Amrita School of Computing, Chennai\

Department of Computer Science and Engineering (Artificial Intelligence)

21BIO201 – Intelligence of Biological Systems 3

Capstone Project Title: Brain MRI-based Alzheimer Detection and Classification: A novel approach using Neural Networks and Machine Learning

Abstract

First Discovered in 1906, Alzheimer's disease is now a major cause of concern among the majority of the world's population. Detection and classification of Alzheimer's disease (AD) are a demanding field of research in medicine. The goal of this research is mainly aimed at diagnosing the disease in its early stages. Recently, deep-learning-based approaches have been proposed for the classification of neuroimaging data related to Alzheimer's disease (AD), and significant progress has been made. Our aim is to apply Artificial Intelligence with the help of a few machine learning and deep learning models to help classify the extent of the spread of Alzheimer's disease in the brain. We use the ADNI dataset which consists of images of numerous MRI scans of patients with and without the disease. The images are preprocessed which are then used for extracting the raw features. We then apply various machine learning modules like Convolutional Neural networks and Recurrent Neural Networks to help classify these images to produce a prediction. We obtain prediction accuracy by comparing the test images and the validation images. At the end of this project, we can see that the highest classification accuracy was obtained by the Recurrent Neural Network (RNN) with an accuracy percentage of 98.59%. The Convolutional Neural Network has given us an accuracy of 93.61%.

Key words: CNN, machine learning, classification, Alzheimer's disease, neuroimaging, MRIs.

S.No	***Roll Number***	***Name***	***Marks (30)***
1.	CH.EN.U4AIE21101	Abhivyakti Yadav	
2.	CH.EN.U4AIE21112	Gottipati Koushitha	
3.	CH.EN.U4AIE21117	Jayant Toleti	
4.	CH.EN.U4AIE21119	Kaif Ahmed R	
5.	CH.EN.U4AIE21142	Sai Sruthik Reddy D	

Faculty Name & Signature:

1 Introduction

Alzheimer's disease (AD) is a prolonged, progressive, and unpreventable neurodegenerative condition that clinically emerges as amnesia, cognitive dysfunction, the progressive loss of numerous other brain functions, and the inability to carry out daily activities independently The most prevalent type of dementia, Alzheimer's disease (AD), presents a significant healthcare concern in the twenty-first century. AD affects an estimated 5.5 million adults 65 and over, and it is the sixth most common cause of mortality in the country. AD is an irreversible, progressive brain condition characterized by a lack of cognitive performance without a proven disease-modifying therapy. Now there is no medicine that can fully stop the course of AD or cure it, and the pathogenesis of the illness is still not fully understood. Patients with amnestic mild cognitive impairment (MCI), a stage between cognitively normal ageing and Alzheimer's disease (AD), are more likely to develop the disease than people with age-matched healthy cognition (HC). The majority of current machine learning methods rely on the manual identification of pre-defined brain areas of interest (ROIs) based on recognized MRI characteristics of AD. In order to limit or stop the progression of the disease, a lot of work has been put into developing ways for early identification, particularly at pre-symptomatic phases. In particular, cutting-edge neuroimaging methods like positron emission tomography (PET) and magnetic resonance imaging (MRI) have been created and used to discover structural and molecular indicators for Integrating large-scale, highly dimensional, multimodal neuroimaging data has become difficult due to the quick advancement of neuroimaging technology. As a result, interest in computer-aided machine learning methodologies for integrative analysis has rapidly increased. Support vector machines (SVMs), logistic regression (LRs), linear programming boosting techniques (LPBMs), and support vector machines with recursive feature elimination (SVM-RFEs) have all been employed and show promise for the early identification of AD and the prediction of AD progression.

Such machine learning algorithms must be applied with the proper architectural design or pre-processing processes in place. Four steps are often necessary for classification research utilizing machine learning: feature extraction, feature selection, dimensionality reduction, and feature-based classification method selection. These techniques may be time-consuming and call for specialist knowledge and several optimization stages. These methods' lack of reproducibility has been a problem. To create more informative combinatorial measures, AD-related features, such as mean subcortical volumes, grey matter densities, cortical thickness, brain glucose metabolism, and cerebral amyloid-accumulation in regions of interest (ROIs), such as the hippocampus, are chosen from a variety of neuroimaging modalities.

