An Investigation of Interocular Suppression with a Global Motion Task

by

Peng Zhang

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AUTHOR'S DECLARATION

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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ABSTRACT

Purpose:

Interocular inhibitory interactions appear to underlie the establishment of ocular dominance. The inhibitory effect leads to suppression of the non-dominant eye in certain conditions. While these processes are not fully understood, the relative differences in image contrast appear to be fundamental. By titrating the relative contrast presented to each eye, a balance in the relative inhibitory effects of each eye can be defined. This research looked at whether the interocular contrast ratio at perceptual balance could be used as an index of the ocular dominance in binocular normal population, and the suppression typically found in the amblyopic population. Contrast variation was compared to luminance variation as well as the application of neutral density filters.

Methods:

Balance point measures were obtained by varying the interocular levels of contrast for a global motion task viewed dichoptically. One eye received signal dots moving in a given direction while the other eye received noise dots moving randomly. Subjects were tasked with determining the direction of movement of the signal dots. Balanced dichoptic motion sensitivity was achieved under a specific contrast ratio (or the balance point), depending on the observer's binocular functions. This test was conducted on a control group (n=23) having normal vision and a strabismic amblyopic group (n=10). In addition, a variation of this test was designed with interocular luminance (rather than interocular contrast) serving as the independent variable, and it was conducted to both the control (n=5) and amblyopic groups (n=8). Concurrent eye tracking measures measured changes in eye alignment at the balance point.

Results:

Although most normal vision subjects showed a balance point at close to equal levels of contrast between the eyes, a minority of them were significantly imbalanced. The suppression measured in the strabismic amblyopic group was significantly greater than that of the control group. Varying the interocular luminance instead of contrast failed to affect the coherence motion thresholds. Ocular alignment was not changed when the balance point was reached.

Conclusion:

Consistent with the current model of binocular integration, interocular contrast are uniquely important in establishing sensory dominance and suppression. This suggests that the interocular suppression found in amblyopia could be attenuated by methods that allow the reduction of contrast to the fellow fixing eye. Amblyopia therapy might then be improved where such contrast balancing methods are employed instead of the complete patching of the fellow fixing eye.

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DEDICATION

This work is graciously dedicated to my parents for their love and support.

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CHAPTER 1: LITERATURE REVIEW

1.1 ANATOMICAL AND PHYSIOLOGICAL ORGANIZATION OF THE VISUAL PATHWAY

The functional organization of the visual system is highly specialized. The primary function of vision is to convert the retinal image into perception. However, object perception has numerous attributes such as colour, orientation, and motion. This process involves transforming the pattern of the visual scenes processed by several key structures in the brain, most notably the LGN, the primary visual cortex, and other cortical areas. In fact, there are 32 areas in the monkey cortex devoted to vision[1]. Basic attributes of a stimulus are often analyzed in discreet parallel areas. Visual information regarding the stimulus features seem to be analyzed in a different pathway from that regarding the target's motion[2]. It has been argued that two common cell types in the retina, P (parvocellular) and M (magnocellular) pathways respectively constitute the basis of this differentiation[2].

The lateral geniculate nucleus (LGN) is a folded sheet of neurons composed of six layers that receive direct input from the retina, following a crossing over of nasal fibres at the optic chiasm[2]. Each layer receives information from only one eye. Layers III and V receive primarily P neurons and layer II receives M cells, both from the ipsilateral eye. Layers IV and V receive P cells and layer I receives M cells from the contralateral eye. Similar to the retina, the LGN contains both ON-centre cells and OFF-centre cells[3]. However, differs from the retinal cells, the LGN cell have additional inhibitory interneurons, and those interneurons cause less responses to white light that illuminates the entire receptive field uniformly[4]. The information between the eyes was segregated based upon the layered inputs[5]of LGN. However, there appears to be binocular interaction within a given LGN[6, 7]. Schroeder el al[8] conducted a study on the macaque using flash-evoked multiunit activity, and their result suggested that some activities in the LGN are involved in binocular integration. Additionally, there is evidence in cat studies that the binocular interaction in the LGN is inhibitory[9].

The primary visual cortex (V1), which contains six layers and several sub-layers, is the first site at which the excitatory signals from the two eyes converge onto a single cell. The LGN projects to layer IV of the primary visual cortex. The neurons from the P layer project to sub-layer IVCβ, which then connect with layers II and III and finally to visual areas V2 and V3. The M cells project to layer IVCα, which then connect to layer IVB and on to visual areas V2 and V5. The primary visual cortex contains a variety of cell types responsible for form and motion analyses. These functions are further divided in higher cortical areas (V2 to V5). However, it should be noted that there is considerable cross talk between these two systems throughout the cortex[10, 11]. Cells in the cortex share similar properties due to the way that the anatomical connections are arranged[4]. There is a columnar organization for orientations, as well as ocular dominance. The ocular dominance columns are stripes of neurons in the visual cortex that have certain preference in signal input from one eye or the other. It is found that monocular deprivation in cats may cause the columns to degrade, and those columns serving the non-deprived eye become larger in size[12]. It is believed that the ocular dominance columns must play a role in binocular vision[13], although an opposite view speculates that they are merely by-products of development due to their absence in many squirrel monkeys[14].

1.1.1 The phenomenon of suppression

The concept of ocular dominance has been discussed in the literature for a long time[15]. The establishment of ocular dominance of one eye over the other is useful in determining the suitability of ocular "monovision" therapies, which require one eye to focus in different depth than the other. In this way, presbyopic individuals, who are unable to accommodate may use one eye to focus in the distance while the other eye is focussed for near. Typically this design is used with contact lens[16] and refractive surgery, Eye dominance in such cases is sometimes determined by alternating a plus 1.5 diopter lens in front of each eye, and the eye that best tolerates the blur (confirmed by visual acuity test) is taken as the non-dominant eye. Other times, sighting dominance tests such as Dolman's method or the Porta test are used. These tests determine the subject's preference to use one eye over the other--a phenomenon known as motor dominance. The motor dominance determined by sighting tests is not always consistent with sensory dominance, which is either determined by relative measure of visual sensitivity[17, 18], or by the relative persistence during binocular rivalry paradigms[16, 18-20]. The concept of sensory dominance places emphases on the unequal contribution of visual inputs from the two eyes, which makes it more difficult to be accurately assessed. The two eyes must be dissociated in order to measure their sensory suppression[21, 22]. For binocular normal individuals, they tend not to aware of any sensory imbalance under normal viewing conditions (where the eyes are not dissociated).

1.1.2 Rivalry, Permanent and Anisometropic Suppression

Psychophysical paradigms based on binocular rivalry are common tools to measure sensory dominance[23]. Suppression resulting from binocular rivalry can be induced when projecting two different targets simultaneously to the corresponding retina area in each eye. Binocular rivalry is often experienced when the two targets are comprised of spatial contours that cannot be fused into a single image[23, 24]. For example, a pair of orthogonally oriented contours often induces rivalry. If the observers fail to fuse the dissimilar targets to one single percept, then image fluctuations will be perceived reflecting an alternation of eye dominance and hence suppression. The brain receives ambiguous information at a given location of visual space, thus causing fluctuations between the different neural states[25]. When one eye is experiencing dominant phases, that eye tends to show normal visual sensitivity; but during suppressive phases, the visual sensitivity is attenuated and suppressed. This loss of visual functions during the suppressive phases during rivalry paradigms is termed the rivalry suppression[26].

Compared with rivalry suppression, permanent suppression (as the name suggests) is a more stable form of suppression, which does not cause alternation of dominance. It is induced when a contoured target with high contrast is presented to one eye, and a spatially homogenous image presented to the other eye. The eye that receives the contoured target tends to dominate. The classic "hole-in-the-hand" illusion is an example of permanent suppression. This illusion can be performed by placing a paper tube in front of one eye and then placing a hand approximately 3 inches in front of the other eye. When properly done, one should perceive a hole-in-the-hand illusion[27], as one eye (the eye covered by the hand) is being suppressed by the contoured target that is seen through the tube. In permanent suppression, one perceives a stable, single percept without experiencing fluctuations[24].

The third example of suppression is anisometropic suppression or suppression of blur. Anisometropic suppression can be produced by placing a defocusing lens over one eye[28, 29]. Anisometropia is a natural ocular disorder that occurs in early years of life when the refractive components develop unequally leading to unequal overall ocular powers (hence refractive errors) [30]. The difference of refractive error produces differences in both spatial frequency and contrast[31] of retinal images, which are then projected to the cortex. The spatial frequency attenuation is dependent on the degree of defocus[32]: The lower degrees of relative defocus caused by anisometropia only affects high spatial frequencies, but the attenuation extends to low spatial frequencies as the degree of anisometropia is increased. The resulting contrast differences in the two images may trigger an inhibitory mechanism that causes suppression[33].

All three forms of interocular suppression result in a decrease of sensitivity for detecting stimuli. One fundamental characteristic to the three types of suppression aforementioned is that the suppression zone does not encompass the entire visual field but are rather confined to small areas known as the "suppression scotomas". For example, permanent suppression is retinal locus-specific and only affects the retinal region that corresponds to the inducing stimuli viewed by the fixating eye[24]. In the case of anisometropic suppression, the size of the suppression scotomas depends on the relative degree of defocus, but it is also affected by the amount of fusional details[34]. In other words, less defocusing power is required to produce an equivalent size of suppression scotomas if a greater amount of detail is present in the fusional lock.

Permanent and rivalry suppression are both induced by dissimilar stimuli presented to the two eyes when dissociated. These processes were once considered a similar mechanism with different temporal characteristics[35]. However, studying the attenuation of sensitivity to gratings at different wavelengths suggests that there are differences in their associated mechanisms. Color studies show that the reduction of contrast sensitivity associated with permanent suppression is independent of the wavelength[24]. On the other hand, the attenuation caused by rivalry suppression is wavelength-dependent[36]. Rivalry suppression leads to more substantial attenuation in sensitivity for short wavelength stimuli compared with stimuli with middle and long wavelengths[36, 37].

Moreover, when attempting to induce permanent suppression by the aforementioned means, the severity of sensitivity loss depends on both the contrast and the spatial frequency (in cycles per degree) of the grating stimuli. On the contrary, the attenuation caused by rivalry suppression is much less dependent on the contrast and the spatial frequency of the rivalry-inducing stimuli[35, 38]. The different patterns suggest qualitatively different neural mechanisms that mediate the rivalry suppression and permanent suppression[24].

1.1.3 Strabismus and amblyopia

Strabismus is a disorder where the eyes are not properly aligned with each other. Strabismus may be a result from multiple factors including refractive, sensory, motor, or innervational causes[39]. However, most commonly it results during development in the early months and years of life and is not secondary to pathological causes. When viewing an object, only one eye is aligned to the object, while the other eye is most commonly misaligned about the vertical or horizontal axis or combinations of both. In rare cases, the misalignment can be about the line of sight (cyclotropia). Strabismus can be constant, which often leads to impaired binocular function including fusion and stereoacuity, and it can also be intermittent, where the misalignment is not always present. Further, strabismus can show either a unilateral pattern where one eye is constantly misaligned or an alternating pattern where the misalignment can vary between eyes. When the strabismus is constant and unilateral, typically amblyopia results in the eye that is constantly misaligned, thereby leading to a lack of clear imagery in the constantly turned eye. Amblyopia is less common in cases of alternating strabismus presumably due to the capacity of either eye to adopt fixation [2].

1.1.4 Suppression associated with strabismic amblyopia

In addition to amblyopia, suppression is commonly found among strabismic patients, which is believed to arise in order to avoid diplopia and confusion resulting from the misalignment[40]. There are still disagreements regarding the interactions, which may exist between amblyopia and suppression.[41, 42] One view suggests that suppression simply follows as a consequence of amblyopia as a way to further reduce the deficient input from the amblyopic eye. In other words, it is the monocular visual loss that causes the binocular disruption. An alternate view is just the opposite, which suggests that the suppression developed due to binocular disorders (such as strabismus) produces a chronic deterioration of vision which then leads to amblyopia. The former view provides theoretical support to the occlusion therapies commonly instigated for amblyopes, because occlusion therapies emphasize improving the monocular function of the amblyopic eye. Often times, the binocular vision is not restored as a consequence of correcting amblyopia[43]. The alternate view is supported by evidence of monocular acuity improvements of the amblyopic eye, following an anti-suppression therapy that reduced suppression and strengthened the binocular function[44]. This seems to suggest that amblyopia correction comes as a secondary benefit of suppression reduction.

Strabismic amblyopia demonstrates reduced spatial resolution and contrast sensitivity but is limited to confined areas[45]. The suppression scotomas found in strabismic patients vary in size and do not seem to be correlated to the squint angle[46]. Scotomas can be large enough to encompass both the fovea and the region corresponding to the fixation point of the deviating eye[47], or they also can be relatively reduced and cover only a small region at the fovea[48].

The similarities between strabismic amblyopic suppression and normal suppression lead to the speculations that they may share similar neural mechanism[36]. Some researchers believe that strabismic suppression is similar to permanent suppression due to the short temporal delay between stimuli presentation and perception, and their stable characteristics over time[24]. Some hypothesized that the suppression resulting from binocular rivalry and that from strabismus are related[26, 49], which is supported by Joosse et al.' works on visual evolved potentials (VEP) recordings [46]. However, an alternate view questions this hypothesis because strabismic suppression shows greater attenuation for stimuli with middle or long wavelengths, which is different from the pattern found in normal rivalry suppression.

1.1.5 The site of suppression

There are also numerous studies that attempt to understand the mechanisms of suppression by locating and isolating the neural site of suppression. One psychophysical study concluded that suppression from binocular rivalry occurred beyond the primary visual cortex but no later than V5/MT or its afferent target sites[50]. In another study, strabismic suppression is suggested to occur right at the site of spatial adaptation, which is believed to be within the visual cortex (V1)[51]. Although the psychophysical properties of suppression have been well documented, studies using newer imaging techniques have been conducted in an attempt to resolve the issue of where in the brain suppression occurs. For example, a recent fMRI study demonstrated the LGN's deficient responses in strabismic amblyopes[52]. This not only shows that the suppression mechanism may be more complicated than speculated; it also suggests the need to re-evaluate the current models of suppression.

1.2 BINOCULAR INTERACTION MODELS

1.2.1 Two stage model

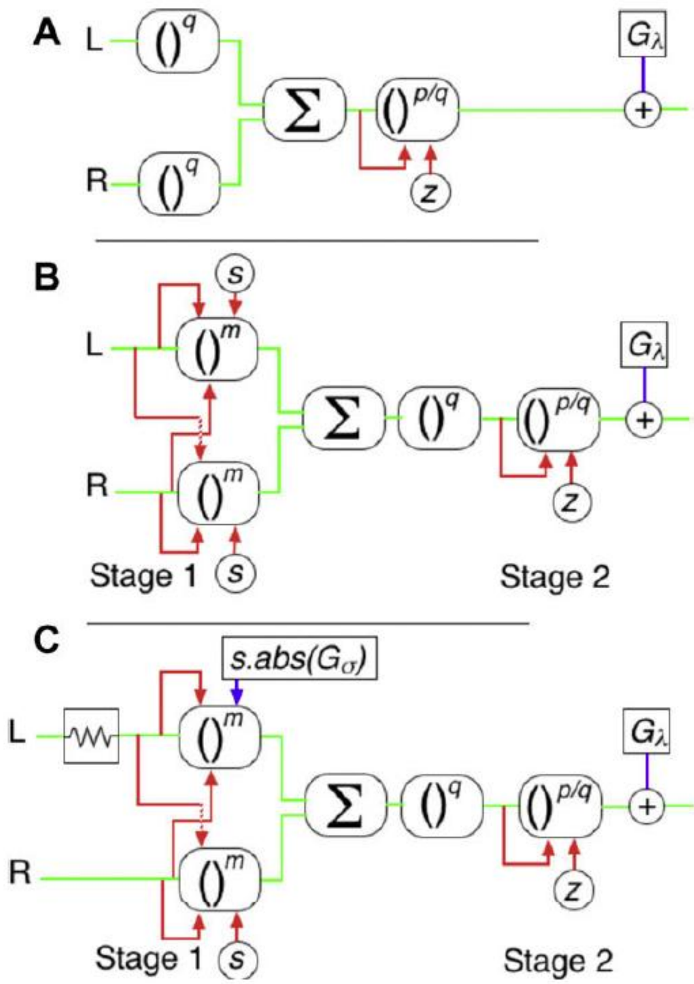
The understanding of suppression can benefit substantially from exploring the architecture of binocular interactions. Legge's early model[53, 54] on binocular contrast summation involved two monocular pathways that processed contrast inputs nonlinearly prior to binocular summation. Although Legge's model only involves excitatory pathways, it provides an excellent framework for further modifications. The two stage model proposed by Meese and colleagues is one of the many subsequent models to incorporate both the excitatory and inhibitory pathways[55]. It provides a better fit to dichoptic contrast matching and high levels of binocular summation. This model features an early stage where each eye receives a suppressive input from each other. The strength of the interocular suppressive drive, according to the model is contrast-dependent.

The neural site of the suppressive drive is not known with certainty. However, there is evidence[9, 56-58] that at least part of the inhibitory processes may occur at the LGN, a relay centre that receives information from the retina. On the other hand, the excitatory site is believed to be located in layer VI of the primary visual cortex [59].

1.2.2 The strabismic amblyopic model

To explore the binocular dysfunction of strabismic amblyopes, a strabismic model of binocular interaction was proposed[60] deriving from the aforementioned two-stage model. According to this model, the strabismic amblyopic eye has additional signal attenuation, more noise, and greater interocular suppressive drive from the fellow fixing eye[44, 60]. The binocular summation stage remains intact, but the imbalanced interocular suppressive drive is responsible for rendering the system functionally monocular. Figure 1-1 illustrates the three models discussed above (the figure was reproduced with permission from Mansouri et al. 2008[22]). As seen in Figure 1-1, the strabismic amblyopic version (Figure 1-1C) of the two-stage model differs from the intact version (Figure 1-1B) in three aspects, all of which occur prior to binocular summation (the second stage of the gain control). First, the amblyopic eye undergoes signal attenuation, which causes reduced contrast input. Second, the (contrast-dependent) interocular suppressive input toward the fellow fixing eye is reduced as a direct result of the reduced contrast input. Last, the amblyopic eye has additional multiplicative noise (Gσ), which contributes to the loss of the visual sensitivity of the amblyopic eye. However, it should be noted that the entire summation stage (Σ) remains intact for amblyopes according to the model.

Figure 1-1: Schematic illustration of three models of binocular interaction



(A) Legge's model, (B) the more recent Two-Stage Model (Messe et al. 2004), and (C) the model of strabismus amblyopia (Baker 2008) derived from model B. The bracket "( )" represents the contrast input to each eye. The green line indicates excitation and the red line indicates inhibition. Note that the strabismic amblyopic (Left) eye has additional signal attenuation, more multiplicative noise (Gσ), and greater interocular suppressive drive from the fellow fixing eye (Right). The second stage, or binocular summation stage (Σ), remains intact. (Figure reproduced from Mansouri et al. 2008[44] with permission.)

