Detection of Alzheimer's disease using Intelligent Selection and Transfer Learning

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***Abstract*—Alzheimer's Disease is an irreversible, progressive brain disorder. It is a neurodegenerative disease, which means there is progressive brain cell death that happens over time. Early diagnosis will considerably decrease the risk of further deterioration. The detection of Alzheimer's Disease from neuroimaging data such as MRI scans through machine learning has been a subject of intense research in recent years. However, the common limitation with such algorithms is the reliance on a large number of training images. The prime objective here is to solve such issues with Transfer Learning and Intelligent Selection, where the VGG Neural Network is initialized with pre-trained weights from large benchmark datasets consisting of natural images like MRI and PET scans from various subjects. The network is then fine-tuned with layer-wise tuning where few of the layers are frozen first and the network is trained. The frozen layers are then unfrozen and the training is done for the whole network.**

Keywords—Deep Learning, Transfer Learning, Intelligent Selection, Convolutional Neural Networks, Entropy.

I. INTRODUCTION

Alzheimer's Disease (AD), also called senile dementia, is a chronic, irreversible neurodegenerative disease. It is a progressive disorder that causes brain cells to degenerate and die. Almost 60–70% of the cases of dementia are associated with AD. The most common symptom is difficulty in remembering recent events. As the disease advances, symptoms can present themselves in the form of mood swings, loss of motivation, not managing self-care, and behavioral issues. As a person's condition declines, they often withdraw from family and society. Gradually, bodily functions are lost, ultimately leading to death. Although the speed of progression can vary, the typical life expectancy following diagnosis is three to nine years. No treatments stop or reverse its progression, though some may temporarily improve symptoms.

The availability of clinical datasets such as MRI, CT, PET scans etc is very scarce. This becomes a huge problem while trying to train a CNN for disease identification, since most CNNs require exhaustive training with huge datasets for providing an accurate and robust classification which is highly essential for fatal diseases like Alzheimer's, for the doctor to make an appropriate diagnosis. This issue is mitigated by the use of Intelligent Selection to select the images to be used for training. The already existing methods for AD detection incur high costs and technical overheads for deployment. This restricts small clinical setups and under-developed hospitals from adopting these techniques. The proposed system can reduce these costs to a good extent. The existing approaches which use models for performing disease classifications and detections, generally require extensive training for long durations to provide good results. This is mitigated by the use of Transfer Learning, where an already pretrained model is taken and tweaked according to the application at hand.

The primary objective is to detect AD by training a Convolutional Neural Network using Transfer Learning and Intelligent Selection to provide a robust classification of the brain scans into one of the three categories AD, MCI or NC. The use of Intelligent Selection helps in significantly reducing the size of the dataset required for training. The dataset used is the benchmark ADNI dataset. The proposed system will be a boon to the field of medicine, especially in the field of Neurology. It can be used as an effective means in various clinics, hospitals and neurology centres to detect the presence of Alzheimer's disease in a patient's brain. Using this method to detect AD, does not mandate the requirement of skilled professionals. Even non-professionals can use this technique to detect AD effectively.

II. LITERATURE SURVEY

Dementia was detected using the Human Electro Encephalogram (EEG) in [2]. This technique helps non-professionals analyze the EEGs. Although a good level of specificity is achieved, the sensitivity achieved is poor. This makes the detection of changes a huge problem.

Even small hospitals with insufficient data samples can perform more robust classification for AD diagnosis using the technique proposed in [3]. Domain adaptation is also used. Factors such as the devices and the setup of technical parameters etc. also play a major role in influencing the sample distribution, resulting in an unclear classification or diagnosis of AD.

Manifold regularization is integrated into the sparse regression model thereby significantly improving the classification performance in [5]. But the optimal parameters used are data dependent and obtaining them automatically is a prevailing issue. Only cortical thickness is used to distinguish AD and MCI, while other features exist.

Since the MR images used are longitudinal, it is easier to observe the pathological changes from MCI to AD using the technique proposed in [6]. It eliminates the need for time consuming processes like non-linear registration and tissue segmentation. The computational cost is exacerbated. Landmark feature selection may require manual correction.

Each brain's MRI was first non-linearly registered onto multiple templates and then the feature sets were extracted in [8]. The learning from multiple templates is induced through relationships. The registration process requires large computational resources. The different feature representations that were generated had the same dimensionality.

