

Chapter I

STRATEGIES TO GET CLEAR VISION OF MOVING OBJECTS

In order to get clear vision of an object of interest moving across the visual field, the projection of this object onto the retina must be stabilized on the fovea, which is the region of the retina with the highest visual acuity. Therefore, in everyday life, humans orient their visual axis to targets of interest. While scanning their environment, humans perform multiple saccades (rapid eye movements that correct for a position error between eye and target) to align their visual axis with objects of interest. Humans are also able to track objects that move in their environment by means of smooth pursuit eye movements (slow eye movements that stabilize the projection of the moving target onto the fovea and correct for any velocity error between eye and target, i.e. for any retinal slip).

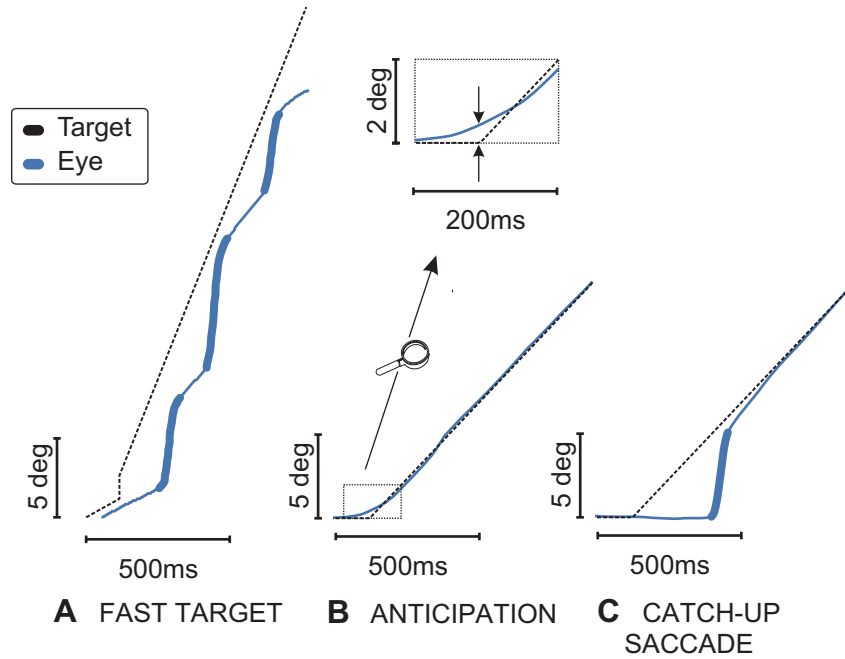


Figure I-1: Oculomotor strategies in visual tracking. For each panel, eye and target position are represented versus time. **A:** The eye velocity saturates and cannot match target velocity. Therefore, catch-up saccades are triggered (thick traces). Target velocity is 50 deg/s. **B:** The oculomotor system predicts the time of target motion onset and the eyes begin to move before the target does. The inset provides a zoom around target motion onset. The arrows highlight the advance in position of the eye with respect to the target at its onset. **C:** A catch-up saccade (thick blue trace) is executed to suppress the position error around 200ms after target motion onset. For B and C, target velocity is 18 deg/s.

The appearance of a moving stimulus in the environment elicits smooth pursuit eye movements with a latency of around 100ms. Accordingly, the smooth pursuit system accounts for a change in the trajectory of a moving target with a similar delay. This delay is largely due to the early processing of visual inputs by the visual system and cannot be eliminated. Because of this inherent delay, large position errors arise during the visual tracking of a stimulus that changes its trajectory abruptly. Moreover, the maximum smooth eye velocity and acceleration that can be achieved is limited, i.e. the change in smooth

eye velocity is not instantaneous. Consequently, smooth eye movements cannot reach large velocities in a short period of time and cannot track very fast targets (Fig. I.1.A), which results in an accumulation of position error. Due to these limitations, the oculomotor system needs to develop strategies to avoid the build up of position error during tracking of a moving target. To do so, the oculomotor system uses prediction to try and anticipate the future target trajectory during smooth pursuit eye movements (Fig. I.1.B; Dallos & Jones, 1963; Bahill & McDonald, 1983b; Barnes & Asselman, 1991). However, this strategy is limited to conditions where target trajectory is predictable. In particular, it fails in all conditions where the target undergoes unpredictable changes in trajectory, as they cannot be anticipated by the subject. For instance, most people probably experienced how difficult it is to track and catch a mosquito on-the-fly. Indeed, even though its velocity is low, the flight trajectory of a mosquito is very unpredictable. Thus, it is a very good example of a very frustrating condition (especially in the middle of a short night) of a task that seems quite easy due to the small velocity of the target but turns out to be very difficult because predictive mechanisms cannot be used. In sum, the smooth pursuit system cannot manage unpredictable or very fast moving targets on its own (Fig. I.1.A and I.C).

Therefore, primates do combine pursuit and saccades in visual tracking of unpredictable moving targets to avoid large position error and the eye lagging behind the target (Fig. I.1.C). The execution of a saccade helps to catch up with the target quickly (hence their name:

catch-up saccades). In contrast with saccades towards stationary targets that only take the position error into account, catch-up saccades also need to consider the relative motion of the eye with respect to the object of interest to be accurate (de Brouwer *et al.*, 2001). Besides, saccades deteriorate vision during their execution, i.e. large changes in the visual world occurring during saccades are not detected (Bridgeman *et al.*, 1975). Thus, the oculomotor system faces a trade-off between short epochs of poor vision (due to catch-up saccades) and poor tracking (eye lagging behind the target).

In sum, the smooth pursuit system needs to collaborate with the saccadic system in order to improve tracking of a target that moves in an unpredictable way. The collaboration starts at the level of the visual inputs (position and velocity errors) that must be shared between both systems and at the level of the decision, i.e. whether an error must be corrected by the smooth pursuit system on its own or by a catch-up saccade. The two inputs are mediated by different brain pathways that were primarily attributed to only one of the oculomotor subsystems (position pathway to saccades and motion pathway to smooth pursuit). However, as I have emphasized in this introduction, saccadic and smooth pursuit systems work hand in hand to optimize visual tracking of moving targets. In this first part of this chapter, I will first describe the contribution of the motion and position pathways to both saccadic and smooth pursuit eye movements. I will then introduce the synergies developed by the brain to track moving targets in a very efficient way. Finally, I will present the neural substrate underlying the interaction between saccades and pursuit. In

the second part of the chapter, I will review the main characteristics of the prediction mechanisms. Finally, I will sketch a model to account for the observed behaviours.

Saccades and Pursuit: Two Outcomes of a Single Sensorimotor Process

BOTH POSITION AND MOTION PATHWAYS CONTRIBUTE TO SACCADDES AND PURSUIT

CONTRIBUTION FROM THE POSITION PATHWAY TO THE SACCADIC SYSTEM

Saccades typically respond to a sudden step of the target and correct for the position mismatch between the visual axis and the object of interest (see Leigh & Kennard, 2004 for a review). Saccades are fast eye movements (up to 1000deg/s) and their duration is very short (30-80ms). Their peak velocity, duration and amplitude show consistent relationships (the main sequence, Bahill *et al.*, 1975). This relationship issues from a speed-accuracy trade-off as predicted by optimal control theory, i.e. increasing the peak velocity of the saccade increases the noise of the motor command and reduces the saccadic accuracy (Harris & Wolpert, 1998, 2006). On average, saccades undershoot stationary targets and only account for ~90% of the distance between the eye and the target (Becker, 1991). As their duration is very short, saccades cannot be controlled by continuous visual feedback, which is characterized by a delay of around 100ms, but instead by an internal feedback loop based on an efference copy of

the motor command sent to the motoneurons (see Bridgeman, 1995 for a review).

Saccades have a typical latency of around 200ms. This latency can be dramatically reduced if the target is presented repeatedly. For instance, if two targets are presented alternately with a fixed pacing frequency, saccades can occur before the next target appears (Ross & Ross, 1987). This predictive behaviour appears for a certain range of pacing frequencies (around 1Hz) but not at lower frequencies (around 0.25Hz). Interestingly, there exists an abrupt transition between reactive and predictive saccades. This transition is located at different frequency depending if you go from reactive to predictive or from predictive to reactive saccades (hysteresis phenomena, Shelhamer & Joiner, 2003).

The distribution of the latency of reactive saccades is known to follow a recinormal distribution (inverse Gaussian distribution, Carpenter & Williams, 1995). This distribution can be explain by a linear rise to threshold model (LATER model, Carpenter & Williams, 1995), i.e. the decision to trigger a saccade is taken as soon as a decision signal, starting from an initial level, reaches a particular decision threshold. The rate of rise of the decision signal is not fixed but follows a Gaussian distribution, which explains the recinormal distribution of the saccade latency (Carpenter & Williams, 1995). This model can also account for the speed-accuracy tradeoff, i.e. the larger the saccadic reaction time, the more accurate the saccade (Reddi & Carpenter, 2000; Reddi *et al.*, 2003), for the effect of Parkinson

disease on saccadic latencies (Michell *et al.*, 2006) and reaction times in a saccade countermanding task (Asrress & Carpenter, 2001).

From the visual input to the motor command generating the saccade, the position signal undergoes a sensorimotor transformation that consists in mapping the position error vector to a motor command, which is then sent to the extra-ocular muscles. This sensorimotor transformation, which underlies the generation of the saccades, is subserved by a cortical network (Leigh & Zee, 2006) consisting of the saccadic part of the frontal eye fields (FEF), the supplementary eye fields (SEF) and the lateral intraparietal area (LIP). The cortical eye fields project to the brainstem, to the superior colliculus (SC), either directly or through the basal ganglia, and to pontine nuclei which relay the information to the saccadic region of the cerebellum (dorsal vermis and fastigial nucleus). The SC, which contains a retinotopic map of the visual field, codes the position error signal. Both the cerebellum and the SC project to the premotor circuit located in the brainstem that sends the command to the ocular motoneurons (see Keller & Missal, 2003 for a model of the premotor circuitry; see Ramat *et al.*, 2007 for an overview of the brainstem circuitry).

The motor command sent to the extra-ocular muscles can be roughly divided into two parts: a pulse (phasic component) and a step (tonic component). The pulse corresponds to the torque needed to overcome the viscous forces of the orbital tissue so that the eye will quickly move. The step is the torque required to maintain the eye steady after the saccade and to counteract tissue elasticity that tends to

return the eye to central position. Therefore, the step must be computed (or integrated) from the pulse as there is a specific relationship between the pulse and the step in order to prevent the eye from drifting toward primary position after saccades. If this relationship is broken because of disease or maldevelopment, the eye drifts after saccades (Kapoula *et al.*, 1986; Kapoula *et al.*, 1997; Yuksel *et al.*, 2005).

CONTRIBUTION FROM THE POSITION PATHWAY TO THE SMOOTH PURSUIT SYSTEM

Because the retinal position of the target influences the eye acceleration just after pursuit onset (Pola & Wyatt, 1980; Lisberger & Westbrook, 1985), several experiments were designed to assess the contribution of the position pathway to the smooth pursuit system in primates. For example, a sudden jump of the target during motion elicits a change of the smooth eye velocity to correct for position error (Carl & Gellman, 1987; Segraves & Goldberg, 1994). Moreover, the stabilization of the target onto the retina with a small offset with respect to the fovea elicits smooth pursuit eye movements that aim to correct for the artificially created position error (Wyatt & Pola, 1981; Lisberger *et al.*, 1987; Morris & Lisberger, 1987; Barnes *et al.*, 1995). However, these experiments have been largely ignored for years, partly because they could only bring indirect evidence of a position input to the smooth pursuit system and could be influenced by concurrent retinal slip. In contrast, experiments in the cat shed light on how the position pathway influences smooth pursuit and which brain structures mediate this influence.

Saccades in cats are rather inaccurate in comparison with saccades in primates and are characterized by a much lower and variable gain. Therefore, when cats orient their visual axis towards an eccentric target, they usually perform multiple saccades interleaved with slow eye movements towards the target (Missal *et al.*, 1993). These slow eye movements were the first evidence in the cat of a contribution of the position pathway to the smooth pursuit system, which was consistent with modelling studies (Lefevre & Galiana, 1992; Lefevre *et al.*, 1994). In addition, stimulation in the SC, which is part of the position pathway, evokes smooth eye movements in the cat (Missal *et al.*, 1996; Missal *et al.*, 2002a).

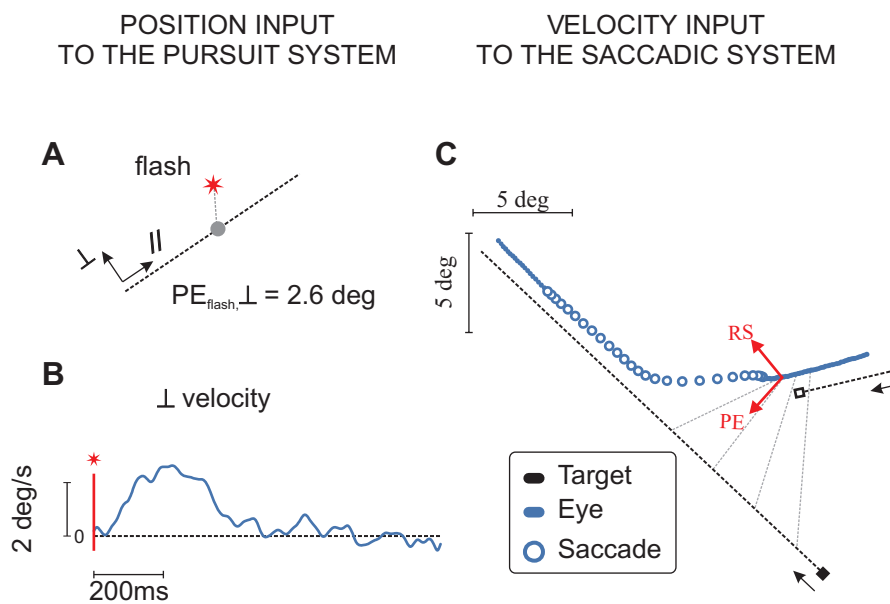


Figure I-2: Position input to the smooth pursuit system. A: Schematic representation of the paradigm: the target follows a linear path and a second target (red star) is flashed during ongoing smooth pursuit. The position of the moving target at the time of the flash is represented by the grey disk. For the illustrated trial, the target velocity is 27 deg/s along the // axis. The target is flashed for 10ms at 2.6 deg perpendicularly to the target path (along the $\perp$ axis). B: Representation of the eye velocity perpendicular to the target

trajectory ($\perp$ axis) versus time. Eye velocity perpendicular to the target path increased after the apparition of the flash (red vertical line). Velocity input to the saccadic system. C: A curved saccade (blue circles) occurring after both position and velocity steps of the target (black dashed lines) is presented in two dimensions. Target positions just before and after the target step are represented by the open and closed squares respectively. Before and after the saccade, smooth pursuit eye movements (solid blue lines) are present to track the target. The grey dotted lines represent isochronic lines that connect eye and target at the same moment in time. Red arrows give the position error (PE) and retinal slip (RS) orientation before the saccade. The saccade is elicited with an initial orientation close to the orientation of PE and final orientation close to the orientation of RS.

Finally, as a proof of a direct position input to the smooth pursuit system in primates, smooth eye movements were elicited towards a target that was briefly flashed (10ms duration) aside the path of an ongoing moving target that is being tracked (left panel of Fig. I.2, Blohm *et al.*, 2005a). Importantly, this only occurs when the flash is a relevant target (the flashed object has to be foveate) and not if it is a distractor (the flashed object has to be ignored). In addition, the smooth eye velocity elicited by such a flash is modulated by the amplitude of the position error, i.e. the larger the distance between the flash and the eye, the larger the smooth response heading toward the flash. Finally, the elicited response was not due to apparent motion of the flashed target because the duration of the flash was too short (only 10ms).

In sum, the position pathway contributes both to the saccadic and the smooth pursuit system. This contribution is preponderant in the case of the saccadic system and is less prevalent in the case of the smooth pursuit system as position error is generally not sufficient to elicit robust smooth pursuit eye movements.

CONTRIBUTION FROM THE MOTION PATHWAY TO THE SMOOTH PURSUIT SYSTEM

The motion pathway contributes to the execution of smooth pursuit eye movements in order to stabilize the visual axis on the object of interest (see Thier & Ilg, 2005 for review). The smooth pursuit eye movements are elicited by retinal slip (or velocity error) but are also modulated by position (see previous section) and acceleration errors (Krauzlis & Lisberger, 1994). They cannot be performed at will but require the percept of a moving visual stimulus (Steinbach, 1976; Braun *et al.*, 2006). Classically, the smooth pursuit system is presented as a closed loop system with a negative feedback of the eye velocity (Robinson *et al.*, 1986). During the first 100ms of pursuit, the smooth eye movements are considered as open-loop, before visual feedback closes the loop (Lisberger *et al.*, 1987). Moreover, an online gain mechanism regulates the smooth pursuit system (Churchland & Lisberger, 2002). This gain is set to zero during fixation and to around one during visually-guided pursuit. It is regulated by the pursuit region of the FEF (Tanaka & Lisberger, 2001).

Smooth pursuit eye movements are subserved by a cortical network involving the medial temporal area (MT), the middle superior temporal area (MST) and the pursuit subregion of the FEF (Leigh & Zee, 2006). These regions project to the pontine nuclei that relay the information to the cerebellar cortex (dorsal vermis, flocculus and paraflocculus). The cerebellar nuclei (fastigial and medial vestibular) receive inputs from the cerebellar cortex and transmit the information

to the ocular motoneurons. It is worth to stress the importance of MT within this network (Born & Bradley, 2005). Indeed, MT codes both the velocity (Priebe *et al.*, 2001; Priebe & Lisberger, 2004) and the acceleration (Lisberger & Movshon, 1999; Price *et al.*, 2005) of the target. Stimulation of MT disrupts target motion perception (Komatsu & Wurtz, 1989) but motion perception has been reported in the absence of MT activity (Ilg & Churan, 2004). Moreover, lesions of MT abolish smooth pursuit eye movements (Dursteler & Wurtz, 1988). In sum, MT processes motion signals and feeds the network with them.

CONTRIBUTION FROM THE MOTION PATHWAY TO CATCH-UP SACCADDES

As I emphasized in the introduction, catch-up saccades are necessary to overcome the limitations of the smooth pursuit system. They superimpose their response to the smooth pursuit response (de Brouwer *et al.*, 2002a) and greatly improve the tracking of a target that moves unpredictably. Cats particularly need these catch-up saccades because their smooth pursuit gain is low and more variable than in humans (Missal *et al.*, 1995; de Brouwer *et al.*, 2001).

Catch-up saccades do differ from saccades towards stationary targets, as their main sequence is different (de Brouwer *et al.*, 2002a). Their amplitude is not related to the position error only (Keller & Johnsen, 1990; Gellman & Carl, 1991; Kim *et al.*, 1997) because if it were the case, saccades directed towards a moving target would always fall short. Therefore, the motion of the target must be taken into account in the programming of saccade amplitude. Catch-up

saccade amplitude is programmed using both the position error and the retinal slip, i.e. the amplitude of catch-up saccades is the sum of a term related to the position error plus a term related to the prediction of the relative motion of the eye with respect to the target (de Brouwer *et al.*, 2001). The existence of these two separate components is confirmed by their different neural substrate. The term related to the position error is coded in the SC that lays in the position pathway (Keller *et al.*, 1996b). In contrast, the term related to the velocity error originates from the motion pathway. Indeed, when MT is lesioned, saccades made to stationary targets are normal (position pathway is intact) but catch-up saccades are not (motion pathway is disrupted, Newsome *et al.*, 1985; May *et al.*, 1988).

The outputs of these two pathways are not synchronized: the position error influences the saccade first. This asynchrony can yield curved catch-up saccades where the initial orientation of the saccade is correlated with the orientation of the position error and the final orientation of the saccade is correlated with the velocity error orientation (right panel of Fig. I.2, Schreiber *et al.*, 2006). Similarly, in one dimension, the asynchrony implies that the motion pathway mainly influences the deceleration phase of the catch-up saccades, not their acceleration phase (Guan *et al.*, 2005). As a result, the velocity profiles of catch-up saccades are more skewed and variable than the profiles of saccades made to stationary targets.

IMPORTANCE OF STUDYING VISUAL TRACKING ACROSS DIFFERENT SPECIES

A historical perspective on the progress made in the last decade on the interaction between saccades and pursuit clearly demonstrates the critical importance of studying similar tasks across species. In particular, the apparent limitations of the oculomotor system in the cat (limited oculomotor range, undershooting saccades and saturation of smooth pursuit velocity) turned out to be a critical feature in our understanding of the interactions between saccades and pursuit. Indeed, when the performance of a system is less efficient, as it is the case in the cat compared to the monkey, the synergy between the different subsystems becomes vital. This explains why the observation of the influence of position error on smooth pursuit (Missal *et al.*, 1993; Lefevre *et al.*, 1994; Missal *et al.*, 1996) and velocity error on catch-up saccades (de Brouwer *et al.*, 2001) is more obvious in cats. Thus, their investigation in the cat was a critical step to design experiments addressing the same questions in primates.

SYNERGIES

The saccadic and smooth pursuit systems share the same inputs, i.e. the position and motion inputs. In this section, I will review how these inputs are combined in order to align the visual axis with the target for both types of eye movements.

TRIGGER MECHANISM OF CATCH-UP SACCADDES

In the introduction, I have shown that the smooth pursuit system needs help from the saccadic system to track accurately a moving target. Indeed, when a target starts moving, position error is

accumulating because of the latency of smooth pursuit eye movements (Fig. I.1.C). Therefore, the oculomotor system generates a saccade to compensate for this position error. Similarly, the smooth pursuit system fails to increase the eye velocity to match the velocity of very fast moving targets (Fig. I.1.A). In this case, catch-up saccades are triggered to compensate for the accumulation of position error due to the retinal slip. In sum, both position error and retinal slip can elicit catch-up saccades during smooth pursuit eye movements.

The combination of position error and retinal slip can also prevent the execution of catch-up saccades because the oculomotor system anticipates that the future target motion will decrease the current position error. For example, if the target steps in one direction (say leftward) before moving in the other direction (say rightward), the oculomotor system predicts that the rightward target motion will reduce the leftward position error (this typical motion of the target is called the Rashbass paradigm). Therefore, the probability of observing a catch-up saccade can be very low if the size of the step is adapted to the target velocity (Rashbass, 1961). The probability of occurrence of a catch-up saccade is minimized when the target crosses its initial position 200ms after the step (Carl & Gellman, 1987). In contrast, when a target begins to move abruptly, the probability of observing a saccade is very high (Fig. I.1.C). This example shows that when the brain predicts that the target trajectory will cross the eye position in a near future, no catch-up saccade is triggered because target motion per se will reduce the position error. In sum, triggering a saccade depends

on the relative motion of the eye with respect to the target and is therefore related to the prediction of the future position of the target.

During foveal pursuit, the relative motion of the eye with respect to the target can be quantified by a parameter, the eye-crossing-time, which corresponds to the time-to-contact between eye (visual axis) and target (de Brouwer *et al.*, 2002b). The eye-crossing-time is the time that the eye would need to catch the target on the basis of the extrapolation of its current motion (Fig. I.3.A). It is computed by dividing the opposite of the position error between eye and target by the relative velocity of the eye with respect to the target (retinal slip). When the eye-crossing time is outside the smooth zone (< 40ms or > 180ms), the decision to trigger a catch-up saccade is taken and a saccade is executed around 125ms later (Fig. I.3.B and C). However, as long as the eye-crossing-time remains within the smooth zone, the smooth pursuit system can correct for the error by modulating the smooth eye velocity (Fig. I.3.D).

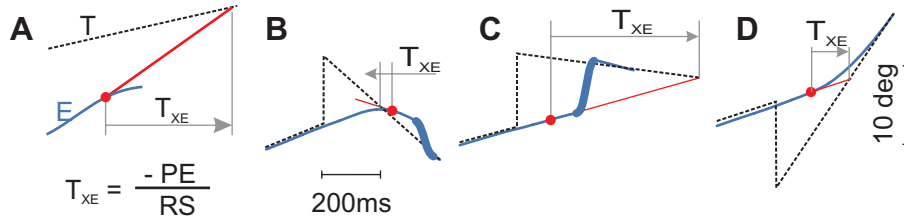


Figure I-3: Trigger mechanism. A: Illustration of the eye-crossing-time parameter which corresponds to the time that the eye trajectory would need to cross the target at constant velocity (position vs. time representation with T: target; E: eye; PE: position error; RS: retinal slip; T_{xe}: eye-crossing-time). To evaluate the eye-crossing-time at a certain instant in time (red dot), I compute the tangent (red line) to the eye trace (blue line representing smooth pursuit eye movements). The distance from the defined instant in time and the intersection between target and tangent yields the eye crossing time. B, C, D: Representation of eye and target position vs. time for three different trials that illustrate the trigger mechanism of the catch-up saccade (thicker traces). About

100ms (red dots) before the saccade, I have represented the eye-crossing-time parameter following the definition of panel A. In trials B and C, the eye-crossing-time is outside the smooth zone (B: <40ms and C: >180ms). For trial D, there is no saccade because the eye-crossing-time remains within the smooth zone.

In sum, during ongoing tracking of a moving target, the oculomotor system tries to optimize the visual feedback of the object of interest by using both the saccadic and the smooth pursuit system in synergy. Somehow, it could be hypothesized that the brain tries to minimize the cost of foveating the target, which is a combination of sensory costs. Indeed, executing a saccade alters vision (cost related to saccade execution) whereas holding a saccade increases the cost related to poor vision (cost related to misalignment between the eye and the target). Within this context, saccade triggering can be interpreted as an optimal control problem, similar to the ones solved by the brain in the control of our actions (Harris & Wolpert, 1998; Todorov & Jordan, 2002; Todorov, 2004; Harris & Wolpert, 2006). In this particular case, the outcome of this optimal control problem would consist in inhibiting saccades only for a specific range of eye-crossing-times.

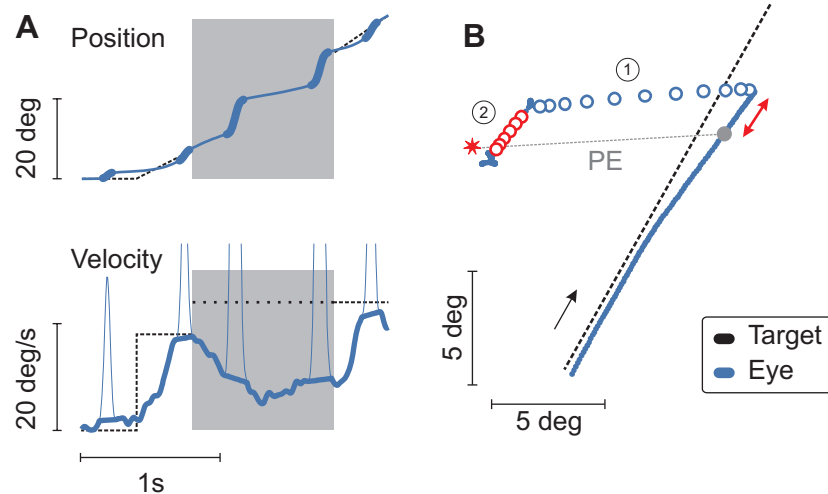


Figure I-4: Extraretinal interactions. A: Illustration of the compensation for a decrease in the smooth eye velocity by the saccadic system during the occlusion of a pursuit target. The upper panel represents position vs. time while the lower panel gives the velocity vs. time. During the occlusion (grey areas), the smooth eye velocity tends to decrease (thick trace on velocity panel). To compensate for this decrease, saccades are generated during the occlusion (thick traces on the position panel). The collaboration between saccades and pursuit yields a small position error at target reappearance (at the right of the grey area on the upper panel). B: Representation of how the saccadic system can integrate the smooth eye velocity to account for the smooth eye displacement while localizing a stationary target (same paradigm as in Fig. I.2: position input to the smooth pursuit system). During ongoing pursuit (blue solid line for the eye and dashed black line for the target), a second target is flashed (red star). The position of the eye at the time of the flash is represented by the grey disk. A first saccade (blue circles) is triggered with a short latency toward the flashed target and the saccade vector matches the position error at the instant of the flash (grey dashed line). Subsequently, a second saccade (red circles) is triggered and accounts for the smooth eye displacement (SED, red arrow) following the flash.

EXTRARETINAL INTERACTIONS

The trigger mechanism of catch-up saccades is based on sensory inputs coming from the position and motion pathways. However, in some cases, the saccadic and smooth pursuit systems can cooperate despite the absence of retinal signals. In this case, internal models and efference copies provide the oculomotor system with an estimation of the position and velocity signals.

For instance, when an ongoing pursuit target is temporarily occluded (Fig. I.4.A), the decrease in the smooth pursuit response is compensated by the release of one or several saccades during the occlusion in order to maintain the performance of the oculomotor system (Mitrani & Dimitrov, 1978; Becker & Fuchs, 1985; Masson & Stone, 2002; Bennett & Barnes, 2003; Churchland *et al.*, 2003; Madelain & Krauzlis, 2003; Bennett *et al.*, 2007). Interestingly, these saccades are scaled to the reduction in smooth eye velocity, demonstrating that efference copies provide information about ongoing smooth pursuit response to the saccadic system (Orban de Xivry *et al.*, 2006). In addition, when a target is flashed either during anticipation of a pursuit target (Blohm *et al.*, 2003a) or during ongoing pursuit of a moving target (Blohm *et al.*, 2005b), the oculomotor system is able to direct the visual axis towards the flashed target position (Fig. I.4.B). When the saccadic reaction time is too short ($<175\text{ms}$), the oculomotor system does not have sufficient time to compensate for ongoing smooth eye displacement and saccades are parallel to the retinal position error (McKenzie & Lisberger, 1986; Blohm *et al.*, 2005b). In contrast, saccades that are initiated with longer reaction time ($>175\text{ms}$) compensate for the ongoing smooth eye displacement (Blohm *et al.*, 2005b). Localization of the flashed target is accurate even though it has been reported that the so-called flash-lag effect (Nijhawan, 1994) can alter the memorized position of the flash (Blohm *et al.*, 2003b). Again, to orient to the remembered target position, the saccadic system must have access to an efference copy of the ongoing smooth eye movement and integrate it to

compensate for the smooth eye displacement (Blohm *et al.*, 2006). Interestingly, the extra-retinal information related to the relative motion of the eye with respect to the target is not available at very short latency but takes some time to be reconstructed. A direct consequence of this dynamical process is that the longer the reaction time the more accurate the eye movement. These experiments emphasize that the oculomotor system can increase its performance by cooperation between its two subsystems on the basis of extraretinal signals.

INITIATION

Before executing an eye movement, the oculomotor system must first detect the target within the environment and program the motor command that will be sent to the ocular motoneurons. These two steps take some time and impose a delay (latency) between the appearance of the target and the execution of the eye movement. Interestingly, saccades and pursuit do not have the same latency (100ms for pursuit and 200ms for saccades) but their latency vary in a similar way with the paradigm being used. For instance, the latency of both types of eye movements decreases when the fixation point is extinguished a few hundreds of milliseconds before the target appears (gap effect; for saccades : Fischer & Boch, 1983; Merrison & Carpenter, 1995; for pursuit : Knox, 1996) by the same amount (around 50ms, Krauzlis & Miles, 1996a, b). Neuronal correlates of the gap effect have been found in SC where the buildup activity that occurs before eye movements increases during the gap whatever the type of eye movement that will follow (Krauzlis, 2003). Similarly, the

latency of saccades and pursuit increases in the presence of a distractor (Krauzlis *et al.*, 1999). Although the latency of saccades and pursuit are quite different in response to the sudden appearance of a stimulus, they become comparable and highly correlated when the target appears before the disappearance of the fixation point (overlap paradigm, Erkelens, 2006). Finally, both pursuit and saccades exhibit a similar dependence on movement preparation time, i.e. their latency exhibits a similar sharp transition between the reactive and predictive responses (Joiner & Shelhamer, 2006).

Thus, the paradigm being used has similar influence on the latency of saccades and pursuit. This suggests the existence of a common decision process to generate both types of eye movements. This process should account for the gap and overlap effects but also for the saccade latency variability that follows a recinormal (inverse Gaussian) distribution. For saccades, as stated earlier, a linear rise to threshold model was proposed to account for the features of the saccadic latency (LATER model, Carpenter & Williams, 1995). Recently, evidence showed that the decision signal is common to both saccades and pursuit but the decision thresholds are not, the saccadic threshold being higher than the pursuit threshold (Krauzlis *et al.*, 1999; Krauzlis & Dill, 2002). The LATER model can account for the gap effect if it is assumed that the gap increases the initial level of the decision signal. Therefore, the time to reach the thresholds is decreased by the same amount for saccades and pursuit. This model nicely mirrors observed behavior but it relies on the hypothesis that both saccades and pursuit initiation follow a LATER process.

However, until now, it has never been reported that a LATER process underlies the generation of smooth pursuit eye movements, though a common initiation process has been evidenced.

TARGET SELECTION

Initiation of an eye movement occurs after the presentation of an object toward which the gaze needs to be oriented. However, when multiple targets are presented simultaneously, the target of interest must first be selected before an eye movement can be initiated. As the initiation mechanism is shared between saccades and pursuit, I expect a single target selection mechanism to subserve both saccades and pursuit.

When two stimuli (one target and one distractor) moving in opposite directions are presented, smooth pursuit and saccades tend to select the same target, even if they choose the distractor (Krauzlis *et al.*, 1999). Because of the difference in latency between saccades and pursuit, smooth pursuit eye movements are initiated first toward the selected target. On some occasions, when the smooth pursuit system selects the wrong target, a correction can occur on line in such a way that, at the time of the saccade, both pursuit and saccadic systems have selected the same target (Liston & Krauzlis, 2003). In this case, the saccade is delayed until corrective pursuit occurs. In sum, the state of the target selection mechanism is used early by the smooth pursuit system at the expense of the accuracy while the saccadic system waits longer to elicit a saccade directed to the target at the expense of the latency. So target selection takes place in the common preparatory stage and reflects a trade-off between speed and accuracy; the smooth

pursuit system favors the speed because it can be corrected online whereas the saccadic system favors the accuracy because a saccade cannot be corrected on-the-fly. Interestingly, it has also been demonstrated that the execution of a saccade has a strong influence on the high-level motion processes involved in motion perception in the vicinity of the selected target (Gardner & Lisberger, 2001; Schoppik & Lisberger, 2006; Wilmer & Nakayama, 2007).

These behavioral data suggest that both subsystems share the same decision signal (race model). The race model (Logan *et al.*, 1984; Osman *et al.*, 1986; Hanes & Schall, 1995; Hanes & Carpenter, 1999) consists of a decision signal that fluctuates between two thresholds, one for each stimulus. As soon as the decision signal reaches one of the two thresholds, an eye movement is made toward the corresponding target. However, the thresholds for the pursuit target selection and the saccade target selection are different, which means that overall, there are four thresholds for two potential targets: one for the pursuit and one for the saccade for each stimulus. The pursuit thresholds are lower than the saccade thresholds (Liston & Krauzlis, 2005), which can reflect the differences observed in the trade-off between speed and accuracy. The decision signal reaches a pursuit threshold faster but reaching the saccade threshold means that the system has accumulated more evidence (i.e. the confidence in the selection is higher).

The superior colliculus has a prevalent role in the common mechanism of target selection as its neuronal activity allows to predict target selection for both pursuit and saccades (Krauzlis & Dill, 2002).

Furthermore, the stimulation of neurons in SC biases the target selection process in favor of the contralateral target whatever the planned eye movement, which suggests a causal role of SC in the target selection process (Carello & Krauzlis, 2004). The observed bias is related to the location of the target, not to its direction, which can be linked to the primacy of spatial information on target selection for both oculomotor systems (Adler *et al.*, 2002) or to the involvement of SC in the position pathway. Regarding the hypothesized mechanism of target selection (common decision signal and different thresholds for pursuit and saccades), the stimulation of neurons in SC induces a bias of the initial level of the decision signal toward the contralateral target (Carello & Krauzlis, 2004). Hence, the duration needed to cross the pursuit and saccade thresholds is shorter (longer) for the contralateral stimulus (ipsilateral) in stimulated trials (Carello & Krauzlis, 2004). In sum, saccades and pursuit share a common target selection mechanism that is based on a race model. Neuronal correlates of this common mechanism can be found in the SC.

CANCELLATION OF AN EYE MOVEMENT

The sudden appearance of a novel object in the environment can require the inhibition of the planned action as circumstances that led to its planning have changed. Cancellation is often tested by the presentation of a stop-signal just before the initiation of the prepared saccade (Hanes & Schall, 1995; Hanes & Carpenter, 1999) or smooth pursuit eye movement. The success of the cancellation depends on the delay between the presentation of the stimulus and the stop-signal (Logan *et al.*, 1984). An eye movement can easily be cancelled if this

delay is close to zero. Accordingly, the longer the delay, the less successful is the stop-signal. Nevertheless, it takes an additional 20ms to cancel a saccade (75ms) in comparison with the cancellation of a smooth pursuit response (55ms) (Kornyló *et al.*, 2003). It has been suggested that this additional delay of 20ms is inherent to the existence of a period of 20ms before the saccade during which it cannot be aborted anymore. This observation is related to processes that precede saccade onset too closely to have an inhibitory influence (point of no return, Osman *et al.*, 1986). A similar period does not exist for smooth pursuit. In sum, saccades and pursuit share a common cancellation mechanism even though the minimum period to cancel a saccade or smooth eye movement differs due to the existence of a point of no return for saccades but not for smooth eye movements.

The neural substrate of the cancellation mechanism is likely located in the brainstem premotor circuit, which is known to generate and control saccades. Within this premotor circuit, omnipause neurons (OPNs) inhibit the release of saccades and pause during their execution (Ramat *et al.*, 2007). The existence of a common mechanism for eye movement cancellation is supported by the modulation of OPNs during both types of eye movements and the fact that their electrical stimulation interrupts saccades and reduces ongoing smooth eye velocity (Keller *et al.*, 1996a; Missal & Keller, 2002).

