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The research study of the adaptive neuro-fuzzy interference system (ANFIS) for the diagnostics of endogenous intoxication syndrome with chronic kidney disease

The article presents information on the application of the neuro-fuzzy diagnostics method of endogenous intoxication syndrome (EIS) in patients suffering from the chronic renal failure and undergoing long-term ambulatory hemodialysis. Early diagnostic task of the endogenous intoxication syndrome is of great importance, as the prevalence rate of chronic kidney disease (CKD) is not less than 10%, reaching 20% or more in certain categories of persons.The publication offers a less expensive and more accessible diagnostic method of EIS. The method is based on the application of the neuro-fuzzy network. The systems based on neuro-fuzzy networks make conclusions on the basis of the knowledge data base which contains a priori expert's experience, and the membership functions parameters are configured using learning algorithms of neural networks.They used an adaptive neuro-fuzzy interference system (ANFIS), implemented in the software environment "Matlab". The article presents the structure of fuzzy neural network consisting of five layers for the diagnostics of EIS. Specified parameters and actions carried out on each network layer are described in details. A fuzzy knowledge data base is set up for modeling of the patient's state. The knowledge data base includes 18 rules of fuzzy production that correspond to the consistency condition. For ANFIS network learning a back propagation of error algorithm was used, which allows to prepare better the neuro-fuzzy network for solving of specific problems in less time.Conducted experiments showed that by virtue of the use of the neuro-fuzzy network for the diagnostics of endogenous intoxication syndrome, it became possible to provide a sufficiently high accuracy of the diagnostics.

Key words: chronic kidney disease, neuro-fuzzy network, adaptive neuro-fuzzy interference system ANFIS, knowledge data base, membership function, linguistic variable.

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Исследование адаптивной нейро-нечеткой сети ANFIS для диагностики синдрома эндогенной интоксикации с хронической почечной недостаточностью

В статье представлены сведения о применении нейро-нечеткого метода диагностики синдрома эндогенной интоксикации (СЭИ) у больных с хронической почечной недостаточностью, находящихся на программном амбулаторном гемодиализе.Задача ранней диагностики синдрома эндогенной интоксикации имеет большое значение, поскольку распространенность хронической болезни почек (ХБП) составляет не менее 10%, достигая 20% и более у отдельных категорий лиц.

В работе предлагается менее дорогостоящий и более доступный метод диагностики СЭИ. Метод основан на применении нейро-нечеткой сети. Системы на основе нейро-нечетких сетей выводы делают на основе базы знаний, в которой заключен априорный опыт эксперта, а параметры функций принадлежности настраиваются с использованием алгоритмов обучения нейронных сетей. Использовалась адаптивная нейро-нечеткая сеть ANFIS, реализованная в программной среде Matlab. В статье представлена структура нечеткой нейронной сети из пяти слоев для диагностики СЭИ. Подробно расписаны задаваемые параметры и действия, выполняемые на каждом слое сети. Построена нечеткая база знаний для моделирования состояния больного. База знаний содержит 18 правил нечетких продукций, которые удовлетворяют условию непротиворечивости. Для обучения сети ANFIS использовался алгоритм обратного распространения ошибки, что дает возможность лучше подготовить нейро-нечеткую сеть для решения конкретных задач с меньшими затратами времени. Проведенные эксперименты показали, что благодаря использованию для диагностики синдрома эндогенной интоксикации нейро-нечеткой сети, стало возможным обеспечить достаточно высокую точность диагностики.
Ключевые слова: хроническая почечная недостаточность, нейро-нечеткая сеть, ANFIS, база знаний, функция принадлежности, лингвистическая переменная.