We are using deep learning techniques like convolutional neural networks (CNN), recurrent neural networks (RNN), and SVM to get beyond these challenges. We used these to identify two: one for Alzheimer's disease detection, which determines if the patient has the disease or not, and the other for Alzheimer's classifier, which determines the patients' stages of the disease.

1.1 Alzheimer's Disease

Dementia is a syndrome or group of syndromes associated with a steep decline in brain functioning. It affects memory, thinking and social abilities severely and interferes with daily life activities. Alzheimer's Disease is a progressive condition and is a prevalent condition of dementia. Current estimates suggest that 44 million people live with dementia worldwide at present. This is predicted to more than triple by 2050 as the population ages. In coming years, the largest increase in dementia prevalence is expected in low- and middle-income countries, which show patterns of increased cardiovascular disease, hypertension, and diabetes.

1.2 Biology of Alzheimer's Disease

In the years following the discovery of the Alzheimer's disease, Dr Alzheimer identified multiple abnormal deposits which he termed plaques and tangles. Plaques are commonly made up of dense clusters of protein scattered throughout the brain. The buildup of these substances can block crucial pathways in your brain. This means the synapses between different brain cells cease to exist. This may play a crucial role in causing the brain cells to die which leads to the gradual decline of cognitive function.

Tangles are made up of protein clusters called tau. Tau Proteins are considered parallel pathways in our brain. They help in transporting nutrients and other important materials within the brain. In an unhealthy brain, these tau proteins can prove to be destructive. The tau protein can collapse and form twists. This causes the formation of tangled clumps of fibers and protein. The cells will have no way to receive vital nutrients.

When braincells are no longer able to function and cell death occurs, the brain dramatically shrinks in some areas of the brain. This shrinkage continues as the severity of the disease slowly increases.

1.3 Classification of Alzheimer's Disease

The clinical classification of Alzheimer's is based on the extent of the decline of cognitive abilities and brain function. This also includes histopathological alterations. This classifies the disease into 4 stages.

1. Preclinical Alzheimer's Disease

   In this stage, the symptoms of the disease are mild and often considered the onset of Alzheimer's Disease. This stage marks the beginning of mild histopathological changes. It affects the entorhinal cortex first and then slowly progresses towards the hippocampus.

2. Mild Alzheimer's Disease

   In this stage, the cognitive decline starts to display symptoms. The pathological changes have now spread to the cerebral cortex. This stage can give birth to symptoms such as minor memory loss, and loss of the ability to hold the latest information and patients may start to suffer from frequent confusion and disorientations.

3. Moderate Alzheimer's Disease

   In this stage, the symptoms gradually start to get worse. The pathological damage has now reached the parts of the brain that controls functions concerned with language, reasoning, and sensory functions. Subjects of the disease at this stage are prone to behavioral problems along with language disorders and impairment of spatial and visual skills.

4. Severe Alzheimer's Disease

   In the final stage of this disease, the patients completely lose their independency from daily activities. The pathological damage has now covered all the regions of the brain. The affected subjects have lost all cognitive abilities and more complex symptoms start to appear which include akathisia, olfactory dysfunction, and a decline in motor skills.

This classification of the Alzheimer's Disease is famously known as the Braak Staging.

