observe the effect of establishing a history in the timekeeping system via entrainment with a smooth-pursuit target, then switching the stimulus to a saccadic target near the point of critical fluctuations when transitioning between predictive and reactive tracking. Our primary goal was to provide evidence of a complete transfer of timing history which was established through entrainment with one type of eye movement to the latter phase of the task when using the alternative type of eye movement. We hypothesize that, if a timekeeping process is globally represented, regardless of the type of eye movement used to entrain the clock, the history of the timing system will influence response latencies after switching the type of eye movement.

Our second experiment was constructed as an extension to that of Collins et al. (1998). We began by replicating their methods of a synchronization/continuation task and decomposing the variability in series of response intervals from the unpaced continuation phase using saccadic movements. However, as previously discussed, the traditional synchronization/continuation cannot be performed with smooth-pursuit movements. This is because smooth-pursuit tracking requires a moving target, which is inherently absent from the continuation phase of these experiments. To overcome this limitation, and with similar intentions as the first experiment to analyze the transfer of timing between types of eye movements, subjects were shown a stimulus-train with either saccadic or smooth-pursuit targets during the synchronization phase and following the removal of the entraining target, static targets were shown and subjects continued self-paced responses with saccades. This design allowed us to analyze the effect of synchronization condition on the WK decomposed variability during the continuation responses. In accordance with the expectations of our first experiment, we hypothesize that, if the timekeeping networks have no effector related dependencies for entraining a clock, we would observe series of continuation phase responses with similar WK decomposed variability when comparing synchronizing conditions.

Chapter 2 – Methods

2.1 Subjects

Seven healthy subjects, 2 female and 5 male, were recruited from the student population. The subjects' age fell between 20 and 25 years, and none had any history of neurological pathologies. Consent forms were presented to, and signed by all participants and the University of Ottawa's Research Ethics Board approved the study.

2.2 Apparatus

For recording eye movements, we used the EyeLink II head mounted eye tracker from SR Research. Visual stimuli were constructed using the eye tracker's bundled software package, Experiment Builder, and presented using a 30-inch LCD Cinema Display, Apple Inc. Cupertino, CA. Prior to each testing session we calibrated the EyeLink II for use with each participant. Although both eyes were used in the calibration process, we recorded monocular data from the eye that had the least average error when validating the calibration.

2.3 Experimental Procedure and Data Analysis

The current study examined the timing of periodic eye movements in two complimentary experiments. Consistent with previous research, visual targets were red circular similar to the size of a typical light emitting diode. Subjects sat at a comfortable height, and distance from the screen was between 25 and 30 inches.

During Experiment 1, subjects tracked a pacing target that was visible for the entire duration of each trial. In this experiment, our analysis examined the latencies of saccades in response to target motion. Consequently, Experiment 2 required participants to follow a pacing target for a predetermined number of repetitions (the synchronization phase) at which point the target was extinguished and the subjects were instructed to continue making movements with the same timing (the continuation phase). Analysis of Experiment 2 involved calculating response intervals between successive saccades during the continuation phase.

Chapter 3 - Experiment 1

3.1 Procedure

The first experiment comprised of four trial conditions, and subjects completed two iterations, or blocks, of each trial. In all of the trials, the target oscillated horizontally between ±15° of the center of the screen, and subjects were instructed to "look at the targets." Response latencies were recorded at target pacing for seven major frequencies, 0.165Hz, 0.2Hz, 0.3Hz, 0.5Hz, 0.7Hz, 0.9Hz, and 1.0Hz for fifty responses. To make transitioning between pacing each frequency smoother, between each major frequency was a minor frequency that lasted for 10 target intervals at 0.175Hz, 0.25Hz, 0.4Hz, 0.6Hz, 0.8Hz, and 0.95Hz. Only major frequencies were used for calculating response latencies.

The first two trials were constructed to examine the hysteresis effect of saccade latencies relative to target motion when pacing was monotonically changed over the duration of the trial. For these trials, target trajectories were programmed as a square wave when plotting position versus time. See Figure 3 for a plot of typical target trajectory. The associated target motion is thus jumping between two points on the screen. Since faster pacing evokes predictive movements, subjects would be making some saccades to an anticipated spatial location. To assist subjects in making properly directed saccades of appropriate amplitude, there were two static points on the screen, one quarter the area of the target's size, at the locations between which the target would jump.

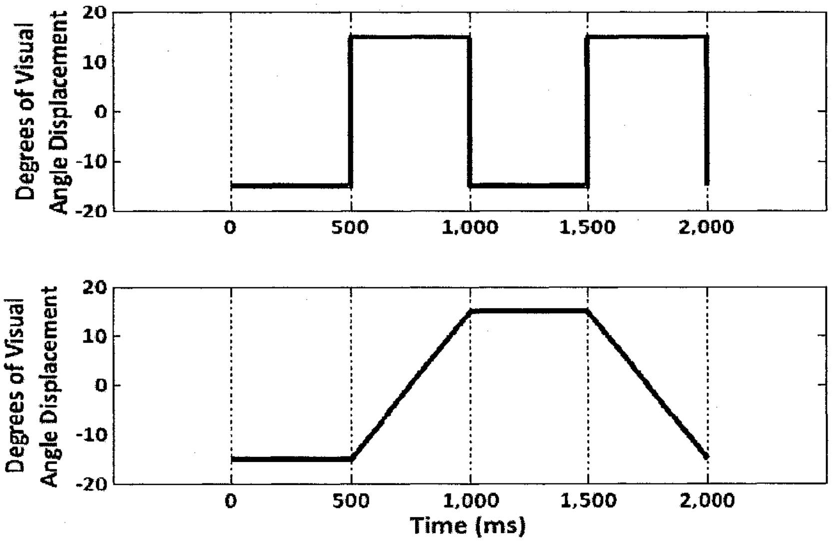


Figure 3. Plots of saccadic and pursuit target trajectories at 1.0Hz pacing. The top plot is representative of target motion for a saccadic target, whereas the bottom plot illustrates the trajectory of a pursuit target with similar timing of its discrete components. Although there are two periods of the square waveform, and only one of trapezoidal waveform, there is the same number of discrete events.

In trial 1, the target pacing began at the slowest rate and increasing in frequency as the trial progressed. Trial 2 was the reverse scenario, with the target beginning at the fastest pacing and gradually slowing. Trials lasted approximately 9 minutes each, and subjects completed one iteration of each trial, and following a brief rest repeated both trials a second time.

Following completion of these trials, we analyzed the response latency distributions for each subject to determine their respective behavioural transitions between reactive and predictive modes. By comparing latency distributions between each trial condition, we used a Fisher's PLSD test to find when a subject had significantly lower latency behaviour during Trial 2 versus Trial 1, thus classifying when predictive behaviour persists and the hysteresis of the system was apparent. The pacing at which this difference was significant will be referred to as the point of behavioural transition. These data were used in the construction of Trials 3 and 4, specifically tailoring them to each subject's respective performance characteristics.

The visual tracking target for Trials 3 and 4 was identical to that used in Trials 1 and 2, however we varied the type of movement path that the target followed. Whereas Trials 1 and 2 were saccade only tracking, Trials 3 and 4 began with smooth-pursuit tracking which was switched to saccadic tracking at a predetermined time during the trial. Of the smooth-pursuit and saccadic phases of these final trials, only the response latencies of the saccadic phase were used for data analysis. This was done because we were mainly concerned with the nature of response latencies following a switch in movement types, which reflects separate underlying motor control networks. Furthermore, we chose to analyze saccadic latencies because accurately calculating the time when smooth-pursuit began is made difficult by anticipatory drift of the eyes when preparing for onset of target movement.

