Early Diagnosis of Alzheimer's Disease on the basis of Orthogonal Locality Preserving Projections and Multi Support Vector Machine

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Abstract : In recent years, several brain scans are collected from different tools to analyze human brain activities for Alzheimer disease detection. Among the available tools, Magnetic Resonance Imaging (MRI) is an effective tool to analyze the functions of the human brain. Initially, the MRI scans were collected from a dataset: Minimal Interval Resonance Imaging in Alzheimer's Disease (MIRIAD). After the collection of brain scans, pre-processing and skull stripping were performed by using histogram equalization and Otsu thresholding approaches. Then, segmentation was carried-out using modified- Kernelized Fuzzy C-Means (KFCM) for segmenting brain tissues: white matter, Cerebro-Spinal Fluid (CSF), and grey matter from the pre-processed brain scans. In addition, hybrid feature extraction (Histogram of Oriented Gradients (HOG), and Dual tree complex wavelet transform (DTCWT)) was used to extract the feature values from the segmented brain tissues. After extracting the feature values, Orthogonal Locality Preserving Projections (OLPP) approach was used for selecting the optimal feature values. Finally, the dimensionally reduced feature vectors were given as the input for multiclass classifier: Multi Support Vector Machine (MSVM) to classify three Alzheimer classes: normal, Alzheimer disease and Mild Cognitive Impairment (MCI). The experimental result showed that the proposed system improved the classification accuracy up to 15% as compared to the existing systems.

IndexTerms **- Dual tree complex wavelet transform, histogram of oriented gradients, kernelized fuzzy c-means, multi support vector machine, and orthogonal locality preserving projections.**

I. INTRODUCTION

Alzheimer's disease is a progressive neuro-degenerative disorder that is characterized by deterioration of cognitive and memory functions. Presently, over 20-30 million people are affected by Alzheimer's disease worldwide [1]. In recent periods, several neuroimaging systems are broadly used in Alzheimer's disease detection and clinical diagnosis, which includes positron emission tomography, MRI, computed tomography, etc. [2, 3]. In that, MRI is a promising one that is utilized for detecting the hippocampal volume and also determine its significance as an indicator of Alzheimer's disease neuropathology. In addition, the MRI brain scans are utilized for identifying the non-demented elderly with Alzheimer's disease neuropathology, so the clinician can able to slow the progression of Alzheimer disease by determining the risk factors of Alzheimer's disease patients [4, 5]. The manual analysis (clinicians or doctors) of Alzheimer's disease is highly significant, but it may not be precise all the time. So, automatic Alzheimer's disease detection system has made an impact in the research community, because of its numerous functional applications [6, 7]. In the field of automatic Alzheimer's disease detection, one of the major problems is that the sample size of medical data is very small, while the dimension is relatively high. Usually, the extracted feature values are higher dimension in nature, so it is essential to transform the high dimensional feature space into low dimensional feature space. At present, a few dimensionality reduction approaches are available in Alzheimer disease detection in order to diminish the "curse of dimensionality" issue [8]. The traditional methodologies: principal component analysis [9], linear discriminant analysis [10] are highly affected by the number of samples in the training and testing sets. To address this concern, a new system was developed in this research paper for improving performance Alzheimer disease classification.

In this research, an effective system is developed to improve the classification accuracy of Alzheimer disease. At first, the brain images were collected from a dataset: MIRIAD. After the collection of brain images, histogram equalization was applied to enhance the quality of collected brain images. The main aim of histogram equalization is to provide a linear trend to the cumulative probability function related to the brain images. The pre-processed brain images were given as the input for Otsu thresholding approach in order to perform skull stripping. After skull stripping, image segmentation was performed by applying modified-KFCM for segmenting the brain tissues like white matter, CSF, and grey matter. The main advantage of modified-KFCM was very robust to the clustering parameters that effectively reduces the computational complexity of the proposed system. Then, hybrid feature extraction (DTCWT and HOG) was carried-out on the segmented brain tissues for extracting the feature values. The hybrid feature extraction method extracts the local and global features from the segmented images that effectively reduce the semantic gap between the low and high-level features. After attaining the feature values, OLPP method was used to reduce the dimensions of the extracted feature values. The dimensionality reduction is the process of achieving the optimal feature sub-sets from the set of extracted features by the rejection of irrelevant or redundant features. The output of dimensionality reduction was given as the input for MSVM classifier in order to classify the stages of Alzheimer disease stages: normal, Alzheimer disease, and MCI. Finally, the performance of the proposed system was compared with other existing systems in terms of precision, recall, error rate, classification accuracy.

