Can we predict and prevent the onset of seizures?

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Can we learn from data when it is not Gaussian nor linear?

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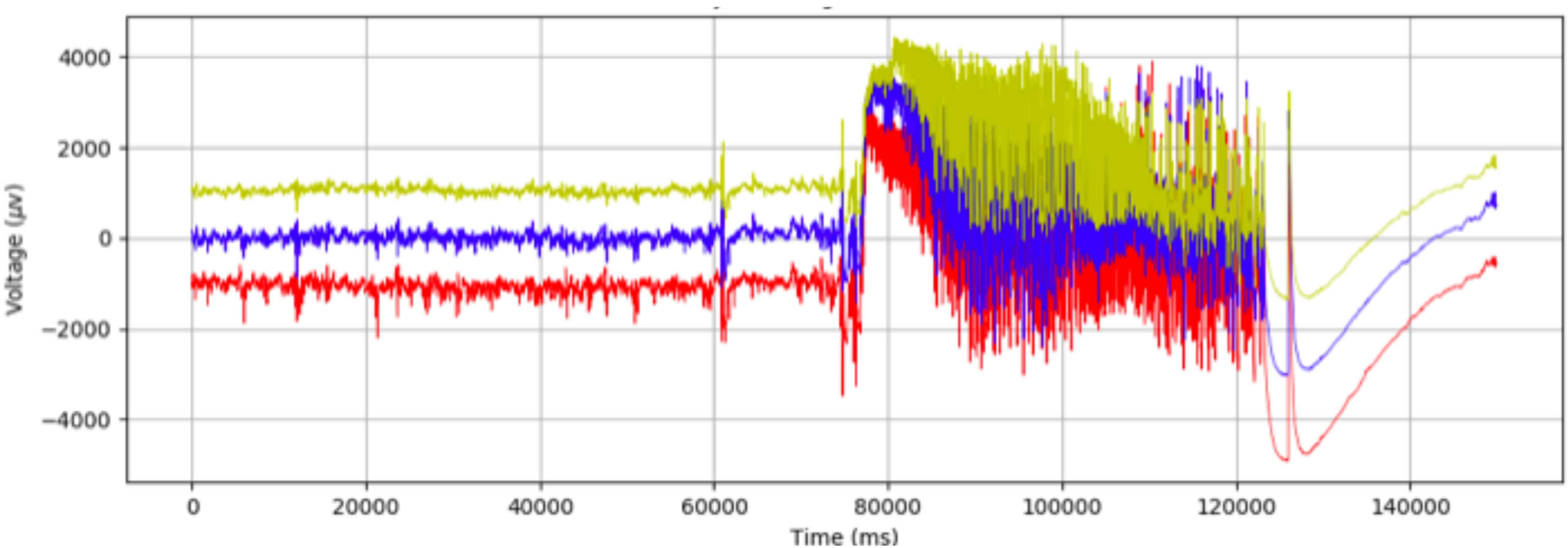
Example



4000
2000
0
−2000
−4000
Voltage (μv)
0
20000
40000
60000
80000
100000
120000
140000
Time (ms)

Can we predict and prevent the onset of seizures?

- less focus on the application
- more emphasize on tools
- let's step back with a few more fundamental questions

How can engineers contribute to medicine?

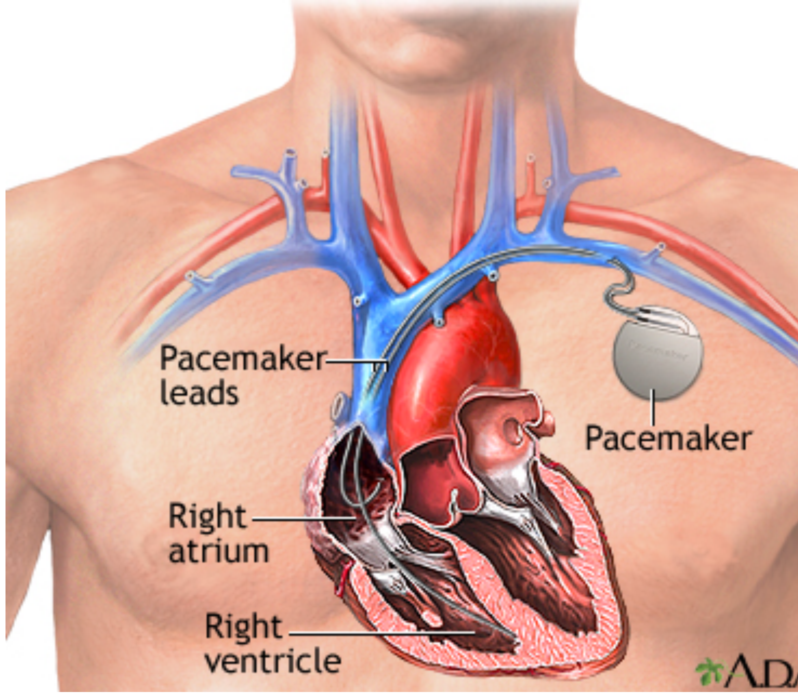
- from data to understanding various disorders
- developing therapies
  - patient-specific
  - episode-specific
  - scalability
  - cost

Engineers

- problem solving with constraints
- developing tools
  - sense and measure
    - nano-electronics
  - control—modulation, stimulation, pacing
    - machine learning and data analytics
    - nonlinear and non-Gaussian

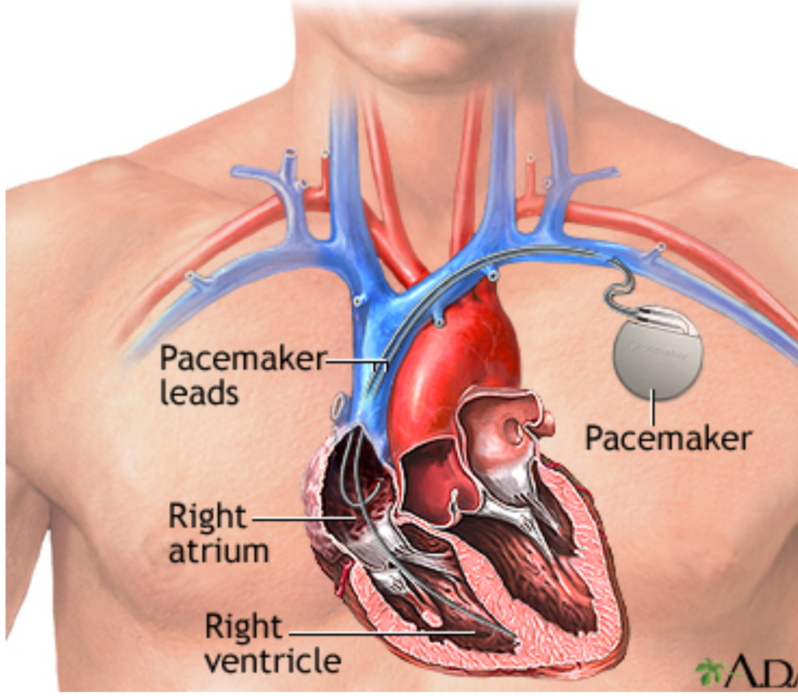
Example

- pacemakers



Example

- pacemakers
- can we modulate our neurological circuit?
    - 86 billion neurons
    - 10 micron diameter
    - 100 Hz clock speed
    - 100 trillion synapses
    - complicated functionality with only 20 W of power



What am I excited about?

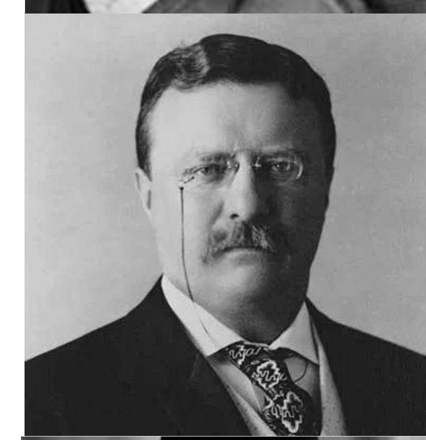
- can data analytics predict the onset?
- can we develop spatiotemporally precise modulation protocols to prevent the onset of seizures?

Epilepsy

- unprovoked and recurring seizures
- seizure
  - no standard definition
  - abnormally hyper-excited neuronal activities

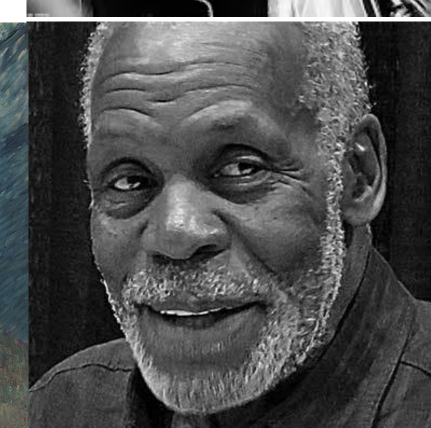
Epilepsy

- celebrities



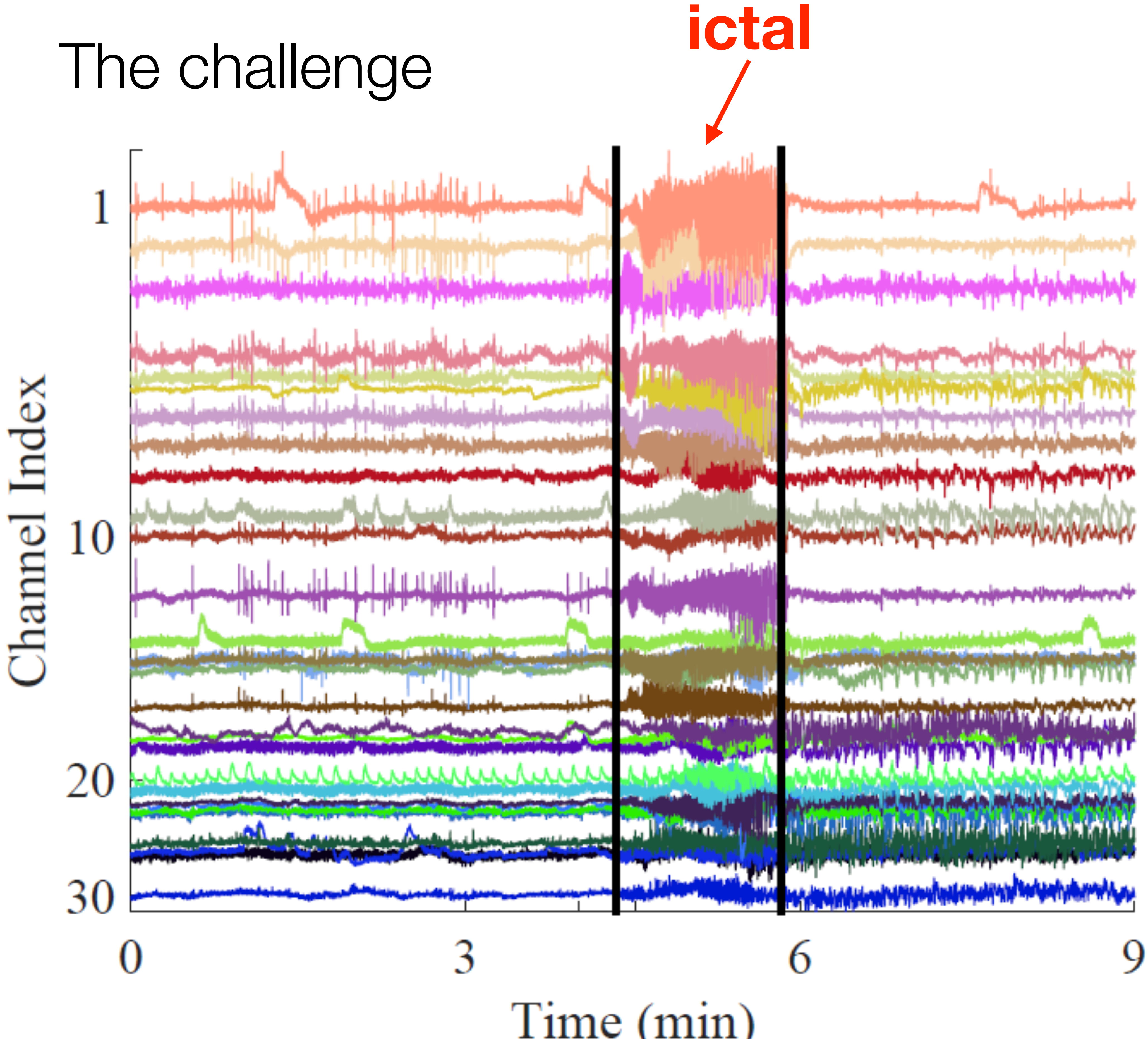


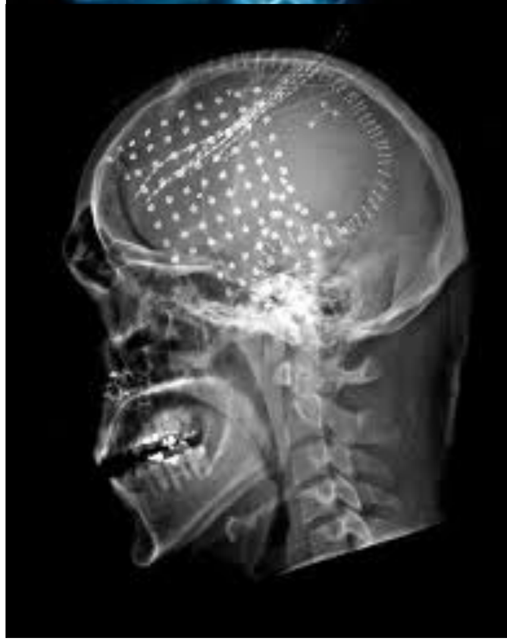


Epilepsy

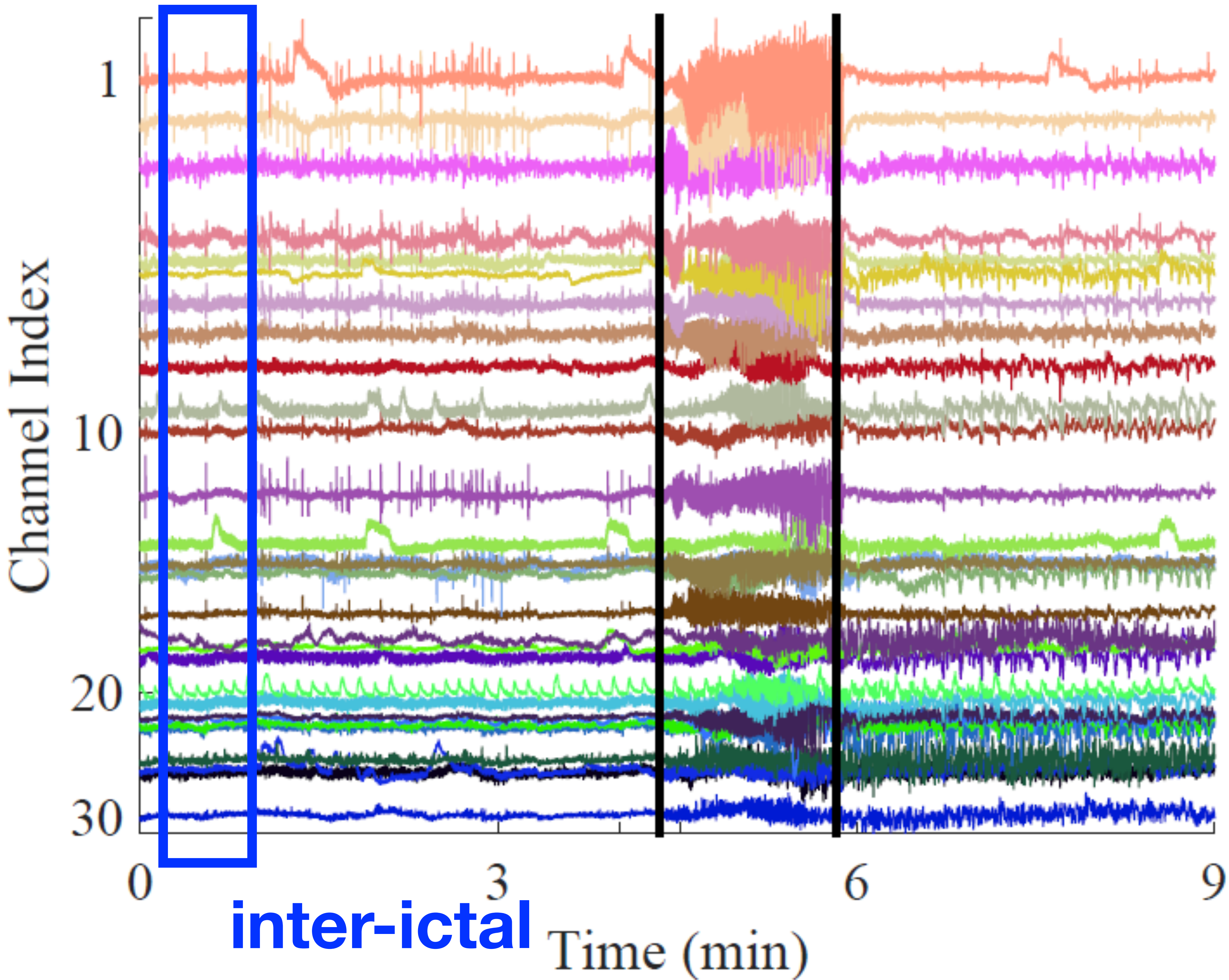
- 1% of world’s population
- causes: stroke, tumors, infection, genetic, developmental,…
- 1/3 of patients do not respond to medication
    - resection!!!!!
    - deep brain stimulation?

