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Diagnosing Hepatitis B Using Artificial Neural Network Based Expert System

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Abstract:- Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus. The virus interferes with the function of the liver while replicating in hepatocytes. It is a major global health problem and the most serious type of viral hepatitis. It can cause chronic liver disease and puts people at high risk of death from cirrhosis of the liver and liver cancer. In medicine, diagnosis is "the recognition of a disease". An extensive amount of information is currently available to clinical specialists, ranging from details of clinical symptoms to various types of biochemical data and outputs of imaging devices. Each type of data provides information that must be evaluated and assigned to a particular pathology during the diagnostic process. To streamline the diagnostic process in daily routine and avoid misdiagnosis, artificial intelligence methods especially computer aided diagnosis and artificial neural networks can be employed. These adaptive learning algorithms can handle diverse types of medical data and integrate them into categorized outputs. Artificial neural networks are finding many uses in the medical diagnosis application. In this paper we have proposed a Generalized Regression Neural Network (GRNN) based expert system for the diagnosis of the hepatitis B virus disease. The system classifies each patient into infected and non-infected. If infected then how severe it is in terms of intensity rate.

Keywords: **Expert System, Artificial Neural Networks, Generalized Regression Neural Network (GRNN), Hepatitis B virus (HBV), Hepatitis B nomenclature, Hepatitis B Diagnosis.**

I. INTRODUCTION

Since the Conventional manual data analysis techniques are not effective in diagnosis, using computer based analyses are becoming inevitable in disease diagnosis. So, it is the time to develop modern, effective and efficient computer based systems for decision support. There are a number of data analysis techniques: statistical, machine learning, expert system and data abstraction [1]. Medical analysis using expert system techniques has begun to be conducted for last twenty years. The advantages of using expert system schemes in medical analysis have caused human support and costs to decrease and caused diagnosis accuracy to increase. Hepatitis B is caused by a virus that attacks the liver. The virus, which is called hepatitis B virus (HBV), can cause lifelong infection, cirrhosis (scarring) of the liver, liver cancer, liver failure, and death. According to the recent world health organization (WHO) reports, there are nearly 400 million HB infected in the world and 50 million persons are added to them annually. This disease ranked as the third infectious one. The importance of surveying and designing an intelligence system has been sensed in this field. A comparative Analysis of all neural networks proved that generalized regression neural network will be the best suitable network in diagnosis of Hepatitis B. The capability of Generalized Regression Neural Network to get trained faster compared to other networks and achieving results for even the few missing attribute makes it used for diagnosis process [2]. GRNN is a very useful tool to perform predictions and comparisons of system performance in practice.

II. HEPATITIS B OVERVIEW

HBV is classified in the family Hepadnaviridae. It occurs as seven distinct genotypes, designated A to G, but it is controversial as to whether the outcome of the infection is influenced by the genotype [3]. HBV has a double-stranded DNA genome of approximately 3200 base pairs organized into four partially overlapping open reading frames, which encode the envelope, core (precore/core), polymerase and X proteins. The envelope proteins are surface glycoprotein collectively designated as hepatitis B surface antigen (HBsAg). In virus-infected liver cells, HBsAg is produced in excess and secreted into the blood, where it serves as a marker for active infection and infectivity. Currently, recombinant HBsAg is used for HBV vaccination, and the development of antibody to HBsAg is typically associated with protective immunity.

A. Data

Applied data in this research for diagnosing the rate of HB intensity have been chosen from the patients. There are 300 records and each record has 8 fields. H_B (Intension Diagnosis hepatic B) is the 8th field. This field is the specialist diagnosis that divides HB intensity levels into 4 parts:

- Normal situation (virus has not hurt vital organs yet).
- Light situation (virus has just started its destroying activity).
- Severe situation (some parts of vital organs have been destroyed).
- Hyper-severe situation (necessarily, patient needs intensive cares and even patient's life is in danger).

The above situations have been put into a table (table 1) according to the specialist's diagnosis in order to compare the resulting together after designing the expert system and the convention system.

