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Analysis for Alzheimer's Disease Using Cross Correlation of EEG Data

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ABSTRACT: Alzheimer Disease is the Neuro-degenerative disease, which consists of the common form of dementia. It is the most expensive disease in the modern society & characterized by cognitive, intellectual as well as behavioral disturbance. Due to this, the early diagnosis of the disease is essential as it helps the patients & also his family to take preventive measures. EEG can be used the standardized tool for diagnosis of Alzheimer disease. Various abnormalities are found in the EEG signals of the patients suffering from Alzheimer disease.

Hence, the need is to develop the detection of the disease in early stage called as Dementia, the first stage called Mild Cognitive Impairment (MCI). Role of EEG in diagnostic & clinical research of Alzheimer disease has become more useful in present decades. In present, the most critical task includes the diagnosis of the AD & its early detection in the preclinical stage. The need is to improve the diagnosis accuracy of the EEG signal. This project presents the ideas of increasing the accuracy of the signal by using various methods. Basically, abnormalities in the EEG signals are characterized by slowing of signals, shift of power spectrum to low frequencies etc. In this way, EEG can be as the tool for the early diagnosis of Alzheimer disease.

I. INTRODUCTION

Alzheimer disease is one of the Neuro-degenerative diseases which are found to be complex in the present scenario. It is the common form of dementia & by the time it affects the brains cells . Its prevalence in the world is assumed to be doubled in next 20 years . In 2012, the World Health Organization and Alzheimer's disease International released a report calling on governments to implement national dementia plans focusing on 1) Raising public awareness about the disease and reducing stigma, 2) Improving early diagnosis, and 3) Providing better care and more support to Caregivers. As AD is assumed to be increased in the near future due to the aging phenomenon, several measures are taken into the consideration for the early diagnosis of disease in the early stage. AD is mainly characterized by the neuronal widespread loss of cells, neurofibrillary tangles, and senile plaques in Hippocampus, entorhinal cortex, neocortex and other brain regions [5]. In the pre-clinical stage of the disease, there are no basically reliable and valid symptoms detected to allow a very early diagnosis. In the mild stage of the disease, memory impairment & loss are noticed. In the moderate stage of dementia, language difficulties become more such as word finding difficulties, paraphasia etc. As the disease goes in progression, several deficits are found in cognitive abilities such as judgment, abstract or logical reasoning, planning, and organizing [6].

In the final stage called as the severe AD, almost all cognitive functions are severely damaged, and motor functions including chewing and swallowing are profoundly disturbed . Presently, it was estimated that there are 44.4 millions of people suffering from dementia in the world. It was also estimated that this number will increase till 75.6 million in 2030, and 135.5 million in 2050. It was also observed that 61% of the people suffering from dementia are from the developed countries. The fastest growth in the elderly population is taking place in China, India, and their south Asian and western Pacific neighbors. There are basically no proper symptoms for cause of AD.

But, some cases are generally accepted for the genetic differences. Some of the hypothesis are used for the understanding the cause of AD. Some of the common hypothesis includes the genetics, cholinergic hypothesis, Amyloid hypothesis, tau hypothesis etc. Another hypothesis is also made that AD is also caused by the age related myelin breakdown in the brain. Air pollution is also one of the contributing factors for the development of theAlzheimer disease. Early diagnosis of the disease in early stage is essential in both the Mild AD & MCI stage as

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medications can be applied in an early stage. Early diagnosis of the disease also raises the chances of treating the disease at a nascent stage. It allows the patients family to take financial decisions related to the disease, and to plan for the future needs and care of the patients.

Motivation:

Alzheimer's Disease (AD), also known as just Alzheimer's ,isa chronic neurodegenerative disease that usually starts slowly and gets worse over time. It is the cause of 60% to 70% of cases of dementia. The most common early symptom is difficulty in remembering recent events (short-term memory loss). As the disease advances, symptoms can include problems with language, disorientation, mood swings, loss of motivation, not managing self-care, and behavioral issues.

Alzheimer's Disease (AD) is a neurodegenerative disorder of the brain characterized by neurofibrillary tangles, amyloid plaques, and loss of neurons and cognitive decline of mental functions with aging. Several studies confirm the ability of Magnetic Resonance Imaging (MRI) to distinguish AD subjects from Normal Controls (NC), Mild Cognitive Impairment (MCI) subjects who later convert to AD from those who do Not and the fast rate of atrophy in AD subjects that is observed in comparison with the age-matched non-demented controls. To provide appropriate care to AD patients, it is very important to quantify the degree of atrophy in thalamus, hippocampus, entorhinal cortex and neocortical areas in the early and later stages of the disease.

Such kind of assessment is known as Region Of Interest (ROI) based analysis and is normally focused on the analysis of specific brain regions during the disease progression. Voxel Based Morphometry (VBM) and Tensor Based Morphometry (TBM) are two most widely used methods for ROI analysis. A region of interest is a selected subset of samples within a dataset identified for a particular purpose. The concept of a ROI is commonly used in many application areas.

