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Design of a Fuzzy-based Decision Support System for Coronary Heart Disease Diagnosis

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Abstract In the present paper, a fuzzy rule-based system (FRBS) is designed to serve as a decision support system for Coronary heart disease (CHD) diagnosis that not only considers the decision accuracy of the rules but also their transparency at the same time. To achieve the two above mentioned objectives, we apply a multi-objective genetic algorithm to optimize both the accuracy and transparency of the FRBS. In addition and to help assess the certainty and the importance of each rule by the physician, an extended format of fuzzy rules that incorporates the degree of decision certainty and importance or support of each rule at the consequent part of the rules is introduced. Furthermore, a new way for employing Ensemble Classifiers Strategy (ECS) method is proposed to enhance the classification ability of the FRBS. The results show that the generated rules are humanly understandable while their accuracy compared favorably with other benchmark classification methods. In addition, the produced FRBS is able to identify the uncertainty cases so that the physician can give a special consideration to deal with them and this will result in a better management of efforts and tasks. Furthermore, employing ECS has specifically improved the ability of FRBS to detect patients with CHD which is desirable feature for any CHD diagnosis system.

Keywords Coronary heart disease · Fuzzy rule-based system · Transparency · Data mining · Medical diagnosis

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Introduction

Background

Coronary heart disease (CHD) refers to the narrowing of arteries that supply blood and oxygen to the heart, causing serious cardiovascular complications including myocardial infarctions (heart attack) and angina [1]. It is the most common type of heart disease and the leading cause of death worldwide [2, 3]. Early detection of CHD in patients, however, can result in significant life saving [4, 5] when followed by adequate medical treatments.

In fact, CHD diagnosis is a quite challenging task, since the physician needs to carefully examine a combination of symptoms and signs that may overlap with other causes [5]. In addition, the information available about the patient is inherently uncertain [6]. In order to help deal with this problem in a more efficient way, many approaches have been proposed to assist the physician's decision making about whether CHD is likely to exist or not.

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Invasive coronary angiography is the gold-standard clinical method used for diagnosing CHD. Its use, however, is restricted to a limited population due to the high cost and high-level technical expertise and technological required to perform this procedure [7]. In addition, a substantial number of patients referred to this modality appear free from CHD [8]. Consequently, attention has shifted to the use and development of relative cost-effective and reliable non-invasive methods so that all the patients with suspected CHD would be able to afford the medical test and those who have an active CHD can be accurately identified at early stage [9]. The noninvasive methods include the widely used exercise electrocardiogram (ECG) test [10] and a number of noninvasive imaging modalities. These modalities include electron-beam computerized tomography (EBCT) [11], single-photon emission computed tomography (SPECT) [12], positron emission tomography (PET) [13], (contrast) stress echocardiography [14], magnetic resonance angiography(CMRA) [15] and most recently Multislice computed tomograph (MSCT) [16].

The data obtained from the above mentioned modalities and other sources such as clinical and historical data are employed by a computer based decision support system (DSS) to classify the patients as either having or not having evidence of CHD. Several techniques were proposed to build these DSSs that can help the physician in the decision making process by providing a rapid and accurate diagnosis of CHD.

Related Works

Soft computing techniques which indicate a number of methodologies used to find approximate solutions are successfully applied in many real-world problems including medical diagnosis problem [17]. Their use in developing disease diagnosis systems are motivated by their ability to handle uncertain information upon which medical diagnosis is usually based [6].

Artificial neural networks (ANNs) [18–28] and recently SVMs [28–31] are the most commonly used soft computing methods in developing CHD diagnosis system. Overall, the performances obtained by these systems appear promising as they achieved relatively good classification accuracy, and thus can serve as reliable decision support system for CHD detection.

Despite the advantage of being highly accurate, ANNs and SVMs have been criticized due to their lack of transparency as they are black box systems, i.e the user is prevented from knowing about the decision process of their inner systems [32].

Transparency or interpretability which refers to the ability of a system to express its behavior in an understandable way, has recently gained more attention and it is considered as an important criterion for medical diagnosis systems [32–34]. One of the advantages that a transparent diagnosis system may offer is its capability to give a response on how a particular decision of diagnosis was made. This feature is of great importance as it may allow the physician to: (1) either consider or reject the decision made by the diagnosis system (2) identify CHD risk factors which helps in its diagnosis and treatment in early and reversible stages [35].

Unlike ANNs and SVMs, Fuzzy rule-based systems offer a convenient format for representing the knowledge underlying a system in the form of transparent and linguistic conditional statements. These statements are in the form of "if condition(s) then action(s)" [36]. Such kind of format is humanly understandable as it uses a language close to the natural language which makes it a suitable tool for interpretation and analysis. In addition, FRBSs use a fuzzy logic-based reasoning scheme to draw conclusions that simulates in some respects the human thinking mechanism [37]. The aforementioned advantages make FRBSs a suitable method for developing diagnosis system for CHD.

Typically, fuzzy rules are generated using two methods: expert-driven approach and data-driven approach. In the first approach, the values of fuzzy rule parameters such as interval boundaries and membership functions are defined and set manually by the expert, while these values are defined automatically from a set of representative examples using a learning method in the other approach [37].

Recently, data-driven rule generation methods have dominated the development of fuzzy-based CHD diagnosis systems partly due to the cost and difficulty of manually setting the rules, and partly due to the availability of historical patient data and the recent development of efficient machine learning algorithms. [38–42]. Their only objective is however, getting higher diagnostic accuracy, disregarding the transparency issue. Hence, fuzzy approach adopted by these systems is a kind of black-box system that is used only for calculating rather than inferencing the diagnosis label. The design of fuzzy rule-based diagnosis system has to consider both the accuracy and the transparency.

