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Forecasting of Patients Condition in the Monitoring Medical Systems on the Example of Prostate Diseases

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Abstract. The mathematical models and computational methods with implementing them applied information technology of decision support in monitoring medical system are proposed. The method of construction robust monitoring indices based diagnostic models for criteria quality assessment of the systems elements condition is described. The informativeness (significance) assessment method of the systems diagnosing models variables, obtained based on artificial neural networks (ANN) theory instrument is developed. The forecasting method of multivariate time series obtained on the monitoring indices based variables of the dynamic systems condition is developed. The method for solving the condition classification problem of the complex systems

elements is improved. The decision support computer system in medical monitoring systems is developed. Application examples of the described methods on diagnosis of medical patients are presented.

Keywords: Decision Support Software System, Reasoning Methods, computational methods, clinical medicine.

1 Introduction

The defects development in technical or biomedical systems (BMS) is complex dynamic process. Subject field experts can't always predict how quickly they will be developed. They are not always manage to reach a consensus on what the developmental stage defects are and as a consequence, what methods for defects eliminating should be applied.

Considering in further only biomedical systems should be noted, that the major advances in understanding disease in the post-genomic era, still a majority of all drugs are effective only for a limited number of patients. The aspiration to provide more effective therapeutic interventions (treatment services) tailored to the individual or groups of individuals with common properties remains unfulfilled.

The object of this research are forecasting processes of the patients' state as decision-making processes stage in the medical monitoring systems. The attributes of these processes are state variables elements, diagnostic models, informative state variables of a model, a condition monitoring models and condition classification of the systems elements.

The problems in the decision-making process in the health monitoring systems, at the stage of diagnosis, are as follows:

- a high error probability (3rd type) at the recognizing patient condition based on the monitoring data because, depending on the condition of the patient is assigned an individual treatment program;
- the choice of monitored state variables is individual for each patient with aim to subsequent efficiency analysis of the designated treatment program.

At present, these problems are aimed only to formalizing but decisions on choosing a treatment program for each patient are accepted subjectively, based on the personal experience of the physician.

The subject of research in this work is mathematical models and computational methods with implementing them applied information technology of decision support in monitoring medical system.

Diagnostic models are developed and used for analysis of quality criteria values of the BMS elements condition depending on state variables values. For this reason it is important from the decision-maker (DM) practical activity point of view to define which of the variables have more or a less impact on the quality criteria that characterized BMS elements condition.

Solving the forecasting problem requires to structure a mathematical model of the condition monitoring (MMCM), the so-called trend, which represents a functional

dependency that reflects a bond between the subsequent and previous values of the time series that describes adequately the time series. Because time series of evolutionary processes are dynamical systems discrete MMCM, they usually contain parametric uncertainty, which are non-stationary and noisy.

While solving the classification problem (about the class choices that owns the analyzed element) one runs into the problems with the estimation of an elements condition for several monitoring variables and with the correctness of these estimates when they are generalized or shared at the step of decision-making by DM.

Great number of the papers devoted to the description of mathematical models and methods of diagnosing technical and BMS (look at, e.g., [1]) have been published by the present moment.

Papers [2],[3],[4],[5] describe in enough detail the generalities of the theory of the trainable artificial neural networks (ANN) which are widely used for the formal mathematical models construction (diagnostic models) in the form of regression equations.

Two main types of the informativeness assessment (significance) methods of monitored variables condition elements of the systems and processes can be single out, based on the literature data analysis [2],[5],[6],[7],[8],[9], such as the differential informativeness method and the method of the structure-parametric analysis and the synthesis of regression models.

In addition, there are three types of the condition monitoring statistical models [2], [10] of the dynamical systems and processes based on the analysis of publications: models of stochastic filtering, regression (structural-parametric models) and probabilistic models.

Works [2],[3],[12] consider the perspectives for the applying and development of methods for the condition classification (pattern recognizing): formation of informative state variables; training samples based classification; taking into account the state variables dynamics of the control objects.

It should be noted in the majority of works devoted to diagnosing solving problems, informativeness assessment and prediction of the dynamic systems state variables based on ANN, there is no analysis of the variables significance for nonlinear models that consider their correlation (cointegration of the «particular» time series) and measurement accuracy.

The practical application of the automated computer systems for the condition monitoring and diagnostic (ASMD) can help decision-makers and/or patients (if the BMS are considered) to make decisions that provide the best values of the technical systems work quality criteria or survival and patients life quality (meaning the biomedical systems). However, information support which is developed to date, does not allow with a sufficiently high level of confidence to solve the MBS condition forecasting problems monitoring indices based.

