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ABSTRACT

of the dissertation for the degree of Doctor of Philosophy

DEVELOPMENT OF METHODS FOR PREDICTING AND DETECTING THE DEVELOPMENT OF PATHOLOGICAL PROCESSES IN THE HUMAN CARDIOVASCULAR SYSTEM

Specialty: 3337.01 - Information-measuring and control systems (in (the chemical industry)

Field of science: Technical sciences

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GENERAL CHARACTERISTICS OF WORK

Relevance and degree of research of the topic. The human cardiovascular system is one of the most complex biological systems and takes the main place from the point of view of the vital activity of the body. It reacts sensitively to slight changes in the state of the internal organs and the environment. Visual observation of the patient's electrocardiogram is traditionally one of the main methods of obtaining information about the patient's condition. At the same time, in recent years, medical institutions show more and more interest in methods of automatic monitoring of the state of the human cardiovascular system. In cardiology (as in other fields of medicine), the instrumental approach is traditionally based on the comparison of some quantitative indicators characteristic of the norm and various pathologies. At this time, the diagnosis is based on the compliance of the measured parameters with the data collected as a result of previous experience and the results obtained by other methods (clinical analysis, medical history, etc.). For example, due to long-term observations of practicing cardiologists and researchers, it became clear that certain pathologies of the cardiovascular system lead to specific changes in the shape of the electrocardiogram (ECG). Therefore, measuring the mutual location, shape and size of ECG wave has become an important part of the process of diagnosing diseases of the cardiovascular system. The development of the technique made it possible to record the sequence of time intervals between heartbeats - the rhythmogram - along with the ECG. The process of reconciling the parameters of the rhythmogram with other data about the patient's condition led to the identification of a clear relationship between the indicators of heart rhythm changes and the state of the body. The application of the calculation technique in medical institutions made it possible to expand the scope of the indicated indicators of the rhythmogram.

The more indicators are recorded, the more accurately the issue of diagnosis is solved, because different indicators have different sensitivity to specific pathologies.

In the last decade, a large number of studies carried out by specialists in the field of processing physiological data by mathematical methods allowed to determine that the dynamics of many physiological processes occurring in the human body are chaotic. Nonlinear chaotic dynamics provide many functional advantages to the organism. Systems in which deterministic chaos is detected are capable of operating in a wide range of conditions and therefore easily adapt to environmental changes. Chaotic behavior is apparently detected by the variability of the recorded data. The decrease of variability accompanied by the clearly expressed periodicity of the observed data means the detection of pathological changes in the body.

To evaluate the chaoticity of RR intervalograms, the characteristics of fractal clusters such as fractal Hausdorf dimension, correlation and information dimension, Herst index, generalized dimension and phase space dimension are used.

Spectral-temporal analysis methods of heart rhythm variability (HRV) are currently well studied, and their further improvement should be focused only on increasing the accuracy of obtained values and developing software and hardware tools for fully automatic measurement of HRV parameters. At the same time, it is confirmed that the algorithms aimed at studying the dynamics of cardiointervals and transition states of HRV have not been sufficiently developed. It should also be taken into account that the availability of such methods and algorithms could significantly improve the understanding of the processes leading to various changes in heart rhythm.

The study of the application of nonlinear dynamics methods for the analysis of heart rhythm changes and also the development of mathematical models and algorithms for better adaptation of the measurement principles to the physiological nature of the heart rhythm are currently the most priority research directions, which confirms the **relevance of the topic** of the current dissertation.

The purpose of the dissertation work. To determine the functional state of the cardiovascular system, it is the detection of new informative signs and the adoption of diagnostic decisions taking into account the periodic sequence of cardiosignals.

Research object: The research object in the dissertation work is the cardiovascular system of the human body and the electrical biological potentials produced by it.

The main issues of the study. The set goal is achieved by solving the following issues:

1) Choosing a method of studying heart rhythm variability based on comparing a pair of adjacent cardiointervals, taking into account fractal features in the dynamics of heartbeat.

2) Development of methodology and algorithms for determining new informative signs of repeated heart beat intervals, which are used for the diagnosis of various diseases of the cardiovascular system based on ECG analysis;

3) Development of a procedure for predicting the state of the cardiovascular system based on determining the extreme values of heart beat intervals.

4) Evaluating the effectiveness of using short-term and long-term correlation dependences of repetitive intervals of heartbeats when predicting jumps of dynamic series with fractal characteristics.

5) Comparative analysis of the methods of predicting the dynamics of heartbeat in the presence of noise in the initial data using information about short-term and long-term dependencies.

6) Prediction of the functional state of the cardiovascular system based on the development of non-stationary electrocardiography signal segmentation algorithms and determination of the boundaries of repetitive intervals.

