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DETAILED ANALYSIS OF SLOW OSCILLATORY MOVEMENTS OF EYE POSITION

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To my family

ABSTRACT

Our eyes make continuous movements even when attempting to fixate a stationary object. The involuntary eye movements occurring during fixation are referred to as *fixational eye movements*. There is a general agreement on three types of eye movements occurring during visual fixation: tremor, drift and microsaccade.

Previously, in a 20-minute long recording of eye position during visual fixation, we observed a slow periodic fluctuation in the eye position signal. The characteristics of this fluctuation did not match any of the three known components normally occurring during visual fixation on healthy subjects.

The hypothesis in this thesis has been that the slow fluctuation found in the recording is a never before described, fourth component of the fixational eye movement system.

The aim of the project has been to test this hypothesis and to further elaborate the underlying control mechanism of this slow eye movement component. Study 1: The main purpose of this first study was to prove that the fluctuation was not an artifact due to recording system, sampling frequency or filtering technique. The analysis procedure to filter out the fluctuation was developed and tested. Study 2: The influence of different visual stimuli was evaluated to investigate the perceptual influence on the oscillation. Study 3: The effect of increased extraocular muscle tonus was explored during a convergence task.

The results indicate that a slow oscillatory movement occurs during visual fixation together with tremor, drift and microsaccade. This slow eye movement has a low frequency of 0.04 to 0.10 Hz and amplitude of less than 0.50 degrees. The underlying control mechanisms for amplitude and frequency are different: visual perception seems to have an effect solely on the amplitude whereas varying muscle force only changes the frequency.

It has not been the purpose to describe the underlying reason for why the eyes oscillate and we still have no clear idea of why this oscillation is present in normal healthy subjects. We speculate that the light energy in the optical focus is distributed in an oscillatory mode around the fovea that might be a retina protective mechanism.

LIST OF PUBLICATIONS

- I. Pansell T, Zhang B, Bolzani R, Ygge J. Slow oscillatory eye movement during visual fixation. *Exp Brain Res*. 2011 Mar; 209 (1):1-8. Epub 2011 Jan 15.

- II. Zhang B, Pansell T, Ygge J, Bolzani R. Visual influence on the slow oscillatory eye movement discovered during a visual fixation task. *Vision Res*. 2011 Oct 1; 51(19):2139-44. Epub 2011 Aug 18.

- III. Zhang B, Bolzani R, Öqvist Seimyr G, Ygge J, Pansell T. The influence of horizontal convergence on slow oscillatory eye movements during a visual fixation task. Submitted.

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LIST OF ABBREVIATIONS

FEM	Fixational eye movements
SOM	Slow oscillatory movement
MR	Medial rectus
LR	Lateral rectus
SR	Superior rectus
IR	Inferior rectus
SO	Superior oblique
IO	Inferior oblique
SIFs	Single innervated muscle fibers
MIFs	Multiply innervated muscle fibers
IRDs	Infrared reflection devices
IR	Infrared reflection
TFT	Thin film transistor
VOG	Video-oculography
SSC	Sclera search coil
AC	Alternating current
LCD	Liquid crystal display
DFT	Discrete Fourier transformation
FFT	Fast Fourier transformation
BCEA	Bivariate contour ellipse area
MANOVA	Multivariate analysis of variance

1 INTRODUCTION

1.1 VISION AND EYE MOVEMENTS

Vision is one of the most important sensory modality in humans. It is estimated that the largest part of sensory information reaching the central nervous system is provided by vision. The prerequisite for distinct and sharp vision is that the optical system of the eye can accurately form an image of the object of interest. Then the image of the object should be held stable on the retina. The image motion beyond the range that can be tolerated will deteriorate vision (Burr and Ross, 1982). In addition, the image of the object should be positioned close to the fovea of the retina, which has the higher density of photoreceptors with smaller receptive fields than the peripheral retina. The central part of the retina has the largest representation in the primary visual cortex. This retino-cortical magnification of the receptive fields indicates the importance of correctly identifying objects.

Eye movements are crucial for clear vision. Eye movements align the visual axes to the object of interest and thereby position the object of interest onto the fovea. Also they can track a moving object and thereby hold the image of the object stable on the retina. Based on the requirement to serve vision, eye movements can be divided into two main types: the one type are *those that stabilize gaze and so keep images steady on the retina*, and the other type are *those shift gaze and so redirect the line of sight to a new object of interest* (Leigh and Zee, 2006).

This thesis will focus on the first category of eye movements that stabilize gaze, and present a never before described component of fixational eye movements.

1.2 FIXATIONAL EYE MOVEMENTS

The involuntary eye movements occurring during visual fixation are referred to as fixational eye movements (FEM). It has long been known that our eyes are never still, even when fixating a stationary object (Ratliff and Riggs, 1950; Ditchburn and Ginsborg, 1953; Cornsweet, 1956). The most probable reason is that visual perception habituates its response to a uniform stimulation of the retinal receptor; and the eye movements during visual fixation can keep the retinal receptor continuously receiving the stimulation and overcome vision disappear due to the neural adaption (Martinez-Conde, Macknik and Hubel, 2004). There is a general agreement of three components

of eye movements during visual fixation in humans: tremor, drifts and microsaccades (Yarbus, 1967; Steinman, Cushman and Martins, 1982; Carpenter, 1988).

1.2.1 COMPONENTS OF FIXATIONAL EYE MOVEMENTS

1.2.1.1 Tremor

Tremor is an aperiodic, wave-like movement of the eyes (Riggs, Ratliff, Cornsweet and Cornsweet, 1953), with a frequency of up to 100 Hz (Spauschus, Marsden, Halliday, Rosenberg and Brown, 1999) and small amplitudes (Steinman, Haddad, Skavenski and Wyman, 1973), which are about the diameter of a cone in the fovea. Tremor is generally thought to move independently in the two eyes (Riggs and Ratliff, 1951; Spauschus et al., 1999). The contribution of tremor to the maintenance of vision is unclear. Recently some studies suggested that tremor might maintain neural activity in the early visual system (Spauschus et al., 1999; Martinez-Conde, Macknik and Hubel, 2002; Greschner, Bongard, Rujan and Ammermuller, 2002).

1.2.1.2 Drift

Drifts occur simultaneously with tremor and are usually identified as the period between two successive microsaccades. Based on that definition, drifts are low-velocity (<0.50 degree/s) movements with an amplitude typically smaller than 0.1 degrees (Ditchburn and Drysdale, 1973; Engbert and Kliegl, 2004). Drifts are non-conjugate movements and were initially supposed to be random movements of the eye as a result of the instability of the oculomotor system (Ditchburn and Ginsborg, 1953; Cornsweet, 1956). Later, drifts were found to have a compensatory role in maintaining accurate visual fixation when compensation by microsaccades was poor or absent (Steinman, Cunitz, Timberlake and Herman, 1967). It is generally thought that drift plays a role in fixation control and prevention of perceptual fading (Collewijn and Kowler, 2008; Rolfs, 2009).