BRAIN AREAS SUBSERVING SACCADDES AND PURSUIT

Classically, neuroscientists considered that the position pathway fed the network subserving saccades whereas the motion pathway fed the smooth pursuit system with little if any interaction between the two systems and their sensory inputs. However, the recent behavioural evidence described in the previous sections contradicts this view and suggests that both pathways influence both oculomotor subsystems. Somehow, the experimental evidence of the integration of the position and motion signals has changed the view of the neuronal network subserving the oculomotor system from two segregated networks into intertwined ones (Fig. I.5).

The brain networks subserving the oculomotor system originate at the level of the retinal inputs. These inputs are then spread into two parallel cortical pathways, subserving mainly the saccadic or the smooth pursuit system. Within these pathways, the frontal and supplementary eye fields (FEF and SEF) contain a population of neurons with saccade-related activity and a separate population with pursuit-related activity (Tian & Lynch, 1996; Heinen & Liu, 1997; Rosano *et al.*, 2002). For the FEF, these two populations are located in different subregions. The LIP, which is interconnected with FEF and SEF, contains both saccade-related and pursuit-related neurons (Kurylo & Skavenski, 1991). In sum, the cortical networks subserving saccades and pursuit look similar, as confirmed by fMRI studies (Berman *et al.*, 1999), but are largely based on different areas and

neuronal populations. From the cortex, several descending pathways convey information and motor commands to the ocular motoneurons.

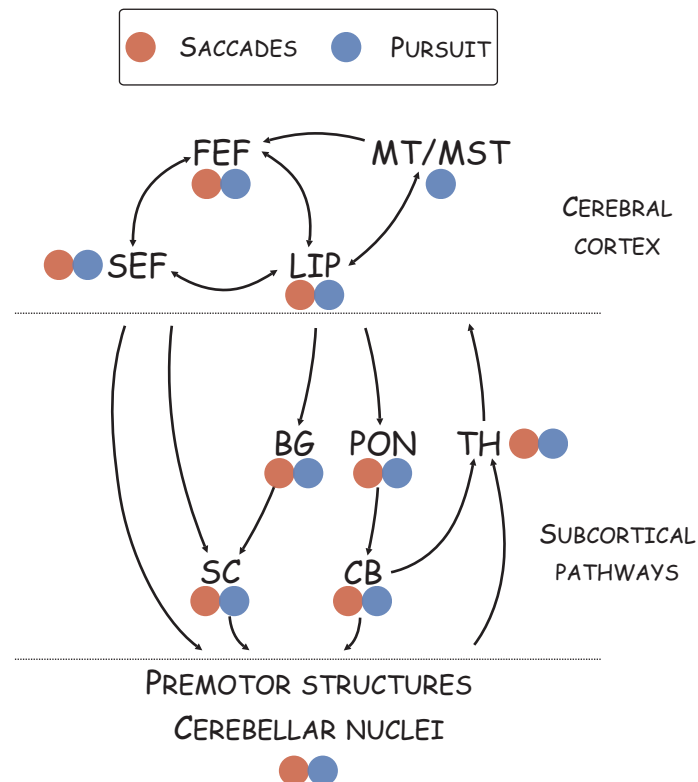


Figure I-5: Brain circuitry subserving saccades and pursuit. Colours were assigned to each brain area following its involvement in each motor pathway (saccade- or pursuit-related activity; red or blue disks). BG: basal ganglia; CB: cerebellum; FEF: frontal eye field; LIP: lateral intraparietal area; MST: medial superior temporal area; MT: middle temporal area; PON: pontine nuclei; SC: superior colliculus; SEF: supplementary eye field; TH: thalamus.

The cortico-ponto-cerebellar (cortex – dorsolateral pontine nuclei – flocculus, paraflocculus and vermis) pathway was traditionally considered as the descending pathway of the smooth pursuit system. However, some areas within this pathway also contain saccade-related activity. For instance, the cerebellar vermis is

involved in the control of both saccades and pursuit (Noda & Fujikado, 1987; Krauzlis & Miles, 1998; Takagi *et al.*, 1998, 2000). In addition, recent experiments demonstrated that pursuit-related neurons in the dorsal pontine nuclei are also saccade-related and sensitive to both position and velocity (Dicke *et al.*, 2004). Moreover, the dorsolateral pontine nuclei receive afferents from the SC (Harting, 1977), a key structure in the position pathway controlling saccades. Another descending pathway, which conveys signals from the cerebral cortex to the SC (either directly or via the basal ganglia), primarily subserves the saccadic network. However, the basal ganglia also contain pursuit-related neurons (Cui *et al.*, 2003; Basso *et al.*, 2005) and the SC provides a position signal to the smooth pursuit system (Basso *et al.*, 2000; Krauzlis, 2003). Moreover, there is evidence that the SC codes the motor goal whatever the type of eye movement and not only the classical motor map of saccade endpoints (Krauzlis *et al.*, 1997).

These pathways terminate either on cerebellar nuclei or on brainstem premotor circuits. These structures often contain saccade- and pursuit-related signals. For example, the fastigial oculomotor region (FOR), a cerebellar nucleus that receives the output of the vermis, does influence both pursuit and saccades. Neurons in FOR burst at the start of contraversive saccades and at the end of ipsiversive saccades and also show pursuit-related activity (Fuchs *et al.*, 1993, 1994). In the pathway between SC and the oculomotor nuclei, several premotor areas contain both saccade- and pursuit-related neural activity. For instance, some neurons in the nucleus of

the optic tract (NOT) fire during smooth pursuit and small saccades (Missal *et al.*, 2002b). Moreover, brainstem premotor nuclei, which generate the burst of activity necessary to elicit a saccade (reviewed in Ramat *et al.*, 2007), receive afferents from SC and from the saccadic and pursuit subregions of the FEF (Yan *et al.*, 2001). They also contain some classes of neurons that are modulated during both saccades and pursuit. Among them, the omnipause neurons, which are known to inhibit the release of saccades, are also modulated during smooth pursuit eye movements (Missal & Keller, 2002). Consistently, large brainstem lesions impair both saccades and smooth pursuit (Bogousslavsky & Meienberg, 1987). Similarly, other premotor areas that control horizontal and vertical gaze respond to both saccades and pursuit (Chubb & Fuchs, 1982; Missal *et al.*, 2000; Keller & Missal, 2003). From the cerebellar nuclei and the brainstem premotor circuits, the neural commands are conveyed to the oculomotor nuclei that innervate the extra-ocular muscles.

Finally, an ascending pathway that plays a central role in the feedback loop is included in both the saccadic and smooth pursuit systems. These feedback signals are mainly conveyed by the cerebellum and the thalamus, which has recently been shown to mediate saccadic and pursuit signals (Sommer & Wurtz, 2002; Sommer, 2003; Sommer & Wurtz, 2004a, b; Tanaka, 2005).

In sum, the brain networks subserving oculomotor functions do not resemble the classical view of separate networks for saccades and pursuit (Petit & Haxby, 1999). In accordance with recent

behavioural findings, the two brain networks rather seem intertwined (Krauzlis, 2004; 2005).

CONCLUSION

Classically, the oculomotor system was viewed as the juxtaposition of the saccadic and smooth pursuit systems. The experimental evidence of shared retinal inputs, common brain areas and synergies emphasizes that saccades and smooth pursuit are not subserved by distinct systems but are rather included in a more integrated system. Of course, in some cases, one or the other type of eye movement is better suited for the specified goal; hence saccades re-orient gaze to stationary targets and smooth eye movements are restricted to track moving targets. However, in many circumstances, there is evidence that the central nervous system takes advantage of the complementary characteristics of both types of eye movements in order to optimize visual information. Smooth and saccadic eye movements reflect different modes in the trade-off between speed and accuracy during initiation and target selection. The brain monitors the smooth pursuit response in order to generate saccades when necessary. The synergy between saccades and pursuit increases the oculomotor performance in different contexts (tracking, target localization, prediction, target selection) and allows humans to perform skilled motor acts (like smashing a mosquito in flight).

Collaboration between saccades and pursuit provides a good opportunity to investigate how the central nervous system combines different modes of motor control to achieve a common goal. Indeed, saccadic and smooth pursuit systems are clearly much more integrated

than has been classically proposed. This is compatible with the existence of a single controller that maximizes the performance of a common tracking goal, as has been reported recently in the fly (Boeddeker & Egelhaaf, 2005).

Predictive mechanisms in smooth pursuit

As stated earlier, the smooth pursuit system has an inherent delay of 100ms before reacting to the appearance of a moving target in the environment or to a change in the trajectory of the target being tracked. To overcome this delay or the bound of the smooth eye acceleration, the brain has developed strategies consisting in predicting future target motion and anticipating target motion onset.

Prediction and anticipation arise very early in the development from newborn to adult. A 5-month child can learn target dynamics (Rosander & von Hofsten, 2004). One month later, he can extrapolate the path of a moving target that is occluded (von Hofsten *et al.*, 1998; Jonsson & von Hofsten, 2003). At 12 months, children can predict the intended goal of people's action (Falck-Ytter *et al.*, 2006). The oculomotor system is able to use these predictions early. For instance, pursuit and saccades show signs of prediction in 6-month old children (Gredeback *et al.*, 2005) and are adult-like in 9-month children (Gredeback *et al.*, 2002).

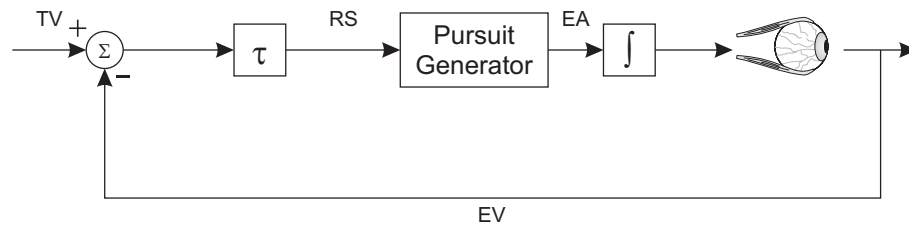


Figure I-6: Schematic representation of the smooth pursuit system. In this schema, the retinal slip (target velocity minus eye velocity, RS) drives the smooth pursuit system.

PERPETUATION OF THE SMOOTH PURSUIT RESPONSE

The smooth pursuit system is often described as a negative feedback control system, i.e. the difference between the output of the system (the eye velocity) and the reference (target velocity) is fed back into the system, which means that the velocity error (or retinal slip) drives the smooth pursuit system (Fig. I.6). Models that described the pursuit response to a target ramp must account for the acceleration saturation during pursuit initiation, for the ringing of eye velocity around target velocity and for perpetuation of eye movement when the target is electronically stabilized on the retina (Morris & Lisberger, 1987; van den Berg & Collewijn, 1987; Newsome *et al.*, 1988; Stone & Lisberger, 1990; Barnes *et al.*, 1995). Two classes of models account for these features: "internal feedback" models and "image motion" models.

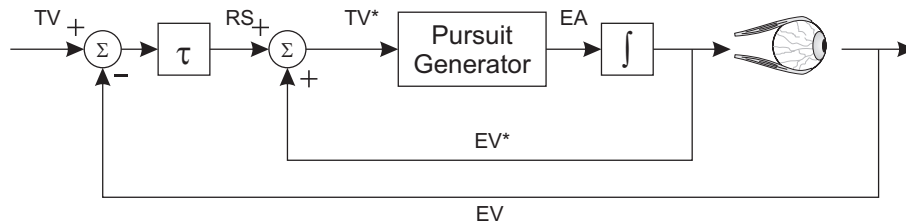


Figure I-7: Schematic representation of an internal feedback model. In this schema, an estimation of target velocity (TV^*) in world coordinates drives the smooth pursuit system. This estimation is obtained by the addition of the retinal slip (RS , target velocity minus eye velocity) and an efference copy of eye velocity (EV^*). The loop that conveys EV^* is the internal feedback loop. Adapted from Robinson et al. (1986)

Internal feedback models (Robinson *et al.*, 1986) state that target motion is reconstructed in world coordinates by adding current eye velocity and retinal slip (Fig. I.7). Other models emphasize that perceived object motion, rather than raw retinal object motion, drives the smooth pursuit response as it is evidenced by smooth pursuit response to partially occluded objects (Stone *et al.*, 2000) and to tilted lines (Masson & Stone, 2002). In the "internal feedback" models, current eye velocity is computed from a copy of the eye motor command (called efference copy or corollary discharge). In this case, the dynamics of pursuit is ascribed to the motor pathway and is mainly determined by the ways the different delays are allocated among the different branches. In the "image motion" models (Lisberger *et al.*, 1987; Krauzlis & Lisberger, 1994), visual inputs related to acceleration and velocity drive the smooth pursuit system (Fig. I.8). In this case, the dynamics of pursuit is determined by the processing of the visual inputs.

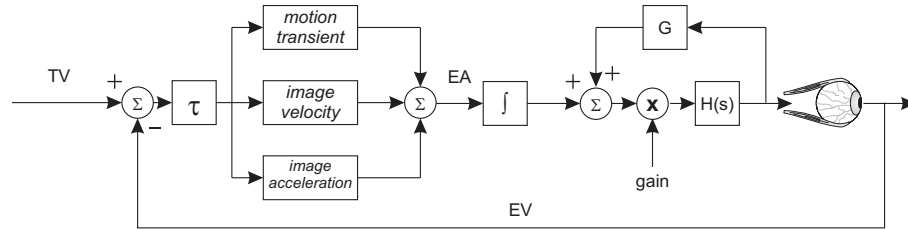


Figure I-8: An example of "image motion" models. In this model, the inputs are related to motion onset transient, image velocity and image acceleration. The hence obtained desired eye acceleration (EA) is integrated and then sent to the leaky integrator ($H(s)$). G is a positive gain that is part of the efferent positive feedback loop. Adapted from Krauzlis and Lisberger (1994)

An efference copy (or corollary discharge) loop is present in both categories of models. The presence of the efference copy loop is responsible for the perpetuation of pursuit when the target is electronically stabilized on the fovea (Morris & Lisberger, 1987; van den Berg & Collewijn, 1987; Newsome *et al.*, 1988; Stone & Lisberger, 1990; Barnes *et al.*, 1995).

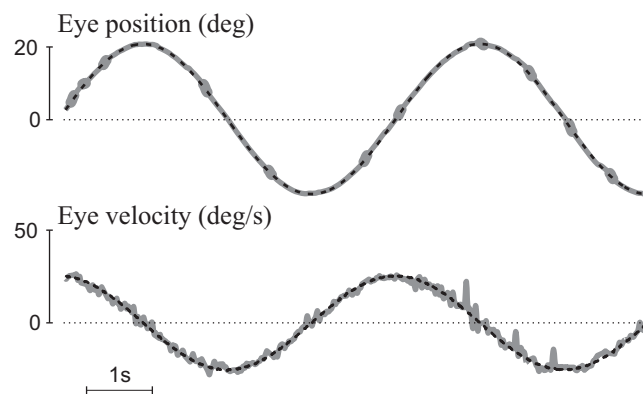


Figure I-9: Zero phase-lag pursuit of a predictable target. Both eye (grey) and target (dashed black) position and velocity are represented vs. time. On the position panel, thicker traces represent saccades.

ONLINE PREDICTION

The two previous categories of models does not account for the zero phase lag between eye and target observed during tracking of

a target moving sinusoidally (Dallos & Jones, 1963; Bahill & McDonald, 1983b) (Fig. I.9). In order to simulate this zero phase-lag pursuit, prediction of future target motion is required in order to overcome the delay in sensory processing (80ms). Online prediction can be based either on the extrapolation of upcoming target motion based on current target velocity (Fig. I.10) (Bahill & McDonald, 1983a; van den Berg, 1988; Deno *et al.*, 1995; Kettner *et al.*, 1997; Shibata *et al.*, 2005) or on a short-term velocity store (Fig. I.11) (Barnes *et al.*, 1987; Barnes & Asselman, 1991; Barnes, 1994). Memory charge require some repetitions of target motion in order to learn target dynamics (Dallos & Jones, 1963). A predictor extrapolates target motion on a short-term scale (around 100ms) as its goal is to overcome the delays present in the sensory processing. In contrast, short-term velocity store contains target motion attributes (such as peak velocity) that are sufficient to characterize the whole target trajectory. In this case, the information held in memory is released under the control of a periodicity estimator (Barnes & Asselman, 1991). The effects of such predictive mechanisms are observed after unexpected changes in target motion or target stabilization (Barnes *et al.*, 2000) and can be observed for up to 400ms after target perturbation.

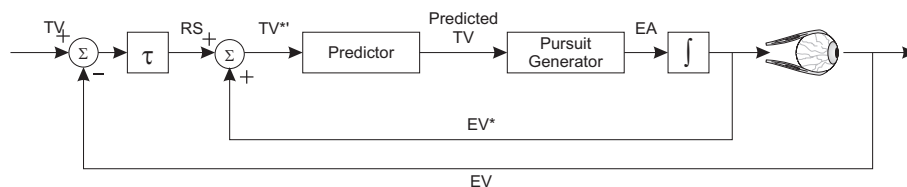


Figure I-10: Model that simulates the predictive component of smooth pursuit eye movements. In this model, future target velocity (Predicted TV) is computed from an estimate of target velocity (TV*). The predictor is a

Kalman filter. The rest of the model is similar to the model described in Fig. I.8. Adapted from Deno et al. (1995).

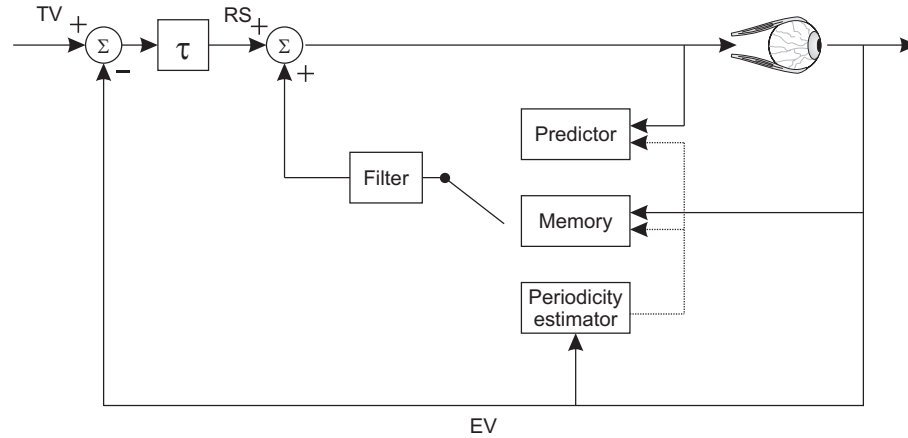


Figure I-11: Model that simulates the predictive component of smooth pursuit eye movements based on a short-term memory that holds velocity. The output of the memory is released under the control of a periodicity estimator. On some occasions, the output of the memory can be replaced by a predictor similar to the one presented in Fig. I.10. Adapted from Barnes & Asselman (1991).

Interestingly, tracking one's hand exhibits predictive features similar to online prediction (Gauthier *et al.*, 1988), which tends to show that signals related to arm motion are available to the smooth pursuit system. These signals are translated into a prediction of upcoming target motion (i.e. arm motion) (Scarchilli *et al.*, 1999). This prediction is then used in order to drive predictive smooth pursuit eye movements.

EXPECTATION

To explain the prediction mechanism based on expectation, I use to say: "If you expect something to move in a certain direction and at a certain instant in time, then your eyes will begin to move before the target". This sentence somehow summarizes the four different

features of this kind of prediction mechanisms: 1) expectation of an event; 2) knowledge of target motion in advance (i.e. direction or speed); 3) knowledge of its timing; 4) eye motion onset occurs before target motion onset. This predictive mechanism exists both for smooth pursuit eye movements and for hand movements (Barnes & Marsden, 2002).

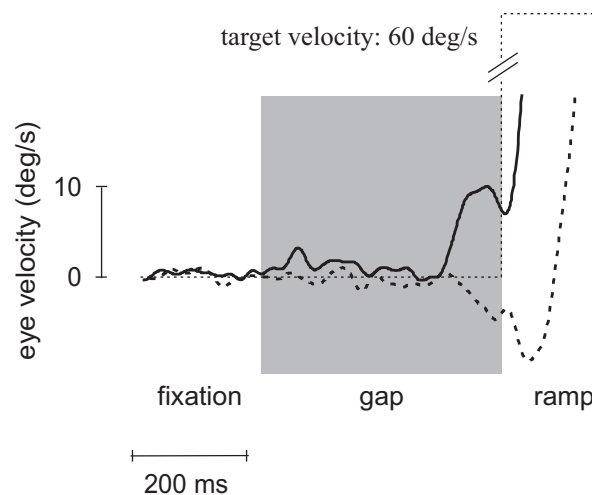


Figure I-12: Anticipatory smooth eye movements in prediction of future target motion. Horizontal eye velocity vs. time for both eye (continuous or dashed traces) and target (dotted black trace). In this paradigm, the target appears in the centre of the screen, disappears during a gap of 400ms, then reappears and immediately starts to move. Target velocity is 60 deg/s. Future target motion direction is not cued and anticipation is produced from subject's expectation about upcoming target direction. In some trials, the eye velocity builds up in a direction compatible with the future target direction (continuous trace). In other trials, it builds up in the incompatible direction (dashed trace). Example from de Hemptinne et al. 2006.

In a series of studies, Kowler and Steinman (1979a; 1979b; 1981) gave the first evidence of an anticipation mechanism in the smooth pursuit system. When subjects track repetitive target steps at different frequencies (providing the expectation, target parameters and timing), the eyes smoothly drifted toward the next target before its

appearance (Kowler & Steinman, 1979a). These drifts also occurred before single target steps or single target ramps (Kowler & Steinman, 1979b), which is a linear target motion with constant velocity. Even if the target direction is unpredictable, humans try to anticipate for future target motion and smooth eye movements are observed before target motion (Kowler & Steinman, 1981; Heinen *et al.*, 2005). This last result does not fit with one of the features of anticipation: the knowledge of target motion in advance. However, the expectation of an event is able to overcome this lack of information by guessing the future target direction (Fig. I.12). Therefore, in some cases, the guessed direction is wrong (dashed trace in Fig. I.12) while, in other cases, the guess is right (continuous trace in Fig. I.12). Guessing the future direction of the target is partially influenced by the target direction in the previous trials (Kowler *et al.*, 1984; Krauzlis & Adler, 2001) but can also be guided by cognitive cues. For example, when a target moves downward into an inverted Y-shape and then continues at the same velocity in either the right or left branch of the inverted Y, horizontal smooth eye velocity can increase before the target reaches the intersection of the two branches. In the absence of cue, the anticipation of the future target direction (either right or left branch) is based on the previous trials (Kowler *et al.*, 1984). In contrast, when future target direction is yielded by either a voice cue (aloud left or right instruction) or a visual cue (one branch is closed by a barrier), anticipation of the future target direction is stronger than in the no cue condition (Fig. I.13, Kowler, 1989).

Slow eye movements occurring before the onset of a target are often referred to as anticipatory smooth eye movements. Interestingly, they are facilitated by the disappearance of the fixation point a few hundreds milliseconds before target motion onset (gap paradigm, Boman & Hotson, 1988; Knox, 1996, 1998) and their velocity is scaled to target velocity. In addition to their occurrence before target motion onset, anticipatory eye movements can take place before target motion offset. In this case, the eye velocity decays before the end of the target motion (Boman & Hotson, 1988; Barnes *et al.*, 2005). Anticipatory and reactive smooth pursuit eye movements are governed by a common mechanism as they exhibit similar accelerations, velocities and inter-individual variability (Kao & Morrow, 1994).

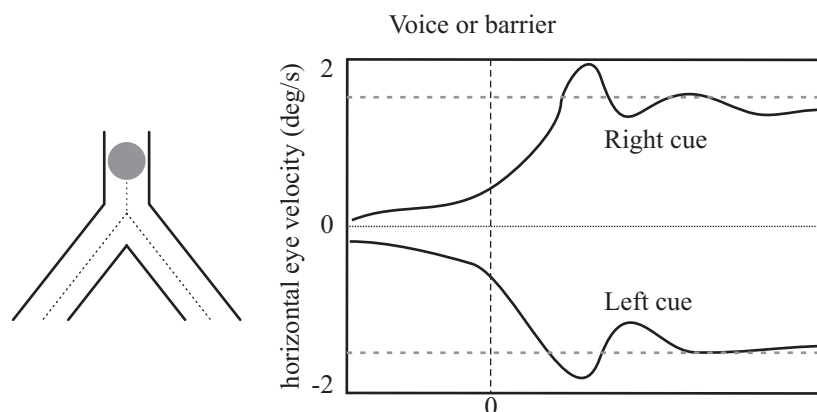


Figure I-13: Cognitive factors influencing anticipatory smooth eye movements. Left panel: In this paradigm, the target is moving through an inverted Y-shape and then changes its direction to move downward through one of the two branches. The future target direction (branch) is given either by a voice cue ("left" or "right") or by a barrier that closes one of the two branches. Right panel: horizontal eye velocity vs. time when either a left or right cue is given. Zero represents the time at which the target crosses the intersection of the two branches. Example from Kowler et al. 1984.

Several lines of evidence show that anticipatory eye movements are based on a memory of the magnitude of target velocity (Barnes & Asselman, 1991; Barnes, 1994; Barnes & Wells, 1999). This velocity memory has many different properties. It can be charged by viewing without pursuing the moving target (Barnes *et al.*, 1997) and its content decays over time (Wells & Barnes, 1998). It can store multiple target velocities together (Barnes & Schmid, 2002; Collins & Barnes, 2005). Its output can be charged by a target motion in one direction and transferred to the other direction using directional cues (Jarrett & Barnes, 2001; de Hemptinne *et al.*, 2006). Finally, the output of the velocity memory is under volitional control, i.e. it can be scaled using precues (Jarrett & Barnes, 2002).

In addition to the velocity memory, the timing of target motion is stored in a memory that is independent from the velocity memory (Barnes & Donelan, 1999). The timing of the target motion onset can be cued either by the gap duration (the gap corresponds to the period before the target motion onset during which the fixation point has already disappeared) or by external cues (Badler & Heinen, 2006). Moreover, in the presence of a gap, behavioural evidence shows that primates time their anticipatory eye movements on the basis of the elapsed time since gap onset (de Hemptinne *et al.*, 2007).

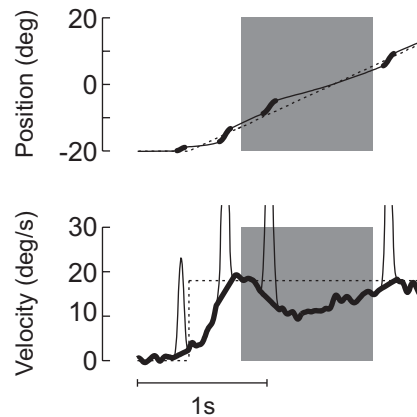


Figure I-14: Oculomotor response during occlusion of the pursuit target. Both position (upper panel) and velocity (lower panel) are represented vs. time. Dashed traces give target position and velocity. On the position panel, solid traces yield eye position. Thicker traces represent saccades. On the velocity panel, solid traces represent eye velocity (thicker traces represent smooth eye velocity).

PREDICTION DURING OCCLUSION

The mechanisms of prediction play a major role during transient disappearance of an ongoing target (temporary occlusion paradigm, see Fig. I.14). This paradigm has been pioneered by Mitrani and Dimitrov (1978) who showed that the eye velocity exponentially decays 100ms after target disappearance. When the target is expected to reappear, the eye velocity decays toward a plateau value (the residual eye velocity, approximately 60% of target velocity). Conversely, when the target is not expected to reappear, it decays exponentially towards zero (Krauzlis & Miles, 1996c; Pola & Wyatt, 1997). The residual velocity results from the output of the velocity store attenuated by a variable gain element. This gain is close to unity during visually-guided pursuit but is reduced during pursuit of an invisible target (Becker & Fuchs, 1985; de Brouwer *et al.*, 2001). Surprisingly, the eye velocity can increase before the end of the

occlusion if the duration of the occlusion is fixed (Bennett & Barnes, 2003). This eye velocity recovery is scaled to target velocity at reappearance (Bennett & Barnes, 2004, 2006b; Orban de Xivry *et al.*, 2006) and is supposed to be timed with the moment of target reappearance (Bennett & Barnes, 2005).

The smooth pursuit response during the occlusion of a pursuit target has been modelled in different ways. Some authors claimed that the residual velocity is based on the efference copy loop, which induces perpetuation of the pursuit response during occlusion (Churchland *et al.*, 2003; Madelain & Krauzlis, 2003). Other authors hypothesized that the residual velocity is based on the output of a short-term velocity store that contains a fixed representation of target velocity obtained during the visual pursuit before the occlusion (Bennett & Barnes, 2003, 2004, 2006b). This short-term velocity store is the same as the one driving predictive smooth pursuit response during visually-guided pursuit (Barnes & Asselman, 1991). In both types of models, the output of the efference copy or memory is under the control of a variable gain element, which decreases at target disappearance and which is responsible for the predictive eye velocity recovery before target reappearance.

NEURAL SUBSTRATE

The cortical network subserving predictive mechanisms has been studied by both fMRI and cell recording techniques. From these studies, it appeared that many areas convey corollary discharge but that the frontal oculomotor regions (SEF and FEF) play a major role in

prediction mechanisms (Schmid *et al.*, 2001; Lencer *et al.*, 2004; Nagel *et al.*, 2006).

In order to distinguish retinal (visual) and extraretinal signals, scientists use two different techniques: electronic stabilization of the pursuit target on the retina or target blanking during short intervals. Extraretinal signals that are related to eye motion are thought to convey efference copy signals of the pursuit response. Such signals were found in MST (Newsome *et al.*, 1988; Kawano *et al.*, 1994; Ilg & Thier, 2003; Churchland & Lisberger, 2005), in the medio-dorsal thalamus (Tanaka, 2005) and in the cerebellum (Noda, 1986; Stone & Lisberger, 1990; Suh *et al.*, 2000). Moreover, the cerebellum is often described as the locus of forward models where the copy of an effector motor command (i.e. the eye motor command) is interpreted in order to predict its effect on the effector (Wolpert & Miall, 1996; Karniel, 2002; Mehta & Schaal, 2002).

Cell recording studies evidenced that SEF and FEF play a role in online prediction. Indeed, neurons recorded in the SEF preferentially discharge during predictive eye motion such as those based on the short-term memory (Heinen & Liu, 1997). Similarly, transcranial magnetic stimulation over the SEF or the FEF affects pursuit of predictable target motion (Gagnon *et al.*, 2006; Drew & Donkelaar, 2007). In addition, lesions of the FEF (Keating, 1991; MacAvoy *et al.*, 1991; Keating, 1993) or the SEF (Lekwuwa & Barnes, 1996a) impair predictive pursuit in such a way that predictable target motion cannot be pursued with zero phase lag anymore. Besides the frontal regions, the flocculus and the

paraflocculus show activity related to online prediction. Indeed, the pursuit-related discharge of floccular neurons led eye motion by an interval of time larger than the time of transmission delay between flocculus stimulation and eye motion (Suh *et al.*, 2000). However, though cerebellar disease lowers the gain of smooth pursuit, it spares its predictive component (Waterston *et al.*, 1992).

The same areas also play a significant role during the anticipation of a pursuit target. For instance, stimulation of neurons of the SEF during anticipation of a pursuit target facilitates anticipation (Missal & Heinen, 2004). Similarly, lesions of the FEF (MacAvoy *et al.*, 1991), different types of cerebral lesions (Lekwuwa & Barnes, 1996b) or cerebellar degeneration (Moschner *et al.*, 1996; Moschner *et al.*, 1999) impair anticipatory smooth eye movements but do not abolish them. Finally, during target blanking, FEF neurons carry a signal related to both target position and velocity (Fukushima *et al.*, 2002; Barborica & Ferrera, 2003, 2004; Xiao *et al.*, 2006).

In sum, the frontal oculomotor regions (FEF and SEF) play a major role in the different predictive mechanisms. However, their role in the different predictive mechanisms appears to differ. Indeed, when TMS is applied over FEF and SEF during predictive tracking or pursuit initiation, its effects on smooth pursuit eye movements are different (Gagnon *et al.*, 2006; Drew & Donkelaar, 2007). The functional role of each of these brain structures to predictive mechanisms remains to be uncovered.

A reference model

The two previous sections described the mechanisms that allow primates to get clear vision of a moving object: interaction between saccades and pursuit and prediction. These mechanisms have been modeled separately and I will present here a unified model of prediction and saccade-pursuit interaction. This unified model is sketched in Fig. I.15. This model is an extension of the model presented in the thesis of Sophie de Brouwer (de Brouwer, 2001), which was the first to simulate both saccades and pursuit.

In this model, retinal inputs are used to estimate both position error and retinal slip (RS, i.e. velocity error). These estimates are then processed by the saccadic and pursuit systems into motor commands. In parallel, the decision whether or not to trigger a saccade is taken (trigger). When a catch-up saccade is released, its motor command is added to the ongoing smooth pursuit command at the premotor level. The initiation, target selection and cancellation mechanisms, which are not represented in the figure, gate the execution of saccades and pursuit in parallel to the input processing (Krauzlis, 2005). The prediction mechanism is embedded within the smooth pursuit system as represented in Fig. I.16.

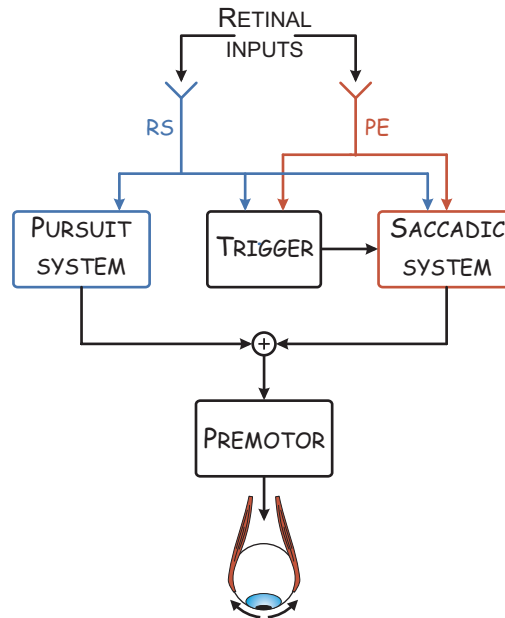


Figure I-15: Model of the synergies between saccades and pursuit. The retinal inputs are processed into retinal slip (RS, blue lines) or position error (PE, red lines). Estimates of position and velocity errors are sent to both saccadic and pursuit systems, which process them into motor commands. The trigger uses these inputs to decide whether a catch-up saccade should be triggered. Pursuit and saccadic commands are then summed up and conveyed to the premotor structures.

The pursuit subsystem of the model belongs to the category of "image motion" model (Krauzlis & Lisberger, 1994). In order to reproduce predictive smooth pursuit eye movements, a memory element was added to the smooth pursuit model similarly to Bennett & Barnes (2006b). The saccadic model was an extension of the model of Scudder (1988) where desired eye displacement is the input of the saccadic system.

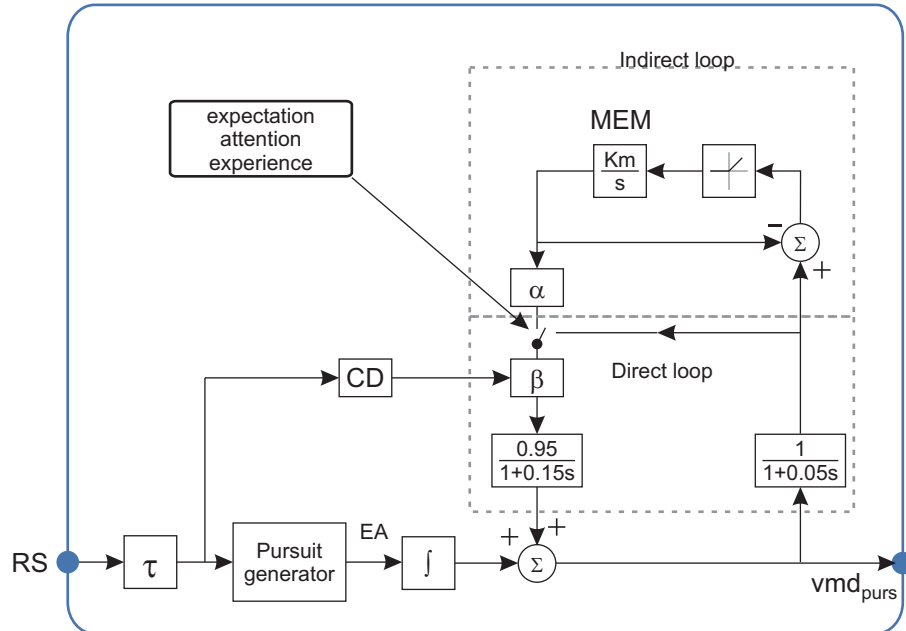


Figure I-16: Model of the smooth pursuit system. This model is an adapted version of the model proposed by Bennett and Barnes (2006b). The retinal slip (RS) is processed by the pursuit generator (see Fig. I.17) which translates it into an eye acceleration motor command that is then integrated. Either the output of the direct loop (efference copy loop) or the output of the indirect loop (Memory (MEM) of the visuomotor drive, vmd) is subsequently added to this motor command. The result of the summation yields a visuomotor drive for pursuit (vmd_{purs}). The switch between the direct and indirect loop is controlled by expectation, attention, experience... The conflict detector (CD) decreases the gain of the loops (β) after target disappearance.

SMOOTH PURSUIT SUBSYSTEM

The proposed smooth pursuit subsystem (Fig. I.16) is a combination of two models, one proposed by Krauzlis and Lisberger (1994) and the other by Bennett and Barnes (2006b). The latter is capable of simulating anticipatory smooth pursuit eye movements, predictive pursuit to sinusoidally moving targets and predictive smooth pursuit response during occlusions (Barnes & Asselman, 1991; Barnes & Wells, 1999; Bennett & Barnes, 2003, 2004, 2006b).

The model of Krauzlis and Lisberger nicely accounts for the dynamics of pursuit during pursuit initiation and maintenance. The retinal slip is processed by the pursuit generator that transforms velocity and acceleration signals into a visuomotor drive (vmd_{purs}) for pursuit eye movements (Fig. I.17). The transient motion branch is only activated for the first 50ms after a sudden change in target trajectory. This information is yielded by a step detector that tracks target steps as described by de Brouwer (2001).

