

Automated diagnosis of liver disorder using multilayer neuro-fuzzy



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ABSTRACT

For the last couple of decades, diagnosis is performed by expert physicians who spend a year or two to understand the complex phenomena of an organ disorder. Still, the diagnosis is not robust and there are errors due to tiredness or complexity of the disease. Our objectives are to propose an automated framework for a liver disorder which is based on the methodology of neural network techniques and fuzzy logic approaches. Abnormality of the liver is measured in a patient through a series of blood and function tests. The symptoms in a patient direct our proposed framework to suggest the procedure for the diagnosis whether it may be liver function test or liver blood test. The proposed intelligent system generates the level of abnormality based on outcomes of 4 different tests that form the input of the liver blood test in our fuzzy system. Our results show that the proposed system is not only accurate but it provides a baseline for automated systems that are robust and provide objectivity in the diagnosis and reduce the human error.

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1. Introduction

Liver is a fundamental organ in a human body which is positioned at the right side of abdomen under human rib cage. It's a vital organ and its size is nearly equal to a football. Liver plays an important role in the functionality of human body. Its main function is to produce protein, digest food, glucose, maintaining cholesterol in blood and clear substance toxic. The main causes for liver disorder include use of alcohol, smoking, and intake of energy drink, unprotected sex, drugs injections and viruses. It can also be genetic (inherited). Viruses damage the liver through semen or blood, low quality water, or close interaction with an infected person. With the passage of time, the continuous damage results in cirrhosis, this may trigger liver failure, and results in liver cancer.

The concept of fuzzy logic (FL) emerged in 1965 with fuzzy set theory by Lotfi Zadeh (1965). Fuzzy logic explores the theory of probabilistic or valued logic (based upon many terms). It provides the reasoning of approximation rather than exact and

fixed reasoning. In other words, FL can have distinct values instead of fixed number of values. Just like binary sets theory (which consists of 0-1, true or false values), FL is also based on different values in the range from 0 to 1 and these are known as truth values. The advantage of these truth values is (which make it more reliable) that either it may be in complete true value range or it may be in complete false value range. That's the fundamental reason for fuzzy logic to be used in control theory and different intelligent systems.

FL is based on membership function which tells the range of a variable (how many times it comes in given set) (Zahra et al., 2017). These variables are based on different probability notions, known as "Probability Theory". The probability theory computes the probability of variables in a given set. Recently fuzzy systems are also used in medical sciences and help the specialists to assist and perform diagnosis of patients. Our main aim of this research is to design a fuzzy based system to help in the diagnosis of a patient and determine his/her disease by just entering the symptoms in this intelligent system.

Neural network is a combination of nodes which are highly interconnected. NN are generalizing from data or training patterns and have learning ability. NN can perform different pattern-matching task with faster algorithmic computation just like humans, while traditional machines are inefficient for

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performing these task. Non-model based system control, robotics, image processing and decision based systems are forms of pattern matching. NN have an ability to perform same information processing as our brain performs which make it more reliable and efficient system, like fuzzy logic decision system (Lin and Lee, 1991).

In this proposed system, a general concept of neural-network is used with fuzzy logic to make a control system. This proposed technique, fuzzy logic technique is combined with the idea of feed-forward multilayer an NN structure, which make control system super-efficient with learning abilities that are integrated with NN based fuzzy logic.

This decision network automatically train itself with learning ability when it is integrated with FL. Different nodes are used in this system, some nodes are for input and some are for output which gives the control at the decision signal. Some nodes are working as rules and MF's and these nodes are resided in hidden layer. At input layer (in general) have u input nodes for n patterns of input. Diagnosed class nodes are composed at output layer.

1.1. Diseases of liver

Cirrhosis: In cirrhosis scar tissues take the place of healthy tissues of liver (soft tissues are replaced by hard scar tissues). Scar tissue functionality is such that it stops the blood flow in liver that causes the liver function to slow down. Different possibilities are presented below that can form the causes of liver dieses "Cirrhosis" (Lin and Lee, 1991; Yim and Lok, 2006), as describe in Fig. 1.

1. Alcoholic diseases: When the metabolism is fast, carbohydrates and proteins are blocked, it affects the liver normal functions. This affect is known as "Alcohol Injuries".
2. Chronic Infection: Inflation and liver damage is due to hepatitis (A, B, C, and D) that can cause for "Chronic Infection".
3. Fatty Liver: Due to obesity and diabetes, normal functions of Liver are affected which cause the "Cirrhosis".
4. Hemochromatosis: Iron disposition and excessive absorption is the cause of disease known as "Hemochromatosis".
5. Inherited Diseases: Some diseases are spread from family to family and nation to nation, such as deficiency of "Alpha-1 antitrypsin". Glycogen, Wilson and Cystic Fibrosis are known as inherited diseases.

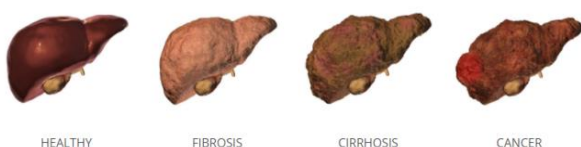


Fig. 1: Liver disorder stages

2. Fuzzy rule-based system

Just like If-Then rule theory in programming, FL also based on rules known as "Linguistic Rules". General representation of FRBS is "IF X then Y". Here X is premise variable and Y is rule consequence and in combine form they both known as "Linguistic Variables" (Zahra et al., 2017). Because of that nature "If-Then", FL has a capability to precise data like a human thinking and maintains its focus at decision related information.

