# EARLY DETECTION OF ALZHEIMER’S DISEASE

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# Table of Contents

# Introduction

AD

Alois Alzheimer

# Introduction

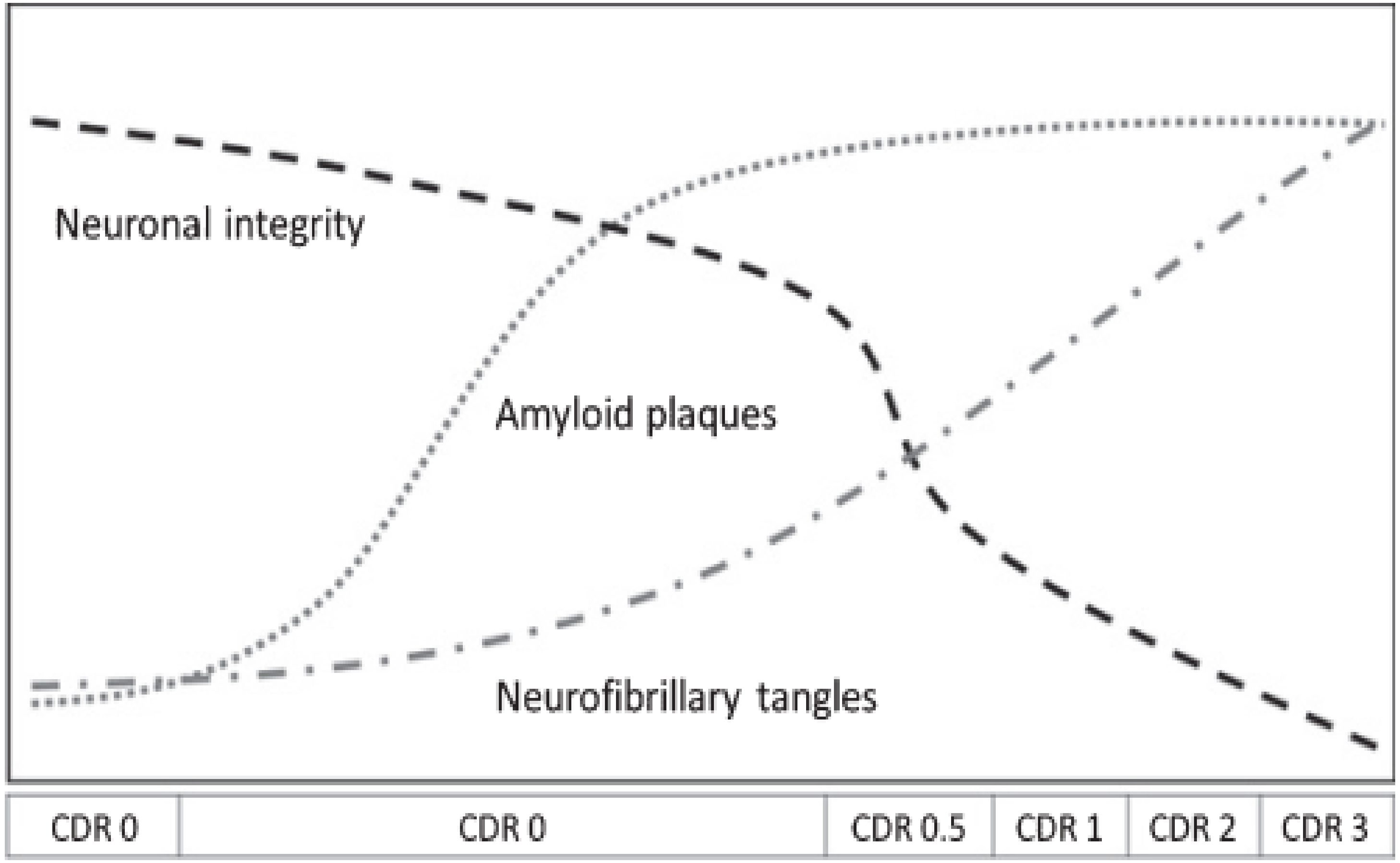
## Stages Of Disease:

- Normal
- Very Mild Dementia
- Mild Dementia
- Moderate Dementia
- Severe Dementia

# Introduction

## AD diagnosis methods

- Amyloid-beta (Aβ)
  - Begins up to 20 years



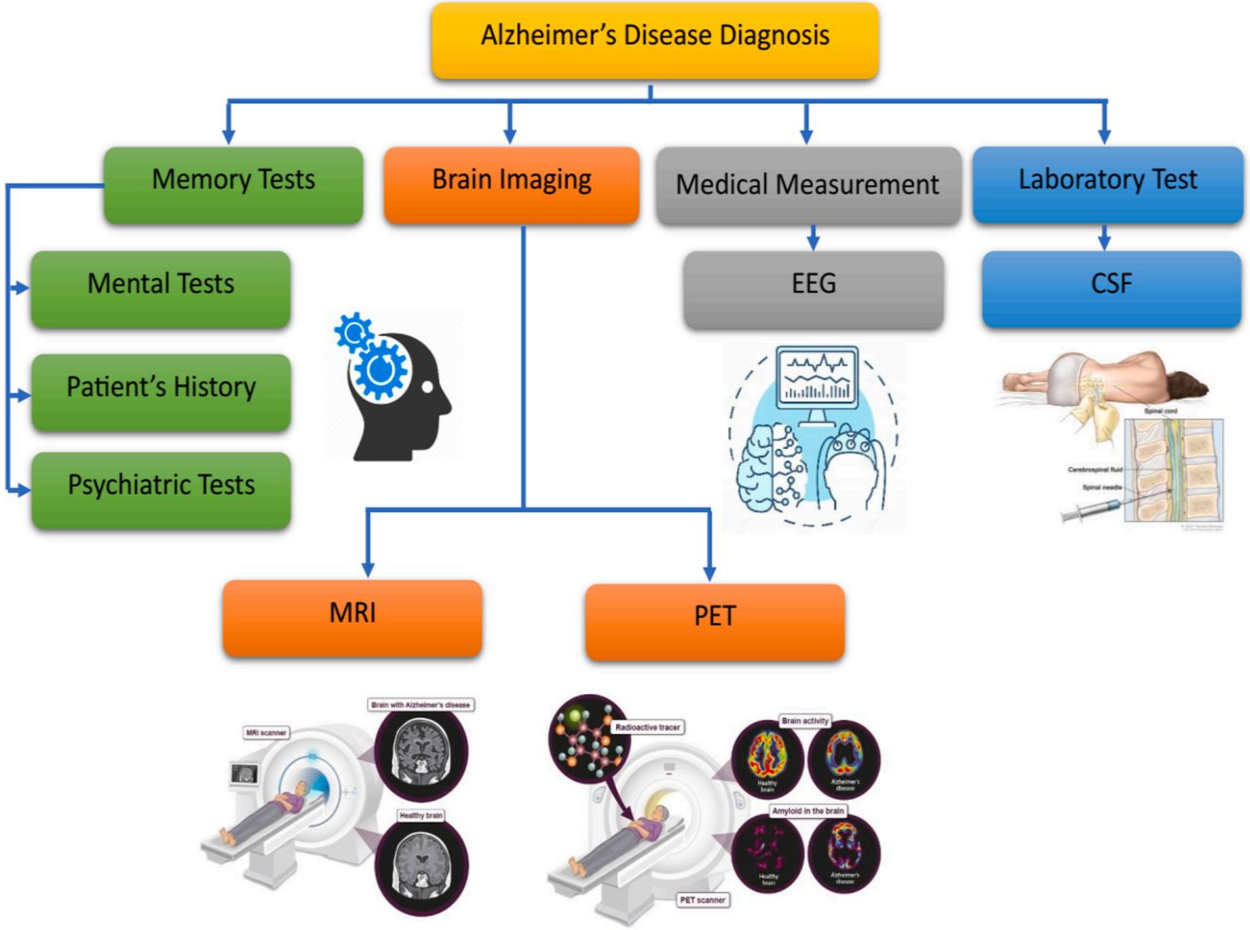
# Introduction

## Alzheimer

- 30% of people are misdiagnosed
- Mentioning the type of MCI
- aMCI affects the hippocampus and is detectable in MRI while it is not easy for naMCI.
- naMCI via an EEG-based biomarker can be more valuable

# Introduction

AD diagnosis methods



# Introduction

## AD diagnosis methods

Comparison of the medical techniques

| Technique | Invasive | Costly | Accessibility |
|---|---|---|---|
| MRI | No | Yes | Low |
| SPECT | Yes | Yes | Low |
| PET | Yes | Yes | Low |
| EEG | No | No | High |
| MEG | No | Yes | Low |

# Introduction

## AD diagnosis methods

- Medical imaging techniques
  - Voxels and features are extracted
- EEG is processed in the time and the frequency domains.
- MRI, CT, and PET, EEG recording methods provide good temporal resolution

# EEG

- Electroencephalography signals (EEG)
    - Detecting electrical activity in the brain

# EEG

EEG Disadvantages :

- Noisy raw data
- Low spatial resolution
- Artifacts
    - Power line, bad electrode contact and broken electrodes
    - Eye movements, muscle activity, and cardiac signals

# EEG

Stages:

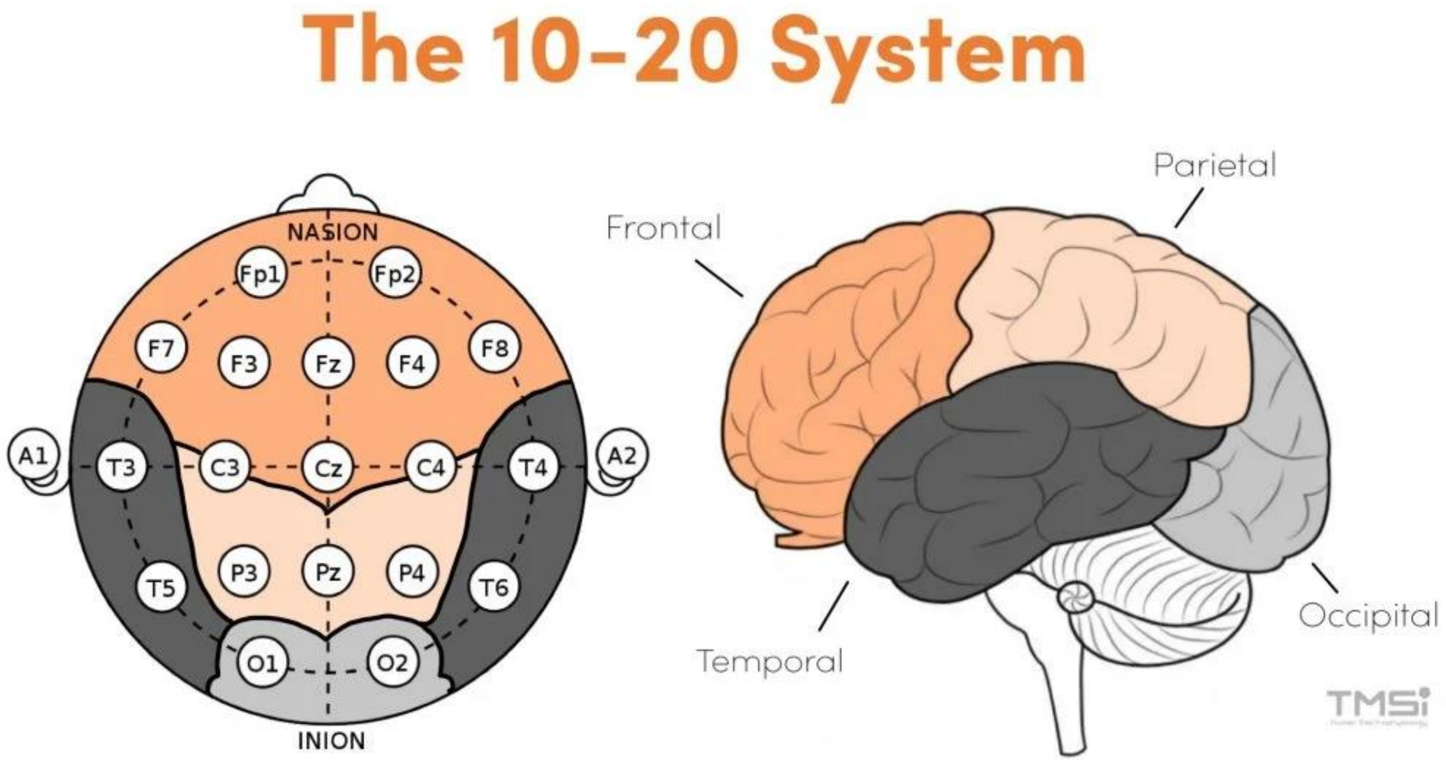
- Data acquisition
- Signal denoising
- Feature extraction
- Classification.

# EEG

- 200 Hz
- In a 10-min eye-closed resting state
- Participants were required to remain awake during the entire recording
- Capture neural events in milliseconds
- spatial resolution is limited by the number of electrodes

