

SeizAlert: Seizure Forewarning via Scalp EEG

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Abstract-- SeizAlert is a low-cost, wearable device to forewarn of an impending epileptic seizure. The technology, covered by eight patents, presently uses brain-wave data from four scalp electrodes at the front of the scalp, removes eye-blink (and other muscular) artifacts that would otherwise confound the analysis, converts the artifact-filtered data into a statistical distribution function (DF), and compares the DF for the baseline period with subsequent DFs via statistical measures of dissimilarity. Several hours forewarning of an impending event is provided by multiple, successive occurrences of the dissimilarity measures above a threshold. The resultant total true rate is 93% with a false positive rate that is more than an order of magnitude below the clinically acceptable value. R&D Magazine awarded its prestigious R&D100 Award to SeizAlert in 2005 [1].

I. INTRODUCTION

The problem of epilepsy afflicts nearly three million people in the US. Two-thirds of patients have events that are controllable by anti-seizure drugs, but the medications frequently have debilitating side effects (e.g., sleepiness, fuzzy thinking, and disorientation). Another 7-8% can be cured by epilepsy surgery, which may result in cognitive impairments. No available therapy is effective for the remaining 25% of patients (intractable epilepsy) causing severe impacts on quality of life. Extreme epileptic events require immediate medical intervention to avoid concomitant injury or sudden unexplained death, which is characterized by fatal cardiac arrhythmia and/or breathing cessation. Multiple hospitalizations are typically associated with diagnosis and ongoing treatment of seizure disorders; thus, significant medical costs are incurred.

The potential benefits of SeizAlert would allow preventive action, reduction in morbidity and mortality, and improvement in patients' quality of life. SeizAlert offers a new treatment paradigm of constant monitoring, rather than continuous medication. Reliable, long-lead-time forewarning would allow the patient to stop hazardous activity, lie down in a quiet place, undergo the seizure, and then return to

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normal activity. Other timely preventive steps may include taking medication to preclude the impending seizure for those responsive to anti-seizure drugs, requesting emergency responders, and/or alerting caregivers or one's physician. SeizAlert could also have utility as add-on software in epilepsy monitoring units and for drug discovery.

II. METHODOLOGY

Protopopescu and Hively [2], [3] recently reviewed their phase space dissimilarity measures (PSDM) methodology for both machine and biomedical applications. The PSDM approach is much more sensitive and consistent in detecting condition change than other methods, because biomedical data such as EEG and ECG are noisy, complex, and nonlinear, in some cases with chaotic features. Efforts to detect or forewarn of significant condition change in such data by conventional statistical measures (CSM) or by traditional nonlinear measures (TNM) failed to give consistent or reliable results.

The time-serial EEG data are acquired at 250 Hz in the 10-20 International System. A higher sampling rate is better, because the PSDM method is a data-hungry, statistical method. The stream of time-serial data is divided into contiguous, non-overlapping windows (cutsets) of N data points. The artifact signal is removed from each cutset with a novel zero-phase quadratic filter [4], using a moving window of data points, e_i , with the same number of data points, w , on either side of a central point. A quadratic curve is fit for this window in the least-squares sense by taking the central point of the fit as the low-frequency artifact, f_i . The residual value, $g_i = e_i - f_i$, has essentially no low-frequency artifact activity. This artifact filter has been highly successful in removing eyeblink and other muscular activity artifact from EEG data, in removing breathing artifact from electrocardiogram (ECG) data, and removing artifacts from machine data. This filter removes artifacts from nonlinear data without distorting the nonlinear features of the dynamics, unlike standard linear filters. All subsequent analysis uses these artifact-filtered data. Ten consecutive baseline segments (or "cutsets," typically having on the order of 20,000 points) from the baseline period are analyzed to provide a basis for comparison with subsequent test-case cutsets. These ten cutsets represent almost 13.33 minutes of data for a baseline. The optimal length of a cutset is one of the parameters that must be determined empirically to give the best forewarning results.

