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A Hybrid Fuzzy-GA Approach Applied to an Expert System for Diagnosis of Liver Tumor

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***Abstract*— Applications of soft computing techniques have been concentrated for management of the uncertainty associated to the medical diagnosis, in the recent decade. This article presents a Fuzzy Expert System (FES) for diagnose of metastasis in the liver which is one of the most common malignant hepatic tumors. Furthermore, the proposed FES has been optimized using a hybrid Fuzzy-GA approach. The purpose of the hybrid Fuzzy-GA approach is to optimize the membership function parameters of the FES to enhance the trades-off between accuracy and interpretability of the FES. To experiment the proficiency of the hybrid Fuzzy-GA model, performance of the system was evaluated with a real dataset of patients collected from the Noor Medical Imaging Center in Tehran. The FES performance was compared to the diagnosis of specialists before and after optimization with the Fuzzy-GA method. The results demonstrate that proposed system has high capability in the diagnosis of metastasis in liver. The hybrid Fuzzy-GA approach for hepatic tumors diagnosis is promising to assistant the specialists for early diagnosis of this type of cancer and saving more human lives.**

***Keywords*— Soft computing, Fuzzy inference system, Fuzzy-GA, Genetic Algorithm, Hepatic metastasis, Computer aided medical diagnosis.**

I. INTRODUCTION

Fuzzy systems have high capability to manage uncertainties in the input of the system as well as their inference process. These systems are useful in the design of the medical systems and other diagnosis systems. The medical practices are associated with uncertainties. The main sources of uncertainty associated to the medical diagnosis are summarized as follows [16]:

1) *Inter-uncertainty: between physicians in diagnosis of a common case*
2) *Inter-uncertainty: of a specialist for the same case in different circumstances*
3) *Imprecision of numbers obtained from the measurement instruments*
4) *Low quality of information acquired from their sources such as resolution of the images provided by imaging devices*

Fuzzy systems are very practical in the design of the systems with abovementioned uncertainty source. The fuzzy inference is conducted using linguistic terms and rules. Thus, fuzzy reasoning is highly understandable and the system decisions provide a great amount of certainty.

This work proposes a fuzzy inference system for diagnosis of metastasis in the liver. Metastasis is a kind of malignant hepatic tumors that is mostly common in Hepatic patients. There are different ways to diagnose hepatic tumors [1]:

1) *Abdominal Ultrasound*
2) *Biopsy from liver, blood test for the examination of hepatic enzymes*
3) *Magnetic resonance imaging (M.R.I) from liver*
4) *Measurement of blood’s alpha image-proteins*
5) *Diagnosis of liver lesion using Computed tomography (CT) scans images*

In this study, an expert system for medical diagnosis of hepatic metastasis using the information provided from the CT scan images of the liver has been proposed. In these images, hepatic metastasis is demonstrated as solid tumors. In the CT scan images, after the injection of contrast agent, this material gradually enters the tumor at a period of less than 15 minutes and then moves to the center and surrounding area of the whole tumor. The next section provides a brief overview of the current related works.

In this paper, a hybrid Fuzzy-GA model has been proposed for detection of metastases in the liver with a new idea of improving the trade-off between accuracy and interpretability using the information obtained from the CT scan images collected from medical imaging center in Tehran.

II. REVIEW OF RELATED WORKS FOR DIAGNOSIS OF LIVER DISEASES

Current advances related to the applying intelligent models for diagnosis of liver disease are presented in this section. Then it follows by an overview of the optimization techniques applied to the intelligent systems designed for diagnosis of the liver diseases.

A. *Review of intelligent systems presented for diagnosis of the liver disease*

Fuzzy inference system has been concentrated as an intelligent expert system for medical diagnosis in various applications including leukemia, breast and lung cancer diagnosis [2]-[3], in the recent decade. However, a few studies have been conducted for hepatic metastasis diagnosis.