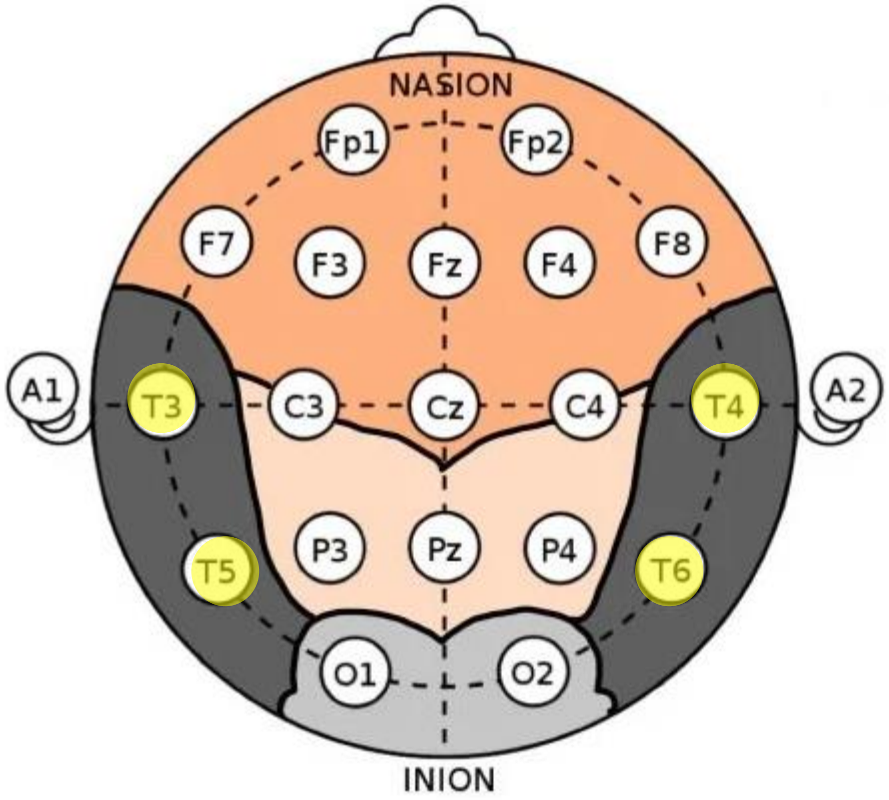
# EEG

## Recording



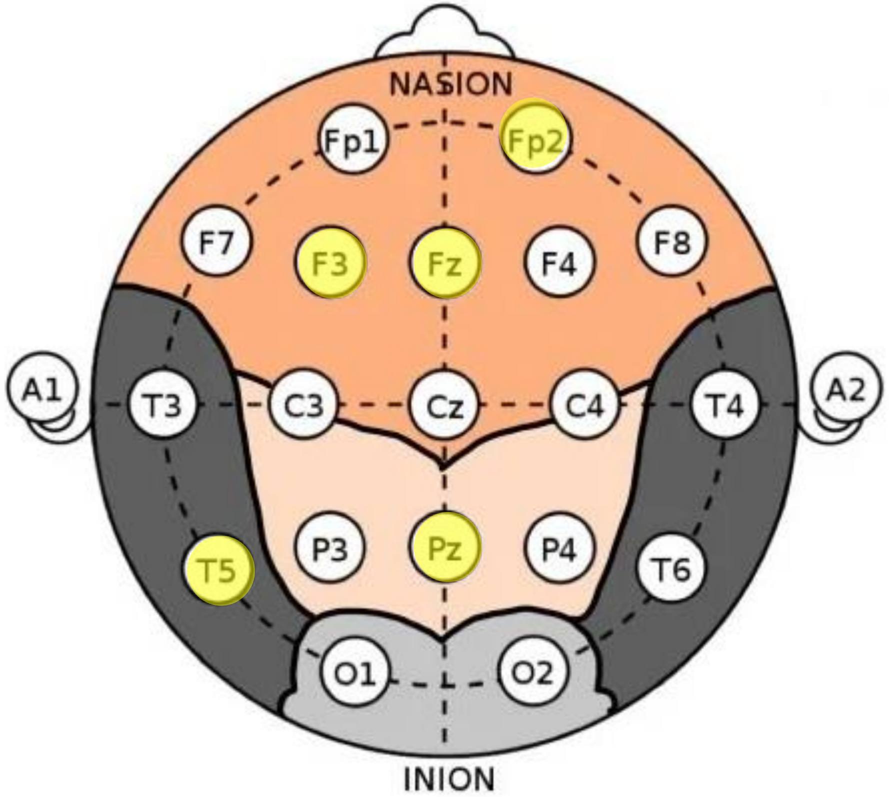
# EEG

## Recording



# EEG

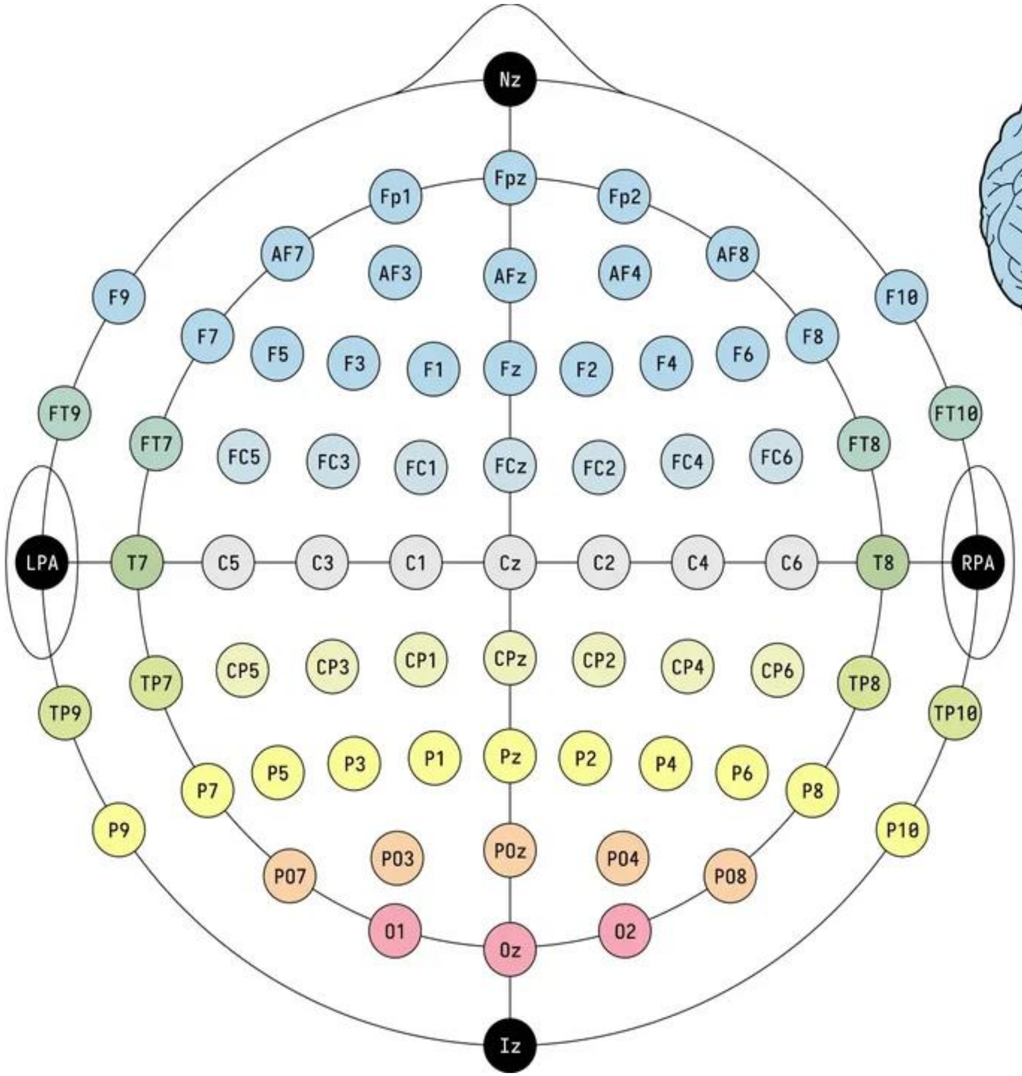
## Recording

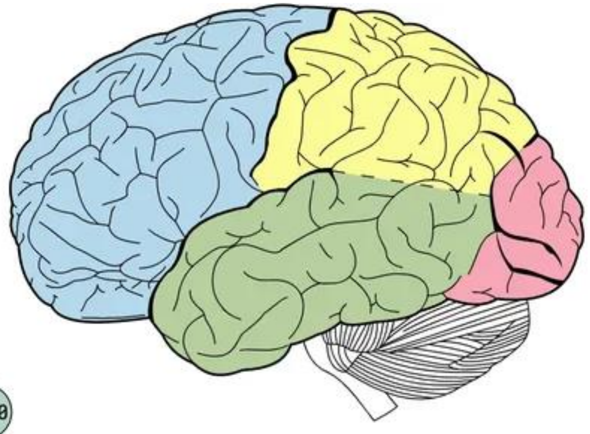


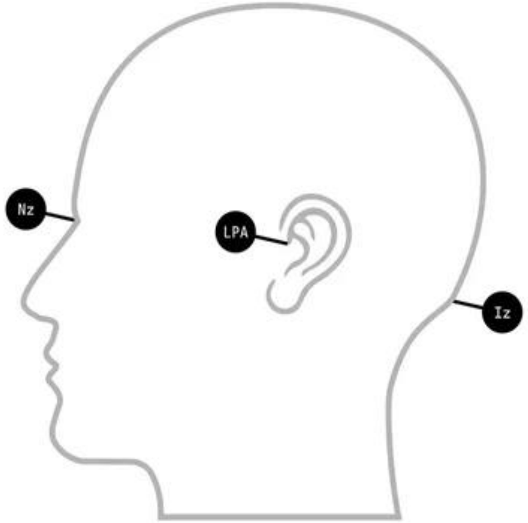
# EEG

## Recording

10-10 system

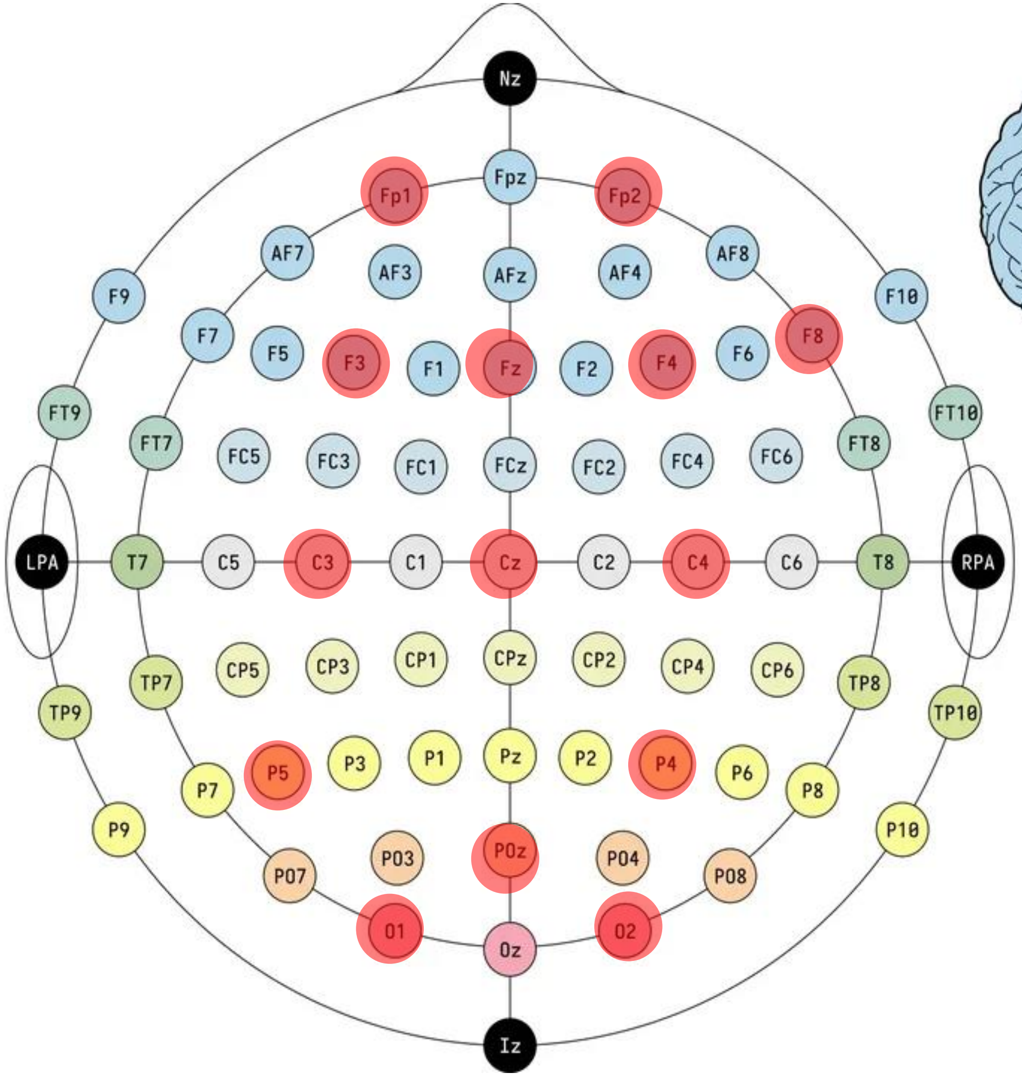


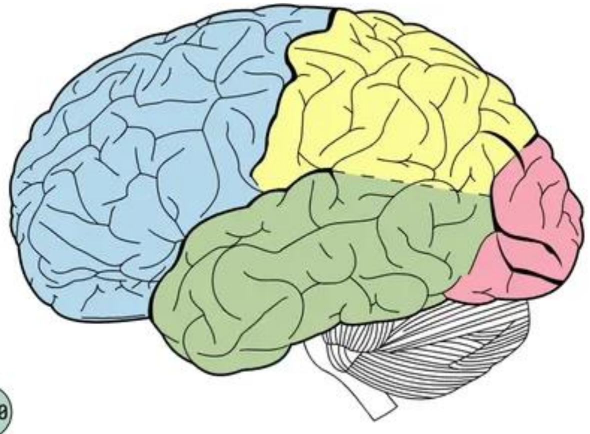



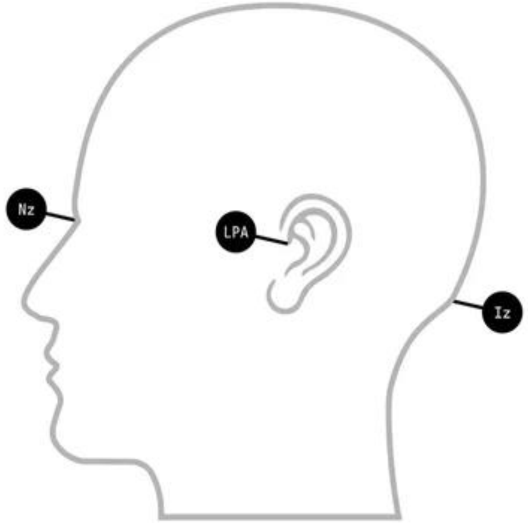


# EEG

## Recording



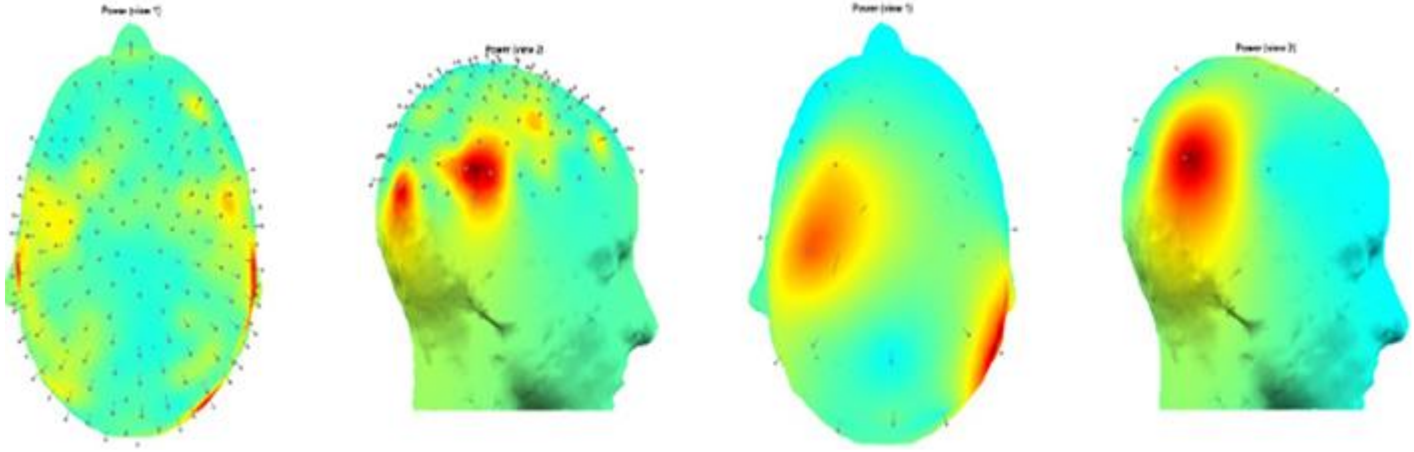





# EEG

## Recording

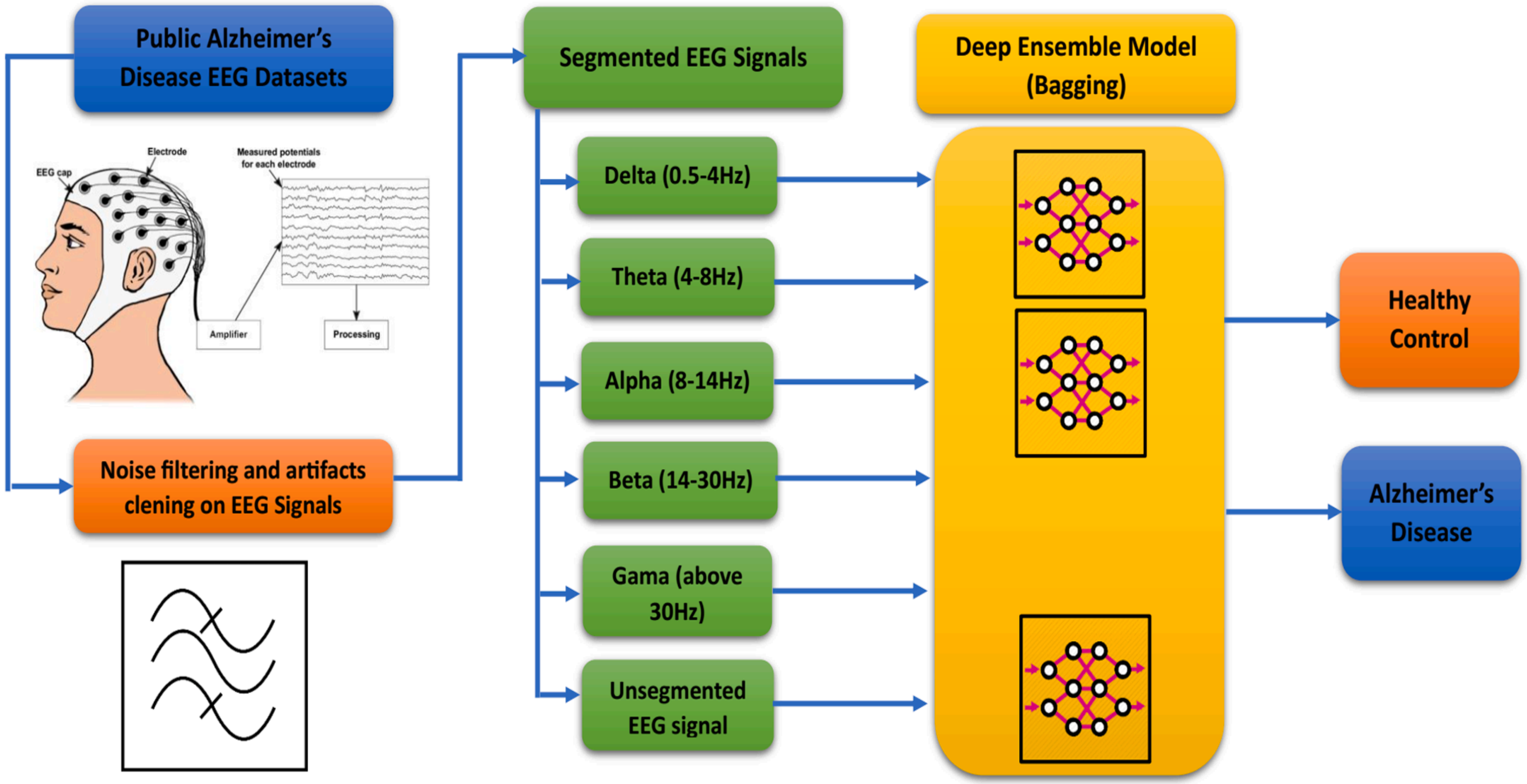
3D scalp topography of the power of the EEG recording is shown