While the transparency feature is maintained in expert-driven approach, it is usually lost during the learning process, and to preserve it, many approaches have been proposed [43–47]. Genetic-based approaches are among the most successful ones. Basically, they try to find a fuzzy system that has the required balance between the accuracy and transparency

using the powerful search of genetic algorithm. This approach is, however, computationally costly when it applies for our problem as the number of inputs is relatively high. Thus, it is desirable to apply a feature selection method to select only the most relevant features. This preprocessing step is used to reduce the complexity and the time needed for the optimization process.

In addition, the fact that some approaches generate highly transparent fuzzy rules with clear linguistic meaning such in [46, 47], their consequent parts do not include enough information about the rules. While most of these approaches include only the certainty (or confidence) degree which is important for assessing the classification ability of the rules, it is important to incorporate also the degree of support of rules which indicates how often these rules occur in a data set. By giving these two information measures about each rule, the decision maker can effectively assess the degree of importance and certainty of each rule.

Objectives

In this study, a transparent and a relatively accurate fuzzy rule-based system is designed for CHD diagnosis. The concept of transparency is extended to include not only the traditional measures such as the number of rules and fuzzy sets, but also to include the degree of certainty and the support of each rule. The development of our fuzzy rule-based system involves four main steps. In the first step which is a preprocessing step aiming at reducing the complexity of the data set, a feature selection method is applied to select the most discriminative subset of features. After generating all the possible fuzzy rules in the second step, multi-objective genetic algorithms are utilized to obtain a subset of a small number of rules with the highest classification ability in the third step. The result of this step is a set of fuzzy rules that incorporate at the consequent part in addition to their class labels, their degree of certainty and confidence.

To enhance further the accuracy capabilities of the produced fuzzy rules, we introduce in the fourth step a new method where the decision or classification made by a rule which its degree of confidence is less than threshold value is supported by an ensemble of selected classifiers in order to get a more reliable decision. This ensemble classifiers strategy (ECS) is inspired by common medical practice where more than one expert's opinion should be considered in complicated cases that have low diagnostic certainty. Finally, the results achieved by our FRBS are evaluated and compared with other benchmark methods.

The rest of the paper is organized as follows. Section "Data Set" describes the data set used in this study while Section "Methodology" details the steps and features of the proposed methodology. The results obtained and their discussions are given in Section "Results and Discussions" while conclusion is drawn in Section "Results and Discussions".

Data Set

The data set used in this study was obtained from UCI Repository of Machine Learning Databases. It was collected from Cleveland Clinic Foundation, Cleveland, Ohio and supplied by Robert Detrano, M.D., Ph.D. of

Table 1 Description of Cleveland heart disease data set

Attributes	Description	Type	Value
Age	Age	Integer	[29 77]
Sex	Sex	Integer	1 = male; 0 = female
Pc	Chest pain type	Integer	1 = typical angina; 2 = atypical angina; 3 = non-anginal pain; 4 = asymptomatic
Trestbps	Resting blood pressure (in mm Hg on admission to the hospital)	Integer	[94,200]
Chol	Serum cholestoral in (mg/dl)	Integer	[126,564]
Fbs	Fasting blood sugar (>120 mg/dl)	Integer	1 = true; 0 = false
Restecg	Resting electrocardiographic results (values 0, 1, 2)	Integer	[0, 2]
Thalach	Maximum heart rate achieved	Integer	[71,202]
Exang	Exercise induced angina	Integer	1 = 4 yes; 0 = no
Oldpeak	ST depression induced by exercise relative to rest	Real	[0.00, 62.00]
Slope	The slope of the peak exercise ST segment	Integer	1 = upsloping; 2 = flat; 3 = downsloping
♯ of MajorVessels	Number of major vessels (0–3) colored by flourosopy	Integer	[0, 3]
Thal	Thal	Integer	3 = normal; 6 = fixed defect; 7 = reversable defect
CHD	Coronary heart disease diagnosis	Integer	0 = absent; 1 = present

the V.A. Medical Center, Long Beach, CA [48]. Originally, the data had 76 attributes, out of which only 13 attributes were selected for use. The selected attributes represent the clinical and noninvasive test results of 303 patients undergoing angiography. Removing the cases containing missing values, 270 cases were considered in study, out of which 120 cases are identified as patients with CHD while 150 cases are diagnosed as patients without CHD.

Table 1 gives a brief description of Cleveland data attributes and their respective values.

Methodology

The proposed methodology composed of four main steps:

Feature Selection

Feature selection is a preprocessing step aims at reducing the number of features by selecting the subset of features that can produce the best model according to a certain criterion. The literature shows that the most effective feature selection methods are the Sequential Floating Forward Selection (SFFS) [49] and the genetic algorithms (GAs) [50]. While many studies [50–53] suggest the superiority of SFFS over the sequential search algorithms , there is no clear cut case study of which of the two methods—SFFS and GAs—is better than the other [50]. In our study, SFFS is selected as it is much faster than the GAs method.

Since we are dealing with classification problem, the criterion used for selection is the classification accuracy. For each candidate feature subset, SFFS performs 10-fold cross-validation method and the subset that achieves the least misclassification error (or the best classification accuracy) is selected. In the following is a brief description of the SFFS algorithm applied at this step.

Sequential Floating Forward Selection (SFFS) The standard Sequential Forward Search (SFS) starts from an empty feature set and creates candidate feature subsets using the following procedure:

(1) evaluate the feature sets of size 1 and select the single best feature;
(2) evaluate the feature sets of size 2 that includes the feature from 1 and select the best one;
(3) evaluate the feature sets of size 3 that includes the features from 2 and select the best one;
(4) and so on until the stopping criteria is reached.