The main scientific theses for the defense:

-methodology and system of criteria for diagnosing various diseases of the cardiovascular system based on the analysis of repetitive intervals of heart beats;

- the selection of statistics of repetitive intervals of heartbeats based on the application of RIA (return intervals approach), which allows to speed up the procedure of predicting the state of the cardiovascular system and increase the degree of accuracy of the obtained prediction;

- the possibility of assessing the correct prediction of the state of the cardiovascular system when using information about both short-term and long-term dependences of repeated intervals of heartbeats;

- method of segmentation of non-stationary physiological signals into quasi-stationary segments after rejecting (eliminating) the trend organizer, taking into account the change points of instability;

- a complex prediction algorithm of the state of the cardiovascular system when determining the boundaries of quasi-stationary areas, taking into account the method of evaluating the change point of the instability of the time series of cardiac signals.

Scientific novelty of the research:

1. New informative signs of repeated heartbeat intervals were proposed, and algorithmic and software solutions were developed to evaluate the effectiveness of using long-term correlations in the differential diagnosis of the functional state of the cardiovascular system.

2. In order to realize the process of predicting the state of the cardiovascular system and increase its authenticity, it was proposed to study the probability distribution functions of repeated intervals, as well as their long-term dependencies (autocorrelation function, conditional recurrence periods, etc.).

3. The effectiveness of using the short-term and long-term correlation dependences of the repeating intervals of the heartbeat when predicting the jumps of the dynamic series with fractal characteristics was analyzed and evaluated.

4. The effectiveness of predicting the state of the cardiovascular system in the presence of normal and regularly distributed additive noise, taking into account the linear and non-linear components of long-term memory, was evaluated.

5. Taking into account the non-stationarity of the electrophysiological signals, a modified method of predicting the state of the cardiovascular system was proposed based on the determination of the boundaries of the quasi-stationary areas of the time series.

Methods of research. The theoretical part of the dissertation work was performed on the basis of correlation analysis, multifractal analysis, signal theory, probability theory, statistical analysis methods. The results of the research were obtained in Microsoft Excel, Matlab software tools.

The degree of accuracy of the results. The theoretical results obtained in the dissertation were proven by medical and mathematical experiments and applied in the teaching process. The results of the dissertation work were used in the state-funded scientific-research work carried out by the "Biomedical Engineering" department of Azerbaijan Technical University.

Theoretical and practical significance of the research. The practical significance of the studies performed in the dissertation is that the use of algorithms and programs developed for the processing of electrocardiographic signals, as well as methods of predicting the functional state of the cardiovascular system, will allow to increase the authenticity of the results obtained in electrocardiographic studies and, therefore, to increase the effectiveness of diagnostic decisions made based on them. .

Also, the results of theoretical and practical studies were applied in the teaching of a number of subjects.

Personal presence of the author. The scientific issues raised in the dissertation work and the main results obtained were obtained directly by the author independently. As a result of the calculation experiment, normal and pathological signals were studied, fractal methodology was applied to the analysis of electrocardiographic signals, repeated intervals of heartbeats were analyzed and algorithms were developed to predict the state of the cardiovascular system, algorithms for the collection and analysis of information about the value of the intervals between jumps of heart signals, those segmentation between jumps and development of algorithms that determine time series change points was performed with the participation of the applicant.

Approbation and application. The main results of the dissertation were presented and discussed at the following conferences, symposiums and seminars:

Materials of the dissertation work was presented and discussed at the VIII International Conference "Problems and Perspectives of IT-Industry Development", Kharkiv, Ukraine, 2016; XII International scientific conference "Physics and radioelectronics in medicine and ecology", Vladimir-Suzdal, Russia, 2016; International scientific and technical conference "Modern state and development prospects of information and communication technologies", Baku, 2016; IX International scientific-practical conference "Problems and Perspectives of IT-Industry Development", Ukraine, Kharkiv, 2018, XII International scientific conference - 2018, Vladimir, Russia; VII International scientific-practical conference "Signal processing and non-Gaussian processes", Ukraine, Cherkassy, 2019; 1st international scientific-practical conference "Modern information, measurement and control systems: problems and prospects", Baku, 2019.

The name of the organization where the dissertation work was performed: It was carried out at the "Biomedical Engineering" department of Azerbaijan Technical University.

Scientific works published on the topic of the dissertation. The main results of the dissertation work were published in 25 printed works, including 1 monograph, 17 articles, 6 international and national conference theses.

The total volume of the dissertation with a sign, indicating the volume of the structural units of the dissertation separately. Chapter I consists of 35919 symbols, Chapter II has 55453 symbols, Chapter III has 51883 symbols, and Chapter IV has 255672 symbols, including 63760 symbols.

The dissertation consists of an introduction, four chapters, a conclusion, and a list of references (136).

The total volume of the dissertation is 186 pages. and in total, the dissertation consists of 255672 symbols. The main text of the thesis is explained in 186 pages including 25 pictures, 3 tables and 3 listings.

