Accurate Neural Network Classification Model for Schizophrenia Disease Based on Electroencephalogram Data

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Abstract

Electroencephalogram is a useful interface system that translates the human electrical brain activity into voltage signals. By these means, the recorded brain waves can be employed to characterize, classify, or diagnose mental disorders. A novel neural network model to classify patients with schizophrenia based on electroencephalograms is presented. The proposed model decomposes the multichannel electroencephalogram records into a group of multivariate novel radial basis functions using a fuzzy means algorithm. The decomposition permits to extract different electroencephalogram channel information and distinguish between two sort of classes i.e., schizophrenic patients and healthy controls. Results show improved accuracy compared to classical algorithms reported in the literature i.e., Support Vector Machine, Bayesian Linear Discriminant Analysis, Gaussian Naive Bayes, K-Nearest Neighbour or Adaboost. As a result, the method presented in this paper achieves the highest balanced accuracy, recall, precision and F1 score values, close to 93 % in all cases. The model presented in this paper may be integrated in real time tools involved during the diagnostic of schizophrenia.

1. Introduction

Schizophrenia is a disorder of crucial public health significance affecting more than 21 million people worldwide, being more common in men (12 million) than in women (9 million) [1]. Schizophrenia may cause a combination of serious disturbances in thinking and behavior, hallucinations, and delusions [2–3]. It usually involves lifelong treatment, where early detection can help to control symptoms and can improve the long-term prognosis [4–5]. The exact causes of schizophrenic disorder are unknown, although current research suggests a combination of hereditary and environmental factors [6–7]. The genetic predisposition maybe the primarily motive, but external factors such as stressful life situations or substance abuse can act as triggers. Diagnosis of schizophrenia is generally based on a comprehensive evaluation of the person's illness history and a clinical interview carried out by psychiatrists. In this interview, signs and symptoms are carefully analyzed, and all possible close sources are asked: family, friends, neighbors, or work, to name a few. For its diagnosis, two manuals that classify psychiatric diseases are used i.e., the Diagnostic and Statistical Manual of Mental Disorders (DSM) of the American Psychiatric Association, and the International Classification of Diseases (ICD) of the World Health Organization (WHO). The last versions of both tests are DSM-V and ICD-10, respectively.

Currently, there is no objective examinations that can confirm the disease. Nevertheless, the monitoring of neurophysiological activity through encephalograms (EEGs) provides decisive information that can lead to a possible diagnosis [8–11]. EEGs offers an effective means of evaluating brain function, remaining an essential tool in neurology, particularly in serious neurological conditions. Besides, it can be employed with relative low damage to patients due to its non-invasive nature [12–15]. Although the EEG does not precisely determine the etiology of the brain disfunction, the subsequent processing of the data recoded by the electrodes can be very helpful to make diagnostics.

Additionally, recent research studies focused on machine learning have significantly helped to develop new classification techniques using EEG records [16–19]. By these means, different brain diseases, including schizophrenia, have been successfully identified compared with healthy controls by examining the neuronal activity of the brain. Generally, machine learning is classified in supervised learning, unsupervised learning, deep learning, and reinforcement learning [13, 20], but during the last years, methods based on deep learning employed for classification have increased significantly due to its interesting properties. For instance, deep learning systems can create new features from datasets without human intervention, it is able to work with unstructured data or allows to develop efficient models at learning complex features due to the use of multiple hidden layers.

In this particular study, a novel deep leaning method based on radial basis function (RFB) using a fuzzy means algorithm is presented. An RBF network is a non-linear artificial neural network that uses complex functions to predict the possible outputs from the input data [21–24]. The RBF network has three different layers in total, the input layer (it transmits the input signals to the hidden neurons without performing any processing operation), the hidden layer (it performs non-linear and local transformations by means of the radial basis functions) and the output layer (it combines the activation of the hidden neurons to obtain the outputs). Thus, these types of networks build approximations that are linear combinations of multiple non-linear local functions. In addition, the training phase is extremely fast, the analysis of hidden layers is simple and present easy network configurations. On the other hand, fuzzy clustering is a class of clustering algorithm where each element could belong to more than one cluster [25–27]. This sort of system is developed to solve exclusive grouping (which considers that each element can be unambiguously grouped with the elements of a specific cluster). The similarity between new elements and clusters is obtained by an analytical function named membership function. Values close to one denote maximum similarity, whilst values close to zero indicate minimum similarity. Thus, the main aim of the fuzzy clustering consists of finding the optimal membership function. More specifically, fuzzy C-means algorithm is a method used in fuzzy grouping based on objective functions (normally least squares error functions) [28–31]. These algorithms define a grouping criterion depending on the objective functions that are iteratively minimized to obtain the optimal fuzzy cluster.

By these means, the use of RBF deep learning methods combined with fuzzy grouping have shown a great accuracy to classify patients with schizophrenia and healthy controls compared with other classical methods. As a result, the proposed algorithm improved the results obtained up to date and could be used in current psychiatry for real time clinical diagnosis. The paper is organized as follows: Section 2 introduces the materials used in this study. Section 3 presents our proposed classification approach. The description of the experiments and the discussion of the results are given in Sections 4 and 5, respectively. Finally, the conclusions of this paper are summarized in Section 6.