The aim of this work is to improve the quality of patient treatment through the use of targeted therapies, optimizing interventions for each individual patient, thereby achieving greater success in treating or curing a patient. Improving the quality of patient treatment, in turn, possible due to improving the quality of the patients' condition diagnosis by developing robust mathematical models, computational

methods, and the applied decision support information technology in the medical monitoring system.

This work is dedicated to the development of the forecasting methodology of the elements condition of biomedical systems depending on the individual current state with the correlated dynamic systems state variables and the accuracy of their measurements, cointegration of the «particular» time series with aim to improve the diagnosis process quality.

2 Problem definition of the condition forecasting

The forecasting problem is formulated as follows: from the resulting measurement values of the monitored variables $\overset{P}{X}$, is necessary to predict the subsystems condition (functional elements) in which have appeared defects, in the future. As a result of the decomposition an overall condition forecasting methodology can be represented as a sequence of methods for solving interrelated problems:

- condition monitoring (values selection and measurement of monitored variables of the system condition at fixed intervals);
- formation precedent database such as experimental and verifiable samples of the registered variables that characterize the observed patients condition: let there be a multi-dimensional condition matrix $X = \{x_{i,j}\}$ ($i = 1..I, j = 1..J$), where I is a number of monitored patients in the sample, J is a number of the measured state variables. Traditionally, rows of this matrix are called precedents;
- cluster analysis is a task of selecting condition classes in terms of mathematically formalized criteria (the formation of classes for classification tasks);
- building diagnostic model: selection of quality criteria, the model structure (type of trained ANN) and the training method. It is necessary in a predetermined vector-function of the training pairs set $(\overset{P}{X}^{(0)}, d)_p$, $p = 1..P$, where is an input vectors of the dimension H_0 , and exit with dimension H_{K+1} , respectively, to approximate a given sample. As a result of solving the problem is have to be a mathematical mechanism, as a result of work which it would be possible to obtain any value of the vector function $\overset{P}{Y}^{(K+1)}(\overset{P}{X}^{(0)})$, which is represented of the training sample, in a predetermined input vector within the range that is bounded by the input data;
- the informativeness (significance) assessment of «particular» monitored state variables, which reflect properties of the elements (data reduction it's an assessment of the variables informativeness when some input variables are less informative and overabundant). Criteria selection of the informativeness (significance) assessment of the state variables depends on what should be distinguished from what i.e. from the type and dimension of the state variables set X of considered system elements or process, and the type of decision functions Π . For each task an own informative subset of the state variables should find.

The initial set of state variables (set X_0) is assigned by nonformalized way based on the specialists experience of subject area. Formal methods are applied when the training sample A is being analyzed to test this set of data on the necessity and sufficiency. Among all the possible subsets of variables B the subset is considered sufficient when X_0 and Π provides cost N , not exceeding a certain threshold N_0 . Under the expenses N here meant the cost measuring of the monitored the state variables (N_x) and cost of losses caused by the recognizing errors (N_r): $N = N_x + N_r$.

A sufficient subset of the minimum dimension is a necessary. So actually on the training set A the problem of exhaustive search type is solved:

$$\beta = \arg \min_{\beta \in B} N(X_\beta) / X_0, \Pi, A, N_0$$

This problem of simultaneous minimization of the N_x and N_r . The costs of measurement depends on how much and what kind of the state variables have to be registered and what is accuracy required of measurement results. From the viewpoint of the diagnosing practice would be a logical statement about the appropriateness of measuring the costs of informative variables for which signal/noise ratio are significant. At the same time, according to the general trends of the scientific and technological progress development, such measurements are becoming more costly. Thus, the actual task is reducing count of the measured state variables ie, the search informative subset X_β of minimum dimension, where $X_\beta \subset X_0$ [9];

- recasting the monitoring indices in the form suitable for regression analysis (additional processing and formation of samples, taking into account informative variables for the trend models construction);
- the mathematical model of the condition monitoring (MMCM) construction. We will consider in further the time series that relate to the persistent class (with the presence of long-term memory). There is prescribed $D_Q = \{q^\circ(t+l)\}$, $q^\circ(t+l) = (\Pi^\circ(t+l), U^\circ(t+l), \Phi^\circ(t+l))$, $l = -K..L$, is a finite set of design and regime parameters Π° , control variables U° , phase variables Φ° , constituting time series. Here t is a forecast moment, K and L are forecast horizons. Her $D_Q \in Q$, Q is a time series space.

