

# Applied Intelligence

## Automated Detection of Cyclic Alternating Pattern and Classification of Sleep Stages Using Deep Neural Network --Manuscript Draft--

<b>Manuscript Number:</b>	
<b>Full Title:</b>	Automated Detection of Cyclic Alternating Pattern and Classification of Sleep Stages Using Deep Neural Network
<b>Article Type:</b>	Original Submission
<b>Keywords:</b>	Sleep stages; cyclic alternating pattern (CAP); classification; Electroencephalogram (EEG); deep learning; CAPSLPDB; CNN
<b>Corresponding Author:</b>	Rajendra U ACHARYA Ngee Ann Polytechnic SINGAPORE
<b>Corresponding Author Secondary Information:</b>	
<b>Corresponding Author's Institution:</b>	Ngee Ann Polytechnic
<b>Corresponding Author's Secondary Institution:</b>	
<b>First Author:</b>	Hui Wen Loh
<b>First Author Secondary Information:</b>	
<b>Order of Authors:</b>	Hui Wen Loh
	Chui Ping Ooi
	Shivani G. Dhok
	Manish Sharma
	Ankit A. Bhurane
	Rajendra U ACHARYA
<b>Order of Authors Secondary Information:</b>	
<b>Funding Information:</b>	
<b>Abstract:</b>	<p>The visual sleep stages scoring by human experts is the current gold standard for sleep analysis. However, this method is tedious, time-consuming, prone to human errors, and unable to detect microstructure of sleep such as cyclic alternating pattern (CAP) which is an important diagnostic factor for the detection of sleep disorders such as insomnia and obstructive sleep apnea (OSA). The CAP is only observed as subtle changes in the electroencephalogram (EEG) signals during non-rapid eye movement (NREM) sleep, making it very difficult for human experts to discern. Hence, it is important to have an automated system developed using artificial intelligence for accurate and robust detection of CAP and sleep stages classification. In this study, a deep learning model based on 1-dimensional convolutional neural network (1D-CNN) is proposed for CAP detection and homogenous 3-class sleep stages classification, namely wakefulness (W), rapid eye movement (REM) and NREM sleep. The proposed model is developed using raw and standardized EEG recordings. Our developed CNN network achieved the sensitivity of 76.23% and 79.23% for unbalanced and balanced sleep dataset, and 92.06% and 80.29% for unbalanced and balanced CAP dataset, respectively. Our proposed model also demonstrated good performance for 3-class sleep stages classification with an accuracy of 83.14% using unbalanced sleep dataset and correctly identified 11.6% of A-phases which comprised only 12.6% in the unbalanced dataset. The performance of the developed prototype is ready to be tested with more data before clinical application.</p>

COVER LETTER

U Rajendra Acharya, MTech, Ph.D., DEng, DSc

Ngee Ann Polytechnic, Singapore

Adjunct Professor, University of Malaya, Malaysia

Adjunct Professor, University of Southern Queensland, Australia

Adjunct Professor, Asia University, Taiwan

Associate faculty in SUSS, Singapore

Email: [aru@np.edu.sg](mailto:aru@np.edu.sg)

**Website:** <https://scholar.google.com.sg/citations?user=8FjY99sAAAAJ&hl=en>

**ResearchGate:** [https://www.researchgate.net/profile/U\\_Rajendra\\_Acharya](https://www.researchgate.net/profile/U_Rajendra_Acharya)

**Publons:** <https://publons.com/researcher/2836800/rajendra-u-acharya/>

**Scopus:** Author ID: 7004510847

Highly Cited Researcher for *five* consecutive years (2016 to 2020) in Computer Science <http://highlycited.com/>

Prof. (Dr) Hamido Fujita

Editor in Chief, Applied Intelligence Journal

**Sub: Submission of manuscript to Applied Intelligence**

Dear Prof. Fujita,

We are submitting our research paper titled “*Automated Detection of Cyclic Alternating Pattern and Classification of Sleep Stages Using Deep Neural Network*” to **Applied Intelligence** journal for possible publication. This manuscript, or specified parts of it, has not been and will not be submitted elsewhere for publication. All the co-authors have read the papers and have recommended submission to this journal.

We would also like to declare that there is no real or potential conflict of interest in conjunction with the submission of this manuscript. Should you have any other enquiries, please do not hesitate to write to us.

I, on behalf of all the co-authors, would like to kindly request you to review this paper at the earliest and submit the decision.

Thank you very much.

Best Regards, Raj

**Date:** 30/12/2020

# Automated Detection of Cyclic Alternating Pattern and Classification of Sleep Stages Using Deep Neural Network

Hui Wen Loh<sup>1</sup>, Chui Ping Ooi<sup>1</sup>, Shivani G. Dhok<sup>4</sup>, Manish Sharma<sup>5</sup>, Ankit A. Bhurane<sup>6</sup>, U. Rajendra Acharya<sup>1,2,3,7,8,\*</sup>

<sup>1</sup> School of Science and Technology, Singapore University of Social Sciences, Singapore; Hui Wen Loh (ORCID: 0000-0003-3114-6523); Chui Ping Ooi (ORCID: 0000-0002-0293-3280)

<sup>2</sup> School of Engineering, Ngee Ann Polytechnic, Singapore,

<sup>3</sup> Department of Bioinformatics and Medical Engineering, Asia University, Taiwan,

<sup>4</sup> Department of Electronics and Communication Engineering, Indian Institute of Information Technology Nagpur (IIITN), Nagpur, India; Shivani G. Dhok (ORCID: 0000-0003-1443-2624)

<sup>5</sup> Department of Electrical and Computer Science Engineering, Institute of Infrastructure, Technology, Research and Management (IITRAM), Ahmedabad, India

<sup>6</sup> Department of Electronics and Communication, Visvesvaraya National Institute of Technology (VNIT), Nagpur, India; Ankit A. Bhurane (ORCID: 0000-0001-8181-7685)

<sup>7</sup> International Research Organization for Advanced Science and Technology (IROAST) Kumamoto University, Kumamoto, Japan

<sup>8</sup> School of Management and Enterprise, University of Southern Queensland, Australia

\* Corresponding author: U Rajendra Acharya ([aru@np.edu.sg](mailto:aru@np.edu.sg)); (ORCID: 0000-0003-2689-8552)

## Abstract

The visual sleep stages scoring by human experts is the current gold standard for sleep analysis. However, this method is tedious, time-consuming, prone to human errors, and unable to detect microstructure of sleep such as cyclic alternating pattern (CAP) which is an important diagnostic factor for the detection of sleep disorders such as insomnia and obstructive sleep apnea (OSA). The CAP is only observed as subtle changes in the electroencephalogram (EEG) signals during non-rapid eye movement (NREM) sleep, making it very difficult for human experts to discern. Hence, it is important to have an automated system developed using artificial intelligence for accurate and robust detection of CAP and sleep stages classification. In this study, a deep learning model based on 1-dimensional convolutional neural network (1D-CNN) is proposed for CAP detection and homogenous 3-class sleep stages classification, namely wakefulness (W), rapid eye movement (REM) and NREM sleep. The proposed model is developed using raw and standardized EEG recordings. Our developed CNN network achieved the sensitivity of 76.23% and 79.23% for unbalanced and balanced sleep dataset, and 92.06% and 80.29% for unbalanced and balanced CAP dataset, respectively. Our proposed model also demonstrated good performance for 3-class sleep stages classification with an accuracy of 83.14% using unbalanced sleep dataset and correctly identified 11.6% of A-phases which comprised only 12.6% in the unbalanced dataset. The performance of the developed prototype is ready to be tested with more data before clinical application.

**Keywords** Sleep stages · cyclic alternating pattern

(CAP) · classification · Electroencephalogram (EEG) · deep learning · CAPSLPDB · CNN

---

## 1 Introduction

Sleep is often taken for granted by the public, but it is crucial for our physical and mental health [1]. Approximately 50 to 70 million Americans are reported to have sleep disorders [2] and at least 25 million Americans have obstructive sleep apnea (OSA) [3]. Also, 30% of the adults in the United States of America are diagnosed with insomnia [4]. Sleep disorders like OSA and insomnia are also associated with numerous health problems such as stroke [5], cardiovascular disease [6], and obesity [7]. However, sleep problem is a global issue that is not just unique to America. In 2012, Stranges et al. [8] investigated the prevalence of sleep problem from 8 countries across Asia and Africa, using two publicly available datasets: International Network for the Demographic Evaluation of Populations and Their Health (INDEPTH) and the World Health Organization Study on Global Ageing and Adult Health (WHO-SAGE). They reported that 16.6% of the adults ( $\approx 150$  million) included in their study had sleep problems and this number is expected to exceed 260 million by 2030 because adults, especially in low-income settings, are ignorant of the detrimental health effect of sleep problems. Another global sleep problem study by Konayagi et al. [9] had analyzed data from the World Health Organization's World Health Survey (WHS) across 70 countries. They reported that the odds of having sleep problems for an individual with a known psychotic symptom is 2.41 (p-value < 0.001); more than two times increase in the risk of having sleep problems. Hence, sleep problem is becoming a serious public health issue on a global scale and an accurate diagnostic tool of sleep disorder is needed [10, 11].

