2019-01-01

HFO Detector Based On EEG Mean Energy Change Detection

Raul Ontiveros
University of Texas at El Paso

HFO DETECTOR BASED ON EEG MEAN ENERGY CHANGE DETECTION

RAUL ONTIVEROS

Master's Program in Electrical Engineering

APPROVED:

_____
Rodrigo Romero, Ph.D., Chair

_____
Sergio Cabrera, Ph.D., Co-Chair

_____
Yoonsik Cheon, Ph.D.

_____
Stephen L. Crites, Jr., Ph.D.
Dean of the Graduate School

HFO DETECTOR BASED ON EEG MEAN ENERGY CHANGE DETECTION

by

RAUL ONTIVEROS, B.S

THESIS

Presented to the Faculty of the Graduate School of

The University of Texas at El Paso

in Partial Fulfillment

of the Requirements

for the Degree of

MASTER OF SCIENCE

Department of Electrical and Computer Engineering

THE UNIVERSITY OF TEXAS AT EL PASO

December 2019

Acknowledgements

I would like to thank Dr. Rodrigo Romero and Dr. Sergio D. Cabrera for their mentorship through this entire research. I would also like to give a very special thanks to my parents for their sacrifice and undying support to get me through my education and making it the best experience possible. I would like to personally thank my brother for the countless times he took responsibility to make sure I made it to where I had to be always on time and helping me in the most stressful times. I would also like to thank my friends that made everything bearable until the end of this research. I would like to thank Jazmine Covarrubias for always being on my side and making me acknowledge how everything is possible even when things look horribly bad. Lastly but not least, I would like to thank Aubrey and Aurora, your presence is always felt and your existence is a gift to this world.

Abstract

The main goal of this work is to support automated seizure prediction by identifying preictal states using multiple detectors of high-frequency oscillations (HFOs). Assessment of HFOs from a seizure onset zone may be facilitated using automatic HFO detectors. However, studies have shown that HFOs can be generated by physiological or pathological brain processes. Distinguishing between pathological and physiological HFOs is challenging due to a lack of discriminant information in signals' morphology and other characteristics. Other complicating factors include a lack of consistency in definitions of HFO frequency ranges, the need for expert verification of HFO detection, and lack of robustness of automatic HFO detectors. In addition, artifacts, spatial subsampling, and filtering of spikes and their high-frequency harmonics may introduce uncertainty and make automatic HFO detection difficult. This work introduces an automatic HFO detector based on detecting changes in signal mean energy through cumulative sum computation with the aim of including it in a consensus detector. Leveraging a set of automatic HFO detectors is justified by the expectation that detection must be accurate to automatically identify changes from the interictal state to the preictal state in electroencephalogram (EEG) signals, but there is no single automatic HFO detector with a positive detection rate sufficiently close to one hundred percent and a sufficiently low false detection rate. Even though the cusum detector performed lowly it is better if combined with other methods.

Table of Contents

List of Tables

List of Figures

Chapter 1: Introduction

As the result of a brain injury or a disorder, whether genetic or acquired, an individual may develop epilepsy, which is characterized by unpredictable, unprovoked seizures. Electrical activity of the brain can suddenly change during a seizure and affect movement, feeling, and sensation of the body. Epilepsy may be treated through medication or surgery. When treatment results with medication are inadequate, surgery may be undertaken. Although it is only effective in 10% of cases [8]. For surgery to be successful, the location of the epileptogenic zone (EZ) or zones, i.e., brain tissue that initiates seizures, must be accurately established, as resection of incorrect tissue is even more detrimental to patients than the effects of untreated epilepsy per se. While presurgical examination for resective surgery aims at delineating the epileptogenic zone, its localization depends on determining spatially related zones including the irritative zone which generates interictal discharges, the seizure onset zone (SOZ), the epileptogenic lesions, and the functional deficit zone. The authors indicate that removal of tissue that generates high-frequency oscillations (HFOs), which oscillate faster than typical clinical brain signals, has been related to improved postsurgical outcomes compared to results from resecting only the SOZ.

Epileptogenic zone identification can prove difficult, however, because its activity cannot be measured directly and diagnostic tests must be utilized to identify it [2]. Such tests may include a history of seizure semiology, electroencephalogram (EEG) recordings, and magnetic resonance imaging. Intracranial depth electrodes and observation of interictal EEG spikes can help finalize epileptogenic zone localization. HFOs could help also to locate the epileptogenic zone. In order to detect HFOs, at least an 800Hz sampling rate with surface and depth electrodes may be needed. While HFOs can be physiological or pathological, there is a difference between HFOs. On the one hand, the former are bound to have HFOs during deep sleep and while recalling information. On

the other hand, HFOs in patients with epilepsy will be associated also with epileptogenic brain zones. Results using HFOs for epileptogenic zone localization are still inconclusive since the number of studied patients so far is very small.

Treatment or removal of an epileptogenic zone may reduce or eliminate seizures, but seizure source location and identification of epileptogenic zones are active research areas. For patients with untreatable epilepsy, i.e., those whose seizures cannot be eradicated through medication or surgery, seizure prediction may be an alternative. Work in this area started in the 1970's with an aim to identify precursors of seizures that could be used either to generate warnings for patients and care-givers or to trigger mechanisms to suppress impending seizures [8]. Reliable indicators remain unknown, but recent studies have identified HFOs, especially signals above the high gamma range, as promising biomarkers of the SOZ and preictal indicators [1]. HFOs are defined as either ripples or fast ripples covering the frequency range from high gamma to 250 Hz and above 250 Hz, respectively. While expert visual inspection of EEGs to detect HFOs is the gold standard for their identification, it can be a time-consuming, tedious, and unpredictable process, as events may be misclassified or missed [11]. Instead, automatic detectors can be used to inspect signals to detect and classify HFOs in an accurate fashion. The goal of automatic detectors is to detect the same events a neurologist would.

1.1 Problem statement

The main goal of this work is to support automated seizure prediction by using multiple detectors. Assessment of HFOs from SOZs may be facilitated using automatic HFO detectors. However, studies have shown that HFOs can be generated by physiological or pathological processes within the brain [9,19]. Distinguishing between pathological and physiological HFOs is nontrivial due to a lack of discriminant information in signals' morphology and other characteristics [9]. A second complicating factor is the lack of consistency in definitions of HFO frequency range. For instance, some authors define high gamma signals in the 80 – 150Hz range, ripples in the 150 – 250Hz range, and fast ripples in the >250Hz range, with the latter being associated with pathological activity by some authors [9]. However, other authors define these ranges differently [5,3,21,22]. A third complicating factor is that detected HFOs must be visually verified by experts, which is a time-consuming, and can also become very tedious [11] A fourth complicating factor is that automatic HFO detectors have yet to reach a large consensus [24]. In addition, artefacts, spatial subsampling, and filtering of spikes and their high-frequency harmonics may introduce uncertainty and make automatic HFO detection difficult. This work will leverage results from a set of automatic HFO detectors as references for the performance and analysis of a proposed detector based on detecting changes in signal mean RMS energy through computing the cumulative sum of mean RMS energy [29]. This approach is justified by the expectation that HFO detection must be accurate to automatically detect changes from the interictal state to the preictal state in EEG signals but there is no automatic detector with a one hundred percent HFO detection rate [19]. This work will evaluate the utilization of a cumulative sum detector for automatic detection of HFOs.