A fuzzy expert system for assessment of the risk of liver cancer, Hepatocellular carcinoma (HCC), was proposed in [4]. This system includes the fuzzy variable of the Alpha-fetoprotein (AFP) input, tumor degree, tumor size, lymph nodes, and albumin, and it considers the risk of getting liver cancer type (HCC) in the output.

The accuracy of this system was not investigated and reported on real patients. Another fuzzy expert system to diagnose of hepatic diseases was presented in [5]. The inputs of this system are Serum glutamic-pyruvic transaminase (SGPT), Serum Glutamic-Oxaloacetic transaminase (SGOT), Alkaline phosphatase (ALP), Mean corpuscular volume (MCV), Gamma GT (Glutamyl transpeptidase), and Drink, and the output is differentiating patients into two classes of healthy and unhealthy. In this system, the type of the disease was not reported. The accuracy of this system is 91%. An automatic computer aided diagnosis for hepatic tumors in the CT scan images was presented in [6]. The output of the system determines two types of the HCC and Hemangioma tumors. The accuracy of this system was reported as 96.7%. A neural network method for hepatic tumors tissue analysis in the CT scan images was reported in [7]. This is an automatic CAD system that diagnoses Hepatodenoma (HA), Hemangioma, HCC, Colangiocarcinema (CC) in the output. The differential diagnosis of hepatic focal lesions through CT-scan images based on the categorized group was proposed in [8]. This CAD system automatically diagnoses the hepatic lesion. It also uses the neural network to classify the outputs into five classes. The average accuracy of five categories in this system was reported as 73.356%. A fuzzy expert system and an MLP neural network were designed by the authors in [15]. Accuracy of the FES was 93.5% and for the neural network was 91% for diagnosis of the hepatic metastasis.

In this paper, a Mamdani fuzzy inference system has been designed, with a new idea of improving the trade-offs between accuracy and interpretability for the detection of metastases in the liver using the information obtained from the CT scan images. The main difference of the proposed system with other systems reviewed in this section are using Mamdani inference model which provides the capability to manage uncertainty in the input and reasoning of the system. In addition, the inputs and outputs of the system are obtained from the information in the reports provided after taking a liver CT scan images from patients. Furthermore, this work utilizes the evolutionary nature of the genetic algorithm to optimize the fuzzy system parameters and consequently improves overall performance of the fuzzy system.

B. *Review of the optimization techniques applied to expert systems for diagnosis of the liver disease*

This section reviews related works have been proposed for optimization of fuzzy expert system. A general fuzzy system was designed for classification of the medical datasets in [9]. Accuracy of this system for medical data classification was 92.93%. This system uses the genetic algorithm for optimization of the rule set of the system. A decision support system was designed in [10]. Evolutionary strategy used to develop learning-based decision, and to improve the efficiency of learning based on a genetic optimization algorithm. This system was applied on 5 medical datasets of breast cancer and liver fibrosis, and the accuracy of system before the optimization for Self-organizing map (SOM) and Probabilistic neural network (PNN) methods were 71.61% and 57.85% and average accuracy of system after the optimization by GA was 96.92%. An invasive weed optimization algorithm for liver CT scan clustering was proposed in [11]. This system uses the K-mean method in [11]. The accuracy of the system after optimization was 87%. The system proposed in [12], uses the genetic algorithm for optimizing rule set of the fuzzy system for medical data classification. The goal of optimization was to increase accuracy of the fuzzy system by improving rule set. This system was applied to the Indian liver disorder dataset, accuracy of system after optimization was 75.21%.

A feature selection method based on particle swarm optimization for liver disease was proposed in [13]. Optimization was performed with the purpose of increasing the performance and accuracy of the system. Accuracy of system on training set and testing set after optimization was 100% and 97.9%.

III. THE PROPOSED FUZZY INFERENCE SYSTEM FOR DIAGNOSIS OF THE HEPATIC METASTASIS

The structure of a fuzzy system demonstrated in Figure 1 a fuzzy inference system consists of the following components [14]:

1) *Fuzzifier*

The inputs of a fuzzy system are numeric inputs associated with uncertainty. The fuzzifier produces membership values related to certain input numbers.

