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COMBINED DELAY AND GRAPH EMBEDDING OF EPILEPTIC DISCHARGES IN EEG REVEALS COMPLEX AND RECURRENT NONLINEAR DYNAMICS

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Abstract

The dynamical structure of the brain's electrical signals contains valuable information about its physiology. Here we combine techniques for nonlinear dynamical analysis and manifold identification to reveal complex and recurrent dynamics in interictal epileptiform discharges (IEDs). Our results suggest that recurrent IEDs exhibit some consistent dynamics, which may only last briefly, and so individual IED dynamics may need to be considered in order to understand their genesis. This could potentially serve to constrain the dynamics of the inverse source localization problem.

Keywords

Electroencephalography (EEG); Manifold Learning; Graph Signal Processing; Nonlinear Dynamics

1. INTRODUCTION

Identifying and analyzing the dynamics of the brain's electrical behavior are important problems in medicine and research. Here we are particularly concerned with epileptic discharges in electroencephalographic (EEG) measurements from scalp electrodes, cortical surface electrodes, and depth electrodes. The discharges that occur between seizures, known as *interictal epileptiform discharges* (IEDs), are usually analyzed together by first segmenting the data into time-aligned epochs and then looking at their ensemble average. This is done to improve the signal-to-noise ratio (SNR), and it is thought to succinctly summarize the commonalities across epochs while suppressing the background "noise."

However, the dynamics of IEDs are potentially quite complex, and in order to more comprehensively investigate the genesis of these discharges and their possible relationship to seizures, it may be important to analyze epochs individually, but also look for commonalities that are not necessarily preserved by simply averaging. Here we propose an algorithm that combines techniques from the fields of nonlinear dynamics and machine learning to characterize the similarities and dissimilarities in the dynamics of individual IED epochs. In addition, we suggest that this method has the potential to serve as a dynamic constraint for EEG source localizations.

Methods for analyzing the nonlinear dynamics in signals have been studied for some time [1], and the topic continues to be of interest to the EEG analysis community [2]. However, many of the available methods for analyzing nonlinear dynamics in EEGs are only focused on characterizing dynamic complexity. Others are useful for identifying consistent dynamics in single channel time series, but do not present a clear method for doing so in multi-channel EEGs. In this work, we are concerned with identifying consistent IED dynamics across multiple epochs of multi-channel EEG recordings.

Recently there has been some interest in analyzing low-order nonlinear dynamics with manifold learning techniques, which can reduce the dimensionality of data when they can be modeled as points sampled from a low-dimensional manifold embedded in a vector space [3, 4, 5, 6]. Indeed, many of those methods also use ideas from nonlinear dynamical analysis (*e.g.*, [3, 5, 6]). The manifold learning method we use here, Laplacian Eigenmaps [7], has roots in graph theory. Recently, graph signal processing [8], with similar roots in graph theory, has emerged as a family of techniques for dealing with signals that possess, or can be endowed with, graph structure. This is a potentially attractive relationship, because it suggests that the dynamic structure identified from the analysis methods here can be leveraged in future graph signal processing algorithms, most notably in algorithms for constraining and solving the EEG source localization problem.

We have previously applied manifold learning methods to characterize electrocardiographic (ECG) signal dynamics [4] and then we later built low-order models based on those characterizations of dynamics in order to constrain the ECG inverse problem [9]. While the dynamics observed in ECG signals are generally less complex than those in EEGs, we have found dynamic manifolds in both types of data using similar manifold learning techniques. A key difference between our previous work and the present work is the introduction of delay embedding as an attractor reconstruction technique prior to manifold learning. In our experience, this step of the algorithm is important for recovering the manifold geometry underlying EEG data, and we believe that this is in part because of the increased dynamic complexity of EEGs as compared to ECGs, as well as the signal attenuation between sources in the brain and measurement electrodes, which obscures the dynamic contribution of deeper brain sources unless delay-embedding is utilized. This will be described in greater mathematical detail using a nonlinear state space model in Sec. 2.1

In the sequel, Sec. 2 contains both the background and methods for the algorithm proposed in this work, in Sec. 3 we describe experiments and results with data recorded from intracranial electrodes and scalp surface electrodes, and in Sec. 4 we discuss the results from the experiments, as well as future work and conclusions.

2. BACKGROUND AND METHODS

In this section we will present background on state space modeling of IEDs, which will then be used to describe the motivation for the two methods whose description will follow afterwards. Our contribution is in combining these methods to make a new method for analyzing recurrent dynamics of IEDs.

