

## Hepatitis B Diagnosis Using Logical Inference and Self-Organizing Map

<sup>1</sup>Ghumbre Shashikant Uttreshwar and <sup>2</sup>A.A. Ghatol

<sup>1</sup>College of Engineering, Pune University, Pune, India

<sup>2</sup>Dr. Babasaheb Ambedkar Technical University Vidyavihar, Lonere, Maharashtra, India

---

**Abstract:** Despite all the standardization efforts made, medical diagnosis is still regarded as an art owing to the fact that that medical diagnosis requires an expertise in handling the uncertainty which is unavailable in today's computing machinery. Though artificial intelligence is not a new concept it has been widely recognized as a new technology in computer science. Numerous areas such as education, business, medical and manufacturing have made use of artificial intelligence. **Problem statement:** The proposed study investigated the potential of artificial intelligence techniques principally for medical applications. Neural network algorithms could possible provide an enhanced solution for medical problems. This study analyzed the application of artificial intelligence in conventional hepatitis B diagnosis. **Approach:** In this research, an intelligent system that worked on basis of logical inference utilized to make a decision on the type of hepatitis that is likely to appear for a patient, if it is hepatitis B or not. Then kohonen's self-organizing map network was applied to hepatitis data for predictions regarding the Hepatitis B which gives severity level on the patient. **Results:** SOM which is a class of unsupervised network was used as a classifier to predict the accuracy of Hepatitis B. **Conclusion:** We concluded that the proposed model gives faster and more accurate prediction of hepatitis B and it works as promising tool for predicting of routine hepatitis B from the clinical laboratory data.

**Key words:** Medical diagnosis, artificial intelligence, neural networks, hepatitis B, expert system, logical inference, kohonen's self-organizing map, Hepatitis B Virus (HBV), hepatitis B DNA, spleen palpable, spiders, hepatitis B surface antigen (AGHBS)

---

### INTRODUCTION

The utilization of Artificial Intelligence (AI) in medical applications has extensively been recognized in the recent past. AI in medicine comprises of interpretation of medical images, diagnosis, Expert systems to aid general practitioners, monitoring and control in intensive care units, design of prosthetics, design of drugs and intelligent tutoring systems for diverse phases of medicine. The area of application of Artificial Intelligence in medicine may either be in diagnostic and educational systems, in expert laboratorial information systems, or machine learning systems that possibly involve new forms of knowledge<sup>[1]</sup>. Certainly, modern-day Medicine has come far away from perceiving diseases in isolation, to recognize that illness happens at a complex system level; i.e., by perceiving things at a Meta level one can comprehend what being diseased actually means and how that condition may be inverted<sup>[2]</sup>. Artificial intelligence could facilitate the creation and application of medical knowledge, explicitly in the generation of

alerts or reminders, provision of diagnostic support, judging on therapy critiquing and planning.

Machine learning techniques should have good comprehensibility (i.e., the transparency of diagnostic knowledge and the explanation ability)<sup>[3]</sup> so as to support computer-aided medical diagnosis, as medical diagnosis demands highly reliable performance. The machine learning techniques could be beneficial once it is possible to check and describe the diagnostic process. Symbolic and connectionist are the two common categories of machine learning techniques. These learning techniques have been applied comprehensively in Medical diagnoses<sup>[4]</sup>. Another class of machine learning techniques is the Artificial Neural Networks. However these are regarded as incomprehensible due to the fact that the knowledge learnt is hidden in multiple connections and is not visible to the user.

Since neural networks are appropriate for numerous real world issues, they have been employed effectively in a variety of industries already. Neural networks are suitable for diverse forecasting necessities like sales forecasting, industrial process control,

---

**Corresponding Author:** Ghumbre Shashikant Uttreshwar, Dr. Babasaheb Ambedkar Technical University Vidyavihar, Lonere, Maharashtra, India

customer research, data validation, risk management, target marketing and more, owing to their ability to identify patterns or trends in data<sup>[5]</sup>. A learning methodology that incorporates numerous artificial neural networks is trained to solve the same problem. Being capable of enhancing the generalizing ability of learning systems based on artificial neural networks, this has attracted attention from both machine learning and neural computing communities and has previously been attempted on diverse medical tasks<sup>[6,7]</sup>. Nevertheless the comprehensibility of an ensemble comprising of multiple artificial neural networks is inferior to that of a single artificial neural network. This may obstruct the extensive recognition of this technique in medicine.

In recent years, Artificial Neural Networks (ANN) has become a fascinating research area in the field of medicine. It is believed that in near future, they will be extensively applied to biomedical systems<sup>[1]</sup>. Diverse areas of medicine, for instance, diagnostic systems, biochemical analysis, image analysis and drug development have successfully applied ANN, in the past. In the mid-1980s, an application known as the “instant physician” stored a large number of medical records by training an auto associative memory neural network. Information regarding symptoms, diagnosis and treatment for a particular case were stored in all the records. Once the training is completed, a set of symptoms will be presented as input to the net. Consequently, the full stored pattern representing the “best” diagnosis and treatment is identified by the net. In our research hepatitis B is diagnosed by utilizing ANN which provides the severity level on the patient.