1.2 Related work

Par A number of methods for automatic detection of HFOs in EEG signals have been proposed by several authors as discussed below. No approach has proven successful in general because of variations in algorithms used, the need for data-specific adjustments, and the lack of a widely accepted set of evaluation parameters and a corpus that offer a reference for performance appraisal of detection algorithms.

1.2.1 Algorithms to detect high frequency oscillations in human intracerebral EEG (Rahul Chander, 2007)

Chandler developed an automatic baseline detector to remove any ambiguity introduced by visual identification of the signal baseline, which is the background activity surrounding HFOs. Detection methods used are modifications of previously introduced detectors [25,26] to support time-invariant modes. The first method can detect HFOs but not classify them into ripples or fast ripples. The second method can have arbitrary resolution in the frequency or the time domain. The dataset used comprises interictal EEGs from 5 epileptic patients. The reviewer went over non-rapid eye movement (NREM) sleep, as interictal HFOs occur more frequently in NREM sleep than when the subject is awake. EEG signals were visually reviewed and classified into one of four categories: background, HFO's (oscillations, Spikes-with-HFO's), Spikes-without-HFO's, and grey areas. Then, EEGs were separated into training and validation sets. Algorithms were applied with different parameters to compute the sensitivity and discovery rates for each patient dataset. The HFO's were correctly identified in certain cases with a method but not with the other.

1.2.2 Pitfalls of high pass filtering for detecting epileptic oscillations: A technical note on "false rippled (C.G. Benar et al, 2009)

EEG recordings of brain activity have proved useful in recent studies for HFO detection and classification. Signals of interest are classified according to their fundamental frequencies into a number of ranges including delta (2-4Hz), theta (4-7Hz), alpha (7-13Hz), beta (13-25 Hz), gamma (30-100 Hz), and higher frequencies (200-500 Hz), which include ripple and fast ripple signals. Normal ripples are different from pathological ones in their frequency range and location. Recorded signals, however, lose some frequency components when filtered. By the same token, some signal components are not band-limited and their energy may spread over very wide ranges. To study the effects of such signals, the authors simulate Gaussian spikes, sinusoidal oscillations, triangular spikes, and triangular oscillations. They also recorded signals from rats. Both simulated and rat signals were filtered with a band edge set at multiple frequencies: 40 Hz (low gamma band), 80 Hz (high gamma band), and 250 Hz (fast ripple band). For anti-aliasing, they low-pass filtered signals at 600Hz. Authors show that the presence of sharp transients and harmonics of non-sinusoidal signals, may introduce artifacts in filtered signals that are very similar to HFOs and raise the false positive detection rate of automatic detection algorithms. This should not affect the results of visual inspection, as reviewers compare filtered and raw signals to ensure identification of only true HFOs.

1.2.3 Automatic detection of fast oscillations (40-200 Hz) in scalp EEG recordings (Nicolas Von Ellenrieder et al, 2012)

Von Ellenrieder et al. define fast oscillations (FOs) as having frequencies above the low gamma range and they propose a two-stage algorithm for automatic FO detection in scalp EEGs. Their definition of FOs is consistent with HFO definitions by other authors, except for focusing on events in the 40—200 Hz range, i.e., the high-gamma to low-ripple range, which they refer to as the broadband. The first stage of their algorithm extracts events from the background and the second stage classifies FOs while ignoring artifacts. The first stage detects approximately sinusoidal signal segments as RMS power increments within 10Hz bands. This produces greater, more detectable increments than changes over the whole broadband and reduces the number of false positives. Detector performance is evaluated against the performance of an expert in terms of finding events at the same time and channel with the goal of determining whether their detector would provide automatic support for finding the epileptogenic zone, which would be related to the channels with a high number of FOs.

1.2.4 A comparison between detectors of high frequency oscillations (R. Zelmann et al, 2012)

Zelmann et al. state that HFOs can be detected in the epileptogenic zone during interictal periods and they may be accompanied by spikes. This leads to a higher identification of HFOs within SOZs than in any other areas in the brain, which indicates the location in the brain where epileptic seizures originate. The authors sampled EEG signals from intractable epileptic patients at 2KHz and filtered them at 500Hz to detect HFOs. Data from 45 patients was gathered, but 20 were randomly selected and one was excluded due to artifacts. Two experienced reviewers visually

identified HFOs in the 80—250Hz range as ripples and in the 250—500Hz range as fast ripples. HFOs found by reviewers were used as the gold standard to determine automatic detector performance. Three previously designed detectors, referred to by Zelmann as the RMS detector, the Line Length detector, and the Hilbert detector, were compared against a detector designed at Montreal Neurological Institute (MNI). The utilized automatic detectors find events by comparison of the signal energy level vs. a per-detector threshold within EEG epochs. While detectors where designed for different HFO-generating brain regions, energy thresholds, and event morphologies, they all improve when tuned for the test dataset and using the same filters.

1.2.5 Automatic detection and classification of high-frequency oscillations in depth-EEG signals (Nisirine Jrad et al, 2017)

Authors present an HFO detector classifier for gamma (30—80Hz), high-gamma (80—120Hz), ripples (120—250Hz), and fast ripple (250—600Hz) EEG signals. Using event energy ratios and duration for detection and a support vector machine (SVM) for classification, the algorithm finds HFOs and rejects artifacts, which results in a low FDR. A Gabor transformation is applied to EEGs to determine their components in each band of interest. Then the Gabor RMS energy of each band is used to find events longer than 6.5 ms and over an optimal threshold. Finally, events found are classified based on their energy ratio using a SVM. Compared to Staba's RMS detector [25], this detector classifier achieves a higher sensitivity and a lower false detection rate.

1.2.6 Estimating the dominant frequency of high frequency oscillations in depth EEG signals (M. Shamas, 2017)

The authors evaluate methods to determine the dominant frequency of HFOs to enable keeping their morphological and spectral features, which may be related to the cortical regions that generated the HFOs. Using a biophysical simulation model, the authors can tune the oscillation frequency of epileptic patches in the model to generate synthetic HFOs for algorithmic performance analysis of estimators. They conclude that the HFO median frequency suffices to find its dominant frequency, but they warn that energy of slow components will shift down the median frequency.

1.2.7 The viability of high-frequency oscillations analysis in EEG signals for seizure prediction (B.D Kern, 2016)

People affected by epilepsy are about one percent of the world population. To avoid having to deal with seizures, epileptic medication may help up to 80% of the patients. For the rest, brain surgery is their next possible option. About ten percent may be successfully treated with surgery. Remaining patients have no other means of eliminating their seizures. In this case, seizure prediction could provide an alternative for those who cannot undergo surgery. If available, seizure prediction could be useful for imminent seizure suppression. To determine whether HFOs can be used as preictal correlates of imminent seizures for a reliable seizure prediction, Kern uses the Ripplelab implementation of the MNI detector to locate potential HFOs in EEG recordings. His dataset includes EEGs recorded during slow wave sleep, which includes a number of seizures, and interictal EEG recordings when the patient is awake. HFOs detected by the MNI detector are manually verified. This ensures a correct identification and classification of HFOs since a high

sensitivity is used for automatic detection and this produces a large number of false positives. In addition, preprocessing was used to search and find the SOZ using intracranial grid electrode recordings. Since the dataset comprises many hours of recordings with a full grid, looking for HFO's in data from electrodes next to or within an SOZ reduces significantly the amount of data to process.