The number of selected features can be predefined by the user or can be automatically defined by the algorithm. SFFS method improves SFS by dynamically changing the number of features included or eliminated at each step according to a certain criterion. In addition, this method allows the reconsideration of features included or removed at the previous steps [49].

Fuzzy Rule-based System Generation

Extending the Format of Fuzzy Rules

In medical diagnosis problem, the physician, based on the symptoms exhibited by the patients, classifies the patient's disease to one of the two classes, namely, patient with CHD and patient without CHD (binary classification). Thus, medical diagnosis problem falls under the classification problems.

Formally, diagnosis problem can be solved by finding a suitable classifier or mathematical function f that maps a set of symptoms $\mathbf{X}$ to a diagnosis class label c_j. This function can be written as follow:

$$f : \mathbf{x} \rightarrow c_j$$

where $\mathbf{x} = \{x_1, x_2, ..., x_n\}$ is a set of symptoms, and c_j where $j \in \{1, 2\}$ is the class label. The classifier can be ANNs or decision tree or any other classification method.

In fuzzy set theory, the classifier f is a set of fuzzy rules where the kth rule has the following format:

$$R_k : \text{ if } x_1 \text{ is } A_1^k \text{ and } x_2 \text{ is } A_2^k \text{ and } ... \\ \text{and } x_n \text{ is } A_n^k \text{ then } Y \text{ is } c_j \quad (1)$$

where A_j^k are fuzzy sets of the input variables (x_1, x_2, x_n) represented by linguistic values such as low, moderate and high while c_j is the class label of the class variable Y (which in this case is either $Y = c_1$ for present class or $Y = c_2$ for absent class).

Some studies (see for example [47]) used an extended format of (1) that includes the degree of certainty or confidence r_k of the kth rule where $r_k \in [0\,1]$. The value r_k represents also the certainty's degree of the decision made by this rule. This feature allows the physician to know about the degree of confidence of the decision made by the fuzzy classifier or more precisely by the winner rule and whether to consider it or not.

This format of fuzzy rule-based system can be written as follows:

$$R_k: \text{ if } x_1 \text{ is } A_1^k \text{ and } x_2 \text{ is } A_2^k \text{ and } ... \text{ and } x_n \text{ is } A_n^k \text{ then } Y \text{ is } c_j \text{ with certainty } r_k \quad (2)$$

where r_k is the degree of certainty of the kth rule.

Although (2) gives more information about the kth rule than (1), it does not allow the decision maker to know the degree of importance of the rule and precisely how many times R_k rule holds true in the training data. This concept is known in data mining field as *support* and it is important criterion to assess the rules. Using the degree of certainty alone might cause a mislead in the decision making, for example assume that the degree of certainty of the R_k is $r_k = 1$ (100% classification accuracy) but it covers only very few cases in the training data. As a result, R_k has a low support and cannot be used alone to generalize relations or draw conclusions. In addition, this value of support helps also in handling partial contradictions between the rules and considering special cases. In our study, in order to provide more information about rules, the format of fuzzy rules is extended to include the support value of the rule. This extended format can be written as follows:

$$R_k: \text{if } x_1 \text{ is } A_1^k \text{ and } x_2 \text{ is } A_2^k \text{ and ... and } x_n \text{ is } A_n^k \text{ then } Y \text{ is } c_j \text{ with certainty } r_k \text{ and support } s_k \quad (3)$$

where s_k is the support value of the kth rule.

Fuzzy Rule Generation Procedure

Let T_i be the number of linguistic values associated with the input variable x_i. One of these linguistic values is used as the fuzzy antecedent A_i^k for the input variable x_i in each rule R_k. In addition *"dont care"* is an additional linguistic value that represents the irrelevant fuzzy antecedents that can be deleted without affecting the fuzzy systems performance. Thus, the number N of possible combinations of the antecedent part in this case is:

$$N = (T_1 + 1) * (T_2 + 1) * (T_3 + 1) * ... * (T_n + 1) \quad (4)$$

Using this method, all the possible antecedents of fuzzy rules can be generated, but when the number of inputs is high (high-dimensional data set), the number of rules generated will be exponentially increased. Since we are applying feature selection procedure at the pre-processing stage, the number of inputs will be adequate to apply this approach. After defining the antecedents of fuzzy rules, the consequent class of the rule R_k, its degree of certainty [54], and support can calculated as follows:

(a) *Calculate the consequent class*

(1) For each training pattern $\mathbf{x}_t = (x_{t1}, x_{t2}, ..., x_{tn})$, its compatibility grade $\mu_k(x_t)$ with the rule R_k is calculated as

$$\mu_{R_k}(x_t) = \mu_{k1}(x_{t1}) * \mu_{k2}(x_{t2}) * ... * \mu_{kn}(x_{tn}), \quad t = 1, ..., m \quad (5)$$

where $\mu_{ki}(.)$ is the membership function of the fuzzy set A_j^k.

(2) for each class, calculate the sum of compatibility grades of the training patterns with the fuzzy rule R_k as:

$$\beta_{\text{Class h}}(R_k) = \sum_{x_t \in \text{Class h}} \mu_{R_k}(x_t), h = 1, 2. \quad (6)$$

(3) find the class c_j that has the maximum value of $\beta_{\text{Class h}}(R_k)$:

$$\beta_{\text{Class c}_j} = \max\{\beta_{\text{Class 1}}(R_k), \beta_{\text{Class 2}}(R_k)\} \quad (7)$$

if the consequent class of the fuzzy rule cannot be uniquely defined, we do not generate the fuzzy rule R_k.

