Detecting inter-areal functional connectivity using artificial neural network

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***Abstract*—In present paper we introduce an extended machine-learning-based approach to detect inter-areal functional connectivity based on artificial neural network (ANN). We prove the efficiency of the proposed method by applying multilayer perceptron to find functional relations between the cortex and thalamus of the pathological WAG/Rij rats during the epileptic seizure based on the multivariate electrocorticography (ECoG) recordings. We show that the proposed algorithm is able to reconstruct the increased coupling within a thalamo-cortical network during the seizure versus a baseline activity.**

Keywords—machine learning, artificial neural networks, multilayer perceptron, functional connectivity, absence epilepsy, generalized synchronization

I. Introduction

Functional connectivity is a concept developed to analyze integrative brain activity through evaluation of the neural synchronization between remote brain areas [1,2]. Recent studies show that the brain activity, normal as well as abnormal, is associated with an interaction between remote brain areas [3-10]. Therefore, studies of the functional connectivity patterns are of great demand to understand the way in which the different brain areas are integrated to process healthy and pathological states.

To predict the functional dependencies in the brain neural network, we propose a method that uses a well-known phenomenon called generalized synchronization (GS) [11-13]. GS refers to the presence of a functional relation between the drive and response states and implies that the response state can be predicted by the drive state [14,15]. Recently, we have developed a method to evaluate sensor-to-sensor functional connectivity using a feed-forward neural network [16] which is often used for processing neuroscience data for classification [17-19]. Here, we extend this approach to reveal functional connectivity between the brain areas, each represented by a set of sensors. We use this concept to define the interaction between the states of somatosensory cortex and anterior thalamic nucleus before and during the absence epilepsy seizure in WAG/Rij rats [20]. To approximate the synchronous behavior in these two brain areas, we apply a machine learning based model to the ECoG dataset separated on short time series, threating the target activity as the response state and the input activity as the drive state. In particular, we focus on the multilayer perceptron (MLP), which is a most widely used model highly relevant in classification, prediction, approximation and recognition tasks [21-23]. The sufficient ability of MLP to map nonlinear data makes it a proper choice to detect the functional relations.

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II. Materials and Methods

A. Experimental data and preprocessing

In present paper we focus on the evolution of the functional connectivity during the onset of spike-wave discharges (SWD) evaluated from ECoG data. The original dataset consisted of the ECoG recordings taken from WAG/Rij strain of rats implanted with stainless steel electrodes in 3 layers of somatosensory cortex (ctx4, ctx5, ctx6), posterior, ventral-postero-medial and anterior thalamic nucleus (PO, VPM, ANT). The data were recorded with the WINDAQ-recording-system and sampled at 2048 Hz. We also applied the band-pass filter in the range from 4 to 100 Hz, as well as with the 50 Hz Notch filter to avoid the power line noise. Each considered trial contained 6 seconds of normal background activity followed by 5 seconds of SWD (see Fig. 1A).

B. Multilayer perceptron

MLP is an efficient computational model that requires relatively low computational costs to reveal the complex relationships in nonlinear data. In present study, we use MLP to approximate the functional dependence between two multivariate sets: cortical activity recordings ctx = {ctx4,ctx5,ctx6} (training dataset) and thalamic recordings thl = {PO, VPM, ANT} (target dataset). To reduce the dimensionality we applied Principal Component Analysis (PCA) to both training and target data. Afterwards, we extracted n_1 and n_2 independent components using Independent Component Analysis (ICA) from training and target sets, respectively, where n_1 and n_2 are the number of independent components in the trading and target sets identified by the PCA. If the number of independent components was identified as 1, then this component was embedded. Considered ANN model had one hidden layer with 10 softmax neurons and the output layer with linear activation function. The number of neurons in both input and output layers was defined by the embedding dimension $D = 5$ of the original time series determined by the false nearest neighbor method [24]. The delay time $\tau = 5$ time points was calculated using the mutual information method [25].

C. The MLP training process

The training process was performed with the Adam optimizer (*learning rate* = 0.001). The MLP algorithm was implemented with the Keras library with Tensorflow backend developed in Python 3.4 [26].

We considered the training and the target datasets x=ctx and y=thl in the 1 sec floating window with 0.5 sec step (see Fig. 1B). Since both x and y are multivariate datasets, we apply the independent component analysis to select the most informative components before proceeding with the MLP training. Then, we consider the phase space trajectory of the current 1-sec time series restored according to the Takens embedding theorem [27] with $D = 5$ and $\tau = 5$ as the embedding

