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Automatic Early Detection of Alzheimer's Disease based on 2D-VMD and Deep Convolutional Neural Network

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Abstract: ***In this paper, the classification of normal controls (NC), very mild cognitive impairment and the early stage of Alzheimer's disease (AD) known as mild cognitive impairment (MCI) from magnetic resonance imaging (MRI) is proposed, based on the two dimensional variational mode decomposition (2D-VMD) and deep convolutional neural network (DCNN). The 2D-VMD is applied to decompose the MRI scans into a discrete number of band limited intrinsic mode functions (BLIMFs). The automatic feature extraction, selection and optimization are performed using the proposed DCNN. The classification accuracy and learning speed of the 2D-VMD-DCNN method are compared with DCNN by taking the MRI data as input. The superior classification accuracy of the proposed 2D-VMD-DCNN method over DCNN method as well as other recently introduced prevalent methods is the major advantage for analyzing the biomedical images in the field of health care.***

Keywords: ***Alzheimer's disease (AD), Magnetic resonance imaging (MRI), Deep convolutional neural network (DCNN), Two-dimensional variational mode decomposition (2D-VMD)***

I. INTRODUCTION

Dementia is largely defined as a clinical syndrome characterized by forgetfulness, limited social skills and cognitive impairment [1].The most common cause of dementia is the Alzheimer's disease (AD) and as indicated by a study, individuals who is experiencing dementia everywhere throughout the world is around 47 million and it is evaluated that there will be one individual with AD in each 85 individuals by 2050 [2]. The pathological changes in the brain such as loss of cortical neurons and synapses, and gathering of amyloid plaques and neurofibrillary tangles are identified as the main cause of AD. As a result, the ability of reading, writing as well as memorizing gets seriously affected and even it becomes difficult for an AD patient to recognize own family members [3]. The problem compounds over the time in such a way that the parts of the brain responsible for heart functionality and breathing gets destroyed leading to death. Therefore, detection of AD at its early stage, known as mild cognitive impairment (MCI) is of utmost importance to alleviate the abnormal degeneration of neurons, so that the progress of AD can be under control and the cost of patient care can be reduced to ensure better management. Unlike computer tomography (CT), magnetic resonance imaging (MRI) contributes adequate information regarding neurological diseases and many researchers have shown interest in analyzing the MRI data of brain. It gives prevalent delicate tissue differentiation, high spatial resolution, and better contrast and can even distinguish small abnormalities in the brain [4]. Further, the information present in the MRI data has been augmented using computerized applications and exact labeling of the data to distinguish a normal control from AD subject [5]. Initially, larger part of the process of analyzing the MRI scans was practiced by the clinicians to estimate the region of interest (ROI) present in MRI scans. Because of the bottlenecks of ROI based methods it was important to concentrate on exploring other important biomarkers to detect the affected MRI scans as segmentation of the complete MRI is of more importance [6]. Therefore, computer aided automatic approaches are used to help the physicians to diagnose the disease from the MRI. A few artificial intelligence (AI) techniques have been proposed for the exact determination of AD. The surmised volume estimation [7] and the cerebral metabolic rate of glucose (CMRGlc) [8], were regularly processed from fragmented 3-D brain region of interest (ROI) and were utilized for AD classification with support vector machine (SVM) [9], and Bayesian method [10].

At present, many neurologists and medicinal experts have been investing significant amount of time and energy in examining various methods to detect the early stage of AD, and empowering results have been often achieved [11]. The conventional machine learning approaches like support vector machine (SVM) [12], and logistic regression models have provided significant results in classifying the MRI data of brain images affected with AD, but recently, the classical methods are getting completely outperformed by a large margin with the application of deep learning methods. Deep learning methods separate the important features automatically using different layers and activation functions [13]. Brosch and Tam used a multi layered deep learning structure to report that the proposed algorithm effectively identifies the variation in the shape of the brain region such as ventricle size [14]. Suk *et al.* [15], proposed a combined effect of stacked autoencoders (SAEs) and multi-kernel support vector machine (MKSVM) for the classification of AD from the NC but this type of framework may ignore the

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synergy between different modalities in the feature learning. Liu *et al.* [16], developed a multimodal stacked autoencoder network using zero-masking strategy by applying the concept of unsupervised feature engineering and softmax to classify four stages of AD. Liu and Shen used supervised and unsupervised methods for the training of a developed deep neural network to classify Ad and MCI patients [17].