It is necessary to obtain a functional dependence, reflecting the relation between the subsequent and previous values of the time series which satisfies the system preferences of DM, for a given forecast horizon: $q^\circ(t+L) = F(q^\circ(t+L-1), \dots, q^\circ(t-K)) + \varepsilon_t^\circ$, and also, to take into account the uncertainty in the choice of the models structure and parameters (in the multidimensional case the «particular» time series can be cointegrated);

- the calculation of the predicted values of the time series in the range which is limited with the forecast horizons, with applying MMCM and respective them confidence intervals;
- the classification problem is an attribution of the current state of a precedent to one of the classes: based on the MMCM and on the obtained results of solving forecasting problem, the classification problem of the BMS elements condition is solved (it is correlating the predicted values to one of the formed diagnostic classes). Let $\overset{P}{X}^*$ be a variables vector that describes the precedents condition, M is a set of classes numbers (scenarios). It is known the number of possible failures system scenarios in general, and also for each scenario (class) the subsets of monitored state variables (symptoms) have been formed. Based on the values of the vector projections $\overset{P}{X}^*$ precedent is referred to one of the possible sets of R_m , where $m = 0..M - 1$. It is necessary to find such an m-th scenario, for which the maximum conditional probability density function of $\overset{P}{X}^*$ occurrence have a precedent with m-th scenario.

Having the aim in a correct solution the classification problem the factor analysis of the patient's state variables was performed. The factor analysis based on principal component analysis was used as a method of state variables aggregation into complexes that would be are pairwise poorly-correlated variables (an orthogonalization) with a view to the subsequent reduction of the space dimension of the state variables.

3 The method of constructing robust diagnostic models

The approximation problem solution with vector function of a vector variable in order to build diagnostic models was accomplished through the theory of trainable ANN [4]. To approximate data were used unidirectional multilayer (UMNN) and radial-basis (RBNN) neural networks.

The input data to approximate the data with the ANN are: the input state variables of the system elements $\{Y_{ph}^{(0)}\}$; the output parameters of the $\{d_{pi}\}$.

The simplest ANN with one hidden layer ($K=1$) have been used. Let there $\{Y_{ph}^{(0)}\}$ be a set of input data, $\{Y_i^{(k)}\}$ be a set of output data of k-layer; k is the number of layer, $k = 1..(K+1)$, K is the number of hidden layers; $p=1..P$, P is the analogues number; $\{w_{ij}^{(k)}\}$ is a set of weights of k-layer; i is an element of k-layer; j is an element of $(k - 1)$ -layer; H_0 is the count of network inputs; H_1 is the count of neurons in the hidden layers; H_2 is the count of network outputs.

The structure of the unidirectional multilayer network (UMN) has the form:

$$Y_i^{(2)} = f\left(s_i^{(2)}\right), \quad (1a)$$

$$s_i^{(2)} = w_{i0}^{(2)} + \sum_{j=1}^{H_1} w_{ij}^{(2)} Y_j^{(1)}, \quad i = IK \ H_2, \quad j = IK \ H_1; \quad (1b)$$

$$Y_j^{(1)} = f\left(s_j^{(1)}\right), \quad (1c)$$

$$s_j^{(1)} = w_{j0}^{(1)} + \sum_{h=1}^{H_0} w_{jh}^{(1)} Y_h^{(0)}, \quad h = IK \ H_0, \quad (1d)$$

where $f(s) = th(\beta s) = \frac{e^{\beta s} - 1/e^{\beta s}}{e^{\beta s} + 1/e^{\beta s}}$ is the chosen transfer function,

$f'_s = \beta \left[1 - f^2(s) \right]$ is the derivative of transfer function.

As the scalar convolution of choice functions in finding a solution of the approximation problem with UMN were used a function of form [4]:

$$E = \frac{1}{2PH_{K+1}} \sum_{p=1}^P \gamma^{P-p} \sum_{i=1}^{H_{K+1}} f_{\text{fit}}[\Delta_{\text{pi}}^2(M)] + \frac{1}{2} \beta_{t+1} I(M_{t+1}, D_{\text{int}}), \quad (2)$$

where M is the model parameters, D is a vector measurement data;

$I(M_{t+1}, D_{\text{int}})$ is a transmitted information;

γ, β is the regularization parameters;

$\Delta_{\text{pi}} = Y_{\text{pi}}^{(K+1)} - d_{\text{pi}} - \hat{Y}_{\text{pi}}^{(0)}$, $f_{\text{fit}}(\Delta_{\text{pi}}^2) = 1 - \exp(-L_{\text{fit}} / 4) \Delta_{\text{pi}}^2$, $L_{\text{fit}} \geq 4$.

The solution is an approximating functions of form $Y_i^{(K+1)} - \hat{Y}_i^{(0)}$ which were found with stochastic approximation method based on the conjugate gradient ravine method. At training the regularizing algorithm was used, that implements the interruption in the iterative process in cases of accumulation of computation errors [4].