2.1. State Space Model of Interictal Epileptiform Discharges (IEDs)

As background, we present a state space model to describe the dynamics of IEDs in the sources and their relationship to the measured signals. We begin by presenting the general model and then discuss how properties of the model enable analysis from the perspective of nonlinear dynamics on manifolds. The standard nonlinear state space model used in this work is

$$\dot{x}(t) = f(x(t)) \quad (1)$$

$$y(t) = Ax(t) + \eta(t), \quad (2)$$

where x describes the state of the electrical sources in the brain at any time t , $f(\cdot)$ describes their continuous evolution in time, and A contains a numerical solution to Poisson's equation, the partial differential equation (PDE) used to model the “forward” mapping from electrical sources in the brain to measurements made either on the scalp surface, cortical surface, or in the rest of the brain “volume.” Here $y(t)$ are the electrode measurements, and the measurement noise, η , is assumed to be independent and identically distributed (IID) in space and time. A is an ill-conditioned matrix when it describes measurements on the scalp, and the problem of determining electrical source locations and strengths in the brain from scalp measurements is a well-known ill-posed inverse problem.

Here we are concerned with the dynamics of IEDs contained in M epochs of regularly-sampled intervals (consisting of N discrete samples each), $\mathcal{E}_j = \{t_1^j, \dots, t_N^j\}$, $j = 1 \dots, M$. In typical analyses, a single ensemble average, $\bar{y}(t_i)$, is computed from these epochs as $\bar{y}(t_i) = \sum_{j=1}^M y(t_i^j)$. However, the genesis of IEDs can be complex and ensemble averaging may obscure variations across epochs that are important for understanding the underlying mechanisms.

In our work, we consider another approach to studying the dynamics in these epochs. When f is a diffeomorphism, thus describing a specific type of nonlinear dynamical system, at each time instant the states lie on a smooth manifold $\mathcal{N}$. Then the sequence of states in each epoch, $\{x(t_1^j), \dots, x(t_N^j)\}$, are point samples from a dynamic “flow” (*i.e.*, an integral curve satisfying Eq. 1) on that manifold. Variations in dynamics from epoch-to-epoch cause each such flow to traverse a different path on the manifold. If we could perform computations with $x(t)$ directly, we could use almost any technique from the family of machine learning methods for performing “manifold learning” in order to study the manifold $\mathcal{N}$. This will be discussed further in Sec. 2.3. Similarly, if A was a diffeomorphism, the same could be done with $y(t)$, but the properties of A preclude this possibility. Specifically, A has a large null space and, in general, the resulting projection destroys the topology of the manifold. However, in some cases it is still possible to reconstruct the topology of such a manifold (or attractor) from the observed time series, $y(t)$, and this will be discussed next in Sec. 2.2.

2.2. Attractor Reconstruction with Delay Embedding

Attractors are manifolds in the state (or phase) space of a dynamical system. The term “attractor reconstruction” refers to a process that recovers the topology of the state space manifold from observations of the signal. It has been shown that, under certain conditions, delay embedding can be used for attractor reconstruction. Given a generic observation function, h , of a flow, $x(t)$, on a d -dimensional manifold, $\mathcal{N}$, Takens’ Embedding Theorem [1] states that the trajectories can be embedded in a Euclidean vector space of dimension greater than $2d$, by forming vectors of at least $2d+1$ appropriately delayed samples of $h(x(t))$. In this paper, we take $h(x(t)) = y(t)$, as in Eq. 2, and obtain delay-embedded observations $\tilde{y}(t)$ according to the following equation:

$$\tilde{y}(t_i) = \begin{bmatrix} y(t_{i-w})^T & y(t_{i-w+1})^T & \cdots & y(t_i)^T \end{bmatrix}^T, \quad (3)$$

where $w = 2d$ is the parameter that controls the number of delay samples. This is performed for each epoch separately, which results in M “delay-embedded epochs” consisting of $N - w$ time samples each.

2.3. Manifold Learning with Graph Signal Embedding

Attractor reconstruction by delay embedding increases dimensionality to gain the possibility of recovering the topological manifold underlying the data, at the cost of reduced interpretability. Manifold learning is concerned with finding mappings from low-dimensional manifolds embedded in high-dimensional spaces, such as these, to low-dimensional Euclidean spaces that more succinctly represent the manifold topology. The topology of the manifold is actually unknown, but these methods attempt to “learn” the topology by preserving some of the properties of the original dataset *locally* in data space.

A number of these methods do this by first embedding the point samples in a graph, and then employing methods from graph theory (much like what is done in graph signal processing) to obtain simplifications of the graph structure. Suppose the input is a set of points, $P = \{p_i\}_{i=1}^K$. Then the methods proceed by constructing a graph with K nodes, one for each point in P , and edges that encode distance relationships between points in P . Laplacian Eigenmaps is one such method, which we will describe in these terms next.

Given a set of points, P , as described above:

1. Construct an adjacency matrix, W , representing the graph: Calculate a matrix of pairwise distances between points $R_{r,k} = \|p_r - p_k\|_2$ and choose a tuning parameter, σ , which we always set as $\sigma = \sqrt{\max(R)}$. Calculate a matrix $W_{r,k} = \exp\left(-R_{r,k}^2 / \sigma^2\right)$ and a degree matrix $D = \text{diag}(\sum_r W_{r,:})$ (where $W_{r,:}$ denotes the r -th row of W).
2. Perform a spectral decomposition of the graph Laplacian of W : This is equivalent to solving for the singular value decomposition of $D^{-1}W = USV'$. The columns of V represent the new coordinate directions, and thus row r of V is the result of applying Laplacian Eigenmaps to point p_r . The new coordinate directions are

ranked by magnitude of singular values, and the first one is typically discarded because it is constant. Thus from here on the “first d ” coordinates refers to columns 2, 3, ..., $d + 1$ of the matrix V .