(b) *Calculate the certainty grade*
Certainty grade can be calculated as follows:

$$CF_j = \left\{\beta_{\text{Class C}_j}(R_k) - \bar{\beta}\right\} / \sum_{h=1}^{2} \beta_{\text{Class h}}(R_k) \quad (8)$$

Where

$$\bar{\beta} = \sum_{h=1, h \neq C_k}^{2} \beta_{\text{Class h}}(R_k) \quad (9)$$

(c) *Calculation of the support*

Calculate the support s_k with the following formula:

$$s_k = \frac{NCC_{R_k}}{m_j}, R_k \in \text{FRBS}_{c_j} \quad (10)$$

where NCC_{R_j} is the number of training patterns correctly classified by the rule R_k, m_j is the number of training patterns belonging to the class c_j and FRBS_{c_j} is the set of fuzzy rules associated with the class c_j.

Fuzzy Reasoning Method

The fuzzy reasoning adopted in this study is based on a single rule winner [54]. A new pattern $x_t = (x_{t1}, x_{t2}, ..., x_{tn})$ is assigned to the consequent class of the winner R_w. That is the rule which has the highest combination between the matching degree of the pattern with the antecedent-part and the certainty degree of classes. The winner rule can be determined as follows:

$$\mu_{R_w}(x_t).CF_w = \max\{\mu_{R_j}(x_t).CF_k | R_k \in \text{FRBS}\} \quad (11)$$

The classification of the new pattern is rejected in the case where two or more rules with different classes have the same maximum value in Eq. 11.

Fuzzy Rule-based System Optimization

After generating all possible rules, the optimization procedure is applied to search for a subset of a small number of rules (within all possible rules) with the highest classification ability. The first objective represents the accuracy of FRBS while transparency (a subset with small number of rules) defines the second objective. These two modeling objectives of our FRBS can be written as follows:

$$\text{Maximize } f_{\text{acc}}(\text{FRBS}), \text{Minimize } f_{\text{rule}}(\text{FRBS}) \quad (12)$$

Where f_{acc}(FRBS) is the accuracy of FRBS measured by the rate of classification accuracy, f_{rule} (FRBS) is the number of fuzzy rules of FRBS. To optimize simultaneously the above mentioned objectives, controlled NSGA-II is utilized, and the results of the optimization are Pareto-front solutions that represent a number of different FRBSs solutions with their corresponding 2-tuple of values t_{FRBS} where t_{FRBS} = (accuracy of FRBS, rules' number of FRBS). The selection between these solutions usually depends on user preference and the type of problem under investigation. In our case, since the accuracy in medical diagnosis is critical, the FRBS with the highest accuracy is selected. In the following subsection, a brief description of the multi-objective genetic algorithm used is introduced.

Multi-objective Genetic Algorithms

Genetic algorithms are heuristic techniques inspired by natural evolution for searching for optimum solution. Multi-objective genetic algorithms (MOGAs) are classes of genetic algorithms which are mainly applied for optimization problems that have multiple and even conflicting objectives [55]. MOGAs use two approaches in handling multi-objectives optimization problems. In the first approach, various objective functions are combined into a single function using weight factors. The difficulty of this approach lies in the determination of the proper weight values that characterize the user preference. The second approach searches for non-dominated Pareto optimal compromises between the conflicting objectives. It is more practical, as it offers the decision maker multiple alternatives that have the same cost. There are a number of MOGAs proposed in the literature [55–57], of which NSGA-II algorithm [58] is the most commonly used multi-objective genetic algorithms to handle this kind of problem.

Non-dominated genetic algorithm II NSGA-II is an efficient MOGAs introduced by Deb et al. [58] to overcome some of the NSGAs [59] drawbacks such as computation complexity, the need for specifying a sharing parameter, and non-elitism approach [58]. The advantages of NSGA-II with respect to other MOGAs is the preservation of diversity and the fast non-dominated sorting of individuals. The concept of non-dominated relation can be defined as follows. Solution S_A dominates S_B if the following two conditions hold:

1. S_A is strictly better than S_B in at least one objective, and
2. S_A is no worse than S_B in all objectives.

Controlled elitist genetic algorithm It is an enhanced version of NSGA-II proposed by Deb and Goel [60] for controlling the extent of elitism to certain portion defined by the user. This approach allows for better convergence comparing with original NSGA-II. The following subsection describes the chromosome representation used in our implementation.

Chromosome Representation

Let N be the total number of fuzzy rules generated and S is the subset of rules selected, where $S \leq N$. The chromosome is coded as binary string of length N and each binary bit represents one rule. When the value of qth bit is set to 1, the qth rule is selected while in the other case (qth bit is set to 0), the qth rule is not

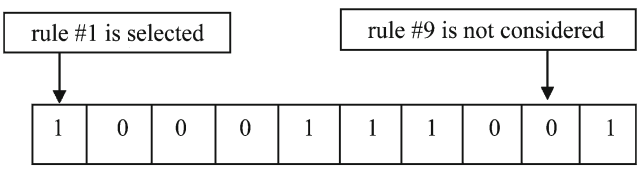

Fig. 1 Chromosome coding of rule selection procedure with $N = 10$, $S = 5$

considered. Figure 1 shows an example of chromosome coding of rule selection procedure with total number of rules $N = 10$, and number of selected rules $S = 5$. The rules number 1,5,6,7 and 10 are selected to form a candidate fuzzy rule-based system while rules number 2,3,4,8 and 9 are ignored.

Enhancing the Classification Accuracy of the Fuzzy Rule-based System by an Ensemble Classifiers Strategy (ECS)

After producing the fuzzy rule-based system, we propose an approach to enhance the performance of the FRBS by supporting its decision (classification) by an ensemble of classifiers in the case where the classification decision is made by a rule (winner rule) which its degree of certainty is below a threshold α where α is defined by the user, in this study $\alpha = 0.5$.