The Machine Learning based approach proposed in [4] calculates the biomarker sequence which is most cost effective for diagnosis of AD. It is capable of providing a personalized diagnosis for AD patients. The dependency on a large no. of biomarkers for AD diagnosis is reduced. The accuracy is on the lower side and so it cannot be used to fully replace the clinical diagnosis methods.

A diagnostic framework proposed in [7] using the zero-masking for the extraction of complementary information based on deep learning was developed. The requirement of labelled data was minimized. Since multimodal architectures are parametric, a larger dataset is required for a more accurate classification of AD.

Intelligent selection was used for picking out the images for the training phase in the approach proposed in [1]. The most informative slices were picked out cautiously by calculating the entropy value, thereby reducing the dependency on a large dataset for training. High accuracy was achieved than other methods for the detection of AD.

The multi-response regression-based method proposed in [9] can simultaneously locate the subregions of the brain that contribute to the disease and infer multiple responses. This model can be used for the diagnosis of both AD and MCI. But the quality of the recovered signal is heavily affected by insufficient or excessive penalty. Also, a more flexible model means dealing with a large no. of unknown parameters.

Alzheimer's Disease was predicted using a Long Short-Term Memory (LSTM) model in [10]. This LSTM model processes time series data to make the prediction of AD six months in advance. Although the model could carry out the future state prediction, it could not classify current state diagnosis.

The prediction of AD was carried out in [11] by collecting data about certain behavioral features of 29 subjects like mobility, patterns of eating and cooking, outgoing activities, walking speed. The data was collected by the behavior of the subjects inside what is called a 'Smart Home' by using various embedded sensors for monitoring. All these real-life data could be collected in a naturalistic manner to offer a complete view of the adult's behavior. The shifts in the home-based behavior when mapped to AD could potentially help in overcoming some disadvantages like older adults having to travel to health centers to receive invasive and costly diagnostic testing.

Domain transfer learning used in [12] helps in the assessment of the conversion of MCI to AD by acquiring knowledge from various cross domains. The Support Vector Machine being used entails the requirement of a large number of parameters. The accuracy of prediction achieved is low.

III. PROPOSED SYSTEM

A. Dataset

The dataset used is the benchmark dataset for deep learning-based Alzheimer's disease diagnosis named Alzheimer's Disease Neuroimaging Initiative (ADNI).

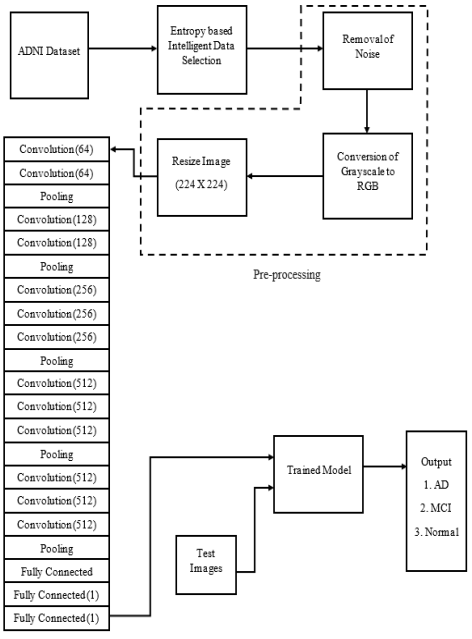

Fig. 1. Architecture of the proposed system

ADNI is an ongoing, multi-centre study designed to develop clinical, imaging, genetic, and biochemical biomarkers for the early detection and tracking of Alzheimer's disease. The ADNI study began in 2004 and is now in its third phase. The dataset used here consists of 50 patients in each one of the three classes: Alzheimer's Disease, Mild Cognitive Impairment (MCI), and Normal Control (NC), resulting in a combined total of 150 subjects. Clearly, it is difficult to pick up visual differences between the three classes. The aim is to provide a robust classification of the stage of Alzheimer's disease, whether it is AD or MCI or NC.

B. System Architecture

The fundamental architecture of the system proposed for the detection of Alzheimer's disease using VGGNet as the underlying CNN is illustrated in Fig.1. The system consists of various modules like Image Preprocessing, Intelligent Selection of data to reduce the size of the dataset for training, and the VGGNet itself, which when trained, is expected to provide a good classification for the detection of AD.