# EEG

## Processing

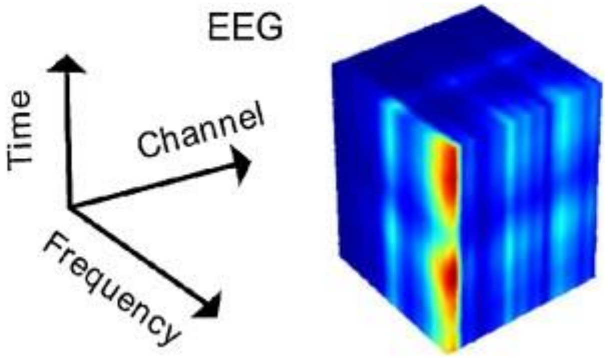
- AD diagnosis model



# EEG

## Preprocessing

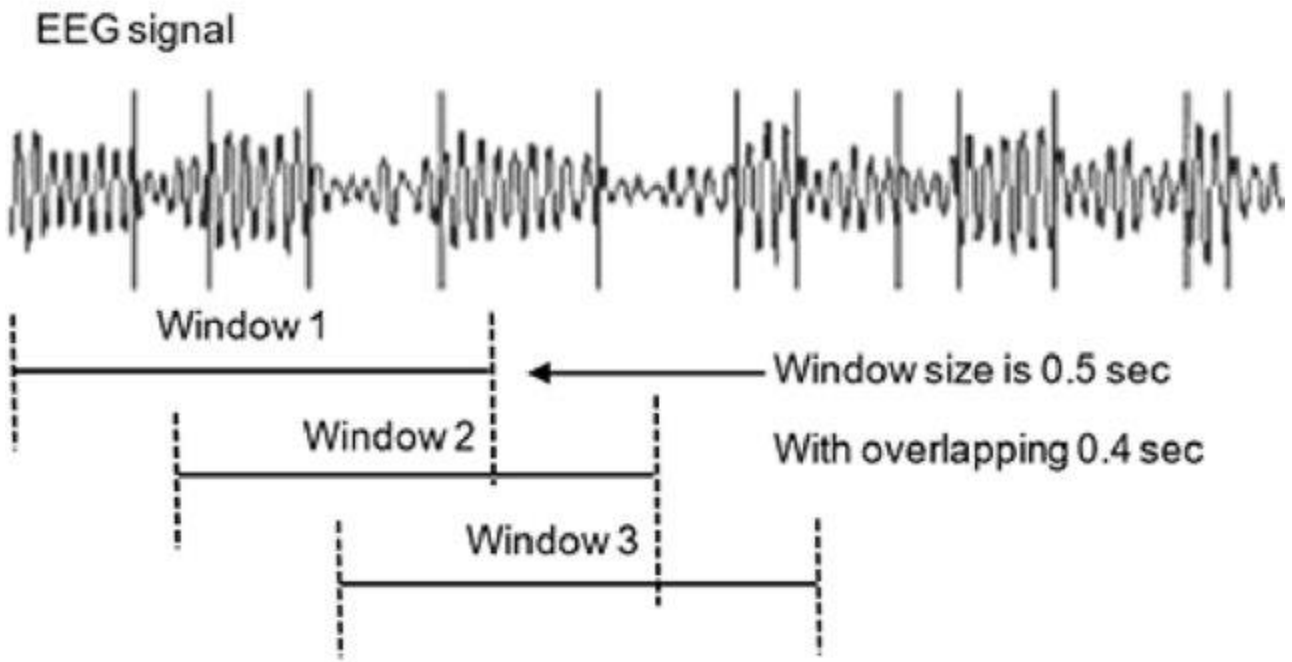
- Filtering and EEG rhythm calculation
- Artifact reduction algorithms
- Expert supervision
- Data reduction
- Source localization
- Data augmentation
- Normalization, and input generating for Deep Neural Network (DNN)



# EEG

## Preprocessing

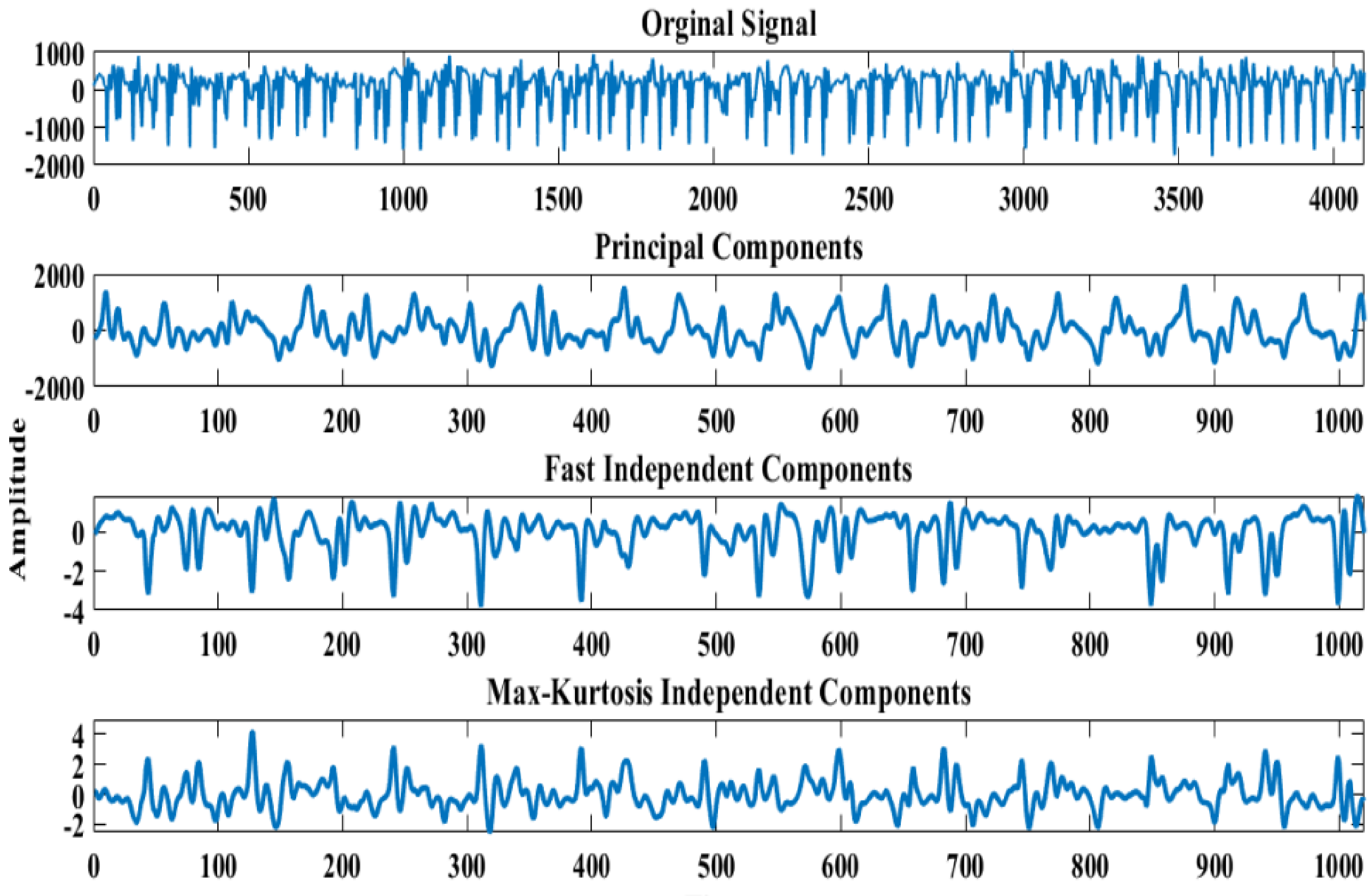
Determining of the window size



# EEG

## Preprocessing

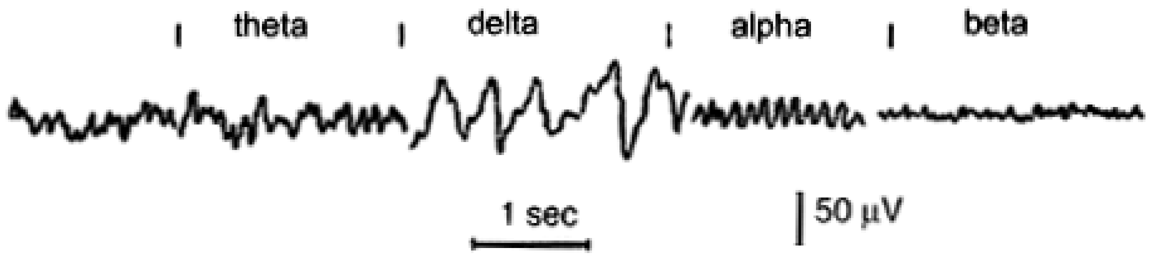
Dimension reduction



# EEG

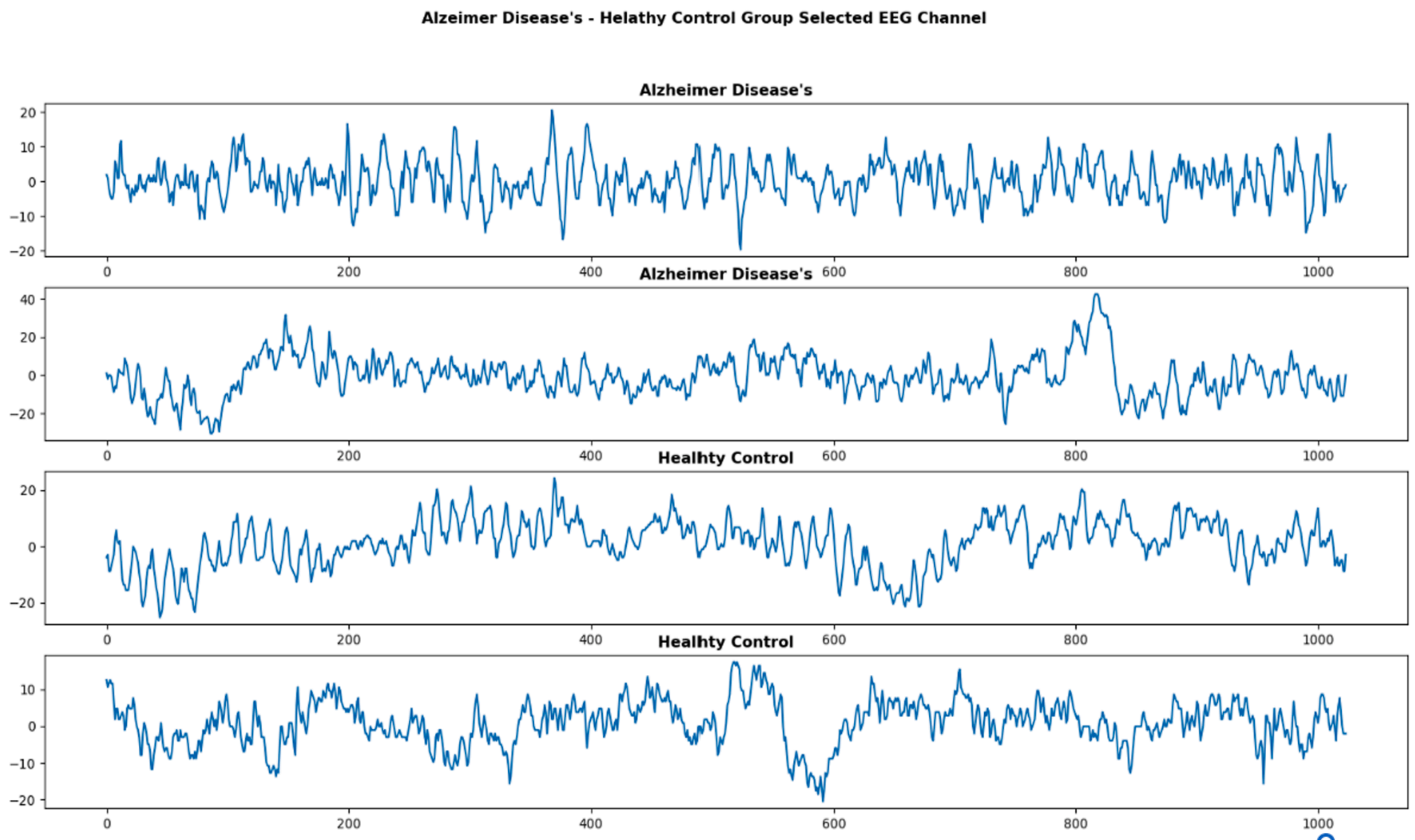
## Preprocessing

- Delta: has a frequency of 3 Hz or below
- Theta: has a frequency of 3.5 to 7.5 Hz
- Alpha: has a frequency between 7.5 and 13 H
- Beta: : has a frequency between 13 and 25 Hz



# EEG

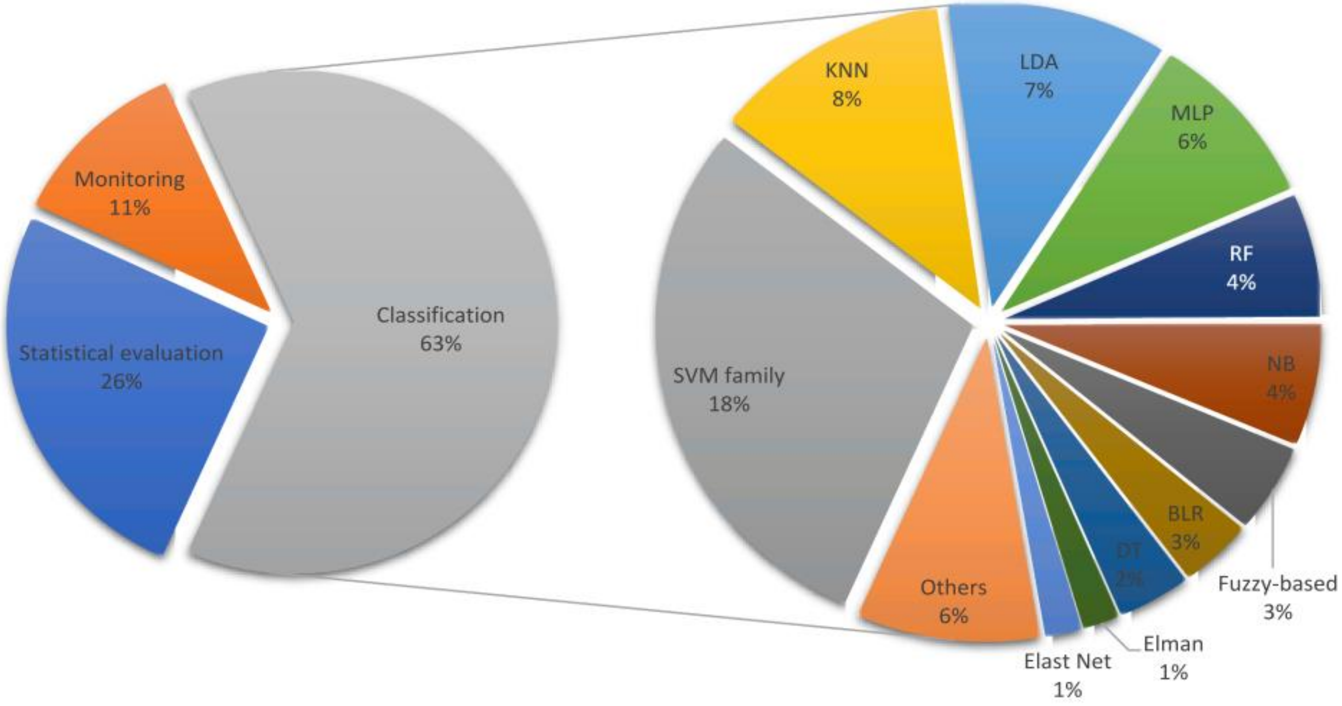
## Processing



# EEG

## Overview of Studies

Pie chart of the percentages of Decision-making approaches



# EEG

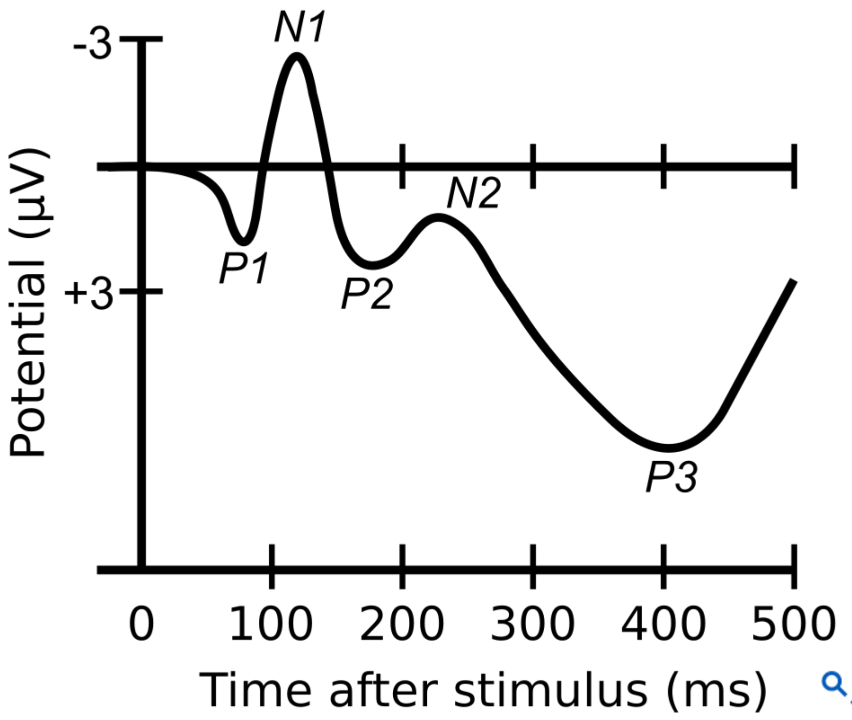
## Feature Extraction

- Transformed to the frequency domain using
  - Fourier methodology such as Fast Fourier Transform (FFT)
  - Welch Power Spectral Density (PSD) analysis
- Transformed to the time-frequency domain using decomposition such as
  - Discrete Wavelet Transform (DWT) **
  - Empirical Mode Decomposition (EMD)