The continuous artifact-filtered data, x_i , are first converted into S discrete symbols, ranging from 0 to $S-1$ via the transformation, $s_i = \text{INT}[S(x_i - x_n)/(x_n - x_1)]$. Here, the

minimum and maximum in the data are x_n and x_x , respectively; INT converts a decimal number to the next lower integer. The s_i -data are then converted into a d-dimensional “phase-space” vector, $y(i) = [s_i, s_{i+1}, s_{i+2} \dots]$, spanning S^d discrete states. A statistical distribution function (DF) is obtained by binning the occurrences and location of each of these discrete states. Q_J and R_J denote the population of the J -th DF bin for the baseline, and for a test cases, respectively. The test case is compared to the baseline by dissimilarity measures:

$$\chi_N^2 = \sum_J (Q_J - R_J)^2 / (Q_J + R_J), \quad (1)$$

$$L_N = \sum_J |Q_J - R_J|. \quad (2)$$

The χ^2 statistic is a relative measure of the dissimilarity between DFs, not an unbiased statistic for accepting or rejecting a null hypothesis. The analysis can be enhanced by connecting successive phase-space points as prescribed by the underlying dynamics, $y(i) \rightarrow y(i + 1)$. This process flow can be represented by adjoining two successive vectors: $Y(i) = [y(i), y(i + 1)]$. $Y(i)$ is a $2d$ -dimensional, connected-phase-space (CPS) vector. Dissimilarities between successive CPS states are also determined by the measures in Eqs. (1)-(2). For the CPS, χ_C^2 and L_C denote dissimilarities between the CPS states; χ_N^2 and L_N denote the non-connected PS dissimilarities. Small dissimilarities indicate unchanging dynamics, while the converse is true, in that large dissimilarities are indicative of large changes in the dynamics of the data. Several successive occurrences of the dissimilarities above a threshold for all of the PSDM are required to indicate significant condition change for forewarning. The much higher sensitivity of the PSDM is achieved by first subtracting the corresponding values of the DFs and then summing the absolute value of the differences. In contrast, TNM first average over the global dynamics and then take the difference of the averages, giving a much less sensitive measure.

III. RESULTS

Sixty physician-characterized temporal lobe epilepsy data sets of up to 8 hours in length have been analyzed; these include data of both adult and pediatric patients. These data were obtained in the course of a CRADA project with Nicolet Biomedical (1999-2000). Twenty data sets contained no seizure; the remainder contained seizures as determined by physician review, with the onset marked relative to the start of the data set. Several data sets contained multiple seizures; the analysis stopped with the first seizure as the method has not been extended to handle multiple seizures. Figure 1 shows typical results obtained via PSDM analysis compared to the TNM, correlation dimension, in subplot (b) and Kolmogorov entropy in subplot (c). Raw data in subplot (a) have very complex, non-periodic features that are typical of brain waves. The seizure event occurred at 110.7 minutes, denoted by the solid vertical line in subplots (d) and (e). The TNM show no event forewarning. The isolated peaks at 42 and 58 minutes in subplot (c) are not significant.

At 27 minutes an event forewarning is provided by $U(\chi^2)$ in subplot (d) and $U(L)$ in subplot (e), with two (or more) successive occurrences above the threshold of 5 (dashed horizontal line) at 85 minutes (vertical dashed line). The best total true rate (true negatives plus true positives) to date is 56/60 (93%). The false-positive rate is 1 per 87 hours or more than an order of magnitude below the clinically acceptable value. The PSDM analysis of temporal lobe seizure data provides up to 5.3 hours of forewarning, with most occurring 1 to 3 hours prior to the seizure onset [5].

IV. DISCUSSION

Other investigators have used a variety of approaches detailed in several recent reviews of seizure prediction/forewarning in the *Journal of Clinical Neurophysiology* (May 2001) and *IEEE Transactions on Biomedical Engineering* (May 2003). Litt and Echauz reviewed this research in 2002 [6]. This work includes traditional nonlinear measures, time- and frequency domain analysis, neural networks and other artificial intelligence approaches. Nearly all of this work used intracranial EEG data, thus requiring highly invasive procedures, unlike scalp EEG.

Anticipated additional applications of the ORNL technology to biomedical endpoints include forewarning of atrial fibrillation in post-coronary artery bypass graft surgery patients via ECG data, discrimination of traumatic brain injury from normal EEG data, and detection of changes in alertness via EEG and associated eyeblink artifact data.

