Artificial Immune System using Fuzzy Logic for Optimal Reply

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***Abstract*— There was developed a functional scheme of the immune system for optimal control of therapeutic doses of sulfonamides for the pyelonephritis therapy. Obtained the results of the neuro-fuzzy network training in the form of optimal values of the therapeutic doses of the system. Obtained the results of modeling in the MATLAB environment of three phases of chronic pyelonephritis by the urosulfan therapy on the basis of the results of the neuro-fuzzy setting of the regulator. Presented the comparative analysis of the modeling results of the change in the amount of microorganisms at pyelonephritis depending on time. Developed a software product was developed on the basis of the ANFIS editor of MATLAB environment, in conjunction with the mathematical model of optimal control of an immune object.**

Keywords— artificial system; immune system; fuzzy logic; optimal reply

I. INTRODUCTION

Nowadays, there are a wide range of activities in the field of medicine, concerning the development of methods of computing and information technologies to get the results of data processing for diagnosis and treatment of diseases. Due to the fact that the problems associated with questions of medicine, have a high complexity and uncertainty, there are used methods of fuzzy systems.

In many areas of medicine, for example in the treatment of kidney diseases, cancer and asthma diagnostics, there were developed approaches based on fuzzy logic [1]. The control system based on fuzzy logic helps doctors make quick and effective decisions regarding the dose of the drug, taking into account all factors. With this system, medical errors are minimized, possible complications are prevented. Moreover, reliability of this method has been proven and accepted by statistical studies [2, 3].

Today, there are a wide range of works related to the development of methods of fuzzy logic theory to the class of models that have found their application in medicine [4–9]:

- for the analysis of Parkinson's disease [4];
- for the analysis of psychosomatic disorders [5];
- to determine the ophthalmic artery disorders [6];
- for the diagnosis of breast cancer [7];
- for the diagnosis of diabetes [8];
- to predict heart diseases [9].

This paper is organized as follows. Section 2.1 presents results of a systematic approach to the processing of structural data about the age and weight of a person, taking into account the effect of these properties on the organism on the choice principles and methods of dosing drugs, using the methodology of fuzzy sets. So section 2.1 is devoted to the linguistic variables of the control action and sulfonamides dosing at pyelonephritis. Section 2.2 describes the synthesis of the artificial immune system. We end the paper in section 3 with some conclusions.

II. OPTIMAL CONTROL OF THERAPY USING ARTIFICIAL IMMUNE SYSTEM

A. Optimal control of sulfonamide therapy with neural-fuzzy tuning

In order to form a set of variables of the system of neuro-fuzzy output, at the decisions making in the processes of diagnosis and therapy, it is necessary to have processed information accumulated by specialists in medicine [10, 11]. Significant experience and knowledge of relevant experts in their field allows to create extended databases on the basis of which it is possible to conduct differential diagnosis and differentiated treatment.

Synthesis of a neuro-fuzzy network to solve the problems of body therapy, decision-making in differential treatment, is based on the processing of certain information about the patient and is based on the use of accumulated knowledge, where the developed systems are able to help the doctor to choose the tactics of treatment. The aim is to create an intelligent system for personalized medical diagnostics, which is constructed on expert clinical recommendations and computer knowledge representation tools.

Problem statement. To develop software for neuro-fuzzy output for sulfonamides therapy, with formulated recommendations of the expert data formation, a way to describe and present them. To develop a functional diagram and mathematical model of artificial immune system of optimal reply.

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In order to develop a database of input and output variables of the system for the diseases therapy by various medical preparations, we will compile an expert table. To the main input and output variables affecting the therapy conduction, it is proposed to attribute the following ones [12]: the properties of the drug; laboratory indicators of the disease; body properties; therapeutic doses of drugs.

Each of the input variables corresponds to a linguistic name, designation, unit of measure and fuzzy sets represented by the degree of belonging. All variables, and the corresponding to them fuzzy sets, are formed on the basis of expert opinion. The output variables corresponding to the therapeutic doses of the preparations are described by the functions of the Sugeno fuzzy inference system.

For the sulfonamides therapy of such a disease as pyelonephritis there are used various sulfanilamide preparations. Each of the preparations differs by the specific use for different indications. For each drug at the construction of a system of fuzzy output it is necessary to make a basis of rules of pyelonephritis therapy strategies using sulfanilamide preparations. As an example, there was chosen a variant of human body therapy with urosulfan.

