SCIENTIFIC Publishing Limited

Digital Technologies Research and Applications
http://ojs.ukscip.com/index.php/dtra

Article

Artificial Intelligence-Assisted Care for Human Newborns with Neurological Impairments

Ejay Nsugbe *

Nsugbe Research Labs, UK

* Correspondence: ennsugbe@yahoo.com

Received: 14 June 2022**; Accepted:** 4 August 2022**; Published:** 18 August 2022

Abstract: Seizures are a widespread condition affecting 50~65 million people in the world, and newborns are also susceptible to them. EEG is used to monitor the brain activity of newborns with suspected brain injuries, followed by a qualitative waveform interpretation by a group of clinical experts, where the means towards detection of seizures include a set of distinct characteristics in the waveform. This means of seizure detection has been critiqued, particularly due to subjectivity where, at times, waveform reviewing clinicians fail to reach a consensus on the presence of seizure activity in the brain of a newborn. As a means towards dealing with this problem, the author investigated the use of Artificial Intelligence-driven prediction machines capable of an automated diagnosis of seizure, based on a newborn's EEG waveform. This approach used a reduced selection of EEG electrodes, the Linear Series Decomposition Learner (LSDL), an ensemble of a group of features, and performance comparison across multiple classification models. Secondary work was also carried out, which leveraged the patient information available alongside the EEG dataset. This involved the use of EEG towards predicting the level of asphyxia within the neonatal brain. The results from the seizure prediction exercise showed an increment in prediction performance of the seizures when preprocessed with the LSDL. The results spanned a range of figures (depending on the classification model), with the highest accuracy of 88.1%, while a probabilistic approach towards predicting the extent of seizures provided a maximum accuracy of 93.5%. The results from the secondary analysis showed a maximum accuracy for asphyxia prediction of 89. 1%. The obtained results have helped to demonstrate that a reduced selection of electrode segments, alongside the selected algorithms, can serve towards the prediction of seizures for newborns within a neonatal intensive care unit.

Keywords: neonates; newborns; artificial intelligence; signal decomposition; SVM; machine learning

1. Introduction

Epileptic seizures are disorders of the nervous system which manifest themselves in the form of hyperactivity within the cortex of the brain. It is estimated that 50~65 million people actively suffer epileptic seizures, and are — based on epidemiological statistics— highly prevalent in developing countries [1–3]. Epileptic seizures can be broken down into three primary types, namely: 1) generalized seizures, which are global across the brain, influencing the electrical activity of all neurons within the brain, and may result in impairment; 2) partial epilepsy, which is characterized by more localized manifestations where focal epilepsy is evidenced amongst a cluster of neurons within a particular hemisphere within the human brain [4–6]; and finally 3) intermittent seizures, where the onset is unknown [1]. It can also be noted that over 50% of epileptic seizures have been deemed to be drug resistant [1]. A hierarchical breakdown of the various kinds of seizures can be seen in Figure 1.Human newborns have shown a high proneness to seizures, which is largely attributed to a high excitability alongside low levels of the inhibitory neurotransmitter gamma-aminobutyric acid [7,8]. As can be expected, a rapid response is required for treating newborns with these conditions due to a potential subsequent impact on their neurological development, where imaging exercises in children who had been subject to neonatal convulsions have shown a reduction in myelination [7]. Seizures in newborns are frequently associated with neurological conditions such as ventricular hemorrhage, stroke, hypoglycemia, cerebral malformations and hypoxic ischemic encephalopathy [7]. Acute care must be taken when dealing with and treating seizures, as although the episodes may be brief, membrane damage from seizures releases glutamate – an excitotoxic substance – which triggers subsequent epileptic activities [7].The time and onset of seizures tends to vary in newborns, with hypoxic ischemic encephalopathy being the prime cause of seizures in the immediate neonatal period [7]. Pyridoxine -caused seizures can occur within the womb and manifest themselves as increased in-utero movement, while other seizures take place typically within a 12–48 hour window following the birth of a newborn [7]. In neonates, four main types of seizure can occur; a summary of their characteristics, alongside their manifestations, can be seen in Table 1.

