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# A NOVEL HYBRID CLASSIFICATION METHOD WITH PARTICLE SWARM OPTIMIZATION AND K-NEAREST NEIGHBOR ALGORITHM FOR DIAGNOSIS OF CORONARY ARTERY DISEASE USING EXERCISE STRESS TEST DATA

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Abstract. *The aim of this study is to investigate the effectiveness of a novel hybrid method, particle swarm optimization with k-nearest neighbor classifier (PSOkNN), on determination of coronary artery disease (CAD) existence upon exercise stress testing (EST) data. The PSOkNN method is composed of two steps. At the first step, one particle which demonstrates the whole samples optimally in training dataset is generated for both healthy and unhealthy patients. Then, at the second one, the class of the test sample is determined according to the distance of the test sample to the generated particles utilizing k-nearest neighbor algorithm. To demonstrate the effectiveness of this novel method, the results of PSOkNN are compared with the classification results of the artificial immune recognition system and k-nearest neighbor algorithm. Besides, reliability of the proposed method on determination of CAD existence upon EST data is examined by using classification accuracy, k-fold cross-validation method and Cohen's kappa coefficient.*

**Keywords:** Coronary artery disease, Exercise stress testing, Particle swarm optimization, Artificial immune recognition system

1. **Introduction.** Developing new insights for researchers, artificial intelligence and machine learning techniques are considered as the best available methods for development due to their common usage. Especially the studies carried out for the diagnosis in medical field are used effectively as a supplementary tool for the conventional methods due to their advantages in terms of speed or cost.

Considering widespread application of artificial intelligence and machine learning techniques in the diagnosis of heart diseases, several successful studies focusing on the diagnosis of the heart valve diseases were carried out in the past decade [1-6]. Artificial neural network (ANN) [1,2], support vector machine (SVM) [3-5] and hidden Markov model [6] methods were used in these studies regarding heart valve diseases which were certainly diagnosed by echocardiography, and these studies were usually intended for the classification of the signals obtained by using devices like Doppler. In addition to the studies regarding heart valve diseases, it is possible to reach many others evaluating the diagnosis of the arrhythmias [7-10]. These studies, in which SVM [7], ANN [8], artificial immune recognition system (AIRS) [9-11] and probabilistic artificial neural network methods were used as the classifiers, were implemented by being devoted to classifying the signals obtained from the electrocardiography device with the help of pre-processing and post-processing techniques.

Coronary artery disease (CAD), which is defined as a significant stenosis at least in a major epicardial coronary artery, is the leading cause of death among both men and women worldwide. In the literature, there are some studies relating to the diagnosis of CAD, employing different methods on various data. Zhao [12] proposed a method to diagnose CAD as non-invasive based on the instantaneous frequency estimation of diastolic murmurs. The author used SVM as the classifier. Kurt et al. [13] used demographic and medical data in order to predict the presence of CAD and compared the performances of some machine learning approaches including logistic regression, classification and regression tree, multi-layer perceptron, radial basis function and self-organizing feature maps. Scott et al. [14] used clinical, exercise and imaging data in order to predict the presence of CAD by using ANN. Mobley et al. [15-17] studied on the ANN method and designed ANN models to predict coronary stenosis among men and women based on demographic and medical data. Antanavicius et al. [18] proposed a computerized system for the diagnosis of CAD based on the descriptors obtained from the electrocardiographical data including nonlinear dynamics descriptors, recurrences percentage, mutual information, fractal dimension and embedding dimension error.

Although many diagnostic tools are used to diagnose CAD, exercise stress test (EST) is the most commonly preferred method for the diagnosis of CAD by cardiologist. It is a non-invasive, inexpensive, easily operable, safe and reproducible method. Nonetheless, relatively low sensitivity and specificity of EST for diagnosing CAD has led to a limitation in its clinical usage [19,20].

Most researchers did not use EST in the diagnosis of CAD in the machine learning approach; they preferred ECG, demographic and medical data in their experiments. Due to relatively low sensitivity and specificity of EST for diagnosing CAD conventionally, this study aims to improve the classification accuracy of the diagnosis of CAD by implementing a novel hybrid method, particle swarm optimization with k-nearest neighbor classifier (PSOkNN), as well as k-nearest neighbor algorithm (kNN) and AIRS.

