Independent Component Analysis for Processing of Retinal Responses to Patterned Stimuli

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Abstract—**To permit the non-invasive study of the response of the retina to spatially patterned stimuli, an optical imaging apparatus that can deliver a video-based visual stimulus to the retina while imaging the functionally correlated intrinsic signal response in the rear infrared (IR) was developed. Measured changes in reflectance in response to the visual stimulus are on the order of 0.1% to 0.5% of the total reflected intensity level, which makes the functional signal difficult to detect by standard methods because it is masked by the other physiological signals. In this paper, we apply Principal Component Analysis (PCA) and Independent Component Analysis (ICA) methods such as JADE and Fast-ICA to extract the signals present on the resulting videos. From our dataset of 140 different experiments performed on cats, in 65 % of the cases the algorithms can detect and extract the patterned stimuli. Careful analysis of the results may give an insight of the processes present during the stimulation of the retina.**

Keywords—**Optical Imaging, Functional Imaging, Independent Component Analysis, Retina.**

I. INTRODUCTION

A fundus camera was modified to permit collection of retinal images with a cooled CCD camera in the near IR, while delivering a visible patterned stimulus generated by a computer driven LCD display. The patterns of visual stimuli tested included counter flickering checkerboards of differing spatial extent, designed to systematically map the imaged field. Recordings were conducted in 20 sec blocks with a 3 sec stimulus period. The IR illumination wavelengths ranged from 750 to 860 nm. Measured changes in reflectance in response to the visual stimulus are on the order of 0.1% to 0.5% of the total reflected intensity level which makes the functional signal difficult to detect by standard methods since it is masked by the other signals that are present.

Figure 1 shows the frames from a single experiment. Response changes in the reflected intensity due to the stimulus are not readily apparent. In this work PCA and two methods for ICA: Joint approximate diagonalization of eigen-matrices (JADE) [11] and the fast fixed-point algorithm (Fast-ICA) [12] are applied in an attempt to separate and to understand the signals present in the cat retina during the period of stimulation. The better we understand the functionality of the cat retina, which is anatomically simpler than the human retina, the better we will understand the functional activity of the human retina.

As early as 1949, Hill and Keynes linked the activity of the nerve cells with changes in their optical properties [1]. In 1986, Grinvald et al. [2] showed that changes in the optical properties of the tissue could be used to study the functional architecture of the cortex. Villringer and Chance [3] used near-infrared light to measure non-invasively brain activity in humans through the skull. Kardon *et al.* [4] reported the first device, called the Optical Imaging Device for Retinal Function (OID-RF) to directly image the human retina to record changes in 700 nm light caused by retinal activation in response to a 535 nm stimulus. Barriga *et al.* [5, 6] used ICA to extract the functional signal from the videos obtained with the OID-RF. T'so *et al.* [7] used a device similar to the OID-RF to image the response of a cat's retina to a patterned stimuli.

II. METHODOLOGY

A. Data Pre-processing

The data set contains 7 files with 20 different experiments, each one generating an epoch (video). An epoch consists of 20 frames of 144x192 pixels each, at a frame rate of 2 Hz for a total recording time of 10 sec. A sample of the resulting frames is shown in figure 1. As we mentioned before, no significant change in the images can be seen during the period of stimulation (second row of images). The basic pre-processing procedure consists of averaging each two frames and then subtracting the first averaged frame to measure only changes due to the stimulation. The result is 9 averaged frames, where the first frame is baseline (no stimulus), the next three are stimulus and the remaining five frames are post-stimulus. Figure 2 shows a sample of these 9 frames.

