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## SLOW EYE MOVEMENTS

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**Abstract**—Monkeys and humans are able to perform different types of slow eye movements. The analysis of the eye movement parameters, as well as the investigation of the neuronal activity underlying the execution of slow eye movements, offer an excellent opportunity to study higher brain functions such as motion processing, sensorimotor integration, and predictive mechanisms as well as neuronal plasticity and motor learning. As an example, since there exists a tight connection between the execution of slow eye movements and the processing of any kind of motion, these eye movements can be used as a biological, behavioural probe for the neuronal processing of motion. Global visual motion elicits optokinetic nystagmus, acting as a visual gaze stabilization system. The underlying neuronal substrate consists mainly of the cortico-pretecto-olivo-cerebellar pathway. Additionally, another gaze stabilization system depends on the vestibular input known as the vestibulo-ocular reflex. The interactions between the visual and vestibular stabilization system are essential to fulfil the plasticity of the vestibulo-ocular reflex representing a simple form of learning. Local visual motion is a necessary prerequisite for the execution of smooth pursuit eye movements which depend on the cortico-pontino-cerebellar pathway. In the wake of saccades, short-latency eye movements can be elicited by brief movements of the visual scene. Finally, eye movements directed to objects in different planes of depth consist of slow movements also. Although there is some overlap in the neuronal substrates underlying these different types of slow eye movements, there are brain areas whose activity can be associated exclusively with the execution of a special type of slow eye movement. © 1997 Elsevier Science Ltd

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## ABBREVIATIONS

AOS	Accessory optic system	MT	Middle temporal area
CEHT	Combined eye/head tracking	MTN	Medial terminal nucleus of the accessory optic tract
cFm	Coarse Fourier motion	NOT	Nucleus of the optic tract
COR	Cervico-ocular reflex	NPH	Nucleus prepositus hypoglossi
dbm	Drift-balanced motion	NRTP	Nucleus reticularis tegmentis ponti
DLPN	Dorsolateral pontine nucleus	OFR	Ocular following response
DMPN	Dorsomedial pontine nucleus	OKAN	Optokinetic after-nystagmus
DTN	Dorsal terminal nucleus of the accessory optic tract	OKN	Optokinetic nystagmus
EMD	Elementary motion detector	PG	Parietal gyrus
eOKAN	Early optokinetic nystagmus	PIVC	Parietoinsular vestibular cortex
FEF	Frontal eye field	PO	Parieto-occipital area
fFm	Fine Fourier motion	SC	Superior colliculus
FST	Floor of temporal sulcus	SCC	Semicircular canal
FTN	Flocculus target neurons	SPEM	Smooth pursuit eye movements
IO	Inferior olive	STP	Superior temporal polysensory area
LED	Light-emitting diode	STS	Superior temporal sulcus
LIP	Lateral intraparietal area	tm	Theta motion
lOKN	Late optokinetic nystagmus	tVOR	Translatory vestibulo-ocular reflex
LPN	Lateral pontine nucleus	VIP	Ventral intraparietal area
LTN	Lateral terminal nucleus of the accessory optic tract	VN	Vestibular nucleus
MST	Middle superior temporal area	VOR	Vestibulo-ocular reflex
		VVOR	Visual enhanced vestibulo-ocular reflex

## 1. INTRODUCTION TO SLOW EYE MOVEMENTS

This review will concentrate on the neuronal substrate of each of the different types of slow eye movements. Therefore, most of the studies reviewed here consist of recordings of single-unit response types from various brain areas of trained rhesus monkeys together with behavioural measurements such as eye movement recordings. In addition, investigations will be presented examining human subjects and their eye movements as well as their perception in various conditions. Only occasionally will reports of deficits in patients suffering from brain damage be presented.

There are three perpendicular axis of eye rotation: horizontal, vertical, and torsional axis, respectively. The rotations of the eye are caused by contractions of the six extraocular muscles receiving innervation from motoneurons located in three motor nuclei (oculomotor, trochlear, and abducens nucleus) in

the brainstem. Of course, rotations around each axis can be slow. However, the slow eye movements presented here consist exclusively of horizontal and vertical eye movements; there will be neither a presentation of torsional eye movements nor the interactions between all three rotational axis known as Listing's Law.

There are a number of other reviews with sharper or broader perspectives available. With respect to smooth pursuit eye movements, Keller and Heinen (1991) gave an excellent insight in the underlying neuronal substrate, Thier *et al.* (1994) and Stein and Glickstein (1992) described the cortico-ponto-cerebellar pathway, not only necessary for the execution of smooth pursuit eye movements but also for other visual guided movements. Pola and Wyatt (1991) explained the smooth pursuit eye movements with special interest in predictive behaviour and Krauzlis (1994) focused on the comparison between rabbit, cat, and monkey. Collewijn (1981) described

the optokinetic system of the rabbit. A complete overview concerning all types of eye movements was given by Robinson (1981) and Carpenter (1988).

### 1.1. Classification of Eye Movements

At the beginning of this century, Raymond Dodge (1903) proposed that the oculomotor behaviour of humans could be divided into five different subsystems: stationary eyes during fixation, quick eye movements in between two phases of fixation called saccades, the vestibulo-ocular reflex (VOR), optokinetic nystagmus (OKN) and vergence eye movements. Fifty years later, Gerald Westheimer (1954b,c) applied the linear system analysis approach to the field of oculomotor research and described saccades and smooth pursuit in two separate papers. The reason why this approach was not totally successful is due to the major influence of predictive mechanisms on all types of eye movements. As a consequence, at the end of this century, there is increasing evidence that the number of oculomotor subsystems could be reduced to only two systems: simply, a fast and a slow system (Steinman *et al.*, 1990). The slow system, with all its different aspects, is the topic of this review. According to a very naive assumption, it can be differentiated simply between moving and non-moving eyes, or saccades and fixation, respectively. A prominent feature of human eye movements is that frequently they are performed involuntarily. So we do think that during fixation our eyes do not move, but this can be disproved easily. If the reader fixates the white spot in Fig. 1 for about 20 sec to generate an after-image, the miniature movements during subsequent fixation of the central black spot can be

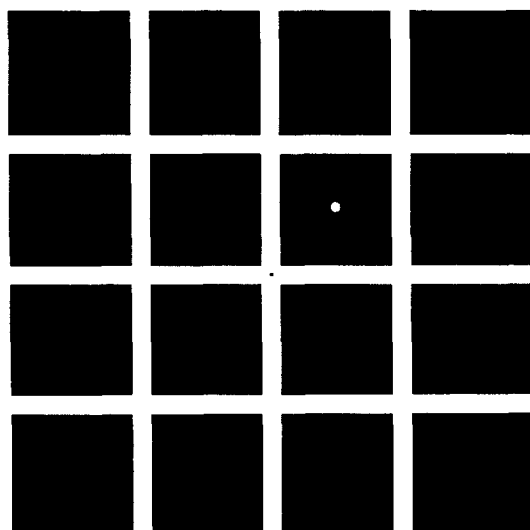


Fig. 1. Demonstration of miniature eye movements during fixation (Verheijen, 1961). The white spot has to be fixated for about 20 sec to generate an after-image of the black-and-white pattern; subsequently the small black spot in the centre should be fixated and the miniature eye movements can be observed by the movements of the after-image onto the black-and-white pattern.

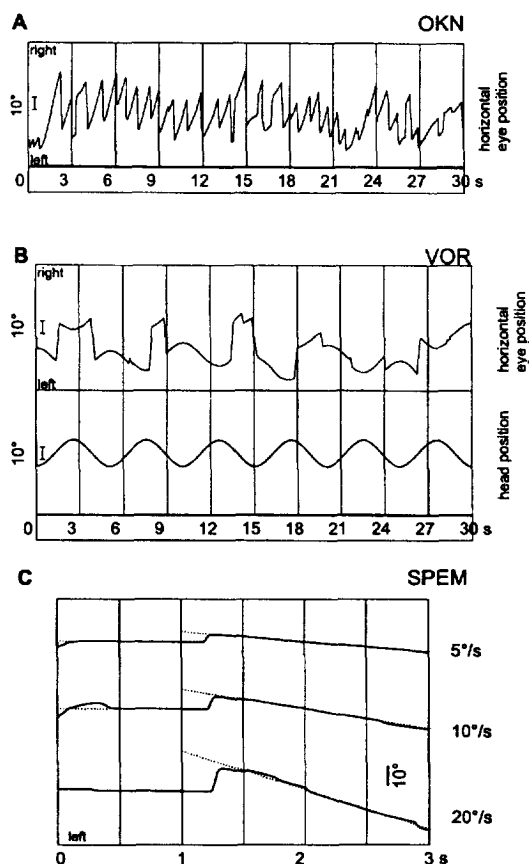


Fig. 2. Major types of slow eye movements recorded from a rhesus monkey. (A) An example of optokinetic nystagmus elicited by global motion. The horizontal eye position of the monkey looking at a moving black-and-white stripe pattern (size  $90 \times 90^\circ$ , spatial frequency  $0.25 \text{ cyc}/^\circ$ , velocity  $60^\circ/\text{sec}$ ). (B) The vestibulo-ocular reflex elicited by head motion is shown. Horizontal eye and head position of the monkey in darkness during sinusoidal head movements ( $0.2 \text{ Hz}$ ,  $10^\circ$  amplitude) is displayed. (C) Three trials of smooth pursuit eye movements elicited by local motion. Horizontal eye and target position are shown for target movement at  $5$ ,  $10$  and  $20^\circ/\text{sec}$ , respectively, to the left. Note the increased number of saccades for high target velocity.

observed by the interactions of the image and the after-image (Verheijen, 1961).

These miniature eye movements can be divided into three different classes: slow drift, miniature saccades and tremor. Their amplitude in humans is always less than  $30 \text{ min of arc}$  (Robinson, 1981). Figure 2 informs about the major classes of slow eye movements discussed in this review: OKN, elicited by global visual motion; VOR, elicited by head movements in darkness; and smooth pursuit eye movements (SPEM), elicited by local visual motion. These eye movements were recorded using the search coil technique from a rhesus monkey in the context of other investigations of our laboratory.

It is important to note in the beginning of this review that the execution of slow eye movements is tightly connected to the processing of movement, either movement of objects in external space or to movement of the subject itself. In primates, the pro-

cessing of visual motion is mainly a cortical phenomenon. The analysis of slow eye movements give some insight in the cortical processing of motion. As will be explained in the course of this review, the cortex provides the necessary information for subcortical structures to perform all the different slow eye movements, at least for all slow eye movements dependent on visual motion processing.

### 1.2. Velocity Range of Slow Movements

The differentiation between slow and fast saccadic eye movements can be done easily according to the relation of velocity and duration of the eye movements: during saccades, the eye speed reaches several  $100^\circ/\text{sec}$  and the duration of the movement is around 100 msec, depending on the amplitude of the eye movement. A fixed relationship between peak velocity and amplitude, as well as between duration and amplitude of the saccade, was shown and named "main sequence" (Robinson, 1964; Becker and Fuchs, 1969). In contrast, the duration of slow eye movements is usually much longer, as long as the motion of the stimulus or the subject continued. There is only a small overlap in the velocity domain of slow and fast eye movements since the upper limit of smooth pursuit in humans was close to  $100^\circ/\text{sec}$  eye velocity. Below stimulus velocities to  $100^\circ/\text{sec}$ , the eye velocity is equal to target velocity; if the target velocity exceeds  $100^\circ/\text{sec}$ , the eye velocity saturates (Meyer *et al.*, 1985). However, the overlap in the velocity domain in squirrel monkeys is even larger: these monkeys are able to generate OKN up to a stimulus velocity of  $400^\circ/\text{sec}$  yielding an eye velocity during slow phase of  $150^\circ/\text{sec}$  (Behrens and Grüsser, 1988). Since the peak velocity during saccades, especially for very small saccades, is smaller than  $100^\circ/\text{sec}$ , a differentiation between saccades and slow eye movements cannot be done solely based on a velocity criterion. But the fixed re-

lationship between velocity and amplitude during saccades allow the differentiation between saccades and "slow" eye movements, even if the "slow" eye movements are faster than saccades. The lower end of stimuli velocity producing an eye movement response was observed in frogs which move their eyes as slow as  $5^\circ/\text{hr}$  in response to a visual moving stimulus. The ability to see and to perform such slow movements suggested that frogs can even see and track the movement of the sun in the sky which prevents them from image fading (Dieringer and Daunicht, 1986). Similarly, rabbits are able to respond to black-and-white stripes moving as slow as  $0.003^\circ/\text{sec}$  equal to  $10.8^\circ/\text{hr}$  (Collewijn, 1969).

## 2. SLOW EYE MOVEMENTS REFLECTING GLOBAL MOTION PROCESSING (OPTOKINESIS)

An essential prerequisite for the sophisticated processing of visual information in primates consists of a sharp retinal image that does not move. In addition to the accommodation system ensuring correct refraction of the lens, there are two different gaze-stabilizing reflexes preventing the retinal image to move: the VOR and the OKN.

### 2.1. Optokinetic Nystagmus

In the last century, Jan Evangelista Purkinje (1825) described an observer's eye movements while watching a parade as a saw-tooth-like pattern with slow phases, during which the retinal image of the parade was stabilized, and quick phases resetting the eye. In modern environments, this eye movement pattern can be observed in a train passenger looking out the window of the moving train. This saw-tooth-like eye movement pattern is called OKN and is performed reflexively if large components of the visual surroundings move coherently. In Fig. 3(A),

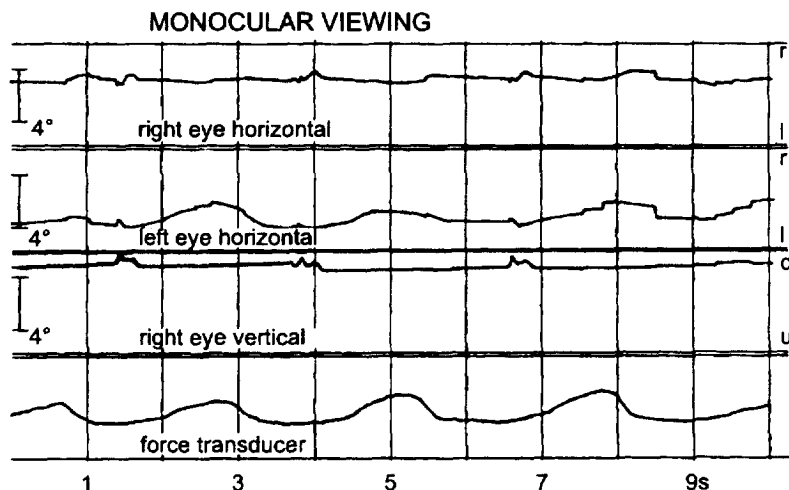


Fig. 3. The left and right eye position during eye press. The horizontal position of both eyes of the subject were measured with two scleral search coils. The right eye was pressed gently, as shown by the force transducer trace. It is evident that the right rectus lateralis muscle compensated for the pressure to yield a stable right eye axis, the left eye received the same innervation and moved nasally (reproduced with permission from Ilg *et al.*, 1989).

the saw-tooth-like pattern of the OKN of a rhesus monkey is shown. The monkey was not trained or instructed to track the horizontally moving black-and-white stripes. For moderate stimulation velocities up to 30°/sec, the velocity of the slow phases matched the stimulus velocities in humans (Honrubia *et al.*, 1968). As earlier mentioned, squirrel monkeys can follow stimulation velocities up to 400°/sec (Behrens and Grüsser, 1988). From the linear system approach, the optokinetic system can be understood as a simple negative feedback system that minimizes retinal image motion. To examine the characteristics of the optokinetic system, it is necessary to cut this feedback loop. This can be done by immobilization of one eye, stimulation of the immobilized eye and measurement of the movements of the patched non-seeing contralateral eye. The measured movements of the patched eye show the open-loop response to the stimuli presented to the immobilized eye (Ohm, 1926). The other possibility to cut the feed-back loop is to compensate for the eye movements by moving the visual stimuli identically to the eye; additional retinal image motion can be added (Collewijn and van der Mark, 1972; Pola and Wyatt, 1985). The approach with the immobilized eye revealed that the optokinetic system cannot be understood as a simply linear integrator: the velocity of the patched eye increases steadily until it reaches a value typically greater than the stimulus velocity (Ter Braak, 1936; Koerner and Schiller, 1972). If the optokinetic system were a linear integrator, then the eye velocity would have increased in this condition without limit. Additionally, it was shown that retinal image motion in the range of 20–30°/sec in man and monkey (Waespe *et al.*, 1983; Maioli, 1988) and below 10°/sec in rabbits (Collewijn, 1972) produced the most precise adjustment in slow-phase eye velocity to target velocity. The reason for this velocity-tuned behaviour of OKN is most probably due to velocity sensitivity of directional selective neurons in the afferent branch of the optokinetic system, which will be explained later.

The analysis of the main sequence of the quick phases of OKN in monkeys revealed that the quick phases during the execution of OKN have the same parameters as visually guided saccades (unpublished observation from author's own laboratory). Thus, it might be speculated that the phylogenetic origin of saccades, representing typical fovea dependent eye movements, might be identical to the optokinetic system of avoate vertebrates. The neuronal circuitry in the brainstem responsible for the programming of action potential salves in the motoneurons of the extraocular muscles necessary for the execution of a saccade therefore was present already in lower avoate vertebrates and used to generate quick phases of OKN. Later in the evolution towards foveate mammals, these circuits might be used for a different system: the goal-directed saccades.

## 2.2. Suppression of OKN

As already stated, OKN is executed reflexively. Therefore, animal studies are easy to perform, since

there is no special training necessary to elicit OKN in an experimental animal. On the other hand, human subjects are not able to suppress OKN voluntarily. But as soon as a stationary target among the optokinetic stimulation is present, subjects or rhesus monkeys are able to fixate and thereby to suppress the ongoing OKN. Occasionally, slow eye movements are observed in the opposite direction to the optokinetic stimulation during fixation of a stationary target (Waespe and Schwarz, 1987). These slow eye movements cannot possibly be due to an incomplete suppression of OKN, since they are directed in an opposite direction to the stimulation. It seemed more likely that these eye movements in monkeys were equivalent to the perception of a human observer seeing induced motion: if a subject fixates a single spot embedded into a moving background, the subject perceives an apparent movement of the fixation spot in an opposite direction to the background motion, called induced motion (Duncker, 1929). The question of whether rhesus monkeys do actually perceive induced motion is not yet answered, although this is very likely, since neurons in two different parts of the medial superior temporal sulcus (MST) did respond to induced motion (Wurtz *et al.*, 1990; Tanaka *et al.*, 1993).

