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PHD PROGRAM IN BIOENGINEERING AND ROBOTICS

Novel Methods for Assessing and Rehabilitating Binocular Sensorimotor System in Virtual Reality

Sensory and Motor Contributions in Visual Perception

by

Federico Ferracini

Thesis submitted for the degree of *Doctor of Philosophy* (38° cycle)

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Declaration

I hereby declare that except where specific reference is made to the work of others, the contents of this dissertation are original and have not been submitted in whole or in part for consideration for any other degree or qualification in this, or any other university. This dissertation is my own work and contains nothing which is the outcome of work done in collaboration with others, except as specified in the text and Acknowledgements.

Federico Ferracini
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Abstract

The ability to coordinate the two eyes to achieve a stable and unified perception of the world is a fundamental aspect of human vision. This process, which relies on the continuous interaction between sensory and motor components, allows us to perceive depth and maintain precise alignment during everyday activities. When this coordination fails, as in strabismus or amblyopia, binocular function deteriorates, leading to abnormal fixation, loss of stereopsis, and suppression of one eye. Despite technological advances, quantitative and ecologically valid tools for assessing and treating binocular sensorimotor coordination are still limited, particularly in clinical contexts where eye misalignment hinders the use of conventional eyetracking systems. With these premises in mind, the general goal of my PhD research was to develop and validate novel methodologies for the quantitative assessment of binocular coordination in immersive virtual environments, and to extend the use of HMD-based eye tracking to individuals with atypical binocular vision. The first step was the implementation of a monocular calibration framework for head-mounted displays with integrated eye trackers, capable of providing accurate gaze estimation even when built-in calibration fails due to asymmetric fixation or ocular deviation. Modelling headset–eye system individual geometric and optical parameters allowed a precise monocular gaze mapping that could overcome the limitations of standard manufacturer procedures. Building upon this, I developed a digital version of the clinical cover test, which enables direct measurement of ocular deviations in VR while controlling viewing parameters such as head orientation, occlusion timing, and fixation distance. Experimental results demonstrated that the monocular calibration significantly improves spatial accuracy and reduces systematic bias across the visual field compared to standard methods. Validation was carried out on both healthy participants and individuals with binocular misalignment, confirming the robustness of the approach in clinical conditions. The digital version of the cover test revealed consistent patterns of phoria modulation with head rotation and provided quantitative evidence for optimal occlusion durations required to capture full eye realignment dynamics. Overall, the methods and tools developed in this work offer a new experimental framework for studying binocular sensorimotor coordination with high precision and ecological validity. These advances pave

the way for future applications of virtual reality in clinical research, offering non-invasive, adaptive, and quantitative tools for the assessment and potential rehabilitation of binocular visual disorders.

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Chapter 1

Introduction

1.1 Motivation and objectives

Binocular vision relies on the coordinated interaction between sensory and motor processes that jointly support a unified percept of the environment from the two retinal images. Through precise integration of visual signals and tightly controlled eye movements, the visual system constructs a three-dimensional representation of space that enables accurate perception and action. This synergy between sensory fusion and oculomotor alignment is fundamental for depth perception, spatial orientation, and visually guided behavior in everyday life.

Crucially, binocular vision is not only a perceptual phenomenon but also a sensorimotor one. Accurate eye movements depend on reliable sensory representations of depth, while stable sensory fusion depends on precise motor alignment of the eyes. Disruption at any level of this loop—particularly during development—can lead to persistent binocular vision disorders. These may manifest as sensory impairments such as amblyopia, diplopia, suppression, or reduced stereopsis, and/or as motor impairments such as strabismus and vergence insufficiency. Together, these conditions affect millions of individuals worldwide and have profound consequences for visual function, quality of life, and clinical outcomes.

Despite the sensorimotor nature of binocular vision, current clinical assessment and rehabilitation strategies remain largely fragmented. Standard treatments for amblyopia, such as occlusion or penalization therapy, primarily target monocular visual acuity and do not explicitly promote binocular integration or eye movement coordination. Likewise, surgical and optical treatments for strabismus often focus on mechanical alignment without systematically addressing the underlying sensory and motor interactions that support stable binocular vision. These limitations are partly due to a lack of practical tools for quantitative assessment of sensorimotor function and partly due to the absence of coordinated therapeutic approaches that engage both sensory and motor plasticity.

Recent advances in eye tracking, virtual reality (VR), and stereoscopic display technologies provide new opportunities to bridge this gap. These tools enable precise measurement of eye movements and perceptual responses in controlled yet ecologically meaningful environments. At the same time, growing evidence shows that both sensory and motor components of the visual system retain substantial plasticity even in adulthood. While many recent rehabilitation approaches have focused on sensory plasticity through dichoptic games or perceptual training, considerably less attention has been directed toward motor plasticity, or to interventions that explicitly combine sensory and motor rehabilitation within a unified framework.

In this dissertation, I adopt a sensorimotor perspective on binocular vision, aiming to develop and evaluate assessment and rehabilitation methods for binocular sensorimotor disorders using immersive and quantitative technologies. The central hypothesis is that coordinated sensory-motor approaches can lead to more effective, stable, and generalizable improvements in binocular visual function than treatments targeting either component alone.

Specifically, this work addresses two research questions:

1. **How can binocular sensory and motor deficits be quantitatively assessed in realistic three-dimensional environments?**

2. **How can combined sensory-motor interventions promote and maintain functional binocular vision?**

Focusing on binocular integration, oculomotor control, and visual plasticity, this dissertation examines:

- The development of quantitative metrics for sensory and motor impairments in binocular vision.

- The impact of altered eye alignment on three-dimensional visual representations across the visual field.

- The potential of feedback-based, VR-mediated rehabilitation to support ocular alignment and binocular fusion.

1.2 Overview

1.2.1 Thesis Organisation

Background The first part of this dissertation provides the theoretical and methodological background underlying the present work. It introduces key concepts and reviews relevant literature on binocular vision, visuomotor disorders, and current clinical and technological approaches (Chapters 2 and 3). This section contextualizes the research questions and highlights the main challenges that motivate the development of the methods proposed in this thesis.

1.2.2 Dissemination

Within the context of the work presented in this thesis, have published some preliminary studies on peer-reviewed conference proceedings and later extended such results targeting international journals with widespread attention from the research community. Below is a list of such publications:
Peer-reviewed conference proceedings:

- **Ferracini, F.**, Peveri, F., Borsani Villa, E.A., Sabatini, S.P., Gibaldi, A., Canessa, A. (2025). *"Custom Monocular Calibration for Enhanced Eye-Tracking Accuracy"*. Proceedings of the IEEE Engineering in Medicine and Biology Conference (EMBC) 2025.

Poster presentations:

- *“VR-CUT, the Cover-Uncover Test in Virtual Reality: Easy and Accurate Assessment of Strabismus Across Gaze Eccentricities and Fixation Distances.”* Association for Research in Vision and Ophthalmology (ARVO) 2025 Annual Meeting.

- *“Head- gaze related influences on heterophorias revealed by an HMD-based cover test.”* Vision Sciences Society (VSS) 2024 Annual Meeting.

- *“Enriching Strabismus Evalua- tion through Immersive Virtual Reality and Comprehensive Cover Test Protocols.”* European Conference on Visual Perception (ECVP), 2024.

Chapter 2

Binocular Visuomotor Disorders

2.1 Physiological Basis of Stereopsis

2.1.1 Physiology of Stereopsis

Stereopsis represents one of the most sophisticated capabilities of the human visual system and constitutes the perceptual basis of three-dimensional (3D) depth perception derived from binocular vision. It arises from the integration of slightly different images projected onto the retinas of the two eyes, a phenomenon known as binocular disparity (1; 2). Because the eyes are horizontally separated by an average interocular distance of approximately 6–7 cm, each retina receives a slightly different view of the same visual scene (3). The visual system exploits these positional differences to infer the relative depth of objects in the environment (3).

The neural computation of binocular disparity constitutes a fundamental mechanism underlying fine depth discrimination, particularly within the peripersonal space, where precise spatial information is required for visually guided actions. Tasks such as reaching, grasping, and object manipulation rely heavily on accurate estimation of relative distances, for which stereopsis provides highly reliable and high-resolution information (4; 5). Under optimal viewing conditions, humans can detect binocular disparities as small as a few arcseconds, demonstrating the remarkable sensitivity of the stereoscopic visual system (1; 2).

This mechanism originates from the geometric configuration of the two eyes and their coordinated vergence movements. When fixating a target in space, the eyes rotate in opposite directions so that the image of the object falls on corresponding retinal locations. As illustrated in Figure 2.1, this oculomotor behavior produces slightly different projections of the same object on the two retinas, generating retinal disparity.

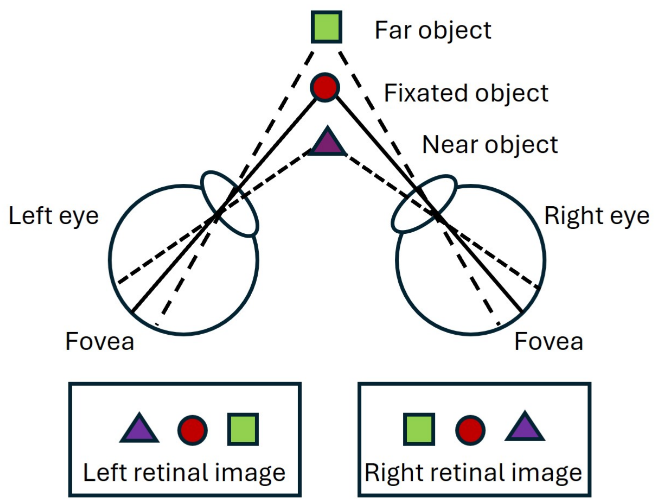

Figure 2.1 Geometric principle of binocular disparity. Because the two eyes observe the scene from slightly different viewpoints, the projections of an object on the two retinas differ. The visual system exploits this disparity to estimate relative depth, particularly in the near (peripersonal) space.

Although binocular disparity provides highly precise depth information at short viewing distances, it operates in conjunction with several additional visual cues. Monocular cues such as perspective, occlusion, shading, and texture gradients contribute to the perception of spatial layout, particularly at larger distances where binocular disparities become less informative (3).

Motion-based cues, such as motion parallax, also play a significant role in depth perception. When an observer moves relative to the environment, objects located at different depths generate different retinal motion patterns, providing additional information about spatial structure (6).

The contribution of these cues depends strongly on the viewing distance. While binocular disparity is the dominant cue in the peripersonal space, where high spatial precision is required, monocular and motion-based cues become increasingly relevant for the perception of far space and for navigation in complex environments. The integration of multiple depth cues enhances the robustness of spatial perception, allowing the visual system to maintain stable depth estimates even when individual cues are degraded or ambiguous (3).

Retinal Correspondence, Horopter, and Binocular Disparity

The geometric basis of stereopsis relies on the concept of retinal correspondence, which describes the relationship between points on the two retinas that are stimulated by the same object in space. When a point in the visual scene projects onto corresponding retinal locations in both eyes, it is perceived as single and located in a specific position in depth.

From a geometric standpoint, retinal correspondence defines a set of spatial locations that project onto matched retinal coordinates in the two eyes. The locus of all such points forms a surface in three-dimensional space known as the horopter (3; 7). Therefore, the horopter can be interpreted as the set of points in space that produce zero binocular disparity for a given fixation condition, as illustrated in Figure 2.2.

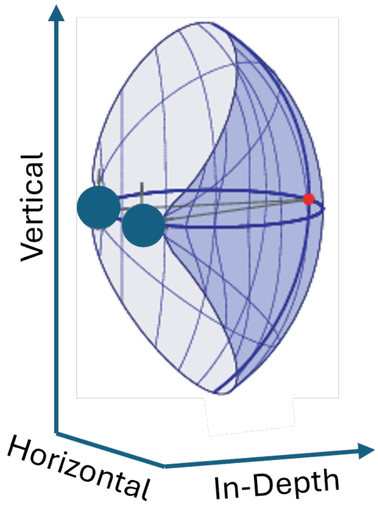

Figure 2.2 Three-dimensional schematic representation of the horopter. Given a fixation point, the horopter defines the surface in space that produces zero binocular disparity. Additional fixation points are also illustrated to highlight how the shape and position of the horopter change depending on the gaze direction.

In an idealized geometric model, the horopter corresponds to the Vieth–Müller circle, which passes through the fixation point and the nodal points of the two eyes. However, empirical measurements have shown that the actual horopter deviates systematically from this theoretical construction, reflecting both anatomical asymmetries and perceptual adaptations of the visual system.

Objects located on the horopter are perceived at the same depth as the fixation point, as they generate no disparity between the retinal images. In contrast, objects positioned either closer or farther than the horopter produce binocular disparity, which serves as the primary cue for depth perception in binocular vision.

Specifically, objects located closer than the fixation point generate crossed disparities, while objects located farther away generate uncrossed disparities. These disparities arise from the relative horizontal shift of the retinal projections in the two eyes and provide information about the spatial arrangement of the scene (3; 8).

From a quantitative perspective, disparity can be defined as the angular difference between the projections of a visual target onto the two retinas. This quantity depends on both the spatial position of the object and the fixation point of the observer, and it varies systematically across the visual field. The horopter therefore represents the zero-disparity reference surface against which all depth variations are encoded.

The visual system is capable of detecting extremely small disparities. Behavioral measurements of stereoacuity indicate that humans can discriminate disparities as small as 5–10 arcseconds under optimal conditions (1; 3). This high sensitivity enables precise depth discrimination and supports visually guided actions in complex environments.

Overall, the relationship between retinal correspondence, the horopter, and binocular disparity provides the fundamental geometric framework underlying stereoscopic vision and accurate depth perception.

Functional Role of Stereopsis

Stereopsis plays a crucial role in visually guided motor tasks that require high spatial precision, particularly within the peripersonal space. Experimental studies have demonstrated that binocular vision significantly improves the accuracy and reliability of reaching and grasping movements compared to monocular viewing conditions (5). The availability of disparity information allows the visual system to estimate relative distances with high precision, enabling fine motor coordination during object interaction.

In addition to supporting motor actions, stereopsis contributes to perceptual organization of the visual scene. Variations in binocular disparity provide a powerful cue for segmenting objects from their background and for reconstructing the three-dimensional structure of complex environments. This process facilitates figure-ground segregation and enhances the perception of spatial relationships between objects (9).

Furthermore, stereopsis plays an important role in maintaining stable and coherent spatial perception. By providing consistent depth information, it contributes to reducing ambiguity in visual scenes, especially when other depth cues are limited or conflicting. This integration is particularly important in dynamic environments, where rapid and accurate interpretation of spatial layout is required.

From a functional perspective, impairments in stereopsis can significantly affect both perceptual and motor performance. Reduced or absent binocular vision may lead to difficulties in depth judgment, decreased precision in object manipulation, and increased reliance on compensatory cues. These limitations are particularly evident in individuals with binocular vision disorders, such as strabismus, where abnormal ocular alignment disrupts the normal processing of disparity information.

Overall, stereopsis represents a key component of the visual system, supporting both action and perception by providing precise and reliable information about the three-dimensional structure of the environment.

Development of Stereoscopic Vision

Stereopsis does not emerge immediately after birth but develops progressively during infancy. Behavioral studies indicate that coarse stereopsis begins to appear between three and five months of age, coinciding with the maturation of binocular cortical circuits (8). The development of stereoscopic vision depends critically on balanced visual input from both eyes during early life, allowing the sensory and motor fusional mechanisms to establish a coherent binocular representation of the environment.

Binocular vision function relies on the close interaction between sensory fusion, which constructs a single percept from the two retinal images, and motor fusion, which ensures precise ocular alignment. A disruption in either component during sensitive periods of development can lead to persistent deficits in binocular vision. Sensory impairments may manifest as amblyopia, diplopia, or suppression, while oculomotor impairments may include strabismus or insufficient vergence responses. Importantly, accurate binocular eye movements themselves depend on the presence of a stereoscopic sensory representation, creating a reciprocal relationship between sensory and motor subsystems. Failures in this intertwined system can compromise both the perception of depth and the capacity to execute precise binocular movements.

Recent research has also highlighted the considerable plasticity of both sensory and motor systems, even beyond early development. This plasticity suggests that, under the appropriate conditions and with targeted interventions, deficits in stereoscopic vision may be mitigated or rehabilitated, emphasizing the importance of early detection and the potential for adaptive therapies (10).

Clinical Implications

Disruptions in binocular alignment or sensory integration can profoundly affect stereoscopic perception. Conditions such as strabismus, amblyopia, and anisometropia interfere with normal binocular correspondence, preventing the establishment of a stable stereoscopic perception (11; 12). When one eye is suppressed to avoid diplopia, the development of stereoscopic depth perception is further compromised, even if monocular vision remains functional.

The clinical management of binocular vision deficits traditionally treats sensory and motor impairments separately. Monocular therapies for amblyopia do not directly address binocular integration or the coordination of eye movements, while interventions for strabismus focus primarily on ocular alignment without considering perceptual fusion. This segmented approach may limit the overall therapeutic efficacy. Emerging evidence suggests that simultaneous targeting of sensory and motor plasticity could provide synergistic benefits, enhancing both depth perception and ocular control. Laboratory and virtual reality-based assessments offer precise, quantitative endpoints to evaluate these sensory-motor interactions, enabling a more detailed characterization of binocular dysfunction and potentially guiding personalized rehabilitation strategies; however, these approaches still face important limitations related to calibration accuracy, ecological validity, inter-individual variability, and the translation of experimental measurements into clinically actionable outcomes. (13).

2.1.2 Physiology of Eye Movements

Eye movements play a fundamental role in visual perception by allowing the visual system to acquire, stabilize, and integrate information from the surrounding environment. Because the fovea occupies only a small portion of the retina and provides the highest spatial resolution, precise control of ocular motility is necessary to direct the line of sight toward relevant visual targets (14). The oculomotor system therefore operates as a highly coordinated sensorimotor control system, integrating visual, vestibular, and proprioceptive information to ensure stable and accurate gaze behavior (15).

Human eye movements are generated by six extraocular muscles for each eye, which are controlled by motor nuclei located in the brainstem. These muscles enable rotations of the eyeball along three principal axes: horizontal, vertical, and torsional. The neural control of these muscles involves complex interactions between cortical areas, subcortical structures, and brainstem circuits (16).

Several distinct classes of eye movements have been identified, each serving specific functional purposes. Among the most relevant for binocular vision are saccades, smooth pursuit movements, and vergence movements. In addition, accommodation mechanisms interact closely with vergence to maintain clear and single vision across different viewing distances (17).

Extraocular Muscles and Neural Control

Each eye is controlled by six extraocular muscles: the medial rectus, lateral rectus, superior rectus, inferior rectus, superior oblique, and inferior oblique. These muscles act in coordinated pairs to produce precise rotations of the eyeball (18). The anatomical organization of the extraocular muscles responsible for ocular rotations is illustrated in Figure 2.3.

