**Krzysztof PENKALA, Tomasz ROGALA, Andrzej BRYKALSKI**
SZCZECIN UNIVERSITY OF TECHNOLOGY, INSTITUTE OF ELECTRONICS, TELECOMMUNICATIONS AND COMPUTER SCIENCE

# Selected Methods of the Pattern Electroretinogram Signal Analysis

**Ph.D. Krzysztof PENKALA**

Graduated from the Faculty of Electrical Engineering, Poznań University of Technology (1972, speciality: Control Engineering). In 1972 – 1976 he was at the Academy of Medicine in Poznań. Since 1976 he has been at the Szczecin University of Technology. He obtained his Ph.D. at the Faculty of Electrical Engineering in 1984. His research and education activities are within the area of Biomedical Engineering, in particular: visual system testing, electrophysiology of vision, modeling retinal structures as well as analysis of bioelectric visual signals.

*e-mail: Krzysztof.Penkala@ps.pl*

**Prof. Andrzej BRYKALSKI**

Graduated from the Faculty of Electrical Engineering, Szczecin University of Technology, (1979, speciality: automatic control engineering and electric metrology). He received Ph.D. in electrical engineering (1983), D.Sc. degree (habilitation) in electrical engineering (1991). From the beginning of his professional career he has been engaged in research on computer analysis of eddy-current problems, screening of electromagnetic fields, diffusion processes, chosen acoustic problems and recently on processing of biomedical signals.

*e-mail: Andrzej.Brykalski@ps.pl*

**Ph.D. Tomasz ROGALA**

Graduated from the Faculty of Electrical Engineering, Szczecin University of Technology (2002, speciality: electronics and telecommunication). Obtained Ph.D. degree in Electrical Engineering from the Szczecin University of Technology in 2005. His thesis was describing analysis and processing of bioelectrical signals originating in human visual system. He is also interested in the field of electromagnetic tomography. His papers were published in Pattern analysis and Applications and Compel journals.

*e-mail: Tomasz.Rogala@ps.pl*

**Abstract**

In the paper a short review of methods applied for pattern electroretinogram signal analysis is presented. Various possible alternatives for classical method used in medical practice are described. The capabilities and disadvantages of each method as well as relevant results are briefly presented and/or references are cited. The described algorithms are: statistical regression analysis, continuous wavelet transform, discrete wavelet transform, artificial neural networks, principal components analysis and independent component analysis. The aim of the paper is to give a short review of previously taken activity in the field of pattern electroretinogram analysis particularly for diagnostic purposes, and present a guide for possible approaches to be applied for other bioelectrical signals.

**Keywords**: signal analysis, pattern electroretinogram, PERG, statistical analysis, continuous wavelet transform, discrete wavelet transform, artificial neural networks, principal components analysis, independent component analysis.

## Wybrane metody analizy sygnału Elektroretinogramu wywołanego wzorcem

**Streszczenie**

W artykule przedstawiono przegląd metod zastosowanych do analizy sygnału elektroretinogramu wywołanego wzorcem. Zaprezentowano szereg możliwych technik alternatywnych w stosunku do procedur używanych w praktyce klinicznej. Przedyskutowano zalety i ograniczenia każdego z algorytmów, przedstawiając pokrótce wyniki doświadczeń lub cytując odpowiednie pozycje literatury. Opisane algorytmy to: statystyczna analiza regresji, ciągła i dyskretna transformata falkowa, sztuczne sieci neuronowe, analiza składowych głównych (PCA) oraz analiza składowych niezależnych (ICA). Celem niniejszego artykuły jest usystematyzowanie wcześniejszych działań autorów w dziedzinie analizy elektroretinogramu wywołanego wzorcem, w szczególności dla potrzeb diagnostyki, oraz zaproponowanie metodologii badań sygnałów bioelektrycznych o podobnym charakterze.

