A New Method for Diagnosis and Predicting Blood Disorder and Cancer Using Artificial Intelligence (Artificial Neural Networks)

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Abstract: This paper represents a novel use of artificial neural networks in medical science. The proposed technique involves training a Multi Layer Perceptron (MLP) (a kind of artificial neural network) with a BP learning algorithm to recognize a pattern for the diagnosing and prediction of five blood disorders, through the results of blood tests from H1 machine. The blood test parameters and diagnosis of physician about the diseases of 450 patients from Taleghani Hospital in Kermanshah, Iran, are used in a supervised training method to update network parameters. This method was implemented to diagnose these disorder and cancer: Megaloblastic Anaemia, Thalassemia, Idiopathic thrombocytopenic pupura (ITP), Chronic myelogenous leukemia and Lymphoproliferative.

Keywords: Artificial Neural Network, Multilayer Perceptron (MLP), Multi-Variable Non-linear Regression, Blood Disorder, Cancer, Megaloblastic Anaemia, Chronic Myelogenous Leukemia.

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Introduction

One of the major problems in medical life is giving a diagnosis. A lot of applications have been tried to help experts in offering a solution. This paper describes how artificial intelligence, for example artificial neural networks can improve this area of diagnosis.(1)

On average, the human body contains five liters of blood, and your red blood cells are replaced every 120 days. Blood diseases can range from anaemia, which is common, to rare disorders that affect only a few. Many different diseases affect blood. Many people have some form of blood disease, either detected or not. In the United States alone, approximately 72,000 people have sickle cell anaemia with about 2,000,000 people carrying the trait. There are 20,000 hemophilia patients in the U.S. Each year, nearly 27,000 adults and more than 2,000 children in the United States learn that they have leukemia (statistics are from NIH and Cancernet web sites).

The health of a population, which is based primarily on the result of medical research, has a strong impact upon all human activities. Hematologic disorder are one of the important branches of internal medicine.With the accelerated progress which has been implemented in recent years in this field, we think that special attention to improve conventional methods is needed. With this as background, we have presented a new idea in the diagnosis widespread disorders.

We know that in the medical sciences, a good interpretation of data and giving a correct, early diagnosis are very important. These can be the base of a good and effective treatment, especially in hematology, as it would be in other fields of internal medicine disorders. Medical decision making becomes a very difficult activity because experts who have to make decisions, can hardly process the huge amounts of data. Physicians usually suffer from an absence of good, accurate analysis of these laboratory data. They need a tool that would help them to make good decision. An expert system or artificial neural networks, which are part of artificial intelligence would prove to be very useful.(1)

According to this view and to use this as a good referral system in making decision for patients, we have presented a new method with a high quality (and quantity) analytic potency that resolves these problems.

Because of that the number of hematologists (hematologist: physicians specialized in hematology; Hematology: is the branch of biology, pathology, clinical laboratory, internal medicine, and pediatrics that is concerned with the study of blood, the blood-forming organs, and blood diseases. Hematology includes the study of etiology, diagnosis, treatment, prognosis, and prevention of blood diseases. The lab work that goes into the study of blood is performed by a medical technologist) are limited and in most small towns and clinics, there is not any physician. This method, therefore can be very beneficial and can be used in any general hospital, clinic and even in laboratories for primary diagnosis which can be sent to hematologists.

At first, we searched for disorder diagnosis and prediction with the artificial neural network. We found that maximum research and solutions in medicine branch are not usually thoroughly done. For example, most artificial neural network were used in detecting this disorders: breast cancer [there tends to an integrated view of implementing automated diagnostic systems for breast cancer detection(2,3,4,5)], prostate cancer (using with an extended biopsy, they developed and validated multivariate models predicting prostate cancer with an initial biopsy and examined whether these extended biopsy-based models(6,7) and a neural network model which is compared with logistic regression to predict this cancer,(8,9,10), heart disease like coronary artery disease,(11) or to classify heart disease,(12) Alzheimer's disease,(13,14) brain disease such as a biomedical system based on fuzzy, discrete hidden Markov models for the diagnosis of brain diseases,(15) cervical cancer,(16) dermatologic diagnosis in order to improve diagnosis,(17) diabetes such as the prediction of the progression of diabetic nephropathy,(18) optic nerve disease,(19) ovarian cancer,(20) pancreatitis and pancreatic cancer.(21)