For example, in medical imaging, the boundaries of a tumor may be defined on an image or in a volume, for the purpose of measuring its size. Alzheimer's Disease (AD) is the most common typeof dementia that is affecting the elderly population worldwide.

Relevance:

Alzheimer's disease (AD) is the most popular dementia in elderly people worldwide. Its Expectation is 1 in 85 people will be affected by 2050 and the number of affected people is double in the next 20 years. Alzheimer's disease was named after the German psychiatrist and pathologist Aloes Alzheimer after he examined a female patient (post mortem) in 1906 that had died at age 51 after having severe memory problems, confusion, and difficulty understanding questions. Alzheimer reported two common abnormalities in the brain of this patient:

1. Dense layers of protein deposited outside and between the nerve cells.
2. Areas of damaged nerve fibres, inside the nerve cells, which instead of being straight had become tangled". Moreover, these plaques and tangles have been used to help diagnose AD there are three phases of AD: preclinical, mild cognitive impairment, and dementia. Preclinical means the starting stage of AD. MCI includes "mild changes in memory. Dementia means severity of the disease. The symptoms of AD different between patients.

Symptoms of Alzheimer's:

- Memory loss that disrupts daily life.
- Challenges in planning or solving problems.
- Confusion with time or place.
- Trouble understanding visual images and spatial relationships.
- Decreased or poor judgment.
- Withdrawal from work or social activities.

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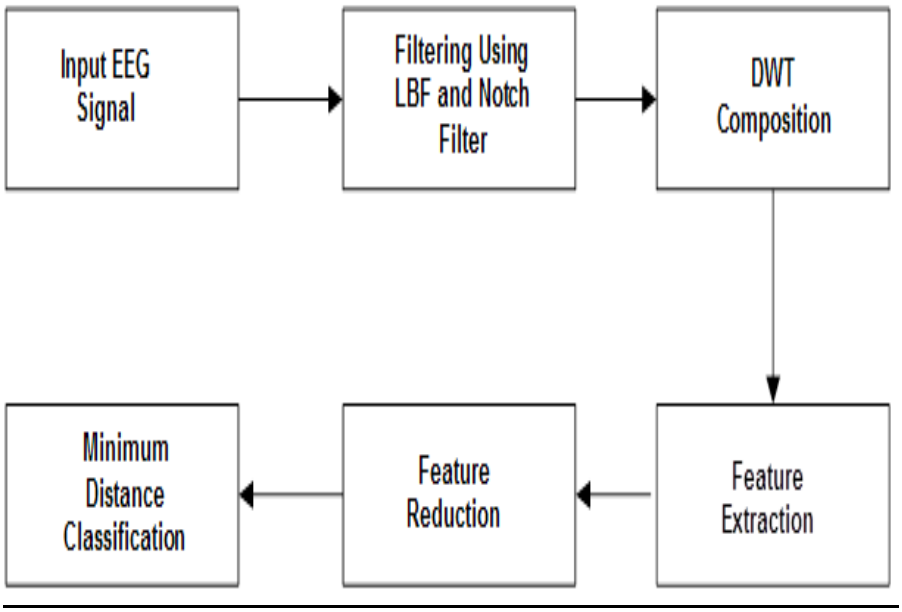
Problem Definition:

Alzheimer's disease (AD) is the most common type of dementia that is affecting the elderly population worldwide.Alzheimer's disease (AD) is a neurodegenerative disorder of the brain characterized by neurofibrillary tangles, amyloid plaques, loss of neurons and cognitive decline of mental functions with aging.

Objectives:

Early diagnosis or detection of Alzheimer's disease (AD) from the Normal Elder Control (NC) is very important. However, the Computer-Aided Diagnosis (CAD) was not widely used, and the classification performance did not reach the standard of practical use. To provide appropriate care to AD patients, it is very important to quantify the degree of atrophy in thalamus, hippocampus, entorhinal cortex and neocortical areas in the early and later stages of the disease. Such kind of assessment is known as Region Of Interest (ROI) based analysis and is normally focused on the analysis of specific brain regions during the disease progression.

II. METHODOLOGY



a) Block diagram of analysis of Alzheimer disease.

Input EEG Signal:

Choose an input EEG signal. Electroencephalography (EEG) signal is the recording of electrical activity along the scalp. EEG measures voltage fluctuations resulting from ionic current flows within the neurons of the brain. In our proposed methodology, EEG refers to the recording of the brain's spontaneous electrical activity over a short period of time, usually 20–40 minutes recorded from multiple electrodes placed on the scalp. For the placement of the electrodes; we are using the standard 10 to 20 electrode system.