The challenge

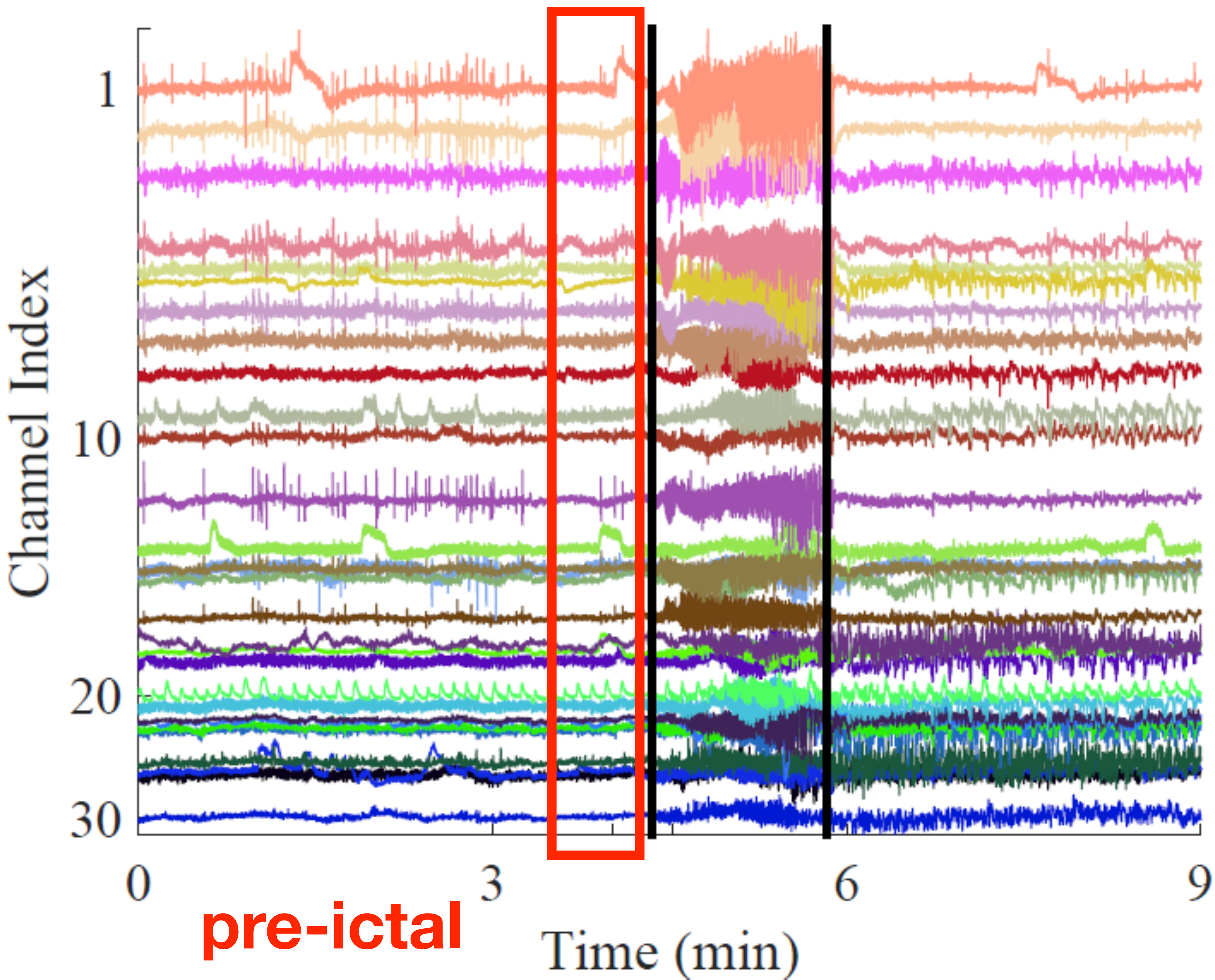


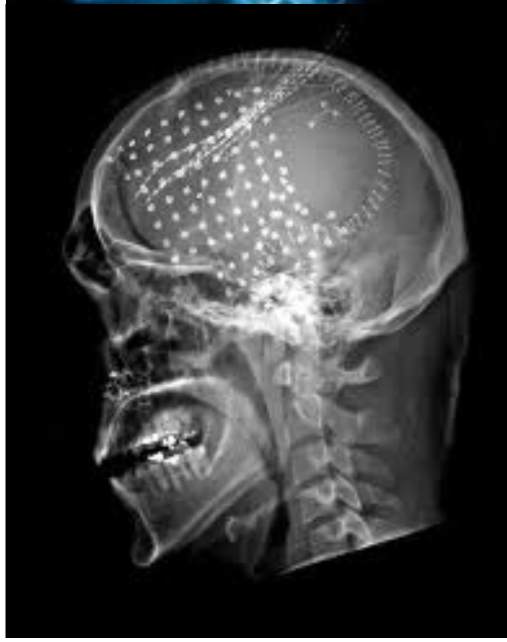


The challenge

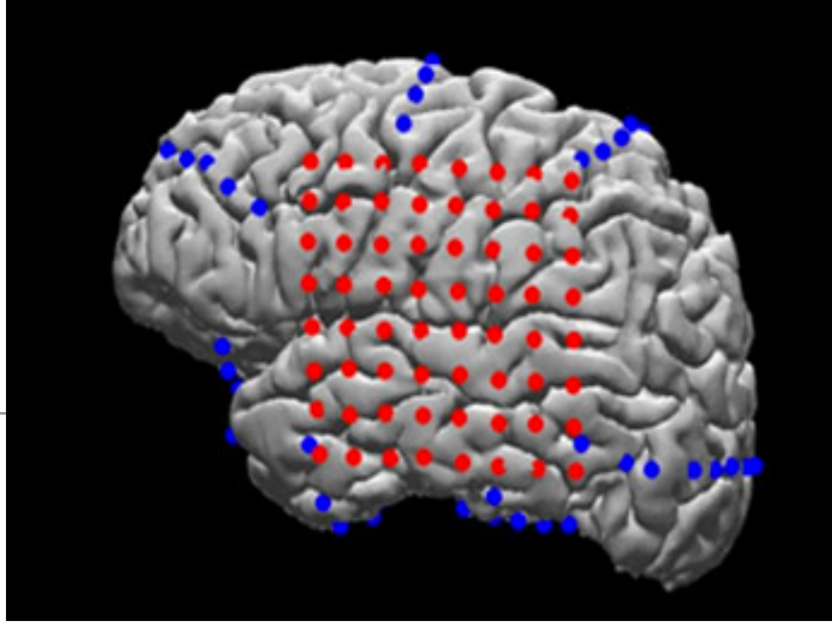


The challenge





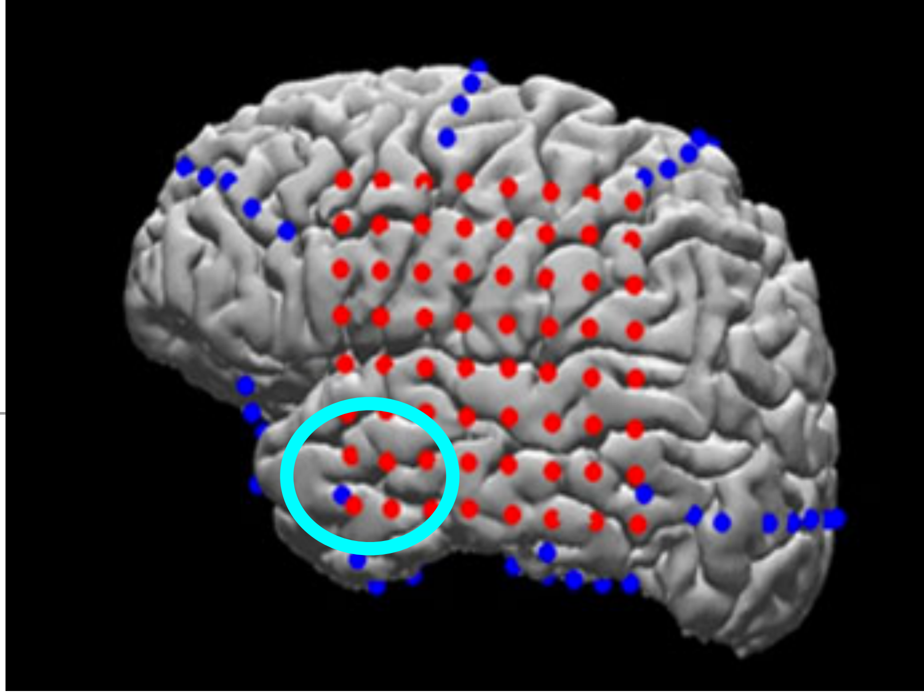
Approach

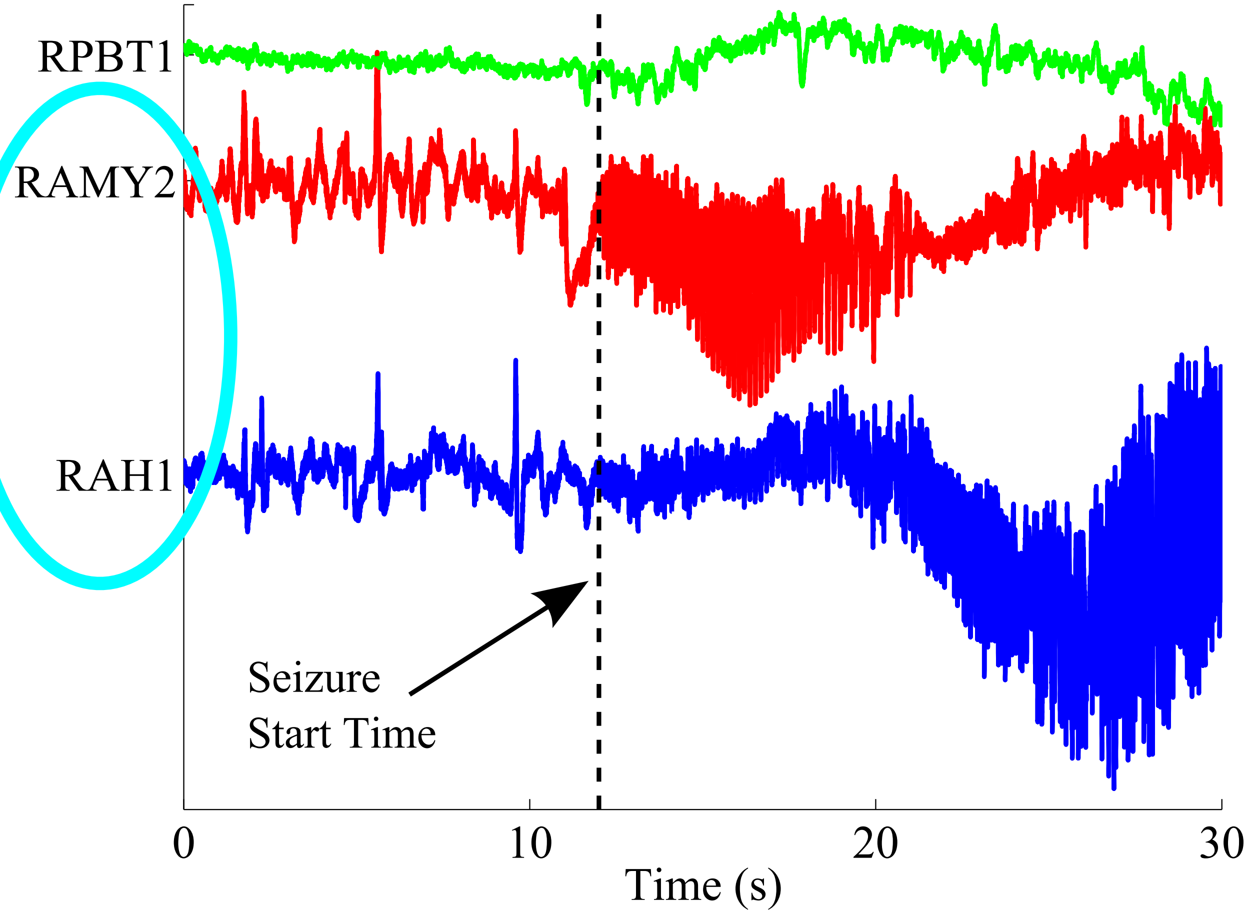


- patient and episode specific
  - identify the seizure onset zone
  - understand the dynamics of the underlying system
    - predict seizures
    - modulate (stimulate) to prevent the onset of seizure

