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NE-nu-SVC: A new nested ensemble clinical decision support system for effective diagnosis of coronary artery disease

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ABSTRACT Coronary artery disease (CAD) is one of the main causes of cardiac death around the world. Due to its significant impact on the society, early and accurate detection of CAD is essential. This study proposes a novel nested ensemble nu-Support Vector Classification (NE-nu-SVC) model which combines several traditional machine learning methods and ensemble learning techniques for effective diagnosis of CAD. We validated our model using two well-known CAD datasets (Z-Alizadeh Sani and Cleveland). To improve the performance of the model, we selected clinically significant features from the datasets using a genetic search algorithm. To further improve our results, we applied a multi-level filtering technique to balance the data using the ClassBlancer and Resample methods. Our base algorithm, nu-SVC, is performed using four well-known kernel functions (linear, polynomial, radial basis (RBF) and sigmoid). The proposed NE-nu-SVC model provided the highest accuracy of 94.66% and 98.60% to predict CAD entities in the Z-Alizadeh Sani and Cleveland CAD datasets, respectively. Our system can aid the clinicians to diagnose CAD accurately and may probably replace other invasive diagnostic techniques.

INDEX TERMS Coronary artery disease (CAD), machine learning, ensemble learning, nested ensemble (NE) model, genetic algorithm.

I. INTRODUCTION

RECENT advances in artificial intelligence (AI) have led to the emergence of new intelligent automatic systems. AI, nowadays, acts as a bridge between different fields such as economics, biology, physics, mathematics, chemistry, etc [1]–[8]. AI methods can be applied to solve a variety of problems existing in those fields, providing more accurate solutions than standard classification methods.

Data mining and machine learning algorithms have been also widely used in the fields of bioinformatics and healthcare science. The volume of data in these fields has been growing very quickly [9]. Moreover, biological and medical data are usually heterogeneous and complex. All these factors motivate a prompt development of new data mining approaches, including the development of specialized machine learning techniques [10]. Machine learning algorithms, such as DTs (decision trees) [11], SVMs (support vector machines) [12]–[14] and ANNs (artificial neural networks) [15], combined to the powerful deep learning approach [16], can be used to tackle various challenging issues arising in bioinformatics and healthcare science, including protein structure prediction and disease identification [17], [18]. Nowadays, one of the most relevant challenges in healthcare science is the improvement of the performance of Clinical Decision

Support Systems (CDSS) [19] meant to predict and cure many important diseases such as Coronary Artery Disease (CAD) and other cardiovascular diseases [20], obesity [21], Chronic Obstructive Pulmonary Disease (COPD) [22], Alzheimer disease [23], prostate cancer [24], etc. CDSSs can be very beneficial to diagnose many of these diseases, including CAD, which is one of the major types of heart diseases [20] According to recent reports, CAD is the most common cardiovascular disease in the United States of America, being the leading cause of heart attacks among both male and female population [25]. As indicated in Nahar et al. [26], CAD is also one of the main causes of death in Australia and the United Kingdom. Therefore, it is very important to provide an efficient approach for CAD prediction, and we propose to do it here using different machine learning techniques.

The primary goal of this work is to introduce and test a new CDSS intended for accurate CAD prediction. Our new model, called Nested Ensemble nu-SVC (NE-nu-SVC), allows one to use different ensemble learning techniques with traditional machine learning algorithms. The proposed nu-SVC model including four different kernel functions was used to analyze two well-known CAD datasets (Z-Alizadeh Sani CAD [27] and Cleveland CAD datasets [25]). In order to eliminate redundant features and thus improve the model's performance, we carried out feature selection using a genetic search algorithm. In addition, the entities in both datasets were reweighted using a multi-level data balancing by the way of the supervised ClassBalancer (CB) method [28] and resampled using both supervised and unsupervised resample approaches [29]. The applied multi-level data balancing led to the prediction accuracy improvement for both minority and majority classes. Then, the proposed NE-nu-SVC model was applied. To achieve a better accuracy, four ensemble learning techniques at three different levels of the model were combined in the framework of NE-nu-SVC. As a result, we could greatly improve the accuracy of the traditional nu-SVC model with all kernel functions for both the Z-Alizadeh Sani and Cleveland CAD datasets [27], [25].

The rest of the paper is structured as follows. In Section II, we discuss the related work in the field. Section III describes materials, methods and the proposed approach. Section IV discusses the experimental results. Finally, Section V presents the conclusions of this study and the ideas for future research.

II. RELATED WORK

Many recent studies address the problem of an early diagnosis of heart disease [27], [30]–[39]. Here, we briefly discuss those which are directly related to our work. Several traditional machine learning methods have been applied by Alizadehsani et al. [27] to predict CAD and some of its instances. The accuracy scores of 86.14%, 83.17% and 83.50% were obtained by these authors as to an early recognition of the LAD (left anterior descending) artery, LCX (left circumflex) artery and RCA artery (right coronary artery) cases of CAD, respectively. In another study, Tayefi et al. [30] put forward a new model to predict CHD (Coronary Heart Disease). To this end, Tayefi et al. described a CHD prediction model using decision trees. Their model provided the average CHD prediction accuracy of 95.3%. Arabasadi et al. [31] introduced a new hybrid machine learning model to detect CAD. To do so, a genetic algorithm and an artificial neural network were combined. The method proposed by Arabasadi et al. provided a relatively good performance on the Z-Alizadeh Sani data with the accuracy, sensitivity and specificity scores equal to 93.85%, 97% and 92%, respectively. On the other hand, Alkeshuosh et al. [32] generated different rules for CAD detection using machine learning. For this purpose, the authors applied the well-known PSO (particle swarm optimization) evolutionary algorithm. Furthermore, the performance of the PSO algorithm was compared to that of the C4.5 algorithm. Alkeshuosh et al. showed that the average accuracy of their PSO method, which outperformed the C4.5 algorithm, was around 87%.

Abdar [33] applied four well-known DT algorithms, including CHAID (Chi-Square Automatic Interaction Detection), C5.0, QUEST (Quick, Unbiased and Efficient Statistical Tree) and CART (Classification And Regression Trees) to analyze the Cleveland CAD data. According to the results of that study, the C5.0 algorithm provided the greatest accuracy of 85.33% among the competing methods. Several simple rules were also generated by C5.0. Babič et al. [34] addressed the problem of CAD detection by applying different machine learning methods to three real CAD datasets. These authors focused on the two following directions: (1) a predictive CAD analysis with SVM, naïve Bayes classifier, neural networks and decision trees, and (2) a descriptive CAD analysis using association and decision rules. Babič et al. indicated that SVM was the best performer among the methods compared in this work. Polat et al. [35] applied the k-NN (k-nearest neighbour) algorithm as a preprocessing step for CAD detection. An AIRS (Artificial Immune Recognition System) based on a fuzzy resource allocation mechanism was then proposed to recognize CAD patients. The best CAD prediction accuracy reported by Polat et al. was 87%.

Acharya et al. [36] tackled the problem of CAD prediction by using the electrocardiogram (ECG) signals as input data for various machine learning techniques. Thus, a new automated diagnostic system for CAD and Myocardial Infarction (MI) detection was proposed. The statistical model described by Acharya et al. included three main methods: DCT (Discrete Cosine Transform), EMD (Empirical Mode Decomposition) and DWT (Discrete Wavelet Transform). The proposed system showed a good performance on real CAD data with an average accuracy of 98.5%. Patidar et al. [37] presented a new approach for CAD prediction using the tunable-Q wavelet transform (TQWT) method. TQWT divides the heart rate signals into different sub-bands in order to improve the diagnostic feature selection. By using LS-SVM (Least-Squares Support Vector Machine) and PCA (Principal Component Analysis), Patidar et al. obtained the average CAD recognition accuracy of 99.72%. Kausar et al. [38] combined an unsupervised clustering method and a supervised classification technique for timely detection of CAD using an ensemble technique. At the first stage, PCA was carried out. Then, the SVM and K-means algorithms were applied. Mahmoodabadi and Tabrizi [39] introduced a new intelligent system, called Imperialist Competitive Algorithm (ICA), to predict CAD. This system included both the decision tree and evolutionary algorithms and provided the average CAD detection accuracy of 94.92%.

III. MATERIALS AND METHODS

In this section, we first present the two real CAD datasets used in our study. Then, we describe our novel method based on the ensemble learning approach. Moreover, we shortly discuss some important features of the traditional machine learning algorithms considered in our work.

