Multivariate Analysis of SEEG Signals During Seizure

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Abstract— **Epilepsy is a neurological disorder that affects tens of millions of people every year and is characterized by sudden-onset seizures which are often associated with physical convulsions. Effective treatment and management of epilepsy would be greatly improved if convulsions could be caught quickly through early seizure detection. However, this is still a largely open problem due to the challenge of finding a robust statistic from the neural measurements. This paper suggests a new multivariate statistic by combining spectral techniques with matrix theory. Specifically, stereoelectroencephalography (SEEG) data was used to generate a series of coherence connectivity matrices which were then examined using singular value decomposition. Tracking the relative angles of the first singular vectors generated from this data provides an effective way of defining the most dominant characteristics of the SEEG during the normal, the pre-ictal, and the ictal states. This paper indicates that the first singular vector has a characteristic direction indicative of the seizure state and illustrates a data analysis method that incorporates all neural data as opposed to a small selection of channels.**

I. INTRODUCTION

Epilepsy is a chronic neurological disorder that affects 50 million people worldwide [1]. It elicits abrupt seizures, which cause disabling convulsions, spasms, and possible loss of consciousness [2], [3]. Medications taken regularly help manage seizures, but results vary largely and are ineffective in over 30% of patients [4]. A promising alternative is deep brain stimulation (DBS) [5], [6], [7], [8], which uses electrical stimulation to suppress approaching seizures. The efficacy of both DBS and medications would be increased significantly if they were administered at the earliest possible point in seizure development. Despite abundant neural recordings obtained from implanted electrodes in epilepsy patients undergoing ablative neurosurgery, early detection of seizures is still largely an open problem.

A. Previous Work

Algorithms have been developed for early detection of seizures from sequential neural measurements [9], [10], [11]. Several approaches use measures from nonlinear systems and

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chaos theory to capture when the brain activity transitions from a less-orderly (or "chaotic") state to an orderly (or "synchronized") state (e.g. Lyapunov exponents [9], correlation dimension [9], correlation density [12], dynamical similarity [13], coarse grained flow average [14], etc.). Other approaches exploit spectral theory and relate seizure onset to significant modulations of power in different frequency bands [15], [16]. Finally, a few studies compute phase synchronization measures between at most two distinct channels and identify a seizure when such synchronization significantly increases [11], [17]. These approaches do not exploit the multivariate nature of the recordings, and may therefore neglect important network information that accounts for the underlying brain physiology. While they can be computed efficiently, these statistics also may not capture network dynamics critical to observing changes in the hidden clinical state.

II. METHODS

A. Data Collection Details

The data analyzed in this study are Stereotactic-EEG (SEEG) recordings performed at the Cleveland Clinic. This stereo-angio-fluoroscopic guided placement of depth electrodes is used for pre-operative monitoring [18]. In comparison to traditional techniques, these electrodes provide more complete coverage of the brain including lateral, intermediate and/or deep structures in a three-dimensional arrangement.

Invasive monitoring digital samples were recorded using the Nihon Kohden 1200A EEG diagnostic and monitoring system (Nihon Kohden America, Foothill Ranch, CA, USA) during the period of extra-operative monitoring at the Epilepsy Monitoring Unit (M60, main campus, Cleveland Clinic). Patient 1 had 14 electrodes implanted with 197 contacts and Patient 2 had 141 contacts. All data was band-pass filtered (0.080 Hz to 250 Hz) and digitized (10 KHz).

B. Multivariate Analysis

In this paper, we describe a method which shows how spectral analysis and matrix theory can be combined to compute a multivariate statistic from multi-site SEEG recordings in epileptic patients. First, multiple simultaneous neural measurements are translated into connectivity matrices that describe the time dependent correlation (spectral coherence [19] at a specific frequency) between channels. Then, the singular value decomposition [20] of each connectivity matrix is computed to analyze how the direction of the first singular vector changes over time. Our approach measures changes in

network structure over time and integrates information from all channels in contrast to single and bivariate statistics.

