33rd Annual International Conference of the IEEE EMBS
Boston, Massachusetts USA, August 30 - September 3, 2011

Noise-Assisted Intrinsic Mode Function Coherence in Seizure Anticipation

Daniel W. Moller, *Student Member, IEEE,* and Alan W. L. Chiu, *Member, IEEE*

Abstract— **Epilepsy is a common neurological disorder characterized by recurrent electrophysiological activities, known as seizures. We explore the applicability of noise-assisted Ensemble Empirical Mode Decomposition (EEMD) for patient-specific seizure anticipation. Intracranial EEG data were obtained from invasive pre-surgical epilepsy monitoring at the Epilepsy Center of the University Hospital of Freiburg. Data from six patients (19 seizure recordings) with hippocampal foci were analyzed. For each recorded channel, twelve levels of intrinsic mode functions (IMFs) were produced. The coherence between the IMFs (denoted as IMF-Coh) between different channel pairs was computed. Statistical distributions of IMF coherence were determined from three hours of interictal data. Patient-, IMF level-, and channel pair-specific IMF-Coh were used to determine the earliest anticipation times for detected ictal events. Our study shows that while not all channel pairs are able to detect every ictal event, in general, low IMFs (containing frequency components greater than 1 Hz) can discriminate between interictal and periictal activities. Our results suggest patient-specific increases in coherence for one or more IMF levels during seizure progression. The anticipation window ranges from 30 to 53 minutes prior to clinical manifestation. We propose an anticipation optimality index as a joint indicator of sensitivity and earliest anticipation times to help select relevant channel pairs and IMF levels. In future work, we will incorporate cross-validation techniques with more interictal data as well as investigate patient-specific, automated selection of high-sensitivity channel pairs.**

I. INTRODUCTION

EPILEPTIC seizures affect as many as 50 million people and often occur without warning or apparent provocation. In many cases, pharmacological, surgical and other therapies for people suffering from epilepsy may have side effects or are unsuccessful in controlling seizures. A capable means of seizure anticipation could dramatically influence the quality of life for people with epilepsy through early warning systems and acute interventional therapy.

In a clinical sense, a seizure state is attributed to the involvement of regional or global neuronal networks experiencing hypersynchronous entrainment. The transitions to seizure activities, however, are unclear and may be based on patient-specific, and possibly seizure-specific, manifestations of abnormal brain dynamics. Better understanding of the dynamical changes preceding ictal events is necessary for the realization of viable seizure anticipation approaches. Researchers have shown neuronal population synchronization changes during periods leading up to seizure activities [1],[2]. Coherence measures have been applied in seizure anticipation algorithms with some success [3],[4]. Over the last three decades, a tremendous amount of research on signal processing has been undertaken to improve the standard coherence technique. In this paper, we explore the spatial coherence of intrinsic mode functions decomposed from a noise-assisted empirical approach and its relationship with the manifestation of seizure activities.

II. METHODS

A. IEEG Data Set

Intracranial EEG (IEEG) data from the grid, strip and depth electrodes were obtained through a publicly-available database of invasive pre-surgical epilepsy monitoring at the Epilepsy Center of the University Hospital of Freiburg. IEEG data were acquired at 256 Hz. Data from six recorded channels (CH1-CH3 within focal region; CH4-CH6 out of focal region) are available for each patient. Data from six patients (19 total seizures analyzed) with temporal (or temporo/occipital) hippocampal foci have been analyzed in this exploratory study. IEEG recordings for each channel were partitioned into non-overlapping 16-sec, normalized (mean: $\mu = 0$, standard deviation: $\sigma = 1$) windows.

B. Intrinsic Mode Function Coherence

For each time window, a noise-assisted (variance: $\sigma^2 = 0.1$) Ensemble Empirical Mode Decomposition (EEMD) [5] was employed to obtain 12 levels of intrinsic mode functions (IMF). IMF1 contains the higher frequency information and IMF12 contains the lower frequency information. The mean coherence of the concurrent time windows for the 15 channel pairs was determined at each IMF level (Fig. 1). These intrinsic mode function coherence measures span the length of each set of analyzed data.