2.1. Fuzzy inference engine

The procedure of formulate mapping of output according to input is known as fuzzy inference in FL. Based on these mapping, decisions are made for system. FIE is consists of three things: 1) MF's, 2) logical operations (min-max) and 3) rules (If-Then). FIE can be implemented with two different toolboxes known as Mamdani and Sugeno. These two types have different determination method from input to output (Tavill, 2001; Amitrano et al., 2000). It has a nature of multidisciplinary, so it can be associated with fuzzy modeling, FRBS, FL controllers, associative memory of fuzzy, expert systems based on fuzzy, and even for both ambiguous and simple approach fuzzy system.

Now a day, fast fuzzy inference systems (FFIS) are used to optimize the implementation of FIE and made it portable. FFIS is supportable in both Takagi-Sugeno and Mamdani model.

2.2. Fuzzy logic control system (FLCS)

This system is also known as "Fuzzy Diagnostic System" and is based on FL. FLCS analyze the logical operators as input values in the form of continuous values in between range of 0-1 (Zahra et al., 2017; Amitrano et al., 2000; Ozyilmaz and Yildirim, 2003; Neshat et al., 2008; Gonçalves et al., 2006; Dragulescu and Albu, 2007). This computation scheme makes this control system a "mathematical system" and design of error and trial methodology makes it as an "empirical method". This system performs the following functionalities:

- Arrange fuzzy set input
- Arrange documentation which consists of specification of system's specification, input and output of system.
- Rule set
- Declaration of defuzzification method.
- To validate system, run the requirement test suite.

3. Proposed system structure

The purposed system is a mixture of fuzzy and expert system which turns its nature into hybrid system nature known as "Fuzzy Expert". This system consists of "Knowledge Base" and "Decision Evaluator" which is further control by "Decision

Making Unit". DE consists of four steps (symptoms, fuzzification, DMU and defuzzification) and itself take the input from the KB. The general description of system is shown in Fig. 2 and whole process is

shown in Fig. 3, and Fig. 4. The Proposed Liver Diagnosis based fuzzy system LFT Layer shown in Fig. 5.

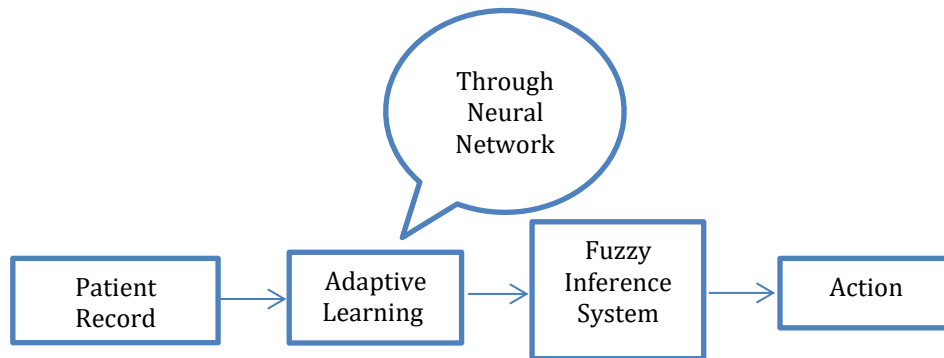


Fig. 2: General structure of proposed diagnosis control system based on multilayer functionality of fuzzy logic and neural network

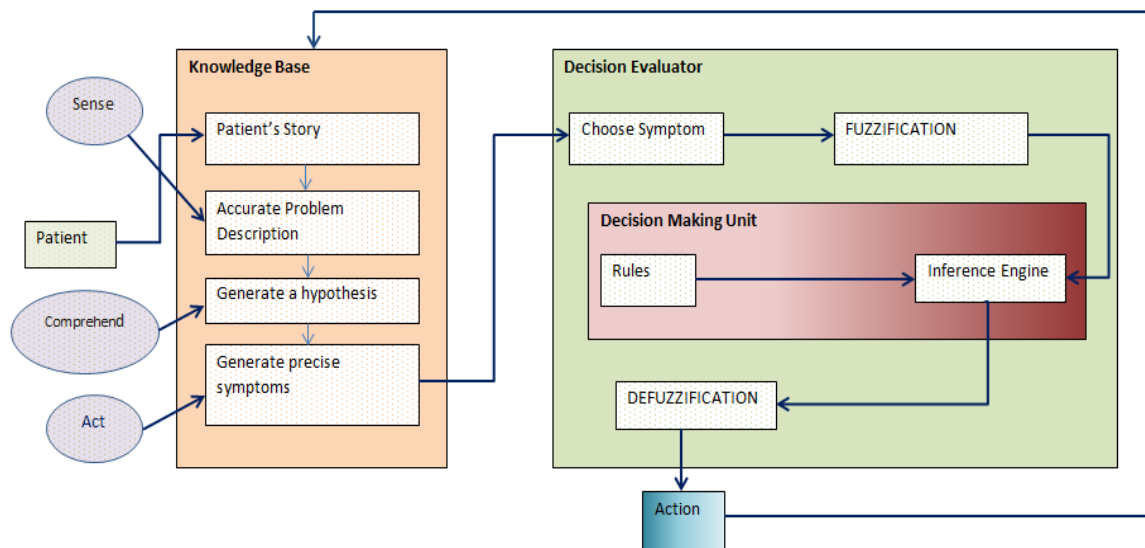


Fig. 3: Proposed diagnosis control system based on ANFIS (Multilayer functionality of Fuzzy Logic)