2) Inference engine

It provides the fuzzy reasoning using rules. The output of inference engine is a fuzzy set.

3) *Defuzzifier*

The result of a fuzzy inference process is a fuzzy set. In fact, defuzzifier accepts the input as a fuzzy set and in the output it produces the real number.

In this study a fuzzy inference system has been designed to diagnose hepatic metastasis through the information collected from radiologist reports on the CT scan images. The input and output variables have been modeled using fuzzy membership functions. This system includes five fuzzy input variables and a fuzzy variable in output. Fuzzy input and output variables are described in the TableI. The Mamdani inference model was implemented.

The rest of this section presents the implementation details of the fuzzy inference system designed for diagnosis of the Hepatic Metastasis tumor.

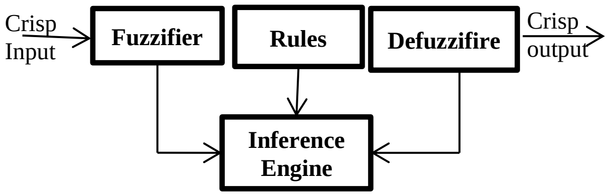

Fig.1.The structure of a fuzzy inference

TABLE I
FUZZY INPUT AND OUTPUT VARIABLES

Fuzzy variables	**Input/output**	Definition
Lesion size	Input	The size of hepatic lesion that can be distinct in CT scan photos should at least be 0.4 mm.
Effect on lymph node	Input	Lymph nodes are oval shape organs that control the proper function of immune system.
Contrast effect	Input	This variable observes the percent of the penetration of contrast in the existed lesion, from the images. If the amount of contrast penetration is low the lesion can be a hepatic metastasis.
Liver size	Input	Change the size of the liver can be a sign of the liver cancer
Effect on thickness kidneys	Input	With the release and growth of tumors in the liver, the change is in the liver size can affect the kidneys thickness.
Metastasis tumor	Out put	the risk of development of the hepatic metastasis tumor

Fuzzy sets and linguistic terms of input and output variables are defined for liver metastasis diagnosis fuzzy system are represented in Tables II to VII.

TABLE II
LINGUISTIC TERM AND FUZZY SETS OF THE VARIABLE LESION SIZE

Variable name: Tumor size	
Intermediate	$X \leq 2cm$
Intermediate or high	$2cm \leq X \leq 5cm$

TABLE III
LINGUISTIC TERM AND FUZZY SETS OF THE VARIABLE LESION SIZE

Variable name: Effect on lymph node	
Intermediate	$1mm \leq X \leq 2mm$
Intermediate or high	$2mm \leq X \leq 6mm$
High	$X > 6mm$

TABLE IV
LINGUISTIC TERM AND FUZZY SETS OF THE LIVER SIZE

Variable name: Liver size	
Small	$X \leq 7cm$
Normal	$7cm \leq X \leq 10.5cm$
major	$X > 10.5$

TABLE V
LINGUISTIC TERM AND FUZZY SETS OF THE CONTRAST EFFECT

Variable name: Contrast effect	
Very low	$X \leq 0.1$
Low	$0.1 \leq X \leq 0.25$
Intermediate	$0.25 \leq X \leq 0.5$
High	$0.5 \leq X \leq 1$

TABLE VI
LINGUISTIC TERM AND FUZZY SETS OF THE THICKNESS KIDNEYS

Variable name: Effect on thickness kidneys	
Normal	$2.5cm \leq X \leq 3cm$
Low	$X \leq 2.5cm$

TABLE VII
LINGUISTIC TERM AND FUZZY SETS OF THE METASTASIS PROBABILITY

Variable name: Metastasis tumor	
Very low	$Y \leq 0.1$
Low	$0.1 \leq Y \leq 0.25$
Intermediate	$0.25 \leq Y \leq 0.5$
High	$0.5 \leq Y \leq 1$

The rules of the fuzzy inference system for diagnose of hepatic metastasis are represented in Table 8. Rules were collected using the knowledge of radiologist and through interviewing with the guidance of a radiologist in the Noor Imaging Centre in Tehran, consulting with a gastroenterologist, and also studies have been done about how contrast affect hepatic lesions.

