The effects of oculomotor instability on visual performance of people with macular disease

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“If we knew what it was we were doing, it would not be called research, would it?” attributed to Einstein

Declaration

I, Antonio Filipe Teixeira Macedo, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Abstract

Background: People with macular disease often face difficulties using their preferred retinal locus (PRL) during visual tasks. These difficulties are due to impaired oculomotor control, amongst other causes. The aim of this work was to investigate whether stabilizing the visual target at the PRL is beneficial for visual acuity and reading. **Methods:** Control of retinal image instability at the PRL was achieved using an eyetracker that moved the target according to the eye movements. Crowded and uncrowded visual acuity was measured at the PRL in people with macular disease and in healthy peripheral retina of control subjects. RSVP reading speed was also measured using the same method of stabilization at the PRL and healthy peripheral retina. **Results:** Results of a series of experiments showed that stabilizing the visual target can improve visual performance in most cases. In healthy peripheral retina crowded visual acuity improved when the image was stabilized and reduced when fixation instability was over-compensated. At the PRL, in patients, no improvement in visual acuity was obtained under stabilized conditions and again visual acuity reduced for over-compensated fixation instability. However, reading speed improved under stabilized conditions, by 20% in healthy peripheral retina of control subjects, and by up to 40% at the PRL of people with macular disease. **Discussion:** Good oculomotor control is critical for complex crowded tasks like reading. The improvement in reading speed found whilst compensating for oculomotor instability at the PRL is encouraging. These results indicate that training programs which aim to improve fixation control are likely to bring benefits for visual tasks. The observed increase in reading speed might be clinically relevant but the technique used to control instability needs simplification to be implemented outside the laboratory.

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Chapter 1. The retina: visual function and eye movements

The human visual system is one of the most complex in nature. It provides ‘snap shots’ of the surrounding world forming vision, the richest source of sensorial information. The optical structures capture and focus light which triggers a photochemical reaction in the photoreceptors of the retina. The signals travel through a complex neural network where they are processed and perceived as an image of the visual scene when they reach the brain.

1.1 The Retina

1.1.1 Anatomy

The retina is nervous tissue that lines the back of the eye. The innermost layer of the functional part is made up of photoreceptors and their neural connections to retinal ganglion cells, amacrine cells, bipolar cells and horizontal cells. The retinal pigment epithelium together with its basal membrane and Bruch’s membrane forms a structure that maintains the

integrity of the barrier between the choroid and the retina. The choroid, mainly a vascular tunic, is sandwiched between the retina and the sclera and forms the main source of blood supply to the outer half of the retina. The retina as it appears when visualized through direct observation of the back of the eye is shown in Figure 1.1.

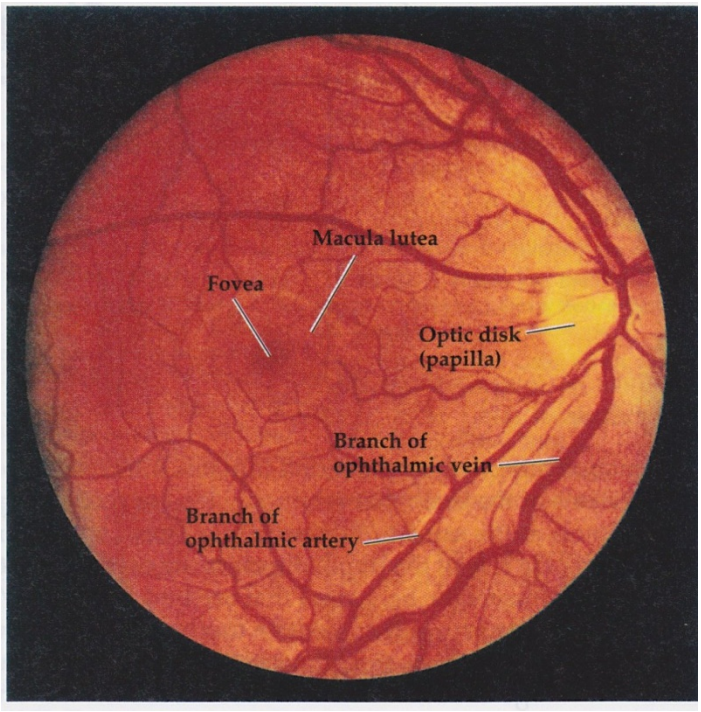

Figure 1.1: The retina as it appears through the Ophthalmoscope. The macula lutea can be seen as a distinct area at the centre where vasculature is absent. The fovea is a depression or pit about 1.5 mm in diameter that lies at the centre of the macula (Purves, Augustine, Fitzpatrick, Hall, LaMantia, McNamara & Williams, 2004).

The photoreceptors transform light into nervous impulses which are conducted through the network of cells in the retina. There are two main types of photoreceptors: cones, sensitive to high levels of illumination, and

rods, sensitive to low levels of illumination. According to spectral tuning, cones are divided into 3 types: short, medium and long-wavelength sensitive.

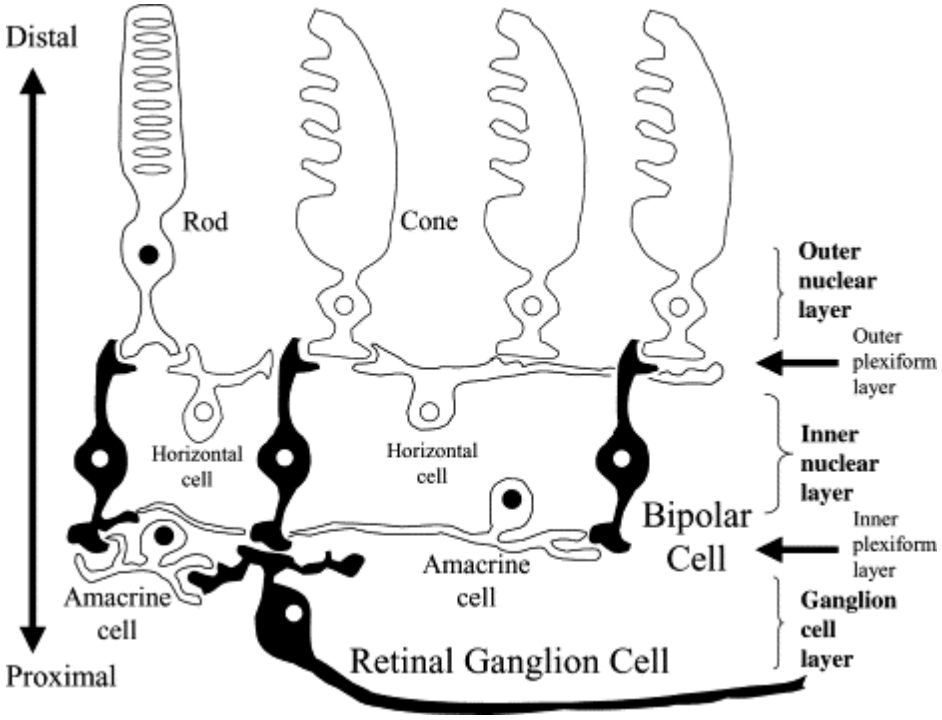

Figure 1.2: The structure of the retina with three nuclear layers. The outer nuclear layer (photoreceptors), the inner nuclear layer (bipolar, horizontal and amacrine cells) and the ganglion cell layer (ganglions). Between the inner and outer nuclear layers is the outer plexiform layer where lateral connections are formed between photoreceptors, bipolar cells and horizontal cell processes. Between the inner nuclear layer and the ganglion cell layer is the inner plexiform layer where lateral connections are formed between bipolar, amacrine and ganglion cells. Information flows from photoreceptors to ganglion cells but there are also many lateral interactions (Clifford & Ibbotson, 2002).

Ganglion cells with their receptive fields receive information from the

receptors and transmit to the optic nerve. A receptive field corresponds to the area of the retina which, when illuminated, produces a response in specific nerve fibres, as shown in Figure 1.3.

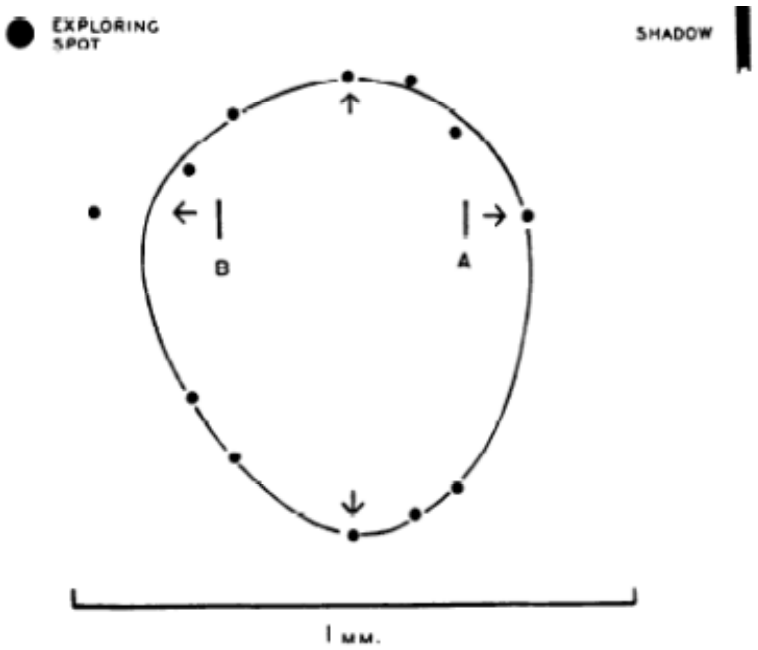

Figure 1.3: Illustration showing the receptive field limits of an optic disc nerve fibre (frog). When the illuminated spot is moved outside the limits the cell stops firing (Hartline, 1940).

Receptive fields of the ganglion cells can be of two types: type “on” (responsive when the centre is illuminated or the intensity of light increases) and type “off” (responsive when the illumination extinguishes or the intensity of light reduces). In both types there is a surround whose response works in the opposite direction of the centre. These cells respond vigorously to small and sudden movements of the retinal image. For

example, a moving spot of light with constant intensity causes a response in visual neurons by alternation between adjacent receptive fields (Hartline, 1940).

The macula is the central part of the retina which subtends approximately 5 degrees of visual field. This area is characterized by an exceptionally high density of neural cells and absence of retinal blood supply (Provis, Penfold, Cornish, Sandercoe & Madigan, 2005). The centre of the macula, the fovea, consists of only two cone types: medium and long wavelength sensitive. With increasing distance from the centre of the fovea (eccentricity) the number of rods increases, as it does the number of short wavelength cones. Figure 1.4 shows the density of cones, rods, and ganglion cells from the centre to the periphery of the retina.

In general, acuity decreases rapidly with eccentricity as can be seen in Figure 1.4. The next section describes in detail how visual function varies with eccentricity and what limits central and peripheral resolution.

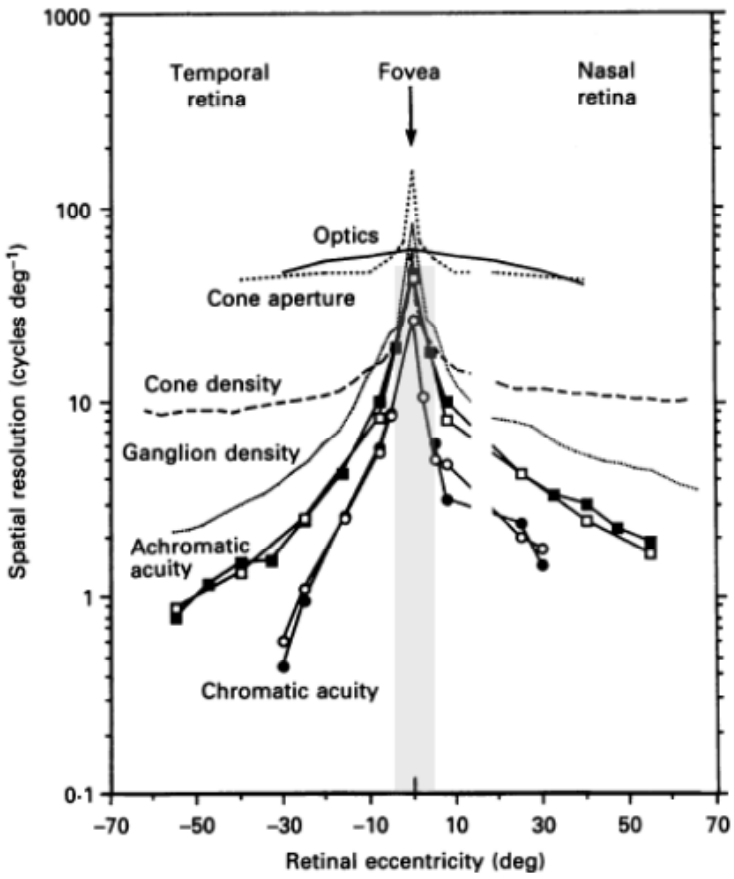

Figure 1.4: Variation of optical, psychophysical and anatomical data for the human eye. The data symbols show achromatic acuity (square symbols) and chromatic acuity (round symbols) as a function of retinal eccentricity along the horizontal meridian. The various continuous, dashed and dotted lines show the maximum spatial resolution (cycles.deg^{-1}) afforded by: the eye's optical properties, the aperture size of individual cones, and the Nyquist limits dictated by cone density and ganglion cell density. All data sources can be seen in the original publication, adopted from Anderson (Anderson, Mullen & Hess, 1991).

In Figure 1.4 the Nyquist limit is defined as the highest sinusoidal spatial frequency (colour or luminance modulation) that can be reconstructed unambiguously from an array of spatially discrete sampling elements

(Anderson et al., 1991). Fringe acuity measurements were based on Young's double-slit interference experiment. Young's interference fringes on the retina are unaffected by optical defocus of the eye or by aberrations in the usual sense (Westheimer, 1960).

1.1.2 Visual function

In the centre of the macula visual acuity reaches its maximum value and finer than 1 minarc^{-1} (Green, 1970). At 5º eccentricity visual acuity is already less than half of this value and the decline continues to the periphery where the density of receptors is lower. Figure 1.5 shows the relationship between cone density and visual resolution.

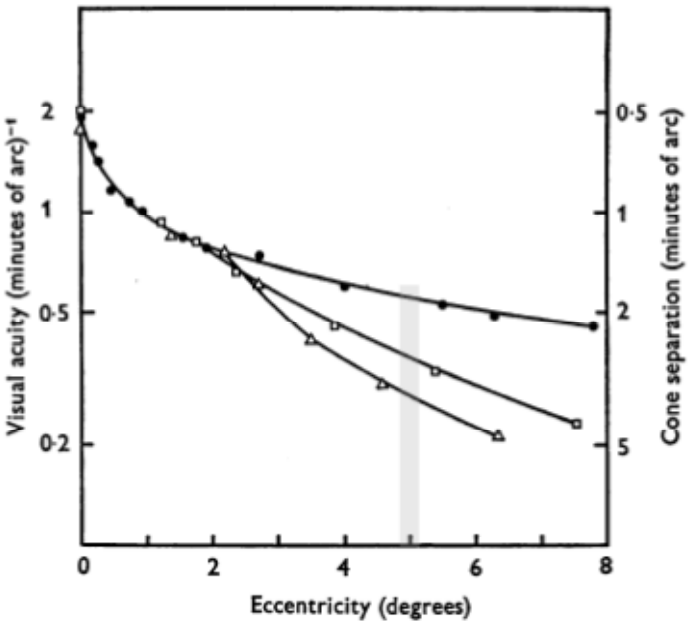

Figure 1.5: Comparison of interference fringe acuity and cone-to-cone separation. Open symbols correspond to acuity of two observers and closed circles show the cone separation. Adopted from Green (Green, 1970).

Limits of resolution in the central retina are imposed by the organization of the mosaic of photoreceptors and by the density of ganglion cells. In the fovea the maximum angle of resolution is proportional to the distance between two adjacent receptors (Williams & Coletta, 1987). In the periphery of the retina the density of photoreceptors is not the main limitation of resolution, here the reduction in the number of ganglion cells per photoreceptor is the main limiting factor. The number of ganglion cells per photoreceptor changes from 3 at around 2º eccentricity to less than 1 at 11º eccentricity (Curcio, Allen, Sloan, Lerea, Hurley, Klock & Milam, 1991). The size of the receptive fields of ganglion cells changes to compensate for the reduction of the ratio ganglion cells/receptor. At the fovea receptive fields are the size of one photoreceptor but they increase with: eccentricity, the area of the retina and the number of receptors connected to each ganglion cell (Sjöstrand, Olsson, Popovic & Conradi, 1999). Thus, the spacing between ganglion cells poses the fundamental limit on the spatial resolution of the peripheral retina (Anderson et al., 1991).

1.1.2.1 *Primary visual cortex and cortical magnification*

Each point of the retina corresponds to an area of the visual cortex, this is known as retinotopic correspondence. The area of the visual cortex devoted to the analysis of a constant-size region of the visual field diminishes progressively for more peripheral locations. The change is defined by the cortical magnification factor, which indicates the linear

extent of cortex in millimetres corresponding to one degree of visual field at various eccentricities (angular distances from the middle fovea). The cortical magnification factor can predict the resolution of the peripheral retina for scaled gratings (Rovamo, Virsu & Nasanen, 1978).

1.1.2.2 *Temporal aspects of vision*

In the central retina the visual system integrates information over approximately 120 msec (Barlow, 1958), which is enough time for a moving object to alternate between receptive fields. This movement can produce motion smear or motion blur (Burr, 1980). The amount of blur depends on: the size of the receptive field, the target's velocity and the target's spatial frequency. Kelly proposed a mathematical equation using these variables to predict the temporal output of receptive fields (Figure 1.6). According to Kelly, if the velocity of the target increases 'within limits' to compensate for reduction in spatial frequency of the target, the visual system can resolve finer patterns with the target moving than when the target is static (Kelly, 1985). The limits of velocity are probably imposed by the integration period. According to Burr (1980) target exposures of 30 msec produce more blur than 100 msec exposures. For moving targets, the higher the velocities the shorter the exposure and higher the amount of motion blur expected. However, the amount of blur is less than would be expected based on this model. Burr (1980) considered that the visual system has mechanisms to detect motion, which only act when the exposure time is long enough to trigger these actions (deblurring

mechanism). For brief exposures the mechanisms are not activated and a moving target is perceived as static and blurred due to motion blur.

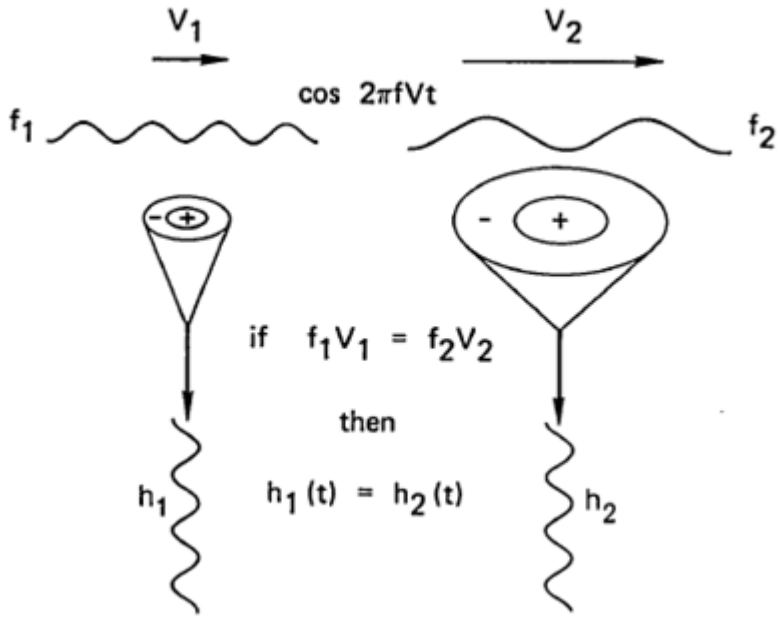

Figure 1.6: Schematic diagram of two receptive fields located at different eccentricities. According to Kelly it is possible to obtain the same temporal output at different eccentricities by inverse scaling of the local velocity and the spatial frequency (Kelly, 1985).

In the peripheral retina, the receptive fields are bigger than in the central retina. According to Kelly's model, resolution should be higher for moving targets. This prediction has been confirmed by several studies (Bex, Dakin & Simmers, 2003, Bex, Edgar & Smith, 1995, Brown, 1972b, Falkenberg, Rubin & Bex, 2007). Resolution would be improved, according to Burr, if the moving target is exposed for long enough to trigger the debluring mechanism and it should be sharper than a static target (Bex, Edgar & Smith, 1995). However, for very high velocities the target will be seen as

blurred. In brief, the peripheral retina has reduced motion sensitivity for moving targets which, within limits, can be seen sharper than static targets (McKee & Nakayama, 1984).

The visual system has a built in mechanism to move the retinal image from one receptive field to another. The fixational eye movements or miniature eye movements (see below) keep the eye moving incessantly during fixation (Barlow, 1952). Different studies have shown that these small displacements of the retinal image are beneficial for central vision (Berry, 1948, Keesey, 1960, Tulunay-Keesey, 1982). Fixational eye movements cause fast changes in illumination on the receptive fields of the visual neurons preventing adaptation (Coppola & Purves, 1996, Ditchburn, 1959, Martinez-Conde, Macknik & Hubel, 2004, Rucci, Iovin, Poletti & Santini, 2007). In other words, fixational eye movements prevent a decline in response of the visual neurons due to the presence of a constant stimulation on the receptive fields of the ganglion cells. In the periphery these miniature eye movements are not enough to prevent image disappearance as demonstrated by Troxler fading, Figure 1.7. Troxler fading consists of the disappearance of the images in the peripheral retina during a steady, prolonged fixation and is due to adaptation of the peripheral visual neurons (Clarke, 1960, Clarke, 1961, Clarke & Belcher, 1962). The occurrence of this phenomenon is consistent with Kelly's model described in the last two paragraphs.

The mechanism responsible for fixational eye movements is still unknown

but recent findings suggest a connection between perception and the generation of fixational eye movements (Engbert & Mergenthaler, 2006, Martinez-Conde, Macknik, Troncoso & Dyar, 2006). Visual information originating in the retina continuously feeds the mechanism controlling the eye movements and is the main source of information for oculomotor control. Section 1.2 describes eye movements and the visual information used to control them.

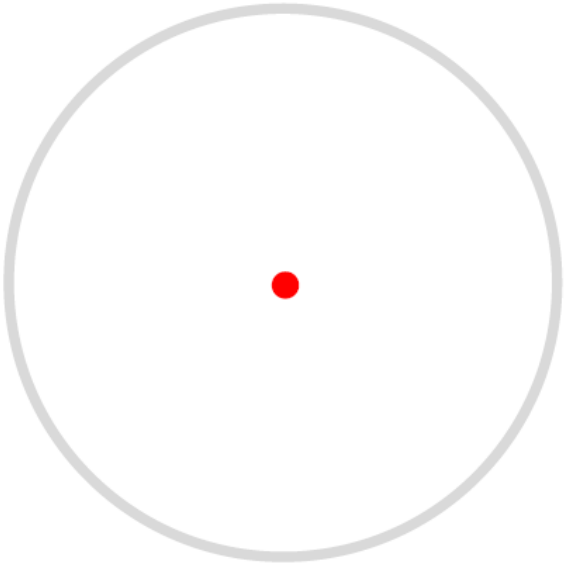

Figure 1.7: Troxler fading phenomenon. During a sustained fixation of the red dot part of the grey circle will fade or disappear. The circle will be perceived again if sustained fixation is interrupted.

1.2 Retinal image stability and eye movements

The eye movements are responsible for stabilizing the image on the retina and for shifting the gaze to the object of interest. The stability of the retinal

image in natural conditions is achieved by interaction between the oculomotor system controlling the eye movements, and other systems. For example, the vestibulo-ocular and optokinetic systems are responsible for the vestibulo-ocular reflex that stabilizes the gaze during head turns (Leigh & Zee, 1999a). A full description of the stabilization process is beyond the scope of this thesis, so only the orienting eye movements will be considered. Orienting eye movements are divided into three types: saccades, smooth pursuit and fixation. The role of these eye movements, together with other systems, is to keep the retinal image stable and aligned with the fovea. In certain eye conditions such as nystagmus the control of eye movements is impaired leading to a significant reduction in vision.

1.2.1 Miniature eye movements

During fixation the fovea is aligned with the object of interest and three types of eye movements occur: tremor, drift and microsaccades. Tremor is an aperiodic wave-like motion with velocities of approximately 20 minarc.s^{-1} and amplitude smaller than the diameter of a foveal cone. Drift movements occur simultaneously with tremor and are larger and slower than tremor, with velocities in the order of 4 minarc.s^{-1} and mean amplitudes of around 2 – 5 minarc. This amplitude corresponds to a movement of the retinal image across a dozen photoreceptors. Fixational microsaccades, also called ‘flicks’ in early studies, are small and fast eye movements that occur during voluntary fixation. Typically with peak velocities above 600 minarc.s^{-1}, their amplitude ranges from 1 to 120

minarc and they carry the retinal image across a width of between several dozen and several hundred photoreceptors (Carpenter, 1988, Martinez-Conde et al., 2004).

1.2.2 Smooth Pursuit

Smooth pursuit is the eye movement which follows moving targets. Approximately 100 msec after a target starts to move, fixation is interrupted by a saccade, which reduces the error between the eye and the target positions accumulated during the latency period. After the saccade the eye moves smoothly in the direction of the target in order to keep it close to the fovea. Visual information is constantly used to guide the eye in the target's direction. The smooth pursuit system is influenced by instantaneous visual information: in other words, it is controlled by a closed loop mechanism (Blohm, 2004, Leigh & Zee, 1999a). The closed loop mechanism uses negative feedback to reduce the relative speed between the eye and the visual stimulus, also called retinal slip. Retinal image slip is considered the main input to smooth pursuit control but positional error and target acceleration also have some influence on smooth pursuit control (Robinson, Gordon & Gordon, 1986).

Smooth pursuit eye movements are slow, with typical velocities below $100^{o}s^{-1}$, and are characterized by gain, the ratio between eye and target velocities. During smooth pursuit the eye acceleration increases to reduce retinal image slip and gain is close to 1. Eye acceleration saturates

between 200ºs^{-2} and 400ºs^{-2} and positional error starts to accumulate. To reduce the error a saccade is generated to maintain the target close to the fovea (Morris & Lisberger, 1987, Segraves & Goldberg, 1994).

1.2.3 Saccades

Saccades are eye movements used to move the direction of the fovea from one visual target to another. Saccades can be made to visual, remembered, tactile, auditory or even imaginary targets. The main input used by the saccadic system to program the amplitude of a saccade is the retinal error (the distance between the retinal location of an image and the fovea) (Leigh & Zee, 1999b).

The saccadic system uses an undershooting strategy whereby the initial saccade covers approximately 90% of the distance towards the target (Becker, 1988, Troost, Weber & Daroff, 1974). The time between the trigger and execution of saccade (latency) is typically under 200 msec (Robinson, 1965). Once started the amplitude of a saccade cannot be modified by visual information. The independence of the visual feedback means they are executed in open-loop. Saccades are the fastest movements of the eye with extremely high acceleration and deceleration (up to 30 000ºs^{-2}) and velocities up to around 500ºs^{-1} (Bahill, Clarke & Stark, 1975).

The fovea is the retinomotor centre, therefore its coordinates play a key role in the planning and execution of eye movements. Macular disease

normally causes fovea destruction and consequently impairs the mechanisms controlling eye movements. Chapter 2 gives an overview of macular disease, implications to visual function and eye movements.

Cortical processes involved in controlling orienting eye movements

The neural control of the orienting eye movements is complex because it requires input from difference sources and computation of information in several areas of the brain. Fundamental input for controlling eye movements originates in the retina. The previous section described how the retina provides essential information about the positional error between the target and the fovea. Visual information is transferred from low visual areas (retina and LGN) to the primary visual cortex (V1) almost without any division. Once visual information reaches the brain it divides to different areas as shown in Figure 1.8.

The neuroanatomical areas associated with the eye movements have been extensively studied in animals, but only a few studies involved healthy humans. A study from Anderson and colleagues in 1994, used PET (positron emission tomography) to study the areas of the brain involved in eye movements control. They monitored the changes in regional cerebral blood flow in humans during two tasks: (1) reflexive saccades and fixation, (2) remembered saccades and fixation. The findings from Anderson's in intact humans were consistent with animal studies. Saccades (reflexive - visually guided) are triggered primarily by the posterior parietal cortex (PPC) and secondarily by frontal eye field (FEF), with inhibition of such saccades by the prefrontal cortex. Single

remembered saccades are thought to be controlled by three successive regions, the PPC (visuospatial integration), dorsolateral prefrontal cortex (memorization and decision) and FEF (triggering) (Anderson, Jenkins, Brooks, Hawken, Frackowiak & Kennard, 1994, Pierrot-Deseilligny, 1991). Anderson's findings also gave evidence that active fixation is mediated by extensive areas of the ventromedial and anterolateral frontal cortex.

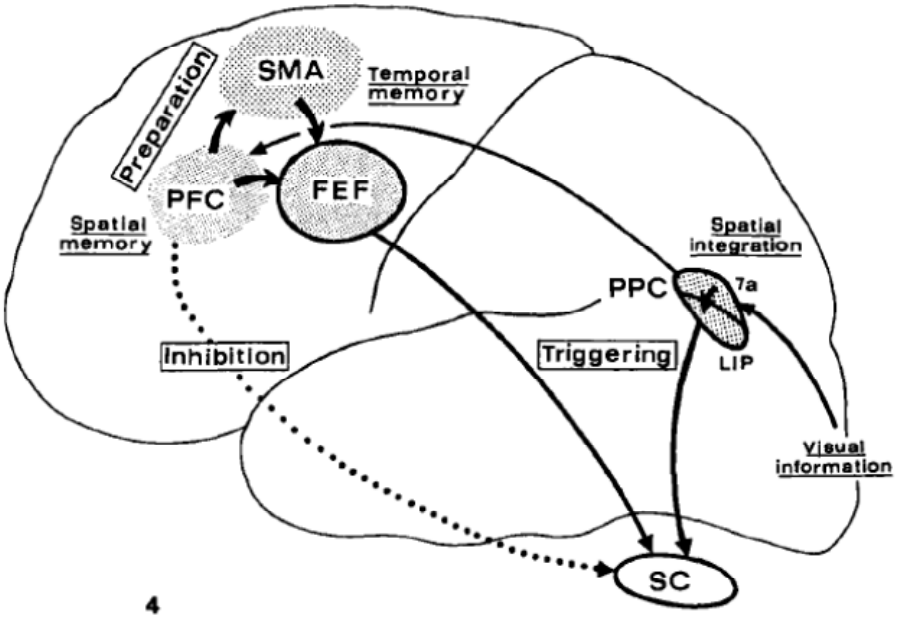

Figure 1.8: Main actions of the different ocular motor cortical areas in saccade initiation, FEF: frontal eye field; LIP: lateral intraparietal area; PFC: prefrontal cortex; PPC: posterior parietal cortex; SC: superior colliculus; SMA: supplementary motor area; 7a: area 7a. Adapted from Pierrot-Deseilligny (Pierrot-Deseilligny, 1991).

The anatomical pathways underlying saccades and fixation, discussed above, are different from the pathways underlying pursuit. However,

saccades and smooth pursuits are synchronized when, for example, following a moving target. Smooth pursuit control includes such cortical regions as the middle temporal area and medial superior temporal sulcus and such subcortical regions as the basilar pons and cerebellum (Ilg, 1997). Some authors speculate that there must be a shared mechanism to target selection for saccades and smooth pursuit (Krauzlis, Basso & Wurtz, 1997). The superior colliculus (SC), a laminated midbrain structure known to be important for the generation of saccadic eye movements, represented in Figure 1.9, is a candidate to be part of the shared mechanism for target selection. The superficial layers of the SC contain visually responsive neurons that form a retinotopic map of visual space, whereas the deeper layers contain saccade-related neurons that form a corresponding motor map. Much importance has been attributed to the SC since the publication of Robinson's classic study in 1972 where he showed that characteristics of the saccade are dependent on the area of the SC actived (Robinson, 1972).

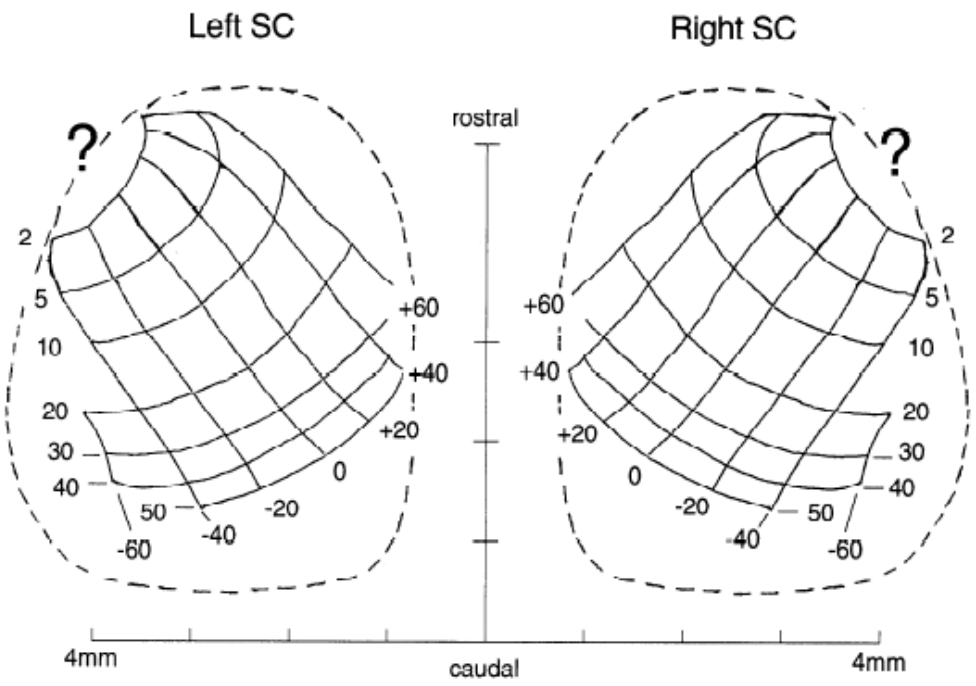

Figure 1.9: Schematic motor map of the intermediate layers of the monkey superior colliculus (SC). Maps of the right and left SC show isodirection lines running from rostrolateral to caudomedial SC (positive numbers represent upward directions, negative represent downward) and isoamplitude lines. The question mark at the rostral pole shows the location of cells with a clear relation to fixation. Adapted from Robinson (1972) by Munoz (Munoz & Wurtz, 1993a, Robinson, 1972).

Particular functions in controlling saccades, such as generating express saccades, have been attributed to the SC. Express saccades are short-latency eye movements (typically below than 200 msec) that form the first mode of a bimodal distribution of saccadic latencies, while the second mode is formed of latencies of regular saccades (typically above 200 msec). If the SC is removed, planned saccades are possible while express saccades are not. Conversely, express saccades are possible without frontal eye fields, but regular saccades are not. Without both structures all

become impossible (Schiller, 1998). If we consider the retinotopic organization of the SC and its role in controlling saccades together, we would expect impaired eye movement control when using the peripheral retina to fixate a “straight ahead target”. As the observer looks at a target with the peripheral retina, the SC plans a saccade to move the fovea to the target. In people with central scotoma, saccades might be planned in the wrong part of the SC, leading to frequent and erratic saccades. Also important is the effect of this structure on controlling steady fixation by inhibition of the saccade system (Munoz & Wurtz, 1993b). The consequences of using the peripheral retina to maintain sustained fixation are discussed in section 2.2.3.3.

Chapter 2. Macular disease

The first part of this chapter describes the most common causes of macular disease and currently available treatments. The second part describes the impact of macular disease on visual function, and the last section describes current rehabilitation tools.

2.1 Causes, types and treatments

Macular disease is the primary cause of legal blindness in the developed world (Friedman, O'Colmain, Munoz, Congdon, Klaver, Klein, Kempen, Taylor, Mitchell & Hyman, 2004). According to its aetiology macular degeneration can be divided into two categories: juvenile (or early onset) macular disease (JMD), and age-related macular degeneration (AMD).

The macula has a high density of photoreceptors that consume more oxygen than any other cell type in the body. Paradoxically, these cells have a restricted blood supply from the retina, depending on oxygen supplied by the choriocapillaris (Linsenmeier & Padnick-Silver, 2000). Choroidal blood flow is independent of metabolism at the photoreceptor level and because of that is

unable to alter blood flow in response to an increase in metabolic demand (Delaey & Van de Voorde, 2000). With aging there is a decrease in the density and volume of the choriocapillaris and a consequential reduction in choroidal blood flow.

2.1.1 Age-related macular degeneration

Characteristics of the macula, such as its high demand of oxygen and restricted blood supply, make it vulnerable to degenerative changes. In the long term, there is accumulation of insoluble substances in Bruch's membrane and in the sub-retinal epithelial space, which then acts as a barrier to the effective diffusion of oxygen and nutrients to the photoreceptors. Oxidative stress and an inflammatory response are the most likely sequelae of such changes, leading, in many cases, to a degenerative process. This degenerative process is known as age-related maculopathy (ARM) which is the precursor to AMD (Neelam, Nolan, Chakravarthy & Beatty, 2009). AMD is subdivided into: neovascular AMD (wet) and geographic atrophy (dry), and is the most prevalent type of macular disease (Bird, 2003, Bjornsson, Syrdalen, Bird, Peto & Kinge, 2006, Jonasson, Arnarsson, Sasaki, Peto, Sasaki & Bird, 2003, Vingerling, Dielemans, Hofman, Grobbee, Hijmering, Kramer & Dejong, 1995).

2.1.2 Treatment of AMD

Treatment options for wet AMD have expanded over the past two decades. Former treatments such as laser photocoagulation proved to be of low benefit in

controlling neovascularisation whilst reducing patients' vision and enlarging the central scotoma (Macular photocoagulation study group, 1991).

The first widely used effective treatment for AMD was photodynamic therapy. This treatment consists of injecting an intravenous infusion of a photosensitive drug (verteporfin). The drug is then activated by a non-thermal light at the wavelength absorbed by the photosensitizer which shrinks neovascularization (Manyak, Russo, Smith & Glatstein, 1988). Photodynamic therapy proved to be relatively efficient in stopping disease progression, but visual acuity rarely improved (Bressler & Bressler, 2000).

More recently, therapies have been developed to control vascular endothelial growth factor (VEGF). VEGF is the principal agent responsible for the development of neovascularisation. Currently available agents include pegaptanib sodium (Macugen; OSI/Eyetech Pharamaceuticals, New York, USA), ranibizumab (Lucentis; Genentech Inc, California, USA) and bevacizumab (Avastin, Genentech Inc, California, USA). These drugs have proved to be safe and effective in slowing down the disease and in some studies improvement of visual acuity has been reported (Rattner & Nathans, 2006, Smith, Joseph & Grand, 2007).

Currently, there is no widely available effective treatment for dry AMD. Extra intake of anti-oxidants may slow the progression of dry AMD (Age-Related-Eye-Disease-Study-Res-Group, 2001, Coleman & Chew, 2007). Surgical treatment such as macular translocation, the shifting of the fovea away from the area of

the choroidal neovascularisation, has been tried in pathological myopia and AMD. Results of this treatment are highly variable with some patients showing little or no improvement (Aisenbrey & Bartz-Schmidt, 2003, Chen, Patel, Uppal, Rubin, Coffey, Aylward & Da Cruz, 2009, MacLaren, Bird, Sathia & Aylward, 2005) and others showing a significant improvement in visual acuity of 3 or more lines (Glacet-Bernard, Benyelles, Dumas, Haddad, Voigt, Razavi, Roquet, Coscas & Soubrane, 2007). These procedures have a significant number of serious post-operative complications such as diplopia, retinal detachment and macular oedema (Chen et al., 2009). Future treatment options for AMD are likely to include gene and stem cell therapy.

2.1.3 Early Onset Macular Degeneration

Macular degeneration of early onset can have a primary genetic cause or can be the consequence of other ocular conditions. Those with a primary genetic cause include: Stargardt disease, photoreceptor dystrophies (Kim & Fishman, 2006, Maia-Lopes, Silva, Silva, Reis, Faria & Castelo-Branco, 2008, Walia & Fishman, 2009), Best disease (Arora, Das, Shroff, Narula & Chauhan, 2007, Goodwin, 2008, Spaide, Noble, Morgan & Freund, 2006, Vedantham & Ramasamy, 2005) and X-linked retinoschisis (George, Yates & Moore, 1995, Pimenides, George, Yates, Bradshaw, Roberts, Moore & Trump, 2005). Of these, Stargardt disease is the most prevalent (Allikmets, Singh, Sun, Shroyer, Hutchinson, Chidambaram, Gerrard, Baird, Stauffer, Peiffer, Rattner, Smallwood, Li, Anderson, Lewis, Nathans, Leppert, Dean & Lupski, 1997, Moradi & Moore, 2007, Sikkink, Biswas, Parry, Stanga & Trump, 2007). Macular

degeneration at a young age can also result from eye disease such as pathological myopia (Glacet-Bernard et al., 2007, Tano, 2002) and punctate inner choriodopathy (Gerstenblith, Thorne, Sobrin, Do, Shah, Foster, Jabs & Nguyen, 2007, Quillen, Davis, Gottlieb, Blodi, Callanan, Chang & Equi, 2004). For simplicity those with any form of early onset macular degeneration will be referred to as having Juvenile Macular Disease (JMD) throughout this thesis.

2.1.4 Treatment for JMD

The aims of treating inherited diseases are: to replace abnormal genes, to prevent progression; to replace dead retinal cells and to restore vision. Treatment for genetic retinal conditions is being tried using genetic therapy in patients with Leber's Congenital Amaurosis (an early-onset, severe retinal dystrophy but not a form of JMD). Studies are evaluating the safety and efficacy of subretinal recombinant adeno-associated virus vector for gene-replacement therapy in patients with RPE65 mutations. Study participants have already been treated in the UK (Al-Karmi & Markowitz, 2006, Bainbridge, Smith, Barker, Robbie, Henderson, Balaggan, Viswanathan, Holder, Stockman, Tyler, Petersen-Jones, Bhattacharya, Thrasher, Fitzke, Carter, Rubin, Moore & Ali, 2008, MacLaren, Pearson, MacNeil, Douglas, Salt, Akimoto, Swaroop, Sowden & Ali, 2006) and the USA (Cideciyan, Hauswirth, Aleman, Kaushal, Schwartz, Boye, Windsor, Conlon, Sumaroka, Roman, Byrne & Jacobson, 2009). Results from the few patients treated are promising, ranging from improvement in visual acuity (Bainbridge et al., 2008) to subjective and microperimetric changes, and self reported improvements (Cideciyan et al., 2009). These procedures remain

at the beginning of their clinical use.

In summary, macular disease can be divided into early onset and age-related form. Wet AMD remains the only form of macular degeneration with effective treatment available.

2.2 Visual function in macular disease

2.2.1 Impact of macular disease on the individual

Macular disease is a very common cause of low vision. The World Health Organization defines a person with low vision as one who has impairment of visual functioning even after full treatment and/or refractive correction but who uses, or is potentially able to use, vision for the planning and/or execution of a task for which vision is essential (Prevention-Blindness, 2010). Visual acuity is typically between 6/18 and light perception, or the visual field is less than 10º from the point of fixation in the better eye. An alternative definition is the one advocated by Dr Gordon Legge in Minnesota who defines low vision as: “The inability to read regular newsprint with optimal refractive correction”. This is better in that it includes a functional statement, but may exclude people who have good reading acuity but are unable to perform other tasks using vision – such as to safely cross a street or to watch television. Leat and colleagues consider low vision as the visual impairment are sufficient to cause a disability and that should be when one or more conditions is satisfied: visual acuity < 6/12; Pelli-Robson contrast less than 1.5 log units; visual field less than 120º

(Leat, Legge & Bullimore, 1999a).

The most common complaint of patients with macular disease is difficulty in reading newsprint and essential correspondence (Dickinson & Fotinakis, 2000, Elliott, TrukoloIlic, Strong, Pace, Plotkin & Bevers, 1997, Farrel, 1991, Faye, 1970, Faye, 1984, Hazel, Petre, Armstrong, Benson & Frost, 2000). Difficulty in reading cannot be fully explained by a reduction in visual acuity as reading is a complex task, requiring significant high and low-level visual resources. Sensory, oculomotor and perceptual deficits of the peripheral visual system (Bedell, 1986, Seiple, Szlyk, McMahon, Pulido & Fishman, 2005) compromising reading are discussed in the next section. Educational and cognitive factors surrounding difficulty in reading are beyond the scope of this thesis and will not be discussed.

2.2.2 Factors affecting reading speed

2.2.2.1 *Sensory deficits: contrast sensitivity and visual acuity*

Contrast

Contrast threshold can be used to predict the optimum print contrast for reading. Contrast reserve (CR) is the ratio between text contrast and threshold contrast sensitivity (Whittaker & Lovie-Kitchin, 1993b). Text contrast of less than 10 times contrast threshold will reduce reading rate and if less than 4 times contrast threshold it will significantly impair reading rate and accuracy (see Table 2.1). Threshold contrast sensitivity rises when the velocity of the visual

target increases (Burr & Ross, 1982), and loss in contrast sensitivity can lead to a reduction in visual span (the number of letters in a line of text that can be recognized reliably during one fixation) and reading speed (Legge, Ahn, Klitz & Lubker, 1997).

Visual acuity

In a study by Legge et al (1985) logMAR visual acuity explained 36% of the variance in reading speed, and Snellen acuity explained 8% of the variance in reading speed (Legge, Pelli, Rubin & Schleske, 1985, Legge, Ross, Isenberg & Lamay, 1992). Legge concluded that visual acuity can predict the best print size but not the reading rate. According to Whittaker & Lovie-Kitchin (1993b) for fluent reading, text must be at least 3× the threshold near visual acuity size: that is, the acuity reserve must be at least 3:1 to read continuous text (Whittaker & Lovie-Kitchin, 1993b). In their results, obtained in a general low vision population, they found that in some cases the optimal character size to read continuous text can be as large as 18× the acuity threshold.

Legge and colleagues developed a new test that assesses reading acuity, reading speed and critical print size, the MNREAD (Legge, Ross, Luebker & Lamay, 1989). Critical print size is the smallest print size which patients can read at their maximum reading speed. This test was used in this thesis to calculate the critical print size. Subramanian's studies provide a detailed discussion of the test results (Subramanian & Pardhan, 2006, Subramanian & Pardhan, 2009).

Table 2.1: Summary of the visual requirements for reading. Visual acuity reserve, contrast reserve and other factors such as the size of the scotoma (eccentricity of fixation) and field of view (Whittaker & Lovie-Kitchin, 1993b).

Visual requirement	**Reading rates words per minute (WPM)**			
	Spot	Fluent	High Fluent	Optimum
	Standard text equivalent			
	40 WPM	80 WPM	160 WPM	
	Observed (6th grade level)			
	44 WPM	88 WPM	174 WPM	
Contrast reserve	3:1	4:1	10:1	>30:1
Field of view (characters)	With scrolled text			
	1	2-5	4-6	4-6
	With stationary text			
	2	5	12	16-20
Acuity reserve	1:1	1.5:1	3:1	6-18:1
Eccentricity of fixation (distance from the fovea)	>15º	<11º	<2º	0º
Scotoma diameter	>30º	22º	4º	none

The effect of scotoma size

The eccentricity of the retina used for reading is normally related to the scotoma size; thus, people with larger scotomas have more difficulties with reading (Chung, 2002, Higgins, Arditi & Knoblauch, 1996, Legge, Mansfield & Chung, 2001). Cummings et al (1985) found that reading speed is inversely proportional to scotoma area. Fixation instability also increases with eccentricity of the target (Sansbury, Skavensk.Aa, Haddad & Steinman, 1973) but it is not clear if it increases with scotoma size (Timberlake, Mainster, Peli, Augliere, Essock & Arend, 1986, White & Bedell, 1990, Whittaker, Budd & Cummings, 1988). It has been established that for eccentricities of fixation of 15º from the fovea,

equivalent to a symmetrical scotoma of 30º, reading is extremely difficult as shown in Figure 2.1 (Whittaker & Lovie-Kitchin, 1993b).

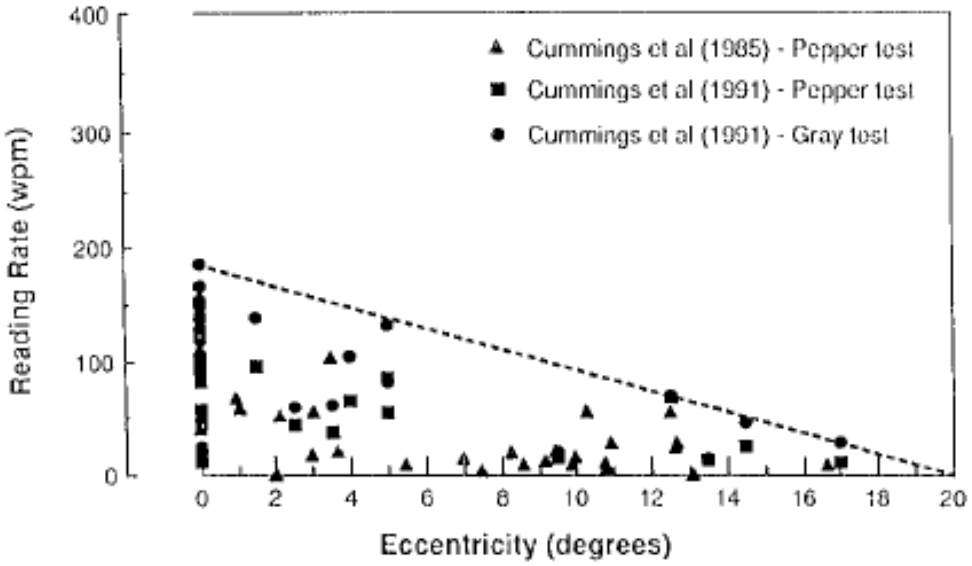

Figure 2.1: The effect of scotoma size on reading speed. Results from Cummings and colleagues plotted by Whittaker (Cummings & Rubin, 1992, Cummings, Whittaker, Watson & Budd, 1985, Whittaker & Lovie-Kitchin, 1993b). The Pepper test measures unconstrained reading of unconnected words. The Gray test measures reading of continuous text. The dashed line represents the upper performance limit that was estimated visually on the basis of the highest recorded performance of individual subjects.

2.2.2.2 *Perceptual deficits*

Perceptual limitations of the peripheral visual system that are known to impose limitations for reading speed are: crowding, slow visual processing and reduced visual span. These limitations that increase with eccentricity may explain why scotoma size is a key variable in predicting reading speed (see Table 2.1).

The effect of crowding

Most visual tasks are crowded and even when the resolution of a single letter is possible it can become impossible if surrounded by other letters. This effect is known as crowding and affects predominantly the peripheral retina (Bouma, 1970, Leat, Li & Epp, 1999b, Levi, 2008). It is known that crowding does not scale with visual acuity in the peripheral retina (Tripathy & Cavanagh, 2002). It is also known that crowding increases when target and flankers have similar shape, attention reduces the effect of crowding (Leat et al., 1999b) and crowding zones are asymmetric (Toet & Levi, 1992). For moving targets the size of the crowding zone varies with target speed (Bex, Dakin & Simmers, 2003).

Crowding predicts that reading with the peripheral retina would be facilitated when letters are more spaced out. However, in the normal peripheral retina, the optimal separation between letters is equivalent to one character (Bernard, Anne-Catherine & Eric, 2007, Chung, 2002). A possible explanation is that the beneficial effect of increasing letter separation would be counteracted by the detrimental effect of declining acuity, contrast sensitivity and visual span. In this thesis I have assessed the effect of fixation instability on crowded and noncrowded acuity to investigate possible interactions between these factors.

The effect of visual span

Visual span is defined as the number of letters in a line of text that can be recognized reliably during one fixation (Legge et al., 1997). Legge found that

visual span reduces when eccentricity increases (Legge et al., 2001). In normal peripheral retina, with low contrast text, or in low vision, reduced visual span imposes a fundamental limitation for reading (Legge, Cheung, Yu, Chung, Lee & Owens, 2007, Levi, 2008). Visual span can reduce by a factor of 10 when contrast changes from 100% to 1.5%. People with low vision usually have reduced visual span even for text at very high contrast and it can reduce to one letter or less in many cases (Legge et al., 1997). Visual span in people with macular disease is more reduced than in normal peripheral retina at the same eccentricity (Cheong, Legge, Lawrence, Cheung & Ruff, 2007, Crossland & Rubin, 2006). This may be due to reduced visual processing speed that has been found in the peripheral retina of people with macular disease (Cheong, Legge, Lawrence, Cheung & Ruff, 2008).

The effect of slow visual processing

The speed of visual processing varies with eccentricity and stimulus features. For stimuli limited by low-level visual mechanisms processing is faster in the periphery than in the centre of the retina. That has been verified with tilt experiments using Gabor patches (Carrasco, McElree, Denisova & Giordano, 2003), with critical frequency for flicker fusion (Raninen, Franssila & Rovamo, 1991, Rovamo & Raninen, 1988), and with pulse detection thresholds (Westheimer, 1983). However, for stimuli such as letters, digits and words which require high-level visual processing, processing is slower in the periphery (Higgins et al., 1996, Seiple, Holopigian, Shnayder & Szlyk, 2001).

Patients with macular disease have slower visual processing than controls.

Cheong et al found slower reading speeds for patients than for controls when reading at the same eccentricity and attributed the findings to slow visual processing and reduced span (Cheong et al., 2007). Reading speed can be affected by temporal and spatial characteristics of the visual span. To capture both these attributes in a single measure, Cheong et al. (2008) defined the rate of information transfer through the visual span as the visual-span size in bits divided by the exposure time in seconds. The later study Cheong found that even with normal visual span patients still having reduced reading speed, with 49% of that reduction being attributed to slow visual processing (Cheong et al., 2008).

It is thought that slower processing and the shrinkage of visual span observed in patients with macular disease can be caused by, among other factors, spread of the disease outside the scotoma area and by poor oculomotor control (Cheong et al., 2007, Cheong et al., 2008).

2.2.2.3 *Oculomotor control*

Oculomotor impairment: saccades

When reading with good vision, forward (left-to-right) saccades are necessary to move along the line of text. The information necessary to guide reading saccades is obtained by the parafovea and extends from 7 to 14 characters to the right of the gaze position (Rayner, Inhoff, Morrison, Slowiaczek & Bertera, 1981). Regressive (right-to-left) saccades occur more frequently in macular

disease than in normal reading (Bullimore & Bailey, 1995, McConkie, Kerr, Reddix & Zola, 1988, Rayner et al., 1981, Rayner, Well & Pollatsek, 1980).

A reduction in reading speed is normally accompanied by a rise in the number of forward (left-to-right) and regressive (right-to-left) saccades (Figure 2.2). Rayner & Bertera found that reading with a mask centred on the macula (equivalent to a central scotoma) covering 7 to 9 characters makes reading impossible (Rayner & Bertera, 1979). In a similar experiment Fine & Rubin (1999) found that when text is scaled to overcome the reduction of acuity in the retinal periphery it is possible to read with a scotoma covering more than 9 characters. This study also showed that the number of letters hidden by the simulated scotoma is more important than the size of the scotoma in degrees (Fine & Rubin, 1999a).

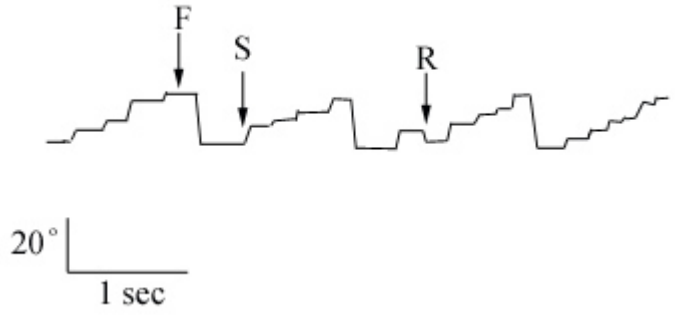

Figure 2.2: Typical eye movements for normal subject during reading text, showing fixations (F), forward saccades (S) and regressive saccades (R). Horizontal axis shows time, vertical axis shows horizontal position on the page. (After Carpenter, (1988) & Crossland (2004))

In people with macular scotoma, reading speed is correlated with the number of

saccades. McMahon et al (1991) found a correlation of 0.79 between reading speed and the number of saccades. Using a different approach, Bullimore et al (1995) also found that reading speed is highly correlated with the number of letters per forward saccade. A more recent study by Rubin & Feely found similar results (Rubin & Feely, 2009).