The structure of the radial-basis network (RBN) with one hidden layer ($K=1$) is similar to that shown UMN has the form:

$$Y_i^{(2)} = s_i^{(2)}, \quad s_i^{(2)} = w_{i0}^{(2)} + \sum_{j=1}^{H_1} w_{ij}^{(2)} \varphi_j^{(1)} \left(Y_j^{(0)}, C_j^{(1)}, \sigma_j^{(1)} \right), \quad i = IK \ H_2, \quad (3)$$

where $\varphi_j^{(l)} = \exp\left[-\frac{1}{2} \sum_{h=1}^{H_0} Z_{jh}^2\right]$ is a radial-basis activation function of the

hidden layer neuron, $Z_{jh} = \frac{Y_h^{(0)} - C_{jh}^{(l)}}{\sigma_{jh}^{(l)}}$, $j = 1 \dots H_1$, $h = 1 \dots H_0$;

$Y^{(0)} = \left[Y_I^{(0)}, K, Y_h^{(0)}, K, Y_{H_0}^{(0)} \right]^T$ is a input data vector of 0-layer;

$C_j^{(l)} = \left[C_{jI}^{(l)}, K, C_{jh}^{(l)}, K, C_{jH_0}^{(l)} \right]^T$, $j=1 \dots H_1$ is a coordinate vector of the centers of the activation function for the hidden layer neurons

$\sigma_j^{(l)} = \left[\sigma_{jI}^{(l)}, K, \sigma_{jh}^{(l)}, K, \sigma_{jH_0}^{(l)} \right]^T$, $j=1 \dots H_1$ is a vector which sets the window width of the activation function of the j-th neuron of the hidden layer;

w_{ij} is a bond weight between the i-th neuron of output layer and j-th neuron of the hidden layer. The bonds weights were found through the SVD method (here is meant, according to the designations, that the $w_{jh}^{(1)} = e_{jh} = 1$, $w_{ij}^{(2)} \equiv w_{ij}$).

As the scalar convolution of choice functions at the correcting nonlinear RBN parameters was used function of the form (2).

The vectors projections specifying the window width and the centers coordinates of the activation function for the hidden layer neurons were found through the method of stochastic approximation based on conjugate gradient ravine method [4].

4 The informativeness assessment method of the state variables

The informativeness measure of the system is defined as its average entropy:

$$\Theta = \int \theta(M) F(dM), \quad (4)$$

where $\theta(M) = -\rho(M) \log_2 \rho(M)$, $F(dM)$ is the priory probability measure of the model M parameters.

We assume that the probability density distribution of the error-free acceptance of the hypothesis about the obtained values reliability of the parameters of the mathematical model M_{t+1} is defined by the law $\rho(M_{t+1}) \sim \exp\left[-\beta_{t+1} I(M_{t+1}, D_{int})\right]$, where $I(M_{t+1}, D_{int})$ is a mutual information \mathfrak{I} , D_{int} is a vector of the random numbers dimensionality H_0 (input data, $D_{int} \subset D$):

$$I(M_{t+1}, D_{int}) = \Theta(M_{t+1}) - \Theta(M_{t+1} / D_{int}). \quad (5)$$

As a criterion for the quality assessment of mathematical models of systems and processes further, we will consider the change of the mutual information (5).

We represent $Y_i(S)$, where $S = \{s_l\}$, $l = 1, \dots, L$, the set of input data as a Taylor series, while retaining only the terms of the first infinitesimal order in the expansion. Obtained function is a linear. For the dispersion of an arbitrary linear function of several random variables estimate holds [5]:

$$D_{Y_i} = (\text{grad} Y_i)^T \Sigma_S \text{grad} Y_i = \sum_{l=1}^L \left(\frac{\partial Y_i}{\partial s_l} \right)^2 \sigma_{s_l}^2 + \sum_{l=1}^L \sum_{\substack{n=1 \\ n \neq l}}^L r_{ln} \frac{\partial Y_i}{\partial s_l} \frac{\partial Y_i}{\partial s_n} \sigma_{s_l} \sigma_{s_n} \quad (6)$$

where Σ_S is the covariance matrix of variables s_l and s_n ;

σ_{s_l} is the standard deviation;

r_{ln} are the correlation coefficients s_l and s_n ($R = [r_{ln}]$).

Usually, if there is the correlation bonds then accept $r_{ln} = 1$, otherwise $r_{ln} = 0$.