CHAPTER 2: BINOCULAR BALANCE IN NORMAL VISION AND ITS MODULATION BY MEAN LUMINANCE

2.1 INTRODUCTION

The current models of binocular vision involve inhibitory as well as excitatory connections[55]. Although the excitatory combination of the signals from the two eyes is well documented and thought to occur in the early layers of the primary visual cortex[59], the inhibitory circuit connected with binocular summation has only recently been appreciated by psychophysicists[61]. Evidence of inhibitory binocular interactions in the lateral geniculate nucleus (LGN) [8, 9, 62] and the cortex[63] has been reported. For a balanced binocular system that does not exhibit any sensory dominance, both the excitatory and inhibitory interocular influences must be in balance. Any imbalance will produce a sensory dominance that has potential clinical implications[64]. For example, the management of monovision associated with contact lenses, refractive and cataract surgery benefits considerably from the knowledge of sensory dominance[65-67], which is something that is not normally assessed in the clinic. Motor dominance, a concept similar to the handedness, is the preference to use a particular eye[68]. Motor dominance is commonly measured by sighting tests such as the Porta’s test and the Dolmen’s method. However, the motor dominance has been shown to be uncorrelated with sensory functions (visual acuity) or persistence in binocular rivalry[69]. Therefore, there is a need for an accurate assessment of sensory dominance for both scientific and clinic purposes.

Suppression associated with amblyopia is the end result of a severe imbalanced binocular system. There is an attenuation of the monocular pathway, and a resultant strong suppressive influence from the fellow fixing eye's input on that of the amblyopic eye. Mansouri and colleagues[56] proposed a psychophysical method with which to measure the degree of imbalance.

They used global motion stimuli in which signal elements moving in a coherent direction were presented to one eye, and noise elements moving in random directions were presented to the other eye. The signals and noises were switched between the eyes from trial to trial during the experiment. Thresholds were represented by the percentage of signal elements associated with correct identification of the signal elements' direction. By manipulating the interocular contrast, a balanced sensitivity on this motion task between the eyes could be achieved, suggesting that two eyes then make an equal contribution under the appropriate interocular contrast. Mansouri et al. proposed that the contrast ratio would be a good measure of the strength of imbalance, and they further advocated its application to quantify the degree of suppression for amblyopes.

If one views interocular dominance in normals as a mild version of suppression, then a similar approach could be taken to quantify the degree of sensory dominance in normals. Li and colleagues[64] applied an abbreviated version of aforementioned psychophysical experiment in a group of normal observers in order to measure their interocular dominance. They showed that the majority of the observers who exhibited mild interocular imbalance demonstrated variability across a range of clinical eye dominance tests (including Worth-4-Dot test, Bagolini test) as well as three sighting tests. On the other hand, there was a small fraction of their participants who exhibited a stronger interocular imbalance and showed a greater consistency with other dominance tests.

One limitation of Li and colleagues' application of the Random Dot Kinematograms (RDK) task to quantify sensory dominance is that they only used one contrast setting (i.e., a high contrast for both eyes). This was done to make the test convenient and practical in a clinical setting. However, the validity of the results depend upon the assumption that measurement of the dichoptic sensitivity ratio for stimuli of equal high contrast also applies to other stimuli of different contrast. As originally suggested by Mansouri et al.,[56] a more complete quantification of dominance should involve dichoptic motion threshold measurements under a range of unequal interocular contrasts at various levels.

This study was conducted with two specific aims. The first was to test the assumption that interocular contrast ratio can be used to quantify sensory dominance in the normal population. The second was to assess whether the balanced performance is susceptible to changes in interocular mean luminance, as well as changes in interocular contrast between the eyes. Since the effects of luminance generally occur at pre-cortical levels, this investigation would then explore whether the site of this balancing operation was cortical or pre-cortical[63]. For example, cells in the LGN do respond to changes in the mean light level as well as the contrast[63] and even though the input from each eye is kept separate in the laminar structure of the LGN, inhibitory interocular interactions have been reported between cells from different lamina [9, 57, 58, 62]. The balance between these subcortical signals may underlie sensory dominance.

2.2 METHODS

2.2.1 Participants

Twenty-five (25) naive observers, whose ages ranged from 19 to 36 years, were recruited from the School of Optometry, University of Waterloo. Informed consent was obtained before the tests, and the study was approved by the Office of Research Ethics (ORE 15,721) of University of Waterloo.

Before the experiments, each subject underwent a series of clinical tests to ensure that specific inclusion criteria were met. These criteria included normal vision with 20/20 or better for each eye after a subjective refraction; the absence of any binocular deficits (i.e., amblyopia); lack of oculomotor abnormalities such as strabismus; normal binocular vision as indicated by stereoacuity of <50 s of arc; and no history of ocular surgery.

Unilateral and alternate cover tests were performed to ensure the absence of strabismus, and the Modified-Thorington-Test (MTT) was used to measure phoria. Logmar visual acuity was assessed with Test Chart 2000 Pro (manufactured by Thomson Software Solutions, Hertfordshire, UK); and stereoacuity was measured with Randot Stereo graded circle test set at 40 cm.

Before the observers started the experiments, two sighting tests were performed to determine their dominance.

The Dolman method[70], also known as "The Hole-in-Card Test" required the observers to hold a card with both hands at about 40 cm from their eyes. They were instructed to align a target at 6 m through a hole in the card with both eyes open. The participants were asked to alternate one eye at a time, and the eye that remained aligning with the target is determined to be the motor dominant eye.

The Porta test [71], or "Point-a-Finger Test" required the observers to extend both arms and put one thumb over the other. They were then asked to align their thumbs to a 6m distant target with both eyes open. Motor dominance was determined by alternating one eye at a time to determine along which line of sight the thumbs were aligned with.

The two sighting tests demonstrated strong agreement between each other and they provide a crude binary estimate of dominance. The motor dominance information was to be used in the subsequent psychophysical experiment, where the contrast to the motor dominant eye was to be varied.

2.2.2 Apparatus

Stimuli were presented using a MacBook Pro laptop computer running Matlab (Mathworks, Natick, MA) and Psychophysics Toolbox, Version 3.19[72]. The stimuli were displayed using a Z800 duel pro head-mounted-display or HMD system (manufactured by eMagin Corporation, Hopewell Junction, NY). This HMD model contains two OLED screens, one for each eye. The screens have mean luminance of 50 cd/m^2, a linear luminance response profile (refer to appendix A for details) and refresh simultaneously at 60 Hz. The most important feature of this device is that it allows different stimuli to be presented to each eye. To achieve this dichoptic presentation, each frame of the dichoptic stimulus was computed as a single image with a resolution of 600 × 1600 (pixels). A Matrox DualHead2Go external video board was then used to split the target into two 800x600 targets, which were projected separately to OLED each screen. A photometer (LS-100 model, manufactured by Konica Minolta, Japan) was used to ensure equal luminance between the two screens.

2.2.3 Stimuli and Task

Stimuli were RDK based on those used by Mansouri et al.[56] discussed early in this chapter (Figure 2-1). In each trial, one eye was presented with a population of "signal" dots that all moved coherently in the same direction (left or right); while the other eye was presented with the "noise" dots that moved in random directions. When properly fused, the observers should perceive a mixture of signal and noise dot, and their objective was to indicate the direction of motion of the signal dots.

Each dot had a radius of 0.5 ° and moved at speed of 6 °/s. The dots had a limited lifetime whereby on any single frame each dot had a 5% chance of disappearing and reappearing in a new spatial position. Dots were presented within a circular display aperture with a radius of 11.1 °, which were framed by a solid black square fusional lock to aid fusion. To avoid interacting with the central dark fixation dot (radius 0.35 °), the stimulus dots were not programmed to enter the central region of the display aperture (radius 2 °). Dots that approached toward the central region disappeared and reappeared on the opposite side of the central area with the appropriate temporal delay to maintain a constant speed.

The total number of dots was fixed at a total of 100, while the percentage of signal dots (%) was varied with a specific psychophysical procedure. A motion coherence threshold was defined when the correct direction of the signal dots to be identified at a rate of 79% or better. The number of signal dots was varied on a trial-by-trial basis, and it was adjusted by a 3-down 1-up staircase procedure with a proportional step size of 50% before the first reversal and 25% thereafter. The starting point for each staircase was 100 signal dots and 0 noise dots. When dots were removed from the signal population, they were added to the noise population. Each staircase consisted of six reversals, and the last five reversals were averaged to determine the threshold. During each set of measurements, 10 staircases were randomly interleaved. This allowed the threshold measurements to be made at five contrast offsets between the two eyes with signal presented to either the dominant or non-dominant eye (based on clinical sighting tests). The contrast of the dots (see Weber's definition of contrast, Equation 2-1 below) in the non-dominant eye was fixed at a high level (80 %); while the contrast of the dots in the dominant eye was varied from 20 to 100%. Therefore, there were five interocular contrast ratios (0.25, 0.50, 0.75, 1.00, and 1.25) being tested. Each full set of measurements took approximately 20 min to complete, and the measurements were performed three times to ensure accurate thresholds were obtained. The data representing the interocular contrast as a function of the dichoptic performance was subjected to a linear fit (orthogonal linear regression) and the balance point derived from the contrast corresponding to the intersection of the linear fits to the data for the dominant and non-dominant eyes[19].

$$C_d = \frac{L_d - L_b}{L_b},$$

(Equation 2-1)

Weber's contrast: L_d and L_b represents the luminance of target dots and the background respectively.

Each participant was familiarized with the task using a demonstration program that is similar to the actual experiment. Once the participants were familiar with the task, the determination of their motion coherence thresholds began with two square frames presented separately to each eye with nonius lines next to the fixation marks. Using the arrow keys on the laptop keyboard, the participants could adjust the frame in the non-dominant eye to ensure that the images in the two eyes were perfectly aligned and properly fused. The participant then initiated the experiment by pressing any key on the keyboard. Once the test started, the left and right arrow keys were the only two keys functional to report the percept of the signal dot motion. The experiment was self-paced with each trial initiated 250 ms after the response to the preceding trial.

2.2.4 Rationale for the Balance Point Measurement

A signal/noise procedure was designed in order to determine when and to what extent information was being combined between the eyes. If the information was rigidly combined between the two eyes, then an obvious decrement in performance would result due to interference from the noise. The signal comprised a group of randomly placed dots all moving in the same direction. The subjects' task was to detect this motion direction. The noise consisted of spatially intermingled dots, each of which moved at the same speed but in random directions (Figure 2-1). The subject's task was to detect this motion direction. If the sensitivity for determining the signal direction was attenuated by the noise dots, then information must had been combined binocularly. In a perfectly balanced visual system (i.e., with no sensory dominance), thresholds for detection of signal dots would not depend on which eye sees the noise and which eye sees the signal. However, if there is an imbalance between the eyes, noise in the dominant eye would be more effective than seen through the non-dominant eye. The degree of imbalance could be quantified by varying the interocular contrast until a balanced performance resulted (i.e., equal thresholds between the eyes).

As stated earlier, one objective of this study was to test whether the sensory balance restored by manipulating contrast was susceptible to the changes of mean luminance. The use of neutral density filters (Kodak Wratten) placed in front of the non-dominant eye effectively reduced the mean luminance. The filter's optical density values varied from 1 (luminance reduction of a factor of 10) to 3 (reduction of a factor of 1000). The mean luminance of the OLED was 50 cd/m^2 so that in the most extreme case (i.e., 3 ND), the filter restricted vision to the upper mesopic level (0.05cd/m^2). Time was allocated for sufficient dark adaptation before testing; however, because the subjects' previous light exposure was restricted to moderate indoor lighting, this could be relatively short (approximately 5 min).

2.2.5 Statistical Procedures

The motion coherence thresholds of both the dominant and non-dominant eye as a function of the contrast shown to the dominant eye were subject to linear regression. The intersection of the two linear fits would determine the balance point. The threshold dominance ratios[64] were defined using only the thresholds for which both eyes were presented with the same contrast, and were calculated as follows:

$$\text{Dominance Ratio} = \frac{\text{nDE threshold} - \text{DE threshold}}{\text{nDE threshold} + \text{DE threshold}}$$

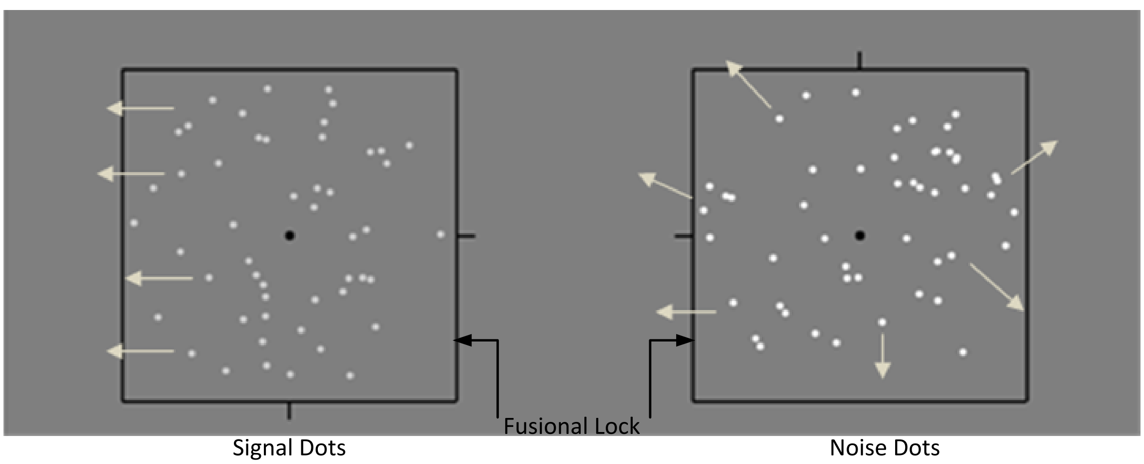
(Equation 2-2)

where nDE is the non-dominant eye, DE is the dominant eye (determined by sighting tests)

Therefore, 0 indicates no difference between the eyes, a positive value indicates a lower threshold for the dominant eye (i.e., better performance by the dominant eye) and a negative value indicates a lower threshold for the non-dominant eye.

One-Sample Kolmogorov-Smirnov Tests were used to test whether the balance point and the motion coherence threshold dominance ratio were normally distributed. If the distributions were shown to be normal, then t-tests were used to assess whether these measures differed from unity between the eyes. The motor dominance determined by sighting tests described above was then compared to the dominance defined from the motion coherence thresholds using a Pearson product moment correlation coefficient. The non-parametric Spearman rho test was used to assess the relationships between variables that did not meet the assumptions for parametric tests.

Figure 2-1: Example stimuli used for the dichoptic motion coherence threshold measurements



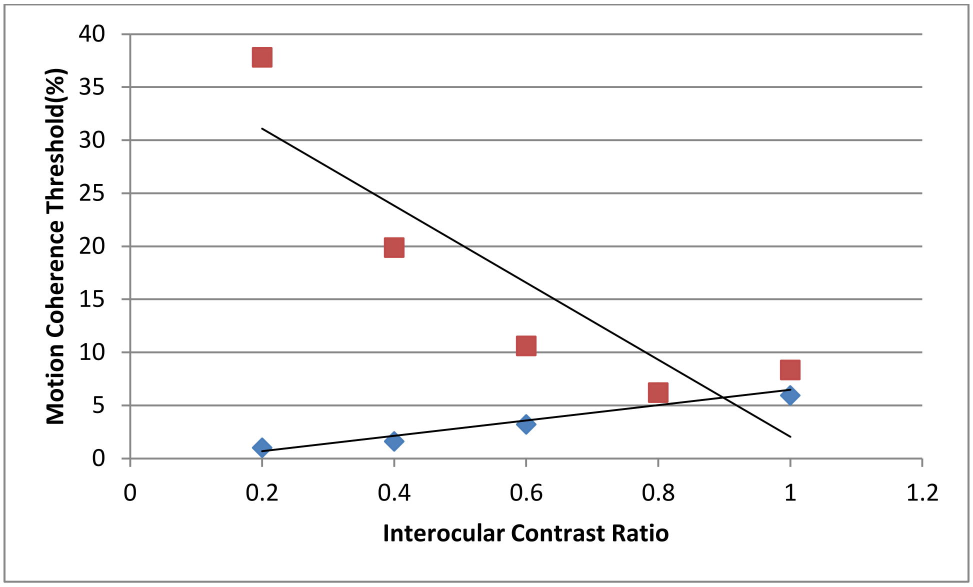
In this schematic representation, all the dots in the left eye are moving to the left, constitute the signal dot population. The dots in the right eye are moving in random directions, constitute the noise population. Facilitated by the fusional lock, the observers perceive a single, fused percept that consists of a mixture of signal and noise. Note that the contrast of the dots in the right eye is higher than that in the left eye.

2.3 RESULTS

2.3.1 Sensory Dominance Measurements

Figure 2-2 shows an example measurement of the balance point using the approach outlined in the previous section. Here, the motion coherence threshold (% signal elements) is plotted against the interocular contrast ratio. The contrast presented to the non-dominant eye (blue rhombus) remains fixed, whereas the contrast presented to the dominant eye (red square) varies from being the same as the contrast shown to the non-dominant eye (interocular contrast ratio of 1) to 20% of the contrast shown to the non-dominant eye (ratio of 0.2). In this case, as the interocular contrast ratio decreases, the threshold of the non-dominant eye decreases, and that of the dominant eye increases. Each data set has been fit with a linear function using orthogonal linear regression. The point of intersection represents the “balance point”, which is a specific interocular contrast ratio that represents equal sensitivity between the eyes. At the balance point, which for this participant was an interocular contrast ratio of 0.9, the contrast reduction of the dominant eye has neutralized its initial advantage (i.e., the sensory dominance). This result suggests that the right eye is the dominant eye and that the degree of dominance is equivalent to a contrast reduction or penalization of 10%.

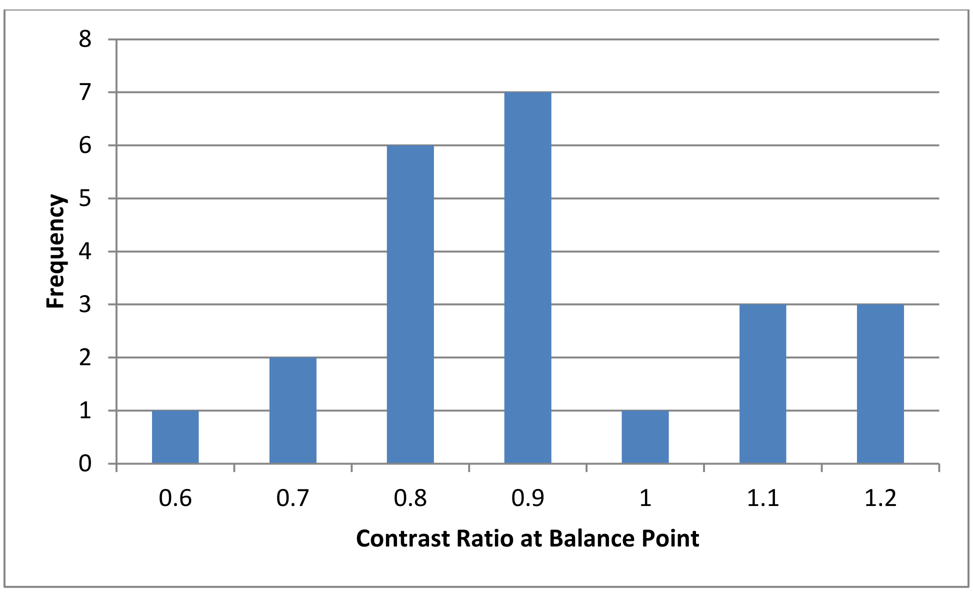
Figure 2-2: The dichoptic motion threshold as a function the interocular contrast ratio



Example data from a single participant illustrating the technique used to determine the balance point. The threshold is plotted against the interocular contrast. As the interocular contrast ratio decreases, the threshold of the non-dominant eye (blue rhombus) decreases, and that of the dominant eye (red square) increases. The balance point is determined from the intersection of the regression lines.