1.2.1.3 Microsaccades

Microsaccades were called "flicks" in early studies and are fast, jerk-like eye movements. Microsaccades occur one to two per second with amplitude less than 0.50 degrees (Zuber, Stark and Cook, 1965; Engbert and Kliegl, 2004). The relationship between microsaccade velocity and amplitude follows the main sequence (Zuber et al., 1965): the saccade peak velocity linearly depends on the saccade amplitude, similar to larger saccades. Microsaccades in the two eyes are executed in the same direction

(conjugate) (Ditchburn and Ginsborg, 1953; Yarbus, 1967; Ditchburn and Drysdale, 1973). The role of microsaccades during visual fixation has been on debate for a long time. Some proposed that microsaccades play an important role in the maintenance of vision (Cornsweet, 1956; Ditchburn, Fender and Mayne, 1959; Nachmias, 1961; Carpenter, 1988) whereas some others argued that microsaccades is useless and merely a kind of nervous tic” (Steinman, Haddad, Skavenski and Wyman, 1973; Kowler and Steinman, 1980). Recent neurophysiological studies verify that microsaccades can generate neural responses in almost every visual area: the lateral geniculate nucleus, MT, the extrastriate area V2 and V4, the primary visual cortex (Martinez-Conde et al., 2004). Together with the quantity characteristics of microsaccades: they carry the retinal image across a large range of photoreceptors (Ratliff and Riggs, 1950; Martinez-Conde, Macknik and Hubel, 2000). It is reasonable that microsaccades serve to visual perception. Some recent studies indicate that microsaccades might help to counteract receptor adaptation on a short timescale and to correct fixation errors on a longer timescale (Engbert and Kliegl, 2004).

1.2.2 VISUAL MODULATION OF FEM

If the main contribution of fixational eye movements to vision is to overcome the image disappearing due to neural adaption, we may expect that the visual perception, as feedback, has some effect on the control of fixational eye movements. The thought has already been proposed and investigated by others. In darkness, fixation stability reduces markedly compared to when fixating a visual stimulus (Skavenski and Steinman, 1970; Sansbury, Skavenski, Haddad and Steinman, 1973; Epelboim and Kowler, 1993). Both microsaccades (St Cyr and Fender, 1969; Matin, Matin and Pearce, 1970)) and drift show larger amplitude (Ditchburn and Ginsborg, 1953; Sansbury et al., 1973) in darkness compared to when a visual target is available. This indicates that one of role of fixational eye movements is to minimize fixation error and to maintain the image within the fovea. Some studies showed that the visual target characteristics, such as size, luminance, color, configuration, and eccentricity, can affect microsaccade rate (Steinman, 1965) and magnitude (Sansbury et al., 1973) as well as drift velocity (Leigh and Zee, 2006) and magnitude (Sansbury et al., 1973). However, Boyce (Boyce, 1967) reported that target luminance and color had no effect on the fixational eye movements; while in his setup the change of the target luminance did not bring up image blur. So man can speculate that if the parameters of the visual stimulus, such as luminance,

color, contrast, size, and shape, render barely visible, the normal fixational eye movements may not sufficiently maintain visibility.

1.2.3 COGNITIVE MODULATION OF FEM

Eye movements are always intertwined with brain activities (Corbetta, Akbudak, Conturo, Snyder, Ollinger, Drury, Linenweber, Petersen, Raichle, Van Essen and Shulman, 1998). Although fixational eye movements are generally considered to be involuntary movements, one of its components, microsaccades, can be suppressed. Several studies has reported that in high accurate visual fixation tasks like threading a needle or rifle shooting, humans or other primates can suppress their microsaccades for several seconds (MacKay and Fiorentini, 1966; Steinman, Cunitz, Timberlake and Herman, 1967; Steinman, Haddad, Skavenski and Wyman, 1973; Bridgeman and Palca, 1980; Hafed and Clark, 2002; Engbert and Kliegl, 2003a-b).

Visual input can drive visual attention shift, so the visual modulation on fixational eye movements can be the byproduct of attentional modulation on fixation eye movements. Recently studies have demonstrated that microsaccade rate and orientation can be strongly modulated by display changes and visual attention in spatial cuing paradigms (Hafed and Clark, 2002; Engbert and Kliegl, 2003a-b)

1.3 SLOW OSCILLATORY EYE MOVEMENTS (SOM)

Five years ago, Pansell and collaborators occasionally observed the slow movement. They recorded the torsional gaze stability over 20-minutes in a healthy subject by a new bought recording system – the C-ETD Video oculography (Chronos Vision Inc. Germany). In a 20-min long recording of the eye position signals (fig. 1), they observed a fluctuation of the signal. In discussion with professor Ygge and professor Bolzani, they concluded that the characteristics of this fluctuation did not match any of the previously identified eye movements during visual fixation and decided to go further.

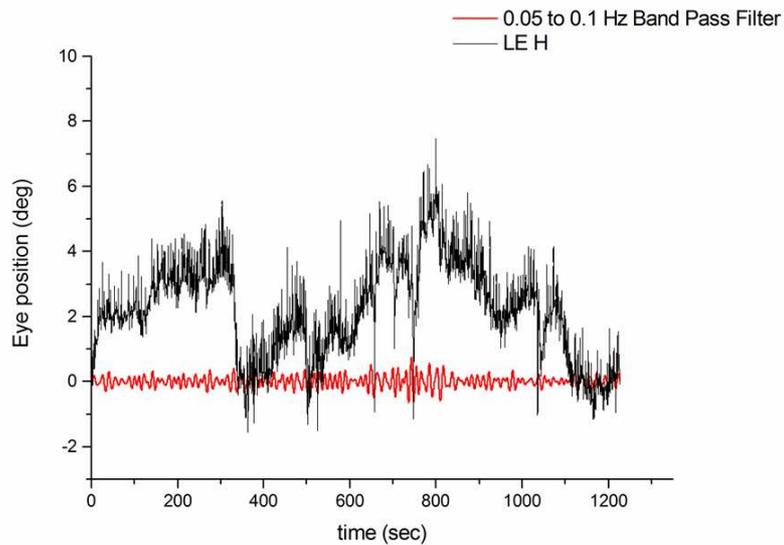


Figure 1. This is the eye position signal recorded by the C-ETD technique. The eye position signal was filtered by a band pass filter (0.05 – 0.10 Hz) and showed fluctuations in the eye position signal of about ± 0.5 deg.