In regards to Trials 1 and 2, we referred to target pacing as frequencies, implying a specific period of oscillation. However, this nomenclature is incongruent when describing a trapezoidal waveform because of more discrete movement onset events in the waveform during one period. Accordingly, we constructed the trapezoidal target motion to provide intervals which matched intervals to the square wave frequencies. For purposes of consistency, naming and referring to specific pacing speeds in both saccadic and pursuit conditions will remain according to the comparable square wave frequency. Refer to Figure 3 for a graphical representation of comparing square wave and pursuit target trajectories with similar timing properties.

Following analysis of Trial 1 and Trial 2 data, we constructed Trials 3 and 4 offline, and for each subject. Consequently, testing for the first and second half of the experiment was split into two sessions, both completed within a week. Similar to the ordering of Trials 1 and 2, in Trial 3 we presented horizontally oscillating targets beginning at a slow pacing and speeding up through the trial, and Trial 4 was the reverse scenario. First the pursuit target was presented, with the subject following fifty target intervals at every major pacing frequency and ten target intervals at every minor frequency. The pursuit target is displayed from the beginning of the trial up to, and including the pacing frequency where the subject elicited the behavioural transition point, as observed during Trials 1 and 2. Following fifty pursuit target repetitions at this pacing, the target switched to a saccadic tracking target and fifty more target intervals were presented. Subsequently the trials continued with saccades, monotonically speeding up in Trial 3, or slowing down in Trial 4. Subjects completed one iteration of each of these trials, and after a short break performed a second iteration.

3.2 Data Analysis

Gaze data was exported from the eye tracker's proprietary data file to an ASCII file and further analyzed in Matlab. In-house scripts were developed to determine saccadic response latencies. This was accomplished by determining saccade onset according to a velocity threshold. Time differentials were calculated progressively between the onset of saccades and the according target movement. At times, subjects blinked, made premature movements and looked back again, or missed some interval. In these scenarios, eye movements were considered to be an inaccurate representation of the intended timing and no response latency was calculated until the next target jump.

Calculation of statistics was done using the Statview software. First, we examined mean latencies for all trials, qualitatively looking for the pacing frequency where the point of behavioural transition likely occurred. We then used Fisher's PLSD post-hoc test to find significant differences between latency distributions from each trial at this pacing frequency.

3.3 Results

Of the seven subjects tested, two, PR and PG, did not show the expected hysteresis, with higher latency responses in Trial 1 and lower latency responses in Trial 2 around the behaviour transition. As this experiment is targeted at examining the effect of switching eye movements on this hysteresis, these subjects were not included in further testing or analysis. From here on, when we refer to *all subjects*, we imply the ones completing the entire Experiment 1 procedure.

Figure 4 shows mean latency data for all subjects. Four of the five subjects had significantly lower latency responses in Trial 2 than in Trial 1 at 0.5Hz. The other subject (JY) had statistically similar results at all pacing frequencies during the transition between predictive and reactive from 0.3Hz to 0.7Hz. However, at 0.3Hz pacing, JY's Trial 2 responses (M = -71.26, SD = 166.12) were only nearing significance to being lower than Trial 1 responses (M = -28.64, SD = 166.34), $p = 0.0927$. While the subject was consistent with the general trend of transitioning to lower latency responses at faster pacing, we regarded 0.3Hz as an appropriate pacing frequency to label as this subject's behavioural transition point. This was chosen because Trial 1 and Trial 2 responses were closest to being significantly different from one another at this pacing.

Table 1 shows all subjects' mean response latencies and standard deviation of the sample for each trial at the point where subjects' behavioural transition was showing effects of hysteresis. Table 2 lists significant differences in groups of response between trial conditions, at the point in time when subjects were transitioning between high and low latency behaviour. This data was used to determine the point at which the hysteresis effect was apparent, as subjects showed significantly lower latency responses in Trial 2 as compared with Trial 1.

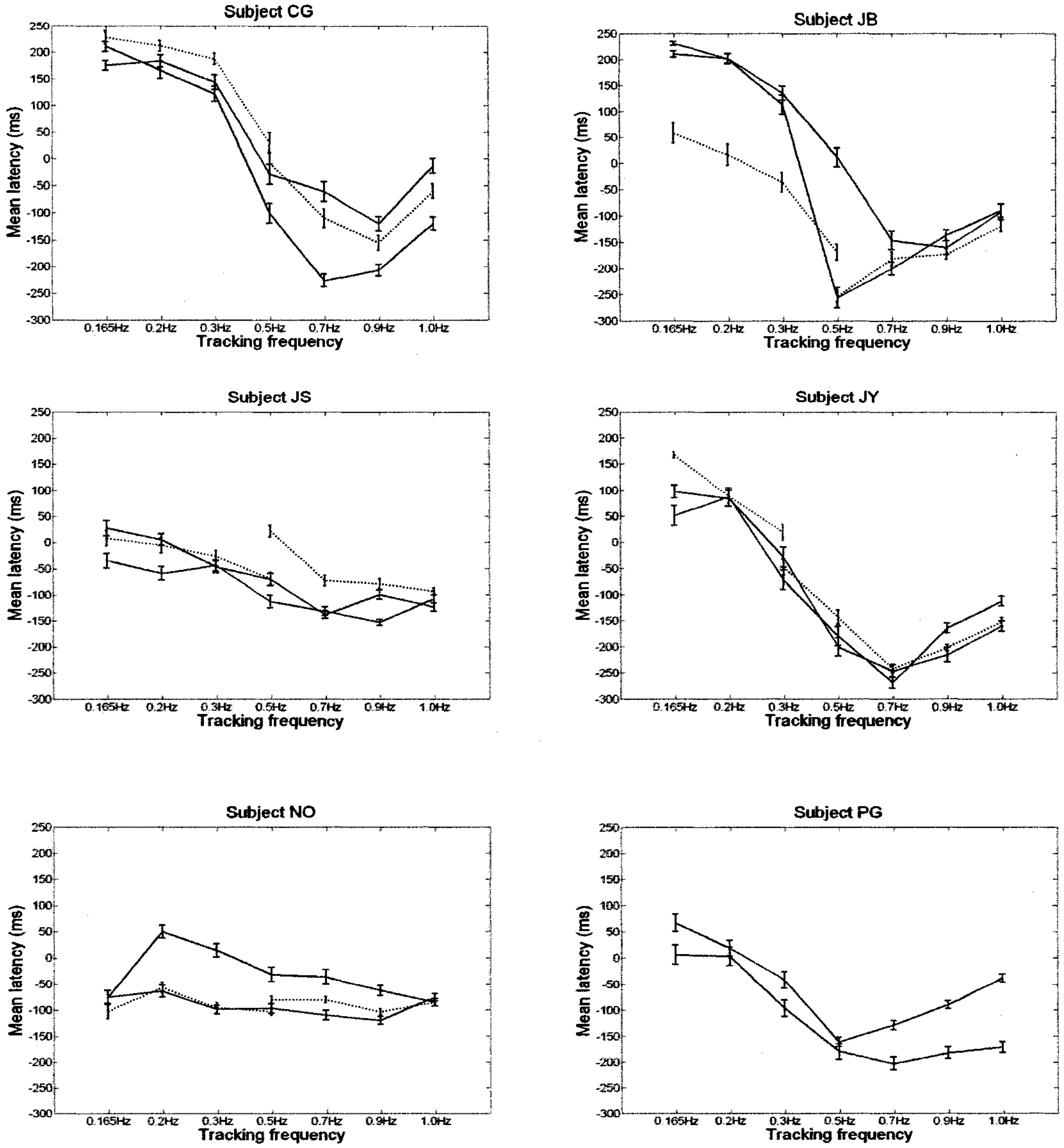
Qualitatively comparing results at the behavioural transition point from Trial 3 and 4 with each other, and to Trials 1 and 2, revealed no ubiquitous intra-subject trend or consistency in response behaviour. However, there are some general patterns of higher or lower response latencies persisting throughout Trial 3 and Trial 4. We did not perform any statistical tests on these sets of data because it would not strengthen any assumptions about the processes generating the responses more so than analyzing the general qualitative trends. In our discussion section, we will highlight what these trends are, and what the implications may be.