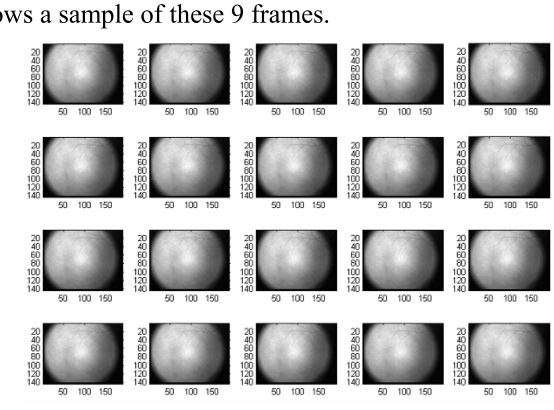

Fig. 1. Frames from a cat video recording

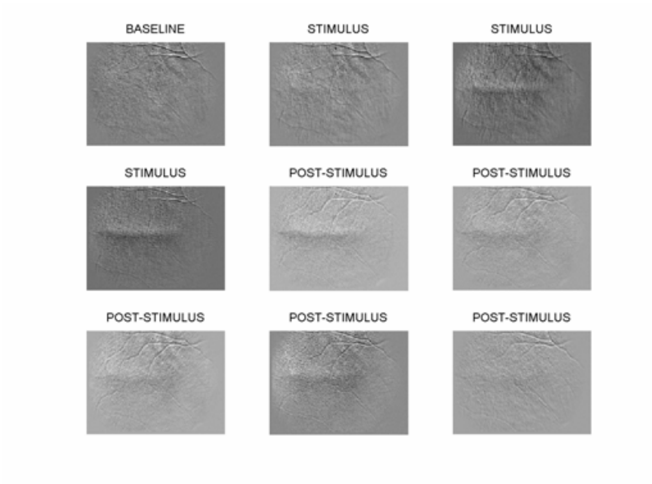

Fig. 2. Resulting frames after pre-processing

B. Principal Component Analysis (PCA)

The purpose of principal component analysis (PCA) is to derive a relatively small number of decorrelated linear combinations (principal components) of a set of random variables while retaining as much of the original information as possible. Using PCA the functional signal can be reconstructed using a subset of the principal components [8].

C. Independent Component Analysis (ICA)

Given a set of observations of random variables $x=[x_1(t),x_2(t),...,x_n(t)]$, assume that they are generated as a linear mixture of independent components $s=[s_1(t),s_2(t),...,s_n(t)]$, as in

$$x = As, \tag{1}$$

where A is some unknown matrix. ICA consists of estimating both the matrix A and the sources s, when we only observe x. ICA methods assume statistical independence between the sources, and use maximization of nongaussian components to separate the sources [9].

There are many methods available for ICA [9, 10], but in this work we applied two of the most successful: Joint approximate diagonalization of eigen-matrices (JADE) and the fast fixed-point algorithm (Fast-ICA).

D. Joint Approximate Diagonalization of Eigen-matrices (JADE)

The JADE algorithm was proposed by Cardoso and Souloumiac in [11] and is based on the joint orthogonalization of the cumulant tensors. The cumulant tensor is defined as a four-dimensional array whose entries are given by the fourth order cross-cumulants of the data as in:

$$Q_x = \left\{cum\left(x_i,x_j,x_k,x_l\right) \mid 1 \le i,j,k,l \le n\right\}. \tag{2}$$

The cumulant matrix $F_{ij}(M)$ associated to any n x n matrix M is defined as:

$$F_{ij}\left(M\right) = \sum_{kl} m_{kl} cum(x_i,x_j,x_k,x_l), \tag{3}$$

where m_{kl} are the elements of the matrix M. We work with the case that the data follows the ICA model with whitened data

$$x = VAs = W^T s, \tag{4}$$

where the whitened matrix is denoted by W^T. Eigenvalue decomposition (EVD) can be viewed as a diagonalization, then the JADE algorithm takes a set of matrices M_i, $i=1,...,m$, and tries to make the matrices $C=WF(M_i)W$ as diagonal as possible. The contrast function to measure the diagonality of the matrix C is:

$$\phi_{JADE}\left(W\right) = \sum_i \left\| diag\left(WF\left(M_i\right)W^T\right)\right\|^2 \tag{5}$$

After some manipulations [11], the contrast function can be expressed as:

$$\phi_{JADE}\left(W\right) = \sum_{i,j,k,l=1,..,n} \left|cum\left(y_i,y_j,y_k,y_l\right)\right|^2 \tag{6}$$

where $y_i=Wx_i$. Maximization of ϕ_{JADE} is one method of joint diagonalization of $F(M_i)$.

