# Synchronization network-based approach for accurate epileptogenic zone identification from short interictal EEG data

*Tonmoy Monsoor, Atsuro Daida, Prateik Sinha, Sotaro Kanai, Shingo Oana, Yipeng Zhang, Lawrence Liu , Gaurav Singh, Chenda Duan, Naoto Kuroda, Shaun A. Hussain, Raman Sankar, Aria Fallah, Richard J. Staba, Jerome Engel Jr., Eishi Asano, Vwani Roychowdhury, Hiroki Nariai*

UCLA Mattel Children's Hospital
Children's Discovery & Innovation Institute
UCLA Samueli School of Engineering

## RATIONALE

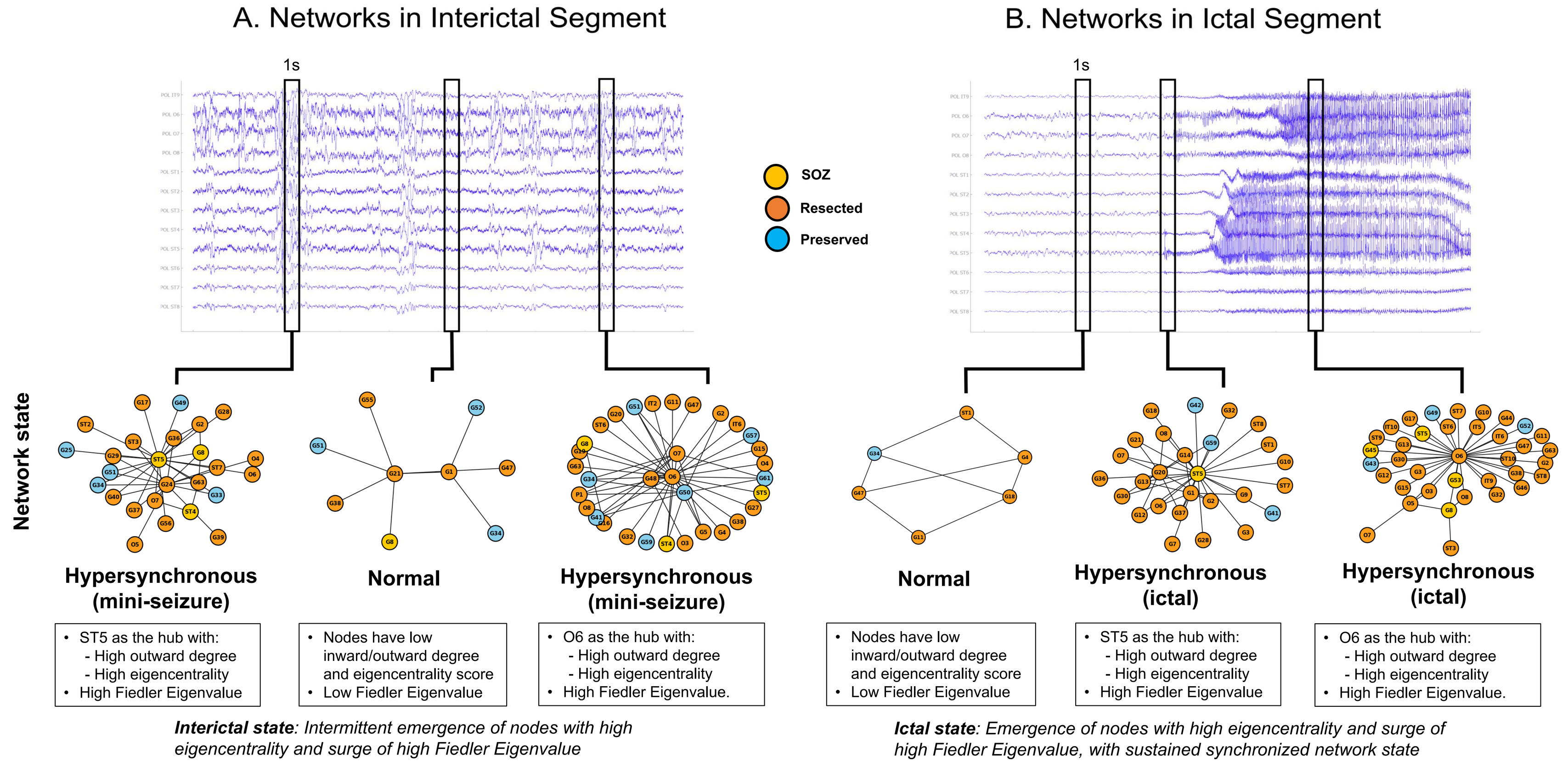
- Identifying epileptogenic zone (EZ) in medication-resistant epilepsy using brief interictal EEG remains an unresolved challenge.
- Current clinical practice requires lengthy monitoring (up to several weeks) of intracranial EEG (iEEG) to analyze ictal segments.
- This approach misses potential seizure onset zones (PSOZ) that could become active with extended observation.
- We hypothesize EZ regions (SOZ+PSOZ) contain subtle ictal signatures within short interictal iEEG segments.