3. For our method, we apply the algorithm above to the set of delay-embedded points from all epochs, $P = \left\{ \tilde{y} \left(t_i^j \right) \right\}$, $i = w + 1, \dots, N$, and $j = 1, \dots, M$. Here $\tilde{y}$ represents delay-embedding, as in Eq. 3, w controls the size of the temporal window in each delay-embedding, $j = 1, \dots, M$ indexes epochs, and $i = w + 1, \dots, N$ indexes the available time samples from each epoch.

3. EXPERIMENTS

The experiments for this work were performed on two different types of data recorded from patients at Boston Children’s Hospital under protocols approved by the institution’s review board.

3.1. Intracranial EEG Data

During a normal two-stage clinical intervention for a single patient, electrodes were implanted in the brain through a craniotomy. Measurements were made simultaneously from 124 channels at a sampling rate of 1kHz. Of those channels, 64 were used for an 8×8 grid of electrodes that was placed on the cortical surface near the suspected seizure focus. The remaining channels were used for 6 depth electrodes, each with 10 contact points, inserted into the cortex, also in the vicinity of the suspected seizure focus. Data was collected over the course of several days in the first stage, and then, upon removal of the electrodes, a resection of the suspected seizure focus was performed during the second stage. The recorded data was reviewed by clinical epileptologists who marked 61 IEDs manually. Epochs were created by taking the data from a window of time consisting of ± 500 milliseconds around the marked times of IEDs. Delay embedding was performed using a window size parameter of $w = 100$ samples, and then Laplacian Eigenmaps (LE) was applied using the algorithm described in Sec. 2.3. The first three coordinate directions resulting from the LE algorithm were visualized and are shown in the first column of Fig. 1.

3.2. Scalp EEG Data

Scalp EEG data was recorded from 5 patients during outpatient studies. Data was recorded from 128 channels simultaneously using a HydroCel GSN (Electrical Geodesics, Inc., Eugene, OR, USA) 128-lead EEG headset. In each case, data was collected for approximately 2 hours at a 500Hz sampling rate. Each record was reviewed by clinical epileptologists who marked IEDs manually. Case 1 had 2792 marked IEDs, Case 2 had 4559, Case 3 had 1069, Case 4 had 26, and Case 5 had 107. Epochs were created by taking the data from a window of time consisting of ± 500 milliseconds around the marked times of IEDs. Delay embedding was performed using a window size parameter of $w = 40$ samples, and then Laplacian Eigenmaps (LE) was applied using the algorithm described in Sec. 2.3. The first three coordinate directions resulting from the LE algorithm, in cases 1-5, were visualized and are shown in columns 2-6 of Fig. 1, respectively.

3.3. Visualization of Laplacian Eigenmaps Results

In general, the dimension of the manifolds analyzed using Laplacian Eigenmaps (LE) in these experiments was greater than three, but the first three coordinate directions of LE are visualized here in Fig. 1 for the purposes of comparison because they represent the most dominant directions in the data as prioritized by the LE algorithm. Each point in each visualization represents a delay-embedded data point. The epochs in each case were separated into three subintervals to highlight the differences in the consistency of dynamics as time approaches a marked IED (a.k.a. a “spike”), the IED occurs, and then time passes the marked IED. In each visualization, the progression of time within each displayed interval (*i.e.*, pre-spike, spike, or post-spike) is indicated by the progression of color shown in the colorbar in the bottom-left of the figure.

4. DISCUSSION

Consistent dynamics were identified across epochs in each case. However, as demonstrated in Fig. 1, the consistency was only noticeable in relatively short intervals surrounding each marked IED. This suggests that techniques modeling all epochs with one underlying signal will struggle to summarize the dynamics outside of these intervals. It may be necessary to consider the dynamics of individual IEDs to understand their genesis. In future work, we plan to use further graph signal processing techniques to leverage the signal structure uncovered by this work in order to dynamically constrain the EEG source localization problem.

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Fig. 1.

Analysis with Laplacian Eigenmaps of intracranial and scalp EEG epochs containing Interictal Epileptic Discharges (IEDs), a.k.a. “Spikes”, reveals consistency of dynamic trajectories during IEDs and across epochs, but shows that patterns may be less consistent both before and after IEDs. The same pre-spike, spike, and post-spike intervals were used consistently across all epochs per case. The progression of time within each interval is indicated by the coloring of points. The consistency of trajectories across epochs, or lack thereof, is noticeable upon inspection of the color progressions. The existence of this trend in both intracranial and scalp data suggests the possibility to analyze IED dynamics on the scalp despite the ill-conditioned forward problem. Even cases with fewer epochs (*e.g.*, 4 & 5) followed this trend, although it is easier to see in the other cases.