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The OMIS Software System: A Module for Analysis of Physiological Processes

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Introduction

Analysis of the time series of *RR*-intervals in electrocardiograms (ECG) is the main method of studying the dynamics of the sinus rhythm [2, 14, 15, 19, 21, 27].

Dynamics of *RR*-intervals is described using standard statistical parameters (simple mean, variance, etc.) and spectra within various frequency ranges (LF, HF, VLF) [2, 7, 15, 19, 27]. Recently, several techniques for automated analysis of the dynamics of other ECG elements have been suggested [24, 26, 29, 30].

Methods for computer analysis of electroencephalograms (EEG) are usually limited to analysis of the frequency spectrum within the ranges of α-, β-, γ-, δ-, and θ-waves and analysis of correlation (cross-correlation functions) between instantaneous values of the source processes [3, 17]. In some cases, the distribution of intervals between the points of EEG intersection with the zero level [4], the amplitude distribution, and some other distributions are analyzed. However, these methods of analysis do not take into account a fundamental property of physiological processes: the relationship of various phases of individual activity cycles to the functional state of the human body [9, 11, 25].

Only methods taking into account the qualitative nonuniformity of the dynamics of physiological processes (inhalation–exhalation, systole–diastole, muscular contraction and relaxation, etc.) can provide comprehensive analysis of these processes. To study the dynamics of various physiological processes it is necessary to know how the preceding phase of a process affects the following phase.

Nonlinear dynamics methods are insufficient to solve this problem. These methods use an autocorrelation function and its spectrum for assessing the fractal dimensionality, so that the information about the fine phase structure of the oscillation process is lost [20].

Methods based on clinical knowledge (typological classification of EEG [13] or ECG [22, 23] or structural description of the ECG elements and the cardiosignal as a whole [5]) also do not provide adequate description of the temporal dynamics of physiological processes.

The methods of analysis of the temporal dynamics of physiological processes considered in this work are based on dividing the source process into individual oscillations and generating discrete series of various characteristics of these individual oscillations. The resulting time series are considered as elements of the source physiological process as a systemic whole [9, 11, 25].

The goal of this work was to describe an information technology used for systemic analysis of the dynamics of characteristics of individual oscillations of physiological processes. So far, this technology provides analysis of ECG, EEG, and respiration-like oscillations (pneumogram, photoplethysmogram (PPG), rheogram). The number of channels for information analysis is now limited to four.

The developed information technology is implemented using the module for analysis of physiological processes of the OMIS software system [12]. The software module implements the following functions.

1. Reliable identification of the critical points of ECG, EEG, PPG, pneumogram, etc.

2. Measurement of various intervals and amplitudes of individual activity cycles.

3. Generation of vector time series consisting of the intervals and amplitudes of individual activity cycles or their average values per several cycles (or per certain time interval).

4. Transformation of time series of characteristics of individual oscillations into binary sequences (decrease of the time series is denoted by 0; increase, by 1).

5. Generation of parameters of the dynamics of characteristics of individual oscillations using both

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conventional statistical methods and such special statistical techniques as estimation of the time series randomness, ψ-matrix method, etc.

6. Use of the research module of the OMIS system [10] for selecting the most valuable information from the obtained set of EEG, ECG, PPG, pneumographic, and rheographic parameters and the relationships between these parameters.

7. Use of the resulting information about the physiological processes for automated development of diagnostic and prognostic algorithms.

Main Menu

The main menu is invoked by selecting the Process field (Fig. 1). The menu contains the following options.

1. *Select process file*. This option provides the process import from ASCII file into the digital case history (patient's record).

2. *Processing of source data*. This option provides identification of the critical points of oscillations and measurement of the characteristics of individual activity cycles.

3. *Slow process*. This option provides analysis of time series consisting of the characteristics of individual oscillations. The frequency of these processes is considerably lower than the frequency of the source processes, so that we denote them as slow processes (source processes are denoted as quick processes).

4. *Integral characteristics of process*. This option provides access to the results of analysis for individual patients.

5. *Determine slow process file*. This option provides import of the obtained time series (slow process) into the digital case history (DCH) with further analysis using all computational resources of the OMIS system. Such procedure is necessary, for example, for analysis of the results of monitoring of blood pressure and pulse (in this case, the source data are presented as a two-dimensional time series).

6. *Information deletion*. This option provides deletion of the source process, the file containing the slow oscillation dynamics, the results of analysis, etc.

Process Import from File into Digital Case History

In the OMIS system (version 2.9), the process import from ASCII file into the digital case history is performed from the Process field. To form the field, it is necessary to specify the number of channels (no more than 4), channel type (ECG, EEG, respiration), and the amplitude variation range.

The process sampling step should be compatible with the digitization frequency. For example, if the frequency is 1000 Hz, the sampling step can be 10, 5, 4, 2, or 1 msec.

The recording time for each process should not exceed 16,300 cycles or periods of the process. For a cardiogram measured at a pulse rate of 75 beats/min,

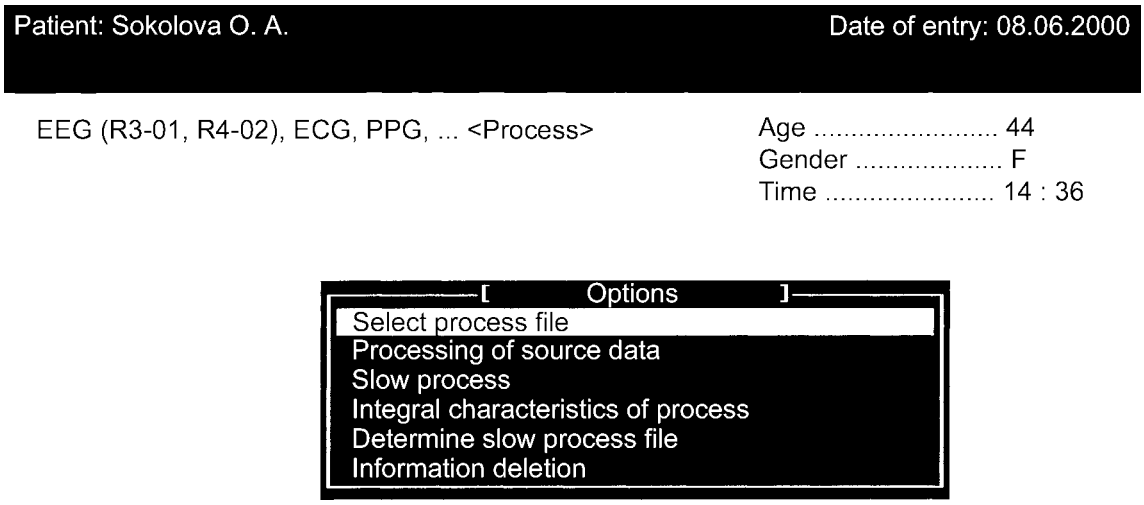

Fig. 1. Main menu of the module for analysis of physiological processes of the OMIS software system.

the recording time is about 3.5 h; for EEG, about 30 min. In the case of multichannel recording, the import duration is limited by the rate of the fastest process. A segmentation mechanism is used for analyzing very long records. It allows processes of any duration to be imported.

A memory volume of 5-6 Mb is required for storing one channel of hour-long ECG record (or ten-minute EEG record), the sampling step being 4 msec. Upon forming time series of characteristics of individual oscillations the source process can be completely or partially deleted. A database stored on a 15-30-Gb hard-disk unit can contain information about dynamics of several thousand ECG, EEG, etc.

The algorithm of identification of critical points of physiological processes and measurement of intervals and amplitudes is initiated by pressing the key F6 (Count).

Measurement of Characteristics of Individual Activity Cycles and Generation of Time Series

Processing of smooth processes (EEG, pneumogram, plethysmogram, etc.) includes only identification of the points of maximum and minimum of each oscillation. This allows the amplitudes V_g and V_d and durations g and d of the ascending and descending waves, respectively, to be calculated. The following characteristics are also calculated:

– period $L = g + d$;
– phase duration asymmetry $\Delta = g - d$;
– mean amplitude of oscillation $V = (V_g + V_d)/2$;
– ascending phase rate V_g/g;
– descending phase rate V_d/d;
– asymmetry of ascending and descending phase rates $\Delta = V_g/g - V_d/d$.

These characteristics can be averaged over a certain time interval or number of oscillations. If a characteristic is averaged over a time interval, time series characterizing different processes are synchronized.

Processing of ECG includes identification of the following critical points:

– initial point P_i of P wave;
– extremum P of P wave;
– initial point Q of QRS complex;
– extremum R of QRS complex (R wave);
– end point S of QRS complex (S wave);
– extremum T of T wave;
– end point T_f of T wave.

The following intervals and amplitudes are measured:

– time interval P_iQ (PQ) from the pulse generation in the sinus node to the beginning of depolarization of the left ventricle;
– time interval P_iT_f (PT) from the beginning of atrial depolarization to the end of ventricular repolarization;
– duration QT_f (QT) of electric ventricular systole;
– cardiac cycle duration RR;
– duration T_fP_i (TP) of electric diastole;
– width QS of QRS complex (duration of ventricular depolarization);
– duration ST of the ascending phase of T wave;
– duration TT_f of the descending phase of T wave;
– duration ST_f of ventricular repolarization;
– total duration QP of systole and diastole;
– amplitude VR of R wave;
– amplitude VT of T wave;
– amplitude VP of P wave.

The amplitude of R wave is determined as the difference between the ordinates of the points R and Q. The amplitude of T wave is determined as the difference between the ordinates of the points T and S. The amplitude of P wave is determined as the difference between the ordinates of the points P and P_i. In addition, the following characteristics are calculated: ratio VR/VT of amplitudes of R and T waves; ratio QT/TP of durations of electric systole and diastole; ratio QT/RR of the electric systole duration to the cardiac rhythm duration; etc.

Then, time series composed of the ECG elements and their ratios are formed.

The algorithm for determination of critical points is not considered in this work. It is based on discrete differentiation and logical testing and has two option sets (for ECG and smooth processes (EEG, respiration, etc.)). It provides determination of the number of discrete readings used for smoothing, localization of extremums and inflection points, etc.

The reliability of identification of the QRS complex is checked using two logical conditions providing localization of the point R if the extremum T is higher than the point R.

Options specified by user are stored in PC memory. Generally, these options are individual for each patient.

An example of identification of critical points for a four-channel process (two EEG leads, ECG lead, and PPG) is shown in Fig. 2.