It is important that the stationary fixation target has to be in the same plane of depth as the optokinetic stimulus to suppress effectively the ongoing OKN (Howard and Simpson, 1989). In addition, very experienced subjects were said to be able to suppress ongoing OKN by fixation of an after-image, but never by fixation of an imaginary target (Howard *et al.*, 1989).

## 2.3. Subtypes of OKN

Very early on, it was discovered that two forms of OKN could be differentiated: Stier-Nystagmus on the one hand and Schau-Nystagmus on the other hand (Ter Braak, 1936). During Schau-Nystagmus (look nystagmus), the subjects track actively single details in the moving stimulus, producing an OKN with large eye movements with no periodic pattern. In contrast, during Stier-Nystagmus (stare nystagmus), the subject does not look actively at specific features in the stimulus. The obtained amplitudes of OKN are small with a regular periodic pattern. In modern studies, a dynamic random dot pattern, consisting of single dots with brief life-times, are used to make it impossible for the subject to track single spots and thereby to force the subject to perform Stier-Nystagmus. A different solution for examination of Stier-Nystagmus was shown by Han Collewijn and colleagues, by concentrating on a species that does not have a fovea: the rabbit. Already Ter Braak has suggested that the Stier-Nystagmus is mediated through subcortical structures, whereas the Schau-Nystagmus depend on the presence of the visual cortex (Ter Braak, 1936). Further, it seemed reasonable to assume that the execution of Schau-Nystagmus is closely related to the execution of smooth pursuit eye movements.

A more recent dichotomy of the optokinetic system is based on the slow phase eye velocity elicited by steps in stimulus velocity. The eye movement response to a step in stimulus velocity consists of two components: the rapid rise (eOKN) followed by a slower rise (IOKN) to steady-state eye velocity. The initial rise of eye speed was suggested to be mediated by the direct path and the subsequent slow build-up mediated by an indirect path (Cohen *et al.*, 1977). Another nomenclature differentiates between early and late OKN, eOKN and IOKN respectively, synonymous to the terms direct and indirect paths. The slow build-up also reflects the perception of circular vection and the execution of optokinetic after-nystagmus (OKAN) with comparable charge (5–6 sec) and discharge times (20–30 sec) in man (Brandt and Dichgans, 1972) that will be presented in the following sections. The execution of IOKN is more prominent in animals with lateral eyes; eOKN also can be generated by small moving stimuli and depends critically on the presence of fovea. The execution of IOKN is suppressed by stationary contours in the peripheral visual field, eOKN does not reveal this sensitivity (Dichgans, 1977). So, although there are most likely different neural mechanisms involved, there seems to exist a correlation between SPEM, eOKN or direct path or Schau-Nystagmus vs IOKN, indirect path and Stier-Nystagmus (Pola and Wyatt, 1985).

It will be explained later that prediction of future stimulus movement is a very important feature of SPEM. Usually, OKN is viewed as a more primitive oculomotor response lacking the capability for predicting future stimulus movement. However, comparing the optokinetic response obtained from sinusoidal stimulation with responses from random-walk lacking any periodicity showed that also the optokinetic system has predictive capabilities, revealed by higher gain and lower phase lag elicited by the sinusoidal stimulation (Wyatt and Pola, 1988). These authors offered three explanations for their results: the first possibility suggested that the optokinetic system located in the brainstem itself has predictive capabilities, the second possibility suggested that the predictive response is due to a pursuit mechanism contributing to the optokinetic response and the third possibility suggested that pursuit and optokinetic systems are not separate in man at all (Wyatt and Pola, 1988).

#### 2.4. Sensation of Circular Vection

During the execution of OKN, some interesting features parallel to the execution of the saw-tooth like OKN can be observed. Firstly, during optokinetic stimulation, the subjects built up the sensation of self-rotation called circular vection (Mach, 1875; Fischer and Kornmüller, 1930; Brandt *et al.*, 1974). This perception represents a very logical conclusion drawn by the brain, since in natural condition it is simply not possible that the entire visual surroundings move coherently. The only possible assumption in real-world conditions is that the subjects himself rotates and that the coherent retinal image movement is a consequence to the ego-motion.

#### 2.5. Average Eye Position During OKN

During the execution of OKN, the quick phases move the average eye position out of the primary position against the direction of stimulus movement (Borries, 1926). This shift in average eye position is called haptation (Borries, 1926). Once more, this eye movement behaviour can be explained as a logical conclusion drawn from the assumption of the constraints a real world. Large-field coherent motion is an indication of self-motion, so if there is an obstacle, the obstacle appears at the most lateral part of the visual field, pointing against the direction of movement. It is obvious that it is important to have the gaze where an obstacle can eventually appear.

It is possible to speculate that the observed haptation during optokinetic stimulation is due to the artificial fixation of head during the experiments: it was shown that during optokinetic stimulation rats whose heads were free to move turned their head in an opposite direction to the optokinetic stimulation, centring their eye movements close to the primary eye position (Dieringer and Meier, 1993).

#### 2.6. Eye Velocity Storage During Execution of OKN

Prolonged optokinetic stimulation yields charging of a velocity storage mechanism, parallel to the sensation of circular vection. The effect of the velocity storage easily can be examined by switching off the lights after prolonged optokinetic stimulation. The subjects continue to produce the saw-tooth-like eye movement pattern, called OKAN (Ohm, 1921; Fox *et al.*, 1931; Ter Braak, 1936). It is important to note that only the indirect path or late OKN charges the velocity storage mechanism or integrator, brief optokinetic stimulations do not produce an OKAN (Cohen *et al.*, 1977). In the rhesus monkey, the charging of the integrator takes 5–10 sec and the OKAN discharges in darkness over 20–60 sec (Cohen *et al.*, 1977). This discharge consists in an initial drop of 10–20% of eye speed followed by a slower, exponential decline in eye velocity. In contrast, in rabbits, the decline in eye speed during OKAN is linear (Collewijn *et al.*, 1980). In primate, the OKAN can be dumped by fixation of a stationary target. If the fixation period is only brief in time (less than 3 sec), the OKAN resumes after the end of fixation (Cohen *et al.*, 1977). The OKAN can be divided into up to at least two different phases with changing directions of slow phases (monkey: Koerner and Schiller, 1972; cat: Maioli and Precht, 1985; comparison of different species: Collewijn, 1985). During OKAN I, the slow phases are in the same direction as during execution of OKN; during OKAN II, the direction of performed slow phases is inverted. OKAN I is thought to be driven by the velocity storage mechanism or integrator (Cohen *et al.*, 1977; Robinson, 1981); OKAN II appears to depend on a second storage element with lower gain and longer time constant (König and Dichgans, 1981). The two storage elements seem to work independently (Brandt *et al.*, 1974; Waespe *et al.*, 1978). The physiological meaning of the OKAN will be discussed in the following chapter in relation with post-rotatory vestibular nys-

tagmus. There are some differences in the optokinetic system between man and monkey: in man the gain of the direct pathway was found to be close to unity, whereas in monkeys it is about 0.6 (Cohen *et al.*, 1977). Thus, it was suggested that humans depend more on the direct pathway, and the velocity storage mechanism contributes less to the execution of OKN in man (Cohen *et al.*, 1981). This explains also why labyrinthectomy affecting the indirect path in humans had a much more limited effect on the execution of OKN than in monkeys (Zee *et al.*, 1976).

### 2.7. Directional Asymmetry of OKN

The primate optokinetic response differs in some respect from the optokinetic response of non-primate mammalian orders. When horizontal OKN is tested monocularly, primates with their frontal eyes show a fully symmetrical response, whereas most other species with lateral eyes exhibit higher slow-phase eye velocity if the stimulus moves in the temporo-nasal (preferred) direction compared to the naso-temporal (non-preferred) direction (Precht, 1981). This asymmetry in lower mammals reflects an adjustment to the naturally occurring retinal stimulation in the lateral eyes during forward locomotion. Similarly, the vertical optokinetic response in man is highly asymmetrical: downward movement yields smaller gain than upward movement (van den Berg and Collewijn, 1988; Murasugi and Howard, 1989). Again, this vertical symmetry can be attributed to the adjustment of naturally occurring retinal stimulation during linear forward locomotion with frontal eyes. Similar to the velocity sensitivity of the optokinetic response, the directional asymmetries can be explained by the characteristics of the sensory neurons in the afferent branch of the optokinetic system.

### 2.8. Eye-Press Experiments

In addition to stimulating the optokinetic system by placing a human subject inside an optokinetic drum, there is another possibility for stimulation of the optokinetic system. Instead of moving the entire visual environment, the eye of a human subject can be moved passively. If a subject presses gently against the temporal canthus of the eye while the contralateral eye is covered, the subject perceives an apparent movement of the world. It was shown that this perception is most likely the consequence of the efference copy of an eye movement command (Ilg *et al.*, 1989). In detail, a subject of an eye-press experiment shows disconjugate eye movements: the pressed eye remained stationary in the orbit, whereas the contralateral eye moved nasally, as shown in Fig. 3. According to Hering's Law, both eyes receive identical innervation in this condition. The rectus lateralis of the pressed eye compensates the external force and the rectus medialis of the contralateral eye moves this eye nasally. Thus, the perceived apparent motion is due most likely to the innervation state influencing perception, since the retinal image does not move. This experiment also shows that information from the proprioceptors in the extraocular muscles could not induce the movement of the contralateral eye, since the movements

of the covered eye would not be present if the eye-press experiment was performed in darkness (Ilg *et al.*, 1989).

### 2.9. Neuronal Substrate Underlying the Execution of OKN

Although the execution of OKN-like eye or head movements can be observed in vertebrates and invertebrates, this chapter focuses on the neuronal substrate underlying the optokinetic response in rabbit and monkey with a brief explanation of the interactions of the retinal and cortical afferents to the nucleus of the optic tract (NOT) in cats.

Before going into detail, it is necessary to introduce the major structures of the afferent branch of the optokinetic system located in the pretectal complex in all species examined so far: the NOT and the nuclei of the accessory optic system (AOS) consisting of the dorsal, lateral, and medial terminal nucleus (DTN, LTN and MTN, respectively). The pretectum is a nuclear complex anterior to the superior colliculus in the transition zone between posterior thalamus and mesencephalon. As will be shown, the NOT is an important structure in rabbits and monkeys, although there are major differences in the input to this nucleus between these two species. In all species examined so far, the NOT neurons responded directionally selective to visual motion; all neurons showed a horizontal preferred direction towards the recording site (ipsiversive) (see Hoffmann, 1988). The preferred directions of neurons of the three AOS nuclei are roughly in register with the planes of action of the antagonistic pairs of extraocular muscles and the planes of the semicircular canals of the inner ear: the MTN neurons prefer upward motion with a posterior component, LTN neurons prefer downward motion with an anterior component and DTN neurons prefer horizontal ipsiversive motion (Simpson *et al.*, 1979; Walley, 1967). It is important to note that the response properties of neurons located in the NOT are very similar to the responses from DTN neurons. Since these two nuclei cannot be differentiated anatomically, the NOT and DTN usually are viewed as an entity.

#### 2.9.1. Optokinetic System of the Rabbit

As a matter of fact, the first description of the AOS derived from Bernhard von Gudden's observation (von Gudden, 1870) in the last century of the surface anatomy of the rabbit brainstem. More recently, thanks to the pioneer work by Han Collewijn and colleagues, the parameters of the optokinetic response of rabbits and the underlying neuronal substrate are well known (Collewijn, 1981). The optokinetic system of rabbit is highly asymmetrical, if stimulated monocularly, only stimulation in the temporo-nasal direction is effective in eliciting OKN. Single-unit recordings revealed the ipsiversive preferred direction of the visual response of NOT neurons (Collewijn, 1975a), lesions of NOT produced a deficit in ipsiversive horizontal OKN (Collewijn, 1975a), and electrical stimulation elicited an OKN-like eye movement pattern (Collewijn, 1975b). It might be speculated that

the reason why the optokinetic system of rabbit lacked the direct or early component is related to the observation that the NOT and the AOS in rabbit do not receive cortical inputs. In concordance, ablation of the cortex in rabbits do not change the OKN (Ter Braak, 1936). The functional role of this cerebral input missing in rabbits will be explained later.

There is a special subclass of retinal ganglion cells in rabbits that respond directionally selective to visual motion (Barlow and Hill, 1963). Directionally selective responses are the key feature of neurons that provide the visual input for the optokinetic system. These ganglion cells, located in the visual streak, project to the NOT and the three nuclei of the AOS (DTN, LTN, and MTN) (Oyster *et al.*, 1980). The visual streak represents a horizontal band in the rabbit retina containing a higher concentration of ganglion cells. Not only the specificity of ganglion cells for direction of motion, but also the specificity for speed is very similar to the relationship between velocity of retinal image motion and slow phase eye velocity (Oyster *et al.*, 1972). This implies that the processing of visual motion already is completed at the level of NOT/DTN, and subsequent processing is only necessary to generate the appropriate slow-phase eye movements. The concept of a non-linear processing of retinal image motion was an important experimental finding that had major influences on the formulation of optokinetic models.

Before presenting this further processing downstream of the NOT, it is important to note that the left- and right-hand NOT, as well as the NOT and the three nuclei of the AOS, are interconnected to each other (Simpson *et al.*, 1988). Most likely, these projections serve to sharpen the directional tuning behaviour of these neurons.

In rabbits, the neurons in the pretectum project to the nucleus prepositus hypoglossi, NPH (Holstege and Collewijn, 1982). The complex of NPH and the vestibular nucleus (VN) is thought to constitute the neuronal substrate of the velocity storage mechanism or integrator (Cannon and Robinson, 1987). Even a projection directly to the relevant ipsilateral abducens nucleus was shown (Holstege and Collewijn, 1982). Stimulation of the NOT by ipsiversive motion yields an activation of the motoneurons in the abducens nucleus that moves the eye in the same direction as the stimulus. A very massive projection from the NOT/DTN is directed towards the ipsilateral dorsal cap of the inferior olive (IO) (Holstege and Collewijn, 1982) providing climbing fibre input to the cerebellum. This projection is most probably responsible for the visual motion input to allow VOR gain adjustments that will be presented in the following section.

### 2.9.2. Optokinetic System of the Monkey

A first statement to the neuronal substrate underlying the OKN in primates is related to the AOS: surprisingly, in primates, the AOS is incomplete: the MTN was not found (Giolli, 1963). The primate LTN contains neurons that are directionally selective for upward motion (Mustari and Fuchs, 1989).

The visual response of LTN neurons revealed a preference for slow retinal image velocities (Mustari and Fuchs, 1989). The responses of NOT/DTN neurons will be explained in detail later. Similarly to the rabbit, there are interconnections between the left and right NOT/DTN, as well as between the NOT and the AOS (Magnin *et al.*, 1990), acting most likely to sharpen the directional tuning of the response to visual motion.

The importance of the primate NOT/DTN for the generation of slow phase OKN was shown by electrophysiological recordings of single-unit activity (Hoffmann *et al.*, 1988), by damage of NOT producing an ipsiversive OKN deficit (Kato *et al.*, 1986, 1988; Schiff *et al.*, 1990; Cohen *et al.*, 1992; Ilg *et al.*, 1993; Yakushin *et al.*, 1994), and by electrical stimulation of NOT yielding OKN-like eye movements (Schiff *et al.*, 1988; Cohen *et al.*, 1992).

Although there are retinal afferents to the pretectum in the monkey (Hutchins and Weber, 1985), it is doubtful whether there are directionally selective ganglion cells in the primate retina which responded directionally selective and whether these types of ganglion cells do actually project to the NOT/DTN. In contrast, motion perception in primates generally is attributed to cortical processing. It was the work of Klaus-Peter Hoffmann and colleagues which showed that the importance of cortical input to the NOT/DTN increased in the evolution of the mammals towards the primates (Ilg and Hoffmann, 1996).

#### 2.9.2.1. Retinal input vs cortical input to the NOT/DTN

In the retina of the adult cat there are retinal ganglion cells with thin axons (w cells) that respond directionally selective to visual motion (Stone and Fukuda, 1974). These cells project to the contralateral NOT/DTN and provide a directional selective input from the retina (Hoffmann and Stone, 1985). In 3-week-old kittens, the attempt to show a functional cortical input failed, the NOT/DTN neurons in these kittens are exclusively driven by contralateral eye (Distler and Hoffmann, 1992). In parallel to this single-unit response types, the OKN of these kittens lacked the response to high retinal image velocities and to stimulation in non-preferred direction as observed in adult cats. These OKN response characteristics in kitten developed during the next 4–5 weeks: the OKN velocity tuning became broader and symmetrical. At the same time, a cortical input reached NOT/DTN, and as a consequence of this input, the NOT/DTN neurons responded to stimulation of both eyes and displayed a broader velocity tuning (Distler and Hoffmann, 1992). It was hypothesized that the retinal input to the NOT might act as a teacher for cortical input. The authors suggested that the cat might be used as a model for the development in man, since the development of the human optokinetic system also reflected an initial asymmetrical phase and a transition to symmetric OKN responses. The nature of the cortical input to the NOT/DTN in monkeys will be addressed in the next paragraph.



### 2.9.2.2. Cortical processing of global visual motion

This is the first description in this review of the cortical processing of visual motion. This processing also will be discussed in the chapters dealing with smooth pursuit eye movements and ocular following response. It is not clear at the present time whether the neuronal substrate is identical or different for these three types of slow eye movements.

The processing of visual motion is a well-examined function of the visual cortex in primates. In the first stage of processing visual information, V1, between 10 and 20% of the neurons respond in a way that is directionally selective to visual motion (Hawken *et al.*, 1988; Mikami *et al.*, 1986b). It has been suggested and shown (Movshon and Newsome, 1996) that especially the directionally selective neurons in V1 contribute to the massive projections that define anatomically the middle temporal area (MT) (Cragg, 1969; Zeki, 1969). Functionally, area MT is defined by a high concentration of directionally selective neurons (Allman and Kaas, 1971; Dubner and Zeki, 1971; Zeki, 1974; Mikami *et al.*, 1986a; Erickson *et al.*, 1989). Neurons in area MT are also sensitive for the velocity of retinal image motion with a maximal response for velocities close to 20°/sec (Maunsell and van Essen, 1983a). Area MT neurons are active during the execution of OKN with pauses in activity during quick phase explained by the velocity sensitivity (Ilg, 1997). Subsequent stages of motion processing involve different parts of MST, which receive dense projections from area MT (Maunsell and van Essen, 1983b; Ungerleider and Desimone, 1986). Area MST neurons display larger receptive fields and more complex visual response types compared with neurons in area MT (for review see Wurtz *et al.*, 1990).