C. Flow Diagram

The working of the VGGNet CNN is illustrated in Fig.2. The images chosen by the Intelligent Selection module, after performing all the preprocessing steps are fed as inputs to the VGGNet for training. The top layers are frozen first, and the rest of the network is trained. Next, the previously frozen layers are unfrozen and then the training is performed for the whole network. This sort of layer wise freezing and training is adopted to modify the necessary parameters to significantly improve the accuracy. This training is done with the aim of obtaining a robust trained model for the detection of AD.

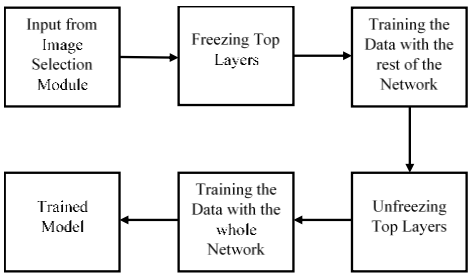

Fig. 2. Inside the VGG Network

D. System Modules

In the intelligent selection module, the image selection carried out is an entropy-based selection. It is done by computing the entropies for each of the image slices and then sorting them in increasing order. In [1], this intelligent selection is performed by sorting the entropies in a decreasing order. But here, the sorting is done in increasing order because the lower the entropy, the higher is the information gain. The algorithm adopted for sorting is the quicksort algorithm since it has the best worst-case time complexity and is much more efficient than other existing sorting algorithms. Entropy is chosen as the parameter for selection because entropy is a measure of the information content in an image. The entropy of each image slice is then calculated. The aim of this module is to obtain as much information from the MRI slices as possible while keeping the number of images to a minimum, in order to reduce the size of training data for a much faster training process. After selecting the images intelligently, only those images are pre-processed in the next module.

In the image pre-processing module, the following steps are carried out:

- Removal of noise
- Conversion of grayscale to RGB
- Resizing of image

The unnecessary noise in the MRI slices is removed using the average or mean filter. This filter works by replacing the current pixel with the average of the neighbourhood pixels.

Generally, the MRI scans are gray scale, single channel images which is helpful for computing their entropies, but that is not the case for the process of training the network because the VGG-16 neural network only accepts three channel RGB images. Hence RGB conversion is done. For each image, the number of color channels is read. If the number of channels in the image is equal to three, then the image is already in RGB format. If it is equal to one, then the image is grayscale. The intensity of each pixel of the gray scale images is calculated and is compared with the 'hot' color map, thus converting them into three channel RGB images.

As the VGG-16 neural network only accepts images in the size 224 X 224, the images are resized to 224 X 224. Bicubic interpolation and anti-aliasing are performed. Bicubic interpolation is an extension of cubic interpolation for interpolating data points on a two-dimensional regular grid. Anti-aliasing is used to reduce the visual defects that occur when high-resolution images are presented in a lower resolution i.e. it softens the harsh stair stepped lines on edges.

CNNs consist of layers which can extract local features in an input image through convolution. Each node in a convolutional layer is connected to a small subset of spatially connected neurons. The weights are shared between the nodes in the convolution layers so that they search for the same features. Each set of convolution layers is followed by a max pooling layer which reduces the size of feature maps by selecting the maximum feature response in local neighborhoods. CNNs typically consist of several pairs of convolutional and pooling layers, followed by a number of consecutive fully connected layers,

and finally a softmax layer, or regression layer, to generate the output labels.

As VGG16 is pretrained, two layers such as the last fully connected layer and the classification layer are replaced to retrain the network on the ADNI dataset. The last fully connected layer is selected, because it is the last layer with learnable weights and the classification layer specifies the output classes of the network. The fully connected layer is replaced with new fully connected layer with outputs equal to the number of classes in dataset. The classification layer is replaced with new layer with no labels, so the new layers are trained properly. The validation images are also given so the network validation is also done in parallel.

The VGGNet CNN generally uses Rectified Linear Unit (ReLU) as the activation function. A further enhanced version of ReLU is the Leaky ReLU (L-ReLU). The major problem in ReLU is the Dying ReLU problem where some ReLU neurons essentially die for all inputs and remain inactive no matter what input is supplied. Here no gradient flows and if large number of dead neurons are there in a neural network, its performance is affected. This issue can be overcome by using Leaky ReLU. In Leaky ReLU, the slope is changed left of x=0 and thus causing a leak and extending the range of ReLU.