C. Equations and Techniques

Recent studies have introduced multivariate schemes that include all electrode channels in their analyses [21], [22]. In these schemes, each electrode is treated as a node in a graph, and any two nodes are considered to be connected (an edge exists between their nodes) if the activity at the two sites are dependent. The connectivity or topology of the graph can then be described by a matrix. Statistics are then computed from the matrix to see if the topology changes significantly in different clinical states (e.g. inter-ictal, pre-ictal). Any significant change in the statistics can then be used to detect a seizure's onset.

1) Coherence: The connectivity matrix, A has been computed using the spectral coherence between the signal in channel i, X_i, and the signal in channel j, X_j, in a specific frequency (see section II, subsection D for more details) [22]. The matrix is recomputed for each stage of a sliding time window. That is,

$$A_{ij} = \frac{\left| P_{X_i X_j} \right|^2}{P_{X_i X_i} P_{X_j X_j}} \quad (1)$$

where $P_{X_i X_j}$ is the cross spectrum, and $P_{X_i X_i}$ and $P_{X_j X_j}$ are the power spectra of signals X_i and X_j at a given frequency, respectively. Coherence is widely used as a measure of correlation in the brain.

2) Singular Value Decomposition: The structure of the multivariate connectivity matrices, generated using the coherence between all channels of the SEEG recording, were analyzed using singular value decomposition [20]. SVD is a representation of a matrix that highlights properties such as the rank, range space, and null space associated with the matrix. The SVD method partitions the connectivity matrix into its column and row spaces and associated null spaces. The vectors that span the column and row spaces correspond to the dominant pathways through the connectivity matrix. The singular value decomposition (SVD) of an m x n matrix A is defined as

$$A = USV^* = U \begin{bmatrix} \sigma_1 & & & \\ & \ddots & & 0 \\ & & \sigma_r & \\ \hline & 0 & & 0 \end{bmatrix} V^* \quad (2)$$

In the SVD, U is an m x m unitary (i.e. $UU^* = 1$) matrix whose columns are the eigenvectors of the matrix AA^*, and V is an n x n unitary matrix whose columns are the eigenvectors of the matrix A^*A. A^* is defined as the complex conjugate transpose of A. SVD has the advantage that, unlike eigenvalue decomposition, it can be extended to future work on non-symmetric connectivity matrices. The matrix S is an m x n matrix whose first r diagonal entries $\sigma_1 \geq \sigma_2 \geq \cdots \geq \sigma_r$ are the nonzero singular values of A. Finally, r is the rank of A [20]. The first r columns of U span the column space of A and the first r rows of V span

the row space of A. When $m = n$ and A is symmetric, the SVD reduces to the conventional eigenvalue decomposition, where the singular values are the square of the eigenvalues of A, $U = V$, and the columns of U and V are the eigenvectors of A [20].

D. Signal Processing

The data were divided into one second windows (500 points) that overlapped by 50%. A Hamming window of the same length was applied and a spectrogram generated for each one second window after subtracting out the window specific mean. The following analysis was done to select the best frequency to evaluate the coherence. The spectrograms were averaged across the pre-ictal period on a frequency by frequency basis. The spectrograms spanning the seizure period were also averaged separately. The average spectrogram from the seizure period was divided by the average spectrogram during the pre-ictal period. The resulting frequency specific ratios were seen as a measure of which frequencies were the most modulated by the seizure event. The frequency showing the most modulation in Patient 1 was 19 Hz and 86 Hz in Patient 2. This was selected to be the frequency at which coherence was calculated between channels. An overview of the signal processing preformed is shown in Fig. 1.

A connectivity matrix was then constructed for each one second window as mention in the previous section where the element (i,j) in the array corresponds to the coherence between the ith and jth channel. The connectivity arrays were averaged together over the span of five seconds (9 windows) where the window that would appear in adjoining time frames due to overlap was disregarded for this analysis to prevent duplication of data between time frames. This results in a series of time frames (matrix $A(j)$), each representing 5 seconds of data. The total number of time frames differed between the two patients due to various lengths of data available.

