LCC - RE1-994
DOI: 10.6084/m9.figshare.5230330

DEVELOPMENT OF MATHEMATICAL MODELS AND METHODS ANALYSIS OF ELECTRORETINOSIGNAL

Mykola Hvostivskyy

Ternopil Ivan Puluj National Technical University

Address for Correspondence: Mykola Hvostivskyy, PhD.

Institutional affiliation: Ternopil Ivan Puluj National Technical University, Ternopil, Ukraine

E-mail: hvostivskyy@ukr.net

Abstract. A new application of periodically correlated stochastic process as an electroretinosignal mathematical model which in its structure takes into account a combination of periodicity and stochastic properties is justified. The human eye retina electroretinosignal analysis methods in ophtalmodiagnostic systems on a valid model basis have been developed, using a formalized and automated procedure that allows the human eye retina at an early diseases stage evaluation with increased reliability.

Keywords: electroretinosignal; macromechanism of generation; periodicity; impulse periodically correlated random process; methods analysis; spectral components; certanty.

Introduction. Visual analyzer takes the main place among the human body sensors, providing about 85% of the environment information perception. The global computerization, poor environment and inactive lifestyle are the factors that cause a negative effect on its condition. Therefore, an important modern medicine objective not only in Ukraine but also worldwide is eye diseases early diagnosis and prevention.

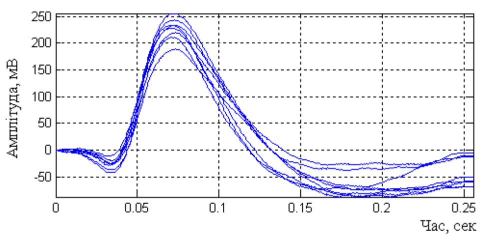
On the visual system electroretinosignal (ERS), which is a human retina response on the light flash, diagnosis urgency pointed out the authors of many medical direction works (Shamshynova A., Volkov V., Bogoslavskyy A., Byzov A., Zislyna N, Mironov E, Karpe G., Henkes H., Kato M. and other). It was established that regular retina diagnostics by ERS enables to detect early functional changes in it and promptly carry out preventive measures for rehabilitation, and in the case of pathological disorders prevent disease appropriate treatment.

The preventive and therapeutic interventions choice effectiveness depends on the ophtalmodiagnostic system proper use which should be based on adequate mathematical models and enable automated accurately and reliably determine the lesion location and track the disease dynamics.

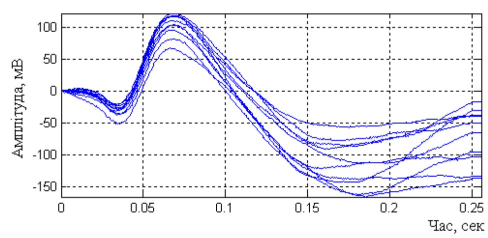
Except deterministic interpretation (Yavorskyy B., Yuzkiv A. [1]), it is known a number of papers Matsyuk O. [2], Tkachuk R. [3,4], Palamar M. [5,6], Rilk A. [7] devoted to ERS stochastic models (linear stochastic process and additive mixture of deterministic and stochastic components). However, these models in their statistical structure do not take into account interconnectedness between the same series observations different responses that is important for the ERS structure phase changes research for the purpose of retina functioning changes early manifestations detection.

Objective. These arguments which point on the ERS mathematical model improvement urgency and analysis methods development for the automated computer ophtalmodiagnostic systems are oriented on the human retina functional state early diagnosis reliability improvement by introducing to ophthalmology a new reliable informative signs class based on a rhythm model as a periodically correlated impulse stochastic process.

Materials and Methods. Figure 1 shows the experimental retina ERS from patients in normal and with pathology (central retina degeneration) registered by "ДСЗО-1" system (Ukraine developers - Tkachuk R., Palamar M., Matsyuk O.).