Critical points are on the screen with color marks. This facilitates visual detection of artifacts and checking of the accuracy of estimation of intervals and amplitudes (another method for revealing artifacts and

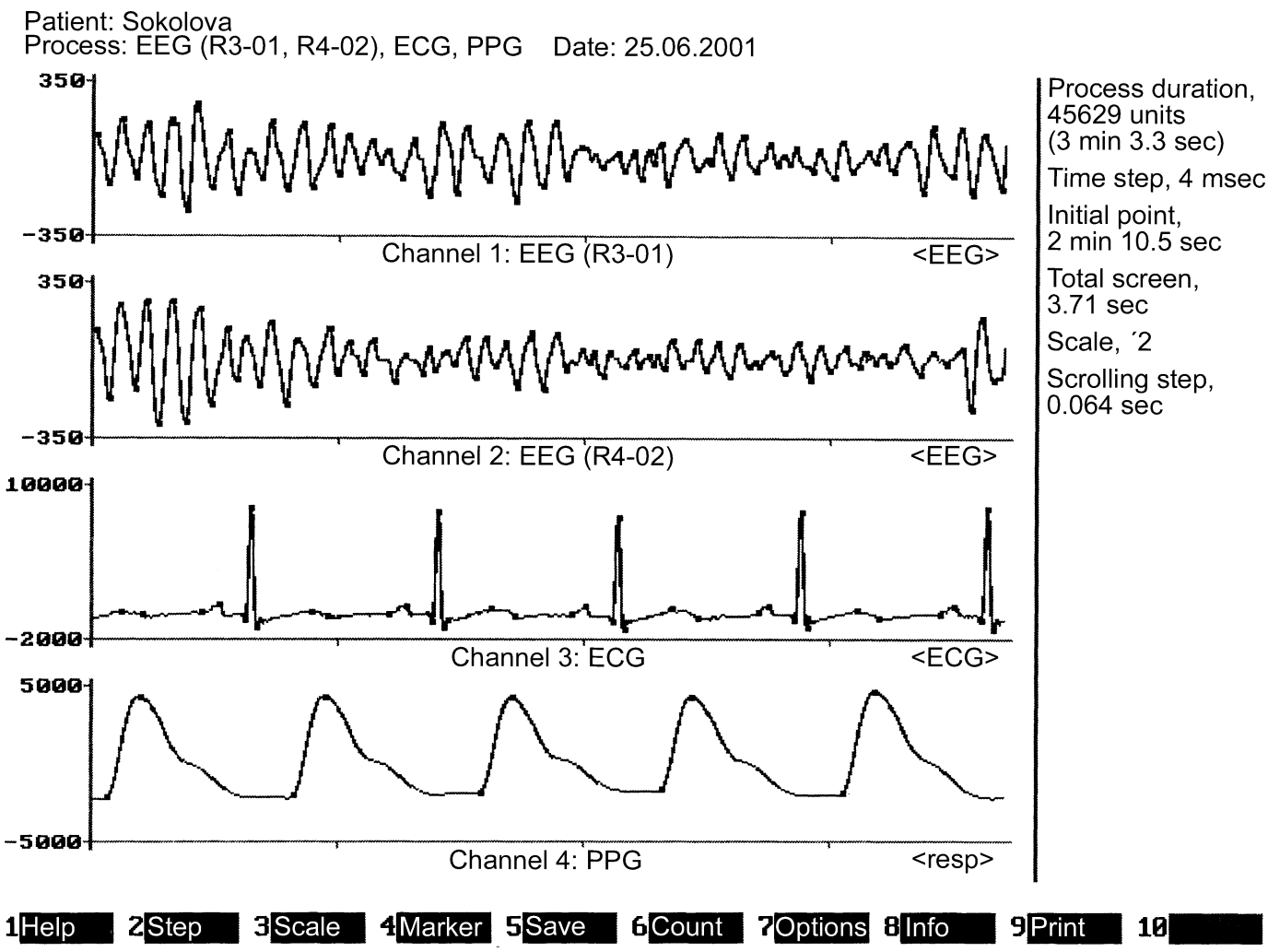

Fig. 2. Results of import of a four-channel process (two EEG leads, ECG lead, and PPG) upon identification of critical points of physiological processes and measurement of intervals and amplitudes.

incorrectly estimated process elements is described below). In some cases, the user can correct errors in identification of critical points. Uncorrectable errors are almost always caused by detection artifacts. Such points should be removed. Correct selection of options provides reliable identification of critical points even in very noisy records (probability of missing a critical point (and, thus, the probability of incorrect measurement) does not exceed 1%).

It should be noted that identification of critical points in standard noiseless records (similar to that shown in Fig. 2) is performed without the user's participation.

In general, the error of measurement of intervals and amplitudes depends on the sampling step. To provide sufficient accuracy of measurement, the sampling step should not exceed 5 msec (sampling with a frequency of 200 Hz). The smaller is the sampling step, the higher is the accuracy of measurement. However, a decrease in the sampling step also causes an increase in the duration of analysis. The algorithm operates at any sampling (digitization) frequency.

The source process can be viewed by scrolling with cursor keys. The scale can be changed 2-10-fold by pressing the key F3.

A marker is activated by pressing the key F4. Using the marker, the limits of a time interval can be determined. This is useful for analysis and removal of artifacts.

Physiological Process as a Time Series of Characteristics of Individual Cycles

Each cycle of the sinus rhythm is described with a set of measured characteristics and their functions. As a result, the ECG is represented as a vector time series denoted as ECG(n) and consisting of various characteristics of individual activity cycles: RR, PQ, PT, QT, TP, ST, TT_f, ST_f, QS, VR, VT, VP, QT/TP, ST/TT_f, and VR/VT:

$$\mathrm{ECG} \to \mathrm{ECG}(n) = \left\{ \begin{array}{c} RR(n) \\ PQ(n) \\ PT(n) \\ QT(n) \\ TP(n) \\ ST(n) \\ TTf(n) \\ STf(n) \\ OS(n) \\ VR(n) \\ VT(n) \\ VP(n) \\ QT/TP(n) \end{array} \right\}, n = 1, 2, 3, \ldots N.$$

Oscillations constituting smooth processes $s(t)$ (EEG, PPG, pneumogram, etc.) are described with another set of components:

$$V_g,\ V_d,\ V,\ g,\ d,\ L,\ \Delta,\ V_g/g,\ V_d/d,\ \Delta'.$$

Corresponding time series are denoted as EEG(n), PPG(n), etc.:

$$s(t) \to \left\{ \begin{array}{c} V_g(n) \\ V_d(n) \\ V(n) = \dfrac{V_g(n) + V_d(n)}{2} \\ g(n) \\ d(n) \\ l(n) = g(n) + d(n) \\ \Delta(n) = g(n) - d(n) \\ V_g^i/g_i \\ V_d(n)/d(n) \\ V_g(n)/g(n) - V_d(n)/d(n) \end{array} \right\}, n = 1, 2, 3, \ldots N,$$

where N is the number on ECG cycles under consideration, EEG periods, respiration cycles, etc. or the sample number. If each sample contains s oscillations, the sample number N is equal to the total number of oscillations divided by s; if τ is the time step, $N = T/\tau$, where T is the total duration of the analyzed process.

Results of measurement of characteristics of individual activity cycles (time series components) are stored in tabular form (Fig. 3).

Tables containing time series components are invoked from the main menu (*Slow process* option) or by moving the cursor to the Process field and pressing Enter. If two or more processes are detected simultaneously, a separate table is generated for each channel. Switching from one table to another is performed by selecting the corresponding (key F3).

The option *Sample* (key F2) provides generation and analysis of time series averaged over different numbers of cycles (periods) or a given time interval. The selected sampling step is entered in the table. For example, the table in Fig. 3 describing the dynamics of characteristics of individual activity cycles of ECG was obtained for a sampling step of 1 period.

The option *Time* (key F4) provides indication of time elapsed from the beginning of the process in minutes and seconds instead of indicating the sequence number of the current activity cycle.

The option *Plot* (key F6) invokes a menu containing types of time series components. The option provides plotting of time curves of selected characteristics (no more than 4) within selected interval. The interval is specified in a special window (invoked by pressing Alt F8) by selecting the cycle numbers or boundary time points.

An example of time curves for RR, QT, TP, and PQ components is shown in Fig. 4.

The curves shown in Fig. 4 represent so-called respiration waves. It can be seen that the wave patterns are different for different elements of the cardiac cycle. Some parameters of slow time series are indicated in the right part of the plot (simple mean (msec); variance (msec^2); variability index *var* = *stddev*/*mean*, where *stddev* is the standard deviation and *mean* is the simple mean, frequency *freq* (Hz)). The software module for analysis of physiological processes provides comprehensive analysis of these time series (dynamics randomness estimation, determination of the power spectrum and ratios between various components, etc.).

The option *Export* (key F7; see Fig. 3) creates an ASCII file for export of already generated time series. There is usually no need for exporting time series to

Patient: Sokolova O. A. Date of entry: 08.06.2000

Process: EEG (R3-01, R4-02), ECG, PPG [time: 3 min 3.3 sec time step: 4 msec]
Channel: ECG [number of points: 246]
Sampling step: 1 period

–	#	RR	PT	QT	TP	QS	ST	TTf	STf	PQ	VR	VT	VP	QT/TP
	1	752	512	340	236	48	212	80	292	172	9299	1413	809	1.441
	2	728	516	344	238	48	204	92	296	172	8850	1586	823	1.444
	3	744	500	348	253	52	208	88	296	152	8466	1618	437	1.373
	4	748	488	348	232	48	200	100	300	140	8863	1123	560	1.500
	5	760	516	344	236	48	200	96	296	172	9051	1247	814	1.458
	6	756	512	336	232	52	196	88	284	176	9089	1330	809	1.448
	7	740	536	348	248	52	212	84	296	188	9040	1644	836	1.404
	8	724	496	348	235	48	204	96	300	148	8635	1607	470	1.483
	9	724	480	336	220	52	204	80	284	144	8519	1516	395	1.527
	10	744	504	332	228	48	216	68	284	172	8917	1247	700	1.456
	11	748	524	344	257	52	212	80	292	180	8973	1302	929	1.339
	12	740	484	336	236	52	192	92	284	148	8930	1509	707	1.424
	13	728	508	340	232	52	200	88	288	168	8904	1430	901	1.466
	14	724	508	352	234	48	208	96	304	156	8463	1613	698	1.506
	15	740	484	344	232	52	224	68	292	140	8462	1413	623	1.483
	16	748	500	332	252	48	204	80	284	168	9122	1327	763	1.317
	17	752	504	340	259	52	192	96	288	164	8851	1389	778	1.310
	18	740	496	340	248	52	200	88	288	156	9083	1285	674	1.371
	19	724	488	336	220	44	208	84	292	152	8842	1652	813	1.527
	20	724	504	340	236	48	224	68	292	164	8400	1551	693	1.443

1Help 2Sample 3Channels 4Time 5Count 6Plot 7Export 8Function 9Print 10

Fig. 3. Time series table containing intervals and amplitudes of ECG elements and their ratios.

external statistical systems because the software module for analysis of physiological processes provides great scope for statistical processing of information.

Analysis of Time Series of Characteristics of Individual Oscillations of Physiological Processes

The option *Function* (key F8) invokes a function menu for analysis of characteristics of individual oscillations of physiological processes (Fig. 5).

The *Main statistical parameters* option provides calculation of various statistical parameters (simple mean (*mean*), variance (*disp*), mean-square difference of successive values of the time series (*s_disp*), k = *s_disp*/*disp*, standard deviation (*stddev*), variability index (*var* = *stddev*/*mean*)) for selected components of the slow process.

The resulting tables for ECG(n), EEG(n), etc., contain valuable information about variability of dynamics of the elements of physiological processes.

The *Pearson correlation matrix* option provides calculation of all pairwise coefficients correlation between data columns containing characteristics of individual oscillations (Fig. 3). An example of such matrix for 534 successive ECG cycles measured in an apparently healthy subject in the state of rest is given in Table 1.

Table 1 contains only significant correlation coefficients (significance level $p < 0.001$). The correlation matrix contains more than 50% of significant correlations between the cardiac rhythm elements measured in apparently healthy subject in the state of rest. This is typical for such matrices. However, only two correlations (*RR–TP* and *PQ–PT*) are always very strong. These correlations are important for understanding the information morphology of the sinus rhythm elements. In particular, the coefficient of correlation between *RR* and *QT* is rather low (0.399 in Table 1; in other patients it is usually lower), so that it can be concluded that the systole and diastole durations are determined by different mechanisms. The rhythm is almost functionally determined by the electric diastole duration.

