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DEVELOPMENT OF MATHEMATICAL MODELS AND METHODS ANALYSIS OF ELECTRORETINOSIGNAL

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Abstract. A new application of a periodically correlated random process as a mathematical model of an electroretinosignal is justified, which takes into account in its structure a combination of the properties of periodicity with stochastic. On the basis of a valid model, methods for the analysis of the electroretinosignal of the human eye retina in ophtalmodiagnostic systems have been developed, using a formalized and automated procedure that allows the evaluation of the retina of the human eye at an early stage of its disease 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 perception of information from the environment. The solid computerization, poor environment and inactive lifestyle are factors that cause a negative effect on his condition. Therefore, an important objective of modern medicine is early diagnosis and prevention of eye diseases not only in Ukraine but also worldwide.

In actuality diagnosis electroretinosignal (ERS) visual system, which is a response to the human retina light flash, the authors pointed out many works medical direction (Shamshynova A., Volkov V., Bogoslavskyy A., Byzov A., Zislyna N, Mironov E, Karpe G., Henkes H., Kato M. and other), as established that regular diagnostics of the retina by ERS enables to detect functional changes in it early and promptly carry out preventive measures for rehabilitation, and in the case of pathological disorders prevent disease appropriate treatment. Effectiveness of choice preventive and therapeutic interventions depends on the proper use ophtalmodiagnostic system which should be based on adequate mathematical models and

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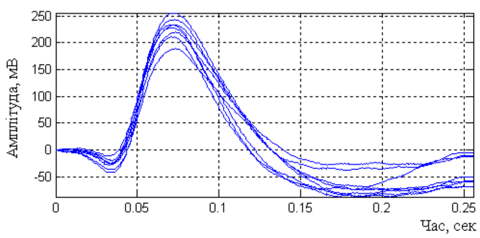
enable automated accurately and reliably determine the location of lesion and track the dynamics of the disease.

Known except deterministic interpretation (Yavorskyy B., Yuzkiv A. [1]), a number of papers Matsyu O. [2], Tkachuk R. [3,4], Palamar M. [5,6], Rilk A. [7] in which to describe ERS applied stochastic models (linear random process and additive mixture of deterministic and random components). However, these models do not allow to take into account in their statistical structure interconnectedness between different opinions of the same series of observations that are important in the study of phase changes ERS structure to detect early manifestations since changes in the functioning of the retina.

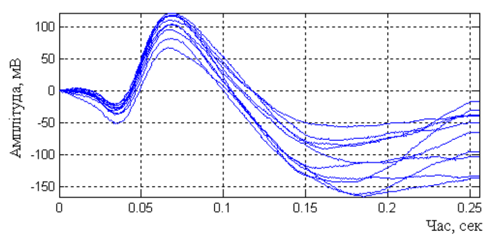
These arguments point to the urgency of improving the mathematical model ERS and development of analysis methods for automated computer ophtalmodiagnostic systems oriented to improve the reliability of early diagnosis of functional state of human retina by introducing a new class area of ophthalmology reliable informative signs based on a model of rhythm a pulse periodically correlated random process.

Objective. Using of microprocessor in the measuring head of the device significantly reduce its weight and size, consumption power, to make the device more versatile, compact, without changing its basic technical and consumer characteristics; use it together with modern computer systems, which greatly enhances its functionality.

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



(patient A in normal)



(patient B with pathology)

Fig.1

To substantiate the mathematical model, 10 implementations (responses) of ERS were used, which were simultaneously decomposed according to the order of the flash (Fig. 2).