Hepatitis B that includes chronic liver disease is rather familiar one which may cause damage to hepatocytes. The healthy carrier and the decompensate cirrhosis may be said as the range of severity. The diagnosis and the prognosis of the hepatitis disease is the prime focus of numerous studies<sup>[8-11]</sup>. Nevertheless, it is necessary to consider the important components of medical care processes, such as, defining the severity level of hepatitis and evaluating alternative treatments, regardless of their unavailability in the literature till date. The infection of Hepatitis B Virus (HBV) is a major health problem in the continent of Asia. In Chinese population, HBV carriers amount up to almost 20%. In the HBV carriers, the people died due to HBV-related complications that include liver cirrhosis and Hepatocellular Carcinoma (HCC), i.e., liver cancer are almost equal to 25%. Our study aims at identifying the genomic markers of the HBV and clinical information which are utilized to predict occurrence of liver cancer and response to therapy.

Our study aims to diagnosis Hepatitis B virus disease and predict the severity level by imbedding an intelligent system with a classification model for HBV DNA and clinical data. Two main branches of artificial intelligence are utilized in the presented intelligent system. First is the traditional one that is represented by expert systems on the basis of Logical inference. Here, the decision of what type of hepatitis is to appear for a patient is made. Second is the connexionist, where artificial neural networks are the most common forms utilized. Here, a high accuracy for HCC diagnosis and prediction is necessitated.

The kohonen Self-Organizing Map (SOM) which is an unsupervised neural-network like algorithm that performs clustering of input data and, at the same time, maps it to a two-dimensional surface, doing both things at the same time. SOM is used to do the predictions regarding the Hepatitis B which gives severity level on the patient and its classification accuracy. In the diagnosis process, choosing valid clinical data is vital, because system has to deal with the patient’s health and even life. We have used a Hepatitis database<sup>[12]</sup> of 155 samples in total with 75 of them having missing attributes, which provides some symptoms of the disease Hepatitis B, measured features of some patients and a group of normal healthy people. The hepatitis is one of the serious diseases which demands expensive treatment and severe side effects can appear very often. Thus it is important to identify those patients who most probably can react to the treatment, so that the others can be protected from a treatment with no benefits by means of setting up a correct diagnosis. Accordingly, the practitioners of medicine have always been lent a helping hand by Artificial Intelligence intended to improving medical diagnosis and treatment.

**Hepatitis B:** Hepatitis B Virus (HBV) illness is a worldwide health issue. Among the 350 million chronic carriers of Hepatitis B it has been predicted that a quarter of them will pass away as a result of Hepatitis B (HB)-related chronic liver diseases. Hepatitis B virus generates huge viral loads through active replication, without killing the infected cell directly and its distinct life cycle of evolution seems to comprise interesting consequences<sup>[17]</sup>. Since HBV makes use of reverse transcription that is devoid of a proofreading function, the copying of its Deoxyribo-Nucleic Acid (DNA) genome results in the emergence of mutant viral genomes frequently. Furthermore both endogenous (host immune clearance) and exogenous (vaccines and antiviral drugs) selection pressures willingly select out these escape mutants. The Hepatitis B Virus (HBV) is commonly a double-stranded DNA virus that belongs to

the hepadnaviridae family<sup>[16]</sup>. The name of the family is derived from hepa, meaning liver; DNA, referring to deoxyribonucleic acid, the virus' genetic material and viridae, which means virus. The genes of the hepatitis B virus comprise of genetic codes to create numerous protein products that include Hepatitis B Surface Antigen (HBsAg), Hepatitis B Core Antigen (HBcAg), Hepatitis B E Antigen (HBeAg) and DNA polymerase<sup>[18]</sup>. These four proteins are of vital significance as they are measured in blood tests and aid in the diagnosis of hepatitis B and it is necessary that we are familiar with the same.

The Hepatitis B virus (HBV), a 3.2 kb orthohepadnavirus is a chief human pathogen. Though the outcome of chronic infection by HBV is uneven it is commonly followed by a complete recovery. A small amount of infections prevail as a chronically infected carrier state where in the virus continues to stay in the liver. Commonly, no particular initial symptoms of the carriage exist yet, in due course, cirrhosis and Hepatocellular Carcinoma (HCC), the chief ailment sequelae of carriage, may result. HBV stays in its human host in the form of eight clusters of viruses, each cluster exhibiting a similarity of sequences (genotypes A-H) and variable antigenicity (serotypes)<sup>[19]</sup>. There is an ascending substantiation that diverse HBV genotypes might possibly be connected to different disease profiles and varying responses to antiviral therapy. Studies in Taiwan and Japan recommend that genotype C is quite frequent in patients having cirrhosis, while HCC is connected with genotype B in patients below 50 years of age and with genotype C in those above 50<sup>[20]</sup>. Besides, it is has become evident that viral response in carriers undergoing sero conversion from comprising HBV e antigen (HBeAg) in their serum to comprising antibody to HBeAg (anti-HBe) is greatly influenced by the HBV genotype.