C. Statistical Analysis Training, Validation and Testing

The running average of the intrinsic mode function coherence data was obtained using a 20-point (20 x 16-seconds ~ 5-min) smoothing function to create the IMF-Coh

---

Manuscript received April 15, 2011. This work was supported in part by the National Institutes of Health (NCRR) - P20RR016456.

D. W. Moller is a graduate student with the Department of Biomedical Engineering, Louisiana Tech University, Ruston, LA 71270 USA (Phone: 318-257-5231; Fax: 318-257-4000; Email: dwm027@latech. edu).

A. W. L. Chiu is an Assistant Professor with the Department of Biomedical Engineering, Louisiana Tech University, Ruston, LA 71270 USA.

978-1-4244-4122-8/11/$26.00 ©2011 IEEE

feature. This is consistent with the 5-min time windows which provided enhanced feature separation as discussed in [3],[6]. The first 6 hours of available interictal data for each patient were partitioned into twelve 30-min blocks. The data was then submitted to the EEMD process for the computation of the IMF-Coh. The training data set consisted of alternate blocks of the interictal IMF-Coh information from each patient. The standard deviation (σ) at each IMF level was calculated and used as the basis for determining the IMF-Coh thresholds. The appropriate IMF-Coh thresholds which can range from 2 to 5 times σ, were identified using the validation set which consists of the remaining IMF-Coh data. The criterion to determine a minimum threshold is called "zero-FP threshold method" in which the false positive (FP) rate of seizure detection is zero. Patient-specific IMF-Coh information containing 60-min preictal and 15-min ictal/postictal (the collection of which is defined here as periictal) were used as the test set. Seizure events were considered to be correctly detected when its IMF-Coh value first exceeded the lowest validation threshold having a FP rate of zero (Fig. 2). The sensitivity or true positive (TP) rate for each patient's test set was calculated from the ratio of correctly identified seizures to total tested seizures. The seizure anticipation time (maximum of 54min 40sec, due to the smoothing parameter) was noted for each detected seizure.

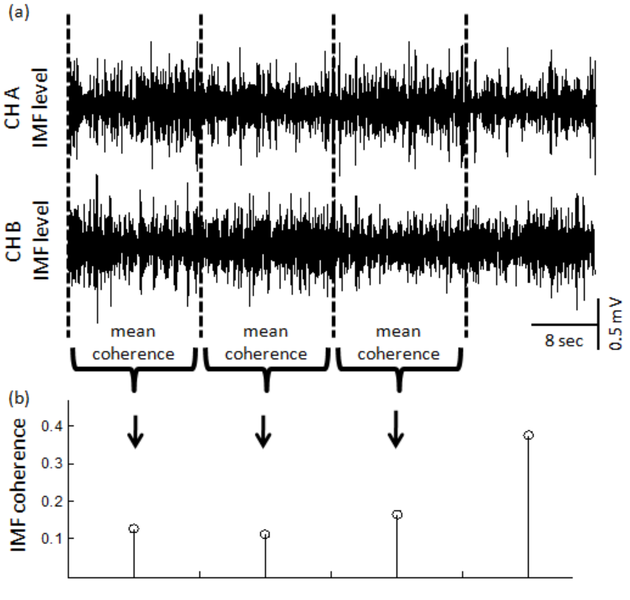

Fig. 1 (a) A single IMF level with four consecutive time windows is shown for two channels. (b) Concurrent IMF time windows are used to determine a channel pair's mean coherence, each producing a single value of IMF coherence information.