As mentioned above, there is a general agreement about three components of fixational eye movements to occur during visual fixation. To put forward a hypothesis about a fourth component requires a thorough investigation to exclude other possible explanations to this fluctuation of eye position.

We applied a fast Fourier transform on the eye position signals and could see a pronounced peak in the band of 0.04 to 0.10 Hz, which means there is a periodic process of the corresponding frequency occurring during visual fixation. We therefore performed band pass filter, which included the peak value in the FFT plot, on the recording and found that the eye position signals could be divided into three components (See fig.2): (1) a slow drift, (2) a middle range component (follows the oscillation movement), and (3) a rapid component, including tremor, microsaccades, blinks, noise etc.

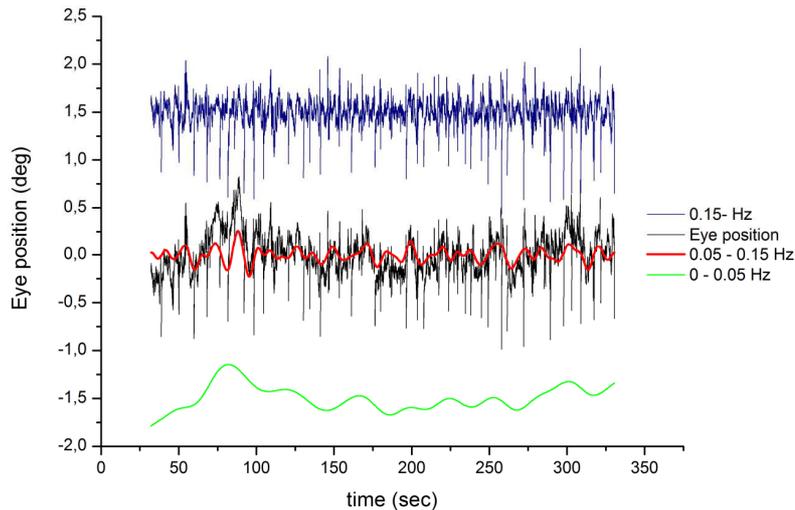


Figure 2. Graph shows the eye position (black) recorded by C-ETD technique during a fixation task over 5 minutes. The signal was decomposed into three components: (1) a low-frequent (green line), (2) a mid-frequent (red line) and (3) a high-frequent component (blue line).

Could this fluctuation be due to an artifact of the recording system, or constructed by the sampling frequency as a result of aliasing? Could the analog-to-digital signal conversion which is built in the recording systems have any effect on the fluctuation of eye positions? Or maybe this fluctuation is created by analysis process. In our first publication, we described how we explored the answers to these questions. From then on, this fluctuation was named as Slow Oscillatory Movement (SOM).

SOM is slow periodic oscillation of eye position, both in the horizontal and in the vertical directions. It has a frequency of 0.04 to 0.10 Hz and amplitude of less than 0.5 degree. When horizontal and vertical SOMs are combined in a XY-plot, the eye position was found to oscillate in a horizontal –vertical elliptical track (fig.3). In our following studies, we found the apparent double dissociation between perceptual effects on amplitude of SOM vs. muscle force effects on frequency of SOM. The less visual information or no visual clue (in darkness) could trigger larger SOM. However, the frequency of SOM cannot be influenced by the visual stimulus. Even in darkness when the subject was instructed to fixate an imagined non-existing target, the frequency of SOM had a similar value compared to when fixating a visual target. In a fixation test under horizontal convergence of varying angles, the frequency of SOM was found to be lowest in the nearest eye-target distance (increased bilateral adduction). Horizontal convergence had no effect on the amplitude of SOM.

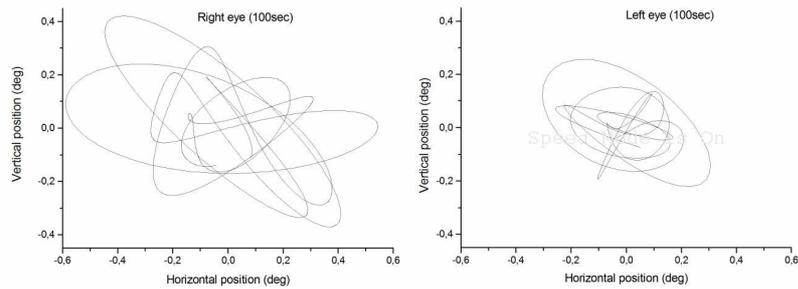


Figure 3. The horizontal and vertical SOM component (100 secs) was combined in a 2-D plot for each eye, displaying an oscillatory elliptical track of eye position.

1.4 ACTIONS OF EXTRAOCULAR MUSCLE

1.4.1 Six muscles and their functions

Each eye has six extraocular muscles in the orbit, which are responsible for rotating the eye globe. There are a pair of horizontal rectus muscles: medial rectus (MR) and lateral rectus (LR), and a pair of vertical rectus muscles: superior rectus (SR) and inferior rectus (IR), and a pair of oblique muscles: superior oblique (SO) and inferior oblique (IO). The four rectus muscles originate from the annulus of Zinn at the apex of the orbit. MR inserts onto the medial side of the globe at approximate $5.3 (\pm 0.7)$ mm from the corneoscleral limbus, and LR inserts onto the lateral side of the globe at approximately $6.9 (\pm 0.7)$ mm from the limbus. MR and LR are antagonistic. Because they lie in the same horizontal meridian, their contractions produce only horizontal eye movement: contraction of MR adducts the globe, whereas contraction of LR abducts the globe.

SR inserts onto the globe superiorly at approximately $7.9 (\pm 0.6)$ mm from the limbus, and IR inserts inferiorly at approximately $6.8 (\pm 0.8)$ mm from the limbus. They subtend a 23 degree angle with the visual axis when the eye is in primary position. SR solely elevates the globe and IR solely depresses the globe when the eye is abducted 23 degrees. In addition to their primary action, SR has a secondary action of incyclotorsion and a tertiary action of adduction, and IR has a secondary action of excyclotorsion and a tertiary action of adduction.

SO also originate from the annulus of Zinn, and passes through the trochlea in the superomedial orbit and extends in a posterolateral direction and inserts onto the superior posterotemporal quadrant of the globe. The trochlea is superior oblique's

functional origin. SO subtends a 54 degree angle with the visual axis when the eye is in primary position. So in addition to its primary action of incyclotorsion, SO has a secondary action of depression and tertiary action of abduction. IO originates from the anterior medial orbital floor, and inserts onto the inferior posterotemporal quadrant of the globe and subtends a 51 degree angle with the visual axis when the eye is in primary position. So in addition to its primary action of excyclotorsion, IO has a secondary action of elevation and a tertiary action of abduction.