**Słowa kluczowe**: analiza sygnałów, elektroretinogram wywołany wzorcem, PERG, analiza statystyczna, ciągła transformata falkowa, dyskretna transformata falkowa, sztuczne sieci neuronowe, analiza składowych głównych, analiza składowych niezależnych.

## 1. Introduction

When the eye is stimulated with an alternating black and white checkerboard (with constant total luminance), a specific bioelectric signal, the so-called pattern electroretinogram (PERG) is recorded from the human retina with a corneal contact electrode. PERG signal originates in the retinal ganglion cells as well as neighboring inner retinal structures. Particular waves reflect the electrical activity of different neural structures involved in visual information processing and are used in assessment of their function [7]. According to the ISCEV (International Society for Clinical Electrophysiology of Vision) standards [4] clinical evaluation of the PERG recordings is based on measurement of implicit times and amplitudes of particular waves (Fig. 1). However, in many cases it is difficult to localize the peaks precisely, so the method of analyzing the PERG parameters in time domain is inaccurate. This disadvantage affects reliability of this very important and valuable electrophysiological test. The aim of our studies was to demonstrate the possibility of finding features of the PERG signal reliable for distinguishing between normal and abnormal cases with better accuracy. In the paper a review is presented of the methods applied by the authors for PERG analysis – mainly for diagnostic purposes.

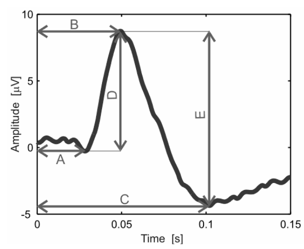


Fig. 1. Parameters of the of the PERG waveform components
Rys. 1. Parametry składowych morfologicznych przebiegu PERG

## 2. Overview of methods

The methods applied for PERG signal analysis can be divided into three groups, with respect to the purpose of calculations. The first group contains techniques used to increase the accuracy of determination of PERG signal parameters. However, the evaluation of the waveform is still performed according to traditional ISCEV recommendations. Second group consists of methods allowing reduction of dimensionality. They may act as preprocessor for classification algorithms. Third group performs automatic classification of PERGs, using their own calculated criteria, which are not human readable. Methods applied by the authors for PERG signal analysis are shown in Fig. 2 and their description is summarized in Tab. 1.

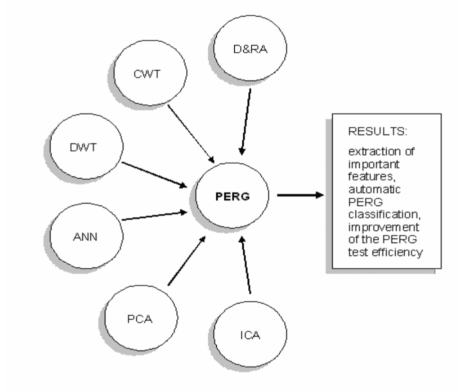


Fig. 2. Diagram showing methods applied for the PERG signal analysis
Rys. 2. Schematyczne przedstawienie metod zastosowanych do analizy sygnału PERG

Tab. 1. Summary of methods applied for PERG signal analysis
Tab. 1. Zestawienie zastosowanych metod analizy sygnału PERG

| Abbrev. | Name | Description | Ref. |
|---|---|---|---|
| D&RA | Discriminant functions and regression analysis (statistical methods) | Classification algorithm allowing finding linear or quadratic functions capable of distinguishing between two classes of learning samples. Requires assumption on normal distribution of features. Results in obtaining reduced set of diagnostically important parameters | [3, 6, 8, 10, 12, 16] |
| CWT | Continuous Wavelet Transform | Improvement of accuracy of implicit times and amplitudes measurement of the waveform in CWT coefficients domain | [8, 9, 11, 13] |
| DWT | Discrete Wavelet Transform | Pre-processor for various classifiers. Used for signal denoising as well as for dimensionality reduction of input data (lossy compression). Improves the performance of classification algorithm by increasing the ratio of learning samples number to their dimension | [13, 15] |
| ANN | Artificial Neural Networks | Well-known classification algorithm. Used for distinction between normal and abnormal recordings. Results in better (than traditional method) classification rate, but acts like a "black box". | [2, 3, 13, 15] |
| PCA | Principal Component Analysis | Used for dimensionality reduction of the input data. Can be used as a preprocessor for a classification algorithm, or as a method of 2-D visualization of multidimensional data. | [2, 14] |
| ICA | Independent Component Analysis | Used for signal denoising and recovery of proper PERG shape | [1, 5] |