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Созылмалы бүйрек жеткіліксіздігі бар эндогендік интоксикация синдромын диганостикалауға арналған ANFIS бейімді нейро-айқын емес желіні зерттеу

Мақалада бағдарламалық амбулаторлық гемодиализдегі созылмалы бүйрек жеткіліксіздігі бар науқастарда эндогенді интоксикация синдромын (ЭИС) диагностикалаудың нейро-айқын емес әдісін қолдану туралы мәліметтер ұсынылған. Эндогенді интоксикация синдромын ерте диагностикалау міндеті зор мағынаға ие, себебі созылмалы бүйрек ауруының (СБА) таралуы кем дегенде 10% құрап, адамдардың жекелеген санаттарында 20% және одан да жоғары шамаға жетеді. Жұмыста ЭИС диагностикалаудың анағұрлым қолжетімді және барынша қымбат емес әдісі ұсынылады. Әдіс нейро-айқын емес желінің қолданылуына негізделген. Нейро-айқын емес желінің негізіндегі жүйелер сарапшының априорлы тәжірибесі қамтылған білім қорының негізінде ұйғарым жасайды, ал қатыстылық функцияларының параметрлері нейрондық желілерді оқыту алгоритмдерін қолдану арқылы бапқа келтіріледі. Matlab бағдарламалық ортасында жүзеге асырылған ANFIS бейімді нейро-айқын емес желісі қолданылған. Мақалада ЭИС диагностикалауға арналған бес қабаттан тұратын айқын емес нейрондық желінің құрылымы ұсынылған. Тағайындалатын параметрлер мен желінің әрбір қабатында орындалатын іс-әрекеттер егжей-тегжейлі көрсетілген. Науқастың күйін үлгілеуге арналған айқын емес білім қоры құрылған. Білім қоры қайшылықсыздық шартын қанағаттандыратын айқын емес өнімдердің 18 ережесін қамтиды. ANFIS желісін оқыту үшін қатені кері тарату алгоритмі қолданылған, бұл уақытты аз шығындап, нақты мәселелерді шешуге арналған нейро-айқын емес желіні жақсырақ дайындау мүмкіндігін береді. Жүргізілген тәжірибелер көрсеткендей, эндогенді интоксикация синдромын диагностикалау үшін нейро-айқын емес желіні қолданудың арқасында диагностикалаудың жеткілікті түрде жоғары дәлдігін қамтамасыз ету мүмкін болды.
Түйінді сөздер:: созылмалы бүйрек жеткіліксіздігі, нейро-айқын емес желі, ANFIS, білім қоры, қатыстылық функциясы, лингвистикалық айнымалы.

1. Introduction

Endogenous intoxication syndrome (EIS) is one of the most common in clinical practice and is characterized by the accumulation in the tissues of biological products, which are a result of responding to damaging factor [1-2]. SEI is the prevalence of chronic renal failure (CRF) [3]. According to the large population-based registries, such as the US Renal Data System and the Russian Register of renal replacement therapy, the prevalence of chronic kidney disease (CKD) is not less than 10%, reaching 20% or more at certain categories of persons (the elderly, patients with diabetes of the second type) [4]. Thus, the problem of early diagnosis of the syndrome of endogenous intoxication is of great importance.

2. Setting of the problem

The problem of early EIS diagnosis is hampered by complexity of using of toxicity specific markers. There are various laboratory techniques for EIS diagnosis but they are expensive, and therefore there is a task of creating of less costly and more affordable diagnostic methods. To make a correct prediction of the disease it is necessary to analyze a large number of risk factors and diagnostic features that lead to disease. For the treatment of biomedical data formal methods are used. Systems based on neuro-fuzzy networks make conclusions on the basis of the knowledge base in which a priori experience of the expert is concluded and parameters of membership functions are configured using the learning algorithms of neural networks. Neuro-fuzzy networks are able to use inaccurate information, acquire new knowledge, to study, to classify images, to predict and in addition may explain this result.

The aim of the study is optimization of EIS computer diagnostics using neuro-fuzzy network in patients with end-stage of CKD.

3. Solution

When the diagnosis of the disease in some patients only a small number of features is enough for accurate diagnosis the others require further examination. Often this is due to the fact that between the healthy and the sick sometimes there is no clear dividing border. In such cases to build a model of diagnosis is advisable to apply neuro-fuzzy network [5]. As such you can use the well-known network of sales in the software environment Matlab — the so-called adaptive neuro-fuzzy network ANFIS (Adaptive Neuro-Fuzzy Inference System). The ANFIS conclusions are based on fuzzy logic and corresponding membership functions are self-adjusted with the help of back-propagation errors algorithm.