The *First-order ψ-state matrix* option is used for generating for given column a 2×2 matrix containing

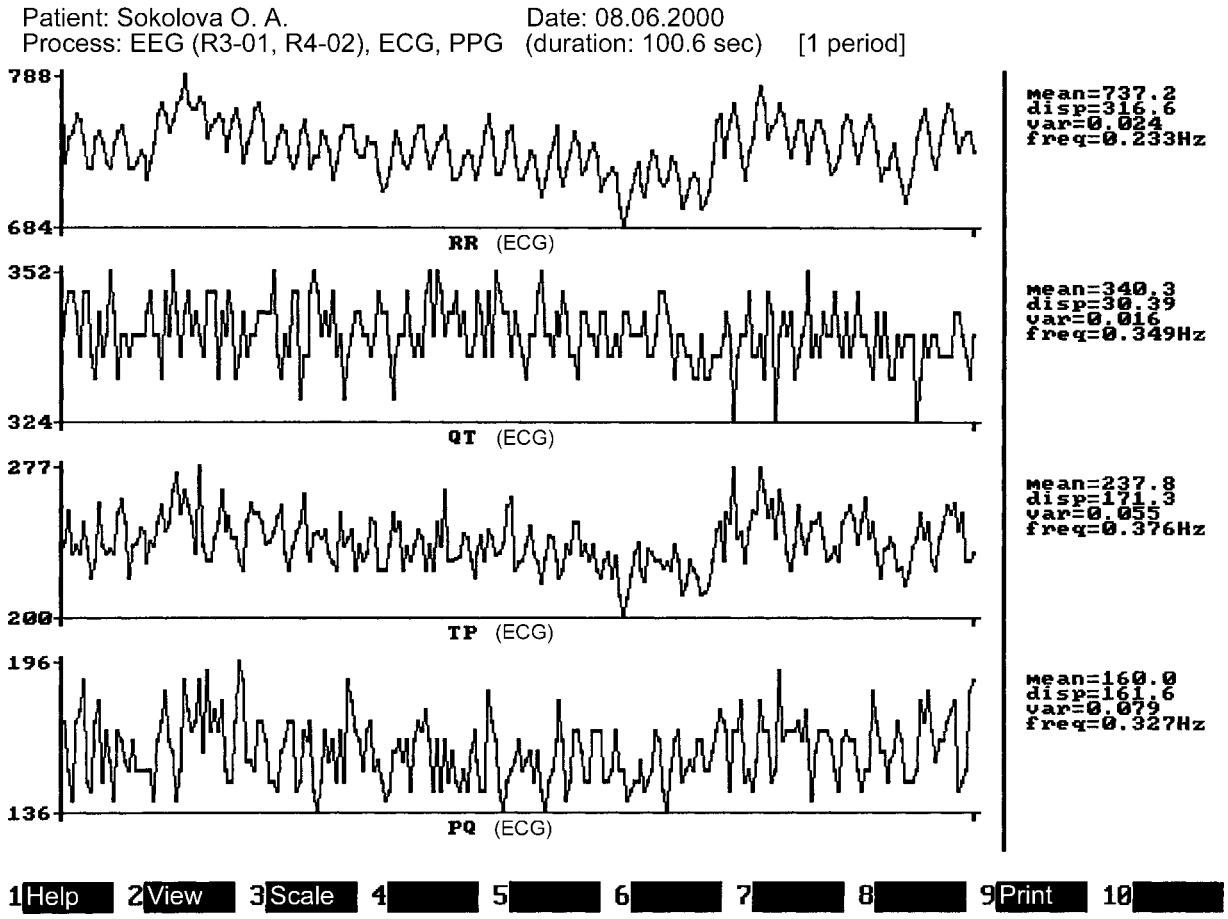

Fig. 4. Dynamics of four ECG elements (*RR*, *QT*, *TP*, *PQ*) for 246 successive ECG cycles.

information about the dynamics of an individual element of the physiological process (a single slow time series).

The *Second-order ψ-state matrix* option is used for generating a 4×4 matrix containing information about the dynamics of two elements of the same process (or measured using two analyzed channels).

The y-state method for generation and analysis of ψ-state matrices [11] is considered below in more detail.

ψ-State Method

Transformation of a Time Series of Characteristics of Individual Oscillations into a Binary Sequence. Consider a component $\{x(n)\}$ (n = 1, 2, 3, ..., N) of a time series of characteristics of individual oscillations. The series can be transformed into a binary sequence $b(n)$ (a time sequence consisting of 0 and 1) by the following rule:

$$b(n) = \left\{ \begin{array}{c} 1,\ x(n) > x(n-1) \\ 0,\ x(n) < x(n-1) \\ x(n-1),\ x(n) = x(n-1) \end{array} \right\}.$$

Thus, the vector process $X(n)$ is transformed into a binary vector process $B(n)$. An example of such transformation of a fragment of time series for 3 ECG characteristics is given below:

RR: 10111011001100110010010001101101100110110011011001101100
QT: 01000001101100001010101010100100010001011011010 0 (*)
TR: 10011011001000110010011001001101100110110011011001101100

There are different approaches to analysis of the resulting time series. The approach implemented in the OMIS software system is considered below.

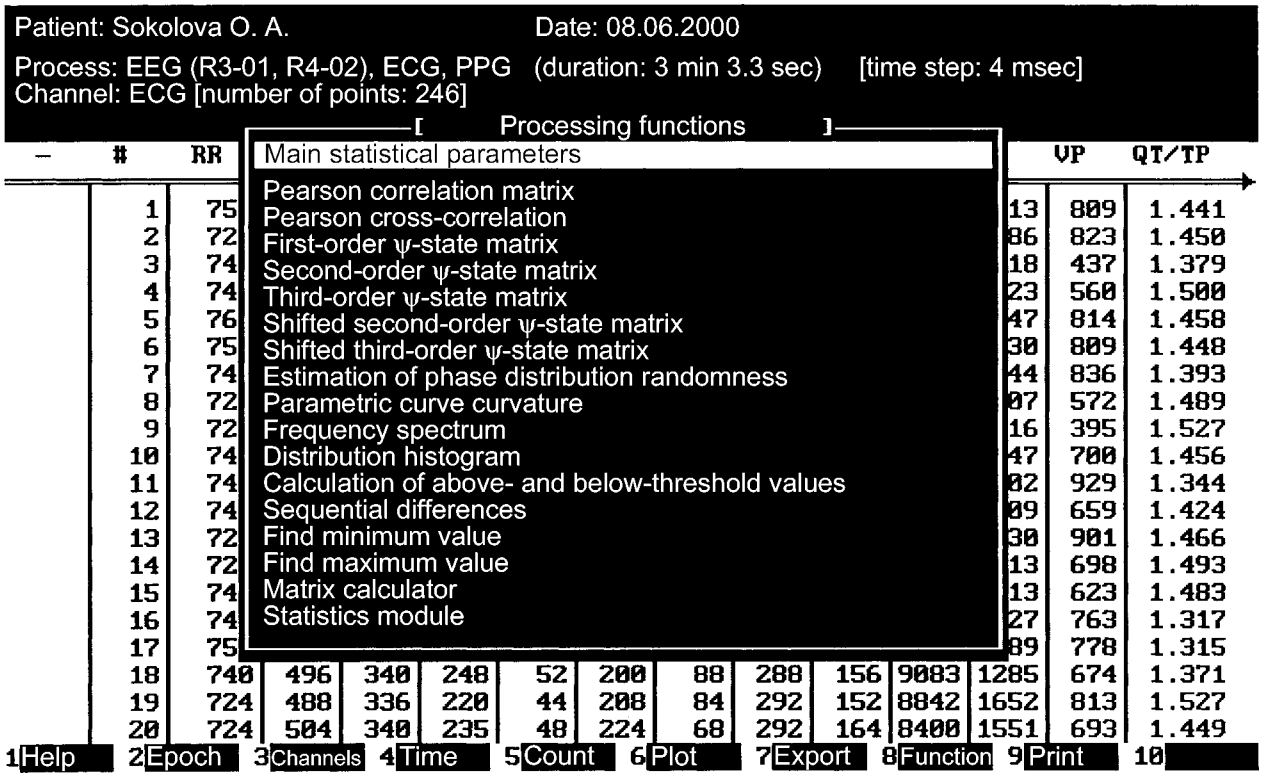

Fig. 5. Function menu for analysis of characteristics of individual oscillations.

First-order ψ-States and Estimation of Their Dynamics. Values of any component of the time series (*) (0 or 1) are denoted as first-order ψ-states. The number of ψ-states for each component of the time series is $N - 1$, where N is the number of oscillations (activity cycles). The dynamics of such binary sequences can be described by a 2 × 2 matrix of 1-1, 1-0, 0-1, and 0-0 transition frequencies (first-order ψ-state matrix).

TABLE 1. Pearson Correlation Matrix

Patient: 6. ECG Date: 03.10.2001
Process: ECG [1 period]. N = 534
Pearson correlation matrix Significant correlations
Number of significant correlations: 35 (53.0%) $p < 0.001$

Characteristic	*RR*	*PT*	*QT*	*TP*	*QS*	*ST*	TT_f	ST_f	*PQ*	*VR*	*VT*	*VP*
RR	1.000											
PT	0.332	1.000										
QT	0.339	0.351	1.000									
TP	0.984	0.295	0.348	1.000								
QS	–	–	0.571	–	1.000							
ST	0.326	0.242	0.427	0.299	–	1.000						
TT_f	0.190	0.260	0.468	0.153	–	–0.423	1.000					
ST_f	0.478	0.468	0.833	0.418	–	0.511	0.562	1.000				
PQ	–	0.811	–0.263	–	–0.418	–	–	–	1.000			
VR	–	–	–	–	0.193	–	–	–	–	1.000		
VT	–	–	–	–	–	–	–0.175	–0.159	–	0.342	1.000	
VP	0.193	0.359	–	0.181	–	0.144	–	–	0.310	0.233	–	1.000

Thus, each component $\{x(n)\}$ of the time series (*) is characterized by the following matrix:

$$\psi(x) = \begin{pmatrix} \psi_{11} & \psi_{12} \\ \psi_{21} & \psi_{22} \end{pmatrix},$$

where ψ_{11}, ψ_{12}, ψ_{21}, and ψ_{22} are the 1-1, 1-0, 0-1, and 0-0 transition frequencies, respectively. The total number of transition frequencies is $\psi_{11} + \psi_{12} + \psi_{21} + \psi_{22} = N - 2$; ψ_{12} can differ from ψ_{21} by no more than 1. The frequencies are normalized as follows:

$$p_{ij} = \psi_{jj}/(N - 2) \ (i = 1, 2; j = 1, 2).$$

In the subsequent discussion, normalized transition frequencies p_{ij} are denoted as ψ_{jj}.

Consider the physiological interpretation of the parameters ψ_{11} and ψ_{22}. The parameter ψ_{11} is the relative frequency of the slow process component increase (it shows how often the given characteristic of the individual oscillation is observed during the phase of the slow process increase). The parameter ψ_{22} shows how often this characteristic of the individual oscillation is observed during the phase of the slow process decrease.

The matrix trace $\mathrm{tr}\psi(x) = \psi_{11} + \psi_{22}$ can be considered as the slow oscillation period expressed in relative units. It indicates the average content of given characteristic in a single oscillation of a slow process.

Second- and Third-order ψ-States and Estimation of Their Dynamics. Second-order ψ-states are used for comparing dynamics of various elements of vector processes ECG(n), EEG(n), etc.

During each activity cycle (oscillation), a selected pair of components is in one of the following second-order ψ-states: ψ_1 (both components increase in comparison with the preceding cycle), ψ_2 (the first component increases, while the second component decreases), ψ_3 (the first component decreases, while the second component increases), or ψ_4 (both components decrease):

$$\psi_1 = \begin{pmatrix} 1 \\ 1 \end{pmatrix}, \psi_2 = \begin{pmatrix} 1 \\ 0 \end{pmatrix}, \psi_3 = \begin{pmatrix} 0 \\ 1 \end{pmatrix}, \psi_1 = \begin{pmatrix} 0 \\ 0 \end{pmatrix}.$$

If time series of characteristics of individual oscillations are obtained by averaging over a time interval longer than the slowest individual oscillation, ψ-states can be used for description of components of different processes.

Dynamics of any two components X and Y for N successive cycles of time series of characteristics of individual oscillations is described by a matrix of transition frequencies of second-order ψ-states:

$$\psi(x, y) = \begin{pmatrix} \psi_{11} & \psi_{12} & \psi_{13} & \psi_{14} \\ \psi_{21} & \psi_{22} & \psi_{23} & \psi_{24} \\ \psi_{31} & \psi_{32} & \psi_{33} & \psi_{34} \\ \psi_{41} & \psi_{42} & \psi_{43} & \psi_{44} \end{pmatrix} \begin{pmatrix} \psi_1 \\ \psi_2 \\ \psi_3 \\ \psi_4 \end{pmatrix},$$

where ψ_{ij} are normalized (divided by N) transition frequencies; the components of the right column matrix are equal to the number of ψ_1, ψ_2, ψ_3, and ψ_4 states occurring within the interval under consideration.

For example, consider two matrices describing the dynamics of correlation between the amplitude (V) and period (L) and between the durations of the ascending (g) and descending (d) phases for a parietooccipital EEG lead (Tables 2 and 3). The sampling step is one oscillation. The duration of EEG recording is 3 min 3 sec (1860 oscillations) (Fig. 2).