IV. RESULT ANALYSIS

The accuracy achieved in training phase is depicted in the graph in Fig.3. It is clear that the accuracy increases with each iteration, while towards the end the growth becomes almost stagnant.

The softmax function as given in Equation 1 is the output unit activation function after the last fully connected layer for multi-class classification problems:

$$P(c_r|x,\theta) = \frac{e^{a_r(x,\theta)}}{\sum_{j=1}^{k} e^{a_j(x,\theta)}} \quad (1)$$

where $0 \le P(c_r|x,\theta) \le 1$, $\sum_{j=1}^{k} P(c_j|x,\theta) = 1$, $a_r = \ln(P(x,\theta|c_r)\,P(c_r))$, $P(x,\theta|c_r)$ is the conditional probability of the sample given class r, and $P(c_r)$ is the class prior probability.

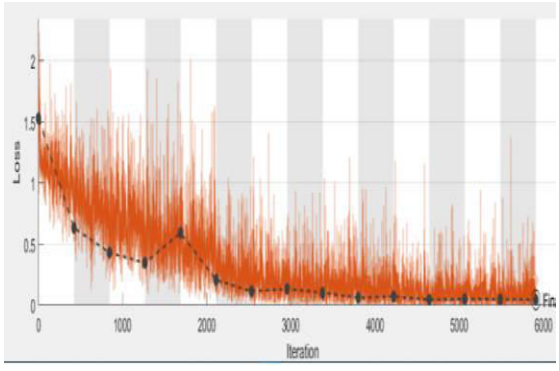

Fig. 3. Training accuracy

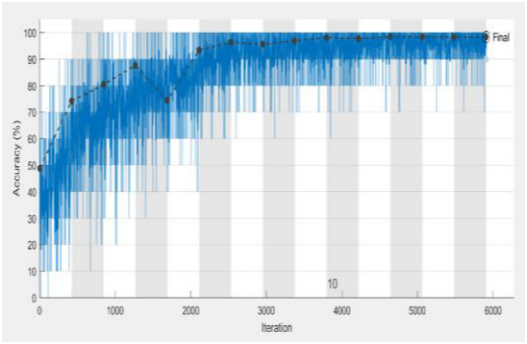

Fig. 4. Loss in each epoch

Loss is a number indicating how bad the model's prediction was on a single sample. If the model's prediction is perfect, the loss is zero; otherwise, the loss is greater. Unit time or Epoch time is a system for describing a point in time. The graph in Fig.4 shows the loss in each epoch of the training phase which is calculated using the formula given in Equation 2.

$$\text{Loss} = - \sum_{i=1}^{N}\sum_{j=1}^{K} t_{ij} \ln y_{ij} \quad (2)$$

where N is the number of samples, K is the number of classes, t_{ij} is the indicator that the ith sample belongs to the jth class, and y_{ij} is the output for sample i for class j, which in this case, is the value from the softmax function. that is, it is the probability that the network associates the ith input with class j.

Most deep learning neural networks such as VGG16make use of ReLU as the activation function. Using the in-built ReLU activation function of VGGNet, the model gave a testing accuracy of 43%. But when this activation function is replaced with Leaky ReLU, the model showed an improved accuracy of 50.68%.

Then batchwise training was performed to further increase the accuracy of detection. After performing this type of training, the accuracy of prediction increased to 70.5%. This accuracy is significantly higher than what was achieved using earlier methods.

V. CONCLUSIONS AND FUTURE WORKS

The system proposed has performed well in the process of effectively detecting the presence of AD in a subject's brain. The usage of transfer learning technique has significantly reduced the dependency on large medical datasets for training the CNN to provide good classification accuracy. This was done to mitigate the problem of scarce availability of such clinical data. Although the VGGNet took a lot of time to be trained, it proved effective in classifying the subject's MRI brain scan as AD, MCI or NC. Since MCI is an earlier stage of the actual AD itself, its timely detection provides time for proper treatment to prolong the onset of AD.

As part of the future work, the objective is to perform the prediction of AD and other types of

dementia by measuring the extent of atrophy or shrinkage in certain brain structures.

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