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Francisco Martinho Cidade

FROM BASIC RESEARCH TO THE CLINIC: CREATION OF AN INTERFACE FOR ANALYSIS OF EYE MOVEMENTS

Thesis submitted to the University of Coimbra in fulfilment of the requirements of the Master's Degree in Physics Engineering under the scientific supervision of Ph. D. João Lemos and Ph. D. João Castelhano and presented to the Physics Department of the Faculty of Sciences and Technology of the University of Coimbra

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Master in Physics Engineering

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Supervisors:
Ph.D. João Lemos
Ph.D. João Castelhano

FCTUC, Physics Department
CHUC, Neurology Department

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que tu segues comigo
Na planície da alegria”

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Resumo

Esta tese pretende estabelecer uma interface padronizada e de fácil utilização para a análise dos movimentos oculares, focando as suas potenciais implicações no contexto das doenças neurodegenerativas. O objetivo principal deste trabalho é formular um protocolo consistente para a avaliação dos movimentos oculares. A execução deste protocolo envolve a utilização de scripts Matlab adaptados para atender aos requisitos analíticos específicos de cada tarefa. Esta fase crucial é facilitada através de uma Interface Gráfica do Utilizador (GUI) intuitiva, garantindo que os clínicos com conhecimentos limitados de codificação Matlab possam navegar eficientemente no processo. O culminar deste processo produz dois resultados. Em primeiro lugar, uma folha de cálculo Excel abrangente fornece uma compilação estruturada dos parâmetros calculados para cada tarefa, oferecendo uma visão geral organizada dos resultados. Em segundo lugar, um conjunto de visualizações meticulosamente elaboradas apresenta aspectos intrincados da dinâmica do movimento ocular. Estas visualizações incluem gráficos de rastreio do olhar, posições de fixação, dispersão do olhar, sequência principal de micro-sacadas e histogramas polares. Estas visualizações oferecem uma perspetiva multidimensional do desempenho do movimento ocular do sujeito, permitindo uma compreensão mais profunda dos seus comportamentos oculares. Os resultados revelaram a eficácia do protocolo padronizado, demonstrando uma reprodutibilidade favorável e o potencial para facilitar a investigação de doenças neurodegenerativas através da análise dos movimentos oculares. Esta abordagem permite um meio sistemático e acessível de estudar os comportamentos oculares, oferecendo informações valiosas sobre a intrincada dinâmica dos movimentos oculares e sua associação com condições neurológicas. Em conclusão, esta tese não só abriu caminho para uma exploração aprofundada da Doença de Parkinson (DP) através da análise do movimento ocular, como também abriu caminhos mais amplos para a investigação de várias doenças neurodegenerativas. Os esforços futuros

poderão estender-se para além da análise do movimento ocular, integrando medições adicionais, como o EEG, para desvendar camadas mais profundas de compreensão no contexto de doenças neurológicas. Esta abordagem holística tem o potencial de fornecer conhecimentos abrangentes para as múltiplas facetas das doenças neurodegenerativas, promovendo uma compreensão mais profunda dos seus mecanismos subjacentes.

Abstract

This thesis aims to establish a standardized and user-friendly interface for analyzing eye movements, focusing on their potential implications in the context of neurodegenerative diseases. The primary objective of this work is to formulate a consistent protocol for assessing ocular movements in a clinical context. The execution of this protocol involves the utilization of tailored Matlab scripts designed to cater to the specific analytical requirements of each task. This crucial phase is facilitated through an intuitive Graphical User Interface (GUI), ensuring clinicians with limited Matlab coding expertise can efficiently navigate the process. The culmination of this process yields twofold outcomes. Firstly, a comprehensive Excel spreadsheet provides a structured compilation of calculated parameters for each task, offering an organized overview of findings. Secondly, an array of meticulously crafted visualizations showcases intricate aspects of eye movement dynamics. These visualizations encompass gaze tracing graphs, fixation positions, gaze dispersion, micro-saccades main sequence, and polar histograms. These visualizations offer a multi-dimensional perspective on the subject's eye movement performance, enabling a deeper understanding of their ocular behaviors. The results revealed the efficacy of the standardized protocol, demonstrating favorable reproducibility and the potential to facilitate the investigation of neurodegenerative diseases through eye movement analysis. This approach enables a systematic and accessible means of studying ocular behaviors, offering valuable insights into the intricate dynamics of eye movements and their association with neurological conditions. In conclusion, this thesis has not only paved the way for an in-depth exploration of Parkinson's Disease (PD) through eye movement analysis but has also unearthed broader avenues for investigating various neurodegenerative diseases. Future endeavors could extend beyond eye movement analysis, integrating additional measurements, such as EEG, to unravel deeper layers of understanding in the context of neurological disorders. This holistic approach has the potential

to provide comprehensive insights that span multiple facets of neurodegenerative diseases, fostering a better understanding of their underlying mechanisms.

List of Acronyms

AD Alzheimer's disease.

CHUC Centro Hospitalar e Universitário de Coimbra.

DBS Deep Brain Stimulation.

EEG Electroencephalography.

GUI Graphical User Interface.

MS Multiple Sclerosis.

PD Parkinson's Disease.

VOG Video-oculography.

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Chapter 1

Introduction

1.1 Motivation and Goals

The study of ocular motor assessment is crucial in advancing our understanding of eye movements and their implications in various neurological and motor disorders. However, a significant challenge in this field arises from the lack of standardization in experimental protocols used by different research groups. As will be mentioned in the following chapter, the absence of a unified approach to conducting eye movement experiments hinders the comparability and reproducibility of results, preventing effective collaboration between laboratories and hindering the translation of research findings into clinical practice.

The primary motivation behind this thesis, titled "From Basic Research to the Clinic: Creation of an Interface for Analysis of Eye Movements," was to bridge the gap between basic research and clinical applications by developing a standardized and accessible interface for analyzing eye movements. This interface aimed to provide researchers and clinicians with a common platform that adheres to a standardized international protocol for ocular motor assessment, allowing consistent data collection, validation, and interpretation in different laboratories and clinical settings. The first goal of this thesis project was to conduct an extensive review of existing research on ocular motor assessment. We identified the strengths and limitations of various approaches by critically analyzing previous studies, including those utilizing custom-designed behavioral paradigms and the DEMoNS protocol [1].

The second goal was to develop an intuitive, user-friendly software interface to accommodate the standardized eye movement assessment protocol. The software was designed to seamlessly integrate with existing eye-tracking device (Eyelink SR Research, 1000Hz), providing real-time data acquisition and analysis capabilities. The interface allowed researchers to customize specific parameters while adhering to the standardized framework, ensuring consistent and comparable results across diverse experimental setups.

The third goal of this project was to validate the developed interface by conducting a series of controlled experiments with human participants. Statistical analysis was employed to evaluate the reliability and reproducibility of the results obtained through the new standardized approach, further reinforcing its credibility.

The final goal of this thesis was to demonstrate the clinical applicability of the standardized interface in assessing eye movements in patients with neurodegenerative and motor diseases. By collaborating with clinical partners and conducting studies on a diverse patient population, we aimed to establish the utility of the interface in diagnosing and monitoring ocular motor abnormalities associated with these conditions. The successful application of the standardized protocol in a clinical setting facilitated more accurate and meaningful comparisons of results across different medical centers, enabling collaborative research and the development of effective intervention strategies.

In conclusion, the "From Basic Research to the Clinic: Creation of an Interface for Analysis of Eye Movements" thesis aimed to advance eye movement research by addressing the critical issue of standardization in ocular motor assessment. By developing a comprehensive and accessible interface, this project seeked to foster collaboration among researchers and clinicians, enhance data comparability and reproducibility, and ultimately pave the way for translating eye movement research findings into improved clinical practices for patients with neurodegenerative and motor diseases.

1.2 Outline of the Dissertation

The structure of this document unfolds as outlined below: Chapter 2 provides the State of The Art for this project. Chapter 3 provides an insight into the employed data acquisition and analysis methodology. In Chapter 4, the attained results are presented and deliberated upon. Lastly, Chapter 5 encompasses the concluding remarks regarding the conducted work and a glimpse into future endeavors.

Chapter 2

State of The Art

2.1 Eye Movements in Neurodegenerative Diseases

The study of eye movements can provide invaluable insight into the mechanisms of neurodegenerative diseases [2–5].

There is substantial clinical and experimental evidence from the last 50 years showing that there are several cortical and subcortical networks responsible for the generation of eye movements, and therefore, ocular motor evaluation has served as a window to the brain, both in healthy individuals and patients [2, 3, 6].

Researchers and clinicians generally divide the eye movements into two classes. The first class of movements includes rotational and translational vestibulo-ocular reflexes, fixation, smooth pursuit, and optokinetic nystagmus, with the goal of stabilizing the fovea in relation to movement of the body or of objects in the surroundings. The second class is used to rapidly shift the fovea and bring its superior acuity and color sensitivity to bear on objects of interest and are called saccades [2].

The majority of studies on eye movements have focused on three types of movements: fixation, pursuit and saccades.

2.1.1 Fixation

The fixation system makes the gaze resting on a small predefined area, however they are not completely still. The eyes are in constant motion during attempted fixation. This happens to prevent visual fading from occurring, which is caused when images are perfectly stabilized on the retina. There are three main components to fixational eye movements: microsaccades, high-frequency low-amplitude tremor, and smooth drift. The control of ocular fixation is shared by several areas in the brain, including the basal ganglia, cerebellum, pariental cortex, and thus, fixation can become unstable in several neurodegenerative disorders, working as a very sensitive marker of brain dysfunction in general. Not surprisingly, disorders such Parkinson's disease (PD) and Alzheimer's disease (AD), etc. greatly affect ocular fixation [6, 7].

2.1.2 Saccades

Saccades are rapid eye movements that shift from a fixation point to another or from an object to another, in order to maintain the fovea directed to the point/object of interest. They include a rage of behaviors that cover voluntary and involuntary shifts of fixation. Saccades have become an important research tool to study a wide range of issues in the neurosciences beyond control of eye movement, due to the ease to distinct their abnormalities and connect them to specific mechanisms. In the most recent years, there are innumerous studies using saccades to investigate not only several aspects of cognition including memory, attention or impulsivity, but also to delineate the ocular motor phenotypes in virtually all neurodegenerative disorders. Importantly, some disorders show specific saccadic abnormalities (e.g., pathological slowing of vertical saccades in progressive supranuclear palsy, or prolonged latency in corticobasal degeneration, both reflecting severe forms of parkinsonism), making them an important diagnostic marker in neurology. The cortical and subcortical saccadic centers of saccades been described in detail and the saccadic network is one the most well studied motor network in neuroscience [7].

2.1.3 Smooth Pursuit

Smooth pursuit takes place when the eyes follow a moving object. Unlike saccades, this movement allows for a clear vision of an object as it moves within the visual field. It has been demonstrated that the velocity of smooth pursuit eye movements match the velocity of the target and that vision remains clear throughout the movement. As in fixations, to achieve this, the image of a moving object must be attended to and kept near to the fovea, whereas smeared images of the stationary background, which move across the rest of the retina due to the eye movements, must be ignored. The parietal cortices, together with the brainstem and cererebellum play a major role in the generation of smooth pursuit. Just like fixation, disturbance of pursuit is a very sensitive marker for signaling the presence of a neurological disorder, including chronic balance disorders such as ataxia [6, 7]

In sum, the analysis of oculomotor function, mainly the one derived from the evaluation of fixations, saccades, and smooth pursuit, show promise for probing both motor and cognitive function in patients with neurodegenerative diseases. Indeed, eye movements can be developed as a biomarker of both disease status and progression. There is a large body of literature demonstrating changes of oculomotor performance in diseases such as Alzheimer's and other neurodegenerative dementias, as well as in PD, Multiple Sclerosis (MS), Spinocerebellar ataxia and Huntington's disease [2–5, 8–11].

2.2 Eye Movement Recording Methods

Being able to record and analyze the above types of eye movements is a valuable tool to understand the functional integrity of brain structures and, consequently, to give insight about the status of neurodegenerative diseases.

Some eye movements abnormalities can be clinically assessed by trained doctors using, for example a fixation targe, Frenzel glasses or ophthalmoscopes [12]. However, such evaluation is gross, often inaccurate, prone to inter- and intra-observer lack of agreement, and lacking precision to be used as a measurement tool over time. Thus, it is often imperative in this context to make accurate measurements, including metrics of saccadic accuracy, latencies with respect to the appearance of the target, or eye velocity peak estimations which are not possible to be done by a clinician. Furthermore, to test cognitive impairment, it is desirable to present stimulus under specific and standardized conditions such as defined targe positions, randomized latency for targets' appearance, constant velocity of a moving target, etc. [6].

Importantly, such measurements can be easily obtained in the laboratory. Recordings of eye movements are highly useful for objective and precise identification of disease status and monitoring of disease progression [6].

Several different methods to assess eye movements have been developed and are currently in use, including electro-oculography [13], scleral search coil system [14], and video-oculography (VOG)/eye tracking [15]. While scleral search coil system remains the gold standard in eye movements research due to its accuracy, its invasiveness, limited time use, and demanding technical requirements only available in a few centers in the world make it a non-feasible option. In the last decades, the emergence of competitive alternatives. mostly based on VOG and eye tracking systems, have revolutionized the field and are progressively replacing scleral search coil system. The former carries the advantages of being non-invasive and allowing for easy test design.

2.2.1 Eye tracking Video-Oculography Techniques

A handful of methods for estimating gaze have recently been published in the literature. These methods can be classified in two categories: appearance-based and feature-based methods. It is clear that the use of a certain methods depends on the application for which it has been designed. Features of the device and the process itself, including the quality of the camera and hardware, the required accuracy, the environmental conditions, the desired cost, and the freedom of head movements constitute some examples which can ultimately influence the choice for a specific system and/or behavioral paradigm [6].

Appearance-based methods

Some studies [16–18] have described strategies for working with low-resolution images in various environments, with appearance-based solutions looking to be a potential choice. With this, it is possible to address the gaze estimation problem by mapping a function and learning from it to give gaze directions from eye images. This method is very robust even when they are applied to low-resolution cameras or under natural illumination. The mapping functions are designed so that the system is trained with eye images of known gaze direction using various regression techniques before it is applied [6, 17, 19–23].

The main problem of these methods is that it is necessary to generate a person-specific training because the appearance of the eye depends on the gaze direction and on the head poses, imaging conditions and eve on the identities of subjects.

The accuracy of appearance-based methods is not high enough for clinical uses and it depends on the quality of the training data.