Table 1: Different Output Situation

S.no	State	Range
1	normal	0 – 3
2	Light	3 – 5
3	High	5 – 7
4	very high	7 - 10

B. Recommended tests to investigate chronic HBV infection and the interpretation of results

Chronic HBV infection is defined by the continued presence of HBsAg in the blood for longer than six months. Table 2 outline the tests used to diagnose most cases of chronic HBV. Test selection should be based on the person's risk factors, vaccination history and findings from previous tests.

Table 2: Primary and Secondary tests to diagnose/monitor hepatitis B virus (HBV) infection

	Marker	**Incubation period**	**Acute infection**	**Past/resolved infection**	**Chronic infection**	**Vaccination**
Primary Diagnostic tests	**HbsAg**	±	+	-	+	-*
	Anti-HBs	-	-	+	-	+
	Anti-HBc-Total	-	±	+	+	-
	Anti-HBc-IgM	-	+	-	±†	-
Prognostic or Monitoring tests	**HbeAg**	±	+	-	±	-
	Anti-Hbe	-	-	±	±‡	-
	HBV-DNA	±§	+	±§	+§	-

* Recent HBV vaccination within one to two weeks can lead to a false-positive test. The vaccine antigen can be detected at low levels

† May be positive in chronically infected individuals.

‡ Patients with chronic HBV infection usually have detectable Hepatitis B e antigen (HBeAg) or antibody to hepatitis B e protein (anti-HBe). Rarely, both HBeAg and anti-HBe can be detected simultaneously.

§ Methods differ in sensitivity and standardization. Anti-HBc Antibody to hepatitis B core protein; Anti-HBs Antibody to hepatitis B surface protein; HBsAg Hepatitis B surface antigen; IgM Immunoglobulin M;

+ Implies positive; **–** Implies negative; ± May be positive or negative

Table 3 gives the usual interpretation for sets of results from Hepatitis B blood(serological) tests.

Table 3: Markers for Hepatitis B diagnosis

Marker	Value
HbsAg	Positive
HbsAg	Negative
HbeAg	Positive
HbeAg	Negative
Anti-VHD	Positive
Anti-VHD	Negative
Anti-VHC	Positive

Rule: If (HbsAg = Positive) and (HbeAg = Positive) and (anti-VHD = Negative) then Hepatitis B

III. ARTIFICIAL NEURAL NETWORKS

An ANN is a mathematical representation of the human neural architecture, reflecting its *"learning"* and *"generalization"* abilities. For this reason, ANNs belong to the field of artificial intelligence. ANNs are widely applied in research because they can model highly non-linear systems in which the relationship among the variables is unknown or very complex. A review of various classes of neural networks can be found in [4] and [5]. Overview of the main applications of artificial neural networks in medicine is shown in the following figure.

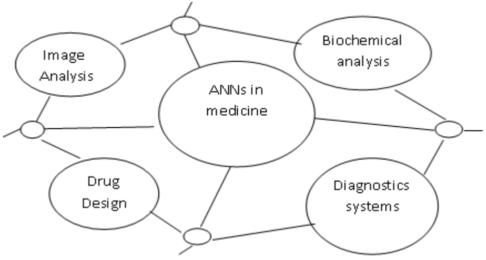


Fig 1: Overview of the main applications of artificial Neural networks in medicine

A. Mathematical Background

A neural network is formed by a series of "neurons" (or "nodes") that are organized in layers. Each neuron in a layer is connected with each neuron in the next layer through a weighted connection. The value of the weight w_{ij} indicates the strength of the connection between the *i*-th neuron in a layer and the *j*-th neuron in the next one. The structure of a neural network is formed by an *"input"* layer, one or more *"hidden"* layers, and the *"output"* layer. The number of neurons in a layer and the number of layers depends strongly on the complexity of the system studied. Therefore, the optimal network architecture must be determined. The general scheme of a typical three-layered ANN architecture is given in Fig.2.