Motor commands originate from three cranial nerve nuclei located in the brainstem: the oculomotor nucleus (cranial nerve III), the trochlear nucleus (cranial nerve IV), and the abducens nucleus (cranial nerve VI). These nuclei receive inputs from multiple cortical and subcortical regions involved in gaze control, including the frontal eye fields, parietal cortex, superior colliculus, cerebellum, and vestibular nuclei (14).

The coordination between the two eyes is ensured by specialized neural circuits that enforce conjugate eye movements during gaze shifts and disconjugate movements during vergence responses. The well-known Hering's law of equal innervation states that corresponding muscles in the two eyes receive equal neural commands during conjugate movements, ensuring synchronized motion

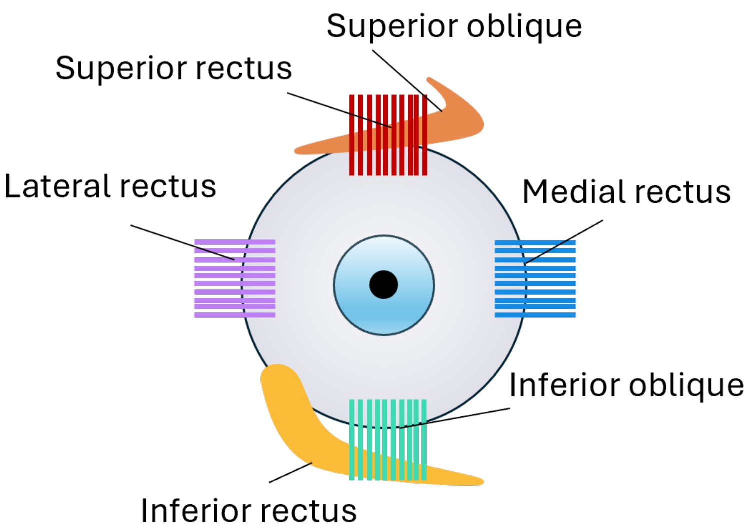

Figure 2.3 Anatomy of the six extraocular muscles responsible for eye rotations. Coordinated activation of these muscles allows precise control of gaze direction.

Saccadic Eye Movements

Saccades are rapid ballistic eye movements that redirect the line of sight from one point of interest to another. They represent the fastest movements produced by the human body, reaching peak velocities of up to 500–700 degrees per second (19). Saccades typically occur several times per second during natural viewing and are essential for exploring complex visual scenes. The typical velocity profile of a saccadic movement, characterized by a rapid increase in velocity followed by a deceleration phase toward the target fixation, is illustrated in Figure 2.4. While Figure 2.4 illustrates the typical velocity profile of a saccade schematically, Figure 2.5 presents actual experimental measurements of saccadic eye movements, showing eye position, velocity, and acceleration over time.

The primary function of saccades is to bring objects of interest onto the fovea, where visual acuity is maximal. Once a target is selected by attentional mechanisms, cortical areas such as the frontal eye fields and parietal eye fields generate motor commands that are transmitted to brainstem saccade generators (14).

Saccadic movements are characterized by their ballistic nature: once initiated, the trajectory cannot be modified by sensory feedback. Instead, accuracy is maintained through internal calibration mechanisms involving the cerebellum (20). Adaptive processes allow the oculomotor system to adjust saccade amplitude in response to systematic errors.

Although saccades are primarily conjugate movements involving both eyes in the same direction, small vergence components may accompany them when gaze shifts occur between objects located at different depths. These combined movements are often referred to as saccade–vergence interactions (17).

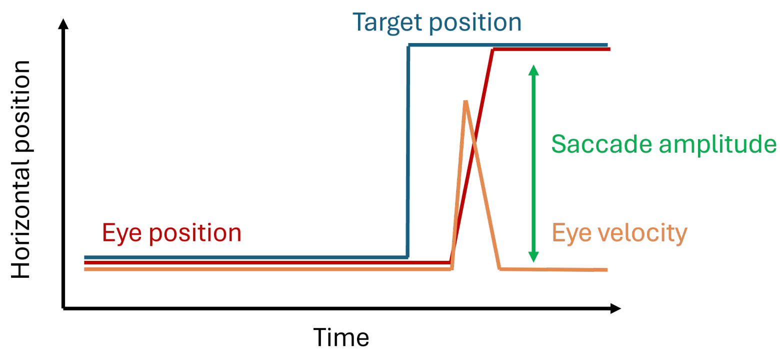

Figure 2.4 Typical velocity profile of a saccadic eye movement. Saccades are characterized by rapid acceleration followed by deceleration toward the fixation point.

Smooth Pursuit Movements

Smooth pursuit movements allow the eyes to track moving objects in the visual field. Unlike saccades, which are rapid and discrete, smooth pursuit movements are continuous and relatively slow, enabling the image of a moving target to remain stabilized on the fovea (21).

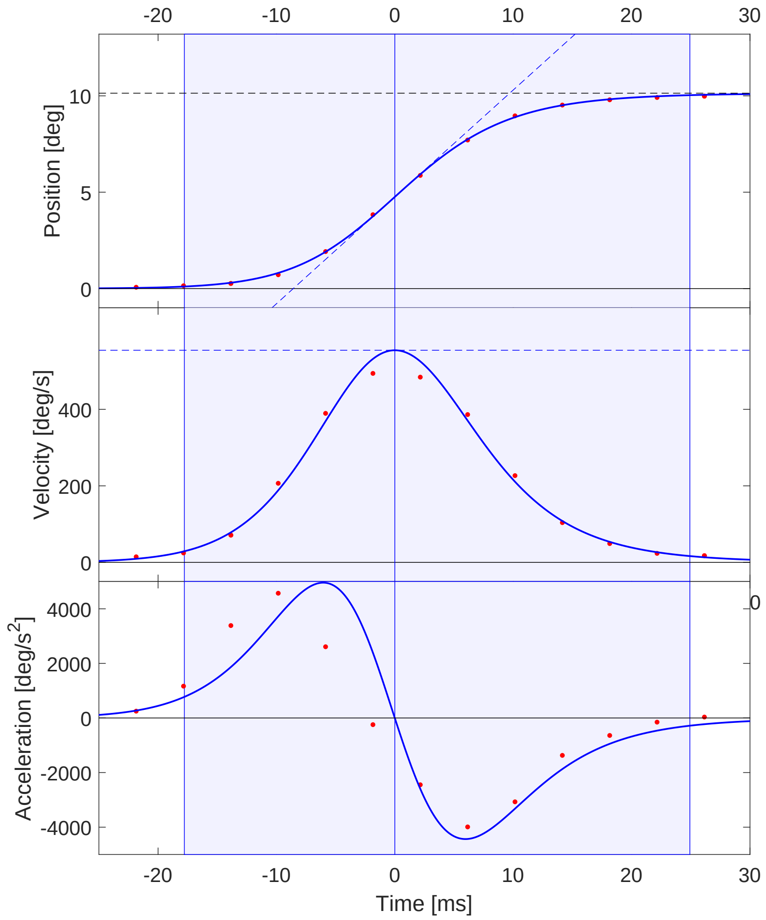

Figure 2.5 Experimental measurements of a saccadic eye movement. Eye position, velocity, and acceleration are shown over time. Red points indicate the sampled data, the blue line represents a continuous interpolating curve, and the vertical line at time zero marks the peak velocity of the saccade.

Smooth pursuit requires the presence of a moving visual stimulus and cannot be generated voluntarily without a target. The neural circuitry underlying smooth pursuit involves cortical motion-processing areas such as the middle temporal area (MT) and medial superior temporal area (MST), which provide motion signals used to guide eye velocity (22).

These cortical signals are transmitted to the cerebellum and brainstem pursuit generators, where motor commands are computed and sent to the extraocular muscles. Smooth pursuit performance depends on both retinal motion signals and predictive mechanisms that allow the brain to anticipate target trajectories (21).

Vergence Eye Movements

Vergence movements represent a distinct class of eye movements that adjust the relative orientation of the two eyes to maintain binocular fixation on objects located at different depths. Unlike conjugate movements, vergence movements are disconjugate: the eyes move in opposite directions (17).

Two main types of vergence movements exist: convergence and divergence. Convergence occurs when the eyes rotate inward to fixate a near object, while divergence occurs when the eyes rotate outward to fixate a distant object, as illustrated in Figure 2.6.

Vergence movements are essential for maintaining single binocular vision and enabling stereopsis. When an object moves closer to the observer, the eyes must converge appropriately to ensure that the image falls on corresponding retinal locations. Failure to maintain accurate vergence alignment may result in diplopia or visual discomfort (17).

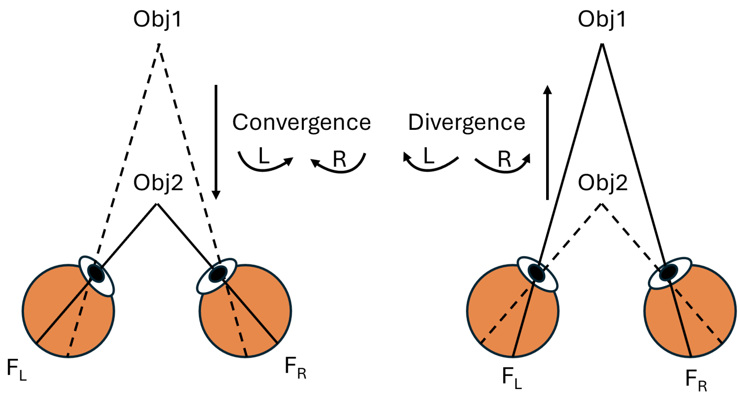

Figure 2.6 Vergence eye movements. Convergence occurs when the eyes rotate inward to fixate a near object, while divergence occurs when fixation shifts toward a distant object.

Accommodation and its Interaction with Vergence

Accommodation refers to the process by which the crystalline lens changes shape to maintain a sharp retinal image of objects at different viewing distances (23). This adjustment is achieved through contraction and relaxation of the ciliary muscles, which modify the curvature of the lens.

Accommodation is tightly coupled with vergence through neural mechanisms known as the near triad, which includes convergence, accommodation, and pupillary constriction. When a person shifts fixation from a distant object to a near one, these three responses occur simultaneously to maintain clear and single vision (17).

Vergence–Accommodation Conflict

Under natural viewing conditions, vergence and accommodation are driven by the same physical distance of the observed object. However, in artificial display systems such as stereoscopic screens or virtual reality head-mounted displays, these cues can become decoupled (24).

In VR environments, binocular disparity cues may indicate that an object is located at a certain virtual depth, while the physical display surface remains at a fixed optical distance from the eyes. As a consequence, vergence responses may correspond to the simulated depth, whereas accommodation remains fixed at the screen distance.

This mismatch between vergence and accommodation is known as the vergence–accommodation conflict. It represents a significant challenge for immersive display technologies and may contribute to visual discomfort, reduced depth perception accuracy, and visual fatigue (24; 25).

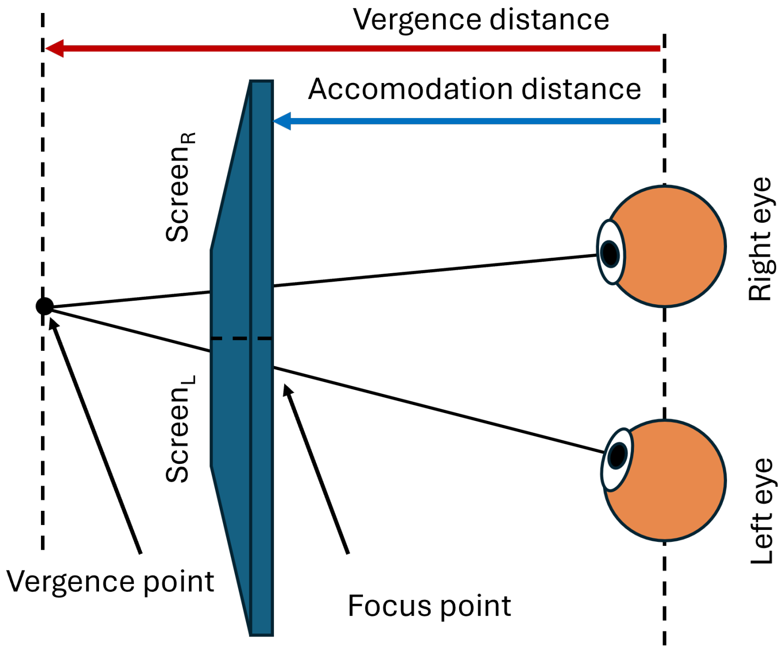

Figure 2.7 Vergence–accommodation conflict in stereoscopic displays. Vergence cues indicate virtual depth, while accommodation remains fixed at the display distance.

Functional Integration in Binocular Vision

The coordination between saccades, pursuit, vergence, and accommodation enables efficient exploration of three-dimensional environments. These oculomotor subsystems operate in close interaction, allowing the visual system to maintain stable fixation while simultaneously updating gaze direction and depth alignment (14).

Disruptions in these mechanisms may lead to binocular vision disorders such as convergence insufficiency, strabismus, or accommodative dysfunctions. Understanding the physiology of eye movements is essential for interpreting clinical measurements of binocular function and for developing immersive visual technologies that exploit or rehabilitate binocular mechanisms (17).

2.1.3 Atypical Development of Binocular Vision

The development of binocular vision is a complex process that relies on the coordinated maturation of sensory and motor components of the visual system. During early infancy, neural circuits responsible for binocular integration undergo rapid functional specialization driven by visual experience (26). Balanced and synchronized input from both eyes is required for the normal development of stereopsis, ocular alignment, and stable binocular perception (12).

When visual input is disrupted during critical developmental periods, the maturation of binocular mechanisms may be altered, potentially leading to persistent visuomotor disorders. Conditions such as strabismus, amblyopia, and anisometropia represent the most common causes of abnormal binocular development (11). These disorders often emerge during early childhood and may produce long-lasting changes in both sensory processing and oculomotor control.

Understanding the mechanisms underlying atypical development is essential for interpreting the clinical manifestations of binocular vision disorders and for designing appropriate diagnostic and therapeutic interventions (27).

Critical Periods in Visual Development

The maturation of binocular visual functions occurs during specific developmental windows known as critical periods. During these periods, neural circuits exhibit heightened plasticity and are particularly sensitive to visual experience (28). Proper alignment and balanced visual input from the two eyes are necessary to establish normal binocular connectivity within the visual cortex.

Experimental studies in animals have demonstrated that disruption of binocular vision during these critical periods can lead to permanent alterations in cortical organization. For example, monocular deprivation experiments in kittens and monkeys revealed that depriving one eye of visual input during early development causes profound changes in the distribution of ocular dominance columns in the primary visual cortex (29; 30).

These findings highlight the importance of early visual experience in shaping binocular neural circuits. In humans, the critical period for binocular vision development is believed to extend through the first few years of life, although some degree of plasticity may persist into later childhood (11).

Strabismus and Disruption of Binocular Alignment

Strabismus is characterized by a persistent misalignment of the visual axes, which prevents the two eyes from simultaneously fixating the same target, as illustrated in Figure 2.8. When strabismus occurs during early childhood, the developing visual system must adapt to the conflicting retinal images generated by the misaligned eyes.

One common adaptive mechanism is sensory suppression. In this process, the brain selectively ignores input from one eye in order to avoid diplopia and visual confusion (31). Although suppression allows the individual to maintain comfortable single vision, it disrupts the normal integration of binocular signals and prevents the development of stereopsis.

Persistent ocular misalignment may also interfere with the normal calibration of vergence eye movements. Because the two eyes no longer receive matched visual information, the neural mechanisms responsible for coordinating binocular alignment may fail to develop properly (17).

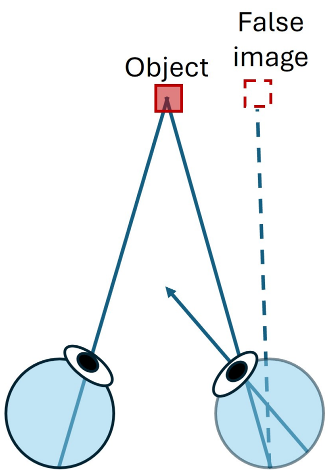

Figure 2.8 Illustration of ocular misalignment in strabismus. When the visual axes are not aligned, the two retinas receive incompatible images that may lead to diplopia or suppression.

Amblyopia

Amblyopia is a developmental visual disorder characterized by reduced visual acuity in one eye that cannot be fully explained by structural abnormalities of the eye (11). It typically arises when one eye provides degraded or inconsistent visual input during early development.

Several conditions may lead to amblyopia, including strabismus, anisometropia (unequal refractive errors between the two eyes), and visual deprivation caused by congenital cataracts or ptosis. In these situations, the brain preferentially relies on the eye that provides clearer visual information, leading to reduced cortical representation of the affected eye.

At the neural level, amblyopia is associated with alterations in binocular neurons within the visual cortex. Studies using neurophysiological recordings and neuroimaging techniques have demonstrated reduced responsiveness to stimuli presented to the amblyopic eye, as well as abnormal binocular interactions (10).

In addition to reduced visual acuity, amblyopia often involves deficits in contrast sensitivity, spatial processing, and binocular depth perception (12). Even when monocular visual acuity is partially restored through treatment, binocular functions such as stereopsis may remain impaired.

Suppression and Abnormal Retinal Correspondence

To avoid the perceptual confusion caused by misaligned retinal images, the visual system may develop suppression mechanisms that inhibit signals from one eye in specific regions of the visual field (31). Suppression is particularly common in individuals with early-onset strabismus and represents an adaptive strategy that allows comfortable single vision despite ocular misalignment.

Another sensory adaptation that may occur in strabismus is abnormal retinal correspondence (ARC). In this condition, the brain reassigns corresponding retinal locations in the two eyes so that non-foveal points in the deviating eye become functionally linked with the fovea of the fixing eye (17). This neural remapping allows some degree of binocular cooperation despite persistent misalignment.

While ARC may reduce diplopia, it typically prevents the development of normal stereopsis because the spatial relationship between retinal points no longer reflects the true geometry of visual space.

Plasticity and Therapeutic Interventions

Although early disruptions of binocular vision can produce long-lasting effects, the visual system retains some capacity for plastic reorganization (10). Recent studies have shown that binocular visual mechanisms in adults remain highly plastic, with short-term manipulations such as monocular deprivation capable of altering sensory eye dominance and interocular balance (32). Traditional treatments for amblyopia, such as occlusion therapy (patching of the dominant eye), aim to promote the use of the weaker eye and restore balanced visual input (11).

More recent therapeutic approaches have focused on binocular training paradigms that attempt to restore cooperation between the two eyes rather than treating them independently (33). These methods often involve perceptual learning tasks or dichoptic visual stimuli designed to reduce suppression and improve binocular integration.

Technological advances, including virtual reality and computer-based visual training systems, have created new opportunities for delivering such interventions in controlled and engaging environments (33; 34). By presenting separate stimuli to each eye and dynamically adjusting visual parameters, immersive platforms may facilitate the recovery of binocular functions even beyond traditional developmental periods.