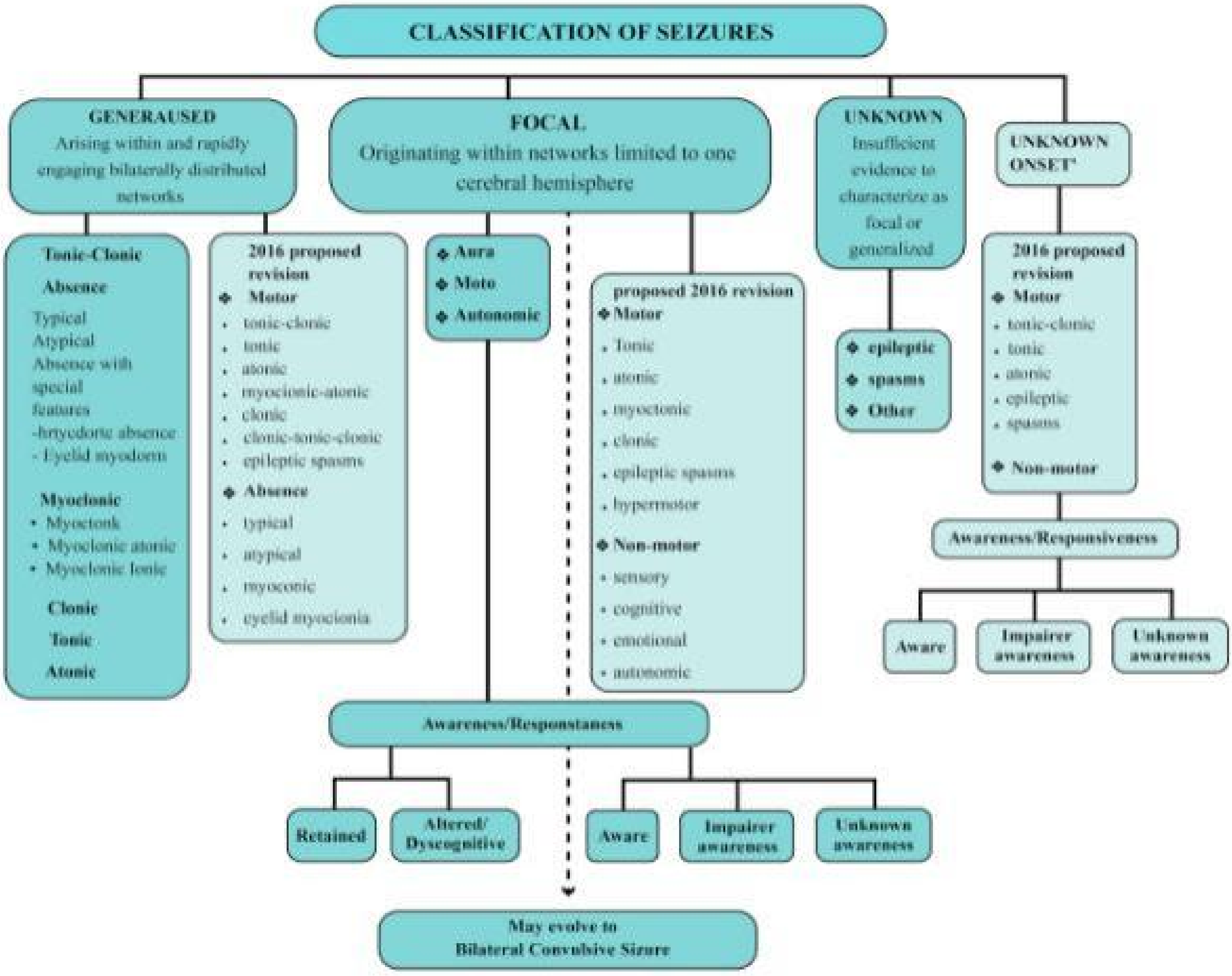

Figure 1. A flow diagram showing the hierarchical structure of the various kinds of seizures. Seizure characteristics established in 2011 are depicted in dark green, while seizure characteristics established in 2016 are depicted in light green. [6]

Table 1. A summary of the various kinds of seizures and their manifestation characteristics.

Variant	Manifestation
Subtle	No EEG changes, primarily ocular manifestations,i.e., fixed open stares, apnea, eye deviation, alongside other characteristics such as swimming movement of limbs, mouthing and chewing
Tonic	Stiffening of limbs, characterized by sharp waves and spikes in the EEG signal
Clonic	Unifocal or multifocal, non-Jacksonian jerking, newborns are mostly unconscious during this seizure, changes normally present in EEG
Myoclonic	Closely resemble salaam spasms, can lead to abnormality in EEG

The physiological changes which occur in newborns during seizures involve fluctuations in blood glucose levels due to the brain's transport system being unable to keep up with the demands, although cerebral blood flow may increase as a result of the need to meet the demands for oxygen and glucose [9] . Spectroscopic measures have provided evidence to suggest that metabolic demands outweigh the normal physiological supply, as embodied by shifts in the spectroscopic spectra from a high energy phosphate towards an inorganic phosphate. Lactate also increases as arterial pH falls, alongside systemic blood pressure increasing [7].

Key means and techniques towards the diagnosing of seizures include the following: EEG, blood glucose measurements, serum magnesium levels, arterial pH, serum sodium levels, serum urea and creatine levels, lumbar puncture, blood cultures, and cranial ultrasound scanning [7]. EEG is the most frequently adopted means towards the diagnosis of seizures in newborns due to its ability to provide a real-time detection and prediction of seizure episodes, while also lending itself to potential automated detection of the condition [10,11].

The expert-based identification of seizures predominantly involves a manual visualization of EEG series, recognizing specific set markers within the time-series that are characteristic of a seizure, before following up with the appropriate care bundle [7,10,12]. Characteristics include a distinct onset alongside a fixed minimum duration, which ultimately implies a qualitative means towards diagnosis that carries subjectivity and can lead to non-consensus amongst a group of reviewing clinicians, as will be discussed later in this paper [7,10,12]. Due to this, there has been an uprise in the notion of the implementation of artificial intelligence-driven prediction machines that are capable of automated seizure detection from a real-time stream of EEG signals from the brain of a newborn. Upon the detection of a seizure, potential medications that can betitrated for newborns include phenobarbitone in combination with phenytoin, both of which are established seizure and epilepsy medications [13,14].

Newborns with seizures and neurological conditions are typically cared for within neonatal intensive care units (NICU), where there are high associated financial and economic implications that vary based on the socioeconomic standing of a nation [15,16]. A study conducted by Cheah et al. [15] has attributed nearly half of the costs from NICU to be associated with preterm births, some of which are also affected by seizure and brain-related conditions. Strategies towards potentially lowering the number of newborns admitted into NICU, and reducing the associated financial cost, are focused on enhancing proactive care of threatened preterm newborns, which are detailed in the series on the topic conducted by Nsugbe et al. [16]. Further investment in NICU by resource holders within government is needed to allow for equivalent parity with adult intensive care facilities. Legislation is required around assisted reproductive therapies and embryo transfers, which have a large margin for error and can lead to imperfect gestations and increased neonatal care needs for the newborns [15, 16].

Needless to say, the ability to detect seizures in newborns could help to prevent brain damage and, in certain cases, potential death. As mentioned, the real-time diagnosis of seizures is a big challenge as the physical manifestations are not satisfactorily distinct in newborns. Although EEG brainwaves are now widely adopted in NICU, their interpretation remains subjective even amidst experienced neonatologists, which often leads to a non-consensus on the diagnosis of the newborn seizures [17]. This is typically carried out with the use of electrodes, carefully placed around the head of a newborn, alongside specialized equipment for the visualization of the waveforms [18]. Although another commonly used variant via EEG waveforms – known as the amplitude-integrated EEG (aEEG) – is also in use, it has been reported to be subjective, often carrying less accuracy in its interpretations [19]. The process towards a clinical expert-based diagnosis involves a manual annotation of EEG series amidst varied sources of interferences

stemming from both artifacts and electronics. Moreover, expertise is not always on hand for the interpretation of seizures, which is amplified in developing nations [20].

This has given rise to the need for automated intelligent systems capable of detecting seizures from a stream of EEG waveforms. These systems are modelled around data-driven frameworks where the art of seizure detection is learned by a machine in a systematic way, and used to serve as a decision support tool in the NICU. Ultimately, this would form an appealing solution to resource-constrained environments, in addition to strongly minimizing the issue of diagnosis subjectivity amongst experts. These automated seizure decision support systems are supported by machine learning models, the design of which can be broadly broken into various stages, including the feature extraction phase. This is where key features — which can succinctly characterize the signal in question — are extracted from the signal to form a feature vector, which is fed into a machine learning classification model as part of the training and validation process [21]. The extracted features tend to be from different domains (i.e ., time, frequency etc.) and provide quantitative information on the stream of EEG information [21].

In the literature, supervised learning methods are primarily used for the design of the classification models which are reliant on the provision of labelled samples (i.e., seizure or no-seizure) for the design of the model [22,23]. The predominant machine learning models used in this area have been particularly focused on support vector ma chines (SVMs) and artificial neural networks, while more recently there has also been upcoming work in the appli cation of deep learning [19,24,25]. Studies in the literature on these machine learning models have used various neonatal seizure databases and different windowing schemes, where different feature groups have also been leveraged and have thus rendered it challenging and largely unfeasible to do an equivalent like-for-like comparison of the different model performances on the recognition of newborn seizures [17–25]. However, the literature has shown favorable results in the use of the SVM machine learning models [17–25].