2. Materials And Equipment

This section describes the data used in this study. EEGs were recorded continuously through a 32-channel brain vision system employing sintered Ag/AgCl electrodes, see Fig. 1. The sampling rate was 500 Hz and

the electrodes were placed following the International System 10–20 [32] with reference points Fpz/Afz/Fz/Cz/Pz/Qz. External interferences and artifacts existing in EEG signals due to electrical distribution network, breathing, eye-blinking, body movements, breathing or sweating were removed via filtering [33–34]. More specifically, a notch filter at 50 Hz and a low pass filter with 40 Hz cut-off frequency were applied.

The clinical interview DSM-IV from the Diagnostic and Statistical Manual of Mental Disorders was provided to all patients, after requiring informed consent and completing baseline assessments, for schizophrenia diagnosis. The interview was designed to be administered by healthcare personnel having experience in performing unstructured diagnostic evaluations. All patients and controls resided in Cuenca, Spain. In addition, all of them were enrolled in the Severe Mental Disorder Program of the Psychiatric Service of Virgen de la Luz Hospital, Cuenca, Spain. All the evaluations and results obtained were approved by the Clinical Research Ethics Committee of the Health Area. It was conducted between May 2013 and April 2020. Three hundred and twelve subjects with schizophrenia and three hundred and twenty healthy controls were examined in order to confirm the classification models proposed in this paper. Inclusion criteria comprised symptoms within at least 6 months and age between 10 to 60 years. Exclusion criteria limited the study to patients with medical instability and pregnant or lactating women.

3. Methodology

During the last years, numerous classic machine learning based methods have been developed for many different applications in medicine, for instance disease classification and diagnosis [36], medical imagining [37], smart health records [38], personalized treatment [39], epidemic control [40], or artificial intelligence surgery [41], to name a few. Among all these methods and applications, the use of deep learning algorithms for diagnosis and disease identification have become of key importance in healthcare and medical services. In this regard, artificial neural networks (ANN) employing RBF architectures have been tested to solve complex problems in classification, showing good performances in nonlinear scenarios [23, 42]. In the present study, a novel RBF technique to improve accuracy using a fuzzy C-means algorithm was developed. The algorithm was directly applied to the pre-processed real EEG signals to classify two different clusters, namely schizophrenic patients, and healthy controls. Figure 2 shows the architecture of the ANN with the input layer, just one hidden layer, and the output layer, as it was mentioned in the introduction section.

The input layer corresponds to the vectors $e_p = [e_{p,1}, e_{p,2}, ..., e_{p,32}]$ recorded by the 32 electrodes for each p patient. The hidden layer is formed by N neurons with associated radial basis function $\mu(r)$ that estimates the Euclidean distance (denoted as r and showed in Eq. 1) of the input vectors with respect to the center of the s_{th} node $c_s = [c_{s,1}, c_{s,2}, ..., c_{s,32}]$ of the RBF neuron (for $s = 1, 2, ..., N$), see Fig. 3:

{r}={r}\left({{e}}_{{p}}\right)=\left(‖{{e}}_{{p}}-{{c}}_{{s}}‖\right)=\sqrt{\sum _{{n}=1}^{{P}}{({{e}}_{{p},{n}}-{{c}}_{{s},{n}})}^{2}} (1)

The RBF function $\mu \left(r\right)$ can be of several types depending on the patterns to be classified. The most common choices are:

Gaussian function

$$\mu \left(r\right)=e^{-\left(\frac{r}{\sigma }_{s}\right)^{2}}$$

Multi-quadratic function

$$\mu \left(r\right)=\sqrt{1+\left(\frac{r}{\sigma }_{s}\right)^{2}}$$

Inverse multi-quadratic function

$$\mu \left(r\right)=\frac{1}{\sqrt{1+\left(\frac{r}{\sigma }_{s}\right)^{2}}}$$

Poly-harmonic Spline Function

$$\mu \left(r\right)=r^{k}, k=1, 3, 5, \dots$$

$$\mu \left(r\right)=r^{k}\text{l}\text{n}\left(r\right), k=2, 4, 6, \dots$$

where $\sigma }_{s}$ is the width of the s_{th} node of the RBF neuron, shown in Fig. 2. Finally, the output of the network can be calculated as a function of the RBF functions and the output weights $w}_{s}$ associated to each neuron as follows:

$$O\left(e\right)=\sum _{i=1}^{N}w}_{i}\mu \left(\|e}_{p,i}-c}_{s,i}\|\right) \quad (2)$$

3.1. Training of the proposed Neural Network

The training process employed for the proposed RBF neural network includes two separate phases:

1.- The hidden RBF layer parameters are obtained. To this aim, a fuzzy means algorithm [21–24] has been employed to initialize the parameter values $c}_{s}$, $\sigma }_{s}$ and calculate the network structure such as the number of hidden layers N. Generally, N is selected by a trial-and-error method or applying the k-means clustering algorithm [43–44]. However, the use of a fuzzy means systems permits to increase accuracy and is faster. The process establishes a fuzzy partition defining several triangular fuzzy arrangements which centers define a multidimensional grid for the input data. Then, the nodes of the grid are stablished as node centers for the hidden layers, where the distance between any pair of center positions is always equal or greater than the smallest edge in the grid. In addition, it is guaranteed that at least one hidden node is designated for any input data.