ANFIS is adaptive neuro-fuzzy inference [5]. ANFIS network is a multilayer neural network of a special structure without feedback input to which are fuzzy linguistic variables with the only way out. A linguistic variable is defined as a tuple [5]:

$$< \beta,\ T,\ X,\ G,\ M > \tag{1}$$

где β — the name of the linguistic variable; T — the set of values of linguistic variable, which is also called the base term-set. Elements of the basic term-set are names of fuzzy variables α; X — the domain of the fuzzy variables included in the definition of linguistic variable β; G — syntactic procedure that describes the formation of a plurality of T new and meaningful in this context for the values of the linguistic variable; M — semantic procedure that allows you to assign a new value to each of the linguistic variable obtained using G procedure, some meaningful content through the formation of the corresponding fuzzy set.

Thus the terms of the input linguistic variables described by the standard membership functions and terms of the output variable is a linear function or permanent facilities. ANFIS network concludes on the basis of fuzzy rules of production which has a constant weight set in 1. Setting of such network parameters is carried out in the course of training on the experimental data. Education on adaptive-neuro fuzzy networks includes two steps: 1. Generation of linguistic rules; 2. Adjustment of the membership functions. The first challenge relates to the problem such as exhaustive search, the second — to the optimization in continuous space. With automatic generation of fuzzy rules is necessary to ensure completeness and consistency.

The mechanism or algorithm of fuzzy inference is a basic part of the architecture of neuro-fuzzy network, the algorithm consists of the following stages: fuzzification of the input variables, development of fuzzy rules and defuzzification (figure 1).

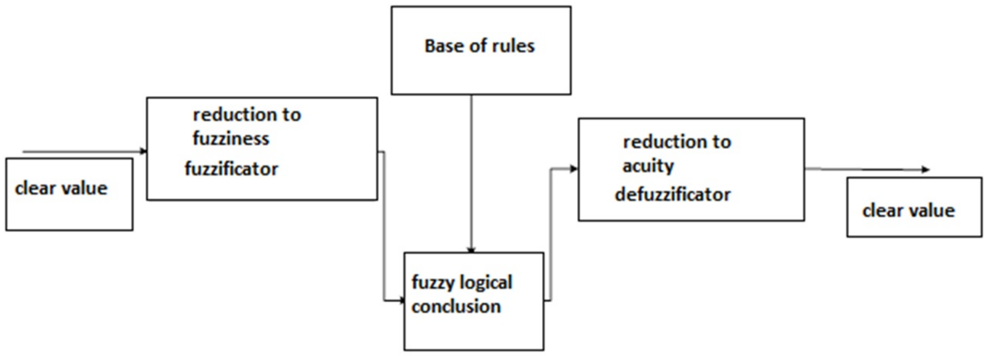

Figure 1 – Diagram of fuzzy logical inference

When fuzzification of input variables compossibility is matched between the specific values of the individual input variables and values of the membership function. At this stage for each of the linguistic terms for all input variables need to be determined by the membership function. Membership functions that were identified after the completion of stage fuzzification used in the premises of the rules of fuzzy inference. Linguistic variables can be determined from the formula (1).

For each linguistic variable required number of values (terms) is determined and each of them is assigned by a value of a physical quantity described [5]. For example, the value of linguistic variable «body temperature» are the terms «reduced», «normal», «increase», «high».

To implement linguistic variable it is necessary to determine the exact physical values of its terms. Under the terms of fuzzy theory sets [5] each value of a physical quantity can be associated with a number from zero to one which determines the degree of membership of the physical value to a particular term of linguistic variable. Before creating a linguistic variable it is necessary to determine how much terms of the variable will be enough to accurately represent the physical quantity. For most systems it is enough to determine from 3 to 7 terms for each linguistic variable. The minimum value of the number of terms is enough to represent a physical quantity since it contains two extreme values (minimum and maximum) and one secondary. The maximum number of terms is not limited and depends entirely on the problem and required accuracy of the system description. The 7 number is determined from short-term memory capacity due to the person which according to modern concepts can be stored for up to seven units of information.

Membership of the exact value of each one of the terms of the linguistic variable is defined by the membership function $\mu_{A_k}(x)$. Its appearance can be completely arbitrary. Usually as the triangular function is selected as membership function [5]:

$$\mu_{A_k}(x) = \left\{ \begin{array}{l} 0,\ x \le a \\ \frac{x-a}{b-a}, a \le x \le b \\ \frac{c-x}{c-b}, b \le x \le c \\ 0,\ c \le x \end{array} \right\}, \tag{2}$$

where $\{a, b, c\}$ — numerical parameters assuming arbitrary real values. Parameters are referred to as *parameters parcels*.