Singular value decomposition was then performed on each time frame independently. Since in this case the connectivity array is symmetric, SVD is equivalent to the eigenvalue decomposition. The first singular vector (first column in V or row in V^*) now points a particular direction in higher dimensional space. This vector has the largest singular value and represents the dominant structure in the connectivity matrix at that time. In fact, the components of this vector are proportional to the *Eigenvector Centrality* of each node, which is a measure of importance of each node in a network [23].

Although visualizing the direction and progression of the vector is difficult, the relative direction can be analyzed throughout the pre-ictal and ictal periods. The first singular vectors were then combined into a matrix B, where the jth column of B is defined as the 1st singular vector V_1 at time frame j.

$$B_{*j} \equiv V_1(j) \quad (3)$$

Finally, the inner product of the mean ictal singular vector and the first singular vector from each time window
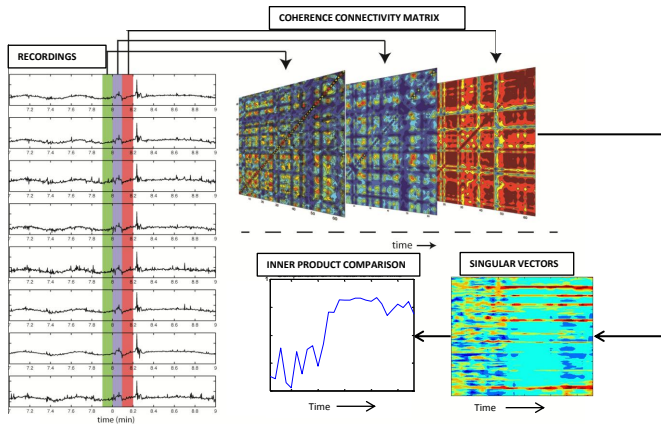
Fig. 1. **Signal Processing Overview** - An overview of the data processing method. The coherence arrays are calculated from raw SEEG data. Singular value decomposition is then performed. The inner product of the average first singular vector from the ictal period with each coherence array(5 second time frame) is computed. This statistic is then tracked over time.

was calculated to determine if the first singular vector had a characteristic direction during seizure and whether the dominant direction of the connectivity matrix changes during seizure onset. We plan to use the time dependent structure of the dominant direction of the connectivity matrix as a way to detect the onset of seizures.

III. RESULTS

A. Spectrogram and Coherence Results

The spectrogram for Patients 1 and Patient 2 are shown in Fig. 2 A. Representative signals from one electrode are shown time-matched to the spectrogram. It can be seen that the increase in power occurs at a higher frequency in Patient 2 as opposed to Patient 1. From these, coherence connectivity matrices were computed. Examples of these connectivity matrices are shown in Fig. 3.