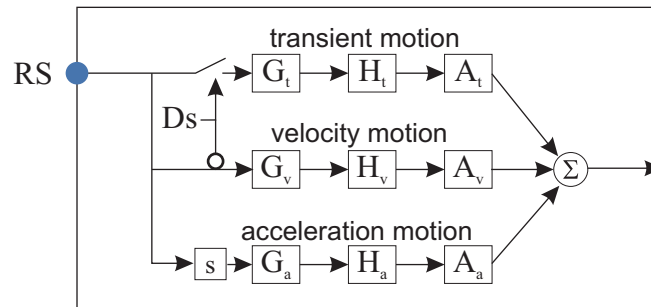


Figure I-17: Schematic diagram of the pursuit generator. The pursuit generator translates retinal slip into desired eye acceleration that will produce the visuomotor drive. The three branches, which process retinal slip, are similar to those described by Krauzlis and Lisberger (1994). The transient motion only intervenes after a sudden change in target motion is detected (Ds). The G_i , H_i and A_i boxes respectively represent non-linear functions, second-order filters and gain elements.

The output of the pursuit generator is added to the output of the efference pathways (see Fig. I.16). These pathways consist of a direct loop, which corresponds to the classical efference copy loop, and an indirect loop, which is responsible for the predictive smooth pursuit. The indirect loop is a short-term memory that stores the maximum visuomotor drive sent to the eye plant. The content of the store can be replayed before target onset to simulate anticipatory smooth eye movements or during steady-state pursuit to elicit

predictive smooth pursuit eye movements (Barnes & Asselman, 1991; Barnes & Wells, 1999). The time of the replay is under the control of a periodicity estimator (not represented). During occlusions, the content of the memory drives smooth pursuit eye movements (Bennett & Barnes, 2003, 2004, 2005, 2006b). Within these loops, the gain β is controlled by the conflict detector (CD) that reduces it as soon as the target disappears or as soon as there is a unexpected change in target trajectory (Barnes *et al.*, 2000).

SACCADIC SUBSYSTEM

The saccadic subsystem used in this model is derived from the work of Scudder (1988). In this subsystem, position error and retinal slip are combined in order to estimate the desired eye displacement (de Brouwer *et al.*, 2002a). In this case, the desired displacement is computed as following:

$$\Delta Ed = 0.95 \cdot (PE + 0.13 \cdot RS)$$

This estimate is then fed to the saccadic model which is based on the negative efference copy loop proposed by Robinson (1974). When a saccade is triggered, the desired eye displacement is transformed into a burst signal. This burst signal is concurrently sent towards the ocular motoneurons and fed back through a resettable integrator that estimates the actual eye displacement and compares it to the desired eye displacement (Robinson, 1974). The trigger of saccades is under the control of OPNs, which gate their execution. The burst signal also inhibits the OPNs. At the end of the saccade (i.e. when the actual eye displacement is equal to the desired eye

displacement), the burst signal stops inhibiting OPN activity and the OPNs are reactivated.

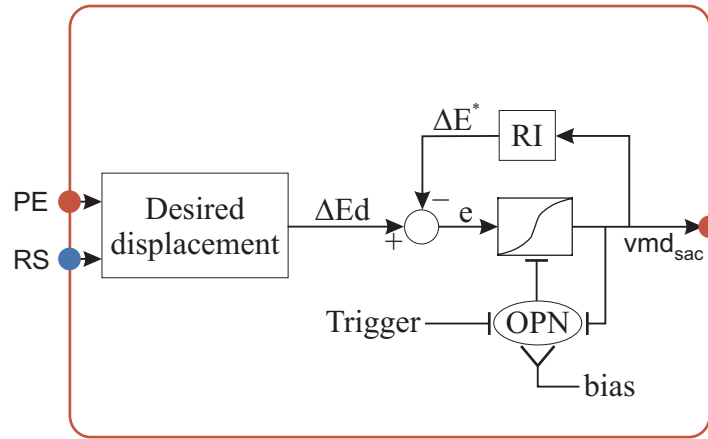


Figure I-18: Saccadic model as proposed by Scudder (1988). The desired displacement (ΔEd) is computed from PE and RS. This signal passes through a non-linear function. The resulting motor command (vmd_{sac}) is simultaneously sent to the premotor circuitry and negatively fed back through a resettable integrator (RI) that computes the eye displacement (ΔE^*). This circuitry is under the inhibitory control of the omnipause neurons (OPN).

TRIGGER MECHANISM

The trigger mechanism is implemented following the results obtained by de Brouwer et al. (2002b). The eye-crossing-time is computed by dividing the opposite of the position error by the retinal slip. As soon as this parameter leaves the smooth zone, the decision to trigger a saccade is taken and a go-signal is released. After a variable delay (computed following the LATER model, Carpenter & Williams, 1995), the saccade is executed.

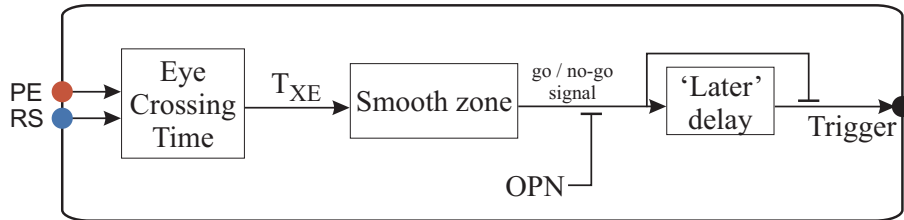


Figure I-19: Trigger mechanism of catch-up saccades during visually-guided pursuit. In this diagram, the eye-crossing-time (T_{xe}) is computed and compared with the limits of the smooth zone. If the T_{xe} is outside the smooth zone, the decision to trigger a saccade is taken (go/no-go signal) and a saccade is executed after a delay predicted by a Later model.

FITTING BEHAVIOURS

The model as presented here accounts for visually-guided pursuit eye movements elicited by target motion (Lisberger *et al.*, 1987; Barnes & Asselman, 1991; Krauzlis & Lisberger, 1994; Barnes & Wells, 1999) and for predictive smooth pursuit response during transient target disappearance (Bennett & Barnes, 2003, 2004, 2006b). It can simulate saccades to stationary and moving targets (Scudder, 1988; de Brouwer *et al.*, 2002a). It can reproduce the trigger mechanism of catch-up saccades during ongoing pursuit (de Brouwer *et al.*, 2002b).

Chapter II

TARGET ACCELERATION CAN BE EXTRACTED AND REPRESENTED WITHIN THE PREDICTIVE DRIVE TO OCULAR PURSUIT.

As we move around and interact within our natural surrounds, it is common to experience accelerating object motion. It is, therefore, not difficult to think of situations where there is potential for serious consequence if the effect of object acceleration is not perceived. For example, misperceiving the changing relationship between two approaching cars can lead to an incorrect braking strategy, possibly resulting in a collision (Lee, 1976). Less severe consequences are evident in interceptive tasks such as pointing and reaching (Port *et al.*, 1997; Brouwer *et al.*, 2003), but still successful performance is dependent on maintaining a precise relationship between the observer and moving object. Physiological and psychological research indicates that these human behaviours are supported by a visual system that comprises highly specific motion processing mechanisms that are capable of extracting information about an object's direction and

speed (McKee, 1981; Anderson & Burr, 1985; Watamaniuk & Heinen, 1999). Interestingly, however, the human visual system is less capable of discriminating object acceleration (Snowden & Braddick, 1991; Werkhoven *et al.*, 1992; Watamaniuk & Heinen, 2003). This is consistent with the finding that in response to target acceleration the firing of neurons in MT, the key motion processing area of the monkey, is not independent of target speed (Lisberger & Movshon, 1999; Price *et al.*, 2005). In fact, the general consensus is that humans do not perceive acceleration directly, but rather perceive acceleration indirectly from change in speed (Price *et al.*, 2005; Price *et al.*, 2006). This conclusion is further supported by psychophysical studies, which have shown that perceptual discrimination of acceleration is influenced by mean velocity over a presentation (Gottsdanker *et al.*, 1961; Schmerler, 1976; Brouwer *et al.*, 2002), and hence is not simply dependent on the magnitude of acceleration per se. For instance, for two presentations of equal duration (e.g., 500ms) with the same target acceleration (e.g., 8deg/s^2) but different initial and final velocity (e.g., 8 and 12deg/s ; 24 and 28deg/s), the former would be more readily discriminated as containing accelerative motion because the percentage change in velocity (i.e., $\text{initial velocity} - \text{final velocity} / \text{mean velocity}$; 41% and 16%, respectively) is well above the reported threshold of 25% (Brouwer *et al.*, 2002).

Although sensitivity to the effect of acceleration on object motion conveys significant advantage, the need to sample and

compare object speeds (for a physiological model based on population coding of MT neurons see Lisberger & Movshon, 1999) could be responsible for the high acceleration discrimination threshold. In other words, while speed discrimination has a low threshold enabling detection of speed differences of less than 5% (McKee, 1981), the process of extracting reliable information on object acceleration appears to introduce error (for a discussion of possible mechanisms see Watamaniuk & Heinen, 2003). This process has been shown to be influenced by presentation duration, with estimates of approximately 100ms being required to differentiate the speed signal (Werkhoven *et al.*, 1992) and 300ms being sufficient for perception to correctly discriminate a 25% between-trial change in velocity due to constant acceleration on 75% of trials (Brouwer *et al.*, 2002). It is likely, therefore, that the inadequacy of acceleration extraction over short stimulus duration accounts for the lack of scaling in the open-loop period of smooth pursuit (i.e., 40-140 ms after onset) to the target velocity resulting from acceleration (Lisberger *et al.*, 1987; Krauzlis & Lisberger, 1994; Watamaniuk & Heinen, 2003).

As a result of poor discrimination of target acceleration over short stimulus presentations, it follows that there will be significant retinal slip and position error both during and after the open-loop period of smooth pursuit. To avoid the mismatch between eye and target motion, it has been suggested that, given sufficient exposure, the oculomotor system employs a corollary discharge mechanism (Robinson *et al.*, 1986) that provides a reference (e.g., efference copy)

to predict the ongoing eye movement. To date, however, although these models of ocular pursuit have incorporated input of an acceleration signal that influences pursuit onset (Krauzlis & Lisberger, 1994), the efference copy has typically been modelled to represent an eye-velocity signal of constant magnitude. Recognising the limitations of such models, others have suggested that a more persistent velocity-based memory can be formed given sufficient opportunity to sample and hold the stimulus characteristics, and that this can account for pursuit of sinusoidal target motion (Barnes & Asselman, 1991). Recent refinement of this latter model has led to the proposal that the velocity-based representation is in fact tuned with a variable gain function in order to produce drive with the desired acceleration characteristics (Bennett & Barnes, 2006b).

Despite attempts to examine pursuit of accelerating target motion there remains a clear need to more fully determine the sensitivity of the oculomotor system to target acceleration. Work on the latency to initiate pursuit (Krauzlis & Lisberger, 1994) and the subsequent 40-140 ms open-loop response (Watamaniuk & Heinen, 2003) cannot verify if the extraction of an acceleration signal that inputs to ocular pursuit improves over a stimulus duration longer than the perceptual-motor delay, and whether this then forms the basis of a predictive response. Further, because only targets with positive acceleration were used, it remains unknown if, like perceptual discrimination (Gottsdanker *et al.*, 1961; Schmerler, 1976; Calderone

& Kaiser, 1989; Babler & Dannemiller, 1993) ocular pursuit also discriminates between negative acceleration and positive acceleration. Longer ramps of accelerating target motion were given in the study of Bennett and Barnes (2006b). However, because stimulus presentation was arranged to enhance predictability, it was not possible to confirm whether the increase in smooth pursuit during the transient target occlusion reflected a prediction made in advance of target motion regarding the expected change in target velocity either side of the occlusion or an on-line extraction and representation of the acceleration signal made during pursuit of the initial visible ramp. Finally, none of the studies to date on pursuit of accelerating target motion have examined the collaboration between the two oculomotor subsystems: saccades and smooth pursuit (Krauzlis & Stone, 1999; Krauzlis, 2004, 2005). This is an important omission because the combined response of saccades and smooth pursuit during transient occlusion can reveal much about how precisely the oculomotor system represents a target's trajectory (Orban de Xivry *et al.*, 2006).

In the present paper we report the results of a study in which we examined smooth and saccadic pursuit during a transient target occlusion where target acceleration and deceleration, initial target velocity and visible duration prior to target occlusion were randomised across trials. By maintaining a fixed start position, this combination of parameters enabled us to decorrelate target position and velocity just prior to occlusion, as well as mean target velocity during the initial visible ramp, from target acceleration. Hence, the

design enabled us to determine whether the pursuit response during a transient occlusion was based upon a measure of target acceleration or target velocity. According to the standard efference copy model of pursuit, eye motion during an occlusion is based upon target velocity just prior to occlusion. In our protocol, the pre-occlusion target velocity was independent of target acceleration. Therefore, there should be no relationship between the oculomotor response and target acceleration if extrapolation were based on pre-occlusion target velocity. Consequently, we will refer to this as the “final velocity” hypothesis. Instead of extrapolating eye motion using the pre-occlusion target velocity, subjects could use a more global measure of target velocity, i.e. mean target velocity during any earlier interval of the initial visible ramp. To reveal any evidence for this effect, we designed the target parameters in such a way that average target velocity was negatively correlated with target acceleration (“average velocity” hypothesis). Finally, if the oculomotor response during the occlusion were based on target acceleration during the initial visible ramp, it would be positively related to target acceleration (“acceleration” hypothesis).

Methods

EXPERIMENTAL SET-UP

Six healthy human subjects (mean age: 27 years), all of whom had previous experience of ocular pursuit tasks, participated after

giving informed consent. Two of the subjects were authors (S3, S5) and the others were naïve to the purpose of the study. All subjects had normal or corrected-to-normal vision, were healthy and without any known oculomotor abnormalities. All procedures were conducted with approval of the Université Catholique de Louvain ethics committee.

Subjects sat in a purpose-built dark room, facing a flat white screen (2x1.5 m) at a viewing distance of 1.5 m. The head was supported with a chin rest that was adjusted to each subject's height. Visual stimuli were projected onto the screen using a CRT projector (Barco Cine8) with a refresh rate of 100Hz and 800x600 spatial resolution. The horizontal motion of the visual stimuli was controlled by a visual stimulus generator (VSG2-5; Cambridge Research Systems Ltd) interfaced with a PC running proprietary software through MATLAB (Mathworks Inc). Eye movements were recorded at 200Hz using a Chronos eye tracker (Skalar Medical BV) and stored to a PC for off-line analysis.

PARADIGM

We performed a standard occlusion experiment over 4 sessions, each lasting approximately 30 minutes. Each session began with a calibration procedure (Orban de Xivry *et al.*, 2006) followed by blocks of 40 presentations that were received in a pseudo-random order. A presentation began with a green central fixation point presented for a period varying randomly between 500 and 1500ms. After the fixation period, the green target was replaced by a co-located

red target that started to move at constant acceleration either leftward or rightward for 200, 500 or 800ms, after which the target disappeared behind an imaginary occluder for 800ms. Initial target velocity was chosen such that target velocity 50ms before occlusion (pre-occlusion velocity) was either 0deg/s or 8deg/s (in absolute value). Therefore, average target velocity during the last 100ms before the occlusion was constant whatever target acceleration. Target acceleration was constant during the entire presentation, hence when the target reappeared for 400ms after the occlusion its motion characteristics were a straightforward extrapolation of the previous trajectory. For pre-occlusion target velocity of 8deg/s, target acceleration was -8, -4, 0, 4 or 8deg/s², whereas for the pre-occlusion target velocity of 0deg/s, target acceleration was 0, 4, 8, 12 or 16deg/s² (see Fig. II.1). Subjects were instructed to track the horizontally moving target as accurately as possible throughout the presentation.

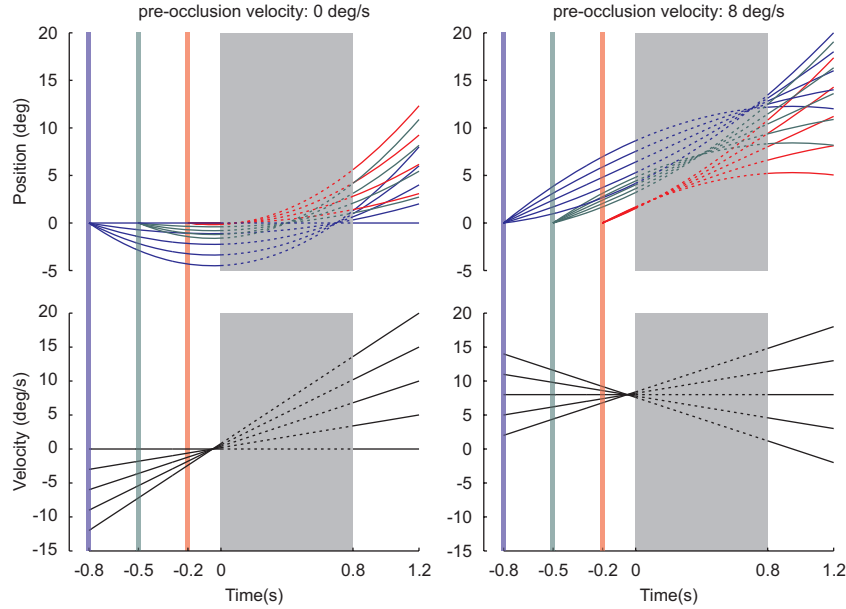


Figure II-1: Representation of pursuit target position (vertical axis in upper panels) and velocity (vertical axis in lower panels) versus time (horizontal axis). Target motion onset is indicated by the thick vertical line. At this time the red pursuit target became visible and moved for 200ms (red), 500 (green) or 800ms (blue) with velocity and acceleration characteristics that brought it to pre-occlusion velocity of 0deg/s (panels on left side) or 8deg/s (panels of right side). The target was then occluded for 800ms (light grey shaded area) and finally reappeared for a further 400ms. Target acceleration was 0, 4, 8, 12 or 16 deg/s² for 0deg/s pre-occlusion velocity (left panel) and -8, -4, 0, 4 or 8 deg/s² for 8deg/s pre-occlusion velocity (right panel). The combination of pre-occlusion target velocity and target acceleration resulted in 10 distinct position trajectories for each initial ramp duration.

Our protocol was designed to disambiguate the different parameters that subjects could use to extrapolate target motion during the occlusion. Therefore, the two different levels of pre-occlusion target velocity were independent of target acceleration. Moreover, the mean target velocity during any interval of the initial visible ramp (apart from the final 50ms) was negatively related to target

acceleration; so was target position at target disappearance. In total, there were 60 different conditions (2 pre-occlusion velocities x 2 directions x 3 ramp durations x 5 levels of acceleration) that were presented, on average, 15 times over the 4 sessions. This minimised the predictive influence of cues (e.g., start velocity of the initial visible ramp, target position at the end of the first ramp) that were ambiguously related to target acceleration. Consequently, our protocol enabled us to discriminate between three potential hypotheses for extrapolating the oculomotor response during a transient occlusion.

DATA ANALYSIS

Eye and target position signals were low-pass filtered at 50Hz using an autoregressive, zero-phase digital filter implemented in MATLAB (Mathworks, Inc). Eye velocity and acceleration were derived from filtered position signals using a weighted central difference algorithm on a $\pm 10\text{ms}$ time interval. Saccades were detected using a 500deg/s^2 acceleration threshold and were considered to occur during the occlusion when their onset was at least 100ms after the start of the occlusion and before its end. The smooth component of the saccadic amplitude was removed using a technique described in de Brouwer et al. (2002a). The computation of the smooth component was obtained by multiplying the saccade duration by the mean smooth eye velocity during the saccade. The raw saccade amplitude data were then corrected by subtracting the smooth

component. The total contribution of the saccadic system to the displacement (SAD) during the occlusion interval was obtained by summing the signed amplitude of all the saccades. To obtain desaccaded smooth eye velocity, we then removed the identified saccades plus 5 additional data points (equivalent to 25ms) at the beginning and end of the identified saccade trajectory from the eye velocity trace. The removed data were replaced by a linear interpolation routine based on the smooth eye velocity before and after the saccade (for more details see de Brouwer *et al.*, 2002a). The contribution of the smooth pursuit system to the displacement (SED) during the occlusion interval was obtained by integrating the smooth eye velocity during this interval. The total eye displacement during the occlusion was computed from the sum of SAD and SED.

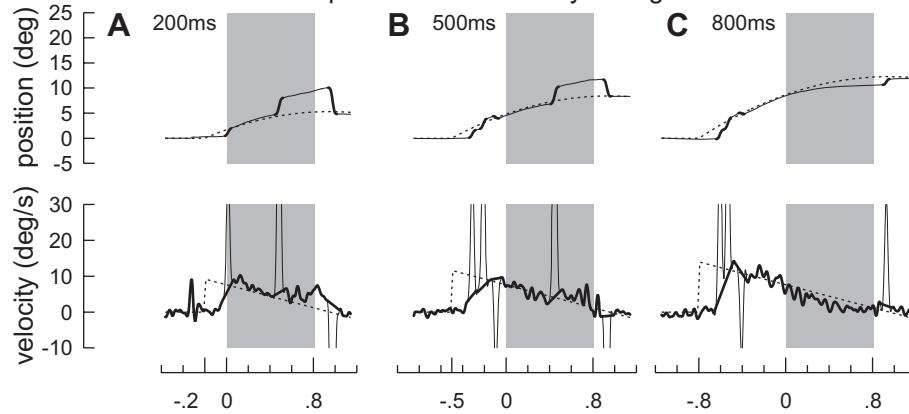
For the purposes of statistical analysis, we calculated intra-subject means for selected measures of the smooth and saccadic eye movements during a presentation. Data from presentations with 0deg/s pre-occlusion velocity and 0deg/s² acceleration were not included in the analysis. These presentations were included in the design in order to reduce anticipatory eye movements prior to target motion onset and to discourage subjects from simply responding with an eye movement of equal magnitude irrespective of target acceleration. Additionally, data were collapsed across leftward and rightward target motion during the occlusion. Because there were a different number of target accelerations where pre-occlusion target velocity was 0 or 8deg/s, the intra-subject mean data for these presentations was submitted to

separate ANOVA. Main and interaction effects were quantified using Tukey's HSD post hoc procedure; this test performs all comparisons while maintaining alpha and the probability of making a Type I error at the specified level. Finally, regression analyses were used to more fully explore the relationship between target acceleration and our dependent measures. To this end, the intra-subject mean data were regressed against corresponding target data; this was done separately for each initial ramp duration.

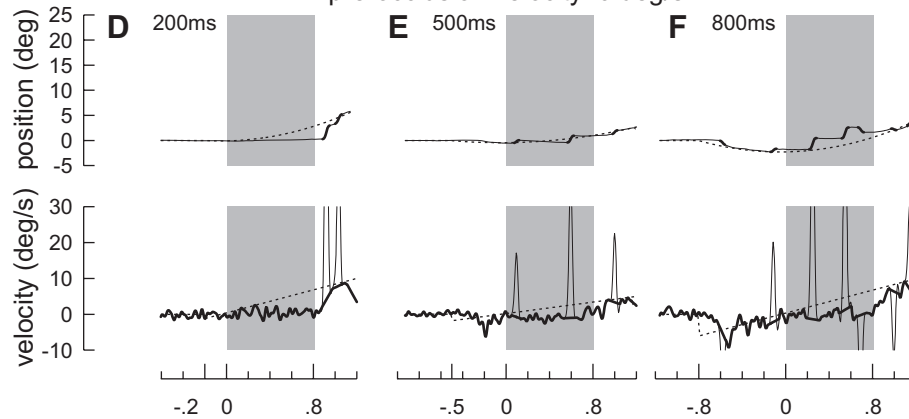
Figure II-2: Representative examples from a single subject (S5) of the position (deg) and velocity (deg/s) vs. time (s) of the eye (continuous traces) and target (thin broken traces). In the eye position traces, the thick parts represent identified saccades. On the eye velocity panels, thick traces represent desaccaded smooth eye velocity and thin traces indicate saccades. In the upper and middle pair of plots for pre-occlusion velocity 8 deg/s (A, B, C) and 0 deg/s (D, E, F), target acceleration is 8 deg/s². In the lower pair of plots (G, H, I) pre-occlusion velocity is 8 deg/s and initial ramp duration is 800ms. Target occlusion is represented by the light grey shaded area.

Influence of time of exposure

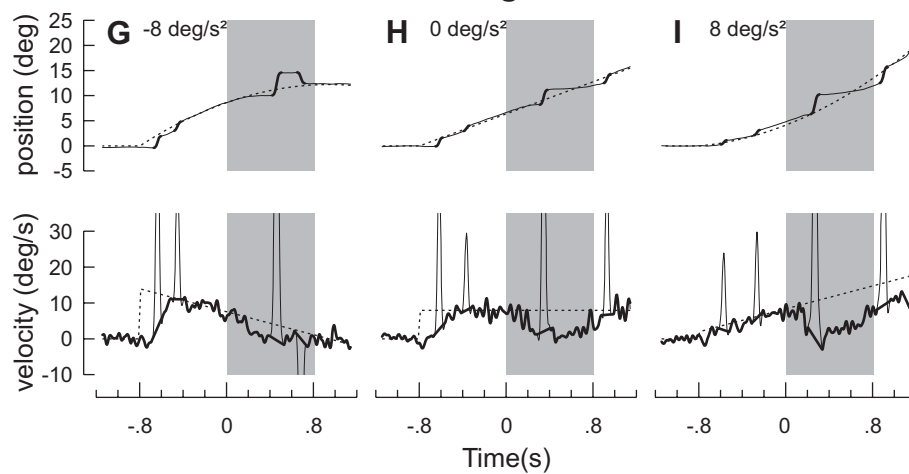
pre-occlusion velocity: 8 deg/s



pre-occlusion velocity: 0 deg/s



Influence of target acceleration



Results

TYPICAL EXAMPLES

Representative examples of the pursuit response on individual trials to various stimulus characteristics are shown in Fig. II.2. As expected given the variability in fixation period combined with unpredictability of the upcoming target speed, acceleration and direction, subjects exhibited very little (if any) anticipatory eye movements (smooth or saccadic). Following pursuit onset, the eyes tracked the target with a combination of smooth and saccadic movements. Around the moment of target occlusion, eye velocity and position were reasonably well matched to target velocity and position for the 500 and 800ms ramps (e.g., panels B, C, E and F). For these two conditions, pre-occlusion smooth eye velocity was similar across the range of ramp duration and target acceleration. For the 200ms ramp (panel A), there was insufficient time for eye velocity to reach a pre-occlusion velocity of 8deg/s, whereas there was very little target motion to drive eye motion when pre-occlusion target velocity was 0deg/s (panel D); target displacement was smaller than 0.2deg for each level of target acceleration.

In all presentations where pre-occlusion target velocity was 8deg/s, subjects exhibited substantial eye motion during the initial ramp, which was then continued during the occlusion interval. In

general, smooth eye velocity decayed following target disappearance and then recovered prior to target reappearance. The recovery differed in line with target acceleration (and velocity) when the target had initially been tracked for 500 and 800ms (e.g., panels G, H and I). In presentations where target velocity remained equal or increased during the occlusion interval, eye velocity was not sufficient to eliminate the developing position error and hence was accompanied by forward saccades (e.g., panels E, F, H, and I). In some instances, the combination of smooth pursuit and forward saccades brought the eye to a position ahead of the target, which was then corrected by reverse saccades; this was particularly evident in presentations with negative target acceleration (panels F and G).

Representative examples from two subjects of total eye displacement resulting from the combined smooth and saccadic response during an 800ms occlusion interval are shown in Fig. II.3. The pursuit response of both subjects discriminated between the different levels of target acceleration, although there was some inter-subject variation. For presentations where pre-occlusion target velocity was 0deg/s (panels A and B), subject 1 exhibited less variation between the different levels of target acceleration than subject 5. This was reflected in a total eye displacement for subject 1 that overshot the displacement of a 4deg/s² target and undershot the displacement of a 16deg/s² target. For subject 5, total eye displacement was well matched to target displacement for each level of acceleration. A somewhat reverse pattern was observed in

presentations where pre-occlusion target velocity was 8deg/s (panels C and D). Total eye displacement for subject 1 was reasonably well matched to the target displacement corresponding to each level of acceleration, whereas for subject 5 there was considerable undershoot except when pursuing a -8deg/s² target.

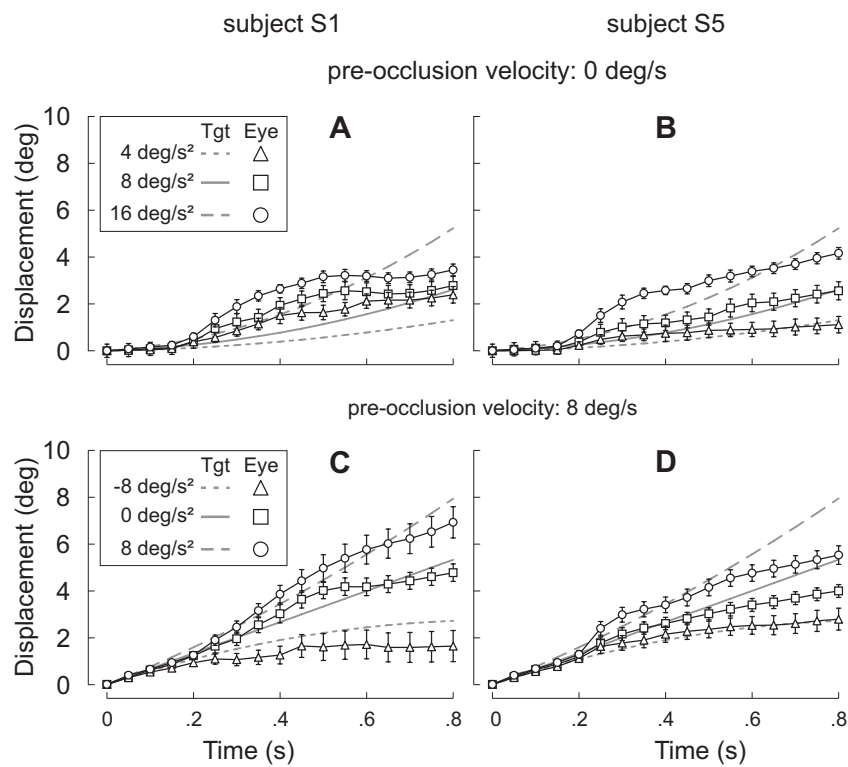


Figure II-3: Representative examples from two subjects (panels A and C – S1; panels B and D – S5) of mean ($\pm$ SE) eye displacement vs. time (s) for targets with 0 deg/s pre-occlusion velocity (upper panels) and 8 deg/s pre-occlusion velocity (lower panels). Initial ramp duration was 800 ms. The pursuit target (grey traces) and eye (black traces with symbols) displacement are normalized to 50 ms into the start of the occlusion interval in order to remove influence of visually-driven response. Symbols and line style indicate response of eye and target, respectively.

END-OCCLUSION SMOOTH PURSUIT

Having observed in our data the general trend of a reduction in smooth eye velocity during target occlusion followed by a recovery, it was important to segregate this global effect from the influence of target acceleration on the smooth response. We achieved this goal by comparing for each initial ramp duration the average eye velocity at end-occlusion pooled across all acceleration levels (dashed line in Fig. II.4) with the response to each acceleration level. This provided a direct way of testing the three proposed hypotheses: final velocity hypothesis (no modulation), average velocity hypothesis (negative relationship with target acceleration) and acceleration hypothesis (positive relationship with target acceleration).

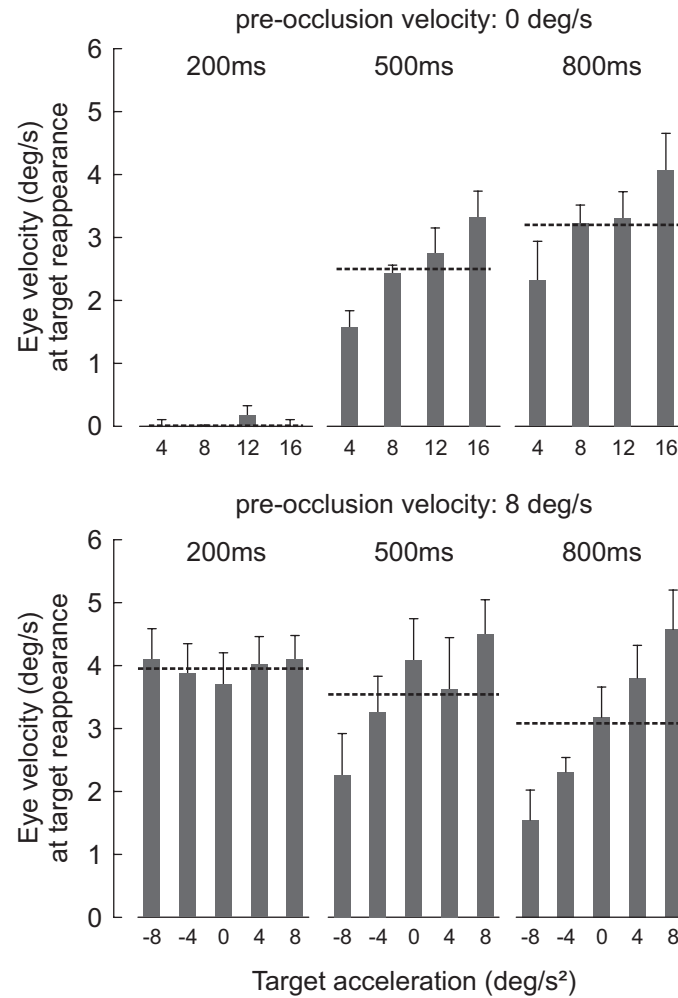


Figure II-4: Group mean (+SE) eye velocity (dark grey bars) at end-occlusion for targets with 0 deg/s pre-occlusion velocity (upper panel) and 8 deg/s pre-occlusion velocity (lower panel). The horizontal dashed lines represent the average eye velocity obtained by collapsing the data across all target accelerations. Left, middle and right columns (i.e., sub-set of bars) correspond to initial ramp duration of 200, 500, and 800ms. Horizontal axis legends represent target acceleration.

Figure II.4 shows the group mean end-occlusion eye velocity for targets with pre-occlusion velocity of 0 and 8deg/s. Here it can be seen that end-occlusion eye velocity remained uninfluenced by target acceleration in presentations where the target was initially visible for 200ms (left column). This was not the case after pursuing the target for a 500 or 800ms ramp (Fig. II.4, middle and right columns) where, for both levels of pre-occlusion target velocity, end-occlusion eye velocity across all target accelerations was modulated positively around average eye velocity. For the 0deg/s pre-occlusion target velocity, the modulation of smooth eye velocity with target acceleration was confirmed by ANOVA (significant interaction between ramp duration and target acceleration; $F(6,30)=2.85$, $p<0.05$). In presentations with either 500 or 800ms ramp duration, end-occlusion eye velocity was significantly higher when pursuing targets with acceleration of 16deg/s² compared to 4deg/s². For the 8deg/s pre-occlusion target velocity, the smooth eye velocity decreased after the start of the occlusion and then recovered, albeit to a level that was below start-occlusion smooth eye velocity. For the two longest initial ramp durations, smooth eye velocity differed as a function of ramp duration and target acceleration ($F(8,40)=4.61$, $p<0.01$). End-occlusion eye velocity was significantly higher when pursuing targets with acceleration of 8deg/s² compared to -8deg/s².

The scaling of smooth eye velocity according to target acceleration was confirmed by regression analysis. As shown in Table II.1, end-occlusion eye velocity did not change in proportion with

target acceleration in presentations where the target was initially visible for 200ms (0 and 8deg/s pre-occlusion velocity). After pursuing the target for either a 500 or 800ms ramp there was a more obvious scaling of end-occlusion eye velocity to target acceleration (0 and 8deg/s pre-occlusion velocity). However, the slope of the regression equations indicates the scaling of end-occlusion eye velocity fell well short of unity.

		0 deg/s			8 deg/s		
		R ²	Slope	p	R ²	Slope	p
EV	200	.001	.002	.90	.001	.003	.94
	500	.310	.156	.01	.146	.140	.04
	800	.193	.148	.03	.352	.212	.01
SAD	200	.014	.033	.58	.001	-.013	.83
	500	.577	.324	.01	.048	.091	.24
	800	.473	.385	.01	.216	.211	.01
TED	200	.000	-.032	.93	.006	.005	.68
	500	.585	.230	.01	.134	.411	.05
	800	.589	.420	.01	.333	.550	.01

Table II-1: Regression statistics for fit of eye data to target data (df=22 and 28 for 0 deg/s and 8 deg/s pre-occlusion target velocity, respectively). EV: eye velocity at target reappearance; SAD: Saccadic eye displacement; TED: total eye displacement.

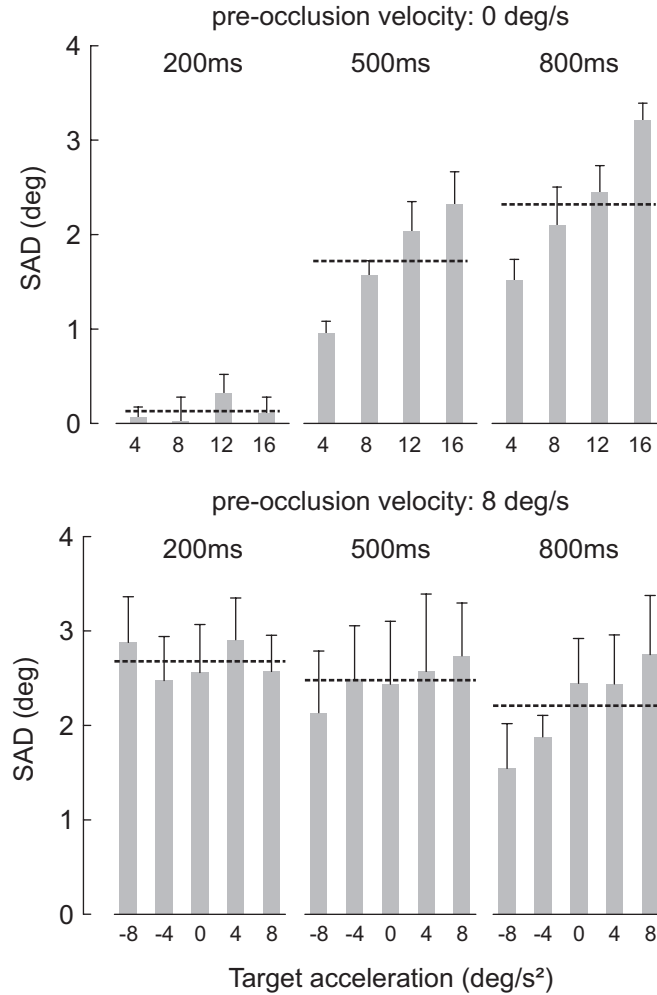


Figure II-5: Group mean (+SE) saccadic eye displacement (light grey bars) during the transient occlusion for targets with 0 deg/s pre-occlusion velocity (upper panel) and 8 deg/s pre-occlusion velocity (lower panel). The horizontal dashed lines represent the mean SAD obtained by collapsing the data across all target accelerations. Left, middle and right columns (i.e., sub-set of bars) correspond to initial ramp duration of 200, 500, and 800ms. Horizontal axis legends represent target acceleration.