If some of the parameters of the model have a «blur», i. e. their exact planned value is unknown then it's better to use so-called triangular fuzzy numbers with triangular shape membership function as an input data (figure 2). These numbers simulate the statement of the form: «A parameter is *approximately equal to* $\bar{a}$ and uniquely in the range of $[\mathrm{a_{min}},\ \mathrm{a_{max}}]$».

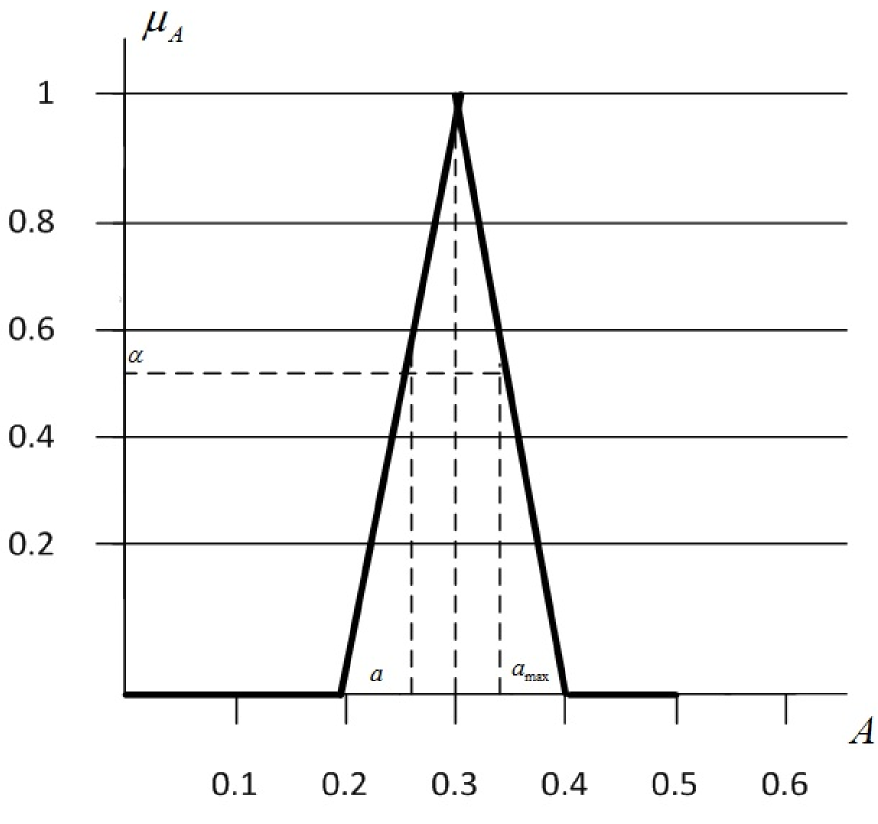

Figure 2 – Triangular membership function of the fuzzy number A

At the stage of «development of fuzzy rules» the rules are determined that link linguistic variables a set of such rules describes the knowledge base. The knowledge base is needed to describe the experience of a priori expert using a formal language in a particular subject area in the form of fuzzy production rules.

Any rule consists of the premises (antecedents: part IF ...) and conclusion (consequent: a part of THEN ...) using linguistic variables. The rule may contain more than one parcel but consequent always contains one conclusion. If there are several parcels they are combined by the logical connectives AND or OR. Customary law is written as: «IF (parcel) (ligament) (parcel) ... (parcel) THEN (conclusion)». Example: IF «Patient has a high temperature», THEN «he is sick», or IF «The patient has a high temperature» AND «low hemoglobin level», THEN «he was sick». A fuzzy rule is as follows:

$$R_k : \text{If } x^1 \in A_k^1 \text{ and ... and } x^n \in A_k^n, \quad \text{then class } y = C_k \text{ with weight } V_k$$

where R_k — mark of rule k, $x = (x^1, \dots x^n)$ — n dimensional vector of input features, y — output feature, A_k^j— fuzzy set of rule precondition R_k, C_k — class mark, V_k — weight or degree of rule reliability.