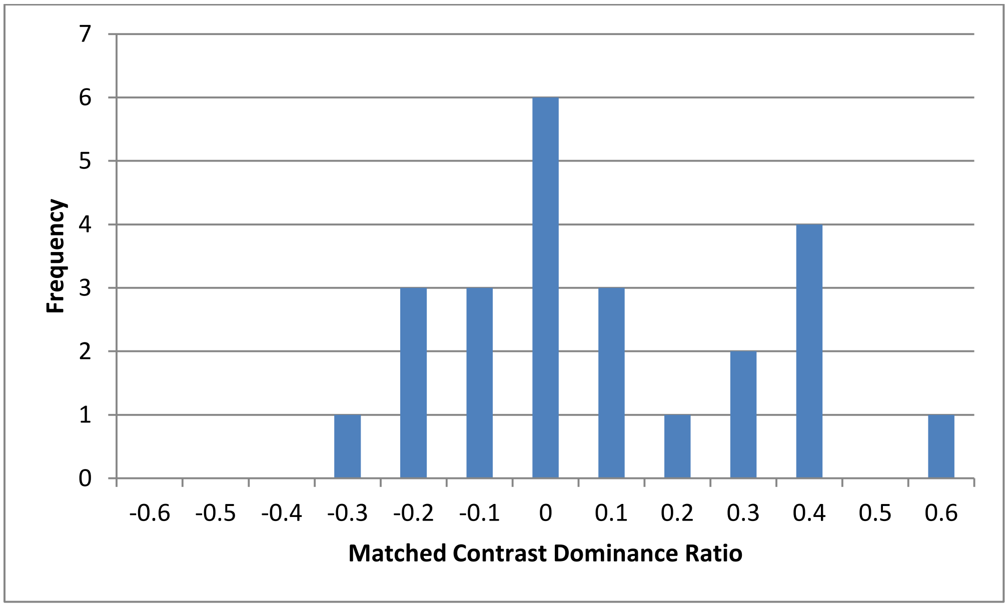
The first question addressed concerns the relationship between the dichoptic motion threshold measured in normals[64] and the interocular contrast ratio associated with balanced dichoptic performance (termed the "balance point"). The mean contrast ratio at the balance point was 0.88 (SD 0.18) indicating that, on average, the dominant eye required 88% of the contrast that was presented to the non-dominant eye to achieve dichoptically balanced motion coherence thresholds. $t_{df=23} = 3.4$, $p = 0.003$. When the two eyes were shown dots of equal contrast, the average threshold dominance ratio was 0.04 (SD, 0.22) indicating a slight, but non-significant ($p > 0.05$) bias toward the dominant eye. Therefore, observers with normal binocular vision had well-balanced interocular inhibitive drive for this global motion task. The distribution of contrast ratios at the balance point is shown in Figure 2-3. It is clear that most of the balance points are close to unity (i.e., value of 1), indicating a well-balanced interocular inhibition. The balance point of six participants exceeded 1, demonstrating the sensory dominance determined from this dichoptic motion coherence test does not agree with their motor dominance defined by the sighting tests. There were also three participants who demonstrated more pronounced sensory dominance between the two eyes with a balance point of 0.7 and below, suggesting a stronger imbalance between the eyes in favor of the motor dominant eye. The distribution of the dominance ratios for motion coherence thresholds when the same contrast was shown to each eye is shown in Figure 2-4. Again, the distribution is bimodal with most participants showing balanced performance between the eyes and a minority of participants showing a stronger imbalance in favor of the dominant eye. There was a significant correlation between the contrast ratios at the balance point and the motion coherence dominance ratios when both eyes saw the same contrast ($r = -0.79$, $p < 0.001$; $n = 24$, Figure 2-4), indicating good agreement between these two measures of interocular suppression. The pattern of eye dominance whereby most observers have weak dominance with a minority exhibiting more pronounced dominance is consistent with previous reports[16, 20, 64, 73].

Figure 2-3: The distribution of the balance points



A value of 1 indicates a perfect balance between the eyes whereby the same contrast was required by both eyes for matched dichoptic motion coherence thresholds. A value <1 indicates that the dominant eye required less contrast than the non-dominant eye and a value of >1 indicates that the dominant eye required more contrast than the non-dominant eye.

Figure 2-4: The distribution of threshold dominance ratios



A dominance ratio of 0 indicates balanced performance between the two eyes. A positive dominance ratio indicates that the dominant eye thresholds were lower than the non-dominant eye thresholds (i.e., less signal dots were required when the noise was presented to the non-dominant eye than when the noise was presented to the dominant eye). Negative dominance ratios indicate the opposite relationship.

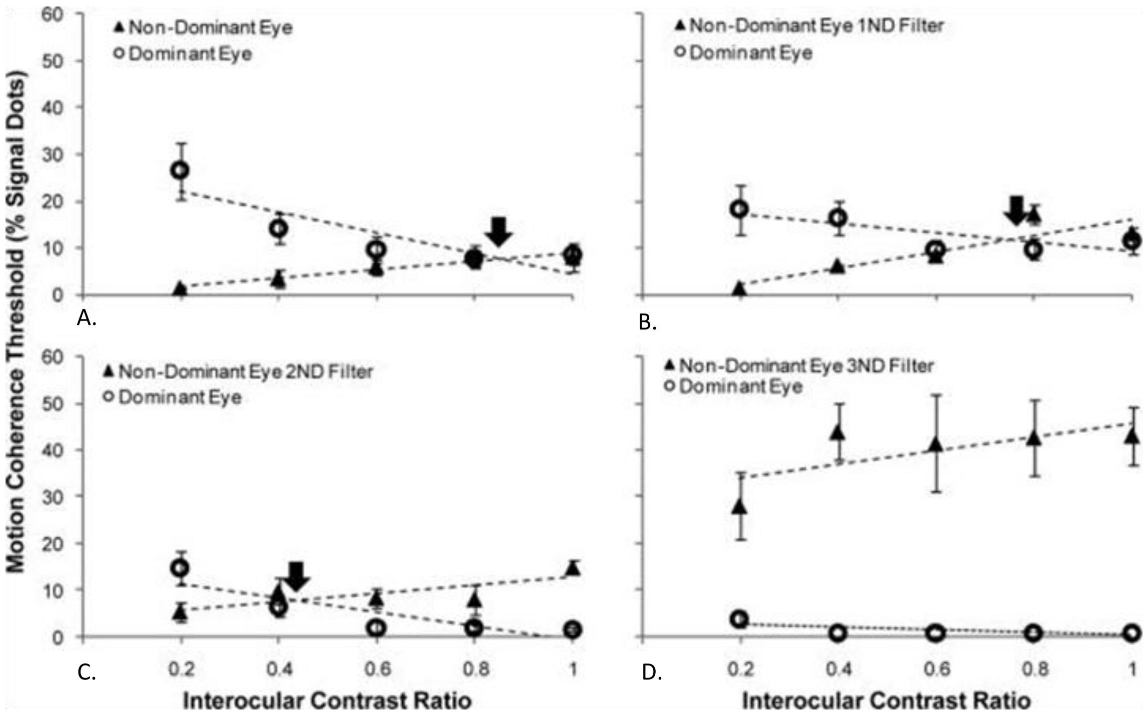
When the stimuli were shown to each eye at the same contrast, the mean motion coherence thresholds, in % signal dots, were 21.1 (SD, 9.6) and 18.6 (SD, 8.1) for the dominant and non-dominant eyes, respectively. The average motion coherence threshold at the balance point was 20.0 (SD, 7.0). As would be expected for a population with normal binocular visual function, no correlation was found between the balance point and interocular acuity difference or the type or magnitude of any phoria.

2.3.2 Effects of luminance reduction

The second question concerns the possible site (or locus along the visual pathway) of the suppressive effects demonstrated in the present study. In particular, I wonder whether the severe suppression one sees in amblyopia could be simulated by reducing the mean luminance to one eye. This was done by neutral density (ND) filters, which could reduce the mean luminance without affecting the contrast. Because cells in the visual cortex are relatively unresponsive to sustained changes in mean luminance compared with their counterparts in the LGN[8], such a simulation would be relevant to potential geniculate involvement in the inhibitory circuit.

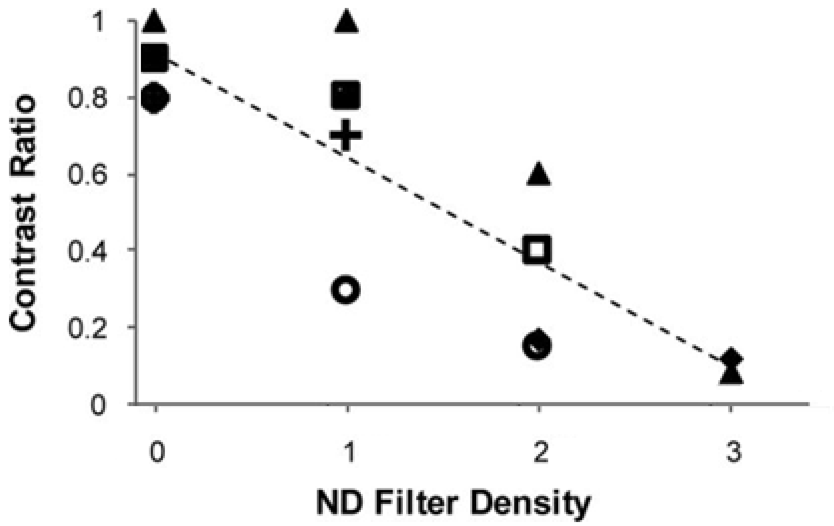
The strong interocular imbalance reported for observers with amblyopia[56, 74, 75]was simulated using the neutral density filter technique in a subset of the observers with normal binocular function. The example simulation results of one observer are shown in Figure 2-5, where the motion coherence threshold for both eyes is plotted as a function of the interocular contrast ratio. Linear fits using orthogonal linear regression were then made for each dataset and the intersection of the fits is the balance point, at which equal performance was achieved between the two eyes. Figure 2-5A shows the thresholds for this participant without any ND filter placing in front of the non-dominant eye. Under these conditions, there is a normal balance between the two eyes. The effects of luminance reduction were demonstrated in Figure 2-5 B-D. The observers' thresholds were measured at the presence of ND filters with various optical density powers (1-3). It is clear that there is a leftward shift of balance point, and the linear fits no longer converge within the range of interocular contrasts provided. This pattern of results is indicative of a gradual increase in the imbalance between the two eyes. Similar results were collected for a group of five normal observers in which the balance point was derived with a series of neutral density filters (0, 1, 2, and 3 optical density) fit in front of the non-dominant eye. These neutral density filter results for a group of normal participants are shown in Figure 2-6.

Figure 2-5: The measurement of balance point as a function optical density



The motion coherence threshold (% signal dots) of the dominant eye (triangle) and non-dominant eye (open circle) is plotted against the interocular contrast ratio. Each data set is fit with a linear function. The contrast corresponding to the intersection of these linear functions represents the balance point. As the optical density power of the neutral density filter increases (from 1 to 3), the balance point is progressively displaced to lower contrasts.

Figure 2-6: Balance point as a function optical density



The interocular contrast ratio corresponding to the balance point (Figure 2-6) is plotted against the optical density of the ND filter (log units). As shown in the individual example in Figure 2-6, results for the group of five subjects show a similar displacement to lower contrast ratios as the value of the neutral density filter increases. The dashed line is the best linear fit.

Figure 2-7 shows how the interocular contrast ratio (corresponding to balanced dichoptic performance) varies with the magnitude of mean luminance reduction (over a range of 3 log units or from 1/10 to 1/1000) in the non-dominant eye. There is an orderly reduction in the contrast of the stimuli seen by the dominant eye required to balance the suppressive effects induced by the reduced mean luminance in the non-dominant eye. In other words, a change in interocular mean luminance can cause strong interocular suppressive effects, similar to that previously reported in amblyopia[56].

2.4 DISCUSSION

Ocular dominance is a measure that is useful in determining the suitability of ocular "monovision" therapies, which require one eye to be focused at different depth than the other. This is often the case for contact lens[16] and refractive surgery correction in presbyopia[67, 76], and for cataract surgery[20]. Eye dominance in such cases is sometimes determined by alternating a plus 1.5 dioptre lens in front of each eye, and the eye that tolerates the blur better is taken as the non-dominant eye. Other times, motor dominance tests such as Dolman's method or Porta test are used. The basis of these tests is not well understood, as sensory dominance correlates poorly with motor dominance[16, 18, 20, 69], and monocular visual sensitivity[69]. Li et al.[64] sought an explanation for the inconsistency based on a recently proposed model of binocular combination[55], which incorporates both inhibitory and excitatory interactions. In particular, Li et al. wondered whether ocular dominance is determined by the extent to which the contralateral inhibitory signals are balanced, and they provided support for this proposition in terms of the dichoptic sensitivity ratio using a motion coherence task. They found a strong correlation between their brief version of the coherence motion test and a more traditional clinical test for sensory dominance and went on to show that the normal population is composed of two overlapping dominance groups, whereby the majority of participants (61%) showed weak dominance, but a significant minority (39%) showed strong dominance. Their conclusion however, was based only on thresholds with stimuli of equal contrast, as the measurements were optimized for clinical utility. To provide a more complete test of this novel idea and a more complete picture of the role that interocular inhibitory interactions may play in eye dominance, both the balance point (i.e., the contrast ratio at which the dichoptic coherence ratio is at unity[56]), as well as the thresholds at matched high contrast, were measured in a group of binocularly normal individuals. A significant correlation between these two measures was found, thus providing further support for the existence of two dominance distributions in the normal population. This was characterized by the majority of subjects exhibiting balanced or weak dominance and a minority exhibiting strong dominance. Knowing the strength of sensory dominance has potential clinical value though at present its measurement is not part of standard clinical practice.

Since dominance cannot be predicted solely on the basis of monocular sensitivity[69], the site along the visual pathway at which eye dominance emerges must be at a stage where neurons receive binocular input. The striate cortex and in particular, layer 4 is where binocular combination first takes place, which makes it an obvious candidate. However, the role of the LGN cannot be discounted because there are reports of inhibitory binocular interactions between cells from right and left eye laminae[9, 57, 58, 62], and also because the feedback from layer 6 of the striate cortex to the geniculate is known to affect both right and left eye inputs[77]. One striking difference between cells in the LGN and cortex relates to their response to the mean light level. Geniculate cells having a high-resting level are very responsive to sustained changes in mean luminance, whereas cortical cells have virtually no resting level [63]and are not sensitive to changes in mean luminance. The question that needs to be answered is whether changes in the mean interocular light level could affect the dominance when the interocular contrast was maintained. If dominance was exclusively cortical, one would not expect such a manipulation of stimuli luminance to have much effect; however, if dominance also involved the LGN, the mean luminance differences between the eyes could well modulate the balance point. It was found in the present study, changes in mean luminance (where stimulus contrast is unaltered) do systematically affect the measurement of the balance point and hence the estimation of dominance; the larger the interocular ratio of mean luminance, the greater the change in dominance. This is also the case for suppression in strabismic amblyopia where changes in mean luminance and contrast have been linked to the suppressed function[78]. One might hypothesize that in normal observers, although the excitatory combination of left and right eye input takes place in the cortex, the inhibitory contralateral effects may occur at the level the LGN.

CHAPTER 3: QUANTIFYING SUPPRESSION IN STRABISMIC AMBLYOPIA AND EVALUATING THE EFFECTS OF INTEROCULAR LUMINANCE

3.1 INTRODUCTION

In the previous chapter, the sensory dominance in a group of normal binocular individuals was successfully quantified by a global motion task. The stimuli were random dot kinematograms that consist of both "noise" and "signal" elements, which were presented dichoptically to measure the each eye's sensitivity to global motion stimuli. The interocular contrast of the stimuli seen by the two eyes (see Figure 2-1) was varied until a balanced sensitivity was reached between the eyes. The interocular contrast ratio at which a perceptual balance occurs is used as a measure of suppression.

Based on the two-stage model of binocular interaction proposed by Meese and colleagues[55], the strength of interocular suppression that takes place prior to binocular summation is contrast-dependent[55]. This lays a foundation for the measurement of the "balance point" by inducing a difference of contrast between the eyes. As reported in chapter 2, the dichoptic motion threshold of both the dominant and non-dominant eye is strongly correlated with the interocular contrast ratio.

Compared with the mild imbalance typically observed in participants with normal binocular vision, people with amblyopia exhibit more severe interocular suppression[60]. Amblyopia is a binocular disorder with attenuation of monocular visual sensitivity that is not due to refractive error, ocular/neurologic disease, or structural abnormalities in the visual pathways[79]. One of the conventional clinical criterions for amblyopia diagnosis is a two-line difference in visual acuity between the eyes[80]. Amblyopia is commonly associated with refractive error differences (anisometropia), visual deprivation (cataract), or oculomotor disorders (strabismus)[81].

Although it is generally agreed that suppression plays important roles in amblyopia[82, 83], the relationship between amblyopia and suppression is unresolved[41, 42]. Some suggests that suppression follows as a consequence of amblyopia as a way to ensure that the amblyopic eye does not disrupt binocular visual perception[41]. An opposite view argues that amblyopic monocular loss is the result of suppression, and it claims that the loss is reversible by reducing suppression via psychophysical training[74, 84]. If the latter view is correct, then amblyopia treatment should be initially directed to the restoration of binocular function[19, 74, 75]. This could have strong therapeutic benefits, as procedures such as patching could be avoided. Here in the present study, the suppression quantification paradigm described in chapter 2 was applied to a group of strabismic amblyopes to investigate the relationship between the sensory suppression and the depth of their amblyopia.

In chapter 2, it was found that reducing the mean luminance by ND filters systematically affects the balance point determination. For the normal observers, ND filters shift the balance point progressively leftward, creating strong binocular imbalance that resemble those from the strabismic amblyopic observers (Figure 2-6). In other words, if the mean luminance of stimuli seen by one eye is reduced, additional increase to the contrast to this eye is needed in order to achieve an interocular balance, despite the fact that ND filters do not alter the image contrast. The observed influence of the mean luminance on the balance point determination may be due to the inhibitory binocular interactions that are hypothesized to occur at the LGN[85]. This hypothesis was suggested by findings that the cells in the LGN are responsive to a sustained change of luminance level, whereas cortical cells are not sensitive to changes in mean luminance[63].

The influence of the interocular differences in luminance on binocularity was explored by a newly designed global motion test where the interocular luminance (rather than interocular contrast) was varied. The mean luminance of the image seen by one eye was manipulated and changed from trial to trial, while the luminance seen by the other eye was maintained constant throughout the entire session. This means that the threshold for global motion could be measured under a range of interocular luminance ratios, while maintaining equal and constant contrast between the eyes. The question that this study will address is whether a measure of suppression could be obtained by manipulating the interocular luminance (with interocular contrast fixed) as have previously shown in the preceding chapter for interocular contrast. The successful simulations of severe suppression by ND filters in chapter 2 suggest that this might be possible.