1.4.2 Neural innervations of extraocular muscles

The oculomotor nerve, cranial nerve III, innervates MR, SR, IR and IO. The trochlear nerve, cranial nerve IV, innervates SO. The abducens nerve, cranial VI, innervates LR. The nuclei of these nerves are closely associated, and coordinate the corresponding extraocular muscles to rotate the eye globe. There are two classical laws to explain how the extraocular muscles are innervated during the eye movement: Sherrington's law of reciprocal innervation and Hering's law of equal innervation. Sherrington elaborated: when one set of muscles is stimulated, muscles opposing the action of the first are simultaneously inhibited. For example, whenever the medial rectus of the right eye receives an excitatory signal to contract, an equivalent inhibitory signal is sent to the lateral rectus, the antagonist muscle of the same eye. The integrated manifestation is the adduction of the right eye. Hering's law proposes that the extraocular muscle responsible for each eye's movement receive the equal innervation during conjugate movements, so that the two eye globes move in the same direction and in the same velocity. This law is questioned now because the premotor neurons were thought to encode conjugate velocity commands for saccades are found to actually encode monocular commands (Zhou and King, 1998; King and Zhou, 2002).

1.4.3 Properties of extraocular muscles

Each extraocular muscle has two layers: an inner "global layer" and an outer "orbital layer". The orbital layer inserts onto the periorbital connective tissue- Tenon's capsule or "pulleys", which forms sleeves around the individual eye muscles. The global layer extends the full muscle length and inserts on the sclera. Extraocular muscle can be divided into two fundamentally categories- the single innervated muscle fibers (SIFs) and multiply innervated muscle fibers (MIFs). The SIFs, called also "twitch" fibers, generate an all-or-nothing contraction on the activation of their centrally lying endplates. The MIFs, called also "nontwitch", are innervated at several places, "en

grappe” nerve endings, along their length. The activation of the nerve fibers of MIFs generates a local contraction which is not propagated throughout the muscle fiber (Büttner-Ennever, 2007). The contraction of MIFs is slowest of other muscle types, but can hold the tension for a long period. Based on the morphological and physiological characteristics of these two muscle sets, the SIF motoneurons and muscles are more suited to driving eye movements, and the MIF motoneurons and muscles to setting the tonic tension in any given eye position.

1.4.4 Tonic strength during tonic vergence

Extraocular muscles show a continuous slight activity even when at rest, called ”tonic activity”. This action is performed by the discharges of the tonic neural activity- the step of innervation. The generation of the vergence movement needs two kinds of neural activities: the pulse innervation and the step innervation (Leigh and Zee, 2006). The pulse innervation discharge a burst of neural activity to the muscle and the muscle generate a powerful contraction to overcome the orbital viscous drag and elastic restoring forces. The eye globe rotates to a new position. The velocity-coded signal can be integrated into the position-coded signal by the vergence integrator (Gamlin and Clarke, 1995). The step innervation raises a new tonic level of neural activity to resist the elastic restoring forces and hold the eye globe in the new position.

2 AIMS

2.1 STUDY 1

The purpose of this study was to test our hypothesis of a slow oscillatory movement existing together with tremor, microsaccade and drift during visual fixation and also to describe the characteristics of this movement.

2.2 STUDY 2

To analyze if SOM is modulated in response to changes of the visual target to better understand the underlying control mechanism of SOM.

2.3 STUDY 3

In study 1 and 2, we did not find any variable that could influence SOM frequency. That raised the question if SOM frequency is an inherent property for each individual, or if it can be modified by variation in the level of motor input to the eye muscles during fixation. In this study, we aimed to test this idea by recording SOM during horizontal convergence at four different fixation distances.

3 MATERIAL AND METHODS

3.1 SUBJECTS

Healthy individuals without a history of neurologic disorders or eye movement disturbances were enrolled in the study. Taking medication with a possible influence on the central nervous system was not allowed. All individuals were examined to ensure normal vision (near va > 0.8 decimal acuity) and stereopsis (LANG stereo <550). In the study 3, each test subject had a normal vision, stereopsis (LANG <200 sec arc) and normal near point of convergence (≤ 10 cm). The dominant eye was determined at close distance. The nature and possible consequences of this study was explained before the test and all individuals gave informed consents. The research adheres to the tenets of the Declaration of Helsinki (World Medical Association; DoH/Oct2008). The research has been approved by the local ethic committee (2009/1583-31/1: Detaljerade studier av fixationsögonrörelser).

Table 1. Subjects involved in each study

Study	Number of subjects (male/fema)	Mean age (range)
1	7 (4/3)	38.9 (27-62)
2	13 (3/10)	39.8 (25-63)
3	14 (4/10)	38.1 (20-65)

3.2 EYE MOVEMENT RECORDING TECHNIQUES

An eye movement recording system detects the eye position and by continuous recording it is possible to evaluate changes in eye position (i.e., eye movements). Each technique has its pros and cons. Some are more invasive than others, requiring topical anesthetics while others are remote with no contact to the body or head at all. Some systems are highly accurate while others are less accurate and suffer from more signal noise. Most systems detect changes in 2 dimensions, horizontal and vertical eye movements, but there are both 1-dimensional as well as 3-dimensional systems available.

The four most popular recording techniques are the Electro Oculo Gram (EOG), infrared reflection devices (IRDs), scleral search coil (SSC) and video-oculography (VOG) (Eggert, 2007). We used the The XY1000 (IOTA Eye Trace System, Sweden), the Tobii T60 (Tobii Inc. Sweden), the C-ETD video oculography (Chronos Vision Inc.

Germany) and the Scleral Search Coil technique (Chronos Vision Inc. Germany) in order to record the eye position signals and investigated the effect of recording technique on SOM.

3.2.1 Infrared reflection devices-XY1000

IRDs use photodiodes to measure the intensity of infrared light reflected from the eye. The eye position is calculated by the individual change in infrared-light intensity between the different photodiodes. The XY1000 consists of a pair of head mounted goggles and a small processing unit. Eight infrared reflection (IR) sensors are built into the goggles, four for each eye. The IR radiation can be reflected from the white sclera, and transmit through the transparent cornea and absorbed by the pigmented iris. The eye position is calculated by the relative change in illumination on the eight sensors. XY-1000 has a high temporal resolution (the sampling frequency is 1000 Hz) and the spatial resolution is 0.01 degree.