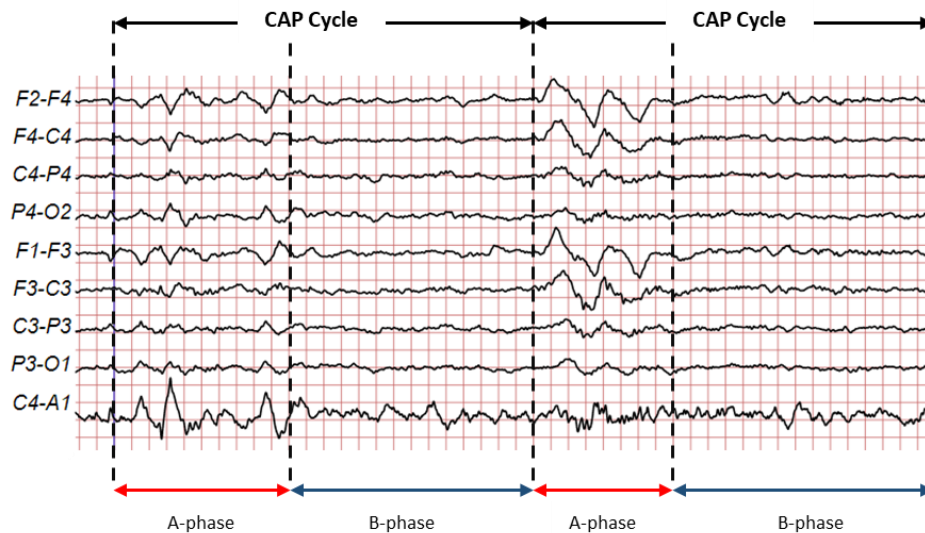
Sleep stages are also known as the macrostructure of sleep and there are initially six stages according to Rechtschaffen and Kales (R&K) rules [12]: Wakefulness (W), Rapid Eye Movement (REM), and Non-REM which is divided into 4 stages (NREM S1- S4). Later, the American Academy of Sleep Medicine (AASM) guidelines [13] classified NREM S3 and NREM S4 together as Slow Wave Sleep (SWS) due to similarity in their characteristics, resulting in a total of five sleep stages. The five sleep stages can be described with electroencephalogram (EEG) characteristic rhythm and other physiological changes as follows:

- **Wakefulness:** Brain activity is in the most active stage and is represented by high frequency alpha rhythms and occasional beta rhythms [14].
- **NREM S1:** Individual proceeds to fall asleep and alpha rhythms disappear while theta rhythms make their appearances [14]. This is the lightest sleep stage where individuals are easily awakened by disruptive noises [2]. Heart rate and breathing begin to slow down and muscle starts to relax as well [15].
- **NREM S2:** Sleep spindles and K-complex will occasionally appear for approximately 1 to 2 seconds [14]. High density sleep spindles are also observed in individuals who learn new task before sleep, hence indicating its relation to memory consolidation [16]. Body temperature begin to drop, and eye movement ceases at this stage [15].
- **SWS (NREM S3 and S4):** Low frequency delta rhythms will appear intermittently in NREM S3 and eventually dominates in NREM S4 [14]. An optimal amount of SWS allows individuals to feel refreshed when they wake up. Heart rate and breathing are the slowest at this stage and muscles are fully relaxed. This is the deepest sleep stage where individuals usually find it hard to wake up [15].

- **REM:** Proceeds immediately after SWS and it is represented by theta rhythms and flattening of EEG signals, accompanied by loss of muscle tone of the body core [14], [17]. Breathing patterns are fast and irregular during REM sleep and heart rate increases to near waking levels. Dreams are known to occur in this stage and REM sleep is accompanied by the loss of muscle tone to prevent individuals from acting out of their dreams [15].

Currently, the visual sleep stages scoring by human experts is the gold standard for sleep analysis [18]. According to the AASM guidelines [13], overnight polysomnogram (PSG) recordings are first segmented into 30s fragments (epochs). Next, each epoch is scored into different sleep stages. It is very often that an epoch may contain two or more sleep stages. Thus, human experts will score each epoch based on the sleep stages which appear many number of times. For instance, an epoch comprises 45% NREM S1 and 55% NREM S2 will be classified as NREM S2 sleep. However, this method results in heterogenous sleep stages scoring [18]. In fact, NREM S3 and S4 are heterogeneously combined as SWS for ease of classification because human experts are incapable of adapting to slow background EEG changes which makes the classification of NREM S3 and S4 challenging, as counting the delta rhythm occurrence is difficult [12, 18]. To address the limitation of heterogenous sleep stages scoring, Kemp et al. [19] and Pardey et al. [20] suggested that NREM sleep should be represented as a continuous function, rather than subdivisions of NREM sleep.

Another challenge regarding the current sleep stages scoring approach is the exclusion of microstructure of sleep which only appears for a few seconds, significantly shorter than an epoch of 30s duration [18]. The microstructure of sleep includes cyclic alternating pattern (CAP), elementary arousal (K-complexes) and micro-arousal [18, 21]. In particular, arousal instability is more evident in the CAP sequence rather than in micro-arousal events. Hence, CAP provides a global framework to measure sleep instability [21]. CAP only appears in periodic EEG activity of the NREM sleep and it is associated with sleep events such as falling asleep, transition in sleep stage, and awakenings [22, 23]. Thus, if there is an appearance of CAP in REM sleep, it could be a prognostic element of sleep disorder [24].



**Fig. 1** CAP waveform recorded from different EEG electrodes in CAPSLPDB, healthy subject N1

CAP can be described as recurrent transient electrocortical events that consist of two distinct phases: A-phase and B-phase [23]. A-phase is a transient phenomenon that has known association with brain activation [24, 25] and it is further broken down into three subtypes described as follows [24, 25]:

- **A1-phase** can be identified by an increase in amplitude to 3 times that of normal background activity and they are usually delta rhythms, K-complexes, and bursts.
- **A2-phase** is a combination of A1 and A3 phase, characterized by a mixture of slow and fast rhythms. This phase also indicated a drop in sleep stability.
- **A3-phase** can be identified by an increase in frequency compared to background activity and they are usually alpha and beta rhythms.

Hence, A-phase is characterized by having either low frequency with high amplitude EEG signals (A1-phase) or high frequency with low amplitude EEG signals (A3-phase) or a combination of these two phenomena (A2-phase) [25]. A-phases can be distinguished from B-phases which are background EEG activities as shown in Figure 1 [11].

A CAP cycle is formed when B-phase immediately follows after A-phase, otherwise, the A-phase is considered to be isolated [24]. A CAP sequence is formed when two or more CAP cycles occur in a sequence. The duration of each CAP phase can vary from 2s to 60s and normally, young adults have a mean duration of two and half minutes of CAP sequence, which consists of six CAP cycles [24, 26]. On the other hand, individuals with sleep disorders such as OSA are found to have higher CAP rate, cycles, and duration. This phenomenon is evident when OSA patients are accompanied by excessive sleepiness as well [27]. Abnormal CAP rates are found in epilepsy [28], insomnia [29], obstructive sleep apnea (OSA) [27], and coma patients [30]. Therefore, CAP is an important marker for unstable sleep that is, unfortunately, not included in visual sleep analysis [18, 26].

As such, there is a need to resolve the limitations of visual sleep analysis, which are heterogenous sleep stages scoring and exclusion of CAP. This can be achieved with the aid of



a computer aided diagnostic (CAD) tool that is superior to human counterparts in detecting the subtle changes in background EEG related to microstructure of sleep like CAP that is commonly left out in sleep stages scoring by human experts [18]. Studies have also shown that CAD performed equally well, if not better, in sleep stages scoring as compared to the human experts [31–33]. In the recent past, numerous studies have attempted to develop CAD tools based on machine learning and deep learning methodology for automated classification of sleep stages and detection of CAP separately. Rahman et al. [34] used EEG signals from the expanded sleep-EDF database in their study for 3-class sleep stages classification (W, NREM & REM) and achieved an accuracy of 94.1% with discrete wavelet transform (DWT) and support vector machine (SVM). Likewise, Yildirim et al. [35] proposed 1-Dimensional Convolutional Neural Network (1D-CNN) model for 3-class sleep stages classification and achieved an overall accuracy of 94.2% using EEG signals in both Sleep-EDF and expanded sleep-EDF database. As for CAP detection, Mendez et al. [36] proposed k-nearest neighbor (KNN) classifier to distinguish A-phases in CAP and achieved 80% accuracy. Hartmann et al. [37] proposed long short-term memory (LSTM) model for A-phase detection in CAP and achieved an accuracy of 82.4%.

In this work, we have attempted to address the limitation of traditional sleep stages scoring and automatic CAP detection using a deep learning model based on 1-Dimensional Convolutional Neural Network (1D-CNN). To the best of our knowledge, this is the first automated model developed for both sleep stages classification and CAP detection. The main contributions of this work are given below:

- The proposed model is compatible for the classification of both macrostructure and microstructure of sleep.
- For CAP detection, the proposed model can be trained with a smaller dataset (Table 4: balanced CAP dataset) and evaluated with a bigger dataset (Table 3: unbalanced CAP dataset). Hence, higher classification efficiency is obtained with shorter training time.
- The proposed model has the potential to be further developed into a CAD tool for clinical application.

## 2 Materials & Methods

Section 2.1 describes the data preparation and preprocessing methods, section 2.2 outlines the experiment setup of this work, and section 2.3 elaborates the architecture of the proposed 1D-CNN model.

### 2.1 Data Acquisition

CAP sleep database (CAPSLPDB) was acquired from PhysioNet [23, 38]. The PSG recordings in CAPSLPDB was obtained from an experiment conducted in the Sleep Disorder Center of the Ospedale Maggiore of Parma, Italy [23]. A total of 108 overnight PSG recordings were collected from 16 healthy and 92 pathological subjects, for a duration of 9-10 hours. The PSG recordings included at least 3 EEG channels, 2 EOG channels, 2 EMG channels, ECG and respiratory signals, which were sampled over a range of sampling frequencies (100Hz, 128Hz, and 512Hz.).

In this paper, we used single-channel EEG recordings (C4-A1 or C3-A2) from 6 healthy subjects that were sampled at 512Hz sampling frequency. The EEG signals were first segmented into epochs of 2 seconds duration, resulting in a length of 1024 timesteps per epoch. For sleep stages classification, substages of NREM sleep are combined into a single sleep stage. Likewise, for CAP detection, A1 to A3 subphase were combined as a single A-phase. Four types of datasets were created: unbalanced sleep dataset (Table 1), balanced sleep dataset (Table 2), unbalanced CAP dataset (Table 3), and balanced CAP dataset (Table 4). In the unbalanced datasets, every epoch was taken into account while the balanced datasets ensured that there was an equal number of epochs for each sleep stage and CAP phases. This means that for the balanced sleep datasets, the number of epochs was the same across the five sleep stages in Table 2(a). In other words, the number of epochs was balanced with respect to the five sleep stages before the substages S1, S2 and SWS were combined into a single NREM sleep stage in Table 2(b). The purpose of doing this was to ensure that the substages of NREM sleep were included in equal proportion. Similarly, for the balanced CAP dataset in Table 4, the number of epochs was the same across the subphases of A-phases before ensuring that the number of epochs was balanced for A- & B-phases. The epochs in the balanced datasets were chosen at random for consistency purposes [25].