In normal reading regressive saccades are rare and are thought to be due to difficulties in comprehension or failures in recognition (Reichle, Rayner & Pollatsek, 2003). In the case of people with central scotoma they are more frequent, as it are progressive saccades, and it has been suggested they serve to compensate for reduced visual span (Bullimore & Bailey, 1995, Crossland & Rubin, 2006). Another possible function of saccades observed in patient is to align the PRL with the text (Safran, 1999).

Oculomotor impairment: fixation

Fixation stability, sometimes referred as fixation accuracy, refers to the precision of gaze position during a sustained fixation. A very precise fixation would be a zero deviation from the attended position; however, normally some deviation occurs due to fixational eye movements. Different authors quantified stability by different metrics. For example, Rattle (1969) quantified fixation stability with the root mean square of the angular deviation of the eye (Rattle, 1969) and Sansbury (1973) used the bivariate contour ellipse (area), also known as BCEA, expressed in minarc^2. BCEA corresponds to the solid angle subtended at the eye by an ellipse projected on the plane parallel to Listing's plane (Sansbury et al., 1973). It became one of the most popular methods of

quantifying fixation stability in people with macular disease (Crossland, 2011) and in normal vision as well (Epelboim & Kowler, 1993). Table 2.2 shows values of fixation stability in normally sighted subjects quantified by BCEA and standard deviations on the horizontal and vertical meridians during fixation for seven different targets. This study gives an example of some of the factors that can cause variability in fixation stability: type of target, eccentricity of target or no fixation target. Also important to consider when analysing fixation stability is the technique used to monitor the eye movements. For example, results from infrared eye trackers produce higher instability than retinal imaging devices such as the scanning laser ophthalmoscope (Crossland & Rubin, 2002).

Table 2.2: Fixation stability of two subjects (AS and RS) summarized by bivariate-contour-ellipse areas (BCEA in minarc^2) and standard deviations, in minarc, on the horizontal (H) and vertical (V) meridians during fixation for seven target arrays. Modified from Sansbury et al. (1973).

Target array	**AS**			**RS**		
	H	**V**	**BCEA**	**H**	**V**	**BCEA**
Centred 1.3º -diameter disk	3.5	7.4	174	3.4	7.5	182
H & V disks, separated 10º	13.3	11.3	1087	8.0	13.8	788
H & V disks, separated 21.8º	11.2	14.8	1142	11.7	17.2	1332
H & V disks, separated 29.5º	16.1	19.5	2060	15.2	23.6	2406
H disks, separated 21.8º	34.4	19.6	3601	14.4	16.7	1676
V disks, separated 21.8º	9.8	12.1	851	12.6	23.7	2134
Complete darkness	30.5	26.1	5591	41.3	28.9	8262

Fixation instability is a common finding in people with macular scotoma which might have a detrimental effect on visual function (Crossland, Culham & Rubin, 2004a, Culham, Fitzke, Timberlake & Marshall, 1993, Schuchard, 2005, Timberlake et al., 1986). Position error caused by fixation instability might also trigger excessive corrective saccades during detailed visual tasks (Whittaker et

al., 1988). In a recent study Crossland et al (2004) measured reading speed in people with macular disease and found that people with good fixation stability can read faster than people with the same acuity but with poor fixation. That suggests a detrimental effect of fixation instability on visual performance.

Stable gaze can be maintained exclusively with drift. Saccades are considered unnecessary. This mechanism is known as slow control (Steinman, Cunitz, Timberlake & Herman, 1967). It is accepted that fixating with the peripheral retina impairs slow control, leading to increased fixation instability (Epelboim & Kowler, 1993). Fixation instability, in the case of people with macular disease, results from increased drift speed and amplitude, and from excessive and imprecise fixational (micro)saccades. Saccades normally correct positional errors caused by large drift that take the eye away from the target. In people with MD saccades are more imprecise; therefore spatial uncertainty of the landing positions increases and contributes to the overall fixation instability (McMahon, Hansen, Stelmack, Oliver & Viana, 1993). Figure 2.3 shows the recording of fixational eye movements in a subject with a macular scotoma. Drifts are followed by saccades to correct eye position (Whittaker et al., 1988).

Increased drift speed and amplitude may be due to a mixture of factors such as: ineffectiveness of the (micro)saccades system, ineffectiveness of the smooth pursuit velocity-correcting system, and/or normal drift characteristics for nonfoveal fixation (Martinez-Conde & S. Martinez-Conde, 2006). Timberlake et al. speculated that macular disease might impair visual function, e.g. velocity discrimination, in the peripheral as well as central retina, leading to slow control

impairment (Timberlake et al., 1986). Heinen, studied the effect of macular scotoma in fixation stability in monkeys and speculated whether increased drift speed would be required for optimal visibility (Heinen & Skavenski, 1992). Additionally, Whittaker et al. suggested that increased drift speed in simulated and pathological scotomas could be caused by the eccentric position of the eye in the orbit plus the fact that the target is the peripheral retina (Whittaker et al., 1988). It is probable that a combination of these factors lead to impaired oculomotor control in people with macular disease.

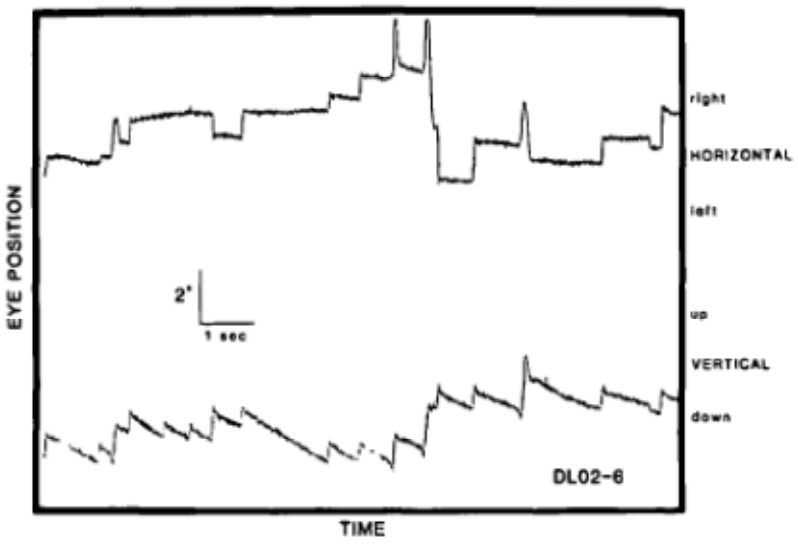

Figure 2.3: Stripchart recording of horizontal and vertical eye positions over a 12s period in a subject with macular disease. The scotoma was above the target, thus a down drift would move the target into the scotoma. The upward saccades directed the target image to functioning retina. Adapted from Whittaker et al. (1988).

Control of fixation by higher cortical areas

Electrophysiological studies have provided evidence that fixation and smooth pursuit activate cells of the rostral pole of the superior colliculus. Here I describe findings relevant to this thesis, see Leigh for a full description of this topic (Leigh & Zee, 1999c). In 1993, Munoz et al. showed in monkeys and cats that a group of cells located in the rostral pole of the SC corresponding to the foveal and parafoveal areas that are responsible for controlling fixation (Munoz & Wurtz, 1993a, Munoz & Wurtz, 1993b). Cells corresponding to the fovea and perifovea increase their firing during fixation and reduce firing during saccades. The authors designated these cells, “fixation cells”. To prove the fixation cell hypothesis Munoz et al. showed that when fixation cells were artificially activated, the monkey was unable to initiate saccades. Conversely, when these cells were inhibited, the monkey exhibited saccades with very low latency, similar to express saccades. Also, the monkey was unable to suppress unwanted intrusive saccades (Munoz & Wurtz, 1993a, Munoz & Wurtz, 1993b). The authors concluded that this group of cells in the rostral pole of the SC were responsible for controlling fixation and for preventing unwanted saccades. Interestingly, fixation cells indentified by Munoz et al. also fired during smooth pursuit.

The idea that the function of fixation cells is exclusively fixation control, as proposed by Munoz and colleagues in 1993, was challenged a few years later. Krauzlis and colleagues recorded the activity of fixational neurons in the rostral SC whilst a monkey fixated a target that was unexpectedly displaced in a stepped manner to an eccentric position (Krauzlis et al., 1997). Such steps

caused changes in the firing rate that began 50 to 70 ms after the target was displaced and often resulted in small corrective saccades. This change in firing rate suggests a mismatch between the eye and target positions, defined as motor error, in a similar fashion to rest of the motor map of the SC associated with saccade control. To add evidence, they recorded the firing rate of fixation cells during pursuit. The firing rate during pursuit displayed a dependence on motor error that was not different from that observed with small target steps imposed during fixation. The authors concluded that neurons in the rostral pole of the SC might encode a more general form of motor error rather than commands for maintaining fixation. According to these findings, involuntary fixational microsaccades and voluntary saccades would have the same purpose (reduce motor error) similar triggering mechanisms. Krauzlis's hypothesis has been reinforced by Hafed and colleagues (Hafed, Goffart & Krauzlis, 2009). Hafed described a model assuming that the rostral pole of the SC is directly involved in the generation of microsaccades during fixation and, as Krauzlis hypothesized, microsaccades during fixation share neural mechanisms with voluntary saccades. A piece of evidence for this hypothesis are the findings by Steinman et al. in the seventies that microsaccades, as voluntary saccades, can be suppressed (Steinman et al., 1967).

Findings arriving from basic eye movement research need to be considered when studying the consequences of macular disease on oculomotor control. As studies above shown, increased motor error in the rostral pole of the SC or reduction in neural activity in this part of the SC would lead to an increased difficulty to control fixation and increased number of unnecessary saccades.

This is likely to be part of the explanation for the impaired fixation control and excessive saccades that can be found in people with macular disease (McMahon, Hansen & Viana, 1991). Further discussion on fixation and oculomotor control can be found in Chapter 3. Figure 2.4 summarizes the factors discussed in the sections above that contribute to the poor visual performance of the peripheral retina and the way these factors interact.

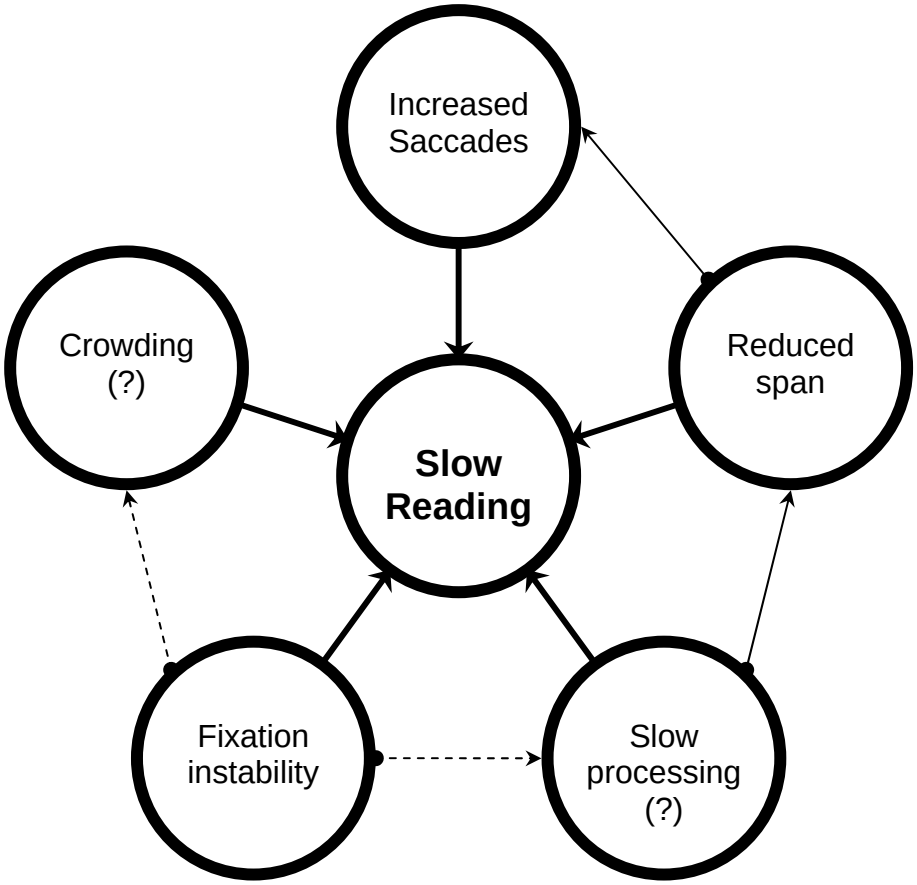

Figure 2.4: Perceptual and oculomotor characteristics of the peripheral visual system that contribute to reduced reading speed in patients with macular disease. The dashed lines show hypothesis that are not fully proven.

In summary, visual function in general and reading in particular is reduced in people with macular scotoma. Apart from the inevitable sensory deficits, imposed by the physiology of the peripheral retina, perceptual and oculomotor factors can, independently or together, contribute to further reduction of visual function.

2.2.3 Eccentric viewing and the preferred retinal locus

Eccentric viewing is a technique used to look at targets using the peripheral retina (Timberlake, Peli, Essock & Augliere, 1987). When looking at a face, for example, people with macular disease may direct their gaze slightly away from it in order to see the facial contours; otherwise, they would be hidden by the central scotoma. In the vast majority of cases, a certain area of the peripheral retina is used more often than others. This area is known as the preferred retinal locus (PRL) (Timberlake et al., 1986, Timberlake et al., 1987, Whittaker et al., 1988). The PRL of a patient with macular scotoma is shown in Figure 2.5**.**

Eccentric viewing is a technique which can develop spontaneously or with formal training. The technique normally improves during adaptation to the disease either by training or simply by practice (Crossland, Culham, Kabanarou & Rubin, 2005). Studies using animals with bilateral lesions showed that they adopted eccentric viewing after one day post-lesion and improved fixation stability after two days (Heinen & Skavenski, 1992). Humans with newly developed macular disease can adopt eccentric viewing in approximately 6 months, without formal training (Crossland et al., 2005).

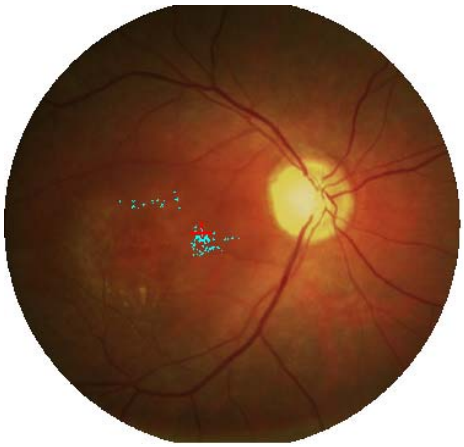

Figure 2.5: Preferred retinal locus in a patient with JMD characterized using the microperimeter MP1 (the technique is described in detail in section 4.4). The patient was fixating a red cross whilst the retinal sensitivity was tested, the blue dots show fixation positions. The dark area, left of the cross, corresponds to the damaged macula.

The preferred retinal locus can be located in different positions relative to the damaged macula. If the macular scotoma was perfectly symmetrical around the damaged macula the theoretically ideal location to develop a PRL would be in the lower visual field, due to physiological and ecological advantages (Previc, 1990). Positioning the PRL in the lower visual field (using superior retina), would be advantageous because the upper retina has a higher density of photoreceptors, the lower field is mostly used for locomotion (Anderson et al., 1991) and has higher attentional resolution (He, Cavanagh & Intriligator, 1996). Further, important visual information for programming the horizontal eye movements would never be hidden by the scotoma or the physiological blind spot at the optic nerve head (Rayner et al., 1980, Rayner, Well, Pollatsek & Bertera, 1982).

2.2.3.1 *PRL location and reading*

People do not always adopt the theoretically most favourable PRL position. A number of studies have shown that the PRL can be in any location relative to the macula. In approximately 3/4 of the cases the PRL is located at the left or below the scotoma, with higher predominance to the left than below (Crossland et al., 2005, Culham et al., 1993, Fletcher & Schuchard, 1997, Fletcher, Schuchard, Walker, Wing & Raskauskas, 2001, Guez, Legargasson, Rigaudiere & Oregan, 1993, Nilsson, Frennesson & Nilsson, 1998, White & Bedell, 1990).

Reading speed is independent of the location of the preferred retinal locus. Two separate studies using a significant number of subjects (Fletcher et al (1999), 99 participants and Crossland et al (2005), 25 participants) failed to find correlation between the PRL quadrant and reading speed (Crossland et al., 2005, Fletcher, Schuchard & Watson, 1999). A similar result has been found by Rubin & Feely (2009). That might be because patients use a PRL for reading which is different from the PRL they use to fixate a single target. When the PRL is defined by using small stimuli such as crosses or single letters they are normally adjacent to the scotoma boundary or even within the lesion (Cummings et al., 1985, Guez et al., 1993). In visual tasks such as reading a PRL away from the scotoma boundary has the disadvantage of poorer resolution than that adjacent to the scotoma. However, this disadvantage would be suppressed by the benefit of avoiding characters being hidden by the scotoma, allowing information essential for reading to be seen (Duret, Issenhuth & Safran, 1999, Fine & Rubin, 1999b).

2.2.3.2 *Eccentric viewing and binocularity*

Visual performance is normally better with both eyes than with the better-seeing eye, due to a phenomenon known as binocular summation. Binocular inhibition occurs when binocular visual function is worse than with the better eye alone. When both eyes have similar vision (i.e., inter-ocular difference of 1.0 ETDRS line or less) binocularity normally causes summation (Rubin, Munoz, Bandeen-Roche & West, 2000). Measurements with neutral density filters inducing unequal monocular contrast sensitivity have shown that summation, which happens when both eyes have similar contrast, switches to inhibition when the difference between the eyes increases. Inhibition starts when the contrast difference between eyes is 0.7 log units and is maximal when the difference is 1.5-2.0 log units (Pardhan, Gilchrist, Douthwaite & Yap, 1990).

People with binocular MD normally have significant inter-ocular differences in acuity and contrast and that might cause binocular inhibition instead of summation. Some studies, measuring contrast sensitivity, found evidence of binocular inhibition when compared with monocular viewing (Faubert & Overbury, 2000, Valberg & Fosse, 2002). More recently, a study by Tarita-Nistor assessed visual acuity at different contrast levels. This study showed that there is a slight advantage of binocular vision for visual acuity. Results from this study also showed that the outcome can be affected by many factors such as unequal scotomas in both eyes, loss of fixation or asymmetrical PRLs (Tarita-Nistor, Gonzalez, Markowitz & Steinbach, 2006a).

The existence of asymmetrical scotomas and acuities might lead to changes in eye dominance in bilateral macular disease. Kabanarou et al (2006) found that most patients shift gaze position in one or both eyes when viewing binocularly compared with monocularly (Kabanarou, Crossland, Bellmann, Rees, Culham & Rubin, 2006). Tarita-Nistor found that patients with MD spend less time using the input of the worse eye than a group of control subjects (Tarita-Nistor et al., 2006a, Tarita-Nistor, Gonzalez, Markowitz & Steinbach, 2006b). In terms of visual function, Kabanarou found no significant differences between monocular and binocular reading speeds (Kabanarou & Rubin, 2006). In line with Tarita-Nistor's results, Kabanarou found that the binocular PRL position is driven by the better eye.

In summary, macular disease induces changes in binocular vision that vary according to individual factors. Studies showed that binocular visual function is mostly determined by the better-seeing eye. Experiments in this thesis were conducted using the better eye. I speculate that the results would be very similar if experiments were conducted binocularly.

2.2.3.3 *PRL location and non-visual factors*

Non-visual factors such as sustained attention influence PRL location. Altpeter et al tested the effect of sustained attention in visual performance in the four quadrants and found better attentional performance in the horizontal meridian than in the vertical meridian either for patients and controls (Altpeter, 2000). Patients in this study were tested in the better eye, with central fixation, for

attention and the poorer eye was tested to define the PRL location using the SLO. They found that the quadrant of the PRL in the poorer eye corresponds to the quadrant with better attentional performance in the good eye (Altpeter, 2000). This and other studies gave evidence that PRL location is correlated with the pre-disease attentional capabilities of the patient (MacKeben, 2009).

2.2.3.4 *The use of multiple PRLs (mPRL)*

In some cases it has been found that patients can have multiple PRLs. For example, it has been found that the used PRL can change according to: illumination (Lei & Schuchard, 1997), size of the target (Guez et al., 1993) and task (Duret et al., 1999). It has been proposed that this is due to an automatic mechanism which aims to maximize patients' vision. Accordingly, if a PRL has the best visual acuity but is too small to accommodate the target, patients may automatically select another healthy retinal area where the entire target can be visualized (Deruaz, Whatham, Mermoud & Safran, 2002, Duret et al., 1999, Fine & Rubin, 1999b).

Multiple PRLs can also be caused by poor adaptation to the disease. With newly developed macular disease fixation control is difficult. The eye alternates between retinal locations stopping when the visual target falls on a healthy area of the retina (Reinhard, Messias, Dietz, MacKeben, Lakmann, Scholl, Apfelstedt-Sylla, Weber, Seeliger, Zrenner & Trauzettel-Klosinski, 2007). It is expected that with longer adaptation, practice, or training, only one PRL would develop. This hypothesis is supported by previous results, in a longitudinal

study Crossland et al (2005) observed the development of the PRL(s) in a group of patients with central scotomas caused by recent onset MD. The number of patients with multiple PRLs reduced from 67% at the baseline to 44% at the end of the study, 12 months after they enrolled.

In summary, a preferred retinal locus usually develops spontaneously in a period of approximately 6 months. Some patients can have more than one PRL and may alternate between PRLs depending on the task and viewing conditions. PRL location is normally in the area of best visual acuity but this is not always in the most favourable, for example, to control the eye movements during reading.

2.3 Rehabilitation in macular disease

The use of low vision devices aims to compensate for sensory deficits of the peripheral visual system while training can be used for re-education of the visual system and better use of low vision devices.

2.3.1 Magnification and light modulation

Magnification compensates for poor resolution and allows to some extent periods of accurate reading producing significant subjective satisfaction in patients (Beckmann & Legge, 1996, Margrain, 2000, Scott, Smiddy, Schiffman, Feuer & Pappas, 1999, Temel & Kazokoglu, 1991). Fluent reading with high magnification is rarely achieved because page navigation is more difficult with

large text and the number of visible characters that can be seen in one fixation is reduced (Dickinson, 1998, Elliott et al., 1997, Faye, 1970, Faye, 1984, Hazel et al., 2000).

There are four main techniques to increase the size of the retinal image (Dickinson, 1998, Wolffsohn, 2007). Relative size magnification involves increasing the size of the object while the working distance is kept constant. Relative distance magnification is the reduction in the object viewing distance (Crossland & Silver, 2005, Margrain, 2000). Angular magnification increases the angle subtense by the object at the eye by viewing through telescopic optical systems (Lowe & Rubinstein, 2000). Finally projection magnification is achieved by projecting or electronically increasing the size of the object. Adequate illumination is also helpful either alone or when combined with magnification (Bowers, Meek & Stewart, 2001, Bullimore & Bailey, 1995).

In summary, light modulation and magnification are commonly prescribed and are of benefit in compensating for sensory deficits in patients with macular disease. In most cases minimal training is necessary to teach people how to use these devices. Other aims of training include re-education of the visual system to compensate for oculomotor deficits or increasing awareness of the PRL.

2.3.2 Training

Reports of training programs for people with macular disease started around 1960. Training aims to teach patients eccentric viewing, which can be achieved by increasing awareness of the PRL to improve gaze control. Evidence that training might be necessary for optimal use of low vision aids and residual vision has been given by better visual performance in people who receive training, compared with those who did not, despite presenting with similar clinical measures (Goodlaw, 1968, Goodrich & Mehr, 1986, Goodrich & Quillman, 1977, Inde, 1978). Prism relocation to redirect the image to the PRL has also been considered. However, results from different studies showed modest or no improvement in visual function with prism therapy (Al-Karmi & Markowitz, 2006, Verezen, VolkerDieben & Hoyng, 1996). A recent randomised control trial provided unequivocal evidence that prism relocation is no more effective than placebo (Smith, Dickinson, Cacho, Reeves & Harper, 2005).

A PRL can be trained in a specific retinal location with the SLO. Timberlake et al (1987) measured reading speed in the adopted PRL and in the “trained PRL” (below the scotoma) and suggested that training a better PRL location might improve reading. This small study, of only 3 patients, was extended by Culham et al (1997). Culham failed to show any effect of training on reading speed (Culham, Fitzke & Marshall, 1996, Culham et al., 1993). In contrast, others have reported dramatic improvements after training (Nilsson et al., 1998, Nilsson, Frennesson & Nilsson, 2003). These contrasting results are probably due to limitations in Nilsson’s studies design which are discussed below.

Training eye movements, such as saccades, is also seen as a way to improve eccentric viewing. In a study involving 12 individuals trained over six weeks, McMahon et al (1993) found mixed results with modest improvements in some but no improvement in other participants. Recently Seiple et al (2005) trained eye movements in patients with MD through a series of exercises. The result was a small but significant improvement in reading speed of 25 words per minute, corresponding to approximately 27.5% of the initial reading speed. The authors suggested that their method of training eye movements could be more efficient than direct reading training.

Visually guided training can be also performed using instruments such as the scanning laser ophthalmoscope (SLO) (Culham et al., 1996, Culham, Fitzke, Timberlake & Marshall, 1992, Culham et al., 1993, Duret et al., 1999, Nilsson et al., 2003, Timberlake et al., 1986, Timberlake et al., 1987). Culham trained patients for six weeks using an SLO leading to an improvement in visual acuity and fixation stability but not reading speed (Culham, Fitzke & Marshall, 1997). Thus, according to Culham's results, training improvements were due to psychological benefits associated with training and the acquisition and perfection of new visual strategies. Very different results were obtained by Nilsson et al (2003) more recently. Nilsson trained a total of 18 patients of which 12 learned how to use a trained PRL and increased reading speed from about 9 wpm to 68 wpm. The remarkable improvement achieved in Nilsson's study is confounded by many factors: for example, magnification was provided simultaneously with training and there was no control group.

Biofeedback training in patients with macular disease has been tried in the past but not pursued until recently (Zeevi, Peli & Stark, 1979). Biofeedback training is based on the principle that when the patient listens to an auditory signal he/she needs to do a certain task. A study in 2002 using an instrument called improved biofeedback integrated system (IBIS) reported improvements in fixation stability, visual acuity and contrast sensitivity, after training (Contestabile, Recupero, Palladino, De Stefanis, Abdolrahimzadeh, Suppressa & Gabrieli, 2002). More recently Vingolo et al (2008) trained patients with the MP1 using biofeedback and also reported improvement in visual function. The authors considered that, during training a “retina motor” PRL was effectively trained and that produced improvements in retinal sensitivity, fixation and saccades. They considered that the feedback sound increases attention, causing the individual to consciously search for the target leading to an effective “lock-in” of the visual target with the PRL. The ultimate consequence of this type of training would be neural changes with remapping of the visual function (Vingolo, Salvatore & Cavarretta, 2009).

In summary, training aims to increase the ability to use a PRL or the best PRL and to achieve better control of eye movements. Better eye movement control would reduce retinal image motion and lead to an improvement in visual performance. The results from past studies are not consistent: more research is necessary to define what training is really effective in improving visual function.

Chapter 3. Oculomotor control and vision

During fixation the oculomotor system maintains foveal alignment with the target by minimizing the visual error signal. Macular disease can cause a shift of fixation control to the peripheral retina due to the foveal damage. The implications for the oculomotor system are discussed here.

When the visual target falls on the peripheral retina it generates an error signal that changes the pattern of eye movements and increases fixation instability. It is thought that fixation instability can be associated with increases of the size of both drift and (micro)saccades (Bedell, Barbeito & Aitsebaomo, 1984, Sansbury et al., 1973). Sansbury et al. suggested that the quality of visual and proprioceptive signals may cause changes in the ratio of saccades.

The effects of macular damage in oculomotor control have been studied in animals. Heinen & Skavenski studied eye movements in monkeys with induced macular scotomas. They damaged the macula of three monkeys with a red krypton laser and monitored their adaptation to the use of

peripheral retina (Heinen & Skavenski, 1992). The size of the lesions was 3 degrees of visual field. All three animals adopted eccentric PRLs and fixation stability increased, returning to almost normal levels in 2 days. Full control of saccades, the function of which is to direct the fovea to the visual target, was never achieved and the level of control varied from animal to animal. One of the animals always failed to reach the target with the PRL and needed saccades to correct the PRL position (Heinen & Skavenski, 1992). These animals with a sudden and small lesion of the macula developed eccentric fixation without extra training in a short period of time, but the eye movements never recovered their original performance.

There are reports of accidental damage to the macula in humans with similar consequences for fixation (Sakaguchi, Ohji, Kubota, Otori, Hayashi, Kusaka, Saito & Tano, 2000, Zwick, Ness, Molchany, Stuck & Loveday, 1997, Zwick, Ness, Molchany, Stuck & Loveday, 1998). Adaptations to macular lesions caused by laser burns give valuable information about the consequences of macular damage. However, unlike macular disease, these lesions are not progressive, are normally small and are not scattered in the retina. Therefore, adaptation to accidental macular damage is not the ideal model to predict adaptation to macular disease.

Many studies used simulated scotomas to predict adaptation to macular disease (Bernard et al., 2007, Cornelissen, 2005, Cummings & Rubin, 1992, Fine & Rubin, 1999a, Fine & Rubin, 1999b, Fornos, Sommerhalder, Rappaz, Pelizzone & Safran, 2006, Petre, Hazel, Fine & Rubin, 2000,

Varsori, Perez-Fornos, Safran & Whatham, 2004). Results produced by studies with simulated scotoma might be different from those produced by pathological scotoma. For example, fixation stability in people with real scotoma is better than in people with equivalent simulated scotoma (Culham et al., 1993, Sansbury et al., 1973, Timberlake et al., 1986, Timberlake et al., 1987). This shows that real scotomas need always to be studied and also suggests that there is a learning process which improves fixation control in people with pathological scotomas (McMahon et al., 1991) and reinforces the importance of studying real scotomas rather than simulations.

Improvement in fixation stability is possible either with or without training. Better fixation stability has been a common finding from various training studies and has been associated with improvement in visual performance (Culham et al., 1997, Stelmack, Robert & Stelmack, 2004, Vingolo et al., 2009). According to these studies, training increases awareness of the scotoma/PRL and allows effective use of the PRL in the peripheral retina leading to reduction in oculomotor instability. Spontaneous improvement is also possible, in a longitudinal study Crossland (2005) found that patients with newly diagnosed macular degeneration can adopt a stable PRL for eccentric viewing in 6 months with corresponding improvements in fixation stability.

Even after long term adaptation to the disease and/or training, saccade control without a fovea remains difficult. Non-foveating saccades have

longer latencies, lower peak velocities and less precision than foveating saccades of same amplitude (Whittaker & Cummings, 1990, Whittaker, Cummings & Swieson, 1991, Zeevi & Peli, 1979). Whittaker et al (1991) suggested that people with macular disease must suppress the foveating saccade mechanism and depend on non-foveating saccades for saccade control. Given the reflexive nature and the limited plasticity of the foveating saccades, people with central scotoma should have a residual tendency to produce foveating saccades (Whittaker et al., 1991). Thus, the ability make non-foveating eye movements is essential to achieve good performance during eccentric viewing.

Other adaptive changes which have been reported include patients describing themselves as looking straight ahead while using a peripheral PRL (White & Bedell, 1990). It was considered that these patients re-referenced their oculomotor system to the PRL. In this study seven patients re-referenced their oculomotor system; however, only 1 out of 7 had AMD, the remaining had JMD (White & Bedell, 1990). Crossland and colleagues followed a cohort of 25 patients (20 with AMD and 5 with JMD). At the 12-month follow-up visit the awareness of using peripheral retina was assessed. Eleven of the AMD and all 5 JMD patients lost awareness of using a PRL. People with juvenile macular disease seem to have faster and more efficient changes in the oculomotor system than AMD patients. This might be explained by the superior plasticity of the oculomotor system in young patients.

Although an almost total re-reference of the oculomotor system would seem possible, based on patients' reports, objective assessments show that is uncommon. For example, some people with long standing disease use multiple PRLs. With a permanent "re-referencing" of the visual system patients should use one not multiple PRLs (Bellmann, Feely, Crossland, Kabanarou & Rubin, 2004, Deruaz et al., 2002, Duret et al., 1999, Whittaker et al., 1988). A recent study using fMRI evaluated cortical networks that underlie oculomotor control during saccades and smooth-pursuit in patients with AMD (Little, Thulborn & Szlyk, 2008). This study showed that patients generally showed increased prefrontal cortex and intraparietal sulci activation, with decreased activation in visual cortex compared with the control subjects. The author concluded that eye movements in patients with AMD required greater involvement of the cortical regions generally implicated in attention and effort.

In summary, people with macular disease exhibit difficulty in controlling saccades and fixation. These changes need to be considered when explaining the reduction in visual function.

3.1 Saccade control in macular disease

People with macular disease use an increased number of saccades when reading (Bullimore & Bailey, 1995, Crossland & Rubin, 2006). This has also been shown for control subjects reading with a simulated scotoma (Fine & Rubin, 1999b, Fornos et al., 2006, Rayner & Bertera, 1979,

Sommerhalder, Rappaz, de Haller, Fornos, Safran & Pelizzone, 2004). This increase is likely to compensate, for example, for the smaller visual span in people with central scotomas (Bullimore & Bailey, 1995, Crossland & Rubin, 2006). The cost of extra saccades is a reduction in reading speed (Bullimore & Bailey, 1995, Crossland & Rubin, 2006, McMahon et al., 1991).

Saccades are rare during fixation of eccentric targets (Sansbury et al., 1973, Zeevi et al., 1979); however, for tasks such as reading with a PRL corrective saccades would be expected. Corrective saccades compensate for fixation selection deficits, caused by the poor definition of the peripheral retina, and for saccades inaccuracy, caused by the spatial error due to the lack of fovea (section 1.2.3).

Impaired saccade control is considered the main oculomotor limitation for reading continuous text in people with central scotoma (McMahon et al., 1993). Evidence that saccades impose an important limitation came from studies using words presented sequentially, which reduces the need for saccades. This method is called rapid serial visual presentation (RSVP) (Forster, 1970). Rubin & Turano (1994) found that people with macular disease read RSVP faster than continuous text but points out that, due to their reduced visual span patients may need saccades during reading RSVP. The authors reported that reading speed fell as the number of intra-word saccades increased (Rubin & Turano, 1994). In the same study reading improved more in control subjects using peripheral retina than in

patients. The authors conclude that poor saccade control was responsible for a substantial fraction, but not all, of the reduction in reading.

If intra-word saccades are a significant limitation on fast reading, scrolled text (which reduces the need for intra-word saccades) should improve reading more than RSVP. Fine & Peli (1995) compared reading speed for RSVP and scrolling text in patients with central scotoma and found no gain between scrolling text over RSVP (Fine & Peli, 1995). When reading from scrolling display optokinetic nystagmus (OKN) is elicited to maintain fixation on a single point. The fast phase of OKN behaves like a saccade; however, unlike a saccade in normal reading, the fast phase of OKN does not require high levels of saccade control (Whittaker & Lovie-Kitchin, 1993a). Recently, Valsecchi and colleagues (2011), reported that reading scrolled text is performed with a combination of smooth tracking movements and fast saccadic movements, not exactly OKN (Valsechi, Schutz & Gegenfurtner, 2011). In any case eye movements would be reflexive, reducing cognitive demand for control and facilitating reading in patients with macular disease. Fine & Peli (1998) compared again RSVP and scrolling text reading and concluded that RSVP can be read faster than scrolling text as long as the text size is 6× or more the acuity reserve. Other studies failed to find any differences in reading speed produced by scrolling, RSVP and continuous text (Bowers, Woods & Peli, 2004, Harland, Legge & Luebker, 1998). It is still unclear if any alternative text format that minimizes saccades brings advantages compared with continuous text for readers with low vision and central scotoma.

Saccades are necessary to align the preferred retinal locus with the target (McMahon et al., 1993, McMahon et al., 1991). Saccades are also needed to select the “best” PRL and to alternate between PRLs (Bullimore & Bailey, 1995, Deruaz et al., 2002, Guez et al., 1993, Safran, 1999). The benefits of alternating PRLs using saccades during the execution of the same visual task, such as word recognition, are debatable. Signals coming from the retina are suppressed every time a saccadic eye movement is performed and that starts about 75 msec before the onset of the saccade (Vallines & Greenlee, 2006). Alternating between PRLs is therefore likely to reduce vision because it requires saccade programming and suppression. Both are likely to reduce visual input (Burr, Morrone & Ross, 1994). Thus, the use of different PRLs for different tasks is more likely to have benefits for patients.

In summary, more saccades are used by people with macular disease. These extra saccades compensate for reduced visual span and align the target with the PRL. An abnormally high saccade rate (saccades/word) reduces reading speed probably because it reduces visual input. Extra saccades require extra planning and execution time. More saccades mean more fixations which add at least 200 msec per fixation. Higher cognitive demands to suppress foveating saccades might also contribute by increasing saccade latency (Little et al., 2008, Whittaker et al., 1991).

3.2 Implications of fixation instability

Excessive motion of the retinal image either due to eye instability or due to target motion is expected to reduce visibility. Blur increases with the velocity of the target and above critical limits, blur increases visual temporal integration (Paakkonen & Morgan, 1994) and reduces resolution (Badcock & Wong, 1990, Morgan & Benton, 1989). Conversely, it is possible to find, in well controlled experiments, conditions in which moving objects look sharper than static objects (Bex et al., 1995). Bex found that the perceived blur of sine-wave gratings and blurred edges is less when drifting than when static. The perceived blur of these images decreased with velocity. That might be because moving targets trigger the deblurring mechanism proposed by Burr (1980), discussed in section 1.1.2.2.

Under normal conditions the retinal image is never perfectly still due to fixational eye movements. When good stabilization is achieved the retinal images fade (Clarke, 1957, Clarke, 1960, Clarke, 1961) (Kelly, 1985). In the peripheral retina this can be easily experienced during a prolonged and steady fixation. Recently, it has been suggested that fixational eye movements, particularly microsaccades are triggered when retinal image slip caused by inter-saccade drift is too low to prevent fading of the image in the fovea (Engbert & Mergenthaler, 2006, Martinez-Conde et al., 2006). Kelly (1985) demonstrated that in the peripheral retina fading is essentially prevented by inter-saccade drift (Kelly, 1985). In summary, normal fixation

instability caused by fixational microsaccades and drift are parts of a mechanism that prevents image fading and ensures sharp and continuous vision.

Based in the explanation of the Troxler phenomenon, discussed in section 1.1.2.2, Deruaz suggested that fixation instability, observed in patients with macular disease, might be beneficial during eccentric viewing (Deruaz, Matter, Whatham, Goldschmidt, Duret, Issenhuth & Safran, 2004). This suggestion is inconsistent with studies which have shown that instability is associated with a reduction in reading speed (Crossland et al., 2004a, Falkenberg, Rubin & Bex, 2007).

In people with macular disease fixation instability is likely to enhance deficits of the peripheral visual system. For example, crowding increases for unstable targets (Bex & Dakin, 2005, Bex et al., 2003). Other interactions such as fixation instability and slow visual processing are also likely (Cheong et al., 2008). These interactions have been discussed in section 2.2.2. The text presentation formats used to reduce the effect of poor oculomotor control in reading, such as RSVP and scrolling text, do not compensate for fixation instability. That might be why these formats failed to produce consistent improvements in reading speed.

In summary, oculomotor instability has the potential to increase motion blur and crowding which might slow visual processing speed leading to reduction in span and general visual performance.

3.3 Thesis hypothesis and justification

3.3.1 Hypothesis

The hypothesis investigated in this thesis is that: compensating for oculomotor instability will improve visual performance of people with macular disease; specifically it will improve visual acuity and reading speed.

As discussed in the proceeding sections some amount of retinal image motion might be more beneficial for visual function in the peripheral retina than a motionless retinal image. In this thesis visual function is assessed with different degrees of compensation for fixation instability to determine which is most beneficial for patients' acuity and reading speed.

3.3.2 Rationale

Compensating for fixation instability is likely to improve visual function in two ways. First, it may improve vision by reducing motion blur caused by excessive retinal image motion. Second, reduction in motion blur might improve visual processing speed and reduce crowding in the peripheral retina.

3.3.3 Aims

The primary aim of this thesis is to clarify if fixation stability is causing a reduction in visual function. The secondary aim is to evaluate the best stabilization settings to compensate for oculomotor deficits and the tertiary aim is to drive conclusions about the possibility of using eye-tracking based stabilization technique to further training and/or devices to improve visual performance in people with macular disease.

Visual performance in controlled fixation conditions is compared with performance in normal conditions to quantify the effect of compensating for fixation instability. The analysis included assessment of the retinal image speed, number of saccades and eye stability.

3.3.4 Thesis plan

Four experiments were conducted. In the first experiment, Chapter 6, visual performance is assessed by letter acuity and crowded letter acuity in normal control subjects with simulated scotomas under four conditions of fixation instability compensation. Here I report and discuss the effect of different conditions of stabilization for isolated and crowded letters and interactions between conditions, retinal eccentricity and retinal quadrant.

In the second experiment, Chapter 7, letter acuity and crowded letter acuity is measured in patients with scotoma caused by macular

degeneration under four conditions of fixation instability compensation. In this chapter I report and discuss that visual acuity can get worse when retinal slip signal caused by fixation instability is very high. I also discuss a theoretical argument that fixation instability might be beneficial for eccentric viewing. This argument is refuted for this group of patients (AMD, and Stargardt's patients) and range of visual acuity.

In the third experiment, Chapter 8, reading speed using rapid serial visual presentation is assessed in normal controls subjects with simulated scotoma under six conditions of text stabilization. In this chapter I report and discuss the effect of compensating fixation stability and the effect of intra-word saccades on reading speed.

In the fourth experiment, Chapter 9, rapid serial visual presentation reading speed is measured in patients with pathological scotoma under four conditions of text stabilization. In this chapter I discuss again the effect of compensating fixation instability and intra-word saccades on reading speed.

Chapter 4. General methods

This chapter has general information about participants and describes equipment and general protocols. Further details can be found in specific methods for each experiment.

4.1 Participants

This project involved participants with low vision due to macular disease (patients) and participants with normal vision (controls). All experiments reported here received ethics approval either from the UCL ethics committee or from the Moorfields & Whittington Research Ethics Committee and conformed to the tenets of the Declaration of Helsinki. All participants gave informed consent. A copy of the ethics forms is in Appendix B.

4.1.1 Control subjects

Source

Control subjects were recruited among work colleagues and students at UCL Institute of Ophthalmology. More information about all control participants is given in Appendix A.

Inclusion criteria

All control subjects had corrected visual acuity better than 0.00 logMAR, correction in glasses was below 4DS but could be above this limit in contact lenses. Whenever possible the testing was with contact lenses because that reduced noise during eye tracking. In total 15 subjects were recruited: 7 were involved in the visual acuity experiments (Chapter 6) and 8 subjects involved in the reading experiment (Chapter 8). Some subjects participated in more than one experiment.

Exclusion criteria

For the reading experiment only subjects whose first language is English were recruited. Subjects were asked if they were affected by any condition that could affect reading such as dyslexia. If so they were excluded.

4.1.2 Macular Disease Patients

Source

Some participants were contacted by letter using information from a database of volunteers that participated in previous studies in the laboratory. They were asked about their willingness to participate in a new study, those who replied were recruited. The remaining participants were recruited in person from the Low Vision Clinic at Moorfields Eye Hospital.

Inclusion criteria

Participants with macular disease had been refracted in the Low Vision Clinic by a qualified Optometrist in the 12 months prior to the study and were asked before taking part if they noticed any changes in vision since the last eye test.

In total 16 patients were recruited, aged between 24 and 89 years, best corrected visual acuity, in the better eye, ranged from 0.4 to 1.2 logMAR. Fixation data from the MP1 microperimeter were analysed to ensure that participants had only one PRL. All had binocular macular disease demonstrated with microperimetry and no secondary eye disease or relevant systemic illness. All spoke English fluently.

Of the 16 patients, 5 had juvenile macular degeneration and the remaining had age-related macular degeneration. Ten patients took part in the visual

acuity experiment, Chapter 7 (8 with AMD and 2 with JMD), six took part in the reading experiment, Chapter 9 (2 with AMD and 4 with JMD). Two patients, one in each experiment, withdrew from the study before conclusion of all testing due to difficulties imposed by the task.

Exclusion criteria

If patients reported any changes in their vision, started any treatment or suffered from illness that could affect vision during the period of testing they were excluded. For the reading experiment only subjects whose first language is English were recruited.

4.2 Clinical tests

4.2.1 Visual acuity

Best-corrected distance visual acuity was tested monocularly in both eyes with retro-illuminated ETDRS charts (Precision Vision, La Salle, IL) viewed at 4 or 2 m, as appropriate for the patient's level of acuity (Bailey & Lovie, 1976).

4.2.2 Eye Dominance

Control subjects used the dominant eye during experiments as verified by the pointing method. The subject was given a piece of cardboard in which

there was a central circular hole and was asked to hold the cardboard with both hands and to view a distant target away through the hole, with both eyes open. Each eye was then occluded in turn. When the dominant eye was covered, the target could not be seen through the hole. Alternatively, when the non-dominant eye was covered, the dominant eye continued to fix the target through the aperture. This test is a forced choice test of dominance, which allows only a right or left eye result (Porac & Coren, 1976).

4.2.3 Critical print size

Critical print size (CPS) is the smallest print size which patients can read at their maximum reading speed (MRS). These two values were assessed monocularly in the eye with better acuity, with the normal near correction (if necessary), in the better eye using the MNread charts. This chart consists of 19 blocks of continuous text, approximately 85% contrast, with print sizes from 1.3 logMAR to - 0.5 logMAR at recommended viewing distance of 40 cm. Each block contains 60 characters including spaces which correspond to 10 standard length words and is printed on 3 lines with even left and right margins (Legge et al., 1989).

The time to read each sentence was recorded with a stop watch. Reading speed is measured in words per minute, and in the case of the MNread charts is given by:

$$\text{Reading speed} = 600 \times (10 - \text{errors}) / (\text{time in seconds})$$

When the number of errors for a print size is 10, reading speed is assumed to be zero. Alternatively, when the full block of 10 words was correctly read, the time can be recorded on a sheet which is marked with the corresponding reading speed. The MRS reported in this thesis was calculated using the mean of the three largest reading speeds. CPS was defined as the smallest print size that supports reading at 90% of the MRS, as shown in Figure 4.1 (Patel, Chen, Da Cruz, Rubin & Tufail).

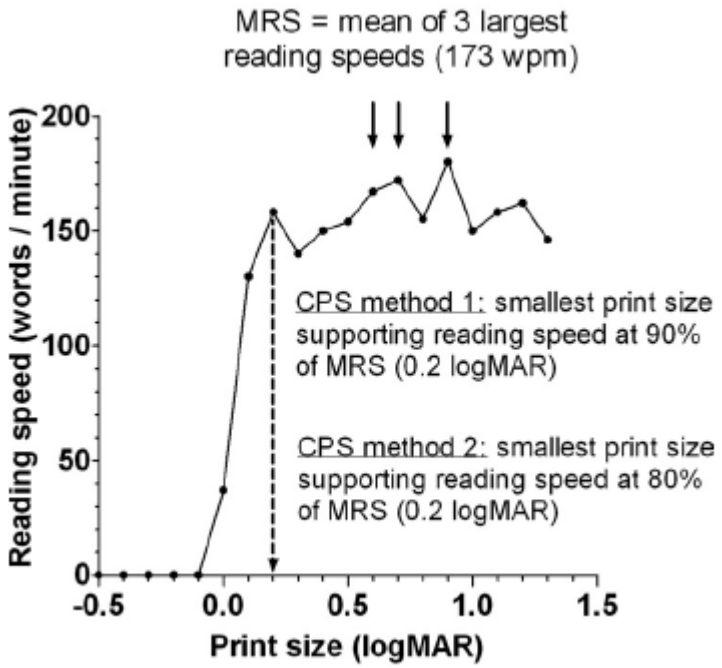

Figure 4.1: Example of MRS and CPS calculations, adapted from Patel et al. (2011). The mean of the 3 largest reading speeds,173 wpm, corresponds to the MRS, and 90% of that (156 wpm) is used to determining the CPS (0.2 logMAR).

4.3 Control of retinal image stability

4.3.1 The eyetracker

The eyetracker used was the Eyelink I Gazetracker (SMI, Tetlow, Germany, now represented by SR Research Ltd., Mississauga, Ontario, Canada). This eyetracker consists of two eye cameras mounted headband mounted and two infrared light sources plus one head camera and 4 infrared light sources on the video monitor. Pupil position is tracked by an algorithm similar to a centroid calculation, with a noise-limited resolution of 0.01º or less, and a velocity noise of less than $3º.s^{-1}$ (manufacturer's specifications). The head camera tracks four infrared markers mounted on the visual stimulus display, so that head motion can be measured and gaze position can be computed.

The cameras produce images at a sampling rate of 250 Hz (4 msec temporal resolution). The Eyelink is used with a PC with dedicated hardware for the image processing necessary to determine gaze position. The Eyelink communicates via a high-speed ethernet connection with a second PC that performs the stimulus display. The ethernet connection transfers information from the eye tracker allowing it to display stimulus gaze-contingent in the monitor connected to the Eyelink Subject PC (Figure 4.2). The average delays from eye movement to position data availability is 6 msec with heuristic filtering disabled, and 10 msec with filtering enabled (manufacturer's specifications). In all experiments the filter

was enabled. With this it is possible to create near real-time gaze-contingent experiments (Cornelissen & van den Dobbelsteen, 1999, Tant, Cornelissen, Kooijman & Brouwer, 2002).

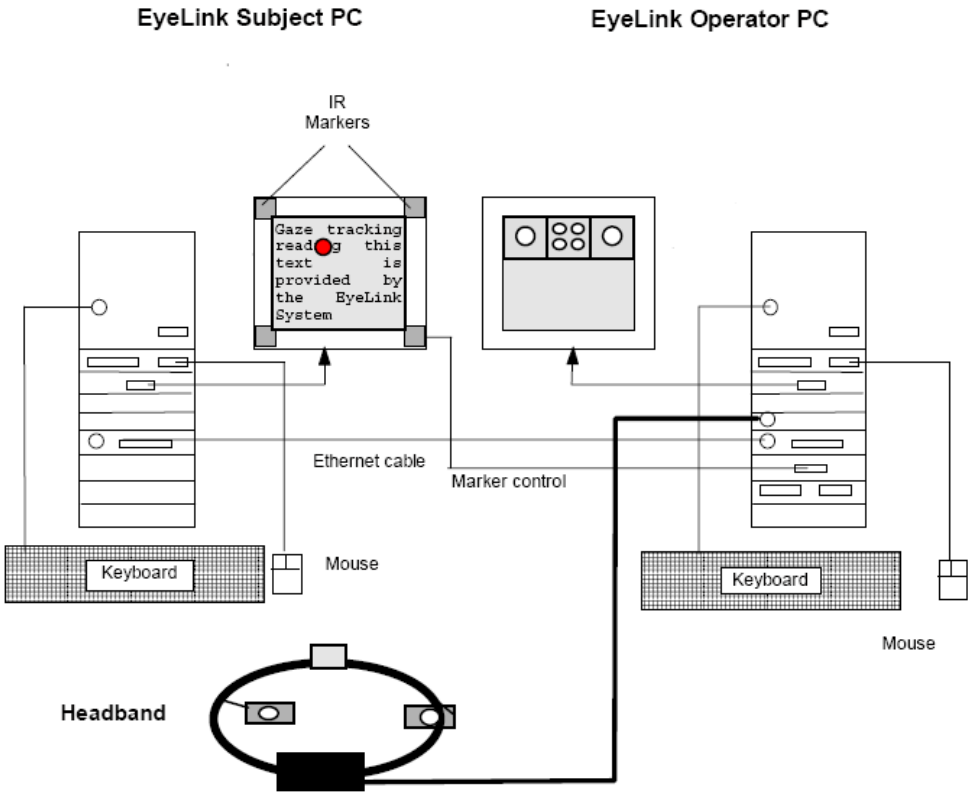

Figure 4.2: Eyelink Setup. Attached to the headband there are two high-speed cameras to track both eyes simultaneously and a third camera tracks four infrared markers mounted on the visual stimulus display. The Eyelink Operator PC communicates via a high-speed ethernet connection with the Eyelink Subject PC that performs the stimulus display.

According to the information provided by the manufacturer there is a delay, for a monitor running at 60 Hz, of 16 msec between the eye movement and the time it reflects in the stimulus monitor. In experiments reported here the monitor was running at 100 Hz, which corresponds to 10 msec of vertical

retrace. Before the vertical retrace the eyelink subject PC (Figure 4.2) controlling the monitor was collecting the newest sample, available through the ethernet, arriving from the eyelink PC. The time the sample takes to travel from one computer to the other is 10 msec (variable). Thus the total delay should be 16-20 msec (total of 4 to 5 eyetracker frames).

The slippage of the head-mounted system can cause variability of the gaze estimate over time that can be minimized by performing drift correction between trials. Saccade parameters and fixation position estimates of the Eyelink have been shown to be highly correlated with those measured using a scleral coil system. The Eyelink's relatively low sampling frequency of 250 Hz results in somewhat noisier parameter estimates in cases of small saccades (Cornelissen, Peters & Palmer, 2002, van der Geest & Frens, 2002).

Reflections from eyeglasses sometimes interfered with the ability of the eye camera to detect the pupil. The effect of lens reflection was minimized by activating the anti-reflection mode (R-mode), a built-in mode of the Eyelink software that performs further image processing to detect the pupil. However, R-mode increases the inaccuracy of the head position detection and pupil-tracking noise. Because of this, it was used only after all other strategies, such as positioning the camera below the trial frame had failed.

In people with macular disease difficulties calibrating the eye tracker increased due to the inaccuracy of fixation whilst looking at the calibration

points. To reduce the number of failed calibrations it was necessary to extend the exposure time of the calibration points from 1000 msec to 1500 msec to ensure that participants were able to look at it. For some participants, calibration points were manually accepted by the experimenter after confirming with the participant that he or she was fixating at their best. The calibration was validated using the software algorithms that provide a qualitative classification of the calibration as “good”, “fair” or “poor”. Only trials where the calibration was categorised as “good” or “fair” were included. In accordance with manufacturer’s specifications, a “good” calibration means that errors are acceptable. “Fair” means that errors are moderate and calibration should be improved whenever possible.

4.3.2 Monitor

Stimuli were displayed on a 21-inch monitor (Trinitron GDM-F500R, Sony, Japan) with peak luminance of 98 $cd.m^{-2}$ set at a refresh frequency of 100 Hz. The monitor resolution was 1280 × 1024 pixels for the visual acuity experiments and 1024 × 768 pixels for the reading experiments.

4.3.3 Procedure and MATLAB programs

4.3.3.1 *Procedure for eye movements collection*

Unless otherwise stated, the viewing distance was 50 cm and subjects were wearing their refractive correction. The eyetracker was adjusted to follow the eye over the entire monitor without losing tracking. The camera threshold was adjusted as it is dependent on the eye colour and room illumination. The room was normally illuminated for the control experiments but the lights were dimmed or switched off for experiments with patients to allow better detection of the target.

4.3.3.2 *General algorithm for data collection*

Programs for running the experiment were written in the Matlab programming environment using elements of the Psychophysics toolbox (Brainard, 1997; Cornelissen, Peters, & Palmer, 2002; Pelli, 1997). The Psychophysics toolbox (Brainard, 1997, Pelli, 1997) is a software package for precise stimulus specification with MATLAB, a high-level interpreted language with extensive support for numerical calculations (The MathWorks, 1993), allowing for rapid and flexible programming of psychophysical experiments. Examples of the programs can be found in Appendix D.

The Eyelink Toolbox, included in the Psychophysics toolbox, was developed by Cornelissen & Peters and is a high-level interface between MATLAB and the Eyelink Gazetracker. The toolbox enables one to measure eye movements while simultaneously executing stimulus presentation routines provided by the Psychophysics Toolbox as well as other MATLAB scripts (e.g., gaze-dependent displays) (Cornelissen et al., 2002).

A typical program would go through these steps:

i) Calibration of the eye tracker

ii) Drift correct

Start recording / Start of a loop

iii) Collect samples from the eye tracker

iv) Instantaneous calculations (see below)

v) Stimulus display until time limit was reached or response

vi) Wait for response (if necessary)

vii) Update psychometric function (Quest, see below)

viii) Drift correct

ix) Next trial: goes to iii)

End of loop / Stop recording

x) Data saving

4.3.3.3 *Calculations*

Eye velocity and acceleration

Gaze position is recorded every 4 msec and used for calculations of eye velocity, acceleration and direction.

