Multilayer perceptron reveals functional connectivity structrure in thalamo-cortical brain network

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***Abstract*— Artificial neural networks (ANNs) are known to be a powerful tool for big data analysis. They are widely used in computer science, nonlinear dynamics, robotics, and neuroscience for solving tasks of classification, forecasting, pattern recognition, etc. In neuroscience ANNs allow recognizing specific forms of brain activity from multichannel electro- (EEG) or magnetoencephalographic (MEG) data and, therefore, widely used as a computational core in various brain-computer interfaces. Another challenging problem is the analysis of connectivity structures in big multivariate data. In neuroscience restoring the functional brain network using multichannel EEG/MEG signals uncovers mechanisms of neuronal interaction during various physiological or cognitive processes. In this report we use recent advances in the area of machine learning known as feed-forward artificial neuronal network to formulate a method for detecting functional dependence in unidirectionally and bidirectionally coupled systems without additional information about them. We apply our method for the first time to reveal functional connectivity structure in the thalamo-cortical network of epileptic brain based on a rodent electrocorticography (ECoG) data set.**

Keywords—functional connectivity, synchronization, artificial neural network, EEG, brain

I. INTRODUCTION (*HEADING 1*)

Brain, being one of the most complex systems in nature, exhibits well-pronounced network properties on both anatomical and functional levels [1]. The latter implies the existence of functional dependence between the states of remote brain areas, which is believed to provide mechanisms for neuronal. communication and information transfer within a distributed brain network. According to the recent theories [2-4], neural interaction between distant brain regions through emergent functional connectivity structures determines normal brain functioning, including cognitive, motor-related activity etc.

At the same time, abnormalities in functional brain networks stand behind various types of brain disorders like epilepsy, Parkinson's and Alzheimer's diseases, brain tumors etc. [5,6].

Thus, restoration of functional connectivity between brain areas is a crucial approach for brain functioning diagnostics in modern neuroscience [7].

In nonlinear dynamics, the presence of a functional relation between the dynamics of coupled chaotic systems is known as a particular type of synchronous behavior called generalized synchronization (GS) [8]. This relation may be very complicated, and its explicit form cannot be found in most cases. The definition of the GS regime in the case of unidirectional coupling accepted hitherto is the presence of a functional relation

$$\mathbf{y}(t) = \mathbf{F}[\mathbf{x}(t)] \qquad (1)$$

between the drive x(t) and response y(t) oscillator states. This definition has been generalized on mutual coupling systems as:

$$\mathbf{F}[\mathbf{x}(t), \mathbf{y}(t)] = 0 \qquad (2)$$

The concept of generalized synchronization may be essentially applied in neuroscience for data-driven functional connectivity restoration based on multichannel EEG/MEG data. However, it has not been systematically used in this context so far. In this context, machine learning, which has already become a useful tool in nonlinear dynamics and neuroscience [9-14], to infer functional links in terms of GS. In this study, we use our feed-forward artificial neural network (FANN) to analyze functional connectivity in small thalamo-cortical network during the onset of epileptic seizure in WAG/Rij rats with genetic predisposition to absence epilepsy. Such seizures manifest as a hyper synchronization of brain activity in thalamo-cortical network, thus they are extremely suitable for demonstration of FANN approach applied for experimental data. We show the emergence of functional interdependence between cortical layers and thalamic nuclei after epileptic discharge onset.

II. METHOD

ANN is known to be a biologically inspired computational system, whose main purpose is to fit unknown and usually complex relationship between input and output data32. Since functional connectivity in coupled systems implies the existence of functional dependence between them, ANN seems to be an essential tool in this context.