E. Fast Fixed-point Algorithm (Fast-ICA).

The Fast-ICA algorithm was developed by Hyvarinen and OJA in [12] and is based on the minimization of the gaussianity based on the *negentropy* concept. To define negentropy we have to use the concept of differential entropy, which is defined as:

$$S\left(p_x\right) = -\int p_x\left(u\right)\log p_x\left(u\right)du, \tag{7}$$

where S is the differential entropy of the random vector X with probability density function p_x. Then, the negentropy is defined as:

$$J\left(p_x\right) = S\left(\phi_x\right) - S\left(p_x\right), \tag{8}$$

where ϕ_x is the gaussian density with the same mean and variance as p_x. The Fast-ICA algorithm then uses a fixed point algorithm to maximize negentropy.

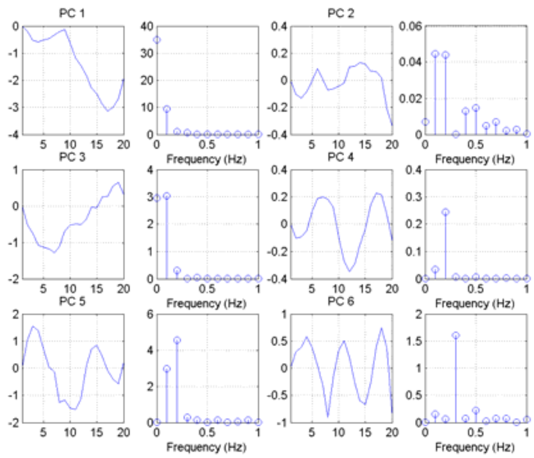

Fig. 3. First six principal components of a video with their correspondent power spectral density.

The algorithm then computes the demixing matrix W in an iterative fashion, computing one row at a time using

$$w_i\left(j+1\right)=E\left(y\left(w_i^T(j)y\right)^3\right)-3w_i\left(j\right), \tag{9}$$

where $w_i(j+1)$ is the i-th row for the (j+1)-th iteration and y is the whitened version of the data.

III. Results

A. Principal Component Analysis

After applying PCA to the data and backprojecting it to the time domain, we noticed that in many cases the components with the highest eigenvalues showed clear sinusoidal patterns. Figure 3 presents the first 6 principal components for an experiment with horizontal stimulus. It is clear how components 4, 5 and 6 have a sinusoidal shape, fact confirmed by its power spectral density (on the right next to the principal components).

B. Independent Component Analysis

Both the JADE and the Fast-ICA algorithms yielded similar results when applied to the data. Figure 4 shows the JADE separation of an experiment with a spot stimulus. It is clear how the stimulus is isolated in the sixth independent component (Fig. 4F).

Figure 5 shows the separation of six input sources as estimated by the Fast-ICA algorithm. This figure shows the stimulus bar applied to the cat retina in the third component (Fig. 5C). Figure 6 shows the JADE separation for the same experiment, here the stimulus bar is on component 1 (Fig. 6A). Comparing both figures we notice similar results for the detection of the stimulus, but the rest of the components are slightly different.

Not all the epochs showed the stimulation signal, in many cases due to changes in the settings of the experiments. From the seven different experiment settings performed, three did not present any response at all. These experiments corresponded to the cases where a background was added to the stimulus and when the LCD display was rotated. From the remaining experiments, in 65% (52 out of 80) of the cases the stimulus signal could be extracted.

IV. Discussion

The sinusoidal patterns seen in the principal components may be attributed to physiological processes. The analysis of the principal components with the ancillary data could lead to a better understanding of these processes. If the physiological processes are decorrelated from the images we may obtain clearer pictures of the nature of the response to the stimulus.

In figure 4 we can see how the JADE algorithm separates the stimulus input from other sources, as seen in the sixth component. Also notice how in the fifth component (Fig. 4E) there are a series of black and white stripes on the upper right corner of the images. These stripes do not correspond to any known physiological event, and are most likely to be caused by an illumination artifact.