The outline of this paper is as follows: in Section 2, details of the ANN method are derived and used architecture is explained. Section 3 presents our numerical results for the various cases of designed artificial neural networks. Section 4 presents conventional methods in order to compare the programmed ANN performance in predicting a aforementioned disorders, with classical methods such as statistic solutions, multivariable nonlinear regression method (with SPSS V.13 software). Results of this method have been thoroughly presented in this section. The last section explains comparison of these two method results to illustrate the efficiency of neural networks, fast convergence and low use of memory in any kind of disorder diagnose.

Method

Neural networks: Neural networks are composed of simple, interconnected processing elements, called *neurons*, which operate in parallel. These elements are triggered by biological nervous systems. As in nature, the network function is determined largely by the connections between elements. We can program a neural network to perform a particular function by adjusting the values of the connections (weights) between elements.

An artificial neuron is a simplistic representation that emulates a signal integration and threshold firing behavior of biological neurons by means of mathematical equations. Like their biological counterparts, artificial neurons can be bound together by connections that determine the flow of information between peer neurons. Stimuli were transmitted from one processing element to another via *synapses* or interconnections, which can be excitatory or inhibitory. If the input to a neuron is excitatory, it is more likely that this neuron will transmit an excitatory signal to the other neurons connected to it. Whereas, an inhibitory input will most likely be propagated as inhibitory. A neuron with a single scalar input shows in Figure-1.

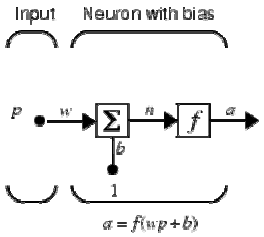

Figure- 1. A neuron with a single scalar input

Commonly neural networks are adjusted, or programmed, so that a particular input leads to a specific target output. There, the network is adjusted, based on a comparison of the output and the target, until the network output matches the target. Typically, many such input/target pairs are needed to program a network. A simple block diagram of a neural network is shown in Figure-2.

complex functions in various fields, including

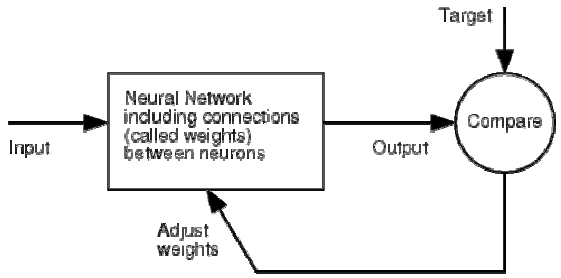

Fig. 2 A simple block diagram of a neural network

Neural networks have been programmed to perform pattern recognition, identification, classification, speech, vision, and control systems. Today, neural networks can be programmed to solve problems that are difficult for conventional computers or human beings. A neural network is superior at fitting functions and recognizing patterns. In fact, there is proof that a fairly simple neural network can fit any practical function.

MLP networks: There are many types of neural networks used for various applications. MLPs are the simplest and therefore most commonly, used neural network architectures programs due to their structural flexibility, good representational capabilities and availability, with a large number of programable algorithms. MLPs are feed forward neural networks and universal approximators, programmed with the standard back propagation algorithm. They are supervised networks so they require a desired response to be trained. They are able to transform input data into a desired response, so they are widely used for pattern classification. With one or two hidden layers, they can approximate virtually any input-output map.
An MLP consists of three layers: an input layer, an output layer and an intermediate or hidden layer. In this network, every neuron is connected to all neurons of the next layer, in other words, an MLP is a fully connected network. Figure-3 shows the structure of an MLP.

