

Midline EEG Functional Connectivity As Biomarker for Conscious States in Sleep and Wakefulness

Anusha A. S. and A. G. Ramakrishnan

Dept. of Electrical Engineering, Indian Institute of Science Bengaluru, India
e-mail: anushas@iisc.ac.in, agr@iisc.ac.in

Abstract—Functional connectivity (FC) between different cortical regions of the brain has long been hypothesized to be necessary for conscious states in several modeling and empirical studies. The work presented herein estimates the FC between two bipolar midline electroencephalogram (EEG) recordings to evaluate its utility in discriminating consciousness levels across wakefulness and sleep. Consciousness levels were defined as Low, Medium, and High depending upon the ability of a subject to self-report their experiences at a later stage. The sleep EDF [expanded] dataset available in the Physionet data repository was used for analyses. FC was estimated using the debiased estimator of the squared Weighted Phase Lag Index (dWPLI2) metric. A total of 40 features extracted from the FC spectra for 10 EEG sub-bands were considered. FC trends demonstrated the highest alpha synchrony in the ‘Low’ conscious state. While the ‘Medium’ conscious state demonstrated superior phase synchronization in the low-gamma band, the ‘High’ conscious state was characterized by comparatively lower phase synchronization in all frequency bands. A Multi-Layer Perceptron (MLP) framework using a combination of 7 features yielded the highest cross-validation accuracy of 95.15% in distinguishing these conscious states. The study results provide a pertinent validation for the hypothesis that midline EEG FC is a reliable and robust signature of conscious states in sleep and wakefulness.

Keywords: Functional connectivity (FC), electroencephalogram (EEG), conscious states, phase synchronization, sleep.

I. INTRODUCTION

Identifying reliable and objective neural signatures for different states of the consciousness continuum [1] poses a crucial medical, scientific and ethical challenge for modern neuroscience. Although the significance of cortico-cortical functional connectivity (FC) in different conscious states has been explored by several empirical and theoretical studies [2]–[4], the utility of the property as a biomarker remains highly debated owing to (i) the range of FC measurement involved [5], [6], (ii) the frequency bands involved in the FC estimation, with heterogeneous proposals ranging from comparatively faster bands like theta, alpha and gamma [7] to slow (0.5–4 Hz) [8], or ultra-slow (< 0.01 Hz) band rhythms [9], and (iii) the lack of uniformity in the general value of FC when comparing different conscious and unconscious states.

This study aims to explore the utility of midline electroencephalogram (EEG) based FC as a biomarker to distinctly identify conscious states in sleep and wakefulness. A prerequisite for such an investigation is a clear definition for a conscious state. A conscious state in this study is defined

as a state during which experiences result in episodic memory formation, thereby making them memorizable and self-reportable at a later stage [10]. Following this definition, wakefulness and sleep may be interpreted as states of varying levels of consciousness that fluidly run into each other.

The work presented here identifies three levels of consciousness across wakefulness and sleep and attempts to distinguish them by incorporating EEG-based FC measures into machine learning frameworks. The Sleep-EDF [expanded] dataset available for public access in the Physionet data repository was used for analyses [11], [12]. The debiased estimator of the squared Weighted Phase Lag Index (dWPLI2) [13] was used as a metric of functional connectivity (FC) between two midline bipolar EEG recordings viz., Fpz-Cz and Pz-Oz. Boruta based feature selection was performed to identify an appropriate feature subset [14], which was further used to develop a Multilayer Perceptron (MLP) framework [15] for discriminating conscious states during wakefulness and sleep.

Section II describes the details of the methodology used in the study. The study results are discussed in Section III and conclusions are presented in Section IV.

II. METHODOLOGY

A. Dataset Description

Whole-night sleep EEG recordings of 32 age and gender-matched subjects [16 females, and 16 males, Age: 55.7 +/- 20.3 years (mean+/-SD)] obtained from the publicly available Physionet Sleep-EDF [expanded] database, were used for the analyses. All subjects were healthy Caucasians who had participated in the Sleep Cassette study and had no sleep-related disorders. A detailed description of this benchmark dataset provided by the PhysioNet organizer can be found in [11], [12].