Epilepsy

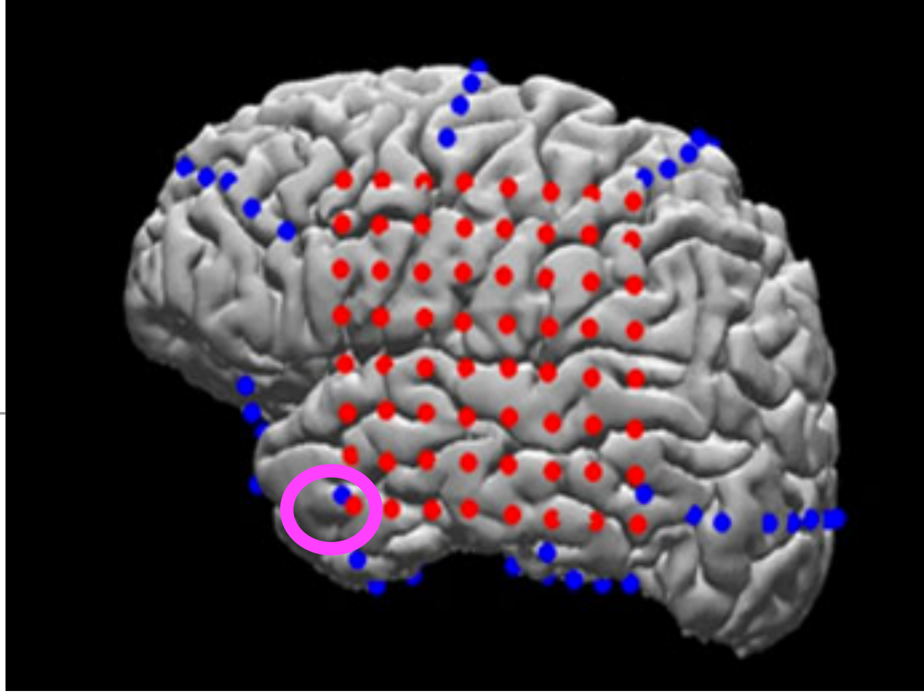
- identify seizure onset zone



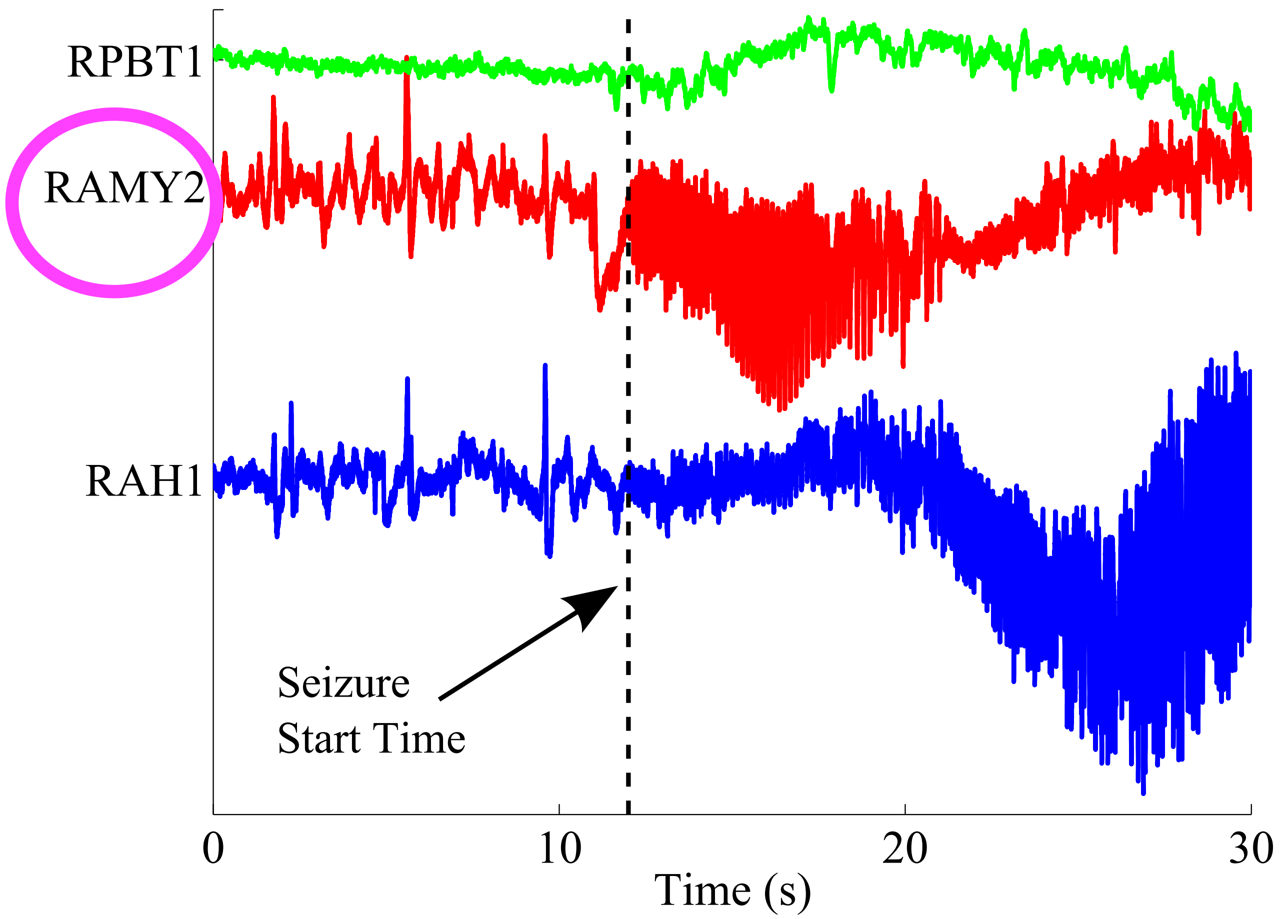


seizure zone

Epilepsy



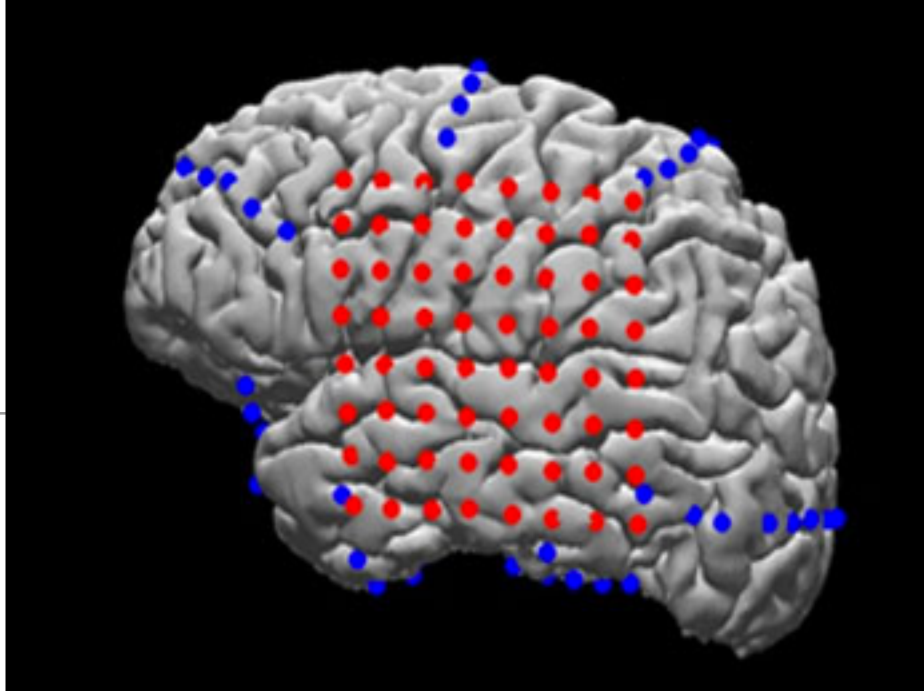
- identify seizure onset zone



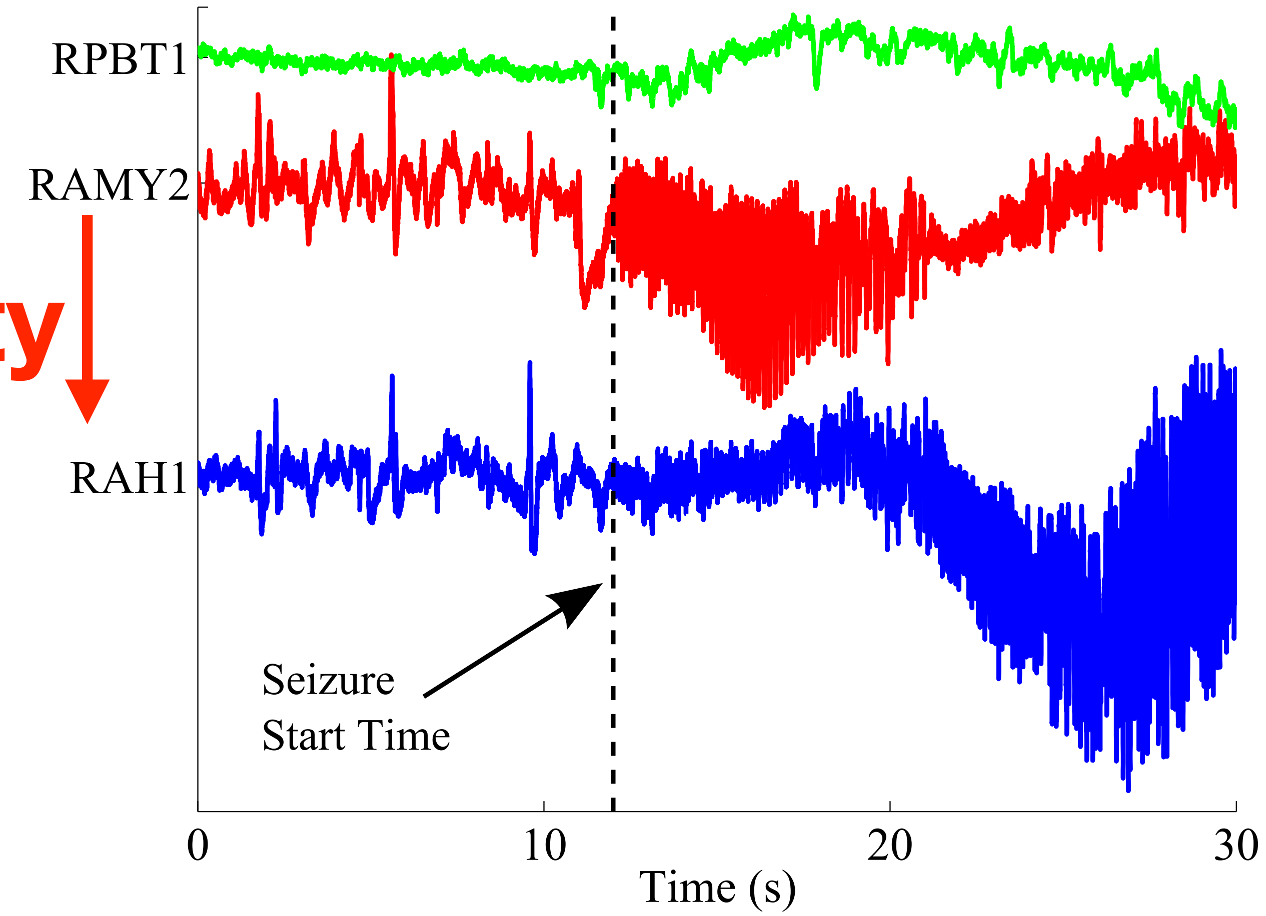
seizure onset zone

Epilepsy

- identify seizure onset zone



causality



Causality

- one time series forecasting another
  - economics
  - transportation
  - …
    - n. wiener (1956), c. granger (1969), h. marko (1973)
    - j. massey (1990), g. kramer (1998),
    - c. quinn, et. al. (2011)

A little background

- directed information and causality

$$I(X_1^N \to Y_1^N) = \sum_{n=1}^{N} I(X_1^n; Y_n | Y_1^{n-1})$$

- directional with temporal information

$$X_1^N \equiv (X_1, X_2, \ldots, X_N) \longrightarrow Y_1^N \equiv (Y_1, Y_2, \ldots, Y_N)$$

A little background

$$I(X_1^N \rightarrow Y_1^N) = \sum_{n=1}^{N} I(X_1^n; Y_n | Y_1^{n-1})$$

- mutual information of time series

$$I(X_1^N; Y_1^N) = \sum_{n=1}^{N} I(X_1^N; Y_n | Y_1^{n-1})$$

- no temporal and no causal information

$$X_1^N \equiv (X_1, X_2, \ldots, X_N) \longrightarrow Y_1^N \equiv (Y_1, Y_2, \ldots, Y_N)$$

$$I(X_1^N; Y_1^N) = H(Y_1^N) - H(Y_1^N | X_1^N)$$

A little background

- directed information of time series

$$I(X_1^N \to Y_1^N) = H(Y_1^N) - H(Y_1^N || X_1^N)$$

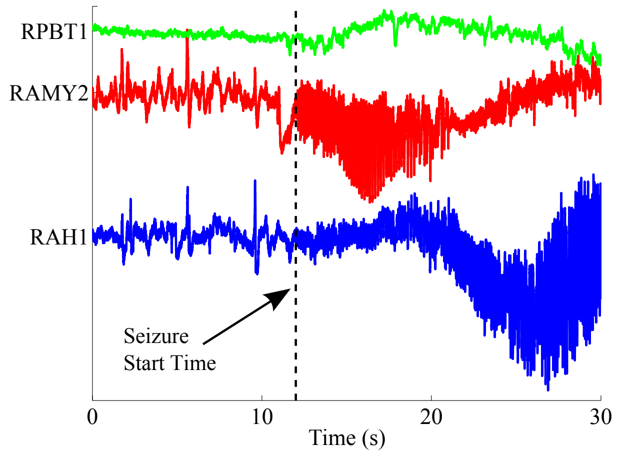
causal conditional entropy

- where

$$H(Y_1^N || X_1^N) = \sum_{n=1}^{N} H(Y_n | Y_1^{n-1}, X_1^n)$$

Back to seizures

- causal relation among electrodes
  - directed information
    - model free—data driven
      - k-nearest neighbor density estimation
- identify time series with largest directed information

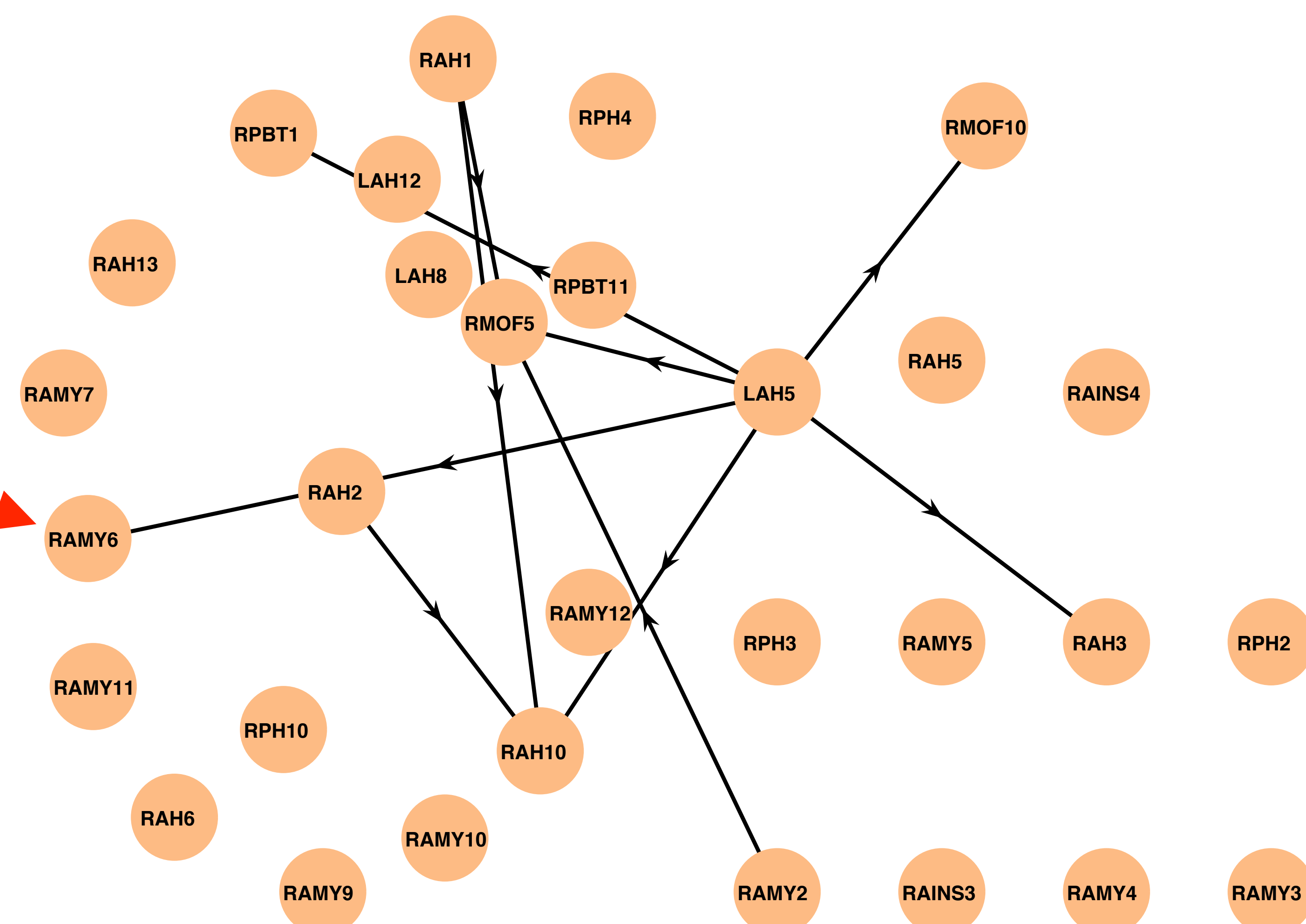


$$\rightarrow \hat{f}_{X,Y} \rightarrow \hat{H}(X), \hat{H}(X,Y) \rightarrow \hat{I}(X \rightarrow Y)$$

Seizure onset zone

- causal influence—directed connectivity
  - a graph with electrodes as nodes and directed information as edge
  - pre-ictal (period prior to seizure)

electrode



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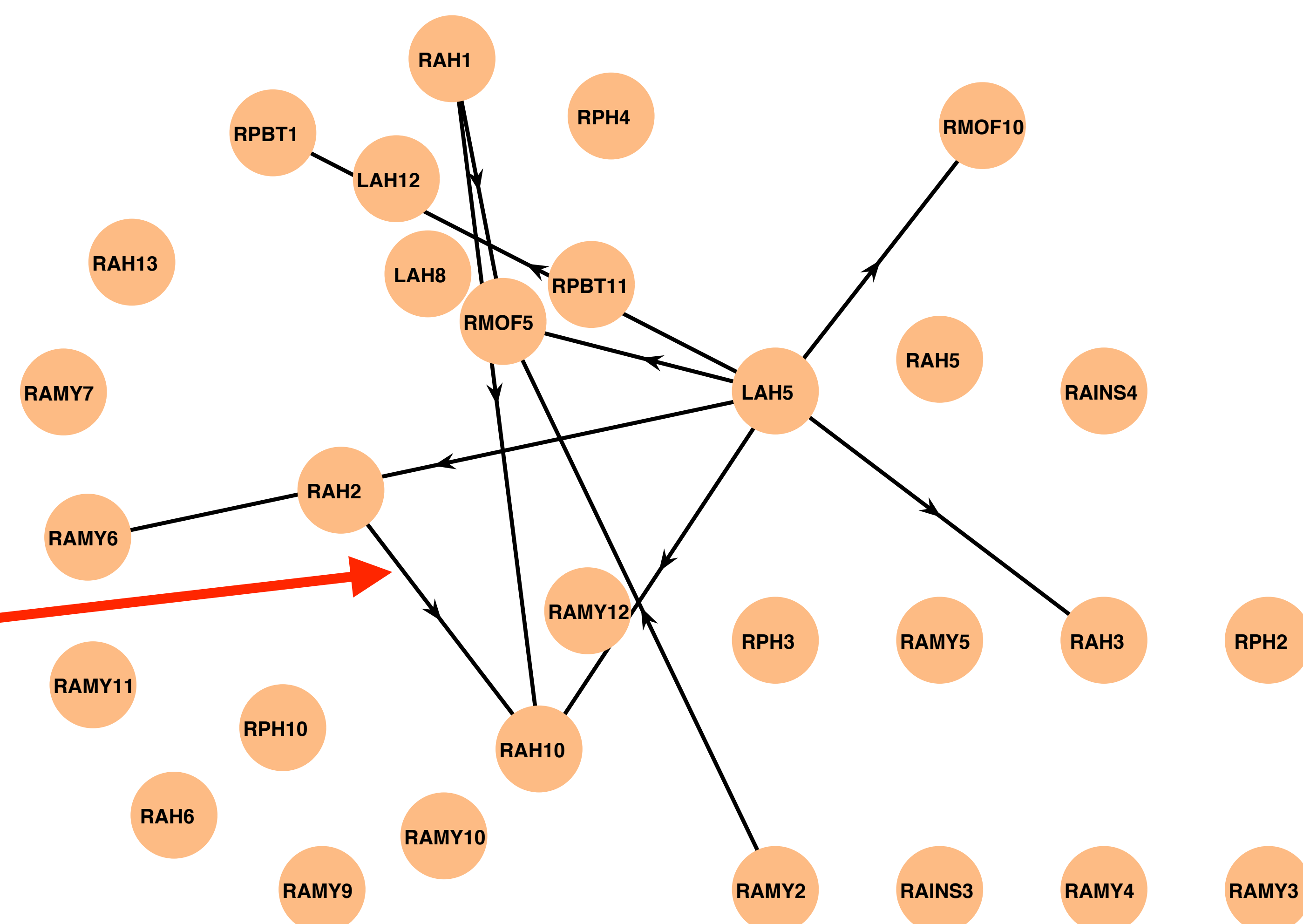
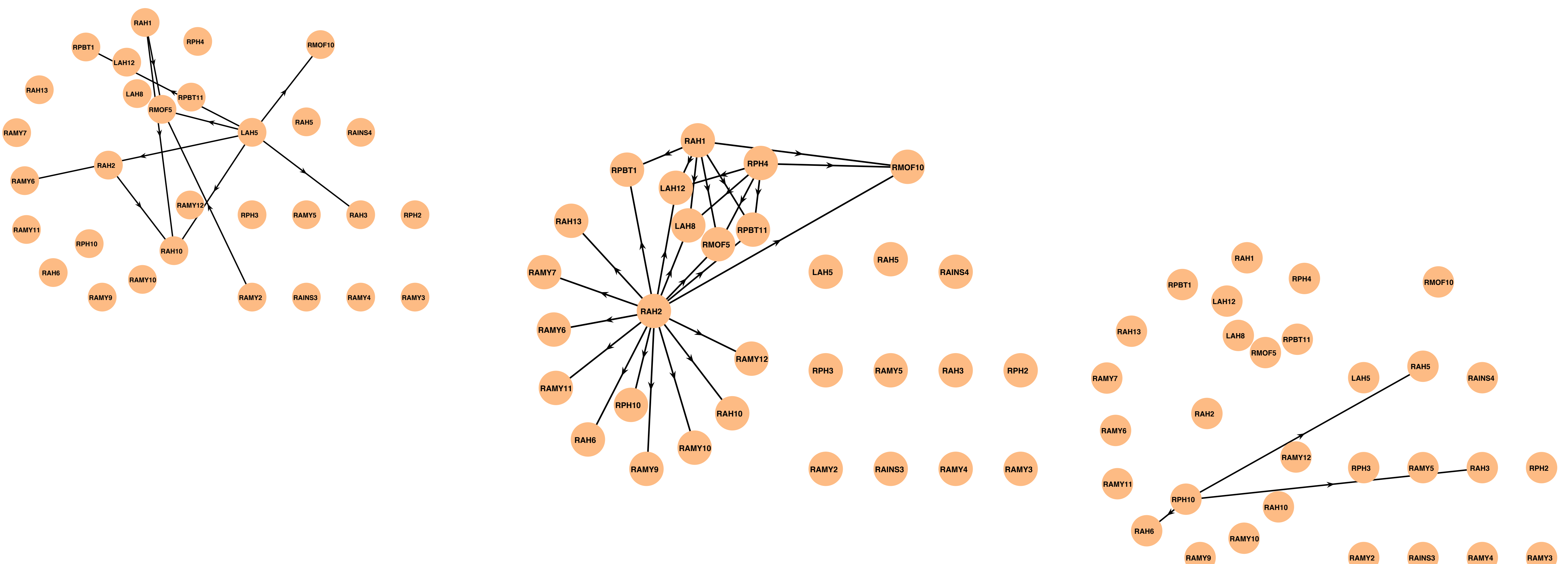
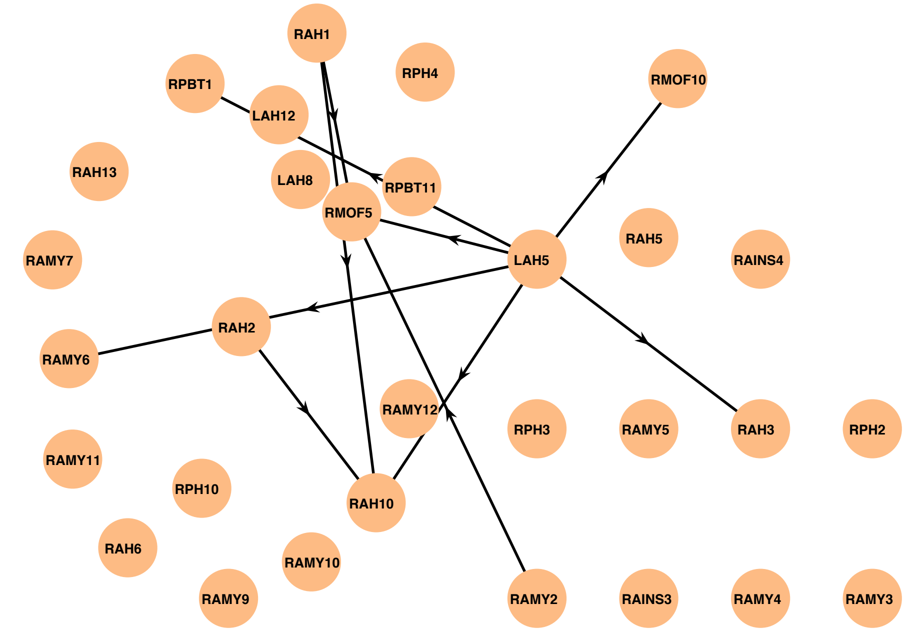


flow between population of neurons

Seizure onset zone

- causal influence—directed connectivity
  - a graph with electrodes as nodes and directed information as edge
  - pre-ictal, ictal, post-ictal





Seizure onset zone

- causal influence—directed connectivity
  - a graph with electrodes as nodes and directed information as edge
  - pre-ictal (period prior to seizure)
  - net degree of a node = out degree - in degree