A. DESCRIPTION OF THE Z-ALIZADEH SANI AND CLEVELAND CAD DATASETS

In order to test our new model, we decided to use two well-known CAD datasets available at the University of California, Irvine, machine learning repository (UCI). Specifically, the Z-Alizadeh Sani [27], [40] and Cleveland [25], [41] datasets were considered. The Z-Alizadeh Sani dataset includes 303 patients' records described by 56 features; 55 of them were selected as input and one as output in our prediction model. Namely, this dataset contains the data for 216 CAD (sick) patients and 87 non-CAD (healthy) patients. Four main types of features are available for these data: echo, symptom and examination, ECG and laboratory, and demographic features (for more information regarding the Z-Alizadeh Sani dataset, see Supplementary Material).

The angiography procedure was used in the study of Alizadeh Sani et al. [27] to measure the stenosis of each artery. When a patient had the diameter that was greater than or equal to 50%, he/she was categorized as a CAD patient, otherwise as a Normal patient. The Z-Alizadeh Sani data include 71% of positive records (CAD-affected patients) and 29% of negative records (Normal patients). This means that these data are not well-balanced. To classify such unbalanced data more effectively, we applied a multi-level balancing approach [28], [29] (the discretization ranges of the Z-Alizadeh Sani data features are reported by Alizadeh Sani et al. [27]). More information regarding the discretization ranges of heart disease features can be found in Braunwald's Heart Book [42].

The Cleveland CAD dataset is another well-known heart disease dataset, which has been widely studied in the literature [25], [41]. This dataset contains 303 records as well, which are described 14 features; 13 of them were chosen as the input of our model and the remaining one was selected as our target attribute. The CAD data patients are categorized into 5 major classes. The first of them represents healthy patients (164 records; Class 1 in our work), whereas the four other classes correspond to different types of CAD patients (139 records in total). Here, we combined the data of the four latter classes into a general class of CAD patients (Class 2 in our work). The detailed information about the main features of the Cleveland CAD dataset is available in [25].

B. DESCRIPTION OF THE NEW MODEL

In this study, we first applied several machine learning methods, including J48, Random Forest, NaiveBayes, BayesNet, Multilayer Perceptron, C-SVC and nu-SVC, to analyze the Z-Alizadeh Sani CAD dataset [27]. We found that the traditional nu-SVC model, which usually works well in practice, provides very average results for the Z-Alizadeh Sani data. This traditional nu-SVC model was used as a core of our new model (the nested ensemble (NE)) with a goal of improving its performance when predicting CAD.

The nested ensemble (NE) approach allows one to combine several ensemble learning techniques within one model [43]. The main idea of this approach consists of using an ensemble learning technique inside of another ensemble learning technique. The general view of an NE model is presented in Fig. 1 and Algorithm 1. Moreover, we can use multiple classifiers (algorithms) with each ensemble learning technique. In general, an NE model can include different numbers of ensemble learning techniques at different levels of the model. In this study, we considered a three-level NE model using four ensemble learning techniques (see Fig. 2).

At the first level, we used the stacking technique as our first ensemble learning technique. The stacking technique has two main components: "classifier" and "metaClassifier". Within the "classifier" component, we used the three following methods: the nu-SVC, SGD (Stochastic Gradient Descent) and Random Forest. Here, the Random Forest classifier was embedded into our stacking ensemble learning technique. The loss function we used for training in SGD was the Hinge Loss (SVM) function. As to "metaClassifier", we used the bagging ensemble learning technique. At the second level, we added one more ensemble learning technique to our model. Finally, we applied a voting ensemble technique (also called the Vote technique) as a classifier at the previous level (bagging technique). This voting technique included the SMO and Naïve Bayes classifiers. The NE model we consider in this study was combined with genetic-based feature selection and multi-level data balancing. The complete schematic view of the Nested Ensemble nu-SVC model proposed in our work is presented in Fig. 2.

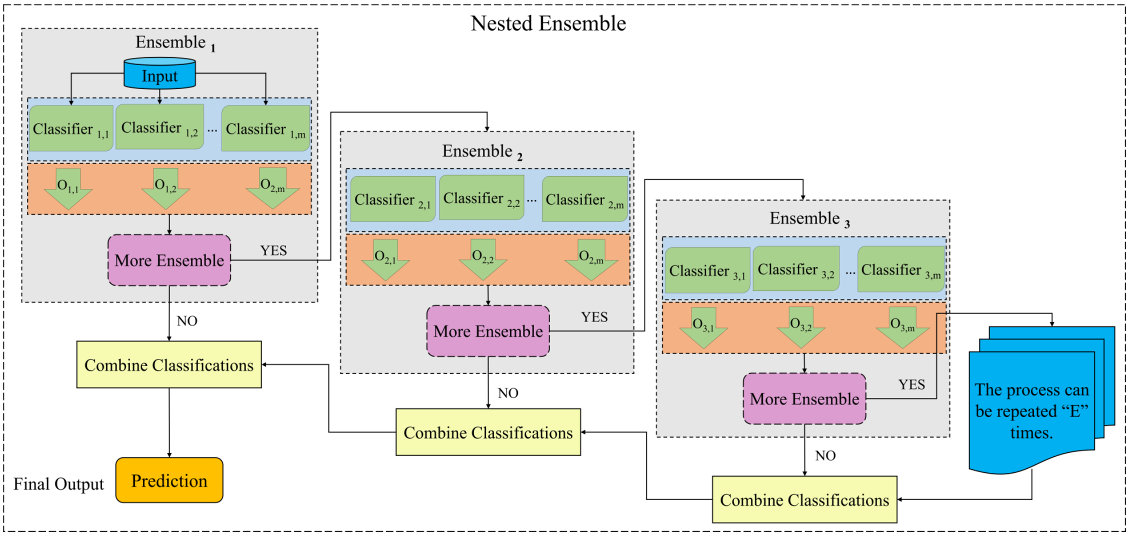


FIGURE 1: General scheme of a nested ensemble (NE) model.

Algorithm 1: A general Nested Ensemble (NE) model

```
Input: CAD dataset: $D = D_{train} \cup D_{test}$
Output: $O_f$: Best classification output
Begin Calculate the portance rate of each feature
  using a feature selection algorithm;
if $D$ is not balanced then
    Balance $D$ using a balancing technique;
end
Select the number of $L$ levels in the NE model;
for $l = 1, \cdots, L$ do
    Train the base machine learning algorithms,
      ensemble learning techniques and
      $metaClassifier$ at different levels of the NE
      model using $D_{train}$;
end
Classify unseen records from $D_{test}$ using the NE
  model;
return Best classification result found;
End
```

As shown in Fig. 2, within our model, we also carry out the K-fold cross-validation technique, in which the value of K is set to 10. Because both real datasets we consider here are not very large (i.e., 303 records in each of them), we can use the K-fold cross-validation technique which is generally very effective with this kind of data. By using the K-fold cross-validation technique, the problem of data bias can be minimized [44]. As mentioned previously, our base nu-SVC algorithm was used with four different kernel functions (linear, polynomial, RBF and sigmoid). We selected the most important data features using a genetic search algorithm. In order to balance the data (this was especially necessary for the Z-Alizadeh Sani dataset), we used the multi-level balancing approach. Our tests suggested that a three-level NE model can generate accurate results while predicting CAD. Since both datasets include categorical features (e.g., gender), we applied one-hot encoding to deal with categorical features since they cannot be directly processed by machine learning algorithms.

1) Problem definition and base algorithms used

In this section, we discuss our nested ensemble model [45], [46]. First, we give the formal definition of a nested ensemble (NE) model and present the NE model parameters used in our work. Let $\mathscr{D} = \{\mathscr{D}_1, \mathscr{D}_2, \mathscr{D}_3, \ldots, \mathscr{D}_n\}$ be a set of n datasets (each dataset includes different numbers of r records), $A = \{A_1, A_2, A_3, \ldots, A_m\}$ be a set of m machine learning algorithms (base algorithms) and $E = \{E_1, E_2, E_3, \ldots, E_k\}$ be a set of k ensemble learning techniques. Let L be the number of levels in the NE model. It should be noted that different machine learning algorithms and ensemble learning techniques can be used at different levels of the model.

We can add ensemble learning techniques and machine learning algorithms to different levels of an NE model till the prediction results improve. By using the union of the sets E_i ($i = 1, 2, \ldots, k$), we get a general NE model: NE = $\{E_1 \cup E_2 \cup E_3 \ldots \cup E_k\}$.

In our work, we used a three-level NE model including four ensemble learning techniques, four machine learning algorithms and two well-known CAD datasets (i.e., $L = 3$, $n = 2$, $m = 4$ and $k = 4$).