1.2.8 Assessing performance of detectors of high frequency oscillations in EEG Signals (Deeksha Seethrama Bhat, 2018)

The gold standard for HFO detection is visual inspection of EEG recordings by trained neurologists. However, this is a very slow and unreliable process as many hours of recordings must be analyzed to find events lasting milliseconds and determinations always differ among groups of experts. This led to the development of algorithms for automatic HFO detection, which started gaining ground within the last few years [11]. Seetharama's work focuses on performance assessment of HFO detectors and the possibility of automatic detection using MATLAB and Alexnet, a deep-learning neural network trained for image classification [REF]. Ripplelab enables visual inspection of EEG signals and provides four automatic HFO detectors. Two detectors were chosen for her work: the Montreal Neurological Institute (MNI) detector and the Short Time Energy (STE) detector. Raw signals from the Epilepsiae database [8,9] were detrended and high-pass filtered before using them for HFO detection with Ripplelab. While filtering is necessary, care must be taken to avoid artefactual HFOs produced by the process of filtering the signals [10]. Ripplelab detector parameters can be adjusted based on EEG signal and target HFO characteristics.

Chapter 2: Theoretical Foundation

This chapter introduces background information including the electroencephalogram (EEG) which is used to record electrical activity of the brain, EEG signal frequency bands which crucial for the discussion and analysis of HFO detection and classification, the SOZ which is a brain region where seizures originate, and cumulative sum computations as a means for HFO detection.

This chapter introduces background information including the electroencephalogram (EEG) which is used to record electrical activity of the brain, EEG signal frequency bands which crucial for the discussion and analysis of HFO detection and classification, the SOZ which is a brain region where seizures originate, and cumulative sum computations as a means for HFO detection.

2.1 HFO Frequency Bands

During brain activity, neurons send electrical pulses for communication with other neurons. They communicate normally when the subject is awake and reduce communication when the subject is asleep. Such communication signals can be detected as aggregate biopotentials by an electroencephalogram (EEG). EEG frequencies vary depending on the action being performed by the subject. HFOs are comprised of ripples (80-250Hz) [12] and fast ripples in the range above 250Hz. There is a likelihood that HFO's are non-exclusively generated by multiple mechanisms at the cellular level. HFO frequencies also depend on the activity being done by the individual. Human cognition has been studied predominantly in the gamma range (30-100Hz). For instance, high frequency oscillations are associated with cognitive processing in human recognition memory [13]. Information retrieved within this frequency range shows neurons that deal with attention, the ability to learn, and memory. For this research, the range considered will include HFOs in the 80Hz-500Hz range.

Clinical EEGs signals are in a lower range including infraslow signals (<0.5Hz), delta (0.5-3Hz), theta (3-8Hz), alpha(8-12Hz), and beta (12-38Hz). Notice that different authors may slightly modify these signal ranges. Infraslow waves of interest, which are difficult to detect due to filtering, oscillate about once per minute and interact with various neural functions that affect cognition states when an individual is awake or asleep [28]. Delta signals are the slowest clinical signals. The deepest period of sleep is called non-REM sleep. These signals are mainly generated and predominate during this stage of sleep, which is why they are also known as deep sleep waves [14]. Theta signals have basic roles dealing with the process of cognition, appear corticohippocampal, and play an important role for signaling microconnections that deal with learning [15]. During the rapid eye movement (REM) sleep stage, these signals mainly deal with dreams and imagination. Alpha signals help with association throughout the brain; 10 Hz trains resonate through several brain structures. Alpha signals also deal with the state of mind and can be seen when an individual is calm and relaxed. Beta signals are involved with movement and are linked with the GABA neurotransmitter (gamma aminobutyric acid). GABA is distributed throughout cortical neurons and contributes with functions such as motor control and vision. These signals also deal with focus for problem solving and decision making. Lower gamma frequencies have been found in an infant's brain as young as four months old when testing brain responses to photographs [16]. The lower gamma signals range from 38Hz to 70 Hz and deal with information processing.

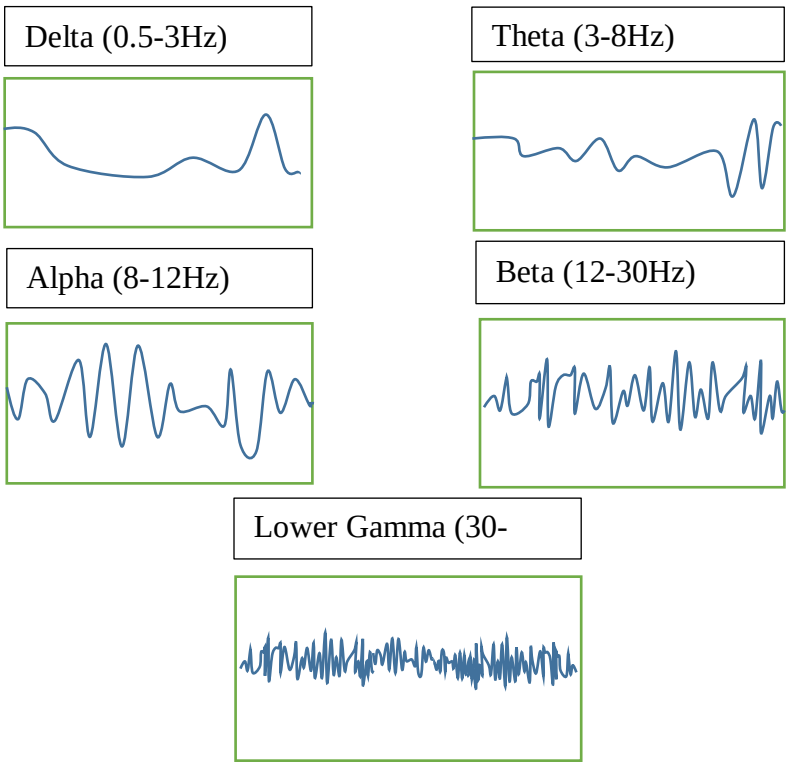


Figure 2.1: Clinical EEG waves

Signals to be tested for this research range from 80Hz to over 500Hz. These visible HFO's will be referred to here as either ripples in the 80-250Hz range or fast ripples in the 250-500Hz range. As mentioned in Chapter One, Bryan Kern found correlation between HFOs and epileptic events. Other studies have shown that HFOs are associated with seizures (High-frequency oscillations (HFO's) in clinical epilepsy, J. Jacobs et al). These ictal HFOs have been determined to reside as locally generated cortical signals that correlate with the SOZ along and seizures.

For HFO detection, authors recommend a sampling rate four times the highest frequency of interest or, preferably, 2KHz or above [7]. They define HFOs as events with at least four consecutive oscillations clearly above baseline in the 80—500Hz range. Alternatively, HFOs have been

defined as an RMS amplitude greater than 5 standard deviations (SD) above background, lasting at least 6ms, and having at least 6 peaks greater than 3 SDs above the mean baseline. Automatic HFO detectors are key for the systematic study and clinical use of HFOs.

2.2 Electroencephalogram

Electroencephalography is an imaging technique High Frequency for recording electrical brain signals or biopotentials to help in the analysis of physiology and pathology of the brain. Signal waves differ based on the state of the brain. In relation to the present work, EEG signals show the amount of high frequency activity [7], EEGs can be recorded non-invasively from the scalp of the subject or invasively from cortical or depth electrodes, which are used when readings from deep structures such as the hippocampus are needed. Invasive EEGs are usually needed to identify the epileptic cortex when a patient is being considered for surgery to treat epilepsy.