Feature-based methods

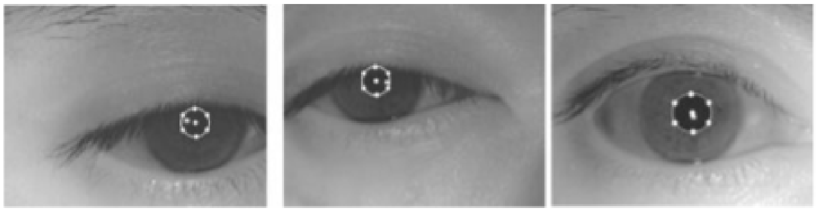


Figure 2.1: Features from high-resolution eye-images, Source: [6]

Feature-based methods are the most popular approach for gaze estimation, extracting local features like contours, eye corners, and eye reflections. For this, it is needed to have access to high-resolution eye images captured by zooming in the user's eyes, as we can see in Fig. 1. These methods can be divided into two main groups: 2D mapping-based gaze estimation methods and 3D model-based gaze estimation methods [6].

The 3D model-based methods directly compute the 3D gaze direction vector from the eye features based on a geometric model of the eye [24,25]. In order to compute the center of the cornea and the eye vector, these models require correct assessment of various user-dependent parameters such as cornea radii, angles between visual and optical axes, the distance between the cornea center and pupil center, etc. [6]. These models can also calculate head movements in a detailed way and with high accuracy but with one disadvantage of complexing the setup of the process. For this, it is needed to use at least a single camera with multiple calibrated light sources [26] or stereo cameras [27–29].

Alternatively, the 2D mapping methods are based in finding a mapping function from 2D feature space like Pupil-Center-Corneal-Reflections, contours, etc. to gaze point such the computer screen coordinates. In this approach, the parameters are implicitly included in the learning of the mapping function which makes the setup process and the calibration process simpler [6, 30, 31].

For the above methods, different features can be used as inputs to the mapping function depending on the application and the image conditions. In recent years, with the increase of studies on eye tracking using low-resolution images and natural light, passive image-based algorithms have been developed for eye localizing and tracking. These works have proposed iris and pupil tracking [16,32]. The pupil tracking has a lot of advantages being one of them the fact that it is less covered by the eyelids, enabling vertical tracking, and also the fact of having a sharper edge between the pupil and the iris provides a higher resolution [6].

Nevertheless, for the purpose of clinical research, where experiments are conducted in a controlled environment, it is not a problem to have infrared lighting and thus active light techniques would be a better option. When a light source (usually infrared) illuminates the eyes at different layers, the boundaries between the lens and the cornea act as convex mirrors and produces some reflections or virtual images [30–33]. When a light source is placed collinearly to the optical axis of the camera, most of the light is reflected back to the camera and the eye image shows a bright pupil. Conversely, when a light source is located away from the camera's optical axis, the image shows a dark pupil. Therefore, eye trackers with active IR illumination can use the difference between dark and bright pupil images by synchronously switching between the two light sources [15].

For detection of the corneal reflections, it's required a narrow field of view camera. Furthermore, these systems compute high-resolution eye images that were captured by zooming in movement-restricted users. Reports of these techniques show good to excellent results but have two major issues. The first is the fact that for each person and each system configuration it's needed a specific mapping function, which requires a tedious calibration procedure. This calibration process is typically made as shown in Fig. 3, where a set of visual targets is presented to the user who has to stare to the computer while the corresponding measurement is being done. Then, from these measurements, the mapping function is calculated. Second, is that once the calibration process is done, the person must be completely still. If head movements are made during the recordings, there will be large errors between the actual and estimated directions. To avoid this from happening, head restraint systems are often used (2.2 and 2.3) [6].

In applications such as clinical research or disease diagnosis, where it is possible to control the conditions of the process, feature-based methods achieve a really high accuracy which is critical to detect subtle abnormalities in oculomotor behavior [34]. Currently, most commercial gaze tracking devices use 2D mapping feature-based methods with Infrared camera and illumination to attain highly accurate performance of gaze estimation.

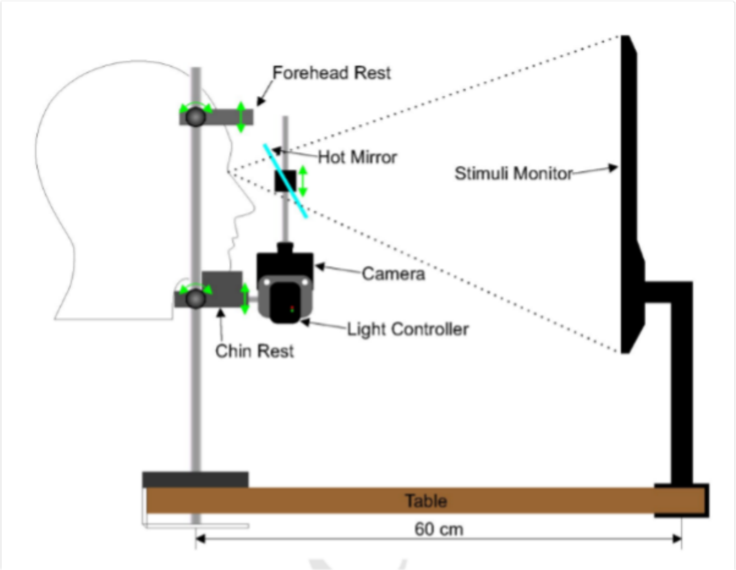


Figure 2.2: Example of a gaze tracker with a restraint system, Source: [6]

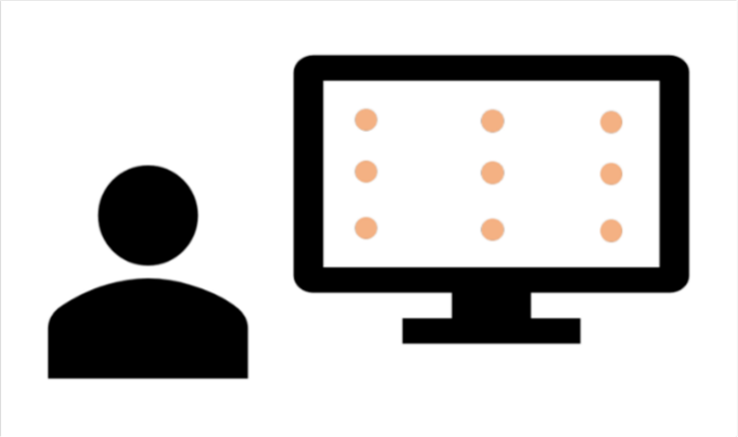


Figure 2.3: Example of calibration points, Source: [6]

Head movements

The eyeball orientation is not the only contributing factor for gaze, the latter is a product of the head pose and the eyeball orientation. Humans usually move their heads to a comfortable position before orienting the eye.

In general, people move their heads while they are using gaze tracker, which makes the measurement of head movements a requirement. 3D model-based methods are the most robust to head pose changes but, as a drawback, they require a really complex and calibrated system setting, difficult their use in common applications.

For clinic applications, tests must be conducted for only a few minutes, and it is not advisable to perform complex calibrations that fatigue the patients. For this reason, the restraint systems are suitable and work very well.

2.3 The importance of bringing the Eye tracker to the Clinic

As stated before, eye tracking is a recent technique that accurately measures eye movement [35]. It has gained popularity as a result of its ability to provide better quantification of ocular motor parameters for big data analysis, in a noninvasive manner. Not surprisingly, eye tracking has become a promising biomarker for the diagnosis and evaluation of neurodegenerative diseases [36–40].

Specifically, when performing an eye movement task, with the eyes looking at the screen of a computer, the tracker captures several parameters, such as the latency, peak and mean velocity, position of the targets and the eyes, the distance between them, etc. If this process is performed with normal people and patients with cognitive impairment, it is made a comparison between the parameters of both. With this, it is possible to find out the differences and judge the status of the disease [41].

Neurodegenerative diseases often damage extensive brain structures and networks, which affect the control of eye movements [5, 40]. Eye-tracking measurements ultimately bridge brain behavioral function and neural processes [40].

There many papers focusing on the importance of Eye tracking in clinic application.

Still, one of the main drawbacks in using an Eye Tracker as a diagnostic tool, relates to its striking underutilization in the clinic, the place where ironically would be most useful. Indeed, most of the available eye trackers are placed in a laboratory environment and are mostly used by psychologists, neuroscientists, engineers in close collaboration with clinicians. While the above research setting has provided extraordinary advances in the knowledge of eye movements and neurological disorders through thousands of seminal publications, it is nevertheless more and more needed the use of eye trackers in a hospital setting, where a large number of patients could easily have access to such tool, apart from a controlled and restricted experimental setting in a laboratory.

One additional drawback relates to the knowledge and required skills to properly operate an eye tracker, since the majority of eye trackers available in the market do not provide a user-friendly interface to be used by non-engineers/mathematicians, and moreover, ocular motor paradigms and results output has to be developed in advance by experts through the use of *Matlab* and/or other related software. Thus, for an eye tracker to be fully operated by clinicians and other health clinicians as a diagnostic tool in a hospital setting, where it would be most needed, the aforementioned drawbacks have to be takin into account and strategies should be developed based on the above gaps.

The biggest drawback is the lack of appropriate combination of parameters to be studied and a standard protocol to perform this procedure.

2.4 The Effort on Standardization

One final matter relates to standardization of ocular motor assessment. So far, each work group has published their research using custom-designed behavioral paradigms, lacking standardization in most instances. And this subject is important in eye movement research, since it is well known that the manipulation of specific parameters in the design of a task such as the size of the stimuli, distance between stimuli, randomized vs. constant order of their appearance, gap vs. overlap saccades, pre-task instructions, feedback during tasks, number of trials, order of tasks, overall difficulty, all relevantly influence the results [7].

As there is no standardized protocol for carrying out eye movement experiments, results from one laboratory cannot be easily compared with those from another [42]. Current research highlights the need for a systematic approach and a generalized protocol of eye movements tests suitable to use in multicenter studies in order to eliminate the lack of data validation and reproducibility.

As an example, for a complex task as the antisaccadic task (in which the saccade must be made in a direction opposite to that of the stimulus), there is a huge number of different possible protocols and each researcher has their favorite procedure, so that when the detailed data is published it can't be compared with other studies [42]. In early stages of research it is important to have different approaches and to evaluate each of them to know which one has the better results. But once the technique has matured, and to apply it clinically as a useful test, it is essential that the results can be compared with other labs and clinics.

For this reason, a protocol was published in 2018, called DEMoNS protocol [1] where the main objective was to provide a standardized and reproducible protocol for infrared oculography measurements of eye movements and analysis.

The protocol was focused on brevity, reliability and reproducibility in order to be more suitable for implementation in a multicenter clinical setting and its results were of excellent reproducibility, being capable of studying eye movements in various neurodegenerative and motor diseases [1].

Chapter 3

Methods

In this chapter, it will be described the design and conditions chosen for this study and the processes and methods used to gather and analyze the data.

3.1 Project description

In *CHUC - Department of Neurology*, there is an eye movement tracking setup (3.1), with eye-tracking equipment (*Eyelink SR Research, 1000Hz*) in Tower Mount (average accuracy of 0.15º and spatial resolution of less than 0.01° RMS), working with a sampling rate of 1000Hz, and acquiring binocular data, calibrating each eye at a time [43, 44].

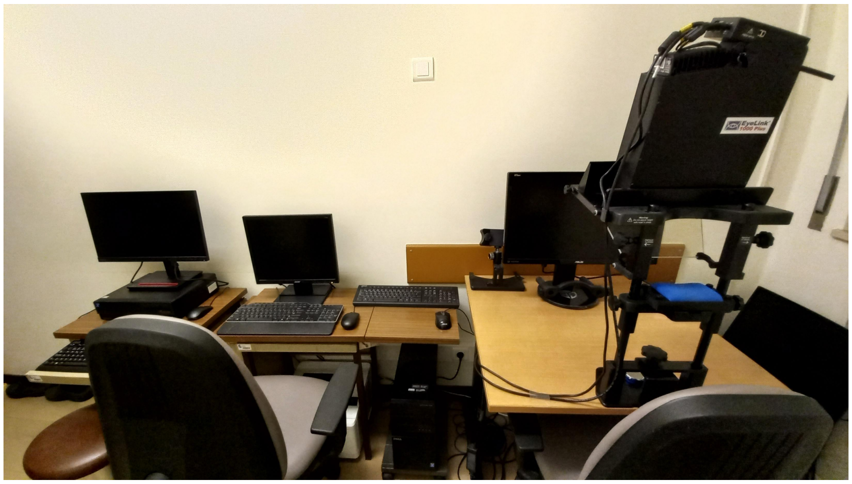


Figure 3.1: Eyetracker CHUC setup

A few adaptations were made to the DEMoNS protocol [1]. Regarding setup, eye-monitor distance was set to 45 cm (and not 92 cm), a tower mount was used instead of a desktop mount, and a 5-point (and not 9) calibration procedure was used. Regarding the measurement protocol, fixation, pro-saccades, and anti-saccades were included, while express saccades (gap paradigm), double-step, and repeated pro-saccades were excluded. During the fixation paradigm, only one (and not two) trials of five fixations were performed, at the center and an eccentric location (15º of visual angle left or right and 15º of visual angle up or down from the center). The horizontal pro-saccades task was split into a fixed distance visual angle task (10º) and a variable distance visual angle task (5º. 8º, 11º and 15º), both of which with 32 saccades randomly directed either to the right or to the left. Two similar paradigms were added along the vertical direction. Anti-saccades task was built using the same criteria as that from pro-saccades. Sinusoidal horizontal and vertical 30º pursuit tasks were added and performed between pro- and anti-saccades protocols. The above changes were made based on recent recommendations on saccade protocols in order to maximize patients' cooperation during the ocular motor task [3, 4], avoid biases (e.g., different amplitudes) that might compromise a fair comparison between vertical and horizontal saccades data, and introduce recent metrics which seem to be a helpful discriminator between health and disease states (e.g., vertical antisaccades) [37].

The monitor has a size (not including the bezel) of 53cm x 29.8cm, its resolution is 1920x1080, and the refresh rate is 144Hz. According to the Visual Angle Calculator (SR Research) [45], using these values, 15o corresponds to 436.8077401 pixels (3.2).

3.2 Measurement protocol

This section will describe all the details of the different paradigms of CHUC's measurement protocol.

All the different domains (fixation, pro-saccades, anti-saccades, multiple pro-saccades, and pursuit) are preceded by a practice task so that the patient can understand what he is supposed to do.