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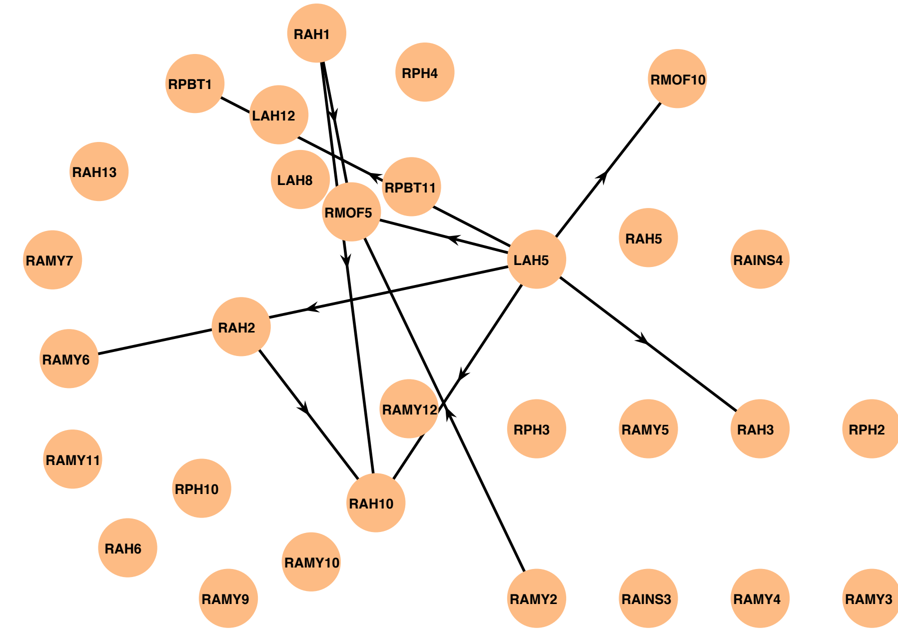
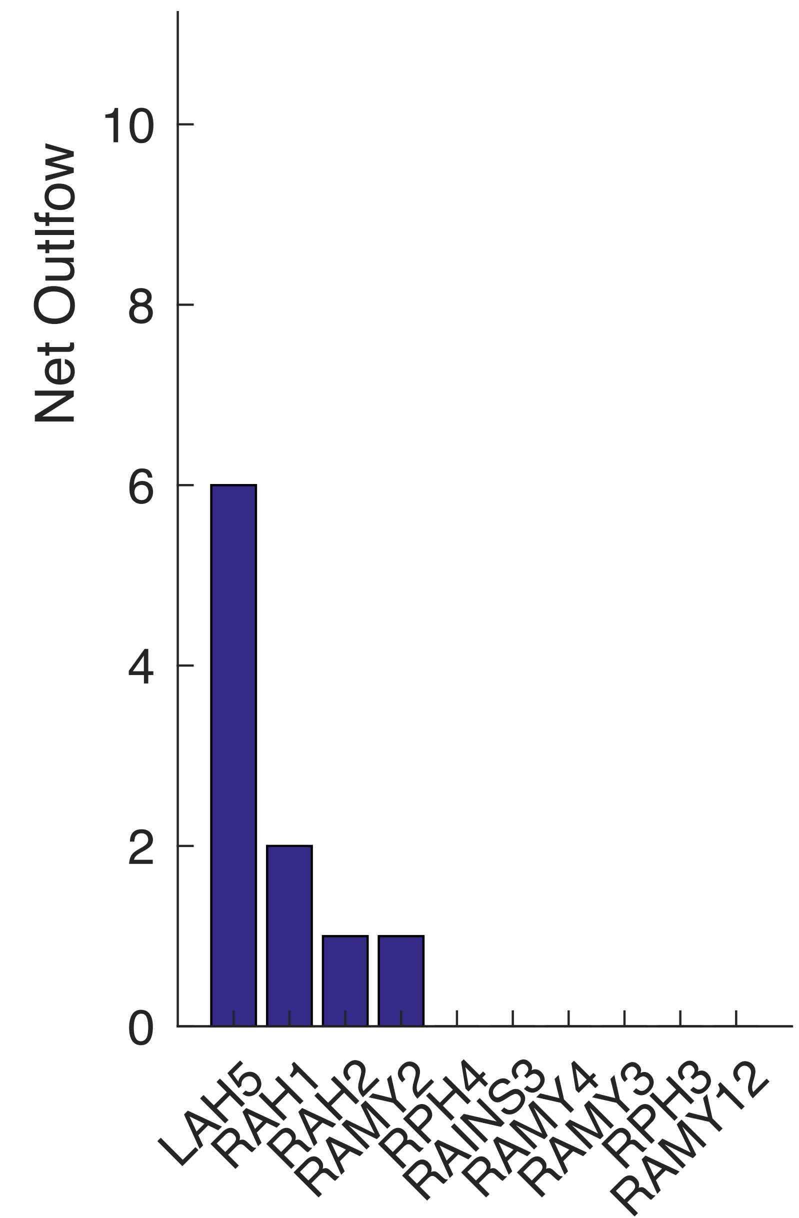
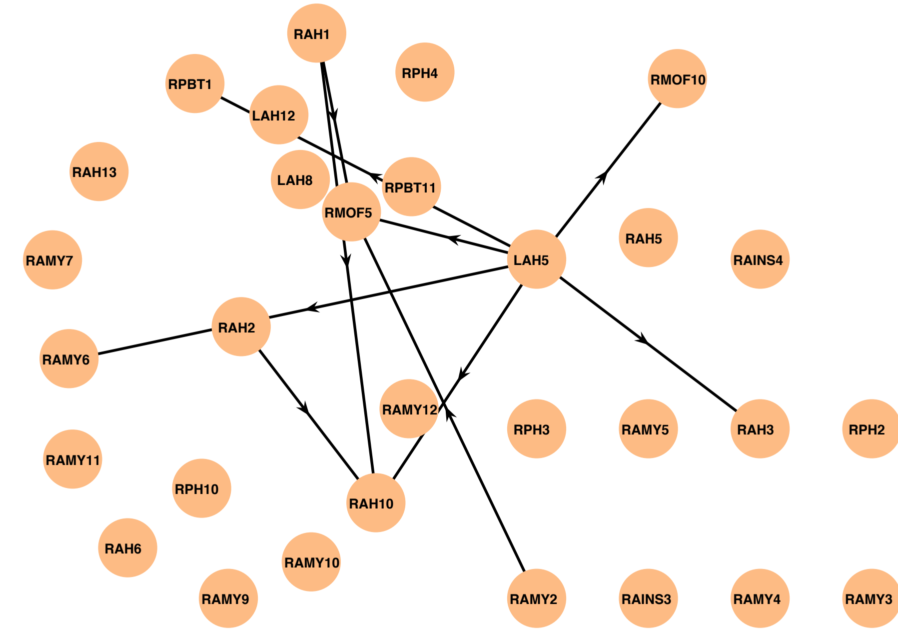




Seizure onset zone



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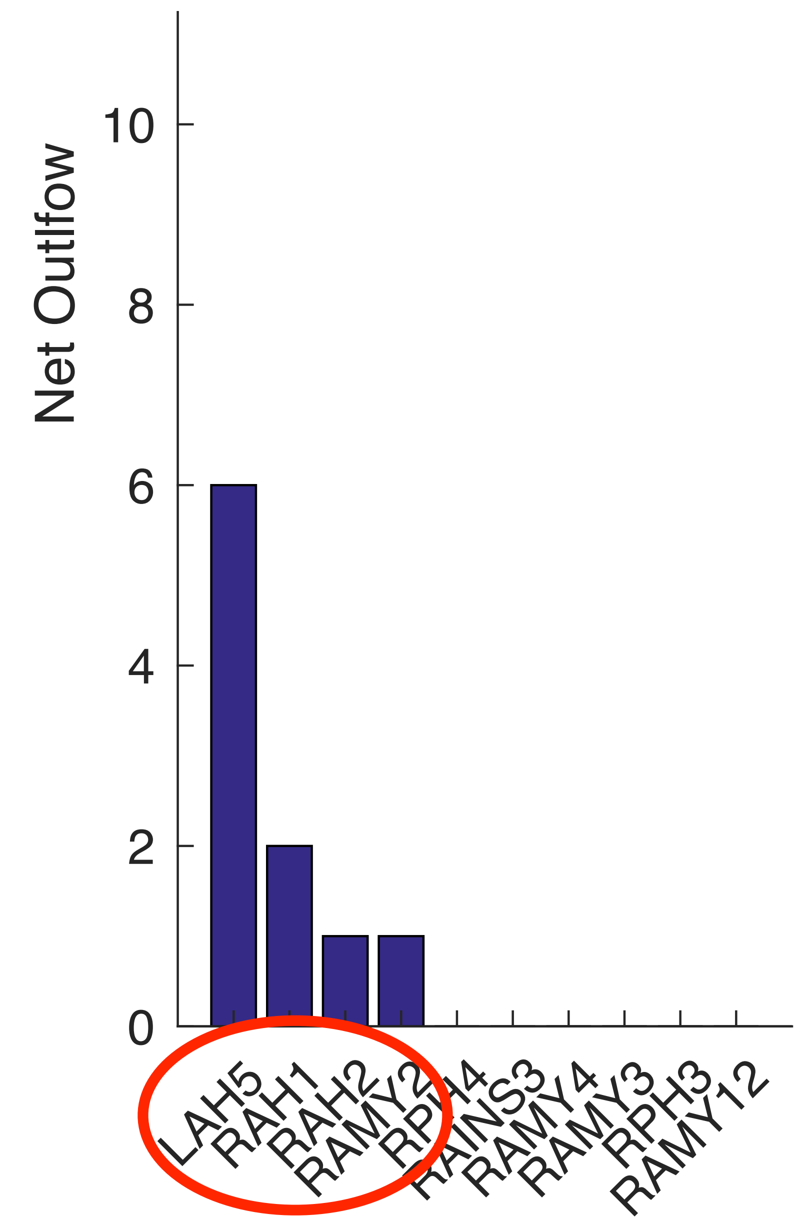
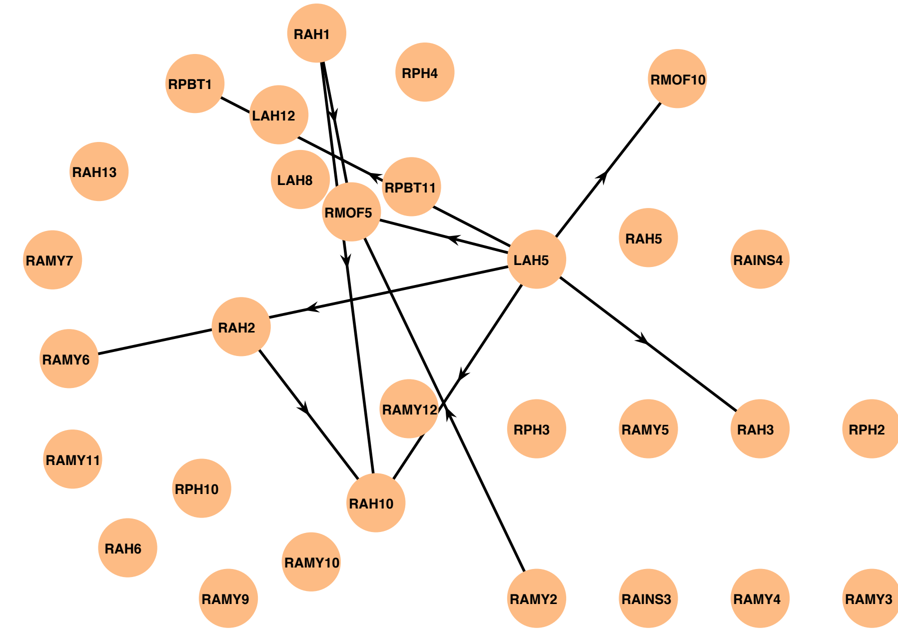


Seizure onset zone



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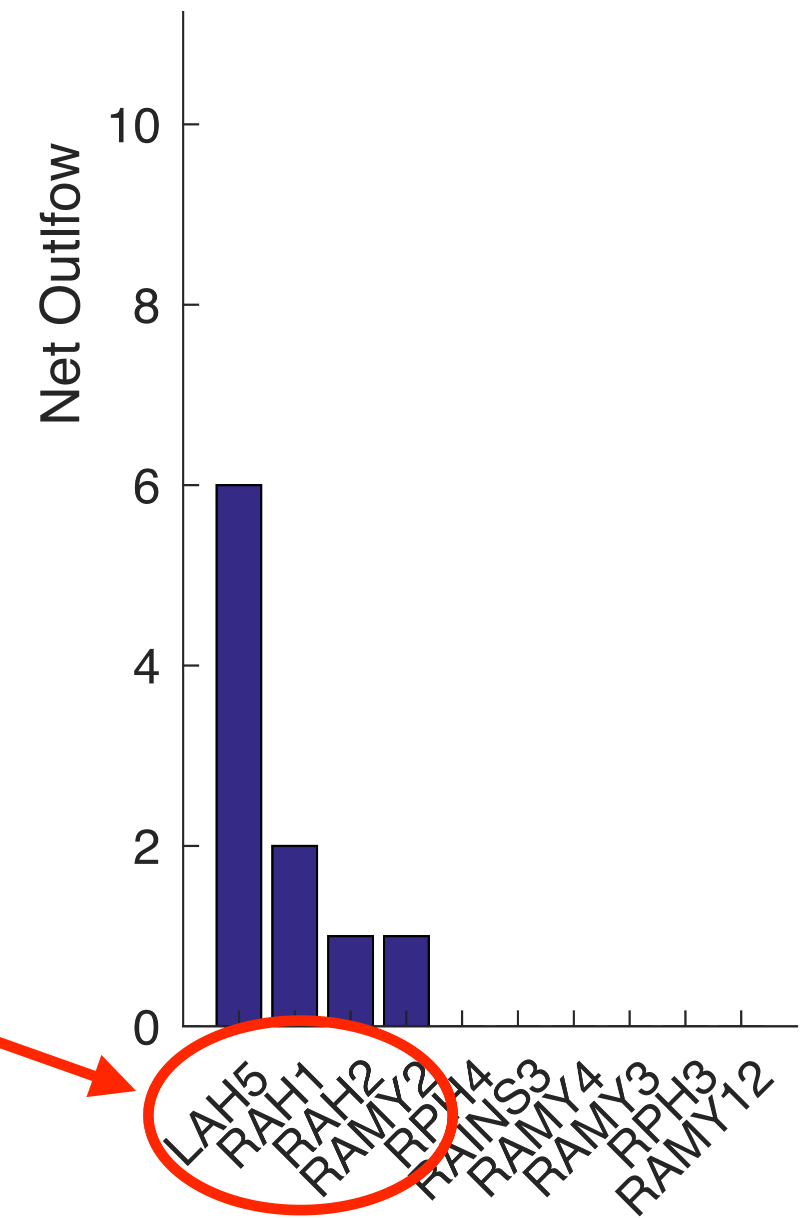
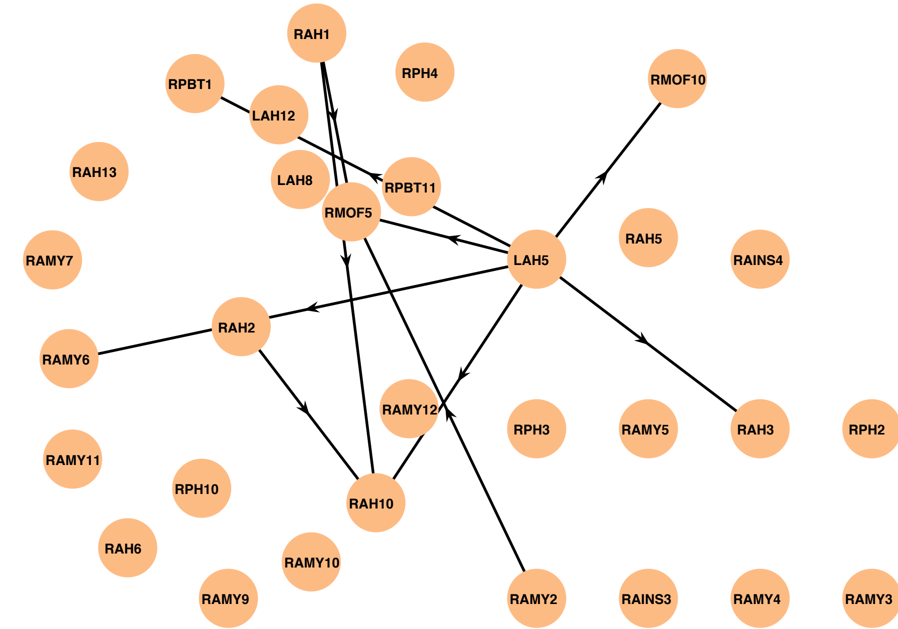
electrodes in seizure onset zone