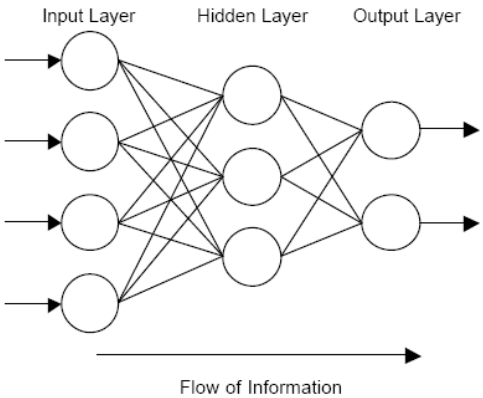

Figure- 2: An MLP network's structure

Processing elements (PE) or neurons in the input layer only act as buffers for distributing the input signals x_i (i show the i-th input PE) to PEs in the hidden layer. Each PE $_j$ (j shows the j-th PE in the hidden layer and output layers) in the hidden layer calculates its input signals x_i after weighting the values of the respective connections w_{ji} from the input layer and computes its output y_j as a function f of the sum, viz., (1)

$$Y_j = f(\sum w_{ji} x_i)$$

There are various choices for the transfer function f which can be globally supported. The only limitation of this function is that it must be derivable (Figure- 4).

Linear: $f(x) = x$ (2)

Log – Sigmoid : $f(x) = \dfrac{1}{1+e^{-x}}$ (3)

Tan – Sigmoid: $f(x) = \dfrac{2}{1+e^{-2x}} - 1$ (4)

The output of processing elements in the output layer is computed similarly. The structure of the multiple layers of neurons can be seen in Figure-5.

Programming the network: Before programming a feed forward network, the weights and biases must be initialized. Once the network weights and biases are initialized, the network is ready to be programmed. Programming a network consists of adjusting its weights using a programming algorithm. The programming process requires a set of examples of proper network response, network input and target output.