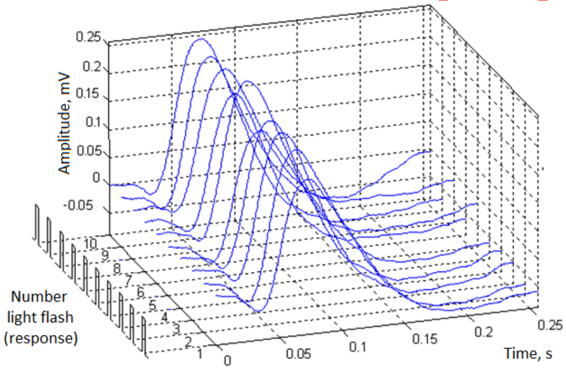
(patient A in normal)



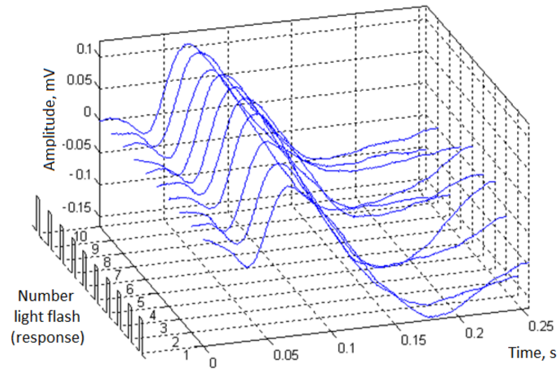
(patient B with pathology)

Fig.1

10 ERS responses simultaneously decomposed according to the flash order were used for the mathematical model grounding, (Fig. 2).



(patient A in normal)

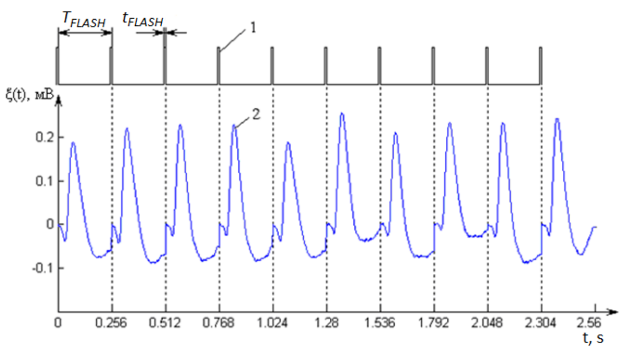


(patient B with pathology)

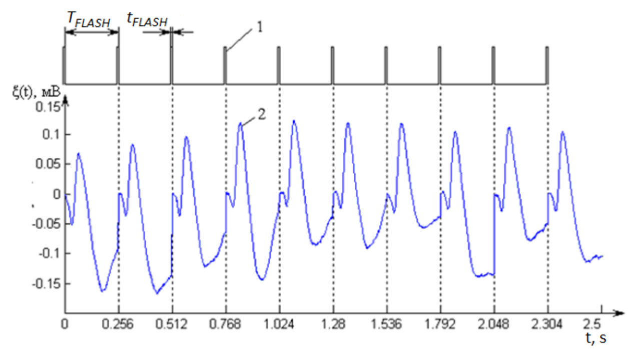
Fig. 2

According to the signal registration methodology ERS is the same eye retina response to the light flashes series which in its structure combines periodicity and stochastic properties, so these ERS responses are depicted on the same time axe as an ensemble that makes it possible to see the retina response time changes dependence from flash to flash.

Figure 3 illustrates ERS at the same time axe depending on the light flashes, where 1 - curve shows the light flash time moment (according to the conditions of the ERS registration, flashes are generated periodically), 2 – shows that the light flash periodicity ensure the signal generation phases uniformity in the time interval equal to the fixed flash period.



(patient A in normal)



(patient B with pathology)

Fig. 3

As the light flashes are periodical with a specified period T_{FLASH} and durations (t_{FLASH}), therefore retinal response (reaction to a flash) also contains periodicity with the same period T_{FLASH}.