This research paper is arranged as follows. Several recent papers in Alzheimer disease classification are reviewed in t section II. Detailed explanation about the proposed system is given in section III. Section IV illustrates the quantitative analysis and comparative analysis of the proposed system. The conclusion is done in section V.

II. LITERATURE REVIEW

L. Khedher, J. Ramírez, J.M. Górriz, A. Brahim, F. Segovia, and Alzheimer' s Disease Neuroimaging Initiative, [11] developed a new system for Alzheimer's disease classification by using partial least squares and principal component analysis. The developed multivariate approaches perform dimensionality reduction in the feature vectors for reducing the small sample size problem. In this research paper the classification was difficult, when the dimension of the feature vectors/values were very high.

R.M. Steketee, E.E. Bron, R. Meijboom, G.C. Houston, S. Klein, H.J. Mutsaerts, and M. Smits, [12] used arterial spin labeling-MRI for the early diagnosis of Alzheimer's disease. The developed method helps to differentiate the two most common types of presenile dementia: frontotemporal dementia and Alzheimer's disease. The structural Region of Interest (ROI) includes the lingual gyrus and cuneus, which shows hypoperfusion in Alzheimer's disease that affects the entire region of cerebral blood flow. So, it was very difficult in segmenting the brain tissues like CSF, white matter and gray matter.

J. Zhang, M. Liu, L. An, Y. Gao, and D. Shen, [13] used landmark-based feature extraction approach for automatic Alzheimer's disease classification. The developed approach shows an efficient diagnostic capability by eliminating inconsistent scan numbers. The learning performance of the subsequent classification model was affected by redundant or noisy features.

J.E. Iglesias, K. Van Leemput, J. Augustinack, R. Insausti, B. Fischl, M. Reuter, and Alzheimer's Disease Neuroimaging Initiative, [14] developed an effective algorithm (Bayesian longitudinal) for automatic Alzheimer's disease classification. The developed system increases the flexibility of the segmentation and also reduced the time complexity of the segmentation. The classification performance was degraded, when the training samples were noisy or mislabeled and placed on the incorrect side.

I. Beheshti, H. Demirel, and Alzheimer's disease Neuroimaging Initiative, [15] used t-test based feature making the approach for Alzheimer's disease classification. The developed method compares the local and global differences of brain tissues; white matter, CSF, and grey matter and then voxel cluster was employed for extracting the feature values. The extracted features were classified by employing support vector machine. At last, the data fusion approach was applied for improving the classification accuracy of Alzheimer disease. SVM was a binary classifier, which supports only two-class classification.

III. PROPOSED METHODOLOGY

In this research paper, the proposed system consists of six phases; image collection, pre-processing, segmentation, feature extraction, dimensionality reduction and classification. Fig. 1 shows the work flow of the proposed system and the detailed explanation about the proposed system is described below.

