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A hybrid Model to Estimate Cirrhosis Using Laboratory Testsand Multilayer Perceptron (MLP) Neural Networks

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Abstract: *Hepatitis C virus (HCV) infection and its complications are one of the most leading health challenges over the world. Where it causes tissue damage, causing cirrhosis of the liver gradually. Liver biopsy and Fibro-scan are the standard methods to measure fibrosis before treatment. however, those methods have its own limitations, risks and cost. Liver fibrosis has been determined using routine laboratory tests. The laboratory tests are Alanine Aminotransferase (ALT), aspartate aminotransferase (AST), platelet count (PLT), Total Bilirubin(TB), Direct Bilirubin (DB), Total Proteins (TP) and Albumin (ALB). The aim of this paper, estimate cirrhosis using laboratory tests and multilayer perceptron (MLP) neural networks. Research applied on 582 liver patient in Egypt. Testing phase is comparison between Fibro-index results and Neural Network result. Visual studio 2015 C# and SQL-Server are used to develop a windows application.*

General Terms
Liver disease
Keywords: *Cirrhosis, Liver, Multilayer perceptron neural networks.*

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I. Introduction

Hepatitis C virus (HCV) infection is a serious human liver health problem. HCV is one of the most dangerous viruses on the liver and most prevalent. It spreads through the blood contact [1].The natural course of chronic hepatitis C is characterized by progressive fibrosis in the inflamed liver with structural and hemodynamic changes leading to cirrhosis, which is followed by end stage complications. Accordingly, the assessment of liver fibrosis in chronic hepatitis C has become of paramount importance; to guide management decisions, predict outcome (prognosis), and monitor disease activity in individual patients [2].Fig.1, represent liver's tissue phases that infected by HCV according life time. According Fig. 1 cirrhosis has 4 levels, F1, F2, F3 and F4 [2].

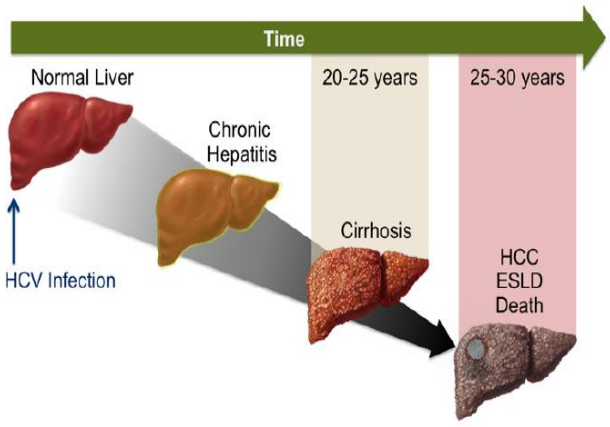


Fig. 1 Time Course of Progression with Chronic Hepatitis C Infection

Masahiko Koda et el [3], presented a simple model consisting of routine laboratory tests. a simple Firbo-Index measurement has been created. the experiment was run on 240 patients whose tested by Fibro-scan. A fibro index equation has been created using platelet count, AST, and serum gamma globulin.
Dakshata Panchal and Seema Shah [4], presented an intelligent system to diagnosis of the Hepatitis B virus disease using as generalized regression and neural network which gives the result for whether the patient is Hepatitis B positive or not and the severity of the patient.

GhumbreShashikant and A.A. Ghatol [5], proposed a Neural network algorithm in conventional hepatitis B diagnosis 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. The kohonen Self-Organizing Map network(SOM) was applied to hepatitis data for predictions regarding the Hepatitis B which gives severity level on the patient. It is a class of unsupervised network was used as a classifier to predict the accuracy of Hepatitis B. 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.

Tamer Sh. Mazen [6] computes the weight of each fibrosis-4 inputs using analytic hierarchy process and coefficient between its inputs. correlation coefficient model, practically proved that there is a relation between SGPT and SGOT but there is no relation or very weak relation between other inputs. Then by using Analytical Hierarchy Process, practically proved that the most important inputs which effect on Fibrosis is SGOT with weight value about 53%, the second input is Age with weight value about 25%, the third input is PLT with value 16% and the last input is SGPT with weight value about 5%.

II. Background

2.1 Neural Network

Neural networks are a new method of programming computers. They are exceptionally good at performing pattern recognition and other tasks that are very difficult to program using conventional techniques. Programs that employ neural nets are also capable of learning on their own and adapting to changing conditions.

