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Differential operator in seizure detection

Kaushik Majumdar

Systems Science and Informatics Unit, Indian Statistical Institute, 8th Mile, Mysore Road, Bangalore 560059, India

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ABSTRACT

Differential operators can detect significant changes in signals. This has been utilized to enhance the contrast of the seizure signatures in depth EEG or ECoG. We have actually taken normalized exponential of absolute value of single or double derivative of epileptic ECoG. This in short we call differential filtering. Windowed variance operation has been performed to automatically detect seizure onset on differentially filtered signal. A novel method for determining the duration of seizure has also been proposed. Since all operations take only linear time, the whole method is extremely fast. Seven empirical parameters have been introduced whose patient specific thresholding brings down the rate of false detection to a bare minimum. Results of implementation of the methods on the ECoG data of four epileptic patients have been reported with an ROC curve analysis. High value of the area under the ROC curve indicates excellent detection performance.

1. Introduction

Broadly speaking signal processing has two parts—(1) decomposing the signal into simpler components, and (2) analyzing the components in search of specific patterns. Because of (2) substantial part of signal processing may be considered as pattern recognition [1,2]. The pattern recognition part acquires an extra importance for biomedical signals in which detection of specific patterns has implications on diagnosis and monitoring of diseases. Electrophysiological signals generated by the human brain are known to carry signatures of epilepsy [3], Parkinson's disease [4], dementia [4], Alzheimer's disease [5] and schizophrenia [6].

In this paper we will concentrate on the identification of patterns in the prolonged brain electrophysiological recordings of the epileptic patients. Since the monitored signal may be several days long, automatic identification of patterns in real time is of practical importance. We are interested in seizure onset and offset detection in the continuously monitored depth EEG or ECoG of the epileptic patients. Ironically, any good detection algorithm tends to produce false detections in the ECoG when there is no seizure at all. This may happen because of presence of artifacts in the ECoG, many of which may look like a seizure. In order to avoid this there need to be sufficient measures to prevent false detections. In this paper we have devised seven such measures.

Second derivative based Laplacian operator is widely used for edge detection in an image [7]. An *edge* can be characterized by an abrupt change in intensity indicating the boundary between two regions of an image [8]. We have applied the same logic in this paper to detect the boundary between seizure and nonseizure in ECoG signals of epileptic patients, which indicates a seizure onset or offset. For automatic seizure detection see [9–11]. Differential operator has been utilized in seizure detection in [12–14]. Earlier first and second derivative of neonatal sleep EEG were used for feature extraction in order to automatically detect the sleep stages [15]. First and second derivative of EEG were also used to extract time domain features for automatic seizure detection in [16].

In the next section we will describe the methods used in this work. In Section 3 data acquisition will be described. Section 4 will contain the results of implementation on depth EEG or ECoG of four epileptic patients. We will use EEG and ECoG interchangeably throughout this letter. The last section contains some concluding remarks.

2. Method

In this letter we will be dealing with digital signals only. Derivative is discrete derivative or difference operation. Let a, b and c be successive time points. If a spike occurs at b then statistically $x(b)-x(a)$ and $x(c)-x(b)$ both have high numerical value, where $x()$ is the signal. The second derivative $x(a)+x(c)-2x(b)$ has an even higher numerical value. Whereas these values for the back ground signal will not be much higher. Let us take the transformation $\exp((1/w)|D^2x|)$, where D^2 is the second derivative, $|.|$ is absolute value and w is a positive valued normalization constant. $\exp((1/w)|D^2x|)$ acts as a spike enhancement filter with respect to the back ground EEG (spike enhancement through appropriate filter for the detection purpose has also been accomplished in [17]). $\exp((1/w)|Dx|)$ too acts the

E-mail address: kmajumdar@isibang.ac.in

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same way, where D denotes the first order derivative. Depending on the data set one gives better results than the other. Both of these two filtering methods will be denoted as *differential filtering*. Fig. 1 gives a schematic block diagram of the seizure onset detection.

Success of windowed variance method in seizure detection is well established [18]. In Section 4 we will see that the above filtering can significantly improve the seizure detection accuracy by windowed variance. Ironically a good seizure onset detection method tends to produce high number of false detection alarms on non-seizure signals. In order to minimize false alarms, following parameters have been introduced. Patient specific threshold needs to be set for each of them in order to avoid false detection to a very large extent. For the detail of implementation see the MATLAB programs with elaborate documentation along with supplementary materials in the author's website [19]. The automatic detection of onset and duration of a seizure for particular patients at any given time slot and channel location are summarized in Fig. 2 (for single differential filter or SDF) and Fig. 3 (for double differential filter or DDF).