Consider the integral dynamic characteristics calculated from the data contained in the second-order ψ-state matrix:

TABLE 2. Second-order ψ-State Matrix Describing the Dynamics of Amplitude-Period Correlation

Patient: Sokolova O. A. Date: 08.06.2000
Process: EEG (R3-01, R4-02), ECG, PPG [1 period]
Component 1: 2-V (EEG (R4-02))
Component 2: 2-L (EEG (R4-02))
Second-order ψ-State Matrix

State	11	10	01	00	Total
11	0.083	0.075	0.049	0.097	567
10	0.061	0.024	0.059	0.047	355
01	0.039	0.054	0.022	0.077	358
00	0.121	0.038	0.062	0.091	580

TABLE 3. Second-order ψ-State Matrix Describing the Dynamics of Correlation between Durations of Ascending and Descending Phases

Patient: Sokolova O. A. Date: 08.06.2000
Process: EEG (R3-01, R4-02), ECG, PPG [1 period]
Component 1: 2-g (EEG (R4-02))
Component 2: 2-d (EEG (R4-02))
Second-order ψ-State Matrix

State	11	10	01	00	Total
11	0.036	0.056	0.060	0.080	431
10	0.052	0.056	0.098	0.061	495
01	0.054	0.103	0.046	0.061	492
00	0.090	0.051	0.061	0.037	442

– parameter <teta> $((\psi_1 + \psi_4)/(\psi_2 + \psi_3))$ is used for estimating the predominance of unidirectional states (11 and 00) over contradirectional (10 and 01);

– parameter <syn> $(\psi_{11} + \psi_{14} + \psi_{41} + \psi_{44})$ indicates the relative frequency of transitions from unidirectional to unidirectional states (synchronous transitions);

– parameter <recip> $(\psi_{22} + \psi_{23} + \psi_{32} + \psi_{33})$ indicates the relative frequency of transitions from contradirectional to contradirectional states (reciprocal transitions);

– parameter <chaos> $(\psi_{12} + \psi_{13} + \psi_{24} + \psi_{34} + \psi_{42} + \psi_{43} + \psi_{21} + \psi_{31})$ indicates the frequency of other (chaotic) transitions;

– parameter <ro> is used for estimating the correlation between two time series.

Second-order ψ-state matrices for physiological processes are almost symmetrical, i.e., the frequencies ψ_{ij} and ψ_{ji} are close to each other [9, 11]. The parameter of symmetry indicates the deviation of the second-order ψ-state matrix from symmetrical. In the case of complete symmetry, the parameter of symmetry is equal to zero.

Consider some general regularities in the EEG dynamics. The second-order ψ-state matrix describing the dynamics of correlation between the amplitude and period contains mainly synchronous transitions, whereas the matrix describing the dynamics of correlation between the durations of the ascending (*g*) and descending (*d*) phases contains mainly reciprocal transitions. The matrices under consideration are almost symmetrical. There are good grounds to believe that the degree of symmetry depends on the functional state of the brain. The parameters <chaos> for two completely different EEG elements could coincide very closely (to the fifth decimal place). Complete coincidence was observed once. For a rather long time interval (several minutes), the parameters <chaos> for (*V*, *L*) and (*g*, *d*) components measured in the state of rest differ insignificantly.

Some second- and third-order ψ-states depend on the sequence order of components. If the sequence order is changed, ψ_2 changes to ψ_3 (and vice versa); ψ_1 and ψ_4 do not depend on the sequence order of components. Changes in the sequence order of components cause the following permutation of ψ-states: $\psi_1, \psi_2, \psi_3, \psi_4 \rightarrow \psi_1, \psi_3, \psi_2, \psi_4$. This transformation is effected by the following permutation matrix:

$$P = \begin{pmatrix} 1000 \\ 0010 \\ 0100 \\ 0001 \end{pmatrix}.$$

The transformed ψ-state matrix $\psi(y, x) = P\psi(x, y)P$ contains the same (although rearranged) frequencies as the initial matrix, so that the information content of $\psi(y, x)$ is the same as of $\psi(x, y)$.

Many integral parameters of the ψ-state matrix (Trace, Norm, Entropy, Symmetry estimate, <syn>, <recip>, <chaos>, <ro>) are unaffected by this transformation.

For third-order ψ-state matrices six permutations (including the initial matrix) are possible: $\psi(y, x, z)$, $\psi(z, x, y)$, $\psi(x, z, y)$, etc. Each permutation is described by a 8×8 permutation matrix: $\psi(y, x, z) = P_1\psi(x, y, z)P_1$, $\psi(z, x, y) = P_2\psi(x, y, z)P_2$, $\psi(x, z, y) = P_3\psi(x, y, z)P_3$, etc. Thus, the information obtained using the ψ-state method does not depend on the sequence order of components. Therefore, it is sufficient to perform analysis of time series for one sequence order. In the software module for analysis of physiological processes, the EEG components are arranged in the sequence order given in Table 4.

Consider, how the ψ-state method allows the correlations between processes with completely different rhythms and shapes to be determined. A second-order ψ-state matrix describing correlation between the EEG period *L* and the duration of the *RR*-interval of ECG is given in Table 5. The sampling step is 1 sec (in ECG under consideration, all *RR*-intervals are shorter than 1 sec).

It can be seen that the frequencies of transitions (10) → (11) and (01) → (11) differ considerably. An increase in the EEG period and a simultaneous decrease in the *RR*-interval are very seldom followed by a simultaneous increase in the EEG period and the *RR*-interval ($\psi_{21} = 0.028$). On the other hand, the probability of transition from a decrease in the EEG period and a simultaneous increase in the *RR*-interval to a simultaneous increase in the EEG period and the *RR*-interval is higher than the probabilities of other transitions ($\psi_{31} = 0.106$).

It should be noted that the parameter <ro> indicates a slight negative correlation between the EEG period and the *RR*-interval averaged over 1 sec.

Permutation matrices 8×8 for third-order ψ-state matrices are determined and constructed in the same manner. For example, consider a matrix for three ECG elements: *RR*-, *QT*-, and *TP*-intervals (record duration, ~1 h) (Table 6). ECG was measured in a first-year student of the Lesgaft Physical Training Institute (age, 17 year; pulse rate, 48 beats/min).

It can be seen that some states (101 and 010) occur rather often, whereas some other states are very seldom or do not occur at all (011 and 100). The latter fact

TABLE 4. Integral Parameters of Second-order ψ-State Matrix

Parameter	Value
Trace of matrix (tr)	0.22001
Norm of matrix	0.27119
Entropy	2.68286
<mu> (tr/cotr)	0.66612
<teta> ((ψ1 + ψ4)/(ψ2 + ψ3))	1.60870
<syn> (ψ11 + ψ14 + ψ41 + ψ44)	0.39215
<recip> (ψ22 + ψ23 + ψ32 + ψ33)	0.15815
<chaos> (ψ12 + ψ13 + ψ24 + ψ34 + ψ42 + ψ43)	0.34911
<ro> (SQRT(syn-recip))	0.48373
<gamma1> ((ψ11 + ψ44)/(ψ14 + ψ41))	0.80000
<gamma2> ((ψ22 + ψ33)/(ψ23 + ψ32))	0.40670
Symmetry estimate	0.04940
Parameter	**Value**
Trace of matrix (tr)	0.17429
Norm of matrix	0.26181
Entropy	2.72641
<mu> (tr/cotr)	0.47025
<teta> ((ψ1 + ψ4)/(ψ2 + ψ3))	0.88450
<syn> (ψ11 + ψ14 + ψ41 + ψ44)	0.24153
<recip> (ψ22 + ψ23 + ψ32 + ψ33)	0.30339
<chaos> (ψ12 + ψ13 + ψ24 + ψ34 + ψ42 + ψ43)	0.34911
<ro> (SQRT(syn-recip))	–0.24872
<gamma1> ((ψ11 + ψ44)/(ψ14 + ψ41))	0.42540
<gamma2> ((ψ22 + ψ33)/(ψ23 + ψ32))	0.50802
Symmetry estimate	0.02409
Parameter	**Value**
Trace of matrix (tr)	0.20112
Norm of matrix	0.26972
Entropy	2.68704
<mu> (tr/cotr)	0.63158
<teta> ((ψ1 + ψ4)/(ψ2 + ψ3))	0.78218
<syn> (ψ11 + ψ14 + ψ41 + ψ44)	0.20112
<recip> (ψ22 + ψ23 + ψ32 + ψ33)	0.31844
<chaos> (ψ12 + ψ13 + ψ24 + ψ34 + ψ42 + ψ43)	0.34637
<ro> (SQRT(syn-recip))	–0.34252
<gamma1> ((ψ11 + ψ44)/(ψ14 + ψ41))	0.71429
<gamma2> ((ψ22 + ψ33)/(ψ23 + ψ32))	0.58333
Symmetry estimate	0.06467

TABLE 5. Second-order ψ-State Matrix Describing Correlation between EEG period and RR-Interval

Patient: Sokolova O. A. Date: 08.06.2000
Process: EEG (R3-01, R4-02), ECG, PPG [1 period]
Component 1: 2-L (EEG (R4-02))
Component 2: 3-RR (ECG)
Second-order ψ-State Matrix

State	11	10	01	00	Total
11	0.061	0.039	0.078	0.067	44
10	0.028	0.050	0.101	0.078	47
01	0.106	0.101	0.067	0.028	54
00	0.050	0.067	0.056	0.022	35

TABLE 6. Third-order ψ-State Matrix Describing Correlation between RR-, QT-, and TP-Intervals

Patient: 16 Date: 27.10.2001
Process: ECG [1 period] Duration: 54 min 28.6 sec
Component 1: RR (ECG) $N = 2647$
Component 2: QT (ECG)
Component 3: TP (ECG)
Second-order ψ-State Matrix

State	111	110	101	100	011	010	001	000	Total
111	0.017	0.008	0.024	0.000	0.000	0.049	0.008	0.023	337
110	0.000	0.002	0.008	0.000	0.002	0.017	0.019	0.006	140
101	0.056	0.028	0.028	0.000	0.002	0.098	0.003	0.015	611
100	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0
011	0.000	0.000	0.000	0.000	0.000	0.002	0.000	0.002	10
010	0.009	0.006	0.096	0.000	0.000	0.066	0.056	0.083	837
001	0.019	0.008	0.015	0.000	0.000	0.037	0.004	0.015	258
000	0.026	0.002	0.060	0.000	0.000	0.047	0.008	0.028	453

can be easily explained. Indeed, in healthy subjects an increase in the *RR*-interval is seldom accompanied by a decrease in the *QT*-, and *TP*-intervals. However, the fact that such state was not once detected in a hour-long ECG record is unique. The probability of a decrease in the *RR*-interval accompanied by an increase in the *QT*-, and *TP*-intervals is also very low. It was also observed that a decrease in the *RR*-interval is often accompanied by an increase in the *QT*-interval and a decrease in the *TP*-interval (010), whereas an increase in the *RR*-interval is often accompanied by a decrease in the *QT*-interval and an increase in the *TP*-interval (101). This is a specific feature of systemic regulation of the cardiac cycle in the examined patient.

Comprehensive testing using the OMIS software system is required to assess the efficiency of the ψ-state method for EEG processing. However, it is already obvious that the ψ-state method provides valuable information about the dynamics of physiological processes.

Method for Estimation of the Time Series Randomness

The method for estimation of the time series randomness provides new possibilities for analysis of physiological processes. This method is used for analyzing phases of successive binary sequences to obtain information about the dynamics of characteristics of individual oscillations (activity cycles).

The K-order phase is the parameter of a binary sequence indicating how often K successive zeroes or ones occur in the sequence under consideration. Ascending and descending phases of physiological time series are functionally nonuniform, so that ascending (successive ones) and descending (successive zeroes) phases should be considered separately. Ascending phases of the first, second, third, and fourth orders are denoted as g_1, g_2, g_3, g_4; descending phases, d_1, d_2, d_3, d_4. If K is greater than four, the phase is considered as the fourth order phase.