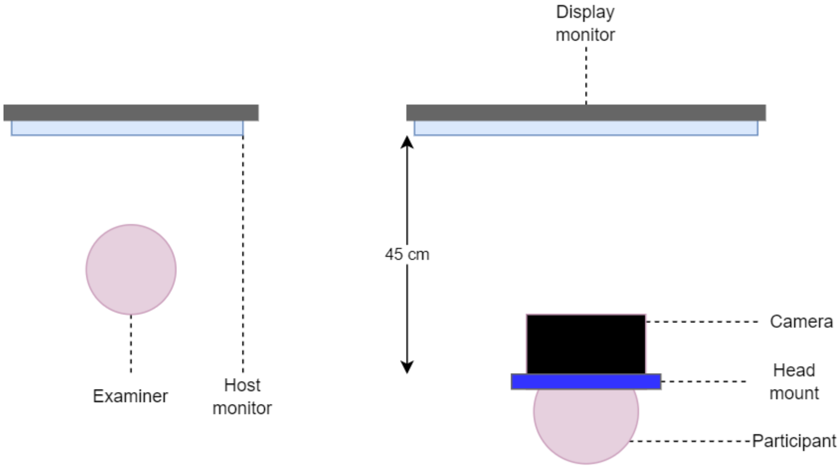


Figure 3.2: Eyetracker CHUC setup (scheme)

3.2.1 Fixation Task

The fixation task includes five practice points to enhance fixation skills, starting with the central fixation point followed by four eccentric locations. Participants perform one block of five fixations during the main task, each lasting 10 seconds. These fixations occur at the center and four eccentric positions (15 degrees of visual angle to the left, right, up, and down from the center). The order of eccentric fixation targets is randomized, while the center fixation is always the starting point. The clinic provides verbal instructions, guiding participants to focus on the white circle and follow its movements as it jumps to different locations. Verbal encouragement is given to promote steady fixation while allowing occasional blinks. All fixation dots at the center or eccentric locations consist of a white fixation circle (3.3).

3.2.2 Horizontal Pro-saccades Task

The pro-saccades task begins with four practice trials, involving horizontal pro-saccades. These practice trials include two eccentric positions on each side (left and right). In the main task, participants perform one block comprising 32 pro-saccades from the center to an eccentric location, either 10 degrees of visual angle to the left or right. Each trial starts with a white central fixation circle displayed randomly between 1440ms and 2304ms. Afterward, an eccentric blue target appears randomly to the left or right for 1 second. The trial ends

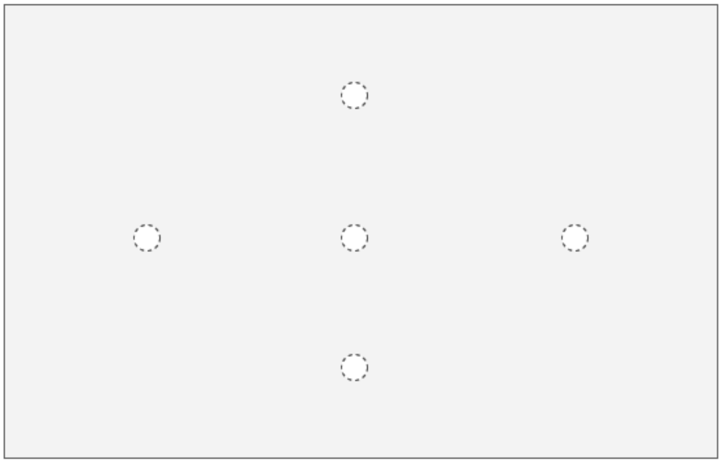


Figure 3.3: Fixation task

with a blank screen shown for 1 second. The timing and position of the eccentric target are randomized and counterbalanced to prevent predictability. The clinic delivers verbal instructions to look at the circle and follow it with a saccade to the eccentric target as soon as it appears, aiming for speed and accuracy. Participants are then instructed to return their gaze to the center and wait for the fixation circle to reappear (3.4).

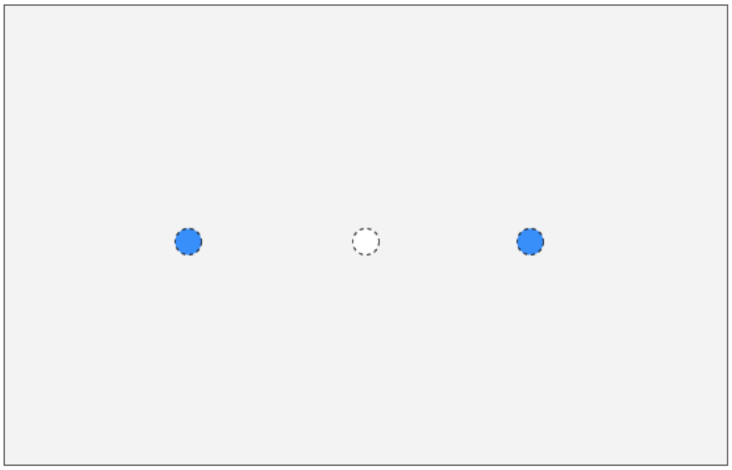


Figure 3.4: Horizontal Pro-saccades Task

3.2.3 Vertical Pro-saccades Task

The vertical pro-saccades task mirrors the horizontal pro-saccades task, with the sole distinction being the orientation of the targets – now positioned upward and downward rather than left and right. The procedure involves an initial phase of 4 practice trials centered on vertical pro-saccades. These practice trials encompass two upward and two downward eccentric positions. In the primary task, participants engage in a single block featuring 32 pro-saccades originating from the center and directed towards an eccentric location, either 10 degrees of visual angle above or below the central fixation point.

Each trial initiation is marked by the appearance of a white central fixation circle, displayed for a variable duration ranging from 1440ms to 2304ms. Following this, an eccentric blue target materializes randomly either above or below, remaining visible for 1 second. The trial concludes with a blank screen presented for 1 second. To ensure unpredictability, the eccentric target's temporal sequencing and position are randomized and counterbalanced. Participants receive oral instructions to fixate upon the central circle, and track its movement with a swift saccade to the eccentric target upon appearance, emphasizing swiftness and precision. Following the saccade, participants are prompted to reorient their gaze to the center and await the reappearance of the fixation circle (3.5).

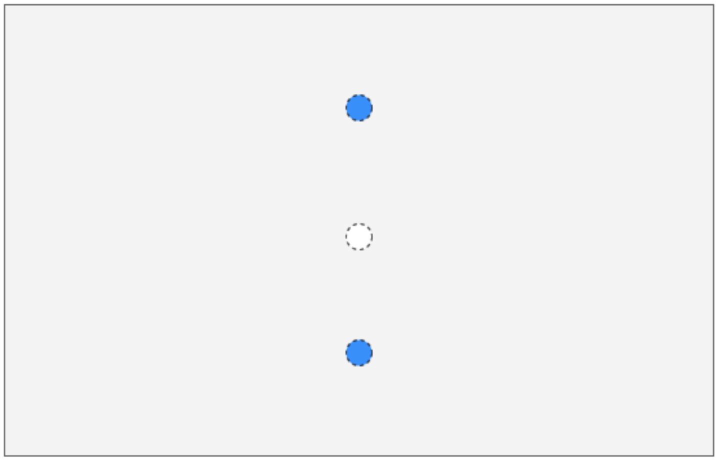


Figure 3.5: Vertical Pro-saccades Task

3.2.4 Horizontal Multiple Pro-saccades task

Participants undergo four practice trials, each presenting a different eccentric target location between 5, 8.33, 11.66, and 15 degrees, with two trials on each side (left and right). The main task comprises one block of 32 pro-saccades, starting from the center to an eccentric location, either 5, 8.33, 11.66, or 15 degrees to the left or right. The duration of the central fixation circle varies randomly between 1440ms and 2304ms. After the central fixation period, an eccentric blue target appears randomly to the left or right for 1 second, followed by a blank screen for 1 second. The first trial is preceded by a practice trial containing four pro-saccades. Verbal instructions from the clinic remain consistent with the previous tasks, guiding participants to follow the circle and make saccades toward the eccentric target promptly and accurately (3.6). Of note, horizontal and vertical (see below) multiple pro-saccades task constitute the only optional block within the protocol, given its specific utility on studying the relationship between the amplitude and velocity of saccades, making it useful only for analyzing patients with diseases where the above relationship is known to be altered (e.g., MS).

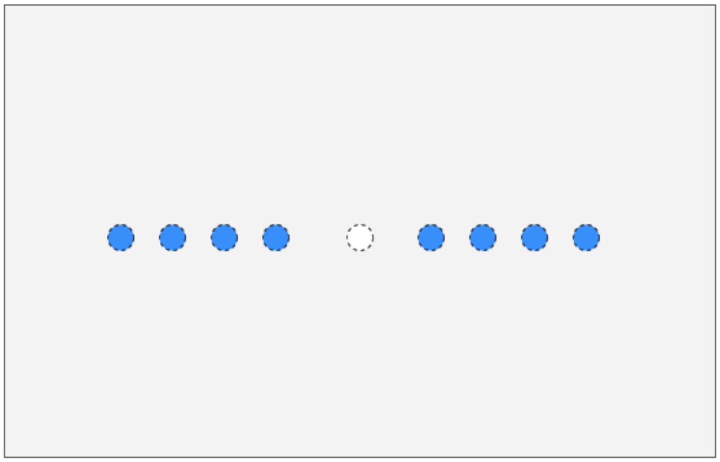


Figure 3.6: Horizontal Multiple Pro-saccades Task

3.2.5 Vertical Multiple Pro-saccades task

The vertical multiple pro-saccades task closely parallels the horizontal multiple pro-saccades task, with the key distinction being the orientation of the targets – now positioned upward and downward instead of left and right. The procedure commences with participants engaging in 4 practice trials, each featuring distinct eccentric target locations set at 5, 8.33, 11.66, and 15 degrees, with two trials on each side (above and below).

The main task encompasses a block of 32 pro-saccades, originating from the center and directed towards an eccentric location. This location can be 5, 8.33, 11.66, or 15 degrees above or below the center. The initiation of each trial is heralded by the appearance of a white central fixation circle, with its duration randomly varied between 1440ms and 2304ms. Following the central fixation period, an eccentric blue target emerges randomly above or below the center, remaining visible for 1 second. Subsequently, a blank screen is displayed for a 1-second duration.

The first trial is preceded by a practice trial involving four pro-saccades. Verbal instructions delivered by the clinic remain consistent with those provided for the prior tasks, guiding participants to fixate upon the central circle, swiftly and accurately executing saccades toward the eccentric target upon its appearance (3.7).

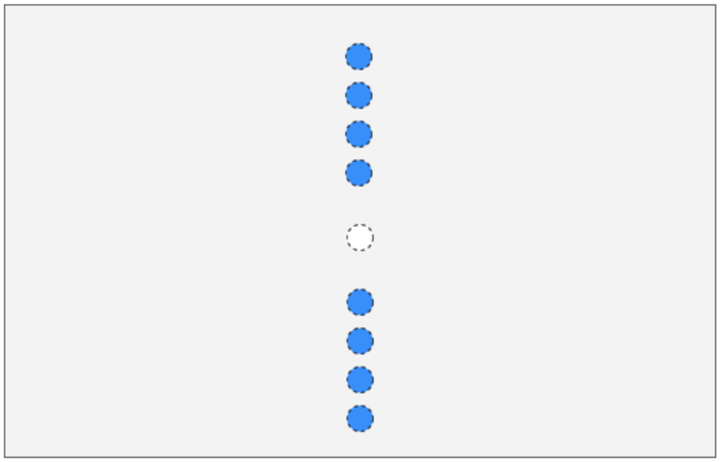


Figure 3.7: Vertical Multiple Pro-saccades Task

3.2.6 Pursuit Task

In the practice task for horizontal sinusoidal pursuit, participants complete one trial involving a target moving from the center to one side, returning to the center, moving to the other side, and finally returning to the center, resulting in two half-circles of horizontal pursuit. In the main task, participants engage in horizontal sinusoidal pursuit, starting with presenting a central blue circle for 1000ms. The target then moves horizontally with a sinusoidal velocity profile, performing eight half circles with a 30-degree amplitude between 15 degrees to the right and 15 degrees to the left, taking 40 seconds. The clinic provides verbal instructions for participants to smoothly and accurately follow the moving target (3.8).

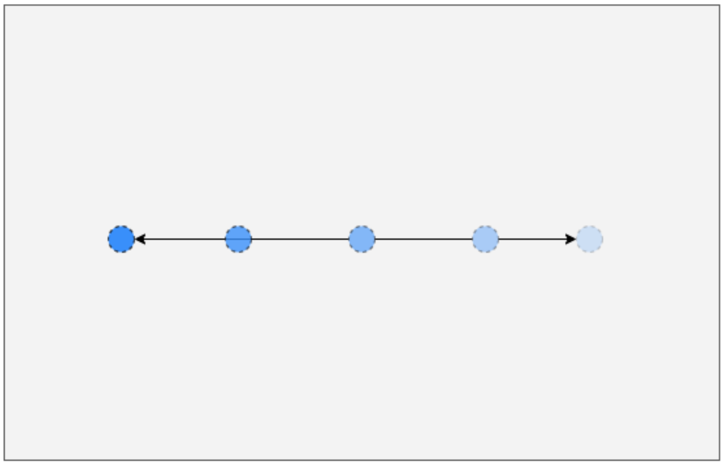


Figure 3.8: Horizontal Pursuit Task

Similarly, the practice and main tasks for vertical sinusoidal pursuit are identical, with the only difference being the direction of movement, now vertical, ranging 15 degrees up and 15 degrees down from the center. The clinic instructs participants to follow the target's vertical movements smoothly and accurately (3.9).

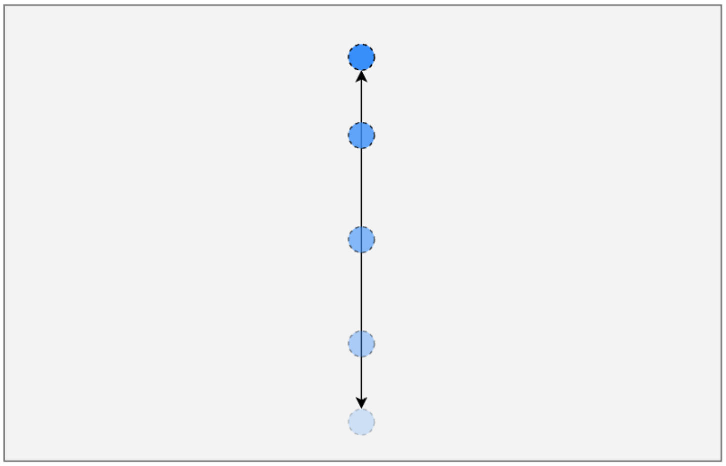


Figure 3.9: Vertical Pursuit Task

3.2.7 Horizontal Anti-saccades Task

The practice task for horizontal anti-saccades consists of 4 trials involving horizontal anti-saccades with two eccentric positions on each side (left and right). The main task for horizontal anti-saccades is similar to the horizontal pro-saccades task but with the critical difference in instructions provided by the clinic. Participants are guided to look at the circle and, when it jumps to the left or right, make a saccade in the opposite direction, mirroring the eccentric target's direction. Verbal instructions inform participants that this task is distinct from the previous one. A practice trial with four anti-saccades precedes the first trial (3.10).