Specifically, the input variable is divided in $a}_{s}$ triangular fuzzy sets named $T}_{s}^{1}$, $T}_{s}^{1},\dots , T}_{s}^{a}_{s}$ with membership functions:

{{\mu }}_{{{T}}_{{s}}^{{l}}}\left({{e}}_{{p}}\right)=\left\{\begin{array}{c}1-\frac{\left|{{e}}_{{p}}-{{t}}_{{s}}^{{l}}\right|}{{{d}}_{{s}}^{{l}}} if e\in \left[{{t}}_{{s}}^{{l}}-{{d}}_{{s}}^{{l}},{{t}}_{{s}}^{{l}}+{{d}}_{{s}}^{{l}}\right] , l=1,\dots ,{{a}}_{{s}} \\ 0 otherwise \end{array}\right. (3)

being {{t}}_{{s}}^{{l}} the central element with membership value equal to unity and {{d}}_{{s}}^{{l}} is half of the respective width. It is worthwhile to mention that for each input variable, the sum up of the membership quantities is the unity. The aforementioned fuzzy partition properties have been represented for an input vector {{e}}_{1} in Fig. 3.

At last, the width {{\sigma }}_{{s}} of the RBF activation functions are calculated. For each i node, the width was estimated using the g heuristic of the nearest neighbour:

{{\sigma }}_{{i}}\left({e}\right)={\left(\frac{1}{{g}}\sum _{{j}=1}^{{g}}{||{{c}}_{{i}-{{c}}_{{j}}||}^{2}\right)}^{1/2} (4)
where {{c}}_{1}, {{c}}_{2}, \dots , {{c}}_{{g}} are closest node centers to the hidden i node. The g value was chosen so that entering an input vector into the system activates a large number of nodes.

2.- The weights{{w}}_{{s}} are calculated by means of a linear regression based on Eq. (2). The solution of the linear regression implies N equations with N unknown weights, that can be expressed in a matrix form as follows:

$$\underbrace{\begin{bmatrix} \mu(\|e_{1,1}-c_{1,1}\|) & \cdots & \mu(\|e_{1,1}-c_{1,N}\|) \\ \vdots & \ddots & \vdots \\ \mu(\|e_{N,1}-c_{s,1}\|) & \cdots & \mu(\|e_{N,1}-c_{N,N}\|) \end{bmatrix}}_{\mu} \underbrace{\begin{bmatrix} w_1 \\ \vdots \\ w_N \end{bmatrix}}_{w} = \underbrace{\begin{bmatrix} O(e_{p,1}) \\ \vdots \\ O(e_{p,N}) \end{bmatrix}}_{O} \quad (5$$

Moreover, a simpler solution corresponding to the exact interpolation obtained as {w}={{\mu }}^{-1} can be applied.

Lastly, in order to train the hidden layer of the neural network, a group of known training pairs of inputs {{e}}_{{k}} and outputs {{O}}_{{k}} (with{k}=1, 2,...,{K})has been employed.

3.2. Validation

The validation of the model proposed was performed by means of a K-fold cross-validation process [45] to assess its predictive capability, see Fig. 4.

It is an iterative procedure that divides the recorded input data from the electrodes randomly into k groups or folds of approximately the same size. K-1 groups are used to train the model and the remaining one is used for validation. This process is repeated K times using a different group for validation in each

iteration. The process generates K estimates of the error, which average is considered the final estimation. In the present study, the input recorded dataset was divided 70% for training and 30% for testing. To avoid overtraining the cross-validation analysis was performed without sharing data across training and validation groups. A comparison among different classical machine learning algorithms i.e., Support Vector Machine (SVM), Bayesian Linear Discriminant Analysis (BLDA), Gaussian Naive Bayes (GNB), K-Nearest Neighbour (KNN) and Adaboost were also included in the study to check the advantages of the proposed model. All the methods were implemented through the machine learning Matlab toolbox [46].

As it is well known, the algorithms need to be adjusted during the training process by means of different hyperparameters like the number of splits, learners, neighbours, distance metric, distant weight, kernel, box constraint level, multiclass method, etc. The hyperparameters of each model were optimized with a Bayesian approach. In this regard, the Bayesian optimization generates a short sequence of simulated experiments with different combinations of the hyperparameters, keeping the values that presents the best area under the curve (AUC) and balanced accuracy.

Finally, the parameters checked to measure performance are:

{R}{e}{c}{a}{l}{l} \left({\%}\right)=\frac{{T}{P}}{{T}{P}+{F}{N}} {x} 100 (6)

{S}{p}{e}{c}{i}{f}{i}{c}{i}{t}{y} \left({\%}\right)=\frac{{T}{N}}{{T}{N}+{F}{P}} {x} 100 (7)

{P}{r}{e}{c}{i}{s}{i}{o}{n} \left({\%}\right)=\frac{{T}{P}}{{F}{P}+{F}{P}} {x} 100 (8)

{B}{a}{l}{a}{n}{c}{e}{d} {a}{c}{c}{u}{r}{a}{c}{y} \left({\%}\right)=\frac{{R}{e}{c}{a}{l}{l}+{S}{p}{e}{c}{i}{f}{i}{c}{i}{t}{y}}{2} {x} 100 (9)

