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Partial Directed Coherence Analysis of Intracranial Neural Spikes in Epilepsy Patients

Hsiao-Lung Chan, *Member,* IEEE, Yu-Tai Tsai, Yao-Chung Wang, Ju-His Ju, Bao-Luen Chang, Tony Wu, Shih-Tseng Lee, and Bor-Shyh Lin

Abstract—**Intracranial electroencephalograms (EEG) provide a direct observation of neural activity by placing an electrode array on the cortical surface near the suspected epileptic foci. The neural spikes appeared during inter-ictal stages are mainly produced by abnormal neural discharges from epileptic foci. The topological mapping of spikes' potentials is commonly used to identify the epileptogenic zone. However, the propagations among multi-channel spikes are also important to identify the epileptic source activity. In addition, the changes of source activities in a series of consecutive spikes reveal the time-varying neural activations during discharge process, which provide alternative information for interpreting epileptic source activity. This paper proposes a spike classification based on the similarity of phase-space features to select candidate spikes from the intracranial EEGs recorded from an 8×8 electrocorticogram grid. Then, the partial directed coherence (PDC), which can provide the flow of source activity, at each spiking time point is computed. The outflow PDCs of all electrodes are therefore displayed on the grid. Our result showed that the derived source activities in the preceding spikes had high concentrated distributions but decreased in latter spikes. This implied the epileptic discharges were initially induced by a small-area cortex neurons and then spread out.**

I. Introduction

Intracranial electroencephalograms (EEG) provide a direct observation of neural activity by placing an electrode array on the cortical surface near the suspected epileptic focus. The neural spikes appeared during inter-ictal stages mainly arise from abnormal neural discharges from the epileptic foci. The spikes with large peak amplitude and early occurrence are usually regarded as the source of abnormal discharges. The geometric mapping of spikes' potentials is commonly used to identify the epileptogenic zone.

There are many spikes in an intracranial EEG recording. The nonlinear energy operator is commonly used to find the candidate spikes at a low signal-to-noise ratio [1]. The detected waves contain both epileptogenic spikes and non-spike waves. Traditionally used features for spike classification include durations, amplitudes, slopes, and sharpness [2–4]. However, extracting these features may be difficult when the spike is contaminated by background EEG or noise. Rather than detecting characteristic points, it is possible to find robust features in noisy data by matching the whole waveform or wavelet coefficients to predefined spike patterns [5,6]. Nevertheless, these methods require prior information about spike patterns and need a reference point. Recently, classification of neuronal action potentials over the reconstructed phase space is proposed. It has an advantage that the spike does not need to be exactly aligned as long as the essential waveform is included [7].

The temporal relationship of epileptic spikes among channels reveals the propagation of spike activity. However, it is not easy to disclose this relationship by potential mapping. Wilke *et al* employed a time-varying causality measure, the adaptive directed transfer function, to identify seizure-onset zone by aggregating the source activities of the selected intracranial spikes [8]. Nevertheless, selecting candidate spikes is an arduous task. In addition, the occurrence of consecutive spikes provides a chance to observe the propagation of spike activity, which would be beneficial for determining the propagation path. This paper proposes a method to find candidate spikes based on the similarity of phase-space features. The partial directed coherence is hereafter used to disclose the source activity.

II. Methods

A. Data Collection

The video-scalp EEG monitoring (Nicolet Biomedical Inc., Madison, WI, USA) for spontaneous seizures was performed to identify epileptogenic zones. The brain surgery was conducted and an 8×8 electrode array was placed on the cortical surface of the suspected epileptic focus. The same video-EEG monitoring was performed to record the intracranial EEGs for refining the location of epileptic focus. The EEG data were retrieved at a sampling rate of 1 kHz for spike detection, phase space reconstruction, and spike classification in the MATLAB 7.5 (The MathWorks, Natick, MA, USA).