MAIN CONTENT OF THE WORK

In the introduction, the relevance of the topic of the dissertation is justified, the goals and issues of the conducted research are stated. Results containing scientific innovation are noted and their practical value is indicated. A brief annotation and structure of the content part of the work is provided.

In the first chapter of the dissertation, in order to analyze the situation of the problem and formulate the research problem, a review of the methods of assessing the functional state of the cardiovascular system and a review based on the characteristics of the heart signals was conducted.

As a rule, for the purpose of operative diagnosis of the functional state of the cardiovascular system, the change in heart rhythm is analyzed. Such an approach is designed to ensure the maximum reliability of measurements in the conditions of different types of obstacles and the analysis of sequences of RR intervals.

The various mathematical processing and analysis methods of biomedical signals and the data used in the study for the analysis and processing of ECG signals are based on the dedicated web portal PhysioNet, which is shown to be accessible to everyone and to allow researchers to expand its content. When performing the computational experiment, signals corresponding to normal rhythm and atrial fibrillation were studied. The regularity of the heart rhythm is normal and the frequency of heart contractions for the specified pathology is determined.

Taking into account the non-stationary nature of electrophysiological signals, the application of fractal methods to the analysis of the electrocardiogram for the purpose of obtaining diagnostic information was viewed as a prospective issue.

In the second chapter, repeated intervals of heartbeats were analyzed to predict random process spikes that would exceed any Q threshold for differential diagnosis of cardiovascular conditions. At this time, a typical predictor of such a jump, i.e., the characteristic behavior of a random process at the time moments before the occurrence of the jump, was searched. In order to determine statistical parameters of heartbeat dynamics, heartbeat intervals were modeled based on a multifractal approach. For the generation of multifractal clusters, the multiplicative random cascade (MRC) process was considered, the MRC process was generated from the initial data by an iterative method by changing the distance between the records in each iteration.

Another algorithm for the generation of multifractal clusters was obtained by applying the multifractal random walk (MRW) method, in which the record value a_i, i=1, ..., N of the signal was first generated. By taking the exponential value of this record and multiplying it by two Gaussian random numbers, the result is a multifractal series:

$$x_i = \left(e^{a_i}\right) \cdot b_i$$

The statistics of the intervals between events exceeding any Q threshold were examined using the MRC and MRW models of the process. An algorithm was developed to calculate the generalized Herst index for obtaining informative signs of repetitive heartbeats, to evaluate the unconditional and conditional distribution density of repetitive intervals exceeding the Q threshold, the conditional recurrence period, the autocorrelation function of repetitive intervals, and to estimate the distribution density of the sizes of clusters of repetitive intervals. The obtained complex of informative signs is used for the diagnosis of various diseases of the cardiovascular system. Numerical realization of the algorithm was performed for differential diagnosis of normal condition and atrial fibrillation.

The following parameters were calculated to determine the re-informative signs of heartbeats:

1. The generalized Hurst exponent of the multifractal set $\{\widetilde{X\iota}\}$

$$F_q(s) \sim s^{h(q)} \tag{1}$$

Here, $F_q(s)$ the generalized fluctuation index, s - is a sequence of s-length cuts, q - deformation parameter (-∞<q<+∞)

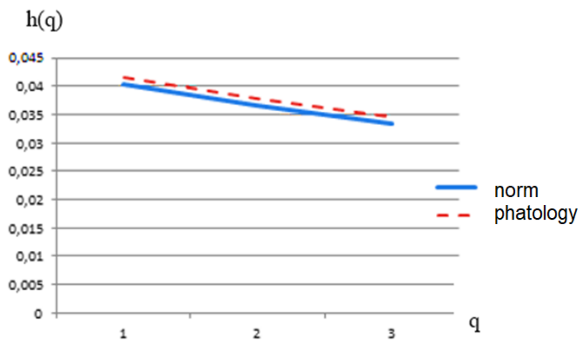

Fig. 1 graph of h(q) dependence

2. The δ(Q) indicator of the scaling relationship was calculated:

$$\ln\left[P_Q(r)\right] = -\delta(Q)\ln\left[r / R_Q\right] \tag{2}$$

Here, $P_Q(r)$ is the density distribution of repetition intervals of length r.

$$P_Q(r) \sim (r / R_Q)^{-\delta(Q)} \tag{3}$$

Here, R_Q is the averaged repetition interval or repetition period, r is the value of the current interval.