Subject	Behavioural Transition Point	Trial	Mean	Std. Dev.
CG	0.5Hz	T1	-28.62	179.41
		T2	-100.47	169.05
		T3	-7.51	192.51
		T4	29.71	184.36
JB	0.5Hz	T1	11.35	173.85
		T2	-255.72	139.18
		T3	-252.71	101.35
		T4	-168.50	145.00
JS	0.5Hz	T1	-70.04	113.78
		T2	-112.11	115.55
		T3	21.98	107.87
		T4	-68.06	114.18
JY	0.3Hz	T1	-28.64	166.34
		T2	-71.26	166.12
		T3	-46.81	147.72
		T4	18.92	147.88
NO	0.5Hz	T1	-31.21	129.20
		T2	-96.27	87.42
		T3	-79.92	68.09
		T4	-102.23	70.50

Table 1. Mean, standard deviation and standard error for all subjects' response latencies at their respective behavioural transition point.

Subject	Interaction	Mean Diff.	Crit. Diff	P-Value
CG	T1, T2	71.85	54.05	< 0.01
	T1, T4	-58.34	53.13	< 0.05
	T2, T3	-92.96	54.05	< 0.001
	T2, T4	-130.19	53.91	< 0.0001
JB	T1, T2	267.07	49.48	< 0.0001
	T1, T3	264.06	42.11	< 0.0001
	T1, T4	179.85	41.99	< 0.0001
	T2, T4	-87.22	49.87	< 0.001
	T3, T4	-84.21	42.58	< 0.001
JS	T1, T2	42.06	32.46	< 0.05
	T1, T3	-92.02	32.29	< 0.0001
	T2, T3	-134.09	32.20	< 0.0001
	T2, T4	-44.04	32.20	< 0.01
	T3, T4	90.04	32.03	< 0.001
JY	T2, T4	-90.17	47.08	< 0.001
	T3, T4	-65.73	44.61	< 0.01
NO	T1, T2	65.06	26.14	< 0.0001
	T1, T3	48.71	26.14	< 0.001
	T1, T4	71.02	26.14	< 0.0001

Table 2. Significant differences in mean latency between trials at the pacing rate when each subject was transitioning between high and low latency behaviour, also referred to as the point of behavioural transition. Significant differences between T1 and T2 were used to quantify when the hysteresis effect was evident.



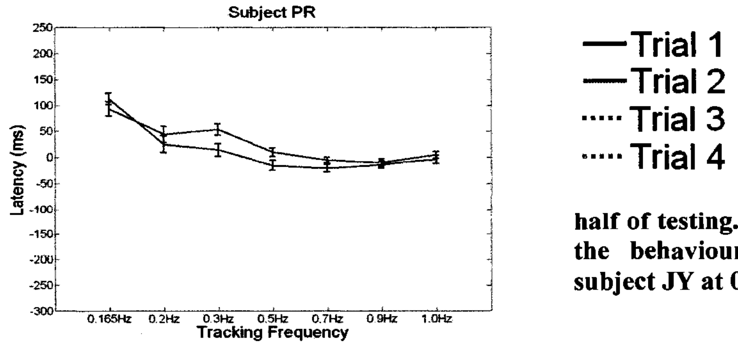


Figure 4. Plots of mean latency of responses for all trials and all subjects, with error bars representing the standard error of the mean. Subjects PG and PR were excluded from the second half of testing. Subjects CG, JB, JS, and NO show the behaviour transition point at 0.5Hz, and subject JY at 0.3Hz.

Chapter 4 – Experiment 2

4.1 Procedure

This experiment was constructed using a synchronization/continuation paradigm in two conditions. Visual targets were similar to those used in Experiment 1. The first condition used only saccade tracking during the synchronization phase. The target oscillated horizontally between the two static points for a total of twenty intervals at which point the continuation phase began and target disappeared but the static points remained. The subjects were instructed to continue making saccadic jumps between the static points at the same rate as the pacing target that had just disappeared. After thirty-two unpaced responses, the trial was over.

The second condition was similar, but the synchronization phase was performed using a pursuit target. This target trajectory was constructed with a triangle wave form, resulting in a constant velocity target which moved from one side to the other, and would appear to be bouncing off of the static points. Subjects were instructed to follow the pursuit target, and when it disappeared to continue making responses between the static points at the same rate with saccades. Similar to the saccade synchronized condition, twenty intervals were performed in synchronization and thirty-two during continuation. We first presented a demo condition to subjects to familiarize them with the nature of the task.

Both saccade and smooth-pursuit synchronized conditions were presented at 500ms, 750ms, and 1000ms for a total of six trials. We recorded five blocks of each trial, and the order of trials within each block was randomized.

4.2 Data Analysis

Using MATLAB™ and in-house developed scripts, inter-response intervals (IRIs) were calculated from continuation phase data for all trials. Because eye movements are made both back and forth across the screen, we corrected for possible effects of directionality in each trial run following methods used by Collins et al. (1998). This was done for each trial run by computing the mean response interval during rightward and leftward movements, and the difference between both means. We then added half of the difference between means to each response interval of the direction that had a smaller mean, and subtracted half from each response interval in the direction having a larger mean.

Series of IRIs from each subject and each trial were exported to Microsoft Excel 2007 for decomposition according to the WK model. To correct for timing drift over the duration of the continuation phase, each series of response intervals was first detrended by

$$I_{n\text{-corrected}} = I_n - (n * m + b) \qquad [4]$$

where the corrected interval $I_{n\text{-corrected}}$ is the detrended interval, I_n is the recorded interval, *n* is the interval number in the series, *m* is the slope of the series, and *b* is the series' y-intercept. We used Equations 2 and 3 to find the variance of the individual components of the WK model. Because these equations are estimations of actual underlying variances, some of the calculations can return negative variances. As is customary with WK decomposition using this method, we replaced the negative variance values with zero.

A 2 (synchronizing condition) x 3 (target interval) ANOVA was performed to investigate the effects on total interval variance, clock variance, motor delay variance, and autocorrelation functions from lags 1-5.

4.3 Results

Six of the seven recruited subjects took part in Experiment 2. For investigations of the WK components of variability, we grouped all subject data together. The first trend we looked for in our data was the effect of target interval and synchronization condition on total interval variance. We expect that total interval variance increases with target interval, which would be consistent with Weber's law.

Firstly, we ran a 2 (synchronization condition) x 3 (target interval) ANOVA. This showed a significant main effect of target interval [F(2,137) = 10.36, p < 0.0001] but no significant effect of synchronization condition [F(1,137) = 1.33, p > 0.05] or of synchronization condition and target interval [F(2,137) = 0.37, p > 0.05]. In Figure 5A, the trendlines show that total interval variance increases with target interval for both synchronization conditions. Also in this plot, we can see that total interval variance in the saccade synchronized condition 500ms trials (M = 3705.48, SD = 3053.95) were significantly less than in the 750ms trials (M = 10678.77, SD = 10605.07), $p < 0.01$. However, total interval variance in the 1000ms trials (M = 10477.45, SD = 8423.35) was not significantly different from in the 750ms trials. This effect was similar to that of the smooth-pursuit synchronized trials, where the 500ms trials (M = 3809.78, SD = 2483.44) showed significantly less total variance than the 750ms trials (M = 12831.34, SD = 17137.63), $p < 0.01$. Again, the 1000ms trials (M = 14206.53, SD = 12680.42) did not have significantly different total variance from the 750ms trials. Overall, we can see no effect of synchronization condition when grouping all target interval conditions and comparing total interval variance. This is evident as the first set of columns in Figure 6 have a similar magnitude.

Next, we looked at the effect of target interval and synchronization condition on the clock variance. Similar to total interval variance, we also expect to see clock variance increase with target interval. This is because Weber's law attributes the relationship of increasing interval variance with target interval to cumulative errors of the internal clocking mechanism.