B. Data Pre-processing and Labelling

For each subject, the dataset provides polysomnography (PSG) signals of about 20 hours, recorded during two subsequent day-night periods at the subjects’ homes. Two bipolar EEG recordings obtained from Fpz-Cz and Pz-Oz electrode locations are used for analyses in this study. Both signals were filtered between 0.1 and 47 Hz, individually inspected, and periods with artifacts were removed. The cleaned EEG data were partitioned into 30s epochs so as to conform to

the guidelines of the American Academy of Sleep Medicine (AASM) [16]. The hypnogram of each subject was used to annotate the epochs.

The dataset uses 8 labels for annotations viz., Wake (W), Stage 1, Stage 2, Stage 3, Stage 4 (corresponding to the range from light sleep to deep sleep), Rapid Eye Movement (REM) sleep (R), Movement (M), and Stage ? for any non-scored segment. Based on the chosen definition of consciousness, wake epochs were labeled as ‘High’, Stage 3 and 4 epochs (deep sleep) were labeled as ‘Low’, and REM epochs were labeled as ‘Medium’. Furthermore, all Stage 2 epochs occurring in the first 90-minute sleep cycle were labeled as ‘High’, while those belonging to the last 90-minute sleep cycle were labeled as ‘Medium’. This differential labeling of stage 2 sleep was based on the literature which suggests that self-reported stage 2 experiences from the first or second 90-minute cycle of sleep are markedly different from those in later cycles, and especially from those occurring at the end of a sleep period in the morning [17]. The circadian peak, which occurs at the end of the sleep cycle in the early morning is known to stimulate better recall of experiences during stage 2 sleep with a greater predominance of attributes such as character interactions, emotional contents, and vividness, much like REM sleep [18]. Studies have also shown that self-reported experiences in stage 2 sleep at the beginning of the sleep cycle are more ‘thought like’, and similar to the wake stage [19], while those towards the last 90-minute sleep cycle are more ‘dream like’, and similar to REM experiences [20]. Table I gives the number of epochs with different levels of consciousness labeled as mentioned above.

TABLE I
SUMMARY OF EPOCHS LABELED WITH DIFFERENT LEVELS OF CONSCIOUSNESS.

	# Epochs		
	Low	Medium	High
Female	1760	4160	31083
Male	1166	3927	30717
Combined	2926	8087	61800

C. Functional Connectivity Estimation

The functional connectivity between the two bipolar EEG signals was computed using the debiased estimator of the squared Weighted Phase Lag Index (dWPLI2). The metric proposed by Vinck et al. [13] is a measure of phase synchronization that is based solely on the imaginary component of the cross-spectrum of two time series and is not spuriously affected by the volume conduction artifacts. Mathematically, dWPLI2 can be expressed as:

$$dWPLI2 = \frac{\sum_{j=1}^N \sum_{k \neq j} Im\{X_j\}Im\{X_k\}}{\sum_{j=1}^N \sum_{k \neq j} |Im\{X_j\}Im\{X_k\}|} \quad (1)$$

where $Im\{X\}$ denotes the imaginary component of the cross-spectrum of the complex-valued random-variable X and N denotes the number of trials.

In comparison to the previous phase synchronization measures based on the imaginary component of the cross-spectrum, the dWPLI2 metric is known to have increased

sensitivity to detect true interactions (even when the interacting sources are spatially close) [13], [21], [22] and increased robustness to noise [23], [24]. Furthermore, the metric also debiases connectivity based on the number of epochs thereby preventing any sample size bias from being introduced by a direct estimator [13]. This debiasing can cause the dWPLI2 to be negative and, therefore its value, ranges from -1 to 1 .

D. Feature Extraction

FC estimations were done in 10 specific EEG bands, and four descriptive statistical features viz., Average FC value, Maximum FC value, Peak frequency (frequency corresponding to maximum FC value), and FC spectrum density (FCSD) were extracted from each band. Thus, a total of 40 features were estimated for each epoch. Table II summarizes the feature set.