To the best of our knowledge, no existing work applied a multi-level NE model to analyze CAD data. The detailed information about the traditional machine learning algorithms and the ensemble learning techniques used in our work can be found in the Supplemental material. These

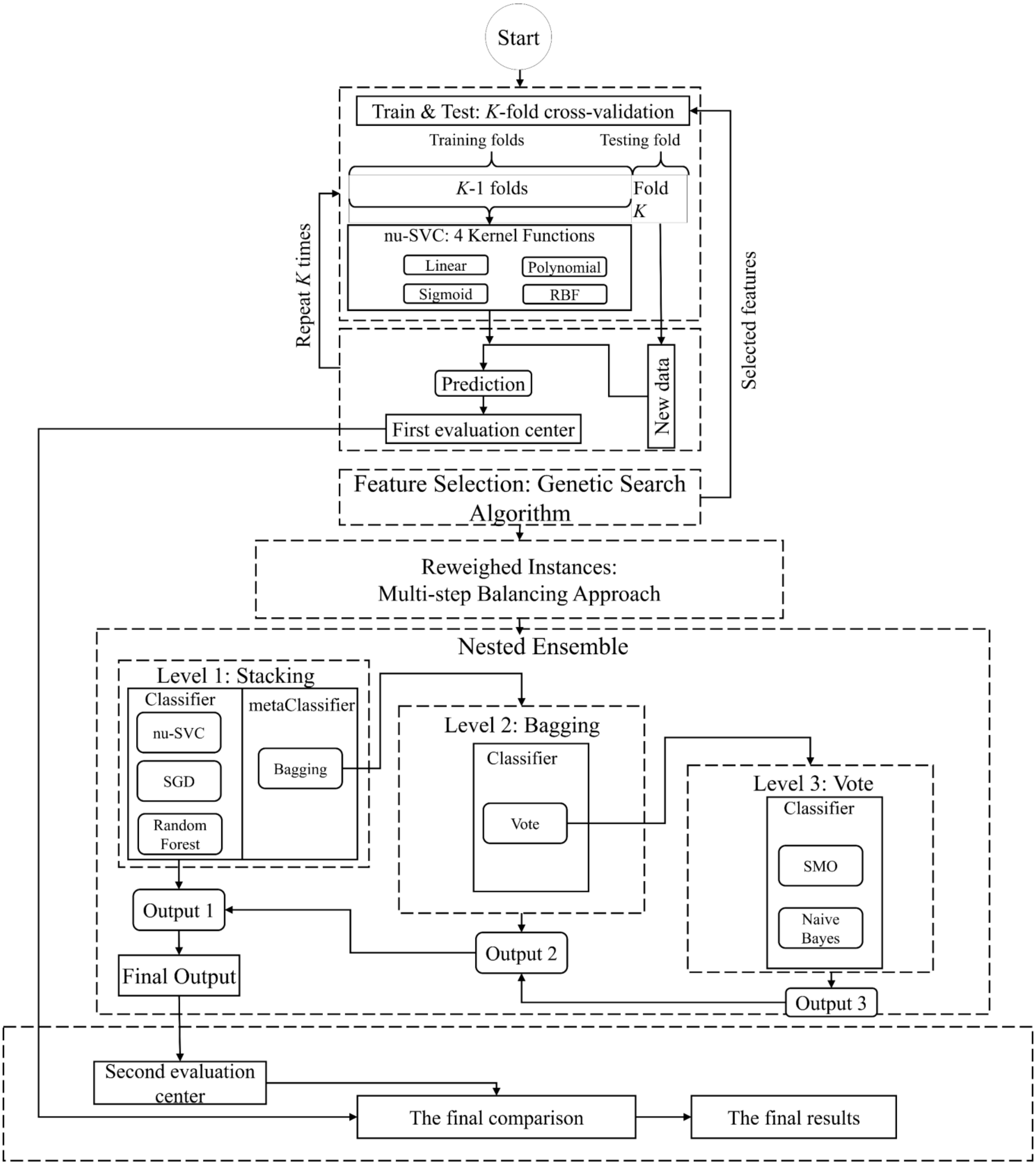


FIGURE 2: A block diagram of the proposed NE-nu-SVC model.

algorithms and techniques are also briefly described there.

IV. EXPERIMENTAL RESULTS

In this section, we discuss the results obtained when analyzing the Z-Alizadeh Sani CAD data with our NE-nu-SVC model. An IBM PC computer, equipped with a 2.30 GHz Intel Core i7 CPU and 8 GB of RAM, was used in our simulations. Our model was implemented using the 3.9.1 version of the WEKA package [29]. In addition, the LIBSVM (a Library for Support Vector Machines) open source machine learning library [47] was used to carry out the nu-SVC algorithm.

A. PERFORMANCE METRICS

Various statistical measures can be considered to evaluate and compare the performance of machine learning methods [48]. Here, we used the following popular metrics: Recall (True Positive Rate (TPR)), False Positive Rate (FPR), Precision, F-Measure, Accuracy, ROC (receiver operating characteristic) area, Kappa statistic, Pc, MAE (Mean Absolute Error) and RMSE (Root Mean Squared Error). These metrics are listed in Eq. (1-9) below:

$$FPR = \frac{FP}{FP+TN}, \tag{1}$$

$$Precision = \frac{TP}{TP+FP}, \tag{2}$$

$$Recall = TPR = \frac{TP}{TP+FN}, \tag{3}$$

$$F-Measure = \frac{2\times(Recall \times Precision)}{Recall + Precision}, \tag{4}$$

$$Accuracy = \frac{TP+TN}{P+N}, \tag{5}$$

$$Kappa-statistic = \frac{Accuracy - P_c}{1-P_c}, \tag{6}$$

$$P_c = \frac{(TP+FP)\times(TP+FN)+(FN+TN)\times(FP+TN)}{(P+N)^2}, \tag{7}$$

$$MAE = \frac{1}{r}\sum_{i=1}^{r}\left|(y_i - \widehat{y}_i)\right|, \tag{8}$$

$$RMSE = \sqrt{\frac{1}{r}\sum_{i=1}^{r}\left|(y_i - \widehat{y}_i)\right|^2}, \tag{9}$$

where N stands for the number of negative records in the data (original), P stands for the number of positive records in the data, TP (true positives) stands for the number of positive records that are classified correctly, *FN* (false negatives) stands for the number of positive records that are misclassified as negative, *FP* (false positives) stands for the number of negative records that are misclassified as positive, *TN* (true negatives) stands for the number of negative records that are classified correctly, r denotes the number of records in the dataset, i denotes the sample index, y_i denotes the actual value of record i and $\widehat{y}_i$ denotes the predicted value of record i.

B. RESULTS OBTAINED PRIOR TO FEATURE SELECTION

This section presents the experimental results obtained using the traditional nu-SVC model when all original features of the Z-Alizadeh Sani CAD dataset were considered. The nu-SVC model was applied with four different kernel functions: linear, polynomial, RBF and sigmoid. The obtained results are presented in Table 1 and Fig. 3.

According to Table 1, the results provided by different kernel functions used within the traditional nu-SVC model vary a lot. On one hand, in terms of TP Rate, FP Rate, Precision, Recall and F-measure, the RBF function yielded good results for the CAD class, whereas it did not show good performance for the Normal class. On the other hand, the sigmoid function provided good results in terms of TP Rate, FP Rate and Recall for the Normal class, but not for the CAD class. Here, our main finding was that traditional nu-SVC had the greatest accuracy when the kernel function was polynomial. Moreover, Figure 3 shows that nu-SVC with the linear kernel function yielded the best results according to the Kappa statistic, and the MAE and RMSE measures.

C. FEATURE SELECTION PROCEDURE

In this step, a genetic search algorithm was carried out to select the most significant features of the Z-Alizadeh Sani CAD data. The applied genetic search algorithm by Goldberg [49], implemented in WEKA, uses a correlation-based variable selection approach to eliminate redundant features [50]. The values of population size, number of generations and report frequency during our feature selection were set to 20. The probability of crossover and the probability of mutation were set to 0.6 and 0.033, respectively. More details on the applied feature selection procedure are presented in Tables A.1 and A.2 (see Appendix A). Initial population features and generated features provided by the genetic search algorithm for the Z-Alizadeh Sani CAD dataset are presented in Tables A.1 and A.2. The numbers in the Subset column in both Tables A1 and A.2 show the feature order in the original data file. Applying this procedure, we selected 16 most significant features which were used in further investigation. The selected features were as follows: Age, DM (Diabetes Mellitus), HTN (Hyper Tension), CRF (Chronic Renal Failure), BP (Blood Pressure), Typical Chest pain, Dyspnea, Atypical, Nonanginal, Q Wave, T-inversion, ESR (Erythrocyte Sedimentation Rate), K (Potassium), EF (Ejection Fraction), RWMA (Regional Wall Motion Abnormality) and VHD (Valvular Heart Disease). It should be noted that we applied feature selection prior to one-hot encoding as suggested by Hasanin et al. [51].