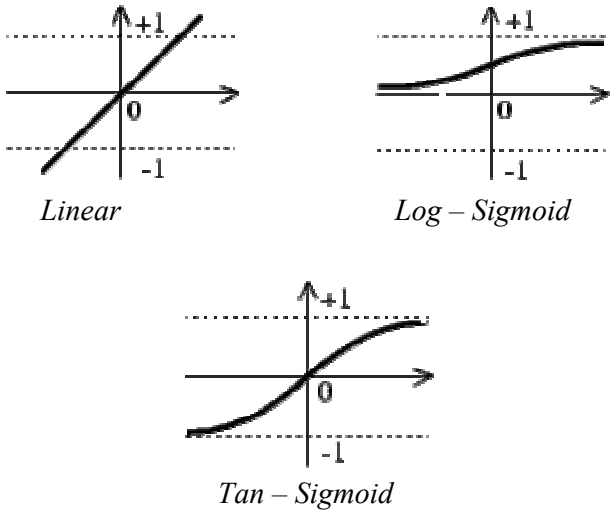

Figure- 4: Some of useful transfer functions

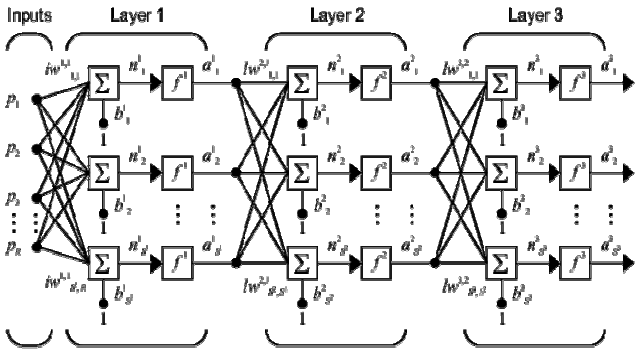

Figure- 5: Structure of the multiple layers of neurons

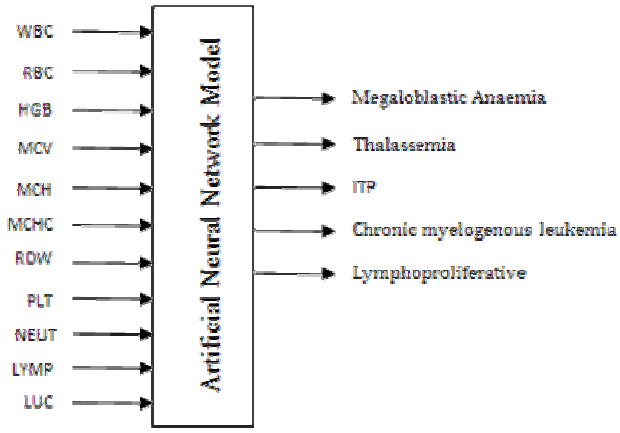

Figure. 6: An Input-output schematic of system

During the programming the weights and biases of the network are iteratively adjusted to minimize the network performance function.

The MLP used in this work is programmed with a backpropagation (BP) programmable algorithm. This programming algorithm optimizes the weights by attempting to minimize the sum of squared differences between the desired and actual values of the output neurons.

$$E = \frac{1}{2}\sum_{j}(Y_{dj} - Y_j)^2 \qquad (5)$$

Where ydj is the desired value of output neuron j and y_j is the actual output of that neuron. Each weight w_{ji} is adjusted by adding the increment Δw_{ji} to it. Δw_{ji} is selected to reduce E as rapidly as possible. The adjustment is carried out over several programming iterations until a satisfactorily small value of E is obtained or a given number of iterations is reached. How Δw_{ji} is computed depends on the programming algorithm adopted.

The backpropagation computation is derived using the chain rule of calculus. The basic backpropagation programming algorithm moves weights in the direction of the negative gradient.

The available ANN software today provides many neural-network structures and programmable algorithms, and also helps users to apply ANN to their specific problems easily. The MATLABTM's Neural-Network Toolbox might be a good example of this software. One can also write ANN software using available compilers. In this paper, we use the MATLABTM's Neural-Network Toolbox to develop the network.

ANN applications to diagnosing and predicting blood disorder and cancers: In this paper, by using the MLP neural networks, a novel applicable method for diagnosing and predicting five blood diseases and cancers through the results of blood tests, has been presented. In order to program and test the network, 450 data series which were obtained from blood tests of 450 patients who had been examined by haematologists, were used. In these blood tests, eleven parameters playing role in diagnose these disorders. These parameters had been used as the input of the network. The developed system is shown in Figure- 6. Its input parameters were white blood cell (WBC), red blood cell (RBC), hemoglobin (HGB), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), platelet (PLT), neutrophil (NEUT), lymphocyte, leukocyte (LUC) [the result parameters of blood tests]. The output is five blood diseases: megaloblastic anaemia, thalassemia, idiopathic thrombocytopenic pupura (ITP), chronic myelogenous leukemia and Lymphoproliferative.

In order to present the problem in mathematical form, a multilayer perceptron network with eleven input and five output data had been created. This network involves three layers (an input layer, a hidden layer, and an output layer). The Number of neurons in input layer is equal to the number of input variables (eleven), and the number of neuron in the output layer is equal to the number in the output data (five). This network had been simulated with a MATLAB Neural Network Toolbox, with 360 series of 450 available data series, which is used to program the network and a 90 series was used to test it.