**Table 1** Summary of the total number of samples (Unbalanced sleep stages dataset) for (a) 5 sleep stages and (b) 3 sleep stages

(a)	Subject	W	S1	S2	SWS	REM	Total
	N1	585	615	8528	5658	3585	18971
	N2	2145	2389	6400	3260	2265	16459
	N3	2040	836	5732	4608	2820	16036
	N5	150	881	6806	5629	3480	16946
	N10	1023	30	4328	5473	3225	14079
	N11	840	136	4323	6193	5700	17192
	Total	6783	4887	36117	30821	21075	99683

(b)	Subject	W	NREM	REM	Total
	N1	585	14801	3585	18971
	N2	2145	12049	2265	16459
	N3	2040	11176	2820	16036
	N5	150	13316	3480	16946
	N10	1023	9831	3225	14079
	N11	840	10652	5700	17192
	Total	6783	71825	21075	99683



**Table 2** Summary of the total number of samples (Balanced sleep stages dataset) for (a) 5 sleep stages and (b) 3 sleep stages

<b>(a)</b>	Subject	W	S1	S2	SWS	REM	Total
	N1	585	585	585	585	585	2925
	N2	2145	2145	2145	2145	2145	10725
	N3	836	836	836	836	836	4180
	N5	150	150	150	150	150	750
	N10	30	30	30	30	30	150
	N11	136	136	136	136	136	680
	<b>Total</b>	3882	3882	3882	3882	3882	19410

<b>(b)</b>	Subject	W	NREM	REM	Total
	N1	585	1755	585	2925
	N2	2145	6435	2145	10725
	N3	836	2508	836	4180
	N5	150	450	150	750
	N10	30	90	30	150
	N11	136	408	136	680
	<b>Total</b>	3882	11646	3882	<b>19410</b>

**Table 3** Summary of the total number of samples for unbalanced CAP dataset

Subject	A1	A2	A3	A-phase	B-phase	Total
N1	1013	354	548	1915	12915	14830
N2	550	327	597	1474	10560	12034
N3	285	284	494	1063	10110	11173
N5	1307	157	377	1841	11460	13301
N10	703	159	445	1307	8550	9857
N11	796	270	386	1452	9210	10662
<b>Total</b>	4654	1551	2847	9052	62805	<b>71857</b>

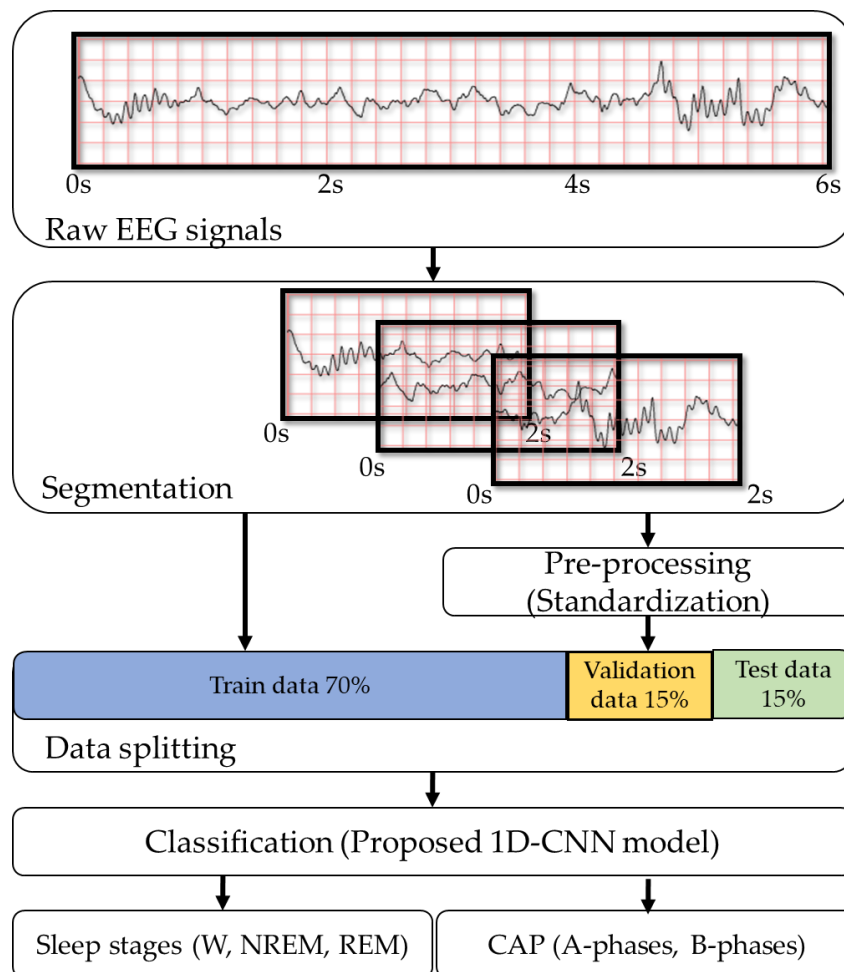
**Table 4** Summary of the total number of samples for balanced CAP dataset

Subject	A1	A2	A3	A-phase	B-phase	Total
N1	354	354	354	1062	1062	2124
N2	327	327	327	981	981	1962
N3	284	284	284	852	852	1704
N5	157	157	157	471	471	942
N10	159	159	159	477	477	954
N11	270	270	270	810	810	1620
<b>Total</b>	1551	1551	1551	4653	4653	<b>9306</b>

## 2.2 Experiment Setup

The workflow of the experimental setup is shown in Figure 2. After segmentation of the raw EEG recordings, the dataset was preprocessed by standardization of EEG signals and split into training set (70%), validation set (15%) and test set (15%). The original dataset with raw EEG signals without any preprocessing operation was also used to compare the difference between standardized and raw EEG signals. Training and validation were initially used during hyperparameter optimization to determine the layer parameters of proposed model. Once the model architecture was fixed, the proposed model was trained 50 times with the training set, and the best model was saved. The test set was then used to evaluate the performance of the saved best model.

The same experimental setup was applied for both unbalanced and balanced sleep datasets. However, an exception was applied for unbalanced CAP datasets that were not split into the respective train, validation and test sets. Instead, the proposed model was trained with the training set of balanced datasets for CAP detection while the performance of the model was evaluated using the test set of balanced datasets and the entire unbalanced CAP dataset. In other words, the unbalanced CAP datasets served as a secondary test set to evaluate model performance for CAP detection.



**Fig. 2** Workflow of experimental setup

### 2.3 Proposed Deep Learning Model (1D-CNN)

A typical 1D-CNN model consists of convolutional and pooling layers that are responsible for feature extraction and the operation of the convolutional layer can be described by the following formula [35]:

$$(S * W)_n = \sum_{i=1}^{|W|} W(i)S(i + n - 1) \quad (1)$$

where  $S$ ,  $W$  and  $*$  represent the 1D input signal, kernel and discrete convolution operation. The dimension of the kernel in 2D-CNN is denoted as  $W(i, j)$  but for 1D-CNN, only  $W(i)$  is concerned. The kernel ( $W$ ) is also the weights in any CNN model and the weights are updated every time the kernel slides over the input signals. The kernel output the feature maps once it runs through the input signals.

The output feature map ( $O$ ) can be described by the following formula:

$$O_n^l = (S_{W(i)} * W(i))_n \quad (2)$$

The features maps are further processed by multiple convolutional and pooling layers to make the features more distinct, thereby increasing the recognition and classification ability of 1D-CNN models. The processed feature maps are then flattened into single list vectors before entering the fully connected layers where classification takes place. The model architecture for the proposed model is based on 1D-CNN and is illustrated in [Figure 3](#). The details of the layer parameters and hyperparameters are provided in [Table 5 and 6](#), respectively.

The proposed model starts with a series of 3 convolutional layers followed by another 3 convolutional layers with 4 pooling layers placed in between them. The input, which is the standardized or raw EEG epochs with 1024 timesteps are convoluted into 64 feature maps with the length of 339 in the first convolutional layer. By the time it reaches the last pooling layer, 32 feature maps with the length of 18 is generated. The flatten layer converts the 32 feature maps from the last pooling layer into single-list vectors with the length of 576, which is used to train the neurons in the fully connected layers. To prevent overfitting of the proposed model, batch normalization is done after every convolutional layer and the regularizer (l2) of each kernel is set to 0.005. Dropout layers are also introduced in between the fully connected layers to prevent overfitting. Finally, the last layer of the proposed model is a SoftMax classifier which contains the same number of neurons as the number of classes for sleep stages (3 classes) and CAP (2 classes) respectively. SoftMax classifier generates probability scores which indicate the likelihood in which the single list vectors are classified into. For instance, a single list vector may have a probability score of 0.85 for A-phase and 0.15 for B-phase, respectively. The sum of the probability score for all the classes will always equate to 1.0. Adam optimizer with 0.001 learning rate and 0.01 decay rate is used in the proposed model.

The proposed model is created using Keras (v2.3.1) with Tensorflow (v1.14.0) backend, and both are deep learning tools from Python programming language. The specification of the

computer used to train and evaluate the model is as follows: Intel Core i7-10875H CPU, RTX 2070 Super 8GB, 32GB RAM, and 500GB NVMe SSD. The training time for each dataset is shown in Table 7.

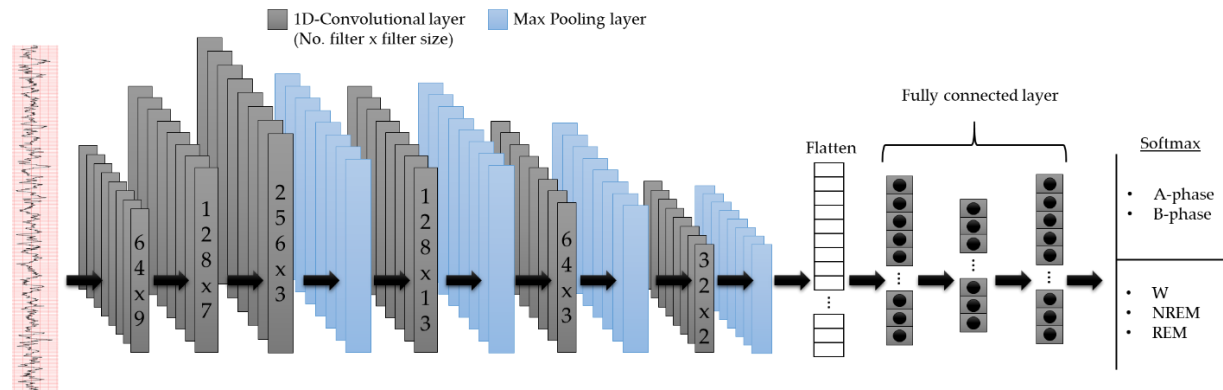


Fig. 3 Proposed 1D-CNN model architecture

Table 5 Detail of layers in proposed 1D-CNN model

No.	Layer	No. filter	Kernel size	Unit size	Parameter	Output shape
1	1DConv	64	9	-	ReLu, Stride = 3	64 x 339
2	BatchNorm	-	-	-	-	64 x 339
3	1DConv	128	7	-	ReLu, Stride = 1	128 x 333
4	BatchNorm	-	-	-	-	128 x 333
5	1DConv	256	3	-	ReLu, Stride = 1	256 x 331
6	BatchNorm	-	-	-	-	256 x 331
7	MaxPool	-	-	2	Stride = 2	256 x 165
8	1DConv	128	13	-	ReLu, Stride = 1	128 x 153
9	BatchNorm	-	-	-	-	128 x 153
10	MaxPool	-	-	2	Stride = 2	128 x 76
11	1DConv	64	3	-	ReLu, Stride = 1	64 x 74
12	BatchNorm	-	-	-	-	64 x 74
13	MaxPool	-	-	2	Stride = 2	64 x 37
14	1DConv	32	2	-	ReLu, Stride = 1	32 x 36
15	BatchNorm	-	-	-	-	32 x 36
16	MaxPool	-	-	2	Stride = 2	32 x 18
17	Dropout	-	-	-	Rate = 0.7	32 x 18
18	Flatten	-	-	-	-	1 x 576
19	Dense	-	-	64	ReLu	1 x 64
20	Dropout	-	-	-	Rate = 0.2	1 x 64
21	Dense	-	-	16	ReLu	1 x 16
22	Dropout	-	-	-	Rate = 0.2	1 x 16
23	Dense	-	-	64	ReLu	1 x 64
24	Dense	-	-	num_class	Softmax	1 x num_class