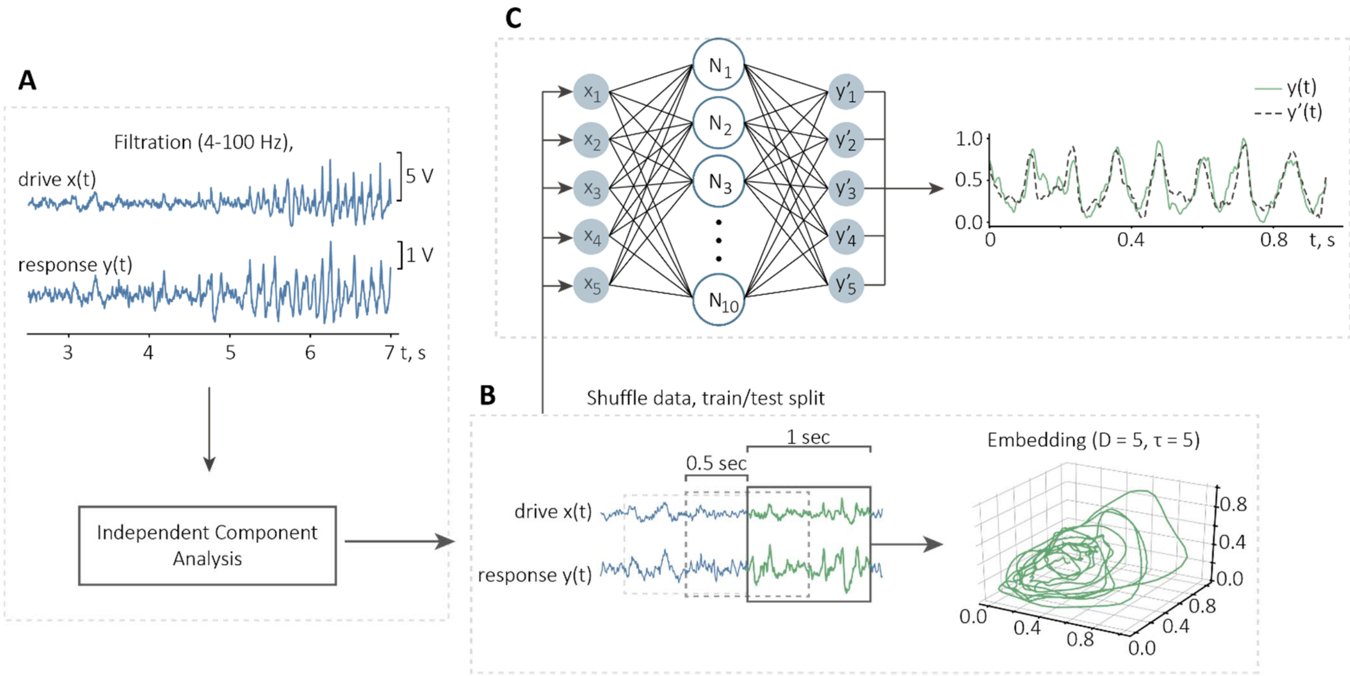

Fig. 1. A. Example of filtered multivariate time series collected from ctx6 (drive *x(t)*) and ANT (response *y(t)*) sensors; B. The training paradigm. The functional dependence between drive and response states was calculated in 1-sec window with 0.5-sec step. Each data segment was embedded, shuffled and splitted on training and validation sets. C. Left panel: MLP model for calculation the prediction state *y'(t)*; right panel: an example of predicted state *y'(t)* and original target state *y(t)*.

dimension and lag, respectively. Obtained datasets were randomly shuffled and equally separated into training and validation sets. Finally, the training sets were fed to the developed MLP model which was trained during the 100 epochs. The result of the MLP was a dataset y', which was a prediction of the target dataset *thl* by the input dataset *ctx* (see Fig1C).

D. Functional dependence estimation

According to the proposed approach, the presence of functional dependence between the states of the two brain areas is defined by the quality of prediction of the response state by the drive state via ANN [28]. In terms of GS framework, we consider the recordings taken from the *ctx* sensors as the drive system $x = \{x(t_1), x(t_2), \dots x(t_N)\}$ and from the *thl* sensors as the response system y= $\{y(t_1), y(t_2), \dots y(t_N)\}$, where N is the length of the trial.

To evaluate the correlation between the original response data *y* and the prediction obtained via MLP, we used the R^2-score measure:

$$R^2 = 1 - \frac{\sum_{d=1}^{D} 1 \sum_{i=1}^{N} \left(y_d(t_i) - y'_d(t_i)\right)^2}{\sum_{d=1}^{D} 1 \sum_{i=1}^{N} \left(y_d(t_i) - \bar{y}_d\right)^2},$$

with D as a number of embedding dimensions,$y'_d(t_i)$, $y_d(t)$, and $\bar{y}_d$ are *d*-th component of predicted and original time series and the mean value of the latter, respectively. The value of R^2-score lies in the range of [0,1] and defines the extent of strength of the relationships between two variables. Therefore, in the course of the study we use it to determine the couple strength of the functional connectivity link between the two considered areas in different states.

III. Results

Proposed method allowed to map the state of the response system based on the state of the drive system, which in our case are the SWD-signals collected from *ctx* and *thl* sensors of the epileptic rats' brain. Fig. 1C shows an example of the mapping $y'(t)$versus the original response time series $y(t)$ corresponding to the absence seizure. The R^2-score for this trial was 0.79 confirming the established functional dependence.

IV. Conclusion

In present paper we extended the ANN-based method to detect inter-areal functional connectivity from the ECoG dataset of WAG/Rij rats with predisposition to the absence seizures. Our method employed the concept of generalized synchronization to successfully detect the degree of functional dependence between the cortical layers and thalamic nuclei during the seizure onset.

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