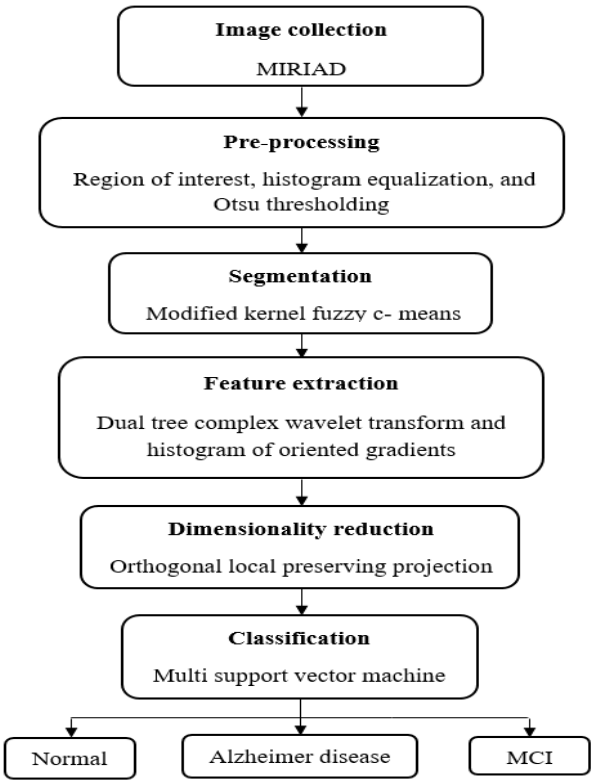


Figure 1. Work flow of proposed system

3.1 Image collection

Initially, the input brain images are collected from a dataset: MIRIAD. The MIRIAD dataset contains T1 708 MRI scans for forty-six subjects. Here, the scans are collected at the intervals of 18 and 24 months or 2, 6, 14, 26, 38, and 52 weeks from baseline. Also, this dataset includes information like age, mini mental state examination scores, and gender. The sample collected brain image is graphically denoted in Fig. 2.

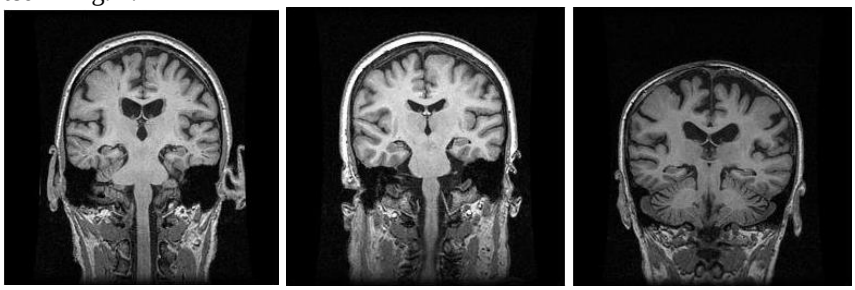
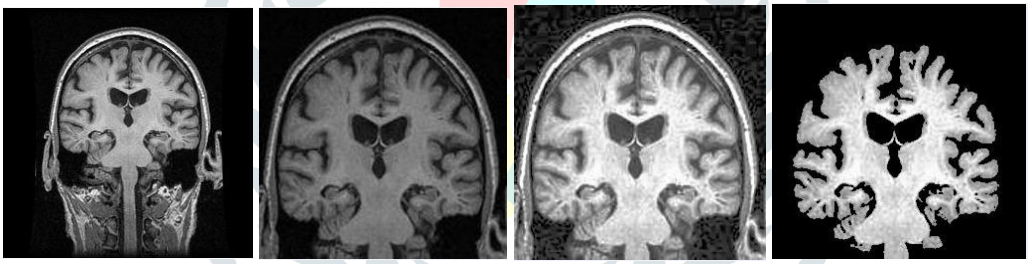


Figure 2. Sample image of MIRIAD dataset

3.2 Image pre-processing

After collecting the brain scans, image pre-processing is carried out for reducing the noise or to enhance the quality of brain images. In this research, the region of interest and histogram equalization are used for pre-processing the brain images. Initially, ROI is performed on the collected brain images, which is defined as a subset of brain image or a database identified for a specific purpose. Then, histogram equalization is carried out on the ROI applied brain image. After histogram equalization, Otsu thresholding approach is applied for skull removal. The undesired brain tissues and artifacts during image collection affects the processing quality that leads to the imprecise diagnosis. So, a vital phase in brain segmentation is skull stripping/removal. Since, the manual skull stripping is a time-consuming task and prone to errors. To address this concern, several methods are developed for removing the additional cerebral tissues without human intervention. Though, each and every skull stripping algorithm has its own merits and limitations. In this research study, the pre-processed brain images are utilized for skull removal by applying Otsu thresholding approach.