B. Spike Detection and Classification

The nonlinear energy operator (NEO) [1] was applied to each channel. A smoothed nonlinear energy (SNE) is derived by a convolution with a Bartlett window. The epileptic spike has larger SNE due to its large-amplitude, sharp characteristics. An adaptive threshold is computed from the

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H. L. Chan, Y. T. Tsai, Y. C. Wang, and J. H. Chu are with the Department of Electrical Engineering, Chang Gung University, Taoyuan, Taiwan (phone: 886-3-2118800-5145; fax: 886-3-2118026; e-mail: chanhl@ mail.cgu.edu.tw).

B. L. Chang, and T. Wu, are with the Department of Neurology, Chang Gung Memorial Hospital, Taoyuan, Taiwan.

S. T. Lee is with the Department of Neurosurgery, Chang Gung Memorial Hospital, Taoyuan, Taiwan.

B. S. Lin is with the Institute of Imaging and Biomedical Photonics, National Chiao Tung University, Tainan, Taiwan.

SNE. To obviate the effect from spikes, we propose a max-energy sorting method which is adapted from the max-min spread sorting, originally developed for detecting neuronal action potentials [9]. The SNE signal is divided into consecutive 0.1-s bins with 50% overlap. The maximal SNE in each bin is inserted into a buffer. The buffer is sorted ascending and the values within 5% and 30% are averaged. An adaptive threshold is therefore set as p times the averaged value. When the instantaneous SNE is greater than the adaptive threshold, searching for largest SNE in the subsequent 0.2 second is continued to prevent the detection of small, connected SNE peak as a separate spike.

The detected spikes contain several epileptic spikes but also false spikes. In order to screen appropriate spikes, post-hoc spike classification is performed. The waveform from -0.1 to 0.2 s around the detected point is extracted and normalized by dividing its maximum magnitude. The waveform is resampled at a 10-time finer resolution by a cubic interpolation in order to give a denser phase space trajectory [7]. Phase space reconstruction expands the interpolated waveform $x(t)$, $t = 0 \ldots T$ to a series of vectors $\mathbf{X}(t)$, $t = 0 \ldots T\text{-}\tau$ by the time-delay technique

$$\mathbf{X}(t) = [\,x(t) \;\; x(t+\tau)\,] \tag{1}$$

where τ is a time delay. Plotting $\mathbf{X}(t)$ in two-dimensional phase space depicts a topological trajectory.

Fig. 1 shows the transformation of spikes to their phase space trajectories. The linear relationship between $x(t)$ and $x(t+\tau)$ still remains when τ=0.01 s is used (left trajectory). Using τ=0.03 s can break this linear relationship, but the produced phase space trajectory is less smooth (right trajectory). Therefore, τ=0.02 s is used in the present study (middle trajectory). The phase space trajectory is then projected onto a one-dimensional major trajectory radius (MTR) curve. The MTR is defined as the radial distances from the origin to major trajectory points at phases from 0 to 2π with 24 partitions. If more than one trajectory points are found at the same angle, the largest one is chosen.

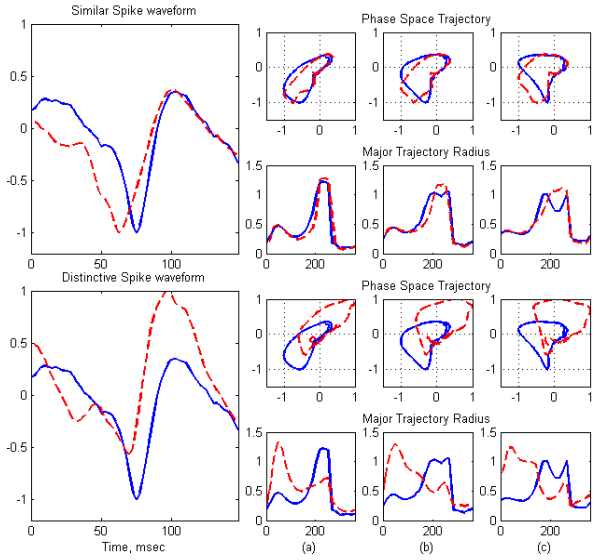

Fig. 1. Phase space reconstruction of spikes with similar waveforms and distinct waveforms, respectively.