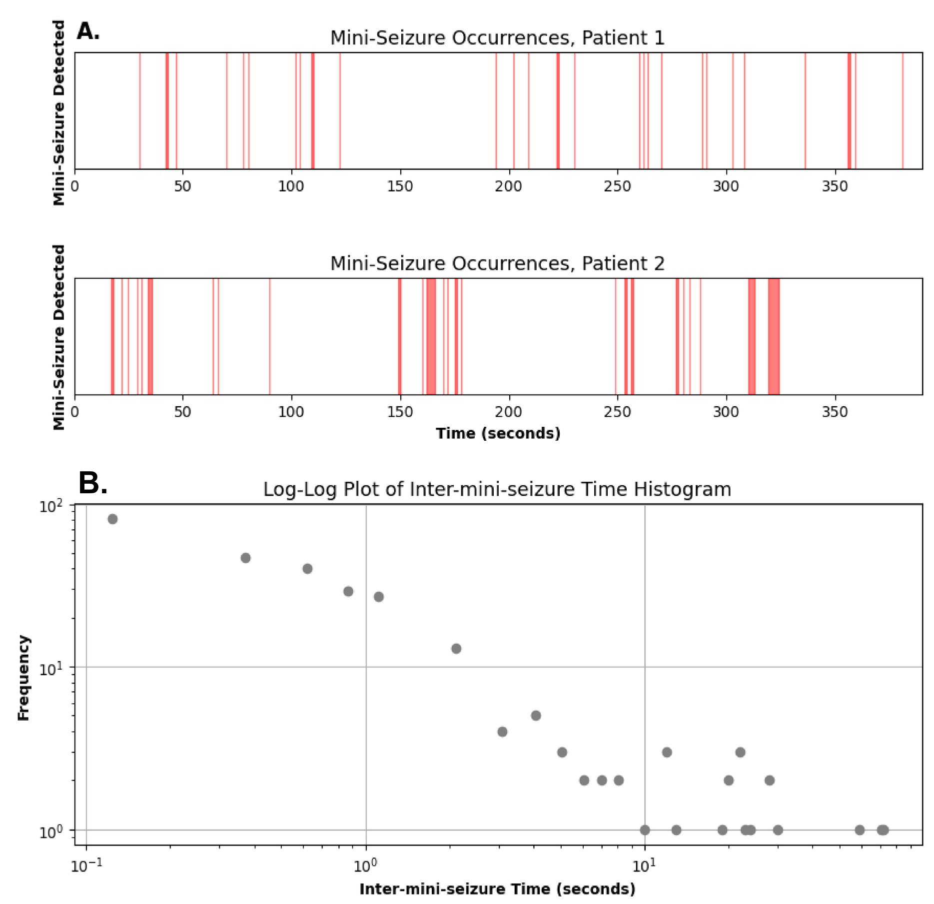
## METHODS

- Study included 159 pediatric patients from UCLA and Wayne State University who underwent chronic iEEG monitoring with either electrocorticogram (n=144) or stereotactic EEG (n=15) grid/strip followed by resection.
- Analyzed interictal iEEG recording (5-90 minutes) by dividing it into 1-second non-overlapping segments
- For each segment, created synchronization networks in 3 frequency bands (50-80, 80-250, 250-300 Hz) using power-phase coupling between channel pairs[1].
- Generated feature vectors from temporal dynamics of the sequence of networks.
- Trained and tested random forest model using leave-one-out cross-validation to estimate likelihood of channels belonging to SOZ.
- Developed prediction model incorporating channel SOZ likelihoods and the channel resection status to predict postoperative seizure freedom probability.

