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DEVELOPMENT OF DEVICE FOR INVESTIGATION OF THE PUPILLARY RESPONSE

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Abstract. *The pupillary dilation and constriction influence the amount of light stimuli that reach the retina and occur due to the sympathetic and parasympathetic nervous system activity. Thus, the measurement of pupil size is a valuable tool for the study of a large number of functions and dysfunctions in the people because to evaluate the behavior of the autonomic nervous system. However, assessment of pupillary dynamics is poorly understood in some aspects and techniques to make diagnoses more accurate are still evolving and depend mainly on equipments. It is therefore of utmost importance the development of technologies that meet these needs since this analysis is able to detect abnormalities in the human body. Consequently, the aim of this work is to present the development of a system of stimulation, acquisition and processing of the pupillary image. The apparatus will allow better understanding of pupillary dynamics since there is evidence in the literature that the pattern of eye's movement/pupil are important parameters for the differential diagnosis. The results show that the device developed is able to provide data that allow the study.*

Keywords: *pupillary movement, autonomic nervous system, dynamic pupillometry system.*

1. INTRODUCTION

The measurement of the pupil size is a non-invasive technique, known as pupillometry, that allows to quantify the pupil behavior with or without the presence of light (Souza, 2012).

In a simplified form, the light first hits the cornea then passes through the pupil. Then, the lens focuses the light as it reaches the retina, which contains photoreceptor cells responsible for transforming the light into electrochemical impulses. Finally, the optic nerve transports these pulses to the brain where the nervous system will decode them into images, Gamlin, *et al.* (2010). Figure 1 depicts some structures of the human eye involved in the passage of light process.

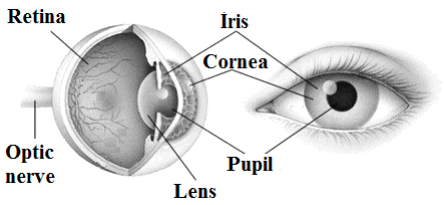


Figure 1. Anatomy of the Human Eye [Adapted from Compuland, 2015]

The pupillary light reflex is a way to regulate the intensity of light that penetrates the eyes. A higher light intensity leads to decrease of the pupils (miosis), allowing less light penetration, while lower intensities cause dilation of the pupils (mydriasis), allowing more light penetration.

Besides the pupillary light reflex, the pupil has a kind of involuntary pulsatile movement known as hippus, which occurs due to excitation and inhibition signals transmitted by the nervous system. The hippus, or pupillary athetosis, causes constant oscillations in the pupil diameter of about 3% and a frequency of approximately 0.2 Hz, independent of the change of light incidence (Leal, 2008).

The stimuli transmission through the optic nerve pass through a region called the optic chiasm (Fig. 2). At the optic chiasm occurs fiber interlacing of the optic nerves, so that approximately half the fibers of the right optic nerve passes to the left optic nerve and vice versa. This makes the reflections by a stimuli applied in an eye also shown in the other eye. This physiological function is called "consensus reflex" (Lund, Klassen and Young, 2000).

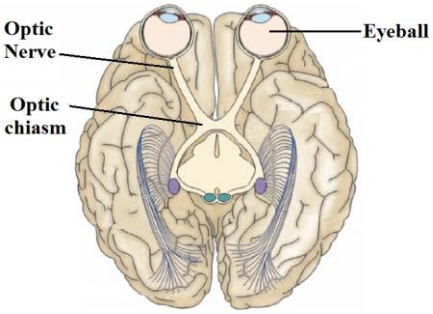


Figure 2. Chiasm optical responsible for consensual reflection [Adapted from Purves, *et al.,* 2005]

The size and the ability of human pupillary response to light are regulated by the action of the sphincter muscle responsible for contraction and dependent on the parasympathetic nervous system, and the dilator muscle, dependent on the sympathetic nervous system (Hachol, *et al.,* 2007). Therefore, the change in pupil size is based on a functional balance between the sympathetic and parasympathetic nervous system (Fotiou, *et al.*, 2009).