1.4 Diagnosis and treatment

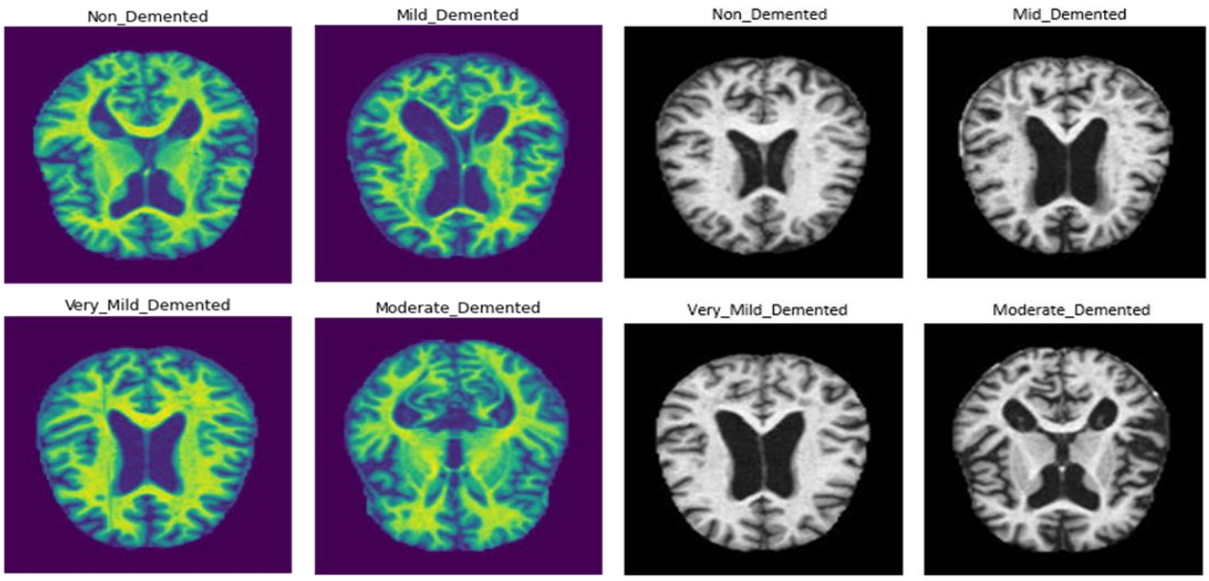
There is no definitive test to diagnose the presence of Alzheimer's Disease in a patient. Doctors usually begin with a basic mental status which tests the functioning of your long-term and short-term memory. After this, if the need arises, they proceed to conduct imaging studies. These tests will image and map your entire brain. The most common Imaging tests are the MRI (Magnetic Resonance Imaging) scans and CT (Computed Tomography) scans. MRI scans can help in picking up key features like inflammation and structural issues. CT scans will look for all the abnormal features in the brain.

Although there are various medicines and drugs available that reduce the effect of certain symptoms, there is no cure that completely gets rid of the Alzheimer's disease.

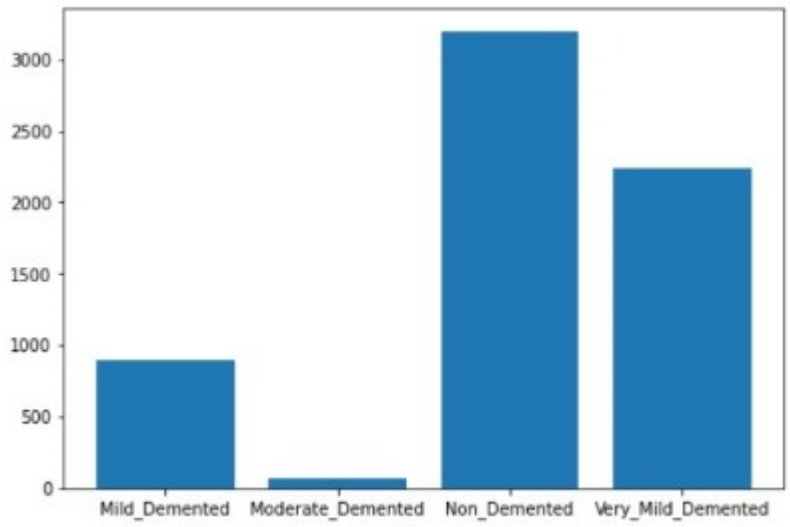
2 Data Preparation

Open-access brain imaging datasets are used for this project. The data used are obtained from Alzheimer's Disease Neuroimaging Initiative (ADNI) database, data.gov (An official website of the *United States government* published by the *Centers for Disease Control and Prevention)* database. The main objective of ADNI has been to determine whether serial MRI, positron emission tomography (PET), other biological markers, clinical evaluation, and neuropsychological testing can be used in conjunction to track the development of MCI and early AD (Alzheimer Disease).

The datasets consist of Brain MRI Image considered in the transverse plane. Each type of Alzheimer has images of its own type. Those images are used to train the machine and based on the pattern of the presence of the cerebrospinal fluid, the type of Alzheimer is classified.



- The information is gathered from several websites, hospitals, and public databases.
- Preprocessed magnetic resonance imaging images make up the dataset.
- All the images are resized into 128 x 128 pixels.
- There are four classes of images in the dataset.
- The Dataset is consisting of total 6400 MRI images.
  Class-1: Mild Demented (896 images)
  Class-2: Moderate Demented (64 images)
  Class-3: Non-Demented (3200 images)
  Class-4: Very Mild Demented (2240 images)



3 Methodology

Prepare the data in 2 separate ways.