Previous work by Nsugbe et al. [26–29] has shown the potential for, and appeal of, signal decomposition methods— in particular the Linear Series Decomposition Learner (LSDL) — in reducing the overall uncertainty in the signal as a preprocessing mechanism prior to modelling of the signal. This has previously been seen to enhance the classification performance of a model, in addition to allowing for the use of classification models with low complexity, which carry a high degree of clinical appeal due to their explanatory potential [26–29]. In this work, we utilized the seizure database by Stevenson et al. [19] in the design of a seizure prediction platform from LSDL decomposed EEG signals capable of working in real-time, and comprising a unique ensemble of features and a reduced selection of elec trode channels. Further to this, as Stephenson et al.'s [19] database is supported by gestation information and indepth diagnoses on the degree of brain damage sustained by the newborns, this information was also leveraged to form secondary investigations around the prediction of various newborn conditions from an acquired EEG wave form. Precisely speaking, the contributions of this manuscript are as follows:

- A comparison of the accuracy of a newborn seizure prediction machine for a preprocessed LSDL signal and state-of-the-art (raw signal) prediction across a range of classification models, including the decision tree (DT),logistic regression (LR), SVM (linear, quadratic and cubic), and artificial neural network;
- The use of probabilistic reasoning towards grading the extent of seizures in newborns to aid the prioritization of care;
- The prediction of asphyxia brain damage in newborns who experience seizures.

2. Methods

2.1 Seizure EEG Waveform Theoretical Representation and Newborn Brain Connectivity

International standards detailed by Clancy et al. [10] define a neonatal seizure as a form of clear ictal event in the waveform, which is sudden and repetitive with a distinct start, mid-point and ending, where a key characteristic of this is the manifestation of an evolving periodicity within an EEG waveform [12]. Given a sample signal x(t) in the absence of noise and interferences, the periodicity in a signal can be defined as x(t+T), where t is time and T represents the period.

Primarily speaking, neonatal seizures exhibit two kinds of time varying periodicity, and are described as follows:

- The first and most common involves a series of epileptic spikes, where those spike morphologies do not vary significantly during the seizure episode and can be mathematically described as Equation (1) [12] :$\mathrm{x(t)} = \mathrm{w(t)} \sum_{n=0}^{N} \delta(t - t_n)$

where t_n represents a time shift, $w(t)$ is the waveform morphology and δ represents an impulse within the time-domain. This particular function is cyclical and takes the form of e^{-t} sin (t^{-2}).

The second embodies a seizure where the waveform is shifted in time and scale, and can be mathematically described as Equation (2) [12] :

$$\mathrm{x(t)} = \sum_{m=0}^{M} a_m \sin\left(2\pi m \int_0^t T(\tau)^{-1} d\tau + \emptyset_m\right) \tag{2}$$

where τ is time in this case, Ø is a phase constant, am and m define the harmonic relationship of the signal, and T(τ) represents the time varying period of a continuous signal.

Brain functional connectivity looks at the functional and effective connectivity within the brain, mostly using brain physiological measurement instrumentation, EEG, which is subject to the investigation carried out in this paper [30,31]. EEG measures ionic current flow in the cortex, and also involves a degree of spatial averaging of electrical dynamical activity within the cortex [30,31].

Connectivity studies have shown that long range connections within the brain of the newborn develop much quicker than short range cortical connections, thus making unilateral autonomous cortical activity in newborn babies to be dominant, with no substantial interhemispheric relationship noted at this point [32]. In the first few months, expansion of neuronal pathways occur, which give rise to dynamic changes in the EEG waveform in due course [32]. The general dynamic characteristic of a newborn's EEG is intermittent and discontinuous activity alongside a mixture of bursts of spontaneous activity transients (SAT), and general low voltage activity, which is distinct from burst suppression activity that mostly appears in newborns with existing brain damage [32].

2.2 Experimental Process

The EEG recordings used in the data set forming part of this research were acquired by Helsinki University [19] in 2010–2014 from infants admitted to NICU. The newborns had gestational ages spanning 35–45 weeks. Each EEG recording spanned approximately one hour, and data were acquired using the Nico One EEG sensor, which was sampled at 256 Hz with an EEG cap comprising 19 electrodes that were positioned using the 1 0–2 0 international electrode standard [19]. A sample image of a newborn wearing an EEG cap with continuous data being collected can be seen in Figure 2.

The acquired EEG wave forms were analyzed and annotated by three experts to qualitatively identify seizure events within the EEG wave forms [19]. The criteria for identifying the seizures were patterns of activity within the waveform where distinct anomalies occurred with a definitive start and end with sustained shape waves, and with rhythmic wave forms spanning 10 seconds or more [19]. The visualization setting for the experts was a paper speed of 30 mm/ sec (12 seconds per screen) , a sensitivity of 100 µV/cm, and a cut-off of 0.5–70 Hz, with the annotation experts receiving authorization to modify the visualization setting as deemed fit with their preferences [19]. Each expert had a minimum of 10 years ' worth of experience of dealing with seizure identifications, and they were not given any prior information regarding the seizures (aside from the fact that there were suspicions of abnormal brain activities) in order to keep the annotation process fair and reflective [19]. All annotations were based on EEG analysis, although there was also an electrocardiogram at hand for reference when required. All data acquisitions were carried out in accordance with the standards of care expected at the Helsinki University Hospital, Finland, where permission to release the patient de-identified data and use for research purposes was granted by the ethics committee at the Children's Hospital, Helsinki University Hospital, Finland [19].

Figure 2. Image of a newborn with an EEG skullcap. [33]

In the opensource database, files marked with seizures by all three annotation experts were termed 'consensus seizure files' [19]. Further, there were files which did not receive full consensus, i.e., all three experts did not agree on the presence of seizure within the EEG waveforms, and finally 'consensus no-seizure files' [19] . Only the consensus files were used for the signal processing exercises, where a total of 34 newborn EEG files were used in this work, comprising 17 seizure cases and 17 nonseizure cases.For the newborn seizure files, the windowing scheme for the EEG signals included portions of the signals with and without seizures in order to make the model design more robust. The windowing scheme involved a size and receptive field of 5 minutes per window.

2.3 Electrode Selection

Alongside creating parsimonious modelling in automated seizure diagnosis, a reduced channel configuration was investigated as part of this work. Work by Webb et al. [34] considered uncertainty analysis in EEG electrodes in newborns and highlighted key electrodes that produce rich signal information and are generally free from noise and uncertainty. A study of Webb et al.'s [34] work showed six key electrodes that are largely uncertainty-free during the acquisition of newborn EEG signals, as indicated in Figure 3: F3C3,FZ -CZ, F4-C4, C3-P3, CZ-P3, CZ-PZ and C4-P4.

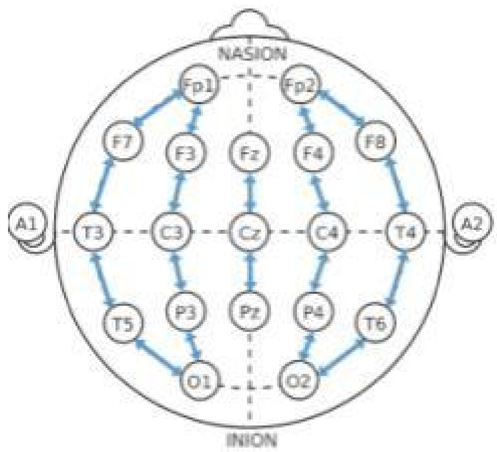

Figure 3. Image of the map of EEG electrodes employed by Stevenson et al. [19] (the orange circle indicates the group of electrodes used in this study).

