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A new method for prediction of the hospitalization period in ICU using neural networks

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ABSTRACT

Introduction:APACHE (Acute Physiologic and Chronic Health Evaluation) score is a medical tool designed to measure the severity of disease for adult patients admitted to Intensive Care Units (ICU). However, it is designed based on the American patients' data and is not well suited to be used for Iranian people. In addition, Iranian hospitals are not equipped with High Dependency Units which is required for original APACHE.

Method: We aimed to design an intelligent version of APACHE system for recognition of patients' hospitalization period in ICUs. The new system can be designed based on Iranian local data and updated locally. Intelligence means that the system has the ability to learn from its previous results and doesn't need manual update.

Results: In this study, this new system is introduced and the technical specifications are presented. It is based on neural networks. It can be trained and is capable of auto-learning. The results obtained from final implemented software show better performance than those obtained from non-local version.

Conclusion: Using this method, the efficiency of the prediction has increased from 80% to 90%. Such results were compared with the APACHE outputs to show the superiority of the proposed method.

Keywords: Health status indicators, Hospitalization, Intensive care unit, Classification system, Neural networks

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Introduction

Considering the increasing development of software and its application in solving the problems in different disciplines of industry and medicine, the researchers are more inclined toward using different types of software. One of the main applications of software in industry is the prediction in different fields including economy, environment, and medical sciences to aid individuals in living a better life and more success in different areas. Among the current predictive types of software, Exchange Market Prediction (1, 2), Earthquake Prediction (3), Weather Forecast Prediction (4) can be mentioned.

After designing different types of software for application in industry and medicine, the researchers found that some parts of this software lose their quality after some time and don't show acceptable results. On the other hand, some kinds of software in different fields like the predictive software lose the accuracy after a while for different reasons. As a result, the designers of such software should be updated to produce a new version. In creating different designs which are costly and time-consuming, the researchers are inclined more toward some methods for making software systems intelligent so that the need to various versions of such systems is removed. Intelligence means that the system has the ability to learn from its previous results and doesn't need manual update. Methods used in the design of predictive and intelligent software are artificial intelligence methods. Of these methods, genetic algorithm, fuzzy logic, and neural network can be referred to which are used by researchers for prediction and making intelligence.

As to the issues pertaining to medicine including disease diagnosis, choosing and selecting the best treatment method, researchers have been and still are seeking to find some software solutions to solve them. Diagnosis of breast cancer (5) and recognition of disease severity (6) are the examples of such cases. As mentioned earlier, recognition of disease severity has been one of the main concerns of physicians for a long time. On one hand, this diagnosis

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has been more considered by the researchers for patients in ICU due to lack of equipment, high cost and many references to this section. Therefore, researchers seek to find some software-based solutions for the diagnosis of disease severity and prediction of hospitalization period so that they can determine the proper method of disease treatment and make use of the equipment of this sector in the most proper way.

Among the designed software types for this issue, SAPS , APACHE can be mentioned. APACHE software is among the most successful software kinds in this area. It uses the physiological information in the patients' profile for diagnosis of disease severity. It can also estimate the hospitalization time in ICU and help the physicians in selecting the best treatment method. However, the use of this software system in Iran has three main problems, the first two being among the main non-local system of APACHE. The first problem is that for the use of this system in different areas, its local version should be designed based on the data related to that area (according to APACHE designers). The second problem lies in manual update of this software during creation of different versions. The third issue is that Iran's hospitals are not equipped with HDUs or High Dependency Units. While for non-local systems (such as APACHE), it is designed in a manner that patients will be transferred to HDU after some time of being hospitalized in ICU.

Therefore, we aimed to design an intelligent version of APACHE system for prediction of patients' hospitalization period in ICUs. The new system can be designed based on Iranian local data and it can be updated locally (7). Intelligence here means that the system has the ability to learn from its previous results and doesn't need manual update. In this study, this new system is introduced and the technical specifications are presented. The proposed system is based on neural networks. It can be trained and it has the ability of auto-learning. The results obtained from final implemented software show better performance than those obtained from non-local versions. Using this method, the efficiency of the prediction has increased from 80% to 90%. The results were compared with the APACHE outputs to show the superiority of the proposed method.