The signal energy is determined as:

$$E_i = \sum_{l=1}^L |D_{Y_i/s_l}|, \quad (7)$$

where the dispersion of the signal at the selected variable is calculated according to the following expression:

$$D_{Y_i/s_l} = \left(\frac{\partial Y_i}{\partial s_l} \right)^2 \sigma_{s_l}^2 + \left(\sum_{\substack{n=1 \\ n \neq l}}^L r_{ln} \frac{\partial Y_i}{\partial s_n} \sigma_{s_n} \right) \frac{\partial Y_i}{\partial s_l} \sigma_{s_l}. \quad (8)$$

The informativeness coefficient (of the contribution significance) is defined through the variable s_l in the signal $Y_i(S)$:

$$\beta_{il} = \frac{|D_{Y_i/s_l}|}{E_i}, \quad \sum_{l=1}^L \beta_{il} = 1. \quad (9)$$

The influence coefficient of the variable s_l on the signal value $Y_i(S)$ is determined as:

$$\varphi_{il} = \frac{D_{Y_i/s_l, r_{ln}=0}}{\sigma_{s_l}^2} = \left(\frac{\partial Y_i}{\partial s_l} \right)^2. \quad (10)$$

The value of the mutual information between the Gaussian random variable is determined, according to [2], as follows:

$$I(Y_p, S_p) \sim \ln \left[\frac{\det(\Sigma_{Y_p})}{\det(\Sigma_{S_p})} \right], \quad (11)$$

where the covariance matrix are:

$$\Sigma_{Y_p} = \begin{bmatrix} r_{in} \sqrt{D_{Y_{pi}}} \sqrt{D_{Y_{pn}}} \end{bmatrix}, \quad (12a)$$

$$\Sigma_{S_p} = \begin{bmatrix} r_{in} \sigma_{s_{pl}} \sigma_{s_{pn}} \end{bmatrix}. \quad (12b)$$

In the paired comparison of diagnostic models in the form of a linear equation of multiple regression (LMR), ANN (UMN, RBN) we will evaluate the signal dispersion change, which characterizes the robustness of a particular model:

$$D_{Y_i, dB} = 10 \lg_{10} \left(\frac{D_{Y_i}^{(\beta)}}{D_{Y_i}^{(0)}} \right), \text{ decibels; } \beta = 1, 2. \quad (13)$$

Here, as the signal variance estimates in further were used calculated values of residual dispersions for each of the compared diagnostic models.

5 A method of the mathematical model construction of the condition monitoring

We consider the mathematical model of the condition monitoring (MMCM). The MMCM quality essentially depends on the correctness of recasting this monitoring indices in the form suitable for regression analysis (to the normal view), for a specific subject field.

To make a normal distribution, or make a series either stationary or uniform, to stabilize the dispersion and make all data with the positive values, the monitoring indices recasting to the normal view [10].

In this paper, to eliminate the influence of the initial values of the time series $q^\circ(t-K)$ and, as a consequence for reduce the autoregressive order when choosing structure recurrent MMCM, the input data recasting to the normal view was applied:

$$Y_i(t+l) = \ln \left(\frac{q_i(t+l)}{q_i(t-K)} \right), \quad i = 1 \dots I, l = (-K+1) \dots L, \quad (14)$$

where I is the count of these time series (the dimension of the vector is q°).

With the help of neural network models with time delay is possible approximation of nonlinear dependencies between the subsequent time series values from their previous values and the values of the external factors (such as measurement errors). Consider the structure of neural network models with time delay. Let the $\mathbf{Y}^{(k)} = [Y_1^{(k)}, \dots, Y_{H_k}^{(k)}]^T$, $k=0, 1, 2$ is an input data vector of the k -layer, where the H_k is an number of elements in the k -layer. The number of network outputs equal to the number of these time series – $H_2 = I$. In case when the order of the recurrent MMCM with applying neural network models with the time delay is assumed equal to $AR(K)$, the count of network inputs equals $H_0 = I \cdot K$. Synthesis of robust neural network models was implemented through the regularization method [4].

Thus, the calculation of predicted values of multivariate time series can be performed with using the proposed neural network models with time delay.

The values of standard deviation of previous $\sigma_{Y_h^{(0)}}$ (at a given relative accuracy of the measurement variables $\Delta_{Y_h^{(0)}}^o$) and subsequent time series values $\sigma_{Y_i^{(2)}}$ for neural network models with time delay is determined according to the procedures [5], [11].

It is obvious that the proposed recurrent MMCM with the use of neural network models with time delay are cointegration equations. The cointegration rank (the space dimension of cointegrated time series) $rang(Q)$ can be determined based on the variables informativeness assessment of neural network models [5] – by calculating the corresponding informativeness coefficients (the significance of the contribution) of the previous time series values in the following:

$$\beta_{ij} = \sum_{l=-K+1}^{L-1} \beta_{ij}^{(t+l)}, \quad i, j = 1 \dots I. \quad (15)$$

6 The solving method of the BMS elements condition classification problem according to the forecast data

The condition recognizing problem appears as classification problem. In order to avoid multicollinearity, we apply the orthogonalization procedure of the state variables [12]. Further, to solve the classification problem of the object condition the probabilistic neural network was used, the following structure:

- an input layer $F_1^* \dots F_A^*$ – the input elements are the values of the principal component (PC) vector projections of the monitored state variables \mathbf{F}^* of the precedent;
- samples layer $\rho_{1m} \dots \rho_{Mm}$ – are the classes centres of training sample. The count of patterns equals to the number of classes in the training set.