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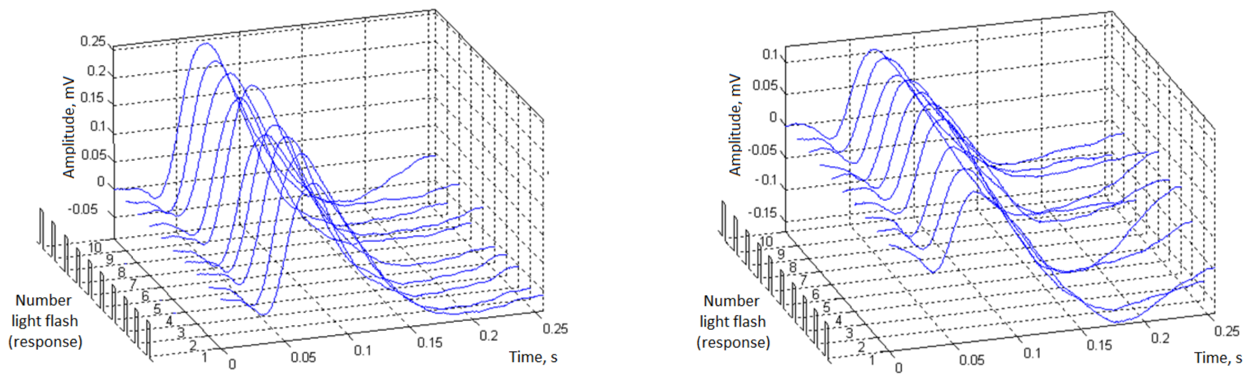
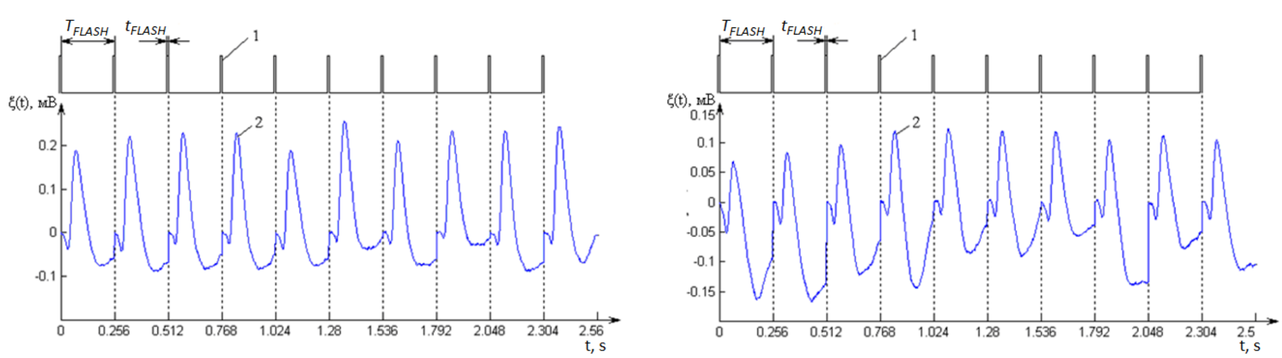


(patient A in normal) (patient B with pathology)

Fig. 2

According to the methodology registration signal ERS is the response of the retina of the same eye to a series of light flashes in the structure of an accident implicitly combine frequency, so these reviews ERS is depicted on one time axis as the ensemble as periodically continued (macromechanism formation) that makes it possible to see the time dependence of the response of the retina from flash to flash.

In Figure 3 illustrated ERS at one time axis depending on the light flashes with 1 - curve shows the time of the light flash (under the terms of the registration ERS flash is periodic), 2 - ERS into account the frequency of outbreaks, which provides uniformity phases of the process of generating a signal in the interval of time equal to the fixed period of the outbreak.



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

Fig. 3

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Since during registration of the conducted studies, the light flashes are fed periodically with a specified period T_{FLASH} and durations (t_{FLASH}), therefore retinal recall (reaction to a flash) will also contain the periodicity of properties with the same period T_{FLASH}.

Given such a macro-mechanism of formation, ERS is presented as a set of reviews, shifted in time with respect to each other for a constant period $T = T_{FLASH}$ in the form of:

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

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

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

T - duration of a response ERS.

The image of the ensemble of ERS in the form of its periodic continuation takes into account in its structure the combination of the properties of periodicity with stochastic, and thus makes it possible to take into account the statistical relationships between various retinal reactions of the same series of observations, is impossible in the case of the traditional representation of the same type of reactions in the form of an ensemble of realizations.

