Functional Signal Detection in Retinal Videos

Eduardo S. Barriga, Peter Soliz, and Paul W. Truitt.

Abstract— **An optical imaging device of retina function (OID-RF) has been developed to perform measurements of changes in blood perfusion due to neural activity resulting from visual stimulation of the photoreceptors in the human retina. Experiments were performed by measuring the changes in reflected long wave visible (700nm) light from the retina caused by the retinal activation in response to a visual stimulus. The problem being addressed is that of detecting the signal from the retinal activation in the presence of noise from other sources, including the unstimulated retinal background and other unknown physiological changes. Preprocessing of the raw data was done to eliminate unwanted artifacts, such as blinking or excessive eye movement. Principal Component Analysis (PCA) was used to isolate the functional signal. The results of the analysis showed that regions of the retina that were stimulated could be detected using PCA.**

Index Terms— **retinal function, optical imaging, functional retinal imaging, infrared reflectance, principal component analysis.**

I. Introduction

Visual field testing (perimetry) remains the gold standard for detection and monitoring progression of diseases of the optic nerve. Perimetry is a functional test of the patient's vision, which is intended to detect defects on the visual field map. The visual field map gives the clinician diagnostic information to help localize the damage. Perimetry has been central to monitoring progression or improvement of the optic nerve diseases over time. Unfortunately, perimetry remains a subjective test that requires the patient to make important judgments during the test that can be clouded by anxiety, fatigue, or lack of concentration. This results in poor repeatability in areas where functional damage is suspected [1]. The optical imaging device for retinal function (OID-RF) device was developed in an attempt to improve the objectiveness of the test and the sensitivity for detection of damage and change over time. This paper presents early results that take the first major step toward achieving this goal.

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II. Bio-chemical basis for Optical Signal

Noninvasive optical recording of neuronal signals from the brain has been demonstrated [2,3]. Changes in the inherent optical properties of active brain tissue due to blood perfusion or metabolic changes (referred to as "intrinsic signals") permit visualization of neuronal activity. Intrinsic signals refer to the change in the percent reflectance of the illumination light occurring as a result of the change in the absorption coefficient due to the conversion of oxyhemoglobin to deoxyhemoglobin in response to the metabolic demands of active neurons. The interrogating light measures the difference in absorption spectra between the oxyhemoglobin and deoxyhemoglobin molecule in the region of 580-720nm.

Direct functional imaging of the human retinal has been previously reported only by our collaborators, Kardon, Kwon, and Ts'o. The device and the methods employed for stimulating the retina and capturing functional images of the retina have been described previously by Kardon, et al [4].

Our initial hypothesis was based on data collected for similar experiments where differential retinal stimulation was observed by imaging visual cortex. In these experiments Villringer [5], for example, observed a pattern in the response signal at 700 nm that appears to show an increase in the reflectance in portions of the visual cortex shortly after the onset of the stimulation to the retina (Figure 1). This characteristic change is consistent with an increase in oxygenated hemoglobin.

III. Methodology

A. Data Collection Procedure

Briefly, the OID-RF device applies a stimulus pattern (Figure 2) to the human subject's retina. One of these patterns are applied during a 13s epoch. The epoch starts

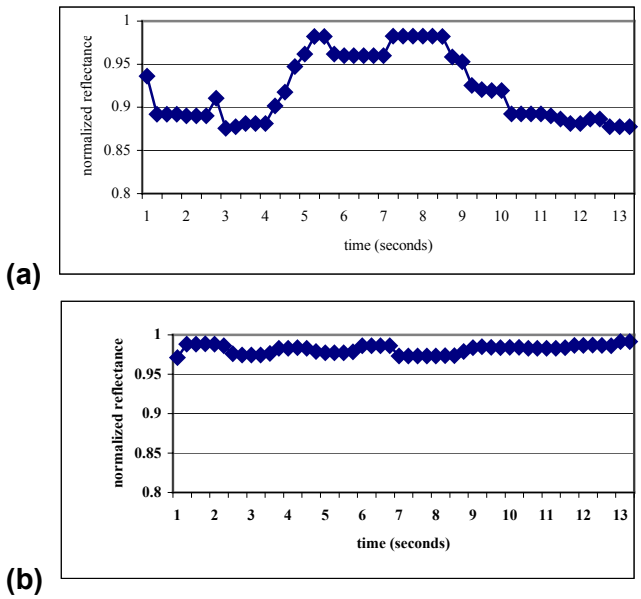

Fig. 1. For a normal subject, a and b shows the expected average reflected intensity over time for one for the superior stimulated retina (a) and inferior unstimulated region of the retina (b).