3.2.8 Vertical Anti-saccades task

The vertical anti-saccades task follows a structure analogous to the horizontal anti-saccades task, with the sole variation being the orientation of the targets – now positioned above and below instead of left and right. To initiate the practice phase, participants engage in 4 trials

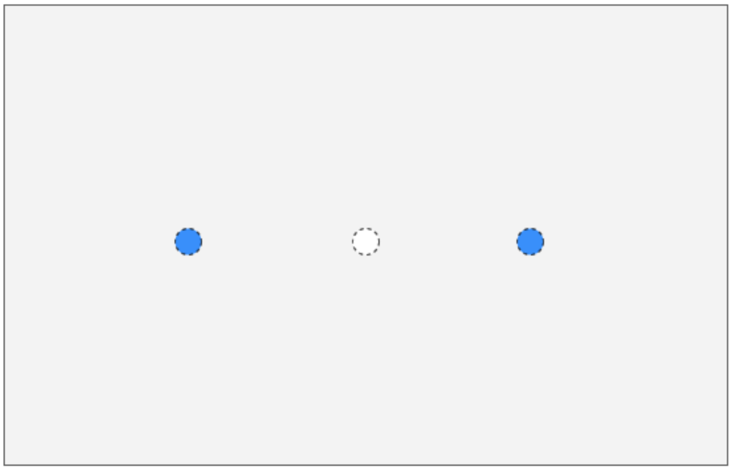


Figure 3.10: Horizontal Anti-saccades Task

involving vertical anti-saccades. These practice trials incorporate two eccentric positions above and below the central point.

The primary task for vertical anti-saccades closely mirrors the vertical pro-saccades task, with the fundamental distinction residing in the instructions provided by the clinic. During the main task, participants are directed to focus on the central fixation circle. However, when the circle shifts its position either upward or downward, participants are instructed to execute a saccade in the precise opposite direction, mirroring the eccentric target's trajectory.

Verbal instructions emphasize the distinct nature of this task compared to the previous ones. The commencement of the first trial is preceded by a practice trial encompassing four anti-saccades, allowing participants to acquaint themselves with the task's execution and expectations (3.11).

Throughout the experiment, the background color is gray (R128 B128 G128), the fixation circle is white (R255 B255 G255), and the eccentric targets are blue (R0 B0 G255), all maintaining specific visual angles as mentioned in the original description.

3.3 Participants

This dissertation will focus on subjects with PD who previously underwent deep brain stimulation (DBS). In brief, DBS is a treatment modality commonly used in moderate to

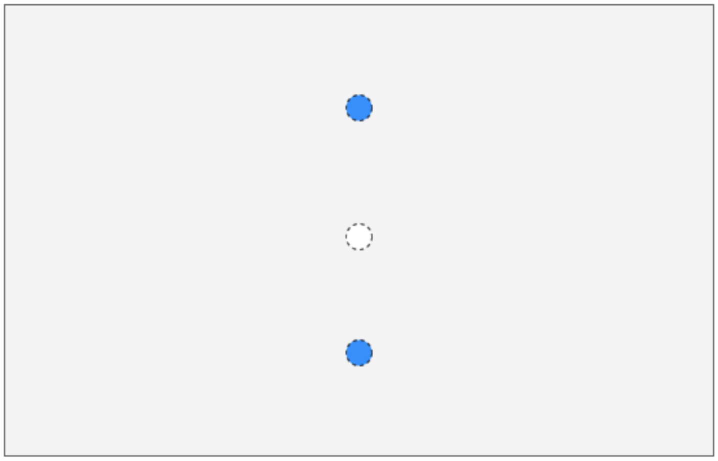


Figure 3.11: Vertical Anti-saccades Task

advanced PD, in which electrodes are implanted in the brain in order to modulate basal ganglia neuronal discharge, ultimately improving motor function in PD patients. However, as will be explained in the Future Work section, the methods applied for PD can also be applied to other neurological diseases mentioned in the State of The Art. Patients with PD were recruited after authorization of the project by the Hospital Ethics Commitee.

There were 23 subjects with Parkinson's disease included in this study, with a mean age of 66,5 (range 49-78), of which 39% were of female gender.

It's important to note that the participants with PD involved in this study underwent the procedure on at least two occasions – once with the DBS system activated (DBS ON) and another with the DBS system deactivated (DBS OFF).

Importantly, the above protocol has been successfully applied in several other diseases so far, including in patients with MS, AD, motor neuron disease.

3.4 Analysis of DEMoNS Protocol Scripts and Functions: Initial Process

The project is based on the DEMoNS protocol mentioned in the State of the Art chapter. The multidisciplinary team that worked on this protocol published the *Matlab* scripts and functions used in it along with some descriptions of the methods applied and instructions of the analysis so that more people could implement the same protocol.

With this in mind, the first step was to analyze the scripts and functions published by the multidisciplinary team in order to understand the workload that would be needed to adapt this protocol to the reality of the Neurology Department of *Centro Hospitalar e Universitário de Coimbra*.

After this analysis, the following conclusions were drawn:

- The analysis and import scripts could not be executed in our reality without significant adaptations.
- Some tasks were deemed irrelevant for our specific context (which will be described ahead).

Implementing the DEMoNS protocol in the Neurology Department revealed several advantages and disadvantages. The advantages include the following:

- Most important parameters of all tasks were pre-calculated, although not all were utilized.
- Most function scripts were created to be used in every task.
- The pre-processing was very consistent.
- The import files procedure was functional but obsolete; it took a considerable amount of time to complete (from 120 to 180 minutes).
- All scripts were written and organized in the same way, creating a homogeneous type of coding and variable creation.
- The documentation provided by the DEMoNS protocol multidisciplinary team explained the scripts thoroughly.
- The calculations, parameters calculated, and conditions were standardized and well-grounded since they were written based on the DEMoNS article.

On the other hand, the protocol also presented some disadvantages:

- The scripts were very lengthy, with some explanation required.
- It took considerable time to feel comfortable with the coding and variable creation.
- Some obsolete code had to be rewritten.

The initial step involves having the subject complete the designated tasks. Subsequently, using the *Eyelink Data Viewer* software, specific parameters are selected, such as:

Parameters	Description
TRIAL_INDEX	Assigns a unique number to each trial, including practice ones.
TIMESTAMP	Records the time from the eye-tracker equipment.
LEFT_GAZE_X	Captures the horizontal position (x) of the left eye.
LEFT_GAZE_Y	Captures the left eye's vertical position (y).
LEFT_IN_BLINK	Indicates '1' when the left eye blinks; otherwise, it's '0'.
RIGHT_GAZE_X	Records the horizontal position (x) of the right eye.
RIGHT_GAZE_Y	Records the right eye's vertical position (y).
RIGHT_IN_BLINK	Indicates '1' during right eye blinks; otherwise, it's '0'.
block	Identifies the trial block, such as 'fixation_prac' or 'fixation'.
sac_location	Provides the target's horz. and vert. position (x, y) for all tasks except pursuit.
TARGET_X_TARG1	Indicates the target's horizontal position for the pursuit task.
TARGET_Y_TARG1	Indicates the target's vertical position for the pursuit task.
SAMPLE_MESSAGE	Contains control messages.

After selecting these parameters, a .txt file is generated for further use.

3.5 Optimizing Script Efficiency

I started my work on the scripts by optimizing the import of the raw data files. I tested different approaches using cells and tables in *Matlab* to import the data acquired through the eye tracker. The conclusion was that using tables to import the files from the .txt file to a .mat file for each task reduced the script's running time. After this rework, instead of 3 hours running the import script, the import took less than 1 min to complete.

3.6 Script Adaptation to Align with Coimbra's Context: In-depth Analysis

In this section, I will delve into the modifications made to the DEMoNS scripts to tailor them to the specific context of CHUC. This adaptation involved several changes to the analysis procedures, enabling the scripts to capture and analyze data in the CHUC's setup effectively. Additionally, I will elaborate on the distinct parameters calculated for each task within this adapted framework.

3.6.1 Pre-processing Workflow for Data Analysis

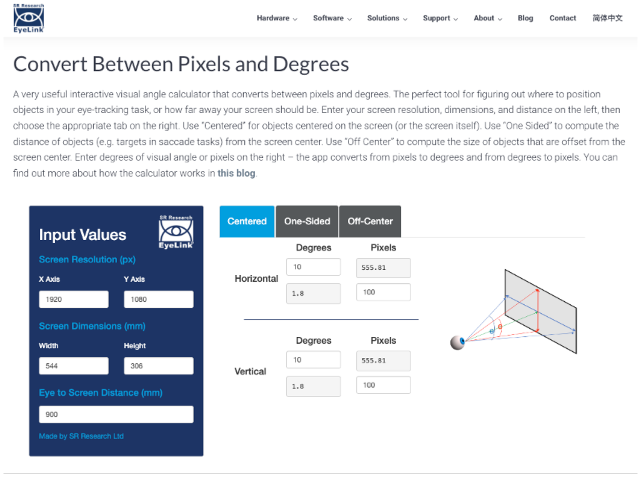
Gaze Position Filtering

The initial stage of the pre-processing process involves applying a filter to the recorded gaze positions obtained during the experimental tasks. Gaze position data are often susceptible to noise, which could adversely impact the precision of subsequent analyses. A suitable filtering technique, such as a second-order low-pass filter with a cutoff frequency set at 10% of the sampling frequency, is applied to counteract this. This approach effectively reduces high-frequency noise while maintaining the fundamental patterns of gaze movement.

It's important to note that the following variables are manual settings that must be aligned with the setup of each clinical site:

- Sample frequency.
- Cutoff frequency of the filter (standard at 10% of the sampling frequency).
- Number of pixels width of the screen.
- Number of pixels height of the screen.
- Locations of the targets in pixels on the screen.
- Width of the screen (cm).
- Height of screen (cm).
- Viewing distance (cm).

The variables in pixels were acquired using the *Visual Angle Calculator* from the SR Research Eyelink [45] (3.12).



Convert Between Pixels and Degrees

A very useful interactive visual angle calculator that converts between pixels and degrees. The perfect tool for figuring out where to position objects in your eye-tracking task, or how far away your screen should be. Enter your screen resolution, dimensions, and distance on the left, then choose the appropriate tab on the right. Use "Centered" for objects centered on the screen (or the screen itself). Use "One Sided" to compute the distance of objects (e.g. targets in saccade tasks) from the screen center. Use "Off Center" to compute the size of objects that are offset from the screen center. Enter degrees of visual angle or pixels on the right – the app converts from pixels to degrees and from degrees to pixels. You can find out more about how the calculator works in **this blog**.

Input Values

Screen Resolution (px)
X Axis: 1920
Y Axis: 1080

Screen Dimensions (mm)
Width: 544
Height: 306

Eye to Screen Distance (mm)
900

Made by SR Research Ltd

	Degrees	Pixels
Horizontal	10	555.81
	1.8	100
Vertical	10	555.81
	1.8	100

Figure 3.12: Visual Angle Calculator

In our case, these settings were tailored to match the configuration at CHUC - Department of Neurology. The manual adjustment of these variables ensures that the filtering process is optimized for the specific setup at the clinical site, enhancing the accuracy and reliability of the subsequent analysis.

Each domain task (fixation, pro-saccades, multiple pro-saccades, and anti-saccades) has its filter gaze position script.

Artefact Removal

Building upon the filtered gaze positions, the subsequent step centers around identifying and eliminating artifacts in the dataset. Artifacts can emerge from various sources, including blinks, rapid eye movements, and sensor-related distortions. To address these issues, a comprehensive strategy is employed:

- **Blink Artefact Removal**: To counteract blink-related artifacts, samples preceding and succeeding blinks are systematically removed from the dataset. This targeted approach ensures that blink-induced distortions are effectively eliminated.

- **Disturbance Removal:** Signal disturbances, originating from factors such as sensor noise, are systematically detected and treated. Spikes in velocity and acceleration values exceeding predefined thresholds are identified and marked for removal.

Saccade Detection

Upon successful artifact removal, the focus shifts to identifying saccadic eye movements. Saccades, rapid shifts in gaze between fixations, offer insights into visual attention patterns. This process involves the following steps:

- **Approximate Saccade Detection:** Applying specific criteria, such as acceleration thresholds, the approximate intervals of potential saccades are identified. These intervals are flagged for further analysis.
- **Merging Saccade Intervals:** Adjacent saccade intervals are merged, streamlining the identification process.
- **Parameterization of Saccades:** Parameters of approximate saccade intervals are determined, including peak velocities and directions.
- **Refinement of Saccade Start and End:** Through a systematic analysis of velocity and acceleration patterns, individual saccades' precise start and end points are pinpointed.
- **Saccade Validation:** Saccades with minimal durations and amplitudes are selected for further analysis.
- **Main Saccade Identification:** A hierarchical approach distinguishes main saccades from post-saccadic oscillations (PSOs) within saccade complexes, considering peak velocities and temporal relationships.

By meticulously following this pre-processing workflow – encompassing gaze position filtering, artifact removal (including blink artifact elimination), and saccade detection – the dataset is refined and prepared for subsequent analysis stages. This pre-processed data forms the foundation for extracting meaningful insights and facilitating in-depth interpretations of gaze behavior and attention dynamics within the study context.

3.6.2 Data Analysis

Fixation Analysis

Overview of Analysis Steps:

1. Detect Target Movements and Fixation Periods
2. Identify and Remove Centrifugal and Centripetal Saccades
3. Classify Saccades
4. Determine Eye Stability Parameters

Detailed Analysis Steps:

1. **Detect Target Movements and Fixation Periods:**
    - Detect movements of the target in variables TargetX and TargetY.
    - Identify centrifugal target jumps for off-center target locations.
    - Detect center fixation periods with center target locations.
    - Record fixation locations and associated parameters.
    - Detect centripetal target jumps (end of off-center fixation period).
    - Identify the end of the center fixation period.
2. **Identify and Remove Centrifugal and Centripetal Saccades:**
    - For centrifugal saccades in left and right eyes:
        - Set activation flags for correct saccades after target movement.
        - Detect correct centrifugal saccades based on timing and amplitude criteria.
        - Record saccade parameters in Target Movements variable.
        - Deactivate flag.
    - For centripetal saccades:
        - Set activation flags for correct saccades after target movement
        - Detect correct centripetal saccades based on timing and amplitude criteria.
        - Record saccade parameters in Target Movements variable.
        - Deactivate flag.
    - Determine which eye had the first and last saccade, and mark samples for acceleration removal.
    - Re-run saccade detection to update acceleration variables.

3. **Classify Saccades:**
   - Classify saccade types for left and right eyes separately.
   - Classify square wave jerk (SWJ), macro SWJ, saccadic intrusion, and microsaccadic intrusion.
   - Identify saccades during fixation periods and record parameters.
4. **Determine Eye Stability Parameters:**
   - Set fixation position codes for different target locations.
   - Organize fixation data into corresponding variables.
   - Calculate stability parameters (mean, SD, correlation, BCEA, velocity, acceleration) for fixation periods.
   - Establish continuous fixation data for the same target positions.
   - Perform linear regression on fixation positions and vergence for different target positions.
   - Compute the standard error of the estimate for regression lines.
   - Record fixation stability parameters and regression coefficients.
   - Create new variables for fixation stability and saccade flags.
   - Exclude short fixation periods (¡3.5 sec) from the analysis.
   - Display statistics on saccades, fixation periods, and mono-ocular saccades.
   - Issue a warning if the detected number of fixation periods is not 10.

