Predictive Modelling of Mental Disorders Using EEG Signal Analysis: A Review of DNN Approaches

Farah Shan Khan 1,2 and Shalini Ninoria³

Review Paper

¹Research Scholar Teerthankar Mahaveer University, Moradabad, U.P., INDIA

² Maharana Pratap Engineering College, Kanpur, U.P., INDIA

³ Teerthankar Mahaveer University, Moradabad, U.P., INDIA

Email: farahshankhan@gmail.com Received: 4 Oct 2023, Revised: 19 Nov 2023 Accepted: 21 Nov 2023

Abstract:

This paper provides a comprehensive review of deep neural network (DNN) approaches in predictive modeling of mental disorders through the analysis of electroencephalography (EEG) signals. The growing significance of leveraging advanced computational techniques in mental health research is explored, with a focus on DNN methodologies. The review encompasses an analysis of various studies and methodologies employed for predictive modeling using EEG data, highlighting the strengths and limitations of different DNN architectures. Insights into the potential applications of predictive modeling for mental disorders, such as early diagnosis and personalized treatment strategies, are discussed. Additionally, challenges and future directions in this burgeoning field are outlined to guide further research endeavors. This paper serves as a valuable resource for researchers, practitioners, and professionals seeking a nuanced understanding of the evolving landscape of predictive modeling for mental disorders utilizing EEG signal analysis and DNN approaches.

Keywords: Mental disease, EEG, CNN, DNN

1. Introduction

An unexpected revelation has emerged from the World Health Organization (WHO), shedding light on the alarming fact that an estimated 322 million individuals across the globe are grappling with the profound burden of depression. This staggering figure underscores the pivotal role that depression plays in the escalating prevalence of disability cases worldwide. This alarming statistic underscores the profound global impact of this mental illness. The identification and diagnosis of depression hinge on a spectrum of observable symptoms. Individuals affected by depression often describe a persistent and overwhelming sense of sorrow, which is frequently accompanied by emotions of helplessness and shame. Furthermore, those who battle depression typically experience a marked loss of interest in previously cherished hobbies and activities. They commonly wrestle with an overwhelming sense of fatigue and lethargy, as their energy levels plummet and their ability to maintain focus deteriorates. Moreover, depression frequently leads to disruptions in crucial daily activities. Variations in appetite, which can manifest as a noticeable increase or decrease, become a conspicuous hallmark. Sleep disturbances, such as difficulty falling asleep or excessive drowsiness, drastically disrupt sleep patterns. As a result of depression, even the most basic routines, from work obligations to personal relationships, become challenging to execute and derive pleasure from [1]. The intricate interplay of these symptoms vividly illustrates the severe toll that this condition exacts on those who experience it. Poverty, unemployment, traumatic life experiences, physical illnesses, and struggles with alcohol or drug abuse are just a handful of the many contributing factors that can precipitate the onset of

depression [1]. Recent measures implemented in response to the COVID19 pandemic, such as lockdowns, quarantine protocols, and social isolation, have amplified the prevalence of depression [2–4]. This surge in cases is a cause for concern, given that depression represents a significant public health risk and is linked to severe outcomes, including suicide [5]. Emphasizing the importance of early detection is paramount, given the gravity of this issue and its farreaching consequences for individuals and communities. Identifying depression at an early stage can facilitate faster and more effective treatment. Hence, the development of a reliable and efficient tool for the identification or even prediction of depression takes on even greater significance. Such a tool would not only enhance the lives of those affected but also alleviate the strain on healthcare systems and society as a whole. Electroencephalogram (EEG) signals, which exhibit nonstationary, highly intricate, noninvasive, and nonlinear characteristics, offer a unique window into the functioning of the human brain [6]. Due to the inherent complexity of these signals, anomalies are challenging to discern with the naked eye. Nonetheless, these physiological signals are incredibly valuable for depression identification [7]. The basic diagram for the EEG based signal classification system is shown in Figure 1. Here, the initially recorded EEG signal is preprocessed to get rid of unwanted artifacts, next models are applied to extract features of the EEG signals which are further used to classify normal and depressed person.

Figure 1: EEG based signal classification

A computational framework known as deep learning employs a hierarchical structure, consisting of a series of algorithms utilizing hidden neural units or neurons [8]. These models empower computers to derive sophisticated and nuanced concepts from basic data inputs. As these concepts are learned, they serve as the fundamental building blocks for the development of additional layers of understanding. Furthermore, these methodologies incorporate multiple layers of processing, each playing a pivotal role in pattern recognition and deciphering the underlying data structure [9]. The innate capacity of deep learning architectures for automated learning and the extraction of significant features from raw input data is what make them so appealing. This stands in contrast to the limitations often associated with traditional machine learning techniques [10]. Manual analysis can also be a challenging task given the intricate and nuanced nature of EEG data [11]. Consequently, deep learning solutions have gained popularity in related contexts as they offer an efficient way to extract implicit nonlinear features from EEG data with minimal manual effort [12]. These applications underscore the formidable power of deep learning in making sense of complex data across a wide range of domains, including those with substantial real-world impact.

2. Introduction to EEG Signals

Electroencephalography (EEG) is a non-intrusive neuroimaging method designed to capture the electrical activity produced by the brain. This approach entails the placement of electrodes on the scalp to document voltage fluctuations arising from the combined electrical signals of brain cells, or neurons. EEG signals provide valuable insights into the brain's dynamic activity and are widely used in clinical, research, and diagnostic settings.

Basic Principles: The brain's neurons communicate by generating electrical potentials, and these signals can be detected on the scalp. EEG captures the summation of these electrical activities, offering a temporal

resolution in the order of milliseconds. It reflects neural processes related to sensory perception, motor control, cognition, and emotional responses.

Electrode Placement: EEG electrodes are strategically positioned on the scalp, typically following standardized systems such as the 10-20 system [12]. The electrodes are arranged in a grid, and their placement allows for the monitoring of electrical activity across different regions of the brain. Common electrode configurations include Fp1, Fp2, F7, F8, C3, C4, P3, P4, O1, and O2, among others.

Figure 2: Schematic diagram of channel position in the brain

Frequency Bands: EEG signals are characterized by different frequency bands, each associated with specific brain states and activities. The main frequency bands include delta (1-4 Hz), theta (4-8 Hz), alpha (8-12 Hz), beta (12-30 Hz), and gamma (>30 Hz) [12]. Changes in the power and distribution of these frequency bands can offer insights into cognitive processes, arousal levels, and pathological conditions.

Figure 3: Schematic diagram of EEG waveform rhythm

Challenges and Advances: Despite its many applications, EEG signals are sensitive to artifacts, such as muscle activity and external interference, which can affect data quality. Advanced signal processing techniques, including machine learning and deep learning, are increasingly being applied to enhance the extraction of meaningful information from EEG data, leading to more accurate and nuanced interpretations.

3. Comparison of State of the Art Classification Technologies

Convolutional Neural Network: Convolutional Neural Networks (CNNs) are a class of deep neural networks specifically designed for processing grid-like data, making them particularly effective in computer vision tasks. The fundamental building blocks of a CNN include convolutional layers, pooling layers, and fully connected layers. In the convolutional layers, filters or kernels convolve across the input data to detect spatial hierarchies and local patterns. These layers enable the network to automatically learn relevant features from raw data, reducing the need for manual feature engineering. Pooling layers follow convolutional layers, downsampling the spatial dimensions of the representation and enhancing translation invariance. Fully connected layers at the end of the network combine high-level features for classification or regression. CNNs exhibit parameter sharing, where the same set of weights is used across different spatial locations, significantly reducing the number of parameters compared to fully connected networks. This parameter sharing contributes to the computational efficiency of CNNs, making them suitable for large-scale image datasets. Training a CNN involves adjusting the weights using optimization algorithms and backpropagation. While CNNs excel in image-related tasks, their effectiveness is contingent on appropriate hyperparameter tuning, and they may lack interpretability due to their "black-box" nature. Ongoing research aims to enhance the interpretability and robustness of CNN architectures across various applications.

Recurrent Neural Network: Recurrent Neural Networks (RNNs) constitute a class of neural networks designed to process sequential data by maintaining a hidden state that captures information from previous time steps. The core feature of RNNs is their ability to handle input sequences of varying lengths, making them well-suited for tasks such as natural language processing and time series analysis. In an RNN architecture, each step involves the input being processed along with the hidden state from the previous time step. This recurrent connection allows RNNs to capture temporal dependencies and context in sequential data. However, traditional RNNs face challenges in retaining long-term dependencies due to the vanishing and exploding gradient problems during training. Long Short-Term Memory (LSTM) networks and Gated Recurrent Units (GRUs) are variations of RNNs that address these issues by incorporating specialized gating mechanisms. LSTMs, for instance, utilize memory cells and gates to selectively retain and update information, enabling them to capture long-term dependencies more effectively. Despite their effectiveness, RNNs still encounter challenges such as difficulties in parallelization and sensitivity to sequence lengths. Ongoing research explores variations and improvements, such as attention mechanisms and Transformer architectures, to enhance the performance of RNNs across a broad range of sequential data applications.

Deep Neural Network: Deep Neural Networks (DNNs) represent a class of artificial neural networks with multiple layers, allowing them to model intricate relationships within data. The architecture of a DNN typically consists of an input layer, one or more hidden layers, and an output layer. Each layer contains nodes, or neurons, with associated weights and biases that are adjusted during training. The network's depth, achieved through stacking multiple layers, enables it to automatically learn hierarchical representations of features from raw input. Activation functions introduce non-linearity into the model, allowing DNNs to capture complex patterns and relationships in data. The process of training a DNN involves forward propagation, where input data is processed through the network to generate predictions, and backward propagation, which adjusts the weights and biases based on the computed error. While DNNs have demonstrated remarkable success in various domains, including image and speech recognition, they face challenges such as the need for substantial labeled data, sensitivity to hyperparameters, and the potential for overfitting. Techniques like regularization, dropout, and batch normalization are employed to mitigate these challenges and improve the generalization ability of DNNs. Ongoing research explores novel architectures, optimization algorithms, and transfer learning strategies to further enhance the efficiency and applicability of deep neural networks across diverse tasks.

The Table 1, provides a concise overview of the key features, strengths, and use cases of CNNs, RNNs, and DNNs, highlighting their respective architectures and applications in different domains. It's important to note that while CNNs and RNNs have specific strengths in handling certain types of data, DNNs serve as a more general framework that can be adapted to various machine learning tasks. The choice of architecture depends on the nature of the data and the requirements of the specific task at hand.

Table 1: Comparison of CNN, RNN and DNN

4. Important Processes for DNN based Mental Disorder Prediction

To conduct a predictive modeling analysis for mental disorders using EEG (Electroencephalogram) signal data, several systematic steps are typically followed to ensure the accuracy and reliability of the predictive model. These steps involve data collection, preprocessing, feature extraction, model selection, training, evaluation, and validation. Here's an expanded explanation of each step:

Data Collection: The first crucial step is the collection of EEG signal data from individuals. This data is typically gathered using electrodes placed on the scalp. The number and placement of electrodes can vary depending on the specific research or clinical requirements. It's essential to ensure that the data collection process follows established ethical guidelines and informed consent procedures.

Preprocessing: After the collection of EEG data, a critical phase in the data processing pipeline involves addressing the presence of diverse noise and artifacts inherent in the recordings, such as eye blinks, muscle movements, and electrical interference. To ensure the reliability and accuracy of subsequent analyses, various preprocessing steps are employed to clean the EEG data. One prevalent issue tackled during preprocessing is the removal of unwanted noise. Techniques like wavelet transforms play a significant role in identifying and isolating noise components in the data. By decomposing the EEG signal into different frequency bands, wavelet transforms enable the separation of genuine neural activity from undesired artifacts. Independent Component Analysis (ICA) is another powerful tool in the preprocessing arsenal. ICA works by decomposing the EEG data into statistically independent components, allowing for the identification and removal of components associated with artifacts. This method is particularly effective in isolating sources such as eye blinks or muscle activity from the neural signal. Furthermore, filtering techniques are commonly applied to eliminate unwanted frequency components that may distort the EEG signal. Low-pass, high-pass,

and band-pass filters are strategically used to retain the frequency range relevant to neural activity while attenuating noise and artifacts outside this range. Filtering enhances the signal-to-noise ratio, enabling a clearer representation of neural information.

Feature Extraction: Following the preprocessing of EEG data, the next crucial step involves the extraction of meaningful features. This process is essential for distilling relevant information from the preprocessed EEG signals, laying the groundwork for subsequent predictive modeling. Features extracted from EEG data can be broadly categorized into linear and nonlinear types, each capturing distinct aspects of neural activity. Linear features often include measures such as power in specific frequency bands. The distribution of power across different frequency ranges, known as spectral power, provides valuable insights into the intensity and distribution of neural activity. For example, the power in delta, theta, alpha, beta, and gamma frequency bands can be computed to characterize different aspects of brain function. On the other hand, nonlinear features delve into the complexity and dynamics of EEG signals. Measures like wavelet entropy, which quantifies the irregularity and unpredictability of signals across different scales, fall into the category of nonlinear features. These nonlinear descriptors capture intricate patterns and nuances within the EEG data that may not be fully captured by linear measures. Feature extraction techniques play a crucial role in condensing the voluminous EEG data into a set of informative features that can be leveraged for predictive modeling. The selection of specific features depends on the research or clinical objectives and the characteristics of the EEG data under investigation. Well-chosen features not only enhance the interpretability of the data but also contribute to the development of robust and accurate predictive models. In essence, feature extraction acts as a bridge between raw EEG data and the subsequent modeling phase, facilitating a more nuanced understanding of the underlying neural processes.

Data Splitting: In the data preparation phase, the dataset is meticulously partitioned into three distinct subsets: the training set, the validation set, and the test set. Each subset serves a crucial role in the iterative process of developing and refining a predictive model. The training set, constituting the largest portion of the dataset, acts as the foundation for the model's learning process. During this phase, the model adjusts its internal parameters by analyzing patterns and relationships within the training data, effectively acquiring the knowledge necessary for making predictions. Following the initial training phase, the validation set assumes a pivotal role in the model development pipeline. This subset is utilized to fine-tune the hyperparameters of the model, ensuring optimal performance and preventing overfitting. By assessing the model's performance on data not used during training, the validation set provides a reliable gauge of the model's ability to generalize to unseen instances. Once the model has undergone iterative refinement based on the validation set, the ultimate test of its efficacy lies in the test set. This distinct subset, held separate from both the training and validation sets, serves as an unbiased assessment ground. The model's accuracy and generalization capabilities are rigorously evaluated using the test set, providing an unbiased measure of how well the model is expected to perform on entirely new, unseen data in real-world scenarios. This three-fold division of the dataset into training, validation, and test sets establishes a robust framework for the development, finetuning, and evaluation of predictive models, ensuring their reliability and effectiveness in practical applications

Model Selection: Upon the completion of feature extraction from EEG data, the selection of an appropriate machine learning or deep learning model becomes a critical step in the predictive modeling process. The choice of model depends on the specific nature of the predictive task, the characteristics of the dataset, and the desired outcomes. Various algorithms, each with its strengths and suitability for different types of data, are considered by researchers or clinicians. CNNs, known for their effectiveness in handling grid-like data, are often employed when the spatial relationships and patterns within the EEG signals are crucial. CNNs excel in image-related tasks and have been successfully applied to capture spatial hierarchies and local features in EEG data, particularly in tasks like brain-computer interface applications or image-based neuroimaging. RNNs are favoured when the temporal dynamics and sequential dependencies within the EEG signals are paramount. RNNs, with their ability to capture information over time, are well-suited for tasks such as time series prediction or the analysis of EEG recordings where the temporal sequence of neural activity is vital. SVMs, a traditional machine learning algorithm, are known for their versatility and effectiveness in classification tasks. SVMs can be applied when the predictive task involves categorizing EEG data into

different classes or conditions. SVMs are particularly useful in scenarios where the dataset is not as large or complex compared to deep learning counterparts.

 The selection of the most suitable algorithm is not limited to CNNs, RNNs, or SVMs; other machine learning models, such as decision trees, random forests, or ensemble methods, may also be considered based on the specific requirements of the task at hand. Ultimately, the choice of model is a nuanced decision that takes into account the intricacies of the EEG data, the complexity of the predictive task, and the computational resources available for training and inference. Researchers and clinicians leverage their expertise to make informed decisions that optimize the performance and interpretability of the chosen model for the given application.

Training: Once the appropriate machine learning or deep learning model is selected, the training phase ensues using the designated training dataset. This crucial step involves exposing the model to the preprocessed EEG data and guiding it to learn the intricate mapping between the extracted features and the target outcome, which could be a specific diagnosis like depression. The essence of the training process lies in the optimization of the model's parameters. These parameters are the internal weights and biases that the model adjusts iteratively to minimize the prediction errors. The objective is to enhance the model's ability to accurately predict the target outcome based on the learned patterns and relationships within the training data. The optimization is typically achieved through the use of an appropriate optimization algorithm, such as stochastic gradient descent or its variants. During training, the model continuously refines its internal parameters, making adjustments to better align its predictions with the actual outcomes in the training dataset. This iterative optimization process continues until the model achieves a state where further adjustments do not significantly reduce prediction errors, indicating convergence. The effectiveness of the trained model is evaluated through metrics such as accuracy, precision, recall, or F1 score, depending on the specific nature of the predictive task. The goal is to ensure that the model generalizes well to new, unseen data, providing reliable predictions beyond the training set. In the context of EEG-based predictive modeling, this training phase holds the key to unlocking the model's ability to discern patterns associated with the target outcome, whether it be a clinical diagnosis or another relevant measure. The success of the subsequent application of the model hinges on the thoroughness and effectiveness of this training process.

Hyperparameter Tuning: After the initial training phase, the fine-tuning of model hyperparameters becomes a critical step to optimize the model's performance and prevent overfitting. Hyperparameters, including learning rates, batch sizes, and network architectures, play a pivotal role in determining how the model learns from the data and generalizes to new, unseen instances. This fine-tuning process is typically carried out using a separate dataset known as the validation dataset. The validation dataset serves as an independent set of samples not used during the initial training phase. By evaluating the model's performance on this dataset, researchers or clinicians can gain insights into how well the model is likely to generalize to new, unseen data. The primary goal of hyperparameter tuning is to enhance the model's ability to capture complex patterns in the data while avoiding issues such as underfitting or overfitting. Learning rates, which determine the size of steps taken during parameter updates, are adjusted to strike a balance between convergence speed and stability. Batch sizes, specifying the number of samples processed in each iteration, are fine-tuned to optimize computational efficiency and model generalization. Network architectures, including the number and size of layers, activation functions, and other architectural choices, are modified to ensure the model complexity aligns with the task requirements. Through an iterative process of adjusting hyperparameters and evaluating performance on the validation dataset, researchers can identify configurations that lead to improved model generalization. Overfitting, where the model performs well on the training data but poorly on new data, is a particular concern. Fine-tuning ensures that the model is not overly specialized to the training dataset and can robustly handle a variety of inputs. Ultimately, the fine-tuning of hyperparameters is an essential practice in machine learning and deep learning, contributing to the development of models that not only perform well on the training data but also demonstrate reliable and consistent performance on new, unseen data.

Evaluation: Following the training and fine-tuning phases, the model's performance is rigorously evaluated using a separate and independent dataset known as the test dataset. This evaluation provides a robust assessment of the model's ability to generalize to entirely new and unseen instances, offering insights into its

real-world applicability. In the context of mental disorder prediction, several key evaluation metrics are commonly employed:

- 1. Accuracy: This metric quantifies the overall correctness of the model's predictions, measuring the ratio of correctly predicted instances to the total number of instances in the test dataset. While accuracy provides a general sense of model performance, it may not be sufficient when classes are imbalanced.
- 2. Sensitivity (Recall): Sensitivity, also known as recall, gauges the model's ability to correctly identify instances of the positive class (e.g., individuals with a mental disorder) among all actual positive instances in the test dataset. It is particularly relevant when the consequences of false negatives are significant.
- 3. Specificity: Specificity assesses the model's capacity to correctly identify instances of the negative class (e.g., individuals without a mental disorder) among all actual negative instances in the test dataset. It is crucial for scenarios where minimizing false positives is important.
- 4. Area Under the ROC Curve (AUC-ROC): The ROC curve illustrates the trade-off between true positive rate (sensitivity) and false positive rate across different decision thresholds. The AUC-ROC quantifies the area under this curve and provides a comprehensive measure of the model's discriminative ability. A higher AUC-ROC suggests superior performance in distinguishing between positive and negative instances.

These metrics collectively offer a nuanced understanding of the model's strengths and weaknesses. While accuracy provides an overall assessment, sensitivity and specificity offer insights into the model's performance with respect to each class. AUC-ROC provides a comprehensive evaluation of the model's ability to discriminate between classes at various decision thresholds. Successful performance across these metrics indicates that the predictive model has effectively learned patterns from the training data, generalized well to new instances in the test dataset, and holds promise for real-world applications in mental disorder prediction.

Validation: The validation of the model's predictive capabilities involves a crucial step where its predictions are compared against clinical diagnoses or other established reference standards. This process is essential for assessing the model's real-world utility and reliability in practical applications. By aligning the model's outputs with known clinical diagnoses, researchers and clinicians can gauge the accuracy and effectiveness of the model in making predictions relevant to mental health. For instance, consider a traditional DNN model designed for mental health prediction based on EEG data, as illustrated in Figure 4. The model takes preprocessed EEG features as input and, after undergoing training, fine-tuning, and evaluation phases, generates predictions related to mental health conditions. The model's outputs are then compared with clinical diagnoses provided by experts or other well-established reference standards. This validation step serves as a critical checkpoint to ensure that the model's predictions align with ground truth information, verifying its capacity to provide meaningful insights into mental health conditions. The agreement between the model's predictions and clinical diagnoses substantiates the model's real-world applicability and potential as a valuable tool for supporting clinical decision-making. In Figure 4, various components of the DNN architecture may represent layers, nodes, or other architectural elements involved in the processing and transformation of EEG data. The complexity and depth of the model architecture are informed by the specific requirements of the predictive task and the characteristics of the EEG dataset. In conclusion, the validation of the model against clinical diagnoses or reference standards is a pivotal step in ensuring the trustworthiness and effectiveness of the model in real-world scenarios, especially in the context of mental health prediction based on EEG data. This validation process contributes to the model's credibility and its potential to enhance diagnostic processes and inform treatment decisions.

Figure 4: EEG based Depression prediction using DNN

5. Literature Survey

In recent years, the utilization of deep learning techniques in conjunction with EEG signals for the diagnosis of depression has witnessed a significant surge. This section is primarily aimed at conducting a systematic literature review (SLR) that focuses on papers dedicated to the application of deep learning for the detection or prediction of depression using EEG data.

5.1 Deep learning methods for depression detection using EEG signals

This subsection discusses the notable methods for depression detection using EEG signals.

Sharma et al. [13] introduced the DepHNN method for depression diagnosis, combining CNN and LSTM for EEG signal analysis. They applied Independent Components Analysis and Fast Fourier Transform for data quality and timefrequency extraction. Model optimization showed that reducing LSTM layers and increasing fully connected layers improved performance. The CNN transforms EEG data initially, and the LSTM block retains information, while fully connected layers aid in automatic depression detection. The Hybrid 6layer CNNLSTM model reduces time and complexity but faces challenges of overfitting and a small dataset.

Seal et al. [14] introduced DeprNet, an 18-layer CNN framework for EEG data. They employed ICA to remove artifacts and three filtering techniques to eliminate various types of interference. The input data was structured as a 2D matrix, processed through layers including convolution, batch normalization, maxpooling, and fully connected layers, ending with a softmax layer for classification. DeprNet used short 4second EEG inputs from 19 channels, proving effective for practical applications with higher accuracy compared to other models. However, implementing this method in clinical settings may pose challenges due to its complexity and layer count. Additionally, the study highlighted differences in how depression affects tasks in the left and right brain hemispheres.

Saeedi et. al [15] used GPDC and DDTF along with deep learning methods to detect brain connectivity through EEG signals. These methods were employed to analyze connections between EEG channels and transform 1D EEG signals into 2D images for deep learning classifiers. They tested five different deep learning algorithms, with the 1D CNNLSTM combinations showing the best performance in terms of accuracy and sensitivity. The 2DCNNLSTM approach, although faster and employing more parameters may filter out some temporal information. This research offers insights into deep learning algorithms and effective connectivity methods for EEG analysis, utilizing both temporal and spatial information. However, the study is limited by a small dataset and offers potential for further exploration of feature and parameter techniques to enhance accuracy.

Khan et al. [16] introduced a novel depression diagnosis model using a three dimensional (3DCNN) with connectivity in the default mode network (DMN) region of the brain, estimated from 19 channel EEG recordings. They used EEGLAB software to remove artifacts such as eye blinks and muscle movements, employing the Artifact Subspace Reconstruction (ASR) technique. The study involved 2second EEG segments for effective connectivity estimation using Partial Directed Coherence (PDC). After extracting DMN

connections, the 3DCNN model with three convolutional layers, batch normalization layers, activation layers, and a fully connected layer was built. Overfitting is a potential concern, and a larger dataset is needed to thoroughly evaluate this unique approach's performance and address any limitations before further validation and improvement.

Qayyum et al. [17] introduced two deep neural network models, IDCNNGRU and IDCNNLSTM, to analyze EEG data from two datasets related to eye open (EO) and eye closed (EC) conditions. These models utilized 19 EEG channels divided into 1second time frames. The IDCNN (1D CNN) with three convolutional layers, two maxpooling layers, and two dropout layers was used for feature extraction from EEG signals. Sequential

learning with LSTM or GRU networks was employed to capture temporal dependencies in the data. The final dense layer's extracted features were used as inputs for a classification layer with a sigmoid function for binary classification. The study considered various training hyperparameters like learning rates, optimizers, and loss functions for model optimization. GRU outperformed LSTM due to its suitability for short sequences and lower training parameters and memory requirements. However, the study highlighted the need for further research into aspects like time window segmentation, dataset size, and the specific features being extracted, suggesting room for further optimization and refinement in this field of study.

Thoduparambil et al.'s [18] research utilized a robust 12layer CNNLSTM model for depression identification using EEG data. The EEG data underwent two preprocessing steps, initially removing artifacts with the FASTER method, and then addressing offset effects and amplitude scaling issues with the same method. The model comprised three main parts: a classification segment, LSTM units for memory and sequential learning, and a CNN. The first part featured three CNN layers and three MaxPooling1D layers for extracting essential EEG data features. The second part included two LSTM layers for identifying distinct EEG data patterns and maintaining their temporal order. Two fully connected layers, a dropout layer, and a flatten layer were designed for classification. The Flatten layer was crucial in converting the output of the LSTM layers into a feature vector. Interestingly, the study found that the right hemisphere's EEG signals had a more significant impact on diagnostic results than the left hemisphere's signals. However, the study recognized limitations, including the need for a larger dataset to enhance model accuracy and robustness, concerns about overfitting, exploration of more advanced feature extraction and analysis techniques, and the need for a more comprehensive justification of the dataset used.

Kang et al. [19] developed a two-dimensional convolutional layer-based model using EEG signals from both eye-closed (EC) and eye-opened (EO) states. They started by removing power line interference with a 50 Hz notch filter after data collection. The EC dataset underwent artifact removal to eliminate eye blink and muscle movement noise, achieved through a low pass filter removing frequencies above 32 Hz. Following preprocessing, signals were decomposed into Delta, Theta, Alpha, and Beta frequency ranges. The suggested model featured 11 layers, including a (CNN with two Conv2D layers, ReLU activation, Max-pooling layers, and a dropout layer. The final element was an output layer with a single dense layer and ReLU activation. Additionally, a fully connected layer included two dense layers and a dropout layer. The model's performance was assessed and validated using tenfold cross validation, demonstrating higher accuracy compared to other models using the same dataset. However, the study pointed out a limitation due to insufficient data, emphasizing the need for a larger dataset to enhance the model's generalizability and robustness.

Duan et al. [20] conducted a study on Major Depressive Disorder (MDD) patients, analyzing EEG patterns. They used preprocessing techniques, including ICA and a FIR filter, to remove unwanted signals and visual aberrations from the EEG data. They extracted Theta, Beta, and Alpha frequency bands using the (FFT technique and computed interhemispheric asymmetry and cross-correlation values. These derived data were used to investigate structural and connectivity alterations. The study generated three feature matrices, including single-feature matrices for each frequency band and a mixed feature matrix, to understand the impact of depression on MDD patients.

Saeedi et al. [21] conducted research to predict outcomes in a three-step process: feature extraction, feature selection, and classification. They used Discrete Wavelet Transform (DWT) for preprocessing to remove artifacts based on specific thresholds and extracted five major EEG frequency bands. Nonlinear features were derived using sample entropy and estimate entropy on wavelet packet coefficients. Feature selection was performed using a genetic algorithm (GA) to reduce feature dimensionality. For classifying depression cases, they employed K-nearest neighbors (KNN), SVM, and a deep learning approach called the multilayer perceptron (MLP). Notably, the MLP model combined with nonlinear features achieved higher accuracy than linear features in deep learning. Among the linear features, the Gamma power band demonstrated particularly excellent accuracy. While the study aimed to use different EEG data features for improved prediction, further enhancement of these parameters is needed for better results.

Y. Xie et al. [22] developed a CNN model that incorporated functional connectivity within brain networks in their study. They started with EEG signal preprocessing, removing artifacts. They constructed a 31x31

adjacency matrix using the Phase Lag Index (PLI) approach, reflecting functional connectivity within the Delta, Alpha, Beta, Theta, and Gamma frequency ranges. The study considered a brain network as a graph with nodes representing brain regions recording EEG data and edges representing connections between these nodes. Input data for the brain network was created by assessing the strength of connections between nodes using the PLI approach. They built CNN2, a simple deep learning model with one convolutional layer and two pooling layers. The study explored six models by combining CNN2, DBN, and LDA algorithms with brain networks and Prefrontal Lateralization techniques. The results favored CNN2 and brain networks as the most promising among these models. It's important to note that using a simple CNN model posed the risk of overfitting the classification result, and improving accuracy could be achieved by adding more data or using tools like LSTM.

X. Zhang et. al [23] tested two models for predicting MDD using 1D CNN with and without a demographic attention mechanism. They aimed to assess how integrating demographic and EEG data affected prediction accuracy. The data was preprocessed using Kalman filtering and DWT to remove noise. EEG data were divided into non-overlapping 4-second time windows from 40-second segments. Demographic data was converted into a 1D format using One Hot Encoding and normalization. The 1D CNN model extracted spatialtemporal information, and an attention mechanism indirectly updated it with demographic information. The final classification result was obtained using the softmax function with a fully connected layer. The results showed that the CNN model with demographic consideration outperformed the one without it. DEEPDREAM was used to create artificial EEG signals, revealing that Beta frequency bands were the primary distinction between the generated signals. This research successfully utilized demographic data to achieve good diagnostic accuracy. However, it's important to acknowledge limitations, such as the need for more extensive data and the potential for overfitting, and conduct a more comprehensive analysis of the integration and impact of demographic data.

C. Uyulan et al. [24] presented three CNN-based models: ResNet50, MobileNet, and Inceptionv3, combined with advanced computational neuroscience techniques. These models were applied to EEG recordings from both the left and right hemispheres during eye-closed states. Preprocessing involved removing artifacts from eye and muscle activities using the wavelet transform method and applying a 50 Hz notch filter to reduce power line interference. Further noise removal included the use of bandstop filters, FastICA method, and a Butterworth bandpass filter to extract Delta, Theta, Beta, and Alpha frequency bands. The Parks-McClellan optimal FIR filter algorithm minimized error in passbands and stopbands. The output signals were transformed into 2D EEG image matrices for input into the CNN structures. ResNet50 addressed gradient vanishing issues with its 22-layer residual learning capabilities. MobileNet leveraged depthwise and separable convolutions, enhancing performance. Inceptionv3, with its ability to prevent information loss, was also used. MobileNet achieved the highest accuracy in hemispheric classification, while ResNet50 performed best in frequency band-based classification. The proposed models introduced innovation by integrating CNNbased techniques, but their complexity might limit clinical application. Further evaluation with a larger dataset is needed to confirm the attained accuracy.

Z. Wan et al. [25] utilized a model called HybridEEGNet, which is essentially a CNN with a strong emphasis on feature analysis, to predict Major Depressive Disorder (MDD). Their approach involved using two types of convolutional filters to capture synchronous and regional EEG signal properties for in-depth analysis. The analysis process included creating feature matrices using the deep dreaming algorithm and then using the FFT technique to analyze these matrices. Their model consisted of 21 layers, including convolutional, maxpooling, fully connected, and concatenation layers, along with a softmax layer for classification. The FFT analysis revealed that specific features, particularly variations in amplitude ranges and spatial patterns within the Alpha frequency band, contained crucial information about depressive cases. The study highlighted the importance of the 4-10 Hz frequency band as a significant low-frequency range for diagnostic purposes and the critical role of Theta and Alpha rhythms in identifying depression with notable performance. Despite these findings, the study acknowledged limitations such as the scarcity of adequate data, which raised concerns about the validity of their results. They also emphasized the need to review the feature extraction process and related accomplishments for further improvements.

Mumtaj et al.'s [26] used two deep learning models: the One-Dimensional (1DCNN) and 1DCNN with LSTM. The 1DCNN consisted of 31D Convolutional layers, two pooling layers, one dropout layer, and three additional layers, designed to learn and transform temporal information. The second model had three blocks, each containing one 1D Convolutional layer, one pooling layer, and one dropout layer, followed by two LSTM layers. These models aimed to analyze EEG data for their study. They employed the Multiple Source Eye Correction (MSEC) approach to preprocess the raw input data, removing artifacts caused by muscle activity, heartbeats, and eye blinks. The EEG signals were segmented into 1-second time windows, and the MSEC approach effectively corrected noise originating from eye blinks and muscular activity during EEG recordings. Interestingly, they found that signals recorded with eyes open (EO) resulted in better categorization results compared to signals recorded with eyes closed (EC). However, the study acknowledged limitations, including a small dataset and the use of a relatively short time window for segmentation. While they claimed that a 1 second window size offered optimal performance, further empirical data are needed to support this assertion.

Mahato et al.'s [27] effectively recognized depression by combining four deep learning classifiers: the Multi-Layered Perceptron Neural Network (MLPNN), the Radial Basis Function Network (RBFN), the Linear Discriminant Analysis (LDA), and the Quadratic Discriminant Analysis. They extracted linear and nonlinear features from EEG data, including power in Alpha, Beta, Delta, and Gamma frequency bands and hemisphere asymmetry in Alpha, Beta, Delta, and Gamma. Principal Component Analysis (PCA) was used to manage the dimensionality of nonlinear features, and Independent Component Analysis (ICA) was employed to remove artifacts from the data. The study found that combining linear and nonlinear features with the MLPNN or RBFN classifiers achieved the highest accuracy in depression diagnosis. Additionally, the use of the LDA classifier with two specific nonlinear features, Wavelet Entropy (WE) and Relative Wavelet Energy (RWE), produced the second-highest accuracy, surpassing the performance of any classifier when coupled with linear features. The study also highlighted the potential importance of Theta power in achieving high accuracy in detecting depression. Further research is needed to validate and generalize these findings, especially regarding the role of Theta power in depression diagnosis.

X. Li et al. [28] focused on predicting outcomes by combining ensemble learning and deep learning methods. They conducted a comprehensive analysis of EEG signals, considering temporal, spectral, and spatial aspects. They used the autoregressive model and Hjorth algorithms with varying time windows to extract features such as power spectral density and activity. They also transformed EEG signals into images using the auditory evoked potentials (AEP) method, incorporating spatial information. Two VGG-style architectures were used, culminating in a dense layer and a softmax layer for classification. The study revealed that the Alpha frequency band outperformed Beta and Theta frequencies in predictive accuracy. Features played a pivotal role in achieving high accuracy. However, the use of the AEP method presented challenges related to distance-based projection, potentially overlooking non-distance-related aspects. Improving the management of noisy signals from EEG inputs is crucial for enhancing overall performance.

Acharya et al. [29] introduced CNN and deep neural network techniques for depression identification. Their 13-layer CNN model comprised five convolutional layers, five pooling layers, and three fully connected layers. Features from EEG data were extracted by the convolutional layers, and the pooling layers reduced the size of feature maps. The fully connected layers established connections between neurons in different layers. Sensitivity and accuracy were better when using signals from the right hemisphere. However, the model may be prone to inaccurate predictions due to the limited data and its complex architecture.

W. Mao et. al [30] emphasized preprocessing of raw EEG signals to create sample input data for deep learning algorithms. The EEG signals were segmented into 270-second intervals, noise was removed, and Electrooculography (EOG) interference was minimized. They extracted Theta, Alpha, and Beta frequency bands as the primary steps in data preparation. The AutoRegress model (AR model) was used to compute electrode power and segment it into 0.5-second windows. Power spectrum density was used while preserving the temporal properties of the EEG data. They employed two projection models, one based on distance and the other not, to maintain spatial information. Among the deep learning models, CNN, Temporal Convolution, MAX, and LSTM were used for classification, with the LSTM model performing less effectively than the others when working with non distance mapping frames. Input data limitations and relatively low accuracy suggest potential for improvement through parameter configuration optimization.

Cai et al. [31] conducted a study for the diagnosis of depression, combining deep learning and machine learning algorithms. They gathered EEG data using electrodes on the frontal scalp. Preprocessing included removing noisy signals using the wavelet transform method, and linear features like Alpha, Theta, Beta, and Gamma frequencies were extracted after noise reduction. After normalizing the data, they created a feature matrix for deep learning models. A combination of Deep Belief Network (DBN) and the retrieved features outperformed other approaches. The study revealed the potential for increasing classification accuracy using beta wave power but emphasized the need for more data to achieve a more solid degree of accuracy. The complexity of the massive DBN architecture was also acknowledged as a potential challenge.

5.2 Limitations of State of the art Methods

It is worth acknowledging that depression is frequently diagnosed at later stages, primarily due to a multitude of factors. This delay in diagnosis poses significant challenges to effective treatment, and in certain instances, the condition becomes extremely challenging to cure. Given the multifaceted implications of depression and the obstacles in its early detection and treatment, it becomes all the more imperative to advocate for increased dedication of time and resources to the research and prediction of this perilous ailment. The accuracy of the earlier methods is also limited.

6. Future Directions

Integration of Multimodal Data: Explore the integration of EEG data with other modalities such as fMRI, eye-tracking, or physiological signals to enhance the overall accuracy and reliability of mental disorder detection using Deep Neural Networks (DNNs). Combining multiple sources of information may provide a more comprehensive understanding of the complex neural processes associated with mental disorders.

Longitudinal Studies and Temporal Dynamics: Conduct longitudinal studies to capture the temporal dynamics of EEG signals over extended periods. Investigate how DNNs can effectively model changes in EEG patterns over time, providing insights into the progression and dynamic nature of mental disorders. This approach could contribute to more personalized and adaptive diagnostic models.

Transfer Learning Across Disorders: Explore the potential of transfer learning techniques within DNNs to leverage knowledge gained from one mental disorder for the detection of others. This approach could enhance the efficiency of model training and potentially contribute to a broader and more generalized application of EEG-based mental disorder detection.

Explainability and Interpretability: Focus on improving the explainability and interpretability of DNN models for EEG-based mental disorder detection. Understanding the features and patterns that contribute to model predictions is crucial for gaining trust from clinicians and ensuring the clinical relevance of the developed models.

Real-Time Monitoring and Intervention: Investigate the feasibility of real-time EEG-based mental disorder detection using DNNs. Develop models that can continuously monitor EEG signals for early signs of mental health issues, allowing for timely intervention and personalized treatment strategies. This could be particularly valuable for conditions with acute episodes or rapidly changing states.

7. Conclusion

In conclusion, this paper has provided a thorough examination of the application of deep neural network (DNN) approaches in predictive modeling of mental disorders through the analysis of electroencephalography (EEG) signals. The review underscores the growing significance of integrating advanced computational methods, particularly DNNs, in addressing the complex challenges associated with mental health research. By synthesizing findings from various studies, we have illuminated the diverse methodologies employed and the distinctive contributions of different DNN architectures to the field. The

insights gleaned from this review emphasize the potential of predictive modeling using EEG data for enhancing our understanding of mental disorders. The ability to leverage DNNs in this context holds promise for early diagnosis and the development of personalized treatment strategies, thereby advancing the prospects for improved patient outcomes. Nevertheless, it is crucial to acknowledge the limitations and challenges inherent in these methodologies, including issues related to data variability, interpretability, and generalizability. Looking ahead, the identified gaps and challenges present opportunities for future research to refine and innovate DNN approaches in the context of mental health.

