Neural Network Architecture for the Classification of Alzheimer's Disease from Brain MRI

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***Abstract*—Alzheimer's Disease (AD) is a neurological condition in which the decline of brain cells causes memory loss and cognitive decline. Various Neuroimaging techniques have been developed to diagnose AD; among those, Magnetic Resonance Imaging (MRI) is one of the most prominent ones. Historically, expert radiologists were solely responsible for making decisions of a patient's AD situation by manually analyzing brain MR images. However, the recent progress in medical image analysis using deep learning especially has automated this task significantly. Although the state-of-the-art architectures have achieved human-level performance in classifying AD images from Normal Control (NC), they often require predefined Regions of interest as a basis for feature extraction. This condition not only requires specialized domain knowledge of the human brain but also makes the overall design complicated. In this paper, we designed a 14 layer Neural network architecture that can facilitate AD diagnosis without being dependent on any neurological assumption. The network was tested over ADNI-1, a benchmark MRI dataset for AD research, and found an accuracy of 87.06% (AUC = 0.93).**

***Index Terms*—Alzheimer's Disease, Magnetic Resonance Imaging, Convolutional Neural Network**

I. Introduction

Alzheimer's Disease (AD) is an irreversible, progressive neurodegenerative disease that slowly but indeed deteriorates one's memory and other cognitive skills [1]. It is one of the most common causes of dementia for adults older than 65 [4]. People with advanced age, possessing symptoms of Mild Cognitive Impairment (MCI), have the highest risk of developing AD [3]. About 50 million people were affected by various forms of dementia [2]. Alarmingly, by 2050, one new case of AD is expected to develop every 33 seconds, which is nearly 1 million new cases per year [2]. AD treatment is expensive as it alone costs the United States Government approximately $100 billion each year [5]. Making things worse, most of the affected are not in well-developed regions [6], which quickly becomes a reason for many people to take proper treatment only at a late stage of AD. Thereby, early diagnosis of AD becomes a crucial factor for adequate treatment.

MRI has been widely used as a common AD biomarker to accurately detect its onset as it gives a detailed representation of the brain's structure which is necessary for identifying symptoms co-related to AD [7].

Recently, machine learning techniques from a wide range have been developed to automate the diagnosis of AD using MR images [8]. We characterized these techniques into two main groups- linear statistical learning and deep nonlinear learning. Regardless of the group, convolution is seen as a standard method for feature extraction [9]. Since features correlated to AD consist of multiple modalities, nonlinear classifiers like Convolutional Neural Network (CNN) generally outperform linear classifiers like Support Vector Machne (SVM) or Random Forest [10], [9]. Due to this superior performance in classification, and the availability of sufficiently large dataset like ADNI [11], MIRIAd [12], and OASIS [13], numerous research has been conducted focusing on CNN exclusively [14], [15], [18], [19].

In 2017, Korolev et al. designed a 21 layers Residual Neural Network and a 17 layers 3D Convolutional Neural Network (3D-CNN) for the binary classification of different AD stages [15]. In an experiment conducted over the ADNI dataset, these two architectures achieved 80% (AUC = .88) and 79% (AUC = .87) classification accuracy, respectively, after running 50 epochs.

In the same year, Li et al. designed a "Y shaped" residual network architecture, where two identical sub-networks with residual blocks extracted features from the Right and Left Hippocampus separately [16]. Later in a fully connected (FC) layer, outputs from these two networks were merged for binary classification. This network was trained on the ADNI I dataset and validated on ADNI Go & ADNI 2 datasets, achieving 0.939 AUC.

In 2018, Khvostikova et al. designed a 3D-CNN that was somewhat similar to the previously mentioned network in the sense that it also leveraged separate identical networks and merged their output in an FC layer [17]. However, unlike relying on two major brain components al a whole (Right and Left Hippocampus) and running two sub-networks, they considered several Regions of Interest (ROI) throughout the hippocampus and generated that number of sub-networks for feature extraction. They experimented on ADNI several times with varying numbers of RoI- ranging from 28 to 48. This experiment achieved a maximum of 96.7% accuracy while considering 48 RoI.

In the same year, Liu et al. conducted a similar study from a different paradigm. Instead of extracting features from pre-defined RoI, they used a fixed patch landmark detector for identifying landmarks throughout the brain before using those in a pre-trained CNN for binary classification [18]. They used three independent datasets (ADNI-1,2 and MIRIAD) and achieved 91%-92% accuracy every time for AD vs. NC classification.