From figure 5 a horizontal stripe is noticeable in component 3 that corresponds to the stimulus applied. Again as in the previous result, components 2, 3 and 4 (Fig. 4B, C and D) show the illumination artifact in the upper right corner of the images. In this case we only considered 6 inputs for the algorithm; this helped us to avoid redundancy in the separation of the signals. Although it is not completely known how many physiological processes are present during the stimulation of the eye, but our long-term objective is to identify as many as we can in order to isolate the response of the retina to the stimuli.

V. Conclusion

Retinal responses to the patterned stimuli could be identified and isolated by the ICA algorithms. Future research is oriented to the analysis of a large amount of data from cat and macaque experiments. Given that the cat retina is simpler than the human retina, it will give us useful information to better understand the phenomena present during stimulation of the human eye.

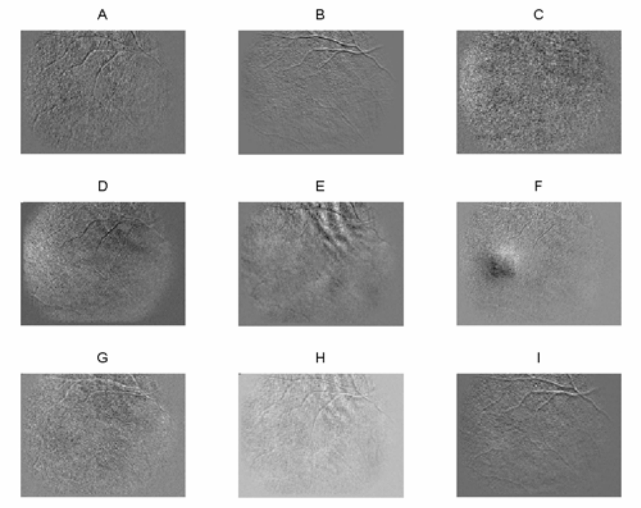

Fig. 4. Separation of the sources using the JADE algorithm.

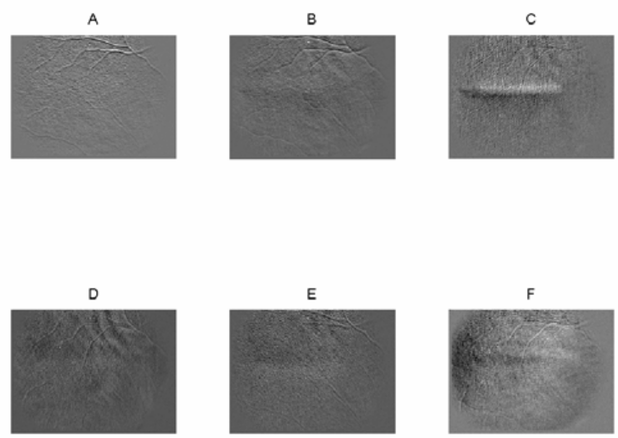

Fig. 5. Separation of sources using the Fast-ICA algorithm.

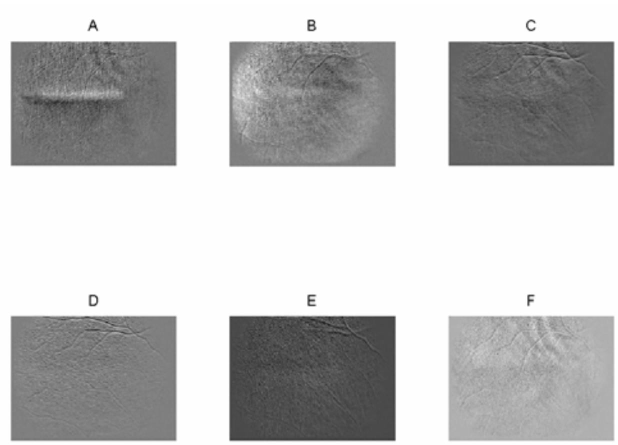

Fig. 6. Separation of sources using the JADE algorithm.

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