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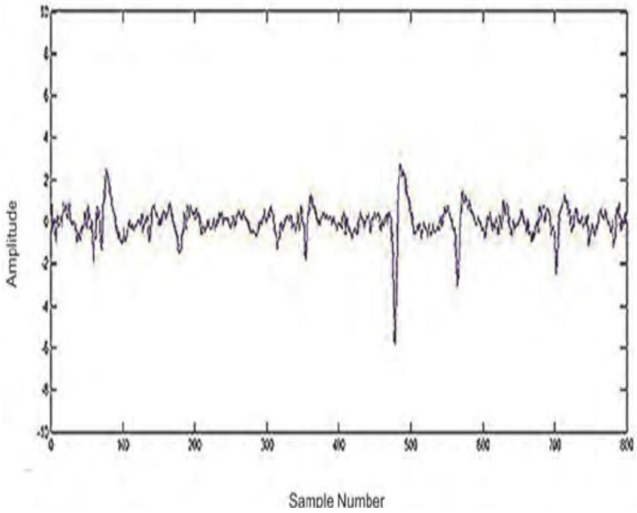

b) Normal EEG signal when a person is relax.

Filtering Using LPF and Notch filter:

Filtering of the EEG signal to remove artifacts is a common pre-processing step but introduces temporal distortions in the signal. Digital filtering is a common preprocessing step when analyzing EEG data. The typical practice in EEG signal processing is to apply a high-pass filter to filter out slow frequencies less than 0.1 Hz or often even 1 Hz and a low-pass filter to filter out frequencies above 40 or 50 Hz Hz. Although filters (and there are many types of them!) can be extremely useful in reducing and/or separating noise from the signal of interest, they are not entirely harmless. Numerous studies demonstrate that filtering can affect and distort the shape/temporal structure of EEG signals or event related potential (ERP) data (1-4).In our approach we use Notch filter and LPF Filter to reduce noise from signal.

DWT Composition:

Feature Extraction is performed by using DWT and the Decomposition of EEG signals is extracted for 8 levels using “db4” wavelet.

DWT chooses only a subset of scales and positions. DWT works as filters where the signals are divided into two bands at each a specified level called approximations and details signals. The approximations (A) are the high-scale, lowfrequency components of the signal. The details (D) are the low-scale, high-frequency components. The samples of the signal are dividing by 2 and this is called sub-sampling, as shown in Fig. The data obtained after normalization stage serves as the input data to the DWT decompositions, which is also known as Sub-band Coding, and could be repeated for further decomposition. At every level, the sub-sampling will result in half the number of samples. The procedure of the sub-band coding of the EEG data can be visualized [11], as shown in Fig. 5. In this work, a four-level multi-resolution decomposition using Daubechies4 wavelets is implemented. Each level could characterize the frequencies of the EEG data band.

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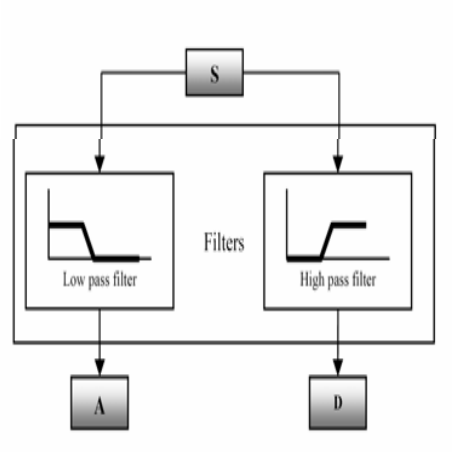
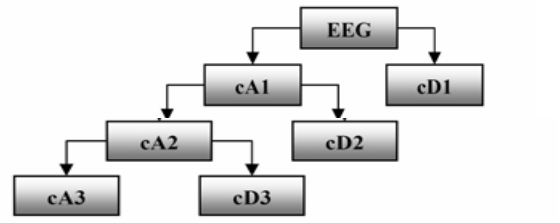


c) The filtering process of the DWT

Fast Fourier Transform (FFT) of each level in DWT levels: Fourier analysis is extremely useful for data analysis, as it breaks down a signal into constituent sinusoids of different frequencies. For sampled vector data, Fourier analysis is performed using the discrete Fourier transform (DFT).

The fast Fourier transform (FFT) is an efficient algorithm for computing the DFT of a sequence; it is not a separate transform. It is particularly used in area such as signal processing, where its uses range from filtering and frequency analysis to power spectrum estimation. Computation using FFT of each level gives an indication to the frequencies that the bands contained in. Fig. 6 summarizes the flow chart of the EEG waves classification software.



d) Sub-band coding algorithm of the DWT

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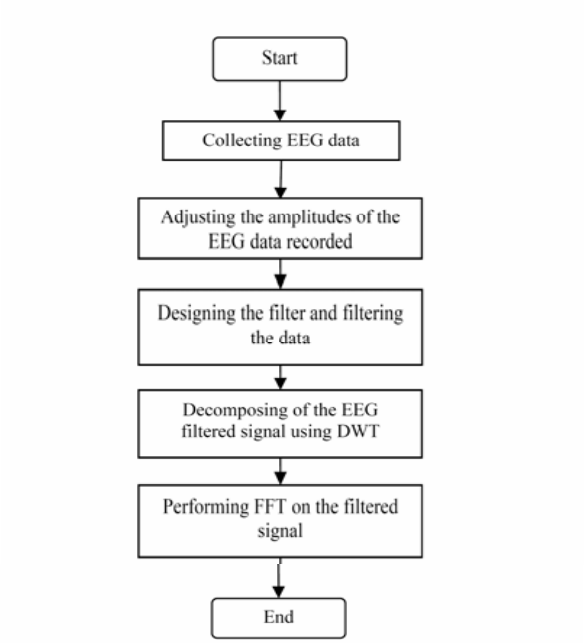

e) Flow chart of EEG waves classification procedure.