In 2020, Lian et al. designed a Hierarchical Fully Convolutional Network (H-FCN) for the same purpose. Unlike the previously mentioned 2 staged networks, this architecture was three-stage, and the same network was responsible for both the region proposal and classification [19]. As a result, the feature extraction became coupled with the classification process. This H-FCN was trained by the ADNI-1 dataset and tested over ADNI-2 dataset-achieving 90% accuracy (AUC = 0.95) in AD vs. NC classification.

These are some of the existing literature in AD diagnosis using MRI, all of which disclosed significant findings. Nevertheless, we are addressing some of the points which can be explored differently. Most importantly, some of the studies were heavily dependent on the domain knowledge of brain anatomy for feature selection. For example, [16] considered features extracted only from the hippocampus on the assumption of a higher concentration of correlated features. [17] considered 28 to 48 pre-defined RoI based on specialized neuroimaging knowledge. In the same way, [18] identified 1741 landmarks by the statistical measurement of brain anatomy and utilized 50 of them as information regions. Besides the additional specialized knowledge requirement, all but one of the mentioned studies used multi-staged architecture, which can be considered complex from a design perspective. For example, [16], [17] and [18] used two-staged networks, and their primary stages have consisted of a minimum of 2 to a maximum of 50 sub-networks. Moreover, [19] designed 3 staged hierarchical network which was comparatively more complex. Last but not least [15] did use a single-stage architecture, and that was also not dependent on specialized knowledge; however, its sub-optimal performance comparing to other mentioned works creates room for improvement.

This leads to the conclusion that a simple but robust Architecture needs to be designed from the domain of Deep learning exclusively. Addressing this need, we designed a 14 layer Convolutional Neural Network that is able to assist us in the early detection of Alzheimer's Disease by employing various Deep Learning techniques to distinguish between different stages of dementia using structural MRI scans. The rest of the paper is organized as follows. In section II, we have described our proposed methods for work for the whole study. In section III, we have discussed about our experimental results and its implications. Finally, In section IV, we concluded our study with our plans for the future of this study.

II. Proposed Method for Alzheimer's Detection

This section describes the architecture and construction of our proposed model for Alzheimer's detection using MRI scans. The model performance is evaluated based on factors such as accuracy, precision, f1 score etc.

A. Data collection

During dataset selection, we decided to go with the collection of MRI images provided by the Alzheimer's Disease Neuroimaging Initiative (ADNI). The ADNI dataset

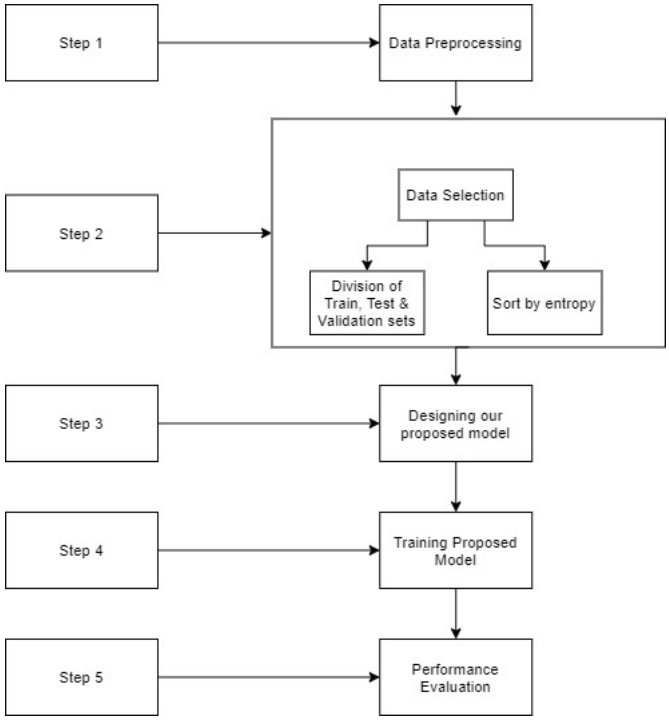


Fig. 1: Proposed Method for Alzheimer's Detection

is comprised of several collections of MRI images which are all taken in different lo- cations and different times. For this experiment, we decided to use the 3T baseline image collection.This particular image collection is comprised of the MRI images of 75 subjects. Among these 75 subjects, 25 subjects are tagged as Alzheimer's Disease (AD), 25 with Mild Cognitive Impairment (MCI) and the rest of the 25 subjects are labeled as Control Normal (CN).