## 2. Materials and Methods.

**2.1. Data collection.** Four hundred and eighty patients who underwent EST and coronary angiography (CAG) were included in the study. Baseline demographic characteristics, rest and peak exercise heart rate, blood pressure, and exercise time were recorded. The EST results were evaluated by 2 experienced cardiologists (human-based CAD assessment). ST segment depression and elevation occurred 60 ms after the J point were recorded at each derivation in peak exercise. According to human-based method, an exercise test result was considered positive if there was $\geq 1$ mm horizontal or downsloping ST depression or ST elevation in two contiguous leads. Within the first month following the EST, CAG was performed to all patients, and the angiographic images were evaluated by 2 experienced cardiologists. Presence of $\geq 50\%$ narrowing in left main coronary artery, or $\geq 70\%$ narrowing in other major epicardial coronary arteries indicated significant CAD. The patients with bundle branch blocks (right or left), pre-excitation syndromes, atrial fibrillation, left ventricular hypertrophy and those taking the digoxin were excluded from the study. The EST dataset was obtained from Selçuk University Meram Faculty of Medicine and the descriptive features of the dataset are ST state changes and heart rate at resting, age, sex, peak stage (1 to 5), exercise duration (in seconds), heart rate at peak stage, metabolic equivalent, reason for termination (target heart rate, ST depression or others), chest pain, previous myocardial infarction and values of the 12 derivations (D1, D2, D3, aVR, aVL, aVF, V1, V2, V3, V4, V5, V6) at peak stage which obtained from the EST, and presence of coronary artery disease which obtained from CAG.

2.2. **Particle swarm optimization.** Particle swarm optimization (PSO) is an optimization technique which was developed being inspired by the social behaviors of swarms like bird flocking or fish schooling by Eberhart and Kennedy [21]. The algorithm is firstly used for optimizing the weights in the artificial neural networks [22]. Because PSO is an easily applicable and fast method, it is widely used in many areas [23-25].

In PSO method, each potential solution is referred as a particle and each particle has positions ($x_{i,j}$) and velocities ($v_{i,j}$) in a $j$-dimensional feature space [26]. The solution set which consists of the particles is called as swarm. At the beginning of the algorithm, each particle is generated by taking random values from the solution space. The success of each particle is determined employing a fitness function. Through the iteration process, the best instance of each particle and the swarm is kept as local bests ($P_{best_{i,j}}$) and global best ($G_{best_{i,j}}$), respectively. For each iteration, the velocity and position of each particle is updated utilizing (1) and (2).

$$v_{i,j}(t+1) = wv_{i,j}(t) + c_1R_1(p_{best_{i,j}} - x_{i,j}(t)) + c_2R_2(g_{best_{i,j}} - x_{i,j}(t)), \quad (1)$$

$$x_{i,j}(t+1) = x_{i,j}(t) + v_{i,j}(t+1), \quad (2)$$

where $i$ is the index of the particle, $j$ is the index of the position in particle, $t$ shows the iteration number, $v_{i,j}(t)$ is the velocity of the $i$th particle in the swarm on $j$th index of the position in the particle and $x_{i,j}(t)$ is the position. $R_1$ and $R_2$ are the random numbers uniformly distributed between 0 and 1. $c_1$ and $c_2$ are the acceleration numbers and default values are 2 and $w$ is the inertial weight.

The original procedure for implementing PSO is as follows [27]:

1. *Generate each particle randomly within the $j$-dimensional feature space.*
2. *Evaluate the success of each particle using the fitness function.*
3. *If the success of the current particle is better than the success of $P_{best_{i,j}}$ then determine $P_{best_{i,j}}$ as the current particle.*
4. *If the success of the current particle is better than the success of $G_{best_{i,j}}$ then determine $G_{best_{i,j}}$ as the current particle.*
5. *Update the velocity and position of the particle using (1) and (2).*
6. *Repeat the steps from 2 to 5 until the stopping criteria or maximum iteration is reached.*

Inertial weight was introduced by Shi and Eberhart [28,29] embedding it into original PSO algorithm firstly introduced by Kennedy and Eberhart [21]. Inertial weight is a parameter used to assign a path which is employed to find optimal solution from local and global solution space. Thus, this parameter prevents the solution to be attached to the local or global solutions. Depending on the studies in literature [28,29], inertial weight is used as the following equation in this study,

$$w = \frac{t_{\max} - t}{t_{\max}}, \quad (3)$$

where $w$ is inertial weight, $t$ corresponds to the current iteration number and $t_{\max}$ corresponds to the maximum iteration number.