- The input layer and the samples layer are constitute fully-connected structure. An element activity of the layer-samples was determined by the dependence of the corresponding probability distribution density according to the Student's t -law (it is appropriate for the limited samples;
- the output layer $m^*, \rho(F_m^* | R_{m^*})$ (output element) is a discriminator of the threshold value indicating the samples layer element with a maximum activity value (ie, the class to which belongs an unknown precedent).

It should be noted that the values of the t-Student's statistic depend on the basis choice, in which the closeness degree between the precedent and samples is assessed (in solving the classification problem), as well as between samples (in the analysis of the distances significance between classes). Therefore, there is a need for further structuring of additional statistical decision rule selecting of a single (reference) basis. According to the principle of maximum likelihood as the decision rule of the reference basis m^* selection was made a rule:

$$\exists! m^* \in C_m(t_{lm}) (l, m = 0..M-1): \min_l t_{lm} \rightarrow \max, \quad (16)$$

where the $C_m(t_{lm})$ is a set of m-th statistics indexes.

7 Information technology tools of the decision support in forecasting the MBS elements condition

IDEF-model of the applied information technology of the decision support in forecasting patients condition in medical monitoring systems based on the observed values of the state variables with a known instruments measurement accuracy, developed based on the proposed methodology are presented in Fig. 1.

The proposed information technology includes the following number of stages corresponding to a sequence of interrelated tasks described in claim 2.

The computer interactive decision support system (CI DSS) in forecasting of the complex dynamic systems condition «RMICP®» in the uncertainty conditions of the input data which implements the proposed methodology was developed. The information technology of calculations in the environment developed by CI DSS was proposed.

Thus the decision maker proceeds to test hypotheses based on the received information (of the projected values of the state variables, taking into account the boundaries estimates of their confidence intervals): about the availability of changing tendency in time of the variables deviations from their permissible values, about the belonging the observed condition to one or another class. If testable hypothesis will be true, then the decision on the need to adjust the treatment program is accepted. The presented information technology can be used to forecast the elements condition of the BMS on the current and further stages of treatment.

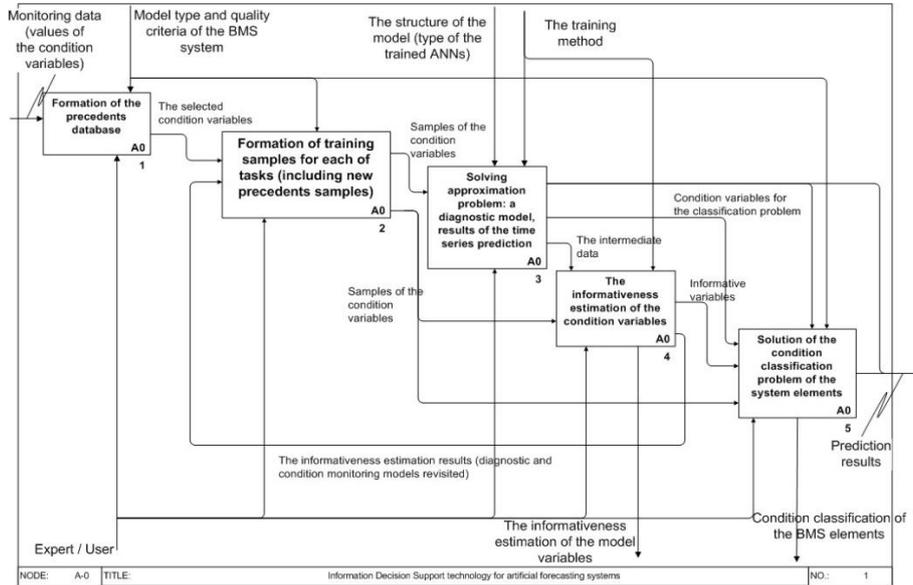


Fig. 1. IDEF - functional model of the applied information technology of the decision support at forecasting the BMS elements condition

8 A practical application example of the proposed methodology

Based on the system analysis of the diagnosing process of the BMS elements the following hierarchy diagnosing stages was identified: laboratory diagnostic, visual diagnostic and monitored patients' variables that appropriate for each stage. The initial dimension of the state variables set was equal to 24. An experimental training set of the monitored variables that characterize the condition of the observed patients for selected disease was formed. The sample was divided into 4 classes: 50, 45, 51 and 33 people. As a feature, classification at dividing total sample into classes the disease progression level was chosen.