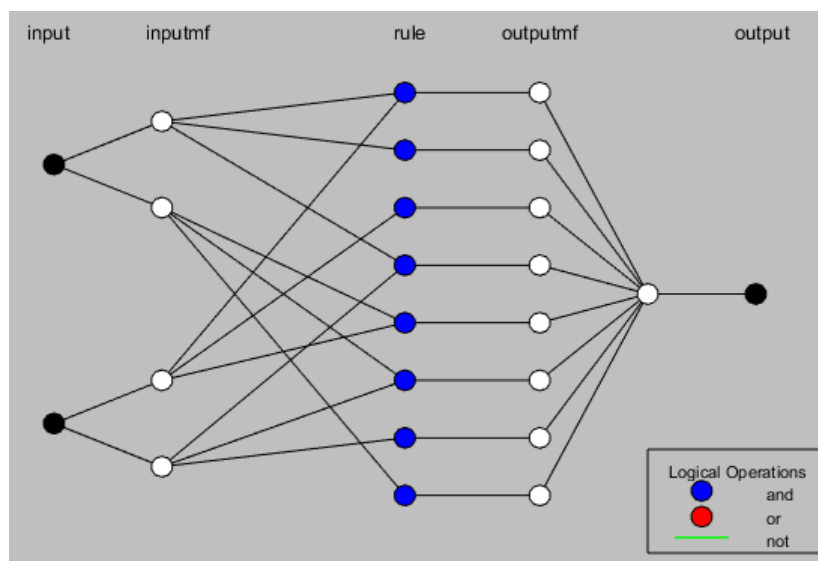


Fig. 4: Proposed multi-layered liver diagnosis in detailed based on ANFIS

This system is working for "Liver Disorder Diagnosis" based on "Liver Function Test" (LFT) and "Liver Blood Test" (LBT) and generates the liver

abnormality in terms of three parameters, high, medium and low abnormalities. This section of paper define the intelligent system based on ANFIS process

model with is implemented in MATLAB by using the simulation of fuzzy techniques. First part of system is description of input, output variables which are used in fuzzy system. At next step membership functions are defined for all the variables. In second step output variables are defined with membership function. Then next session describe the fuzzy system rules, process of fuzzification, and defuzzification.

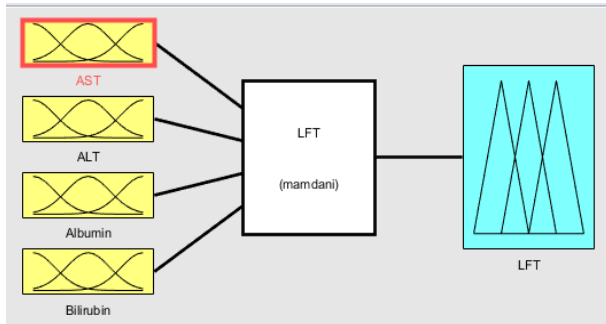


Fig. 5: Proposed liver diagnosis based fuzzy system LFT layer

3.1. Expert personal

To design an expert system we use the knowledge of expert personal, (Liver Consultant) that have skills and experienced in the specific field. In past, unfortunately the knowledge of expert personal was unavailable or unknown to others. May be expert personal solved problems are remain unsolved for others or he/she can provide most efficient results and solution for the particular case (liver disorder diagnosis). To keep in mind that point we design a knowledge base which can help other personals by maintain a relationship between the diagnosis and expert suggestions. By adding the cognition (sense, comprehend and act) this system generate automated and more accurate results.

3.2. Input variables

3.2.1. Liver function test (LFT)

LFT are used to check the liver health by determine the protein levels, enzymes range and existence of bilirubin in blood. Many tests are available for determining the functionality of liver but issue is that the overall liver performance is doesn't calibrate by most of them. Most commonly test that are preferred by doctors are 1) Alanine transaminase test (ALT), 2) Aspartate aminotransferase test (AST), 3) Albumin test, 4) Bilirubin test, 5) Alkaline phosphatase test (ALP), 6) international normalized ratio (INR) and 7) Platelets (PLT) [ss3].

Our intelligent system is based on first four tests respectively. The detail of these test are as follow:

Alanine transaminase test (ALT)

Metabolize protein in body is checked by ALT. ALT is released into blood when liver is not

function/working properly. Improper working is the cause to increase ALT level. If the value is increase with the given range of values then that increase value will damage the liver. As per the Mayo Clinic report range of ALT is among 7 to 55 units per liter (7-55 U/L).

```
if given_value > range
    "liver damage"
else
    "no issue means no damage"
// ALT Condition
```

Aspartate aminotransferase test (AST)

AST is based on particles known as enzyme which reside in different body parts, even in muscles and heart too. Doctors check AST for liver problem with ALT because levels of AST are not distinct for liver disorder. Doctor use ratio of AST with ALT in diagnosis. If the liver is damaged or generate high values, then AST and make a bad effect at muscles and livers. AST normal range is among 8 to 48 U/L.

```
if given_value > range
    "AST in blood stream"
else
    "no health issue "
// AST Condition
```

Albumin test

Our liver produce a main protein known as albumin, and albumin performs a lot of main function of body. Such as 1) fluid leaking is stop by Albumin, 2) Tissues are nourished by albumin, 3) Allow/Preform movement of vitamins hormones and other useful particles in human body.

