A Diagnostic System for Automatic Epiletogenic Zone Localization

Team 23

Adam von Paternos, Paige Murphy, Stephen Schmidt & Shaheer Hassan

Sabato Santaniello, Ph.D.

University of Connecticut, Storrs, CT 06269 USA

***Abstract*— Patients who suffer from drug resistant epilepsy (DRE) may be candidates for resective surgery of epileptogenic zone or where seizures originate. However, the pre surgical screening currently requires several days of gathering iEEG data for clinical review and identified by hand. For this reason, we are proposing to automate the epileptogenic localization process through the use of high frequency oscillations as a biomarker along with a novel ranking index for seizure onset zone (SOZ) identification to assist clinicians with their presurgical iEEG review. Based off of preliminary data, the detection algorithm identifies and is validated from reports of patients who have been previously undergone resection surgery, the electrode channels within and around the resected volume have been identified at a prediction time where the amount of data necessary would significantly decrease the amount of iEEG data, and thus patient recording time needed. The identified zone from this algorithm will run on a Raspberry Pi hardware and upload results, consisting of the identified SOZ along with a brain density map, to Amazon Web Services that can then be accessed via a secure web portal for clinical interpretation**.

Keywords—*Seizure onset zone (SOZ); epilepsy; High frequency oscillations (HFO); detection algorithm*

I. INTRODUCTION

This project is about designing, implementing and testing a system that will assist with the localization of the seizure onset zone (SOZ). The designed system will be unsupervised, use intracranial electroencephalogram (iEEG) signal that is collected at the bedside by a microcontroller, and rely on a newly developed algorithms for SOZ identification based on the occurrence of high frequency oscillation (HFO) events. The system will interface with end users, for example a team of clinicians that are monitoring the patient, via a secure web-based infrastructure to guarantee portability, mobility and security. This project attempts to address the challenges of finding an index for SOZ mapping, deciding a rule for SOZ selection, and determining a time window necessary for SOZ localization.

The SOZ located by this system will be displayed as a color density map of the recording electrode grids to be utilized by a team of trained professionals as an assistive tool in pre surgical screening. Information will then be uploaded to the Amazon S3 storage cloud via Wi-Fi. A specifically designed web portal with secure login credentials will allow for a team of clinicians to access and download the data for display. The overall data flow for this system is shown in Figure 1 below.

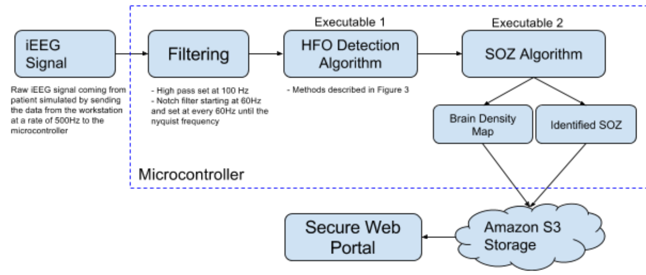

Figure 1*: Overall design schematic*

SOZ localization using current techniques has been proven to be quite difficult through visual inspection of iEEG recordings. For this reason we are attempting to utilize HFOs as a biomarker based off of the reviewed literature, there has been promise for the correlation between these events and SOZ, which may lead to improved surgical specificity and surgical outcomes in patients who undergo resections. [1]

II. METHODS

A. Software

Through peer review the Staba automated HFO detector has been utilized and validated on both short and prolonged iEEG datasets [2] when combined with multiple artifact filtering techniques. [3] These methods are used to identify and select candidate HFO events that will later be used in the spatial localization algorithm to infer the patient's SOZ based on analysis of the HFOs in both time and space. Figure 2 below displays data processing flow through the HFO detection algorithm for this system.

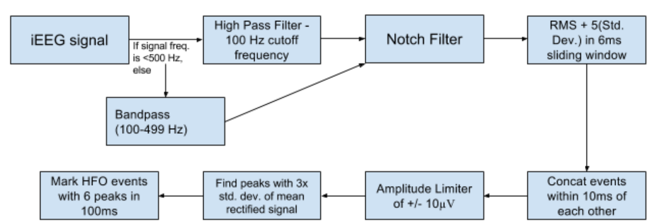

Figure 2*: Flow diagram of HFO detection algorithm*

In order to determine the SOZ, a novel index was implemented based off of each channels frequency of HFOs occurring within each 10 minute window determines the rank of each channel. Utilizing this ranking, an index will be developed for each channel at that respective time stamp as shown in Equation 1 following. Equation 1 is an exponential index based on the current and previous channel ranking where *i* is the time stamp.

$$Index_i = e^{-rank_i+1} * e^{-rank_{i-1}+1} \qquad (1)$$

B. Hardware

The software will be implemented on a Raspberry Pi 2 Model B. The data for the system is first received through a TCP/IP socket. A python script on the Pi listens to the socket streaming data and saves the data in a binary file. The HFO detection algorithm then processes this data. Because the software for the HFO detection was written in MATLab, the design utilizes Simulink in order to create standalone executable files to run on the Raspberry Pi. The design collects 10 minutes of data, saves this data to a file, and then calls the executable as a sub-process. This process then continues until data is exhausted. The processed information from the Raspberry Pi is then transferred to a secure web portal that can be accessed by the consulting physicians for further review.