SACCADES DURING OCCLUSION

The total saccadic eye displacement (SAD) during the occlusion was quantified using the same approach as in the previous section (i.e., comparing for each initial ramp duration the average SAD pooled across all target acceleration levels (horizontal dashed lines in Fig. II.5) with the response to each acceleration level). Group mean in Fig. II.5 shows that for targets with 0deg/s pre-occlusion velocity, there was no modulation of saccadic eye displacement with target acceleration following an initial 200ms ramp (left column, upper panel); there was almost no saccadic response during the occlusion interval. However, there was clear modulation of saccadic eye displacement around the mean following an initial 500 or 800ms ramp (middle and right columns, upper panel). This was confirmed by the presence of a significant interaction between ramp duration and target acceleration; $F(6,30)=2.78$, $p<0.05$. Post hoc testing indicated that the saccadic eye displacement during the transient occlusion was significantly greater when pursuing targets with acceleration of 16deg/s^2 compared to 4deg/s^2 . These effects were also evident in the regression analysis, which showed that saccadic eye displacement changed in proportion with target acceleration in presentations where the target was initially visible for 500ms or 800ms (Table II.1).

For targets with 8deg/s pre-occlusion velocity there was a less obvious modulation of saccadic eye displacement to target acceleration (Fig. II.5 lower panel), although contrary to the response

to targets with 0deg/s pre-occlusion velocity, there was a notable contribution from saccades during the occlusion following all initial ramp durations. Once again there was a lack of modulation of saccadic eye displacement around the mean following an initial 200 ramp (significant main effect of initial ramp duration; $F(2,10)=4.29$, $p<0.05$). Figure II.5 (right column, lower panel) shows that a difference in saccadic eye displacement during the transient occlusion was only evident between target accelerations of -8 and 8deg/s² in presentations with an 800ms initial ramp. This less robust scaling of saccadic eye displacement to target acceleration was confirmed by regression analysis (Table II.1). Saccadic eye displacement did not change in proportion with target acceleration in presentations with an initial 200ms or 500ms ramp. Furthermore, although significant, the slope of the regression on presentations with an initial 800ms ramp was lower than that observed for presentations of the same initial duration and 0deg/s pre-occlusion target velocity.

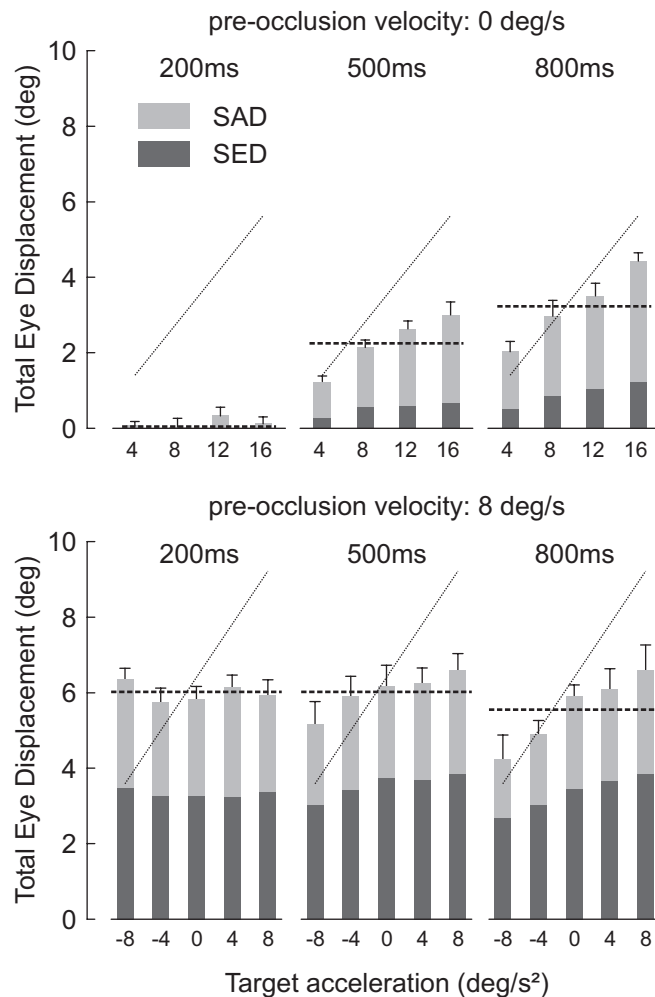


Figure II-6: Group mean (+SE) total eye displacement during the occlusion interval for target with 0deg/s pre-occlusion velocity (upper panel) and 8deg/s pre-occlusion velocity (lower panel). Diagonal lines represent target displacement. Dark and light grey bars represent contribution to displacement from SED and SAD, respectively. The horizontal dashed lines represent the mean total eye displacement obtained by collapsing the data across all target accelerations. Left, middle and right columns (i.e., sub-set of bars) correspond to initial ramp duration of 200, 500, and 800ms. Horizontal axis legends represent target acceleration.

COMBINATION OF SMOOTH PURSUIT AND SACCADDES FOR THE CONTROL OF EYE DISPLACEMENT

Having shown that both the smooth and saccadic eye movements discriminated between the different levels of target acceleration for the longer initial visible ramp durations, we sought to determine how the response of these two systems (i.e., total eye displacement) during the occlusion interval was combined in an attempt to match the target displacement. Again, the average total eye displacement was computed (horizontal dashed lines in Fig. II.6) and compared with the response to each acceleration level.. This revealed a significant interaction between ramp duration and target acceleration for both the 0deg/s and 8deg/s pre-occlusion velocity conditions; $F(6,30)=5.34$, $p<0.01$, $F(8,40)=3.47$, $p<0.01$, respectively. Group mean data in Fig. II.6 (left column) shows that, as expected given the findings for the measures of smooth and saccadic eye motion reported above, total eye displacement did not differ with target acceleration for an initial ramp duration of 200ms. There was a complete lack of eye displacement from either smooth pursuit or saccades during the occlusion interval for the 0deg/s pre-occlusion target velocity (upper panel), which resulted in total eye displacement close to zero. For the 8deg/s condition (lower panel), there was substantial eye displacement during the occlusion for the 200ms ramp duration but there was, however, no difference in total eye displacement across the different levels of target acceleration. Conversely, the middle and right columns

of Fig. II.6 show that when the target was initially presented for 500 or 800ms, total eye displacement differed according to target acceleration for both the 0deg/s (upper panel) and 8deg/s (lower panel) pre-occlusion velocity conditions. The regression statistics shown in Table II.1 indicate that the change in total eye displacement was proportional to target acceleration in presentations with 500 or 800ms initial ramp. Still, across all initial ramp durations, the combined response from SAD and SED failed to match well the target displacement for the higher levels of acceleration (e.g., 4 and 8deg/s² for the 8deg/s pre-occlusion target velocity) and resulted in significant undershoot.

Comparison of the individual contribution from the saccadic and smooth pursuit system to total eye displacement for the 0deg/s pre-occlusion target velocity shows that when there was substantial eye motion during the occlusion interval (500 and 800ms ramps) this was dominated by the saccadic system. Averaged over the different target accelerations, there was 3.3 (500ms ramp) and 2.6 (800ms ramp) times more contribution from saccades than smooth pursuit to total eye displacement. In contrast, comparison of the individual contribution from the saccadic and smooth pursuit systems to total eye displacement for the 8deg/s pre-occlusion target velocity indicated that eye motion during the occlusion interval was not dominated by one eye movement system. Averaged over the different target accelerations, there was 0.8 (200ms ramp), 0.7 (500ms ramp) and 0.7

(800ms ramp) times less contribution from saccades than smooth pursuit to total eye displacement.

Discussion

In this study we investigated the ocular pursuit response of human subjects to accelerating target motion. To determine if the drive underlying ocular pursuit is modified according to an on-line prediction of target acceleration made during pursuit of the initial visible ramp, we examined smooth and saccadic eye movements during the transient occlusion of a moving target. A combination of target parameters were chosen that enabled us to disambiguate whether ocular pursuit was driven according to target acceleration or a measure of target velocity. Specifically, we arranged presentations such that target velocity just prior to the transient occlusion did not differ with target acceleration, and hence was not related to the ensuing target velocity. This design enabled to distinguish between the following three hypotheses. First, if subjects based their extrapolation on the pre-occlusion target velocity, their oculomotor response should not change in accord with target acceleration (final velocity hypothesis). Second, if the oculomotor response were based on the mean target velocity of any period of the initial visible ramp, it would be negatively related with target acceleration (mean velocity hypothesis). Third, if the extrapolated response during the transient occlusion were based on the different levels of target acceleration

(acceleration hypothesis), this should be reflected in the smooth and saccadic eye movements.

In line with previous studies of human ocular pursuit (Becker & Fuchs, 1985; Bennett & Barnes, 2003, 2005; Orban de Xivry *et al.*, 2006), we observed that a combination of smooth pursuit eye movements and saccades was made in response to the disappearance of a moving target. More importantly, and consistent with the acceleration hypothesis, we found that both types of eye movement showed signs of acceleration discrimination when target motion was visible for at least 500ms. During the initial, visible part of the target motion leading up to the transient occlusion, the smooth eye velocity was appropriately scaled to target velocity (0 or 8deg/s) generated by the different levels of target acceleration (4, 8, 12, 16 or -8, -4, 0, 4, 8 deg/s²). The smooth eye velocity then deflected from its pre-occlusion trajectory, but recovered to a level that was positively scaled, albeit with some error in absolute magnitude, to target velocity at reappearance. This would not have been expected if smooth eye velocity were controlled using a measure of target velocity taken just prior to the transient occlusion (final velocity hypothesis). Furthermore, the difference in recovery for each level of target acceleration was not consistent with an extrapolation based on a measure of mean target velocity during the initial ramp, which was negatively related to target acceleration (mean velocity hypothesis).

In the longer presentations where there was evidence of scaling the oculomotor response to target acceleration, there was still significant retinal slip when target acceleration was -8 to 8deg/s^2 . These results are qualitatively similar to those from Bennett and Barnes (2006b) in which they found no difference between start-occlusion and end-occlusion eye velocity when presentations of accelerating target motion (4 and 8deg/s^2) were received in random order (Bennett & Barnes, 2006b). Thus, it would seem that while information related to target acceleration can be extracted on-line during the initial visible ramp, the process is not entirely sufficient to drive a fully predictive oculomotor response in the absence of visual input. This contrasts with the improved tracking of an occluded accelerating target that is presented in blocked order, where there is a strong expectation in advance of the upcoming target motion (Bennett & Barnes, 2006b).

In addition to the effects on smooth pursuit, the saccadic eye displacement (SAD) was also positively related to target acceleration in presentations with the longer initial visible ramp durations. For presentations in which pre-occlusion target velocity was 0 or 8deg/s after 500 or 800ms of target motion, there was a difference in SAD during the transient occlusion between the most extreme levels of target acceleration. In other words, subjects exhibited more saccadic eye displacement in presentations where the target displacement was only partially compensated by the smooth eye displacement. Consistent with our previous work (Orban de Xivry *et al.*, 2006), it

would appear that the smooth and saccadic eye movements work in combination to maintain eye displacement towards the trajectory defined by target acceleration, even in the absence of the target. Further support for this notion was evident in the proportional contribution made by the saccadic and smooth pursuit systems to total eye displacement during the transient occlusion. In presentations with 0deg/s pre-occlusion target velocity, subjects responded with relatively little smooth eye displacement (SED) during the transient occlusion. This was probably due to the fact that they had to first reverse the smooth eye movement, and then slowly build it up again during the transient occlusion. Nonetheless, subjects compensated for the lack of smooth eye displacement with a large contribution from the saccadic system. Conversely, when pre-occlusion target velocity was 8deg/s, subjects exhibited a similar contribution from smooth eye displacement and saccadic eye displacement.

Interestingly, despite showing greater smooth eye displacement in presentations with pre-occlusion target velocity of 8deg/s compared to 0deg/s, in combination with SAD this was not sufficient to eliminate the position error at the moment of target reappearance for the 4 and 8 deg/s² targets (Fig. II.6). This might seem surprising given that the contribution from saccades was not particularly large. However, there are several reasons why this might have occurred. First, it is possible that by using a relatively short occlusion interval, subjects did not have sufficient time to exhibit

more than 1 or 2 saccades (see Bennett & Barnes, 2005). Second, it is important to remember that subjects were instructed to maintain pursuit of the target during the transient occlusion, and as such, it would not have been appropriate to make particularly large saccades that took towards the predicted reappearance position and hence long ways off the occluded trajectory. Finally, and related to both the above, it is possible that subjects only had a relatively primitive prediction regarding the upcoming target motion because the experimental design only permitted this to be formed on-line during pursuit of the initial visible ramp.

Together, the observed smooth and saccadic eye movements provide clear evidence that subjects extracted target acceleration on-line when the initial visible ramp was at least 500ms, and used this to control pursuit prior to and during the transient occlusion. It would appear that an initial exposure of 200ms was insufficient to perform these operations. First, there was a lack of scaling of eye velocity to target velocity leading up to the transient occlusion. Second, and most important, the lack of scaling observed leading up to the transient occlusion was still evident at the moment of target reappearance. For presentations with 0deg/s pre-occlusion target velocity, target displacement had changed by a further 1.62 to 6.6deg, whereas target velocity had increased between 3.6 to 14.4deg/s (4 and 16 deg/s²). These values are well within the range of established displacement (Watamaniuk & Heinen, 1999) and velocity (McKee, 1981) sensitivity. Still, eye displacement and velocity did not change during

the occlusion interval and therefore failed to match the corresponding characteristics of target motion (Fig. II.6). For presentations with 8deg/s pre-occlusion target velocity, eye displacement and velocity changed by a similar amount during the occlusion interval. This shows that even when there was sufficient time to exhibit a recovery during the transient occlusion, an initial ramp of 200ms was not sufficient to discriminate target acceleration and use this to accurately control the oculomotor response. Instead, subjects exhibited a default response that provided a reasonable balance between overshooting and undershooting the different target trajectories experienced in the experiment, which is consistent with the final velocity hypothesis

Our finding that ocular pursuit does not scale to target acceleration following an initial 200ms ramp indicates either that the temporal limits of this process are longer than those required to extract target velocity or that larger target displacement are required in order to extract acceleration compared with extraction of velocity. Evidence concerning the time to extract velocity comes from experiments by Lisberger (1998), who examined normal pursuit initiation, which is often characterized by the occurrence of an initial saccade with a latency of approximately 200ms. Lisberger demonstrated that, although pre-saccadic smooth eye velocity was much lower than the target, post-saccadic smooth eye velocity closely matched target velocity, implying that target velocity had been effectively extracted during the first 200ms. Interestingly, though, our finding that 200ms

was not sufficient to scale ocular pursuit to target acceleration is in accord with the temporal limits of acceleration discrimination reported in psychophysical studies. For example, it has been shown that perceptual discrimination of target acceleration for an absolute judgment task (i.e., judge acceleration per se and not whether acceleration differs between presentations) is more accurate when the target motion is presented for 600ms compared to 300ms (see Fig.3 in Brouwer *et al.*, 2002). Indirectly, then, the results of the present study provide further evidence for the suggestion that pursuit and perception share inputs from a common motion processing stage (Beutter & Stone, 1998; Madelain & Krauzlis, 2003; Stone & Krauzlis, 2003). Finally, in our experiment, the relatively short target presentation before occlusion was associated with relatively small target displacement. Therefore, target displacement for the 200ms condition did not fully activate MT neurons, which have large receptive fields (between 4 and 25 deg, Felleman & Kaas, 1984). This partial MT activation could result in a poor estimation of target acceleration. Following this hypothesis, larger target acceleration, which would produce larger target displacement, would be detected even if the duration of the presentation does not exceed 200ms.

If it is accepted that the processing of accelerating motion in humans is not achieved directly via acceleration sensitive cells, it follows that on-line extraction of acceleration could be achieved indirectly through a process of sequential sampling of the velocity signal. This requires a mechanism in which velocity information from

the immediate past is temporarily stored so that it can be “compared” with current velocity. There is evidence for such behaviour from motion perception tasks (Greenlee *et al.*, 1995). The notion of sampling and temporarily storing velocity information is also one that we have previously put forward to explain the ability to make anticipatory smooth pursuit movements (Barnes & Asselman, 1991), which can be scaled to several different levels of velocity presented in a sequence (Barnes & Schmid, 2002; Collins & Barnes, 2005). In addition, we have shown that a good approximation to the acceleration/deceleration characteristics of sinusoidal target motion can be achieved by sampling and storing velocity information from a single half cycle at 250 ms intervals (Barnes, 1994; Barnes *et al.*, 2000). Most recently, we proposed a modified version of this process, which enabled us to generate realistic simulations of the smooth pursuit eye movements made in response to an accelerating motion signal that underwent a transient occlusion (Bennett & Barnes, 2006b). The results of the present study are consistent with the general logic of this approach to representing velocity-based information, and indicate that at least for the control of ocular pursuit, 200ms is insufficient to acquire the minimum of two samples required for this process.

As we have previously acknowledged, using on-line prediction demands a different mode of operation to that where subjects have a very clear expectation of the upcoming target motion characteristics in

advance of the presentation. By randomising presentation order and using several different combinations of target motion characteristics, it would be behaviourally unrealistic for subjects to generate a persistent representation of the upcoming target motion that could be fed forward to the oculomotor controller. Instead, if subjects were to predict the upcoming target motion, this would have to be generated on-line by extracting the relevant velocity and acceleration signal from the initial visible ramp. Here, it is crucial to emphasize the point that on-line prediction does not equate to using efference copy to perpetuate eye motion. For human ocular pursuit, efference copy-based models are unnecessarily restrictive and do not account well for voluntary influences. Moreover, in such models, efference copy reflects only the most recent eye velocity and hence does not incorporate information regarding target acceleration. As we have shown in the present study, eye velocity at 50ms into the transient occlusion does not relate well to eye velocity at the end of the transient occlusion. We suggest that on-line prediction may be an early stage in the process of representing target motion, whereby the comparison between two or more velocity samples provides only an approximation of the future target motion.

Chapter III

EVIDENCE FOR SYNERGY BETWEEN SACCADES AND SMOOTH PURSUIT DURING TRANSIENT TARGET DISAPPEARANCE

Introduction

Visual tracking of a moving target is a common process in our everyday life. This ability allows us to play sports requiring hitting and catching balls, and is also used in our everyday life when navigating within our surrounds (Land & Furneaux, 1997; Rushton & Wann, 1999; Land & McLeod, 2000; Rodrigues *et al.*, 2002; Brouwer *et al.*, 2003). Estimating the final position of moving objects may not always be sufficient to perform these actions because it does not account for unexpected changes in the target motion. Instead, it is typical to continuously predict the target motion in order to maintain the target image on the fovea. The oculomotor system can achieve this form of prediction using a corollary discharge mechanism (Robinson *et al.*, 1986) that feeds the system with an efference copy of the ongoing eye movement. As well as enabling the oculomotor system to

overcome the inherent perceptual-motor delay, prediction is particularly useful when the target moves behind another object. In this case, visual feedback is no longer available to correct for any small mismatch between the eye and object motion, and therefore prediction of occluded target motion is required to minimize position and velocity errors between eye and target at reappearance (Filion *et al.*, 1996).

Visual tracking of a moving target is usually achieved by the collaboration between two oculomotor subsystems: saccades and smooth eye movements (see Krauzlis & Stone, 1999 for reviews; Krauzlis, 2004). In the event that eye and target position are not perfectly matched, for example after an unexpected change in the target path, eye and target have to be realigned. The saccadic system is used to compensate for position mismatch between eye and target by triggering corrective saccades. During visually guided pursuit, the amplitude of catch-up saccades is based on the prediction of the difference between eye and target position at the end of the saccade (de Brouwer *et al.*, 2001; de Brouwer *et al.*, 2002a). However, even when the target suddenly disappears, the saccadic system is able to trigger saccades to the expected position of the invisible target (Barborica & Ferrera, 2004). Indeed, Filion *et al.* (1996) showed that primates can approximately predict target position when it has disappeared behind an occluder. The smooth pursuit system is used to compensate for velocity mismatch (i.e., retinal slip) between eye and

target, and achieves this during visually guided pursuit by increasing gain. However, when the target is occluded and retinal slip is not available, there is an exponential decay of eye velocity (Pola & Wyatt, 1997; de Brouwer *et al.*, 2001), which continues to zero if the target is not expected to reappear (Mitrani & Dimitrov, 1978). In contrast, when the target is expected to reappear, eye velocity decreases until it reaches a plateau value where it is maintained (Becker and Fuchs 1985; Pola and Wyatt, 1997), or recovers in anticipation of target reappearance (Becker & Fuchs, 1985; Bennett & Barnes, 2003). The eye velocity trajectory during a transient target disappearance can be modelled by a modification of the pursuit gain (Bennett & Barnes, 2003; Churchland *et al.*, 2003; Madelain & Krauzlis, 2003; Bennett & Barnes, 2004), and simulates well the finding that the decrease in eye velocity is dependent on the experience of the subject (Madelain & Krauzlis, 2003), and that the scaling of the recovery is modified according to expectation of target velocity at reappearance (Bennett & Barnes, 2004).

It has also been shown that subjects use a combination of saccades and smooth pursuit to continue eye motion during target blanking. In a recent study, Bennett and Barnes (2005) reported that the saccades were triggered and directed to the expected target position, and by generally overshooting they combined with the reduced eye velocity to match the target displacement reasonably well. However, to date, there has been no quantitative analysis of how saccades triggered during target blanking interact with the

contribution from the smooth pursuit system. Therefore, to examine this issue we used a target blanking paradigm where both position and velocity of target at reappearance could vary independently. This paradigm allowed us to show that the hypothesised gain increase which elicits the predictive recovery was influenced only by the velocity of the target at reappearance, not by its position. Moreover, we showed that the saccadic system accounted for the target position at reappearance, not velocity, and furthermore that it took into account the variability of the smooth eye displacement. Therefore, beside the interaction between saccadic and smooth pursuit systems based on retinal signals, we demonstrated here that there is a synergy between both systems when there is no visual input, and hence a combining of information from efference copy of saccadic and smooth eye movements.

Methods

EXPERIMENTAL SET-UP

Six healthy human subjects (mean age: 28.7 years), all of whom had previous experience of ocular pursuit tasks, participated after giving informed consent. All subjects had normal or corrected-to-normal vision, were healthy and without any known oculomotor abnormalities. The experiments were carried out according to a protocol approved by the University of Manchester local ethics committee and in accordance with the Declaration of Helsinki.

Subjects sat in a purpose-built dark room, facing a flat white screen (1.5x1.5 m) at a viewing distance of 1.7 m. Their head was restrained with head clamps and a chin rest. We projected onto the screen a green fixation target, with a diameter of 0.6 deg and luminance of 0.5 cd/m², and a red pursuit target, consisting of a ring of 12 light emitting diodes that were optically reduced to form a ring of dots with a diameter of 1.2 deg and luminance of 0.5 cd/m². The green fixation target was illuminated throughout the experimental sessions, and remained stationary at a position of -20 deg to the left of the screen center. The red pursuit target was reflected from a mirror galvanometer, which controlled its horizontal movement across the screen. Visibility of the red pursuit target was controlled by toggling the illumination of the diodes. Eye movements were recorded at 200 Hz using a Chronos eye tracker (Skalar Medical BV) which is based on high-frame rate CMOS sensors (Clarke *et al.*, 2002). The eye tracker has a resolution better than 0.1 deg in a range of measurement of ± 40 deg. A calibration procedure was performed in which subjects pursued the red target following an ellipsoidal path with horizontal amplitude of 20 deg and vertical amplitude of 10 deg at a frequency of 0.195 Hz.

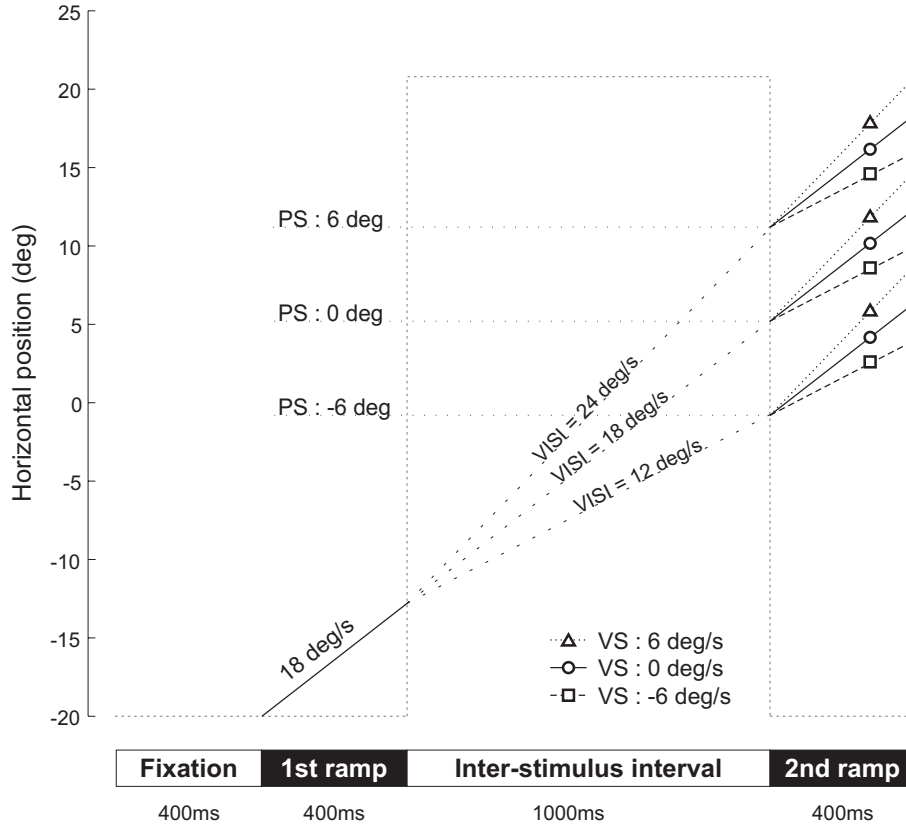


Figure III-1: Representation of pursuit target position versus time across a presentation. Vertical axis gives horizontal target position (deg) and horizontal axis time (ms). When time bar (on the bottom of the graph) is black, red pursuit target was visible. During first ramp interval, target had a constant velocity 18 deg/s. The inter-stimulus interval is delimited by the light grey dotted line that is low outside ISI and high during ISI. The oblique dashed line represented during ISI gives the three possible paths for the virtual target which corresponded to the three different PS. During the 2nd ramp interval, pursuit target path had 9 possible paths, three for each possible PS. For one given PS, the possible paths were defined by the three possible target velocities of the 2nd ramp. Triangle shape superimposed on a dotted line, circle shape superimposed on a continuous line and square shape superimposed on a dashed line corresponded, respectively, to 2nd ramp velocity of 12, 18 and 24 deg/s.

PARADIGM

Subjects performed 11 blocks during which they were required to visually track the red pursuit target. Presentations were received in blocks in order to maximise stimulus predictability, and differed according to the visibility of the red pursuit target and its motion characteristics. In the initial part of each presentation, prior to pursuit target motion onset, subjects were presented with the green fixation target alone at a position located -20 deg to the left of screen centre for 2000 ms (rest period). An audio cue was then given for 80 ms to signal the start of the presentation. The start of the audio cue corresponded to the start of the fixation period which lasted 400ms. After this fixation period, the red pursuit target began to move rightward at a velocity of 18 deg/s.

In the first two blocks subjects received 8 presentations during which the pursuit target was visible for 1800ms of constant velocity motion (continuous build-up presentation), followed by 8 presentations in which the pursuit target was visible for only 400ms (interrupted build-up presentation). They then received a further 9 blocks of 10 presentations each consisting of 2 continuous build-up presentations, followed by 8 test presentations. In the test presentations the pursuit target first appeared for a 400ms ramp but then was occluded for 1000ms inter-stimulus interval (ISI), before reappearing for a further 400 ms ramp motion. All presentations lasted

4210ms in order to give sufficient time for subjects to return their gaze to the green fixation in preparation for the upcoming presentation.

The target motion characteristics were modified during the ISI such that the target reappeared at one of three possible positions and with one of three possible velocities (see Fig. III.1). The reappearance positions were computed as if the pursuit target moved from the endpoint of the first 400 ms ramp at a velocity of 12, 18 or 24 deg/s during the ISI (V_{ISI}). When V_{ISI} was equal to 18 deg/s the reappearance position was a simple linear extrapolation from the first ramp and resulted in zero position step. On the other hand, when V_{ISI} was equal to either 12 or 24 deg/s, the target appeared either closer (negative position step) or further (positive position step) than expected from the extrapolation of the first ramp. By varying V_{ISI} we effectively created a position step (PS) at the moment of target reappearance of -6 deg, 0 deg, or 6 deg. A similar procedure was used to generate the velocity step (VS), which thus represented the difference between actual and expected (from the first 400 ms, 18 deg/s) target velocity at reappearance. By modifying target velocity at the moment of reappearance we created a VS of -6 deg/s, 0 deg/s, 6 deg/s, which was independent of the reappearance position and hence PS.

To represent all possible combinations of the target motion parameters (3 PS and 3 VS), subjects received 9 blocks (preceded by 2 blocks of build-up presentations) in a single run of the experiment. A

particular combination of these three parameters remained constant within a block, but the order in which they were received was randomised across subjects to minimize sequence effects. The calibration procedure was performed prior to every four blocks. Three of the subjects performed two runs of the experiment giving a total of 18 experimental blocks, while the other three subjects performed four runs of the experiment giving a total of 36 experimental blocks. Each run of the experiment was performed on a separate day. Subjects were instructed to track the horizontal target as accurately as possible throughout the presentations. They were also told that a block always started with two continuous build-up presentations but they did not know what parameters to expect before the first test presentation of each experimental block.

DATA ANALYSIS

Eye and target positions were sampled at 200 Hz and stored for offline analysis with Matlab (Mathworks, Inc). Position signals were low-pass filtered using a zero-phase digital filter (autoregressive, forward and backward filter, cutoff frequency: 35 Hz). Eye velocity and acceleration were derived from position signals by means of a central difference algorithm. Saccades were detected using an acceleration threshold of 500 deg/s^2 , and were considered to occur during the ISI if their onset fell 100 ms after the start, and before the end of the ISI. Their latency was then computed with respect to the start of ISI. Saccades were labelled forward if their

velocity peak was in the same direction as the target velocity, otherwise they were labelled as backward. The total contribution of the saccadic system to the displacement during the ISI (SAD) was obtained by summing the signed amplitude of all the saccades. To obtain desaccaded smooth eye velocity, we then removed the identified saccades plus an additional 5 data points (equivalent to 25 ms) at the beginning and end of the identified saccade trajectory from the eye velocity trace. The removed data were replaced by a linear interpolation routine based on the smooth eye velocity before and after the saccade (for more details see de Brouwer *et al.*, 2002a).

To calculate the characteristics of the saccadic movements we subtracted the contribution of the smooth pursuit system from the saccadic amplitude. The smooth eye displacement during the saccade was obtained by multiplying the estimate of the mean smooth eye velocity during the saccade (obtained by linear interpolation) by its duration. The contribution of the smooth pursuit system to the displacement during the ISI was obtained by integrating the smooth eye velocity during this period.

To compute the magnitude of occurrence of minimum velocity reached during the ISI, we first filtered the desaccaded smooth eye velocity traces at 20 Hz. We then simply searched the eye velocity data during the ISI for the minimum velocity and the corresponding time. The eye velocity data for each presentation were presented on screen and visually inspected, so that when minima were incorrectly

identified by the automatic analysis they could be corrected under interactive control. In some trials, there was no clear minimum velocity during the ISI, and hence no minimum velocity was computed.

We analyzed the steady-state response to the manipulation of target reappearance position and velocity (test presentations 3-8 within each block). To determine if there was an effect of PS and VS on our measures of the smooth and saccadic response, the intra-block mean data for each dependent variable were submitted to separate 6 subject by 3 PS (-6, 0, +6 deg) by 3 VS (-6, 0, +6 deg/s) analysis of variance (ANOVA) with repeated measures on the last two factors. Where we sought to determine if there was a difference between two separate measures of eye velocity (e.g., eye velocity minimum compared to eye velocity at the moment of target reappearance), these were included as an additional repeated measure in the ANOVA design. Main and interaction effects were further analysed using Tukey's HSD post hoc procedure (alpha level was $p < 0.05$).

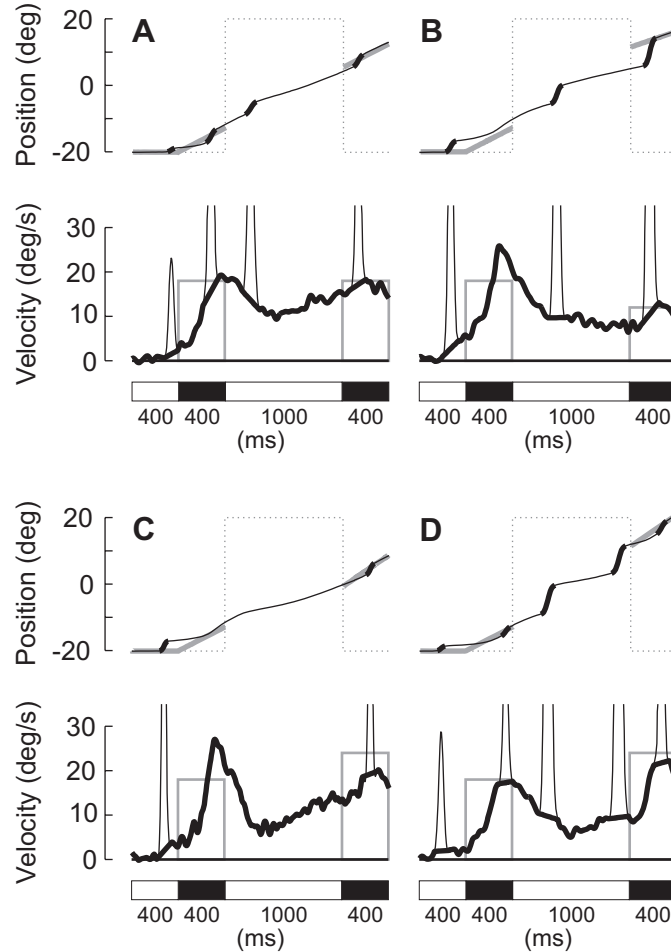


Figure III-2: Representation of eye (black traces) and pursuit target (grey traces) position (deg, upper traces) and velocity (deg/s, lower traces) vs. time (ms) for 4 typical presentations of a single subject (panels A, B, C, D) where PS (deg) and VS (deg/s) were equal to (0,0), (6,-6), (-6,6) and (6,6). When time bars (at the base of graphs) are black, pursuit target was visible. On the position panels: thin dotted line is high during ISI and low otherwise; thin eye traces correspond to smooth eye movements; overlaid thick eye traces represent saccades. On the velocity panels: thick eye traces represent desaccaded smooth eye velocity; thin eye traces represent saccades that were removed and replaced by linear interpolation.

Results

TYPICAL EXAMPLES

Representative examples of the pursuit response to various test presentations are shown in Fig. III.2. As expected given the predictability of the fixation period, subjects exhibited anticipatory eye movements (smooth and saccadic) before the target appeared for the first 400 ms ramp. Eye velocity continued to increase during the first ramp until it matched target velocity. Subjects then continued to move their eyes during the ISI, although smooth eye velocity was reduced compared to that in continuous build-up presentations ($VS=0$, $PS=0$). In general, smooth eye velocity decayed following target offset and then recovered to a level that was scaled to target velocity at reappearance (panel A, C, and D). In presentations with a -6 deg/s VS (panel B) the recovery was represented by a sustained eye velocity at a reduced level. This pattern of decay followed by a scaled recovery during the ISI occurred in 86.4% of all test presentations, and confirmed that the response was both anticipatory and predictive of target reappearance. While there was evidence of corrective saccades during the visible portions of the presentations, the reduced smooth eye movements during the ISI were also often combined with one (panel A and B) or several saccades (panel D) despite there being no visual feedback. This was not always the case, and as can be seen for a presentation with a negative position step and positive velocity step (panel C), smooth eye movements alone were sufficient to align gaze

to the target position at reappearance. Smooth eye movements alone represented 8% of all the responses ($N=882$).

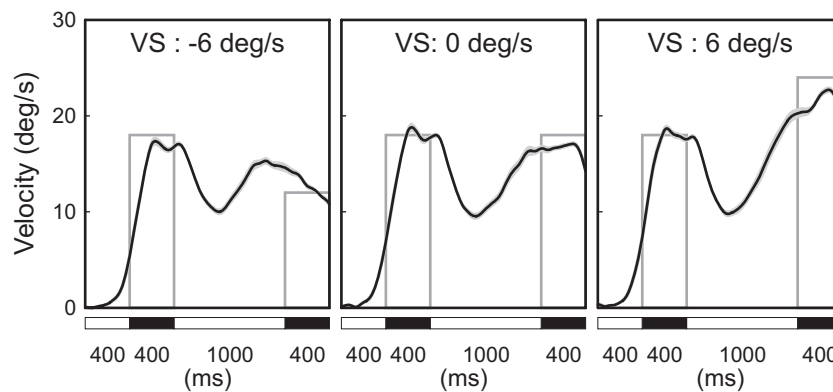


Figure III-3: Representation of the mean eye velocity (deg/s) of one subject vs. time (ms) for the three different VS when PS was zero ($V_{ISI} = 18$ deg/s). Black lines represent mean eye velocity; Dark grey lines represent target velocity; light grey surface around eye velocity traces corresponds to standard error (SE). When time bars (on the bottom of the graphs) are black, pursuit target was visible.

