



Computer aided decision making for heart disease detection using hybrid neural network-Genetic algorithm



Zeinab Arabasadi^a, Roohallah Alizadehsani^{b,*}, Mohamad Roshanzamir^c, Hossein Moosaei^d, Ali Asghar Yarifard^a

^a Department of Computer Engineering, University of Bojnord, Bojnord, Iran

^b Department of Computer Engineering, Sharif University of Technology, Azadi Ave, Tehran, Iran

^c Department of Electrical and Computer Engineering, Isfahan University of Technology, Isfahan, Iran

^d Department of Mathematics, Faculty of Science, University of Bojnord, Iran

ARTICLE INFO

Article history:

Received 11 September 2016

Revised 18 December 2016

Accepted 12 January 2017

Keywords:

Cardiovascular disease

Coronary artery disease

Neural network

Genetic algorithm

ABSTRACT

Cardiovascular disease is one of the most rampant causes of death around the world and was deemed as a major illness in Middle and Old ages. Coronary artery disease, in particular, is a widespread cardiovascular malady entailing **high mortality rates**. Angiography is, more often than not, regarded as the best method for the diagnosis of coronary artery disease; on the other hand, it is associated with high costs and major side effects. Much research has, therefore, been conducted using machine learning and data mining so as to seek alternative modalities. Accordingly, we herein propose a highly accurate hybrid method for the diagnosis of coronary artery disease. As a matter of fact, the proposed method is able to **increase the performance of neural network by approximately 10% through enhancing its initial weights using genetic algorithm which suggests better weights for neural network**. Making use of such methodology, we achieved accuracy, sensitivity and specificity rates of 93.85%, 97% and 92% respectively, on **Z-Alizadeh Sani dataset**.

© 2017 Elsevier B.V. All rights reserved.

1. Introduction

Data mining refers to the extraction of valid patterns, hidden information and relationships from large datasets [1]. This interdisciplinary subfield is employed in banking, insurance, and marketing for **cost reduction and quality improvement** [2]. Recent years have witnessed a surge of interest in utilizing machine learning and data mining in the field of medicine for early diagnosis [3–10].

Cardiovascular disease is the most widespread cause of death the world over. Particularly, coronary artery disease (CAD) is the most common cardiovascular condition.

CAD occurs when **at least one of the left anterior descending (LAD), left circumflex (LCX), and right coronary (RCA) arteries is stenotic** [11].

In order to diagnose CAD, physicians currently employ different methods, among which angiography is widely regarded as the most precise method. It is, however, associated with high costs and major side effects, hence researchers have long sought to **devise precise diagnostic modalities**. In fact, a large number of in-

vestigations have been conducted in this field [12–34], with the **UCI datasets** [35] being the most frequently utilized sets. These datasets, however, are **not up-to-date**.

In the present study, given the **risks of invasive diagnostic procedures such as angiography** and auspicious experiences in the field of data mining, attempts were made to propose a model for identifying coronary arteries disease.

The suggested detection model, based on artificial neural networks and genetic algorithms, can detect coronary artery disease based on clinical data without the need for invasive diagnostic methods.

The present research primarily introduces the required background information; in the subsequent four sections, the proposed method, experimental results, related works and conclusions will be discussed.

2. Background

2.1. Dataset

The present research used Z- Alizadeh Sani dataset, containing information on 303 patients, 216 of whom suffered from CAD. **Fifty-four features** were collected for each patient. These features

* Corresponding author.

E-mail addresses: alizadeh_roohallah@yahoo.com, ro_alizadeh@alum.sharif.edu (R. Alizadehsani).

Table 1
Features of Z-Alizadeh Sani dataset.

Feature type	Feature name	Range
Demographic	Age	30–86
	Weight	48–120
	Sex	Male, Female
	BMI (Body Mass Index Kg/m ²)	18–41
	DM (Diabetes Mellitus)	Yes, No
	HTN (Hypertension)	Yes, No
	Current smoker	Yes, No
	Ex-smoker	Yes, No
	FH (Family History)	Yes, No
	Obesity	Yes if BMI > 25, No otherwise
	CRF (Chronic Renal Failure)	Yes, No
	CVA (Cerebrovascular Accident)	Yes, No
	Airway disease	Yes, No
	Thyroid disease	Yes, No
Symptom and examination	CHF (Congestive Heart Failure)	Yes, No
	DLP (Dyslipidemia)	Yes, No
	BP (Blood Pressure mm Hg)	90–190
	PR (Pulse Rate ppm)	50–110
	Edema	Yes, No
	Weak peripheral pulse	Yes, No
	Lung rales	Yes, No
	Systolic murmur	Yes, No
	Diastolic murmur	Yes, No
	Typical chest pain	Yes, No
	Dyspnea	Yes, No
	Function class	1, 2, 3, 4
	Atypical	Yes, No
	Nonanginal chest pain	Yes, No
ECG	Exertional chest pain	Yes, No
	Low Th Ang (low-Threshold angina)	Yes, No
	Rhythm	Sin, AF
	Q wave	Yes, No
	ST elevation	Yes, No
	ST depression	Yes, No
	T inversion	Yes, No
	LVH (Left Ventricular Hypertrophy)	Yes, No
Laboratory and echo	Poor R-wave progression	Yes, No
	FBS (Fasting Blood Sugar mg/dL)	62–400
	Cr (Creatine mg/dL)	0.5–2.2
	TG (Triglyceride mg/dL)	37–1050
	LDL (Low-Density Lipoprotein mg/dL)	18–232
	HDL (High-Density Lipoprotein mg/dL)	15–111
	BUN (Blood Urea Nitrogen mg/dL)	6–52
	ESR (Erythrocyte Sedimentation Rate mm/h)	1–90
	HB (Hemoglobin g/dL)	8.9–17.6
	K (Potassium mEq/lit)	3.0–6.6
	Na (Sodium mEq/lit)	128–156
	WBC (White Blood Cell cells/mL)	3700–18,000
	Lymph (Lymphocyte %)	7–60
	Neut (Neutrophil %)	32–89
	PLT (Platelet 1000/mL)	25–742
	EF (Ejection Fraction %)	15–60
	Region with RWMA	0,1,2,3,4
	VHD (Valvular Heart Disease)	Normal, Mild, Moderate, Severe

encompass the data on the patients' demographic characteristics, symptoms and the results of physical examinations, electrocardiography, echocardiography, and laboratory tests. These features are shown in Table 1. In this dataset, if at least one of the LAD, LCX, and RCA has a stenosis of higher than 50%, the patient is diagnosed with CAD.