Thus, the use of pupillometry permits to identify abnormalities in the human body since it allows evaluating the autonomic nervous system behavior (Fotiou, *et al*., 1998) and may have several clinical applications (Sargsyan, *et al*., 2009).

Currently, the interest in pupillometry for most of the eye clinics is limited practically to its use to aid in surgeries. However, over the past decades, the range of pupillometry application expanded considerably, both basic research and clinical practice due to the growing evidence that confirms the use of pupillary response as an objective physiological marker and noninvasive of the normal and abnormal functioning of the central nervous system (Souza, *et al*., 2013) and indicative of various diseases (Ellis, 1979).

According to Jackson (2000), pupillometry has been shown to be applicable in the detection of people under the influence of drugs, since the consumption interferes in the functioning of the nervous system, modifying the reaction of the pupil to light. In literature, several studies relate pupil data with the use of different drugs (Ogle *et al*., 1966; Bye *et al*., 1979; Murray and Loughnane, 1981; Giakoumaki *et al.*, 2005).

The increased prevalence of drugs beyond alcohol has received increasing attention as a possible threat to road safety and this has been reported by several authors (Drummer *et al*., 2004; Schwilke *et al*., 2006; Poncel and Leyton, 2008). Although alcohol is the psychoactive substance most found in fatal traffic accidents, other drugs, legal or illegal as marijuana, amphetamine derivatives, opiates and benzodiazepines, have also been frequently detected (Del Rio and Alvarez, 2000; Holmgren *et al*., 2005).

One of the few studies conducted in Brazil showed the prevalence of 7% of drugs found in urine analysis of truck drivers (indicating recent use, but not necessarily that the driver was under the influence of this) and 3% in blood tests, indicative that they were under the influence of drugs. The substance most commonly found was ethanol, followed by amphetamines, used primarily to maintain wakefulness (Yonamine, 2004).

Curcio, *et al*. (2001) and Smolensky, *et al*. (2011) found a high incidence of accidents related to excessive sleepiness negatively affecting public safety. Several studies demonstrate the successful implementation of pupillometry to drowsiness detection and fatigue states (Lowenstein *et al*., 1963; Wilhelm *et al*., 2001; Souza *et al.*, 2013).

Thus, a specific pupillometry system for the detection of sleep and/or drug effect provide an improvement in diagnostic capacity, prognostic and preventive, as well as technological innovation, because although there are devices that measure the pupillary variation, it was not found any currently marketed models that are able to detect if a person is in its normal state. It should be noted the reliability of this test once the size of the pupil and their reactions cannot be manipulated or falsified by being involuntary and unconscious.

Thus, this paper presents a preliminary study regarding the development of a stimulation and capture system of the pupillary response using stimuli of different wavelengths in the visible spectrum. It is also demonstrated the development of an algorithm capable of analyzing the obtained data of the pupil size.

2. METHODOLOGY

In literature many works and equipments can be found related to pupil analysis, such as Ferrari (2008), Souza (2012), Leal (2008), Costa (2009) and Pedroni (2011). From the literature data, we designed a hardware that performs the stimulus and capture of pupillary dynamics and, consequently, as well as developed a software using computer

vision techniques, able to process images (*frames*) of the human eye, identifying the area of the pupil in function of time variation. In the following sections are shown details of these two development stages of pupillometry system

2.1 Hardware Development

In order to capture images we used an infrared camera (IR). This measure was adopted to meet the need of capturing images in low visible light and to contrast difference between dark irises (very pigmented) and the pupil.

According to Ferrari (2008) with the infrared illumination there is not pupil reaction. Thus, the IR light will not influence the results of pupil size.

Aspects regarding the image capture were addressed in this paper, since there is no consensus in literature about which would be the most suitable parameters for pupillometry. Thus, these details will be shown in the discussion of results.