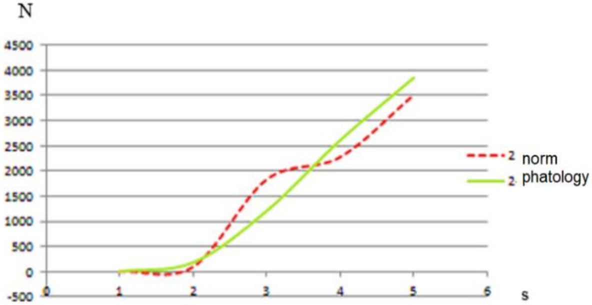

Fig. 2. Graph of δ(Q) dependence
(N is the number of points in the intervals)

3. Evaluation of conditional recurrence period.

For $r_0 \geq R_Q$ values, the conditional recurrence period is calculated, which is defined as the average value of all r_0 intervals following recurrence intervals with a certain r_j value:

$$\ln[R_Q(r_0)] = \nu(Q)\ln[r_0] \tag{4}$$

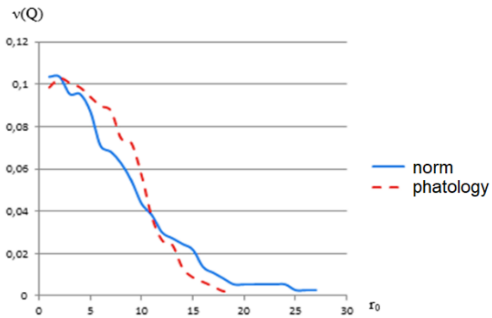

Fig. 3 graph of *v(Q)* dependence

4. Evaluation of the autocorrelation function of repeated intervals. The evaluation was performed as follows:

$$C_Q(s) \sim s^{-\beta(Q)} \quad (5)$$

Here, the β indicator reflects the direct dependence on the size of the quantile. For example, β=0.46, 0.49, 0.56 correspond to R_Q=10,70,500 periods.

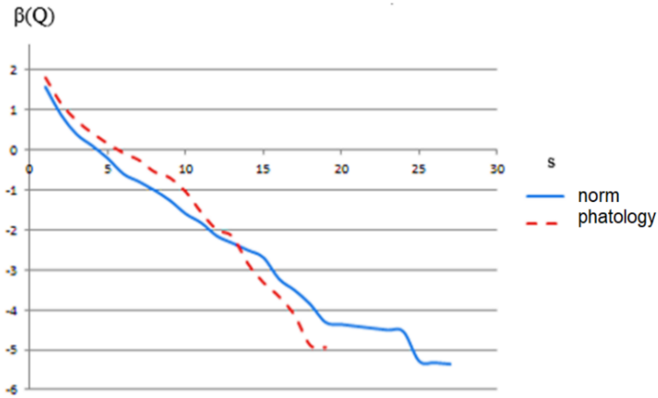

Fig. 4. Graph of β(Q) dependence

5. Evaluation of the distribution density of the sizes of clusters of repeated intervals. Note that the distribution of k cluster quantities is calculated with the frequency *v*(k)>1/2 (above the median) and with the frequency *v*(k)<1/2 (below the median). Assuming P(k)≈(k), the probability distributions $P_1(k)$ and $P_2(k)$ of measures k are calculated for repeated intervals above and below the median, respectively.

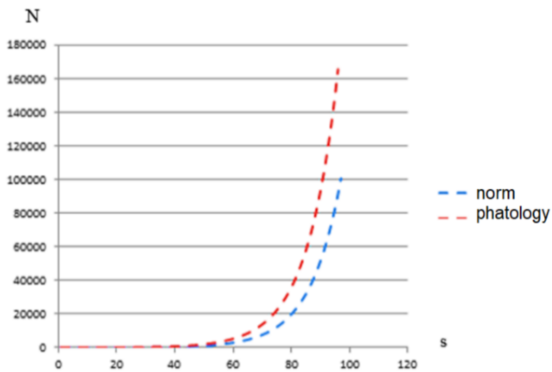

Fig. 5. Graph of dependence P(k).

As a result of the mentioned 5 stages, the entire palette of informative signs of heartbeat repetition intervals is determined.

An approach to the problem of predicting large recurring intervals using long-term RIA (return intervals approach) memory is considered.

The probability $W_Q(t,\Delta t)$ is the probability that at least one Q - interval of a heartbeat will occur during the time units Δt after the last Q - event, provided that the Q - event interval until this last Q - event occurs within t time units.

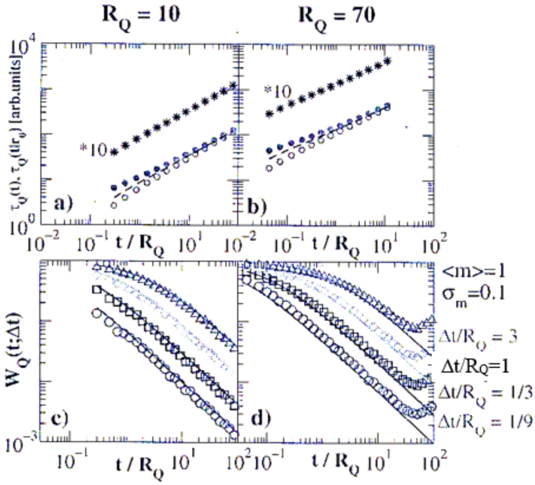

Fig. 6. $\tau_Q(t)$ and $W_Q(t,\Delta t)$ graphs

The values of the global $\tau_Q(t)$ and conditional $\tau_Q(t|r_0)$ quantities of the expected time units until the next event occur are shown (Fig. 6). Their numerical values were obtained for the MRC-model: (a) for $R_Q = 10$ and (в) for $R_Q = 70$. r_0 values were considered only when $r_0 = 1$ and $r_0 = 3$.