2.2. Feature selection

For feature selection, four famous ranking methods were considered, namely Gini index, weight by SVM, information gain and principal component analysis (PCA). Gini Index shows the probability of incorrectly labeling a randomly chosen element according to the distribution of labels in the subset if it is randomly labeled [36]. Information Gain shows the expected reduction in entropy owing to partitioning records based on a given attribute [36]. In

weight by SVM, attribute weights are the coefficients of the normal vector of a linear SVM [37]. PCA converts a set of correlated variables into a smaller number of uncorrelated variables employing an orthogonal transformation [38].

Weight by SVM uses F-score so as to measure feature weights. If we have training instance x_i , and $i = 1, 2, \dots, L$ (L: Number of instances), the F-score of feature j is calculated as shown in Eq. (1). The higher the F-score, the more discriminative the feature will be [39].

$$F(j) = \frac{(\bar{x}_j^{(+)} - \bar{x}_j)^2 + (\bar{x}_j^{(-)} - \bar{x}_j)^2}{\frac{1}{n_+ - 1} \sum_{i=1}^{n_+} (x_{i,j}^{(+)} - \bar{x}_j^{(+)})^2 + \frac{1}{n_- - 1} \sum_{i=1}^{n_-} (x_{i,j}^{(-)} - \bar{x}_j^{(-)})^2} \quad (1)$$

where n_+ and n_- are the number of positive and negative samples, respectively. The j th feature average of the whole, and the positive-labeled and negative labeled samples are shown with

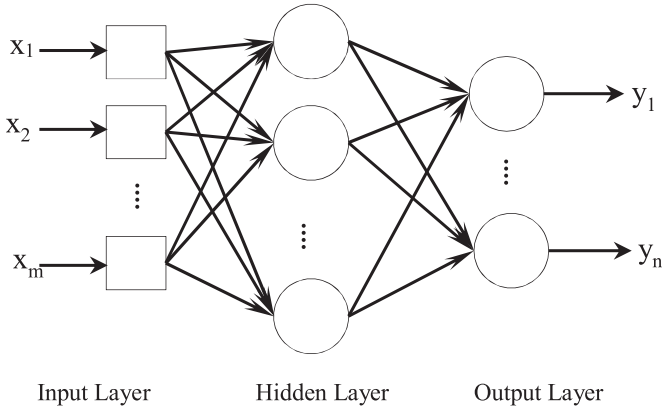


Fig. 1. The MLP structure of NN.

\bar{x}_j , $\bar{x}_j^{(+)}$, $\bar{x}_j^{(-)}$, respectively. The j th feature of the i th positive and negative instance are $x_{i,j}^{(+)}$ and $x_{i,j}^{(-)}$, respectively.

In this equation, the numerator shows the inter-class variance, with the denominator indicating the sum of the variance within each class.

2.3. Neural network

An artificial neural network is comprised of input variables, output variables and weights. The network behavior is dependent on the relationship between input and output variables. In general, there are three types of layers, each made of a number of processing units called neurons (cells, units or nodes):

The first layer is the input layer which receives the raw data fed into the network.

The second layer is the hidden layer. There may be several hidden layers depending on the structure of the neural network. The performance of a hidden layer is determined by inputs and their relationship with other hidden layers. The weights of input and hidden units determine the activation time of a hidden unit.

The last layer is the output layer. The performance of output layer depends on the activity of hidden layers and the weights of hidden and output units [40]. The number of layers and neurons in each layer is specified by the designer throughout the process of trial and error.

There exists many methods to train networks and modify weights in order to achieve minimum error, the most common of which is error back propagation algorithm [40]. Based on their structures, artificial neural networks are divided into two main groups: Multi-layer perceptron (MLP) and radial bases function (RBF).

In the present work, as illustrated in Fig. 1, we made use of error back propagation algorithm in artificial neural network with MLP structure and sigmoid exponential function.

In each iteration of the neural network training phase, the weights of connections are updated according to Eq. (2).

$$w_{ji} = w_{ji} + \eta \delta_j x_{ji} \quad (2)$$

where x_{ji} is the i th input to unit j , w_{ji} is the weight associated with the i th input to unit j , and η is the learning rate. If w is the weight of the output layer units, δ is updated as Eq. (3) while, if w is the weight of the hidden layer units, δ is updated as Eq. (4).

$$\delta_k = o_k(1 - o_k)(t_k - o_k) \quad (3)$$

$$\delta_h = o_h(1 - o_h) \sum_{k \in \text{Outputs}} w_{kh} \delta_k \quad (4)$$

where o_k and o_h are the outputs generated by output unit k and hidden unit h , respectively, and t_k is the target output of unit k . k is between 1 and the number of output layer units while h is between 1 and the number of hidden layer units [40].