## 3. Discriminant functions and regression analysis, Bayesian classifiers

These methods are relatively simple (compared to other approaches listed in table 1), since they are based on statistical concepts. They are well known to medical staff and this approach would be probably the easiest - of proposed procedures - to introduce in clinical practice.

Statistical methods: discriminant analysis, regression analysis were used by the authors for distinguishing between normal and abnormal PERGs and obtained results (mathematical models and their optimization using Fisher *F(n1,n2)* test, classification algorithms, their preliminary clinical evaluation) were presented in several papers [e.g. 8, 10].

In opposition to "peak-based" approach another promising way of PERG description based on wavelet compression by Discrete Wavelet Transform was proposed [15]. Recently statistical pattern recognition methods [2] were also used for the PERG signals. In this study [16] Bayesian classification was applied for supervised learning. Two types of feature sets were compared: features of PERG waveform in time domain and in DWT domain, and efficiency of both approaches was assessed. Surprisingly, the conventional approach produced higher efficiency. The influence of patient age was also examined and separate models for two age categories were applied. It occurred that the age factor might be ignored for analyzed data.

Statistical analysis was also used by the authors [12] in order to evaluate the efficiency of interpretation of PERG recordings in the domain of Continuous Wavelet Transform coefficients, as compared with the previously obtained results in time domain.

The results of statistical analysis of PERG signals in time domain as well as in the CWT/DWT coefficients domain revealed that efficient distinguishing between normal and abnormal waveforms is dependent only on the values of reduced set of parameters. These results also showed the possibility of creating classification algorithms based on simple mathematical models. Classification of the PERG waveforms based on statistical methods was found useful in preliminary interpretation of the recordings as well as in supporting clinical decision-making in "borderline" cases, for more accurate assessment of clinical data [8, 10].

## 4. Wavelet transform

The Continuous Wavelet Transform (CWT) is defined as follows:

$$CWT_f(\tau,s) = \left\langle f(t), \psi_{\tau,s}(t) \right\rangle = \frac{1}{\sqrt{|s|}} \int_{-\infty}^{\infty} f(t)\psi(\frac{t-\tau}{s})dt\,,$$

where the function $\Psi$ is a shifted and scaled version of a "mother" wavelet function:

$$\psi_{s,\tau}(t) = \frac{1}{\sqrt{s}}\psi\left(\frac{t-\tau}{s}\right),$$

$s$ and $t$ are the "scale" and time, which create the domain of CWT operation. The result is a set of coefficients having two parameters: scale (often interpreted as an inverse of frequency) and time. They may be plotted as a two argument function in three-dimensional Cartesian coordinate system. In Fig. 3 example of the PERG recording and its CWT representation are shown.

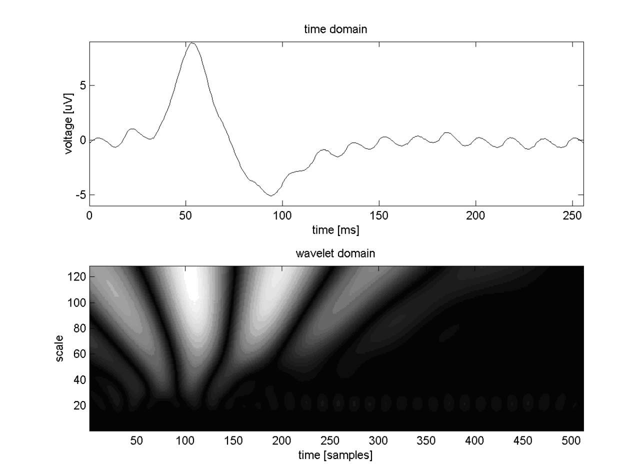


Fig. 3. PERG waveform in CWT domain
Rys. 3. Przebieg PERG w dziedzinie współczynników falkowych