In saccade synchronized trials, the clock variance was statistically similar between all of the target interval conditions. Yet, examining the trendline between target interval conditions as seen in Figure 5B, clock variance generally increased with interval duration. A 2 x 3 ANOVA confirmed this trend, showing a significant main effect of target interval [$F(2,137) = 3.08$, $p < 0.05$]. However, there was no significant effect of synchronization condition [$F(1,137) = 3.18$, $p > 0.05$] or interaction of synchronization condition and target interval [$F(2,137) = 0.81$, $p > 0.05$].

Post-hoc analyses of smooth-pursuit synchronized trials revealed a significant increase from the 500ms trial runs ($M = 1435.16$, $SD = 1022.16$) compared to those from the 750ms trials ($M = 5945.54$, $SD = 13076.12$), $p < 0.05$. Again, the clock variance in the 1000ms trials ($M = 5351.41$, $SD = 7133.38$) was not significantly different than that calculated from the 750ms trials. Fitting a trendline showed that variance increased with target interval. These relationships can be seen in Figure 5B with all target interval and synchronization conditions plotted separately. As the second group of columns in Figure 6 is similar in magnitude, we did not observe a significant effect of synchronization condition on clock variance when grouping all target intervals.

The remaining component of the WK model for variance decomposition was to examine the effect of target interval and synchronization condition on the motor delay component. A 2 x 3 ANOVA showed significant main effects of target interval [F(2,137) = 10.06, $p < 0.0001$]. However, there was no significant effects of synchronization condition [F(1,137) = 0.03, $p > 0.05$] or of synchronization condition and target interval [F(2,137) = 0.24, $p > 0.05$]. In Figure 5C, we can see that in saccade synchronized trials, there was an increase in motor delay variance from the 500ms trials (M = 1154.17, SD = 1089.93) to 750ms trials (M = 4263.49, SD = 5770.91), $p < 0.01$, but no significant differences between the 750ms and the 1000ms trial runs (M = 4139.96, SD = 4783.87). The smooth-pursuit synchronized trials showed similar trends. In the same plot, we see that the 500ms trials (M = 1191.25, SD = 1110.71) had significantly lower motor variance than the 750ms trials (M = 3552.22, SD = 3055.74), $p < 0.05$, while the 750ms and 1000ms trials (M = 4473.86, SD = 4134.72) were not significantly different from one another. Fitting a trendline to Figure 5C shows that both saccade synchronized and smooth-pursuit synchronized trials had increasing motor delay variability with increasing target interval. Similar to the effect on both total interval variance and clock variance, the effect of synchronization condition on motor variance was not significant, and the third set of columns in Figure 6 are nearly identical in magnitude.

Aside from decomposing total variability into separate components as per the WK model, we also examined the long-term correlations within each trial run. A plot of these data from lag-1 to lag-5 for each subject is located in the appendix as Figure 9. Seen in this figure, subject PR exhibited very atypical trends, with the majority of trials having a positive autocorrelation coefficient across all lags. Consequently, we excluded this subject from the pooled data. We then grouped the rest of the subjects and plotted the mean autocorrelation coefficient for all trials in Figure 7.

Furthermore, Figure 8 shows these data grouped according to synchronization condition for examining the effect of these conditions on long-term correlations within trial sequences. Because the WK model predicts a lag-1 autocorrelation coefficient between 0 and -0.5, and a value of 0 at higher lags, Figure 8 is important in seeing in which synchronization condition and at which lags the data conforms to or violates the model. Since we are comparing the data sets to constant values there is no need for statistical tests comparing the distributions of each group to one another.

We can see in Figure 8 that both conditions obeyed the WK prediction of having a lag-1 autocorrelation coefficient between 0 and -0.5. At higher lags, the saccade synchronized trials mostly obey the predictions of being at, or near 0 and are within standard error. The greatest non-0 value of these data being at lag-5 (M = 0.0706, SD = 0.157). However, the mean autocorrelation coefficients for smooth-pursuit synchronized trials are further from zero, with the standard error of the distributions being outside of 0 at lag-2 (M = -0.06, SD = 0.17), at lag-3 (M = 0.05, SD = 0.14805), and at lag-5 (M = 0.03, SD = 0.16).

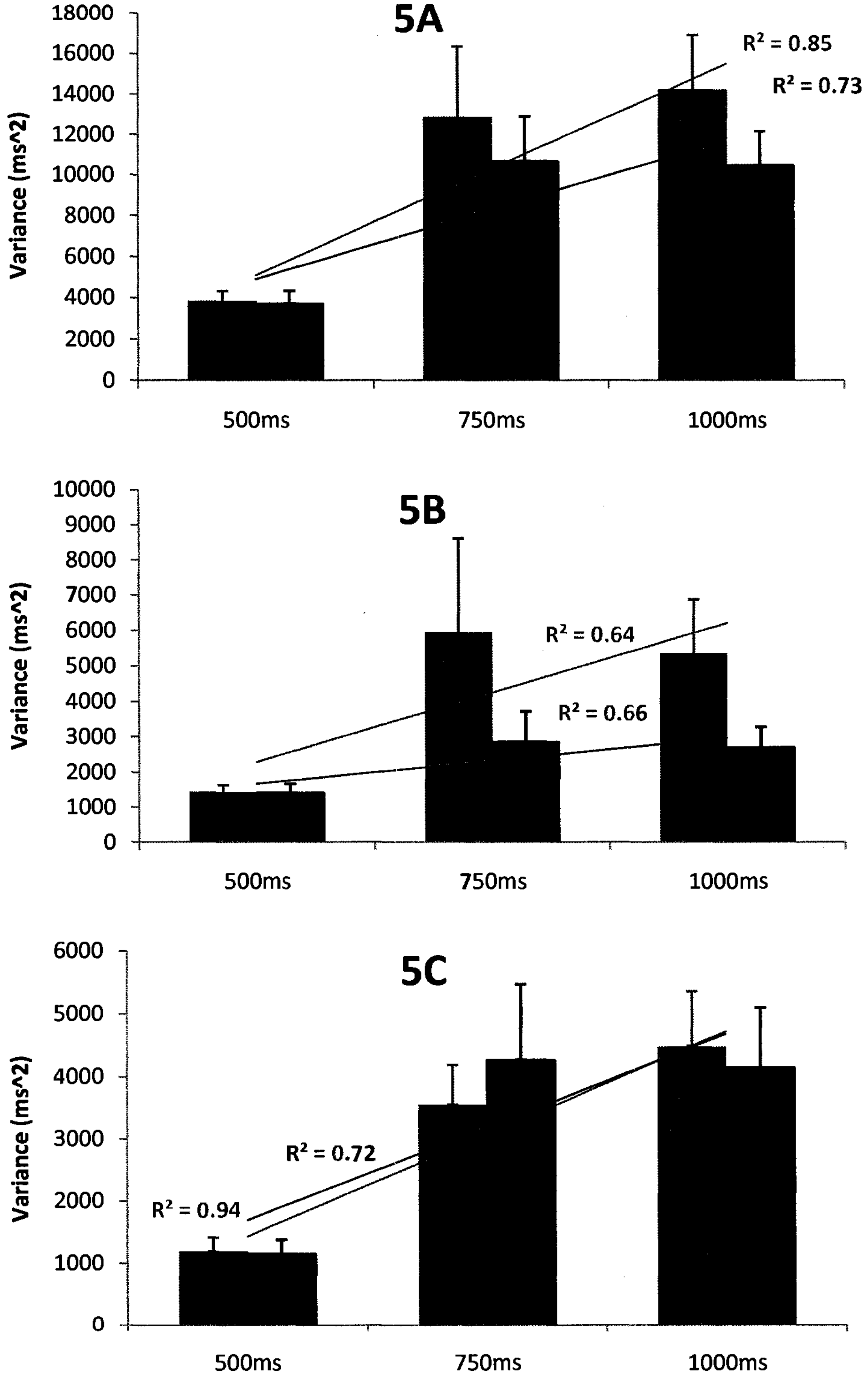


Figure 5. Wing and Kristofferson decomposed variability of timed responses from Experiment 2. Subplots A, B, and C represent total interval variance, clock variance, and motor variance respectively. Error bars represent the standard error of the mean.