The process of fuzzy rule calculating is called fuzzy logical conclusion and is divided into two steps: synthesis and conclusion.

The first step is to determine the degree of generalization of all rule antecedents. For this purpose modified methods of fuzzy logic are used: MIN (...) and MAX (...) [5]. When you use the MIN (...) the minimum value of the degree of affiliation of all the antecedent is calculated, and using the second method — the maximum value of the degree of affiliation of all the antecedent is calculated:

$$(\mu_1 \cap \mu_2)(x) = \min(\mu_1(x), \mu_2(x))$$
$$(\mu_1 \cup \mu_2)(x) = \max(\mu_1(x), \mu_2(x))$$

where μ_1, μ_2 — membership functions of rule antecedents related to a bunch of AND and OR [5].

Using of one or other operator depends on the bunch connecting parcel in the rule. If a bunch AND is used operator MIN (...) is applied. If it's combined by OR bunch you must apply the operator MAX (...). Well, if there is only one parcel in the rule operators are not needed. The operation described above is fulfilled for each rule in the knowledge base.

Consider an example. Suppose we have the following rule:

IF CREATININE LEVEL = high
AND LEVEL OF UREA = high,
THEN PACIENT = sick.

After the fuzzification of input data we find that the degree of membership to the term *high* of a linguistic variable CREATININE LEVEL is 0.9 and the degree of membership to the term high of a linguistic variable LEVEL OF UREA is 0.8. For our example we apply operator MIN (...) because AND bunch is used. So, we get the following:

$$\min(0.9; 0.8) = 0.8$$

Consequently the degree of membership of the rule antecedent is 0.8

Next step - we find the fuzzy value of the output variable. To give the result it is necessary to bring to the stage of definition it is going to bring on the stage of defuzzification. At the stage of defuzzification transition from fuzzy values of quantities to certain physical parameters is fulfilled. At this stage various methods are used, one of them method of the center of a maximum, a method of center of gravity, a method of the largest of maxima [5].

As several terms of output variable can be a result of the fuzzy inference the rule defuzzification must determine which term should be chosen. When you use the center of the maximum defuzzification typically selects the maximum of the obtained values of the output variable.

Experiments were carried out using fuzzy inference algorithm Sugeno [5, 6, 7]. Its main feature is that the conclusion of the rule are set not by vague terms but by a linear function of the inputs [5]. The structure of the fuzzy neural network is shown in figure 3.