B. Data Prepossessing

In order to remove unnecessary details of MRI images that might cause poor training of our classification task, we perform various prepossessing tasks on our data. These processes are:

1) Motion correction and conform:: This process is responsible for correcting minor motions between multiple sources of a volume by averaging them together

2) Non Uniform intensity normalization: Also known as N3, this process corrects MR data by removing non-uniform intensity of the image. This process is performed with the help of the following equation:

$$I(x) = U(x)f(x) + n(x) \tag{1}$$

Where, I is the given image, U is uncorrupted image, f is the bias field and n is the noise.

3) Talairach transform computation:: This process converts all the pixel co-ordinates of the image into talairach co-ordinates and applies an affine transformation to the newly obtained co-ordinates.

4) Intensity normalization:: This step helps to correct for fluctuations on intensity. It does this by scaling intensities of all voxels by taking the mean intensity of white matter as 110.

5) Skull Stripping:: In this process we remove the skull and any other visible organs other than the brain in the MRI so that the final image only contains the necessary features for classification.

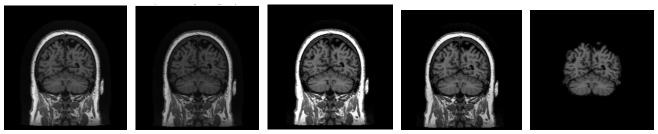


Fig. 2: Transformation of a slice after going through all pre processing steps.

C. Data selection:

After prepossessing, we have images of 75 patients, with each subject having 256 slices of images. Among these 256 images, only a few are needed for classification as a limited sample size would raise the chances of success of the model. So, in order to choose the best possible slices, we only choose to only include the first 32 slices with the highest entropy values for each subject. After the necessary slices were chosen we decided to divide the dataset into separate training, test and validation sets.

D. Construction of proposed model

In this section we discuss the construction and architecture of our proposed model that is responsible for the early detection of Alzheimer's. Our proposed model is based on five basic components, namely, the convolutional layer, pooling layer, flatten layer, dense layer and activation function. A detailed discussion of each component is given below:

1) Convolutional Layers: This layer is responsible for most of the computations of a CNN model such as ours, and thus it is the most important part of the model. In this layer, the convolution process is initiated from which the entire model is able to extract the necessary features from images. It contains various parameters and hyper-parameters such as filters, kernels, K etc. Convolutional layers extract features using the aforementioned filters, which are then used to compare images segment by segment to distinguish the similarities and differences among them. The main goal of a convolutional layer is to extract and identify high level features like edges, circles etc. Moreover, this layer also performs various other operations such as blur, sharpen etc by applying filters to input images. It should be noted that, we decided to use five convolutional layers in our model.

2) Pooling Layer: The Pooling layer is used in conjunction with the convolutional layer to reduce the size of the volume of the image when it is too large. This layer is responsible for making computation relatively fast, prevents overfitting and reduces strain on memory. There are carious kinds of pooling layers which makes use of different techniques to accomplish such feats. Pooling layers such as the Max Pooling layer only takes the largest values from the feature map, while others like Average pooling take the average of all values from the feature map and feed it forward. Note that, in our model we have taken a Max Pooling layer for every Convolutional layer, taking five Max pool layers in total.

3) Flatten layer: The Flatten layer takes all the outputs of both the convolutional and pooling layers and transforms the entire pooled feature map into a single column. We used one such flatten layer in our model, after which it is passed along the neural network for further processing.

4) Dense Layer: The Dense layer, also known as fully connected layers take input from previous layers, using which they decide which features seem more likely to match a particular class. It does this by assigning weights to specific features, using which certain high level features are specifically highlighted while others effect on the overall classification is dimmed. In our model we have used 3 dense layers, which takes the takes inputs from the flatten layer and uses it to detect certain features that may be responsible for the detection of Alzheimer's

E. Activation function

We have used the softmax and relu activation function with our own dense layers. These functions have been observed to have the best performance with our model. The activation functions are shown as follows:

$$softmax(x_i) = \frac{exp(x_i)}{\sum_j exp(x_j))} \tag{2}$$

$$relu(x_i) = max(0, x_i) \tag{3}$$

In the above equations, x is a real valued number. The value of the softmax function always ranges from 0 to 1. It is used in the neural network to normalize the output of a network to a probability distribution over the specified output classes. The rectified linear unit (ReLU) on the other hand is much more simple and absolute in nature. It is a piecewise linear function that will output the input only when the input is positive, otherwise the output will be zero. We use the ReLU activation function on the first two dense layers while the last dense layer uses the softmax function for the best evaluation.