Taking into consideration such a macro-mechanism formation, ERS is presented as a set of responses, shifted in time relative to each other for a constant period $T = T_{FLASH}$ as:

$$\xi(t) = \sum_{k \in Z} \chi_{D_k}(t) \cdot \xi_{\text{response}_k}(t - kT), \quad t \in R, \tag{1}$$

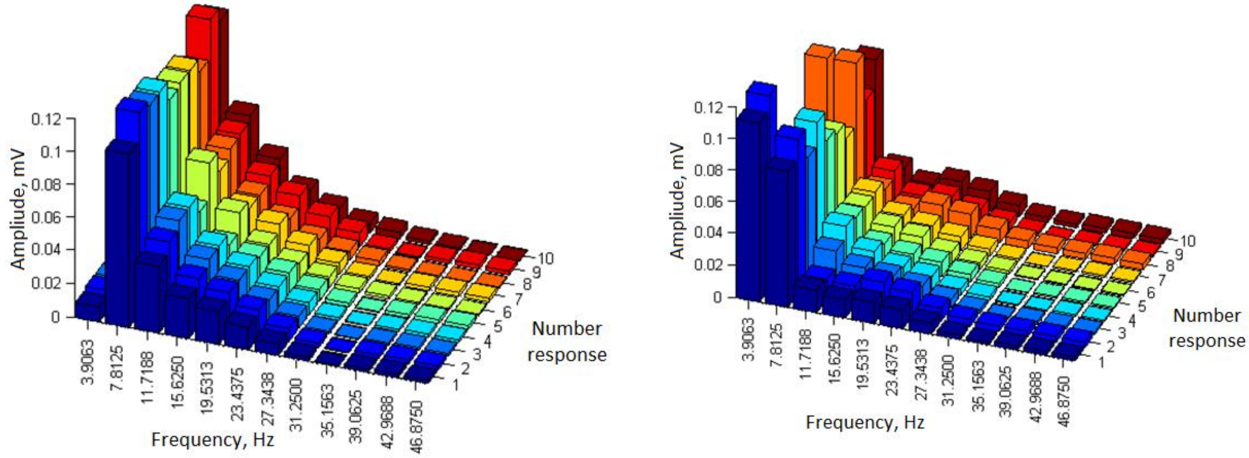
where $\chi_{D_k}(t) = \begin{cases} 1, \ if \ t \in D_k \\ 0, \ if \ \notin D_k \end{cases}$ - D_k set indicator function;

$D_k = [kT, (k+1)T)$ - time range of the k response $\xi_{\text{response}_k}(t), t \in [0, T)$ duration;

T - certain ERS response duration.

The ERS ensemble representation as its periodic continuation takes into account in its structure the combination of the periodical and stochastic properties, and thus enables to consider the statistical relationships between the various retinal reactions of the same observations series, which is impossible in the case of the traditional representation the same type reactions series as an realizations ensemble.

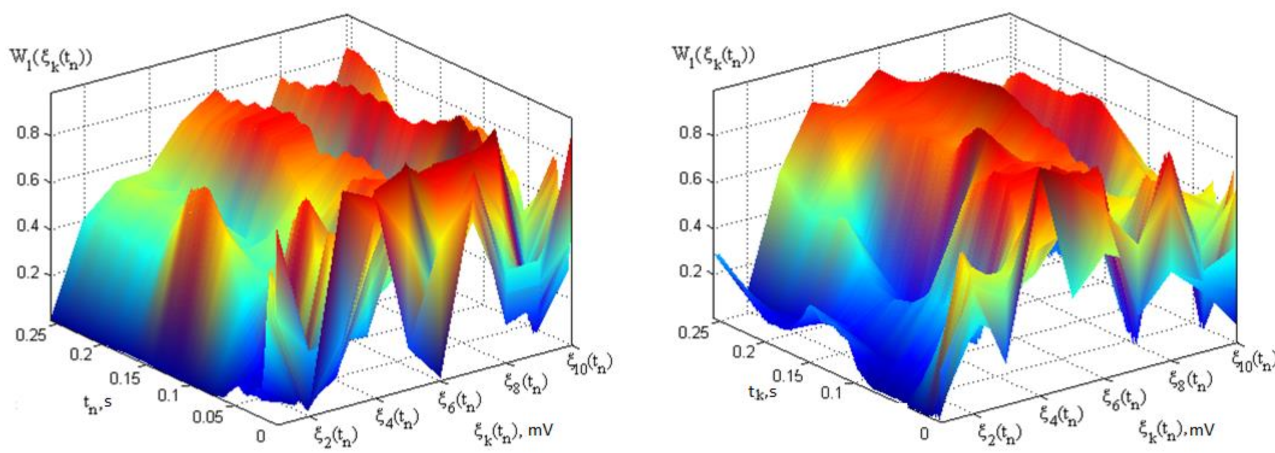
The results of the ERS analysis by harmonic analysis methods within the deterministic approach confirmed that the obtained ERS responses amplitude spectrum (Fig.4) are variable, which indicates the stochastic component presence in the signal.