# EEG

## Time domain features

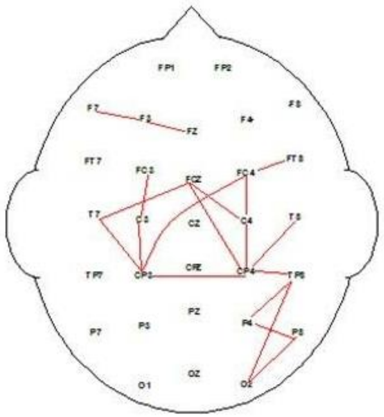
- Event-related potentials (ERP)
    - ERP are electric potentials elicited in the brain as a response to an auditory or visual stimulus.
- Complexity
    - Lower complexity and irregularity compared to HC

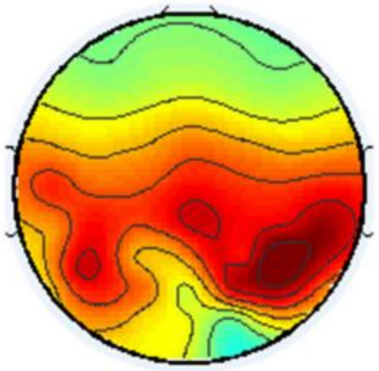


# EEG

## Frequency domain analysis

- Coherence
  - This metric evaluates the synchrony between two signals
  - Increase of coherence in delta and theta rhythms, and a decrease in alpha and beta rhythms in MCI and AD
- Relative power
  - This metric quantifies the proportion of power that is contained in an EEG sub band, compared to the total power of the signal.
  - Relative power in the fast rhythms (alpha and beta) decreases, while the relative power in the slow rhythms (delta and theta) increases.





# EEG

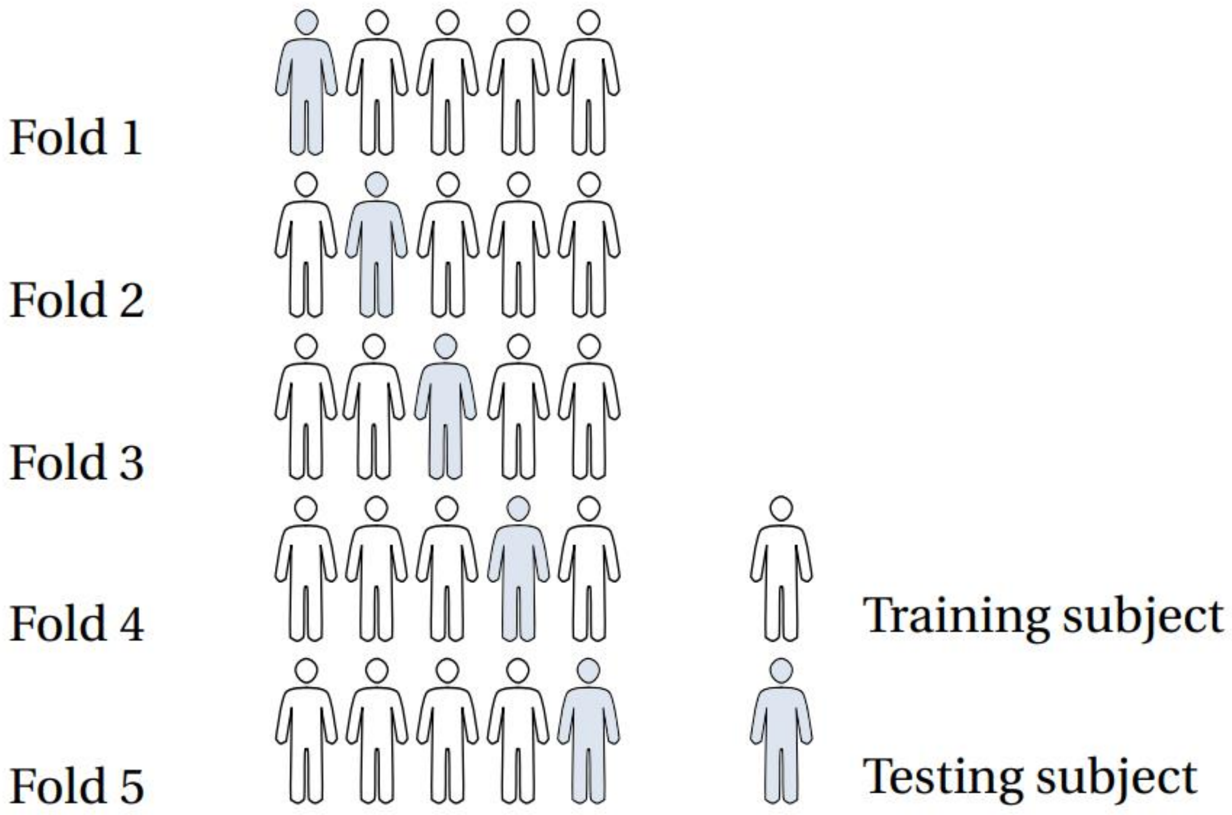
## Frequency domain analysis for AD detection

- Fourier transform
  - Wavelet transform
- Amplitude modulation
  - Combines temporal and frequency analysis

# Evaluation Methods

LOSO CV (Leave-One-Out Cross-Validation)

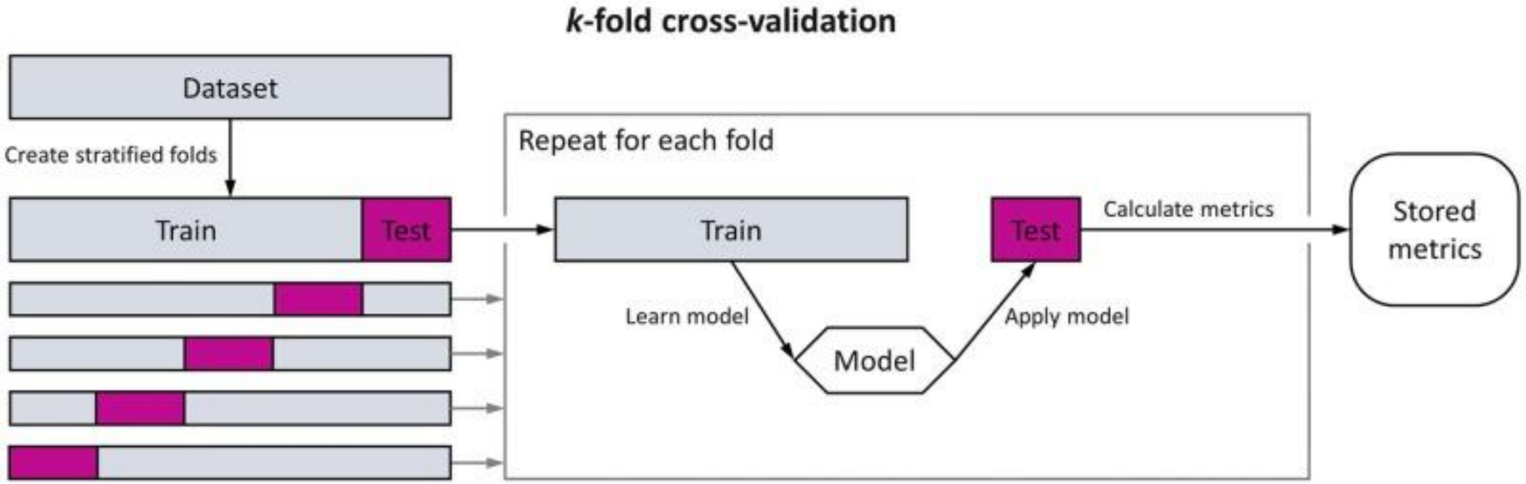
- Splitting a dataset into a training set and a testing set
- Using all but one observation as part of the training set



# Evaluation Methods

K-fold

- Dataset is randomly split into k equal-sized folds
- Each fold is then used as a test set once, while the remaining k-1 folds are used as the training set
- This process is repeated k times, with each fold serving as the test set exactly once.



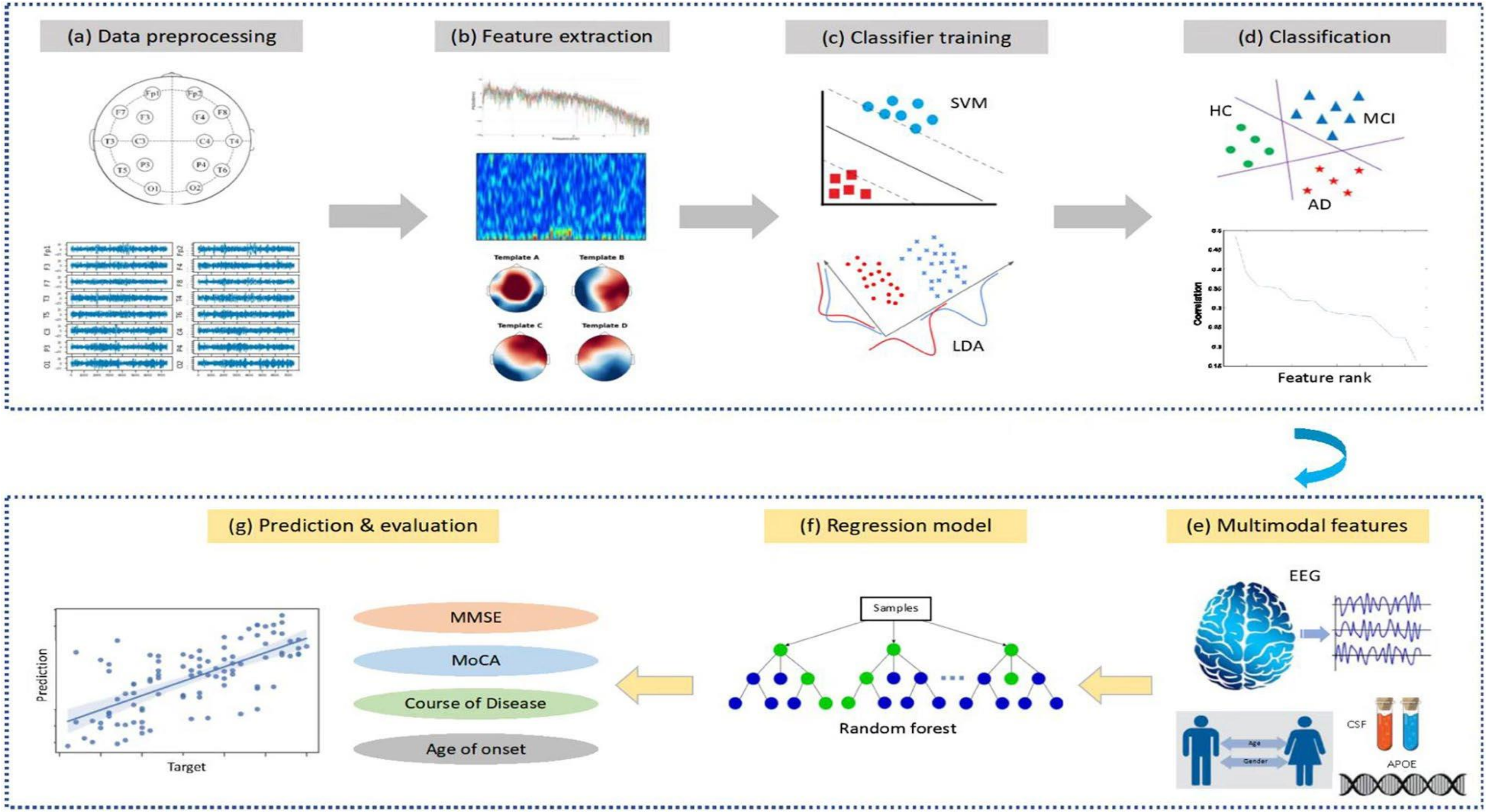
# Methods

- Deep learning techniques in AD assessment:
  - Convolutional neural network (CNN)
  - MC-DCNN (Multi-Channel Deep Convolutional Neural Network )
  - Stacked autoencoder (SAE)
  - Spatial Temporal Convolutional Networks (ST-CNN)

# Methods

## Overview

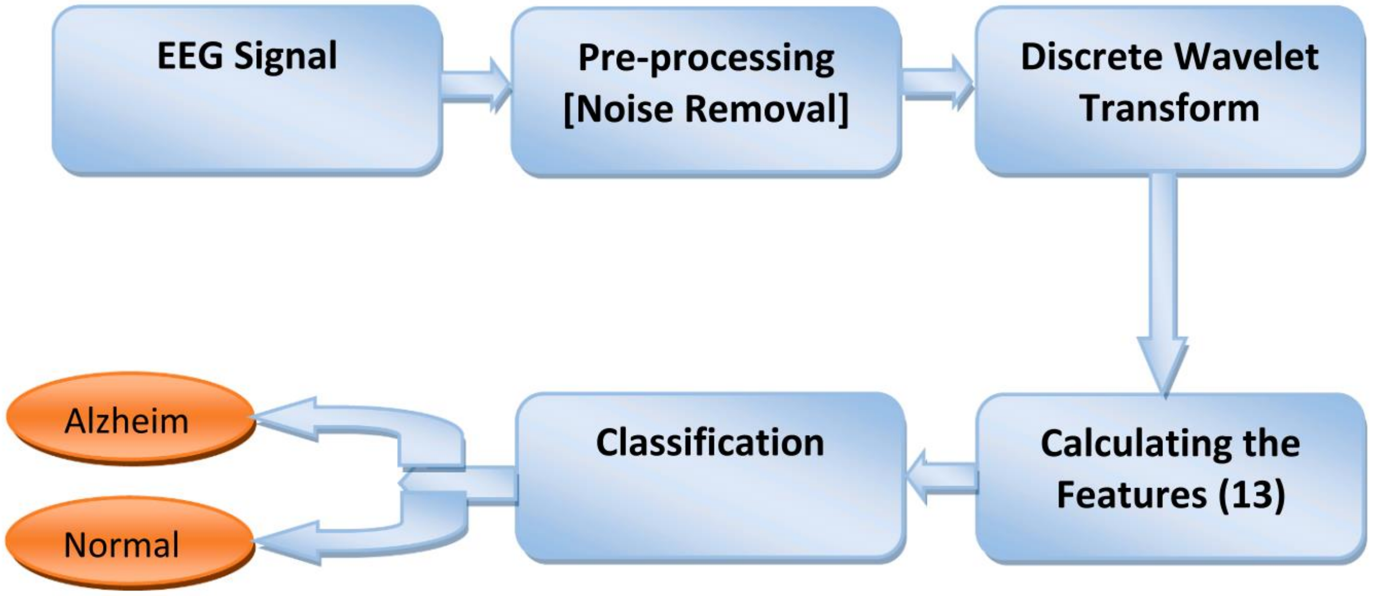
- 890 participants
  - 189 MCI
  - 330 AD
  - 125 other dementias
  - 246 Healthy




Jiao B, Li R, Zhou H, Qing K, Liu H, Pan H, et al. Neural biomarker diagnosis and prediction to mild cognitive impairment and Alzheimer's disease using EEG technology. Alzheimer's Research & Therapy. 2023;15(1):32.

# Methods

- Use three central lobe electrodes
- Dataset
  - 7 MCI
  - 59 AD
  - 102 NC
- Performance is 96.55%




Fouad IA, El-Zahraa M. Labib F. Identification of Alzheimer’s disease from central lobe EEG signals utilizing machine learning and residual neural network. Biomedical Signal Processing and Control. 2023;86.