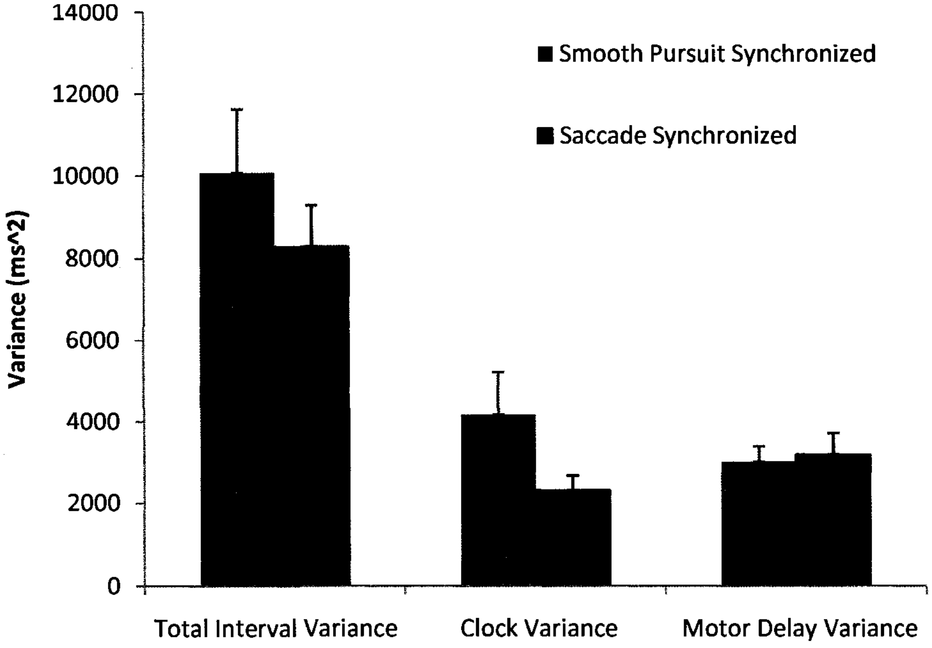


Figure 6. The effect of synchronization condition on Wing and Kristofferson decomposed variability from Experiment 2.

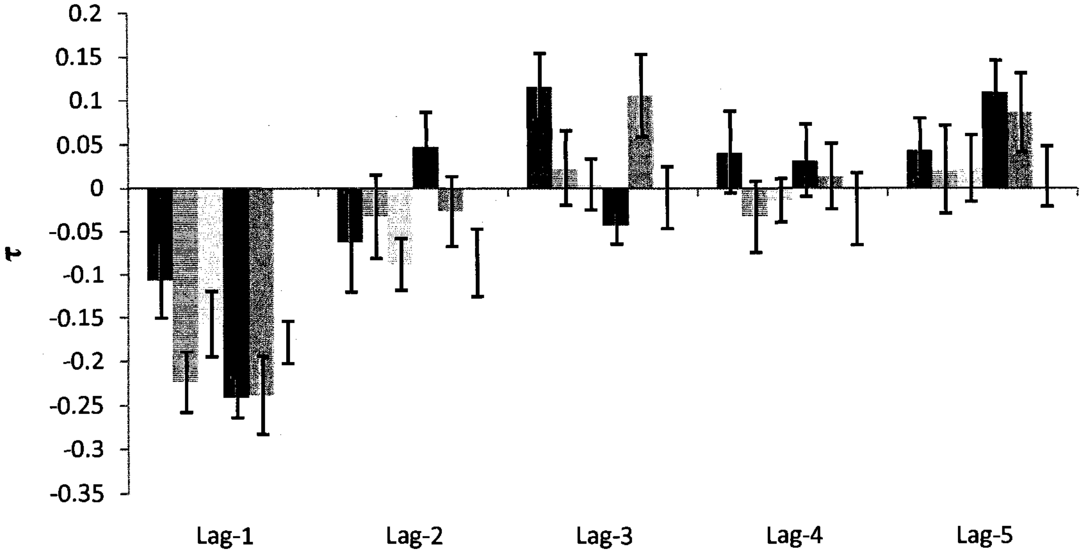


Figure 7. Mean correlation coefficient from lag-1 to lag-5 for pooled subject data, excluding subject PR. Error bars represent standard error of the mean, calculated from the pooled data.

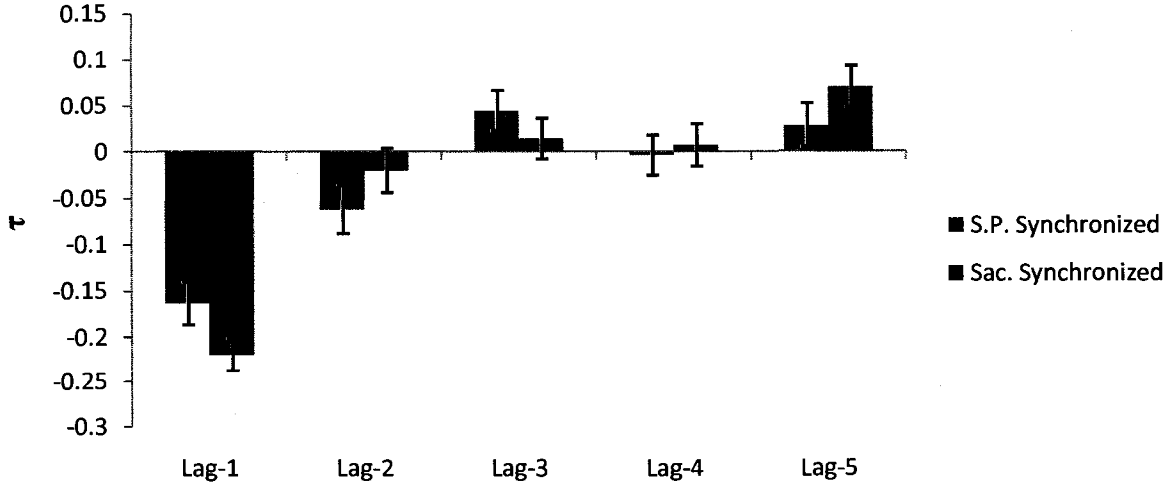


Figure 8. Mean autocorrelation coefficient from lag-1 to lag-5 for data grouped according to synchronization condition. These data excluded subject PR, and the error bars represent the standard error of the mean calculated from all trial runs within each synchronization condition.

Chapter 5 – Discussion

5.1 Experiment 1

Results from our first experiment showed that some subjects were able to track a periodic saccadic target with similar behaviour regardless of the method used for entrainment. This suggests that a central clocking mechanism exists that does not have effector dependent characteristics that are non-transferrable in sharing timing with other effectors.

The first two trials of Experiment 1 were designed to replicate the findings of Shelhamer & Joiner (2003). Data collected from five of the seven participants were exemplary of the trends which we expected to observe, and we excluded the other two participants from further investigation. The five subjects who completed the entire Experiment 1 procedure all tracked the saccade target with higher latency (reactive) responses at slower pacing frequencies, and lower latency (predictive) responses at faster pacing frequencies. As discussed in our introduction, it is important to note that predictive behaviour is not necessarily less than 0ms, below which point the eyes lead the target motion. Revisiting the literature of Bruce & Friedman (2002), we must consider the minimum time required to make a stimulus driven reaction. As observed during express saccades, it is possible for one to make a reactive saccade to a newly displayed visual target with no less than 80ms latency. Thus, a saccade made in anticipation of target motion, also considered to be driven by an internal clocking mechanism, includes responses that are less than 80ms in latency.