The sequence variation inside the HBV genome is categorized into eight genotypes A-H that are defined by the variations in their full-length genome >8%<sup>[22]</sup>. These differ from the serological subtypes that are described by the antigenicity of the HBV Surface Antigen (HBsAg)<sup>[21]</sup>, calculated by the amino acids at particular remains in the 'a' determinant of HBsAg. Despite the continuous enhancements in molecular biology, computational power and phylogenetic algorithms supporting the characterization and genotyping of the full-length HBV genome, several genotype predictions are frequently computed practically by sequencing a relatively small area of the genome, typically the surface antigen<sup>[23]</sup>. The subsequent table gives a brief account of the protein products and symptoms of Hepatitis B Virus (Table 1).

Table: 1 Hepatitis B protein products and symptoms

Protein products	Symptoms
<b>Hepatitis B Diagnosis:</b>	
Hepatitis B surface Antigen (HBsAg), Hepatitis B surface Antibody (HBsAb), Hepatitis B e-Antigen (HBeAg), Hepatitis B DNA.	Tiredness, fever, headache, nausea and vomiting, diarrhea or constipation, muscle aches, Joint pain, skin rash, yellowing of the skin and eyes (jaundice).

Exposure to an infected body or the body's secretions spread the Hepatitis B virus. Blood, semen, vaginal discharge, breast milk and saliva contain the maximum concentration of hepatitis B virus. Urine contains minimal concentration of the hepatitis B virus and the feces do not have any. Thus it is evident that neither food and water nor casual contact results in the spread of hepatitis b virus. Moreover blood transmission do not aid in the spread of hepatitis b anymore since all the blood utilized for transfusion are screened (tested) to forbid contamination with hepatitis B virus.

**Artificial intelligence in medicine:** A branch of computer science, which intends to make computers more intelligent, is known as Artificial intelligence. Learning is the fundamental necessity for any intelligent behavior. A majority of contemporary researches are of the unanimous opinion that there can be no intelligence without learning. Thus machine learning is one of the significant branches of Artificial Intelligence<sup>[24,25]</sup> and undoubtedly one of the rapidly growing subfields of Artificial intelligence research. Numerous researches have supported the potential of AI in medicine which is subsequently summarized:

- Proffers a laboratory to examine, organize, represent and catalogue the medical knowledge
- Builds new tools to facilitate medical decision-making, training and research
- Merges the medical, computer, cognitive and other scientific activities
- Provides a content-rich discipline for future scientific medical specialty

Numerous intelligent systems have been built so as to improve health care and proffer enhanced facilities at reduced cost. Intelligent systems were built to assist the users (chiefly doctors and patients) and to provide early detection and prediction to avoid serious illnesses<sup>[26,27]</sup>. Manual practice of diagnosis in several disease domains have been outperformed by early studies in intelligent medical system such as MYCIN, CASNET, PIP and Internist-I. The studies in intelligent system were improved in the 1990s so as to apply the system for current needs. Several other studies merged two or

more methodologies and applied the function to ensure system performance.

Data mining, one of the major AI techniques is employed for knowledge discovery in large databases. This method is applicable for gathering concealed information for medical purposes<sup>[28]</sup>. Fuzzy logic is another area of Artificial intelligence that deals with the uncertainty in knowledge that simulates human reasoning in incomplete or fuzzy data<sup>[29]</sup>. Further, a branch of AI that is capable of learning a set of data and building weight matrixes to denote the learning patterns is known as Neural Network (NN). NN is a network if several simple processors or units. NN simulates the functions of a human brain so as to carry out tasks in a way a human does. For instance a study on approximation and categorization in medicine with incremental neural network illustrates the finer generalization performance in comparison with other classification models<sup>[30]</sup>. Numerous medical applications including coronary artery; Myocardial Infarction<sup>[32]</sup>, cancer<sup>[31]</sup>, pneumonia<sup>[34]</sup> and brain disorders<sup>[33]</sup> utilize NN. Identification of abnormalities within the same images with high accuracy was facilitated by a NN that was implemented as a hybrid along with textual description method in Karkanis *et al.*<sup>[31]</sup>. The proposed study utilizes Neural Network for the diagnosis of Hepatitis B virus.

**Intelligent system for hepatitis B diagnosis:** The proposed research intends to Apply Artificial Neural Networks (ANNs) and related analysis methods to Health care, precisely to the management of Hepatitis B virus patient. The research is carried out to convert the diagnosis process into an over flow diagram or the effective parameter datasets (machine readable format) for the Hepatitis B disease followed by the evaluation the effective set of symptoms by utilizing expert systems on basis of Logical inference and artificial neural network techniques.