$$\tau_Q(t) \sim (t/R_Q)^{\xi(Q)} \quad (6)$$

satisfies a power law, where the exponent ξ(Q) decreases as Q increases (ξ=0.6; for R_Q=10 and ξ=0.47; for R_Q=70). The conditional expected number $\tau_Q(t|r_0)$ of time units can also be described by a power law with an exponent approximately as $\xi(Q,r_0)$, as a global quantity ξ(Q) for $r_0 = 1$.

$$W_Q(t;\Delta t) = \frac{(\delta(Q)-1)\Delta t/R_Q}{t/R_Q+(\delta(Q)-1)\Delta t/R_Q} \quad (7)$$

Fig. 6(c) and 6(d) show the W_Q graphs for recordings of the MRC-model characterized by the power spectrum in the form of 1/f when R_Q=10 and R_Q=70, respectively.

In the third chapter, it is shown that the approach is effective when studying records with non-linear (multifractal) long-term memory. Two indicators were used to evaluate the prognosis: sensitivity (sensitivity) that characterizes the share of correctly reported Q-events in advance and a special indicator that characterizes the share of non-Q-events that are correctly reported in advance – specify (specify) Spec. To increase the effectiveness of the forecast, an analysis is used by applying a signal reception operator called ROC-analysis (receiver operator characteristic). When using information about both short-term and long-term dependencies, the correct prediction (Sens) at the same values of the probability of a false alarm (Spec) is approximately the same probabilities are obtained. Using long-term memory (RIA-approach) recordings of heartbeats has an advantage over PRT (pattern recognition technique), which uses only short-term memory.

Additional consideration of information about the value of the previous interval between jumps can be obtained by switching to basic probabilities calculated on the basis of conditional probabilities.

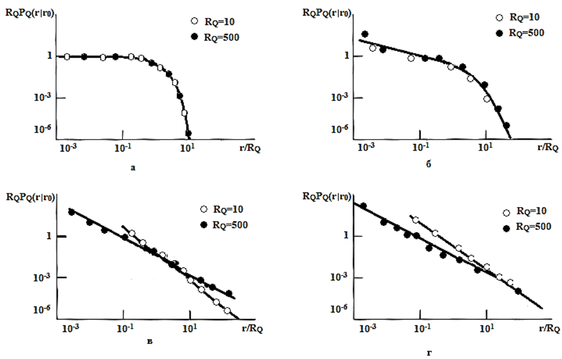

Fig. 7. Conditional density of $P_Q(r/r_0)$.

Conditional densities $P_Q(r|r_0)$ of the probability distribution are shown in fig. 7 are given for the intervals after the first bin (outlined markers) and after the fourth bin (filled markers). By switching to the conditional probabilities $W(t;\Delta t|r_0)$ obtained by replacing $P_Q(r)$ with $P_Q(r|r_0)$, the information about the value of the previous interval between shots can be additionally taken into account

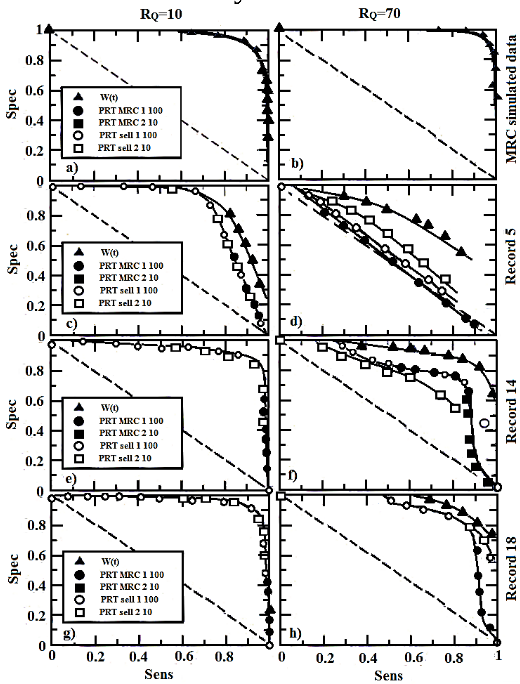

Fig. 8. Dependence of Spec and Sens parameters on Q

Fig. 8(a) and 8(b) show the ROC curves reflecting the prediction efficiency according to the existing MRC model. The MRC model records are obtained in $l = 2^{21}$ and for values of $R_Q = 10$ and $R_Q = 70$ and have a linear correlation with a 1/f power spectrum. It can be concluded from these figures that in these cases the statistics are effective (compared to the records obtained from directly observed data), the prediction efficiency in both cases is very high, and the predictions are comparable to each other. Figures 8(c)-(h) show the ROC curves obtained for three given values 5,14,18 of heartbeat interval records (out of twenty records). These images also show the corresponding results obtained for the records observed with the PRT technique. The figure shows that in all three records considered, both the ROC curve and the RIA technique provide reasonably good comparable predictions when $R_Q = 10$, while when $R_Q = 70$ the RIA predictions exceed the accuracy characterized by the ROC curves in all three cases, especially Sens=1 near prices.