The importance of the processing of visual motion in area MT for the generation of OKN also was shown by the use of transparent stimuli. These stimuli provide at least two different motion signals not spatially separated. If a human subject watches two groups of dots moving horizontally left- and rightwards, the subject performs antagonistic optokinetic nystagmus with distinctly reduced slow phase eye velocity compared with the unilateral stimulation (Niemann *et al.*, 1994). This reduction in eye speed during transparent stimulation can be explained by a reduction in response of area MT neurons to transparent motion compared to unidirectional motion (Snowden *et al.*, 1991). Interestingly, the early stage of processing, area VI, does not show this reduction in response (Snowden *et al.*, 1991).

It was successfully suggested that the cortical processing of visual information consists in two different pathways: a ventral stream related to object recognition (what) and a dorsal stream related to spatial location (where) (Ungerleider and Mishkin, 1982). Motion processing clearly is a part of the dorsal stream, although the spatial information is irrelevant for the optokinetic system and therefore is lost in the further processing.

### 2.9.2.3. Functional grouping of the cortico-pretectal projection

It is not surprising that, following unilateral lesion of the NOT in monkeys, the OKN becomes asymmetrical; especially, the ipsiversive OKN towards the lesion is abolished (Kato *et al.*, 1986; Kato *et al.*, 1988; Schiff *et al.*, 1988; Ilg *et al.*, 1993). This can be explained easily since the visual response of all neurons in the NOT/DTN have the same, ipsiversive preferred direction. After unilateral damage of NOT/DTN, the neuronal representation of this

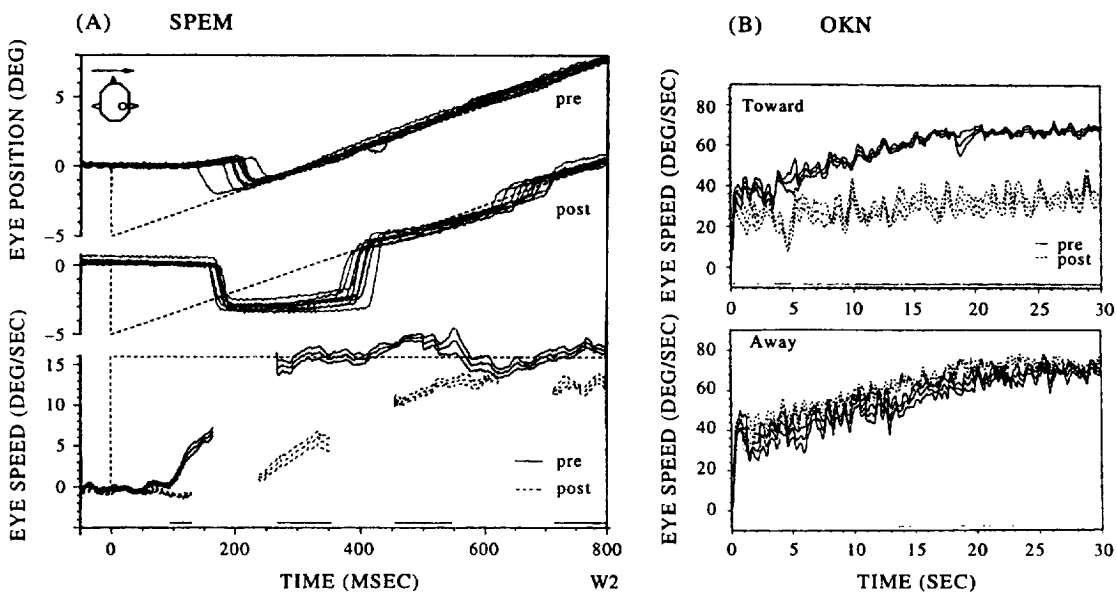


Fig. 4. Ipsiversive SPEM (A) and OKN (B) deficit following two different lesions in primate area MST. (A) Eye position and eye velocity traces of 10 trials pre- and post-lesion, together with target position and velocity. (B) Mean eye velocity ( $\pm$ SD) during pre- and post-lesion OKN. Note that in both cases the eye movements toward the lesion site were impaired (reproduced with permission from Dürsteler and Wurtz, 1988).

direction of motion is missing. More puzzling was the observation, that, true for monkey and man, cortical lesion of the posterior parietal cortex also produces an ipsiversive deficit in the execution of OKN and smooth pursuit eye movements (monkey: Dürsteler *et al.*, 1987; man: Thurston *et al.*, 1988; Morrow and Sharpe, 1990). Figure 4 shows the deficits in SPEM and OKN following a chemical lesion in area MST of a rhesus monkey. Even lesions in the frontal cortex of patients produced such an ipsiversive deficit in SPEM and OKN (Rivaud *et al.*, 1994). In case of a lesion in the posterior parietal cortex or in the frontal cortex, the neurons of the lesioned tissue do not show a clear anisotropy in the distribution of preferred directions predicting the direction of the deficit. A possible answer for this problem arose when it was shown by antidromic identification and collision test that the cortical output to the NOT/DTN is highly selective with respect to preferred directions: only neurons with an ipsiversive preferred direction project to the ipsilateral NOT/DTN (Hoffmann *et al.*, 1992; Ilg and Hoffmann, 1993a). Although the concept of functional grouping of the cortical input to the NOT/DTN solves the problem concerning the ipsiversive deficit, a puzzling problem persists: the anatomical reconstruction of the STS of the experimental monkeys revealed that the backfired cells are in area MT. But the observed response types, especially the big receptive fields with a huge extension into the ipsilateral visual field, do not fit to our present knowledge of MT neurons response properties. So

the question of which area projects to the NOT/DTN still waits for an answer (Hoffmann *et al.*, 1992; Ilg and Hoffmann, 1993a).

#### 2.9.2.4. Response types of primate NOT/DTN neurons

The recordings of single-unit activity of NOT in awake monkeys revealed a new response property not observed before in the studies with anaesthetized and paralysed monkeys. About 50% of the recorded units stopped to respond to a moving visual stimulus if the monkey fixated a stationary target, while the remaining did not change their response due to fixation, as shown in Fig. 5 (Ilg and Hoffmann, 1991, 1996).

The two types of neurons also can be distinguished based on their response during smooth pursuit eye movements across a structured background. The neurons that stopped to respond during fixation responded only to the movement of the pursuit target, therefore these neurons are called *target velocity cells*. The other type of neurons responded to the passive retinal image motion due to the background and are therefore called *background velocity cells* (Ilg and Hoffmann, 1996). Neither type of neurons showed an eye movement-related modulation of activity, for that reason it can be excluded that the lack of response of the *target velocity cells* during fixation was due to the lack of eye movements in this condition. These two types of NOT/DTN neurons might be similar to two NOT/DTN response types found in another study (Mustari and Fuchs,

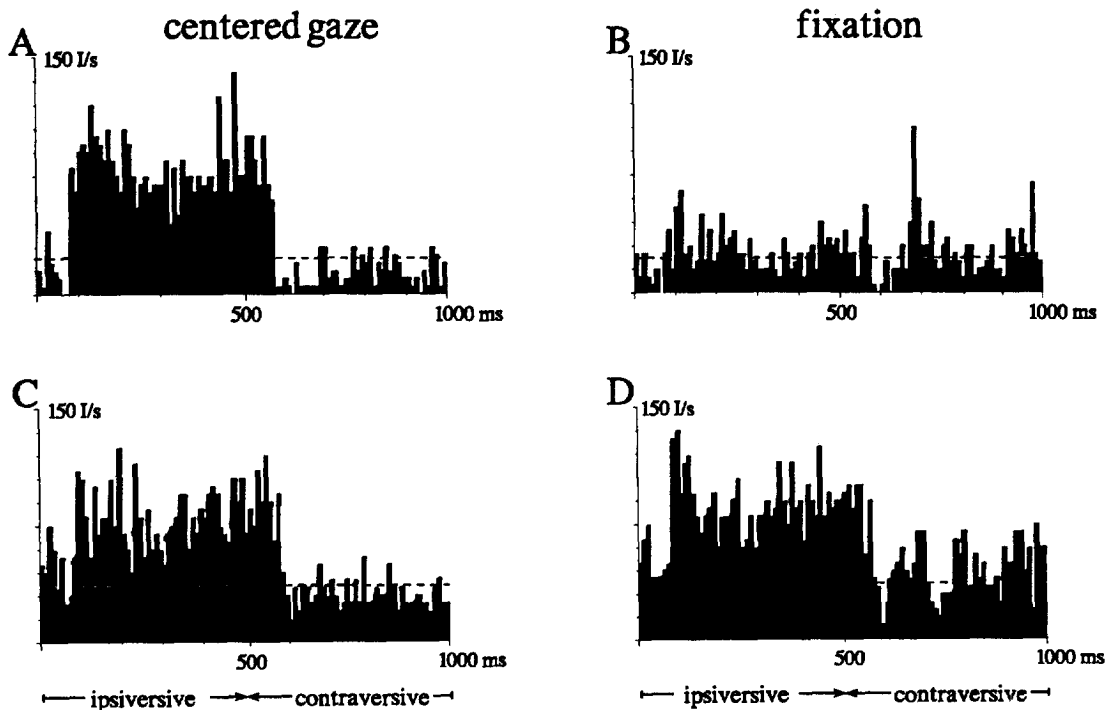


Fig. 5. Responses to background movement ( $40^\circ/\text{sec}$ ) in preferred (500 msec) and non-preferred direction (500 msec) during fixation [(B) and (D)] and centred gaze [(A) and (C)] of two different NOT/DTN neurons are shown. The horizontal dashed lines show the spontaneous activity. The *background velocity cell*, [(C) and (D)] responded in both cases, whereas the *target velocity cell* only responded in the centred gaze condition (A), but not during fixation (B) (reproduced with permission from Ilg and Hoffmann, 1996).

1990): one type of neurons responded only to large moving stimuli and the other type to small moving stimuli. The former might be the *background velocity cells* and the latter the *target velocity cells*.

In addition to the already described sensitivity for the direction of retinal image motion, NOT/DTN neurons in primates are also sensitive for the velocity of motion. Most neurons show the maximal response to stimuli moving on average at  $21^\circ/\text{sec}$ , which is very close to the retinal image velocity (between  $20$  and  $30^\circ/\text{sec}$ ) that yields the highest slow-phase eye velocity (Waespe *et al.*, 1983; Maioli, 1988). Interestingly, the inhibition caused by movement in the non-preferred direction is not velocity-dependent (Ilg and Hoffmann, 1996). Another study resulted in a slightly different preferred velocity of  $64^\circ/\text{sec}$  of NOT/DTN neurons (Mustari and Fuchs, 1990). The explanation of this difference consists of different experimental procedures: Mustari and Fuchs (1990) stimulated with different velocities while the monkey fixated a stationary target, whereas Ilg and Hoffmann (1996) calculated the velocity sensitivity based on data during the execution of optokinetic nystagmus. As already explained, the response to a moving stimulus frequently was reduced by fixation of a stationary target, probably affecting mainly the response to slow retinal image motion. The velocity sensitivity of the NOT/DTN responses also predicted the observed pauses in activity during quick phases (Mustari and Fuchs, 1990; Ilg and Hoffmann, 1996), since the velocity of retinal image motion was increased dramatically during quick phases. These pauses in activity were very similar to the pauses observed in the activity of neurons in area MT (Ilg, 1997).

A very important finding of the groups of Albert Fuchs and Klaus-Peter Hoffmann was that NOT neurons were active during horizontal SPEM in ipsiversive direction. (Mustari and Fuchs, 1990; Ilg and Hoffmann, 1991; Ilg and Hoffmann, 1996). It was shown that the pursuit response is purely visual since the activity drops as soon as the pursuit target was turned off briefly (Mustari and Fuchs, 1990). This visual origin of pursuit activity in primate NOT/DTN neurons also was suggested earlier by the result that, in paralysed monkeys, NOT/DTN neurons responded to the movement of a single, small object (Hoffmann *et al.*, 1988). In addition, the NOT/DTN activity is modulated during the suppression of VOR. Brief disappearances of the VOR suppression target reveal that this modulation is also visual in origin (Mustari and Fuchs, 1990). From the anatomical studies, there is no reason to assume vestibular input to the NOT/DTN. The finding of pursuit-related activity in NOT/DTN clearly shows that there is some overlapping in the neuronal substrate underlying the different types of slow eye movements. In concordance with this result, a lesion of the NOT/DTN does produce an ipsiversive SPEM deficit in addition to the well-known optokinetic deficit (Ilg *et al.*, 1993).

#### 2.9.2.5. NOT/DTN efferent systems

It was suggested (Ilg and Hoffmann, 1996) that there are three major efferent projections from

NOT/DTN serving different functions. Firstly, especially the *target velocity cells* projecting to the dorsolateral pontine nuclei DLPN (Magnin *et al.*, 1990; Mustari *et al.*, 1994; Büttner-Ennever *et al.*, 1996) are thought to back-up the major pursuit path and cerebellar function that will be presented in detail later. Interestingly, lesion of the DLPN not only produced an ipsiversive pursuit deficit, but also a deficit in eOKN, supporting the idea that eOKN and SPEM reflect identical neuronal processing (May *et al.*, 1988). Secondly, especially the *background velocity cells* are thought to project to the NPH and VN (Magnin *et al.*, 1990; Mustari *et al.*, 1994; Büttner-Ennever *et al.*, 1996) to charge the integrator representing the indirect path of the optokinetic system (Cohen *et al.*, 1977). This is supported by the finding that neuronal activity in VN continued during the execution of OAKN without visual stimulation (Waespe and Henn, 1977). Thirdly, both types of NOT/DTN neurons project to the dorsal cap of the inferior olive (IO) (Simpson *et al.*, 1988) and provide information about retinal image motion via climbing fibres to the cerebellum, where it may be used for another function of the cerebellum, consisting of the calibration of compensatory slow eye movements during rotation of the head. In the cerebellar flocculus, the majority of Purkinje cells could be classified as type I cells (i.e. they are activated during ipsiversive optokinetic stimulation) (Markert *et al.*, 1988). Additionally, neurons in the uvula also were driven by prolonged optokinetic stimulation (Heinen and Keller, 1996). The Purkinje cells project reciprocally to the vestibular nuclei VN (Langer *et al.*, 1985b), which is in close relationship to the oculomotor nuclei.

It was suggested that the indirect path including the velocity storage mechanism responsible for the slow build-up of eye velocity should be related to neuronal activity in VN (Waespe *et al.*, 1983). The direct path was suggested to correlate with floccular Purkinje cell activity (Waespe and Henn, 1981, 1985). It is important to note that this implies that the neuronal substrate of the direct path of the optokinetic system is identical to the substrate of SPEM.

The NOT/DTN projection to the pontine nuclei may also include the mediodorsal part of the pons (MDPN) where very similar response types as the responses of NOT neurons were recorded (Keller and Crandall, 1983). Especially the sensitivity for slow retinal image velocity ( $5\text{--}10^\circ/\text{sec}$ ), the response during smooth pursuit, and the immediately return to spontaneous activity after cessation of optokinetic stimulation are very similar to the responses obtained from NOT/DTN neurons. Therefore, the MDPN might act as a parallel relais structure to the DLPN to provide mossy fibre input to the cerebellum (Brodal, 1979). In the adjacent nucleus reticularis tegmenti pontis (NRTP), no responses to optokinetic stimulation could be shown; these neurons seem to respond before and during saccades only (Keller and Crandall, 1981).

Figure 6 tries to visualize the information given in the last paragraphs emphasizing the cortico-preecto-olivo-cerebellar pathway represented by the solid lines and the interactions with the SPEM sys-

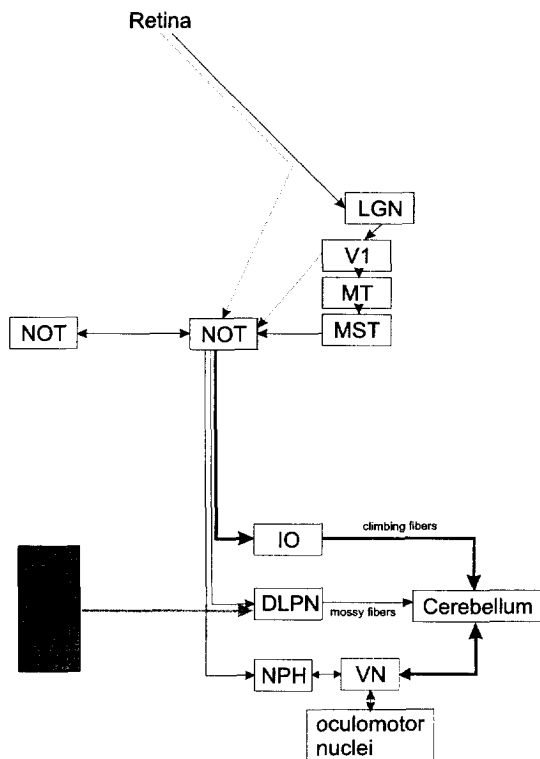


Fig. 6. Neuronal substrate responsible for the execution of horizontal OKN in monkeys. The bold lines represent the cortico-preecto-olivo-cerebellar pathway. See text for further explanation.

tem by the grey lines. The dotted lines represent retinal (Hoffmann *et al.*, 1988) and striate cortex projections (Hoffmann *et al.*, 1991) to the NOT/DTN which were demonstrated anatomically but might not function in the adult monkey as earlier explained, exemplary in cats.

The differentiation of neuronal responses related to the execution of OKN from the execution of SPEM system is very difficult, if not impossible; therefore, many investigations of the optokinetic system were done with afoveate mammals such as the rabbit, which simply do not have the fovea-dependent SPEM system. The already presented lesions of the posterior parietal cortex and the related ipsiversive deficit in SPEM and OKN (monkey: Dürsteler and Wurtz, 1988; man: Baloh *et al.*, 1980) emphasizes that the afferent parts of both systems might be similar. Another site of interaction between the system underlying OKN and SPEM was shown in the primate NOT/DTN, where lesions not only produced ipsiversive OKN deficits, but also SPEM deficits (Ilg *et al.*, 1993; Yakushin *et al.*, 1994). Further processing seems to be different for the optokinetic and pursuit system: while the DLPN is essential for the generation of SPEM, the IO is essential for the execution of OKN. So, returning to the assumptions drawn by Wyatt and Pola (1988), based on their finding that the optokinetic system also displays predictive capabilities, it seems that the suggestion of pursuit system contributions to the optokinetic system might be more realistic than the

suggestion that the OKN and SPEM are not separate systems at all in man (Wyatt and Pola, 1988).

In addition to this overlap in the neuronal substrate underlying OKN and SPEM, the optokinetic system also provides important visual information for the calibration and adaptation of the VOR and might interact with the ocular-following system, explained later in this review.

