35th Annual International Conference of the IEEE EMBS
Osaka, Japan, 3 - 7 July, 2013

Seizure Prediction Using Adaptive Neuro-Fuzzy Inference System

Ahmed F. Rabbi, *Student Member*, *IEEE*, Leila Azinfar, *Student Member*, *IEEE*, and Reza Fazel-Rezai, *Senior Member, IEEE*

***Abstract*— In this study, we present a neuro-fuzzy approach of seizure prediction from invasive Electroencephalogram (EEG) by applying adaptive neuro-fuzzy inference system (ANFIS). Three nonlinear seizure predictive features were extracted from a patient's data obtained from the European Epilepsy Database, one of the most comprehensive EEG database for epilepsy research. A total of 36 hours of recordings including 7 seizures was used for analysis. The nonlinear features used in this study were similarity index, phase synchronization, and nonlinear interdependence. We designed an ANFIS classifier constructed based on these features as input. Fuzzy if-then rules were generated by the ANFIS classifier using the complex relationship of feature space provided during training. The membership function optimization was conducted based on a hybrid learning algorithm. The proposed method achieved highest sensitivity of 80% with false prediction rate as low as 0.46 per hour.**

I. Introduction

Epilepsy is one of the most common neurological disorders that affect 1-3% of the world's population. In the United States, almost 200,000 new cases of Epilepsy are diagnosed every year [1]. The estimated clinical cost related to epilepsy and seizure is approximately $17.6 billion [1]. Hence, a desirable solution is to prevent the side effects of seizure attacks by predicting the attack time few minutes to several hours earlier before a seizure event happens. A warning device equipped with a highly efficient and reliable prediction algorithm would significantly improve the life of an epilepsy patient as well as lower the economical effect of prevalence of epilepsy.

Growing number of literature demonstrate the possibility of seizure prediction with varying degrees of limited success. The large number of algorithms found in literature can be classified into several broad categories. First of all, most of the methods developed are based on applying a threshold procedure to a seizure prediction method, such as phase synchronization [2]. Another group of study applied clustering based techniques [3]. In machine learning based approaches, artificial neural network (ANN), support vector machine (SVM) classifiers were used with multiple features [4], [5]. These algorithms make use of multiple characteristic features extracted from EEG recordings. However, they are supervised in nature and require training from pre-ictal and ictal datasets. In another approach, combining epileptic seizure prediction methods using Boolean "AND"/"OR" logic was proposed and the superiority of this method over a single method was shown [6]. Recently, a patient specific rule-based approach on spatial and temporal combination was proposed [7]. A fuzzy rule-based system was proposed for epileptic seizure detection from intracranial EEG for taking advantage of the combination in the feature domain as well as in the spatial domain [8]. In a previous study, we applied adaptive rule-based fuzzy inference systems in seizure onset detection from intracranial EEG [9]. Fuzzy membership parameters were optimized using fuzzy c-means clustering and fuzzy if-then rules were developed based on human knowledge reasoning for temporal-spatial combination of the features and the channels [9].

The approach of combining multiple methods might open up new possibilities in prediction research. Application of fuzzy logic based approaches can be very useful as Boolean logic can combine only two methods. Although it is not proven clearly that linear feature extraction methods are better than nonlinear dynamical systems based methods [9], the prediction studies are biased in utilizing the exciting computational aspects of nonlinear dynamical systems based methods in quantifying the subtle and rather smooth changes in brain dynamics toward seizures [6]-[14]. In a previous study, we developed a fuzzy rule-based soft threshold method applied to correlation dimension features extracted from intracranial EEG [15].

This paper introduces the application of adaptive neuro-fuzzy inference system (ANFIS) in epileptic seizure prediction. The approach combines multiple epileptic seizure predictive features, both nonlinear univariate and bivariate. We applied an ANFIS network to combine the feature patterns in identifying the pre-ictal state [16], [17]. ANFIS efficiently performs the nonlinear input output mapping by taking account the complex relationships of the feature space [16], [17]. The advantage over other classification techniques, such as ANN, is that it provides the output as a linear regression time series rather than integer values representing classes. This aspect of ANFIS is advantageous, as it allows the performance analysis within the framework

Manuscript received February 1, 2013. This work was supported in part by the North Dakota Space Grant Consortium and ND EPSCoR under Grant #EPS-0814442.