(a) Maximum of the windowed variance B of the differentially filtered data (single channel ECoG signal). Each window has a fixed length. We have taken this length to be 4000 time points across all the data sets.
(b) Maximum of the windowed variance of absolute value of the data C.
(c) $|\max(B)-mm(1)|$, where $mm(1)$ is the variance of the differentially filtered data in the window next to the window of the

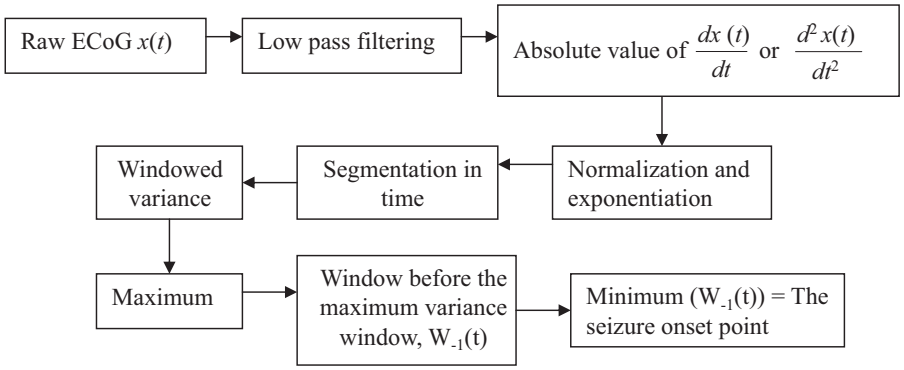

Fig. 1. A schematic block diagram of the automatic seizure detection algorithm. It has three major subparts, namely enhancement (accentuate the seizure part of the signal compared to the background), filtering and detection (which actually identifies the seizure onset point).

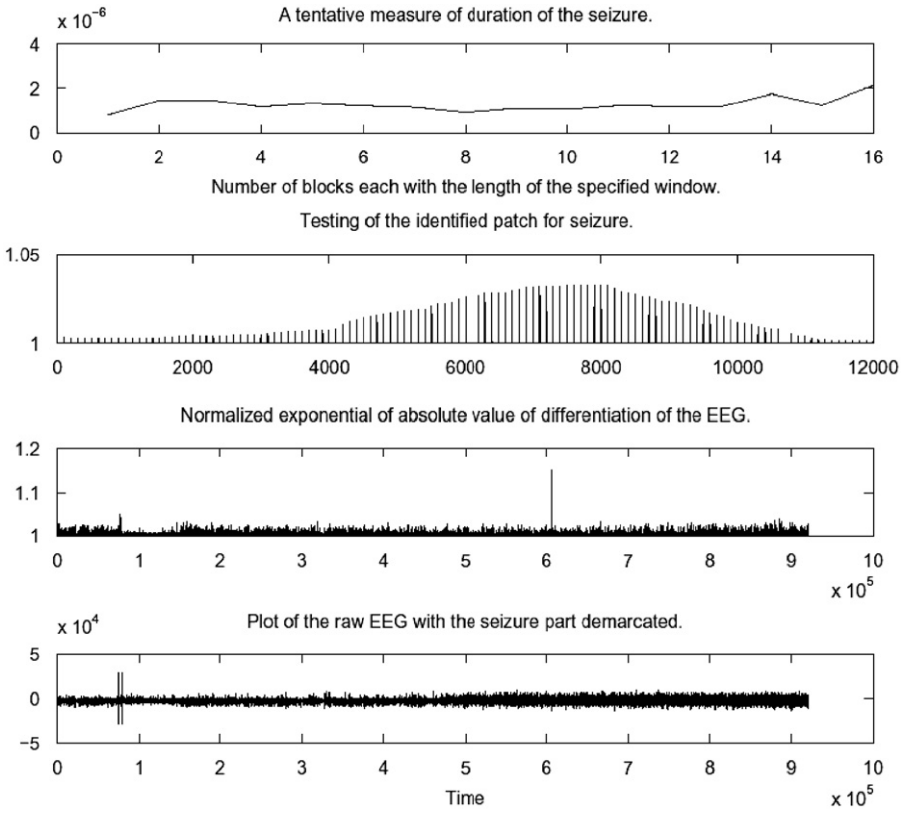

Fig. 2. Automatic detection of seizure and its duration at a single channel for patient 1. Seizure part has been demarcated by parallel vertical lines in the plot of raw EEG at the bottom panel. In the second panel from the bottom the filtered (based on single derivative) signal has been plotted, in which the seizure part is appearing as a distinct pillar like structure with respect to the back ground. The third panel from below plots DE, whose distinct shape corresponds to seizure. The top panel plots mm, which determines a tentative duration of the seizure. Automatic detection is from 74,501 to 78,501 time points, whereas the actual seizure occurred from 73,382 to 78,125 time points. 256 time points = 1 s.