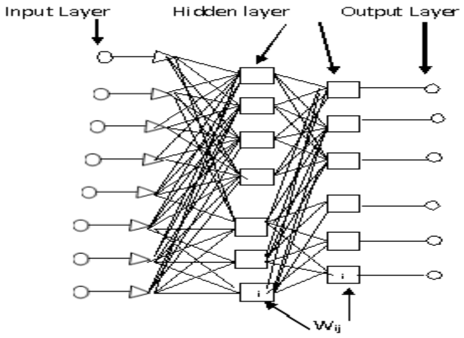


Fig 2: General structure of a neural network with two hidden layers

The neurons in the input layer receive the data and transfer them to neurons in the first hidden layer through the weighted links. Here, the data are mathematically processed and the result is transferred to the neurons in the next layer. Ultimately, the neurons in the last layer provide the network's output. The *j*-th neuron in a hidden layer processes the incoming data x_i by:

(i) calculating the weighted sum and adding a "bias" term (θ_j) according to Eq. 1:

$$\mathrm{net}_j = \sum_{i=1}^{m} (x_i \times w_{ij} + \theta_j)$$

Where (j = 1 , 2 , 3 , …, n) (1)

(ii) transforming the net_j through a suitable mathematical "transfer function"

(iii) Transferring the result to neurons in the next layer.

Various transfer functions are available[6]. However the most commonly used is the sigmoid one:

$$f(x) = \frac{1}{1+e^{-x}} \qquad (2)$$

B. Neural Network Learning

The mathematical process through which the network achieves "learning" can be principally ignored by the final user. In this way, the network can be viewed as a "black box" that receives a vector with m inputs and provides a vector with n outputs (Fig. 3).

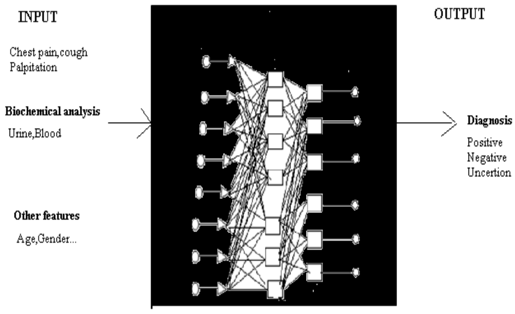
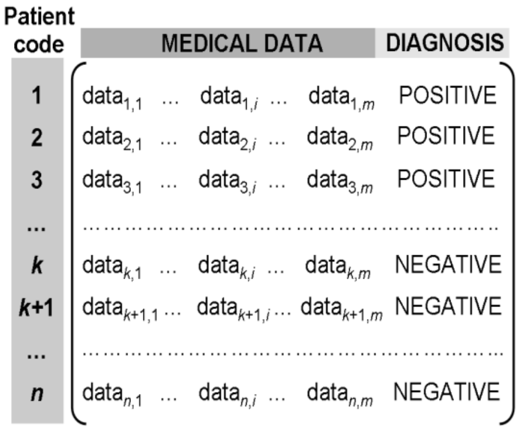


Fig.3 Details of input and output items concerning ANNs-based diagnosis

The network *"learns"* from a series of *"examples"* that form the *"training database"* (Fig. 4). An *"example"* is formed by a vector $X_{im} = (x_{i1}, x_{i2}, \ldots, x_{im})$ of inputs and a vector $Y_{in} = (y_{i1}, y_{i2}, \ldots, y_{in})$ of outputs. The objective of the training process is to approximate the function *f* between the vectors X_{im} and the Y_{in}:



Patient code	MEDICAL DATA					DIAGNOSIS
1	$\mathrm{data}_{1,1}$	…	$\mathrm{data}_{1,i}$	…	$\mathrm{data}_{1,m}$	POSITIVE
2	$\mathrm{data}_{2,1}$	…	$\mathrm{data}_{2,i}$	…	$\mathrm{data}_{2,m}$	POSITIVE
3	$\mathrm{data}_{3,1}$	…	$\mathrm{data}_{3,i}$	…	$\mathrm{data}_{3,m}$	POSITIVE
…	………					
k	$\mathrm{data}_{k,1}$	…	$\mathrm{data}_{k,i}$	…	$\mathrm{data}_{k,m}$	NEGATIVE
k+1	$\mathrm{data}_{k+1,1}$	…	$\mathrm{data}_{k+1,i}$	…	$\mathrm{data}_{k+1,m}$	NEGATIVE
…	………					
n	$\mathrm{data}_{n,1}$	…	$\mathrm{data}_{n,i}$	…	$\mathrm{data}_{n,m}$	NEGATIVE

Fig. 4. Example of training database structure. Each row refers to a different patient labeled with a numerical code. The element data *k,i* refers to the *i*-th medical data(symptom, laboratory data, etc.) of the k-th patient.

IV. GENERALIZED REGRESSION NEURAL NETWORK (GRNN)

The generalized regression neural network was originally proposed for system modelling and prediction [6]. It has been used to learn the same problems as the back-propagation network, the radial basis function network, the probabilistic neural network, and the modular neural network. The network has a relationship to the probabilistic neural network and has sometimes been used in place of it for classification problems.

This network has certain characteristics:

- Fast learning
- Good convergence with a large number of training examples
- Handling of sparse data well
- Possible memory hog
- Possible computing time issues

GRNN falls into the category of probabilistic neural networks. This neural network like other probabilistic neural networks needs only a fraction of the training samples a back propagation neural network would need. The data available from measurements of an operating system is generally never enough for a back propagation neural network. Therefore the use of a probabilistic neural network is especially advantageous due to its ability to converge to the underlying function of the data with only few training samples available. The additional knowledge needed to get the fit in a satisfying way is relatively small and can be done without additional input by the user. This makes GRNN a very useful tool to perform predictions and comparisons of system performance in practice.

A. Architecture

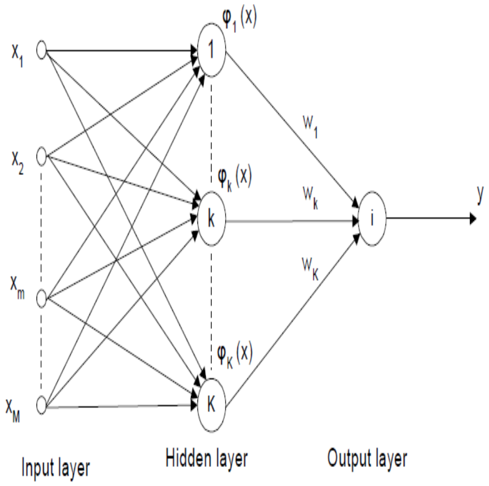


Fig 5: Generalized Regression Neural Network Architecture

As it can be seen from Figure 1, the Generalized Regression Network consists of three layers of nodes with entirely different roles:

- The input layer, where the inputs are applied,
- The hidden layer, where a nonlinear transformation is applied on the data from the input space to the hidden space; in most applications the hidden space is of high dimensionality.
- The linear output layer, where the outputs are produced

B. Algorithm

The probability density function used in GRNN is the Normal Distribution. Each training sample, *Xj*, is used as the mean of a Normal Distribution.

$$Y(X) = \frac{\sum_{i=1}^{n} Y_i exp\left(-D_i^2/2\sigma^2\right)}{\sum_{i=1}^{n} \exp\left(-D_i^2/2\sigma^2\right)} \qquad (3)$$

$$D_i^2 = (X-X_i)^T \cdot (X-X_i)$$

The distance, Dj, between the training sample and the point of prediction, is used as a measure of how well the each training sample can represent the position of prediction, X.If the Distance, Dj, between the training sample and the point of prediction is small, exp(-Dj2/σ2), becomes big. For Dj =0, exp(-Dj2/2σ2) becomes one and the point of evaluation is represented best by this training sample. The distance to all the other training samples is bigger. A bigger distance, Dj , causes the term exp(-Dj2/2σ2) to become smaller and therefore the contribution of the other training samples to the prediction is relatively small. The term Yj* exp(-Dj2/2σ2) for the jth trainng sample is the biggest one and contributes very much to the prediction. The standard deviation or the smoothness parameter, σ , as it is named in is subject to a search. For a bigger smoothness parameter, the possible representation of the point of evaluation by the training sample is possible for a wider range of X. For a small value of the smoothness parameter the representation is limited to a narrow range of X,respectively.