2.4 Signal Preprocessing

Signal decomposition was employed as a preprocessing method for the newborn EEG signal as previous work has shown that this approach contributes towards the enhancement of recognition and classification accuracies [28]. Generally, the concept of signal decomposition involves a systematic deconvolution and separation of a timeseries signal to obtain and converge at a region within the signal, minimizing uncertainty and enhancing the overall prediction accuracy, where the applications of signal decomposition methods are disperse [28].

The Linear Series Decomposition Learner (LSDL) is an intelligent, metaheuristically-driven decomposition method that works with set linear basis functions, and was originally conceived by Nsugbe et al. as part of a set of source separation exercises [26,28] . Comparisons with the wavelet decomposition showed the LSDL's ability to surpass the wavelet transform in terms of prediction accuracy and overall computation time [26,28].

In addition to its original case study, the applications of the LSDL have been broad and span areas of clinical medicine such as rehabilitation and pregnancy medicine, where the LSDL has resulted in an enhanced prediction when compared with the current state of the art analysis [28,29]. Assuming an absolute signal |Sn |, a comprehensive list of the tuning methods and heuristics used as part of the LSDL are reported in Nsugbe et al. [28] , while the various parameters used in the implementation of the method can be seen in Table 2. A tree-like flow of the decomposition sequence of the LSDL is shown in Figure 4.

From a mathematical perspective, the LSDL decomposition series can be expressed as follows:

$$|s_n| = \left(\int_0^T (T_{l_{upper_1}})(|s_n|)dn + \int_0^T (T_{l_{upper_2}})(|s_n|) \ldots\ldots \int_0^T (T_{l_{upper_n}})(|s_n|)dn\right) + \left(\int_0^T (T_{l_{lower_1}})(|s_n|)dn + \int_0^T (T_{l_{lower_2}})(|s_n|)dn \ldots\ldots \int_0^T (T_{l_{lower_n}})(|s_n|)dn\right) \tag{3}$$

$$|s_n| = \int_0^T (upr_n(|s_n|) + \int_0^T (Lwr_n(|s_n|) \tag{4}$$

2.5 Feature Extraction

The features used in this study represent a select subset of features that have been used in prior studies for the modelling and characterization of physiological signals [35–38]. The features comprise a unique ensemble spanning low order statistics, frequency features and nonlinear features, where a concatenation of these is believed to provide an effective characterization of the physiological signal in question from multiple perspectives [35–38].

Table 2. Threshold parameters for the LSDL.

where Tl_upper_n and Tl_lower_n are the thresholds for the upper and lower amplitude regions of the signal.

Iteration	**1**	**2**	**3**	**n**
Upper threshold region parameter (Upper)	$T_{l\_uppeT\_1} = 50\%\ \text{of}\ \max |s_n|$	$T_{l\_uppeT\_2} = \frac{\max s_n + T_{l\_uppeT\_1}}{2}$	$T_{l\_uppeT\_3} = \frac{\max |s_n| + T_{l\_uppeT\_2}}{2}$	$T_{l\_uppeT\_n} = \frac{\max |s_n| + T_{l\_uppeT\_n-1}}{2}$
Lower threshold region parameter (Lower)	$T_{l\_loweT\_1} = 50\%\ \text{of}\ \max |s_n|$	$T_{l\_loweT\_2} = \frac{T_{l\_lower\_1}}{2}$	$T_{l\_loweT\_3} = \frac{T_{l\_lower\_2}}{2}$	$T_{l\_loweT\_n} = \frac{T_{l\_lower\_n-1}}{2} t$

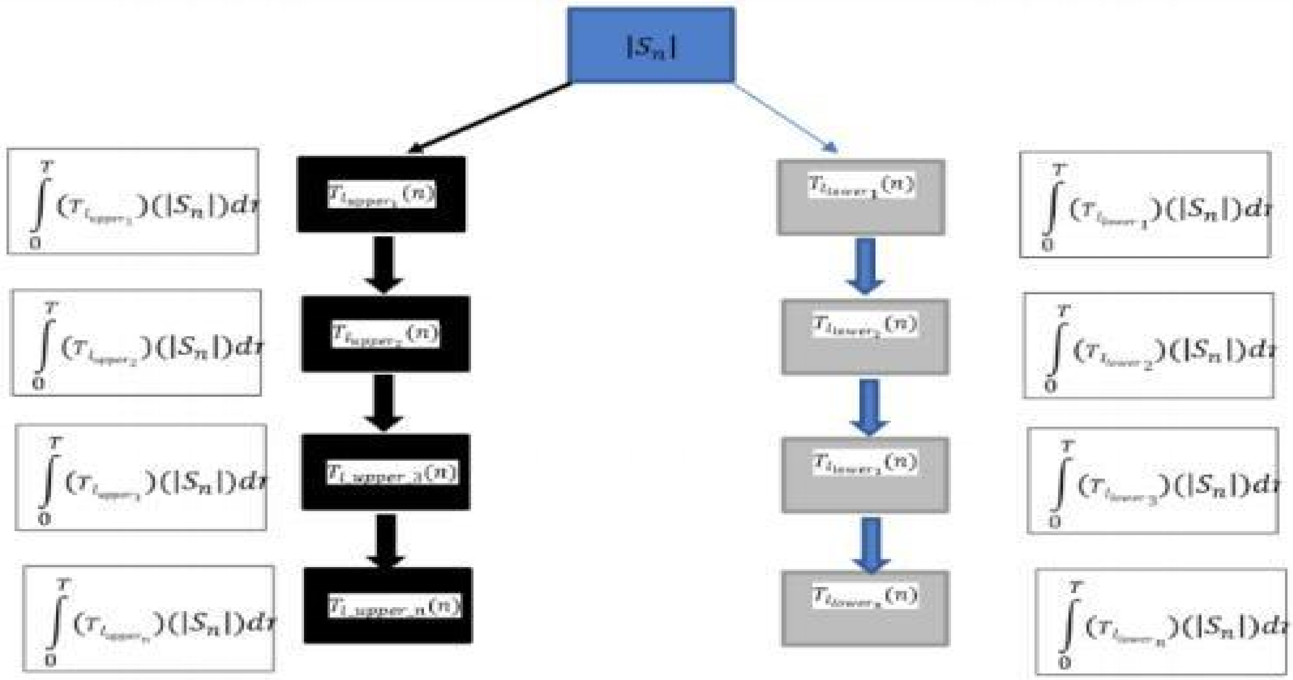

Figure 4. Decomposition tree representation for the LSDL (where T indicates the length of the candidate signal). [35]

The list of features is as follows: mean absolute value (MAV),waveform length (WL), zero-crossing (ZC), slope sign change (SSC), root mean square (RMS),fourth order autoregression (AR), sample entropy (SampEN), cepstrum (Ceps), maximum fractal length (MFL), median frequency (MedFrq),peak frequency (PeakFrq), number of peaks (NP), simple squared integral (SSI) and variance (VAR) [35–38]. The value of 1 µv was chosen for every feature requiring a threshold, while 2 and 0.2 were the chosen values of m and r for the sample entropy.