Implications for Binocular Visuomotor Disorders

The mechanisms described above illustrate how early disruptions in visual experience can affect both sensory and motor aspects of binocular vision. Because the development of stereopsis, vergence control, and binocular integration are tightly interconnected, alterations in one component often influence the others (12; 17).

Patients with atypical binocular development may therefore exhibit a wide range of visuomotor deficits, including impaired depth perception, unstable fixation, reduced vergence accuracy, and abnormal eye movement coordination. These deficits can significantly impact everyday visual tasks and may persist into adulthood if not addressed during early developmental stages (11).

For this reason, early detection and precise characterization of binocular dysfunctions are essential components of clinical practice. Advances in measurement technologies and immersive visual environments may provide new tools for assessing these complex visuomotor interactions and for designing more effective rehabilitation strategies (33; 34).

2.1.4 Social Impact of Binocular Visuomotor Disorders

Binocular visuomotor disorders, such as strabismus and amblyopia, have substantial implications not only for sensory and motor function but also for psychosocial development and quality of life. These disorders can interfere with the performance of everyday tasks that rely on accurate depth perception, such as reading, driving, or navigating complex environments (35; 36). The inability to integrate visual input effectively from both eyes may lead to difficulties in spatial judgment and object manipulation, affecting both occupational and educational outcomes.

A failure in either part of the binocular vision system, especially during development, can lead to sustained impairment of the oculomotor and sensory systems, including strabismus and amblyopia, which have a prevalence of approximately 2–5% (37) and are known to have a significant negative impact on quality of life.

In children, early-onset strabismus and amblyopia have been associated with delays in motor coordination, reduced participation in sports, and challenges in tasks requiring fine visuomotor skills (38). The psychosocial consequences include lower self-esteem, increased risk of social anxiety, and potential stigmatization due to visible ocular misalignment (36). Several studies report that children with noticeable strabismus are often subject to teasing or social exclusion, which may affect long-term psychological well-being.

In adults, residual deficits from untreated or partially treated binocular dysfunctions can compromise driving safety and workplace performance. Depth perception errors may increase the risk of accidents in tasks requiring accurate distance judgment, such as operating machinery or driving vehicles (35). Moreover, adults with persistent amblyopia or strabismus may continue to experience eye strain, headaches, and difficulty with prolonged near-vision tasks, which can reduce occupational efficiency.

Beyond individual functional limitations, binocular disorders impose a broader societal burden. The economic impact includes costs related to clinical care, corrective surgery, vision therapy, and assistive technologies (36). Early detection and treatment have been shown to reduce long-term healthcare expenses by preventing severe visual impairment and improving functional outcomes. For example, timely occlusion therapy for amblyopia or surgical correction of strabismus during childhood can restore binocular function and minimize the need for ongoing interventions in adulthood (11).

Education and public health interventions play a critical role in mitigating these impacts. Screening programs in early childhood allow for the identification of strabismus, anisometropia, and other risk factors for amblyopia before critical periods of visual development close (12; 38). Early intervention not only enhances visual outcomes but also reduces the psychosocial burden on affected children and their families.

Emerging technologies, including virtual reality and eye-tracking-based assessment tools, offer new possibilities for quantifying the functional impact of binocular disorders in realistic environments (33; 34). Such tools can simulate daily life scenarios, evaluate depth perception performance, and monitor improvements following therapy. This approach provides more ecologically valid measures of functional vision compared to traditional clinical tests and may inform individualized rehabilitation strategies.

The clinical relevance of understanding social impact extends to designing patient-centered care plans. For instance, interventions that combine visual rehabilitation with psychosocial support can address both the functional and emotional challenges associated with binocular dysfunctions (36). Moreover, clinicians can provide education to families and educators regarding the potential academic and social difficulties, promoting supportive environments that encourage participation and inclusion.

Finally, binocular visuomotor disorders highlight the interplay between physiological deficits and daily life activities. Impaired stereopsis, convergence, or accommodation affects not only the accuracy of motor tasks but also confidence and independence in interacting with the environment (35). Recognizing the social and functional dimensions of these disorders underscores the necessity for timely diagnosis, targeted interventions, and ongoing monitoring to optimize both visual and psychosocial outcomes.

In summary, binocular visuomotor disorders carry significant functional, psychosocial, and economic consequences. Early detection and intervention, combined with emerging assessment technologies and patient-centered rehabilitation strategies, are essential for mitigating the negative impact of these conditions and improving quality of life for affected individuals.

2.2 Clinical Assessment Procedures

2.2.1 Visual Acuity and Dominant Eye

Visual acuity is the fundamental measure of the eye's ability to resolve fine spatial detail and is a critical component of binocular vision assessment. Clinical evaluation of visual acuity typically employs standardized optotypes, such as Snellen letters or logMAR charts, under controlled lighting conditions (39). Differences in visual acuity between the two eyes, often referred to as interocular imbalance, can significantly impact binocular integration and stereopsis.

A dominant eye is defined as the eye preferentially used when performing monocular tasks, such as aiming or sighting. Eye dominance can be measured using several methods, including the Miles test, the Porta test, and sighting-through-a-hole tasks (40). Dominance is not always absolute and may vary depending on the visual task or context. Clinically, understanding the relationship between visual acuity and eye dominance is essential for interpreting binocular performance and planning interventions.

Clinical Measurement of Visual Acuity Visual acuity assessment begins with monocular testing of each eye, with the fellow eye occluded. This approach allows identification of refractive errors, amblyopia, or other ocular pathologies affecting one eye more than the other. Standardized scoring in logMAR units provides a continuous scale that enables sensitive detection of small differences between eyes (39). The assessment procedure is illustrated in Figure 2.9a.

Interocular differences in acuity greater than one line on the logMAR chart may indicate an underlying binocular imbalance. Such imbalances can contribute to suppression of the weaker eye during binocular viewing, particularly in patients with early-onset strabismus or anisometropic amblyopia (11). The magnitude of the interocular difference is correlated with the severity of stereopsis deficits and may influence treatment decisions.

Assessment of Eye Dominance Eye dominance evaluation complements visual acuity testing by identifying the preferred eye during monocular tasks. In sighting dominance tests, the individual is asked to align a target with a reference aperture or pointing task using both eyes open and then each eye individually (40). The eye maintaining alignment is considered dominant. This assessment scheme is illustrated in Figure 2.9b.

Sighting dominance is generally consistent in adults but may fluctuate in children or individuals with visual disorders. Clinical assessment should consider both sensory dominance (preference based on input quality) and motor dominance (preference based on oculomotor control) (41). Recognition of dominance is particularly relevant in planning occlusion therapy for amblyopia, where the stronger eye may need to be patched to stimulate the weaker eye.

Implications for Binocular Function Unbalanced visual acuity and eye dominance have direct consequences for binocular integration. In cases where one eye provides lower-quality input, the visual system may develop suppression mechanisms to avoid diplopia and visual confusion (17). Persistent suppression can lead to deficits in stereopsis, reduced depth perception, and impaired vergence control.

Furthermore, the interplay between acuity imbalance and dominance affects the efficacy of binocular therapies. For example, dichoptic training paradigms for amblyopia rely on presenting high-contrast stimuli to the weaker eye while reducing contrast for the dominant eye, effectively leveraging eye dominance to promote balanced binocular vision (33). Accurate assessment of both visual acuity and eye dominance is therefore crucial for individualizing therapeutic interventions.

Technological Enhancements in Assessment Emerging technologies have improved the precision of visual acuity and eye dominance measurements. Digital optotype charts allow adaptive presentation of stimuli and automated scoring, reducing examiner bias and increasing reliability (39). Eye-tracking devices integrated with psychophysical tasks enable real-time monitoring of fixation stability and ocular preference during binocular viewing, providing more detailed insights into interocular imbalance (42).

Virtual reality platforms are increasingly used to simulate complex, ecologically valid visual environments while assessing visual acuity and eye dominance under dynamic conditions (34). Such immersive systems can reveal deficits that may not be apparent in conventional clinical settings and can inform tailored rehabilitation strategies for individuals with binocular dysfunctions.

Monocular visual acuity and eye dominance are foundational components of binocular assessment. Unbalanced acuity and dominant-eye preference influence suppression, stereopsis, and vergence accuracy. Standardized clinical tests, complemented by modern technological tools such as digital optotypes and eye-tracking, provide a comprehensive understanding of these factors. Accurate evaluation is essential for diagnosis, prognosis, and the design of effective therapeutic interventions targeting binocular visuomotor disorders.

2.2.2 Stereoacuity (Discrimination Thresholds)

Stereoacuity is the measure of the visual system's ability to detect small differences in depth between objects, arising from binocular disparity (12; 43). It represents a key functional output of binocular vision, reflecting the precise integration of visual information from both eyes. Clinically, stereoacuity is a sensitive indicator of binocular performance and is often assessed using psychophysical tests that measure the smallest detectable depth difference, expressed in arcseconds.

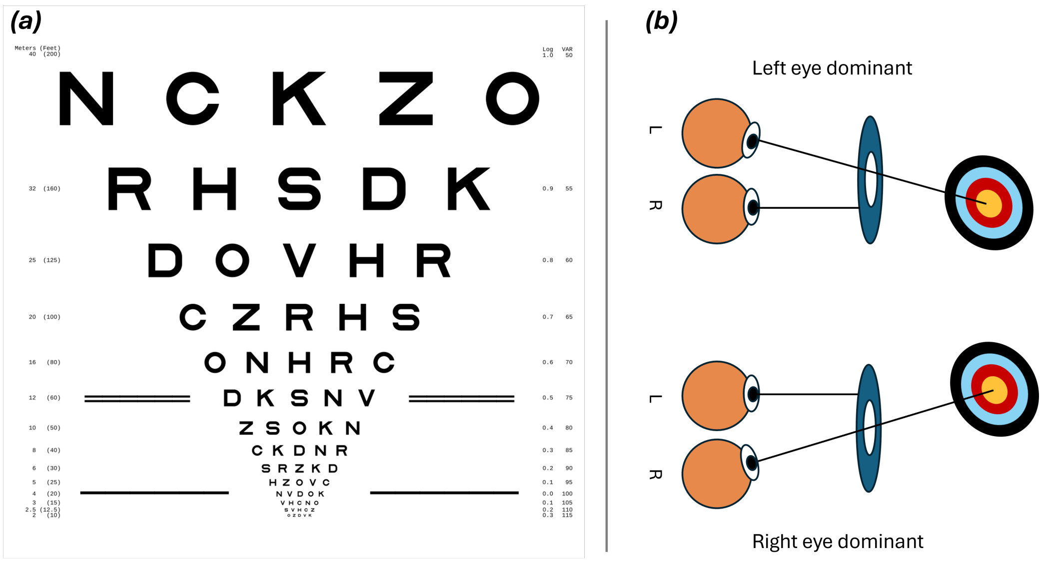

Figure 2.9 Clinical assessments for monocular visual function: (a) logMAR visual acuity, where interocular differences are measured to detect unbalanced visual function; (b) eye dominance evaluation, identifying the preferred eye for monocular fixation and visual tasks.

Principles of Stereoacuity Measurement Stereoacuity arises from the brain's capacity to compare the retinal images projected onto the left and right eyes, detecting disparities caused by the slightly different viewpoints of each eye (43). This binocular disparity provides critical information about relative depth and three-dimensional structure. High stereoacuity indicates the ability to perceive minute depth differences, whereas reduced stereoacuity is indicative of impaired binocular integration.

Factors Affecting Stereoacuity Several factors influence stereoacuity, including the quality of visual acuity in each eye, ocular alignment, and the presence of suppression (12). Even mild amblyopia can reduce stereoacuity significantly, as the impaired eye provides unreliable input that the brain cannot integrate effectively. Similarly, strabismus disrupts the correspondence between retinal points, limiting depth discrimination. The angular size of the stimulus and viewing distance are critical parameters. Smaller stimuli at near viewing distances can detect higher stereoacuity thresholds, whereas large or distant targets may only reveal coarse stereopsis (44). Clinical protocols often standardize these parameters to allow reliable comparisons across individuals.

Neural Basis of Stereoacuity Stereoacuity depends on the activity of binocular neurons in the primary visual cortex (V1) and higher visual areas such as V2 and V3 (45). These neurons are tuned to specific disparities and contribute to the perception of relative depth. The precision of disparity coding determines the limits of stereoacuity, and disruptions in cortical organization due to amblyopia or early-onset strabismus can compromise depth discrimination (12). Functional imaging studies have revealed that higher-level visual areas, including the dorsal and ventral streams, integrate disparity information to support tasks such as object recognition, navigation, and motor coordination (46). Therefore, stereoacuity is not only a perceptual measure but also an indicator of sensorimotor integration.

Clinical Protocols for Stereoacuity Testing Common clinical tests include:

- **Titmus Fly Test:** Uses large disparity targets to assess gross stereopsis.
- **Randot Stereotest:** Provides a range of disparity levels for fine stereoacuity measurement.
- **TNO Test:** Employs anaglyph glasses and random-dot stereograms to assess global stereopsis.

Patients are asked to identify shapes appearing in depth or to align objects until perceived as coplanar. Thresholds are recorded in arcseconds, with lower values indicating higher stereoacuity. Repeated measurements under controlled conditions are recommended to account for learning effects and attentional fluctuations. An example of the Randot stereotest setup is shown in Figure 2.10.

Figure 2.10 Example of a Randot stereotest. Patients are required to identify shapes or figures that appear in depth, assessing their stereoacuity.

Limitations and Considerations Traditional stereotests have limitations. Monocular cues may inadvertently aid performance, particularly in tests with visible outlines or shadows (47). Test-retest reliability can vary with patient age, attention, and cooperation. Emerging technologies, such as digital stereoscopic displays and virtual reality environments, offer more precise control over stimulus parameters and reduce monocular cue confounds (33; 34). Eye-tracking integrated with stereoscopic stimuli enables continuous monitoring of fixation stability, vergence alignment, and ocular dominance during testing, providing richer datasets for clinical assessment.

Implications for Therapy Stereoacuity assessment guides both diagnosis and therapy. Reduced stereoacuity indicates the presence of suppression or binocular misalignment and informs the design of interventions, including patching for amblyopia, vision therapy for convergence insufficiency, and dichoptic training (33). Progress in stereoacuity can serve as an objective outcome measure for treatment efficacy. Stereoacuity testing provides a sensitive and functionally meaningful assessment of binocular integration.

2.2.3 Cover Test and Prism Cover Test

The cover test and prism cover test are cornerstone clinical procedures for assessing ocular alignment and binocular function. These tests allow the detection and quantification of heterotropias (manifest strabismus) and heterophorias (latent deviations), providing crucial information for diagnosis, prognosis, and therapy planning (7; 48).

Principles of the Cover Test The cover test evaluates the presence of ocular misalignment by alternately occluding each eye while the patient fixates on a target (Figure 2.11). In the *cover-uncover test*, one eye is covered while the other maintains fixation; the examiner observes the uncovered eye for movement, which indicates a manifest deviation (tropia) (48). No movement suggests proper ocular alignment.

The *alternate cover test* involves covering one eye and then the other in rapid succession. This procedure disrupts binocular fusion, allowing latent deviations (phorias) to manifest as corrective movements when the cover is removed (17). By observing the direction and magnitude of eye movement, clinicians can classify deviations as esotropia/exotropia or hypertropia/hypotropia.

Prism Cover Test for Quantification Once a deviation is detected, the prism cover test is employed to measure its magnitude in prism diopters (Δ) (Figure 2.12). Prisms of known

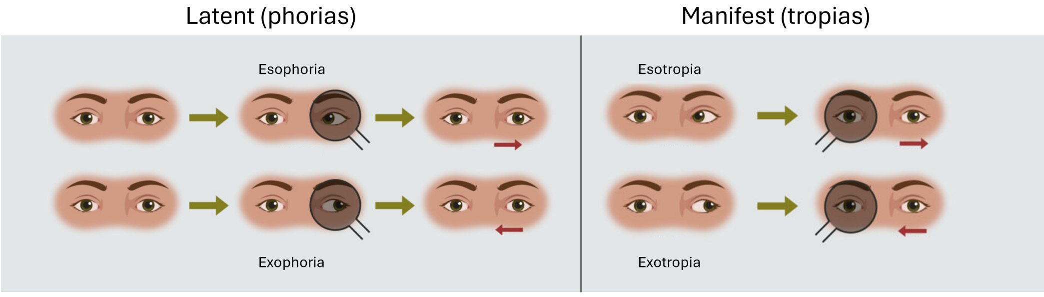

Figure 2.11 Schematic of the cover test. Occlusion can be used to assess both manifest and latent strabismus by observing eye movements.

dioptric strength are placed in front of one eye, and the cover test is repeated until no corrective movement is observed, indicating neutralization of the deviation (7). This method provides a precise, quantitative assessment of ocular misalignment.

Prism diopters correspond to the angular displacement required to shift an image from the fovea of the deviating eye onto the fovea of the fixating eye. For example, a 10 prism diopters deflects light by approximately 5.7 degrees, allowing the examiner to translate observed eye movements into standardized units (48).

Clinical Protocols and Standardization Standardized protocols are essential to ensure reliability of cover and prism cover tests. Tests should be performed at both near (40 cm) and distance (2 m) fixations, as some deviations are distance-dependent (17). he choice of fixation target (accommodative vs. non-accommodative) can influence measured deviation, particularly in patients with convergence insufficiency or accommodative anomalies.

Repeated measures improve accuracy, especially in pediatric populations where attention and cooperation may fluctuate. In cases of intermittent strabismus, measurements should be taken during periods when the deviation is evident, and parents or caregivers may provide observational input about daily occurrences (48).

Interpretation of Findings Cover and prism cover tests yield both qualitative and quantitative information. The direction of movement indicates the type of deviation: inward movement reveals esotropia, outward movement indicates exotropia, and vertical movements reveal hypertropias or hypotropias (7). The magnitude measured in prism diopters allows classification into mild, moderate, or severe deviations, which informs treatment decisions such as occlusion therapy, vision therapy, or surgical correction.

Detection of phorias versus tropias has prognostic implications. Phorias, latent deviations controlled by fusional mechanisms, may become symptomatic under stress or fatigue, leading to asthenopia, diplopia, or headaches (17). Tropias, manifest deviations, indicate more pronounced dysfunction and often require more intensive intervention.

Litterature Recent advances have introduced digital and eye-tracking-based enhancements to cover and prism cover tests. Eye trackers can provide continuous, objective measurements of ocular movements during dissociation, improving precision and reducing observer bias (33; 42). Virtual reality environments can simulate real-world fixation targets at various distances and depths, allowing assessment of deviations under controlled but ecologically valid conditions.

Automated or semi-automated systems may record eye movement trajectories, quantify the magnitude of deviation in real-time, and store longitudinal data for monitoring therapy progress. These innovations increase reproducibility and allow integration with other metrics such as vergence and accommodation responses.