Because of the output of network, there are always two values, 0 or 1. the log-sigmoid transfer function for the output-layer was selected. To achieve the best transfer function for the input and hidden layers several trials were made. The best result was obtained with a network using a tan-sigmoid transfer function in both the input and hidden layers. There are many choices for the number of neurons in the hidden layer. In order to achieve the

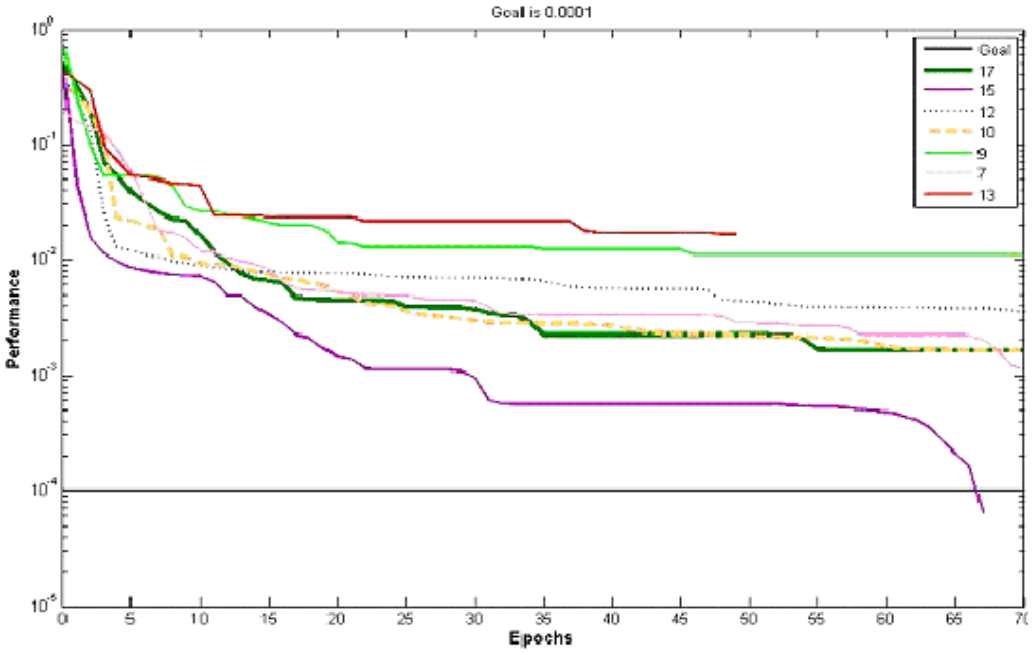

Figure. 7 Ttraining networks having different number of neurons in hidden layer

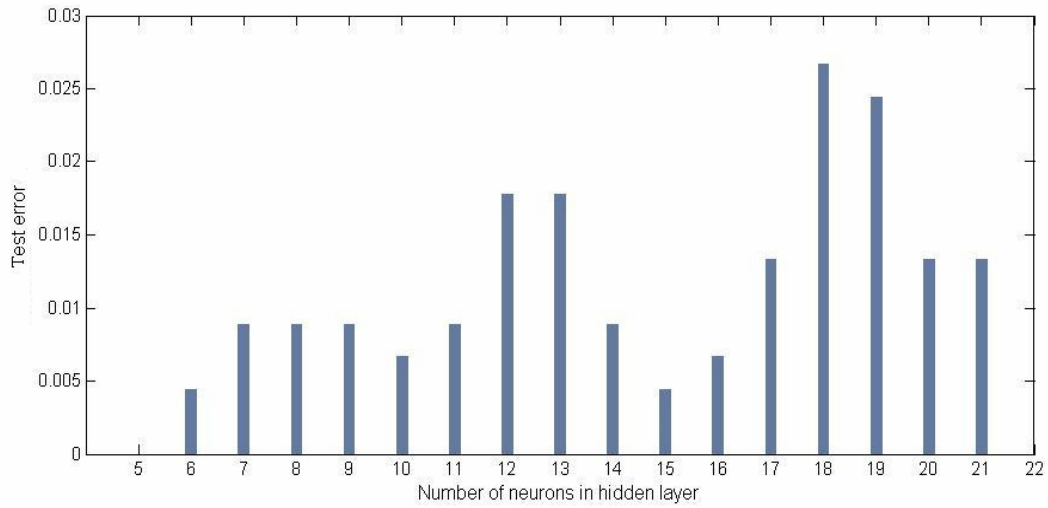

Figure- 8. Comparison of training error in networks having different number of neurons in hidden layer