The mathematical form of the sigmoid function for the transfer of data to the output layer is as follows:

$$F(n) = \frac{1}{1 + e^{-n}} \quad (5)$$

To assess the results of artificial neural network models and compare the outcomes with the observed values, the following statistical parameters were utilized:

$$R^2 = \frac{\sum \{(X_{est} - \bar{X}_{est}) \times (X_{obs} - \bar{X}_{obs})\}}{\sqrt{\sum (X_{est} - \bar{X}_{est})^2 \times \sum (X_{obs} - \bar{X}_{obs})^2}} \quad (6)$$

$$RSME = \sqrt{\frac{\sum (X_{obs} - X_{est})^2}{n}} \quad (7)$$

In the above equations, X_{obs} is refers to the actual values, X_{est} is the values estimated from the model, \bar{X}_{obs} is the mean real values, \bar{X}_{est} is the mean estimated values of the model network and n is the number of samples. R^2 demonstrates the correlation between empirical and estimated data, i.e. values close to one, indicating higher correlation between the empirical and estimated data. RMSE shows the root mean square error. Unlike R^2 , it is more preferable that RMSE be closer to zero.

2.4. Genetic algorithm

Genetic algorithm, first put forth by John Holland, is a method for finding approximate solutions to optimization and search issues. Such algorithm is a specific form of evolutionary algorithms in which evolutionary biology techniques such as inheritance and mutation are used. In genetic algorithms, to obtain the optimal solution, the appropriate responses of a generation are combined based on the principle of the survival of the fittest in living organisms [41].

2.4.1. Basic operations of genetic algorithm

In genetic algorithms, so as to combine the qualified members of the current generation with the aim of probably producing more qualified members, a number of operators are employed [41], among which, the following can be made mention of:

Selection operator: In this operator, based on the fitness criterion, a member of a generation which is supposed to participate in the reproduction process is selected. In this operator, the members of the current generation with more compatibility are more likely to generate the next population. There are certain selection operators such as roulette wheel (RW) and stochastic universal sampling (SUS) in genetic algorithm [42]. In the former, also known as fitness proportionate selection, the selection probability of each individual is calculated as Eq. (8).

$$p_i = \frac{f_i}{\sum_{k=1}^N f_k} \quad (8)$$

where p_i shows the probability of individual i selection, f_i shows the fitness of individual i and N is the number of individuals in the population.

Substitution operator: This operator conduces to the propagation and transfer of members from one generation to the next.

Recombination operator: Using this operator, the substrings of two members belonging to a chosen generation are substituted in each other in an intersectional manner. There exist some approaches for recombination such as single-point crossover, two-point crossover and uniform crossover [43].

Table 2

Weights assigned to selected features using weight by SVM.

Feature	Weight
Typical chest pain	1.0
Atypical	0.88
Age	0.88
Nonanginal	0.58
DM	0.44
Tinversion	0.44
FH	0.42
Region RWMA	0.40
HTN	0.40
TG	0.35
PR	0.33
Diastolic murmur	0.32
Current smoker	0.31
Dyspnea	0.31
ESR	0.29
BP	0.27
Function class	0.25
Sex	0.24
FBS	0.24
St depression	0.23
St elevation	0.21
Q wave	0.20

Table 3

Neural network performance with different numbers of hidden neurons.

Number of neuron	RMSE Train set	R ²
3	0.58	0.8015
4	0.57921	0.88275
5	0.257	0.94581
6	0.464	0.89625
7	0.35	0.86984
8	0.4581	0.90441

Mutation operator: This operator is used to make changes in the genes of a member of the current generation in order to produce a new member. **Boundary operator, uniform and non-uniform operator and Gaussian operator** are among the mutation methods [43]. In Gaussian operator, a random value from the normal distribution is added to the selected gene. If $x \in [a, b]$ is the gene chosen for mutation, it is changed to x' according to Eq. (9).

$$x' = \min(\max(N(x, \sigma), a), b) \quad (9)$$

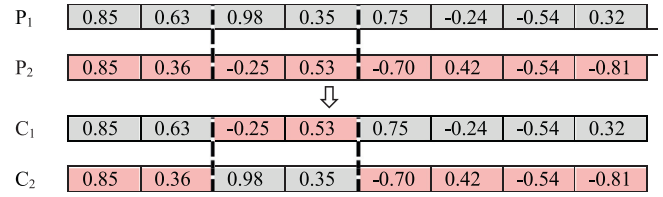
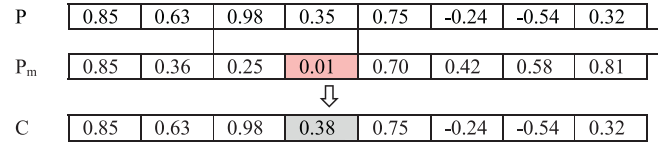
where σ depend on the length of interval or time.

3. Proposed method

One of the factors affecting the performance of artificial neural network is the initial weights utilized in the network structure. In this regard, the proposed model sought to ameliorate the performance of neural network through enhancing the primary weights used in it.

In this study, the **initial weights of neural network were identified via genetic algorithm**. Then, the neural network was learned using training data. In the neural network, we employed feed forward structure with one hidden layer. Inputs are features shown in Table 2, and the output pertains to disease diagnosis. We have **22 inputs, 5 neurons in one hidden layer and one output specifying whether or not the patient has CAD**. As it is shown in Table 3, five hidden neurons are chosen as it has the best performance on our training data.

In genetic algorithm, at first, 100 chromosomes were produced in an aleatory fashion. Then, their **fitness function is calculated according to the RMSE of the untrained neural network output**. It must be noted that, in this research, we were looking for the

**Fig. 2.** Two-point crossover. P_1 and P_2 are the selected parents while C_1 and C_2 are the generated children.**Fig. 3.** Gaussian mutation. P is the selected parent. P_m is the mutation probability and C is the generated child.

minimum RMSE. For parent selection, RW method was used and for substitution, we selected 10% of the best individuals from the current generation and supplanted them with the worst individual belonging to the next generation. For recombination, two-point crossover was used with $P_c = 1$, meaning that recombination was done in each iteration. A simple two-point crossover is demonstrated in Fig. 2.