A. F. Rabbi is with the Biomedical Signal and Image Processing Laboratory, Electrical Engineering Department, The University of North Dakota, Grand Forks, ND 58202 USA (e-mail: ahmed.rabbi@my.und.edu).

L. Azinfar, is with the Biomedical Signal and Image Processing Laboratory, Electrical Engineering Department, The University of North Dakota, Grand Forks, ND 58202 USA (e-mail:leila.azinfar@my.und.edu).

R. Fazel-Rezai is with team Biomedical Research And INovation (BRAIN) and the Director of Biomedical Signal and Image Processing Laboratory, Electrical Engineering Department, University of North Dakota, Grand Forks, ND 58203 USA (e-mail: reza@engr.und.edu . phone: 701-777-3368, fax: 701-777-5253).

of seizure prediction characteristics [18]. Moreover, ANFIS is capable of accommodating human knowledge and reasoning as well as machine learning capabilities [16], [17].

II. Methods and Materials

A. EEG Datasets

The EEG datasets used in this study were obtained from the recently available one of the most comprehensive Epilepsy EEG databases, the European Epilepsy Database [19]. The database provides long-term EEG recordings (both surface and invasive recordings) [19]. EEG datasets were selected from one of the patient's (Patient id # FR_253) data for feature extraction which included long-term recordings with 7 seizures. All the 7 seizures available for this patient's EEG recordings were analyzed. A total 36 hours of EEG recordings having 7 seizures were used for feature extraction. The data sets were divided into three sets for training and testing purpose as described in sub-section *D*. Since identification of the pre-ictal state in the intracranial recording was the goal, at least three hours of recordings prior to a seizure event were taken for each analyzed seizure.

B. Preprocessing

EEG recordings were analyzed using a sliding window analysis technique [2]. The length of each window was 10 sec with 5 sec overlap between the adjacent windows. To reduce the high frequency noise and low frequency artifacts, a fourth order digital Butterworth IIR bandpass filter was applied to all the EEG segments in all channels. The cutoff frequencies were set at 0.5 Hz – 100 Hz. In addition, to remove the effect of power line noise, a second order notch filter at 60 Hz cutoff frequency was applied. For both the filters zero phase digital filtering was used.

C. Feature Extraction

One univariate and two bivariate seizure predictive features were extracted from two channels located in the epileptic region.

1) Univariate Nonlinear Features: Dynamical Similarity Index (DSI) quantifies the changes in dynamics of a test window relative to a constant reference window [10]. It was described by Le Van Quyen *et al.* in 1999 and applied to EEG signals in identifying preictal state from interictal baseline [11]. This feature had also been applied in pre-ictal state identification in rat EEG [13].

2) Bivariate Nonlinear Features: Bivariate features are known to be more sensitive in detecting pre-ictal changes [10]. Two bivariate features, nonlinear interdependence, and mean phase coherence were extracted from two channels located in the epileptic region [12], [20]. The nonlinear interdependence is considered as a measure of generalized synchronization between two EEG signals from different channels whereas mean phase coherence is known as measure of phase synchrony. Generalized synchronization occurs when the dynamical state of one of the coupled oscillators is determined by the other oscillator. On the other hand, phase synchronization measures the phase difference between two coupled chaotic oscillators. Mormann *et al.* reported significant decrease in mean phase coherence prior to a seizure event [12].

D. Preparation of Data for ANFIS training and testing

A total of 35 hours of invasive EEG data having 7 seizures were used for evaluation of the algorithm from recordings for one patient (patient id # FR_253) [19]. Data were divided into two portions for two-fold validation purpose. The training and checking dataset each contained 1 seizure with interictal and preictal recordings. The length of the training and checking dataset was 4.74 and 5 hours respectively. The ANFIS model was tested on the rest of the dataset which contained 5 seizures with total length of 26.12 hours.