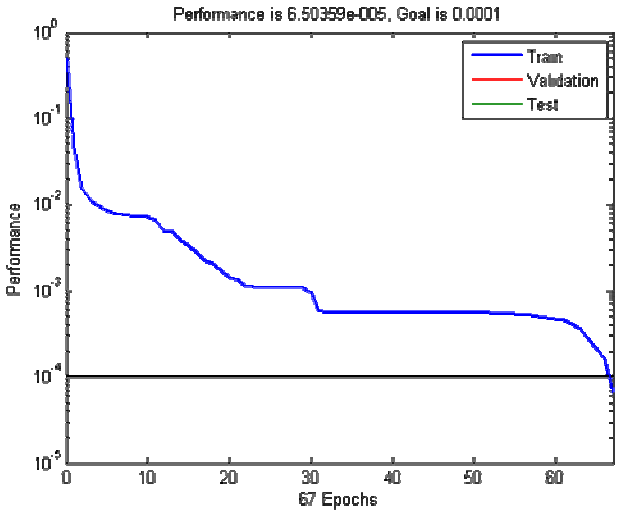

Figure- 9. Performance changes in the course of network training

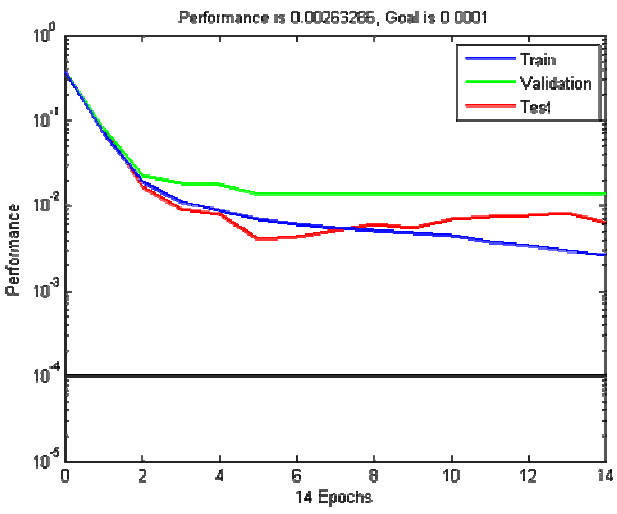

Figure.10 Performance changes in the course of network training

Table-1. Comparison of error in networks having different numbers of neurons in hidden layers

Network	Number of neurons in hidden layer	Test error	Number of epochs
ANN.1	6	0.004444	113
ANN.2	7	0.008889	92
ANN.3	8	0.008889	171
ANN.4	9	0.028889	112
ANN.5	10	0.006667	131
ANN.6	11	0.008889	38
ANN.7	12	0.017778	75
ANN.8	13	0.017778	49
ANN.9	14	0.008889	91
ANN.10	15	0.004444	67
ANN.11	16	0.006667	53
ANN.12	17	0.013333	98
ANN.13	18	0.026667	57
ANN.14	19	0.024444	23
ANN.15	20	0.013333	46
ANN.16	21	0.013333	100

Table- 2. A comparison of programming errors with different programming functions

Network	Number of neurons in hidden layer	Train function	Percent of test error	Number of epochs
ANN.10.1	15	Trainlm	0.004444	67
ANN.10.2	15	Trainscg	0.008889	976
ANN.10.3	15	Traingdm	0.006667	5000
ANN.10.4	15	Trainrp	0.006667	481

Table- 3. Optimal structure of a developed MLP neural network to obtain a minimum prediction error

Number of hidden layers	1
Number of neurons in hidden layer	15
Hidden layer Transfer Function	Tan-sigmoid
Output layer Transfer Function	Log-sigmoid
Training function	Trainlm
Test error	0.004444
Number of epochs	67