For mutation, **Gaussian operator was used. Each gene mutated with probability $P_m = 0.2$** . A simple mutation is shown in Fig. 3. **Weights change between -1 and 1 while σ is 1 .**

Each gene shows one weight of the Neural Network and a chromosome consists of all the Neural Network weights.

The proposed algorithm, named “Hybrid CAD prediction method”, is shown in Fig. 4.

4. Results

4.1. Feature selection results

For feature selection, we used weight by SVM as it has the best performance on the training data. Table 2 illustrates the results. We selected the features which weights were more than 0.20 as they indicated the highest performance on the training data.

4.2. Classification results

Table 4 compares the results related to the application of Neural Network and the proposed method to Z-Alidadeh Sani dataset using **10-fold cross validation**. As observed, our proposed method has a much better performance comparisons to Neural Network. Receiver operating characteristic (ROC) curve of standard neural network and Hybrid CAD prediction methods are shown in Figs. 5 and 6 respectively.

Sensitivity, specificity and accuracy are calculated according to Eqs. (10)–(12).

$$\text{Sensitivity} = \frac{TP}{TP + FN} \quad (10)$$

$$\text{Specificity} = \frac{TN}{TN + FP} \quad (11)$$

$$\text{Accuracy} = \frac{TN + TP}{TN + TP + FN + FP} \quad (12)$$

where TP, FP, TN and FN are the mean number of samples correctly identified, incorrectly identified, correctly rejected and incorrectly rejected respectively.

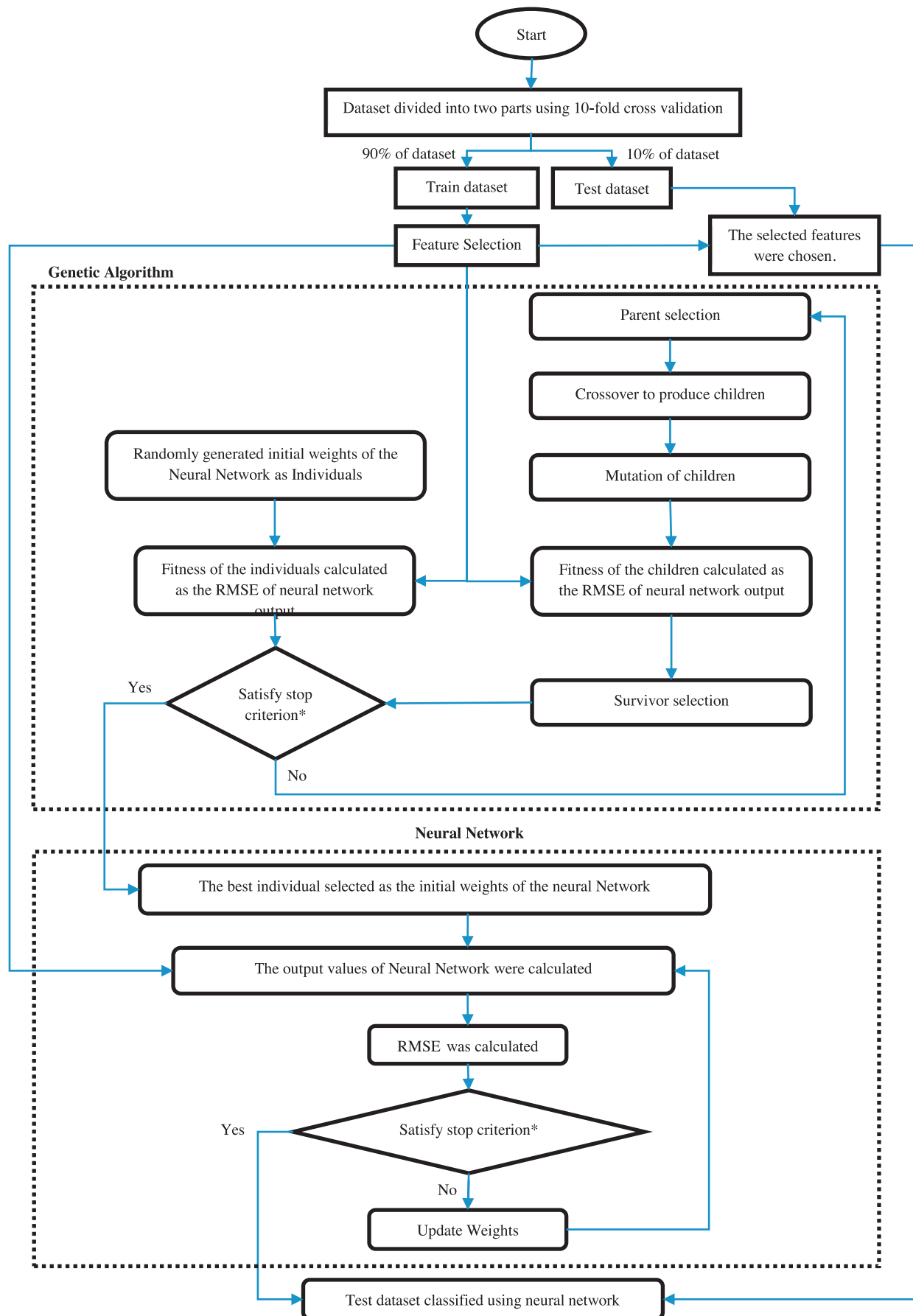
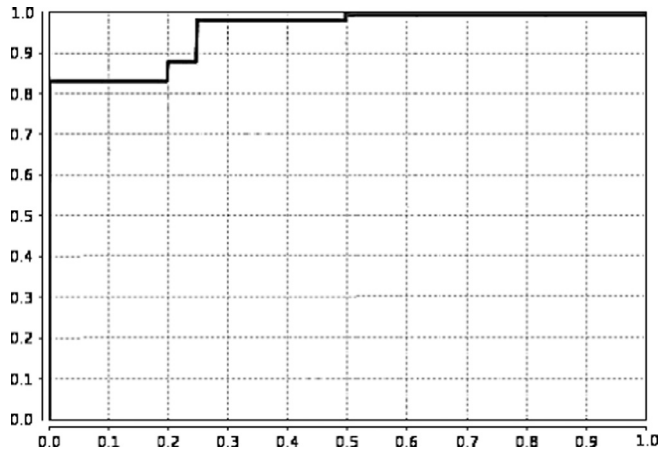
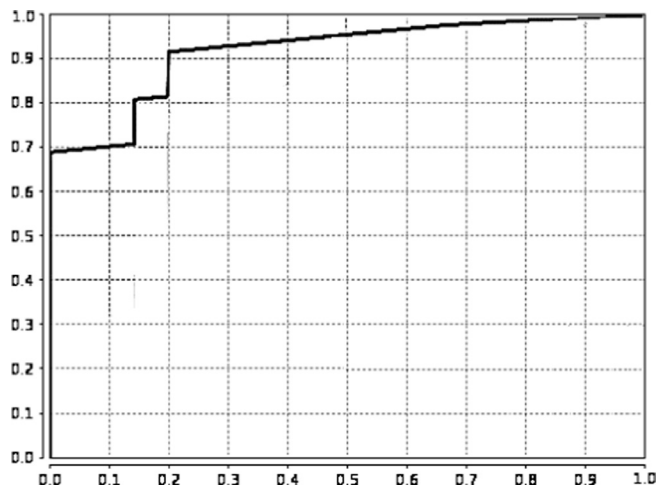