Eye velocity (*v*) and eye acceleration (*a*) were calculated by equations 1 and 2 below, where *i* is the index of the i^{th} sample collected from the eye tracker and, *x* and *y* are the horizontal and vertical positions of the eye. *t* represents time of sample collection.

$$v_i = \frac{\sqrt{(x_{i-1} - x_i)^2 + (y_{i-1} - y_i)^2}}{t_i - t_{i-1}} \qquad (1)$$

$$a_i = \frac{\sqrt{(v_i - v_{i-1})^2}}{t_i - t_{i-1}} \qquad (2)$$

Gain

Stimulus velocity during fixations was modulated by a gain factor:

$gain = v_{target} / v_{eye}$

Changing the value of the ratio between the velocity of the stimulus and the velocity of the eye (gain) the amount of retinal image motion can be controlled.

When the target was moving with the eye movements, gain 1.0, the retinal

image motion was at a minimum. Due to a delay between the movement of the eye and the availability of that information to update the target position on the screen, estimated to vary between 16 and 20 msec, the retinal image was not totally stabilized. Compared with normal fixation, retinal image motion was reduced (gain 0.1), fully compensated (gain 1) or overcompensated (gain 10).

Quest

The size of the stimulus, in visual acuity experiments, and the stimulus exposure time, in the reading experiments, was controlled by Quest staircases. Depending on the number of positions assessed, in one block, single or multiple Quests were used. (Brainard, 1997, Watson & Pelli, 1983). The Quest adaptive algorithm uses a maximum likelihood procedure to estimate threshold letter size (acuity) or word exposure (reading). For each trial the value tested is based on the mode of the maximum likelihood function produced by the all of the preceding values tested.

4.3.3.4 *Stimuli*

Visual acuity

Visual acuity was expressed in logarithm base 10 of the minimum angle of resolution in minutes of arc (logMAR), where 1.0 logMAR is equivalent to a minimum angle of resolution of 10 minarc (20/200) and 0.0 logMAR is

equivalent to a minimum angle of resolution of 1 minarc (20/20).

Visual acuity was measured with a Landolt C with 80% Michelson contrast. This optotype consists of a ring with a thickness (stroke width) equal to 1/5 of its diameter and a gap equal to stroke width. In each trial the gap was presented in one four positions: left, right, up, down.

The crowded visual acuity was measured with the Landolt C described above but here four flankers (bars) were presented alongside the target, as shown in Figure 4.3. The bar width was equal to stroke of the ring, the length was equal to the diameter of the ring and the distance from C to flankers was two strokes.

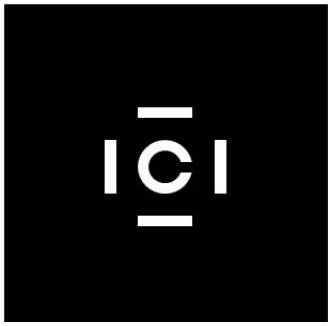

Figure 4.3: Landolt C surrounded by four flankers.

4.3.3.5 *Reading sentences*

Sentences used in Chapter 8 were randomly selected from a database supplied by Dr Elisabeth Fine of Harvard Medical School, MA., USA. This database is formed of sentences with similar properties to those used on the MNRead card (Legge et al., 1989). The number of words per sentence

was reduced to 4 in Chapter 9 because 5 word sentences caused memorization problems given the long exposure times.

Sentences for the reading experiment in Chapter 9 were obtained from a sentence database with MNread type sentences and generated using a sentence generator described by Crossland et al (Crossland, Legge & Dakin, 2008). In brief, it consists of a corpus of words arranged into three categories: quantifiers, objects and descriptions. Each sentence is constrained to have the following structure: first, a noun is selected at random from one of 414 words currently in the corpus (such as "architects", "penknives", "ale" or "music"). Second, a grammatically appropriate two-word description (which may be true or false) is selected from a set constrained to the item or category in question: for example, a human trait ("read books"), a non-living-object trait ("don't breathe") or a specific trait ("design buildings", "aren't sharp", "is jazz"). At present there are over 1,000 unique descriptions in the database, although not all descriptions can be applied to all nouns. Finally a quantifier is chosen from the set "no", "some" or "all". The combination of quantifier and description is selected such that half of all of the sentences are true. Double negative sentences (e.g. "No alligators can't read") are prohibited (Crossland et al., 2008).

Examples of sentences used in the reading experiment with patients, Chapter 9:

“some Audis are clever”

“some foxes have beaks”

Words were presented as white letters in Courier New font against a black background. Courier is a fixed-width font in which each character occupies an equal amount of horizontal space. The text size was based on the *x*-height.

Rapid serial visual presentation - RSVP

Sentences were presented using an RSVP paradigm, as introduced in section Chapter 3. With RSVP each word is presented sequentially at the same location. The exposure time was controlled by Quest.

4.4 Microperimetry

4.4.1 Instrument

The MP-1 microperimeter (Nidek Technologies, Italy) was used to identify the PRL location using the convention shown in Figure 4.4. The Microperimeter is a device combining the capabilities of a fundus camera with live video, microperimetry and eye tracking. Visualization of the retina and tracking of the eye are fundamental for the correct characterisation of the retinal function in people without central fixation.

The tracking system follows a landmark in the retina at 25 Hz that allows

the projection of the stimuli in the region with correspondence with the photography of the fundus. There is a delay of approximately 2 frames (~80 msec) in the tracking system. Currently, this device is used for classification and rehabilitation of macular disease (Seiple et al., 2005, Vingolo et al., 2009), Microperimetry with this device is also known as “fundus driven microperimetry”.

4.4.2 Microperimetry strategy

The MP-1 measures retinal sensitivity at each stimulus testing location in dB units. The background luminance is 1.27 cd.m^{-2}, the brightest level of the stimuli corresponds to 0 dB attenuation (127 cd.m^{-2}) or 100% contrast, and the dimmest level of the stimuli corresponds to 20 dB attenuation (1.27 cd.m^{-2}) or 1% contrast.

Fixation location was determinate as shown in Figure 4.4. A quick microperimetry assessment was performed using a strategy that consisted of a pattern of 68 stimulus locations centred on the fovea and arranged over a 20º diameter. Stimuli used were Goldmann V (white, circular stimuli, 104 minarc diameter), presented on a black background for 200 msec. During perimetry testing, stimuli locations were presented randomly once at 0 dB attenuation (that is, with the brightest stimulus only). Participants indicated detection of a stimulus by depressing a button on a handheld joystick.

A B

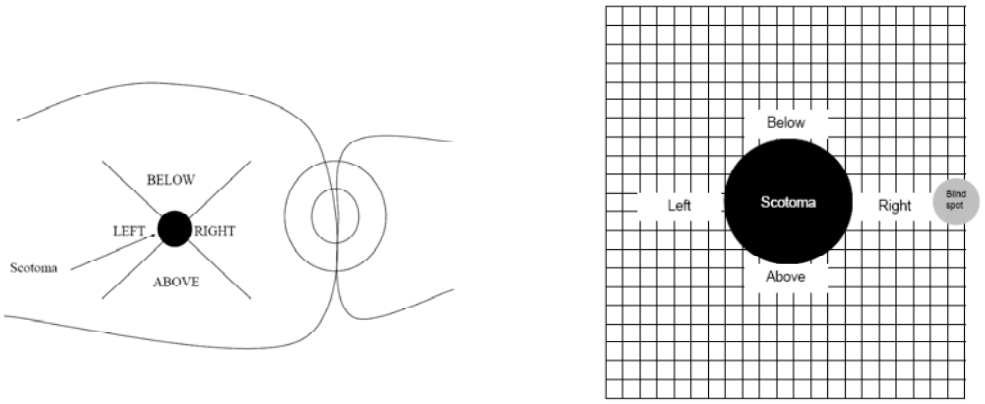

Figure 4.4: (A) Convention used to describe PRL location with respect to the scotoma in visual field space (right eye). (B) How the convention translates when the patients looks at the Amsler grid. In this example, a patient with a right PRL would fixate things that are straight ahead by moving the scotoma to the left field of view (obscuring the left field with the scotoma).

4.5 Data analysis

Eye movements data were analysed using programs written in Matlab (Version R2007a, The MathWorks, Inc., Natick, MA). Prior to statistical analysis data were normalized and/or transformed using Microsoft Excel 2007. Graphs were plotted using OriginPro 8 SR1 (Version 8.0773, OriginLab Corporation, Northampton, MA, USA).

4.5.1 Repeated measures analysis

Repeated measurements of variables in different conditions were analysed

with Linear Mixed Models using SPSS (versions 13 and 15; SPSS Inc., Chicago, IL, USA). Linear mixed models are an alternative to analysis of variance when the design is unbalanced, for example, when the number of repeated measurements was not the same for all the participants. Unlike ANOVA, linear mixed models do not require homogeneity of variance.

4.5.2 Fixation stability quantification

Fixation stability was quantified with the bivariate contour ellipse area (BCEA). The BCEA describes the region over which the eye is fixating for P% of the time (Crossland & Rubin, 2002, Steinman, 1965) and is given by the equation below.

$$BCEA = 2K\pi\sigma_H\sigma_V(1-\rho)^{1/2}$$

Where BCEA is the bivariate contour ellipse area, σ_H and σ_V are the standard deviation of point location over the horizontal meridian and vertical meridian, respectively, and ρ is the product-moment correlation of these two position components. The value *K* is dependent on the probability area chosen

$$P = 1 - e^{-K}$$

where *e* is the base of the natural logarithm. Therefore, P = 63.2 %, *K* = 1, and the BCEA measures the area where the eye was 63.2% of the time. Larger areas correspond to more instability. Different authors have used different values of P, such as 63.2% (Steinman, 1965), 68% (Crossland & Rubin, 2002, Culham et al., 1993) or 95% (Schuchard & Raasch, 1992a).

4.5.3 Multiple PRL assessment

Multiple PRL assessment was made using the maximum likelihood and expectation maximization method. Mathematical details have been published by Crossland et al. (Crossland, Sims, Galbraith & Rubin, 2004b). In brief, the method looks for multimodality in the eye position distribution and uses an expectation-maximization algorithm to define clusters of fixation positions. The method computes mean, variance and number of fixation samples contained within the limits of the variance defined around the mean for each cluster. Multiple preferred retinal loci were defined when the number of samples in each cluster was higher than 20% of the total and the distance between clusters' means was more than twice the sum of the standard deviations for each cluster.

Chapter 5. Development of method

A series of preliminary experiments was performed to test instrumentation limits and experimental setup.

5.1 Qualitative analysis of the eyetracker

This project was devoted to study questions of retinal image stabilization in the peripheral retina of patients with impairment of oculomotor control. This preliminary test was performed to determine whether the eye-tracking system available in our laboratory is fast and precise enough to stabilize the retinal image in real time. The test consisted of generating a retinal afterimage and asking subjects to superimpose this afterimage on a gaze-contingent target presented on the monitor (Barlow, 1963, Debie, 1985, Riggs & Schick, 1968).

After fitting the eyetracker to the observer, a retinal afterimage was produced by activating a camera flash unit with a dot shaped mask, approximately 3 mm diameter. A gaze linked grey dot (0.3º of visual angle)

was displayed on the monitor against a white background. A qualitative analysis of the dot superimposition with the after image was done by 2 experienced observers.

The afterimage was superimposed on the target for the first 3 s to 5 s and was aligned throughout normal fixational eye movements. However, large saccades, from one extreme of the monitor to the other (~30º), and blinks disrupted this effect. Recently, Aguilar and Castet (2011) tested the limitations of gaze contingent experiments using an infrared eye tracker, similar to the one used in these experiments (Aguilar & Castet, 2011). The comprehensive analysis of the gaze contingent window limitations agreed with the preliminary tests of this thesis. The questions raised by Aguilar's work are more important for experiments that involve continuous reading or long target exposures. Eye tracker compensation gets worse for large saccades. Spatial shift is approximately 1 deg at the time of the first monitor refresh (L1, Figure 5.1, first vertical arrow) and approximately 4 deg at the second refresh of the monitor (L2) during the saccade flight. In the experiments of Chapter 6 and Chapter 8 the crucial moment was L1, because that was the time when the program would make an action. The actions were: (1) blanking the screen if a saccade was detected or (2) repeating the trial. Thus I believe that results are not significantly influenced by this spatial shift. Another limitation the authors point out is the disruption of tracking caused by blinks. Again, in experiments reported here, if a blink occurred during target exposure the trial was repeated.

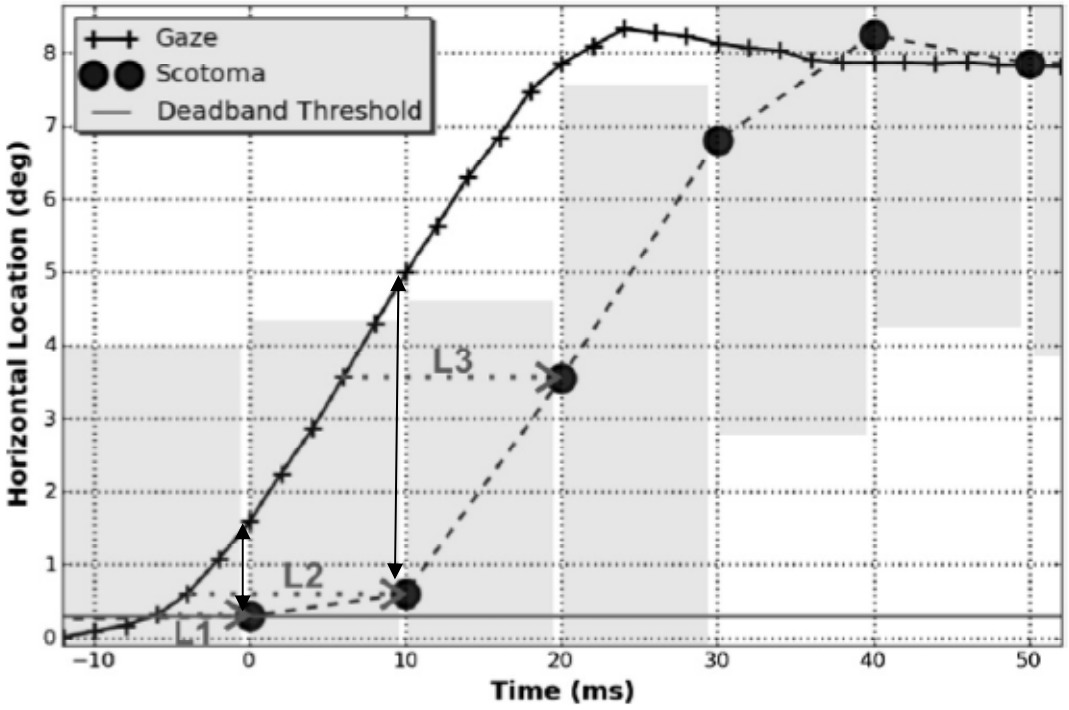

Figure 5.1: Latency of a simulated scotoma. According to Aguilar & Castet (2011) there is a shift between the eye and scotoma positions during saccades that is caused by the inherent delay of the gaze contingent window controlled by infrared eyetrackers. The latency (L1) of the scotoma is relevant for the experiments reported here as described in the text above.

In short, the preliminary results of the testing agreed with the limitations reported recently by Aguilar e Castet (2011). Extra care was needed during the planning of these experiments. For example, in the experiment measuring visual acuity in the peripheral retina, trials during which the eye velocity went above $100^{o}.s^{-1}$ were repeated

5.2 Selection of appropriate screen refresh rate

Visual persistence is the apparent visibility of the stimulus that extends beyond its physical duration (Coltheart, 1980, Farrell, 1984). In simple terms, visual persistence consists of the visualization of stimuli that are not physically present. Visible persistence in cases of static stimulus is about 100 msec. Persistence is dependent of the spatial and temporal separation of the stimulus and increases with the distance between successive stimuli (Allport, 1968, Farrell, 1984).

In some of conditions tested, gain 10, the amplitude of the target's jitter was large. Even when the eye was fixating that would lead to perception of multiple targets due to visual persistence. We determined the optimum image update frequency (monitor refresh rate) that minimized visual persistence effects.

The monitor was set at different refresh rates between 60 and 150 Hz. A gaze contingent Landolt C was presented with motion modulated by gain 10 during fixations. The displacement of the visual target in the screen was analysed and the number of perceived targets registered.

The optimum rate was found to be 100 Hz. This frequency minimized the number of stimuli visible during high velocities of the visual target and no

significant spatial error between the visual target position and the real eye position was observed. In these conditions the visual target position was updated every 8 or 12 msec.

This experiment established the refresh rate of monitor to be used in experiments using gaze contingent targets. Visual persistence was reduced but not totally avoided.

5.3 Selection of most appropriate target flankers

Previous research has shown that the effect of oculomotor instability in visual acuity is not always evident when a single letter is presented (Leat et al., 1999b). Further, the real world is not made of single characters or objects. In order to obtain more realistic results in the experiment where fixation instability was overcompensated crowding should be introduced. Crowding can be added by placing four flankers (bars) around the visual target. Unlike in the central retina the crowding effect in the periphery is not uniquely dependent on the physical characteristics of the stimulus. An experiment was conducted to determine the optimal distance between the stimulus and flankers to test crowded letters in peripheral retina.

Visual acuity was measured under two crowding conditions. In condition 1, the distance between the stimulus and the flanking bars was maintained at a constant visual angle. This angle was selected according to previous

measures made in this laboratory and reported in the literature (Bex et al., 2003, Toet & Levi, 1992). In condition 2, the distance between the optotype and the flanking bars changed with the size of the optotype. The separation between the optotype-centre and the flankers-centre was equal to the size of the optotype (Toet & Levi, 1992), section 4.3.3.4 (Figure 4.3).

Feature interaction was noticeable in both conditions, with a reduction in visual acuity for all gains. The effect obtained with condition 2 was consistent at all eccentricities and positions tested, whilst the results for condition 1 showed inconsistency amongst positions.

Therefore, the flanking bars used in this thesis were scaled with optotype size. This has the added benefit of being more similar to target-flanker separation in normal text, so this crowding technique is also the most suitable to predict the effects of fixation instability during reading.

Chapter 6. Peripheral visual acuity with compensation for fixation instability

The contents of this chapter have been published in Journal of Vision. A copy of the paper can be seen in Appendix C.

Fixational eye movements move the visual target across groups of receptors on the retina. These movements generate a signal which is a mean of the combined activity of all receptors stimulated and not only those corresponding to the size of the visual target (Andersen & Weymouth, 1923, Keesey, 1960). This mechanism explains why it is possible to discriminate Vernier offset of about 1-secarc while the finest foveal receptors subtend about 24-secarc (Berry, 1948, Keesey, 1960). The visual system must cope with the eventual blur resulting from the retinal image slip caused by these movements (Ahissar & Arieli, 2001). When the amount of retinal movement is above the capacity of neutralization of the visual system the image is perceived as blurred due to motion smear (Burr, 1980). An immediate consequence of blur is a

reduction of resolution (Burr & Ross, 1982, Morgan & Benton, 1989).

Several studies have measured resolution in the peripheral retina with static (Banks, Sekuler & Anderson, 1991, Green, 1970, Mandelbaum & Sloan, 1947, Toet & Levi, 1992) and moving targets (Bex et al., 2003, Brown, 1972b, Falkenberg et al., 2007). Brown found that in the peripheral retina visual resolution can be improved when a target has a velocity of approximately $10^{o}.s^{-1}$. The linear or rotational movement used in these studies is likely to be less effective than the more random movement caused by fixational eye movements (Ditchburn & Drysdale, 1977, Rucci et al., 2007, Sharpe, 1972).

A limitation of these previous studies is that retinal image movement has been simulated by asking subjects to fixate a central target whilst a peripheral target is jittered (Bex et al., 2003, Falkenberg et al., 2007), whereas fixational eye movements cover a large range of directions and velocities (Barlow, 1952, Ditchburn, 1959, Hubel & Wiesel, 1959, Martinez-Conde et al., 2004) that cannot be accurately simulated by simple target jitter. It is known that resolution in the peripheral retina is strongly affected by crowding (Leat et al., 1999b, Toet & Levi, 1992) and that crowding increases for unstable targets (Bex & Dakin, 2005, Bex et al., 2003). Thus, another question investigated here is the effect of fixation instability, causing large retinal image slip, on crowded acuity.

Studying the implications of fixation instability on visual performance of the

normal peripheral retina will help to explain its role in patients relying on the peripheral retina during eccentric viewing. In this chapter I report 2 experiments measuring peripheral visual acuity for a crowded and noncrowded target moving in synchrony with the fixational eye movements. The aim was to assess the effect of different levels of retinal image slip on peripheral visual acuity.

6.1 Specific method

6.1.1 Participants

Seven observers participated: 2 subjects were aware of the purpose and 5 subjects were naïve to the purpose of this study. Five observers participated in each experiment; 3 were common to both experiments. All had normal or corrected to normal vision; further information can be found in section Chapter 4 and Appendix A, Appendix Table 1.

6.1.2 Apparatus

The general algorithm to run the experiment has been described in section 4.3.3.2 and an example of the program is in Appendix D. The stimulus was displayed on the monitor described in section 4.3.2 within a central square window of 30 × 30 cm with a black background. The stimulus was a Landolt “C” with 80% Michelson contrast. The size of the stimulus was controlled by multiple Quest staircases, applied to each position independently (Brainard, 1997, Watson & Pelli, 1983).

Eye position was measured with an eyetracker using Eyelink software (version 2.04). During each block, drift correction was performed every five trials. During stimulus presentation the velocity of the target was modulated by gain, see section 4.3.3.3. Four gain factors were used: 0 (no compensation, corresponds to the baseline condition), 0.1 (reduced retinal image slip), 1.0 (null retinal image slip) and 10 (increased retinal image slip). For each frame a circular artificial scotoma was centred on the point of gaze. This ensured that the target could not be seen if it came closer to the fovea than the specified eccentricity. Figure 6.1A shows the target window. The distance between the scotoma boundary and the target, *d*, remained constant in relation to the size of the gap ($d = 2.5 \times g$). Responses were given via a response box.

6.1.3 Procedure – experiment 1

Observers sat 60 cm from the monitor and a chin rest was used to minimize head movements and to maintain a constant viewing distance. Observers viewed the display monocularly with an eye patch covering their non-dominant eye. Participants practiced the task until they were able to finish an entire block of trials with fewer than 10% of trials having large saccades (defined below).

Visual acuity was measured at four isoeccentric positions: right, left, up and down, at two eccentricities, 5º and 10º. The minimum number of

blocks for each subject for the gaze contingent conditions was: 2 (eccentricities) × 4 (gains) × 3 (repetitions) = 24 blocks. In each block acuity was tested in four positions and each position was tested 60 times per block. The gain and the order of positions tested in each block were selected randomly. Each block started with an observer's button press and the first trial for each position was preceded by an auditory signal. The orientation of the Landolt C was generated at random with the gap in one of four cardinal positions: up, down, right or left. Participants were asked to report the orientation of the target by means of a button press. Observers were instructed to respond after the target disappeared to reduce the number of large saccades being made. The sequence of events during each trial is shown in Figure 6.1B. The cue, a gaze contingent grey circle of 33% contrast and of the same size as the target, was present at the eccentricity being tested. This cue duration was selected to maximize discrimination in the periphery (Cheal & Lyon, 1991). The cue disappeared after 100 msec and was replaced by the gaze contingent Landolt C presented up to a maximum of 500 msec. If during target presentation no response was given it was abruptly replaced by a mask (not gaze contingent) that remained visible until a response was received.

The target was visible only during fixations; it was replaced by a black screen during saccades. During frames in which the monitor was blanked the target position was updated based on the real eye movement (not modulated by gain), to avoid possible positional errors in the first frame after a saccade. A saccade was defined when eye velocity was greater

than 30º.s^{-1} and/or acceleration was greater than 8500º.s^{-2}. These saccade detection criteria were used to allow small microsaccades during the measurements, given their useful role in central vision (Martinez-Conde et al., 2006, Rucci et al., 2007).

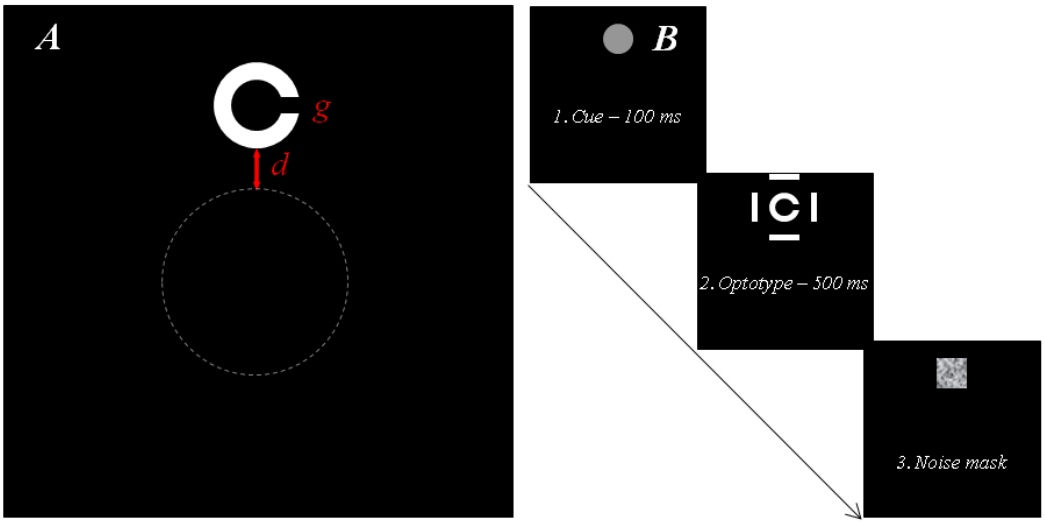

Figure 6.1: Details of target window and presentation sequence. A - Landolt C (orientation – right), the dotted circle delimits the artificial scotoma; g – represents the gap, equivalent to 1/5 of the Landolt C size; d – represents the maximum distance that Landolt C could move before entering the area of the artificial scotoma. The size of the scotoma was varied such that: target size / d = 0.5. B – Sequence of stimulus presentation; the Landolt C was presented with and without flankers.

The delay between eye movement and screen update is 20 msec or less (Cornelissen, 2005). This means that the distance between the eye and the target could be significantly reduced if a fast eye movement (large saccade) occurred during this period. Trials where a “large saccade” occurred were repeated. “Large saccades” were defined when the velocity

was higher than 100º.s^{-1}, corresponding to a saccade of approximately 1º amplitude and 25 msec duration (van der Geest & Frens, 2002). An auditory alert was played to signal the occurrence of these saccades. Blocks were stopped if the number of trials repeated reached 10% of the total number of trials.

For the baseline condition, observers were instructed to fixate a white dot (size: 0.3º) presented in the centre of the monitor. The fixation target was needed to "anchor" participants' gaze. Without a fixation target the eye would move around the screen and the target would be presented at random retinal locations. The eyetracker was used to monitor fixation, but not to change the target position. To avoid saccades towards the target (and therefore multiple repetitions of each trial) the optotype duration was reduced to 200 msec (Carpenter, 1988, Keesey, 1960). According to Keesey, the short exposure time used here, 200 msec, would not significantly alter the final resolution obtained. The implications of dividing attention while attending two locations on the screen are discussed in section 6.3.

6.1.4 Procedure – experiment 2

Experiment 2 was similar to experiment 1 but the target was presented with flankers. Four flankers (bars) were presented alongside the target, as shown in Figure 6.1B. The bar width was equal to g, length was equal to the Landolt C, and the distance from target to flankers was equal to 2 × g.

The viewing distance for this experiment was 50 cm. The size of the target was adjusted for the viewing distance.

6.1.5 Statistical analysis

For statistical analysis, the mean value of visual acuity obtained for gain 0 (baseline visual acuity) was computed. Visual acuity for each eccentricity and position was normalized by the mean baseline visual acuity for each observer. Linear mixed models were used to determine the effects of gain, position, eccentricity, and their interactions, on peripheral visual acuity. For right dominant participants, right position corresponds to nasal retina and left position to temporal retina. Subject (S1) was left dominant, therefore data from right and left positions were swapped before analysis.

6.2 Results

6.2.1 Experiment 1 – Peripheral visual acuity without crowding

Mean visual acuity results for each gain value at each position and eccentricity are summarised in Figure 6.2 (variation of visual acuity with gain, means of all observers). Individual results are presented in Appendix C, Appendix Table 4.

Visual acuity improved when the target was presented under gaze contingent conditions (gain: 0.1, 1.0, 10) compared with the no gaze contingent condition (gain 0). The mean improvement from gain 0 to gain 0.1 was 0.04 logMAR ($p = 0.013$). In the gaze contingent conditions peripheral visual acuity improved slightly with increased retinal image slip: visual acuity with gain 10 was significantly better than that for gain 0.1 (mean improvement = 0.04 logMAR, $p < 0.001$). There was no improvement in VA from gain 0.1 to gain 1.0 ($p = 1.00$) but an improvement was seen for gain 10 compared to gain 1.0 (mean improvement = 0.03 logMAR, $p = 0.01$).

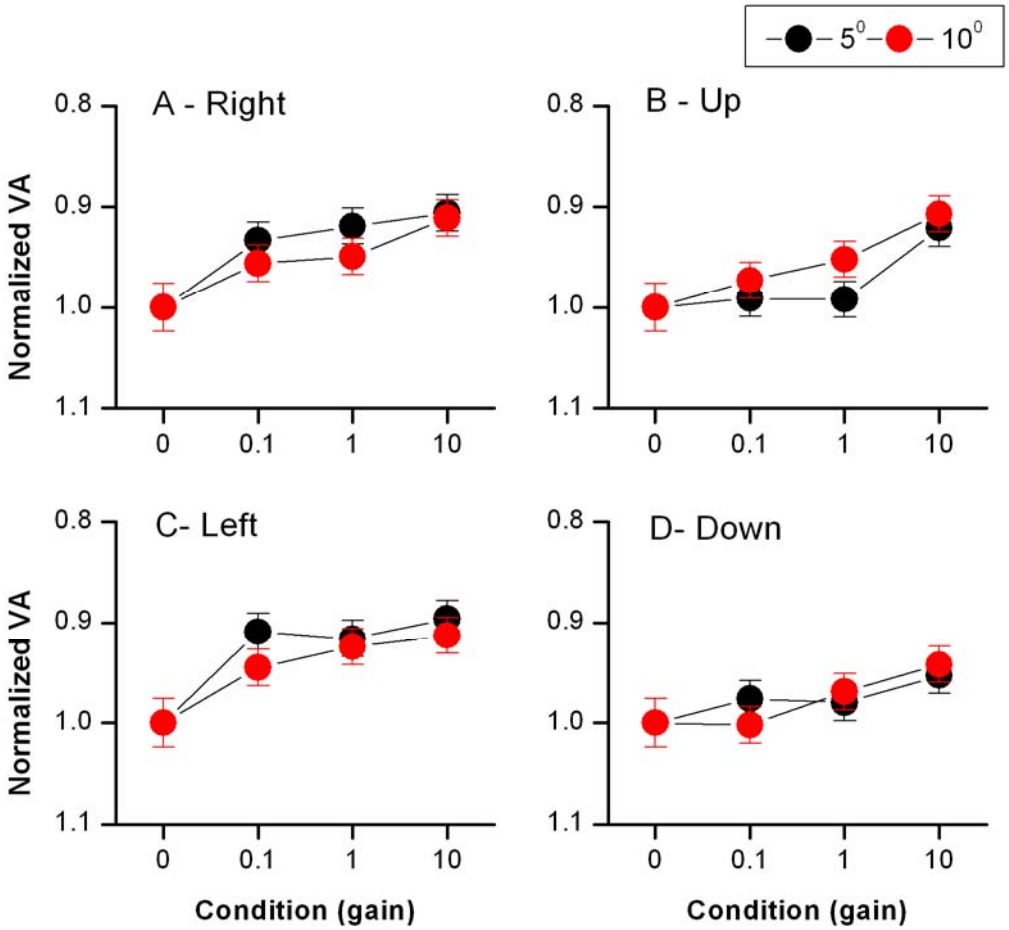

Figure 6.2: Variation of peripheral acuity, measured with a noncrowded Landolt C, for the four motion conditions of the target. Gain 0 corresponds to the non gaze contingent measurements. Each panel shows results for a different screen position. Black circles: 5º eccentricity. Red circles: 10º eccentricity. Error bars show one standard error.

There was no interaction of gain × position or gain × eccentricity. These results are shown in Figure 6.3A and Figure 6.3B, respectively. Thus, the effect of gain was not significantly different at 5º and 10º eccentricity and it was also not significantly different between the four positions tested.

The interaction eccentricity × position was not significant, demonstrating that the variation in acuity with position was not significantly different from 5º to 10º eccentricity.

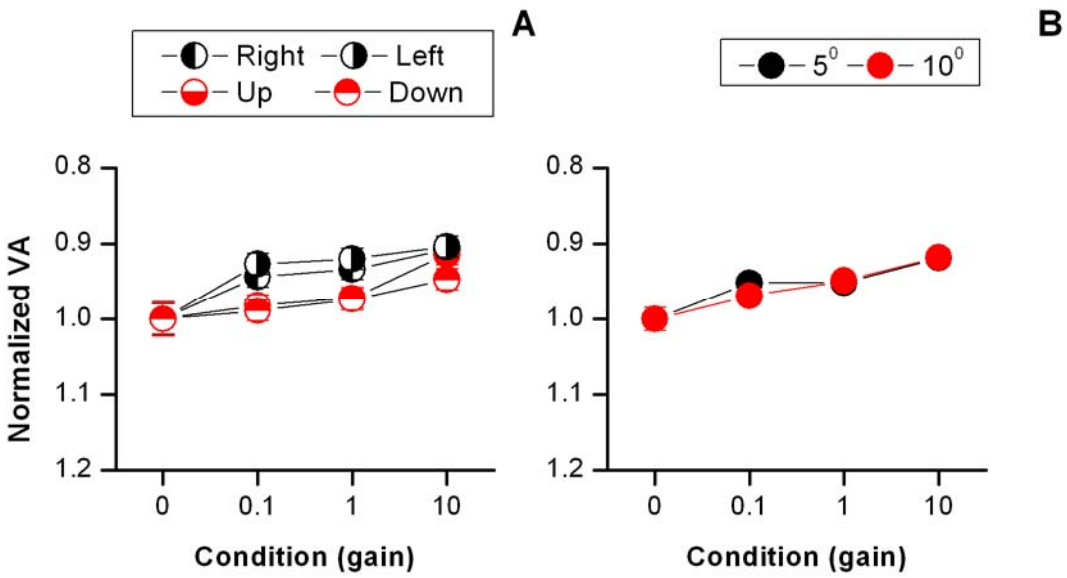

Figure 6.3: The interaction between (A) gain × position and (B) gain × eccentricity for experiment 1. A: each curve corresponds to one position, mean values for positions in the horizontal meridian are shown in black and mean values for positions in the vertical meridian are shown in red. B: each curve corresponds to one eccentricity. Black circles: 5º eccentricity. Red circles: 10º eccentricity. Error bars show one standard error in A and B.

6.2.2 Experiment 2 – Peripheral visual acuity with crowding

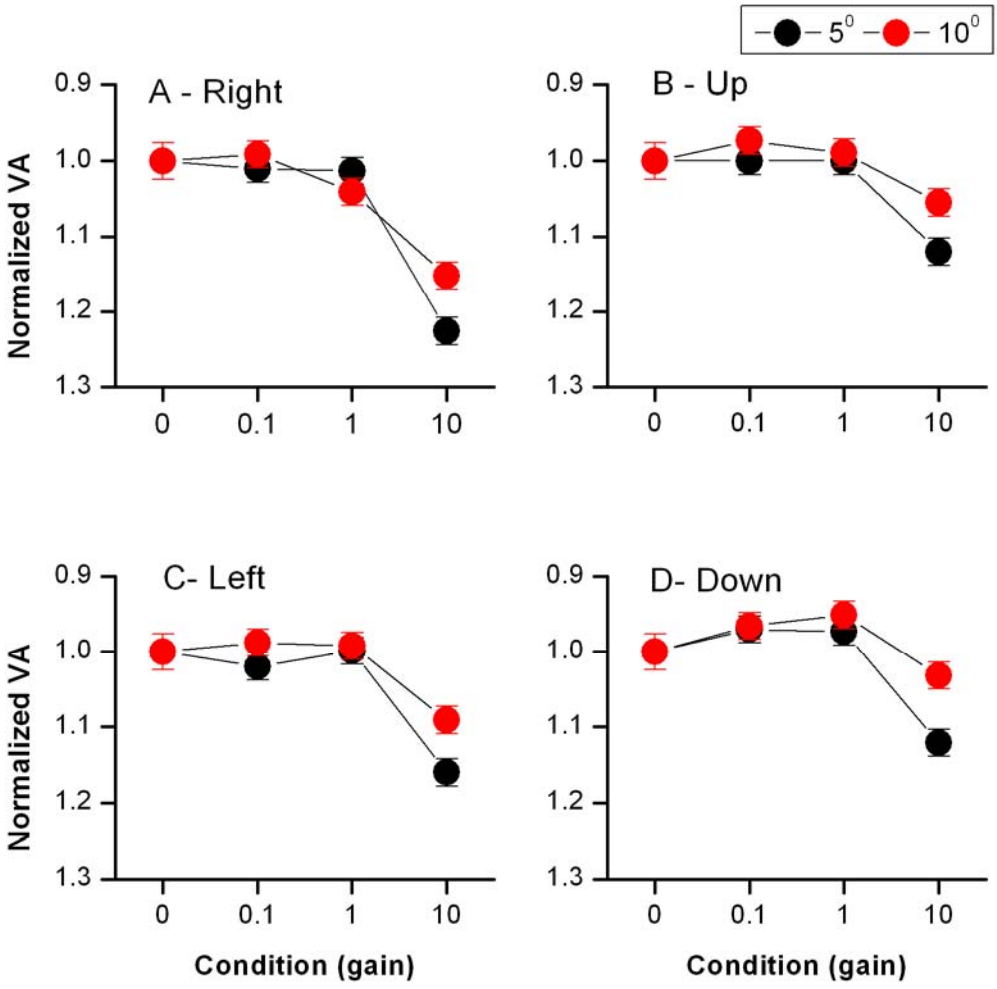

Figure 6.4: Variation of peripheral acuity, measured with a crowded Landolt C, for the four motion conditions of the target. Gain 0 corresponds to the non gaze contingent measurements. Each panel shows results for a different screen position. Black circles: 5º eccentricity. Red circles: 10º eccentricity. Error bars show one standard error.

Mean visual acuity results for each gain value at each position and

eccentricity are summarised in Figure 6.4. Individual data are presented in Appendix C, Appendix Table 5. Gain, position and eccentricity all had significant effects on peripheral visual acuity. The difference between gain 0, gain 0.1 and gain 1 was not statistically significant. In contrast with experiment 1 for gain 10 visual acuity reduced significantly compared to all other gains.

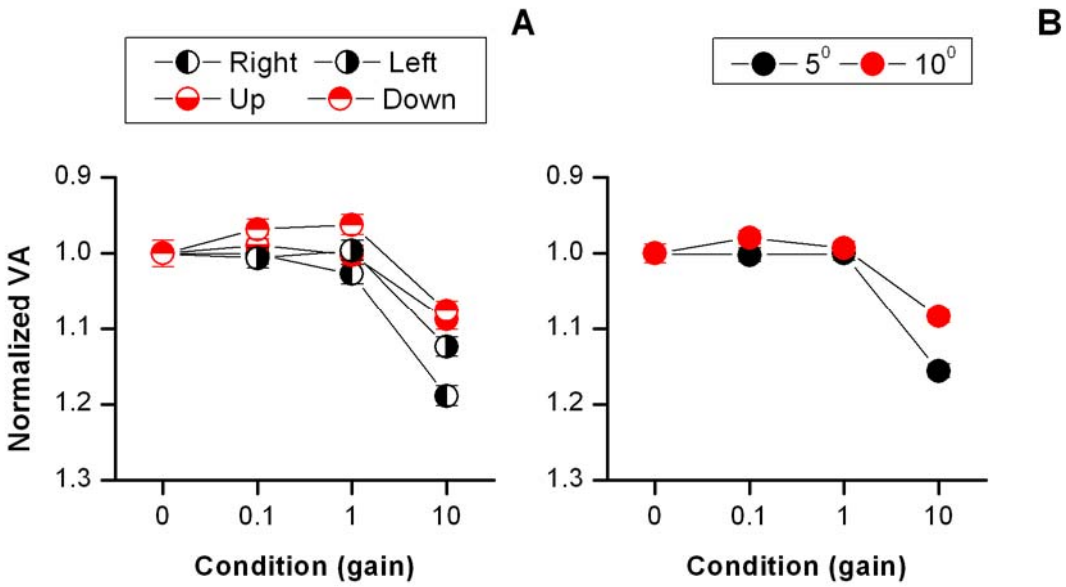

Figure 6.5: The interaction between (A) gain × position and (B) gain × eccentricity for experiment 2. A: each curve corresponds to one position, mean values for positions in the horizontal meridian are shown in black and mean values for positions in the vertical meridian are shown in red. B: each curve corresponds to one eccentricity. Black circles: 5º eccentricity. Red circles: 10º eccentricity. Error bars show one standard error in A and B.

The interaction of gain × position was significant ($p = 0.002$) indicating that

the effect of gain was different depending on the position. The interaction is shown in Figure 6.5A. The interaction of gain × eccentricity was also significant ($p < 0.001$), indicating that the effect of gain was different for different eccentricities. This interaction is shown in Figure 6.5B. All values are presented in Appendix C, Appendix Table 6.

6.3 Discussion

In these two experiments I investigated the effect of increasing, reducing and nullifying the retinal image slip generated by fixational eye movements on peripheral visual acuity. Visual acuity under these conditions was compared to visual acuity measured with no compensation for fixational eye movements.

Peripheral visual acuity measured without crowding (experiment 1) improved slightly with increased retinal image slip, when compared with the other motion conditions. In contrast, under crowded conditions (experiment 2), peripheral visual acuity decreased markedly with increased retinal image slip. Different effects of retinal image slip on crowded and noncrowded conditions have previously been reported in people with nystagmus (equivalent to an increased retinal image slip) (Chung & Bedell, 1995, Pascal & Abadi, 1995).

In both experiments increased retinal image slip would cause blur due to motion smear. In the crowded condition this would lead to superimposition

of the flankers on the target, impairing the ability of observers to detect the gap position within the target. In the noncrowded condition, there are no flankers to interfere with target detection. Other authors investigating the effect of target motion on central visual acuity have found that the effect of motion depends on target configuration: a task that involves a component of localization, such as a Vernier task, is only minimally affected by stimulus motion (Bedell, Chung & Patel, 2000, Carpenter, 1988, Westheimer & McKee, 1975), whereas the ability to discriminate the spacing between two moving bars is greatly impaired by the same amount of motion (Burr & Ross, 1982, Morgan & Benton, 1989). Morgan (1989) suggested this happens because, unlike the Vernier targets, the two lines are very close and their trajectory falls in the same part of the retina reducing the luminance-valley cue to a single-peaked distribution that is no longer resolvable.

Peripheral visual acuity was worse when observers were instructed to fixate the central dot (baseline condition). VA for gain 0 might have been reduced due to the presence of two objects on the monitor compared with the other gains where only the peripheral target was visible. When performing peripheral resolution tasks with foveal vision observers were less likely to orient their attention to the peripheral target than when there was no fixation target. This can induce variability in the peripheral visual performance as is the case with the baseline condition compared with all other conditions (Posner, 1980).

In both experiments peripheral visual acuity measured under reduced and null retinal image slip was similar. These results are in agreement with other authors who have measured central (Keesey, 1960) and peripheral (Millodot, 1966) visual acuity with non stabilized and stabilized retinal images.

Increased retinal slip can improve peripheral vision. Previous studies have found a slight improvement in peripheral visual acuity for targets with velocities above the limit imposed by normal fixational eye movements (Bex et al., 2003, Brown, 1972b). Recent research has reinforced the fundamental role of normal fixational eye movements in central vision (Martinez-Conde et al., 2006, Rucci et al., 2007) yet they cannot prevent visual adaptation in the peripheral retina (Clarke, 1960, Clarke, 1961). Results from experiment 1 are in agreement with these findings.
The effect of gain changed with eccentricity. It has previously been shown that the effect of image stabilisation gets smaller with increasing eccentricity (Millodot, 1966). The second experiment also shows that the change in visual acuity with different gains is more pronounced at 5º than 10º eccentricity, suggesting that retinal image slip is better tolerated with eccentricity. This may be due to the increased size of more peripheral receptive fields (Drasdo, 1989, Hubel & Wiesel, 1960) and changes in the size of spatial interference zones (Bex et al., 2003, Toet & Levi, 1992, Tripathy & Cavanagh, 2002).

In both experiments, peripheral visual acuity in horizontal positions was different from vertical positions (Figure 6.3 A, Figure 6.5A and Appendix

C). This asymmetry between positions is in agreement with other studies and can be caused by anatomical properties of the human retina (Curcio & Allen, 1990), attentional factors (Cameron, Tai & Carrasco, 2002, Talgar & Carrasco, 2002, Yeshurun & Carrasco, 1999) and/or crowding asymmetries (Toet & Levi, 1992). An offline analysis was performed to analyse the possible interaction between the orientation of the gap and the meridian of the position. These results showed no consistent relationship between these two variables.

A limitation of the experimental setup is that the stabilization system with gain 1.0 does not reduce retinal image slip to zero due to the imprecision of head-mounted video eyetrakers and the delay between the movement of the eye and the movement of the target on the screen. One sign of perfect stabilisation is image fading, which was not reported under any condition. However, image fading would have been unlikely given the very high target contrast: even with perfect stabilization it requires exposures far longer than 500 msec for the image to fade (Keesey, 1960, Tulunay-Keesey, 1982).

To quantify the error in the system, an offline analysis was performed to determine if the eye was moving towards or away from the target between each monitor retrace. In periods during which the eye moved away from the target the value of gain would effectively be reduced, whereas when the eye moved towards the target the gain would effectively increase compared to the initially defined value. Despite some variance, for all three gains the value of the mean differed by no more than 1/10 of the defined

value. For a typical set of 4 repetitions per gain for the same observer, the mean and 95% confidence interval was: 0.099 ± 0.0008 for gain 0.1; 0.99 ± 0.005 for gain 1.0; and 10.53 ± 0.5 for gain 10.

A further consequence of system delay would be a time lag between the onset of a saccade and screen blanking. The maximum distance the eye could travel during a saccade is approximately 0.12º every 4 msec. Thus, the maximum distance the eye could travel towards the target during a saccade before the blanking of the monitor was less than 0.5º. I retrospectively computed typical target amplitude, measured between monitor frames, for the non-zero gain conditions. The mean amplitudes of the target movements for 5º eccentricity were 1.8 minarc for gain 0.1; 18 minarc for gain 1.0 and 33.6 minarc for gain 10. The amplitude for gain 0.1 was many times below the limit of 1 pixel. Therefore, the difference in the mean amplitude of the target movement between gain 0.1 and gain 1.0 was not large enough to produce changes in peripheral visual acuity (Brown, 1972b, Westheimer & McKee, 1975). However, performance differences between these two gains would exist if there was a systematic difference in the number of microsaccades due to different amounts of retinal image slip (Engbert & Mergenthaler, 2006). This was not the case: no systematic change was found in the number of microsaccades with increasing gain. At 5º eccentricity the mean number of microsaccades was 107.5 (range 272 – 53) at gain 0.1, 98.0 (range 289 – 13) at gain 1.0 and 110.1(range 489 – 18) at gain 10.

A further potential limitation of the experimental technique is that subjects

wore the same refractive correction for 5º and 10º eccentricity. Whilst it is known that there are small differences in refractive error with increasing eccentricity (Gustafsson & Unsbo, 2003, Millodot, Johnson, Lamont & Leibowitz, 1975, Millodot & Lamont, 1974) this effect would have the same impact under each gain and would not alter the results systematically.

Previous studies in people with macular scotomas caused by diseases such as age-related macular degeneration have shown that they have poor fixation stability (increased retinal image slip) (Bellmann et al., 2004, Culham et al., 1993) and that their reading speed decreases if instability increases (Bellmann et al., 2004, Seiple et al., 2005). These results confirm that fixation instability has a significant effect on peripheral visual acuity.

6.4 Conclusion

Increased retinal image slip improves peripheral visual acuity for isolated targets but worsens acuity when targets are crowded. These results have two important implications: first, measurements of peripheral visual acuity performed with isolated letters are not likely to be good predictors of visual function under normal crowded conditions; second, in real visual tasks poor fixation stability may be a limiting factor for visual function in the peripheral retina.

Chapter 7. Visual acuity at the PRL

The content of this chapter has been accepted for publication in Investigative Ophthalmology and Vision Science. The paper can be found in Appendix C.

In Chapter 6 I assessed the effect of fixation instability on visual acuity of the normal peripheral retina. Here I explore the same in people with macular disease. In section 2.2 and Chapter 3 I reviewed the consequences of macular disease for visual function.

In brief, in advanced macular disease patients use eccentric viewing (Crossland et al., 2005, von Noorden & Mackensen, 1962). Most of them develop a preferred retinal locus (PRL) and have increased fixation instability (Crossland et al., 2005, Culham et al., 1993, Fletcher & Schuchard, 1997, Timberlake et al., 1986, Timberlake et al., 1987, Whittaker et al., 1988). In normal vision tolerance to retinal image motion is relatively low: resolution starts to reduce for velocities above $2.5^{o}.s^{-1}$ (Morgan & Benton, 1989, Westheimer & McKee, 1975). In the peripheral

retina, where retinal stabilized images fade easily, linear velocities of up to $10.0^{o}.s^{-1}$ can improve resolution (Bex et al., 2003, Brown, 1972b, Falkenberg et al., 2007).

In 2004 Deruaz and colleagues suggested that fixation instability could be part of a beneficial adaptation mechanism to improve peripheral visual function (Deruaz et al., 2004). Two studies, investigating the trigger for microsaccades in central vision, showed that when retinal image slip drops to values close to zero a dynamic triggering mechanism generates a microsaccade that increases instability (Engbert & Mergenthaler, 2006) and avoids perceptual fading (Martinez-Conde et al., 2006). If a similar mechanism exists during eccentric viewing, eye instability would be beneficial and instability would increase when retinal motion is reduced.

In this experiment I investigated the effect of fixation instability on visual acuity for crowded and noncrowded letters in patients with central scotomas caused by macular disease. The amount of retinal image motion was controlled by an eye tracking system. I anticipated that the results would be similar to those for control subjects: acuity would improve by reducing the amount of retinal image motion caused by fixation instability and the effect would be more pronounced for crowded letters. However, if Deruaz's hypothesis is correct, increased retinal image motion might improve visual acuity. Additionally, if fixation instability is caused by a mechanism triggered by low retinal image motion the eye stability would change during measurements under different conditions. I quantified

fixation stability to verify if the eye instability was affected by retinal image motion. In other words, compensation for instability should improve acuity but would lead to more eye instability.

7.1 Specific method

7.1.1 Participants

Participants were recruited from the Low Vision Clinic at Moorfields Eye Hospital in London. All subjects gave their informed consent to participate, see Chapter 4 for more information. All participants had a central scotoma identified by microperimetry (MP1 microperimeter, Nidek Technologies, Italy). The MP1 microperimeter was also used to determine the location of the preferred retinal locus, the complete protocol has been described in section 4.4. Microperimetry images can be seen in Appendix C, Appendix Table 7.

7.1.2 Apparatus and procedure

The stimuli and procedure were the same as for control subjects in Chapter 6 except for the following: positions tested - visual acuity was measured only at the PRL; exposure time - the target was presented for 700 msec (Figure 7.1); calibration - the eyetracker was calibrated using a 5 point grid; number of blocks (16) - 4 gains × 2 acuities × 2 repetitions (in random order); trials per run - 40 trials; practice - before the first session of

data collection crowded and noncrowded visual acuity was measured for two different gains per visual acuity.

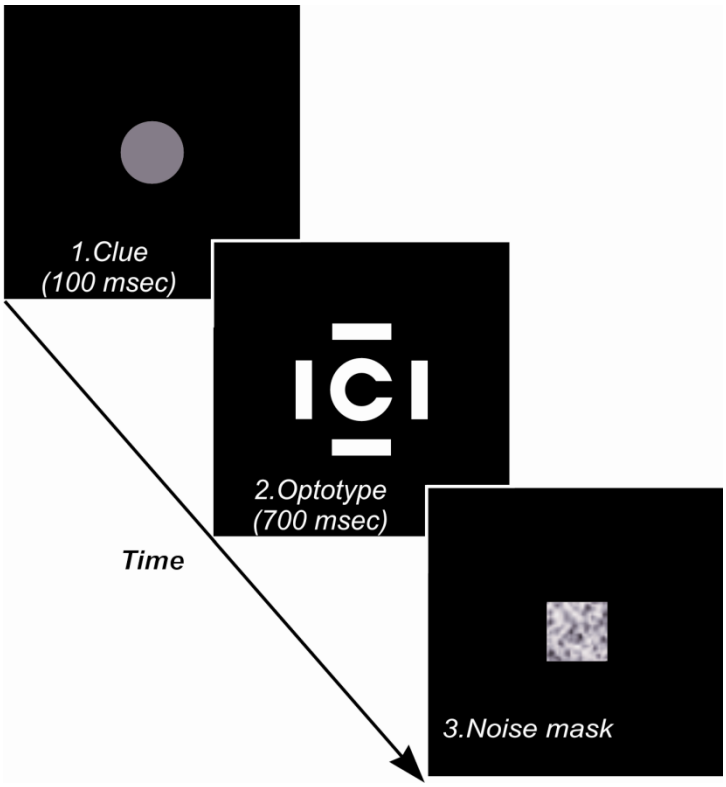

Figure 7.1: Sequence of stimuli in each trial. The optotype was preceded by a cue reducing spatial uncertainty and followed by a noise mask, visible until a response was given.

7.1.3 Statistical analysis

Eye movements were analyzed offline to measure fixation stability. Periods when the optotype was visible were isolated from raw data; trials containing blinks or outliers (data collected outside the calibration area) were excluded from analysis. Eye positions from inter-saccadic intervals were used to calculate the bivariate contour ellipse area (BCEA), in $minarc^2$, containing 68% of the eye positions (Crossland & Rubin, 2002,

Timberlake et al., 1986), mathematical details have been described in section 4.5.2. Prior to statistical analysis all visual acuities were normalized against noncrowded visual acuity for gain 0.

7.2 Results

Eleven subjects were recruited, two subjects had been diagnosed with juvenile macular degeneration and the remainder had age-related macular degeneration. One subject with age-related macular disease withdrew from the study due to the difficulties imposed by the task. The condition was bilateral in all participants and all subjects had dense central scotomas on microperimetry, with the exception of S9 who had relative central scotomas. Age ranged from 25 to 89 yr old and visual acuity in the better eye was between 0.7 and 1.2 logMAR. No patient had more than one PRL identified on either the eyetracker or the MP1 fixation data. A summary of the clinical characteristics of the participants are in Appendix A - Appendix Table 2 and Appendix C- Appendix Table 7. There was a trend for people with JMD to have slightly better visual acuity although this did not reach statistical significance ($p = 0.06$) perhaps due to the small sample size. Mean fixation stability was not significantly different between the JMD and AMD subjects ($p = 0.49$).

7.2.1 Variation of visual acuity with gain

Figure 7.2 shows visual acuity obtained for each condition: A – noncrowded acuity and B – crowded acuity. The effects of gain and crowding on visual acuity were tested using linear mixed models. Both crowding ($p < 0.001$) and gain ($p < 0.001$) had significant effects on visual acuity and the interaction gain × crowding was not significant ($p = 0.601$). Non-crowded visual acuity was better than crowded acuity for all gains, with mean difference of 0.071 logMAR ($p < 0.001$).

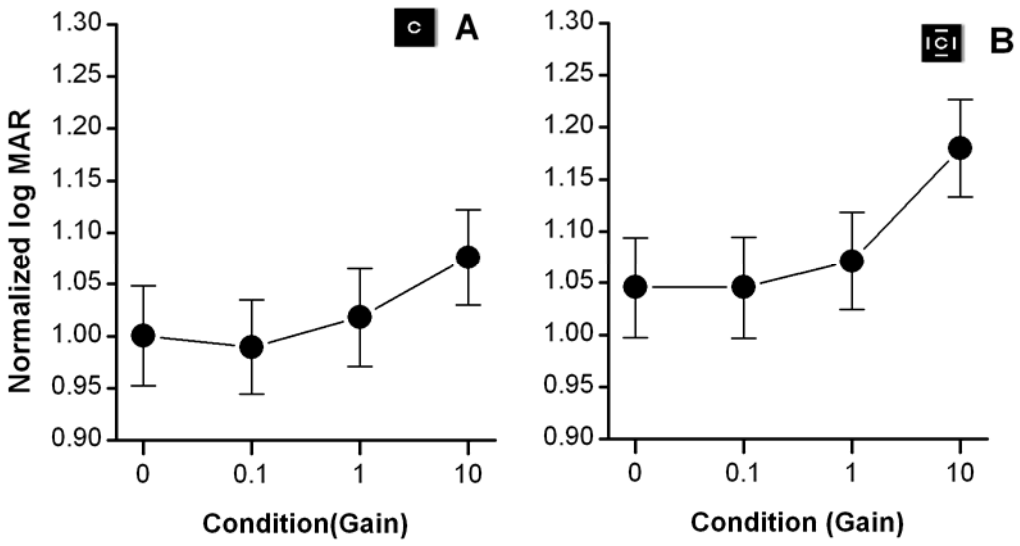

Figure 7.2: Variation of noncrowded (A) and crowded (B) visual acuity with gain. Symbols show the mean for all participants for each gain as estimated by mixed models, the error bars show the 95% confidence interval. All acuities were normalized prior to statistical analysis against noncrowded acuity obtained with gain 0.