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

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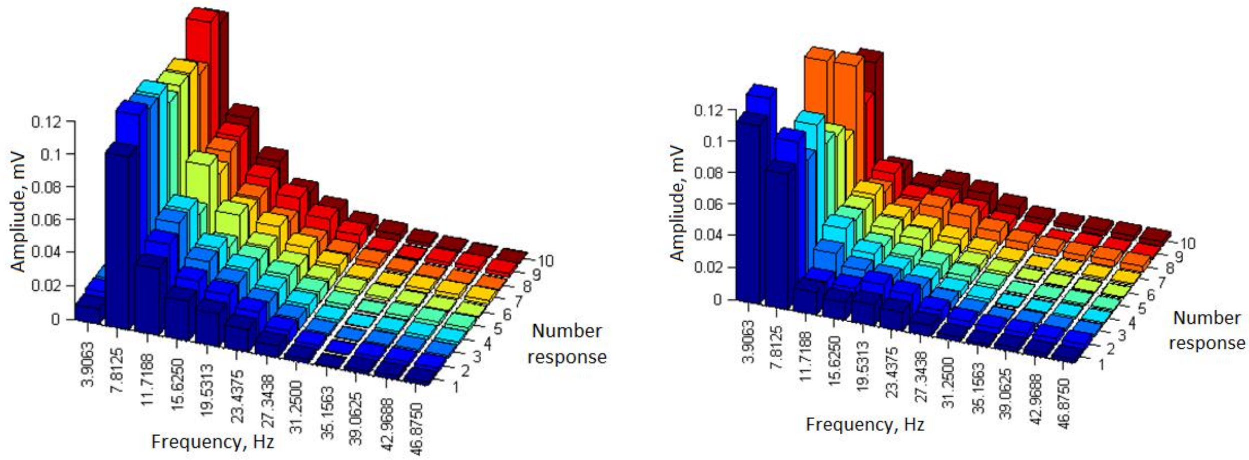
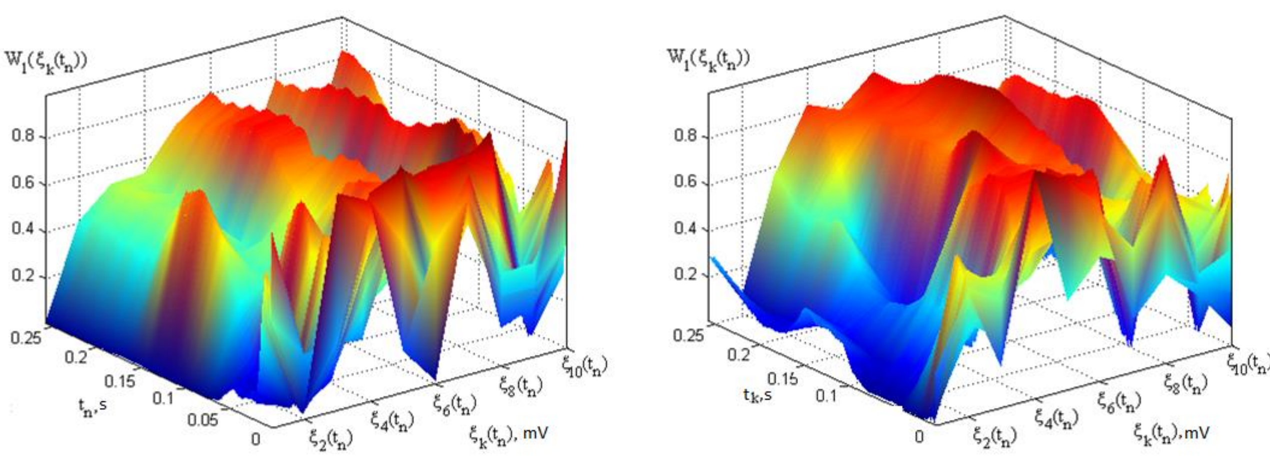


(patient A in normal) (patient B with pathology)

Fig. 4

Considering the signal within the stationary model, observed that the density distribution function (Fig. 5) are transformed over time,