2.6 Machine Learning Models

In this work, four different machine learning classification models were considered, each with its own unique discriminant function and level of classifier complexity, and level of interpretability. The list of machine learning models is as follows:

Logistic Regression (LR): This is an interpretable, statistically-driven binary classification method; its outputs ranging from 0–1, where classes are assigned based on the final output value relative to a designated threshold [39]. Logistic regression supersedes the classical linear regression for pattern recognition exercises due to its enhanced ability to deal with outliers through the nature of its sigmoidal decision function [40].

Decision Tree (DT): These classification models refer to grey-box models whose classification approach is based around the use of a Boolean logic-like approach towards the sorting of data into different classes in a tree-like hierarchical fashion [40]. The white-box characteristic of the DT implies that it carries interpretability. Thus its decision making process is transparent to a degree [40].

Support Vector Machine (SVM): This approach is based around the projection of the data vector into a higher dimensional space, where the class boundaries are implemented in an iterative fashion with the aid of a small subset of the data (known as support vectors),followed by a downward projection of the data, while preserving the structure of the class boundaries implemented in a higher dimensional space, in a feat known as the 'kernel trick ' [41]. Due to the transformations involved as part of the general operability of the model, the SVM has been seen to be relatively computationally expensive to run, although capable of running in real-time [41]. As part of this work, three different kernel types were explored, namely, the linear SVM (LSVM), quadratic SVM (QSVM) and cubic SVM (CSVM). This choice of kernels served as different kinds of class boundaries that were used to separate data classes using the SVM approach.

Multi-Layer Perceptron Neural Network (MLPNN): This is a version of the feed forward neural network which mainly consists of an input layer, a hidden layer with an user-definable amount of neurons, and an output layer that maps out predicted class labels [42] . The MLPNNs are nonparametrically able to map the relationship between input data and output label given sufficient training data using typically nonlinear boundaries, and are commonly referred to as the nonlinear function approximators [42]. The implemented version of the MLPNN utilized the sig-moid activation function, 30 units in the hidden layer, the iterative back propagation algorithm for the training, and a SoftMax function as part of the output layer [42]. Due to the nature of the hidden layers of the MLPNNs, interpretation of the output from the network has typically been viewed as challenging and at times infeasible, thus they are typically referred to as black-box classifiers with minimal interpretabilities [42].

All classifiers were validated using the k-fold cross-validation approach with k chosen as 10. The MLPNN was validated with a data split of 70% for training, 15% for validation, and 15% for testing. All other classifiers were validated using a split of 80% of the data for training, with the remaining 20% used for validation purposes.

3. Results

For the characterization of the seizure prediction power of the various designed models, the classification accuracy was calculated. This represents a statistical figure for the number of correct predictions made by a model, expressed as a percentage of the total amount of samples. The results of the various prediction exercises with the newborn EEG signals are as follows.

3.1 Seizure Prediction

The results of the LSDL decomposition exercise are shown in Table 3, where it can be noted that the optimal decomposition level is within the fourth iteration of the lower threshold region. The implication of this is that the rich information of the signal—which is crucial for the classification and pattern recognition exercise—lies within the lower amplitude region of the signal. Thus, all subsequent signals that underwent LSDL preprocessing utilized the parameters corresponding to the optimal decomposition level for the signal decomposition.

Table 3. LSDL decomposition results.

	Iteration 1	Iteration 2	Iteration 3	Iteration 4
Upper	n/a*	n/a*	n/a*	n/a*
Lower	2.0001	2.0019	2.0240	2.0510

* n/a indicates decompositions that could not be carried out due to a constrained number of samples

The results for the seizure prediction exercise contrasting the Raw Signal (which represents the state of the art) with the bespoke LSDL across six different classification models, are shown in Table 4. At first glance, it can be seen that the LSDL does indeed lead to an increase in the prediction accuracy of the presence of seizures across all the various classifications considered. The impact of the LSDL is more pronounced in the classification performance of the classifier with a lower complexity, i.e., the LSVM, while for the other classifiers with a higher order complexity (and therein less interpretability) the LSDL still appears to outperform the Raw Signal, although in a marginal sense with increasing classifier complexity.

Table 4. Results of the seizure prediction classification exercise.

Classification Model	Raw Signal (%)	LSDLPreprocessed (%)
LR	61.4	68.1
DT	79.5	80.7
LSVM	60.1	70.1
QSVM	79.0	81.5
CSVM	87.6	88.1
MLPNN	74.0	82.4

The best performing classification model is seen to be for the CSVM for the LSDL Preprocessed signal, which once again showcases the compatibility of the kernel classification models for distinguishing between signals of this kind. It is worth mentioning that the best model in this case is the cubic variant of the SVM, which carries a high computational complexity. This reduces the potential of model explainability, which could be met with skepticism by clinical regulatory bodies. However, this seizure prediction model is intended for an auxiliary source of information which supports and helps to inform clinical decisions regarding care through a clinical expert, as opposed to independently driving care decisions. Furthermore, the use of high-order classification models breeds the potential for model overfit, which has strongly negative impacts in a clinical environment. Thus, if complex models such as the CSVM are to be adopted, care should betaken to ensure that a broad and diverse training set is used as part of the model training and design.

Amongst the models that carry interpretability, the LSDL preprocessed DT appears to have produced the higher accuracy and could also be an option for a model to be deployed in a clinical setting where decision making can be explained. However, this interpretability comes at a tradeoff of accuracy where it can be seen that the DT performs slightly lower than the CSVM.

As the LSDL produced the superior prediction accuracies (shown in Table 4), all subsequent analysis done as part of the results section utilized the LSDL preprocessing.

3.2 Probabilistic Seizure Prediction

Much of the literature has presented the seizure prediction case as part of a binary prediction solution where, given an EEG signal, a trained model predicts whether a seizure is present. Although informative, this does not give an insight into the severity and intensity of the seizure, which can make it difficult, if not arbitrary, to prioritize the delivery of care to the neonates within NICU settings.

A computational means towards tackling this shortcoming can involve the use of probabilistic learning, which is a learning method where numerical values are assigned towards the various samples classified within a certain category, with the assigned value allowing for the inference of the magnitude of a particular prediction/ diagnosis, which in this case is a seizure in a newborn. From the prior section, and from the literature, it is seen that the kernel approach shows a good compatibility with newborn EEG, thus for this exercise a probabilistic SVM (PSVM) learner was used to assign probability values to the samples. These were classified in terms of having seizures and followed by splitting the probability values into two groups, which reflected the severity of the seizure; from here a classification model was used to design the automatic recognition of these cases [43] .