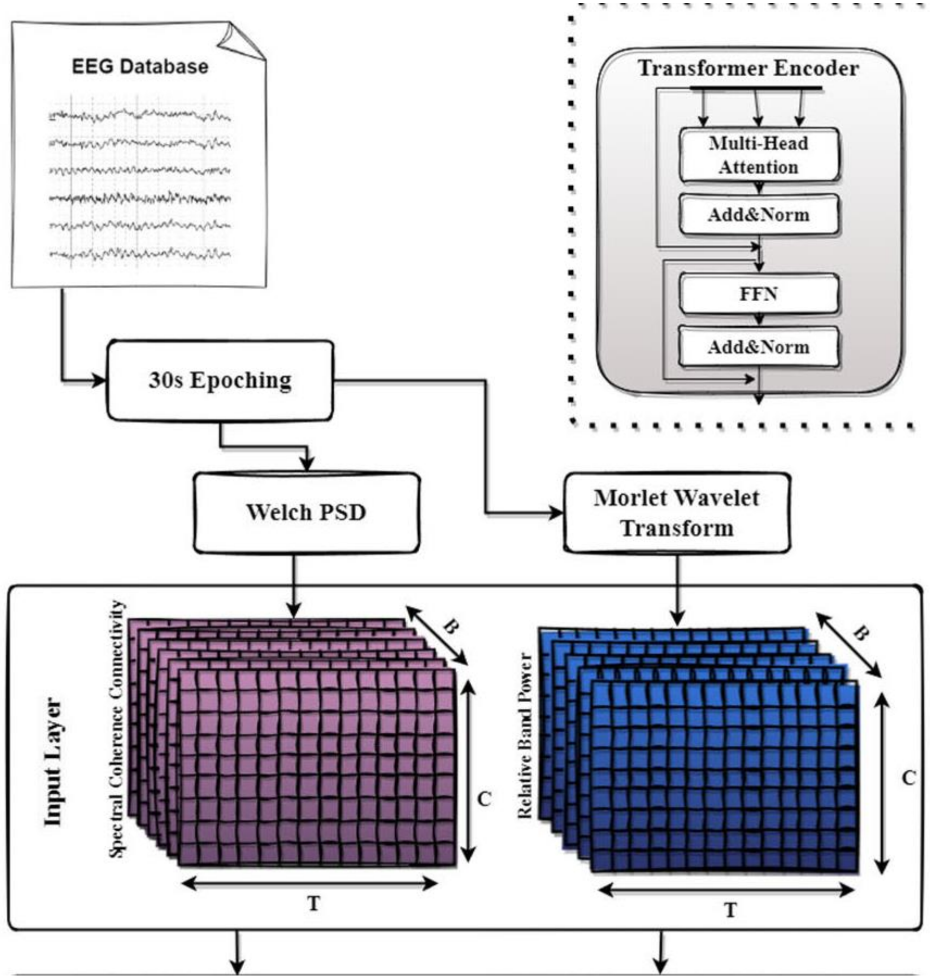
# Methods

- Using a Dual-Input Convolution Encoder Network
- Public dataset from Department of Neurology of AHEPA General University Hospital of Thessaloniki
    - 36 AD
    - 23 Frontotemporal dementia (FTD)
    - 29 CN

Miltiadous A, Gionanidis E, Tzimourta KD, Giannakeas N, Tzallas AT. DICE-Net: A Novel Convolution-Transformer Architecture for Alzheimer Detection in EEG Signals. IEEE Access. 2023;11:71840-58.

# Methods

- Extract two biomarkers
  - Relative Band Power (RBP): increase in Theta/Alpha ratio in AD patients
  - Spectral Coherence Connectivity (SCC): decreased synchronization likelihood in AD patients
- Express them in image-like representations (3d matrixes)

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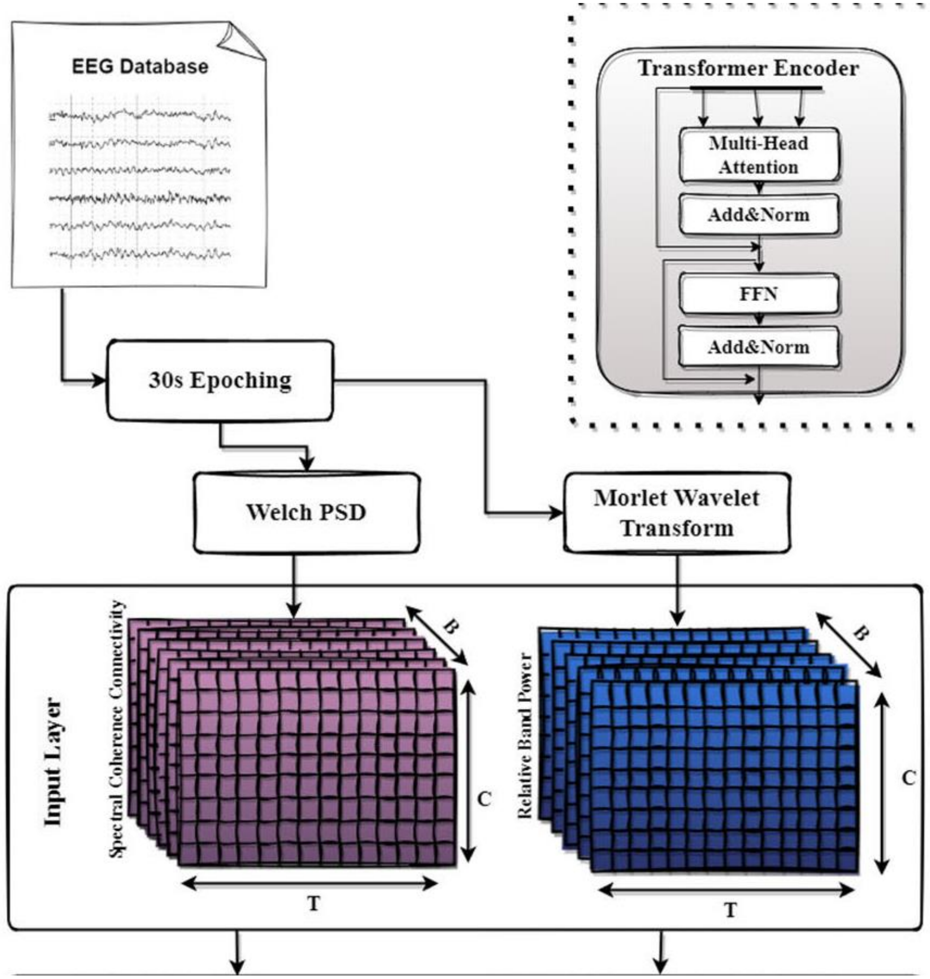
# Methods

- Preprocessing pipeline
  - Butterworth band-pass filter 0.5-45 Hz
  - Re-referenced to A1-A2
  - Automatic artifact reject method
    - ASR

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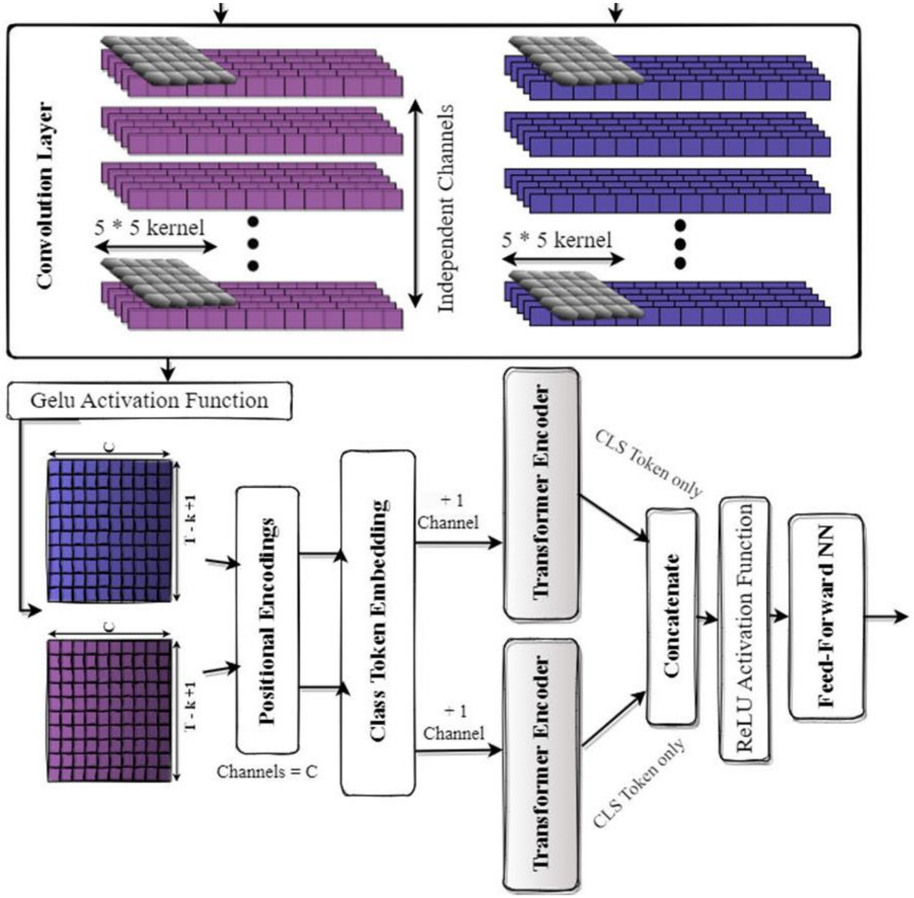
# Methods

- Fed in 2 parallel Convolution blocks
- Accuracy of 83.28% LOSO validation




Miltiadous A, Gionanidis E, Tzimourta KD, Giannakeas N, Tzallas AT. DICE-Net: A Novel Convolution-Transformer Architecture for Alzheimer Detection in EEG Signals. IEEE Access. 2023;11:71840-58.

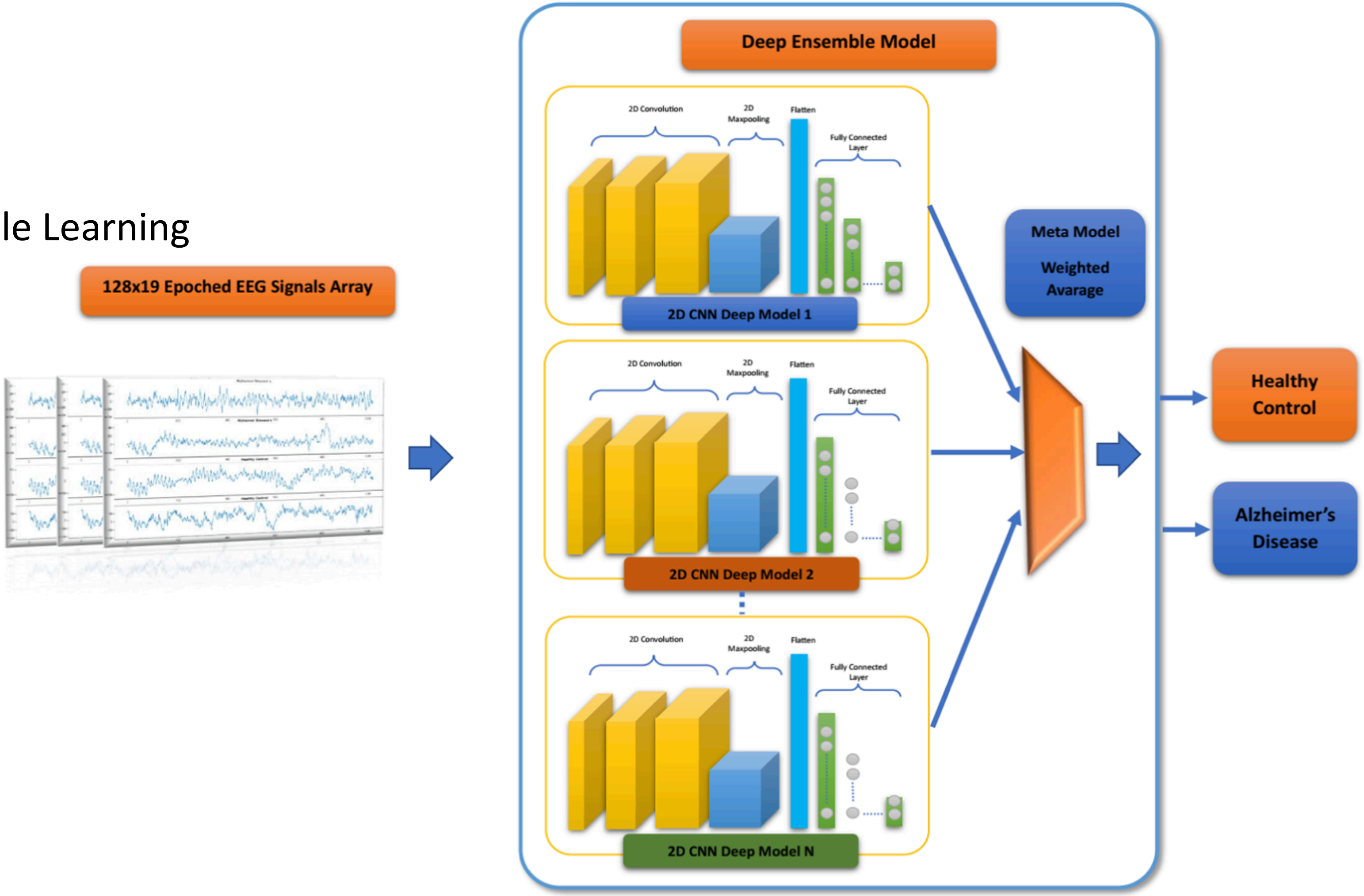
# Methods

- Two datasets were used
- Divides EEG signals into 5 frequency bands with a Butterworth band-pass filter
- Signals recorded as 8 s in the datasets were segmented into 1 s epochs
- An epoch was converted into a 2D array of 128x19. A total of 1120 epochs consist of two datasets combined
- Then, EEG signals for each frequency band (delta, theta, alpha, beta, and gamma) were segmented into 1 s epochs (128x19 2D array) and given as input to ensemble learning
- Accuracy of 97.9%

Nour M, Senturk U, Polat K. A novel hybrid model in the diagnosis and classification of Alzheimer's disease using EEG signals: Deep ensemble learning (DEL) approach. Biomedical Signal Processing and Control. 2024;89.

# Methods

- The proposed Deep Ensemble Learning




Nour M, Senturk U, Polat K. A novel hybrid model in the diagnosis and classification of Alzheimer's disease using EEG signals: Deep ensemble learning (DEL) approach. Biomedical Signal Processing and Control. 2024;89.

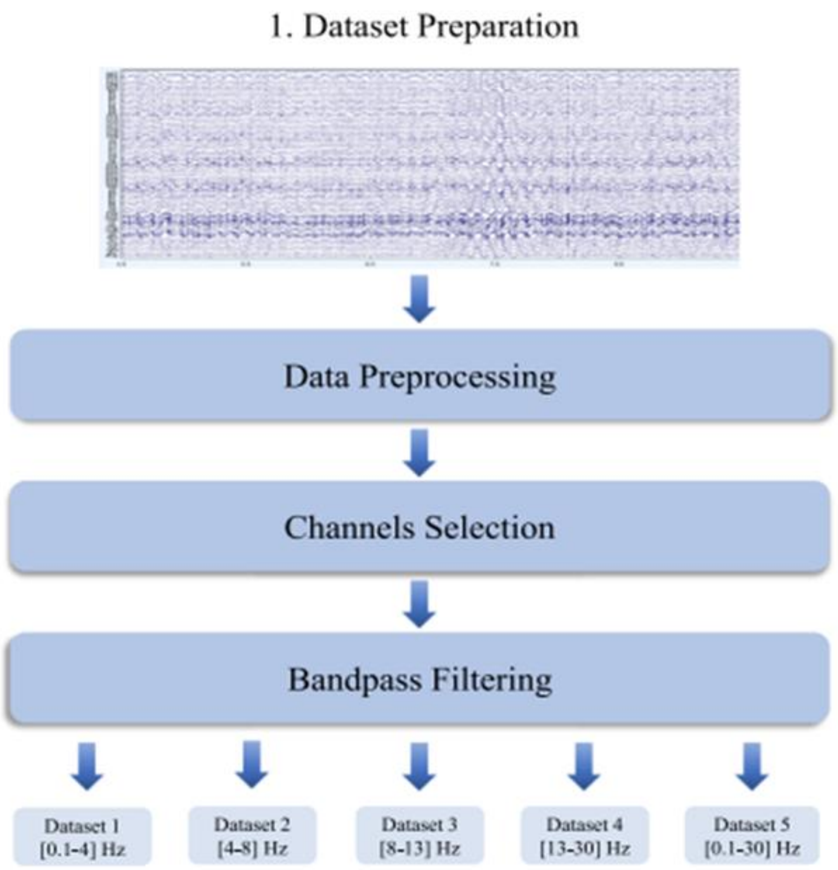
# Methods

- Transformers
  - Higher ability to deal with long-range dependencies
  - Recognize patterns in sequences of data
  - More interpretable decision-making processes
  - Recent efforts in exploring their applications on timeseries data, such as EEG or electromyography signals are showing interesting results

Sibilano E, Brunetti A, Buongiorno D, Lassi M, Grippo A, Bessi V, et al. An attention-based deep learning approach for the classification of subjective cognitive decline and mild cognitive impairment using resting-state EEG. Journal of Neural Engineering. 2023;20(1):016048.

# Methods

- Best performances
  - delta dataset
  - Performance of 0.807
- Performance with a minimum features is higher than 0.74
- Adding available 61 EEG channels, instead of a cluster of 19 channels, not only did not improve the performances of the model

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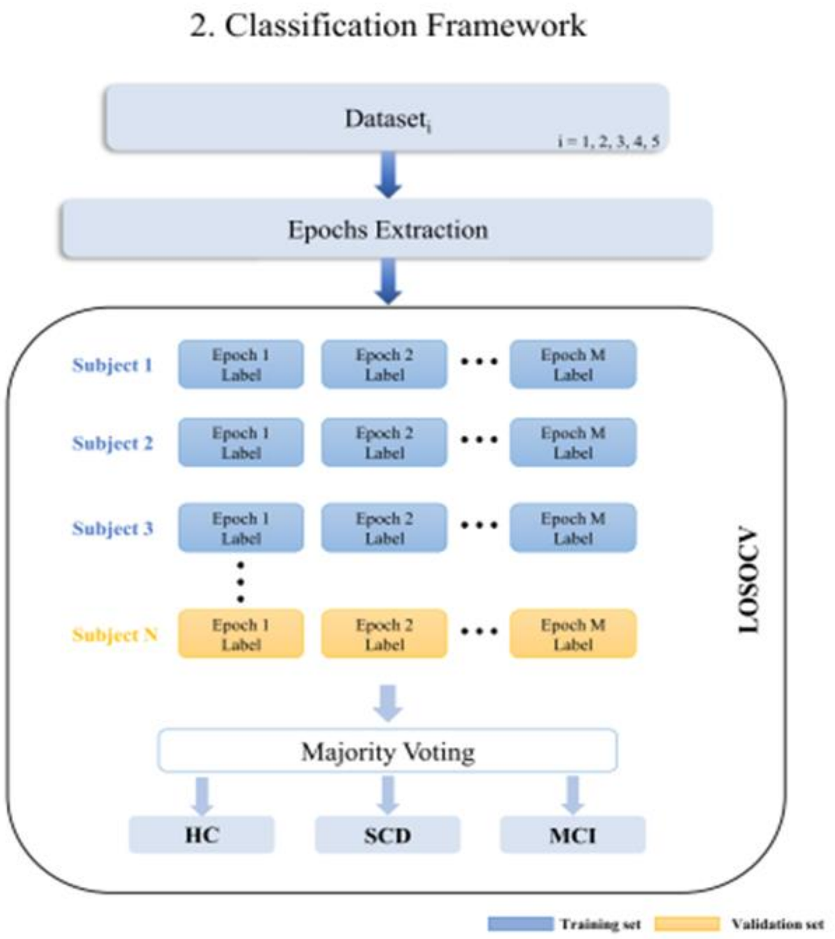
# Methods

Workflow of the proposed method

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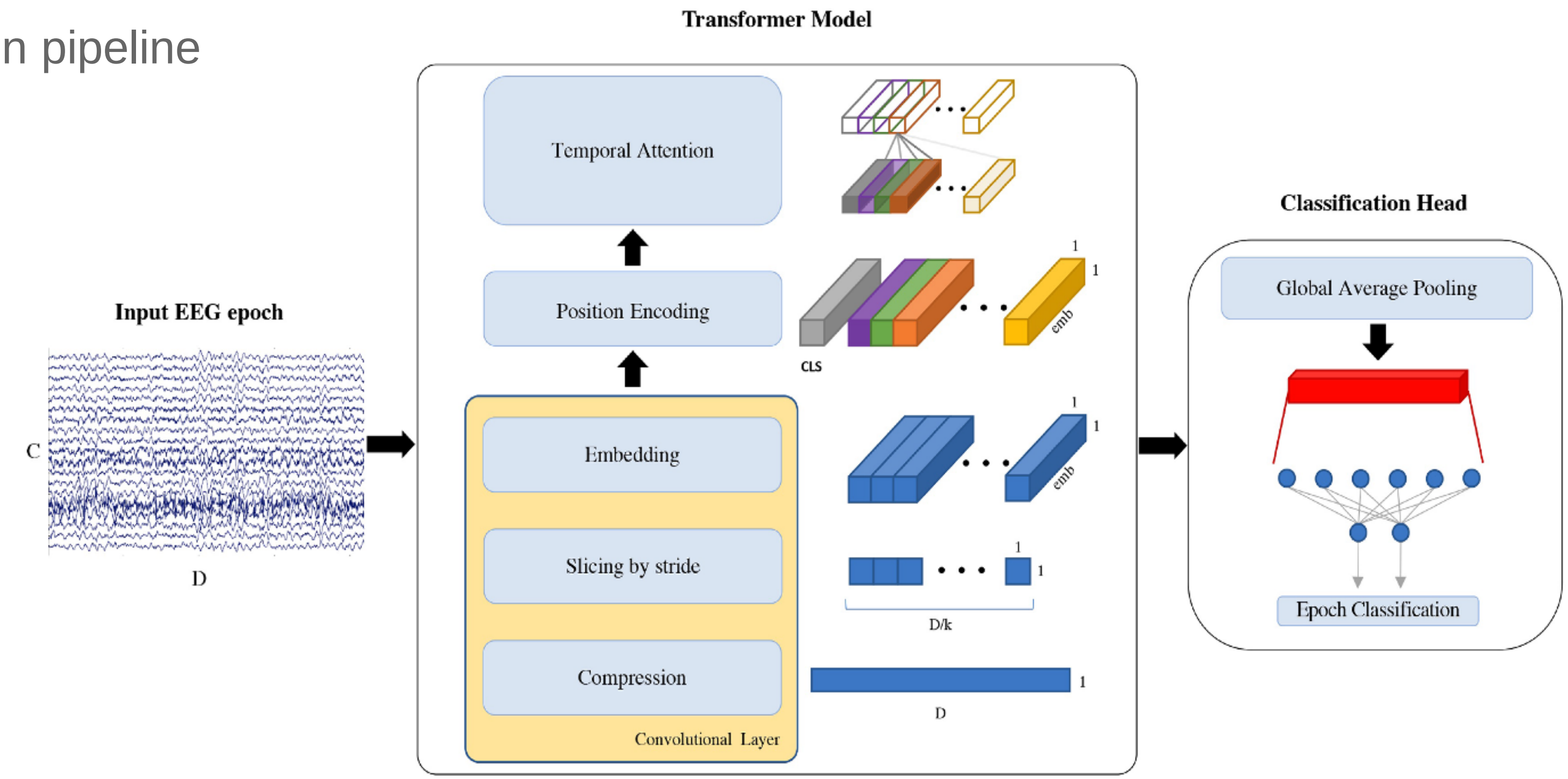
# Methods

EEG epoch classification pipeline

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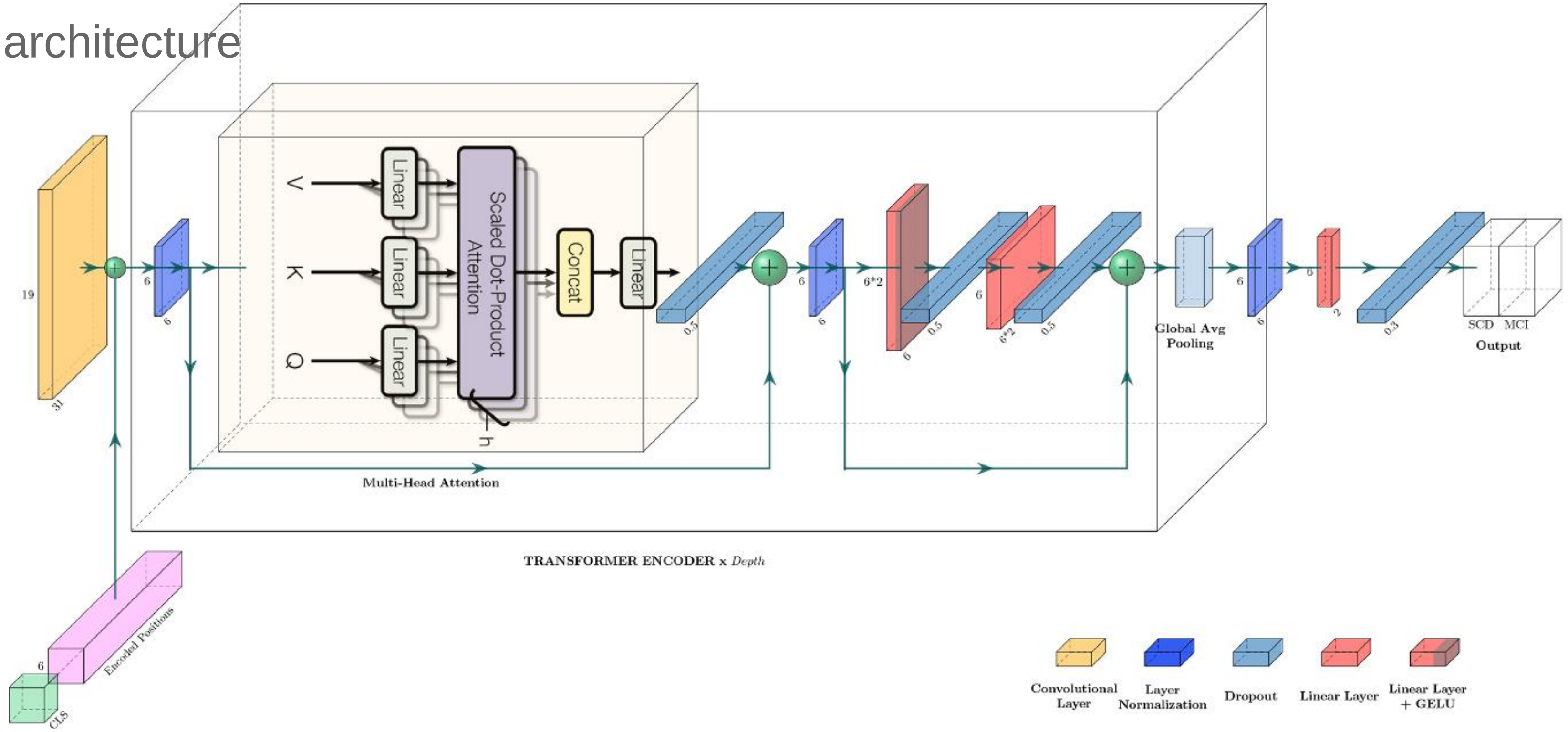
# Methods

Proposed transformer architecture



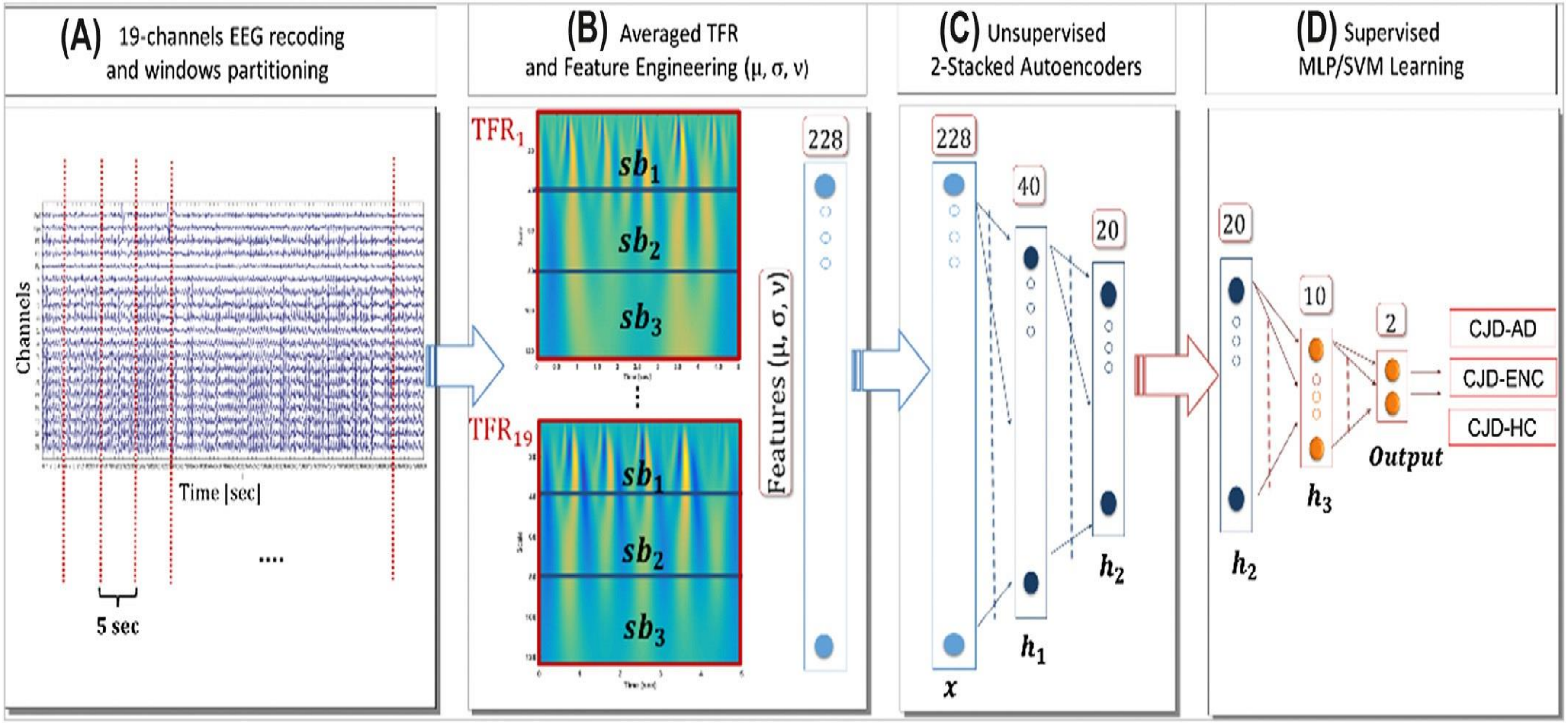

Sibilano E, Brunetti A, Buongiorno D, Lassi M, Grippo A, Bessi V, et al. An attention-based deep learning approach for the classification of subjective cognitive decline and mild cognitive impairment using resting-state EEG. Journal of Neural Engineering. 2023;20(1):016048.

# Methods

- The 19-channel EEG recording is partitioned into N nonoverlapping 5s windows
- For each EEG epoch, and for every EEG channel a time-frequency representation (TFR) is computed. The TFRs are averaged over epochs resulting in 19 averaged TFRs (one per channel). Each averaged TFR is subdivided into three sub bands, and then, the mean (μ), the standard deviation (σ), and the skewness (v) are estimated both for the sub bands and for the whole TFR.
- The first autoencoder compresses the input representation in 40 parameters . The second autoencoder compresses the 40 learned features in 20 higher-level paraments
- A classifier with a single hidden layer of 10 neurons is trained

Morabito, F. C., et al. (2017). "Deep Learning Representation from Electroencephalography of Early-Stage Creutzfeldt-Jakob Disease and Features for Differentiation from Rapidly Progressive Dementia." Int J Neural Syst 27(2): 1650039.

# Methods




Morabito, F. C., et al. (2017). "Deep Learning Representation from Electroencephalography of Early-Stage Creutzfeldt-Jakob Disease and Features for Differentiation from Rapidly Progressive Dementia." Int J Neural Syst 27(2): 1650039.