## RESULTS

**Figure 1: Interictal mini-seizures mimics ictal network states.**



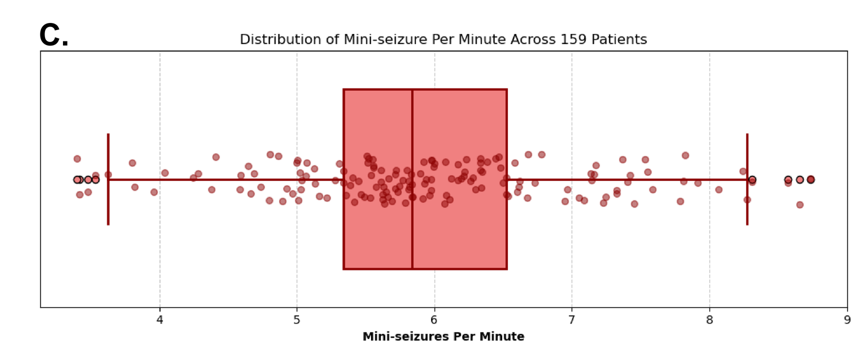




**Figure 2: Mini-seizures frequently occur in bursts and inter-mini-seizure interval statistics follow power law distribution.**
(A) Raster plots showing the occurrences of mini-seizures over time for two patients, where each red line represents a detected mini-seizure. For both patients, mini-seizures occur in bursts.
(B) X-axis represents inter-mini-seizure time interval and Y-axis represents the frequency of that inter-mini seizure time interval occurring, where both axes are on a logarithmic scale. The plot, aggregated across 159 patients, show that inter-mini-seizure time interval follows a power law distribution found in inter-seizure statistics
(C) Each dot represents a patient's mini-seizure rate at the group level, with a mean occurrence of approximately 6 mini-seizures per minute.

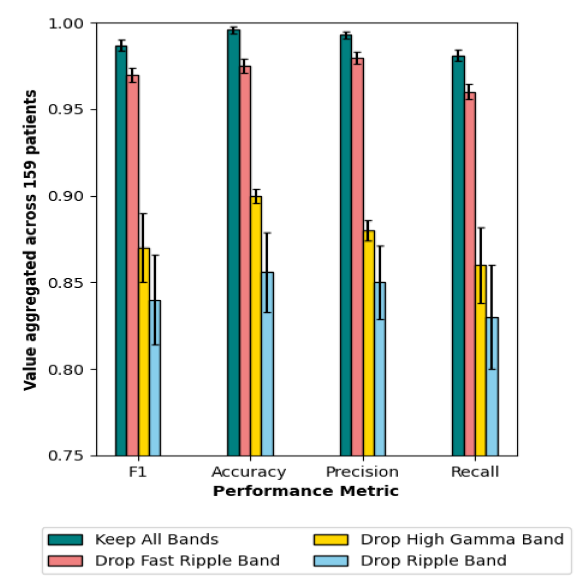



**Figure 3: Random forest model accurately predicts SOZ status, with ripple band features being the most informative.** A leave-one-out cross validation approach was used to validate the performance of the SOZ classification model. X-axis represents the 4 performance metrics and Y-axis represents value of the performance metric averaged across 159 patients with error bar showing the variance. The model using all frequency bands generalizes well as shown by the high average F1 score of 0.97 and small variance in F1 score across 159 patients. However, when the ripple frequency band was dropped, the model performance decreased significantly to an average F1 score of 0.84 showing the importance of ripple band in SOZ classification.