All conditions and decision criteria were retained from the DEMoNS protocol scripts. The modifications were aimed at adapting the protocol to Coimbra's setup and refining the target detection process. These adjustments were necessary to ensure compatibility and accuracy within the specific context of *CHUC - Department of Neurology.* The comprehensive analysis outlined above incorporates the original framework while addressing the unique requirements of the clinical site's setup and procedures.

Horizontal Pro-saccades Analysis

Overview of Analysis Steps:

1. Detect Target Movements
2. Identify Correct Pro-saccades and Calculate General Parameters
3. Determine Fixation Period after Saccade
4. Calculate Area Under the Curve (AUC)
5. Compute First-pass Amplitude (FPA)
6. Check for CF Saccade Start Time Discrepancy
7. Calculate Versional Dysconjugacy Index (VDI)

Detailed Analysis Steps:

1. **Detect Target Movements:**
   - Analyze the TargetX variable.
   - Detect centrifugal target jumps at two specific locations:
     - Identify off-center locations in consecutive samples.
     - Ensure the previous sample doesn't indicate an off-center position.
     - Count these jumps using Target_CF.
   - Detect centripetal target jumps:
     - Identify central locations in consecutive samples.
     - Confirm the previous sample doesn't indicate central position.
     - Ensure Target_CF is not 0.
2. **Determining Saccade Parameters:**
   - For each centrifugal target movement and eye:
     - Record off-center target location.
     - Set CF_activate and CP_activate for selecting saccades.
   - Detect correct centrifugal saccades in Saccades variable:

  - Check criteria including timing, amplitude, and direction.
  - Record saccade parameters.
  - Reset CF_activate.
- Record off-center target location in Saccades variable.
- Detect correct centripetal saccades in Saccades variable:
  - Check criteria for timing and amplitude.
  - Record start time in Target movements.
  - Reset CP_activate and add a code to the Saccades variable.

3. **Fixation Period after Saccade:**
   - Iterate through CF_saccades for each centrifugal saccade and eye:
     - Define the start of the fixation period.
     - Determine the end of fixation based on conditions.
     - Calculate mean gaze X during fixation.
     - Calculate the horizontal gain of the saccade.
     - Reset sum and count variables.

4. **Calculating Area Under the Curve (AUC):**
   - Iterate through CF_saccades for each centrifugal saccade:
     - Determine start and end times for AUC calculation.
     - Calculate AUC by summing X amplitude changes.
     - Record AUC values.
     - Reset variables.
     - Assign 0 to AUC parameters if no centrifugal saccade is detected for one eye.

5. **Peak Velocity Divided by Amplitude and Acceleration:**
   - Calculate Pv/Am by dividing peak velocity by amplitude.
   - Calculate Pa/Am by dividing peak acceleration by amplitude.
   - Record calculated values.

6. **First-pass Amplitude (FPA) Calculation:**

- For each centrifugal saccade, search for the first-pass sample:
    - Check criteria including time window and gaze position.
    - Calculate first-pass horizontal gain.
    - Record the horizontal gain.

7. **Checking CF Saccade Start Time Discrepancy:**
    - Compare CF_saccades start times between eyes.
    - Remove saccade with the lowest amplitude if start time difference exceeds a threshold.
8. **Calculating Versional Dysconjugacy Index (VDI):**
    - Iterate through CF_saccades variables for both eyes:
        - Calculate VDI values by comparing abducting and adducting eye values.
        - Write VDI values and calculate the area under the curve difference.

It's crucial to emphasize that the DEMoNS protocol, as outlined in various articles and studies that were referenced, provided a robust foundation for our analysis. Throughout the process, we ensured that all the predefined conditions and decision criteria from the Demons protocol scripts were meticulously upheld. This commitment to consistency allowed us to build upon established methodologies and ensure the integrity of our work. Additionally, my contribution involved adapting these protocols to Coimbra's specific experimental setup and meticulously reconfiguring the target detection procedures to align with the project's unique requirements.

Horizontal Anti-saccades Analysis

Overview of Analysis Steps:

1. Detect Target Movements
2. Determine Correct Saccades
3. Determine Fixation Period after Saccades

Detailed Analysis Steps:

1. **Detect Target Movements:**

Iterate through the TargetX variable:

- Detect centrifugal target jumps for each of the two target locations:
  - Identify an off-center location in the current and next sample of the TargetX variable.
  - Ensure the previous sample does not indicate an off-center location (higher for leftward movement, lower for rightward movement).
  - Verify that the sample 20 msec before this sample does not contain the other off-center location.
  - Count this jump using the Target_CF variable.
  - Record the location and the sample number.
- Detect centripetal target jumps:
  - Identify a central target location in the current and next sample of the TargetX variable.
  - Ensure the previous sample does not indicate a central location.
  - Confirm that Target_CF is not 0.
  - Record the sample number.

2. **Determine Correct Saccades:**

For each centrifugal target movement and for each eye separately:

- Record the off-center target location.
- Set CF_activate, CP_activate, and RF_activate to 1 for selecting the first correct saccade after the target movement.
- Detect correct centrifugal saccades in the Saccades variable:
  - Check for CF_activate status, saccade start time within the specified range, start location criteria, amplitude criteria, and direction matching target jump.
  - Record saccade parameters in CF_saccades variable: start time, end time, latency, startpositionX, endpositionX, amplitude, peak velocity, peak acceleration, direction.

  - Set CF_activate to 0.
  - Record off-center target location in the 16th column of the detected saccade in the Saccades variable.
- Determine if the detected centrifugal saccade is a correct anti-saccade:
  - Check for the difference between the saccade and target directions, and categorize as correct or incorrect anti-saccade.
- If the main saccade starts more than 3 degrees from the center, assign value 0 to the second column of CF_saccades and reset CF_activate.
- For incorrect anti-saccades, search for a corrective saccade:
  - Search for a corrective saccade from the end until 1500 msec after the main saccade.
  - Criteria include a different direction than the main saccade and passing the horizontal center.
  - Record corrective saccade parameters in CF_saccades columns and indicate as a corrective saccade.

3. **Determine Fixation Period after Saccade:**

For every centrifugal saccade and for each eye separately:

- Determine the start of the fixation period:
  - Use the end of the last-ended saccade or 50 msec after the end of the last-ended main saccade.
- Calculate the sum of gaze positions during the fixation period and calculate mean gaze positions.
- Calculate the gain of the main saccade and fixation period and assign it to corresponding columns.
- Calculate the X and Y error of the endpoint of the main saccade and fixation period and assign them to columns.

It's essential to highlight that strict adherence to the conditions and decision criteria outlined in the Demons protocol scripts was diligently maintained throughout the analysis process. The work involved adapting these protocols to suit the specific setup at Coimbra and revamping the target detection methodology. Notably, it's essential to acknowledge that our project diverges from the original Demons protocol because we don't incorporate a refixation after each eccentric target appearance, necessitating modifications to the analysis approach to suit our unique context.

Horizontal Multiple Pro-saccades Analysis

When dealing with Multiple Pro-saccades, the analysis procedure closely mirrors the standard pro-saccades. However, a notable distinction arises from using six targets instead of only two.

3.6.3 Generation of New Files: Expanding Content and Functionality

Vertical Approaches

As an extension of the analysis methodologies applied to horizontal pro-saccades, horizontal anti-saccades, and horizontal multiple pro-saccades, this section delves into the development of vertical pro-saccades, vertical anti-saccades, and vertical multiple pro-saccades analyses. The underlying logic guiding these new approaches' creation remains consistent with their horizontal counterparts, emphasizing meticulous adaptation to Coimbra's experimental setup while maintaining the established DEMoNS protocol scripts.

Vertical Pro-saccades Analysis:

Following the principles of the horizontal pro-saccades analysis, a similar framework was applied to vertical pro-saccades. By considering the unique context of vertical target movements, the process involved detecting target shifts, identifying correct pro-saccades, determining fixation periods, calculating the area under the curve (AUC), computing first-pass amplitude (FPA), checking for saccade start time discrepancies, and calculating the versional dysconjugacy index (VDI). As with horizontal pro-saccades, strict adherence to the Demons protocol conditions ensured methodological consistency.

Vertical Anti-saccades Analysis:

Adapting the horizontal anti-saccades analysis to the vertical axis presented a parallel challenge. Key steps such as detecting target movements, identifying correct saccades, and determining fixation periods were carefully adjusted to align with vertical target shifts. The detailed process involved discerning centrifugal and centripetal target jumps, detecting correct saccades, classifying saccade types, and calculating eye stability parameters. Again, the commitment to maintaining DEMoNS protocol criteria was pivotal in ensuring robust and reliable results.

Vertical Multiple Pro-saccades Analysis:

Expanding the analysis scope to vertical multiple pro-saccades entailed a consistent methodology akin to its horizontal counterpart. Despite six targets, the approach remained faithful to the core principles established earlier. This analysis offered valuable insights into eye movement patterns and behavior by considering the nuanced interactions of multiple pro-saccades in the vertical domain.

In this manner, the generation of new analysis approaches not only broadened the scope of the study but also contributed to a comprehensive understanding of eye movements in various contexts. By meticulously extending the existing methodologies to vertical tasks, the research aimed to uncover insights that could further enhance clinical understanding and aid in treating and assessing neurological conditions.

Generation of Output Report

In the final phase of the analysis pipeline, generating an output report serves as a comprehensive summary of subject parameters. This report is meticulously compiled into an Excel file, with columns dedicated to the various parameters and rows delineating subdivisions within those parameters. The process involves extracting and organizing data from the earlier analysis tasks, providing a concise and structured representation of the acquired insights.

Fixation Task:

A pivotal step in generating the output report involves crafting a table structure to capture the essence of fixation analysis. This table spans 18 rows and 61 columns, aptly capturing the diverse range of fixation-related parameters. To facilitate this process, temporary variables such as Leftfix and Rightfix are employed to temporarily store parameters associated with the left and right eyes, respectively. These parameters offer a detailed understanding of gaze stability, vergence, velocity, acceleration, and the occurrence of specific eye movement patterns. Here's a summarized overview of the critical parameters captured by each column:

- Number of fixation periods included maximum 10 total.

- Mean horizontal and vertical gaze position in fixation periods.
- Standard deviation of horizontal and vertical gaze position in fixation periods.
- Mean horizontal and vertical vergence in fixation periods.
- Standard deviation of horizontal and vertical vergence in fixation periods.
- BCEA of vergence in fixation periods.
- Mean horizontal and vertical velocity in fixation periods.
- Standard deviation of horizontal and vertical velocity in fixation periods.
- Mean acceleration in fixation periods.
- Standard deviation of acceleration in fixation periods.
- etc. (up to 61 parameters calculated).

The rows in the output report represent distinct categories and subsets of fixation conditions, each providing insights into the subject's eye movement behavior during various fixations. Here's a summarized overview of the key categories captured by each row:

- Total: The mean of all fixation directions and both eyes, offering an overall perspective on the subject's fixation behavior.
- Total_lefteye: The mean of all fixation directions of the left eye, providing insights specific to the left eye's fixation behavior.
- Total_righteye: The mean of all fixation directions of the right eye, offering insights specific to the right eye's fixation behavior.
- Central: The mean of the central fixations of both eyes, focusing on fixation behavior when the target is centrally located.
- Central_lefteye: The mean of the central fixations of the left eye, providing insights into the left eye's fixation behavior during central fixation.
- Central_righteye: The mean of the central fixations of the right eye, offering insights into the right eye's fixation behavior during central fixation.

- Right: The mean of rightward eccentric fixations of both eyes, highlighting fixation behavior for targets located to the right.
- Right_lefteye: The mean of rightward eccentric fixations of the left eye, focusing on the left eye's behavior when fixating on rightward targets.
- Right_righteye: The mean of rightward eccentric fixations of the right eye, offering insights into the right eye's behavior when fixating on rightward targets.
- Left: The mean of leftward eccentric fixations of both eyes, showcasing fixation behavior for targets to the left.
- Left_lefteye: The mean of leftward eccentric fixations of the left eye, providing insights into the left eye's behavior when fixating on leftward targets.
- Left_righteye: The mean of leftward eccentric fixations of the right eye, offering insights into the right eye's behavior when fixating on leftward targets.
- Up: The mean of upward eccentric fixations of both eyes, focusing on fixation behavior for targets located above.
- Up_lefteye: The mean of upward eccentric fixations of the left eye, highlighting the left eye's behavior when fixating on upward targets.
- Up_righteye: The mean of upward eccentric fixations of the right eye, offering insights into the right eye's behavior when fixating on upward targets.
- Down: The mean of downward eccentric fixations of both eyes, showcasing fixation behavior for targets located below.
- Down_lefteye: The mean of downward eccentric fixations of the left eye, providing insights into the left eye's behavior when fixating downward targets.
- Down_righteye: The mean of downward eccentric fixations of the right eye, offering insights into the right eye's behavior when fixating on downward targets.

By systematically compiling this array of data, the output report encapsulates the subject's eye movement parameters across various fixation conditions. This comprehensive documentation is invaluable for clinical interpretation, further research, and aiding in diagnosing and treating neurological conditions.

Horizontal Pro-saccades Task:

For this phase, initial adjustments are made to ensure accurate data representation in the output report. Parameters receive zero values when no saccade start time is detected, and the FPG value becomes zero if the FPG time aligns with or precedes the saccade's start time.

An output table with 9 rows and 34 columns is generated, encapsulating the essential metrics derived from horizontal pro-saccade analysis. Each column is dedicated to a specific parameter, while rows represent distinct conditions, yielding a comprehensive analysis of the subject's horizontal pro-saccadic eye movement patterns.

The columns in the output table for horizontal pro-saccades analysis provide a detailed set of parameters that characterize the characteristics of centrifugal saccades and their associated eye movement patterns. These parameters include saccade velocity, acceleration, latency, gain, and dysconjugacy indices. The columns also encompass statistics related to the saccade trajectory, such as the area under the curve (AUC) and metrics that compare peak velocity and peak acceleration to amplitude. Additionally, columns related to saccadic detection thresholds and standard deviations are included for both horizontal and vertical acceleration signals. The output is organized to represent different conditions, target directions, and eye-specific analyses, providing a comprehensive understanding of the subject's horizontal pro-saccadic behaviors.

The rows in the output table for horizontal pro-saccades analysis correspond to various conditions and directions of saccades and eye-specific analyses. They capture aggregated data and metrics for different types of centrifugal saccades, target directions, and eye combinations. The rows include summaries for various target eccentricities (left and right targets) and eye-specific analyses (left and right eye). Additionally, some rows provide overall means for all centrifugal saccades and both eyes, offering a comprehensive overview of the subject's horizontal pro-saccadic behavior under various conditions.

This detailed structure encompasses the diverse insights from horizontal pro-saccade analysis, offering a comprehensive overview of the subject's eye movement behavior in response to various visual targets and directions.

Horizontal Anti-saccades Task:

In this case, the process is initiated by initializing parameter cells with zero values when no start time is detected for a saccade.