Seizure onset zone



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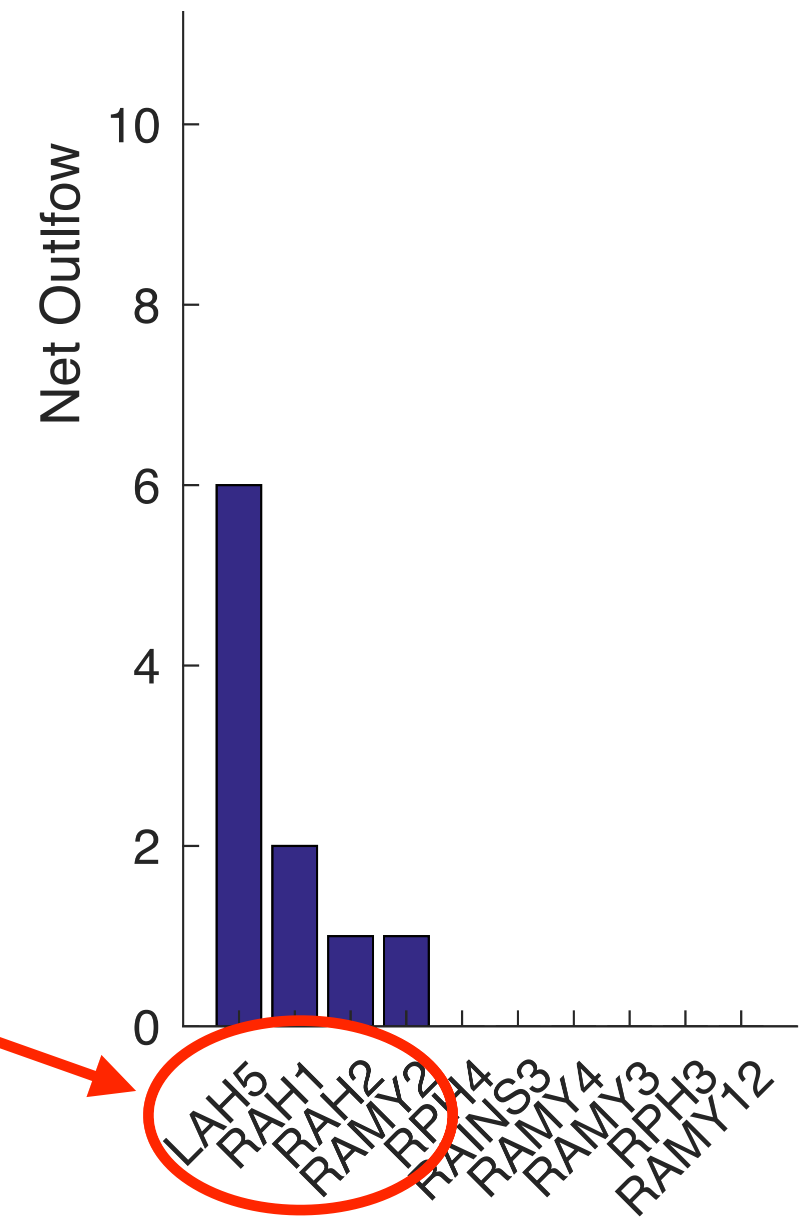
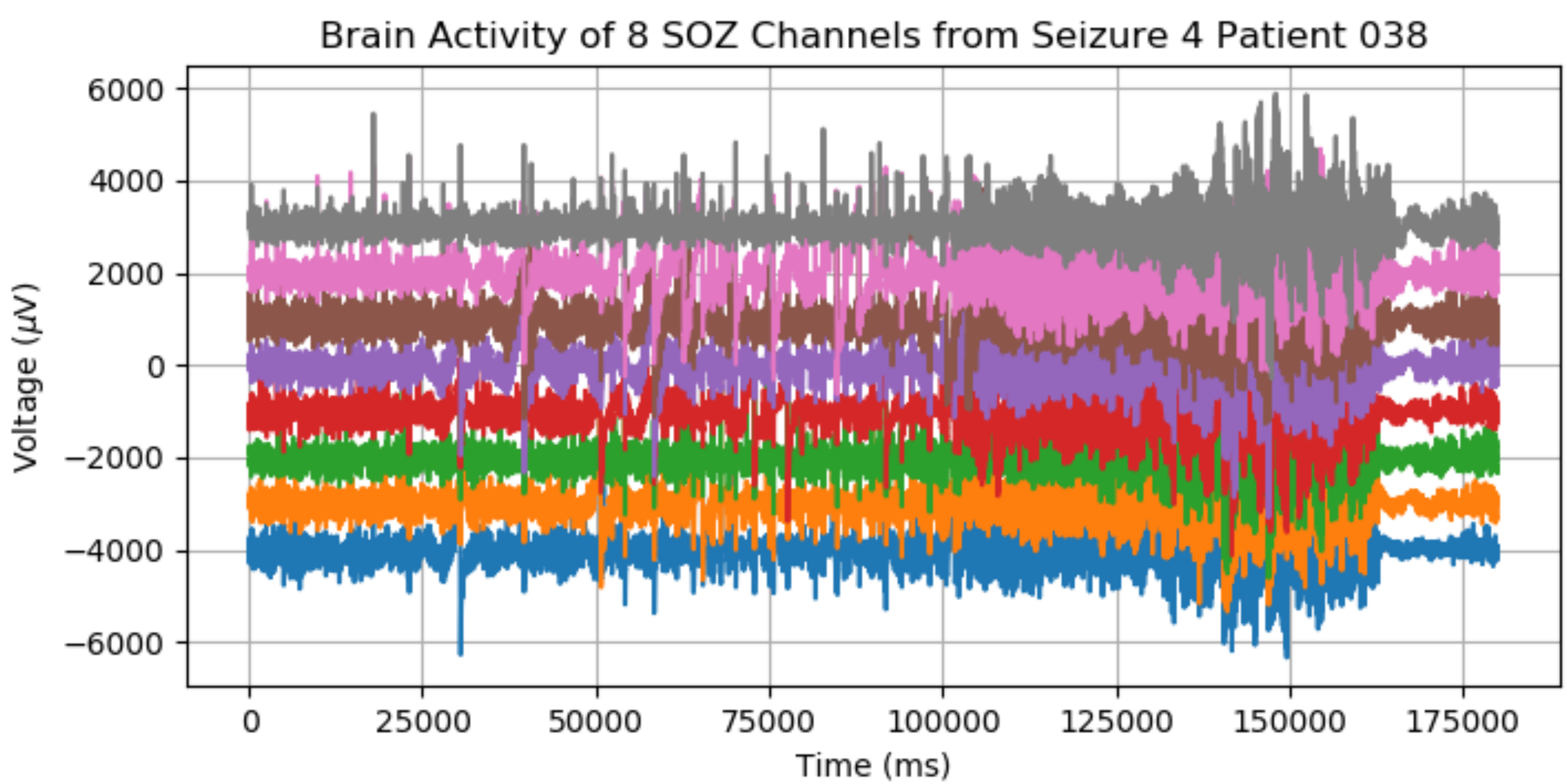


electrodes in seizure onset zone

nearly perfect match with the neurologist for all 12 patients

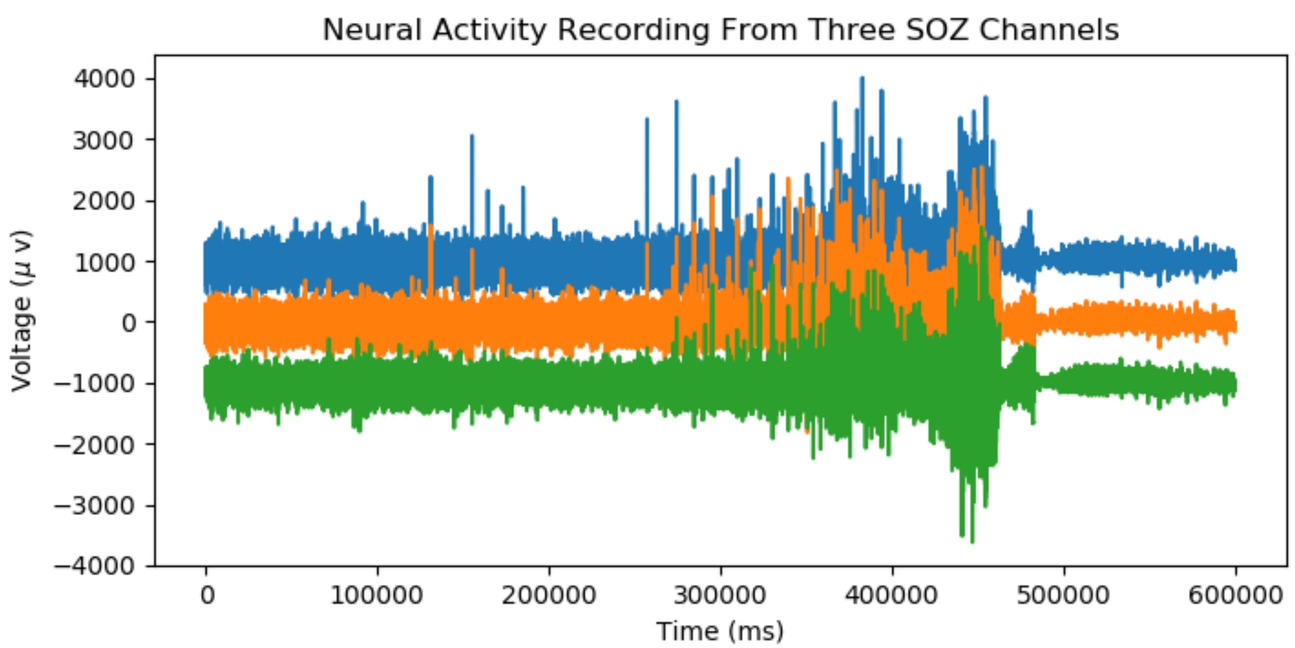
Epilepsy

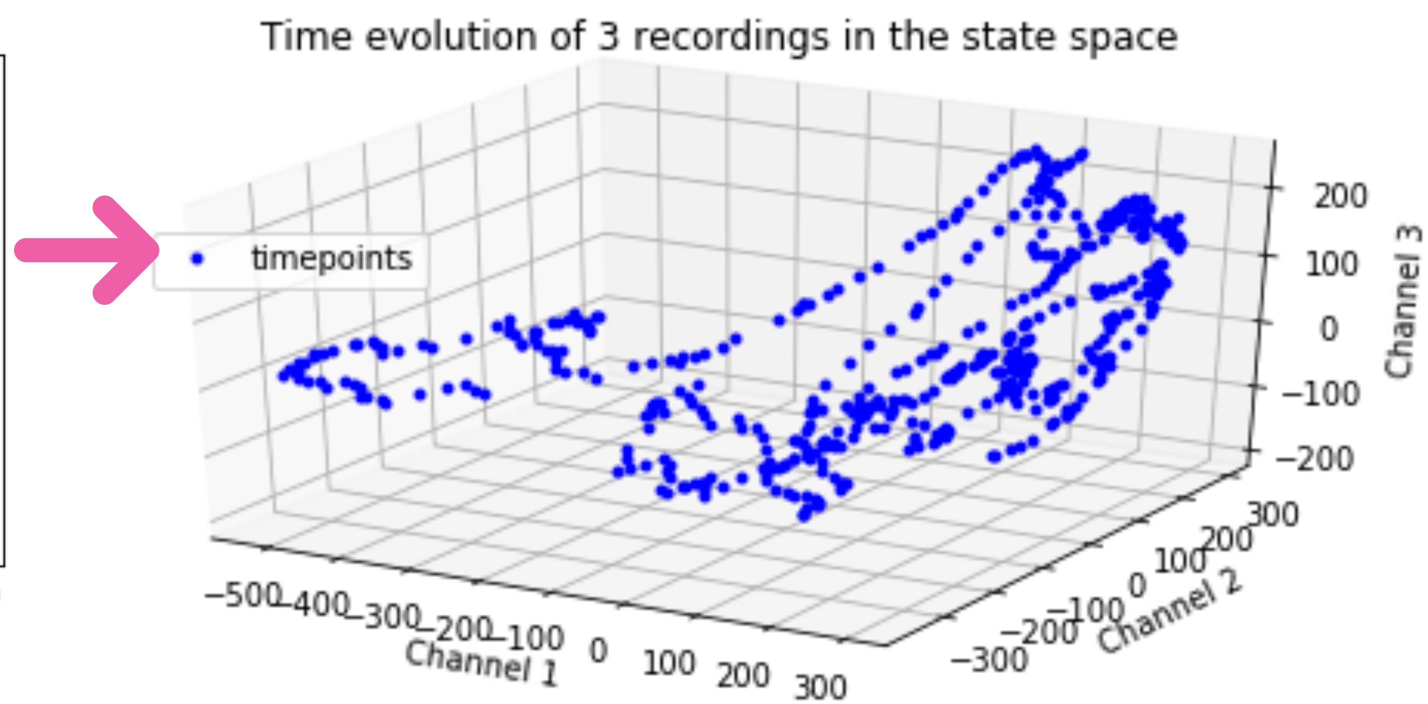
- focus on electrodes in the seizure onset zone—250 electrodes down to 6-10
- dynamics of time series to predict seizures



State space

- trajectory is nonlinear

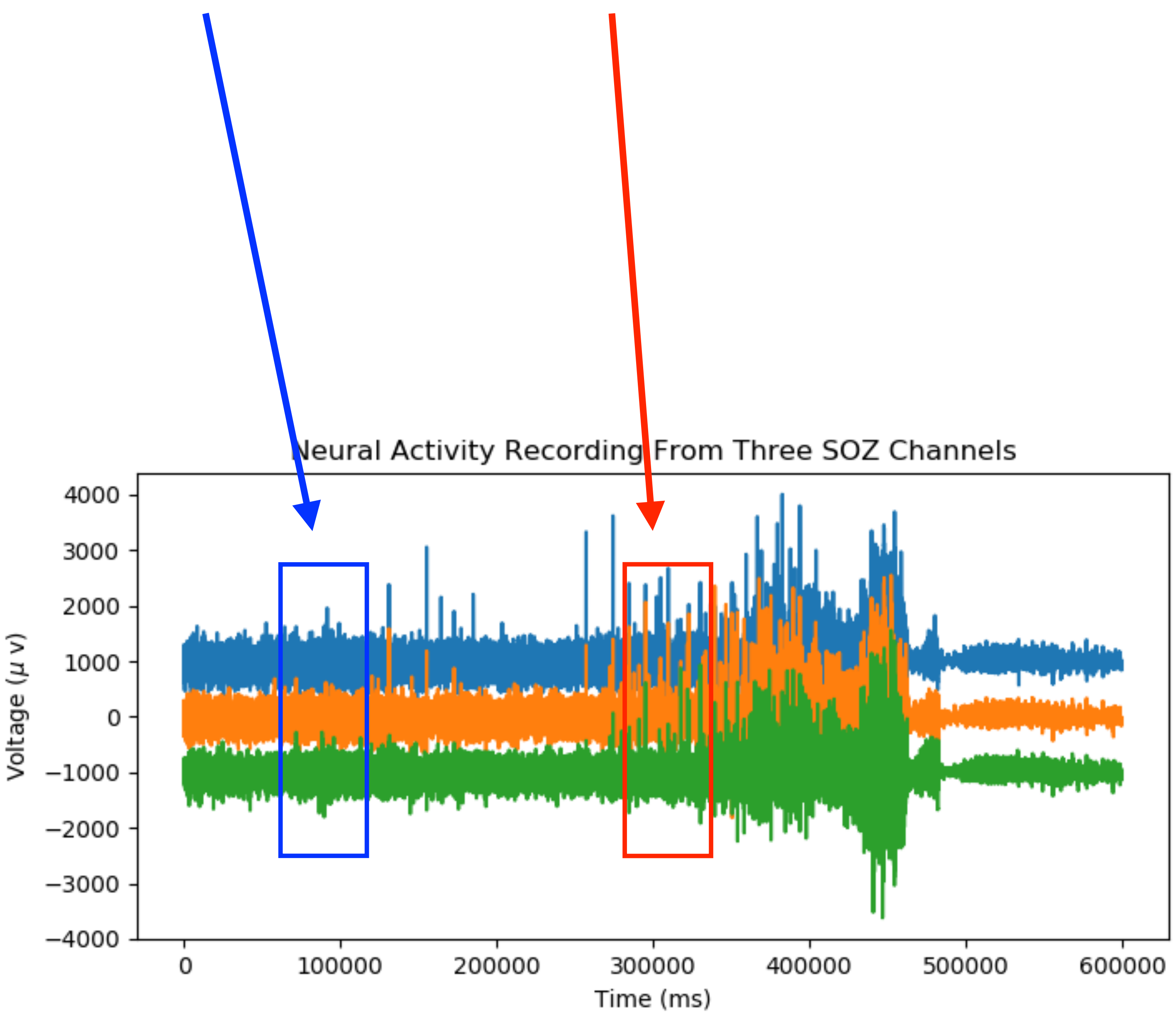




State space

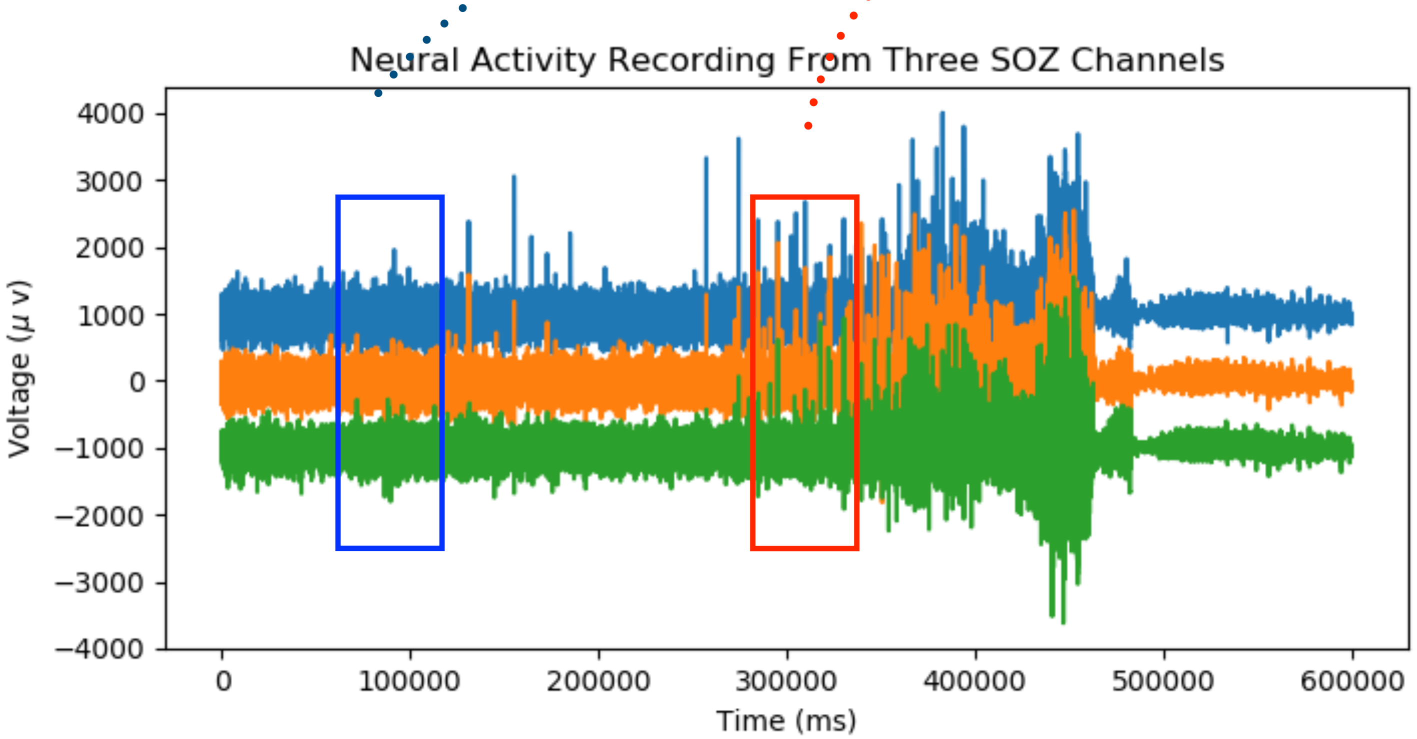
- trajectory is nonlinear

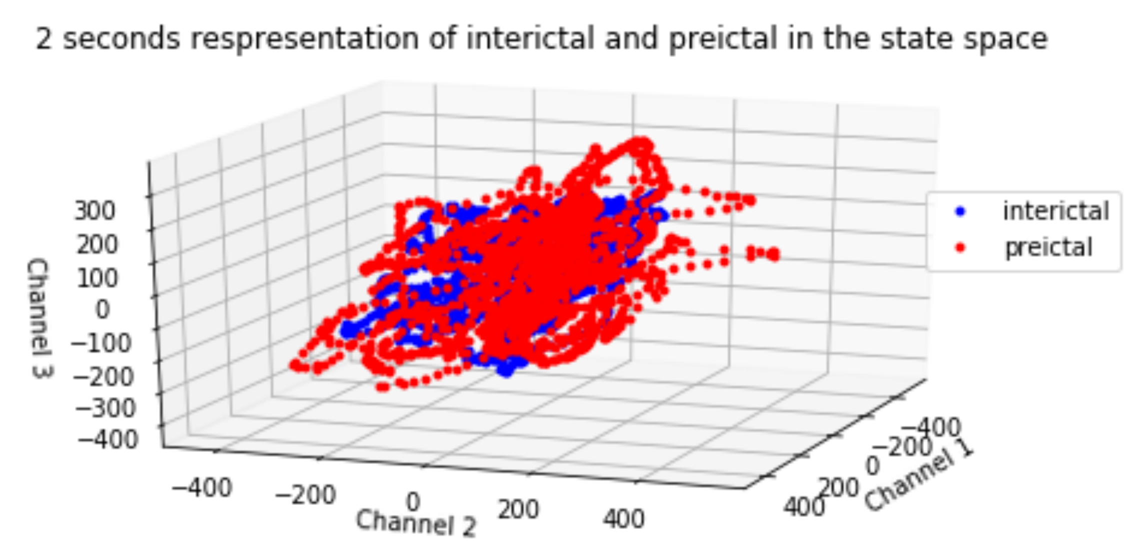
- inter-ictal and pre-ictal



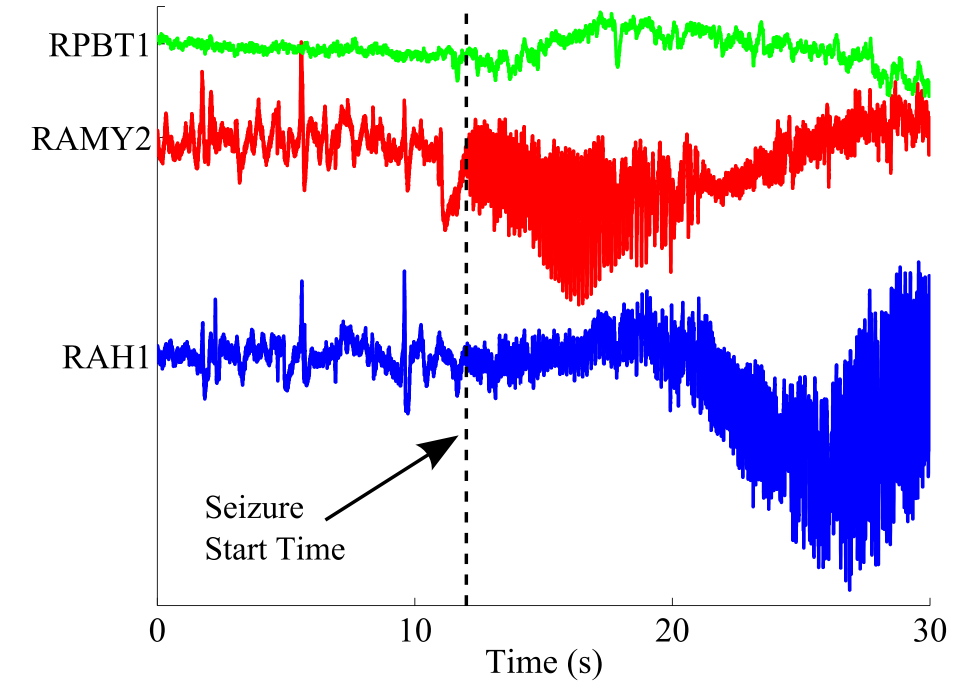
State space

- trajectory is nonlinear
- inter-ictal and pre-ictal periods are not distinguishable