Fig. 4. Hybrid CAD prediction method.
 * 1000 iterations are done or RMSE is <0.001 .

Table 4

The comparison between the performance of our proposed method and classic neural network on Z-Alizadeh Sani dataset.

	Sensitivity %	Specificity %	Accuracy %	FPR	TPR
Proposed method (Genetic + NN)	97	92	93.85	0.08	0.97
NN	86	83	84.62	0.17	0.86

**Fig. 5.** ROC curve of standard neural network.**Fig. 6.** ROC curve of Hybrid CAD prediction method.

4.3. Results of the proposed method on other datasets

In this section, so as to compare the performance of our proposed method with neural network, we present the results pertaining to their application to four famous heart disease datasets: Hungarian, Cleveland, long-beach-va and Switzerland datasets [35], which have 294, 303, 200 and 123 samples respectively. In those datasets, a total of 14 attributes are presented: Age, sex, chest pain type, resting blood pressure, serum cholesterol in mg/dl, fasting blood sugar, resting electrocardiographic results, the obtained maximum heart rate, exercise-induced angina, ST depression, the slope of peak exercise ST-segment, the number of major vessels, thal and heart disease diagnosis.

Table 5 summarizes the performance of the proposed method and Neural Network on these datasets. As seen, our proposed method indubitably augments the performance of the neural network.

Table 5

Experimental results related to other datasets.

Datasets	Methods	Sensitivity %	Specificity %	Accuracy %
Hungarian dataset	Proposed method	85	88	87.1
	NN	76	86	82.9
Cleveland dataset	Proposed Method	88	91	89.4
	NN	81	88	84.8
long-beach-va dataset	Proposed method	93	33	78.0
	NN	91	25	74.0
Switzerland dataset	Proposed method	78	50	76.4
	NN	75	25	71.5

5. Discussion of the related works

As mentioned in Section 1, researchers have employed various methods in detecting and predicting CAD. More often than not, these studies made use of Electrocardiogram (ECG) signals. In [44], for instance, multilayer perceptron indicated a high accuracy for detecting CAD.

Acharya et al. [45] employed KNN algorithm for classification using 13 bispectrum features. In [46], Kumar et al. used the ECG signals of 40 normal and seven CAD subjects. These signals were segmented into beats which were further decomposed via flexible analytic wavelet transform. For classification, least squares support vector machine and radial basis function kernel were utilized.

Patidar et al. [47] put forth a novel method based on tunable Q wavelet transform in order to diagnose CAD, using heart rate signals. A novel CAD risk index was also proposed to detect CAD subjects. PCA was applied to the extracted features so as to transform the number of features; finally, least squares support vector machine classifier was employed for CAD detection.

In [48], for CAD diagnosis, wavelet analysis and artificial neural networks were used to analyze the heart sounds recorded synchronously with ECG. As far as CAD diagnosis, Zhao et al. [49] proposed an intelligent noninvasive diagnosis system based on Empirical Mode Decomposition-Teager Energy Operator to estimate instantaneous frequency of diastolic murmurs and Back-Propagation neural network to classify the murmurs.

Giri et al. [50] employed ten features from the data related to the full time series heart rate. They showed that the Gaussian Mixture Model classifier had a better performance in comparison with Principal Component Analysis (PCA), Linear Discriminant Analysis (LDA) and Independent Component Analysis (ICA).

To automate CAD detection, Acharya et al. [51] extracted the heart rate from the ECG signals and used them as the base signal for further analysis. They further analyzed the heart rate signals of both normal and CAD subjects in the time and frequency domain.

In [52], where heart rate variability signals were used, Least Squares-Support Vector Machine, Morlet wavelet and Radial Basis Function kernels were proven to have the highest classification accuracy in as far as CAD diagnosis.

In [44], nonlinear features were extracted from the HRV signals using recurrence plots, Poincare plots, and detrended fluctuation analysis. Principal component analysis was conducted in order to select the important features which were later appraised making use of eight classification techniques, among which, multilayer perceptron method had the highest classification accuracy.