Regarding the light stimuli, Kohn and Clynes (1969) demonstrated that at the time that stimuli of different wavelengths or different intensities reach regions of the retina, they stimulate differentially the receptors that evoke different pupillary constriction.

Thus, the initial prototype has different stimuli in the visible wavelength: red, blue and green, with varying intensity. To provide light stimulation to the human eye and observe the response of the pupil, an illumination system composed of LEDs was developed. The control of the flashes fired by LEDs was implemented using a microcontroller (MSP430G2452/Texas Instruments), programmed by the Code Composer™ Studio.

The lighting system consists of first lighting an infrared LED that will remain lit, illuminating the eye filmed during the whole process of data acquisition. After the period of pupillary accommodation the system triggers a blue LED. Subsequently, the blue LED goes off and two blue LEDs are lit. This process will be repeated for the other two colors LEDs (green and red). Therefore, for each individual will be obtained a total of 6 pupillary responses (two different intensities for the 3 kinds of wavelengths).

The illumination range of each LED is next to the largest absorption wavelengths of the cones (cells in the retina), Fig. 3.

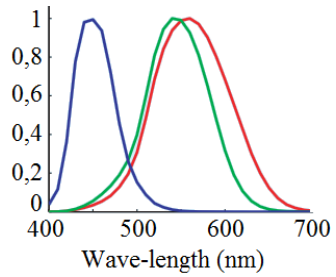


Figure 3. Sensitivity of the cones [Adapted from Trussel, Saber e Vrhel, 2005]

The arrangement of the lighting system was made for LEDs of each color to stay arranged in such a way that would enable all colors influence the eye in equivalent manner. The distance between the position of the eye and the center of the lighting apparatus is about 0.1 meter. According to Souza (2012), even when only one eye receives stimulus, reaction in both pupils is observed. This action is known as a consensual response and is due to the optic chiasm.

Thus, the mechanical components are designed so that the light stimulus was issued in the left eye and the equipment to capture images of the pupillary response of the right eye.

The designed hardware and its components are shown in Fig. 4. It's possible to observe two cylinders where will be encased part of the camera, LEDs, wires and the microcontroller. It is also observed the facial plug which seals the face so that no external light stimulus can influence in the tests.

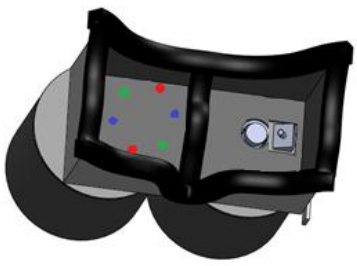


Figure 4. Prototype designed

2.2 Software Development

Computational techniques, properly applied, may be a promising way for the efficient detection and diagnosis of diseases studied nowadays. In the case of disorders associated with viewing this is no different.

Thus, this study developed a software, compiled with Microsoft Visual C ++ Express Edition with the OpenCV (Open Source Computer Vision Library) for image analysis of the eye of an individual in order to evaluate the variation process of pupil size when subjected to a light stimulus.

OpenCV is a library that enables the implementation of computer vision tools. It is written in C or C ++ and runs on Linux, Windows and Mac OS X. One of the goals OpenCV computer vision is to provide an infrastructure that helps people to quickly implement various techniques in image or video input (Bradski and Kaehler , 2008).

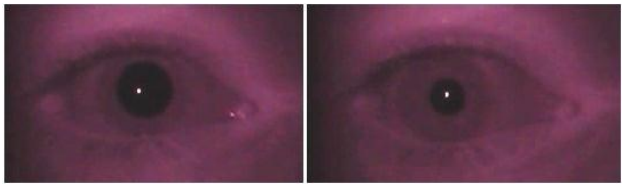
As this work, as many other stakeholders in the eye dynamic, focuses to computer vision techniques for the detection of circular shapes of the eye. The most widely used and commonly recommended form involves the use of circular Hough Transform.

The Hough transform is a method for finding lines, circles or other shapes parameterized (Bradski and Kaehler, 2008) and this algorithm is implemented in the library openCV.