**Expert system for diagnosis:** Though expert systems proffer pre-selected rules for decision-making within specialized domains of knowledge they are restricted by the fixed number of options and by the date of the expert opinions embodied in the decision rules. Medical expert systems are developed with the intention of providing the physicians with both structured questions and structured responses in the medical domains of particular knowledge or experience<sup>[35]</sup>. The structure of the program is represented by the advice of one or more medical experts, who as well propose the optimal questions to be considered and proffer the most accurate conclusions from the answers the physician

chooses. An inference machine and architecture of neural networks are the two significant components that facilitate the system in the exploration and manipulation of the multifunctional database. The evolution of biological indicators is presumed with the aid of a trained artificial neural network. The expert system is capable of specifying the evolution in time of the illness as soon as the patients' personal data and the results of the tests taken at the onset of the treatment are provided along with the postulated code of reaction. Expert systems can be implemented with the aid of either logical inference or the statistical inference. The proposed system makes use of logical inference so as to predict the diagnosis of hepatitis B and the evolution in the infected victim.

**Logical inference:** Logical inference is employed to facilitate the advancement of expert systems in medicine by providing a diagnosis with the aid of a set of premises. The prospect of constructing an expert system is based on a set of rules provided that it implements human reasoning to a substantial degree. These systems are known as Rules based experts systems and are applied widely in medical diagnosis<sup>[36]</sup>. The expert system resembles a graph structure and is managed by the chain logical evaluation. These systems are extremely uncomplicated to implement and are simple to operate by a non-engineer since the rules of the aforesaid expert system synchronize with that of natural medical language.

In case of the diagnosis of hepatitis B the specification of the factors that define various kinds of hepatitis becomes an inevitable first step. This is followed by the design of an expert system. The type of hepatitis found in the patient organism is adjudged after a thorough analysis of a set of markers (AgHBs → Positive/ Negative, AgHBe → Positive/ Negative, anti-VHD → Positive/ Negative, anti-VHC → Positive).

The logical model consist of the following rules:

- IF (AgHBs = Positive) AND (AgHBe = positive) AND (anti-VHD = Negative) THEN Hepatitis B

This type of expert system is easy to be implemented for simple rules like 'logical premises → conclusion'.

**Artificial neural network for prediction:** Artificial neural networks are fundamental replicas of biological nervous system and hence have obtained motivation from the kind of computing carried out by a human brain. ANN encompasses a category of robust nonlinear regression and discriminant model, data reduction models and nonlinear dynamical systems<sup>[37]</sup>. The enormously parallel structure and the capability to learn

from experience are the reasons behind the supremacy of a neural network. The efficiency of training influences the accuracy of classification. The knowledge obtained by the learning experience, hoarded as connection weights aid in the decision making on fresh input. Neural Networks (NN) have been widely recognized as dominant and flexible computational tools for the organization and correlation of information in a manner that is beneficial in solving certain types of problems that are too complex, too poorly understood, or too resource-intensive to manage with conventional computing technologies. Lately Neural networks techniques have been deployed in several medical diagnosis problems<sup>[38]</sup>. Neural Network (NN) is a powerful AI technique possessing the ability to learn a set of data and build weight matrixes to denote the learning patterns.

Pattern classification, pattern completion, function approximation, optimization, prediction and automatic control are some of the applications that extensively utilize neural networks. Supervised learning and unsupervised learning are the two common categories of ANNs. Supervised learning necessitates the presence of a desired output result for each input vector while training the network. Back-Propagation Neural Networks (BPNN), Radial Basis Function Networks (RBFNN)<sup>[39,40]</sup>, Probabilistic Neural Networks (PNN) and Generalized Regression Neural Networks (GRNN) are the common networks belonging to the supervised learning kind. This research employs unsupervised learning for the HBV diagnosis. In case of unsupervised learning the training of the network is completely triggered by data and the target results for the input data vectors are not specified.

**Self-organizing map:** A computational data structure called the Self-Organizing Map (SOM) was introduced by Tuevo Kohonen in 1982. The Self-Organizing Map<sup>[41]</sup> is a neural network model that facilitates the analysis and visualization of high dimensional data. This is a part of the competitive learning network. The SOM is a feed forward neural network devoid of hidden layers<sup>[14]</sup>. A grid map of neurons interconnected with weights to other neurons form the output layer. A 2-dimensional rectangular or hexagonal interconnection structure is the general and widespread topology of the map. The generation of a low dimensional (usually 2-dimensional) projection of the data set besides conserving the topological properties of the data set is the chief intent of a SOM. This offers us with a way to visualize low-dimensional views of high-dimensional data<sup>[13]</sup>.

Topographic maps of input signals are generated as a result of optimization where the most significant

relationships among the input signals are transformed into associations amid the neuron positions. This is similar to an abstracting capability that restrains details of futile importance and maps the most significant features along the map dimension. On the whole, it is possible to say that the Kohonen networks aim to transpose the resemblance of sensorial input signals to the neighborhood of neuron positions.