In this paper, first, we propose a novel deep convolutional neural network (DCNN) to automatically extract the discriminative features for the classification of normal controls (NC), very mild cognitive impairment and the early stage of Alzheimer's disease known as mild cognitive impairment (MCI). Second, two-dimensional variational mode decomposition based deep convolutional neural network (2D-VMD-DCNN) is proposed for classification purpose. 2D-VMD is applied to decompose the input MR images into a discrete number of band limited intrinsic mode functions (BLIMFs) and the decomposed images are fed to DCNN for detection of the MCI subjects. Finally, the 2D-VMD-DCNN method proves its superiority with better classification accuracy and higher learning speed over the DCNN method. The block diagram of the proposed three-class classifiers to detect the demented, very mild demented and MCI subjects are shown in Fig. 1.

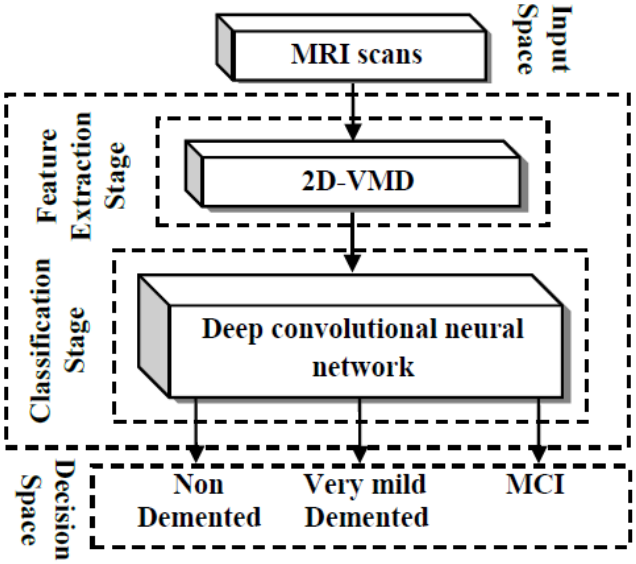
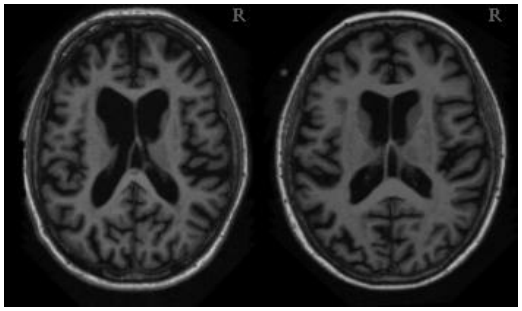


Fig. 1. The block diagram of the proposed classifier.

The rest of the article is organized as follows, section II contains the information about the selected dataset for classification, section III provides a brief introduction of the 2D-VMD, section IV represents the proposed DCNN classifier, section V discusses the results obtained followed by the conclusion in section VI.

II. MATERIALS AND METHODS

In this article, the publicly available Open Access Series of Imaging Studies (OASIS) dataset is used. It is a project of preparing MRI scans to make publicly available for the scientific community to facilitate the diagnostic process and research progress in the field of clinical neuroscience. The OASIS dataset has both cross-sectional and longitudinal MRI images of brain and the authors have selected the cross-sectional data known as "cross-sectional MRI data in young, middle aged, non-demented and demented older adults".



(a) (b)

Fig. 2. MRI dataset sample of (a) NC and (b) MCI.