The parameters $c_1$ and $c_2$ are utilized to determine new particles solutions trend to local or global solutions in solution space. Earlier studies on particle swarm optimization in literature showed that trend constants $c_1$ and $c_2$ are both equal to 2 for almost all applications. Thus, $c_1$ and $c_2$ are used being both equal to 2 in this study.

2.2.1. *Classification with particle swarm optimization.* In basic classification process using PSO, the $N$-dimensional dataset having $C$ classes is divided into $C$ separate subsets. $C$ distinct optimum centroid vectors that could present each class optimally in each subset are obtained using basic PSO algorithm. For these $C$ distinct optimum centroid vectors, $N$-dimensional particles and velocities can be given as [30],

$$P_i = (p_i^0, p_i^1, \ldots, p_i^N), \tag{4}$$

$$V_i = (v_i^0, v_i^1, \ldots, v_i^N), \tag{5}$$

where $i$ is the class index and $1 \leq i \leq C$, $P$ is the particle and $V$ is the velocity of the particle. During the PSO algorithm process, $C$ distinct optimum centroid vectors are found using the fitness functions like Euclidean distance.

After obtaining $C$ optimum centroid vectors for $C$ classes using PSO, the classification process is employed using classifiers like kNN.

2.3. **Artificial immune recognition system.** Artificial immune recognition system is inspired from the immune system which recognizes foreign substances and constitutes a defense system against these substances. In other words, being an evolutionary algorithm, AIRS is developed by Watkins [31], and it is a computational system inspired by the principles and processes of the vertebrate immune system that typically exploit the immune system's characteristics of learning and memory to solve a problem.

The main objective of the AIRS is to generate the memory cells which are going to be used in the classification. The generation of the antibody which will best classify the training antigen is implemented by utilizing the artificial recognition ball (ARB) pool. This pool includes the antibody which will best classify the training antigen together with the antibodies previously added and mutated. A brief explanation of the AIRS algorithm is given below:

a) **Initialization.** *Dataset normalization and determination of the constants of the AIRS like mutation rate, affinity threshold, affinity threshold scalar, stimulation threshold, clonal rate and the number of the resources are assigned in this stage.*
b) **Constitution of the ARB pool.** *The optimum conjugate antibody which has the best stimulation value with the training antigen is found within the memory cells. This antibody is called as MCMatch and added to the ARB pool by mutating it. In this phase, the number of the clones is determined by multiplying the threshold value between the training antigen and MCMatch, hypermutation rate and the cloning rate.*
c) **Improvement of the ARB pool.** *Allowed resource numbers of each antibody is calculated by employing the cloning rate and the stimulation rates of antibodies within the ARB pool. The whole antibodies within the ARB pool are mutated until the stopping criteria are reached.*
d) **Constitution of the memory cell.** *The antibody which has the best stimulation to the training antigen is found within the ARB pool. This antibody is called as the candidate antibody. If the stimulation value between the candidate antibody and the training antigen is bigger then the stimulation value between the candidate antibody and MCMatch, the candidate antibody is added into the memory cells. If the candidate antibody is added into the memory cells and the stimulation value between the candidate antibody and MCMatch is smaller than the affinity threshold scalar multiplied by the affinity threshold, then the MCMatch is extracted from the memory cell.*
e) **Classification.** *Steps b), c) and d) are repeated for all training antigens. Following the training of all training antigens, test samples are classified using the memory cells obtained and the kNN classifier system.*

