Bionic models for identification of biological systems

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Abstract. This article proposes a clinical decision support system that processes biomedical data. For this purpose a bionic model has been designed based on neural networks, genetic algorithms and immune systems. The developed system has been tested on data from pregnant women. The paper focuses on the approach to enable selection of control actions that can minimize the risk of adverse outcome. The control actions (hyperparameters of a new type) are further used as an additional input signal. Its values are defined by a hyperparameter optimization method. A software developed with Python is briefly described.

1. Introduction

Improvement of intellectual support for decision making aimed at minimizing adverse outcomes is commonly discussed nowadays [1-4]. Clinical decision support systems are developed to aid functional diagnostics.

Data analysis and machine learning can be efficiently used to improve diagnostic systems. In particular, solutions based on deep learning, Gradient Boosting and Random Forest [5, 6] perform strongly. However, they can rarely be observed in practice and are mainly used for research purposes.

This project is aimed at developing a clinical decision support system that can be used to identify functional statuses of biosystems in the context of energy-information processes. The following tasks have been set to reach the overall objective:

1. To characterize behaviors of biological systems in clearly defined functional states (diagnostics).
2. To define control actions that can minimize the risk of system transition into adverse conditions.

Let us consider the following algorithm for the proposed clinical decision support system:

1. To create an operational image of an investigated biosystem based on functional characteristics of the system at some time t_i.
2. To calculate integral parameters I^*_{adapt} for time t_i. To construct cumulative curves.
3. To forecast changes in functional characteristics over time (across different forecast horizons).
4. To identify the forecasted functional state. To calculate forecasted values I^*_{adapt} and functional reserves.
5. To select optimal control actions at $t_{i+1}, t_{i+2}, \ldots$.
6. To display possible control actions to enable selection of the optimal action.

2. Materials and methods

For the needs of this study, a bionic model is a mathematical model and a related software that reflect functioning and organization of a biosystem.

Presentation of a diagnosed subject (biosystem) in the form of a bionic model that is based on neural networks (NS), genetic algorithms (GA) and immune systems (IS) can facilitate identification of developing systems. Thus, each diagnosed subject (each functional state of a human) is described in a bionic model <NS, GA, IS, A> where A stands for tuning algorithms.

Combination of NS, GA and IS in bionic models allows an exchange of information and control actions among systems, which enables improved operability and interpretability of obtained values.

2.1. Energy-informational approach for integral evaluation of functional states

An approach [7] where the Fullback information measure is considered as a measure of preferred behavior of a biological object is used to evaluate a functional state of a biosystem in the developed clinical decision support system. For that matter, the problem of calculating the informational integral parameter to characterize a functional state of a human can be summarized by the following equation:

$$I = \sum_{j=1}^{n} P_0(\Delta x_j) \ln \frac{P_0(\Delta x_j)}{P_1(\Delta x_j)} = \sum_{j=1}^{n} P_0(\Delta x_j) \ln(P_0(\Delta x_j) - P_1(\Delta x_j)),$$

where n is a number of parameters;

$P_0(\Delta x_j)$ is the probability that characterises a preferable state of the object, i.e. the situation when deviation of j from its normal value is 0.

A normal value is a state when all variables stay within their standard range (for homogeneous groups of diagnosed subjects).

$P_1(\Delta x_j)$ is the probability that x_j stays within its standard range:

$$P_1(\Delta x_j) = P(|x_j - x_0| < \delta) = 2F\left(\frac{\delta}{\sigma}\right) - 1,$$

where x_0 is the average value of x_j; δ is some assigned deviation value;
σ is standard deviation of x_j; F is the Laplace's function.

$P_0(\Delta x_j)=1$, because the preferred state is set at the 0 deviation. Thus, the integral parameter of an object's functional state can be calculated as (1):

$$I_{adapt} = \frac{1}{n} \sum_{j=1}^{n} \ln \frac{1}{P_1(\Delta x_j)}, \quad (1)$$

where n is a number of parameters;
$P_1(\Delta x_j)$ is a probability of deviation of x_j from its preferred state.

Threshold values were obtained for $I_{adapt,}$ on the basis of the levels used in biocybernetics (see Table 1).

Table 1. Correlation of biological object's states to threshold values.

Threshold values	Gradation level	Object's state
$I_n = 0.507$	$\|x - x_0\| < \pm 0.5\sigma$	Satisfactory adaptation
$I_{ten} = 2.01$	$\|x - x_0\| < \pm 1.5\sigma$	Tension of functional systems
$I_{st} = 3.09$	$\|x - x_0\| < \pm 2.0\sigma$	Supertension of functional systems
$I_f = 4.39$	$\|x - x_0\| < \pm 2.5\sigma$	Failure of adaptation

Note: Integral parameter of satisfactory adaptation (I_n), integral parameter of tensed functional system (I_{ten}), integral parameter of supertensed functional system (I_{st}), integral parameter of failed adaptation (I_f).