In the present study, this newly designed test was applied to a group of strabismic amblyopic observers, as well as a group of normal observers. Would interocular luminance provide a measure of interocular suppression in the absence of contrast variation? If the threshold of the eyes reached an equal level at a particular interocular luminance ratio, then it would provide an alternative measure of the degree of suppression. Furthermore, it would implicate the potential roles of the LGN's inhibitory pathway in providing the greater interocular suppressive drive from the fellow fixing eye. The inhibitory connection may occur prior to binocular summation as suggested by the strabismic model of binocular interaction by Baker's and colleagues[60]. Alternatively, if luminance variations are not successful in providing balanced interocular performance we are left to conclude that contrast is uniquely important in this regard.

3.2 METHODS

3.2.1 Participants

Ten (10) strabismic amblyopic observers (refer to table 3-1, for their clinical details) whose ages ranged from 21 to 45 years, were recruited from the School of Optometry, University of Waterloo. Five (5) normal binocular observers were recruited to the control group for comparison purposes. Informed consent was obtained from all participants before the experiment, and the study was approved by the Office of Research Ethics (ORE 15721) of University of Waterloo.

Prior to the experiments, each subject underwent a series of clinical tests to ensure the inclusion criteria were met. For the amblyopic group, the inclusion criteria specifically included the followings: 1) amblyopia with unilateral constant strabismus with squint angle of less than 15 degree ($<30\Delta$); 2) two or more lines of visual acuity difference between the eyes (with subjective refraction); and 3) no history of ocular surgery or other neurological diseases.

The inclusion criteria for the control group were consistent with those described in chapter 2, which included the following: normal vision with 20/20 or better after a subjective refraction; the absence of any binocular deficits; lack of oculomotor abnormalities such as strabismus; normal binocular vision as indicated by stereoacuity of <50 s of arc; and no history of ocular surgery. Unilateral and alternate cover tests were performed to ensure the absence of strabismus, and the Modified-thorington-test (MTT) was used to measure the phoria of normal observers. Visual acuity was assessed by Test Chart 2000 Pro (manufactured by Thomson Software Solutions, Hertfordshire, UK) on LogMAR scale, and stereoacuity was measured with Randot Stereo graded circle test set at 40 cm.

Table 3-1: The clinical details for ten amblyopic observers including identifier, age, strabismus, refraction, visual acuity, cover test results, stereo acuity, and patching history.

Observer ID	Age	Type	Refraction			Acuity (OD OS)	Strabismus	Stereo (sec of arc)	History
YP	40	RE Strab	+4.5DS	-0.75	135	20/126	ET +2Δ	200	Not patched
			+0.5DS			20/25			
TR	21		+0.5DS	-1.25	90	20/20	ET +14Δ	Gross	patched
		LE Strab		-1	75	20/40			
SA	28		-2.5DS	-1.25	180	20/15	ET +10Δ	Gross	patched
		LE Strab	+0.5DS	-1.5	180	20/30			
MA	25	RE Strab	N/A			20/126	ET +6Δ	200	Not patched
						20/25			
SM	21		N/A			20/20	ET +2Δ	None	patched
		LE microtropia				20/70			
AM	22		+0.5DS	-0.5	180	20/20	ET + 3Δ	200	patched
		LE Strab	+2.5DS	-0.5	65	20/60			
LB	21	RE strab	plano			20/400	XT -22Δ	None	patched
			-4.5DS	-1	10	20/15			
CZ	26	RE strab	-1.25DS			20/40	ET +6Δ	Gross	not patched
			-1DS			20/20			
SS	20	RE microtropia	+1DS			20/100	ET	140	patched
			+1DS			20/20			
CP	45	RE strab	+1.25DS	-0.5	90	20/25	XT -30Δ	400	patched
			-0.5DS	-0.5	90	20/20			

Two sighting tests, the Dolman method[70] and the Porta Test[71], were performed on the observers from the control group to identify their motor dominance. The dominance information was used in the subsequent psychophysical experiments, where the contrast or mean luminance to the dominant eye was to be varied.

3.2.2 Apparatus

The apparatus used in the present study were the same as those used in chapter 2. Stimuli were presented using a laptop running Matlab (Mathworks, Natick, MA) and Psychophysics Toolbox (Version 3.19). The stimuli were displayed using a Z800 duel pro head-mounted display or HMD (manufactured by eMagin Corporation, Hopewell Junction, NY). This HMD system contains two OLED screens, one for each eye a refresh rate of 60 Hz. A Matrox DualHead2Go external video board split the 1600x600 resolution viewing target into two 800x600 targets, which were projected to each screen. A photometer (LS-100 model, manufactured by Konica Minolta, Japan) was used to ensure accurate luminance of the two screens.

3.2.3 Rationale

The rationale of measuring thresholds was described in chapter 2. A total of one hundred (100) dots were displayed via the two OLED screens of the HMD goggle device. In each trial, one eye was presented with a population of “signal” dots that all moved horizontally in one direction (left or right). The other eye was presented with the “noise” dots that moved in random directions. The task required the observers to identify the signal populations from the noise, and then to determine the direction of the signal’s motion. With the total number of dots (signal + noise) fixed at 100, the task difficulty was finely controlled by the number of signal elements. For example, a threshold of 30 indicates that the observer requires 30 signal dots to correctly determine the direction of the coherent stimuli.

The dichoptic motion coherence thresholds measurement required 79% correct performance. The number of signal dots was varied on a trial-by-trial basis using a three-down one-up staircase procedure (to counter balance the effects of guessing rate) with a proportional step size of 50% before the first reversal and 25% thereafter. Each staircase consisted of six reversals, and the last five reversals were averaged to estimate threshold. During each set of measurements, 10 staircases were randomly interleaved. The thresholds measured, which ranged from 100 to 1, indicated the minimum number of signal dots required to perceive the correct direction. The threshold measured using this approach was influenced by the interocular contrast ratio. And there is evidence that unequal interocular luminance may exert an effect on the balance point (Figure 2-6). As a result, the interocular contrast ratio and interocular luminance ratio were independently manipulated and served as the independent variables, which lead to the two following tests.

3.2.4 Test A: Contrast-defined Balance Point task

In Test A, the mean luminance of the both OLEDs was maintained at an equal level (80 cd/m^2) throughout the entire session. The stimulus contrast presented to the amblyopic eye was kept high at 80% (see Weber's definition of contrast, Equation 2-1), while the contrast to the fixing eye was varied from 100% to 20%. The dichoptic motion coherence threshold was measured under a range of interocular contrast ratios at five different levels: 1.25, 1.00, 0.75, 0.50, and 0.25. For the example illustration of the stimuli, see Figure 2-1 in chapter 2.

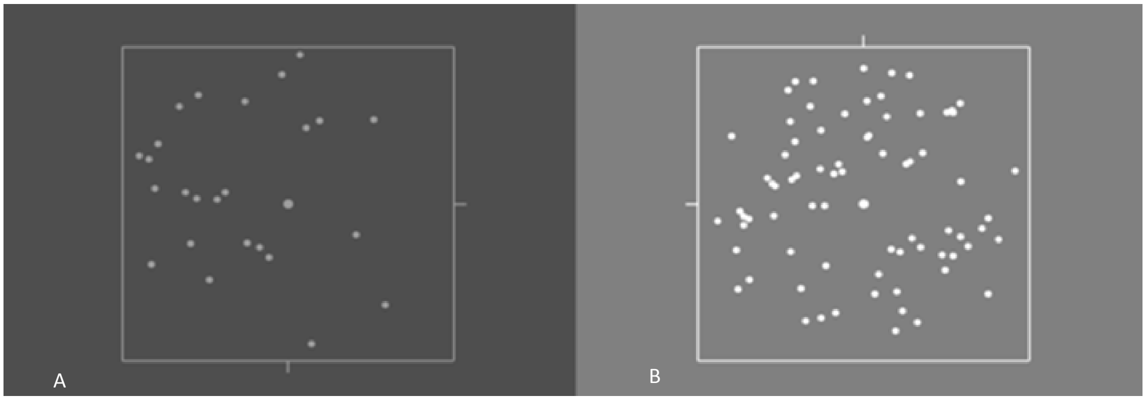
Each full set of measurements took approximately 20 minutes to complete. The dichoptic motion threshold as a function of the interocular contrast ratio was subjected to orthogonal linear regression. The intersection of the regression lines represented the “balance point”, which is the contrast ratio corresponding to equal sensitivity between the eyes. This test was already performed in a group of normal participants in chapter 2 and Figure 2-2 shows an example balance point determination. Here in the present study, test A was applied to the observers from the amblyopic group and the balance point determination followed the same rationale.

3.2.5 Test B: The luminance-defined Balance point task

The luminance-defined balance point task is modified from Test A by varying the interocular mean luminance rather than the interocular contrast. The rationale of the threshold measurements was identical to test A, which was outlined in detail in chapter 2. The mean luminance presented to the amblyopic eye was set to 103 (RGB unit, equivalent to 75 cd/m^2), whereas the luminance to the fellow-fixing eye varied from 28 to 128 (RGB unit, equivalent to 4 ~110 cd/m^2). Example stimuli presentation with luminance varying test is shown in Figure 3-1.

One session of test B typically comprises 500 individual trials, which takes 20 minutes to complete. The coherence motion thresholds of each eye under various luminance conditions were measured. Linear fit regressions to the thresholds were made, and the point where the two linear regressions intersected was taken as the balance point.

Figure 3-1: The stimuli used for dichoptic motion coherence threshold measurements of Test B.



In this schematic representation, the mean luminance seen by the right eye (B) is greater than that seen by the left eye (A). The interocular luminance ratio is varied throughout the study while the Weber contrast is fixed. Note that a fixation lock that comprises a squared shape frame and a dot in the centre is always present throughout the study.

The luminance is controlled by Matlab program with the flowing formula[86] (Equation 3-1):

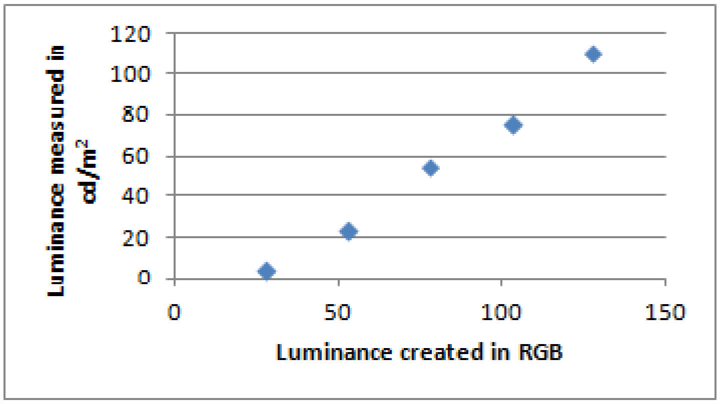
$$\text{Luminance in RGB} = 0.3\ \text{R} + 0.59\ \text{G} + 0.11\ \text{B}$$

(Equation 3-1)

Where R, G, B represent Red, Green, and Blue, respectively. The relationship between the actual luminance measured by photometer in cd/m^2 and the luminance in RGB is shown in Table 3-2.

Table 3-2: The relationship between the luminance settings in RGB unit simulated by Matlab and the corresponding grayscale luminance in cd/m^2 measured by a photometer

Luminance inRGB unit	Luminance measured in cd/m^2
128	110
103	75
78	54
53	23
28	4



3.3 RESULTS

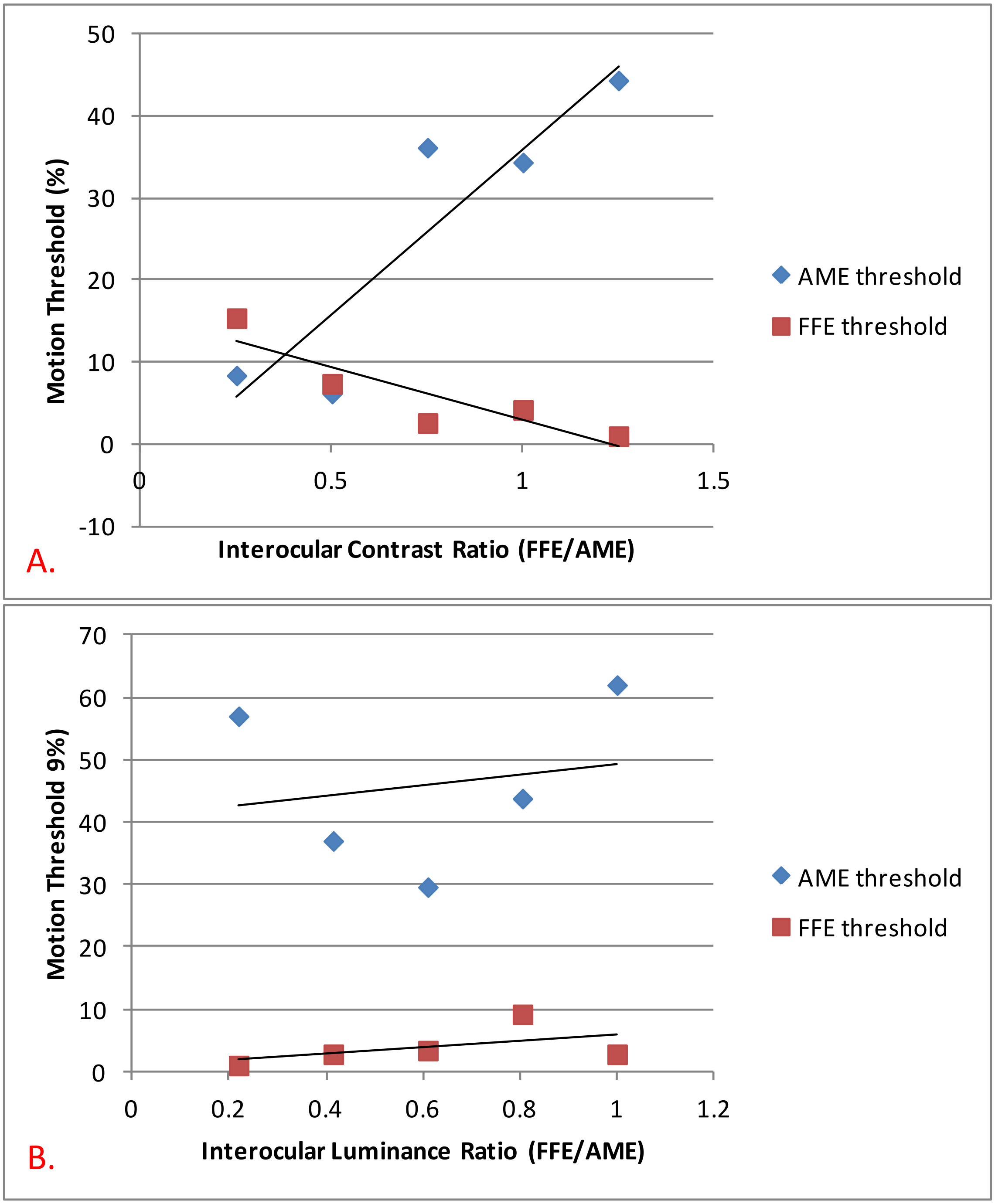
Ten (10) strabismic amblyopes successfully completed test A, and eight (8) of them managed to complete test B. The two tests were also conducted on five (5) binocular normal observers for comparison purposes.

Figure 3-2 shows an example observer's threshold measurements as a function of contrast (test A) and luminance (test B). In Figure 3-2A, the coherent motion threshold measured when signal elements were presented to the amblyopic eye (AME, shown by rhombus symbols) and when they were the fellow fixing eye (FFE, shown by square symbols) is plotted against the interocular contrast ratio. The intersection of the two linear regression lines defines the balance point, which measures the level of suppression.

Figure 3-2B shows the coherent motion thresholds of the two eyes measured relative to the interocular luminance ratio. The luminance presented to the amblyopic eye remains fixed to 103, whereas the luminance presented to the fellow fixing eye varies from 28 to 128. The horizontal axis represents the luminance ratio, which is defined by dividing the mean luminance presented to fellow fixing eye by the mean luminance presented to the fellow-fixing eye

(FFE/AME). Each dataset had been fit with a linear function. However, as shown in Figure 3-2b, the two regression lines did not intersect, showing that varying the interocular mean luminance did not result in the equal coherence motion sensitivity of the two eyes. As a result, no balance point could be obtained by varying the interocular luminance.

Figure 3-2: Example dichoptic motion threshold measurements of a single amblyopic observer (subject SM) obtained from test A and B



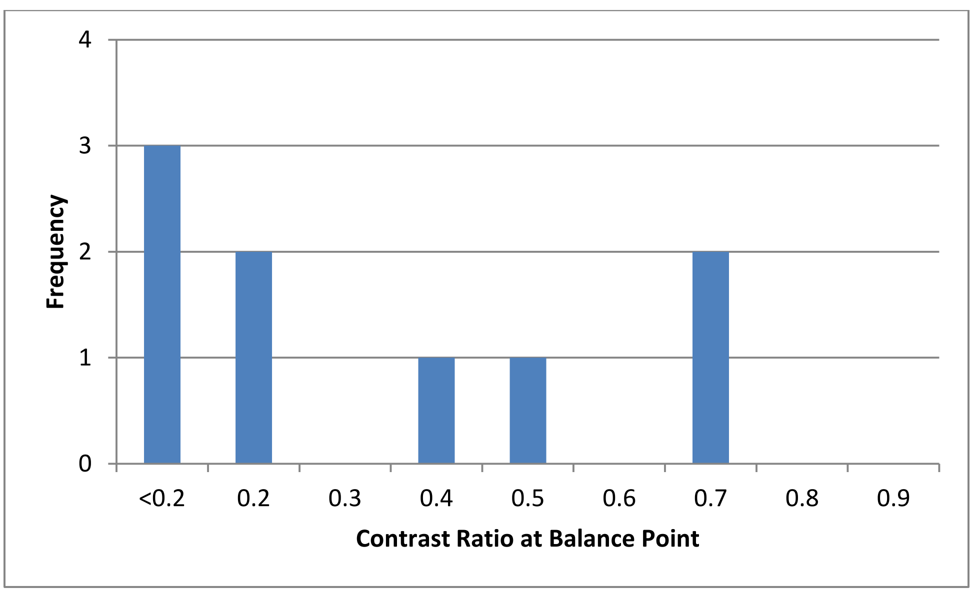
(A) Example results from test A where the interocular contrast is varied. The dichoptic motion threshold is plotted against the interocular contrast ratio, and the intersection of the regression lines represents the balance point. (B) Example results from test B where the interocular luminance is varied. The dichoptic motion threshold is plotted against the interocular mean luminance (FFE/AME). The regression lines do not intersect so that no balance point is obtained. Signal to the AME: rhombus symbols; signal to the fellow fixing eye: square symbols.

3.3.1 The distribution of balance points obtained from Test A

With only one exception (whose suppression was too strong to fall within the range tested), all other 9 observers from the amblyopic group successfully achieved a perceptual balance by varying the interocular contrast ratio. The distribution of the balance points defined by the interocular contrast ratio is shown in Figure 3-3.

The balance point distribution figure shows that the majority (7 out of 9) of the observers has a balance point less than 0.5, indicating that they needed the contrast to be reduced to at least 50% in the fellow fixing eye to reduce its suppressive drive over the amblyopic eye. Over half of the observers (5/9) demonstrated severe suppression, with the balance point equal or less than 0.2.

