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A model-based method for computation of correlation dimension, Lyapunov exponents and synchronization from depth-EEG signals

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ABSTRACT

In order to predict epileptic seizures many precursory features, extracted from the EEG signals, have been introduced. Before checking out the performance of features in detection of pre-seizure state, it is required to see whether these features are accurately extracted. Evaluation of feature estimation methods has been less considered, mainly due to the lack of a ground truth for the real EEG signals' features. In this paper, some simulated long-term depth-EEG signals, with known state spaces, are generated *via* a realistic neural mass model with physiological parameters. Thanks to the known ground truth of these synthetic signals, they are suitable for evaluating different algorithms used to extract the features. It is shown that conventional methods of estimating correlation dimension, the largest Lyapunov exponent, and phase coherence have non-negligible errors. Then, a parameter identification-based method is introduced for estimating the features, which leads to better estimation results for synthetic signals. It is shown that the neural mass model is able to reproduce real depth-EEG signals accurately; thus, assuming this model underlying real depth-EEG signals, can improve the accuracy of features' estimation.

1. Introduction

Epileptic patients constitute about 1% of the world's population [10]. Life quality of epileptic patients depends on the use of anti-epileptic drugs. Long-term usage of these drugs may create unavoidable side effects. Since seizures occur without any obvious herald, the possibility of predicting seizures will open new horizons of remedies to prevent, or at least control, seizures. Reduction of drug dosage, confining the use of drugs to emergencies, stimulation of the vague nerve, and other techniques will improve the quality of patients' lives by reducing their intense feelings of helplessness.

Different algorithms have been used to assess whether seizures can be anticipated or not. These algorithms involve extracting some characteristic features from signals, consisting of both uni-variate features, like correlation dimension [9,24] and Lyapunov exponents [15], and bi-variate features, like synchronization [32] and dynamical entrainment [16–18].

Three main features that have dominated the seizure prediction field during the last years are correlation dimension, largest Lyapunov exponent, and synchronization.

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Elger and Lehnertz [9,24] applied the correlation dimension, as a measure of dynamical complexity, to discriminate between inter-ictal and pre-ictal states. But, later, by some studies [2,14] the ability of the correlation dimension to predict seizures was questioned. For example, data by which Martinerie and his colleagues [28] distinguished pre-ictal and inter-ictal states, *via* correlation density, were re-evaluated by [30], who showed that this measure reflects only the variance of EEG signals. In fact, it was suspected if the presence of non-linearity in a signal can justify the use of non-linear and complicated measures to characterize dynamical changes (see also [36]). It is important to prove that whether these complicated methods indeed outperform simpler linear measures or not (see also [4]). However, correlation dimension is still considered for seizure prediction, *e.g.*, in combination to other features [1,31].

On the other hand, since seizure generation is attributed to synchronous firing of neurons, something like regularity of neural networks; so, by taking the complex brain as a chaotic system, one would think of seizure as a state of decrement in chaotic behavior [15] estimated the largest Lyapunov exponent as an indicator of this phenomenon. They showed a decrease in chaoticity of the brain some minutes before an epileptic seizure. Then, studies by Lai et al. [22,23] raised doubts about the suitability of the Lyapunov exponent for seizure prediction.

Furthermore, Mormann et al. [32] considered the variation of synchronization between different brain areas before and during seizure. They measured phase synchronization between signals recorded from two channels, and observed such patterns of phase synchronization before seizure that were not found in seizure-free recordings. Le Van Quyen et al. [25,26] confirmed these findings through the study on eight patients suffering from neocortical epilepsy. Then, in the controlled studies comprising defined groups of patients with pre-ictal and inter-ictal control recordings, phase synchronization [33,34] was shown to be suitable for distinguishing between inter-ictal and pre-ictal data. In 2003, Chavez et al. [5] claimed that pre-ictal changes in phase synchronization occur predominantly in the beta band. Also, pre-ictal synchronization changes were found to be locally, restricted to specific channels, rather than a global phenomenon. Although using the concept of seizure time surrogates [3] bi- and multivariate measures were reported to have better performance than uni-variate measures [17,27,35], power of synchronization measures in seizure prediction is still under debate [11].

Briefly, none of these features can predict seizures accurately enough to be applied in the clinical care. This failure may be a result of the complex nature of seizures, which prohibits determination of a unique pattern for pre-seizure state in different seizures, even in one single patient. One the other hand, it is possible that the aforementioned features are not computed accurately, *i.e.*, the features may be approximated in such a way that prevents the prediction to be accomplished. In the absence of a ground truth for the real signals, performances of the features' computation methods are under question.

In this paper, at first, a multi-channel depth-EEG model is explained, and then *via* a parameter identification procedure, it is shown that this model is able to reproduce real depth-EEG signals. So, according to the synthetic signals produced by this spontaneous seizure generation model [40,41], we showed that the conventional methods lead to inaccurate estimations of features. From this point of view, it is not of main importance which seizure generation scenario underlies the synthetic signals [7], or what kind of seizure is simulated by them. The important thing is that some depth-EEG-like signals are at hand, by which it is possible to show that conventional methods can not compute their features accurately that may be the first reason of preventing seizures to be predicted.

Then, it is shown that thanks to the proposed algorithm that is based on parameter identification procedure, the features of synthetic multi-channel signals are obtained accurately. Although this good result is due to the exact matching of the synthetic signals and the assumed model; but, because of the ability of model to produce real depth-EEG signals, the proposed algorithm can be generalized to real depth-EEG signals. Nevertheless, it is noteworthy that more feasible the assumed model, more accurate the features.

The conventional synchronization measures have been taken into consideration in [41], in which it has been shown that in contrast to the conventional synchronization measures, the connectivity values identified based on the realistic depth-EEG model, would effectively quantify the synchronization between different areas of brain. But it is not discussed there [41] if the proposed algorithm still works in conditions in which the connectivity values change during time or not. Here, the concept of time varying connectivity values is covered.

Thus, the structure of this paper is as follows. At first, the model generating depth-EEG signals is illustrated, and similarity if its output signals to the real depth-EEG signals is validated. Then the conventional algorithms of feature extraction, as well as the proposed one based on knowledge about the signal generation mechanism, are described. These algorithms are applied to the synthetic signals, and it is shown that the proposed algorithm can extract features of synthetic signals more accurate than the conventional techniques.

2. Materials

2.1. *The seizure generator model*

Although all factors playing role in ictogenesis procedure are not exactly known, unbalanced excitation and inhibition activity of populations of neurons are supposed to be the cause of seizure initiation [43]. In Shayegh et al. [40] neuronal excitation and inhibition variation are assumed to be stochastic processes, *i.e.*, it is supposed that both excitatory and inhibitory gains of neural synapses change randomly. Thereupon, in this paper a two level stochastic model is assumed for generating depth-EEG signals in which the first layer simulates the stochastic variation of excitation and inhibition parameters. In the second layer there is a seizure genesis neural mass model whose parameters are excitation and inhibition properties of populations of neurons. This two-layer model is well described in [42] and is repeated in the Appendix A, and here we suffice to a short review of it.

In the first layer of model four physiological parameters, including excitation gain, excitation time constant, fast