The SOM algorithm for classification is summarized below:

- Initialize input nodes, output nodes and connection weights: Use the top (most frequently occurring) N terms as the input vector and create a two-dimensional map (grid) of M output nodes. Initialize weights  $w_{ij}$  from N input nodes to M output nodes to small random values
- Present each set in order: Describe each set as an input vector of N coordinates
- Compute distance to all nodes: Compute Euclidean distance  $d_j$  between the input vector and each output node j:

$$d_j = \sum_{i=0}^{N-1} (x_i(t) - w_{ij}(t))^2 \quad (1)$$

where,  $x_i(t)$  can be 1 or 0 depending on the presence of  $i$ th term in the document presented at time  $t$ . Here,  $w_{ij}$  is the vector representing position of the map node  $j$  in the document vector space. From a neural net perspective, it can also be interpreted as the weight from input node  $i$  to the output node  $j$ :

- Select winning node  $j^*$  and update weights to node  $j^*$  and its neighbors: Select winning node  $j^*$ , which produces minimum  $d_j$ . Update weights to nodes  $j^*$  and its neighbors to reduce the distances between them and the input vector  $x_i(t)$  :

$$w_{ij}(t+1) = w_{ij}(t) + \eta(t)(x_i(t+1) - w_{ij}(t)) \quad (2)$$

After such updates, nodes in the neighborhood of  $j^*$  become more similar to the input vector  $x_i(t)$ . Here,  $\eta(t)$  is an error-adjusting coefficient ( $0 < \eta(t) < 1$ ) that decreases over time.

The classification rules are offered by Kohonen's SOM or a feature map<sup>[15]</sup>. SOM merges competitive learning and dimensionality reduction through the smoothing of clusters in accordance with an a priori grid. In SOM the clustering is produced when

numerous units compete for (training) data. Eventually, the unit whose weight vector is closest to the data turns out to be the winner in order to approach closer to the input data. The weights of both the winner and that of the nearest neighbors are regulated. This technique is known as the Winner Takes All (WTA) approach. A topology among the input data is presumed by SOM. Since the identical inputs are anticipated to stay adjacent to each other, the aforesaid organization is assumed to form a SOM map.

### RESULTS AND DISCUSSION

The proposed research employs Artificial Neural networks so as to forecast the treatment response of a hepatitis B virus infected patient. Owing to the fact that hepatitis B is a widespread and severe disease the examination of its evolution throughout the treatment is considered to be of vital significance. Despite the efficiency of the hepatitis B treatment being enhanced steadily the intensity of this infection would still raise critical concerns in the years to come. Numerous intricate processes including evaluation of information in relation to the apparition of the hepatitis infection, its evolution, the antecedents and symptoms, the results of the laboratory tests and the evolution of some explicit biological indicators all through the treatment comprise are encompassed in this application. A multifunctional database is built and an expert system is implemented so as to detect diverse kinds of hepatitis besides realizing a few forecasts in connection with its volition in the patient and the response to the treatment. The primary phase supports the diagnosis of the disease for a new patient to be carried out on basis of the Markers. To begin with, the system aims to diagnose the type of hepatitis: B or others. The values of the three markers, Hepatitis B surface Antigen (AgHBs), anti-VHC and anti-VHD (Fig. 1) to be precise, are to be specified. This portion of the system has been built with the aid of a customary procedure of actualization of human reasoning known as Logical inference. The expert system necessitates the specification of the features of the patients: Sex, age, living conditions, symptoms and the results of laboratory tests so as to test the same. Conclusions obtained are greatly influenced by logical inference.

If (AgHBs = Positive) and (AgHBe = Positive) and (anti-VHC = Negative) and (anti-VHD = Negative) then Hepatitis B

Once the patient is diagnosed positive for hepatitis B the system predicts its evolutionary category and henceforth the corresponding treatment to be applied (Fig. 2).