This test tells how the functionality of proteins that mention above are working properly or not if the generated value is lower than range it indicates range than liver is not working in proper manner. Albumin range lie from 3.5 to 5.0 and it measure in grams per deciliter (g/dL).

```
if given_value > range
    "Liver is not working properly"
else
    "Not mentioned"
// Albumin Condition
```

Bilirubin test

When red-blood-cells are breakdown, it generates a waste product known as bilirubin. This process is done by liver. Before going to stool it passes through liver. It not directly mentions the liver damaged level abnormality in blood. If generated value is greater than the given range that it indicates the functionalities of liver are not working properly. Range of bilirubin is 0.1 to 1.2. It also measures in milligrams per deciliter (mg/dL) like albumin; the only difference is it deals with milligrams whereas albumin is deal in grams.

```

if given_value > range
    "High level of abnormality in
    blood which case liver problem"
else
    "Not mentioned"
// Bilirubin Condition

```

Symptoms of LFT

There are some symptoms through which a patient should perform a LFT. If these symptoms are exist then they became the input of test layer. Following are the symptoms of LFT:

- Weakness
- Weight loss
- Jaundice (yellow skin and eyes)
- Vomiting
- Nausea
- Diarrhea
- Abdominal pain

Input variables of LFT

Liver blood test (LBT): The existence of abnormality in liver is evidence by LBT. Liver test are based on blood sample. Most commonly test that is preferred by doctors is "Aminotransferases", commonly known as AST/ALT.

Aminotransferases AST/ALT

As discuss earlier that aminotransferases are basically enzymes, which are found able in different tissues, liver, muscle's and they are part of metabolic process. Other name of ALT is Serum-Glutamic-Pyruvic-Transaminase (SGPT) and AST are Serum-Glutamic-Oxaloacetic-Transaminase (SGOT). ALT and AST are directly checked by blood sample. Range of AST is 10-40 U/L (units per liter) and ALT is 7-56 U/L (unit per liter).

Input Variables

AST/ALT Ratio: AST/ALT of LBT ratio is describe in Table 1, whereas input variables of LFT are define in Table 2 with their ranges, semantic sign and cutoff values which indicate if the generated/resulted value is small than 2; the condition is normal or if is more than 2 it show liver abnormality, and in medical term it shows alcoholic presence in liver. Membership functions of AST/ALT are triangular and trapezoidal as mention in Fig. 5.

Table 1: Layer-LFT input variables of LFT for proposed Liver diagnosis expert fuzzy system

Input Parameters	Ranges	Semantic Sign	Range / Cut off value
AST	$G_T > 47$	Danger	10 - 40 U/L
	$L_T < 48$	Normal	
ALT	$G_T > 53$	Danger	7 - 56 U/L
	$L_T < 55$	Normal	
Albumin	$G_T > 4.8$	Danger	3.5 - 5.0 g/dL
	$L_T < 5.0$	Normal	
Bilirubin	$G_T > 1.0$	Danger	0.1-1.2 mg/dL
	$L_T < 1.2$	Normal	

U/L = Unit per Liter, mg/dL = milligrams per deciliter, g/dL = grams per deciliter, G_T = Greater_Value, Less_Than_Value

Table 2: Layer-LBT input variables of LBT for proposed liver diagnosis expert fuzzy system

Input Parameters	Ranges	Semantic Sign	Range / Cut off value
AST	$G_T > 37$	Danger	10 - 40 U/L
	$L_T < 40$	Normal	
ALT	$G_T > 54$	Danger	7 - 56 U/L
	$L_T < 56$	Normal	

U/L = Unit per Liter, G_T = Greater_Value, Less_Than_Value

Symptoms of LBT

There are some symptoms through which a patient should perform a LBT. If these symptoms are exist then they became the input of test layer. Following are the symptoms of LBT:

- Malaise
- Fever
- Jaundice (yellow skin and eyes)
- Vomiting
- Nausea
- Itching
- Abdominal pain
- Fatigue

Output Variables: The design purpose of the system is to identify the abnormality level of liver as a disease. Our system output value lie in the range of 0 to 5 to representing abnormalities in three different levels; high, medium and low respectively. These fuzzy set output variables are named as high_abn, medium_abn and low_abn which are shown in the Table 3 with its ranges and fuzzy set membership functions shown in Fig. 4.

Table 3: Layer-LFT, Layer-LBT and output variables of proposed Liver diagnosis expert fuzzy system

	Range	Semantic Sign
Layer-LFT	AST-LFT	Danger
		Normal
	ALT-LFT	Danger
		Normal
	Albumin-LFT	Danger
		Normal
Layer-LBT	Bilirubin-LFT	Danger
		Normal
	AST-LBT	Danger
		Normal
	ALT-LBT	Danger
		Normal
Output Layer	Liver Disorder	No Liver Disorder
		Acute Liver Disorder
		Chronic Live Disorder
		Disorder

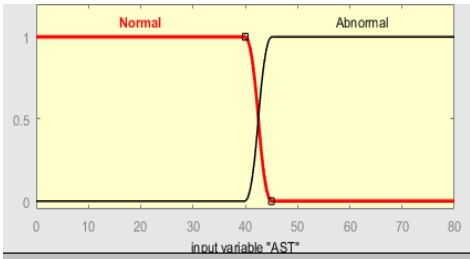
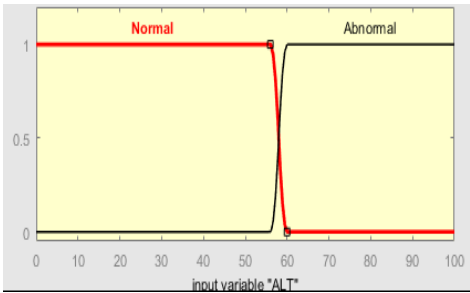
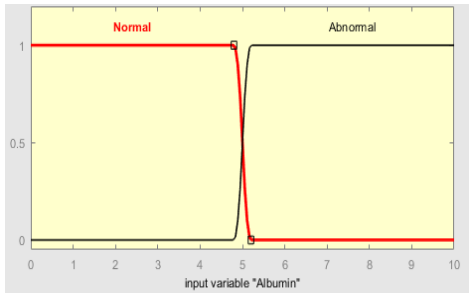
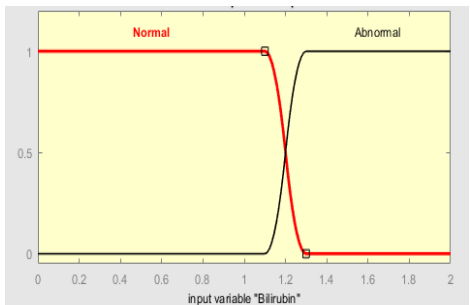
Membership function: The membership function of our intelligent system gives the mathematical function of input and output variables. These mathematical functions are defined in Table 4.