The XY-1000 is very sensitive to relative translations of the photodiodes to the eye. A translational movement of the goggles of 1 mm for an eye radius of 1.25 cm will lead to an eye position error of almost 5 degrees (Eggert, 2007). The goggles should therefore be stabilized to the head during recording. Eye lid artifacts are more pronounced in this system compared to other recording techniques since lid movements also induce changes in illumination, especially in the vertical direction. The system requires a thorough calibration procedure using a nonlinear calibration, since the system suffers from nonlinearity.

3.2.2 Infrared reflection devices - Tobii T60

This system, called double Purkinje image eye tracker, uses light reflections from the cornea and the lens to measure the orientation of the eye without having any contact with it. An infrared camera is embedded at the lower part of the TFT monitor (resolution: 1280 × 1024 pixels). The IR camera detects the shape and position of the pupil and also tracks the Purkinje images. Tobii has a limitation that there is a field nonlinearity component due to mainly the curvatures of the relevant optical surfaces of the eyes and to some extent also the change in pupil size. A deflection of eye position will change the perspective of the round pupil into an ellipse and the Purkinje images will change their relative position to each other. Another artifact is due to the lack of rigidity between the corneal surface and the lens of the eye ball (Crane and Steele,

1985). The temporal resolution of the system is 50 Hz and the spatial resolution is 0.2 deg. The device is easy to use with simple setup. The relative low spatial resolution makes this system not so suitable for recording fixational eye movements.

3.2.3 Video-oculography (VOG) - C-ETD Video Oculography

Video-based eye movement recording systems record the anterior surface of the eye. In the CET-D system the video cameras are virtually positioned in front of the eyes at the visual axis by using semi-transparent mirrors. The cameras and mirrors are attached to the head on a helmet. The C-ETD system has two miniature cameras (one for each eye) with CMOS image sensors. The eye position is analyzed by detecting the pupil form and approximating the visual axis to pass the center of the pupil circle. The temporal resolution of the video system is 200 Hz and the spatial resolution is <0.1 degrees. The system suffers from the pupil diameter fluctuation artifacts, especially for slow eye movements (Walsh, 1988; Engbert, Mergenthaler, Sinn and Pikovsky, 2011). We first believed that the SOM signal might include a signal artifact caused by slow oscillation of the pupil diameter. To test this question, we made a control experiment by comparing the fluctuation trace of the pupil diameter with the SOM (see second publication).

3.2.4 Sclera search coil technique (SSC)

The sclera search coil system is based on the electromagnetic induction theory. One or two coils are molded in a soft contact annulus which can be attached to the eyeball surface. Subject is positioned in an AC magnetic field. The system measures the voltages in the coil and the eye position can be calculated from the induced current in the coil. The temporal resolution of the system can be set to maximum 1000 Hz and the spatial resolution was 0.01 deg.

The SSC technique suffers from coil slippage on the ocular surface due to eye lid movement. This will cause a transient displacement of the coil at every blink. It has also been shown that the peak velocities of saccades are significantly lower within subjects with the SSC technique than with an IR-technique (Träisk, Bolzani and Ygge, 2005). The authors hypothesize this might be caused by coil slippage during the accelerating phase of the saccades.

In study 1 four different recording techniques were used: The XY1000 (IOTA Eye Trace System, Sweden), the Tobii T60 (Tobii Inc. Sweden), the C-ETD video oculography (Chronos Vision Inc. Germany) and the Scleral Search Coil technique (Chronos Vision GmbH, Germany). The C-ETD video oculography was used to record eye fixational movement in study 2 and 3 for its convenience to operate and the low noise in the recording signals.

3.3 VISUAL STIMULUS AND PARADIGMS

In study 1 and 2, the visual stimulus was displayed on a LCD-screen (res 1600 ×1200px; contrast 900:1; 60Hz) at 50 cm eye-screen distance (100 cm for XY1000 recording system) with the center of the screen at the same level as the eyes of the subject. The screen subtended a visual angle of 47° (24° for XY1000) in the horizontal direction and 36° (18° for XY1000) in the vertical direction. In study 3, the visual stimulus was a small red lamp built into a black box (7.5×8.5×9.5 cm) illuminating a hole (3×3 mm) with transparent adhesive tape on its front side, creating a sharp visible red dot. This box was mounted on a stand, allowing it to be moved in the room in front of the subject. A binocular eight-point horizontal and vertical calibration (amplitude 4 and 8°, respectively) was conducted prior to each recording. The visual stimulus was projected at the same level as the subject's eyes. The subject was sitting on a chair, using a chinrest and a bite bar to reduce unintended head movements. The instruction was to concentrate and maintain fixation on the fixation target during the entire test session.

3.3.1 Study 1

The visual stimulus was a photo of a city scene with a red fixation dot in the center (visual angle: 0.29°, 0.14° for XY1000). The viewing condition was binocular. Study 1 included three test sessions.

3.3.1.1 Session 1

In the first session, eye movements were recorded in all seven subjects with the XY1000, C-ETD and Tobii T60 technique. The purpose was to investigate if the slow oscillation could be recorded with different techniques with fundamentally different principles of detecting eye position. Eye movements are sampled in time by the recording systems, and are converted into a discrete eye position signal. The process of generating discrete time samples from an analog signal is sampling. The numbers of

eye positions per second is the sampling frequency of the recording system. We can consider an analog sinusoidal signal $x(t) = A \cos(\omega t + \phi)$, ω is the angular velocity and $1/t$ is the frequency.

If this signal is sampled at $t = n T_s$ (T_s is the sampling time interval), the following discrete signal is generated:

$$x[n] = A \cos(\omega n T_s + \phi) = A \cos(\theta n + \phi), n = 0, 1, 2, \dots$$

Based on the relationship between the analog and digital frequencies, we can draw the following inferences: for the three used recording systems, we cannot obtain identical eye position signals even if they record the same eye movement. If this diversity of eye position signals does not impact on the SOM, then we can ascertain that SOM is not created by the recording process.

3.3.1.2 Session 2

If sampling frequency is much lower than the original signal, aliasing will occur. For example, if the original signal is a sinusoidal function and its frequency is 1.6 Hz.