Dynamics of time series is described by matrices G and D. The matrix $G = (gd_{ij})$ contains the frequencies of transition from the state g_i to the state d_j. The matrix $D = (dg_{ij})$ contains the frequencies of transition from the state d_i to the state g_j. G_1, G_2, G_3, and G_4 are the frequencies of occurrence of first through fourth order ascending phases (total of the ascending phase frequencies in the rows of the matrix G). D_1, D_2, D_3, and D_4 are the frequencies of occurrence of first through fourth order descending phases (total of the descending phase frequencies in the rows of the matrix D) (Table 7).

Let us assume that $\sum_{i=1}^{4} G_i = \sum_{i=1}^{4} D_i$. Actually, the total of the ascending phases can differ from the total of the descending phases by no more than 1 (end effect). This difference can be neglected.

The total of phases $Nphase = \sum_{i=1}^{4} G_i + \sum_{i=1}^{4} D_i$. The number of oscillations of the slow process is $Nphase/2$. Thus, the mean frequency W_1 of oscillations of the slow process (Hz) is equal to $Nphase/2T$, where T is the time interval of observation of the source process.

TABLE 7. Matrices G and D

			G		
	d_1	d_2	d_3	d_4	Total G
G_1	gd_{11}	gd_{12}	gd_{13}	gd_{14}	G_1
G_2	gd_{21}	gd_{22}	gd_{23}	gd_{24}	G_2
G_3	gd_{31}	gd_{32}	gd_{33}	gd_{34}	G_3
G_4	gd_{41}	gd_{42}	gd_{43}	gd_{44}	G_4
			D		
	g_1	g_2	g_3	g_4	Total D
d_1	dg_{11}	dg_{12}	dg_{13}	dg_{14}	D_1
d_2	dg_{21}	dg_{22}	dg_{23}	dg_{24}	D_2
d_3	dg_{31}	dg_{32}	dg_{33}	dg_{34}	D_3
d_4	dg_{41}	dg_{42}	dg_{43}	dg_{44}	D_4

The mean number W_2 of oscillations (activity cycles) of the source process per one oscillation of the slow time series is equal to $2N/Nphase$, where N is the number of oscillations (activity cycles) of the source process.

The mean durations of the ascending and descending phases of the slow process can be estimated by the following formulas:

$$\overline{G} = \frac{G_1 + 2G_2 + 3G_3 + 4G_4}{G_1 + G_2 + G_3 + G_4},$$
$$\overline{D} = \frac{D_1 + 2D_2 + 3D_3 + 4D_4}{D_1 + D_2 + D_3 + D_4}.$$

To increase the accuracy of estimation of $\overline{G}$ and $\overline{D}$, phases of the fifth and higher orders should be taken into account separately instead of being considered as fourth order phases.

The parameters $\overline{G}$ and $\overline{D}$ indicate the number of oscillations of the source process per one ascending (descending) phase of the slow process. If the slow process observed in the time series of RR-intervals is respiration-related, parameters $\overline{G}$ and $\overline{D}$ indicate the number of RR-intervals per inhalation (exhalation). The slow oscillation period is equal to $\overline{G} + \overline{D} = W_2 = 2N/Nphase$.

The number of averaged oscillations of the slow process depends on the sampling step. If the sampling step is s oscillations, we obtain that $W_2 = 2[N/s]/Nphase$, where $Nphase/2$ is the number of oscillations of the corresponding slow process. If the sampling step τ is measured in seconds, $W_2 = 2[T/\tau]/Nphase$, where T is the duration of the source process.

The structure of slow oscillations of a time series element varies from patient to patient. For example, in [14] dynamics of RR-intervals was described using nine different types of the autocorrelation function. Differences in the time series dynamics of various elements of the cardiac rhythm can be easily observed in the same patient (Fig. 4). The regularity index indicates the difference between the number of extremums of the slow process (number of phases $Nphase$) and the number of extremums of a corresponding random time series. The latter value can be calculated as a function of the number N of oscillations of the source process.

It was shown in [28] that under the assumption of randomness of $Nphase$ we obtain that $Nphase = 2/3(N - 2) - 1$.

In the subsequent discussion the parameter $regul = Nphase/(2/3(N - 2) - 1)$ is used. The smaller is this

TABLE 8. Matrices of Frequencies of Transition from Ascending to Descending Phase and vice versa

Patient: 15			Date: 03.10.2001		
Process: ECG [1 period]			Duration: T = 655 sec		
Component: RR (ECG)			N = 528		
			G		
Phase	d_1	d_2	d_3	d_4	G
g_1	12	25	11	12	60
g_2	13	21	10	8	52
g_3	0	4	5	2	12
g_4	1	1	2	0	4
			D		
Phase	g_1	g_2	g_3	g_4	D
d_1	15	8	3	0	26
d_2	24	20	3	4	51
d_3	11	14	3	0	28
d_4	10	10	3	0	23

parameter, the less is the number of fast irregular oscillations. If *regul* > 1, the slow process is chaotic.

Using vectors (G_1, G_2, G_3, G_4) and (D_1, D_2, D_3, D_4), we can estimate the correlation between successive values of time series containing characteristics of individual oscillations of physiological processes.

Under several assumptions allowing the successive values to be considered as independent the theoretical average of distribution of the first through fourth order phase frequencies can be determined. The criterion of the time series randomness can also be obtained.

It was shown in [28] that under the assumption of independence of the successive values of the time series first order phases constitute 5/8 of the total number of phases; second order phases, 11/40; third order phases, 19/240; and fourth and higher-order phases, 1/48. The results described in [28] were obtained for the total number of phases. However, the same method can be used for separate estimation of randomness of the ascending and descending phases of time series.

In the module for analysis of physiological processes of the OMIS software system the time series randomness (independence) is estimated by comparing the theoretical and experimental frequencies of time series of characteristics of individual oscillations. Estimation is performed using the Kuhlbak approach [18].

Consider an example of the use of the method for estimation of the time series randomness for studying the dynamics of 528 successive *RR*-intervals measured in a first-year student of the Lesgaft Physical Training Institute (age, 18 year) (Table 8). It can be seen that the vectors of frequencies of the ascending (G) and descending (D) phases differ considerably. First-order phases are mainly ascending, whereas third and fourth order phases are mainly descending.

Indices of randomness rand$G$ and rand$D$ for frequencies (G) and (D) (14 and 230) show that the dynamics of both ascending and descending phases is nonrandom. The descending phases are considerably more ordered than ascending phases (for descending phases the significance level of randomness is equal to zero with an accuracy of 0.00001). The indices of randomness for ascending and descending phases differ considerably. This difference is estimated by the randomness asymmetry index. In the case under consideration, this index is equal to 0.061. It should be noted that such relationship between the randomness indices is not general. Moreover, in ECG measured in healthy subjects in the state of rest the randomness index is usually greater for the ascending phases. In approximately 60% of cases the randomness asymmetry index is greater than 1. In 40 healthy subjects whose ECG were studied in this work this index reached 5.2.

Matrices G and D are often similar to each other if the frequencies of the g_i–d_j transition are close to the frequencies of the d_j–g_i transition. The index of similarity of matrices G and D' (transpose of the matrix D) is used for assessing the regularity of the process dynamics. In the case under consideration, this index is equal to 11.3. In general, the randomness and similarity indices depend on the number of oscillations of the slow process; thus, it is more expedient to use normalized indices.

One of the important characteristics of matrices G and D is Shannon entropy. It was shown experimentally that this parameter indicates nontrivial regularities in the cardiac rhythm dynamics.

The expediency of use of matrices of frequencies of ascending–descending phase transition and some of their integral characteristics (Table 9) for assessing the dynamics of physiological processes was pointed out in [9]. In [9], in contrast to the present work, a single 8×8 matrix for eight states g_1, g_2, g_3, g_4, d_1, d_2, d_3, d_4 is considered. The method for estimation of similarity of matrices G and D considered above is equivalent to the method for estimation of the symmetry of this 8×8 matrix.

Power Spectrum

The *Power spectrum* option provides calculation of the spectrum of the autocorrelation function of any characteristic of individual oscillations using a standard algorithm [6]. The results of the spectrum calcu-

TABLE 9. Integral Characteristics of Phase Transition Matrices

Characteristic	Ascending phase (G)	Descending phase (D)	Characteristic	Value
Index of randomness (rand)	14.03	230.08	Randomness asymmetry index (rand$G$/rand$D$)	0.061
Randomness criterion significance	0.00286	0.00000	Similarity index	11.281
Correlation index	0.023	0.019	Mean frequency (Hz) W_1 ($Nphase/2T$)	0.197
Correlation index significance	0.75344	0.85127	Mean period ($G + D$)	4.117
Mean phase duration	1.695	2.422	Mean asymmetry of duration ($G - D$)	–0.727
Entropy	2.326	2.340	Number of phases ($Nphase$)	256
First eigenvalue	0.114	0.110	Regularity index ($Nphase/(2/3(N - 2) - 1)$)	0.734

lation are presented in graphical and tabular form. The table contains the total power values for four frequency ranges and the values of the relative power contribution (in %) for three frequency ranges (*LF*, 0.04-0.15 Hz; *HF*, 0.15-0.4 Hz; *VHF*, > 0.4 Hz) [27]. The normalized power contribution is calculated by the formulas $LF\% = LF/(TP - VLF)\cdot 100$ (for *LF* range) and $HF\% = HF/(TP - VLF)\cdot 100$ (for *HF* range), where *TP* is the total power, and *VLF* is the power contribution for the very low frequency range (<0.04 Hz). The table also contains additional information about the slow process spectrum. An example of the results of the power spectrum calculation is given in Fig. 6.

The algorithm of calculations is based on the Fourier transform of the autocorrelation function [6] instead of the fast Fourier transform because it provides calculation for any number of points (fast Fourier transform can be used only for 2^m points). Calculation of the power spectrum of an hour-long ECG took less than 3 sec.

In the power spectrum under consideration, the maximum value is attained at high frequencies (*HF*).

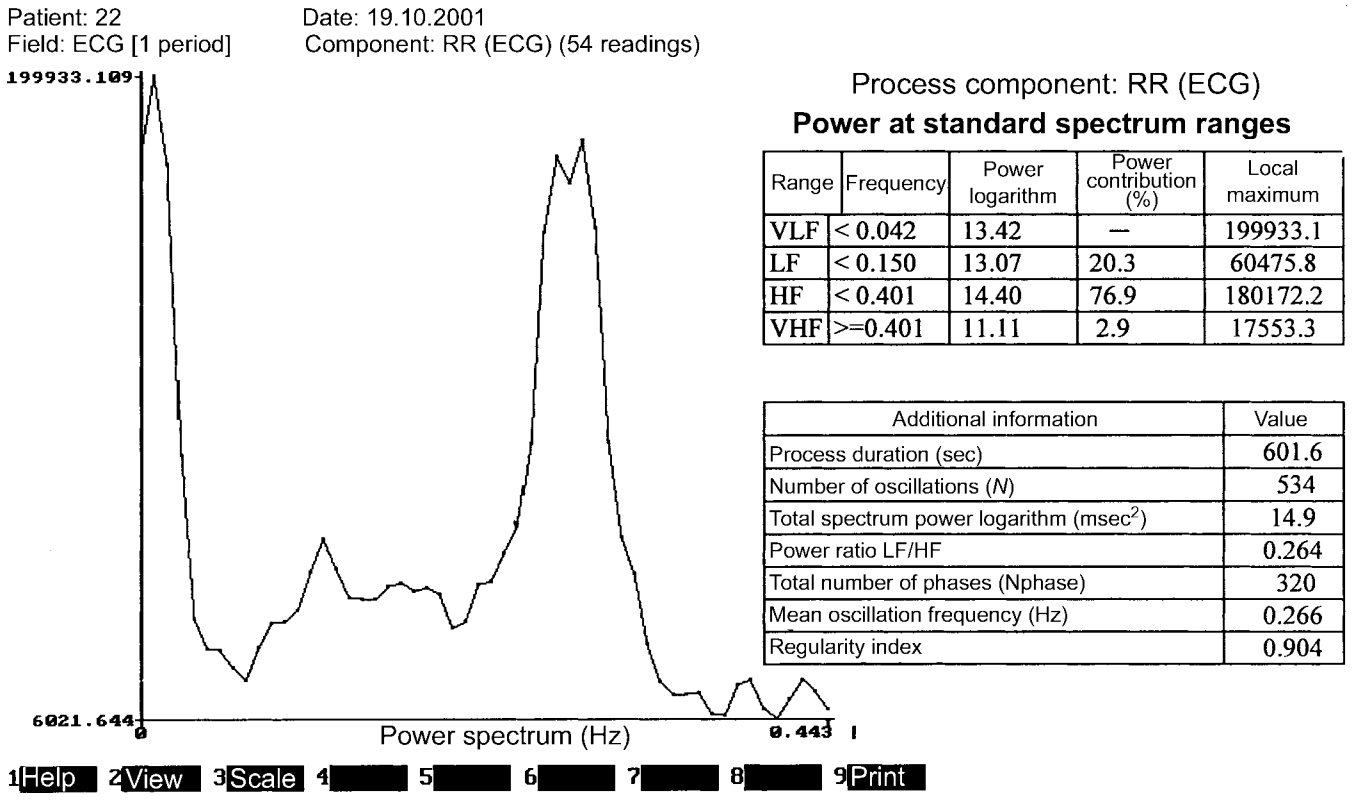

Fig. 6. Results of the power spectrum calculation.