Clinical Implications The cover test and prism cover test remain gold-standard procedures for the detection and quantification of binocular misalignment. Accurate measurement of ocular deviations informs diagnosis, guides therapy selection, and provides outcome measures for treatment efficacy. Knowledge of both the presence and magnitude of deviations is critical for managing conditions such as strabismus, convergence insufficiency, and amblyopia (17).

Furthermore, precise assessment allows clinicians to monitor developmental changes, detect early-onset deviations, and evaluate responses to therapeutic interventions, including vision therapy or surgical alignment procedures. Integration with modern digital tools enhances the ecological validity, objectivity, and longitudinal tracking of binocular function.

2.2.4 Limitations of Conventional Clinical Methods

Traditional clinical methods for assessing binocular vision—including visual acuity testing, stereopsis measurements, and cover/prism cover tests—remain indispensable in ophthalmology and optometry. However, these procedures present intrinsic limitations that may affect accuracy, reproducibility, and ecological validity (17).

Most conventional tests rely on the clinician's visual observation and interpretation of patient responses. For instance, cover test outcomes depend on detecting subtle corrective movements of the eyes, while stereoacuity assessments require subjective judgments of depth perception (47). Observer experience, fatigue, and attentional factors may introduce variability, limiting inter- and intra-rater reliability. This issue is particularly relevant in pediatric populations, where attention span, comprehension, and motivation may fluctuate

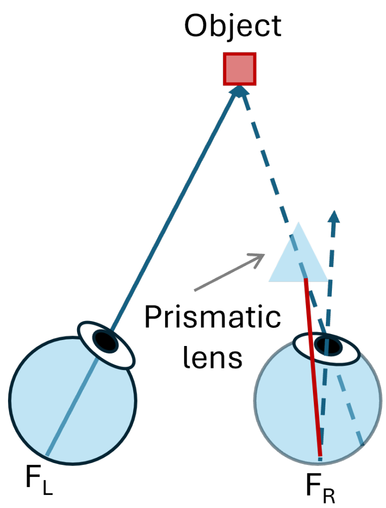

Figure 2.12 Illustration of the effect of prisms on ocular alignment. Prisms deviate light to compensate for eye misalignment, demonstrating how prism diopters alter visual direction.

during testing. Consequently, repeated testing or alternative methods may be necessary to confirm findings and ensure reliable assessment.

Although the prism cover test provides a standardized measure of ocular deviation in prism diopters, its resolution is constrained by the discrete increments of available prisms. Small deviations below the minimum measurable step may go undetected, particularly in cases of microstrabismus or intermittent phorias (7). Similarly, stereoacuity tests often report thresholds in relatively coarse increments, such as 40, 60, or 80 arcseconds, limiting sensitivity to subtle improvements or deterioration. Visual acuity charts, including Snellen or LogMAR, also exhibit finite resolution and can be influenced by environmental factors such as lighting, contrast, and patient cooperation (49). These limitations hinder the precise quantification of minor deficits, which may be critical for early detection of amblyopia or mild binocular dysfunctions.

Conventional clinical methods are also affected by monocular cues and environmental conditions. Many stereotests and fixation tasks are susceptible to monocular cues, such as shadows, outlines, or relative size, which may allow patients to infer depth or alignment without true binocular integration (47). Ambient lighting, target contrast, and viewing distance can further influence outcomes, making standardization across different clinical settings challenging. Additionally, traditional tests are typically conducted under static, simplified conditions, which may not accurately reflect the dynamic and complex visual environments encountered in daily life. Binocular coordination and oculomotor performance in natural, three-dimensional contexts may differ substantially from results obtained in the clinic (33).

Most conventional procedures primarily evaluate static or quasi-static aspects of binocular function. For example, the cover test provides information about ocular alignment at a single fixation distance, while standard stereoacuity tests present isolated, static stimuli (17). Dynamic components, such as vergence tracking during moving targets, fixation stability during saccades, or adaptation to changes in depth, are not captured by these methods. As a result, functional deficits—particularly in patients with intermittent strabismus, subtle suppression, or convergence insufficiency—may remain undetected. This limitation underscores the need for complementary objective assessment tools that can capture real-world visuomotor performance.

Children, elderly patients, and individuals with cognitive impairments may struggle to follow instructions, sustain attention, or provide consistent responses (47). Similarly, patients with neurological disorders, nystagmus, or ocular motility restrictions may yield inconsistent or non-interpretable results. Certain subtle conditions, such as microstrabismus or anomalous retinal correspondence, may not be reliably detected using conventional methods alone (14). Clinicians must therefore combine multiple assessments, interpret results cautiously, and consider longitudinal observations to obtain a complete understanding of binocular function.

Despite these limitations, conventional methods remain essential for clinical practice due to their simplicity, rapid administration, and interpretability. However, awareness of these constraints is crucial for accurate diagnosis, treatment planning, and monitoring. Clinicians should consider technological solutions that complement traditional tests. Eye-tracking systems enable continuous, objective measurements of ocular alignment, vergence, and fixation stability, providing detailed quantitative data beyond what is possible with observer-based methods (42). Virtual reality environments allow controlled presentation of dynamic, stereoscopic stimuli at varying depths, improving ecological validity and revealing subtle deficits that may be missed in static tests. Digital stereotests and automated analysis tools can enhance resolution, reduce observer bias, and facilitate longitudinal monitoring.

Integration of conventional methods with these modern technologies allows clinicians to retain the familiarity and interpretability of standard tests while expanding quantitative precision, functional assessment, and reproducibility. Such hybrid approaches are particularly valuable for evaluating treatment outcomes, guiding individualized interventions, and advancing research in binocular visuomotor disorders. Understanding the limitations of traditional clinical methods also informs the design of new assessment paradigms and emphasizes the importance of objective, repeatable, and functionally relevant measurements (50).

In summary, while visual acuity testing, stereopsis measurements, and cover/prism cover tests provide indispensable clinical information, they are limited by subjectivity, resolution constraints, environmental sensitivity, and restricted functional assessment. Awareness of these limitations is essential for interpreting clinical data accurately and for incorporating emerging technological solutions that enhance the assessment of binocular vision.

2.3 Eye Trackers in Research

Eye tracking has emerged as a pivotal technology for assessing binocular vision and visuomotor function in both clinical and research settings. Eye trackers provide objective, continuous measurements of ocular position, movement dynamics, and binocular coordination, overcoming many of the limitations inherent to traditional observer-based methods (51).

Principles of Eye Tracking Eye trackers measure the position and movement of the eyes relative to the head or visual environment. The most common technologies include video-based infrared (IR) eye trackers, which illuminate the eye with IR light and track reflections from the cornea and pupil, and scleral search coil systems, which provide high-precision measurements via a small coil placed on the eye within a magnetic field. Modern video-based systems can track both eyes simultaneously, enabling the assessment of vergence, fixation disparity, and binocular coordination in real time(52).

Calibration procedures are essential to ensure accuracy. Typically, participants are asked to fixate a series of known targets at varying positions, allowing the system to map eye positions to corresponding points in visual space. For binocular measurements, calibration must account for the geometry of both eyes, including interpupillary distance and potential alignment deviations (53).

Applications in Binocular Vision Research Eye trackers have been instrumental in understanding the dynamics of binocular control. They allow researchers to quantify vergence movements, including both convergence and divergence responses, under static and dynamic conditions (54). High temporal resolution enables the study of fast vergence components, such as phasic responses to sudden disparity changes, as well as slow, tonic adjustments during sustained fixation.

In stereopsis research, eye trackers facilitate the measurement of fixation stability, ocular drift, and micro-saccades, which are crucial for fine depth discrimination. Abnormalities in

Figure 2.13 Schematic of a binocular video-based eye-tracking setup. Infrared light illuminates the eyes, and cameras record reflections from the cornea and pupil. The system computes gaze direction and binocular coordination.

these oculomotor parameters are often associated with amblyopia, strabismus, or convergence insufficiency (55). Eye-tracking data can reveal subtle deficits that conventional clinical tests might miss, providing a richer understanding of binocular function.

Eye trackers also allow the study of dynamic visual tasks, such as tracking moving targets, reading, or interacting with three-dimensional virtual environments. These applications are particularly relevant for assessing functional performance, as real-world tasks often involve continuous coordination of saccades, smooth pursuit, vergence, and accommodation (56).

Clinical and Pre-clinical Applications Eye-tracking technologies have become a cornerstone in behavioral, cognitive, and clinical research, supported by recent advances in computer vision and artificial intelligence (57). In clinical research, eye trackers provide quantitative biomarkers for diagnosing binocular vision disorders and monitoring treatment outcomes. Objective and automated approaches to the assessment of heterophoria have been proposed to overcome the subjectivity and limitations of traditional clinical methods such as the cover test (58). For example, objective measurements of vergence dynamics can inform the severity of convergence insufficiency, quantify intermittent exotropia, and evaluate response to vision therapy or occlusion treatment (59).

Pre-clinical research benefits from eye tracking by enabling non-invasive, high-resolution studies of oculomotor physiology. Animal studies using scleral search coils have elucidated the neural mechanisms underlying vergence and binocular coordination, providing insight into three-dimensional eye movement control (60). These insights translate into improved diagnostic and therapeutic strategies for human patients.

Technical Considerations Several factors influence the precision and accuracy of eye-tracking measurements. Pupil size, eye morphology, lighting conditions, and calibration quality all affect signal reliability (61). Head movements must be compensated, either via chin rests, bite bars, or head-mounted systems, to maintain measurement fidelity. Additionally, real-time binocular tracking requires careful synchronization of camera data and compensation for parallax, particularly in immersive or three-dimensional environments.

Sampling frequency is critical for capturing fast oculomotor events. High-speed eye trackers (500–1000 Hz) are required to accurately analyze saccades, microsaccades, and phasic vergence responses, whereas lower sampling frequencies may suffice for tonic or slow eye movements (62).

Integration with Virtual and Augmented Reality Eye trackers have been increasingly integrated into virtual reality (VR) and augmented reality (AR) systems, allowing simultaneous assessment of binocular function and interaction with immersive environments. Head-mounted eye trackers measure gaze and vergence while participants navigate three-dimensional scenes, providing ecologically valid data on binocular coordination and visual behavior (63). Such integration is particularly valuable for evaluating visual performance under naturalistic viewing conditions and for designing interactive vision therapy interventions.

For example, eye-tracking data can guide adaptive stimulus presentation, where visual targets are dynamically adjusted based on real-time gaze position, improving training efficacy and patient engagement. VR-based eye tracking also enables the study of vergence–accommodation conflicts and other perceptual phenomena relevant to stereoscopic displays (25).

Advantages Over Conventional Clinical Methods Compared to standard clinical assessments, eye trackers offer several advantages. They provide objective, high-resolution data that are reproducible across sessions and observers. Continuous recording captures dynamic behavior, including subtle deficits in vergence, fixation stability, and binocular coordination. Eye trackers also facilitate longitudinal monitoring (64), allowing quantitative evaluation of therapy progress and recovery of binocular function .

Moreover, eye-tracking technology can detect movements and dynamic adjustments that are invisible to the naked eye, revealing underlying oculomotor strategies and compensatory mechanisms. This capability is particularly valuable for research into amblyopia, intermittent strabismus, and other subtle binocular dysfunctions (65).

Limitations and Challenges Despite their advantages, eye trackers have limitations. Calibration can be challenging in young children or patients with strabismus. Data quality may be compromised by excessive head movement, eyelid occlusion, or low contrast pupils (66). High-speed, high-precision systems can be expensive and require technical expertise, limiting widespread clinical adoption. Additionally, interpretation of eye-tracking metrics requires understanding of oculomotor physiology and careful integration with other clinical data.

2.3.1 AR/VR-based Vision Therapy Systems

Augmented reality (AR) and virtual reality (VR) technologies have emerged as effective tools for the assessment and rehabilitation of binocular vision disorders. Immersive systems allow the presentation of controlled three-dimensional visual environments in which binocular disparity, depth cues, motion trajectories, and target properties can be precisely manipulated, offering unique opportunities to evaluate and train visual and oculomotor functions (50). In addition, VR-based platforms have been successfully applied to the treatment of vergence and accommodative dysfunctions, demonstrating their potential as flexible and engaging alternatives to conventional clinical approaches (67).

Virtual reality therapy typically employs head-mounted displays that deliver separate images to each eye, generating binocular disparity cues that simulate depth. By controlling the position, motion, and properties of visual targets, VR systems can elicit specific vergence responses, train convergence and divergence, and provide immediate feedback to guide patients toward improved binocular coordination. Patients with convergence insufficiency can practice maintaining binocular alignment on near targets while performing tasks of increasing complexity or duration. The controlled nature of VR environments allows precise modulation of visual parameters such as target size, contrast, and motion, enabling graduated and adaptive training protocols (68).

Augmented reality overlays virtual objects onto the real environment, allowing patients to interact with natural surroundings while receiving controlled visual stimuli. This approach is particularly useful for tasks requiring visuomotor integration, such as reaching, grasping, and spatial navigation. By combining visual and proprioceptive feedback, AR systems support the training of binocular coordination in functional contexts, offering a bridge between laboratory exercises and everyday tasks. The immersive and interactive nature of these systems enhances patient engagement, which is a key factor in sustaining compliance and optimizing therapeutic outcomes (69).

Several studies have demonstrated the effectiveness of immersive visual systems for binocular training. VR-based exercises have been applied to improve stereopsis in children with amblyopia, showing measurable gains in depth discrimination and binocular cooperation after repeated sessions (68). Similarly, VR paradigms targeting vergence control have been employed in adults with intermittent exotropia, leading to increased convergence amplitude, reduced suppression, and improved fixation stability. These interventions rely on precise control of stimulus parameters and the ability to adjust task difficulty based on real-time performance, ensuring that patients are challenged appropriately without inducing fatigue or frustration (69).

The design of AR and VR therapy tasks frequently incorporates principles of perceptual learning, which propose that repeated exposure to targeted stimuli can induce neural plasticity and improve visual performance (69). Tasks are structured to challenge binocular integration while providing immediate feedback, promoting the use of both eyes and reducing suppression of the weaker eye. Adaptive difficulty adjustment ensures that the patient remains within an optimal range for inducing neural adaptation, maximizing the effectiveness of training sessions (68).

Immersive systems also enable integrated assessment. Eye-tracking technologies embedded in head-mounted displays allow continuous monitoring of gaze direction, fixation stability, saccadic accuracy, and vergence responses. This capability provides objective and high-resolution data on oculomotor function and binocular coordination, complementing conventional clinical measurements. Real-time monitoring allows clinicians to quantify patient progress and adjust training parameters dynamically, offering individualized therapy based on measurable performance metrics (70).

The versatility of AR and VR systems extends to the simulation of a broad spectrum of visual conditions, from simple static targets to complex dynamic environments with multiple depth layers and moving objects. This capability facilitates the assessment of functional performance in tasks that resemble daily activities, such as reading, navigation, or object interaction in three-dimensional space (71). It also enables controlled investigation of perceptual phenomena like the vergence–accommodation conflict, where vergence cues indicate a virtual depth while accommodation remains fixed at the display distance (25).

Despite their advantages, immersive visual systems require careful calibration and technical optimization. Head-mounted displays must be adjusted for interpupillary distance and lens distortion, while eye-tracking systems must be calibrated for accurate mapping of gaze within the virtual environment. Display properties, including resolution, latency, and field of view, can influence both the quality of therapy and the precision of assessments.

Patient-specific factors, such as susceptibility to motion sickness or difficulty maintaining attention, must also be considered, particularly in pediatric populations or individuals with neurological impairments.

Immersive visual systems have been implemented in both research and clinical contexts. In research, VR and AR provide platforms for controlled experimentation on binocular function, oculomotor control, and perceptual learning. Clinically, these technologies enable individualized therapy protocols tailored to specific deficits and dynamically adjusted according to performance. By combining assessment and training in a single immersive platform, these systems allow precise evaluation of oculomotor function and targeted interventions that are challenging to achieve with conventional methods alone (69).

Comparative studies indicate that AR and VR platforms can detect subtle binocular coordination deficits that may be overlooked in standard clinical tests. Patients with intermittent strabismus, mild suppression, or subclinical convergence insufficiency can exhibit measurable impairments in immersive tasks even when conventional assessments suggest normal function (70). These findings emphasize the sensitivity of immersive systems and support their role as complementary tools for both assessment and rehabilitation of binocular vision disorders (68).

In conclusion, AR and VR technologies offer controlled, interactive, and dynamic visual environments for the assessment and rehabilitation of binocular vision. By allowing precise manipulation of visual stimuli and integration with eye-tracking measurements, immersive systems enhance the evaluation of oculomotor function and support targeted training of binocular coordination. While technical and patient-related factors must be carefully addressed, AR and VR platforms constitute a significant complement to conventional clinical methods, providing new possibilities for both research and therapy in binocular vision disorders (68).

2.3.2 Digital Amblyopia Treatments

Digital technologies have increasingly been applied to the treatment of amblyopia, offering alternatives and complements to conventional occlusion therapy. These approaches leverage computer-based programs, tablet applications, and serious games to deliver targeted visual stimuli in a controlled, engaging, and adaptive manner (72). Digital treatments are designed to promote binocular cooperation, reduce suppression of the amblyopic eye, and improve visual acuity and stereopsis, capitalizing on the plasticity of the visual system, particularly during critical periods of development.

A key advantage of digital amblyopia therapy is the ability to present dichoptic stimuli, in which each eye receives a different visual input that is carefully balanced to encourage the use of both eyes simultaneously. In traditional patching therapy, the stronger eye is occluded, forcing the amblyopic eye to work independently. While effective in improving monocular acuity, patching does not address binocular dysfunction and can lead to poor compliance, especially in children. Dichoptic digital therapies, by contrast, aim to reduce suppression and restore binocular integration through interactive tasks that require the cooperation of both eyes (72).

Several types of digital interventions have been developed. One common approach is the use of video games specifically designed for amblyopia therapy. These games present tasks in which elements visible to the dominant eye are reduced in contrast or occluded, while the amblyopic eye receives high-contrast stimuli. The game mechanics are structured to ensure that successful performance depends on the participation of both eyes. Studies have shown that such game-based training can lead to improvements in visual acuity, contrast sensitivity, and stereoacuity, with the added benefit of higher engagement and adherence compared to traditional patching (72).

Tablet-based applications are another popular format for delivering digital therapy. These systems often include a variety of visual tasks that target different aspects of visual function, including spatial resolution, contrast discrimination, and depth perception. The software can adapt in real time to the user's performance, increasing difficulty as improvement is detected. This adaptive approach maintains the tasks within an optimal range for inducing perceptual learning and neural plasticity, maximizing therapeutic benefit (72).

Digital treatments can also integrate eye-tracking technologies to monitor fixation, gaze stability, and binocular coordination during therapy sessions. Eye-tracking provides objective measures of patient performance, enabling the system to adjust stimuli dynamically and giving clinicians quantitative feedback on progress. For instance, the system can detect when the amblyopic eye is underused and increase stimulus contrast or adjust the presentation to encourage its engagement (73).