Dynamics



- capturing dynamics of recordings

$$X_{m+1} = f(X_m)$$

- *K* recordings in time *m* are

$$X_m = \begin{bmatrix} x_m^{(1)} \\ x_m^{(2)} \\ \vdots \\ x_m^{(K)} \end{bmatrix}$$

- a linear approximation is often insufficient to capture the dynamics

$$X_{m+1} = AX_m \text{ where } A \text{ is } K \times K$$

Dynamics

- time embedding

$$\mathcal{X}_1 = \begin{bmatrix} X_1 & X_2 & \dots & X_{M-h+1} \\ X_2 & X_3 & \dots & X_{M-h+2} \\ \vdots & \vdots & \ddots & \vdots \\ X_h & X_{h+1} & \dots & X_M \end{bmatrix}$$

- dynamics result in

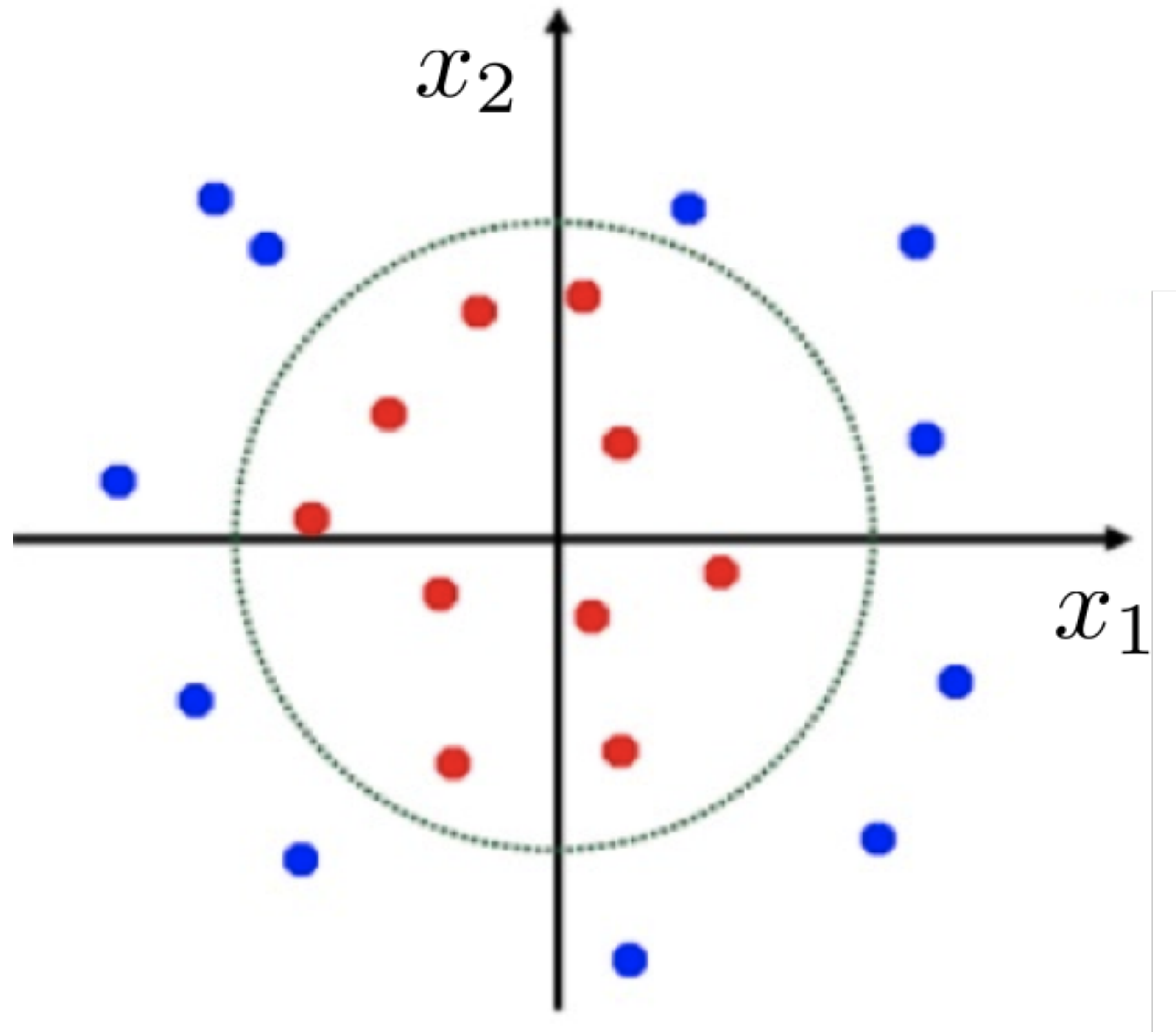
$$\mathcal{X}_2 = \begin{bmatrix} X_2 & X_3 & \dots & X_{M-h+2} \\ X_3 & X_4 & \dots & X_{M-h+3} \\ \vdots & \vdots & \ddots & \vdots \\ X_{h+1} & X_{h+2} & \dots & X_{M+1} \end{bmatrix} = f(\mathcal{X}_1)$$

- a linear approximation has shown to be sufficient in many applications

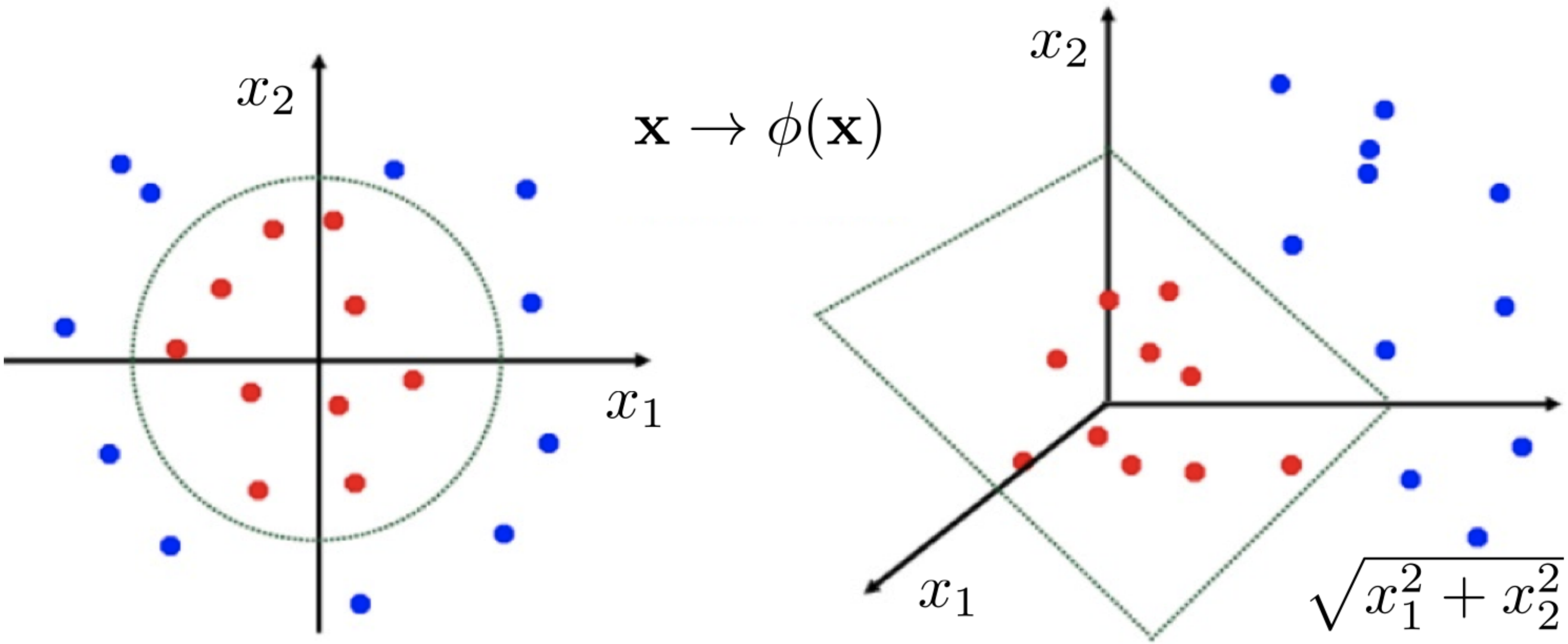
$$\mathcal{X}_2 = \mathcal{A}\mathcal{X}_1 \text{ where } \mathcal{A} \text{ is } Kh \times Kh$$

I. Mezic´"Spectral properties of dynamical systems, model reduction and decompositions," Nonlinear Dynamics

Example



Example



Dynamic mode decomposition

- the main objective is to estimate $\mathcal{A}$

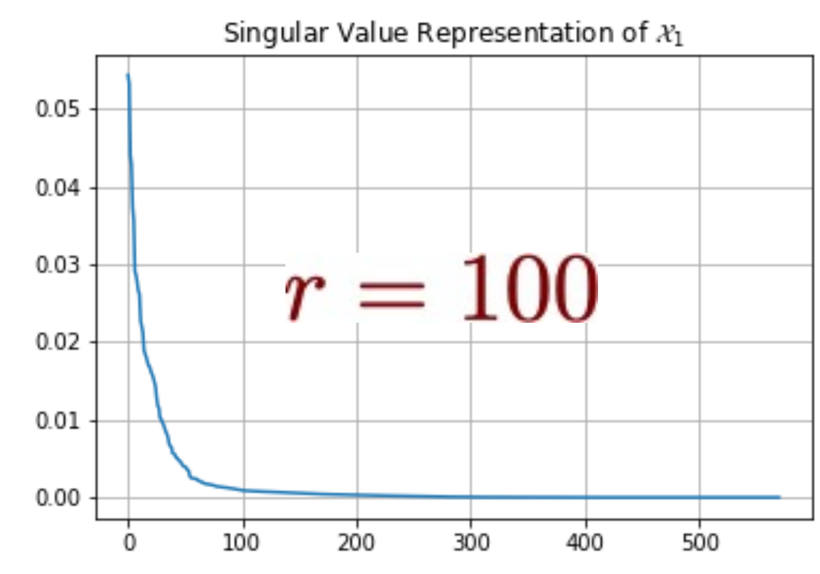
$$\mathcal{A} = \mathcal{X}_2 \mathcal{X}_1^{-1} = \mathcal{X}_2 \mathcal{U} \mathcal{S}^{-1} \mathcal{W}^\top$$

- dynamics of the system is captured by eigenvector and eigenvalues of $\mathcal{A}$

$$\mathcal{A} = \mathbf{\Phi} \mathbf{\Lambda} \mathbf{\Phi}^{-1}$$

- the *Kh x Kh* matrix can be approximated by a smaller matrix

$$\tilde{A} = \mathcal{W}_r^\top \mathcal{A} \mathcal{W}_r = \mathcal{W}_r^\top \mathcal{X}_2 \mathcal{U}_r \mathcal{S}_r^{-1}$$



Extracting key feature

- spatiotemporal feature extraction

$$\mathbf{\Phi} = [\phi_1 \quad \phi_2 \quad \dots \quad \phi_r]$$

DMD Power

$$|\mathbf{\Phi}| = [|\phi_1| \quad |\phi_2| \quad \cdots \quad |\phi_r|]$$

DMD Phase

$$\angle\mathbf{\Phi} = [\angle\phi_1 \quad \angle\phi_2 \quad \cdots \quad \angle\phi_r]$$

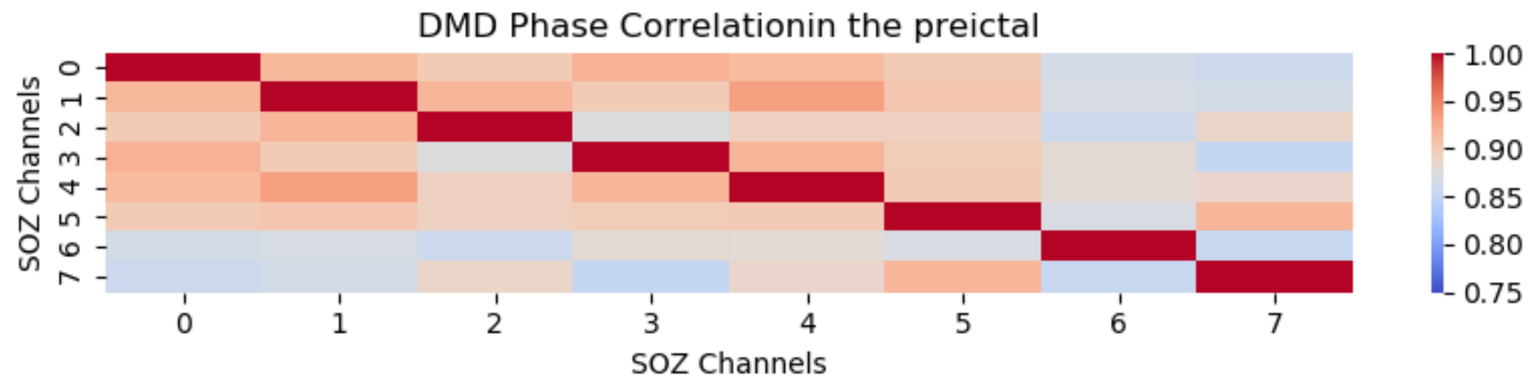
I. Mezic´“Spectral properties of dynamical systems, model reduction and decompositions,” Nonlinear Dynamics

Features

- DMD phase correlations among electrodes and power versus frequencies

Feature 1:

$$\begin{bmatrix}\angle\phi_1 & \angle\phi_2 & \cdots & \angle\phi_r\end{bmatrix} \cdot \begin{bmatrix}\angle\phi_1^T \\ \angle\phi_2^T \\ \vdots \\ \angle\phi_r^T\end{bmatrix}$$

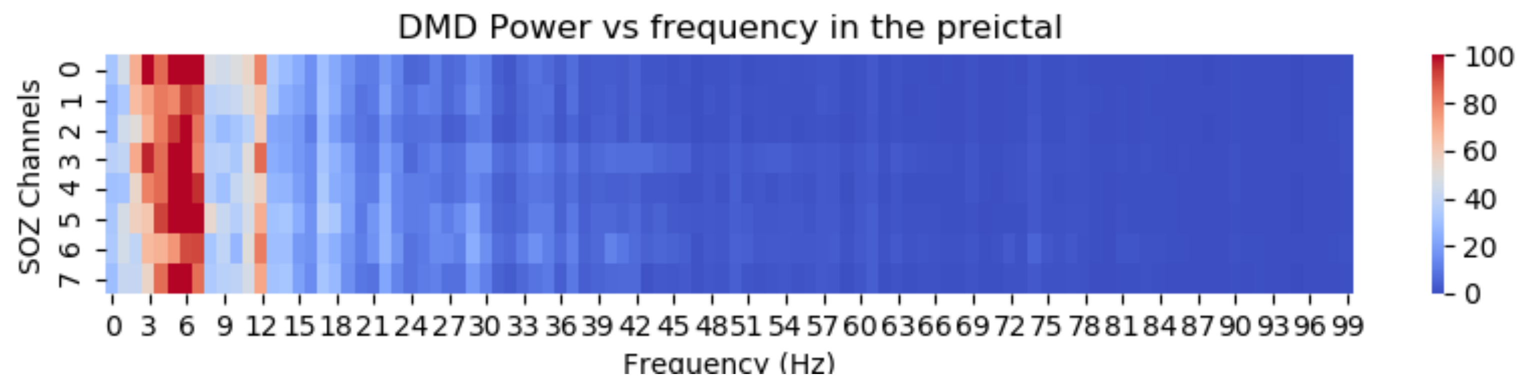


Feature 2:

$$\begin{bmatrix}|\phi_1| & |\phi_2| & \cdots & |\phi_r|\end{bmatrix}$$

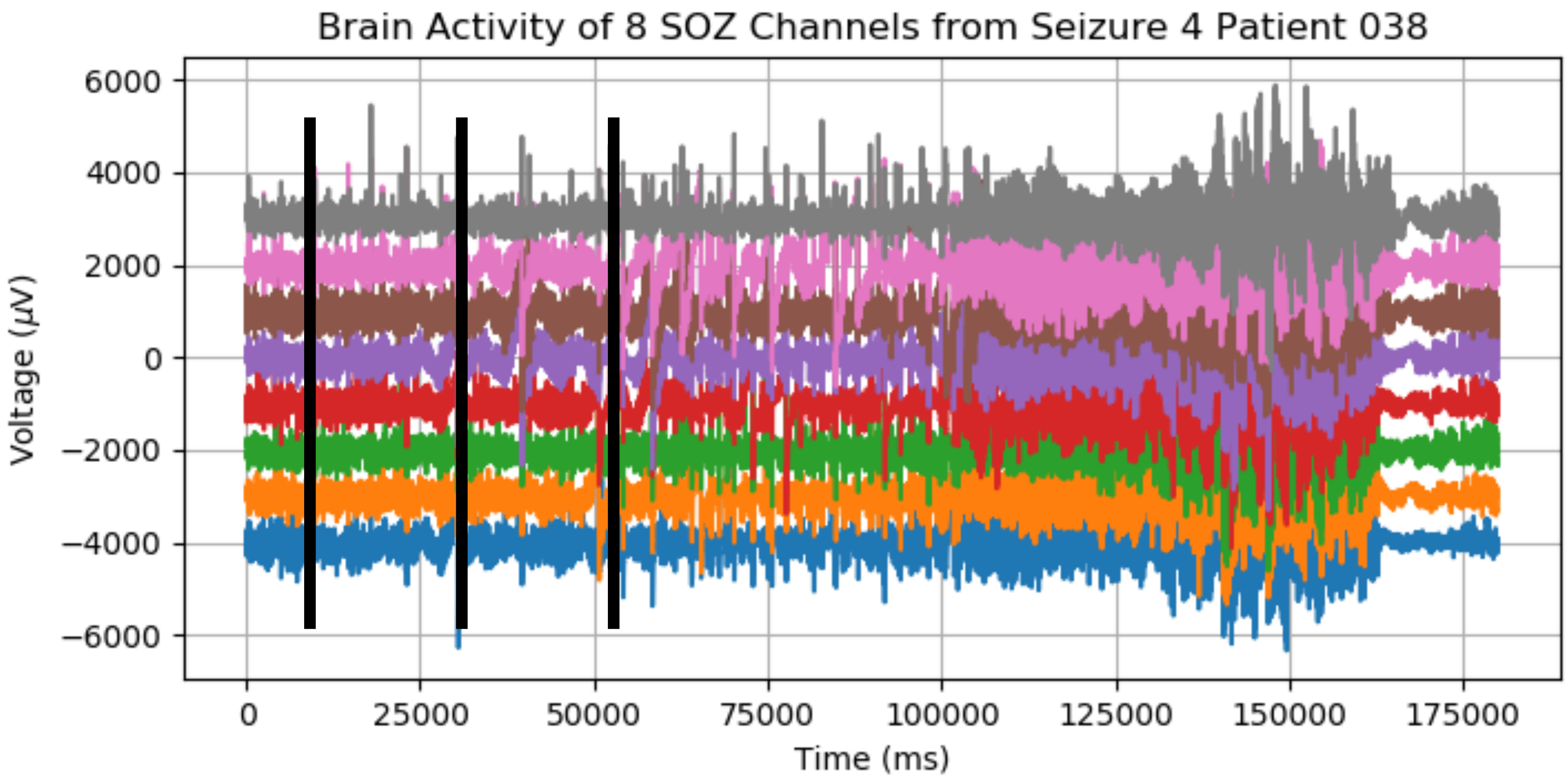
vs.