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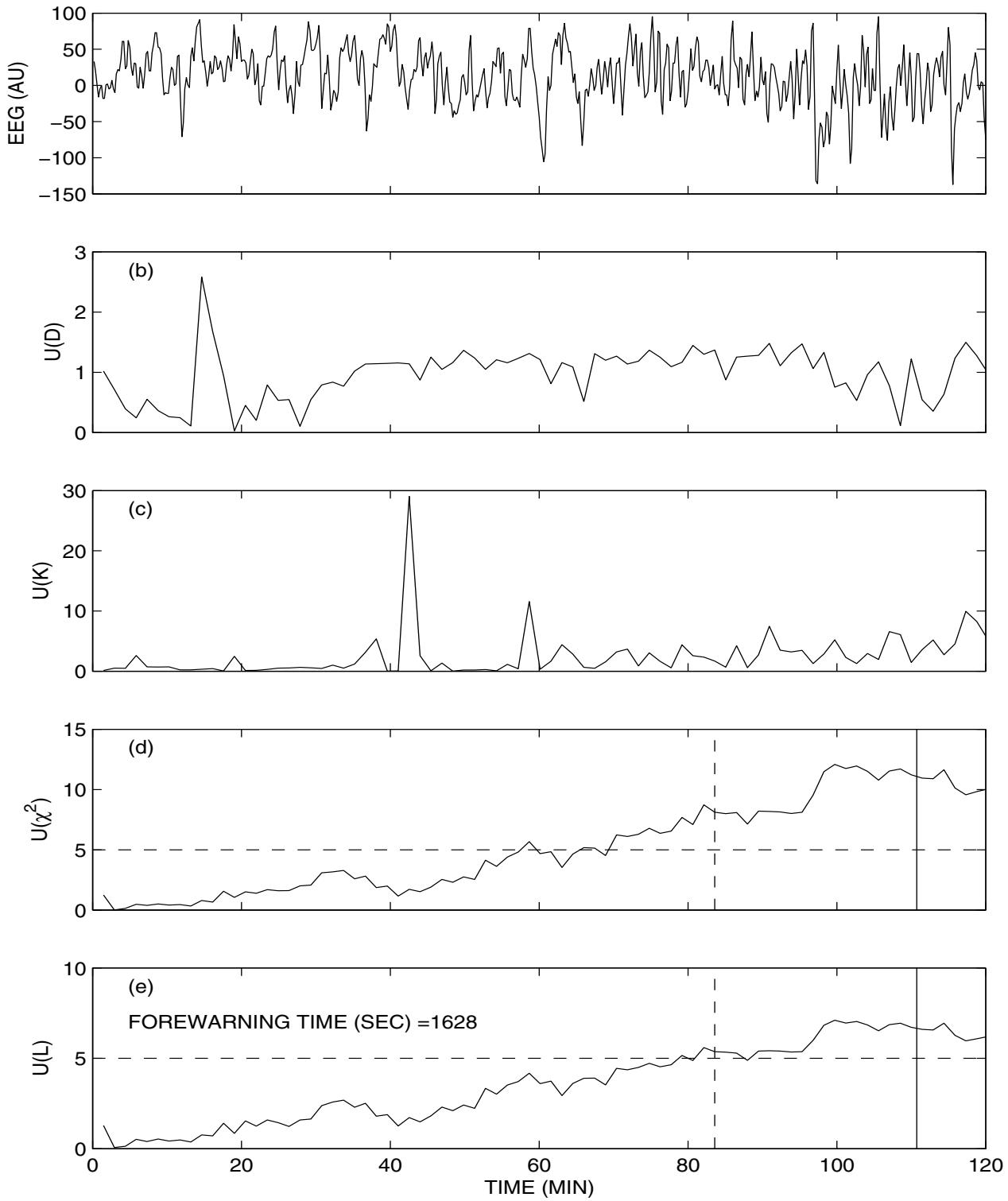


Figure 1: Results for human electroencephalogram channel 5 of dataset #PVM006, showing time-serial plots for: (a) 2.4 seconds of raw data collected at 250Hz, (b) correlation dimension, D , (c) Kolmogorov entropy, K , (d) $U(\chi^2)$, and (e) $U(L)$. The phase-space dissimilarity measures in subplots (d) and (e) are for $d = 3$, $S = 20$, $\lambda = 17$, and after removal of eye blink artifacts. Each cutest has $N = 22,000$ points, corresponding to 88 seconds. We have successfully applied this analysis to over sixty human datasets.