Fig. 2 shows an image of the collected data set depicting the pictorial difference between the MRI of a normal control and an early stage of AD patient. The selected dataset contains the T1 weighted MRI scans of 416 subjects aged between 18 to 96. The demographic data of cohorts include the necessary information about the subjects such as handedness, age, education, gender (M/F), mini mental state examination (MMSE) and the clinical dementia rating (CDR). The mini mental state examination (MMSE) is a short 30-point questionnaire test generally conducted to observe the state of very mild dementia and mild cognitive impairment. Clinical dementia rating (CDR) is a number within a range of zero to four, estimating the seriousness of different stages of dementia. The statistical information about the subjects from which the 196 samples are selected is presented in Table I.

Table-I. Cohort's statistical data.

Factors	Normal Controls	Very mild cognitive impairment	Mild cognitive impairment
No. of patients	98	70	28
Age	75.91 ± 8.98	74.87± 7.64	77.75 ± 6.99
CDR	0	0.5	1
MMSE	28.95 ± 1.20	27.28± 1.71	21.67 ± 3.75
Gender(M/F)	26/72	29/41	9/19

III. FEATURE EXTRACTION

Variational mode decomposition (VMD) has been efficiently used to decompose stationary and non-stationary signals into a discrete number of sub-signals known as band-limited intrinsic mode functions (BLIMFs). Similarly, to decompose a two-dimensional signal such as image, two-dimensional variational mode decomposition (2D-VMD) is used for sifting out the spectral bands with oscillatory characteristics. The 2D-VMD, an extension of one-dimensional variational mode decomposition (1D-VMD), is a non-recursive fully adaptive variational method which sparsely decomposes digital images into a discrete number of band limited intrinsic functions. The objective of 2D-VMD is to reduce the bandwidth of each mode around the center frequency ω_k . For each mode the analytic signal is computed by applying Hilbert transform to produce a unilateral frequency spectrum [18].

To compute the bandwidth, frequency spectrum of each mode is combined with an exponential function which shifts the spectrum to baseband. The variational constraint model of 2D-analysis is given as,

$$\min_{u_k, w_k}\left\{\sum_k \alpha_k \left\|\nabla\left[u_{AS,k}(x)e^{-j(\omega_k, x)}\right]\right\|_2^2\right\} \text{ such that,}$$

$$\forall x : \sum_k u_k(x) = f(x)$$

(1)

where u_k represents the set of each mode after 2D mode decomposition and $f(x)$ is the input digital image and $u_{AS,k}(x)$ is the analytic signal. This minimization problem is made unconstrained by introducing a quadratic penalty and Lagrangian multiplier [19], and is represented as,

$$L(\{u_k\},\{\omega_k\},\lambda) := \sum_k \alpha_k \left\|\nabla\left[u_{AS,k}(x)e^{-j(\omega_k, x)}\right]\right\|_2^2$$

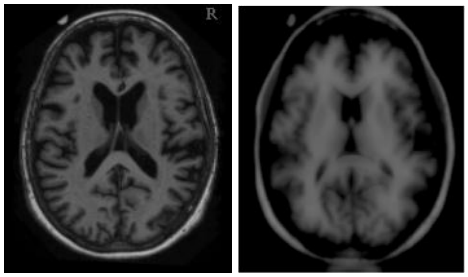
$$+\left\|f(x)-\sum_k u_k(x)\right\|_2^2 + \left\langle \lambda(x), f(x)-\sum_k u_k(x)\right\rangle$$

(2)

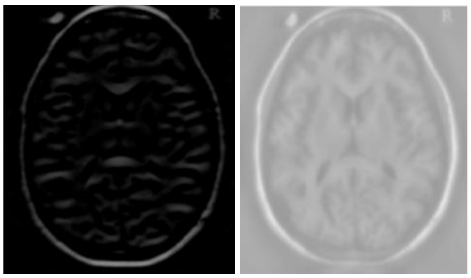
Similar to 1D-VMD, the optimization problem stated in (2) is solved by an iterative method known as alternate direction method of multiplier (ADMM). Then, the constrained problem is,

$$\min_{u_k, w_k} \max_{\lambda} L(\{u_k\},\{\omega_k\},\lambda) \quad (3)$$

Where λ is the Langrangian multiplier and α_k is the balancing parameter of the data fidelity constraint.