- Alzheimer Detection: Whether the patient has the Alzheimer or not (non vs all other categories)
- Alzheimer Classifier: Define what stage the patient is in the Alzheimer.

3.1 SVM for Alzheimer Detection and Alzheimer Classification:

The SVM's linear kernel model gives a very promising result for the task. Considering that this model is not those of so-called 'State-of-the-Art', the performance is quite stellar.

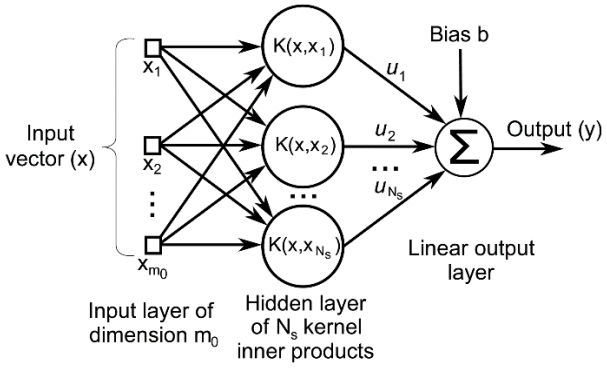
Linear Kernel is used when the data is Linearly separable, that is, it can be separated using a single Line. It is the most basic type of kernel, usually one dimensional in nature. It proves to be the best function when there are lots of features. Linear kernel functions are faster than other functions. Surprisingly, as the kernel gets more complex, the overall performance does not necessarily rise. Advantages of using Linear Kernel: 1) Training a SVM with a Linear Kernel is faster than with any other Kernel. 2) When training a SVM with a Linear Kernel, only the optimization of the C-Regularization parameter is required.

4.1.1 Linear Kernel Function:

F(x, y) = sum(x.y)

Here, x and y represent the data we are trying to classify.

A linear kernel is suitable for an 'Alzheimer detector' as it can be distinguished just by looking at the thickness of the grey matter and the size of the ventricles. For an Alzheimer classifier, more complex kernel would be better. Rbf kernel is also a Gaussian kernel which projects the high dimensional data and then searches a linear separation for it.

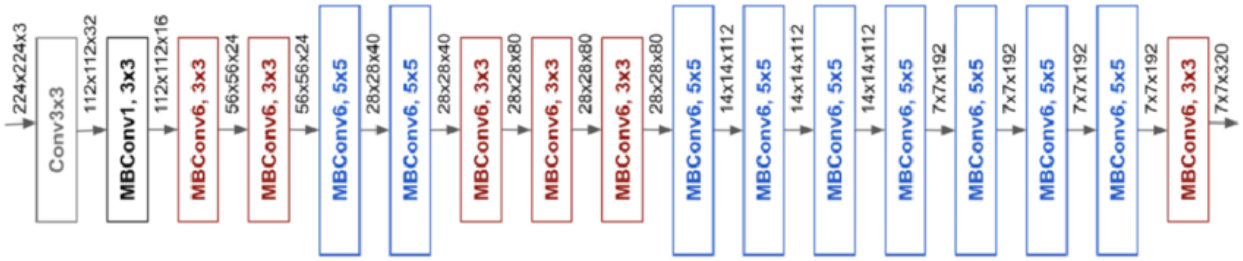


SVM Complex model (RBF Kernel)

The linear kernel still works the best for the classification compared to other complex kernels. Considering that kernel is used to separate the data with its shape, the data is very well separated linearly in the upper dimension, hence the accuracy of the linear kernel SVM model is higher than the more complex models.

3.2 CNN model for Alzheimer Classification (EfficientNetB0):

Rather than using the typical and basic models, we tried the state-of-the-art EfficientNet model. Depending on the input data's shape, EfficientNet changes slightly. However, for the smallest shape (usual input is 224x224) EfficientNetB0 is used. The EfficientNet-B0 has 237 layers.



Baseline model Architecture for EfficientNet-B0.