Recent studies have highlighted the efficacy of digital binocular therapies in both children and adults. Children with amblyopia undergoing dichoptic training have demonstrated improvements in visual acuity and stereopsis over a period of several weeks, even in cases where traditional patching was insufficient (73). In adults, who have traditionally been considered less responsive to amblyopia therapy due to reduced neural plasticity, dichoptic digital interventions have produced measurable gains in binocular function, suggesting that targeted perceptual learning can induce cortical changes beyond the critical period (69).

Digital amblyopia treatments also allow for precise customization of therapy parameters. The contrast, size, motion, and position of stimuli can be individually adjusted to accommodate specific deficits, and therapy can be conducted at home under remote supervision. This flexibility addresses some of the limitations of clinic-based therapy, including accessibility and adherence, and facilitates higher-frequency training sessions, which are associated with better outcomes (72).

Beyond visual acuity, digital therapies can target multiple aspects of binocular vision. Training protocols can incorporate tasks designed to improve vergence control, reduce suppression, and enhance stereoacuity, supporting a more holistic rehabilitation of the visual system. By engaging both sensory and oculomotor mechanisms, these therapies aim to restore functional binocular vision, rather than solely improving monocular performance (68).

Compliance is a critical factor in amblyopia therapy. Conventional patching often suffers from poor adherence due to discomfort or social stigma. Digital therapies, by providing gamified, interactive experiences, can significantly improve patient engagement. Feedback, rewards, and adaptive difficulty all contribute to maintaining motivation, which is particularly important in pediatric populations (72).

While digital amblyopia treatments have shown promise, challenges remain. Ensuring adequate monitoring of patient performance at home is essential to maintain therapeutic efficacy. Moreover, long-term retention of gains and generalization to real-world visual tasks require further investigation. Integration with eye-tracking and virtual reality platforms may further enhance therapy by providing immersive, three-dimensional stimuli that mimic natural viewing conditions (71).

In summary, digital amblyopia treatments offer a flexible, engaging, and adaptive approach to vision therapy. By leveraging dichoptic stimulation, serious games, and eye-tracking feedback, these interventions promote binocular cooperation, reduce suppression, and improve multiple aspects of visual function. Their advantages in terms of compliance, adaptability, and remote delivery position them as a valuable complement or alternative to conventional therapies, supporting the rehabilitation of both sensory and oculomotor aspects of binocular vision (68; 71; 72).

Chapter 3

Methodological Challenges

3.1 A Virtual Reality Implementation of the Cover–Uncover Test

3.1.1 Clinical Cover Test

The Cover–Uncover Test is one of the most widely employed clinical procedures for evaluating ocular alignment and diagnosing binocular visuomotor disorders in both orthoptic and ophthalmologic practice. The test consists of alternately occluding one eye while the patient fixates a visual target, allowing clinicians to observe refixation movements of the uncovered eye. These observations enable the identification of manifest deviations (tropias) as well as latent deviations (phorias) when binocular fusion is disrupted (14). Owing to its simplicity, rapid administration, and diagnostic relevance, the Cover–Uncover Test remains a cornerstone of clinical assessment of ocular motility and binocular vision.

Despite its clinical utility, the procedure is predominantly qualitative or, at best, semi-quantitative. In routine practice, clinicians rely on visual inspection of eye movements, often supported by prisms or synoptophore devices to estimate the magnitude of deviation (74). This reliance on subjective judgment limits the sensitivity of the test, particularly for detecting small deviations or subtle oculomotor instabilities, such as those observed in intermittent strabismus. Furthermore, measurement accuracy is influenced by several factors, including clinician expertise, patient cooperation, fixation stability, and testing conditions such as viewing distance and gaze direction.

Previous studies have highlighted the variability introduced by factors such as fixation instability and small head or eye movements during binocular testing. Even during attempted steady fixation, involuntary fixational eye movements can alter interocular alignment, potentially obscuring subtle latent deviations or exaggerating manifest misalignments (75). In addition, comprehensive evaluation of binocular function across multiple gaze positions is time-consuming and may induce visual fatigue or reduced cooperation, particularly in pediatric or clinical populations, limiting the feasibility of fully quantitative assessment in routine practice (76).

To address these limitations, recent research has explored the use of digital technologies, including video-based eye tracking and automated testing systems, to provide more objective and reproducible measurements of ocular deviations. These approaches aim to preserve the clinical rationale of the Cover–Uncover Test while improving measurement sensitivity and repeatability. Importantly, they do not directly replace clinical evaluation, but rather extend it by enabling quantitative characterization of ocular alignment under controlled conditions (70; 77). Such developments are particularly relevant for studies requiring fine-grained analysis of binocular coordination and for the implementation of VR-based paradigms.

3.1.2 Translating the Cover Test into Virtual Reality

Recent advances in immersive technologies have created new opportunities to translate classical orthoptic examinations into controlled digital environments where eye movements can be measured quantitatively. Head-mounted displays (HMDs) equipped with integrated eye trackers enable the implementation of binocular vision tests within virtual environments, while simultaneously recording gaze direction, fixation stability, and relative ocular alignment with high temporal resolution (52). This capability allows continuous monitoring of refixation dynamics during cover–uncover paradigms and supports automated, observer-independent analysis.

A growing body of work has investigated the use of virtual reality (VR) for the assessment of binocular visual function. VR-based systems have been successfully employed for stereopsis measurement, dichoptic stimulation, and binocular training, demonstrating that immersive environments can provide reliable and reproducible visual assessments under controlled conditions (**?**). The ability to present independent stimuli to each eye enables the implementation of dichoptic paradigms and controlled monocular occlusion, which are difficult to achieve with conventional display systems. For instance, occlusion can be simulated by selectively suppressing the visual input to one eye, while virtual stimuli can be presented at controlled depths and eccentricities (77).

Beyond replicating traditional clinical procedures, VR offers significant advantages in terms of experimental control and standardization. Virtual environments allow precise manipulation of head orientation, stimulus position, and binocular disparity, thereby reducing variability associated with uncontrolled head movements or inconsistent fixation. Moreover, data acquisition is automated and digitized, minimizing observer bias and enabling high-throughput analysis (51; 78). These features are particularly advantageous when testing populations with limited compliance, such as children or patients with visuomotor impairments.

Importantly, translating the Cover–Uncover Test into VR does not simply reproduce the clinical procedure, but introduces a framework for quantitative analysis of oculomotor behavior under controlled yet flexible conditions. However, it should be noted that VR-based measurements rely on eye-tracking signals and therefore provide an indirect estimate of ocular alignment, which may not be strictly equivalent to clinical measures obtained with prism-based methods. Within this context, VR approaches should be interpreted as complementary tools that extend, rather than replace, traditional clinical assessments. This perspective is essential when evaluating their potential application in both research and clinical settings.

3.1.3 Implementation of the VR Cover–Uncover Test

In the present work, we implemented a digital version of the classical Cover–Uncover Test within an immersive virtual reality environment, with the goal of establishing a controlled and quantitative framework for studying binocular visuomotor behavior. The test was performed using a head-mounted display (HTC Vive Pro Eye) equipped with an integrated Tobii eye tracker, enabling continuous binocular recording of gaze direction at 120 Hz, with a nominal spatial accuracy of approximately 1° of visual angle (78).

Monocular occlusion was simulated digitally by selectively disabling the visual output of one display panel of the headset, thereby restricting visual stimulation to a single eye while maintaining effective occlusion of the contralateral eye. This approach reproduces the essential structure of the clinical Cover–Uncover Test, while allowing precise control over stimulus timing, viewing conditions, and gaze monitoring. In contrast to conventional clinical procedures, the VR implementation enables systematic manipulation of head orientation, fixation distance, and stimulus eccentricity within a unified experimental framework.

Eye movements and fixation behavior were continuously monitored using the integrated eye tracker. For each eye, the system provides a three-dimensional gaze direction vector expressed in the headset reference frame. From this signal, horizontal and vertical components of gaze were derived to obtain angular estimates of eye orientation. In particular, the horizontal gaze direction (azimuth) was computed as:

$$\theta_{\text{azimuth}} = \arctan\left(\frac{x}{z}\right)$$

where x and z represent the horizontal and forward components of the gaze direction vector, respectively. The resulting angle was expressed in degrees of visual angle. An analogous computation was used to derive the elevation component. These quantities provide an estimate of eye orientation relative to the eye tracker coordinate system and constitute the basis for quantifying changes in ocular alignment across occlusion conditions.

During the Cover–Uncover procedure, deviations in ocular alignment were inferred from changes in gaze direction of the uncovered eye following removal of occlusion. Specifically, the refixation movement required to re-establish fixation on the target was quantified in terms of angular displacement in azimuth and elevation. Within this framework, the measured deviation represents an indirect estimate of ocular misalignment, derived from eye-tracking signals rather than a direct clinical measurement of extraocular muscle imbalance.

Gaze data were synchronized with head orientation signals obtained from the HMD's inertial measurement unit, allowing compensation for small head rotations and translations. This integration ensured that variations in gaze direction could be interpreted with respect to a stable reference frame, reducing the impact of head motion on the estimation of ocular alignment.

Overall, this implementation establishes a reproducible VR-based framework for the quantitative assessment of eye alignment, combining automated data acquisition with the conceptual structure of a classical clinical test, while explicitly acknowledging the indirect nature of the measurement.

3.1.4 Fixation Target

The fixation stimulus consisted of a 1.4° Maltese cross, over which a rotating ellipse was superimposed, with a major axis of 0.8° and a minor axis of 0.4° (Figure 3.1).

The visual appearance of the stimulus was carefully controlled: the background, the Maltese cross, and the rotating ellipse were rendered in distinct shades of gray to optimize contrast while minimizing visual adaptation effects. This configuration ensured sufficient saliency of the fixation target without introducing excessive luminance differences that could

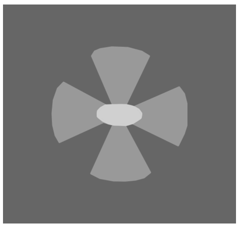

Figure 3.1 Fixation stimulus used in the virtual reality cover test. The target consists of a 1.4° Maltese cross with a centrally superimposed rotating ellipse (0.8° × 0.4°). The stimulus is rendered in distinct shades of gray to optimize contrast while minimizing visual adaptation effects.

lead to afterimages or visual discomfort, thereby promoting stable fixation over time within a naturalistic viewing condition.

The fixation stimulus used in the digital cover test consisted of a Maltese cross presented within the virtual environment. The stimulus subtended 1.4° of visual angle and was selected due to its well-defined geometry and high-contrast structure, which provide clear spatial references along both horizontal and vertical axes. These characteristics are known to facilitate precise and stable fixation, and for this reason the stimulus is widely adopted in both clinical practice and experimental studies on oculomotor behavior.

The continuous motion of the ellipse was therefore designed to sustain the participant's engagement and promote foveation on the central region of the stimulus, which is critical for accurate eye-tracking measurements. The introduction of this dynamic element was also supported by observations from preliminary experiments, indicating that purely static stimuli may lead to reduced attention over time and increased fixation variability.

The stimulus was implemented in a custom Unity3D environment with dedicated shaders to ensure consistent luminance, contrast, and temporal dynamics across trials. This design aimed to promote stable fixation while reducing potential confounds such as afterimages, flicker, or unintended accommodative responses (51; 52). In particular, independent images were presented to each eye according to the calibrated geometry of the head-mounted display, allowing precise control over binocular disparity and vergence demand. This design choice enables the system to replicate the natural visual conditions of clinical cover testing, where binocular fusion is established during the uncovered phases. Additionally, stereoscopic rendering ensures that the spatial position of the fixation target is accurately perceived in depth, which is essential for maintaining stable vergence and for preventing the introduction of artificial disparities that could bias the measurement of ocular alignment.

3.1.5 Emerging Methodological Challenges

While VR provides powerful tools for precise stimulus control and quantitative measurement of gaze behavior, translating the Cover–Uncover Test into an immersive environment introduces methodological challenges that are largely absent in traditional clinical settings. In particular, the reliability of ocular alignment estimates in VR critically depends on the accuracy and stability of eye-tracker calibration. Even small calibration errors can propagate into systematic biases in gaze estimation, especially when assessing subtle deviations or when measurements are performed under monocular viewing conditions.

Prolonged use of head-mounted displays may also induce visual fatigue and discomfort, potentially affecting fixation stability, vergence responses, and pupil dynamics. Although HMDs allow natural head movements, these movements can introduce geometric distortions in gaze estimation due to changes in the relative position between the eyes and the display optics. In addition, compensatory eye movements driven by vestibular and proprioceptive inputs may interact with the measured signal, complicating the interpretation of ocular alignment.

Another intrinsic limitation of stereoscopic HMDs is the vergence–accommodation conflict, arising from the mismatch between the vergence distance required to fixate a virtual object and the fixed focal distance of the display. This dissociation can influence binocular coordination, particularly in tasks involving multiple fixation distances or peripheral targets, which are relevant in comprehensive Cover–Uncover Test paradigms.

Rather than treating these factors as secondary limitations, we explicitly investigated their impact on VR-based measurements through a series of pilot experiments. Each study was designed to isolate a specific methodological factor and quantify its effect on gaze estimation and alignment measures. In particular, we examined the influence of monocular versus binocular calibration, assessed the impact of visual fatigue on signal stability, quantified the effect of head rotations on gaze accuracy, and evaluated measurements across different fixation distances to characterize the role of vergence–accommodation conflict.

These analyses provide a methodological foundation for interpreting VR-based estimates of ocular alignment and highlight both the potential and the current limitations of immersive technologies for quantitative assessment of binocular visuomotor function.

3.2 Eye-Tracker Calibration

3.2.1 The Critical Role of Calibration in VR-Based Ocular Alignment Measurement

Accurate calibration of eye-tracking systems represents a fundamental prerequisite for obtaining reliable gaze measurements. In video-based eye trackers, calibration establishes the mapping between the detected pupil features and the corresponding gaze direction in the visual scene. Errors in this mapping process can lead to systematic deviations between the estimated gaze vector and the true visual direction, thereby compromising the reliability of gaze-based measurements (51; 52).

In the context of immersive virtual reality (VR), calibration becomes even more critical. Head-mounted displays (HMDs) integrate compact infrared cameras that track eye movements within a constrained optical geometry. While modern systems provide built-in calibration routines, these procedures are primarily designed for general gaze interaction tasks rather than for precise scientific measurements. Several studies have shown that eye-tracking accuracy in VR headsets may vary substantially across participants and viewing conditions, with typical errors ranging from fractions of a degree to several degrees of visual angle (78). Such variability can significantly affect experiments that require precise estimation of gaze direction or ocular alignment.

This issue is particularly relevant when studying binocular visuomotor function. Many paradigms in vision science rely on the accurate estimation of the gaze direction of each eye independently in order to compute vergence angles or evaluate ocular misalignment. Even small calibration errors can propagate into large uncertainties in the estimation of binocular coordination, potentially masking subtle deviations or producing artificial disparities between the two eyes. Therefore, calibration accuracy represents a critical factor for the reliable implementation of binocular assessment paradigms in VR environments.

3.2.2 Calibration Challenges in Binocular Measurements

Standard calibration procedures implemented in commercial VR headsets typically rely on binocular calibration, in which both eyes are calibrated simultaneously while the participant fixates a set of targets distributed across the visual field. While this approach is sufficient for many consumer applications, it may introduce limitations when applied to studies of binocular vision. In particular, the calibration algorithm implicitly assumes consistent and symmetric gaze behavior across both eyes, an assumption that may not hold in individuals

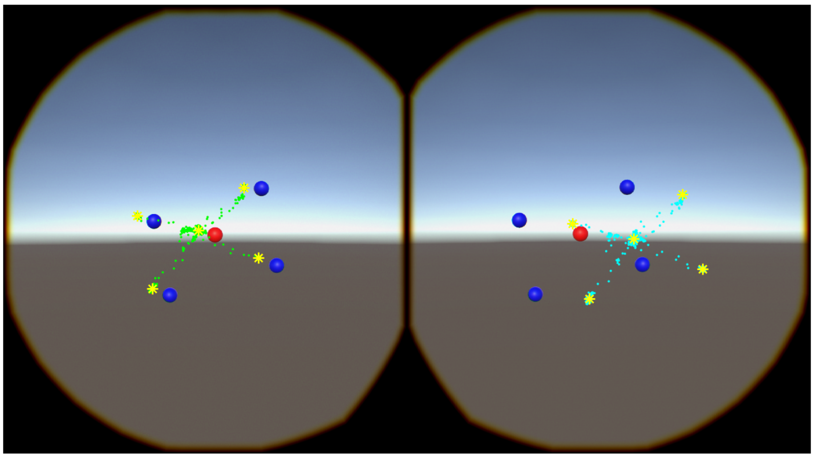

Figure 3.2 Example of gaze estimation error produced by standard binocular calibration in a VR headset. Small calibration inaccuracies can lead to systematic offsets between the estimated gaze direction and the true fixation target, affecting the reliability of ocular alignment measurements.

with binocular asymmetries, ocular dominance differences, or subtle ocular misalignments (79).

In the context of a VR-based Cover Test, these limitations become particularly critical. The test relies on detecting small refixation movements and measuring the relative alignment of the two eyes during monocular viewing conditions. Any systematic calibration bias affecting one eye more than the other may therefore introduce errors in the estimation of ocular deviation.

Figure 3.2 illustrates how small calibration inaccuracies can produce systematic offsets between the measured gaze direction and the true target position. When binocular measurements are derived from these estimates, such offsets may lead to incorrect estimation of vergence angles or ocular deviations.

3.2.3 Pilot Investigation of Calibration Accuracy

To quantify the reliability of the built-in calibration procedure, we conducted a pilot study involving a small group of participants ($n = 7$). Participants aged 20–30 years included healthy individuals and two subjects with binocular disorders, one of whom presented with a clinically diagnosed 5° strabismus. Exclusion criteria included ocular deviations exceeding 20° and conditions prone to cybersickness. All participants provided informed consent,

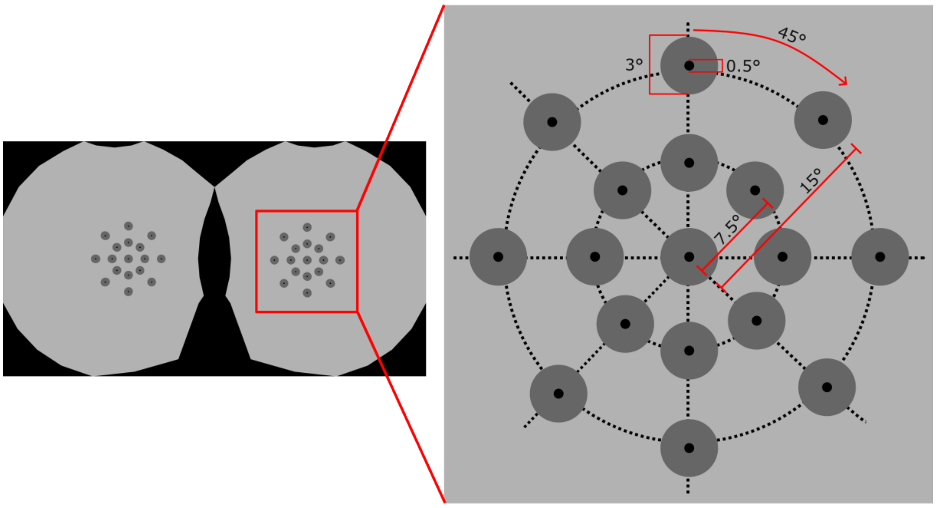

Figure 3.3 Spatial distribution of fixation targets used during the pilot calibration experiment. Targets were distributed across central and peripheral regions of the visual field in order to evaluate gaze estimation accuracy across the workspace.

and the protocol was approved by the University of Genoa Ethics Committee (Protocol ID 2025/07).