To summarize, the NOT/DTN is an important relais structure between cortical and subcortical structures for the execution of horizontal optokinetic nystagmus. Additionally, the NOT/DTN is thought to provide information for other functions of the visual systems such as SPEM, VOR and ocular following (see Büttner-Ennever *et al.*, 1996).

### 2.10. Nystagmus as a Pathological Indication

The term "nystagmus" is derived from two different words in Greek: "*nustagmos*" meaning drowsiness and "*nustazein*" meaning to be sleepy. This implies the pathological character of the saw-tooth like eye movement pattern made up of alternating slow and quick phases. In addition to the already described optokinetic nystagmus, after-nystagmus and the vestibular nystagmus that will be explained in the next chapter, there is a report in the literature of a subject that was able to elicit "voluntary nystagmus" (Westheimer, 1954a). Rebound nystagmus occurs after prolonged periods of eccentric gaze; the slow phases are in the direction of previous gaze deviation. Many kinds of nystagmic eye movements can be "dumped", i.e. the saw-tooth-like eye movement pattern can be stopped by a stationary fixation target similar to OKAN (Chung and Bedell, 1995).

The pathological character of spontaneous nystagmus is related to an imbalance of neuronal activity in the left and right brain. Following unilateral lesions of the VIII nerve, lesions of NOT/DTN (Ilg *et al.*, 1993) or MST (unpublished observations so far), spontaneous nystagmus can be observed and is superimposed onto the regular eye movement repertoire of the monkey or patient. Recovery of stable eye axis or disappearance of nystagmus can be led back to the recovery of balance in neuronal activity of left and right brain. In the case of VIII lesions, this recovery happens within weeks or months, depending on the age of the patient (Smith and Curthoys, 1989); after NOT/DTN lesion in a rhesus monkey, the stability of gaze was reached after the first week post-lesion (Ilg *et al.*, 1993).

### 3. SLOW EYE MOVEMENTS CAUSED BY HEAD MOVEMENTS

In the preceding section, the optokinetic system was introduced and described as visual stabilization. In addition to this visual system, there is a second gaze-stabilizing system using vestibular information to achieve stable gaze in space. The report of the physician JC (1952) who lost his vestibular sensation due to lesion of the hair cells with streptomycin, demonstrate the major contribution of the vestibular system: JC was unable to read in bed unless stabiliz-

ing against the headboard and was unable to recognize anyone without artificially stabilizing his head (JC, 1952).

The vestibular sense organs consisting of the hair cells of the three semicircular canals (SCC), and also the utricle and saccule forming the otolith, transduce head acceleration into neuronal activity. Rotational acceleration is transduced by SCC, sensing the inertia of the endolymph, and linear acceleration is transduced by the otolith sensing the inertia of calcareous granules in the jelly filling of utricle and saccule. Head acceleration causes a dynamic eye movement response called vestibulo-ocular reflex (VOR). As shown in Fig. 3(B), if a subject or a rhesus monkey is rotated sinusoidally around his pitch axis, the eyes perform compensatory, horizontal movements in antiphase to the head movement. In addition, the otolith activity is also influenced by changes in orientation with respect to the earth's gravity (Fernandez *et al.*, 1972) demonstrated by the counter-rolling of the eyes following head tilt in the frontal plane, called the otolith-ocular reflex. This static reflex generally is weak in species with frontal eyes such as man and monkey, compared with SCC-driven VOR (Krejčova *et al.*, 1971). Another reason to neglect this type of rotational eye movement in my review is that this reflex involves interactions of three-dimensional eye position (horizontal, vertical and torsional) expressed as Listing's Law, which will not be discussed in this review.

### 3.1. Eye Movements Elicited by Rotational Acceleration

One might ask why evolution produced two different gaze stabilization reflexes? The answer is, as usual, easy: the two systems work in two different frequency domains: for low frequencies (<1–2 Hz), the optokinetic system compensates, whereas for high frequencies (>1–2 Hz), the VOR becomes active. For sinusoidal head movements in darkness, the VOR works up to 6–8 Hz and provides quite good compensation, i.e. the gain is close to unity and the phase lag is small (man: Skavenski *et al.*, 1979; monkey: Keller, 1978). The analysis of power spectra of human head movements revealed 7 Hz as upper limit (Skavenski *et al.*, 1979), so evolution adapted the sensitivity to the natural demands.

If a subject is rotated at constant speed in darkness, the eye velocity that initially compensates the body rotation, returns exponentially to zero. Otherwise, if the rotation stops, a post-rotatory nystagmus with slow phases in opposite direction is performed, whose velocity decays with a time constant of 21 sec for man (Malcolm and Mevill Jones, 1970). Under normal conditions, the post-rotatory nystagmus interacts with the OKAN to gain as fast as possible stable eye axis following self-motion of the subject. It is important that the decay in eye speed during post-rotatory nystagmus and OKAN do have similar time constants. Therefore, after rotation in light, the action of the post-rotatory nystagmus balances the action of the charged velocity storage mechanism and results in stable eye axis immediately after the end of rotation.

The three SCCs (horizontal, anterior, and posterior) of one side are arranged mutually perpendicularly, with pairs of them coding head rotational acceleration in a push-pull arrangement: the right vs the left horizontal canal, the left anterior vs the right posterior canal, and the left posterior vs the right anterior canal. Very similarly, each eye is moved by the three pairs of extraocular muscles also arranged in a mutually perpendicular manner. The afferents of each canal affect the extraocular muscles whose action to the eye axis is closest to the arrangement of the canal: horizontal canal afferents affect the horizontal recti, left anterior and right posterior canal affect left vertical recti and right obliques, right anterior and left posterior canal affect right vertical recti and left obliques (Lorente de Nó, 1933).

After bilateral lesion of the vestibular organ, patients and monkeys still could perform some compensatory eye movements elicited by head movements. They used either proprioceptive inputs from the neck muscles to compensate the head movement or elicited centrally pre-programmed eye and head movement pattern (monkey: Dichgans *et al.*, 1973; man: Kasai and Zee, 1978).

#### 3.1.1. Neuronal Substrate and Plasticity of the VOR

The signal from the SSC codes quite precisely the head acceleration and elicits high-gain compensatory eye movements during rotations in darkness. It is easy to see that the gain of the VOR must be subject to adaptation during the life-span of a human subject with juvenile growth of eye and adolescent weakening of the extraocular muscles. Under normal conditions, head movements not only stimulate the vestibular organs, but also generate global retinal image motion. In an experiment, the gain of VOR can be modified: wearing magnifying spectacles causes an increase in VOR gain, miniaturizing spectacles or goggles with small hole-limited visual field cause a decrease of VOR gain (Miles and Eighmy, 1980; Lisberger and Miles, 1980). This long-term adaptation constitutes a very simple example of motor learning and offers a handle to reveal some neuronal mechanisms underlying learning (Lisberger, 1988). In addition to this long-term adaptation of VOR, a short-term adaptation can be demonstrated as VOR suppression by fixation of a target that moves exactly with the subject.

A detailed analysis of the latency of the VOR revealed that the very first eye movement response (latency around 14 msec) of rhesus monkeys to head rotation in darkness is not subject to gain modification. Gain modification-dependent changes become visible later (19 msec) (Lisberger, 1984). This finding suggests multiple neuronal systems underlying the VOR response. There are three major pathways described responsible for the VOR (Lisberger, 1988): firstly, the shortest reflex arc underlying the VOR consists of three neurons: hair cells in the cupula of the SCCs transduce head acceleration into neuronal activity, which is transmitted via a vestibular primary afferent neuron that contacts a VOR interneuron in the VN. This interneuron drives the responsible extraocular

motoneuron. The second pathway includes a flocculus target neuron (FTN) acting as an interneuron in the medial VN with monosynaptic inhibition from the flocculus. Thirdly, the Purkinje cell receives tri-synaptic vestibular input via collaterals of the vestibular primary afferent neuron to the granule cells, which contacts the Purkinje cells.

It has been shown that the short-term modification depends critically on the flocculus. The line of evidence is as follows: caloric nystagmus can be suppressed if a stationary visual environment is present (Takemori and Cohen, 1974a). If the flocculus is lesioned, the caloric nystagmus can be elicited as normal in darkness, but the monkey is not able to suppress the caloric nystagmus with visual information (Takemori and Cohen, 1974b). It has been shown that vestibulocerebellectomy abolished reversing prism-induced VOR gain adaptation (cat: Robinson, 1976; rabbit: Ito and Miyashita, 1975). Additionally, Purkinje cells in the flocculus showed no modulation if a monkey was rotated in darkness and performed normal VOR, but showed a deep modulation if VOR was suppressed (Lisberger and Fuchs, 1974). The suppression therefore can be explained as a result of the inhibitory influence of the Purkinje cell onto the post-synaptic VN neuron. The lack of modulation during rotation and VOR can be explained by opposite influences related to eye and head movements converging onto the Purkinje cell (Lisberger and Fuchs, 1978).

The convergence of visual and vestibular inputs is a prerequisite for the long-term VOR gain adaptation. This convergence was suggested to be achieved in the flocculus. Masao Ito (1972) formulated that a persistent error signal from the optokinetic system arriving over the climbing fibres, as explained in the preceding section, could serve to modify slowly the efficacy of vestibular mossy fibre synapses on flocculus Purkinje cells to promote a learning process. In support of this hypothesis, recordings from primary afferents showed no change in sensitivity or in dynamic response properties in association with changed VOR gain (Miles and Braitman, 1980).

Unfortunately, there are different results from the laboratories of Masao Ito and Frederick Miles: firstly, in Ito's laboratory, it was shown that Purkinje cells in the flocculus changed their firing pattern as a result of VOR gain adaptation and therefore suggested the flocculus as site of motor learning (Watanabe, 1984). The influence of head movement-related input onto the firing rates of Purkinje cells increased if the VOR gain was lowered. The results of this study are difficult to interpret, since the monkey performed VOR during the experiment. Purkinje cells receive not only head movement-related input but also eye movement-related input, so the change in firing rate can be due to either an increase in the sensitivity to vestibular input or to a decrease in sensitivity to eye movement-related input.

Secondly, in Frederick Miles' laboratory, the firing patterns of Purkinje cells or vestibular afferents were found not to be subject to VOR adaptation (Miles *et al.*, 1980). Frederick Miles avoided the above-described conflicting condition by asking the

monkeys to suppress their VOR by fixating a target that moved together with the monkeys. He found only modest changes in the vestibular transmission, and this modification was found to be in the wrong direction, since a decrease in VOR gain produced a decrease in vestibular sensitivity of Purkinje cells (Miles *et al.*, 1980).

Based on these contradicting results, it was suggested that there must be two sites of VOR-gain adaptation: firstly, vestibular inputs to the cerebellar cortex of the flocculus; secondly, the vestibular input to these VN neurons that receive monosynaptic inhibition from the flocculus. A recent study showed two components of VOR modification, separated for pulse-like and sinusoidal head movements. The authors suggest that the two components reflect the two different sites of learning (Raymond and Lisberger, 1996).

### 3.1.2. Cortical Areas Responding to Vestibular Stimulation

So far, only subcortical structures are regarded to be related to the compensation of head movements by the VOR. In addition, vestibular information is necessary to achieve correct orientation of the subject in three-dimensional space. This processing is very likely based on cortical areas listed here: the parietoinsular vestibular cortex (PIVC) (Grüsser *et al.*, 1990), area 2v at the border of area 2 in the immediate vicinity of areas 5 and 7 (Büttner and Büttner, 1978), the vestibular part of area 3a (3aV) (Ödkvist *et al.*, 1974), visual-tracking neurons in area 7 (Kawano *et al.*, 1984), the ventral intraparietal area (VIP) (Bremmer *et al.*, 1997b), and the lateral part of MST (Thier and Erickson, 1992a,b). The majority of cortical neurons that respond to vestibular stimulation also respond to optokinetic stimulation. This supports the notion of the tight interactions between these two gaze stabilization systems. In addition, many vestibular responding neurons also respond during the execution of SPEM. Since the preferred directions of the head and eye movement-related activity are frequently in register, it is necessary to suppress the VOR to obtain a vestibular driven activity. During the execution of VOR, the activity is not modulated at all, since the eye and head movement-related responses balance.

### 3.2. Eye Movements Elicited by Linear Acceleration

The linear acceleration of the head is sensed by otolith organs. It is important to note that the effects of linear acceleration and gravity are identical. This linear acceleration causes compensatory eye movements called translatory VOR (tVOR). The maximum eye speed of tVOR depends on viewing distance (monkey: Schwarz *et al.*, 1989; man: Busetini *et al.*, 1994). The ocular following response (OFR) that will be discussed later showed the same dependence on viewing distance.

An important note has to be made to translatory head movements: they are very powerful in decoding space. Objects nearer to the fixation point will move in the same direction as the head, whereas objects

behind the fixation point will move in the opposite direction. This enables decoding of space in a monocular viewing condition. Neurons in the dorsal part of MST are especially tuned to decode depth from this arrangement since the preferred direction of their response to visual motion depends on the disparity of the stimulus (Roy and Wurtz, 1990).

To summarize this chapter, the fact that there are two different backup systems must be emphasized: firstly, (rotational) VOR backs up the indirect, delayed component of the optokinetic response. Secondly, tVOR supports the early component of the optokinetic response, which is very similar to the OFR.

## 4. SLOW EYE MOVEMENTS REFLECTING LOCAL MOTION PROCESSING

### 4.1. Smooth Pursuit Eye Movements

The key feature of this chapter is the assumption that the execution of SPEM, as shown in Fig. 3(C), depends critically on the processing of local motion and an internal representation of target trajectory in space. Under normal conditions, subjects are only able to produce high-gain SPEM in the presence of a moving target. The importance of the internal representation of target trajectory is suggested by the following five observations, explained in detail throughout this section: firstly, it is argued that after pursuit initiation, pursuit is "taken over" by the internal representation of target movement, rather than operating on the basis of incoming signals (Jürgens *et al.*, 1988; Barnes and Ruddock, 1989). Secondly, a class of models of the pursuit system is able to predict the generation of SPEM in various conditions based on an internal feedback of the eye movement command and combination with the retinal image motion yielding a signal related to the target movement in space (Robinson *et al.*, 1986). Thirdly, electrophysiological recordings from neurons in various areas of the primate brain revealed activity that seem to reflect the movement of the target in space. Fourthly, the execution of other motor commands, especially head movements and the related combination of eye and head movements to track a moving target, also only can be explained in the presence of an internal representation of target movement. Fifthly, and finally, even perceptual stability despite eye movements benefits from the internal representation of target movement.

Already, in the 1950s, Gerald Westheimer (1954c) investigated SPEM and realized that there are factors of three different levels affecting the execution of SPEM: the A level describes the mechanical aspects of the orbit, basically how the action potentials of the motoneurons are transformed into an eye movement. The B level refers to reflexive mechanisms to keep the target on the fovea. The C level operates at higher levels of complexity, such as predictive mechanisms (Westheimer, 1954c).

An important notion is related to the importance of prediction of the target movement and two different time domains which will be considered here: firstly, short-term prediction is important if the tar-

get moves at constant velocity, the underlying time/distance relationship allows prediction of where the target will be at a given time. Secondly, long-term prediction is useful to estimate future target position for periodic movements (Deno *et al.*, 1995). The prediction is not an exclusive feature of SPEM, even if we are asked to track a target moving according to a square wave trajectory with saccades, the saccade latency will be reduced and the subject will anticipate the target movement.

To summarize, if a study is supposed to address the processing of visual motion necessary to elicit SPEM, special care has to be taken to prevent the subject from any type of anticipation or, more globally, to use any kind of non-retinal information. A simple way to achieve this, used by the majority of modern studies of the pursuit system, is to analyse eye movement parameters only in brief time windows to brief and unpredictable target movements. Under these circumstances, the execution of SPEM depends solely on the processing of retinal image motion and therefore can be used as a biological probe for this processing.

### 4.2. Fovea-Dependence of SPEM

In order to maintain the high spatial resolution of the fovea, we are able to track moving objects to keep the retinal image located on the fovea. To be able to identify the facial expression of a walking person, we need to track the face, thereby using the high spatial resolution of our foveal vision. The velocity of the eye matches closely the velocity of the target. Since, under everyday conditions, the targets are real objects that move continuously or smooth, and the eye movements are a replica of the object movements, these eye movements are called SPEM.

Theoretically and very simplistically, SPEM could therefore be equivalent to fixation of a moving target. There is only one experimental evidence suggesting that this assumption is correct: fixation cells in the rostral part of the primate superior colliculus (SC) respond similarly if the monkey fixated a stationary target or performed SPEM (Munoz and Wurtz, 1993b). In contrast, there is much evidence suggesting the incorrectness of this assumption: firstly, the firing rates of the motoneurons of extraocular muscles can be described by a first-order differential equation if distinctions are made between fixation and SPEM (Eckmiller and Mackeben, 1978). Secondly, the sensitivity to slight perturbations of the target position or vibrations is increased if the monkey performs SPEM compared with fixation of a stationary target (Morris and Lisberger, 1987; Goldreich *et al.*, 1992; Schwartz and Lisberger, 1994). Thirdly, in the posterior parietal cortex, the response properties of single neurons suggest that fixation and SPEM drives two different pools of neurons: some cells fire during fixation of a stationary target and other cells fire during the execution of SPEM in preferred direction (Lynch *et al.*, 1977; Mountcastle *et al.*, 1975). Fourthly, and finally, dynamics of eye movements are different at the onset of pursuit to the cessation of pursuit, especially the ringing of eye velocity; oscillations can only be observed during pursuit, never during fix-

ation (Robinson *et al.*, 1986; Wyatt and Pola, 1987; Goldreich *et al.*, 1992). Additionally, the presence of a structured background changed the initiation of SPEM, but not the cessation (Mohrmann and Thier, 1995).

The notion that the presence of retinal image motion is a necessary prerequisite to elicit SPEM has to be slightly modified. There is one big exception to this rule: if the feedback loop between movements of the eye and retinal image motion is opened, normal and untrained subjects are able to perform SPEM without retinal image motion. This is not surprising when the loop is opened during steady-state SPEM and simply reflects once more the importance of extra-retinal signals for the maintenance of SPEM (Morris and Lisberger, 1987). But even pursuit initiation is shown to be possible in the open-loop condition. There are two possibilities to cut the feedback loop: either the measured eye position can be fed back to affect the target position or, more easily, by evoking an after-image. Using the after-image technique, it was shown that small eccentricity of the after-image elicits SPEM, bigger eccentricity elicits a sequence of saccades, although the actually performed eye movement pattern is influenced heavily by the attentional state of the subject (Kommerell and Klein, 1971; Grüsser, 1986). The open-loop technique also is used to test the validity of the eye position signals: a horizontal offset of 1° of the fixation target yields a cascade of saccades, symmetrical to both directions (Morris and Lisberger, 1987).