D. *Performance Assessment*

An optimality index [7] was modified to assess the performance of our anticipation algorithm for the IMF-Coh data for each channel pair. We define our anticipation optimality index (aO) as

$$aO = \frac{TP + (1 - FP)}{2} + \frac{T_a}{T_d} \qquad (1)$$

where FP is forced to be zero by the threshold selection method, T_d is the time of smoothed preictal data available (here, 54min 40sec), and T_a is the average anticipation time of seizures that were identified (positive if prior to the seizure onset, negative if after). For IMF level / channel pair cases in which no seizure was detected, T_a was set to be zero. In this analysis, the possible range for the anticipation optimality measure is $0.23 \leq aO \leq 2$, where higher aO values indicate better sensitivity and earlier detection anticipation.

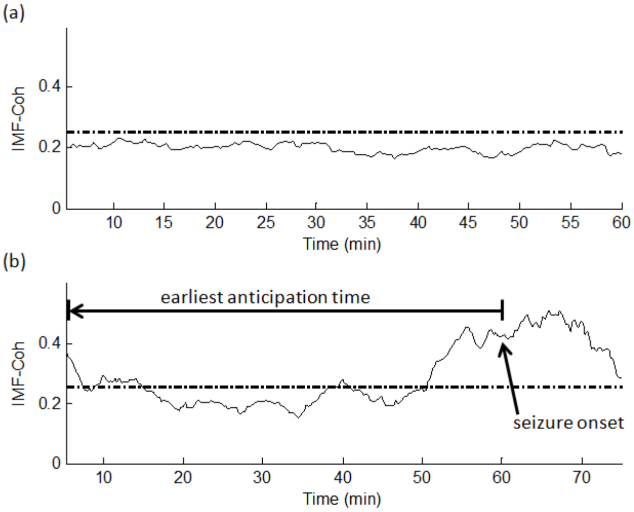

Fig. 2 IMF-Coh data for a single channel pair is shown for a subset of interictal validation data in subplot (a) and for one set of periictal test data containing a single seizure event in subplot (b). The threshold (dot-dash lines) in the validation and test data subplots illustrates zero false positives and seizure anticipation nearly an hour before onset, respectively.

III. RESULTS

Our results indicate that IMF-Coh data from some channel pairs were capable of distinguishing between interictal and periictal dynamics for patients with hippocampal epileptic foci. Fig. 3 shows weighted TP percentages for each channel pair at the first four IMF levels. The interconnectivity for different patients vary, suggesting that IMF-Coh analysis is highly subject dependent. Some channel pairs proved to be unsuccessful in anticipating any tested seizure event for some patients, while many others resulted in correct identification of most test cases. Channel pairs associated with successful seizure anticipation at one particular IMF level did not always support presupposition of success at other IMF levels, evincing that increased levels of coherence between channels result from narrow-band preictal frequency information not present in the interictal validation data. Analysis for some patients (e.g., Patient 12) showed high connectivity in all four IMF levels suggesting more broadband information present for patient-specific manifestations of seizure events. These results indicate applicability of this intrinsic mode function coherence measure should be evaluated on a patient-specific basis, though specific channel pairs may be sufficient to provide good sensitivity.