An output table with 9 rows and 33 columns is created to showcase the results of the horizontal anti-saccades analysis task.

The table encompasses essential parameters that shed light on various critical aspects:

Starting the "Number of Saccades" it provides a count of included centrifugal saccades. The "Peak Velocity for Correct Saccades" column displays the average peak velocity of correct anti-saccades, accompanied by the corresponding standard deviation. Similarly, the "Peak Acceleration for Correct Saccades" column offers insights into the average peak acceleration of correct anti-saccades, along with its standard deviation.

The "Latency" column reveals the mean latency of centrifugal saccades. In contrast, the "Latency for Correct Saccades" column focuses specifically on the average latency of correct anti-saccades, both accompanied by their respective standard deviations. In contrast, the "Latency for Incorrect Pro-saccades" column provides an average latency for incorrect pro-saccades and the corresponding standard deviation.

Moving on to the "Gain for Correct Saccades," this column indicates the average gain of correct anti-saccades, and the associated standard deviation provides insights into the variability. The "Horizontal and Vertical Errors" columns reveal the average errors in the horizontal and vertical directions for correct anti-saccades, complemented by their standard deviations.

The "Number of Errors" column tallies the count of incorrect pro-saccades, while the "Proportion of Errors" column quantifies the proportion of incorrect pro-saccades in relation to other saccades. The "Latency of Corrective Saccades after Incorrect Pro-saccades" column uncovers the average latency of corrective saccades that follow incorrect pro-saccades, accompanied by the standard deviation.

Shifting the focus to the "Gain of Final Eye Position," this column displays the average gain of the final eye position, offering insights into the accuracy of these movements. The subsequent "Errors of Final Eye Position" columns provide average errors in horizontal and vertical directions for the final eye position, supported by their corresponding standard deviations.

Additionally, the "Absolute Error of Final Eye Position" column calculates the average absolute error of the final eye position, providing a comprehensive measure of accuracy. The "Absolute Error of Final Eye Position for Correct Saccades" column, with its corresponding standard deviation, specifically quantifies the average absolute error for correct anti-saccades.

The final columns, "SD Acceleration in Horizontal Direction" and "SD Acceleration in Vertical Direction," offer the standard deviations of horizontal and vertical acceleration signals, which serve as thresholds for saccadic detection.

This table structure provides an in-depth understanding of horizontal anti-saccadic behavior, capturing various conditions, target directions, and eye-specific analyses.

Horizontal Multiple Pro-saccades Task:

The output generated by the horizontal multiple pro-saccades task closely resembles that of the horizontal pro-saccades task, with a notable distinction: introducing multiple targets on each side. This variation in target placement enriches the analysis by offering insights into more complex saccadic behaviors involving various stimuli.

Much like the horizontal pro-saccades task output, the horizontal multiple pro-saccades task output provides a comprehensive set of parameters that characterize various aspects of centrifugal saccades and their associated eye movement patterns. These parameters encompass saccade velocity, acceleration, latency, gain, and dysconjugacy indices, among others. The output also includes statistics related to saccade trajectories, such as the area under the curve (AUC) and metrics that compare peak velocity and acceleration to amplitude. Moreover, columns dedicated to saccadic detection thresholds and their standard deviations are present for horizontal and vertical acceleration signals.

Incorporating three targets on each side introduces a more nuanced analysis of saccadic behaviors. This allows for the exploration of how multiple targets influence saccadic characteristics, potentially revealing differences in response strategies and eye movement patterns. The output remains organized to represent diverse conditions, different target directions, and eye-specific analyses, thus providing an enhanced understanding of the subject's saccadic behaviors in scenarios with multiple stimuli on each side.

Vertical Approaches:

Indeed, the analysis encompassed the creation of vertical variations for three distinct tasks: vertical anti-saccades, vertical pro-saccades, and vertical multiple pro-saccades. In these task outputs, the fundamental parameters and calculations remained consistent with their corresponding horizontal counterparts—however, the main alteration involved adjusting the positioning of the targets in a vertical orientation.

The vertical anti-saccades task output allowed for the assessment of how subjects responded to vertical stimuli, emphasizing the ability to inhibit saccades towards these vertically placed targets. Similarly, the vertical pro-saccades task output enabled the exploration of vertical-oriented quick eye movements, providing insights into saccadic behaviors towards vertically positioned targets. Lastly, the vertical multiple pro-saccades task output extended this analysis to scenarios with various vertically situated targets, thereby investigating simultaneous eye movements toward different vertical stimuli.

By introducing these vertical variations while maintaining the same analytical parameters, the study aimed to uncover potential differences in saccadic responses and eye movement patterns in relation to the vertical placement of the stimuli. This approach added depth to the investigation and enhanced the understanding of how individuals engage with stimuli across both horizontal and vertical dimensions.

Visual Insights for Comprehensive Analysis: Generation of Plots

Beyond the meticulous data processing and task-specific output reports, another facet of the comprehensive analysis was the creation of insightful visual representations that are set to be unveiled in the forthcoming Results and Discussion chapter. These plots encapsulate a range of eye movement dynamics, shedding light on nuanced aspects of the experimental results. Gaze tracing graphs offer a visual narrative of the eye's trajectory during different tasks, unraveling the intricate interplay between fixations, saccades, and gaze shifts. Fixation positions are graphically depicted to provide an intuitive understanding of the eye's points of focus, showcasing patterns and variations that might underpin specific task-related behaviors.

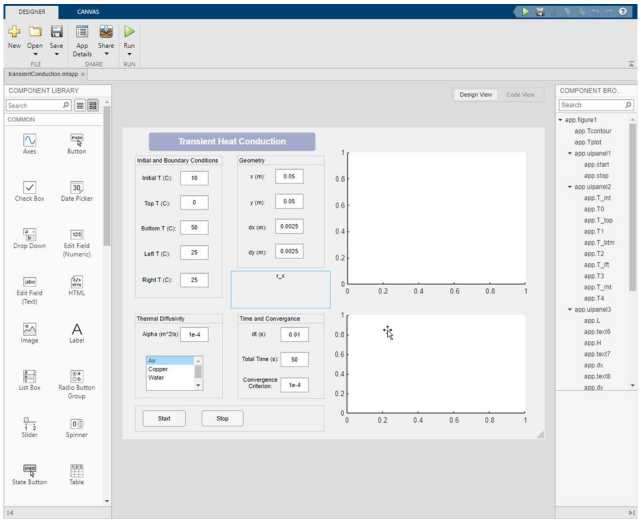
Including gaze dispersion plots amplifies the richness of the visual analysis, showcasing the distribution of gaze points across different tasks and conditions. This spatial insight aids in deciphering the extent of gaze exploration and its variability across participants. Additionally, the portrayal of the micro-saccades main sequence, a quintessential representation of micro-saccadic behavior, promises to unravel the relationship between micro-saccade characteristics such as amplitude and peak velocity. Rounding out the visual repertoire are the polar histograms that encapsulate saccadic directions, unveiling potential biases and tendencies in eye movement patterns. Collectively, these meticulously crafted visualizations not only augment the interpretive depth of the study but also provide a bridge between complex data and intuitive comprehension, fostering a comprehensive understanding of the experimental outcomes.

User-Friendly Interface: Consolidated App Development for Eye Movement Analysis Tasks

To streamline the utilization of complex analysis scripts and offer a seamless experience for clinicians, a single comprehensive user interface app was developed using the *Matlab* tool *App Designer* (3.13). This consolidated app was a centralized hub that housed all the essential scripts and functionalities for the various eye movement analysis tasks. By integrating the multiple scripts into a unified interface, clinicians were empowered to execute different analyses – including the fixation task, horizontal and vertical anti-saccades, horizontal and vertical pro-saccades, and horizontal and vertical multiple pro-saccades – within a user-friendly application.

The essential advantage of this approach was its accessibility. Clinicians with limited coding knowledge could effortlessly navigate the app's intuitive graphical interface, input relevant parameters, and initiate the desired analysis tasks. The app seamlessly executed the underlying scripts, conducting the complex calculations and data processing required for each task. As a result, clinicians could obtain comprehensive insights into eye movement behaviors without the need to delve into intricate coding processes.

By incorporating all relevant scripts into a single app, the development simplified the analysis process and enhanced the visualization of results. Clinicians could readily interpret and assess the outcome of their analyses through interactive plots and reports generated within the app. This innovative user interface marked a significant step toward bridging the gap between sophisticated eye movement analysis and practical clinical application, empowering clinicians to harness the power of advanced techniques with ease and efficiency.



Initial T (C): 10
Top T (C): 0
Bottom T (C): 50
Left T (C): 25
Right T (C): 25
x (m): 0.05
y (m): 0.05
dx (m): 0.0025
dy (m): 0.0025
Alpha (m^2/s): 1e-4
Air
Copper
Water
dt (s): 0.01
Total Time (s): 50
Convergence Criterion: 1e-4

Figure 3.13: App Designer

3.7 Complete Procedure Summary

The culminating steps that lead to the comprehensive analysis of an individual subject's data are outlined below in a systematic sequence:

1. **Task Performance**: The subject embarks on the designated tasks, engaging in controlled eye movements to elicit diverse eye tracking patterns.

2. **Data Collection and Export**: Leveraging the *Eyelink Data Viewer*, a meticulously detailed .txt file is generated. This file encapsulates crucial parameters such as 'TRIAL_INDEX', 'TIMESTAMP', 'LEFT_GAZE_X', 'LEFT_GAZE_Y', 'LEFT_IN_BLINK', 'RIGHT_GAZE_X', 'RIGHT_GAZE_Y', 'RIGHT_IN_BLINK', 'block', 'sac_location', 'TARGET_X_TARG1', 'TARGET_Y_TARG1', and 'SAMPLE_MESSAGE'.

3. **Data Import and Segmentation**: The information extracted from the.txt file is skillfully imported into MATLAB to facilitate further analysis. The data is meticulously segmented and organized into separate .mat files, each aligned with a specific task.

4. **Script Execution**: The *Matlab* scripts, tailored to the analytical requirements of each task, are executed. This pivotal step can be seamlessly simplified through a user-friendly Graphical User Interface (GUI), streamline the process for clinicians without

extensive *Matlab* coding expertise.

5. **Attainment of Outcomes**: The outcomes materialize, presenting a two-fold result. First, an Excel spreadsheet encapsulates a comprehensive overview of the parameters calculated for each task, presenting a structured tabulation of the findings. Secondly, an array of meticulously crafted visualizations showcases diverse aspects of eye movement dynamics, including gaze tracing graphs, fixation positions, gaze dispersion, micro-saccades main sequence, and polar histograms, offering a multifaceted perspective on the subject's performance.

In essence, this structured sequence constitutes the foundation upon which the thorough analysis of an individual's eye movement behaviors is built, culminating in a coherent presentation of insights through tabulated data and visually immersive plots.

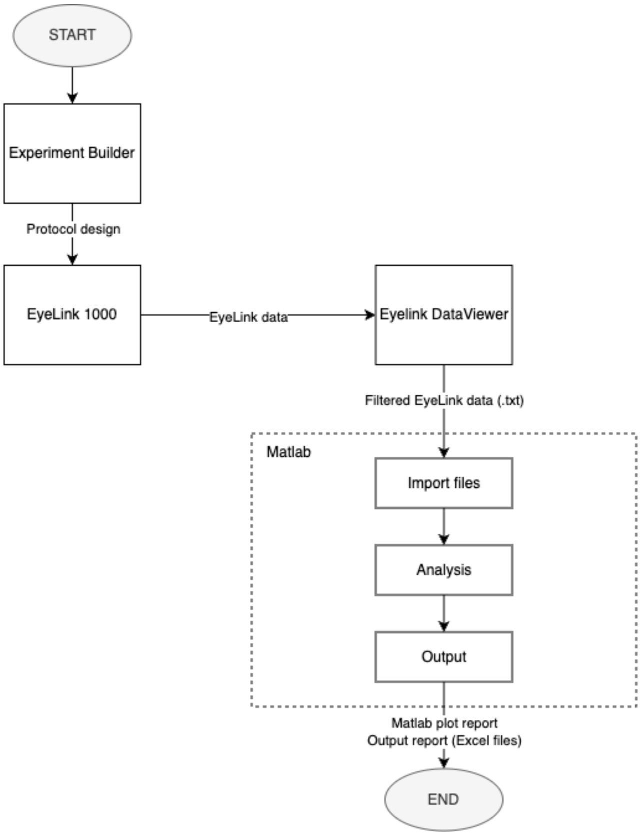


Figure 3.14: Complete Procedure

Chapter 4

Results and Discussion

In the following chapter, the results of the comprehensive eye movement analysis will be presented and discussed, showcasing the outcomes obtained by applying the methods described in the previous chapter.

4.1 Results obtained

This section will center on the achieved results concerning the output reports generated for each task, along with creating plots designed to visualize key parameters of significance. Every parameter calculated underwent a thorough review process with the clinician (J.L.), ensuring their fidelity to established literature and prior studies.

4.1.1 Fixation Task

In this section, we present the results derived from applying the methods described in the previous chapter. Following the well-established DEMoNS protocol, we meticulously generated output reports encapsulating various parameters. These outputs offer a comprehensive overview of the subject's performance during the Fixation task.

Additionally, a collection of illustrative plots was created to enhance the visualization of key parameters. These plots are invaluable tools for facilitating a nuanced understanding of the results.

Fixation Dispersion

Introducing the Fixation Dispersion plot, a pivotal visualization tool that encapsulates the dispersion of eye movements during fixation on various targets within the Fixation task. Specifically designed for subjects with Parkinson's Disease (PD), this plot presents a concise yet comprehensive insight into gaze stability. By focusing on fixations on both center and eccentric targets, this visualization aids in identifying potential patterns unique to PD subjects. This graphical representation and quantitative data enhance our grasp of Fixation task outcomes and their implications in PD cases (4.1).

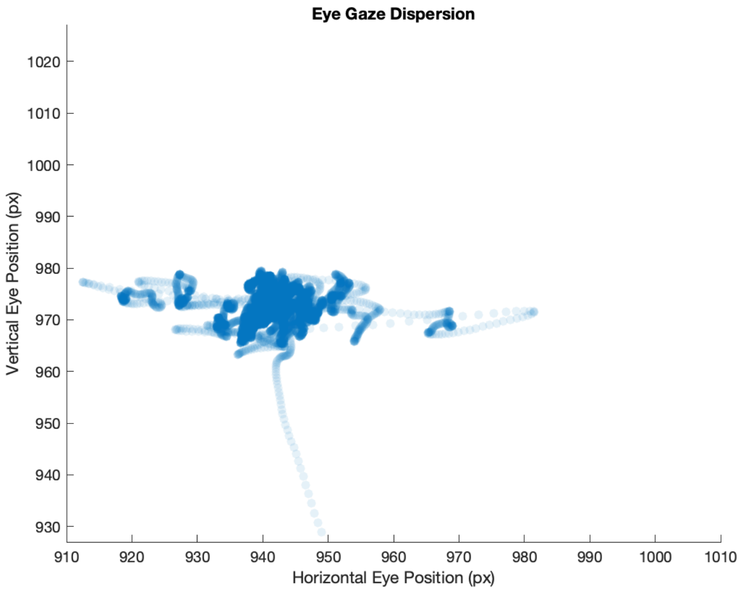


Figure 4.1: Fixation Dispersion up target position OD

Gaze Tracings

The Gaze Tracings plot offers a dynamic perspective by displaying each eye's horizontal and vertical positions in relation to the corresponding target positions. This plot is a powerful tool for evaluating the precision of gaze fixation and tracking throughout the task. By juxtaposing the eye trajectories with the intended target positions, insights emerge into the accuracy of visual fixation and any potential deviations. This visual representation provides a tangible way to assess the alignment between gaze behavior and task requirements, contributing to a more holistic understanding of the subject's performance within the task (4.2).