# Methods

- The study analyzed a total of eight EEG features obtained from 21 channels.
- Used two public datasets that are both available

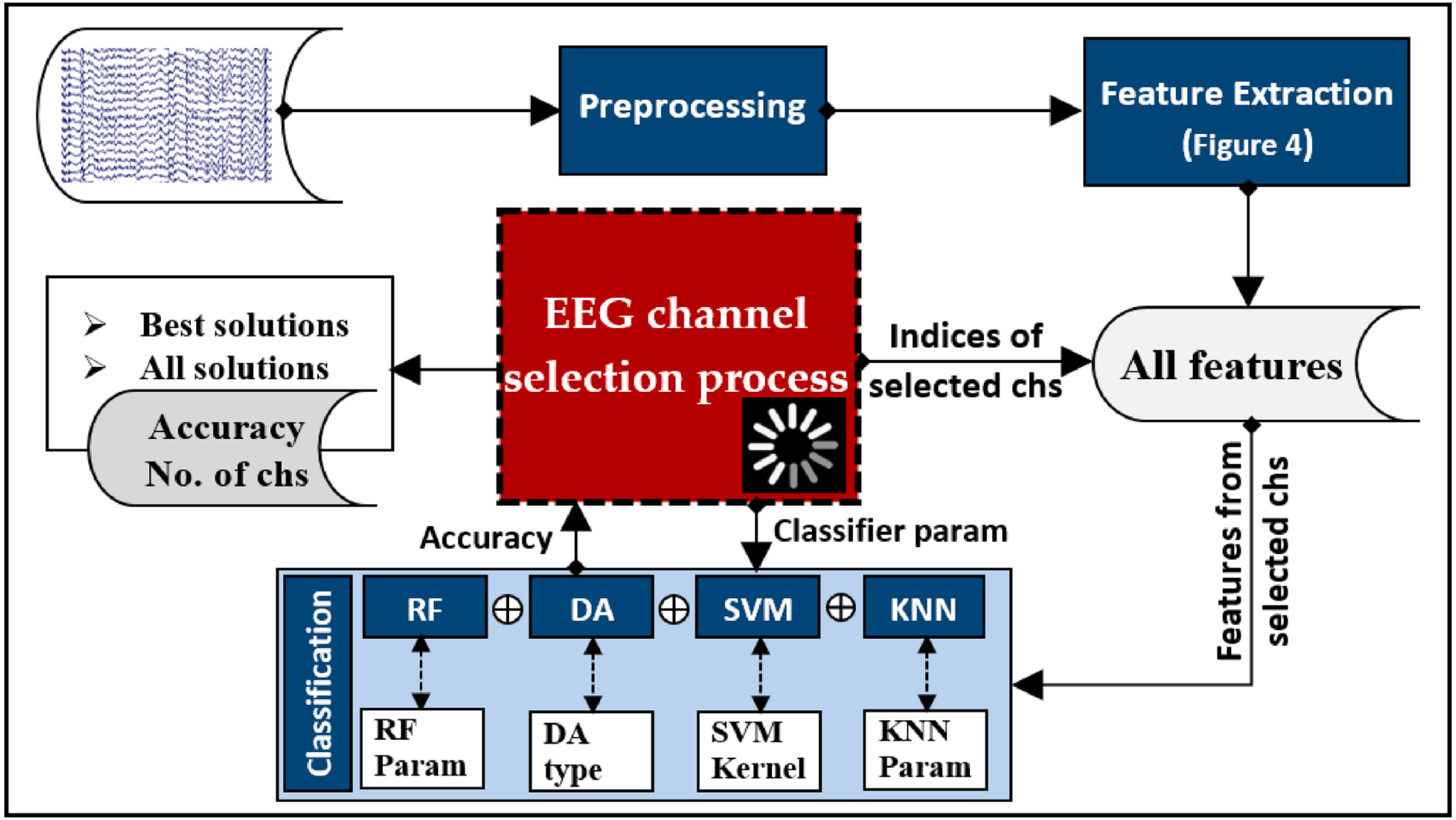
Subject’s demographics.

| Characteristic | HC (mean ± st) | MCI (mean ± st) |
|---|---|---|
| No. of cases | 32 | 29 |
| Ages (years) | 63.8 ± 4.3 | 65.7 ± 4.9 |
| Education (years) | 8.7 ± 2.3 | 8.3 ± 1.8 |
| MMSE scores | 28.8 ± 0.9 | 26.9 ± 0.7 |
| NUCOG scores | 92.5 ± 3.1 | 81.5 ± 2.4 |

Aljalal, M., et al. (2024). "Mild cognitive impairment detection with optimally selected EEG channels based on variational mode decomposition and supervised machine learning." Biomedical Signal Processing and Control 87.

# Methods

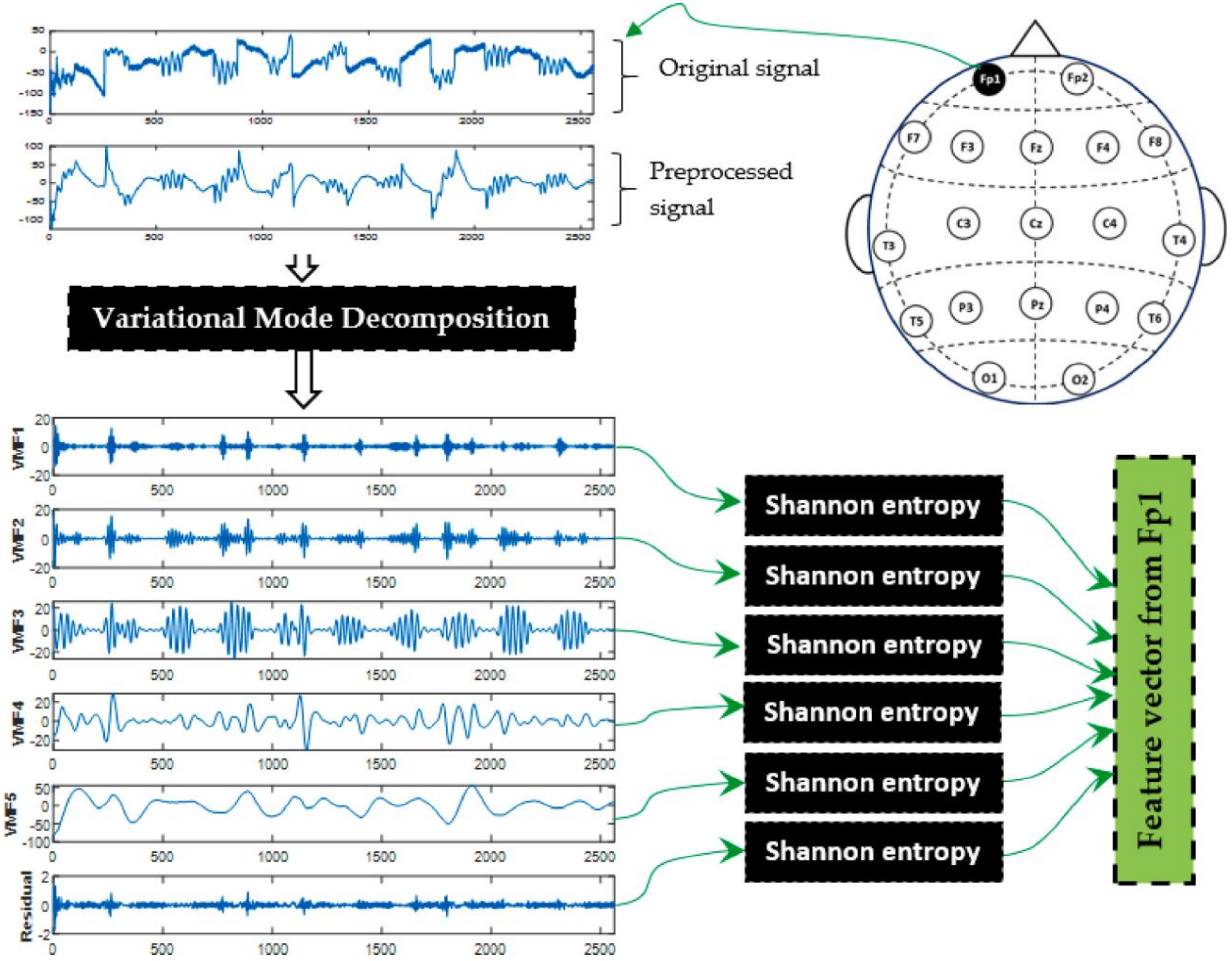
## Overview




Aljalal, M., et al. (2024). "Mild cognitive impairment detection with optimally selected EEG channels based on variational mode decomposition and supervised machine learning." Biomedical Signal Processing and Control 87.

# Methods

- Example of feature extraction from a 10 sec segment using VMD and Shannon entropy.

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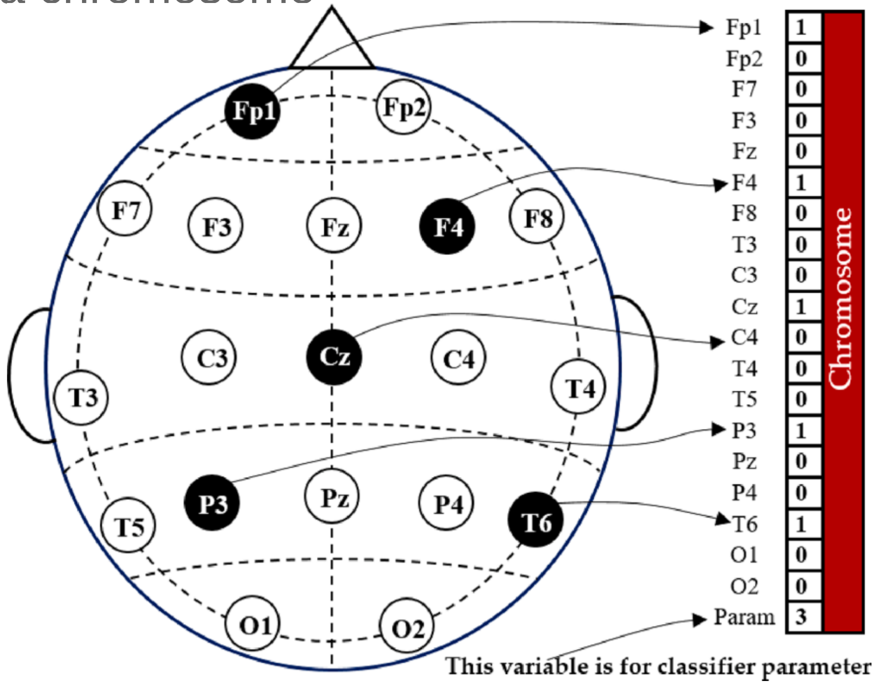
# Methods

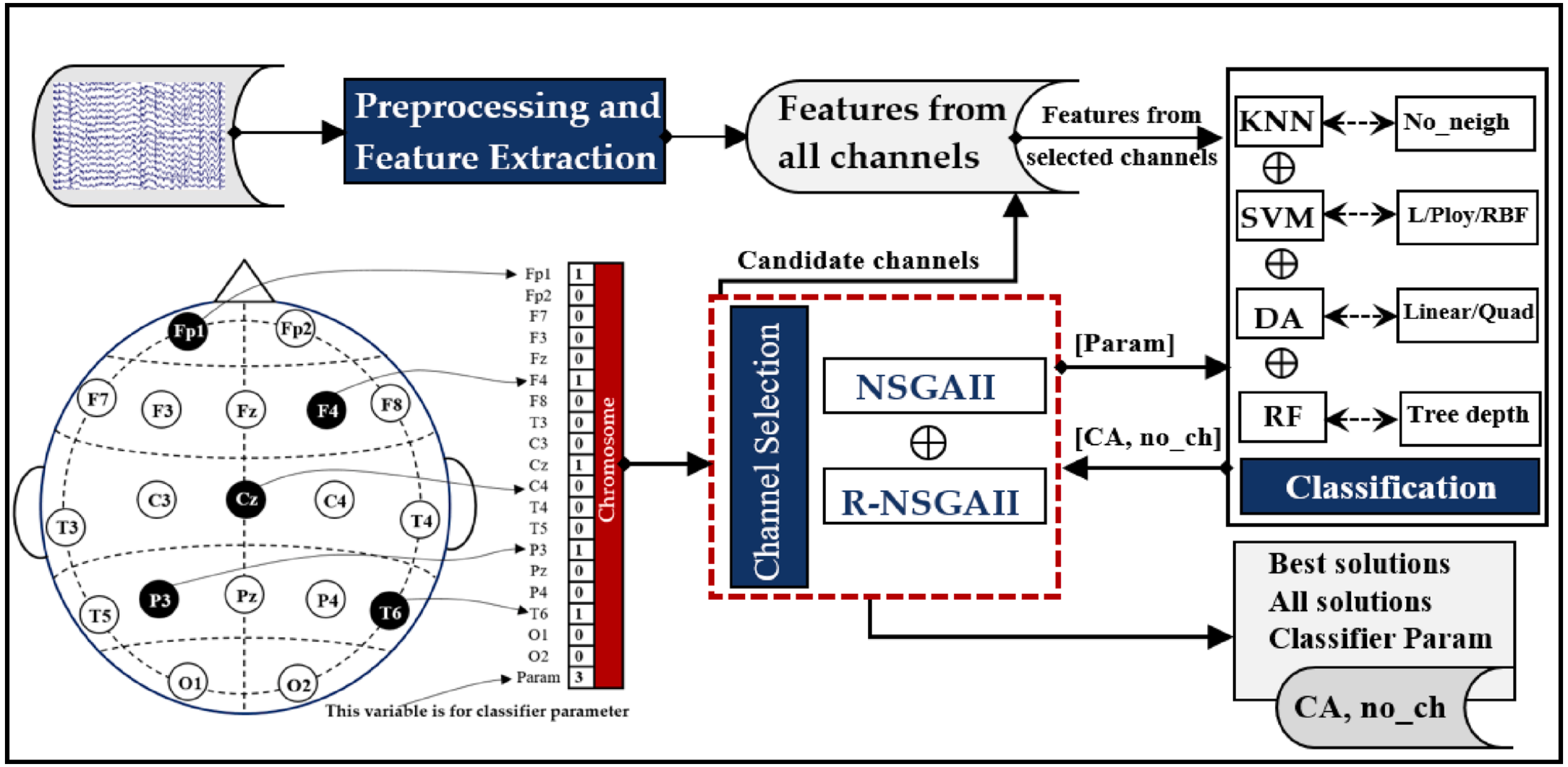
Example of channel representation in a chromosome




Aljalal, M., et al. (2024). "Mild cognitive impairment detection with optimally selected EEG channels based on variational mode decomposition and supervised machine learning." Biomedical Signal Processing and Control 87.

# Methods

- EEG channel selection using NSGA for MCI classification
- Accuracy using all 19 EEG channels is 99.51%




Aljalal, M., et al. (2024). "Mild cognitive impairment detection with optimally selected EEG channels based on variational mode decomposition and supervised machine learning." Biomedical Signal Processing and Control 87.

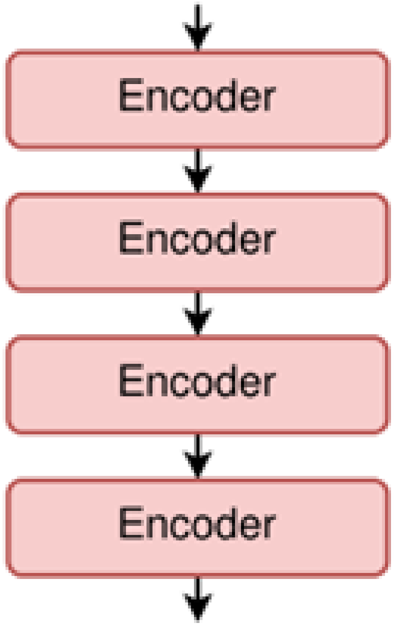
# Methods

- EEG with a window size of 0.25 s
- Independent component analysis (ICA) is applied
- Bad channels are manually removed
- Accuracies of 94.68% were achieved
- This proves the effectiveness of the transformers for processing raw EEG data
    - Can reduce the need for feature extraction in EEG .

Siddhad, G., et al. (2024). "Efficacy of transformer networks for classification of EEG data." Biomedical Signal Processing and Control 87: 105488.

# Methods

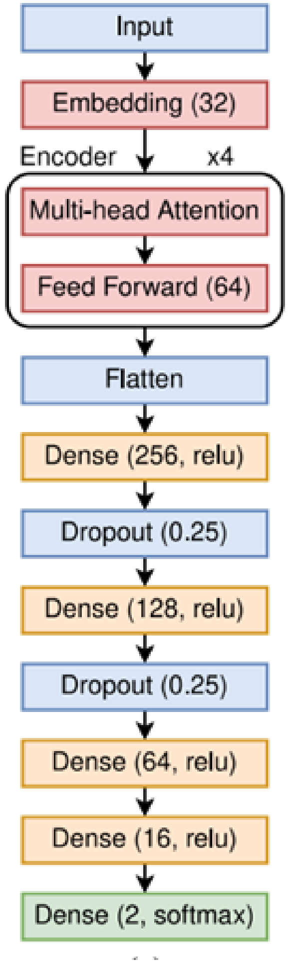
Stack of 4 encoders are used in the proposed method




Siddhad, G., et al. (2024). "Efficacy of transformer networks for classification of EEG data." Biomedical Signal Processing and Control 87: 105488.