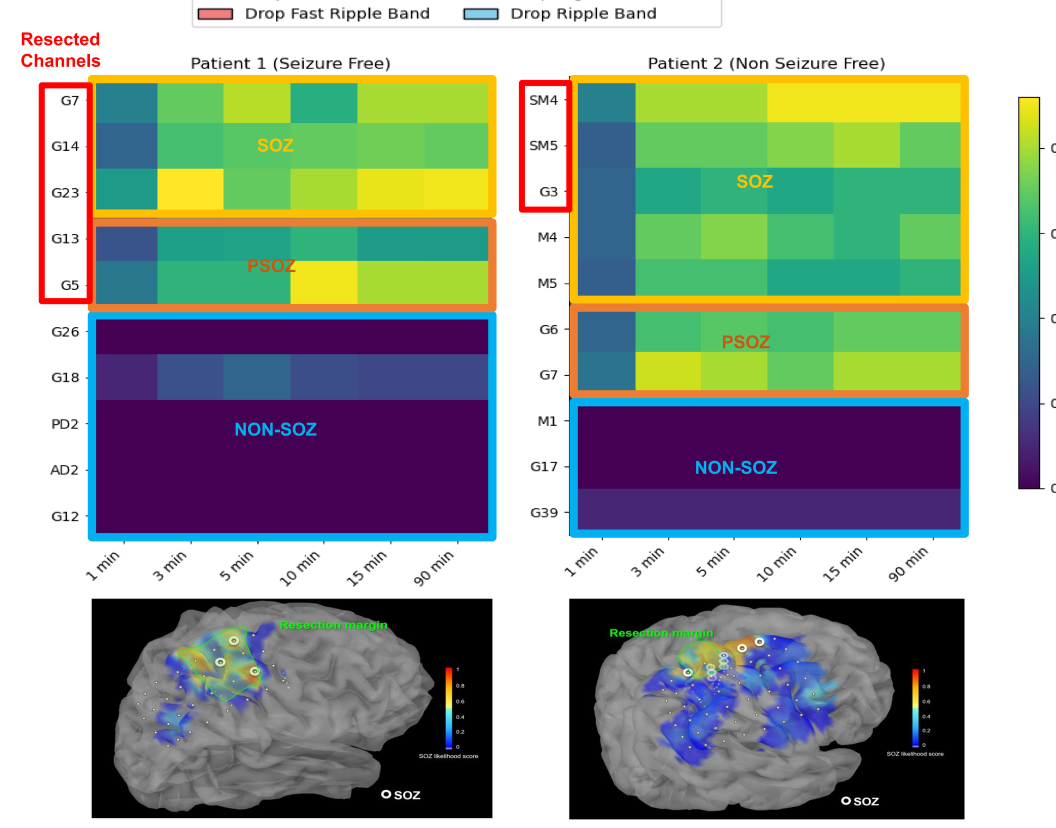
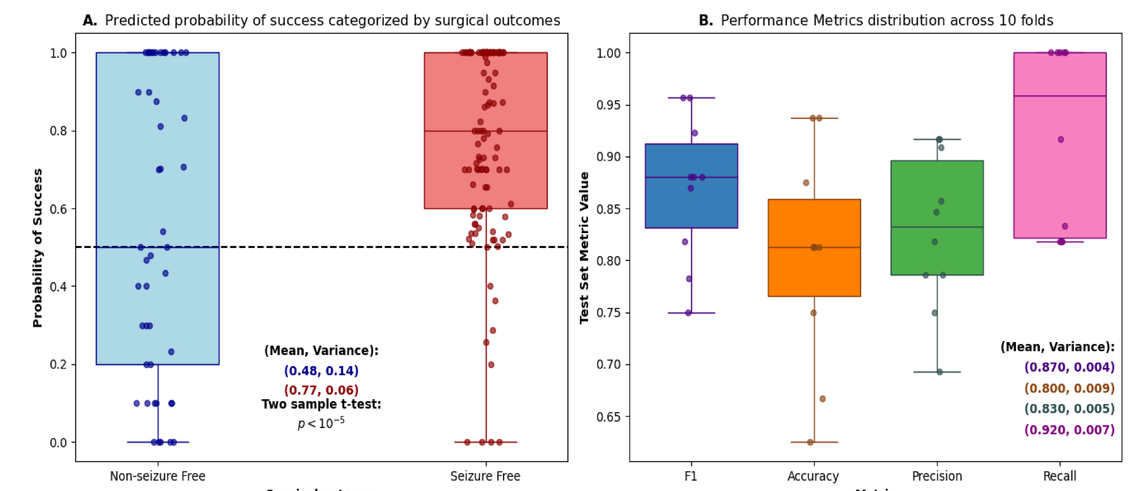



**Figure 4: Short interictal iEEG segments may be sufficient for high confidence EZ identification.**
(A) Heatmap of SOZ likelihood scores for two patients are shown with rows representing the channels and columns representing the duration of the iEEG epoch used to train the SOZ classification model. We can identify SOZ (overlapping with doctor's annotated SOZ [dSOZ]) and PSOZ with high confidence from iEEG epochs with duration as short as 3 minutes.
(B) SOZ likelihood score distribution when overlaid on the brain forms distinct contiguous hotspots reflecting potential foci of the EZ. A patient where the resection margin included all the foci, became seizure-free. Conversely, a patient where resection margin did not cover all the foci, it did not become seizure free.