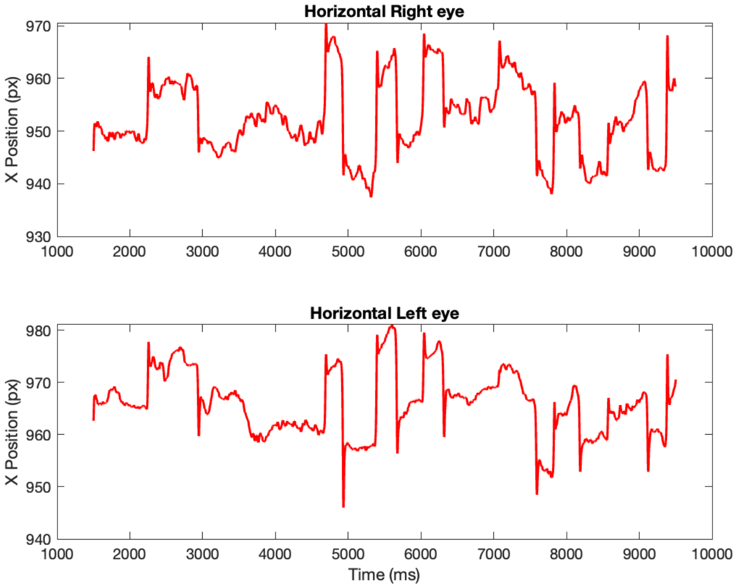


Figure 4.2: Gaze tracing center target position

Micro-Saccade Main Sequence

The Micro-Saccade Main Sequence plot delves into the intricate relationship between microsaccade amplitude and peak velocity. This plot captures the essence of microsaccade dynamics by showcasing the distribution of detected microsaccades as dots, each corresponding to a specific combination of amplitude and peak velocity. The plot's linear model, represented by the line, offers an estimated trajectory that elucidates the general pattern of this relationship. Through this visual representation, it becomes evident how the amplitude and velocity of microsaccades interact, allowing for insights into the fine-scale oculomotor behavior of the subject. This analysis enriches our understanding of microsaccade characteristics and their potential implications in the context of the Fixation task, adding a layer of depth to the overall interpretation of the data (4.3).

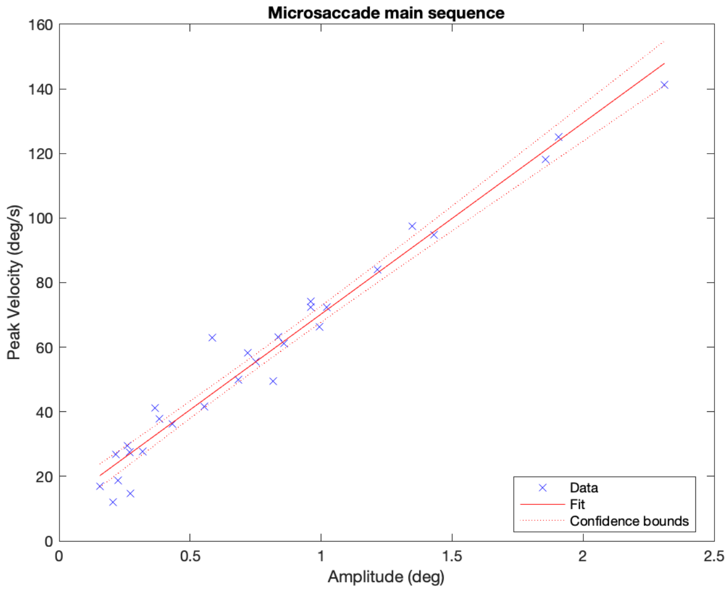


Figure 4.3: Micro-saccade Main Sequence

Micro-Saccade Direction

The Micro-Saccade Direction plot offers a comprehensive view of the distribution of microsaccade directions through polar histograms. By aggregating the frequency distribution of microsaccade directions, these histograms visually present the predominant directions in which microsaccades occur. The angular spread of the histograms provides insights into the subject's oculomotor behavior, revealing any directional biases or preferences. This visual representation unveils the underlying patterns in the microsaccade directions, shedding light on the interplay between the subject's eye movements and the task's requirements. The polar histograms are a powerful tool for understanding the directional dynamics of microsaccades and offer a glimpse into the subject's visual exploration strategy during the Fixation task (4.4).

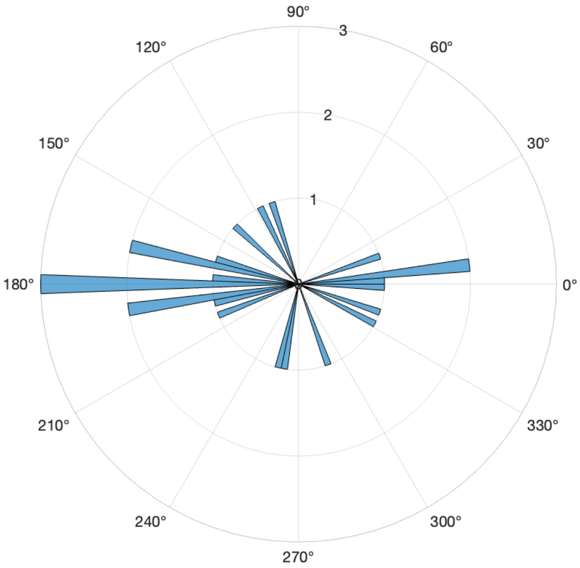


Figure 4.4: Micro-saccade Direction left eye

4.1.2 Horizontal and Vertical Pro-saccades Tasks

Within this section, we delve into the outcomes of applying our methodology to horizontal and vertical pro-saccades tasks. Initially, we obtain the output reports, which encapsulate the quantitative results obtained from our analysis. Furthermore, we enhance our comprehension by creating illustrative plots, facilitating the visualization of these outcomes. Through this combined approach of numerical data and graphical representation, we understand the intricacies underlying the execution and performance of both the horizontal and vertical pro-saccades tasks.

Gaze Tracings

The initial plot illustrates the Gaze Tracings associated with the horizontal and vertical pro-saccades tasks. This visual representation enables a direct comparison between the gaze positions of the left and right eyes in horizontal and vertical directions, juxtaposed with the intended horizontal and vertical target positions (4.5,4.6).

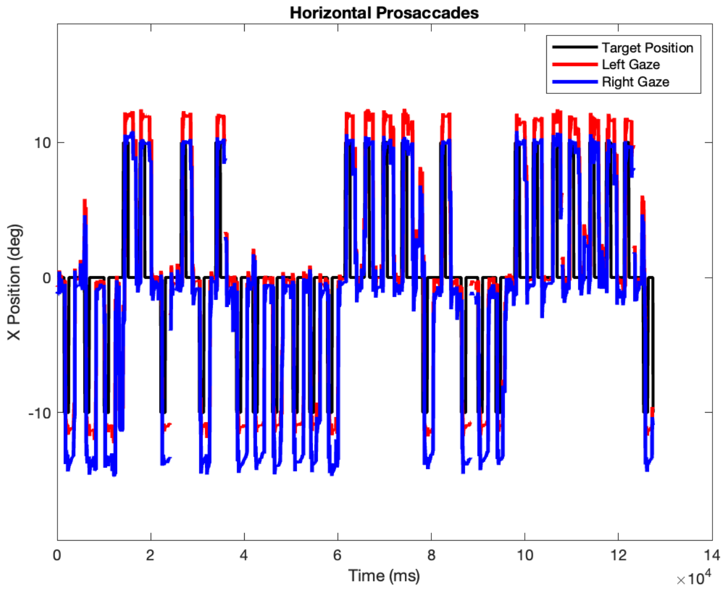


Figure 4.5: Horizontal Pro-saccades: Gaze Tracing

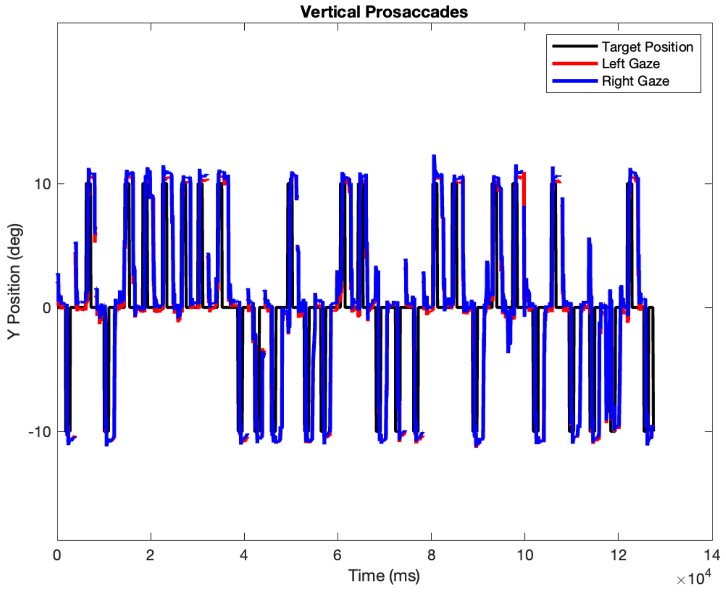


Figure 4.6: Vertical Pro-saccades: Gaze Tracing

Trajectories of Saccades

Next, the subsequent plot, once more about the horizontal and vertical pro-saccades tasks, portrays the trajectories of a participant's saccades (measured in degrees) as a function of time (measured in milliseconds). These ocular saccades encompass movements directed both horizontally and vertically toward visual targets. Notably, the temporal axis starts at 0, signifying the instance when the eccentric stimulus becomes visible. It is important to note that these plots are created for both left and right gaze (4.7,4.8).

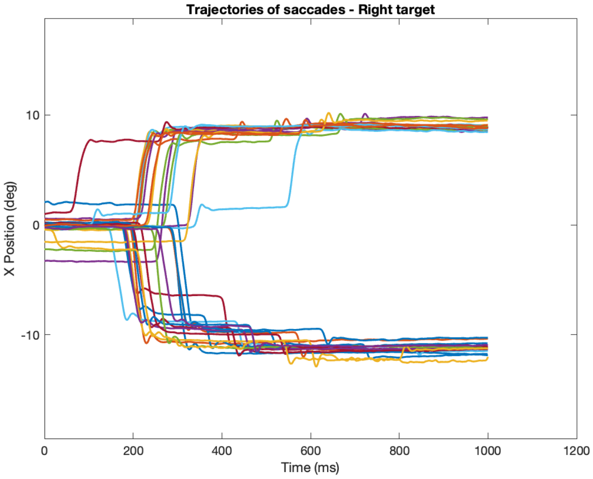


Figure 4.7: Horizontal Pro-saccades: Trajectories of Saccades

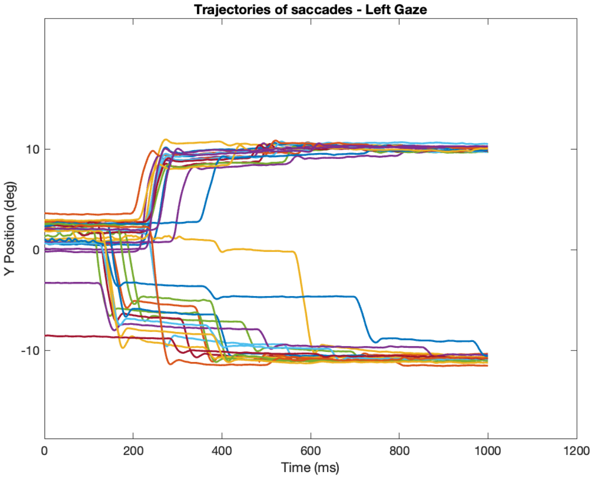


Figure 4.8: Vertical Pro-saccades: Trajectories of Saccades

4.1.3 Horizontal and Vertical Multiple Pro-saccades Tasks

In the subsequent section, focusing on the horizontal and vertical multiple pro-saccades tasks, we delve into an analysis that closely parallels the earlier approach for the horizontal and vertical pro-saccades tasks. Consequently, the outcomes derived from this analysis and the visual representations in the form of plots closely resemble those from the earlier tasks. This alignment underscores the consistency and adaptability of the analytical framework, demonstrating its effectiveness across varying task scenarios.

Furthermore, the horizontal and vertical multiple pro-saccades tasks were exclusively performed using a subject diagnosed with MS. This deliberate selection highlights the versatility of the developed methodology, showcasing its potential applicability to various neurodegenerative diseases. By including this task, the thesis underscores its ability to accommodate different conditions, making it adaptable for various studies. This choice reinforces the thesis's aim to provide insights into various neurological conditions, illustrating its utility in understanding eye movement behaviors in the context of neurodegenerative diseases (4.9, 4.10, 4.11, 4.12, 4.13).