At this point, PRT forecasts based on “learning” from observed records are better than forecasts learned from model records. The reason for this fact is that there is a rather good level of learning statistics and the limited ability of the MRC model to describe short-term dynamics of heartbeat intervals, including individual changes in physiological regulation.

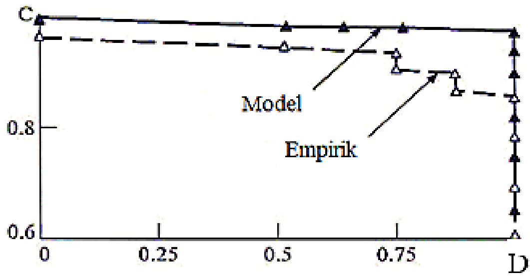

Fig. 9. ROC curve for value $W(t;\Delta|r_0)$
Here C=Spec and D=Sens

It can be seen from Fig. 9 that the ROC curve for the $W(t;\Delta|r_0)$ value obtained using the approximation of the $P_Q\,(r/r_0)$ characteristics for the multifractal model shown with a solid line is above the ROC curve obtained using the empirical $P(r|r_0)$ value for the real data (dashed line) at all values of the threshold. A curve bounded by two curves characterizes the resulting gain.

The studied random signal of the real heart rhythm is distorted by additive noise for two main reasons. The first of them consists in the possibility of the random nature of the measurement noise, which is caused by the limited accuracy of the measuring equipment.

A comparative analysis of the effectiveness of forecasting is carried out with the help of PRT and RIA-technologies that use linear and non-linear organizers of long-term memory. In the presence of normal and regularly distributed additive noise, the robustness of prediction in both approaches was considered. When analyzing the recorded random signals generated by physiological systems (in particular, the cardiovascular system), the influence of noise factors during measurement and measurement errors are very large, and assuming the absence of noise can lead to a decrease in the validity of the result.

When analyzing real recordings of the heart rhythm, using additional analysis (Sens sensitivity operator, which shows the frequency of correct predictions of Q events, that is, events greater than the Q limit, and Spec specification operator, which shows the frequency of correct predictions of non-Q events, that is, events not greater than the Q limit), instead of prediction based on RIA has been given. This analysis, called “receiver operator characteristic” (ROC), has been more effective in most cases.

Let us denote the number of correct and incorrect predictions of Q events by N_{11} and N_{01}, and the number of correct and incorrect predictions of non-Q events by N_{00} and N_{10}. Then the number of wrong predictions

$$D = N_{11}/(N_{11} + N_{01}) \text{ və } \alpha = N_{10}/(N_{00} + N_{10}) \qquad (8)$$

correspondingly will be equal to the fraction of correct predictions of Q events and incorrect predictions of non-Q events. The plot of D versus α is called ROC curve

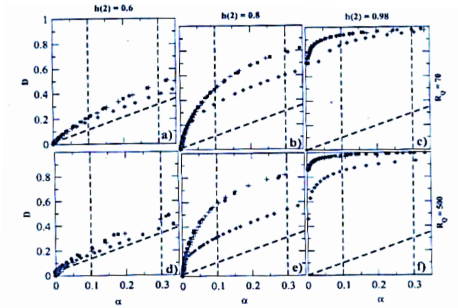

Fig. 10. Dependence graphs of D and α

Let's compare the effectiveness of RIA and PRT analysis when predicting jumps based on information about the linear complex of long-term dependence on the basis of synthetic data obtained according to the MRC model with the addition of additive Gaussian noise and averaged according to 20 different Gaussian distributions of noise. At this time, let's take the length of the sequence $L = 2^{21}$, obtained with values of $h(2) = 0.6, 0.8$ and 0.98 ($\gamma =$

0.8; 0.4 and 0.04) (γ=0.8,0.4 and 0.04), respectively. In PRT, the length of the precursor sample is k=2,3 and 4, in MRC we will choose the number l so that the total number of samples l^k is equal to 10^4. Fig. 11a-c for $R_Q = 70$ when α≤0.35, fig. 11 d-f shows the graphs of ROC curves for $R_Q = 500$.

