Machine learning to predict clinical outcomes from RNS background ECoG

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Description

Some patients with refractory epilepsy are implanted with a responsive neurostimulation device (RNS NeuroPace, Inc., Mountain View, CA). The RNS is an FDA-approved device which delivers brief pulses of electrical stimulation upon detection of abnormal EEG patterns to terminate seizures. Physicians program RNS detection and stimulation parameters to potentially reduce seizure duration and frequency. Current practice is empirically driven, and physicians are limited by a lack of evidence for guiding stimulation settings. A data-driven approach could help physicians reach optimal therapeutic stimulation parameters more quickly, and avoid seizure exacerbation.

We propose two data mining projects to address this clinical problem. The RNS system continuously stores EEG recordings, which provides a large and rich dataset to develop improved methods for optimizing RNS therapy.
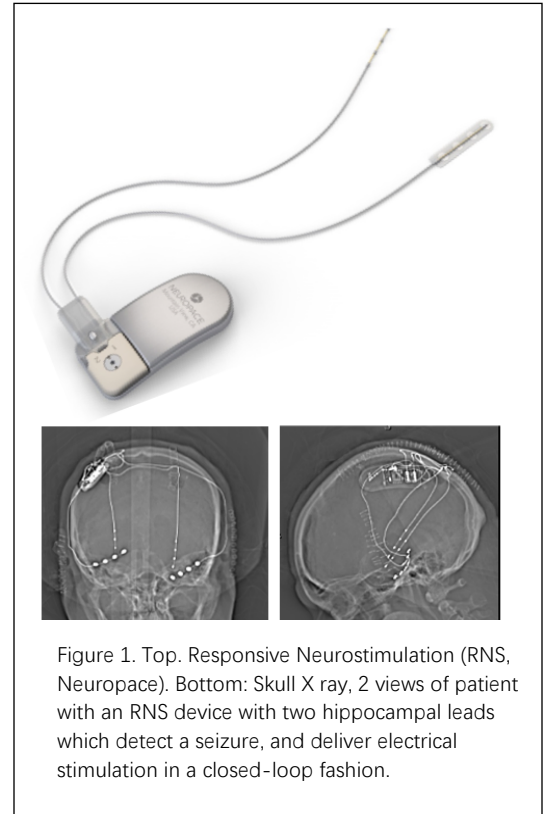

Figure 1. Top. Responsive Neurostimulation (RNS, Neuropace). Bottom: Skull X ray, 2 views of patient with an RNS device with two hippocampal leads which detect a seizure, and deliver electrical stimulation in a closed-loop fashion.

1) Examine long-term neuromodulatory effects of chronic electrical stimulation. Patients undergoing RNS therapy routinely meet with their physicians during office visits to adjust RNS parameters. Periods among office visits with stable EEG detection settings and antiepileptic medication doses will be identified, and parsed into 1-month epochs. The first month (immediately following an office visit) will serve as a baseline. Subsequent epochs will be classified as a "good " if they demonstrate at least a 50% improvement in EEG metrics, while bad epochs will be defined as those that exhibit at least 50% worsening of EEG metrics. EEG metrics will include total abnormal detections, total number of long episodes (programmed detections which exceed a set threshold), and seizure count. Scheduled EEG segments recorded daily at preset times during all "Good" and "Bad" epochs will be pooled respectively as samples reflecting background EEG activity in the two classes. This will be followed by feature extraction from individual EEG segments based on frequency-time domain as well as pathological characteristics, such as spectral power in standard frequency bands, total spectral power, inter-ictal discharge rate *etc*. Machine learning algorithms (starting with K-nearest neighbor classifier and Support Vector Machine) will be applied to the features to calculate classification accuracy. The goal of this analysis is to build reliable classifiers for prediction of "Good" versus "Bad" epoch outcomes based on background EEG patterns. These classifiers will help physicians to assess the efficacy of RNS parameter adjustments by using readily available scheduled EEG segments, as opposed to clinical seizure rate which may be subject to error in reporting or long durations between seizures.