An Artificial Neural Network (ANN) is an information processing paradigm that is inspired by the biological nervous systems, such as the human brain's information processing mechanism. It has been applied to an increasing number of real world problems of varying complexities [7].

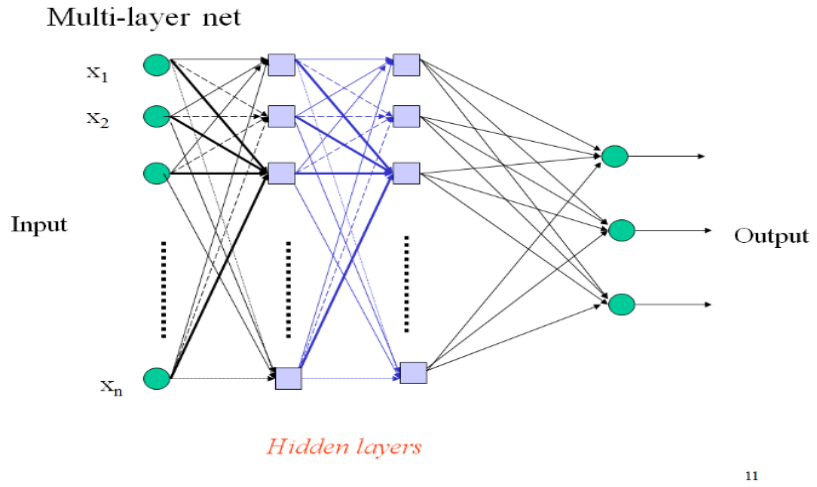


Fig. 2 Multi-Layer Neural Network

(Fig. 2) Represent the consists of ANN multi-layer where

- Input Layer - The activity of the input units represents the raw information that Is fed into the network.
- Hidden Layer - The activity of each hidden unit is determined by the activities of the input units and the weights on the connections between the input and the hidden units.
- Output Layer - The behavior of the output units depends on the activity of the hidden units and the weights between the hidden and output units.

The key element of this paradigm is the novel structure of the information processing system. It is composed of a large number of highly interconnected processing elements (neurons) working in unison to solve specific problems. NNs, like people, learn by try and error. An NN is configured for a specific application, such as pattern recognition or data classification, through a learning process. Learning in biological systems involves adjustments to the synaptic connections that exist between the neurons. This is true of NNs as well. Their greatest advantage is in solving problems that are too complex for conventional technologies, such as problems that do not have an algorithmic solution or for which an algorithmic solution is too complex to be found. In general, because of their derivation from the biological brain, ANNs are well suited to problems that people are good at solving, but for which computers are not. These problems include pattern recognition and forecasting. The later techniques require the recognition of the trends in data. Other advantages of neural networks include; adaptive learning for example an ability to learn to do tasks based on the data given for training or initial

experience. An ANN can create its own organization or representation of the information it receives during learning time and real-time operation. [8].

In using neural networks, the entire available data set is usually randomly divided into a training (in-sample) set and a test (out-of-sample) set. The training set is used for neural network model building and the test set is used to evaluate the reductive capability of the model. While this practice is adopted in many studies, the random division of a sample into training and test sets may introduce bias in model selection and evaluation in that the characteristics of the test may be very different from those of the training.

2.1.1 Training Multilayer Perceptron Networks

The goal of the training process is to find the set of weight values that will cause the output from the neural network to match the actual target values as closely as possible. The most basic method of training a neural network is trial and error. If the network isn't behaving the way it should, change the weighting of a random link by a random amount. If the accuracy of the network declines, undo the change and make a different one. It takes time, but the trial and error method does produce results.

2.1.2 Learning Rule to Adapt weight

We provide the specific output for each example we offer to the network, and thus learn the network (modify the weights) by knowing the difference between the current output and the output target output, and the most famous learning algorithms with the method of the Backpropagation method. Fig. 3 represent a flowchart to learn rule to adapt weight, in instruction using a router.