The diagnostic model (DM) in the form of LRM equation and trained ANN (UNN and RBN) based on the set of normalized variables, which included all of the data, with using the generalized method of least squares (LSM) and ANN training methods were obtained.

In Fig. 2, as an example, the diagram of the informativeness assessments of the monitored state variables are shown (24 state variables) obtained by the RBN and the LMR analysis for the elements corresponding mathematical expectations of state variables values for different classes. Numbers of the most informative state variables are represented along the abscissa and the informativeness coefficients values obtained by LMR and RBN analysis for different classes elements represented the ordinate. These results were obtained at a given relative accuracy measurements of continuous variables - 1%, Boolean - 25%, enum - 10% or 15%, respectively. The correlation matrix was determined for samples containing data for four classes.

Further, similar results were obtained for 17 (were excluded Boolean variables) and 14 (were excluded Boolean and enumerated types variables) monitored state variables.

Analysis of the results shows that the most informative (significant) in the present case are 6 of Boolean type, 3 of enumerated type and 7 of continuous variables (total 16 monitored state variables).

It is obviously, that the informativeness (significance) evaluation of the variables LMR does not depend on the condition (belonging to a particular class) BMS element. The subsets of informative (significant) variables, which identified based on the RBN analysis for elements of biomedical systems belonging to the different classes, are not equal.

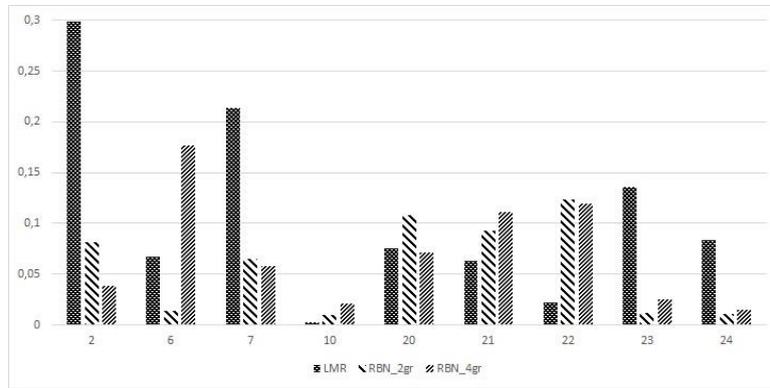


Fig. 2. The results of the estimation informativeness variables LMR and RBN for elements of different classes (24 monitored state variables)

Further, the monitoring of the BMS elements condition that belong to the 4th class was carried out. The experimental test sample of the state variables of the BMS elements was formed: $D_Q = \{q_p^o(t+l)\}$, $l = -K..L$, $q_p^o(t+l) = \{q_{pi}(t+l)\}$, $i = 1..I$, $p = 1..P$. In the present case, we had: the quantity of observed elements – $P = 17$, the quantity of monitored continuous state variables – $I = 7$, forecast horizons – $K = 4$ and $L = 1$. Recasting the input data to the normal form was carried out in accordance with (14) was carried out in this paper. Thus, the proposed recurrent MMCM with the use of neural network models with time-delay in the form of (1, 3) had a quantity of inputs $H_0 = 21$, the quantity of outputs $H_2 = 7$, the quantity of neurons in the hidden layer is assumed to be equal to the quantity of observed patients $H_1 = P$.

According to data, based on the received information (the predicted values of the state variables with estimates of their confidence intervals borders) the treating physician proceeds to verify the hypothesis about presence a trend change in time of the variables deviations from their permissible values. If the tested hypothesis is true, then the decision on the need to adjust the treatment program is accepted.

Informativeness influence analysis of previous time series values to the next was carried out for the purpose of estimating cointegration rank $\text{rang}(Q)$ (as an example look at the Fig. 3, for the second and seventh variable) with using MMCM RBN according to (15) for the selected BMS element. It is revealed, that in the considered case the $\text{rang}(Q) = 5$ at the $I = 7$, i.e. $\text{rang}(Q) < I$. In particular, it is clear that the greatest contribution to the prediction error of the second and seventh variables make the measurement error of the second, fourth and fifth variables in the previous steps condition monitoring.