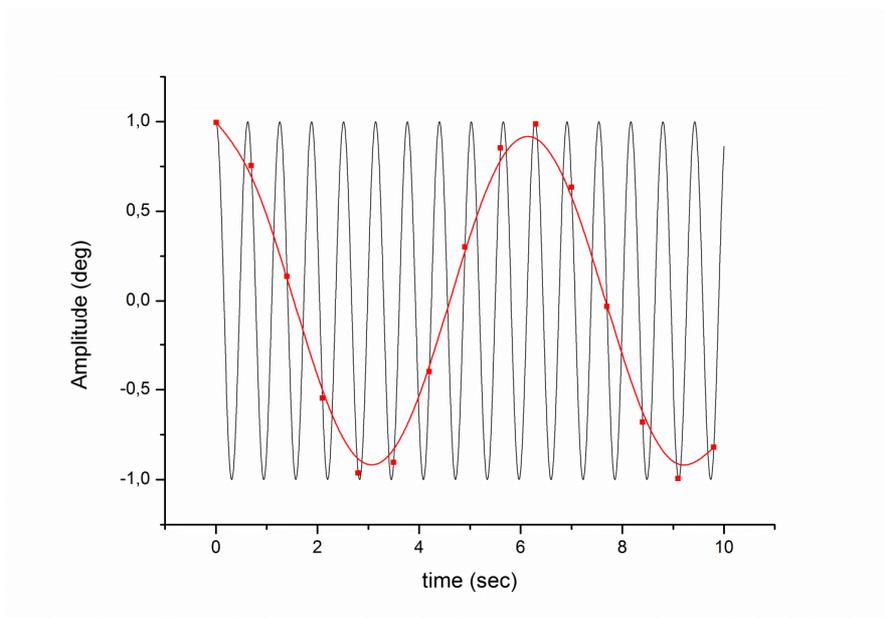


Figure 4. The dots represent the sampled data. Because of few sampled data points, the reconstructed signal is a poor representation of the original.

Since the SOM frequency is much lower than the system frequency, this might be an artifact due to aliasing effect. In the second session, fixational eye movements were recorded with five different sampling frequencies (120, 140, 160, 180 and 200 Hz) in one subject using the search coil technique to investigate the possible influence of aliasing.

3.3.1.3 Session 3

In the third session, the same signal from one eye (left eye vertical) was synchronously filtered by two different filters (analogue and digital) to investigate the effect of filtering technique. Each recording in study 1 lasted for five minutes.

3.3.2 Study 2

Study 2 included three sessions and each session has a different stimulus. In the first session two different backgrounds were evaluated. The first was a photo of a city scene (i.e. structured background) and the second with a black background (i.e. non-structured background). The same fixation target (a red dot, visual angle 0.29°) was superimposed on the center of the backgrounds. The viewing condition was binocular. In the second session the size of the target was evaluated. The target was a red round disc with different visual angles (target 1: 0.29° ; target 2: 3.72° ; target 3: 7.44° ; target 4: 11.14°) that was superimposed on the center of the city scene. The viewing condition was monocular and the dominant eye was chosen for fixation. In the third session, the visual stimulus was an imagined non-existing dot (i.e. no visual stimuli) in a completely dark room (i.e. no visual feedback). The stimulus with a red dot (visual angle: 0.29°) on the photo of a city scene was used as control to the recording in dark. The viewing condition was monocular and the dominant eye was chosen for fixation. Each recording in study 2 lasted for five minutes.

3.3.3 Study 3

The visual stimulus was placed in the midline in front of the subject at four different distances, 120 cm, 60 cm, 30 cm and 15 cm. There were two recording orders, either from far-to-near (from 120 to 15cm) or from near-to-far (from 15 to 120cm). Each test subject was randomized for either test order. The viewing condition was binocular. Each recording lasted for three minutes.

3.4 DATA ANALYSIS AND STATISTICS

3.4.1 The analysis procedures of the eye position signals

All systems save eye position recordings in ASCII-files with one horizontal and one vertical channel per eye. The eye position signals were first calibrated to convert the deflection of the signal (arbitrary unit) into degrees eye rotation. This was done with JR software (setup in our laboratory). Next the horizontal and vertical eye position data were imported into the Origin 8.0 software (Origin Lab Inc.) for evaluation.

To offset the signal drift, a regression line was fitted and subtracted from the original eye movement signal to obtain a track with no trend of linear drift of the signal. The entire track was tilted to horizontal and shifted to $y = 0$ to approach and vary around the base line. All blinks were removed by cutting the signal amplitudes outside of $\pm 1^\circ$. In this way, the signal displacement and the linear drift would not affect the following analysis.

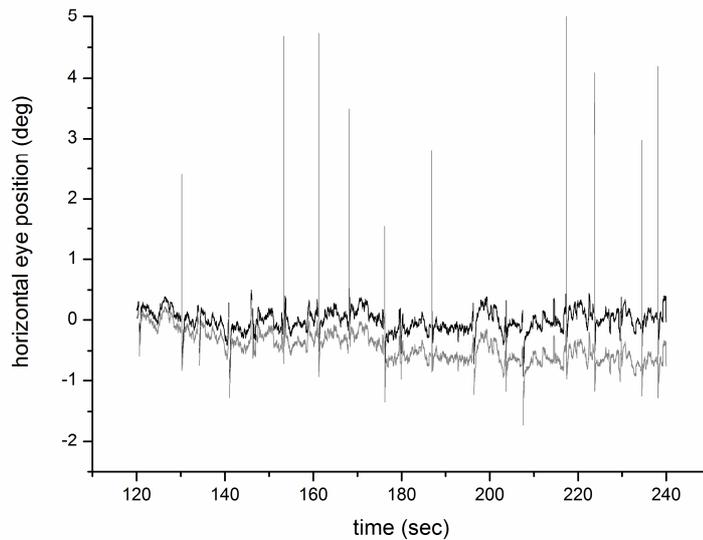


Figure 5. The grey line represents the eye position signals recorded by the C-ETD system, and the black line represents the position signals after linear regression and blinks cleaning.

3.4.2 Fast Fourier transform (FFT) - the first step of searching for SOM

A famous French mathematician, Joseph Baron Fourier presented in his book *The Analytical Theory of Heat* how heat diffuses in solid bodies and proposed that any function could be written as an infinite sum of the trigonometric functions of cosine and sine, as follows,

$$y = 1/2 a_0 + (a_1 \cos x + b_1 \sin x) + (a_2 \cos 2x + b_2 \sin 2x) + \dots$$

The series above, the Fourier series, are named after the famous mathematician. The study of Fourier series generated *Fourier analysis*, a method used to find the frequencies present in a complex signal; also known as *frequency analysis* (Ridpath, 2012). Fourier analysis decomposes a function mathematically into the sum of simple oscillations of various frequencies. The decomposition process is called a *Fourier transform*. Fast Fourier transform (FFT) is an algorithm that computes the discrete Fourier transform accurately and efficiently (Daintith and Wright, 2008) Discrete Fourier transform (DFT) is a kind of discrete transform used in Fourier analysis. In

DFT, the input function should be discrete, for example the eye position over time. DFT can reveal periodicities in input data as well as the relative strengths of any periodic components.

