Real Time Pupil Size Monitoring As a Screening Method for Diabetic Retinopathy

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Abstract— **This paper reports an accurate pupil size monitoring and analyzing system designed for a new method for screening diabetic retinopathy. The system monitors the pupil size change under stimulation of circular or annular objects of different sizes and brightness produced on a LCD screen facing the subject. Pupil response is captured by digital cameras and the eye images acquired are processed in real time. A novel algorithm is designed to calculate the pupil size to provide data input for the screening procedure of diabetic retinopathy. To distinguish real pupil size changes from artifacts like blinking, eyelid drop or reflections, we use several image processing techniques to estimate the pupil size when the pupil shape is partially occluded.**

Index Terms — **Diabetic retinopathy, image processing, ellipse detection, pupil size.**

I. INTRODUCTION

Diabetic retinopathy (DR) is one of the potential complications of diabetes that may cause blindness. The primary effect of DR is that it can cause vascular damage on the retina before the patient develops more severe symptoms. The damage on the retina is not uniformly distributed, which means the relation of pupil response to light stimulus on the center of the retina and on the peripheral of the retina will be different for a patient with DR and a healthy person. The approach of using pupil response as a biosensor for retinal function has been studied and validated by prior research [1][2][3]. However, its application as a broad screening approach for DR requires both the optimization of the testing system and extensive statistical analysis over the patient data.

The method of using pupil response to screen DR was initially proposed by Gorin in 2006 [4]. Compared to existing methods including examination by the ophthalmologist using ophthalmoscopy, using trained grader to assess disease severity based on nonmydriatic fundus imaging, a digital image based pupillometry and analyzing system has the advantages that it provides an objective test result, is fast, non-invasive, easy to use, and does not require extensive training for operators. In this paper, we propose a new algorithm to perform more accurate and robust pupil area monitoring.

Since the system is supposed to be used to perform tests among general population when a wide range of conditions exist, the system needs to facilitate a rapid test, be robust to interference, and provide accurate information. Most existing eye tracking systems focus on eye position detection instead of the pupil size change. Existing pupil size estimation systems either assume the artifacts, including cornea reflex and eye lid occlusion, are negligible [5], or are not designed to detect the pupil change in real time and are not fully automatic (depending on the eyelid position) [6]. In [7], the horizontal diameter of the pupil is used to estimate the pupil size. While this seems like a reasonable approach, the horizontal diameter of the pupil can suffer from artifacts such as cornea reflex.

We implemented a pupil size monitoring system that presents stimulus on a LCD screen facing the subject and uses high speed digital cameras to capture the left and right eye response. We also developed a pupil extracting algorithm using a combination of blob analysis and edge detection techniques to ensure both real time performance and robustness. The algorithm assumes that the pupil appears as a circle at the central position and looks elliptical when at eccentric positions. The system sampling rate is 60 Hz.

The remainder of this paper is organized as follows. In section II, we discuss the related work. In section III, we present an overview of the system we developed. In section IV, we provide the details of the ellipse estimation and pupil size calculation method. In section V, we present the preliminary test results obtained. The intended method to develop a norm for DR screening is discussed in section VI. Finally, in section VII we summarize the main findings of our study.

II. RELATED WORK

Ellipse estimation based on edge information is a widely used object extraction technique, but generally faces the dilemma of utilizing Hough transform in a large parameter space which consumes lots of computation power, or using local edge feature, like gradient information, to deduce the parameter space, which suffers from poor consistency and accuracy [8]. In [8], global geometric symmetry of ellipses is used to reduce the dimension of the parameter space. It still assumes that major part of ellipse edge is detected correctly; especially the vertical scan assumes the upper and lower part of the edge is not occluded. Given that the upper eye lid drop is a frequent scenario, the method proposed in [8] is not suitable for our application.

Starburst is an eye tracking system using RANSAC algorithm iteratively to fit a subset of detected edge points to an ellipse [9]. Like most algorithms based on RANSAC, the estimation result may not be accurate when a significant portion of edge points are outliers, i.e., when the pupil is partially occluded. In [10], a threshold on the curvature of edge points is determined to eliminate outliers before fitting edge points to an ellipse, which is computationally expensive and the determination of curvature threshold is not trivial.