In these equations, *TP* indicates the number of positive cases, *TN* is the true negatives, *FN* the false negatives and *FP* indicates the false positive cases.
In addition, the {{F}}_{1} score and Matthew's correlation coefficient (*MCC*) were employed during the study. The {{F}}_{1} score is defined as:

{{F}}_{1} {s}{c}{o}{r}{e} \left({\%}\right)=\frac{{P}{r}{e}{c}{i}{s}{i}{o}{n}\bullet {R}{e}{c}{a}{l}{l}}{{P}{r}{e}{c}{i}{s}{i}{o}{n}+{R}{e}{c}{a}{l}{l}} {x} 100 (10)

and the *MCC* [47], that measures the overall model performance, is described as:

{M}{C}{C} \left({\%}\right)=\frac{{T}{P}\bullet {T}{N}-{F}{P}\bullet {F}{N}}{\sqrt{({T}{P}+{F}{P})({T}{P}+{F}{N})({T}{N}+{F}{P})({T}{N}+{F}{N})}} {x} 100 (11)

Lastly, two additional metrics assessing the overall model performance, namely Cohen's Kappa (*CK*) and degenerated Younden's index (*DYI*) [47], have also been included in the study.

4. Results

The results obtained for schizophrenia classification employing the proposed method and different classical algorithms are presented subsequently. The experiments were carried out on an Intel Xeon dual-core computer and 32 GB RAM. The machine learning toolbox included in MATLAB was used for preprocessing of EEG data and developing the machine/deep learning models. Performance metrics (balanced accuracy, recall, precision and F_1 score) for all methods (SVM, BLDA, GNB, KNN, Adaboost, and RBF) are shown in Table 1.

Table 1
Values of balanced accuracy, recall, precision and F_1 score of the machine learning models and the proposed method implemented.

Method	Balanced Accuracy (%)	Recall (%)	Precision (%)	F_1 score (%)
SVM	84.74	84.84	84.64	84.14
BLDA	81.95	82.05	81.84	81.34
GNB	75.60	75.68	75.50	75.12
KNN	87.94	88.08	87.81	87.68
Adaboost	89.05	89.16	89.05	88.44
RBF	93.40	93.49	93.30	92.73

The proposed method achieved the highest metrics. Compared to RBF, Adaboost and KNN algorithms had the subsequent best values of metrics. Balanced accuracy, recall, precision and F_1 score were in all cases 4% and 6% below the proposed method based on radial basis functions, respectively. SVM, BLDA, GNB, presented lower values in all the parameters evaluated.

Additionally, the results for the AUC, MCC, DYI and Kappa index are given in Table 2. Again, the best performance is obtained for the model presented in this study with parameter values AUC, DYI and Kappa index close to 93% and MCC 83%. Both models, Adaboost and KNN, behaved with lower performance values and SVM, BLDA, GNB exhibited considerably lower classification capability. Therefore, it can be concluded that the RBF model was significantly more accurate than classical systems employed currently in machine learning classification approaches.

Table 2
Values of AUC, MCC, DYI and Kappa of all the tested machine learning models and the proposed method implemented.

Method	AUC (%)	MCC (%)	DYI (%)	Kappa (%)
SVM	84	75.19	84.74	74.64
BLDA	81	72.71	81.95	72.80
GNB	75	66.51	75.59	67.35
KNN	87	77.94	87.94	78.12
Adaboost	89	78.97	89.15	79.37
RBF	93	83.13	93.40	83.02

For clarity, Fig. 5 displays the aforementioned values of metrics and indexes as radar charts, divided into two different graphs corresponding to training and test dataset. As it can be observed, among all algorithms analyzed the RBF model has the best shape, close to the maximum values in both cases, the training and test records. The rest of the methods showed lower accuracy following the next precision (from highest to lowest accuracy): Adaboost, KNN, SVM, BLDA, and GNB.

At last, the overall diagnostic accuracy of the method has been checked by means of the receiver operating characteristic (ROC) that represents the sensitivity versus (1-specificity). ROC is a curve of probability so that values close to 1 denotes a perfect predictive capability of the method analyzed, and it is closely related to the area under a given ROC curve. In this regard, the higher the AUC, the better the prediction accomplished by the model is. A 0 AUC value indicates a totally inaccurate prediction, and a 1 AUC value reflects a completely accurate test. Likewise, an AUC value of 0.5 indicates that the method is not able to discriminate schizophrenic patients and healthy controls, and the ROC curve falls on the diagonal. AUC values above between 0.7 to 0.8 are considered acceptable, between 0.8 to 0.9 are considered excellent, and AUC values beyond 0.9 are considered outstanding. See Fig. 6 for the ROC curves obtained in the case of data presented in Table 2. As it can be expected, the RBF proposed system reaches the best prediction accuracy for schizophrenia disease.

5. Discussion

In this analysis, a novel method based on neuronal networks for schizophrenia classification has been presented. More specifically, a method employing RBF functions combined with fuzzy C-means clusters was developed. It showed a high accuracy in the diagnostic prediction, improving the classification capability compared to other classical algorithms. In the analysis, the configuration of the RFB system was firstly determined using the machine/deep learning toolbox of MATLAB following the expressions described in Section 3.1. To this aim, the method was trained by means of three hundred and twelve patients affected with schizophrenia and three hundred and twenty controls, thus, validating the method with a large number of patients and healthy volunteers.