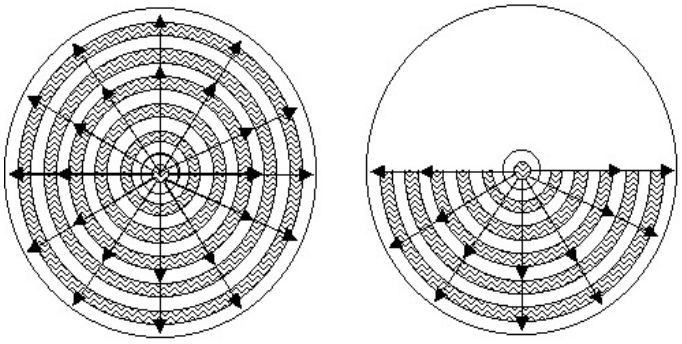

Fig. 2. Two stimulus patterns used in the study. Patterns radiate from the center at 2 cycles per second. The spatial frequency varies from 10 cycles per degree (cpd) in the parafovea to 0.2cpd in the periphery. The polarity of the hemifield pattern (b) could be changed to present a pattern in the superior half.

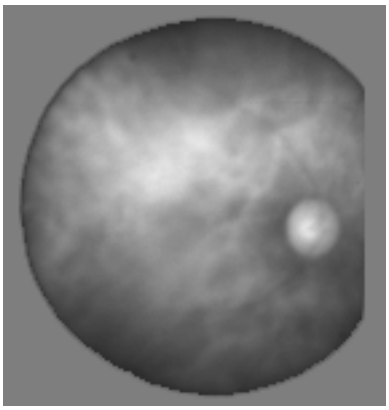

Fig. 3. A typical fundus image of the retina using the reflected interrogation light (700nm). The image shown is from the right retina and the optic disc is to the right side of the image.

with 3s of baseline data, followed by 5s of stimulus, and 5s of recovery time when, as with the baseline measurements, no stimulus is applied. A digital video camera operating at about 3 Hz collects 160 x 160 pixel frames of a 40° field of view centered on the fovea. A typical frame is shown in figure 3. Camera characteristics, as well as a full description of the OID-RF device have been previously reported [6].

B. Basic Preprocessing

In this paper we present the analysis of two normal patients, M6 and M8. The data set consisted in 30 epochs for M8, with both superior and inferior retinal stimulus and 60 epochs for M6, with full field, superior and inferior retinal stimulus. Each epoch consisted of 53 image frames of data. The first step was to determine which epochs presented unwanted artifacts, for this we calculated the standard deviation of the pixels intensity over each epoch. It was shown that epochs with high standard deviation had artifacts; therefore those epochs were removed from the analysis. Next, the epochs with the same stimulus condition were averaged to reduce random noise. The result was an average epoch also consisting of 53 frames, where each of the 53 averaged frames came from the same frame in the sequence for each epoch. Each stimulus condition resulted in an average epoch.

The number of frames is further reduced by calculating average frames that represent blocks of time in the epoch. For example, two blocks of five frames each represent the base period, three blocks for the stimulus period and three blocks for the recover period. Finally, to perform a First Frame Analysis [7], the first block was subtracted from the rest of the block. First Frame Analysis allows one to measure only the changes produced by the stimulus, eliminating the background level. At this stage of the preprocessing seven images represent the time course of each stimulus condition.

C. Principal Component Analysis

The analysis of the data showed an unexpected similarity in the response of the unstimulated and stimulated areas of the retina. This motivated us to apply a source separation method to extract the functional signal from the background and noise signals present in the images. PCA determines an appropriate subspace of dimensionality smaller than the dimensionality of the original feature space of the images. Using PCA the functional signal can be reconstructed using a subset of the principal components [8,9].

Our data set has the time series of each pixel in the image, and the principal components can be found as the solution of

$$SE = \Lambda E' \tag{1}$$

Where S is the sample covariance matrix of the data set, the matrix E contains the eigenvectors e_n and Λ is the diagonal matrix of the eigenvalues λ_n, which represents the variance of the data along the principal axes. The n-th principal component is given by

$$y_n = \lambda_n^{-1/2} v_n^T X \tag{2}$$

The functional signal $\hat{X}$ can be reconstructed using a combination of the principal components, and can be calculated by

$$\hat{X} = \sum_n v_n (v_n^T X) = \sum_n v_n \lambda_n^{1/2} y_n \tag{3}$$

IV. Results

Our analysis was focused in two regions of the retina, a superior and an inferior Region of Interest (ROI), both of 30x40 pixels size. After applying first frame analysis to the images, we obtained the mean intensity value over the ROI and plotted the values through time, as shown in Figure 4. Recall that the data point 1 is baseline (no stimulus); points 2, 3, and 4 are stimulus; 5, 6 and 7 are post stimulus.

Calculations showed that the first principal component accounts for 95-98% of the information, and reproduces the general illumination level. The principal components 2 through 5 contain most of the information about the functional signal, and the rest contain information about noise and movement. In Figure 5 the time series of the first 10 principal components (applied to the images without binning) are shown. Here one can see how the second principal component shows the functional signal.

In figure 6 we show the ROI's intensity after applying PCA. The principal components are selected by studying the time series, such as shown in Figure 5, to isolate the functional signal.