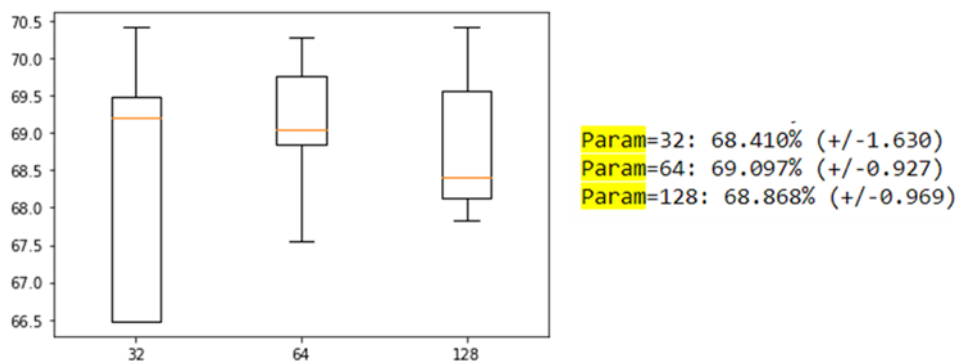
**Table 6** Details of hyperparameters in proposed 1D-CNN model

Hyperparameters	
Batch size	64
Kernel regularizer (l2)	0.005
Optimizer	Adam
Learning rate	0.001
Decay rate	0.01
Loss function	Categorical crossentropy

**Table 7** Training time of proposed 1D-CNN model in each respective sleep and CAP dataset

Datasets (EEG signals)	Training time (hh:mm:ss)
Unbalanced sleep dataset ( <i>raw</i> )	04:12:38
Unbalanced sleep dataset ( <i>standardized</i> )	04:13:59
Balanced sleep dataset ( <i>raw</i> )	00:49:31
Balanced sleep dataset ( <i>standardized</i> )	00:48:46
Balanced CAP dataset ( <i>raw</i> )	00:23:49
Balanced CAP dataset ( <i>standardized</i> )	00:23:24

The parameters in Table 5 and 6 are decided through numerous trials and errors. An example of layer parameters and hyperparameters optimization is shown in Figure 4, where the parameter of 32, 64, and 128 nodes for a fully connected layer is tested. For each parameter, the model is trained and evaluated for 5 rounds with training and validation set respectively. The box and whiskers plot summarizing the mean, median, and standard deviation for each parameter is summarised in Figure 4. From the plot in Figure 4, the parameter of 64 is chosen as the parameter for the fully connected layer because it has the highest overall accuracy and lowest standard deviation.

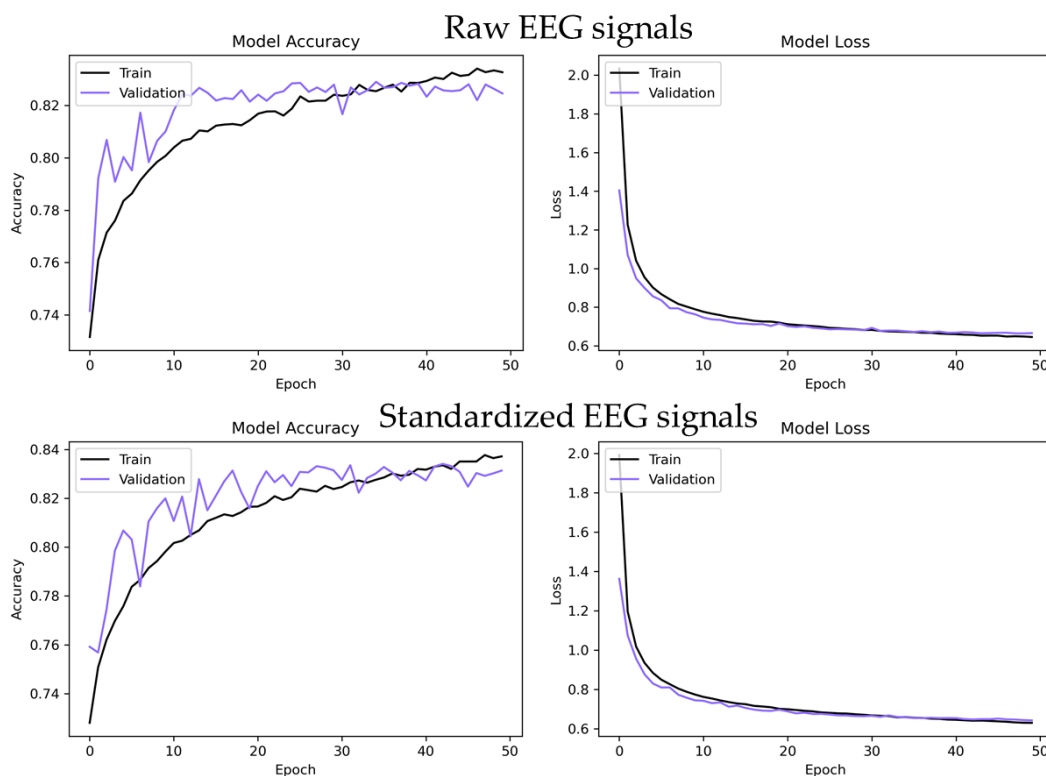
**Fig. 4** Hyperparameter optimization for the 19<sup>th</sup> fully connected layer in Table 5

### 3. Results

This section reports the major findings of the experiment. The experimental results for sleep stages classification is presented in *section 3.1* (unbalanced dataset), and *section 3.2* (balanced dataset). CAP detection is described in *section 3.3* and *section 3.4* summarizes the major findings of this work.

#### 3.1 Sleep Stages Classification with Unbalanced Dataset

In the unbalanced sleep dataset, the proposed model was individually trained with raw and standardized EEG signals, and the respective test sets obtained from these two training experiments were used to evaluate the performance of the model. Here, the same layer parameters and hyperparameters were used for both these two experiments. The performance graph obtained during model training is shown in [Figure 5](#). There was negligible gap between the training and validation loss for both raw and standardized models. The gap between training accuracy and validation accuracy for both raw and standardized models decreases until it reached 30-40 epochs and began to increase again. Also, the validation accuracy for both models remained stable at 82-83%. Hence, there was no overfitting problem for both raw and standardized EEG signals in the unbalanced sleep dataset.



**Fig. 5** Performance graph of proposed 1D-CNN model for raw and standardized EEG signals (unbalanced sleep dataset)

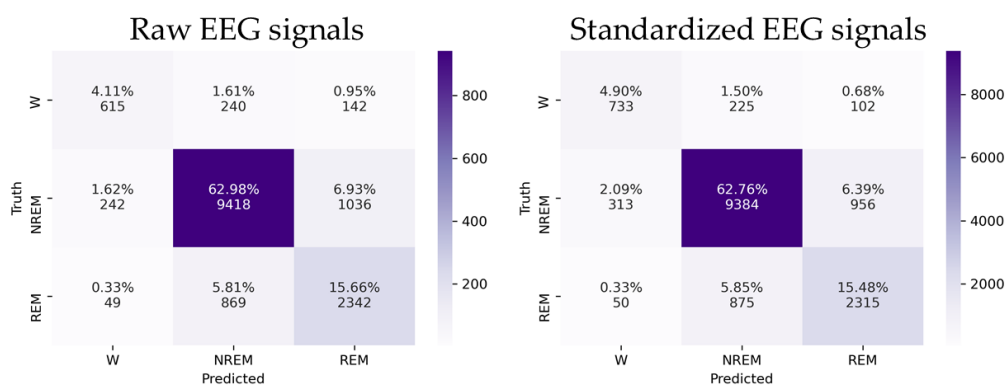
The highest validation accuracy of 82.91% and 83.41% were obtained for raw and standardized models respectively ([Table 8](#)). It can also be seen in [Table 8](#) that the performance of the standardized model was better than the raw model with higher training, validation, and test accuracy values.



**Table 8** Model accuracy (%) for raw and standardized EEG signals (unbalanced stages dataset)

	Training	Validation	Test
<b>Raw EEG signals</b>	84.16	82.91	82.76
<b>Standardized EEG signals</b>	85.53	83.41	83.14

Figure 6 shows the confusion matrix for raw and standardized EEG signals when evaluated with the test sets of unbalanced sleep datasets. The values in the confusion matrix represent the ratio of sample to the entire test set in percentage (%) and the number of samples for each sleep stages classification. The values that lie along the diagonal line in the confusion matrix are correctly classified by the model, hence they appear darker in color while values outside the diagonal line are wrongly classified. Take for instance, there were a total of 10,696 samples for NREM sleep in the test set of raw EEG signals. From that, 9,418 samples were correctly classified while the others were wrongly classified as wakefulness (W) (242 samples) and REM sleep (1036 samples).