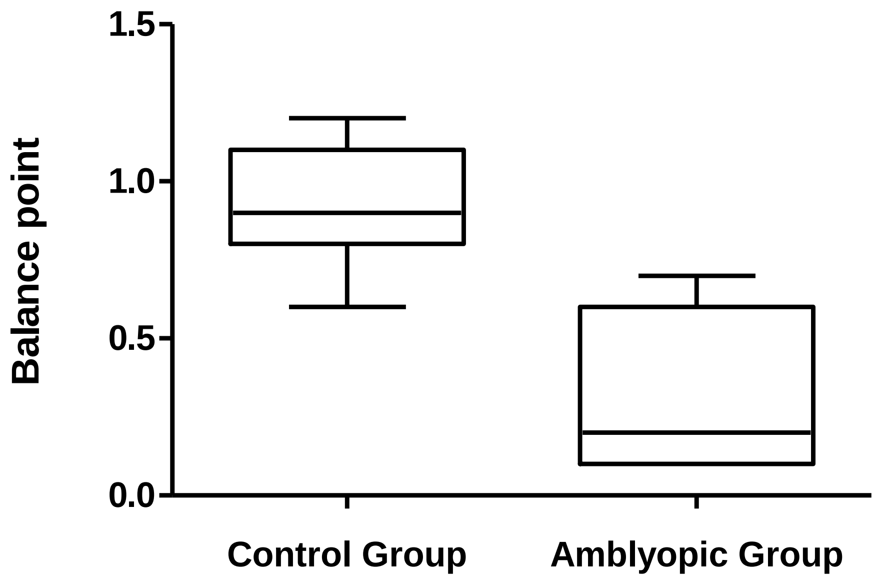
Figure 3-3: The distribution of the "balance points" of strabismic amblyopic observers obtained from Test A



Serving as a measure of interocular suppression, a balance point of 0.5 indicates that the fellow eye requires the contrast to be reduced to 50% in order to achieve perceptual balance.

Comparing with the sensory dominance of the normal group (Figure 2-3 of chapter 2), the suppression manifested by the amblyopic observers is much more severe. As shown in Figure 3-4, the mean balance point of the amblyopic group (M=0.33 SD 0.25) was significantly lower than that of the control observers (M = 0.91 SD 0.17) $t_{df=30}$ =7.610, $p<0.05$

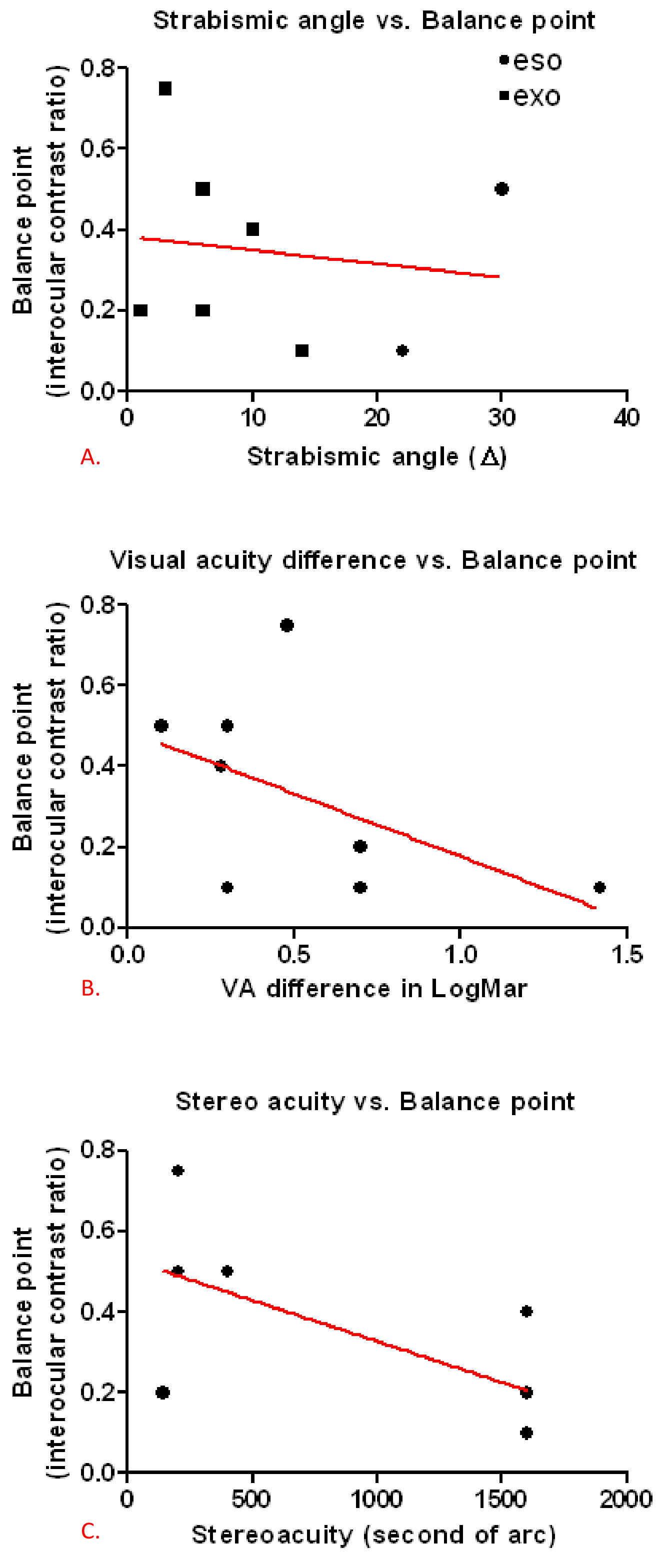
Figure 3-4: A comparison of the mean balance point between the control and the strabismic amblyopic group



The mean balance point of the control group (n=23) is significantly greater than that of the amblyopic group (n=9), suggesting greater suppression exhibited by the amblyopic observers. The box and whiskers plot compares the median of the two groups, where the central rectangle spans the first (25%) and third (75%) quartiles and the whiskers below and above show the minimum and maximum value of balance point.

Linear regression analysis (Figure 3-5) was performed to explore the possible correlation among the strength of suppression (i.e. balance point), the angle of deviation, visual acuity difference (in LogMAR scale), and stereo acuity. It was shown that the angle of deviation (F=0.13, P>0.05) was not correlated with the degree of suppression, thus suggesting a lack of relationship between sensory suppression and strabismic deviation. Although neither the visual acuity difference ($F=2.69$, $P=0.145$), nor the stereoacuity ($F = 4.208$, $P=0.086$) was statistically correlated with the balance point, a clear trend with negative slope could be found in both graphs. Despite the lack of statistical significance, the trend shows that greater sensory imbalance tends to be associated with greater VA difference and poorer stereoacuity. This is consistent with the previous report using a similar approach by Li and others[41], who demonstrated a significant positive correlation between the level of amblyopia and the degree of suppression.

Figure 3-5: The relationships between the balance point and strabismic angle, visual acuity difference or stereo acuity



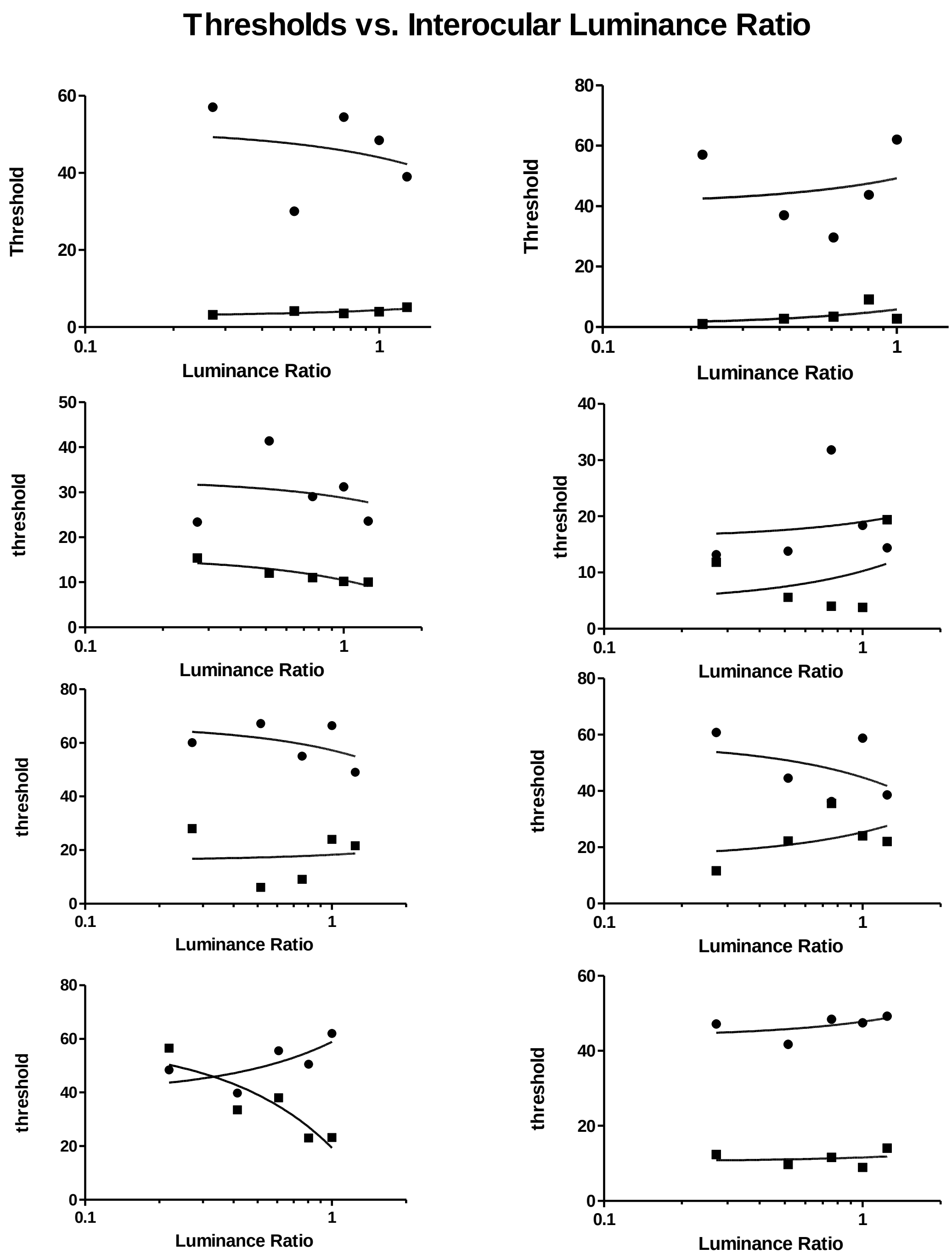
(A) The balance point plotted against the strabismic angle in prism dioptres; $F=0.13$, $P>0.05$ (B) The balance point plotted against visual acuity difference between the eyes in LogMAR scale; $F=2.69$, $P=0.145$, and (C) The balance point plotted against stereoacuity; $F = 4.208$, $P=0.086$. Each dataset is fit with a linear regression function. Despite the lack of statistical significance, the trend shows that greater sensory imbalance tends to associate with greater VA difference and poorer stereoacuity.

3.3.2 Luminance defined balance points Test

There are 8 amblyopic observers who completed test B with luminance being varied from 128 to 28 (RGB unit). As shown in Figure 3-6, the dichoptic motion threshold is plotted as a function of the interocular luminance ratio. There was no correlation found between the dichoptic motion threshold and the interocular luminance ratio. The vast majority demonstrated flat slopes, which indicated a lack of response to the mean luminance change.

T-tests revealed a significant difference between the mean AME's threshold (M=42 SD=13.7) and the FFE's threshold (M=11.5, SD=7.0). $t_{df=7}=5.607$, $p<0.05$ This means that during the luminance range adopted in the present study, the fellow fixing eye was always more sensitive to the motion stimuli than the amblyopic eye.

Figure 3-6: The coherence motion thresholds (vertical axis) of both amblyopic eye (closed circle) and fellow fixing eye (square), measured under various interocular luminance ratio (horizontal axis)



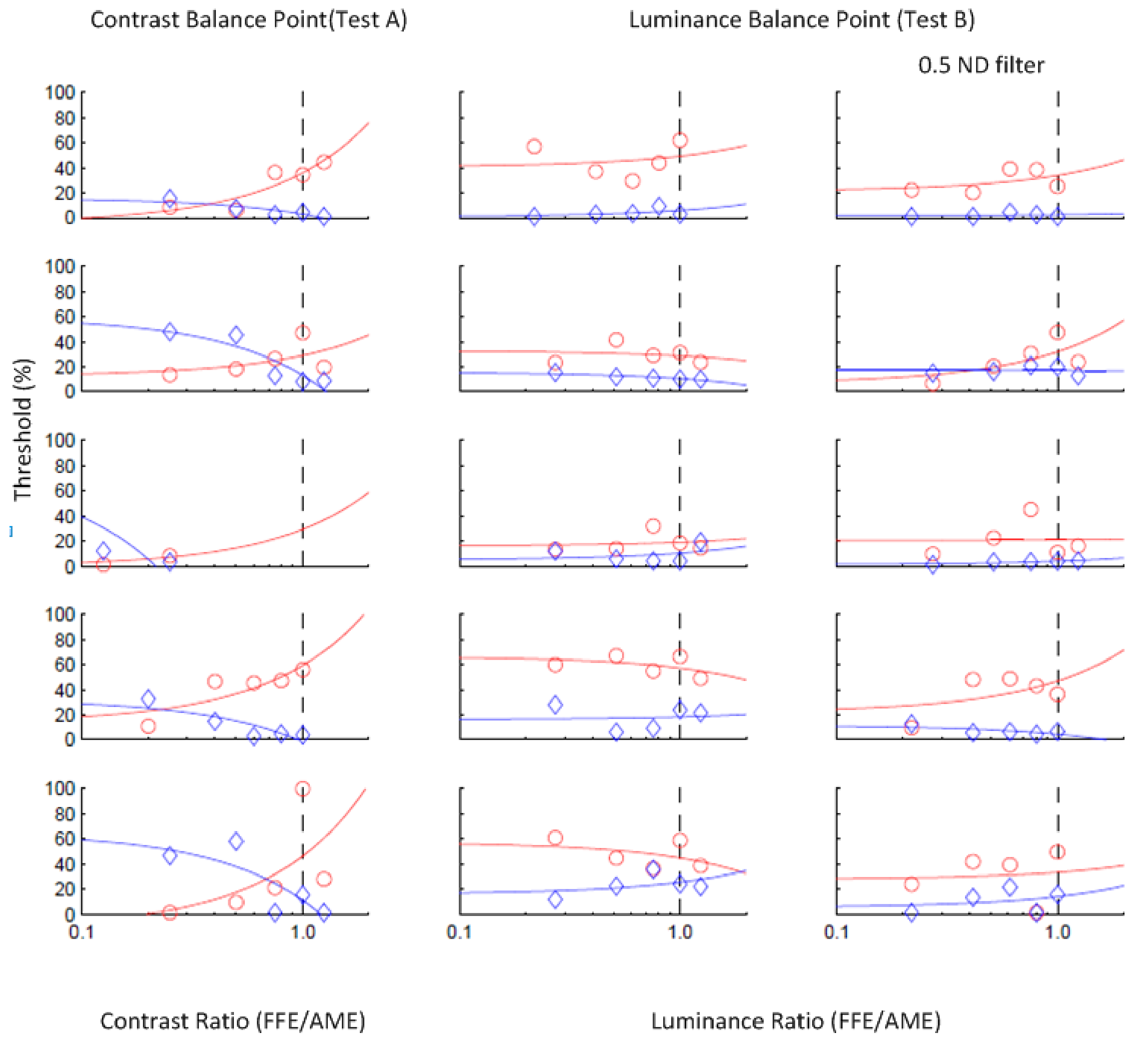
The horizontal axis represents the interocular luminance ratio displayed in log scale. The intersection is observed in only one subject (bottom left), and no balance point was obtained from the others. Square symbols: signal to the fixing eye; circle symbols: signal to the amblyopic eye.

3.3.2.1 Test B w/ ND 0.5: Extending the range of luminance

Unlike the interocular contrast that can be accurately and finely controlled, the luminance range displayed by HMD has limitations at the low end if the contrast is to be kept constant. This means that when controlled digitally, the luminance range is very limited. To overcome this limitation, an additional ND filter was placed over the fellow fixing eye to extend the luminance range over which the relative luminance could be controlled digitally without affecting the image contrast. As a result, a ND filter with an optical density of 0.5 (which reduces light transmission by 68%, to brightness of 35.2-1.28 cd/m^2) was placed over the fellow fixing eye to further reduce the luminance.

Five amblyopic observers were retested with this procedure that extended the luminance range. Thus, we could test whether the limitation of the luminance range was the cause for failure to define a balance point. During this measurement, an ND filter was placed over their fellow fixing eye. The results from Test A and Test B were paired up for comparison, and they are shown in Figure 3-7.

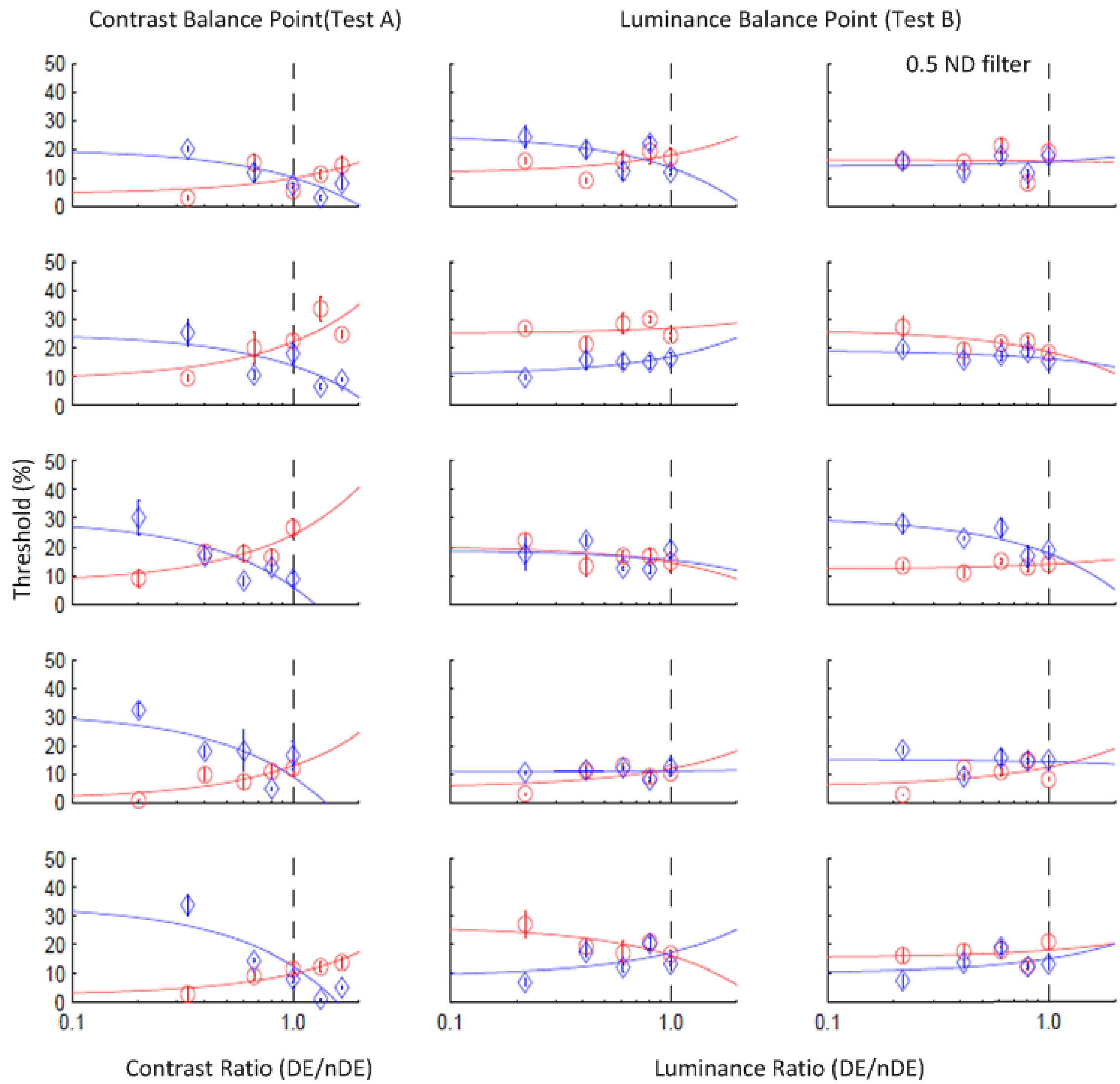
Figure 3-7: The measurement of the balance point of five amblyopic observers using test A (contrast-varying), test B (luminance varying), and test B with 0.5ND



The horizontal axis is in log scales. Rhombus symbols: signal to the fixing eye; circle symbols: signal to the amblyopic eye.