With (Eqn.3) it is possible to

- predict behavior of systems based on few training samples
- predict smooth multi-dimensional curves
- Interpolate between training samples.

In (Fig.5) a prediction performed by GRNN is shown. The circles represent the data points or training samples used to predict the solid line going through most of these samples. The bell shaped curves are the individual terms of (Eqn.3) Each of these curves is one term, Yj * exp(-Dj2/2σ2)/∑i=1nexp(-Dj2/2σ2) of the whole equation (Eqn.3) used in GRNN for the prediction. These terms are normalized normal distributions. Summing up the values of the individual terms at each position yields the value of the prediction, the solid line going through most of the data points. The smoothness parameter was arbitrarily chosen to σ =0.1.

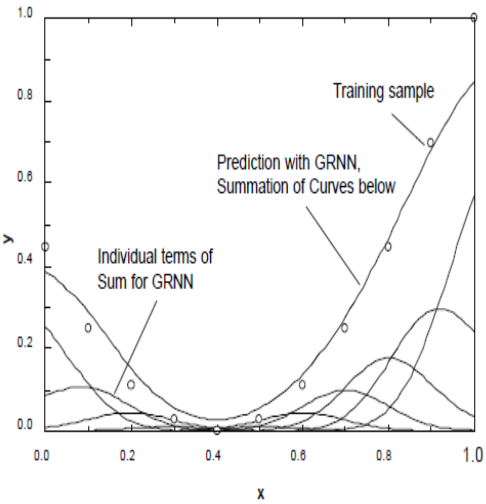


Fig.6: GRNN with individual terms contributing to prediction. ***σ*** **=0.1**

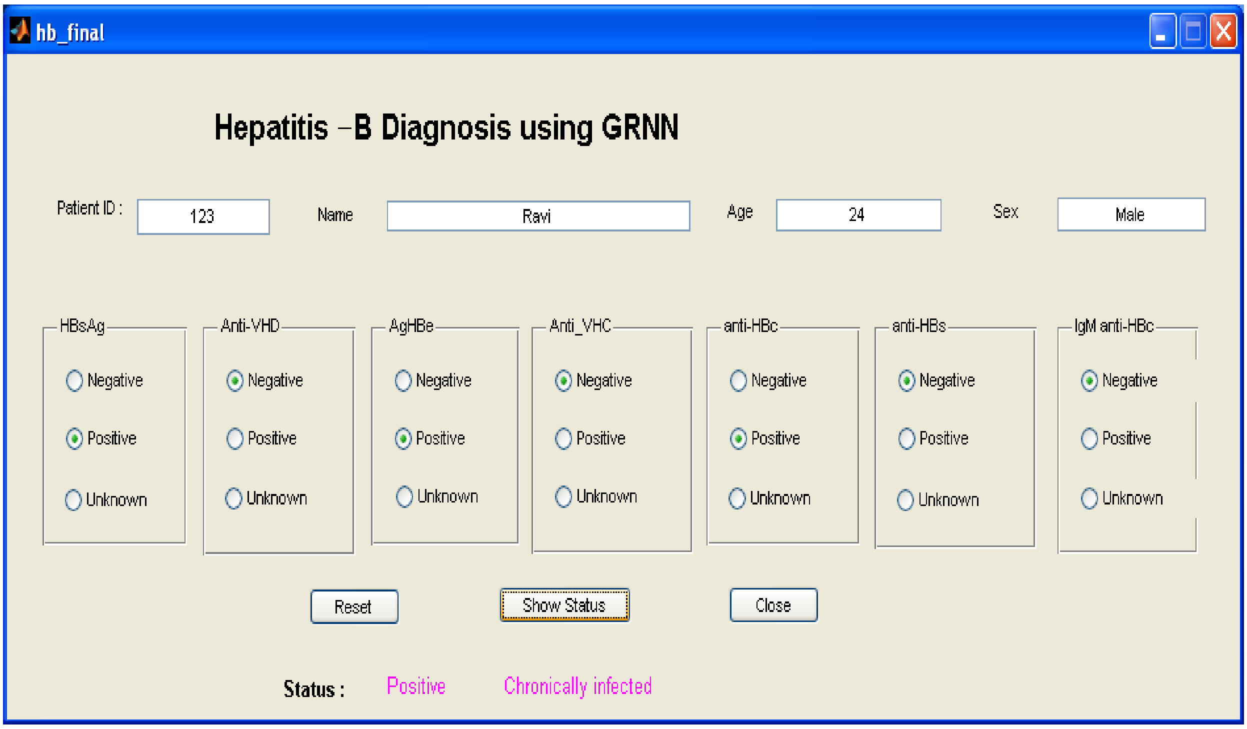
V. EXPERIMENTAL RESULT

The diagnosis of the disease for a new patient to be performed on basis of the makers is facilitated by the primary phase. At the outset, the system intends to diagonis the kind of hepatitis: B or others: It is necessary to specify the values of the three markers namely Hepatits B surface Antigen AgHBs),anti VHC and anti-VHD. Table 4 shows a few sample results

HBsAg	Anti VHD	HbeAg	Anti VHC	HBc Anti	HBs Anti	HBc Anti IgM	Result	Status of Patient
0	0	0	0	0	0	0	0	Susceptible, Not infected, not immune
0	0	0	0	0	1	1	0	Immune due to Hepatitis B Vaccination
1	0	?	?	1	0	0	1	Chronically Infected
1	0	0	0	1	0	0	1	Chronically Infected
1	0	0	0	1	0	1	1	Acutely infected

Table 4. Shows a few sample results

Fig 7: Hepatitis B Diagnosis Generalized regression natural network



hb_final

Hepatitis -B Diagnosis using GRNN

Patient ID : 123
Name Ravi
Age 24
Sex Male

HBsAg: ○ Negative ● Positive ○ Unknown