In FIS, rule based perform an important role at which input and output of desire system is based (Zahra et al., 2017). Following shows the proposed liver diagnosis Expert Fuzzy System Rules of layer-LFT and layer-LBT.

Rule surface of LBT and LFT of proposed Liver diagnosis Control System Based on Multilayer

functionality of Fuzzy Logic are defined in Fig. 6 and Fig. 7.

Table 4: Input membership functions of proposed Liver diagnosis expert fuzzy system

Sr. #	Input Variables	Membership Function (MF)	Graphical representation of μ
1	AST ($\mu_{AST(M)}$)	$\mu_{AST,N}(M) = \begin{cases} 1, & M \leq 57 \\ 1 - 2\left(\frac{M-40}{5}\right)^2, & 40 \leq M \leq 42.5 \\ 2\left(\frac{M-45}{5}\right)^2, & 42.5 \leq M \leq 45 \\ 0, & \text{and } M \geq 45 \end{cases}$	
		$\mu_{AST,AN}(M) = \begin{cases} 1, & M \leq 57 \\ 2\left(\frac{M-40}{5}\right)^2, & 40 \leq M \leq 42.5 \\ 1 - 2\left(\frac{M-45}{5}\right)^2, & 42.5 \leq M \leq 45 \\ 0, & \text{and } M \geq 45 \end{cases}$	
2	ALT ($\mu_{ALT(N)}$)	$\mu_{ALT,N}(N) = \begin{cases} 1, & N \leq 57 \\ 1 - 2\left(\frac{N-60}{3}\right)^2, & 57 \leq N \leq 58.5 \\ 2\left(\frac{N-57}{3}\right)^2, & 58.5 \leq N \leq 60 \\ 0, & \text{and } N \geq 60 \end{cases}$	
		$\mu_{ALT,AN}(N) = \begin{cases} 1, & N \leq 57 \\ 2\left(\frac{N-57}{3}\right)^2, & 57 \leq N \leq 58.5 \\ 1 - 2\left(\frac{N-60}{3}\right)^2, & 58.5 \leq N \leq 60 \\ 0, & \text{and } N \geq 60 \end{cases}$	
3	Albumin ($\mu_{Albumin(O)}$)	$\mu_{Albumin,N}(O) = \begin{cases} 1, & O \leq 4.8 \\ 1 - 2\left(\frac{O-5.2}{0.4}\right)^2, & 4.8 \leq O \leq 5 \\ 2\left(\frac{O-4.8}{0.4}\right)^2, & 5 \leq O \leq 5.2 \\ 0, & \text{and } O \geq 5.2 \end{cases}$	
		$\mu_{Albumin,AN}(O) = \begin{cases} 1, & O \leq 4.8 \\ 2\left(\frac{O-4.8}{0.4}\right)^2, & 4.8 \leq O \leq 5 \\ 1 - 2\left(\frac{O-5.2}{0.4}\right)^2, & 5 \leq O \leq 5.2 \\ 0, & \text{and } O \geq 5.2 \end{cases}$	
4	Bilirubin ($\mu_{Bilirubin(P)}$)	$\mu_{Bilirubin,N}(P) = \begin{cases} 1, & P \leq 1.1 \\ 1 - 2\left(\frac{P-1.1}{0.2}\right)^2, & 1.1 \leq P \leq 1.2 \\ 2\left(\frac{P-1.3}{0.2}\right)^2, & 1.2 \leq P \leq 1.3 \\ 0, & \text{and } P \geq 1.3 \end{cases}$	
		$\mu_{Bilirubin,AN}(P) = \begin{cases} 1, & P \leq 1.1 \\ 2\left(\frac{P-1.1}{0.2}\right)^2, & 1.1 \leq P \leq 1.2 \\ 1 - 2\left(\frac{P-1.3}{0.2}\right)^2, & 1.2 \leq P \leq 1.3 \\ 0, & \text{and } P \geq 1.3 \end{cases}$	

At the inference engine of proposed Liver diagnosis Ech layer. Figs. 6 and 7 show the De-fuzzification of proposed Liver diagnosis Expert Fuzzy System.

To generate simulation results, we use R2017a MATLAB tool. MATLAB is an efficient tool for data analysis, programming, computing and visualization. Following figures shows the result simulation of proposed Liver diagnosis Expert Fuzzy System. Lookup diagrams for LFT and LBT of proposed Liver diagnosis Control System Based on Multilayer functionality of Fuzzy Logic are define in Fig. 8 and their different values are define in Table 5 and Table 6. If AST = 29.8, ALT=36.6, Albumin= 3.2 and Bilirubin=1.07 then LFT generated value is 0.33. Table 5 contains different values of four parameters and as in result have corresponding LFT values.

Same as in Table 6, different generated values of LBT are defining with a set of input parameter values.