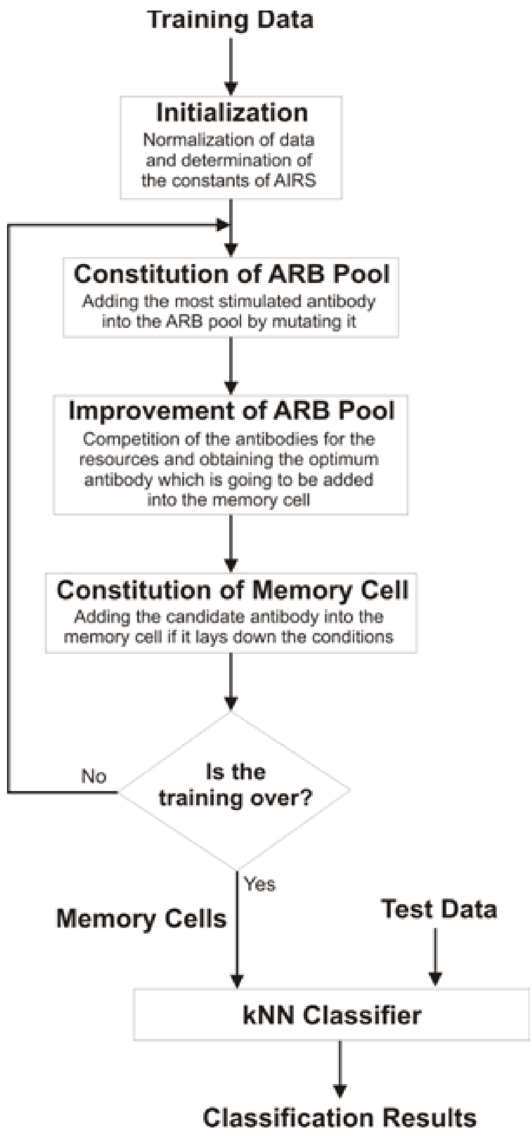


FIGURE 1. The AIRS algorithm

The AIRS algorithm is diagrammatized in Figure 1, and more detailed information about the AIRS system could be obtained from several studies like Watkins, Kodaz and Polat [10,31,32].

2.4. **K-nearest neighbor algorithm.** kNN is one of the simplest and most commonly used classification methods. kNN is a fast classification method because it does not have any training stages unlike most others. In this method, $k$ training samples are obtained for each test sample using a distance measure like Euclidean distance (6). The class of the test sample is classified using majority voting within these $k$ samples obtained [33]. Euclidean distance can be given as follows:

$$d = \sqrt{\sum_{i=1}^{N} (p_i - q_i)^2}, \tag{6}$$

where $p$ and $q$ are test and training samples respectively, $i$ is the index of the feature within $p$ and $q$, and $N$ is the number of the features.

3. **Results and Discussions.** In the study, EST dataset of 23 distinct features for 480 patients obtained from Meram Faculty of Medicine is used. Before the classification processes, the dataset is normalized to range $[-1, 1]$.

In PSOkNN classification process, two particles (one for healthy patients, the other for unhealthy ones) are generated. The test dataset is classified using these two particles with kNN classifier. During the obtaining process of the two optimal particles, the inertial weight is used as defined at (3). The parameters $c_1$ and $c_2$ are used as both equal to 2, and $k$-value for kNN is used as 1.

PSOkNN method is implemented within the varying range of iterations and different particle sizes in the swarm. Table 1 demonstrates the PSOkNN parameter search grid. The optimum results are obtained from the PSOkNN model with 150 iterations and 65 particles in the swarm.

Table 1. PSO parameters search grid

| ***Prm*** | ***SVal*** | ***EVal*** | ***Int*** |
|---|---|---|---|
| *NoI* | *50* | *1000* | *50* |
| *NoP* | *5* | *100* | *5* |

Prm, Name of the parameter; SVal, Start value of the parameter; EVal, End value of the parameter; Int, Interval of the parameter between start value and end value; NoI, Number of the iterations; NoP, Number of the particle in the swarm.

In AIRS algorithm, mutation rate, hyper clonal rate, stimulation threshold and $k$-value for kNN are used as 0.1, 3, 0.9 and 5, respectively. Clonal rate, the number of resources and affinity threshold scalar parameters are used in various ranges given in Table 2. The parameters clonal rate, number of resources and affinity threshold scalar for the optimum AIRS model are obtained as 1.5, 100 and 0.95, respectively.