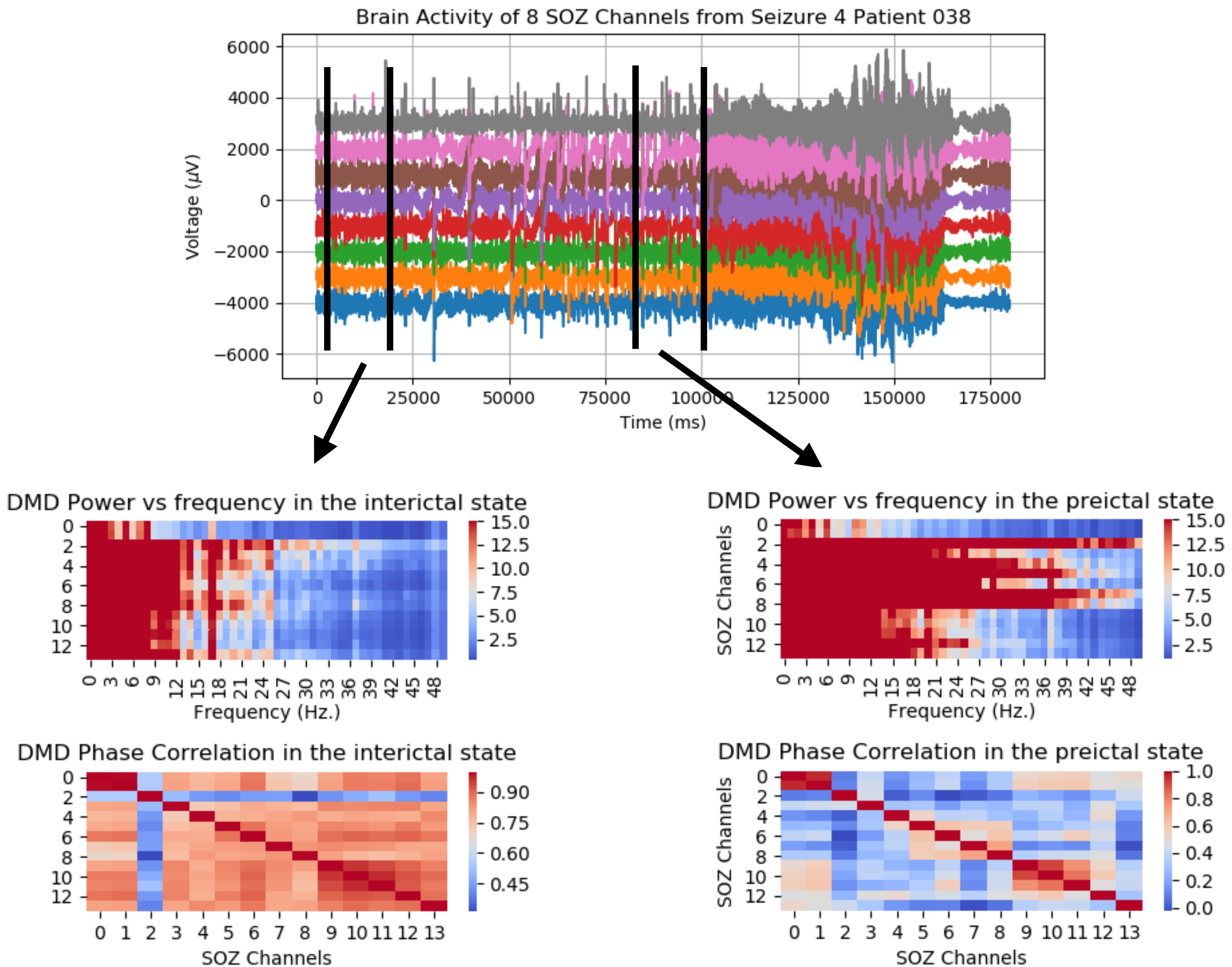
$$\begin{bmatrix}\lambda_1 & \lambda_2 & \dots & \lambda_r\end{bmatrix}$$



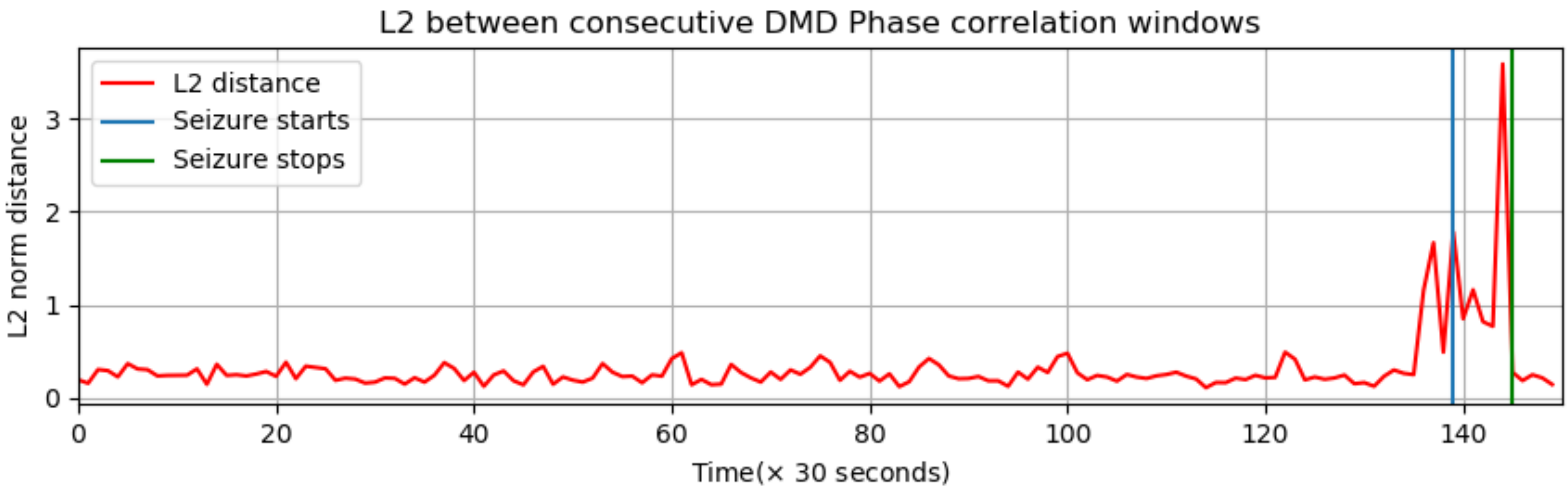
Back to seizure prediction

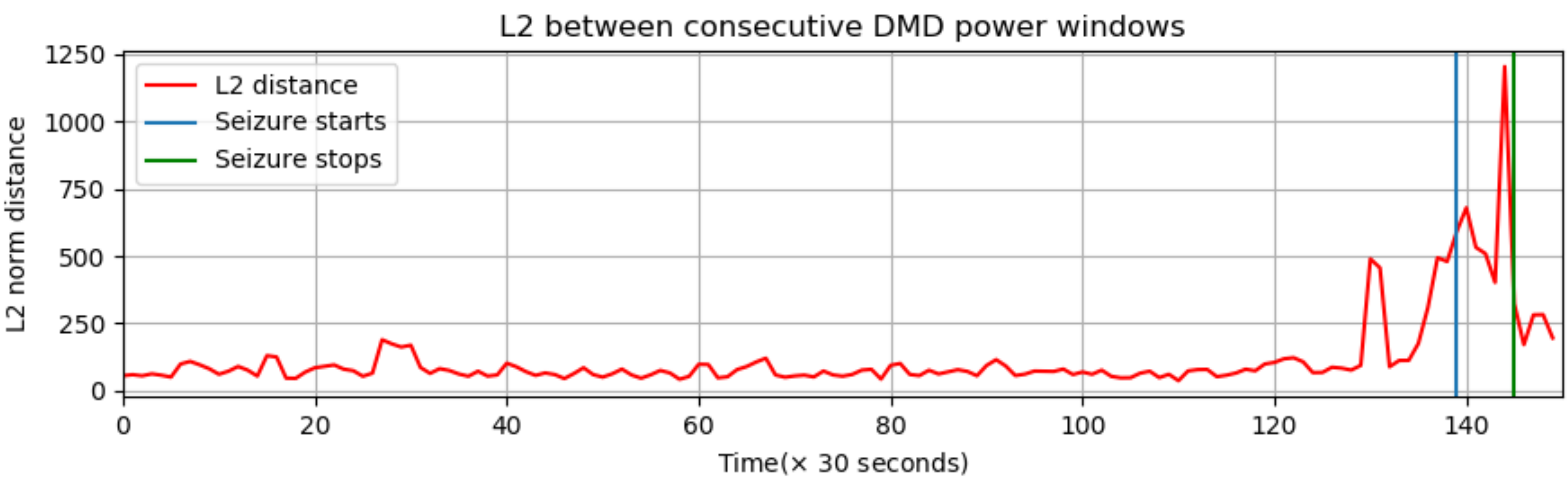
- dynamics $$\mathcal{X}_{m+1} = \mathcal{A}_m \mathcal{X}_m$$

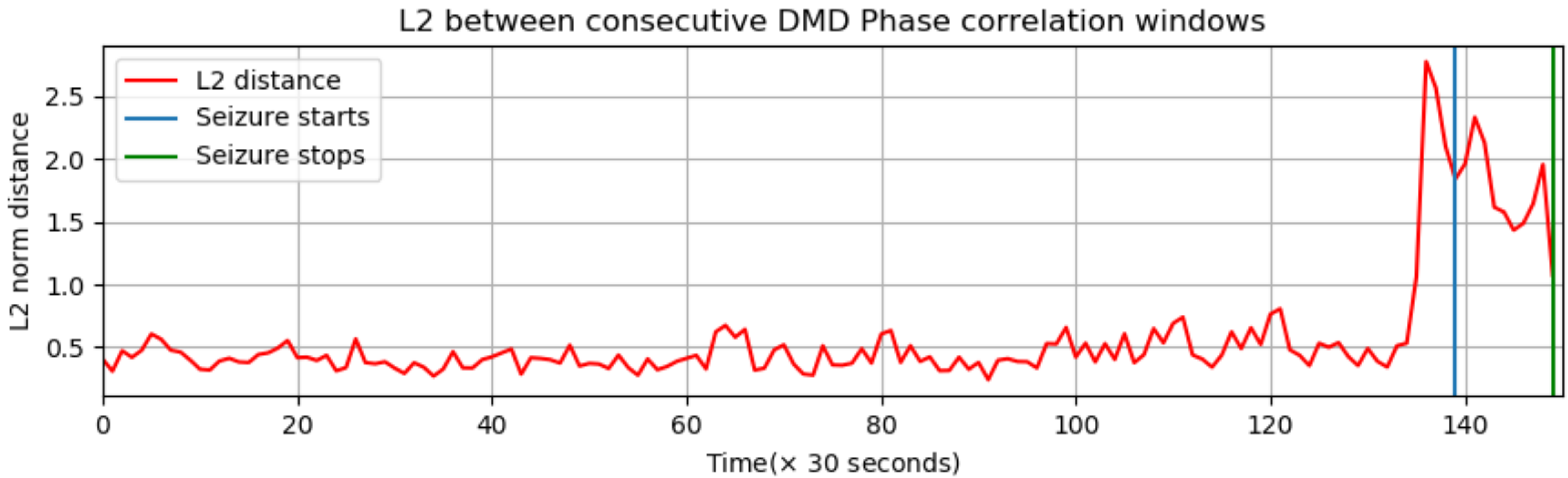


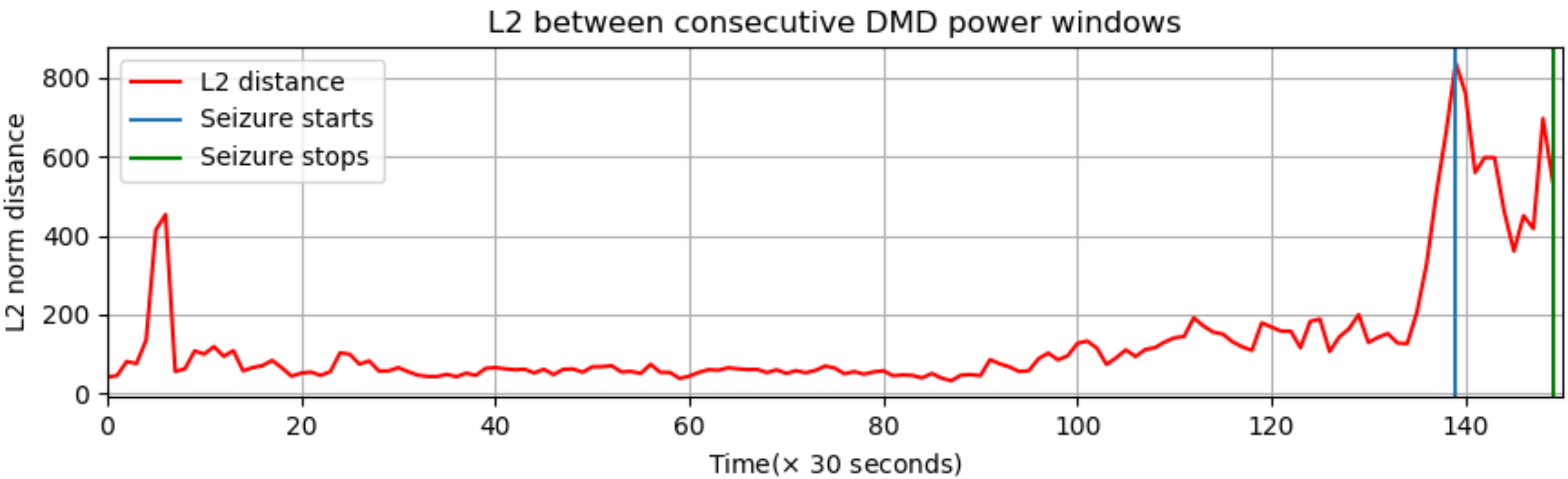


Brain Activity of 8 SOZ Channels from Seizure 4 Patient 038
Voltage (μV)
Time (ms)
DMD Power vs frequency in the interictal state
Frequency (Hz.)
DMD Power vs frequency in the preictal state
SOZ Channels
Frequency (Hz.)
DMD Phase Correlation in the interictal state
SOZ Channels
DMD Phase Correlation in the preictal state
SOZ Channels
SOZ Channels

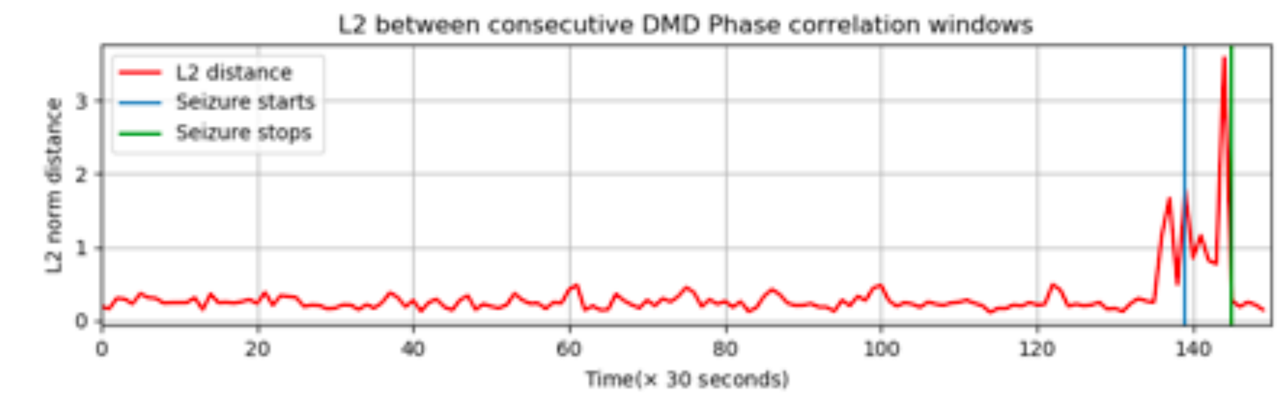

L2 between consecutive DMD Phase correlation windows
L2 distance
Seizure starts
Seizure stops
L2 norm distance
0
1
2
3
0
20
40
60
80
100
120
140
Time(× 30 seconds)