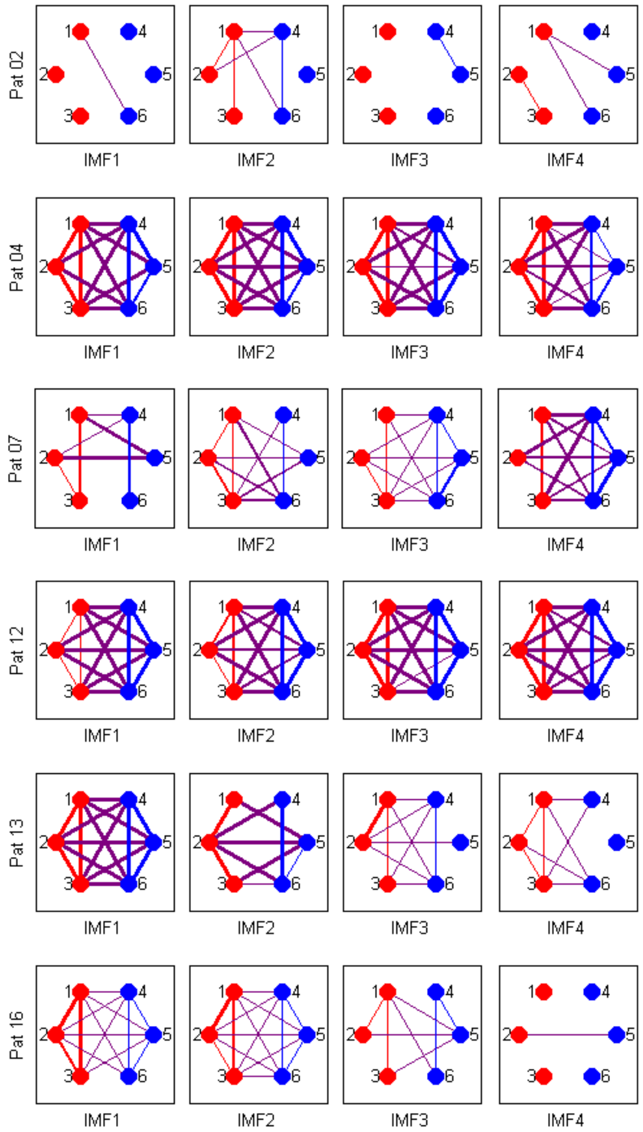

Fig. 3 Connectivity plots of channel pairs at the first four IMF levels (higher frequency) for each patient show correct detection of periictal dynamics. Channels 1-3 (red nodes) are identified as focal electrodes, while channels 4-6 (blue nodes) are extrafocal electrodes. The line width is proportional to TP. Results indicate IMF-Coh measures may be suitable for some patients, but not others, requiring evaluation of applicability on a patient-specific basis. Information regarding anticipation time is not included in the plots.

We also found long anticipation times for the majority of the correctly detected seizure events. Channel pairs showing perfect TP rates had earliest anticipation times ranging within 30 to 53 min prior to seizure onset almost exclusively. In some cases, anticipation times were shortened, but remained on the order of several minutes. The anticipation optimality index provides a unified indicator of the sensitivity and anticipation window available for IMF-Coh testing. It can be used to identify “high-impact” channel pairings, in addition to a general estimation of performance. Table I lists the averaged *aO* values for the 15 channel pairs as well as the maximum *aO* for each IMF level. In several cases, the maximum *aO* was exhibited by multiple channel pairs, also detailed in Table I.