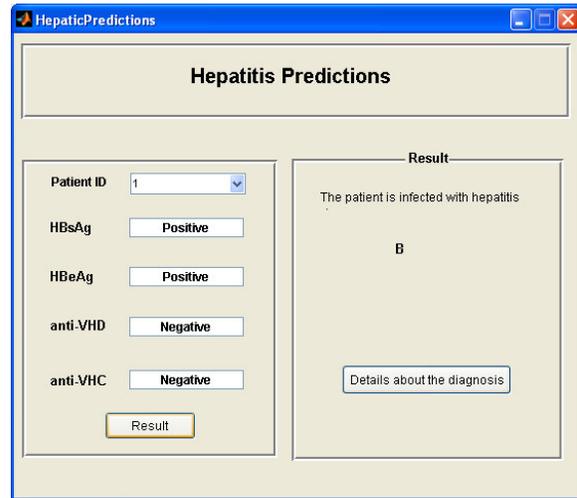


Fig. 1: Hepatitis B diagnosis

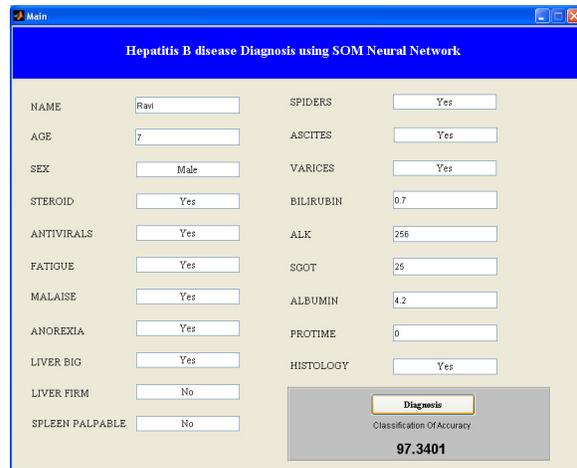


Fig. 2: System's predicts of evolutionary category and corresponding treatment

Self organising map neural network is used in devising this system for further accuracy of prediction. The total amounts of cases for all subjects have been divided into two groups, one for training and the other for testing of the algorithm. The symptoms of the disease Hepatitis B levels were used as an input to the SOM classifier. SOM which is a class of unsupervised network is used as a classifier to predict the accuracy level of hepatitis B. For example, when the AgHBs and AgHBe are positive and both anti-VHD and anti-VHC are negative in a patient then he is said to be tested positive for hepatitis B. It is always possible for the human expert to utilize the remaining two branches if at all he is in need of more predictions with regard to the diagnosis. Figure 2 can be obtained by clicking on the

button 'Details about the diagnosis' in Fig. 1. Therefore, the proposed expert system diagnoses hepatitis B using logical inference. Only when the patients' features such as sex, age, living conditions, symptoms and the results of laboratory tests are provided by the user will further classifications be supported. This phase would be succeeded by the diagnosis with the implemented algorithm and eventually by the determination of the plausibility scores for the evolutionary type and the classification accuracy of hepatitis B (as is shown in the later half of Fig. 2).

### CONCLUSION

The characteristics of medical diagnosis and prediction with the aid of artificial intelligence techniques will build an interactive consultation environment. Expert systems and fuzzy logic will be appropriate techniques for clinical decision making since it innately involves handling partial evidence and uncertainty regarding the effects of projected interventions. Neural networks have displayed better prediction capabilities than other techniques (like statistics). The proposed research projects an intelligent system for the diagnosis of Hepatitis B disease with the aid of unsupervised learning neural network known as the Self Organizing Map (SOM) and an expert system that works on logical inference. Thus the hepatitis B diagnosis was done with a wide variety of data samples from diverse patients. Experimental results demonstrated that both artificial neural networks and logical methods perform equivalently well in the diagnosis of hepatitis B.

### REFERENCES

1. Brause, R.W., 2001. Medical analysis and diagnosis by neural networks. Proceedings of 2nd International Symposium on Medical Data Analysis, Oct. 08-09, Springer-Verlag, London, UK., pp: 1-13.  
<http://portal.acm.org/citation.cfm?coll=GUIDE&dl=GUIDE&id=691037>
2. Victor Alves, Paulo Novais, Luís Nelas, Moreira Maia and Victor Ribeiro, 2003. Case based reasoning versus artificial neural networks in medical diagnosis. Proceedings of the IASTED International Conference Artificial Intelligence and Applications, pp: 1-5.  
<http://repositorium.sdum.uminho.pt/bitstream/1822/934/1/AIA2003.pdf>
3. Zhi-Hua Zhou and Yuan Jiang, 2003. Medical diagnosis with C4.5 rule preceded by artificial neural network ensemble. IEEE Trans. Inform. Technol. Biomed., 7: 37-42. DOI: 10.1109/TITB.2003.808498
4. Richards, G., V.J. Rayward-Smith, P.H. Sönksen, S. Carey and C. Weng, 2000. Data mining for indicators of early mortality in a database of clinical records. Artif. Intel. Med., 22: 215-231. DOI: 10.1016/S0933-3657(00)00110-X
5. Sarma, D.J., 2000. Neural networks and their applications in industry. DESIDOC Bull. Inform. Technol., 20: 29-36.  
<http://publications.drdo.gov.in/gsd/collect/dbit/index/assoc/HASH4e6e.dir/dbit2001029.pdf>
6. Setiono, R., 2000. Generating concise and accurate classification rules for breast cancer diagnosis. Artif. Intel. Med., 18: 205-219.  
<http://citeseerx.ist.psu.edu/viewdoc/summary?DOI=10.1.1.45.9593>
7. Zhou, Z.H., Y. Jiang, Y.B. Yang and S.F. Chen, 2002. Lung cancer cell identification based on artificial neural network ensembles. Artif. Intel. Med., 24: 25-36. DOI: 10.1016/S0933-3657(01)00094-X
8. Lin, W. and J. Tang, 1999. DiagFH: An expert system for diagnosis of fulminant hepatitis. Proceedings of the 4th Annual IEEE Symposium on Computer-Based Medical Systems, May 12-14, IEEE Xplore Press, Baltimore, MD., USA., pp: 330-336. DOI: 10.1109/CBMS.1991.128988
9. Buscher, H.P., Ch. Engler, A. Führer, S. Kirschle and F. Puppe, 2004. Hepato consult: A knowledge-based second opinion and documentation system. Artif. Intel. Med., 24: 205-216. DOI: 10.1016/S0933-3657(01)00104-X
10. Jajoo, R., D. Mital, S. Haque and S. Srinivasan, 2002. Prediction of hepatitis c using artificial neural network. Proceedings of the 7th International Conference on Control, Automation, Robotics and Vision, Dec. 2-5, IEEE Xplore Press, USA., pp: 1545-1550.  
[http://ieeexplore.ieee.org/xpls/abs\\_all.jsp?arnumber=1235004](http://ieeexplore.ieee.org/xpls/abs_all.jsp?arnumber=1235004)
11. Bonfa, I., C. Maioli, F. Sarti, G.L. Milandri and P.R. Dal Monte, 2004. HERMES: An expert system for the prognosis of hepatic diseases. Proc. IEEE., 92: 1759-1779. DOI: 10.1109/ANNES.1993.323033
12. Hepatitis Dataset 2003. Hepatitis B disease diagnosis using artificial neural networks.  
<http://www.ics.uci.edu/pub/ml-repos/machine-learning-databases/>, 2003.ax
13. Ali, A.H., 2008. Self-organization maps for prediction of kidney dysfunction. Proceedings of the 16th Telecommunications Forum TELFOR, Nov. 25-27, Serbia, Belgrade, [http://www.telfor.org.yu/files/radovi/09\\_13.pdf](http://www.telfor.org.yu/files/radovi/09_13.pdf)