V. Discussion

A. Intensity Profiles

Figure 3 presented the time course of the measured changes in reflectance from the first block image that represents the base (pre-stimulus) reflectance. Based on data collected from imaging of the brain by other researchers [5,7], the hypothesis is that stimulated retinal tissue will

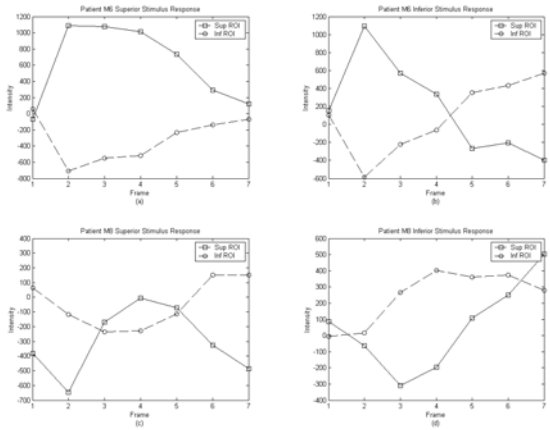

Fig. 4. Intensity plots of the ROI's after First Frame Analysis. The upper frames are for Subject M6. Lower frames are Subject M8. Left frames are the superior stimulus. Right frames are the inferior stimulus. Dashed lines are the response of the inferior, while the solid lines are for the superior response.

behave in a manner similar to the visual cortex experiments. That is, there will be an increased reflectance for stimulated retinal tissue and change in reflectance for unstimulated retina. The waveform patterns observed in Figure 4 do not quite agree with the previous measurements of the visual cortex. For subject M8 (Figure 4 C and D), there is clearly an increased reflectance for the stimulated ROI. In Figure 4C, when the superior ROI (solid line) is stimulated, one observes an increased reflectance while the retina was being stimulated, then a decrease during the post stimulus period. Conversely, in Figure 4C, the inferior ROI (dashed line), which is not being stimulated, shows a decrease in reflectance. This decrease has been observed in other subjects and is not yet well understood. The other plots show similar behavior in the reflectance of the stimulated and

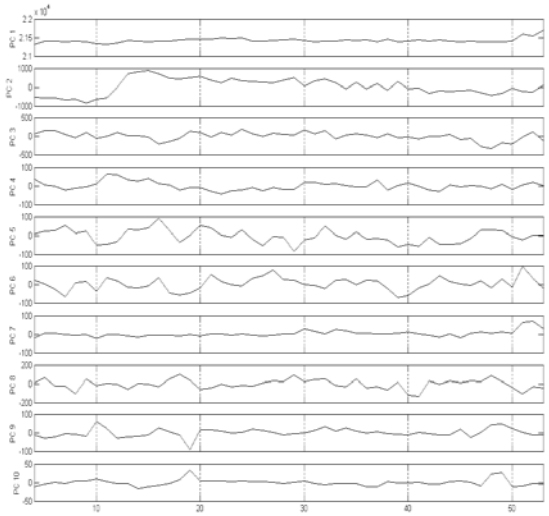

Fig. 5. Time series of the intensity values of the first 10 principal components

unstimulated ROI's. The exception is Figure 4B, where the stimulated ROI shows a decrease in reflectance, while the unstimulated ROI shows an increase in reflectance.

B. Intensity Profiles of Principal Components

Figure 6 presents the changes in reflectance for the same experiments in Figure 3, except that the data in these plots have been processed by principal components. By selecting the appropriate principal components the ambiguity or inconsistency in the signal produced by Subject M6 (inferior stimulus), Figure 4B, is corrected in Figure 6B. Now the reflectance of the inferior ROI increases as the stimulus is applied and the superior ROI decreases.

VI. CONCLUSIONS

To our knowledge, this paper is the first report the application of principal components in the analysis of functional retinal imaging obtained in a human eye using changes in the reflection of near infrared light (700nm) as a means of detecting a response to a visual stimulus (530nm). From the results of this pilot study, it is not yet clear which retinal layers are contributing to the functional signal. It is our goal to continue to collect functional imaging data in order to assess whether the tigroid pattern that was observed in many of the high order principal components may correspond to the pattern of deeper lying choroidal vessels. This observation may imply that one of the signals that are being isolated by the principal components may result from changes in the oxyhemoglobin concentration in the deep choroidal vessels.

Through continued application of techniques like principal components and blind source separation, we expect to separate the potentially large number of linear and non-linear physiological responses. From the preliminary data presented here, the results for separating such functional activation of the retina from other retinal signals appears to be promising.

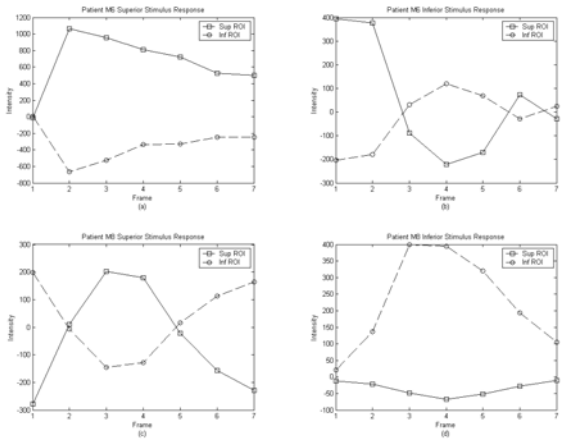

Fig. 6. Intensity plots of the selected Principal Components. Notice the inverse behavior of the inferior and the superior ROI's.

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