In this paper, we propose an algorithm that first locates horizontally symmetric edge points, finds the midpoint, and fits the locus of these midpoints to a straight line, i.e., the vertical (or close to vertical) axis of the ellipse, then calculates the horizontal distance of each edge points to the vertical axis, eliminates those points which have a discontinuous change in the distance, and finally fits an ellipse to the remaining points. Since occlusion at the left and right side of the pupil is typically small, vertical axis usually can be located accurately and provides a good baseline for locating other edge points. The algorithm is fast, robust, and does not need to set tricky parameters; it satisfies the real time and robustness requirements of the diabetic retinopathy application.

III. SYSTEM OVERVIEW

The system components and the block diagram of the software used are shown in Figure 1. Figure 1.-(a) shows the block diagram of system components. Digital cameras are installed on a frame that can exclude ambient illumination. The subject is instructed to put both eyes onto the frame, in front of which half mirrors are installed, with one eye looking directly to the LCD screen and stimulated by the light from the screen, while the other eye is occluded. The mirrors reflect the eye image to cameras installed on the side. The responses from both eyes are captured by the digital cameras and analyzed by our software. We use a Dell desktop system to run our control and analysis software. Infrared off-axis lighting is used for image acquisition to produce a black pupil effect so that the pupil area is easy to extract.

The software block diagram is shown in Figure 1-(b). The software is developed on the Labview 7.1 platform using its vision module. The stimulation module generates circular or annular bright objects on the LCD screen in order to stimulate the central or the peripheral sections of the retina, respectively. According to different test requirements, different brightness, color, size and time interval of the visual stimulation can be specified. A small fixation point is shown on the center to help the subject to focus. In the mean time, given the visual stimulation and the resulting eye response, the image acquisition and processing module captures and processes the eye image in real time. After the test, the analysis module analyzes the data collected and provides input for the screening procedure for DR.

The system reaches a processing rate of 60Hz (120 images/second) at real time on a 3 GHz Pentium IV desktop system.

IV. ELLIPSE ESTIMATION AND PUPIL SIZE CALCULATION

To extract the pupil and estimate its size, first the approximate location of the pupil is located by a simple threshold and blob analysis operation on a down-sampled low pixel-density resolution image in the same way described in [11]. Next, pupil edge points are detected by scanning the full pixel-density resolution image horizontally. The edge detection procedure is applied on a small window enclosing the approximate area of the pupil. This ensures both a high speed operation and no lost of edge points.

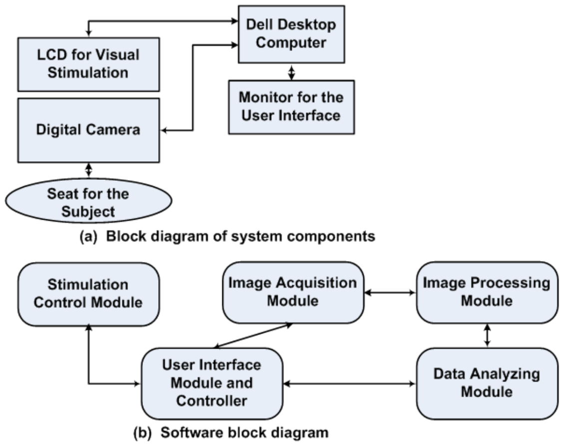

Figure 1. System components and the software diagram

The edge points detected from the previous step can include outliers, such as points from the cornea reflections, eye lid edges, or other sources of noise. To select edge points, we employ two major properties of the elliptical pupil boundary.

A. Symmetric property

It can be proven that for any group of parallel chords of an ellipse, the locus of their midpoints is a straight line. If we scan the pupil area horizontally, locating the two edge points and the midpoints, these midpoints form a straight line. We name the line deduced from the midpoints of horizontal chords as the vertical axis, although it may not be strictly vertical depending on the orientation of the ellipse.

B. Horizontal chord length property

By assuming that the pupil is a circle at the central position and appears as an ellipse at eccentric position, based on the perspective projection relationship, we have proved a property (details omitted for lack of space) for the length of the horizontal chord as:

$$\frac{\partial\left(r\frac{\partial r}{\partial y}\right)}{\partial y}=-\frac{4\cdot\cos^2(\theta)}{\cos^2(\varphi)}, \tag{1}$$

where r is the chord length, as shown in Figure 2, φ is the vertical rotation angle of the eye ball in the 3D space, and θ is the horizontal rotation angle of the eye. In Figure 2, X_L and X_R represent the left and right edge points detected respectively, and O_l is the midpoint. Since sometimes only one side of the edge points (X_L or X_R) is detected, we can use the half chord length to replace r after the vertical axis is located. In addition, φ and θ are only determined by the position of the eye in the 3D space and are the same for all horizontal chords; therefore, the right side of Eq. (1) is a constant while the eye position is determined. This constant value is defined as the horizontal chord length coefficient. In practice, we do not really need to calculate the exact pupil rotation angle φ and θ before we estimate the ellipse.