Basically, Ensemble method uses a set of relatively accurate and diverse classifiers to classify all new cases by taking a weighted vote of their classifications [61]. For our case, we are using FRBS for classification and we are not calling Ensemble method in all the cases (as the traditional way) but only on the uncertainty cases, i.e. where the certainty of the FRBS classification is low. And the reason behind proposing this method can be resumed as the following: in the cases where the certainty of the FRBS classification is high (FRBS classification is most likely to be correct), we prefer to keep using FRBS to get the interpretation of the cases, while we use Ensemble method (Bagging method with simple majority vote) in the uncertainty cases (the certainty degree of FRBS is low) to enhance the likelihood of their correct classification.

To compose the ensemble of classifiers, we select, in addition to our FRBS, six other popular classifiers, out of which 3 are non-fuzzy based methods and the others are fuzzy-based methods. The non-fuzzy based methods are: Artificial Neural Networks (ANNs) [62], the popular decision tree algorithm C4.5 [63] and statistical method Linear Discriminant Analysis (LDA) [64] while the fuzzy based methods are: FH-GBML [46], SLAVE [43], and GP-FCS [65]. These algorithms are included in many non-commercial tools such as Weka [66], Keel [67], and Orange [68].

Fuzzy Rule-based System Evaluation

Transparency Measures

While the transparency concept is difficult to convert into measurable metrics, many researchers agree on some properties of transparency related to the fuzzy systems such as the number of rules, and the number of antecedent conditions in each rule [46, 47]. In addition, there is a special emphasis on the use of linguistic variables that have clear meaning [44, 45]. In this study, we consider all the above stated measures and we highlight also the importance of providing more information about degree of certainty and support of each rule, so that transparent and informative rules will be produced.

Performance Measures

To assess the discriminating power of the fuzzy rule-based system, two well known measures are employed. The first and conventional method is the percentage of correctly classified testing patterns (PCC) while the second is the area under the Receiver operating characteristic (ROC) curve or AUC for short. The latter measure is commonly used in the medical community to evaluate the diagnostic power of tests for diseases [69]. In addition, 10-fold cross-validation method is used to estimate the classification accuracy of our fuzzy rule-based system [70]. The results achieved by our system are compared with existing benchmark methods.

Results and Discussions

Feature Selection Procedure

In this step, SFFS method was applied to select the subset of features that can produce the best classification model. The results of this step are shown in Table 2. As can be noted from the table, SFFS selects the subset that includes the following four features: sex, chest pain type, ♯ of MajorVessels and Thal. In addition, while the number of features decreases from 13 to only 4, the classification accuracy of the model is still maintained at almost 83% which reflects the ability of SFFS method in handling feature selection problem.

Table 2 Results of feature selection procedure

	All features	Selected features
♯ of features	13	4
Description	See Table 1	2 (sex), 3 (chest pain type), 12 (♯ of major vessels), 13 (Thal)
Misclassification error	17.07%	17.04%

Table 3 the number of fuzzy rules and fuzzy sets selected in the optimization step

Subsets	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10	Average
♯ of rules	7	8	8	10	8	10	6	7	7	9	**8**
♯ of initial fuzzy sets	28	32	32	40	32	40	24	28	28	36	**32**
♯ of selected fuzzy sets	17	22	20	27	20	25	15	15	17	21	**19.9**
♯ of fuzzy sets/rule	2.4	2.8	2.5	2.7	2.5	2.5	2.5	2.1	2.4	2.5	**2.5**

Fuzzy Optimization

This step aims at: (1) maximize the classification accuracy and (2) minimize the number of fuzzy rules in the fuzzy rule-based system. The results of this step are shown in Tables 3, 4, 5, 6, 7 and 8.

Transparency Criterion

The total number of generated fuzzy rules are $N = 300$ rules, from which S rules are selected to represent the fuzzy rule-based system. The results of this selection are Pareto non-dominated solutions that represent fuzzy rule-based systems with different levels of accuracy-number of rule values. As stated before, the priority is given to the accuracy of the systems, that is, the FRBS with the higher accuracy is selected. Table 3 shows the number of rules, fuzzy sets and number of sets per rule for different folds. As can be seen from Table 3, fuzzy rules selected from 300 rules have relatively small number with an average of 8 rules per fold. The difference in the number of rules between folds is due to the changing of training data from a fold to another. Another improvement is in the number of fuzzy sets selected per rule which decreases from 4 to 2.5 per rule. In addition, as can be seen in Fig. 2—which depicts the fuzzy rules of fold2-, the fuzzy rules use understandable description of the antecedent conditions in the form of if-then rules and they include in addition to their class labels, their degree of certainty and support. The linguistic description helps the physician to understand the relations between the factors or symptoms and the diagnosis outcome while degree of certainty degree helps to know how well this relation is accurate. This kind of reasoning matches with the human thinking which allows partial truth to exist.

Rule's support at the other hand allows knowing to what extent this relation can be generalized. For example, in Table 4, which contains information about the rules of fold2, the 8th rule has a certainty degree of 1 which means perfect classification ability while it covers only 2 cases in the training data. This kind of relations can be seen as special cases and cannot be generalized. On the other hand, rules 1, 2, and 3 have correctly classified 82, 56 and 30 cases respectively out of 243 cases (the total cases of training data). These rules should have special importance in the analysis and in drawing conclusions when comparing with the others as they have dominant position in the diagnostic process.