E. Feature Selection and Classification

Feature selection is an important pre-processing step in the machine learning pipeline which helps to identify a subset of the most pertinent features and enhance predictive modeling [25]. Boruta, an “all-relevant” feature selection algorithm was used in this study, to identify a subset of relevant features. Unlike the popular feature selector algorithms, Boruta yields a set of all appropriate features from the feature set instead of selecting only the non-redundant ones. The algorithm identifies a feature as being relevant if there is a subset of attributes in the dataset among which the feature is not redundant when used for prediction [14].

The Boruta-selected features were further ranked by computing a score for each feature independently according to the Fisher criterion [26]. The identification of conscious states during sleep and wakefulness was formulated as a 3-level classification problem. As can be seen from Table I, the longer duration of the wakefulness phase in the data collection protocol has resulted in a class imbalance. Such an imbalance may bias the classification algorithms for always predicting the majority class thereby giving high accuracy but a low generalization. Therefore an imbalance correction using Synthetic Minority Over-sampling Technique (SMOTE) [27] was performed.

A Multilayer Perceptron (MLP) model - one of the proficient methods of classification from the artificial neural network (ANN) domain - was chosen as the classifier [15]. In order to identify the minimal-optimal feature subset, the ranked features were fed as input to the MLP model, starting from the first feature (with the highest Fisher score) and subsequently adding other features, one at a time, in the decreasing order of Fisher score. The 10-fold cross-validation accuracy was chosen as the performance index.

III. RESULTS AND DISCUSSIONS

As mentioned in section II.D, the dWPLI2 metric was computed for every epoch in the ‘Low’, ‘Medium’, and ‘High’ conscious states. Fig. 1 illustrates the grand average of the dWPLI2 spectra for three conscious states across 32 subjects in the 0.5 - 45 Hz range.

TABLE II
LIST OF ALL FEATURES CONSIDERED FOR ANALYSIS

EEG Band	Delta	Low Delta	Delta-Theta	Theta	Theta-Alpha	Alpha	Alpha-Beta	Beta	Beta-Gamma	Low Gamma
Frequency range (Hz)	0.5-4	1-2.5	2-5	4-8	4-10	8-12	8-20	12-30	16-40	30-45
Feature	Feature ID									
Average FC	F01	F02	F03	F04	F05	F06	F07	F08	F09	F10
Maximum FC	F11	F12	F13	F14	F15	F16	F17	F18	F19	F20
Peak frequency	F21	F22	F23	F24	F25	F26	F27	F28	F29	F30
FCSD	F31	F32	F33	F34	F35	F36	F37	F38	F39	F40

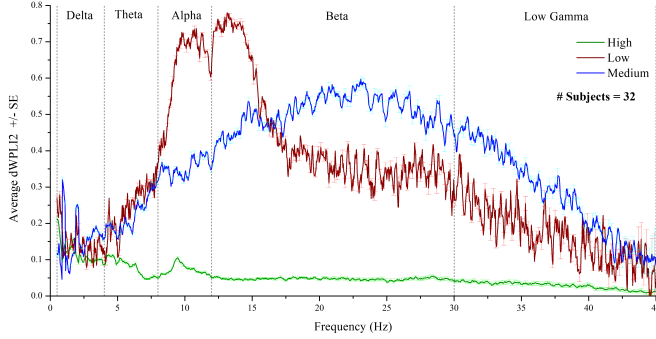


Fig. 1. dWPLI2 spectra of Low, Medium, and High conscious states, averaged across 32 subjects.

As can be seen, the ‘High’ conscious state is characterized by comparatively lower phase synchronization in all frequency bands. This is in line with the existing literature which suggests that EEG in the head midline is desynchronized during conscious wakefulness, as different regions of the brain are involved in different functions [28]. While the ‘Low’ conscious state exhibited the highest alpha synchrony, the ‘Medium’ conscious state illustrated superior phase synchronization in the low-gamma band. The episodic memory formation during the ‘Medium’ conscious state which enables self-reporting of experiences at a later stage can be attributed to the low-gamma band synchronization, which provides for the optimal temporal relationship between two signals to produce long-term synaptic changes that have been theorized to underlie episodic memory formation [29].