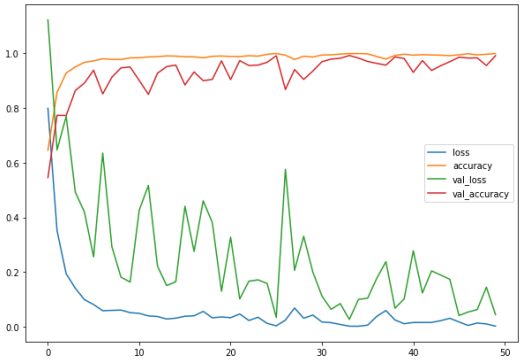
3.2.2 Tuning Parameters

The resolution remains the same as for the whole family. The kernel size may change or remain the same. The number of layers is already shown above in the above figure. The number of channels varies and it is calculated from the information seen from each model's summary and is presented in the table below:

Stage i	Operator $\hat{\mathcal{F}}_i$	Resolution $\hat{H}_i \times \hat{W}_i$	#Channels $\hat{C}_i$	#Layers $\hat{L}_i$
1	Conv3x3	224×224	32	1
2	MBConv1, k3x3	112×112	16	1
3	MBConv6, k3x3	112×112	24	2
4	MBConv6, k5x5	56×56	40	2
5	MBConv6, k3x3	28×28	80	3
6	MBConv6, k5x5	14×14	112	3
7	MBConv6, k5x5	14×14	192	4
8	MBConv6, k3x3	7×7	320	1
9	Conv1x1 & Pooling & FC	7×7	1280	1

Kernel Size, resolution, channels, and no. of layers information

By having a different seed, the accuracy drops or gains significantly with correspondence to a right sized learning rate. Also, the shape of the data input is 128x128 rather than 224x224, which is the input expected for EfficientNetB0.

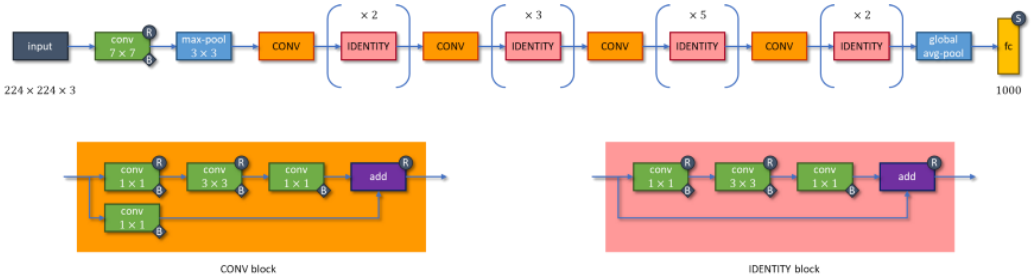


Accuracy measurement parameters for EfficientNet-B0.

3.3 CNN model for Alzheimer Classification (ResNet-50):

The ResNet-50 is an advanced model which has 26 million parameters and 50 layers. Residual block architecture:

1) Identity block: consists of 3 convolution layers with 1×1, 3×3, and 1×1 kernel sizes, all of which are equipped with BN. The ReLU activation function is applied to the first two layers, while the input of the identity block is added to the last layer before applying ReLU.
2) Convolution block: same as identity block, but the input of the convolution block is first passed through a convolution layer with 1×1 kernel size and BN before being added to the last convolution layer of the main series.



ResNet-50 architecture

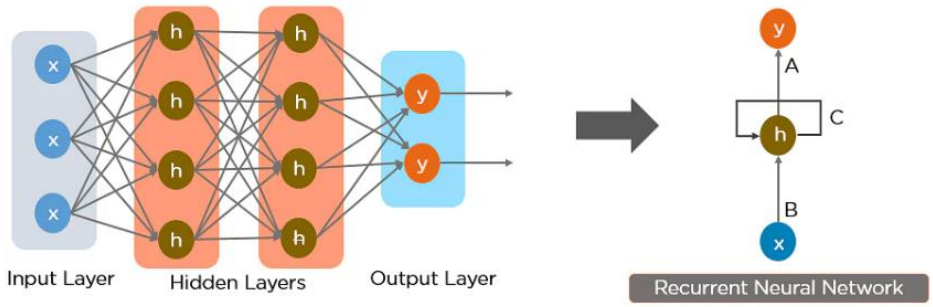
In total, there are:

- 1 convolution layer with BN then ReLU is applied, followed by
- 9 layers that consist of 1 convolution block and 2 identity blocks, followed by
- 12 layers that consist of 1 convolution block and 3 identity blocks, followed by
- 18 layers that consist of 1 convolution block and 5 identity blocks, followed by
- 9 layers that consist of 1 convolution block and 2 identity blocks, followed by
- 1 fully connected layer with SoftMax.

The first convolution layer is followed by a 3×3 max-pooling and the last identity block is followed by a global-average-pooling. Default ResNet-50 accepts colored images with dimensions 224×224 and outputs one of the 1000 classes.

