Graph neural network for fMRI and EEG brain data analysis

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Outline

- **Extracting Default Mode Network Based on Graph Neural Network for Resting State fMRI Study**

Donglin Wang, Qiang Wu, and Don Hong, *Frontiers in Neuroimaging*, 2022. https://doi.org/10.3389/fnimg.2022.963125

- **REM Sleep Stage Identification with Raw Single Channel EEG**

Gabriel Toban, Khem Poudel, and Don Hong, manuscript submitted to Bioengineering, July 2023.

Extracting Default Mode Network Based on Graph Neural Network for Resting State fMRI Study

- Resting state fMRI (rs-fMRI) is used in brain mapping to evaluate brain networks (RSN) that occur in a resting state, one of them is the default mode network (DMN). Classical methods rely on prior assumptions, and the result of analysis is subjective, this research propsosed to using graph neural network (GNN) to extract DMN.

Introduction: Resting state functional magnetic imaging (rs-fMRI)

Functional magnetic resonance imaging (fMRI) is a brain image technique which is non-invasive, excellent spatial and good temporal resolution.

It works by detecting the blood-oxygen-level-dependent signal (**BOLD**), reflecting the changes of deoxyhemoglobin in blood flow.

rs-fMRI measures the brain activity when the brain is in resting state without external stimulus.

Several common RSNs include: the default mode network (DMN), Somatomotor network (SMN), Visual network (VIN), Dorsal attention network (DAN), Salience netwrok (SAN), left and right Frontoparietal network (FPN).

Mental health disorder is related to RSNs, for example, DMN more active with depression, anxiety, SMN more active with bipolar disorder.

Common methods to extract DAN include: seed-based correlation method, independent component method, dictionary learning method.

Common algorithms to extract Dorsal attention network (DAN)

Seed-based correlation method (SBC) method calculates the Pearson correlation coefficient between two voxels or region of interests (ROIs) based on two time series. SBC needs to choose a prior seed as base before analysis.

Independent component analysis (ICA) assumes the observed data (non-Gaussian) is a linear combination of sources which are statistically independent, and its main goal is to separate independent source signals from mixed signals by solving the inverse mixing matrix. ICA is a decomposition method and looking for non-gaussian sources, most ICA algorithms often use principle component analysis (PCA) to remove gaussian signals in the observed data.

Dictionary learning (DL) is another linear decomposition technique which emphasizes the sparsity between components. The idea of DL is to decompose the observed data into two matrices: dictionary D, a collection of elements (atoms) and spare coefficient matrix A so that it optimizes the observed value vector Y and the matrix product DA.

GraphSAGE algorithm

GraphSAGE (Sample and Aggregate) is an inductive deep learning technique and help extract node embedding (node features). It has ability that can generalize to unseen node (data).

The unsupervised GraphSAGE model with K layers for node embedding of voxels or ROIs (v) can be implemented accordingly.

The purpose of preprocessing is to remove all kinds of noise from the fMRI signal to the greatest extent for the subsequent statistical analysis.

In this project, we use the DPABI: data processing & analysis for (resting-state) brain imaging (Neuroinformatics, 14(3):339–351, 2016) for data preprocessing. The first ten time points are removed, temporal filtering is in the range of 0.01 ~ 0.1Hz, and spatial smoothing with a Gaussian kernel of full width with half maximum(FWHM) equal to 6mm.

Data introduction

- The data set is from the open shared neuroimage data resource (`http://fcon_1000.projects.nitrc.org/fcpClassic/FcpTable.html`), namely, 1000 Functional Connectomes Project. All data sets are collected independently from 33 different sites around the world.

- The data is summarized in the table below:

Table 1: Data summary

Total	84
Female	41
Male	43
Age	7 ~ 49
Repetition Time (TR)	2 seconds
Slice	39
Time Points	192

Structural brain

The structural brain of one randomly chosen subject with dimension $256 \times 176 \times 256$ is shown below:
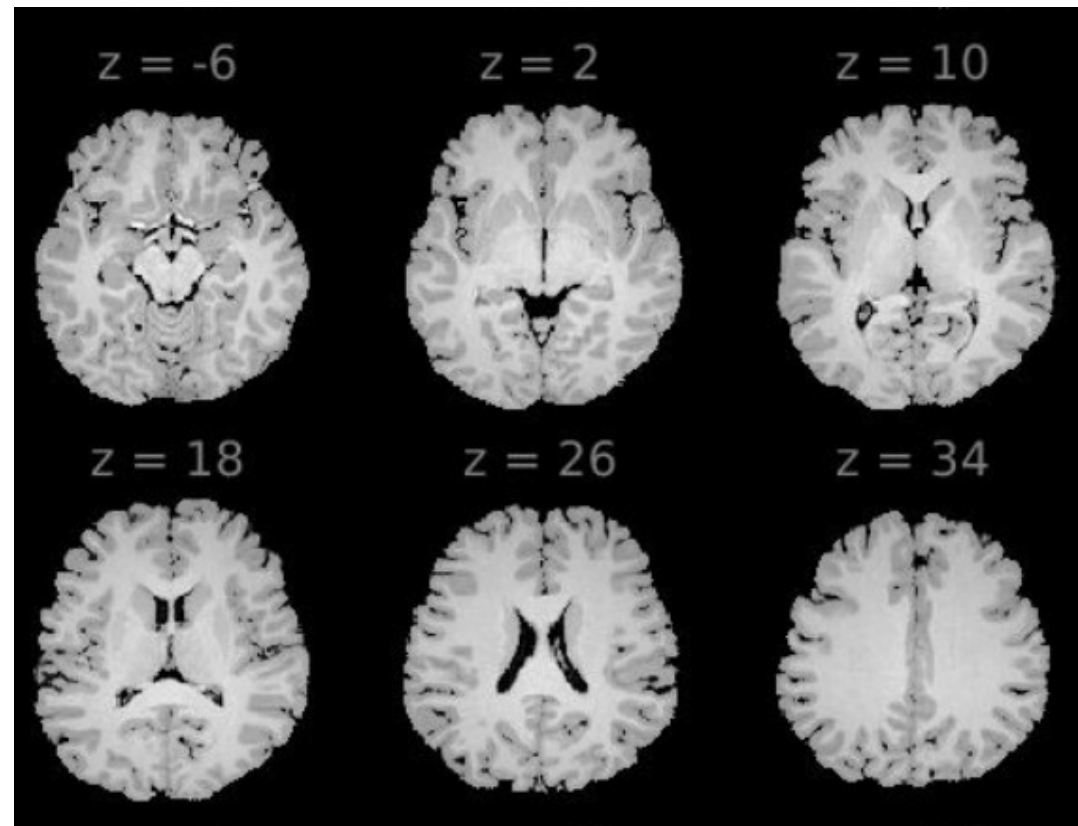
Figure 1: The structural brain of one randomly chosen subject

Functional brain

The functional brain of the same subject in Figure 4 with dimension $64 \times 64 \times 39 \times 192$ is shown below:
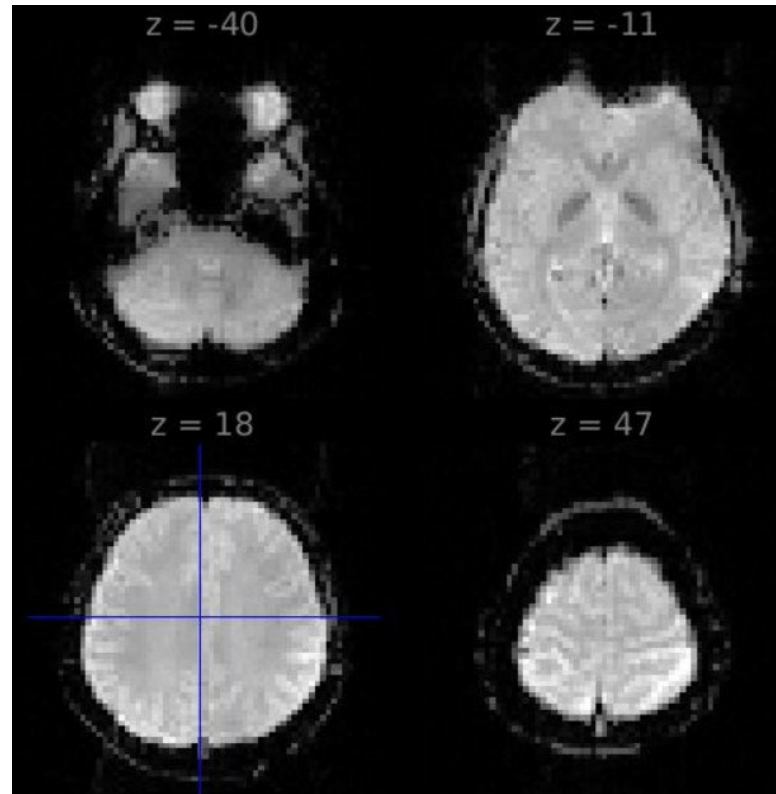
Figure 2: The functional brain of one randomly chosen subject

Data analysis: classical methods

The below table shows the parameters for the analysis of traditional methods:

Table 2: Parameters for each model

Model	P^1	FWER^2	Seed^3	Components^4	Sparsity^5	DF^6
SBC	<0.0001	<0.01	PCC	-	-	83
ICA	<0.0001	<0.01	PCC	10	-	83
DL	<0.0001	<0.01	PCC	10	15	83

[1]Voxel threshold p-uncorrected value.
[2]Familywise error rate p-value controlling the probability of false positive.
[3]PCC: Posterior cingulate cortex seed.
[4]The number of independent components.
[5]The parameter of control sparsity.
[6]Degree of freedom.

Data analysis: graphSAGE

Based on the atlas of Schaefer(2018), 800 nodes (ROIs) were extracted, each subject has $G(800, 319, 600)$, correlation calculated between every two nodes based on 192 time series data; each node has 800 values as the original features.

Table 3: Parameters for two layers graphSAGE

Input	84 graphs, with 800 features each node per graph
1 hop neighbors per node	50
2 hop neighbors per node	10
Number of neurons first layer	200
Number of neurons second layer	100
Dropout rate	0.15
Activation function	RELU, tanh
Learning rate	0.005
Output(node embedding)	matrix with dimension 800 x100

Visualize the node embedding with the first two principal components from PCA anaysis, and it shows about seven groups. Then K-means [12] cluster algorithm is performed with components extracted from PCA to group ROIs into seven parts.
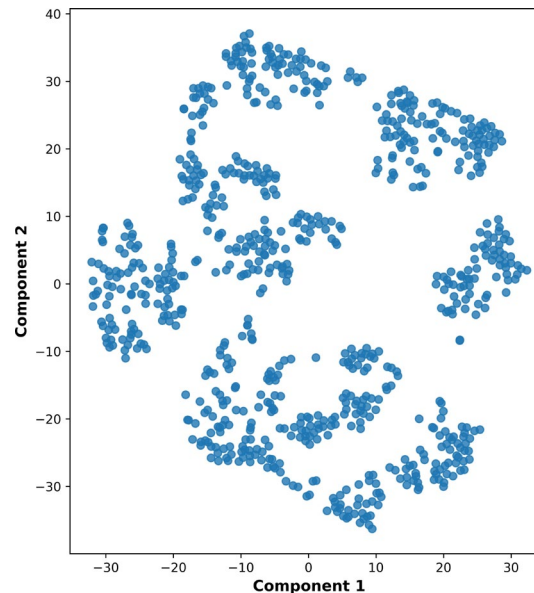
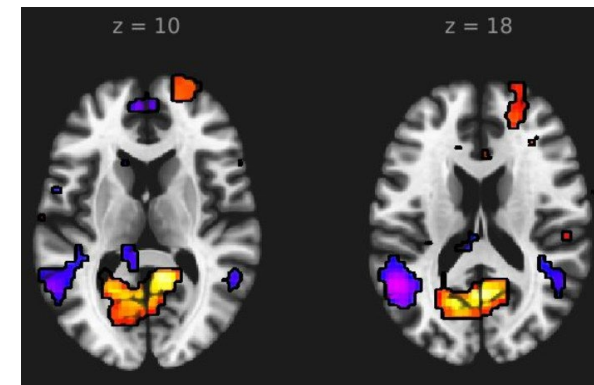Figure 3: Plot of node embedding with first two components

Result comparison
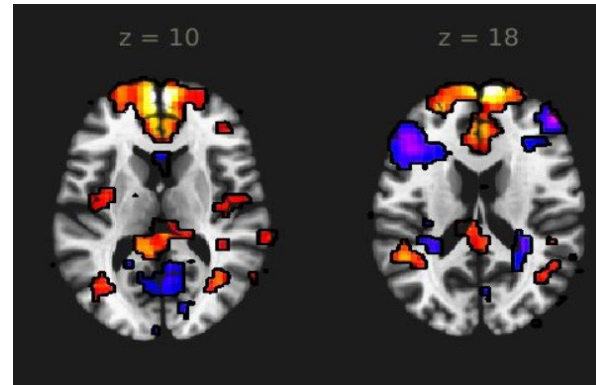
(a) SBC
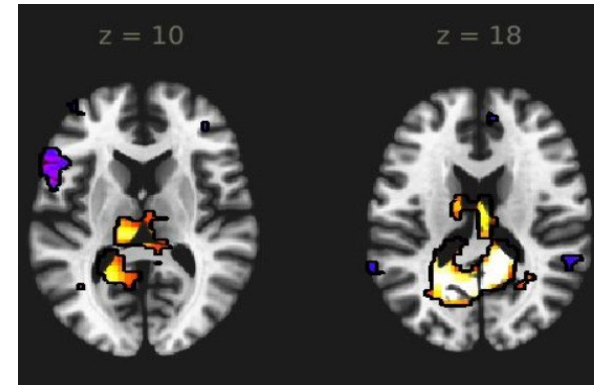
(b) ICA
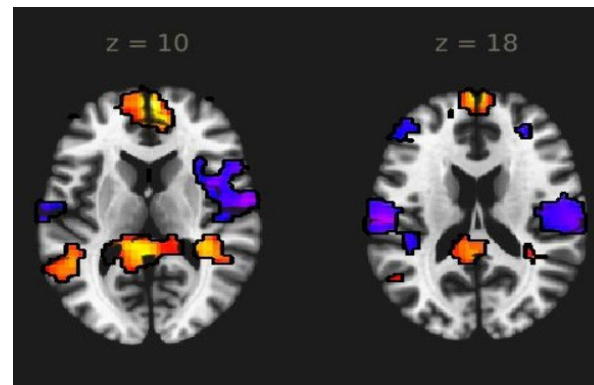
(c) DL

(d) graphSAGE

Figure 4: Result comparison: DMN

Summary

- It is important to explore and identify RSNs, to help better understand the functional RSNs, especially for discovering the difference of functional changes of RSNs between healthy and unhealthy individuals.

- GraphSAGE can extract/detect not only the DMN also other RSNs; compared with other algorithms, it is no prior assumption and robust. This provides an approach to exploit the RSNs.

- The algorithm is used to explore the bio-marker among the different mental disorders, like depression, autism, anxiety, Alzheimer, and so on.

- The result is published in the paper:

- Donglin Wang, Qiang Wu, and Don Hong, *Extracting Default Mode Network Based on Graph Neural Network for Resting State fMRI Study,* Frontiers in Neuroimaging, 2022.

  https://doi.org/10.3389/fnimg.2022.963125

REM Sleep Stage Identification with Raw Single Channel EEG

- This work focuses on creating an interpretable model for automatic Rapid Eye Movement (REM) sleep stage scoring using a single-channel electroencephalogram (EEG).

- Accurate scoring of sleep stages is clinically important for diagnosing sleep disorders. While polysomnography using multiple physiological signals provides the gold standard, there is a need for simplified techniques that can be used at home. Our work aims to develop an automated approach using only a single EEG channel, which reduces measurement complexity.

- This method uses discrete wavelet transforms to decompose the EEG signal into different frequency bands that are each input to a separate 1D convolutional neural network. The outputs are concatenated and input to a bidirectional GRU network to incorporate temporal information. When tested on the public Sleep-EDF Expanded dataset, our model achieved 97% accuracy, 93% precision and 89% recall in identifying REM sleep, competitive with more complex models in the literature. Importantly, the convolutional filters learned by the model correspond to known electrophysiological markers of sleep stages.

- Sleep disorders are commonly seen in patients with neurodegenerative diseases. Specifically, (Rapid Eye Movement) REM sleep behavior disorder (RBD) may be the initial manifestation of neurodegenerative diseases such as Parkinson's disease, dementia, and multiple system atrophy.

- By creating a CNN model with fewer filters based on EEG frequency bands, the filters and individual CNN sub models become relatable to clinical markers. This project focuses on the first step in that process: reducing the number filters per EEG frequency band to a number that can be easily reviewed and understood.

- The convolutional part usually consists of 5 CNN's. There is 1 CNN for each of the delta, theta, and alpha EEG bands and 2 CNNs for the beta EEG band for a total of 5 CNNs. Each CNN has a filter size that allows the frequency of the filter to fit within the specified frequency band. Each CNN was trained independently on the 30 second epochs to score REM.

Data

- This study used the "Sleep Recording and Hypnograms in European Data Format (EDF)" data set or "The Sleep-EDF Database [Expanded]" from physionet.org: The Sleep-EDF Database [Expanded].

- The portion of the database used is from a study on healthy patients from 1987-1991. There are 20 patients avaialable. There are 10 males and 10 females ranging from age 25-34 years old.

- The EEG has a recording every 10 milliseconds. There are 3000 recordings per epoch. This implies that the maximum decomposition level is 8. Each decomposition level produced a different number of coefficients.

Sleep Study and Polysomnogram
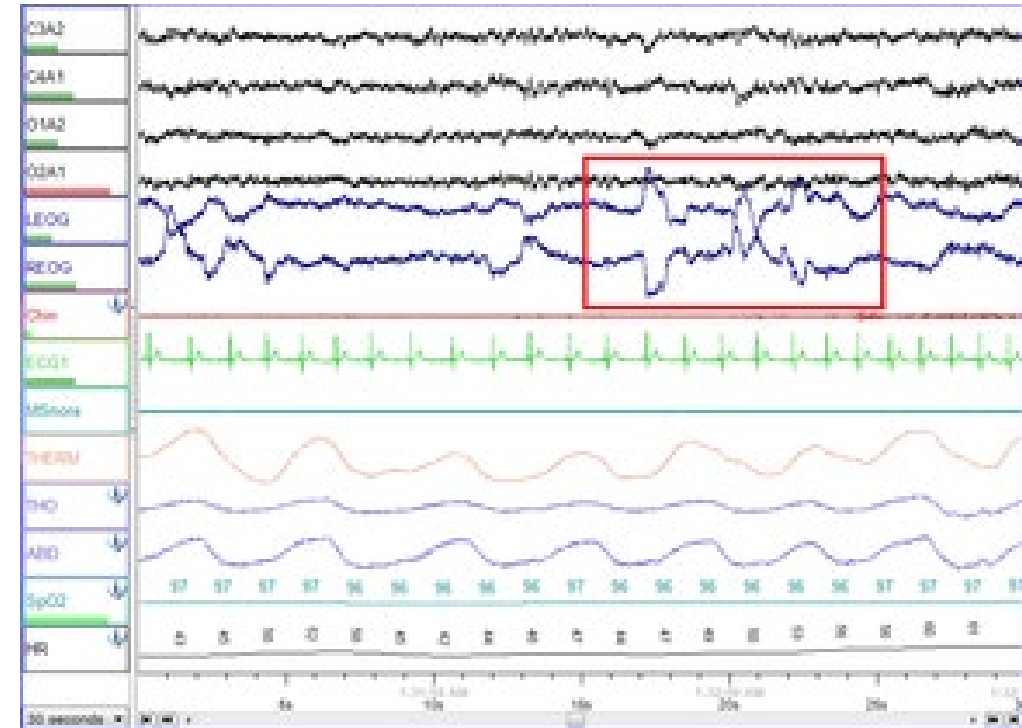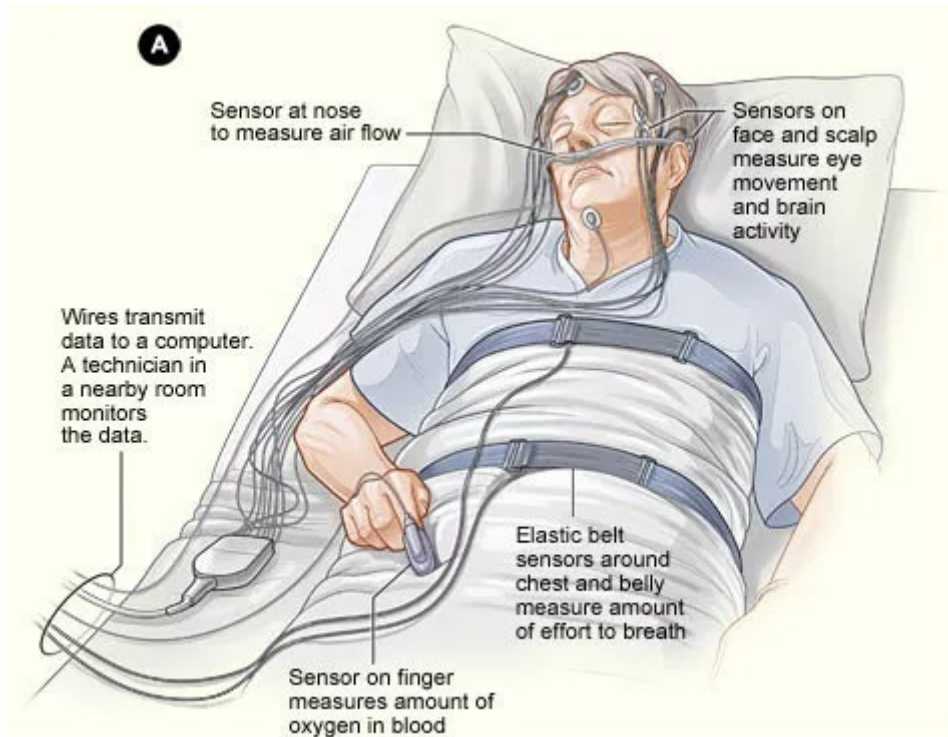
Sleep Study Outcomes/Diagnoses

Sleep Apnea

Sleep Staging

Wakefulness (W)
Non-REM 1 (N1)
Non-REM 2 (N2)
Non-REM 3 (N3)
Rapid Eye Movement (REM)

REM Sleep Disorder
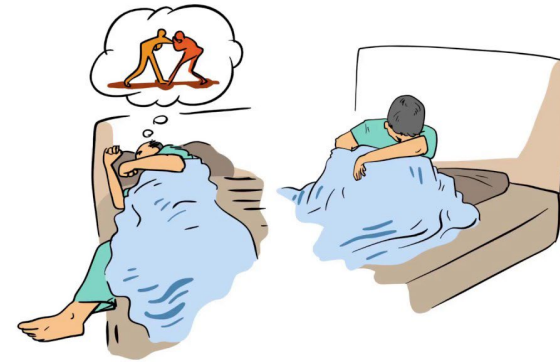
Technician's Analysis

8 Hours of Sample Signal with 30 Second Epoch Highlighted

Time (hours)
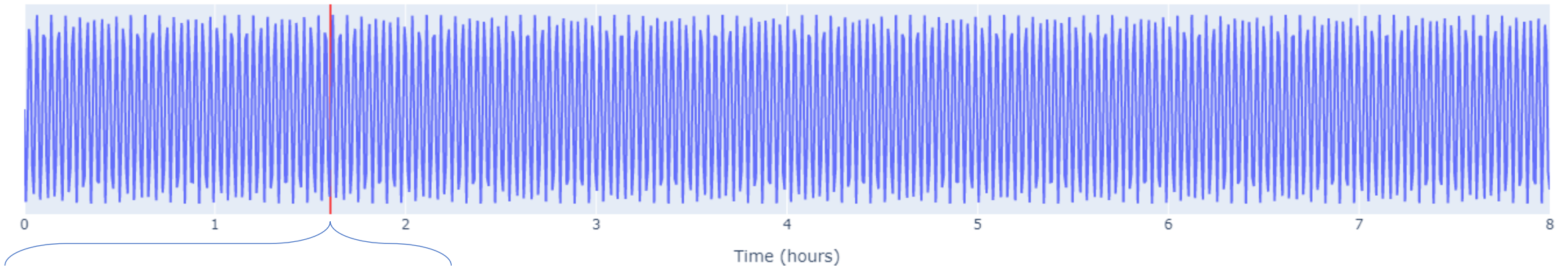
30 Second Epoch

Clinical Markers

V-Wave   **K-complex**

Outcome/Diagnosis

| Wakefulness (W) |
| Non-REM 1 (N1) |
| Non-REM 2 (N2) |
| Non-REM 3 (N3) |
| Rapid Eye Movement (REM) |
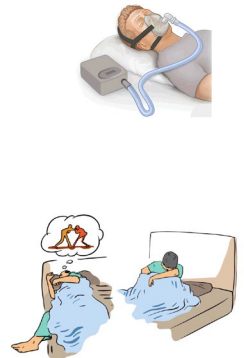
Automated Analysis

8 Hours of Sample Signal with 30 Second Epoch Highlighted
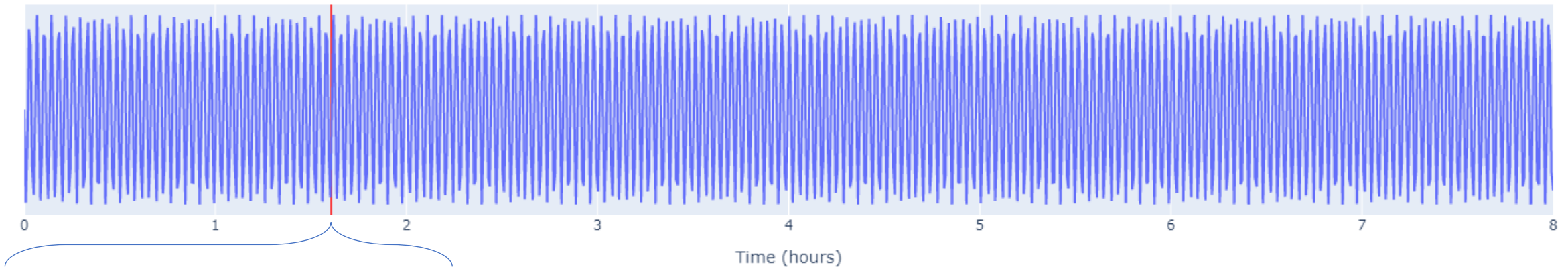
30 Second Epoch
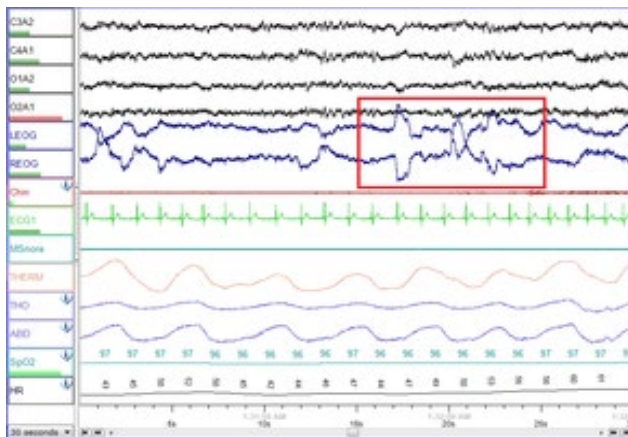
**Algorithm
Clinical Markers**

?

Outcome/Diagnosis

Wakefulness (W)
Non-REM 1 (N1)
Non-REM 2 (N2)
Non-REM 3 (N3)
Rapid Eye Movement (REM)

One Common Approach

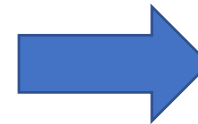8 Hours of Sample Signal with 30 Second Epoch Highlighted

Time (hours)
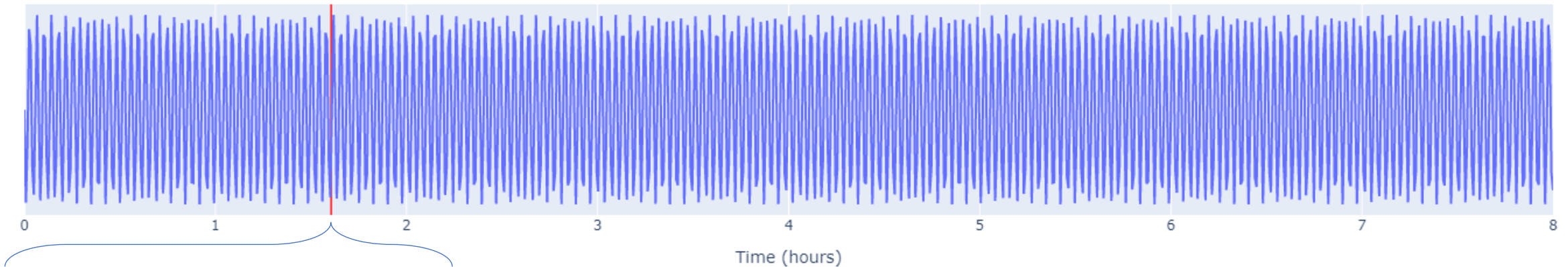
30 Second Epoch of EEG
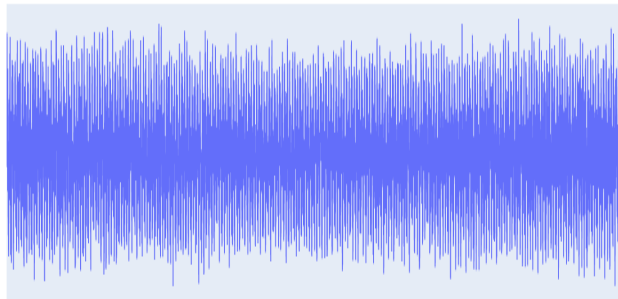
Algorithm = Convolutional Neural Networks
Clinical Markers = Filters
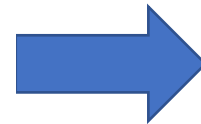
REM Sleep Staging

Rapid Eye Movement (REM)

$$\begin{pmatrix} f_1 * g_1 + f_2 * g_2 + \ldots + f_n * g_n \\ f_2 * g_1 + f_3 * g_2 + \ldots + f_{1+n} * g_n \\ \vdots \\ f_{k-n+1} * g_1 + f_{k-n+2} * g_2 + \ldots + f_k * g_n \end{pmatrix}$$
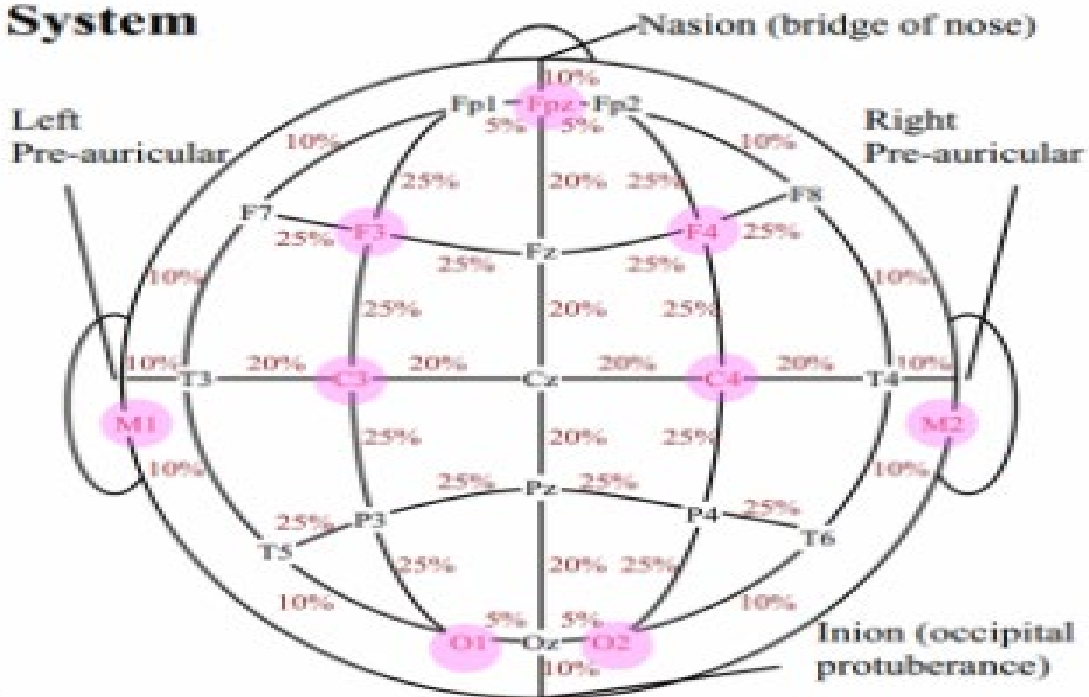
The 10/20 System for EEG

International 10/20 System

The following EEG electrode sites are used in a standard overnight sleep study:

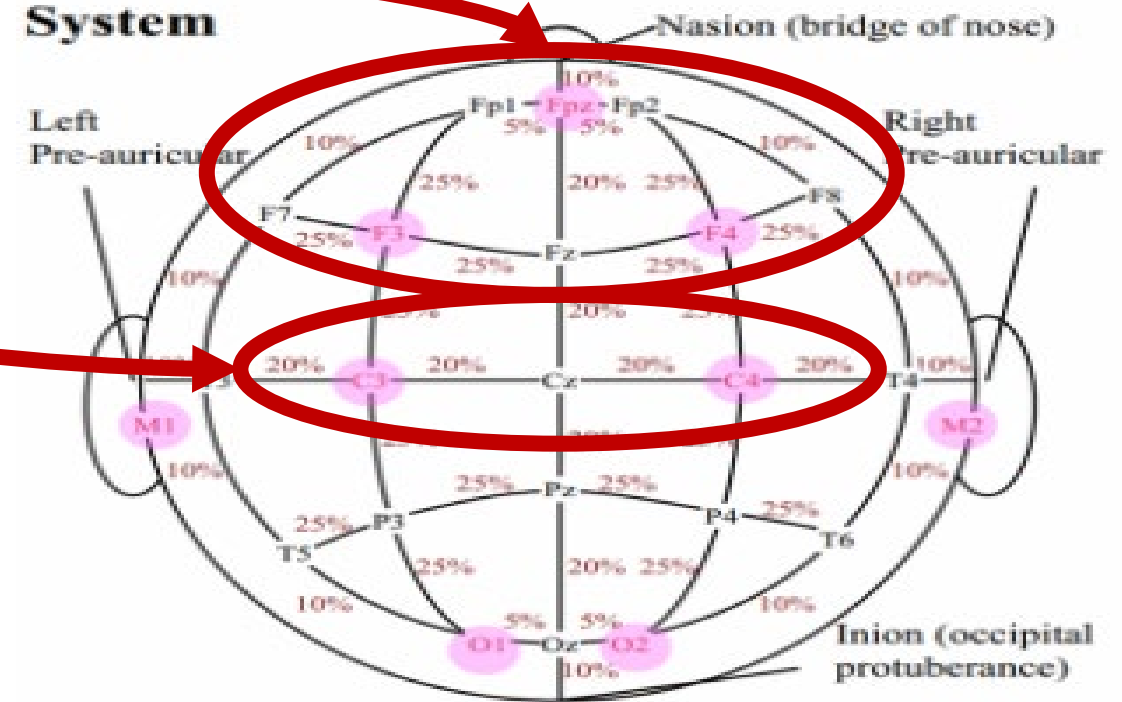- F3
- F4
- C3
- C4
- O1
- O2
- M1
- M2
- FpZ

EEG Channel to Clinical Markers

| Clinical Markers	Frontal	Central	Occipital	Fz-Cz	E1-Fpz
Slow Wave				No	Yes
V-Waves		Maximal			
K-complexes	Maximal				
Spindles		Maximal			
Sawtooth		Maximal			
Alpha		Adequate	Maximal		

Data

Sleep-EDF Database Expanded

Fpz-Cz Channel

30 Second EEG Epoch from Fpz-Cz Channel

Convolutional Neural Network (CNN)

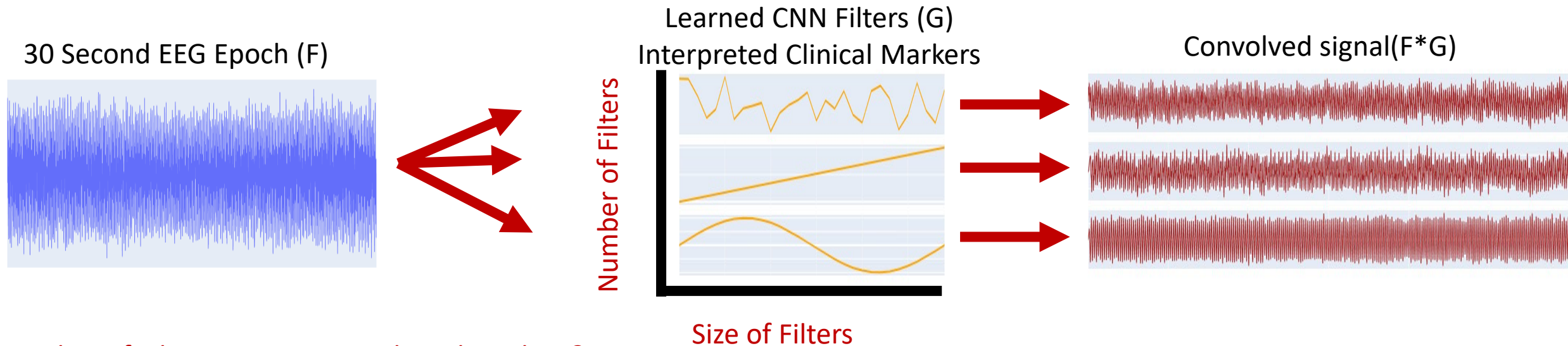30 Second EEG Epoch (F)

Learned CNN Filters (G)
Interpreted Clinical Markers
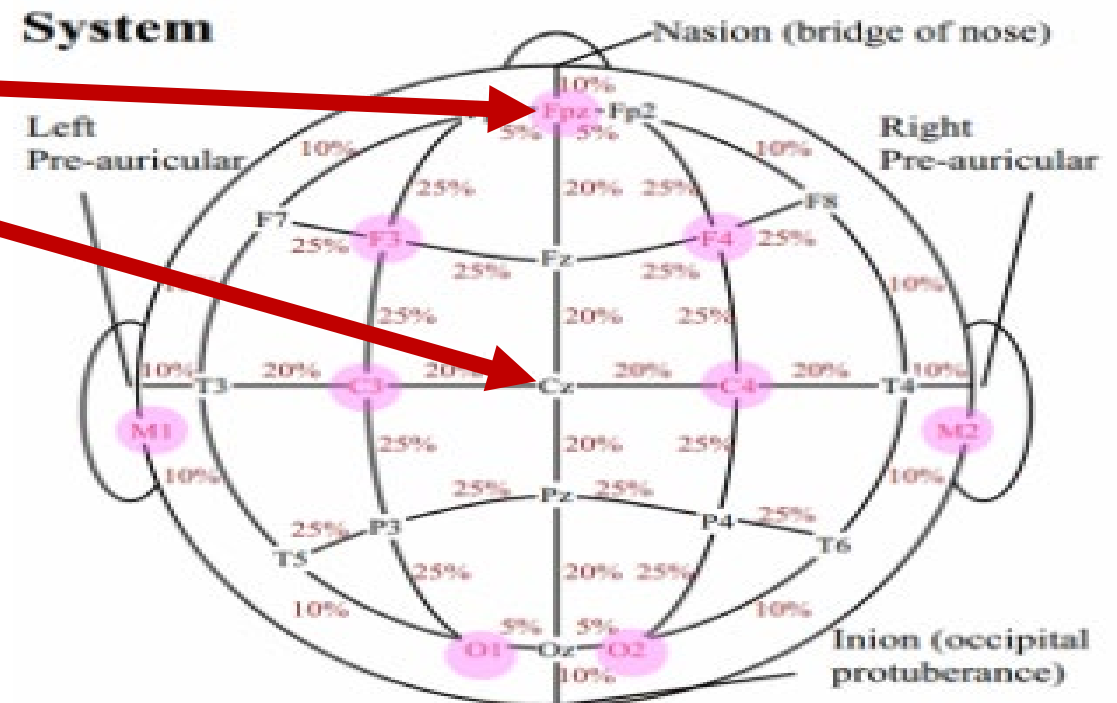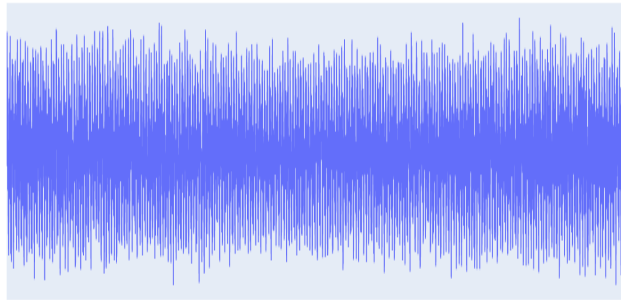
Convolved signal(F*G)
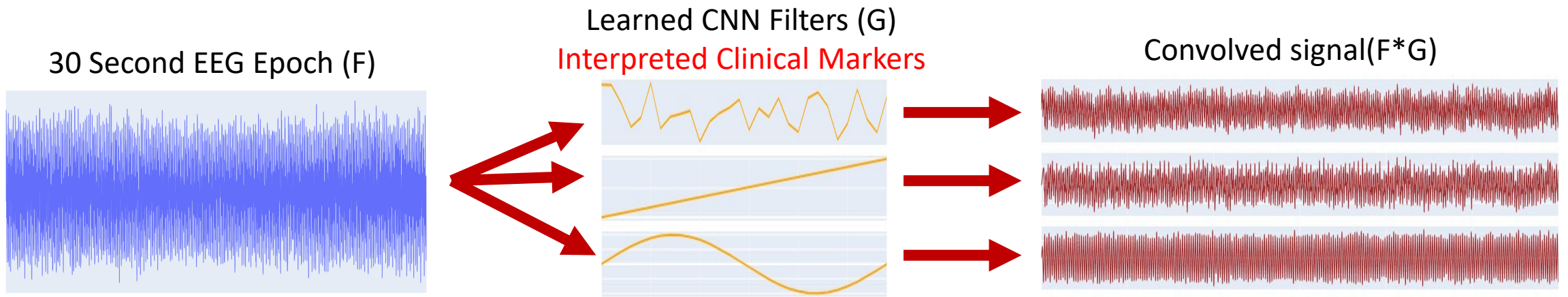
$$\text{convolved signal} = F * G = \begin{pmatrix} f_1 * g_1 + f_2 * g_2 + \ldots + f_n * g_n \\ f_2 * g_1 + f_3 * g_2 + \ldots + f_{1+n} * g_n \\ \vdots \\ f_{k-n+1} * g_1 + f_{k-n+2} * g_2 + \ldots + f_k * g_n \end{pmatrix}$$

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Convolutional Neural Network (CNN)

30 Second EEG Epoch (F)

Learned CNN Filters (G)
Interpreted Clinical Markers

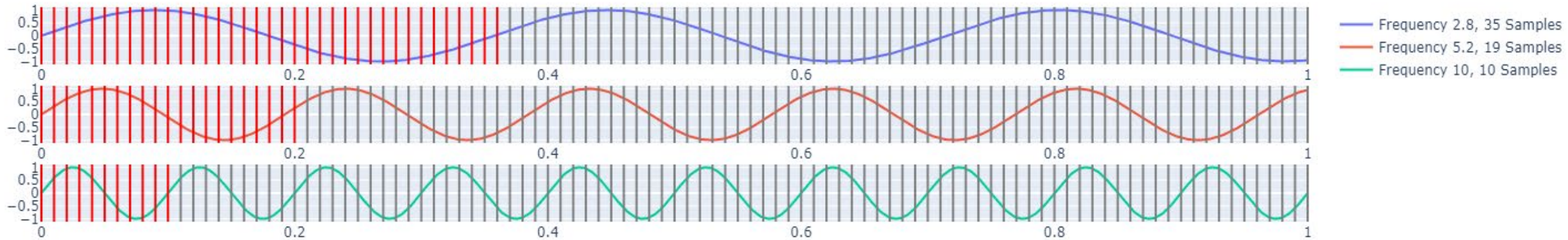Convolved signal(F*G)

Number of Filters

Size of Filters

Number of Filters = How many clinical markers?
Size of Filters = Frequency band

$$\text{CNN Filter Size} \approx \frac{\text{Sample Rate}}{\text{CNN Filter Frequency}}$$

Frequency to Samples Per Wave

Number of Samples for 1 Wave

— Frequency 2.8, 35 Samples
— Frequency 5.2, 19 Samples
— Frequency 10, 10 Samples

$$\text{Number Of Samples} \approx \frac{\text{Sample Rate}}{\text{Frequency}} = \frac{100}{\text{Frequency}}$$

5 Frequency Bands to Filter Size
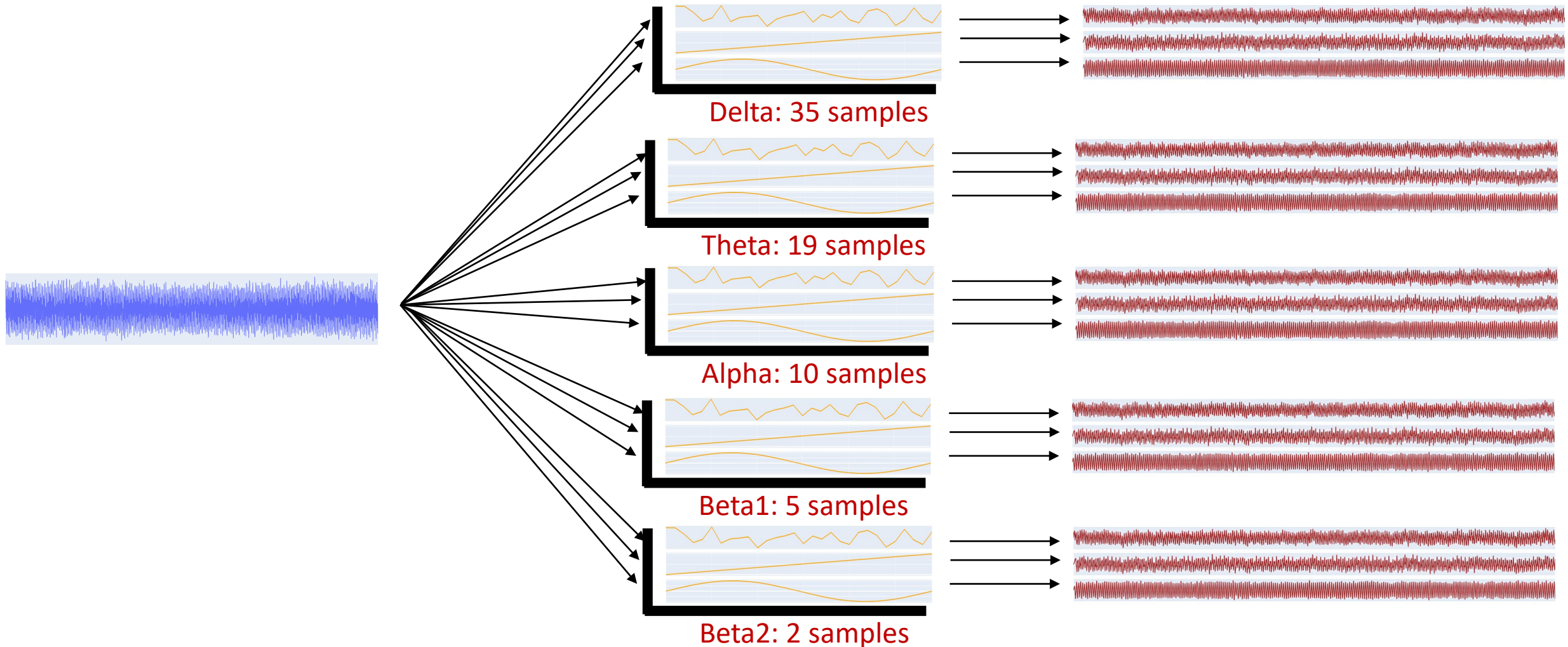
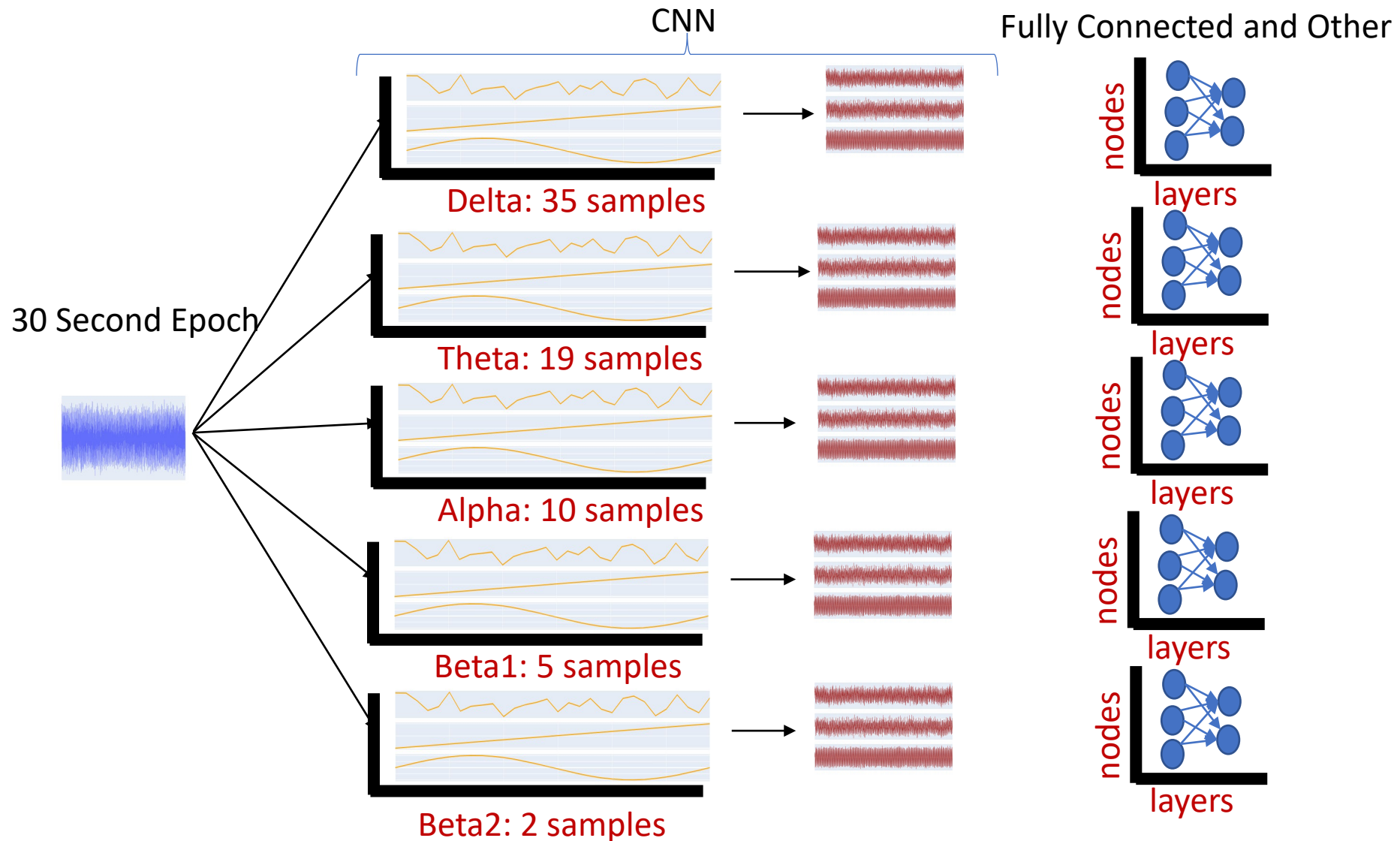| EEG Frequency Band (Hz)	CNN Filter Frequency (Hz)	CNN Filter Size (samples)
Delta (0-3.99)	2.8	35
Theta (4-7.99)	5.2	19
Alpha (8-13)	10	10
Beta1 (>13)	20	5
Beta2 (>13)	50	2

$$\text{CNN Filter Size} \approx \frac{\text{Sample Rate}}{\text{CNN Filter Frequency}}$$

Convolutional Neural Network (CNN)

30 Second EEG Epoch (F)

Learned CNN Filters (G)
Interpreted Clinical Markers

Convolved signal(F*G)

Delta: 35 samples

Theta: 19 samples

Alpha: 10 samples
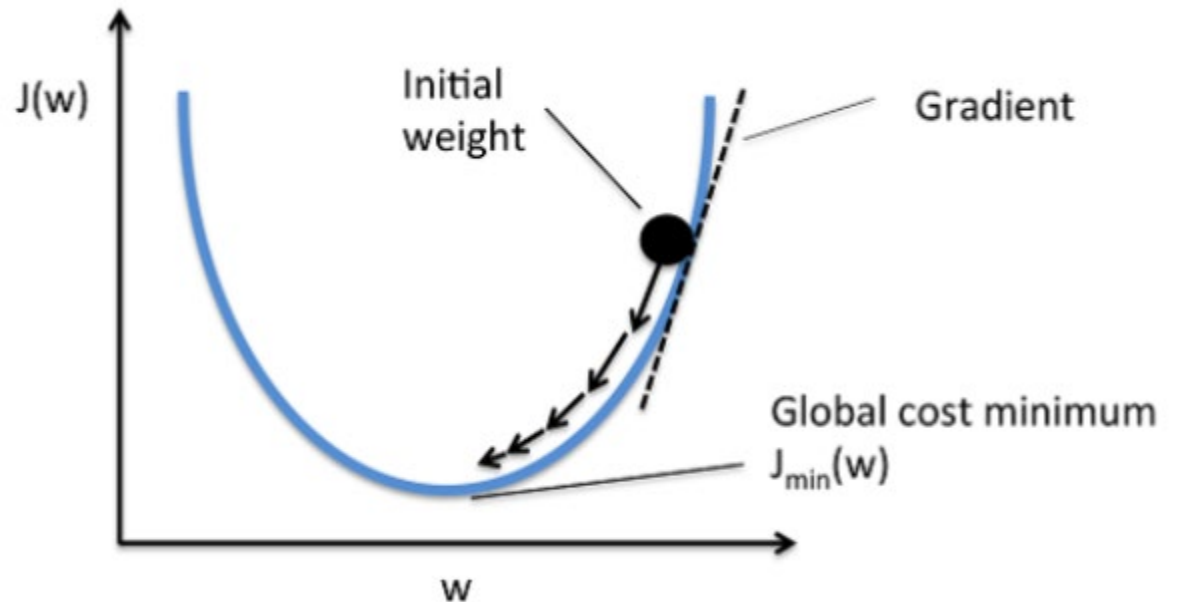
Beta1: 5 samples

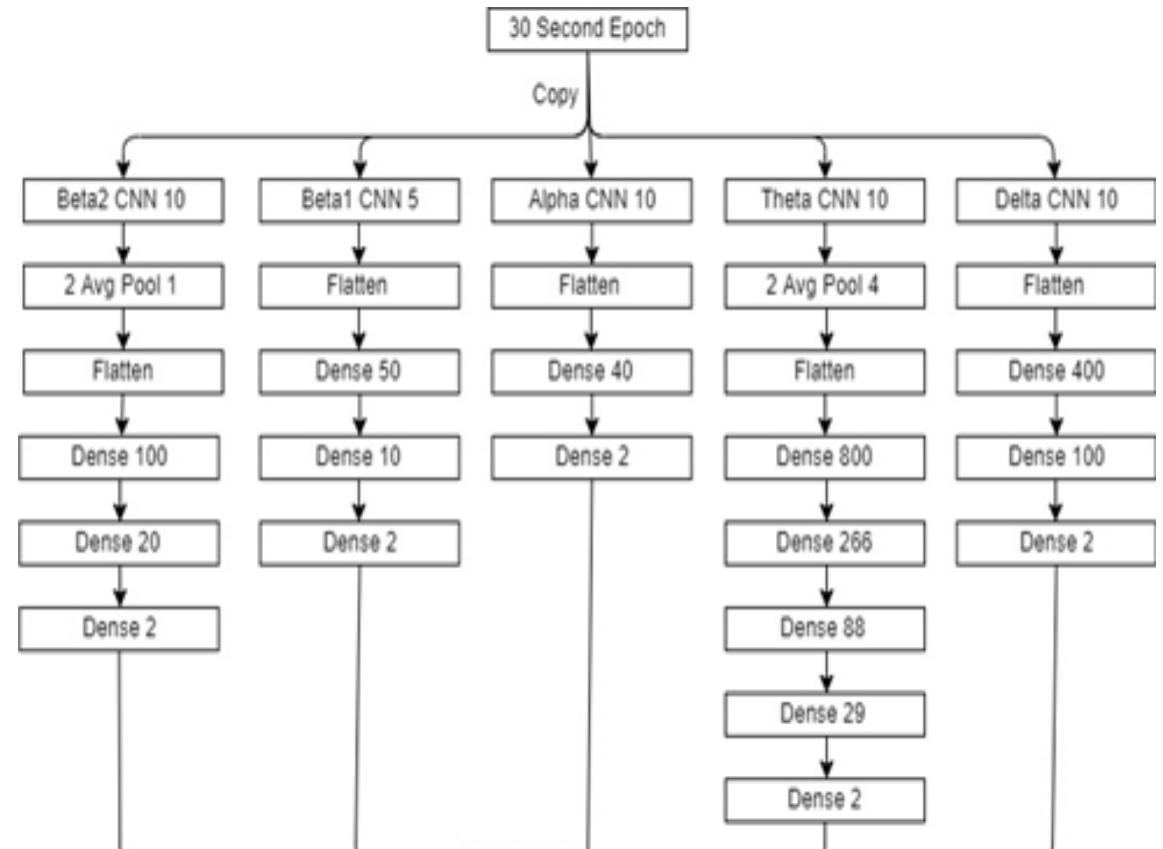Beta2: 2 samples

Convolutional Neural Network (CNN)

Hyperparameter Optimizer

- CNN
  - Number of Filters
- Full Connected
  - Number of layers
  - Number of Nodes in each layer
- Flatten layer or not
- Pooling or not
- Optimization functions to solve (gradient descent, adam)
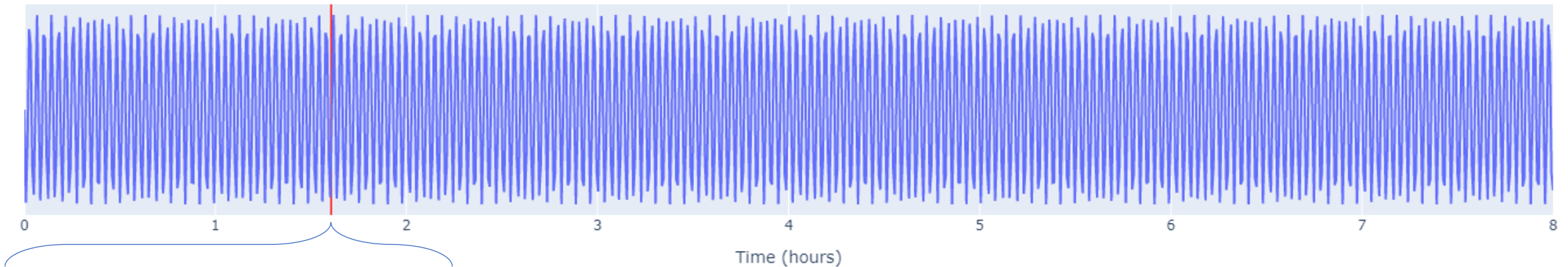- Activation functions (tanh, sigmoid, softmax)

CNN Model

- CNN Level
  - 1 30 second epochs
  - 5 CNN
    - 1 frequency size per frequency band
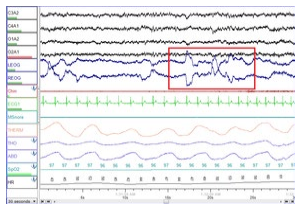 - 5 or 10 filters per band
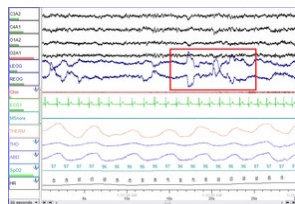 - 1-hot-encoded REM vs not REM

Technician's Analysis: 3 epochs

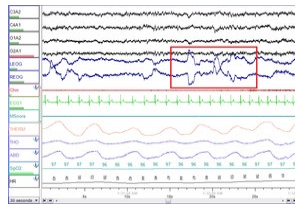8 Hours of Sample Signal with 30 Second Epoch Highlighted

Time (hours)

30 Second Epochs

Pre Epoch   **Target Epoch**   **Post Epoch**

Clinical Markers

V-Wave   K-complex

Outcome/Diagnosis

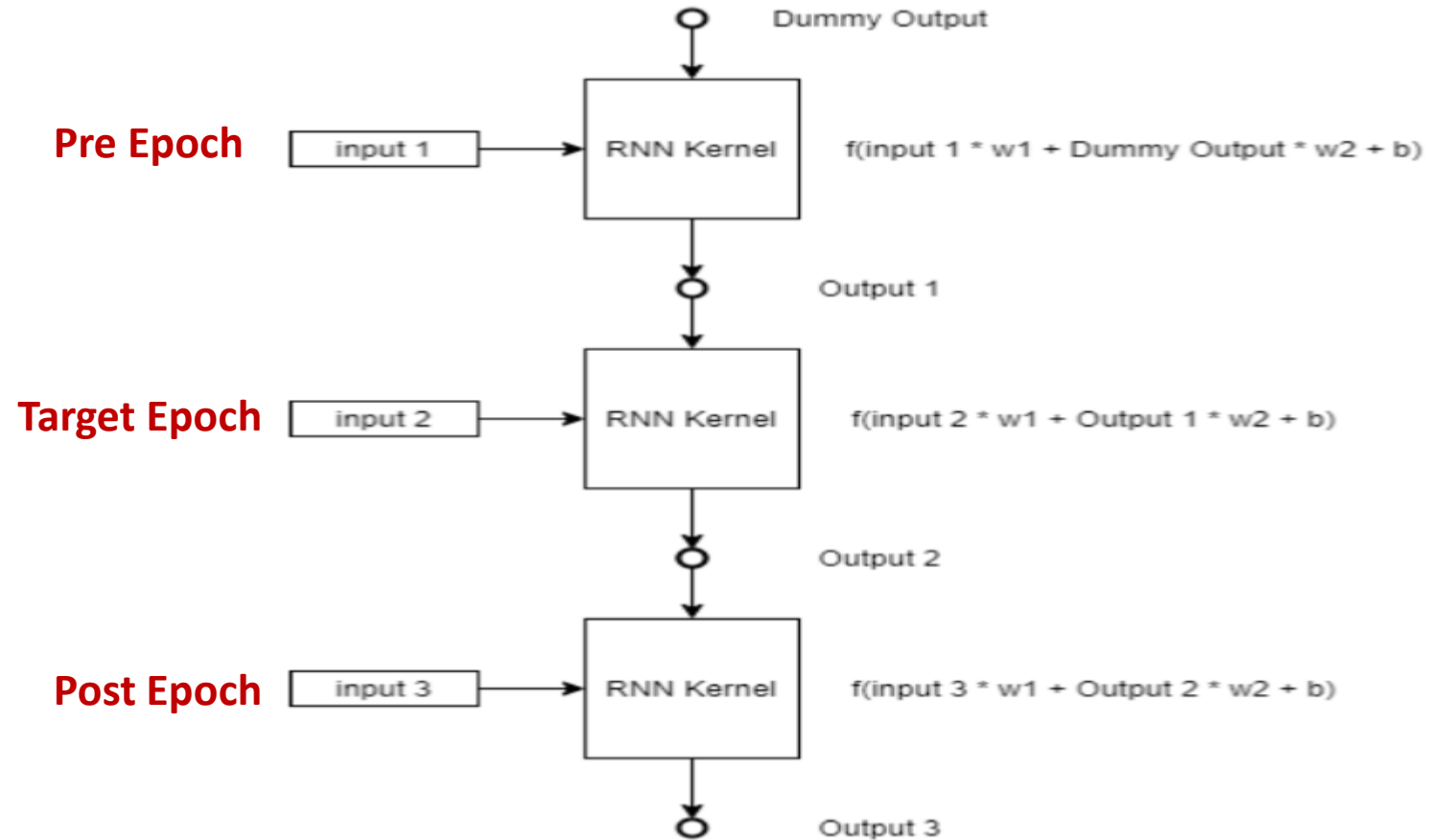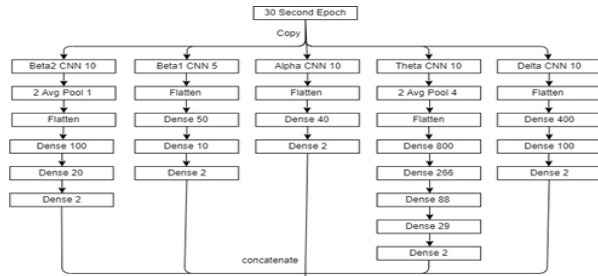| |
|---|
| Wakefulness (W) |
| Non-REM 1 (N1) |
| Non-REM 2 (N2) |
| Non-REM 3 (N3) |
| Rapid Eye Movement (REM) |

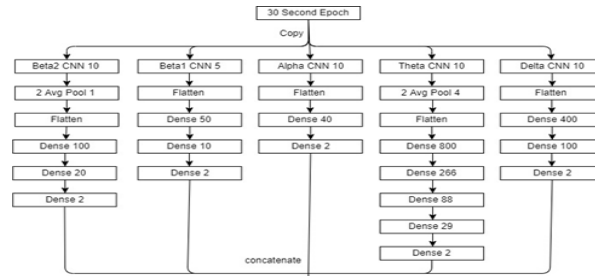# Deep Learning: Recurrent Neural Network (RNN)

- Memory
- Simple RNN
- GRU

Dummy Output

Pre Epoch   input 1 → RNN Kernel   f(input 1 * w1 + Dummy Output * w2 + b)

Output 1

Target Epoch   input 2 → RNN Kernel   f(input 2 * w1 + Output 1 * w2 + b)

Output 2

Post Epoch   input 3 → RNN Kernel   f(input 3 * w1 + Output 2 * w2 + b)

Output 3

RNN Model
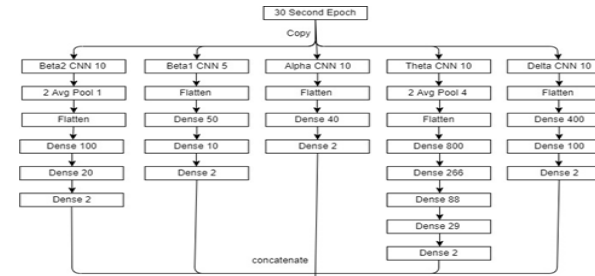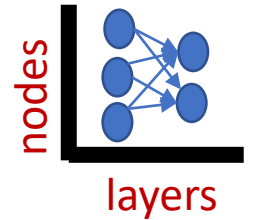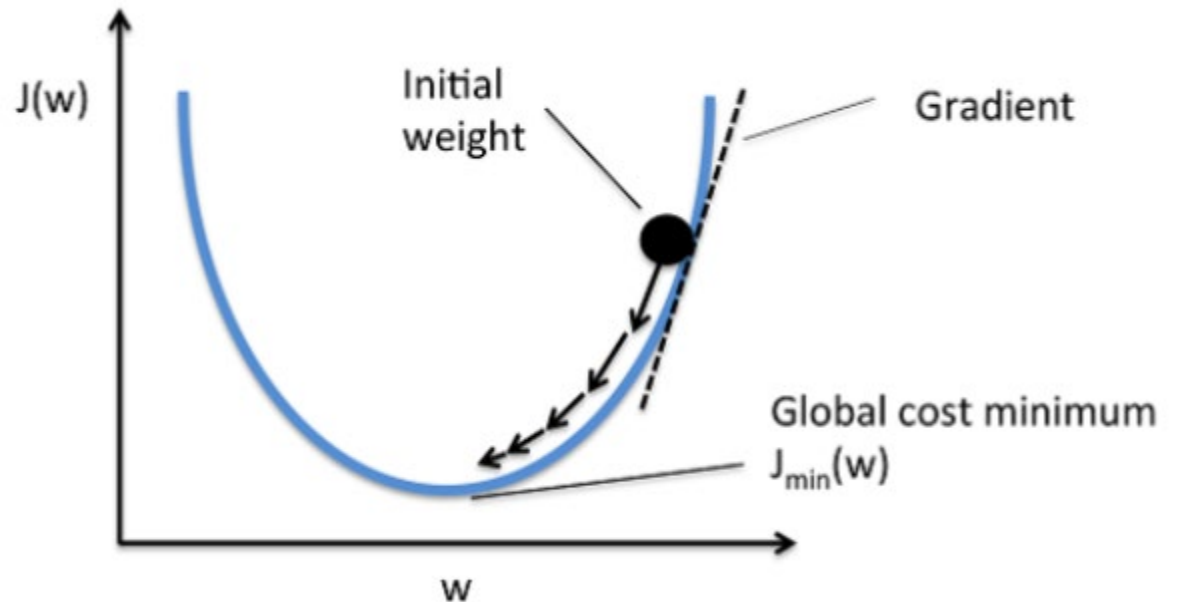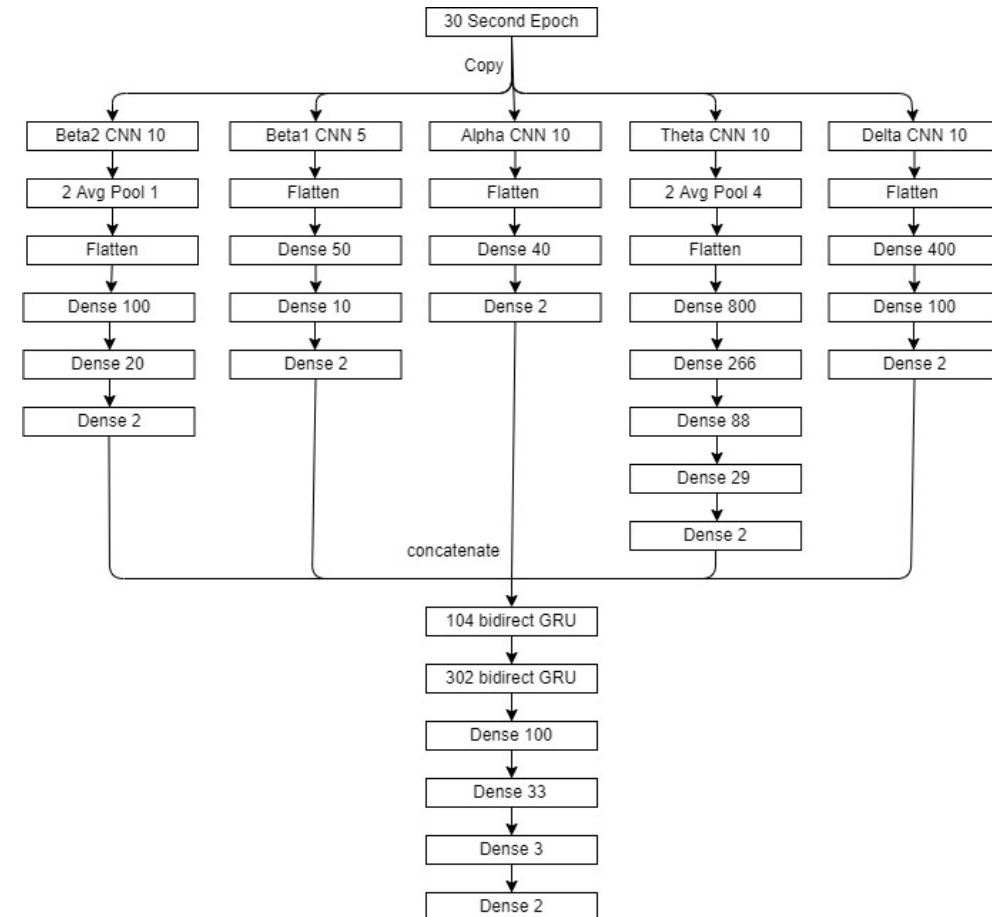
Hyperparameter Optimizer

- RNN
  - GRU, LSTM, Bidirectional
- Full Connected
  - Number of layers
  - Number of Nodes in each layer
- Flatten layer or not
- Pooling or not
- Optimization functions to solve (gradient descent, adam)
- Activation functions (tanh, sigmoid, softmax)

Model

- **CNN Level**
  - 1 30 second epochs
  - 5 CNN
    - 1 frequency size per frequency band
  - 5 or 10 filters per band
  - 1-hot-encoded REM vs not REM
- **RNN level**
  - 3 outputs from CNN Level
  - Bidirectional GRU
    - Better than LSTM
  - 1-hot-encoded REM vs not REM

Methods

- "The Sleep-EDF Database [Expanded]" from physionet.org
  - 2-12 patients
  - Fpz-Cz Channel
  - Removed leading awake epochs
- Custom hyperparameter optimizer
  - F1 Score
  - Raw signal
  - CNN -> Feed Forward -> Bidirectional GRU

Training Parameters

- dataFiles: input002.csv, input142.csv

- cvFolds: 10

- validation_split: 0.1

- epoch: 100

- batchSize: 177

- normSTD : 28.2862

- normMean : 0.6683
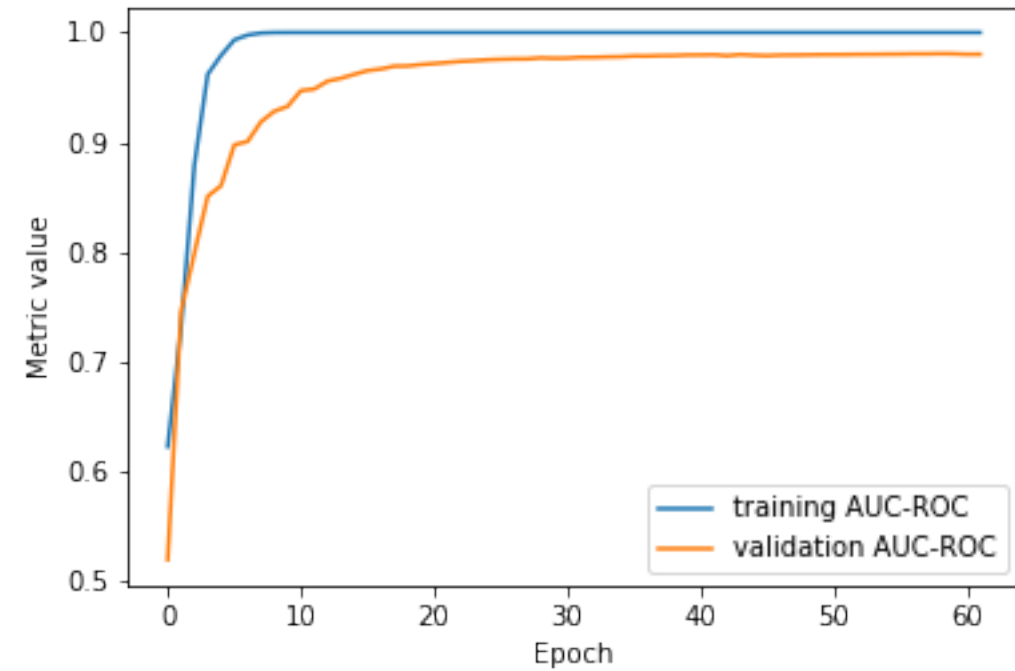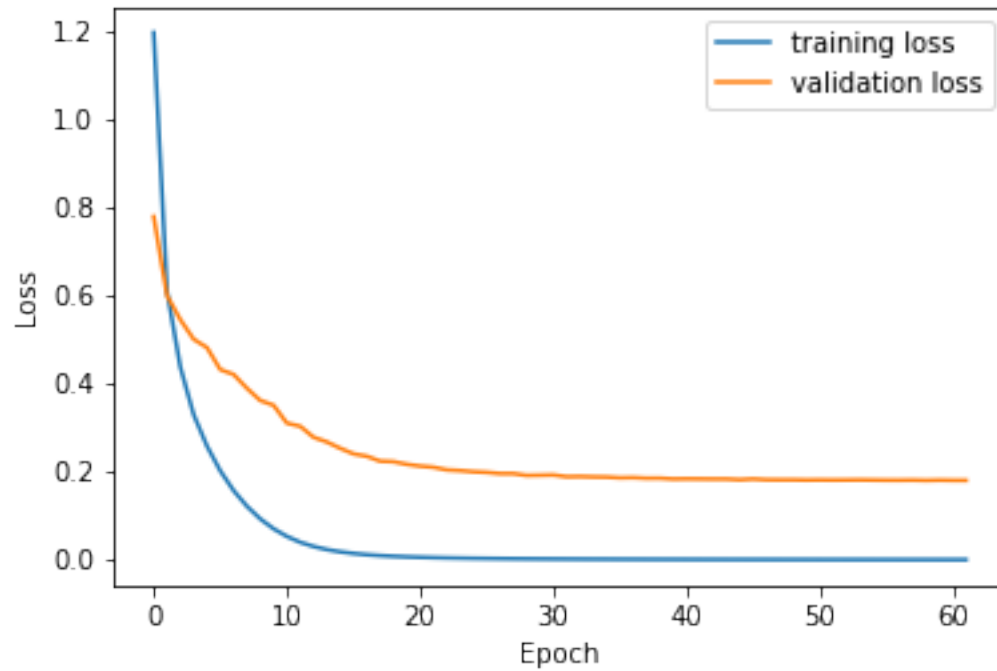
- Given 2-digit patient number *PP* and 1 digit night number *n*

dataFiles format = input*PPn*.csv

- Given record count R, number of cross validation folds C, and validation split V

batchSize = int((R*(1 - V))/C + 1)

Fit Histories

Results: Number of True/False

	REM	False REM	False NotREM	NotREM
Actual	1344	0	0	8330
Beta2	1007	585	337	7745
Beta1	5	40	1339	8290
Alpha	781	90	563	8240
Theta	143	34	1201	8296
Delta	1134	195	210	8135
RNN	1212	107	132	8221

Results: Percent of True/False

	REM	False REM	False NotREM	NotREM
Actual	13.89%	0.00%	0.00%	86.11%
Beta2	10.41%	6.05%	3.48%	80.06%
Beta1	0.05%	0.41%	13.84%	85.69%
Alpha	8.07%	0.93%	5.82%	85.18%
Theta	1.48%	0.35%	12.41%	85.76%
Delta	11.72%	2.02%	2.17%	84.09%
RNN	12.53%	1.11%	1.36%	85.00%

Results: Comparison

Model	Accuracy	Precision	Recall	F1-Score	Kappa
GACNN	91.00	92.00	91.00	91.00	90.00
DeepSleepNet		80.90	83.90	82.40	
SleepEEGNet		81.63	88.71	85.02	
This Model	97.30	93.08	89.32	90.86	90.00

Results: Comparing to Clinical Markers

	Slow Wave	V-Waves	K-complexes	Spindles	Sawtooth	Alpha
Frontal			Maximal			
Central		Maximal		Maximal	Maximal	Adequate
Occipital						Maximal
Fz-Cz	No					
E1-Fpz	Yes					

CNN Filters
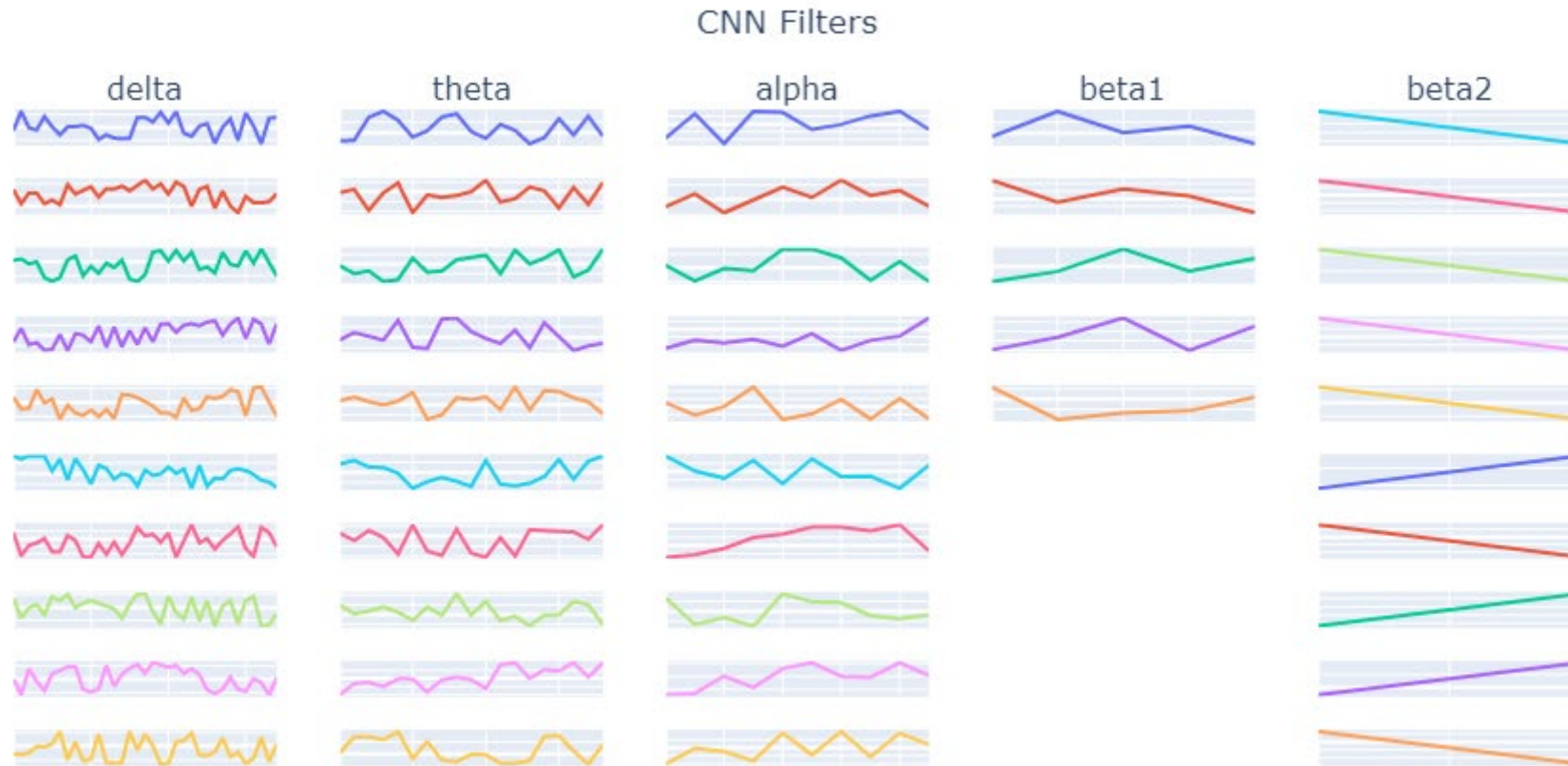
CNN Filters

CNN Filters -> Clinical Markers

CNN Filters

delta   theta   alpha
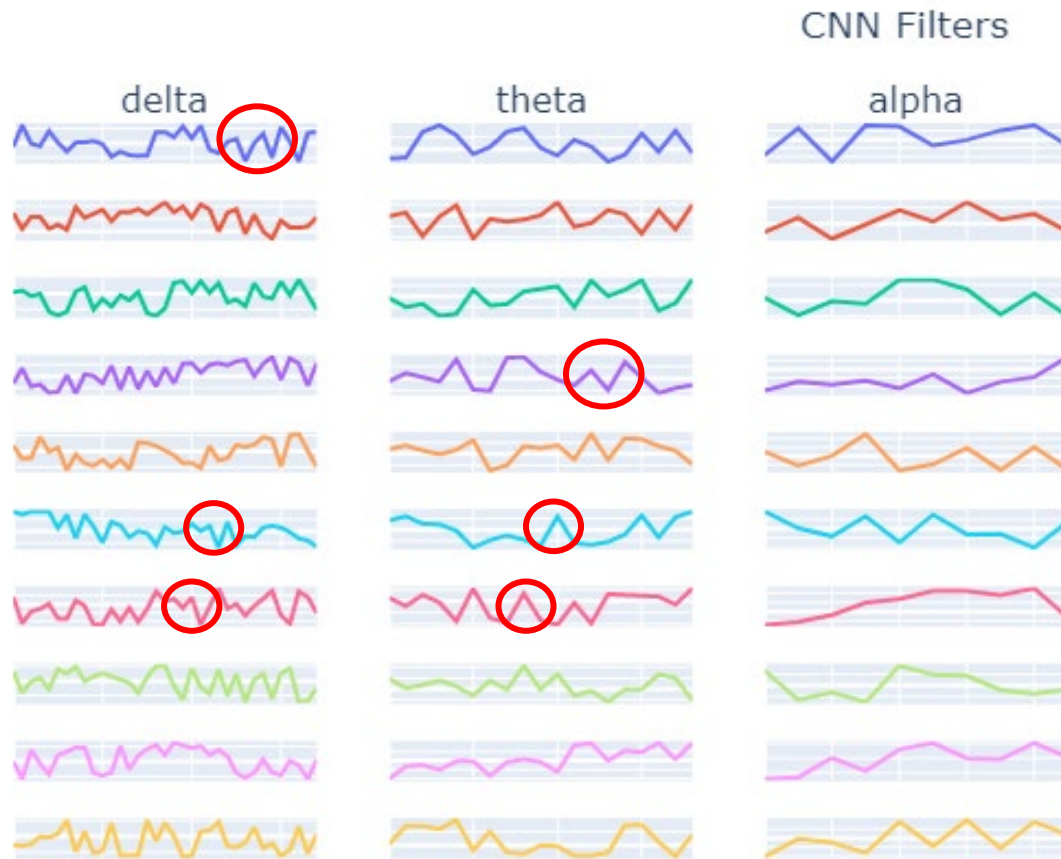
V-Wave   **K-complex**

- We demonstrate accurate REM detection from a single EEG channel, with performance approaching multi-channel polysomnography. Our model is also more interpretable, with the learned filters providing insights into how the network recognizes sleep stages. The simplified setup enables at-home sleep monitoring to aid diagnosis of sleep disorders.

- We believe these findings significantly advance the state-of-the-art in automatic sleep stage classification using reduced physiological measurements.

- The result of this research has been submitted recently:

- Gabriel Toban, Khem Poudel, and Don Hong, *REM Sleep Stage Identification with Raw Single Channel EEG,* manuscript submitted to Bioengineering, July 2023.