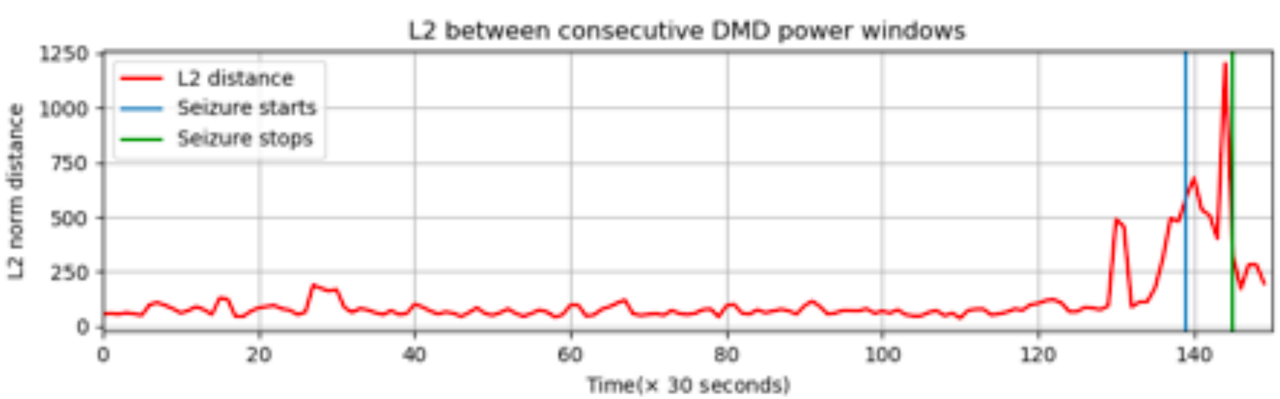

L2 between consecutive DMD power windows
L2 distance
Seizure starts
Seizure stops
L2 norm distance
0
250
500
750
1000
1250
0
20
40
60
80
100
120
140
Time(× 30 seconds)


L2 between consecutive DMD Phase correlation windows
L2 distance
Seizure starts
Seizure stops
L2 norm distance
Time(× 30 seconds)

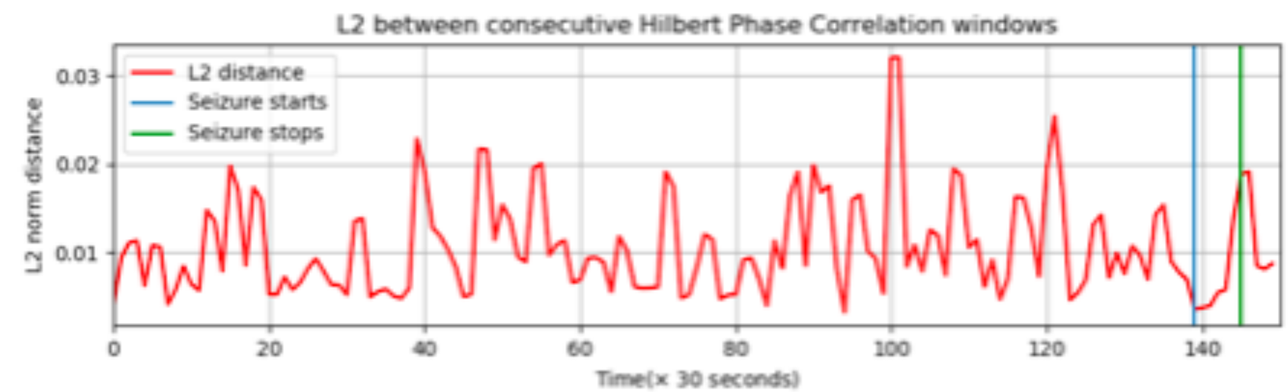

L2 between consecutive DMD power windows
L2 distance
Seizure starts
Seizure stops
L2 norm distance
Time(× 30 seconds)

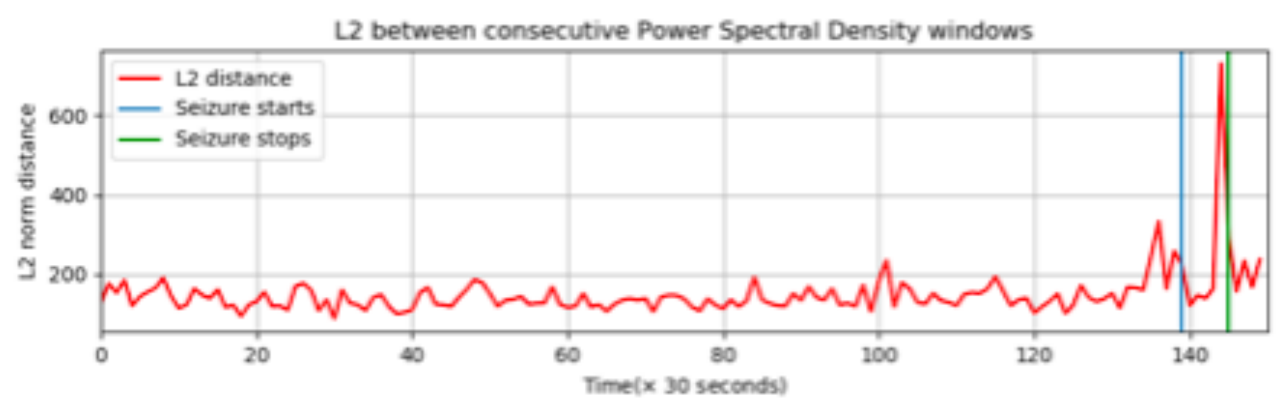
EmDMD



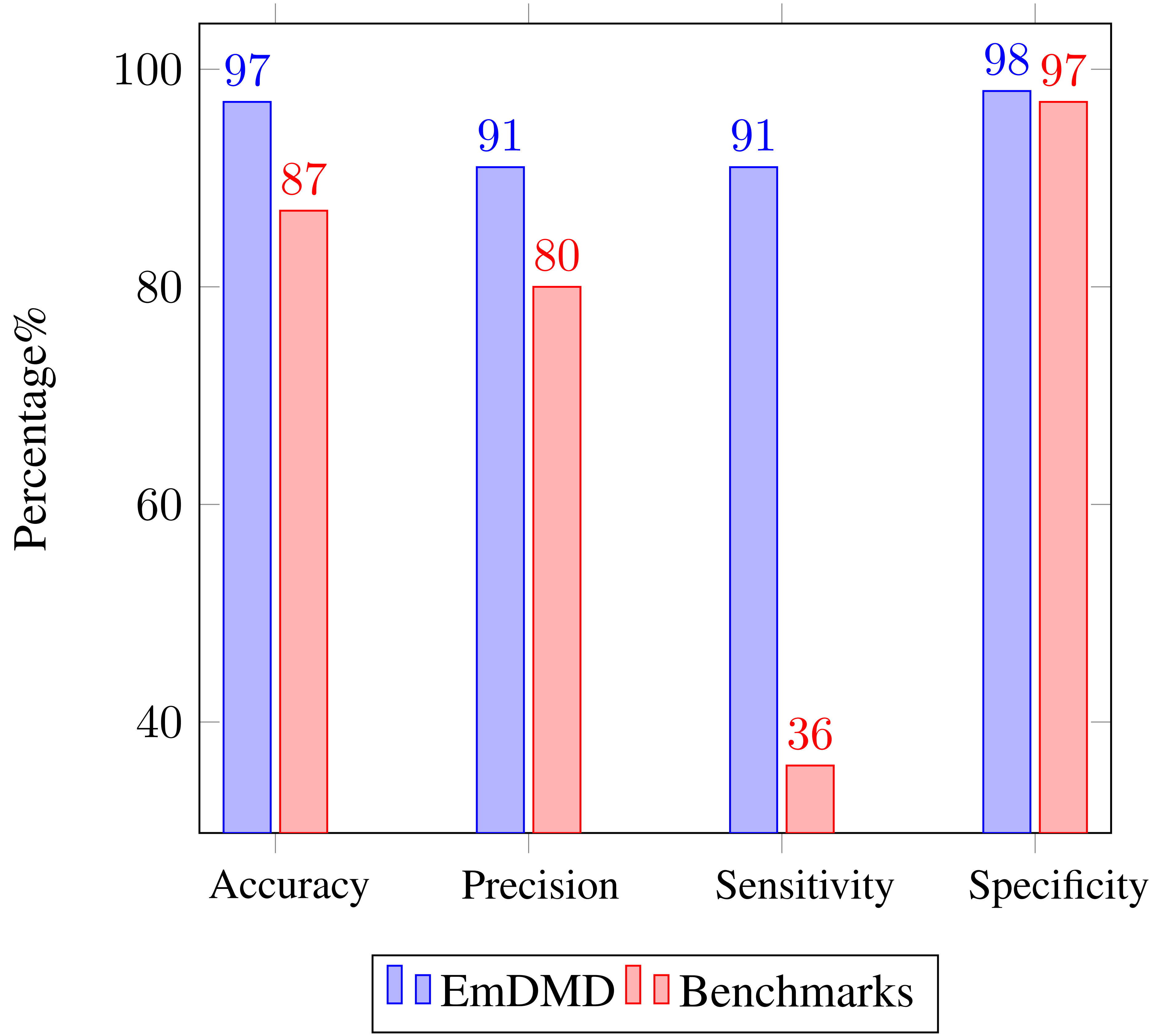


Benchmark

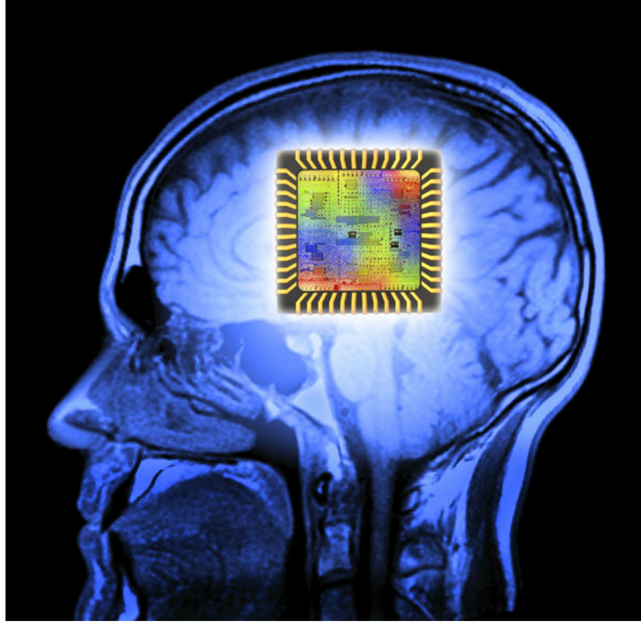




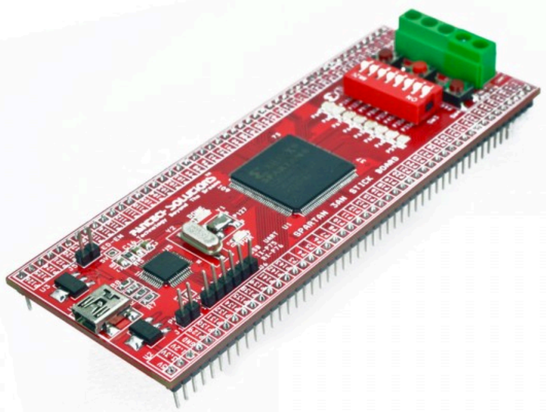
SVM with kernel



Seizure prediction



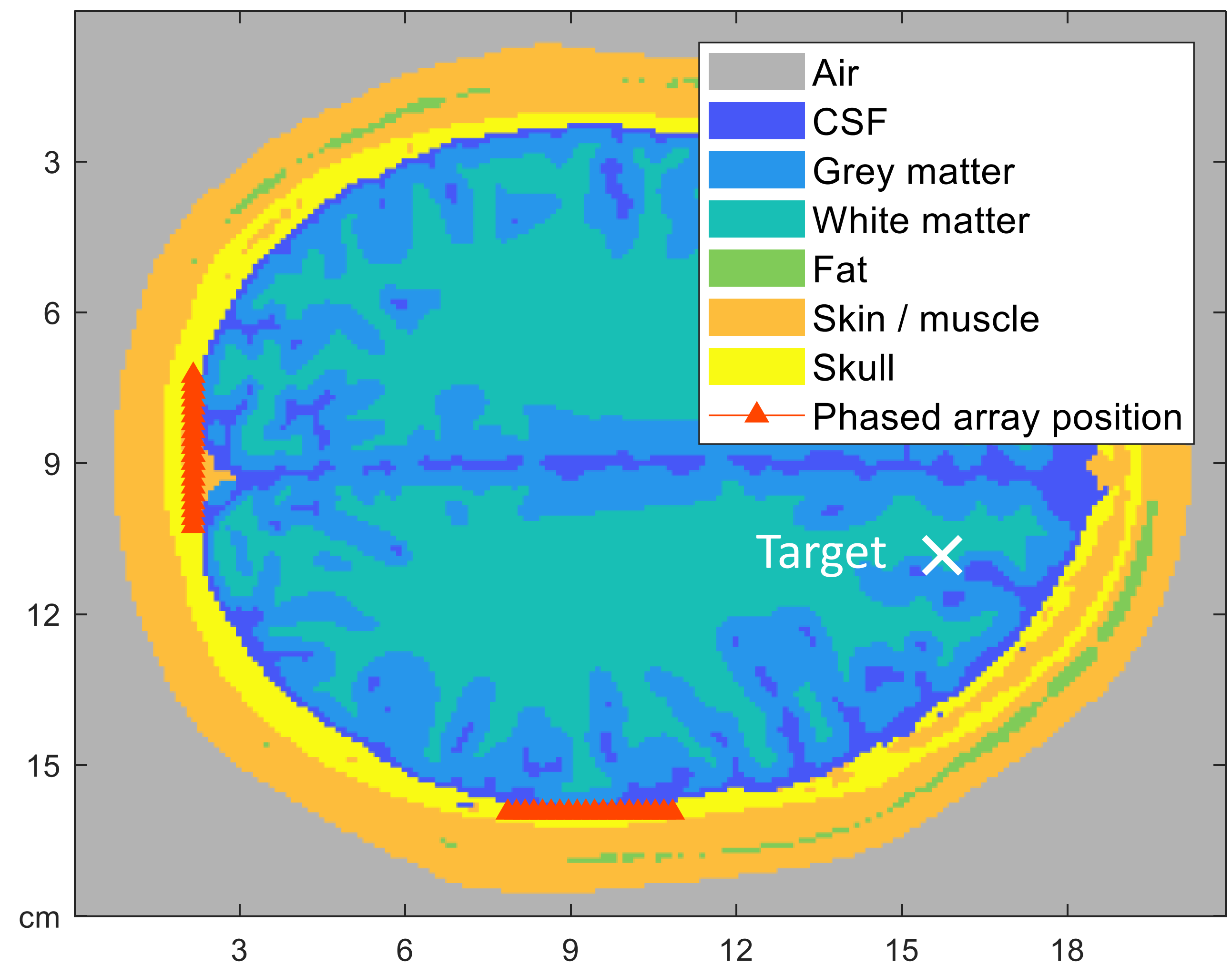
- promising data analytic tools
  - directed information, mutual information in frequency (coherence)
  - coherence graphs, directed graphs, EmDMD, SVM
- patient specific
- real-time processing
  - non-Gaussian and nonlinear



Control

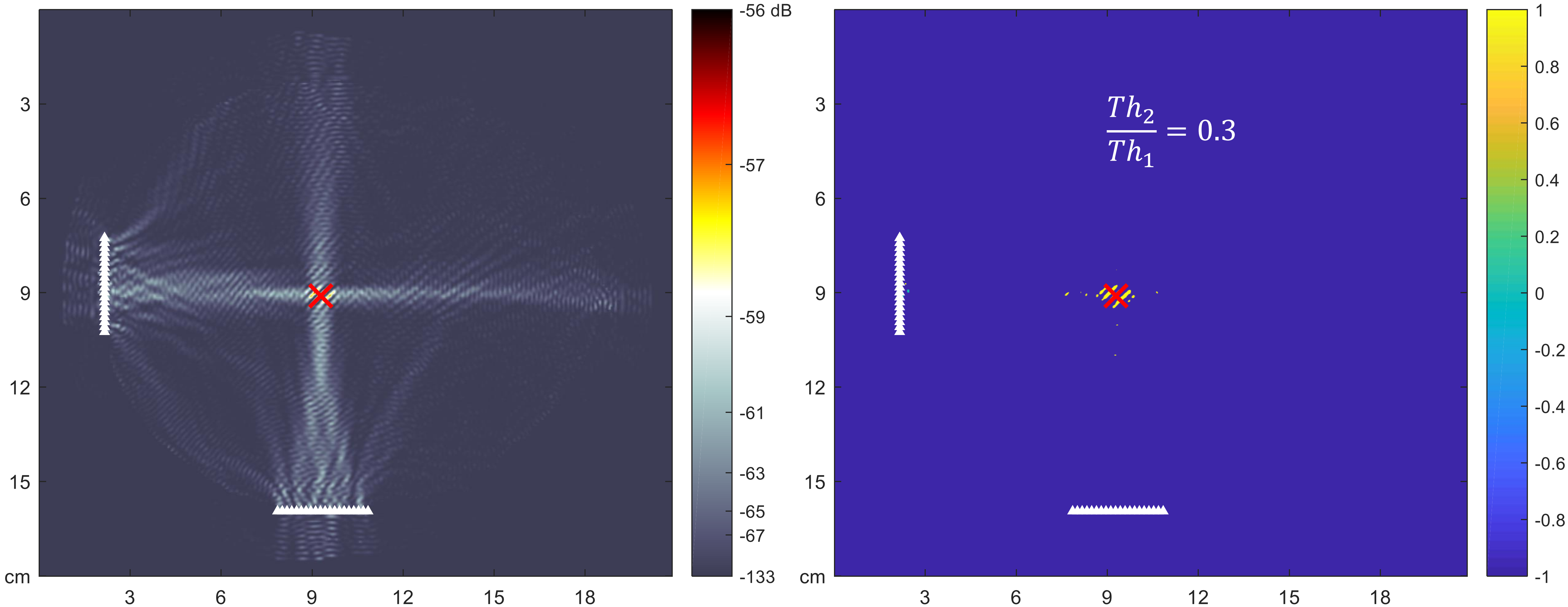
- spatiotemporally focused modulation
- data driven model of dynamics $\mathcal{X}_{m+1} = \mathcal{A}_m \mathcal{X}_m$
- control model

$$\mathcal{X}_{m+1} = \mathcal{A}_m \mathcal{X}_m + \mathcal{B}_m \mathcal{U}_m$$



Ultrasound and electromagnetic modulation

- optimized beams



Take-home message

- learning from non-Gaussian and nonlinear data
  - control and modulation
    - non-invasive or minimally invasive

A happy and well funded team

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National Institutes of Health

NSF

THE ROBERT AND JANICE
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FOUNDATION

THE DAN L. DUNCAN INSTITUTE
FOR
CLINICAL AND TRANSLATIONAL RESEARCH

Bench to Bedside to Community

Projects

- optimization of MU-MIMO wireless network *(su)*
- non-invasive deep brain stimulation *(ahsan, fan)*
- wireless multisite modulation of the diseased heart *(cosentino, banta)*
- real-time closed-loop modulation for depression *(erfanian)*
- learning and socialization in primates *(yellapantula)*
- understanding olfactory circuit *(jyoung)*
- modulation of epileptic circuit *(moghaddam)*