This shows that the slow process has a manifested periodic component. The mean frequency calculated as the ratio between the number of oscillations of the slow process *Nphase*/2 and the ECG duration *T* is equal to 0.266 Hz. This corresponds to a frequency of 16 oscillations per minute.

Such manifested periodic component (whether in the *HF* or *LF* range) is observed rather seldom. The variety of the observed ECG spectra is in good agreement with the classification of the correlation functions of time series of *RR*-intervals given in [14]. The presence of a manifested periodic component usually indicates the nonrandomness of the time structure of the process. Nevertheless, in the case under consideration the number of extremums (*Nphase*) is close to the number of extremums calculated theoretically under the assumption of randomness ($Nphase = 2/3(N - 2) - 1$). The regularity index (0.814) is close to 1. Unconditionally irregular processes are observed if the regularity index is greater than 1.

One of the specific features of the *Power spectrum* option is that it allows the boundaries of the frequency ranges to be varied. Thus, the *LF*%/*HF*% ratio can be calculated for various boundaries of these ranges. The ranges given above were specified for *RR*-intervals [17, 25]. For other elements of ECG and other processes the boundaries of frequency ranges providing physiological information are unstudied. Some recently obtained data about the power spectrum of *RR*-intervals also contradict conventional clinical and physiological concepts [19].

The *Power spectrum* option was used for processing time series of the values of asymmetry of phase durations in successive EEG intervals. The boundaries of the frequency ranges were changed. Local maximums were detected within the range from 0.1 to 0.35 Hz. Such oscillations of the asymmetry of durations of EEG phases have been studied and described by many scientists [1, 8].

Sequential Differences and Other Options

The *Sequential differences* option is used for forming first differences of time series consisting of characteristics of individual oscillations.

Process: EEG (R3-01, R4-02), ECG, PPG [1 period]
Sequential differences of process components

=	#	3-RR	3-PT	3-QT	3-TP	3-QS	3-ST	3-TTf	3-STf	3-PQ	3-VR	3-VT	3-VP	3-QT/TP
	1	-24	4	4	2	0	-8	12	4	0	-449	173	14	0.003
	2	16	-16	4	15	4	4	-4	0	-20	-384	32	-386	-0.071
	3	4	-12	0	-21	-4	-8	12	4	-12	397	-495	123	0.127
	4	12	28	-4	4	0	0	-4	-4	32	188	124	255	-0.042
	5	-4	-4	-8	-4	4	-4	-8	-12	4	38	83	-6	-0.009
	6	-16	24	12	16	0	16	-4	12	12	-49	314	27	-0.044
	7	-16	-40	0	-13	-4	-8	12	4	-40	-405	-37	-366	0.079
	8	0	-16	-12	-15	4	0	-16	-16	-4	-116	-91	-75	0.044
	9	20	24	-4	8	-4	12	-12	0	28	398	-269	305	-0.071
	10	4	20	12	29	4	-4	12	8	8	56	55	229	-0.117
	11	-8	-40	-8	-21	0	-20	12	-8	-32	-43	207	-222	0.085
	12	-12	24	4	-4	0	8	-4	4	20	-26	-78	193	0.042
	13	-4	0	12	2	-4	8	8	16	-12	-441	183	-203	0.041
	14	16	-24	-8	-2	4	16	-28	-12	-16	-1	-200	-75	-0.024
	15	8	16	-12	20	-4	-20	12	-8	28	660	-86	140	-0.165
	16	4	4	8	7	4	-12	16	4	-4	-271	62	14	-0.007
	17	-12	-8	0	-11	0	8	-8	0	-8	232	-103	-104	0.061
	18	-16	-8	-4	-28	-8	8	-4	4	-4	-241	367	139	0.156
	19	0	16	4	16	4	16	-16	0	12	-442	-101	-121	-0.085
	20	4	-12	0	2	4	-24	20	-4	-12	486	-231	-135	-0.009
	21	8	0	0	8	-4	0	4	4	0	2	48	200	-0.047
	22	-4	0	0	-3	4	4	-8	-4	0	74	113	-142	0.015
	23	-16	4	4	-16	-4	4	4	8	0	21	159	84	0.118

1 Help 2 3 4 5 6 Plot 7 Export 8 Function 9 Print 10

Fig. 7. First differences of time series consisting of characteristics of individual oscillations.

A table containing first differences of time series given in Fig. 3 is shown in Fig. 7. Dynamics of the first differences can be visualized by pressing the key F6. It is also possible to apply functions considered above to the first differences (key F8).

The *Matrix calculator* option provides various operations with ψ-state matrices 2×2, 4×4, and 8×8. This option is used for revealing various regularities in the matrix form.

The *Statistics module* option provides use of additional computational resources of the OMIS system for analyzing individual data [10]. Such functions as monofactorial variance analysis (for studying variability of parameters within segmented intervals), partial correlation (for studying the dependence of the revealed correlation between two elements of the cardiac rhythm on other elements), correlation graph analysis, regression analysis (for studying regression interdependence between various elements of the cardiac rhythm), etc. As an example, consider the use of regression analysis for analyzing the strong dependence between the durations of the *RR*-interval and the electric diastole discussed above (Fig. 8).

The dependence of the electric diastole duration on the duration of the *RR*-interval shown in Fig. 8 is almost linear. Such dependence is typical for healthy subjects in the state of rest, but can be also observed under other conditions [14]. Visualization of this and other correlations between the ECG elements allows the points departing considerably from the general dependence to be detected. The user can easily find the corresponding activity cycle of the source process and remove it if the deviation is caused by an artifact.

Analysis of Grouped Data

The OMIS software system combines a module for compilation of the digital case history with a research

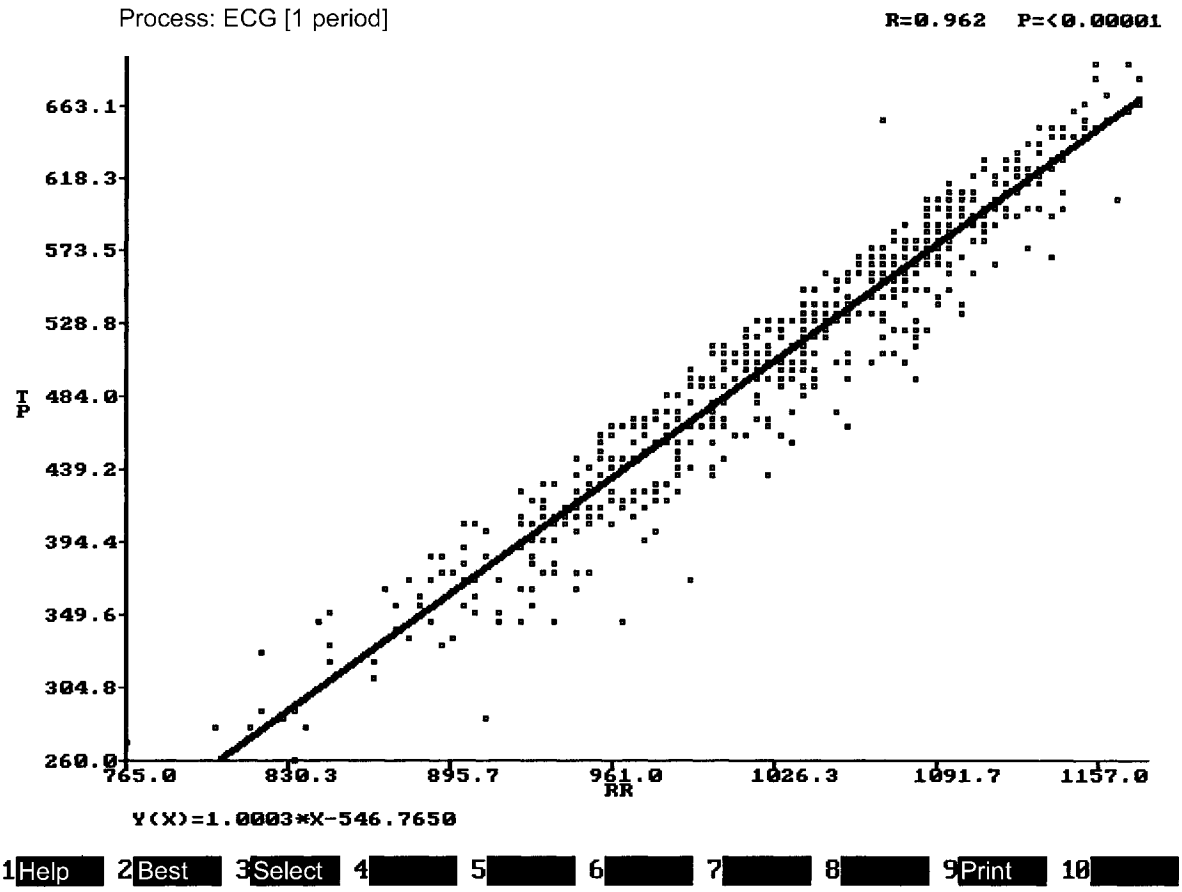

Fig. 8. Regression dependence between the durations of the *RR*-interval and the electric diastole measured in a single patient.

module and a knowledge base containing the results of analysis of data from DCH [10].

Only the Process field of the module for analysis of physiological processes was considered above. Other information about the patient (personal information, various clinical, laboratory, and instrumental data) is usually entered from the keyboard into special fields.

The algorithm for generation of parameter sets on the basis of DCH parameters entered from the keyboard is similar to that used in the preceding version of the OMIS software [10]. It presents no difficulties for the user.

The algorithm for generation of sets of parameters obtained by analysis of the Process field is somewhat different. The differences are due to the fact that the clinical and laboratory data from DCH database are imported directly into the research module, whereas the database used for analysis of processes contains time series of characteristics of individual oscillations (or the detected process if it is not removed). Thus, the parameters to be analyzed should be determined using the module capabilities considered above, and only then the information about the processes should be imported into the research module. For this purpose, the parameter window is slightly modified in comparison with the window used for generation of sets of parameters entered from the keyboard [10]. It contains two additional columns (Fig. 9).

The column *Number of computable parameters* is used for generating computable parameters in the module for analysis of physiological processes and exporting them into the research module of the OMIS system. For this purpose, the cursor is moved to this column and the key Enter is pressed to invoke the menu for selection of functions (main functions from the menu shown in Fig. 3). On this menu, the functions required for obtaining the computable parameters are selected using the Insert key. Then the cursor is moved to this column and the key Enter is pressed to invoke the menu for selecting the elements of the process. The elements required for generating computable parameters are selected using the Insert key, and the key Enter or Esc is pressed. As a result, a column containing the number of computable parameters obtained using the selected functions and elements of the physiological processes is formed (Fig. 10).