SMOOTH EYE VELOCITY

Figure III.3 shows a representative example of an individual subject's average eye velocity profiles as a function of the different velocity steps for the case where there was no position step; the results were similar for negative and positive position steps. Again, it can be seen that for this subject there was decay in smooth eye velocity during the ISI, which then recovered to a level that increased as target velocity at reappearance increased. Note that in the $VS = -6$ deg example, eye velocity increased prior to target onset and then decreased towards target velocity. When examined as a group with all individual-subject data pooled together (collapsed across velocity and

position steps), the minimum velocity declined, on average, to 47% (N=761, SE=0.01%) of the eye velocity at the beginning of the ISI (mean=17 deg/s, SE=0.08 deg/s). In those examples where there was a clear minimum, repeated measures ANOVA between eye velocity at the start of the ISI and minimum eye velocity indicated that the decay was significant (Post-Hoc Tukey HSD test, $p < 0.05$) for each subject in each condition (except for one condition in one subject). This decay was neither influenced by PS ($p = 0.27$) nor by VS ($p = 0.47$).

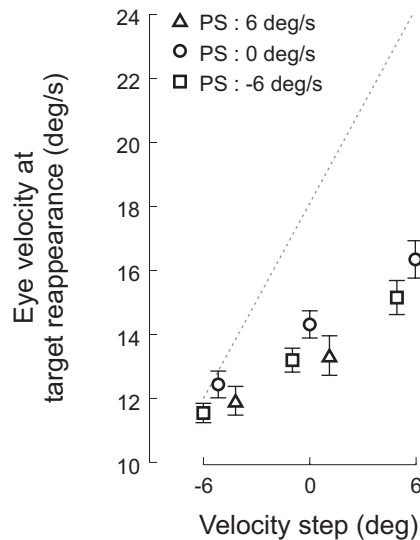


Figure III-4: Eye velocity at target reappearance (deg/s) for each combination of VS (horizontal axis) and PS. Triangle shape, circle shape and square shape correspond, respectively, to a position step of -6, 0 and 6 deg/s. Grey dotted lines correspond to target velocity at reappearance.

Further ANOVA indicated that there was a significant difference between the eye velocity minimum compared to eye velocity at the moment of target reappearance ($p=0.0095$). Post-hoc analysis (Tukey HSD test) confirmed this effect was evident across

each combination of PS and VS in 5 of the 6 subjects. It was also confirmed that eye velocity at reappearance was scaled to target velocity ($F(2,878)=40.92$, $p<0.0001$), and this effect was present in 5 out of the 6 subjects (F-test, $p<0.05$). For a negative VS, eye velocity at target reappearance was approximately equal to target velocity at reappearance ($99.7\%\pm 1.6\%$ (SE)), whereas for a zero or positive VS, eye velocity reached 75% ($\pm 1.9\%$) and 66% ($\pm 1.8\%$) of the expected reappearance velocity, respectively (see Fig. III.4). Therefore, although smooth eye velocity at the moment of target reappearance was scaled to the expected VS, it did not match well the actual target velocity and resulted in considerable retinal slip. As can be seen in Fig. III.4, which shows the group mean eye velocity at target reappearance as a function of PS and VS, the scaling of eye velocity at target reappearance was not influenced by PS ($p>0.12$).

Thus, during the ISI, there appeared to be two phases. In the first phase (decay), the smooth eye velocity was neither influenced by PS nor by VS, thus there was no influence of target parameters. In contrast, in the second phase (recovery) which is related to the anticipation of target reappearance, smooth eye velocity at target reappearance was influenced by VS alone. We tested whether the influence of VS on the smooth response occurred at a fixed time during the ISI. To estimate the time when VS begins to influence the smooth response, we performed a Tukey Post-Hoc test on each of the 200 samples along the ISI. For each subject, PS and sample, we tested

whether the mean eye velocities were different between $VS=0$ and $VS=-6$, between $VS=0$ and $VS=6$ and between $VS=-6$ and $VS=6$. We found that the time of divergence varied from 0.2 to 0.9 s from the beginning of the ISI. This shows that there was no clear segregation in the timing of the decay and recovery phases.

SACCADES

As previously noted (see Fig. III.2A, B and D), saccades also contributed to the eye displacement during the ISI, although observation of the individual-subject data indicated that they appeared less prevalent when there was a negative PS. This could be because fewer saccades were required to match eye displacement to a smaller target displacement during the ISI when PS was negative. To test this hypothesis we examined the contribution of saccades (i.e., saccadic occurrence, amplitude and endpoint location) to eye displacement during the ISI as a function of PS and VS.

Firstly, we found that the number of saccades increased significantly (F-test, $F(12,881) = 12.6$ $p < 0.0001$) with PS (on average 1.27, 1.61 and 2.14 saccades per presentation for $PS = -6, 0$ and 6 deg), although they were independent of VS. As a consequence, there was an increase in the number of presentations without any saccades as PS decreased. For example, the percentage of presentations in which there was only pure smooth eye movement was 18% when there was a negative PS, compared to 5% and 1% when there was a zero or positive PS, respectively. Furthermore, when saccades were

separated into two categories (i.e., forward and backward saccades, made in the same or opposite direction to the target), we found that there was a greater percentage of backward saccades (approximately 25% of the total number of saccades) triggered during the ISI when PS was negative. Saccades thus tended to counter the rightward smooth eye displacement in order to match the expected negative step in target displacement. In contrast, with a positive PS, subjects exhibited more saccades, of which the majority (92%) were forward in the direction of the target. In this case, saccades contributed to the rightward smooth eye displacement as expected target displacement increased.

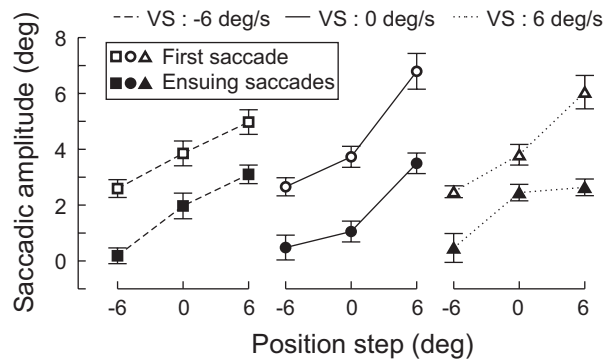


Figure III-5: Average amplitudes (deg) of first saccades (open symbols) and subsequent saccades (closed symbols) during ISI as a function of PS for each VS. Triangle shape superimposed on a dotted line, circle shape superimposed on a continuous line and square shape, superimposed on a dashed line correspond, respectively, to 2nd ramp velocity of 12, 18 and 24 deg/s.

Saccadic amplitude (first and subsequent) was likewise influenced by PS ($F(2,889) = 70.95$, $p < 0.0001$ and $F(2,688) = 66.31$, $p < 0.0001$ for first and subsequent saccades, respectively), but was independent of VS ($F(12,879) = 0.07$, $p = 0.99$ and $F(12,678) = 0.08$, $p = 0.99$ for first and subsequent saccades respectively) (see Fig. III.5). However, the amplitude of the first saccade exhibited during the ISI (Fig. III.5, open symbols) was larger than subsequent saccades (closed symbols) (F-test, $F(1,1581) = 168.05$, $p < 0.0001$). Forward saccades represented 87, 95 and 98% of the first saccades for negative, zero and positive PS ($N=187$, 237 and 237 respectively). Therefore, the smaller average amplitudes of subsequent saccades can be explained by the increased proportion of backward saccades as a function of PS (46% (PS = -6, $N=71$), 22% (PS = 0, $N=143$) and 14% (PS=6, $N=235$) respectively).

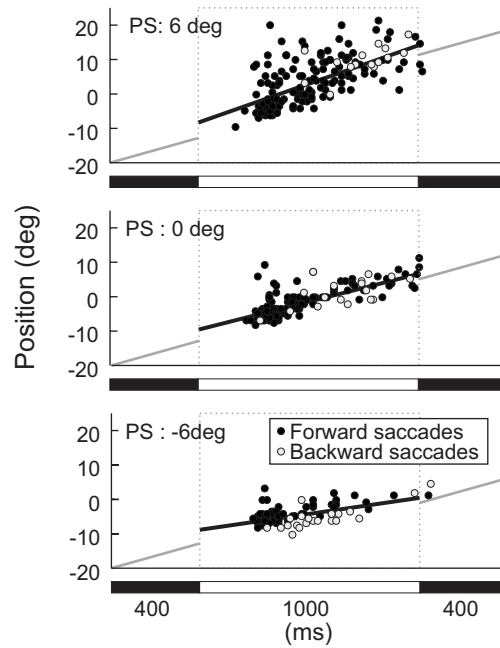


Figure III-6: Offset position (deg) from a single subject vs. time (ms) of saccades during ISI for each PS when VS was zero. Closed symbols represent forward saccades and open symbols backward saccades. Black oblique lines represent linear best-fit. Grey lines correspond to target position before and after ISI. Time bar (bottom of the graphs) is black when pursuit target is present. The ISI is delimited by the light grey dotted line that is low outside ISI and high during ISI. Dots beyond the end of the ISI correspond to saccades starting during the ISI.

PS (deg)	VS (deg/s)	R	α	β
-6	-6	.76	-9.8	10.3
-6	0	.60	-8.8	9.3
-6	6	.53	-8.3	8.1
0	-6	.75	-10.2	18.6
0	0	.76	-9.6	16.3
0	6	.72	-9.5	16.4
6	-6	.7	-8.2	20.3
6	0	.65	-8.3	22.4
6	6	.78	-9.4	22.7

Table III-1: Parameters related to the regression fit presented in Fig. III.6. First and second columns, respectively, represents PS and VS values. Third column shows correlation coefficient. Fourth and fifth columns provide the intercept and slope coefficient of the fit line ($y = \alpha + \beta \cdot (t-0.4)$).

The scaling of the saccadic response to PS during the ISI can also be seen in Fig. III.6, which shows how the endpoint of saccades fell in the neighbourhood of the virtual target path corresponding to a PS alone (VS of 0 deg/s). Regression lines appeared to be reasonably parallel to the virtual path that the target would have followed according to the change in V_{ISI} and hence PS, resulting in coefficients for the slope that matched well the unseen target velocity (see Table III.1). In order to see if PS or VS and saccadic offset time interact in influencing the saccadic endpoint, we performed a Homogeneity-of-slopes test which revealed that the relation between endpoint of saccades and times of saccadic offset was influenced by PS ($p < 0.0001$) but independent of VS ($p = 0.9$). In other words, the slope of the regression lines was dependent on PS and not on VS, as shown

in Table III.1. To verify that the saccades were directed to the unseen target path and not to a fixed location such as the reappearance target position, we examined the end position of first and ensuing saccades. If these saccades were aimed towards the same fixed location, the end positions should be similar. However, this was not found to be correct; the end position of first and second saccades were significantly different ($p < 0.0001$).

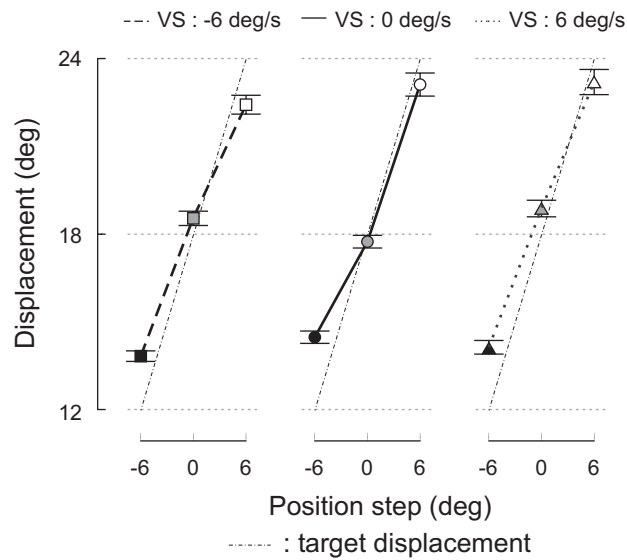


Figure III-7: Eye (dashed, continuous and dotted lines with symbols) and target (point and bar lines) displacement (deg) vs. PS for each VS. Horizontal dotted grey lines correspond to the different target displacements. Triangle symbol superimposed on a dotted line, circle symbol superimposed on a continuous line and square symbol superimposed on a dashed line correspond, respectively, to 2nd ramp velocity of 12, 18 and 24 deg/s. Black, grey and white symbols correspond to negative, zero and positive PS, respectively.

CONTROL OF EYE DISPLACEMENT

Having shown that the saccadic system adapts to the position step, while the smooth pursuit system scales the smooth eye velocity according to the expected target velocity at reappearance (VS), we sought to determine whether the combined response of these two systems led to an eye displacement over the ISI that matched well the target displacement. Figure III.7 shows that the total eye displacement (saccades + smooth eye displacement) was, in fact, scaled to the target displacement during ISI. For the three different VSs, there was a very similar pattern of total eye displacement. For a negative PS (black symbols), the position error at the moment of target reappearance was negative, with the eyes ahead of the target by 1.5 deg on average ($N=290$ and $SE=0.12$ deg). When there was no PS (grey symbols) the position error at target reappearance was almost zero (mean=0.15 deg, $SE=0.14$ deg and $N=298$). Finally, for a positive PS (white symbols), the eyes were behind the target, resulting in a position error equal to 1.5 deg on average ($SE=0.23$ deg and $N=194$). In conclusion, eye displacement during the ISI was influenced by target displacement (ANOVA, $p<0.0001$) but not by target velocity at reappearance (ANOVA, $p=0.1$).

INTERACTION BETWEEN SACCADIC AND PURSUIT SYSTEMS.

Up to this point we have shown that the contribution from the smooth pursuit and saccadic systems brought gaze to approximately

the right position at the right time and with a scaled velocity. However, it remains to be verified if both systems worked in synergy to produce this response. To examine this issue we performed additional analysis on each individual subject's response to multiple presentations with identical target parameters (positive PS and VS). Representative data from a single subject are shown in Fig. III.8 (I, II, III and IV, N.B. these are selected examples and were not received sequentially). In these examples the smooth response during the ISI becomes stronger from presentation I to IV, and as a consequence there are fewer saccades during the ISI in presentation IV than in the other presentations. Additionally, comparison of presentations I to III, shows that the saccade amplitudes tend to decrease as smooth response during the ISI increased. Finally, it is noteworthy that in each of these 4 presentations there was a relatively small position error at target reappearance. Therefore, it would appear that this subject achieved this level of performance using a different combination of smooth eye movements and saccades during the ISI.

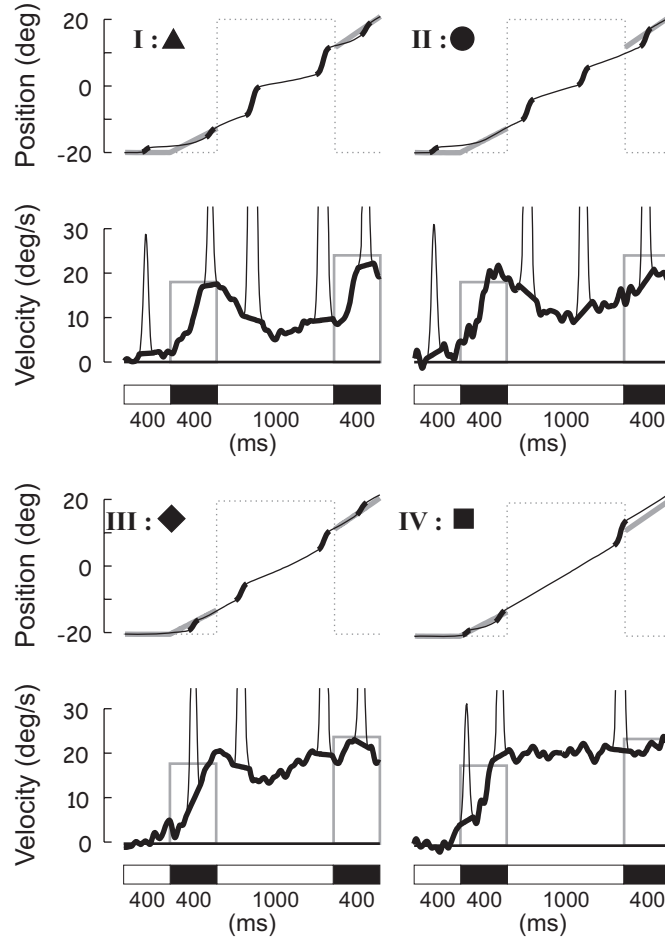


Figure III-8: Representation of eye (black traces) and pursuit target (grey traces) position (deg, upper traces) and velocity (deg/s, lower traces) vs. time (ms) for 4 typical presentations (panels I, II, III, IV) of the same combination of PS (=6deg) and VS (=6deg/s). When time bars (on the bottom of the graphs) are black, pursuit target was visible. On the position panels: thin dotted line is high during ISI and low outside; thin eye traces correspond to smooth eye movements and thick eye traces to saccades. On the velocity panels, thick eye traces represent desaccaded smooth eye velocity and thin eye traces saccades

To analyse these presentations in more detail we computed the contribution of both the smooth pursuit (i.e., smooth eye displacement

- SED) and saccadic systems (i.e., saccadic displacement - SAD) to the eye displacement during the ISI, and then determined how they covaried. In the examples of Fig. III.8 presentations I to IV were ranked in ascending order of SED (9.9, 13.3, 17.8 and 21.1 deg respectively). SED was related to the minimum eye velocity reached during the ISI ($r=0.9$, $p<0.001$), a smaller minimum occurring with a reduced SED. Conversely, SAD decreased from presentation I to IV (14.6, 9.1, 7.2 and 5.4 deg respectively). Therefore, the implication is that SED and SAD compensated for each other such that when there was a smaller (larger) SED, this was matched by a larger (smaller) SAD.

To investigate whether this compensatory role between the smooth and saccadic systems existed across each of the different combinations of PS and VS, we plotted separately for each combination of target parameters the relationship between SED and SAD during the ISI for all subjects' individual presentations (see Fig. III.9). Focusing on the upper right panel which corresponds to a positive PS and VS, and from which examples of Fig. III.8 were extracted, regression analysis revealed that the relationship between SED and SAD had a negative trend. The regression equation (for upper right panel: $SAD = 20.3 - 0.65 \cdot SED$) gives an idea of the mean compensation between saccadic and smooth pursuit system, and shows that in this case saccades compensated for 65% of the variation of smooth eye displacement. There was a significant relationship

between SAD and SED for all combinations of PS and VS (slope ranging from -0.49 to -0.82 , all $p < 0.001$, see first column of Table III.2), confirming the fact that SED increased as SAD decreased (see Table III.2). Comparison against the line representing the ideal compensation between SED and SAD (dashed line with a slope of -1) shows that the position error at target reappearance was relatively low.

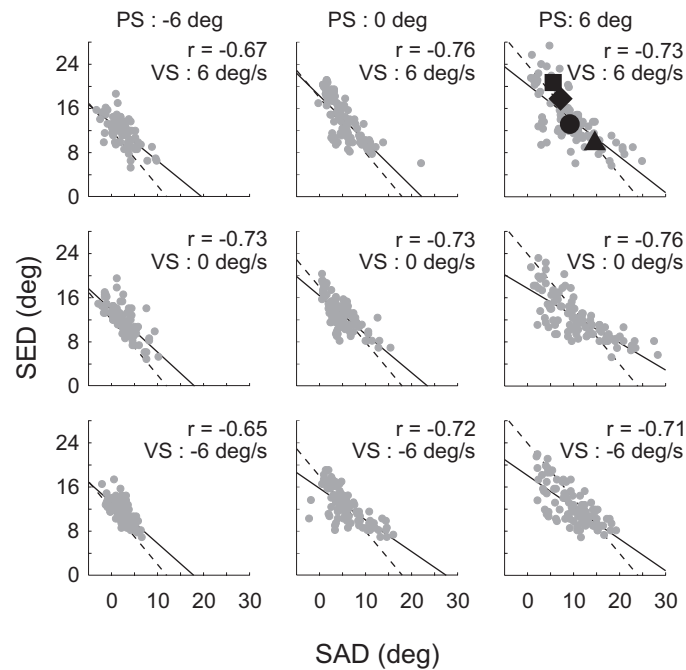


Figure III-9: Scatterplot of smooth eye displacement during ISI (SED, deg) vs. sum of saccadic amplitudes (SAD, deg) for each combination of PS and VS. Continuous lines represent linear best-fit. Dashed lines represent ideal compensation (see text). On the right upper panel, the four black symbols correspond to presentations shown in Fig. III.8.

Although it would appear in Fig. III.9 that there is considerable variability in the way participants combine their smooth and saccadic response during the ISI, we found that each subject demonstrated a

relationship between these two systems that was reasonably similar to that described in the group data. The correlation and slope coefficients for each subject as a function of PS and VS are given in Table III.2. For a zero or positive PS, the relationship between SED and SAD was negative and significant in the majority of the target conditions. However, for a negative PS, the correlation coefficients were rarely significant because the range of the parameters was too small (smaller than for zero or positive PS, as visible on Fig. III.9). Overall, though, these data confirm that each subject exhibited mutual compensation between the smooth pursuit and saccadic system in order to bring their gaze to the expected position at the expected time of reappearance.

		Inter-Subject		S1		S2		S3		S4		S5		S6	
PS	VS	r	β	r	β	r	β	r	β	r	β	r	β	r	β
-6	-6	-.65*	-.74*	-.63*	-.69*	.07	.15	.14	.3	-.46	-.45	-.4	-.4	-.09	-.07
-6	0	-.73*	-.77*	-.09	-.1	-.45	-.42	.7*	1.14*	.17	.16	-.67*	-.84*	.07	.04
-6	6	-.67*	-.68*	-.17	-.29	-.54*	-.8*	-.3	-.29	-.6*	-.42*	-.64	-.34	.84	.6
0	-6	-.72*	-.57*	-.63*	-.5*	-.67*	-.4*	-.14	-.15	-.71*	-.26*	-.15	-.05	-.27	-.13
0	0	-.73*	-.7*	-.49*	-.38*	-.56*	-.4*	-.41	-.9	-.81*	-.38*	-.15	.06	-.86*	-.59*
0	6	-.76*	-.82*	-.46*	-.5*	-.61*	-.27*	-.54*	-.67*	-.8*	-.25*	-.5	-.11	-.93*	-.68*
6	-6	-.71*	-.57*	-.28	-.16	-.64*	-.21*	-.8*	-.59*	-.4	-.17	-.62	-.2	-.95*	-.48*
6	0	-.76*	-.49*	-.82*	-.46*	-.62*	-.16*	-.49*	-.39*	-.73*	-.28*	-.51	-.14	-.92*	-.57*
6	6	-.73*	-.65*	-.74*	-.53*	-.54*	-.33*	-.01	-.01	-.78*	-.34*	.06	.03	-.89*	-.51*

Table III-2: correlation (r) and slope (β) coefficients for each target parameter and subject separately. An asterisk indicates that the value is significant ($p < 0.05$).

Discussion

In this study we investigated the ocular pursuit response of human subjects to the transient disappearance of a moving target under conditions where the target reappeared in a predictable way at a different velocity and/or different position to that expected from the first part of the motion. This enabled us to examine independently the response of the smooth and saccadic systems to different but predictable combinations of target position and velocity steps. In line with previous studies (Bennett & Barnes, 2006a), we observed that a combination of smooth pursuit eye movements and saccades was made in response to the disappearance of a moving target. The smooth pursuit component of this response, which has been studied in cats (de Brouwer *et al.*, 2001), monkeys (Kawano *et al.*, 1994; Churchland *et al.*, 2003) and humans (Becker & Fuchs, 1985; Bennett & Barnes, 2003; Madelain & Krauzlis, 2003), decayed following target disappearance and then recovered to a level that was scaled to the expected target velocity (Bennett & Barnes, 2004). However, there was no effect of a predictable velocity step on the discrete measures of the saccadic response. In addition, we found that the discrete measures of the smooth pursuit response during the transient (e.g., eye velocity minimum) were not influenced by the predictable position step, and hence change in target reappearance position. Rather, subjects modified their saccadic response in order to deal with the predictable position step and hence the change in eye displacement required to

align gaze at the moment of target reappearance. For example, when the target reappeared with a -6 deg position step, more saccades were made in the direction opposite to the smooth eye movement (backward saccades). In contrast, when the target appeared with a 6 deg position step, saccadic amplitudes were larger and mainly forward, in the direction of the smooth eye movement.

Initially, then, it appeared that given predictable changes in target parameters during the transient, the resulting smooth eye velocity was dependent on target velocity and independent of target position, whereas the saccadic response was dependent on target position and independent of target velocity. Our data thus shed light on an important issue related to the influence of position and velocity steps on smooth pursuit during transient target disappearance. Contemporary models of pursuit assume that target disappearance causes a modification of the gain of the internal efference copy feedback loop, which is responsible for the decay and subsequent recovery of smooth eye velocity (Bennett & Barnes, 2003; Churchland *et al.*, 2003; Madelain & Krauzlis, 2003; Bennett & Barnes, 2004). The decrease in gain to a non-zero value enables smooth eye velocity to be maintained at a reduced level, as observed experimentally (Becker and Fuchs, 1985). In order to obtain a predictive reacceleration, it is necessary to assume that this gain is then predictively increased prior to target reappearance. The fact that eye velocity at reappearance is independent of the position step implies

that the gain increase is dependent on expected target velocity at reappearance, not on expected target position.

The foregoing evidence gives the impression that the saccadic and smooth pursuit systems appear to be independent and aim to achieve different goals. However, in other contexts, both systems have been shown to collaborate in achieving a common goal. Indeed, retinal slip (velocity error) is used by the saccadic system to compute saccadic amplitude by taking eye and target velocity into account (2001; de Brouwer *et al.*, 2002a). In the present study, we also showed that eye displacement matched target displacement in an efficient way, indicating that the addition of the responses of both systems yields an appropriate result. This occurs despite the large variability of the smooth response across trials for the same target parameters. Thus we further investigated this interaction to determine whether there was compensation between the smooth and saccadic systems across individual trials. This revealed that the saccadic and smooth pursuit systems worked in synergy during target blanking. Indeed, although there was a tendency to maintain the smooth eye velocity during the occlusion interval, there was considerable variability in the smooth response from one presentation to another. In response to this variability, we found that the saccadic system modified its contribution to the total eye displacement to compensate for changes in the smooth eye displacement (see Fig. III.9). Whatever the magnitude of the smooth eye movement, corrective saccades tended to allow the overall eye displacement to closely match target

displacement. Thus, when smooth pursuit eye movements contributed less to the eye displacement during the ISI (quantified by the smooth eye displacement), the saccadic system increased its contribution. On average 65% of smooth eye displacement variability was taken into account by the saccadic system. This compensation for the variability of the smooth response occurred without any visual feedback, which suggests that extra-retinal signals derived from efference copy of smooth eye velocity are available to the saccadic system. This hypothesis is supported by Blohm et al. (2005b), who suggested that an efference copy of the smooth eye displacement is available to the saccadic system during a target localization task. These authors showed that when a target is flashed during smooth pursuit, the saccadic system can compensate for the smooth eye displacement that takes place after the moving target disappears and maintain space constancy. Interestingly, Blohm et al. (2005b) reported that, on average, a similar proportion of smooth eye displacement (55%) was taken into account.

In the Blohm et al experiment, the eye was directed towards a single point in space, whereas, in the current experiment, the eye appeared to be directed towards the continuing trajectory of the target, even though that target could not be seen. This implies that the subjects have access to an internal representation of the expected target trajectory and that they are able to compare this with an internal representation of eye position so as to make corrective saccades that

will minimize the difference between them. An alternative and simpler hypothesis might be that subjects learned the timing and position of target reappearance in allocentric coordinates and that they used this to compensate for any variability in their smooth eye movements. However, in this case it might be expected that the oculomotor system would release one corrective saccade towards the end of the ISI rather than multiple saccades (both forward and backward) throughout the ISI. The finding that saccades occurred throughout the ISI and that the endpoints of first and subsequent saccades were significantly different argues against this conclusion. Moreover, even if the subject did operate on the basis of directing gaze towards the target reappearance position during target blanking, the saccadic system would still need an internal representation of concurrent eye position to trigger well-fitted saccades.

NEUROPHYSIOLOGICAL SUBSTRATE

The smooth pursuit system of non-human primates is known to depend on several cortical areas, of which the most studied are the middle temporal (MT) and medial superior temporal (MST) areas (see Krauzlis, 2004 for a review). MT and MST receive retinal velocity error signals from the primary visual cortex (V1) but MST also receives extra-retinal inputs which are necessary to maintain smooth pursuit eye movement during transient disappearance of the target (Newsome *et al.*, 1988; Kawano *et al.*, 1994; Ilg & Thier, 2003). Extra-retinal signals were also found in the ventral intraparietal area

(VIP), which is highly connected with MST (Schlack *et al.*, 2003), and in the frontal eye field (FEF) (Fukushima *et al.*, 2002; Barborica & Ferrera, 2003), which also communicates with MST. Apart from the role of FEF in the saccadic system, an adjacent region of FEF is also involved in smooth pursuit (Tanaka & Fukushima, 1998; Tanaka & Lisberger, 2002a, b), and has been associated with the regulation of pursuit gain (Lekwuwa & Barnes, 1996b, a; Tanaka & Lisberger, 2001). Activation of this cortical network during pursuit eye movements has been described in several fMRI studies in humans (Petit & Haxby, 1999; O'Driscoll *et al.*, 2000; Schmid *et al.*, 2001; Lencer *et al.*, 2004).

In one such study, Lencer *et al.* (2004) reported that amongst other areas, FEF and LIP remained activated in humans during target blanking. This is consistent with findings in monkeys by Barborica and Ferrera (2004), who showed that activity in FEF is related to target velocity during fixation and, moreover, is maintained during target blanking. In addition, these authors showed that the monkeys were able to make a corrective saccade to the predicted position of the target at reappearance; this was taken to indicate that the activity in FEF might be integrated to obtain a representation of the unseen target trajectory. Extending upon this, Bennett and Barnes (2006a) proposed that, even when the eye is in motion and there is no visual feedback, the target velocity-related activity in FEF could be derived from extraretinal input. Integration of this signal would provide a

continuous internal representation of expected target trajectory, as described earlier. This could then be compared with an internal representation of eye position, and used by the saccadic system to trigger saccades directed towards the unseen target trajectory. It is noteworthy, however, that this representation of eye position should ideally take account of the combination of prior smooth and saccadic eye movements.

At present, the form of this internal representation is unknown. It could be a single position-coded signal derived from the brainstem or alternatively it might be derived from the combination of separate representations of smooth and saccadic components further upstream. The likely recipient of this position-coded signal (Bremmer *et al.*, 1997) is area LIP, which has an established role in remapping the visual scene when keeping track of saccades (Duhamel *et al.*, 1992; Heide *et al.*, 2001; Medendorp *et al.*, 2003) and of smooth pursuit eye movements or the vestibulo-ocular reflex (Powell & Goldberg, 1997; Snyder & Harper, 1999; Snyder, 2000), and could thus keep track of self-motion as proposed by Blohm *et al.* (2005b). We suggest that LIP is thus the most likely area where internal signals representing the continuing target trajectory and current position are compared during target blanking for the purpose of deriving corrective saccades.

Chapter IV

A DYNAMIC REPRESENTATION OF TARGET MOTION DRIVES PREDICTIVE SMOOTH PURSUIT DURING TARGET BLANKING

Prediction is a feature inherent to various motor systems. When lifting and moving an object, we are able to adjust the grip force in a predictive way to counteract the variation of the load force (Flanagan & Wing, 1998; Wolpert & Flanagan, 2001; Flanagan *et al.*, 2003). Similarly, prediction allows the oculomotor system to track a target moving along a predictable path with zero phase-lag by overcoming the inherent delays present in the oculomotor system (Dallos & Jones, 1963; Bahill & McDonald, 1983b; Barnes & Asselman, 1991; Barnes *et al.*, 2000).

The predictive mechanisms driving the smooth pursuit response during occlusion of a moving target have been widely studied in one dimension (Mitrani & Dimitrov, 1978; Becker & Fuchs, 1985). In this condition, both position (Filion *et al.*, 1996; Barborica & Ferrera, 2004) and velocity (Barborica & Ferrera, 2003; Ilg &

Thier, 2003) of the occluded target are available to the oculomotor system. However, around 100ms after target disappearance, the eye velocity starts to decay exponentially to zero if the target is not expected to reappear (Pola & Wyatt, 1997; de Brouwer *et al.*, 2001) or to a plateau value otherwise (Mitrani & Dimitrov, 1978; Becker & Fuchs, 1985). This eye velocity decay might be due to a decrease in the gain that regulates smooth pursuit eye movements (Tanaka & Lisberger, 2001; Churchland & Lisberger, 2002) or to the weakening of target motion signals held in short-term memory. In addition, when the duration of the occlusion is known in advance, a predictive eye velocity recovery takes place before the end of the occlusion (Bennett & Barnes, 2003, 2004, 2005). The level of this recovery is scaled to the expected target velocity at reappearance (Bennett & Barnes, 2004, 2006b; Orban de Xivry *et al.*, 2006). In these studies, the pre-occlusion target velocity determined the plateau value whereas the putative modulation of the gain during occlusions regulated eye velocity at target reappearance. Therefore, a static internal representation of pre- and post-occlusion target velocities was sufficient to drive the predictive smooth pursuit response during occlusions. However, it has never been investigated how the predictive smooth pursuit response looks like when post-occlusion target velocity is not available (for instance, when occlusion duration is not known in advance) and when pre-occlusion target velocity is not sufficient to drive the predictive smooth pursuit response during

occlusions (for instance, when target velocity varies during occlusions). In this condition, a dynamic internal representation of target motion (i.e. that evolves with time) is required to drive predictive smooth pursuit eye movements. However, the existence of such dynamic representation has never been demonstrated.

Recent behavioral and neurophysiological experiments showed that pursuit and saccades strongly cooperate in order to foveate moving objects (as reviewed in Krauzlis, 2005; Orban de Xivry & Lefevre, 2007a, b). This is also the case during occlusion of a pursuit target where there is a synergy between the smooth and the saccadic responses, i.e. saccades compensate for the variability of the smooth eye displacement (Orban de Xivry *et al.*, 2006). However, the possible influence of predictive saccades onto predictive smooth pursuit response has never been considered. The emphasis of this influence during occlusions in one dimension is complex because saccadic amplitudes are correlated to smooth eye velocity (Orban de Xivry *et al.*, 2006). Hence, the causality between these two factors is difficult to establish. For instance, contemporary models of the predictive smooth pursuit response during occlusions presume that this response is not influenced by the occurrence of predictive saccades (Bennett & Barnes, 2003; Churchland *et al.*, 2003; Madelain & Krauzlis, 2003).

In sum, the present study addresses two questions related to the predictive smooth pursuit response during occlusion of a pursuit target. The first question is related the nature of the internal

representation of target motion driving the smooth pursuit response (static vs. dynamic). The second question is related to the influence of position error on the predictive smooth pursuit response during occlusions. To address these issues, we asked subjects to pursue a target that moved along a circular path and that transiently disappeared in order to address these two open questions.

Methods

SUBJECTS

Six human subjects participated in the experiment after informed consent. Their age ranged between 22 and 40. Two of them were completely naive. They all had normal or corrected-to-normal vision and did not have any known oculomotor abnormality. All procedures were approved by the Université catholique de Louvain ethics committee and were in agreement with the Declaration of Helsinki. One of the subjects (#6) exhibited very few saccades during occlusions. Therefore, his data were systematically withdrawn from analyses related to saccades.

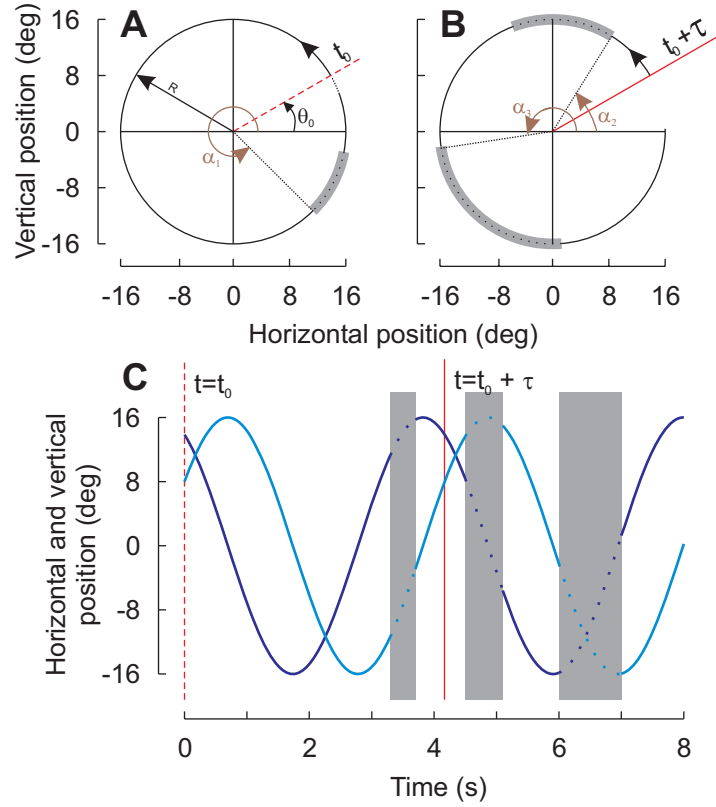


Figure IV-1: Representation of target motion in XY plots (panels A and B) and in position vs. time plot (panel C). In the XY plots, panel A represents the first revolution of the target along the circular path of radius R . At time t_0 , the target appears at (R, θ_0) in polar coordinates (represented by the dashed red line) and begins to move counter-clockwise along the circular path. The second revolution of the target is represented in panel B and begins at time $t_0 + \tau$ where τ is the period of target motion (represented by the continuous red line). During the revolutions of the target, it is occluded three times (dotted black lines on grey thick lines). The starting angles of the occlusions are α_1 , α_2 and α_3 . In panel C, we represented horizontal (dark blue) and vertical (sky blue) target position vs. time of the same two revolutions than in panels A and B. Dotted lines on grey bars represented the occlusion periods. Time correspondence between panels A and B and panel C is provided by the red dashed and continuous line that delimited the starting time of each of the two revolutions.