Five observers from the control group had their dichoptic motion thresholds determined from the three experiments aforementioned (Figure 3-8). Comparing with the amblyopic group, the thresholds determined between the eyes was much closer in observers with normal binocular vision. Unlike their amblyopic counterparts, two control observers demonstrate a visual balance as we altered the interocular luminance ratio. However, the presence of intersection may be artefactual as it could not be replicated using the 0.5 ND filter measurement.

Figure 3-8: The measurement of balance point of five normal observers obtained from the three types of psychophysics tests described: contrast (Test A), luminance (Test B), and luminance with ND filter from left to right

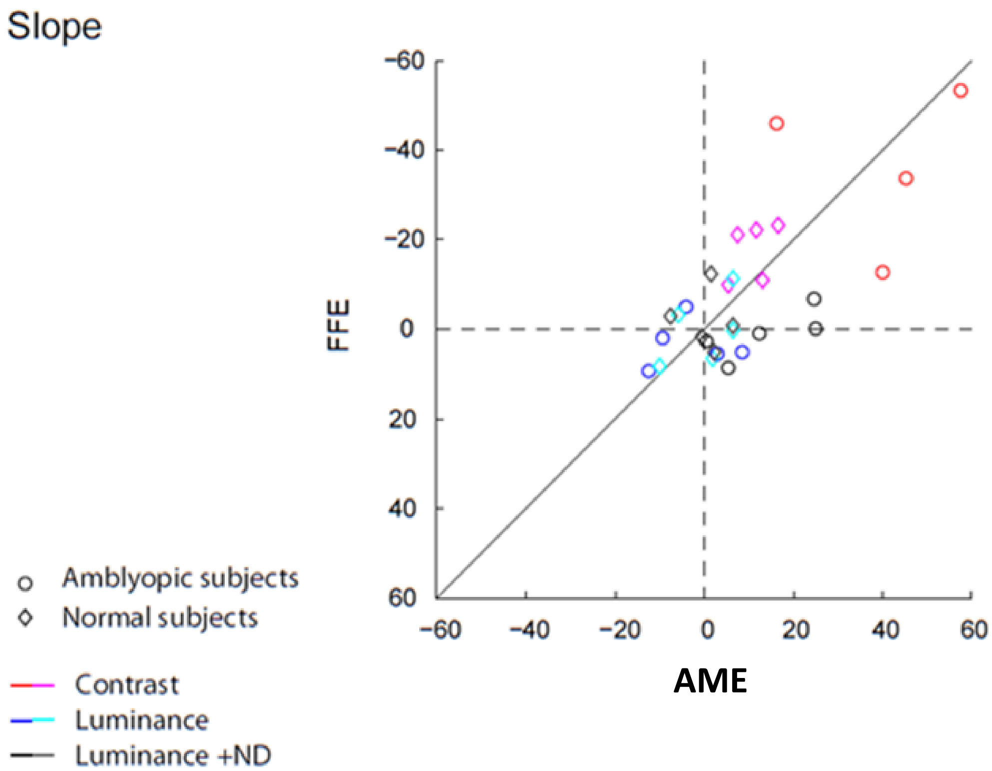


Rhombus symbols: motor dominant eye (DE); circle symbols: non-dominant eye (nDE).

3. 3.3 Correlation analysis

To explore the relationship between the dichoptic motion threshold and interocular contrast or luminance, the slopes obtained from different tests were analyzed. A slope represents the strength with which a particular variable (such as interocular contrast or interocular mean luminance) affects the thresholds. A steep slope represents a greater likelihood of an intersection occurring between the dichoptic motion threshold's regression lines. As one would expect, the example results seen in Figure 3-2 from an amblyopic observer yielded a high positive slope for the amblyopic eye and a high negative slope for the fellow eye. High magnitude of positive and negative slopes suggest that there will be an intersection of the linear regression, which means the sensory balance point can be defined within the testing range. If both slopes are flat and close to 0, then for the above reasons the absence of sensory balance is an inevitable consequence within the testing range. In Figure 3-9, the slope of linear regressions, fit from AME thresholds, is plotted on the horizontal axis, and the slope obtained from FFE thresholds of the same subject is plotted on the vertical axis. It can be seen that the data obtained from the interocular contrast manipulation are found mostly in the upper right quadrant, indicating positive slopes of AME thresholds and negative slopes for FFE thresholds. This is consistent with the observations that almost every observer (9 out 10) had their balance point determined within the tested contrast ratio range. On the contrary, the slopes of regressions obtained from the luminance experiments (test B), with or without ND filter, tend to cluster near the origin (0,0). The small magnitudes of best fit slopes of thresholds suggest the lack of responsiveness to the change of luminance. Consequently, a valid balance point cannot be obtained by varying the interocular mean luminance under these test conditions, which indicates that changing the luminance ratio is not a suitable approach to quantify suppression.

Figure 3-9: The scatter plot of the slopes obtained from the three types of balance point tests



Each point represents the results of AME thresholds (horizontal coordinate) and FFE thresholds (vertical coordinate) of one subject. This figure contains both amblyopic subjects and normal subjects who are represented by the circle and rhombus, respectively. The color indicates the test type at which the data were obtained (please refer to the electronic version).

Control group results

Results obtained from the subjects with normal vision revealed some degree of balance at a particular luminance ratio. Although a balance point was found in two out of five normal observers, the slope analysis (shown in Figure 3-9 and Figure 3-10) reveals poor fit of the linear model, indicating that there is little correlation between the luminance ratio and the threshold. In addition, normal observers tend to achieve a perceptual balance close to the natural viewing conditions (i.e., equal interocular luminance and contrast). The intersections found in the normal observers lack significance, as the thresholds of the two eyes were very close.

3.4 DISCUSSION

Presenting random dot kinematograms stimuli dichoptically can effectively measure one's motion thresholds[41, 44]. Inducing unequal contrasts to the eyes modulates the dichoptic motion thresholds in a predictable manner. In general, as the contrast to one eye is reduced, the dichoptic motion threshold of that eye increases while the threshold of the other eye decreases. The well correlated relationship between the interocular contrast ratio and the dichoptic motion threshold is consistent with the notion that interocular suppressive drive is contrast-dependent[44, 60]. Therefore, the interocular contrast ratio is a reliable measure to quantify the level of suppression.

3.4.1 The relationship among suppression, amblyopia, and strabismus

Here in the present study, the balance point test that measures suppression was applied to a group of strabismic amblyopic observers. Consistent with the previous application to quantify the sensory dominance of normal binocular observers, the dichoptic motion threshold of amblyopic observers is well correlated with the interocular contrast ratio. Using this technique, it appears that the suppression of strabismic amblyopes is significantly greater than that of the normal binocular subjects. The majority of the observers were shown to have a balance point less than 0.5, indicating that they need at least 50% contrast reduction to their fellow fixing eye to achieve a binocular sensory balance. This is explained by Baker et al.'s model[60] of binocular interaction for strabismic amblyopia. The model suggests that the amblyopic monocular pathway differs from a normal one in three ways; it exhibits additional signal attenuation, more noise, and greater interocular suppressive drive from fellow eye (For the illustration of the model, refer to

Figure 1-1). Additionally, the interocular suppressive drive is contrast dependent[60, 87], which means that reducing the image contrast presented to the fellow eye can reduce the suppressive drive to the amblyopic eye.

In an attempt to explore the relationship between suppression and the visual acuity difference and stereoacuity, linear analysis was conducted. Although not statistically significant (P value: 0.145 and 0.086 for VA and stereoacuity), it was found that greater suppression tends to be associated with greater VA differences and poorer stereoacuity. This trend is consistent with a previous report using a similar technique by Li and others[41], who demonstrated a significant positive correlation between amblyopia and suppression. Linear analysis also suggests that there is no relationship between the degree of strabismic deviation and the level of suppression. It appears that the strabismic deviation is not only unrelated to the size of suppression scotoma[46], it is also unrelated with strength of suppression-- a finding consistent with Li et al.'s recent results as well as many other literatures[41, 51, 82].

3.4.2 The effects of interocular mean luminance

More importantly, a modified version of the coherence motion task was described and tested in the present study. This test measures the thresholds when the eyes attempt to fuse two targets with unequal mean luminance. The novelty of this technique is that interocular mean luminance (rather than interocular contrast) is the independent variable. The aim of modifying the test was to evaluate the effects of unequal interocular luminance and to compare this technique with the balance point defined by interocular contrast.

Based on the results of 8 strabismic amblyopic observers, it was found that the magnitude of the slope (obtained from Test B) is very shallow, indicating a lack of response to the interocular luminance change.

The results from the control group show that the difference of sensitivity between the eyes is significantly lower than what is observed in the amblyopic group. This is not surprising as the interocular suppressive force is believed to be a lot greater for observers with strabismic amblyopia[60, 88]. Further analysis on the possible relationship between the interocular luminance and the threshold reveals poor linear fit and lack of correlations. On the other hand, the contrast-defined balance point tests performed on the same observers show much better linear fits. The greater magnitudes of slopes and better R^2 observed clearly reveals that contrast is a better measure to assess sensory suppression.

However, the previous results in chapter 2 suggest that the mean luminance difference between the eyes of normal observers can simulate suppression in amblyopia. The simulated imbalance can be counteracted by manipulating the interocular contrast. This discrepancy is not unexpected since the magnitude of the interocular luminance difference used in chapter 2 to simulate suppression was a lot more substantial. For example, a ND filter with optical density of 2 causes a 100-fold reduction in the mean luminance. For these magnitudes of luminance differences, there appeared to be changes in the sensitivity. Although the physical contrast in the image is unaltered, stimulus detectability is affected. This is why ND filters can simulate suppression as they change the gain of the visual system, which in turn leads to a suppressive imbalance that then can be measured by adjusting the stimulus contrast.

3.4.3 Summary

In conclusion, the strength of suppression of strabismic amblyopic observers was shown to be significantly greater than that of the binocular normal participants. Although not statistically significant, there was a clear trend for suppression to correlate positively with the degree of amblyopia. No significant correlation was found between the angular magnitude of strabismic deviation and the depth of suppression. As demonstrated in chapter 2, placing ND filters were effective in simulating amblyopic suppression in normal observers. On the other hand, the dichoptic motion threshold was not very responsive to the change of mean luminance when it is manipulated digitally in this experiment. The effect of ND filters could be complex. In part, it may be due to the fact that they reduced luminance sufficiently to change the contrast sensitivity of the visual system despite leaving the contrast of the target unchanged. ND filters produced a luminance-dependent contrast change that cannot be thought of simply in terms of a luminance change per se. In conclusion, within the confines of the parameters used in this experiment, the manipulation of interocular contrast, not luminance affects sensory dominance in normals and suppression in amblyopes. This is most likely due to the fact that interocular balance involves the inhibitory monocular contra-lateral drives to the contrast gain control mechanisms of each eye, which is consistent with the two-stage model of binocular interaction.

CHAPTER 4: A QUANTITATIVE ANALYSIS OF OCULOMOTOR FUNCTIONS OF STRABISMIC AMBLYOPIA DURING A DICHOPTIC GLOBAL MOTION TASK

4.1 INRODUCTION

Strabismus is a disorder where the eyes are not properly aligned with each other. Suppression is a common sensory adaptation which is believed to arise in order to avoid diplopia and confusion resulting from the misalignment[40].

In chapter 3, a group of eight constant and unilateral strabismic observers with amblyopia were tested and shown to have severe suppression. The balance point experiment, which varied the interocular contrast between the eyes, quantified the degree of interocular suppression of the strabismic amblyopes. The results revealed a non significant, yet clear correlation between the level of suppression and the degree of amblyopia.

However, the investigation conducted in chapter 3 had focused primarily on the sensory aspect of the observers, while their oculomotor function was not mentioned. Given that, this chapter explores the oculomotor status of these strabismic amblyopes, and whether there is a change to the ocular misalignment, when suppression was reduced at their balance point. This objective could be fulfilled by comparing the relative eye position quantitatively at various interocular contrast settings induced during a balance point determination.

4.2 METHODS

4.2.1 Participants

This study was conducted at the same time as the balance point was measured, and the inclusion criteria are identical to what had been described in chapter 3. Eight[1] (8) constant and unilateral strabismic amblyopes with deviations less than 30Δ and ages which ranged from 18 to 40 years were included in the study. The study was approved by the Office of Research Ethics (ORE 15721) of University of Waterloo, and informed consent was obtained from each participant prior to testing. The detailed clinical information of the strabismic amblyopic subjects can be found in Table 3-1 in chapter 3.

4.2.2 Apparatus

The apparatus and methods for this study were described in chapter 2 and 3 with regard to the measurement of the balance point. As discussed previously, a 13 inch Macbook laptop was used to generate the stimuli and output it to a head-mounted display (HMD) goggle system. Additionally, the HMD system was equipped with a pair of infrared cameras-based eye-trackers (manufactured by Arrington Research, Scottsdale, AZ). The company specifications indicated that the eye-trackers' spatial resolution is 0.15 degrees and accuracy is 0.25 - 1 degree. The GigE-60 software program (Arrington Research) was run to perform the calibration, and to record the eye movements during the balance point experiment. Table 4-1 below summarizes the apparatus and the software programs used in the present study.

[1] The subjects included the following individuals: YP, AM, TR, MA, SS, CZ, SM, SA. Please refer to Table 3-1 for their clinical information.

Table 4-1: A summary of the apparatus and software used

Purpose	Apparatus	Software program
Stimuli presentation	Z800 Duel Pro Head mounted Display (EMargin Corporation) with a resolution of 1600 X 600	Matlab(Mathworks) and Psychtoolbox V3
Eye-Tracking	Mountable eyetracking system(Arrington Research) with sampling frequency of 60 Hz	GigE-60
Tracking data processing and analysis		Matlab-based analysis package (written by S. Clavagnier, Vision Research, McGill University)

4.2.3 Stimuli Presentation

The stimuli were Random dot kinematograms used in an earlier study[89] that were described in detail in chapter 2 and 3. An example illustration of the stimuli can be found in Figure 2-2. As previously described, the stimuli were presented dichoptically by the HMD goggle device. In each trial, one eye was presented with signal dots that all moved coherently either to the right or left, whereas the other eye was presented with noise dots that moved in random directions. The stimuli always moved within the frame, and they did not interfere with the fixation dot in the centre. During the experiment, a fusional lock that consists of a square-shaped frame and a dot in the centre was always present to facilitate fusion between the eyes. The observers combined the information received from both OLED screens and fused them into a single percept. The objective was to identify the direction of the signals' motion -- a process requiring the observers to integrate information from both eyes. The duration of the stimuli presentation was 1 second (or 1000 msec) per trial, after which an empty field with only the fusional lock was shown (for the illustration of the fusional lock, please refer to Figure 2-1) until the observers make a response.

4.2.4 Eye-tracking system calibration

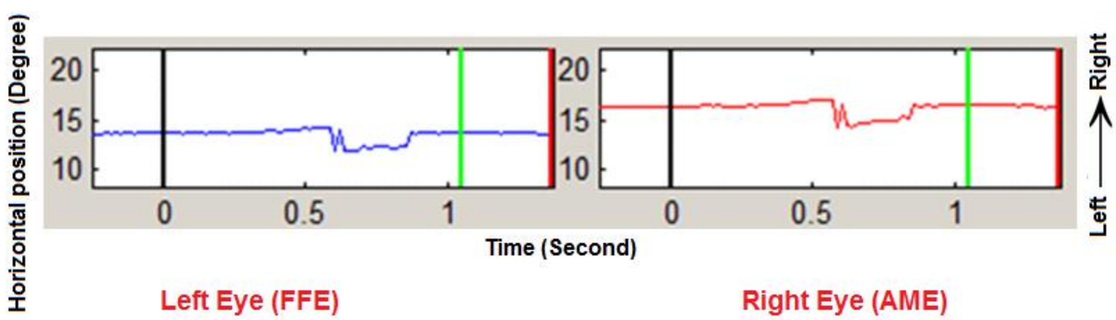
A calibration of the visual field was performed on each eye dichoptically before the experiment started. 16 dots that covered the entire visual field were presented in sequence for each eye to fixate on. Since the eyes were calibrated in two independent visual spaces separately, each eye would be registered to the same positional coordinate following the calibration unless there was a change to the relative alignment of the eyes. In other words, the relative position between the eyes (i.e., the difference of the position value of the two eyes) at resting should be 0 for normal observers.

4.2.5 Calculating the change of ocular alignment in a single trial

The horizontal position of each eye was recorded throughout the entire session, which consisted of approximately 500 trials and took about 20 minutes to complete. The relative eye position was analyzed only during the time when the stimuli were perceived, which means that the eye movements recorded before and after the stimuli presentation were discarded. Artefacts could arise occasionally from situations such as blinking which might lead to temporary loss of fixation by the eye-trackers. Saccades, the rapid and conjunctive eye movements to quickly direct the gaze, were also commonly observed. Saccades and artefacts were removed for better accuracy of the alignment calculations. Blink artefacts were manifested as sharp spikes with large amplitudes while saccades were evident by rapid velocity changes in the eye tracker recordings, with smaller amplitude and could be recognized by examining the positional change of the traces. Figure 4-1 below shows a pair of horizontal eye traces in one single trial for a strabismic amblyope. The horizontal axis shows the time (in second) and the vertical axis labels the eye position (in degrees). The two (black and green) bars mark the beginning and the end of the stimuli presentation in a trial, and the region in between was extracted and analyzed to calculate the alignment. In the example illustration (Figure 4-1), the value of the left eye's position fluctuates at around 14 degree, which indicates the distance between the left eye's gaze and the reference point (0,0). The absolute value may change over the course of the 20-min test depend on the observer's gaze of fixation. It was the difference of the position between the eyes that was calculated in order to find the change of alignment.