B. Singular Value Decomposition Results

In Fig. 2 C, a visual break can be seen in the data where the dashed black line marks the onset of the seizure. This is quantified in Fig. 2 D where the average first singular vector is computed from the ictal time, and the inner product is taken with each subsequent first singular vector. The 80 seconds of seizure data were used to generate the average ictal first singular vector for both Patient 1 and Patient 2. As can be seen in Fig. 2 D, the inner product remains low during the pre-ictal period but climbs quickly around the onset time. This leads to a key discovery. The direction of the first singular vectors during the seizure time are similar (high inner product), but distinct from the direction of the first singular vectors throughout the pre-ictal period (low inner product). This indicates that the first singular vector has rotated and the structure of the network is changing significantly as the seizure develops.
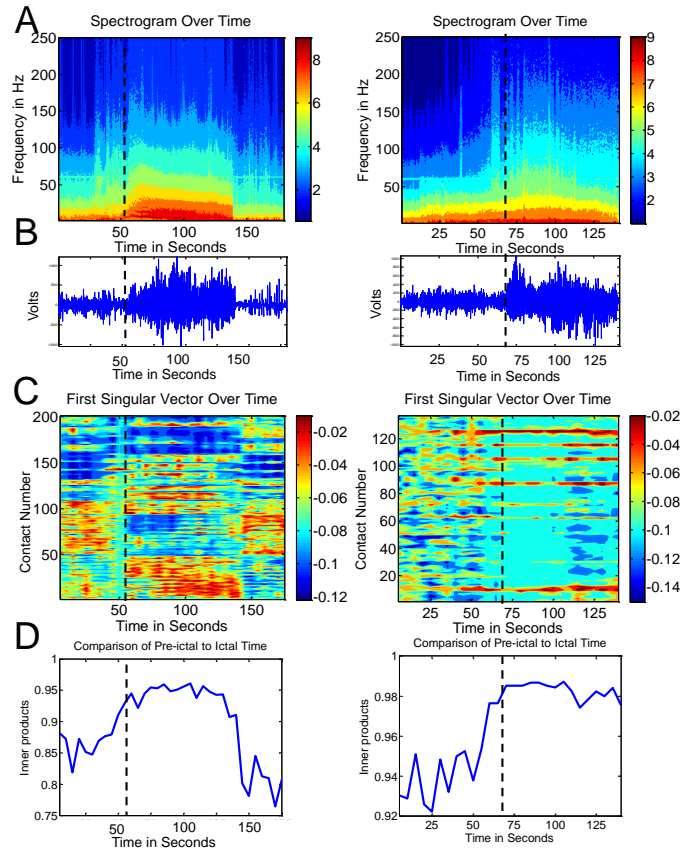

Fig. 2. **Aligned Signals** - The left column represents Patient 1 and the right, Patient 2. A is a spectrogram generated from the full SEEG data. B is the voltage reading from a representative electrode. C is matrix B for each patient with each column representing a five second period from the SEEG recording. D is the inner product result of an average first singular vector taken from the ictal period with the first singular vector at each time.

IV. DISCUSSION

The data indicate that the first singular vector achieves a characteristic direction during seizure. This is indicated by the high inner products between singular vectors from times throughout the seizure duration and the average ictal vector. In addition, this direction seems to be distinct from the typical direction during the pre-seizure time period as indicated by a low inner product between the average ictal vector with those in the pre-ictal period. This direction seems both stable throughout the seizure duration and different from the normal behavioral state of the brain. If this pattern continues throughout all seizures in an individual, tracking the direction of the first singular vector in high-dimensional space may provide a powerful statistic for accurately detecting clinical seizure onset.

V. CONCLUSION AND FUTURE WORKS

Confirming the usefulness of tracking the direction of the first singular vector from connectivity matrices will require validation with multiple data sets from each individual. In addition, epileptic events from a wide variety of subjects should be studied to ensure that the direction of the first
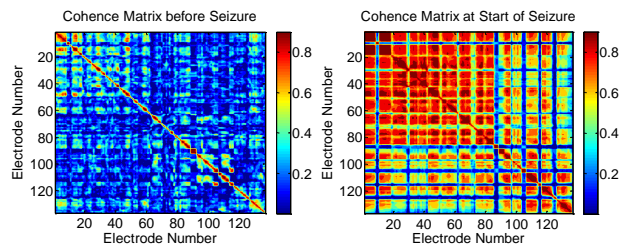
Fig. 3. **Coherence Matrix Examples** - $A(5)$ and $A(12)$, two examples of connectivity matrices from Patient 1 are shown above. The left, $A(5)$, is from the pre-ictal period and the right, $A(12)$, is from the start of the ictal period.

singular vector is a robust statistic for seizure detection across individuals. With this information a system could be built that would warn the subject when the first singular vector of their neural activity (viewed as a connectivity matrix) rotates towards a direction known to be associated with their seizures.

VI. ACKNOWLEDGMENTS

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