F. Training of model

After constructing our model, we train our model for 3 way classification of the three categories of AD, MCI and CN. The AD class contains MRI images of patients with Alzheimer's while the MCI contains images of patients suffering from Mild Cognitive Impairment and the CN group

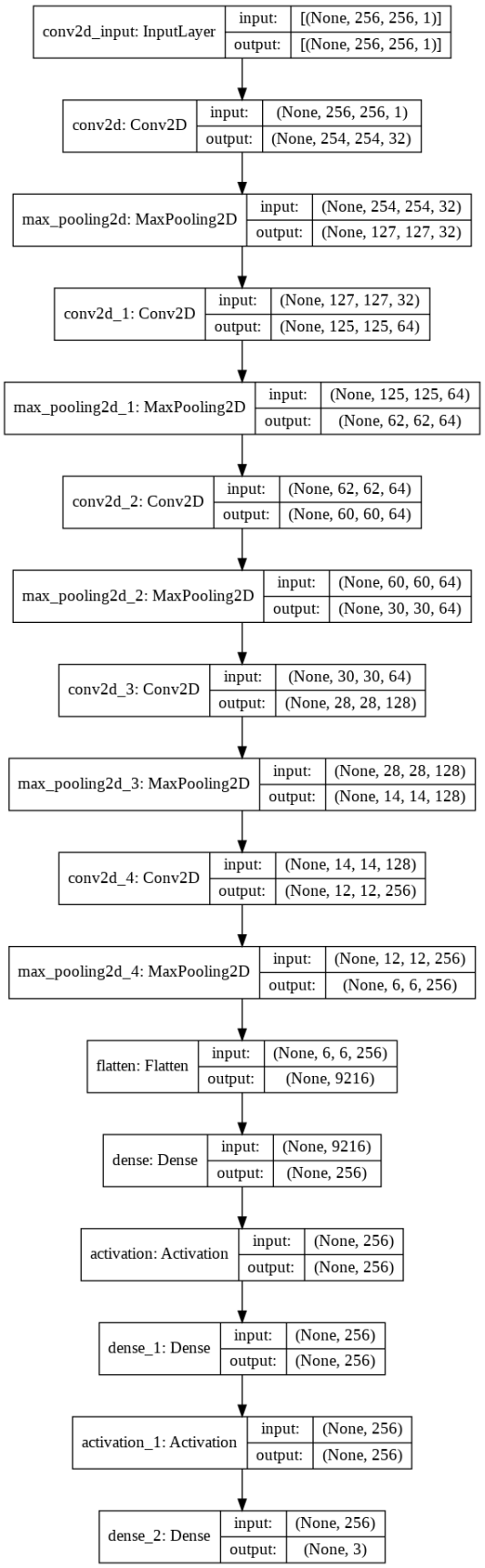
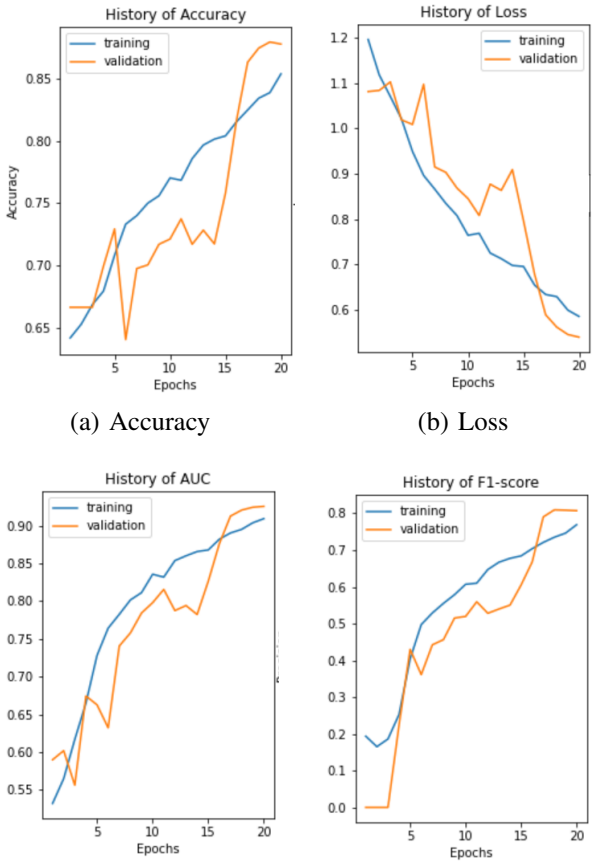


