Quantifying Frequency Modulation in Seizures of Patients Undergoing Responsive Neurostimulation

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Motivation

Changes in the pattern of seizure progression can differentiate responders and non-responders treated using closed-loop brain stimulation

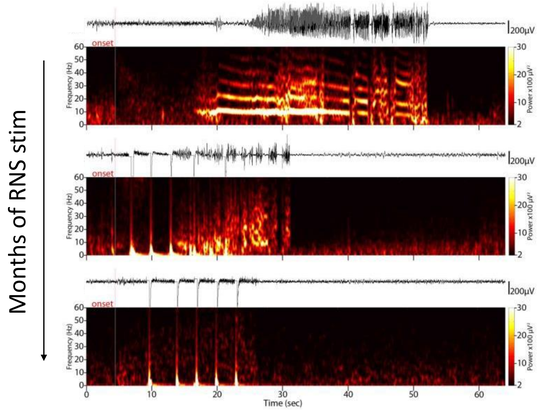
(Kokkinos et al., JAMA Neurology, 2019)

A neurophysiological biomarker correlated with patient response to neurostimulation: **indirect frequency modulation**

This biomarker challenges the current understanding of RNS' mechanism, as a direct and instantaneous inhibitor of seizures

Frequency Modulation

Characterized by a significant change in the frequency content of the seizure pattern over several months of RNS treatment



Previous study qualitative: we need concrete statistical tools to ***quantitatively*** evaluate seizure progression

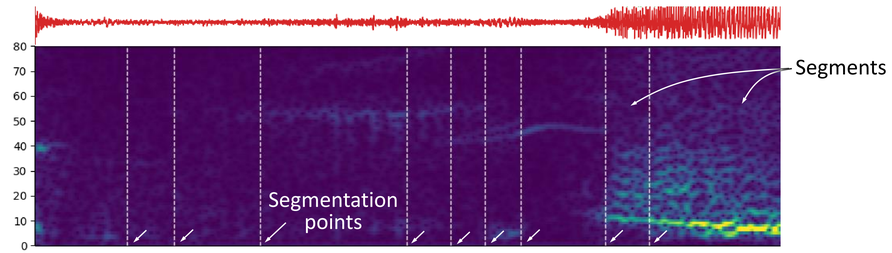
Future Potential

Quantifying seizure evolution may inform tuning of RNS parameters, forming the first step towards personalized RNS therapy

Methods

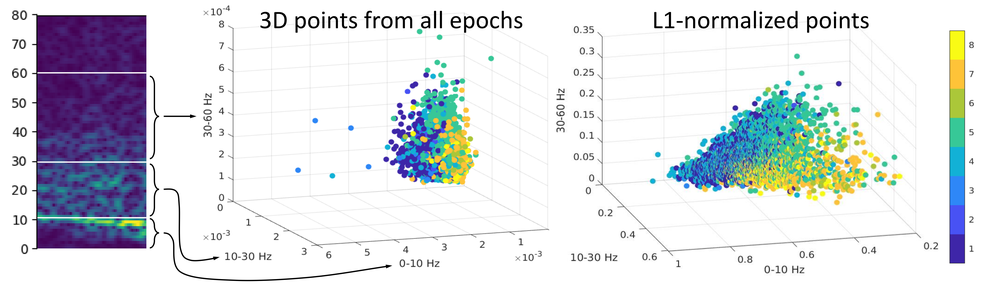
Step 1. Select a representative channel for each patient, and partition each of their seizures into segments with distinct spectral content

(Venkatesh et al., AES annual meeting 2019)



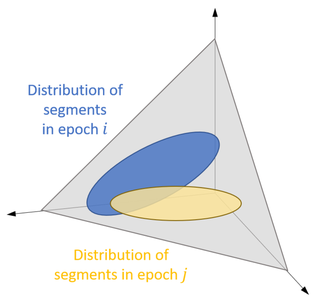
Step 2. Convert each segment into a 3D point, by computing the average frequency magnitude in three bins: 0-10Hz, 10-30Hz, and 30-60Hz

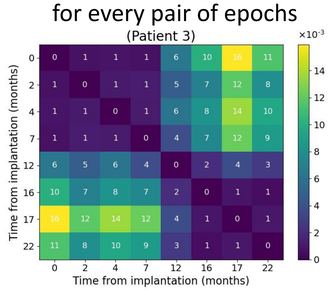
Step 3. Collect all 3D points from every RNS programming epoch (epochs shown in different colors below) and normalize each vector by its L1-norm

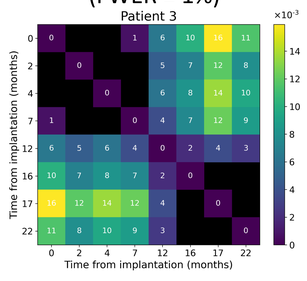


Step 4. Compute Earthmover's distances between point clouds for every epoch pair

Step 5. Compute statistical significance against a null hypothesis of zero distance using a permutation test

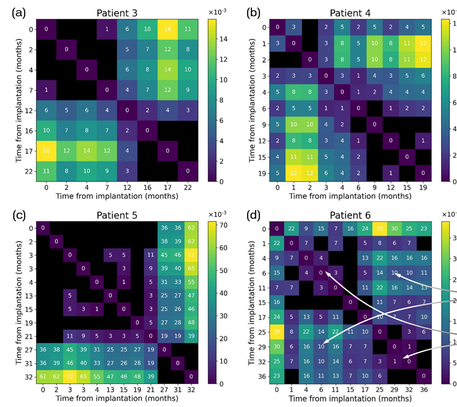






Results

Patients that show frequency modulation



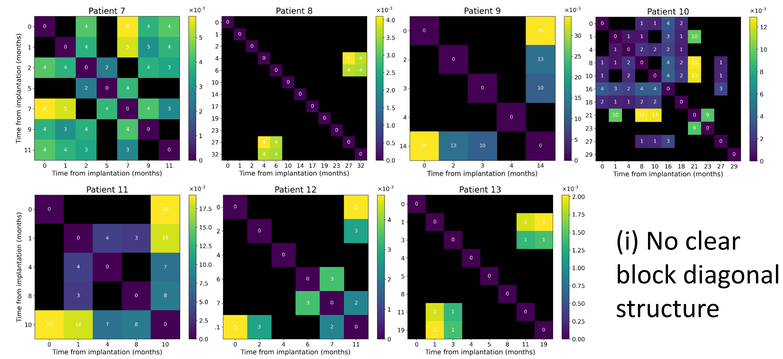
(i) Larger Earthmover's distances on average (14×10^{-3} vs 5×10^{-3})

(ii) Pairwise distance matrix shows clear block diagonal structure

Large off-diagonal blocks

Small or statistically insignificant diagonal blocks

Patients that do not show frequency modulation



(i) No clear block diagonal structure

(ii) Smaller or statistically insignificant Earthmover's distances

Acknowledgements

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References

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Praveen Venkatesh, Vasileios Kokkinos, R Mark Richardson, Pulkit Grover, "An Automated Configurable Seizure Segmentation Tool for Tracking the Evolution of Seizures", *AES abstract (2019)*