The functional scheme of the neuro-fuzzy immune system of the optimal control of sulfanilamides therapeutic doses has the form of a control system, the optimal control unit of which is complemented by neuro-fuzzy settings (Fig. 1). This scheme allows adjustment and training of the setting block. In this case, the control system using the apparatus of artificial neural networks and fuzzy logic makes it possible to identify the object and to synthesize for it the optimal response, that makes it possible to solve the considered problem of system synthesis under uncertainty conditions on the basis of available experimental data obtained at the facility [13].

Based on the methods of fuzzy logic, it is possible to design a therapy system that can function effectively in the presence of information about a control object of only a qualitative nature (Fig. 1).

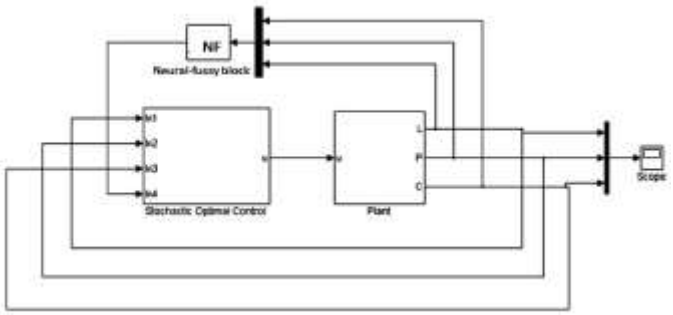

Fig. 1. Structure of optimal stochastic control with a neural-fuzzy adjustment block in the MATLAB Simulink environment

The blocks, included in the scheme (Fig. 1) in the MATLAB environment, are the elements associated with the equations developed in [13]:

- Plant: mathematical model of the sulfonamides therapy of the human body;
- Stochastic Optimal control (SOC);
- NF: Neuro-fuzzy setting block with gibrid_medicine.fis software.

In accordance with these blocks, the fuzzy control device generates a control, u_k, based on a fuzzy set of control actions in order to achieve the quality criterion [13]. All the initial information about the control strategy is stored in the bases of the membership functions, $\mu(x)$, and the conditional logical inference rules database. A fuzzy set of control actions corresponds to the membership function, $\mu(u)$, which is formed on the basis of the selected quality criterion and constraints in SOC block.

For the development of rules of fuzzy logic there were obtained membership functions of sulfonamides duration of excretion, acetylation of sulfonamides and laboratory parameters of pyelonephritis phases [13]. The fuzzy system takes into account that in order to prevent complications it is necessary to keep up strictly to the age and weight doses and to intervals between them, in other words, to take into account the input linguistic variables "age" and "weight". According to the analyzed data there were defined fuzzy set "age", presented by the terms: "children", "young people", "adult", "old" and fuzzy set of the weight "centiles," associated with the levels of centile table: "low" "normal", "high".

In order to adjust the parameters of the control impact "therapeutic doses of drugs" there were developed linguistic variables, denoted by degree of membership to the fuzzy sets. As a programming environment there was used MATLAB environment with the package of fuzzy inference Fuzzy Logic Toolbox (Fig. 2).

Fig. 2. The interface for viewing rules in the RuleEditor of the generated system

Let's obtain the modeling results of the optimal control scheme with the neural-fuzzy setting block in the MATLAB environment, using the result, u=2.35, with the use of ursulfan therapy [13].

B. Функциональная схема иммунной системы оптимального управления терапевтическими дозами

The mathematical model of pyelonephritis therapy is described by discrete equations of the intellectual immune system developed in [13]. In this case, the mathematical model of pyelonephritis therapy is described by the discrete equations

of an artificial immune system linking the dynamics of changes, L, P, C:

$$\begin{cases} L_{k+1} = \left(-\gamma - fP_k - gC_k\right) L_k T + L_k \\ P_{k+1} = \left(-\beta + \lambda\left(1/L_k\right) - \rho C_k\right) P_k T + P_k \\ C_{k+1} = \left(-\alpha + \eta P_k\right) \cdot C_k T + C_k + u_k \end{cases} \quad (1)$$

where L – quantitative representation of body resources (the variable is associated with the symptoms of chronic pyelonephritis depending on the amount of leukocytes, active leukocytes, ESR);

P – the change in the amount of microorganisms at pyelonephritis depending on time (associated with bacteriuria and the presence of microorganisms) (Fig. 3);

C – the change in the amount of detected microorganisms and inhibition, due to sulfonamides, in microbes of the enzyme that synthesizes folic acid, which is a factor of growth and reproduction for microorganisms.

γ – rate of natural increase in body resources;

f – amount of resources for the microorganism;

g – amount of body resources for reaction to sulfanilamides, estimates the side effect of the drug;

β – rate of change in the number of microorganisms in the absence of body resources; $-\beta+\lambda$ – cascade growth of the number of microorganisms due to resources;

ρ – probability of detection of a microorganism;

α – coefficient associated with the duration of excretion of sulfanilamides from the body;

η – therapeutic dose of sulfonamides, taking into account the duration of their removal from the body;

u_k – control.