(a) MCI sample (b) BLIMF 1



(c) BLIMF 2 (d) BLIMF 3

Fig. 3. The MCI sample and three BLIMFs of 2D-VMD.

The solution of the unconstrained problem provide the updated forms of modes, center frequency and Lagrangian multiplier as given below in (4), (5) and (6) respectively.

$$(\hat{u}_k)^{n+1} = \frac{\hat{f}(w) - \sum_{i\neq k}\hat{u}_i(w) + \hat{\lambda}(w)/2}{1+2\alpha_k|w-w_k|^2}$$

(4)

where the numerator contains the Fourier transforms of the 2D input signal $f(x)$, modes $u(x)$ and the Lagrangian multiplier λ. The number of iteration is denoted as n.

The half-plane integration path is used in order to update the center frequencies.

$$(w_k)^{n+1} = \frac{\int_{\Omega_k} w\left|(\hat{u}_k)^{n+1}(w)\right|^2 dw}{\int_{\Omega_k}\left|(\hat{u}_k)^{n+1}(w)\right|^2 dw}$$

(5)

The updated Lagrangian multiplier is given as

$$\lambda^{n+1}(x) = \lambda^{n+1}(x) + \tau[f(x) - \sum_k u_k{}^{n+1}(x)]$$

(6)

Readers may refer to [19] for the detailed explanation of the algorithm. Fig. 3. shows an MCI sample and corresponding three BLIMFs extracted using 2D-VMD.

IV. DEEP CONVOLUTIONAL NEURAL NETWORK (DCNN)

Artificial neural network (ANN) has been a very useful tool for binary as well as multiclass classification. But especially in case of image classification ANN is sensitive to shift deviation and translation resulting in a poor classification performance. Convolutional neural network (CNN) is an extended version of ANN which stands unreceptive to shift deviation and translation. The recently developed deep learning classifiers have been producing significant results in the field of pattern classification [20-24]. The deep learning method we propose is a variant of convolutional neural network and called as the deep convolutional neural network (DCNN). The DCNN extracts the local features of the input MRI data through convolution operation.

The DCNN architecture comprises of five layers:

1. Convolutional layer, 2. Rectified linear unit (ReLU) layer, 3. Pooling layer, 4. Fully connected layer, and 5. Softmax layer.

A. Convolutional layer

It is the core building block of the proposed DCNN. The prime objective of convolutional layer is to extract the meaningful features of the input MRI data automatically. Similar to CNN, selected filters are allowed to slide over the input image to produce the feature map or activation map. The output of convolutional layer is given as,

$$C_j = \sum_{i=0}^{n-1} f_i S_{j-i} \quad (7)$$

where S is the input signal, f is the filter applied for convolution operation, n is the number of data points in the input signal, i indicates the i^{th} element of the filter vector, j corresponds to the j^{th} output element presented in (7).

B. Rectified linear unit (ReLU) layer

The ReLU activation function is applied on the convolution layer output for sparse and nonlinear representation.