Table- 4. Comparison networks training with Cross-Validation and without it

Network	**Number of Training data series**	**Number of Validation data series**	**Number of Testing data series**	**error**	**epochs**
Training without cross-validation	360	-	90	0.004444	67
Training with cross-validation	270	90	90	0.003333	14

Table- 5. Case Processing Summary

Unweighted Cases		N	Percent
Selected Case	Train Included in Analysis	318	70.7
	Missing Cases	0	0.0
	Total	318	70.7
Unselected Cases(test)		132	29.3
Total		450	100.0

Table- 6. Dependent Variable Encoding

Original Value	Internal Value
0	NO
1	YES

Table- 7. Analyzes results for Megaloblastic Anemia

			Predicted					
	Predicted		Selected Cases(train)			Unselected Cases(test)		
			Megaloblastic Anaemia		Percentage	Megaloblastic Anaemia		Percentag
	Observed		No	Yes	Correct	No	Yes	e Correct
Step 1	Megaloblastic Anaemia	No	316	0	100.0	131	1	99.2
		Yes	0	2	100.0	0	0	.
	Overall Percentage				100.0			99.2
Step 2	Megaloblastic Anaemia	No	316	0	100.0	131	1	99.2
		Yes	0	2	100.0	0	0	.
	Overall Percentage				100.0			99.2

Table- 8. Analyzes results for Thalassemia

	Predicted		Predicted					
			Selected Cases(train)			Unselected Cases(test)		
			Thalassemia		Percentage Correct	Thalassemia		Percentage Correct
	Observed		NO	YES		NO	YES	
Step 1	Thalassemia	NO	317	0	100.0	131	1	99.2
		YES	1	0	0.0	0	0	.
	Overall Percentage				99.7			99.2

Table- 9. Analyzes results for ITP

	Predicted		Predicted					
			Selected Cases(train)			Unselected Cases(test)		
			ITP		Percentage Correct	ITP		Percentage Correct
	Observed		NO	YES		NO	YES	
Step 1	ITP	NO	313	0	100.0	132	0	100.0
		YES	5	2	0.0	0	0	.
	Overall Percentage				98.4			100.0
Step 2	ITP	NO	312	1	99.7	132	0	100.0
		YES	4	1	20.0	0	0	.
	Overall Percentage				98.4			100.0

Table- 10. Analyzes results for Chronic Myelogenous Leukemia

	Predicted		Predicted					
			Selected Cases(train)			Unselected Cases(test)		
			Chronic Myelogenous Leukemia		Percentage Correct	Chronic Myelogenous Leukemia		Percentage Correct
	Observed		NO	YES		NO	YES	
Step 1	Chronic Myelogenous Leukemia	NO	312	0	100.0	131	0	100.0
		YES	6	0	0.0	1	0	0.0
	Overall Percentage				98.1			99.2
Step 2	Chronic Myelogenous Leukemia	NO	312	0	100.0	131	0	100.0
		YES	6	0	0.0	1	0	0.0
	Overall Percentage				98.1			99.2

Table- 11. Analyzes results for Lymphoproliferative

	Predicted		Predicted					
			Selected Cases(train)			Unselected Cases(test)		
			Lymphoproliferative		Percentage Correct	Lymphoproliferative		Percentage Correct
	Observed		NO	YES		NO	YES	
Step 1	Lymphoproliferative	NO	314	0	100.0	131	1	99.2
		YES	3	1	100.0	0	0	.
	Overall Percentage				100.0			99.2
Step 2	Lymphoproliferative	NO	314	0	100.0	131	0	99.2
		YES	2	2	100.0	0	0	.
	Overall Percentage			100.0				99.2
Step 3	Lymphoproliferative	NO	314	0	100.0	130	1	99.2
		YES	2	2	50.0	1	0	0.0
	Overall Percentage				99.4			98.5