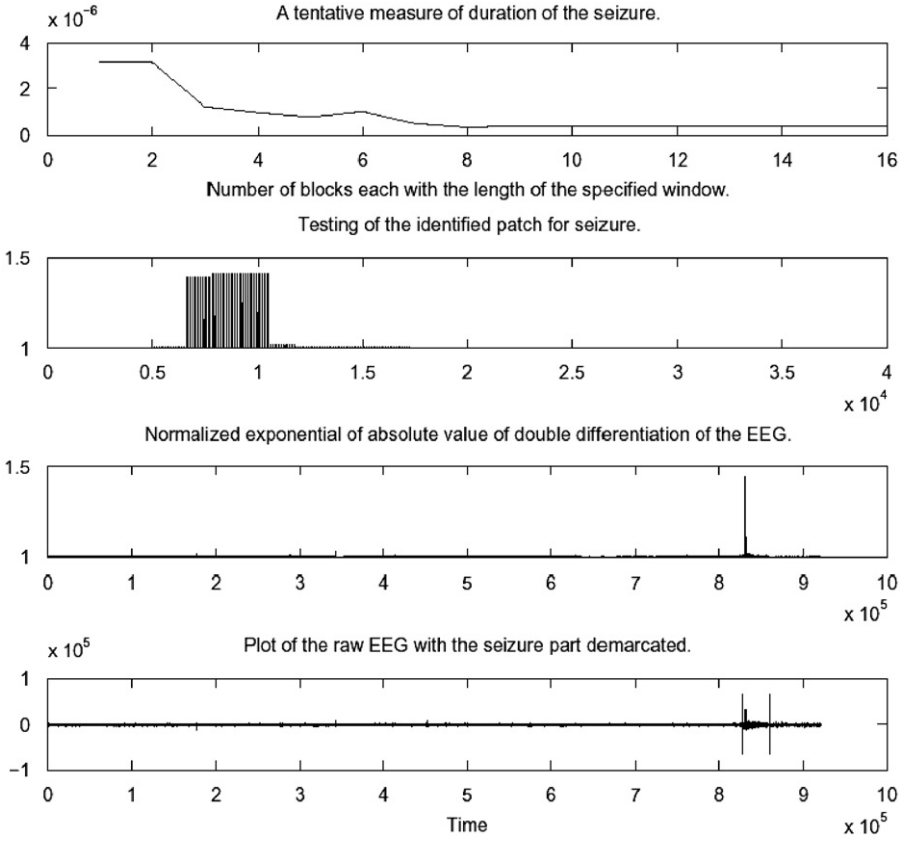

Fig. 3. Same as in Fig. 1, but for patient 2. In this case the filter is based on double derivative of the signal. Automatic detection is from 827,901 to 859,901 time points, whereas the seizure has been identified by epileptologist is from 819,373 to 857,094 time points. 256 time points = 1 s.

maximum variance. If there are more than one windows with maximum variance then $mm(1)$ is the window after the first window of maximum variance.

(d) $mm(i)$ is the variance of filtered data at the ith window after the first maximum window. Now let us take a stipulated number of windows after the first window of maximum variance. Here we have taken the stipulated number as 16. Let the first of the windows with minimum variance among the stipulated number of windows be the $n1(1)$th window. If M is the starting point of $\max(B)$ then $N1 = M +$ (number of time points in a window) $*$ $n1(1)$. M has been treated as the onset of seizure in this paper (in majority of the cases it happens to be several seconds after the actual onset) and $N1$ is the offset (usually several seconds after the actual offset). E is an array consisting of windowed variance of the filtered data starting from two windows before M up to $N1$. x is an array consisting of maximum values of E. F is another array consisting of values of E, which are greater than or equal to $(3/4)\max(E)$. We have observed that $||mean(F) - x(1)||$ is a quantity whose threshold distinguishes between seizure and non-seizure EEG.

(e) $|std(F)|$, where std stands for standard deviation, which distinguishes between seizure and non-seizure ECoG subject to a threshold.

(f) $DE = \exp((1/\nu)|D^2E|)$, where ν is a positive valued normalization constant. K is an array consisting of values of DE, which are greater than or equal to $0.999\max(DE)$. Length of K, whose threshold distinguishes between seizure and non-seizure EEG.