To create these subclasses, the seizure probabilities were split as follows:

Class 1 Seizure/Minor-Moderate: 0.5–0.85

Class 2 Seizure/Severe: 0.85

The implemented PSVM model works in a similar way to the discrete SVM classifier, but also utilizes the Platt scaling, which serves as a conversion mechanism to transform classifier scores into a form of probability distribution where, as mentioned, each sample assigned to a class is accompanied by a probability score [43]. The Platt scaling, which is an integral part of this process, works by transforming output scores into probabilistic representations by utilizing the logistic regression model, which can be defined as Equation (5) [44]: $\frac{1}{1+exp(Af(x)+B}$

Where f (x) is the classifier score, and A and B are learned values during the model fitting process.

As part of the work done in this section, the SMOTE synthetic sample generation algorithm was employed as a mean towards ensuring that both created classes were balanced as part of the model design process [45]. A flow diagram of the model design process is shown in Figure 5, while the results for all models considered can be seen in Table 5.

Table 5. Probabilistic seizure results.

Classification Model	Classification Accuracy (%)
LR	80.5
DT	90.5
LSVM	86.3
QSVM	93.3
CSVM	93.5
MLPNN	88.8

From Table 5, it is evident that the trend carries on to this section with the LR, which carries the greater amount of interpretability and least amount of complexity, thus producing the lowest classification accuracy, while the high-order SVM produced the highest accuracy. The presence of this probabilistic prediction model allows for the deeper exploitation of data to produce prediction models which can help inform and prioritize care measures, as mentioned. It is worth noting that, depending on the preference and overall clinical needs, further seizure classes can be created from the probability measures in order to gain further granularity in the seizure extents, as required.

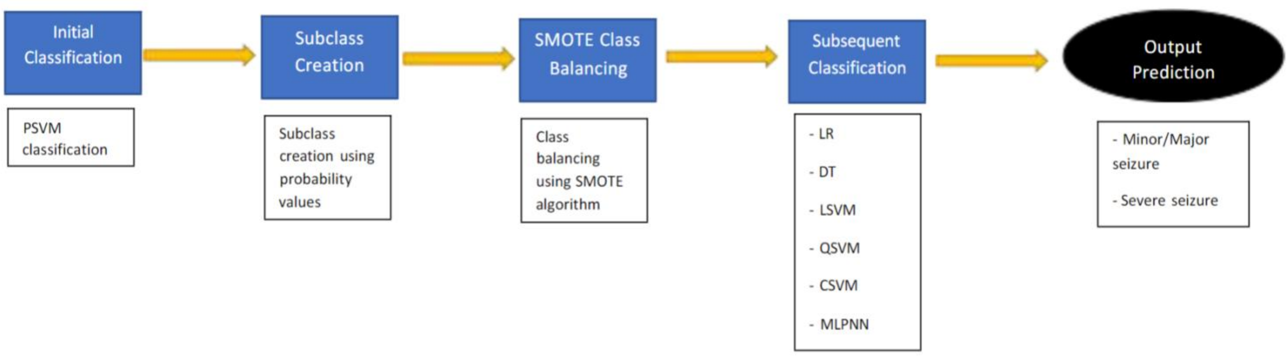

Figure 5. A diagram of the probabilistic prediction model design flow.

3.3 Birth Asphyxia Prediction

Asphyxia refers to the process by which the brain becomes oxygen deficient. In newborns, asphyxia does not have distinct characteristics and manifests itself with a deficiency in brain function, alongside the accumulation of waste acids in the body [46,47]. The level of damage and harm depends on the length of oxygen deprivation for the newborn, in addition to how swiftly remedial treatment was administered [46,47]. Asphyxia involves a reduction in blood flow where both the brain and cells become oxygen deprived; this is followed by reperfusion injury, which occurs as the brain begins to receive oxygen and slowly returns to baseline levels [46,47]. The diagnosis of immediate birth asphyxia involves multiple stages, the first of which utilizes an Apgar score that immediately rates the skin and muscle tone, heart rate, reflexes and breathing pattern of a newborn, where a low Apgar score at 1 and 5 minutes of life is frequently a sign of birth asphyxia [46,47] . Combined with results from arterial and venous cord blood sample pairs, asphyxia is more likely to be diagnosed as per Malin et al. [48].

Following this, a specialist clinician could observe factors such as abnormal breathing, urination frequency, lethargy, blood clotting anomalies, and blood pressure [46,47] . For the less severe asphyxia, an immediate source of breathing support is offered to the newborn alongside close monitoring, while for more severe versions of asphyxia a combination of medication, body cooling, kidney dialysis and targeted breathing support is required to maintain ventilation of the newborn [46,47] .

Newborn asphyxia is also accompanied by seizure episodes, as was seen to be the case with a select number of the newborns whose EEG formed part of the seizure dataset [46,47]. Due to the kinds of asphyxia that occur, it is inferred that these newborns would have reperfusion -related asphyxia at various stages. In this section, it will first be investigated to see if asphyxia can be predicted from a newborn's EEG signal recording, where further work could potentially consider providing an inference of the extent and stage of the asphyxia.

For this aspect, a total of 16 neonatal EEG recordings were used for the prediction exercise, 8 of which had been diagnosed with asphyxia by clinical experts, and 8 of which were deemed to be asphyxia free. The results of the prediction exercise can be seen in Table 6.

Thus, it can be seen that the prediction results for asphyxia are generally high, with the lower complexity classifiers also showing a high prediction result. Once again, the high-order SVM produced the highest accuracy across the different models. This demonstrates that EEG signals from newborns can be used to predict and monitor asphyxia brain injuries, although in order to confirm this theory a larger and more diverse sample size would be needed as part of further work.

Table 6. Results from the prediction of asphyxia using EEG signals.

Classification Model	Classification Accuracy (%)
LR	78.8
DT	82.6
LSVM	77.4
QSVM	88.5
CSVM	89.1
MLPNN	76.4

As can be expected with decision support models, their presence can be expected to reduce diagnosis subjectivity and provide auxiliary sources of information which, in the long term, can inform clinical care strategies as previously described. Probabilistic modelling can also be employed as part of prediction sequences to help grade the various stages of asphyxia experienced by the newborns.

3.4 Feature Ranking Exercise

A feature selection exercise was conducted in order to uncover the most common features that influence the classification decision [49] . The feature ranking work was done using the ReliefF method, which is a filter-based means towards a weighted ranking of a feature group [49]. It is renowned for being computationally efficient —when compared to the wrapper and embedding methods— due to being based on a statistical underpinning [49].

A summary illustrating the features that carried a considerable weighting, and therein discriminatory power, is shown in Table 7, where 10 nearest neighbors were considered.

From the results, it can be seen that five of the six topranked features are time-domain features which are able to characterize the EEG signal from multiple perspectives based on the feature characteristics. The other feature in the group is a complexity-based feature which, although showing effectiveness in characterizing nonlinear physiological signals, is computationally expensive to calculate.

