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Wavelet based electroretinographic signal analysis for diagnosis

Surya S. Nair*, K. Paul Joseph[1]

Electrical Engineering Department, National Institute of Technology, Calicut, Kerala 673601, India

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ABSTRACT

In this paper we have made a humble attempt to automate an ophthalmologic diagnostic system based on signal processing using wavelets. Electroretinographic signals indicate the activity of the retinal cells from different layers of the inner retina and therefore these signals are used to predict various dreadful diseases. In this work we have analyzed 95 subjects from four different classes viz. Controls, Congenital Stationery Night Blindness (CSNB), rod-cone dystrophy and Central Retinal Vein Occlusion (CRVO). The signal features extracted by wavelets are used for morphological and statistical analysis and for getting the subtle parameters like entropy. The results found comprises of difference in the values of wavelet coefficients, *a*-wave and *b*-wave amplitude in the case of normal and pathological signals. The colour intensity distribution of scalograms shows highlighting variations in the case of maximum response and oscillatory potentials of the ERG signals for specific type of diseases. Furthermore, we propose an Electroretinographic Index (ERI) from different entropy parameters which can be used to distinguish between the normal and abnormal classes. This new method based on ERG signal analysis can be reliable enough to build a solution for the constraints in the field of ophthalmology.

1. Introduction

All the physiological signals exhibit complex behaviour which reflects the non-deterministic and non-linear dynamics of a biological system. To be specific, the bio-signals can contain more information which is not visible to our naked eye. By using conventional tools, such hidden information cannot be extracted. For this reason, wavelets are used for obtaining the subtle parameters like entropy and are used in the context of non-linear signals for the analysis of biomedical time-series [1,2].

1.1. Electroretinogram

Electroretinogram is the time-varying potential that arises from the different layers of the retina. It is elicited by a brief flash of light which will produce a repeatable waveform. It is recorded clinically with a contact lens type electrode that carries a silver chloride wire. The electrode is in the shape of a cup, filled with saline and is placed on the cornea. The reference electrode can be placed either on the forehead, temple or earlobe. The amplitude of ERG depends upon the physiological and stimulating conditions, and it is in the range of tenths of a millivolt [3].

Each portion of the ERG waveform is contributed by different layers of the retina. Fig. 1 shows the cross-section of human retina along with the origin of signals from various retinal cells. A typical ERG signal comprises of R_1 and R_2 early receptor potential (ERP), *a*-wave (a_1 and a_2), oscillatory potentials, *b*-wave (cone *b*-wave and rod *b*-wave) and *c*-wave. The first and the primary portion of the signal are generated by the initial changes in the photo pigment molecules of the photoreceptor (cones and rods) due to the action of stimulus (flash). This gives rise to a positive R_1 deflection followed by R_2 deflection which comprises of ERP. It is then followed by a 2 ms delay, after which a late receptor potential (LRP) which forms the main constituent of the *a*-wave and is a corneo-negative waveform [3]. The *a*-wave forms two dips a_1 and a_2 which are attributed to the photoreceptor (cones and rods) contribution respectively. It lasts for about 30 ms [1,2]. By applying appropriate stimuli, these cones and rods can be separated. For instance, a dim blue light with the dark-adapted environment extracts a rod ERG, whereas a bright red light with a light-adapted environment will exhibit a cone ERG. The second wave which is corneo-positive is the *b*-wave. In the inner-retinal cells, there are Muller cells which contribute to the *b*-wave. The Muller cells have no synaptic link to the retinal cells. Now, the trans-membrane potential of these cells depends upon the extra-cellular changes of potassium, the release of which causes the activation of photo-receptors. Muller response can be either from cone or rod photo-receptors separately. The oscillatory potentials are small amplitude wavelets which occur in the light-adapted rising edge of the *b*-wave. They reflect the activity of inner retinal layers especially the amacrine cells. The *c*-wave is a slower

* Corresponding author. Tel.: +91 08891622925.
E-mail addresses: surbiomed@gmail.com (S.S. Nair), paul@nitc.ac.in (K. Paul Joseph).
[1] Tel.: +91 0495 2287233.