Considering two coupled processes, whose dynamics is represented by multivariate signals $\mathbf{x}(t)$ and $\mathbf{y}(t)$, functional connectivity implies $\mathbf{y}(t) = \mathbf{F}[\mathbf{x}(t)]$. Since from a mathematical point of view ANN defines a function $f\colon \mathbf{x} \rightarrow \mathbf{y}$, one may use ANN to build a model of the unknown relation $\mathbf{F}[\bullet]$ and predict the **y** state based on the **x** state. Thus, if a true functional relation $\mathbf{y}(t) = \mathbf{F}[\mathbf{x}(t)]$ exists, ANN is able to approximate it and give a precise prediction $\mathbf{y}'(t)$ of the $\mathbf{y}(t)$ state based on $\mathbf{x}(t)$. On the contrary, if functional dependence is not established, ANN fails to learn it and therefore is not able to predict the **y**-state accurately enough. Summarizing the above, the criterion for functional connectivity inference is equality of predicted and actual values of y processes: $\mathbf{y}'(t) = \mathbf{y}(t)$.

We use the traditional FFANN architecture – multilayer perceptron – to build an ANN-model of functional dependence **F**[•] between interacting systems. MLP consists of 2 hidden layers, each containing 10 softmax units. The number of both inputs and outputs is determined by the embedding dimensions of coupled systems. Output artificial neurons have a linear activation function. To build a proper ANN-model of relationship between **x** and **y** we normalize the data in range [0;1], shuffle it and keep 50% of the dataset to train ANN and the other 50% to validate prediction accuracy. To train the network we use a popular and efficient Adam optimizer with learning rate 0.001 implemented in Keras API33. To quantify the degree of functional dependence establishment we use a metric called R^2-score (coefficient of determination).

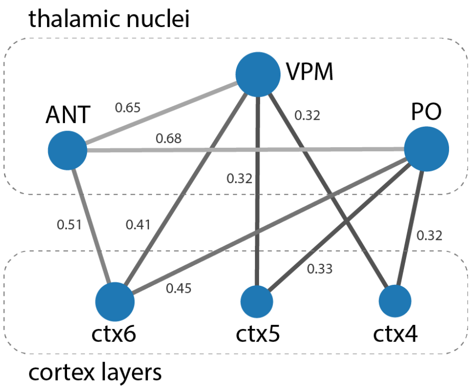

Fig. 1. For all presented plots, t is time, sec, with audio command placed in 0 and marked with red line. (a) Raw EEG signal corresponding to the movement; (b) wavelet surface of corresponding EEG signal; (c) averaged mu-rhythm energy W_μ; (d) recurrence plot of considering time series; (e) matched EMG signal; (f) RQA metrics.

III. Results

We analyzed a multichannel set of ECoG recordings taken from Wistar Albino Glaxo from Rijswijk (WAG/Rij) rats – a genetic animal model giving rise to spontaneous absence seizures [15]. In the experiments 6-month-old WAG/Rij rats were chronically implanted with stainless steel electrodes in layer 4 to 6 of the somatosensory cortex (ctx4–6), as well as in the (i) posterior (PO), (ii) ventral-postero-medial (VPM), and (iii) anterior thalamic nucleus (ANT), respectively. Two weeks after surgery, ECoG signals were recorded from these structures in freely moving animals. Signals were filtered by a band pass filter with cut-off points at 1(HP) and 100(LP) and a 50 Hz Notch filter and digitized by WINDAQ-recordingsystem (DATAQ-Instruments Inc., Akron, OH, USA) with a constant sampling rate of 2048 Hz. Experiments were carried out in accordance with the Ethical Committee on Animal Experimentation of University of Münster.

Based on the considered approach for functional connectivity diagnostics in experimental time series identified on a pair of ECoG channels, we have reconstructed the structure of functional links in the thalamo-cortical network during background (3 s prior SWD onset) and pathological (1 s after SWD onset) activity. To reveal the functional network, we considered changes in $R2$-score in pathological activity with respect to background via t-test for related samples with Bonferroni correction (critical α-level = 0.003). One can see that the pathological activity shown in Fig. 1 is accompanied primarily by the appearance of functional links between between the thalamic nuclei and cortical layers (ctx4-PO, ctx4-VPM, ctx5-PO, ctx5-VPM, ctx6-PO, ctx6-VPM, ctx6-ANT). Notable, intra-thalamic functional connectivity intensifies as well (ANT-PO, ANT-VPM).

IV. Conclusion

In conclusion, we have proposed a machine learning based method for detecting functional connectivity in unidirectionally and mutually coupled systems without additional information about analyzed systems.

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