The underlying algorithm is handling the frames captured by the camera used in the manipulation, isolation of colors to finally define geometries understood by one color in question in the presence of contrast and thereby obtain object desired exposed on screen. In other words, the basic algorithm for the software of the developed task of being able to detect an object that is in contrast and define its geometry, in this case, the size of the pupil.

3. RESULTS AND DISCUSSION

Pupil images, obtained using the apparatus designed with the IR camera, without visible light stimulus (a) and with the light stimulus (b) are shown in Fig. 5.

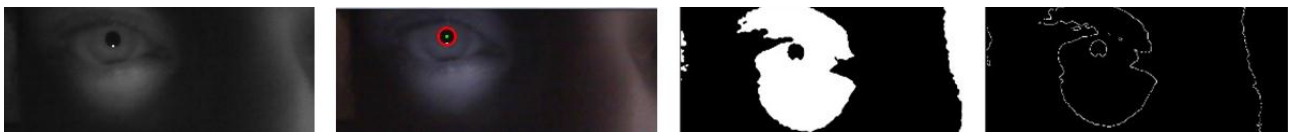


(a) (b)

Figure 5. Pupil image without light stimulus (a) and with light stimulus (b)

The results after implementing the program can be seen in Fig. 6 illustrating separately the windows displaying the software running.

Figure 6 (a) shows the image processed by the infrared camera. Figure 6 (b) illustrates a window of the software at the time that occurs the Hough Transform function for circles location that is performed in order to distinguish the region of the pupil in relation to other objects. It notes that as the pupil changes its approximate diameter, the red circle that distinguishes it from other elements tends to accompany this change, which allows a view of the pupil ratios. Figure 6 (c) and (d) exposes the images presented previously, but in black/white and contour detection, allowing easy pupil circle distinction in relation to any other geometry observed in the image, in other words, any other element of the face, the same as the iris, which is also circular.



(a) (b) (c) (d)

Figure 6. Pupil image acquired by the camera (a) and detection of circles made by the software (b). Images in black/white (c) and contour detection (d)

In the literature there is still divergence of information as to which image capture rate is more suitable for pupillometry and works using some different rates is shown in Tab. 1. Thus, this study addressed this aspect, in order to see if there is considerable difference between the acquired values.

Table 1. Literature data about the pupil image capture rate

Literature	Capture rate (frames/second)
Leal (2008)	15
Lee *et al.* (2005)	30
Pedroni (2011)	24
Tilmant *et al.* (2005)	25
Ferrari (2008)	30

Tests with different pupillary image capture rates were carried out simultaneously, three videos and during them there were no visible light stimulus. The place had low visible illumination intensity, but as the pupil is very sensitive to variation in brightness and an oscillation size always exist (*hippus*) it was necessary to position three cameras with different capture rates and the same resolution to capture the same movement of the pupil. A camera captured videos with 15 frames per second (fps), another with 30 fps and the last with 60 fps. These values were chosen based on the ranges found in the literature and results are shown in Fig. 7, where it is possible to observe the variation of pupillary area (in the unit px^2, being "px" the side of a pixel).

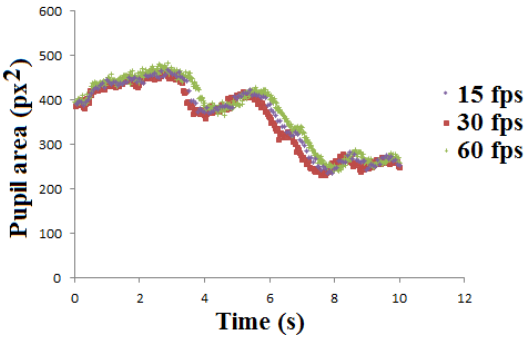


Figure 7. Graph of pupillary area *x* time for different image capture rates

Given the results presented in Fig. 7, one can notice a slight difference between the curves, especially in times between 3 to 4 seconds and 6 to 8 seconds, which are the periods that occurs greater decrease in pupillary area. One cause for this difference can occur due to having 03 different cameras and each being a different angle relative to the pupil. Anyway, the results for the different image capture rates are very close even in these times.