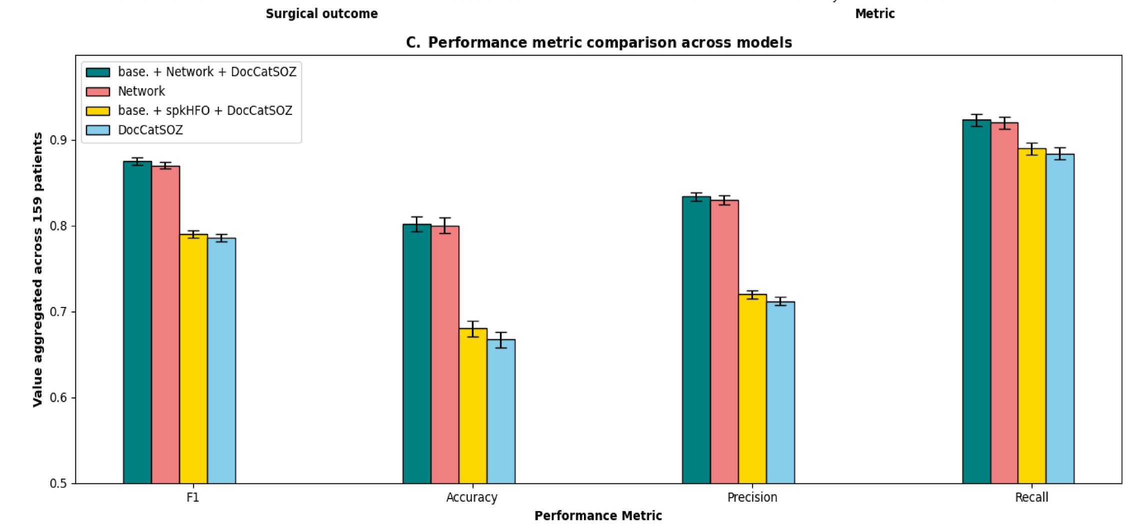




**Figure 5: Network based model accurately predicts post-operative seizure outcome**
A 10-fold cross-validation (CV) approach was used to validate the performance of the surgical outcome prediction models.
(A) The synchronization network based model outputs a seizure freedom probability ($P_s$) for each patient. Each dot represents one patient and dots are color-coded by surgical outcome. For the network based model, the majority of patients with a successful surgical outcome (red dots) had $P_s$ values greater than the threshold (dotted line) whereas patients with a failed surgical outcome generally had $P_s$ values below the threshold
(B) Box plots show distributions of each performance metric across the 10 CV folds. The network based model generalizes well as shown by the high mean F1 score of 0.87 and a low variance of 0.004 across the 10 CV folds.
(C) Four surgical outcome prediction models are compared in terms of 4 performance metrics. The synchronization network based model ( mean F1 score - 87%) outperforms the HFO based model (mean F1 score - 79%) and SOZ resection status based model (current clinical standard) (mean F1 score - 78%) on all the 4 performance metrics.

## CONCLUSIONS

- Interictal hypersynchronous events, termed "mini-seizures," occurred frequently and mimicked ictal network signatures.
- The ripple band (80-250 Hz) appeared to play a key role in generating these networks.
- This network-based approach to interictal synchronization could potentially delineate the epileptogenic zone (EZ) from brief interictal iEEG data, aiding in resection planning and reducing the duration of iEEG monitoring.

Correspondence: Tonmoy Monsoor[1] (mtonmoy@g.ucla.edu), Vwani Roychowdhury[1] (vwani@g.ucla.edu), and Hiroki Nariai[2] (hnariai@mednet.ucla.edu)
1: The UCLA Henry Samueli School of Engineering and Applied Science, Los Angeles, CA, USA
2: Division of Pediatric Neurology, Department of Pediatrics, UCLA David Geffen School of Medicine, Los Angeles, CA, USA

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Reference: [1] Wang, Shuo, et al. "Inferring dynamic topology for decoding spatiotemporal structures in complex heterogeneous networks." Proceedings of the National Academy of Sciences 115.37 (2018)