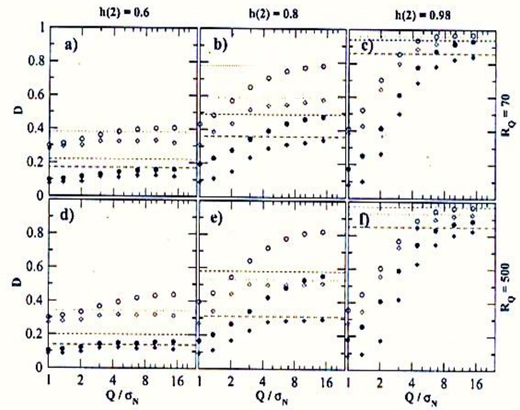

Fig. 11 graph of Q and S/N dependence

As the S/N value, they usually take the correct ratio of the amplitude S of the signal to the standard deviation σ_N of the noise. Since we are interested in events larger than Q, we can assume that $S/N=Q/\sigma_N$. It can be seen from Fig. 11 that the predictions by PRT are still better than those by RIA, even in the presence of strong obstacles.

The fourth chapter deals with the problem of segmentation of non-stationary time series given by electrocardiograms. This allows to determine the boundaries separating qualitatively different components of the rhythmogram according to their statistical characteristics. In order to find the change points of the time series, the method of non-parametric estimation of structural change points in time series models with instability was used. This method is a generalization of the iterative cumulative sum of squares algorithm (ICSS algorithm).

Iterative cumulative sums of squares (ICSS) method was proposed to detect multiple change points of the instability function.

The essence of the method consists of the following.

Consider a stationary time series $\{a_t\}$ with zero mean and variance σ_t^2 $(t = 1, \ldots, T)$. Suppose that the cumulative sum of the series $\{a_t\}$ is of the form $C_k = \sum_{R=1}^{n} a_k$ and

$$D_k = \frac{C_k}{C_T} - \frac{k}{T},\ k = 1, \ldots, T,\ v\text{ə}\ D_0 = D_T = 0 \qquad (9)$$

İs the centered (and normalized) cumulative sum of squares.

For a constant $\sigma_t = \sigma$ variance, the sequence $\{D_k\}$ oscillates around zero. If sudden changes in the variance of σ_t are possible, then the plot of dependence of D_k on k will most likely be within certain limits. These bounds are calculated by analyzing the asymptotic distribution of D_k given any constant variance

$$k^* = \arg\max_k |D_k| \qquad (10)$$

If this maximum exceeds the above-mentioned boundary conditions $|D_k|$ with a value level a, then k^* can be considered as the value of the change point of the dispersion.

In order to more accurately detect the boundary where the dynamic system is realized, along with the initial signal, a derivative evaluation signal constructed according to the values of the fractality index of the local fractal dimension is used. The main quantitative characteristic of the fractal set A is the fractal dimension D. This measure was introduced by Hausdorf in the following formula:

$$D = \lim_{\delta \to 0} \frac{lnN(\delta)}{\ln(\frac{1}{\delta})} \qquad (11)$$

Here N(δ)– is the minimum number of spheres of radius δ covering the set A. The basis for the determination of (4.56) is the asymptotics for δ for fractal sets determined by the following expression:

$$\text{if } \delta \to 0 \text{ then } N(\delta) \sim (1/\delta)^D \qquad (12)$$

The fractal dimension of a time series can be directly calculated using the cell dimension D_c, which is also called the Minkowski dimension or box dimension.

Regularly divide the segment [a,b] by the points $t_1, \ldots t_{m-1}$:

$$\omega_m = [a = t_0 < t_1 \ldots < t_{m-1} < t_m = b]\ , \delta = \frac{b-a}{m} \qquad (13)$$

and construct the graph of the function $y = f(t)$ with rectangles of width δ and height $A_i(\delta)$ (fig. 14)

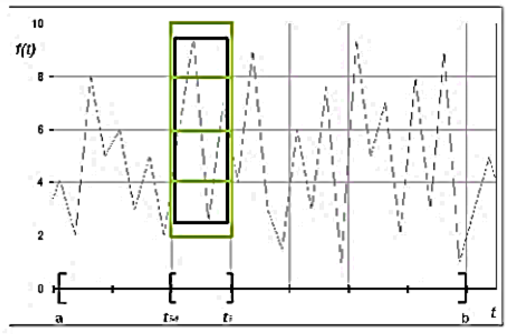

Fig. 12. The fragment of the maximal (gray rectangle) and minimal (black rectangle) coverages on the $[t_{i-1}, t_i]$ segment of the graph of the fractal function.

$$\mu = D_\mu - 1 \tag{14}$$

The indicator μ is called the fractality index, and the dimension D_μ is called the minimal covering dimension. The value of μ is related to the stability of the time series: the more stable the behavior of the initial series itself (that is, the oscillations occur near a level), the larger the value of μ, in which case the opposite is also true.

If *f(t)* is a realization of a Gaussian process, then the Herst exponent H is related to the dimension D_μ and hence also to the index μ by the following expression:

$$H = 2 - D_\mu = 1 - \mu \tag{15}$$

So, in this case $H = H_\mu = 1 - \mu$. However, real physiological time series are not Gaussian series in general, and so H_μ and H can differ greatly.