This study is organized as follows: In Section 2, different versions of APACHE as our non-local system have been explained. Section 3 focuses on general overview of the proposed new system. Furthermore, data and the considered parameters are presented in this section along with the proposed algorithm. Sections 4 and 6 include the results of experiences and conclusion, respectively.

APACHE has been developed based on the assumption that disease severity can be measured by determining the abnormality of several physiologic variables. The reason why researchers use this method is that one of the main applications of intensive care unit is observation and treatment of physiologic disorders; thus, a classified system should be designed based on physiological measurements. Furthermore, this system should be applicable to a wide range of diagnoses, easy to use and based on real data of hospitals (8). To select the weighting of physiologic variables, researchers used a set of credit group processes. This process follows Gostafson's recommendations and is suitable for creating disease severity indices. Moreover, it provides the possibility of reaching the self-stability principle. APACHE original version prepares weighting for 34 physiologic variables (parameters), sum of which show the severity of disease (8).

APACHE is a reliable tool for classification of ICU patients. Increase of system ranking means the increase of death probability. On the other hand, the efficiency of APACHE in evaluation of intensive care results and success of various treatment methods has been practically proved.

APACHE II

The early APACHE system was complex and needed official validation of several institutes. In fact, the aim of APACHE II was simplification and provision of a more accurate and beneficial classification system. For this reason, APACHE II was introduced by Knaus et al in 1985; it is a widely used system for determining the extent of patient's injury in ICU. APACHE II used a rating system with 12 physiologic parameters, age and previous health status (the number of physiologic parameters has reduced from 34 to 12. Some physiologic parameters like the amount of lactic acid, which have been rarely calculated, have been eliminated since their effects were observed in other parameters) to prepare an integrated measurement of the disease severity. High score means direct relation with death risk which has been designed based on 58.5% of ICU admissions from 13 hospitals.

By creating a collection consisted of medical parameters and accurate evaluation of the role of extra physiologic parameters concerning their effect in survival, the number of next parameters has been reduced. Each parameter has been removed after hospital investigations, and then this decision was validated by multivariable comparison with APACHE system.

When the score of APACHE II combines with accurate description of the disease, it can classify similar diseases (in terms of risk severity) and help the researchers to compare the success of the new method or change their method. This scoring index can be used for evaluation of the use of hospital resources and efficiency of ICU in different hospitals during the times (8).

The validity of APACHE II was assessed with the related mortality rate test by the use of a high number of admissions in ICU from 13 hospitals. Patients were categorized in different special groups regarding the reason for their admission (8).

APACHE III

APACHE III is better than APACHE II in terms of more accurate results and better classification. This version has been designed within two main procedures consisting of the collection of proper database and analysis for designing the final system. First, a list was selected containing physiologic variables along with questions related to five predictive variables (appropriate category with disease, physical injury, age, previous disease and the time of patient selection). Then for determining the main reason for admission in ICU, a list consisting of 212 disease categories was created; then, the patients were classified in these categories concerning three elements of medical or surgical status, the main injured organ, and the reason for disease (if possible). These data were obtained from medical profile of patients in the first 24 hours of admission in ICU (9, 10).

The researchers selected 20 physiologic variables for measuring the severity of disease concerning their past experiences and medical knowledge. Data used for APACHE III design were taken from the database including 17440 patients from 40 hospitals in 1995. It seems necessary to note that the whole hospitals were included in 16 categories; the classification was done based on geographical situation (north, south, east and west), number of beds and the training status, each one being given a random number to be used for random selection of hospitals (9, 10).

Researchers used multi-variable regression for analysis of the relationship between mortality rate and 20 physiologic variables, so that 19 other variables were considered along with data related to age, health condition, operational status and classification of specific disease by the use of both absolute and continuous weighting. Furthermore, the mutual effect of physiological variables has been investigated through separated and combined weighting of variables.