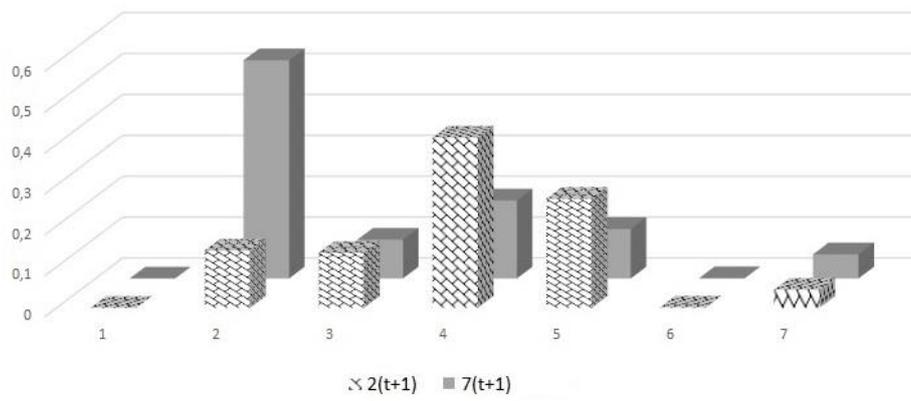


Fig. 3. The results of the informativeness influence evaluation of previous time-series values on the next for the selected BMS element

The results of the informativeness influence assessment of the previous time-series values on the next selected BMS element, as an example, for the second and seventh variables that shown in Fig. 4.

From these results, it is possible to judge about the information usefulness from the time. It is obviously from the viewpoint of the attending physician that the patient's condition monitoring, at each step after the prescribed treatment is an important point to verify the treatment efficacy.

The results of solving classification problem of the condition BMS elements for the type of disease were obtained. Based on informativeness analysis and variables aggregation the space dimension reduction of the state variables was made. The dimension reduction of the PC space based on the Kaiser's criterion at the factor analysis stage was conducted. It was decided to leave the 16 PC out of the 24 PC, which made it possible to reduce the space dimension of the state variables.

The distance significance analysis between the classes, which take into account selected quantity of state variables and the quantity of precedents in the classes was carried out. The distances between the centers of classes in each of the selected basis spaces were determined through Student's t-statistics $\{t_{lm}\}$. Student's statistical decision rule (the hypothesis of means equality) was used [11]. It was found that the

distance between the classes are significant, as evidenced by the excess of critical values of Student statistics. Following the decision rule (16) a zero-class '0' basis was selected as a reference. The itself-recognition probability of the class exceeds 80%.

The results of solving the classification problem about belonging precedents of test sample to the class '3' based on the monitoring indices is 100%.

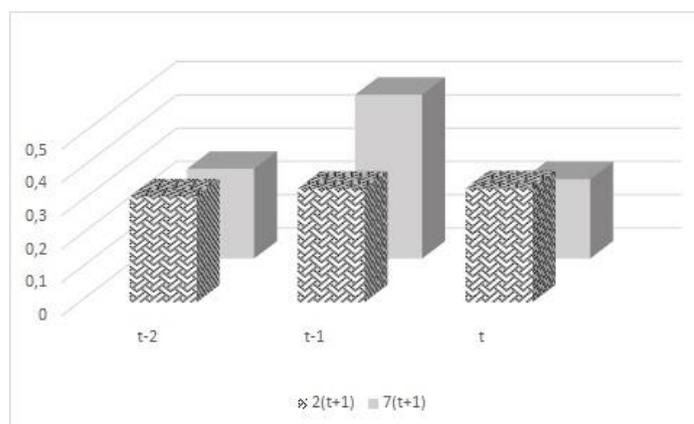


Fig. 4. The results of the informativeness influence evaluation of previous values of all time-series on the next for the selected BMS element

9 Conclusion

The system mathematical model, methodology and implementing them applied information technology of the patients condition forecasting in monitoring medical system in condition of uncertainty input data trend-analysis concept based that are brought to the level of engineering techniques were proposed.

As an example the forecasting problems solution results of the patients condition in the monitoring medical systems for a definite type of disease were obtained.

The informativeness assessments of monitored variables state of the biomedical system elements that takes into a count the accuracy of their measurements with using linear and nonlinear diagnosis models was obtained. It is shown that a subset of informative (significant) variables that were identified on the basis of the non-linear models analysis for different elements condition of BMS can be non equals.

A comparison of the forecasting quality using the proposed neural network models was done. It is shown that in this case the cointegration rank less than the dimension of the original space of time series.

Based on informativeness analysis and variables aggregation the reduction of the space dimension of the state variables was made.

A computer interactive decision support system (CI DSS) when forecasting the condition of complex dynamic systems «RMICP[®]» under input data uncertainty,

which implements the proposed methodology. The information technology of calculations in the environment developed by CI DSS was proposed.

It was found that with the using developed method and its implementing CI DSS the itself- recognizing probability of the class exceeds 80%.

The proposed methodology and implementing their applied information technology can be used for the forecasting elements conditions as BMS as well as technical systems.

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