PARADIGM

Subjects were asked to pursue a visual target following a counter-clockwise circular path (see Fig. III.1). After a period of fixation for 500ms, the target began to move and remained visible for at least a half-circle (3.3 to 4s). Subsequently, there were three successive periods of target occlusion (represented by grey bars in Fig. III.1.C) ranging from 400 to 1000ms. After each of the three occlusions, the target reappeared for a period ranging between 800ms and 1500ms. Thus, each test trial consisted of four periods of visible target interleaved with three periods of occlusion. At the end of each trial, the target was switched off for about 2s.

The characteristics of the circular path varied randomly across trials. Both radius (9.6, 12.8 and 16 deg) and frequency (0.15, 0.2 and 0.25Hz) varied. The combination of the different radii and frequencies led to 5 different vectorial target velocities ranging from 9 to 25deg/s. The starting point of the circular trajectory (θ_0) was chosen at random on the circular path for each trial.

Experimental sessions consisted of several blocks of 13 test trials, lasting a maximum of 30 minutes. Each subject performed at least 4 experimental sessions which led to a minimum of 810 periods of occlusion per subject (maximum: 1125). At the beginning of each session, a learning block was presented to the subjects. It consisted of 13 learning trials during which the visual target moved counter-clockwise on a circular path with parameters (radius and frequency)

chosen in the same set as the test trials. However, the target was never switched off but remained visible for the whole duration of the learning trials (5s).

EXPERIMENTAL SETUP AND DATA ANALYSIS

Subjects sat in complete darkness in front of a translucent screen which was at a distance of one meter and covered a field of ± 40 deg horizontally and vertically. The target (0.2 deg) was a red laser spot which was back-projected onto the screen by two mirror-galvanometers. The galvanometers were controlled by a dedicated real-time computer which controlled their position and illumination (detailed description of the setup in Blohm *et al.*, 2003a). Eye movements were recorded using the scleral coil technique (Robinson, 1963; Collewyn *et al.*, 1975).

Eye and target position were sampled at 500 Hz and stored on a hard disk for offline analysis which was performed using Matlab (Mathworks Inc.). Position signals were low-pass filtered using a zero-phase digital filter (autoregressive, forward and backward filter, with a cutoff frequency of 48 Hz). Velocity and acceleration signals were derived from position by means of a central difference algorithm. All the trials were visually inspected and abnormal trials were eliminated from the database (blinks). In addition, we removed from the data all occlusions that were interpreted by the subjects as the

end of the trial (outlier analysis based on three standard deviations, which led to the rejection of 2.5% of the trials).

Saccades were detected using an acceleration threshold of 500 deg/s^2 , and were labeled predictive if their onset occurred at least 170 ms after the start of the occlusion and before its end. The first visually-guided saccades after the end of the occlusion were selected if their onset occurred in a time interval ranging from 75 to 400ms after the end of the occlusion. Measures of position error or heading direction were taken 25ms before and after saccades. To evaluate the smooth pursuit response, we analyzed both the vectorial eye velocity profile and the pursuit heading direction. The heading direction of the smooth pursuit response was computed as the direction of the tangent to the smooth eye position trace. The time courses of eye and target heading direction during the occlusions were measured relative to the heading of the target at the start of the occlusion.

Moreover, the horizontal and vertical eye velocity profiles (EV) were fitted with a non-linear function resulting from the multiplication of target velocity (TV) by a negative exponential (Fig. III.2). For the static memory model, TV is constant and equal to corresponding component of target velocity at target disappearance. For the dynamic memory model, TV varies in function of time and is equal to the actual target velocity. The parameters of the fit were: g , the eye velocity gain at the start of the occlusion; T , the time of eye velocity decay; G , the value of the eye velocity gain after the

exponential decay and τ , the time constant of the negative exponential. The constants were: R , the radius of the circular path, ω , the angular velocity of the target and ϕ , the angular target phase at the start of the occlusion. The non-linear fit was performed on the average velocity profiles using a least-square approximation (lsqcurvefit in Matlab). Vectorial eye velocity profiles were fitted with the same non-linear function with TV equal to the vectorial target velocity.

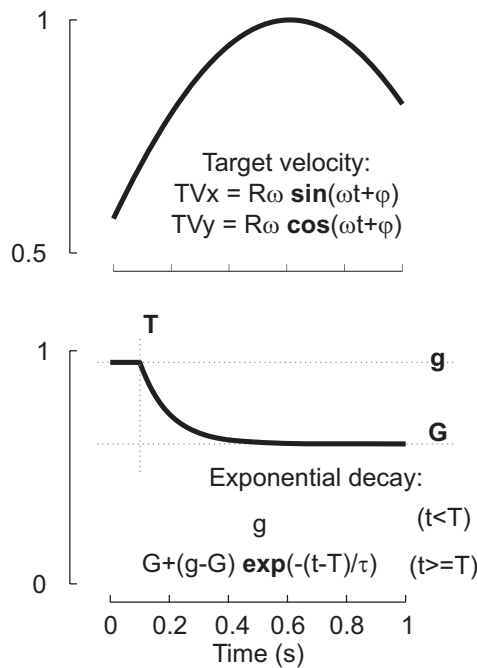


Figure IV-2: Illustration of the non-linear function used to characterize the eye velocity profile during the occlusions. This function resulted from the multiplication of target velocity (upper panel) with a negative exponential (lower panel). Y-scales are arbitrary. The parameters to fit were g , the gain at start of the occlusion; G the plateau value, T , the time of eye velocity decay, and τ , the time constant of the exponential. The constants were R , the radius of the circle, ω , the target angular velocity and ϕ , the angular position of the target at the start of the occlusion.

Statistical analyses (Anova, T-test) were performed using Statistica (Statsoft, Tulsa, OK). Sample means were compared using T-tests. To account for multiple comparisons, the p-values were corrected by means of the false discovery rate procedure (Curran-Everett, 2000).

Finally, throughout the analyses, some measures were expressed in polar coordinates (such as the angular target velocity). The angular component of the polar coordinates was expressed in degrees, noted deg_p , to avoid confusion with the degree unit of visual angle, noted deg . The three frequencies (0.15, 0.2 and 0.25 Hz) of the target led to angular velocities of 54, 72 and 90 deg_p/s .

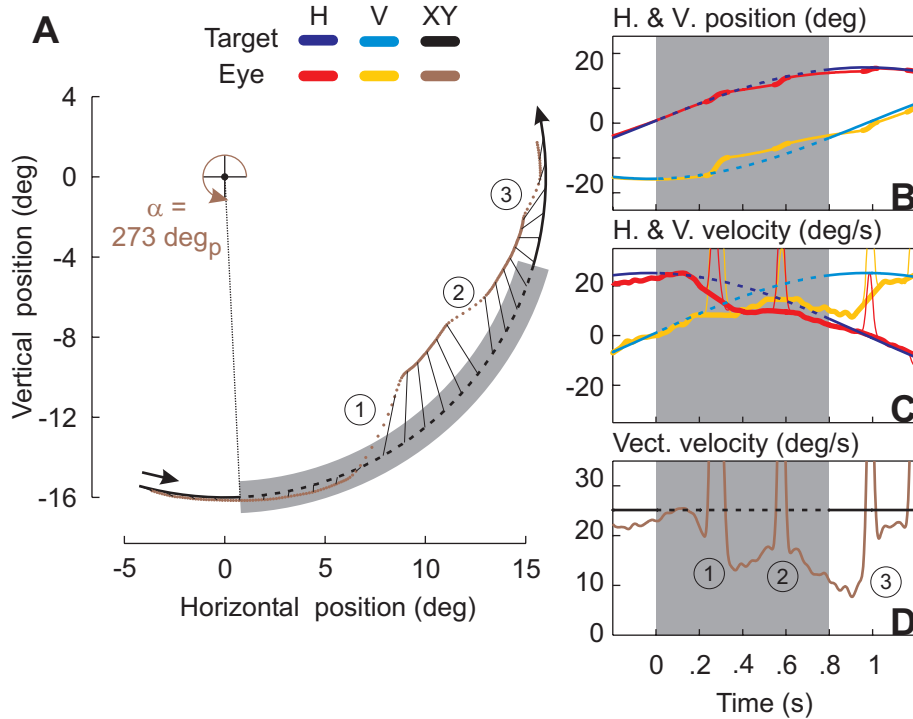


Figure IV-3: Typical oculomotor response to an occlusion during which the target was moving with the fastest target velocity. The color code for the four panels is given on top of panel A (H: horizontal; V: Vertical; XY: 2D or vectorial). Panel A: XY plot of both eye and target from 200ms before the occlusion until 400ms afterwards. The origin of the reference frame coincides with the centre of the circular path and the occlusion had a starting angle of 273 deg_p . Brown dots represent eye position every 6ms. Saccades are labelled 1, 2 and 3. Panels B, C and D respectively position, velocity and vectorial velocity vs. time for both eye and target. In panel B, the saccades are represented by a thicker trace. In panel C, the desaccaded smooth eye velocity is given by the thicker trace. Occlusion period is delimited by the grey area. H: horizontal; V: vertical; Vect: vectorial.

Results

Fig. III.3 shows a typical example of the oculomotor response during occlusion of a target moving along a circular path. The

occlusion of the pursuit target was associated with a decay of vectorial and angular smooth eye velocity that was often accompanied by the release of one or several predictive saccades (Fig. III.3, saccades #1 and #2). However, the vectorial eye velocity did not decay to zero but to a plateau value. The pattern of response (decay in vectorial eye velocity and predictive saccades) was typical of our trial population as the decay occurred in about 90% of the occlusions (84 to 95% depending on the subject). In addition, more than 75% of the smooth pursuit responses were accompanied by at least one saccade (75 to 91% across subjects, except for subject #6, 19%). Typically, a visually-guided catch-up saccade corrected for the position error at the end of the occlusion (Fig. III.3, saccade #3).

There was a general tendency for the first saccades in the occlusion to be centripetal, which means that they brought the eye towards the centre of the circle. In contrast, the second saccades were generally parallel to the circular path of the target (Fig. III.3.A). Both first and second saccades gave a phase advance to the eye with respect to the target. This feature appears clearly on Fig. III.3 by mean of the isochronic lines, connecting eye and target at the same instant in time (thin black lines in Fig. III.3.A). Indeed, before the saccades, the eye lagged behind the target whereas it was ahead afterwards. Isochronic lines also show that at the end of the occlusion, eye and target were in phase for this particular example (Fig. III.3). This phase synchronization between the eye and the target resulted from the

combination of saccadic and smooth pursuit predictive eye movements.

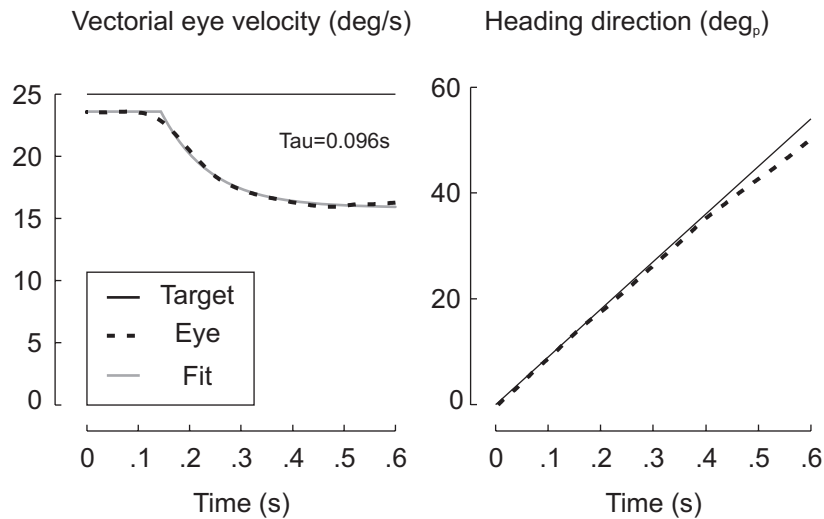


Figure IV-4: Average smooth pursuit response of all the subjects during the first 600ms of the occlusions. Left panel: average of vectorial velocity vs. time for both eye (dashed black curve) and target (black line). A negative exponential was fitted on the eye trace (dark grey curve, see Methods). Standard error of the mean was smaller than 1deg/s. Right panel: average of heading direction for both eye (dashed black curve) and target (black line). All the heading directions were computed with respect to the heading direction of the target at the start of the occlusion. Standard error was smaller than 1 deg_p. Only occlusions lasting more than 600ms and with the largest target velocity were selected for these graphs.

SMOOTH RESPONSE

As illustrated in the typical example, smooth eye velocity tended to decay during the occlusions (Fig. III.3.D). In agreement with previous studies in 1D, we found that vectorial eye velocity exponentially decayed after the target disappearance as shown in Fig. III.4.A. The time constant of the exponential ranged from 0.07 to

0.13s depending on the subject, except for subject #6 who had a time constant of 0.033s. This decay in the smooth response usually did not last for the whole occlusion. After a few hundreds of milliseconds, vectorial eye velocity reached a plateau, the gain of which varied across subjects (from 0.54 to 0.85) and across target velocities (Anova, $p < 0.001$). Surprisingly, this gain did not depend on the duration of the occlusion for four of the six subjects (ANOVA, $p > 0.05$ in at least 7 out of the 9 target conditions). The two last subjects showed a significant decrease of their gain with occlusion duration in the majority of the target conditions (7 and 8 of the nine conditions).

In two dimensions, the vectorial eye velocity is not sufficient to characterize the smooth pursuit response. The heading direction (namely the orientation) of the pursuit response must also be taken into consideration. Thus, the heading direction was computed relative to the target heading direction at target offset (see Methods). During the course of the occlusion, the heading direction of the target evolved over time (solid trace in Fig. III.4.B). Interestingly, the oculomotor system was able to predict accurately the heading of the target (dashed trace in Fig. III.4B). Indeed, the pursuit heading direction matched target heading direction almost perfectly during the first 600ms of the occlusions. This required a good knowledge of timing and an accurate representation of target heading direction over time.

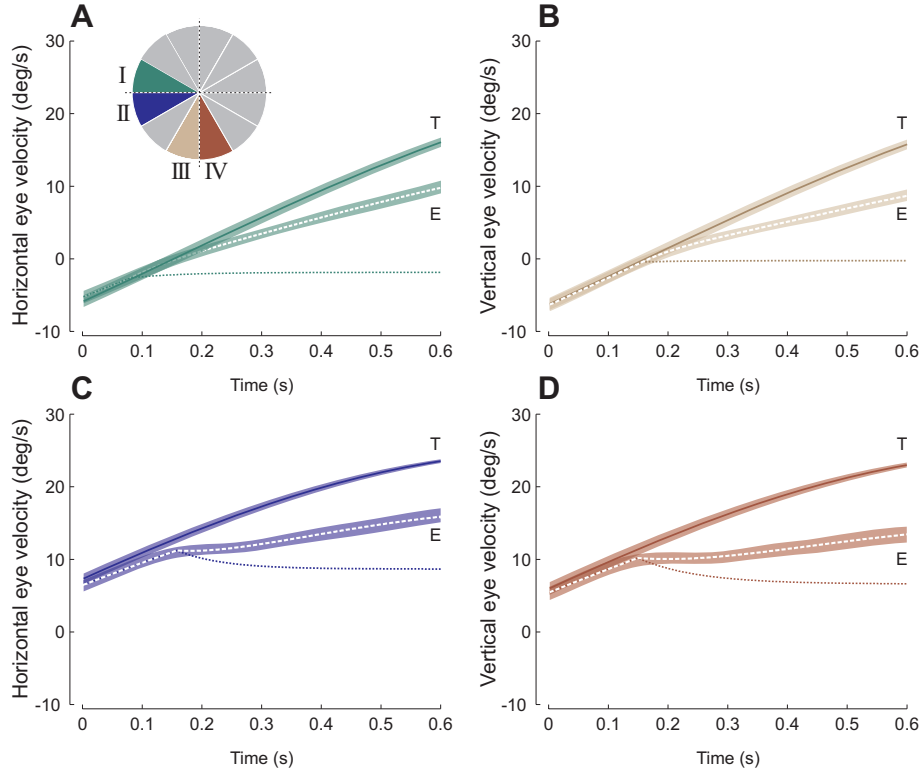


Figure IV-5: Description of the horizontal and vertical eye velocity components for different groups of occlusions. A, B, C and D: Horizontal and vertical components of target velocity (solid colored traces) vs. time for different groups of trials (I, III, II and IV, respectively). The confidence interval of the mean eye velocity traces is represented by the colored area (means not shown). The fit of the static memory model is represented by the thin dotted line. The fit of the dynamic memory model is represented by white dashed traces (see Methods). Inset: Categorization of the occlusions regarding their starting angle (see Fig. III.1) by bins of 30 deg_p. Groups I and III (resp. II and IV) gathered the occlusions starting just before (resp. after) the crossing of the horizontal or vertical axis, i.e. group I contains the occlusions with a starting angle between 150 and 180 deg_p and between 330 and 0 deg_p (with a reversed sign). A color was assigned to each group and is used in panels A and B.

The change in pursuit orientation during the occlusion implies that horizontal and vertical components of smooth pursuit remained

strongly coupled. Indeed, the longest occlusion duration combined with the largest target frequency yielded a target displacement of a quarter of a circle during the occlusions, which obliged the subjects to adapt their horizontal and vertical components of the pursuit response in synergy; i.e. one component of eye velocity increased while the other decreased. Therefore, these components remained scaled to the corresponding horizontal or vertical component of target velocity. For instance, when the occlusion started a few hundred milliseconds before the target crossed the horizontal or vertical axis, one component of target velocity reversed its sign during the occlusions. Accordingly, the sign of the horizontal or vertical eye velocity changed (group I, Fig. III.5.A and group III, Fig. III.5.B). Moreover, when the target was occluded just after one of the four cardinal points (Fig. III.5.C, group II and Fig. III.5.D, group IV), one of the components of target velocity was initially low and increased along the first 600ms of the occlusion. Accordingly, the corresponding eye velocity component increased in parallel.

The components of eye velocity did not perfectly match their respective component of target velocity. The difference between eye and target velocity seemed to increase along the occlusions as shown in Fig. III.5. However, Fig. III.4.A indicated that the vectorial eye velocity reached a plateau value after the exponential decay. Thus, we checked whether each component of eye velocity did exponentially decay with respect to either the corresponding component of target

velocity sampled during the pre-occlusion interval (static memory model) or the actual corresponding component of target velocity (dynamic memory model, see Methods). Fig. III.5 clearly rejected the static memory model as it did not predict the horizontal or vertical eye velocity during the occlusions. In contrast, the dynamic memory model yielded good fits of the data. Indeed, the fits lie within the confidence interval of the mean eye velocity profiles (white dashed trace in Fig.5). Moreover, mean fitted values ($\pm$ SE) for the time of velocity decay (152 ± 4 ms) and for the time constant of the exponential (107 ± 8 ms) matched the values found in the literature (Becker & Fuchs, 1985). Similar results were obtained when the fits were performed for each subject separately (time of velocity decay: 153 ± 2 ms; time constant of the exponential: 126 ± 5 ms).

SACCADES

During visually-guided pursuit of a moving target, the role of catch-up saccades is to correct for the position mismatch between eye and target. This is particularly true for the first visually-guided catch-up saccades after occlusions (see saccade #3 in Fig.3 for illustration). In this case, the Euclidean position error (PEEucl, illustrated in Fig. III.6.A) between eye and target is reduced by the occurrence of the first visually-guided catch-up saccade after occlusions (Fig. III.6.B, label "V"). In contrast, the position mismatch between the eye and the invisible target was not reduced by predictive saccades during

occlusions as illustrated by the first and second predictive saccades of Fig. III.3 (saccades #1 and #2). Indeed, on average, the first predictive saccades increased PEEucl (Fig. III.6.B, label "F"). In addition, the second predictive saccades maintained PEEucl at a similar level (Fig. III.6.B, label "S").

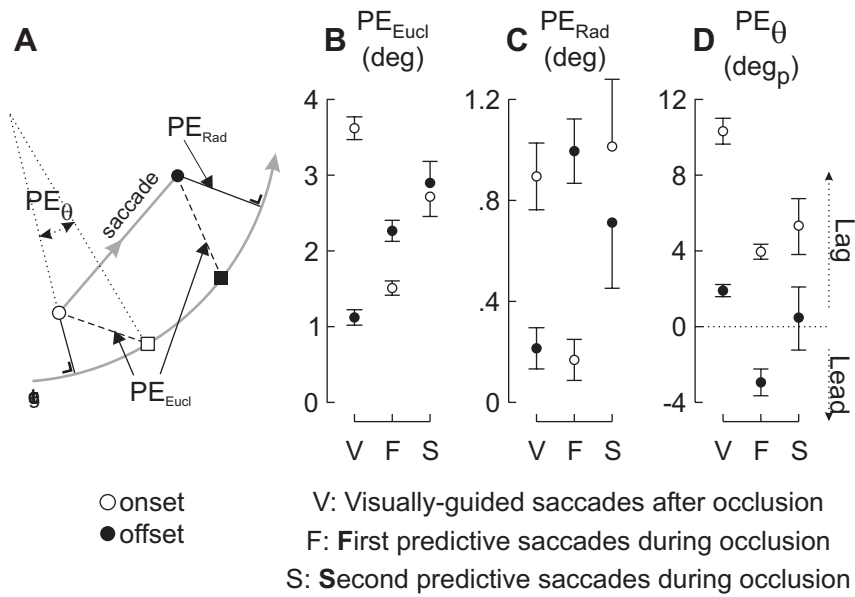


Figure IV-6: Evolution of different measures of position error around the time of saccades. A: Schematic representation of the three error measures. The target path is represented by the grey arc, the saccade by the grey arrow. Eye and target position at the moment of saccade onset (resp. offset) are indicated by an open (resp. filled) circle and an open (resp. filled) square. B, C and D: Mean Euclidean (PE_{Eucl}), radial (PE_{Rad}) and angular (PE_{θ}) position error ($\pm$ confidence interval) for the first visually-guided saccades (V) after the occlusions, the first (F) and second (S) predictive saccades during the occlusion. Positive values of PE_{Rad} correspond to eye position inside the circle and positive values of PE_{θ} correspond to phase lag.

However, some of the features of the predictive saccades described in Fig. III.3 are not reflected by the analysis of PE_{Eucl} .

Indeed, we noticed that the first predictive saccade brought the eye toward the centre of the circle whereas the second did not. In addition, we observed that after the first predictive saccades, the eyes were ahead of the target. Therefore, we tested other parameters such as radial (PE_{Rad}) and angular (PE_{θ}) position errors. PE_{Rad} represents the smallest distance between eye and the circular target path and PE_{θ} the difference of angular position between eye and target (Fig. III.6.A). Analysis of PE_{Rad} confirmed that on average, the first predictive saccades during occlusions brought the eye towards the centre of the circle whereas the second did not (Fig. III.6.C). On the other hand, PE_{θ} was reduced by both the first and second predictive saccades during occlusions (Fig. III.6.D). Furthermore, PE_{θ} was negative after the first predictive saccades, which indicated that the eye was in advance of the target (lead, Fig. III.6.D).

These observations were confirmed by statistical comparisons (T-tests) for each target velocity separately. The increase in PE_{Eucl} and PE_{Rad} resulting from the first predictive saccades were highly significant for all levels of target velocity ($p < 0.0001$). The second predictive saccades did neither decrease nor increase PE_{Eucl} ($p > 0.15$) but decreased PE_{Rad} for two of the five target velocities ($p < 0.05$). Finally, PE_{θ} was reduced by both the first and second predictive saccades and for each target velocity ($p < 0.01$). At the end of first predictive saccades, PE_{θ} was negative for all target velocities (T-tests,

$p < 0.01$). The multiple comparison procedure confirmed all these results.

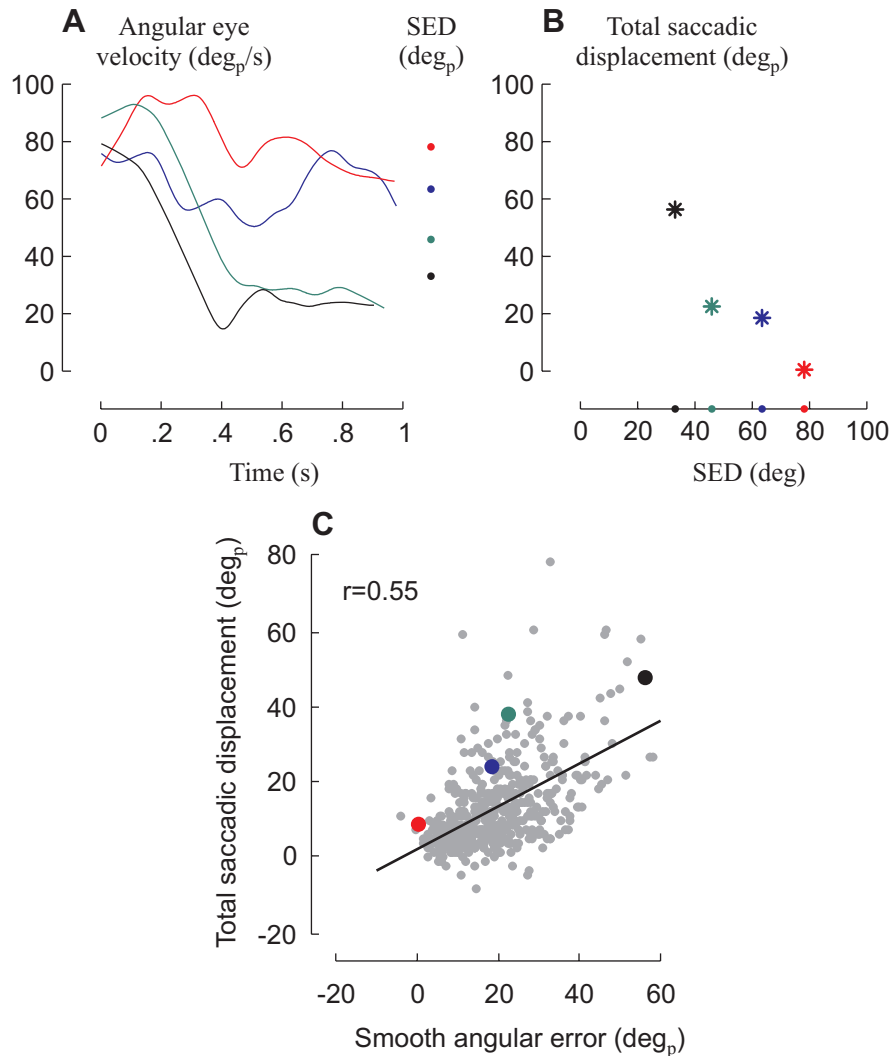


Figure IV-7: Saccades compensate for the variability of the predictive smooth pursuit response. A: Four typical angular smooth pursuit responses during occlusions from a single subject (#2). The illustrated responses occurred during occlusions that lasted more than .9s and with target velocity equal to 90 deg_p/s .

These four profiles (deg_p/s) are represented vs. time (s). The smooth eye displacement (SED, in deg_p) achieved during each of these trials is given on the right of the panel (colored points). B: The total angular saccadic displacement (sum of angular saccadic amplitudes, in deg_p) is represented vs. SED (deg_p) for each of the four typical profiles of panel A. The color points corresponded to the values of SED given in panel A. C: Correlation between total saccadic displacement (deg_p) and smooth angular error (deg_p) for the largest target velocity. The smooth angular error corresponds to the difference between the total angular displacement of the target during the occlusion and the total angular smooth eye displacement during the same occlusion. The four colored points correspond to the responses illustrated in panel A and B.

INFLUENCE OF VELOCITY SIGNALS ON PREDICTIVE SACCADES

During occlusions, the predictive smooth pursuit response was highly variable across occlusions (Fig. III.7.A). For instance, though the smooth angular velocity profiles presented in Fig. III.7.A were taken from a single subject, the angular smooth eye displacement (i.e. the integral of the angular smooth eye velocity) achieved during these occlusions varied between 33 deg_p and 78 deg_p for an angular target displacement around 85 deg_p . Interestingly, predictive saccades compensated for the difference between the angular smooth eye displacement and the angular target displacement (i.e. the smooth angular error). Indeed, for these four trials, the sum of the angular saccadic amplitudes (i.e. the total saccadic displacement) was negatively correlated with the angular smooth eye displacement (Fig. III.7.B). In other words, the lower the smooth eye displacement, the larger the total saccadic displacement. This indicates that the smooth angular error was accounted for by predictive saccades. We confirmed

this result by demonstrating that for the whole population of occlusions, the total angular saccadic displacement was correlated with the smooth angular error (Fig. III.7.C, $r=0.55$, target velocity of 25 deg/s, all subjects pooled together). This correlation was significant for each target condition (all subjects pooled together, correlation coefficient between 0.21 and 0.49). Finally, it was significant in 34 of the 45 conditions (5 subjects x 3 frequencies x 3 radii).

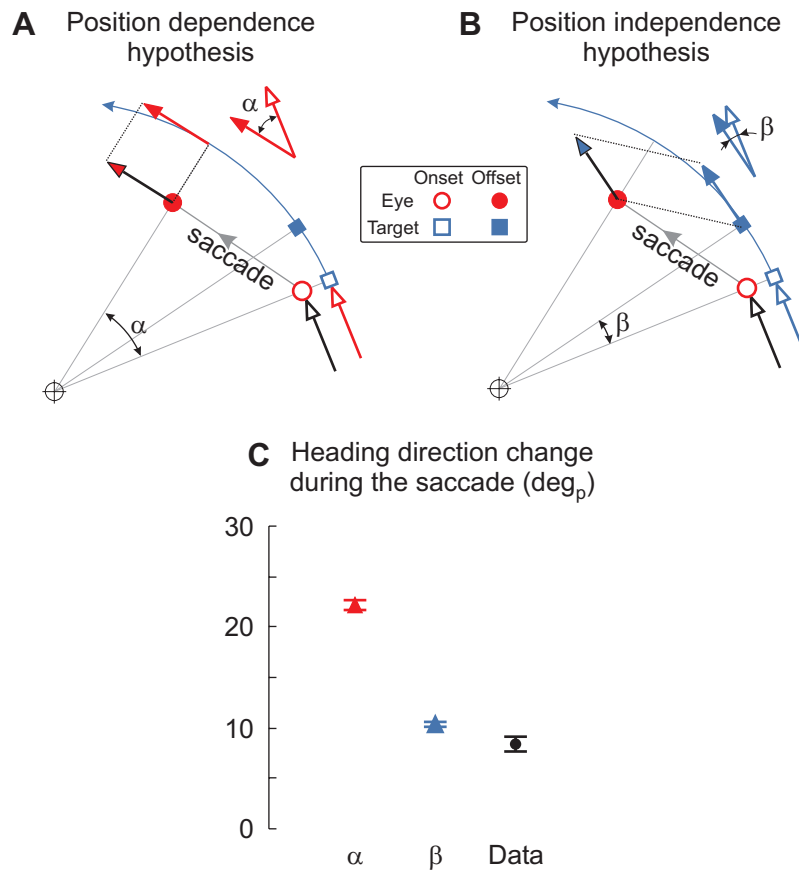


Figure IV-8: Hypothesized and actual change of heading direction around the time of saccades. A and B: The eye (resp. target) positions at saccade onset and

offset are represented with red open and filled disks (resp. blue open and filled squares). Heading directions at saccade onset and offset are represented with open arrows and filled arrows, respectively. Target path is represented by the thin blue line. Angular position of eye and target at saccade onset and offset are given by the thin grey line (radii of the circle). The centre of the circle is given by the small circle. **A:** Illustration of the position dependence hypothesis. It states that pursuit heading direction after the saccades (dark outlined and red filled arrow) is parallel to the circular target path (filled red arrow). The angle α represents the predicted change of pursuit heading direction during the saccades following the position dependence hypothesis. **B:** Illustration of the position independence hypothesis. This hypothesis states that pursuit heading direction after the saccades (black outlined and blue filled arrow) is parallel to the current target heading direction (blue filled arrow). The angle β represents the predicted change of pursuit heading direction during the saccades following the position independence hypothesis. **C:** Comparison between predicted and actual heading direction changes between saccade onset and offset. (All subjects and conditions pooled together) α : prediction from the position dependence hypothesis; β : prediction from the position independence hypothesis; Data: actual data.

INFLUENCE OF POSITION SIGNALS ON THE PREDICTIVE SMOOTH PURSUIT RESPONSE.

The predictive smooth pursuit response during occlusions was characterized by a decrease in vectorial eye velocity but an accurate heading direction on average (Fig. III.4). This accurate heading direction pleads in favor of a dynamic internal representation of target motion. However, such accurate average heading direction could also be obtained by a static internal representation of the circular target path. To test for this possibility, we investigated whether eye position influenced the heading direction of pursuit during occlusions. Indeed, if the predictive pursuit was driven by the circular path, pursuit heading direction should be parallel to the target path at any instant in time. Therefore, pursuit heading direction should be determined by the

angular position of the eye relative to the circular path (position dependence hypothesis), which only requires a static representation of the circular target path. In contrast, if pursuit heading direction was parallel to the current target heading direction at any instant in time (position independence hypothesis), pursuit heading direction should be determined by the current angular position of the target independently of eye position. Following this hypothesis, predictive pursuit should be driven by a dynamic internal representation of target motion. In sum, testing the influence of eye position on pursuit heading direction should reveal the nature of the internal representation (static or dynamic).

To disambiguate both hypotheses, we tested the influence of eye position on pursuit heading direction around the time of the first predictive saccades (Fig. III.8). Indeed, saccades largely modified the angular position of the eye (Fig. III.6.D) in a short period of time. Therefore, during saccades, angular eye position varied largely but angular target position was only slightly modulated. Thus, if the position dependence hypothesis was true, the pursuit heading direction should change as much as angular eye position during saccades (α in Fig. III.8.A) and, after the saccades, pursuit heading direction should be parallel to the target path. In contrast, if the position independence was true, the pursuit heading direction should change as much as the angular target heading direction during saccades (β in Fig. III.8.B). Therefore, after the saccades, pursuit heading direction should be

parallel to the actual target heading direction. To increase the difference between α and β , we selected saccades that brought the eye at least 6 deg_p ahead of target (30% of the first predictive saccades). Across all subjects and conditions (Fig. III.8.C), eye position jumped 22.1 deg_p (α) on average during the selected saccades whereas target position increased only by 10.4 deg_p (β). Interestingly, the actual average change in pursuit heading direction during the saccades was equal to 8.5 deg_p (Fig. III.8.C), which pleads in favor of the position independence hypothesis.

This intuition was confirmed by statistical comparisons for each of the conditions separately (3 target frequencies x 3 target radii x 5 subjects). For all conditions, the change in heading direction predicted by the dependence hypothesis was significantly larger than the actual one (T- tests, $p < 0.05$), which was confirmed by the multiple comparison procedure. In contrast, the prediction of the heading change during the selected saccades by the independence hypothesis compared to the actual change were not significantly different in the 35 of the 45 conditions (T-test, $p > 0.05$). The prediction from the position independence hypothesis overestimated the actual change in the remaining 10 conditions (T-tests, $p < 0.05$). However, the significance of these 10 comparisons was rejected by the multiple comparison procedure. The same results were found when the heading was measured 50ms after saccade offset rather than at saccade offset. In sum, pursuit heading direction was parallel to the actual heading

direction and pleaded in favor of the position independence hypothesis, namely in favor of a dynamic internal representation of target motion.

The rejection of any influence of position signals on the predictive smooth pursuit response should be confirmed by the analysis of the effect of the radial component of these saccades onto the vectorial eye velocity. Indeed, as these first saccades draw the eye towards the centre of the circle, vectorial eye velocity should decrease in such a way that angular eye velocity matched angular target velocity. To do so we correlated the change in radial position with the change in vectorial eye velocity during these saccades. Again, we found no evidence of influence of the saccades onto the predictive smooth pursuit response. Indeed, the correlations were non-significant (p-levels between 0.07 and 0.86, all subjects pooled together) in the nine conditions. This analysis rejected the possible influence of position signals on the predictive smooth pursuit response on the basis of extraretinal signals.

Discussion

During occlusion of a target moving along a circular path, we observed that vectorial smooth eye velocity decayed exponentially whereas the heading direction of smooth pursuit accurately matched target heading direction. This is the first experimental evidence that the smooth pursuit response during occlusion is driven by a dynamic

internal representation of target motion. In addition, we demonstrated that predictive saccades compensate for the variability of predictive smooth pursuit during occlusions whereas position signals do not influence the heading of predictive pursuit in 2D.

The smooth pursuit response during the occlusion of a pursuit target has been widely studied (Mitrani & Dimitrov, 1978; Becker & Fuchs, 1985; de Brouwer *et al.*, 2001; Mrotek & Soechting, 2006) and modeled in one dimension (Bennett & Barnes, 2003; Churchland *et al.*, 2003; Madelain & Krauzlis, 2003; Bennett & Barnes, 2004, 2005; Voss *et al.*, 2006). In these models, the exponential decrease in eye velocity after the disappearance of the tracked target was explained by a diminution of the gain element that regulates the smooth pursuit response (Tanaka & Lisberger, 2001; Churchland & Lisberger, 2002) or by the weakening of the motion signals held in the short-term memory. In addition, during target blanking, these models hypothesize that the retinal information is replaced by the output of a short-term velocity store that contains a static internal representation of target motion (Bennett & Barnes, 2003, 2004; Voss *et al.*, 2006). During occlusions in our data, we observed the effect of the putative gain reduction as evidenced by the exponential decay of the vectorial eye velocity toward a plateau value (Fig. III.4.A). However, how can we reconcile this gain reduction with the accurate matching between target and pursuit heading directions along the occlusions (Fig. III.4.B)? Indeed, though their gain exponentially decreased, both

components of eye velocity remained scaled to their corresponding component of target velocity (Fig. III.5). Therefore, this scaling demonstrated that the content of the short-term velocity store must be dynamic and closely represent the current target motion (Whittaker & Eaholtz, 1982). This dynamic internal representation could either be obtained by extrapolation of the pre-occlusion target motion (Bennett *et al.*, 2007) or built up by repetition of the same target motion (Bennett & Barnes, 2006a; Orban de Xivry *et al.*, 2006). Neural correlates of this dynamic representation has been found in the frontal eye fields (FEF) where the neuronal activity reflects an up-to-date estimation of target motion during occlusions (Barborica & Ferrera, 2003, 2004; Xiao *et al.*, 2006).