Fig. 3: Architecture for the proposed model.



(a) Accuracy (b) Loss

(c) AUC curve (d) F1 score

Fig. 4: Graphs describing (a) Accuracy, (b) Loss, (c) AUC curve and (d) F1 score of the model

contains MRI images from patients from the control group. Our model was implemented using the keras, tensorflow and scikit image libraries.The experiment was carried out on Google Colabrotory Ubuntu server with a Tesla K80 GPU. We trained the model using our own prepared dataset and with the RMSprop optimizer. We Take 0.00001 as the value for the learning rate and 32 as the batch size with 20 epochs.

III. Results and Discussion

This section includes the experimental performance and performance of our proposed method. In evaluating the model we have used accuracy as the primary evaluation metric in the compilation. In keras, accuracy is calculated as:

$$Accuracy = \frac{\sum_i^n B^i}{n} \tag{4}$$

Where, n is the number of samples and B^i is a Boolean function for the ith sample. Its true class label is defined as y^i_{true} while the predicted class label is called $y^i_{predicted}$ Using this metric we have managed to achieve an accuracy of 87.06% on our validation set, by training it for 20 epochs with the same optimizer and loss function.

Besides accuracy we also used other metrics such as loss, Area under the curve(AUC) and f1 score. The loss function of the neural network describes the rate of error of the

network. As such, a graph with decreasing loss indicates that the networks error rate is decreasing , while a rising score means an increase in errors in the network. Here, our according to figure 4, we see that our model is experiencing a relatively low loss for both the training and test sets, signifying constantly decreasing error rates for the model.

The area under the curve on the other hand measures the ability of the classifier to distinguish between classes. The higher the AUC curve, the better the ability of the classifier to distinguish between classes. According to the results of 4, our model boasts a very high AUC score 92.8% making the model be very adept at distinguishing classes making false negative and true positive predictions.

Lastly, the f1 score determines the accuracy of the tests performed on the model at hand. It is calculated form both the precision and recall at hand. It is calculated in the following way.

$$F_1 = 2.\frac{precision.recall}{precision + recall} \tag{5}$$

In the figure 4, we see our model has a very high F1 score of 81.2% which bodes very well for our model as it describes our model to have relatively balanced precision and recall, both of which are independently used as measures of a models effectiveness. A performance comparison is given in Table 01.

Table 01

Performance comparison of different models

Study	Sample Size	Feature	Network Type	Accuracy	AUC
Korolev et al. [15]	231	Whole Brain image	Single Stages	80%*	0.87
Li et al. [16]	1776	Right and Left Hippocampus	Two Stages	-	0.939
Khvostikov et al [17]	214	48 Predefined RoI from Hippocampus	Two Stages	97%*	-
Liu et al [18]	1457	50 pre calculated Landmarks	Two stages	91%*	0.96
Lian et al [19]	1457	120 automatically proposed Locations	3 stages	90%	0.95
Proposed Model	75	Whole brain image	Single stage	87.06%	0.93

*Multiple experiments conducted. Best considered.

IV. Conclusion

Neurodegenerative diseases like Alzheimer's Disease (AD) are a common sight on elderly and senior populations. The advent of modern medical imaging technologies such as, Magnetic Resonance Imaging (MRI) has taken great strides to make accurate diagnosis easier to achieve than ever before.To this end, various Deep learning Models have been developed to detect Alzheimer's by using various predefined regions of interest of the brain as bio-markers for specific stages of dementia. And while this method is accurate, it requires hefty amount of data preprocessing and computational power in order to derive these specific qualities from these regions of interest. Thus, we hope to adopt our model for accurate and early diagnosis of Alzheimer's by only relying on the structural MRI data without the help of such regions of interest to facilitate a quicker and more efficient diagnosis.

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