The upper trace of Fig. 1 demonstrates similar phase space trajectory. Similar MTR curves are produced for spikes with similar waveform. On the other hand, distinct spikes have different trajectories and different MTRs (the lower trace).

C. Partial Directed Coherence

The partial directed coherence is computed based on a time-variant multi-variate autoregressive (AR) model:

$$\begin{bmatrix} x_1(n) \\ \vdots \\ x_M(n) \end{bmatrix} = \sum_{k=1}^{P} \mathbf{A}_k \begin{bmatrix} x_1(n-k) \\ \vdots \\ x_M(n-k) \end{bmatrix} + \begin{bmatrix} w_1(n) \\ \vdots \\ w_M(n) \end{bmatrix} \tag{2}$$

where $x_1(n),\ldots,x_M(n)$ are M-channel intracranial EEG signals [10,11]. These signals are modeled by AR coefficient matrix with order P driven by the uncorrelated M-dimensional Gaussian process $\mathbf{W}(n)$ with zero mean

$$\mathbf{A}_k = \begin{bmatrix} a_{11}(k) & \cdots & a_{1M}(k) \\ \vdots & \ddots & \vdots \\ a_{M1}(k) & \cdots & a_{MM}(k) \end{bmatrix} \tag{3}$$

The Fourier transform is then applied to the derived AR parameters by

$$\begin{aligned} A_{ij}(f) &= 1 - \sum_{k=1}^{P} a_{ij}(k) z^{-k} \Big|_{z=e^{-j2\pi f}} \quad \text{for } i = j \\ &= \sum_{k=1}^{P} a_{ij}(k) z^{-k} \Big|_{z=e^{-j2\pi f}} \quad \text{for } i \neq j \end{aligned} \tag{4}$$

The Grange causality is represented by the PDC in frequency domain:

$$\pi_{i\to j} = \frac{|A_{ji}(f)|}{\sqrt{\sum_{k=1}^{M} A_{ki}^{*}(f) A_{ki}(f)}} \tag{5}$$

The PDC $\pi_{i\to j}(f)$ take values between 0 and 1. It provides a measure of the direct linear influence of x_i on x_j at frequency f, i.e. an outflow activity from electrodes i to j. Higher PDC means a higher strength of source activity from electrode i.

III. Results

Fig. 2 shows a series of consecutive spikes. An interval was selected (marked by a darker box). The spikes within this interval were detected by adaptive thresholds. The detected spikes were then classified based on their phase space features.

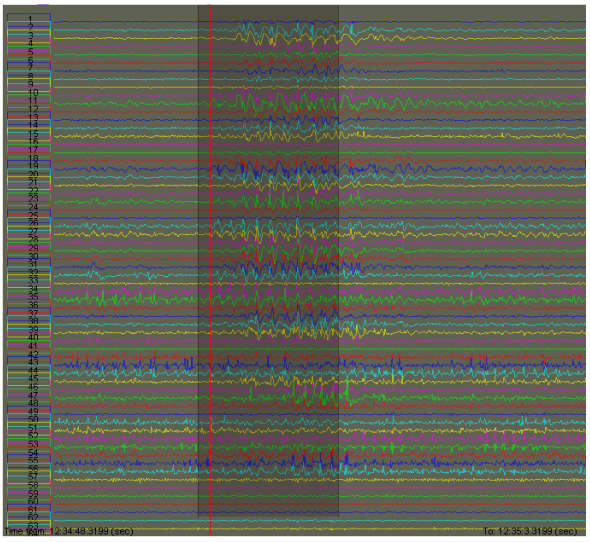

Fig. 2. A series of consecutive epileptic spikes recorded from an 8×8 electrocorticogram grid

Fig. 3 shows the topological mapping of negative peak potentials or the least potentials around reference points. The red color in the mapping means extremely negative voltages in that area. In the first six spikes, the negative voltage (red color) mainly appeared near the right middle region. After that, the concentrated region started to move to another site (form the sixth to the ninth).