Subsequent work could involve an exhaustive selection exercise with further features similar to the top driving ones, and strategically added to the feature vector while being optimal towards the overall cost of their computations [51]. Likewise, low ranked features may be pruned out as required to boost overall parsimony and prevent the likelihood of model overfit, which is highly relevant for this area of research.

Table 7. Summary of the top features in the classification process.

Feature	Property	Reference
SSI	Quantifies the amount of power and energy in a signal	[Spiewak et al. 2018]
WL	A time-domain-based method towards quantifying frequency information from a signal	[Nsugbe et al. 2020]
AR1st Coefficient	A stochastic quantification of time-series information which varies with the state of a biological system	[Nsugbe et al. 2020]
MFL	Complexity feature capable of capturing faint neuronal firing	[Nsugbe et al. 2021]
NP	Quantifies the filtered firing rate of neurons using a peak detection algorithm and a defined threshold	[Nsugbe et al. 2021]
AR-2nd Coefficient	A stochastic quantification of time-series information which varies with the state of a biological system	[Nsugbe et al. 2020]

4. Conclusions

Seizures are brain-based disorders which affect 50–65 million individuals globally. They can manifest in newborns, and EEG is commonly used to visualize brain activity alongside clinical expertise in the qualitative interpretation of the EEG waveforms. The use of qualitative means towards diagnosis breeds subjectivity, leading to cases of non-consensus in the interpretation of the seizures amongst clinical experts. This has given rise to the need for AI-driven machines that can predict the presence of seizures in a newborn from an acquired EEG signal. Thus, the work done in this paper is centered around the use of AI-driven prediction machines for the prediction of seizures in newborns using a reduced channel representation of six electrodes, LSDL decomposition alongside a unique ensemble of features, and comparison of four different classification models. Using the dataset and supplementary patient information, further exercises were developed

in the use of probabilistic reasoning for grading the extent of seizures in newborns, along with the prediction of asphyxia.

The results of the seizure prediction exercise initially showed an increment in the prediction accuracy when the LSDL decomposition was used, across a range of all classifiers. It was seen that the highorder kernel classifier with the CSVM produced the highest classification accuracy, showing in the process that it is feasible to use a low-channel representation towards a high and reliable prediction of seizures in newborns. This was followed by the probabilistic prediction of the SVM towards predicting the extent of the seizures, where two subclasses were created based on the probabilistic grading, and where the classification results showed a high accuracy of up to 93.5% for the two subclasses.

The final prediction exercise looked at the use of EEG to predict asphyxia in newborns where, as an investigation into the problem, the extent to which this could be predicted from an EEG signal was explored.

The results were seen to be generally high for all classifiers, with the CSVM once again providing the highest accuracy and demonstrating the suitability of kernel-based classification models towards prediction exercises based around newborn EEG signals.

Future work in this area will involve the validation of the devised methods using a larger sample set of newborns with a diverse range of ethnicities where possible, along with the utilization of probabilistic reasoning towards grading the various severities of asphyxia, as well as feature selection exercises to prune for features that can further boost the prediction accuracies in the various exercises whilst maintaining overall model parsimony. In addition to this, further work would also be done on the computation of additional statistical metrics for the best performing and optimal models from the various sets of case studies carried out, in order to robustly observe and characterize the model's capability across different quantitative perspectives.

Acknowledgment

The author would like to thank Dawn Adams and Michael Provost for providing feedback on the manuscript, and Brian Kerr from Kerr Editing for proofreading this manuscript.

Conflict of Interest

There is no conflict of interest.

References

1. Shoeibi, A. , Ghassemi, N. , Khodatars, M. , et al., 20 2 1 . Applications of Epileptic Seizures Detection in Neuroimaging Modalities Using Deep Learning Techniques: Methods, Challenges, and Future Works. arXiv:210514278 (cs, eess] (Internet). (cited 2022 Feb 24); Available from: http://arxiv.org/ abs/2105.14278.