Participants were instructed to fixate a set of targets distributed across the visual field while gaze data were recorded using the integrated HTC Vive Pro Eye tracker (Tobii SDK). The spatial coordinates of each target were known a priori within the virtual environment, allowing the estimation of gaze error as the angular deviation between the measured gaze vector and the true target direction. The target distribution used in the pilot experiment is illustrated in Figure 3.3, covering central and peripheral regions of the visual field.

Preliminary observations suggest that binocular calibration is generally adequate for participants with normal binocular vision and no ocular deviations. However, in individuals with binocular visual disorders, standard binocular calibration often fails or produces inaccurate and unreliable gaze estimates, compromising the precision of ocular alignment measurements.

3.2.4 Custom Monocular Calibration Procedure

To overcome these limitations, we implemented a custom monocular calibration procedure, designed to independently calibrate each eye, following a rationale consistent with clinical needs: in participants with strabismus, amblyopia, or other binocular dysfunctions, one eye may be suppressed or misaligned during standard binocular calibration, introducing systematic bias (52; 78).

The procedure consisted of 17 fixation targets: one central, and two concentric rings at 7.5° and 15° eccentricity, with eight targets per ring. Targets were 3° gray disks with a 0.5° black dot at the center, displayed against a gray background to reduce visual adaptation. Participants used a controller to trigger recording once they perceived stable fixation for one second per target, and could rest their eyes between fixations.

Calibration was performed in two computational steps:

1. **Rigid co-registration:** The 3D gaze vectors were projected onto the image plane using Unity's `WorldToScreenPoint`. Each centroid of measured gaze points was paired with the corresponding target location. A rigid transformation (rotation + translation, without scaling) aligning the measured and target point clouds was computed using the Kabsch-Umeyama algorithm (80; 81), ensuring optimal alignment of the gaze data in the planar projection.

2. **Nonlinear distortion correction:** Residual spatial nonlinearities were corrected using a generalized quadratic polynomial lens distortion model. This 7-parameter model accounts for three Radial Rotationally Invariant (RRI) coefficients (k_1, k_2, k_3) and a combination of radial and tangential displacements weighted by parameters (t_1, t_2, p, q). The distortion correction is applied as:

$$\begin{pmatrix} \Delta x \\ \Delta y \end{pmatrix} = \begin{pmatrix} x \\ y \end{pmatrix} \left(k_1 r^2 + k_2 r^4 + k_3 r^6\right) + p \begin{pmatrix} t_1 & -t_2 & 0 \\ 0 & t_1 & -t_2 \end{pmatrix} + q \begin{pmatrix} 0 & t_2 & t_1 \\ -t_2 & -t_1 & 0 \end{pmatrix} \begin{pmatrix} x^2 \\ xy \\ y^2 \end{pmatrix}$$

where $(\Delta x, \Delta y)$ are the corrections applied to the distorted fixation points (x, y), $r^2 = x^2 + y^2$, $k_1, k_2, k_3 \in \mathbb{R}$ are the RRI coefficients, $t_1, t_2 \in \mathbb{R}$ are radial and tangential displacement coefficients, and $p, q \in \mathbb{R}$ weight their contribution. Parameters were estimated using nonlinear least-squares minimization to minimize the Euclidean distance between corrected gaze points and target locations, allowing flexible compensation beyond standard radial-tangential models.

3.2.5 Pilot Study Conditions and Results

To evaluate the impact of calibration strategies on gaze accuracy, we tested four conditions: hybrid binocular-monocular and monocular-only calibrations in healthy participants ($n = 5$) and participants with binocular disorders ($n = 2$). Monocular testing involved activating only one HMD display panel at a time, isolating the stimulated eye.

First Condition: Hybrid Binocular–Monocular Calibration in Healthy Subjects

In healthy participants, we first assessed the effect of combining standard binocular calibration with a subsequent monocular correction. Gaze centroids were compared to the fixation targets across nine validation positions, and RMSE was computed for each eye.

As shown in Figure 3.4 panel A, the hybrid calibration reduced the average RMSE from 0.76° ± 0.20° (95% CI: [0.62°, 0.90°]) in the binocular-only condition to 0.59° ± 0.13° (95% CI: [0.50°, 0.69°]) after applying monocular correction. A paired t-test confirmed that this reduction was statistically significant ($p = 0.0440$), indicating that even in healthy participants, a hybrid approach can improve gaze accuracy, particularly for subtle eye alignment differences.

Second Condition: Monocular Calibration Only in Healthy Subjects

We then evaluated the custom monocular calibration without performing the system's built-in calibration. RMSE values were compared between the raw uncalibrated centroids and the monocularly calibrated centroids.

Results (Figure 3.4, panel B) showed a substantial reduction in gaze error, from 3.20° ± 1.33° (95% CI: [2.25°, 4.15°]) in the uncalibrated condition to 1.50° ± 0.62° (95% CI: [1.05°, 1.95°]) after monocular calibration, with a statistically significant difference ($p = 0.0118$). This demonstrates that monocular calibration effectively improves accuracy even when standard system calibration is not performed.

Third Condition: Hybrid Calibration in Participants with Binocular Disorders

For participants with binocular visual disorders (BD1 and BD2), we first attempted the built-in binocular calibration. Both participants were able to complete the calibration, likely due to moderate motor impairments; however, they reported diplopia and discomfort during the process.

The same analysis as in healthy subjects was performed, comparing raw binocular centroids to the hybrid calibrated centroids. Figure 3.5 illustrates the improvement in gaze alignment for both eyes. Hybrid calibration partially improved accuracy but residual deviations persisted, suggesting that binocular calibration alone may be insufficient for participants with ocular misalignment.

Fourth Condition: Monocular Calibration Only in Participants with Binocular Disorders

Finally, monocular-only calibration was applied to the two participants with binocular disorders. As shown in Figure 3.6, the monocular calibration corrected for misalignment of the affected eye, resulting in reliable estimation of gaze direction and ocular alignment. RMSE values dropped substantially compared to the raw uncalibrated condition, and fixation centroids closely matched the target positions.

Table 3.1 summarizes the RMSE values across all four conditions for both participants with binocular disorders. No significant outliers were observed in any of the conditions, supporting the robustness of the calibration method.

Summary of Pilot Results

Across all conditions, the pilot study confirmed the critical role of calibration in VR-based binocular measurements. Key observations include:

- Hybrid binocular-monocular calibration improves accuracy even in healthy participants, reducing systematic offsets between eyes.
- Monocular calibration alone is particularly effective for participants with binocular disorders, enabling reliable assessment of ocular alignment and vergence where binocular calibration fails or produces inaccurate results.
- Errors generally increase with target eccentricity, consistent with characteristics of video-based eye trackers.

These findings highlight that careful consideration of calibration procedures is essential for reliable quantitative assessment of binocular visuomotor function in immersive VR environments.

Table 3.1 RMSE values for participants with binocular disorders across calibration conditions.

Participant	Binocular Only	Hybrid Binocular+Monocular	Raw Uncalibrated	Monocular Only
BD1	2.009°	1.302°	2.794°	1.457°
BD2	1.417°	0.857°	2.283°	1.496°

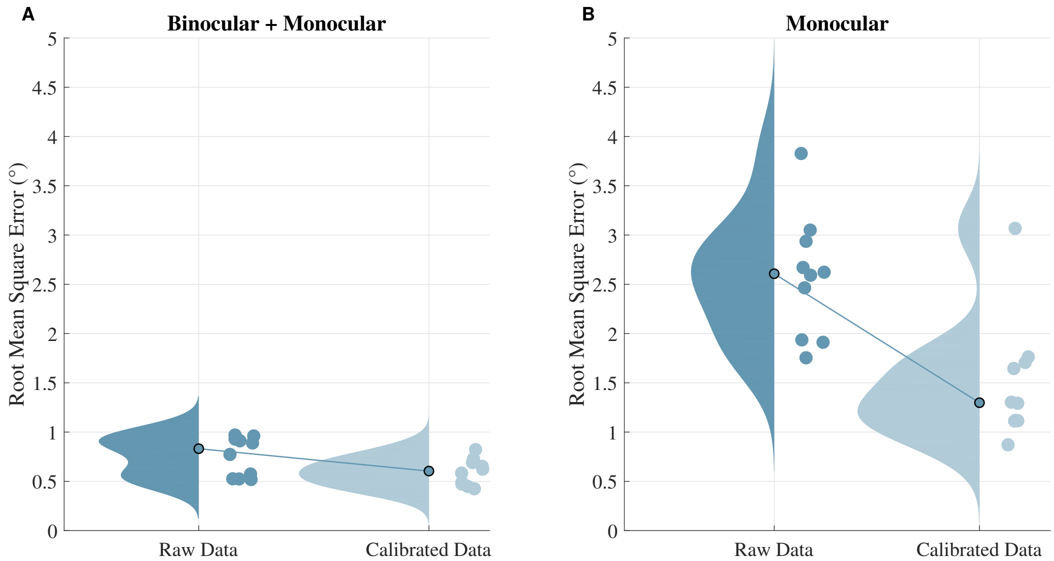

Figure 3.4 RMSE comparison for Hybrid Binocular-Monocular Calibration in healthy participants. Each cluster shows right and left eye centroids across five subjects.

3.3 Visual Fatigue in Head-Mounted Displays

Prolonged use of head-mounted displays (HMDs) has been widely reported to induce visual fatigue and cybersickness in users (82; 83). Symptoms can include eye strain, blurred vision, headache, and, in some cases, nausea. In the context of eye-tracking studies and binocular assessment, visual fatigue may influence oculomotor behavior, potentially altering fixation stability, saccade dynamics, or vergence responses. Therefore, it is critical to evaluate whether the experimental protocol itself introduces artifacts in gaze measurements due to fatigue.

3.3.1 Impact of Visual Fatigue on Oculomotor Measurements

Eye strain or fatigue can manifest as increased variability in gaze position, reduced fixation stability, or slower saccadic reactions (84). In the context of a VR-based Cover Test, such changes could obscure subtle refixation movements, bias measurements of ocular alignment, or affect the estimation of vergence angles. Moreover, HMDs introduce additional sources of fatigue, including prolonged accommodation-convergence conflicts, limited field of view, and the optical properties of stereoscopic displays.

Quantifying these effects is particularly important when testing participants with binocular visual disorders, as they may be more susceptible to fatigue-related performance decrements.

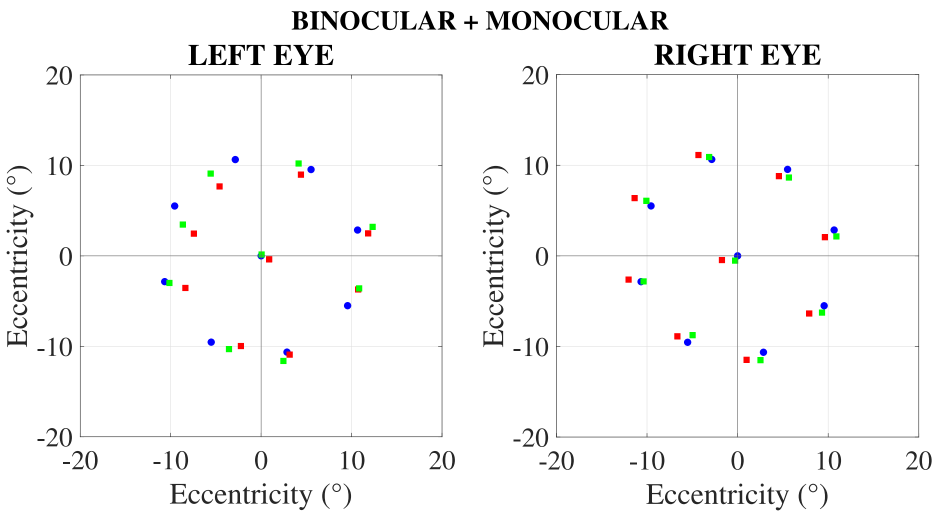

Figure 3.5 Hybrid calibration results in participants with binocular disorders (BD1 and BD2). Residual deviations remain, highlighting limitations of standard binocular calibration.

A systematic evaluation allows us to distinguish between true oculomotor deviations and artifacts introduced by the experimental setup or prolonged exposure to VR stimuli.

3.3.2 Pilot Experiment on Visual Fatigue

To investigate the potential impact of VR exposure on eye movements, we conducted a pilot study with the same participants involved in the calibration experiments ($n = 10$). Participants performed repeated Cover Test trials in the VR environment over a session lasting approximately 20–30 minutes.

During the session, gaze data were continuously recorded using the integrated eye tracker. Fixation stability was evaluated by examining the repeatability of the measured ocular alignment across trials. In this pilot study, we focused on healthy participants, some of whom exhibited latent deviations (phoria). For each participant, the measure was assessed over 60 consecutive trials to investigate the consistency of the measurement over time and its potential sensitivity to visual fatigue.

3.3.3 Results

Analysis of gaze data focused on the repeatability of ocular alignment measurements across trials in healthy participants, some of whom exhibited latent deviations (phoria). Each participant completed 60 consecutive trials, allowing us to evaluate the consistency of the measurement over time and the potential impact of visual fatigue.

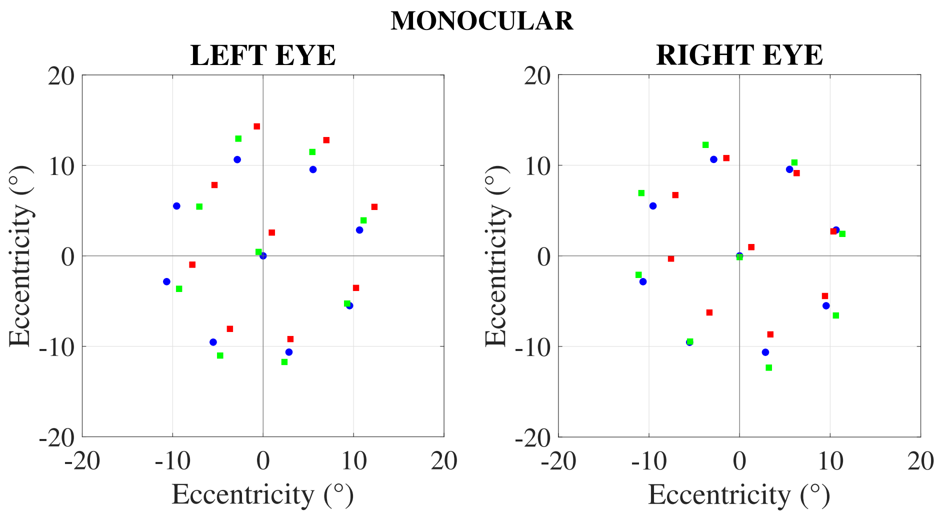

Figure 3.6 Monocular calibration in participants with binocular disorders. Calibration successfully aligns gaze centroids with target positions for both eyes.

As shown in Figure 3.7, the measured ocular deviations remained stable across trials, with no systematic drift or increase in variability. This indicates that the VR-based Cover Test provides reliable measurements of ocular alignment even during extended sequences of repeated fixations. Subjective reports of fatigue were minimal.

These findings demonstrate that short-to-moderate VR testing sessions do not compromise the reliability of binocular measurements due to visual fatigue, supporting the feasibility of using HMD technology to implement a VR-based Cover Test protocol. The results provide a methodological foundation for future studies assessing binocular visuomotor function under ecologically realistic conditions.

3.4 Head Orientation and Eye Alignment Measurement

3.4.1 Impact of Head Orientation on Eye-Tracking Accuracy

Accurate measurement of ocular alignment is essential for assessing binocular visuomotor function. In immersive virtual reality (VR) environments, head-mounted displays (HMDs) allow participants to move freely, enabling more naturalistic visual behaviors. However, head rotations can significantly influence eye-tracking measurements if not properly accounted for (51; 52). Even small head tilts or translations may alter the relative position of the eyes with respect to the display and to the eye-tracker cameras, potentially introducing systematic errors in vergence and ocular alignment estimates.

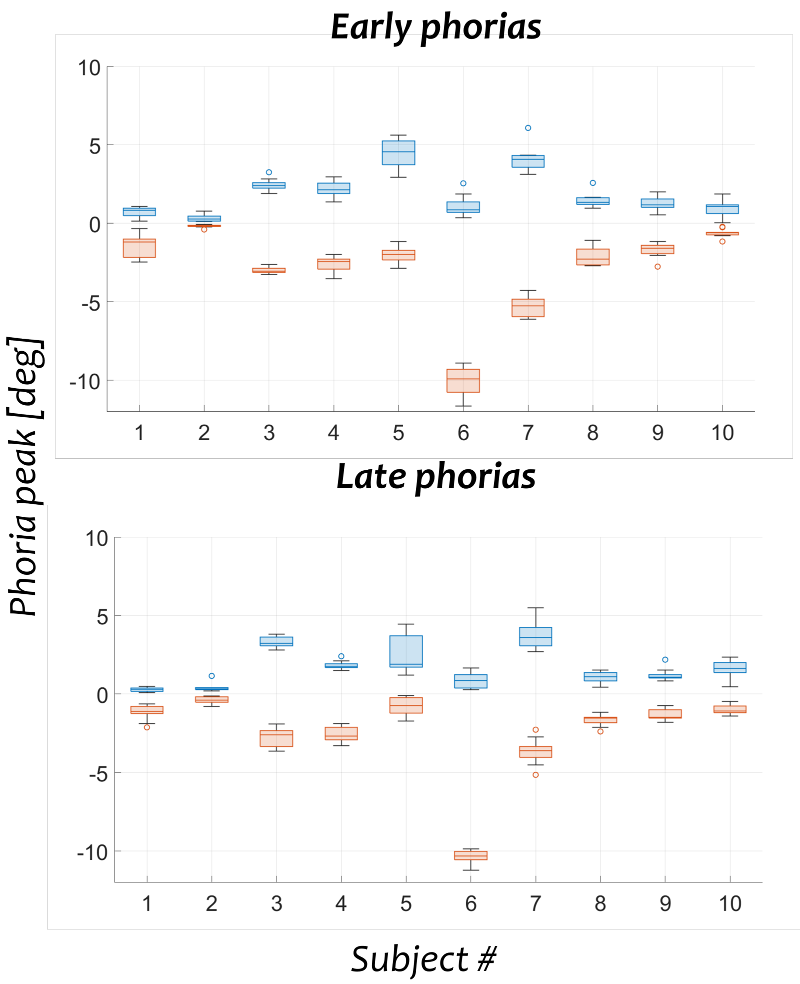

Figure 3.7 Comparison of measured phoria across the VR Cover Test in healthy participants. Boxplots show the distribution of phoria values during the first 10 trials (early) versus the last 10 trials (late).