Table.12 The final results of regression analyze

Disorder	Error percentage	
	Selected cases (train)	Unselected cases (test)
Megaloblastic Anemia	0	0.8
Thalassemia	0.3	0.8
ITP	1.6	0
Chronic Myelogenous Leukemia	1.9	0.8
Lymphoproliferative	0.6	1.5
Average	0.88	0.78

best network with optimum parameters, a comparison among networks by different neurons in the hidden layer has been done. The result of testing networks with 6, 7, 8... 21 neurons in the hidden layers is shown in Table-1, Table-2, Figure- 7 and Figure- 8.
the best result for this problem (Not to be forgotten is that increasing the number of neurons in the hidden layers may cause an overfitting problem in the network. To prevent this problem, the number of neurons must be fewer than the cases in the programming algorithm). It must be said that regarding this problem, the value of a test error is more important than the number of occurrences, so the error value was the main guide used in our decision making. Table- 3 and Figure- 9 show the final network stracture and the results of its performance.

The network calculates the programming set and does not generalize well when the network is programmed too much (over-fitting). Correct programming holds the key to an accurate solution, so the criterion to end programming must be very well described. Cross-validation is a highly recommended criterion for ending the programming of a network. When an error in the cross- validation increases the programming should be stopped. A practical way to find an overall view is to use a small percentage (around 10%) of the programming set for cross-validation.(22)

An obtain a better overall view of the networks presented in this work, 90 series of programming data (which were selected randomly) were used as cross- validation sets. The values of error for 2 different programming algorithms with and without cross-validation are given in Table- 4 and Figure- 10. As can be seen from Table- 4, training of the MLP with cross-validation has less error value.

Conventional method: In order to show the ability, accuracy and capability of ANN applications in predicting diseases, we compared the ANN method with one of the conventional methods which can similarly do this task.(23, 24) One of these conventional methods is using statistical solutions. The statistic method that we used is the multivariable nonlinear regression method to find a relation between each disease and input data to analyze cases, as well as predicting diseases for new cases, based on the relationships. With this method, all 450 cases were randomly divided into two sets, consisting of selected cases for analization and unselected cases. Results of this method are

A comparison between the range of test error and the number of epochs that is required to reach the minimum performance of 0.0001, shows that a network with fifteen neurons in a hidden layer and *trainlm* function as its programming function, give

defined in Table- 5 to Table-11 (These analyses were done using SPSS 14th version software).

The final results of regression analyses for the output and the average of these five diseases is shown in Table- 12. To compare the accuracy of this method with the ANN method, we should have an average error figure from all of the output data, because the ANN method simulates and calculates all five output errors simultaneously. From these results we can compare these two methods.

Conclusion

The first topic that needs to be discussed is the data that was sampled to program and test the MLP network. The data was collected from blood test results of 450 patients who had been examined by hematologists, at the Taleghani Hospital in Kermanshah, Iran. The data samples were used for training, validating and testing the neural network (60-20-20 ratio for training with cross-validation and 80-20 ratio for training without it) and also for multivariable nonlinear regression analysis (70-30 ratio). The number of hidden layers and neurons in each layer were determined through trial and error to be optimal including with different transfer functions as tangent-sigmoid and log-sigmoid. After several trials, the best result was obtained from a three-layered network. In this network the tangent-sigmoid function is used in the input and hidden layer, and log-sigmoid function in the output layer. and the most suitable network configuration found was 11 x 15 x 5. It means that the number of neurons were 15 for the hidden layer. For training network with backpropagation learning algorithm, The MSE performance function with 0.0001 goal value, and *trainlm* function were used and cross-validation method was used to stop training in order to prevent over-fitting problem. From the results achieved in two last chapters, the designed neural network has 0.3333 error percentage but the SPSS analysis has 0.78 error percentage. By these results we can conclude that the artificial neural network is more applicable by reason of high accuracy, fast convergence and low use of memory for diagnosis and predicting disorder.Another eminent property of this network is its ability to diagnose all five mentioned disorder simultaneously unlike multi

variable nonlinear regression that can do analysis only for one disorder in each time.

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