Using property A and B, one can eliminate the outliers from the detected edge points, and after that, the algorithm fits an ellipse to the remaining points, and then the pupil size is estimated as the area of the ellipse. Since for the application of the DR screening, we are mostly interested in the change of pupil area when the subject is fixating in one direction (although this direction may not be the central location), the system needs no additional effort in translating the elliptical pupil area into its real area by perspective projection. The details of the algorithm are shown in Table 1 .

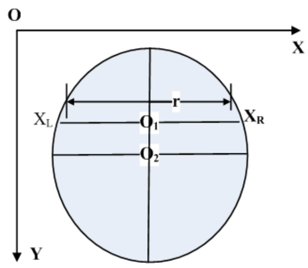

Figure 2. Horizontal chord on the ellipse

Table 1. Edge detection and ellipse estimation algorithm

1. Scan horizontally. For each row (i), find edge points X_L, X_R and the midpoint O_i.
2. Fit the locus of all midpoints O_i detected in step 1 to a straight line using Labview line estimation VI (Virtual Instrument): "IMAQ Fit Line".
3. For all edge points X_L and X_R that satisfy the symmetric property, add them to the candidate point array Cp, and calculate the horizontal chord coefficient (using difference as the approximation of the partial directive), and find the average value of the horizontal chord coefficient.
4. For all other edge points, calculate the horizontal chord coefficients; if they satisfy equation (1), then add them to Cp.
5. Fit an ellipse to all points in Cp using the Labview ellipse estimation VI: "IMAQ Fit Ellipse 2".
6. Calculate the area of the ellipse obtained in step 4 as the pupil size.

V. TEST RESULTS

Figure 3 shows results of two tests when the eyes are at two different positions and with different levels of occlusion. The left column shows result when the eye is at position (φ =0, θ =15°), and the right column shows result when the eye is at position (φ =0, θ =20°). The top row shows the result when there is no occlusion from eye lid drop and this result is used as the "true" eye area as a benchmark. The middle row and bottom row show test results with the same degree of occlusion at that particular eye position. The middle row is the test result when using a simple ellipse estimation algorithm that fits the ellipse to all edge points detected directly. The bottom row is the test result of the algorithm we have presented in this paper. In all six images, the white curve shows the final ellipse detected; the small window overlaid at the left top corner is the result in the low resolution image when using blob analysis to detect the approximate position of the pupil. Table 2 shows the accuracy of the two algorithms in terms of measurement error. We can see that for both cases, our algorithm results in much better accuracy in measurement. Measurement error is calculated as the difference in percentile between the measured position and the "true" position.

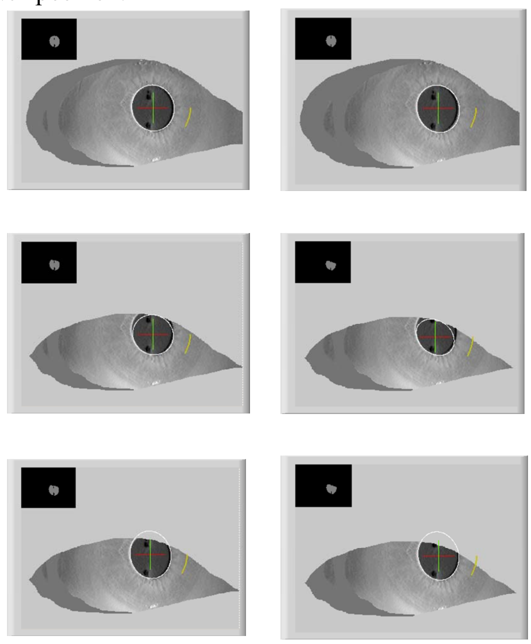

Figure 3. Processing results for the proposed algorithm and a simple algorithm that fits an ellipse to edge points directly. The left column and right column describe two tests while the eye is in different positions.