Distribution of implicit times of the PERG characteristic waves (denoted as P50 and N95, according to their polarity and peak time in milliseconds) shows that in certain cases characteristic features of abnormal recordings lie in the same range that normal waveforms' features (Fig. 4). The difference between normal and pathological values is often very small. The purpose of our first investigation [11] was to find features in time-frequency domain, which are more reliable for distinguishing the cases. In this study, 15 normal PERG waveforms and 7 recordings obtained in some precisely diagnosed retinal diseases were chosen. The recordings were obtained with the LKC UTAS-E 2000 (USA) system. In the abnormal PERGs, P50-wave implicit time was increased (in 4 recordings) as well as N95-wave implicit time (in 3 recordings).

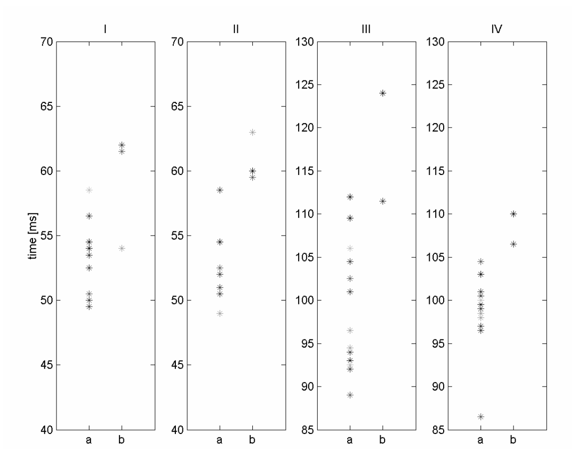


Fig. 4. Comparison of P50-wave and N95-wave implicit times: a – normal, b – abnormal waveforms; I – P50 (time method), II – P50 (time-scale method), III – N95 (time method), IV – N95 (time-scale method); some points overlap: group b should have 4 points (I, II) and 3 points (III, IV); Mexican Hat was used as a mother wavelet function

Rys. 4. Porównanie czasów pików P50 i N95 dla przebiegów: a – prawidłowych, b – nieprawidłowych; I – P50 (pomiar w dziedzinie czasu), II – P50 (pomiar w dziedzinie czas-skala), III – N95 (pomiar w dziedzinie czasu), IV – N95 (pomiar w dziedzinie czas-skala); część punktów nakłada się na siebie: grupa b powinna liczyć 4 punkty (I, II) i 3 punkty (III, IV); zastosowano falkę Mexican Hat

Further steps of CWT analysis were performed with a new set of PERG data obtained in the Department and Clinic of Ophthalmology in Szczecin with the RetiPort/RetiScan system (Roland Consult, Germany) in 60 eyes of healthy subjects, in 2 age groups [8, 9]. Better "consistency" of normal values obtained with the CWT method was obtained, especially for the N95-wave implicit time. This is a very important result because traditional measurements of the N95-wave latency are difficult and often lead to significant errors.

More recently, in our unpublished research (paper in preparation) it was shown that also amplitude parameters can be determined with better accuracy after performing CWT analysis of the PERG signal. This improvement is observed as significantly smaller standard deviation values of the parameters as compared to the values obtained in traditional way, i.e. measurements with cursors placed on the peaks of a particular recorded waveform. As a consequence, control normal values for this important test show much less scatter and reliability of the PERG examinations can be improved.