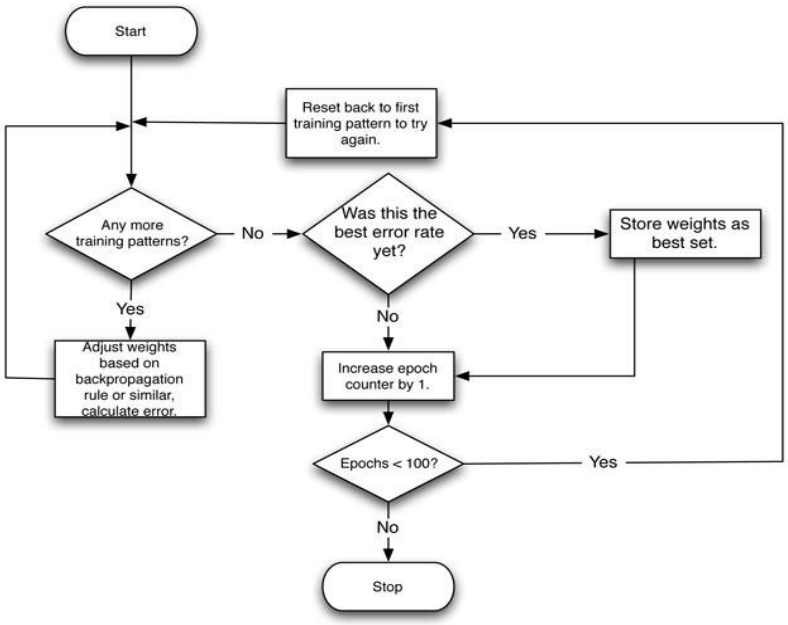


Fig. 3A Flowchart to Adept weight

Cross-validation will be used to accurately describe the predictive performance of the neural networks. Cross validation is a re-sampling technique which uses multiple random training and test sub samples. The advantage of cross validation is that all observations or patterns in the available sample are used for training the model. The cross-validation analysis will yield valuable insights on the reliability of the neural networks with respect to sampling variation.

2.2 Fibro Index

Fibrosis-4 score uses to estimate cirrhosis. Cirrhosis has estimated using four parameters (Age, SGOT, SGPT and PLT) [8]. Fibrosis-4 estimated by [9]

$FBI = \frac{Age \times AST}{PLT \times \sqrt[2]{ALT}}$ ……..(2)

Where:

Aspartate Aminotransferase (AST or SGOT)[U/L]

Alanine Aminotransferase (ALT or SGPT)$[U/L])^{1/2}$

Platelet Count (PLT) $[10^9/L]$.

Table1 represents the interpretation of FBI equation results.

Table 1 FBI results Interpretation

FBI Results		
F0 - F1	If FBI <= 1.54	Normal Liver
F2	If 1.54 < FBI < 3.25	Chronic
F3-F4	If FBI > 3.26	Cirrhosis

III. Research Experiment

While the searcher was thinking to using neural network to estimate liver Cirrhosis, there are two important questions need to be addressed:

1- What is the appropriate neural network architecture for this particular data set?

2- How robust is the neural network performance in predicting the Cirrhosis status in terms of sampling variability?

For the first question, there are no definite rules to follow since the choice of the architecture also depends on the classification objective. For example, if the objective is to classify a given set of objects as well as possible, then a larger network may be desirable. However, if the network is to be used to predict the classification of unseen objects, then a larger network is not necessarily better.

The experiments run on real-life data sets. this data consists of 582 Egyptian liver patient. Dataset had been divided to 75% as training and 25% for testing.

Testing is comparison between Fibro-index results and Neural Network result.

Windows application was developed by researcher using visual studio 2015 C# and SQL server 2008.

3.1 Neural Network

The input layer for Neural Networks is consists of eight neurons. Each one for one test as seen in Fig. 3

