EN.580.694: Statistical Connectomics Final Project Proposal

Michele Lohr · April 21, 2015

Characterizing epileptic brain network response to mental effort

Opportunity Epilepsy is considered a network phenomenon characterized by "hypersynchronous" atypical activity during seizure, at both the single neuron level and higher neural populations [1][2]. Evidence of seizure cessation in epileptic patients through mental effort exercises (e.g., spelling or mathematical problem solving) has been observed [3], but it is not fully understood how this stimulus works and how to characterize when it will work.

Challenge A number of tools can be applied to understand epileptic networks, e.g. neuroimaging (MRI, fMRI), and electromagnetic recordings (ECoG, MEG) [4]. ECoG data are localized, instantaneous, gridded measurements of brain electrographic activity and useful for monitoring epileptic patients prior to resection surgery and for real-time testing of seizure response to stimuli [5]. However, the complexity of the brain electrical activity and the high-dimensionality of the ECoG time series data are challenging from a network modeling perspective.

Action We propose to test a connectivity feature derivable from ECoG data that can be used to characterize a patient's response (positive/negative) to mental effort stimulus at the onset of abnormal brain activity. Specifically, we will implement a variant of an approach [5][6] leveraging connectivity features (centralities) that have shown promise in correctly locating seizure foci based on ECoG data over time, but adapt to our problem, to determine (1) if there is evidence that there is a characterizable pre-ictal state, and (2) if so, can we use use this information to develop a classifier or predictor. We will analyze an ECoG dataset collected on patients prior to resection surgery, with positive and negative (no) response to mental effort stimulus. Noting potential trends in the calculated features (centralities), we will take steps to develop a classifier and test on a testing ECoG dataset. The hypothesis is that the stimuli affect strength of region connectivity over time, which is the primary feature of the applied approach [5]. Specifically, the region connectivity effects are hypothesized to be global for effective seizure mitigation through mental effort.

- 1. Implement variant of current approach [5] for calculating strength of region connectivity over time for an ECoG dataset, using several different centralities.
- 2. Apply to the training set of ECoG data with known outcomes following stimuli application (i.e., seizure or other abnormal brain activity stopped/not stopped following math problem posited to patient to solve).

- 3. Note trends in the features calculated above (e.g., strength of region connectivity over time) for cases of positive or negative outcome, that can be used to characterize outcome. If trends are noted, build a predictor or "classifier."
- 4. Apply classifier to a set of random/permuted graphs generated in same format as 1.) for determining classifier performance on null distribution.
- 5. Apply classifier to a test dataset, i.e., an ECoG dataset not used in the training above, and assess performance.

Resolution We will gain insight into the utility of connectivity features (centralities) currently used in other seizure studies for the characterization of epileptic brain network responses to mental effort.

Future Work One likely difficulty of this project will be the high dimensionality of the datasets. Additional graph classification approaches, e.g. using signal-subgraphs [7], may provide a more intuitive approach to deal with the data dimensionality and learning aspect of the problem.

Statistical Decision Theoretic

- **Sample Space** G = (V, E, Y) Graphs of ECoG data, where V is each electrode (node), E is the region connectivity as calculated by approach in [5][6], and $Y \in \{0, 1\}$, where 0 is negative effect (no seizure cessation) and 1 is positive effective (seizure cessation).
- **Model** $H = (V, E) \in \mathcal{H}$ Graphs of the raw ECoG data without the known classifications.
- Action Space $\hat{Y} \in \mathscr{Y}$ Outcomes of classifier, i.e. $\{0,1\}$, where 0 is negative effect (no seizure cessation) and 1 is positive effective (seizure cessation).
- **Decision Rule Class** $f: \mathcal{H} \to \mathcal{Y}$; $f = thresh[cluster[rank(x(i) = \sum_{i=1}^{n} H_{ij}x(j))]]$ this is a mapping of the graph or connectivity matrix H_{ij} to the classes \mathcal{Y} by a thresholding of a ranked and k-clustered centrality feature derived from the centrality vector which is a function of the eigenvector \vec{x} [5].
- **Loss Function** Loss functional: (TBD) $\ell(\hat{Y}, Y) = a ROC$ curve comparison of some kind between our sample space classes, and our action space classes.
- **Risk Function** Risk functional: $R = E[\ell]$.

REFERENCES REFERENCES

References

[1] Yaffe R, Borger P, Megevand P, Groppe D, Kramer M, Chu C, Santaniello S, Meisel C, Mehta A, and Sarma S 2015 Physiology of functional and effective networks in epilepsy Clinical Neurophysiology

- [2] Netoff T, Clewley R, Arno S, Keck T, and White J 2004 Epilepsy in small-world networks Neurobiology of Disease
- [3] Lesser R, Lee H, Webber W, Prince B, Crone N, and Miglioretti D 2008 Short-term variations in response distribution to cortical stimulation *Brain* (add additional 1999 stim paper and poster, and Holmes and Tucker paper on cross-freq coupling)
- [4] Holmes M and Tucker D 2013 Identifying the epileptic network Frontiers in Neurology
- [5] Yaffe R, Burns S, Gale J, Park H, Bulacio J, Gonzalez-Martinez J, and Sarma S 2012 Brain state evolution during seizure and under anesthesia: a network-based analysis of stereotaxic EEG activity in drug-resistant epilepsy patients 34th Annual International Conference of the IEE EMBS, San Diego, CA, 28 August 1 September 2012.
- [6] Burns S, Santaniello S, Yaffe R, Jouny C, Crone N, Bergey G, Anderson W, and Sarma S 2014 Network dynamics of the brain and influence of the epileptic siezure onset zone *PNAS*
- [7] Vogelstein J, Gray W, Vogelstein R, and Priebe C 2013 Graph classification using signalsubgraphs: applications in statistical connectomics *IEEE Transactions on Pattern Anal*ysis and Machine Intelligence 7 (35)