In [45], Higher-Order Statistics and Spectra bispectrum and cumulant features were extracted from each ECG beat. Principal Component Analysis was done in order to reduce the dimension. After that, Principal Component Analysis coefficients were ranked through such different methods as Bhattacharyya and entropy methods. K-Nearest Neighbors and Decision Tree methods showed the highest classification performance.

Using Demographic, Symptom and Examination, ECG, Laboratory and Echo features, Alizadehsani et al. [37] diagnosed the stenosis of three major coronary arteries, separately. In [53], binary particle swarm optimization and genetic algorithm techniques were used for feature selection. Support vector machine with k-fold cross-validation was used as the classification method. They utilized 23 features obtained from patients who had undergone exercise stress test and coronary angiography.

Arafat et al. [54] used combined uncertainty methods, which compute a fuzzy-probabilistic composite, and ECG signals in their detection of CAD. Subsequently, for classification, they employed three model examples computing fuzzy, probabilistic, and combined uncertainty models. Combined uncertainty model entailed better results compared with using only fuzzy or probabilistic models.

In [55], a suitable prediction model was proposed to improve the reliability of medical examinations and CAD treatments. From ECG signals, linear and nonlinear features of HRV were extracted. Six different classification methods were then used, among which SVM outperformed the other classifiers.

Through various linear and nonlinear measures of HRV, Kim et al. [56] proposed a multiple discriminant analysis method for CAD detection. In [57], a methodology for the automatic diagnosis of CAD was proposed via extracting HRV signals from ECG in time, frequency and nonlinear domains. PCA was employed in order to reduce the dimension in the extracted features, while for classification, SVM was used.

Acharya et al. [58] employed Discrete Cosine Transform, Discrete Wavelet Transform and Empirical Mode Decomposition extracted from ECG signals so as to obtain the respective features which were further reduced using Locality Preserving Projection. These features were then ranked using F-value. The high ranked features were used as inputs for the K-Nearest Neighbor classifier.

Verma et al. [59] presented a novel hybrid method where for feature selection, particle swarm optimization search method and K-means clustering algorithms were used. They finally employed supervised learning algorithms such as multi-layer perceptron, multinomial logistic regression, fuzzy unordered rule induction algorithm and C4.5 for classification.

6. Conclusion and future works

We proposed a new hybrid method to augment the performance of neural network. The method was tested on some heart disease datasets so as to check any improvement in its performance. The method put forth can ameliorate the performance of neural network as concerns CAD detection. Specifically, using this method, CAD can be detected without angiography which can help eliminate high costs and major side effects.

In addition to genetic algorithm, there exist many powerful evolutionary and swarm intelligence methods such as evolution strategy and particle swarm optimization. As the future works, we can use these methods instead of genetic algorithm as they may enhance the performance of our proposed method.

Meanwhile, other versions of neural networks can be tested and compared. **Parameters like learning rate, and momentum factor can also be optimized for this work.**

Finally, new data with some other features must be checked by this algorithm.