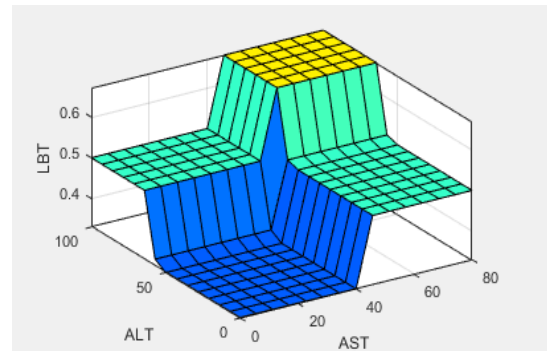


Fig. 6: Rule surface of LBT of proposed Liver diagnosis control system based on multilayer functionality of Fuzzy Logic

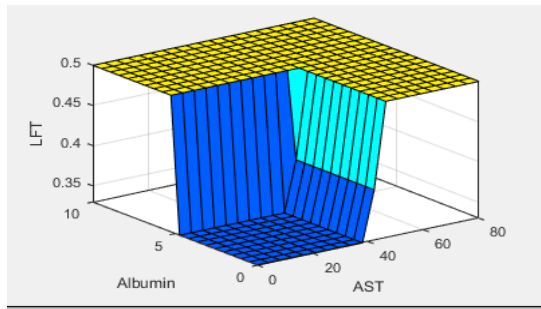


Fig. 7: Rule Surface of LFT of proposed Liver diagnosis control system based on multilayer functionality of fuzzy logic

For example if the value of AST=12.8 and ALT=13.2 then LBT generate 0.33 value in Result. And proposed system analysis is shown able in Fig. 8. Fig. 9 mentions the total number of epochs in x-axis (in our case 24 epochs) and mean-squared-error (MSE) at y-axis of the proposed multilayer diagnosis control system. The red color line shows the proposed multilayer diagnosis control system testing which converges at epochs 12 to get MSE at $10^{-2.02}$. Green color line represents the validation of proposed system; this line converges at epoch 17 with MSE at $10^{-3.07}$. The blue line curve represents the phase of training; it generates MSE 10^{-4} at Epoch number 22.

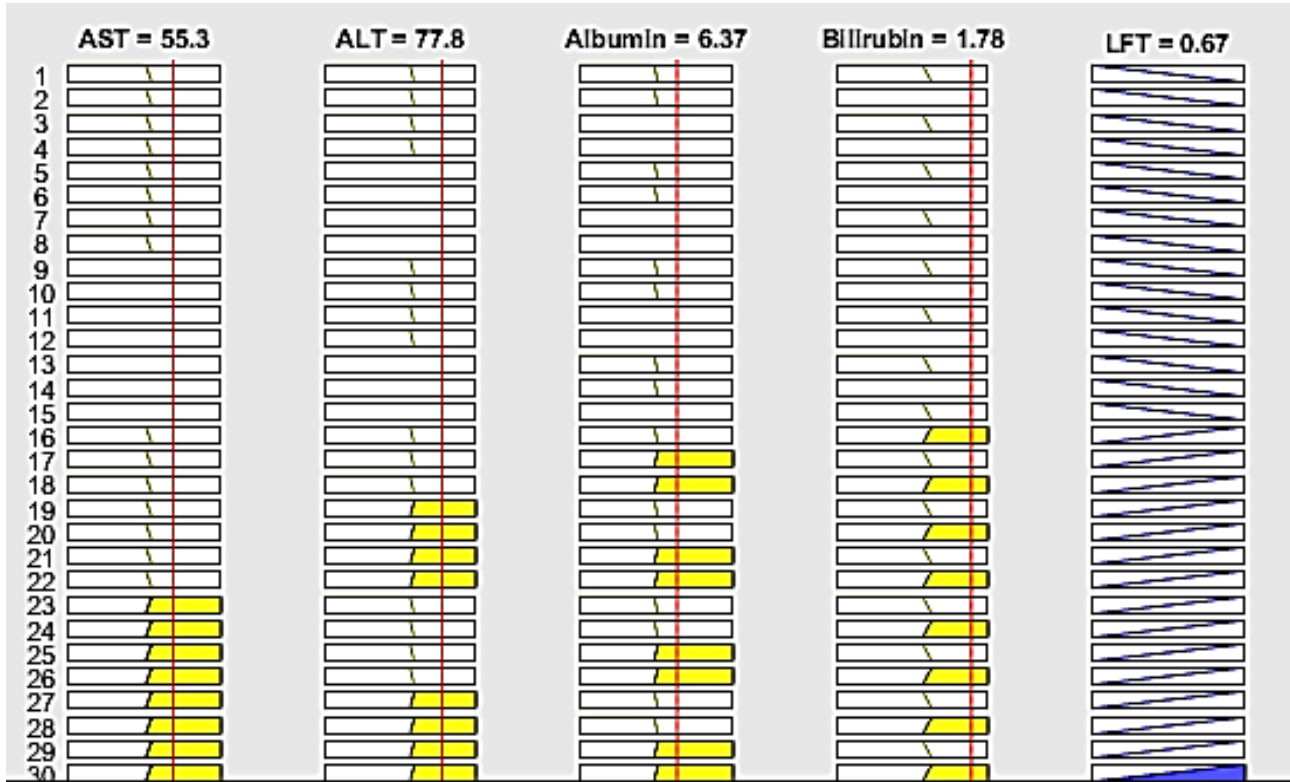


Fig. 8: Lookup diagram for LFT of proposed Liver diagnosis control system based on multilayer functionality of fuzzy logic

Table 5: Lookup diagram for LFT of proposed Liver diagnosis control system based on multilayer functionality of fuzzy logic