Thus, the results below were with capture rate of 30 frames per second, a rate that will not generate a high computational cost and reliability features.

The results shown in Fig. 6 it is possible to observe the clear distinction of the iris and the pupil, and because this is possible to quantitatively obtain the area of the pupil of the variation with respect to time. Thus videos were obtained when the pupil is subjected to intermittent light stimulation with variable intensity and wavelength, Fig. 8. The lighting system consists in first lighting infrared LED that will remain illuminated, illuminating the eye for all the process of data acquisition. After, the system gives a pulse of light with only a blue LED. Thereafter, when the blue LED is off, there is a period with no visible light (about 10 seconds) and another pulse of light is given, now with two blue LEDs. This process is repeated for the green LEDs and red LEDs for the order with the same time intervals and the same light pulse (about 1 second).

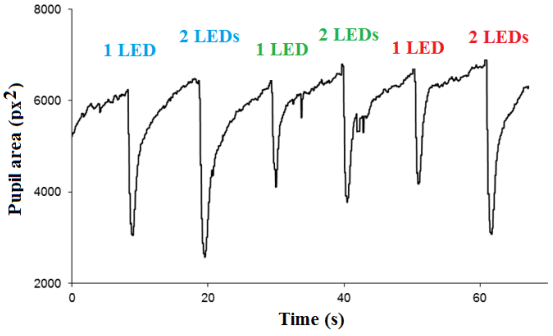


Figure 8. Graph of pupillary area *x* time

When comparing the light intensities, it is observed that there is greater constriction of the pupil area of the greater intensity on stimuli, so, two LEDs (regardless of visible wavelength) will cause pupil constriction greater than just the same length LED wave. Yet this perspective, it is observed that there is no significant difference in pupillary constriction when the eye is illuminated by a green LED and two green LEDs.

Comparing the wavelengths, was realized that two red LEDs cause the same pupillary constriction that a blue LED and the lower pupillary area is obtained when the eye is illuminated by two blue LEDs.

The graph also shows that the pupil constriction occurs with greater speed compared to pupillary dilation.

Finally, Figure 9 shows the same result as above, however, considering the uncertainty. As the area we want to know the size (pupil) has the next form of a circle and the pixels have quadrangular format, our main mistake is in relation to approach these areas. Thus, the uncertainty will be considered half of the pupil perimeter for each time point (*frame*).

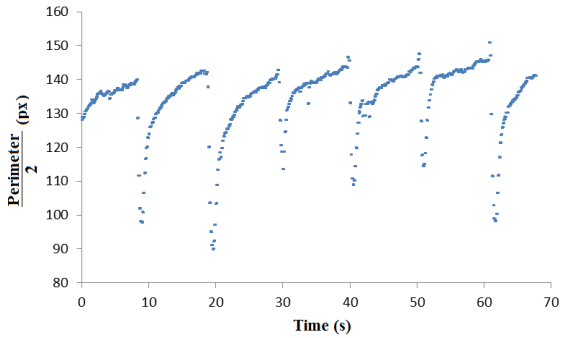


Figure 9. Graph of uncertainty

4. CONCLUSION

In this study was addressed the question of neurovisual changes and the importance of developing techniques for diagnosis and treatment progress. Some physiological aspects were also highlighted that help in the design and development of study.

Thus, based on the understanding of the need for more objective equipment and specific to study the dynamics of vision, and knowledge of the challenges of development thereof, the work shows the design and assembly of a device that stimulates neurovisual system and provides images of the pupil at different times and processes providing quantitative information on the pupillary reflex.

In this way, the results shows that the system developed provides preliminary subsidies for various studies involving the dynamics of the vision and development of equipment for pupillary measuring.

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