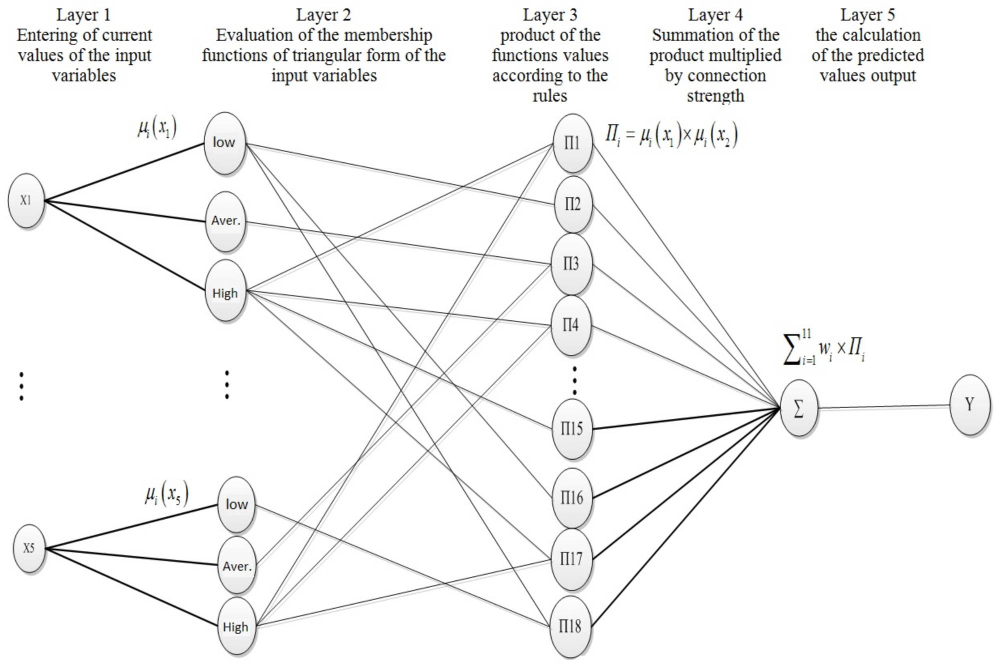

Figure 3 – The structure of the fuzzy neural network for EIS diagnostic

On the first layer fuzzy terms of input variables are determined. These are the five selected indicators — a total protein, urea, creatinine, albumin, bilirubin. The only way out of the network is a sign «ill- health». Symptom «healthy» was coded by output value $y = 1$, the symptom "patient"was coded by output value $y = -1$. In this way model of neuro-fuzzy network of patient status was developed depending on five indicators: x_1 — total protein, x_2 — bilirubin, x_3 — urea, x_4 — creatinine, x_5 — albumins.

On the second layer each variable is represented by three membership functions of triangular type (formula 2). This function is used to define sets of properties that characterize uncertainty such as «approximately», «average value», «is located in the interval».

As the term set of linguistic variables «Total protein», «Bilirubin», «Urea», «Creatinine», «Albumin» set was used $T_{1...5}$ ={«low level», «average level», «high level»}. As the term set of output linguistic variable «The patient's condition» set was used T_y={«sick», «healthy»}. Intervals of membership functions for the terms «low level», «average level», «high level» have been obtained in the study sample consisted of data on patients in the terminal and in the early stages of CKD and on the basis of medical data [8, 9, 10, 11]. For the output variable a linear function from inputs is used $y = -1$, $y = 1$, because Sugeno algorithm of fuzzy inference is used. For shorthand of term linguistic variables the following designations are used: x_1 — first input linguistic variable named «Total protein», x_2 — second input linguistic variable named «Bilirubin», x_3— third input linguistic variable named «Urea», x_4 — fourth linguistic input variable called «Creatinine», x_5 — fifth input linguistic variable named «Albumin». Generalized conclusions are presented in table 1.

Table 1 – The values of membership functions for linguistic variables

	Term set of linguistic variable	Lower boundary	Higher boundary
1	High	83	90
	Average	64	83
	Low	42	64
2	High	50	62
	Average	35	50
	Low	24	35
3	High	5.9	149.8
	Average	2.5	6.4
	Low	2.5	3
4	High	109	2650
	Average	62	115
	Low	50.08	68
5	High	17.1	205
	Average	3.4	17.1
	Low	2	3.4

On the third layer of fuzzy neural network creation of knowledge base rules is fulfilled [5]. Third layer node is connected to the nodes of the second layer, which form the respective antecedents of the rule.

To solve this problem knowledge base was built. When it was being the main condition was that the patient is considered to be sick if at least one parameter exceeds the permissible level. Built knowledge base includes 18 of the rules of fuzzy production which satisfies consistency and contains the rules of the following form:

RULE 1: IF "x_1 is a high level " AND "x_2 is a high level "
THEN "y is sick"

Other rules given in table 2 where x_1, x_2, x_3, x_4, x_5 — input variables, y — output variable. Antecedents elements of fuzzy rules are associated by logical operations AND (rules 1-16), OR (rules 17-18).

On the fourth layer significance of the rules is adjusted and then particular fuzzy subsets are defined in which the membership function of the output is scaled using the calculated degree of rule truth preconditions.

On the fifth layer output of the network is calculated.

After defining of neuro-fuzzy network structure preprocessing of input data was carried out using *k–means* clustering algorithm and then gaps were filled in.

Learning of ANFIS networks to determine the parameters of membership functions of Sugeno fuzzy inference systems can use backpropagation algorithm. The main feature of this approach is that setting of membership functions parameters is carried out without modifying of rules base [5]. Given a training set consisting of a set of examples $x_1^{(k)}, x_2^{(k)}, ..., x_m^{(k)}$ — values of the input variables $x_1, x_2, ..., x_m,$ $y^{(k)}$ — reference value of the output variable y in $k-$ example, K — the total number of examples in the training set. Note that for Neuro-Fuzzy ANFIS network with using of Sugeno algorithm configurable parameters are the parameters of membership functions of the formula (2), where a_{ij} — center of membership function, b_{ij} — width of this function.