2. Iasemidis, L.D., 2003. Epileptic seizure prediction and control. IEEE Transactions on Biomedical Engineering. 50(5), 549–558.
3. Siddiqui, M.K., Morales-Menendez, R., Huang, X., et al., 2020. A review of epileptic seizure detection using machine learning classifiers. Brain Informatics. 7(1), 5.
4. Hussein, A., Gomes, C., Habash, Q., et al., 2018. Focal and non-focal epilepsy localization: a review. IEEE Access. 6, 49306–49324.
5. Nair, D.R., Laxer, K.D., Weber, P.B., et al., 2020. Nine-year prospective efficacy and safety of brain-responsive neurostimulation for focal epilepsy. Neurology. 95(9), e1244–e1256.
6. Ngoh, A., Parker, A.P., 2017. New developments in epilepsy management. Paediatrics and Child Health. 27(6), 281–286.
7. Rennie, J.M. , 1997. Neonatal seizures. European Journal of Pediatrics. 156(2), 83–87.
8. Moshé, S.L., 1993. Seizures in the developing brain. Neurology. 43(11 Suppl 5), S3-S7.
9. Younkin, D.P., Delivoria-Papadopoulos, M., Maris, J., et al., 1986. Cerebral metabolic effects of neonatal seizures measured within vivo 31P NMR spectroscopy. Annals of Neurology. 20(4), 513–519.
10. Clancy, R.R., Legido, A., 1987. The exact ictal and interictal duration of electroencephalographic neonatal seizures. Epilepsia. 28(5), 537–541.
11. Scher, M.S., Hamid, M.Y., Steppe, D.A., et al., 1993. Ictal and interictal electrographic seizure durations in preterm and term neonates. Epilepsia. 34(2), 284– 288.
12. Tapani, K.T., Vanhatalo, S., Stevenson, N.J., 2019. Time-Varying EEG Correlations Improve Automated Neonatal Seizure Detection. International Journal of Neural Systems. 29(4), 1850030.
13. Gilman, J.T., Gal, P., Duchowny, M.S., et al., 1989. Rapid sequential phenobarbital treatment of neonatal seizures. Pediatrics. 83(5), 674–678.
14. Goldberg, H.J., 1983. Neonatal convulsions--a 10 year review . Archives of Disease in Childhood. 58(12), 976–978.
15. Cheah, I.G.S., 2019. Economic assessment of neonatal intensive care. Translational Pediatrics. 8(3) , 246–256.
16. Nsugbe, E., 2021. A cybernetic framework for predicting preterm and enhancing care strategies: A review. Biomedical Engineering Advances. 2, 100024. [17] Temko, A., Thomas, E., Marnane, W., et al., 2011.
17. EEG-based neonatal seizure detection with Support Vector Machines. Clinical Neurophysiology. 122(3), 464–473.
18. O'Shea, A., Lightbody, G., Boylan, G., et al., 2020. Neonatal seizure detection from raw multi-channel EEG using a fully convolutional architecture. Neural Networks. 123, 12–25.
19. Stevenson, N.J., Tapani, K., Lauronen, L., et al., 2019.A dataset of neonatal EEG recordings with seizure annotations. Scientific Data. 6(1), 190039.
20. Daly, A., O'Shea,A., Lightbody, G., et al., 2021. Towards Deeper Neural Networks for Neonatal Seizure Detection. Annual International Conference of the IEEE Engineering in Medicine and Biology Society. 920–923.
21. Deburchgraeve, W., Cherian, P.J., De Vos, M., et al., 2008. Automated neonatal seizure detection mimicking a human observer reading EEG. Clinical Neurophysiology. 119(11), 2447–2454.
22. Greene, B.R., Marnane, W.P., Lightbody, G., et al., 2008. Classifier models and architectures for EEGbased neonatal seizure detection. Physiological Measurement. 29(10), 1157– 1178.
23. Runarsson, T.P., Sigurdsson, S., 2005. On-line Detection of Patient Specific Neonatal Seizures using Support Vector Machines and Half-Wave Attribute Histograms. International Conference on Computational Intelligence for Modelling, Control and Automation and International Conference on Intelligent Agents, Web Technologies and Internet Commerce (CIMCA-IAWTIC'06). pp. 673–677.
24. Aarabi,A., Grebe, R., Wallois, F., 2007.Amultistage knowledge-based system for EEG seizure detection in newborn infants. Clinical Neurophysiology. 118(12), 2781–2797.
25. Thomas, E.M., Temko, A., Marnane, W.P., et al., 2013. Discriminative and generative classification techniques applied to automated neonatal seizure detection. IEEE Journal of Biomedical and Health Informatics. 17(2), 297–304.
26. Nsugbe, E., 2017. Particle size distribution estimation of a powder agglomeration process using acoustic emissions (Internet) (Thesis). (cited 2021 Dec 27). Available from: http://dspace.lib.cranfield.ac.uk/ handle/1826/14378.
27. Nsugbe, E., Ruiz-Carcel, C., Starr, A., et al., 2018. Estimation of fine and oversize particle ratio in a heterogeneous compound with acoustic emissions. Sensors. 18(3), 851.
28. Nsugbe, E., William Samuel, O., Asogbon, M.G., et al., 2021. Contrast of multi-resolution analysis approach to transhumeral phantom motion decoding. CAAI Transactions on Intelligence Technology. 6(3), 360–375.
29. Nsugbe, E., Sanusi, I., 2021. Towards an affordable magnetomyography instrumentation and low model complexity approach for labour imminency prediction using a novel multiresolution analysis. Applied AI Letters (Internet). (cited 2021 Dec 27). 2(3). DOI:https://onlinelibrary.wiley.com/doi/10.1002/ail2.34
30. Vanhatalo, S., Kaila, K., 2006. Development of neonatal EEG activity: from phenomenology to physiology. Seminars in Fetal and Neonatal Medicine. 11(6), 471–478.
31. Friston, K.J., 1994. Functional and effective connectivity in neuroimaging: A synthesis. Human Brain Mapping. 2(1–2), 56–78.
32. Omidvarnia, A., 2014. Newborn EEG connectivity analysis using time-frequency signal processing techniques (Internet) (PhD Thesis) . The University of Queensland. (cited 2022 Feb 25). Available from: http://espace.library.uq.edu.au/view/UQ:341333.
33. Neuroscience NewsNeuroscience News, 2017 . Artificial Intelligence to Evaluate Brain Maturity in Preterm Infants (Internet). Neuroscience News. (cited 2022 Feb 25). Available from: https://neurosciencenews.com/ai-preterm-brain-7823/.
34. Webb, L., Kauppila, M., Roberts, J.A., et al., 2021. Automated detection of artefacts in neonatal EEG with residual neural networks. Computer Methods and Programs in Biomedicine. 208, 106194.
35. Nsugbe, E., Al-Timemy, A.H., Samuel, O.W. Intelligence combiner: a combination of deep learning and handcrafted features for an adolescent psychosis prediction using EEG signals. Unpublished results.
36. Nsugbe, E., Samuel, O.W., Asogbon, M.G., et al., 20 2 1 . Phantom motion intent decoding fortranshumeral prosthesis control with fused neuromuscular and brain wave signals. IET Cyber-Systems and Robotics. 3(1), 77–88.
37. Nsugbe, E., Phillips, C., Fraser, M., et al., 2020. Gesture recognition for transhumeral prosthesis control using EMG and NIR. IET Cyber-Systems and Robotics. 2(3), 122–131.

38. Nsugbe, E., Obajemu, O., Samuel, O.W., et al., 2021. Enhancing care strategies for preterm pregnancies by using a prediction machine to aid clinical care decisions. Machine Learning with Applications. 6, 100110.
39. Molnar C. 5. 2 Logistic Regression. Interpretable Machine Learning (Internet). (cited 2022 Feb 25). Available from: https://christophm.github.io/interpretable-ml-book/logistic.html.
40. 1.10. Decision Trees (Internet). scikit-learn. (cited 2022 Feb 25). Available from: https://scikit-learn/stable/modules/tree.html.
41. Noble, W.S., 2006. What is a support vector machine? Nature Biotechnology. 24(12), 1565–1567.
42. Hopfield, J.J., 1988. Artificial neural networks. IEEE Circuits and Devices Magazine. 4(5), 3–10.
43. Jinglin, Y., Li, H.X., Yong, H., 2011. A probabilistic SVM based decision system for pain diagnosis. Expert Systems with Applications. 38(8), 9346–9351.
44. Böken, B. , 2021 . On the appropriateness of Platt scaling in classifier calibration. Information Systems. 95, 101641.
45. Wang, J., Xu, M., Wang, H., et al., 2006. Classification of Imbalanced Data by Using the SMOTE Algorithm and Locally Linear Embedding. 2006 8th international Conference on Signal Processing.
46. Birth Asphyxia Seattle Children's (Internet). Seattle Children's Hospital. (cited 2022 Feb 25). Available from: https://www.seattlechildrens.org/conditions/birth-asphyxia/.
47. Gillam-Krakauer, M., Gowen Jr, C.W., 2022. Birth Asphyxia . StatPearls (Internet) . Treasure Island (FL): StatPearls Publishing (cited 20 2 2 Feb 25) . Available from: http://www.ncbi.nlm.nih.gov/books/ NBK430782/.
48. Malin, G.L., Morris, R.K., Khan, K.S., 2010 . Strength of association between umbilical cord pH and perinatal and long term outcomes: systematic review and meta-analysis. British Medical Journal. 340, c1471.
49. Urbanowicz, R.J., Meeker, M., La Cava, W., et al., 2018. Relief-based feature selection: Introduction and review. Journal of Biomedical Informatics. 85 , 189–203.
50. Spiewak, C., Islam, M.R., Assad-Uz-Zaman, M., et al., 2018. A Comprehensive Study on EMG Feature Extraction and Classifiers. Open Access Journal of Biomedical Engineering and its Applications.
51. Chandrashekar, G., Sahin, F., 2014. A survey on feature selection methods. Computers & Electrical Engineering. 40(1), 16–28.