Based on the developed model (1), taking into account the estimation of the random parameter, ρ, it was obtained the results of modeling in the MATLAB environment of the three phases of chronic pyelonephritis (Fig. 3), which are classified according to the activity of the inflammatory process in the kidney (ESR and bacteriuria are considered as symptoms) [13]:

- Phase of active inflammatory process:

a) ESR – above 12 mm/hour in 50-70% of patients;

b) bacteriuria – 100 000 pcs. and more in 1 ml of urine.

- Phase of the latent inflammatory process:

a) COЭ – not higher than 12 mm/h;

b) bacteriuria is absent or does not exceed 10 000 in 1 ml.

- The phase of remission or clinical recovery:

a) ESR – less than 12 mm/h;

b) bacteriuria – No.

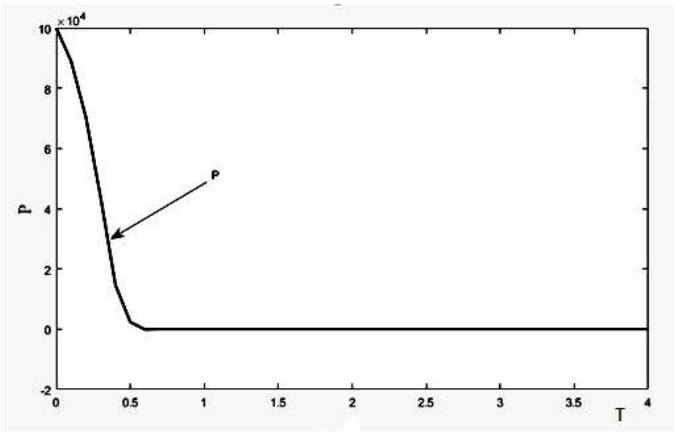

Fig. 3. Results of modeling the change in the number of microorganisms with pyelonephritis, *P*

Let's given the initial conditions and parameters for modeling the processes of chronic pyelonephritis with sulfanilamide therapy of the first group (short-term action): L_0=5mm/h, P_0=10, C_0=1, α= –0.0001, β= –0.0001, γ= –0.0001, f= –0.0001, g = –0.0001, ρ – random parameter with binomial distribution law, η=1.

Based on the developed model, the modeling results (Fig. 3) differ from the modeling results without fuzzy logic (Fig. 4) obtained in [13].

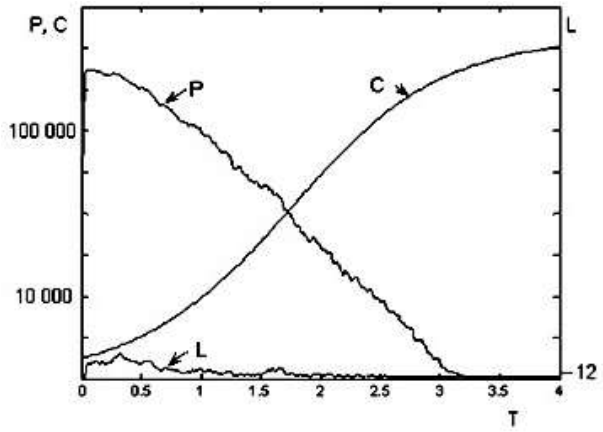

Fig. 4. Modeling results [13], *P, C, L*

Comparative analysis of the results presented in Fig. 3 and Fig. 4 shows that the dose calculated on the basis of the neuro-fuzzy setting of the regulator is more effective (Table 1).

TABLE I. COMPARATIVE ANALYSIS OF THE RESULTS

Phases of the inflammatory process	**Amount of microorganisms**	
	Figure 2	***Figure 3***
Active	not more than 100.000 pcs.	100 000 pcs. and more
Latent process	No	not more than 10
Remission phase	No	No

The developed software product on the basis of the ANFIS editor of MATLAB environment in conjunction with the mathematical model of optimal control of the immune object allows to obtain the control with neural-fuzzy setting of the optimal regulator.

III. CONCLUSION

During the investigation implementation the following results were obtained: created the algorithm of the creation of a neuro-fuzzy network for the artificial immune system of sulfanilamide therapy in the MATLAB programming environment, using the Fuzzy Logic Toolbox, NNTool and Anfis packages. There is used a fuzzy multi-layered neural network in which the layers act as elements of a fuzzy inference system. Obtained the results of the neuro-fuzzy network training in the form of optimal values of the therapeutic doses of the system.

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