A total of 40 features were extracted from the dWPLI2 spectra, as explained in Section II.D. Further, an “all-relevant” feature subset was identified using Boruta. Boruta identified 24 of these features to be relevant. Fig. 2 summarizes the results.

As one can see, all FC-based features from the delta, delta-theta, and theta bands were rejected by Boruta, indicating that they are weakly relevant to the classification problem under consideration. Fisher score was computed for the selected features and they were ranked based on their scores, as shown in Fig. 3.

Ranked features were further used as input to construct MLP classifier models using sigmoid functions, and trained with standard backpropagation algorithm. The number of hidden layers, learning rate, and momentum rate for the backpropagation algorithm was carefully chosen for every input feature set, to achieve the best prediction. Fig. 4 shows the cross-validation accuracies achieved as a function of

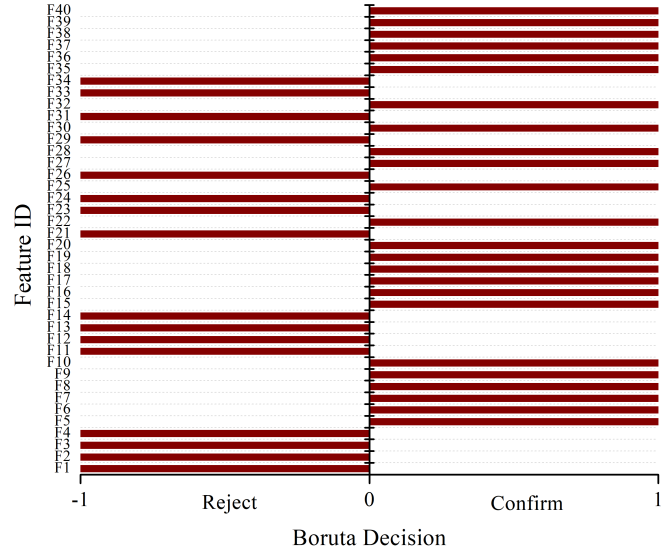


Fig. 2. Feature selection using Boruta. 1 indicate features confirmed as significant. -1 indicate features rejected by Boruta.

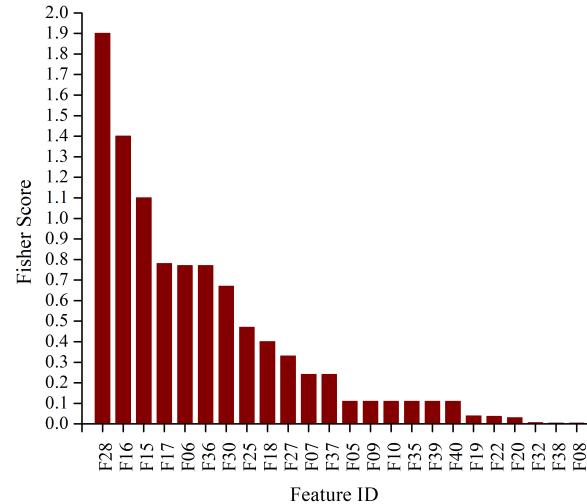


Fig. 3. Fisher score based ranking of Boruta-selected features.

increasing number of features, included in the decreasing order of Fisher score.

As one can see, a combination of 7 features yielded the highest classification accuracy of 95.15%. The model involved 4 hidden layers. A learning rate of 0.59 and a momentum rate of 0.48 were chosen for the model. Selected features corresponded to 5 EEG bands viz., Alpha, Beta, Low-Gamma, Theta-Alpha, and Alpha-Beta. The predomi-