Furthermore, similar models based on machine learning algorithms, namely SVM, BLDA, GNB, KNN, and Adaboost, generally employed in disease detection were generated. The proposed method was tested employing eight factors (balanced accuracy, recall, precision, F_1 score, AUC, MCC, DYI and Kappa index) to check the performance during the classification of diagnosticated patients with schizophrenia and healthy individuals. The best metrics were obtained for the proposed model (balanced accuracy = 93.40%, recall = 93.49%, precision = 93.30%, F_1 score = 92.73%, AUC = 93%, MCC = 83.13%, DYI = 93.40%, and Kappa = 83.02%). The other classic methods mentioned previously always showed lower values i.e., between 4% – 18% points lower, for the metrics analyzed. Additionally, ROC results for the methods included in the analysis indicated that the best prediction algorithm was the proposed RBF system. Therefore, the outcomes achieved proved that the classification algorithm proposed improves the existing classical classifiers.

The enhanced classification properties of RBF algorithms combined with fuzzy C-means can provide important advantages for classification. First, RBF systems have good generalization ability, stability, robust tolerance to noise, and simplify the configuration of the network as they only have one hidden layer. This implies very fast training and rapid classification. Furthermore, the algorithm integrates a fuzzy initialization of the network that improves the approach capabilities, where it is not necessary to have a fixed number of cluster prior training stages.

6. Conclusions

In conclusion, in this study an RBF model initialized with a fuzzy C-means algorithm have been developed. This analysis proposes the combination of methods to improve classification properties to discriminate schizophrenic patients from healthy individuals. Moreover, other recent machine learning methods i.e., support vector machine, bayesian linear discriminant analysis, gaussian naive bayes, K-nearest neighbour, or Adaboost, have also been included in the study to compare the performance of the model presented in this paper. The results obtained show that RBF algorithms combined with fuzzy clusters provides the best classification accuracy in classifying patients affected by schizophrenia and healthy controls. In particular, balanced accuracy, recall, precision, F_1 score, AUC, DYI parameters around 93% and, MCC and Kappa indexes around 83.13%, were achieved. The proposed RBF classifier presented important advantages compared to other classic methods such as simplicity, good generalization ability and robust tolerance to noise. These results indicate that the application of RBF artificial neural network techniques to data acquired by means of encephalograms can potentially help during the automatic classification of patients in medical environments.

Declarations

Author Contributions: M.A.L. and A.L.B. wrote the main manuscript text. M.A.L., J.M.S and J.L.S. prepared the experiments, measurements. M.A.L., J.M.S. and A.L.B. carried out the simulations and signal processing.

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Figures

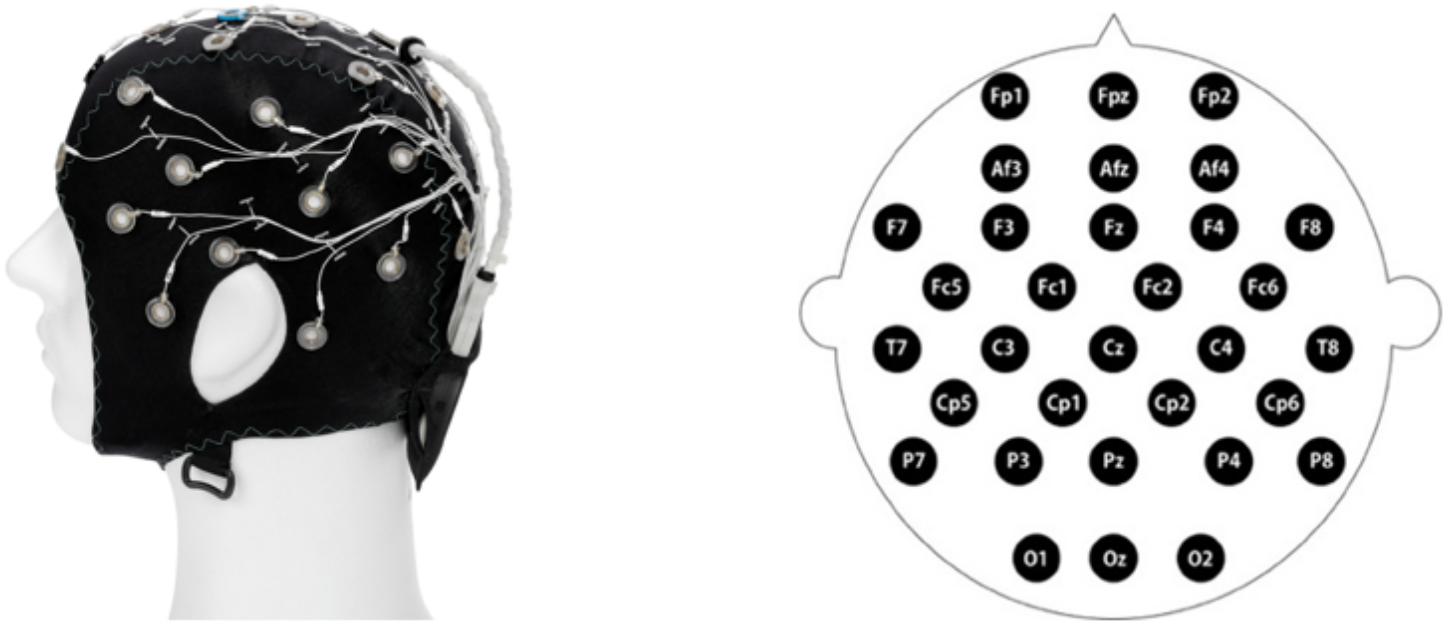

Figure 1

Brain vision system employed to record EEG datasets and electrode positions [35].