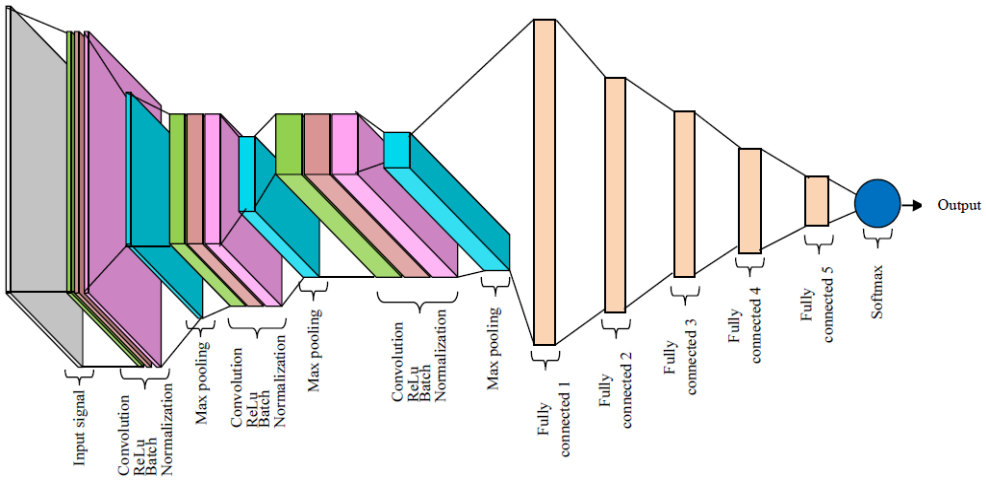


Fig. 4. Architecture of deep convolutional neural network (DCNN).

The main objective of ReLU activation function is to reduce nonlinearity by thresholding operation.

It assigns zero to the values less than zero and a fixed value to the values greater than zero and is given by the following equation

$$f(m)=\begin{cases} M; m \geq 0 \\ 0 \;; Otherwise \end{cases} \quad (8)$$

Further, ReLU layer follows a batch normalization operation for regularization to reduce the problem of over fitting.

C. Pooling layer

Max pooling is the most used pooling operation to reduce the computational complexity after each output of the convolutional layer. The main function of the pooling layer is to reduce the dimension of feature map preserving the important features. In this work max pooling operation is used with a stride of two.

D. Fully connected layer

After all the intermediate normalization operation, the final normalized output is flattened and fed to the first fully connected layer. In FC layer the neurons of the present layer and the previous layer are all fully connected to each other. The last fully connected layer contains n number of neurons where n is the no of classes used for the classification problem. The output of FC layer is given as,

$$x_i = \sum_j w_{ji} y_j + b_i \quad (9)$$

where x and y are the outputs of current and previous layer respectively with w weights and b biases.

E. Softmax layer

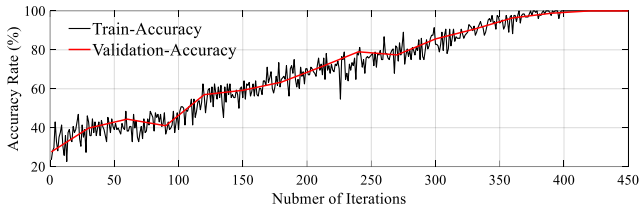
Finally, the softmax function is used for classification by receiving the inputs from the last fully-connected layer. It predicts the class of a signal applied at the input and the value of the output of the softmax layer lies between zero and one. The softmax activation function is given as,

$$P_i = \frac{e^{x_i}}{\sum_m^k e^{x_i}} \quad (10)$$

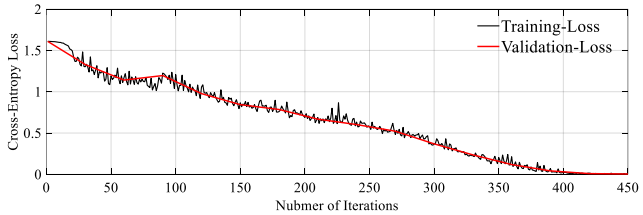
where $P(x_i)$ is the probability of the input to belong to the class of x_i .

V. RESULT AND DISCUSSION

In this work, the publicly available Open Access Series of Imaging Studies (OASIS) dataset known as "cross-sectional MRI data in young, middle aged, non-demented and demented older adults "dataset is used to verify the proposed work in an Intel core i5-8000U CPU at 2.6 GHz processor of 16GB RAM using MATLAB/Simulink software environment to detect the early stage of Alzheimer's disease known as mild cognitive impairment (MCI) from the brain MRI images. The proposed DCNN structure is used for automatic computation, selection and optimization of the most discriminate features. The architecture of the novel DCNN comprising of three sets of convolutional layer followed by five fully connected layers is presented in Table II. The developed architecture of the proposed DCNN is shown in Fig. 4, where same padding is used before each max-pooling layer to eliminate the possibility of losing any data during the max pooling operation.