	LFT				Results
	AST	ALT	Albumin	Bilirubin	
1	5.44	50	5	1	0.432
2	5.45	41.6	059	0.119	0.33
3	27.3	15.3	1.89	0.681	0.32
4	7.25	21.6	2.33	1.17	0.362
5	16.3	27.8	3.14	1.16	0.346
6	17.8	31.6	3.45	1.18	0.386
7	23.3	39.1	4.44	1.27	0.499
8	29.3	44.1	5	1.24	0.492
9	32.8	47.2	5.43	1.28	0.5
10	43.3	60.3	6.55	1.57	0.636
11	46.8	60.4	6.57	1.57	0.67
12	8.75	70.9	7.55	1.77	0.5
13	74.3	92.2	8.79	1.42	0.67
14	72.8	67.2	2.52	0.356	0.5

Fig. 10 shows that Gradient of the proposed system is 0.000184, step size is 0.0042 when number of validation checks fail are 6 at epoch 24.

Table 6: Lookup diagram for LBT of proposed Liver diagnosis control system based on multilayer functionality of fuzzy

Sr. No.	LBT		Results
	AST	ALT	
1	12.8	13.2	0.33
2	20.2	57.7	0.398
3	44.4	57.7	0.539
4	57.6	69.5	0.67
5	73.8	6.82	0.5
6	12.8	73.2	0.5

Fig. 11 shows the validation data set through ANN by doing a comparison between predicted and experimental models. Fig. 11 also shows the proposed system residues graph by whole available data set points used in ANN. For example, available data set is used for testing, validation and training. For training 70 % of data set is used, for validation 15 % of data set is provided and for testing purpose 15 % data set is used. It is examining during testing, validation and training that predicted and

experimental values are extremely tie in $R=1$, $R=1$, and $R = 0.99$ respectively. It also examines that

overall proposed system is extremely correlated with the value $R= 0.91$.

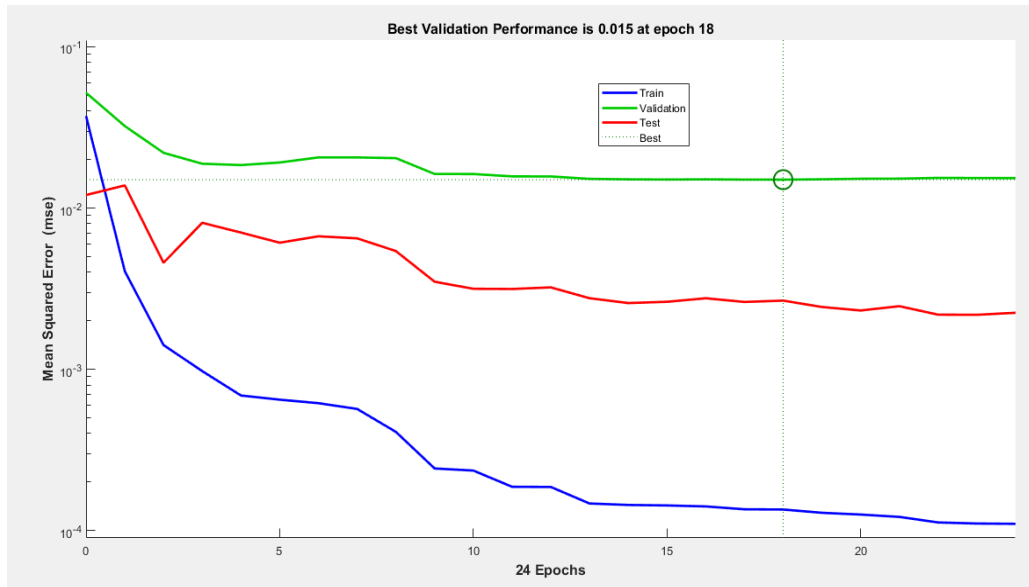


Fig. 9: Mean squared error (MSE) vs. number of epochs for proposed multilayer diagnosis control system based on ANFIS