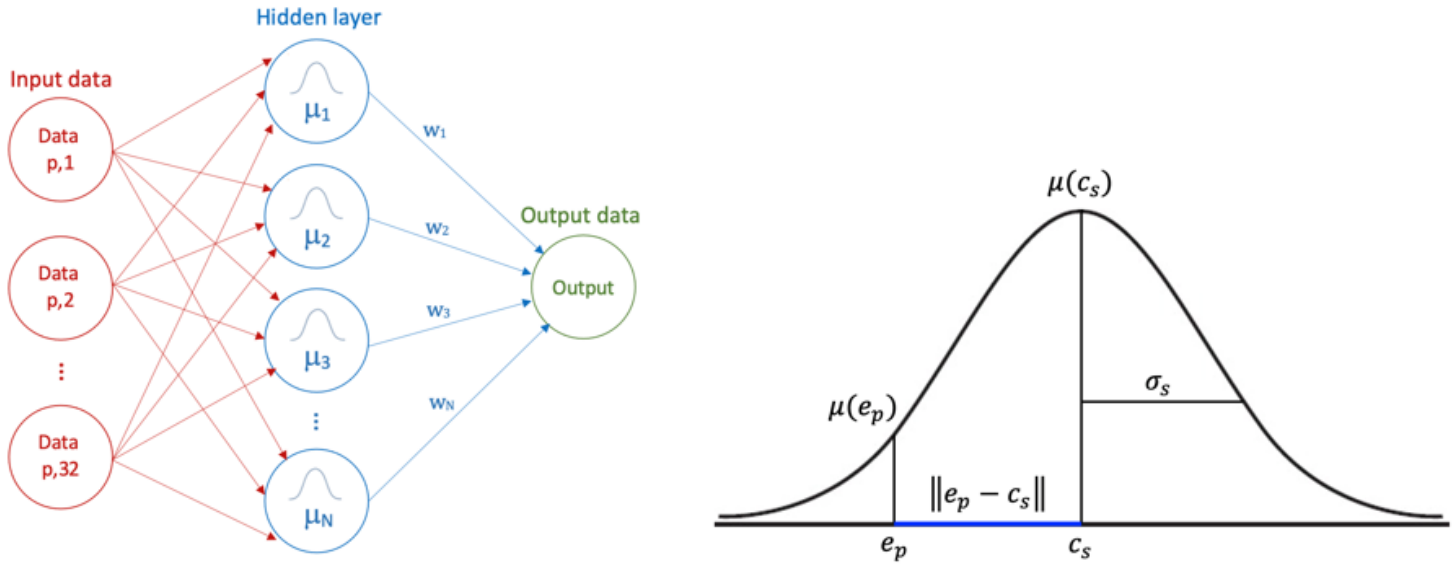

Figure 2

Structure of the proposed RBF network and RBF Gaussian neuron.