The Otsu thresholding approach works on the basis of discriminates analysis in order to determine the maximum separability of classes and also the Otsu thresholding approach is used for performing histogram shape image thresholding. The Otsu thresholding approach identifies the threshold value on the basis of statistical information of the brain image. After skull stripping, segmentation is done by applying modified KFCM clustering for segmenting the brain tissues; white matter, CSF, and grey matter from the skull removed the brain image. The sample input and pre-processed brain image of MIRIAD dataset are represented in Fig. 3.



(a) (b) (c) (d)

Figure 3. a) Input image, b) region of interest, c) pre-processed image, and d) skull removed image for MIRIAD dataset

3.3 Image segmentation using modified KFCM

The pre-processed brain images are used for tissue segmentation. In this research study, an effective approach: modified-KFCM is undertaken for segmenting the brain tissues: normal, Alzheimer disease, and MCI. This segmentation approach considers I as a pre-processed brain image that comprises of a set of grayscale images p_i at pixel $i(i = 1,2, \dots, N)$ and $P = \{p_1, p_2, p_3 \dots p\} \subset R^k$, respectively in the $k-$dimensional area. The cluster centers in the brain images are denoted as $Q = \{q_1, q_2, q_3 \dots q_c\}$, where c is represented as a positive integer $(2 < c \ll N)$ and u_{ij} is denoted as a membership value for each pixel i in j^{th} cluster $(j = 1,2, \dots c)$. The clusters formed in the image space are combined by assigning a separate membership value to all the pixels in modified KFCM algorithm. The general equation or objective function of modified KFCM is mathematically given in the Eq. (1).

$$J_{KFCM} = \sum_{i=1}^{N} \sum_{j=1}^{c} u_{ij}^{m} \left\| p_i - q_j \right\|^2 , 1 \le m < \infty \quad (1)$$

Where, c is represented as the number of clusters, N is denoted as the data points, u_{ij} is stated as the degree of membership, m is represented as an exponent of regularization to the degree of fuzziness, $m > 1$ and $\left\| p_i - q_j \right\|^2$ be the gray-scale Euclidean distance between i and q_j, which is mathematically represented in the Eq. (2).

$$\sum_{j=1}^{c} u_{ij} = 1, u_{ij} \in [0,1], 0 \le \sum_{i=1}^{N} u_{ij} \le N \quad (2)$$

The cluster centres and membership function are updated in an alternating procedure, which is named as alternate optimization. The cluster centres and membership function are mathematically given in the Eq. (3) and (4).

$$q_j = \frac{\sum_{i=1}^{N} u_{ij}^{m} p_i}{\sum_{i=1}^{N} u_{ij}^{m}} \quad (3)$$

$$u_{ij} = \frac{1}{\sum_{k=1}^{c}\left(\|p_i - q_j\|^2 / \|p_i - q_k\|^2\right)^{1/(m-1)}} \quad (4)$$

Generally, the objective function does not comprise of any local information, so the conventional FCM is very sensitive to noise and artifacts. In this proposed approach, the presence of noise is decreased by adding a spatial information of neighbouring pixels that is denoted in the Eq. (5).

$$J_{KFCM-S} = \sum_{i=1}^{N}\sum_{j=1}^{c} u_{ij}^{m} \|p_i - q_j\|^2 + \frac{\alpha}{N_R}\sum_{i=1}^{N}\sum_{j=1}^{c} u_{ij}^{m} \left(\sum_{r\epsilon N_i}\|p_r - q_j\|^2\right) \quad (5)$$