Acuity for gain 10 (overcompensation condition) was reduced compared to the no compensation condition by 0.10 logMAR ($p<0.001$), for both crowded and noncrowded stimuli. These results show that reducing retinal image motion (gains 0.1 and 1) had no effect on patients' visual acuity; however, increased retinal image motion (gain 10) had a detrimental effect on acuity. All results are summarised in Table 7.1.

Table 7.1: Mean visual acuity, in logMAR, obtained for different conditions for crowded and noncrowded targets. Values in brackets show the 95% confidence interval.

	gain 0 (baseline)	**gain 1**	**gain 2**	**gain 3**
noncrowded	1.27 (±0.14)	1.27 (±0.13)	1.27 (±0.13)	1.37 (±0.17)
Crowded	1.31 (±0.16)	1.33 (±0.14)	1.34 (±0.11)	1.45 (±0.12)

7.2.2 Variation of fixation stability with gain

Figure 7.3 shows the variation of fixation stability with gain during visual acuity measurements: A – noncrowded acuity and B – crowded acuity. Gain had a significant effect on fixation stability ($p < 0.001$), but there was no effect of crowding ($p = 0.23$) or interaction of gain × crowding ($p = 0.18$).

Fixation stability for crowded and noncrowded stimuli gain 0 (mean BCEA: 9795 minarc^2) was significantly better than all other gains (mean BCEA: 21748 minarc^2, $p = 0.001$ for gain 0.1; mean BCEA: 21748 minarc^2; $p <$

0.001 for gain 1; mean BCEA: 17783 minarc^2; p = 0.014 for gain 10). There was no significant difference in fixation stability between gain 0.1, 1.0, and 10. BCEA values were in the same range as those found in previous studies (mean: 20361 minarc^2, 95 %: 10160 minarc^2 - lower limit: 30561 minarc^2 - upper limit) (Bellmann et al., 2004, Crossland et al., 2004b, Fletcher & Schuchard, 1997, Macedo, Nascimento, Gomes & Puga, 2007).

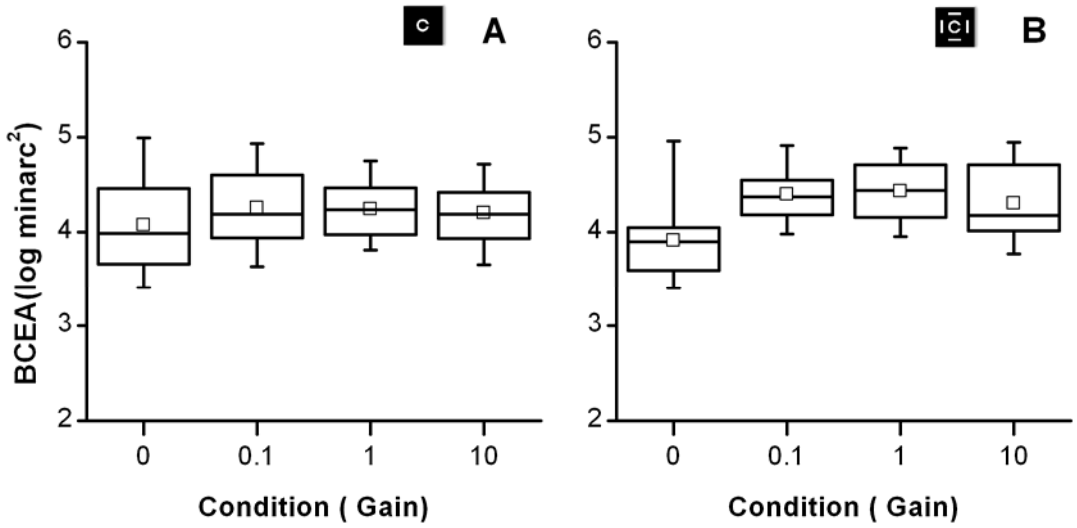

Figure 7.3: Variation of fixation stability with gain during noncrowded (A) and crowded (B) visual acuity measurements. The length of the box is the interquartile range (25th – 75th percentiles) and whiskers represent the 5th – 95th percentiles. Inside the box: squares show the means and the horizontal lines show the median. BCEA was calculated in minarc^2 and log10 transformed before statistical analysis to approximate a normal distribution.

7.2.3 Effect of gain on retinal image speed

Figure 7.4 shows the variation of the eye speed and retinal image speed calculated offline during a typical trial for gain 10. In this trial no saccades were detected by our criteria. Frames when the retinal image speed was very high correspond to large overshoots of the target in the monitor that sometimes caused the perception of multiple targets.

Retinal image speed was calculated for the inter-saccadic drift. Microsaccades were included because they were not detected by the saccade detection criteria. The baseline retinal image speed (gain 0) was 8.7º.s^{-1}, significantly higher than gain 0.1 (v = 4.8º.s^{-1}) and gain 1 (v = 3.0º.s^{-1}); but significantly lower than gain10 (v = 12.4º.s^{-1}).

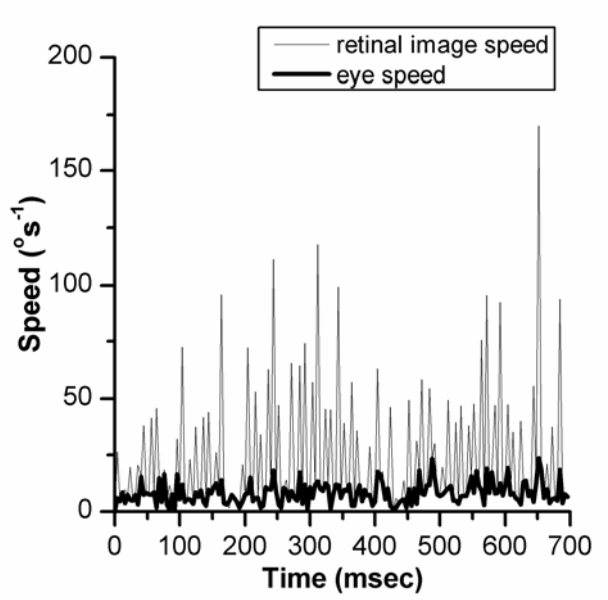

Figure 7.4: Profile of the eye speed (thick line) and retinal image speed (thin line) of the target during a typical trial for gain 10.

7.3 Discussion

In this experiment I measured crowded and noncrowded visual acuity whilst compensating for fixation instability by controlling retinal image motion in patients with macular scotomas. The effects of controlling retinal image motion on visual acuity and on fixation stability are discussed separately.

7.3.1 Effect of gain on visual acuity

Compensating for fixation instability in people with macular disease failed to improve visual acuity: no compensation (gain 0), partial compensation (gain 0.1) and total compensation (gain 1) all produced similar acuity. These results suggest that fixation instability of these patients does not reduce visual acuity for briefly exposed stimuli.

These results are in agreement with studies showing no reduction or some improvement in normal peripheral visual acuity for moving targets. In these studies retinal image motion was caused by normal fixational eye movements or was increased by manipulating the target's velocity (Brown, 1972b, Falkenberg et al., 2007, Millodot, 1966). In people with macular scotoma I expected improvement of visual acuity when motion was compensated because retinal image motion is naturally increased due to their fixation instability. The lack of a difference across gain 0, gain 0.1, and gain 1 for both crowded and uncrowded visual acuities might indicate

that:

(i) Patients have adapted to the amount of retinal image motion caused by their “normal” fixation instability;

(ii) Independently of any adaptation, fixation instability in patients is within the tolerance of the part of the retina they use during eccentric viewing (and that might be part of the reason why that area is used as the PRL);

(iii) Limitations of our stabilization system reduced the size of any observed effect (see below).

Crowded visual acuity was worse than noncrowded visual acuity. The difference of 0.071 logMAR units between acuities is within values found in previous studies. In other studies involving patients, the reduction for crowded acuity varied from 0.006 logMAR units (Pardhan, 1997) to 0.11 logMAR units (Cacho, Dickinson, Reeves & Harper, 2007). Other studies found higher differences, up to 0.15 logMAR units, in healthy peripheral retina (Leat et al., 1999b).

The effect of gain did not differ between crowded and noncrowded acuity. Previous studies showed that visual acuity measured with isolated letters would be minimally affected by very high levels of retinal image motion (Badcock & Wong, 1990, Deruaz et al., 2004). However, I expected higher variation between gains under crowded conditions because crowding would increase blur for high levels of retinal image motion (Morgan & Benton, 1989). In a study measuring peripheral acuity in healthy retina with jittering targets, Falkenberg et al. (2007) failed to find any interaction

between jitter and crowding. In the same study, reading speed for sequentially presented words reduced when jitter increased. The authors suggested that this occurred because jittering words increased crowding.

Another contribution to the lack of interaction between gain and crowding is likely to be the characteristics of the participants. The group was small and heterogeneous regarding the PRL location. PRLs were in different directions from the fovea and at different eccentricities (as indicated by the visual acuity that can be seen in Appendix C), and it is known that retinal location changes the effect of crowding (Toet & Levi, 1992, Tripathy & Cavanagh, 2002). The number of patients was not sufficient to test the interaction between gain, PRL eccentricity and PRL direction (Fine & Rubin, 1999a, Fine & Rubin, 1999b, Petre et al., 2000).

7.3.2 Effect of gain on fixation stability

When retinal image motion was controlled by the eyetracker, the magnitude of eye movement during fixation increased when compared to no compensation (gain 0). However, it remained constant under all compensation conditions (gains 0.1, 1.0, and 10). Reduction in eye stability under compensation conditions was probably caused by target motion. Atypical smooth pursuit can occur when the target is perceptually moving despite the retinal image speed is zero, for example, when following an after image (Dubois & Collewijn, 1979, Wyatt & Pola, 1983).

Under the three compensation conditions eye instability (BCEA) remained constant. If fixation instability was caused by a mechanism to increase retinal image motion in order to maintain target's visibility, the three gains should yield variation in eye stability. Accordingly, reduced retinal motion (gain 0.1 and gain 1) would increase eye instability and increased retinal motion (gain 10) would reduce eye instability. Based on their results, Deruaz et al. (2004) argued that training fixation control, leading to a reduction in retinal image motion, might reduce patients' vision. They considered that fixation instability could be part of a mechanism to maintain the visual target moving between adjacent or separated loci in the retina. Our results show that eye instability was independent of the retinal image motion imposed by the 3 gains. This argues against a possible mechanism increasing eye instability to prevent low retinal image motion leading to improvements in patients' vision. Recently, Reinhard et al (2007) observed that patients with macular disease tend to use separated or adjacent loci during visual tasks but they attributed that to patients' poor adaptation to the disease (Reinhard et al., 2007). These results add evidence that fixation instability is a consequence of poor oculomotor control and not a strategy to enhance eccentric viewing.

7.3.3 Limitations of the study

The stabilization system has limitations due to the delay between the real eye movement and the time its effect is visible in the screen. Due to this delay the mean retinal image velocity for gain 0, gain 0.1 and gain 1 was

always below $10^{o}.s^{-1}$, which might have reduced the size of any effect of these gains on visual acuity. Also, unstable fixation is likely to affect the overall effect of stabilization because relatively widely separated retinal areas might have been used for different eyetracker calibrations and/or drift corrections. This would lead to the optotype being stabilized in the peripheral retina but not always in the same area.

A further limitation is that measurements were performed monocularly. These effects are likely to be applicable when viewing binocularly because binocular oculomotor behaviour is thought to be driven by the better eye (Kabanarou et al., 2006, Tarita-Nistor et al., 2006b).

7.4 Conclusion

This experiment shows that stabilizing the retinal image does not improve visual acuity in patients with macular disease. Increasing retinal image motion reduces visual acuity for crowded and noncrowded targets. This study gives further evidence that fixation instability is a consequence of impaired oculomotor control rather than an adaptation made to improve visual function. Training oculomotor control can improve reading speed without a significant improvement in acuity (Seiple et al., 2005). The next 2 experiments explore the effects of correcting fixation instability in reading.

Chapter 8. Reading with simulated scotoma

The ability to read with the peripheral retina is reduced by its poor resolution (Banks et al., 1991, Green, 1970, Mandelbaum & Sloan, 1947), reduced visual span (Cheong et al., 2008, Crossland & Rubin, 2006, Legge et al., 1997, Legge et al., 2007) and crowding (Bex et al., 2003, Leat et al., 1999b, Levi, 2008, Toet & Levi, 1992). Peripheral retina is also less able to control eye movements although the effect of this oculomotor impairment remains under scrutiny.

There is evidence that poor saccade control leads to a reduction in reading speed (Bullimore & Bailey, 1995, Crossland & Rubin, 2006, McMahon et al., 1991, Rubin & Feely, 2009). People with macular scotoma make more forward and more regressive saccades than normal readers. Reading RSVP, instead of continuous text, reduces the need for saccades and leads to faster reading in simulated (Chung, Mansfield & Legge, 1998, Fine & Rubin, 1999b) and pathological scotoma (Rubin & Turano, 1994). RSVP reading can be faster when the exposure time is modulated by word size (Aquilante, Yager, Morris & Khmelnitsky, 2001, Arditi, 1999). Arditi et al

(1999) suggested that effect is caused as the time needed to read the word is based on its size and difficulty. RSVP reading is slower in people with pathological scotomas than in control subjects reading at similar eccentricities. People with pathological scotomas need to make intra-word saccades during RSVP and this might be due to their reduced visual span. Different authors proposed that occurs because peripheral retina used by normal-vision subjects is healthier than the peripheral retina used by low-vision subjects (Cheong et al., 2007, Legge et al., 1997 350, Rubin & Turano, 1994).

The need to make intra-word saccades can be reduced by presenting scrolling text. However, there is no difference between scrolled reading speed and RSVP reading speed for a low vision populations (Fine & Peli, 1995, Fine & Peli, 1998). Neither RSVP nor scrolled text eliminates the effect of fixation instability that has been linked with reduced reading performance (Crossland et al., 2004a, Rubin & Feely, 2009, Seiple et al., 2005). Unstable fixation might increase motion blur (Chung & Levi, 1997) to levels that lead to a reduction in contrast (Burr & Ross, 1982), reduction of visual span (Cheong et al., 2007, Cheong et al., 2008) and an increase of crowding (Bex et al., 2003, Falkenberg et al., 2007).

In this experiment reading speed was measured in subjects with simulated scotoma whilst modulating the retinal image speed by presenting gaze-contingent words. Reading speed was also assessed when intra-word saccades were possible (the screen was not blanked during saccades),

and when intra-word saccades were not possible (the screen was blanked during saccades) with words visible always left justified during fixations. Reading was assessed in upper and lower visual field to verify the optimal region of retina to read with.

My expectation was that the fastest reading speed would be achieved when fixation instability was compensated and the screen was not blanked during saccades, in the lower visual field.

8.1 Specific method

8.1.1 Participants

Eight normally sighted subjects served as observes in this experiment. All were naïve to the purpose of the study. One subject participated in the acuity experiment (Chapter 6). Subjects were aged between 25 and 31 years old and no participants had any eye or neurological disease. All were native English speakers. See section Chapter 4 for further participants information.

8.1.2 Apparatus

The eyetracker and monitor settings have been described in sections 4.3 and Chapter 6. The exposure time was controlled by two Quest staircases, applied to the upper and the lower field independently, as described in section 4.3.3.3.

8.1.3 Stimuli

Sentences were presented using RSVP. Font size was selected based on the resolution obtained in Chapter 6. At 5 deg eccentricity, crowded visual acuity was 1.3 logMAR at 50 cm, (x-height 1.8 cm, equivalent to a visual angle of 1.7º). This text size has been used in other reading studies at the same eccentricity (Chung, 2002). The sentence database was generated using the method described in section 4.3.3.5. Sentences were constructed of 5 words (Crossland, 2008). The profile of word length, in characters, is shown in Figure 8.1.

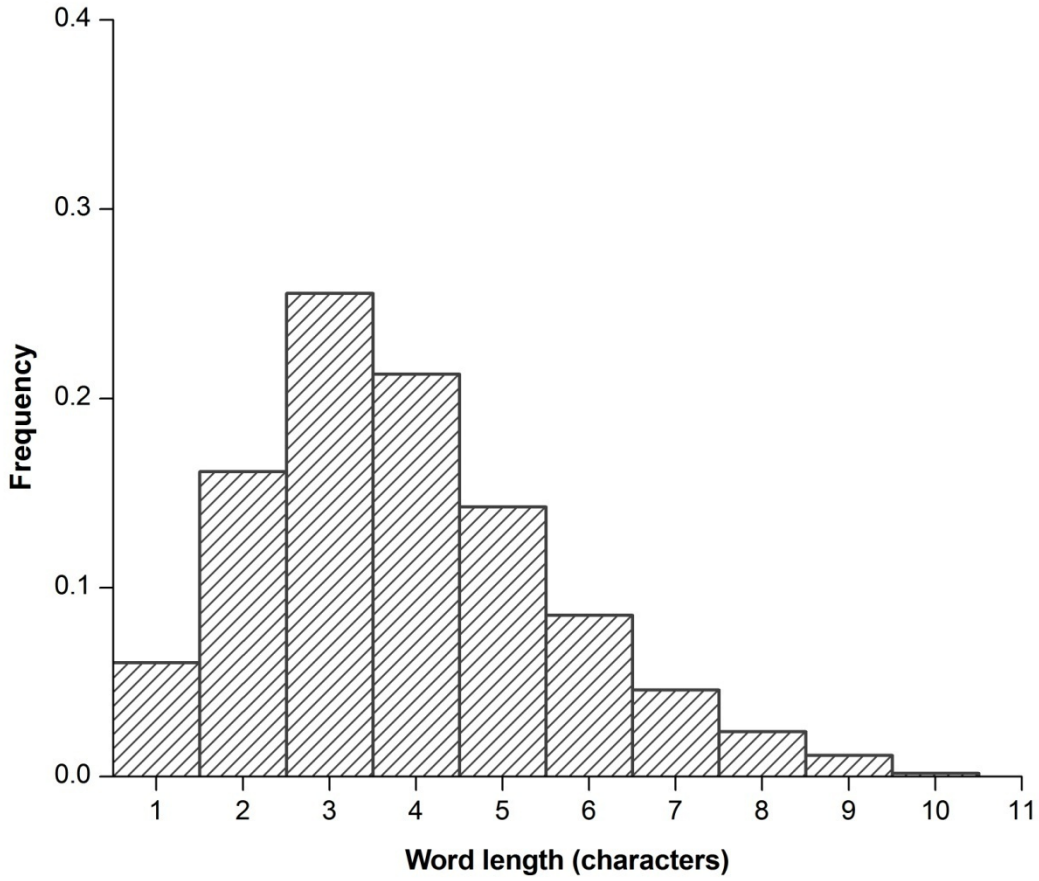

Figure 8.1: Distributions of word lengths in the sentence database.

Words were presented, left justified at 5º (distance gaze position-centre of the letter) above or below the fovea as shown in Figure 8.2. The first word was preceded by a row of capital Xs and a beep. The last word was followed by a noise mask. No feedback was given.

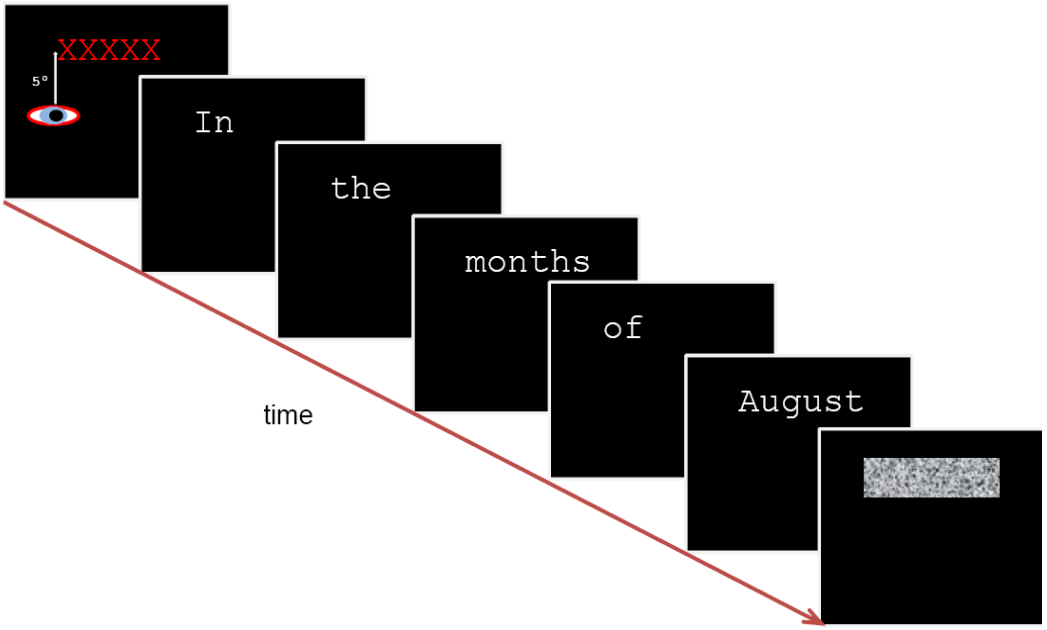

Figure 8.2: The sequence of stimuli in the monitor in a complete trial during RSVP. Text was white against a black background. The cartoon in the first panel shows the distance, in visual angle, between the eye and the word centre that was kept constant at 5º.

8.1.4 Procedure

Observers were positioned 50 cm away from the monitor resting the chin in a chinrest. Reading speed was measured using the dominant eye and the fellow eye was patched. To read aloud subjects were allowed to raise their chin, slippage of the eyetracker headband was corrected by drift correction

before every trial. Two blocks of practice was performed, under randomly chosen conditions, before data collection. In addition, one block of practice was performed each day that new data were collected. Different sets of sentences were used for data collection and practice.

Six blocks were performed in each data collection session, with the two sessions being separated by one week or more. A break was given every two blocks. Sentences did not repeat within a session.

Table 8.1: The 6 conditions in which reading speed was measured

Condition	word velocity	gain	screen during saccades
1	0	NA (0)	not blanked
2	eye vel.	1	blanked
3	10 × eye vel.	10	blanked
4	0.1 × eye vel	0.1	not blanked
5	eye vel.	1	not blanked
6	10 × eye vel.	10	not blanked

Word motion was modified according to the conditions in Table 8.1. Baseline data (condition 1) were collected with stationary words being presented in the monitor centre. In all other conditions words were presented under gaze-contingent conditions using the eyetracker. Eye movements were modulated by gain as described in section 4.3.3.3 to change the stability of the words during fixations. Saccades were detected by the criteria described is section Chapter 6. Briefly, gain 1 corresponds to compensated fixation instability, gain 10 corresponds to over-compensated fixation instability, and gain 0.1 corresponds to semi-

compensated fixation instability.

In conditions 2 & 3 the screen was blanked during saccades. During fixations words were visible and moved in accordance with the fixation compensation level of the condition. The screen was blanked during saccades. During frames in which the monitor was blanked the word position was updated based on the real eye position (not modulated by gain), to avoid possible positional errors in the first frame after a saccade.

In conditions 4-6 intra-word saccades were possible because the screen was not blanked. As in the previous conditions, during fixations words moved in accordance with the fixation compensation level of the condition. During saccades, words remained fixed on the screen horizontally but were moved vertically to compensate the vertical component of saccades. Trials were repeated if the vertical amplitude of saccade was >1º or any part of the word was placed outside the screen. Drift correction was applied between sentences.

Sentences were considered as correct when four of five words were reported correctly (80% accuracy criterion).

8.1.5 Data analysis

Eye movements were computed offline using a program written in Matlab which computed the number of saccades per run, drift amplitude, drift

velocity, and retinal image speed during periods when the words were visible. Saccades were detected by the eyetracker algorithm according to the criteria defined in Chapter 6 and were selected from the raw data file using a Matlab program, see Appendix D for a program example.

8.2 Results

8.2.1 Reading speed

Reading speed for condition 2 (compensated fixation instability, screen blanked during saccades) was significantly higher than baseline, with a mean improvement of 23% (p = 0.039). Reading speed was not significantly different to baseline for all other conditions. Results for each condition are summarized from Table 8.2 and Figure 8.3.

Table 8.2: Summary of the effects of each condition on reading speed. Differences were obtained by subtracting results for conditions in the first column from the condition defined in the remaining columns headings.

	Cond. 1	**Cond. 2**	**Cond. 3**	**Cond. 4**	**Cond. 5**	**Cond. 6**
Cond. 1	-	-0.23*	0.15	-0.076	-0.21	0.14
Cond. 2	-	-	0.38***	0.16	0.018	.037***
Cond. 3	-	-	-	-0.23*	-0.36***	0.01
Cond. 4	-	-	-	-	-0.14	0.22
Cond. 5	-	-	-	-	-	-0.35***

§ Significance levels are: 0.05 (*), 0.01 (**), and 0.001 (***)

Reading speed improved from the first to the second data collection

session, mean improvement 20.9% (p = 0.01). Reading speed in the upper field was similar to that in the lower field (p = 0.41).

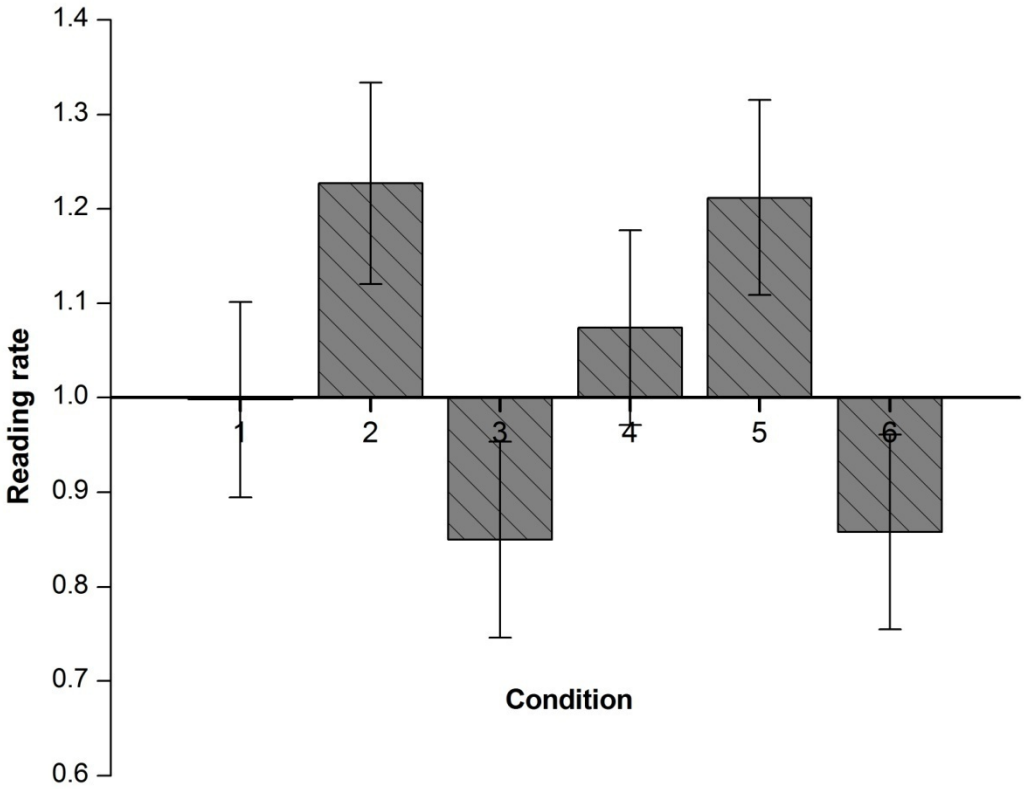

Figure 8.3: Reading rate for 6 conditions, rates shown were obtained after dividing results for each condition by results for condition 1. *condition 1*: baseline - no compensation; *condition 2*: gain 1 & screen blanked during saccades; *condition 3*: gain 10 & screen blanked during saccades; *condition 4*: gain 0.1 & screen not blanked during saccades; *condition 5*: gain 1 & screen not blanked during saccades; *condition 6*: gain 10 & screen not blanked during saccades.

8.2.2 Retinal image speed during fixations

As expected retinal image speed was much higher than baseline for conditions with gain 10 and reduced to about ½ of baseline RIS for conditions with gain 1. RIS for gain 0.1 was not significantly different from baseline. All results are summarized in Figure 8.4 and Table 8.3

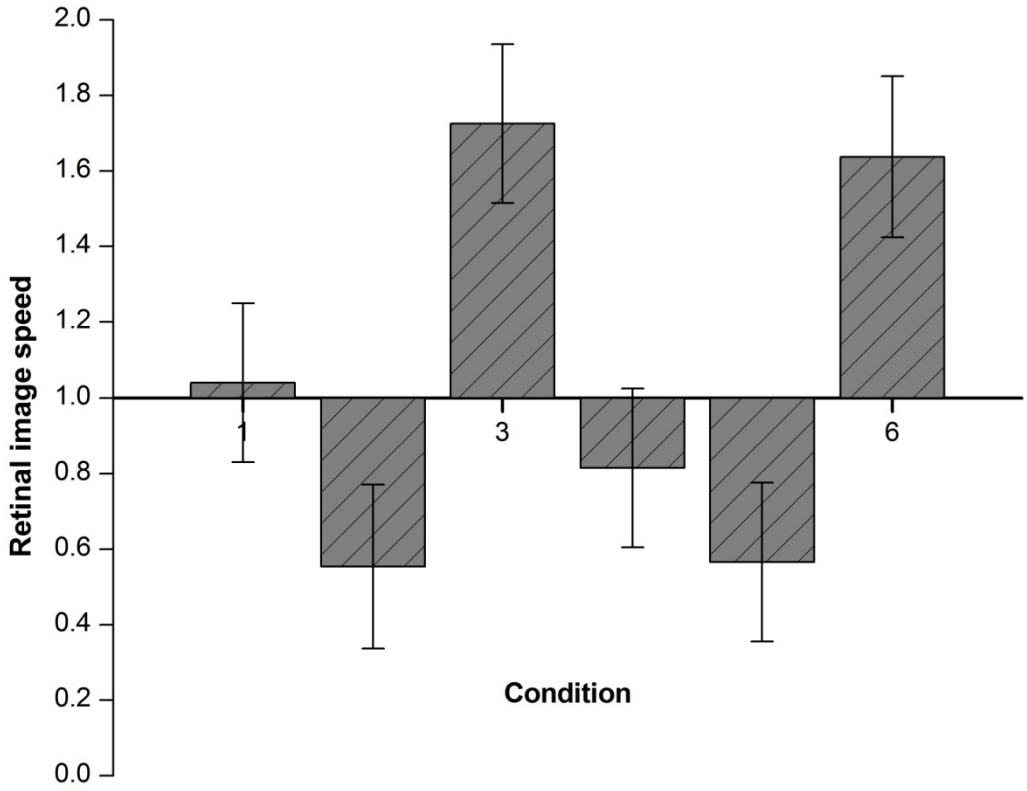

Figure 8.4: Retinal image speed for the 6 conditions. *condition 1*: baseline - no compensation; *condition 2*: gain 1 & screen blanked during saccades; *condition 3*: gain 10 & screen blanked during saccades; *condition 4*: gain 0.1 & screen not blanked during saccades; *condition 5*: gain 1 & screen not blanked during saccades; *condition 6*: gain 10 & screen not blanked during saccades.

Table 8.3: Comparison of the retinal image speed in all conditions. Differences were obtained by subtracting results for conditions in the first column by the condition defined in the remaining columns headings.

	Cond. 1	**Cond. 2**	**Cond. 3**	**Cond. 4**	**Cond. 5**	**Cond. 6**
Cond.1	-	0.49***	- 0.68***	0.23	0.48***	-0.59***
Cond. 2	-	-	-1.17	-0.26	-0.01	-1.08***
Cond. 3	-	-	-	0.91***	1.16***	0.08
Cond. 4	-	-	-	-	-0.25	-0.82***
Cond. 5	-	-	-	-	-	1.07***

§ Significance levels are: 0.05 (*), 0.01 (**), and 0.001 (***)

8.2.3 Fixation duration

The effect of gain was significant for fixation duration ($p = 0.002$) as it was the effect of session ($p < 0.001$). Fixation duration for conditions 3 & 6 was significantly prolonged compared with condition 5, mean difference was 15% in both cases ($p = 0.02$). The mean reduction in fixation duration from session 1 to session 2 was 10%.

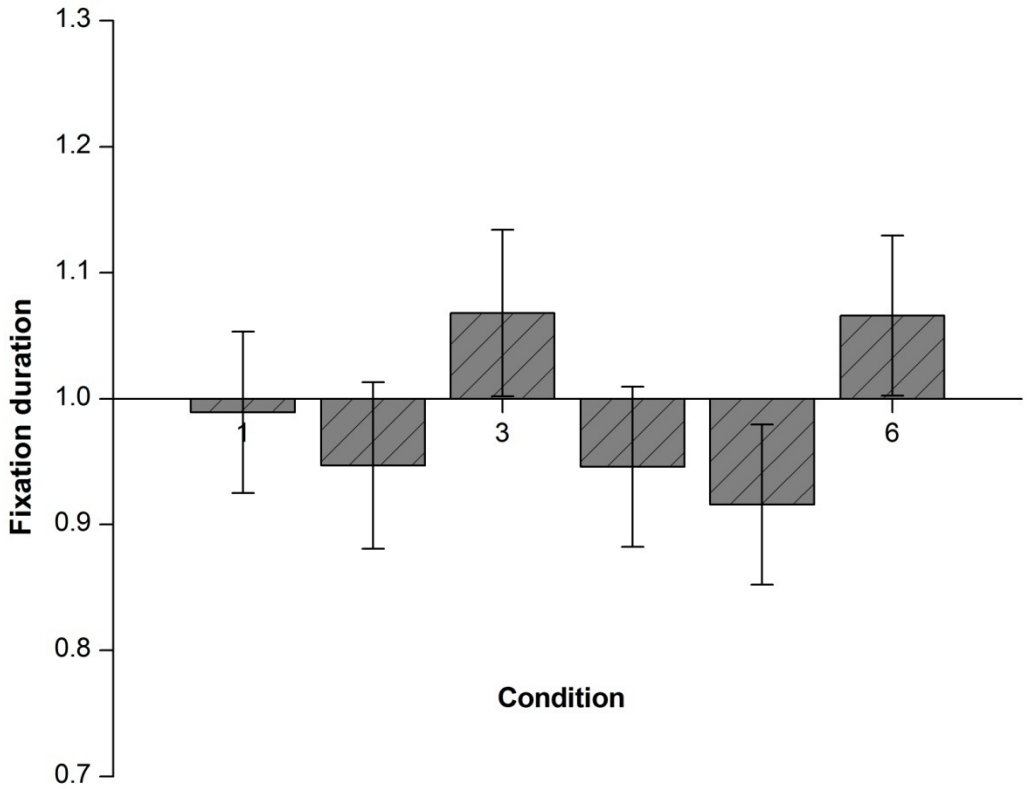

Figure 8.5: Fixation duration for the 6 conditions. *condition 1*: baseline - no compensation; *condition 2*: gain 1 & screen blanked during saccades; *condition 3*: gain 10 & screen blanked during saccades; *condition 4*: gain 0.1 & screen not blanked during saccades; *condition 5*: gain 1 & screen not blanked during saccades; *condition 6*: gain 10 & screen not blanked during saccades.

8.3 Discussion

This experiment investigated the effect of fixation instability when reading with simulated central scotoma. Reading speed increased when fixation

was compensated (gain 1)[1] and reduced when fixation was over-compensated (gain 10).

When fixation was over-compensated retinal image speed was ~60% more than the limit that observers would experience normally. Unstable fixation is likely to cause a reduction in reading due to motion blur by:

i) Increasing spatial thresholds (Burr, 1980, Burr & Ross, 1982, Chung & Bedell, 2003, Chung & Levi, 1997) as seen in Chapter 6 for crowded letters;

ii) Increasing spatial interference (Bex et al., 2003, Chung & Bedell, 1995, Chung, Legge & Tjan, 2002, Falkenberg et al., 2007, Levi, Klein & Aitsebaomo, 1985);

iii) Indirectly, by reducing contrast sensitivity (Burr & Ross, 1982) that reduces visual span (Legge et al., 1997).

It is surprising that in condition 5 reading speed was not different from baseline. Here fixation was compensated and intra-word saccades were allowed, which should allow scanning of longer words and effective reading. Legge et al (2001) estimated that visual span at 5º eccentricity in normal retina should be 10 or more characters (Legge et al., 2001). Given the size of the words used (10 characters or less, Figure 8.1), scanning should not be necessary because the visual span covered all characters. In these conditions intra-word saccades were not important for reading.

[1] Fixation compensated and screen blanked during saccades

Fixation duration was higher for gain 10 (condition 3 & 6) than for all other conditions. Legge et al (1997) found that prolonged fixations occur when contrast is reduced. In the current experiment over-compensating fixation instability might also have caused contrast reduction due to motion blur. Falkenberg et al (2007) speculated that the additional time it takes to read scaled text has to do with moving “peripheral attention” along the word due to a limited visual span. These two explanations are linked because, as Legge et al (1997) showed, contrast reduction results in shrinkage of visual span, leading to prolonged viewing (Legge et al., 1997).

No difference has been found between the upper and the lower visual field. The distribution of retinal ganglion cells implies better resolution in the lower field (Curcio & Allen, 1990, Green, 1970), but reading does not correlate with resolution and cannot be predicted by cell density (Legge et al., 1992, Petre et al., 2000). Factors such as attention (Altpeter, 2000, He et al., 1996) and oculomotor control (Skrandies, 1987) also influence reading rates. An additional source of variability in reading speed is word information from the upper part of a word (Fiset, Blais, Ethier-Majcher, Arguin, Bub & Gosselin, 2008). The lack of control for these variables may explain the reason why the field effect was not visible in this experiment.

Reading speed improved from session 1 to session 2. Practice normally leads to better performance in the peripheral retina. This is due a combination of improvements in attention, oculomotor control (Fornos et al., 2006, He et al., 1996, Lee, Kwon, Legge & Gefroh, 2010, Zeevi & Peli,

1979) and, eventually, perceptual learning (Yu, Legge, Park, Gage & Chung, 2010).

8.3.1 Limitations

The limitations of our stabilization system have been discussed in section 6.3.

8.4 Conclusion

In summary, when fixation instability was compensated reading speed increased and reduced when fixation instability was over-compensated. Fixation instability increases retinal image motion which might be causing motion blur leading to worse visual performance.

Chapter 9. Reading with compensation for fixation instability at the PRL

People with central scotoma read RSVP more slowly than control subjects, reading at the same eccentricity, or subjects with low vision but without central scotoma. While comparing page reading with RSVP, Rubin & Turano (1994) found that in patients with central scotoma RSVP reading speed increases by a factor of 1.5 and in patients without central scotoma, it increases by a factor of 2.1. The modest improvement observed in patients was justified by the time that patients need for planning and execute intra-word saccades and by a possible extension of the retinal lesion outside the visible area. It has been suggested that scrolling text, that does not require saccades planning, could be more beneficial than RSVP. Fine & Peli (1995) compared RSVP with scrolling text and failed to found differences in reading speed in these two formats. Fixation instability is likely to have a role on reducing reading speed but none of these formats compensates for it. Results of the previous experiment (Chapter 8) showed that fixation instability can be detrimental for RSVP in normal

control subjects.

In this experiment reading speed was measured in subjects with macular disease whilst modulating retinal image speed by presenting gaze-contingent words. The aim was to assess the effect of compensating for fixation instability on RSVP reading speed. It was expected that reading speed would improve for conditions where fixation instability was compensated, particularly, when intra-word saccades were permitted.

9.1 Specific method

9.1.1 Participants

Five patients with macular disease and dense central scotomas in both eyes were recruited. Two subjects had also participated in the acuity experiment (Chapter 7). No participants had any eye or neurological disease and all were native English speakers. Relevant clinical information about these subjects is summarized in Table 9.1.

Table 9.1: Participants' characteristics including PRL location. PRL location was defined according to the convention defined in section 4.4. The images of microperimetry can be seen in Appendix C. CPS: Critical Print Size at 20 cm; MRS: Maximum Reading Speed.

ID	**Age/Sex**	**VA** (LogMAR)	**Eye tested**	**CPS** (LogMAR)	**MRS** (wpm)	**PRL location**
S1	71/F	1.0	RE	1.7	80	Left
S2	54/F	0.7	LE	1.5	120	Below
S3	86/F	0.9	RE	1.5	60	Right/Below
S4	57/M	0.8	RE	1.2	150	Left
S5	54/M	1.0	RE	1.4	150	Right

9.1.2 Clinical tests

Distance visual acuity measurements were made with an ETRDS chart. Critical print size was assessed using the MNREAD acuity chart at 20 cm. For testing at 20 cm appropriate refractive correction was provided. Clinical tests have been described in section 4.2.

9.1.3 Apparatus

The eyetracker and monitor settings have been described in section 4.3. Participants had their PRL location characterized by microperimetry as described in section 4.4, microperimetry results can be seen in Appendix C, Appendix Table 8. Word exposure time was controlled by a Quest staircase (section 4.3.3.5).

9.1.4 Stimuli

Words were presented centred with respect to gaze position. Text size was scaled according to the critical print size measured by the MNREAD test (Table 9.1, see section 4.2.3 for details).

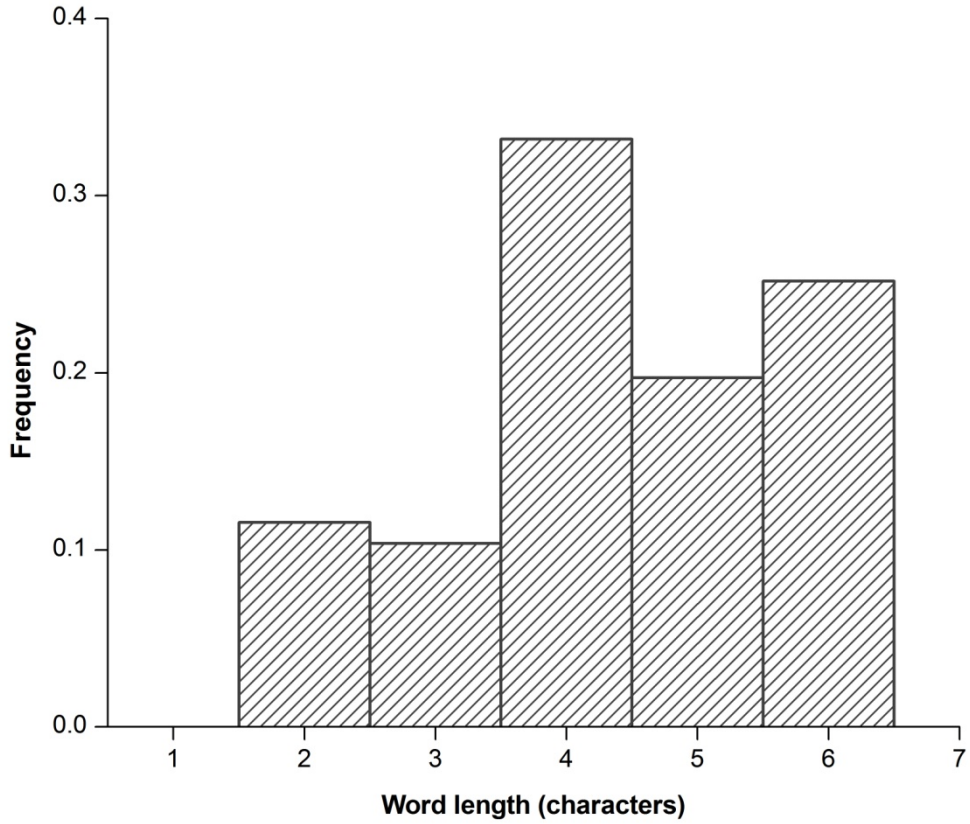

Figure 9.1: Distribution of word lengths in the sentence database.

The sentence database was generated using the method described in section 4.3.3.5 (Crossland et al., 2008). The original set of sentences was filtered to exclude those with maximum word length of more than six characters. This was needed to reduce the number of times the word reached the boundaries of the monitor given the large size of the text. The distribution of word length is shown in Figure 9.1. The number of

characters per sentence was between 16 and 20 plus spaces. The first word was preceded by a row of capital Xs and a beep; the last word was followed by a noise mask (Figure 9.2). No feedback was given.

9.1.5 Procedure

The eye with the best visual acuity was tested at a viewing distance of 50 cm. The fellow eye was occluded with an eye patch. The procedure for data collection and pre-experiment practice were the same as those described in section 8.1.4. In brief, in condition 1, words appeared at a fixed location at the centre of the screen (no compensation). In condition 2 the word location was updated every 10 msec to compensate for fixation instability. If the patient made a saccade the screen was blanked and the eye and word velocities were the same (gain 1, screen blanked during saccades). Condition 3, compensation for fixation instability and during saccades the text remained visible (gain 1; screen not blanked during saccades). In condition 4, instability was over-compensated, the text velocity was 10× the eye velocity. During saccades the text remained visible and static (gain 10; screen not blanked during saccades). Reading speed was assessed twice under each of the four conditions (Table 9.2), for a total of 8 blocks of 30 sentences each.

Trials were repeated when the eyetracker lost eye position or the word went out of the screen. Sentences were considered as correct when 3 out of 4 words were read correctly (75% accuracy criterion).

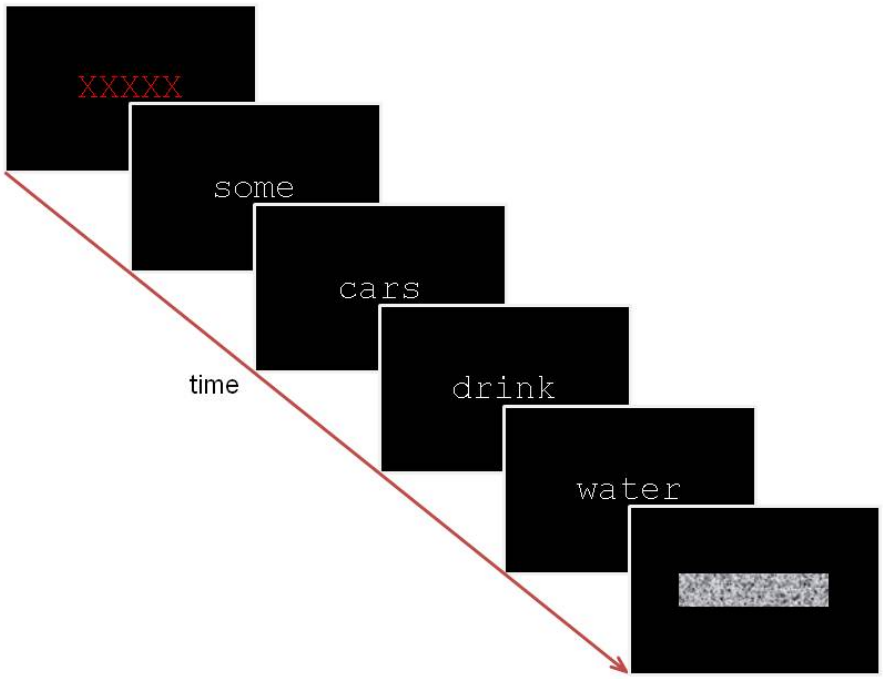

Figure 9.2: The sequence of stimuli in the monitor in a complete trial during RSVP. Text was presented white against a black background. The first word was preceded by a row of Xs and the last word was followed by a noise mask.

Table 9.2: Conditions in which reading speed was measured

Condition	word velocity	gain	screen during saccades
1	0	NA (0)	Not blanked
2	eye vel.	1	Blanked
3	eye vel.	1	Not blanked
4	10 × eye vel.	10	Not blanked

9.1.6 Data analysis

As in the previous experiment (Chapter 8) a Matlab programme was used to select the eye movements data (see Appendix D). Results for conditions 2, 3 & 4 were normalized with respect to condition 1 (no compensation), prior to statistical analysis to factor out differences in baseline reading speed across subjects.

9.2 Results

9.2.1 Reading speed

Figure 9.3 shows individual reading speed for all conditions. Inter-individual results are variable but results for each condition are consistent. Figure 9.4 shows the comparison between conditions considering mean results from all participants.

Reading with gain 1 (condition 3) was 40% faster ($p = 0.034$) than baseline (condition 1), and 55% ($p = 0.01$) faster than in condition 4 (gain 10). Reading speed for condition 4 (gain 10) was not significantly different from baseline. Values are given in Table 9.3.

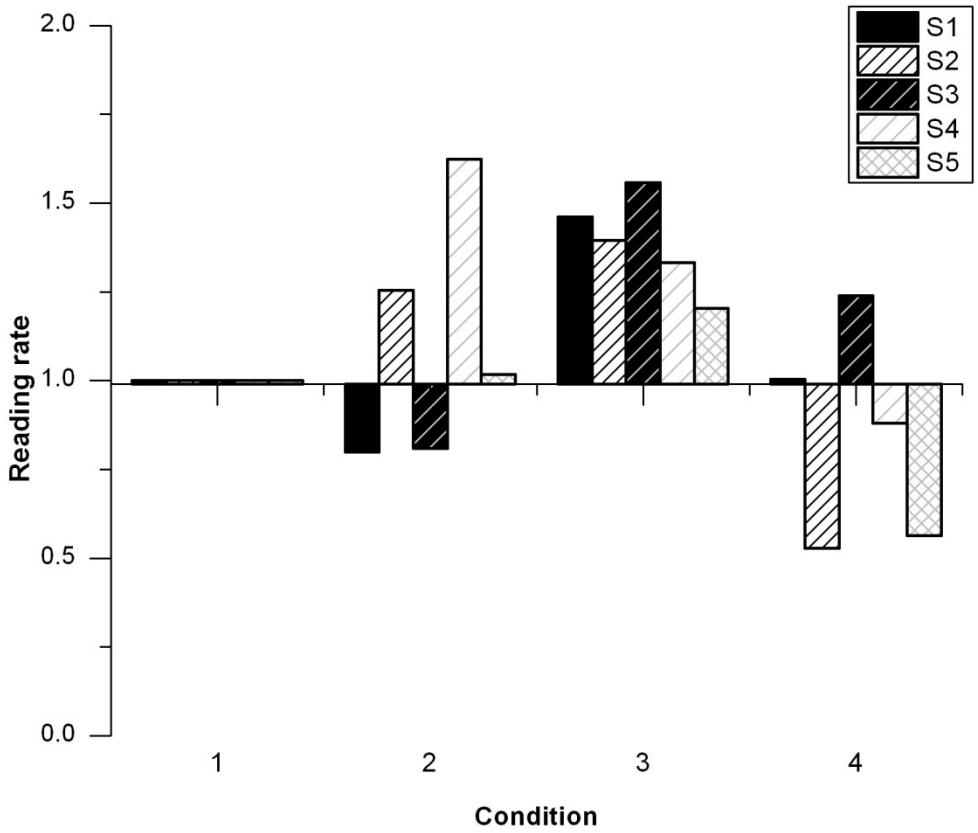

Figure 9.3: Individual reading speeds for the four conditions. The black columns represent slow readers, S1 & S3, and white columns, fluent readers. A fluent reader was defined as someone reading more than 80 words per minute and a slow reader as someone reading less than that. See Table 2.1.

The Ratio RSVP/MNREAD in the last column of Table 9.3 does not aim to show any advantage of RSVP over MNREAD because these values are not directly comparable. The most evident difference is in the metric. MNREAD was measured at 100% correct while RSVP was measured at 75% correct. This ratio only reassures that in this experiment RSVP reading was generally faster. The opposite would contradict the assumptions of this thesis (Chapter 3).

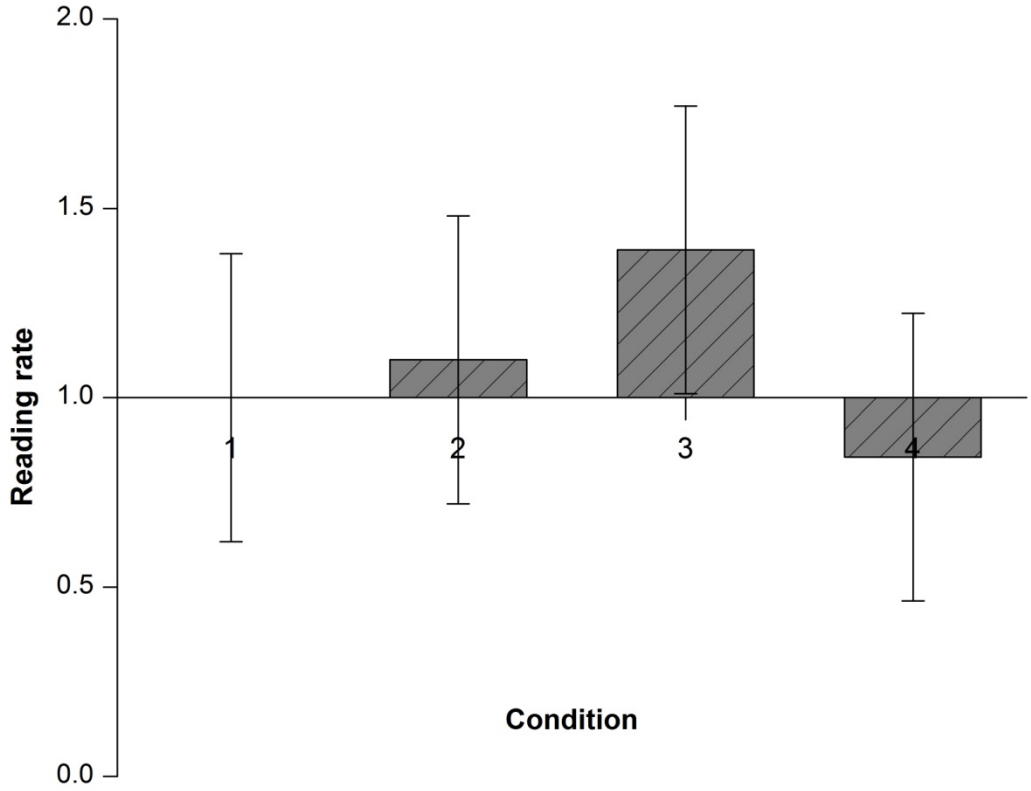

Figure 9.4: Variation of reading speed with condition. *Condition 1*: baseline - no compensation; *condition 2*: gain 1 & screen blanked during saccades; *condition 3*: gain 1 & screen not blanked during saccades; *condition 4*: gain 10 & screen not blanked during saccades.

Table 9.3: Summary of the main results. The summary includes mean value for: retinal image speed (RIS), reading speed in words per minute (wpm) and the RSVP gain compared with MNread in the last column. Numbers in square brackets show 95% confidence intervals.