2.2. Bionic models in forecasting functional states

In the designed clinical decision support system, neural networks are responsible for forecasting changes in the parameters that characterize functional states over time and for selecting appropriate control actions. The choice of neural networks is determined by

- High efficiency of forecasting;
- Possibility to implement a committee of models to enable optimal forecasting;
- Possibility to use recursive neural networks for variable structure vectors.

Let us consider some object, which functional state is characterised with parameters x_i and actions u that affect the object's functional state. The functional state is defined by the energy-informational approach.

Let us assume that the value of the i-th parameter at some time t+1 can be calculated by the following equation:

$$x_i(t+1) = f(x_i(t), x_i(t-1), \ldots, u_j) .$$

Then it is the problem of time series forecasting. To solve this problem, a neural network is created for each parameter and trained on the basis of available data sampling.

Forecasting algorithms are based on recurrent neural networks [8, 9] that enable precise identification of behavior. Sequence-to-sequence learning is the main advantage of the aproach with a random length vector at the entry and a random length vector at the output.

2.3. Selection of control actions and minimization of the risk of system transition into an adverse functional state

Any functional state of a diagnosed subject at any specific time is characterized by integral parameter, $I_{adapt,}$ which is a function of parameters. Besides, values of control actions $U = \{u_1, u_2, \ldots\}$ are assigned for each diagnosed subject. Let us assume that desirable values $I_{кр}(t), t \in [t_0, t_k]$ are assigned for a preset control horizon at any specific time. The loss function [10] is calculated as a difference between the desired value of the functional state and the current state at some time $C_t = I_n - I_{adapt}$. Then, the optimization algorithm can take the following form:

$$J(x;u) = \frac{1}{k}\sum_{i=t_0}^{t_k} (I^*_{adapt_i} - I_{n_i})^2 \rightarrow min,$$

where $J(x;u)$ is an objective function; $I^*_{adapt_i}$ is a forecasted value of the integral parameter.

The use of the genetic algorithm takes the form of generating optional control actions on the basis of parameters obtained by the proposed energy-informational approach. The generated control actions should be aimed at minimizing the risk of adverse outcome.

The genetic algorith is operated according to the following procedure:

1. The initial population of n chromosomes is generated.
2. Each chromosome is evaluated.
3. A pair of parent chromosomes is selected by one of selection methods.
4. A crossover of two parents is carried out with pc probability to generate two offspring chromosomes.
5. The offspring chromosomes mutate with pm probability.
6. Steps 3-5 are repeated until a new generation with n chromosomes is produced.
7. Steps 2-6 are repeated until a termination criterion is reached.

2.4. Identification of functional states of biological systems and detection of inter-state transition based on implementation of an immune system

Immune systems are integrated into the bionic model to identify functional states based on the informational model. The use of the immune algorithm is reasonable, because an addition of new state parameters results in the change of the algorithm only (addition of cells in the immune algorithm); it does not affect formal characterization, neither requires additional training or retraining.

A negative selection algorithm is used as a base algorithm [11, 12]. The number of systems that use the characteristics of immune systems corresponds to the number of states. Each immune system responds to its state and neglects other states. Thus, we not only understand the current state of the object, but also detect where it can transition. Overlapping characteristics in several states can be considered as the level of immunity.

A control action (type of intervention) is created at the output of the immune algorithm and sent to the genetic algorithm.

3. Software development

Currently, a software is being developed for the clinical decision support system based on a multidimensional grid. Each cell of the grid contains values that reflect efficiency of solutions obtained for specific hyperparameters of the model and of the used numerical technique. The number of hyperparameters depends on the dimension of the grid.

In this study hyperparameters are sets of a priori assigned parameters of a model. Hyperparameters remain unchanged during training. In a neural-network-based model, hyperparameters can include the number of layers and neurons, the type of activation functions and their factors, as well as interconnections between the neurons.

Hyperparameters of the learning algorithm include a training pace; a type of parameter initialization; an objective function; a regulation mechanism; an approach to divide training data into training, test and validation sets; and the type of data normalization.

The designed software enables the use of several hyperparameters as input signals. Such hyperparameters are called control actions. To forecast some value $x(t)$, it is defined on the basis of previous values $(x(t-1), x(t-2), \ldots, x(t-p))$ and control action $u(t)$. In the medical context, *u(t)* can be interptreted as a therapeutic intervention.

Software optimization of hyperparameters is based on the genetic algorithm, where the fitting function is determined by the difference in integral parameters.

The software of the clinical decision support system is developed in Python and consists of the main module and secondary modules (pybrain, numpy, pandas and scikit_learn) that can be connected while running the code of the main module. These modules are complete forecasting models including neural network models and training algorithms. The main module is responsible for importing two dataframes with initial data and hyperparameters that are used as arguments in the instance constructors of the Model and Teacher classes. It also fills the grid cells.