Gaze Tracings

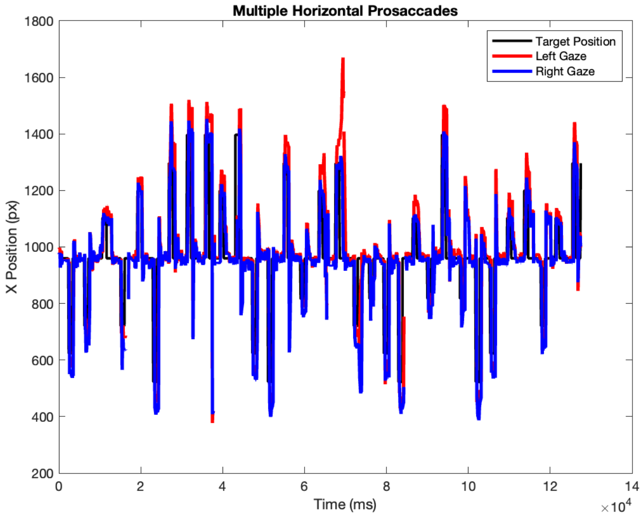


Figure 4.9: Multiple Horizontal Pro-saccades: Gaze Tracing

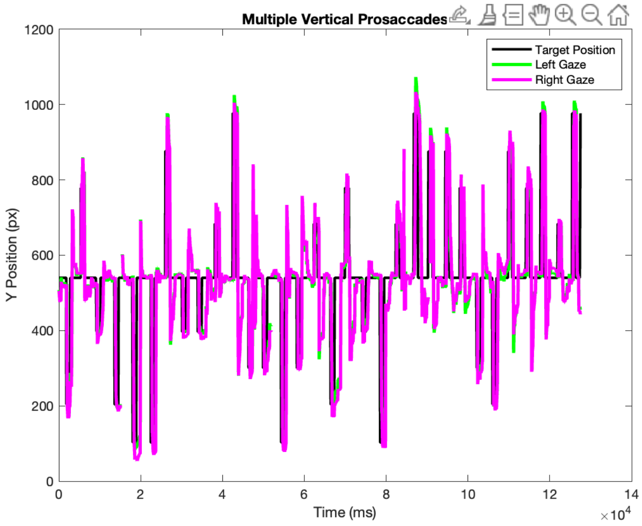


Figure 4.10: Multiple Vertical Pro-saccades: Gaze Tracing

Trajectories of Saccades

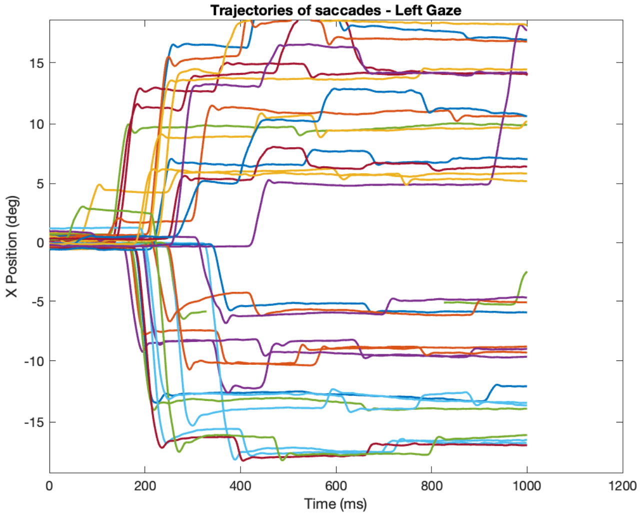


Figure 4.11: Multiple Horizontal Pro-saccades: Trajectories of Saccades

Saccade Main Sequence

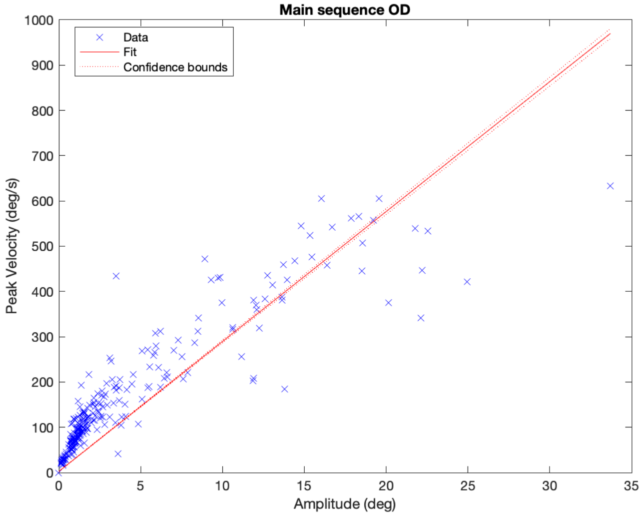


Figure 4.12: Multiple Horizontal Pro-saccades: Saccade Main Sequence OD

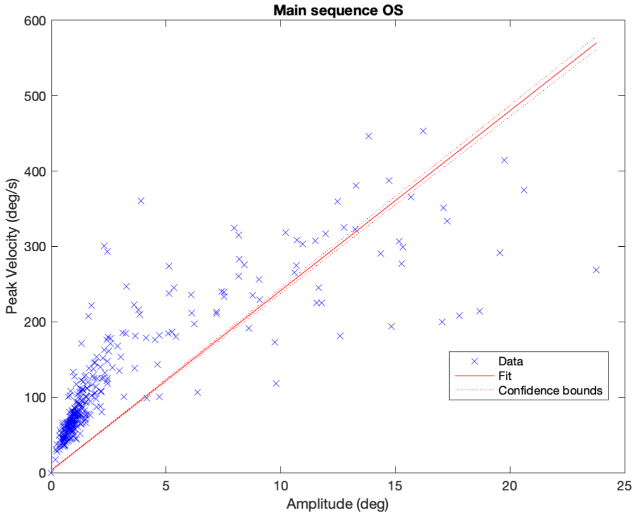


Figure 4.13: Multiple Vertical Pro-saccades: Saccade Main Sequence OS

4.1.4 Horizontal and Vertical Anti-saccades Tasks

Turning to the horizontal and vertical anti-saccades Tasks, the analysis followed a similar pattern of generating output reports and constructing plots for visualization. In this context, particular attention was given to differentiating between correct and incorrect saccades. Notably, the focus extended to identifying and assessing the saccades that were corrected after an initial erroneous attempt. This distinction added depth to the analysis, providing insights into the dynamics of corrective eye movements. These nuances are readily observable in the trajectories of saccades plots, where the interplay between correct and incorrect responses is visually evident. This comprehensive examination enriches the understanding of the subject's ocular behavior in the context of anti-saccade tasks (4.15, 4.15, 4.16, 4.17).

Gaze Tracing

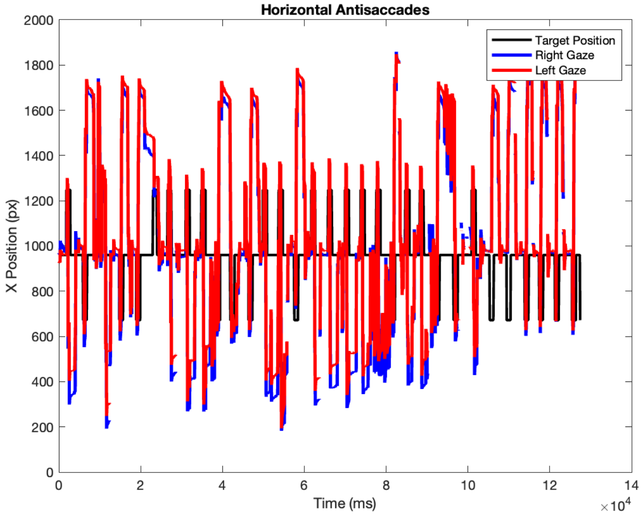


Figure 4.14: Horizontal Anti-saccades: Gaze Tracing

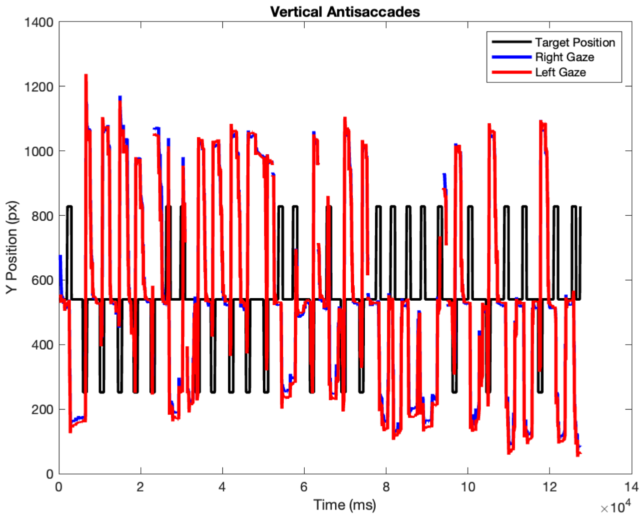


Figure 4.15: Vertical Anti-saccades: Gaze Tracing

Trajectories of Saccades

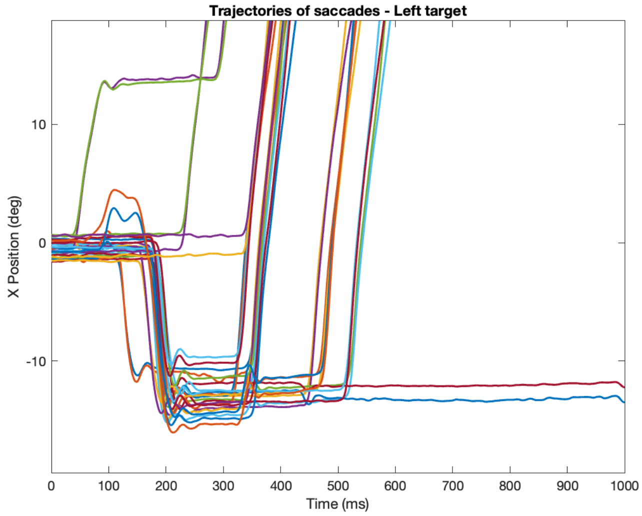


Figure 4.16: Horizontal Anti-saccades: Trajectories of Saccades

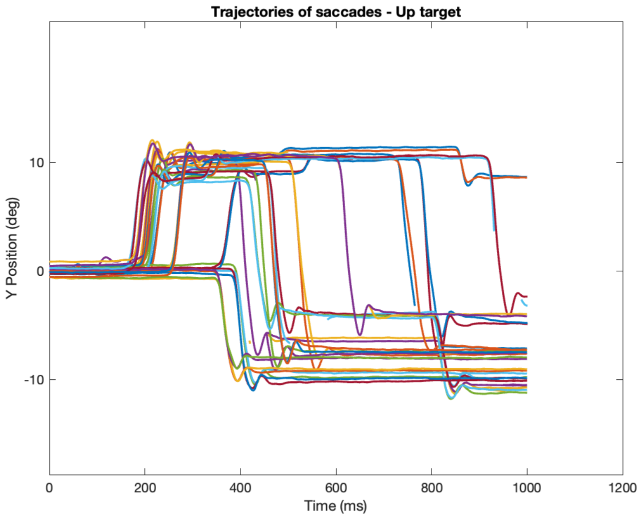


Figure 4.17: Vertical Anti-saccades: Trajectories of Saccades

4.1.5 Graphical User Interface (GUI)

Moving forward to the Graphical User Interface (GUI) section, the culmination of the project's development efforts will be showcased. This interface is the platform that encapsulates the functionalities of the *Matlab* scripts discussed in the Methods chapter. By harmonizing the intricacies of these scripts and offering a user-friendly environment, the GUI grants clinicians and researchers access to the output reports and visualization plots. The overarching objective behind this development was to present a streamlined and intuitive means of executing the analysis tasks. The GUI empowers users to execute the scripts without necessitating an in-depth understanding of *Matlab* coding, thereby making the analytical process accessible to a broader range of professionals (4.18).

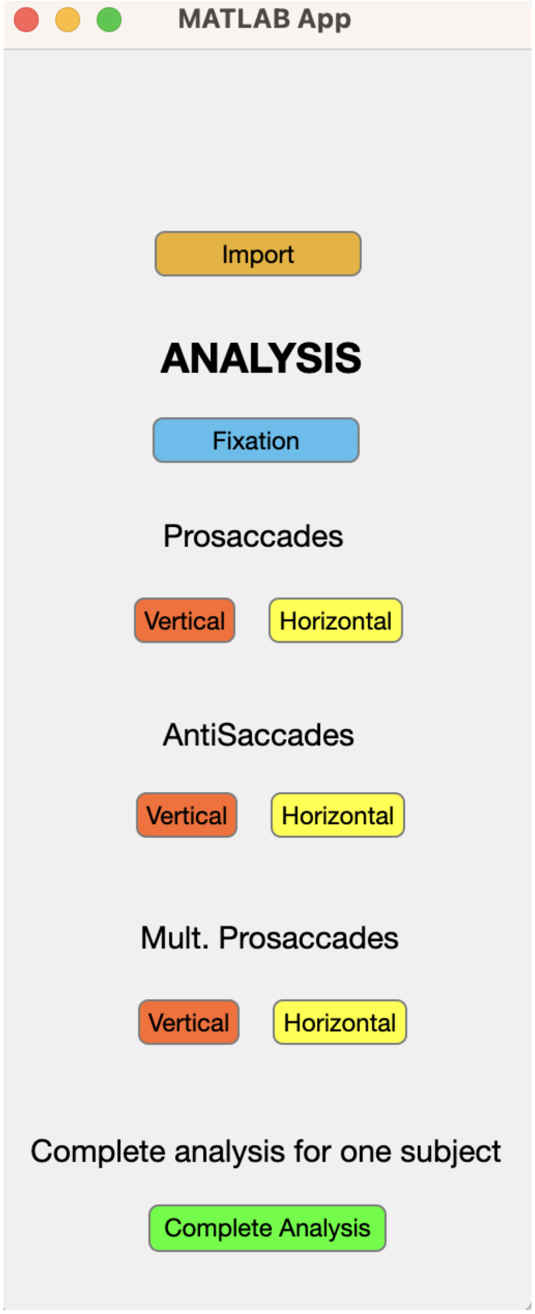


Figure 4.18: Graphical User Interface

Chapter 5

Conclusion

The successful implementation of the DEMoNS protocol represents a significant milestone in ocular motor assessment. This achievement equips the *CHUC - Department of Neurology* with a comprehensive and accessible procedure for analyzing eye movements, strengthening its capabilities for clinical studies and advancements in neurology. Importantly, this analytical framework bridges the gap between clinical investigators and medical doctors, eliminating the prerequisite for extensive *Matlab* coding knowledge. This democratization of eye movement analysis expedites the process and ensures its widespread applicability within the clinical community.

As we peer into the future, it's evident that the horizons of this research extend beyond Parkinson's disease. The methodologies and protocols developed herein can be readily adapted and applied to other neurodegenerative diseases, opening doors for broader explorations and enabling the comprehensive examination of ocular motor behaviors across various clinical contexts. Additionally, this dissertation's findings are set to reach a wider audience, as it's been submitted for presentation as a poster at the Portuguese Neurological Society Meeting in November 2023. This platform will facilitate the dissemination of knowledge and foster valuable discussions within the scientific community, furthering the understanding of eye movements in neurological disorders.

Expanding upon the groundwork in this research, future work may encompass the analysis of horizontal and vertical pursuit tasks, which are unexplored by the DEMoNS protocol. Investigating these aspects will provide a more holistic perspective on ocular motor behavior and contribute to a deeper comprehension of neurodegenerative diseases. Furthermore, applying eye movement analysis in subjects with PD undergoing DBS therapy holds promise for groundbreaking insights. An upcoming article submission detailing this application is poised to contribute substantially to the field, potentially paving the way for future enhanced clinical interventions and treatments. In conclusion, this thesis marks not just an endpoint but also a new beginning in exploring eye movements' vital role in understanding and managing neurodegenerative diseases.

Furthermore, the prospects for future work in eye movement analysis are notably promising. Beyond the confines of this dissertation, the application of the developed protocol and methodologies extends into diverse horizons. One notable endeavor is the upcoming master thesis by Carolina Bugalho [46], which harnesses the same approach for alternative applications. Carolina's pilot project aims to unravel the in vivo cortical and subcortical eye movement-related activity in PD patients, employing synchronized data from DBS, Electroencephalography (EEG), and Eye Tracking during eye movement paradigms.

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