2) Assess the role of long episode duration as a biomarker of acute response to electrical stimulation.
RNS electrical stimulations are delivered to disrupt ongoing abnormal EEG activity which may evolve into clinical seizures. The length of long episodes may be a biomarker for seizure duration and severity. We hypothesize that long episode duration may be a good measure of the acute efficacy of neurostimulation. We will track long episodes immediately following any adjustments to stimulation settings (intensity, duration etc), as well as those occurred later on, to identify stimulation parameters that are associated with reductions in the long episode duration, which we predict will coincide with meaningful reductions in clinical seizure frequency. This approach may result in more efficient and reliable assessment of RNS parameter adjustments to help physicians more quickly reach optimal settings.

Learning objectives for the course
At the end of the course, I will finish a paper that will be submitted to a journal that focus on neural simulation and epilepsy.

Number of credits and meeting/contact hours
3 credits and 8 meeting/contact hours

Schedule of work to be done:
I have been working on this project for the last 7 months. Therefore, in this semester we will focus on conducting further research into new feature engineering, writing the paper and submitting to the conference.

1-4 weeks: The machine learning classifiers will produce different performance when using different number of days as an epoch. Look into the effect of the number of days on the performance and examine the results from the perspective of neural science. Make the poster and present the poster at the American Clinical Neurophysiology Society Conference, Las Vegas.

5-8 weeks: Investigate if features other than the power in different frequency bands can help improve the performance of the prediction model. Look into whether long episode duration can help boost the classifier performance.

9-18 weeks: write the paper and submit it to the journal.

Reading:

1. The Scientist and Engineer's Guide to Digital Signal Processing By Steven W. Smith http://www.dspguide.com/, Chapter 1 to Chapter 11
2. Handbook of EEG Interpretation, Second Edition by William Tatum IV DO Chapter 1 to chapter 4
3. Baud, M. O., Kleen, J. K., Mirro, E. A., Andrechak, J. C., King-Stephens, D., Chang, E. F., & Rao, V. R. (2018). Multi-day rhythms modulate seizure risk in epilepsy. *Nature Communications*, *9*(1), 1614. http://doi.org/10.1038/s41467-017-02577-y
4. Sun, F. T., & Morrell, M. J. (2014). The RNS System: responsive cortical stimulation for the treatment of refractory partial epilepsy. *Expert Review of Medical Devices*, *11*(6), 563–572. http://doi.org/10.1586/17434440.2014.947274
5. Changes in the electrocorticogram after implantation of intracranial electrodes in humans: The implant effect. (n.d.). Changes in the electrocorticogram after implantation of intracranial electrodes in humans: The implant effect. Retrieved January 29, 2019, from https://reader.elsevier.com/reader/sd/pii/S1388245717311446?token=CEF8807D1801F5D038 835E4A2451FE536041743219001B4EF4DA1DB2254D95508307E6C4ACEEF5F27290FC405 59B0D0E

Work to be evaluated by the instructor:
A poster and a paper will be produced before the end of the semester. The paper will be at least 6 pages long.

Syllabus:

February:

The machine learning classifiers will produce different performance when using different number of days as an epoch.

Look into the effect of the number of days on the performance and examine the results from the perspective of neural science.

Make the poster and present the poster at the American Clinical Neurophysiology Society Conference, Las Vegas.

 Reading:

1. The Scientist and Engineer's Guide to Digital Signal Processing By Steven W. Smith http://www.dspguide.com/, Chapter 1 to Chapter 11
2. Handbook of EEG Interpretation, Second Edition by William Tatum IV DO Chapter 1 to chapter 4

March:

Investigate if features other than the power in different frequency bands can help improve the performance of the prediction model.

Look into whether long episode duration can help boost the classifier performance.

Reading:

1. Baud, M. O., Kleen, J. K., Mirro, E. A., Andrechak, J. C., King-Stephens, D., Chang, E. F., & Rao, V. R. (2018). Multi-day rhythms modulate seizure risk in epilepsy. *Nature Communications, 9*(1), 1614. http://doi.org/10.1038/s41467-017-02577-y
2. Sun, F. T., & Morrell, M. J. (2014). The RNS System: responsive cortical stimulation for the treatment of refractory partial epilepsy. *Expert Review of Medical Devices, 11*(6), 563–572. http://doi.org/10.1586/17434440.2014.947274

April:

Write the paper and submit it to the journal.

Reading:

1. Changes in the electrocorticogram after implantation of intracranial electrodes in humans: The implant effect. (n.d.). Changes in the electrocorticogram after implantation of intracranial electrodes in humans: The implant effect. Retrieved January 29, 2019, from

I approve the above proposal

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1/30/19