References

- [1] P.-N. Tan, Introduction to Data Mining, Pearson Education, India, 2006.
- [2] I.H. Witten, E. Frank, Data Mining: Practical Machine Learning Tools and Techniques, Morgan Kaufmann, 2005.
- [3] U.R. Acharya, O. Faust, N.A. Kadri, J.S. Suri, W. Yu, Automated identification of normal and diabetes heart rate signals using nonlinear measures, *Comput. Biol. Med.* 43 (2013) 1523–1529.
- [4] C. Barbieri, F. Mari, A. Stopper, E. Gatti, P. Escandell-Montero, J.M. Martínez-Martínez, J.D. Martín-Guerrero, A new machine learning approach for predicting the response to anemia treatment in a large cohort of end stage renal disease patients undergoing dialysis, *Comput. Biol. Med.* 61 (2015) 56–61.
- [5] L. Hu, G. Hong, J. Ma, X. Wang, H. Chen, An efficient machine learning approach for diagnosis of paraquat-poisoned patients, *Comput. Biol. Med.* 59 (2015) 116–124.
- [6] B. Robson, S. Boray, Implementation of a web based universal exchange and inference language for medicine: sparse data, probabilities and inference in data mining of clinical data repositories, *Comput. Biol. Med.* 66 (2015) 82–102.
- [7] S.A. Izad Shenaz, B. Raahemi, M. Hossein Tekieh, C. Kuziemy, Identifying high-cost patients using data mining techniques and a small set of non-trivial attributes, *Comput. Biol. Med.* 53 (2014) 9–18.
- [8] V.K. Sudarshan, U.R. Acharya, E.Y.K. Ng, R.S. Tan, S.M. Chou, D.N. Ghista, Data mining framework for identification of myocardial infarction stages in ultrasound: a hybrid feature extraction paradigm (Part 2), *Comput. Biol. Med.* 71 (2016) 241–251.
- [9] P. Gifani, H. Behnam, Z.A. Sani, Noise reduction of echocardiographic images based on temporal information, *IEEE Trans. Ultrason. Ferroelectr. Freq. Control.* 61 (2014) 620–630.
- [10] Z. Alizadeh Sani, A. Shalhaf, H. Behnam, R. Shalhaf, Automatic computation of left ventricular volume changes over a cardiac cycle from echocardiography images by nonlinear dimensionality reduction, *J. Digit. Imaging* 28 (2015) 91–98.
- [11] R.O. Bonow, D.L. Mann, D.P. Zipes, P. Libby, Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine, ninth ed., Elsevier Science, 2011.
- [12] I. Maglogiannis, E. Loukis, E. Zafropoulos, A. Stasis, Support vectors machine-based identification of heart valve diseases using heart sounds, *Comput. Methods. Programs. Biomed.* 95 (2009) 47–61.
- [13] R. Alizadehsani, J. Habibi, M.J. Hosseini, H. Mashayekhi, R. Boghrati, A. Ghandeharioun, B. Bahadorian, Z.A. Sani, A data mining approach for diagnosis of coronary artery disease, *Comput. Methods. Programs. Biomed.* 111 (2013) 52–61.
- [14] R. Alizadehsani, J. Habibi, B. Bahadorian, H. Mashayekhi, A. Ghandeharioun, R. Boghrati, Z.A. Sani, Diagnosis of coronary arteries stenosis using data mining, *J. Med. Signals Sensors* 2 (2012) 153–159.
- [15] I. Babaoglu, O.K. Baykan, N. Aygul, K. Ozdemir, M. Bayrak, Assessment of exercise stress testing with artificial neural network in determining coronary artery disease and predicting lesion localization, *Expert Syst. Appl.* 36 (2009) 2562–2566.
- [16] I. Babaoglu, O. Findik, M. Bayrak, **Effects of principle component analysis on assessment of coronary artery diseases using support vector machine**, *Expert Syst. Appl.* 37 (2010) 2182–2185.
- [17] C.-M. Chu, W.-C. Chien, C.-H. Lai, H.B. Bludau, H.-J. Tschai, L. Pai, S.-M. Hsieh, N.F. Chu, A. Klar, R. Haux, **A Bayesian expert system for clinical detecting coronary artery disease**, *J. Med. Sci.* 29 (2009) 187–194.
- [18] R. Das, I. Turkoglu, A. Sengur, **Effective diagnosis of heart disease through neural networks ensembles**, *Expert Syst. Appl.* 36 (2009) 7675–7680.
- [19] D. Itchhaporia, R. Almassy, L. Kaufman, P. Snow, W. Oetgen, **Artificial neural networks can predict significant coronary disease**, *J. Am. Coll. Cardiol.* 25 (1995) 328.
- [20] S. Kara, F. Dirgenali, A system to diagnose atherosclerosis via wavelet transforms, principal component analysis and artificial neural networks, *Expert Syst. Appl.* 32 (2007) 632–640.
- [21] M.A. Karaolis, J.A. Moutiris, D. Hadjipanayi, C.S. Pattichis, Assessment of the risk factors of coronary heart events based on data mining with decision trees, *Trans. Info. Tech. Biomed.* 14 (2010) 559–566.
- [22] N. Lavesson, A. Halling, M. Freitag, J. Odeberg, H. Odeberg, P. Davidsson, Classifying the severity of an acute coronary syndrome by mining patient data, in: The Swedish AI Society Workshop, Linköping University Electronic Press, May 27–28, 2009, pp. 55–63.
- [23] N. Lavrač, Selected techniques for data mining in medicine, *Artif. Intel. Med.* 16 (1999) 3–23.
- [24] H.G. Lee, K.Y. Noh, K.H. Ryu, A data mining approach for coronary heart disease prediction using HRV features and carotid arterial wall thickness, in: Proceedings of International Conference on BioMedical Engineering and Informatics, IEEE Computer Society, 2008, pp. 200–206.
- [25] C. Ordóñez, E. Omiecinski, L.d. Braal, C.A. Santana, N. Ezquerro, J.A. Taboada, D. Cooke, E. Krawczynska, E.V. García, Mining constrained association rules to predict heart disease, in: Proceedings of IEEE International Conference on Data Mining, IEEE Computer Society, 2001, pp. 433–440.
- [26] C.E. Pedreira, L. Macrini, E.S. Costa, **Input and data selection applied to heart disease diagnosis**, in: Proceedings of IEEE International Joint Conference on Neural Networks, 2005, pp. 2389–2393.
- [27] K. Polat, S. Güneş, A hybrid approach to medical decision support systems: combining feature selection, fuzzy weighted pre-processing and AIRS, *Comput. Methods. Programs. Biomed.* 88 (2007) 164–174.