Where, α is represented as the spatial information with $0 < \alpha \leq 1$, N_i and N_r are denoted as the set of pixels and cardinality of the pixels, and $\acute{p}$ is indicated as a colour scale filtered image. In addition, the conventional FCM algorithm is computationally expensive. So, the term $\frac{1}{N_R}\sum_{r\epsilon N_i}\|p_i - q_j\|^2$ is replaced with $\|\acute{p}_i - q_j\|^2$ in order to avoid the neighbourhood function. The updated objective function is represented in the Eq. (6).

$$J_{KFCM-S(1,2)} = \sum_{i=1}^{N}\sum_{j=1}^{c} u_{ij}^{m} \|p_i - q_j\|^2 + \alpha\sum_{i=1}^{N}\sum_{j=1}^{c} u_{ij}^{m} \left(\|\acute{p}_i - q_j\|^2\right) \quad (6)$$

Then, the modified-KFCM calculates the parameter η_j at every step of the iterations in order to replace α for each cluster. Here, the correlation distance measure is used for calculating the parameter value that is mathematically represented in the Eq. (7).

$$\eta_j = \frac{min_{j' \neq j}\left(1 - C\left(q'_j, q_j\right)\right)}{max_k\left(1 - C\left(q_k, \acute{p}\right)\right)} \quad (7)$$

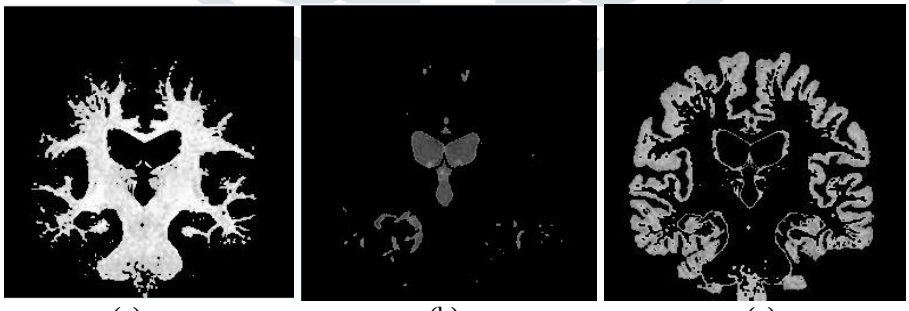
Where, C is represented as the correlation distance measure or correlation function. Generally, the identification of C requires a large number of patterns and also several cluster centers are needed for finding the optimal value for η_j. To address this concern, a combination of scale information and spatial context are developed by using a fuzzy factor. The fuzzy factor F_{ij} is included in the objective function of the modified-KFCM, which is stated in the Eq. (8).

$$J_{C-KFCM} = \sum_{i=1}^{N}\sum_{j=1}^{c}\left[u\left|ij^m\right|\|p_i - q_j\|^2 + F_{ij}\right] \quad (8)$$

The altered fuzzy factor F'_{ij} is derived by using the Eq. (9).

$$F'_{ij} = \sum_{C\epsilon N_i, i \neq k} w_{ik}\left(1 - u_{ij}\right)^m \quad (9)$$

Where, w_{ik} is represented as the fuzzy factor i and $1 - C\left(p_i, q_j\right)$ is denoted as the correlation metric function. Here, the altered fuzzy factor F'_{ij} controls the local neighbour relationship and also replace the distance with a correlation distance measure. The segmented brain tissues of MIRIAD dataset is graphically denoted in the Fig. 4.