**Fig. 6** Confusion matrix for raw and standardized EEG signals (unbalanced sleep dataset)

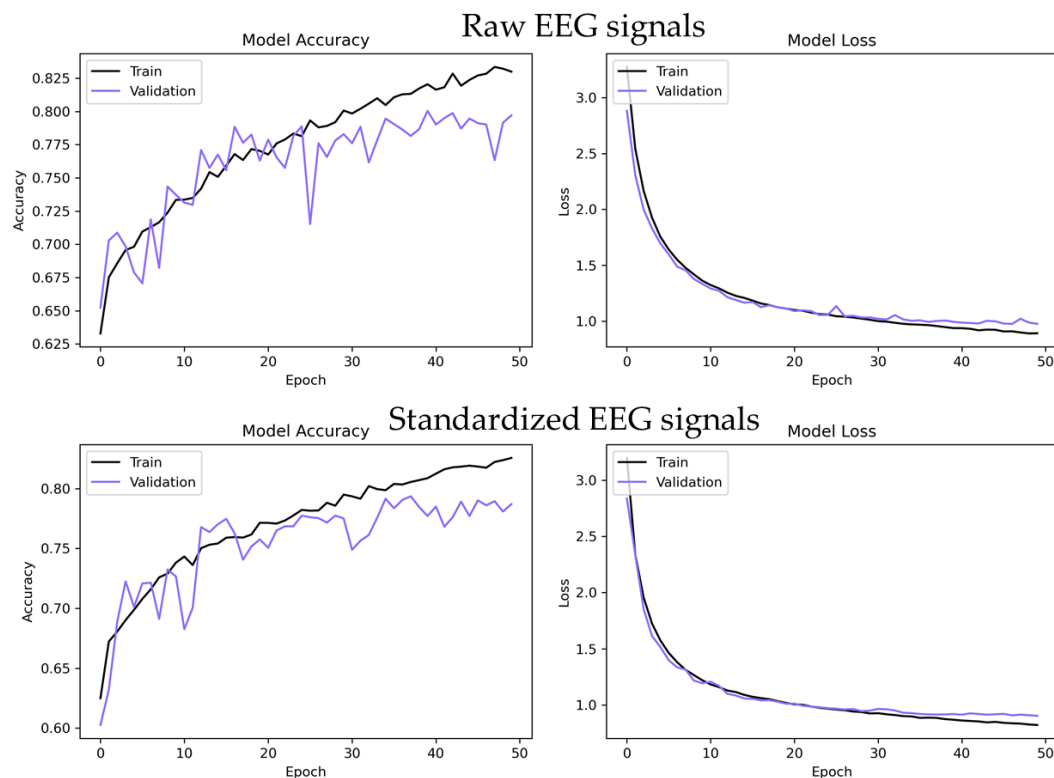
Various performance parameters evaluated using the test sets of raw and standardized EEG signals respectively are shown in Table 9. It can be noted that, NREM stages obtained the highest sensitivity of 88.05% and 88.09% for raw and standardized models respectively, since the majority of the samples were from this stage. Likewise, the lowest sensitivity of 61.69% and 69.15% were seen in the W stage of raw and standardized models respectively, which have the least number of samples.

**Table 9** Various performance values (%) for raw and standardized EEG signals (unbalanced sleep dataset)

EEG Signals	Sleep Stages	Precision	Sensitivity	F1	Samples
Raw	W	67.88	61.69	64.63	997
	NREM	89.47	88.05	88.75	10696
	REM	66.55	71.84	69.09	3260
Standardized	W	66.88	69.15	68.00	1060
	NREM	89.51	88.09	88.79	10653
	REM	68.63	71.45	70.01	3240

### 3.2 Sleep Stages Classification with Balanced Dataset

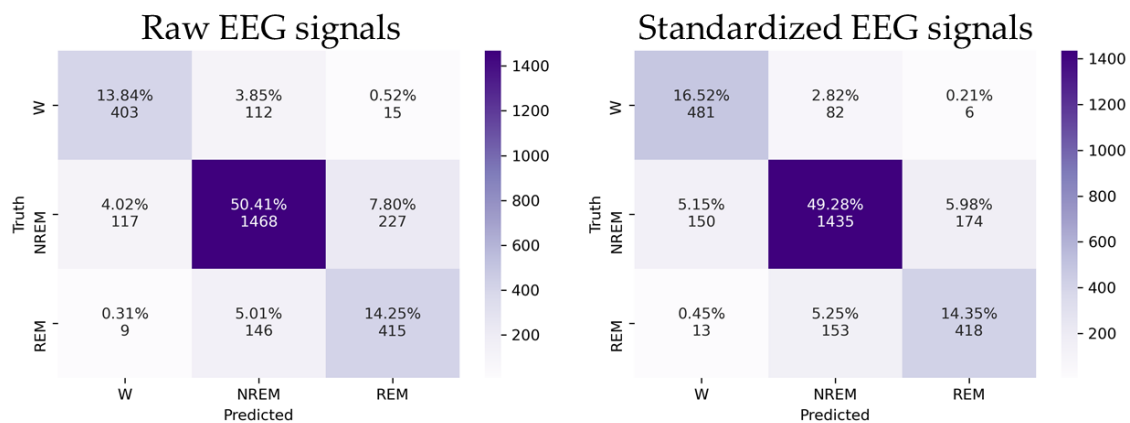
The same layer parameters and hyperparameters of the model were used for the balanced sleep dataset. With a smaller dataset, the model displayed signs of overfitting as shown in Figure 7. By looking at the model loss for both raw and standardized EEG signals, it can be noted that the overfitting problem started at around 30 epochs for both models. However, more fluctuation in the validation accuracy and loss were observed in the raw model, as compared to the standardized model. Hence, raw EEG signals were more prone to overfitting problem than standardized EEG signals.

**Fig. 7** Performance graph of proposed 1D-CNN model for raw and standardized EEG signals (balanced sleep dataset)

The highest validation accuracy obtained during model training was 80.04% and 79.35% for raw and standardized models, respectively, as shown in Table 10. Higher test accuracy was observed with standardized EEG signals; i.e. 78.50% and 80.15% for raw and standardized models, respectively. Another important factor to note was the difference between the test and training accuracy; the differences were greater in raw model (78.50-85.29%) as compared to standardized model (80.15-85.19%). It can be concluded that the proposed model has better generalization ability when standardized EEG signals were used.

**Table 10** Model accuracy (%) for raw and standardized EEG signals (balanced sleep dataset)

	Training	Validation	Test
<b>Raw EEG signals</b>	85.29	80.04	78.50
<b>Standardized EEG signals</b>	85.19	79.35	80.15



**Fig. 8** Confusion matrix for raw and standardized EEG signals (balanced sleep dataset)

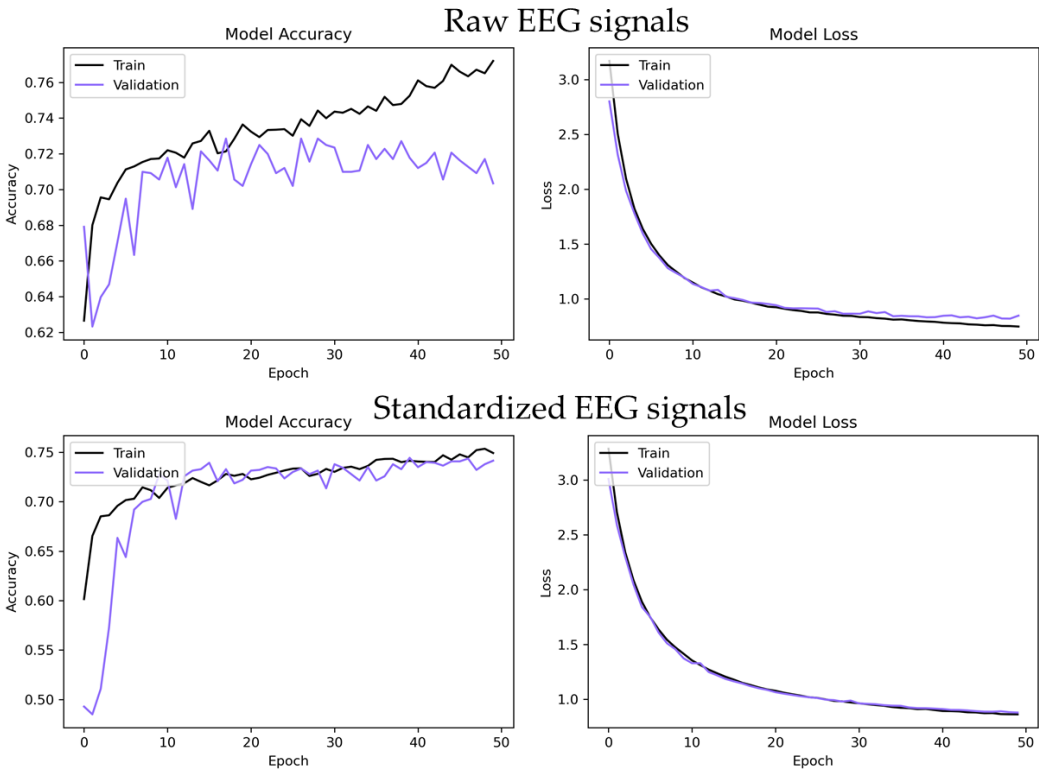
Unlike the unbalanced sleep stages dataset, the highest sensitivity (84.53%) was observed in the W stage of standardized model (Table 11). This is unexpected as the number of samples in W stage was significantly lower than the NREM stage. The REM stage had the lowest sensitivity of 72.81% and 71.58% for both raw and standardized model, respectively (Table 11). Figure 8 also showed that both models misclassified  $\approx 5\%$  of REM sleep in each dataset, while the misclassification for W stage is 4.37% and 3.03% for raw and standardized models respectively. This indicates that the proposed model had difficulty in recognizing the EEG characteristics rhythm of REM sleep for both raw and standardized EEG signals. Hence, balanced sleep dataset may not be a suitable dataset to train the proposed model. However, it could be used to detect the model's weakness, which is the inability to pick up the characteristic rhythms of REM sleep, in this case.

**Table 11** Various performance values (%) for raw and standardized EEG signals (balanced sleep dataset)

EEG Signals	Sleep Stages	Precision	Sensitivity	F1	Samples
Raw	W	76.18	76.04	76.11	530
	NREM	85.05	81.02	82.98	1812
	REM	63.17	72.81	67.64	570
Standardized	W	74.69	84.53	79.31	569
	NREM	85.93	81.58	83.70	1759
	REM	69.90	71.58	70.73	584

3.3 CAP Detection

The experiment for CAP detection differs from sleep stages classification. The raw and standardized models were individually trained with balanced CAP dataset (training set), while the performance of the model is evaluated by the test set of balanced CAP dataset and the entire unbalanced CAP dataset. The performance graph in Figure 9 shows negligible gap between training and validation loss in standardized EEG signals while a growing gap was observed in the raw EEG signals at around 30 epochs. The same phenomenon was also observed in the model accuracy of raw and standardized EEG signals, where the gap between training and validation accuracy was wider in the raw as compared to standardized EEG signals. Hence, raw EEG signals were more prone to overfitting problems, which was consistent with the results observed in sleep stages classification.