E. Application of ANFIS

ANFIS is a Sugeno type fuzzy inference system with added neural-network learning capabilities proposed by Roger Jang in 1993 [16]. The antecedent or the premise part is linguistic in nature. Thus, the premise part performs qualitative fuzzy reasoning. The consequent parameter is a liner function of the input variables. Fuzzy if-then rules performs the logic "AND" operations on the inputs provided. The fuzzy if-then rules are defined as follows:

$$If\ (F_1\ is\ A_i)\ and\ (F_2\ is\ B_i)\ and\ (F_3\ is\ C_i)\ and\ (F_4\ is\ D_i)$$
$$then\ (f_i = p_iF_1 + q_iF_2 + r_iF_3 + s_iF_4 + t_i) \tag{1}$$

where F_i $(i = 1, 2, \dots, 4)$ is the input, A_i, B_i, C_i, and D_i are the fuzzy sets, and p_i, q_i, r_i, s_i, and t_i are the linear design parameters. The linear parameters are adaptable. A simplified ANFIS architecture with four inputs and one output is shown in Fig. 1.

For simplicity, all the nodes in layer 2, layer 3, and layer 4 were not shown. The square nodes are adaptive whereas circular nodes are fixed [16]. Fuzzifications of the input variables are performed in the first layer and all the nodes of the first layer are adaptive nodes. Fuzzy input membership function parameters and the design parameters were optimized using a hybrid learning algorithm as described by Roger Jang [16].

The outputs of the first layer are the fuzzy membership grades of the inputs. The membership grade parameters are used to adaptively estimate the membership grades during training to better map the input/output relationships. The second layer nodes perform the product operation (logic operation "AND") to calculate the firing strength of each rule. The third layer performs the data normalization. The fourth layer performs the following operation.

$$O_i^4 = \bar{w}_i\,(p_iF_1 + q_iF_2 + r_iF_3 + s_iF_4 + t_i) \tag{2}$$

where $\overline{w_i}$ is the output of the previous layer, F_i $(i = 1, 2, \dots, 4)$ is the input, and $\{p_i, q_i, r_i, s_i, t_i\}$ is the first order polynomial parameter set [16], [17].