2.2 Seizure Onset Zone

The area on the brain from which seizures originally propagate is called the seizure onset zone (SOZ). The amount of gamma and fast ripple waves increases within the SOZ [18]. Electrode positioning that includes the SOZ is used for identifying the right location for surgery. Then the electrodes from the EEG can then be used as a marker for the location of the SOZ.

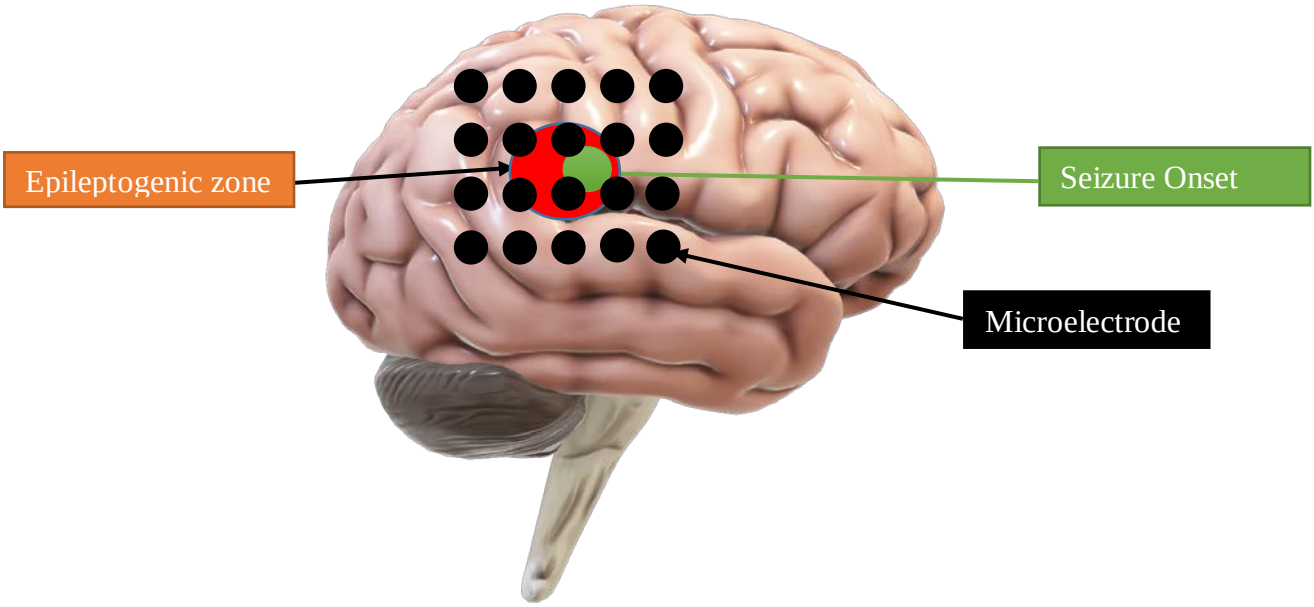


Figure 2.2: Epileptogenic Zone (EZ) and Seizure Onset Zone (SOZ)

2.4 Cumulative Sum

For this work, a cumulative sum is a sequence of partial sums of a function of an EEG signal channel. Given a channel and a function S(•) of its values. The cumulative sum of S(k), k = 1, n, is the sequence $\{S_1,\ S_1 + S_2, S_1 + S_2 + S_3, \ldots\}$. In essence, each partial sum P_k in the sequence is computed as $P_k = \sum_{n=1}^{k} S_n$. In our case, we are interested in defining an S(•) for change point analysis to detect HFOs. Specifically, we are looking for changes in the mean of the signal RMS energy. Thus, the cusum sequence we will use has terms defined as $S_k = S_{k-1} + (X_k - \bar{X})$, where $\bar{X} = \frac{1}{n}\sum_{i=1}^{n} x_i$ is the arithmetic mean of the channel signal. In addition, the sequence will include an initial term $S_0 = 0$. Not knowing the underlying physiological and pathological processes that generate signal values and without loss of generality, we will assume that each channel signal is a sequence of independent identically distributed zero-mean Gaussian variables. To detect HFOs, we must set a change threshold θ_h which, like in the case of energy threshold detector covered in Chapter one, may be a function of the channel standard deviation. However, in this case we will be using the standard deviation of the change in signal mean. To be conservative, we will use three standard deviations to detect HFOs. Since the computed cumulative sums will be partial sums of the differences between the signal RMS energy and the channel mean RMS energy, when energy is above average, the cusum will increase. Thus, positive slopes of the cusum will occur during periods when energy tends to be above average. Once the cusum crosses the HFO detection threshold, we will assume the signal contains a potential HFO which will be referred to in general as an event. Based on the cusum definition, the beginning of each event will the previous point in the sequence where the cusum had a local minimum. For ease of visual verification of events found through cusum computation, its values can be plotted as $S'_k = S_k - \theta_h$ in order to quickly identify all positive cusum values as values over the detection threshold.

To further simplify computations, we will use the implementation of cusum available in MATLAB. A cumulative sum as used in MATLAB shows the cumulative sum of the elements of an array. The elements that are plotted will be shown in ranges and will spot the element that will have drifted more than one standard deviation away from the norm.