Condition	**Vel. drift** ($^{o}s^{-1}$)	**Amp. drift** (minarc)	**RIS** ($^{o}s^{-1}$)	**Reading** (wpm)	**Ratio** **RSVP/MNREAD**
1	5.8 [±1.2]	18.0 [±5.0]	5.8 [±1.2]	161.0 [±71.1]	1.4
2	6.9 [±1.6]	42.9 [±17.3]	3.0 [±0.7]	189.4 [±98.5]	1.5
3	6.5 [±1.7]	42.0 [±19.4]	2.9 [±0.7]	215.8 [±96.3]	1.8
4	6.7 [±1.8]	40.1 [±16.6]	12.4 [±2.9]	110.9 [±29.3]	1.0

9.2.2 Retinal image speed

Retinal image speed was calculated offline by computing the slip of the retinal image during fixation. RIS for conditions 2 and 3 were 48% lower than for condition 1 ($p = 0.004$). RIS for condition 4 was 114% higher than condition 1, more than twice the normal RIS. RIS for condition 4 (overcompensation) was 162% higher than condition 2 and 3, that is, almost three times RIS for the compensated conditions (see Table 9.3 for a summary)

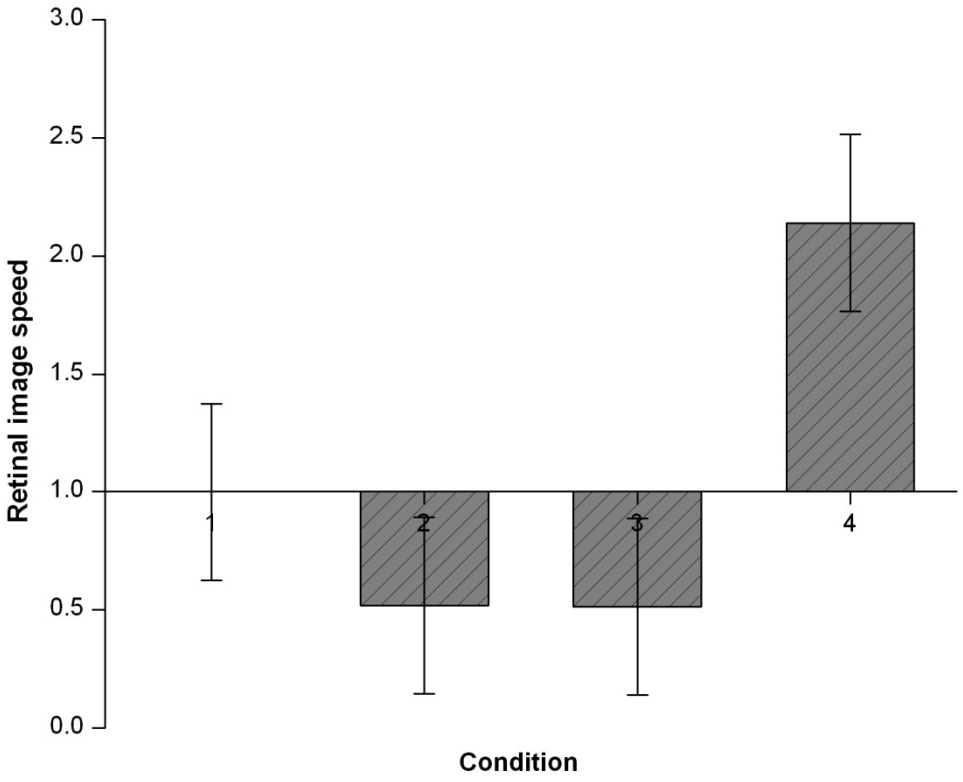

Figure 9.5: Variation of retinal image speed (RIS) during fixation. *Condition 1*: baseline - no compensation; *condition 2*: gain 1 & screen blanked during saccades; *condition 3*: gain 1 & screen not blanked during saccades; *condition 4*: gain 10 & screen not blanked during saccades.

9.2.3 Saccade rate

Saccade rate (saccades per word) remained constant for all conditions with a mean value of 1.45 saccades per word (range 0.6 - 2.7). The ratio of saccades per word was correlated with word length (Pearson's correlation coefficient = 0.131, p = 0.032).

9.2.4 Fixation duration and drift amplitude

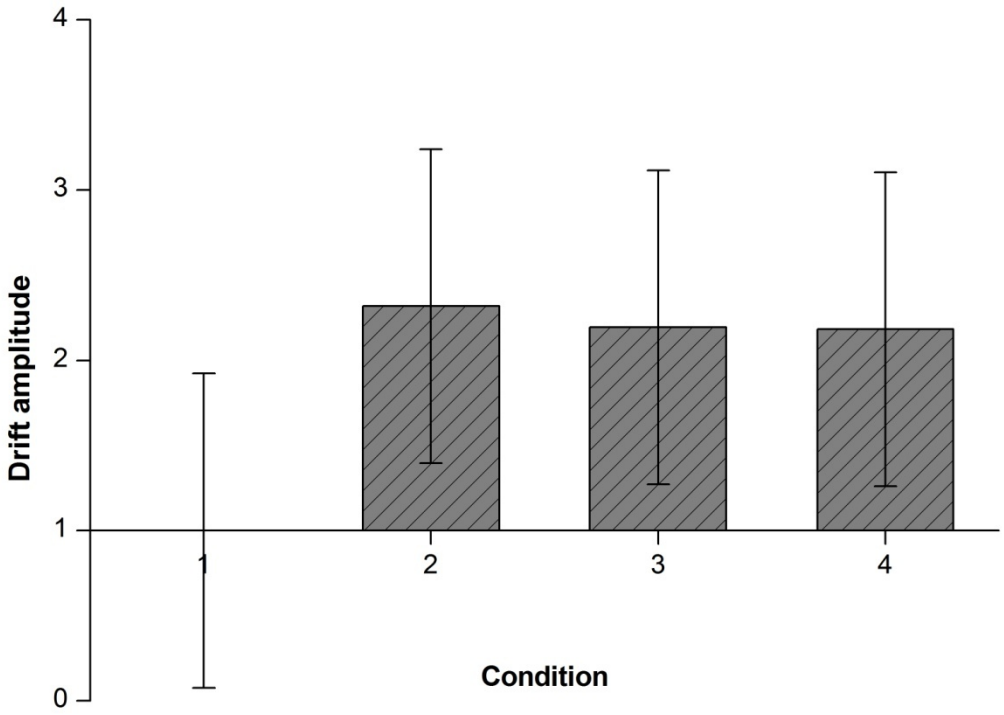

Figure 9.6: Variation of drift amplitude with condition. *Condition 1*: baseline - no compensation; *condition 2*: gain 1 & screen blanked during saccades; *condition 3*: gain 1 & screen not blanked during saccades; *condition 4*: gain 10 & screen not blanked during saccades.

Drift amplitude for conditions 2, 3 and 4 was higher than for baseline. The mean difference for condition 2 was 1.3 ($p = 0.001$), for condition 3 was 1.2 ($p = 0.004$) and for condition 4 was 1.2 ($p = 0.005$).

Fixation duration for condition 4 was higher than in condition 2 (mean difference: 0.25; $p = 0.013$). Fixation duration for conditions 2, 3 and 4 were not significantly different from baseline.

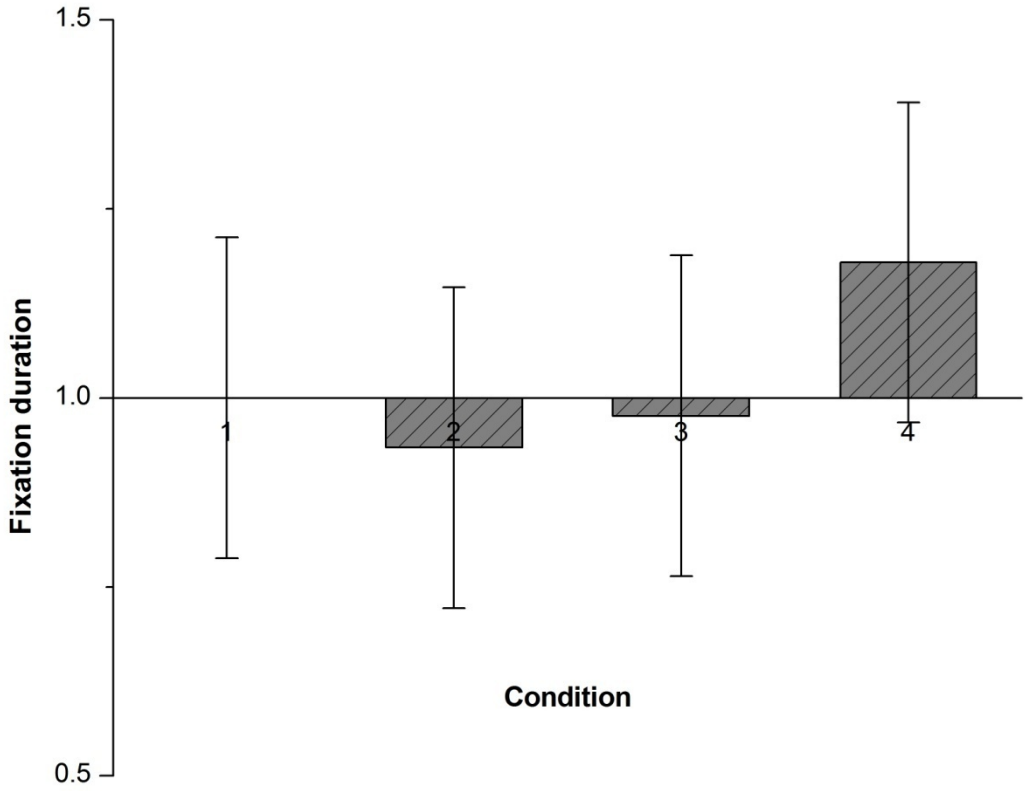

Figure 9.7: Variation of fixation duration with condition. *Condition 1*: baseline - no compensation; *condition 2*: gain 1 & screen blanked during saccades; *condition 3*: gain 1 & screen not blanked during saccades; *condition 4*: gain 10 & screen not blanked during saccades.

9.3 Discussion

In this experiment RSVP reading speed of five patients with macular disease was measured under four conditions. Reading speed improved, compared with baseline, for condition 3, where fixation instability was compensated (gain 1) and the screen was not blanked during saccades. That is in agreement with the results obtained in Chapter 8 with normal sighted subjects reading with the peripheral retina; unlike in Chapter 8, for people with real scotoma intra-word saccades were necessary. All participants improved in condition 3. Slow readers did not seem to slow further in condition 4 but read slower in condition 2. Fluent readers improved in condition 2, but reduced in condition 4. These results seem to indicate that slow readers rely more on intra-word saccades and are more tolerant to high RIS than fluent readers.

Improvement in reading speed is likely to be due to reduction in motion blur achieved through reduction in retinal image speed. The difference between normal RSVP and condition 3, where patients read faster, is essentially retinal image speed, because in both cases intra-word saccades were possible. There is further evidence that high RIS is detrimental for reading. For example results obtained in condition 4 (gain 10, high RIS) where the difference condition 4-condition 3 increased by 15% compared with the difference baseline-condition 3. Also, it is known that fixation duration increases with decreasing visibility of the content, that might the reason for prolonged fixations found in condition 4 (Hooge &

Erkelens, 1996).

Compensating for fixation instability might help to maintain the alignment of the PRL with the word but that alone could not explain the improvement in reading (Bullimore & Bailey, 1995, Deruaz et al., 2002). For example, in condition 4 where words were aligned with the PRL but RIS was high, reading speed reduced compared with condition 3. Therefore, fixation instability has a role to play and that is consistent with previous studies showing detrimental effects of fixation instability for reading (Crossland, 2004, Crossland et al., 2004a, Falkenberg et al., 2007).

Intra-word saccades were important during RSVP. Condition 2, with RIS similar to condition 3 but without intra-word saccades, failed to produce higher reading speed than baseline. The ratio of character size to saccade amplitude was approximately: 1 character per saccade (maximum: 2 char/sac; minimum = 0.6 char/sac). Saccade ratio per word and characters per saccade were the same for all conditions. These results are similar to previous studies (Bullimore & Bailey, 1995). Reading rates for the MNREAD test (Table 9.1) show that some participants were below or borderline for fluent reading (80 wpm) which is thought to correspond to a visual span of four characters (Whittaker & Lovie-Kitchin, 1993b). About 80% of the words used in this experiment had 4 or more characters (see Figure 9.1); thus, it is likely that saccades served to scan the words. Previous studies also showed that intra-word saccades are likely to be a consequence of patients' reduced visual span (Cheong et al., 2008, Legge et al., 1997). The number of saccades per word was the same under all

conditions and was correlated with word length, which is in agreement with the hypothesis that patients need intra-word saccades because they have reduced visual span (Crossland & Rubin, 2006, Legge et al., 1997).

Previous studies using scrolling or/and RSVP text showed that it is possible to improve reading by reducing the effect of impaired saccades. Here we extended these findings by showing that further gains in reading speed can be obtained by reducing RIS caused by fixation instability. This contradicts the idea of a beneficial effect of fixation instability for patients, as suggested by Deruaz et al (2004), and is in agreement with studies showing that patients with good fixation normally read faster than patients with similar acuity but poorer fixation (Crossland et al., 2004a).

9.3.1 Limitations

The compensation technique used in this experiment is likely to elicit atypical smooth pursuit as evidenced by the increased drift amplitude found in all stabilized conditions (2-4). As discussed in section 7.3.3, atypical smooth pursuit that can occur when the target is moving despite retinal image speed is close to zero (Dubois & Collewijn, 1979, Wyatt & Pola, 1983). This limitation is in part caused by the limitations of the stabilization instruments discussed in section 6.3. It is particularly important to emphasise the fact that our stabilization system relies in calibration using point targets. Recently, Crossland et al (2010) showed that patients use different PRLs for point targets and reading using the

MP1 microperimeter, although it is not possible to know if the same happens with the eyetracker (Crossland, Crabb & Rubin, 2010).

9.4 Conclusion

This experiment showed that gaze-contingent text can reduce the effect of oculomotor impairment with benefits for reading in patients with macular disease. Reading speed was improved by correcting fixation instability whilst allowing intra-word saccades.

Chapter 10. General discussion

Poor oculomotor control reduces visual function in people with macular scotoma. While saccadic control has been extensively studied and some solutions have been proposed, fixation instability has received considerably less attention. It is possible that fixation has received less attention because it had been considered less detrimental to visual function or because these experiments are technically complex.

Several authors in the 80's and early 90's noticed that people with macular disease have unstable fixation when compared with healthy controls (Culham et al., 1993, McMahon et al., 1991, Timberlake et al., 1986, Whittaker et al., 1988). Whittaker for example stated that for fixations above 300 msec, given the typical drift velocities that he found, the PRL could be moved away from the target. Schuchard (1994) suggested that fixation instability would be a limiting factor for reading and in 2004 Crossland (2004) found that 25% of the variability in reading speed among patients with MD was explained by fixation instability (Crossland, 2004, Schuchard & Fletcher, 1994). Further evidence regarding the importance

of fixation (in)stability was given by Seiple and colleagues in 2005. Seiple administered a training protocol aiming to improve oculomotor control; no direct reading training was provided. Patients improved their reading speed significantly, compared to the baseline. Progress was attributed to improvements in oculomotor control and not due to practice reading (Seiple et al., 2005).

10.1 Primary purpose of this work

The aim of this thesis was to investigate whether compensating for oculomotor instability would improve visual performance for people with macular disease. The primary objective was to illustrate whether fixation instability reduces visual function. Additional aims included the evaluation of the best stabilization settings to compensate for oculomotor deficits.

10.1.1 Visual function assessment

The effect of oculomotor control has been assessed in two visual tasks: visual acuity and RSVP reading. These have different visual, oculomotor and cognitive requirements (Thorndyke, 1977). Cognitive requirements are beyond the scope of this thesis and will therefore not be discussed. Visual acuity requires identification of the visual target and good fixation control (Thibos & Bradley, 1993), whereas reading requires visual input and cognitive processing. In the latter, oculomotor control is more critical, and both good saccade control as well as fixation are necessary (Bouma &

Voogd, 1974, Rayner & Pollatsek, 1987, Starr & Rayner, 2001).

Acuity is reduced by the poor resolution of the peripheral retina, by crowding, and by high retinal image speed (Bex & Dakin, 2005, Bex et al., 2003, Chung & Bedell, 1995, Pascal & Abadi, 1995). Reading, however, is susceptible to further limitations of the peripheral retina, such as reduced visual span (Bouma, 1970, Legge et al., 2007), slow visual processing (Cheong et al., 2007), and poor oculomotor control (Bouma & Voogd, 1974, Bullimore & Bailey, 1995, Oregan, 1980, Rayner & McConkie, 1976). The different requirements for acuity and reading limit the comparisons between experiments. Results from reading and acuity are generally discussed separately.

10.1.2 Real and simulated scotoma

This thesis studied peripheral visual function with simulated scotoma and scotoma caused by macular disease. There are several differences between simulated and real scotoma, one principal difference is its awareness. In many cases simulated scotoma is visible to the subjects; however, it is believed that people with real scotoma do not see it neither see its contours (Fletcher & Wichita, 2010). Furthermore, people with central scotomas caused by macular disease are often unaware that they use a PRL in the peripheral retina (Crossland et al., 2005, Schuchard & Raasch, 1992b, White & Bedell, 1990).

Simulated scotoma are different from those caused by macular disease because they correspond to an acute change in vision. Contrary to simulated, scotoma caused by dry macular disease cause progressive loss of central vision giving people time to develop new viewing strategies. People performing visual tasks with simulated scotoma do not have time to develop equivalent viewing skills. Additionally, in simulated scotoma the peripheral retina is completely healthy while in macular disease that might not be the case (as discussed below). Simulated scotoma used in this thesis was invisible so as to minimize the visual cues to our normal sighted participants. Despite these limitations, results from simulated scotoma remain the best way to study functional changes in macular disease when it is not desirable or possible to involve patients.

10.2 Main findings

In normal peripheral retina compensation of fixation instability caused by simulated scotoma (gain 0) had distinct effects on reading and on visual acuity. In the case of the positions and eccentricities tested, acuity improved very slightly in some of the gaze contingent conditions compared with gain 0 (the baseline condition). For noncrowded acuity there was an improvement of 0.04 logMAR for gain 0.1 and gain 1 compared with gain 0. For crowded acuity no significant difference was found between gains: 0, 0.1 and 1. Interestingly, gain 10 caused improvement in nonwcrowded visual acuity of 0.03 logMAR compared with gain 1 and gain 0.1. Conversely the same gain 10 resulted in an equivalent reduction for

crowded acuity (the amount of reduction varied with eccentricity and position).

For reading, a detrimental effect of typical fixation instability was found (typical fixation instability corresponds to condition 1 - gain 0). By comparing condition 1 to conditions 2 and 5 (conditions with gain 1) in Chapter 8, an improvement in reading speed of 23% was observed for condition 2 (instability compensated and screen blanked during saccades). Interestingly the difference between condition 1 and 5, where the screen was not blanked during saccades (intra-word saccades were possible), was not statistically significant. Possible causes of the lack of improvement in condition 5 have been discussed in Chapter 8.

In people with macular disease the effect of compensating for fixation instability was also different for visual acuity and reading. No significant improvement in acuity was obtained when comparing fully compensated fixation instability (gain 1), to no compensation (gain 0 corresponds to typical fixation instability). This result was similar for both acuities: crowded and nonwcrowded. For reading, compensating for fixation instability (condition 3, gain 1 and screen not blanked during saccades) led to an improvement in reading speed of 40%. In condition 3 intra-word saccades were permitted. This was fundamental to the obtained consistent improvements for all participants (Chapter 9). When intra-word saccades were not permitted (condition 2) poor readers read slower compared with normal RSVP reading(condition 1), probably because saccades are

necessary to compensate for their narrow visual span. Fluent readers only reduced reading speed when fixation instability was over-compensated (gain 10 - condition 4), though this did not cause poor readers read slower (compared with condition 1). The resistance that poor readers showed to high levels of retinal image speed might be explained by their baseline poor reading speed. The longer word exposures they require make motion blur less detrimental to reading than it does to fluent readers.

In brief, fixation instability was compensated for by using three main conditions full-compensation of instability (gain 1), over-compensation of instability (gain 10) and semi-compensation of instability (gain 0.1). In the reading experiments further conditions were introduced by making intra-word saccades permitted or not permitted. The condition that produced the best visual performance was different for participants with macular disease and participants with simulated scotoma. Similarities and differences between these experiments are discussed below.

10.2.1 The best condition with simulated scotoma

The most interesting result in nonwcrowded visual acuity was the improvement observed when fixation instability was over-compensated (gain 10). Despite being statistically significant this improvement is clinically irrelevant (less than half a line difference on an ETDRS acuity chart (Bailey & Lovie, 1976)). As reported above, there was also improvement for gain 0.1 and gain 1 compared with gain 0. These results

are not totally comparable because for gain 0, acuity was measured with a fixation target and the optotype was exposed only for 200 msec. The reasons for using these settings and their implications have been discussed in Chapter 4 and Chapter 6. Essentially, in the baseline condition it was always necessary to use a fixation target though this eliminated the principle of a simulated scotoma.

Reading improved significantly in only one of the five conditions: when fixation instability was compensated and intra-word saccades were not possible (Condition 2). The effect of allowing intra-word saccades was not visible in control subjects (condition 5), presumably due to their fast reading speed. The word exposure time was between 120-160 msec, less than the typical saccadic latency (Carpenter, 1988). All this provides evidence that the combination of simulated scotoma size and word length permits the processing of all word information during one fixation. As discussed before, the number of characters of most words was within the visual span expected for 5º eccentricity, as it was found in previous research (Legge et al., 2001).

10.2.2 The best condition with macular disease

In macular disease neither crowded nor noncrowded acuity improved under the conditions that were tested. The resolution (visual acuity) obtained for participants in the experiment described in Chapter 7 was very low compared with the resolution of the simulated scotoma (Chapter 6). As

a consequence of poor resolution the visual system gets more tolerant to higher amounts of retinal image motion. This has previously been discussed by Kelly and in section 1.2.2 of this thesis (Kelly, 1985). Given these characteristics of the visual system, even with more efficient stabilization the effect would probably not be visible for such reduced resolutions.

Reading speed improved when fixation was compensated and intra-word saccades were possible. With full compensation, gain 1, a reduction of approximately 50% in retinal image speed was obtained, Figure 9.5. Reading is a more complex task than resolution thus here, reduction in retinal image motion blur was beneficial. Reduction in motion blur might help to relieve deficits of the peripheral retina that influence reading (previously discussed in section 2.2). The need for saccades, contrary to what was found in simulated scotoma, is likely to be due to the reduced visual span that is typical in people with macular disease (Cheong et al., 2008, Rubin & Turano, 1994).

10.2.3 Retinal image speed reduction: oculomotor consequences

Some authors have suggested that low retinal image speed in the central retina could trigger a mechanism that disrupts eye stability (Engbert & Mergenthaler, 2006, Martinez-Conde et al., 2006). These findings would give some credit to the suggestion made by Deruaz in 2004 that fixation instability observed in people with a macular scotoma might be part of the

strategy of the visual system to improve perception (Deruaz et al., 2004). However, contrary to what Deruaz suggested, compensating instability (gain 0.1 or gain 1) did not reduced acuity and in fact over-compensating instability did (Chapter 7). Additionally, when retinal image speed was reduced by stabilization, the visual system did not seem to try to "unstabilize" the eye. As seen in Chapters 1 and 2, people with macular disease might have disturbances in the flow of information through the pathways responsible for fixation control. An eventual attempt by the visual system to increase retinal image speed would enhance oculomotor impairment. These predictions do not agree with BCEA values found in Chapter 7.

Results of this thesis are not in agreement with what has been found in central retina by Engbert and Mergenthaler (2006) nor with the suggestion made by Deruaz et al. (2004) for people with macular disease. Fixation instability measured under different conditions gives evidence that instability is not a strategy of the visual system but a consequence of poor oculomotor control.

10.3 Why does stabilization work?

Previous studies have shown that patients with macular disease improve performance by reading text formats where saccades are not necessary or are kept to a minimum (Forster, 1970, Rubin & Turano, 1994). This thesis shows that further gains can be achieved if fixation instability is

compensated. These findings agree with the initial hypothesis that compensating for fixation instability is beneficial for people with poor oculomotor control. The main reason for the improvement is likely to be a reduction in motion blur (Georgeson & Hammett, 2002, Hammett, 1997, Packer & Williams, 1992).

Visual performance is reduced by motion blur because it enhances the deficits of the peripheral retina. It is understood that motion blur is responsible for reducing resolution (Badcock & Wong, 1990, Morgan & Benton, 1989) and contrast (Burr & Ross, 1982) and for increasing crowding (Bex & Dakin, 2005, Bex et al., 2003). Consequently, when contrast reduces saccades become less precise (Brown, 1972a) and visual span shrinks (Legge et al., 1997). Thereby, contrast reduction enhances the oculomotor difficulties of the peripheral retina to plan saccades. Poor contrast also increases fixation time in normal reading (Rayner, 1978, Rayner, 1998). In people with central scotoma, prolonged fixations increase the probability of taking the PRL away from the target. A positive effect in the various deficits would thereby be expected from a reduction in fixation instability.

10.4 Text formats compensating for poor oculomotor control

The two most common text formats experimentally used to reduce poor oculomotor control are RSVP and scrolled text. The gain in reading speed,

compared with page reading, is about 40% in both formats (Fine & Peli, 1995). The results reported in Chapter 9 corroborate these findings, despite the use of different metrics for MNREAD and RSVP. It is expected that voluntary saccades are not necessary for reading scrolled text. However, in normal sighted readers scrolled text causes a combination of smooth tracking movements and saccades (Valsechi et al., 2011). According to some authors eye movements whilst reading scrolled text are reflexive (do not require programming) and because of that, they are less likely to interfere with reading speed (Bowers et al., 2004). Bowers and colleagues tried to reduce the interference of poor oculomotor control in reading by presenting vertically scrolled text for horizontally shifted PRLs, that is, perpendicular to the PRL. They failed to show differences between reading scrolled texts presented orthogonally or radially to the PRL. Recent work by Yu and colleagues also explored the effect of reducing oculomotor deficits of the peripheral retina by presenting text in vertical format. They studied whether vertical text could be beneficial for lateral PRLs (right or left of the scotoma) in people with simulated central scotoma. Yu found much slower reading speed in the vertical format than the horizontal (Yu, Park, Gerold & Legge, 2010).

In summary, various attempts to compensate for poor oculomotor in people with scotoma during reading were not successful. Since 1994 when Rubin & Turano showed that people with scotoma read faster text presented as RSVP, there have been no progress in techniques to reduce the effect of poor oculomotor control. None of the attempts described

above reduced the effects of fixation instability. This thesis shows that further gains in RSVP are possible if a stabilization system is used. The technique was not tested in continuous text and the possibility of its implementation needs therefore to be confirmed.

10.5 Factors interfering with oculomotor control

10.5.1 Simulated vs pathological scotoma

The relevant aspects interfering with compensation that vary from simulated to pathological scotoma have been discussed in section 10.1.2.

10.5.2 Age-related vs juvenile macular degeneration

The time onset of the macular disease might be important for oculomotor control adaptation. People with early onset diseases start to develop oculomotor strategies when the visual system has more plasticity than people with age related macular degeneration. Hence, White & Bedell hypothesised that people with early onset macular disease (JMD) shift their oculomotor reference more easily than people with AMD (White & Bedell, 1990). In the experiments reported in this thesis, due to a small number of participants with JMD, it was not possible to verify whether compensation of oculomotor instability in AMD differed from JMD. Interestingly, Calabrese et al. found differences in visual performance

(reading) between people with wet and dry AMD. Those with wet AMD performed better than those with dry.(Calabrese, Bernard, Hoffart, Faure, Barouch, Conrath & Castet, 2010). This goes against the general idea that people with dry AMD should have better performance because they have had more time to adapt to central vision loss. Therefore, the effect of compensating oculomotor instability as shown in this thesis may also be affected by the level of plasticity of the oculomotor system and/or by the type of disease (Tita-Nistor, Gonzalez, Mkowitz & Steinbach, 2009). These are questions that need to be addressed by future studies.

10.5.3 Eccentricity of the PRL

People with MD normally develop their PRL close to the boundary of the scotoma in the area with the best visual acuity (Cacho et al., 2007). It is expected that patients with good visual acuity have a PRL close to the fovea and better fixation stability than patients with poorer vision (Ergun, Maar, Radner, Barbazetto, Schmidt-Erfurth & Stur, 2003, Whittaker et al., 1988). At large eccentricities fixation instability causes less blur due to the enlarged receptive fields of the far periphery of the retina (Drasdo, 1989). Therefore, a patient with a PRL relatively close to the fovea but poor fixation, is more likely to have reduction in visual performance caused by poor fixation than patients using more eccentric PRL. In the experiment reported in Chapter 6, fixation instability was less detrimental for crowded visual acuity measured at 10º than for the same measure at 5º. That is in agreement with Kelly's model for moving targets in the periphery, as

discussed in section 1.1.2.2. According to Kelly, if the velocity of the target increases 'within limits' to compensate for reduction in spatial frequency of the target, the visual system can resolve finer patterns with a moving target than with a static target (Kelly, 1985).

10.5.4 The PRL location

From a theoretical perspective the most appropriate place to develop a PRL for reading is below the scotoma in the visual field of view (Figure 10.1). A PRL below the scotoma does not mask text information and would give visual information in order to programme the eye movements orthogonal to the fixation point (Bowers et al., 2004, Peli, 1986). Similar oculomotor conditions would be found above the scotoma but the upper retina (lower field) has some physiological and ecological advantages. These include a higher density of photoreceptor and better attentional deployment (Altpeter, 2000, Curcio & Allen, 1990, He et al., 1996). Vertical PRLs also minimise text eccentricity, for example, for a circular scotoma with 10º diameter centred on the fovea and a word subtending 5º, the middle of the word (where gaze normally lands) for a vertical PRL, would be at 5º eccentricity. For the same conditions, but for a horizontal PRL the middle of the word would be at 7.5º eccentricity and would fall easily into the scotoma (Petre et al., 2000). Thus, horizontal PRLs would be less favourable for reading than vertical PRLs.

Regarding PRL location, results of thesis can not be generalized because only five participants with macular disease participated in the reading experiment. However, it is still interesting to discuss what was observed. Subjects S4 and S5 had horizontal PRLs and relatively poor acuity compared with S2 (vertical PRL), but S4 and S5 achieved higher reading speed. These findings are not in full agreement with the theoretical considerations above. Studies with more participants (99) showed that it is not possible to predict reading ability based on PRL location (Fletcher, 1999). Fletcher pointed that other variables such as oculomotor abilities (related with the PRL location) and/or cognitive factors are key to determine reading ability.

The oculomotor abilities of people with horizontal PRLs between the scotoma and the physiological blind spot (for example: right PRL in the right eye) are probably more compromised than in all other locations. In Chapter 9, S3 and S5 had PRLs between the scotoma and the blind spot. Subject S3 complained frequently of missing the first characters of the word during the stabilized condition, curiously S5 never complained. A possible explanation is that, S3 was calibrating the eye tracker with a PRL very close to the scotoma. With the middle of the word centred with on the PRL the first characters would certainly fall into the scotoma. Eventually S5, who had a smaller scotoma (see Appendix Table 8) and healthier retina around the PRL, missed fewer characters. Also as subject S3 read larger print, the word would go further into the scotoma than for patient S5. In theory, PRLs located between the scotoma and the blind spot are also

disadvantageous for using the eye tracking technique to compensate for instability. However, this thesis does not provide enough evidence of that. Previous studies showed that for some persons with PRLs at unfavourable locations, training a new PRL is possible and leads to significant visual improvement (Tita-Nistor et al., 2009).

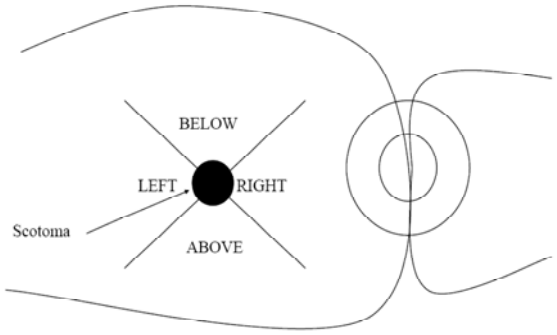

Figure 10.1: Convention used to describe PRL location with respect to the scotoma in visual field space (right eye).

10.5.5 Multiple PRLs

The use of multiple PRLs (mPRLs) is frequently reported in literature, but the definition of multiple PRLs varies significantly from author to author (Crossland et al., 2004b, Deruaz et al., 2002, Duret et al., 1999, Guez et al., 1993, Macedo et al., 2007, Whittaker et al., 1988). To date there is no evidence to suggest that without using mPRLs this group of people would have worse performance. The use of multiple PRLs is not compatible with the compensation technique used here because: firstly, multiple PRLs would cause errors during calibration and, secondly, because the system

keeps the targets permanently in the same retinal area making it impossible to alternate between PRLs.

10.5.6 Binocular vision

All experiments reported in this thesis were performed monocularly in the better eye, despite in daily life most people with macular disease use both eyes. Kabanarou and colleagues have found that oculomotor control is dominated by the eye with better vision in people with binocular AMD (Kabanarou et al., 2006). However, they noticed a shift in gaze position in one or both eyes when viewing binocularly compared with monocularly. If scotoma size and visual acuity is similar in both eyes, it is possible that oculomotor dominance could be less consistent and monocular experiments might not be predictive of visual performance under binocular conditions.

10.6 Limitations

The limitations regarding the stabilization setup have been explained in detail in previous chapters. To summarise, errors may have been induced by the delay between the eye movements and the update of the image position in the monitor and the fact that the eyetracker relies on calibration with the PRL. Further, presenting words at the PRL used for fixation might not be an appropriate strategy for all patients. It has recently been shown that one retinal area is used for fixating single calibration dots and a

different PRL is used for reading (Crossland et al., 2010).

It was only possible to test a relatively small number of people with macular disease and the patients were clinically heterogeneous. Therefore it was impossible to determine the effect of the compensation strategy for people with different types of scotoma or different durations of vision loss. More participants would be required to generalise the findings in relation to everyone with macular disease or even to predict for whom this technique would be advantageous.

Chapter 11. Thesis conclusion and suggestions for future research

11.1 Thesis conclusion

Oculomotor instability is detrimental to visual performance for both normal peripheral retina and for people with macular disease. For people with macular disease, RSVP reading speed improves when fixation instability is compensated. This study has further shown that compensating for fixation instability is possible using an infrared eyetracker. This technique has the potential to be part of future assistive devices for people with macular disease.

11.2 Implications of this study

The results of this thesis might have implications for three aspects of the macular disease rehabilitation. First, eccentric viewing training protocols should focus more on oculomotor training, in particular training fixation control. As Seiple and colleagues showed, a protocol based on eye movements control can improve visual tasks without direct practice of the tasks (Seiple et al., 2005). It is expected that better control of fixation will also lead to better adaptation to low vision aids (Dickinson & Fotinakis, 2000, Goodrich & Mehr, 1986).

Second, the introduction of gaze-contingent PRL training may be useful. This type of training would avoid people frequently losing the target, making the use of the peripheral retina more constant during practice.

Finally, this study has shown that new assistive devices should compensate for poor oculomotor control. Eye-trackers can be easily incorporated in devices such as head mounted displays, but more research is necessary to define the best way to integrate this fixation compensation with devices for the visually impaired (Efron, David, Apter, Thirer, Zedaka, Bogillo, Weyl, Levy & Salasnik, 2008, Levy, Apter & Efron, 2006).

11.3 Suggestions for future research

Future research investigating oculomotor control in people with macular disease should aim to compensate for oculomotor deficits of the peripheral retina using cost-effective techniques. Cost-effect techniques would be,for example, more effective training offered by therapists or more technologically elaborate devices that compensate for fixation instability.

In order to consolidate the results of this thesis and future development of techniques based on eye-tracking, the effect of practising RSVP reading under stabilized conditions should be examined. The impact of this training on conventional page mode reading is another potential area for future study.

A significant advancement in compensation would be a technique that does not rely on calibration to ensure text stabilization at the correct PRL. A similar system to that of the scanning laser ophthalmoscope, where the stimulated area could be visualized by the experimenter, would be ideal if that could transfer to clinical practice. However, before further effort is expended in training PRLs, it is important to ensure PRL training is absolutely beneficial. Further research in this area is warranted.

References

Age-Related-Eye-Disease-Study-Res-Group (2001). The age-related eye disease study system for classifying age-related macular degeneration from stereoscopic color fundus photographs: The Age-Related EyeStudy Report Number 6. *American Journal of Ophthalmology, 132* (5), 668-681.

Aguilar, C., & Castet, E. (2011). Gaze-contingent simulation of retinopathy: Some potential pitfalls and remedies. *Vision Research, 51* (9), 997-1012.

Ahissar, E., & Arieli, A. (2001). Figuring space by time. *Neuron, 32* (2), 185-201.

Aisenbrey, S., & Bartz-Schmidt, U. (2003). Macular translocation with 360-degree retinotomy for management of age-related macular degeneration with subfoveal choroidal neovascularization. *American Journal of Ophthalmology, 135* (5), 748-749.

Al-Karmi, R., & Markowitz, S.N. (2006). Image relocation with prisms in patients with age-related macular degeneration. *Canadian Journal of Ophthalmology-Journal Canadien D Ophtalmologie, 41* (3), 313-318.

Allikmets, R., Singh, N., Sun, H., Shroyer, N.F., Hutchinson, A., Chidambaram, A., Gerrard, B., Baird, L., Stauffer, D., Peiffer, A., Rattner, A., Smallwood, P., Li, Y., Anderson, K.L., Lewis, R.A., Nathans, J., Leppert, M., Dean, M., & Lupski, J.R. (1997). A photoreceptor cell-specific ATP-binding transporter gene (ABCR) is mutated in recessive Stargardt macular dystrophy. *Nature Genetics, 15* (3), 236-246.

Allport, D.A. (1968). Phenomenal simultaneity and perceptual movement hypothesis. *British Journal of Psychology, 59*, 395.

Altpeter, E., M. Mackenben, S. Trauzettel-klosinski (2000). The importance of sustained attention for patients with maculopathies. *Vision Research, 40*, 1539-1547.

Andersen, E.E., & Weymouth, F.W. (1923). Visual perception and the retinal mosaic: I. Retinal mean local sign - an explanation of the fineness of binocular perception of distance. *American Journal of Physiology, 64* (3), 561-594.

Anderson, S.J., Mullen, K.T., & Hess, R.F. (1991). Human peripheral spatial-resolution for achromatic and chromatic stimuli: limits imposed by optical and retinal factors. *Journal of Physiology-London, 442*, 47-64.

Anderson, T.J., Jenkins, I.H., Brooks, D.J., Hawken, M.B., Frackowiak, R.S.J., & Kennard, C. (1994). Cortical Control of Saccades and Fixation in Man - a Pet Study. *Brain, 117*, 1073-1084.

Aquilante, K., Yager, D., Morris, R.A., & Khmelnitsky, F. (2001). Low-vision patients with age-related maculopathy read RSVP faster when word duration varies according to word length. *Optometry and Vision Science, 78* (5), 290-296.

Arditi, A. (1999). Elicited sequential presentation for low vision reading. *Vision Research, 39* (26), 4412-4418.

Arora, R., Das, S., Shroff, D., Narula, R., & Chauhan, D. (2007). In vivo microscopy of Best's Vitelliform Macular Dystrophy: optical coherence tomography study of combined stage III and IV lesions. *Clinical and Experimental Ophthalmology, 35* (3), 287-288.

Badcock, D.R., & Wong, T.L. (1990). Resistence to positional noise in human vision. *Nature, 343* (6258), 554-555.

Bahill, A.T., Clarke, M.R., & Stark, L. (1975). The main sequence, a tool for studying human eye movements. *Mathematical Biosciences, 24*, 191-204.

Bailey, I.L., & Lovie, J.E. (1976). New design principles for visual-acuity letter charts. *American Journal of Optometry and Physiological Optics, 53* (11), 740-745.

Bainbridge, J.W.B., Smith, A.J., Barker, S.S., Robbie, S., Henderson, R., Balaggan, K., Viswanathan, A., Holder, G.E., Stockman, A., Tyler, N., Petersen-Jones, S., Bhattacharya, S.S., Thrasher, A.J., Fitzke, F.W., Carter, B.J., Rubin, G.S., Moore, A.T., & Ali, R.R. (2008). Effect of gene therapy on visual function in Leber's congenital amaurosis. *New England Journal of Medicine, 358* (21), 2231-2239.

Banks, M.S., Sekuler, A.B., & Anderson, S.J. (1991). Peripheral spatial vision: limits imposed by optics, photoreceptors, and receptor pooling. *Journal of the Optical Society of America A - Optics Image Science and Vision, 8* (11), 1775-1787.

Barlow, H.B. (1952). Eye movements during fixation. *Journal of Physiology-London, 116* (3), 290-306.

Barlow, H.B. (1958). Temporal and spatial summation in human vision at different background intensities. *Journal of Physiology-London, 141* (2), 337-350.

Barlow, H.B. (1963). Slippage of contact-lenses and other artifacts in relation to fading and regeneration of supposedly stable retinal images. *Quarterly Journal of Experimental Psychology, 15* (1), 36-51.

Becker, W. (1988). Saccades. In: R. Carpenter (Ed.) *Movements of the eyes* (pp. 95-137). London: Pion.

Beckmann, P.J., & Legge, G.E. (1996). Psychophysics of reading--XIV. The page navigation problem in using magnifiers. *Vision Research, 36* (22), 3723-3733.

Bedell, H.E. (1986). Some constraints on peripheral visual functioning - Introduction. *American Journal of Optometry and Physiological Optics, 63* (2), 91-93.

Bedell, H.E., Barbeito, R., & Aitsebaomo, P.A. (1984). The precision of oculocentric direction and its role in the stability of fixation. *Vision Research, 24* (10), 1157-1161.

Bedell, H.E., Chung, S.T.L., & Patel, S.S. (2000). Elevation of Vernier thresholds during image motion depends on target configuration. *Journal of the Optical Society of America A - Optics Image Science and Vision, 17* (6), 947-954.

Bellmann, C., Feely, M., Crossland, M.D., Kabanarou, S.A., & Rubin, G.S. (2004). Fixation stability using central and pericentral fixation targets in patients with age-related macular degeneration. *Ophthalmology, 111* (12), 2265-2270.

Bernard, J.B., Anne-Catherine, S., & Eric, C. (2007). Page mode reading with simulated scotomas: A modest effect of interline spacing on reading speed. *Vision Research, 47* (28), 3447-3459.

Berry, R.N. (1948). Quantitative relations among vernier, real depth, and stereoscopic depth acuities. *Journal of Experimental Psychology: General, 38* (6), 708-721.

Bex, P.J., & Dakin, S.C. (2005). Spatial interference among moving targets. *Vision Research, 45* (11), 1385-1398.

Bex, P.J., Dakin, S.C., & Simmers, A.J. (2003). The shape and size of crowding for moving targets. *Vision Research, 43* (27), 2895-2904.

Bex, P.J., Edgar, G.K., & Smith, A.T. (1995). Sharpening of drifting blurred images. *Vision Research, 35* (18), 2539-2546.

Bird, A.C. (2003). Towards an understanding of age-related macular disease. *Eye, 17* (4), 457-466.

Bjornsson, O.M., Syrdalen, P., Bird, A.C., Peto, T., & Kinge, B. (2006). The prevalence of age-related maculopathy (ARM) in an urban Norwegian population: the Oslo Macular Study. *Acta Ophthalmologica Scandinavica, 84* (5), 636-641.

Blohm, G. (2004). The use of extraretinal information to compensate for self-movement. *Laboratory of Neurophysiology and Center for Systems Engineering and Applied Mechanics,* PhD Thesis (Louvain: University Catholique de Louvain.

Bouma, H. (1970). Interaction effects in parafoveal letter recognition. *Nature, 226* (5241), 177-178.

Bouma, H., & Voogd, A.H.D. (1974). Control of Eye Saccades in Reading. *Vision Research, 14* (4), 273-284.

Bowers, A.R., Meek, C., & Stewart, N. (2001). Illumination and reading performance in age-related macular degeneration. *Clinical and Experimental Optometry, 84* (3), 139-147.

Bowers, A.R., Woods, R.L., & Peli, E. (2004). Preferred retinal locus and reading rate with four dynamic text presentation formats. *Optometry and Vision Science, 81* (3), 205-213.

Brainard, D.H. (1997). The Psychophysics Toolbox. *Spatial Vision, 10* (4), 433-436.

Bressler, N.M., & Bressler, S.B. (2000). Photodynamic therapy with verteporfin (visudyne): Impact on ophthalmology and visual sciences. *Investigative Ophthalmology & Visual Science, 41* (3), 624-628.

Brown, B. (1972a). Effect of target contrast variation on dynamic visual acuity and eye movements. *Vision Research, 12* (7), 1213.

Brown, B. (1972b). Resolution thresholds for moving targets at the fovea and in the peripheral retina. *Vision Research, 12* (2), 293-304.

Bullimore, M.A., & Bailey, I.L. (1995). Reading and eye movements in age-related maculopathy. *Optometry and Vision Science, 72* (2), 125-138.

Burr, D. (1980). Motion smear. *Nature, 284* (5752), 164-165.

Burr, D.C., Morrone, M.C., & Ross, J. (1994). Selective suppression of magnocellular visual pathway during saccadic eye movements. *Nature, 371* (6497), 511-513.

Burr, D.C., & Ross, J. (1982). Contrast sensitivity at high velocities. *Vision Research, 22* (4), 479-484.

Cacho, I., Dickinson, C.M., Reeves, B.C., & Harper, R.A. (2007). Visual acuity and fixation characteristics in age-related macular degeneration. *Optometry and Vision Science, 84* (6), 487-495.

Calabrese, A., Bernard, J.B., Hoffart, L., Faure, G., Barouch, F., Conrath, J., & Castet, E. (2010). Wet vs. Dry Age-Related Macular Degeneration in Patients With Central Field Loss : Different Effects on Maximum Reading Speed. *Invest. Ophthalmol. Vis. Sci., 51* (5), 3063-.

Cameron, E.L., Tai, J.C., & Carrasco, M. (2002). Covert attention affects the psychometric function of contrast sensitivity. *Vision Research, 42* (8), 949-967.

Carpenter, R. (1988). Movements of the eyes. (London: Pion).

Carrasco, M., McElree, B., Denisova, K., & Giordano, A.M. (2003). Speed of visual processing increases with eccentricity. *Nature Neuroscience, 6* (7), 699-700.

Cheal, M.L., & Lyon, D.R. (1991). Central and peripheral precuing of forced-choice discrimination. *Quarterly Journal of Experimental Psychology Section a - Human Experimental Psychology, 43* (4), 859-880.

Chen, F.K., Patel, P.J., Uppal, G.S., Rubin, G.S., Coffey, P.J., Aylward, G.W., & Da Cruz, L. (2009). A Comparison of Macular Translocation with Patch Graft in Neovascular Age-Related Macular Degeneration. *Investigative Ophthalmology & Visual Science, 50* (4), 1848-1855.

Cheong, A.M.Y., Legge, G.E., Lawrence, M.G., Cheung, S.H., & Ruff, M.A. (2007). Relationship between slow visual processing and reading speed in people with macular degeneration. *Vision Research, 47* (23), 2943-2955.

Cheong, A.M.Y., Legge, G.E., Lawrence, M.G., Cheung, S.H., & Ruff, M.A. (2008). Relationship between visual span and reading performance in age-related macular degeneration. *Vision Research, 48* (4), 577-588.

Chung, S.T.L. (2002). The effect of letter spacing on reading speed in central and peripheral vision. *Investigative Ophthalmology & Visual Science, 43* (4), 1270-1276.

Chung, S.T.L., & Bedell, H.E. (1995). Effect of retinal image motion on visual acuity and contour interaction in congenital nystagmus. *Vision Research, 35* (21), 3071-3082.

Chung, S.T.L., & Bedell, H.E. (2003). Velocity dependence of Vernier and letter acuity for band-pass filtered moving stimuli. *Vision Research, 43* (6), 669-682.

Chung, S.T.L., Legge, G.E., & Tjan, B.S. (2002). Spatial-frequency characteristics of letter identification in central and peripheral vision. *Vision Research, 42* (18), 2137-2152.

Chung, S.T.L., & Levi, D.M. (1997). Moving vernier in amblyopic and peripheral vision: Greater tolerance to motion blur. *Vision Research, 37* (18), 2527-2533.

Chung, S.T.L., Mansfield, J.S., & Legge, G.E. (1998). Psychophysics of reading. XVIII. The effect of print size on reading speed in normal peripheral vision. *Vision Research, 38* (19), 2949-2962.

Cideciyan, A.V., Hauswirth, W.W., Aleman, T.S., Kaushal, S., Schwartz, S.B., Boye, S.L., Windsor, E.A.M., Conlon, T.J., Sumaroka, A., Roman, A.J., Byrne, B.J., & Jacobson, S.G. (2009). Vision 1 Year after Gene Therapy for Leber's Congenital Amaurosis. *New England Journal of Medicine, 361* (7), 725-727.

Clarke, F.J.J. (1957). Rapid light adaptation of localised areas of the extra-foveal retina. *Journal of Modern Optics, 4*, 69-77.

Clarke, F.J.J. (1960). A study of Troxler's effect. *Journal of Modern Optics, 7* (3), 219 - 236.

Clarke, F.J.J. (1961). Visual recovery following local adaptation of the peripheral retina (Troxler's effect). *Journal of Modern Optics, 8* (2), 121 - 135.

Clarke, F.J.J., & Belcher, S.J. (1962). On the localization of troxler's effect in the visual pathway. *Vision Research, 2* (1-4), 53-68.

Clifford, C.W.G., & Ibbotson, M.R. (2002). Fundamental mechanisms of visual motion detection: models, cells and functions. *Progress in Neurobiology, 68* (6), 409-437.

Coleman, H., & Chew, E. (2007). Nutritional supplementation in age-related macular degeneration. *Current Opinion in Ophthalmology, 18* (3), 220-223.

Coltheart, M. (1980). Iconic Memory and Visible Persistence. *Perception & Psychophysics, 27* (3), 183-228.

Contestabile, M.T., Recupero, S.M., Palladino, D., De Stefanis, M., Abdolrahimzadeh, S., Suppressa, F., & Gabrieli, C.B. (2002). A new method of biofeedback in the management of low vision. *Eye, 16* (4), 472-480.

Coppola, D., & Purves, D. (1996). The extraordinarily rapid disappearance of entoptic images. *Proceedings of the National Academy of Sciences of the United States of America, 93* (15), 8001-8004.

Cornelissen, F.W. (2005). The influence of artificial scotomas on eye movements during visual search. *Optometry and Vision Science, 82* (1), 27-35.

Cornelissen, F.W., Peters, E.M., & Palmer, J. (2002). The Eyelink Toolbox: eye tracking with MATLAB and the Psychophysics Toolbox. *Behavior Research Methods Instruments & Computers, 34* (4), 613-617.

Cornelissen, F.W., & van den Dobbelsteen, J.J. (1999). Heading detection with simulated visual field defects. *Visual Impairment Research, 1* (2), 71-84.

Crossland, M.D. (2004). The development of viewing strategies in patients with macular disease. *Institute of Ophthamology,* PhD Thesis (London: University College London).

Crossland, M.D. (2011). The impact of fixation stability on visual function in eye disease. ECEM 2011, Marseille.

Crossland, M.D., Crabb, D.P., & Rubin, G.S. (2010). Task specific fixation behaviour in macular disease. *Investigative Ophthalmology & Visual Science, 52* (1), 411-416.

Crossland, M.D., Culham, L.E., Kabanarou, S.A., & Rubin, G.S. (2005). Preferred retinal locus development in patients with macular disease. *Ophthalmology, 111* (9), 1579-1585.

Crossland, M.D., Culham, L.E., & Rubin, G.S. (2004a). Fixation stability and reading speed in patients with newly developed macular disease. *Ophthalmic and Physiological Optics, 24*, 327-333.

Crossland, M.D., Legge, G.E., & Dakin, S.C. (2008). The development of an automated sentence generator for the assessment of reading speed. *Behavioral and Brain Functions, 4*, 4-14.

Crossland, M.D., & Rubin, G.S. (2002). The use of an infrared eye tracker to measure fixation stability. *Optometry and Vision Science, 79* (11), 735-739.

Crossland, M.D., & Rubin, G.S. (2006). Eye movements and reading in macular disease: Further support for the shrinking perceptual span hypothesis. *Vision Research, 46*, 590–597.

Crossland, M.D., & Silver, J.H. (2005). Thirty years in an urban low vision clinic: Changes in prescribing habits of low vision practitioners. *Optometry and Vision Science, 82* (7), 617-622.

Crossland, M.D., Sims, M., Galbraith, R.F., & Rubin, G.S. (2004b). Evaluation of a new quantitative technique to assess the number and extent of preferred retinal loci in macular disease. *Vision Research, 44* (13), 1537-1546.

Culham, L.E., Fitzke, F.W., & Marshall, J. (1996). Training of patients with ace-related macular disease (AMD) using a scanning laser ophthalmoscope (SLO). *Investigative Ophthalmology & Visual Science, 37* (3), 561-561.

Culham, L.E., Fitzke, F.W., & Marshall, J. (1997). Training of patients with age-related macular disease (AMD) using a scanner laser ophthalmoscope (SLO). *Ophthalmic and Physiological Optics, 17* (6), 542-542.

Culham, L.E., Fitzke, F.W., Timberlake, G.T., & Marshall, J. (1992). Use of scrolled text in a scanning laser ophthalmoscope to assess reading performance at different retinal locations. *Ophthalmic and Physiological Optics, 12* (3), 281-286.

Culham, L.E., Fitzke, F.W., Timberlake, G.T., & Marshall, J. (1993). Assessment of fixation stability in normal subjects and patients using a scanning laser ophthalmoscope. *Clinical Vision Science, 8* (6), 551-561.

Cummings, R.W., & Rubin, G.S. (1992). Reading speed and saccadic eye movements with artificial paracentral scotoma. *Investigative Ophthalmology and Visual Science, 33(suppl)*, 1418 (abstract).

Cummings, R.W., Whittaker, S.G., Watson, G.R., & Budd, J.M. (1985). Scanning Characters and Reading with a Central Scotoma. *American Journal of Optometry and Physiological Optics, 62* (12), 833-843.

Curcio, C.A., & Allen, K.A. (1990). Topography of ganglion cells in human retina. *The Journal of Comparative Neurology, 300* (1), 5-25.

Curcio, C.A., Allen, K.A., Sloan, K.R., Lerea, C.L., Hurley, J.B., Klock, I.B., & Milam, A.H. (1991). Distribution and morphology of human cone photoreceptors stained with anti-blue opsin. *The Journal of Comparative Neurology, 312* (4), 610-624.

Debie, J. (1985). An afterimage vernier method for assessing the precision of eye movement monitors - results for the scleral coil technique. *Vision Research, 25* (9), 1341-1343.

Delaey, C., & Van de Voorde, J. (2000). Regulatory mechanisms in the retinal and choroidal circulation. *Ophthalmic Research, 32* (6), 249-256.

Deruaz, A., Matter, M., Whatham, A.R., Goldschmidt, M., Duret, F., Issenhuth, M., & Safran, A.B. (2004). Can fixation instability improve text perception during eccentric fixation in patients with central scotomas? *British Journal of Ophthalmology, 88* (4), 461-463.

Deruaz, A., Whatham, A.R., Mermoud, C., & Safran, A.B. (2002). Reading with multiple preferred retinal loci: implications for training a more efficient strategy. *Vision Research, 42*, 2947-2957.

Dickinson, C. (1998). Low Vision: principles and practice. v3 (Oxford).

Dickinson, C.M., & Fotinakis, V. (2000). The limitations imposed on reading by low vision aids. *Optometry and Vision Science, 77* (7), 364-372.

Ditchburn, R.W. (1959). Vision with controlled movements of the retinal image. *Journal of Physiology-London, 145* (1), 98-107.

Ditchburn, R.W., & Drysdale, A.E. (1977). Effect of retinal-image movements on vision. II. Oscillatory movements. *Proceedings of the Royal Society of London Series B-Biological Sciences, 197* (1129), 385-406.

Drasdo, N. (1989). Receptive-field densities of the ganglion-cells of the human retina. *Vision Research, 29* (8), 985-988.

Dubois, M.F.W., & Collewijn, H. (1979). Optokinetic reactions in man elicited by localized retinal motion stimuli. *Vision Research, 19*, 1105-1115.

Duret, F., Issenhuth, M., & Safran, A.B. (1999). Combined use of several preferred retinal loci in patients with macular disorders when reading single words. *Vision Research, 39* (4), 873-879.

Efron, U., David, I., Apter, B., Thirer, N., Zedaka, I.B., Bogillo, O., Weyl, M., Levy, O., & Salasnik, M. (2008). An Image Transceiver-Based, Low Vision Goggle. *Vision 2008* (Montréal).

Elliott, D.B., TrukoloIlic, M., Strong, J.G., Pace, R., Plotkin, A., & Bevers, P. (1997). Demographic characteristics of the vision-disabled elderly. *Investigative Ophthalmology & Visual Science, 38* (12), 2566-2575.

Engbert, R., & Mergenthaler, K. (2006). Microsaccades are triggered by low retinal image slip. *Proceedings of the National Academy of Sciences of the United States of America, 103* (18), 7192-7197.

Epelboim, J., & Kowler, E. (1993). Slow control with eccentric targets: Evidence against a position-corrective model. *Vision Research, 33* (3), 361-380.

Ergun, E., Maar, N., Radner, W., Barbazetto, I., Schmidt-Erfurth, U., & Stur, M. (2003). Scotoma size and reading speed in patients with subfoveal occult choroidal neovascularization in age-related macular degeneration. *Ophthalmology, 110* (1), 65-69.