At the first stage of training for each example from the training set by the values of input variables $x_1^{(k)}, x_2^{(k)}, ..., x_m^{(k)}$ fuzzy network calculates values of output variable $y'^{(k)}$.

At the second stage error function is calculated for all the examples of learning sample:

$$E^{(k)} = \sum \frac{\left(y'^{(k)} - y^{(k)}\right)^2}{2}, \ k = 1, ..., K \tag{3}$$

In this case the error function can be written as a function depending on the following arguments:

$$E^{(k)} = E^{(k)}\left(a_{ij}, b_{ij}\right) = \frac{1}{2}\left(y'^{(k)}\left(a_{ij}, b_{ij}\right) - y^{(k)}\right)^2, \ k = 1, ..., K \tag{4}$$

At the third stage values are corrected (a_{ij}, b_{ij}) for each instance of learning sample based on the relatives:

$$\begin{array}{l} a_{ij}\left(t+1\right) = a_{ij}\left(t\right) - \eta \frac{\partial E^{(k)}(t)}{\partial a_{ij}(t)}, \\ b_{ij}\left(t+1\right) = b_{ij}\left(t\right) - \eta \frac{\partial E^{(k)}(t)}{\partial b_{ij}(t)}, \end{array} \tag{5}$$

where t — number of learning iterations, $\eta \in [0, 1]$ — coefficient characterizing the speed of learning.

Stages 1-3 are repeated iteratively and routine adjustment of all parameters is considered completed if the value of error function for each example of learning sample does not exceed some predetermined threshold:

$$E^{(k)} < \varepsilon, \ k = 1, ..., K,$$

or estimate of the average total error of fuzzy network with all the examples of learning sample does not exceed a set threshold:

$$E = \frac{1}{K}\sum_{k=1}^{K}\left(y'^{(k)} - y^{(k)}\right)^2 < \varepsilon.$$

In this case it is considered that the fuzzy network successfully learned.

When learning using back propagation algorithm uniqueness property representation is ensured by linguistic terms related adaptation parameters of membership functions. Thus from the above analysis it is clear that using the algorithm of back propagation optimal refinement of membership functions occurs which gives opportunity of better preparation of neuro-fuzzy network for specific tasks in less time.

Learning samples were drawn into two groups of observations. The first group included observations on patients in end-stage of CKD, the second group of observations — data on patients in the early stages of CKD. The allowable change of step size per iteration is — 20%. The number of training cycles of created fuzzy neural network was 100 epochs. The network was trained on the basis of historical data on patients in the terminal and in the early stages of CKD. After that it has been tested on a sample of data that were not used in the learning sample.

Table 2 – Fuzzy knowledge base for modeling of patient's condition (logic operation AND, OR)

№	x_1	x_2	x_3	x_4	x_5	y
1	High	High	High	High	High	Sick
2	Low	Low	Low	Low	Low	Sick
3	Average	Average	Average	Average	Average	Healthy
4	High	Low	High	Low	High	Sick
5	High	Low	High	Low	Low	Sick
6	Low	High	Low	High	Low	Sick
7	Low	High	Low	High	High	Sick
8	Average	High	Average	High	Average	Sick
9	High	Average	High	Average	High	Sick
10	Average	Low	Average	Low	Average	Sick
11	Low	Average	Low	Average	Low	Sick
12	Average	Low	Average	Low	High	Sick
13	High	High	High	-	High	Sick
14	Low	Low	Low	-	Low	Sick
15	High	High	-	High	-	Sick
16	Low	Low	-	Low	-	Sick
17	High	High	High	High	High	Sick
18	Low	Low	Low	Low	Low	Sick

6. Conclusion

It was established experimentally that the neuro-fuzzy network data on the basis of patients with end-stage CKD results in an error — 7.14%. And on the basis of patients on the early stages of CKD network gives an error of 19,03% [12-13]. Summarizing we can say that thanks to the use of the neuro-fuzzy network for endogenous intoxication diagnosis it was possible to provide a sufficiently high diagnostic accuracy.

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