14. Teuvo Kohonen, 2001. Self-Organizing Maps. 3rd Edn., Number 30 in Springer Series in Information Science, Springer, ISBN: 3540679219, pp: 501.
15. Yanagida, T.T. Miura and I. Shioya, 2003. Classifying news corpus by self-organizing maps. Proceedings of the IEEE Pacific Rim Conference on Communications, Computers and signal Processing, Aug. 28-30, IEEE Xplore Press, USA., pp: 800-803. DOI: 10.1109/PACRIM.2003.1235902
16. Zhenming, Xu, T.S. Benedict Yen, W. Lanying, R.C. Madden, W. Tan, B.L. Slagle and Jing-hsiung Ou, 2002. Enhancement of hepatitis B virus replication by its x protein in transgenic mice. *J. Virol.*, 76: 2579-2584. DOI: 10.1128/JVI.76.5.2579-2584.
17. Locarnini, S., 2004. Molecular virology of hepatitis B virus. *Seminars in Liver Disease*, <http://medicine1.bjmu.edu.cn/PBL/200507gy/ckwx/2.pdf>
18. Ding, X., M. Mizokami, G. Yao, B. Xu, E. Orito, R. Ueda and M. Nakanishi, 2001. Hepatitis B virus genotype distribution among chronic hepatitis B virus carriers in Shanghai China. *Intervirology*, 44: 43-47. DOI: 10.1159/000050029
19. Myers, R., C. Clark, A. Khan, P. Kellam and R. Tedder, 2006. Genotyping hepatitis B virus from whole- and sub-genomic fragments using position-specific scoring matrices in HBV STAR. *J. General Virol.*, 87: 1459-1464. DOI: 10.1099/vir.0.81734-0
20. Kao, J.H., P.J., Chen, M.Y. Lai and D.S. Chen, 2000. Hepatitis B genotypes correlate with clinical outcomes in patients with chronic hepatitis B. *Gastroenterology*, 118: 554-559. DOI: 10.1016/S0016-5085(00)70261-7
21. Courouce, A.M., H. Lee, J. Drouet, M. Canavaggio and J.P. Soulier, 1983. Monoclonal antibodies to HBsAg: A study of their specificities for eight different HBsAg subtypes. *Develop. Biol. Standardisat.*, 54: 527-534. <http://www.ncbi.nlm.nih.gov/pubmed/6653898>
22. Norder, H., A.M. Courouce, P. Coursaget, J.M. Echevarria, S.D. Lee, I.K. Mushahwar, B.H. Robertson, S. Locarnini and L.O. Magnius, 2004. Genetic diversity of hepatitis B virus strains derived worldwide: Genotypes, subgenotypes and HBsAg subtypes. *Intervirology*, 47: 289-309. DOI: 10.1159/000080872
23. Peters, M.G., 2007. Diagnosis and Management of Hepatitis B Virus and HIV Coinfection. *IAS-USA. Topic in HIV Med.*, 15: 163-166. <http://www.ncbi.nlm.nih.gov/pubmed/18073452>
24. Mitchell, T., 1997. *Machine Learning*. MC-Graw Hill, pp: 414.
25. Ryszard, S. Michalski, Ivan Bratko and Miroslav Kubat, 1998. *Machine Learning and Data Mining: Methods and Applications*. John Wiley and sons Inc., ISBN: 10: 0471971995, pp: 456.
26. Manickam, S. and S.S.R. Abidi, 1999. Experienced based medical diagnostics system over the World Wide Web (WWW). Proceedings of the 1st National Conference on Artificial Intelligence Application in Industry, Kuala Lumpur, pp: 47-56. <http://citeseerx.ist.psu.edu/showciting?jsessionid=C6227E681EF947AB2343526B6A50FF?cid=27100>
27. Zelic, I., N. Lavrac, P. Najdenov and Z. Rener-Primec, 1999. Impact of machine learning to the diagnosis and prognosis of first cerebral paroxysm. *Machine Learning and Applications: Machine Learning in Medical Applications*, Chania, Greece, pp: 24-26. <http://citeseer.ist.psu.edu/old/270320.html>
28. Neves, J., V. Alves, L. Nelas, A. Romeu and S. Basto, 1999. An information system, that supports knowledge discovery and data mining in medical imaging. *Machine Learning and Applications: Machine Learning in Medical Applications*, Chania, Greece, pp: 37-42. [http://www.iit.demokritos.gr/skel/eetn/acai99/Workshops/w13/w13\\_07.pdf.gz](http://www.iit.demokritos.gr/skel/eetn/acai99/Workshops/w13/w13_07.pdf.gz)
29. Cunningham, P., J. Carney and S. Jacob, 2000. Stability problems with artificial neural networks and the ensemble solution. *Artif. Intel. Med.*, 20: 217-225. DOI: 10.1016/S0933-3657(00)00065-8
30. Jankowski, N., 1999. Approximation and classification in medicine with incnet neural networks. *Machine Learning and Applications, Machine Learning in Medical Applications*, Chania, Greece, pp: 53-58. <http://citeseer.ist.psu.edu/old/268056.html>
31. Karkanis, S.A., G.D. Magoulas, M. Grigoriadou and M. Schurr, 1999. Detecting abnormalities in colonoscopic images by textual description and neural networks. *Machine Learning and Applications: Machine Learning in Medical Applications*, Chania, Greece, pp: 59-62. <http://citeseerx.ist.psu.edu/viewdoc/summary?DOI=10.1.1.2.2938>
32. Heden, B., M. Ohlsson, R. Rittner, O. Pahlm, W.K. Haisty, C. Peterson and L. Edenbrandt, 1996. Agreement between artificial neural networks and human expert for the electrocardiographic diagnosis of healed myocardial infarction. *J. Am. College Cardiol.*, 28: 1012-10s16. <http://citeseerx.ist.psu.edu/viewdoc/summary?DOI=10.1.1.32.5662>