Table 2 Measurement error of the test result for two algorithms

	Our algorithm	Simple ellipse fit algorithm
Test 1	3.32%	17.5%
Test 2	2.58%	32.7%

Figure 4 shows the test result for a volunteer healthy subject whose eye is stimulated by interleaved circular and annular bright objects on the LCD screen, stimulating the central and peripheral part of the retina respectively. The stimulus is on for a short period of time and off for a relatively longer time waiting for the pupil to recover and then the next stimulus is on again. Only response from one eye is shown here and there is no significant difference for the other eye in this particular test. Figure 4-(a) shows the full range time of the test. From left to right, the stimulus is increasing in brightness and one can observe that in region R2, the pupil response amplitude is increasing accordingly. Region R3 is the area that the pupil becomes saturated and the pupil response does not increase with the increasing stimulus level. The initial period in region R1 shows the duration when the subject adapts to the test. Region R2 is the region that we are interested in because that is the region the pupil response is sensitive to the stimulus level.

Figure 4-(b) shows one short episode. The valleys denoted by triangles are the response to peripheral stimulation and the ones denoted by arrows are response to central stimulation.

One can observe that the two different responses have varying amplitudes. Investigating the degree of difference in amplitude or other features between the peripheral and central response is a major topic for future research, because they can indicate the presence of DR.

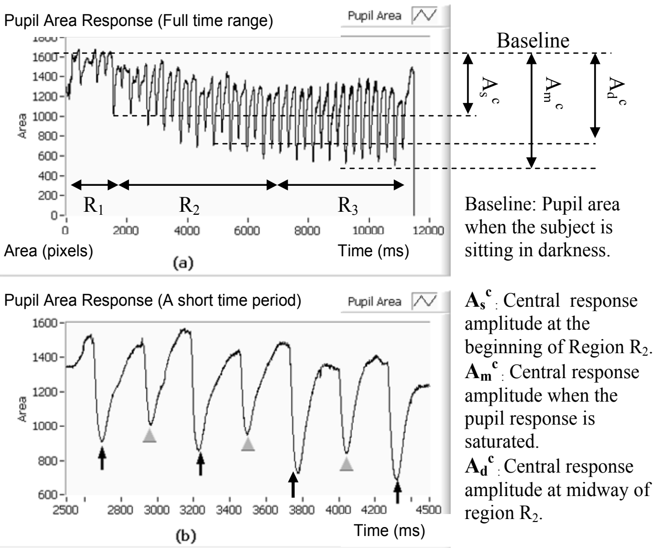

Figure 4. Test result for a volunteer healthy subject stimulated by interleaved circular and annular bright objects.

VI. DISCUSSION

It is well known that the pupil size and response can be affected by many factors including age, iris color, media opacities, and medication, or even the anxiety level. It is difficult to collect enough statistics to address all of these aspects. To control these variations, we plan to use the central response of the pupil within the same eye as an internal benchmark and compare the peripheral response with it. The overall light sensitivity of the central part of retina is usually stable until later stages of DR. The idea of using this intraocular comparison method for DR screening is proposed by Gorin in [4] and he proposes to use the ratio of stimulus levels when central and peripheral responses reach the same amplitude as the major criterion. We plan to use a slightly different ratio metric, which we believe might be a more direct measurement.

While we have not yet started collecting data on diabetic patients and developing a norm for the purpose of DR screening, as a general outline of the approach, we intend to find the response amplitude at the midway of region R_2 for both peripheral and central stimulus, denoted by A_d^p and A_d^c respectively. Figure 4 shows an example of how to obtain A_d^c. If necessary, at the same stimulus level where A_d^p and A_d^c are collected, the pupil constriction rate can also be measured for both peripheral and central stimulus, denoted by V_p and V_c respectively. For each subject, we calculate two ratios: $R_a=A_d^c/A_d^p$, $R_v=V_c/V_p$.

In the two dimensional sample space shown in Figure 5, if the distributions of healthy subjects and subjects who have developed DR are sufficiently apart from each other, it is then possible to draw a decision boundary and develop a norm for the screening method with an acceptable error rate.

VII. CONCLUSION

This paper presents an accurate and robust image based pupillometry designed for the screening of diabetic retinopathy based on different pupil response to peripheral and central stimulus. Test results on pupil area measurement show that the designed system provides a more accurate measurement of the pupil size under interference and satisfies the real time requirement. Preliminary tests on healthy volunteer subjects clearly show that stimulations to central and peripheral sections of the retina result in different pupil responses. Further research is needed to analyze the data on pupil response to set up normality for the purpose of screening DR or determining the degree of pathology.

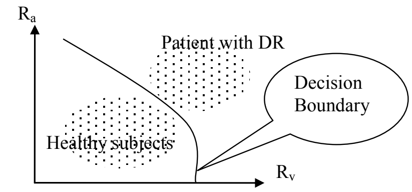

Figure 5. Two dimensional sample space and decision boundary

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