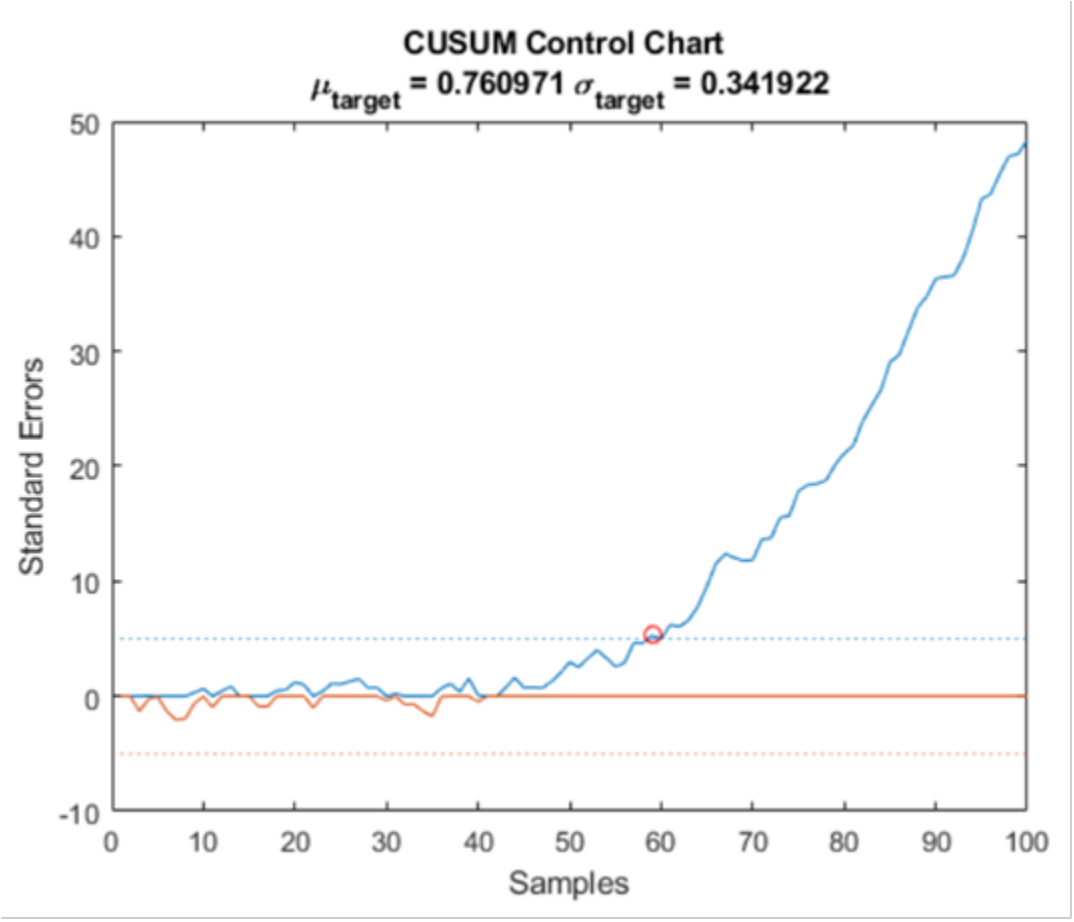


Figure 2.3: Cusum Chart showing increasing standard errors

Chapter 3: Methodology

Given that the gold standard for HFO detection is the result of expert visual classification, different algorithms have different underlying assumptions about EEG data and have been tested with different datasets, and neither the definition of HFO nor detection performance criteria are the same across all studies, no automatic detector has been proven infallible. Thus, the approach followed in this work is to add a cusum detector to the set of available detectors, given it is not a simple energy threshold detector, with an aim to diversify detection approaches and to identify a set of the detectors to use for increased robustness with respect to results from any single detector. This section starts by describing the database used for seizure detection testing. Next Ripplelab is discussed to understand the other classifiers used here and how they work. Finally, we will describe a consensus function to leverage results from the different classifiers in order to produce the best HFO detection performance achievable with them. Classification will be based on results obtained with Ripplelab and the MATLAB cusum function.

3. 2 Cumulative sum implementation

The Page-Hinkley algorithm (PHA) uses the cumulative sum to detect changes in the mean of a sequence. According to [19] this method in combination with the Gabor transformation of EEG signals is more accurate than previously used HFO detectors. PHA uses a cumulative sum to compute a signal moving average to detect HFOs as hypotheses testing on a piecewise stationary sequence energy. Where $\varepsilon_{(Tot)}(t)$ is the piecewise stationary energy sequence, and $u(t)$ is the mean of the piecewise stationary sequence energy at time t and $\phi_{(Tot)}(t)$ is a sequence of mutually independent random variables with zero mean. Thus, we obtain the following:

$$\varepsilon^{(Tot)}(t) = \mu(t) + \phi^{(Tot)}(t)$$

$$m(t_c) = \sum_{t=1}^{t_c} \left(\varepsilon^{(Tot)}(t) - \mu_0 - \frac{\delta_P}{2} \right).$$

Figure 2.4: Page Hinkley Equations

where m(0) = 0.

3. 3 Ripplelab

HFO detection algorithms are based on computationally intense, somewhat intricate procedures to correctly detect events and classify them as HFOs when meeting followed criteria. A research group of Colombia developed the Ripplelab MATLAB application to simplify use of HFO detection algorithms. Ripplelab provides implementations of the four detectors analyzed in [3] EEG signal plotting, and support for manual visual detection of HFOs. Included detectors are the short-time energy algorithm (STE), the short line length algorithm (SLL), the Hilbert transform algorithm (HIL), and the Montreal Neurological Institute detector (MNI). From these detectors, the MNI and STE detectors will be used for research purposes. The STE detector consists in band-passing an EEG signal within a high frequency range and using Root Mean Squared (RMS) to compute the signal energy. A selectable number of standard deviations are defined in order to detect potential HOF events. Depending on whether RMS energy or wavelet entropy is used, the MNI detector can detect events either using an energy baseline or using activity from channels with continuous high-frequency activity.

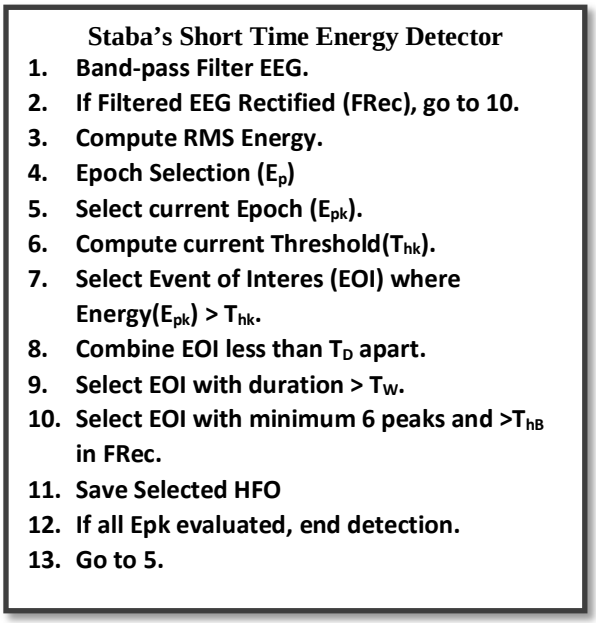


Figure 3.2: STE detector flow

MNI Wavelet Energy Detector

1 Band-pass Filter EEG.
2 If RMS Energy, go to 7.
3 Autocorrelation.
4 Wavelet Entropy (WEn).
5 Baseline Detection, WEn > Th_{WE}.
6 If Baseline > T_B, go Detect Events with Baseline.
else go to 9. Detect Events with Cont. HF Activity.
7 Compute RMS Energy.
8 If Baseline, go Detect Events with Baseline.
9 Epoch Selection (E_{CC})
10 Select current Epoch (E_{CCk}). $S_{CCk} = E_{CCk}$
11 Compute current Threshold (T_{hCCk}).
12 Select EOI. Energy(S_{CCk}) > (T_{hCCk}).
13 If New EOI Detected,
13a. Remove EOI Segments
13b. Update $S_{CCk.}$
13c. go to 11.
Else
13d. Select EOI. Energy(S_{CCk}) > (T_{hCCk}).
13e. Combine EOI less than T_D apart.
13f. Select EOI with duration > T_W.
14 Save Selected HFO
15 If all E_{CCk} evaluated, End detection.
16 Go to 10.

MNI Detect Events with Baseline

1. Epoch Selection (E_{CB})
2. Select current Epoch (E_{CBk}).
3. Compute current Threshold (T_{hCBk}).
4. Select EOI. Energy(S_{CBk}) > (T_{hCBk}).
5. Combine EOI less than T_D apart.
6. Select EOI with duration > T_W.
7. Save Selected HFO
8. If all E_{CBk} evaluated, End detection.
9. Go to 2.

Figure 3.3: MNI Wavelet Energy Detector and Baseline

Chapter 4: Experiments

Two experimental studies are included in this work. The first one is a continuation from work done by Bryan Kern [8] and Deeksha Seetharama-Bhat [9]. The second one processes patient data with a cusum detector for comparison against Ripplelab outputs.

Study 1 – Using the detectors from Ripplelab for detection in 20-minute intervals

Work by B. Kern had located the SOZ of the patient under a small subset of grid electrodes that were subsequently used for the rest of his work, Deeksha Seetharama-Bhat's, and the present work. D. Seetharama-Bhat's research was based on automatic HFO classification with Ripplelab's MNI and the STE detectors. Using 2500Hz Epilepsiae EEG data, she found that the total with both detectors included more events with more true HFOs than by using any of these detectors alone. Events found were compared by time stamp and raw signal shape to determine whether they had been detected by only one detector or by both. In some instances, the MNI detector outperformed the STE detector, but combining results from both detectors was an improvement in general.