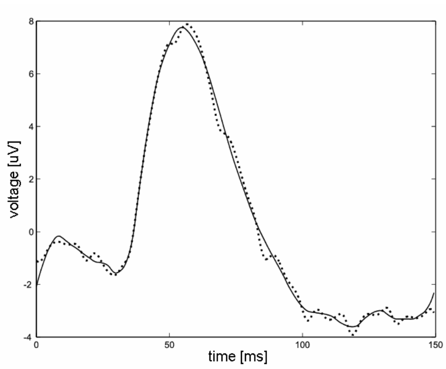


Fig. 5. PERG waveform (solid line) restored from its 16 wavelet coefficients (dotted line)

Rys. 5. Przebieg PERG (linia ciągła) odtworzony z jego 16 współczynników DWT (linia punktowa)

A Discrete Wavelet Transform (DWT) is computed when the values of time and scale are shifted in discrete steps. Such an operation can be also described as signal decomposition using a set of lowpass and highpass filters. The filter coefficients depend on the chosen wavelet function. DWT can be then treated as a lossy compression of signal and method of its dimensionality reduction [15]. In described case it allowed representing the 256 samples of time waveform as 16 DWT coefficients (Fig. 5). Therefore, from pattern classification point of view, the dimension of the feature vector was reduced sixteen times. The procedure of choosing the transform parameters and coefficients rejection procedure was described in [15].

## 5. PCA and ICA

Principal Components Analysis (PCA) is a method of simplifying a data set, by reducing multidimensional data sets to lower dimensions for analysis. The operation is an orthogonal linear transformation that transforms the data to a new coordinate system such that the greatest variance by any projection of the data comes to lie on the first coordinate (called the first principal component). The first principal component accounts for as much of the variability in the data as possible, and each succeeding component accounts for as much of the remaining variability as possible.

Nonlinear PCA (NLPCA) can be seen as a nonlinear generalization of standard principal component analysis (PCA) that generalizes the principal components from straight lines to curves. This can be done by using neural networks with autoassociative architecture, such as multilayer perceptrons that perform an identity mapping [3]. The middle layer of the MLP network acts a bottleneck, reducing the dimension of the data. It provides desired components which can be nonlinear.

Such a technique was used by authors to present multidimensional PERG data in 2-D Euclidean space [14]. This was done in order to increase the separability of the learning patterns. Exemplary results are presented in Fig. 6. However, the method has an important disadvantage. It is not repeatable, because each time different network coefficients are obtained.

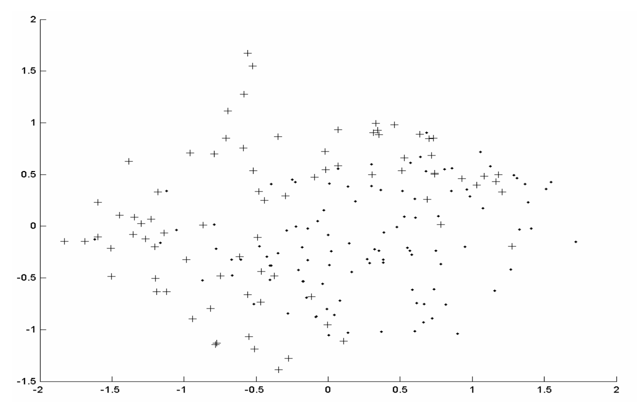

Fig. 6. Nonlinear PCA used for graphical presentation of six-dimensional feature space (crosses denote correct waveforms, points – incorrect ones)

Rys. 6. Nieliniowa PCA wykorzystana do przedstawienia sześciowymiarowej przestrzeni cech na płaszczyźnie (krzyżyki oznaczają zapisy nieprawidłowe, punkty – prawidłowe)

When the frequency range of a given signal overlaps with noise and electrical activity of other organs, the method of Independent Component Analysis (ICA) proposed by Comon [1] may be effective. ICA is based on the assumption that the electrical activity from a given bio-source and the artifacts are physically, anatomically and physiologically independent processes. This separation is reflected in statistical independence between the different source signals (independent components) contributing to a linear mixture of signals recorded in particular experimental conditions.