TABLE VIII

THE FUZZY RULES FORHEPATIC METASTASIS DIAGNOSIS

1	If (tumor-size is small-size) and (effect on lymph-node is intermediate) and (female-_liver-size is normal) and (effect on thickness-kidney is normal) and (contrast-effect is very low) then (metastasis tumor is very-low)
2	If (tumor-size is small-size) and (effect on lymph-node is high) and (female-_liver-size is small) and (effect on thickness-kidney is normal) and (contrast-effect is low) then (metastasis-tumor is high)
3	If (tumor-size is small-size) and (effect on lymph-node is high) and (female-_liver-size is major) and (effect on thickness-kidney is normal) and (contrast-effect is low) then (metastasis-tumor is high)
4	If (tumor-size is small-size) and (effect on lymph-node is intermediate) and (effect on thickness-kidney is normal) and (contrast-effect is very low) and (mail-liver-size is normal) then (metastasis-tumor is very-low)
5	If (tumor-size is small-size) and (effect on lymph-node is high) and (effect on thickness-kidney is normal) and (contrast-effect is low) and (mail-liver-size is small) then (metastasis-tumor is high)
6	If (tumor-size is small-size) and (effect on lymph-node is high) and (effect on thickness-kidney is normal) and (contrast-effect is low) and (mail-liver-size is major) then (metastasis-tumor is high)
7	If (tumor-size is intermediate-size) and (effect on lymph-node is high) and (female-_liver-size is small) and (effect on thickness-kidney is normal) and (contrast-effect is low) then (metastasis-tumor is high)

The following parameters have been used in the design of the inference engine and defuzzification of the fuzzy system for diagnosis of the hepatic metastasis.

Defuzzification: Centroid

And operator: Minimum

Or operator: Maximum

T-norm operator: Product

S-norm operator: Maximum

The sources of the uncertainty in the input variables for diagnosis of the liver metastasis are managed through the fuzzy sets associated to input and output variables and the overlaps between the associated fuzzy membership functions. The proposed FES utilizes the Mamdani fuzzy inference model with the capability of managing uncertainty in the knowledge of expert during the fuzzy reasoning process.

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IV. THE PROPOSED HYBRID FUZZY-GA APPROACH FOR OPTIMIZATION OF FUZZY SYSTEM FOR DIAGNOSIS OF HEPATIC METASTASIS

This section explains the proposed hybrid Fuzzy-GA method applied to parameter optimization of fuzzy system for diagnosis of the hepatic metastasis tumor. This study takes advantages of the evolutionary nature of the GA through implantation of the selection, crossover and mutation to keep the exploration and exploitation behaviors in multi-dimensional problem space. It also employs the meta-heuristic derivative-free random search in states space to find the optimum solution. Genetic algorithm is one of the commonly applied methods in soft computing paradigm for optimization of the database or rule base of a fuzzy system. The hybridization improves the static deficiency of the fuzzy systems to adapt and learn from the environment.

In this study, Genetic algorithm was used for optimization of the database of fuzzy expert system. The purpose of this work is optimization of fuzzy expert system database including membership function parameters using Genetic algorithm for diagnosis of the hepatic metastasis. For this, the hybrid Fuzzy-GA approach is applied to improve the accuracy, flexibility, performance of the fuzzy system. The steps of the proposed hybrid fuzzy-GA approach are described in Figure 2.