Study 2- Applying the Cusum detector.

D. Seetharama-Bhat used the MNI and the STE detectors implemented in Ripplelab. Likewise, for this study we incorporated the same detectors to compare event detection results after processing through those detectors against results obtained through the cusum detector being evaluated in this work. B. Kern [8] and D. Seetharama-Bhat [9] chose five electrodes located on the SOZ. The same electrodes are being used to evaluate the cusum detector for identification of events and true HFOs. Preictal detection periods used by Kern and Seetharama were 20 minutes and 40 minutes, respectively. In this work we chose a 15 min. preictal period. After testing results with 40 min. and 20 min. detection periods, Seetharama-Bhat did not find a significant difference for detecting the

preictal period and did the rest of her work with a 20 min. period. After all, the main goal of her work was to compare detector performance independently and in combination, not to determine the possibility of seizure prediction through detection of a preictal period, which was Kern's goal. With our dataset, Seetharama-Bhat found that the MNI algorithm detects more events than the STE algorithm, yet it also misses some events detected by the latter. For this research we aim to evaluate the detection performance of the cusum detector and its potential for supporting research based on HFO detection. The EEG dataset created by Seetharama-Bhat was used as the basis for this research to accomplish a meaningful comparison of detector performance against her results. The cumulative sum detector was implemented using the vector cusum function in MATLAB as a building block.

For the second study we first converted data into a ".mat" file to simplify computations with MATLAB software. A total of eight recordings from the dataset that were used. Recordings were all separated into individual channels to compute their cumulative sum. Next, a cumulative sum with 5 standard deviations was calculated. Each channel signal was individually processed in 1 min. segments. We used the cumulative function to detect changes in the mean RMS energy of the signal by plotting the cusum results and to inspect the graph looking for these changes. Positive slopes in the plot would mean a change in the mean that could indicate a potential HFO event.

Since filtering may introduce artifacts and false events in a signal [9, 10] this approach allows artifact identification and prevents false detections as well. One of the first channels processed with the cumulative sum detector is shown in Figure XX. In the first 1000 iterations there is a part between 200 and 300 where the output shows a steep positive slope that indicates an event, i.e., a potential HFO.

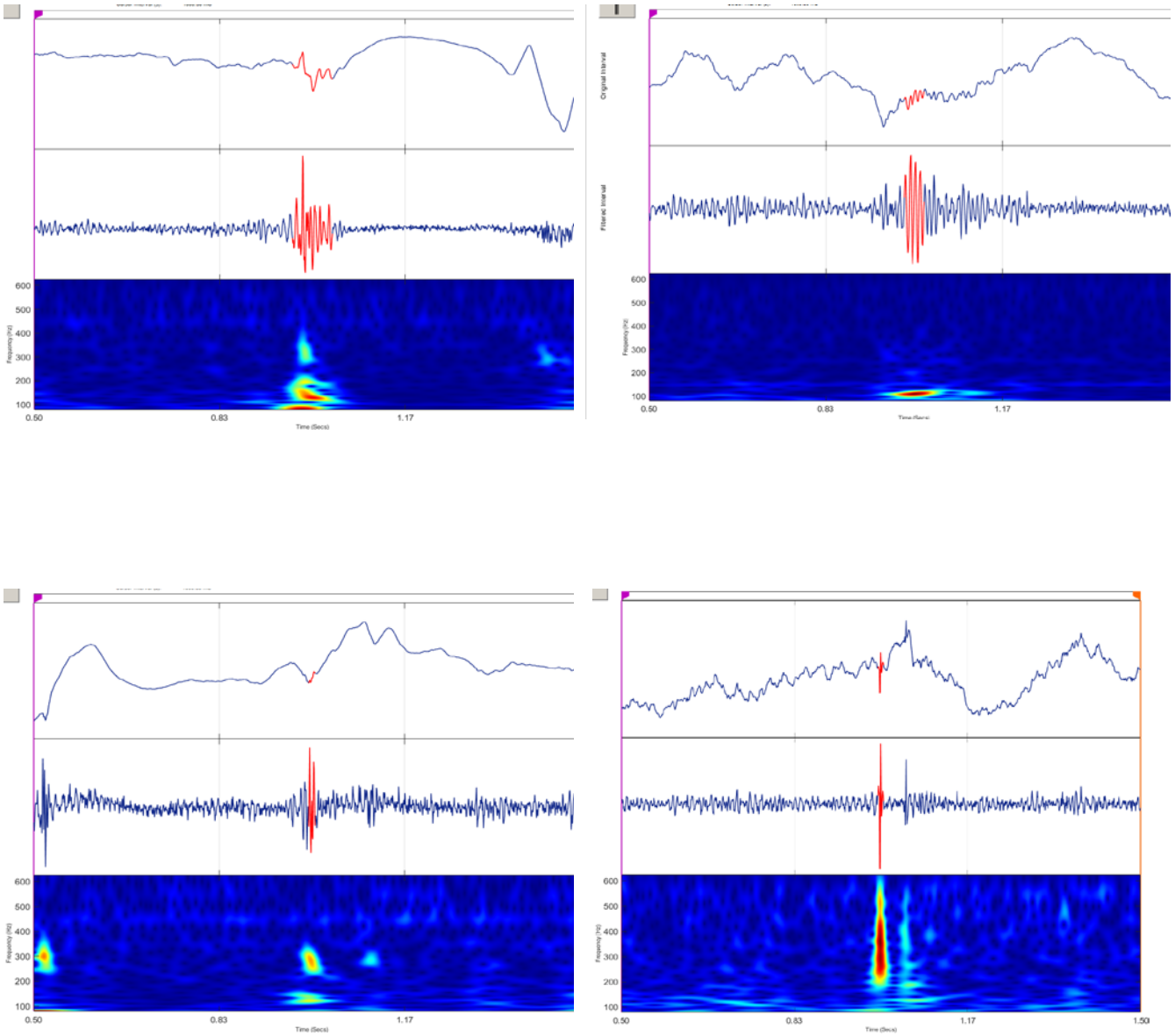
4.1 HFO Detection

The MNI detector uses two different thresholding techniques for event detection. The first one detects a signal baseline based on wavelet entropy over a threshold. The second one is for signals that contain no baseline. The MNI detector defaults to a threshold of 99.9999% for a detected baseline, and to 95% for signals without a baseline. However, the user can change the parameters for the thresholds of each type of signal. Seetharama-Bhat found that using a 98% threshold with a baseline of 95% worked best for our dataset to detect events with a relatively low impact from signal noise. For this reason, we will use the same detection parameters for this research. The STE detector has an RMS window of 3 seconds with a 6ms epoch time, a minimum of 6 peaks, and 5 standard deviations above the background RMS energy for event detection. Ripplelab also allows users to set filter parameters.

4.2 Event Analysis for HFO detection

Using the given parameters, each detector can find events automatically. Each detected event is considered as a candidate event to be visually inspected for rejection or HFO identification. Considering detector differences in algorithms, parameters, and assumptions about the probability density functions of EGG signals, coincidence of event detection by multiple detectors is expected to ultimately achieve enough robustness to obviate the need for expert visual confirmation – the main difficulty for a true automatic detection of HFOs for research and clinical application. For the purpose of this work, detector outputs will be tested to determine their degree of agreement on event detection. Visual inspection will still be used to reject or confirm events and HFOs from the different detectors. Having all the detectors coincide on events with a low false detection rate will lead to possible automatic detection requiring a minimal if not null visual inspection.