TABLE I
AVERAGE (AND MAXIMUM) ANTICIPATION OPTIMALITY INDICES AT INTRINSIC MODE FUNCTION LEVELS

<table>
<tr><th>Patient</th><th>IMF1</th><th>IMF2</th><th>IMF3</th><th>IMF4</th></tr>
<tr><td>02</td><td>0.57±0.25
(1.48)
1|6</td><td>0.84±0.43
(1.50)
1|6</td><td>0.52±0.07
(0.78)
4|5</td><td>0.68±0.38
(1.66)
1|6</td></tr>
<tr><td>04</td><td>1.65±0.41
(2.00)
1|4, 2|4, 3|4</td><td>1.63±0.34
(2.00)
1|4, 2|4, 3|4</td><td>1.52±0.33
(1.93)
1|4, 3|4</td><td>1.42±0.51
(1.93)
1|4, 2|4</td></tr>
<tr><td>07</td><td>0.98±0.55
(1.72)
1|3</td><td>1.11±0.41
(1.67)
4|6</td><td>1.32±0.39
(1.77)
5|6</td><td>1.41±0.46
(1.99)
3|4</td></tr>
<tr><td>12</td><td>1.92±0.15
(2.00)
1|4, 1|5, 1|6, 2|4, 2|6, 3|4, 3|6, 4|5, 4|6, 5|6</td><td>1.83±0.20
(2.00)
1|4, 3|4, 3|6, 4|5, 4|6, 5|6</td><td>1.88±0.30
(2.00)
1|2, 1|6, 2|3, 2|6, 4|5</td><td>1.79±0.32
(2.00)
1|2, 2|3, 4|5</td></tr>
<tr><td>13</td><td>1.53±0.38
(1.92)
1|3, 1|4, 1|6, 2|3, 3|4, 4|6</td><td>1.11±0.53
(1.92)
2|3</td><td>1.29±0.59
(1.75)
1|3, 1|4, 1|6, 2|4, 2|6, 3|4, 3|6, 4|6</td><td>1.17±0.65
(1.75)
1|2, 1|3, 1|4, 1|6, 2|3, 2|6, 3|4, 3|6</td></tr>
<tr><td>16</td><td>1.46±0.37
(2.00)
1|2</td><td>1.55±0.11
(1.72)
1|2</td><td>0.86±0.44
(1.46)
4|5</td><td>0.54±0.17
(1.14)
2|5</td></tr>
</table>

Average values (bold) with standard deviation and maximum values (in parentheses) for *aO* across channel pairs are shown for each patient’s first four IMF levels. Values for *aO* are bounded such that $0.23 \leq aO \leq 2$. All channel pairs having the indicated maximum *aO* value are listed as CHA|CHB.

IV. DISCUSSION

Our data suggest that intrinsic mode function coherence may provide a useful measure for patient-specific seizure anticipation. In many cases, periictal dynamics were successfully identified by one or more IMF/channel pair combination(s) using the “zero-FP threshold method” outlined earlier. An anticipation optimality index is proposed as a relevant measure jointly representing sensitivity and anticipation information. This allows for a quantitative comparison in the performance of seizure anticipation between patients, IMF levels or channel pairs.

Noise-assisted EEMD was utilized in this exploratory analysis. This method was selected in order to better represent the true dynamics underlying the recorded IEEG signals. Although twelve IMF levels were produced, we chose to analyze only the first four IMFs since they contained the majority of the IEEG signal information content (at frequencies greater than ~1 Hz). This, however, does not preclude possible benefits in dynamical analysis of very low frequency components associated with higher IMF levels. EEMD can perform the same function as filtering without the introduction of phase shifts which may hinder the coherence measure. Using the signals from IMF1 to IMF4, the frequency content of interest could be targeted. The IMF coherence information within each time window can be reduced to a single mean value. Smoothing of these values allows for a meaningful comparison of trends between interictal and periictal activities. The approximate 5-min sliding average we have employed appears to adequately represent the differences in IMF-Coh features between normal and abnormal data.

We intentionally constrained the IMF-Coh thresholds to produce a zero FP rate in the validation set. The reasons for this choice are twofold. Firstly, our preliminary analysis is limited to only about one quarter of the available interictal data for each patient. Having a sufficiently high threshold would limit the number of possible FP in future analysis. Future work would include training and validation of the statistical distributions for all available interictal data for each patient in order to evaluate this consideration. Secondly, use of a zero FP rate IMF-Coh threshold can aid circumvention of potential negative effects in acute interventional therapy. It should be noted that by forcing a zero FP rate, the detection rates and anticipation times of ictal events may be reduced. We also utilized relatively coarse threshold steps in our analysis, which could result in underestimation of sensitivity. However, threshold tuning could be adapted to allow for higher sensitivity, though potentially at the expense of lower specificity. In a patient-application scenario, the thresholds could be easily adjusted to more accurately reflect the particular patient's seizure occurrence rate.