(a) (b) (c)

Figure 4. a) Segmented white matter, b) Segmented CSF, c) Segmented grey matter of MIRIAD dataset

3.4 Feature extraction and dimensionality reduction

After segmenting the brain tissues, feature extraction is carried out by using DTCWT [16] and HOG [17] for extracting the feature value/vector from the segmented brain images. The extracted features are given as the input for OLPP in order to perform dimensionality reduction. In recent periods, dimensionality reduction is used for reducing the large dimensional features to low dimensional features without the loss of useful information. The number of irrelevant features decreases the accuracy of classification. So, an effective dimensionality reduction approach: OLPP is applied for reducing the feature space without losing or affecting the classification accuracy. Here, OLPP algorithm helps to decrease the measurement of feature values that highly increases the accuracy of classification. In conventional methodologies, it is hard to remake the information and also the existing algorithms are ordinarily non-orthogonal. To address this concern, an effective dimensionality reduction approach: OLPP is used in this research for Alzheimer disease classification [18]. After dimensionality reduction, Alzheimer disease classification is carried out by using M-SVM.

3.5 Alzheimer disease classification using multi support vector machine

Usually, regular SVM is a two-class classification approach. In order to extend normal SVM to multi classification, it is necessary to modify the multi binary classification issues. In SVM, the multi-class classification is reformed into n^{th} two class and i^{th} two-class issues, where class i is separate from the residual classes. In SVM, two most prominent methodologies are One-Against-All (1-a-a) and One-Against-One (1-a-1). In this scenario, the 1-a-a solution creates a binary classifier for every class that distinct the objects belong to the same class. In n^{th} class, the 1-a-a approach generates n^{th}binary classifiers, and the i^{th} classifier is trained with the samples in i^{th} class with positive labels and the remaining samples are trained with negative labels. The outcome of n^{th} class in 1-a-a approach relates to the 1-a-1 approach for obtaining the highest output value. In addition, the 1-a-1 approach is the resultant of previous researches on two class classifier.

The idea behind MSVM is to generate all possible two class classifiers from a training set of n^{th} classes, each and every classifier trained only two out of n^{th}classes, and there would be $n \times (n-1)/2$ classifiers. In MSVM, decision function is an effective way to moderate the multi-class problems that is constructed by assuming all the n^{th} classes. The M-SVM classification technique is an extension of SVM, which is mathematically represented in the Eq. (10), (11), and (12).

$$min\Phi(w,\xi) = 1/2\sum_{m=1}^{k}(w_m.w_m) + c\sum_{i=1}^{l}\sum_{m\neq yi}\xi_i^m \quad (10)$$

Subjected to,

$$\left(w_{yi}.x_i\right) + b_{yi} \geq \left(w_{yi}.x_i\right) + b_m + 2 - \xi_i^m, \quad (11)$$

$$\xi_i^m \geq 0, i = 1,2,3 \ldots l, m, yi \in \{1,2,3 \ldots k\}, m \neq yi \quad (12)$$

Where, ξ_i^m is stated as slack variables, l is considered as the training data point, c is represented as the user's positive constant, yi is denoted as the class of training data vectors x_i, and k is stated as the number of classes. At last, the decision function is represented in the Eq. (13).

$$f(x) = arg\,max[(w_i.x) + b_i], i = 1,2,3,..k \quad (13)$$

IV. Experimental results and discussion

This section described about the experimental result and discussion of the proposed system. Also, detailed about the experimental setup, performance metric, quantitative analysis, and comparative analysis. Here, the proposed system was experimented by using MATLAB (version 2018b) with 8 GB RAM, 1 TB hard disk, 3.0 GHz Intel i5 processor. The performance of proposed system was related to other dimensionality reduction techniques and existing research papers on a dataset; MIRIAD for evaluating the effectiveness of the proposed system. The performance of proposed system was evaluated by means of precision, recall, error rate, and accuracy.

4.1 Performance metric

Performance metric is defined as the regular measurement of results and outcomes that develops a reliable information about the efficiency and effectiveness of the proposed system. The general formula to evaluate precision, recall, accuracy, and error rate of Alzheimer disease detection is mathematically represented in the Eq. (14), (15), (16) and (17).

$$Precision = \frac{TP}{TP+FP} \times 100 \quad (14)$$

$$Recall = \frac{TP}{TP+FN} \times 100 \quad (15)$$

$$Accuracy = \frac{TN+TP}{TN+TP+FN+FP} \times 100 \quad (16)$$

$$Error\ rate = (1 - accuracy) \times 100 \quad (17)$$

Where, FP is represented as false positive, TP is denoted as true positive, FN is indicated as false negative, and TN is specified as true negative.