For consistency with previous work by Kern and Seetharama-Bhat, detected events will be classified as HFO if they have at least 4 oscillations clearly visible above the background [3, 7, 9] with a duration of at least 25 ms [3,7].



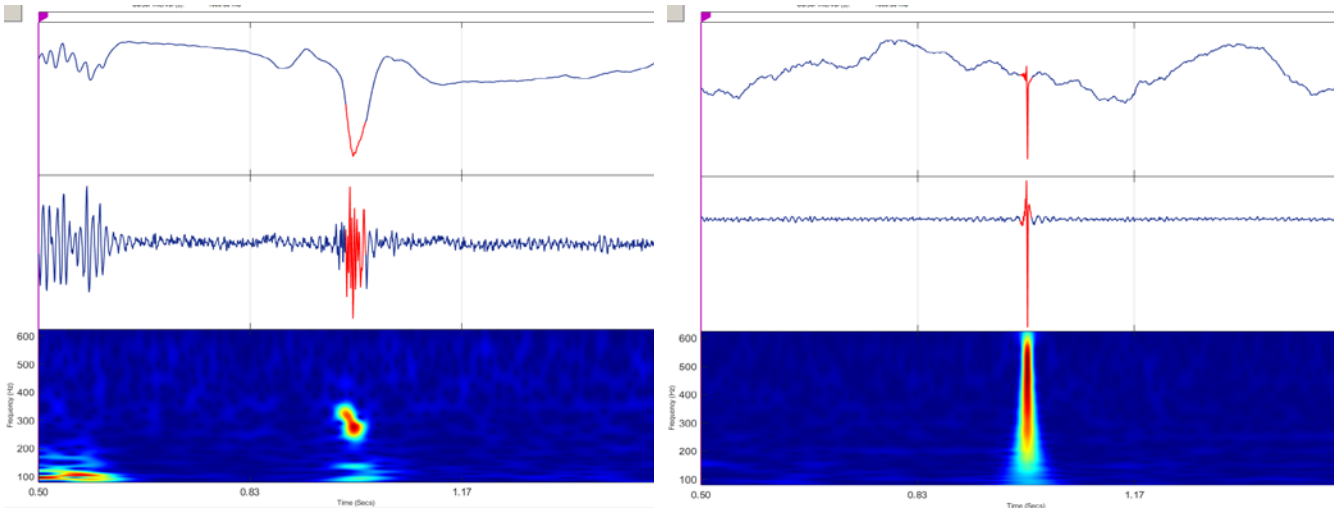


Figure 4.1: Accepted and Rejected events (Top two Accepted, Middle two rejected, last two accepted and rejected respectively)

Chapter 5: Results

In study 1 we noticed that the MNI detector was able to detect more candidate events and HFOs than the STE detector. In agreement with the Ripplelab detectors, the cusum detector found changes of mean RMS energy for several events. Variations in results, as in previous work, were introduced by variations in dataset signals, detection algorithms, and processing parameters. Detection results are shown in the following table. In study 2, the cusum detector identified more events than the other detectors in channel B7 as shown in the following table. However, the MNI detector sets an upper bound on the number of events over which all detectors agree. The time for seizure one to be processed by the MNI detector was 16 minutes with 12 seconds with the threshold moved to 150-500 Hz. The STE detector took 33 seconds with the same frequency limits. For Seizure 2 the MNI detector took 21 minutes and 47 seconds at the same threshold while the STE detector took only 34 seconds. For seizure 3 the MNI detector took 41 minutes to be processed. Many of the processes varied between these times, while the cusum was almost always less than a minute to output. However, the cusum method implemented did need to be visually identified in order to distinguish actual events and to be able to compare with the MNI and STE detectors. The detectors are from Ripplelab which shows the event with the time stamp. For the cusum since it's a method being used outside of Rippleab has to have visual identification and correlation of samples with Ripplelab time. The algorithm was not so complex in order to let computations run smoothly and fast.

Table 5.1: Average Findings Through Detectors in study 1

	Av.MNI	Av.STE	Av. cumsum	Av.Common in all
B6	22	15.2	30	22.4
B7	22.4	21.2	39.2	27.6
B8	16	21	29	22
D7	32	16.4	32.2	26.9
F2	47.4	60.2	65	57.5

Table 5.2: MNI and STE comparison in study 2

Seizure 1	MNI	STE	Common in both
B6	55	32	3
B7	83	30	1
B8	28	15	1
D7	88	34	2
F2	116	88	3

Table 5.3: Cusum and MNI comparison in study 2

Seizure 1	MNI	Cusum	Common in bpth
B6	55	18	6
B7	83	49	13
B8	28	46	10
D7	88	28	17
F2	116	72	42

Table 5.4: Cusum and STE comparison in study 2

Seizure 1	Cusum	STE	Common in both
B6	18	32	5
B7	49	30	1
B8	46	15	1
D7	28	34	15
F2	72	88	31

Conclusion and future work

The cusum detector, which is based on the detection of changes in the RMS energy mean, was used to detect events and HFOs in a dataset with 2500Hz EEG signals of an epileptic patient. The cusum detector performance was evaluated against performance previously obtained with the same dataset using the MNI and STE detectors in Ripplelab. Event detection agreement between detectors was based on comparison of raw signal shape and event time stamp. Output from the cusum detector was plotted for verification through visual inspection. Few events were shared by all three detectors, which indicates that a combination of results from the three detectors may be better than any single detector [9], but stating this as a general conclusion will require additional testing and data from more epileptic patients. MNI and STE had even fewer common events making the cusum a better alternative to use with the other two detectors. The MNI was the detector that was able to detect the most events while also having 50% or more wrongly classified events [8] making the use of a combination of these detectors more crucial. The contribution to this research is that while other works were able to introduce an energy thresholding technique [19], this one deals with the average change in a signal. Future work will include further exploration of the cusum detector with additional data and algorithmic modifications with the goal of achieving truly automatic HFO detection through agreement of a number of detectors for true HFO identification and rejection of false HFOs. The implementation of the cusum in this research was kept simple with an aim to implement it for portable devices while maintaining its fast and robust detection.

References

[1] Ellenrieder, Nicolás von, Luciana P. Andrade-Valença, François Dubeau, and Jean Gotman. "Automatic Detection of Fast Oscillations (40-200 Hz) in Scalp EEG Recordings." *Clinical Neurophysiology: Official Journal of the International Federation of Clinical Neurophysiology* 123, no. 4 (April 2012): 670–80.

[2] Gloss, David, Sarah J. Nolan, and Richard Staba. "The Role of High-Frequency Oscillations in Epilepsy Surgery Planning." *The Cochrane Database of Systematic Reviews*, no. 1 (January 15, 2014): CD010235.

[3] Zelmann, R., F. Mari, J. Jacobs, M. Zijlmans, F. Dubeau, and J. Gotman. "A Comparison between Detectors of High Frequency Oscillations." *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology* 123, no. 1 (January 2012): 106–16.