APACHE IV

The aim of APACHE IV was to improve the accuracy of APACHE for prediction of mortality rate in critically ill adults and evaluate the changes in the accuracy of older APACHE models. The test environment includes 104 ICUs in 45 hospitals of America. Patients selected in this system were a collection of 131618 consecutive admissions of ICU in 2002-2003 (11).

The studies which have used APACHE III in independent ICUs database reported mortality rates much different from what was really observed. The reasons proposed for this difference include insufficient diagnosis data, regional and international differences, changes in patients' referral pattern, difference in selection and timing of ICU admission. Besides, the predicted results were possibly affected by changes in the effect of treatment methods during, before treatment and after ICU admission (11).

In 2004, the accuracy of the first version of APACHE III was re-designated by the use of collected data, indicating that this equation needs remodeling. Consequently, by the use of data related to patients admitted in 1986 to1993, the remodeling was done and by the use of data collected in 2002 to 2003, the revalidation was done in 2004 which yielded acceptable results. Thus, APACHE IV, which is the improved and updated model for prediction of mortality rate of critically ill patients, was proposed for prediction of mortality rate.

The researchers' attempt led to introduction of new regression equation and coefficients for each parameter in the sample of ICU patients. Instead, they could introduce new predictive parameters by the use of data related to critically ill patients and make use of modified statistical methods for development and validation of the improved predictive model that existed publicly (11).

Method

The New Proposed System

Design

There are several reasons for the necessity to localize APACHE system for different areas and regions. APACHE IV has been just evaluated in America by the use of American hospitals' data; however, it should be noted that every region has different and unique conditions in terms of ICU facilities, type of the patients, criteria selection, pre- and post-ICU treatment and its effect on individuals and consequently on the provision of APACHE software. Due to the aforementioned reasons, it seems necessary to localize, reconstruct and evaluate APACHE system for every region and country so that it would be possible to draw other criteria and construct the new system for prediction of hospitalization in ICU.

On the other hand, since the Iranian hospitals are not equipped with HDU, the efficiency of this system is not proven for Iranian patients. Based on this, a new predictive system of patients' hospitalization in ICU wards was designed. By the tests done on data in the medical profiles of ICU patients of Nemazee hospital in Shiraz, southern Iran, the efficiency of the new proposed method against APACHE method has been shown. Neural network method has been used for designing and making this system intelligent.

Training Data

The samples in general and central ICUs of Shiraz Nemazee hospital were used as the training data (it should be noted that the software is data independent; however, since the intended data were not available in ICU of other hospitals, data related to general and central ICUs of Shiraz Nemazee Hospital were used).

To make the software intelligent and capable of automatic updating, first a sample consisting of 1000 individuals in general and central ICUs was used for the beginning of the study as the required data. The selection method was random with uniform distribution from general and central ICU patients. It should be noted that the sample included medical and surgical patients and every adult patient hospitalized in general and central ICUs. The sample of training data has been presented in table 1.

It worth noting that diagnosis on admission, motor response, verbal response and eye opening parameters are initialized. The reason for numerical initialization is that every field of these parameters has been given a numerical value. The initialization started from 1.

This data were initialized 24 hours before registration of the patient's status. Furthermore, a part of data used has been directly drawn from the patients' medical profile and the remaining has been delivered by the specialists of ICU ward. Data were available in https://apachefoundations.cernerworks.com, which is used for specialists of ICU wards and the collected data were stored in.