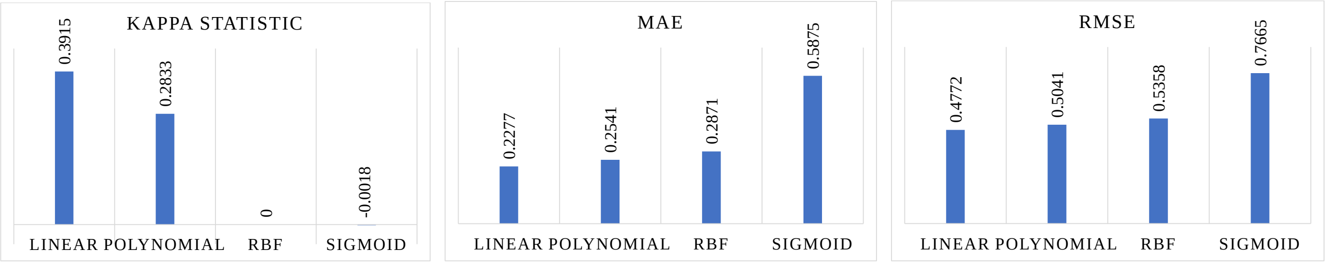
D. RESULTS OBTAINED AFTER FEATURE SELECTION

This section describes the results provided by the traditional nu-SVC model after feature selection. The nu-SVC model was applied with four kernel functions as discussed earlier. The results obtained when the 16 selected features of the Z-Alizadeh Sani CAD dataset were used are presented in Table 2 and Fig. 4.

As shown in Table 2 and Fig. 4, the general trends observed when using only the 16 selected features of the Z-Alizadeh Sani dataset are similar to those found for the original Z-Alizadeh Sani data. In other words, we can notice that traditional nu-SVC had a good performance either for the CAD class or for the Normal class. However, the accuracy results, especially in the case of the linear and polynomial kernel functions, were generally much better after the feature selection. According to Fig. 4, the traditional nu-SVC model with the linear kernel provides the best CAD detection having with the highest value of the Kappa statistic (0.6496), and the lowest values of MAE (0.1386) and RMSE (0.3723), followed by the polynomial kernel. The traditional nu-SVC model with the sigmoid kernel does not show a good performance compared to the three other kernels. We can see that the sigmoid

TABLE 1: The results provided by the traditional nu-SVC model when all original features of the Z-Alizadeh Sani CAD dataset were considered.

Measures		**nu-SVC**			
		Linear	**Polynomial**	**RBF**	**Sigmoid**
FPR	CAD (%)	54.00	66.70	100	29.90
	Normal (%)	10.20	8.80	0.0	70.40
	Average (%)	41.40	50.10	71.30	41.50
Precision	CAD (%)	80.50	77.30	71.30	71.10
	Normal (%)	64.50	60.40	0.0	28.60
	Average (%)	75.90	72.40	50.80	58.90
Recall	CAD (%)	89.80	91.20	100	29.60
	Normal (%)	46.00	33.30	0.0	70.10
	Average (%)	77.20	74.60	71.30	41.30
F-measure	CAD (%)	84.90	83.70	83.20	41.80
	Normal (%)	53.70	43.00	0.0	40.70
	Average (%)	75.90	72.00	59.30	41.50
ROC Area	CAD (%)	67.90	62.30	50.00	49.90
	Normal (%)	67.90	62.30	50.00	49.90
	Average (%)	67.90	62.30	50.00	49.90
Accuracy(%)		**77.22**	74.58	71.28	41.25

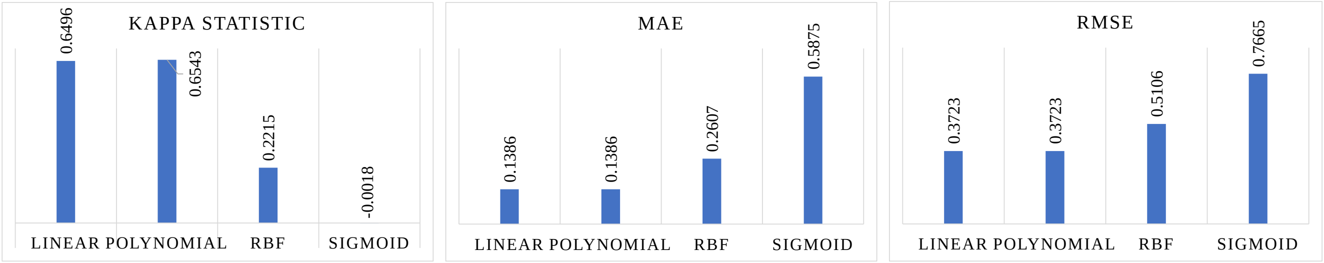


(a) (b) (c)

FIGURE 3: Comparison of the results provided by the traditional nu-SVC model with different kernel functions when all original features of the Z-Alizadeh Sani CAD dataset were considered: (a) Kappa statistic, (b) MAE and (c) RMSE.

TABLE 2: The results provided by the traditional nu-SVC model using the 16 selected features of the Z-Alizadeh Sani CAD dataset.

Measures		**nu-SVC**			
		Linear	**Polynomial**	**RBF**	**Sigmoid**
FPR	CAD (%)	31.00	27.60	75.90	29.90
	Normal (%)	6.90	8.30	6.00	70.40
	Average (%)	24.10	22.10	55.80	41.50
Precision	CAD (%)	88.20	89.20	75.50	71.70
	Normal (%)	80.00	77.80	61.80	28.60
	Average (%)	85.80	85.90	71.50	58.90
Recall	CAD (%)	93.10	91.70	94.00	29.60
	Normal (%)	69.00	72.40	34.70	70.10
	Average (%)	86.10	86.10	73.90	41.30
F-measure	CAD (%)	90.50	90.40	83.70	41.80
	Normal (%)	74.10	75.00	34.70	40.70
	Average (%)	85.80	86.00	69.60	41.50
ROC Area	CAD (%)	81.00	82.00	59.10	49.90
	Normal (%)	81.00	82.00	59.10	49.90
	Average (%)	81.00	82.00	59.10	49.90
Accuracy(%)		**86.13**	**86.13**	73.92	41.25



(a) (b) (c)

FIGURE 4: Comparison of the results provided by the traditional nu-SVC model with different kernel functions when the 16 selected features of the Z-Alizadeh Sani CAD dataset were considered: (a) Kappa statistic, (b) MAE and (c) RMSE.

kernel has generated a negative Kappa statistic value (-0.0018), and very high MAE (0.5878) and RMSE (0.7665) values.

E. RESULTS OBTAINED AFTER DATA BALANCING

As mentioned earlier (see section III, subsection A), most of the entities (216 out of 303) of the Z-Alizadeh Sani CAD dataset belong to the CAD class and only 87 entities to the Normal class. In the previous section, we observed that the nu-SVC model provided different performances for these two classes (see the results in Tables 1 and 2). We can argue that the Z-Alizadeh Sani dataset is unbalanced (or weakly balanced). Hence, we used an approach to deal with such weakly balanced data.

Precisely, the multi-step balancing technique was carried out as follows. The Z-Alizadeh Sani dataset was first reweighted so that each class could get the same total weight. The supervised ClassBalancer (CB) method was used here. Since the CB method did not improve significantly the performance of the proposed model, the unsupervised resample method was also applied. Such a balancing approach is called a multi-step balancing. This two-step balancing allowed us to improve the prediction results for the Z-Alizadeh Sani dataset. It is worth mentioning that one can use different levels of balancing (two steps or more) to get a better performance. Since we used 10-fold cross validation, the balanced data were randomized using an unsupervised instance filter to avoid the overfitting problem. The results obtained after the supervised data balancing (using CB) and the two-step balancing (using both CB and resampling) are reported in Tables 3 and 4, respectively.

TABLE 3: Reweighted records obtained for the Z-Alizadeh Sani CAD data using the supervised ClassBalancer (CB) technique.

No.	Label	Weight
1	CAD	151.5
2	NORMAL	151.5

TABLE 4: Final reweighted records obtained for the Z-Alizadeh Sani CAD data using two-step balancing, including both the supervised and unsupervised resample techniques.

No.	Label	Weight
1	CAD	152.903
2	NORMAL	148.017

After the data balancing, we applied the nu-SVC model once again using the same four kernel functions. We carried out our method 10 times with each kernel function to find out whether the obtained results were stable or not. The average results generated after our two-step balancing are shown in Table 5 and Fig. 5.

It can be noted from Table 5 that the accuracy of the nu-SVC model with the RBF and sigmoid kernel functions increased (compared to the results presented in Table 2), whereas it decreased for the linear and polynomial kernels. In general, we can argue that the prediction of both CAD and Normal patient classes improved when the two-step balancing procedure was applied.