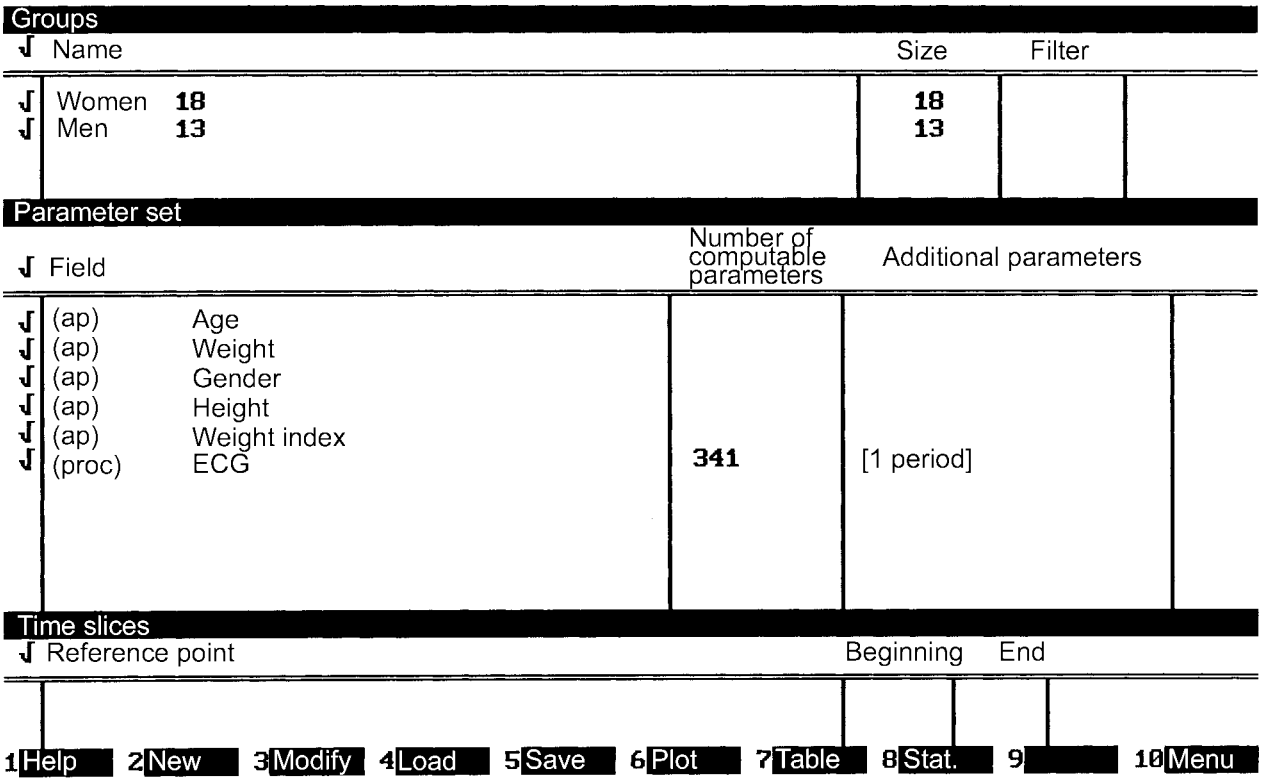

Fig. 9. Main window of the research module (analyzed parameters include characteristics of the Process field).

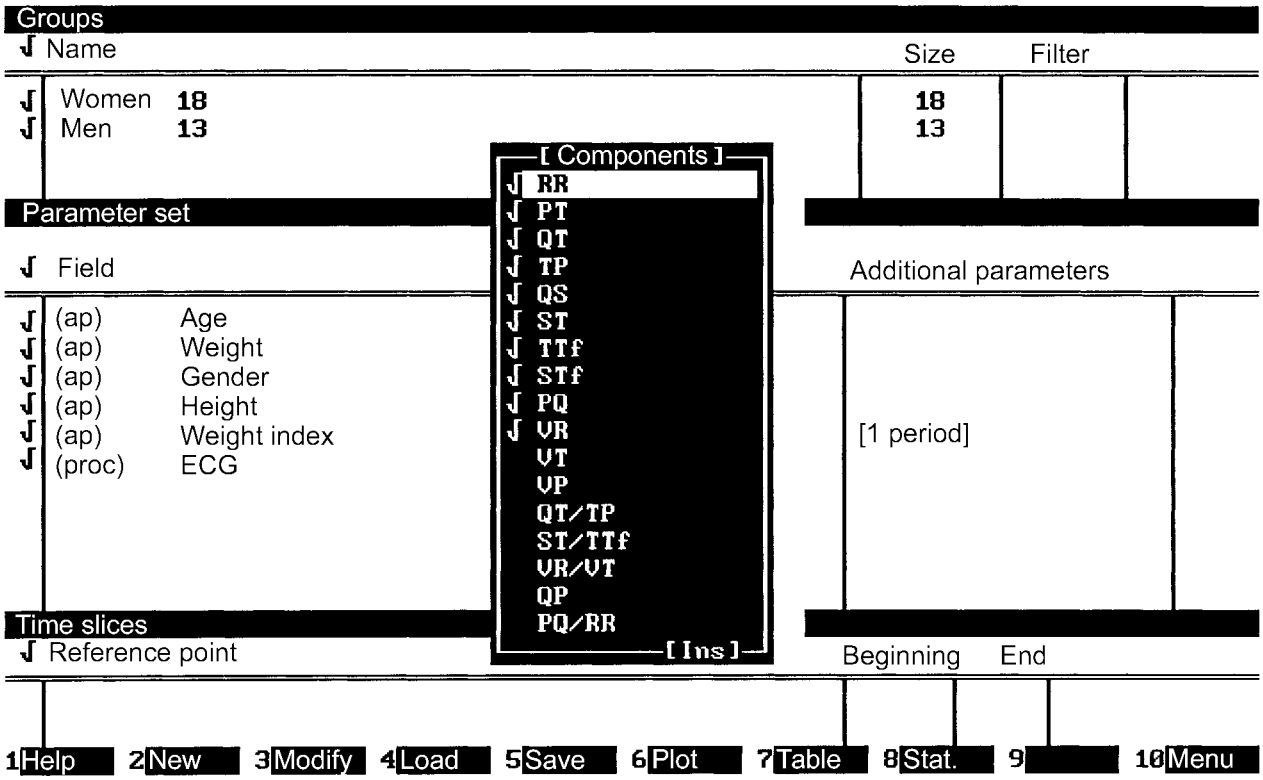

Fig. 10. Menu for selecting elements of a single-channel ECG for analysis using previously selected functions.

For example, if 10 ECG elements were selected, application of the function *Main statistical parameters* allows 50 parameters (5 for each element) to be obtained. The function *Pearson correlation matrix* generates 46 parameters (45 different correlation coefficients and the first eigenvalue of the correlation matrix); the function *Dynamics randomness estimation* generates 120 parameters (12 parameters for each element); the function *Power spectrum* generates 90 parameters. Thus, application of these four functions to 10 elements of characteristics of individual oscillations provides the generation of 306 parameters.

Functional capabilities of the system provide analysis of 1000-1200 parameters (correlation matrix analysis is limited to 300 parameters). By default, the parameters are calculated for elements of all oscillations and the total source process stored in DCH. The user can change the minimum sampling step and analyze the dynamics of values averaged over a certain number of oscillations or a certain time. The process can also be segmented so that information about each segment is imported separately to the research module. To do this, the cursor is moved to the column *Additional parameters* and the key Enter is pressed to invoke the window for selecting the sampling step type (periods or seconds) and duration (Fig. 11). The sampling step type can be specified both for grouped and individual data.

For analysis of individual data, the process can be segmented into segments containing a selected number of periods (cycles) or into a selected number of segments.

If two or more processes should be analyzed, a time interval should be selected as the sampling step in the column *Additional parameters*. This time interval should exceed the maximum duration of the period of the slowest process. Then, the menu for separate selection of parameters of each channel is invoked.

Forming of clinical situations using the values of computable parameters obtained by analysis of the *Process* field can involve certain difficulties. For example, it is rather difficult to form groups varying in the duration or variability of the *RR*-interval or the *LF*/*HF* ratio. The number of parameters can be too great to fit into a standard DHC field for the results of analysis of physiological processes. For example, a second-order ψ-state matrix for four elements generates 186 param-

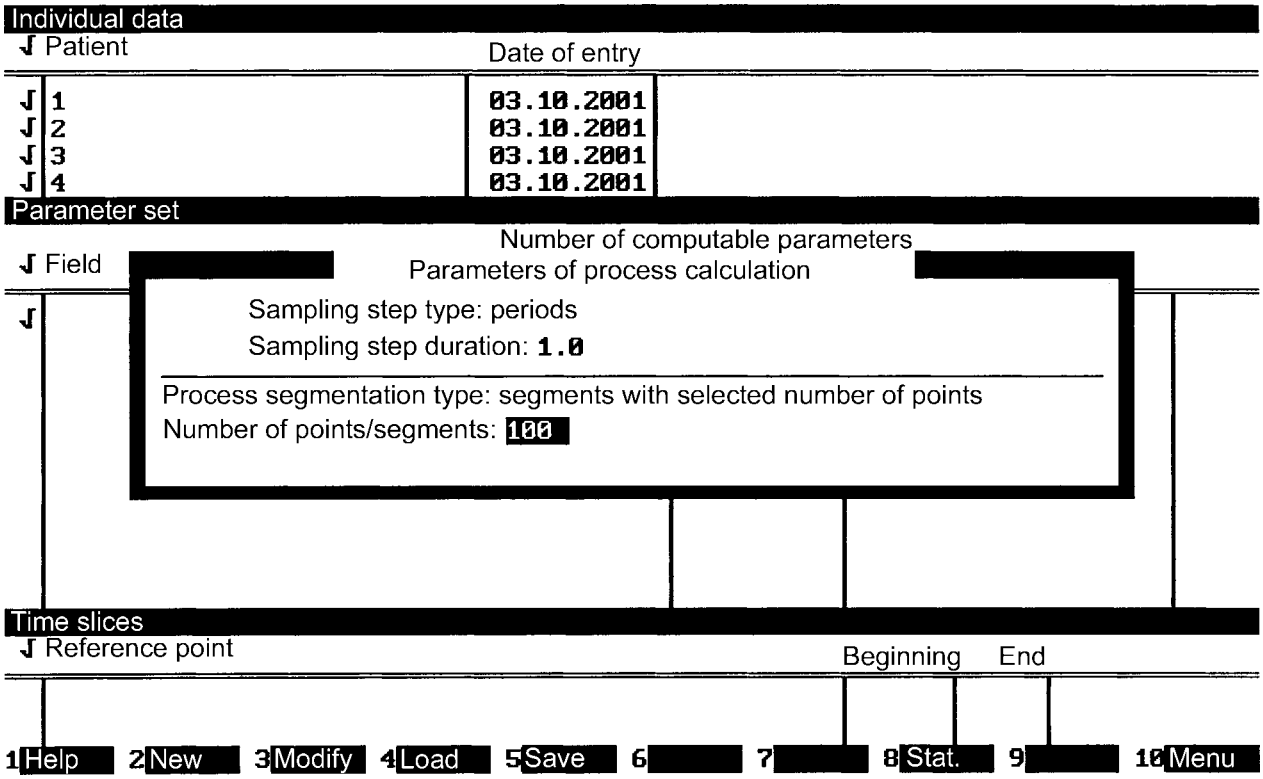

Fig. 11. Sampling step selection (number of oscillations or time interval in seconds) and segmentation of ECG (each segment contains 100 cycles). Segmentation can also be performed for a specified number of segments.

eters, whereas the total number of parameters can exceed 1000.

Another difficulty involved in the development of a unified database for the results of analysis of physiological processes is that the number of parameters depends on the user's requirements. For example, one user can be interested only in analysis of ECG; another user, in analysis of ECG and EEG; the third user, in analysis of ECG, EEG, and respiration; and so on. It is hardly expedient to fill the database with fields for parameters never to be used. On the other hand, the adjustment of the database to the user's requirements is too labor consuming to be done by the user.

The lack of a mechanism for generation of groups using computable parameters of physiological processes would deteriorate the information processing technology used in the OMIS software system [10]. In the last version of the OMIS system the mechanism for generation of groups consists of the following steps.