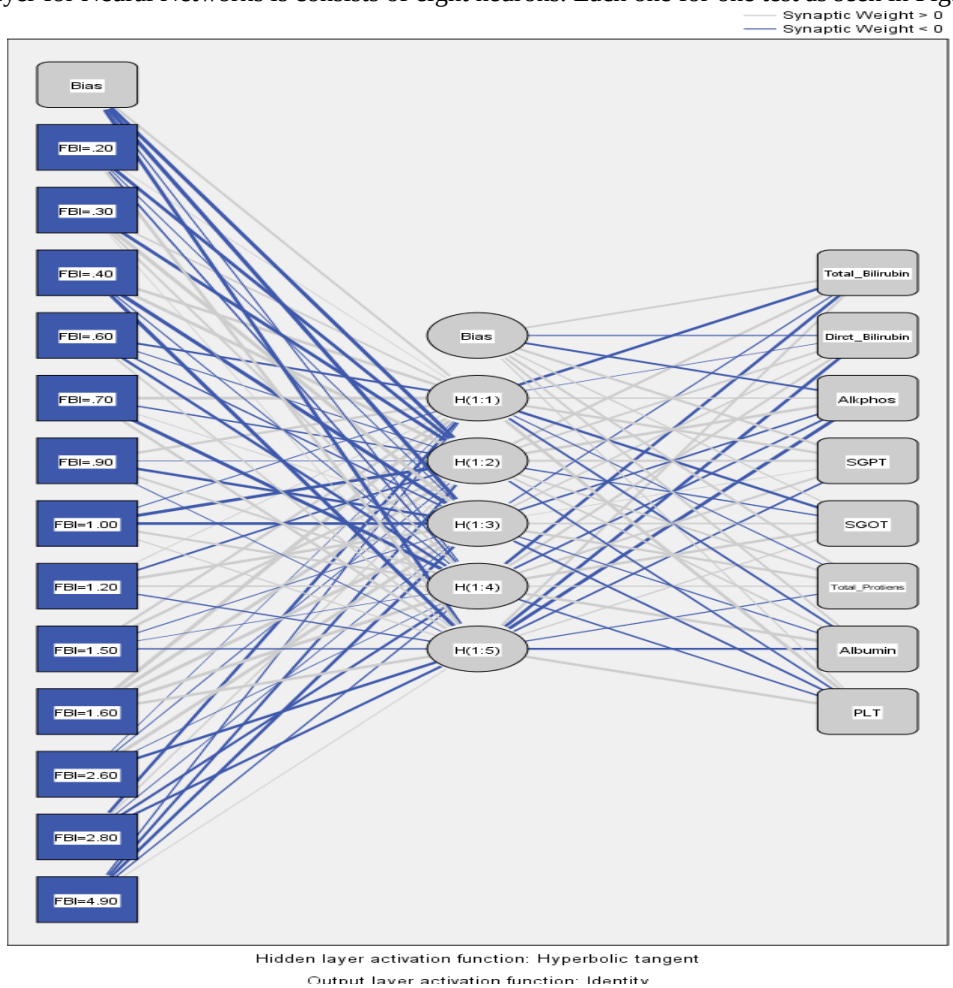


Fig. 4 Researcher Neural Network

Results

Table 2 Model Summary – Training phase

Model Summary -Training	
$\sum e^2$	73.85
Average Relative Error	1.02
Relative Error for Scale Dependents	
Total Bilirubin	1.01
Direct Bilirubin	0.96
Alkphos	1.05
SGPT	1.14
SGOT	0.96
Total Proteins	1.04
Albumin	1.02
PLT	0.97

Table 3 Model Summary– Testing phase

Model Summary - Testing	
$\sum e^2$	52.55
Average Overall Relative Error	1.09
Relative Error for Scale Dependents	
Total Bilirubin	1.62
Direct Bilirubin	0.95
Alkphos	1.13
SGPT	1.03
SGOT	1.22
Total Proteins	0.88
Albumin	0.89
PLT	1.26

Table 4 The Sigmoid Function results.

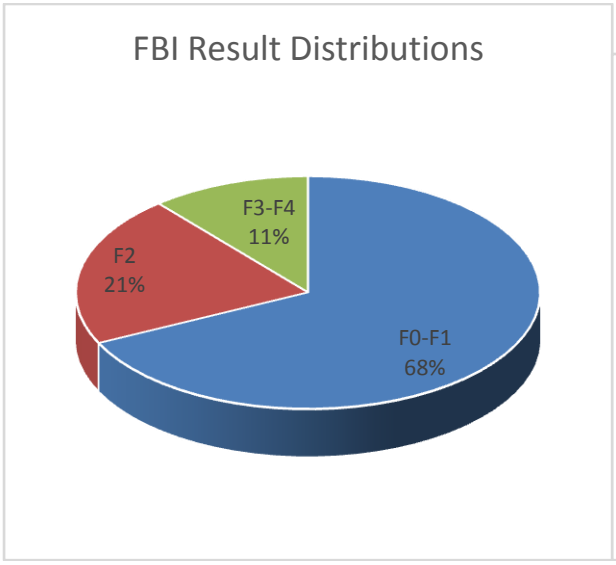
sigmoid function	
Normal Liver	-1
Chronic	0
Cirrhosis	1

Table 2 represents the results of training phase in model.
Table 3 represents the results of testing phase in model.
Table 4 represents the Sigmoid function results that classify liver cirrhosis, where (-1) represents Normal Liver, (0) represents Chronic Liver and (1) represents Cirrhosis Liver.