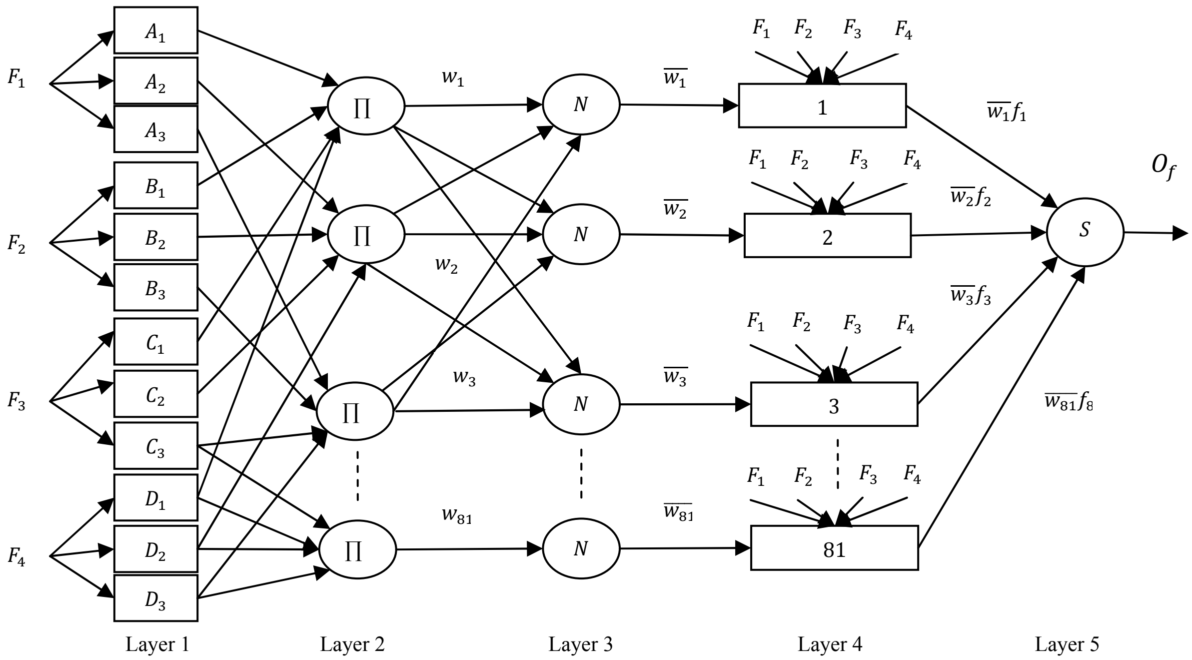

Fig. 1. The ANFIS architecture for four inputs with three membership functions and one output. For simplicity, not all the nodes of the middle layers (layer 2, layer 3, and layer 4) were shown. There would be a total 27 nodes in the middle layers.

The polynomial parameters represent the first order Sugeno type fuzzy model. The final layer consists of a single node, S which is responsible for performing the summation of all the incoming signals coming from previous layer. This fuzzy output variable which is a mapped output of all the input features was used for issuing the seizure prediction alarm. The algorithm was simulated in MATLAB® 7.8.

III. Results and Discussion

A threshold procedure was applied to the final fuzzy output variable to convert it to an alarm space. Since it is better to predict a seizure then to miss it, the threshold parameter was optimized for better sensitivity and lower false positive rates. In post-processing step, short length predictions were minimized by setting up a criterion. The short length predictions might be due to the inherent noise or artifacts in the EEG recordings. The primary alarm time series is processed in a minute-by-minute basis. A criterion was set that no prediction results smaller than 35 seconds will be considered as true predictions. This value was found empirically to obtain the best results. In addition, when an alarm was issued no further alarms were produced for the duration of the specified seizure prediction horizon (SPH). The SPH duration were varied from 15 to 45 minutes with 15 minutes step size. If an alarm is followed by a seizure event the alarm is considered as true positive. Otherwise, the alarm was considered as false positive.

The temporal patterns of the features for the training and testing datasets are shown in Fig. 2 and Fig 3 respectively. The checking dataset was used as a safeguard against over fitting of the model during the training. Finally, the algorithm was tested on out-of-sample testing data set.

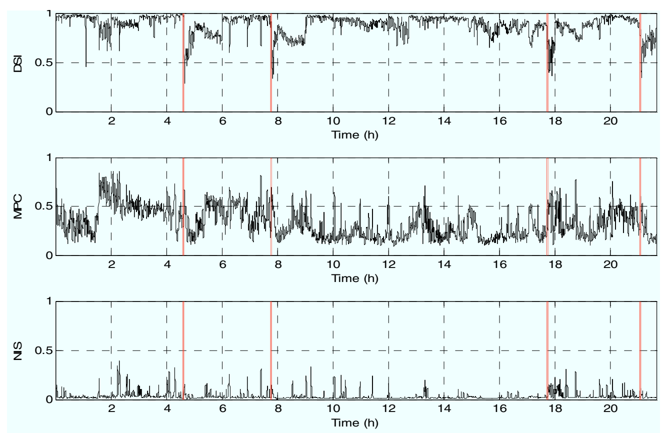

Fig. 2. The temporal profile of three features, dynamical similarity index (DSI), mean phase coherence (MPC), and nonlinear interdependence, S (NIS) extracted from 22 hours of test data. The start and stop time of the seizures are marked by red vertical lines.