1. A wide group (for example, a group of all patients with DCH containing the Process field or a group of all patients with certain characteristic (age, gender, etc.)) is formed using already available DCH fields.

2. A function providing calculation of the parameter required for group generation is selected. For example, if it is necessary to form groups of patients varying in the *RR*-interval range, the function *Main statistical parameters* should be selected.

3. The key F8 (Stat.) is pressed. In the case under consideration, the software prepares 5 parameters for statistical analysis. Then, the second window of the research module is invoked [10].

4. The key F2 (Hist.) is pressed to plot a histogram of any of the computable parameters.

A histogram of the standard deviation of the *RR*-interval dynamics (*RR-stddev*) in 35 apparently healthy subjects is shown in Fig. 12. Each segment of the histogram contains 100 cycles.

At the top of the histogram, the automatically generated computable parameters are listed. Parameters are named in the following manner: name of function–process element–name of parameter. For example, *main-RR-mean* means the mean value (*mean*) of *RR*-interval calculated using the function *Main statistical parameters* (*main*); *rand-QT-randG* means the normalized randomness index of the ascending phase (*randG*) of the

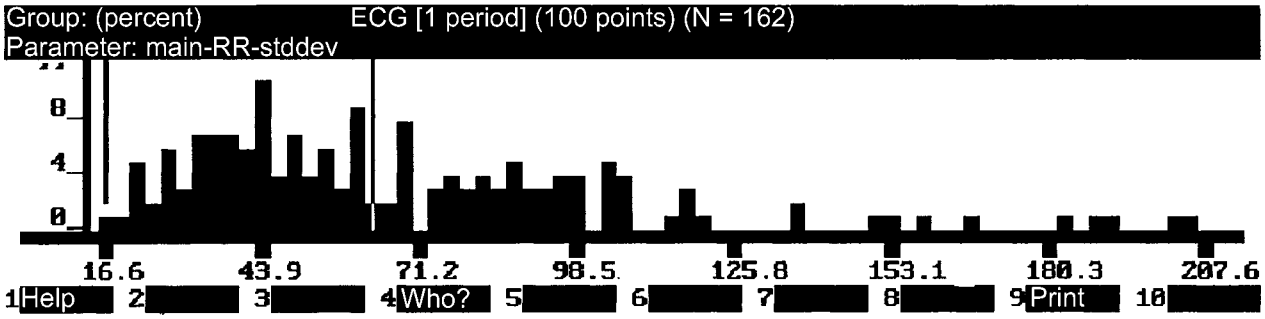

Fig. 12. Histogram of the standard deviation (each of 192 segments of the histogram contains 100 cycles).

systole duration (*QT*) calculated using the function *Time series randomness* (*rand*); *Spectr-RR-LF/HF%* means the power ratio (*LF/HF%*) for the dynamics of *RR*-intervals calculated using the function *Power spectrum* (*Spectr*). All contracted notations of parameters are listed in User's Manual and in the Help file.

5. Using a frame a subset is selected in the histogram. In the case under consideration, all ECG fragments with the standard deviation less than 60 cm were selected.

6. The selected group is stored in PC memory by pressing the key F5 (Group).

Thus, two or more groups with given values of computable parameters of physiological processes can be calculated.

One of the main disadvantages of the method of group generation described above is that it does not allow groups meeting more than one condition (for example, patients with *RR-mean* > 1000 msec and *LF/HF%* < 1) to be generated.

The group generation is the final functional operation of the module for analysis of physiological processes. The information about groups is then processed by the research module of the OMIS system, and various group statistics (mean values, correlations, etc.) are calculated. This provides determination of parameters containing valuable information, automated development of diagnostic and prognostic algorithms, and forming of an expert system containing computable parameters of physiological processes.

Implementation

The development and testing of the module for analysis of physiological processes of the OMIS system was completed in September 2001. To test the module performance, the results of processing of 40 ECG records of 10-15-min duration measured in young healthy subjects, one ECG record of 54-min duration, and one four-channel polygraphic record of EEG, ECG and PPG (Fig. 2) were analyzed.

A personal computer Celeron-750 with 128-Mb RAM and 15-Gb HDD was used for testing the module performance. The results of testing are presented below:

– time required for importing one channel of a 5-10-min ECG record (digitization frequency, 0.005 sec), 20 sec;

– time required for importing a 3-min 4-channel polygraphic record (two EEG leads, one ECG lead, and one PPG lead) into DHC (digitization frequency, 0.004 sec), 50 sec;

– time required for identification of the critical points of a 5-10-min ECG record and generation of 15 time series of characteristics of individual oscillations, 3-5 sec;

– time required for identification of the critical points of a 3-min 4-channel polygraphic record and generation of 15 time series of characteristics of individual ECG oscillations and 10 time series for PPG and two EEG leads, 11.8 sec;

– time required for applying any function from the menu shown in Fig. 7 to a 54-min ECG record, no more than 3 sec;

– time required for generating 1200 parameters of single-channel ECG records of 40 patients and exporting them to the research module of the OMIS system, 5 min.

Work is now underway toward the optimization of some segments of the program. In particular, attempts are made to decrease the time of import of ASCII files into the PC.

The software module installed on a PC with average performance allows forty 5-10-min ECG records available as ASCII-files on a CD to be analyzed during

one day. The results are available in the graphical and tabular form.

Architecture of the Module for Analysis of Physiological Processes of the OMIS System

In conclusion, consider the block diagram of the module for analysis of physiological processes (Fig. 13).

In the last version of the OMIS system, the block *Functions for analyzing the source process* contains only a function providing calculation of the Pearson correlation matrix for instantaneous values of the process (for example, EEG).

The links between the expert system of the OMIS software system (version 2.9), the module for algorithm development, and the obtained parameters of physiological processes are illustrated in Fig. 13. The structure of these links is the same as in the preceding version of the OMIS system (OMIS 2.8) [8].

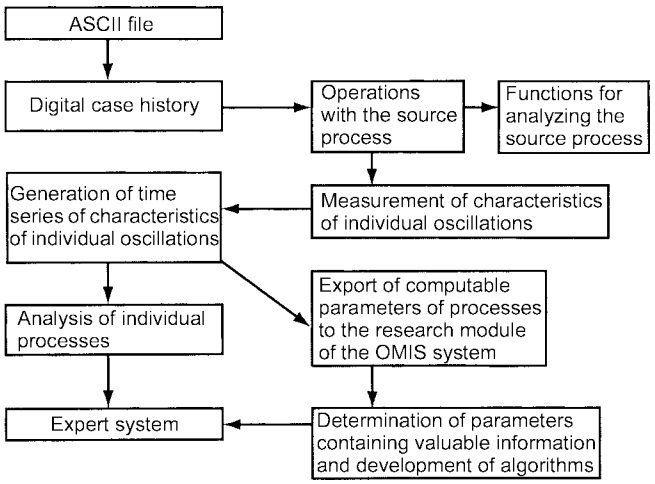

Fig. 13. Block diagram of module for analysis of physiological processes.

Conclusion

An information technology used for systemic analysis of dynamics of characteristics of individual oscillations of ECG, EEG, and other physiological processes is described. The technology is implemented based the OMIS software complex (version 2.9, 1992-2001). It provides analysis of ECG, ECG, and respiration-like processes (pneumogram, PPG, rheogram, etc.) available as ASCII-files with an arbitrary digitization frequency. The number of channels for information analysis is limited to four. The error in identification of critical points normally does not exceed 1% of the number of oscillations. These errors are usually caused by artifacts in records.

Computable parameters of dynamics of characteristics of individual oscillations are generated using both conventional statistical methods and such special statistical techniques as estimation of the time series randomness, ψ-matrix method, etc. (Fig. 5). All functions of the module provide generation of up to 1200 different parameters.

Computable parameters of physiological processes are available to the research module of the OMIS system. Thus, the process of estimation of the information value of physiological information and its correlation with clinical and laboratory data can be automated.

The OMIS software system supplied with the module for analysis of physiological processes (version 2.9) can be effectively used for obtaining new medical and physiological information and studying the time organization of vital activity of the human body.

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REFERENCES

1. E. Yu. Artem'eva, L. D. Meshalkin, and E. D. Khomskaya, in: Mathematical Analysis of Electrical Activity of the Brain [in Russian], Moscow (1965), pp. 87-92.
2. R. M. Baevskii, O. I. Kirillov, and S. Z. Kletskin, Mathematical Analysis of Cardiac Rhythm Variations Caused by Stress [in Russian], Moscow (1984).
3. Yu. G. Balasanov, A. N. Doinikov, M. F. Koroleva, et al., in: Application Study of Time Series Using the Evrista Software [in Russian], Moscow (1991).
4. S. S. Bekshaev, N. N. Vasilevskii, N. B. Suvorov, et al., in: Adaptive Response of the Brain and Its Prognosis [in Russian], Leningrad (1978), pp. 117-123.
5. O. M. Belotserkovskii, A. V. Vinogradov, and S. V. Shebeko, in: Computer Simulation and Progress in Medicine [in Russian], Moscow (2001), pp. 91-100.
6. G. Bendat and A. Piersol, Measurement and Analysis of Random Processes [Russian translation], Moscow (1971).
7. Vestn. Aritmol., **16** (2000).
8. A. A. Genkin, Dokl. AN SSSR, **200**, No. 4, 1003-1006 (1971).
9. A. A. Genkin and V. I. Medvedev, Prognosis of Psychophysiological States [in Russian], Leningrad (1973).

10. A. A. Genkin, New Information Technology for Analysis of Medical Information [in Russian], St. Petersburg (1999).
11. A. A. Genkin, in: New Information Technologies in Medicine and Ecology. Proc. Conf. IT + ME'99, Gurzuf (1999), pp. 155-158.
12. A. A. Genkin, Proc. VII Int. Conf. Regional Informatics, St. Petersburg (2000), Vol. 2.
13. E. A. Zhirmunskaya, In Search of Explanation for EEG Phenomena [in Russian], Moscow (1996).
14. V. M. Zatsiorskii and S. K. Sarsaniya, in: Mathematical Methods of Analysis of Cardiac Rhythm [in Russian], Moscow (1968), pp. 31-50.
15. E. V. Zemtsovskii, Sports Cardiology [in Russian], St. Petersburg (1995).
16. V. A. Kalantar and A. V. Sivachev, Med. Tekh., No. 4, 37-39 (1999).
17. A. P. Kulaichev, Computer Electrophysiology in Clinical and Research Practice [in Russian], Moscow (1999).
18. S. Kuhlback, Information Theory and Statistics [Russian translation], Moscow (1967).
19. L. M. Makarov, Halter Monitoring [in Russian], Moscow (2000).
20. N. I. Muzalevskaya and V. M. Uritskii, in: Telemedicine: New Information Technologies on the Eve of XXI Century [in Russian], St. Petersburg (1998), pp. 209-252.
21. G. V. Ryabykina and A. V. Sobolev, Cardiac Rhythm Variability [in Russian], Moscow (1998).
22. L. V. Chireikin, D. Ya. Shurygin, and V. K. Labutin, Automated Analysis of Electrocardiograms [in Russian], Leningrad (1977).
23. V. V. Shchakin, Computational Electrocardiography [in Russian], Moscow (1981).
24. P. E. Dilaveris, P. Farbom, V. Batchvarov, et al., Ann. Noninvasive Electrocardiol., **6**, No. 2, 92-97.
25. A. A. Genkin, in: Mathematical Analysis of Electrical Activity of the Brain, Harvard (1968), pp. 65-80.
26. D. Govreen-Segal, M. M. Radai, Y. Sivan, and S. Abboud, Comput. Biomed. Res., **32**, No. 4, 336-354 (1999).
27. "Heart Rate Variability. Standards of Measurement, Physiological Interpretation, and Clinical Use", Eur. Heart J., **17**, 354-381 (1996).
28. M. Kivelovith and J. Vilar, J. Sci. Meteorol., **5**, No. 17, 21 (1953).
29. W. J. Kostis and J. C. Bedina, Angiology, **51**, No. 11, 905-911 (2000).
30. A. Porta, G. Baselli, E. Caiani, et al., Med. Biol. Eng. Comput., **36**, No. 1, 27-34 (1998).