Examining the transition between these tracking modes across subjects revealed some variability. Subjects CG, JY and JB had the most distinct transitions between the maximal and minimal response latencies. These took place rather abruptly, exhibiting a steep slope between the mean response latencies at the pacing frequencies across the transition. At the pacing frequencies on either side of the transition, there was variability in the mean response latency, yet subjects' behaviour remained in a relatively constant bracket. In other words, when we observed predictive behaviour at faster pacing frequencies, the latency measures showed variability between each pacing level, fluctuating about the expected negative latency values and did not suddenly switch back to high latency responses. The same was true for the high latency reactive tracking mode at the slower pacing frequencies, which also showed variability but no spontaneous low latency behaviour.

Of the other two subjects, JS transitioned between the higher and lower latency behaviour as expected, yet the mean latencies had maxima and minima across the pacing frequencies were not as extreme as compared with the other subjects. Subject NO had a more distinct behavioural transition in Trial 1 than in Trial 2. During Trial 1, this subject had relatively stable low latency tracking at and above 0.5Hz, and when tracking slower targets, had the expected higher latency responses. However, this subject's tracking behaviour at the slowest pacing, 0.165Hz, had much lower latency than at 0.2Hz and 0.3Hz. It is possible that pacing was so slow and responses being so imprecise that the subject decided to try to guess the target pacing, resulting in inaccurately timed responses with a non-clock driven anticipation. Nevertheless, when comparing Trial 2 results to those of Trial 1, this subject had lower latency responses as expected by the hysteresis.

The purpose of Trials 3 and 4 was to create a condition with which we could analyze the transfer of timing between two visual tracking tasks that involve two different types of eye movements. Because the initiation of saccades and smooth-pursuit have separate motor pathways, presumably any dissociations between the motor and timing systems would be apparent in data recorded using this paradigm. As timing has been shown to be generally transferrable between effectors, whether this transfer is complete or partial is less understood. Thus, we are looking for evidence of any effector dependent effects for entraining the timekeeping networks.

Trials 1 and 2 provided a benchmark for what we can expect in a purely saccadic tracking task. Trials 3 and 4 began by entraining the timing of movements to a smooth-pursuit target, and after a switch to saccadic tracking the trial continued with similar conditions to Trials 1 and 2, respectively.

We hypothesized that if a single, globally represented timing mechanism exists, we would find support in that saccadic response latencies in Trial 3 would closely mimic those of Trial 1, as well as between Trial 4 and Trial 2. By exploiting the hysteresis of the directionality of changes to target pacing, similar behaviour between these trials should only be observed if the history of the system is established without effector dependencies. Our hypothesis relies on the assumption that, when nearing the transition between stimulus driven reactions and internally anticipated responses, critical fluctuations in responses are observed that indicate a fragile balance exists between sensory and timing systems. Thus, we anticipate that, although timing information may be shared between effectors, if there is even a slight loss or lack of transfer, the effects of this loss would most likely be observable around this unstable time.

Conversely, evidence in favour of our null hypothesis would be that the history of the timing system does not fully transfer through the switch of eye movement patterns. Such data would support that the combined dynamics of all task-related neural systems are responsible for the self-organized emergence of task performance. This carries the notion that temporal organization is influenced by the motor system and that a central source of timekeeping is not likely.

As noted in the results section, when analyzing the latency distributions from all four trials at the point of behavioural transition, there was no single trend observed throughout all of the subjects. Consequently, we propose that factors unique to each subject's experience with timing tasks and interpretation of the current experiment must have influenced their response behaviour. Thus, to search for more definitive trends, we decided to look further into the relationships of response latencies at all of the pacing frequencies for all four experimental conditions, and did not restrict our analysis to the response at the point of transition. We consider that the switch between saccades and smooth-pursuit movements was perceived as a perturbation in the task. Although the subjects knew the switch would occur, the exact timing of the switch was not known which added an element of surprise when the switch occurred.

Examining Trial 4 results reveals that subjects CG, JY and JS all had similar trends in that these response latencies were higher as compared with their respective Trial 2 responses. As tracking at these pacing frequencies was guided by stimulus driven reactions, it may seem strange that the history of the timing system affects responses in this pacing range. We suggest that this change in reactive behaviour reflects an adverse effect to the perturbation of switching between eye movements on a higher level of processing. It is possible that this adverse effect changed the subjects' respective strategies for performing the task, and primed them to be less anticipating of the timing characteristics of the target. For that reason, subjects may have hindered their own reaction times by engaging inhibition mechanisms while dedicating more attention to following the target passively. Alternatively, it may seem that these data could support the dynamical systems approach to timing. There are two likely perspectives on this argument.

Firstly, one may posit that the interplay of all task-related neural networks, including sensory systems, is affected by the entire history of the timing task. In consideration of this, the higher latencies in Trial 4 as compared with Trial 2 could be a result of the entirety of the task, and the smooth-pursuit portion effecting subsequent saccade timing. However, support for this quickly ends when revisiting the research by Joiner & Shelhamer (2006a) which indicates no clocking processes, and consequently no long-term correlations being evident in series of reactive saccades. On the other hand, this is limited to reactive saccade tracking, whereas the subjects also tracked at higher than baseline latency immediately following the target switch.

Secondly, one may also argue that these data support Schöner's (2001) view on applying the dynamical systems theory to timekeeping. This thought considers that these three subjects did not show a complete transfer of timing when looking specifically at the point of transition, thus taking on a reactive mode of tracking. This may be indicative that entraining the internal clock during the smooth-pursuit portion of the task resulted in an effector specific representation of time. Following the switch to saccades, subjects approximated the timing entrained with the pursuit target, yet the history of the timing system did not transfer and subjects defaulted to reactive tracking. This would support the notion that entraining the internal clock involves effector-dependent characteristics. Nonetheless, as a brief counterpoint to this argument, of these three subjects, JY and CG both had Trial 4 response latencies at all pacing rates that were even higher as compared with Trial 1. As this purely stimulus-driven reactive mode of tracking is influenced compared to the baseline responses in Trial 1, higher-level effects are almost certainly contributing to the slower reaction times, and are also likely affecting the response latencies immediately following the behavioural transition point.

Contrasting the behaviour of these three subjects, NO maintained almost identical behaviour in Trial 4 as in Trial 2 while JB's Trial 4 response latencies had a slight increase initially as compared with Trial 2, then continued at a much lower latency. We propose that the same higher-level networks previously discussed are intervening, but with different tracking strategies being initiated. Instead of the adverse effects of the perturbation of switching eye movements and engaging a more passive following strategy, we suggest that these subjects employed a more active attempt to anticipating the target.

As previously discussed, subject NO had a much more distinct behavioural transition during Trial 1 than in Trial 2, as well as unexpectedly low latency behaviour at 0.165Hz during Trial 1. Since we have established that this subject is likely taking active attempts to anticipate target motion at a pacing frequency that are known to be unfavourable to natural clock driven behaviour, it is not unlikely that this subject took the same strategic approach to recovering from the eye movement perturbation during Trial 4.

We can apply a similar explanation to JB's response behaviour. Despite the initially higher latency tracking at the behavioural transition point, JB continued producing responses at a lower latency than either Trial 1 or 2. The modification of these responses, which should be under sensory driven control, is likely being modified by cognitively mediated tracking strategies.

Our notion that tracking strategy can vary between subjects and that response latencies can be affected by these differences is supported by other related literature. Isotalo et al. (2005) researched the effects of instruction on the response latencies during a saccade task. In this experiment, the authors gave subjects two task instruction conditions, with one being worded to imply a predictive behaviour and the other implying a passive behaviour. In the former condition, subjects were instructed to "move your eyes in time with the lights," and in the latter "follow the lights." Results of this study showed that subjects often tracked with higher latencies during the passive instruction condition and with lower latencies during the other. However, this effect was not apparent with all subjects, or even in all trials for subjects who exhibited this effect. Relating this to our research is intuitive and we can say with near certainty that subjects employed different tracking strategies based on their respective reactions to the perturbation, motivation levels, previous training in timing tasks and music, or one of many other factors.