The alignment was to be determined by the following three steps: 1) remove saccades and artefacts; 2) take the mean of all data points for each fixation period defined as the time (sampling frequency is 60/sec) between the two bars for each eye, and 3) subtract the means obtained from the two eyes. In the example trial below, the misalignment was determined to be approximately 2 degrees. The calculation was repeated for all the trials in a session by a computerized analysis program (written by S. Clavagnier, Vision research unit, McGill University).

Figure 4-1: Example horizontal eye movements of a strabismic amblyopic observer recorded in a single trial



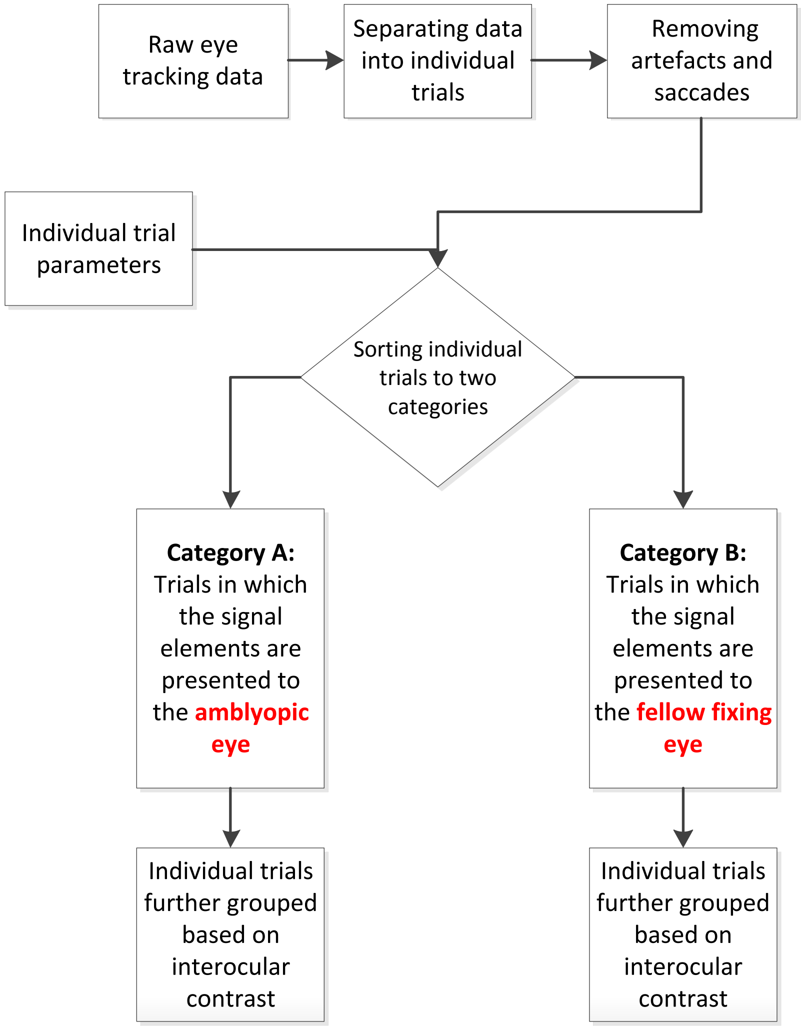
The horizontal axis shows the time (in seconds) and the vertical axis labels the horizontal eye position (in degrees). The black and green bar marks the beginning and the end of the stimuli presentation in a single trial and the position of fixation within the two bars are to be analyzed. The alignment for this trial is to be calculated by subtracting one eye's position from the other. The right eye is the amblyopic eye. The contrast settings and the direction of the stimuli are not known with certainty as the trial was taken randomly for illustration purpose.

4.2.6 The eye-tracking data processing and analysis of the whole testing session

A typical testing session consisted of approximately 500 trials, and each trial contained stimuli with different contrasts used to determine a balance point. In order to investigate the effect of unequal interocular contrast on the oculomotor status, a number of parameters needed to be considered. These parameters included the contrast of the stimuli, the direction of signals, and whether the stimuli were displayed to the amblyopic eye (AME) or the fellow fixing eye (FFE). All the trials in a session were sorted into two groups depending on the eye that received the signal (either the FFE trials or the AME trials), and then they were further separated into five subgroups based on the interocular contrast level.

Figure 4-2 is a flowchart that illustrates this sorting process. At the end of this process, the FFE stimuli trials and AME stimuli trials were differentiated and different contrast ratios were grouped together. This allowed the mean alignment at various contrast ratios to be compared. Moreover, to test whether there is an impact to the ocular alignment when signal elements were sent to amblyopic eye (as opposed to the fellow fixing eye), the FFE trials and AME trials were analyzed separately.

Figure 4-2: A flowchart illustrating the sorting process of the oculomotor data



A typical balance point test consists of approximately 500 trials and these trials are grouped to two categories depending on the eye (AME or FFE) that perceives the signal dots. Each category is further divided into 5 subgroups based on the interocular contrast ratio, thus allowing the ocular alignment information across various contrast ratios to be compared.

4.3 RESULTS

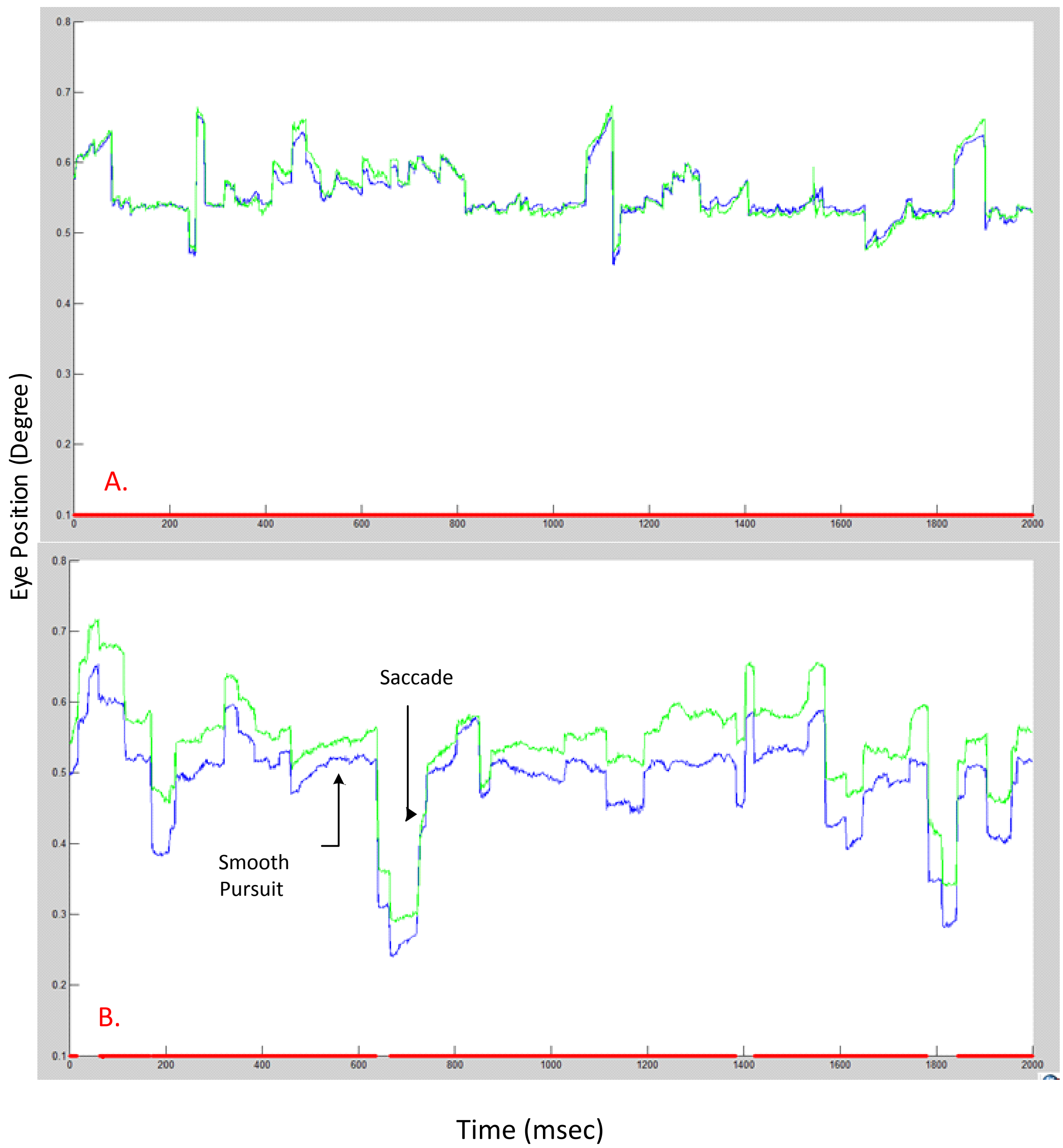
4.3.1 Eye movement recordings

This study investigated the oculomotor status during the psychophysical testing of sensory suppression. The eye movements were continuously recorded throughout the entire session of the psychophysical test. 20-second example eye movement recordings during the dichoptic viewing of a global motion are shown in Figure 4-3 for illustration purposes. During the 20 seconds, several RDK trials were completed, and each trial was conducted with different parameters. As mentioned previously, these parameters included the contrast settings, direction of the signals, and to which eye the signal elements were presented, all of which were randomized over the course of the 20 seconds. The horizontal axis represents the time in milliseconds, and the vertical axis represents the horizontal eye position in degrees, with the two eyes (FFE and AME) illustrated separately by different colors.

Figure 4-3A shows the recording of a normal subject, the two traces are superimposed because the eyes are converged to a similar position independently between their respective screen fields. The superimposing of the traces indicates that the relative eye position was not changed after the pre-test calibration, demonstrating a well maintained ocular alignment for the normal participants throughout the experiment.

For the strabismic amblyopic observer, however, there is a noticeable gap between the traces of the two eyes (Figure 4-3B). The presence of this offset gap indicates a change of alignment between the initial calibration and the actual balance point experiment. This suggests that the angle of strabismus must change temporarily from the resting value, which is set by the initial calibration. The offset gap is wider in some regions showing that the magnitude of the misalignment was not constant during the test when the coherent motion dots were displayed dichoptically. Smooth pursuits and saccades were commonly observed in both amblyopes and normals, as the subjects attempted to follow the signal dot with their fovea (Figure 4-3A and B). It appears that the variations of misalignment tend to arise following quick saccadic movements from the example eye traces (Figure 4-3, and 4-4). It is not testable whether the change is significant or not, and it is not conclusive whether a pattern really exists.

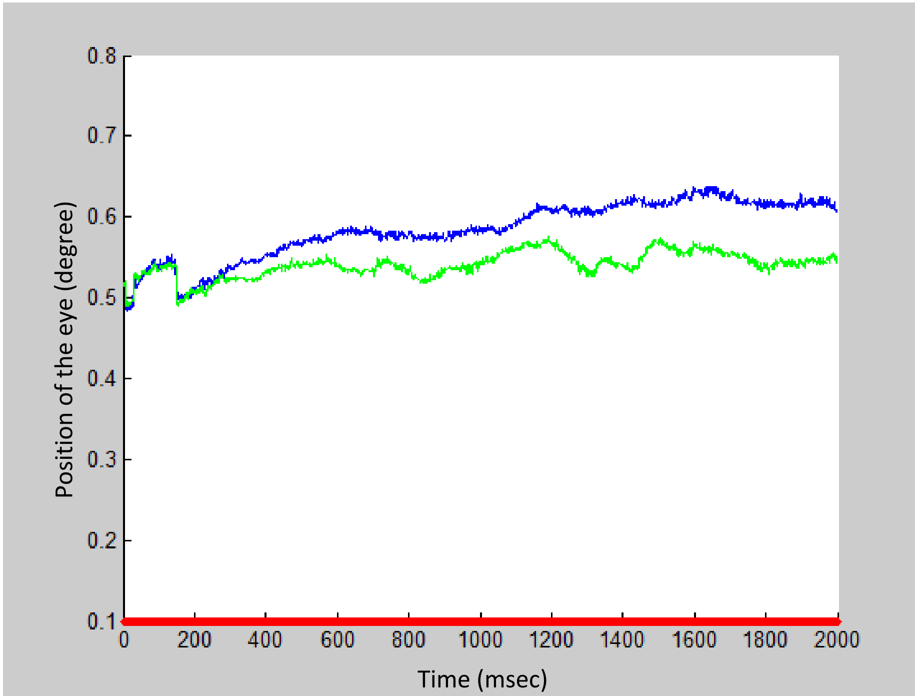
Figure 4-3: Example recordings of the horizontal eye movement



A) example recording of a binocular normal observer where the there is no offset; B) example recording of a strabismic (unilateral and constant) amblyopic observer where there appears to have constant offset which is present in steady fixation, smooth pursuit and saccades. The horizontal axis represents the time in millisecond, and the vertical axis shows the horizontal eye position in degrees. This example eye-trace was taken randomly for illustration purposes. During the 20 seconds, five trials of were completed and each trial was presented with different parameters including contrast settings, direction of the signals, and which eye perceive the signals that were not known with certainly. Green: left eye (amblyopic eye), blue: right eye (fellow fixing eye).

It should be noted that in the case of amblyopes, the two eyes were conjugate as they moved in the same direction just like normal observers. Motor coordination was maintained throughout the experiment, and the amblyopic eye was used as well as the fellow fixing eye. A change of alignment might also occur smoothly during prolonged fixations. This is because the amblyopic observers might choose a reference point (such as the dot in the centre) to fixate, and used their peripheral vision to gauge the global motion of the signal dots. In the example figure 4-4, the angle of strabismus smoothly changed, although this change may not be significant relative to the misalignment.

Figure 4-4: Example recordings of the horizontal eye movement of an amblyopic observer illustrating a change of the ocular alignment

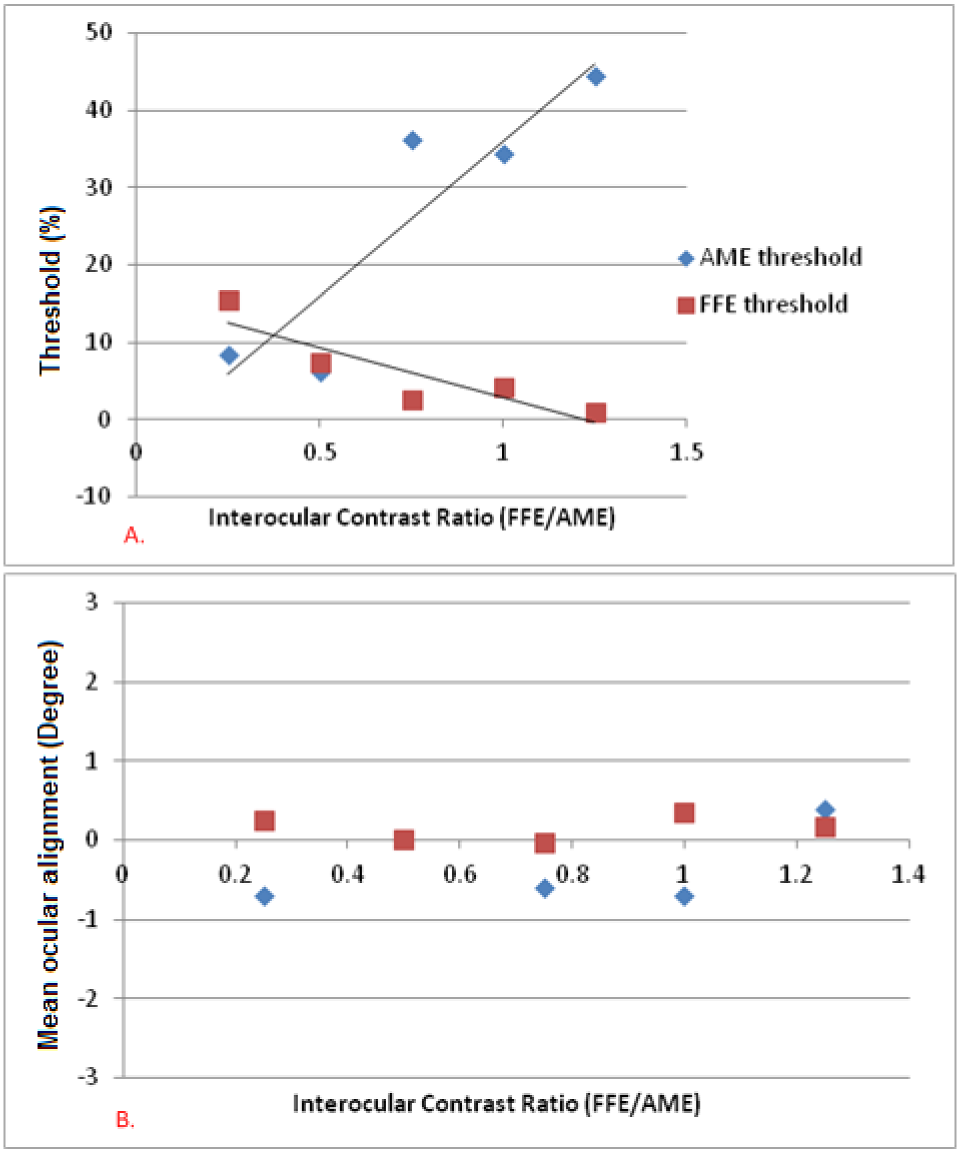


The horizontal axis represents the time in millisecond, and the vertical axis shows the horizontal eye positions in degrees. Note that following a saccadic eye movement the deviation changes in a smooth manner. Green: left eye (amblyopic eye), blue: right eye.

4.3.2 Analyzing individual alignment along with their sensory information

The effect of contrast on ocular alignment was quantitatively analyzed using the detailed procedures outlined in Figure 3-2. The relationship between the mean ocular alignment and the interocular contrast ratio of a strabismic subject is illustrated in Figure 4-5B. The dichoptic motion threshold relative to the interocular contrast ratios is shown in Figure 4-5A, and it can be seen that the balance point was determined to be 0.4.