Falkenberg, H.K., Rubin, G.S., & Bex, P.J. (2007). Acuity, crowding, reading and fixation stability. *Vision Research, 47* (1), 126-135.

Farrel, H. (1991). Optometric management of visual handicap. (Oxford: Blackwell).

Farrell, J.E. (1984). Visible persistence of moving-objects. *Journal of Experimental Psychology-Human Perception and Performance, 10* (4), 502-511.

Faubert, J., & Overbury, O. (2000). Binocular vision in older people with adventitious visual impairment: Sometimes one eye is better than two. *Journal of the American Geriatrics Society, 48* (4), 375-380.

Faye, E. (1970). The low vision patient - clinical experience with adults and children. (New York: Grune and Stratton).

Faye, E. (1984). Clinical Low Vision. (Boston: Little, Brown and Company).

Fine, E.M., & Peli, E. (1995). Scrolled and rapid serial visual presentation texts are read at similar rates by visually-impaired. *Journal of the Optical Society of America a-Optics Image Science and Vision, 12* (10), 2286-2292.

Fine, E.M., & Peli, E. (1998). Benefits of rapid serial visual presentation (RSVP) over scrolled text vary with letter size. *Optometry and Vision Science, 75* (3), 191-196.

Fine, E.M., & Rubin, G.S. (1999a). Reading with central field loss: number of letters masked is more important than the size of the mask in degrees. *Vision Research, 39* (4), 747-756.

Fine, E.M., & Rubin, G.S. (1999b). Reading with simulated scotomas: attending to the right is better than attending to the left. *Vision Research, 39* (5), 1039-1048.

Fiset, D., Blais, C., Ethier-Majcher, C., Arguin, M., Bub, D., & Gosselin, F. (2008). Features for Identification of Uppercase and Lowercase Letters. *Psychological Science, 19* (11), 1161-1168.

Fletcher, D., & Wichita, K. (2010). Where is the PRL? (results of large cross-sectional PRL studies). Envision Meeting 2010, San Antonio.

Fletcher, D.C. (1999). Relative locations of macular scotomas near the PRL: Effect on low vision reading. *Journal of Rehabilitation Research and Development, 36* (4), 356-364.

Fletcher, D.C., & Schuchard, R.A. (1997). Preferred retinal loci relationship to macular scotomas in a low-vision population. *Ophthalmology, 104* (4), 632-638.

Fletcher, D.C., Schuchard, R.A., Walker, J.P., Wing, G.L., & Raskauskas, P.A. (2001). Preferred retinal locus (PRL) eye movement performance by eccentric distance in low vision patients. *Investigative Ophthalmology & Visual Science, 42* (4), S856-S856.

Fletcher, D.C., Schuchard, R.A., & Watson, G. (1999). Relative locations of macular scotomas near the PRL: Effect on low vision reading. *Journal of Rehabilitation Research and Development, 36* (4), 356-364.

Fornos, A.P., Sommerhalder, J., Rappaz, B., Pelizzone, M., & Safran, A.B. (2006). Processes involved in oculomotor adaptation to eccentric reading. *Investigative Ophthalmology & Visual Science, 47* (4), 1439-1447.

Forster, K.I. (1970). Visual perception of rapidly presented word sequences of varying complexity. *Perception & Psychophysics, 8* (4), 215-221.

Friedman, D.S., O'Colmain, B.J., Munoz, B., Congdon, N., Klaver, C.C.W., Klein, R., Kempen, J., Taylor, H.R., Mitchell, P., & Hyman, L. (2004). The Eye Diseases Prevalence Research, Group. Prevalence of Age-Related Macular Degeneration in the United States. *Archives of Ophthalmology, 122* (4), 564-572.

George, N.D.L., Yates, J.R.W., & Moore, A.T. (1995). X-linked retinoschisis. *British Journal of Ophthalmology, 79* (7), 697-702.

Georgeson, M.A., & Hammett, S.T. (2002). Seeing blur: 'motion sharpening' without motion. *Proceedings of the Royal Society of London Series B-Biological Sciences, 269* (1499), 1429-1434.

Gerstenblith, A.T., Thorne, J.E., Sobrin, L., Do, D.V., Shah, S.M., Foster, C.S., Jabs, D.A., & Nguyen, Q.D. (2007). Punctate inner choroidopathy a survey analysis of 77 persons. *Ophthalmology, 114* (6), 1201-1204.

Glacet-Bernard, A., Benyelles, N., Dumas, S., Haddad, W.M., Voigt, M., Razavi, S., Roquet, W., Coscas, G., & Soubrane, G. (2007). Photodynamic therapy vs limited macular translocation in the management of subfoveal choroidal neovascularization in pathologic myopia: A two-year study. *American Journal of Ophthalmology, 143* (1), 68-76.

Goodlaw, E.I. (1968). Homework for low vision patients. *American Journal of Optometry and Archives of American Academy of Optometry, 45* (8), 532-&.

Goodrich, G.L., & Mehr, E.B. (1986). Eccentric viewing training and low vision aids - Current practice and implications of peripheral retinal research. *American Journal of Optometry and Physiological Optics, 63* (2), 119-126.

Goodrich, G.L., & Quillman, R.D. (1977). Training eccentric viewing. *Journal of Visual Impairment & Blindness, 71* (9), 377-381.

Goodwin, P. (2008). Hereditary retinal disease. *Current Opinion in Ophthalmology, 19* (3), 255-262.

Green, D.G. (1970). Regional variations in visual acuity for interference fringes on retina. *The Journal of Physiology, 207* (2), 351.

Guez, J.E., Legargasson, J.F., Rigaudiere, F., & Oregan, J.K. (1993). Is there a systematic location for the pseudo-fovea in patients with central scotoma. *Vision Research, 33* (9), 1271-1279.

Gustafsson, J., & Unsbo, P. (2003). Eccentric correction for off-axis vision in central visual field loss. *Optometry and Vision Science, 80* (7), 535-541.

Hafed, Z.M., Goffart, L., & Krauzlis, R.J. (2009). A neural mechanism for microsaccade generation in the primate superior colliculus. *Science, 323* (5916), 940-943.

Hammett, S.T. (1997). Motion blur and motion sharpening in the human visual system. *Vision Research, 37* (18), 2505-2510.

Harland, S., Legge, G.E., & Luebker, A. (1998). Psychophysics of reading. XVII. Low-vision performance with four types of electronically magnified text. *Optometry and Vision Science, 75* (3), 183-190.

Hartline, H. (1940). The receptive fields of optic nerve fibers. *American Journal of Physiology, 130*, 690-699.

Hazel, C.A., Petre, K.L., Armstrong, R.A., Benson, M.T., & Frost, N.A. (2000). Visual function and subjective quality of life compared in subjects with acquired macular disease. *Investigative Ophthalmology & Visual Science, 41* (6), 1309-1315.

He, S., Cavanagh, P., & Intriligator, J. (1996). Attentional resolution and the locus of visual awareness. *Nature, 383* (6598), 334-337.

Heinen, S.J., & Skavenski, A.A. (1992). Adaptation of saccades and fixation to bilateral foveal lesions in adult monkey. *Vision Research, 32* (2), 365-373.

Higgins, K.E., Arditi, A., & Knoblauch, K. (1996). Detection and identification of mirror-image letter pairs in central and peripheral vision. *Vision Research, 36* (2), 331-337.

Hooge, L.T.C., & Erkelens, C.J. (1996). Control of fixation duration in a simple search task. *Perception & Psychophysics, 58* (7), 969-976.

Hubel, D.H., & Wiesel, T.N. (1959). Receptive fields of single neurons in the cats striate cortex. *Journal of Physiology-London, 148* (3), 574-591.

Hubel, D.H., & Wiesel, T.N. (1960). Receptive fields of optic nerve fibers in the spider monkey. *Journal of Physiology-London, 154* (3), 572-580.

Ilg, U.J. (1997). Slow eye movements. *Progress in Neurobiology, 53* (3), 293-329.

Inde, K. (1978). Low vision training in Sweden. *Journal of Visual Impairment & Blindness, 72* (8), 307-310.

Jonasson, F., Arnarsson, A., Sasaki, H., Peto, T., Sasaki, K., & Bird, A.C. (2003). The prevalence of age-related maculopathy in Iceland - Reykjavik eye study. *Archives of Ophthalmology, 121* (3), 379-385.

Kabanarou, S.A., Crossland, M.D., Bellmann, C., Rees, A., Culham, L.E., & Rubin, G.S. (2006). Gaze changes with binocular versus monocular viewing in age-related macular degeneration. *Ophthalmology, 113* (12), 2251-2258.

Kabanarou, S.A., & Rubin, G.S. (2006). Reading with central scotomas: Is there a binocular gain? *Optometry and Vision Science, 83* (11), 789-796.

Keesey, U.T. (1960). Effects of involuntary eye movements on visual acuity. *Journal of the Optical Society of America, 50* (8), 769-773.

Kelly, D.H. (1985). Visual processing of moving stimuli. *Journal of the Optical Society of America a-Optics Image Science and Vision, 2* (2), 216-225.

Kim, L.S., & Fishman, G.A. (2006). Comparison of visual acuity loss in patients with different stages of Stargardt's disease. *Ophthalmology, 113* (10), 1748-1751.

Krauzlis, R.J., Basso, M.A., & Wurtz, R.H. (1997). Shared Motor Error for Multiple Eye Movements. *Science, 276* (5319), 1693-1695.

Leat, S.J., Legge, G.E., & Bullimore, M.A. (1999a). What is low vision? A re-evaluation of definitions. *Optometry and Vision Science, 76* (4), 198-211.

Leat, S.J., Li, W., & Epp, K. (1999b). Crowding in central and eccentric vision: the effects of contour interaction and attention. *Investigative Ophthalmology & Visual Science, 40* (2), 504-512.

Lee, H.-W., Kwon, M., Legge, G.E., & Gefroh, J.J. (2010). Training improves reading speed in peripheral vision: Is it due to attention? *Journal of Vision, 10* (6)

Legge, G.E., Ahn, S.J., Klitz, T.S., & Lubker, A. (1997). Psychophysics of reading - XVI. The visual span in normal and low vision. *Vision Research, 37*, 1999-2010.

Legge, G.E., Cheung, S.-H., Yu, D., Chung, S.T.L., Lee, H.-W., & Owens, D.P. (2007). The case for the visual span as a sensory bottleneck in reading. *Journal of Vision, 7* (9), 1-15.

Legge, G.E., Mansfield, J.S., & Chung, S.T.L. (2001). Psychophysics of reading XX. Linking letter recognition to reading speed in central and peripheral vision. *Vision Research, 41* (6), 725-743.

Legge, G.E., Pelli, D.G., Rubin, G.S., & Schleske, M.M. (1985). Psychophysics of reading -1. Normal vision. *Vision Research, 25* (2), 239-252.

Legge, G.E., Ross, J.A., Isenberg, L.M., & Lamay, J.M. (1992). Psychophysics of reading - Clinical predictors of low vision reading speed. *Investigative Ophthalmology & Visual Science, 33* (3), 677-687.

Legge, G.E., Ross, J.A., Luebker, A., & Lamay, J.M. (1989). Psychophyssics of reading.VIII: The Minnesota low-vision reading test. *Optometry and Vision Science, 66* (12), 843-853.

Lei, H., & Schuchard, R.A. (1997). Using two preferred retinal loci for different lighting conditions in patients with central scotomas. *Investigative Ophthalmology & Visual Science, 38* (9), 1812-1818.

Leigh, R.J., & Zee, D.S. (1999a). The Neurology of Eye Movements. *Contemporary Neurology Series* (New York: Oxford University Press).

Leigh, R.J., & Zee, D.S. (1999b). The saccadic system. In: *The Neurology of Eye Movements* (pp. 90-150). New York: Oxford University Press.

Leigh, R.J., & Zee, D.S. (1999c). Smooth Pursuit and Visual Fixation. In: *The Neurology of Eye Movements* (pp. 151-197). New York: Oxford University Press.

Levi, D.M. (2008). Crowding - An essential bottleneck for object recognition: A mini-review. *Vision Research, 48* (5), 635-654.

Levi, D.M., Klein, S.A., & Aitsebaomo, A.P. (1985). Vernier acuity, crowding and cortical magnification. *Vision Research, 25* (7), 963-977.

Levy, O., Apter, B., & Efron, U. (2006). Low vision goggles: Optical design studies - art. no. 62890I. In: J.M. Sasian, & M.G. Turner (Eds.), *Novel Optical Systems Design and Optimization IX,* 6289 (pp. I2890-I2890).

Linsenmeier, R.A., & Padnick-Silver, L. (2000). Metabolic dependence of photoreceptors on the choroid in the normal and detached retina. *Investigative Ophthalmology & Visual Science, 41* (10), 3117-3123.

Little, D.M., Thulborn, K.R., & Szlyk, J.P. (2008). An fMRI study of saccadic and smooth-pursuit eye movement control in patients with age-related macular degeneration. *Investigative Ophthalmology & Visual Science, 49* (4), 1728-1735.

Lowe, J.B., & Rubinstein, M.P. (2000). Distance telescopes: A survey of user success. *Optometry and Vision Science, 77* (5), 260-269.

Macedo, A., Nascimento, S.M., Gomes, A.O., & Puga, A. (2007). Fixation in patients with juvenile macular disease. *Optometry and Vision Science, 84*, 852-858.

MacKeben, M. (2009). Making the Best of Remaining VisionThe Role of Focal Attention. *Neuro-Ophthalmology, 33* (3), 127-131.

MacLaren, R.E., Bird, A.C., Sathia, P.J., & Aylward, G.W. (2005). Long-term results of submacular surgery combined with macular translocation of the retinal pigment epithelium in neovascular age-related macular degeneration. *Ophthalmology, 112* (12), 2081-2087.

MacLaren, R.E., Pearson, R.A., MacNeil, A., Douglas, R.H., Salt, T.E., Akimoto, M., Swaroop, A., Sowden, J.C., & Ali, R.R. (2006). Retinal repair by transplantation of photoreceptor precursors. *Nature, 444* (7116), 203-207.

Macular photocoagulation study group (1991). Argon laser photocoagulation for neovascular maculopathy. Five-year results from randomized clinical trials. Macular photocoagulation study group. *Archives of Ophthalmology, 109* (8), 1109-1114.

Maia-Lopes, S., Silva, E.D., Silva, M.F., Reis, A., Faria, P., & Castelo-Branco, M. (2008). Evidence of widespread retinal dysfunction in patients with Stargardt disease and morphologically unaffected carrier relatives. *Investigative Ophthalmology & Visual Science, 49* (3), 1191-1199.

Mandelbaum, J., & Sloan, L.L. (1947). Peripheral visual acuity - with special reference to scotopic illumination. *American Journal of Ophthalmology, 30* (5), 581-588.

Manyak, M.J., Russo, A., Smith, P.D., & Glatstein, E. (1988). Photodynamic therapy. *Journal of Clinical Oncology, 6* (2), 380-391.

Margrain, T.H. (2000). Helping blind and partially sighted people to read: the effectiveness of low vision aids. *British Journal of Ophthalmology, 84* (8), 919-921.

Martinez-Conde, S., Macknik, S.L., & Hubel, D.H. (2004). The role of fixational eye movements in visual perception. *Nature Reviews Neuroscience, 5* (3), 229 -240.

Martinez-Conde, S., Macknik, S.L., Troncoso, X.G., & Dyar, T.A. (2006). Microsaccades counteract visual fading during fixation. *Neuron, 49* (2), 297-305.

Martinez-Conde, S., & S. Martinez-Conde, S.L.M.L.M.M.J.M.A.a.P.U.T. (2006). Fixational eye movements in normal and pathological vision. In: *Progress in Brain Research,* Volume 154, Part 1 (pp. 151-176): Elsevier.

McConkie, G.W., Kerr, P.W., Reddix, M.D., & Zola, D. (1988). Eye movement control during reading. 1- The location of initial eye fixations on words. *Vision Research, 28* (10), 1107-1118.

McKee, S.P., & Nakayama, K. (1984). The detection of motion in the peripheral visual field. *Vision Research, 24* (1), 25-32.

McMahon, T.T., Hansen, M., Stelmack, J., Oliver, P., & Viana, M.A.G. (1993). Saccadic eye movements as a measure of the effect of low vision rehabilitation on reading rate. *Optometry and Vision Science, 70* (6), 506-510.

McMahon, T.T., Hansen, M., & Viana, M. (1991). Fixation characteristics in macular disease. Relationship between saccadic frequency, sequencing, and reading rate. *Investigative Ophthalmology & Visual Science, 32* (3), 567-574.

Millodot, M. (1966). Foveal and extra-foveal acuity with and without stabilized retinal images. *British Journal of Physiological Optics, 23* (2), 75-106.

Millodot, M., Johnson, C.A., Lamont, A., & Leibowitz, H.W. (1975). Effect of dioptrics on peripheral visual-acuity. *Vision Research, 15* (12), 1357-1362.

Millodot, M., & Lamont, A. (1974). Refraction of periphery of eye. *Journal of the Optical Society of America, 64* (1), 110-111.

Moradi, P., & Moore, A.T. (2007). Molecular genetics of infantile-onset retinal dystrophies. *Eye, 21* (10), 1344-1351.

Morgan, M.J., & Benton, S. (1989). Motion-deblurring in human vision. *Nature, 340* (6232), 385-386.

Morris, E.J., & Lisberger, S.G. (1987). Different responses to small visual errors during initiation and maintenance of smooth-pursuit eye movements in monkeys. *Journal of Neurophysiology, 58* (6), 1351-1369.

Munoz, D.P., & Wurtz, R.H. (1993a). Fixation cells in monkey superior colliculus I. Characteristics of cell discharge. *Journal of Neurophysiology, 70* (2), 559-575.

Munoz, D.P., & Wurtz, R.H. (1993b). Fixation cells in monkey superior colliculus. II. Reversible activation and deactivation. *Journal of Neurophysiology, 70* (2), 576-589.

Neelam, K., Nolan, J., Chakravarthy, U., & Beatty, S. (2009). Psychophysical Function in Age-related Maculopathy. *Survey of Ophthalmology, 54* (2), 167-210.

Nilsson, U.L., Frennesson, C., & Nilsson, E.G. (1998). Location and stability of a newly established eccentric retinal locus suitable for reading, achieved through training of patients with a dense central scotoma. *Optometry and Vision Science, 75* (12), 873-878.

Nilsson, U.L., Frennesson, C., & Nilsson, S.E.G. (2003). Patients with AMD and a large absolute central scotoma can be trained successfully to use eccentric viewing, as demonstrated in a scanning laser ophthalmoscope. *Vision Research, 43* (16), 1777-1787.

Oregan, J.K. (1980). The control of saccade size and fixation duration in reading - The limits of linguistic control. *Perception & Psychophysics, 28* (2), 112-117.

Paakkonen, A.K., & Morgan, M.J. (1994). Effects of motion on blur discrimination. *Journal of the Optical Society of America a-Optics Image Science and Vision, 11* (3), 992-1002.

Packer, O., & Williams, D.R. (1992). Blurring by Fixational Eye-Movements. *Vision Research, 32* (10), 1931-1939.

Pardhan, S. (1997). Crowding in visually impaired patients: contour interaction and/or gaze-selection defects? *Neuro-Ophthalmology, 18* (2), 59-65.

Pardhan, S., Gilchrist, J., Douthwaite, W., & Yap, M. (1990). Binocular inhibition - Psychophysical and electrophysiological evidence. *Optometry and Vision Science, 67* (9), 688-691.

Pascal, E., & Abadi, R.V. (1995). Contour interaction in the presence of congenital nystagmus. *Vision Research, 35* (12), 1785-1789.

Patel, P.J., Chen, F.K., Da Cruz, L., Rubin, G.S., & Tufail, A. Test-Retest Variability of Reading Performance Metrics Using MNREAD in Patients with Age-Related Macular Degeneration. *Investigative Ophthalmology & Visual Science, 52* (6), 3854-3859.

Peli, E. (1986). Control of Eye Movement with Peripheral Vision: Implications for Training of Eccentric Viewing. *Optometry and Vision Science, 63* (2), 113-118.

Pelli, D.G. (1997). The VideoToolbox software for visual psychophysics: transforming numbers into movies. *Spatial Vision, 10* (4), 437-442.

Petre, K.L., Hazel, C.A., Fine, E.M., & Rubin, G.S. (2000). Reading with eccentric fixation is faster in inferior visual field than in left visual field. *Optometry and Vision Science, 77* (1), 34-39.

Pierrot-Deseilligny, C. (1991). Cortical control of saccades. *Neuro-Ophthalmology, 11* (2), 63-75.

Pimenides, D., George, N.D.L., Yates, J.R.W., Bradshaw, K., Roberts, S.A., Moore, A.T., & Trump, D. (2005). X-linked retinoschisis: clinical phenotype and RS1 genotype in 86 UK patients. *Journal of Medical Genetics, 42* (6)

Porac, C., & Coren, S. (1976). Dominant eye. *Psychological Bulletin, 83* (5), 880-897.

Posner, M.I. (1980). Orienting of attention. *The Quarterly Journal of Experimental Psychology, 32* (1), 3 - 25.

Prevention-Blindness, W.H.O. (2010). ICD update and revision platform: Change the definition of blindness. 2010 (Geneva: www.who.int/blindness/Change%20the%20Definition%20of%20Blindness.pdf.

Previc, F.H. (1990). Functional specialization in the lower and upper visual fields in humans: Its ecological origins and neurophysiological implications. *Behavioral and Brain Sciences, 13* (03), 519-542.

Provis, J.M., Penfold, P.L., Cornish, E.E., Sandercoe, T.M., & Madigan, M.C. (2005). Anatomy and development of the macula: specialisation and the vulnerability to macular degeneration. *Clinical and Experimental Optometry, 88* (5), 269-281.

Purves, D., Augustine, G., Fitzpatrick, D., Hall, W., LaMantia, A.-S., McNamara, J., & Williams, S.M. (2004). Central Visual Pathways. In: D. Purves (Ed.) *Neuroscience* (p. 259). Sunderland: Sinauer Associates, Inc.

Quillen, D.A., Davis, J.B., Gottlieb, J.L., Blodi, B.A., Callanan, D.G., Chang, T.S., & Equi, R.A. (2004). The white dot syndromes. *American Journal of Ophthalmology, 137* (3), 538-550.

Raninen, A., Franssila, R., & Rovamo, J. (1991). Critical flicker frequency to red targets as a function of luminance and flux across the human visual field. *Vision Research, 31* (11), 1875-1881.

Rattle, J.D. (1969). Effect of Target Size on Monocular Fixation. *Optica Acta: International Journal of Optics, 16* (2), 183-190.

Rattner, A., & Nathans, J. (2006). Macular degeneration: recent advances and therapeutic opportunities. *Nat Rev Neurosci, 7* (11), 860-872.

Rayner, K. (1978). Eye-Movements in Reading and Information-Processing. *Psychological Bulletin, 85* (3), 618-660.

Rayner, K. (1998). Eye movements in reading and information processing: 20 years of research. *Psychological Bulletin, 124* (3), 372-422.

Rayner, K., & Bertera, J.H. (1979). Reading without a fovea. *Science, 206* (4417), 468-469.

Rayner, K., Inhoff, A.W., Morrison, R.E., Slowiaczek, M.L., & Bertera, J.H. (1981). Masking of foveal and parafoveal vision during eye fixations in reading. *Journal of Experimental Psychology-Human Perception and Performance, 7* (1), 167-179.

Rayner, K., & McConkie, G.W. (1976). What guides a readers eye movements. *Vision Research, 16* (8), 829-837.

Rayner, K., & Pollatsek, A. (1987). Eye movements in reading - A tutorial review. *Attention and Performance,* (12), 327-362.

Rayner, K., Well, A.D., & Pollatsek, A. (1980). Asymmetry of the effective visual field in reading. *Perception & Psychophysics, 27* (6), 537-544.

Rayner, K., Well, A.D., Pollatsek, A., & Bertera, J.H. (1982). The availability of useful information to the right of fixation in reading. *Perception & Psychophysics, 31* (6), 537-550.

Reichle, E.D., Rayner, K., & Pollatsek, A. (2003). The E-Z Reader model of eye-movement control in reading: Comparisons to other models. *Behavioral and Brain Sciences, 26* (04), 445-476.

Reinhard, J., Messias, A., Dietz, K., MacKeben, M., Lakmann, R., Scholl, H.P.N., Apfelstedt-Sylla, E., Weber, B.H.F., Seeliger, M.W., Zrenner, E., & Trauzettel-Klosinski, S. (2007). Quantifying fixation in patients with Stargardt disease. *Vision Research, 47* (15), 2076-2085.

Riggs, L.A., & Schick, A.M.L. (1968). Accuracy of retinal image stabilization achieved with a plane mirror an a tightly fitting contact lens. *Vision Research, 8* (2), 159-169.

Robinson, D.A. (1965). Mechanics human smooth pursuit eye movement. *Journal of Physiology-London, 180* (3), 569-591.

Robinson, D.A. (1972). Eye mevements evoked by collicular stimulation in the alert monkey. *Vision Research, 12*, 1795-1808.

Robinson, D.A., Gordon, J.L., & Gordon, S.E. (1986). A model of the smooth pursuit eye movement system. *Biological Cybernetics, 55* (1), 43-57.

Rovamo, J., & Raninen, A. (1988). Critical flicker frequency as a function of stimulus area and luminace at various eccentricities in human cone vision - A revision of Granit-Harper and Ferry-Porter laws. *Vision Research, 28* (7), 785-790.

Rovamo, J., Virsu, V., & Nasanen, R. (1978). Cortical magnification factor predicts photopic contrast sensitivity of peripheral vision. *Nature, 271* (5640), 54-56.

Rubin, G.S., & Feely, M. (2009). The Role of Eye Movements During Reading in Patients with Age-Related Macular Degeneration (AMD). *Neuro-Ophthalmology, 33* (3), 120-126.

Rubin, G.S., Munoz, B., Bandeen-Roche, K., & West, S.K. (2000). Monocular versus binocular visual acuity as measures of vision impairment and predictors of visual disability. *Investigative Ophthalmology & Visual Science, 41* (11), 3327-3334.

Rubin, G.S., & Turano, K. (1994). Low-vision reading with sequential word presentation. *Vision Research, 34* (13), 1723-1733.

Rucci, M., Iovin, R., Poletti, M., & Santini, F. (2007). Miniature eye movements enhance fine spatial detail. *Nature, 447* (7146), 851-854.

Safran, A.B., Florence Duret , Marc Issenhuth, Christhphe Mermoud (1999). Full text with a central scotoma: Pseudo regressions and pseudo line losses. *British Journal of Ophthalmology, 83*, 1341-1347.

Sakaguchi, H., Ohji, M., Kubota, A., Otori, Y., Hayashi, A., Kusaka, S., Saito, Y., & Tano, Y. (2000). Amsler grid examination and optical coherence tomography of a macular hole caused by accidental Nd : YAG laser injury. *American Journal of Ophthalmology, 130* (3), 355-356.

Sansbury, R.V., Skavensk.Aa, Haddad, G.M., & Steinman, R.M. (1973). Normal fixation of eccentric targets. *Journal of the Optical Society of America, 63* (5), 612-614.

Schiller, P.H. (1998). The neural control of visually guided eye movements In: J.E. Richards (Ed.) *Congnitive neuroscience of attention: a developmental perspective* (pp. 3-50).

Schuchard, R.A. (2005). Preferred retinal loci and macular scotoma characteristics in patients with age-related macular degeneration. *Canadian Journal of Ophthalmology, 40*, 303-312.

Schuchard, R.A., & Fletcher, D.C. (1994). Preferred retinal locus: a review with applications in low vision rehabilitation. *Ophthalmology Clinics of North America, 7*, 243-256.

Schuchard, R.A., & Raasch, T.W. (1992a). Retinal locus for fixation - Pericentral fixation targets. *Clinical Vision Sciences, 7* (6), 511-520.

Schuchard, R.A., & Raasch, T.W. (1992b). Retinal locus for fixation: Pericentral fixation targets. *Clinical Vision Science, 7*, 511-520.

Scott, I.U., Smiddy, W.E., Schiffman, J., Feuer, W.J., & Pappas, C.J. (1999). Quality of life of low-vision patients and the impact of low-vision services. *American Journal of Ophthalmology, 128* (1), 54-62.

Segraves, M.A., & Goldberg, M.E. (1994). Effect of stimulus position and velocity upon the maintenance of smooth-pursuit eye velocity. *Vision Research, 34* (18), 2477-2482.

Seiple, W., Holopigian, K., Shnayder, Y., & Szlyk, J.P. (2001). Duration thresholds for target detection and identification in the peripheral visual field. *Optometry and Vision Science, 78* (3), 169-176.

Seiple, W., Szlyk, J.P., McMahon, T., Pulido, J., & Fishman, G.A. (2005). Eye-movement training for reading in patients with age-related macular degeneration. *Investigative Ophthalmolology and Vision Science, 46* (8), 2886-2896.

Sharpe, C.R. (1972). The visibility and fading of thin lines visualized by their controlled movement across the retina. *Journal of Physiology-London, 222* (1), 113-134.

Sikkink, S.K., Biswas, S., Parry, N.R.A., Stanga, P.E., & Trump, D. (2007). X-linked retinoschisis: an update. *Journal of Medical Genetics, 44* (4), 225-232.

Sjöstrand, J., Olsson, V., Popovic, Z., & Conradi, N. (1999). Quantitative estimations of foveal and extra-foveal retinal circuitry in humans. *Vision Research, 39*, 2987-2998.

Skrandies, W. (1987). The upper and lower visual field of man : Electrophysiological and functional differences. In: Springer-Verlag (Ed.) *Progress in Sensory Physiology,* 8 (pp. 1-93). Berlin.

Smith, B.T., Joseph, D.P., & Grand, M.G. (2007). Treatment of neovascular age-related macular degeneration: past, present and future directions. *Current Opinion in Ophthalmology, 18* (3), 240-244.

Smith, H.J., Dickinson, C.M., Cacho, I., Reeves, B.C., & Harper, R.A. (2005). A randomized controlled trial to determine the effectiveness of prism spectacles for patients with age-related macular degeneration. *Archives of Ophthalmology, 123* (8), 1042-1050.

Sommerhalder, J., Rappaz, B., de Haller, R., Fornos, A.P., Safran, A.B., & Pelizzone, M. (2004). Simulation of artificial vision: II. Eccentric reading of full-page text and the learning of this task. *Vision Research, 44* (14), 1693-1706.

Spaide, R.F., Noble, K., Morgan, A., & Freund, K.B. (2006). Vitelliform macular dystrophy. *Ophthalmology, 113* (8), 1392-1400.

Starr, M.S., & Rayner, K. (2001). Eye movements during reading: some current controversies. *Trends in Cognitive Sciences, 5* (4), 156-163.

Steinman, R.M. (1965). Effect of target size, luminance and color on monocular fixation. *Journal of the Optical Society of America, 55* (9), 1158-1165.

Steinman, R.M., Cunitz, R.J., Timberlake, G.T., & Herman, M. (1967). Voluntary Control of Microsaccades during Maintained Monocular Fixation. *Science, 155* (3769), 1577-1579.

Stelmack, J.A., Robert, W.M., & Stelmack, T.R. (2004). Is there a standart of care for eccentric viewing training? *Journal of Rehabilitation Research and Development, 41* (5), 729-738.

Subramanian, A., & Pardhan, S. (2006). The repeatability of MNREAD acuity charts and variability at different test distances. *Optometry and Vision Science, 83* (8), 572-576.

Subramanian, A., & Pardhan, S. (2009). Repeatability of Reading Ability Indices in Subjects with Impaired Vision. *Investigative Ophthalmology & Visual Science, 50* (8), 3643-3647.

Talgar, C.P., & Carrasco, M. (2002). Vertical meridian asymmetry in spatial resolution: visual and attentional factors. *Psychonomic Bulletin & Review, 9* (4), 714-722.

Tano, Y. (2002). Lix Edward Jackson memorial lecture - Pathologic myopia: Where are we now? *American Journal of Ophthalmology, 134* (5), 645-660.

Tant, M.L.M., Cornelissen, F.W., Kooijman, A.C., & Brouwer, W.H. (2002). Hemianopic visual field defects elicit hemianopic scanning. *Vision Research, 42* (10), 1339-1348.

Tarita-Nistor, L., Gonzalez, E.G., Markowitz, S.N., & Steinbach, M.J. (2006a). Binocular function in patients with age-related macular degeneration: a review. *Canadian Journal of Ophthalmology-Journal Canadien D Ophtalmologie, 41* (3), 327-332.

Tarita-Nistor, L., Gonzalez, E.G., Markowitz, S.N., & Steinbach, M.J. (2006b). Binocular interactions in patients with age-related macular degeneration: Acuity summation and rivalry. *Vision Research, 46* (16), 2487-2498.

Temel, A., & Kazokoglu, H. (1991). Low vision aids in Stargardt disease. *Ophthalmologica, 202* (3), 142-146.

Thibos, L.N., & Bradley, A. (1993). New methods for discriminating neural and optical losses of vision. *Optometry and Vision Science, 70* (4), 279-287.

Thorndyke, P.W. (1977). Cognitive structures in comprehension and memory of narrative discourse. *Cognitive Psychology, 9* (1), 77-110.

Timberlake, G.T., Mainster, M.A., Peli, E., Augliere, R.A., Essock, E.A., & Arend, L.E. (1986). Reading with a macular scotoma .1. Retinal location of scotoma and fixation area. *Investigative Ophthalmology & Visual Science, 27* (7), 1137-1147.

Timberlake, G.T., Peli, E., Essock, E.A., & Augliere, R.A. (1987). Reading with a macular scotoma .2. Retinal locus for scanning text. *Investigative Ophthalmology & Visual Science, 28* (8), 1268-1274.

Tita-Nistor, L., Gonzalez, E.G., Mkowitz, S.N., & Steinbach, M.J. (2009). Plasticity of fixation in patients with central vision loss. *Visual Neuroscience, 26* (5-6), 487-494.

Toet, A., & Levi, D.M. (1992). The two-dimensional shape of spatial interaction zones in the parafovea. *Vision Research, 32* (7), 1349-1357.

Tripathy, S.P., & Cavanagh, P. (2002). The extent of crowding in peripheral vision does not scale with target size. *Vision Research, 42* (20), 2357-2369.

Troost, B.T., Weber, R.B., & Daroff, R.B. (1974). Hypometric saccades. *American Journal of Ophthalmology, 78* (6), 1002-1005.

Tulunay-Keesey, Ü. (1982). Fading of stabilized retinal images. *Journal of the Optical Society of America, 72* (4), 440-447.

Valberg, A., & Fosse, P. (2002). Binocular contrast inhibition in subjects with age-related macular degeneration. *Journal of the Optical Society of America a-Optics Image Science and Vision, 19* (1), 223-228.

Vallines, I., & Greenlee, M.W. (2006). Saccadic suppression of retinotopically localized blood oxygen level-dependent responses in human primary visual area V1. *Journal of Neuroscience, 26* (22), 5965-5969.

Valsechi, M., Schutz, A.C., & Gegenfurtner, K.R. (2011). Eye movements in reading drifting text. *ECEM 2011, Marseille* (p. in press): Journal of Eye Movement Research.

van der Geest, J.N., & Frens, M.A. (2002). Recording eye movements with video-oculography and scleral search coils: a direct comparison of two methods. *Journal of Neuroscience Methods, 114* (2), 185-195.

Varsori, M., Perez-Fornos, A., Safran, A.B., & Whatham, A.R. (2004). Development of a viewing strategy during adaptation to an artificial central scotoma. *Vision Research, 44* (23), 2691-2705.

Vedantham, V., & Ramasamy, K. (2005). Optical coherence tomography in Best's disease: An observational case report. *American Journal of Ophthalmology, 139* (2), 351-353.

Verezen, C.A., VolkerDieben, H.J., & Hoyng, C.B. (1996). Eccentric viewing spectacles in everyday life, for the optimum use of residual functional retinal areas, in patients with age-related macular degeneration. *Optometry and Vision Science, 73* (6), 413-417.

Vingerling, J.R., Dielemans, I., Hofman, A., Grobbee, D.E., Hijmering, M., Kramer, C.F.L., & Dejong, P. (1995). The prevalence of age-related maculopathy in the Rotterdam study. *Ophthalmology, 102* (2), 205-210.

Vingolo, E.M., Salvatore, S., & Cavarretta, S. (2009). Low-Vision Rehabilitation by Means of MP-1 Biofeedback Examination in Patients with Different Macular Diseases: A Pilot Study. *Applied Psychophysiology and Biofeedback, 34* (2), 127-133.

von Noorden, G.K., & Mackensen, G. (1962). Phenomenology of Eccentric Fixation. *American Journal of Ophthalmology, 53* (4), 642-661.

Walia, S., & Fishman, G.A. (2009). Natural History of Phenotypic Changes in Stargardt Macular Dystrophy. *Ophthalmic Genetics, 30* (2), 63-68.

Watson, A.B., & Pelli, D.G. (1983). Quest - a bayesian adaptative psychometric method. *Perception & Psychophysics, 33* (2), 113-120.

Westheimer, G. (1960). Modulation Thresholds for Sinusoidal Light Distributions on the Retina. *Journal of Physiology-London, 152* (1), 67-74.

Westheimer, G. (1983). Temporal order detection for foveal and peripheral visual stimuli. *Vision Research, 23* (8), 759-763.

Westheimer, G., & McKee, S.P. (1975). Visual acuity in presence of retinal-image motion. *Journal of the Optical Society of America, 65* (7), 847-850.

White, J.M., & Bedell, H.E. (1990). The oculomotor reference in humans with bilateral macular disease. *Investigative Ophthalmology & Visual Science, 31* (6), 1149-1161.

Whittaker, S.G., Budd, J., & Cummings, R.W. (1988). Eccentric fixation with macular scotoma. *Investigative Ophthalmology & Visual Science, 29* (2), 268-278.

Whittaker, S.G., & Cummings, R.W. (1990). Foveating saccades. *Vision Research, 30* (9), 1363-1366.

Whittaker, S.G., Cummings, R.W., & Swieson, L.R. (1991). Saccade control without a fovea. *Vision Research, 31* (12), 2209-2218.

Whittaker, S.G., & Lovie-Kitchin, J. (1993a). Eccentric scrolling and eye movements in people with macular scotoma. *Optometry and Vision Science, Suppl, 70* (1), 129.

Whittaker, S.G., & Lovie-Kitchin, J. (1993b). Visual requirements for reading. *Optometry and Vision Science, 70* (1), 54-65.

Williams, D.R., & Coletta, N.J. (1987). Cone spacing and the visual resolution limit. *Journal of the Optical Society of America A - Optics Image Science and Vision, 4* (8), 1514-1523.

Wolffsohn, J.S. (2007). Magnification. In: N.J. Rumney, & A.J. Jackson (Eds.), *Low Vision Manual,* 1 (Philadelphia: Butterworth-Heinemann).

Wyatt, H.J., & Pola, J. (1983). Smooth Pursuit Eye-Movements under Open-Loop and Closed-Loop Conditions. *Vision Research, 23* (10), 1121-1131.

Yeshurun, Y., & Carrasco, M. (1999). Spatial attention improves performance in spatial resolution tasks. *Vision Research, 39* (2), 293-306.

Yu, D., Park, H., Gerold, D., & Legge, G.E. (2010). Comparing reading speed for horizontal and vertical English text. *Journal of Vision, 10* (2), 1-17.

Yu, D.Y., Legge, G.E., Park, H., Gage, E., & Chung, S.T.L. (2010). Development of a training protocol to improve reading performance in peripheral vision. *Vision Research, 50* (1), 36-45.

Zeevi, Y.Y., & Peli, E. (1979). Latency of peripheral saccades. *Journal of the Optical Society of America, 69* (9), 1274-1279.

Zeevi, Y.Y., Peli, E., & Stark, L. (1979). Study of eccentric fixation with secondary visual feedback. *Journal of the Optical Society of America, 69* (5), 669-675.

Zwick, H., Ness, J.W., Molchany, J.M., Stuck, B.E., & Loveday, J. (1997). Neural motor ocular strategies associated with the development of a pseudofovea following laser induced macular damage and artificial macular occlusion. Is the fovea replaceable? In: *Ilsc'97 - Proceedings of the International Laser Safety Conference, Vol 3* (pp. 175-181).

Zwick, H., Ness, J.W., Molchany, J.M., Stuck, B.E., & Loveday, J. (1998). Neural motor ocular strategies associated with the development of a pseudofovea following laser induced macular damage and artificial macular occlusion. Is the fovea replaceable? *Journal of Laser Applications, 10* (3), 144-147.

Appendix A

Participants in the experiments described in Chapter 6

Appendix Table 1: Additional information for participants in experiments of Chapter 6.

Subject ID	Experiment	Age/Sex	Glasses	Contact lens
S1	1 & 2	32 / M	No	Yes
S2	1 & 2	35 / F	No	No
S3	1 & 2	31 / M	No	No
S4	1	41 / F	No	No
S5	1	32 / M	No	No
S6	2	41 / F	No	No
S7	2	26 / M	Yes	No

Participants in the experiment described in Chapter 7

Appendix Table 2: Additional information for participants in experiments of Chapter 7. PRL: preferred retinal locus. The PRL location is defined in visual field space determined according to the convention defined in section 4.4.2. VA: visual acuity. AMD: age-related macular disease. JMD: Juvenile macular disease.

Sub. ID	Age/Sex	Diagnosis	Eye	VA	PRL location
S1	84 / F	AMD	LE	0.7 logMAR	Left
S2	87 /F	AMD	RE	1.0 logMAR	Above
S3	89 / M	AMD	RE	1 logMAR	Left
S4	72 / F	AMD	RE	1 logMAR	Left
S5	54 / F	JMD	LE	0.7 logMAR	Below
S6	73 / M	AMD	RE	1.2 logMAR	**
S7	88 / M	AMD	RE	1.1 logMAR	Below
S8	89 / F	AMD	RE	1.0 logMAR	Below
S9	81 / M	AMD	RE	0.4 logMAR	Central
S10	24 / F	JMD	LE	0.8 logMAR	Below

** PRL was not clearly defined

Participants in the experiments described in Chapter 8

Appendix Table 3: Additional information for participants in experiments of Chapter 8.

Subject ID	Sex	age	Glasses	Contact lens
S1	M	26	Yes	No
S2	F	25	No	No
S3	F	27	No	Yes
S4	F	31	No	No
S5	F	31	No	Yes
S6	M	27	Yes	No
S7	F	30	No	Yes
S8	F	26	No	Yes

Appendix B

Consent form for normal subjects

Information Sheet for Participants in Research Studies

You will be given a copy of this information sheet.

Title of Project: **Visual acuity of peripheral retina for unstable targets**

This study has been approved by the UCL Research Ethics Committee [**Project ID 1047/001**]:

Name, Address and Contact Details of Investigators:

Gary S. Rubin & Antonio Filipe Macedo
UCL - Institute of Ophthalmology,
Vision Rehabilitation Research,
11-14 Bath Street, London ECIV 9EL

Email: g.rubin@ucl.ac.uk
a.macedo@ucl.ac.uk

We would like to invite you to participate in this research project. You should only participate if you want to; choosing not to take part will not disadvantage you in any way. Before you decide whether you want to take part, it is important for you to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or you would like more information.

Details of Study

We are investigating the effects of eye movement and image movement on the ability to see objects. This interests us as people with certain eye diseases are less able to keep their eyes still when observing an object.

We will ask you to look at a computer monitor and identify the orientation of a series of letter C's presented away from the centre of your vision. To control where the letter is presented, we will be monitoring your eye position using an infrared eyetracker, which is a non-invasive device consisting of three infrared (non-visible light) cameras mounted on a headband. The experiment will take approximately thirty minutes to complete.

It is up to you to decide whether or not to take part. If you decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason.

All data will be collected and stored in accordance with the Data Protection Act 1998.

Informed Consent Form for Participants in Research Studies

(This form is to be completed independently by the participant after reading the Information Sheet and/or having listened to an explanation about the research.)

Title of Project: **Visual acuity of peripheral retina for unstable targets**

This study has been approved by the UCL Research Ethics Committee **[Project ID 1047/001]**:

Participant's Statement

I agree that I have

- read the information sheet and/or the project has been explained to me orally;
- had the opportunity to ask questions and discuss the study;
- received satisfactory answers to all my questions or have been advised of an individual to contact for answers to pertinent questions about the research and my rights as a participant and whom to contact in the event of a research-related injury.

I agree to be contacted in the future by UCL researchers who would like to invite me to participate in follow-up studies.

I understand that I am free to withdraw from the study without penalty if I so wish and I consent to the processing of my personal information for the purposes of this study only and that it will not be used for any other purpose. I understand that such information will be treated as strictly confidential and handled in accordance with the provisions of the Data Protection Act 1998.

Signed: Date:

Investigator's Statement

I ANTONIO FILIPE MACEDO

confirm that I have carefully explained the purpose of the study to the participant and outlined any reasonably foreseeable risks or benefits (where applicable).

Signed: Date:

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Consent form for patients

Moorfields Eye Hospital NHS
NHS Foundation Trust

City Road
London
EC1V 2PD

Tel: 020 7253 3411
www.moorfields.nhs.uk

Centre:
Study Protocol Number: 08/H0721/5
Patient ID Number (affix label): 01

CONSENT FORM

Study Title: Stabilising eye movements in people with macular disease – an exploratory study

Researchers: Professor Gary Rubin, Dr Michael Crossland, Mr Antonio Filipe Macedo

Please initial box

1. I confirm that I have read and understood the information sheet dated 07/12/2007 (version 2) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐

3. I understand that relevant sections of any of my medical notes and data collected during the study may be looked at by responsible individuals from this Hospital, the UCL Institute of Ophthalmology and from regulatory authorities, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐

4. I understand that some eye tests for this study will be carried out in the Visual Rehabilitation Unit of the UCL Institute of Ophthalmology, and I agree to this. ☐

CONSENT FORM (continued)

Study Title: Stabilising eye movements in people with macular disease

Researchers: Professor Gary Rubin, Dr Michael Crossland, Mr Antonio Filipe Macedo

Please initial box

5. I would like / would not like (delete as appropriate) my GP to be informed about my participation in this study ☐

6. I agree to take part in the above study. ☐

Patient Name	Signature	Date
Researcher	Signature	Date
Person taking consent (if different from researcher)	Signature	Date

1 copy for patient; 1 for researcher site file; 1 (original) to be kept in medical notes.

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Appendix C

Additional results for Chapter 6

Appendix Table 4: Individual mean values of peripheral visual acuity in logMAR for each observer (S), gain and position for experiment 1.

	Gain	**5º**				**10º**			
		Right	Up	Left	Down	Right	Up	Left	Down
S1	0	0.75	0.85	0.66	0.82	0.94	1.10	0.93	1.02
	0.1	0.60	0.79	0.56	0.73	0.87	1.04	0.84	0.98
	1	0.55	0.74	0.53	0.76	0.78	1.03	0.81	0.97
	10	0.57	0.70	0.57	0.70	0.76	0.97	0.77	0.88
S2	0	0.71	0.91	0.72	0.81	0.97	1.12	0.95	1.02
	0.1	0.62	0.83	0.64	0.72	0.91	1.06	0.92	1.04
	1	0.69	0.90	0.66	0.75	0.89	1.02	0.81	0.98
	10	0.66	0.87	0.70	0.80	0.88	1.03	0.98	0.98
S3	0	0.69	0.81	0.73	0.84	0.87	1.17	0.99	1.13
	0.1	0.77	0.93	0.72	0.93	0.89	1.19	0.96	1.12
	1	0.69	0.88	0.67	0.87	0.92	1.18	0.97	1.14
	10	0.72	0.84	0.71	0.91	0.92	1.13	0.93	1.07
S4	0	0.69	0.81	0.64	0.80	0.95	1.10	0.92	1.06
	0.1	0.61	0.76	0.61	0.75	0.91	1.08	0.89	1.12
	1	0.64	0.78	0.68	0.79	0.90	0.99	0.81	1.02
	10	0.61	0.68	0.58	0.72	0.86	0.93	0.81	1.05
S5	0	0.71	0.87	0.73	0.81	1.00	1.13	0.97	1.14
	0.1	0.72	0.92	0.64	0.86	0.96	1.11	0.91	1.12
	1	0.70	0.94	0.65	0.83	0.99	1.13	0.98	1.10
	10	0.67	0.85	0.58	0.79	0.91	1.07	0.90	1.08

Appendix Table 5: Individual mean values of peripheral visual acuity in logMAR for each observer (S), gain and position for experiment 2.

	Gain	**5º**				**10º**			
		Right	Up	Left	Down	Right	Up	Left	Down
S1	0	0.80	1.00	0.83	1.08	1.16	1.29	1.06	1.40
	0.1	0.80	0.93	0.84	0.94	1.04	1.25	0.98	1.23
	1	0.83	0.97	0.84	0.97	1.05	1.24	0.98	1.25
	10	1.05	1.13	0.98	1.16	1.28	1.41	1.23	1.42
S6	0	0.90	1.12	0.99	1.02	1.09	1.35	1.24	1.24
	0.1	0.90	1.12	0.93	1.02	1.07	1.26	1.22	1.31
	1	0.87	1.12	0.88	0.96	1.13	1.35	1.17	1.28
	10	1.03	1.24	0.92	1.11	1.21	1.40	1.24	1.34
S7	0	0.91	1.10	0.89	0.96	1.11	1.40	1.26	1.32
	0.1	0.84	1.07	0.89	0.95	1.12	1.34	1.12	1.33
	1	0.84	1.06	0.86	1.03	1.29	1.39	1.15	1.25
	10	1.03	1.17	1.05	1.11	1.26	1.42	1.27	1.33
S4	0	0.73	0.83	0.75	0.94	0.91	1.17	0.97	1.29
	0.1	0.78	0.91	0.84	0.90	1.00	1.16	1.07	1.21
	1	0.79	0.92	0.83	0.90	1.02	1.19	1.09	1.17
	10	0.96	1.02	0.98	1.06	1.19	1.29	1.19	1.33
S5	0	0.88	1.12	0.87	0.91	1.11	1.40	1.15	1.33
	0.1	0.89	1.12	0.91	0.95	1.07	1.39	1.15	1.31
	1	0.88	1.13	0.86	0.92	1.10	1.36	1.17	1.33
	10	1.02	1.17	1.00	1.05	1.20	1.40	1.16	1.37

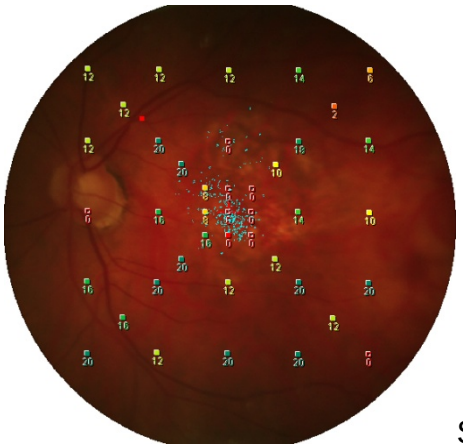
Appendix Table 6: Summary of the main differences in visual acuity between positions of the two experiments described in Chapter 6. Differences were obtained by subtracting results for conditions in the first column by the condition defined in the remaining columns headings.

	Noncrowded			
	Right	**Up**	**Left**	**Down**
Right	-	-0.20	0.09	-0.31*
Up	-	-	0.29	-0.11
Left	-	-	-	-0.40**
	Crowded			
	Right	**Up**	**Left**	**Down**
Right	-	0.34**	0.23	0.53***
Up	-	-	-0.11	0.18
Left	-	-	-	0.30*

§ Significance levels are: 0.05 (*), 0.01 (**), and 0.001 (***)

Additional results for Chapter 7

Appendix Table 7: Microperimetry results for participants with macular disease in the visual acuity experiment, Chapter 7.



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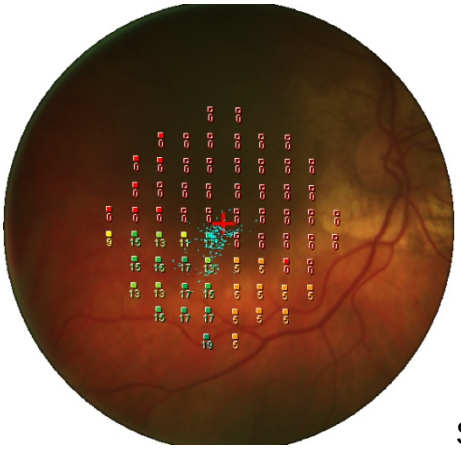

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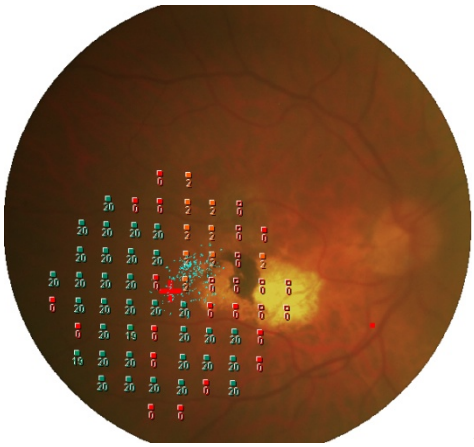

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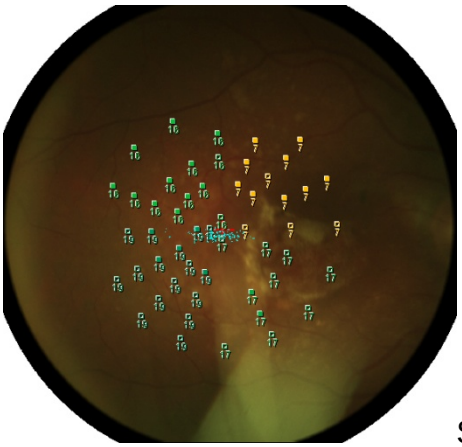

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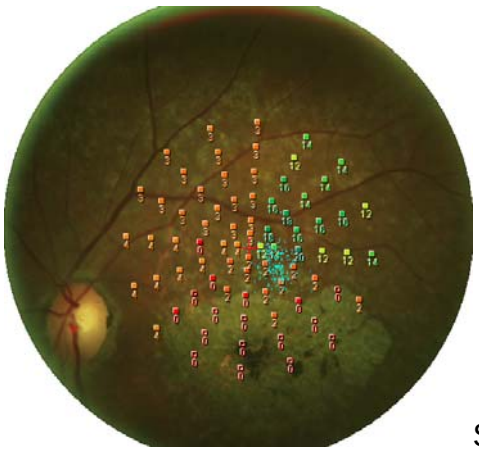
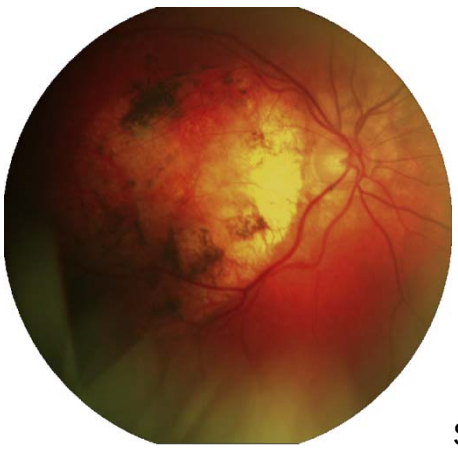
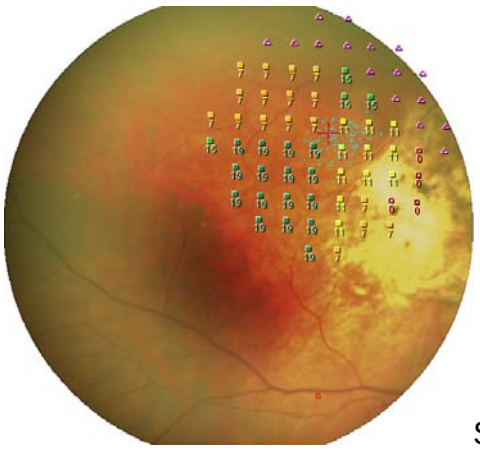


S5



S6

Appendix Table 7 (continued)



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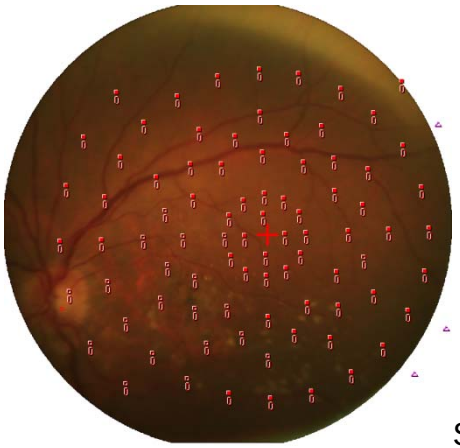
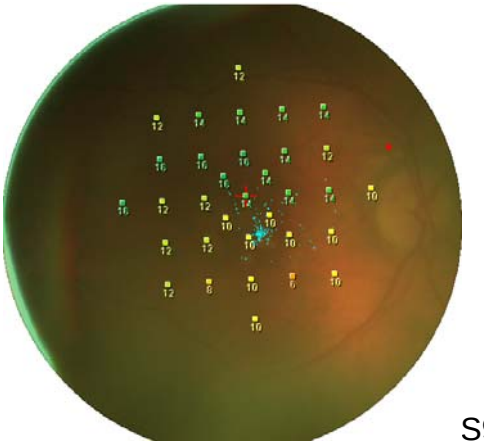
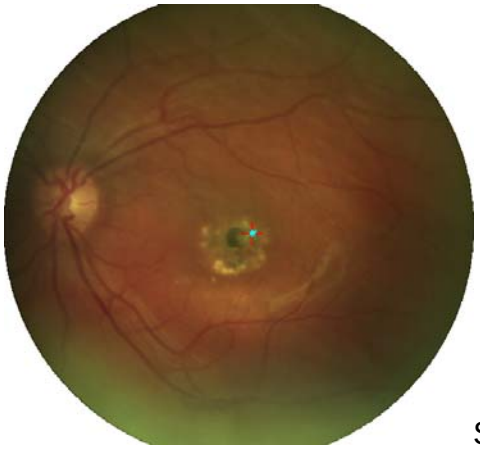


S8



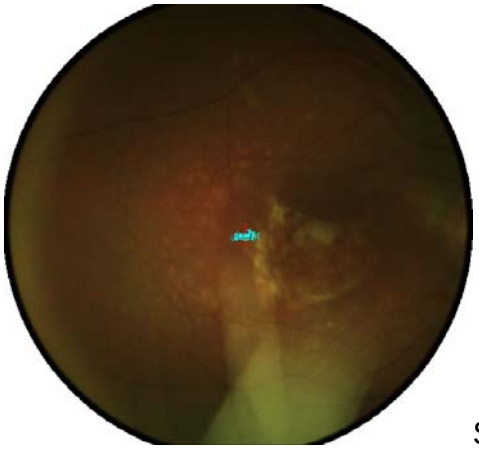
S9



S10

Additional results for Chapter 9

Appendix Table 8: Microperimetry results for participants with macular disease in the reading experiment, Chapter 9.