Feature Extraction:

Features can be extracted from EEG signals in various ways. We have found that the following different features and electrode combinations are efficient for EEG-based emotion recognition Integrated EMG, Mean absolute value, Simple square integral, Variance of EMG, Root mean square, Waveform length, Difference absolute standard deviation value, Autoregressive, Hjorth activity, Hjorth mobility, Hjorth complexity from the EEG signals. We computed the traditional features using Time Domain and Frequency domain such as LCD, technique Most of these methods are well established and can readily be implemented in real time. Recently, advanced computational methods have been proposed to evaluate emotional arousal.

a)Integrated EMG:

Integrated EMG (IEMG) is normally used as an onset detection index in EMG non–pattern recognition and in clinical application.

$IEMG=\sum_{i=1}^{n} I\, xi\, I$

b)Mean absolute value:

Mean absolute value (MAV) is one of the most popular used in EMG signal analysis. It is similar to IEMG feature which is used as an onset index, especially in detection of the surface EMG signal for prosthetic limb control .

$MAV=\frac{1}{n}\sum_{i=1}^{n} I\, xi\, I$

c)Modified mean absolute value type 1:

Modified mean absolute value type 1 (MAV1) is an extension of MAV feature.

$MAV1=\frac{1}{n}\sum_{i=1}^{n} wi\, I\, xi\, I$

d)Simple square integral:

Simple square integral (SSI) or integral square uses energy of the EMG signal as feature.

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$SSI=\sum_{i=1}^{n} xi^2$

e)Variance of EMG:

Variance of EMG (VAR) is another power index. Generally, variance is defined as an average of square values of the deviation of that variable; however, the mean value of EMG signal is close to zero (~10-10).

$VAR=\frac{1}{n-1}\sum_{i=1}^{n} xi^2$

f)Root mean square:

Root mean square (RMS) is another popular feature in analysis of the EMG signal. It is modeled as amplitude modulated Gaussian random process whose relate to constant force and non–fatiguing contraction.

$RMS=\sqrt{\frac{1}{n-1}\sum_{i=1}^{n} xi^2}$

g)Waveform length:

Waveform length (WL) is a measure of complexity of the EMG signal. It is defined as cumulative length of the EMG waveform over the time segment.

$WL=\sum_{i=1}^{n-1} Ix_{i+1} + x_i$

h)Difference absolute standard deviation value:

Difference absolute standard deviation value (DASDV) is look like RMS feature, in other words, it is a standard deviation value of the wavelength.

$yt=a_1y_{t-1} + a_1y_2 + \cdots a_ny_{1-n} + \mathcal{E}_t = \sum_{i=1}^{n} a_iy_{t-1} + \mathcal{E}_t$

where*a1* to *an* are the autoregressive coefficients, *yt*is the time series under investigation, *n* is the order of the AR model (*n* = 4) and *ε* is the residual or Gaussian white noise. With *n* = 4, then there are four features were obtained using (9)

$Hjorth\_1=\frac{1}{n}\sum_{i=1}^{n} I\ xi - \bar{x}\ I^2$

i)Hjorth mobility:

The mobility parameter represents the proportion of standard deviation of the power spectrum.

$Hjorth\_2=\frac{\sigma^1}{n\sigma^x}$

j)Hjorth mobility:

The mobility parameter represents the proportion of standard deviation of the power spectrum.

$Hjorth\_3=\frac{\sigma^1}{n\sigma^x}$

k)Hjorth complexity:

The complexity parameter represents the change in frequency. The parameter compres the signal's similarity to a pure sine wave, where the value converge to 1 if the signals is more similar. $Hjorth\_4=\frac{\sigma_x^{''}/\sigma_x'}{\sigma_x^{''}/\sigma^1}$

Feature Reduction:

Feature selection also constitutes a key development phase of pattern recognition. Extensive research into feature selection has been carried out over the past four decades. The feature selection is inherently a combinatorial optimization problem that is a NP-hard problem. There are many searching algorithms used to determine the promising

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feature subset candidates, such as exhaustive search, branch and bound search (BB), sequential forward selection (SFS), Tabu search (TB), Simulated annealing algorithm (SA), Genetic Algorithm (GA), Binary Particle Swarm Optimization (BPSO) and etc. Exhaustive search algorithm can get the optimal feature subset but its computing complexity increases exponentially with the number of original features increasing. In our project we use PCA Techniques for feature reduction purpose.