Everybody can do a similar experiment: in bright conditions, we are able to perceive small moving dark circles in our visual field. They are objects in the vitreal body of the eye close to the retina (von Helmholtz, 1867). These objects, called "*mouche volant*" (flying flies), move with respect to the eye due to inertia and gravity, and move with respect to the visual surround due to the executed eye movements. The gravity-induced movement can be reduced easily if the eye axis is vertical. In this condition, the flies can elicit SPEM without retinal image motion, very similar to the after-image technique. The subject can perceive his own smooth eye movements by the movement of the flies, similar to the demonstration of the micromovements during fixation in the beginning of this review.

#### 4.3. Parameters of SPEM

If a target starts to move unpredictably for a subject, the eyes of the subject first accelerate after a latency period and the eye velocity approaches target velocity. This acceleration will produce a lag of the eye behind the target; this error will be compensated by the later performed initial saccade (Rashbass, 1961). The statistical analysis of the scatter of pursuit latencies (around 100 msec) and the scatter of initial catch-up saccade latencies (around 170 msec) revealed that the two different eye movement responses are independent of each other (Merrison and Carpenter, 1994).

If the initial parameters of SPEM are addressed, the initial saccade disturbs the analysis to a large degree. To overcome this problem, Cyril Rashbass

developed a special paradigm: the initial saccade is avoided by a step in opposite direction to the movement of the target. The amplitude of the step has to be equal to the product of pursuit latency times target velocity in order to create a target trajectory that can be tracked without an initial saccade (Rashbass, 1961).

It is mainly the work of Steven Lisberger and colleagues which revealed the exact parameters of pursuit initiation in man and monkey: they describe an early component (20 msec) and a late component (20 to 100 msec) of pursuit initiation. During the early phase, the eye accelerates towards the correct direction, but no adjustment of eye velocity to target velocity is observed. This adjustment is achieved in the late phase of pursuit initiation (monkey: Lisberger and Westbrook, 1985; man: Tychsen and Lisberger, 1986).

The exact pursuit latency is found to be in the order of 100 msec for a target moving at 30°/sec, the latency increases for slower target velocities. Additionally, the pursuit latency is a function of target contrast (Lisberger and Westbrook, 1985). The initial eye acceleration is inversely proportional to the retinal eccentricity of the target. Finally, the acceleration is proportional to the target velocity (monkey: Lisberger and Westbrook, 1985; man: Tychsen and Lisberger, 1986).

During steady-state SPEM, low-frequency oscillations in eye velocity, called "ringing", were observed (Goldreich *et al.*, 1992; Robinson, 1976). It was shown that the frequency of this ringing is affected by the time delay of an artificial feed-back of the eye position onto target position. The "ringing" was never observed during fixation. Additionally, the gain of visuo-motor transmission is increased during the execution of SPEM compared to fixation (Schwartz and Lisberger, 1994). These observations constitute a clear argument against the hypothesis that SPEM can be interpreted as fixation of a moving target.

#### 4.4. Express Pursuit

For the execution of saccades, it is known that a temporal gap between the disappearance of the fixation and appearance of the saccade target enables the execution of "express saccades" and reduces the latency of regular saccades (Boch and Fischer, 1986). This reduction in latency is explained by the disengagement of fixation by the temporal gap. Under regular conditions, without a gap between the disappearance and appearance of fixation and saccade target, the first step to execute a saccade is to stop the fixation process. Following this line of arguments one would also expect the execution of "express-pursuit" if a temporal gap between fixation and pursuit target is used. Results from monkeys showed clearly that the latency of pursuit is slightly reduced by a temporal gap, but there is no express pursuit similar to express saccades (Krauzlis and Miles, 1996). This finding is consistent with the hypothesis that the SC is responsible for the execution of express saccades (lesion: Schiller *et al.*, 1987; recordings: Munoz and Wurtz, 1993a; Edelman and Keller, 1996). The primate SC is definitely not



involved in the generation of SPEM. Unfortunately, there exists a different study with human subjects on this issue: Merrison and Carpenter (1995) reported the existence of express pursuit in humans. However, as pointed out in detail by Krauzlis and Miles, the difference might not be a difference between man and monkey, but a difference in the experimental set-up: the express pursuit obtained in the human study might be due to the execution of anticipatory pursuit by the human subjects.

#### 4.5. Targets for SPEM

There are reports in the literature that human subjects are able to perform SPEM without a moving visual target. In contrast to the literature reviewed so far, these reports do not analyse the eye movement pattern in detail; usually they only present selected examples and therefore should not be compared with the latter reports. Firstly, there is an old report that a special skilled person, namely the author himself, was able to perform horizontal smooth pursuit in the direction of everyday motion experience while looking out the window of a moving train (Gertz, 1916). Additionally, either somatosensory or efferent information can be used to elicit SPEM: in total darkness some subjects can track the movement of their own thumb, frequently displaying massive asymmetries (Gertz, 1916; Steinbach, 1969; Gauthier and Hofferer, 1976; Glennly and Heywood, 1979). One of the most bizarre reports is the finding that subjects are not able to perform SPEM towards their own moving thumb if there is an opaque screen between the eyes and the thumb of the subject. It is the knowledge that the screen was present that inhibits the execution of SPEM, not the vision of the screen, since the experiments are done in total darkness (Gertz, 1916; Glennly and Heywood, 1979).

It is also reported that subjects are able to track moving auditory stimuli smoothly after some practice (Zambarbieri *et al.*, 1981). A more recent study compared SPEM elicited by a visual, somatosensory, or acoustic sinusoidal moving target as well as

the imaginary moving target in darkness (Hashiba *et al.*, 1996). It is shown that the attempt to track the imaginary target produced a sequence of saccades without any slow eye movements as shown in Fig. 7. Additionally, the SPEM gain decreases during tracking of an auditory or somatosensory target compared to the visual target. It can be concluded that the SPEM executed towards somatosensory and acoustic targets are mainly due to the predictive mechanisms involved in the generation of SPEM since the eye movements revealed huge phase leads to the target movement (Hashiba *et al.*, 1996).

It has also been shown that expectation can elicit slow eye movements without retinal image motion. If a target steps periodically, the subjects start to move their eyes as early as 350 msec before the expected step at a velocity of  $0.5^\circ/\text{sec}$  (Kowler and Steinman, 1979). It is very clear that these slow eye movements are in a different velocity domain from SPEM to moving visual targets. Furthermore, the importance of the predictor mechanism for the execution of SPEM is able to explain a strange contradiction in the literature. If the pursuit target moving at constant velocity is removed briefly, the eye speed decreases with a time constant between 100 and 200 msec (Becker and Fuchs, 1985; Ilg and Thier, 1997). In contrast, if a periodically moving target is tachistoscopically presented, i.e. the target is only briefly displayed (10–320 msec) during the zero-crossing of its triangular path, human subjects are able also to perform SPEM (Barnes and Asselman, 1992). This contradiction highlights the importance of the prediction of the future target position maximally enabled by a periodic target trajectory.

Taken together, it seems that a normal, not highly trained subject actually performs high-gain SPEM exclusively if a visual target moves.

The quality of SPEM can be improved, i.e. the slow eye speed matches exactly the target speed and the number of catch-up saccades is reduced, if the subject can move the target himself. It is suggested that subjects can use the efference copy (outflow) that produces the target movement (Steinbach, 1969). However, SPEM was upgraded not only if

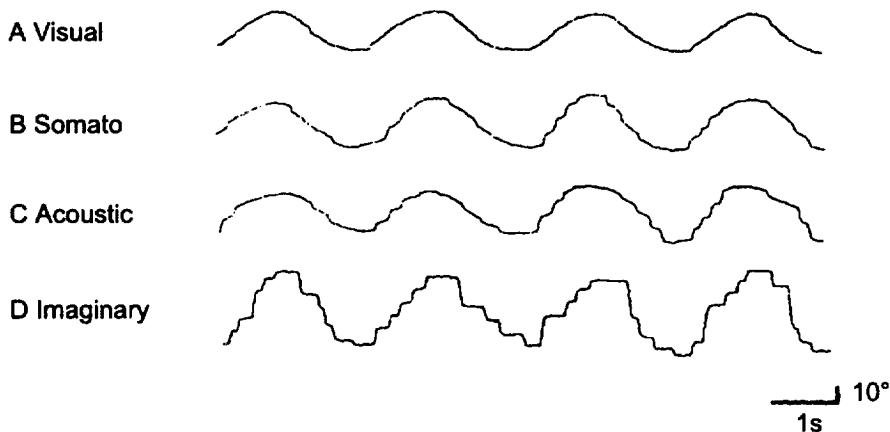


Fig. 7. Horizontal eye movement records during tracking of a (A) visual; (B) somatosensory; (C) auditory; and (D) imaginary target moving sinusoidally (frequency 0.4 Hz, amplitude  $15^\circ$ ) (reproduced with permission from Hashiba *et al.*, 1996).

the subject moved the target himself, but also if the subject tracked the target simultaneously by his hand (Mather and Putschat, 1983; Collewijn *et al.*, 1985; Gauthier *et al.*, 1988), with the restriction that the target movement has to be periodic (Koken and Erkelens, 1992), emphasizing the importance of the predictor mechanism.

It is not necessary for it to be a retinal target, it is also possible to pursue an imaginary target defined by extrafoveal cues. Human subjects are able to track the hidden corner of a moving diamond (Steinbach, 1976) or the centre of two moving dots (Wyatt *et al.*, 1994). Inspired by these results from human subjects, we asked recently whether rhesus monkeys can be trained to pursue an imaginary target, as shown in Fig. 8 (Ilg and Thier, 1997).

We compared the SPEM velocity elicited by the moving real hourglass (size  $20^\circ$ ), the imaginary hourglass lacking information in a central  $12^\circ$  field and simple  $6^\circ$  parafoveal tracking of a single spot. The steady-state gain of SPEM, defined as the quotient of eye velocity divided by target velocity obtained from two rhesus monkeys towards real (0.95) and imaginary (0.88) targets, are quite similar, with only a slight decrease in eye velocity during pursuit of the imaginary target as shown in Fig. 7. The gain elicited by the imaginary figure (0.88) is statistically significantly different from the gain elicited by parafoveal pursuit of a single spot (0.72) (Ilg and Thier, 1997). It was reported earlier that human subjects also show a clear reduction in

SPEM gain when they tracked a target parafoveally (Winterson and Steinman, 1978). As will be explained in the context of the neuronal substrate underlying the execution of SPEM, it is important to keep in mind that the imaginary target provides an experimental paradigm in which the rhesus monkey performed quite normal SPEM without any foveal retinal image motion. In contrast, we found marked differences in saccade parameters towards real and imaginary targets (Ilg and Thier, 1997). Firstly, the latency of the initial saccade during tracking of an imaginary target is increased compared with tracking the real figure, reflecting additionally neuronal processing in the former condition. Secondly, the peak velocity of the initial saccades towards imaginary targets is reduced compared with the peak velocity of saccades towards a real target, a similar difference in peak velocities for visually guided saccades and memory guided saccades (Becker and Fuchs, 1969), acoustic targets (Zambarbieri *et al.*, 1981) and antisaccades (Smit *et al.*, 1987) has been described by others.

So far, there is evidence presented that the execution of SPEM is closely connected to the occurrence of retinal image motion. Movement defined by the change in position of a luminance-defined object (first-order or "Fourier" motion) can be decoded by a simple elementary motion detector of the correlation type (EMD), often referred to as the Reichardt-detector (Hassenstein and Reichardt, 1956; Reichardt, 1961). This concept is functionally

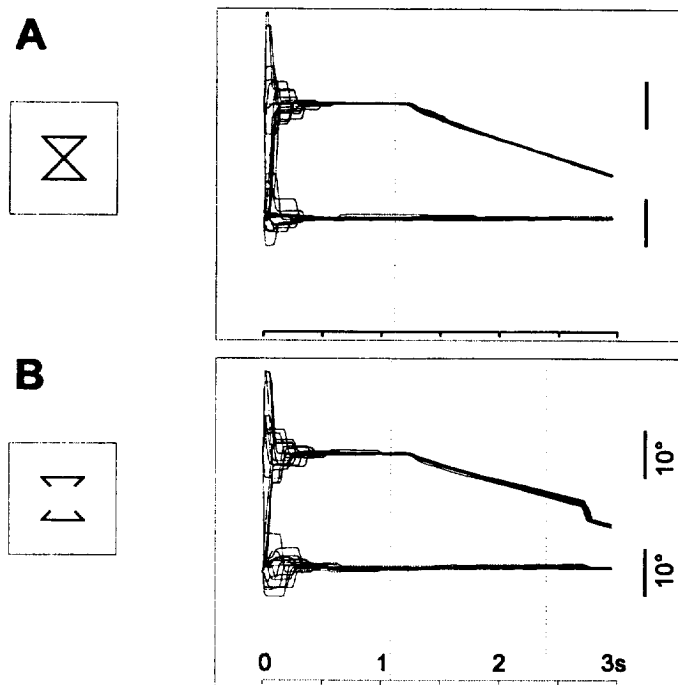


Fig. 8. Single trials ( $n = 20$ ) of horizontal and vertical eye position of a rhesus monkey tracking a real (A) and imaginary (B) target shown in the left panel, moving at  $10^\circ/\text{sec}$  leftwards. The onset of target motion is indicated by the first vertical dashed line, the second vertical dashed line in (B) indicates the time the imaginary target transformed into the real target (reproduced with permission from Ilg and Thier, 1997).

equivalent to other operators widely discussed in the literature called “energy models” (Adelson and Begen, 1985; von Santen and Sperling, 1985), and therefore can be used as a specific representative of a general luminance-based mechanism. However, neither of these models is appropriate to explain motion perception elicited by “non-Fourier” motion or second-order motion stimuli (Chubb and

Sperling, 1988), in which the average luminance distribution is not shifted at all, or is even shifted in a direction different from the one perceived.

We asked whether the eye movements of subjects tracking objects defined by second-order motion reflect the direction of single dots or the direction of the moving objects (Butzer *et al.*, 1997). Figure 9 shows a sketch of the used stimuli: in front of a

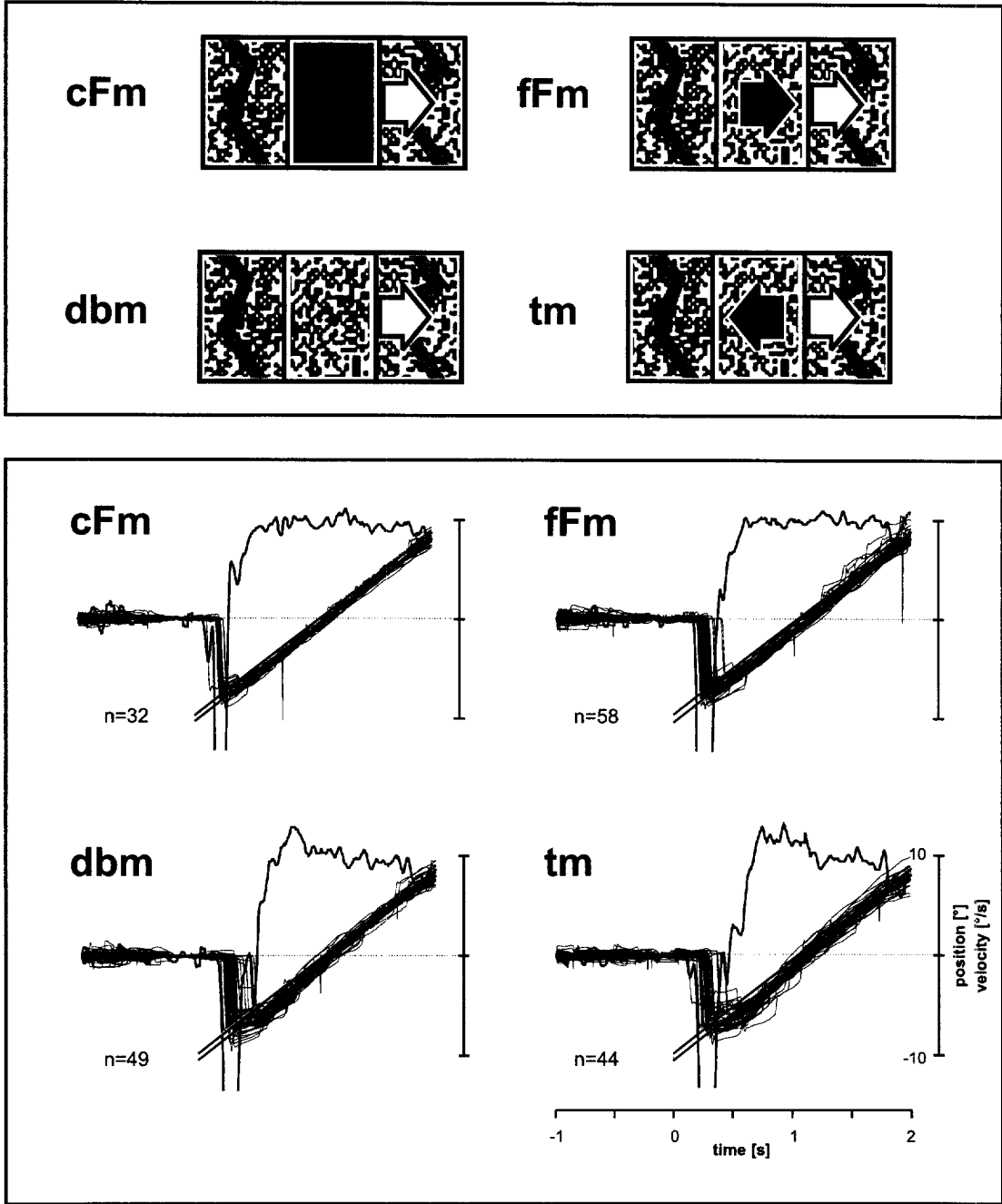


Fig. 9. (Top) Four different stimuli defined by first- and second-order motion are shown. Abbreviations: cFm, coarse Fourier motion; fFm, fine Fourier motion; dbm, drift-balanced motion; tm, theta motion. (Bottom) The horizontal eye position traces of single trials with the average eye velocity are displayed while a subject tracked one of these stimuli. For further explanation see text (modified with permission from Butzer *et al.*, 1997).

dynamic random dot pattern, indicated by the grey zigzag lines, moving coarse and fine Fourier motion (cFm and fFm), theta motion and drift-balanced motion (tm and dbm) stimuli indicated by the white arrows, were displayed. In case of tm, the dots of the object moved in one direction, indicated by the black arrow, while the object itself moved in an opposite direction. In the case of dbm, the dots of the bar are stationary while the background was a dynamic random dot pattern as in all other cases (Zanker, 1993). As Fig. 9 additionally shows, the eye position traces individual trials, while the subjects tracked one of the four motion stimuli. It is obvious that the eye movement responses are very similar in all cases, especially in the case of tm, where the eyes followed the stimulus movement, not the direction of retinal image motion elicited by the movements of individual dots (Butzer *et al.*, 1997). The additional neuronal processing necessary for decoding second-order motion is reflected by the longer latencies of the initial saccades during tracking of an object defined by second-order motion (around 260 msec) compared with the latency of saccades towards first-order motion object (around 210 msec). A different study could not produce optokinetic nystagmus with a similar second-order motion stimulus (Harris and Smith, 1992). The reason for these contradictory results might be that, for decoding second-order motion, attention is necessary. During SPEM, attention is engaged maximally, whereas the execution of OKN does not depend on attention.