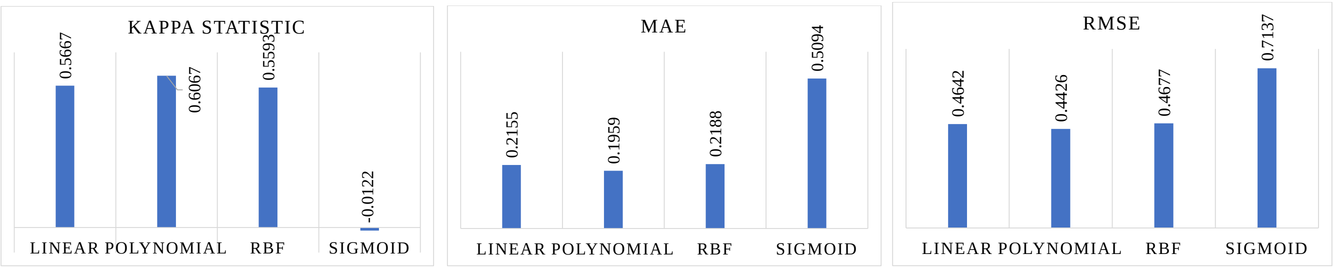
F. RESULTS OBTAINED USING THE NESTED ENSEMBLE NU-SVC MODEL

A good machine learning model should correctly classify the entities of all classes present in a given dataset, whereas the classification results we have obtained so far have been good for one class only, either for the CAD class or for the Normal patient class. Thus, our new Nested Ensemble nu-SVC (NE-nu-SVC) model (see Fig. 2) was applied at this stage to improve the performance of the traditional nu-SVC model. This NE-nu-SVC model incorporates four well-known ensemble learning techniques: stacking, random forest, bagging and voting, which are used together. NE-nu-SVC was applied to the Z-Alizadeh Sani data after the feature selection and two-step balancing of the entities were carried out (as explained in the previous sections). The detailed results provided by NE-nu-SVC are presented in Table 6 and Fig. 6.

The results presented in Table 6 and Fig. 6 suggest that the application of the NE-nu-SVC model allowed us to improve drastically the prediction results for all kernel functions, compared to the traditional nu-SVC model (see Table 5 and Fig. 6). In order to verify the stability of the

TABLE 5: The results provided by the traditional nu-SVC model using feature selection and two-step balancing for the Z-Alizadeh Sani CAD dataset.

Measures		nu-SVC			
		Linear	**Polynomial**	**RBF**	**Sigmoid**
FPR	CAD (%)	37.60	31.80	43.50	30.60
	Normal (%)	6.00	7.80	0.90	70.60
	Average (%)	22.10	20.00	22.60	50.30
Precision	CAD (%)	72.10	75.00	70.20	49.80
	Normal (%)	91.00	89.40	98.30	48.70
	Average (%)	81.40	82.10	84.00	49.30
Recall	CAD (%)	94.00	92.20	99.10	29.40
	Normal (%)	62.40	68.20	56.50	69.40
	Average (%)	78.50	80.40	78.10	49.10
F-measure	CAD (%)	81.60	82.70	82.20	36.90
	Normal (%)	74.00	77.40	71.70	57.30
	Average (%)	77.90	80.10	77.00	46.90
ROC Area	CAD (%)	78.20	80.20	77.80	49.40
	Normal (%)	78.20	80.20	77.80	49.40
	Average (%)	78.20	80.20	77.80	49.40
Accuracy(%)		78.45	**80.41**	78.12	49.05

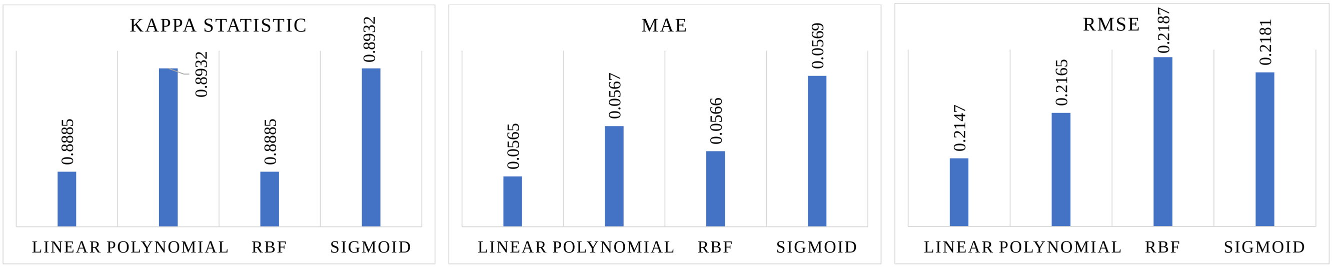


(a) (b) (c)

FIGURE 5: Comparison of the results provided by the traditional nu-SVC model with different kernel functions when the feature selection and two-step balancing of the entities of the Z-Alizadeh Sani CAD dataset were carried out: (a) Kappa statistic, (b) MAE and (c) RMSE.

TABLE 6: The results provided by the proposed NE-nu-SVC model for the Z-Alizadeh Sani data (after applying the feature selection and two-step balancing of the entities).

Measures		NE-nu-SVC			
		Linear	**Polynomial**	**RBF**	**Sigmoid**
FPR	CAD (%)	7.10	7.00	7.10	7.10
	Normal (%)	4.10	3.70	4.10	3.70
	Average (%)	5.60	5.40	5.60	5.40
Precision	CAD (%)	93.30	93.40	93.30	93.40
	Normal (%)	95.60	96.10	95.60	96.10
	Average (%)	94.50	94.70	94.40	94.70
Recall	CAD (%)	95.90	96.30	95.90	96.30
	Normal (%)	92.90	92.90	92.90	92.90
	Average (%)	94.40	94.70	94.40	94.70
F-measure	CAD (%)	94.60	94.80	94.60	94.80
	Normal (%)	94.30	94.50	94.30	94.50
	Average (%)	94.40	94.70	94.40	94.70
ROC Area	CAD (%)	96.60	96.60	96.50	96.50
	Normal (%)	96.60	96.60	96.50	96.50
	Average (%)	96.60	96.60	96.50	96.50
Accuracy(%)		94.43	**94.66**	94.43	**94.66**



(a) (b) (c)

FIGURE 6: Comparison of the results provided by the proposed NE-nu-SVC model with different kernel functions for the Z-Alizadeh Sani data (after applying the feature selection and two-step balancing of the entities): (a) Kappa statistic, (b) MAE and (c) RMSE.

proposed NE-nu-SVC model, it was applied 10 times for each kernel function. Very stable results were generated for all the evaluation metrics under consideration (see Eq.(1-9)). The running time is another important factor to be considered in CDSSs. Table 7 shows the average running time on the transformed records (obtained after applying the feature selection and two-step balancing of the entities) of the Z-Alizadeh Sani dataset before and after using the NE approach within the nu-SVC model.

Observing the results presented in Table 7, we can conclude that even though the proposed NE-nu-SVC model including several nested machine learning techniques requires more running time for the RBF and sigmoid kernel functions, compared to nu-SVC, it needs less running time for the linear and polynomial kernels. Thus, we can argue that, in general, our NE-nu-SVC model is not very time-consuming. The running time of our new model is very reasonable compared to the gain in accuracy it provides. Both good performance and low runtime are the key factors for a CDSS.

Moreover, we compared the accuracy provided by the proposed NE-nu-SVC model for the Z-Alizadeh Sani data with the results yielded by some recent studies dedicated to the analysis of this well-known CAD dataset. Table 9 presents a comprehensive comparison of the results generated by different classification models which were used to analyze the Z-Alizadeh Sani data. As reported in this table, our model has the highest accuracy (94.66%) among the competing approaches. It is worth mentioning that the proposed NE-nu-SVC model also provided very competitive results in terms of other metrics considered, including Recall, F-measure, ROC area, Kappa statistic, MAE and RMSE.

The time complexity of ensemble learning methods should be considered with pruning procedure and without pruning procedure [52]. Suppose that m base algorithms are trained using an ensemble learning model. The total time complexity of training for the ensemble learning model without pruning procedure is $O(m \times t_{train})$, whereas the time complexity of prediction for unseen data (unknown instances) is $O(m \times t_{test})$ [52], where t_{train} is average time required to train the model with one algorithm and t_{test} is average time required to test the model with one algorithm. It should be noted that t_{train} depends on two factors: 1) the size of training set, and 2) the specific base training algorithms being used, while t_{test} depends on the specific machine learning algorithms being used. Table 8 provides the time complexity of the ensemble learning techniques and base machine learning algorithms used in our study.