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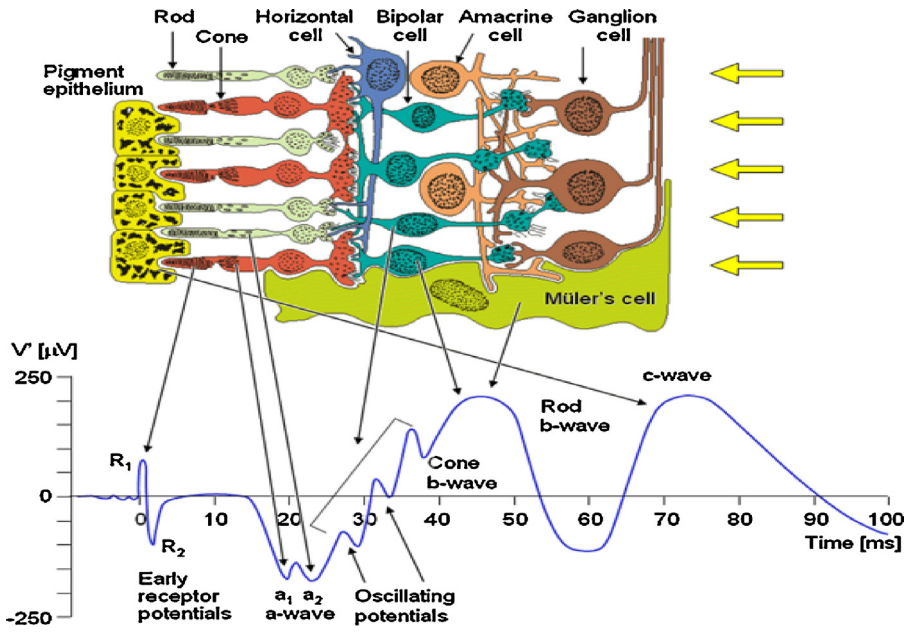

Fig. 1. The cells of retina and the standard ERG waveform.
Courtesy: Jaakko Malmimo and Robert Plonsey, 'Bioelectro-magnetism-Principles and Applications of Bioelectric and Biomagnetic fields'.

positive wave and is generated by the retinal pigment epithelium (RPE) as a result of interaction with the rod cells [3].

1.2. Steps for recording the ERG signal

According to the International Standards for Clinical Electrophysiology of Vision (ISCEV) [4], five commonly obtained responses are:

1.2.1. Rod response

The patient has to be dark-adapted for atleast 20 min. It is the first signal measured with the standard stimulus of dim white flash (2 s between the flash) of 2.5 log units or a blue stimulus [4].

1.2.2. Maximal response

It is the combined response of both cone and rod cells. It is produced by the white standard flash (10 s between the flash) [4].

1.2.3. Oscillatory potentials

It can be obtained either from dark-adapted eye (15 s between flash) or light-adapted eye (1.5 s between flash) using white standard flash. The frequency of interest is set by the band pass filter i.e. 75–100 Hz on the lower end and 300 Hz and above at the higher end [4].

1.2.4. Cone response

Patients should be light adapted for atleast 10 min before recording the cone response. The interval between the flash (white or bright-red) should be 0.5 s [4].

1.2.5. 30 Hz flicker responses

Flashes are presented at the rate of 30 stimuli per second. Rods will follow the flickering light up to 12–17 Hz and cones will follow up to 60–70 Hz [4].

The first remarkable work done by Bornschein et al. was the study of ERG in normal, colour-blind and night blind subjects under different status of adaptation of varying stimuli [20]. Another work was by Barraco et al. in which the results indicate the occurrence of three frequencies in the range 20–200 Hz [1]. They had also analyzed the time-frequency behaviour of the *a*-wave and concluded that there is an absence of the second dip in CSNB patients [2,12]. Garry et al. evaluated cone and cone-driven retinal function in patients with Smith–Lemli–Opitz Sydrome [18]. Tomasz Rogala and Andrzej Brykalski created a wavelet based feature space for the classification of Pattern ERG's. Principal Component Analysis were used to visualize both time-domain features and wavelet features and found that PERG waveforms are better separable in wavelet feature space than time-domain feature space [17].

In all the existing methods, they have analyzed either cone response or rod response of the ERG signal. In our proposed work we are dealing with all the five steps of the ERG signal and got the classification accuracy of 90.5%. To the best of our knowledge, no work is reported yet, attempting five steps in ERG analysis for the diagnosis of the ophthalmological diseases. In all the existing methods the authors have analyzed the *a*-wave of the ERG signal for the diagnosis of CSNB. But in our work, we have formulated an index to differentiate the classes and scalogram analysis is also performed to distinguish between the classes which have more reliability over the existing methods.

2. Materials and methods

Digital data is collected using the machine TOMEY EP 1000 version 3.0.4 from 95 patients with their consent. These patients under the study were those suffering from Congenital Stationery Night Blindness (CSNB), Cone Rod Dystrophy (CRD) and Central Retinal Vein Occlusion (CRVO). Rod response, Cone response, Maximal response, Oscillatory potentials and Flicker response were recorded from the above subjects and the same set of responses were obtained from normal Control subjects. In this work, we have collected the data from four different classes: 30 Controls, 20 CSNB, 30 CRD and 15 CRVO. Proper informed consent was obtained from both the clinicians and the staffs of Little Flower Hospital and Research Centre, Angamaly, India before collecting the data for this study.

The data collected are analyzed by wavelets and several subtle features are extracted. The details regarding the clinical situation and the brief description about the parameters are given below: