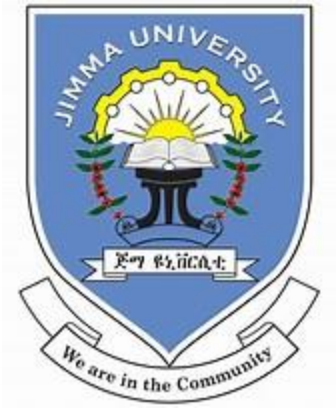

Jimma University

Jimma Institute of Technology

School of Biomedical Engineering

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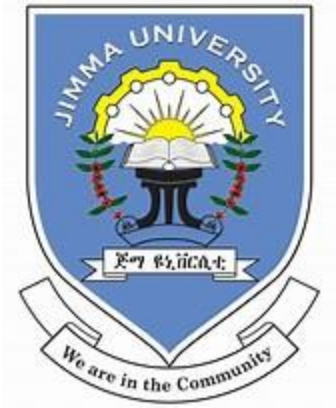
Detection and Grade Identification of Neonatal Seizure Using Deep Convolutional Neural Networks

By: Biniam Seifu Debelo

A thesis submitted to the School of Graduate Studies of Jimma Institute of Technology in partial fulfillment of the requirements for the Degree of Master of Science in Biomedical Engineering (Bioinstrumentation Engineering).

April 30, 2022

Jimma, Ethiopia.



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Main advisor: T. Bheema Lingaiah (Ph.D.)

Co-advisor: Mr. Ahmed Ali (M.Sc.)

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Jimma, Ethiopia

Declaration

I declare this thesis research entitled **"Detection and Grade Identification of Neonatal Seizure Using Deep Convolutional Neural Networks"** is my original work and has not been presented for a degree in any other University and I assure it with my signature.

Mr. Biniam Seifu		4/30/2022
	Signature	Date

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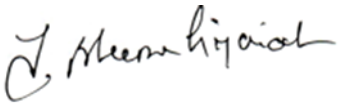
T. Bheema Lingaiah (Ph.D.)		4/30/2022
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Mr. Ahmed Ali (M.Sc.)		4/30/2022
Co-Advisor	Signature	Date

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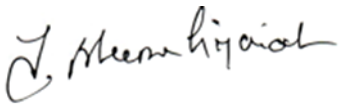
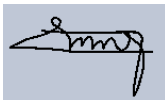
T. Bheema Lingaiah (Ph.D.)		4/30/2022
Main Advisor	Signature	Date
Mr. Ahmed Ali (M.Sc.)		4/30/2022
Co-Advisor	Signature	Date

As a member of Board of Examiners of the MSc. Thesis Open Defense Examination, we certify that we have read, evaluated the thesis prepared by Biniam Seifu and examined the candidate. We recommended that the thesis could be accepted as fulfilling the thesis requirement for the Degree of Master of Science in Bioinstrumentation Engineering.

Melkamu Hunegnaw Asmare (Ph.D)		6/10/2022
External Examiner	Signature	Date
Solomon Gebru (M.Sc.)		10/10/2022
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Abstract

Neonatal seizures are one of the most frequent neurological events in newborn infants which reflects a variety of pre or postnatal disorders of central nervous systems and usually indicates serious neurological dysfunction. These seizures may have nonexistent or subtle clinical manifestations, patterns like oscillatory or spike train start with very low amplitude and gradually increase over time. This makes neonatal seizure detection very difficult and inaccurate if it solely relies upon clinical observation. Although, it has been shown that the most accurate method for their detection or diagnosis is visual interpretation of continuous multi-channel neonatal Electroencephalogram (EEG) along with video by an expert clinical neurophysiologist, such interpretation is extremely labor intensive, time-consuming, and importantly relies on special expertise which is not available continuously around hospital neonatal intensive care units (NICUs).

A reliable and accurate automated neonatal seizure detection and classification using multi-channel EEG can be a very important supportive tool, particularly for the NICUs. However, identifying a core set of features is one of the most challenges in the development of an automated neonatal seizure detection. In most of the published studies describing features and seizure classifiers, the features were hand-engineered (feature selected manually), which may not be optimal and the results claimed from previously proposed automation techniques are less accurate and unreliable. Furthermore, the system that can detect neonatal seizure and identification of the seizure grade from neonatal EEG dataset has not been previously done.

*In this thesis, the detection and grade identification of neonatal seizure from multi-channel EEG signal was proposed using deep convolutional neural network models. The proposed system was developed using MATLAB software. The multi-channel neonatal EEG became preprocessed, segmented and the two dimensional matrix changed to raw waveform image with defined size prior to feeding to the custom CNN and pre-trained Alexnet models. The developed system was capable of detecting the neonatal seizure using binary classification as well as grade level identification using multiple classification techniques. The test result showed that the Alexnet perform better result during binary classification with accuracy of 92.6% and custom CNN performs better result on grade level identification (multi-classification) with accuracy of 88.6%.***Keywords:*** *Alexnet; CNN; Grade; Multi-channel EEG; NICUs; Neonatal Seizure.*

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Finally, I would like to express my deepest gratefulness to my families and friends who supported me in every direction of my life and for their encouragement.

Preface

In this thesis, the diagnosis of neonatal seizure from EEG signal using deep convolutional neural network model using custom CNN which is trained from scratch and the pre-trained Alexnet models were proposed. The objectives of the models were detection of neonatal seizure and classification of grade levels for the resulting seizures based on binary and multi-class classification methods respectively. The main activities done in this thesis involves collecting neonatal EEG data, preprocessing EEG, splitting EEG dataset, forming equivalent temporal EEG waveform image with defined size, and training using custom CNN and pre-trained Alexnet models. The study has a positive impact on clinical practice of professional's decisions accuracy and efficiency of EEG based diagnosis and treatment systems in neonatal intensive care unit.

The first chapter of this thesis describes the background of the study, clinical significance, existing solutions and their gaps, problem statement, objectives of the study and the scope of these work. The second chapter focuses on related works (literature reviews). The third chapter describes the method proposed including the procedures followed, techniques and materials used. Results and discussion are discussed in chapter four. The fifth or last chapter concludes the main findings of this thesis. A sample Matlab source code and clinical information of neonates are provided in the appendices.

Acronyms

ANN Artificial neural network

AUC Area under curve

CNN Convolutional neural network

DL Deep learning

ECG Electrocardiogram

EEG Electroencephalogram

ECoG Electro-oculogram

FCNN Fully convolutional neural network

FT full term neonates

GAP Global Average Pooling

GUI Graphical user interface

IOA Inter observer agreement

IQR Interquartile range

LSTM Long short-term memory

MATLAB Matrix Laboratory

NICU Neonatal intensive care unit

PPV Positive Predictive Value

PT Pre-term neonates

ReLU Rectified Linear Unit

SVM Support vector machine

WHO World health organization

WUNEMMCSH Wachamo University Nigist Eleni Mohamed Memorial Compressive Specialized Hospital

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CHAPTER ONE

1. Introduction

1.1. Background of the Study

Neonatal seizures are common emergency condition in intensive care unit, occurring in about 1-7 per 1,000 neonates born at full-term or FT (37 to 42 weeks gestation), more common in pre-term or PT neonates (less than 37 weeks gestation) about 57-132 per 1000 [1]. The children brought to hospitals in resource poor nations frequently have acute seizures. In Sub-Saharan Africa, however, there is limited information on prevalence, causes, and outcomes of newborn seizures. The lowest incidence, aetiology, and immediate outcome of seizures in neonates hospitalized to a Kenyan rural district hospital were determined. Seizure were documented in 142/1572 (9%) of neonatal admissions. The incidence was 39.5 per 1000 live births (95 percent confidence interval (CI) 26.4 – 56.7) [2]. One hospital based study in Ethiopia found a rate of 13.6% per 1000 live births [3].

They are epileptic fits occurring from birth to the end of the neonatal period, the incidence increases as gestational age (GA) and birth weight of the infant decrease [4]. The neonatal period is the most vulnerable of all periods of life for developing seizures particularly in the first 1–2 days to the first weeks from birth. They may be short-lived events lasting for a few days only. However, they often signify serious malfunction or damage to the immature brain and constitute a neurological emergency demanding urgent diagnosis and management.

Based on clinical and experimental data, the longer the duration of seizure, the greater the difficulty in controlling the seizure. Furthermore, seizures can have immediate and long term serious consequences on the immature and developing brain [5]. Irrespective of immediate actions to suppress the neonatal seizure with antiepileptic drugs (AEDs), the risk for subsequent neuro-developmental deficits and early death is substantial.

Newborn infants with seizures are at risk for death, whereas survivors are at risk for neurological impairment, developmental delay, later epilepsy and cognitive impairment [6]. Therefore, it is important to conduct early diagnosis using simple, low cost, accessible, and automated methods to determine the optimal treatment regimens for the management of neonatal seizures.

1.2. Characteristics of Neonatal Seizure

Neonatal seizures as with any other type of seizure are paroxysmal, repetitive and stereotypical events. The Neonatal seizures can be difficult to diagnose because the seizure may be short and difficult to distinguish. The duration of neonatal seizures is usually brief (10 s to 1-2 min), the voltage must be larger than 2μV, frequency between 0.1Hz and 12Hz and repetitive with a median of 8 min in between each seizure [7]. In addition, symptoms of neonatal seizures may mimic normal movements and behaviors seen in healthy babies. The seizures often are fragmentary because the infant's brain is still developing, thus unable to make the coordinated responses seen in a typical generalized seizures.

Neonatal seizures differ from those of older children and adults. During this stage, the neonatal brain is immature. Therefore, neonatal seizures have unique pathophysiology and electrographic findings resulting in clinical manifestations that can be different when compared to older age groups [8]. The most frequent neonatal seizures described as subtle occurrence with probability 51%, thus the clinical manifestations are frequently overlooked. Subtle seizures are far more common than other types of neonatal seizures, they imitate normal behaviors and reactions [9].

Some specific characteristics of neonatal seizure are:-

- Ocular movements, which range from random and roving eye movements to sustain conjugate tonic deviation with or without jerking. Eyelid blinking or fluttering, eyes rolling up, eye opening, fixation of a gaze or nystagmus may occur alone or with other ictal manifestations.
- Oral-buccal-lingual movements (sucking, smacking, chewing and tongue protrusions).
- Progression movements (rowing, swimming, pedaling, bicycling, thrashing or struggling movements).
- Complex purposeless movements (sudden arousal with episodic limb hyperactivity and crying).
- The baby's facial expression, breathing, and heart rate may change.
- Impairment of responsiveness (which is critical in defining many types of seizures) is difficult to assess in newborns.

1.3. Main Types of Disorder which Causes Neonatal Seizures

The main cause of neonatal seizure are described in the table 1 below.

Table 1: Main types of disorders which causes neonatal seizures.

Type of disorders	Causes
Hypoxia-ischaemia [10].	✚ Prenatal (toxaemia, fetal distress, abruption placentae, cord compression) and (iatrogenic, maternal haemorrhage, fetal distress). ✚ Postnatal (cardio-respiratory causes such as hyaline membrane disease, congenital heart disease, pulmonary hypertension).
Haemorrhage and intracerebral infarction [10].	✚ Intraventricular and periventricular (mainly preterm neonates). ✚ Intracerebral (spontaneous, traumatic), Subarachnoid, Subdural haematoma, Cerebral artery and vein infarction.
Trauma [10].	✚ Intracranial haemorrhage, cortical vein thrombosis
Infections [10].	✚ Encephalitis, meningitis, brain abscess ✚ Intrauterine (rubella, toxoplasmosis, syphilis)
Metabolic [10].	✚ Hypoglycemia (glucose levels <20 mg/d in preterm and, <30 mg/d in full-term babies ✚ Neonates of diabetic and toxemic mothers, Pancreatic disease, Glucagon storage disease (idiopathic)
Malformations of cerebral development [10].	✚ All disorders of neuronal induction, segmentation, migration, myelination and synaptogenesis
Neuro cutaneous syndromes [10].	✚ Tuberous sclerosis, incontinentia pigmenti

Drug withdrawal and toxic [10].	Withdrawal from narcotic analgesics, sedative-hypnotics, and alcohol; heroin and methadone-addicted mothers; barbiturates.

1.4. Neonatal Seizure Diagnosis

Major diagnostic systems include:-

I. Differential diagnosis:

Differential diagnosis for neonatal seizure includes the followings:

- During the neonatal period any unusual repetitive or stereotypic movement may represent a seizure.
- Alteration in automatic functions such as blood pressure or heart rate may represent seizure activity.
- Distinguishing seizure from jitteriness and benign neonatal sleep myoclonus.

II. Assessment method:

Assessment method for neonatal seizure diagnosis involves:

- Review family history of seizures, maternal diabetes, maternal drug use, infections, and evidence of fetal destress in labour and history of birth trauma to provide vital clues to the etiology of the seizures.
- Perform physical and neurological examinations.

III. Pathology test:

Pathology test for neonatal seizure diagnosis include:

- Blood glucose level (BGL).
- Serum electrolytes, calcium and magnesium.
- Full blood examination (FBE), Blood cultures and arterial blood gas (ABG).

IV. Neuroimaging:

Appropriate neuroimaging used for neonatal seizure diagnosis includes the following:

- Cranial ultrasound to exclude intracranial haemorrhage.
- MRI (or CT if MRI is unavailable) is required if there are seizures following traumatic delivery, particularly if there is significant head trauma or if the seizure type are clonic [11].

- Magnetoencephalography (MEG) or nuclear magnetic resonance spectroscopy (NMR or MRS).

V. Neurophysiology:

- If seizures are difficult to control, and/or requires the use of multiple anticonvulsants, an EEG or electrocorticography (ECoG) device assist to determine the cause of seizure as well as guiding treatment.

1.5. Introduction to Electroencephalography

1.5.1. Definition of EEG

Electroencephalography (EEG) is an electrophysiological monitoring method to record electrical activity of the brain. It is typically noninvasive, with the electrodes placed along the scalp. EEG measures voltage fluctuations resulting from ionic current within the neurons of the brain. Clinically, EEG refers to the recording of the brain's spontaneous electrical activity over a period of time, as recorded from multiple electrodes placed on the scalp [12].

EEG is used in clinical circumstances to determine changes in brain activity that might be useful in diagnosing brain disorders, especially epilepsy or another seizure disorder. An EEG might also be helpful for diagnosing or treating the disorders such as brain tumor, brain damage from head injury, brain dysfunction that can have a variety of causes (encephalopathy), inflammation of the brain (encephalitis), stroke, and sleep disorders. All frequency bands of EEG signal are described in the table 2 below.

1.5.2. Comparison of EEG bands

Table 2: Comparison of EEG frequency bands [13].

Band	Frequency(Hz)	Location
Delta	<4	Frontally in adults, posteriorly in children; high-amplitude waves
Theta	4-7	Found in locations not related to task at hand
Alpha	8-15	Posterior regions of head, both sides, higher in amplitude on dominant side. Central sites (c3-c4) at rest
Beta	16-31	Both sides, symmetrical distribution, most evident frontally; low-amplitude waves

Gamma	>32	Somatosensory cortex

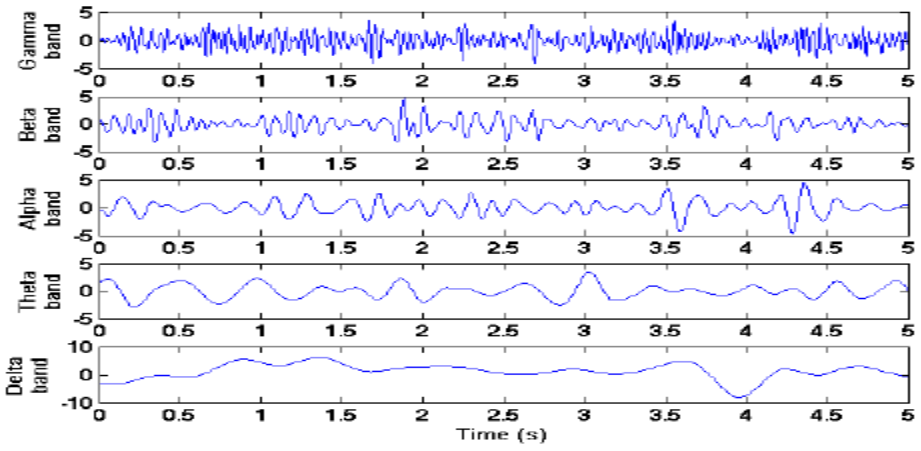


Figure 1: All frequency bands of EEG signal [14].

1.5.3. Characteristics of neonatal EEG

One of the most application areas of EEG are neonatal intensive care unit (NICU) through visual interpretation of long-duration measurements EEG signal by specialized expertise. Neonatal EEG is an objective test to measure the functional integrity of the immature neonatal brain. The indications of EEG in neonates in general includes assessment of neonatal seizure caused by different types of disorders listed on section 1.3.

There are some prominent differences in EEG recording methods in the neonate as compared to adults. These differences are primarily because neonates have a smaller head size and there is a relative lack of EEG activity noted in the extreme front polar head regions, the patient's inability to cooperate, and fragile nature make electrode application and running these test difficult. The sensitivity are 70µV/mm and filter settings for the various channels are 0.1 to 1Hz low frequency filter (LFF) and 70Hz high frequency filter (HFF) [15].

Some unique considerations in the technical aspects of performing a neonatal EEG are discussed in the following section:

1) Equipment:

   There are some important difference in EEG recording methods in the neonate as compared to adults. These differences are primarily because neonates have a smaller head size and also there is a proportional lack of EEG activity noted in the extreme front polar head regions. Due

to these differences, the international 10-20 system of electrode placement has done modification for neonatal EEG recordings.

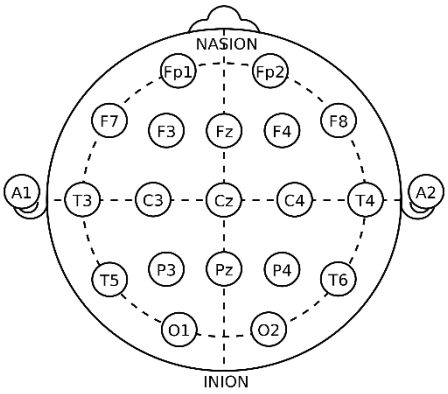


Figure 2: Electrode location of international 10-20 system for EEG [16].

2) Electrodes and Montages: The standard neonatal montage includes at least eight scalp electrodes (FP2, C4, T4, O2, FP1, C3, and O1), EKG, and respiration efforts. Additional three electrodes (Fz, Cz, Pz) may be included to improve coverage. Electrode location of international 10-20 system for EEG is described in the figure 2 above.
3) Recording time: Neonatal EEG should be recorded for a longer period than the routine adult pattern. It is more suitable if the neonate cycles through wakefulness, active sleep, and quiet sleep during the tracing. Since particularly a neonate takes 50 to 60 minutes to cycle through all three stages, a neonatal EEG should be run for at least 60 minutes. If possible, the EEG should be scheduled near the feeding time of the neonate [15]. Sample Multi-channel EEG electrode placed to detect neonatal seizure shown in the figure 3 below.

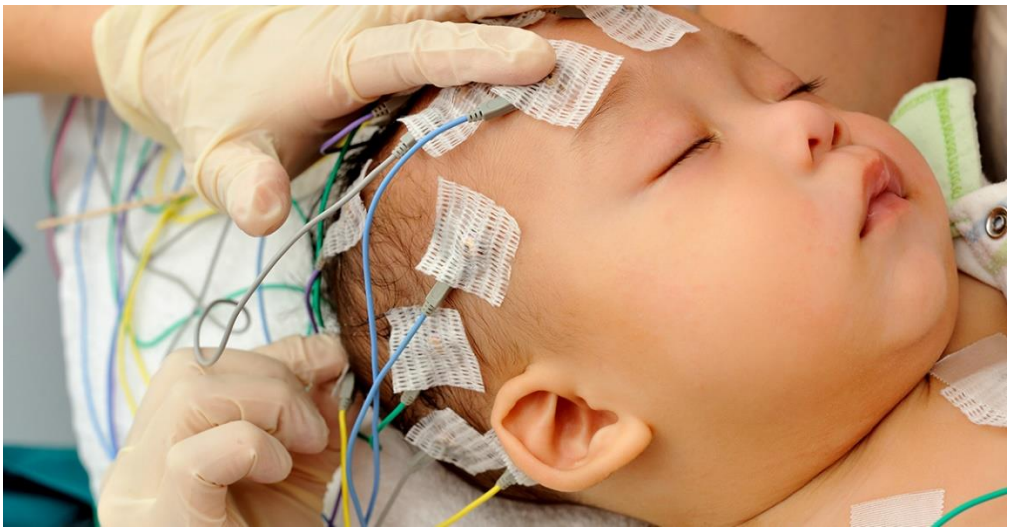


Figure 3: Multi-channel EEG electrode placed to detect neonatal seizure [17].

1.5.4. Advantage of using EEG over other diagnostic techniques

Despite the relatively poor spatial sensitivity of EEG, it possesses multiple advantages over other techniques:

- Hardware costs are significantly lower than those of most other techniques [18].
- EEG has very high temporal resolution, on the order of milliseconds rather than seconds. This high temporal resolution allows for neural dynamics analyses to be made on neurologically-relevant timescales, e.g. calculation of high-fidelity signal analysis methods [19].
- Extremely non-invasive, unlike electrocorticography, which actually requires electrodes to be placed on the surface of the brain.
- EEG does not involve exposure to radio ligands.
- EEG does not involve exposure to high-intensity (>1 tesla) magnetic fields, as in some of the other techniques, especially MRI and MRS (nuclear magnetic resonance spectroscopy).
- EEG is relatively tolerant of subject movement, unlike most other neuroimaging techniques. There even exist methods for minimizing, and even eliminating movement artifacts in EEG data [20].
- EEG is a powerful tool for tracking brain changes during different phases of life.

1.6. Introduction to EEG Data Analysis

1.6.1. Machine Learning Based EEG Analysis

The machine learning is a subfield of artificial intelligence (AI). The goal of machine learning generally is to understand the structure of data and fit that data in to models that can be understood and utilized by people. It used to automatically solve classification problems by computing and encoding hand crafted features of a data (shape, texture, color, etc.) [21]. The Figure 4 shows the schematic representation of terms of AI, machine learning and deep learning techniques.

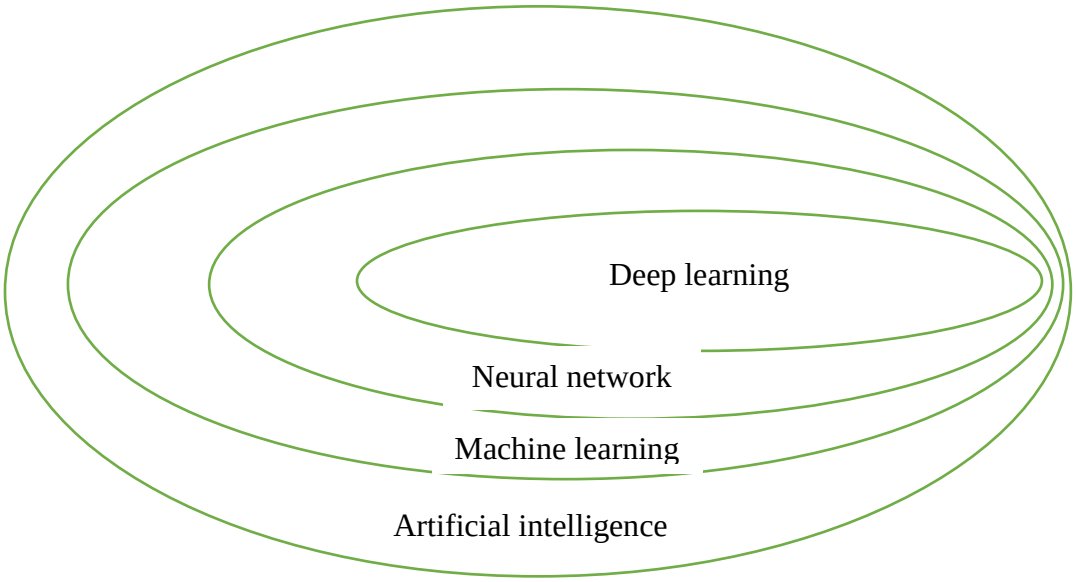


Figure 4: Schematic representation of terms of AI, machine learning and deep learning techniques

1.6.2. Deep Learning Based EEG Analysis

Deep learning is a branch of machine learning which has ability to learn completely based on artificial neural networks with many layers. As neural networks deep learning imitates the way human brain gain certain type of knowledge.

Neural networks are layers of nodes, similarly the human brain also made up of neurons. Nodes within individual layers are connected to adjacent layers. The network is called deeper based on the number of layers it has. A single neuron in the human brains receives thousands of signals from other neurons. In an artificial neural network, signals travel between nodes and assign corresponding weights. A signal with heavier weight node will exert more effect on the next layer

of nodes. The final layers compiles the weighted input to produce the output. Finally, output layer is used to classify the image and obtain the output class label.

Deep learning techniques include convolutional neural networks (CNN) which are highly applicable in medical image classification problems. Figure 5: shows schematics of deep learning based EEG processing pipeline and related terminology.

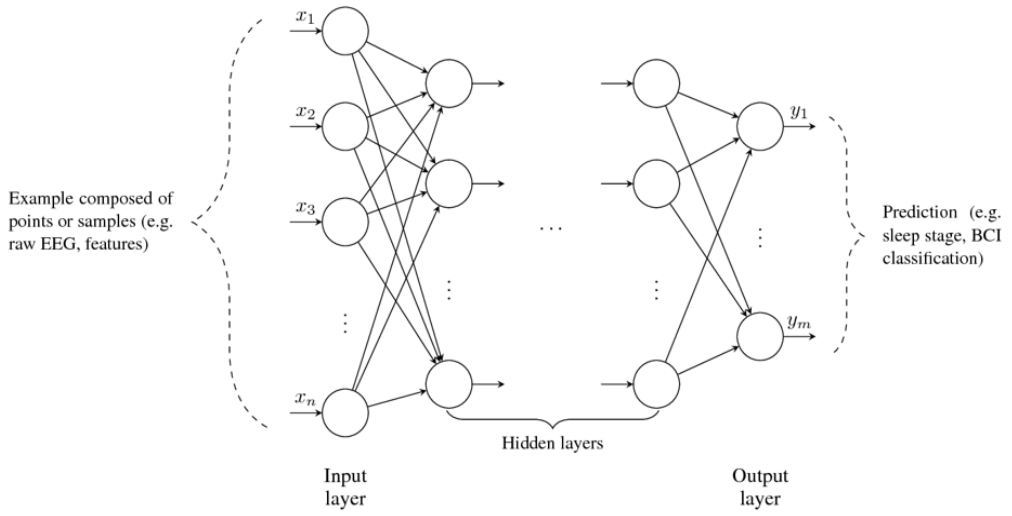


Figure 5: Deep learning based EEG processing pipeline and related terminology [22]

1.6.2.1.Convolutional neural networks which train from scratch

Convolutional neural networks are usual neural networks that assume that the input to the network are image. They are used to analyze and classify images. Cluster images by similarity and perform object recognition by frame. The input images are made up of pixels, each pixel is represented by a number between 0 and 255. Therefore the image has digital representation which is how computers can understand and work with images. There are four operations in CNN image detection or classification such as, convolution, activation map, max pooling and fully connected layer. Example of two dimensional convolutional neural network architecture are described in the figure 6 below.

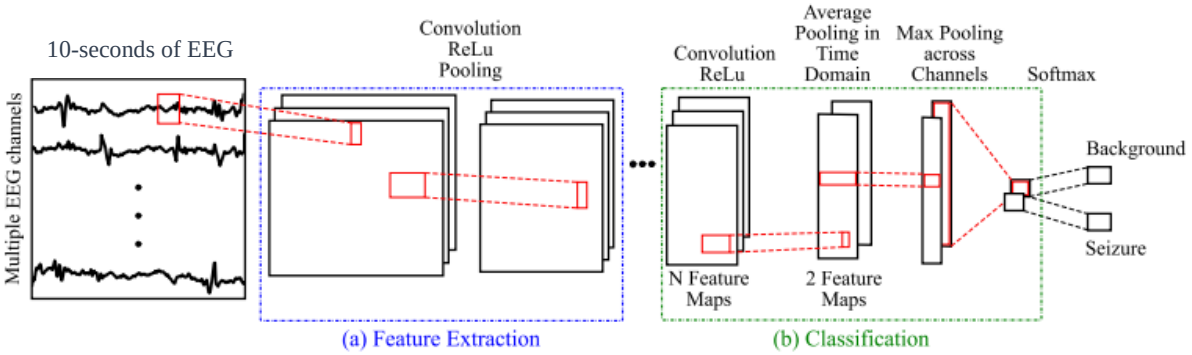


Figure 6: Two dimensional convolutional neural network architecture

1.6.2.2.Transfer Learning Approach

Transfer learning is generally refers to a process in which model trained on one problem is used in the same way on the second related problem. In deep learning, transfer learning is a technique where by a neural network model is first trained on a certain task similar to the problem that is being solved. One more layers from trained model are then used in new model trained on the problem of interest.

The weights in layer used again may be used as the starting point for the training process and adapted in response to the new problem. These usage behave toward transfer learning as a type of weight initialization scheme. Transfer learning has advantage of decreasing the training time for a deep neural network model and can result in lower generalization error.

Currently, there are different pre-trained models which can be used for image classification, prediction, feature extraction and fine-tuning (with weights trained on ImageNet). Example, Alexnet, Squeeznet, Resnet, and etc [23]. . General description on transfer learning approaches are depicted in the figure 7 below.

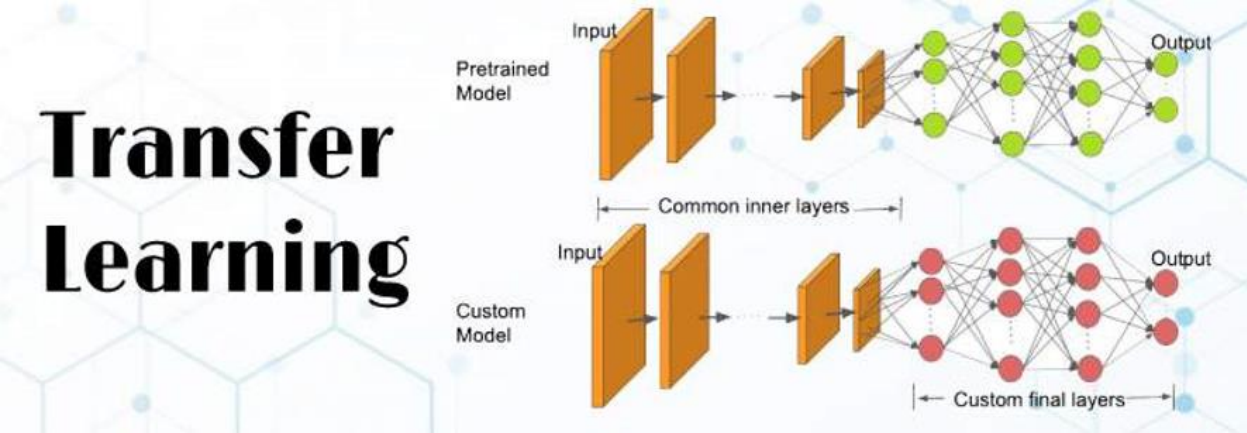


Figure 7: General description on transfer learning approaches [24].

1.6.2.3.Hyper-Parameters and Parameters of deep Learning Models

When training a neural network, there are two key things that need to be considered. These are Hyper-parameters and parameters. Hyper-parameters are parameters whose values control the learning process and determine the value of model parameters that a learning algorithm end up learning. Hyper-parameters are said to be external to the model because the model cannot change its values during learning or training. Some common hyper-parameters are: train/test split ratio, activation function, cost or loss function, number of hidden layer, the drop-out rate, number of iteration, number of clusters, kernel or filter size and batch size.

Parameters on the other hand are internal to the model. Because, they are learned purely from the data during training as the algorithm used tries to learn the mapping between the input features and the labels/targets. Some examples of parameters are: the coefficients (or weights) of linear and logistic regression models, weights and biases of a neural networks and the clusters and centroids in clustering.

1.7. Statement of the Problem

Neonatal seizure are one of the most frequent neurological events in newborn infants which reflects a variety of pre or postnatal disorders of central nervous systems and usually indicates serious neurological dysfunction. These may range from hypoxic ischemic encephalopathy, stroke, epilepsy, meningitis, benign, haemorrhage and intracerebral infarction, potentially worsen brain injury to sever prolonged of life threatening disorders. Recognition of seizures is vital because they often show characteristic sign of an underlying neurological condition, false treatments for non-

seizure events exposes infants to unnecessary harmful drugs. On the other hand early detection allow medical practitioners to begin treatment promptly, potentially preventing further injuries.

The diagnosis and interpretation of neonatal seizures is challenging for clinicians because, unlike the epileptic seizures observed in older children and adults majority of neonatal seizures are acute symptomatic events, have nonexistent or subtle clinical manifestations, and the patterns (oscillatory or spike) train start with a very low amplitude and gradually increase over time. These seizures may have difficult to analyze precisely clinical manifestations and hard to distinguish from the normal and clinical signs.

Despite the availability of EEG in some neonatal intensive care units (NICUs) and the growth of neonatal neuro critical care systems and accurate diagnosis of seizures and prompt treatment remain a challenge. One of the other seizure burden is a measure of the percentage of time spent or duration in a seizure state. Common available method for detection and visual interpretation of continuous multichannel EEG (cEEG) and amplitude integrated EEG (aEEG) along with video by an expert clinical neurophysiologist. However, such interpretation was extremely labor-intensive, time-consuming, expensive, and importantly needs special expertise which is not available around the clock in many hospital neonatal intensive care units (NICUs) as a worldwide, especially in developing countries.

A practical current attempts for the current progress in multi-channel conventional EEG based neonatal seizure diagnosis or newborn brain monitoring in general has been automated by machine learning to support clinical diagnostic and treatment methods. Although there have been many attempts to develop neonatal seizure detection algorithms, the outputs of these methods have not achieved the benchmark of inter observer agreement between human experts.

1.8. Objectives of the Study

1.8.1. General Objectives

- To develop a model for detection and grade level classification of neonatal seizure from continuous multi-channel EEG signals using deep convolutional neural network techniques.

1.8.2. Specific Objectives

- To collect, pre-process and window raw neonatal multi-channel EEG signals

- To classify the preprocessed signal as neonatal seizure or non-seizure using deep convolutional neural networks.
- To classify the grade of neonatal seizure using deep convolutional neural networks.
- To measure specific characteristics and compare accuracy of different neural network models

1.9. Motivation

There are several facts that motivates the interest in automatic clinical EEG for the diagnosis of neonatal seizure these are:

- The development of automated system for screening neonatal seizure could support clinicians by reducing the workload and allows for earlier detection.
- Interpretation of neonatal EEG requires years of training to assess abnormality in clinical EEG recordings.
- The clinically, expert interpretation of continuous EEG without computer aid is frequently a time consuming, exhausting process and erroneous [25].

1.10. Significance of the Study

Some of the importance of using automatic detection technique for neonatal seizure diagnosis are but, not limited to:

- Reduce diagnosis time.
- Detect neonatal seizure automatically.
- Prevent misdiagnosis due to over fatigue of neurologist.
- Enable clinical practice of professional's decisions accuracy and efficiency of EEG based diagnosis and treatment systems in neonatal intensive care unit.
- The study will provide information and recommendations for future researches.

1.11. Scope of the Research

The research aim is to develop neonatal seizure diagnosis system from multi-channel EEG with at least 19 scalp electrodes signals using deep learning algorithm. The research started by gathering relevant data from different sources. The data will be acquired from local hospitals neonatal intensive care units (NICUs) by trained professionals during normal clinical procedures under supervision of neurologists, and more data collected from publicly available dataset which was annotated by international experts. The gathered neonatal EEG recordings are used as input to train and test the proposed deep neural network.

CHAPTER TWO

2. Related Works

2.1. Introduction

Unlike in older children and adults, seizure symptoms are not sometimes clinically visible in babies or neonates which makes them difficult to detect. The detection of seizures in newborn babies are a clinically important task which has motivated a large body of work in the area of developing and testing automated seizure detection algorithms to support clinical decision making. Deferent researchers had done development of computer based automated seizure detection algorithms [26] [27] [28]. Although these automated seizure detection algorithms can raise an alarm system and provide objective decision support to clinicians aiding the prompt detection and treatment of seizures, the performance was determined by the quality of the chosen features and finding appropriate features was a big challenge, which was typically performed by trial and error, signal stationarity assumed over small intervals.

Early automated seizure detection routines relied on heuristic rules and thresholds. W. Deburchgraeve *et al.* [29] Developed heuristic model that mimics a human EEG reader, the complete algorithm was tested on multi-channel EEG recordings of 21 patients with and 5 patients without electrographic seizures, totaling 217 h of EEG. Sensitivity of the combined algorithms was found to be 88%, Positive Predictive Value (PPV) 75% and the false positive rate 0.66 per hour. Even if the algorithm significantly improves neonatal seizure detection and monitoring comparing with previously available systems, there are also some limitations, output of the heuristic algorithm is not continuous, due sensitivity to spikes or artifact related high amplitude signals the false alarm rate is high. The performance of the trainable classifiers will be improved by adding more training datasets, while the heuristic algorithm are untrainable methods or will not be improved easily.

2.1.1. Related works for Neonatal Seizure Detection Using Machine Learning Techniques

Several feature based study has done to detect and classify neonatal seizures [30] [31] [32], the features are usually extracted from the time, frequency and information theory domains to provide energy, frequency, temporal and structural descriptors of the neonatal EEG, giving an informative characterization of each segment of EEG. Most algorithms used the same feature set including 28

features from the frequency domain, 23 from the time domain, and four from information theory (in total 55 features). However all the algorithms relies on pre-defined features and, these features needs strong and precise labels in each channels during the training stage that means seizure events annotated both time and space and some weak label signals could be missing. Feature based algorithms has large computational load or time and chaos theory on time-frequency analysis. Due to neonatal seizure has subtle characteristics, weak amplitude and inaccessible signals the feature based system is ineffective. Slow processing time, challenging for automatic or real time applications.

Temko *et al*. [33] Presents a multi-channel patient-independent neonatal seizure detection system based on the Support Vector Machine (SVM) classifier, a machine learning algorithm (SVM) is used as a classifier to discriminate between seizure and non-seizure EEG epochs. In total, 55 features are extracted and the resulting system was validated on a large clinical dataset of 267 h of EEG data from 17 full-term newborns with seizures. The performance of the system using event-based metrics was reported. The system was able to achieve an average detection rate of 89% with one false seizure detection per hour. Although the proposed system has showed the best up-to-date performance of a neonatal seizure detection system, allow for its practical application in neonatal intensive care units there some gaps found such as the algorithms are dependent on previously defined feature, needs strong and precise labeling of experts in each channels. The number of subject in which study has done was small and the number of channel of EEG electrode used was not enough because as a channel increase the information recorded also increases, thus the characteristics of seizure information could lost as a number of channel minimized. The algorithm relies on recording long hour duration of signals which is also gold standard for resource limited countries.

2.1.2. Related Works for Neonatal Seizure Detection Using Deep CNN Techniques

Progress in deep learning based research has been utilized in the development of new EEG classification algorithms that do not require a feature extraction stage. These deep learning models can take temporal or spectral EEG as input and using back propagation, they can learn both feature extraction and segment classification routines in one end-to-end optimization procedure. Deep learning algorithms have been applied to pediatric and adult EEG for a variety of different tasks, such as brain computer interfaces, seizure detection and feature extractions [34] [35] [36].

O'Shea *et al*. [37]. Proposed a single-channel based CNN for neonatal seizure detection. In this method, the network uses 8 s of a single-channel EEG signal as input to the CNN. Then, a post-processor was applied on the outputs of the CNN. However measurement period 8 s are not enough for extracting evolutionary features of EEG, which have been shown to be important EEG characteristics for discrimination of brief-lasting seizures (<10 s) from short artifacts. Other gaps found in this study was using single channel EEG, due to some basic information regarding to diagnosis treatment neonatal seizure cases missing comparing with multi-channel EEG recorded data.

A.H. Ansari *et al.* [38]. Also proposed Neonatal Seizure Detection Using Deep Convolutional Neural Networks, The main goal of the present paper was using deep Convolutional neural networks (CNNs) and random forest to automatically optimize feature selection and classification. The input of the proposed classifier was raw multi-channel EEG and the output was the class label: seizure or non-seizure. This resulted false alarm rate of 0.9 per hour and seizure detection rate of 77% using a test set of EEG recordings of 22 neonates that also included dubious seizures. Although proposed classifier takes the raw multi-channel EEG data and automatically optimizes the features and classifier at the same time, there is still needs more works to be done due to low performance due to small number of datasets and small number of subjects, which decreases the performances of neural networks, the scored or annotated seizures used for training and testing were labeled by only one expert clinical neurophysiologist, The data used in this paper were recorded from one center only. The system don't have a more generalizable comparison, because the methods did not tested on an extensive and multi-rated, multi-center database.

Gordon Lightbody *et al.* [39] Proposed Neonatal seizure detection from raw multi-channel EEG using a fully convolutional neural networks. This architecture was designed to detect seizure events from raw electroencephalogram (EEG) signals of 834h in duration using only convolutional layers in order to process the time domain signal and was designed to exploit the large amount of weakly labelled data in the training stage. The developed system had achieved a 56% relative improvement with respect to a feature-based algorithms, reaching an AUC of 98.5%; this also compares favorably both in terms of performance and run-time. Although, presented work was a novel way of developing a neonatal seizure detection algorithm through end-to-end optimization of the feature extraction and classification, the convolutional layer applied was too shallow to get

various features from limited datasets, the number of subject the study had done was small, the method did not tested on an extensive and multi-rated, multi-center database. The neonatal seizure grade level classification was not done in this work.

2.2. Major Gaps on the Previous Works

Major gaps in the previous researches are summarized as follows:

- Machine learning algorithms are dependent on only manually defined features, and has large computational load and chaos theory on time-frequency analysis.
- The scored seizures used for training and testing were labeled by less than two expert clinical neurophysiologists.
- The number of subject the study had done was small.
- Pre-term neonates are excluded from most of the studies and the grade level identification study was not done in neonatal level.

CHAPTER THREE

3. Materials and Methodology

3.1. Research Methods

3.1.1. Introduction

This chapter presents the proposed scheme for diagnosis of neonatal seizure from multichannel EEG signals using deep learning techniques. In this work, data has been collected from publicly available online datasets called Zenodo. It was taken from 79 term and some preterm neonates admitted to the NICU at the Helsinki University Hospital, Finland [40], additionally some local datasets were collected from Wachamo University Collage of Health Science Nigist Eleni Mohamed Memorial Compressive Specialized Hospital Department of Neurology. The preprocessed EEG waveforms used to train and test the proposed deep neural network models. The overall methodology of the system is summarized in Figure 8.

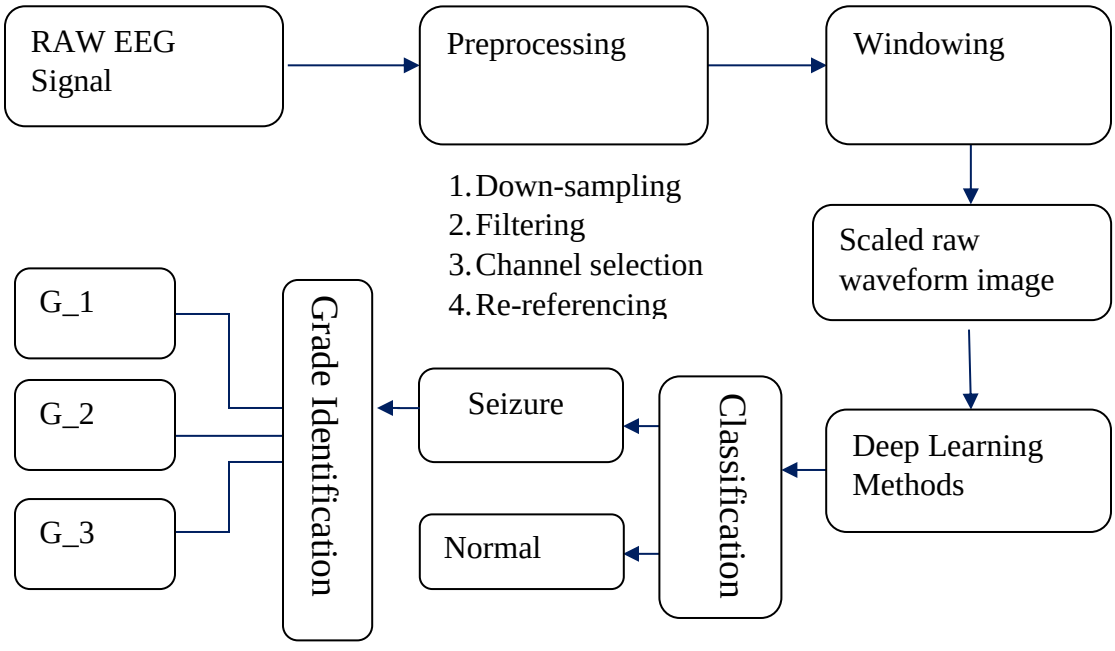


Figure 8: The overall methodology of the proposed system

3.1.2. Dataset

The source of multi-channel EEG signal datasets used in this study were:

A. Publicly available online datasets.

This dataset contains 19-channel recorded using the 10-20 placement system EEG which was recorded from 79 neonates admitted to the NICU at the Helsinki University Hospital. All the recordings were performed between 2010 and 2014, Finland. The median recording duration was 74 min (IQR: 64 to 96min), signals are sampled at 256Hz [40].

The presence of seizures in the EEGs was annotated independently by three international experts. This event was defined as a seizure if it was over 10 s in duration. Initial settings were a paper speed of 30mm/sec (~12s per screen), a sensitivity of 100μV/cm with frequency cut-offs of 0.5Hz (low) and 70Hz (high), but experts were permitted to alter these settings for each recording to achieve the best possible performance. An average of 994 seizures were annotated per expert in the dataset; 57 neonates had seizures and 22 were seizure free, by consensus. A summary of the annotations of three reviewers is described table 3 below.

Table 3: A summary of the annotations of three reviewers.

	A (n = 46)	B (n = 45)	C (n = 53)
Seizure Burden (mins)	10.2 (4.3-23.7)	15.0 (6.6-30.3)	8.6 (2.1-22.5)
Mean Seizure duration (s)	98 (48-246)	103 (67-288)	82 (38-175)
Seizures	5 (2-12)	6 (2-13)	6 (3–11)

A bipolar montage was generated for annotation according to the standard longitudinal bipolar layout (a.k.a. ‘double banana’): Fp2-F4, F4-C4, C4-P4, P4-O2, Fp1-F3, F3-C3, C3-P3, P3-O1, Fp2-F8, F8-T4, T4-T6, T6-O2, Fp1-F7, F7-T3, T3-T5, T5-O1, Fz-Cz and Cz-Pz [40]. (See Fig. 2).

The clinical data, extracted from patient reports, are presented in a spreadsheet (CSV file format) which are attached on appendix 2. Furthermore, the Annotations were stored in a Matlab MAT format and CSV file format. The MAT file contains a cell array with 79 elements, where each element corresponds to a study neonates ID number. Each element of the cell array was an M by N array, where M is the number of experts (M = 3), N was the duration of the annotation in seconds (variable) and each second described by 1 (denoting seizure) or 0 (denoting non-seizure). There are three CSV files (A, B, C), where each file contains the annotations of an expert. The overall structure of database shown in the figure 9.

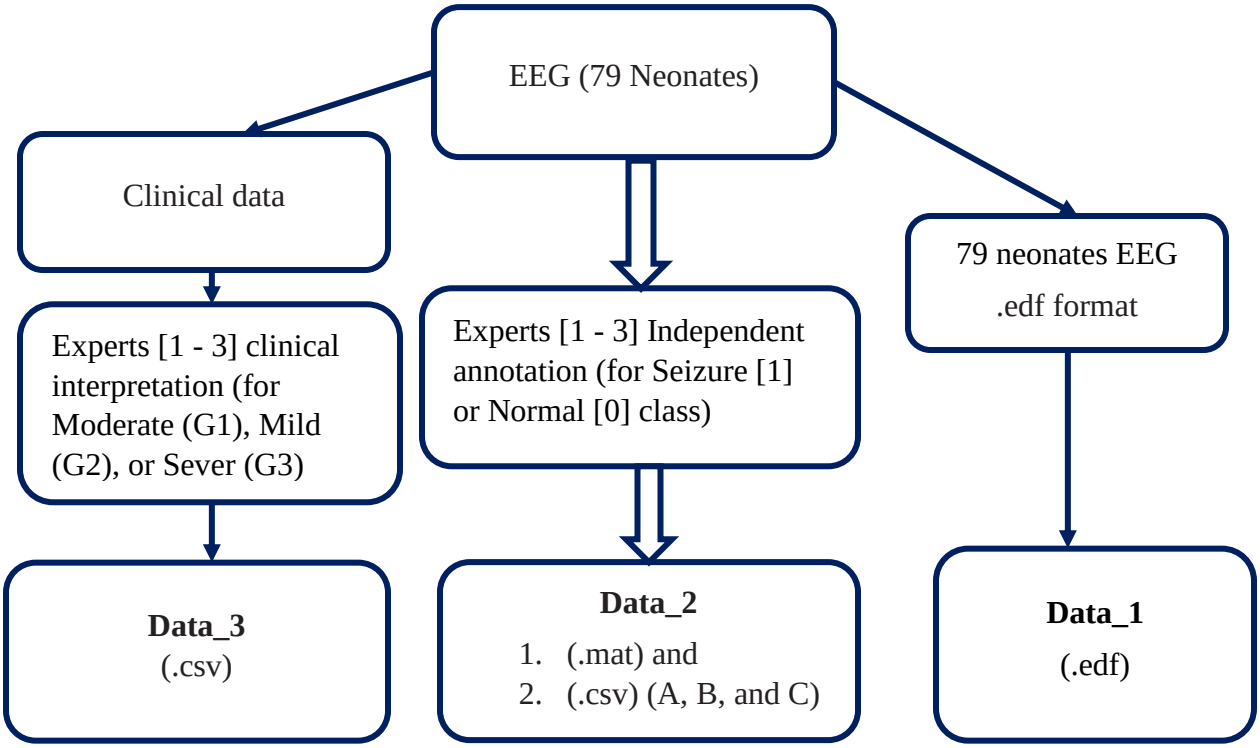


Figure 9: The overall structure of public database

The dataset can be used as a reference set of neonatal seizures, in studies of inter-observer agreement and for the development of automated methods of seizure detection and other EEG analyses [40].

B. Locally acquired data.

The Data acquired using EEG machine with brand EEG-1200 which is 10-20 electrode based arrangement, provides up to 256 channels, and sampling rate 256 Hz. The data was

taken from Wachamo University School of health science Nigist Eleni Mohamed Memorial Compressive Specialized hospital's neonatal intensive care units (NICU) by trained professionals during normal clinical procedures. The conformation letter of data and corresponding clinical information collection for this research work is attached on appendix 4.

Comparison between public and locally collected datasets discussed in table 4 below.

Table 4: The comparison between public and local datasets

	Public dataset (Zenodo)	Local collected dataset
Sampling frequency	256Hz	256Hz
Average recorded time	74min	40min
Number of electrode	19	19
Electrode placement system	10-20	10-20
Number of subject	79	17

3.1.3. Preprocessing

In general, preprocessing is a series of actions of transforming raw data in to a format that is more appropriate for further analysis and interpretable for user. In case of EEG signals, preprocessing usually refers to removing noise or unwanted portion of signals from whole data to get closer to the true neural signals.

There are reasons why preprocessing is necessary for EEG data these are:

- The signals that are picked up from the scalp are not necessarily an accurate depiction of the signals originating from the brain, as spatial information of the signal gets lost.
- EEG signals tends to contain a lot of noise which cannot discovered weaker EEG signals and artifacts such as blinking or muscle movement can contaminate the data and distort the pictures.
- Furthermore, separate the relevant neural signals from random neural activities that occurs during EEG recordings.

In this work the main preprocessing steps involves band pass filtering, down-sampling, removing bad signals, removing bad or unwanted channels and re-referencing the electrodes.

The overall preprocessing steps shown in figure 10 below. The pre preprocessing was done using MATLAB library or toolbox called EEGLAB.

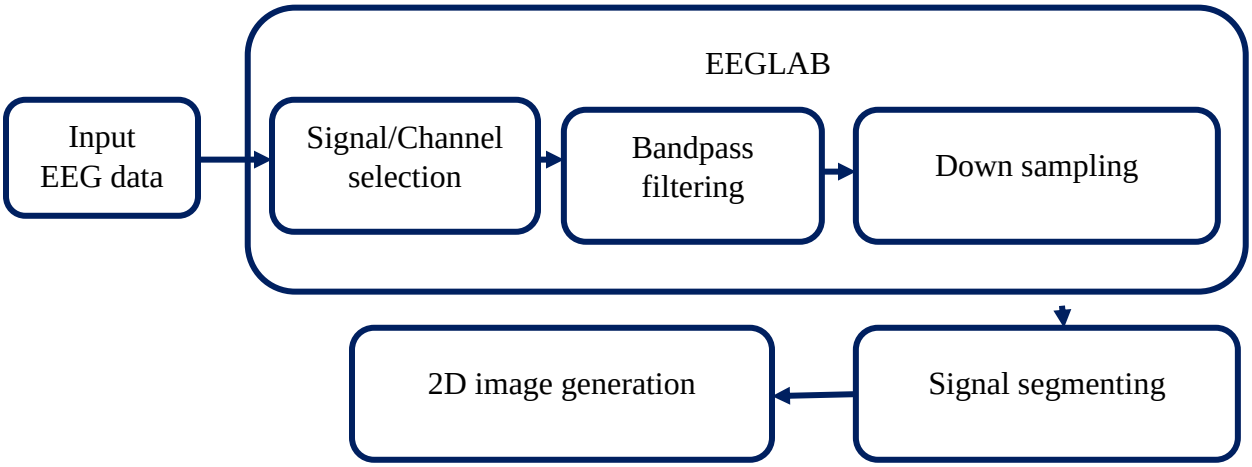


Figure 10: Overall preprocessing steps

EEGLAB is an interactive MATLAB toolbox distributed under the free (Berkeley Software Distribution) BSD license for processing continuous data in about 20 binary file formats from EEG and other electrophysiological signals. Together with all the basic processing tools, EEGLAB implements ICA (Independent Component Analysis), time-frequency analysis, artifact rejection and several modes of data visualization of singe trial or multichannel data. It also incorporates extensive tutorial and help windows, plus a command history function that facilitates user transition from GUI based data exploration to building and running or custom data analysis scripts [41]. The sample EEGLAB window is shown in the figure 11 below.

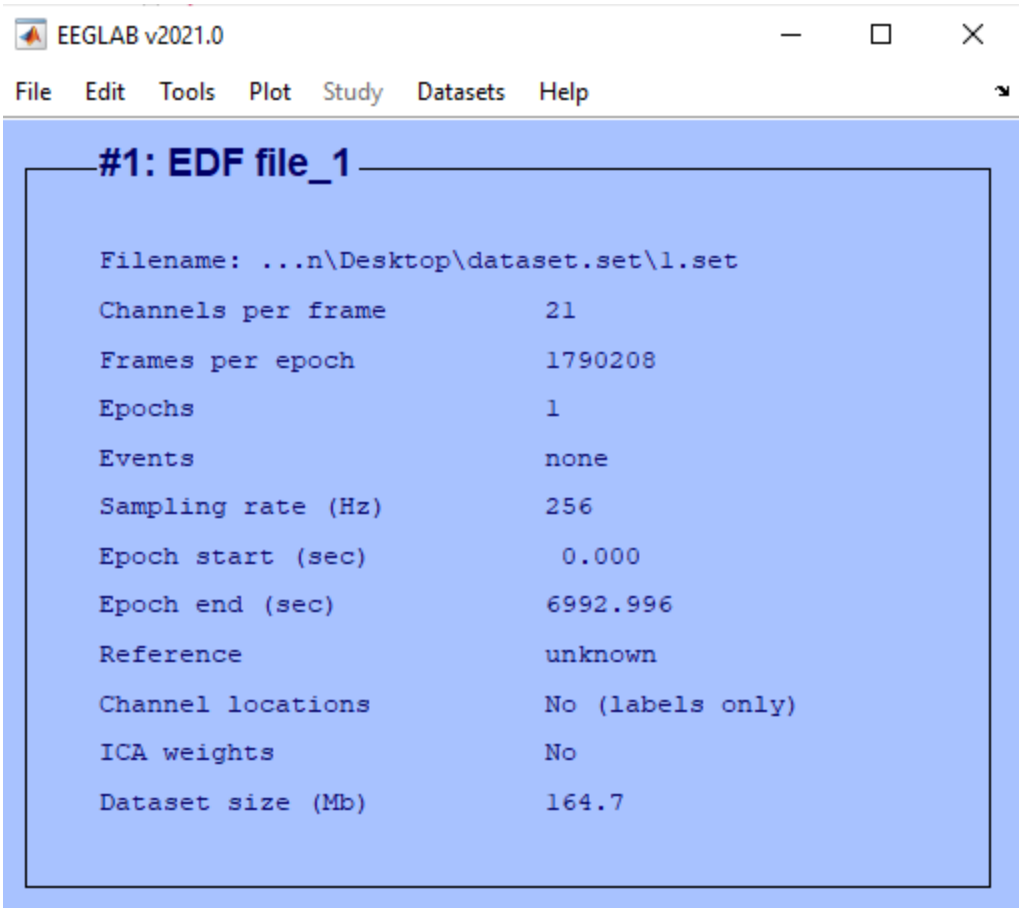
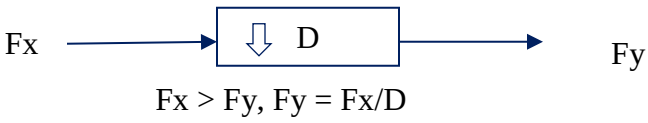


Figure 11: EEGLAB toolbox window

3.1.4. Down-sampling

It is a technique to reduce the number of samples used, while performing down-sampling hopefully maintaining the information that is needed. To make clear description the EEG system with 19 channels, and a sampling rate of 256 samples per second (256 Hz). If we are representing each sample as a 32-bit float, this is (19 * 256 * 32) = 524,288 bits per second, or 530kb/sec of data.

Let as consider Fx be the input function and Fy be the output function, Fx is greater than Fy because, Fy is the down-sampled version Fx by the rate of D.



Fx > Fy, Fy = Fx/D

Figure 12: Down-sampling relation between input and output variables

Due to neonatal seizure characterized by very low amplitude (>100μV/cm) as well as low frequency (0.1 to 12 Hz) compared with adults and in order to decrease the complexity of the CNN network 256 Hz multichannel EEG signal became down-sampled to 32 Hz [42] [43].

3.1.5. Filtering

When looking at the frequencies of digital signal, such as EEG or other signals, a popular thing to do is to filter certain frequencies, such that either some frequencies are removed or possibly some frequencies remain. There are number of type of filters applied in this work such as:

- Low pass filter: Frequencies below a certain value are kept (they pass), while high frequencies are removed. This is called high cut filter.
- High pass filter (low cut): Only high frequencies remain, and only those below a certain value are removed.
- Band pass filter: Combining the two, this keeps only frequencies between a lower and bound and upper bound. In this proposed work the multi-channel EEG signal is band-pass filtered between 0.1 Hz and 15 Hz. Because, the neonatal seizure appears at frequency range from 0.1Hz to 12Hz [42].

3.1.6. Re-referencing

In EEG signal, the voltage for each electrode is recorded relative to the other electrodes. The reference, which can be one or a combination of electrodes, is what voltage will be relative to electrodes. When picking a reference consideration important that the electrodes that we are selecting as reference have as little influence on the locations of our signal of interest as possible.

Some common choices of reference include:

- Mastoids (electrodes placed roughly behind a person's ears): because of being relatively far from the brain yet to close to the other electrodes.
- The average of the two earlobes is also commonly used, for similar reasons as the mastoids.
- Cz (the central electrode) is frequently chosen, when looking at activity that is distant from that location.
- The average of all electrodes

In this work average referencing technique was applied to local neonatal EEG signals due to the following reasons.

- Most recording collected during sleep stages
- The anti convulsant drugs administered before start of recording

3.1.7. Removing Bad Signals or Bad (Unwanted) Channels

Sometimes EEG signals contains bad channels that do not allow accurate information. It is important to remove those from analysis because, keeping that data will affect further analysis. There are few reasons why a channel might be excluded:

- The channel is not functioning well for some reason
- The electrode was not properly placed or didn't have contact with the scalp.
- (If working with wet electrodes) Two or more channels are bridged
- (If working with wet electrodes) The electrode got saturated

3.1.8. Split (window) EEG data

Signal Segmenting is one of the signal processing techniques in which the raw continuous EEG signal become split into specified time intervals. Initially EEG signal was recorded at sampling frequency of 256 Hz. Seizure appears in EEG as sudden, repetitive, stereotyped, evolving waveforms that last at least 10s and have the definite beginning, middle and end [44].

Manual segmentation refers to the process in which an experts put segments and labels an EEG signals file by hand, referring only to the spectrogram and/or waveform. In this work each of these segments includes 10 second of EEG data was prepared using manual segmentation from all available channels. The manual segmentation of multichannel EEG signal has been performed based experts annotated data.

3.1.9. 2D Image generation from Multichannel EEG Time Series Signals

The segmented EEG signal has 19 electrodes of 10 second lengths with sampling frequency of 32 Hz, resulting 19 * 320 array, where the first and second terms correspond to number of the input channel and number of sample in specified time interval respectively. These raw waveform images are the inputs to the proposed CNN. Before using these images data as input to train or test deep neural networks, 19*320 must be rescaled based on requirements of proposed deep CNN models.

3.1.10. Convolutional Neural Network

Convolutional neural networks (CNNs / ConvNets) are made up of neurons that have learnable weights and biases. Each neuron receives some inputs, performs a dot product of the convolution

kernel with layers input matrix and optionally follow it with a non-linearity. As the convolution kernel slides along the input matrix for the layer, the convolution operations generates feature map, which in turn provides to input of the next layer. This followed by other layers such as pooling layers, fully connected layers and normalization layers. Generally CNNs consists of an input layers, hidden layers which performs convolution and an output layers which performs classification tasks. The architecture overviews are described below.

❖ Layers used to build CNNs/ConvNets

- Convolution Layer (`CONV`)

  The Convolutional layer is the building block of the convolutional neural network that does most of computational activities. It is the first layer which can extract features from images of dimension (Height) x (Breadth) x (Number of channel, e.g., RGB). These layer will compute the output of neurons that are connected to local regions in the input, each computing a dot product between their weights and a small regions. An example of input 5x5 image (left) going to convolve with a laplacian kernel (right) is shown in the figure 13.

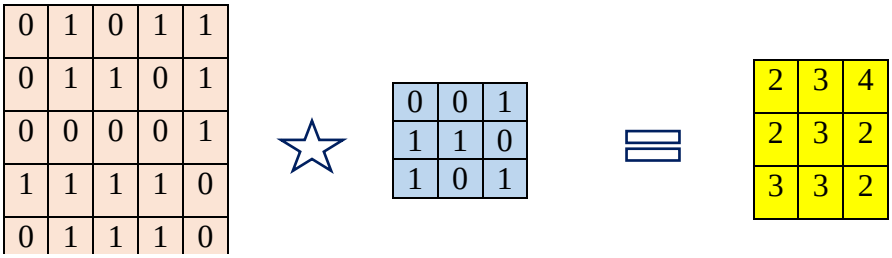


Figure 13: The sample convolution operation

To summarize, the `CONV` layer

- Accepts an input volume of size W(input) x H(input) x D(input), the input size are normally square
- Requires four parameters:
  - ✓ The number of filters K (which controls the depth of the output volume).
  - ✓ The receptive field size F (the size of the K kernels used for convolution and is early always square, which means yielding FxF kernel).
  - ✓ The stride S.

- ✓ The amount of zero-padding P.

- The output of the `CONV` layer is then W(output) x H(output) x D(output), where:
  - ✓ W(output) = ((W(input) – F + 2P) / S) + 1 ---------- (1)
  - ✓ H(output) = ((H(input) – F + 2P) / S) + 1 and ---------- (2)
  - ✓ D(output) = K ---------- (3)

- Pooling Layer (`POOL`)

  Pooling layers reduce the dimension of the data by combining the outputs of neuron clusters at one layer in to a single neuron in the next layer, help with overfitting problem. An example of max pooling operation, with input 4x4 volume, Right: Applying 2x2 max pooling with a stride of S = 1, Bottom: Applying 2x2 max pooling with S = 2 is demonstrated in the figure 14 below.

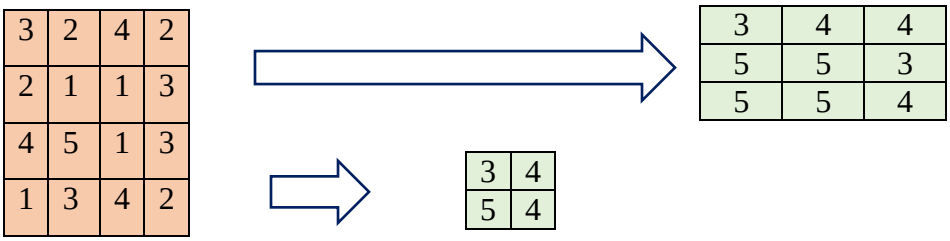


Figure 14: Sample max pooling operation

The POOL layers accepts an input volume of size W(input) x H(input) x D(input), they require two parameters, these are the pool size F and the stride S. Applying `POOL` operation yields an output volume of size W(output) x H(output) x D(output), where:

- W(output) = ((W(input) – F) / S) + 1, ----------(4)
- H(output) = ((H(input) – F) / S) + 1 and ---------- (5)
- D(output) = D(input). ---------- (6)

- The ReLU activation (`RELU`)

  ReLU (Rectified Linear Units) refers to the real non-linear function defined by

  ReLU(x) = max(0,x) ---------- (7)

  Visually, represented in the figure 15 below:

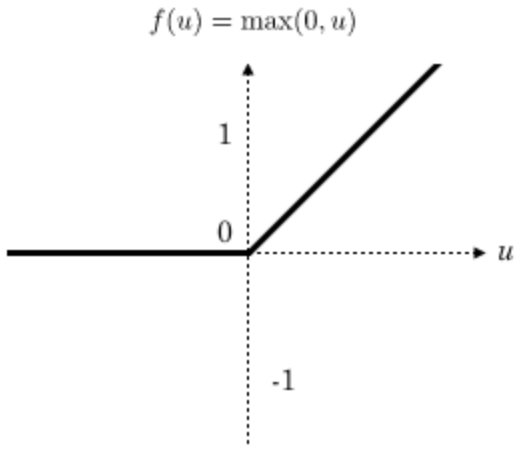


Figure 15: Graphical representation of activation ReLU [45].

An activation layer accepts an input volume of size W (input) x H (input) x D (input) and applies the given activation function as shown in the figure 16. The ReLU correction layer replaces all negative values received as inputs by zeros. It also act as an activation function.

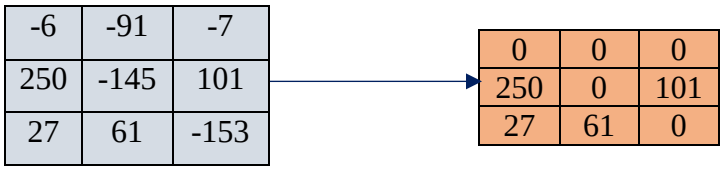


Figure 16: An example of an input volume going through a ReLU activation, max(0,x).

- Fully-Connected Layers (FC)

  The fully connected layer is always the last layer of a neural network, classifies the image as an input to the network. It's common to use one or two FC layers before applying the softmax classifier which will compute our final output probabilities for each class.

- Batch Normalization layers (BN)

  Batch normalization layers, as the name indicates, are used to normalize the activation of a given input volume before passing it into the next layer in the network.

  If we consider x to be our min-batch of activations, then we compute the normalized $\dot{x}$ via the following equations:

$$\dot{x} = \frac{(xi-\mu_\beta)}{\sqrt{\sigma_\beta^2+\varepsilon}} \text{ ---------- (8)}$$

During training, we compute the μ_β and σ_β over each mini-batch β, where

$$\mu_\beta = \frac{1}{M}\sum_{i=1}^{m} xi \ , \ \sigma_\beta^2 = \frac{1}{M}\sum_{i=1}^{m}(xi-\mu_\beta)^2 \text{ ---------- (9)}$$

We set ε equal to a small positive value such as $1e^{-7}$ to avoid dividing by zero. Applying this equation implies that the activations leaving a batch normalization layer will have approximately zero mean and unit variance (i.e., zero-centered).

At testing time we take place of the min-batch μ_β *and* σ_β with running averages of μ_β *and* σ_β computed throughout the course of the training process. This ensures that we can pass images through our network and still obtain accurate predictions without being biased by the μ_β *and* σ_β from final mini-batch passed through the network at training time.

- Dropout:

  Dropout is actually a form of regularization that aims to keep from overfitting by increasing testing accuracy, perhaps at the expense of training accuracy.

3.1.11. Customized CNN Model

In this section, a deep convolutional neural network (CNN) which train from scratch was proposed to recognize seizures in neonates. Constructed CNN consists of 5 convolution layer, 3 * 3 filters and 1 * 1 strides. The network used ReLU activation function, maximum pooling layer, and fully connected layer to compute final output probabilities for each classes. To normalize the outputs of fully connected layer a softmax layer was used, cross entropy loss function was used for learning, for training the proposed deep CNN the gradient descent with momentum, and a learning rate was fixed to 0.001. The maximum epoch number set to 30.

3.1.12. Alexnet Model

Alexnet is the name of a convolutional neural network (CNN) architecture in which designed by Alex Krizhevsky in together with Ilya Sutskever and Geoffery Hinton [46]. The architecture was developed in 2012, and was major breakthrough in CNN development.

The major advantage in using Alexnet architecture are, because of major innovations were made through the use of training on multiple GPU's using augmented version of the image data for training, using the ReLU activation function, using overlapping pools, and utilized dropout.

Therefore, these method reduces complex adaptations of neurons and forces the model to learn more robust features.

The architecture of Alexnet contains 61 million total parameters within 8 total layers: five convolutional layers, and three fully connected layers. We can load a pertained version of the network trained more than million images from the image database [46]. The pertained network can classify images in to 1000 object categories, such as mouse, keyboard, pencil, coffee, many animals. Therefore, the network has learned rich features representations for wide range of images. The pre-trained Alexnet architecture is shown in figure 17.

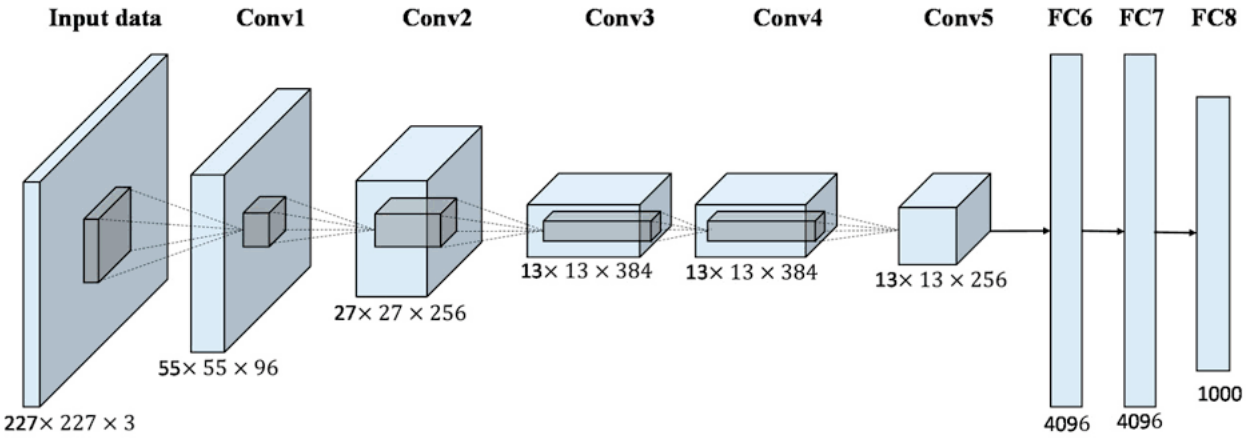


Figure 17: The Alexnet architecture [47].

Transfer learning achieved by taking pertained network and use it as a starting point to learn a new task. Fin-tuning a network with transfer learning is usually much faster and easier than training network with randomly initialized weights from scratch. To use pertained network Alexnet we have to replace last three layers with a fully connected layer, a softmax layer, and a classification layer. The options of the new fully connected have to be the same size as a number of classes in the new data. The network requires input image of size 227-by-227. The pretrained Alexnet architecture for Binary classification is shown in the figure 18 below.

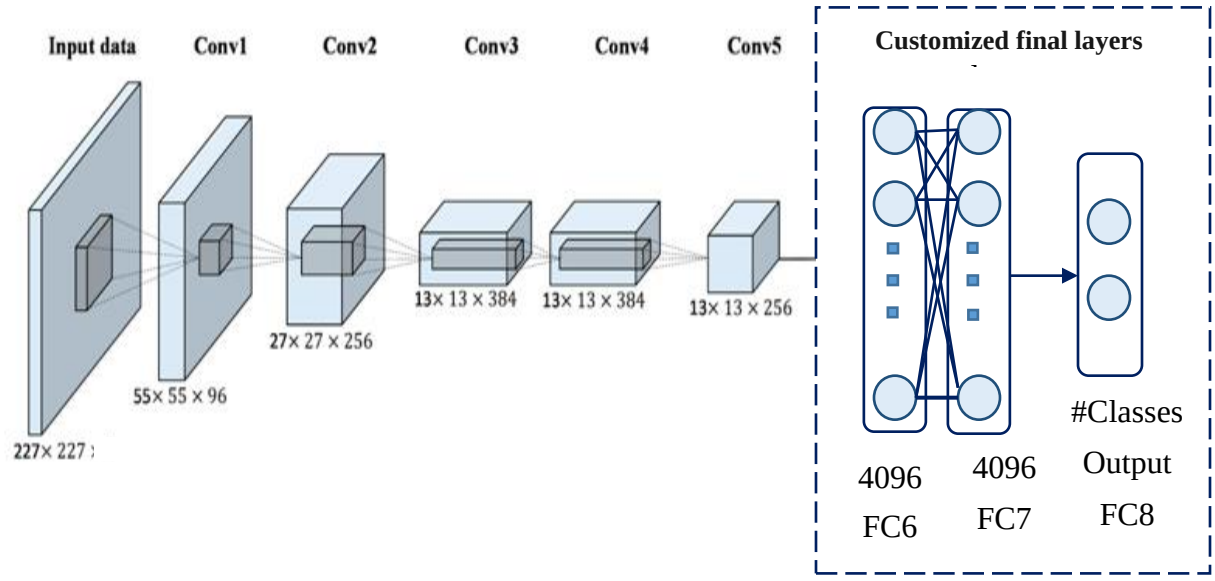


Figure 18: The proposed Alexnet architecture (Binary classification)

3.1.13. Hyper Parameters of the Proposed Models

The hyper-parameters of the network considered and modified during training were summarized in the following table 5.

Table 5: The hyper parameters of proposed models

	Custom CNN	Alexnet
Number of layer	5	8
Activation function	ReLU	ReLU
Learning rate	0.001	0.001, 0.0001
Maximum epoch	30	10
Input image size	256-by-256	227-by-227
Batch number	1 to 30	1 to 50

3.1.14. Performance Evaluation Metrics

After building a model and training the network, its performance must be evaluated so as to know the actual result. There are different ways of evaluating a model. The first one is by using a confusion matrix and getting the TP, TN, FP and FN rates of the predicted values. The second is by calculating and getting the precision, recall, F1-score and over all accuracy values of a model.

For example: Given a binary classifier of class A and class B, a model can be evaluated using confusion matrix. Table 6 indicates the TP, TN, FP and FN components for class A. From the table we can see that the green shaded part indicates the TP and TN part [48].

- A TP (True Positive) value indicates that what is predicted is true.
- A TN (True Negative) value indicates that the predicted class is truly negative.
- A FP (False Positive) value indicates that a thing is predicted as if it is part of the class while it is not.
- FN (False Negative) the prediction indicates that it is not part of the class while it is.

Table 6: Example of confusion matrix

		Predicted class	
		A	B
Actual class	A	TP	FN
	B	FP	TN

Once the confusion matrix is ready, the classification report containing the precision, recall and f1-score can be done. So, given a class prediction from the classifier, the precision is the one which answers the question “how likely is it to be correct?” It is calculated using equation (10), recall or sensitivity will indicate the answer for “will the classifier detect it?” It is calculated using equation (11); F1-score is the harmonic mean of precision and recall. It is calculated using equation (12). The model is said to be performing good if we have high F1-score and specificity is the one which determines the proportion of actual negatives that are correctly identified. To measure the proportion of actual negatives that are correctly identified, the specificity of the model was calculated using equation (13). Finally, the models performance was measured using the accuracy metrics using equation (14). The performance metrics were calculated using the equations given below [48]:

Precision = TP / (TP + FP) ---------- (10)

Recall = TP / (TP + FN) ---------- (11)

F1-score = (2 * Precision * Recall) / (Precision + Recall) ---------- (12)

Specificity = TN / (TN + FP) ---------- (13)

Accuracy = (TP + TN) / (TP + TN + FN + FP) ---------- (14)

3.2. Materials Used in this Research

MATLAB ("MATrix LABoratory") is a proprietary multi-paradigm programming language and numeric computing environment developed by MathWorks. MATLAB allows matrix manipulations, plotting of data and functions, implementation of algorithms, creation of the user interfaces and interfacing with programs written in other languages. It is an interactive system whose basic data element is an array that does need dimensioning. This helps us to solve many technical problems, especially those with matrix-based languages and vector formulations, in a fraction of time it could take to write a program in scalar non-interactive language such as C or FORTRAN.

Additionally, with MATLAB, we can code and debug a new capability much faster than with other programing languages and specifically, MATLAB allows deep learning easy in terms of tools and functions for managing large datasets with just few lines of code and allows to perform deep learning without being an expert. It also offers specialized toolboxes for working with machine learning, neural networks, computer vision and automated driving Therefore, MATLAB is easiest and most productive computing environment for engineers and scientists [49].

In this work, MATLAB 2019b with deferent add-on or libraries such as EEGLab, Biosignal interface, Alexnet architecture were used to design the proposed deep neural networks. In addition, EDF browser software were used to view, highlight and annotate EEG signals from .edf or .edf+ format. The Nicolet EEG Viewer to view, highlight and annotate the EEG signal from different formats. In addition to the above mentioned software's, the EEG machine connected with desktop computer and other miscellaneous hardware's were used. The summary of hardware and software materials used for this research are shown in the table 7 below.

Table 7: hardware and software materials used for the research

Hardware	Software
❖ Laptop Computer • 4GB RAM • 128GB SSD and 500GB HDD • TOSHIBA, Satellite C855, Intel(R) Core(TM) i3-2370M CPU @ 2.40GHz	❖ MATLAB 2019b with • EEGLab2021 • Bio-signal interface • Alexnet Architecture
❖ 32GB USB and 1TB hard disc	❖ EDF Browser2021
❖ EEG Machine • Model: JE-921A • Brand: NIHON CODEN • Accessories used: Desktop computer, Electrode junction box, Flash lamp assembly, Photic stimulator control unit, Cart, Stand and LCD display	❖ Nicolet EEG Viewer2021

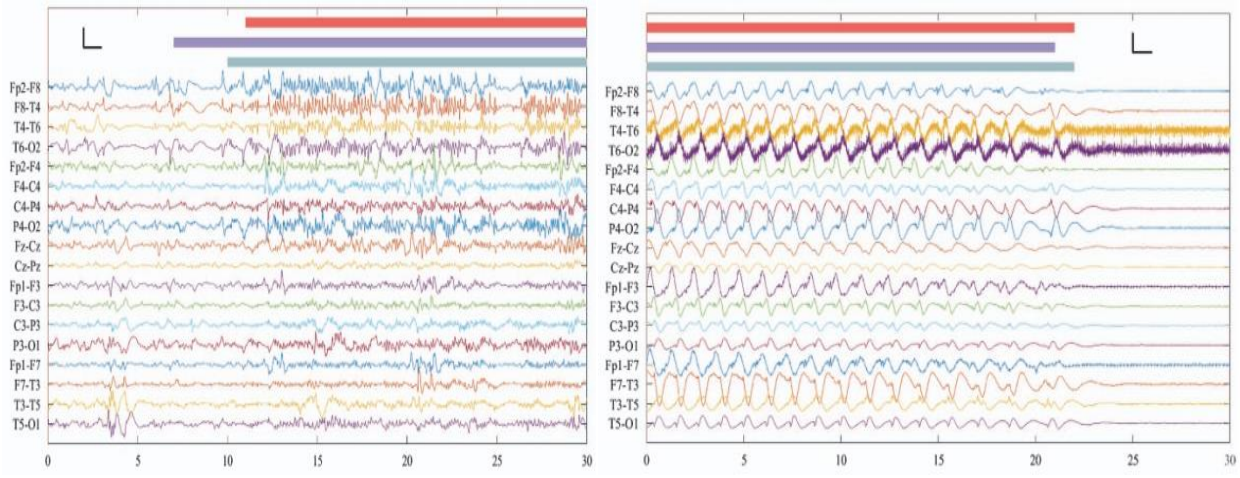
CHAPTER FOUR

4. Results and Discussion

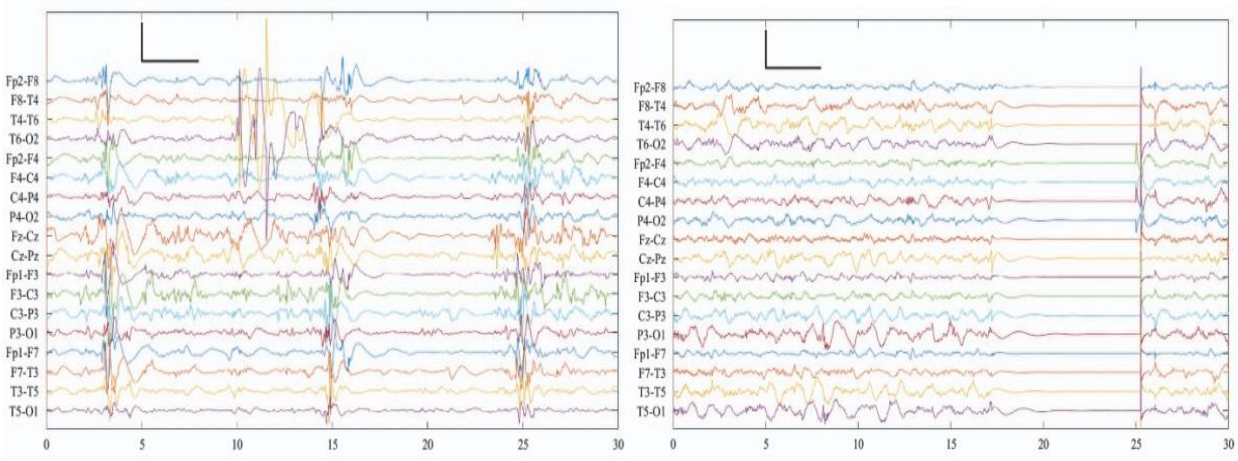
4.1. Data collection, Preparation and Annotation Results

Firstly EEG signals collected from publicly available dataset of neonatal EEG recordings with annotations of seizures from multiple experts [40]. Each EEG file was annotated for seizures by three experts using the Nicolet Reader software (Natus, USA). Annotations were then exported into a text file using the start and duration of each seizure, considering all available derivations, with one second resolution. Each EEG recording lasted approximately one hour; median recording duration was 74 mins. In this study EEG recordings from 79 neonates are used to training, testing and validation of proposed deep neural networks.

The EEG signal of 30s segments from the dataset are shown in the figure 19 below. (19a) The onset of a neonatal seizure discharge in a neonate with a right temporal hemorrhage (neonate 50; at 37 min 39 s), (19b) The cessation of a widespread seizure discharge in a neonate with severe asphyxia (neonate 44; at 5 min 53 s), (19c) a period of burst suppression in a neonate with non ketotic hyperglycinemia interrupted by a high amplitude artefact at approximately 10 s on the T4-T6 and T6-O2 derivations (neonate 26; at 1hr 2 min 34 s), (19d) Recording pause expressed as zero EEG amplitude for approximately 8 s (neonate 42; at 38 min 6 s). In (a) and (b), annotations are plotted above the EEG signals (red, purple and green bars). Each bar denotes an independent, blinded annotation of the seizure by one expert.



19 (a) 19 (b)



19 (c) 19 (d)

Figure 19: Sample 30 second segments from public dataset

The EEG signals were recorded with a NicOne EEG amplifier (sampled at frequency 256 Hz; with model of machine Natus, USA) and EEG caps (sintered Ag/AgCl electrodes; Waveguard, ANT-Neuro, Germany) with 19 electrodes positioned as per the international 10 – 20 standard, including a recording reference at midline.

In addition local EEG data was collected by using machine with model EEG-1200 from Wachamo University Compressive Specialized Hospital. The EEG data were collected from 17 neonates, the recording was done approximately 40 min. 21 scalp electrodes were applied to collect EEG signals. The collected signals were annotated by three neurologist. Furthermore, the clinical data was also accessed based on permission from department as well as hospital governments. The details of clinical data as well as other information are shown in the appendix 3. A sample of 30 sec segment from locally collected dataset is described in the figure 20 bellow.

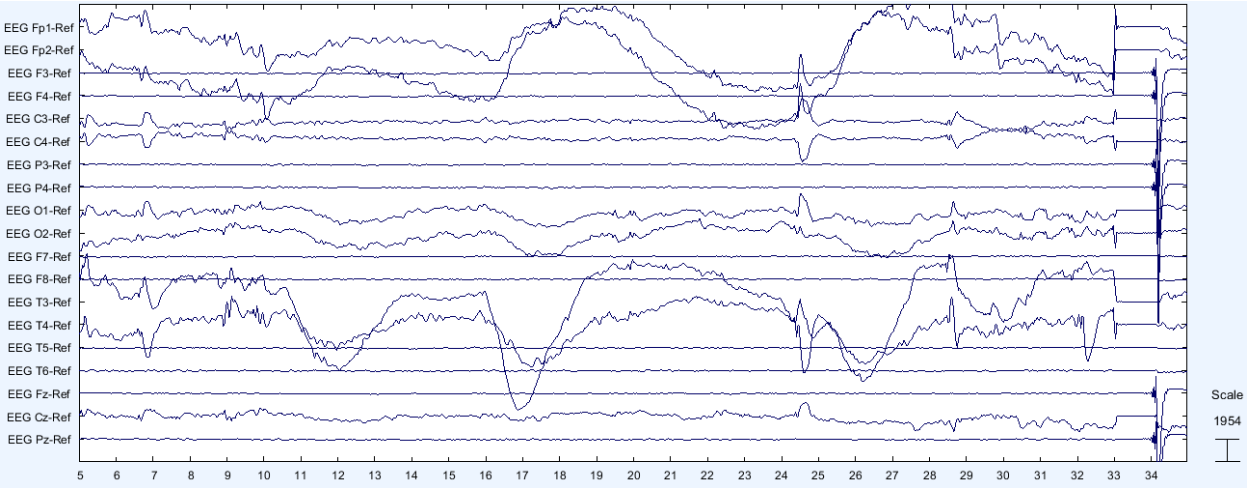


Figure 20: A sample segment of locally collected neonatal EEG with clinical card name 706905 between from time range 30 sec to 60 sec.

4.2. Preprocessing Results

4.2.1. Filtering Result

In this proposed work the neonatal multi-channel EEG signal was filtered between 0.1Hz as lower cut frequency (high pass filter), whereas 15Hz as higher cut frequency (low pass filter) with transition band width 0.5 Hz. figure 21 shows the frequency response of the EEG signal from public dataset with clinical information moderate asphyxia (neonate 1; at 1 min 54 s to 2 min 3 s), figure 22 shows the original neonatal EEG signal before band pass filtered (neonate 1; at 1 min 54 s to 2 min 3 s), and figure 23 shows the neonatal EEG signal filtered between 0.1Hz and 15Hz (neonate 1; at 1 min 54 s to 2 min 3 s).

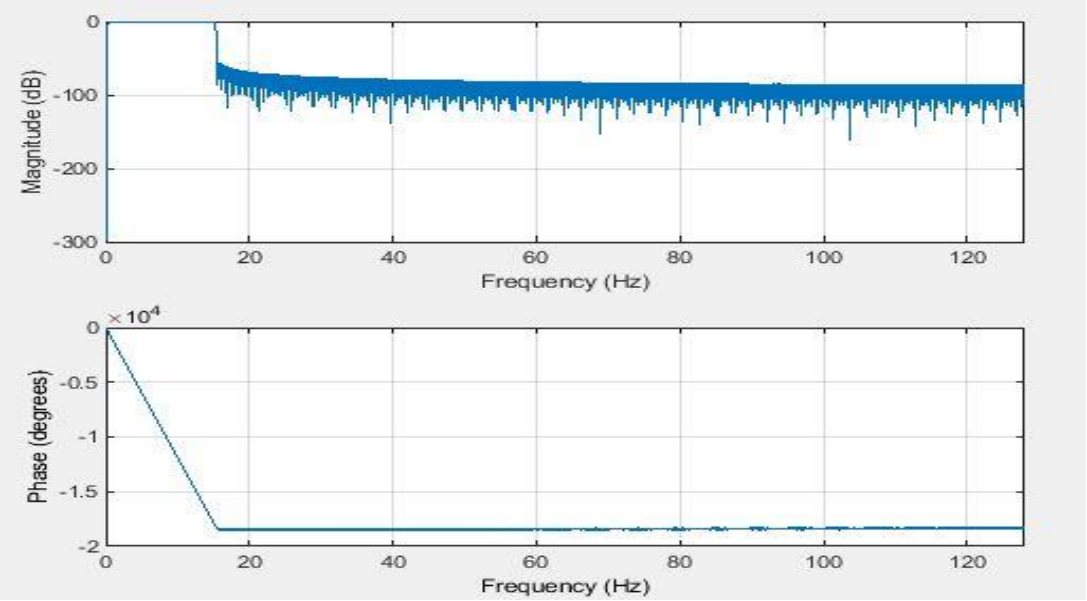


Figure 21: The frequency response of bandpass filtering of the continuous neonatal EEG (Neonate 1)

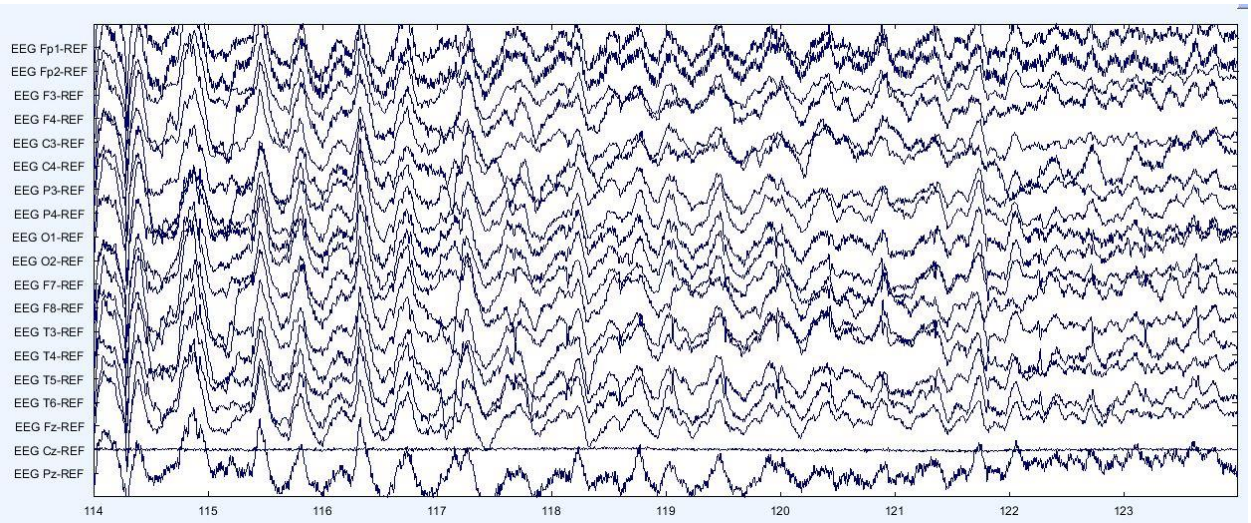


Figure 22: The neonatal EEG signal (neonate 1; at 1 min 54 s (114s) to 2 min 3 s(124s))) with clinical information moderate asphyxia before filtered

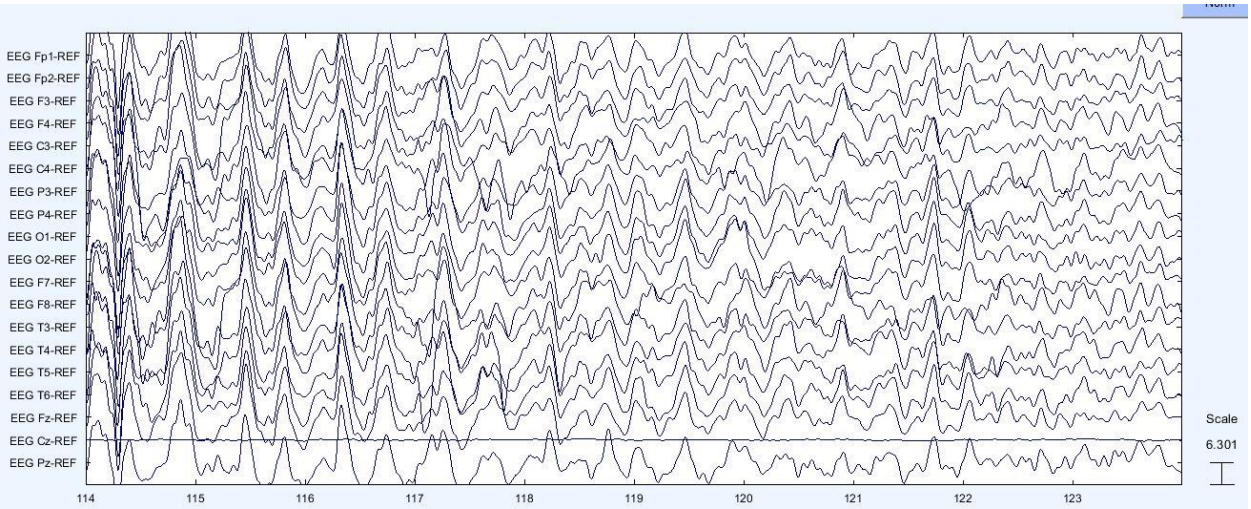


Figure 23: The neonatal EEG signal filtered between 0.1Hz and 15Hz (neonate 1; at 1 min 54 s to 2 min 3 s).

4.2.2. Down-Sampling Result

In order to decrease the complexity of the CNN network, the EEG is down-sampled to 32 Hz. The down-sampling was done based on Nyquist sampling theorem which provides a prescription for the nominal sampling interval required to avoid aliasing. It stated simply as follows. "*The sampling frequency should be at least twice the highest frequency contained in the signal*" [50].

Or mathematical terms:

$$f_s \geq 2f_c, \quad (15)$$

Where f_s is sampling frequency (how often samples are taken per unit of time or space), and f_c is the highest frequency contained in the signal.

Figure 24 shows the EEG signal record of neonate (neonate 1; 5 min 29 s to 5 min 39 s) with mild/moderate asphyxia with sampled at 256Hz, and figure 25 shows the neonatal EEG signal down-sampled from 256Hz to 32Hz (neonate 1; 5 min 29 s to 5 min 39 s).

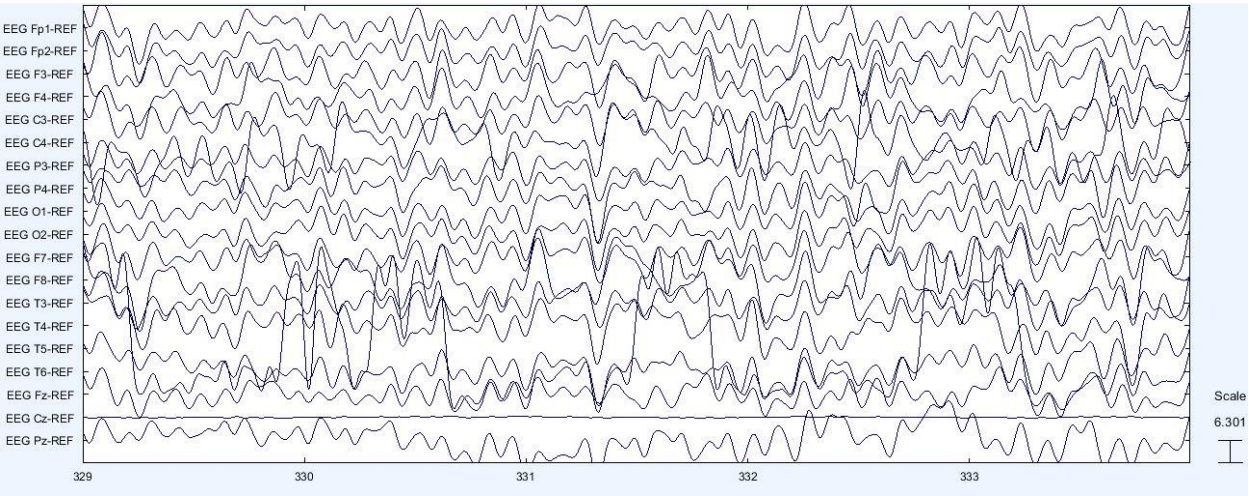


Figure 24: The EEG signal record of neonate with moderate asphyxia with sampled at frequency 256Hz

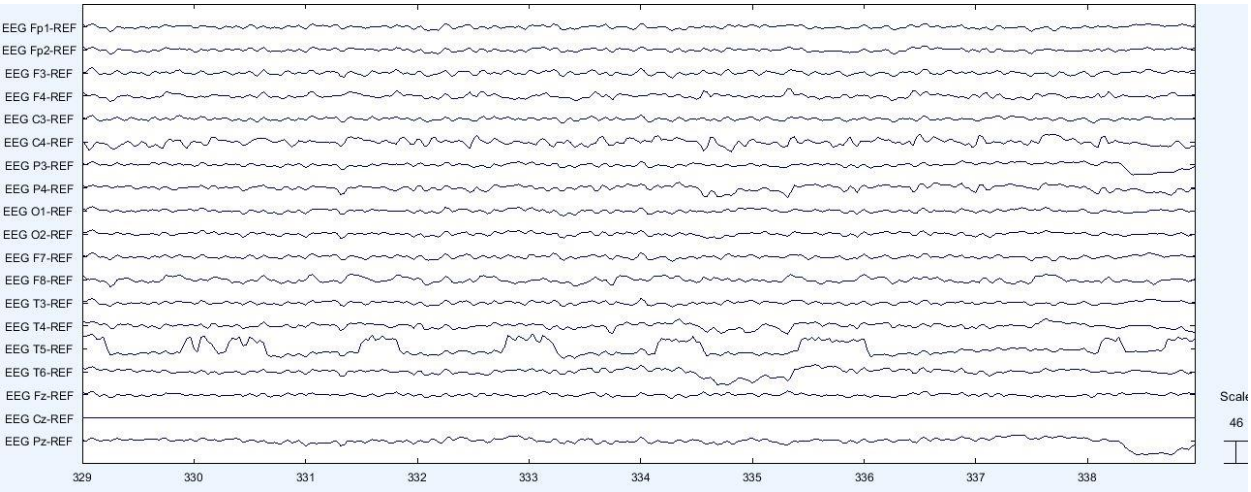


Figure 25: The neonatal EEG signal down-sampled from 256Hz to 32Hz

4.2.3. Re-referencing Result

Due to local EEG recording was stimulated by hyperventilation, photic stimulation and drug administration there is large amplitude variation in the EEG. Therefore average referencing technique was done on locally collected datasets. When applying the common average reference, the new reference is average electrical activity measured all scalp electrode channels. In this case, re-referencing was achieved by creating an average of all scalp channels and subtracting the resulting signal from each channel. Figure 26 shows the neonatal EEG before referencing (neonate 1; 1 min 1 s to 1 min 31 s) and figure 27 shows the neonatal EEG after referencing (neonate 1; 1 min 1 s to 1 min 31 s).

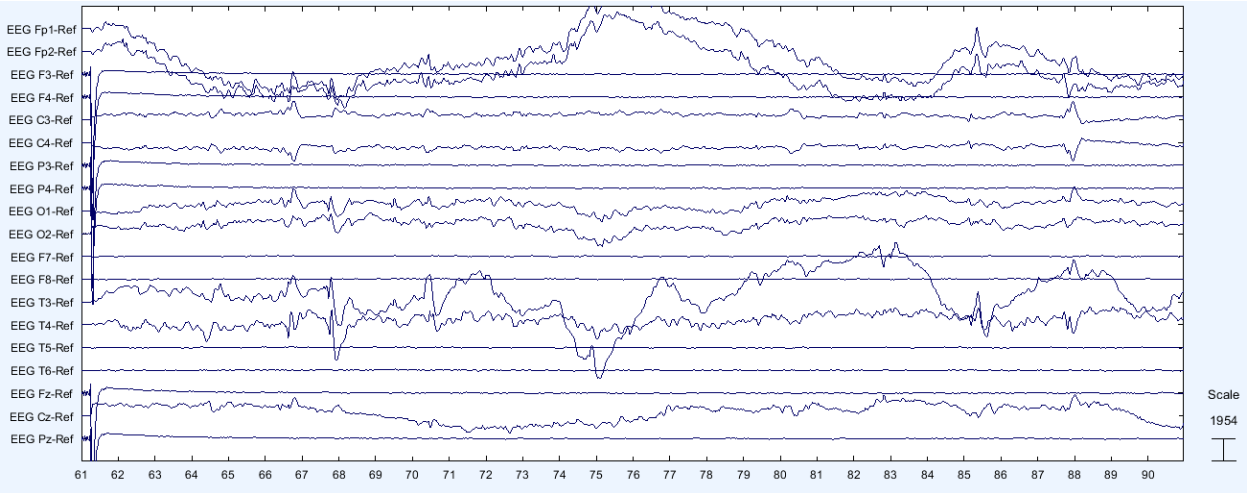


Figure 26: The neonatal EEG before referencing (neonate 1from local data)

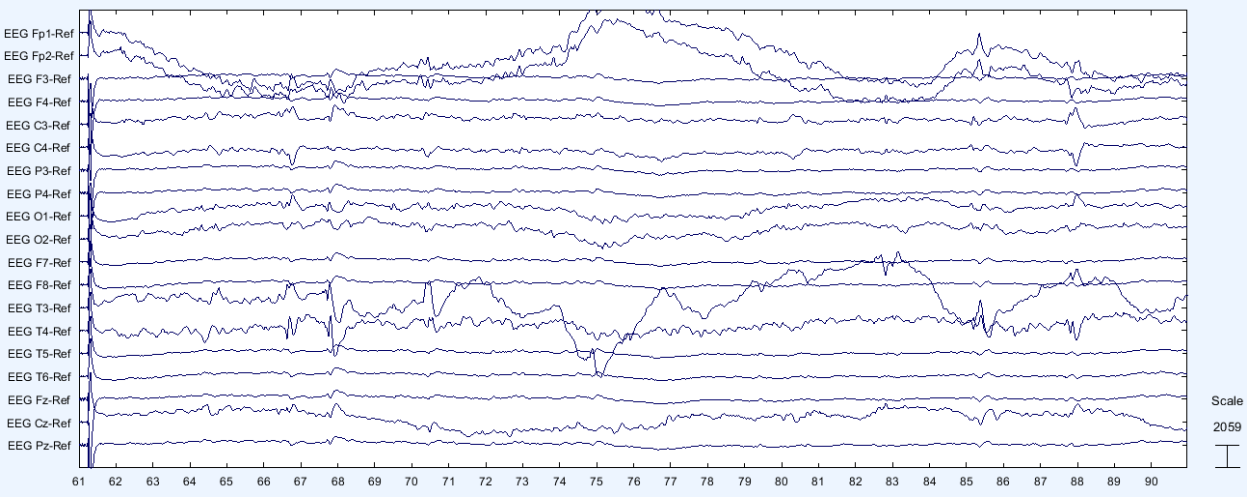


Figure 27: The neonatal EEG after referencing (neonate 1, from local data)

4.2.4. Removing Bad Signals and/or Unwanted Channel

Neonatal EEG signal is low voltage signal which are contaminated by various types of noises or artifacts such as electrical interference, physiological noise, ECG movement of muscle (EMG), ocular signal (EOG). Although, these all noises are not preventable, there are some signals full of noises which could affects the interpretation of wave forms. Additionally there are also deferent sensors connected together with scalp electrodes to monitor other physiological variables such as Pulse-oximetry (SPO2), Electrocardiography and more. Therefore, removing bad signals as well as unwanted channels is important to focus on specific targeted applications. In this work, spo2 and ECG signals were removed from both public and local datasets to focus on signals only generated from head of neonates. On the other hand 24 empty signals removed from locally collected datasets. Figure 28 shows the neonatal EEG signal before removing any signal or channels (neonate 1(public dataset); 1 min 33 s), figure 29 shows the neonatal EEG signal after removing spo2 and ECG channels (neonate 1(public dataset); 1 min 33 s).

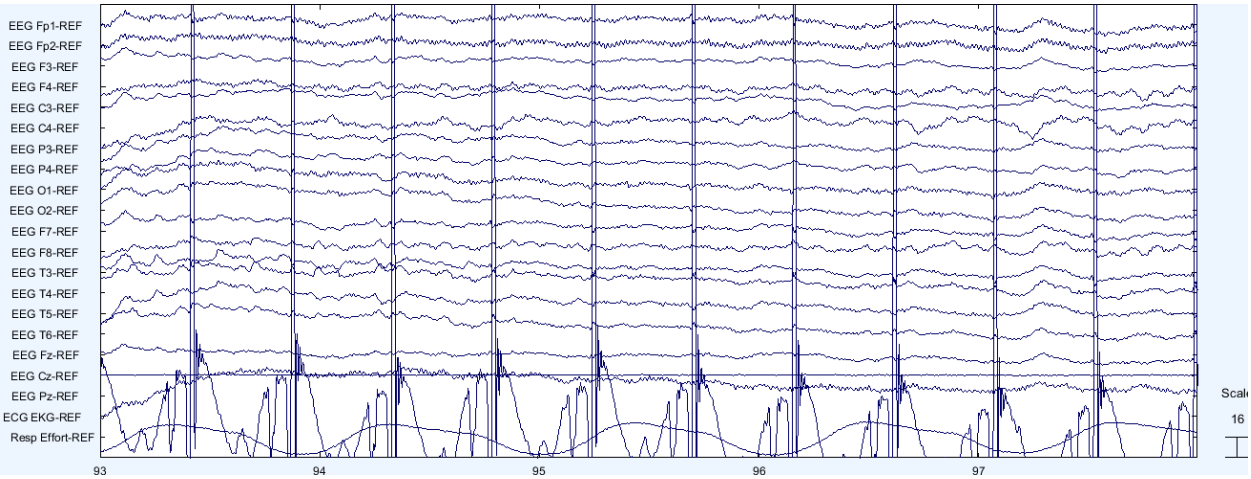


Figure 28: The neonatal EEG signal before removing any signal or channels (neonate 1 from public dataset)

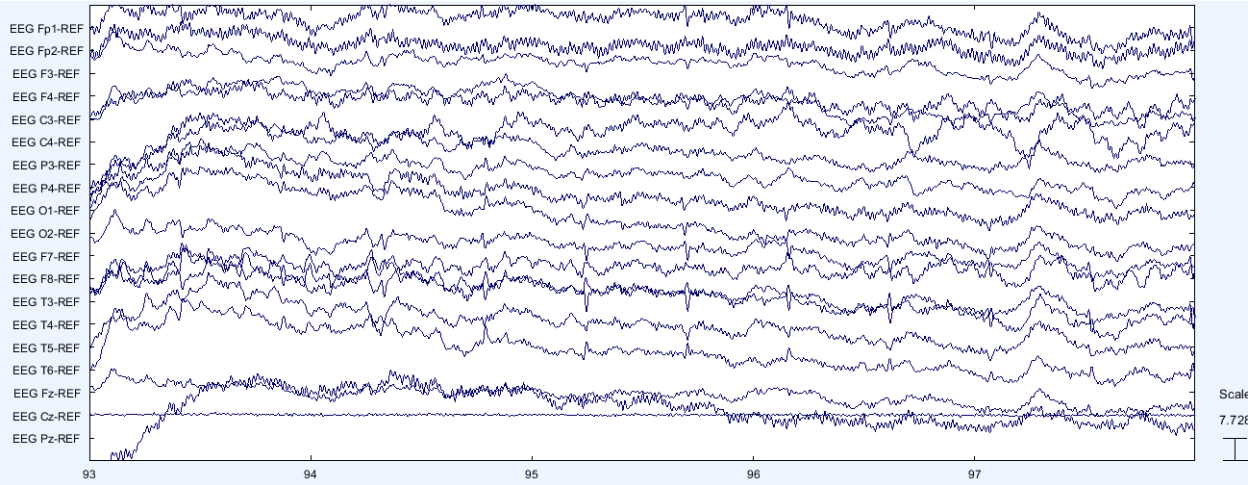


Figure 29: The neonatal EEG signal after removing spo2 and ECG channels (neonate 1 from public dataset)

4.2.5. Signal Segmenting Result

In order to view distinct characteristics of EEG signal, the continuous EEG segmented in to small portion of time. In this thesis EEG recorded approximately 1 hour became segmented in to 10 sec which used as input to deep neural network models. Figure 30 shows the neonatal EEG signal segment of 60 s (neonate 1; from 1 min, 33 sec to 2 min 33 s, figure 31 shows the neonatal EEG signal segment of 10 s (neonate 1; from 1 min, 33 sec to 1 min 43 sec).

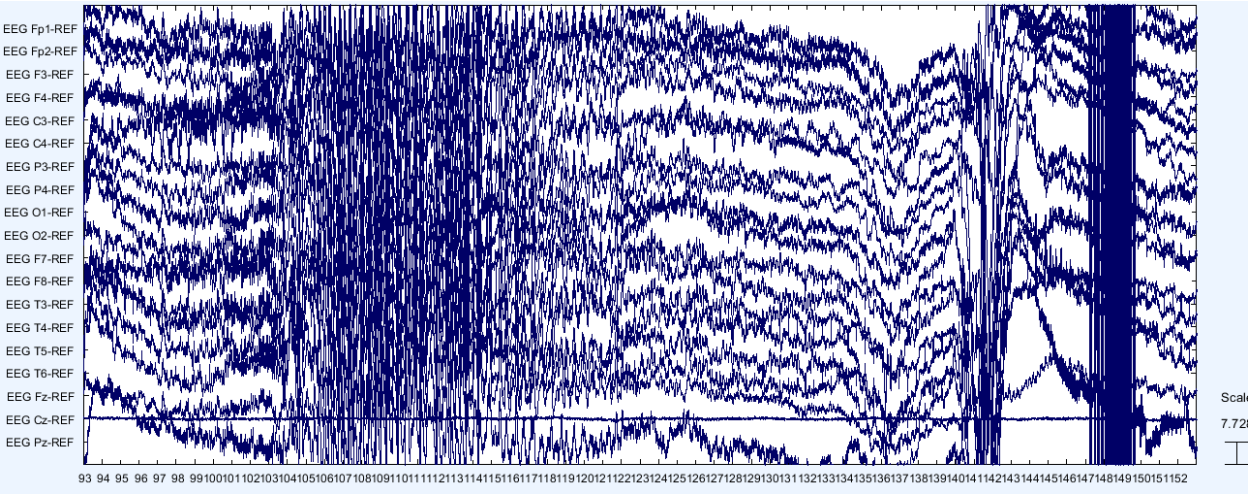


Figure 30: The neonatal EEG signal segment of 60 s

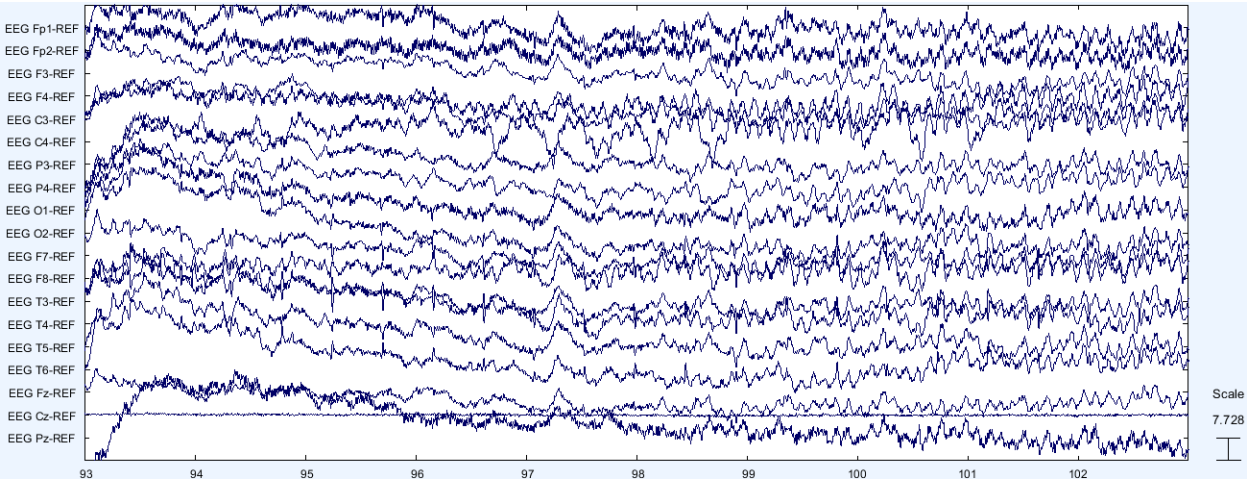


Figure 31: The neonatal EEG signal segment of 10 s

4.2.6. 2D Image generation from Multichannel EEG Time Series Signal Result

For the proposed deep neural networks each segment of EEG, which is 19 channels, 10 second sampled at 32Hz window resulting 19 * 320 array, where the first and second terms corresponds to number of the input channel and number of sample in specified time interval respectively. These raw waveform images are the inputs of the proposed CNN. The CNN can be the most suitable network structure for automated seizure detection when applied to the images of raw EEG waveforms, since CNN can effectively learn a general spatially-invariant representation of seizure patterns in 2D representations of raw EEG [51]. The networks with raw waveform inputs showed the ability to learn the underlying characteristics of EEG [37]. Figure 32 shows the corresponding

raw waveform image of 19 channel and 10 s segment sampled at 32Hz i.e., (19 * 320) of (neonate 1 public dataset; 1 min, 54 s to 2 min, 4 s), and figure 33 shows the rescaled raw waveform image from 19 * 320 to 227 * 227 of (neonate 1 from public dataset; 1 min, 54 s to 2 min, 4 s).

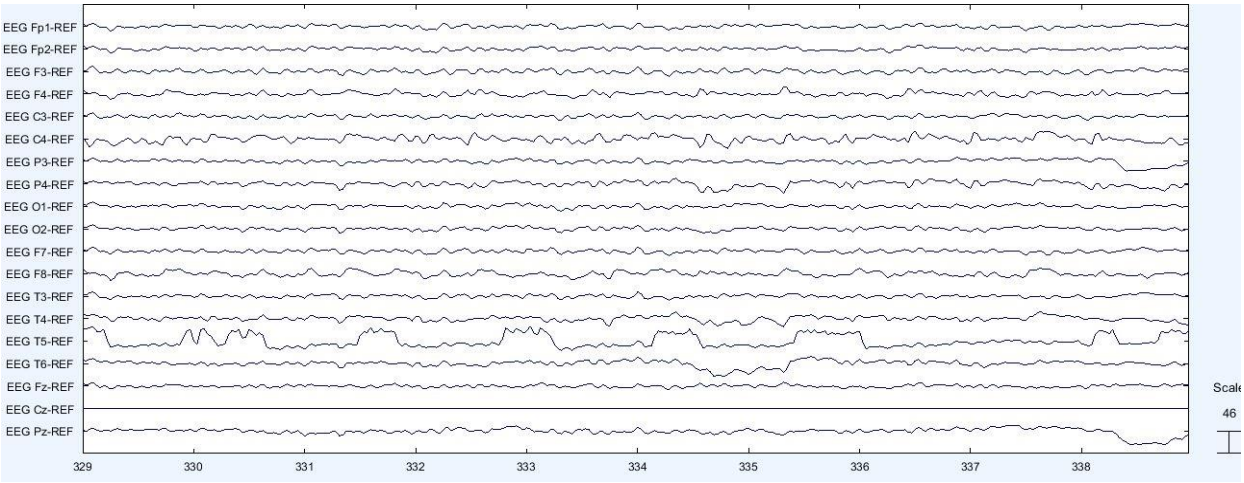


Figure 32: The corresponding equivalent raw waveform image of 19 channel and 10 s window sampled at 32Hz i.e., 19 * 320 (neonate 1 from public dataset; 1 min 54 s to 2 min 4 s)

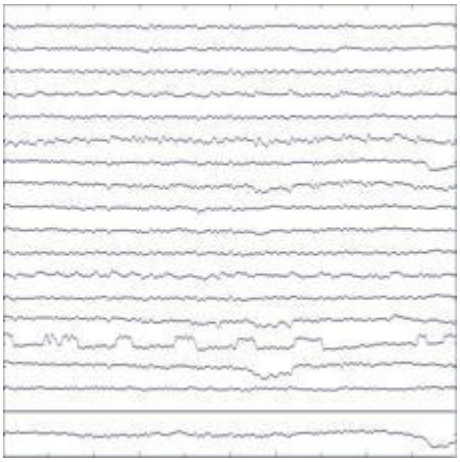


Figure 33: The rescaled raw waveform image from 19 * 320 to 227 * 227 sampled at 32Hz i.e., (19 * 320) (neonate 1 from public dataset; 1 min 54 s to 2 min 4 s)

To train proposed models the pre-processed continuous EEG data segmented or windowed then raw waveform saved in .jpg image format. The image became rescaled to 256-by-256 for custom CNN whereas, 227-by-227 for pre-trained Alexnet models. The number of image data to train,

validate and test the proposed models during binary and grade classification is described in the table 8 and 9 respectively.

Table 8: The training, test and validation image data for binary classification

		Train data	Validation data	Test data
Public dataset	Seizure	1009	202	202
	Normal	1001	200	200
Local dataset	Seizure	200	40	40
	Normal	200	40	40
Total		2410	482	482
Grand total				**3374**

Table 9: The training, test and validation image data for grade classification

		Train data	Validation data	Test data
Public dataset	Grade_1	329	82	52
	Grade_2	273	68	30
	Grade_3	208	52	22
Total		810	202	104
Grand total				**1116**

4.3. Model Training Results

4.3.1. Training result of binary classification for seizure detection

In this study, binary classification indicates the classification of given input neonatal EEG in the form of image with pre-defined size into normal or seizure type. As per the data split ratio used, the number of data used for training the systems were one thousand two hundred one (1201) images for normal class and one thousand two hundred nine (1209) images for seizure class. That was, a total of two thousand four hundred ten (2410) image data taken as a training set. And two hundred forty two (242) images taken as a validation data from seizure class and 240 images from normal class. Likewise, for the test set a total of two hundred forty (240) images taken for each class as a test set.

Once data split and other preprocessing procedures were complete custom convolutional neural network, Alexnet models were trained to perform the classification task. Hence, the models were trained using the training dataset and validated with the validation dataset. Finally the learning and generalizability performance of the models were measured using a learning curve. Figure 34 and figure 35 show the training and validation accuracy plot on epoch versus accuracy and loss of Alexnet and custom CNN respectively.

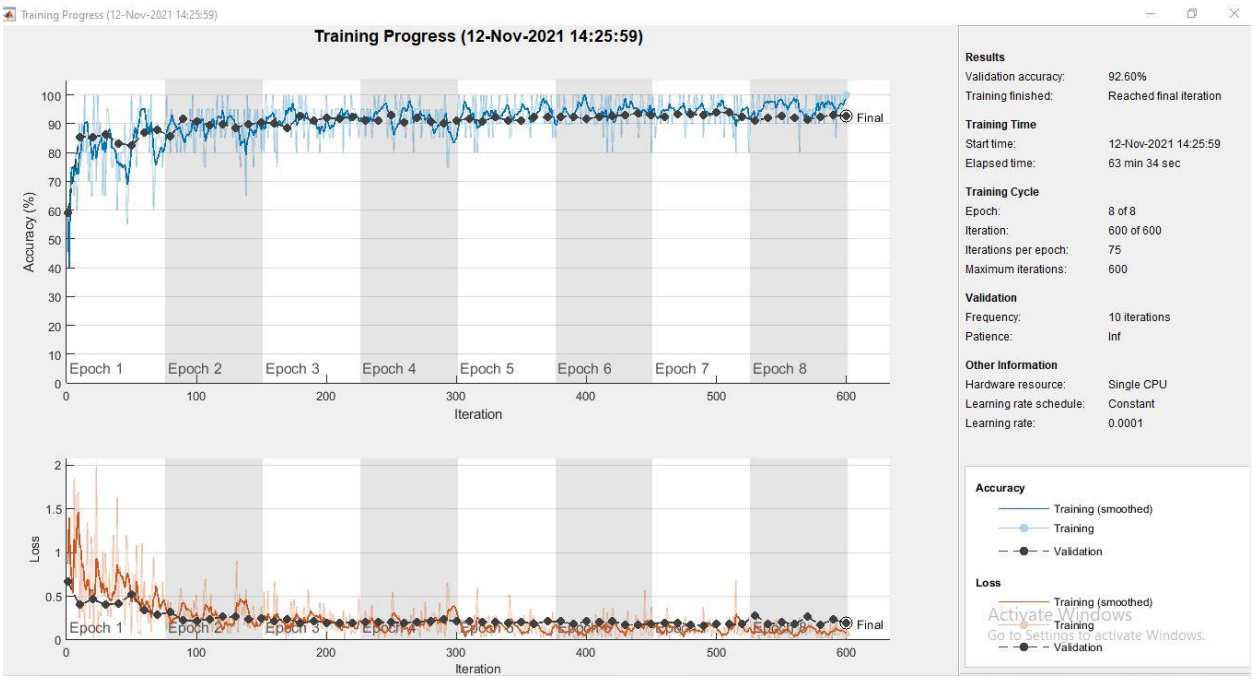


Figure 34: The Binary classification training and validation accuracy plot on epoch versus accuracy and loss of Alexnet model

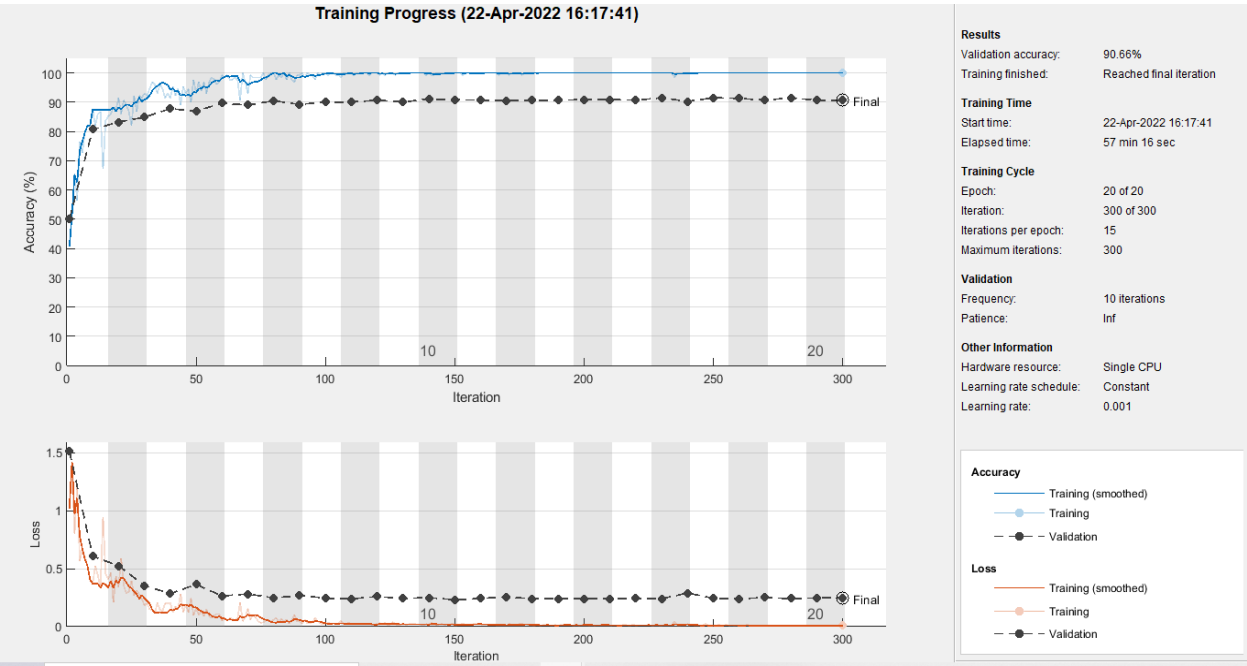


Figure 35: The Binary classification training and validation accuracy plot on epoch versus accuracy and loss of custom CNN model

In this phase, better validation loss was achieved using Alexnet at the 8^{th} epoch with validation loss of 0.141. Therefore, the model was saved the weight value acquired at the last epoch for doing the classification task. As a result, 98.6% training accuracy and 92.6% validation accuracy were achieved. On the other hand custom CNN also trained and the validation loss was achieved at the 20^{th} epoch with loss validation of 0.25. Therefore, the model was saved the weight value acquired at the last epoch for doing the classification task. As a result, 99.8% training accuracy and 90.66% validation accuracy was achieved.

4.3.2. Training phase of multi classification for neonatal seizure

The grade indicates the particular level of rank or aggressiveness of the neonatal seizure type. It was classified into three classes Grade 1, Grade 2 and Grade 3. Of the total (810) images, three hundred twenty nine (329), two hundred seventy three (273) and two hundred eight (208) images were taken for grade 1, grade 2 and grade 3 classes as a training set respectively. Moreover, eighty two (82) from grade 1, sixty eight (68) images from grade 2, and fifty two (52) images from grade 3 were taken as a validation set for both models.

Finally the data was fed to the models and their learning and generalization ability performance were measured using the training and validation curve respectively. During training pre-trained Alexnet the lowest validation loss was realized at the 10^{th} epoch, that was, 0.4 validation loss values attained. At this point, a validation accuracy of 86.54 percent was achieved. Whereas, during training custom CNN the lowest validation loss was realized at the 30^{th} epoch, that was, 0.3 validation loss values was attained. At this point, an accuracy of 88.6 percent validation accuracy was achieved. Figure 36 and Figure 37 shows the results obtained during training phase of epoch versus accuracy or loss for the grade level of Alexnet and custom CNN classification respectively.

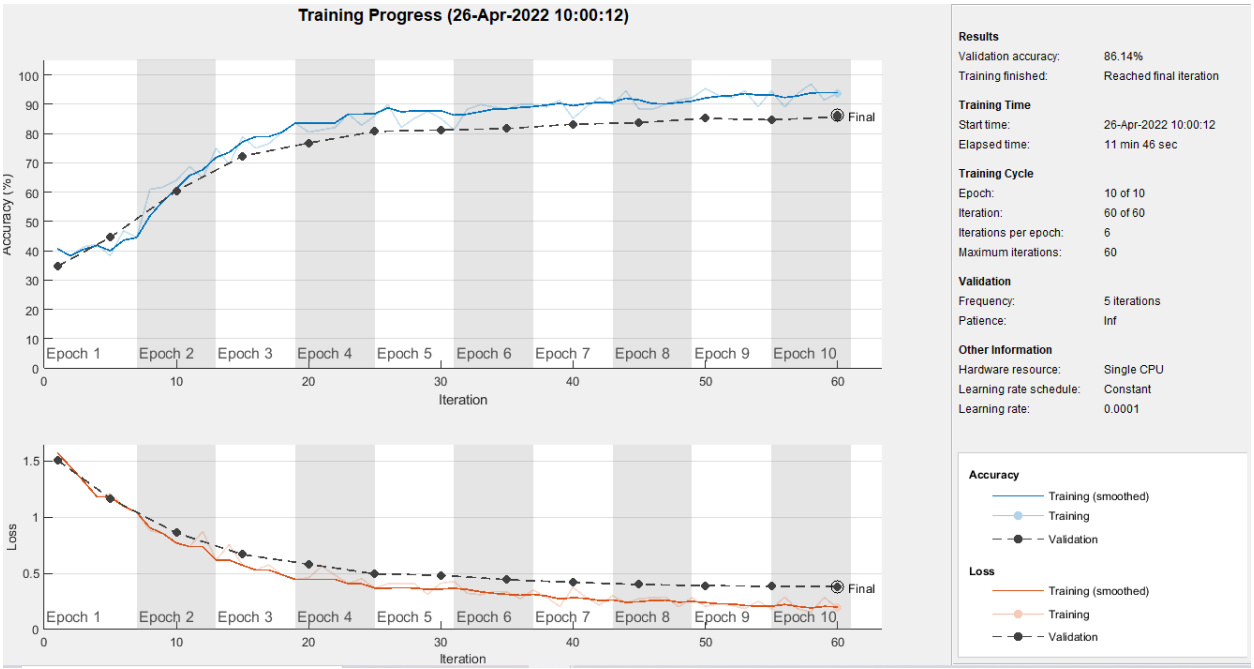


Figure 36: The grade level classification training and validation progress using Alexnet model

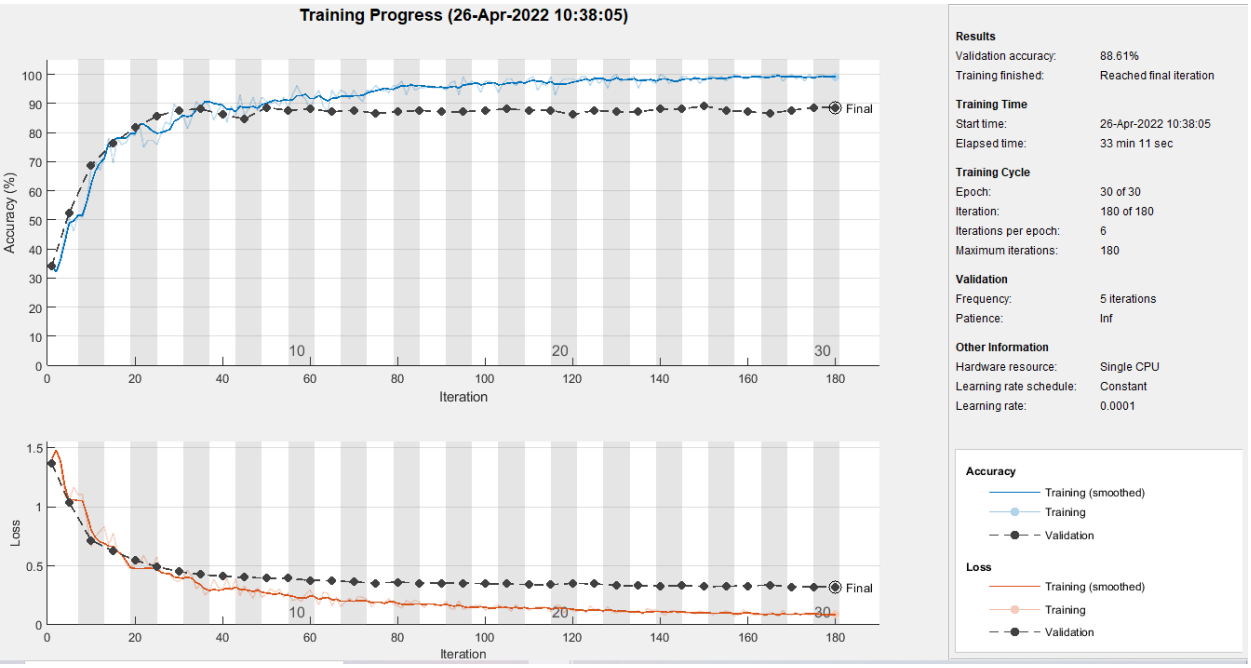


Figure 37: The grade level classification training and validation progress curve of custom CNN

4.3.3. Summary of training results

The overall result of training phase of the system including the training accuracy, validation accuracy, training loss and validation loss for the binary classifiers using Alexnet and custom CNN summarized in the Figure 38 below and table 10. The training accuracy, validation accuracy, training loss and validation loss for the multi classifiers using Alexnet and custom CNN summarized in the table 11 and Figure 39 below.

Table 10: The summary of training accuracy, validation accuracy, training loss and validation loss of the binary classifiers

	Training accuracy	Training loss	Validation accuracy	Validation loss
Alexnet	0.99	0.09	0.94	0.16
Custom CNN	0.98	0.08	0.92	0.23

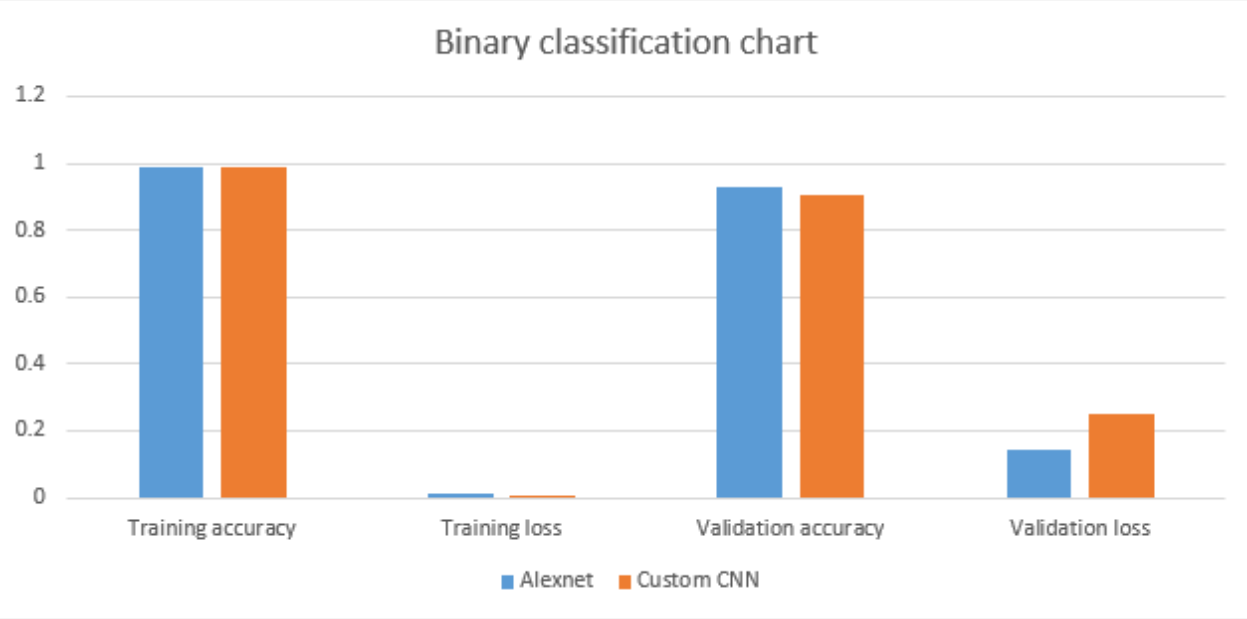


Figure 38: The summary chart of training accuracy, validation accuracy, training loss and validation loss of the multi classifiers

Table 11: The summary chart of training accuracy, validation accuracy, training loss and validation loss of the multi(grade) classifiers

	Training accuracy	Training loss	Validation accuracy	Validation loss
Alexnet	0.96	0.25	0.89	0.4
Custom CNN	0.98	0.15	0.9	0.25

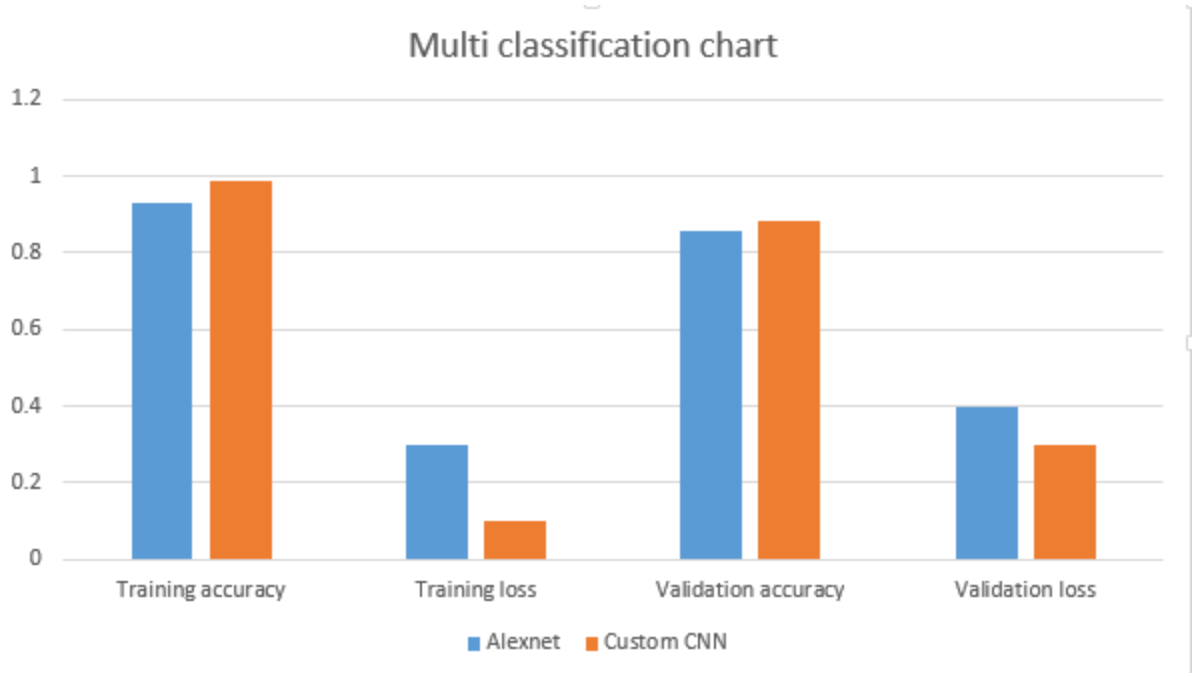


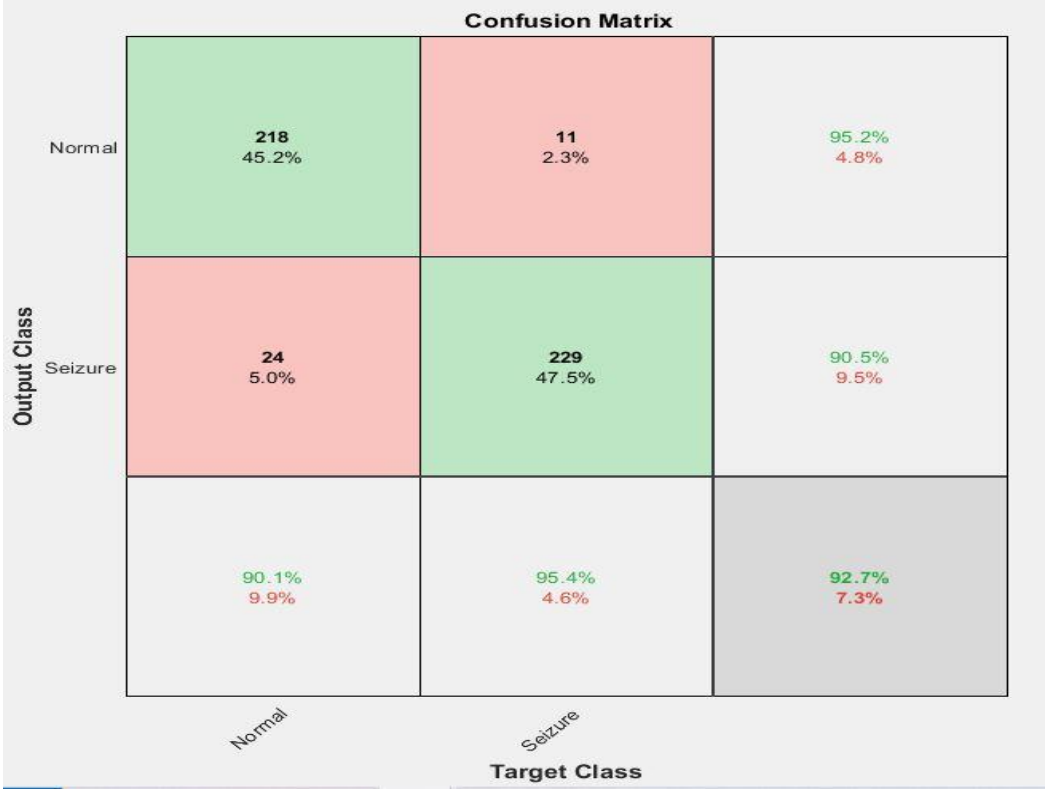
Figure 39: The summary chart of training accuracy, validation accuracy, training loss and validation loss of the multi(grade) classifiers

4.4. Testing Phase Results

4.4.1. Testing Phase of binary classification for Seizure Detection

In the binary classification, the models were expected to categorize given images into normal or seizure classes. “Normal” represents the normal class whereas, “Seizure” represents the seizure or abnormal class. To do this, 242 images for normal and 240 images for seizure were considered from each class. Based on the actual and predicted values a confusion matrix was generated. The binary classifier using Alexnet model confusion matrix shown in the table 12 below. Out of the 242 images in the normal class, 218 images were correctly classified as normal types, while 24 of the images were predicted as seizure class. On the other hand, for the seizure class, out of the 240 images, 229 images were correctly classified as seizure, whereas 11 of the images were predicted as non-seizure or normal types.

Table 12: The resulted confusion matrix for the binary classifier (normal or seizure) using Alexnet



Once the confusion matrix was done, the TP, TN, FP and FN values were easily known. And from those values the precision, recall, specificity, f1-score and test accuracy were calculated. Table 13 shows the overall result of binary classification using Alexnet.

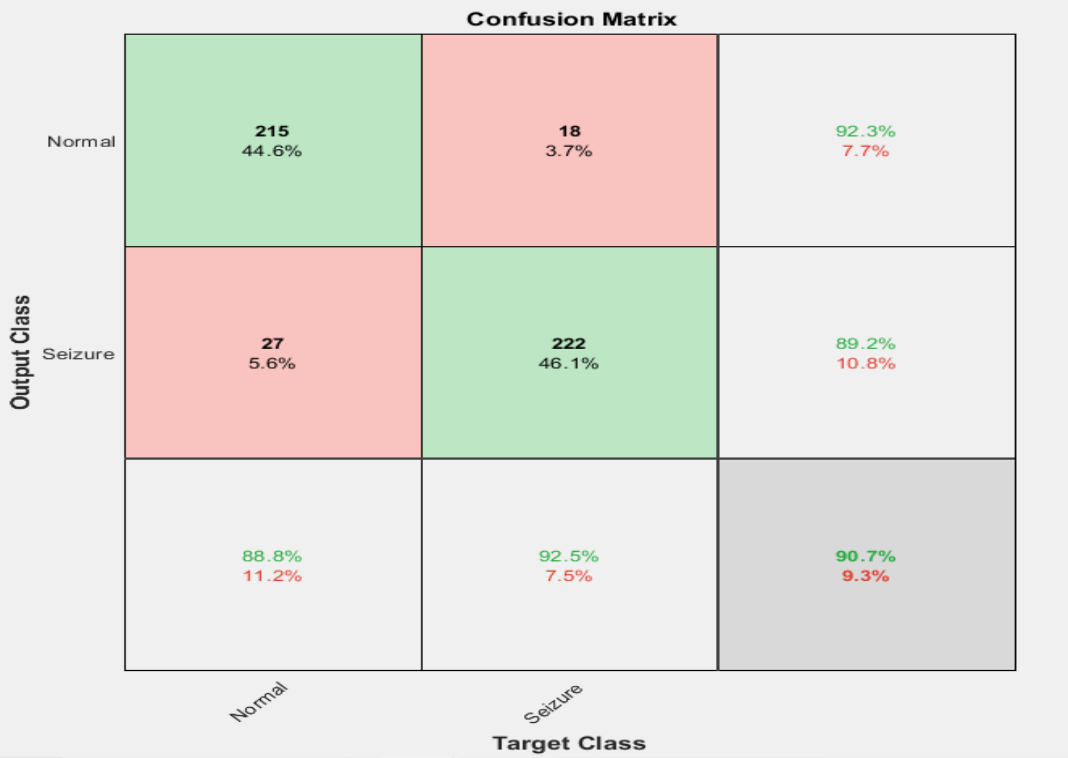
Table 13: The overall result of binary classification using Alexnet

	Precision	Recall	F1-score	Specificity	Accuracy
Seizure	95.4	90.05	92.6	95.2	92.6
Normal	90.4	95.2	92.9	90.5	92.6

Finally average test accuracy of the model for binary classification was calculated using the average of the accuracies of the two classes. As a result, 92.6% test accuracy, 92.9% precision, 92.62% recall, 92.7% F1-score and 92.85% specificity was achieved.

The binary classifier using custom CNN model confusion matrix shown in the table 14. Out of the 242 images in the normal class, 215 images were correctly classified as normal types, while 27 of the images were predicted as seizure class. On the other hand, for the seizure class, out of the 240 images, 222 images were correctly classified as seizure, whereas 18 of the images were predicted as non-seizure or normal types.

Table 14: The resulted confusion matrix for the binary classifier (normal or seizure) using custom CNN



The values of precision, recall, specificity, f1-score and test accuracy were calculated. Table 15 shows the overall result of binary classification using custom CNN.

Table 15: The overall result of binary classification using custom CNN

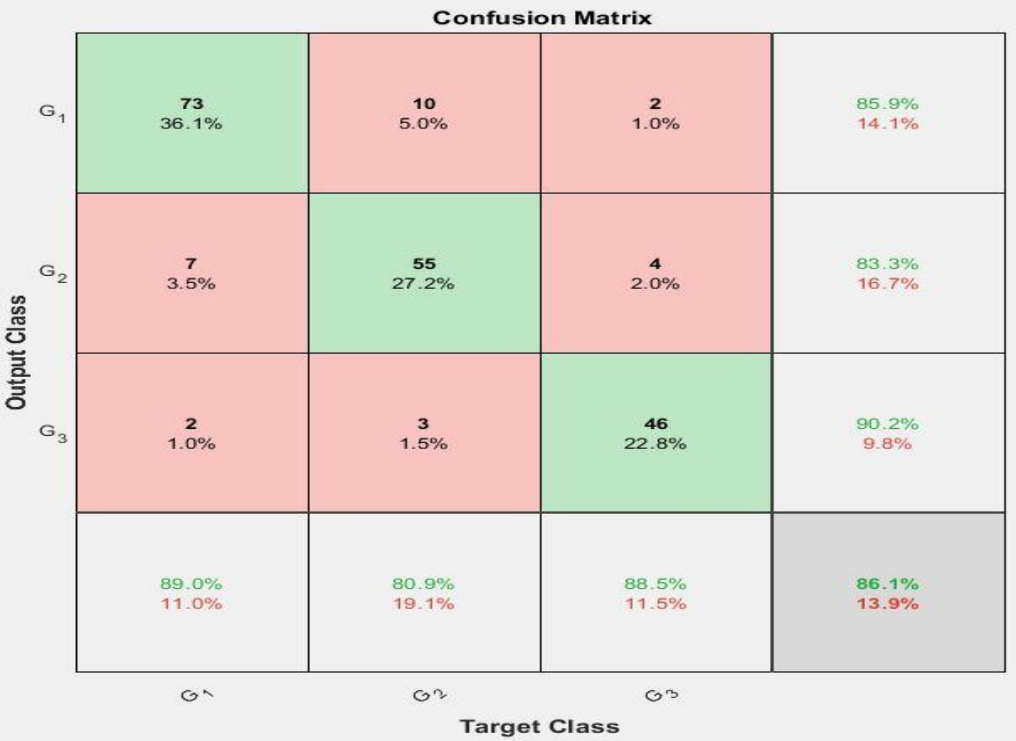
	Precision	Recall	F1-score	Specificity	Accuracy
Seizure	92.5	92.3	90.82	89.1	90.66
Normal	88.8	89.2	90.51	92.2	90.66

Finally average test accuracy of the model for binary classification was calculated using the average of the accuracies of the two classes. As a result, 90.66% test accuracy, 90.65% precision, 90.75% recall, 90.7% F1-score and 90.65% specificity was achieved.

4.4.2. Testing phase of multi classification for neonatal seizure grade

In the confusion matrix, the grade levels were labeled as, "G_1" representing grade 1, "G_2", representing grade 2 and "G_3" representing grade 3. The training result of Alexnet model for multi classification indicated using a confusion matrix shown in the table 16. Out of the 82 images in the grade_1 class, 73 images were correctly classified as grade_1 types, while 7 of the images were predicted as grade_2 and 2 images as grade_3 classes. Out of 68 images in grade_2 class, 55 images were correctly classified as grade_2 types, while 10 images wrongly classified as grade_1 classes and 3 images as grade_3 classes. Out of 52 images in grade_3 classes, 46 images were correctly classified as grade_3, while 2 images wrongly classified as grade_1 and 4 images as grade_2 classes.

Table 16: The resulted confusion matrix for the neonatal seizure grade level classifier using Alexnet



From the result found using the confusion matrix, the precision, recall, specificity, F1-score and test accuracy results were calculated. Table 17 shows the grade classification results using Alexnet model.

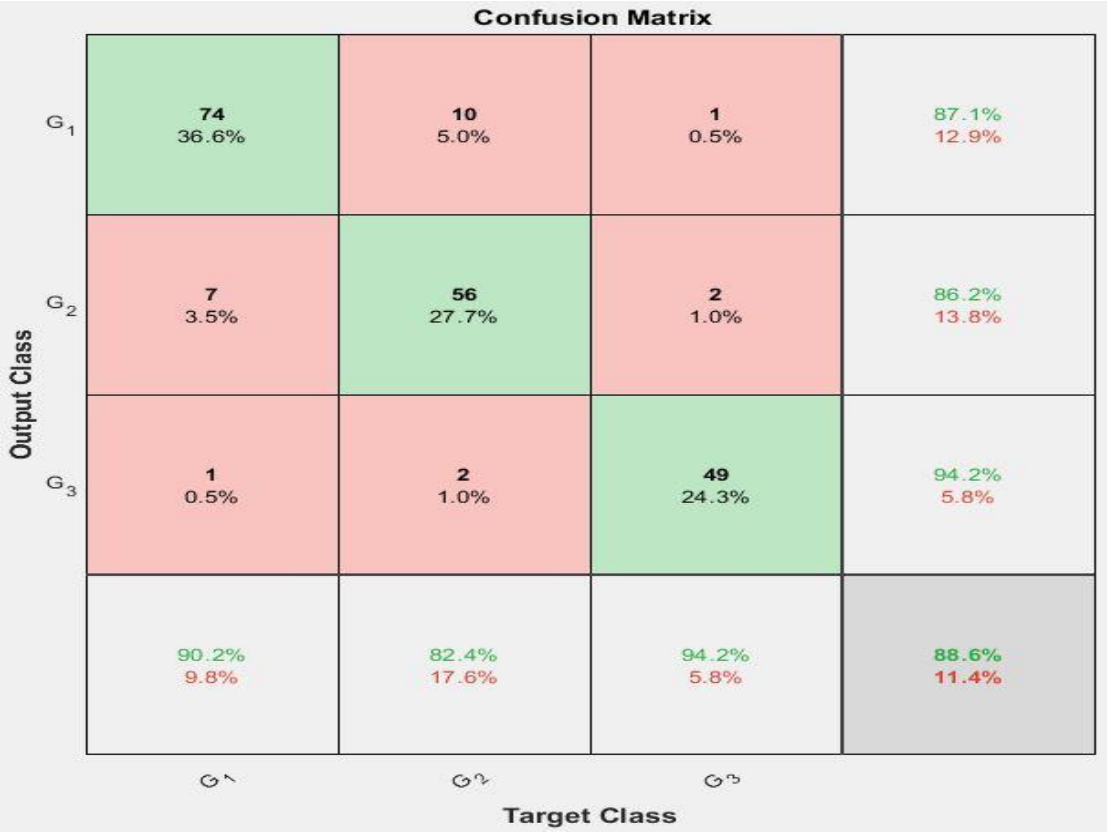
Table 17: The overall grade classification results using Alexnet model

	Precision	Recall	F1-score	Specificity	Accuracy
Grade 1	89.0	85.9	87.4	86.18	86.1
Grade 2	80.9	83.3	82.08	91.02	86.1
Grade 3	88.5	90.2	89.34	99.35	86.1

Finally, the general performance of the developed model for classifying the grade of a given image was assessed and an average test accuracy of 86.1%, precision rate of 86.13%, recall rate of 86.5%, f1 score of 86.27% and specificity of 92.18% was achieved.

The training result of custom CNN model for multi classification indicated using a confusion matrix shown in the table 18. Out of the 82 images in the grade_1 class, 74 images were correctly classified as grade_1 types, while 7 of the images were predicted as grade_2 and 1 images as grade_3 classes. Out of 68 images in grade_2 class, 56 images were correctly classified as grade_2 types, while 10 images wrongly classified as grade_1 classes and 2 images as grade_3 classes. Out of 52 images in grade_3 classes, 49 images were correctly classified as grade_3, while 1 images wrongly classified as grade_1 and 2 images as grade_2 classes.

Table 18: Confusion matrix of multi classification using custom CNN model



From the result found using the confusion matrix, the precision, recall, specificity, F1-score and test accuracy results were calculated. Table 19 shows the grade classification results using custom CNN model.

Table 19: The overall grade classification results using custom CNN

	Precision	Recall	F1-score	Specificity	Accuracy
Grade 1	90.2	87.1	88.6	86.18	88.6
Grade 2	82.4	86.2	84.3	91.02	88.6
Grade 3	94.2	94.2	94.2	80.35	88.6

Finally, the general performance of the developed model for classifying the grade of a given image was assessed and an average test accuracy of 88.6%, precision rate of 88.93%, recall rate of 89.16%, f1 score of 89.03% and specificity of 85.85% was achieved.

4.5. Discussion

Neonatal seizure is a sudden, abnormal and excessive electrical activity in the brain caused by deferent metabolic disorders listed in section (1.2) during neonatal periods. It is a common emergency intensive care condition, occurring in about 1 to 7 out of 1,000 neonates born at full-term, more common in pre-term neonates 57 to 132 out of 1000[1].

Neonatal seizure can be diagnosed using deferent method such as the differential diagnosis applied to distinguish seizure from jitteriness and benign neonatal sleep myoclonus by comparing movement and some body functioning tests blood pressure or heart rate activities, the assessment method which involves reviewing family history of seizures, maternal diabetes, maternal drug use, infections, and evidence of fetal destress in labour and history of birth trauma to provide vital clues to the etiology of the seizures, the pathology test method uses blood glucose level (BGL), serum electrolytes, calcium and magnesium, the neuroimaging techniques which includes cranial ultrasound, MRI, MEG or NMR, and the neurophysiology techniques such as EEG and ECoG.

EEG is an electrophysiological monitoring method to record electrical activity of the brain. One of the most application areas of EEG are neonatal intensive care unit (NICU) through visual interpretation of long-duration measurements EEG signal by specialized expertise. Neonatal EEG is an objective test to measure the functional integrity of the immature neonatal brain. However, EEG has relatively poor spatial sensitivity of EEG, it possesses multiple advantages over some of these techniques some are hardware costs are significantly lower than those of most other techniques, EEG has very high temporal resolution, on the order of milliseconds rather than

seconds which allows for neural dynamics analyses to be made on neurologically-relevant timescales, e.g. calculation of high-fidelity signal analysis methods, EEG is extremely non-invasive, unlike Electrocorticography (ECoG), which actually requires electrodes to be placed on the surface of the brain.

Although, EEG is advantageous tool to monitor or diagnose neonatal seizure, the interpretation of the EEG data are extremely labor-intensive, time-consuming, expensive, and importantly needs special expertise which is not available around the full hours in many hospital neonatal intensive care units (NICUs) as a worldwide, especially developing countries. Therefore automated system supports the general care giving personnel in terms of making decision or interpretation on EEG based clinical activities around NICU.

In this study the diagnosis of neonatal seizure from EEG signal using deep convolutional neural networks were done. The objectives of the models were detection of neonatal seizure and classification of grade levels of resulting seizures based on binary and multi-class classification methods respectively. For model training and testing were acquired from two online data sets (the Zenodo from Helsinki University Hospital) and local data from WUNEMMCSH. The main activities done in this thesis involves collecting neonatal EEG data, preprocessing EEG, splitting EEG dataset to specific time window, forming equivalent raw waveform image with defined size, training using custom CNN and pre-trained Alexnet models.

The aim of preprocessing EEG signal was to improve the signal quality by suppressing unwanted distortions and/or enhancing some important neonatal EEG features, so that the model can take advantages from improved data which was used for further analysis. Deep learning models performance are highly dependent on the type of the data and the total number of training data. As the number of data used for training and the quality, the number of features to be learnt by the model increases and boosting the classification performance. Furthermore, the EEG signal was segmented or split into 10 second long data, then the raw waveforms of each segmented EEG data scaled and saved in image .jpg format so that, the deep CNN trained and classify after training on these images.

The size of input image for the proposed networks are 227 * 227 where first and second terms corresponding to row of matrix, column of matrix respectively. In this work the number of data for each class were prepared separately based on expert annotation and clinical data. Therefore, a

total of two thousand four hundred ten 2410 images were generated from all the classes of the EEG data for training and validation. Out of these, 1209 images prepared for seizure class and 1201 images for normal used for binary classification. Whereas, four hundred twelve 412, three hundred forty two 342 and two hundred sixty 260 images were taken for grade 1, grade 2 and grade 3 classes generated for training and validation.

The major aim of this study was to classify neonatal seizure into normal or abnormal/seizure classes and to determine the grade level of resulting seizure. To achieve this, two different classifying models were developed these are custom CNN and Alexnet. Better result was achieved by training a fine tuned Alexnet for binary classification and custom CNN for grade classification. The hyper parameters for the proposed network custom CNN and Alexnet are described in the section (3.7).

The learning performance of the model over 8 epochs for Alexnet and 30 epochs for custom CNN were evaluated by plotting a learning curve during each training phase as shown in the figure 34 and 35 for binary classification and whereas, figure 36 and 37 for neonatal seizure grade classification. During the performance evaluation of the model using learning curve, two different metrics were used. These are the accuracy and loss metrics. These metrics help to see how the models were optimized according to cross-entropy loss and to evaluate the model according to the classification accuracy. Good result was obtained when the accuracy curve increases and the loss curve decreases with increasing number of epochs for both training and validation datasets. As a result both metrics plots were created for each training task. As a result, from the plots it was concluded that the model has learned well and has good generalizability performance for all classification tasks.

To classify the grade level of neonatal seizure, the first step was classifying a given image of neonatal EEG data segment into binary class (Normal or Seizure). This was achieved by using the developed binary class classifying model. The models' performance was tested using a separate dataset and a good result was achieved. Finally average test accuracy of the model for binary classification was calculated. Hence, 92.6% test accuracy, 92.6% precision, 92.9% recall, 92.59% F1-score and 92.9% specificity was achieved. After binary class classification, the identified seizure type has been further classified into their subtypes (grade levels). After model training for seizure grade classification, the performance was measured in terms of accuracy, precision, recall

and specificity, and a result of an average test accuracy 88.6%, precision 88.06%, recall 83.67%, F1 score 85.61% and specificity 92.18% was achieved. This will have significant advantage in aiding physicians to have good treatment plans.

Generally, based on the test results, the final model of this research work is prepared by taking best preformed networks. As result Alexnet perform better during binary classification, the network will be used as final binary classifier. And custom CNN perform better result during multi classification therefore it will be used as final multi classifier. In other word the network of binary classification by pre-trained Alexnet and multi classification by custom CNN to be taken as final model of this work. The performance of the final Alexnet and custom CNN models are summarized in Table 20 and figure 40 below.

Table 20: The summery of the performance of the Alexnet for binary classification and custom CNN

	Precision	Recall	F1-score	Specificity	Accuracy
Binary Classification	92.9	92.62	92.59	92.9	92.6
Grade Level Identification	88.93	89.16	89.0	85.38	88.6

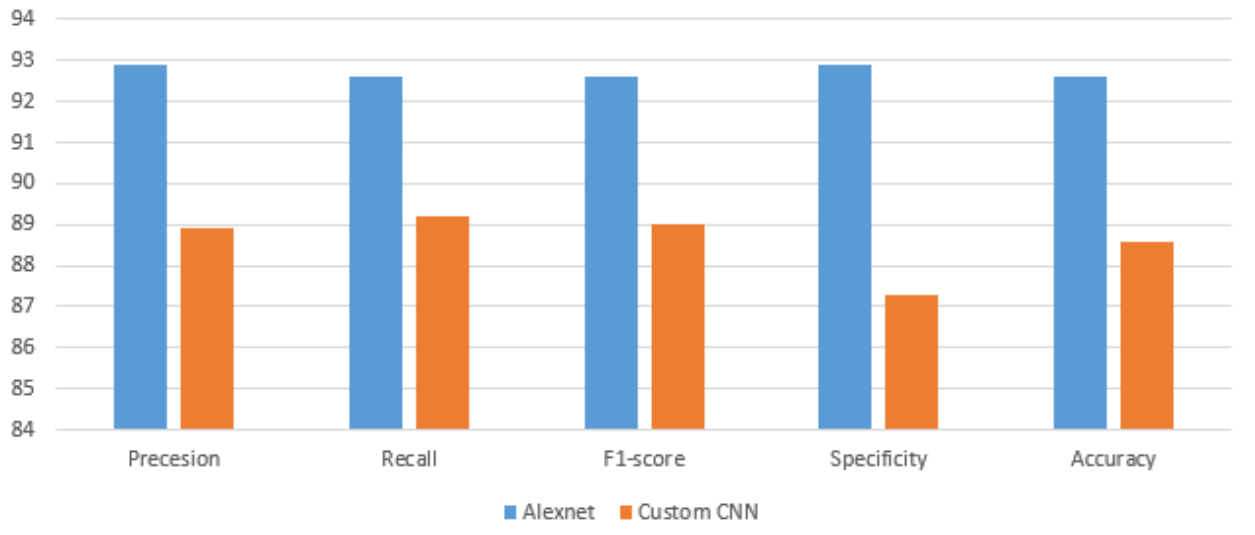


Figure 40: The summery of the performance of the final custom CNN and Alexnet models chart

Comparing the result of this study with the studies done using the Zenodo dataset [52] [53] as benchmark, we can conclude that, the developed system can classify neonatal EEG dataset in the form of images with better classification accuracy. Furthermore, the developed system has overcome the gap of further classification of neonatal EEG (seizure classes) into their grade level (G_1, G_2 or G_3).

4.6. Limitations of the Study

In this study, data has been collected from online available dataset and local data from WUNEMMCSH. But while collecting the local data, it was difficult to find variety of neonatal EEG data having seizure and as well as different grade types. This has been one challenge that hinders the study from being trained by variety of data sources.

The other limitation was lack of highly trained EEG technicians with experience, because the quality of EEG data acquired from patient depends on proper arrangements and the noise minimization during recording. Therefore, the quality of acquired EEG signal was low.

Furthermore, the number of EEG dataset in the form of image was not high enough to train deep CNN models to learn very deep features of the signals because limited annotated seizure class available in Zenodo dataset and small seizure class was available in locally collected datasets.

CHAPTER FIVE

5. Conclusion and Recommendation

5.1. Conclusion

This study proposed system of detection and classification of neonatal seizure from multi-channel neonatal EEG signal which was pre-processed and segmented in to defined time (10sec) so that, to further characterize distinct features of the signal. The segmented signal was changed to equivalent two dimensional image with defined size which was input to the proposed deep CNN models.

Two deferent models such as custom CNN which train from scratch and Alexnet which was pertained CNN are used to detect the neonatal seizure and classify the grade levels of the seizure. During training the Alexnet was performed better result in binary classifications (Normal or Seizure), whereas custom CNN perform better in multiclass or grade level classification (Grade 1, Grade 2 and Grade 3). Moreover, in case of binary class type the system has the ability to classify given image or segment of EEG signal into its class Normal and Seizure with accuracy of 92.6% and in case of grade level classification of average accuracy 88.6%.

This developed system can be used as a decision support system in the diagnosis of neonatal seizure, and this will have a great impact by helping neurologists, especially in those low resource settings where both the expertise and the means is in scarce.

5.2. Recommendation

As a researcher I recommend different researchers at different level of education to see the opportunity of recent methods in detection and classification of Neonatal EEG abnormalities by corresponding with deferent causes or diseases.

The dataset from online used in this research was the only available neonatal EEG dataset used for neonatal seizure studies. It can be seen from the literatures that most works were done using specifically private datasets. Even in this study only small amount of local data was included due to unavailability of similar cases and lack of local data repositories. So, I recommend the researcher can gather local data or form local repositories corresponding to different categories of studies prior to start the study in this areas.

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Appendix 1: Sample MATLAB Codes

```
Close all
clc
%==============================%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
% preprocessing The EEG signal using EEGLAB Library
%==============================%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
% EEGLAB history file generated on the 27-Dec-2021
% ------------------------------------------------------------------------
[ALLEEG EEG CURRENTSET ALLCOM] = eeglab; % Opening eeglab library
EEG = pop_biosig('C:\Users\bin\Desktop\datasets.edf\eeg1.edf',....
    'importevent','off','importannot','off');
%loading the neonatal EEG dataset from .edf format
[ALLEEG EEG CURRENTSET] = pop_newset(ALLEEG, EEG, 0,'gui','off');
%saving the corresponding EEG dataset in the form of .set format
EEG = eeg_checkset( EEG );
pop_eegplot( EEG, 1, 1, 1);% ploting the channel data scroll
EEG = eeg_checkset( EEG );
% removing unwanted signals in this case the ECG and Respiratory signals
% removed
EEG = pop_select( EEG, 'nochannel',{'ECG EKG-REF','Resp Effort-REF'});
[ALLEEG EEG CURRENTSET] = pop_newset(ALLEEG, EEG, 1,'savenew',....
    'C: \\Users\\bin\\Desktop\\eeg1.set','gui','off'); % Data saved again
EEG = pop_eegfiltnew(EEG, 'locutoff',0.1,'hicutoff',15,'plotfreqz',1);
% the neonatal EEG dataset filtered b/n 0.1 and 15 hz
[ALLEEG EEG CURRENTSET] = pop_newset(ALLEEG, EEG, 2,'savenew',...

'C:\\Users\\bin\\Desktop\\after_filtering_eeg1.set_0.5and15hz.set','gui','off
');
EEG = eeg_checkset( EEG );
% The filtered neonatal EEG dataset downsampled at 32Hz
EEG = pop_resample( EEG, 32);
[ALLEEG EEG CURRENTSET] = pop_newset(ALLEEG, EEG, 3,'savenew',...

'C:\\Users\\bin\\Desktop\\after_filtering_eeg1.set_0.5and15hzand_sampledat32H
z.set','gui','off');
EEG = eeg_checkset( EEG );% The downsampled EEG data set was saved
% The EEG dataset performed Average re-referncing
EEG = pop_reref( EEG, []);
[ALLEEG EEG CURRENTSET] = pop_newset(ALLEEG, EEG, 4,'savenew',...

'C:\\Users\\bin\\Desktop\\after_filtering_eeg1.set_0.5and15hzand_sampledat32H
z.setand_average_referanced.set','gui','off');
EEG = eeg_checkset( EEG );%The rereferenced data became saved
pop_eegplot( EEG, 1, 0, 1);
EEG = eeg_eegrej( EEG, [254 284] );
%Some unwanted portion of data became removed
[ALLEEG EEG CURRENTSET] = pop_newset(ALLEEG, EEG, 5,'savenew',...
    'C:\\Users\\bin\\Desktop\\before_filtering and after
removing_some_portion_ofdata__eeg1.set','gui','off');

%==============================%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
% %Program to recognize Neonatal Seizure
% using Custom Convolutional Neural Network
%==============================%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

%Giving path of dataset folder
```

```
EEGDatasetPath='C:\Users\bin\Desktop\EEG_Neonate_Dataset_Normal_and_Seizure';

%Reading EEG Images from Image Database Folder
EEGimages=imageDatastore(EEGDatasetPath,'IncludeSubfolders',true,...
    'LabelSource','foldernames');

%Distributing Images in the set of training and testing
numTrainFiles=800;%numTrainFiles=0.75(75%)
[TrainImages,TestImages]=splitEachLabel(EEGimages,numTrainFiles,...
    'randomize');


%----------------------Building CNN----------------------------------------

layers=[
    imageInputLayer([227 227 3],'Name','Input')

    convolution2dLayer(3,8,'Padding','Same','Name','Conv_1')
    batchNormalizationLayer('Name','BN_1')
    reluLayer('Name','Relu_1')
    maxPooling2dLayer(2,'Stride',2,'Name','Maxpool_1')

    convolution2dLayer(3,16,'Padding','Same','Name','Conv_2')
    batchNormalizationLayer('Name','BN_2')
    reluLayer('Name','Relu_2')
    maxPooling2dLayer(2,'Stride',2,'Name','Maxpool_2')

    convolution2dLayer(3,32,'Padding','Same','Name','Conv_3')
    batchNormalizationLayer('Name','BN_3')
    reluLayer('Name','Relu_3')
    maxPooling2dLayer(2,'Stride',2,'Name','Maxpool_3')

    convolution2dLayer(3,64,'Padding','Same','Name','Conv_4')
    batchNormalizationLayer('Name','BN_4')
    reluLayer('Name','Relu_4')

    fullyConnectedLayer(2,'Name','FC')
    softmaxLayer('Name','SoftMax');
    classificationLayer('Name','Output Classification');
    ];

    lgraph = layerGraph(layers);
    plot(lgraph);%Plotting Network Structore

    %-------Training Options---------------------------------------------

    options =
trainingOptions('sgdm','InitialLearnRate',0.01,'MaxEpochs',20,'Shuffle',...
        'every-
epoch','ValidationData',TestImages,'ValidationFrequency',10,...
        'Verbose',false,'Plots','training-progress');

    net = trainNetwork(TrainImages,layers,options);%Network Training
```

```
    YPred = classify(net,TestImages);%Recognizing digits
    YValidation = TestImages.Labels;%Getting Labels
    accuracy = sum(YPred == YValidation)/numel(YValidation);%Finding age
accuracy

    % Plotting Confusion Matrix
plotconfusion(YValidation,YPred)

%============================%%%%%%%%%%%%%============================
% The AlexNet Network
%============================%%%%%%%%%%%%%============================

% Training and Validation using Alexnet
DatasetPath = 'C:\Users\bin\Desktop\Grade_classification';
%Reading Images from image Database Folder
images = imageDatastore(DatasetPath,'IncludeSubfolders',true,...
    'LabelSource','foldernames');
%Distributing Images in the set of Training and Testing
numTrainFiles = 200;
[TrainImages,TestImages] = splitEachLabel(images,numTrainFiles,'randomize');
net = alexnet; %Importing pretreined Alexnet (Rquires support package)
% layersTransfer = net.Layers(1:end-3);
%Preservig all layers except last three
numClasses = numel(categories(TrainImages.Labels));
% numClasses = 3; %Number of output classes: Seizure,Non-Seizure
%Defining layers of Alexnet

% layers = [layersTransfer
%     fullyConnectedLayer(numClasses,'WeightLearnRateFactor',20,...
% 'BiasLearnRateFactor',20)
%     softmaxLayer
%     classificationLayer];

params =
load("C:\Users\bin\Desktop\Trial_EEG_neonate\params_2021_11_13__15_37_35.mat"
);


layers = [
    imageInputLayer([227 227 3],"Name","data","Mean",params.data.Mean)
    convolution2dLayer([11 11],96,"Name","conv1","BiasLearnRateFactor",2,...
    "Stride",[4 4],"Bias",params.conv1.Bias,"Weights",params.conv1.Weights)
    reluLayer("Name","relu1")
    crossChannelNormalizationLayer(5,"Name","norm1","K",1)
    maxPooling2dLayer([3 3],"Name","pool1","Stride",[2 2])
    groupedConvolution2dLayer([5 5],128,2,"Name","conv2",...
    "BiasLearnRateFactor",2,"Padding",[2 2 2 2],"Bias",params.conv2.Bias,...
    "Weights",params.conv2.Weights)
    reluLayer("Name","relu2")
    crossChannelNormalizationLayer(5,"Name","norm2","K",1)
    maxPooling2dLayer([3 3],"Name","pool2","Stride",[2 2])
    convolution2dLayer([3 3],384,"Name","conv3","BiasLearnRateFactor",2,...
    "Padding",[1 1 1 1],"Bias",params.conv3.Bias,"Weights",...
    params.conv3.Weights)
    reluLayer("Name","relu3")
```

```
    groupedConvolution2dLayer([3 3],192,2,"Name","conv4",...
    "BiasLearnRateFactor",2,"Padding",[1 1 1 1],"Bias",params.conv4.Bias,...
    "Weights",params.conv4.Weights)
    reluLayer("Name","relu4")
    groupedConvolution2dLayer([3 3],128,2,"Name","conv5",...
    "BiasLearnRateFactor",2,"Padding",[1 1 1 1],"Bias",...
    params.conv5.Bias,"Weights",...
    params.conv5.Weights)
    reluLayer("Name","relu5")
    maxPooling2dLayer([3 3],"Name","pool5","Stride",[2 2])
    fullyConnectedLayer(4096,"Name","fc6_new","BiasLearnRateFactor",10,...
    "WeightLearnRateFactor",10)
    reluLayer("Name","relu6")
    dropoutLayer(0.5,"Name","drop6")
    fullyConnectedLayer(4096,"Name","fc7_new","BiasLearnRateFactor",10,...
    "WeightLearnRateFactor",10)
    reluLayer("Name","relu7")
    dropoutLayer(0.5,"Name","drop7")
    fullyConnectedLayer(3,"Name","fc8_new","BiasLearnRateFactor",15,...
    "WeightLearnRateFactor",15)
    softmaxLayer("Name","prob")
    classificationLayer("Name","classoutput")];
plot(layerGraph(layers));

% Training options
options = trainingOptions('sgdm',...
    'MiniBatchSize',20,...
    'MaxEpochs',8, ...
    'InitialLearnRate',1e-4,...
    'Shuffle','every-epoch', ...
    'ValidationData',TestImages,...
    'ValidationFrequency',10, ...
    'Verbose',false,...
    'plots','training-progress');

% Training the AlexNet
netTransfer = trainNetwork(TrainImages,layers,options);

% Classifying Images
YPred = classify(netTransfer, TestImages);
YValidation = TestImages.Labels;
accuracy = sum(YPred == YValidation)/numel(YValidation);

% Plotting Confusion Matrix
plotconfusion(YValidation,YPred)


%=========================================================================
% =========================================================================
% BINIAM SEIFU 2022
% Matlab Program to test CNN model for Neonatal Seizure detection and grade
level identification
%Read image for classification
%=========================================================================
%=========================================================================
[filename,pathname]=uigetfile('*.*','Select the Input RGB Image');
```

```
filewithpath=strcat(pathname,filename);

I = imread(filewithpath);
figure
imshow(I)
b = netgrade;
c = netTransfer;
%Classify the image using the network

label1 = classify(c,I);
label2 = classify(b,I);
m = char(label1);
n = 'Normal';
tf = strcmp(m,n);
if tf == 1
title(['Recognaized Signal is ' char(label1)])

else
 title(['Recognaized Signal is ' char(label1) ' and grade type is '
char(label2) ])
end
```

Appendix 2: Clinical Information from Zenodo Dataset

ID	EEG file	Gender	BW (g)	GA (week	EEG to PM	Diagnosis	Neuroimaging F	PNA of I	Numb	Primary Lo	Other
1	eeg1	f	less than 2	37 to 38	37 to 38	mild/moderate as	widespread isch	0 to 4	3	both hemispheres; a	
2	eeg2	m	less than 2	35 to 36	37 to 38	prematurity	ultrasound norn	0 to 4	1		
3	eeg3	m	N/A	40 to 41	41 to 42	N/A	N/A		0		
4	eeg4	m	3000 to 35	39 to 40	39 to 40	mild/moderate as	bilateral waters	4 to 7	3	right centro-parietal	
5	eeg5	f	2500 to 30	39 to 40	39 to 40	asphyxia (undefir	haemorrhage in	0 to 4	3	left hemisphere	
6	eeg6	f	2500 to 30	39 to 40	39 to 40	mild asphyxia	ultrasound norn	0 to 4	1		
7	eeg7	m	2500 to 30	38 to 39	38 to 39	infarction	right arteria cer	0 to 4	3	right hemisphere	
8	eeg8	m	2500 to 30	36 to 37	36 to 37	severe asphyxia	left arteria cere	greater	2		
9	eeg9	f	greater th	40 to 41	40 to 41	mild/moderate as	normal	4 to 7	3	left frontc	left hemis
10	eeg10	f	3000 to 35	41 to 42	42 to 43	severe asphyxia	diffuse edema i	0 to 4	0		
11	eeg11	N/A	3000 to 35	38 to 39	39 to 40	kernicterus	left side subdur	4 to 7	3	right posterior quadr	
12	eeg12	m	N/A	34 to 35	38 to 39	N/A	N/A		1		
13	eeg13	m	3500 to 40	38 to 39	39 to 40	cardiac anomalies	ultrasound norn	4 to 7	3	bilateral	
14	eeg14	f	3000 to 35	38 to 39	38 to 39	developmental bi	microcephaly; c	4 to 7	3	right; posterior quad	
15	eeg15	m	2500 to 30	36 to 37	36 to 37	asphyxia	ischemic change	4 to 7	3	near vertex; central	
16	eeg16	m	3000 to 35	41 to 42	41 to 42	mild/moderate as	severe bilateral	0 to 4	3	right hemisphere	
17	eeg17	f	less than 2	34 to 35	36 to 37	drug withdrawal s	ultrasound norn	4 to 7	3	near vertex; central	
18	eeg18	m	N/A	N/A	43 to 44	N/A	N/A		0		
19	eeg19	f	N/A	40 to 41	44 to 45	N/A	N/A		3	left hemisphere; alte	
20	eeg20	m	2500 to 30	38 to 39	38 to 39	severe asphyxia	ultrasound norn	0 to 4	3	left frontc	bilateral
21	eeg21	m	less than 2	36 to 37	40 to 41	hypoplastic left h	right side intrav	greater	3	right hem	bilateral
22	eeg22	f	3500 to 40	40 to 41	43 to 44	meningitis	cortical ischemi	greater	3	both posterior hemis	
23	eeg23	f	2500 to 30	35 to 36	36 to 37	congenital kidney	ultrasound: righ	0 to 4	2		
24	eeg24	f	3500 to 40	41 to 42	42 to 43	respiratory distre	ultrasound norn	0 to 4	1		
25	eeg25	N/A	N/A	38 to 39	40 to 41	N/A	N/A		3	both hemispheres; a	
26	eeg26	f	3500 to 40	40 to 41	41 to 42	nonketotic hyper	ultrasound: hyp	0 to 4	1		
27	eeg27	m	2500 to 30	36 to 37	38 to 39	mild prematurity;	ultrasound norn	0 to 4	0		
28	eeg28	m	N/A	37 to 38	39 to 40	not known	ultrasound norn	0 to 4	0		
29	eeg29	f	3500 to 40	38 to 39	38 to 39	respiratory distre	ultrasound: abn	0 to 4	0		
30	eeg30	m	greater th	41 to 42	41 to 42	infarction	left arteria cere	0 to 4	0		
31	eeg31	f	greater th	41 to 42	41 to 42	brain infarction; h	right arteria cer	0 to 4	3	right hemisphere	
32	eeg32	m	3500 to 40	41 to 42	41 to 42	undefined brain c	hypoplasia of p	0 to 4	0		
33	eeg33	m	3000 to 35	36 to 37	37 to 38	congenital toxopl	ultrasound: per	0 to 4	2		
34	eeg34	f	3500 to 40	41 to 42	41 to 42	severe asphyxia; i	infarction	0 to 4	3	right hem	bilateral
35	eeg35	f	3500 to 40	40 to 41	41 to 42	N/A	N/A		0		
36	eeg36	m	3500 to 40	38 to 39	40 to 41	status post cardia	ultrasound norn	0 to 4	3	bilateral	
37	eeg37	m	3500 to 40	38 to 39	39 to 40	status post resusc	ultrasound norn	0 to 4	0		
38	eeg38	m	greater th	41 to 42	42 to 43	mild asphyxia; ne	ultrasound norn	0 to 4	3	left frontc	bilateral
39	eeg39	m	3500 to 40	41 to 42	41 to 42	moderate asphyx	large infarctions	0 to 4	3	left hemis	alternatin
40	eeg40	m	greater th	39 to 40	40 to 41	severe asphyxia	ischemic change	0 to 4	3	left parieto-occipital	
41	eeg41	f	2500 to 30	37 to 38	38 to 39	mild/moderate as	normal	0 to 4	3	right hem	bilateral
42	eeg42	f	2500 to 30	38 to 39	39 to 40	asphyxia	small haemorrh	4 to 7	0		
43	eeg43	m	2500 to 30	38 to 39	38 to 39	newborn apnea a	mild subdural h	4 to 7	1		
44	eeg44	f	3500 to 40	41 to 42	41 to 42	severe asphyxia	severe bilateral	0 to 4	3	bilateral	
45	eeg45	m	2500 to 30	40 to 41	40 to 41	fetal severe intra	Right side wate	4 to 7	0		
46	eeg46	f	2500 to 30	36 to 37	36 to 37	severe asphyxia	severe bilateral	0 to 4	1		
47	eeg47	f	3000 to 35	40 to 41	41 to 42	severe asphyxia; r	extracranial her	4 to 7	3	bilateral	
48	eeg48	m	N/A	36 to 37	39 to 40	not known	N/A		0		
49	eeg49	f	3000 to 35	37 to 38	39 to 40	undefined epilep	N/A		0		
50	eeg50	f	3500 to 40	39 to 40	39 to 40	brain haemorrhag	right temporal h	0 to 4	3	right hemisphere	
51	eeg51	f	2500 to 30	40 to 41	40 to 41	severe asphyxia	bilateral symme	0 to 4	3	left hemisphere	
52	eeg52	m	N/A	35 to 36	43 to 44	N/A	N/A		3	bilateral	
53	eeg53	f	3500 to 40	40 to 41	40 to 41	severe asphyxia	normal	4 to 7	0		
54	eeg54	m	N/A	40 to 41	40 to 41	N/A	N/A		2		
55	eeg55	m	3500 to 40	41 to 42	42 to 43	neonatal withdra	ultrasound norn	greater	0		
56	eeg56	m	3500 to 40	40 to 41	40 to 41	severe asphyxia	bilateral ischem	4 to 7	1		
57	eeg57	m	3500 to 40	42 to 43	42 to 43	cranial anomaly; s	ultrasound norn	0 to 4	0		
58	eeg58	m	N/A	39 to 40	42 to 43	N/A	N/A		0		
59	eeg59	m	N/A	42 to 43	43 to 44	not known	N/A		0		
60	eeg60	m	3500 to 40	42 to 43	42 to 43	mild asphyxia; inf	widespread infa	0 to 4	0		
61	eeg61	f	N/A	41 to 42	42 to 43	not known	N/A		1		
62	eeg62	m	3500 to 40	40 to 41	40 to 41	severe asphyxia	bilateral ischae	0 to 4	3	bilateral	
63	eeg63	f	greater th	39 to 40	39 to 40	severe asphyxia	right arteria cer	0 to 4	3	right hemisphere	
64	eeg64	f	2500 to 30	35 to 36	35 to 36	severe asphyxia	severe bilateral	0 to 4	2		
65	eeg65	f	N/A	39 to 40	39 to 40	N/A	N/A		1		
66	eeg66	f	2500 to 30	41 to 42	43 to 44	infarction; neona	right side infarc	greater	3	right centro-parietal	
67	eeg67	f	3000 to 35	40 to 41	40 to 41	severe asphyxia	right frontal lob	0 to 4	3	both hemispheres; a	
68	eeg68	m	greater th	39 to 40	40 to 41	infarction	left arteria cere	N/A	2		
69	eeg69	m	N/A	40 to 41	42 to 43	sepsis	sinus sagittalis s	4 to 7	3	both hemispheres; a	
70	eeg70	m	greater th	40 to 41	40 to 41	asphyxia	MRI normal	0 to 4	0		
71	eeg71	m	less than 2	36 to 37	39 to 40	hypothalamic han	temporal lobe c	0 to 4	3	bilateral	
72	eeg72	m	N/A	37 to 38	37 to 38	N/A	N/A		0		
73	eeg73	f	3500 to 40	39 to 40	39 to 40	severe asphyxia	severe bilateral	0 to 4	3	left frontc	bilateral
74	eeg74	m	2500 to 30	34 to 35	35 to 36	severe asphyxia	post-ischemic s	0 to 4	2		
75	eeg75	m	greater th	38 to 39	38 to 39	mild/moderate as	left parietal ant	4 to 7	3	left fronto-central;pa	
76	eeg76	m	3500 to 40	41 to 42	41 to 42	ischaemia (classif	Right infarction	0 to 4	3	right; posterior quad	
77	eeg77	f	3000 to 35	41 to 42	41 to 42	mild/moderate as	severe bilateral	0 to 4	3	left centro-parietal	
78	eeg78	f	3500 to 40	41 to 42	41 to 42	acute ischaemia; i	right anteria cer	4 to 7	3	right hemisphere	
79	eeg79	f	2500 to 30	40 to 41	41 to 42	severe asphyxia; r	right side ischae	4 to 7	3	right front	left hemis

Appendix 3: Clinical Information from Local Dataset

ID	EEG	Gende	BW (g)	GA	Discription(Nurologist)	Interpretation(Nur	Nu	Primary Localisa	time of rec
706905	52	F	2600g		moderate amount of delta t	generalized epileps	3	posterior electrod	40min
452912	75	M	2500g		moderate amount of 7-Hz r	NORMAL	3	posterior electrod	50min
621661	89	M	3000g		moderate amount of 11- to	ABNORMAL	3	maximally over tl	40min
730570	108	M	3200g		normal wave form seen	NORMAL	3	NA	40min
318400	100	M	2800g		large amplitude 3 to 4 hz pc	ABNORMAL	3	anteriorly bilatera	40min
599171	74	F	3100g		normal wave form seen	NORMAL	3	NA	30min
692516	73	F	3000g		normal wave form seen	NORMAL	3	NA	40min
572414	39	M	3500g		large amplitude, diffuse, po	ABNORMAL	3	NA	40min
660322	28	F	2700g		moderate amount of 8-Hz r	NORMAL	3	occipital electrod	40min
470015	31	M	2800g		moderate amount of 9-Hz r	NORMAL	3	anteriorly bilatera	40min
584891	46	M	3200g		A small amount of symmet	NORMAL	3	anteriorly bilatera	40min
555234	110	M	3300g		There are ample movemen	NORMAL	3	central and anteri	30min
719770	77	M	3500g		moderate amount of 11- to	ABNORMAL	3	anteriorly bilatera	40min
431224	85	M	3300g		moderate amount of 11-Hz	NORMAL	3	posterior electrod	40min
725118	86	M	3000g		moderate amount of 11- to	NORMAL	3	posterior electrod	40min
555234	5	M	2600g		A small amount of symmet	NORMAL	3	anteriorly bilatera	40min

Appendix 4: Conformation letter of data and information collection

Date Feb 8, 2022

Subject: Conformation letter of Data and Information Collection for Research Work

To Whom It May Concern

This is to certify that Mr. BINIAM SEIFU is a genuine student of MSc Biomedical Engineering, Bio-Instrumentation. He is conducting a research entitled "**Detection and Grade Identification of Neonatal Seizure using Deep Convolutional Neural Networks**" under supervision of T. BHEEMA LINGAIAH. (Ph.D.) and Mr. AHMED ALI (MSc.). He successfully collected neonatal EEG data and corresponding clinical information from Wachamo University collage of Health Science Nigist Eleni Mohamed Memorial Compressive Specialized Hospital.

Best Regards

Name, Signature and organization stamp

Dr. Adane Des
Chief Clinical Director

Wachamo University
Mohammed Memorial Referral Hospital

TEL: 046 – 555 – 43 – 79 046 – 555 – 43 – 78 POST: P.O.BOX 22 FAX: 046 – 555 – 22 - 93