3.4 RNN (Recurrent Neural Network) model for Alzheimer Classification:

RNN operates on the tenet that each layer's output is saved and fed back into the system's input to forecast that layer's output.



The neural network's input is received by the input layer "x," which processes it before sending it to the middle layer.

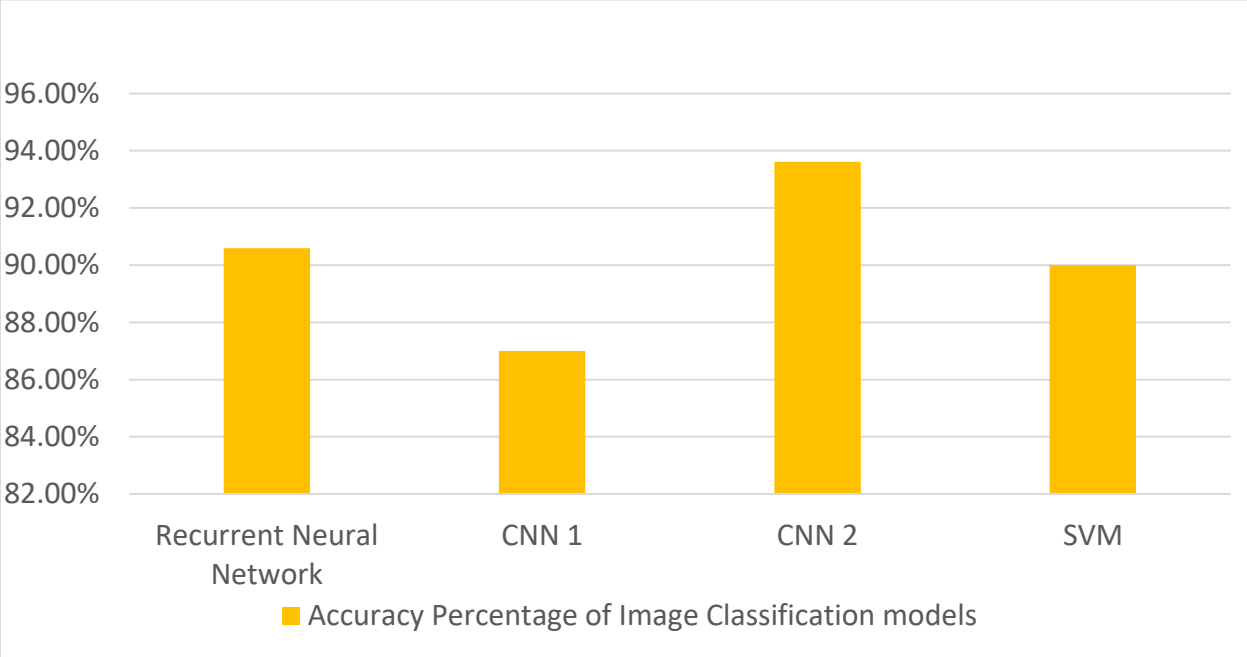
Multiple hidden layers with unique activation functions, weights, and biases may make up the middle layer "h." Recurrent neural networks can be used if you have a neural network without memory, meaning that the various parameters of the different hidden layers are unaffected by the previous layer.

This type of neural network is known as the Vanilla Neural Network. It's used for general machine learning problems, which has a single input and a single output.

4 Result comparison

Overall, from the performance, this data really seems to fit well on SVM in the detection, which runs faster than CNN. For the task of classification, EfficientNetB0 gives an accuracy of 98.2%,

Rbf kernel SVM gives an accuracy of 96%, the ResNet CNN gives an accuracy of 90.12% and RNN gives a relatively low accuracy of 79.90%. The accuracy for CNN model varies by changes the high learning rate. On choosing the ' right sized learning rate ', EfficientNetB0 is the most suitable model for Alzheimer Classification task. Whereas SVM (linear kernel) gives the best results for Alzheimer Detection task.



Conclusion and future scope

ML research associated with neurological studies can offer a more precise analysis of AD. We proposed a framework based on supervised learning models in the classification of AD patients into four categories, i.e., either AD, non-AD, mild AD, very mild AD.

Three Deep-Learning models (2 CNN, 1 RNN) and 1 SVM classifier are used to successfully classify the AD. The most potential model is found to be RNN as it produces higher accuracy at relatively lesser number of Epochs

More sophisticated prediction models with detailed subject data and clinical features around the world should be investigated in future studies, which include more of biological parameters.