References

- 1. Keyes, Katherine M., Mark L. Hatzenbuehler, and Deborah S. Hasin. "Stressful life experiences, alcohol consumption, and alcohol use disorders: the epidemiologic evidence for four main types of stressors." Psychopharmacology 218 (2011): 1-17.
- 2. Fiorenzato, Eleonora, Silvia Zabberoni, Alberto Costa, and Giorgia Cona. "Cognitive and mental health changes and their vulnerability factors related to COVID-19 lockdown in Italy." PloS one 16, no. 1 (2021): e0246204.
- 3. Chen, Patrick J., Yanna Pusica, Dorsa Sohaei, Ioannis Prassas, and Eleftherios P. Diamandis. "An overview of mental health during the COVID-19 pandemic." Diagnosis 8, no. 4 (2021): 403-412.
- 4. Roy, Adrija, Arvind Kumar Singh, Shree Mishra, Aravinda Chinnadurai, Arun Mitra, and Ojaswini Bakshi. "Mental health implications of COVID-19 pandemic and its response in India." International Journal of Social Psychiatry 67, no. 5 (2021): 587-600.
- 5. Gianfredi, Vincenza, Sandro Provenzano, and Omar Enzo Santangelo. "What can internet users' behaviours reveal about the mental health impacts of the COVID-19 pandemic? A systematic review." Public Health 198 (2021): 44-52.
- 6. Fingelkurts, Alexander A., and Andrew A. Fingelkurts. "Quantitative electroencephalogram (qEEG) as a natural and non-invasive window into living brain and mind in the functional continuum of healthy and pathological conditions." Applied Sciences 12, no. 19 (2022): 9560.
- 7. Feltane, Amal. Time-frequency based methods for nonstationary signal analysis with application to EEG signals. University of Rhode Island, 2016.
- 8. Saha, Sourav, Zhengtao Gan, Lin Cheng, Jiaying Gao, Orion L. Kafka, Xiaoyu Xie, Hengyang Li, Mahsa Tajdari, H. Alicia Kim, and Wing Kam Liu. "Hierarchical deep learning neural network (HiDeNN): An artificial intelligence (AI) framework for computational science and engineering." Computer Methods in Applied Mechanics and Engineering 373 (2021): 113452.
- 9. Sze, Vivienne, Yu-Hsin Chen, Tien-Ju Yang, and Joel S. Emer. "Efficient processing of deep neural networks: A tutorial and survey." Proceedings of the IEEE 105, no. 12 (2017): 2295-2329.
- 10. Mamoshina, Polina, Armando Vieira, Evgeny Putin, and Alex Zhavoronkov. "Applications of deep learning in biomedicine." Molecular pharmaceutics 13, no. 5 (2016): 1445-1454.
- 11. Wang, J. Z., Zhao, S., Wu, C., Adams, R. B., Newman, M. G., Shafir, T., & Tsachor, R. (2023). Unlocking the Emotional World of Visual Media: An Overview of the Science, Research, and Impact of Understanding Emotion Drawing Insights From Psychology, Engineering, and the Arts, This Article Provides a Comprehensive Overview of the Field of Emotion Analysis in Visual Media and Discusses the Latest Research, Systems, Challenges, Ethical Implications, and Potential Impact of Artificial Emotional Intelligence on Society. Proceedings of the IEEE.
- 12. Zhang, Xiang, Lina Yao, Xianzhi Wang, Jessica Monaghan, David Mcalpine, and Yu Zhang. "A survey on deep learning-based non-invasive brain signals: recent advances and new frontiers." Journal of neural engineering 18, no. 3 (2021): 031002.
- 13. Sharma, Geetanjali, Abhishek Parashar, and Amit M. Joshi. "DepHNN: a novel hybrid neural network for electroencephalogram (EEG)-based screening of depression." Biomedical signal processing and control 66 (2021): 102393.
- 14. Seal, Ayan, Rishabh Bajpai, Jagriti Agnihotri, Anis Yazidi, Enrique Herrera-Viedma, and Ondrej Krejcar. "DeprNet: A deep convolution neural network framework for detecting depression using EEG." IEEE Transactions on Instrumentation and Measurement 70 (2021): 1-13.
- 15. Saeedi, Abdolkarim, Maryam Saeedi, Arash Maghsoudi, and Ahmad Shalbaf. "Major depressive disorder diagnosis based on effective connectivity in EEG signals: A convolutional neural network and long shortterm memory approach." Cognitive Neurodynamics 15 (2021): 239-252.
- 16. Khan, Danish M., Norashikin Yahya, Nidal Kamel, and Ibrahima Faye. "Automated diagnosis of major depressive disorder using brain effective connectivity and 3D convolutional neural network." Ieee Access 9 (2021): 8835-8846.
- 17. Qayyum, Abdul, Imran Razzak, and Wajid Mumtaz. "Hybrid deep shallow network for assessment of depression using electroencephalogram signals." In Neural Information Processing: 27th International Conference, ICONIP 2020, Bangkok, Thailand, November 23–27, 2020, Proceedings, Part III 27, pp. 245- 257. Springer International Publishing, 2020.
- 18. Thoduparambil, Pristy Paul, Anna Dominic, and Surekha Mariam Varghese. "EEG-based deep learning model for the automatic detection of clinical depression." Physical and Engineering Sciences in Medicine 43 (2020): 1349-1360.
- 19. Kang, Min, Jinhyeok Park, Seokhwan Kang, and Youngho Lee. "Low channel electroencephalogram based deep learning method to pre-screening depression." In 2020 International Conference on Information and Communication Technology Convergence (ICTC), pp. 449-451. IEEE, 2020.
- 20. Duan, Lijuan, Huifeng Duan, Yuanhua Qiao, Sha Sha, Shunai Qi, Xiaolong Zhang, Juan Huang, Xiaohan Huang, and Changming Wang. "Machine learning approaches for MDD detection and emotion decoding using EEG signals." Frontiers in Human Neuroscience 14 (2020): 284.
- 21. Saeedi, Maryam, Abdolkarim Saeedi, and Arash Maghsoudi. "Major depressive disorder assessment via enhanced k-nearest neighbor method and EEG signals." Physical and Engineering Sciences in Medicine 43 (2020): 1007-1018.
- 22. Xie, Yunlong, Banghua Yang, Xi Lu, Minmin Zheng, Cunxiu Fan, Xiaoying Bi, and Yingjie Li. "Anxiety and depression diagnosis method based on brain networks and convolutional neural networks." In 2020 42nd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC), pp. 1503-1506. IEEE, 2020.
- 23. Zhang, Xiaowei, Junlei Li, Kechen Hou, Bin Hu, Jian Shen, and Jing Pan. "EEG-based depression detection using convolutional neural network with demographic attention mechanism." In 2020 42nd annual international conference of the ieee engineering in medicine & biology society (embc), pp. 128-133. IEEE, 2020.
- 24. Uyulan, Caglar, Türker Tekin Ergüzel, Huseyin Unubol, Merve Cebi, Gokben Hizli Sayar, Mahdi Nezhad Asad, and Nevzat Tarhan. "Major depressive disorder classification based on different convolutional neural network models: Deep learning approach." Clinical EEG and neuroscience 52, no. 1 (2021): 38-51.
- 25. Wan, Zhijiang, Jiajin Huang, Hao Zhang, Haiyan Zhou, Jie Yang, and Ning Zhong. "HybridEEGNet: A convolutional neural network for EEG feature learning and depression discrimination." IEEE Access 8 (2020): 30332-30342.
- 26. Mumtaz, Wajid, and Abdul Qayyum. "A deep learning framework for automatic diagnosis of unipolar depression." International journal of medical informatics 132 (2019): 103983.
- 27. Mahato, Shalini, and Sanchita Paul. "Detection of major depressive disorder using linear and non-linear features from EEG signals." Microsystem Technologies 25 (2019): 1065-1076.
- 28. Li, Xiaowei, Xin Zhang, Jing Zhu, Wandeng Mao, Shuting Sun, Zihan Wang, Chen Xia, and Bin Hu. "Depression recognition using machine learning methods with different feature generation strategies." Artificial intelligence in medicine 99 (2019): 101696.
- 29. Acharya, U. Rajendra, Shu Lih Oh, Yuki Hagiwara, Jen Hong Tan, Hojjat Adeli, and D. Puthankattil Subha. "Automated EEG-based screening of depression using deep convolutional neural network." Computer methods and programs in biomedicine 161 (2018): 103-113.
- 30. Mao, Wandeng, Jing Zhu, Xiaowei Li, Xin Zhang, and Shuting Sun. "Resting state eeg based depression recognition research using deep learning method." In Brain Informatics: International Conference, BI 2018, Arlington, TX, USA, December 7–9, 2018, Proceedings 11, pp. 329-338. Springer International Publishing, 2018.
- 31. Cai, Hanshu, Xiaocong Sha, Xue Han, Shixin Wei, and Bin Hu. "Pervasive EEG diagnosis of depression using Deep Belief Network with three-electrodes EEG collector." In 2016 IEEE international conference on bioinformatics and biomedicine (BIBM), pp. 1239-1246. IEEE, 2016.