Classification Accuracy Criterion

Tables 5 and 6 show respectively the PCC and AUC values of our FRBS before applying ensemble classifiers strategy (ECS) and it is named in the table as B-FRBS and after using this strategy (A-FRBS). In addition, the two Tables 5 and 6 show also the PCC and AUC values of a number of benchmark methods namely, (1) the decision tree C4.5, (2) Multilayer Perceptron (MLP) which is the most popular supervised neural networks architecture, (3) HF-GBML [46], a fuzzy hybrid genetic-based machine learning for generating interpretable fuzzy rules, (4) SLAVE, a GA

Table 4 list of classification rules of subset 2 and their corresponding values of support, confidence and classification accuracy

				Training			Testing		
♯ of rule	Class label	Confidence	Support	Total	Correct	Incorrect	Total	Correct	Incorrect
1	0	0.28	0.337	101	82	19	9	9	0
2	1	0.80	0.231	62	56	6	9	8	1
3	0	0.72	0.124	35	30	5	3	3	0
4	1	0.27	0.074	20	18	2	3	3	0
5	1	0.74	0.037	12	9	3	1	1	0
6	0	1.0	0.033	8	8	0	2	2	0
7	0	1.0	0.012	3	3	0	/	/	/
8	1	0.20	0.004	2	1	1	/	/	/
				243	207	36	27	26	/

Table 5 Classification accuracy of FRBS before (B-FRBS) and after (A-FRBS) applying Ensemble Classifier Strategy (ECS) and a number of benchmark classifier algorithms using 10-fold cross-validation method

Methods	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10	Average
Training data											
C4.5	86.80	85.10	86.40	86.40	86.00	86.80	86.80	85.10	87.20	86.40	**86.30**
ANNs	87.60	85.50	86.80	87.20	86.00	87.20	87.60	85.50	87.60	87.20	**86.80**
HF-GBML	86.83	85.19	85.19	86.42	86.01	86.01	87.24	85.60	86.83	86.83	**86.21**
SLAVE	82.70	85.50	86.80	87.20	82.70	86.80	86.80	84.30	85.10	82.30	**84.80**
GP-FCS	78.60	78.10	78.10	79.80	78.60	77.70	79.40	81.40	83.90	79.00	**79.50**
LDA	81.4	83.50	83.90	84.70	83.50	83.50	86.00	83.50	85.10	85.10	**83.90**
B-FRBS	83.54	85.19	85.54	87.24	86.01	81.89	86.42	85.19	84.77	87.24	**85.30**
A-FRBS	86.83	85.19	85.54	86.42	86.01	86.83	86.83	85.19	85.19	86.42	**86.04**
Testing data											
C4.5	77.70	88.80	85.10	85.10	88.80	81.40	74.00	96.20	77.70	77.70	**83.30**
ANNs	77.70	96.20	85.10	74.50	77.70	77.70	77.70	96.20	70.30	81.40	**81.40**
HF-GBML	77.78	96.30	85.19	70.37	92.59	77.78	77.78	93.10	70.37	81.48	**82.27**
SLAVE	74.00	96.20	81.40	77.70	81.40	70.30	74.00	92.50	77.70	77.70	**80.30**
GP-FCS	70.30	85.10	88.80	77.70	77.70	81.40	74.00	88.80	59.20	77.70	**78.10**
LDA	77.70	92.50	88.80	81.40	92.50	74.00	70.30	92.50	77.70	77.70	**82.50**
B-FRBS	70.37	96.30	85.19	85.19	88.89	66.67	77.78	96.30	74.07	77.78	**81.85**
A-FRBS	77.78	96.30	85.19	85.19	88.89	81.48	77.78	96.30	77.78	77.78	**84.44**

learning method for generating fuzzy rules, (5) GP-FCS, a genetic programming algorithm for optimizing fuzzy classifiers, and (6) the statistical method Linear Discriminant Analysis (LDA).

As can be seen from Tables 5 and 6, the initial results show that the ensemble classifiers strategy applied to support the classification of rules with certainty value less than 0.5 has improved the accuracy from 81.85% to 84.44% and from 0.812 to 0.839 for PCC and AUC respectively. This accuracy is comparable or even better than the other classifiers listed in Tables 5 and 6. This result also indicates that more reliable classification decision can be obtained when combined with other classifiers known by their precision ability. This conclusion is shared by West et al. [71] who suggested that the accuracy of a set of classifiers is generally better than the best single classifier. In fact, it is common in medical practice to have more than one opinion in cases where the degrees certainty of the diagnosis is weak. Thus, these classifiers are playing the role of experts who provide their opinions about complicated cases that have low degree of certainty.

Table 6 AUC Values of FRBS before (B-FRBS) and after (A-FRBS) applying Ensemble Classifier Strategy (ECS) and a number of benchmark classifier algorithms using 10-fold cross-validation method