(patient A in normal) (patient B with pathology)

Fig. 4

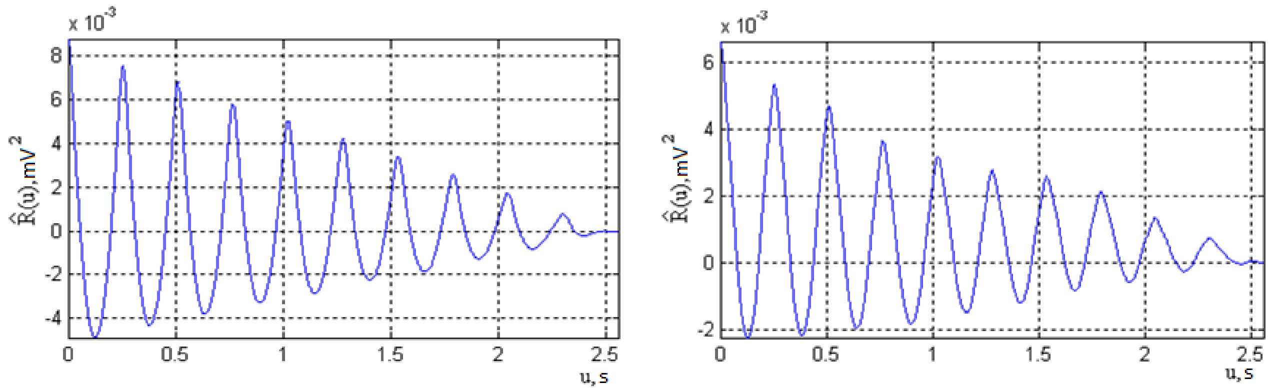
Considering the signal within the stationary model approach, it was noted that the density distribution functions (Fig. 5) change in time,



(patient A in normal) (patient B with pathology)

Fig. 5

and the ERS correlation function as a continuous implementation is periodic in time t and cyclically-damped by displacement u (Fig.6).



(patient A in normal) (patient B with pathology)

Fig.6

It is obvious that the adequate ERS model must possess the properties of stochastic, harmonic and periodic of its statistical characteristics. The stochastic stationary model reflects the ERS complexity in the spectral power distribution, but does not reflect its phase-time structure, which is an important indicator of the signal phase-time changes. In the energy theory terms, these requirements are met by a model as a periodically correlated stochastic process, which has means to account both the harmonic components coupling and the probability characteristics changes.

Periodically correlated stochastic process (PCSP) π^T [8] class – is a process which correlation function satisfies the conditions $r_\xi(t+T, s+T) = r_\xi(t,s)$, $T>0$ for all t, $s \in \mathbf{R}$ and $M_t(r(t,t)) < \infty$.

Considering the eye responses after each flash as PCSP implementation, in the time intervals $[kT,(k+1)T)$ the set of it may be interpreted as PCSP representation through translational components as:

$$\xi(t) = \sum_{p\in Z}\sum_{k\in N} \alpha_k(p)\Phi_k(t-pT), \qquad (2)$$

where $\alpha(p) = [\alpha_k(p)]_{k\in N}, p \in Z$ – a vector stationary sequence;

$\{\Phi_p(t), p \in N, t \in [pT,(p+1)T)\}$ – a translational functional space $L^2(0,T)$ basis;

$\{\alpha(n), n \in \mathbf{Z}\}$ – a sequence of translational stationary components.

An expression (2) is adequate to the pulse signal formats and is efficient in ERS modeling as pulse PCSP. But based on the PCSP representations through translational components (2) and through the stationary components equivalences:

$$\xi(t) = \sum_{k\in\mathbf{Z}} \xi_k(t) e^{ik\frac{2\pi}{T}t}, t \in \mathbf{R}, \qquad (3)$$

where $\xi_k(t)$ – the ERS stationary components as the PCSP,

$\mathbf{Z}$ - the set of integers,

such representations are advisable to treat as the implementations of the last named one, which justify the applicability of the known statistical processing methods (synphase, component) to them for their statistical estimates and probabilistic characteristics that are the human retina state indicators calculating.