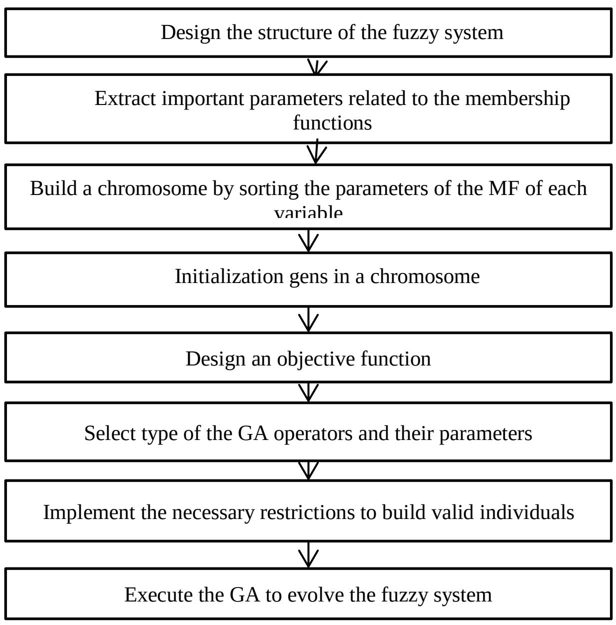

Fig.2. Flowchart of the proposed hybrid Fuzzy-GA approach

This work utilizes a hybrid Fuzzy-GA approach to optimize the fuzzy expert system for diagnosis of the Hepatic metastasis. For this, membership function parameters have been represented as gens in a chromosome. The initialization of the genes was performed using the knowledge of medical experts. The proposed Fuzzy-GA algorithm is described in the following steps:

1) *Design the structure of fuzzy system:*

This includes selecting input and output variables, and the type of membership functions (MF) and fuzzy rules for the fuzzy inference systems (FIS), using the details provided in Section 3. For the FIS for diagnosis of the Hepatic metastasis tumor, the system has 5 fuzzy inputs and one fuzzy output variable. The types of the MFs have been considered Gaussian as described in Tables 2 to 6 and the rules are described in Table VIII.

2) *Chromosome representation*

Construct a chromosome by sorting the parameters of the MF of each fuzzy variable. Chromosome is formed according to the number of linguistic terms related to each fuzzy variable. In the proposed Fuzzy-GA approach for the Hepatic tumor diagnosis, chromosome includes 48 genes consisting of the Gaussian membership function parameters related to the linguistic terms of fuzzy variables systems.

3) *Chromosome initialization*

Gens of the chromosome are initialized with the value of the MF parameters.

4) *Design a fitness function*

An evaluation function is needed to verify fitness of each chromosome in a population. In this study, fitness function for evaluation was considered as mean square error (MSE) to compare the results of the FES to the real diagnosis.

5) *Select the parameters of GA operators*

Genetic algorithm uses the genetic operator such as crossover, mutation and selection in each generation to build chromosomes for the next generation. Each operator is applied with a probability. The GA operators have been selected for the proposed Fuzzy-GA for diagnosis of Hepatic metastasis is shown in Table 9. The crossover and mutation probabilities have been heuristically selected as shown in Table 10.

6) *Implement the necessary restrictions*

To building valid individuals such as lower and upper bounds of the variables.

7) *Execute the genetic algorithm to evolve the fuzzy system*

In this part the genetic algorithm attempts to optimize the membership function parameters of the fuzzy system and produces optimal parameters by passing through several generations of the GA.

V. EXPERIMENTAL RESULTS AND PERFORMANCE EVALUATION OF THE HYBRID FUZZY-GA APPROACH

Fuzzy inference system of hepatic metastasis was designed using fuzzy logic Toolbox in MATLAB. The fuzzy system was evaluated using 100 real dataset of patients obtained from Noor Medical Imaging Center. For the evaluation purpose, the mean square error was used as performance measure. The applied genetic operators are presented in Table IX.