Table 1. Sample Data Used

LOS	4.07	2.38	0.81	11.98
Status	A	A	A	A
Admitting Diagnosis	340	327	192	282
Age	64	27	51	42
Sex	m	m	m	f
Temperature: °C	35.7-36.1	36.1-37.5	36-37	36.1-38.1
Systolic BP (mm /Hg)	100-150	110-130	105-148	98-159
Diastolic BP (mm/ Hg)	60-90	48-77	70-95	66-101
Heart Rate (/min)	80-120	94-117	57-85	65-82
Respiratory Rate (/min)	11-35	23-60	11-24	11-13
Altitude above sea level	1500	1500	1500	1500
Fio2 (%)	80	60	21	40
PH	7.18	7.38	7.4	7.49
PO2	84.6	31.4	73	104.9
PCO2	54.5	37	49	30.2
Sodium (mmol/L)	137-141	141-143	136-140	135-136
Glucose	93-123	75-97	105-139	109-131
Creatinine	3.8-4.2	1.6-1.6	0.8-1	1.1-1.2
Urine Output (ml/24hrs)	1050	1830	1900	1750
Albumin	3.7	3.7	4.1	3.9
Bilirubin	0.5	0.6	1.2	0.7
Motor Response	1	1	1	4
Verbal Response	5	1	1	5
Eye Opening	1	1	1	2
Glasgow Coma Score	10	15	15	7

Defined Parameters

According to previous studies and recommendation of ICU specialists of Nemazee Hospital, APACHE IV with some modifications has been used for data collection and was later used for designing the new proposed method. This modification is due to the fact that Iranian hospitals are not equipped with HDU between ICU and general wards, so it is not possible to transfer the patients who are a bit better to this section to recover and then to transfer them to general ward.

It should be noted that for designing this new system, gender was also added to parameters after consulting with specialists of ICU sector since men and women have different capacities and physical powers to cope with disease. However, APACHE designers have not considered this parameter.

The eliminated parameters in data collection form mostly related to HDU are as follows:

Admitted from, Pre-ICU LOS (days), Post-Operative, Emergency Surgery, Readmission, Ventilated at any time (first 24 hrs).

Furthermore, parameters used in data collection include:

Temperature, Systolic BP(systolic blood pressure), Diastolic BP (diastolic blood pressure), Heart Rate, Respiratory Rate, Altitude above sea level, Fraction of inspired oxygen (Fio2), Power of hydrogen)PH), oxygen partial pressure (tension)(PO2), carbon dioxide partial pressure(PCO2), Sodium, Glucose, Creatinine, blood urea nitrogen(BUN), Urine Output, Albumin, Bilirubin, Hematocrit(HCT), White blood cells (WBC), Verbal Response, Eye Opening, Motor Response, Glasgow Coma Score, Admitting Diagnosis, Age, Sex.

As seen, 24 physiologic parameters along with gender and age related parameters were used for collecting data related to patients hospitalized in ICU. Data collection form is shown in Figure 1.

The main point which should be considered is the parameter of disease type. According to the studies and consultation with specialists, it becomes clear that this parameter is of the greatest significance as compared to other parameters. As an example, if we do not consider this parameter, a record from one patient's data might be very similar to that of another. In this case, these two patients are seen almost the same in terms of predictive system and they should be hospitalized in ICU for the same period. However, adding the disease type might change the result to a great extent. In other words, even one patient might die and another survive.

Diseases were classified into 415 categories. Concerning the data, most selected patients were put into 45 out of 415

categories (i.e. patients in ICU of Shiraz Nemazee hospital suffer from such diseases). Some categories of diseases, which are more frequent, are as follows:
Cardiac arrest, CHF (Congestive heart failure), CVA (cerebrovascular accident/stroke), Hemorrhage/ hematoma.intracranial,Meningitis,drugoverdosewithSedatives.hypnotics.antipsyonotics.benzodiazepines, Emblus pulmonary.

Figure 1. Data collection form

Removing of Incompatible Data
To specify the incompatible data, first the desired range for each parameter was specified by consulting with specialists of ICU, studying the collected data and investigating the data on APACHE site. Then, concerning the value of each parameter in the record of patients, in case that parameter was not in its specified range, it was regarded as incompatible data and the record of that patient was removed. The range of each parameter was between minimum and maximum value.