4. Results

The clinical decision support system based on the bionic model was tested on data from pregnant women during all three trimesters of pregnancy. The following therapeutic measures were considered as control actions $u(t)$ [13]: 1) therapeutic exercises, respiratory gymnastics, music therapy, aqua gymnastics; 2) therapeutic exercises, respiratory gymnastics, pharmacotherapy; 3) aqua gymnastics, respiratory gymnastics.

Integral parameters [12] were calculated and cumulative curves were constructed (Figure 1) at the first stage of the investigation to characterize functional states of each diagnosed subject.

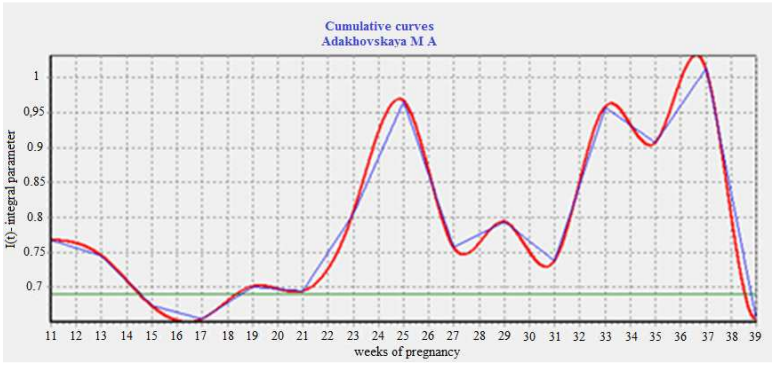

Figure 1. A sample cumulative curve calculated by (1) where blood substances were used as x_i parameters.

At the second stage, forecasted values of the obtained parameters, i.e. blood parameters of the pregnant women, and a forecasted value of $I^*_{adapt_i}$ were calculated by neural networks.

The genetic approach was used to minimize the risk of deviation of the obtained integral parameter [14] from its desired value (healthy performance) and select therapeutic intervention at the final stage. The resulting values are given in Table 2.

Table 2. Selected control actions to minimize the risk of adverse outcome

Trimester	Values of loss function C_t calculated for women with somatic diseases		
	Therapeutic measures. Group 1	Therapeutic measures. Group 2	Therapeutic measures. Group 3
1	0.4	0.7	0.1
2	0.2	0.7	0.3
3	0.1	0.5	0.4

The values in Table 2, calculated for a specific woman, impose therapeutic measures of groups 3-1-1 in appropriate trimesters of the pregnancy.

5. Conclusion

Neural networks, genetic and immune algorithms can be used to create bionic models that can be trained with joint gradient and bionic algorithms. In this paper, the influence of independent variables on dependent parameters is studied with due regard to control actions.

Efficient determination of parameters and hyperparameters in the model and the training algorithm allows minimization of the risk of deviation between actual and desired integral parameters. This enables selection of optimal control actions.

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References

[1] Shcherbakov M, Kamaev V and Shcherbakova N 2013 *Proceedings of the 7th IFAC Conference on Manufacturing Modelling, Management, and Control* **46(9)** 1027-1032

[2] Yurchenko M , Kochegurova E, Fadeev A and Piletskaya A 2015 *Proceedings of the 2014 International Conference on Engineering Technologies, Engineering Education and*

Engineering Management 847-851
[3] Massel L and Massel A 2012 *Bulletin of Tomsk Polytechnic University* **321(5)** 135-140
[4] Kochegurova E and Gorokhova E 2015 *Lecture Notes in Computer Science* **9330** 512-519
[5] http://scikit-learn.org/stable/modules/generated/sklearn.ensemble.RandomForestClassifier.html
[6] Carmesin H 1994 *Physics Letters* **A 188(1)** 27-31
[7] Fokin V, Pekker Ya, Berestneva O and Gerget O 2012 *Bulletin of Tomsk Polytechnic University* **321(5)** 120-124
[8] Wang H and Song G 2014 *Neurocomputing* **134** 289-295
[9] Gerget O, Marukhina O and Cherkashina Yu 2016 *Key Engineering* **685** 957-961
[10] Scherbakov M, Brebels A, Scherbakova N, Tyukov A, Yanovsky T and Kamaev V 2013 *World Applied Sciences Journal* **24(24)** 171-176
[11] Dasgupta D 2006 *Iskusstvennuye immunnye sistemy i ih primeneniye* (Artificial immume systems and their applications, Moscow: Fizmatlit) Russian
[12] D'haeseleer P, Forrest S and Helman P 1996 *Proceedings 1996 IEEE Symposium on Security and Privacy* 110-119
[13] Krivonogova T, Evtushenko I, Trenkaeva N, Gladkih L and Gerget O 2008 *Kompleksniy podhod k ozdorovleniuy beremennyh zhenschin* (Complex approach to health improvement of pregnant women, Tomsk) p. 183 Russian
[14] Gerget O and Kochegurov A 2012 *Bulletin of Tomsk Polytechnic University* **135(5)** 117-120