In Table 8, $O(E_i)$ $(1 \leqslant i \leqslant k)$ is the time complexity of ensemble learning technique E_i, k is the number of ensemble learning techniques used in stacking, r is the number of records in the dataset and v is the size of the adopted feature vector. In the SGD algorithm, *mtry* is the number of used features, *ntree* is the number of trees in Random Forest, d is the depth of the Random Forest tree. Also, T is the number of iterations and t is the average running time of an individual machine learning algorithm used in Ne-nu-SVC, T' is the number of trials, h is the number of hypotheses for voting and *dl* is the dictionary length. Thus, based on Table 8, we get the following time complexity for the proposed NE-nu-SVC model:

$$\begin{aligned} Time-Complexity(NE-nu-SVC) = \\ O(r \times v) + O(r) \\ +O(ntree \times mtry \times d \times r) \\ +O(T \times T' \times h \times t) \\ +O(r^{2.3}) + O(dl \times r). \end{aligned} \tag{10}$$

G. APPLICATION OF THE NE-NU-SVC MODEL TO THE CLEVELAND DATA

In order to confirm the effectiveness of the proposed methodology, the NE-nu-SVC model was also used to analyze the Cleveland CAD dataset [25], [41], [73]–[75].

As previously, the NE-nu-SVC model was used with the linear, polynomial, RBF and sigmoid kernel functions. We then applied the genetic search algorithm for feature selection, as explained in the previous section. As a result, seven original features of the Cleveland CAD dataset were selected for further analysis. These features are as follows: CP (Chest pain), Restecg (Results of resting electrocardiographic), Thalach (Maximum heart rate), Exang (Exercise

TABLE 7: Running times obtained for the Z-Alizadeh Sani dataset before and after using the Nested Ensemble method with different kernel functions within the nu-SVC model.

Runtime (seconds)	**Model**							
	nu-SVC				**NE-nu-SVC**			
	Linear	**Polynomial**	**RBF**	**Sigmoid**	**Linear**	**Polynomial**	**RBF**	**Sigmoid**
Time 1	1.65	1.99	0.04	0.01	0.61	0.64	0.64	0.59
Time 2	1.38	2.07	0.04	0.01	0.66	0.67	0.65	0.59
Time 3	1.42	2.09	0.04	0.01	0.62	0.66	0.65	0.63
Time 4	1.39	2.08	0.04	0.01	0.64	0.65	0.65	0.60
Time 5	1.38	2.12	0.04	0.01	0.63	0.65	0.65	0.59
Time 6	1.38	2.08	0.04	0.01	0.64	0.64	0.65	0.60
Time 7	1.39	2.05	0.04	0.01	0.63	0.65	0.65	0.61
Time 8	1.38	2.06	0.04	0.01	0.62	0.65	0.66	0.59
Time 9	1.61	2.05	0.04	0.01	0.62	0.65	0.66	0.60
Time 10	1.42	2.03	0.04	0.01	0.74	0.65	0.66	0.59
Average	1.44	2.062	0.04	**0.01**	0.641	0.651	0.652	**0.599**

TABLE 8: Time complexity of all ensemble learning and base machine learning algorithms used in this study. See Section F for detailed information about the methods and variables being used.

Algorithm	**Study**	**Time complexity**
Stacking	Zhao et al. (2018) [53]	$O(E_1 + E_2 + E_3 + ... + E_k)$
nu-SVC (SVM)	Hsieh et al. (2016) [54]	$O(r \times v)$
SGD	Chen et al. (2018) [55]	$O(r)$
Random Forest	Gupta and Rana (2019) [56]	$O(ntree \times mtry \times d \times r)$
Bagging	Zhao et al. (2018) [53]	$O(T \times t)$
Vote	Mesterharm (2007) [57]	$O(T' \times h \times t)$
SMO	Ouyang and Gray (2010) [58]	$O(r^{2.3})$
Naive Bayes	Jia et al. (2012) [59]	$O(dl \times r)$

TABLE 9: Comparison of the accuracy of the NE-nu-SVC model with state-of-art techniques for the Z-Alizadeh Sani CAD data.

Study	**Model**	**Accuracy in (%)**
Alizadehsani et al. (2012) [60]	SMO	82.16
Alizadehsani et al. (2012) [61]	SMO 1-1	92.74
Alizadehsani et al. (2012) [62]	SMO	92.09
Alizadehsani et al. (2012) [63]	Ensemble (Naïve Bayes-SMO)	88.52
Alizadehsani et al. (2013) [64]	Bagging-C4.5	79.54 (LAD) 61.46 (LCX) 68.96 (RCA)
Alizadehsani et al. (2013) [65]	Information gain-SMO	94.08
Yadav et al. (2014) [66]	Improved ARM	93.75
Alizadehsani et al. (2016) [27]	arteries-SVM Combined information gain for all	86.14 (LAD) 83.17 (LCX) 83.50 (RCA)
Arabasadi et al. (2017) [31]	Neural network-genetic algorithm	93.85
Qin et al. (2017) [67]	EA-MFS	93.70
Babič et al. (2017) [34]	SVM	86.67
Hu et al. (2018) [68]	Variational finite inverted Beta-Liouville (IBL) Mixture Model (Var- IBLMM)	81.84
Kiliç and Kayakeles et al. (2018) [69]	Artificial Bee Colony+Sequential Minimal Optimization (ABCSMO)	89.43
Zhang et al. (2018) [70]	Extend correlation Restricted Boltzmann machine (Exp-CRBM)	88.95±3.84
Abdar et al. (2019) [71]	N2Genetic-nuSVM	93.08
Khan et al. (2019) [72]	Neural Network + Gini Index + Backward Weight Optimization	88.49
Proposed method	***NE-nu-SVC + feature selection + multi-step balancing***	***94.66***

induced angina), Oldpeak (ST depression induced by exercises relevant to rest), Ca (Number of major vessels) and Thal. It should be noted that 6 original records included missing values. Therefore, they were eliminated from the dataset (i.e., 297 out of 303 original records were analyzed in our work). The obtained results are reported in Table 10 and Fig. 7.

The reduced dataset was balanced using the above-discussed multi-level balancing procedure. For the Cleveland data, we applied a five-step balancing in order to maximize the performance of NE-nu-SVC. The balancing procedure was carried out five times: one time using the ClassBalancer technique (supervised), three times using the resample technique (supervised) and once using the resample technique (unsupervised). The main reason for applying a five-step balancing was that a two-step balancing, which worked well with the Z-Alizadeh Sani data, led to a lower accuracy for the Cleveland data. The detailed results provided by NE-nu-SVC on the modified Cleveland data, obtained after applying the feature selection and five-step balancing of entities, are presented in Table 11 and Fig. 8. Table 12 reports the average running times of our program for the modified records of the Cleveland CAD dataset, obtained after applying the feature selection and five-step balancing of the entities when running the nu-SVC and NE-nu-SVC models.

A comparison of the accuracy provided by the proposed NE-nu-SVC model with state-of-art CAD detection methods for the modified Cleveland CAD data is presented in Table 13. It can be noted that our NE-nu-SVC model provided the highest accuracy (98.60%) among the competing methods. Even though our results are very promising, we cannot ignore the role of specialists in the diagnostic process. However, we can argue that this new model might be appropriate as an assistant during an implementation of clinical guidelines.

There are several advantages and disadvantages of the proposed model which we should report. For example, our model can be also used as a deep ensemble learning model which allows us to include in it different numbers of ensemble learning techniques and classical machine learning algorithms. Importantly, even though our new model comprises several algorithms at different levels, its running time remains reasonable. However, there are also some disadvantages of the proposed methodology which should be addressed in future work. First, the weights of classifiers have not been considered in this study. To do so, one has to apply different evolutionary algorithms to find the proper weights for classifiers at different levels. Moreover, the proposed model should be tested on different datasets, including big data. Finally, our study does not consider the impact of ECG signals [94]–[97] and ultrasound images [98], which should be investigated in the future.