Overall, our results indicate that it is possible for timing information to transfer between effectors without losing the entrainment history of the system. This supports the notion of a central mechanism for timing where the effector used to entrain the clock is not necessarily a component of the clocking mechanism. In regard to providing evidence for or against the dynamical systems theory, results only provide inconclusive evidence and we cannot draw solid conclusions in this respect. However, in consideration that strong evidence already exists for self-organized dynamical systems in the timekeeping processes, we might add that it seems the motor system's contribution to timing related functions is rather limited.

5.2 Experiment 2

The purpose of our second experiment was to observe the transfer of timing information between effector pathways from a perspective that compliments that of Experiment 1. Whereas we previously used a paced tracking task to examine the transfer of timing history, Experiment 2 differed in that we looked at the unpaced responses from the continuation phase of a synchronization/continuation task with two synchronization conditions. Mirroring our hypothesis in Experiment 1, we posited that a central source of timing exists that can be utilized by one of many downstream effector pathways. Hence, we would expect that the decomposed variability of each WK component should be similar when comparing the continuation responses from both synchronization conditions.

The data supported our hypothesis, and there was no significant effect of synchronization condition on the total interval variance, clock variance, and motor delay. Thus, the data suggests that timing is represented globally and can be used by any effector pathway downstream of this source of timekeeping. However, this is not adequate information to say that a central neural structure that is solely dedicated to timekeeping is any more likely than a distributed system. Further investigation into the physiology and locus of the timing networks will require contribution from studies involving patients with neurological lesions, or techniques such as brain imaging and transcranial magnetic stimulation (TMS).

Even though the variance distributions from each synchronization condition were within significance of each other, there was a slight increase in the clock variance component and consequently total variance in the smooth-pursuit synchronized condition. On the other hand, mean motor variance was nearly identical between the conditions. That clock variability slightly increased while motor delay variability remained the same strengthens the WK model's assumption that the variability in motor plan remains relatively constant for each effector and is independent from the clock component. As subjects used saccades in continuation phase for both conditions, it seems that there is no influence of the clock component on the variability of the delay for motor implementation. These data are compatible with findings by Verstynen et al (2006) and Levit-Binnun et al. (2007). By means of a repetitive finger tapping task, the authors of both studies used TMS with the idea of teasing apart the processes of the motor cortex with those of timing networks. The conclusions of both studies indicate that a TMS perturbation to the motor cortex that disrupts the implementation of impending motor commands leaves the underlying timekeeping processes relatively unaffected. Collectively, these observations and those from the present study suggest that the relationship between the clock and motor components is bi-directionally independent.

Consistent with a growing number of studies, our results from running autocorrelation analyses question the WK model's assumption that successive clock intervals are independent. Collins et al. (1998) have noted violations of the WK predictions in saccade only trials, and our results show that the occurrence of such violations are more frequent during the pursuit synchronized condition. We suggest that switching from pursuit to saccades adequately perturbs the timing system to engage broader scale correction strategies. It may be tempting to question our recent discussion that the motor and timekeeping systems are mutually independent. Yet, it is possible to maintain our previous suggestion by attributing the WK violations as an artifact of possible self-monitoring characteristics of the timekeeping process. This process involves some speculation about possible physical models that describe the internal clocking mechanism.

Since changing the motor execution pathway, as we did in the pursuit-synchronized condition in Experiment 2, resulted in an increased rate of basic WK violations at higher lags, there may be an alternative explanation to simply perturbing the timekeeper and engaging error correction strategies. As an alternate explanation, a single locus of timekeeping may exist, but could perhaps be comprised of multiple coupled clocks which facilitate the sharing of timing between effectors. It is possible that each of these clocks drive separate motor output pathways for movement execution. These ideas are purely philosophical, and drawing any solid conclusions would require much more data acquired using many different paradigms. With the status of timing literature, at this time this would likely be beyond the scope of any one study.

5.3 Conclusion and future directions

The main finding of our research is support for a globally represented source of timing that is independent of the motor execution pathways used for entrainment of the clock. Although we indicate the likelihood of a timekeeping model that seems to be entrained independent of effector pathway, we do not intend to contradict evidence supporting the dynamical system theory and the emergence of timing properties. However, the measures we used in the present study to examine the timekeeping processes are not dependent on the dynamics of the motor networks.

There are both advantages and limitations to a global timekeeping mechanism. Having a central timekeeper may provide flexibility in motor learning and contribute to the generalization of learned motor tasks. Schmidt (1975) proposed that motor schemas represent the organization of a movement plan. In this view, a global timekeeping mechanism could explain the transferable nature of the relative temporal organization of learned motor programs. Yet, an important limitation of a single timekeeper is that interference can occur in tasks requiring bimanual coordination. During bimanual finger tapping, it has been shown that the coordinative pattern of the fingers favours an in-phase mode (Haken et al., 1985). Therefore, tasks requiring the dissociation of temporal organization between multiple effectors in both implicitly and explicitly timed movements are difficult to perform.

Even though coordinative interference is observed in both implicit and explicit timing tasks, there is no correlation between the two tasks as a predictor of general timing ability (Zelaznik et al., 2000). Interestingly, patients with lesions of the cerebellum had impaired performance on explicitly timed movement, but no change was observed in the temporal variability of continuous movements. As the cerebellum is implicated in both explicit timing and the coordinative dynamics of compensating for multi-joint interaction forces, the absence of a correlated timing impairment between the two tasks was surprising. Evidence suggests that the timekeeping processes involved in explicit timing tasks are separate than those contributing to the temporal consistency in tasks that do not have salient pacing goals. Presumably, different control strategies are engaged in accordance with task goals and constraints (Ivry et al., 2002).

In regards to furthering our study, more investigations are needed to explain the inter-subject variability in behavioural responses during Experiment 1, as well as the slight changes in autocorrelation between saccade and smooth-pursuit synchronized conditions in Experiment 2. In expansion of the Experiment 1 protocol, modified paradigms that may provide intriguing new data could look into trials comprised of hundreds of switches between saccades and pursuit. This would allow researchers to look for consistent patterns in the autocorrelation of response latencies for a short period following the switch. Such data could have the potential to provide a more detailed understanding as to how the timing system reacts after a change in effector pathway. Specifically, such a design may be able to tease out the nature of self-organizing properties within the timing system. It is possible that effects of the motor system on timing functions do exist, but were masked by other factors in our experiments. By examining a much larger number of trials, it may be possible to average multiple data sets and draw further conclusions relating to subtle interactions.

In addition to monitoring the effects of switching motor pathways mid-trial, other paradigms may find interest in examining the coupling properties between two effectors. Combined eye movement and finger tapping experiments could lead to a better understanding of the interactions between motor and timing systems. This could be accomplished with perturbations to one motor system, and analyzing the following responses made with both effectors. A likely source of perturbation would be TMS, as it allows specifically targeted interference to finger related motor areas, eye related motor areas, or even the cerebellum, which may be implicated in both motor pathways and timing functions. Similar usage of TMS perturbation could be incorporated into synchronization/continuation tasks, furthering the results of Experiment 2. It would be particularly interesting to investigate the long-term correlation structure within series of responses following stimulation of the cerebellum. Such a task has implications in further understanding the role of the cerebellum in timing error correction. This type of design could also be used as a new perspective on investigating the self-organized characteristics used by the timing system to recover from a perturbation.

Overall, the results of both experiments in the current study provide interesting data that furthers research in the timing field. We have examined some important aspects of timing tasks that were previously unknown, and provided some new understandings for future research to build upon. In closing, we provide evidence in two paradigms that timing can indeed be transferred between motor execution pathways with great accuracy. Collectively, our results indicate that a globally represented source of timing is likely to exist.