(g) For seizure EEG $\max(DE)$ must lie within an interval.

Let us mention once again that all the thresholding in the above parameters and the interval in (g) are patient specific. In this work duration of seizure has been calculated as described in (d). Each of the operations executes in linear time. The whole method is extremely fast—takes less than 4 s for a 1 h long signal with 15.625 s window length and 15.234 s overlap on an Intel Core 2 Duo Processor T8100 (2.1 GHz/800 MHz FSB, 3M L2 cache), Ubuntu machine with 4 GB RAM. The implementation was in MATLAB.

3. Data acquisition

Four medically intractable focal epileptic patients' ECoG data that have been analyzed in this work have been provided by the Seizure Prediction Project of the Albert-Ludwig-Universitat Freiburg, Germany [20]. In order to obtain a high signal to noise ratio (SNR), fewer artifacts and to record directly from focal areas intracranial grid, strip and depth electrodes were utilized. The ECoG data were acquired using Neurofile NT digital video EEG system (It-med, Usingen, Germany) with 128 channels, 256 Hz sampling rate, and a 16 bit analog to digital converter. In all cases the ECoG from only six sites have been analyzed. Three of them from the focal areas and the other three from outside the focal areas. See Table 1 for the patient details. A superset of the patient population has been studied in [21].

4. Results

4.1. Preprocessing

Since the data were collected over a couple of years, the conditions under which the data had been collected are likely to

Table 1
Patient details.

Patient	Sex	Age	Seizure type	H/NC	Origin	# Seizures
1	F	15	SP,CP	NC	Frontal	4
2	M	38	SP,CP,GTC	H	Temporal	3
3	M	14	SP,CP	NC	Frontal	5
4	F	26	SP,CP,GTC	H	Temporal	5

SP=simple parietal, CP=complex parietal, GTC=generalized tonic–clonic, H=hippocampal, NC=neocortical.

Table 2
Detail of the patient specific preprocessing.

Patient	Cut-off freq. (Hz)	Montage
1	100	Com. ref.
2	50	Com. ref.
3	100	Com. ref.
4	50	Bipolar

be different from patient to patient. We have performed different preprocessing for different patients for the optimum results. We have chosen the method by trial and error. Gaussian low pass filter, with cut off frequencies either 50 or 100 Hz depending on the patient, has been used to remove muscle contraction artifacts. Montage change from common reference to bipolar has helped to suppress chewing artifacts in patient 4 to some extent. See Table 2 for the details. For patient 4 the three in-focus electrodes have been put in bipolar reference among themselves and three out-focus electrodes have been put in bipolar reference among themselves (although intensity of seizure decreases due to subtracting one channel from another, which may result in detection failure, in this particular case it helped to eliminate artifacts to a large extent while still preserving the strength of the signal, which has turned out to be sufficient for the detection purpose).

4.2. Automatic detection

The detection algorithm was run on one hour long segments of ECoG of the patients containing one seizure per segment. Running the algorithm on longer data segments gives us a better opportunity to test the efficacy of our method in presence of artifacts. Window length of 4000 time points (15.625 s) with 3900 (15.234 s) time points overlap (i.e., sliding by 100 points) has been used. Seizure portions were identified by certified epileptologists at the place of origin of the data at each given time slot. The algorithm was implemented on each channel to automatically detect onset and offset of a seizure. Onset of the seizure has been taken to be the earliest point detected as onset among all the channels. For offset also the earliest point detected among the channels has been taken to be the offset.

The SDF has been applied on patients 1 and 4. The DDF has been applied on patients 2 and 3. Data of 1 and 4 contain more artifacts or noise than those of 2 and 3. DDF could not detect some of the seizures of patient 1. In relatively artifact free signals DDF usually gave more accurate measure of the seizure onset than SDF. In the ECoG of patient 1 windowed variance could not detect seizures in the preprocessed signals. But after filtering with the SDF all the seizures could be detected by windowed variance.

For the first three patients seizures were detected with cent percent accuracy. Data of the last four out of five seizures of patient 4 were heavily contaminated by chewing artifact. First seizure has been detected nicely on all channels. Second and fourth seizures have been detected on all focal channels. The third and the fifth seizures have been detected in two out of three focal channels and in one the seizure could not be detected although it showed up clearly in the plot (see supplementary materials in [19]). The fifth seizure ECoG of patient 4 required a very special and unique preprocessing (suppression of all values ≥ 0.15 of the maximum value regardless of sign), and therefore we will treat it as a failure to detection. For patients 1, 3 and 4 seizure free data for 24 h were available on which the detection algorithm was run to test for false positives. There were 4 false detections for patient 1, 5 for patient 3 and 0 for patient 4.