Table 2. AIRS parameters search grid

| ***Prm*** | ***SVal*** | ***EVal*** | ***Int*** |
|---|---|---|---|
| *Crate* | *1* | *5* | *0.5* |
| *NoS* | *100* | *50* | *500* |
| *AthS* | *0.55* | *0.5* | *0.95* |

Prm, Name of the parameter; SVal, Start value of the parameter; EVal, End value of the parameter; Int, Interval of the parameter between start value and end value; CRate, Cloning rate; NoS, Number of the sources; AthS, Affinity threshold scalar.

As well as comparing results of the proposed method (PSOkNN) and AIRS, kNN classifier in itself is used to classify the dataset. Euclidean distance equation which is given in (6) is used as the distance measure and $k$-value for kNN classifier is taken as 5.

All three classification methods are implemented by using $k$-fold cross validation method, and $k$ is used as 5. Cohen's kappa ($\kappa$) is a statistical measure utilized to represent the reliability of the consistency between two raters [34,35]. In order to demonstrate the reliability and comparison of PSOkNN, AIRS and kNN classification techniques, area under the ROC curve and Cohen's kappa values are obtained in all classification processes. Area under the ROC curve values and Cohen's kappa values obtained from the optimum models of the three classification methods are also given in Table 3.

Results of our previous studies on the diagnosis of CAD existence from EST data comparing feature selection models [36] and evaluating principle component analysis (PCA)

Table 3. Test results

| *Method* | *ACC (%)* | *SEN (%)* | *SPE (%)* | *PPV (%)* | *NPV (%)* | *AUC* | $\kappa$ |
|---|---|---|---|---|---|---|---|
| *AIRS* | *76.46* | *86.40* | *53.92* | *81.52* | *57.94* | *0.7098* | *0.362* |
| *PSOkNN* | *92.49* | *97.39* | *79.94* | *92.87* | *93.13* | *0.8956* | *0.806* |
| *kNN* | *72.71* | *79.19* | *55.97* | *82.28* | *51.02* | *0.7660* | *0.341* |

ACC, Diagnostic accuracy; SEN, Sensitivity; SPE, Specificity; PPV, Positive predictive value; NPV, Negative predictive value; AIRS, Artificial immune recognition system; PSOkNN, Classification with novel PSOkNN method; kNN, k-nearest neighbor; $\kappa$, Cohen's kappa coefficient.

Table 4. Comparative results of the studies

| *Method* | *ACC (%)* |
|---|---|
| *BPSO-FST* | *81.46* |
| *GA-FST* | *79.17* |
| *SVM* | *76.67* |
| *PCA-SVM* | *79.17* |
| *AIRS* | *76.46* |
| *PSOkNN* | *92.49* |
| *kNN* | *72.71* |

ACC, Diagnostic accuracy; BPSO-FST, SVM classification utilizing binary particle swarm optimization as a feature selection technique; GA-FST, SVM classification utilizing genetic algorithms as a feature selection technique; PCA-SVM, SVM classification utilizing principle component analysis preprocessing method; AIRS, Artificial immune recognition system; PSOkNN, Classification with novel PSOkNN method; kNN, k-nearest neighbor.

on classification process [37] are compared with the results of the study. The comparative results are given in Table 4.

Cohen's kappa is generally thought to be a more robust measure than a simple assessment. According to the test results given in Table 3, Cohen's kappa measure shows that the novel hybrid method (PSOkNN) has almost perfect agreement with the CAG results. Besides, diagnostic accuracy, sensitivity, specificity, positive predictive value and negative predictive value of PSOkNN highlight the effectiveness of the algorithm on EST data for diagnosis of CAD. The high area under ROC curve value for PSOkNN also shows that the novel method gives more reliable results than the others.

Upon comparing results of this study and those of our previous studies, it is seen that PSOkNN is more accurate algorithm on EST data for diagnosis of CAD (see Table 4).

4. **Conclusions.** In current study, a novel hybrid method, PSOkNN, is proposed on determination of CAD existence upon EST data. According to the proposed method, one particle which demonstrates the whole samples optimally in the training dataset is generated for both healthy and unhealthy individuals. Afterwards, the class of the test sample is determined according to the distance obtained from kNN between the test sample and generated particles.

Considering the test results, the novel PSOkNN method proposed is more effective than the AIRS and kNN methods on determination of CAD existence upon EST data. Besides, when the results of this study are compared with those of our previous studies, it is observed that PSOkNN method achieves more accurate results on the same dataset.

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