# Methods

Proposed architecture for Age and Gender dataset

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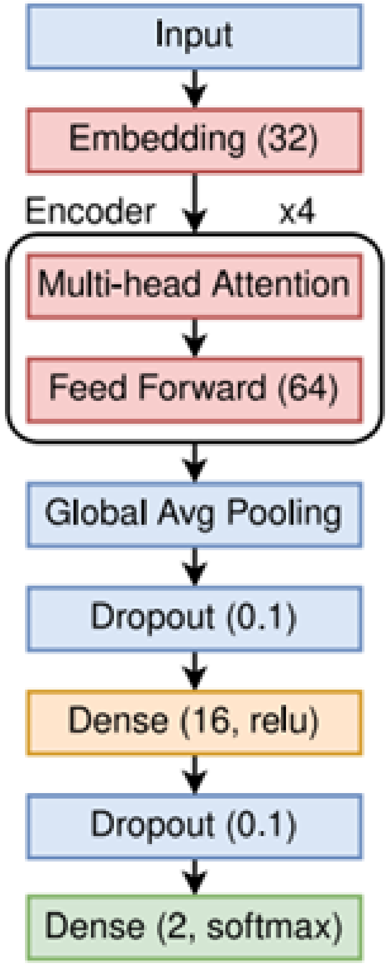
# Methods

Proposed architecture for STEW dataset




Siddhad, G., et al. (2024). "Efficacy of transformer networks for classification of EEG data." Biomedical Signal Processing and Control 87: 105488.

# Methods

Multimodal neuroimaging system and their aim in AD assessment

| Aim | Multimodal set |
| --- | --- |
| prediction of AD severity level | EEG + sMRI |
| Detection of AD from aMCI | EEG + sMRI |
| Detection of AD | EEG + sMRI |
| Detection of aMCI | EEG + fMRI |
| Mild AD detection | EEG + fNIRs |
| Detection of AD | EEG + fNIRs |
| Prediction of β-amyloid occurrence and neurodegenerative disease | EEG + sMRI + fMRI + PET |

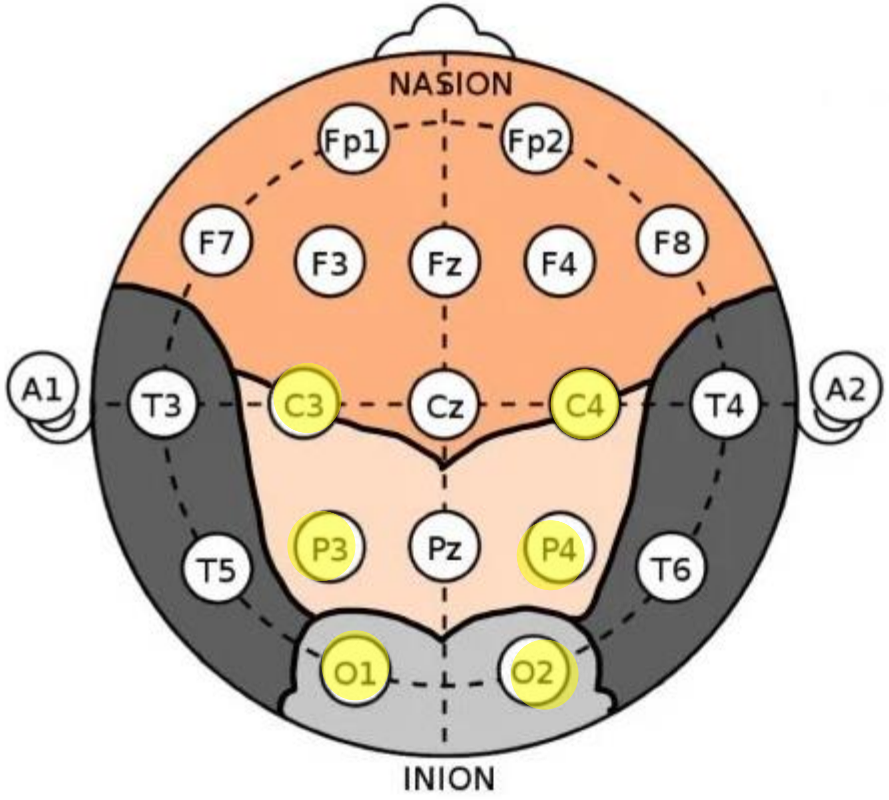
Modir, A., et al. (2023). "A systematic review and methodological analysis of EEG-based biomarkers of Alzheimer's disease." Measurement 220.

# Methods

- Monitoring of AD progression in **large** populations with **few** electrodes in **low-cost** devices
- Data acquired in hospital settings (10-20 montage) from 75 ADMCI participants and 70 age-, education-, and sex-matched normal elderly controls (Nold) were available in an Italian-Turkish archive (**www.pdwaves.eu**).
- Standard spectral fast fourier transform (FFT) analysis of rsEEG data for individual delta, theta, and alpha frequency bands was computed from 6 monopolar scalp electrodes to derive bipolar C3-P3, C4-P4,O1 and O2 markers

Tucci, F., et al. (2023). "What a single electroencephalographic (EEG) channel can tell us about Alzheimer's disease patients with mild cognitive impairment." Alzheimer's & Dementia 19(S2): e062375.

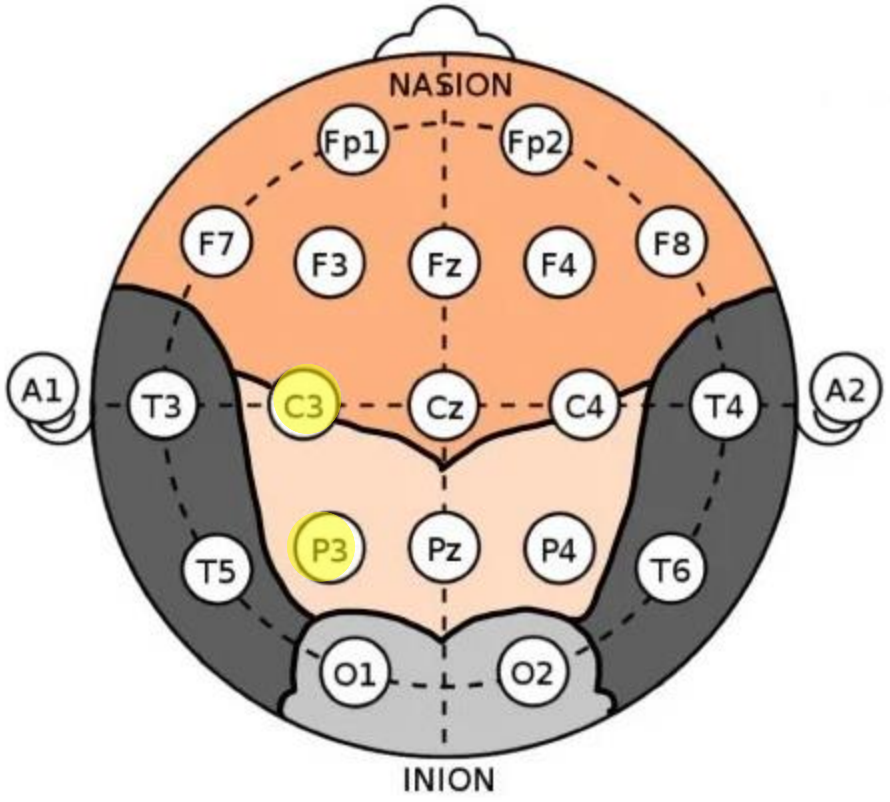
# Methods




Tucci, F., et al. (2023). "What a single electroencephalographic (EEG) channel can tell us about Alzheimer's disease patients with mild cognitive impairment." Alzheimer's & Dementia 19(S2): e062375.

# Methods

- The ADMCI group showed increased delta and decreased alpha power density
- Best classification accuracy between the ADMCI and Nold individuals reached 81% using Alpha2/Theta power density computed at the C3-P3 bipolar channel..




Tucci, F., et al. (2023). "What a single electroencephalographic (EEG) channel can tell us about Alzheimer's disease patients with mild cognitive impairment." Alzheimer's & Dementia 19(S2): e062375.

# Methods

- Demographic and clinical data in Nold and ADMCI
- To evaluate the study hypotheses, clinical, neuropsychological, anthropometric, genetic, cerebrospinal fluid (CSF), MRI, and rsEEG data in 70 Nold and 75 ADMCI subjects from an international archive were used in the present study

| | Nold | ADMCI |
|---|---|---|
| **N** | 70 | 75 |
| **Age** | 69.5 ± 0.9 | 69.7 ± 0.7 |
| **Gender (M/F)** | 28/42 (40% male) | 32/43 (43% male) |
| **Education** | 11.0 ± 0.5 | 11.1 ± 0.5 |
| **MMSE** | 28.7 ± 0.1 | 25.1 ± 0.2 |

Tucci, F., et al. (2023). "What a single electroencephalographic (EEG) channel can tell us about Alzheimer's disease patients with mild cognitive impairment." Alzheimer's & Dementia 19(S2): e062375.

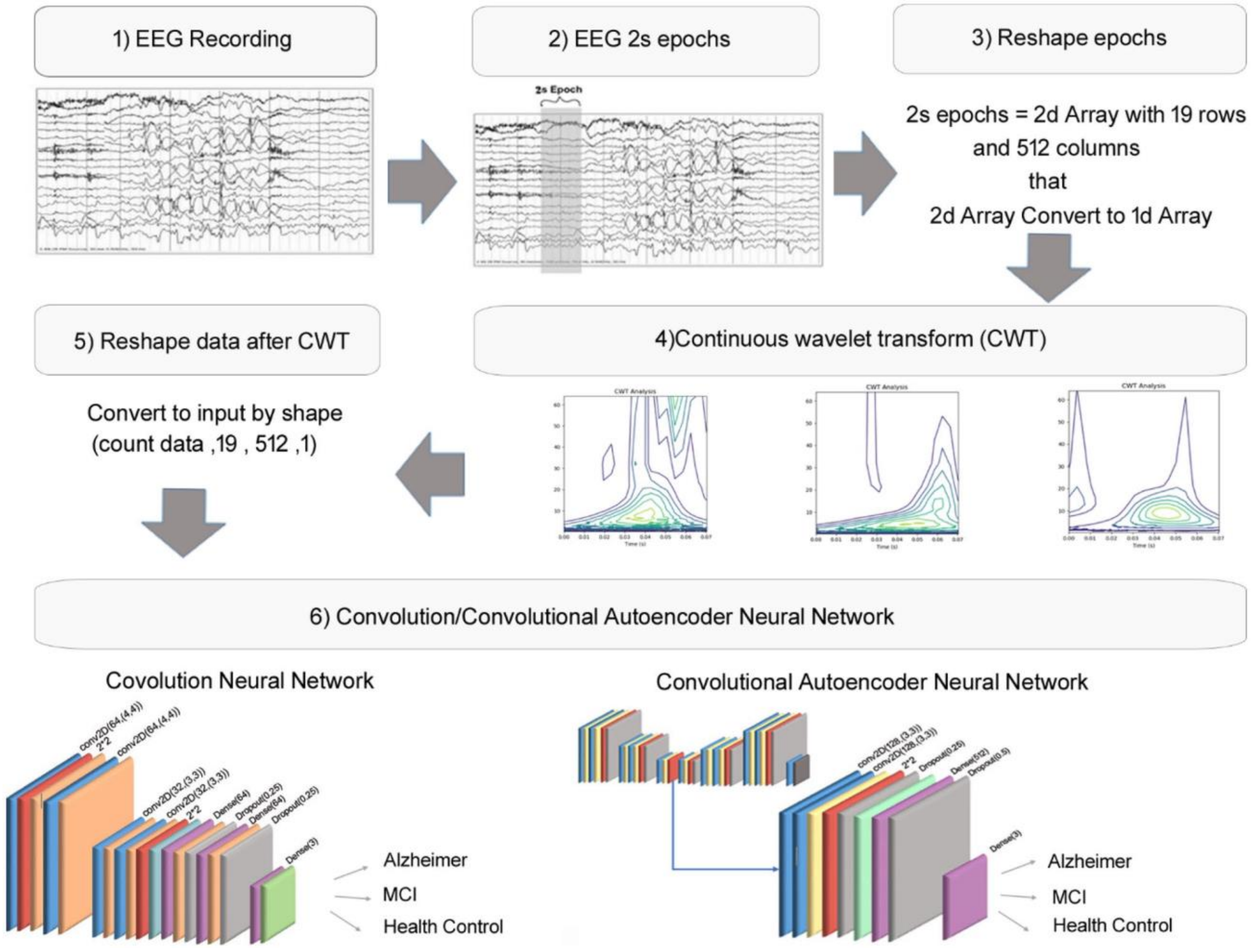
# Methods

- Two different deep learning (DL) architectures
    - Modified convolutional (CNN) with accuracy  92%
    - Convolutional autoencoder (Conv-AE) neural networks (NNs) with accuracy 89 %

Fouladi, S., et al. (2022). "Efficient Deep Neural Networks for Classification of Alzheimer’s Disease and Mild Cognitive Impairment from Scalp EEG Recordings." Cognitive Computation 14(4): 1247-1268.

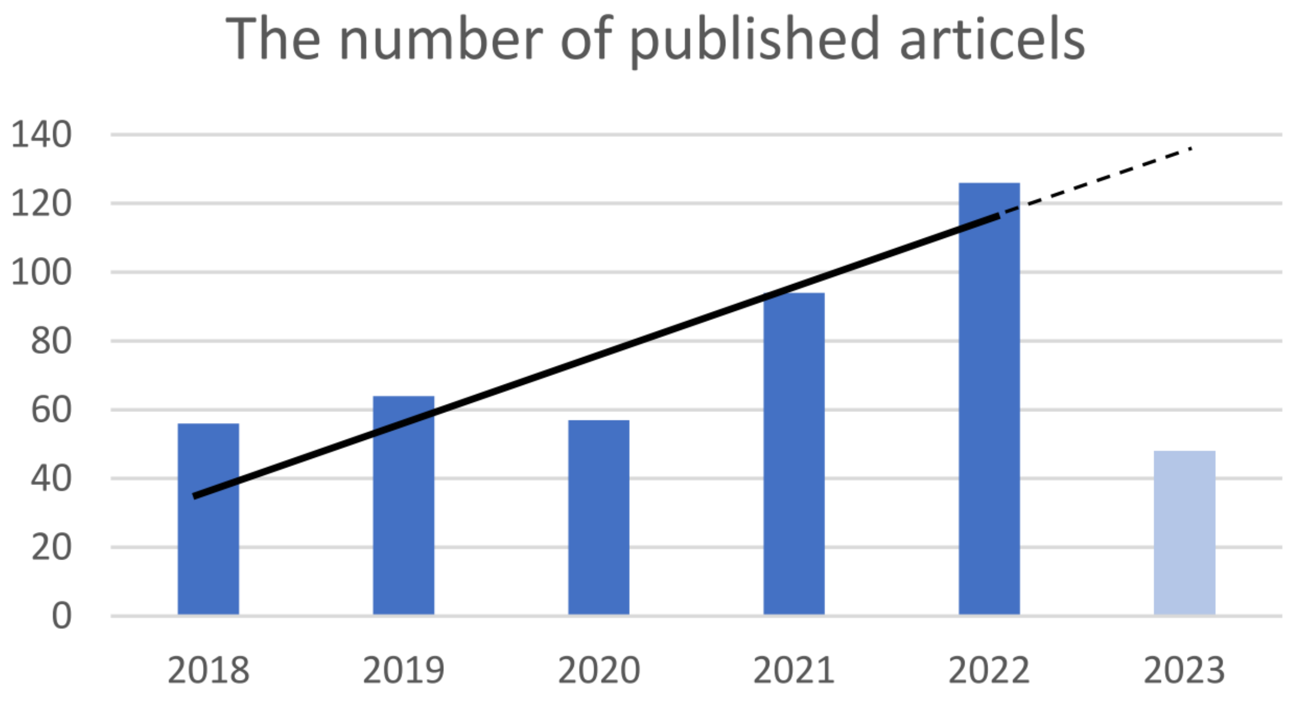
# Methods

- 19-channel
- 90 subjects
    - 37 AD
    - 37 MCI
    - 16 HC
- Recorded in 5-m




Fouladi, S., et al. (2022). "Efficient Deep Neural Networks for Classification of Alzheimer’s Disease and Mild Cognitive Impairment from Scalp EEG Recordings." Cognitive Computation 14(4): 1247-1268.

# Conclusion


The number of published articels
140
120
100
80
60
40
20
0
2018
2019
2020
2021
2022
2023

# Conclusion

- Need to provide an open-access and proper EEG database
- Almost all the researchers applied their own database and it makes the comparison among the performance of studies very challenging
- 95% of the studies were conducted with fewer than 100 participants
- Public medical imaging databases like ADNI or OASIS is a common practice in AD

# Future Works

- Longitudinal studies
- Other neurological disorders,
  - Parkinson’s
  - epilepsy
  - stroke

# Future Works

- In transformer model
  - Add spatial attention module on the EEG channels
- Study of new features that support the early detection of AD

# Future Works

- Multi modal EEG-based biomarker
  - Combined with neuroimaging techniques
  - Novel deep neural network architecture
    - Explains its reason for each output prediction

# Thank You