Classification:

The features extracted in the previous stage are the input for the classifier. The classifier can be anything from a simple linear model to a complex non-linear neural network that can be trained to diagnose the disease. In our proposed methodology, we used minimum distance classifier for the classification.

Diagnosis:

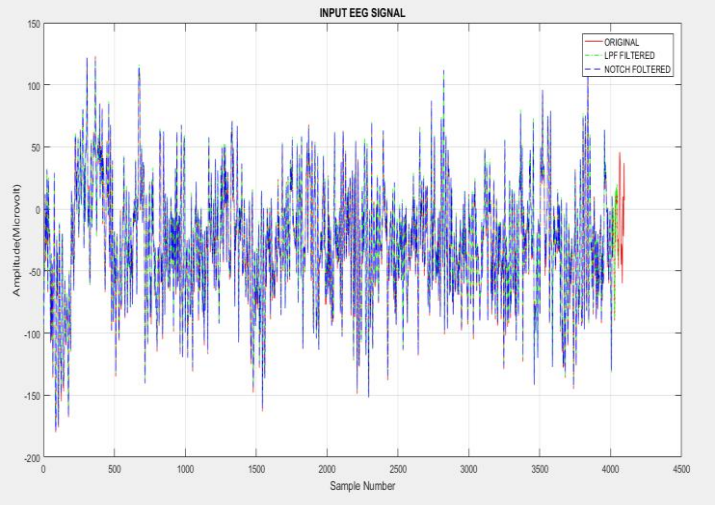
Based on the output of the Classifier, we can detect whether the person is suffering from Alzheimer Disease or he is in the early stage of the AD called as the Mild cognitive impairment (MCI).

EEGLAB is found to be an interactive MATLAB toolbox which is used for processing the continuous and event-related EEG, MEG and other electrophysiological data using independent component analysis (ICA), time/frequency analysis, and other methods including artifact rejection. EEGLAB provides an interactive graphic user interface (GUI) allowing users to flexibly and interactively process their high-density EEG and other dynamic brain data using independent component analysis and/or time/frequency analysis (TFA), as well as standard averaging methods.

III. RESULT

It is expected that we get the high accuracy (upto 95%) of the EEG signal for detection of the Alzheimer disease. By watching the nature of the above signal according to the frequency bands classified we can also detect stage of the Alzheimer disease for example the early stage dementia, later stage Mild cognitive impairment (MCI) & last stage Severe Alzheimer disease.

Filtering (Original):



f) Filtered image of EEG signal

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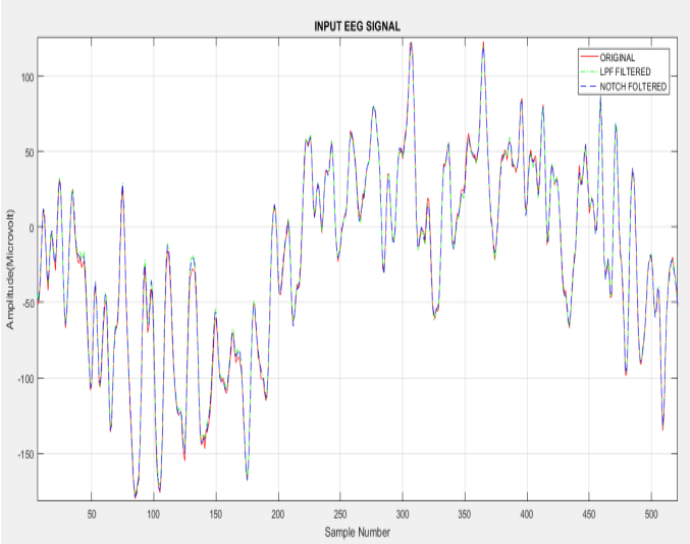
A low-pass filter allows signal frequencies below the low cut-off frequency to pass and stops frequencies above the cut-off frequency. It is commonly used to help reduce environmental noise and provide a smoother signal.

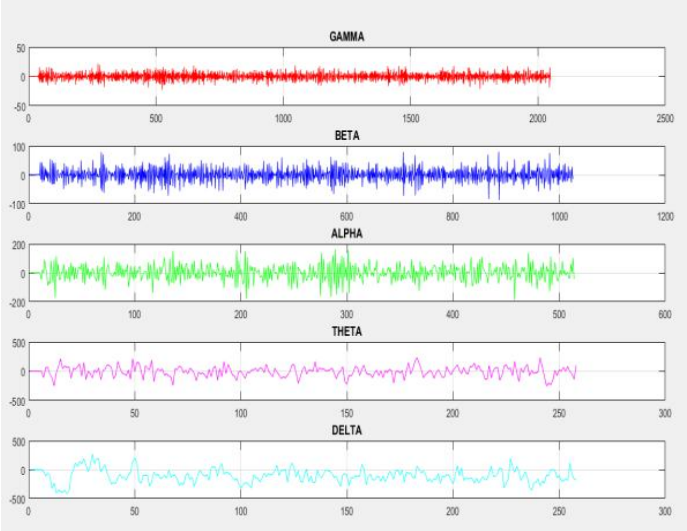
A notch filter removes a particular frequency from a signal and has a frequency response that falls to zero over a narrow range of frequencies (i.e. a 50 Hz notch may block signals from 49.5 – 50.5 Hz). Notch filters are available in all ADInstruments Bio Amps (Animal [ML136], Single [ML132], Dual [ML135] and Dual Bio/Stim [ML408])