Data Normalization
Due to the fact that normalized data which are to be used in neural network have better result and the network show better efficiency, data normalization was done. Data normalization means that the range of entering data is transferred to the intended range and the data are transformed to intended range. This is done through equation 1.

1) $$x_{scaled} = x_{real} * S + O$$

On one hand, when normal data are applied to neural network, the output will also be normalized. Thus, the output should be adjusted to its real range by denormalization. Denormalization was done through equation 2.

2) $$x_{real} = \frac{x_{scaled} - O}{S}$$

S and O are abbreviations Scale and Offset which are obtained through equations 3 and 4.

3) $$S(scale) = \frac{High - Low}{Max - Min}$$

4) $$O(offset) = \frac{Max * Low - Min * High}{Max - Min}$$

Low and high parameters also specify the range to which data should be transferred. Furthermore, Min parameter indicates the smallest and Max indicates the biggest value among entering numbers. By these explanations, data collected to be used and tests were normalized through the equations specified for normalization and in case of returning, they were returned to real range by denormalization equation. This was done for every parameter. The range of each parameter was the permitted range of each parameter. Normalization range has been considered as [1, 0].

Implementation
As explained, artificial intelligent methods were used for designing the new intelligent and predictive software. Evolution algorithm, fuzzy logic, decision tree and neural networks can be mentioned. Bayes method is mostly based on probability and mathematics. Fuzzy logic was proposed by Lotfizadeh based on binary logic. The only difference is that the phenomenon doesn't have just two values of zero or one, they could have the values between zero and one (12). Concerning what was mentioned so far, neural networks had more efficiency and application in

prediction of related issues and still have. For example, it has application in economy like exchange market prediction (1) and inflation rate (13), environmental issues like earthquake prediction (3), in medicine like prediction of breast cancer (5), and some applications like optimal routing of metro lines (14) and estimation of earth series reflection (15).

As to the studies on neural networks (12, 16) and the initial design of this new system by the use of neural network and observing its proper efficiency as compared to APACHE system, the proposed method of this study is multilayer perceptron [MLP] network.

Thus, the use of this method in software design was done so that first the intended neural network was selected; it can be any network with different local features. That is, every network has some properties depending on its type which should be adjusted. For example, for MLP, the number of inner layers, neurons of each layer, error threshold, number, frequency … should be adjusted.

With regard to the normalization and denormalization of used data as the input of neural network, a general picture of the neural network would be as depicted in Figure 2.

main parameters of MLP network are as follow:

Training function which could be Trainlm and Traingdm

Performance function which could be MSE, SSE and This parameter specifies the error calculation method among which MSE is more used as the calculation of error square.

Number of layers which specifies the number of network layers.

Number of neurons which specifies the number of neurons for that layer.

Transfer function which specifies the transfer function of each layer. As mentioned, Tansig and Logsig or Purelin are used. Depending on the selection of transfer function, there are other parameters.

In the proposed method, multi-layer perceptron with training function was used. Furthermore, the used performance function was MSE function and the number of layers was also 3. Logsig transfer function was used in the first and second layers, and for the last layer, Tansig function was used. For this method, various tests have been done with different initialization of the intended network parameters (10 tests for changing each parameter). Mean network error used in the tests was almost 11% which is

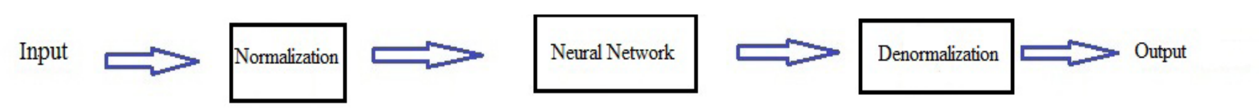

Figure 2. The network figure used for data normalization or denormalization

The test by neural network is such that after making the network, a portion of data are used as network training, some is used for validation and the remaining are used for testing the accuracy of network. In the case of error and if it exceeds the determined threshold, the network parameters (weights and biases) are modified by the use of the error, and the inputs are reapplied to network to repeat this trend (Figure 3). Training and error detection algorithms are various which should be regulated and used according to the need.