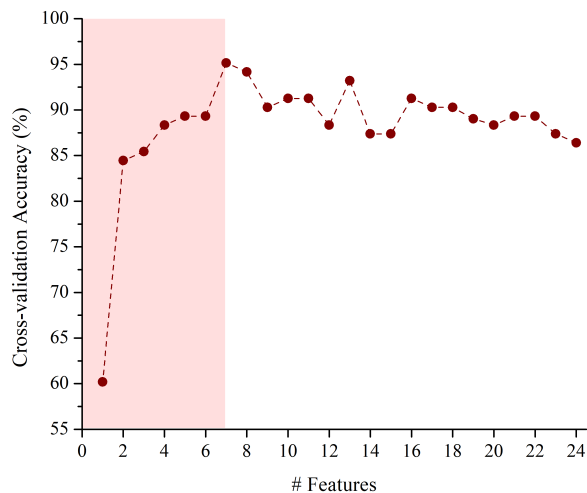


Fig. 4. Cross-validation accuracy for the MLP classifier during step-by-step inclusion of features, in the decreasing order of Fisher Score.

nance of features from comparatively higher frequency bands is in line with the existing literature which suggests that episodic memory formation and recall is associated with synchronized activity in the theta and gamma bands, as well as desynchronized activity in the alpha and beta bands [30]. It also strengthens the rationale that different conscious states are associated with different levels of memory formation and retrieval.

IV. CONCLUSIONS

The work presented here establishes the utility of midline EEG functional connectivity as a means to identify conscious states in sleep and wakefulness. Further studies involving whole-brain and cortico-cortical connectivity across different brain regions are required to identify if any specific FC patterns are associated with these states.

The study utilized memory formation and recall levels associated with conscious wakefulness and sleep stages to differentiate the conscious states. As such, this can be envisaged as the first step towards understanding the role of memory in the underlying neural mechanisms of consciousness and its alterations. Extending this line of thought to other conscious states like anesthesia, meditation, breath-focused yoga, and coma is the way forward.

REFERENCES

[1] J. F. Kihlstrom, "The continuum of consciousness," *Consciousness and Cognition*, vol. 2, no. 4, pp. 334–354, 1993. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S1053810083710287>

[2] E. Amico *et al.*, "Mapping the functional connectome traits of levels of consciousness," *NeuroImage*, vol. 148, pp. 201–211, 2017.

[3] J. S. Crone *et al.*, "Altered network properties of the frontoparietal network and the thalamus in impaired consciousness," *NeuroImage Clin.*, vol. 4, pp. 240–248, 2014.

[4] M. Boly *et al.*, "Consciousness in humans and non-human animals: Recent advances and future directions," *Front. Psychol.*, vol. 4, 10 2013.

[5] S. Laureys and N. D. Schiff, "Coma and consciousness: Paradigms (re)framed by neuroimaging," *NeuroImage*, vol. 61, pp. 478–491, 2012.

[6] V. A. F. Lamme, "Towards a true neural stance on consciousness," *Trends Cogn. Sci.*, vol. 10, pp. 494–501, 2006.

[7] N. D. Schiff, T. Nauev, and J. D. Victor, "Large scale brain dynamics in disorders of consciousness," *Curr. Opin. Neurobiol.*, vol. 25, pp. 7–14, 2014.

[8] B. J. He and M. E. Raichle, "The fMRI signal, slow cortical potential and consciousness," *Trends Cogn. Sci.*, vol. 13, pp. 302–309, 2009.

[9] P. Bartfeld *et al.*, "Signature of consciousness in the dynamics of resting state brain activity," *Proc. Natl. Acad. Sci.*, vol. 112, no. 3, pp. 887–892, 2015. [Online]. Available: <https://www.pnas.org/content/112/3/887>

[10] L. Naccache and S. Dehaene, "Unconscious semantic priming extends to novel unseen stimuli," *Cognition*, vol. 80, no. 3, pp. 215–229, 2001.

[11] A. L. Goldberger *et al.*, "Physiobank, Physiotookit, and Physionet: Components of a new research resource for complex physiologic signals," *Circulation*, vol. 101, no. 23, pp. e215–e220, 2000.

[12] B. Kemp *et al.*, "Analysis of a sleep dependent neuronal feedback loop: The slow-wave microcontinuity of the EEG," *IEEE Trans. Biomed. Eng.*, vol. 47, pp. 1185–1194, 2000.