The synphase method is based on the fact that the ERS samples value through the correlation period for different starting point (initial phase) $t_0 \in [0,T)$ form a stationary ergodic vector stochastic sequence $\{\xi(t_0), t_0 \in [0,T)\}$, where $\xi(t_0) \equiv \{\xi(t_0 + kT), k \in Z\}$. On this method basis the ERS characteristics (covariance components $\hat{b}_\xi(t,u)$), which make it possible to estimate the signal temporal variability are obtained used the expression:

$$\hat{b}_\xi(t,u) = \frac{1}{N}\sum_{k=0}^{N} \overset{0}{\xi}(t+u+kT)\overset{0}{\xi}(t+kT), \qquad (4)$$

where $\overset{0}{\xi}(t) = \xi(t) - \hat{m}(t)$ - centered ERS $\xi(t)$.

Component method assumes that ERS characteristics are periodic functions of time so are represented using Fourier series type expansions:

$$\hat{b}_\xi(t,u) = \sum_{k \in Z} \hat{B}_k(u)\exp\left(ik\frac{2\pi}{T}t\right), \qquad (5)$$

where $\hat{B}_k(u)$ – the spectral components estimates that quantitatively characterize the ERS phase-time structure:

$$\hat{B}_k(u) = \frac{1}{T}\int_0^T \hat{b}_\xi(t,u)\exp\left(-ik\frac{2\pi}{T}t\right)dt, \; k \in Z. \qquad (6)$$

It is founded that the synphase analysis method has two realization ways, in particular: to take into account and not to take into account the components cross-correlation relationships, which made it possible to develop this method. The ERS spectral components estimates as a periodically correlated stochastic discrete sequences obtained by the synphase method considering the cross-correlation relationships are obtained by the expression:

$$\hat{B}_k(u) = \frac{1}{N_T}\sum_{n=0}^{N_T-1} \hat{b}_\xi(n\Delta t, u)\exp\left(-ik\frac{2\pi}{N_T}n\right), \qquad (7)$$

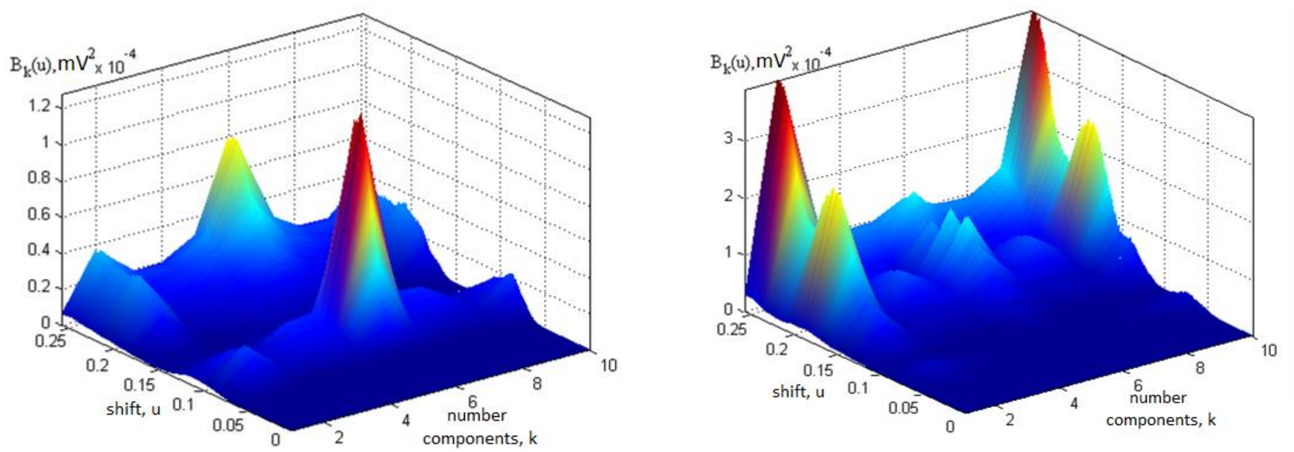
where N_T – ERS discrete correlation period, $N_T = T \cdot \Delta t$, u – shift, Δt – sampling step, $\hat{b}_{\xi}(n\Delta t, u) = \frac{1}{N} \sum_{k1=0}^{N_K-1} \overset{0}{\xi}(n\Delta t + u + k1N_T)\overset{0}{\xi}(n\Delta t + k1N_T)$ – the covariance components estimate, where N_k – a number of ERS responses.