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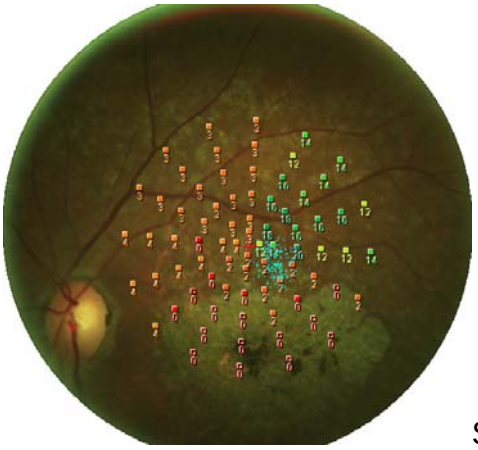

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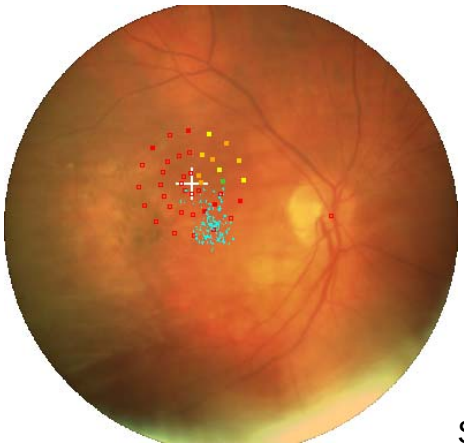

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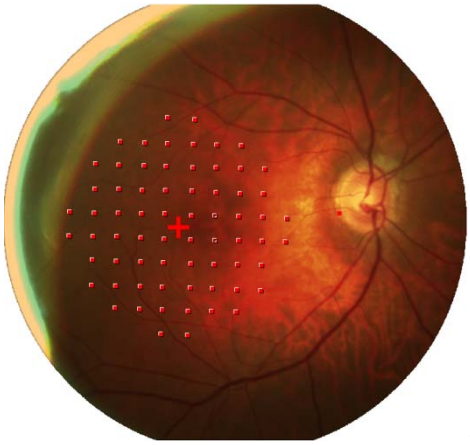
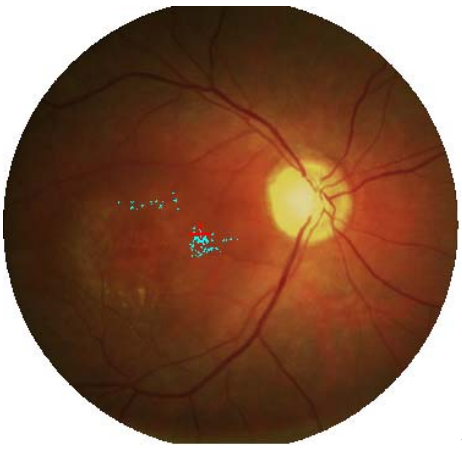


S4



S5

Publications

Papers

Appendix D

Example of a Matlab program to run the peripheral visual acuity experiment

```
function Crowded2Bars
try
clear all;home; tic
fprintf('*PERIPHERAL VA FOR UNSTABLE TARGETS*\n');
fprintf('Performed on ''%s''\n', datestr(now));
 % initialize eyelink            home;
if EyelinkInit()~= 1; %
    return;
end;
fprintf('\n');option='n';%dir('*.mat');
% difining header
while ~strcmp('y',option)
[matFileName,t_index,current_s,h,i_done]= trialsOrder;
h.distance=50;
h.sizeM=[40.5 30] ;
switch h.eccentricity
    case 0
    h.start_va=0.3;
    case 5
    h.start_va=0.8;
    h.crowd_d=0.5;
    case 10
    h.start_va=1.3;
    h.crowd_d=1;
end
% if strcmp(h.initials,'CA'); h.crowd_d='2bars';end
h.start_sd=0.3;h.crowd_d='2bars';
if strcmp(h.initials,'TT')
    h.trialsDesired=20;
else
    h.trialsDesired=60;
end
look4file=exist( matFileName,'file');
fprintf('\n\tPlase make sure the distance is "%g"
cm\n\n\t',h.distance);
if ~strcmp(h.initials,'TT')
```

```
    if look4file==2;fprintf('\tTHIS FILE ALREADY
EXIST!...REPLACE?\n\n\t')
    else fprintf('New file!\n\n\t');end
    option=input('PROCEED?  [y/n]:     ','s' );
else
  fprintf('\tDEMO TRIAL!\n\n\t');option='y';end
end %while option='n'
if
(h.distance~=50&&h.eccentricity==10)||(h.distance~=125&&h.eccentricity
==0)||(h.distance~=50&&h.eccentricity==5);
    error('This is not the correct distance for this test');end
% Do filename i/o
screenNumber=max(Screen('Screens'));
[h.filename,eyefilename,myerr] = getfilenames(h,screenNumber);
% prompt for file name
if myerr
% exit on errors in inputs
    shutdown(oldRes); error('Filename Input Fatal Error');
end;
% SET UP TRACKER CONFIGURATION
eyelink('command','calibration_type = HV5');
eyelink('command','enable_automatic_calibration = YES');
eyelink('command','automatic_calibration_passing = 1500');
eyelink('command', 'saccade_velocity_threshold = 30');
eyelink('command', 'saccade_acceleration_threshold = 8500');
eyelink('command', 'file_sample_data  = LEFT,RIGHT,GAZE,AREA');
eyelink('command', 'file_event_data = GAZE,GAZERES,AREA, VELOCITY');
eyelink('command', 'file_event_filter = LEFT, RIGHT, FIXATION,
SACCADE, BLINK, MESSAGE');
eyelink('command', 'link_sample_data = GAZE,GAZERES,HREF,AREA');
eyelink('command', 'link_event_data =
GAZE,GAZERES,HREF,AREA,VELOCITY');
AssertOpenGL
doublebuffer=1;
%because we reseized the useful space of the monitor we need to set
that here to avoid conversion mistakes
[blackBack,blackR] = Screen('OpenWindow', screenNumber, 0,[], 32,
doublebuffer+1);
if blackR(3)~=1280&& blackR(4)~=1024;error('Check
resolution');return;end
windowRectSizeH=blackR(3)*h.sizeM(2)/h.sizeM(1);
% calculating the horizontal size-small square
windowBegin=[(blackR(3) -windowRectSizeH)/2 1];
windowEnds=[blackR(3)-(blackR(3)-windowRectSizeH)/2 blackR(4)-1];
[w, wRect] = Screen('OpenWindow', screenNumber, 0,round([windowBegin
windowEnds]), 32, doublebuffer+1);
sm=[29.4 30.4];%size monitor
res=[wRect(3) wRect(4)]; %screen resolution
KbName('UnifyKeyNames');
priorityLevel=MaxPriority(w);
home
Screen('BlendFunction', w, GL_SRC_ALPHA, GL_ONE_MINUS_SRC_ALPHA);
if ~IsLinux
    Screen('TextFont', w, 'Arial');
    Screen('TextSize', w, 40);
end
white=WhiteIndex(screenNumber);
el=EyelinkInitDefaults(w);
windowSize = Screen(w,'Rect');
xwcenter=windowSize(3)/2;
```

```
ywcenter=windowSize(4)/2;
Eyelink('openfile', eyefilename);
sendheader(h);
HideCursor
text_ecc=sprintf('TESTING "%g" DEGREES',h.eccentricity);
Screen('DrawText', w, text_ecc,xwcenter-195,ywcenter-60,white*0.5);
Screen('DrawText', w, 'LOOK DOT (S) -- PRESS TOP BUTTON',xwcenter-
325,ywcenter+10,white*0.5) ;
Screen('Flip',w);
while KbCheck;end;
KbWait;
while KbCheck;end;
EyelinkDoTrackerSetup(el);
EyelinkDoDriftCorrection(el);
while Eyelink('ButtonStates');end
prev_state=Eyelink('ButtonStates');
while Eyelink('ButtonStates')==prev_state;
Screen('DrawText', w, 'ANY BUTTON TO START',xwcenter-
195,ywcenter,white*0.5);
Screen('Flip',w);
end
while Eyelink('ButtonStates');end
if h.eccentricity==0;n_pos=1;else n_pos=4;end
% control the number of positions tested/number of quest's created
    tGuess=h.start_va;
    tGuessSd=h.start_sd;
    pThreshold=0.82;
    beta=3.5;delta=0.01;gamma=0.5;
    for i=1:n_pos

q(i)=QuestCreate(tGuess,tGuessSd,pThreshold,beta,delta,gamma);%,grain,
4
        q(i).normalizePdf=1;
    end
    trialsDesired=h.trialsDesired;
% gap positions
    orientation=Shuffle(repmat((1:4)',trialsDesired/n_pos,1));
    orientation=repmat(orientation,n_pos,1);
% position randon selection
    for
i=1:n_pos;testpos.(strcat('p',num2str(i)))=ones(trialsDesired,1)*i;end
    rand_sel=Shuffle(randperm(n_pos));
    for i=0:n_pos-1;    ini=i*trialsDesired+1;fini=ini+trialsDesired-
1;

positions2testRand(ini:fini,1)=[testpos.(strcat('p',num2str(rand_sel(i
+1))))];
    end
trials=1; % controling the number of trials
time2rest=GetSecs;
switch positions2testRand(trials)
            case 1; writePosition='RIGHT =>';
            case 2;writePosition='TOP ^ ';
            case 3;writePosition='<= LEFT ';
            case 4;writePosition='BOTTOM ';
end
while GetSecs-time2rest<3
    if n_pos==1; text1=sprintf('CENTRAL TEST      WAIT  "%1.0g" ', 4-
(GetSecs-time2rest));text2=sprintf('');
    else
```

```
    text1=sprintf('"%s"         WAIT  "%1.0g" ', writePosition,4-
(GetSecs-             time2rest));
    end
    Screen('DrawText', w, text1,xwcenter-195,ywcenter,white);
    Screen('Flip',w);
end
sound_sacc(3000,0.1)
% convertion factores
    px2cm=[sm(1)/res(1) sm(2)/res(2)]; % converts px to cm
% converting sizeM from cm to deg
    sm_d=[atand((sm(1)/2)/h.distance)*2
atand((sm(2)/2)/h.distance)*2];
% size of the monitor in deg
    px2deg=[sm_d(1)/res(1) sm_d(2)/res(2)]; % converts px to deg

    WaitSecs(0.1);
    Eyelink('StartRecording');
    eyetracked = Eyelink('EyeAvailable');

[oldxe,oldye,oldxt,oldyt,oldve,tLastS]=dummyConnected(el,eyetracked);
    xe=oldxe;ye=oldye;
%initial values for the loop --- external function
    Eyelink('message','SYNCTIME');
    Eyelink('command', 'begin_realtime_mode');

    countT=0;% table with importante values to control de experiement
setup
    send2driftcorrection=0; % send to drift correct every 5 trials
    fps=Screen('FrameRate',w);% now defining the time for correct
presentations
    if fps<95;
        Eyelink('shutdown')
        error('The frame rate is below 100 Hz!');
    end
    ifi=Screen('GetFlipInterval',w);
    if fps==0
        fps=1/ifi;
    end
    waitframes=1;
    vbl=Screen('Flip',w);
    Priority(priorityLevel);
    for i=1:n_pos;        drawMessage(i)=trialsDesired*(i)+1;    end

prev_result=0;prev_state=Eyelink('ButtonStates');count_vs=1;repeat=0;
%  Trial loop starts here
while trials<=trialsDesired*n_pos
%-------------------------------------
    ini_time=GetSecs;
    sendNewTargMsg=1;
    sendEndTargMsg=1;
    loops=0;hideT=3;
    %-----------------------------gap
    gaps=randperm(4);orientation2test=gaps(1);
    if repeat==0
    orientation2test=orientation(trials);
    pos=positions2testRand(trials);%-gap
    tTest=QuestQuantile(q(pos));
    send2driftcorrection=send2driftcorrection+1;
    Eyelink('message',strcat('Pos',num2str(pos)));
    Eyelink('message',num2str(tTest));
```

```
    %---/calculating the size of "C"/---
    angDeg=(10^tTest*5)*0.0167;%--/equivalent /60;
    st_px=[angDeg angDeg]./px2deg; %size t_arget H and V (total)
    rectCircle=[0 0 st_px];
    r_gaph=ScaleRect(rectCircle,0.4,0.2);
    r_gapv=ScaleRect(rectCircle,0.2,0.4);
    size_d= mean(rectCircle(3:4));
    s_Sides=[h.eccentricity h.eccentricity].*(1./px2deg);
% size of S from centre2centre
    sel_d=[cosd((pos-1)*90) -sind((pos-1)*90)];
% dist in px for each position
    dtc=s_Sides.*sel_d;
    rectScotoma=floor(s_Sides-st_px); %give S with tolerance
    noise_size=ceil(max(rectCircle));
    end
% it repeats the question if a fast saccade is made
    repeat=0;
    prev_state=
Eyelink('ButtonStates');pen=(r_gaph(4)+r_gapv(3))/2;vlimit=30;
            while  Eyelink('ButtonStates')==prev_state; %LOOP
CONDITION
                        [control,secs,keyCode]=KbCheck;
                        loops=loops+1;loopTime=0;   pupil=0; blink=0;
                        if control==1;
                              error('Keyboard pressed
                        illegaly');return;end
                              errorEl=Eyelink('checkrecording');
                        if (errorEl~=0)
                            return
                        end
%----/EYE---EYE---EYE---EYE/----
                         if Eyelink('isconnected') == el.connected
                             while ~IsInRect(xe,ye,wRect)||pupil==0
                                sample = Eyelink(
'newfloatsampleavailable');
                                if sample
% get the sample in the form of an event structure
% get current gaze position from sample
                                evt = Eyelink( 'newestfloatsample');
                                xe = evt.gx(eyetracked+1);
% +1 as we're accessing MATLAB array
                                ye = evt.gy(eyetracked+1);
                                tS = evt.time(1);
                                pupil=evt.pa(eyetracked+1);
                                if pupil==0;
                                    blink=1;
                                end
                                end % if sample
                            end
                         else
%DEMO MODE --- MOUSE----MOUSE ----MOUSE----MOUSE
                                tS=GetSecs;countT=countT+1;
                                [xe,ye]=GetMouse;pupil=1;
                         end %eyelink('isconnected') == el.connected
        countT=countT+1;
%---/vlimit= ... & alimit= .../---
        time=(tS-tLastS)*0.001; invtime=1/time;tLastS=tS;
%---/calculating eye movement in deg(ped=position-eye-degrees/---
        ped=[xe ye].*px2deg;
        oldped=[oldxe oldye ].*px2deg;
```

```
        vxe=(ped(1)-oldped(1))*invtime; vye=(ped(2)-
oldped(2))*invtime;
        ve=sqrt(vxe^2+vye^2);ae=(ve-oldve)*invtime;
%---/target movements/---
        xt=(xe-oldxe)*h.gain+oldxe;  yt=(ye-oldye)*h.gain+oldye;
        hideT = ve>30||ae>8500;
        if vbl-ini_time<=0.6; % condition 1
                if vbl-ini_time<=0.1;%  condition 1.1
                    xy_e=[xe,ye]+dtc;xt=xe;yt=ye;

r_cue=CenterRectOnPoint(rectCircle,xy_e(1),xy_e(2));
                    Screen('FillOval', w,white*0.4,r_cue);%cueing
                else %condition 1.2
                        if sendNewTargMsg==1;xt=xe;yt=ye;
                  Eyelink('message','TargetVisible');sendNewTargMsg=0;
            end
                        switch hideT
                            case 1     %    condition 1.2.1
                  Screen('FillRect',w,white*0);xt=xe; yt=ye;
%that insures the reset position after saccades
                                    if ve>100
                                        if repeat==0;
                                        sound_sacc(1000,0.1);
                  fastSac(count_vs,:)=[ve,ae,tS,trials,tTest];
fprintf('\n\t# Fast saccade during trial "%g" velocity "%g"--size
"%1.2g" will be repeated',trials,ve,tTest);
                                      count_vs=count_vs+1-blink;
                                        end; repeat=1;
                                  if
length(fastSac))>trialsDesired*n_pos*0.10;
error('Please repeat the run, but looking the centre of the
monitor');end
                                  end
                              case 0    %    condition 1.2.2
      xy_t=[xt,yt]+dtc;cf_g=rectCircle(3)*0.15;vlimit=30;
%this factor correct the centring of gap
rectArc=CenterRectOnPoint(rectCircle,xy_t(1),xy_t(2));
                  switch orientation2test
                  case 1
                  r_gap=CenterRectOnPoint(r_gaph,rectArc(3)-
                  cf_g,xy_t(2));
                  case 2
                  r_gap=CenterRectOnPoint(r_gapv,xy_t(1),rectArc(2)+cf
                  _g);
                  case 3
                  r_gap=CenterRectOnPoint(r_gaph,rectArc(1)+cf_g,xy_t(
                  2));
                  case 4
                  r_gap=CenterRectOnPoint(r_gapv,xy_t(1),rectArc(4)-
                  cf_g);
                 end
                  if noise_size>63
                  Screen('FrameArc',w,white,rectArc,0,360,pen,pen);
                  else
                  Screen('DrawDots', w,xy_t',size_d,white,[],1);
                  Screen('DrawDots', w,xy_t',size_d*0.6,white*0,[],1);
                  end
      crowding(rectCircle,xy_t,rectArc,white,w,px2deg);
% PLEASE COMMENT HERE TO AVOID CROWDING
```

```
        rectScotoma=[([xe ye]-floor(s_Sides-1.5*st_px)) ([xe
        ye]+floor(s_Sides-1.5*st_px))]; %give S with tolerance
        Screen('FillRect',w,white*0.0,r_gap);
                                    if
        n_pos>1&&RectWidth(rectScotoma)>5&&RectHeight(rectScotoma)>5
        Screen('FillOval', w,white*0.0,rectScotoma);end %SCOTOMA
        Screen('DrawingFinished',w);      loopTime=  vbl-ini_time;
                  end % end of condition 1.2.1 and condition 1.2.2
                  end % end of condition 1.1 and condition 1.2
         else %   condition 2
                          if sendEndTargMsg==1;
                             Eyelink('message','TargetNotVisible');
                          if ~IsInRect(xy_t(1),xy_t(2),wRect);
                              [xt,yt]=RectCenter(wRect);end
                              xy_noise=[xt,yt]+dtc;sendEndTargMsg=0;end
                             noise_in(xy_noise,w,noise_size,1)
         end   % end of condition 1 and condition 2
         vbl=Screen('Flip',w,vbl+(waitframes-0.5)*ifi);
         timeControl(countT,:)= [tS time ve ae xe xt ye yt loops
loopTime];
                  oldxe=xe;    oldye=ye;   oldxt=xt;   oldyt=yt;
oldve=ve;
end % END OF LOOP CONDITION
              if
sendEndTargMsg==1;Eyelink('message','TargetNotVisible');end
              prev_result=Eyelink('ButtonStates');
              while Eyelink('ButtonStates');end
              prev_state=Eyelink('ButtonStates');
              switch prev_result
                  case 4
                      result =2;
                  case 1
                      result =3;
                  case 8
                      result=4;
                  case 2
                      result=1;
              end
              response=isequal(result,orientation2test);
              gapDirection=num2str(orientation2test);
fprintf('\n\tposition"%g"gap"%c"response"%g"result"%g"trial
number"%g"\n',pos,gapDirection,result,double(response),trials);
              if repeat==0
              answer=num2str(result);
              results2edfAns=strcat(answer);
Eyelink('message',results2edfAns);
              results2edfGap=strcat(gapDirection);
Eyelink('message',results2edfGap);
              q(pos)=QuestUpdate(q(pos),tTest,response) ;
              trials=trials+1;
%   do a drift correction every five trials
                      if send2driftcorrection==5
                          if
trials>=length(positions2testRand);break;end
                          send2driftcorrection=0;
                          EyelinkDoDriftCorrect(el);
                          while Eyelink('ButtonStates');end
                              if ismember(trials,drawMessage)
                                  time2rest=GetSecs;
                                      switch positions2testRand(trials)
```

```
                                                    case 1;
writePosition='RIGHT =>';
                                                    case 2;writePosition='TOP
^ ';
                                                    case 3;writePosition='<=
LEFT ';
                                                    case
4;writePosition='BOTTOM ';
                                            end
      while GetSecs-time2rest<3
      text1=sprintf('"%s"         WAIT  "%1.0g" ', writePosition,4-
      (GetSecs-time2rest));
      text2=sprintf(' "%g" per cent done', ((trials-
1)/(trialsDesired*4))*100);
      Screen('DrawText', w, text1,xwcenter-195,ywcenter,white);
      Screen('DrawText', w, text2,xwcenter-195,ywcenter+60,white*0.7);
      Screen('Flip',w);
      end
                                  sound_sacc(3000,0.1)
      end
                         WaitSecs(0.1);
                         Eyelink('StartRecording');
                         eyetracked = Eyelink('EyeAvailable');
                    end %end do drift correction
            end %repeat==0
          clear ini_time
end %while trials desired
%---AFTER ALL TRIALS----
for j=1:n_pos
    t(j)=QuestMean(q(j));
%Add the new datum (actual test% intensity and observer response) to
the database.
    sd(j)=QuestSd(q(j));%the after your trial loops (they suggest 60)
put this
end
sound_sacc(1000,1)
    home;fprintf('TEST DURATION: "%1.2g" minutes\n\n',toc/60)
    text_final=sprintf('\nEND OF TEST \n WELL DONE! \n');
    Screen('DrawText', w, text_final,xwcenter-250,ywcenter,white);
    Screen('Flip',w);
    WaitSecs(1);
    Eyelink('closefile');
    Eyelink('Stoprecording');
    wd=cd;d_edf=strcat(wd,'\EDF_FILES');
        if Eyelink('isconnected') == el.connected
            cd(d_edf);
            status = Eyelink('receivefile',eyefilename,eyefilename);
            if status < 0, fprintf('Error in receiveing file!\n');
end;
            cd ..
        end
    Eyelink('Shutdown');
    Screen('CloseAll');
    avFinalResults_logMAR=extractVaThreshold(q);
    [file,path]=uiputfile(matFileName,'Save Workspace As');
    save(h.filename);

    colour=['rgbk'];
    for i=1:n_pos
```

```
        set(gca,'YGrid','on'); ylabel('VA (logMAR)');xlabel('Trials');
        axis([0 60 0.4 2]);
        plot(q(i).intensity,colour(i));
        hold on
    end

    [PATHSTR,NAME,EXT,VERSN] = fileparts(matFileName);
    nome=sprintf('%1.8s.fig',NAME);
    d_plots=strcat(wd,'\PLOTS');
    cd(d_plots)
    saveas(gcf,nome);close()
    cd ..
fprintf('\n\t');warning('MAKE SURE THIS IS A VALID TRIAL BEFORE
PROCEED!!');
    proceed1=0;proceed2=0;
    while proceed1==proceed2
valid_t=input('PROCEED TO DELETE IN YOUR DATA BASE?  [y/n]: ','s' );
        proceed1=strcmp(valid_t,'y');
        proceed2=strcmp(valid_t,'n');
    end
    d_subjects=strcat(wd,'\SUBJECTS_FILES ');
    if  proceed1
        cd(d_subjects);
        load(current_s);
        t_order=(Tant et al., 2002);
        t_done{i_done,1}=matFileName;%t_done=t_done';
        save(h.initials,'t_order','t_done');
        cd ..
    else
        warning('THIS RUN WAS NOT VALID!!');
fprintf('\n\t');
error('ERASE MANUALLY THE DATABASE OTHERWISE THIS RUN WILL BE
REPEATED!!!')
        return
    end
    clear all
    return
catch
    Eyelink('Shutdown');
    Screen('CloseAll');
    clear all
    rethrow(lasterror)
end %try
end % end of the program
% %-------------------------------------------------------------------
-----
function
[oldxe,oldye,oldxt,oldyt,oldve,tLastS]=dummyConnected(el,eyetracked)
if   Eyelink('isconnected') == el.connected
%     if Eyelink( 'newfloatsampleavailable')
        % get the sample in the form of an event structure
        evt = Eyelink( 'newestfloatsample');
        %                     if we do, get current gaze position from
sample
        oldxe = evt.gx(eyetracked+1); % +1 as we're accessing MATLAB
array
        oldye  = evt.gy(eyetracked+1);
        oldxt = evt.gx(eyetracked+1); % +1 as we're accessing MATLAB
array
```

```
        oldyt  = evt.gy(eyetracked+1);
        tLastS = evt.time(1);
        oldve = 0;
%     end
    else
        tLastS=GetSecs;
        [oldxe, oldye]=GetMouse;
        [oldxt, oldyt]=GetMouse;
        oldve = 0;
end

end
%-------------------------------------------------------------------------
---
function sendheader(h)
% sends header structure to eyelink as a series of messages
% empty strings not allowed

names = fieldnames(h);                  % get list of field names
n = size(names);                        % figure number of fields
n = n(1,1);                             % must be better way?

for i= 1:n,
    myfield = names(i);
    myvalue = getfield(h,myfield);
    if ischar(myvalue)                  % handle strings and numbers
separately
        m = strcat('HEADER <>  ',myfield{i},' "',myvalue,'"');
        Eyelink('message',m);
%       fprintf('%s\n',m);
    elseif isnumeric(myvalue)
        m = strcat('HEADER <>  ',myfield{1},':  ',num2str(myvalue));
        Eyelink('message',m);
%       fprintf('%s\n',m);
    else
        fprintf('ERROR: Sendheader: must use strings or numeric
values');
    end
end
end
%-------------------------------------------------------------------------
---
function [filename,eyefilename,myerr] = getfilenames(h,window)
% getfilenames returns file names for main data and eye data.
% strict error checking on file names

myerr = 0; eyefilename = '';

% get main file name
[shortfilename, filepath] = uiputfile(h.filename, 'Data file name?');
cd(filepath);                           % update current path

if isempty(shortfilename) | 0 == shortfilename  % if empty, exit
program
    fprintf('File name required.\n');
    myerr = 1;
    return
end;
```

```
if isempty(filepath)
    filepath = pwd; end;                % use default path if empty

filename = strcat(filepath,shortfilename);

% figure default for eye data file name
place = findstr('.mat',shortfilename);  % based on main datafile
if isempty(place)                       % if no .mat, exit program
    fprintf('Suffix .mat required in file name.\n');
    myerr = 1;
    return
end

% create name for eye data file
eyefilename = strcat(shortfilename(1:place),'edf');
end
%-------------------------------------------------------------------------
---
function avFinalResults_logMAR=extractVaThreshold(q)
    start_column=(1:2:7);avFinalResults_logMAR=zeros(1,4);  writeWs=0;
for i=1:length(q)
    if ~isempty(q(i).intensity)
        writeWs=1;%if all the trial are wrong there is an error in
/line 514

avAllResults(1:length(q(i).intensity),start_column(i):start_column(i)+
1)=[q(i).intensity',q(i).response'];

avFinalResults_logMAR(1,i)=avAllResults(max(find(avAllResults(:,start_
column(i)+1)==1)),start_column(i));
    else
        i=i+1;
    end
end
end
%-------------------------------------------------------------------------
---
function noise_in(xy_noise,w, rectSize,scale)
xc=xy_noise(1);yc=xy_noise(2);

objRect = SetRect(0,0, rectSize, rectSize);

dstRect(1,:)=CenterRectOnPoint(objRect*scale, xc, yc);

noiseimg=(50*randn(rectSize, rectSize) + 128);
tex=Screen('MakeTexture', w, noiseimg);
Screen('DrawTexture', w, tex, [], dstRect(1,:), [], 0);
Screen('Close', tex);
end
%-------------------------------------------------------------------------
---
function crowding(rectCircle,xy_e,rectArc,white,w,px2deg,crowd_d)

bar_v=ScaleRect(rectCircle,0.2,1);
bar_h=ScaleRect(rectCircle,1,0.2);
if nargin <7
    crowd_d='2bars';
```

```
   dist_px=ceil([(RectWidth(bar_v)*2) (RectHeight(bar_h)*2)]);
%change *3 to change boundaries separation
else
    dist_px=crowd_d./px2deg;
end
dist_px=dist_px+[(RectWidth(bar_v)*0.5) (RectHeight(bar_h)*0.5)];
rc.r=CenterRectOnPoint(ceil(bar_v),rectArc(3)+dist_px(1),xy_e(2));
rc.u=CenterRectOnPoint(ceil(bar_h),xy_e(1),rectArc(2)-dist_px(2));
rc.l=CenterRectOnPoint(ceil(bar_v),rectArc(1)-dist_px(1),xy_e(2));
rc.d=CenterRectOnPoint(ceil(bar_h),xy_e(1),rectArc(4)+dist_px(2));
Screen('FillRect',w,white*1,rc.r);
Screen('FillRect',w,white*1,rc.u);
Screen('FillRect',w,white*1,rc.l);
Screen('FillRect',w,white*1,rc.d);
end
%-------------------------------------------------------------------------
---
function [matFileName,t_index,current_s,h,i_done]= trialsOrder
try
    correctName=0;
        while correctName==0
                fprintf('\t') ;h.initials=input('Subject initials:
', 's');
                letter2number=double(h.initials);
                if length(letter2number)>2; fprintf('\t\tOnly 2
initials please!\n\n');continue;end
                for i=1:length(letter2number)
                    if letter2number(i)>=97&& letter2number(i)<=122
                       letter2number(i)=letter2number(i)-
32;correctName=1;
                    elseif letter2number(i)>=65 &&
letter2number(i)<=90

letter2number(i)=letter2number(i);correctName=1;
                    else correctName=0;    end %if
                end;%for
        end;
        initials=char(letter2number);
wd=cd;d_subjects=strcat(wd,'\SUBJECTS_FILES ');

cd(d_subjects);
current_s=strcat(initials,'.mat');
look4file=exist(current_s,'file');

if look4file==0
    fprintf('\n\tYou are creating the trials database\n')
    gain={'M1' 'Z0' 'P1'};
    trial_nc={'T1' 'T2' 'T3'};
%     trial_nc={'T1' 'T2'};
    ecc={'10' '05' '00'};
ii=1;
for i_ecc=1:length(ecc)
    for i_trial=1:length(trial_nc)
        for i_gain=1:length(gain)

t_order{ii,1}=strcat(initials,ecc{i_ecc},gain{i_gain},trial_nc{i_trial
});
            ii=ii+1;
        end
```

```
    end
end
save(initials,'t_order');
end
%
load(current_s);
all_done=1;t_remaining=0;
for i_test=1:length(t_order)
    if ~
isempty(t_order{i_test});all_done=0;t_remaining=t_remaining+1;end
end
%test if all are done
if all_done==1;fprintf('\n\tTHIS PERSON HAS DONE ALL RUNS
ALREADY!\n\t'); error('All tests completed');end
if ~exist('t_done')
    i_done=0;
else
    i_done=length(t_done);
end
if i_done<(length(t_order)*2/3)
%randonly selection of a different run
            allt_index=randperm(length(t_order)*2/3);
            t_index=allt_index(1);
        while isempty(t_order{t_index})
            allt_index=randperm(length(t_order)*2/3);
            t_index=allt_index(1);
        end
else
            allt_index=randperm(length(t_order)-length(t_order)*2/3);
            t_index=allt_index(1);
        while isempty(t_order{t_index})
            allt_index=randperm(length(t_order)-length(t_order)*2/3);
            t_index=allt_index(1)+length(t_order)*2/3;
        end
end
%now we now all the data we need
matFileName=strcat(t_order{t_index},'.mat');
h.initials=matFileName(1:2);
h.filename=matFileName;
h.trialNumber=matFileName(8);
h.eccentricity=str2double(matFileName(3:4));
signal=matFileName(5);
switch double(signal)
    case 77
        h.logGain=str2double(strcat('-',matFileName(6)));
    case 80
        h.logGain=str2double(matFileName(6));
    case 90
       h.logGain=str2double(matFileName(6));
end
h.gain=10^h.logGain;
h.daterun=datestr(now);
i_done=i_done+1;
fprintf('\n\tTHIS IS RUN "%g" FOR "%s" -- NAME "%s"\n\n\tTHERE ARE
"%g" RUNS REMAINING\n',length(t_order)-(t_remaining-
1),initials,matFileName,t_remaining-1);
if length(t_order)-(t_remaining-
1)>20;fprintf('\n\t');warning('"%g"\tTESTS TO FINISH AT
NEAR!',t_remaining-1-(length(t_order)*1/3));fprintf('\t');end
catch
```

```
    cd ..
    rethrow(lasterror)
    return;
end
cd ..
end
%
function sound_sacc(type,dur)
freq = 44100;
mynoise(1,:) = 0.9 * MakeBeep(type, dur, freq);
mynoise(2,:) = mynoise(1,:);
Snd('Play', mynoise, freq, 16);
end
```

Example of a Matlab program to run the reading experiments in patients

```
function readv4pat
% MODIFIED VERSION -- INITIAL CODE FOR CONTROLS'
% Author: Filipe Macedo
% Version: 02.09
% Started, long time ago...
% updated, 29 Jan 08
% Updated, 7 Jan 2009
% Updated, 6 Jan 2009
try
clear all;home; tic
fprintf('\n\n\t\t**READING** \n\t\t');
fprintf('\n\t\tPerformed on ''%s''\n\n\t', datestr(now));
% initialize eyelink
if EyelinkInit()~= 1; %
    return;
end;
fprintf('\n');option='n';%dir('*.mat');


% difining header
while ~strcmp('y',option)
[matFileName,t_index,current_s,h,i_done,t_i] = trialsOrder;
h.distance = 50;
% is that really necessary?
switch h.eccentricity
    case 0
    h.start_time = 2;fprintf('\n\t')
    visualAc = input('Reading Acuity?.: ','s');
    fprintf('\n')
    h.visualAc = str2num(visualAc);
    case 5
    h.start_time = 2;
    h.visualAc = 1.10;
    case 1
    h.start_time = 0.5;
    h.visualAc = 1.38;
end
% deals with the plot window to display the graph
screenNumber=max(Screen('Screens'));
scrsz = get(0,'ScreenSize');
FIGNAME = strcat('BLOCK CONTROL','--', matFileName(1:8));
if screenNumber == 2;
width = scrsz(3)- 400; height = 600;
figure('Name', FIGNAME,'NumberTitle','off','Position',[scrsz(1)
scrsz(4)-(height+80) width height]);
else
  figure('Name', FIGNAME,'NumberTitle','off')
end
% conversion factors
```

```
px2pt = 1.6922;
px2cm = [0.0393 0.0393];
px2deg = [0.0428 0.0437];
angleMAR = 10^str2num(visualAc);
angleDEG = angleMAR/60;
sizeCm = tand(5*angleDEG)*h.distance; % 1/5 of the total size
sizePx = sizeCm*(1/px2cm(1));
sizePt = floor(sizePx*px2pt);
fprintf('\n text Size is.: %g - size cm.: %g - size px.:
%g\n',sizePt,sizeCm,sizePx);
h.ts = sizePt;
h.start_sd = h.start_time;
if strcmp(h.initials,'TT')
    h.trialsDesired = 5;
else
    h.trialsDesired = 30;
end
% deals with file to save in the current directory
look4file = exist( matFileName,'file');
fprintf('\n\tPlase make sure the distance is "%g"
cm\n\n\t',h.distance);
if ~strcmp(h.initials,'TT')
        if look4file == 2
                fprintf('\tTHIS FILE ALREADY EXIST!...REPLACE?\n\n\t')
        else
                fprintf('New file!\n\n\t')
        end
            option=input('PROCEED?  [y/n]:     ','s' );
else
            fprintf('\tDEMO TRIAL!\n\n\t');
            option='y';
end
end %while option

AssertOpenGL;
doublebuffer=1;
[h.filename,eyefilename,myerr] = getfilenames(h,screenNumber);
% prompt for file names
if myerr                                % exit on errors in inputs
    shutdown(oldRes);
    error('Filename Input Fatal Error');
end;
%  TRACKER CONFIGURATION
eyelink('command','calibration_type = HV5');
eyelink('command','enable_automatic_calibration = NO');
eyelink('command','automatic_calibration_passing = 1500');
eyelink('command', 'saccade_velocity_threshold = 30');
eyelink('command', 'saccade_acceleration_threshold = 8500');
eyelink('command', 'file_sample_data  = LEFT,RIGHT,GAZE,AREA');
eyelink('command', 'file_event_data = GAZE,GAZERES,AREA, VELOCITY');
eyelink('command', 'file_event_filter =
LEFT,RIGHT,FIXATION,SACCADE,BLINK,MESSAGE');
eyelink('command', 'link_sample_data = GAZE,GAZERES,HREF,AREA');
eyelink('command', 'link_event_data =
GAZE,GAZERES,HREF,AREA,VELOCITY');
%
doublebuffer=1;
oldVisualDebugLevel = Screen('Preference', 'VisualDebugLevel', 3);
```

```
oldSupressAllWarnings = Screen('Preference', 'SuppressAllWarnings',
1);
[w, wRect] = Screen('OpenWindow', screenNumber, 0,[], 32,
doublebuffer+1);

m = 21;
% PLEASE SET THE MONITOR SIZE IN -- inches
% warning('PLEASE VERIFY THE MONITOR SIZE, NOW SET AT:  "%g" ',m)
if m == 19
   hvratio = 5/4;
elseif m == 21
    m = 19.8;
    hvratio = 4/3;
else
    error('Monitor dimensions unknown');
end

  monitorSize_cm = m* 2.54;
  sm(2) = sqrt(monitorSize_cm^2/(1 + hvratio^2));
  sm(1) = sm(2)*hvratio;
  h.sizeM = sm;
%
res = [wRect(3) wRect(4)]; %screen resolution
fps = Screen('FrameRate',w);% frame rate

KbName('UnifyKeyNames');
priorityLevel = MaxPriority(w);
Screen('BlendFunction', w, GL_SRC_ALPHA, GL_ONE_MINUS_SRC_ALPHA);


if ~IsLinux
    Screen('TextFont', w, 'courier new');
    Screen('TextSize', w, floor(h.ts*0.8));
    Screen('TextStyle', w,1)
end

white = WhiteIndex(screenNumber);
red = [255 0 0];
green = [0 255 0];
el = EyelinkInitDefaults(w);

if Eyelink('isconnected') == el.connected
    if res ~= [1024 768] % resolution check
        error('Check resolution');
        return
    end
    if fps<95;  % verify frame rate
        Eyelink('shutdown')
        error('The frame rate is below 100 Hz!');
    end;
end

windowSize = Screen(w,'Rect');
[xwcenter ywcenter] = WindowCenter(el.window);
Eyelink('openfile', eyefilename);
sendheader(h);
%
testC = 'TEST INFO.';
```

```
testC1 =strcat('RES..: ', num2str(res(1)), 'x' ,num2str(res(2)));
testC2 =strcat('DIST.: ', num2str(h.distance),' cm');
testC3 =strcat('ECC..: ', num2str(h.eccentricity),' deg');
testC4 =strcat('FILE.: ',matFileName(1:8));
cTx  = Screen('TextBounds',w,testC);

Screen('DrawText', w, testC ,10,0.25*cTx (4),red);
Screen('DrawText', w, testC1,10,1.25*cTx (4),white);
Screen('DrawText', w, testC2,10,2.25*cTx (4),white);
Screen('DrawText', w, testC3,10,3.25*cTx (4),white);
Screen('DrawText', w, testC4,10,4.25*cTx (4),white);
Screen('Flip',w);
while KbCheck;end;
KbWait;
while KbCheck;end;
%
text1 =  'LOOK AT DOT';
cTx  = Screen('TextBounds',w,text1);
Screen('DrawText', w, text1,10,ywcenter-cTx(4)*0.5,white);
Screen('Flip',w);

while KbCheck;end;
KbWait;
while KbCheck;end;

EyelinkDoTrackerSetup(el);
if Eyelink('isconnected') == el.connected
% EyelinkDoDriftCorrection(el,wRect(3)/4,ywcenter);
EyelinkDoDriftCorrection(el,xwcenter,ywcenter);
end

% number of position measured/number of quest(s) created
if h.eccentricity == 0;
    n_pos = 1;
else
    n_pos = 2;
end

    tGuess = h.start_time;
    tGuessSd = h.start_sd;
    pThreshold = 0.82;
    beta=3.5;
    delta = 0.01;
    gamma = 0.5;
    for i = 1:n_pos
        q(i) =
QuestCreate(tGuess,tGuessSd,pThreshold,beta,delta,gamma);
        q(i).normalizePdf = 1;
    end
trialsDesired = h.trialsDesired;
trials = 1; % controling the number of trials
oldymax = tGuess; oldymin =tGuess;
time2rest = GetSecs;
while GetSecs - time2rest < 2
     text1 = sprintf('WAIT %g', round (2 - (GetSecs-time2rest)));
     cTx  = Screen('TextBounds',w,text1);
    Screen('DrawText', w, text1,xwcenter-cTx(3)*0.5,ywcenter-
cTx(4)*0.5,white);
    Screen('Flip',w);
```

```
end
%--convertion factores
    px2cm=[sm(1)/res(1) sm(2)/res(2)];
% given a measure in px,converts to cm
%--converting sizeM from cm to deg
    sm_d=[atand((sm(1)/2)/h.distance)*2
atand((sm(2)/2)/h.distance)*2];
% size of the monitor in deg
    px2deg=[sm_d(1)/res(1) sm_d(2)/res(2)];
% given a measure in px,converts to deg
%----//----
if ~IsLinux
    Screen('TextSize', w, h.ts);
end
    WaitSecs(0.1);
    Eyelink('StartRecording');
    eyetracked = Eyelink('EyeAvailable');
    [oldxe,oldye,oldxt,oldyt,oldve,tLastS] =
dummyConnected(el,eyetracked);
    xe = oldxe;ye = oldye;
     %initial values for the loop --- external function
    Eyelink('message','SYNCTIME');
    Eyelink('command', 'begin_realtime_mode');
% now defining the time for precise presentations
    ifi = Screen('GetFlipInterval',w);
    if fps == 0
        fps = 1/ifi;
    end
    waitframes=1;
    vbl = Screen('Flip',w);
    Priority(priorityLevel);

    for i=1:n_pos;
        drawMessage(i) = trialsDesired*(i)+1;
    end

% defining some keys
stopkey=KbName('DELETE');
right = KbName('Return');
wrong = KbName('0');
yes = KbName('y');
no = KbName('n');
% load text before presenting
load('sentences.mat')
words = d;
% words = new6cstcs-- ini some variables
workd = cd; % working directory
cd(strcat(workd,'\SUBJECTS_FILES '));  % save information about the
subject
load(strcat(h.initials,'.mat')); % load existing information
line1= lastLine;
cd ..
% variables in use to control the loop
wd = 1;
prev_result=0;
count_vs=1;
wordCount = 0;
nThres = 1;
show = 0;
```

```
pos_op = randperm(1);
pos = pos_op(1);
add = 0;
countT = 0;
%
gazeArea = CenterRectOnPoint([0 0 2./px2deg],xwcenter, ywcenter);
ecc = str2num(matFileName(3));
loops = 0;
oldClueSize = [ 0 0 0 0];
stFrame = 1;
repeat = 0;
% opens a text file to save bolck information
fid = fopen(strcat(matFileName(1:8),'.txt'),'wt+');
fprintf(fid,'date.:\t%s\nfile name.:\t%s\n',
datestr(now),matFileName(1:8));
fprintf(fid,'tS\ttime\tve\tae\txe\txtar\tasac\tye\tytar\tloops\tcond\t
[vbl-ini_time]\tword\n');
%  ---Trial loop starts here---
while trials <= trialsDesired*n_pos
%
myword = textscan(words{1,1}{randstc(line1),1},'%s','delimiter','% ');
word = myword{1,1}{wd,1};
wordCount = wordCount +1;

if nThres
    tTest = QuestQuantile(q(pos));
    ymax = max(tTest,oldymax);
    ymin = min(tTest,oldymin);
    nThres = 0;
end

textmask(1,1:size(word,2)) = '+';
clueSize = Screen('TextBounds',w,word);
vbl = Screen('Flip',w);
% this is a key moment in time for the experiment during this frame,
the target will never be presented thus the "ini_time" needs to be add
"ifi" because if conditions are satisfied the target will be presented
in the next frame
ini_time = vbl + ifi;
if wd ~=1
    Eyelink('message',strcat('StartOf',num2str(wd),'-',num2str(vbl)));
end

sSac = 0; % end of the saccade
eSac = 1; % start of the saccade
xsSac = 0; % "x" here saccade starts
xeSac = 0; % "x" here saccade lands
aSac =[0 0]; % aSac is zero every new word
stS = 0;
while 1
                        hideT = 0;
                        pupil = 0; %this reset pupil var while pupil
== 0 loop
                        errorEl = Eyelink('checkrecording');
                        if (errorEl~=0)
                            return
                        end
%---EYE---EYE---EYE---EYE/----
                         if Eyelink('isconnected') == el.connected
```

```
                                sample = Eyelink(
'newfloatsampleavailable');
                                if sample
%get the sample in the form of an event structure
                                evt = Eyelink( 'newestfloatsample');
%get current gaze position from sample
                                xe = evt.gx(eyetracked+1);
% +1 as we're accessing MATLAB array
                                ye = evt.gy(eyetracked+1);
                                tS = evt.time(1);
                                pupil = evt.pa(eyetracked+1);
                                end % if sample
%                              end %while
                            Else
%----/MOUSE----MOUSE ----MOUSE----MOUSE
                                tS = vbl;
                                [xe,ye] = GetMouse;
                                pupil = 1;
                            end %eyelink('isconnected') == el.connected
% vlimit & alimit
        time = (tS - tLastS)*0.001;
        if Eyelink('isconnected') ~= el.connected
            time = time*1000;
        end

        invtime = 1/time;
        tLastS = tS;
%---/calculating eye movement in deg(ped=position-eye-degrees/---
        ped = [xe ye].*px2deg;
        oldped = [oldxe oldye ].*px2deg;
        vxe = (ped(1)-oldped(1))*invtime;
        vye = (ped(2)-oldped(2))*invtime;
        ve = sqrt(vxe^2+vye^2);
        ae = (ve-oldve)*invtime;
        repCriteria = 2*(ve > 700);
%---/target movements/---
       if strcmp(matFileName(4:5),'NN');
           xt = xwcenter; yt = ywcenter;
       end

       if strcmp(matFileName(4:5),'FN')
        xt = (xe-oldxe)*h.gain+oldxe;
        yt = (ye-oldye)*h.gain+oldye;
        hideT = ve > 30 || ae > 8500;
        aSac = [0 0];
        if hideT
          xt = xe;
          yt = ye;
          hideT = 0;
        end
       end

        if strcmp(matFileName(4:5),'FS')
        hideT = ve > 30 || ae > 8500;
            if hideT
                xt = oldxt;
                yt = oldyt;
                if ~sSac
                    sSac = 1;
```

```
                    xsSac = xe;
                    eSac = 0;
                end
                hideT = 0;
                aSac = [0 0];stS = 1;
            elseif ~hideT
                xt = (xe-oldxe)*h.gain+oldxe;
                yt = (ye-oldye)*h.gain+oldye;
                if ~eSac && sSac && stS
                   eSac = 1;
                   xeSac = xe;
                   aSac = [xeSac-xsSac 0];
                   sSac = 0;
                end
            end
        end

tg = [xt yt] - [clueSize(3:4)]*0.5 - [aSac];%"tg" is the target
position
inScreen = IsInRect(xe,ye,wRect);
% this bit is only to avoid "flicker" during cond "11" see below
if stFrame
    hideT = 0;
end
if [xe ye] == el.MISSING_DATA  % need ????
    inScreen = 0;
end

switch hideT
case 0 % case hide T is zero starts - shows target/op1
                if wd == 1    % wd = 1 / op.1
                    if stFrame % if 1st frame - op1
                       show = IsInRect(xe,ye, gazeArea);
                       ini_time = vbl + ifi;% please see notes in the
start of this loop about "ifi"
                        if show
                            stFrame = 0;
                            cond = 11;
                        elseif ~show
                            Screen('DrawDots', w,[xe
ye],10,white,[],1);
                            Screen('DrawDots', w,[xwcenter ywcenter] ,
30, red, [],1);
                           cond =12;
                        end
                    elseif ~stFrame % if 1st frame - op2
                        if vbl-ini_time < tTest % if time < tTest op1
                            noise_in(tg,w,clueSize,1);
                           Screen('DrawText', w,
textmask,tg(1),tg(2),red);
                            cond = 13;  sendmsg = 1;
                        elseif vbl-ini_time  < 2*tTest  % if time <
tTest op2
                            if sendmsg
Eyelink('message',strcat('Pos',num2str(pos),'tTest',num2str(tTest)));
                                Eyelink('message','TargetVisible');
Eyelink('message',strcat('StartOf',num2str(wd),'-
',num2str(ini_time)));
                            sendmsg = 0;
```

```
                            end
                           Screen('DrawText', w,
word,tg(1),tg(2),white);
                           cond = 14;
                         else % if time < tTest op3

Eyelink('message',strcat('EndOf',num2str(wd),'-',num2str(vbl-
ini_time)));
                            break
                         end
                     end    % if 1st frame - end!!
                elseif 2 < wd <= 4 % wd = 1/op.2
                    if(vbl-ini_time) < tTest % test Time/op.1
                      Screen('DrawText', w, word,tg(1),tg(2),white);
                      cond = 21;
                    else % test Time/ op.2
                      Eyelink('message',strcat('EndOf',num2str(wd),'-',
num2str(vbl-ini_time)));
                      break
                    end      % test Time/ends
                 else % wd = 1/op.3
                    break
                 end % wd = 1 --- ends!!
case 1       % case hide T is 1 - blank monitor/op2
  xt = xe;
  yt = ye;
  Screen('FillRect',w,white*0)
  cond = 31;
end  % case hide T -- ends !!
        loops = loops +1;
fprintf(fid,'%.0f\t%.5f\t%.2f\t%.2f\t%.2f\t%.2f\t%.0f\t%.2f\t%.2f\t%.0
f\t%.0f\t%.4f\t%s\n',tS,time,ve,ae,xe,xt,aSac(1),ye,yt, loops,cond,
(vbl-ini_time),word);
        vbl = Screen('Flip',w,vbl+(waitframes-0.5)*ifi);
        oldxe = xe;    oldye = ye;   oldxt = xt;   oldyt = yt;   oldve
= ve;
end % END OF LOOP CONDITION
clear textmask cond
% now! -- new sentence if wd = 4; new word otherwise
if wd == 4
Eyelink('message',strcat('TargetNotVisible','R',num2str(repCriteria+(~
inScreen))));
noiseSize = clueSize;
if oldClueSize(3) > clueSize(3)
   noiseSize = oldClueSize;
end
oldClueSize = clueSize;
                hold on
                if trials == h.trialsDesired + 1;
                    oldymin = tGuess;
                    ymax = tTest;
                end
                % axis off
                if trials <= h.trialsDesired
                    t_plot = trials + add;
                end
                set(gca,'xlim',[(t_plot - 2) (t_plot + 2)], 'ylim',
[(oldymin - oldymin*0.1) (ymax +
ymax*0.05)],'XColor','w','YColor','w');
                if repeat
```

```
                        title(strcat('POS - ','PRL'));
                        plot(t_plot,tTest,'-
r*','LineWidth',2,'MarkerSize',12);
                    str2graph = num2str(randstc(line1));
                else
                        plot(t_plot,tTest,'-
g*','LineWidth',2,'MarkerSize',6);
                        str2graph =
strcat(num2str(randstc(line1)),':',sprintf('%s-%s-%s-%s-%s',
(myword{1,1}{1:wd,1})));
                end
            text(t_plot,tTest,str2graph,'FontSize',8);
            drawnow
            oldymax = ymax; oldymin = ymin;
    if ~repeat
        fprintf('\nLINE n.: %g - Trial %g || %s  - %s - %s - %s -%s
\n\n', randstc(line1),trials,(myword{1,1}{1:wd,1}));
        while 1
                [touch, secs, keyCode] = KbCheck;
                noise_in(tg,w,noiseSize,1);
                if keyCode(wrong); % wrong
                    result = 0; % wrong
                    break
                elseif keyCode(right); % right
                    result = 1; % right
                    break
                elseif keyCode(stopkey);
                        fprintf('\n\n'); error('STOP KEY PRESSED');
                         return;
                end
                Screen('Flip',w);
        end
        % update quest
            q(pos)=QuestUpdate(q(pos),tTest,result) ;
            assignin('base','quest',q);
        % move to another sentence -- new trial
            trials = trials + 1;
            line1 = line1 + 1;
            add = 0;
            wd = 1;
            nThres = 1;
            show = 0;
    end % end of ~ repeat
        if repeat
            line1 = line1 + 1;
            add = add + 1;
            wd = 1;
        end

        if ~rem(trials,(h.trialsDesired+1)) && n_pos > 1
            vbl = Screen('Flip',w);
            pos = pos_op(2);
            Screen('DrawText', w,'position change',50,ywcenter,green);
            vbl = Screen('Flip',w);
            WaitSecs(1.5)
        end

        if trials <= trialsDesired*n_pos
            repeat = 0; wd = 1; show = 0;
```

```
            EyelinkDoDriftCorrection(el,xwcenter,ywcenter);
            WaitSecs(0.1);
            Eyelink('StartRecording');
            eyetracked = Eyelink('EyeAvailable');
            [oldxe,oldye,oldxt,oldyt,oldve,tLastS] =
dummyConnected(el,eyetracked);
            clear keyCode
            stFrame = 1;
            vbl = Screen('Flip',w);
        end
else
    wd = wd+1;
end

clear ini_time
end %while trials desired
%---AFTER ALL TRIALS----
for j=1:n_pos
    t(j)=QuestMean(q(j));%Add the new datum (actual test% intensity
and observer response) to the database.
    sd(j)=QuestSd(q(j));%the after your trial loops (they suggest 60)
put this
end
    fprintf('\n\nTEST DURATION: "%1.2g" minutes\n\n',toc/60)
    sound_sacc(1000,0.05);
    WaitSecs(0.25);
    sound_sacc(1000,0.05);
    Screen('Flip',w);
    text1='thank you';
    cTx  = Screen('TextBounds',w,text1);
    Screen('DrawText', w, text1,10,ywcenter-0.5*cTx(4),green);
    Screen('Flip',w);
    Eyelink('closefile');
    Eyelink('Stoprecording');
while KbCheck;end;
KbWait;
while KbCheck;end;
    workd = cd;
    d_edf=strcat(workd,'\EDF_FILES');
        if Eyelink('isconnected') == el.connected
            cd(d_edf);
            status = Eyelink('receivefile',eyefilename,eyefilename);
            if status < 0, fprintf('Error in receiveing file!\n');
end;
            cd ..
        end
    Eyelink('Shutdown');
    Screen('CloseAll');
while KbCheck;end;
KbWait;
while KbCheck;end;

    [file,path]=uiputfile(matFileName,'Save Workspace As');
    save(h.filename);

    colour=['rgbk'];
    hold on
    for i=1:n_pos
        plot(q(i).intensity,colour(i));
```

```
        set(gca,'xlim',[1 (h.trialsDesired)], 'ylim',
[min(q(i).intensity) max(q(i).intensity)],'XColor','w','YColor','w');
        hold on
    end
    [PATHSTR,NAME,EXT,VERSN] = fileparts(matFileName);
    nome=sprintf('%1.8s.fig',NAME);
    d_plots=strcat(workd,'\PLOTS');
    cd(d_plots)
    saveas(gcf,nome);
    close('all')
    cd ..
     fprintf('\n\tVALIDE BLOCK?\n\t')
     fprintf('\n\tDELETE BASE? \n\t PRESS - - (y)es OR (n)o - - to
finish\n\n\n\t' );
     while KbCheck; end
     KbWait;
     while KbCheck; end
     clear keyCode
      while 1
            [touch, secs, keyCode] = KbCheck;
            while KbCheck; end
            if keyCode(yes);
               proceed1 = 1;
               warning('This block is now completed');
               break
            elseif keyCode(no);
               proceed1 = 0;
                warning('This block will be REPEATED!');
                break
            end
      end
% proceed1 = strcmp(proceed,'y');
%     proceed1 =1;
    d_subjects = strcat(workd,'\SUBJECTS_FILES ');
    if  proceed1
        cd(d_subjects);
        load(current_s);
        t_done{i_done,1} = matFileName;
        t_i(1)=[];
        lastLine = trials+line1;
       save(h.initials,'t_order','t_i','t_done','lastLine','randstc');
        cd ..
    elseif ~proceed1
        fprintf('\n\t');
        warning('ERASE MANUALLY THE DATABASE OTHERWISE THIS RUN WILL
BE REPEATED!!!')
    end
    clear all
    return
catch
    Eyelink('Shutdown');
    Screen('CloseAll');
    ShowCursor;
    workd = cd;
        cd(strcat(workd,'\SUBJECTS_FILES'));
        load(current_s);
        lastLine = trials + line1;
       save(h.initials,'t_order','t_i','lastLine','randstc');
        cd ..
    % Restore preferences
```

```
    Screen('Preference', 'VisualDebugLevel', oldVisualDebugLevel);
    Screen('Preference', 'SuppressAllWarnings',
oldSupressAllWarnings);
    clear all
    fprintf('\n\n');
    rethrow(lasterror)
end %try
end % end of the program
% %-------------------------------------------------------------------
-----
function [oldxe,oldye,oldxt,oldyt,oldve,tLastS] =
dummyConnected(el,eyetracked)
if   Eyelink('isconnected') == el.connected
%     if Eyelink( 'newfloatsampleavailable')
        % get the sample in the form of an event structure
        evt = Eyelink( 'newestfloatsample');% if we do, get current
gaze position from sample
        oldxe = evt.gx(eyetracked+1); % +1 as we're accessing MATLAB
array
        oldye  = evt.gy(eyetracked+1);
        oldxt = evt.gx(eyetracked+1); % +1 as we're accessing MATLAB
array
        oldyt  = evt.gy(eyetracked+1);
        tLastS = evt.time(1);
        oldve = 0;
%     end
    else
        tLastS=GetSecs;
        [oldxe, oldye]=GetMouse;
        [oldxt, oldyt]=GetMouse;
        oldve = 0;
end
end
%-------------------------------------------------------------------
---
function sendheader(h)
% sends header structure to eyelink as a series of messages
% empty strings not allowed
names = fieldnames(h);                  % get list of field names
n = size(names);                        % figure number of fields
n = n(1,1);                             % must be better way?

for i= 1:n,
    myfield = names(i);
    myvalue = getfield(h,myfield{1});
    if ischar(myvalue)                  % handle strings and numbers
separately
        m = strcat('HEADER <>  ',myfield{1},' "',myvalue,'"');
        Eyelink('message',m);
    elseif isnumeric(myvalue)
        m = strcat('HEADER <>  ',myfield{1},':  ',num2str(myvalue));
        Eyelink('message',m);
    else
        fprintf('ERROR: Sendheader: must use strings or numeric
values');
    end
end
end
```

```
%-------------------------------------------------------------------
---
function [filename,eyefilename,myerr] = getfilenames(h,window)
% getfilenames returns file names for main data and eye data.
% strict error checking on file names
myerr = 0; eyefilename = '';
% get main file name
[shortfilename, filepath] = uiputfile(h.filename, 'Data file name?');
cd(filepath);                           % update current path
if isempty(shortfilename) | 0 == shortfilename  % if empty, exit
program
    fprintf('File name required.\n');
    myerr = 1;
    return
end;
if isempty(filepath)
    filepath = pwd; end;                % use default path if empty

filename = strcat(filepath,shortfilename);
% figure default for eye data file name
place = findstr('.mat',shortfilename);  % based on main datafile
if isempty(place)                       % if no .mat, exit program
    fprintf('Suffix .mat required in file name.\n');
    myerr = 1;
    return
end
% create name for eye data file
eyefilename = strcat(shortfilename(1:place),'edf');
end
%-------------------------------------------------------------------
---
function prev_state = wait4buttonpress(el,prev_state)
            if Eyelink('isconnected') == el.connected
               while prev_state==Eyelink('ButtonStates');end;
               prev_state=Eyelink('ButtonStates');
            else
                while KbCheck;end;
                prev_state=rand(1);
            end
end
%-------------------------------------------------------------------
---
function noise_in(xy_noise,w, rectSize,scale)

objRect = SetRect(0,0,rectSize(3),rectSize(3));
dstRect =[xy_noise xy_noise] + rectSize;
noiseimg=(10*randn(rectSize(3), rectSize(3)));
tex = Screen('MakeTexture', w, noiseimg);
Screen('DrawTexture', w, tex,[],dstRect,[], 0);
Screen('Close', tex);
end
%-------------------------------------------------------------------
---
function crowding(rectCircle,xy_e,rectArc,white,w)
cf_h= ceil(rectCircle(3)*0.4); % rc-means rect to
crowding(r_right,l_left...)
cf_v= ceil(rectCircle(4)*0.4);
bar_v=ScaleRect(rectCircle,0.2,1);
bar_h=ScaleRect(rectCircle,1,0.2);
```

```
rc.r=CenterRectOnPoint(ceil(bar_v),rectArc(3)+cf_h,xy_e(2));
rc.u=CenterRectOnPoint(ceil(bar_h),xy_e(1),rectArc(2)-cf_v);
rc.l=CenterRectOnPoint(ceil(bar_v),rectArc(1)-cf_h,xy_e(2));
rc.d=CenterRectOnPoint(ceil(bar_h),xy_e(1),rectArc(4)+cf_v);
Screen('FillRect',w,white*1,rc.r);
Screen('FillRect',w,white*1,rc.u);
Screen('FillRect',w,white*1,rc.l);
Screen('FillRect',w,white*1,rc.d);
end
%--------------------------------------------------------------------
---
function [matFileName,t_index,current_s,h,i_done,t_i]= trialsOrder
try
    correctName=0;
        while correctName==0
                fprintf('\t') ;h.initials=input('Subject initials:
', 's');
                letter2number=double(h.initials);
                if length(letter2number)>2; fprintf('\t\tOnly 2
initials please!\n\n');continue;end
                for i=1:length(letter2number)
                    if letter2number(i)>=97&& letter2number(i)<=122
                       letter2number(i)=letter2number(i)-
32;correctName=1;
                    elseif letter2number(i)>=65 &&
letter2number(i)<=90

letter2number(i)=letter2number(i);correctName=1;
                    else correctName=0;    end %if
                end;%for
        end;
        initials=char(letter2number);
workd=cd;
% opensentence database
load('sentences.mat')
words = d;

d_subjects=strcat(workd,'\SUBJECTS_FILES ');
cd(d_subjects);
current_s = strcat(initials,'.mat');
%first chechs -- skips this procedure if the file is already there**
look4file=exist(current_s,'file');
%
if look4file==0 %sC1
     fprintf('\n\tNEW BLOCK DATABASE\n')
ecc={'0'};
t_order(1,1) =strcat(initials,ecc,'NN','Z0','1');
t_order(2,1) =strcat(initials,ecc,'FN','Z0','1');
t_order(3,1) =strcat(initials,ecc,'FS','Z0','1');
t_order(4,1) =strcat(initials,ecc,'FS','P1','1');
t_i = randperm(length(t_order));
randstc = Shuffle([1:1:size(words{1},1)])';
lastLine = 1;
save(initials,'t_order','t_i','lastLine','randstc');
end %eC1 -- if there is a file already**
load(current_s);
% test if all are done
if isempty(t_i);fprintf('\n\tTHIS PERSON HAS DONE ALL TRIALS
ALREADY!\n'); error('All tests completed');end
```

```
if ~exist('t_done')
    i_done = 0;
else
    i_done = length(t_done);
end
t_i = Shuffle(t_i);
t_index = t_i(1);
save(initials,'t_order','t_i','lastLine','randstc');
%now we now all the data we need
matFileName = strcat(t_order{t_index},'.mat');
h.initials=matFileName(1:2);
h.filename=matFileName;
h.trialNumber=matFileName(8);
h.eccentricity=str2double(matFileName(3));
signal=matFileName(6);
switch double(signal)
    case 77
        h.logGain=str2double(strcat('-',matFileName(7)));
    case 80
        h.logGain=str2double(matFileName(7));
    case 90
       h.logGain=str2double(matFileName(7));
end
h.gain = 10^h.logGain;
h.startLine = lastLine;
h.daterun = datestr(now);
i_done = i_done+1;
fprintf('\n\tTHIS IS BLOCK "%g" FOR "%s" -- NAME "%s"\n\n\tTHERE ARE
"%g" BLOCKS AFTER THIS\n',(length(t_order)-
length(t_i)+1),initials,matFileName,length(t_i)-1);
%
catch
    cd ..
    rethrow(lasterror)
    return;
end % end of try
cd ..
end  % end of function
%--------------------------------------------------------------------------
-----
function sound_sacc(type,dur)
freq = 44100;
mynoise(1,:) = 0.9 * MakeBeep(type, dur, freq);
mynoise(2,:) = mynoise(1,:);
Snd('Play', mynoise, freq, 16);
end
```