TABLE IX

GENETIC ALGORITHM OPERATORS

Operators	Function
Crossover	*Scattered*
Mutation	*Uniform*
Selection	*Uniform*

TABLE X

DEFFERENT MUTATION AND CROSSOVER RATE

Crossover rate	0.80	0.86	0.86	0.95	0.9
Mutation rate	0.001	0.007	0.01	0.001	0.001
MSE	0.012	0.013	0.013	0.019	0.009

In the Genetic algorithm cross-over rate is usually selected more than 0.5 and Mutation rate is less than 0.2. To choose these parameters, the system accuracy has been investigated through implementation of genetic algorithm with different mutation and cross-over rates, as shown in Table 10. Crossover and mutation rates for the Hepatic metastasis system were selected 0.9 and 0.001, respectively. After performing hybrid Fuzzy-GA approach with these parameters, the error of the system has reached to 0.009.

Genetic algorithm stopping criteria in this system was considered as average cumulative changes in the value of the fitness function over Stall Gen Limit generations. The GA was converged after 341 generations. Figure 3 shows the progression of Genetic algorithm through different generations.

Membership functions of the input and output variables of the fuzzy system before optimization and after GA optimization are shown in Figures 4 and 5.

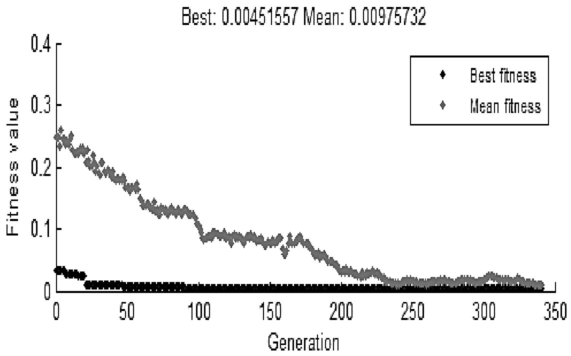

Fig.3. Progression of genetic algorithm

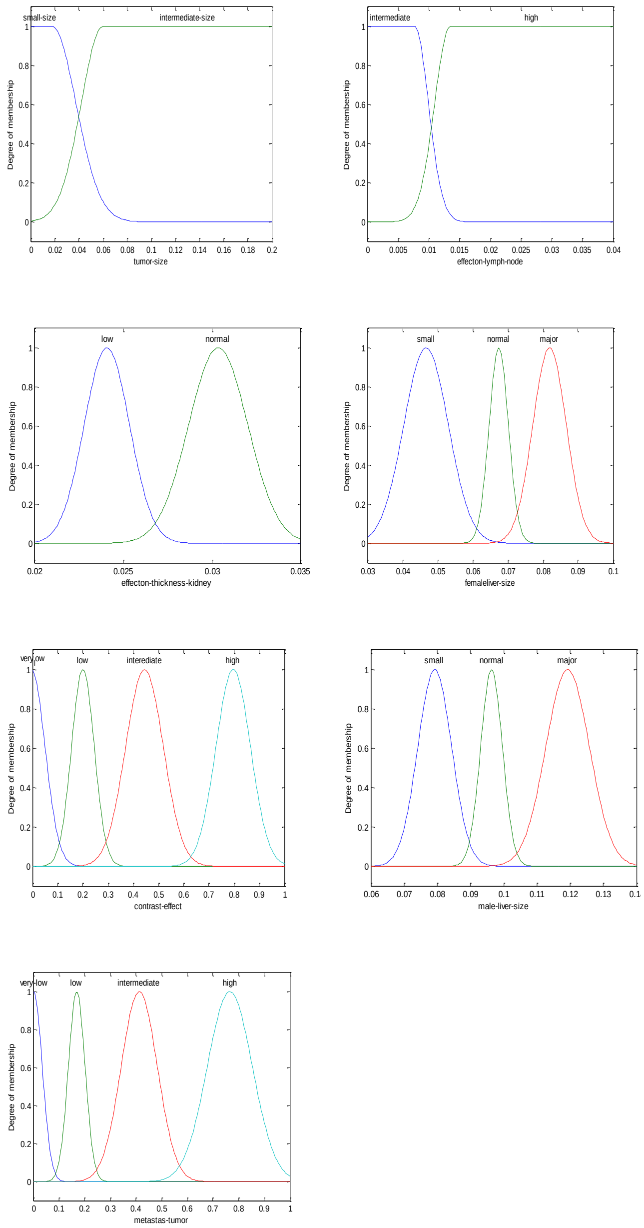