The ERS spectral components estimates obtained by the synphase method not taking into account the cross-correlation relationships are obtained by the expression:

$$\hat{B}_k(n\Delta t) = \frac{1}{N_u} \sum_{u=0}^{N_u} \hat{b}_{\xi}(n\Delta t, u) \exp\left(-ik\frac{2\pi}{N_T}u\right), \qquad (8)$$

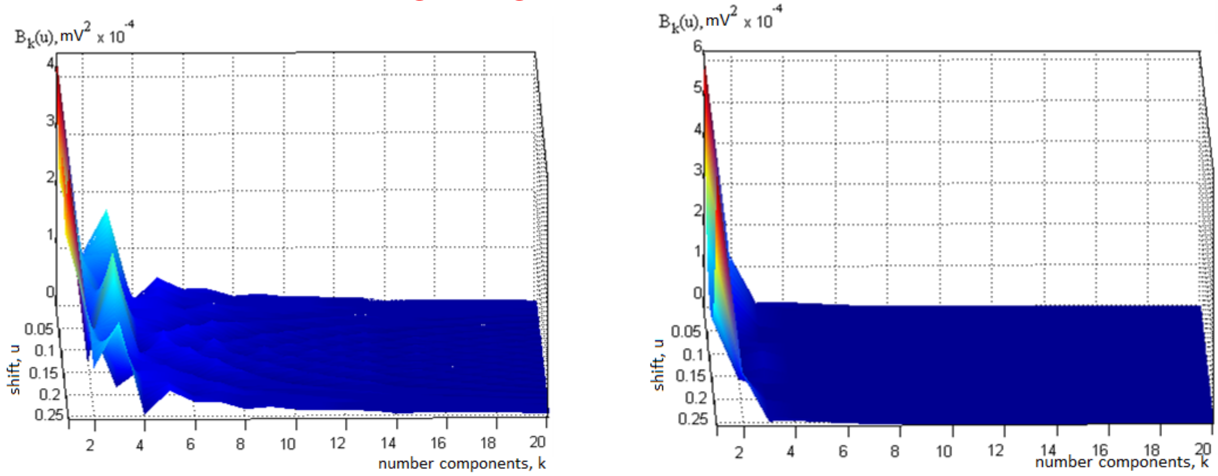
where $\hat{b}_{\xi}(n\Delta t, u) = \frac{1}{N_k} \sum_{k1=0}^{N_k-1} \overset{\circ}{\xi}(n\Delta t + k1 \cdot N_T \cdot \Delta t)\overset{\circ}{\xi}(n \cdot \Delta t + (k1+u) \cdot N_T \cdot \Delta t)$ – covariance component estimates, N_u - shift length.

Results. Taking into account the synphase and component analysis methods expressions (6-8), the obtained results are shown in Fig. 7-9.



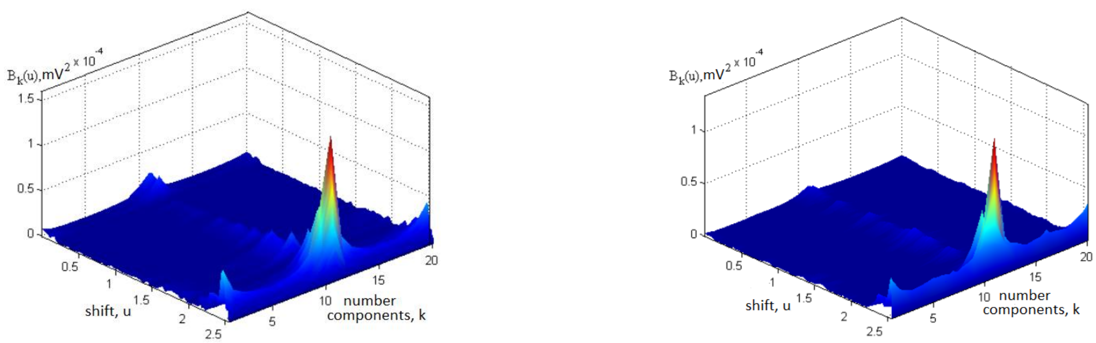
(patient A in normal) (patient B with pathology)