(a)



(b)

Fig. 5. Performance of the proposed method (a) Training accuracy (b) Cross-Entropy loss.

Finally, softmax layer is used for a three-class classification task of the non-demented, very mild demented and the early stage of AD input image data based on the probability function. 70% of the MRI scan images of each class are used for training and remaining 30% for testing, in both the proposed DCNN and 2D-VMD-DCNN methods. The DCNN is trained by taking less number of iterations with maximum training accuracy and minimum training cross-entropy loss as shown in Fig. 5. For testing purpose the remaining 30% images of each class are used both in noise-free and noisy conditions. Further, the 2D-VMD is employed to decompose each input MRI scan image into three BLIMFs and the corresponding BLIMFs are fed to the proposed DCNN method to improve the classification accuracy of multi-class classification. On basis of the processing time of both the classifiers, the DCNN outperforms the 2D-VMD-DCNN but in terms of higher learning speed, minimum training and testing loss, superior classification accuracy and anti-noise performance the 2D-VMD-DCNN classifier stands better than DCNN method. The detail comparisons of classification accuracy of both the DCNN and 2D-VMD-DCNN methods are presented in Table III.

Table-II. The developed structure of the proposed DCNN.

Layer	Name	Output nodes	Filter size	Stride
0-1	Convolution	[204×172×1]×5	5	1
1-2	Rectified linear unit	[204×172×1]×5	1	1
2-3	Batch normalization	[204×172×1]×5	10	10
3-4	Max-pooling	[102×136×1]×5	2	2
4-5	Convolution	[93×127×1]×10	10	1
5-6	Rectified linear unit	[93×127×1]×10	1	1
6-7	Batch normalization	[93×127×1]×10	10	10
7-8	Max-pooling	[47×64×1]×10	2	2
8-9	Convolution	[33×50×1]×15	15	1
9-10	Rectified linear unit	[33×50×1]×15	1	1
10-11	Batch normalization	[33×50×1]×15	10	10
11-12	Max-pooling	[17×25×1]×15	2	2
12-13	Fully connected	6375×1	0	0
13-14	Fully connected	3000×1	0	0
14-15	Fully connected	1000×1	0	0
15-16	Fully connected	100×1	0	0
16-17	Fully connected	3×1	0	0

Finally, Table III concludes that the proposed 2D-VMD-DCNN method is the utmost choice for the detection of AD at its early stage, called as the stage of MCI, efficiently.

Table-III. Comparison of classification accuracy of DCNN method and 2D-VMD-DCNN method.

Proposed model	Noise free condition	SNR values		
		20dB	30dB	40dB
DCNN	95.4	90.3	92.8	94.3
2D-VMD-DCNN	98.9	96.9	97.4	97.9

VI. CONCLUSION

The novel deep convolutional neural network (DCNN) architecture is developed and implemented to detect the early stage of Alzheimer's disease known as mild cognitive impairment, from brain magnetic resonance images as input. Two dimensional variational mode decomposition (2D-VMD) is used to decompose the input brain MRI images into band limited intrinsic mode functions (BLIMFs). Three BLIMFs of each MRI scan are fed to the proposed deep convolutional neural network structure to extract the discriminative feature at the last fully-connected layer automatically. The extracted features are fed to the softmax layer to classify the non-demented, very mild demented and the early stage of AD patients with superior classification accuracy. The higher learning speed and superior classification accuracy of the proposed 2D-VMD-DCNN method prove its superiority over DCNN method in both noise-free and noisy environments. Finally, the robustness of the proposed method suffices its application to other digital image classification.

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