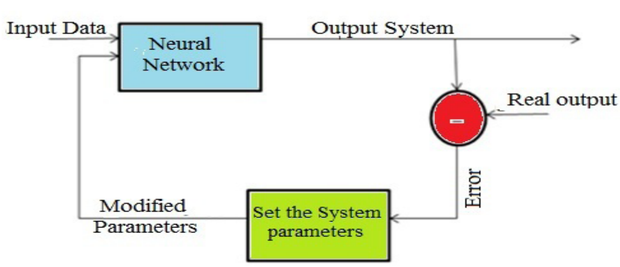

Figure 3. The overall system architecture

It considered that the use of neural network doesn't have certain criteria. That is, it cannot be argued whether, for a certain case, the neural network is responsive or not. In other words, the performance accuracy of this method is calculated based on test and trial method.

Experimental Results

To build a network, its parameters should be regulated. Although these parameters have default values, for better performance of the network, they could be regulated. The

better than the proposed methods in (7) in terms of efficiency.

The best network output is obtained when the parameters are initialized according to parameters shown in Table 2. The result obtained from this test has the least error and most efficiency among the tests done on the intended network. Network error in this test was 0.05% which means the efficiency of this network is 95%. The network output for training, validation and test are represented in Figure 4. It should be noted that the number of layers in this method is changed to four and then the test was done again with different initializations of network parameters; the best output is presented in Figure 5. The values of this parameter are displayed in Table 2.

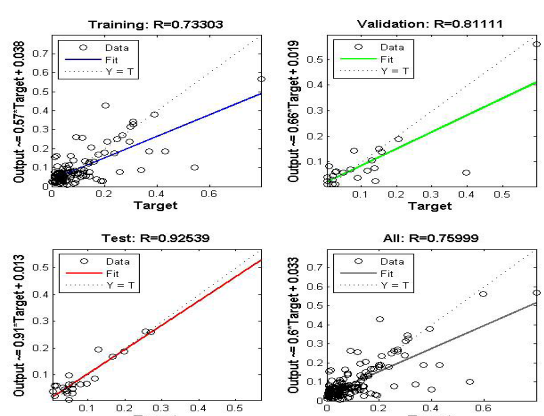

Figure 4. The output of the network test with Trainrp function

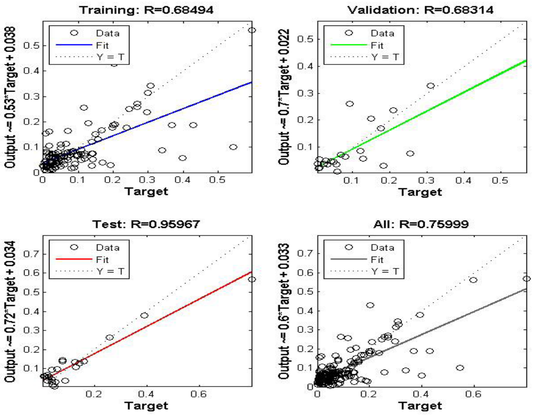

Figure 5. The output of the network test with Trainrp function

Discussion

Based on the tests and the results, it was indicated that the efficiency of the proposed method based on the use of neural network with training function and the use of 3 layers was better than that of the method used in designing of local intelligent predictive system of patients' hospitalization in ICU for Iran presented in (7).

On one hand, concerning the comparison of efficiencies of the new proposed method, the method used for designing local system in Iran and APACHE system designed in America, the optimal efficiency of the proposed method becomes clear. The mean error of tests for proposed method was 12.77. This error means that the mean efficiency value is almost 87.3, while the efficiency of the method used in designing of the local system of Iran and APACHE system designed in America are 80.5% and 44%, respectively.