Methods	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10	Average
Training data											
C4.5	0.863	0.844	0.859	0.858	0.853	0.864	0.864	0.846	0.869	0.859	**0.858**
ANNs	0.843	0.837	0.854	0.835	0.819	0.856	0.852	0.824	0.802	0.847	**0.837**
HF-GBML	0.863	0.844	0.849	0.858	0.853	0.860	0.868	0.849	0.864	0.863	**0.857**
SLAVE	0.819	0.848	0.862	0.866	0.815	0.836	0.865	0.834	0.844	0.811	**0.840**
GP-FCS	0.795	0.844	0.805	0.797	0.831	0.800	0.854	0.764	0.815	0.860	**0.817**
LDA	0.809	0.834	0.840	0.846	0.834	0.817	0.859	0.835	0.854	0.849	**0.838**
B-FRBS	0.826	0.844	0.847	0.866	0.853	0.814	0.860	0.846	0.841	0.867	**0.846**
A-FRBS	0.863	0.844	0.847	0.858	0.853	0.864	0.865	0.846	0.844	0.859	**0.854**
Testing data											
C4.5	0.767	0.892	0.842	0.850	0.900	0.800	0.742	0.958	0.750	0.783	**0.828**
ANNs	0.883	0.933	0.842	0.825	0.833	0.800	0.675	0.925	0.692	0.783	**0.819**
HF-GBML	0.767	0.967	0.842	0.692	0.933	0.767	0.775	0.917	0.675	0.817	**0.815**
SLAVE	0.717	0.967	0.800	0.767	0.808	0.675	0.742	0.917	0.750	0.783	**0.793**
GP-FCS	0.750	0.892	0.842	0.742	0.833	0.708	0.642	0.842	0.633	0.817	**0.770**
LDA	0.767	0.933	0.883	0.825	0.933	0.717	0.708	0.925	0.758	0.783	**0.823**
B-FRBS	0.683	0.967	0.842	0.850	0.900	0.642	0.775	0.958	0.717	0.783	**0.812**
A-FRBS	0.767	0.967	0.842	0.850	0.900	0.800	0.775	0.958	0.750	0.783	**0.839**

Table 7 Sensitivity values of FRBS before (B-FRBS) and after (A-FRBS) applying Ensemble Classifier Strategy (ECS) and a number of benchmark classifier algorithms using 10-fold cross-validation method

Methods	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10	Average
Training data											
C4.5	0.815	0.778	0.815	0.806	0.787	0.824	0.824	0.796	0.843	0.815	**0.810**
ANNs	0.833	0.815	0.833	0.833	0.815	0.852	0.852	0.833	0.833	0.806	**0.831**
HF-GBML	0.815	0.778	0.776	0.806	0.789	0.861	0.824	0.787	0.824	0.815	**0.807**
SLAVE	0.741	0.778	0.806	0.806	0.704	0.769	0.833	0.750	0.778	0.704	**0.767**
GP-FCS	0.694	0.778	0.676	0.750	0.833	0.704	0.870	0.676	0.741	0.787	**0.751**
LDA	0.759	0.824	0.843	0.833	0.824	0.796	0.852	0.833	0.870	0.824	**0.826**
B-FRBS	0.741	0.778	0.785	0.806	0.787	0.769	0.824	0.796	0.778	0.815	**0.788**
A-FRBS	0.815	0.778	0.785	0.806	0.787	0.824	0.833	0.796	0.778	0.815	**0.802**
Testing data											
C4.5	0.667	0.917	0.750	0.833	1.000	0.667	0.750	0.917	0.500	0.833	**0.783**
ANNs	0.833	1.000	0.750	0.917	1.000	0.667	0.750	0.917	0.583	0.833	**0.825**
HF-GBML	0.667	0.875	0.750	0.583	1.000	0.667	0.750	0.833	0.417	0.833	**0.738**
SLAVE	0.500	1.000	0.667	0.667	0.750	0.417	0.750	0.833	0.500	0.833	**0.692**
GP-FCS	0.500	0.917	0.750	0.750	1.000	0.417	0.750	0.750	0.333	0.833	**0.700**
LDA	0.667	1.000	0.833	0.917	1.000	0.500	0.750	0.917	0.583	0.833	**0.800**
B-FRBS	0.500	1.000	0.750	0.833	1.000	0.417	0.750	0.917	0.500	0.833	**0.750**
A-FRBS	0.667	1.000	0.750	0.833	1.000	0.667	0.750	0.917	0.500	0.833	**0.792**

Sensitivity and Specificity

ROC curves of FRBS before and after applying ensemble classifiers strategy (ECS) are displayed in Fig. 3 with blue and green colors, respectively. These curves are graphical plots of the sensitivity vs. (1-specificity) values of the two systems. They also represent the values of true positives (TP), the false positives (FP), the true negative (TN) and the false negatives (FN) for each system. In our case the positive class is the existence of CHD while the negative is the absence of CHD. We notice from Tables 7 and 8 as well as Fig. 3 that the specificity value for FRBS is clearly higher than the sensitivity value. This observation is also true for all classifiers (expect for MLP algorithm) and especially for fuzzy systems such as SLAVE, HF-GBML and B-FRBS where the difference between the specificity and the sensitivity is very significant, for example the specificity in B-FRBS is 0.873 while the sensitivity is 0.750. Another observation is that the non-fuzzy classifiers generally have better sensitivity values than the fuzzy systems and as a result exhibits better ability in

Table 8 Specificity values of FRBS before (B-FRBS) and after (A-FRBS) applying Ensemble Classifier Strategy (ECS) and a number of benchmark classifier algorithms using 10-fold cross-validation method