Anti-VHD: ● Negative ○ Positive ○ Unknown
AgHBe: ○ Negative ● Positive ○ Unknown
Anti_VHC: ● Negative ○ Positive ○ Unknown
anti-HBc: ○ Negative ● Positive ○ Unknown
anti-HBs: ● Negative ○ Positive ○ Unknown
IgM anti-HBc: ● Negative ○ Positive ○ Unknown

Status : Positive Chronically infected

VI. CONCLUSION

Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus. It is a major global health problem and the most serious type of viral hepatitis. It can cause chronic liver disease and puts people at high risk of death from cirrhosis of the liver and liver cancer. Worldwide, an estimated two billion people have been infected with the hepatitis B virus and more than 240 million have chronic (long-term) liver infections. About 600 000 people die every year due to the acute or chronic consequences of hepatitis B.A vaccine against hepatitis B has been available since 1982. Hepatitis B vaccine is 95% effective in preventing infection and its chronic consequences, and is the first vaccine against a major human cancer. Hepatitis B virus is transmitted between people by direct blood-to-blood contact or semen and vaginal fluid of an infected person. Modes of transmission are the same as those for the human immunodeficiency virus (HIV), but the hepatitis B virus is 50 to 100 times more infectious. Unlike HIV, the hepatitis B virus can survive outside the body for at least seven days. During this time, the virus can still cause infection if it enters the body of a person who is not protected by the vaccine. GRNN (Generalized regression N/N) will be the best suitable Neural Network for Hepatitis B diagnosis which will help in reducing extra time consumption in treatment. Even if there is any number of missing parameters in blood test, the diagnosis will be done by artificial intelligence using generalized regression neural networks.

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