First detection algorithm identifies a window in which seizure is supposed to have occurred. Then the threshold values according to (a) to (g) of Section 2 are calculated. The available seizure ECoG was rather scarce for each patient (at most five seizures). So, the threshold values are set in such a manner that none of the seizures goes undetected. At the same time the threshold values are chosen to be bare minimum or bare maximum as the case may be so that the actual seizures are all detected.

Then the effectiveness of the method was tested by the number of false positives on the 24 h long seizure free signals, with the threshold values that were set on the seizure data. Performance measure has been given in terms of the area under the ROC curve in the subsection 4.3. The average seizure onset detection time lag is 20.45 s after the epileptologist determined onset, which is 9.3 s in [10]. The average seizure offset detection time lag is 26.49 s after the epileptologist determined offset.

4.3. ROC curve analysis

ECoG recording of 28 h for patient 1 is available. For patient 2 the recording is of 3 h duration (the 24 h seizure free data is not available). For patients 3 and 4 it is for 29 h each. The receiver operator characteristic (ROC) curve has been plotted as true positive rate (TPR, plotted along the *Y*-axis) vs. false positive rate (FPR, plotted along the *X*-axis) following [22] (Fig. 4). For the purpose of the ROC curve plotting we have assigned 5 false detections to patient 2 in 24 h, which is the highest in the poll of patients under study. For a discussion on missing values conventions see ref. [23]. $FPR = 1 - \text{specificity} = 1 - (TN/TN + FP)$ and $TPR = \text{sensitivity} = (TP/TP + FN)$ [22]. The area under the curve is ≈ 0.98, which indicates excellent identification accuracy.

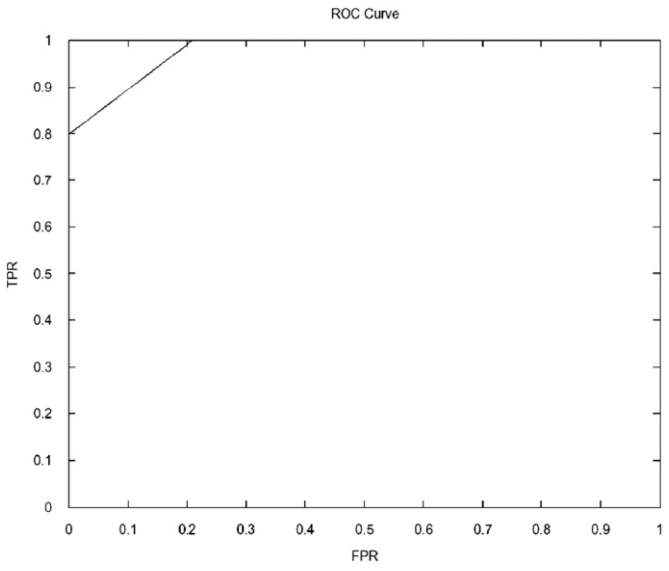

Fig. 4. The ROC curve of seizure detection. TPR=true positive rate and FPR=false positive rate. The area under the curve is ≈ 0.98.

5. Conclusion

In this paper the power of first order and second order differential operators in detecting significant changes in one dimensional signals such as single channel ECoG has been studied. Excellent accuracy has been observed in detecting clinical seizure onsets with a small number of false detections. The method made up of differential operators, exponentiation and variance has turned out to be extremely fast. Seven parameters have been identified whose patient specific threshold can distinguish between seizure and non-seizure signals for a given patient with impressively high automatic onset detection and low false detection rate. Further improvements in elimination of false detection are possible with multidimensional statistical analysis of these parameters. Wavelet based feature detection of the filtered signal followed by appropriate clustering techniques may result in further improvement in reducing the gap between the detection time and the actual onset time.

The current method has shown promising success on ECoG, which is relatively noise free, but not artifact free. The proposed filter can greatly enhance isolated spikes with respect to the back ground and therefore may be a potential tool for spike detection in single cell recordings. It can also suppress low frequency artifacts like those generated by eye blinks. The same is true for low intensity noise. It is yet to be tested for strong event related potential (ERP) detection in scalp EEG. However it is likely to give good results for automatic quake detection in seismological signals. Particularly many low intensity quakes are difficult to detect, yet they contain important information about the inside of our planet. At times they may even be precursor to an impending major earth quake.

Conflict of interest statement

I am the only author, hence there cannot be any conflict of interests.

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