Several mechanisms contribute to this potential source of measurement bias. First, head rotation changes the geometric relationship between the eyes and the eye-tracking cameras embedded in the HMD, which can lead to shifts in the estimated gaze vectors (78). Second, the optical configuration of the headset may introduce slight distortions when the display is viewed from non-central angles, potentially affecting the perceived disparity of stereoscopic targets. Third, head orientation interacts with the oculomotor system through vestibular and proprioceptive pathways. When the head moves or tilts, the vestibulo-ocular reflex (VOR) generates compensatory eye movements that stabilize the retinal image. These responses may alter the statistics of eye movements and influence the measured alignment, particularly in tasks involving prolonged fixation or peripheral gaze positions.

These considerations are particularly relevant when adapting classical clinical tests, such as the cover–uncover test, to immersive VR environments. Traditional clinical assessments are typically performed with the head aligned with the trunk and the gaze directed toward a fixed target in primary position. In contrast, VR setups allow more flexible viewing configurations, making it necessary to verify whether head orientation introduces systematic biases in the estimation of ocular deviation.

To address these methodological challenges, our experimental setup incorporated both hardware and software strategies to monitor and compensate for head orientation. The HMD used in this study was equipped with an integrated inertial measurement unit (IMU), which provided real-time information about head orientation along three rotational axes: pitch, yaw, and roll. These signals were synchronized with eye-tracking data in order to compute gaze direction in head-centered coordinates and to correct vergence estimates accordingly (78). By incorporating these corrections into the analysis pipeline, we aimed to ensure that ocular alignment measurements remained independent of participant head movements, preserving the validity of the collected data.

3.4.2 Pilot Study: Head Rotation Effects on Ocular Alignment

To empirically assess whether head orientation affects ocular alignment measurements in VR, a pilot experiment was conducted with six healthy participants (21–32 years old) with normal or corrected-to-normal vision and no history of diagnosed strabismus. Participants performed a digital implementation of the cover–uncover test within a VR environment while adopting different head orientations.

The experiment was implemented in Unity3D and delivered through an HTC Vive Pro Eye headset, which integrates a binocular eye-tracking system sampling at 120 Hz. The device provides an average gaze accuracy of approximately 1.1° within a central field of view of about 20°. In addition to eye tracking, the headset provides precise head tracking, allowing simultaneous recording of both eye and head movements during the experimental task.

Participants performed the cover–uncover test under three head rotation conditions about the vertical axis: no rotation (H 0°), left rotation (H -45°), and right rotation (H $+45^\circ$). Within each block, participants fixated targets located at three retinal eccentricities: primary position (PP), 10° left (LP), and 10° right (RP). The fixation stimulus consisted of a Maltese cross presented at a virtual distance of 40 cm, with a rotating ellipse at its center to facilitate

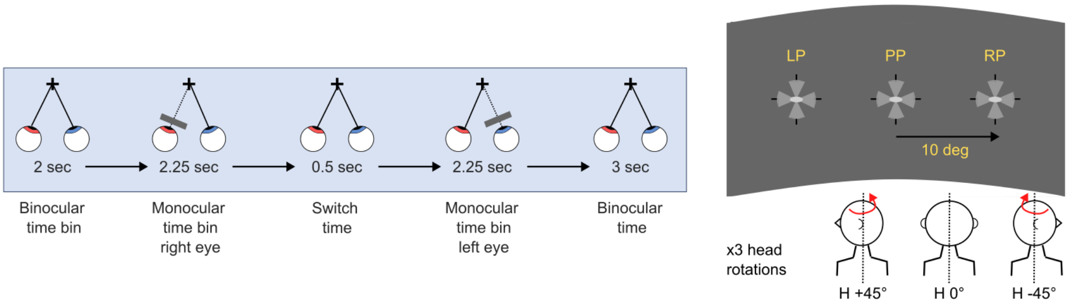

Figure 3.8 Schematic representation of the VR-based cover–uncover test procedure and experimental conditions.

stable fixation. A schematic overview of the experimental procedure and trial timeline is shown in Figure 3.8.

Each trial began with a binocular fixation phase, followed by sequential monocular occlusions of the left and right eyes. Occlusion was implemented digitally by switching off the display corresponding to the occluded eye. This approach allowed direct observation of the behavior of the covered eye through the eye-tracking system. Head alignment for each experimental block was guided by reference fixation crosses to ensure consistent head orientation relative to the visual stimuli.

Eye-tracking data were preprocessed to remove artifacts such as blinks and tracking losses (51). Clean gaze signals were reconstructed using singular value decomposition (SVD), retaining the principal components that preserved between 85% and 90% of the original signal variance. From the reconstructed signals, peak ocular deviations occurring during the monocular occlusion phases were extracted and used as an estimate of phoria. Because the data did not satisfy normality assumptions, statistical comparisons between head rotation conditions were performed using the Wilcoxon rank-sum test (85).

Results revealed heterogeneous patterns of phoria modulation across participants at the single-subject level, with some individuals showing modest variations across head rotation conditions. However, when considering the population as a whole, no consistent trend emerged. Median maximal phoria values were comparable across the three head rotation conditions (Figure 3.9), indicating that moderate head rotations do not systematically influence ocular alignment measurements in healthy individuals.

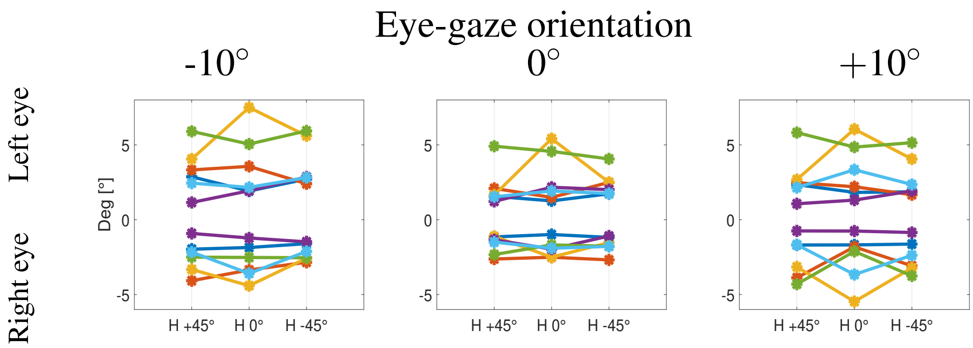

Figure 3.9 Median maximal phorias across head rotation conditions for all participants. Positive and negative values correspond to deviations measured in the left and right eyes, respectively. No systematic population-level trend is observed, suggesting that head rotations up to ±45° do not significantly bias ocular alignment measurements.

3.4.3 Correction Strategies and Methodological Implications

Even when monocular calibration procedures are applied, small variations in head orientation can alter the effective alignment between the eye-tracker cameras and the visual axis. Integrating head orientation data into the analysis therefore enables dynamic adjustment of gaze estimation and calibration mappings, compensating for postural deviations and improving measurement accuracy (78).

The results of the pilot study suggest that moderate head rotations do not introduce systematic population-level biases in phoria measurements. This finding supports the feasibility of allowing natural head movements during VR-based assessments of binocular alignment. At the same time, monitoring head orientation remains important to ensure consistent experimental conditions and to interpret individual variability in oculomotor responses.

Head posture may also interact with visual fatigue mechanisms. Sustained fixation with tilted head positions can increase oculomotor strain, particularly when targets are presented at peripheral retinal locations (52). For this reason, our protocol combined head-centered gaze correction with additional monitoring of ocular metrics sensitive to fatigue, such as fixation stability and pupil diameter. This approach helps disentangle variability arising from head orientation from variability associated with fatigue or attentional fluctuations.

Overall, the methodological framework combining monocular calibration, controlled visual stimuli, synchronized head tracking, and dynamic correction procedures enables reliable assessment of binocular alignment in immersive VR environments. The pilot results indicate that head rotations up to ±45° can be accommodated without introducing systematic measurement biases, supporting the robustness of the proposed VR-based cover–uncover test for future investigations of visuomotor function.

3.5 Vergence–Accommodation Conflict

3.5.1 Intrinsic Challenges in VR-Based Binocular Assessments

Virtual Reality environments inherently introduce a mismatch between vergence and accommodation cues. While the eyes converge according to the perceived depth of a virtual object, the optical focal distance of the head-mounted display (HMD) remains fixed at the physical display plane (84; 86). This phenomenon, known as the vergence–accommodation conflict (VAC), can potentially induce visual discomfort, fatigue, and alterations in binocular coordination.

In the context of clinical assessments of ocular alignment, such as the cover–uncover test, VAC represents a potential methodological concern. If the mismatch between vergence and accommodation cues alters the natural vergence response, it could bias the estimation of phoria or tropia, particularly when stimuli are presented at virtual depths significantly different from the focal plane of the display. Therefore, assessing whether VAC introduces systematic errors in ocular alignment measurements is crucial for validating VR-based diagnostic tools.

3.5.2 Experimental Validation Through Virtual Reality

To evaluate whether the vergence–accommodation conflict (VAC) affects the reliability of binocular alignment measurements in immersive environments, a comparative validation study was conducted on ten participants, including five healthy individuals and five patients diagnosed with strabismus. Specifically, the results obtained with our virtual reality system based on an HTC Vive Pro Eye headset were compared with those obtained by Sam Smithers through his set-up that consisted of a Multi-Depth Plane Display System (MDPDS) (87), which integrates a Pupil Core eye tracker with liquid-crystal shutter technology. This configuration allows the presentation of fixation targets at multiple real physical depths, enabling precise assessment of ocular alignment across both horizontal and vertical gaze directions and at different viewing distances. The system implemented an automated cover–uncover protocol, in which monocular eye positions are recorded during successive fixation periods, while liquid-crystal shutters occlude the eyes to simulate clinical testing conditions.

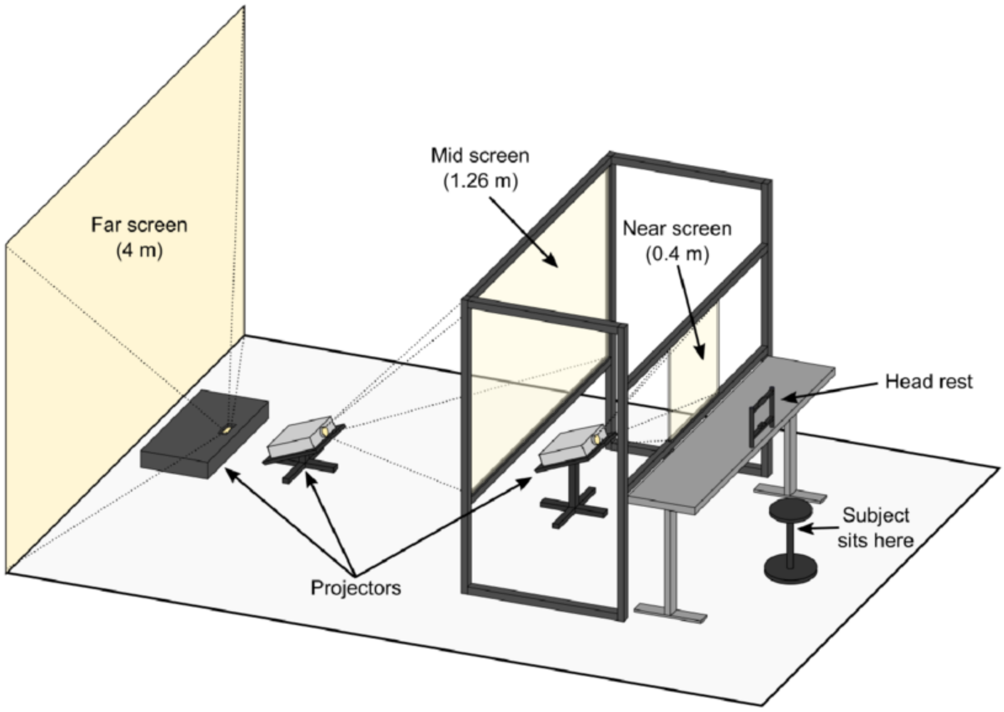

Figure 3.10 Illustration of the multi-depth plane display setup developed and used by S.P. Smithers at the Bex's lab, against which I compared the resuts of my study. Figure by courtesy of Samuel P. Smithers.

Fixation targets were presented at three viewing distances (0.4 m, 1.26 m, and 4 m), arranged across a 3×3 grid of azimuths and elevations covering a visual field of approximately 20°. Each location was tested four times following a structured fixation sequence consisting of binocular fixation, monocular occlusion of the left eye, binocular fixation, monocular occlusion of the right eye, and final binocular fixation. Each fixation interval lasted 2.25 seconds, allowing sufficient time for refixation responses to emerge and stabilize.

From the recorded eye movements, ocular deviation was estimated by quantifying the angular displacement of the eye required to re-establish fixation following occlusion. Horizontal and vertical components of this displacement were computed for each eye at every viewing location, enabling a systematic comparison of alignment measurements across viewing conditions and experimental setups.

The experimental configuration and comparison between the virtual reality–based system and the multi-depth plane display setup are illustrated in Figure 3.10. In addition to the automated measurements, an expert clinician performed an Alternate Prism Cover Test (APCT) to provide a clinical reference for the estimation of ocular deviation.

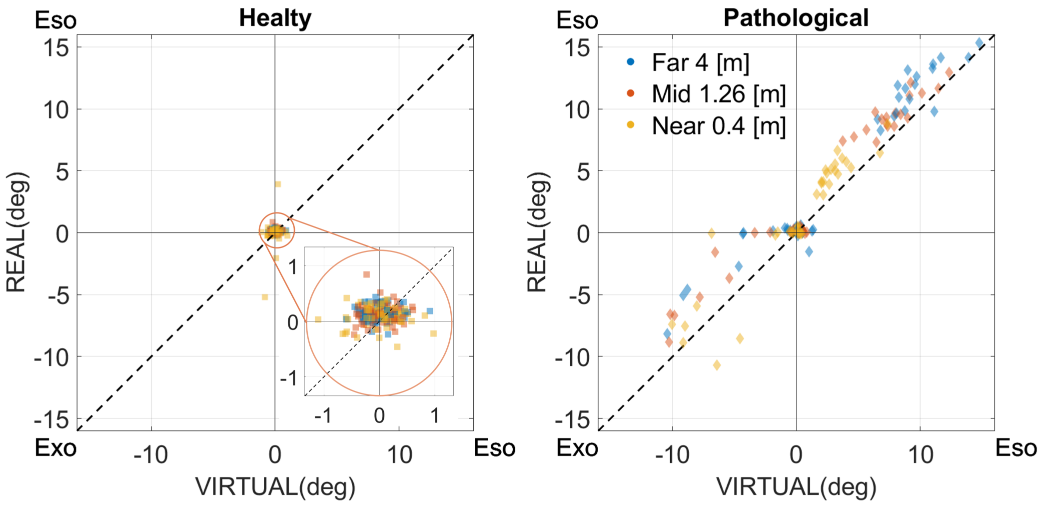

Figure 3.11 Comparison between the VR-CUT setup based on a head-mounted display and the multi-depth plane display system used as a reference. Both systems implemented an automated cover–uncover test to measure ocular alignment across multiple fixation distances and gaze eccentricities.

3.5.3 Results and Observations

The comparison between the virtual reality–based measurements and those obtained using the multi-depth plane display system showed strong agreement in the estimation of horizontal deviations across fixation distances and gaze eccentricities (Figure 3.11). Measurements obtained in the virtual environment closely matched those obtained using real depth planes, suggesting that the vergence–accommodation conflict does not introduce substantial systematic distortions in the estimation of ocular alignment within the tested conditions.

Further comparison with the clinician's APCT measurements demonstrated that the VR-based system reliably detected and quantified strabismic deviations in pathological participants, while correctly identifying the absence of clinically relevant deviations in healthy individuals (Figure 3.12). These results indicate that the measurements derived from the virtual environment are consistent with standard clinical evaluation.

Importantly, the consistency of the measurements across multiple fixation distances suggests that the virtual manipulation of depth does not significantly alter the vergence responses elicited during the cover–uncover procedure. Within the tested range of distances, the influence of VAC appears to be limited and does not compromise the interpretability of the measured deviations.

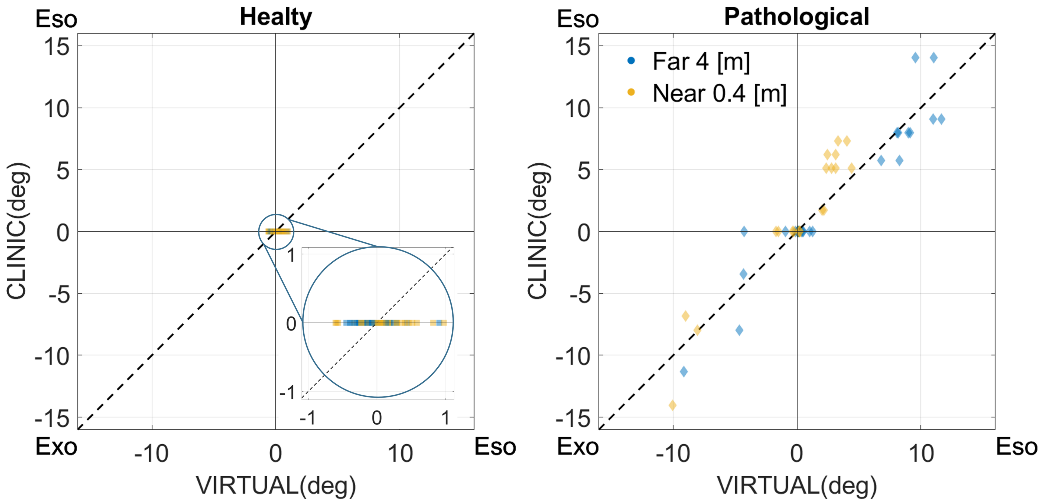

Figure 3.12 Comparison between horizontal deviations measured with VR-CUT and those obtained through the clinician-performed Alternate Prism Cover Test (APCT). Results show strong agreement between the automated VR-based assessment and the clinical reference measurements.

3.5.4 Methodological Implications

The results demonstrate that VR-based implementations of binocular vision tests can provide reliable measurements despite the presence of vergence–accommodation conflict. By enabling controlled manipulation of fixation depth and gaze direction within a compact and portable setup, this system allows the assessment of ocular deviations across conditions that would otherwise require large physical setups.

These findings support the use of immersive VR as a viable platform for automated binocular vision assessment. The ability to reproduce clinical measurements across different fixation distances and gaze eccentricities indicates that the influence of VAC is not sufficient to compromise the diagnostic reliability of the test. Consequently, VR-based systems represent a promising tool for clinical evaluation of binocular disorders, particularly in environments where conventional multi-depth displays or large testing spaces are impractical.