Methods	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10	Average
Training data											
C4.5	0.91	0.911	0.904	0.911	0.919	0.904	0.904	0.896	0.896	0.904	**0.906**
ANNs	0.852	0.859	0.874	0.837	0.822	0.859	0.852	0.815	0.770	0.889	**0.843**
HF-GBML	0.911	0.911	0.933	0.911	0.907	0.859	0.911	0.911	0.904	0.911	**0.907**
SLAVE	0.896	0.919	0.919	0.926	0.926	0.904	0.896	0.919	0.911	0.919	**0.913**
GP-FCS	0.896	0.911	0.933	0.844	0.830	0.896	0.837	0.852	0.889	0.933	**0.882**
LDA	0.859	0.844	0.837	0.859	0.844	0.837	0.867	0.837	0.837	0.874	**0.850**
B-FRBS	0.911	0.911	0.911	0.926	0.919	0.859	0.896	0.896	0.904	0.919	**0.905**
A-FRBS	0.911	0.911	0.911	0.911	0.919	0.904	0.896	0.896	0.911	0.904	**0.907**
Testing data											
C4.5	0.867	0.867	0.933	0.867	0.800	0.933	0.733	1.000	1.000	0.733	**0.873**
ANNs	0.933	0.867	0.933	0.733	0.667	0.933	0.600	0.933	0.800	0.733	**0.813**
HF-GBML	0.867	0.917	0.933	0.800	0.867	0.867	0.800	1.000	0.933	0.800	**0.878**
SLAVE	0.933	0.933	0.933	0.867	0.867	0.933	0.733	1.000	1.000	0.733	**0.893**
GP-FCS	1.000	0.867	0.933	0.733	0.667	1.000	0.533	0.933	0.933	0.800	**0.840**
LDA	0.867	0.867	0.933	0.733	0.867	0.933	0.667	0.933	0.933	0.733	**0.847**
B-FRBS	0.867	0.933	0.933	0.867	0.800	0.867	0.800	1.000	0.933	0.733	**0.873**
A-FRBS	0.867	0.933	0.933	0.867	0.800	0.933	0.800	1.000	1.000	0.733	**0.887**

Fig. 2 Linguistic fuzzy rules of subset 2

Disclaimer: The fuzzy rules listed here should not be used in clinical diagnosis without consulting experienced physicians.

(1) *IF ♯ of MajorVessels is (0) THEN CHD is: (Absent) with Certainty: 0.28 and Support: 0.337*
(2) *IF ChestPainType is (asymptomatic) AND Thal is (reversable defect) THEN CHD is: (Present) with Certainty: 0.80 and Support: 0.231*
(3) *IF Sex is (Male) AND ChestPainType is (non-anginal pain) AND ♯ of MajorVessels is (0) AND Thal is (normal) THEN CHD is: (Absent) with Certainty: 0.72 and Support: 0.124*
(4) *IF Sex is (Male) AND ChestPainType is (asymptomatic) THEN CHD is: (Present) with Certainty: 0.27 and Support: 0.074*
(5) *IF Sex is (Male) AND ChestPainType is (asymptomatic) AND ♯ of MajorVessels is (1) AND Thal is (reversable defect) THEN CHD is: (Present) with Certainty: 0.74 and Support: 0.037*
(6) *IF ChestPainType is (non-anginal pain) AND of ♯ of MajorVessels is (1) AND Thal is (reversable defect) THEN CHD is: (Present) with Certainty: 0.74 and Support: 0.037*
(7) *IF Sex is (Female) AND ChestPainType is (typical angina) AND ♯ of MajorVessels is (0) AND Thal is (normal) THEN CHD is: (Absent) with Certainty: 1.0 and Support: 0.012*
(8) *IF Sex is (Male) AND ♯ of MajorVessels is (2) AND Thal is (normal) THEN CHD is: (Present) with Certainty: 0.2 and Support: 0.004*

detecting patients with CHD while fuzzy-based systems achieve relatively better results in specificity which means better accuracy in detecting patients without CHD. These two observations show that the role of the two sets of classifiers can be complementary and can be used in an ensemble classifier strategy to improve the quality of the FRBS. The results achieved by A-FRBS (after applying ECS) shows that the improvement in sensitivity (from 0.750 to 0.792) is more significant than the improvement in specificity (from 0.873 to 0.887).

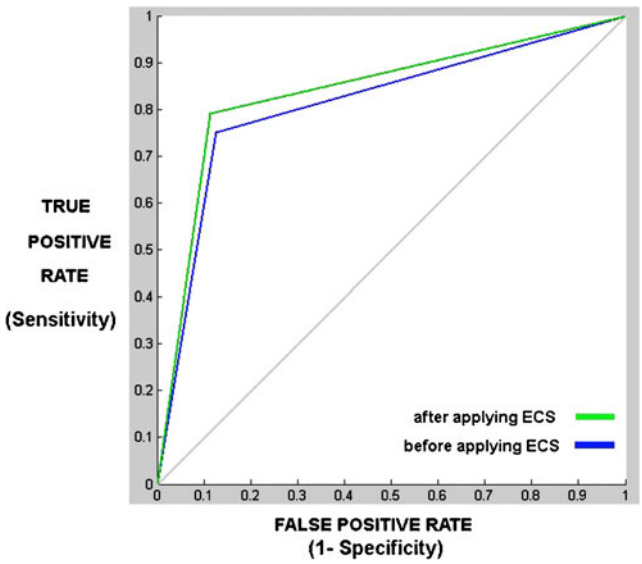

Fig. 3 ROC curve of FRBS before and after applying Ensemble Classifier Strategy (ECS)

Thus, ECS has generally improved the ability of FRBS for CHD diagnosis and specifically for detecting the patient with CHD which is a desirable feature for any CHD diagnosis system.

Conclusions

In this study, a fuzzy rule-based system for CHD diagnosis that considers both the accuracy and the transparency is proposed. The produced fuzzy rules can be easily understood by the physician as they use natural linguistic terms to describe the relations between the factors and the outcome of the diagnosis. In order to enhance the transparency of FRBS, the format of the fuzzy rules is extended to incorporate the certainty degree and the support at the consequent part of each rule so that the physician can check the importance and validity of each rule and whether to consider it in the decision process. In addition, the accuracy of diagnosis decision is improved by employing an ensemble of classifiers strategy (ECS) to support the decision of the FRBS in the case where the degree of certainty of the decision of the winner rule is low. These features make the developed FRBS a suitable tool for CHD diagnosis as it allows the physician not only to detect accurately the existence of CHD but also understand the relations between the factors and the CHD diagnosis. These relations may reveal unexpected findings and knowledge that can be used to detect the CHD existence at early stage which may result in significant life saving.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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