33. Pranckeviciene, E., 1999. Finding similarities between an activity of the different eeg's by means of a single layer perceptron. *Machine Learning and Applications: Machine Learning in Medical Applications*, Chania, Greece, pp: 49-52. <http://citeseerx.ist.psu.edu/viewdoc/summary?DOI=10.1.1.35.9297>
34. Caruana, R., S. Baluja and T. Mitchell, 1996. Using the Future to "Sort Out" the Present: Rankrop and Multitask Learning for Medical Risk Evaluation. *Advances in Neural Information Processing Systems 8*, The MIT Press, Cambridge, pp: 959-965. <http://citeseerx.ist.psu.edu/showciting?jsessionid=565C3D15E030051F6530E8DD4E01AC83?cid=527092>
35. Luger, G.F. and W.A. Stubblefield, 1989. *Artificial intelligence and the Design of Expert Systems*. Illustrated Edn., Redwood City, CA Benjamin/Cummings Publ. Co., ISBN: 10: 0805301399, pp: 600.
36. Petrică, D., 2004. Structure of models for medical knowledge processing. *Trans. Automat. Control Comput. Sci.*, 49: 103-106. <http://conti.ac.upt.ro/2004/conti2004/>
37. Everhart, J.W., J.E. Dickson, W.C. Knowler, W.C. Johannes, R.S., 1988. Using the ADAP learning algorithm to forecast the onset of diabetes mellitus. *Proceedings of the Annual Symposium on Computer Application in Medical Care*, Nov. 9-9, pp: 261-265. <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2245318>
38. Wolberg, W.H. and O.L. Mangasarian, 1990. Multisurface method of pattern separation for medical diagnosis applied to breast cytology. *Proceed. Nat. Acad. Sci., USA.*, 87: 9193-9196. <http://www.pnas.org/content/87/23/9193.full.pdf+html>
39. Park, J. and I.W. Sandberg, 1993. Approximation and radial basis function networks. *Neural Computat.*, 5: 305-316. DOI: 10.1162/neco.1993.5.2.305
40. Venkatesan, P. and S. Anitha, 2006. Application of a radial basis function neural network for diagnosis of diabetes mellitus. *Current Sci.*, 91: 1195-1199. <http://cat.inist.fr/?aModele=afficheN&cpsidt=18507476>
41. Kohonen, T., 1995. *Self-Organizing Maps*. Springer Series in Information Sciences. 2nd Extended Edn., Springer, Berlin, Heidelberg, ISBN: 3-540-67921-9, pp: 501.