Figure 4-5: The threshold and ocular alignment of a strabismic amblyopic observer as a function of the interocular contrast ratio



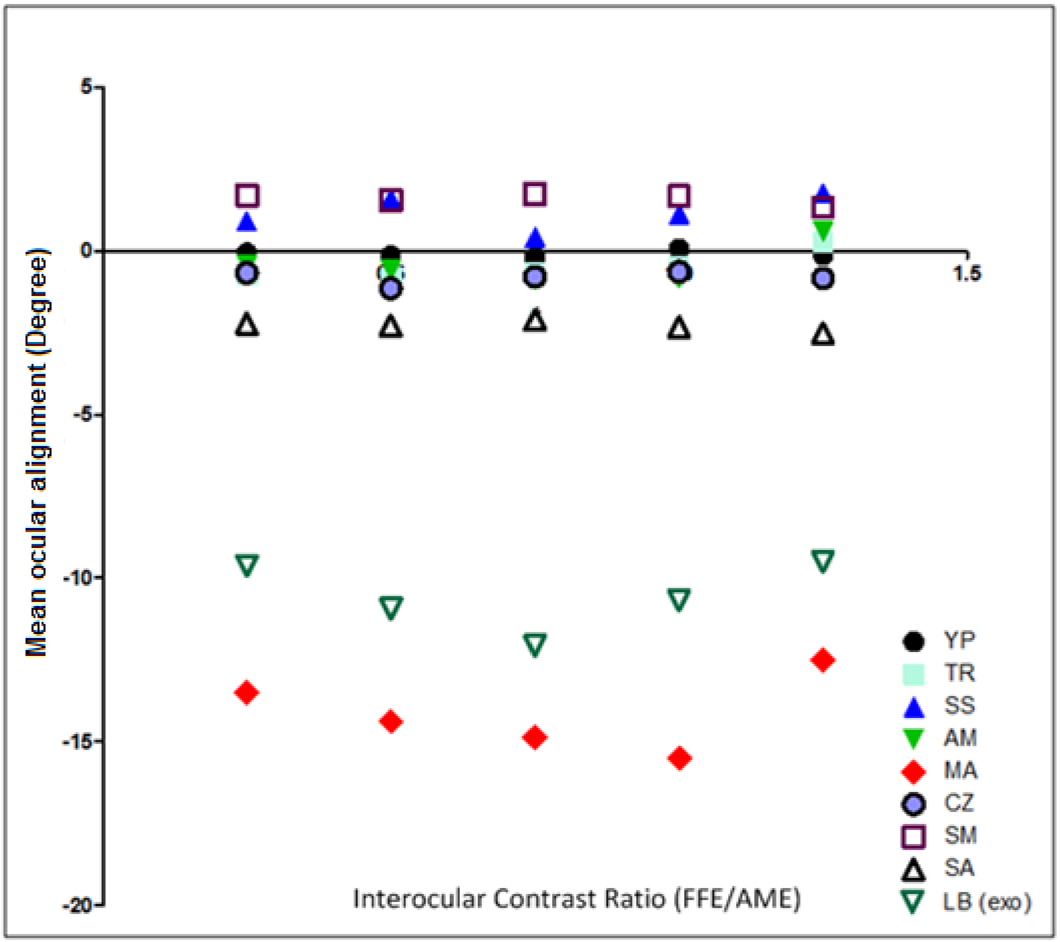
The Upper panel (A) illustrates the motion coherence threshold as a function of the interocular contrast. The intersection of the regression lines is the balance point. The Lower panel (B) shows the mean ocular alignment as a function of the interocular contrast ratio. The trials were separated to FFE and AME trials based on the eye that received the signal elements, and they were represented by square and rhombus symbols, respectively.

4.3.3 The relationship between the ocular alignment and the interocular contrast

There were eight (8) strabismic amblyopic observers who had their eye movements recorded while performing the psychophysical test, 7 constant esotropes and 1 constant exotrope. (For the individual ocular alignment graphs, please refer to Appendix B.) Their alignment information was determined from the mean of all the trials completed (approximately 500 trials), and the associated stimulus parameters (e.g. interocular contrast) were brought in with their eye movement data to explore the effect of interocular contrast.

Their results were collapsed to one graph shown in Figure 4-6, where the mean alignment of each subject was plotted against the interocular contrast ratio. There was no significant change of the relative eye position as a function of the interocular contrast ratio found in any of the observers.

Figure 4-6: The ocular alignment of eight strabismic amblyopic observers across a range of interocular contrast ratios



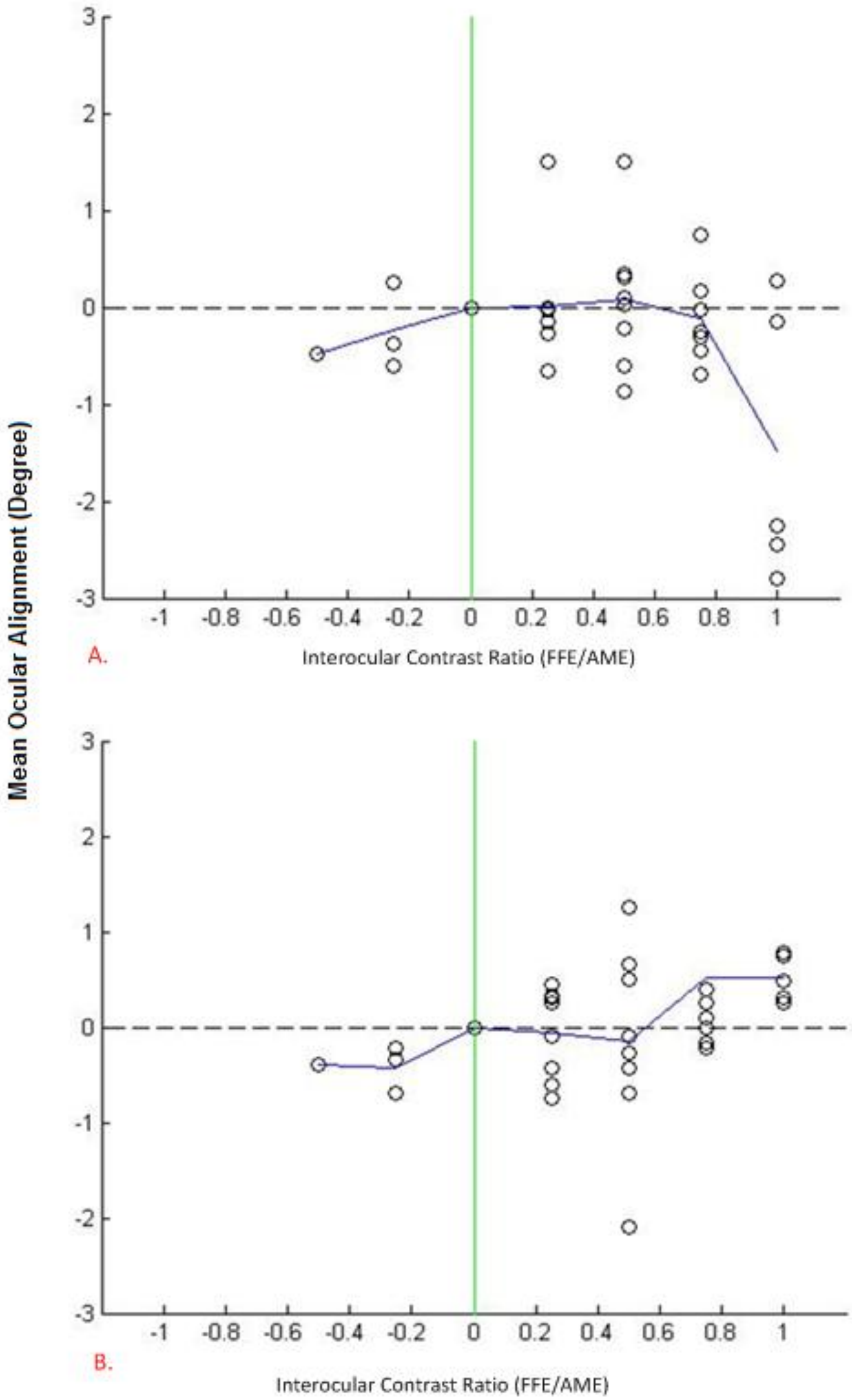
Observers are identified by the symbols of different colors and shapes. 7 subjects are esotropic, and only 1 subject is exotropic. Note that the eye-tracking data contains trials from both FFE and AME presenting signals. Unlike Figure 4-5, AME and FFE trials are not presented separately.

4.3.4 Normalization using the balance point at reference

The purpose of normalization was to create a graph that incorporated the observer's sensory information with their oculomotor status (i.e., the mean ocular alignment). In particular, the data were examined in order to determine a change in the angle of strabismus would occur at the balance point where suppression is reduced, and perhaps some binocular functions may be restored. Using the balance point as reference at the origin (0,0), the change of the mean alignment (y component) is plotted based on how far the respective contrast (x-component) is away from the balance point. For example, subject SA's balance point was determined to be 0.4 (Figure 4-5A), SA's alignment at the balance point is plotted at (0,0), and the calculated mean ocular alignment(y) at the interocular contrast ratio of 0.6 is to be plotted at (+0.2, y), which indicates the difference between a particular contrast ratio and the balance point. Using this approach, the relative eye position of the subjects was well normalized, allowing comparisons among the observers with different degree of suppression.

The relationship between the relative eye position and the level of sensory imbalance after the normalization is shown in Figure 4-7. The upper panel (Figure 4-7A) illustrates this sensory-oculomotor relationship when signals are presented to the amblyopic eye, and the lower panel (Figure 4-7B) illustrates the information when signals are presented to the fellow-fixing eye. A green vertical line shows the balance point, and the x-coordinate represents the level of sensory imbalance from each subject's sensory balance. The majority of subjects demonstrated strong suppression, yielding balance point of small magnitudes (e.g. <0.25). As a result, more information was collected under conditions when the contrast ratio (FFE/AME) is higher than their balance point. Binocular summation would be possible only over the brief range of negative values in Figure 4-7 A & B. Therefore, the right side of the vertical reference bar has a lot more data points, where suppression was strong. As seen in Figure 4-7, the ocular alignment is relative constant throughout the spectrum of contrast ratio range. The only exception occurs at the very right extreme, where the contrast ratio is five stops away from their balance point. This suggests a potential change to the ocular alignment under substantial interocular imbalance when signal elements are presented to the amblyopic eye. However, the overall ocular alignment was not sensitive to contrast gradients. Further, there is no effect when the balance point is reached or exceeded. This suggests that when suppression is attenuated by contrast, there is no evidence that oculomotor changes occur in order to reduce the angle of strabismus.

Figure 4-7: The mean ocular alignment of seven esotropic observers, normalized by contrast at the balance point



The relationship between the ocular alignment and the level of sensory imbalance (defined by the interocular contrast) in esotropic observers. Since the signal elements were presented to either the amblyopic eye (AME trial) or the fellow fixing eye (FFE trial), and it was not with certainty whether this difference pose an impact to the oculomotor status, these two scenarios were treated separately. The upper (A) and lower (B) panel illustrate the ocular alignment of the AME trials and FFE trials, respectively. The vertical axis shows the ocular alignment in degree; and the horizontal axis represents the contrast stops from each subject's balance point, as illustrated by the green vertical line. One contrast stop represents 20% interocular contrast. Blue solid lines connect the mean ocular alignment (by taking an average of all the observers) at various contrast stops. Note that these two graphs are restricted to esotropic observers, and they do not contain the information of the exotropic observer.

4.4 DISCUSSION

4.4.1 The ocular alignment was not affected by interocular contrast

The study conducted in chapter 3 measured the sensory suppression in a group of strabismic amblyopic observers by inducing unequal contrast between the eyes. The interocular contrast ratio was shown to be a good indicator to define the level of suppression. More importantly, the binocular motion sensitivity could be balanced temporally at a particular interocular contrast. Here in the present study, the oculomotor status was explored during these viewing conditions.

The oculomotor status was studied quantitatively by calculating the ocular alignment, or the relative eye position under different interocular contrast levels. The main finding was that overall the ocular alignment was maintained throughout the entire session for the strabismic amblyopic observers. Additionally, no correlation was found between the change of ocular alignment and the degree of sensory imbalance, which is defined by the number of contrast stops from their respective balance point. The ocular alignment was maintained despite the change of interocular contrast. This means that restoring the sensory balance does not lead to a change in the angle of strabismus. Lastly, no effect was found whether the signal elements were presented to the amblyopic eye or the fellow fixing eye.

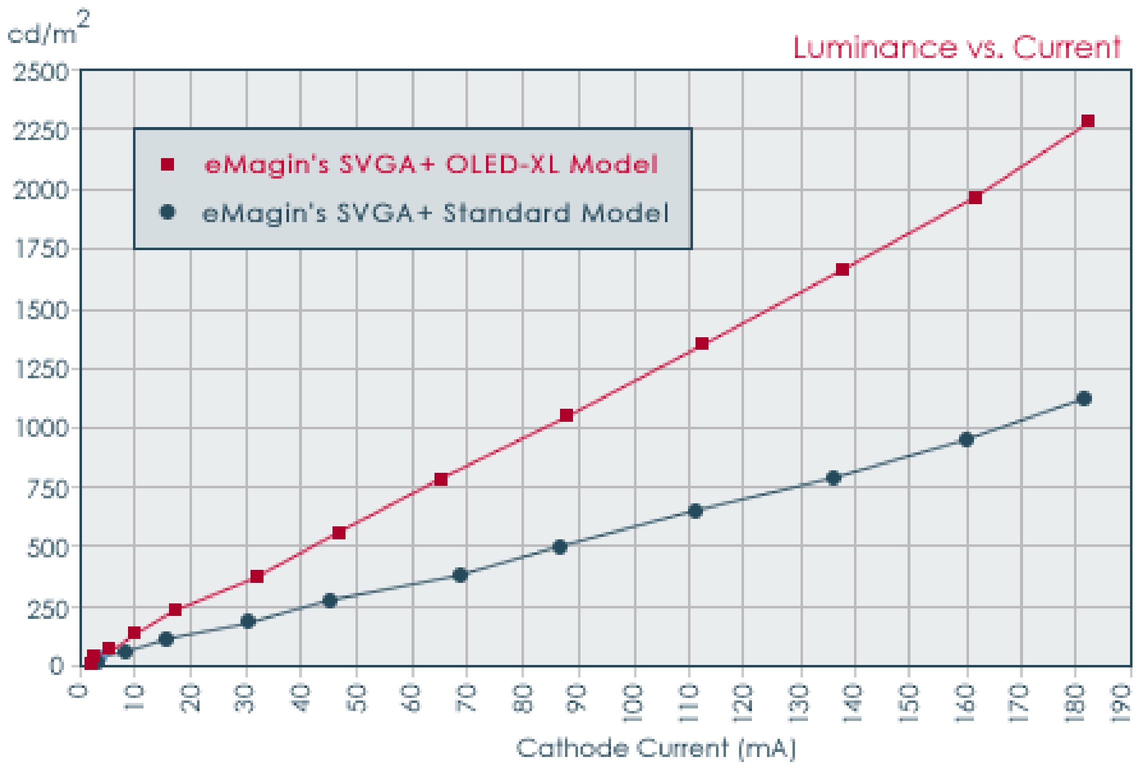
The purpose of inducing unequal contrast between the eyes is to lower the interocular suppressive drive that comes from the fellow eye[44, 60] in order to restore a binocular balance. According to the two stage model of binocular interaction[55] and the derived strabismic amblyopic model[60] (described in chapter 1, refer to Figure 1-1), the interocular suppressive force that takes place in an early stage prior to binocular summation is one of the three main properties that account for the amblyopic eye's deficient visual functions. The other two properties are 1) reduced contrast input and 2) multiplicative noise to the amblyopic eye, both of which contributes to the loss of the monocular visual sensitivity. As discussed in chapter 2, the LGN may play an important role in restoring the interocular balance. The present study reveals that the interocular balance achieved involves only sensory consequences. The oculomotor status, particularly the alignment is not found to be affected by disrupting or restoring sensory balance. Such distinction between motor and sensory pathway is also manifested elsewhere. For example, as discussed in chapter 3, the angle of strabismic deviation is not found to be correlated with the degree of suppression. Moreover, observers with pure amblyopia (sensory deficit) and strabismus (oculomotor deficits) sometimes exhibit different properties in the utilization of disparity vergence[90].

4.4.2 Summary

Overall, the relative eye position was not affected by altering the interocular contrast between the eyes. Consequently, there is no correlation between the ocular alignment and the level of sensory imbalance. The qualitative analysis of the eye-tracker recording reveals that the saccades and pursuits movement were conjugate, which confirms that coordination of the two eyes during the dichoptic viewing.

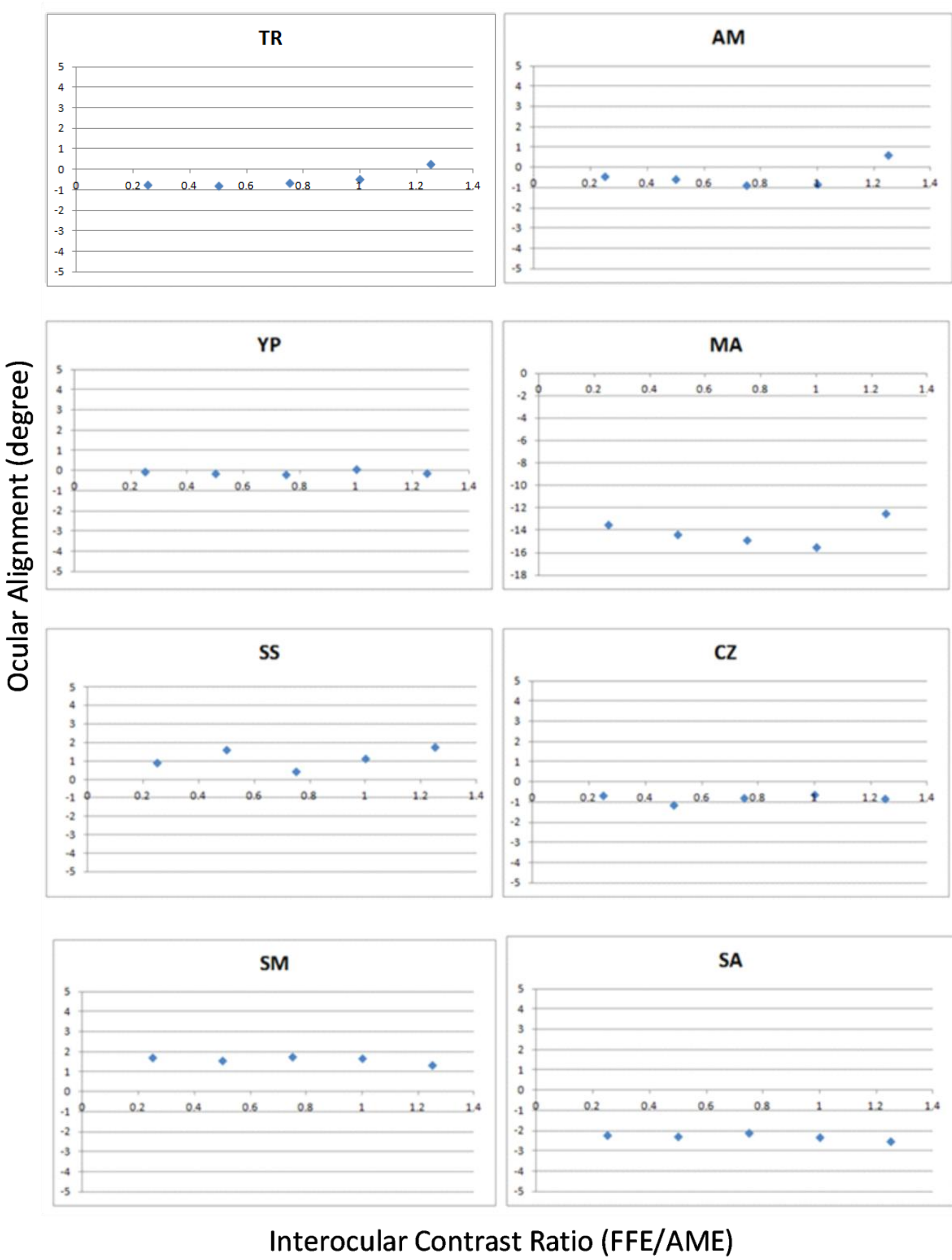
APPENDICES

Appendix A: eMargin's HMD system's luminance profile as a function of Current



The relative amount of light emitted by the LED as a function of the current in mA, the calibration is provided by the manufacturer, eMagin Co. eMagin SVGA +OLED-XL is the model used in this thesis (red line).

Appendix B: The mean ocular alignment (degree) as a function of the interocular contrast ratio



The relative ocular alignment relative to the interocular contrast ratio of eight amblyopic participants displayed separately.

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Vision Research: Figure 1-1, Chapter 1

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