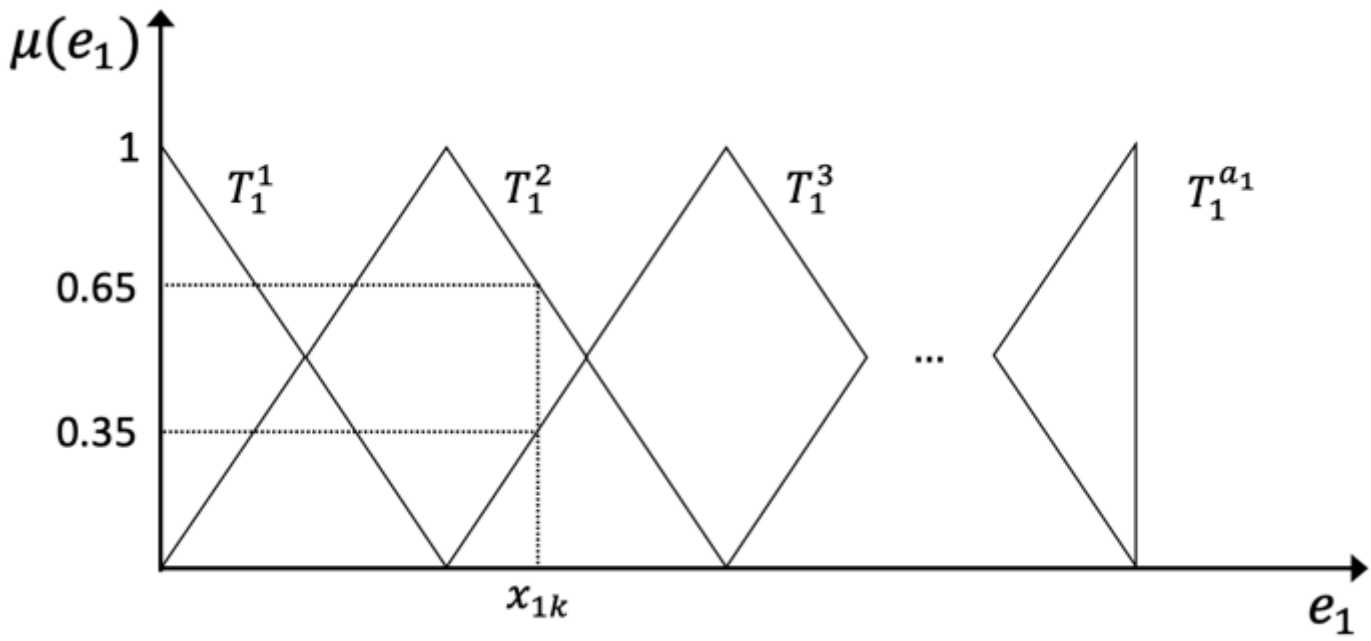

Figure 3

Fuzzy sets selection for a generic input variable.

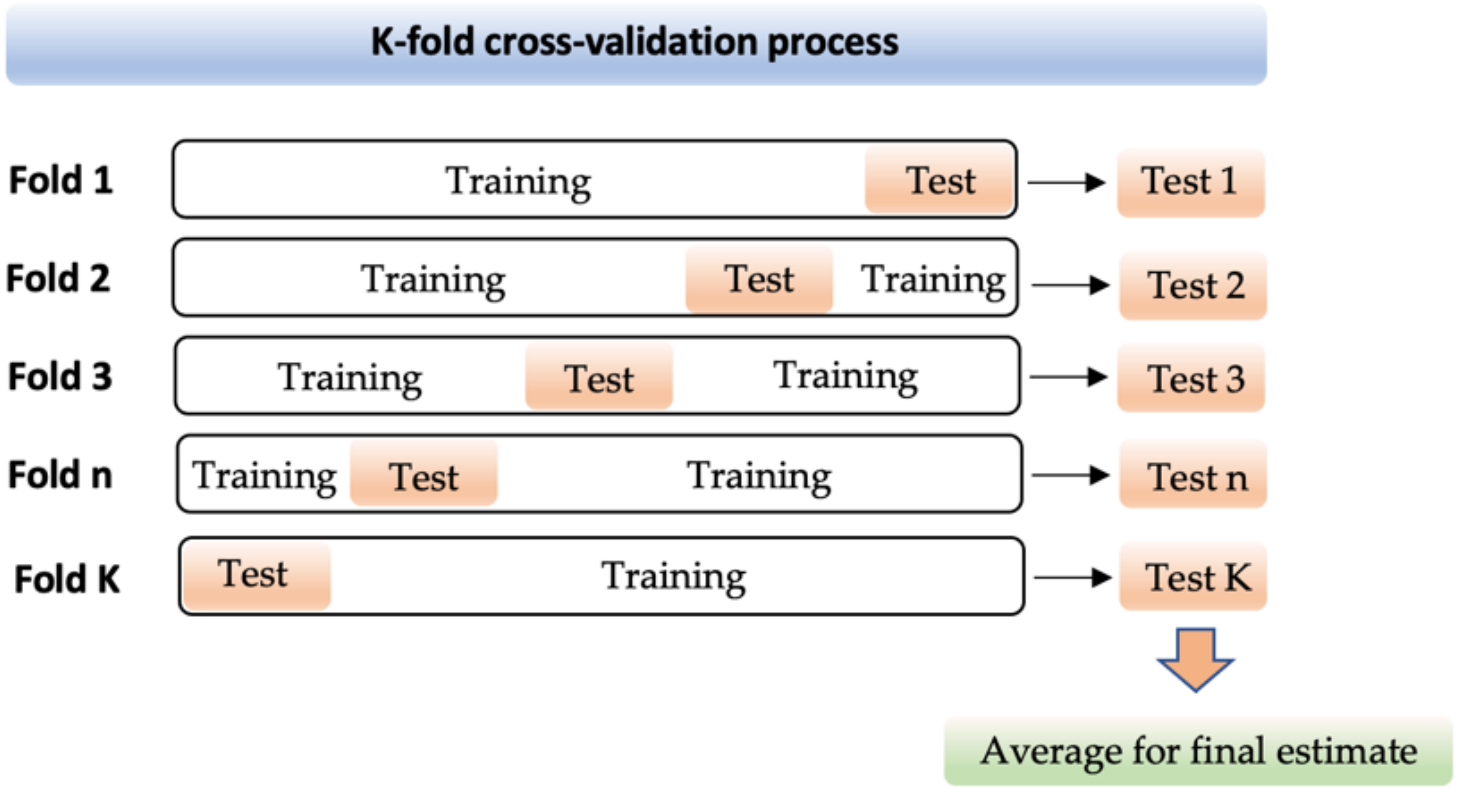

Figure 4

Validation method employed.