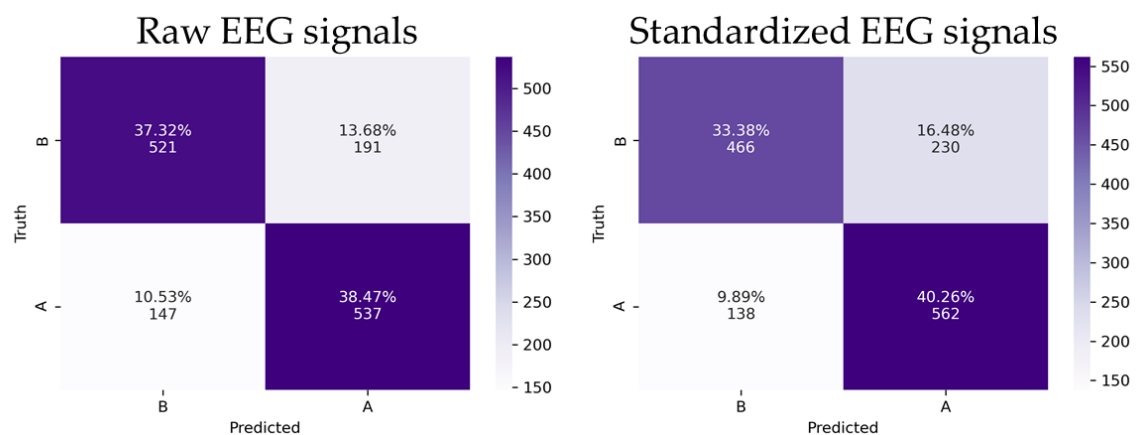


**Fig. 9** Performance graph of proposed 1D-CNN model for raw and standardized EEG signals (balanced CAP dataset)

Likewise, the model was saved when the highest validation accuracies of 72.85% and 74.43% for raw and standardized signals, were obtained for training as shown in Table 12. Higher test accuracy of 75.79% was obtained as compared to the raw model (73.64%). The other performance parameters evaluated using the test set of raw and standardized EEG signals are also shown in Table 12. It can be noted that, standardized signals obtained higher sensitivity (80.29%) than raw signals (78.51%), despite having lower test accuracy. The effect of having higher sensitivity is shown in Figure 10, where a higher percentage of A-phases were correctly identified compared to the B-phases via the standardized signals. Conversely, raw model is skewed towards the B-phases.

**Table 12** Various performance value (%) for raw and standardized EEG signals (balanced CAP dataset)

EEG Signals	Accuracy(%)			Performance parameter (%)			
	Train	Validation	Test	Precision	Sensitivity	F1	Specificity
<b>Raw</b>	74.03	72.85	75.79	73.76	78.51	76.06	73.17
<b>Standardized</b>	75.93	74.43	73.64	70.96	80.29	75.34	66.95

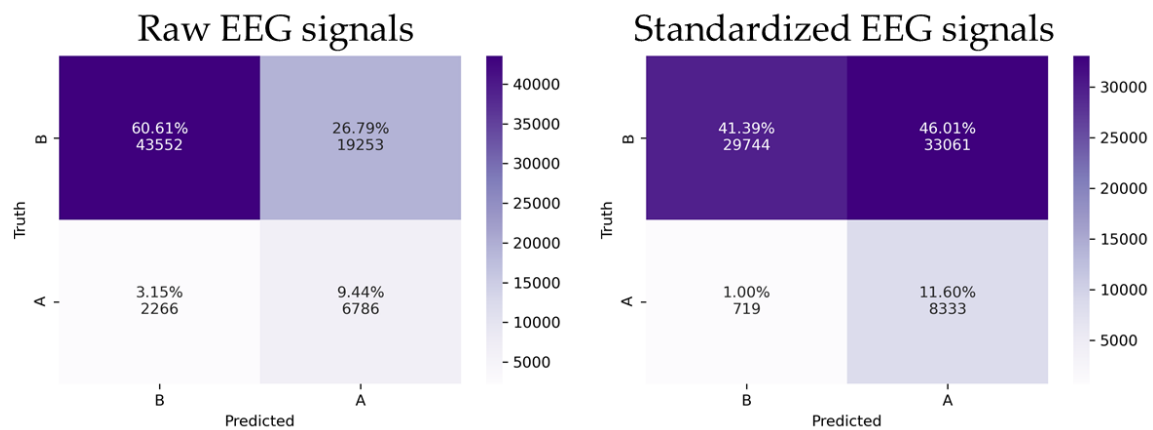


**Fig. 10** Confusion matrix for raw and standardized EEG signals (balanced CAP dataset)

Significant differences between the performance of raw and standardized signals were observed when unbalanced CAP dataset was used to evaluate the respective model. Standardized signal displayed an extremely high sensitivity of 92.06% for A-phases detection (Table 13). This is also evident from the confusion matrix of standardized signal in Figure 11; A-phases comprised only 12.6% in unbalanced CAP dataset and standardized signal correctly identified 11.6% of the A-phases. However, standardized signal did not correctly identify the majority of the B-phases (87.4%) which ended up with a lower accuracy of 52.99% (Table 13). Raw signal, on the other hand, correctly identified the majority of the B-phases, hence securing 60.61% accuracy with just B-phases alone (Figure 11). Even though standardized signal yielded lower accuracies, it was less likely to be affected by the noise caused by B-phases and was able to correctly distinguish the EEG characteristics rhythm of A-phases. Hence, standardized signal was preferred for CAP detection.

**Table 13** Various performance values (%) for raw and standardized EEG signals (unbalanced CAP dataset)

EEG Signals	Accuracy	Precision	Sensitivity	F1	Specificity
Raw	70.05	26.06	74.97	38.68	69.34
Standardized	52.99	20.13	92.06	33.04	47.36

**Fig. 11** Confusion matrix for raw and standardized EEG signals (unbalanced CAP dataset)

### 3.4 Summary of Results

**Table 14** Summary of results (%) obtained from unbalanced and balanced datasets for sleep stages classification and CAP detection

Classifications	Dataset	EEG Signals	Accuracy	Precision	Sensitivity	F1	Samples
Sleep stages	Unbalanced	Raw	82.76	74.63	73.86	74.16	14953
		Standardized	83.14	75.01	76.23	75.60	14953
	Balanced	Raw	78.50	74.80	76.62	75.58	2912
		Standardized	80.15	76.84	79.23	77.91	2912
CAP	Balanced	Raw	75.79	73.76	78.51	76.06	1369
		Standardized	73.64	70.96	80.29	75.34	1369
	Unbalanced	Raw	70.05	26.06	74.97	38.68	71857
		Standardized	52.99	20.13	92.06	33.04	71857

The results for all the sleep stages classification is summarized in Table 14. The average performance parameters of three sleep stages is shown in Table 9 and 11. Raw signals were more prone to overfitting problem in both sleep stages classification and CAP detection, despite having higher accuracy in CAP detection. On the other hand, standardized signals obtained higher overall sensitivity of 0.762 and 0.792 for unbalanced and balanced sleep stages datasets, respectively and 0.803 and 0.921 for balanced and unbalanced CAP datasets respectively. Hence, standardized EEG signals are recommended for both sleep stages classification and CAP detection due to higher sensitivity and no overfitting problem. Also, standardized signals were better at identifying A-phases during CAP detection, as the proposed model was able to correctly identify 11.6% out of 12.6% of the A-phases in the entire unbalanced CAP dataset (Figure 11). On the other hand, the raw signals were influenced by



B-phases which comprised of 87.4% of the unbalanced CAP dataset. Hence, the raw signal was overwhelmed by noise from the B-phases which hindered A-phase detection.

#### 4. Discussion

Many 3-class sleep stages classification studies have been reported based on machine learning and deep learning methods using two popular sleep databases: Sleep-EDF and Sleep-EDFX [19, 38]. To the best of our knowledge, this is the first study to use CAPSLPDB for 3-class sleep stages classification. Table 15 shows the novelty of this work compared to the other sleep stages classification studies. In this study 99,683 and 19,410 samples of EEG signals belonging to unbalanced and balanced datasets respectively were used. This number is higher than the other studies from the sleep-EDF database. However, it has to be noted that the studies conducted using Sleep-EDF and Sleep-EDFX databases obtained an accuracy of more than 90%, while the highest model accuracy obtained in this study for 3-class sleep stages classification was 83.14%. This is because the sampling frequency of the EEG signals used in this study was 512 Hz, which was five times higher than the other studies (100Hz). The duration of epoch had also contributed to the lower accuracy score, where the other studies in Table 15 had used 30s epoch while our study employed 2s epoch, which is extremely precise. Furthermore, CAPSLPDB, Sleep-EDF, and Sleep-EDFX have also scored their PSG recordings with 30s epoch which is heterogenous because an epoch containing 20% W stage and 80% NREM sleep, will be scored as the latter [18]. Hence, when the epoch duration is reduced to 2s, that 20% W stage will be labeled as NREM sleep during data preparation. This may result in classification error where proposed model correctly recognized the epoch as W stage, but in the dataset, the epoch is scored as NREM sleep. Despite the heterogenous sleep stages scoring in the dataset, our proposed model was able to obtain more than 80% accuracy score with standardized EEG signals. Therefore, our proposed model was able to recognize the EEG characteristic rhythm of three sleep stages using EEG signals of higher sampling frequency (512 Hz) and narrow epochs of 2s duration with relatively higher performance.

**Table 15** Summary of automated sleep stages classification studies that uses 3 classes (W, NREM and REM)

Author	Database	Sampling frequency	Approach	No. of samples	Accuracy (%)
da Silveira et al. [39]	Sleep-EDFX	100Hz	DWT + RF	106,376	93.90
Yildirim et al. [35]	Sleep-EDFX	100Hz	1D-CNN	127,512	94.23
Hassan et al. [40]	Sleep-EDF	100Hz	EEMD+RUSBoost	15,188	94.23
Hassan et al. [41]	Sleep-EDF	100Hz	CEEMDAN+Bagging	15,188	94.10
Zhu et al. [42]	Sleep-EDF	100Hz	HVG+SVM	14,963	92.60
Sharma et al. [43]	Sleep-EDF	100Hz	Wavelet filter+SVM	15,139	93.50
Yildirim et al. [35]	Sleep-EDF	100Hz	1D-CNN	15,188	94.20
<u>This work</u>	CAPSLPDB	512Hz	1D-CNN	99,683	82.76
				<b>99,683</b>	<b>83.14</b>
				19,410	78.50
				<b>19,410</b>	<b>80.15</b>

\*Values in **bold** represent results using standardized EEG signals

There are also numerous CAP detection studies which utilized EEG signals from CAPSLPDB, and they are summarized in Table 16. Our study used the same sampling frequency (512Hz) and epoch duration (2s) as Dhok et al. [25]. Hence, we have the same number of samples;

71,862 and 9,306 for unbalanced and balanced data, respectively, as Dhok et al. [25]. Our proposed model performed marginally better in balanced dataset as compared to Dhok et al. [25]. Their proposed machine learning model yielded an accuracy of 73.64% and sensitivity of 80.29% using a balanced dataset. The same model yielded an accuracy of 87.45% using an unbalanced dataset. Despite having lower model accuracy, our proposed model obtained the highest sensitivity score of 92.06% using standardized EEG signals with unbalanced dataset. Our proposed model correctly identified the minority A-phases (12.6% of unbalanced dataset) better than the other studies in Table 16. To date, only Hartmann et al. [37] have proposed deep learning models based on LSTM using EEG signals sampled at 128 Hz sampling frequency. Hence, this study is the first to employ deep learning model based on 1D-CNN for CAP detection using EEG signals of 512 Hz sampling frequency.