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

Fig. 5

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

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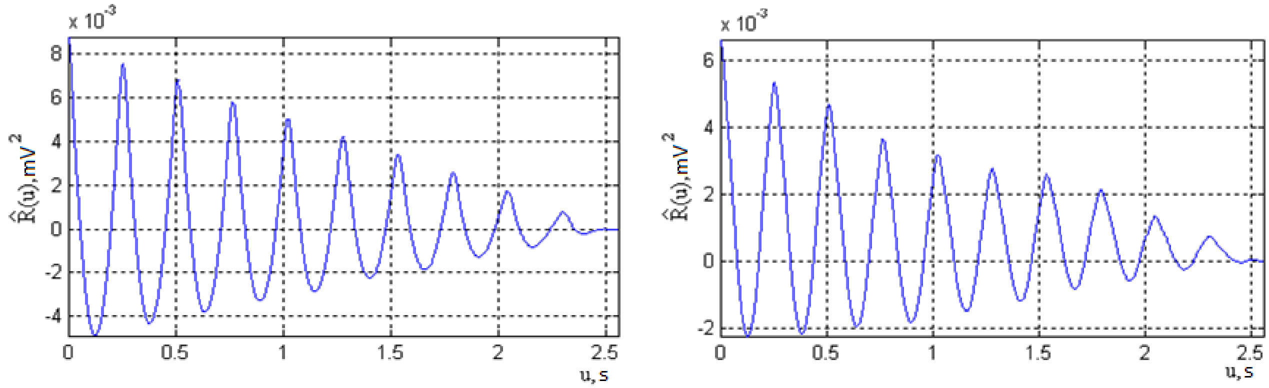

(patient A in normal) (patient B with pathology)

Fig.6

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

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

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

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

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

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

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

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Expression (2) adequate pulse signal formats and efficient in modeling as ERS pulse PCSP, but on the basis of submissions equivalences PCSP through translational components (2) and views them through the stationary components:

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

where $\xi_k(t)$ – the stationary components of the ERS as a PCSP, $\mathbf{Z}$- the set of all integers, it is advisable to treat such implementations as implementations of the last of the named representations, justify the applicability to them of the known methods of statistical processing (synphase, component) for calculating statistical estimates of their probabilistic characteristics that are indicators of the state of the human retina.

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

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

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 as well as representation using Fourier expansions type:

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

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

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structure of the ERS:

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

It is established that the in-phase method of analysis has two ways of realizing, namely, taking into account and without taking into account the cross-correlation between the components, which made it possible to develop this method. Estimates of the spectral components of the ERS as a periodically correlated random discrete sequence obtained by the synphase method with allowance for cross-correlation relationships are calculated from the expression:

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

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

Estimates of the spectral components of the ERS obtained by the synphase method without taking into account the cross-correlation relationships are calculated from expression:

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

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 estimation component, N_u - length shift.

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

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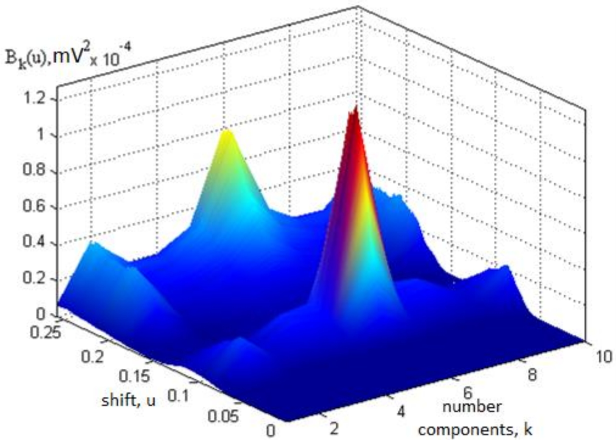
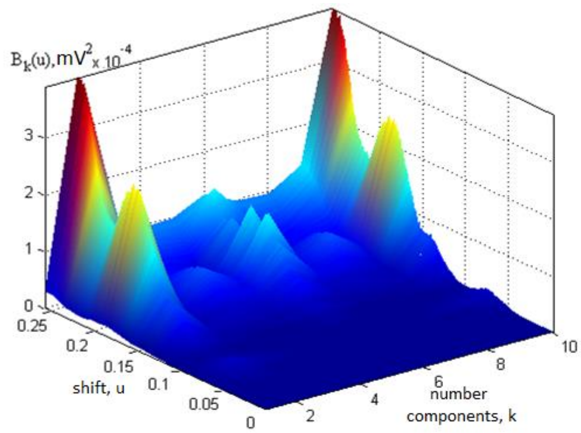
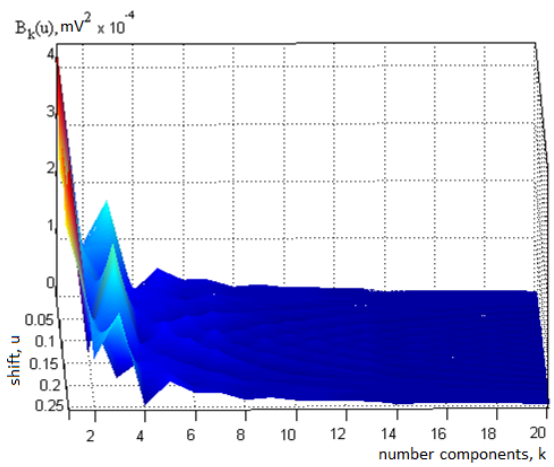