- [28] K. Polat, S. Şahan, S. Güneş, Automatic detection of heart disease using an artificial immune recognition system (AIRS) with fuzzy resource allocation mechanism and k-nn (nearest neighbour) based weighting preprocessing, *Expert Syst. Appl.* 32 (2007) 625–631.
- [29] A. Rajkumar, G.S. Reena, Diagnosis of heart disease using datamining algorithm, *Global J. Comput. Sci. Technol.* 10 (2010) 38–43.
- [30] M. Shouman, T. Turner, R. Stocker, Using decision tree for diagnosing heart disease patients, in: *Proceedings of the Ninth Australasian Data Mining Conference*, Australian Computer Society, Inc., Ballarat, Australia, 2011, pp. 23–30.
- [31] J. Soni, U. Ansari, D. Sharma, S. Soni, Predictive data mining for medical diagnosis: an overview of heart disease prediction, *Int. J. Comput. Appl.* 17 (2011) 43–48.
- [32] K. Srinivas, B.K. Rani, A. Govrdhan, Applications of data mining techniques in healthcare and prediction of heart attacks, *Int. J. Comput. Sci. Eng. (IJCSE)* 2 (2010) 250–255.
- [33] M.G. Tsipouras, T.P. Exarchos, D.I. Fotiadis, A.P. Kotsia, K.V. Vakalis, K.K. Naka, L.K. Michalis, Automated diagnosis of coronary artery disease based on data mining and fuzzy modeling, *Trans. Info. Tech. Biomed.* 12 (2008) 447–458.
- [34] U.R. Acharya, S.V. Sree, M.M.R. Krishnan, N. Krishnananda, S. Ranjan, P. Umesh, J.S. Suri, Automated classification of patients with coronary artery disease using grayscale features from left ventricle echocardiographic images, *Comput. Methods. Programs. Biomed.* 112 (2013) 624–632.
- [35] C. Blake, C. Merz, *UCI Repository of Machine Learning Databases*, University of California, Department of Information and Computer Science, Irvine, CA, 1998.
- [36] T. Pang-Ning, M. Steinbach, V. Kumar, *Introduction to Data Mining*, Pearson Addison Wesley, Boston, MA, 2006.
- [37] R. Alizadehsani, M.H. Zangooei, M.J. Hosseini, J. Habibi, A. Khosravi, M. Roshanzamir, F. Khozeimeh, N. Sarrafzadegan, S. Nahavandi, Coronary artery disease detection using computational intelligence methods, *Knowl.-Based Syst.* 109 (2016) 187–197.
- [38] K. Fukunaga, *Introduction to Statistical Pattern Recognition*, Academic press, 2013.
- [39] Y.-W. Chen, C.-J. Lin, **Combining SVMs with various feature selection strategies, in: Feature Extraction: Foundations and Applications**, 2006, pp. 315–324.
- [40] T.M. Mitchell, *Machine Learning*, first ed., McGraw-Hill, Boston, 1997 (Chapter 4).
- [41] T.M. Mitchell, *Machine Learning*, first ed., McGraw-Hill, Boston, 1997 (Chapter 9).
- [42] A.E. Eiben, J.E. Smith, *Introduction to Evolutionary Computing*, Springer, 2003.
- [43] C. Heitzinger, *Simulation and Inverse Modeling of Semiconductor Manufacturing Processes*, eingereicht an der Technischen Universität Wien, 2002.
- [44] S. Dua, X. Du, S.V. SREE, V.I. Thajudin Ahamed, Novel classification of coronary artery disease using heart rate variability analysis, *J. Mech. Med. Biol.* 12 (2012) 1240017.
- [45] U.R. Acharya, V.K. Sudarshan, J.E.W. Koh, R.J. Martis, J.H. Tan, S.L. Oh, A. Muhammad, Y. Hagiwara, M.R.K. Mookiah, K.P. Chua, C.K. Chua, R.S. Tan, Application of higher-order spectra for the characterization of Coronary artery disease using electrocardiogram signals, *Biomed. Signal Process. Control* 31 (2017) 31–43.
- [46] M. Kumar, R.B. Pachori, U.R. Acharya, Characterization of coronary artery disease using flexible analytic wavelet transform applied on ECG signals, *Biomed. Signal Process. Control* 31 (2017) 301–308.
- [47] S. Patidar, R.B. Pachori, U. Rajendra Acharya, Automated diagnosis of coronary artery disease using tunable-Q wavelet transform applied on heart rate signals, *Knowl.-Based Syst.* 82 (2015) 1–10.
- [48] M. Karimi, R. Amirfattahi, S. Sadri, S.A. Marvasti, Noninvasive detection and classification of coronary artery occlusions using wavelet analysis of heart sounds with neural networks, in: *The 3rd IEE International Seminar on Medical Applications of Signal Processing*, 2005, pp. 117–120.
- [49] Z. Zhao, C. Ma, An intelligent system for noninvasive diagnosis of coronary artery disease with EMD-TEO and BP neural network, in: *International Workshop on Education Technology and Training*, 2008, pp. 631–635.
- [50] D. Giri, U. Rajendra Acharya, R.J. Martis, S. Vinitha Sree, T.-C. Lim, T. Ahamed Vi, J.S. Suri, Automated diagnosis of coronary artery disease affected patients using LDA, PCA, ICA and discrete wavelet transform, *Knowl.-Based Syst.* 37 (2013) 274–282.
- [51] U.R. Acharya, O. Faust, V. Sree, G. Swapna, R.J. Martis, N.A. Kadri, J.S. Suri, Linear and nonlinear analysis of normal and CAD-affected heart rate signals, *Comput. Methods. Programs. Biomed.* 113 (2014) 55–68.
- [52] M. Kumar, R.B. Pachori, U. Rajendra Acharya, An efficient automated technique for CAD diagnosis using flexible analytic wavelet transform and entropy features extracted from HRV signals, *Expert Syst. Appl.* 63 (2016) 165–172.
- [53] İ. Babaoglu, O. Findik, E. Ülker, **A comparison of feature selection models utilizing binary particle swarm optimization and genetic algorithm in determining coronary artery disease using support vector machine**, *Expert Syst. Appl.* 37 (2010) 3177–3183.
- [54] S. Arafat, M. Dohrmann, M. Skubic, Classification of coronary artery disease stress ECGs using uncertainty modeling, in: *ICSC Congress on Computational Intelligence Methods and Applications*, 2005, p. 4.
- [55] H.G. Lee, K.Y. Noh, K.H. Ryu, A data mining approach for coronary heart disease prediction using HRV features and carotid arterial wall thickness, in: *International Conference on BioMedical Engineering and Informatics*, 2008, pp. 200–206.
- [56] W.-S. Kim, S.-H. Jin, Y.K. Park, H.-M. Choi, A study on development of multi-parametric measure of heart rate variability diagnosing cardiovascular disease, in: *World Congress on Medical Physics and Biomedical Engineering*, Berlin, Heidelberg, 2007, pp. 3480–3483.
- [57] A. Davari Dolatabadi, S.E.Z. Khadem, B.M. Asl, **Automated diagnosis of coronary artery disease (CAD) patients using optimized SVM**, *Comput. Methods. Programs. Biomed.* 138 (2017) 117–126.
- [58] U.R. Acharya, H. Fujita, M. Adam, O.S. Lih, V.K. Sudarshan, T.J. Hong, J.E.W. Koh, Y. Hagiwara, C.K. Chua, C.K. Poo, T.R. San, Automated characterization and classification of coronary artery disease and myocardial infarction by decomposition of ECG signals: a comparative study, *Inf. Sci.* 377 (2017) 17–29.
- [59] L. Verma, S. Srivastava, P.C. Negi, A hybrid data mining model to predict coronary artery disease cases using non-invasive clinical data, *J. Med. Syst.* 40 (2016) 178.