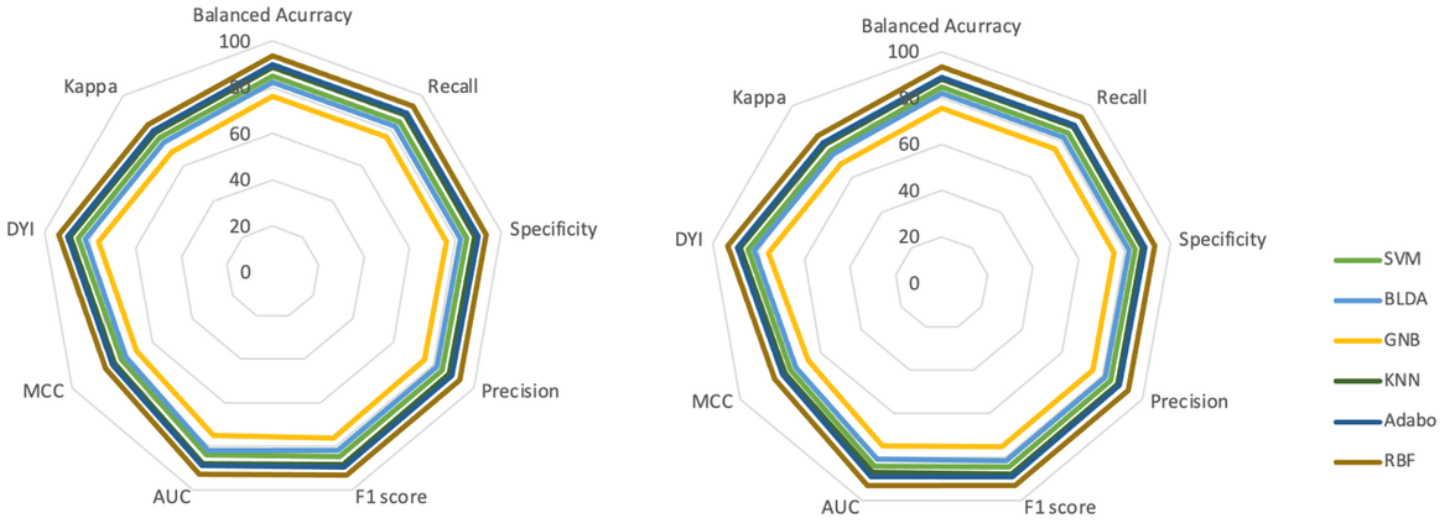

Figure 5

Radarplot of the training phase (above) and test (below) for the classification of bipolar disorder patients.

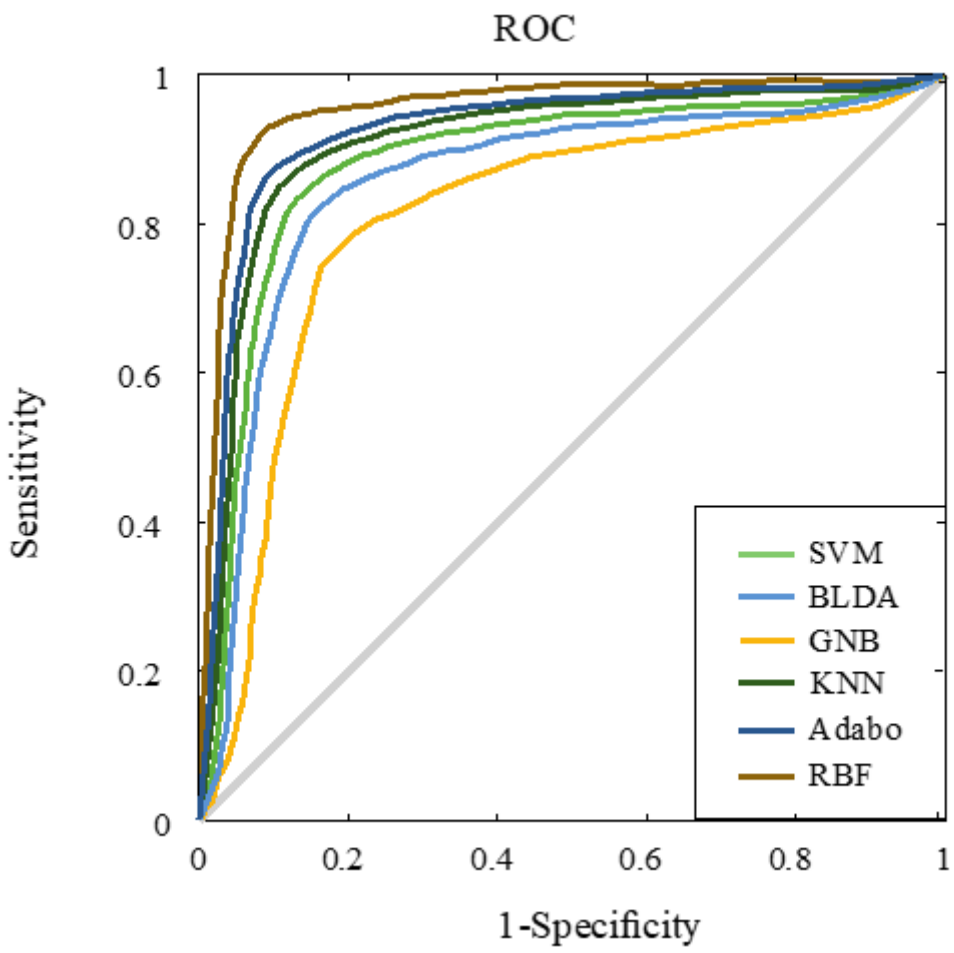

Figure 6

ROC curves of the classification models compared in this study.