Example of a Matlab program to select eye movements information during reading

```
function read4ctrl
%Version.: 2.10
%05MAR10
%- - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - -
- - -
%This program reads the file with reading eye movements info.
%Reads all files starting with the initials inserted in the command
window %If you want read a specific file please insert the full
name
%- - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - -
- - -
%Program needs 4 folders in the working directory
%"EYEMOV_RESULTS" - to save information off all valid eye movements
%"MAIN_SEQUENCES" - to save graphs with the main sequences
%"TxTR" - to save text files with reading speed and saccades
results
%"DRIFT"
%- - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - -
- - -
clear 'global'
version = 'Patients';
author= 'Filipe Macedo';
modified= '28-APR-2010 @ 20:00';
%
fprintf('\n\tOFFLINE_DATA_ANALYSIS \n\tVERSION %s -- %s @ READING
analysis\n\tWritten by %s\n', version,modified ,author)
fprintf('\tPerformed on ''%s'' \n', datestr(now));
    home
    d=dir;
    L=length(d);
    count=0;
%
prompt={'Enter de full name [1 file analysis] or two initials [all
files analysis]'};
name='file Name Input';
numlines=1;
defaultanswer={'KT'};
answer = inputdlg(prompt,name,numlines,defaultanswer);
if ~isempty(answer);  nome_de_referencia=answer{1}; else;
error('error1:badInput','\nerror1\nno file name inserted');end
    wd=cd;
    list={};
    totalFiles = 0;
    for i=1:L
                if regexp(d(i).name,nome_de_referencia)
                    if regexp(d(i).name,'.ASC')
                            home
```

```
                            count=count+1;
                            list(count,1)=strcat({d(i).name(1:8)});
                            f_n = (strcat(d(i).name(1:8)));
                            read_file_1(f_n) %using version 1.1
                    totalFiles = totalFiles +1;
                    end
                end;%length-r2
  end;%for
fprintf('\n\n [ALL LIST FINISHED] %g files analysed \n\n',
totalFiles);
givefeedback(1); waitSecs(.25); givefeedback(1);
end
%new function - - - - - - - - - - - - - - - - - - - - - - - - - - - -
- - -
function read_file_1(f_n)
wd = cd;
fprintf('**now reading the file with function "read_file_1"**')
type='E';
fid = fopen(strcat(f_n,type,'.ASC'), 'r');
file_name=strcat(f_n,'--',type);
if ~fid
    error('Erro na abertura do ficheiro!')
    return
end
%
fprintf('\nNOW READING   " %s\n"',file_name)
tic
%
CellOne= textscan(fid,'%q%q %q%q%q%q%q%q%q%q%q%q%q','delimiter','
\b\t','multipleDelimsAsOne' ,1);
close('all')
n_lines=length(CellOne{1,1});
%
z_Matrix=zeros([n_lines,1],'single');
Time=num2cell(z_Matrix,1);
msgTimeAndx=num2cell(z_Matrix,1);
msgAndTime=num2cell(z_Matrix,1);
msgInfoAndy=num2cell(z_Matrix,1);
CellTimeMsg=num2cell(z_Matrix,1);
msgAndTime=CellOne{1,1};
msgTimeAndx=CellOne{1,2};
msgInfoAndy=CellOne{1,3};
clear n_lines z_Matrix CellTimeMsg sheetNumber temp
fprintf('\n\treading...')
idxv1 = 0; idxv = []; sBk = [];
%new stuff: 12Fev2010
idxsBk = 0;
idxeSac  = 0;
idxsSac = 0; newTrial = 0; trial =0;
%~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~
for idxt = 1:length(msgInfoAndy)
    if strncmp(msgInfoAndy{idxt},'Pos',3)
        idxv1 = idxt;
        position(idxv1,1) = str2num(msgInfoAndy{idxv1}(4));
%21march.ed2
```

```
        if newTrial ==0; last_pos = str2num(msgInfoAndy{idxt}(4));
end
        newTrial = 1;
       while  idxv1 <= length(msgInfoAndy)
                idxv (idxv1,1) = idxv1;
% this 'if' records the start of the 'trial' and stores it in
'blockBounds' column '1'
                if strncmp(msgInfoAndy{idxv1},'TargetVisible',13)
                    blockBounds(idxv1,1) = idxv1; trial = trial +1;
                end
if strcmp(msgAndTime{idxt},'SBLINK')
    idxsBk = idxsBk + 1;
    sBk(idxsBk,1) = [idxt];
    idxsBk2 = idxt + 1;
    while ~strcmp(msgAndTime{idxsBk2},'EBLINK')
          idxsBk2 = idxsBk2 +1;
    end
    sBk(idxsBk,2) = [idxsBk2];
end
% -- saccades
if strcmp(msgAndTime{idxt},'SSACC')
  idxsSac = idxsSac +1;   idxeSac = 1; %write = 1; % ed@22Set09
  sSac(idxsSac,[1 2 4]) = [idxt, idxeSac, last_pos];
  idxSearch = idxt +1;
  while ~strcmp(msgAndTime{idxSearch},'ESACC')
        idxSearch = idxSearch+1;
      if strncmp(msgInfoAndy{idxSearch},'TargetNotVisible',16) ||
strcmp(msgAndTime{idxSearch},'SBLINK')
          sSac(idxsSac,3) = -1; % if saccade finished outside
exposure   sSac(idxsSac,[6,9]) = [idxSearch,trial];
      end
  end
  sSac(idxsSac,5) = [idxSearch];
end
if strcmp(msgAndTime{idxt},'ESACC')  % only if a starting of saccad
existed col.6 is updated
   if idxeSac
      sSac(idxsSac,[6,9]) = [idxt,trial];
%sSac.col6 = frame -- end of saccade
      idxeSac =0; %  this bit resets saccade index and ensures
   elseif idxeSac == 0
       searchBk = idxt;
       while ~strcmp(msgAndTime{idxt},'SSACC')
               searchBk = searchBk -1;
                 if
strncmp(msgInfoAndy{searchBk},'TargetVisible',13)
                   idxsSac = idxsSac + 1;
                   sSac(idxsSac,1:4) = [searchBk, 0, -2,last_pos];
                   sSac(idxsSac,[6,9]) = [idxt,trial];break
% to prevent crash!
                 end
              sSac(idxsSac,1) = [searchBk];
       end % because 'TargetVisible' has been reached
   end  % before the 'SSACC' is maked -2 in col.3
end
          idxt = idxv1 + 1;
```

```
            if strncmp(msgInfoAndy{idxv1},'TargetNotVisible',16)
% till TargetNotVisible - 16 characters
% 'blockBounds', col 2 - index of last frame; col 3 - 'flag' - [1]
if block repeated [0] otherwise
                newTrial = 0;
                blockBounds(idxv1,2) = idxv1-1;
                blockBounds(idxv1,3) =
strncmp(msgInfoAndy{idxv1},'TargetNotVisibleR1',18);
                idxv1 = length(msgInfoAndy); %breaks the 'while' loop
              end%if
                idxv1 = idxv1 + 1;
          end %while
      end%if
end%for
fprintf('\n\tcalculating...')
% to clean 'blockBounds'
[idx col val1] = find(blockBounds(:,1));
[idx col val2] = find(blockBounds(:,2));
val3 = blockBounds(idx,3);
%21march.c1 (position information is recorded)
[idx col val4] = find(position~=0);%21march.ed1
blockBounds=[val1 val2 val3 position(idx)];
repTrial = find(blockBounds(:,3) == 1) ;
blockBounds(repTrial,:) = [];
clear idxv1 idxt col val1 val2 val3 val4 idx
clear i j
%blinks 4by4 msec
if size(sBk,1) >=1
    for i = 1: size(sBk,1)
        bkCell{i,1} = CellOne{1,1}{sBk(i,1),1};%  message
        bkCell{i,2} = CellOne{1,3}{sBk(i,1),1}; %   start of blink
        bkCell{i,3} = CellOne{1,4}{sBk(i,2),1}; %   end of blink
        bkCell{i,4} = CellOne{1,1}{sBk(i,2),1}; % message
    end
    %
    tBk = [str2num(str2mat(bkCell(:,2)))
str2num(str2mat(bkCell(:,3)))];
    tBk(:,1) = tBk(:,1)-4;tBk(:,2) = tBk(:,2)+8;
    tBk(:,3) = tBk(:,2) - tBk(:,1);
        last = 1;
        for i=1:size(tBk,1)
            n4ms = ( tBk(i,2) - tBk(i,1) ) /4+1;%this "+1" is OK
            j = 0;
            while j < n4ms %corrected 24Set09
                    sbkBy4(last+j,1) = tBk(i,1) + 4*j;
                     sbkBy4(last+j,2) = tBk(i,3);
                    j = j+1;
            end
            last= last + n4ms;
        end
    clear last
end
%
eyeMovPositions = {};
load(strcat(f_n,'.mat'),'px2deg','t','q','h')
assignin('base','px2deg',px2deg);
```

```
assignin('base','t',t);
%
for i = 1: size(blockBounds,1);
    st =  blockBounds(i,1);    ed = blockBounds(i,2);    ist =
size(eyeMovPositions, 1);
    rg = ed - (st) +1;    aa = [ist+1:ist+rg]';    bb = [st:ed]';
    for j = 1:size(aa,1)
        eyeMovPositions{aa(j),1} = CellOne{1,1}{bb(j),1};
        eyeMovPositions{aa(j),2} = CellOne{1,2}{bb(j),1};
        eyeMovPositions{aa(j),3} = CellOne{1,3}{bb(j),1};
        eyeMovPositions{aa(j),4} = num2str(i);
        eyeMovPositions{aa(j),5} =  num2str(0);
        eyeMovPositions{aa(j),6} =  blockBounds(i,3);
        eyeMovPositions{aa(j),7} =  num2str(blockBounds(i,4));
    end
end
%
[line col]=size(eyeMovPositions);
eyeMovDataNum=zeros([line col],'single');
eyeMovDataNum=str2double(eyeMovPositions);
%
rawFsac=sSac;   rawFsac(:,7:8)=0;
for i = 1: size(rawFsac,1)
    rawFsac(i,7)= str2double(CellOne{1,3}{rawFsac(i,1),1});
    if isnan(rawFsac(i,7))
       rawFsac(i,7)= str2double(CellOne{1,2}{rawFsac(i,1),1});
    end
    tmax = max( rawFsac(i,6), rawFsac(i,5) );
    rawFsac(i,8)= str2double(CellOne{1,4}{tmax,1});
end
%
last = 1;
for i=1:size(rawFsac,1)
    tmax = max( rawFsac(i,6), rawFsac(i,5) );
    n4ms = (rawFsac(i,8)-rawFsac(i,7))/4+1;%this "+1" is OK
    if tmax > rawFsac(i,1) && ~rem(n4ms,1)
        j = 0;
        while j < n4ms %corrected 24Set09
                rawFsacBy4(last+j,1) = rawFsac(i,7) + 4*j;
                rawFsacBy4(last+j,2) = i;
                j = j+1;
        end
        last= last + n4ms;
    else
        rawFsac(i,4) = -3;
        sSac(i,4) = -3;
    end
end
clear last n4ms
%
if size(repTrial,1)>0
    for i = 1:size(repTrial,1)
        idxnSac= find(sSac(:,9) == repTrial(i) );
        fprintf('\nlast report.:\nsaccade non-valid(REPEATED!) @
trial.: %g\n',idxnSac);
        sSac(idxnSac,:)=[];
```

```
    end
end
idxnSac= find(sSac(:,4) == -3); % why del col.6 == 0
sSac(idxnSac,:)=[];
% col.3 has a control var which tells if saccade was valid or not
idxnSac= find(sSac(:,3) == -1); % why del col.6 == 0
sSac(idxnSac,:)=[];          % col.6:end of saccades,if "0" saccade
ended out of presentation time
idxnSac= find(sSac(:,3) == -2); % why del col.6 == 0
sSac(idxnSac,:)=[];          % col.6:end of saccades,if "0" saccade
ended out of presentation time
for i = 1:size(sSac,1)
    %ALL START
    sacCell{i,1} = CellOne{1,1}{sSac(i,1),1};%MSG
    sacCell{i,2} = CellOne{1,3}{sSac(i,1),1};%TIME START %ALL END
    sacCell{i,3} = CellOne{1,1}{sSac(i,5),1};%MSG
    sacCell{i,4} = CellOne{1,4}{sSac(i,5),1};%TIME END
    sacCell{i,5} = CellOne{1,5}{sSac(i,5),1};%DURATION - TIME
    sacCell{i,6} = CellOne{1,10}{sSac(i,5),1};%AMPLITUDE
    sacCell{i,7} = CellOne{1,11}{sSac(i,5),1};%PEAK VEL.
    sacCell{i,8} = CellOne{1,6}{sSac(i,5),1};%X.START
    sacCell{i,9} = CellOne{1,7}{sSac(i,5),1};%Y.START
    sacCell{i,10} = CellOne{1,8}{sSac(i,5),1};%X.END
    sacCell{i,11} = CellOne{1,9}{sSac(i,5),1};%Y.END
    sacCell{i,14} = num2str(sSac(i,4));%Y.END
end
%it is time 2 delete saccades from the eyeMovDataNum matrix:
22DEZ09
[vints irawSac iEm1] =
intersect(rawFsacBy4(:,1),eyeMovDataNum(:,1));
eyeMovDataNum(iEm1,7)= -2;
% tag blinks
if size(sBk,1)> 1
    [vintb ibK iEm2] = intersect(sbkBy4(:,1),eyeMovDataNum(:,1));
    eyeMovDataNum(iEm2,7)= -3;
end
%
if size(sSac,1)>0 %if saccades are detected
    timeSac= [str2num(str2mat(sacCell(:,2)))
str2num(str2mat(sacCell(:,4))) str2num(str2mat(sacCell(:,6))) ...
                    str2num(str2mat(sacCell(:,8)))
str2num(str2mat(sacCell(:,9))) str2num(str2mat(sacCell(:,10))) ...
                    str2num(str2mat(sacCell(:,11)))
str2num(str2mat(sacCell(:,14))) str2num(str2mat(sacCell(:,7)))
str2num(str2mat(sacCell(:,5)))];%[3x3x4]
direction = rad2deg(atan2(timeSac(:,6)-timeSac(:,4),timeSac(:,5)-
timeSac(:,7)));
for i = 1:size(direction,1)
    if direction(i)<0;  val = direction(i);   direction(i) =
360+val;   end
end; clear val; sdir =  direction;
    for i = 1: size(timeSac,1)
        idx_pos = find(eyeMovDataNum(:,1) == timeSac(i,1) );
        pos_sac(i,1) = eyeMovDataNum(idx_pos,4);
    end
%update saccade cell with direction
```

```
    for i = 1:size(direction,1)
        sacCell{i,12}=direction(i);
        sacCell{i,13}=pos_sac(i);
    end
timeSac(:,6) = pos_sac;% trial
%
    for i = 1:size(sacCell,1)
        ctrlVar(i,1)= str2num(sacCell{i,5});
        ctrlVar(i,2)= str2num(sacCell{i,6});%AMPLITUDE
        ctrlVar(i,3)= str2num(sacCell{i,7});%PEAK.VEL
    end
%METHODS NOTE
%saccades need to be deleted from drift: variable "sacBy4" stores
all the info for further deletion
    last = 1;
    for i=1:size(timeSac,1)
        n4ms = (timeSac(i,2)-timeSac(i,1))/4+1;%this "+1" is OK
        j = 0;
        while j < n4ms %corrected 24Set09
                sacBy4(last+j,1) = timeSac(i,1) + 4*j;
                sacBy4(last+j,2) = i;
                sacBy4(last+j,3) = timeSac(i,8);
                j = j+1;
        end
        last= last + n4ms;
    end
%
plot(ctrlVar(:,2),ctrlVar(:,3),'r*'); % main sequence!
%
cd(strcat(wd,'\SACCADES'));
saveas(gcf,strcat('MS_',f_n(1:8),'.fig'));
close()
%
fid = fopen(strcat('sac',f_n(1:2),'.txt'),'at+');
fprintf(fid,'date.:\t%s\nfile name.:\t%s\n',
datestr(now),f_n(1:8));
fprintf(fid,'sac count.:\t%.0f\n\n',size(sacCell,1));
fprintf(fid,'this time the number of trials
was:\t%g\n\n',h.trialsDesired);
%
    cd ..
else
    fid = fopen(strcat(f_n(1:2),'.txt'),'at+');
    fprintf(fid,'date.:\t%s\nfile name.:\t%s\n',
datestr(now),f_n(1:8));
    fprintf(fid,'sac count.:\t%s\n\n','NO SACCADES!');
end
fprintf('\n\tcalculating...')
clear reading idxvnz
load(strcat(f_n,'.mat'),'reading')
starr = size(reading(1,1).w,2)-10;
if starr>1;
    warning('...MORE THAN 11 COL')
end

i=1;
```

```
while size(reading(i,1).w,2) == size(reading(1,1).w,2)
    lctrol(i,1:11) = reading(i,1).w(starr:starr+10
    i=i+1;
end
clear i
% **lctrol' columns: **
% (1) eye tracker raw time % (2) time between samples [ms]
% (3) vel. eye [deg/sec] % (4) acel. eye [deg/sec/sec]
% (5) xe [px] % (6) xt [px] % (7) horizontal component of saccades
[px]
% (8) ye [px] % (9) yt [px]  % (10) loops [no units] % (11) cond
[no units]
% (12) presntation duration 'vbl-ini_time' [ms]% (13) word
%** Important information during the process of reading data**
% (a) when reading data from 'xxxxxxxx.mat',info. is in 'reading'
structure
% or the txt file with name: 'xxxxxxxx.txt' [in the case of
patients
% (b) 'cond 11' = blank frame, target was visible in next
frame;'TargetVisible' msg sent to file.EDF/ASCI
% (c) 'cond 12' = gaze position not in the red dot
% (d) 'cond 13' = presenting the clue
% (e) 'cond 14' = 'st' word presented; 'cond 21' = remaining words
presented
% (f) 'cond 31' = blank frame due to saccade or missing data % now
using 'cond 11' and 'cond 14' to know the samples corresponding to
the 'clue'
% these sample might contain (31) or (12), these are also deleted;
% %ed.30March
lctrol(:,12)= -4;   lctrol(:,13)= -5;
clueidx_b = zeros(length(lctrol),14);
last = 1; stc = 0;
for i = 1:size(lctrol,1)
    if lctrol(i,10) == 11;  % c1 %
word = 1;
clueidx_b(i,2) = -1;%selects clue frames
        while lctrol(i,10) ~= 14 % c2 % 18July.c1: now column 11
            clueidx_b(i,1) = last;
            i=i+1;
        end % c2 %
clueidx_b(i-1,2) = 1;%last clue frame
stc = stc + 1; %update sentence / trial number
% ed.19July % tags for W1
clueidx_b(i,11) = -1;
stcSeq(stc,word)=lctrol(i,13); % selects first word/first frame
        while lctrol(i,10) ~= 21 % c3 %
                clueidx_b(i,word+2) = 1;
%                 clueidx_b(i,15) = rep;
                clueidx_b(i,word+6) = lctrol(i,1);
                i = i+1;
        end % c3 %
clueidx_b(i-1,11) = 1; % last frame of 1st word
word = word+1; %update word number
i = i + 1; % cx.22July, needs to exist to avoid the 1st=blank frame
% tags for W2 - W? % selects word 1 for w>1 ... number of words in
the sentence
```

```
        while lctrol(i,10) == 21         % c4 %
            clueidx_b(i,10+word) = -1;
            stcSeq(stc,word)=lctrol(i,13);
                while lctrol(i,11) <= lctrol(i+1,11) % c5 %
                    clueidx_b(i,word+2) = word;
                    clueidx_b(i,word+6) = lctrol(i,1);
%                     clueidx_b(i,15) = rep;
                    i = i+1;    if i+1 > length(lctrol); break; end
                end % c5 %
             clueidx_b(i,word+2) = word;% cx.22July, needs to take
the last frame
             clueidx_b(i,word+6) = lctrol(i,1); % cx.22July, needs
to take the last frame
             clueidx_b(i,10+word) = 1;
             word = word + 1;%update word number inside the while %
c4 %
             i = i+2;    if i > length(lctrol); break; end
                % cx.22July, i+2 needs to exist to avoid the
1st=blank frame
        end % c4 %

last = last +1;
    end % c1 %
end
%
a(:,1:6)= [lctrol(:,1), lctrol(:,6), lctrol(:,8),lctrol(:,11),
lctrol(:,2), lctrol(:,10) ];
idx_a_clue = find(clueidx_b(:,1) >=1);
a(idx_a_clue,4) = NaN;
idx_a_dot = find(a(:,6)==12);
a(idx_a_dot,4) = NaN;
%
aizero = find(a(:,1)==0);   a(aizero,:)=[];
idx = 1;
limit = 1;
by4= zeros(300000,6);
for i = 2:size(a,1)/limit
    n4s = (a(i,1)-a(i-1,1))/4;
    j = 0;
    while j < n4s+1
        by4(idx+j,1) = a(i-1,1)+4*j; %col1.time
        by4(idx+j,2) = a(i-1,2); %col2.position of target xx
        if idx+j > 2
            by4(idx+j,3) = by4(idx+j-1,2) - by4(idx+j,2);
%col3.horizontal mov
        end
        by4(idx+j,4) = a(i-1,3); %col4.position of target yy
        if idx+j > 2
            by4(idx+j,5) = by4(idx+j-1,4) - by4(idx+j,4);
%col5.vertical mov
        end
         by4(idx+j,6) = a(i-1,4);%col6.var [0/1]:this tells me when
the screen was blanked due to saccades
             j = j+1;
    end
    idx = idx + n4s;
```

```
end
idx2del =  (idx+1):1:size(by4,1);
by4(idx2del,:) = [];
clear idx2del;
%NOW ALL DRIFT INFO. FROM THE MAT FILE IS IN A 4 BY 4 MSEC FORMAT
b(:,[1 2 4 6 7 8]) = eyeMovDataNum(:,[1:4 6 7]); % column 5 is "0"
but is not necessary!
idxM1 = find(b(:,1)==-1);
b(idxM1,:)=[];
%
idxNan = find(isnan(b(:,1)));
b(idxNan,:)=[];
% to clean repeated blocks data before drift analysis
for i = 2:max(size(b))
    if b(i,6) == b(i-1,6)
        b(i,3)=b(i,2)-b(i-1,2);
        b(i,5)=b(i,4)-b(i-1,4);
    else
        b(i,3)=0;
        b(i,5)=0;
    end

end
[time,idxEye,idxTgt]=intersect(b(:,1),by4(:,1));
[tTE,iT,iE] = intersect(a(:,1),b(idxEye,1));
%
gainCtrl(:,[1 2 3 4 5 6 7 10 11 12 16 22]) = [b(idxEye,[1 2])
by4(idxTgt,2) zeros(size(idxEye,1),1) b(idxEye,4) ...
                                                  by4(idxTgt,4)
zeros(size(idxEye,1),1) by4(idxTgt,6)  zeros(size(idxEye,1),1)...
                                                  b(idxEye,7) b(idxEye,6)
b(idxEye,8)];% b.col.8 corresponds to eyeMovDataNum.col.7
gainCtrl(:,17)= 0.004;
[tGC, iGC, itTE] = intersect(gainCtrl(:,1),tTE);
gainCtrl(iGC,17)= a(iT,5);
gainCtrl(:,18)=gainCtrl(:,17)/0.004-1;
col18 = gainCtrl(:,18);
type = f_n(6:7);
if strcmp(type,'M1')
    gain = .1;  elseif strcmp(type,'Z0');
    gain = 1;   elseif strcmp(type,'P1');
    gain = 10;
end
%x
col2 = gainCtrl(:,2);   col3 = gainCtrl(:,3);
%y
col5 = gainCtrl(:,5);   col6 = gainCtrl(:,6);
%
for i = 2:length(gainCtrl)
%
    if isnan(gainCtrl(i,12))
    %
        if col18(i) == 0
            gainCtrl(i,4) = col2(i)-col2(i-1);
            gainCtrl(i,7) = col5(i)-col5(i-1);
            gainCtrl(i,19) = col2(i)-col2(i-1);
```

```
            gainCtrl(i,20) = col5(i)-col5(i-1);
        elseif  col18(i) ~= 0 && gain ~= 1
            colBack = i-col18(i); if colBack < 1; colBack = i-1;end
            gainCtrl(i,4) = col3(i)-col2(colBack);
            gainCtrl(i,7) = col6(i)-col5(colBack);
            gainCtrl(i,19) = ( col2(i)-col2(colBack) )*gain;
            gainCtrl(i,20) = ( col5(i)-col5(colBack) )*gain;
        elseif col18(i) ~= 0 && gain == 1
            gainCtrl(i,4) = 0;
            gainCtrl(i,7) = 0;
            gainCtrl(i,19) = 0;
            gainCtrl(i,20) = 0;
        end;
     %
    else
            gainCtrl(i,4) = 0;
            gainCtrl(i,7) = 0;
            gainCtrl(i,19) = 0;
            gainCtrl(i,20) = 0;
    end
%
end
col4 = gainCtrl(:,4);   col7 = gainCtrl(:,7); col17 =
gainCtrl(:,17);
delta_x = col4*px2deg(1); delta_y = col7*px2deg(2);
delta_s = sqrt( delta_x.^2 +delta_y.^2); gainCtrl(:,8) = delta_s;
vel = delta_s./col17; gainCtrl(:,13)= vel;

col19 = gainCtrl(:,19); col20 = gainCtrl(:,20);
delta_x1 = col19*px2deg(1);
delta_y1 = col20*px2deg(2);
delta_s1 = sqrt( delta_x1.^2 +delta_y1.^2);  gainCtrl(:,8) =
delta_s;
vel1 = delta_s1./col17; gainCtrl(:,21)= vel1;
% test? 06FEBRUARY2010
for i = 1: size(gainCtrl,1)
%formula.: xe-(xt)^2 + ye-(yt)^2
        gainCtrl(i,8) =
sqrt((gainCtrl(i,4)*px2deg(1))^2+(gainCtrl(i,7)*px2deg(2))^2);%*60;
% slip amplitude
        gainCtrl(i,9) =
rad2deg(atan2(gainCtrl(i,7),gainCtrl(i,4)));
end
%
for i = 2:size(gainCtrl,1)
    if isnan(gainCtrl(i,12)); delta_xd(i,1) = ( col2(i)-col2(i-1)
)*px2deg(1); delta_yd(i,1) = ( col5(i)-col5(i-1) )*px2deg(2);
    else delta_xd(i,1) = 0; delta_yd(i,1) = 0; end
end
delta_sd = sqrt(delta_xd.^2 + delta_yd.^2);   gainCtrl(:,14) =
delta_sd;
gainCtrl(:,15) = gainCtrl(:,14)./.004;
%
idxZ=find(gainCtrl(:,10)==0);
if idxZ
    gainCtrl(idxZ,:) = [];
```

```
end
%
idxM2=find(gainCtrl(:,12)==-2);
if size(idxM2,1)
    gainCtrl(idxM2,:) = [];
end
idxM2=find(gainCtrl(:,22)==-2);
gainCtrl(idxM2,:) = [];
idxM3=find(gainCtrl(:,22)==-3);
gainCtrl(idxM3,:) = [];
idxNan = find(isnan(gainCtrl(:,14) ) );
gainCtrl(idxNan,:) = [];
%
sac = timeSac;
isp1 = find(timeSac(:,8) == 1);
isp2 = find(timeSac(:,8) == 2);
%
sac1 = timeSac(isp1,:);
sac2 = timeSac(isp2,:);
%
timeOfsac = zeros(size(timeSac,1),10);

timeOfsac(:,1:10) = timeSac(:,[1 2 4 5 6 7 8 3 9 10]);
fprintf('\nNumber fo saccades: %g\n',size(timeOfsac,1));
%
% timeOfsac(idxSac,1) =timeOfsac(idxSac,10);  %TIME
% timeOfsac(idxSac,2) = wordBy4(idxWord,1);   %TIME
% timeOfsac(idxSac,3) = wordBy4(idxWord,2);   %WORD.N
% timeOfsac(idxSac,4) = wordBy4(idxWord,3);   %WORD SIZE (CHAR)
% timeOfsac(idxSac,5) = wordBy4(idxWord,3);   %RESERVED! TIME WORD
"ON"
% timeOfsac(idxSac,6) = wordBy4(idxWord,3);   %RESERVED! LATENCY!
% timeOfsac(idxSac,7) = wordBy4(idxWord,4);   %TRIAL N.
% timeOfsac(idxSac,8) = wordBy4(idxWord,5);   %TRIAL RESULT
assignin('base','timeOfsac',timeOfsac);
clear idxouts
load(strcat(f_n,'.mat'),'t','h')
%
%::NOW CALLING ANOTHER FUNC. DO FINISH THE DRIFT JOB!::
[drift2 dist2 distb] = driftcal(gainCtrl,b,by4,px2deg,f_n,t);
%
TxTdir = strcat(wd,'\TxTR');
cd(TxTdir)
%
nf = strcat(f_n(1:2),'-rSpeed','.txt');
fid = fopen(nf,'at+');
count = fprintf(fid,'Function.:\t%s\n','olreadda');
count = fprintf(fid,'Directory.:\t...%s\t%s\n',wd(size(wd,2)-
10:size(wd,2)-5),wd(size(wd,2)-6:size(wd,2)));
count = fprintf(fid,'Date analysed.:\t%s\t%s\nFile name.:\t%s\tDate
recorded.:\t%s\t%s\n\n',datestr(now,1),datestr(now,15),f_n,h.dateru
n(1:11),h.daterun(13:17));
count = fprintf(fid,'x.time[U].:\t%.4f\tsecs\nr.spd[U].:\t%.0f
\twpm\n\n' ,t(1),60/t(1));
%ed.26March - to keep information about saccades
```

```
count =
fprintf(fid,'sac[U].:\t%.0f\tsac[D].:\t%.0f\tsac[UD].:\t%.0f\n',
size(sac1,1),size(sac2,1),size(sac,1));
% mean amplitude
if size(sac1,1)~=0 && size(sac2,1)~=0
count =
fprintf(fid,'amp.[U].:\t%.2f\tamp.[D].:\t%.2f\tamp.[UD].:\t%.2f\n',
mean(sac1(:,4)),mean(sac2(:,4)),mean(sac(:,4)));
% mean peak velocity
count =
fprintf(fid,'p.vel[U].:\t%.1f\tp.vel[D].:\t%.1f\tp.vel[UD].:\t%.1f\
n',mean(sac1(:,3)),mean(sac2(:,3)),mean(sac(:,3)));
else
count =
fprintf(fid,'amp.[U].:\t%.2f\tamp.[D].:\t%.2f\tamp.[UD].:\t%.2f\n',
'--','--',mean(sac(:,4)));
% mean peak velocity
count =
fprintf(fid,'p.vel[U].:\t%.1f\tp.vel[D].:\t%.1f\tp.vel[UD].:\t%.1f\
n','--','--',mean(sac(:,3)));
end
%
fclose(fid);
% saccades info
nfs = strcat(f_n(1:7),'-SACinfo','.txt');
fid = fopen(nfs,'at+');
fprintf(fid,'saccades dir.:\t...%s\n',wd(size(wd,2)-
10:size(wd,2)));
fprintf(fid,'Date analysed.:\t%s\t%s\nFile name.:\t%s\tDate
recorded.:\t%s\t%s\n',datestr(now,1),datestr(now,15),f_n,h.daterun(
1:11),h.daterun(13:17));
fprintf(fid,'sframe\teframe\tpeakvelo.\tamplitude\tangularori\tcomp
x\tcompy\tduration\tposition\n');
for i=1:size(sac,1);
fprintf(fid,'%.0f\t%.0f\t%.2f\t%.2f\t%.2f\t%.2f\t%.2f\t%.0f\n',sac(
i,1),sac(i,2),sac(i,3),sac(i,4),sac(i,5),sac(i,6),sac(i,7),sac(i,8)
);
end
fclose(fid);
cd ..
%
cd(strcat(wd,'\SACCADES'));
fidsac =  fopen(strcat('tOs',f_n(1:8),'.txt'),'w');
legends={'time.start',
'time.end','x.start','y.start','x.end','trial.n','position','amp[de
g]','p.vel[ded/sec]','duration'};
for i=1:size(timeOfsac,2); fprintf(fidsac,'%s\t',legends{i} ); end;
fprintf(fidsac,'date.:\t%s\tfile name.:\t%s\n',
datestr(now),f_n(1:8));
% send the file to a txt file
for i=1:size(timeOfsac,1)
    for j = 1:size(timeOfsac,2)
    fprintf(fidsac,'%.2f\t', timeOfsac(i,j) );
    end
    fprintf(fidsac,'\n');
end
```

```
%
save(strcat('S_',f_n(1:8)),'sacCell','timeSac','timeOfsac');
cd ..
clear CellOne Time msgTimeAndx eyeMovPositions
%
% Please keep this bit below to make sure the file is recorded
cd(strcat(wd,'\EYEMOV_RESULTS'));
save(strcat('R_',f_n));
cd ..
% end of function
fprintf('\n END OF ANALYSIS \n')
% fprintf(fidrpt,'\n\nlast report.:\nEND OF ANALYSIS');
status = fclose('all');
givefeedback(1); %waitSecs(.25); givefeedback(1);
%END OF THE MAIN FUNCTION
end
%%
%AUXILIAR FUNCTION HERE
%
%new function here
function [drift2 dist2 distb] =
driftcal(gainCtrl,b,by4,px2deg,f_n,t)
modified= '28-APR-2010 @ 20:00';
%Update.: 30 September 2009
%Update.: 18 September 2009
%Update.: 03 September 2009
%what is this program doing?
%imports drift information
%first loop goes trough the file and selects,based in the 4 ms
separation,
%the start and end of each fixation
%output var is: drift %col1.start time %col2.end time
%col3.frame start %col4.frame end %col5.fix duration
%EYE
%col6.xx start fix %col7. yy end fix %col8. xx start fix %col9. yy
end fix
%TARGET
%col10.xx start fix %col11. yy end fix %col2. xx start fix %col13.
yy end fix
wd = strcat(cd,'\DRIFT');
px2mina = px2deg*60;
drift = [gainCtrl(1,1),0];  j=1;    i=1;
%
for  i = 1:size(gainCtrl,1)-1
% drift is a small matrix with information about the firt and last
frame of fixation, now i can use drift to calculation about the
maximum slippage
    if gainCtrl(i+1,1)-gainCtrl(i,1)==4
        drift(j,2)= gainCtrl(i+1,1);
        drift(j,4)=i+1;%FRAME.FIX.ENDED
    else
        j=j+1;
        drift(j,1)=gainCtrl(i+1,1);
        drift(j,3) = i+1; %FRAME.FIX.STARTED
    end
%
```

```
end
%
drift(:,5) = drift(:,2) -drift(:,1);%FIX.DURATION
idxDz = find (drift(:,2)==0);%::needed to avoid errors::
drift(idxDz,:)=[];
%eye movement goes to b using drift times and localizes START
% goes to b using drift times and localizes END
[e_tSfix e_idxSb e_idxSdrift] = intersect(b(:,1),drift(:,1));
[e_tEfix e_idxEb e_idxEdrift] = intersect(b(:,1),drift(:,2));
%::to avoid an error::last fix sometimes does not end!
if size(e_idxSb,1)-size(e_idxEb,1) ==1
    e_idxEb( (size(e_idxEb,1))+1,1)=length(b);
end
%
drift(:,6:7) = [b(e_idxSb,2) b(e_idxSb,4)];%EYE.FIX.STAR
drift(:,8:9) = [b(e_idxEb,2) b(e_idxEb,4)];%EYE.FIX.END
drift(:,14) = [b(e_idxEb,8)];%10FEB10: POSITION
%slippage: i_idxSCtrl / i_idxECtrl::THIS BIT IS CLUCIAL AND I NEED
TO KNOW
ddir = rad2deg(atan2(drift(:,8)-drift(:,6),drift(:,7)-drift(:,9)));
for i = 1:size(ddir,1)
    if ddir(i)<0;  val = ddir(i);   ddir(i) = 360+val;   end
end; clear val;
drift(:,15) = ddir;
%slippage: i_idxSCtrl / i_idxECtrl::THIS BIT IS CLUCIAL AND I NEED
TO KNOW
%ACTUAL SLLIPAGE!
[i_tSfix i_idxSCtrl i_idxSdrift] =
intersect(gainCtrl(:,1),drift(:,1));
[i_tEfix i_idxECtrl i_idxEdrift] =
intersect(gainCtrl(:,1),drift(:,2));
%target movement
[t_tSfix t_idxSb t_idxSdrift] = intersect(by4(:,1),drift(:,1));
[t_tEfix t_idxEb t_idxEDrift] = intersect(by4(:,1),drift(:,2));
%
drift(:,10:11) = [by4(t_idxSb,2) by4(t_idxSb,4)];%TARGET.FIX.START
drift(:,12:13) = [by4(t_idxEb,2) by4(t_idxEb,4)];%TARGET.FIX.END
%new block here: maximum drift amplitude:
%e_idxSb -- index starting frame %e_idxEb -- index end frame
%b col.2 gives the xx %b col.4 gives the yy
dist1 = []; dist2 = []; idxorig = 0; idxdist2 = 0;
for i = 1: size(e_idxEb,1)
    ii = 0;idxorig = 0;
    frmIni = e_idxSb(i);
    frmFini = e_idxEb(i)-1;
    for idxorig = frmIni:frmFini
        ii = ii+1;idxorig =  idxorig+1;
        dist1(ii,:) = sqrt(((b(frmIni,2)-
b(frmIni+ii,2))*px2mina(1))^2 + ((b(frmIni,4)-
b(frmIni+ii,4))*px2mina(2))^2);
    end
    idxdist2 = idxdist2+1;
    if max(dist1)~=0
       dist2(idxdist2,1) = log10(max(dist1));
    else
        dist2(idxdist2,1) = 0;
```

```
    end
    dist3{i,1} = dist1; %this is a control var -- no point to save
it
    dist1 = [];i= i+1;
end
%end of the new block
drift2(:,1:4)=[drift(:,8)-drift(:,6) drift(:,9)-drift(:,7)
drift(:,12)-drift(:,10) drift(:,13)-drift(:,11)];
drift2(:,5:6)=[drift2(:,1)-(drift2(:,3)) drift2(:,2)-
(drift2(:,4))];
drift2(:,9) = drift(:,14);
%
for i=1:size(drift2,1)
      drift2(i,7)=log10(sqrt((drift2(i,1)*px2deg(1))^2+(drift2(i,2)
      *px2deg(2))^2)*60);
      drift2(i,8)=rad2deg(atan2(drift2(i,1),drift2(i,2)));
end
% now about slippage
dista = []; distb = []; idxorig = 0; idxdistb = 0;
%col.8 from gain is already in min of arc!
for i = 1:size(i_idxECtrl,1)-1
    ii = 0;
    frmIni = i_idxSCtrl(i);
    idxorig = 0;
    frmFini = i_idxECtrl(i);
    for idxorig = frmIni:frmFini
        ii = ii+1;
        idxorig =  idxorig+1;
        dista(ii,:) = gainCtrl(idxorig,8)*60;
    end
    idxdistb = idxdistb+1;
    if max(dista)~=0    % ADD TO CONTROLS!!
        distb(idxdistb,1) = log10(max(dista));
    else
        distb(idxdistb,1)  = 0;
    end
    distc{i,1} = dista; %this is a control var - no point to save
it
    dista = [];i= i+1;
end
% mean slippage
hist(distb);
mean(distb);
title(strcat('max4slip',f_n,'...mean of max slip =',
num2str(mean(distb)),'...min of arc'));
cd(strcat(wd,'\hist'));
saveas(gcf,strcat('max4slip',f_n,'.fig'));
close()
%
hist(drift2(:,7));
mean(drift2(:,7));
title(strcat('s2e',f_n,'   mean amplitude
=',num2str(mean(drift2(:,7) ) ),' minarc'));
cd(strcat(wd,'\hist'));
saveas(gcf,strcat('s2e',f_n,'.fig'));
close()
```

```
%
hist(dist2);
mean(dist2);
title(strcat('max2',f_n,'   mean amplitude =',num2str(mean(dist2)
),' minarc'));
cd(strcat(wd,'\hist'));
saveas(gcf,strcat('max2',f_n,'.fig'));
close()
cd ..
%file info
fid = fopen(strcat('drift',f_n(1:2),'.txt'),'at+'); GG =
[size(cd,2)-20:size(cd,2)];CD=cd;
fprintf(fid,'\n\n%s\n\ndate.:\t%s\nfile name.:\t%s\n',CD(GG),
datestr(now),f_n(1:8));
fprintf(fid,'\n * * code version date: %s* * \n',modified);
%drift info
i3=find(gainCtrl(:,14)~=0); i4=find(gainCtrl(:,15)~=0);
%
a1 = find(drift2(:,7)~=-Inf );a2 = find(dist2(:,1)~=-Inf );
% %slip info
i1=find(gainCtrl(:,13)~=0); i2=find(gainCtrl(:,8)~=0);
% 10FEB10
for i = 1:4
fprintf(fid,'\n\n * *position: [%g] * * \n',i);
ip = find( gainCtrl(:,22)==i);
 if isempty(ip) == 0
    fprintf(fid,'\nMEDIAN-EyeDriftAmplitude:\t%g\tmin-of-
arc',median(gainCtrl(ip,14))*60);
    fprintf(fid,'\nMEANlog-EyeDriftAmplitude:\t%g\tmin-of-arc',
10^mean( log10(gainCtrl( intersect(ip,i3),14)*60)) );
    fprintf(fid,'\nMEAN-EyeDriftAmplitude:\t%g\tmin-of-
arc',mean(gainCtrl(ip,14))*60);

    fprintf(fid,'\n\nMEDIAN-
EyeDrifVel:\t%g\tdeg/sec',median(gainCtrl(ip,15)));
    fprintf(fid,'\nMEANlog-
EyeDrifVel:\t%g\tdeg/sec',10^mean(log10(gainCtrl(intersect(ip,i4),1
5)) ) );
    fprintf(fid,'\nMEAN-
EyeDrifVel:\t%g\tdeg/sec',mean(gainCtrl(ip,15)));
    ipd2 = find(drift2(:,9) == i);
    fprintf(fid,'\n\nmeanOfS2E-EyeDriftAmplitude:\t%g\tmin-of-
arc\n* * * *\nmean-DRIFT-max:\t%g\tmin-of-arc\n',...
        10^mean( drift2(intersect(ipd2,a1) ,7) ),10^mean(
dist2(intersect(ipd2,a2),1) ) );
    fprintf(fid,'\n\nMEDIAN-
RIVel:\t%g\tdeg/sec',median(gainCtrl(ip,13)));
fprintf(fid,'\nMEANlog-RIVel:\t%g\tdeg/sec',10^mean(
log10(gainCtrl( intersect(ip,i1),13)) ) );
fprintf(fid,'\nMEAN-
RIVel:\t%g\tdeg/sec\n**',mean(gainCtrl(ip,13)));
fprintf(fid,'\n\nMEDIAN-slippage.:\t%g\tmin of arc',
median(gainCtrl(ip,8))*60);
fprintf(fid,'\nMEANlog-slippage.:\t%g\tmin of arc',
10^mean(log10(gainCtrl( intersect(ip,i2),8)*60)) );
```

```
fprintf(fid,'\nMEAN-slippage.:\t%g\tmin of arc',
mean(gainCtrl(ip,8))*60);
fprintf(fid,'\nreadingSpeed:\t%g\tseconds\t=\t%g\twpm\n*\n\n',t(i),
60/t(i));
 end
%
end
%
% send the file to a txt file
fiddft =  fopen(strcat('tD',f_n(1:8),'.txt'),'w');
legends={'fix.start',
'fix.end','frame.s','frame.e','fix.dur(msec)','xe.start','ye.start'
,'xe.end','ye.end','xt.start','yt.start','xt.end','yt.end','positio
n','dir[0-360]','drift.s2e[min arc]'};% 1 extra columns from drift
2
for i=1:size(drift,2)+1; fprintf(fiddft,'%s\t',legends{i} ); end;
fprintf(fiddft,'date.:\t%s\tfile name.:\t%s\n',
datestr(now),f_n(1:8));
for i=1:size(drift,1)
    for j = 1:size(drift,2)
    fprintf(fiddft,'%.0f\t',drift(i,j) );
    end
    fprintf(fiddft,'%.1f\t',10^drift2(i,7) );
    fprintf(fiddft,'\n');
end
%
save(strcat('D_',f_n),'gainCtrl','by4','b','drift2','drift','dist2'
,'dist3','distb','distc');
cd ..
end
%this bit of code calculates saccades latency
%this function is not retriving any resulst because all the info
about
%saccades has been deleted from the "b" - - in the future I can use
%this function but I need to use eyMovDataNum instead
function [lat] = latency(b,timeSac,f_n)
idxTs=find(b(:,7)==1);
%got time target visible and trial number
tT(:,1:2) = b(idxTs,[1 6]);

for i = 1: length(timeSac)
    [t4s itimeSac iB] = intersect(timeSac(:,1),b(:,1));
% can use this index to know where this sac. belongs(trial)
end
n = [b(iB,6) timeSac(itimeSac,1)];
%now doing latency calculations
%n.col.1 = trial n.
%       .2 = time saccade started
%       .3 = time target was exposed
%       .4 = latency first saccade since time col.3 (-) if is the
second saccade
%       .5 = latency second saccades since first
%       .6 = latency since the "clue" exposure (previous +100 msec)
for i = 1:size(tT,1)
    in = find(n(:,1)==tT(i,2)); %find time of expose 4 trial with
saccades
```

```
    n(in,3) = tT(i,1);
    j = 1;
    n(in,4) =  n(in,2) -tT(i,1) ;%does the latency calculations
    if size(in,1) == 2 %if there is more than 1 sac per trial
        j=j+1;
        n(in(j),5) =  n(in(j),2)-n(in(j-1),2) ;
        n(in(j),4) = - n(in(j),4) ;
    elseif  max(size(in)) > 2
        warning('3 saccades in one trial is ridiculus')
    end
end
idxRub = find(n(:,3)==0);
n(idxRub,:) = [];
n(1:size(n,1),5:6) = 0;

for i =1:size(n,1)
    if n(i,4)>0
       n(i,6)=n(i,4)+100;
    elseif n(i,4)<0
         n(i,6)=n(i,5)+100;
    end
end
lat = n;
wd = cd;
cd(strcat(wd,'\SACCADES'));
save(strcat('L_',f_n(1:8)),'lat');
cd ..
%
end
```