Fig.4. Fuzzy membership functions of the input variables before optimization

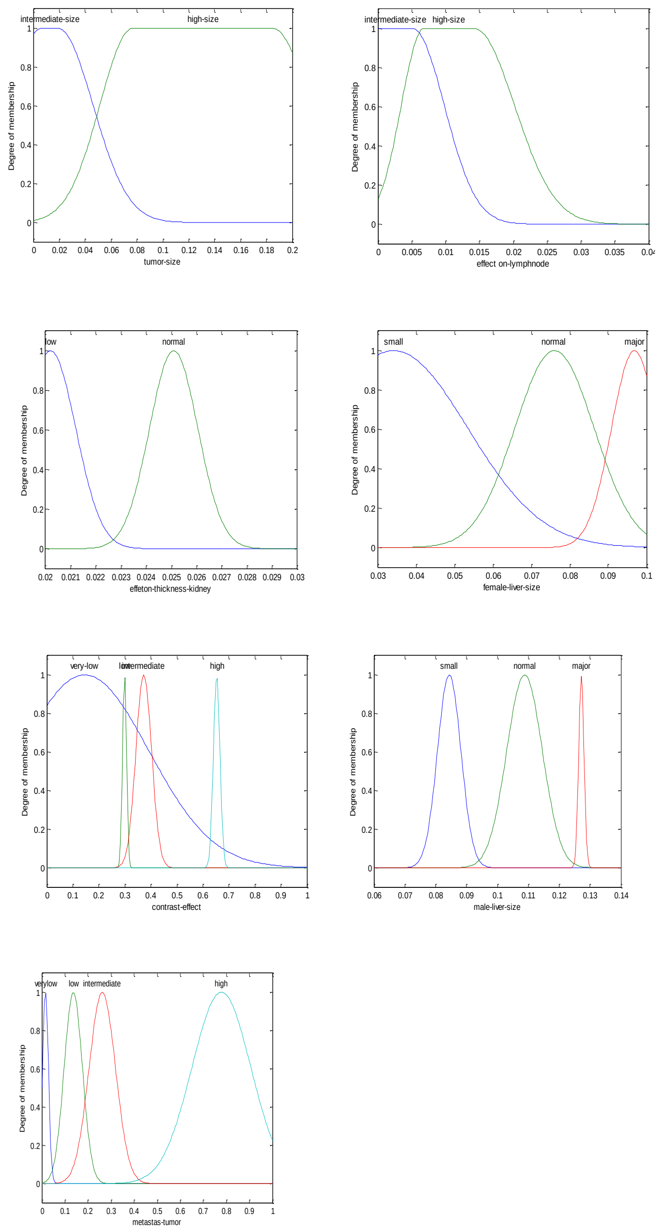

Fig.5. Fuzzy membership functions of the input variables after the GA optimization

A. Comparison of current intelligent systems applied to Hepatic tumor diagnosis

This section presents a comparison of the intelligent methods designed for diagnosis of the liver disease and summarizes the results in Table XI. Table XII shows a comparison of optimization methods applied to the liver disease diagnosis intelligent systems.

In this Section, Table 11 and Table12 show comparison of expert systems and optimization models designed for diagnosis of liver disease, respectively. In this study, a fuzzy inference system for diagnosis of hepatic metastasis using the knowledge of medical expert has been proposed. As shown in Table 11 and 12, this system has improved the tradeoff between accuracy and interpretability by providing a Mamdani inference model with a high accuracy. To evaluate the performance of the FES and Fuzzy-GA approaches, the proposed models were evaluated using the mean square of the error criteria to compare the result of the system to the actual value. Accuracy of the FES before optimization with genetic algorithm was 89.88%, and after optimization using the GA, has reached to 99.3%.