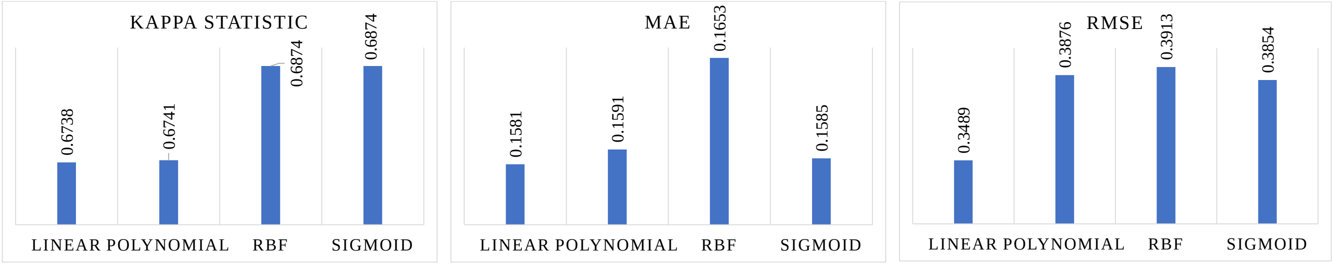
V. CONCLUSION

Nowadays, the impact of Clinical Decision Support Systems (CDSSs) on the individual's health increases gradually. Hence, the improvement of accuracy of statistical models included in CDSSs is a key challenge for clinical researchers, patients and physicians. Coronary artery disease (CAD), being one of the main causes of death worldwide, attracts valuable attention from many researchers worldwide. This study introduces a new hybrid ensemble learning model which can be used in the framework of a CDSS. The proposed model was tested on two well-known CAD datasets: the Z-Alizadeh Sani and Cleveland data from the UCI repository. Our model is a part of the Nested Ensemble (NE) approach. It relies on different traditional machine learning algorithms. In this study, the nu-SVC algorithm, including linear, polynomial, RBF and sigmoid kernels, was selected as the base algorithm of our NE-nu-SVC model. Within an NE model, nu-SVC was combined with other effective machine learning techniques such as SGD (Stochastic Gradient Descent), SMO (Sequential Minimal Optimization), random forest, Naïve Bayes, staking, bagging and voting. Furthermore, both the features selection and data balancing procedures were carried out to enhance the performance of the new model. We applied a genetic search algorithm for feature selection with both CAD datasets we analyzed (Z-Alizadeh Sani and Cleveland data). Since, these datasets were not well-balanced, we also carried out a multi-level balancing, using both ClassBlancer and Resample methods. The NE approach allows one to combine several ensemble learning techniques at different levels of the model. Here, we applied four ensemble learning techniques at three different levels. At the first level, the nu-SCV, SGD and random forest algorithms were combined using the stacking and bagging techniques. At the second level, the voting technique, and at the third level, the SMO and Naïve Bayes algorithms, were used. Our new model provided the accuracy of 94.66% for the Z-Alizadeh Sani data and of 98.60% for the modified Cleveland data. It allowed us to outperform the results provided by the existing machine learning algorithms for these well-known CAD datasets (see Tables 9 and 13). Moreover, we need to point out that the proposed NE-nu-SVC model is efficient in terms of running time. On average, over all four kernels, the execution of our program took 0.635 (s) for the Z-Alizadeh Sani dataset and 0.483 (s) for the Cleveland dataset. In the future, it would be interesting to apply the proposed model in the framework of other CDSSs aimed, for example, at the prediction of such important diseases as breast cancer or stroke. In this study, the number of levels in the NE model was selected manually. It would be essential to adapt an evolutionary algorithm (EA) to select the optimal number of levels automatically.

APPENDIX A

TABLE 10: Experimental results provided by the proposed NE-nu-SVC model for the modified Cleveland CAD dataset after the feature selection and prior to data balancing.

Measures		**NE-nu-SVC**			
		Linear	**Polynomial**	**RBF**	**Sigmoid**
FPR	Normal (%)	19.70	19.00	19.00	19.00
	CAD (%)	13.10	13.80	12.50	12.50
	Average (%)	16.70	16.60	16.00	16.00
Precision	Normal (%)	83.70	84.10	84.30	87.50
	CAD (%)	84.00	83.50	84.70	81.00
	Average (%)	83.80	83.80	84.50	84.50
Recall	Normal (%)	86.90	86.30	87.50	85.90
	CAD (%)	80.30	81.00	81.00	82.80
	Average (%)	83.80	83.80	84.50	84.50
F-measure	Normal (%)	85.30	85.20	85.90	85.90
	CAD (%)	82.10	82.20	82.80	82.80
	Average (%)	83.80	83.80	84.50	84.50
ROC Area	Normal (%)	88.60	89.20	88.60	89.00
	CAD (%)	88.60	89.20	88.60	89.00
	Average (%)	88.60	89.20	88.60	89.00
Accuracy(%)		83.84	83.83	**84.51**	**84.51**

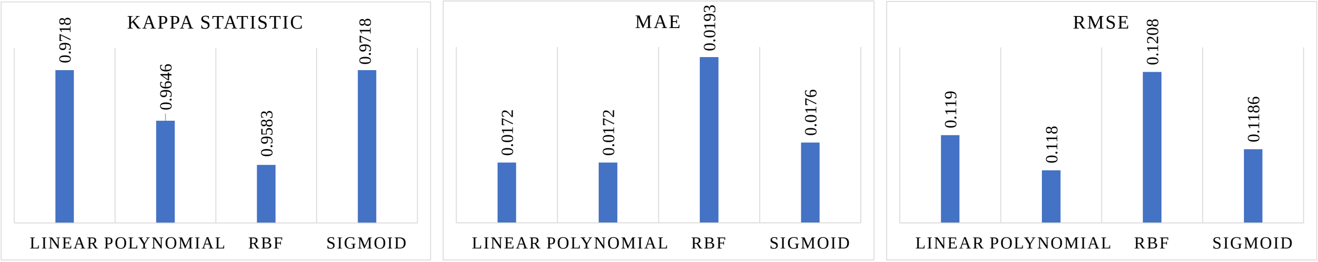


(a) (b) (c)

FIGURE 7: Comparison of the results obtained using the proposed NE-nu-SVC model after the feature selection and prior to data balancing with different kernel functions when 7 selected features of the modified Cleveland CAD dataset were used: (a) Kappa statistic, (b) MAE and (c) RMSE.

TABLE 11: The results provided by the proposed NE-nu-SVC model for the modified Cleveland CAD data, obtained after applying feature selection and five-step balancing of the entities.

Measures		**NE-nu-SVC**			
		Linear	**Polynomial**	**RBF**	**Sigmoid**
FPR	Normal (%)	2.00	2.60	2.60	2.00
	CAD (%)	0.70	0.70	1.40	0.70
	Average (%)	1.30	1.60	1.90	1.30
Precision	Normal (%)	97.60	96.90	96.80	97.60
	CAD (%)	99.40	99.40	98.90	99.40
	Average (%)	98.60	98.30	97.90	98.60
Recall	Normal (%)	99.30	99.30	98.60	99.30
	CAD (%)	98.00	97.40	97.40	98.00
	Average (%)	98.60	98.20	97.90	98.60
F-measure	Normal (%)	98.50	97.70	97.40	98.50
	CAD (%)	98.70	98.40	98.10	98.70
	Average (%)	98.60	98.20	97.90	98.60
ROC Area	Normal (%)	99.10	99.10	99.40	99.20
	CAD (%)	99.00	99.00	99.20	99.10
	Average (%)	99.00	99.00	99.30	99.10
Accuracy(%)		**98.60**	98.24	97.93	**98.60**



(a) (b) (c)

FIGURE 8: Comparison of the results obtained using the proposed NE-nu-SVC model with different kernel functions when selected features of the Cleveland CAD dataset were considered (after applying feature selection and five-step balancing of the entities): (a) Kappa statistic, (b) MAE and (c) RMSE.

TABLE 12: Running times obtained using modified records of the Cleveland CAD dataset before and after using the Nested Ensemble (NE-nu-SVC) model with different kernel functions within nu-SVC.

Runtime (seconds)	**Models**							
	nu-SVC				**NE-nu-SVC**			
	Linear	**Polynomial**	**RBF**	**Sigmoid**	**Linear**	**Polynomial**	**RBF**	**Sigmoid**
Time 1	0.11	0.09	0.02	0.01	0.44	0.49	0.45	0.42
Time 2	0.13	0.09	0.02	0.01	0.55	0.83	0.48	0.47
Time 3	0.03	0.09	0.01	0.01	0.42	0.46	0.45	0.42
Time 4	0.03	0.08	0.01	0.01	0.85	0.64	0.46	0.43
Time 5	0.03	0.08	0.01	0.01	0.46	0.49	0.45	0.41
Time 6	0.03	0.08	0.01	0.01	0.80	0.53	0.44	0.41
Time 7	0.03	0.09	0.01	0.01	0.45	0.46	0.44	0.41
Time 8	0.03	0.09	0.01	0.01	0.43	0.46	0.44	0.41
Time 9	0.14	0.09	0.02	0.01	0.44	0.48	0.44	0.42
Time 10	0.03	0.09	0.01	0.01	0.46	0.47	0.45	0.42
Average	0.059	0.087	0.013	**0.01**	0.530	0.531	0.450	**0.422**

TABLE 13: Comparison of the accuracy of the NE-nu-SVC model with state-of-art techniques for the Cleveland CAD dataset.