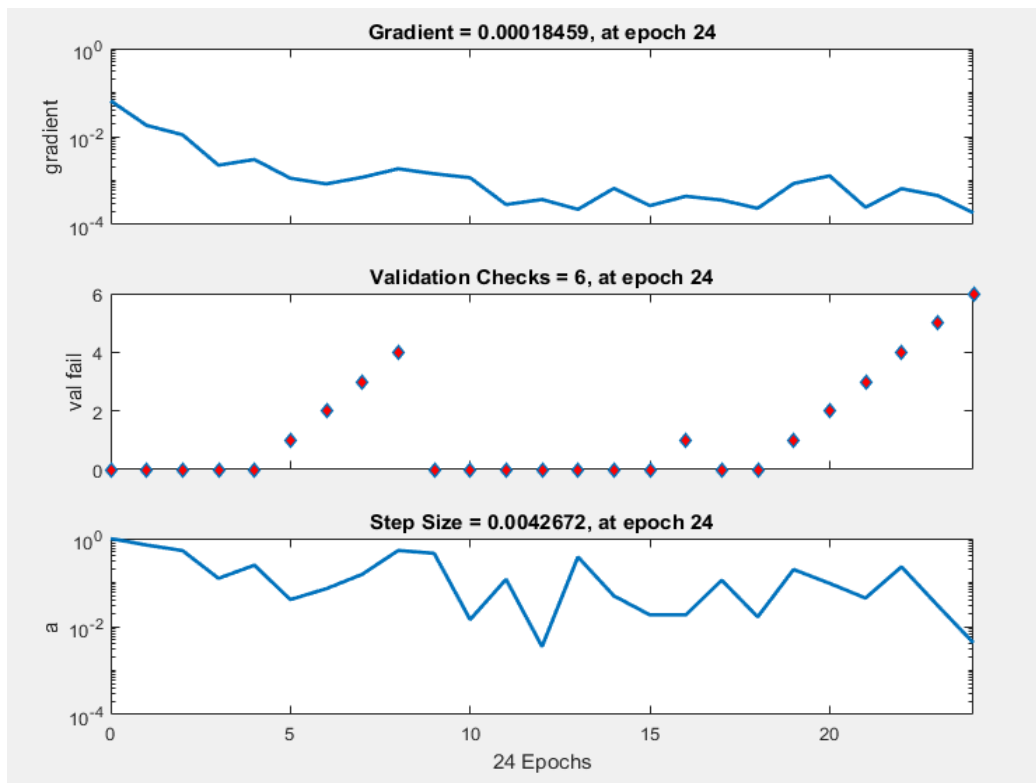


Fig. 10: Result details of diagnosis control system based on ANFIS

Fig. 12 shows the final layer rule surface of the proposed system. It observed that when LBT and LFT both are Normal then No Liver Disorder. In case of Acute Liver Disorder one i/p symptoms is normal and 2nd is danger. But both i/p variables are danger then Chronic Liver Disorder.

4. Conclusion

In this article, proposed a new expert system based on fuzzy system with NN high potential points to detect liver disease. The proposed model of

diagnosis liver disorder can be extendable for any new test as input which is recommended by the doctors. Even we can define the same system structure for hepatitis with just changing in input and output variables. The proposed system carried out fuzzy logic art to diagnosis liver disorder which makes our proposed system into expert control system. The improvement is that our proposed system diagnosis accuracy is 96 %. This expert system appoints the disorder intensity rate, which made it more accurate and complete in diagnosis.

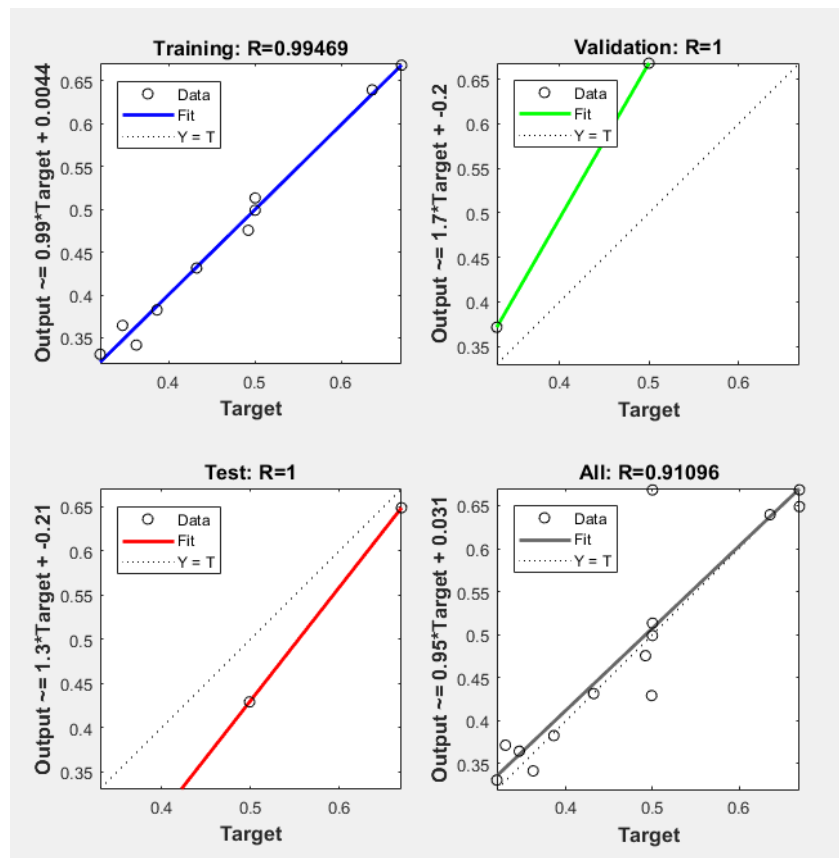


Fig. 11: Scatter plot of observed versus predicted values for proposed system; the fitted line represents the linear regression between observed and artificial neural network (ANN)-predicted values

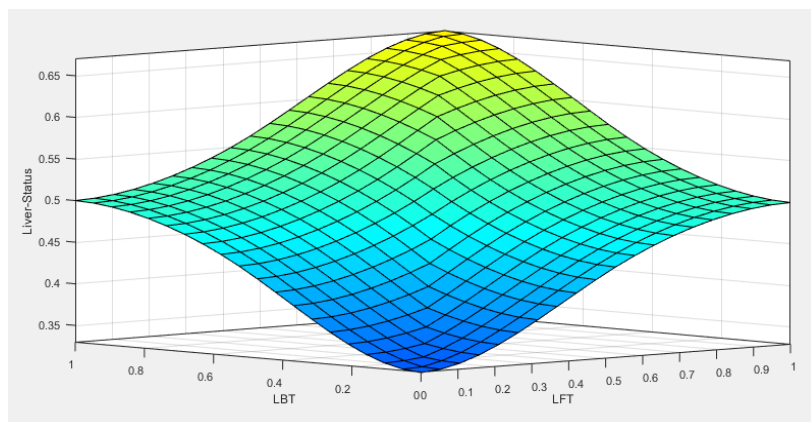


Fig. 12: Final layer Rule Surface of proposed Liver diagnosis control system based on multilayer functionality of fuzzy logic

Compliance with ethical standards

Conflict of interest

The authors declare that they have no conflict of interest.

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