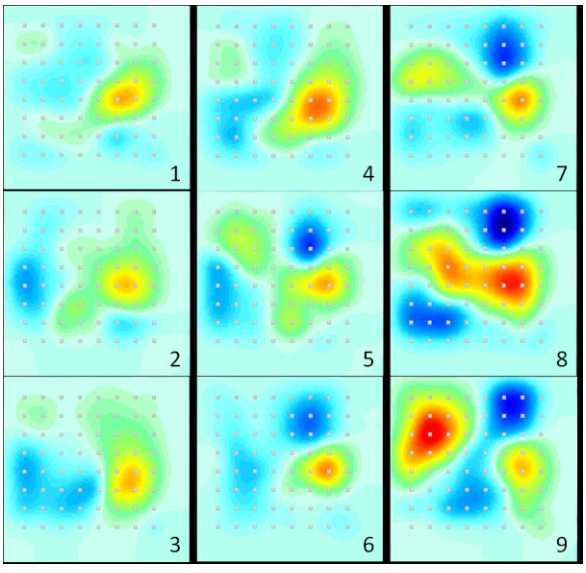

Fig. 3. Potential mapping of negative peaks in a series of consecutive spikes.

Fig. 4 shows the topological mapping of the outflow source activity derived by the PDC. In the first six spikes, high outflow activity (red color) appeared near the similar area as the potential mapping. In the latter spikes, two concentrated areas occurred. Although their locations were also marked by the potential mapping, the represented source activities were not distinct compared to the preceding mapping.

IV. Discussion

Phase space reconstruction does not use absolute time relationships, lending itself to an alignment-free advantage on classification of neuronal action potentials [7], personal identification by electrocardiogram [12], and ventricular extrasystole recognition [13]. In this study, the MTR pattern is little affected by the deviation of the reference point. Quantification based on major trajectory points not only simplify feature extraction but also consider significant morphological information. In addition, manually selecting timelines for selecting spike for mapping is traditionally performed. This work is time-consuming. The proposed phase space-based spike detection and classification is beneficial for reducing these works.

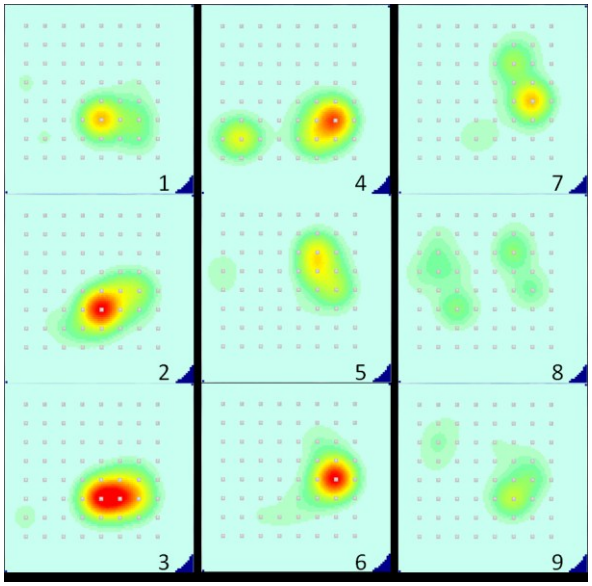

Fig. 4. Mapping of the outflow activity derived by partial directed coherence in a series of consecutive spikes

The topological mapping of spikes' potentials is commonly used to determine the epileptic foci. In our study the potential mapping in a series of consecutive spikes showed the split of the spiking activity. In addition, the PDC mapping suggested the source activities were initially concentrated with high coherences at a small area in the preceding spikes then spread out in the latter spikes. More clinical investigations are needed to associate the mapping patterns with clinical findings.

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