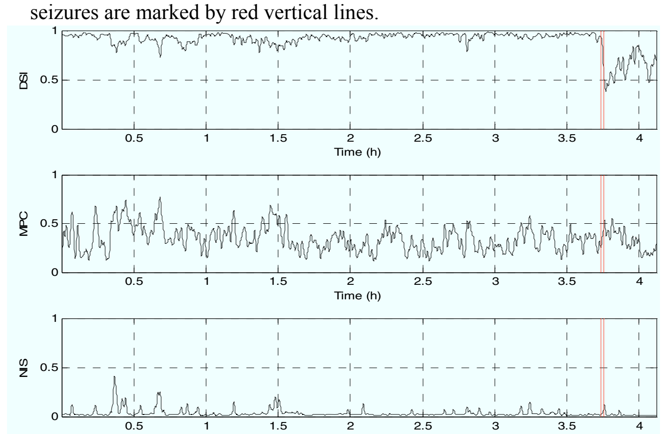

Fig. 3. The temporal profile of the three features extracted from 4.12 hours of continuous recording which constituted testing dataset. The start and stop time of seizure are marked by red vertical lines.

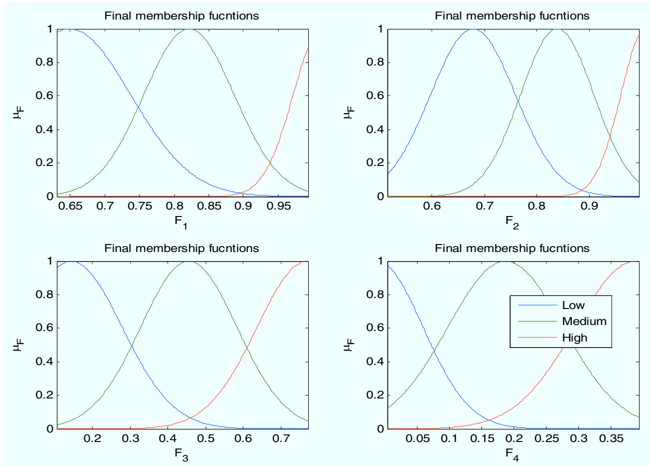

Fig. 4. Final input membership functions after hybrid training. Three levels were considered for fuzzifications of the input feature variables, low, medium, and high.

The input membership functions after training are shown in Fig. 4. We analyzed results for three different values of seizure prediction horizon (SPH) and the results are presented in the following Table 1.

TABLE I
SENSITIVITY AND FALSE PREDICTION RATE PER HOUR WITH VARYING LENGTH OF SEIZURE PREDICTION HORIZON

SPH (min)	Sensitivity (%)	FPR/h
15	20	1.15
30	40	0.73
45	80	0.46

IV. CONCLUSION AND FUTURE WORK

The preliminary results demonstrate the applicability of the ANFIS in seizure prediction. To significantly advance the area of seizure prediction, several important aspects of this problem should be considered. The evaluation of a seizure prediction algorithm requires to be performed in long-term out of sample recordings. In this paper, we have tested our algorithm on data different from the training data set. The algorithm was trained on a different data set than the testing data. The threshold parameter was determined statistically by fitting a normal distribution to a reference window selected from the fuzzy output variable. This threshold parameter is tunable for performance optimization.

Combination of multiple features could open up new window of possibilities in prediction research [6]. ANFIS model or similar neuro-fuzzy approach can be very useful in achieving such goals as these approaches are capable of providing a way to take advantage of both the human knowledge reasoning and machine learning capabilities.

In future, we will apply similar methods with better post-processing to the rest of the 29 patients' data available in the European Epilepsy Database. This would allow studying the inter-patient variability and analyzing the performance of the adaptive capabilities of the algorithm. Finally, we will attempt to analyze the performance of the algorithm against a random predictor and within the frame work of the seizure prediction characteristics [18].

ACKNOWLEDGMENT

Authors would like to thank Dr. Matthias Ihle at the University Hospital of Freiburg for his support with the Epilepsy database.

REFERENCES

[1] http://www.epilepsyfoundation.org/aboutepilepsy/whatisepilepsy/statistics.cfm.

[2] F. Mormann, T. Kreuz, C. Rieke, R. G. Andrzejak, A. Kraskov, P. David, C. E. Elger and K. Lehnertz, "On the predictability of epileptic seizures," *Clinical Neurophysiology*, vol. 116, no. 3, pp. 569-587, 2005.