Table 2. Test parameters of perceptron network with learning function Trainrp

Traning Fun	Performance fun	Number of Layers	Transfer fun for Layers 1 & 2	Transfer fun for Layer3	Min_grad	Delta0	Delta_in	Delta_dec
Trainrp	Mse	3	Logsig	Tansig	1e-009	0.8	0.6	0.5

As can be seen in the Figures, the optimum output has even reached 95%. Concerning the fact that data considered for network test are different from those used for training, this output is desired. Thus, this network can be used for designing APACHE software. It should be noted that the network was assessed for some random data and the negligible error was observed. The full view of the system operation has been designed andshown in Figure 6.

The weak efficiency of APACHE system designed in America is for two reasons: first, the new version of this system should be designed for each area. Second, Iranian hospitals are not equipped with HDU. On the other hand, to make the new system more intelligent for Iran, it was decided to use the new proposed method along with the method used in designing Iran local and new system.

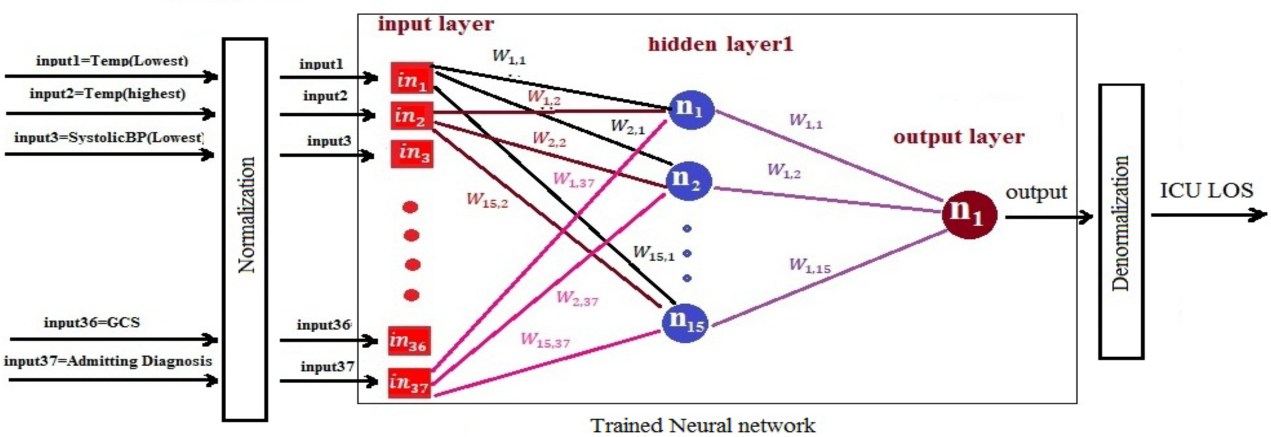

Figure 6. The full view of the system operation has been designed

Comparison of the Efficiency of Proposed Method with the Method Used in APACHE Local and Non-Local Version

To compare the efficiency of local (new method) and non-local versions of APACHE, ten records were randomly selected with uniform distribution. Intended data are those used in [7]. The output of these three systems were compared with real output (real time of hospitalization in ICU) which were in the profile of patients. The error of each record and mean error value of ten records are presented in Table 3.

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Table 3. Comparison of the efficiency of native and non-native Apache

	Apache Result	Apache error	Apache Local Result	Apache Local error	proposed method Result	proposed method	Error actual Result
1	8.47	55	20.878	10.9	19.878	5.6	18.82
2	2.65	31	3.51	8.8	3.749	2.5	3.849
3	5	11	4.56	1.3	4.379	2.6	4.499
4	4.6	61	7.84	32.9	9.2	21.36	11.7
5	2.02	63	3.58	35.2	3.89	29.65	5.53
6	5.53	0.1	3.5	36.5	4.12	25.36	5.52
7	5.26	35.9	4.83	24.8	4.55	17.5	3.87
8	6.49	75.9	24.19	10.2	25.86	4	26.95
9	7.8	150	3.94	26.6	3.69	18.6	3.11
10	7.14	73	25.87	4.2	26.86	0.6	27.02
Mean total error		55.59		20.7		12.77	

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