Such a dynamic internal representation could also come into play during visually-guided smooth pursuit. Indeed, primates have the ability to track a predictable moving target with zero-phase lag (Dallos & Jones, 1963; Barnes *et al.*, 1987; Barnes & Asselman, 1991; Barnes & Wells, 1999; Barnes *et al.*, 2000). This requires the prediction of the ongoing moving target. Up to now, current models predict future target trajectory 100ms in the future on the basis of previous target motion (Bahill & McDonald, 1983b; Kettner *et al.*, 1997; Shibata *et al.*, 2005). However, we demonstrated here that humans are able to predict target motion up to 600ms in the future. Therefore, we suggest that the dynamic internal presentation that drives predictive smooth

pursuit during occlusions could also drive predictive smooth pursuit during visually-guided smooth pursuit.

Thus, we propose that models of the predictive smooth pursuit response should be extended by including a dynamic internal representation of target motion, i.e. a representation that evolves with time. The importance of timing information has been also emphasized in many other contexts (Buonomano & Karmarkar, 2002; Buhusi & Meck, 2005) such as the trigger of catch-up saccades during visually-guided pursuit (de Brouwer *et al.*, 2002b) and anticipation for future events (de Hemptinne *et al.*, 2007). Such timing information is also crucial in order to evoke anticipatory eye movements that occur before target motion onset (Barnes & Asselman, 1991; Barnes & Wells, 1999; Heinen *et al.*, 2005; Badler & Heinen, 2006). In our study, timing information is necessary in order to maintain pursuit heading direction parallel to target heading direction. Their parallelism could facilitate the processing of visual motion by MT cells. Indeed, attending a particular direction of motion enhances the neuronal response to visual stimuli moving along the attended direction (Treue & Martinez Trujillo, 1999). This enhancement changes in function of the similarity between the attended direction and the preferred direction of the neuron (Martinez-Trujillo & Treue, 2004). In addition, some MT cells can even fire in prediction of the direction of the upcoming moving stimulus (Ferrera & Lisberger, 1997), reinforcing the neuronal response to stimuli in the same direction. Therefore,

aligning pursuit heading direction to target heading direction could facilitate motion processing at target reappearance.

In addition to its availability, we demonstrated that the dynamic internal representation of target motion alone drives the predictive smooth pursuit response during occlusions. Indeed, predictive pursuit response is not influenced by position signals during occlusions. This absence of position input to predictive smooth pursuit during occlusions is in contradiction with behavioral evidence of a position input to the smooth pursuit system (see review in Orban de Xivry & Lefevre, 2007b). This difference between predictive and visually-guided smooth pursuit response suggests that the position input might be based on sensory signals (Blohm *et al.*, 2005a), not on extra-retinal signals. In contrast, in this study, we confirmed that the saccadic system takes the predictive smooth pursuit into account and compensates for the variability of the predictive pursuit response even when the occlusion duration is not predictable in 2D (Orban de Xivry *et al.*, 2006). The predictive response of the saccadic system is added to the predictive smooth pursuit response (de Brouwer *et al.*, 2002a), without influencing it. In sum, the link between saccadic and pursuit systems is one-way.

Predictive and visually-guided saccades did not share the same goal. Catch-up saccades corrected for the position mismatch between eye and target (de Brouwer *et al.*, 2001; de Brouwer *et al.*, 2002b) whereas we found that predictive saccades did not correct for it but

gave the eye a phase advance on the target. This phase advance feature highlights the strategy of the subjects. Indeed, the predictive saccades gave the eye an advance with respect to the target even though the oculomotor system has access to an estimation of the target position during the occlusion (Filion *et al.*, 1996; Baker *et al.*, 2001; Barborica & Ferrera, 2004). This is consistent with one-dimensional studies where predictive saccades systematically overshoot the estimated target position (Bennett & Barnes, 2006a; Orban de Xivry *et al.*, 2006), which, in our study, corresponds to a phase advance. This study also reported that the first predictive saccade tended to be centripetal, which is likely related to the "shrinking circle illusion" that biased the perception of a circle into a smaller ellipse (Coren *et al.*, 1975; Bradley & Godiksen, 1984). This centripetal feature of the first saccades showed that internal representation of target trajectory can be biased by illusions.

In conclusion, the present study demonstrated that the predictive smooth pursuit response during target blanking is driven by a dynamic internal representation of target motion. This dynamic internal representation contains crucial timing information related to target trajectory and allows the heading of the predictive smooth pursuit to match instantaneous target heading during the occlusions. However, even though an accurate estimate of timing was available, the smooth pursuit response was dramatically reduced as a consequence of the temporary disappearance of the target.

Interestingly, the large variability of the predictive pursuit response was compensated by the saccadic system. These results highlights that extraretinal signals from the pursuit system are used by the saccadic system but not vice-versa.

Chapter V

WHAT TRIGGERS PREDICTIVE SACCADES DURING OCCLUSION OF A PURSUIT TARGET

Introduction

Optimal vision of a moving object requires that the projection of this object onto the retina falls on the fovea and stays there. Smooth pursuit eye movements aim at aligning the eye and a moving target. However, because the smooth pursuit system reacts to a change of direction or velocity with a delay of 100ms, position error accumulates because eye velocity does not instantly match target velocity. Two different strategies are used by the oculomotor system in order to avoid long-lasting position errors: prediction and saccades. Prediction is used when the target trajectory is known in advance or can be extrapolated from previous information (Kowler & Steinman, 1979a, b, 1981; Kowler *et al.*, 1984; Kowler, 1989, 1990). In these cases, the oculomotor system reacts to an event before it happens. For instance, the eye velocity increases before target motion onset (Barnes *et al.*, 2000). In contrast with prediction that helps minimizing the

position error before it accumulates, catch-up saccades are reactive and correct for an existing position error (de Brouwer *et al.*, 2001; de Brouwer *et al.*, 2002a). Finally, on some occasions, both strategies are used together in order to optimally view a target. For example, saccades and anticipation can occur together before target motion onset (Collins & Barnes, 2006) or during the occlusion of an ongoing moving target (Bennett & Barnes, 2003; Madelain & Krauzlis, 2003; Bennett & Barnes, 2006a; Orban de Xivry *et al.*, 2006).

During such occlusions, eye velocity exponentially decays towards a plateau value (Mitrani & Dimitrov, 1978; Becker & Fuchs, 1985). Models that accounts for this behavior either predict that eye velocity is partially maintained through efference copy (Churchland *et al.*, 2003; Madelain & Krauzlis, 2003) or is driven by the output of a short-term velocity store (Bennett & Barnes, 2003). These models hypothesize that either the efference copy signal or the output of the short-term velocity store are controlled by a gain mechanism (Tanaka & Lisberger, 2001; Churchland & Lisberger, 2002). As eye velocity decays during transient target disappearance, position error accumulates. To correct for this, saccades are generated during the occlusion. From up to now, these saccades have been shown to bring the eye ahead of the target (Bennett & Barnes, 2003) and to compensate for the variability of the smooth pursuit response by adjusting their response to the strength of the smooth pursuit response (Orban de Xivry *et al.*, 2006). Moreover, in the previous chapter

(chapter VI), we have demonstrated that the saccades do not influence the smooth pursuit response, which is driven by an internal representation of target motion. However, the reasons underlying the existence of such predictive saccades have never been investigated.

In contrast, the trigger mechanism of visually-guided catch-up saccades is well understood (de Brouwer *et al.*, 2002b). The decision to trigger a catch-up saccade is taken as soon as the smooth pursuit system alone cannot compensate for the current position error. Whether the smooth pursuit system can or cannot compensate for the current position error depends on the eye-crossing time (or time-to contact between eye and target), i.e. the time that the eye would need to catch the target on the basis of a linear extrapolation of its current motion (de Brouwer *et al.*, 2002b). The eye-crossing-time is obtained by dividing the negative position error by the retinal slip. The decision to trigger a saccade is taken as soon as this parameter is outside a so-called smooth zone, i.e. smaller than 40ms or larger than 180ms. As the eye-crossing-time is closely related to retinal slip, the trigger of catch-up saccades highly depends on the quality of the smooth pursuit response.

In the present study, we demonstrate that the trigger of the predictive saccades is not influenced by the quality of the smooth pursuit response. Inter-session and trial-to-trial analyses showed that smooth pursuit behavior is not a good predictor for saccade occurrence during the occlusions, i.e. it is not possible to predict

whether a saccade would be generated during the occlusions or not on the basis of the smooth pursuit response. However, we determine that the first predictive saccades during the occlusions were likely elicited by the disappearance of the target. Moreover, we showed that the frequency of saccades during occlusions was tightly linked with the probability of observing saccades during visually-guided pursuit, which emphasizes idiosyncratic effects. In sum, we show that the trigger mechanism of visually-guided and predictive saccades totally differs. During visually-guided tracking, a saccade is triggered as soon as position error cannot be corrected by smooth pursuit alone. In contrast, during predictive tracking saccades are generated in order to minimize the position error at target reappearance.

Methods

SUBJECTS

Six human subjects participated in the experiment after informed consent. Their age ranged between 22 and 40. Four of them (#3, #4, #5 and #6) were naive regarding the goal of the experiment. Two of the four had never participated in oculomotor experiment before (subjects #4 and #6). Subjects #1 and #2 were the authors of the study. Our subjects were ranked following the frequency of saccades they exhibited during the first 400ms of the occlusions, subject #1 having the highest frequency and subject #6 having the lowest frequency. The large majority of the results are illustrated with

data from subject #4. They all had normal or corrected-to-normal vision and did not have any known oculomotor abnormalities. All procedures were approved by the local ethics committee and were in agreement with the Declaration of Helsinki.

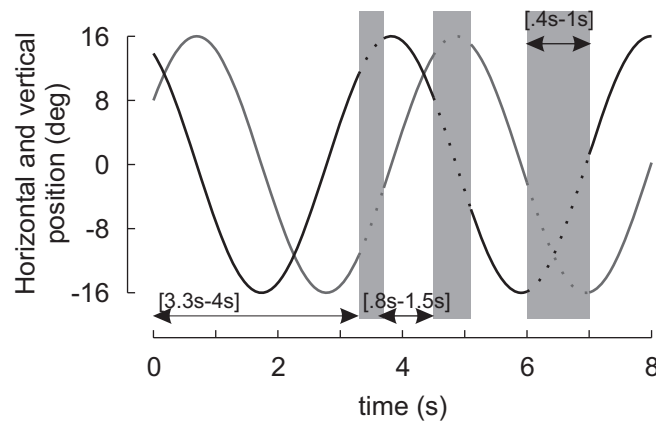


Figure V-1: Horizontal (black) and vertical (grey) target position vs. time along the circular target trajectory. During each trial, the target was occluded three times (grey areas). The occlusion lasted between 400 and 1000ms. The inter-occlusion interval varied from 800 to 1500ms. The period of visible target before the first occlusion lasted between 3300 and 400ms.

PARADIGM

Subjects were asked to pursue a red target dot moving along a circular path (Fig. V.1). After having been displayed at the centre of the screen for 500ms, the target jumped toward a random position along the circular path and began to move counter-clockwise. The target first remained visible for at least half a circle (3.3 to 4s). Then, it disappeared behind an invisible occluder three times (represented by a grey bars in Fig. V.1) for a period lasting from 400 to 1000ms. After each of the three occlusion periods, the circularly moving target

reappeared and continued moving for a period of time ranging between 800ms and 1500ms. The target was finally switched off for about 2s. In sum, each test trial consisted of four periods of visible target motion interleaved with three periods of occlusions.

Target motion varied randomly at each trial. Indeed, the radius of the circular path was chosen randomly between a set of three values (9.6, 12.8 and 16 deg). Moreover, the target moved along the circular path at a frequency assigned from a set of three possible values (0.15, 0.2 and 0.25Hz). Thus, the combinations of radii and frequencies led to nine different target conditions, which led to five different vectorial target velocities ranging from 9 to 25deg/s.

Experimental sessions consisted of several blocks of 13 test trials and lasted a maximum of 30 minutes. Each subject performed at least 4 experimental sessions which lead to a minimum of 810 occlusions per subject. At the beginning of each session, a learning block was presented to the subjects. It consisted of 13 learning trials during which the visual target moved counter-clockwise on a circular path with parameters (radius and frequency) chosen in the same sets as the test trials. However, the target was never switched off but remained visible for the 5s duration of the learning trials.

ACQUISITION AND ANALYSIS

Subjects sat in complete darkness in front of a translucent screen which was at a distance of one meter and covered a field of $\pm$

40deg horizontally and vertically. The visual target was a red laser spot which was back-projected onto the screen by two mirror-galvanometers. The galvanometers were controlled by a dedicated real-time computer which controlled their position and illumination. Eye movements were recorded using the scleral coil technique (Robinson, 1963; Collewyn *et al.*, 1975).

Eye and target position were sampled at 500 Hz and stored on a hard disk for offline analysis that was performed using Matlab (Mathworks Inc.). Position signals were low-pass filtered using a zero-phase digital filter (autoregressive, forward and backward filter, with a cutoff frequency of 47.619 Hz). Velocity and acceleration signals were derived from position by means of a central difference algorithm. All the trials were visually inspected to reject any trials containing blinks. Moreover, we performed an outlier analysis among the occlusion population in order to avoid the occlusions where subjects stopped pursuing the target. This outlier analysis rejected all occlusions for which the eye, at the target reappearance, was too far from the target or had a too low velocity. To do so, we computed the mean and standard deviation of the vectorial position and velocity error and rejected the trials that were further distant from the mean than three times the standard deviation for either the vectorial position or the velocity errors. We thus rejected 2.5% of our trials (# of trials: 6105).

Saccades in the interval from 500ms before the start of the occlusions until its end were detected using an acceleration threshold of 500 deg/s^2 . Saccade frequency during the first 170ms of the occlusions was computed by dividing the number of saccades during this interval by the number of trials for each subject separately. Similarly, predictive saccade frequency was computed by dividing the number of saccades detected from 170ms after the start of the occlusion until its end by the number of trials for each subject. Smooth eye velocity during a saccade was obtained by a linear interpolation routine based on the smooth eye velocity 25ms before and after the saccade (for further details see de Brouwer *et al.*, 2002a). Each eye velocity measure used in the following analyses (e.g. at time T) was computed by averaging the eye velocity over a 20ms interval (e.g. T-10ms to T+10ms). Throughout the analyses, we expressed some parameters in polar coordinates, noted deg_p , and others in degree unit of visual angle, noticed deg .

Finally, we performed numerous statistical comparisons between different populations using Statistica (Statsoft, Tulsa, OK). Sample means were compared T-test. Moreover, to account for multiple comparisons, the p-values were corrected by means of the false discovery rate procedure (Curran-Everett, 2000). We performed statistical comparisons for each subject and conditions separately and thus performed 54 statistical tests (6 subjects x 3 radii x 3 frequencies).

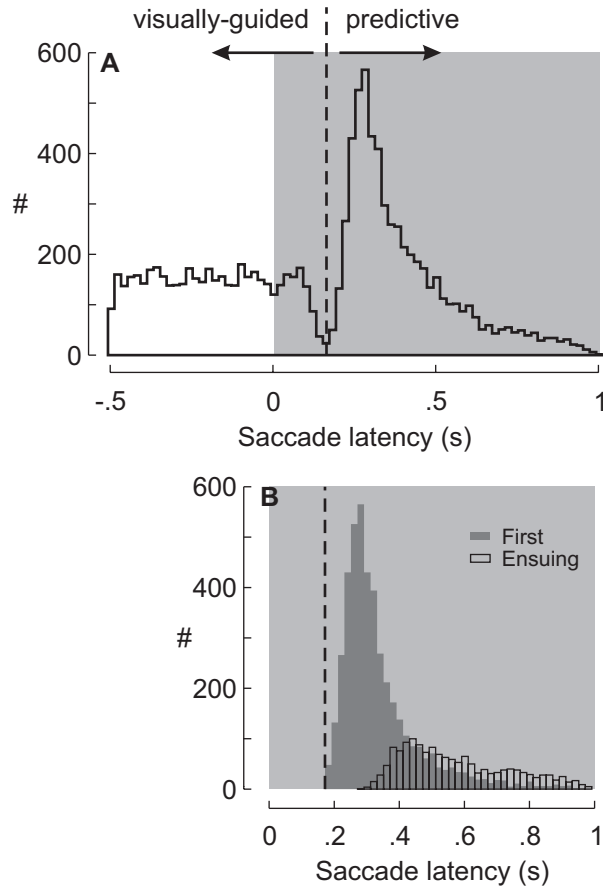


Figure V-2: Distribution function of the saccade latency. The data from all subjects are pooled together. Upper panel: Distribution function for all saccades from 500ms before the occlusion until its end. The grey area represents the occlusion. The dashed vertical line separates the visually-guided and predictive saccades (170ms). Lower panel: Distribution function of the first (dark grey) and ensuing (black outline) predictive saccades. The dashed vertical line represents the separation between the visually-guided and predictive saccades as defined in the upper panel.

Results

During occlusions of the ongoing moving target, the vectorial smooth eye velocity decayed and, most of the time, one or several saccades were executed. The probability of observing saccades during the occlusions was not uniform (Fig. V.2.A). For instance, the probability of observing a saccade was similar during the pre-occlusion interval and during the first 170ms of an occlusion. However, after this time interval, the distribution first reached a minimum 170ms after the start of the occlusion before reaching a peak 120ms later (290ms after the start of the occlusion). From 290ms until the end of the occlusion, the probability of observing a saccade decreased toward zero. The distribution function after 400ms must be handled with caution. Indeed, the probability of observing a saccade at a certain instant in time (say 800ms) was linked to the probability that the occlusion lasted longer than saccade latency (at least 800ms). As the duration of the occlusions was uniformly distributed, the probability that an occlusion lasted at least a certain amount of time decreased with increasing time. For instance, the probability that an occlusion lasted at least 800ms was only 0.33. Consequently, the shape of the distribution function of the latency of the predictive saccades was partially biased after 400ms (the minimum occlusion duration) because of the decrease of the probability that the occlusion lasted a sufficient amount of time.

From the shape of the distribution function, we decided to split the saccade population into two categories. As the plateau of the distribution function before the minimum (170ms) had the same value than the distribution function during visually-guided pursuit, the saccades executed before 170ms were classified as visually-guided. Accordingly, saccades that occurred after 170ms were classified as predictive saccades. The way the saccade population was segregated was consistent with the goal of these saccades. Indeed, visually-guided saccades occurring before the occlusion either reduced the vectorial position error that existed before the saccade (T-test $p < 0.05$ for four subjects) or maintained it constant (T-test, $p > 0.05$ for subjects #4 and #5). In contrast, execution of predictive saccades clearly increased position error (T-test, $p < 0.05$ for five subjects and $p = 0.07$ for subject #5). Saccades occurring during the first 170ms of the occlusions closely mirrored the behavior of visually-guided saccades before the occlusion. Indeed, these saccades either decreased the current position error (T-tests, $p < 0.05$ for subject #3 and #6) or maintained it constant (T-tests, $p > 0.21$ for the four other subjects). The behavior of the saccades nicely fit with our intuition of the minimum of the distribution function. This dip separated out the visually-guided and predictive saccades. Finally, predictive saccades were also segregated into first and ensuing predictive saccades (Fig. V.2.B). Indeed, the probability of occurrence of the first predictive saccade peaked at 290ms (SD: 120ms) whereas the distribution of the

ensuing saccades was more spread with a mean latency of 570ms (SD: 163ms).

The shape of the distribution function was similar for all subjects (Fig. V.3.A). However, the frequency of both visually-guided (before the occlusions or during their first 170ms) and predictive saccades varied largely among them. For instance, almost three quarters of the occlusions (72%, N=5963) contained at least one predictive saccade but one subject exhibited very few saccades (in less than 19% of the occlusion period, subject #6). As expected, among the subjects, the frequency of saccades before the occlusions and during their first 170ms was highly correlated ($r=0.99$, $p=0.0016$). Therefore, subjects who exhibited few saccades during steady-state pursuit also executed few saccades during the first 170ms of the occlusions. Surprisingly, the frequency of predictive saccades was also highly correlated with the frequency of visually-guided saccades among our subjects (Fig. V.3.B, $r=0.885$, $p<0.05$).

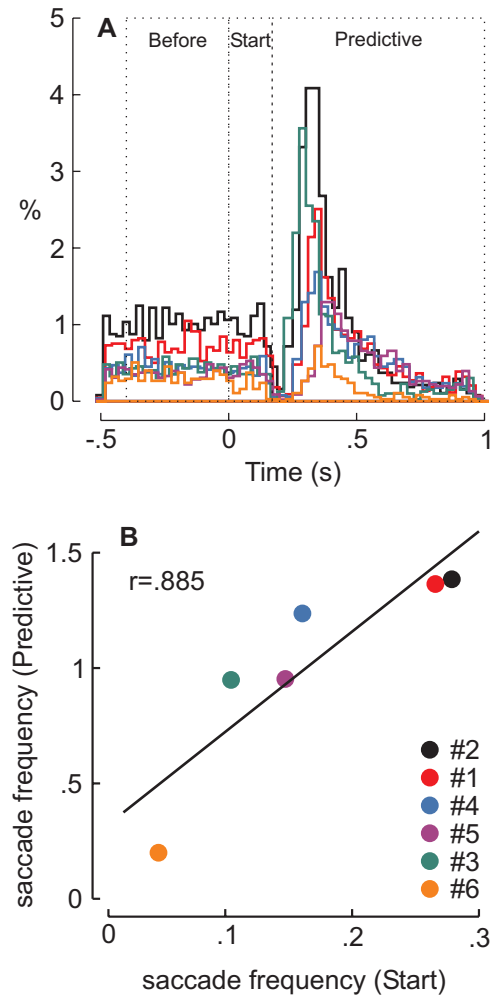


Figure V-3: Idiosyncratic effects on the predictive saccade frequency. Upper panel: same as Fig. V.2.A but for each subject separately (color code given in the right panel). Three time windows are delimited (Before, Start and Predictive). Lower panel: Inter-subject correlation between the frequency of saccade during the Predictive period and the frequency of saccades during the Start period.

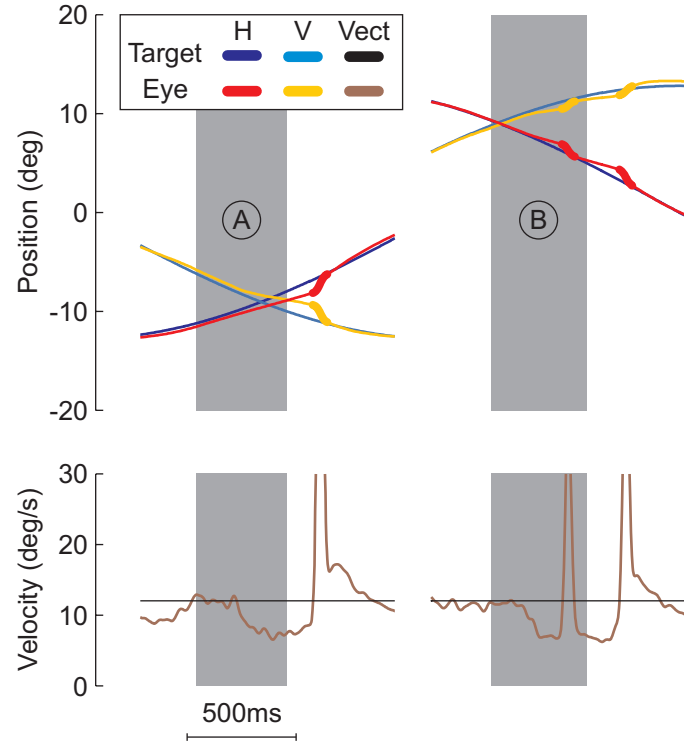


Figure V-4: Illustration of two occlusion periods (grey areas) from a single trial of subject #4. During the first occlusion (A), no predictive saccade was triggered whereas in the second occlusion (B), a predictive saccade was generated. Horizontal and vertical position traces vs. time are given in the upper panels where saccades are represented by thicker traces. Vectorial velocity traces are represented in the lower panels. The colour code is given in the inset. T: target; E: eye; H: horizontal; V: vertical; Vect: vectorial.

Though their frequency can easily be predicted, the occurrence of predictive saccades seems at first unpredictable. For instance, Fig. V.4 represents two occlusions from a single typical trial, during which the vectorial eye velocity decayed in a similar way. However, occlusion A was free of saccades whereas occlusion B contained one predictive saccade. Occurrence of saccades during occlusions yielded

different performance at their end. We measure this performance by computing the angular position error at the end of the occlusions A and B. The angular position error is the difference of angular position (angular component of the polar coordinates) between eye and target with respect to the circular target path. The angular position error was larger at the end of the occlusion A (6.23 deg_p), which was free of saccades, than at the end of the occlusion B (1.46 deg_p). This observation was representative of the whole population. For each subject, the angular position error at the end of occlusions during which predictive saccades were executed was significantly smaller than at the end of occlusions that were free of saccades (Fig. V.5, T-tests, $p < 0.05$). This result highlights the effect of the predictive saccades: minimizing the position error at the end of the occlusion. We will now focus on their trigger mechanism.

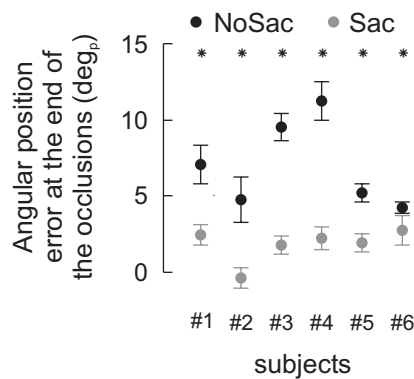


Figure V-5: Influence of predictive saccades on the angular position error at target reappearance. For each subject, mean angular position error is represented in black at the end of occlusions without predictive saccade and in grey at the end of occlusions that exhibited predictive saccades. Asterisks

indicate a significant difference between the two populations (T-test, $p < 0.05$). Spreads represent the 95% confidence intervals.

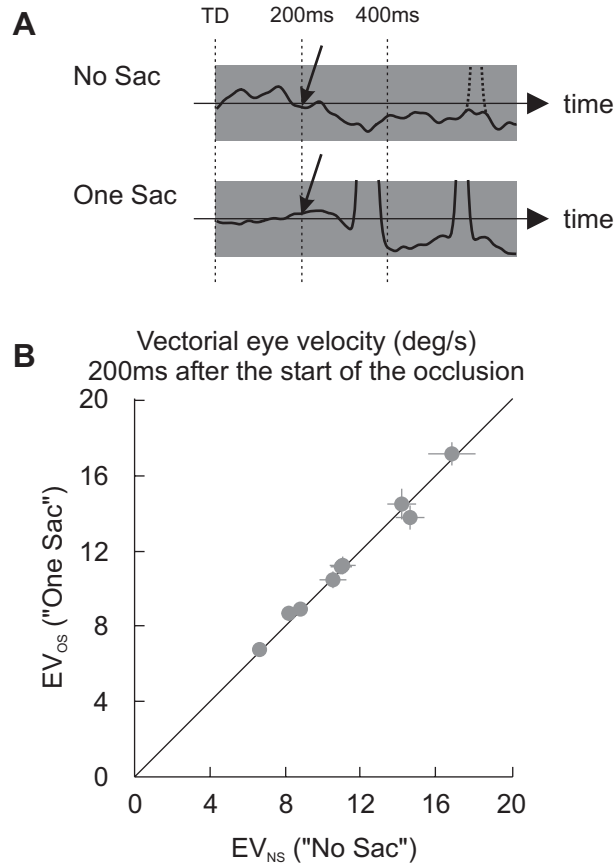


Figure V-6: Comparison of the mean vectorial eye velocity 200ms after the start of the occlusion (TD: target disappearance) between the occlusions with their first saccade during the first 400ms of the occlusion (EV_{OS}; "One Sac") and the occlusions without any predictive saccade during the same interval of time (EV_{NS}; "No Sac"). A: Schematic representation of the two groups of occlusions. The schema represents the vectorial eye velocity vs. time. The saccades are represented by a peak of vectorial eye velocity, which is truncated. In the "No Sac" group, there is no saccade between 200 and 400ms after the start of the occlusion (dashed vertical lines). However, a saccade can occur after 400ms (dashed trace). In the "One Sac" group, a saccade is generated during the first 400ms of the occlusions. The arrows indicate when the smooth eye velocity was measured. B: Average vectorial eye velocity 200ms after target disappearance

for "No Sac" vs. "One Sac". Spreads indicate 95% confidence interval. Oblique line represents the first bisector (no difference between "No Sac" and "One Sac"). Data from subject #4.

DID LOW PURSUIT PERFORMANCE ELICIT THE FIRST PREDICTIVE SACCADDES?

To test the hypothesis that pursuit performance influenced the trigger of the first predictive saccades (H_{ppt}), we segregated the population of occlusions into two different groups: a group of occlusions during which a predictive saccade was triggered within some interval of time ("One Sac") and a group of occlusions that were free of predictive saccades during this same interval ("No Sac"). Then we compared the vectorial and angular eye velocity measured during the occlusions of the "One Sac" group with the same measures taken during the occlusions of the "No Sac" group. For the occlusions of the "One Sac" group, the vectorial and angular eye velocities were measured around 100ms before the average latency of their first predictive saccades. The measures were taken at the same instants in time for the "No Sac" group. We varied the chosen time interval in order to test for the possible influence of other factors such as first predictive saccade latency.

The first analysis aims to predict the occurrence of the predictive saccades during the first 400ms of the occlusions. Therefore, the "One Sac" group gathers all the occlusions with a predictive saccade occurring in their first 400ms (as illustrated in Fig. V.6.A) and the "No Sac" group contains all the occlusions that were

free of saccades during their first 400ms (even if a saccade occurred later in the occlusion). Because the average latency of the first predictive saccades was 286ms, we measured the smooth pursuit response 100ms earlier, i.e. 200ms after the start of the occlusion ($\sim 286\text{ms} - 100\text{ms}$). We postulated that, if H_{ppt} held, the eye velocity measured during occlusions from the "One Sac" group (EV_{OS}) should be smaller than the same measure taken during the occlusions of the "No Sac" group (EV_{NS}). For one subject (#4), we represented the mean EV_{OS} vs. mean EV_{NS} for the nine different conditions (Fig. V.6.B). For this subject, the data points were perfectly aligned with the first bisector (oblique line, 45° from the horizontal). This alignment indicates that the mean EV_{OS} and EV_{NS} did not differ, which was confirmed by the non-significance of the corresponding T-tests ($p > 0.05$). Therefore, the data from this subject rejected H_{ppt} . We repeated this analysis for each subject separately. Across all subjects, H_{ppt} was rejected in the majority of the cases (48 out of 54, T-tests, $p > 0.05$), which indicates that the smooth pursuit response did not influence the trigger of the predictive saccades. In addition, when the p-values were corrected for multiple comparisons (see Methods), the difference between EV_{OS} and EV_{NS} remained significant in only one single case. Accordingly, measures of the angular velocity 200ms after target disappearance did not vary between the "One Sac" and "No Sac" groups in 43 of the 54 cases (T-tests, $p > 0.05$). In this case, the multiple comparison procedure rejected H_{ppt} in the 54 cases.

Therefore, this analysis gave the first clue that the smooth pursuit response did not influence the trigger of the predictive saccades (rejection of H_{ppt}). In the following analyses, we controlled for the latency of the first predictive saccades biasing our conclusion.

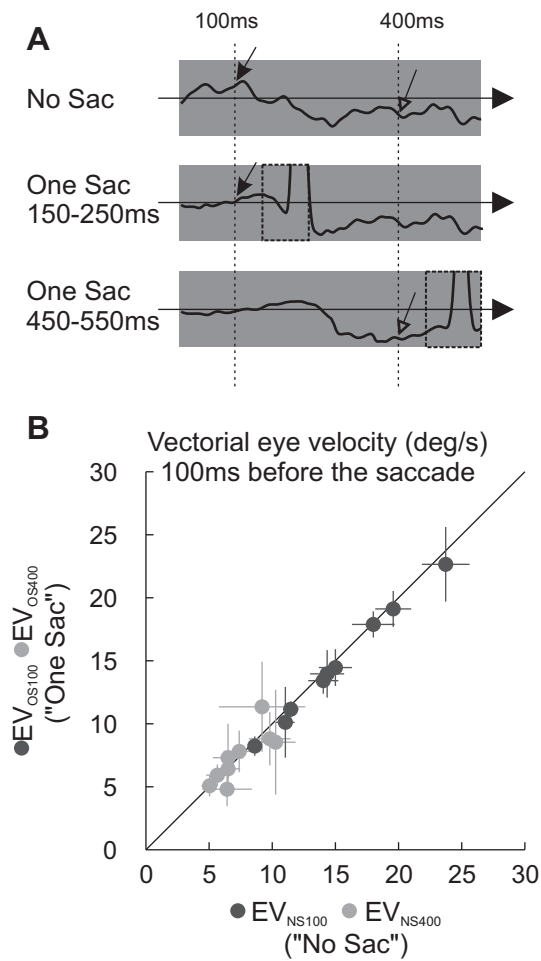


Figure V-7: Comparison of the vectorial smooth eye velocity between occlusions with their first saccade during a certain interval of time (150 to 250ms or 450 to 550ms after target disappearance (TD)) and the occlusions without any predictive saccade during the whole occlusion ("No Sac"). A: Schematic

representation of the different groups of occlusions (vectorial eye velocity vs. time). The saccades are represented by a peak of vectorial eye velocity, which is truncated. Upper row: "No Sac" group contains the occlusions without any predictive saccade. Eye velocity was measured either 100ms or 400ms after TD (EV_{NS100} and EV_{NS400}). Middle row: "One Sac" group that contains occlusions during which the first predictive saccade occurred between 150 and 250ms after TD (dashed rectangle). Eye velocity was measured 100ms after TD (black arrows). Lower row: idem than middle row but the first predictive saccade occurred between 450 and 550ms after TD (dashed rectangle) and the eye velocity was measured 400ms after TD (EV_{OS400} , open arrows). B: Mean EV_{OS100} vs. EV_{NS100} (dark grey points) and Mean EV_{OS400} vs. EV_{NS400} (light grey points). Within each comparison (dark grey or light grey points), each of the nine points represents one single condition. Spreads indicate 95% confidence interval. Oblique line represents the first bisector (no difference between "No Sac" and "One Sac").

The previous analysis only focused on the saccades occurring in the first 400ms of the occlusions. Because this interval did not include all the first predictive saccades (25% of them occurred later than 400ms), other time intervals were considered. For instance, we selected all the occlusions during which the first saccade had a latency between 150 and 250ms after target disappearance (Fig. V.7.A, middle row). For this group of occlusions ("One Sac"), we measured the vectorial eye velocity 100ms after target disappearance (EV_{OS100}). This measure was compared with the measure at the same instant in time (EV_{NS100}) for the occlusions without any predictive saccade ("No Sac", Fig. V.7.A, top row). For subject #4, this comparison was illustrated by a plot of mean EV_{OS100} vs. mean EV_{NS100} (Fig. V.7.B, dark grey points). Each point of this plot was associated with one condition. The superposition of the points with the first bisector indicates that the means did not differ, i.e. that, for the saccades

occurring between 150 and 250ms after target disappearance, H_{ppt} should be rejected. On the same plot (Fig. V.7.B, light grey points), we compared eye velocity 400ms after target disappearance (EV_{OS400}) for a group of occlusions during which the first predictive saccades occurred between 450 and 550ms after target disappearance (Fig. V.7.A, lower row) with eye velocity 400ms after target disappearance for the same "No Sac" group (EV_{NS400}). Again, for this subject, all the data points lie along the first bisector, which indicated that the means of EV_{OS400} and EV_{NS400} did not differ.

We repeated this analysis for each subject and investigated other time windows. To this end, we considered five different "One Sac" groups (first saccade latency between 150 and 250ms, 250 and 350ms, 350 and 450ms and 450 and 550ms) and one "No Sac" group that consisted of all the occlusions without any predictive saccade. For each "One Sac" group, the eye velocity was measured 50ms before the start of the time window (100ms, ..., 500ms), which approximately corresponded to a period of 100ms before the average first predictive saccade latency. Eye velocity was sampled at the same instants in time for the "No Sac" group. Eye velocity measurements from the "One Sac" and "No Sac" groups were then compared in order to further test H_{ppt} . Among the 242 tested cases (5 intervals x 9 conditions x 6 subjects minus 28 cases where no saccade was detected in the time window), the vectorial eye velocity did not significantly vary between the "One Sac" and "No Sac" groups in 224 of the them (93%; T-tests,

$p > 0.05$). The remaining significant differences did not pass the multiple comparison procedure. Accordingly, for the angular velocity, there was no difference in 220 of the 242 cases (91%). Therefore, this analysis rejected the hypothesis that smooth pursuit influenced the trigger of the first predictive saccades in more than 90% of the cases. Again, the significant tests did not pass the multiple comparison criteria. In sum, we can conclude that H_{ppt} was rejected in every comparison.

Subject	N	Q25	Median	Q75
#1	984	0.246	0.276	0.308
#2	747	0.268	0.300	0.356
#3	852	0.230	0.260	0.304
#4	858	0.270	0.322	0.416
#5	705	0.326	0.388	0.500
#6	211	0.286	0.326	0.398

Table V-1: Quartiles of the first predictive saccade latency (s) of each subject. N gives the number of saccades in the population for each subject. The saccades were grouped following the quartiles. Therefore the four groups were [0.17s Q25], [Q25 Q50], [Q50 Q75] and [Q75 1s].