Chapter 4

Iterative VR Cover Test: Set-up, Methodology, Experiment, and Results

4.1 Final VR Cover Test Implementation

Building upon the methodological developments presented in Chapter 3, a final implementation of a digital cover test was developed to provide a fully automated and quantitative assessment of ocular misalignment in virtual reality. The system operates on top of the custom monocular calibration procedure, which establishes subject-specific gaze references and compensates for individual oculomotor offsets prior to testing.

The core challenge addressed in this implementation is the translation of the clinician's manual prism compensation into an automated procedure. To this end, an iterative protocol was introduced, in which the spatial position of the fixation stimulus is dynamically updated based on eye movement responses recorded during the cover–uncover sequence. This mechanism allows the system to progressively compensate for ocular deviations by mimicking prism correction in the virtual domain.

The system was designed to (i) provide controlled stimulus presentation across different vergence and version conditions, (ii) implement an adaptive compensation algorithm robust to eye-tracking inaccuracies, and (iii) ensure reliable signal acquisition through an interactive experimental protocol.

4.1.1 Virtual Stimulus Design

The virtual environment enables precise control of fixation conditions by positioning the stimulus at arbitrary locations in three-dimensional space. In particular, stimulus placement allows independent manipulation of:

- **Vergence demand**, defined by the simulated viewing distance,
- **Version demand**, defined by the angular eccentricity relative to primary gaze.

This flexibility extends the conventional cover test by enabling the assessment of ocular alignment across a broader range of spatial configurations.

4.1.2 Iterative Digital Cover Test Algorithm

Adaptive Compensation Strategy

To reduce the impact of calibration errors and nonlinear gaze distortions, the proposed method estimates ocular deviation indirectly through an adaptive stimulus repositioning strategy.

Instead of relying on absolute gaze measurements, the algorithm iteratively updates the stimulus position based on the corrective movement performed by the eye when fixation is acquired. This approach reproduces the logic of prism compensation used in clinical practice, where the stimulus is shifted until no corrective movement is observed.

Convergence is achieved when the eye remains stable upon uncovering, indicating alignment between the stimulus and the resting oculomotor state.

Iterative Procedure

The adaptive process consists of the following steps:

1. Initial cover–uncover trials are performed to estimate baseline deviation.
2. The stimulus position is iteratively updated based on the measured corrective movement.
3. The procedure terminates when residual movement falls below a threshold (comparable with measurement error) for consecutive trials.

The final stimulus offset provides an indirect estimate of ocular deviation.

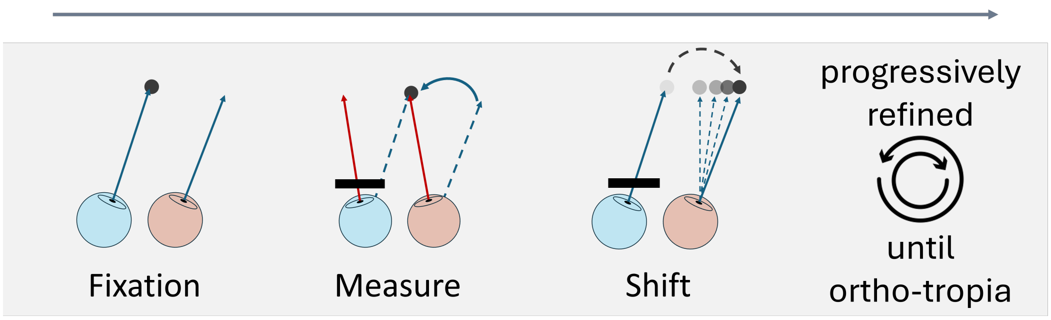

Figure 4.1 Conceptual diagram of the iterative digital cover test algorithm.

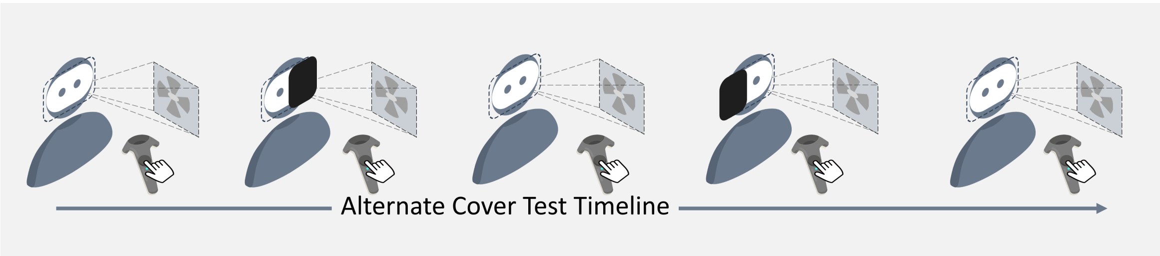

Figure 4.2 Interactive trial structure of the digital cover test.

Convergence Behavior

Convergence was typically achieved within 3 to 9 trials, depending on the magnitude of the deviation. Each trial lasted approximately 9 seconds, resulting in a total acquisition time below 90 seconds.

4.1.3 Interactive Trial Structure

To improve fixation stability, the experimental protocol adopted a participant-controlled timing strategy. Participants triggered transitions between binocular and monocular conditions using a controller, ensuring stable fixation before each occlusion phase.

This approach improved signal quality and reduced variability associated with fixed-timing paradigms.

4.1.4 Data Acquisition

Eye-tracking, head motion, and event data were recorded and synchronized using a common timestamp reference. Controller triggers were used to segment the signals into cover test phases, and preprocessing removed blinks and artifacts.

4.2 Results

4.2.1 Clinical Data Acquisition Campaign

To evaluate the proposed system under realistic clinical conditions, a data acquisition campaign was conducted at the Ophthalmology outpatient clinic of the San Martino Hospital in Genoa.

Data collection was performed on a weekly basis, with participants recruited among patients undergoing routine orthoptic and ophthalmological examinations. After completing standard clinical assessments, patients were asked to perform the VR-based cover test using the proposed system.

This workflow enabled seamless integration of the experimental protocol into routine clinical practice, without requiring dedicated sessions or significant modifications to standard procedures. The full acquisition pipeline—including headset positioning, monocular calibration, and execution of the iterative cover test—was completed within a few minutes per patient, remaining compatible with typical outpatient time constraints.

The clinical setting introduced realistic variability in terms of patient conditions, compliance, and fixation stability. Despite these factors, the system consistently provided reliable eye-tracking data and allowed completion of the adaptive testing procedure.

These observations demonstrate that the proposed VR-based cover test is not only suitable for controlled laboratory experiments, but can be effectively deployed in real clinical environments, supporting its potential as a practical diagnostic tool.

4.2.2 Monocular Calibration Improves Gaze Estimation Accuracy

Calibration performance was evaluated using RMSE between target positions and gaze estimates across 30 participants (15 healthy (H), 15 patients (P)).

Monocular calibration consistently reduced spatial errors, with larger improvements observed in patients, where standard calibration was often unreliable (Figure 4.3).

4.2.3 Iterative Compensation of Ocular Deviation

The iterative algorithm progressively reduced corrective eye movements across trials. Early iterations showed large corrective saccades, while later trials exhibited reduced movement amplitude, indicating progressive alignment of the deviated eye toward the fixation target.

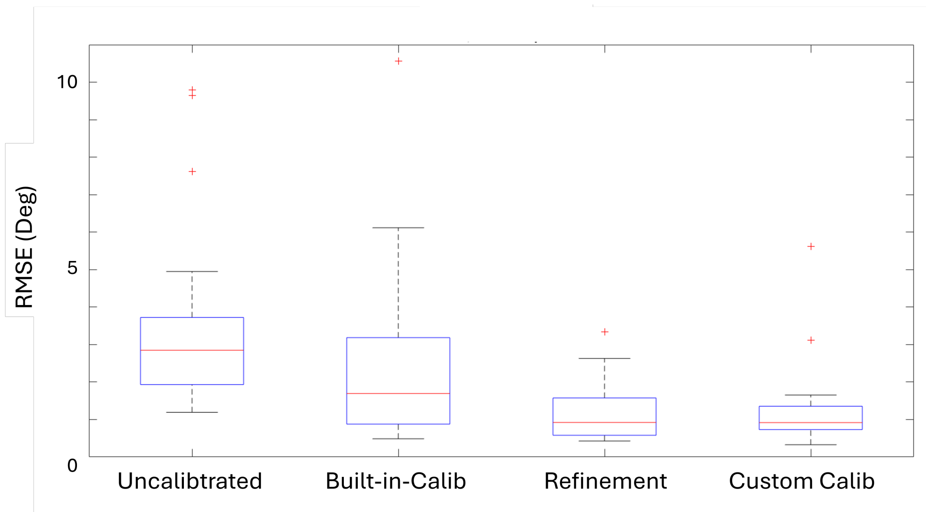

Figure 4.3 Comparison of gaze estimation accuracy for the different conditions considered: fully uncalibrated, built-in binocular calibration, refined monocular calibration in cascade with built-in binocular calibration, and custom monocular calibration only. Each plot shows the RMSE for the validation points. The central line indicates the median, the box represents the interquartile range (25th to 75th percentiles), and whiskers extend to the most extreme data points within 1.5×IQR from the quartiles. Red crosses beyond the whiskers denote outliers.

4.2.4 Convergence and Orthotropic Condition

Convergence was achieved within 3–9 trials. In several participants, the algorithm induced a condition of functional orthotropia, with minimal residual deviation (Figure 4.4).

4.2.5 Comparison with Clinical Measurements

A qualitative comparison was performed between ocular deviation measured by clinicians using prism cover test (expressed in prism diopters) and the values estimated by the VR-based system.

Results show a consistent agreement between clinical and virtual measurements across participants for whom deviation values could be successfully extracted by the system (in degrees) and clinically measured (in prism diopters) (see Table 4.1), providing an initial validation of the proposed method against standard clinical practice.

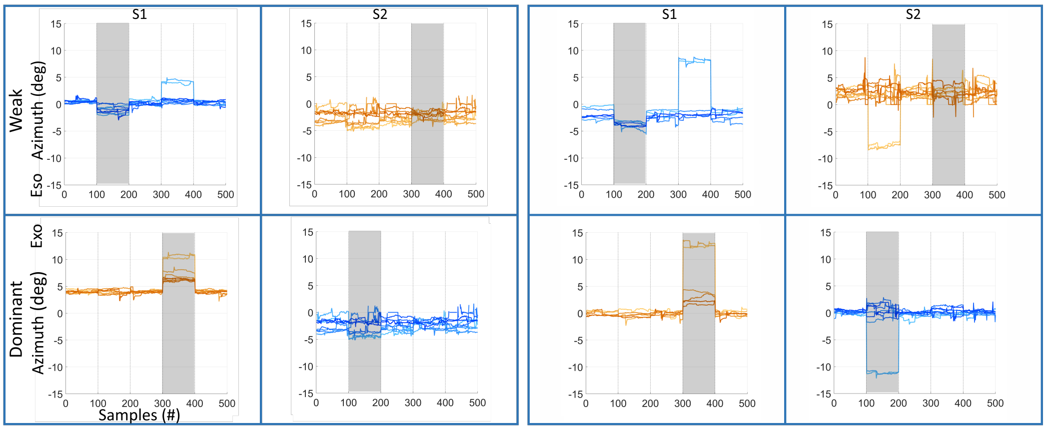

Figure 4.4 Examples of convergence of the automatic procedure for two representative subjects, tested in two different conditions: fixation distances of 40 cm and 2 m. Trace colors indicate the eye: blue for the left eye and yellow for the right eye.

Table 4.1 Comparison between clinical measurements (prism diopters) and VR-based estimates of ocular deviation for a subset of patients (P) and a subset of healthy subjects (H) from the control group.

SBJ NUMBER	CLINIC	HMD
S7 (H)	No	No
S8 (P)	ET, 18 PD	ET, 9°
S9 (H)	No	No
S10 (P)	XT, 75 PD	XT, 37°
S11 (P)	XT, 25 PD	XT, 15°
S12 (P)	ET, 8 PD	ET, 4°
S13 (P)	ET, 20 PD	ET, 11.5°
S14 (H)	No	No
S15 (P)	ET, 12 PD	ET, 8°
S16 (P)	XT, 25 PD	XT, 12.5°
S17 (P)	ET, 20 PD	ET, 8°
S18 (P)	ET, 5 PD	ET, 3.5°

Chapter 5

Discussion and Future Developments

General Considerations The work presented in this thesis introduces a virtual reality implementation of the cover test, combined with an adaptive procedure for compensating ocular deviation. Beyond its role as a measurement tool, this framework enables controlled interaction with the binocular sensorimotor system. Importantly, the approach tries to bridge the gap between traditional clinical assessment and interactive, quantitative evaluation of oculomotor behavior, providing a platform that integrates both observation and manipulation within a single experimental paradigm.

5.1 Orthotropic Alignment in Virtual Reality

A relevant aspect emerging from the results is the possibility of achieving a condition of functional orthotropia within the virtual environment through iterative stimulus compensation. The results indicate that the system can progressively reduce ocular deviation in subjects who initially present with measurable misalignment, guiding the visual system toward a more aligned state.

In several subjects, the adaptive procedure was able to progressively reduce the measured deviation, leading to an orthotropic condition under the specific viewing constraints imposed by the VR setup. This condition is conceptually comparable to what is typically obtained in clinical practice through the use of prisms, although in this case it is achieved through visual stimulation alone. The findings suggest that virtual stimulus manipulation, when combined with precise eye-tracking data, can reproduce some of the compensatory mechanisms employed by clinicians, providing a controlled environment for studying the dynamics of ocular alignment.

5.2 Implications for the Use of the Cover Test

Traditionally, the cover test is used as a diagnostic procedure, aimed at revealing ocular deviations by temporarily disrupting binocular fusion. Its role is therefore limited to assessment. The VR implementation explored in this work introduces additional flexibility, allowing not only the measurement of deviation but also the manipulation of the visual stimulus in response to the observed behavior. This creates a feedback loop in which the system response can be monitored and influenced over time.

Within this framework, the distinction between assessment and interaction becomes increasingly blurred. While the primary purpose of the present work remains evaluative, the same setup could potentially be extended to investigate how the visual system responds to controlled and repeated stimulus adjustments. This represents a shift from purely passive measurement to a more dynamic approach, where the system can provide adaptive feedback, akin to a digital analog of clinical interventions such as prism correction, but implemented entirely through VR.

5.3 Stimulus Manipulation After Alignment

An aspect that deserves further investigation concerns the behavior of the system once an orthotropic condition has been reached. After alignment is achieved, it becomes possible to introduce additional changes to the stimulus position. These changes could be applied in a controlled manner, either gradually or in discrete steps, to observe how the oculomotor system reacts to new spatial configurations.

Such an approach would allow the study of the stability of the achieved condition, as well as the capacity of the system to adapt to further perturbations. It remains an open question whether the system would simply follow the imposed stimulus changes or whether adaptive processes would emerge over repeated trials. The potential to systematically probe these responses provides a unique opportunity to explore the resilience and plasticity of the binocular sensorimotor system under controlled conditions.

5.4 Possible Role of Oculomotor Adaptation Mechanisms

The considerations above can be related to known mechanisms of oculomotor adaptation. In particular, it has been shown that saccadic eye movements can undergo adaptive recalibration in response to systematic errors between expected and actual visual feedback (20).

In classical paradigms, this adaptation is induced by introducing a mismatch between the target position and the final eye position during repeated saccades. Over time, the oculomotor system adjusts the motor command to reduce this error. Similarly, in the context of the present work, controlled displacements of the fixation target starting from an aligned condition could provide systematic discrepancies, potentially engaging similar adaptive mechanisms in binocular viewing.

At this stage, this possibility remains speculative. However, it suggests that the proposed framework could be used not only to observe ocular behavior, but also to investigate the conditions under which adaptation may occur. Exploring these mechanisms could deepen understanding of how binocular alignment can be modified through repeated exposure to controlled visual stimuli, opening avenues for both basic research and clinical applications.

5.5 Perspectives for Rehabilitation-Oriented Applications

The ability to guide the visual system toward orthotropia and to manipulate stimulus conditions raises the question of whether such approaches could be relevant for rehabilitation. Current treatments for binocular vision disorders often address sensory and motor components separately. In contrast, VR-based systems allow simultaneous control of visual input and monitoring of motor response, providing a potentially integrated approach.

The framework presented in this thesis could serve as a basis for exploring such possibilities. For instance, adaptive protocols could be designed to gradually modify stimulus parameters based on individual performance, with the aim of encouraging more stable or balanced oculomotor behavior. By combining precise measurement with controlled visual intervention, the system could support targeted rehabilitation protocols, complementing or enhancing traditional therapies.

Further work is required to determine whether these approaches can produce measurable and lasting effects, particularly in clinical populations. Longitudinal studies would be especially valuable to evaluate whether repeated VR-based interventions can induce persistent improvements in ocular alignment or motor control.

5.6 Limitations and Open Questions

Several limitations should be considered when interpreting the results and their implications. First, the achievement of an orthotropic condition in VR was not observed consistently across all subjects and conditions. In particular, different types and magnitudes of strabismus may respond differently to the adaptive procedure. The current results suggest that the proposed approach is more effective in specific cases, while in others the residual deviation remains even after iterative compensation. This indicates that the method may have limited applicability depending on the underlying oculomotor characteristics.

Second, the adaptive procedure relies on a simplified representation of ocular deviation, primarily treated as a static offset to be compensated through stimulus repositioning. This assumption does not fully capture the complexity of binocular sensorimotor behavior, which may include non-linearities, variability over time, and interactions between vergence and version components.

These aspects highlight the need for further investigation to better characterize the range of applicability and the limitations of the proposed approach. Additional studies could help clarify how different clinical conditions, levels of visual acuity, or age-related factors influence the system's effectiveness.

5.7 Future Directions

Future research could address several of the points raised above. A first direction concerns the systematic study of post-alignment behavior, investigating how the system responds to controlled perturbations after orthotropia is achieved. This includes examining both immediate oculomotor responses and potential longer-term adaptation over repeated trials.

A second direction involves the design of adaptive protocols specifically aimed at eliciting oculomotor adaptation, potentially drawing inspiration from established paradigms in the study of saccadic adaptation. Such protocols could explore how consistent discrepancies introduced via the VR environment influence eye movement control and alignment.

Finally, longitudinal studies will be necessary to evaluate the stability of the observed effects over time and their possible relevance for rehabilitation. Tracking performance across multiple sessions would provide insight into whether the improvements observed in a controlled VR environment can translate to real-world conditions.

Overall, the results presented in this thesis suggest that VR-based approaches may provide a flexible and versatile platform for investigating binocular sensorimotor function, combining assessment and interaction within a single system. The potential extensions of this work range from basic research on oculomotor mechanisms to the development of clinically relevant interventions aimed at improving binocular vision and motor control.

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