Filtering (Zoomed Version of 10 to 500 samples):



g) Zoomed version of filtered image

DWTDecompositio(alpha,beta,gamma,delta,theta):



h) Decomposition of EEG data

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EEG signals are extracted from sophisticated machines in highly secured and de-noised labs are prone to artifacts and several other type of non-separable noise. EEG signal when analyzed has a very low frequency in the range of hertz. These EEG signals can be classified based on their frequency bands. The classification is shown in Table.1 it also mentions the region of brain from where it is extracted.

As we have discussed earlier it very difficult to extract EEG signal from the brain and separate the artifacts, based on the classification of their frequency we generates signals of those frequency. our data will be simulated EEG signals.

Type	Frequency	Location
Delta	up to 4	Frontally in adults, posteriorly in children; high amplitude waves
Theta	4 – 8	Found in locations not related to task at hand
Alpha	8 – 13	Posterior regions of head, both sides, higher in amplitude on non-dominant side
Beta	13 – 30	Both sides of Brain, symmetrical distribution, most evident frontally; low amplitude waves
Gamma	31 - 100	Somatosensory cortex

Table.1 Classification of EEG Signals Based On Their Frequency

Delta wave lies between the range of 0.5 to 4 Hz and the shape is observed as the highest in amplitude and the slowest in waves. It is primarily associated with deep sleep, serious brain disorder and in the waking state.

Theta wave lies between 4 and 8 Hz with an amplitude usually greater than 20 µV. Theta arises from emotional stress, especially frustration or disappointment and unconscious material, creative inspiration and deep meditation.

Alpha contains the frequency range from 8 to 13 Hz, with 30-50m µV amplitude, which appears mainly in the posterior regions of the head (occipital lobe) when the subject has eyes closed or is in a relaxation state. It is usually associated with intense mental activity, stress and tension. Alpha activity recorded from sensorimotor areas is also called mu activity.

Beta is in the frequency range of 13 Hz-30 Hz. It is seen in a low amplitude and varying frequencies symmetrically on both sides in the frontal area. When the brain is aroused and actively engaged in mental activities, it generates beta waves. Beta waves are characteristics of a strongly engaged mind. Beta is the brain wave usually associated with active things, active attentions, and focusing on the outside world or solving concrete problems.

Gamma waves have the frequency from 30 Hz and up. This rhythm is sometimes defined as having a maximal frequency around 80 Hz or 100 Hz. It is associated with various cognitive and motor functions.

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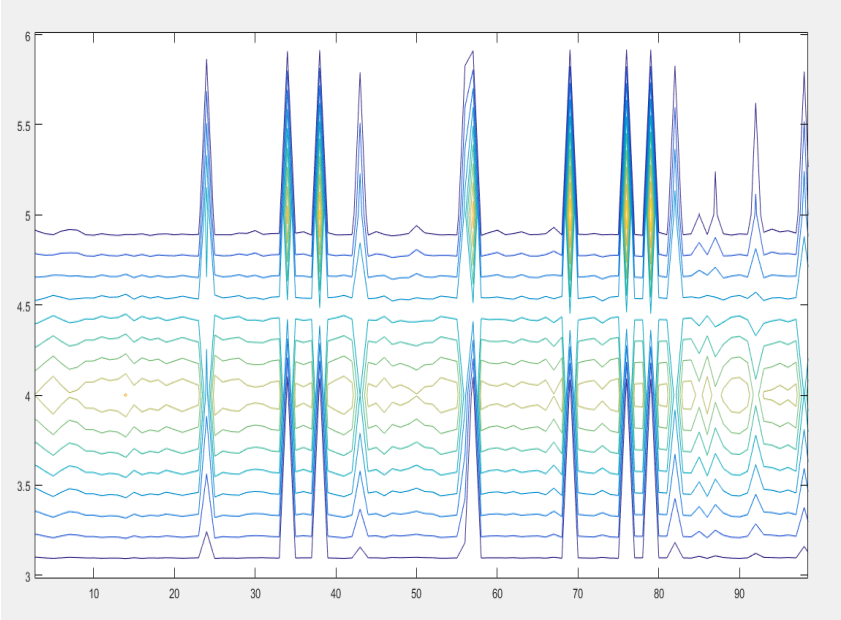
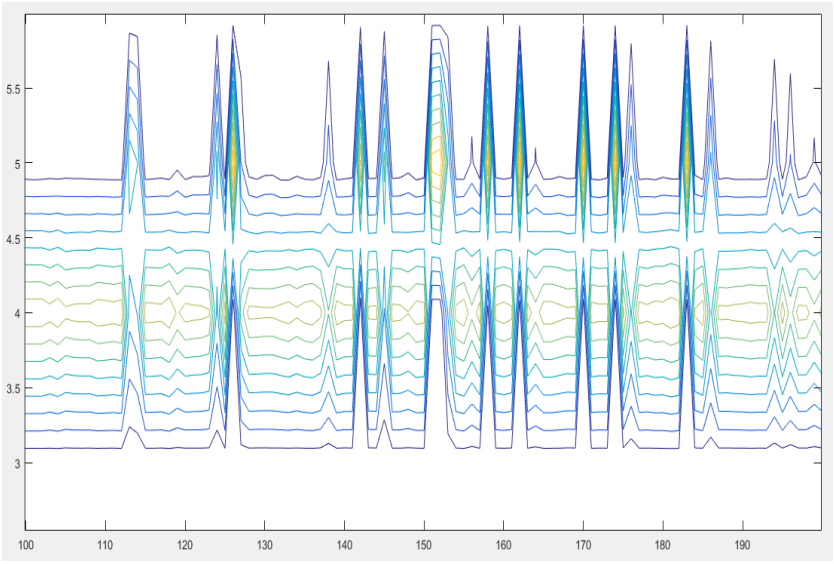
Normal person EEG feature space representation:



i) EEG of normal person

Electrical activity in the brain appears in an EEG as a pattern of waves. Different levels of consciousness, like sleeping and waking, have a specific range of frequencies of waves per second that are considered normal. For example, the wave patterns move faster when you're awake than when you're asleep. The EEG will show if the frequency of waves or patterns are normal. Normal activity typically means you don't have a brain disorder.

AD (Alzheimer's disease) person EEG feature space representation:



j) EEG of AD person

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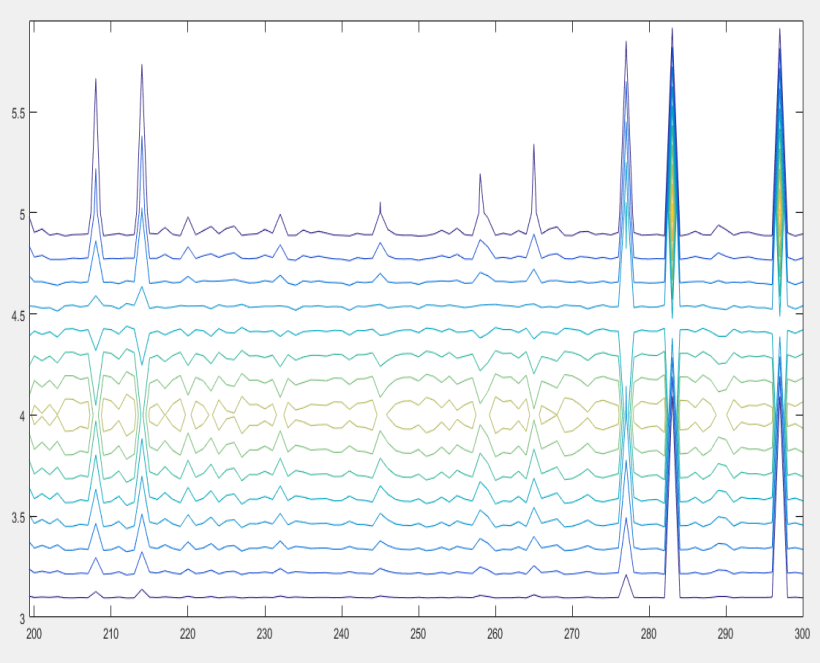
Alzheimer's disease EEG results due to:

- epilepsy or another seizure disorder
- abnormal bleeding or hemorrhage
- sleep disorder
- encephalitis (swelling of the brain)
- tumor
- dead tissue due to a blockage of blood flow
- migraines
- alcohol or drug abuse
- head injury

It's very important to discuss your test results with your doctor. Before you review the results, it may be helpful to write down any questions you might want to ask. Be sure to speak up if there's anything about your results that you don't understand.

VaD (vascular dementia) person EEG feature space representation:



k) EEG of VaD person

Vascular dementia is the second most common form of dementia after Alzheimer disease. It's caused when decreased blood flow damages brain tissue. Blood flow to brain tissue may be reduced. Or it may be completely blocked by a blood clot.

Symptoms of vascular dementia may develop slowly. Or they may develop after a stroke or major surgery, such as heart bypass surgery or abdominal surgery.