[3] A. B. Geva and D. H. Kerem, "Forecasting generalized epileptic seizures from the EEG signal by wavelet analysis and dynamic unsupervised fuzzy clustering," *IEEE Trans. Biomedical Engineering*, vol. 45, no. 10, pp. 1205-1216, 1998.

[4] P. Mirowski, D. Madhavan, Y. LeCun and R. Kuzniecky, "Classification of patterns of EEG synchronization for seizure prediction," *Clinical Neurophysiology*, vol. 120, no. 11, pp. 1927-1940, 2009.

[5] Y. Park, L. Luo, K. K. Parhi and T. Netoff, "Seizure prediction with spectral power of EEG using cost-sensitive support vector machines," *Epilepsia*, vol. 52, no. 10, pp. 1761-1770, 2011.

[6] H. Feldwisch-Drentrup, B. Schelter, M. Jachan, J. Nawrath, J. Timmer and A. Schulze-Bonhage, "Joining the benefits: Combining epileptic seizure prediction methods," *Epilepsia*, vol. 51, no. 8, pp. 1598-1606, 2010.

[7] A. Aarabi and B. He, "Seizure prediction in intracranial EEG: A patient-specific rule-based approach," *Conf. Proc. IEEE Eng. Med. Biol. Soc.*, pp. 2566-2569, Boston, 2011.

[8] A. Aarabi, R. Fazel-Rezai, Y. Aghakhani, "A fuzzy rule-based system for epileptic seizure detection in intracranial EEG," *Clinical Neurophysiology*, vol. 120, pp. 1648-1657, 2009.

[9] A. F. Rabbi and R. Fazel-Rezai, "A fuzzy logic system for seizure onset detection in intracranial EEG. Computational Intelligence and Neuroscience, vol. 2012, 2012. doi:10.1155/2012/705140.

[10] F. Mormann, R. G. Andrzejak, C. E. Elger and K. Lehnertz, "Seizure prediction: The long and winding road," *Brain*, vol. 130, no.2, pp. 314-333. 2007.

[11] M. L. Van Quyen, J. Martinerie, M. Baulac and F. Varela, "Anticipating epileptic seizures in real time by a non-linear analysis of similarity between EEG recordings," *Neuroreport*, vol. 10, no. 10, pp. 2149-2155, 1999.

[12] F. Mormann, K. Lehnertz, P. David and C. E Elger, "Mean phase coherence as a measure for phase synchronization and its application to the EEG of epilepsy patients," *Physica D*, vol. 144, no. 3-4, pp. 358-369. 2000.

[13] X. Li and X. Yao, "Application of fuzzy similarity to prediction of epileptic seizures using EEG signals," *Fuzzy Systems and Knowledge Discovery*, pp. 481-481, 2005.

[14] X. Li and G. Ouyang, "Nonlinear similarity analysis for epileptic seizures prediction," *Nonlinear Analysis*, vol. 64, no. 8, pp. 1666-1678, 2006.

[15] A. F. Rabbi, A. Aarabi and R. Fazel-Rezai, "Fuzzy rule-based seizure prediction based on correlation dimension changes in intracranial EEG," *Conf. Proc. IEEE Eng. Med. Biol. Soc.*, vol. 1, pp. 3301-3304, 2010.

[16] J. S. R. Jang, "ANFIS: Adaptive-network-based fuzzy inference system," *IEEE Trans. on Systems, Man and Cybernetics*, vol. 23, no. 3, pp. 665-685, 1993.

[17] L. H. Tsoukalas and R. E. Uhrig, *Fuzzy and Neural Approaches in Engineering*, 1996.

[18] T. Maiwald, M. Winterhalder, R. Aschenbrenner-Scheibe, H. U. Voss, A. Schulze-Bonhage and J. Timmer, "Comparison of three nonlinear seizure prediction methods by means of the seizure prediction characteristic," *Physica D*, vol. 194, no. 3, pp. 357-368, 2004.

[19] http://www.epilepsy-database.eu.

[20] J. Arnhold, P. Grassberger, K. Lehnertz and C. Elger, "A robust method for detecting interdependences: Application to intracranially recorded EEG," *Physica D*, vol. 134, no. 4, pp. 419-430, 1999.