**Table 16** Summary of CAP detection studies using CAPSLPDB database

Author	Approach	Sampling frequency	Datasets	Performance parameter (%)		
				Accuracy	Specificity	Sensitivity
Mendez et al. [36]	KNN classifier	100 Hz	Unbalanced	80.00	80.00	70.00
Navona et al. [44]	Thresholding	128 Hz	Unbalanced	77.00	90.00	84.00
Mariani et al. [45]	ANN classifier	100 Hz	Unbalanced 240,429	87.19	90.49	69.55
Mariani et al. [46]	SVM, LDA, AdaBoost and ANN	100 Hz	Unbalanced	84.90	86.60	72.50
Mendonça et al. [47]	Feed Forward Neural Network with Finite State Machine	-	Unbalanced ( $\approx$ 50,000)	79.00	80.00	76.00
Hartmann et al. [37]	Variable LSTM	128 Hz	Balanced and unbalanced	82.42	83.90	75.28
Dhok et al. [25]	Wigner-Ville based entropy features	512 Hz	Balanced A-phases: 4653 B-phases: 4653	72.53	69.19	76.76
			Unbalanced 71862	87.45	52.09	87.75
<b><u>This work</u></b>	1D-CNN	512 Hz	Balanced (raw) A-phases: 684 B-phases: 712	75.79	73.17	78.51
			Tested with raw unbalanced data (71862)	70.05	69.34	74.97
			Balanced (standardized) A-phases: 700 B-phases: 696	73.64	66.95	80.29
			Tested with standardized unbalanced data (71862)	52.99	47.36	92.06

The notable aspects of our proposed model are given as follows:

- The same layer parameters and hyperparameters were used for both 3-class sleep stages classification and CAP detection, and high model performance was achieved.
- It was able to capture the EEG characteristic rhythms of three sleep stages and CAP using 2s epochs duration.
- The multifunctional CAD tool comprised of two stages. The first stage separates sleep EEG recordings into three sleep stages (W, NREM and REM) and acts as a filter to simultaneously remove W stage. Subsequently, the second stage detects CAP in NREM and REM sleep to obtain CAP rate, cycle and duration for sleep analysis.
- A completely automated system was successfully generated, thus removing the need for manual feature extraction.
- Large amount of data could be handled with minimal information loss [48].

Machine learning models require features to be extracted from the PSG recordings, and the model may overfit if high dimensional data of PSG recordings are used to train the model in its raw form [49, 50]. However, feature extraction may result in information loss as PSG recordings are converted into a lower dimensional vector feature [49]. Also, feature extraction procedure is done manually, hence more tedious and laborious [51]. Therefore, the proposed deep learning model successfully addressed the limitation of machine learning models by eliminating the need for feature extraction.

The limitations of this study are as follows:

- Proposed model has difficulty in identifying REM sleep during sleep stages classification. Hence, further hyperparameter optimization of the model may be required for better generalization of sleep stages.
- Elimination of noise is extremely challenging, especially in unbalanced CAP dataset as B-phases comprise of 87.4% of the dataset. For this reason, the proposed model was not trained with unbalanced CAP dataset because of the overwhelming number of samples in B-phases had generated data noise that cause our proposed model to predict every sample as B-phases, thus hindering the detection of A-phases.

## 5. Future Work

Our proposed work can be extended in the following ways:

- Consider other physiological signals like electrooculogram (EOG) and electromyogram (EMG) recordings for 3-class sleep stages classification.
- Develop hybrid deep learning models such as the combination of CNN and LSTM for CAP detection since LSTM is known for its ability to learn and predict patterns in sequence.
- Build a cloud-compatible deep learning system so that the CAD tool can conveniently access the required data and apply it immediately.
- Real-time PSG recordings will also be considered for wearable devices that use real time data to track sleep.

## 6. Conclusion

In this study, we proposed a deep learning model based on 1D-CNN for homogenous 3-class sleep stages and CAP detection, using EEG recordings of a high sampling frequency (512 Hz) and narrow epochs of 2 sec duration. The proposed model consists of multiple 1D-convolutional and pooling layers which will extract the salient features from EEG signals of various sleep stages and CAP. Subsequently, the extracted features are used to train the neurons in the fully connected layers for the classification of sleep stages and CAP detection. The performance of the proposed model has been validated with raw and standardized EEG signals. The developed model obtained an average sensitivity score of 76.23% and 79.23% for unbalanced and balanced sleep dataset respectively. Furthermore, our proposed system obtained an average sensitivity score of 92.06% and 80.29% for unbalanced and balanced CAP dataset. Our proposed model achieved an accuracy of 83.14% for unbalanced sleep dataset and 73.64% in balanced CAP dataset. The proposed model is able to identify 11.6% out of 12.6% of A-phases in the entire unbalanced CAP dataset. Hence, the proposed two-stage model is sensitive to the EEG characteristic rhythms of both macro-and micro signatures of sleep EEG signals. The first stage breaks down sleep EEG signals into 3 sleep stages and the second stage identifies the CAP in the respective sleep stages. However, the proposed model needs to be tested with more data before it is ready for clinical application. In future, we intend to improve the model performance by including EOG and EMG recordings for sleep stages classification and develop hybrid deep learning model (CNN-LSTM) for CAP detection.

**Author contributions:** All authors contributed to this article. The idea for the article was provided by HWL and URA. SGD provided MATLAB code for data preparation. HWL developed the model and drafted the first manuscript. Subsequently, CPO, SGD, MS, AAB, and URA edited the manuscript and provided suggestions to improve the manuscript.

**Funding:** This research received no external funding.

**Conflict of interest:** The authors declare that they have no conflicts of interest.

## References

1. Cho JW, Duffy JF (2019) Sleep, sleep disorders, and sexual dysfunction. In World Journal of Men's Health. Korean Society for Sexual Medicine and Andrology 37(3):261–275. <https://doi.org/10.5534/wjmh.180045>
2. Colten HR, Altevogt BM (2006) Institute of Medicine (US) Committee on Sleep Medicine and Research (ed) Sleep Disorders and Sleep Deprivation: An Unmet Public Health Problem. National Academies Press (US). <https://doi.org/10.17226/11617>
3. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM (2013) Increased Prevalence of Sleep-Disordered Breathing in Adults. Am J Epidemiol 177(9):1006–1014. <https://doi.org/10.1093/aje/kws342>
4. Roth T (2007) Insomnia: definition, prevalence, etiology, and consequences. J Clin Sleep Med 3(5 Suppl):S7-10. <http://www.ncbi.nlm.nih.gov/pubmed/17824495>
5. Redline S, Yenokyan G, Gottlieb DJ, Shahar E, O'Connor GT, Resnick HE, Diener-West M, Sanders MH, Wolf PA, Geraghty EM, Ali T, Lebowitz M, Punjabi NM (2010) Obstructive Sleep Apnea-Hypopnea and Incident Stroke. Am J Respir Crit Care Med 182(2):269–277. <https://doi.org/10.1164/rccm.200911-1746OC>
6. Khan MS, Aouad R (2017) The Effects of Insomnia and Sleep Loss on Cardiovascular Disease. Sleep Med Clin 12(2):167–177. <https://doi.org/10.1016/j.jsmc.2017.01.005>

7. Hargens TA, Kaleth AS, Edwards ES, Butner KL (2013) Association between sleep disorders, obesity, and exercise: a review. *Nat Sci Sleep* 1;5:27-35. <https://doi.org/10.2147/NSS.S34838>
8. Stranges S, Tigbe W, Gómez-Olivé FX, Thorogood M, Kandala NB (2012) Sleep Problems: An Emerging Global Epidemic? Findings from the INDEPTH WHO-SAGE Study Among More Than 40,000 Older Adults From 8 Countries Across Africa and Asia. *Sleep* 35(8): 1173–1181. <https://doi.org/10.5665/sleep.2012>
9. Koyanagi A, Stickley A (2015) The Association between Sleep Problems and Psychotic Symptoms in the General Population: A Global Perspective. *Sleep* 38(12):1875–1885. <https://doi.org/10.5665/sleep.5232>
10. Chattu VK, Manzar MD, Kumary S, Burman D, Spence DW, Pandi-Perumal SR (2018) The Global Problem of Insufficient Sleep and Its Serious Public Health Implications. *Healthcare*, 7(1):1. <https://doi.org/10.3390/healthcare7010001>
11. Loh HW, Ooi CP, Vicnesh J, Oh SL, Faust O, Gertych A, Acharya UR (2020) Automated Detection of Sleep Stages Using Deep Learning Techniques: A Systematic Review of the Last Decade (2010–2020). *Appl. Sci* 10(24):8963. <https://doi.org/10.3390/app10248963>
12. Hori T, Sugita Y, Koga E, Shirakawa S, Inoue K, Uchida S, Kuwahara H, Kousaka M, Kobayashi T, Tsuji Y, Terashima M, Fukuda K, Fukuda N, Sleep Computing Committee of the Japanese Society of Sleep Research Society (2001) Proposed supplements and amendments to “A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects”, the Rechtschaffen & Kales (1968) standard. *Psychiatry Clin Neurosci* 55(3):305–310. <https://doi.org/10.1046/j.1440-1819.2001.00810.x>
13. Iber C, Ancoli-Israel S, Chesson AL, Quan SF (2007) The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specification; American Academy of Sleep Medicine: Darien, IL, USA
14. Carley DW, Farabi SS (2016) Physiology of Sleep. *Diabetes Spectr* 29(1):5–9. <https://doi.org/10.2337/diaspect.29.1.5>
15. Brain Basics: Understanding Sleep. National Institute of Neurological Disorders and Stroke. <https://www.ninds.nih.gov/Disorders/patient-caregiver-education/Understanding-sleep>. Accessed: 17-Oct-2020
16. Gais S, Mölle M, Helms K, Born J (2002) Learning-dependent increases in sleep spindle density. *J Neurosci* 22(15):6830–6834. <https://doi.org/10.1523/JNEUROSCI.22-15-06830.2002>
17. Takahara M, Kanayama S, Nittono H, Hori T (2006) REM sleep EEG pattern: Examination by a new EEG scoring system for REM sleep period. *Sleep Biol. Rhythms* 4(2):105–110. <https://doi.org/10.1111/j.1479-8425.2006.00201.x>
18. Schulz H (2008) Rethinking sleep analysis. *J Clin Sleep Med* 4(2), 99–103.
19. Kemp B, Zwinderman AH, Tuk B, Kamphuisen HA, Oberyé JJ (2000) Analysis of a sleep-dependent neuronal feedback loop: the slow-wave microcontinuity of the EEG. *IEEE Trans Biomed Eng* 47(9):1185–1194. <https://doi.org/10.1109/10.867928>
20. Pardey J, Roberts S, Tarassenko L, Stradling J (1996) A new approach to the analysis of the human sleep/wakefulness continuum. *J Sleep Res* 5(4):201–210. <https://doi.org/10.1111/j.1365-2869.1996.00201.x>
21. Halász P (1998) Hierarchy of micro-arousals and the microstructure of sleep. *Neurophysiol Clin Neurophysiol* 28(6):461–475. [https://doi.org/10.1016/S0987-7053\(99\)80016-1](https://doi.org/10.1016/S0987-7053(99)80016-1)
22. Terzano MG, Mancina D, Salati MR, Costani G, Decembrino A, Parrino L (1985) The Cyclic Alternating Pattern as a Physiologic Component of Normal NREM Sleep. *Sleep* 8(2):137–145. <https://doi.org/10.1093/sleep/8.2.137>
23. Terzano MG, Parrino L, Sherieri A, Chervin R, Chokroverty S, Guilleminault C, Hirshkowitz M, Mahowald M, Moldofsky H, Rosa A, Thomas R, Walters A (2001) Atlas, rules, and recording