The two previous analyses compared the smooth eye velocity during the occlusions that contained at least one predictive saccade ("One Sac"), with the smooth eye velocity during the occlusions that were free of saccade ("No Sac"). In contrast, the following analysis will investigate if, 200ms after the start of the occlusion, the level of smooth eye velocity (EV_{200}) indicated if a saccade would occur early or late, i.e. if the smooth eye velocity during the occlusions containing

an early first predictive saccade was smaller than the smooth eye velocity during the occlusions containing a late first predictive saccade. In other words, we looked for a relationship between smooth eye velocity at the start of the occlusions and saccade latency. To do so, for each subject separately, the first predictive saccades were categorized into four groups that were delimited by the three quartiles of their latency distribution (Table V.1). Then, the occlusions that contained at least one predictive saccade were grouped accordingly, i.e. with respect to which saccade group their first predictive saccade belonged to. A main effect ANOVA was then performed in order to look for any difference in EV_{200} among the four groups of occlusions. Among the 54 ANOVAs, only five exhibited a significant main effect of the vectorial eye velocity onto the first predictive saccade latency ($p < 0.05$). In addition, three of them indicated that the saccade latency increased with increasing EV_{200} , which is inconsistent with the hypothesis that predictive saccades were generated because of poor smooth eye velocity. Furthermore, only four ANOVAs (out of 54) showed a significant main effect when comparing the angular eye velocity rather than the vectorial eye velocity. Again, two of them were inconsistent with the tested hypothesis. In sum, we did not find any evidence that the smooth pursuit performance at the start of the occlusion did influence the latency of the first predictive saccades.

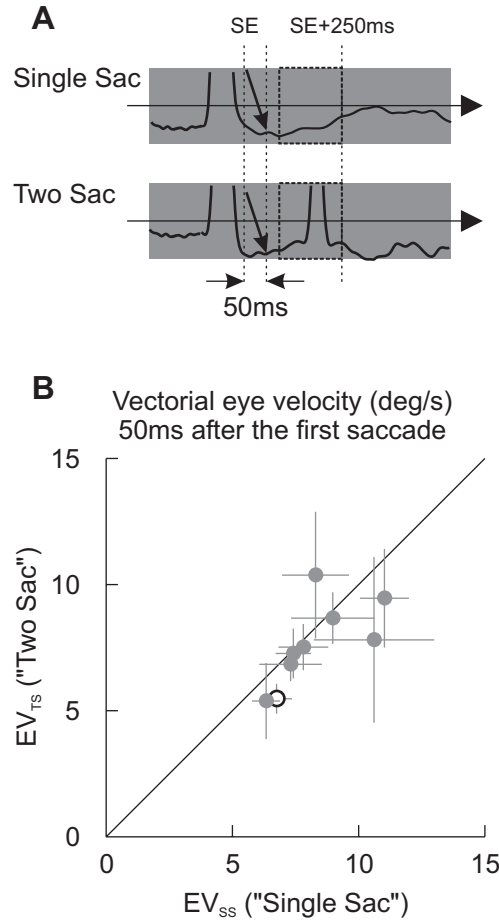


Figure V-8: Comparison of the vectorial smooth eye velocity 50ms after the end of the first predictive saccade (SE) between the occlusions with a second saccade during the next 250ms (EV_{TS}; "Two Sac") and the occlusions with no second predictive saccade during the same interval of time (EV_{SS}; "Single Sac"). A: Schematic representation of the two groups of occlusions (vectorial eye velocity vs. time). The saccades are represented by a peak of vectorial eye velocity, which is truncated. Upper row: "Single Sac" group contains occlusions that did not exhibit saccades from SE+75ms until SE+250ms (dashed rectangle). Lower row: "Two Sac" group gathers the occlusions during which a second predictive saccade was generated during this same time window. The arrows indicate when the smooth eye velocity was measured (50ms after SE). B: Mean EV_{TS} vs. mean EV_{SS}. Each of the nine points corresponds to one single condition. Spreads indicate 95% confidence interval. Oblique line represents

the first bisector (no difference between "Single Sac" and "Two Sac"). Data from subject #4.

*DID LOW PURSUIT PERFORMANCE ELICIT THE
SECOND PREDICTIVE SACCADDES?*

Though many occlusions contained one predictive saccades (72% of all the occlusions), only 26% of them also exhibited a second predictive saccade (19% of all the occlusions). This low percentage could have resulted from the small amount of remaining time after the first predictive saccade (occlusion duration minus time of saccade offset). However, even if the occlusion lasted for more than 250ms after the end of the first predictive saccade (which is larger than the latency of 66% of the second predictive saccades), the occurrence of a second predictive saccade remained low (around 38%) and was not automatic. Therefore, we investigated why some occlusions did ("Two Sac") and others ("Single Sac") did not exhibit a second saccade during a determined interval of time after the first saccade (Fig. V.8.A). This interval started 75ms after the end of the first saccade and ended 175ms later (250ms after the end of the first predictive saccade), which inferred the selection of the occlusions that lasted at least 250ms after the end of the first saccade (N=2173). Moreover, the choice of this interval implied that 34% (or 285) of the occlusions with a second predictive saccades (N=827) were not taken into account because the inter-saccadic time was longer than 250ms (period of time between the offset of one saccade and the onset of the

following one). We then compared the vectorial smooth eye velocity 50ms after the end of the first predictive saccades between the occlusions of the "Two Sac" group (EV_{TS}) and the occlusions of the "Single Sac" group (EV_{SS}). Fifty milliseconds after the first predictive saccade approximately corresponded to the average inter-saccadic interval (143ms) minus 100ms. This analysis was performed for five of the six subjects because the last subject (#6) rarely exhibited two predictive saccades in one occlusion. Similarly to the technique used in the previous section, we compare the mean EV_{TS} and EV_{SS} for each subject and each condition separately. Again, when plotting EV_{TS} vs EV_{SS} for all the conditions of subject #4, we noticed that eight of the nine data points lay on the first bisector (Fig. V.8.B). This superposition on the first bisector implies that the mean of EV_{TS} and EV_{SS} did not differ for eight conditions out of nine. The results were similar for the four other subjects. Indeed, in 38 of the 45 T-tests performed (5 subjects x 9 conditions), EV_{TS} and EV_{SS} did not differ ($p > 0.05$). When the analysis was performed with the angular eye velocity rather than the vectorial eye velocity, 40 of the 45 statistical comparisons were not significant. Again, the multiple comparison procedure rejected the significance of all but one test.

Because the moment at which the eye velocity was measured depended on the latency of the first predictive saccade, we checked if this parameter did not bias our result. We grouped the occlusions with respect to the latency of their first predictive saccades (from the

quartiles, see previous section). For each of the four groups of occlusions, we tested if the mean EV_{TS} differed from the mean EV_{SS} , i.e. if lower eye velocity after the first predictive saccade would elicit a second predictive saccade. Instead, EV_{TS} and EV_{SS} were not significantly different in 139 (resp. 140) of the 153 cases (4 groups x 9 conditions x 5 subjects minus 27 cases where one of the groups was empty). Moreover, three (respectively seven) of the significant T-tests were inconsistent with the hypothesis that the level of the vectorial (respectively angular) smooth eye velocity after the first predictive saccade was responsible for the trigger of a second predictive saccade (EV_{TS} was larger than EV_{SS}). Finally, the multiple comparison procedures rejected all (respectively all but one) significant differences.

Finally, we tested if the second predictive saccades could be elicited on the basis of the position error at the end of the first saccade. To do so, we used the same technique as previously, i.e. we compared the position error after the first predictive saccades between the occlusions of the "Single Sac" and "Two Sac" groups. Again, we found that neither the vectorial position error nor the angular position error were responsible for the generation of a second predictive saccade. Indeed, the vectorial and angular position errors were similar across the two groups of occlusions ("Single Sac" vs. "Two Sac") in 43 of the 45 conditions (5 subjects x 9 conditions, T-tests, $p > 0.05$).

Again, the significant differences failed to pass the multiple comparison procedure.

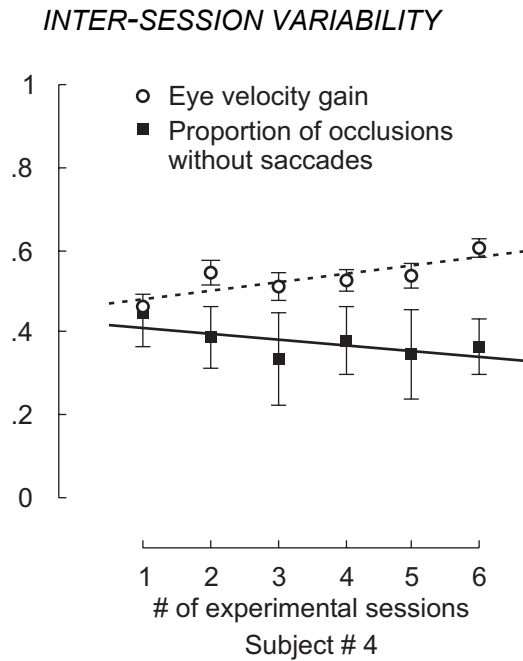


Figure V-9: Evolution of the vectorial eye velocity gain (400ms after target disappearance) and of the proportion of occlusions without any predictive saccades during their first 400ms across the different sessions. Data (from subject #4) are collapsed across all conditions.

As subjects did perform several sessions of the experiment (from 4 to 8), we expected the pursuit gain to evolve over the different sessions. Indeed, we found that the vectorial eye velocity gain at the end of the occlusions increased with the rank of the sessions (F-tests, $p < 0.05$ for each subject, all conditions pooled together). If H_{ppt} was true, then an increase in the smooth pursuit gain should result in an increase in the proportion of occlusions without any predictive

saccade. Again, this was not confirmed by our data as, for the majority of the subjects, the evolution of the smooth pursuit gain (computed 400ms after target disappearance) did not correspond with the evolution of the proportion of occlusions without predictive saccade across sessions (Fig. V.10, subject #4). For five subjects, the vectorial eye velocity gain (400ms after target disappearance) increased with the rank of the session (F-test, $p < 0.05$, all conditions pooled together). For the last subject (#2), there was no significant variation of the mean pursuit gain across sessions. In contrast, the proportion of occlusions without any saccade during their first 400ms did not vary across the different sessions for three subjects (#3, #4 and #6). This proportion decreased for two other subjects (F-test, $p < 0.05$, subjects #2 and #5). Finally, it increased in parallel with the mean pursuit gain for only one subject (F-test, $p < 0.05$, subject #1). Therefore inter-session analyses confirmed that the frequency of predictive saccades is not related to the performance of the smooth pursuit response. These results highlight that predictive smooth pursuit did not drive the trigger mechanism of predictive saccades.

Discussion

During the occlusion of a pursuit target, experimenters observed that the vectorial eye velocity decays more or less strongly (Mitrani & Dimitrov, 1978; Becker & Fuchs, 1985; Churchland *et al.*, 2003) and that predictive saccades can be either frequent or infrequent

(Bennett & Barnes, 2003; Madelain & Krauzlis, 2003; Bennett & Barnes, 2006a; Orban de Xivry *et al.*, 2006). Mechanisms underlying the variability of the eye velocity decay are partially understood. In contrast, the reasons underlying the occurrence of predictive saccades were never addressed. Because the quality of the smooth pursuit response influenced the trigger of catch-up saccades during visually-guided pursuit (de Brouwer *et al.*, 2002b), we sought to determine if, during an occlusion, there was any relationship between the quality of the predictive smooth pursuit response and the occurrence of predictive saccades.

To test the hypothesized influence of the smooth pursuit response on the trigger of the first predictive saccades, we compared the group of occlusions with and without predictive saccade. In the large majority of the cases, we did not find any difference between the two groups of occlusions, which rejected the possible influence of the smooth pursuit system. This rejection is straightforward when considering the saccades that occurred 200ms after the start of the occlusion. Indeed, the decision to trigger these saccades was taken 100ms after the start of the occlusion (100ms before the saccade, de Brouwer *et al.*, 2002b). At that time, smooth pursuit eye movements were yet not modulated by the occlusion of the target because eye velocity started decaying only 150-200ms after target disappearance (Becker & Fuchs, 1985). Therefore, because eye velocity had not yet started decaying, the eye velocity was similar, whether a predictive

saccade was generated later or not. In addition, even when saccade latencies were longer, we were not able to predict if a saccade would be generated based on the eye velocity measures. In sum, our data demonstrate that smooth pursuit response is not a good predictor of the occurrence of predictive saccades.

Two other results confirmed this conclusion. First, the latency of the first predictive saccade was not determined by the quality of the smooth pursuit response at the start of the occlusion. Namely, the smooth eye velocity 200ms after target disappearance did not determine if the first predictive saccade would occur early or late in the occlusion. Second, the increase of the smooth pursuit gain across sessions was not accompanied by a reduction of the number of occlusions with predictive saccades. Therefore, even if the subjects tended to increase their smooth eye velocity across sessions, the frequency of the predictive saccades did not decrease significantly.

If the smooth pursuit behavior did not explain the presence or absence of the predictive saccades, then, they should be triggered by an external event. The distribution of the saccade latency during an occlusion (Fig. V.2) yielded insight into what triggered the first predictive saccades. Indeed, two different behaviors came into play consecutively at the start of the occlusions: continuation of the visually-guided tracking pre-programmed before the occlusion (evidenced by the saccades during the first 170ms of the occlusion) and reaction to the disappearance of the target (evidenced by the huge

peak after 170ms). In other contexts, a perturbation yields first an inhibition of the programmed saccades followed by saccades in response to the perturbation. This was observed while tracking one's own unseen hand of which the trajectory was perturbed (Ariff *et al.*, 2002), or during large gaze shifts when the head was perturbed (Choi & Guitton, 2006). In both cases, saccades were withheld right after the perturbation. Then, around 150ms after the perturbation, saccades were again executed (Ariff *et al.*, 2002). In our data, we did not observe inhibition of the programmed response as we observed saccades during the first 170ms of the occlusions. However, we did observe the peak related to the disappearance of the target.

The disappearance of the target was responsible for the trigger of the first predictive saccades. However, it seemed dubious to postulate that it was also responsible for the trigger of the ensuing predictive saccades. Yet, in this case, we were again not able to conclude that the smooth pursuit system played a major role in the trigger of the second predictive saccades. This result was confirmed by the fact that the inter-subject differences in smooth pursuit gain 400ms after the start of the occlusions was not correlated with the proportion of occlusions with two saccades.

In sum, saccades during predictive tracking differed from saccades during visually-guided tracking. Indeed, during visually-guided tracking, catch-up saccades are triggered on the basis of smooth pursuit response (on the basis of the relative motion between

eye and target, de Brouwer *et al.*, 2002b); their amplitude is correlated with the retinal slip measure 100ms before the saccade (de Brouwer *et al.*, 2002a; Schreiber *et al.*, 2006) and they facilitate motion processing (Schoppik & Lisberger, 2006; Wilmer & Nakayama, 2007). In contrast, during predictive tracking, saccades are not triggered by the quality of the smooth pursuit response (the present study); they do not modify the smooth pursuit response (chapter VI). Yet, the programming of the predictive saccade amplitude takes the smooth pursuit response into account (Chapter V and VI). All these differences indicate that the strategy during predictive tracking is different than the strategy during visually-guided tracking. During visually-guided tracking, humans tend to correct any position error as soon as the time-to-contact between eye and target becomes too long (de Brouwer *et al.*, 2002b). In contrast, during predictive tracking, the trigger of predictive saccades is not related to the smooth pursuit behavior. Indeed, during occlusions, the position error does not require an immediate correction as it does not cost anything. Interestingly, this change of strategy is not due to the impossibility of knowing where the target is. Indeed, an internal representations of target (Filion *et al.*, 1996; Barborica & Ferrera, 2003, 2004; Xiao *et al.*, 2006) and eye positions (Sommer & Wurtz, 2002, 2004a, b; Tanaka, 2005) are available during the occlusion of a moving target. Yet, during predictive tracking, saccades do not correct for a given position error. Rather, saccades landed ahead of the target in order to

minimize the position error at target reappearance (Fig. V.5). This advance in position indicated that subjects used the internal representation of target motion but that the actual target position yielded by this representation was not the goal of the saccade. In the optimal control world (Todorov & Jordan, 2002; Todorov, 2004, 2006), during visual-guided tracking, sensory costs would be associated with poor vision related to position error and with reduced vision related to the execution of saccades. The minimization of a combination of these sensory costs would mirror the trigger mechanism of visually-guided catch-up saccades (de Brouwer *et al.*, 2002b). However, these costs are zero during occlusions, which explains why the trigger of predictive saccades is based on another trigger mechanism. The sensory costs become again non-zero after target reappearance. Therefore, it is reasonable to hypothesize that the role of predictive saccades is to minimize the combination of sensory costs at target reappearance not at each instant in time during the occlusion.

Chapter VI

CONCLUSION AND PERSPECTIVES

The results presented in this thesis evidenced the different strategies taking place during predictive tracking and shed light on a new model for tracking the visible and the invisible. To summarize them, we first reproduced a picture describing oculomotor tracking (Fig. VI.1).

In this figure, the visual scene, which consists of an apple moving rightward, is projected onto a screen. A couple of agents (the sensory agents) extract 1D and 2D local motion information and integrate it in order to estimate the motion of the object of interest. Indeed, the pursuit system needs a simple representation of target motion (one speed signal at a time). This information is then sent to the relay centre in the middle of the tower, who processes it. On top of it, the executive agent relays the information to the low-level controller at the bottom of picture. Finally, this low-level agent instructed the agents that move the eyes how to do it. This low-level agent tells the agents in the tower how the muscle agents react to his

instructions. Links between this picture and the actual oculomotor system are given in Table VI.1.



**Figure VI-1: Schematic view of the brain for oculomotor tracking (see text).
Artwork by K. Nagel. © the Journal of Neuroscience.**

This picture gives a fairly good idea of the internal mechanisms subserving oculomotor tracking. We will now focus on the functions of some of these agents with respect to the results detailed in this thesis.

Part of the picture	Physiological correspondent
screen	retina
sensory agents	visual areas (V1, V2, V3, MT...)
tower	cortical areas (FEF, SEF, MST ...) subcortical areas (SC, CB, TH ...)
low-level controller	premotor structure cerebellar nuclei
muscle agents	extraocular muscles

Table VI-1: Correspondence between the schema (Fig. VIII.1) and the real physiological structure subserving the oculomotor system. V1: primary visual area; V2: second visual area; V3: third visual area; MT: Middle Temporal area; FEF: Frontal Eye Field; SEF: Supplementary Eye Field; MST: Medial Superior Temporal area; SC: Superior Colliculus; CB: Cerebellum; TH: Thalamus.

THE SENSORY AGENTS

The sensory agents have two main functions. They describe the features of the object of interest in order to favor its recognition and they process the motion characteristics of the objects. In this thesis, I



tested which characteristics of target motion the sensory agents can detect. It is well known that target velocity can be estimated very easily by the sensory agents. Whether target acceleration can be estimated as well was still a matter of debate. I showed that, if the

target is presented for a sufficient period of time (larger or equal to 500ms), the sensory agents can estimate target acceleration (Chapter II). Target acceleration can even be kept in mind by the executive controller in order to give instructions to the low-level controller during temporary occlusion of the target.

THE EXECUTIVE AGENT

As outlined in the introduction of this thesis, a single agent controls the oculomotor system and is responsible for the generation of both saccades and smooth pursuit. So the



executive agent can instruct the low-level controller to generate either saccadic or smooth pursuit eye movements. This agent was the main centre of attention of our experiments. We investigated how the executive agent reacts during transient target disappearance and what kind of information about target motion his computer contains. Especially, we have scrutinized how the executive agent combines saccadic and pursuit instructions.

First, the secrets of the executive agent's computer were uncovered. Indeed, the experiments in Chapter IV shows that the executive agent has access to a dynamic representation of the target motion during temporary occlusion of a moving target, i.e. it has access to the prediction of target velocity at each instant during occlusions. This representation is obtained either by extrapolation of

the pre-occlusion target motion (like in Chapter II) or by learning of target trajectory (like in Chapter III, IV and V). In the case of extrapolation, the computer assesses target motion during occlusions on the basis of the target motion parameters during the pre-occlusion interval. In contrast, learning means that the internal representation of target motion is built up by repetition. The executive agent gets this information from his computer and uses it to generate both saccades and pursuit during occlusions of a moving target.

To generate predictive pursuit during occlusion, the executive agent bases his instructions solely on the output of his computer (i.e. on the dynamic internal representation of target motion). Indeed, the computer does not modulate these instructions depending on the relative position of the eyes to the target (Chapter IV). In contrast, we clearly show that the instructions that generate saccades take the smooth eye velocity into account (Chapter III and IV). Indeed, we demonstrated that, during transient target disappearance, the saccades compensate for the variability of the smooth pursuit response. Therefore, we concluded that information about smooth eye velocity is fed back by the low-level controller to the executive controller.

Finally, the last chapter (Chapter V) evidences that the executive agent does not give saccade instructions as soon as the predictive smooth pursuit response is insufficient. Rather, this is the strategy that this agent chooses when the target is visible. In contrast, during transient target disappearance, the strategy of the executive

agent is completely different. He chooses to minimize the position error at target reappearance, not at every instant in time during occlusions.

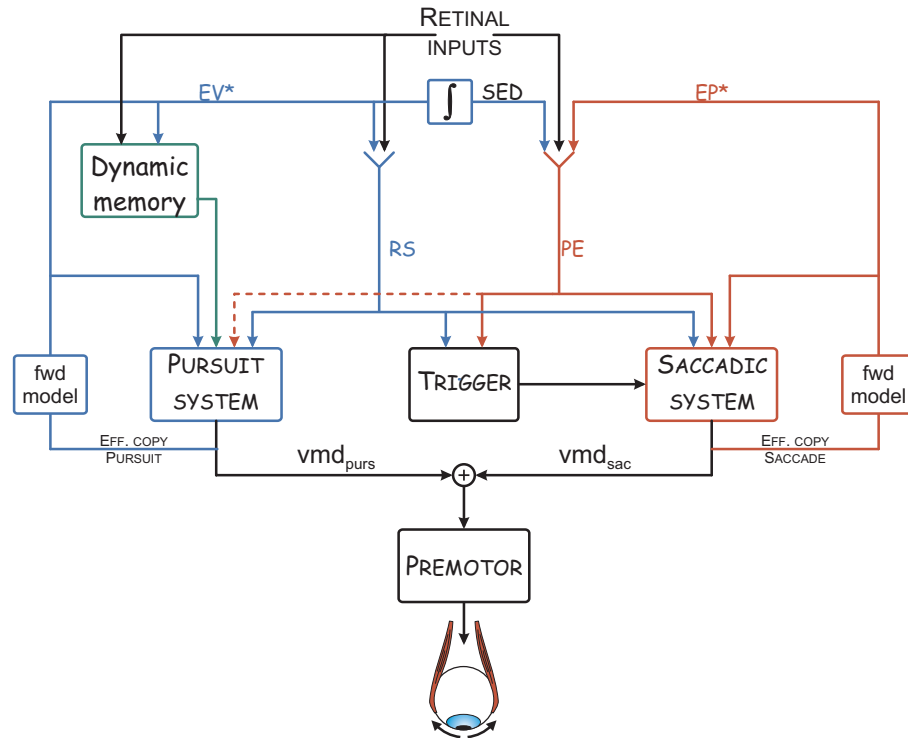


Figure VI-2: Proposed model for tracking the visible and the invisible. Blue and red parts are respectively associated with pursuit and saccadic systems. Green traces are related to the dynamic memory. Black lines are associated with retinal inputs. The retinal slip (RS, velocity error) is estimated by means of retinal inputs and efference copy from the smooth pursuit system. Position error (PE) is estimated by means of retinal and extra-retinal inputs (smooth eye displacement (SED) and efference copy of eye position) depending on the context. The branch that conveys PE to the pursuit system is represented in dashed line as it is not preponderant. The pursuit and saccadic system translates the inputs into visuomotor drives (vmd_{purs} and vmd_{sac}), which are summed up and sent to the premotor circuitry. Forward models (fwd model) predict the future eye position (EP^*) or velocity (EV^*) from an efference copy of the visuomotor drive sent to the premotor circuitry

AN UPDATED MODEL FOR TRACKING THE VISIBLE AND THE INVISIBLE

In conclusion, the results presented in this thesis lead to a new schema of the oculomotor system (Fig. VI.2). This schema has to be compared with the schema presented in Fig. I.15. The updated model contains three major modifications: it contains a dynamic memory that drives the predictive component of the smooth pursuit response, it can explain the synergy between saccades and pursuit during occlusions and it takes into account the position input to the smooth pursuit system.

THE DYNAMIC MEMORY

The major departure from the reference model (see chapter I) consists in the addition of a dynamic memory in the model and its effect on the smooth pursuit system (Fig VI.3). This memory, which is charged by retinal inputs and efference copy of smooth pursuit eye movements, is dynamic in the sense that it yields the evolution of target velocity with time. This memory drives the smooth pursuit response during transient target disappearance (chapter IV) but also during visually-guided tracking (Barnes *et al.*, 2000).

I chose to include a memory that stores information in world-centered coordinates. In contrast, the model proposed by Bennett and Barnes (2006b) contains a memory element that stores the maximum visuomotor drive. Indeed, three different facts suggest that memory could be rather in world-centered coordinates than in motor-centered

ones. First, MST is known to encode target motion in world coordinates (Ilg *et al.*, 2004). As MST neurons carry extraretinal signals related to smooth pursuit eye movements (Newsome *et al.*, 1988), they could participate to the driving of predictive smooth pursuit eye movements during that period. Second, I have presented some evidence in Chapter II that subjects were able to reconstruct target motion during occlusion on the basis of pre-occlusion target motion. However, as the oculomotor plant is non-linear (Quaia & Optican, 2003), extrapolating the visuomotor drive does not seem robust to drive predictive pursuit in such situations. In contrast, extrapolating target motion in world coordinates seems far more natural. Finally, it has been shown that target motion could be stored by viewing, but not pursuing, a target (Barnes *et al.*, 1997). The translation of visual information into visuomotor drive without using it seems a waste of energy. Again, target motion in world-centered coordinates could be simply stored as visual information is processed.

The dynamic memory of target velocity plays a critical role during predictive pursuit (visually-guided or not). Therefore, its existence leads to a modification of the model representing the smooth pursuit system (Fig. VI.3). In this model, the indirect loop that stored the maximum visuomotor drive in the model of Bennett and Barnes (2006b) is replaced by the dynamic memory. As target motion is stored in world-centered coordinates, a transfer function ($H(s)$) is required in order to translate the content of the memory into

visuomotor drive for pursuit. This transfer function could be relatively close to those presented in "internal feedback" models where pursuit is driven by the reconstructed target motion in world coordinates (Robinson *et al.*, 1986). These models were not considered in order to replace the existing model because they do not account for the dynamics of pursuit (Goldreich *et al.*, 1992).

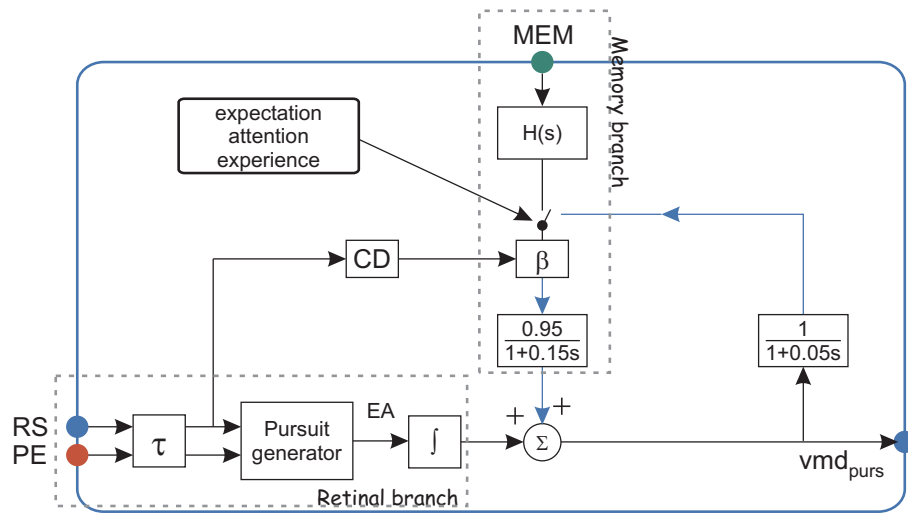


Figure VI-3: Proposed model for smooth pursuit eye movements. The model is an adaptation of the model of Bennett and Barnes as presented in Fig. I. 16. The main difference consists in the suppression of the indirect loop, which is replaced by a dynamic memory input that yields target motion in world-coordinates. This input is translated into a visuomotor drive for pursuit by means of the transfer function $H(s)$.

In addition to the branch related to the processing of stored information into visuomotor drive (memory branch), the smooth pursuit model (Fig. VI.3) also contains a branch dedicated to the translation of retinal information into visuomotor drive (retinal branch). The existence of these two branches looks mirror the two

descending pathways of the smooth pursuit system (Krauzlis, 2004; Thier & Ilg, 2005). The first one goes from MT directly to DLPN and would be associated with the sensorimotor transformation of retinal information. It could be responsible for smooth pursuit initiation and could correspond to early visual pathway. Therefore, this brain pathway could correspond to the retinal branch of my model. The second pathways involved MST and FEF and descends to the DLPN. This pathway could be related to the transformation of the content of the dynamic memory into a visuomotor drive for pursuit, which could be assimilated to the memory branch of my model. Indeed, the saccade-related part of the FEF is supposed to be the locus of a dynamic memory of position during occlusion, i.e. an up-to-date saccade plan (Barborica & Ferrera, 2004; Xiao *et al.*, 2006). It also contains a memory of the invisible target speed (Barborica & Ferrera, 2003). Moreover, it is well known that FEF plays a critical role in driving the predictive smooth pursuit response during predictive tracking (Keating, 1991; Gottlieb *et al.*, 1993; Keating, 1993; Gagnon *et al.*, 2006).

SYNERGY BETWEEN SACCADDES AND PURSUIT

In chapter III, I showed that there was a synergy between saccades and pursuit during transient target disappearance. Therefore, during such occlusions, the saccadic system needs to have access to an estimation of the current position error. This could be achieved easily by taking into account the smooth eye displacement since target

disappearance. Therefore, I hypothesize that the efference copy of the smooth eye velocity was both used to estimate the velocity error and integrated in order to assess the smooth eye displacement. The addition of the smooth eye displacement to the total saccadic eye displacement since target disappearance yields a good estimation of the current position error, which is then used to program the saccadic amplitude.

Such an estimation of the smooth eye displacement is also useful during localization of a target flashed during ongoing pursuit (Blohm *et al.*, 2003b, 2005b; Blohm *et al.*, 2006). In this case, the current position error is computed by adding the retinal position error between eye and flashed target at the moment of the flash to the smooth eye displacement since the flash. Again, the smooth eye displacement is computed from the integration of the efference copy of the smooth pursuit system.

THE POSITION ERROR INPUT TO THE SMOOTH PURSUIT SYSTEM

Apart from the addition of a dynamic memory to the model of the smooth pursuit system and the estimation of the smooth eye displacement, I also considered the position error as an input to the smooth pursuit system. In order to account for this new input, a position motion branch was added in the pursuit generator (Fig VI.4). The position signals that pass through this branch are scaled, filtered and influenced by non-linearities as the signals that pass through the

other branches. As these position signals cannot evoke strong pursuit response during fixation (Morris & Lisberger, 1987), their influence on the smooth pursuit response could be gated by OPNs as hypothesized by Blohm et al. (2005a).

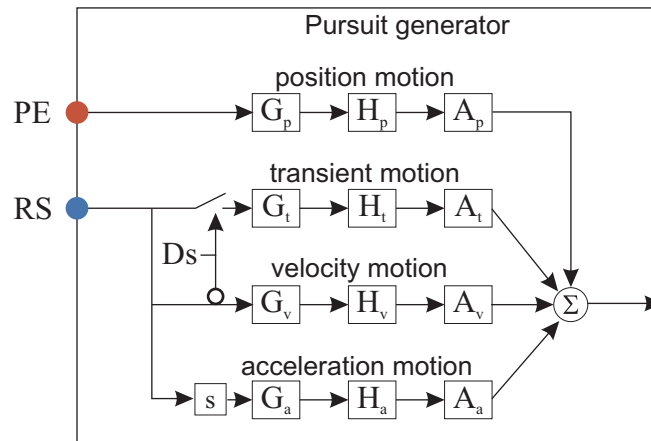


Figure VI-4: Schematic diagram of the pursuit generator. The pursuit generator translates position error and retinal slip into desired eye acceleration that will produce the visuomotor drive. It contains four branches. The three branches that process retinal slip are similar to those described by Krauzlis and Lisberger (1994). The transient motion only intervenes after a sudden change in target motion is detected (Ds). The position motion branch was added to account for the influence of position error onto the smooth pursuit response. The Gi, Hi and Ai boxes respectively represent non-linear functions, second-order filters and gain elements.

PREDICTION AND INTERNAL MODELS

In sum, during tracking of the invisible, smooth pursuit is driven by a dynamic memory that yields prediction about upcoming target motion. In addition, the visuomotor drive of pursuit is both sent to the premotor circuitry and translated into an estimate of eye velocity by a forward model. This prediction of eye velocity allows

the saccadic system to account for the variability of the smooth pursuit system as illustrated in Chapter III. These two elements (dynamic memory and forward models) are essential for tracking the invisible but also to track visible targets as the mechanisms of prediction improve the tracking performance of humans.

OPEN QUESTIONS

The proposed schema summarizes the results of this thesis but also induces new questions. First, in the model, the dynamic memory only contains velocity information. However, it has been demonstrated that the saccade-related part of the FEF contains both position and velocity information (Barborica & Ferrera, 2003, 2004; Xiao *et al.*, 2006). Therefore, one might hypothesize that the dynamic memory contains both position and velocity information. In this case, the model could suggest that the dynamic memory influences both saccades and pursuit, which is currently not the case. Two different cues favor this hypothesis. During transient target disappearance or visually-guided tracking of a predictable target (Van Gelder *et al.*, 1995), saccades use to bring the eye ahead of the target. The existence of such leading saccades suggests that the saccadic system could have access to future target position, which would be held in the dynamic memory. Second, the model states that the forward model is different for pursuit and saccades. However, there is no evidence in favor of either a single or two forward models. Finally, the described trigger mechanism holds during visually-guided tracking but does not account

for the trigger of predictive saccades during occlusions as shown in chapter V. The trigger mechanisms for the predictive saccades have not been uncovered yet. Whether the dynamic memory influences the trigger mechanism of predictive saccades remains an open question.

FURTHER WORK ON THE SENSORY AGENTS

Though we highlighted some skills of the sensory agents, there remain some open questions about their functions. For instance, we uncovered that target acceleration can be extracted by the sensory agents. This sensitivity of the sensory agents to target acceleration might be further challenged. Indeed, in our everyday life, moving objects mainly accelerate because of the gravity, i.e. along the vertical axis. On this basis, we can hypothesize that acceleration perception might be more sensitive during vertical target motion than during horizontal target motion. Our paradigm can therefore be implemented with vertical rather than horizontal target motion and would allow experimenters to test for a possible difference in acceleration perception along the horizontal and vertical axes. This difference will likely appear in the minimum duration of visible target motion necessary to extract target acceleration information.

FURTHER WORK ON THE EXECUTIVE AGENT

SACCADES-PURSUIT INSTRUCTIONS

Many chapters (I, III, IV) of the present thesis highlight the interaction between saccades and pursuit, i.e. the fact that a single

executive agent can give both saccadic and pursuit instructions. However, further experiments are necessary to understand where, in the brain, this interaction happens. The paradigm presented in Chapter V (moving target that is temporarily occluded for a constant duration) is a good testing bench to investigate where saccade pursuit interaction occurs. Indeed, in this case, saccades compensate for the variability of the smooth pursuit response. Therefore, perturbations of the smooth pursuit system could be compensated by the saccadic system if this perturbation occurs upstream from the site of interaction. In contrast, if the perturbation of the smooth pursuit system takes place at a site located downstream from the site of saccade pursuit interaction, the saccadic system would not be able to compensate for the variation in smooth pursuit response. Perturbation of the smooth pursuit response could be obtained either by TMS or by lesions. Different sites would be worth investigating in such a paradigm. For instance, the frontal eye fields, supplementary eye fields, cerebellum, thalamus and dorsolateral pontine nuclei are all involved in the smooth pursuit pathway. Their lesion (either real or obtained by means of TMS) should perturb the smooth pursuit response during occlusions. Last but not least, training and reinforcement can also change the smooth pursuit response during the occlusion of a pursuit target. The adaptation of the saccadic response to these kinds of perturbation should shed some light on the pathways mediating pursuit-saccade interaction.

TRIGGER MECHANISM OF PREDICTIVE SACCADES

In chapter V, we demonstrated that the trigger of predictive saccades is under the control of cognitive functions and that the first predictive saccade is likely elicited by the disappearance of the target. However, we did not investigate the precise distribution of the predictive saccade latency, especially for the ensuing saccades. This distribution could be tested by asking the subjects to perform smooth pursuit eye movements in total darkness. Presenting a moving target several times should allow subjects to learn target parameters. Asking them to pursue the same target that is rendered invisible during its whole motion should remove the perturbation due to target disappearance and shed light on the saccade latency distribution.

COMPUTER OF THE EXECUTIVE AGENT

We have shown that the executive agent based its predictive pursuit instructions on the output of its computer. This computer is able to infer future target motion on the basis of pre-occlusion target parameters or learning. However, we still don't know if the computer is able to adapt its computations to changes of the target characteristics. For instance, if subjects observed different balls bouncing on the ground in such a way that the bounce occurred behind an occluder, would the computer be able to adapt its computations to the actual characteristics of the ball? In other words, can the computer take into account the changing characteristics of the external world in

order to predict upcoming target trajectory? Finally, it should be easy to check if anticipatory smooth eye movement before target motion can also be driven by the dynamic representation of future target trajectory stored in the executive agent's computer. For instance, if subjects are instructed that the target will follow a circular path, anticipatory smooth eye movements might be curved in order to follow future target trajectory.

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