Compared to the neural network designed in [15] for diagnosis of the hepatic metastasis, with an accuracy of 91%, flexibility (in terms of freedom of design parameters constructing the gents in a chromosome) and interpretability (using linguistic terms in the input and knowledge base of the expert system) of the proposed Fuzzy-GA method is more than the neural network. In order to improve the accuracy of this system, a Fuzzy-NN was designed for diagnosis of the hepatic metastasis. The accuracy of this system was 92.5%. However number of the fuzzy rules obtained after training using the Fuzzy–NN method was 300 but number of the fuzzy rules in the Fuzzy-GA was 24. This fact shows that the Fuzzy-GA approach has higher interpretability that the Fuzzy-NN.

The proposed hybrid Fuzzy-GA model has improved the trades-off between accuracy and interpretability. the present hybrid Fuzzy-GA method in this study has provided higher accuracy through tuning membership functions of the FES compared to the Fuzzy-GA system reported in [12] for optimization of the rule set on the UCI Indian liver disorder dataset. The work presented in this study is capable to diagnosis of liver metastasis. The performance of the Hybrid Fuzzy-GA model was investigated using the information provided from the Noor Imaging Centre in Tehran. This is the first time that an intelligent expert system is designed based on the Iranian patients with liver disease which is the third mortal malignant cancer in Iran.

TABLE XI

COMPARISION OF EXPERT SYSTEM FOR LIVER DISEASE DIAGNOSIS

Name	Method	Out put	Accuracy	Difference with this work
A fuzzy expert system to diagnose hepatic diseases [5]	Mamdani fuzzy inference methods	Healthy and unhealthy liver	91%	Recognize normal and abnormal liver, according to the information contained in liver function tests. It does not define different types of the disease.
A fuzzy expert system for assessment of the risk of liver cancer (HCC) [4]	Mamdani Fuzzy inference methods	Risk of hepatocellular Carcinoma	not mentioned	The difference is in the type of input variables and different kinds of diseases detected in the output
An automatic system for medical diagnosis through computer for hepatic tumors in CT scan images[6]	Computer aided diagnosis (CAD)	Detection liver hemangioma and hepatocellular Carcinoma (HCC)	96.7%	Using neural networks for diagnosis of the disease in the system using definitive features for diagnosis
Neural network based method on hepatic tumors tissue analysis in CT scan images[7]	Computer aided diagnosis (CAD)	Hepatodenoma (HA), hemangioma, HCC, colangiocarcinema (CC)	86.85%	Using neural network for diagnosis of the disease in the system and using definitive features for diagnosis
Differential diagnosis of CT focal liver lesions [8]	Computer aided diagnosis (CAD) using texture features, feature selection and ensemble driven classifiers	Clustering liver diseases in 5 cluster	73.36%	Neural network for diagnosis of the disease in the system, and using texture features, feature selection and ensemble driven classifiers.
The Fuzzy Expert System for hepatic tumor diagnosis [This work]	Mamdani Fuzzy inference methods	Risk of hepatocellular Carcinoma	89.88%	

TABLE XII

COMPARISION OF EXPERT SYSTEM FOR LIVER DISEASE DIAGNOSIS

Method	Accuracy	Data base
Evolutionary strategy based on GA for learning-based decision system [10]	97%	Liver fibrosis dataset from a hospital in France
Automatic Liver CT Image Clustering based on Invasive Weed Optimization Algorithm [11]	87%	Liver CT-scan images
Adaptive Genetic Fuzzy System [12]	75.21%	India liver dataset
Improved Feature Selection Based on Particle Swarm Optimization for Liver Disease Diagnosis [13]	Accuracy on train set was 100% and on test set is 97%	Hepatoma and Hemangioma CT-scan images
The MLP neural network for diagnosis of the hepatic metastasis [15]	91%	Information obtained from CT scan Image from the Noor medical image center
The hybrid Fuzzy-GA Approach for diagnosis of hepatic tumor [this work]	The accuracy of the FES before optimization 89.88%, and after optimization was 99.3%.	Information obtained from CT scan Image from the Noor medical image center

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