We performed the FFT analysis on the processed data and in Origin we made a script to perform exactly the same analysis on all data. The frequency spectrum of FFT is related to the input points. The maximum of the frequency value (Nyquist frequency) is equal to the half of the sampling frequency and the fundamental frequency is based on the number of bins and sampling frequency. The number of bins is an integer power of 2 which should be less than or equal to the input points.

We can give an example: in our C-ETD recording, the sampling frequency is 50 Hz, and the maximum frequency is 25 Hz. The period chosen to evaluate is 120 sec, so the input points are 6000. The number of bins should be 2^{12} (4096; $2^{13} = 8192$ more than 6000). The fundamental frequency therefore is $25 \text{ Hz}/4096 = 0.0061 \text{ Hz}$. The frequency value is accumulated by a fundamental frequency in FFT. So it is possible that a frequency value of a periodic function falls in the interval between the two successive FFT frequencies. Therefore, our peak frequency value may be not precise but close to the real SOM frequency. To compensate for this deficiency, we use the peak value in FFT as the initial value and perform the sine fitting function on the eye position data to reveal a more exact frequency value of SOM.

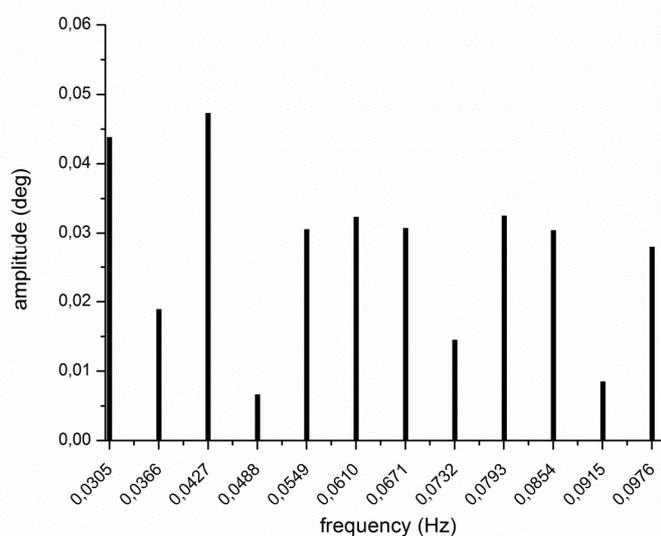


Figure 6. The eye position signals has been performed the FFT and then we can receive the amplitude-over-frequency plot. In the horizontal axis, the frequency values accumulate in fundamental frequency of 0.006 Hz.

3.4.3 Statistical analysis

In study 1, the effect of recording system on the SOM was analyzed by a Kruskal–Wallis test. The effect of sampling frequency was analyzed by a correlation analysis, α -value 5%. In study 2, a bivariate contour ellipse area (BCEA), including all fixational eye movements, was calculated to evaluate the fixation stability for the eye (Steinman, 1965) under different experimental conditions. Stability in terms of bivariate contour ellipse area (BCEA) was calculated, which describes the 95% confidence interval of the distribution area over which the eye was moving during visual fixation. The analysis of variance for the repeated measures was used to analyze the effect of background. Multivariate analysis of variance (MANOVA) for repeated measures was used to investigate the effect of target size on SOM. Paired sample t-test was used to analyze the effect of visual feedback. In study 3, Multivariate analysis of variance (MANOVA) for repeated measure was used to investigate the effect of convergence level on the frequency and amplitude of the SOM. SPSS statistical package version 15.0 has been used for all analysis.

4 RESULTS AND DISCUSSIONS

4.1 HUMAN EYES MAKE A LOW FREQUENCY MOVEMENT DURING VISUAL FIXATION

In the first paper, we described that SOM was discovered in recordings from all four recording systems (fig.7).

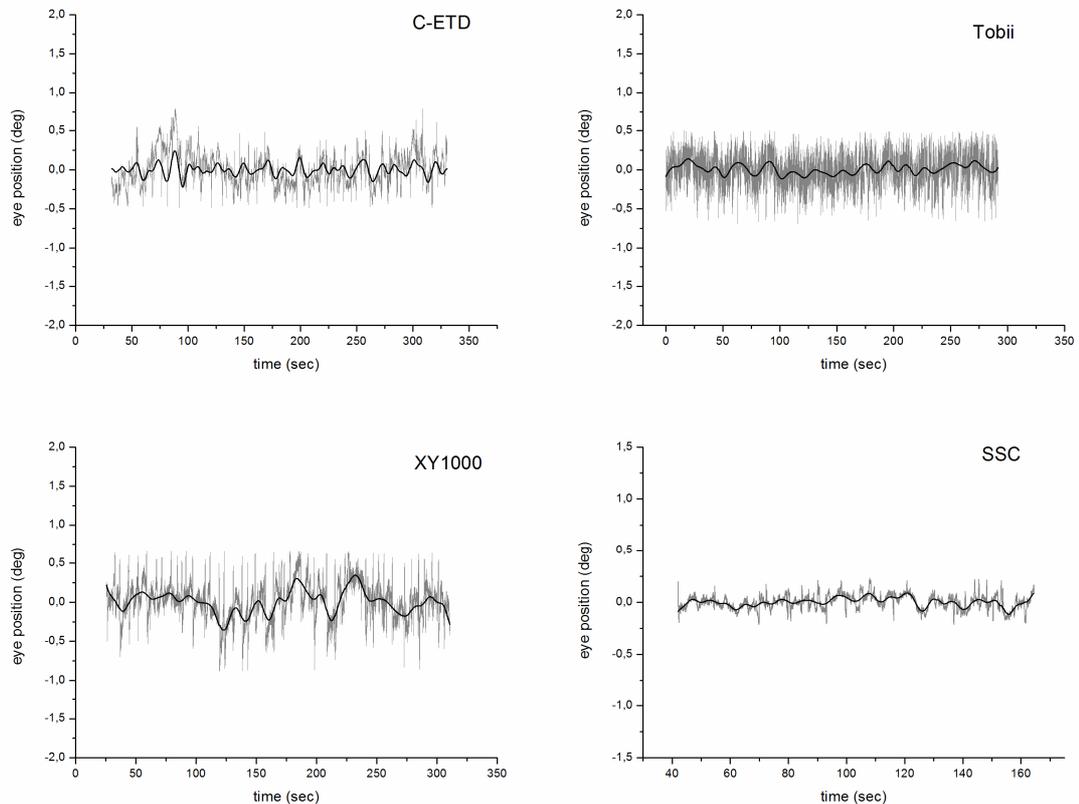


Figure 7. The graphs show the eye position signals (grey lines) recorded by four eye movement recording systems. A slow oscillatory eye movement (black lines) was clearly presented in all the recordings.