4.2 Quantitative analysis on MIRIAD dataset

In this section, the comparative study of existing and proposed work is carried out by using MIRIAD dataset. This dataset comprises of only two classes: normal and Alzheimer disease, so there is no need of multiclass classification. In each class, twenty-three MRI brain images are considered for experimental investigation. Here, the performance evaluation is validated with 80% training data and 20% testing data. Inspecting the table 1, the proposed system outperforms with the classification accuracy of 99.2% as compared to the traditional dimensionality reduction techniques: Principal Component Analysis (PCA) and Kernel PCA (KPCA). In addition, the existing systems achieve minimum precision, recall, and error rate, compared to the proposed system. The graphical comparison of precision, recall, accuracy, and error rate of MIRIAD dataset is shown in Fig. 5.

Table 1 Performance analysis of proposed system using MIRIAD dataset

Dimensionality approach	Accuracy (%)	Precision (%)	Recall (%)	Error rate (%)
PCA	25.2	22.18	27.4	74.8
KPCA	25.1	17.83	22	74.9
OLPP	99.2	100	98.4	0.8

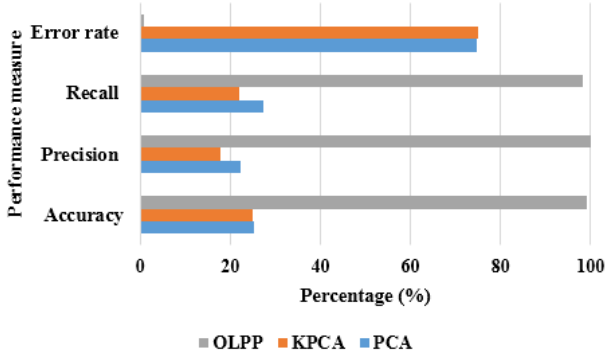


Figure 5. Performance comparison of proposed system using MIRIAD dataset

4.3 Comparative analysis

Comparative study of existing work and the proposed work performance is given in table 2. A. Rueda, F.A. Gonzalez, and E. Romero, [19] developed two-phase visual saliency methodology (combination of top-down and bottom-up approaches) for achieving accurate Alzheimer disease classification. The effectiveness of the developed method was investigated using MIRIAD dataset with 80% training and 20% testing data. The developed research achieved 84.06% of classification accuracy in Alzheimer disease classification. Compared to this existing paper, the proposed work achieved 99.2% of classification accuracy, which was almost 15% higher than the existing system.

Table 2 Comparative analysis of proposed and existing systems

Dataset	Methods	Training and testing (%)	Accuracy (%)
MIRIAD	Two phase visual saliency Model [19]	80% training and 20% testing of data	84.06
	Proposed system		99.2

V. CONCLUSION

In this research article, a new system is presented for classifying the stages of Alzheimer disease from the MRI brain images. The main objective of the experiment is to develop a proper dimensionality reduction and classification approaches for classifying the MRI data by using MIRIAD dataset. In this scenario, a dimensionality reduction algorithm (OLPP) is used for selecting the appropriate/optimal feature values. By selecting the optimal features from the extracted features, a set of the most powerful discriminative features is achieved. The obtained optimal feature values are classified by using the classifier: MSVM. The proposed system has numerous advantages; earlier detection of Alzheimer diseases, assists the clinicians /doctors during surgery, and cost-efficient. Compared to the existing methodology, the proposed scheme delivered an effective performance by means of quantitative and comparative analysis. From the experimental analysis, the proposed system achieved around 99% of accuracy, but the existing methodology attained limited accuracy in MIRIAD dataset. In future work, three dimensional functional MRI brain scans are utilized for further analysing the sub-stages of Alzheimer disease.

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