Fig. 7



(patient A in normal) (patient B with pathology)

Fig. 8



(patient A in normal) (patient B with pathology)

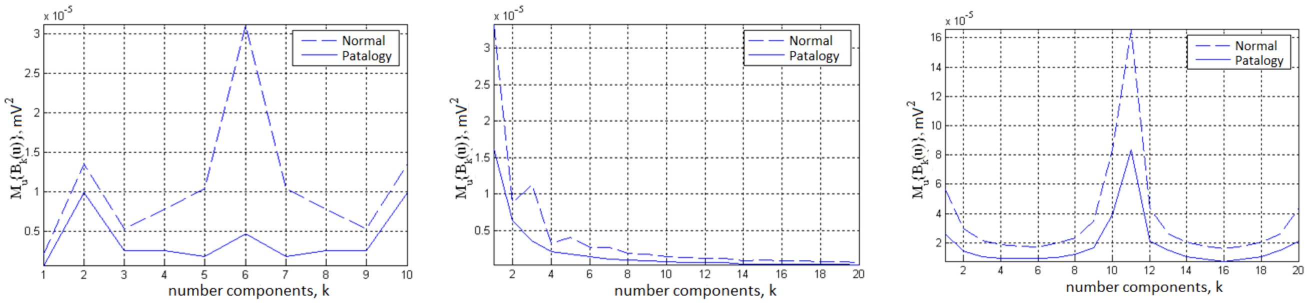
Fig. 9

The spectral components $\hat{B}_k(u)$ realizations mathematical expectation estimations are obtained by the expression:

$$M_u\{\hat{B}_k(u)\} = \frac{1}{N_u}\sum_{u=1}^{N_u}\hat{B}_k(u), \quad u = \overline{1, N_u}, \; k = \overline{1, N_k}, \qquad (9)$$

where k – ERS spectral components number, N_u – a shift length, N_k – a number of components.

The ERS realizations spectral components mathematical expectations are shown in Fig. 10 (a - synphase method (not taking into account the components cross-correlation relationships; b - synphase method (taking into account the components cross-correlation relationships); c - component method).



(a) (b) (c)

Fig. 10

In Fig.10 (a), one can see that the expectations estimates maxima values for the norm and pathology are concentrated at the same frequencies, but the amplitude values differ./ The maximum amplitude for the norm is concentrated at the 8th frequency, for pathology – 2nd frequency. Therefore the expectation estimates are sensitive-quantitative indicators when disparate visual system different states (norm or pathology). In Fig.10 (b) it can be seen that the estimates structure for norm and pathology are very similar, but they differ. From the obtained spectral components expectation estimates by the component method in Fig.10(c) it can be seen that the main components peaks are concentrated at the same frequencies, but differ only in amplitude. This indicates a clear change in the visual system functioning, namely in the retina (norm, cataract, central retinal degeneration or other type of pathology).

The ERS spectral components reliability calculations are reduced to the ERS class (stationary or nonstationary) determination, which is a special case of the hypotheses statistical testing general problem. Under the assumption that the investigated ERS is an additive mixture, two hypotheses have been considered: 1) $H_0 : \xi(t) = \overset{0}{\xi}(t)$ - ERS is stationary: 2) $H_1 : \xi(t) = \overset{0}{\xi}(t) + m_\xi(t)$ - ERS is nonstationary, where $m_\xi(t)$ - periodic deterministic component (in this case, the stochastic process $\xi(t)$), expectation $\overset{0}{\xi}(t)$ - stationary stochastic process (centered stochastic process with zero expectation).