- techniques for the scoring of cyclic alternating pattern (CAP) in human sleep. *Sleep Med* 2(6):537–553. [https://doi.org/10.1016/S1389-9457\(01\)00149-6](https://doi.org/10.1016/S1389-9457(01)00149-6)
24. Machado F, Sales F, Santos C, Dourado A, Teixeira CA (2018) A knowledge discovery methodology from EEG data for cyclic alternating pattern detection. *Biomed Eng Online* 17(1):185. <https://doi.org/10.1186/s12938-018-0616-z>
  25. Dhok S, Pimpalkhute V, Chandurkar A, Bhurane AA, Sharma M, Acharya UR (2020) Automated phase classification in cyclic alternating patterns in sleep stages using Wigner–Ville Distribution based features. *Comput Biol Med* 119:103691. <https://doi.org/10.1016/j.compbiomed.2020.103691>
  26. Parrino L, Ferri R, Bruni O, Terzano MG (2012) Cyclic alternating pattern (CAP): The marker of sleep instability. *Sleep Med Rev* 16(1):27–45. <https://doi.org/10.1016/j.smr.2011.02.003>
  27. Korkmaz S, Bilecenoglu NT, Aksu M, Yoldas TK (2018) Cyclic Alternating Pattern in Obstructive Sleep Apnea Patients with versus without Excessive Sleepiness. *Sleep Disord* 2018:1–7. <https://doi.org/10.1155/2018/8713409>
  28. Parrino L, Halasz P, Tassinari CA, Terzano MG (2006) CAP, epilepsy and motor events during sleep: the unifying role of arousal. *Sleep Med Rev* 10(4):267–285. <https://doi.org/10.1016/j.smr.2005.12.004>
  29. Thomas RJ (2003) Arousals in Sleep-disordered Breathing: Patterns and Implications. *Sleep* 26(8):1042–1047. <https://doi.org/10.1093/sleep/26.8.1042>
  30. Kassab MY, Farooq MU, Diaz-Arrastia R, Van Ness PC (2007) The Clinical Significance of EEG Cyclic Alternating Pattern During Coma. *J Clin Neurophysiol* 24(6):425–428. <https://doi.org/10.1097/WNP.0b013e31815a028e>
  31. Svetnik V, Ma J, Soper KA, Doran S, Renger JJ, Deacon S, Koblan KS (2007) Evaluation of Automated and Semi-Automated Scoring of Polysomnographic Recordings from a Clinical Trial Using Zolpidem in the Treatment of Insomnia. *Sleep* 30(11):1562–1574. <https://doi.org/10.1093/sleep/30.11.1562>
  32. Pittman SD, MacDonald MM, Fogel RB, Malhotra A, Todros K, Levy B, Geva AB, White DP (2004) Assessment of Automated Scoring of Polysomnographic Recordings in a Population with Suspected Sleep-disordered Breathing. *Sleep* 27(7):1394–1403. <https://doi.org/10.1093/sleep/27.7.1394>
  33. Anderer P, Gruber G, Parapatics S, Woertz M, Miazhyńska T, Klosch G, Saletu B, Zeitlhofer J, Barbanoj MJ, Danker-Hopfe H, Himanen SL, Kemp B, Penzel T, Grozinger M, Kunz D, Rappelsberger P, Schlogl A, Dorffner G (2005) An E-Health Solution for Automatic Sleep Classification according to Rechtschaffen and Kales: Validation Study of the Somnolyzer 24 × 7 Utilizing the Siesta Database. *Neuropsychobiology* 51(3):115–133. <https://doi.org/10.1159/000085205>
  34. Rahman MM, Bhuiyan MIH, Hassan AR (2018) Sleep stage classification using single-channel EOG. *Comput Biol Med* 102:211–220. <https://doi.org/10.1016/j.compbiomed.2018.08.022>
  35. Yildirim O, Baloglu UB, Acharya UR (2019) A Deep Learning Model for Automated Sleep Stages Classification Using PSG Signals. *Int J Environ Res Public Health* 16(4). <https://doi.org/10.3390/ijerph16040599>
  36. Mendez MO, Chouvarda I, Alba A, Bianchi AM, Grassi A, Arce-Santana E, Milioli G, Terzano MG, Parrino L (2016) Analysis of A-phase transitions during the cyclic alternating pattern under normal sleep. *Med Biol Eng Comput* 54(1):133–148. <https://doi.org/10.1007/s11517-015-1349-9>
  37. Hartmann S, Baumert M (2019) Automatic A-Phase Detection of Cyclic Alternating Patterns in Sleep Using Dynamic Temporal Information. *IEEE Trans Neural Syst Rehabil Eng* 27(9):1695–1703. <https://doi.org/10.1109/TNSRE.2019.2934828>
  38. Goldberger AL, Amaral LA, Glass L, Hausdorff JM, Ivanov PC, Mark RG, Mietus JE, Moody GB, Peng CK, Stanley HE (2000) PhysioBank, PhysioToolkit, and PhysioNet: components of a new



- research resource for complex physiologic signals. *Circulation*, 101(23):E215-20.  
<https://doi.org/10.1161/01.cir.101.23.e215>
39. da Silveira TL, Kozakevicius AJ, Rodrigues CR (2017) Single-channel EEG sleep stage classification based on a streamlined set of statistical features in wavelet domain. *Med Biol Eng Comput* 55(2):343–352. <https://doi.org/10.1007/s11517-016-1519-4>
  40. Hassan AR, Bhuiyan MIH (2017) Automated identification of sleep states from EEG signals by means of ensemble empirical mode decomposition and random under sampling boosting. *Comput Methods Programs Biomed* 140:201–210. <https://doi.org/10.1016/j.cmpb.2016.12.015>
  41. Hassan AR, Bhuiyan MIH (2016) Computer-aided sleep staging using Complete Ensemble Empirical Mode Decomposition with Adaptive Noise and bootstrap aggregating. *Biomed. Signal Process Control* 24:1–10. <https://doi.org/10.1016/j.bspc.2015.09.002>
  42. Zhu G, Li Y, Wen P (2014) Analysis and Classification of Sleep Stages Based on Difference Visibility Graphs From a Single-Channel EEG Signal. *IEEE J Biomed Health Inform* 18(6):1813–1821. <https://doi.org/10.1109/JBHI.2014.2303991>
  43. Sharma M, Goyal D, Achuth PV, Acharya UR (2018) An accurate sleep stages classification system using a new class of optimally time-frequency localized three-band wavelet filter bank. *Comput Biol Med* 98:58–75. <https://doi.org/10.1016/j.compbiomed.2018.04.025>
  44. Navona C, Barcaro U, Bonanni E, Di Martino F, Maestri M, Murri L (2002) An automatic method for the recognition and classification of the A-phases of the cyclic alternating pattern. *Clin Neurophysiol* 113(11):1826–1831. [https://doi.org/10.1016/S1388-2457\(02\)00284-5](https://doi.org/10.1016/S1388-2457(02)00284-5)
  45. Mariani S, Grassi A, Mendez MO, Milioli G, Parrino L, Terzano MG, Bianchi AM (2013) EEG segmentation for improving automatic CAP detection. *Clin Neurophysiol* 124(9):1815–1823. <https://doi.org/10.1016/j.clinph.2013.04.005>
  46. Mariani S, Manfredini E, Rosso V, Grassi A, Mendez MO, Alba A, Matteucci M, Parrino L, Terzano MG, Cerutti S, Bianchi AM (2012) Efficient automatic classifiers for the detection of A phases of the cyclic alternating pattern in sleep. *Med Biol Eng Comput* 50(4):359–372. <https://doi.org/10.1007/s11517-012-0881-0>
  47. Mendonça F, Fred A, Mostafa SS, Morgado-Dias F, Ravelo-García AG (2018) Automatic detection of cyclic alternating pattern. *Neural Comput Appl* <https://doi.org/10.1007/s00521-018-3474-5>
  48. Faust O, Hagiwara Y, Hong TJ, Lih OS, Acharya UR (2018) Deep learning for healthcare applications based on physiological signals: A review. *Comput Methods Programs Biomed* 161:1–13. <https://doi.org/10.1016/j.cmpb.2018.04.005>
  49. Faust O, Razaghi H, Barika R, Ciaccio EJ, Acharya UR (2019) A review of automated sleep stage scoring based on physiological signals for the new millennia. *Comput Methods Programs Biomed* 176:81–91. <https://doi.org/10.1016/j.cmpb.2019.04.032>
  50. Mirza B, Wang W, Wang J, Choi H, Chung NC, Ping P (2019) Machine Learning and Integrative Analysis of Biomedical Big Data. *Genes (Basel)* 10(2):87. <https://doi.org/10.3390/genes10020087>
  51. Shoeibi A, Ghassemi N, Khodatars M, Jafari M, Hussain S, Alizadehsani R, Moridian P, Khosravi A, Hosseini-Nejad H, Rouhani M, Zare A, Khadem A, Nahavandi S, Atiya AF, Acharya UR (2020) Epileptic seizure detection using deep learning techniques: A Review. <http://arxiv.org/abs/2007.01276>