At present scientists are involved in detecting AD using the neurochips and advanced neural links

References

1) Alzheimer's disease detection and classification using machine learning techniques M. Bachute; N. Vyas; S. Khanna; K. Modi; C. Katpatal
2) Detection and Classification of Alzheimer's disease from cognitive impairment with resting-state fMRI PR. Buvaneswari & R. Gayathri
3) Deep Learning in Alzheimer's Disease: Diagnostic Classification and Prognostic Prediction Using Neuroimaging Data Taeho Jo1,2,3 *, Kwangsik Nho1,2,3 and Andrew J. Saykin1,2,3
4) Early Detection of Alzheimer's Disease Using Magnetic Resonance Imaging: A Novel Approach Combining Convolutional Neural Networks and Ensemble Learning Dan Pan1 , An Zeng1,2 *, Longfei Jia1 , Yin Huang1 , Tory Frizzell3 and Xiaowei Song3 for the Alzheimer's Disease Neuroimaging Initiative (ADNI)
5) A practical Alzheimer's disease classifer via brain imaging-based deep learning on 85,721 samples Bin Lu1,2, Hui-Xian Li1,2, Zhi-Kai Chang1,2, Le Li12, Ning-Xuan Chen1,2, Zhi-Chen Zhu1,2, Hui-Xia Zhou1,2,3, Xue-Ying Li1,13,4, Yu-Wei Wang1,2, Shi-Xian Cui1,13,4, Zhao-Yu Deng1,2, Zhen Fan5 , Hong Yang6 , Xiao Chen1,2, Paul M. Thompson7 , Francisco Xavier Castellanos8,9 and Chao-Gan Yan1,2,10,11*
6) Classifcation and Visualization of Alzheimer's Disease using Volumetric Convolutional Neural Network and Transfer Learning KanghanOh1, Young-ChulChung2,3, KoWoon Kim4, Woo-Sung Kim2,3 & Il-SeokOh1
7) https://adni.loni.usc.edu/
8) https://www.alzheimers.net/
9) https://www.kaggle.com/datasets/jboysen/mri-and-alzheimers
10) https://ieeexplore.ieee.org/document/9521165
11) https://catalog.data.gov/dataset/alzheimers-disease-and-healthy-aging-data
12) https://www.nature.com/articles/s41598-020-79243-9
13) https://cordis.europa.eu/article/id/429468-the-final-epad-dataset-is-now-available-on-the-alzheimer-s-disease-workbench
14) Alzheimer mri preprocessed dataset. (n.d.). Retrieved from https://www.kaggle.com/sachinkumar413/alzheimer-mri-dataset
15) Black and white images on VGG16. (2017). Deep Learning Course Forums. https://forums.fast.ai/t/black-and-white-images-on-vgg16/2479
16) Carpenter, A. (2020,). Neural architecture transfer. Medium. https://towardsdatascience.com/neural-architecture-transfer-54226b2306e3
17) Marius, H. (2021). State-of-the-art image classification algorithm: Fixefficientnet-l2. Medium. https://towardsdatascience.com/state-of-the-art-image-classification-algorithm-fixefficientnet-l2-98b93deeb04c
18) Team, K. (n.d.). Keras documentation: Image classification via fine-tuning with EfficientNet. Retrieved from https://keras.io/examples/vision/image_classification_efficientnet_fine_tuning/

19) Transfer Learning(Vgg16) using MNIST · Issue #11208 · keras-team/keras. (n.d.). GitHub. Retrieved from https://github.com/keras-team/keras/issues/11208
20) Using vgg with greyscale images. (2017). Deep Learning Course Forums. https://forums.fast.ai/t/using-vgg-with-greyscale-images/854
21) https://www.tensorflow.org/guide/keras/rnn
22) https://keras.io/examples/vision/image_classification_efficientnet_fine_tuning/
23) https://towardsdatascience.com/neural-architecture-transfer-54226b2306e3
24) https://towardsdatascience.com/state-of-the-art-image-classification-algorithm-fixefficientnet-l2-98b93deeb04c
25) https://adni.loni.usc.edu/
26) https://ieeexplore.ieee.org/document/9521165
27) https://catalog.data.gov/dataset/alzheimers-disease-and-healthy-aging-data

Link for Code and Respective Data Set