In general, the level of interconnectivity for all IMF levels may provide a rough estimate of the applicability of intrinsic mode function coherence for patient monitoring, however even poorly interconnected plots could include high-sensitivity channel pairs which may prove adequate in seizure anticipation analysis. Determination for the use of an intrinsic mode function coherence-based seizure anticipation system would best be evaluated on a patient-by-patient basis. Fig. 3 illustrates the trends in sensitivity for periictal dynamics for each patient across IMF levels. Our results are relatively consistent with the sensitivities determined in the literature [1]. Patient data showing a relatively low percentage of identified periictal activities using our method were also poor candidates for other measures, such as mean phase coherence and lag synchronization [4]. However, our results show certain channel pairs at certain IMF levels are capable of seizure anticipation despite overall connectivity, which may enhance understanding of important aspects of spatio-frequency dynamics in seizure progression.

Preferential selection of channel pair/IMF-Coh data with high *aO* may adequately generalize some patient-specific factors relating to seizure origin and progression, leading to accurate and timely interventional therapy.

A potential pitfall in this preliminary study may be associated with the selection and the amount of interictal (training and validation) data used. Our selection of the first six available hours of interictal data may result in the inclusion or exclusion of pharmacological, vigilance-state and/or immune response influences when compared to the overall set of interictal data. These influences may affect the validation IMF-Coh threshold values we have determined and thus skew the overall sensitivity.

To explore this method more thoroughly, we intend to incorporate more interictal data along with a cross-validation approach for the rest of the patient database. Other future work includes automated selection of "high-impact" channel pairs through an unsupervised method. Although the analyses proposed here are somewhat computationally expensive, we expect that a real-time application is possible through analysis of intermittent, short-time blocks of data.

V. Conclusion

This exploratory study indicates that intrinsic mode function coherence may be a useful approach in the development of a seizure anticipation method. The proposed anticipation optimality index (*aO*) appears useful for determination of periictal-relevant intrinsic mode function levels and channel pairings, and may also provide selection criteria if evaluating patient candidacy for implementations of seizure anticipation techniques.

Acknowledgment

We would like to thank the Epilepsy Center at the University of Freiburg for providing the public with an excellent resource for epilepsy research. The project described was supported by Grant Number P20RR016456 from the NIH NCRR. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NCRR or the NIH.

References

[1] F. Mormann, R. G. Andrzejak, C. E. Elger, and K. Lehnertz, "Seizure prediction: the long and winding road," *Brain,* vol. 130, pp. 314-33, Feb 2007.

[2] M. Le Van Quyen, J. Soss, V. Navarro, R. Robertson, M. Chavez, *et al.*, "Preictal state identification by synchronization changes in long-term intracranial EEG recordings," *Clinical Neurophysiology,* vol. 116, pp. 559-568, 2005.

[3] P. Mirowski, D. Madhavan, Y. LeCun, and R. Kuzniecky, "Classification of patterns of EEG synchronization for seizure prediction," *Clinical Neurophysiology,* vol. 120, pp. 1927-1940, 2009.

[4] M. Winterhalder, B. Schelter, T. Maiwald, A. Brandt, A. Schad, *et al.*, "Spatio-temporal patient-individual assessment of synchronization changes for epileptic seizure prediction," *Clin Neurophysiol,* vol. 117, pp. 2399-413, Nov 2006.

[5] Z. Wu and N. E. Huang, "Ensemble empirical mode decomposition: a noise assisted data analysis method," *Advances in Adaptive Data Analysis,* vol. 1, pp. 1-41, 2009.

[6] T. Netoff, P. Yun, and K. Parhi, "Seizure prediction using cost-sensitive support vector machine," in *Engineering in Medicine and Biology Society, 2009. EMBC 2009. Annual International Conference of the IEEE*, 2009, pp. 3322-3325.

[7] S. S. Talathi, D.-U. Hwang, M. L. Spano, J. Simonotto, M. D. Furman, *et al.*, "Non-parametric early seizure detection in an animal model of temporal lobe epilepsy," *Journal of Neural Engineering,* vol. 5, p. 85, 2008.