[13] M. Vinck *et al.*, "An improved index of phase-synchronization for electrophysiological data in the presence of volume-conduction, noise and sample-size bias," *NeuroImage*, vol. 55, pp. 1548–1565, 2011.

[14] M. B. Kurska, A. Jankowski, and W. R. Rudnicki, "Boruta - A System for Feature Selection," *Fundam. Inform.*, vol. 101, no. 4, pp. 271–285, 2010.

[15] P. J. Werbos, *The roots of backpropagation: From ordered derivatives to neural networks and political forecasting*. John Wiley & Sons, 1994, vol. 1.

[16] R. B. Berry *et al.*, "The AASM manual for the scoring of sleep and associated events," *Rules, Terminology and Technical Specifications, Darien, Illinois, American Academy of Sleep Medicine*, vol. 176, 2012.

[17] T. Pivik and D. Foulkes, "NREM mentation: Relation to personality, orientation time, and time of night," *J. Consult. Clin. Psychol.*, vol. 32, pp. 144–151, Apr 1968.

[18] T. A. Nielsen, "A review of mentation in REM and NREM sleep: "Covert" REM sleep as a possible reconciliation of two opposing models," *Behav. Brain Sci.*, vol. 23, pp. 851–866, Dec 2000.

[19] S. Scarpelli *et al.*, "Predicting dream recall: EEG activation during NREM sleep or shared mechanisms with wakefulness?" *Brain Topogr.*, vol. 30, no. 5, pp. 629–638, 2017.

[20] H. Suzuki *et al.*, "Dreaming during non-rapid eye movement sleep in the absence of prior rapid eye movement sleep," *Sleep*, vol. 27, no. 8, pp. 1486–1490, 2004.

[21] S. Haufe, V. V. Nikulin, K. R. Muller, and G. Nolte, "A critical assessment of connectivity measures for EEG data: A simulation study," *NeuroImage*, vol. 64, pp. 120–133, 2013.

[22] A. Ewald *et al.*, "Estimating true brain connectivity from EEG/MEG data invariant to linear and static transformations in sensor space," *NeuroImage*, vol. 60, no. 1, pp. 476–488, 2012.

[23] C. J. Stam, G. Nolte, and A. Daffertshofer, "Phase lag index: Assessment of functional connectivity from multi channel EEG and MEG with diminished bias from common sources," *Hum. Brain Mapp.*, vol. 28, pp. 1178–1193, Nov 2007.

[24] G. Nolte *et al.*, "Identifying true brain interaction from EEG data using the imaginary part of coherency," *Clin. Neurophysiol.*, vol. 115, pp. 2292–2307, Oct 2004.

[25] Y. Saeys, I. Inza, and P. Larranaga, "A review of feature selection techniques in bioinformatics," *Bioinformatics*, vol. 23, pp. 2507–2517, 2007.

[26] Q. Gu, Z. Li, and J. Han, "Generalized Fisher score for feature selection," in *Proc. Conf. Uncertainty in Artificial Intelligence*, Arlington, Virginia, USA, 2011, pp. 266–273.

[27] N. V. Chawla, K. W. Bowyer, L. O. Hall, and W. P. Kegelmeyer, "SMOTE: Synthetic Minority Over-sampling Technique," *J. Artif. Int. Res.*, vol. 16, no. 1, pp. 321–357, Jun. 2002.

[28] S. Hanslmayr, B. P. Staresina, and H. Bowman, "Oscillations and episodic memory: Addressing the synchronization/desynchronization conundrum," *Trends Neurosci.*, vol. 39, no. 26763659, pp. 16–25, Jan. 2016.

[29] B. Schack and S. Weiss, "Quantification of phase synchronization phenomena and their importance for verbal memory processes," *Biol. Cybern.*, vol. 92, no. 4, pp. 275–287, 2005.

[30] J. Fell and N. Axmacher, "The role of phase synchronization in memory processes," *Nat. Rev. Neurosci.*, vol. 12, no. 2, pp. 105–118, 2011.