To our knowledge, there are only reports that more difficult tracking conditions such as a decrease in contrast (Winterson and Steinman, 1978), the presence of structured background, high target velocities or losing the attention of the subject, produce an erroneous reduction in smooth eye speed. Our

study with second-order motion as stimulus for SPEM revealed for the first time that difficulties in the execution of SPEM also can produce too fast slow eye movements. The increasing retinal error of the target is compensated by saccades in opposite direction as the SPEM (Butzer *et al.*, 1997).

We made an interesting observation during the previously described experiments: experienced subjects are able to perform smooth pursuit without a moving stimulus across the dynamic random dot pattern, similar to a detuned TV set (Butzer *et al.*, 1997). An older study also showed that the flickering of the background enabled SPEM without a moving stimulus (Ward and Morgan, 1978). The flickering of random dot patterns might be similar to the flickering of LEDs arranged on a circle and the observed sigma movement. If SPEMs are initiated, they can be continued without a moving stimulus (Behrens *et al.*, 1985).

#### 4.6. Influence of a Structured Background on SPEM

If the target for SPEM moves across a structured background, as usually happens under real conditions, two problems arise: firstly, the moving target has to be identified and selected. This problem will affect the parameters of pursuit initiation. Secondly, after onset of SPEM, coherent retinal image motion due to the structured background will be induced by the eye movement, possibly affecting the parameters of steady-state pursuit. As has already been pointed out, coherent motion is the stimulus to drive the optokinetic system. There are reports in the literature that the presence of a structured background reduced steady-state SPEM, the retinal error is compensated by an increase in number of saccades (man: Collewyn and Tamminga, 1984; Yee *et al.*, 1983; monkey: Ilg *et al.*, 1993;

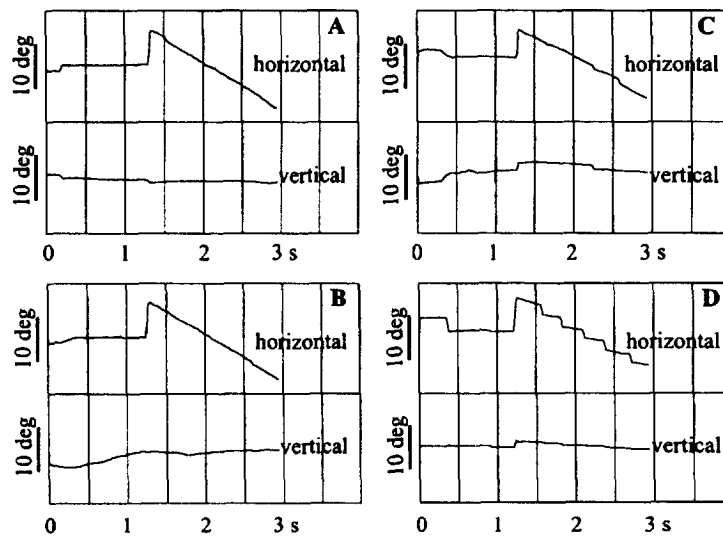


Fig. 10. Examples of different types of visual tracking shown by two different monkeys dependent on the structure of the visual background. Horizontal and vertical eye position traces of a single trial are shown while the monkeys tracked a target moving at  $10^\circ/\text{sec}$  to the left. While monkey I [(A) and (B)] performed SPEM largely independent of the structure of the visual background [(A) homogeneous, (B) random dot pattern], monkey II's pursuit became saccadic when the background was structured (D) as opposed to a homogeneous background (C) (reproduced with permission from Ilg and Thier, 1996).

Mohrmann and Thier, 1995; Ilg and Hoffmann, 1996). In contrast, Keller and Khan (1986) found only marginally reduced steady-state gain in the presence of a structured background. This apparent discrepancy can be explained by major interindividual differences in the sensitivity of the pursuit system to the presence of a structured background: as shown in Fig. 10, we found in a recent study including two rhesus monkeys that one animal showed heavily reduced SPEM gain in the presence of a structured background whereas the other did not change the eye movements at all (Ilg and Thier, 1996).

Additionally, a study on human subjects revealed that the structured background can only affect steady-state SPEM if the background is in the same depth as the moving target (Howard and Marton, 1992).

With respect to pursuit initiation, there is agreement in the literature that the initial acceleration of SPEM of rhesus monkeys is reduced in the presence of a structured background (Keller and Khan, 1986; Kimmig *et al.*, 1992; Mohrmann and Thier, 1995). There are contradicting results on the influence of a background onto the latency of SPEM: Mohrmann and Thier (1995) found a significant increase in latency, Keller and Khan (1986) found a slight, but non-significant increase in latency, and Hubert Kimmig and colleagues found that the latency is not affected by the background (Kimmig *et al.*, 1992). It must be noted that there might be two reasons for these contradictory reports: firstly, as already mentioned, there are major differences between the SPEM performance and the sensitivity of SPEM to the presence of a structured background. Secondly, methodological differences also might be responsible for the contradiction. Since the initial acceleration is reduced in the presence of a structured background, it is easy to see that the obtained latency is apparently increased if a velocity threshold is used to determine SPEM onset as done by these studies (Keller and Khan, 1986; Mohrmann and Thier, 1995) showing the increase in latency. If a correlation technique to assess SPEM onset as changes in the eye velocity profile is used (Kimmig *et al.*, 1992), the reduced acceleration can not affect the measurement of the latency.

So far, the stimulation of the optokinetic system resulted from self-induced retinal image motion. In addition, there are several studies using externally applied global motion together with a moving target for SPEM (Yee *et al.*, 1983; Worfolk and Barnes, 1992). Interestingly, the moving background produced effects that cannot be explained by algebraic summation of independently induced SPEM and OKN stimuli (Yee *et al.*, 1981). More specifically, Graham Barnes used the terms active and passive system, equivalent to the pursuit and optokinetic system. Simultaneous stimulation of both systems was done by a sinusoidal moving small target and a sinusoidal moving background. Since both stimuli moved at different frequencies, the separate gains of both systems can be calculated on the basis of a Fourier transformation of the measured eye velocity. The influence of the active system can be reduced by either tachistoscopic stimulus presentation, eccentric target movement or pseudo-random

target movement (Worfolk and Barnes, 1992). The tachistoscopic stimulation especially needs some explanation: in the control condition, the moving target was displayed continuously, in the tachistoscopic presentation the target is removed for time intervals ranging from 80 to 960 msec. If there is no background visible, the SPEM gain fell from 0.94 (continuous target display) to 0.30 (960 msec interval). If there was a visible moving background, the gain of the passive system stimulated by the background movement increased from 0.08 (continuous target display) to 0.47 (960 msec interval) (Worfolk and Barnes, 1992).

Recently, we were successful in pinpointing the site of interaction between pursuit and optokinetic system: the NOT/DTN seemed to play an important role. If the NOT/DTN was lesioned unilaterally in a rhesus monkey, the inhibitory influence of the structured background on SPEM steady-state eye velocity was reduced for controversial pursuit. The slow eye velocity was increased and the number of saccades was decreased compared to pre-lesion data (Ilg *et al.*, 1993). This result suggests that actually the passive stimulation of the NOT/DTN by the self-induced background motion yields a reduction in pursuit performance.

The presence of a structured background revealed one more argument why SPEM is not simply fixation of a moving target. As already discussed, a structured background is able to affect the parameters of pursuit initiation. In contrast, the pursuit termination was not affected by the structure of the background (Mohrmann and Thier, 1995) suggesting that the transition from fixation to SPEM was different from the transition from SPEM back to fixation.

Overall, the results related to the question whether and how the presence of a structured background affects the parameters of SPEM, or, in other words, how global retinal image motion is processed during the execution of SPEM is not yet enlightened in detail. In a recent study, we tried to solve this problem by "injecting" only briefly global motion during various phases of SPEM (Schwarz and Ilg, 1995). Very robustly, we found that global motion in opposite direction of the target movement does not affect SPEM at all, global motion in the same direction does produce a transient acceleration followed by a deceleration of eye speed. Surprisingly, this asymmetry was not only found in the eye movement pattern but also in the subjects' perception of the target trajectory: in case of injecting global motion in the same direction as the ongoing SPEM, the subjects report a transient apparent deceleration of the target (Schwarz and Ilg, 1995).

#### 4.7. Neuronal Substrate Underlying the Execution of SPEM: Cortico-Ponto-Cerebellar Pathway

A major problem related to the neuronal substrate underlying the execution of SPEM consists in the differentiation of sensory caused neuronal activity from motor-related activity. So there are reports in the literature about "pursuit cells", neurons that responded in a directionally selective manner during the execution of SPEM, which lack a

detailed description of the origin of this "pursuit activity". Without a moving target, as outlined above, neither a human subject nor a rhesus monkey can perform this type of eye movement. So the research on the function of posterior parietal cortex, an important area for the generation of SPEM, has been dominated for many years by a dispute between conflicting interpretations of the response properties of neurons in this part of the brain, leading to very different and even exclusive interpretations of parietal lobe functions. This differentiation between sensory- and motor-related activity and the demonstration of sensorimotor integration is much easier for saccades since memory-guided saccades offer the possibility to dissociate temporally sensory from motor activity (Andersen, 1990). It can be shown that the activity of neurons in the posterior parietal cortex do not reflect pure sensory or motor response properties; rather, they reflected sensorimotor integration necessary to perform goal-directed eye movements to objects in external space.

#### 4.7.1. Cortical Areas Involved in the Generation of SPEM

In the 1970s, neuroscientists began to study the properties of neurons recorded from area 7 using paradigms which required monkeys to direct either their eyes or their hands to visual targets in extrapersonal space (Hyvärinen and Poranen, 1974; Mountcastle *et al.*, 1975). Since many of the neurons studied were active in conjunction with distinct oculomotor behaviour such as fixation, saccades or SPEM, or alternatively, in conjunction with visually directed hand movements, it was suggested that the observed neuronal activity reflected commands for the execution of movements towards objects in extrapersonal space (Mountcastle *et al.*, 1975). Neither group could exclude the possibility that the observed activity was visual and sensory, since firstly the visual background was visible and provided retinal image motion during the execution of SPEM, and secondly the target itself provided visual stimulation. Therefore, not much later, similar neuronal activity was interpreted as visual responses modulated by shifted attention (Robinson *et al.*, 1978). Sakata and colleagues tried hard to test their monkey in total darkness with the pursuit target as exclusive visual stimulation; they recorded pursuit cells in area 7a and the adjacent anterior bank of the superior temporal sulcus (STS) (Sakata *et al.*, 1983). Still, however, there remains the possibility that the pursuit cells responded to residual retinal motion during the execution of SPEM.

In the 1980s, electrophysiological observations suggested that two parieto-occipital areas are involved in the generation of SPEM (Komatsu and Wurtz, 1988; Erickson and Dow, 1989). Both areas are located within STS of rhesus monkeys, the area MT in the posterior bank of the sulcus and the middle superior temporal area (area MST) confined to the anterior bank and the fundus, the latter marking the caudal end of the posterior parietal cortex. As already explained in Section 2.9.2.2, concerning the cortical neuronal substrate underlying the OKN, neurons in area MT respond in a manner

which is directionally selective (Allman and Kaas, 1971; Dubner and Zeki, 1971; Zeki, 1974; Mikami *et al.*, 1986a; Erickson *et al.*, 1989) and receive inputs from directionally selective neurons in V1 (Movshon and Newsome, 1996) and, in turn, project to area MST (Maunsell and van Essen, 1983b; Ungerleider and Desimone, 1986). Both areas are important structures in the dorsal stream of visual processing (Ungerleider and Mishkin, 1982). Different from earlier stages of visual processing as V1 where a lesion abolished initiation of SPEM in the entire contralateral visual field (Segraves *et al.*, 1987), lesions of MT and MST produce a retinotopic and a directional deficit in SPEM (Dürsteler and Wurtz, 1988). Whereas the retinotopic deficit can be interpreted as an artificial scotoma and was produced by every injection of ibotenic acid, the directional deficit was independent of retinal location of the pursuit target and occurred only if the floor or the anterior bank of STS was affected. As earlier stated, the directional deficit affected SPEM as well as OKN.

In both areas, single units are found which were activated by SPEM. William Newsome *et al.* (1988) set out to reveal the nature of the pursuit-related activity found in STS of rhesus monkeys by trying to separate the retinal and eye movement-related factors involved. They adopted two different paradigms which had in common that they tried to remove temporally target image motion while SPEM continued. The first paradigm is based on the assumption that steady-state SPEM should be continued even in the brief absence of the target (blink paradigm). The second approach (stabilization paradigm) is less radical. Rather than turning the target off, they tried to eliminate only residual target image motion by clamping the target image to the retina by electronic means. The rationale underlying these two approaches is as follows: if the activation of pursuit-related activity is not affected by the removal of either the target or the target-related image motion, it obviously cannot have a retinal origin. Neurons of the foveal part of MT which showed pursuit-related activity never continued to respond in these paradigms (Newsome *et al.*, 1988). In contrast, neurons in MST in the anterior bank of STS continued to fire despite the modifications, a finding corroborated by later work (Thier and Erickson, 1992a).

There are methodological difficulties with the paradigms used by William Newsome and colleagues. Firstly, the stabilization does not exclude the possibility that the neurons, similar to fixation cells, respond to the presence of the target. Secondly, it was shown that even brief disappearances of the target yielded reductions in eye velocity (man: Becker and Fuchs, 1985; man and monkey; Ilg and Thier, 1997). This reduction in eye speed is in contrast to the perception of a subject during the blink paradigm: a subject perceives the disappearance of the target as the movement of the target behind an obstacle at constant speed, similar to a train entering and leaving a tunnel. So these experiments reveal a problem: why should the pursuit activity be unaffected while the eye speed drops? This is the reason why we use imaginary figures (see above) to elicit SPEM without foveal retinal image

motion. While neurons in area MT never respond during tracking of an imaginary target, neurons in MST with clearly defined receptive fields also respond during tracking of imaginary figures, although there is no visual stimulation at all of the receptive field as shown in Fig. 11 (Ilg and Thier, 1997).

In contrast to area MT, area MST clearly integrates non-retinal information related to the execution of SPEM. Interestingly, electrical stimulation in area MST is able to modify ongoing SPEM, but unable to overcome fixation and to initiate SPEM (Komatsu and Wurtz, 1989). Usually the stimulation yields an acceleration towards the stimulation site that generates an increasing retinal error which is corrected by saccades. There is a report that electrical stimulation of lateral parts of area PG in the posterior parietal cortex produces ipsiversive SPEM on average at  $9^\circ/\text{sec}$  only if the monkey is in darkness (Kurylo and Skavenski, 1991). Although the authors stated that these stimulation sites are close to area MT, it is difficult to compare their results with those from Komatsu and Wurtz (1989).

In addition to the described areas MT and MST, there are more cortical areas involved in the generation of SPEM. It might be speculated that there are at least two more areas within STS containing neurons with pursuit-related activity: the floor of the sulcus FST and the polysensory areas within the sulcus STP (Bruce *et al.*, 1981). Clear pursuit responses were found in the gyrus anterior to STS, in area 7 (Sakata *et al.*, 1983; Bremmer *et al.*, 1997a). In addition, the visual tracking cells in area 7 receive vestibular input (Kawano *et al.*, 1984). The VIP area within the depths of the intraparietal sulcus contains

a high degree of directionally selective and velocity-selective neurons (80%), which are activated during the execution of SPEM. It has not yet been specified whether the pursuit activity in VIP has visual or non-visual origin (Colby *et al.*, 1993). Adjacent to area VIP, the lateral intraparietal area LIP also was shown to contain neurons that respond in a directionally selective manner during the execution of SPEM (Bremmer *et al.*, 1997a).

Traditionally, the primate frontal eye field (FEF), in the arcuate gyrus of the dorsolateral prefrontal cortex, was thought to be important for the execution of saccades (for review, see Goldberg and Segraves, 1989). Already, David Ferrier (1874) had discovered that saccades can be elicited by electrical stimulation of the FEF. Large saccades can be evoked by stimulation of the dorsolateral part, small saccades by stimulation of the ventrolateral part of the FEF (Stanton *et al.*, 1995). Surprisingly, lesions of FEF only produce trivial deficits in saccades (Schiller *et al.*, 1980) and early single-unit recordings showed that many cells became active after the onset of the saccade (Bizzi, 1968). In later years, evidence was accumulated showing that the FEF is also important for the execution of SPEM, especially for the anticipatory eye movements to predictive target movements. The FEF lesions caused an ipsiversive SPEM deficit (Lynch, 1987; Keating, 1991; MacAvoy *et al.*, 1991), and low-intensity microstimulation yielded SPEM-like eye movements (Gottlieb *et al.*, 1993, 1994). The analysis of single-unit responses during the execution of SPEM revealed the presence of pursuit neurons who increase their activity during the execution of SPEM directionally selectively with a lead on average 19 msec prior to the onset of SPEM. The pursuit ac-

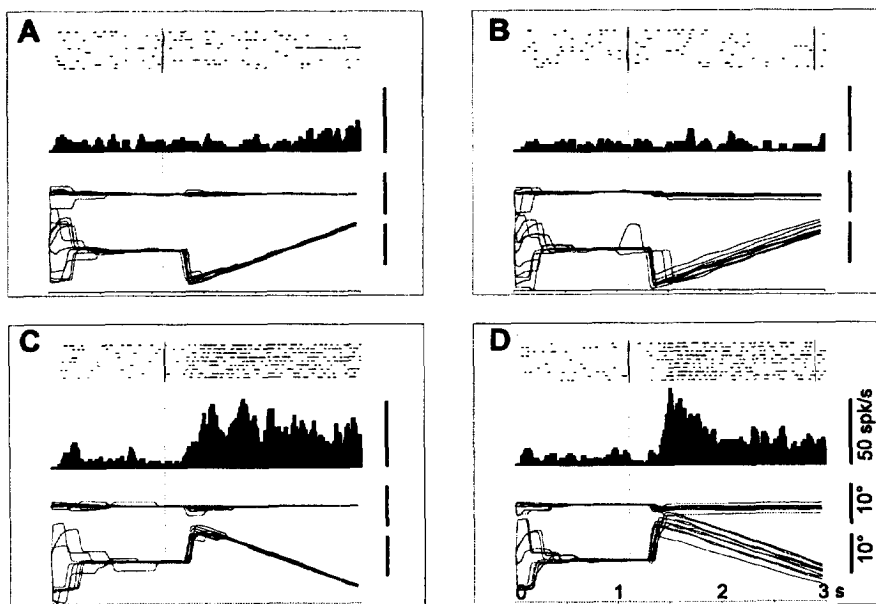


Fig. 11. Directionally selective neuron from area MST during vertical pursuit of a real and imaginary target. The horizontal and vertical eye position profiles of single trials are displayed together with the PSTH and raster plot of the discharge rate ( $n = 10$ ). Note that the neuron was activated during downward pursuit of either a real or imaginary target (reproduced with permission from Ilg and Thier, 1997).

tivity does not simply reflect sensory or motor factors; instead, it seems that similar to the above-described pursuit responses obtained from the posterior parietal cortex, this activity reflected sensorimotor processing necessary to generate SPEM.