Study	**Model**	**Number of classes**	**Accuracy in (%)**
Cheung (2001) [73]	Naive Bayes	N/A	81.48
Polat et al. (2005) [74]	AIRS	2	84.50
Polat et al. (2006) [75]	Fuzzy-AIRS-KNN-based system	2	87.00
Kahramanli and Allahverdi (2008) [76]	ANN and FNN (Fuzzy neural network)	2	86.80
Das et al. (2009) [25]	Neural networks ensembles	2	89.01
Polat et al. (2009) [77]	F-score approach for feature selection and LS-SVM with RBF kernel	2	83.70
Anooj et al. (2011) [78]	Weighted fuzzy rules	2	86.35
Srinivas et al. (2014) [79]	Rough-Fuzzy Classifier	5	46.48
Abdar (2015) [33]	C5.0	5	85.33
El-Bialy et al. (2015) [80]	C4.5	2	78.54
Elsayad and Fakhr, (2015) [81]	Markov Blanket Estimation (MBE)	5	97.92
Alizadehsani et al. (2017) [31]	Neural network and genetic algorithm	2	89.40
Paul et al. (2017) [82]	Weighted fuzzy system ensemble	5	92.31
Uyar and İlhan (2017) [83]	recurrent fuzzy neural networks (RFNN) and GA	2	97.78
Karayılan and Kılıç (2017) [84]	Multilayer Perceptron Neural Network	2	95.55
Alizadehsani et al. (2018) [85]	Feature engineering and SVM	2	93.06
Amin et al. (2018) [86]	Vote with Naive Bayes and logistic regression	2	87.41
Haq et al. (2018) [87]	Logistic regression after features selection	2	89.00
Gokulnath and Shantharajah (2018) [88]	Genetic algorithm with SVM	2	88.34
Khan et al. (2019) [72]	Neural Network and Gini Index and Backward Weight Optimization	5	95.01
Burse et al. (2019) [89]	Multi-Layer Pi-Sigma Neuron Model (MLPSNM) and Principal Component Analysis (PCA)	N/A	94.53
Rajab et al. (2019) [90]	Kernel-based FCM (KFCM)-based ANFIS	N/A	86.00
Terrada et al. (2019) [91]	ANN, KNN, K-means, and K-medoids	2	96.01
Ali et al. (2019) [92]	L_1 Linear SVM, L_2 Linear, and RBF SVM	2	92.22
Akgül et al. (2019) [93]	ANN-GA	2	95.82
Proposed method	***NE-nu-SVC + feature selection + multi-step balancing***	***2***	***98.60***

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TABLE A.1: Initial population features generated by the applied genetic algorithm for the Z-Alizadeh Sani CAD dataset.

Merit	**Scaled**	**Subset**
0.01958	0.02731	4, 5, 7, 9, 11, 12, 13, 20, 21, 23, 24, 27, 29, 30, 32, 34, 36, 37, 38, 39, 41, 43, 44, 46, 47, 49
0.04188	0.03687	1, 4, 6, 7, 9, 11, 13, 14, 16, 18, 21, 22, 23, 25, 26, 28, 32, 34, 36, 40, 41, 43, 44, 45, 46, 48, 49, 52, 53
0.04686	0.03901	5, 6, 7, 8, 11, 12, 14, 21, 23, 25, 26, 27, 28, 30, 31, 32, 34, 37, 38, 39, 45, 46, 47, 48, 49, 50, 52, 53, 54
0.03643	0.03453	1, 2, 5, 7, 8, 12, 15, 17, 18, 22, 23, 24, 25, 27, 29, 31, 33, 35, 38, 41, 42, 44, 46, 48, 49, 50, 51, 52, 53, 54, 55
0.11029	0.06621	7, 12, 13, 16, 18, 25, 26, 28, 34, 35, 37, 47, 50
0.03707	0.03481	1, 2, 4, 5, 7, 9, 10, 11, 12, 15, 16, 17, 19, 20, 21, 23, 24, 28, 29, 31, 32, 33, 35, 36, 37, 38, 39, 40, 45, 46, 49, 50, 53, 54
0.01659	0.02602	9, 10, 29, 44, 46
0.01996	0.02747	1, 2, 5, 7, 8, 9, 10, 12, 13, 14, 15, 17, 20, 21, 24, 27, 29, 30, 31, 33, 34, 35, 36, 37, 38, 43, 44, 46, 47, 49, 50, 51, 55
0.02493	0.02960	5, 12, 13, 16, 24, 26, 49, 52, 54
0.01767	0.02649	5, 11, 24, 55
0.04273	0.03724	4, 13, 18, 21, 23, 28, 29, 34, 35, 38, 42, 43, 46
0.02747	0.03069	1, 2, 3, 4, 5, 7, 9, 11, 12, 14, 15, 17, 18, 20, 21, 24, 28, 29, 30, 32, 33, 36, 39, 41, 42, 44, 45, 49, 50, 51, 52, 55
0.02911	0.03139	1, 6, 14, 20, 23, 27, 30, 36, 41, 48, 54
0.03895	0.03561	1, 4, 6 ,8 ,9, 10, 18, 19, 20, 21, 23, 25, 28, 29, 31, 32, 35, 40, 41, 42, 43, 44, 45, 46, 47, 48, 51, 52, 53, 55
0.02372	0.02908	4, 16, 17, 19, 21, 25, 38, 41, 42, 43, 44, 46, 49
0.00021	0.01900	11, 20
0.03611	0.03439	1, 4, 8, 9, 10, 11, 15, 17, 18, 19, 22, 24, 25, 29, 31, 32, 33, 35, 38, 40, 43, 45, 48, 49, 51
0.02587	0.03000	2, 4, 5, 8, 10, 11, 15, 19, 22, 23, 24, 27, 28, 32, 33, 35, 36, 37, 38, 39, 41, 42, 47, 48, 51, 52, 54, 55
0.02565	0.02991	2, 5, 6, 13, 16, 18, 19, 20, 21, 23, 24, 29, 31, 33, 36, 39, 40, 41, 42, 43, 47, 49, 50, 54
0.04104	0.03651	1, 3, 6, 10, 11, 13, 14, 15, 16, 18, 21, 27, 28, 34, 37, 39, 41, 44, 45, 46, 47, 50, 52, 53, 54, 55

TABLE A.2: Generated features provided by the applied genetic algorithm for the Z-Alizadeh Sani CAD dataset.

[H]

Merit	**Scaled**	**Subset**
0.24654	0.3294	6, 7, 12, 18, 25, 26, 28, 29, 32, 35, 37, 53, 54, 55
0.24654	0.3294	6, 7, 12, 18, 25, 26, 28, 29, 32, 35, 37, 53, 54, 55
0.22603	0.28407	7, 12, 25, 26, 28, 29, 32, 34, 37, 38, 53, 54
0.09750	0.0000	7, 12, 18, 24, 25, 26, 27, 28, 34, 36, 37, 38, 48, 53, 54, 55
0.24626	0.32878	6, 7, 12, 18, 25, 26, 28, 32, 35, 47, 53, 54
0.10218	0.01034	7, 12, 16, 25, 26, 28, 29, 37, 38, 41, 49, 53, 54, 55
0.10619	0.01920	7, 12, 18, 24, 25, 26, 28, 34, 36, 37, 38, 40, 45, 55
0.14178	0.09785	6, 7, 12, 18, 20, 21, 25, 26, 28, 29, 31, 37, 53, 54, 55
0.09832	0.00180	4, 6, 7, 10, 12, 18, 19, 25, 26, 28, 29, 32, 45, 55
0.22071	0.27232	7, 12, 24, 25, 26, 28, 29, 37, 38, 53, 54, 55
0.24654	0.32940	6, 7, 12, 18, 25, 26, 28, 29, 32, 35, 37, 53, 54, 55
0.10440	0.01525	5, 7, 12, 18, 22, 24, 25, 26, 28, 29, 37, 38, 42, 53, 54, 55
0.23369	0.30101	7, 12, 25, 26, 28, 29, 32, 35, 37, 38, 53, 54
0.11147	0.03087	6, 7, 12, 18, 25, 28, 29, 32, 35, 37, 40, 52, 53, 55
0.20152	0.22990	6, 7, 12, 18, 24, 25, 26, 28, 29, 34, 37, 55
0.13983	0.09355	4, 6, 7, 8, 12, 15, 16, 18, 25, 26, 28, 29, 32, 35, 37, 53, 54, 55
0.24940	0.33572	6, 7, 12, 18, 25, 26, 28, 29, 32, 35, 53, 54, 55
0.24654	0.32940	6, 7, 12, 18, 25, 26, 28, 29, 32, 35, 37, 53, 54, 55
0.15224	0.12099	6, 7, 12, 18, 25, 26, 28, 29, 32, 35, 37, 44, 53, 54, 55
0.14370	0.10211	6, 7, 12, 17, 19, 25, 26, 28, 29, 32, 35, 37, 53, 54, 55

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