In our preliminary simulation experiments with the ICA technique application to the PERG signal analysis, the FastICA algorithm for MatLab developed by Hyvaerinen and Oja [5] was used. In this algorithm negentropy (negative entropy) as a measure of the quantity of mutual information shared by the components is applied and maximizing negentropy (minimizing the mutual information) in iterative process is the goal of computations.

The original sample PERG signal was mixed with the line noise, generated by the computer (Fig. 7). The resultant waveforms with two different S/N ratios are also shown in this figure. After ICA processing, the two components were separated with quite good quality.

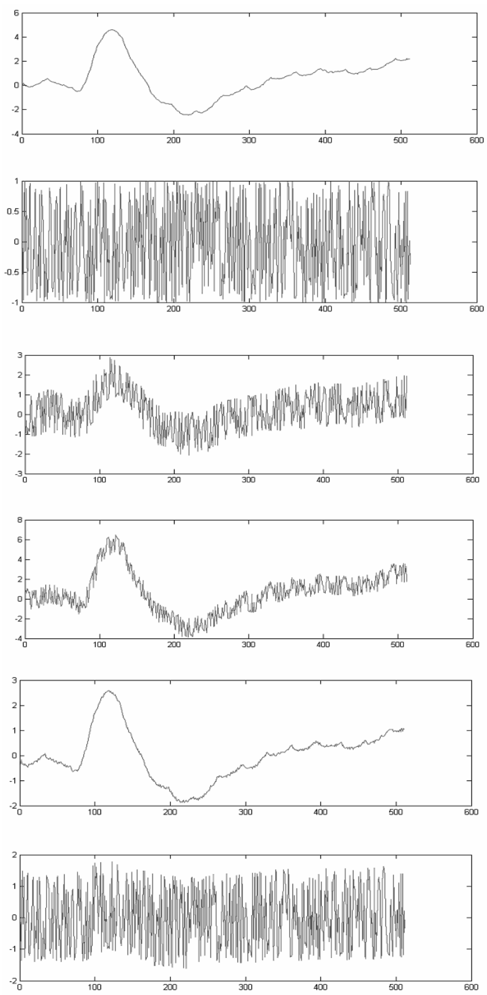

Fig. 7. Original PERG signal and a computer simulation of the 50 Hz noise (two upper figures), two mixtures of PERG and noise (in the middle) and FastICA separation of both waveforms (two lower figures). Numbers of samples on the abscissa, voltage (μV) on the ordinate

Rys. 7. Oryginalny sygnał PERG i komputerowo symulowany szum 50 Hz (u góry), przebiegi zsumowane (środek) oraz sygnały odseparowane przy użyciu FastICA (u dołu). Na osi odciętych – numery próbek, na osi rzędnych – napięcie (μV)

## 6. Neural networks

According to [2] classification has two distinct meanings: there may be given a set of observations with the aim of establishing the existence of classes or clusters in the data, or the number of classes may be known in advance, and the aim is to establish a rule which classifies a new observation into one of the existing classes. The former type is known as unsupervised learning (or clustering), the latter as supervised learning. Therefore, the evaluation of a PERG recording can be treated as a supervised classification task. Among large number of supervised pattern recognition algorithms [3], artificial neural networks (ANN) have enjoyed significant attention, and various network architectures and learning algorithms have been developed for different applications. Currently, the authors are investigating the usefulness of various ANN types and architectures for the PERG signal classification. Preliminary results were described in [15], with focus on proper pre-processing using DWT.

## 7. Conclusions

In the paper the application of different signal processing and classification algorithms for the PERG signal analysis were described. The choice of method is strictly dependent on desired goal. The signals may be de-noised, presented graphically in 2-D space and finally manually and/or automatically classified. Signal processing algorithms may have several primary applications. First, improvement of detection of the PERG components. Second, increase in accuracy of measurement of the most important PERG parameters. And third, they may be aimed at increasing simplicity and/or speed of the test.

As far as the usefulness of chosen methods in medical practice is concerned, one should keep in mind that the main goal is more accurate assessment of clinical data with this electrophysiological test and, as a consequence, improvement of diagnosis.

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