III. Results and Discussion

To validate the index, a series of statistical analyses were performed. The average indexes over the entire recording of focal channels were analyzed versus non-focal channels as seen in Figure 3. For Study 004-2 the focal channels were identified to be 11, 12, 19, 40, 41, 45-48, 53-56, while the rest were deemed non-focal. These decisions were made based off of the interpretation of the resected areas generalized within the patient reports. As can be seen in the box plot, the discrepancy between average index is significant in magnitude and thus statistically significant.

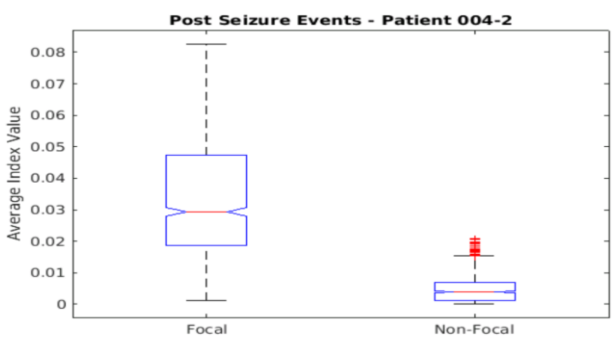

***Figure 3**: Box plot of focal vs non-focal channels*

The resected area was identified and referenced as a golden standard to validate the index. Periods of interictal activity were further investigated to show that the index is seizure independent. Based on these golden standard values found using the previously discussed methods a ROC curve was generated to calculate an AUC for each timestamp of the index throughout the recording. From here a 3-hour average AUC window was tabulated to see the general trend of the index over time. A plot of the AUC values vs time was generated with a 95% confidence interval along with a chance level. This chance level was calculated by randomly changing the vector of index values at every timestamp, 1000 times. From here another ROC analysis was performed on the shuffled average matrix resulting in an AUC value at each timestamp. Again a 3-hour window average was tabulated, which was finally utilized as the chance level. Two standard deviations of the 1000 randomized matrices were utilized to plot the 97% confidence interval of this chance value.

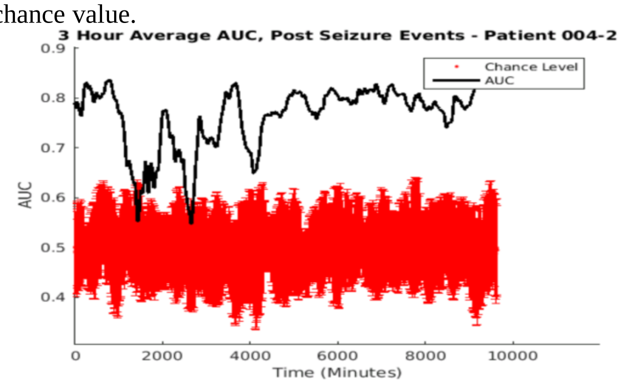

***Figure 4**: Moving AUC plot with chance level 3 hours post seizure activity*

Following these statistical validation plots, the index was plotted and colored for each channel over time. This plot can be seen in Figure 5 below.

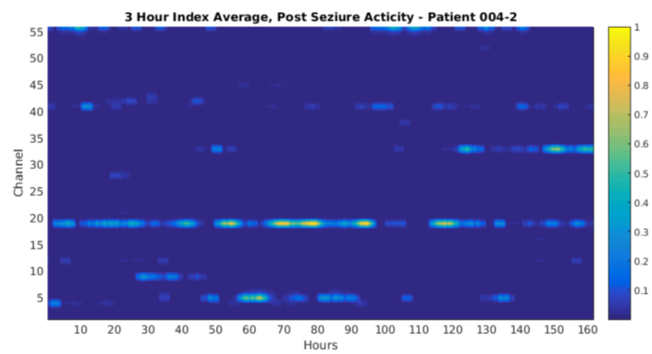

***Figure 5**: Average index 3 hours post seizure activity*

IV. Conclusion

It can be seen from the statistical analysis that the algorithm developed for this project has been validated to be predictive of the SOZ and is seizure independent. This design is run autonomously on a microcontroller and the results are then communicated to physicians via a secure web portal for further patient assessment.

V. Acknowledgments

Team 23 thanks our project advisor Dr. Sabato Santaniello for all of his support and guidance throughout the process.

VI. References

[1] Gliske S V., Irwin ZT, Davis K a., Sahaya K, Chestek C, Stacey WC. "Universal automated high frequency oscillation detector for real-time, long term EEG," *Clin Neurophysiol*. International Federation of Clinical Neurophysiology; 2015;(In Press).

[2] R. J. Staba, C. L. Wilson, A. Bragin, I. F., and J. Engel, "Quantitative Analysis of High-Frequency Oscillations (80 –500 Hz)Recorded in Human Epileptic Hippocampus and Entorhinal Cortex," *J Neurophysiol*;Jun. 2002 pp. 1743–1752,.

[3] Blanco JA, Stead M, Krieger A, Viventi J, Marsh WR, Lee KH, et al. "Unsupervised
classification of high-frequency oscillations in human neocortical epilepsy and control patients," *J Neurophysiol*; 2010 104:2900–12. http://dx.doi.org/10.1152/ Jn.01082.2009.