Table 5 Sample of data and results of FBI and NN

Age	TB	DB	Alkphos	SGPT	SGOT	TP	ALB	PLT	FBI	FBI-Result	NN	NN - Result
65	0.7	0.1	187	16	18	6.8	3.3	274	1.07	F0-F1	-1	F0-F1
62	10.9	5.5	699	64	100	7.5	3.2	615	1.26	F0-F1	-1	F0-F1
62	7.3	4.1	490	60	68	7	3.3	189	2.88	F2	0	F2
58	1	0.4	182	14	20	6.8	3.4	462	0.67	F0-F1	-1	F0-F1
72	3.9	2	195	27	59	7.3	2.4	530	1.54	F2	0	F0-F1
46	1.8	0.7	208	19	14	7.6	4.4	330	0.45	F0-F1	-1	F0-F1
26	0.9	0.2	154	16	12	7	3.5	275	0.28	F0-F1	-1	F0-F1
29	0.9	0.3	202	14	11	6.7	3.6	441	0.19	F0-F1	-1	F0-F1
17	0.9	0.3	202	22	19	7.4	4.1	188	0.37	F0-F1	-1	F0-F1
55	0.7	0.2	290	53	58	6.8	3.4	329	1.33	F0-F1	1	F0-F1
57	0.6	0.1	210	51	59	5.9	2.7	617	0.76	F0-F1	-1	F0-F1
72	2.7	1.3	260	31	56	7.4	3	275	2.63	F2	0	F2
64	0.9	0.3	310	61	58	7	3.4	292	1.63	F2	-1	F0-F1
74	1.1	0.4	214	22	30	8.1	4.1	522	0.91	F0-F1	-1	F0-F1
61	0.7	0.2	145	53	41	5.8	2.7	563	0.61	F0-F1	-1	F0-F1
25	0.6	0.1	183	91	53	5.5	2.3	114	1.22	F0-F1	-1	F0-F1
38	1.8	0.8	342	168	441	7.6	4.4	264	4.90	F3-F4	1	F3-F4
33	1.6	0.5	165	15	23	7.3	3.5	847	0.23	F0-F1	-1	F0-F1
40	0.9	0.3	293	232	245	6.8	3.1	632	1.02	F0-F1	-1	F0-F1

Table 5 represents the sample of dataset (Liver laboratories), also it represents comparison of Fibro Index (FBI) and Neural Network model.



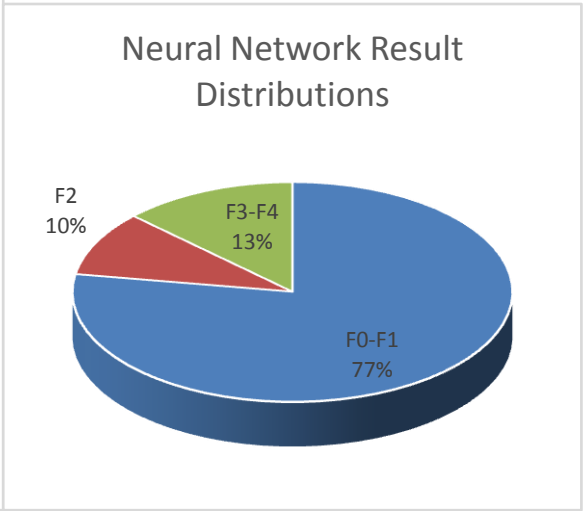


Fig. 5 Distribution of Fibro Index resultsFig. 6 Distribution of Neural Network results

Fig. 5 and Fig 6 are Showing the distribution ratios for the stages of hepatic fibrosis of the samples recorded in the database. As is evident from the two figures The distribution rate in the normal liver stage is 68% according to the FBI and 78% for the neural network model. While the Chronic fibrosis of the liver was distributed, the distribution rate is 21% according to FBI and 9 % for neural network model, finally the distribution rate for Cirrhosis is 11% according to FBI and 13% for neural network model.

IV. Conclusion

In this research, in order to calculate the Fibrosis-4of cirrhosis levels. Cirrhosis determines by Fibro-Index. Fibro- index equation has 4 inputs (SGOT,SGPT, PLT and Age). this research represents new methodology using Multi-Layer Neural Network algorithm to estimate the cirrhosis level. Its inputs are laboratory tests (*Alanine* Aminotransferase (ALT), aspartate aminotransferase (AST), platelet count (PLT), Total Bilirubin(TB), Direct Bilirubin (DB), Total Proteins (TP) and Albumin (ALB)). The algorithm result had been compared to FBI-4 results for same data.

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