An important issue is related to the modification of visual responses by the eye position of the monkey. It is known from the work of Richard Andersen that neurons in areas involved in sensorimotor integration underlying saccadic eye movements, such as the lateral intraparietal area (LIP) and area 7a, showed an influence of the eye position onto the saccade-related activity (Andersen *et al.*, 1990). A recent study revealed that this is also true for the pursuit responses obtained from neurons located in area MT, MST, LIP and 7a (Bremmer *et al.*, 1997a,c). Similarly, some neurons in the FEF showed a modification of their pursuit response due to the orbital position (Gottlieb *et al.*, 1994). This finding might further support the notion that the internal representation of the trajectory of a moving target is encoded in an extra-retinal reference system in these areas of the primate brain.

#### 4.7.2. Subcortical Areas Involved in the Generation of SPEM

So far, only cortical areas involved in the generation of SPEM are introduced. This raises the question of how the cortex might interact with premotor and motor structures in the brainstem. In contrast to the pyramidal cells in the motor cortex which contact the spinal motoneurons directly, no example is known that a cortical neuron can contact an extraocular motoneuron. So there have to be subcortical relays, such as the pontine nuclei, the most prominent candidate, to transmit the information towards motor structures.

The projections to the pontine nuclei do not arise from primary sensory cortical areas such as VI, but instead from association areas such as area MT, PO, LIP, or even FEF (Brodal, 1978; Glickstein *et al.*, 1980; Maunsell and van Essen, 1983b; Tusa and Ungerleider, 1988; Fries, 1990; Boussaoud *et al.*, 1992). Especially the projection from FEF to the DLPN are well described (Leichnetz *et al.*, 1984; Stanton *et al.*, 1988). The neuronal responses obtained from DLPN neurons showed a directional-selective excitation during the execution of SPEM (Suzuki and Keller, 1984; Suzuki *et al.*, 1990a; Thier *et al.*, 1988; Mustari *et al.*, 1988). Lesion of the DLPN produced an ipsiversive deficit in the execution of SPEM (May *et al.*, 1988). There is also a preliminary report that electrical stimulation of the DLPN modified ongoing SPEM (May *et al.*, 1985). Neurons in the DLPN provide the mossy fibre input to the cerebellum (Brodal, 1979). The cerebellum is most probably necessary for the execution of normal SPEM; it was suggested that all pursuit commands pass through the cerebellum before the final pre-oculomotor command can be calculated (Westheimer and Blair, 1974). This suggestion is based on the observation that cerebellectomy abolished SPEM (Westheimer and Blair, 1974); especially sensitive are the following segments of the cerebellum: flocculus (Zee *et al.*, 1981), paraflocculus

(Zee *et al.*, 1981), vermal lobules VI and VII (oculomotor vermis) and lobus IX (uvula). Electrical stimulation of the floccular region elicited slow eye movements (Ron and Robinson, 1973; Belknap and Noda, 1987) and single-unit recordings revealed that these neurons do process retinal image motion (Miles and Fuller, 1975; Noda and Warabi, 1982). The activity profiles showed brief peaks parallel to eye velocity reversals during tracking of a triangular moving target (Lisberger and Fuchs, 1978). Similarly, the activity of Purkinje cells revealed a transient increase at the onset of SPEM, followed by a smaller sustained increase in activity during maintenance of SPEM (Krauzlis and Lisberger, 1994a). There are several reports that Purkinje cells in the floccular region can be described as gaze velocity cells, i.e. they respond not only during smooth eye movements but also during head movements (Büttner and Waespe, 1984; Lisberger and Fuchs, 1978; Miles *et al.*, 1980; Noda and Suzuki, 1979; Noda and Warabi, 1982; Noda and Warabi, 1986; Stone and Lisberger, 1990). So, during suppression of VOR, the activity of floccular Purkinje cells revealed the same preferred direction as during the execution of SPEM (Lisberger and Fuchs, 1978; Miles *et al.*, 1980). If the monkey performed smooth pursuit across a structured background, some floccular Purkinje cells enhanced their modulation of activity compared with pursuit across homogeneous background, whereas other cells showed a nullified response in this condition (Noda and Warabi, 1986). Neurons in the paraflocculus also responded during tracking of a sinusoidal moving target (Noda and Mikami, 1986). There is some contradiction in the literature related to the importance of the vermis (lobules VI and VII) for the execution of SPEM: while Suzuki and Keller (1983) reported in an abstract that the SPEM gain was reduced following lesion of the vermis (Suzuki and Keller, 1983), Optican and Robinson (1980) reported normal SPEM following vermal lesions. The results from single-unit recordings revealed that vermal neurons responded better to retinal image motion than to eye movements (Kase *et al.*, 1979; Suzuki *et al.*, 1981). Nevertheless, it was shown that neurons in the vermis were able to provide a target velocity signal (Suzuki and Keller, 1988a,b). As already stated earlier, neurons in the uvula were activated during prolonged optokinetic stimulation, but only 7% of the examined neurons responded during SPEM (Heinen and Keller, 1996).

The cerebellar Purkinje cells are shown to project reciprocally to the vestibular nucleus (VN) (Langer *et al.*, 1985b). The VN neurons, especially the y-group and medial and superior parts of the VN, are activated during the execution of SPEM (Chubb and Fuchs, 1982; Fuchs and Kimm, 1975; Henn *et al.*, 1974; Keller and Kamath, 1975; Miles, 1974). There is a tight connection between neurons in VN complex and the motoneurons in the three oculomotor nuclei.

Parallel to the just described cortico-ponto-cerebellar pathway, there might be several other pathways, which might also contribute information for the execution of SPEM. First of all, neurons from the FEF are reported to project only sparsely the



DLPN compared to the intensive projections from area MST to DLPN, but FEF projects also to the nucleus prepositus hypoglossi (NPH) (Leichnetz, 1985; Stanton *et al.*, 1988). The NPH is very close to the premotor circuits in the VN complex and oculomotor nuclei. The neurons in NPH are active during horizontal pursuit, mostly with ipsiversive preferred direction, and showed a similar response as neurons from the abducens nucleus (McFarland and Fuchs, 1992). Suggesting this line of evidence, there are projections from NPH and medial VN to abducens nucleus (Langer *et al.*, 1986).

There are several possibilities for interactions between the neuronal substrate of the OKN and SPEM in the brainstem, as already described earlier. Firstly, other pontine nuclei such as NRTP and the dorsomedial pontine nucleus (DMPN) receive input from the pretectal NOT (Büttner-Ennever *et al.*, 1996). Neurons located there respond directionally selective to large field motion, 37% of the recorded neurons responded also during the execution of SPEM (Keller and Crandall, 1983). In the meantime, there are preliminary data available showing that lidocaine lesion within the NRTP produced deficits in SPEM (Suzuki *et al.*, 1990b). Secondly, the NOT projects to the DLPN and might act as a direct back-up of the cortico-ponto-cerebellar system (Magnin *et al.*, 1990; Mustari *et al.*, 1994; Büttner-Ennever *et al.*, 1996). Thirdly, and finally, the NPH also can be the location of interaction between the optokinetic and SPEM system, since it receives projections from the NOT/DTN (Magnin *et al.*, 1990; Mustari *et al.*, 1994; Büttner-Ennever *et al.*, 1996) as well as from the FEF (Leichnetz, 1985; Stanton *et al.*, 1988).

To summarize, Fig. 12 tries to visualize all the information related to the neuronal substrate underlying the execution of SPEM focusing on the cortico-ponto-cerebellar pathway. The interactions with the optokinetic system are represented by the grey lines.

#### 4.7.3. Neuronal Responses to SPEM and Saccades

Having described the various areas in the primate brain involved in the generation of SPEM, the question arises whether there are reasons at all to assume separated systems for the neuronal control of saccades and SPEM, since at the level of the motoneurons these two separate pathways no longer exist. A very recent and preliminary study showed that some DLPN neurons also respond to saccades (Thier *et al.*, 1995) and rejected the view that DLPN constitutes an exclusive neuronal substrate for SPEM. Similarly, an older report of the responses of Purkinje cells in lobulus VI and VII of the vermis showed that these cells also respond during saccades as well as SPEM (Suzuki and Keller, 1988a). The fact that DLPN and vermal Purkinje cells respond during SPEM and saccade might explain the massive interaction between the SPEM and saccade system. If the eye velocity is not adjusted correctly, saccades compensate the retinal error. In addition, if saccades are performed towards a moving object, the saccade amplitude is adjusted to the velocity of

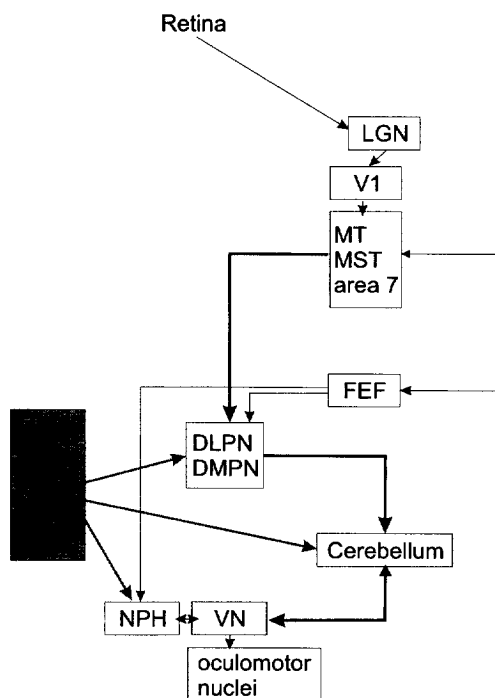


Fig. 12. Neuronal substrate underlying the execution of SPEM in monkeys. The bold lines represent the cortico-ponto-cerebellar pathway. For further explanations see text.

the saccade (man: Gellman and Carl, 1991; monkey: Keller and Steen Johnsen, 1990).

#### 4.8. Effects of Attention on SPEM

There is increasing evidence that different states of attention produce different neuronal responses to physically identical stimuli. Treue and Maunsell (1996) showed that neurons in area MT and MST do change their responses to moving dots depending on the instruction the monkey received prior to the trial. This effect might give some motivation to search for attentional effects on the SPEM parameters. Ferrera and Lisberger (1995) reported that a moving distractor displayed additionally to the pursuit target affected the latency of SPEM initiation but did not affect the initial eye acceleration. These authors claim that target selection processes are responsible for the observed modification of latency and that attention biased the target selection. It must be stated here that the execution of SPEM might not be an appropriate candidate to study attentional effects. The execution of SPEM definitively requires attention, without attending to the moving stimulus, no high-gain SPEM can be performed. If the subject does not direct its attention to the moving target, only Star-OKN is produced, frequently called passive slow eye movements (Pola and Wyatt, 1985; Worfolk and Barnes, 1992). So, instead of explaining the effects of a distractor by an attentional-biased target selection process, these effects might rather be explained by the additional retinal image motion and the well-known background effects on the execution of SPEM.

#### 4.9. Models of SPEM: Retinal Vs Non-Retinal Approaches

The execution of SPEM represents a classical example for system analysis approach, but as already mentioned this approach is only valid for the very early eye movement response, reflecting only visual processing and avoiding any C level processing in Gerald Westheimer's nomenclature (Westheimer, 1954c).

There are two different classes of models predicting SPEM: one class of models is restricted to exclusive visual processing, whereas the other type of model allows the integration of extra-retinal signals. The most elaborated version of the retinal models suggests the analysis of retinal image motion in three parallel pathways for velocity, transient (onset of target motion), and sustained acceleration (smooth changes in target speed) of the retinal image. Combinations of these three channels and subsequent integration produces a signal appropriate to program a SPEM motor plan (Lisberger *et al.*, 1987; Krauzlis and Lisberger, 1989). This approach allows very precise modeling of the initial eye velocity waveform in different experimental conditions. The model also allows calculation of Purkinje cell activity based on the motion parameters of the stimulus and yielded very similar activity profiles to the actually recorded Purkinje cell activity (Krauzlis and Lisberger, 1991). Additionally, the model predicted the actually measured onset and offset of SPEM depended on transient and sustained visual responses (Krauzlis and Lisberger, 1994b), and a similar directional organization (Krauzlis and Lisberger, 1996).

In contrast, the non-retinal models allow interactions between retinal and extra-retinal signals; specifically, they propose an internal feedback of the intended eye movement. The combination of the retinal image velocity with the eye velocity yields the internal representation of target velocity in space (Robinson *et al.*, 1986). Electrophysiological recordings from parietal cortex showed that MST neurons actually seem to include extra-retinal factors and to code for target movement in space (Newsome *et al.*, 1988; Thier and Erickson, 1992a,b; Ilg and Thier, 1997). The experimental findings were used to formulate a neuronal network model depending on an internal representation of target velocity in space to drive smooth eye and head movement (Dicke and Thier, 1995). The exact origin of the observed eye movement-related signal is yet not known: it is unclear whether the origin is an efference copy, or proprioceptive information from the extraocular muscle. But this uncertainty does not influence the concept of the use of extra-retinal signals. A different problem is related to the fidelity of the extra-retinal signal related to the ongoing eye movement. To enable the reconstruction of target velocity in space, the fidelity of this signal must be similar to the fidelity of the retinal image motion. The fidelity of the extra-retinal signal observed in the posterior parietal cortex has not yet been revealed in experimental studies.

An attempt to reveal which model is closer to reality consisted of the analysis of the ringing frequency

and its modifications. Therefore, an artificial feedback was realized by electronically stabilization of the retinal target image. The delay of the feedback system could be varied. Following the internal feedback model, modification of the feedback should not affect the oscillations. In contrast, the image motion model predicted massive influences as observed in these experiments (Goldreich *et al.*, 1992). Although it seems that there is an exclusive relationship between these two types of models, it can be shown easily that they are equivalent: the integration of the retinal model is formally equivalent to the internal feedback in the extra-retinal model. The important issue is that a signal related to the movement of the target in an external coordinate system, definitively not in a retinal co-ordinate system, can be recovered. This signal can be produced by either integration proposed by the retinal models or by feedback proposed by the non-retinal models. As this review tries to show, this internal representation of target trajectory in space is essential not only for the execution of SPEM.

#### 4.10. Combined Eye/Head Tracking

Obviously, if SPEM are examined while the head of the subject or monkey is fixed on a bite bar or by the implant, the experimental situation is highly artificial. Under natural conditions, SPEM are performed in conjunction with head movements called combined eye/head tracking (CEHT). As earlier described, the head movements stimulated the SCC and elicited VOR that moved the eye in the opposite direction of head. Clearly, this would heavily influence our ability to track a moving target with a combined eye and head movement. If the velocity of the head movement matches exactly the target velocity, the eyes remain stationary within the orbita during CEHT. One possible way to explain this is a linear combination of the head movement-related signals from the SCC with the internal representation of target velocity in space as introduced earlier. This linear combination was proposed by the results of the following experiment by Lanman *et al.* (1978): when the head movement of a rhesus monkey tracking a moving target by a combined eye and head movement was suddenly braked, the eyes started to move with a latency of 13 msec following the stop of the head movement. 13 msec is the latency of the VOR. If the vestibular organ was destroyed, the latency of the compensatory eye movement was increased to the visual latency (in the order of 100 msec). These results suggest that the drive for the eye movement during CEHT is derived as the difference of the internal representation of target velocity in space minus the head velocity. If the head movement was braked, the eyes are driven solely by the target velocity.

Interactions between vestibular signals and the internal representation of target trajectory are also shown by passive rotations of monkeys. If the monkey was rotated during the execution of SPEM, a very early component (latency 14 msec) in eye movement due to the head movement independent of the tracking condition was observed. Additionally, a so-called "short-latency tracking"

with a latency of 70 msec, too small to be visual in origin, dependent on the tracking condition was seen (Lisberger, 1990). Since the latency is too small to be visual, the only explanation of the modulated eye movements due to the head movement consists in the already described linear interaction between vestibular signals and the internal representation of target trajectory in space.

As already mentioned, SPEM is not simply equivalent to fixation of a moving target. Therefore, the question appears whether visually enhanced VOR (VVOR) of an earth-fixed target may be equivalent to fixation and suppression of VOR by fixation of a subject-fixed target is similar to pursuit? Data of normal human subjects with respect to oscillations in eye velocity do support this hypothesis: during VVOR no ringing in eye speed was observed, whereas during suppression of VOR the gaze tended to oscillate (Leigh *et al.*, 1994).

#### 4.11. Self-Induced Retinal Image Motion and Perceptual Stability

The execution of eye movements introduces a problem for the visual system: motion within the retinal image can result from movement of objects in space or from an eye movement. To gain perceptual stability the visual system must be able to differentiate these two types of retinal image motion. For the stability of visual perception during saccades there is a very easy solution for the problem: the sensitivity of the visual system is decreased dramatically during saccades, a phenomenon called saccadic suppression, therefore the retinal image motion due to the execution of saccades is not perceived at all (Matin, 1974; Ilg and Hoffmann, 1993b). This easy solution cannot possibly be valid during the execution of SPEM: as earlier pointed out, continuous processing of visual motion is necessary to perform SPEM. Additionally, it is known that SPEM across a structured background introduces an apparent movement of the background in the opposite direction to the SPEM which is called Filehne illusion (Filehne, 1922).