Chapter 6 - References

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Chapter 7 – Appendix

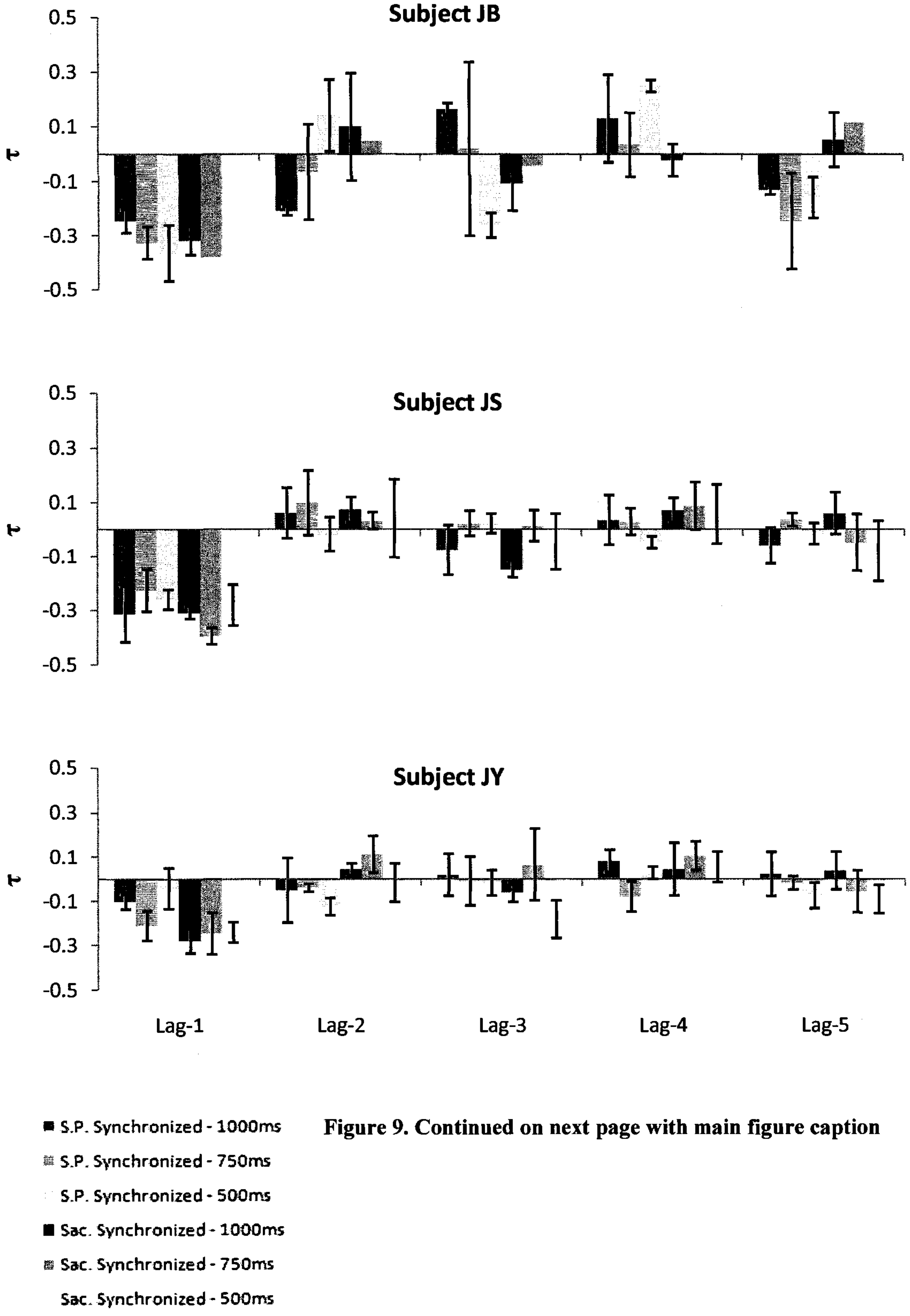

Figure 9. Continued on next page with main figure caption

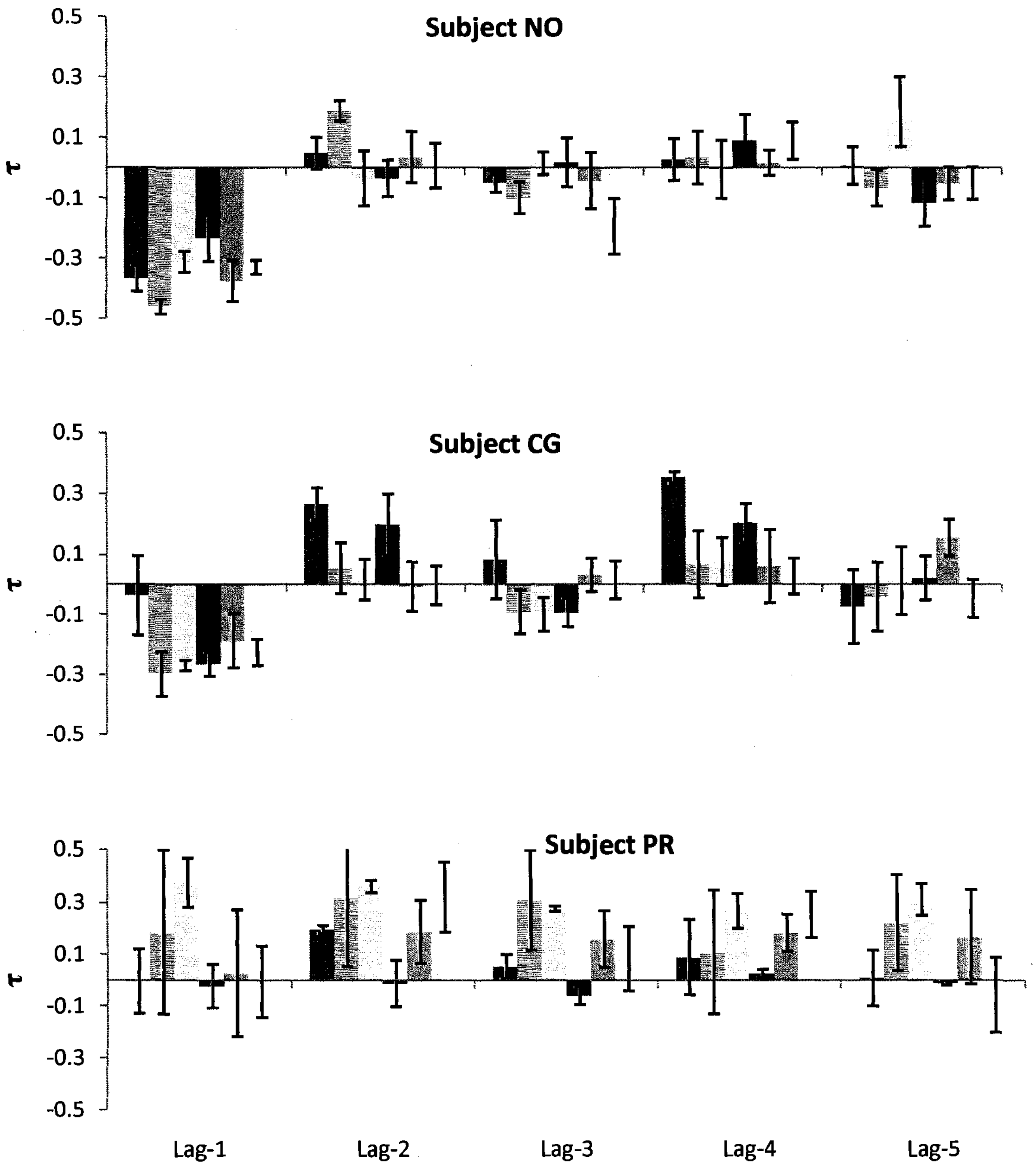

Figure 9 continued. Autocorrelation function from lag-1 to lag-5 for individual subjects. Error bars represent the standard error of the mean for each subject's separate trial runs in from each block of trials.