Since the false solution of one of the hypotheses can lead to undesirable and serious consequences (eg, incorrect treatment of the visual system, which is assigned based on the diagnosis) this is why only such decisions are considered, for which for a given error probability value p_f, the correct decisions probability (reliability) p_d is maximum - Neyman-Pearson criterion. By this criterion, the ERS estimates reliability p_d is determined by the expression:

$$p_d = 1 - \Phi\left(U_0 - m(\xi/H_1) \Big/ \sqrt{D(\xi/H_1)} \right). \qquad (10)$$

where $\Phi(\cdot)$ – normal distribution integral, U_0 – threshold between stationarity and nonstationarity discrimination, $U_0 = \sqrt{D(\xi/H_0)}\Phi^{-1}(1-p_f) + m(\xi/H_0)$; $m(\xi/H_0), D(\xi/H_0)$ - the stationary ERS expectation and dispersion of the spectral density power, $m(\xi/H_1) = \frac{1}{N_u N_k}\sum_u^{N_u}\sum_k^{N_k} B_k(u)$ – expectation and $D(\xi/H_1) = \left(\sum_u^{N_u}\sum_k^{N_k} (B_k(u) - m(\xi/H_1))^2 \right) \Big/ (N_u - 1)(N_k - 1)$ – dispersion of the spectral components of the nonstationary ERS as a PCSP.

The results of the ERS spectral components reliability p_d instantaneous values calculated for a given error probabilities $p_f = (0.001, 0.01, 01)$, which are given in Table 1, indicate that the estimates of the ERS spectral components (Fig. 10) are invariantly informative signs, with the help of which it is possible to assess the retina (norm or pathology) with high reliability (0.989-1).

Table 1

Method of analysis / Error	Synphase by reasonably corrupted calls		Synphase with cross-correlation		Component	
	Norm	Pathology	Norm	Pathology	Norm	Pathology
p_f =0.1	0.999	0.989	0.999	0.999	0.999	0.999
p_f =0.01	1	0.999	1	1	1	1
p_f =0.001	1	0.99	1	1	1	1

Based on the developed ERS mathematical model and analysis method, a package of computer programs for the ERS statistical analysis was created as an integral part of the specialized software of computer ophthalmology automated systems.

Discussion. The ERS model as a pulsed periodically correlated stochastic process is substantiated, which, unlike known ones, reflects the macromechanism of the ERS formation, and allows determining the model characteristics from the experiments results and takes into account the stochasticity and repeatability combination in the signal.

Methods for the of human eye ERS retina statistical analysis have been developed using a formalized and automated procedure that allow to assess the condition of the visual analyzer, in particular its retina at an early stage of its disease.

The obtained spectral components values are the ERS information-invariant signs characteristics with their assessment reliability of 0.989-0.999 with 0.001 error probability and characterize the functional state of the human retina.

A software for electroretinography statistical processing was created which is suitable for use as an integral part of specialized software for computer ophthalmology automated systems

Conflict of interest statement: The authors state that there are no conflicts of interest regarding the publication of this article.

Author Contribution: Conceptualization: Mykola Hvostivskyy. Data curation: Mykola Hvostivskyy. Formal analysis: Mykola Hvostivskyy. Writing - original draft: Mykola Hvostivskyy. Writing - review & editing: Mykola Hvostivskyy.

REFERENCES:

1. Yavorskyy B, Yuzkiv A. Mathematical modeling electroretinograph signals: Bulletin of Ternopil State Technical University. 1997; 2:40-45

2. Matsyuk O, Palamar M. Statistical analysis and harmonic analysis electroretinogram: Bulletin TSTU Ivan Puluj. 1997; 25-28.

3. Tkachuk R., Yavorskyy B. Building a prototype expert system research neurotoxications by human electroretinography: IRTC "Information Technology and Computer Engineering". 2010 May; 44.

4. Palamar M. Adaptive computer measurement and control system for the study biopotentials eye: Control and Local Government of technical systems (Abstracts of 3rd Int. Conf). 1995 Sept; 335-336.

5. Palamar M. Computer measuring system for the study biopotentials visual analyzer: avtoref. dis…. kand. techn. science (05.11.05). Lviv. 1998; 17.

6. Palamar M. Construction and analysis of measurement and control interface with a personal computer registration system ERG-signals: Herald of the Ternopil State Technical University. 1997; 2(2):34-40.

7. Rilk AJ. The Flicker Electoretinogram in Phase Space: Embeddings and Techniques. Aalen; 2003.

8. Dragan Y. Energy theory of linear models of stochastic signals: Lviv Center for Strategic Studies eco-bio-technical systems; 1997