(patient A in normal)

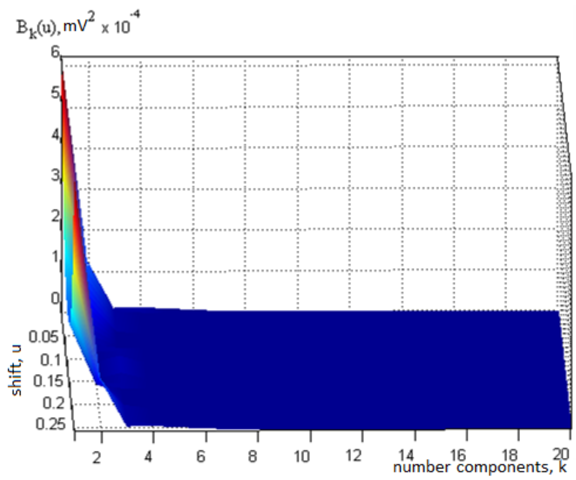


(patient B with pathology)

Fig. 7



(patient A in normal)



(patient B with pathology)

Fig. 9

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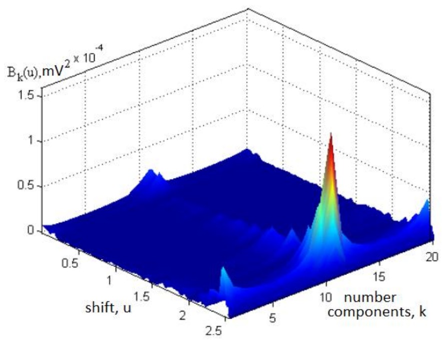
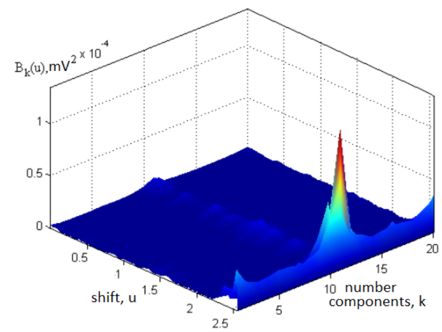


(patient A in normal)



(patient B with pathology)

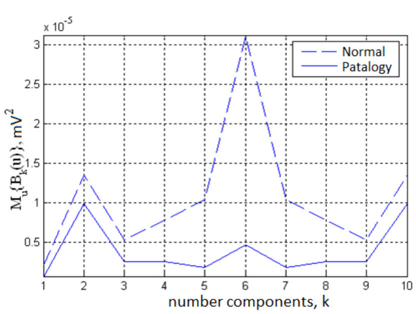
Fig. 10

Estimation of the mathematical expectation of the realizations of the spectral components $\hat{B}_k(u)$, calculated from the expression:

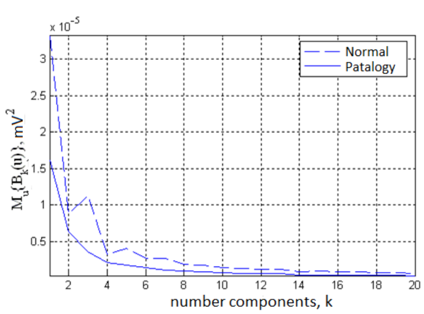
$$M_u\left\{\hat{B}_k(u)\right\} = \frac{1}{N_u}\sum_{u=1}^{N_u}\hat{B}_k(u), \quad u = \overline{1, N_u},\ k = \overline{1, N_k}, \qquad (9)$$

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

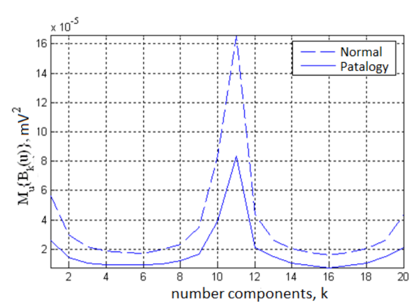
Realizations of mathematics for the spectral components of ERS are shown in Fig. 11 (a - synphase method (without taking into account the cross-correlation between the components; b - synphase method (taking into account interrelationships between components); c - component method).



(a)



(b)



(c)

Fig. 11

In Fig.11(a), we see that the value of the maxima of the estimates of the mathematical expectation for the norm and pathology are concentrated at the same frequencies, but the amplitude values of the estimates differ among themselves, namely for the norm the maximum amplitude of the signs is concentrated at the 8th frequency, for pathology – 2th frequency. Therefore, estimating the mathematical expectation is a sensitive-quantitative indicator when disparate different states of the visual system (norm or pathology). In Fig.11(b) it can be seen that the estimates for norm and pathology are very similar in structure, but they differ. From the obtained estimates of the mathematical expectation of the spectral components by the component method in Fig.11(c) it can be seen that the peaks of the components are concentrated at the same frequencies, but differ only in amplitude, which indicates a clear change in the functioning of the visual system, namely in the retina (norm, cataract, central retinal degeneration or other type of pathology).

The calculation of the reliability of the spectral components of the ERS is reduced to the definition of the ERS class (stationary or nonstationary), which is a special case of the general problem of statistical testing of hypotheses. Considered under the assumption that the investigated ERS is an additive mixture, two hypotheses: 1) $H_0 : \xi(t) = \overset{0}{\xi}(t)$ - ERS stationary: 2) $H_1 : \xi(t) = \overset{0}{\xi}(t) + m_\xi(t)$ - ERS nonstationary, where $m_\xi(t)$ - periodic deterministic component (in this case, the expectation of stochastic process $\xi(t)$), $\overset{0}{\xi}(t)$ - stationary stochastic process (centered stochastic process with zero mathematical 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) because considered only such decisions, for which a given value error probability p_f probability of correct decisions (reliability) maximum p_d - Neyman-Pearson criterion. By this criterion, the reliability of estimates ERS p_d is calculated from the expression:

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

where $\Phi(\cdot)$ – Integral normal distribution, U_0 – threshold of discrimination between stationarity and nonstationarity, $U_0 = \sqrt{D(\xi/H_0)}\Phi^{-1}(1 - p_f) + m(\xi/H_0)$; $m(\xi/H_0), D(\xi/H_0)$ - mathematical expectation and dispersion of the power spectral density of stationary ERS,

$m(\xi/H_1)=\frac{1}{N_u N_k}\sum_u^{N_u}\sum_k^{N_k} B_k(u)$ – mathematical 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 calculated instantaneous values of the reliability p_d of the spectral components of the ERS for given error probabilities $p_f=(0.001, 0.01, 01)$, which are given in Table 1, indicate that the estimates of the spectral components of the ERS (Fig. 13) 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 mathematical model and ERS analysis method, a package of computer programs for the statistical analysis of ERS was created as an integral part of the specialized software of automated systems of computer ophthalmology.

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

Methods for the statistical analysis of ERS retina of the human eye 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.

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

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

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.

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