[4] Navarrete, Miguel, Catalina Alvarado-Rojas, Michel Le Van Quyen, and Mario Valderrama. "RIPPLELAB: A Comprehensive Application for the Detection, Analysis and Classification of High Frequency Oscillations in Electroencephalographic Signals." *PloS One* 11, no. 6 (2016): e0158276.

[5] Jrad, Nisrine, Amar Kachenoura, Isabelle Merlet, Fabrice Bartolomei, Anca Nica, Arnaud Biraben, and Fabrice Wendling. "Automatic Detection and Classification of High-Frequency Oscillations in Depth-EEG Signals." *IEEE Transactions on Biomedical Engineering* 64, no. 9 (September 2017): 2230–40.

[6] Shamas, Mohamad, Isabelle Merlet, Anca Nica, Pascal Benquet, Mohamad Khalil, Wassim El Faou, and Fabrice Wendling. "Estimating the Dominant Frequency of High Frequency Oscillations in Depth-EEG Signals." In *2017 Fourth International Conference on Advances in Biomedical Engineering (ICABME)*, 1–3, 2017.

[7] Zijlmans, Maeike, Premysl Jiruska, Rina Zelmann, Frans S. S. Leijten, John G. R. Jefferys, and Jean Gotman. "High-Frequency Oscillations as a New Biomarker in Epilepsy." *Annals of Neurology* 71, no. 2 (February 2012): 169–78.

[8] Kern, Bryan David. "The Viability of High-Frequency Oscillation Analysis in EEG Signals for Seizure Prediction." *ETD Collection for University of Texas, El Paso*, January 1, 2016, 1–64.

[9] Bhat, Deeksha Seetharama. "Assessing Performance of Detectors of High Frequency Oscillations in EEG Signals." *ETD Collection for University of Texas, El Paso*, January 1, 2018, 1–69.

[10] Bénar, Christian, L. Chauviere, Fabrice Bartolomei, and Fabrice Wendling. "Pitfalls of High-Pass Filtering for Detecting Epileptic Oscillations: A Technical Note on 'False' Ripples." *Clinical Neurophysiology* 121 (2010): 301–10.

[11] Chander, Rahul. "Algorithms to Detect High Frequency Oscillations in Human Intracerebral EEG," n.d., 130.

[12] Frauscher, Birgit, Nicolás von Ellenrieder, Rina Zelmann, Christine Rogers, Dang Khoa Nguyen, Philippe Kahane, François Dubeau, and Jean Gotman. "High-Frequency Oscillations in the Normal Human Brain." *Annals of Neurology* 84, no. 3 (2018): 374–85.

[13] Kucewicz, Michal T., Jan Cimbalnik, Joseph Y. Matsumoto, Benjamin H. Brinkmann, Mark R. Bower, Vincent M. Vasoli, Vlastimil Sulc, et al. "High Frequency Oscillations Are Associated with Cognitive Processing in Human Recognition Memory." *Brain : A Journal of Neurology* 137, no. Pt (2014): 2231–44.

[14] Erbs, Eric, Lauren Faget, Gregory Scherrer, Audrey Matifas, Dominique Filliol, Jean-Luc Vonesch, Marc Koch, et al. "A Mu–Delta Opioid Receptor Brain Atlas Reveals Neuronal Co-Occurrence in Subcortical Networks." *Brain Structure & Function* 220, no. 2 (2015): 677–702.

[15] Basu, Jayeeta, and Steven A. Siegelbaum. "The Corticohippocampal Circuit, Synaptic Plasticity, and Memory." *Cold Spring Harbor Perspectives in Biology* 7, no. 11 (November 2, 2015).
[16] Grossmann, Tobias, Mark H. Johnson, Teresa Farroni, and Gergely Csibra. "Social Perception in the Infant Brain: Gamma Oscillatory Activity in Response to Eye Gaze." *Social Cognitive and Affective Neuroscience* 2, no. 4 (December 2007): 284–91.
[17] Jacobs, J., R. Staba, E. Asano, H. Otsubo, J. Y. Wu, M. Zijlmans, I. Mohamed, et al. "High-Frequency Oscillations (HFOs) in Clinical Epilepsy." *Progress in Neurobiology* 98, no. 3 (September 2012): 302–15.
[18] Andrade-Valenca, L.P., F. Dubeau, F. Mari, R. Zelmann, and J. Gotman. "Interictal Scalp Fast Oscillations as a Marker of the Seizure Onset Zone." *Neurology* 77, no. 6 (August 9, 2011): 524–31.
[19] Jrad, Nisrine, Amar Kachenoura, Anca Nica, Isabelle Merlet, and Fabrice Wendling. "A Page-Hinkley Based Method for HFOs Detection in Epileptic Depth-EEG," 1295–99, 2017.
[20] Litt, Brian, and Javier Echauz. "Prediction of Epileptic Seizures." *The Lancet Neurology* 1, no. 1 (May 1, 2002): 22–30.
[21] Matsumoto, Andrew, Benjamin H. Brinkmann, S. Matthew Stead, Joseph Matsumoto, Michal T. Kucewicz, W. Richard Marsh, Frederic Meyer, and Gregory Worrell. "Pathological and Physiological High-Frequency Oscillations in Focal Human Epilepsy." *Journal of Neurophysiology* 110, no. 8 (October 2013): 1958–64.
[22] Staba, Richard J. "Normal and Pathologic High-Frequency Oscillations." In *Jasper's Basic Mechanisms of the Epilepsies*, edited by Jeffrey L. Noebels, Massimo Avoli, Michael A. Rogawski, Richard W. Olsen, and Antonio V. Delgado-Escueta, 4th ed. Bethesda (MD): National Center for Biotechnology Information (US), 2012.
[23] Roehri, Nicolas, Francesca Pizzo, Fabrice Bartolomei, Fabrice Wendling, and Christian-George Bénar. "What Are the Assets and Weaknesses of HFO Detectors? A Benchmark Framework Based on Realistic Simulations." *PloS One* 12, no. 4 (2017): e0174702.
[25] Staba, Richard J., Charles L. Wilson, Anatol Bragin, Itzhak Fried, and Jerome Engel. "Quantitative Analysis of High-Frequency Oscillations (80-500 Hz) Recorded in Human Epileptic Hippocampus and Entorhinal Cortex." *Journal of Neurophysiology* 88, no. 4 (October 2002): 1743–52.
[26] Khalilov, Ilgam, Michel Le Van Quyen, Henri Gozlan, and Yehezkel Ben-Ari. "Epileptogenic Actions of GABA and Fast Oscillations in the Developing Hippocampus." *Neuron* 48, no. 5 (December 8, 2005): 787–96.
[27] Shamas, Mohamad, Isabelle Merlet, Anca Nica, Pascal Benquet, Mohamad Khalil, Wassim El Faou, and Fabrice Wendling. "Estimating the Dominant Frequency of High Frequency Oscillations in Depth-EEG Signals." In *2017 Fourth International Conference on Advances in Biomedical Engineering (ICABME)*, 1–3, 2017.
[28] Watson, Brendon O. "Cognitive and Physiologic Impacts of the Infraslow Oscillation." *Frontiers in Systems Neuroscience* 12 (October 16, 2018).
[29] "Detect Small Changes in Mean Using Cumulative Sum - MATLAB Cusum."

Vita

Raul Ontiveros was born and raised in El Paso, Texas. The University of Texas at El Paso was his home from 2013 to 2019 from which he was able to complete his bachelor's and master's in the allotted time. His main focus was electrical engineering which his master's was based with a concentration on signals.