The problem that needs to be solved seems to be easy: neurons in various visual areas must be tested for whether they respond similarly or differently to retinal image motion due to object-motion or due to self-motion. While the monkey fixates a stationary target, a stimulus sweeps across the receptive field producing object-motion. During self-motion, the same stimulus remains stationary but the monkey is asked to pursue a moving target, producing identical retinal image motion. Many of these investigations were done by Claudio Galletti and colleagues and early work of this type suggested that even some neurons in V1 of macaque monkey are able to respond exclusively to externally induced retinal image motion (Galletti *et al.*, 1984). The authors named these neurons "real motion cells". About 10 years later, closer examinations of the responses of primate V1 neurons to self- and externally induced retinal image motion revealed that the differential responses are due to different retinal stimulation (Ilg and Thier, 1996). In brief, the retinal stimulation due to the execution of SPEM is not

as precisely matched onto the receptive field as during stimulus movement stimulating the inhibitory side-bands of the receptive fields. If the experimental set-up was modified to guarantee identical retinal stimulation for self- and externally induced motion, neurons in primate area V1 do only show identical responses to both types of retinal image motion (Ilg and Thier, 1996). Area MT neurons share this inability of V1 to differentiate between self-induced and externally induced retinal image motion. In the dorsal aspect of area MST, some neurons do respond differentially to these two stimuli, i.e. they suppress the response to self-induced retinal image motion (Erickson and Thier, 1991, 1992; Thier *et al.*, 1993). This suppression can be explained by visual interactions or flow-field analysis, which is known to be performed in this part of MST (Duffy and Wurtz, 1991; Roy and Wurtz, 1990). These visual interactions are able to explain the suppression of response during pursuit across a structured background only if there is a richly structured background present. If there is only a sparsely textured background, i.e. only a single bar in a otherwise total dark environment, these visual interactions become void. Under these circumstances, the extra-retinal signals during the execution of SPEM may be the internal representation of target trajectory are important suppress the response to self-induced retinal image motion and thereby to keep the perceptual stability (Erickson and Thier, 1991, 1992).

## 5. OCULAR FOLLOWING RESPONSE

The primate OFR, short-latency compensatory eye movements driven by fast movements of large textured stimuli whose parameters are well known due to the work of Frederick Miles and colleagues, serve two function of the visual system: firstly, the OFR is probably involved in getting stable eye axis immediately after the execution of a saccade as fast as possible. Secondly, the OFR might support the already described tVOR. Since the OFR is a very machine-like response with very short latencies and very brief execution times, without any attentional modifications, it is an excellent system to study the underlying neuronal substrate.

Figure 13 shows the post-saccadic enhancement of the eye velocity during OFR, clearly the eye acceleration increases with decreasing delay between end of saccade and onset of stimulus movement (Kawano and Miles, 1986). The latency of the OFR is as short as 51 msec, the latency can be increased if the stimulus was blurred (Miles *et al.*, 1986).

The post-saccadic enhancement of OFR suggest that one proposal of OFR is to serve clear vision as fast as possible following the saccade. It is shown that it is not the motor action of a saccade that enables OFR to occur, since simulation of the retinal image motion caused by saccades during fixation also enhanced the eye movement response. In addition, saccades that do not produce retinal image motion (vertical saccades performed across vertical oriented stripes) are not effective in producing an enhancement of OFR (Kawano and Miles, 1986). Interestingly, when gratings are used instead of ran-

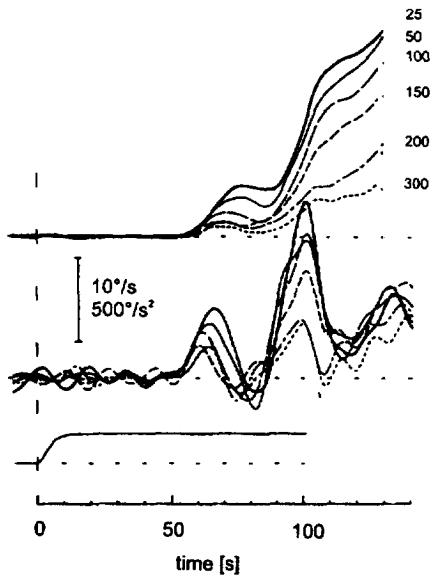


Fig. 13. Post-saccadic enhancement of the ocular following response to a test ramp of  $40^\circ/\text{sec}$  of a rhesus monkey. Displayed are, from top to bottom: eye velocity, eye acceleration, and stimulus velocity profiles with six different stimulus onset times (25–300 msec, as indicated) with respect to the end of the preceding saccade (reproduced with permission from Kawano and Miles, 1986).

dom dot pattern, the latency is solely a function of contrast and temporal frequency indicating that OFR is triggered by local changes in luminance as suggested by Reichardt's elementary motion detector EMD (Hassenstein and Reichardt, 1956; Reichardt, 1961).

Furthermore, the OFR also can be observed if a structured pattern already in motion is presented onto a previously dark background. We used an electronically controlled shutter to enable and disable the projection of a moving random-dot pattern and obtained response latencies in the order of 60 msec in our rhesus monkeys (Ilg *et al.*, 1993). So we conclude that a sharp image on the retina immediately before the onset of background movement is able to prevent OFR to occur. The sharp image can be avoided by either a saccade, simulation of saccade-related retinal image motion, or by darkness (Ilg *et al.*, 1993).

A similar eye movement response to steps of the visual background is observed in man, but for human subjects the response latency is not determined solely by the temporal frequency generated by sine-wave stimuli, the latency varies with the speed and only slightly with the spatial frequency of the stimulus (Gellman *et al.*, 1990).

### 5.1. Other Short-Latency Eye Movements

Recently, a short latency disparity vergence responses was reported (Busetini *et al.*, 1996). Similar to the execution of OFR, this vergence response depends critically on the presence of a previously executed saccade. These experiments are performed under dichoptic viewing conditions and consist of disconjugate steps in the position of large textured

stimuli presented to both eyes of a subject. The eye movement responses to these steps revealed a latency of 52 msec. If the crossed-disparity step is only applied to one eye, the binocular convergence is observed in both eyes, so it cannot possibly be explained by an independent monocular tracking mechanism (Busetini *et al.*, 1996).

The reason why the execution of OFR might be involved in the execution of tVOR is yet indirect: as already shown, the latency of OFR as well as the latency of tVOR is a function of viewing distance (man: Busetini *et al.*, 1994; monkey: Schwarz *et al.*, 1989). Recently, it was shown that monkeys show compensatory eye movements during free-fall with a latency of 16 msec (Bush and Miles, 1996).

### 5.2. Neuronal Substrate Underlying the OFR

As already mentioned, since the OFR is a very machine-like eye movement response, the correlation of neuronal activity with the parameters of eye movements in various brain areas revealed extraordinarily high values.

Thanks to the work of Kenji Kawano and his group, the neuronal substrate underlying the OFR has been identified as an occipito-parieto-ponto-cerebellar pathway, very similar to the pathway underlying the execution of SPEM. In extrastriate area MST, they found neurons that respond with a latency of 42 msec to the background movement of  $80^\circ/\text{sec}$  during the execution of OFR. Out of 214 neurons tested, 166 respond to movement in preferred direction with a latency smaller than 50 msec, that is before the onset of the OFR (Kawano *et al.*, 1990). As already described, there is a strong projection from MT and MST to the pontine nuclei (Brodal, 1978; Glickstein *et al.*, 1980; Maunsell and van Essen, 1983b; May and Andersen, 1986; Ungerleider *et al.*, 1984). The neurons in the dorso-lateral parts of the pons (DLPN) show a latency of their response during OFR smaller than 50 msec, so most neurons (56 out of 77) fire before onset of OFR (Kawano *et al.*, 1992). Or, in other words, 67 neurons of the total of 77 DLPN neurons increase their firing rate before the onset of the eye movement. Figure 14 shows the eye movements and the neuronal responses of a DLPN neuron during rightward OFR. This neuron is directionally selective for rightward visual motion.

Additionally, this study showed that the DLPN might contain two types of neurons: more than the half (68%) of the neurons in this study respond also during SPEM in darkness. Neurons with opposite preferred direction during the execution of SPM and OFR had long latencies ( $> 120$  msec), neurons with same preferred direction in both conditions had shorter latencies (Kawano *et al.*, 1992). This finding seems to support the idea that there are two separate pools of neurons in the pontine nuclei important for the execution of OFR and SPEM, respectively. As already noted, the DLPN provides the input for the cerebellum, mainly to the flocculus and paraflocculus as well as lobules VI and VII of the vermis (Brodal, 1979, 1982; Langer *et al.*, 1985a; Thielert and Thier, 1993). The responses of Purkinje cells in the ventral paraflocculus can be divided into two

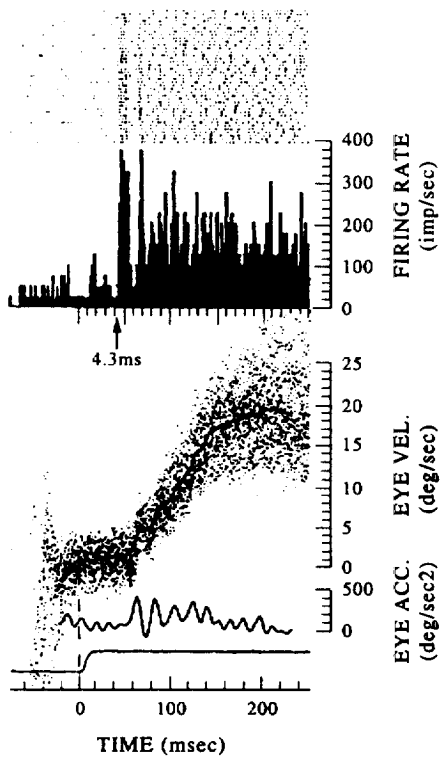


Fig. 14. Response of a DLPN neuron to 38 presentations of a 80°/sec test ramp and executed OFR. The neuronal activity of all recorded presentations is shown as a raster display as well as a PSTH with a bin size of 1 msec, horizontal eye velocity profiles as dots and the average velocity profile as solid line, eye acceleration and stimulus velocity. The arrows represent the estimated time of the response onset (43 msec for the neuronal activity and 56 msec for the eye velocity response) during OFR (reproduced with permission from Kawano *et al.*, 1992).

groups: some Purkinje cells prefer downward motion, others prefer ipsiversive motion. In any case, the majority of Purkinje cells lead the eye movement by 1–9 msec during OFR (Shidara and Kawano, 1993).

Since the OFR is such a machine-like behaviour, it is possible to calculate firing patterns of Purkinje cells based on the observed eye position, velocity and acceleration during OFR by an inverse dynamics model and to compare the calculated with the actually measured firing rates. Originally, an inverse dynamic model was used (Shidara *et al.*, 1993); later, simpler linear time-series analysis was used, enabling even better correlations (Kawano and Shidara, 1994). The firing pattern can be calculated with the formula:

$$F_{(t-\Delta)} = a * e''_{(t)} + b * e'_{(t)} + c * e_{(t)} + d$$

where  $f_{(t)}$  is the firing rate,  $e''$ ,  $e'$  and  $e$  represent the eye acceleration, velocity and position, respectively. The four coefficients ( $a$ ,  $b$ ,  $c$ , and  $d$ ) and the time delay ( $\Delta$ ) had to be determined. It is important to note that the lead of the firing pattern ( $\Delta$ ) of Purkinje cells is 7.1 msec on average (Kawano and Shidara, 1994), which is very close to the latency of

eye movements elicited by electrical stimulation of the ventral paraflocculus (Shidara and Kawano, 1993).

A final note to the neuronal substrate underlying the execution of OFR is related to the pretectal NOT/DTN that constitute a bottleneck-like structure for the optokinetic system. Since NOT neurons showed a response latency to the onset of large-field visual motion that is longer than the latency of OFR (Ilg and Hoffmann, 1996), the NOT/DTN is most likely not involved in transmitting retinal image motion information for the execution of OFR. It is yet not clear whether the neuronal substrate underlying the execution of OFR is identical to the substrate underlying SPEM or whether different pools of neurons are responsible for the execution of these two types of slow eye movements.

### 5.3. Induction of Zero-Latency Post-Saccadic Drift

The post-saccadic drift constitutes similar slow eye movements preceding saccades as OFR (monkey: Optican and Miles, 1985; man: Kapoula *et al.*, 1989). To induce post-saccadic drift, a panoramic presented background pattern moved according to an exponential function after each performed saccade. At the beginning of adaptation, the subject performed a OFR. After 2 hr of adaptation, the compensatory eye movement had a latency of zero and also was observed in darkness without a moving panoramic moving pattern (monkey: Optican and Miles, 1985; man: Kapoula *et al.*, 1989). Twenty years earlier, David Robinson had suggested that the step and pulse-like activity in the motoneurons had to be adjusted exactly to prevent drifts of the eye immediately after the execution of saccades (Robinson, 1964). It was hypothesized that the induction of zero-latency post-saccadic drift might be related to a mismatch of the step and pulse activity of the extraocular motoneurons.

## 6. VERGENCE EYE MOVEMENTS

The eye movements described up to here are conjugate eye movements. The movements of the left and right eye are closely similar in amplitude and direction, resulting from equal innervation of the extraocular muscles of both eyes, which is known as Hering's law (Hering, 1868). The conjugate eye movements provide the ground for binocular fusion of the images on the left and right retinae and enable binocular cells in the visual cortex to use disparity to decode the third dimension of visual space. Now, some disconjugate eye movements related to direct the gaze towards either objects that move in depth of space or towards different objects in different depth will be described.

### 6.1. Vergence Pursuit

If a target moves towards or away from a subject, the subject can track this movement smoothly with appropriate vergence eye movements. It is irrelevant whether a real target is used (Erkelens *et al.*, 1989b; Koken and Erkelens, 1993) or a dichoptic presen-

tation with disparity stimuli (Rashbass and Westheimer, 1961a). Similar to SPEM, the delay of the vergence response becomes negative if periodic movement of the target is used (Erkelens *et al.*, 1989a), revealing the predictive character of vergence pursuit. Different from SPEM, whose quality is upgraded when the subject additionally manually tracked the target (Koken and Erkelens, 1992), the performance of vergence pursuit is not increased when the subject manually tracked the moving target (Koken and Erkelens, 1993).

### 6.2. Saccades to Targets in Different Depth

The classical view of gaze shifts between two targets at different location and depth suggests the following sequence of events: since the vergence system has a shorter latency, the eyes initially start to diverge slowly. About 100 msec later, the saccade, classically viewed as an example for strictly conjugate eye movements, moves both eye axes rapidly towards the direction of the new target. The vergence movements are much slower compared to saccades, so after the cessation of the saccade, the eyes still have to diverge (Yarbus, 1957; Riggs and Niehl, 1960; Rashbass and Westheimer, 1961b; Robinson, 1981). The vergence eye movements are always smooth and reach velocity up to 200°/sec for real targets moving in depth (Erkelens *et al.*, 1989b). The easy scheme of separate vergence and conjugate saccades was refuted when numerous newer studies revealed that saccades can be disconjugate (Erkelens *et al.*, 1989b). Further, it was shown that horizontal saccades are never strictly conjugate (Collewijn *et al.*, 1995). Details will not be gone into here, since saccades end the topic of this review on slow eye movements.

### 6.3. Dichoptic Stimulation

Since the usage of real targets for eye movements introduces serious problems with their handling related to mechanical inertia, many studies are done with a dichotic presentation and the introduction of depth with disparate stimuli. If two random-dot patterns are presented dichoptically and move in counterphase to each other, the subjects perform counterphase smooth eye movements introducing huge vergence without the perception of movement in depth displayed in Fig. 15 (Erkelens and Collewijn, 1985). In a similar study in which the tracking eye movements to transparent horizontal motion were investigated (Niemann *et al.*, 1994), the two simultaneously presented dot patterns were identical, so at a given time the two groups of dots merged. The eye movement response of the subjects to this fusion of dots revealed a huge vergence movement without the perception of movement in depth until the convergent eye movements reached their limits (Niemann *et al.*, 1994):

It seems that real periodic target movement in depth, enabling predictive movements, yielded a shorter time delay of the vergence response (48 msec in Koken and Erkelens, 1993), compared with a delay of 220 msec if only disparity stimuli are used

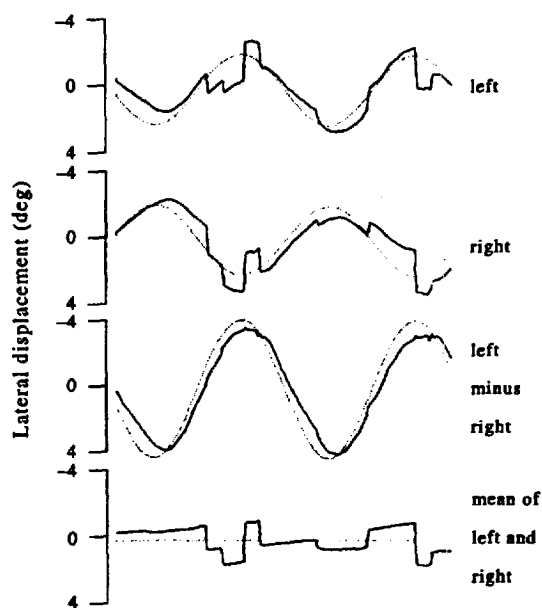


Fig. 15. Left and right eye position of a human observer (solid) and stimulus position (dotted) during counterphase dichoptic stimulation, as well as vergence and version of eye (solid) and image (dotted) are plotted (with permission from Erkelens and Collewijn, 1985).

that did not produce the perception of movement in depth (Erkelens and Collewijn, 1985).

The short-latency vergence response which can be observed in the wake of saccades (Busettoni *et al.*, 1996) has already been introduced in the section explaining the ocular following response.

## 7. EPILOGUE

It is important to summarize at the end that slow eye movements support and serve two different main functions of the visual system: gaze stabilization and tracking of moving objects. With respect to stabilization, rotational acceleration of the head is compensated by the VOR and by the late component of the OKN, linear acceleration stimulates the otolith-dependent VOR, the early component of the OKN and the ocular following response. The tracking of a target moving in front of a structured background asks for interaction between local and global motion processing. This emphasizes that the investigation of isolated types of the slow eye movements represents an insufficient approach; instead, as proposed by Robert Steinman (1986), an eclectic view of the different types of eye movement is needed to understand not only the oculomotor system but rather broader aspects of the visual system. It is important to realize in this context that the study of slow eye movements is not only important to reveal the detail properties of the oculomotor system reflecting sensorimotor integration, but additionally provides a handle to higher functions of the visual system such as visual perception, predictive mechanisms, three-dimensional localization of objects and manoeuvring in three-dimensional space.

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