Dementia and other related diseases and conditions are hard to tell apart because they share similar symptoms. Although vascular dementia is caused by problems with blood flow to the brain, this blood flow problem can develop in different ways. Examples of vascular dementia include:

- **Mixed dementia.** This type occurs when symptoms of both vascular dementia and Alzheimer exist.

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- **Multi-infarct dementia.** This occurs after repeated small, often "silent," blockages affect blood flow to a certain part of the brain. The changes that occur after each blockage may not be apparent, but over time, the combined effect starts to cause symptoms. This is also called vascular cognitive impairment.

The effect of decreased or no blood flow on the brain depends on the size and location of the area affected. If a small area in a part of the brain that controls memory is affected you may be "forgetful." But this doesn't always change your ability to carry on normal activities. If a larger area is affected, you may have trouble thinking clearly or solving problems. These problems may change your ability to function normally.

Researchers think that vascular dementia will become more common in the next few decades because:

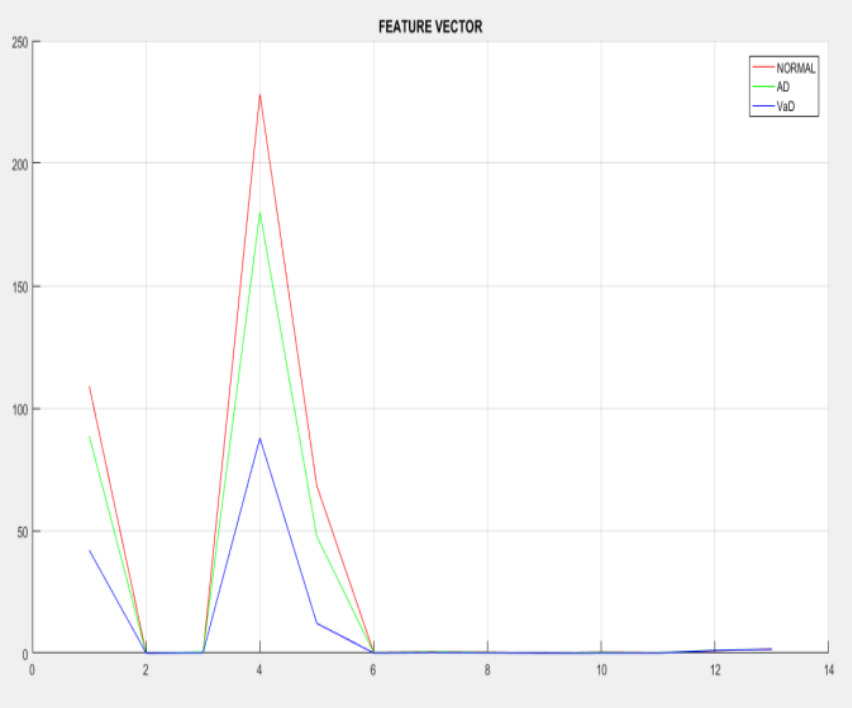
- Vascular dementia is generally caused by conditions that occur most often in older people, such as atherosclerosis (hardening of the arteries), heart disease, and stroke.
- The number of people older than 65 years is growing.
- People are living longer with chronic diseases, such as heart disease and diabetes.

What causes vascular dementia?

Vascular dementia is caused by a lack of blood flow to a part of the brain. Blood flow may be decreased or interrupted by:

- Blood clots
- Bleeding because of a ruptured blood vessel (such as from a stroke)
- Damage to a blood vessel from atherosclerosis, infection, high blood pressure, or other causes, such as an autoimmune disorder

Feature representaion of 3 class on single graph:



l) Feature representaion of 3 class on single graph

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ADVANTAGES, DISADVANTAGES

Advantages

- High accuracy
- High computational speed
- Processing time is less.
- Minimum Distance Classifier are used here. Minimum Distance Classifier are extremely powerful tools for data classification.

Disadvantages

- Sometimes EEG Signals are not very exact
- EEG waveform does not researchers to distinguish between originating in different but closely adjacent locations.

IV. FUTURE SCOPE

In future, multichannel EEG recording from various lobes may be more appropriate to classify AD from normal subject. In future, various different algorithms as well as classifiers such as neural networks can be used for increasing the accuracy of diagnosis of the disease in early stage.

V. CONCLUSION

In this way, we can use EEG as a means of diagnosis of Alzheimer disease. Various abnormalities are found in the EEG signals. Slowing of EEG signals, reduced complexity, Perturbations in synchrony measures are some of the abnormalities found. Various different filtering method,features extraction methods as well as classifiers can be used for early detection of the disease. Thus, EEG can be used as the inexpensive, convenient tool for diagnosis of Alzheimer disease. In future, various different algorithms as well as classifiers such as neural networks can be used for increasing the accuracy of diagnosis of the disease in early stage.

Research Challenges includes the increase of accuracy upto 95% of EEG signal to detect the disease in the early stage, use of different classifiers for classification purpose & to remove the artifacts in EEG signal are some them. In future, the above system can also be made portable.

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