None of the recording systems is perfect one in exactly recording eye position. A good way to analyze the performance of a system is to record the same eye movement through different recording system and compare their data and investigate if their limitations have any effect on the study object (in this case the SOM). FFT plots for the eye position signals recorded by the four different eye trackers cannot be identical due to the different sampling frequencies and different characteristics of the recording systems. The analysis of the SOM with the different recording systems revealed very similar SOM frequency values with all the recording systems. That implies that SOM is not an artifact due to the recording process. Otherwise, the oscillation would be absent or at least very different with some of the recording systems.

The frequency of SOM and sampling frequency has no linear relation which shows that the SOM are not an effect of aliasing. The eye position signals run through the digital filter and an analogue low-frequency filter simultaneously, did not reveal any differences between the SOM components in the recording. Therefore we conclude that the analog-to-digital signal conversion does not create any secondary fluctuations of the signal and that SOM most certainly describes a true movement of the eye.

Fast Fourier transform describe a signal in frequency domain. The amplitude of every component, inclusive all the noise, is presented in the FFT plot. To prove the validity of the peak we chose, we performed the same analysis on a white-noise-signal. White noise signal is a random signal which contains equal amplitude (equal power) within a bandwidth frequency. A white noise signal was created with the same frequency band and the same standard deviation as the eye position signal. The result of this control experiment has been reported in our first paper. No oscillation was found in the noise signal. That certifies that our method is viable and effective.

Before we draw a general conclusion about the experiments for paper I, a last experiment was performed. Could the SOM be a product of eyelid blinking, which can influence both translational and torsional eye movement (Bour, Ongerboer de Visser, Aramideh and Speelman, 2002; Rambold, Sprenger and Helmchen, 2002); or could it be related to breathing movement or carotid pulse? Blinking was easily detected by the video system and its frequency has been compared to the fluctuation. No correlation was found. Breathing was observed during recording of eye position. The small lifting movement of the shoulders indicates the inspiration phase and was counted. Breathing has a higher frequency than the fluctuation. The pulse is higher in frequency and no correlation to the fluctuation was found.

4.2 THE PERCEPTUAL EFFECT AND THE POSSIBLE CONTRIBUTION TO VISION

The purpose of paper II was to elaborate the underlying control mechanism of SOM. It is a good approach to study possible modulation factors for this slow movement. We began from visual perception and hypothesized that visual stimuli has some effect on this slow movement. Our second paper demonstrated that SOM amplitude can be affected by the visual characteristics of the stimuli. SOM showed larger amplitude

when viewing a stimulus (i.e. a red dot) placed on a black background compared to when placed on a structured background. The larger visual targets induced larger SOM amplitude in the horizontal meridian. In darkness when the subject was instructed to look at an imagined non-existing target, the amplitude of SOM showed almost a 20-fold increase in amplitude compared to when fixating a visual target. However, the SOM frequency was not influenced by changing the characteristics of the visual target.

The effect of visual stimuli on the amplitude of SOM is pronounced in darkness, implying that the decrease in visibility triggers larger SOM. The results are consistent with some previous studies (Matin et al., 1970; Skavenski and Steinman, 1970).

When inspecting how SOM contributes to the fixation distribution area (i.e. BCEA), we found that BCEA in darkness was decreased by 10-17% after extracting the SOM. BCEA, when fixating a visible target, did only decrease a little. It seems like SOM plays a potential role in the control of gaze stability that is more effective with visual cues than with no visual cue.

4.3 MUSCLE FORCE EFFECT

In our second paper we found that the SOM amplitude was influenced by the characteristics of the visual target but no change was found in SOM frequency. It seems like the visual sensory transformation into a motor command does not influence the frequency characteristics of the SOM.

In the third paper we focused on the influence of the extraocular muscles tonus on the SOM. If the motor input to the muscles varies, what change will that have on SOM? A fixation target was moved in front of the test subject into four horizontal convergence levels. The results revealed that the frequency of SOM was lowest in the nearest eye-target distance, which corresponds to the largest convergence angle with the highest muscle tonus for the medial rectus. No significant difference was found for the SOM amplitude in the tested convergence levels.

Based on unpublished data from Lennerstrand and Campos, who measured MR force in wake patients by the strain gauges (Showa N51-FA-1-120-11; Showa Measuring Instruments Co., Ltd, Tokyo, Japan), it was found that MR force during symmetric convergence increased proportionally to the convergence angle. Horizontal

convergence changes the forces of MR and LR. Since we found a significant effect at the nearest target distance we assume that the effect on the SOM frequency was due to the changes in muscle force.

The relationship between horizontal convergence and muscle force is not so easily estimated. Miller and his collaborators (Miller, Bockisch and Pavlovski, 2002; Miller, Davison and Gamlin, 2011) used a muscle force measurement of their own design to measure the LR and MR force of monkeys in an asymmetric convergence paradigm. They found that the firing rate in the abducens nucleus during convergence was higher while the muscle force in LR was lower compared to a similar eye position in convergence-relaxed state. The MR force was also found to be lower, similar to the LR force. Demer and co-workers (Demer, Kono and Wright, 2003) scanned the horizontal rectus muscles of humans during convergence and found that horizontal rectus muscle cross-sections did not increase and that the eye globe did not retract. All the above studies suggest that LR and MR do not co-contract in convergence but instead co-relax. One important difference is that Lennerstrand and Campos compared muscle forces in different convergence states, whereas Miller compared muscle forces in convergence with non-convergence. From all the above studies we can conclude one important finding; the muscle force changes with convergence. So our results are in agreement with above mentioned results, irrespective of the muscle tonus has increased or decreased, the change in SOM frequency might be explained by the change in muscle tonus.

5 CONCLUSIONS

5.1 STUDY 1

1. A slow oscillatory movement occurs during visual fixation together with tremor, microsaccade and drift.
2. This slow oscillatory movement is not an artifact due to eye recording technique and analysis procedure.
3. The filtering technique has no effect on the frequency of the slow oscillatory movement.
4. This slow oscillatory movement has a frequency ranging between 0.04 to 0.10 Hz and amplitude less than 0.50 deg.

5.2 STUDY 2

1. A slow oscillatory movement was recorded in all experiment conditions.
2. The visual stimulus had no effect on the frequency of the slow oscillatory movement.
3. The slow oscillatory movement had larger amplitude to non-structured background compared to structured background.
4. The slow oscillatory movement exhibited increasing amplitude with a larger fixation target.
5. Absence of a visual stimulus could trigger a large slow oscillatory movement.

5.3 STUDY 3

1. The SOM is physiological movement of extraocular muscles.
2. The frequency of SOM can be modulated by extraocular muscle force.

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