It would be correct to introduce a function *μ(t)* with μ values defined in the minimal interval τ_μ that precedes the interval *t*. In such an interval, the value of μ can still be calculated with reasonable accuracy. Since the time series in practice is always of finite length, the interval τ_μ is of finite length. When calculating heartbeat rhythmograms, we adopted $\tau_\mu = 24$ *hours*, $\delta = t_i - t_{i1} = 1$ hour, *b-a=30×24=720 hours*, m=*30.*

Let's divide the interval of values (a,b) of the time series f(t) into intersecting intervals of length τ_μ, which are shifted from each other by 1 point (that is, by the value of δ).

Let us denote the jth sliding interval of length τ_μ by $\tau_\mu^{(j)}$ $(j = 1, \dots, m; m = 30)$; Let us put a pair of numbers (b_j, μ_j) against each starting point of the interval $\tau_\mu^{(j)} = \left[t_0, t_{\tau_\mu}\right]$, $\tau_\mu^{(m)} = \left[t_{m-\tau_\mu}, t_m\right]$ and $\tau_k^{(j)}$. Thus, we get the values of b(t) and μ(t) at all $t = t_0, t_1, \dots t_{m-\mu}$ points. Based on the arrays obtained from these values, we calculate the following characteristics: average values of μ and b quantities $\langle\mu(t)\rangle$ and $\langle b(t)\rangle$, maximum and minimum values $\mu_{max,}\mu_{min}, b_{max,}b_{min}$; also characterizes the dispersion (variability) of μ(t) and b(t) values.

By repeating the above calculations several times, we calculate the average values of $< \mu(t) >, < b(t) >, < \delta\mu >$ and $< \delta b >$ for all the obtained realizations, which give an idea of how the local μ and b characteristics behave for the studied time series. Experimental studies conducted for different types of fractal time series show that the quantities μ and b are less variable with less variability of the quantity b. Since the value of b is closely related to the distribution characteristics of the time series increments and hence to the instability of the time series, the initial *f(t)* for dividing the non-stationary series into "quasi-stationary" parts in order to apply a segmentation calculation procedure based on the detection of the jump of the instability function along with the series, it is appropriate to use the series of *b(t)* values and accept the average value of the change points obtained according to the series of the initial *f(t)* and *b(t)* values as the value of the series change points.

Considering this property of the b(t) function, the following method can be proposed for detecting the boundaries of the quasi-stationary parts of the time series. According to the initial f(t) signal, the derivative signal of the estimation of the indicator b(t), which characterizes the local fractal dimension of the time series, is constructed by the sliding window method. Difference points are found in the derivative and the original signal according to the algorithm. The locations of these points are reconciled and the average value is taken, which will be the boundary of the neighboring parts of the quasi-stationarity.

RESULTS

1. Repetitive intervals of heartbeats were analyzed to predict the spikes of the random process consisting of exceeding any Q-threshold for differential diagnosis of the state of the cardiovascular system. In order to determine statistical parameters of heartbeat dynamics, heartbeat intervals were modeled based on a multifractal approach. Another algorithm for generating multifractal clusters is obtained by applying the multifractal random walk method.

As a result, the following informative parameters were determined for the functional diagnosis of the cardiovascular system: the generalized Herst index, the autocorrelation function of repeated intervals greater than the Q-threshold, the density of the distribution of the sizes of clusters of repeated intervals, the probability of the distribution of repeated intervals.

2. The prediction of large Q repetition intervals of the heartbeat is based on long-term memory and the application of repetition interval statistics (RIA), requires less volume and is more useful. To get a more accurate prediction, two indicators are defined for different fixed Q_p values: sensitivity (Sens) and specificity (Spec).

3. A comparative analysis of the methods of predicting the jumps of fractal dynamic series using short-term and long-term information was carried out. An alternative RIA approach using long-term memory performs better in all cases in predicting Q-intervals.

4. When using information about the linear and non-linear complexities of long-term dependence in the presence of additive noise in the repetition intervals of the heartbeat, the effectiveness of the methods of predicting jumps of dynamic series with fractal properties is analyzed and the stability of these methods at different levels of the obstacle is evaluated.

5. Evaluation of statistical properties of physiological signals can be carried out in small time intervals. As a result of increasing the discretization frequency of the continuously analyzed physiological process, by increasing the number of discretized points, it is possible to reduce the evaluation interval to a certain limit. As long as the correlation density between neighboring points is not too large. It is for this reason that the stationarity of real physical processes is limited

from a theoretical point of view, and the concept of quasi-stationarity is practically applied.

6. The calculation procedure for segmentation of fractal non-stationary signals is proposed. Inflection points are found in the derivative and the original signal, their charges are compared, and the average value taken as the value of the border of two adjacent quasi-stationary parts of the non-stationary time series is taken.

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Personal activity of the plaintiff in joint cases with co-authors
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