Real time network modulation for intractable epilepsy

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Electrical and Computer Engineering
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acknowledgement

acknowledgement

- Rakesh Malladi

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- Rakesh Malladi
- Suganya Karunakaran

- Nitin Tandon, MD at UTHSC
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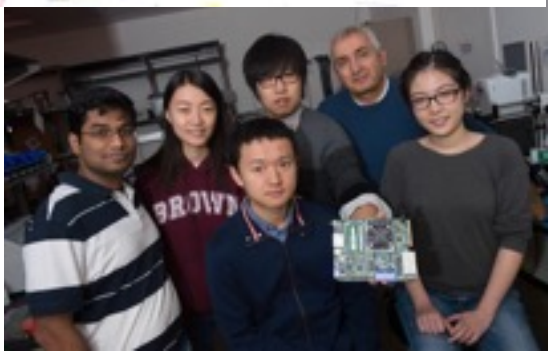
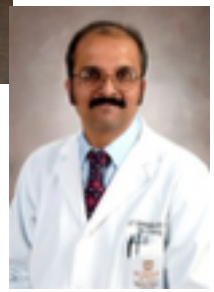
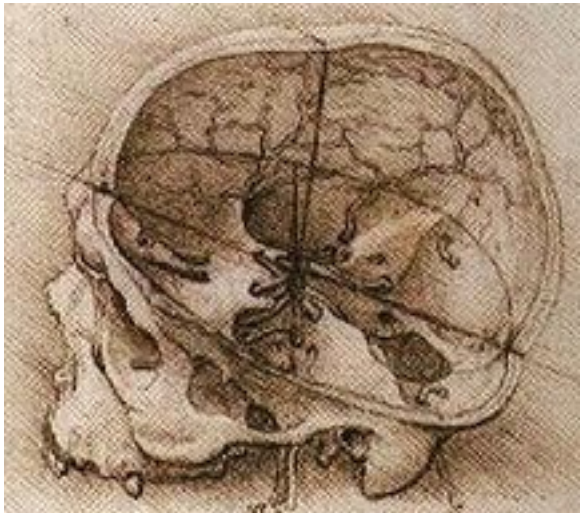




NSF and Texas Instruments

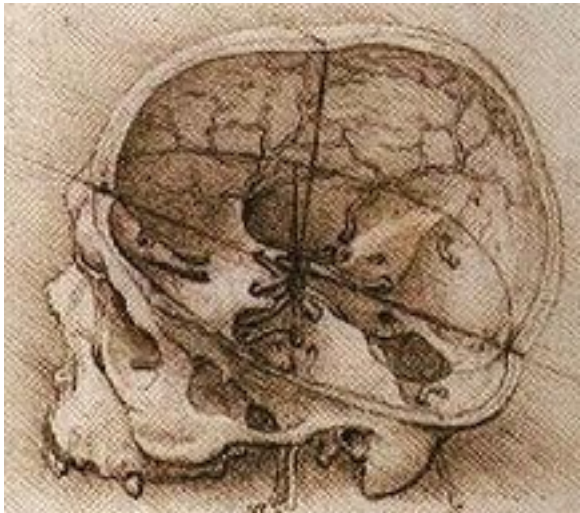
a scientific curiosity

- How does human brain work?



a scientific curiosity

- How does human brain work?
    - Ancient Egypt and Greece
    - Roman empire
    - 19th century
    - USA
        - 90s the “decade of the brain”
        - 2013 “the brain initiative”



grand challenges

- ...
- relation
  - neuronal circuit connectivity and behavior

grand challenges

- ...
- relation
  - neuronal circuit connectivity and behavior
    - transition of neuronal circuits
      - disease state to healthy state
      - learning
- ...

our research focus

- network modulation as a reparative therapy
    - epilepsy, parkinson, alzheimers
- circuits connectivity—behavior

our research focus

- network modulation as a reparative therapy
  - epilepsy, parkinson, alzheimers
- circuits connectivity—behavior
  - common theme
    - tools
    - a network view

this talk

- network modulation as a reparative therapy
    - epilepsy, parkinson, alzheimers
- circuits connectivity—behavior
    - common theme
        - tools
        - a network view

epilepsy

- unprovoked and recurring seizures
- seizure
  - no standard definition

epilepsy

- unprovoked and recurring seizures
- seizure
  - no standard definition
  - abnormally synchronized hyper-excited neuronal activities
  - variations
    - sub-clinical seizure burst———full blown seizure
    - single focal seizure————- multifocal seizure

epilepsy

- strong theories on the cause of seizures
    - imbalance between excitatory and inhibitory activities
- open questions on how seizures end!!

epilepsy

- effects 3 million patients in the USA
    - medication
    - resection
    - stimulation (modulation)
        - neurons respond to electric signals !

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recording-stimulation

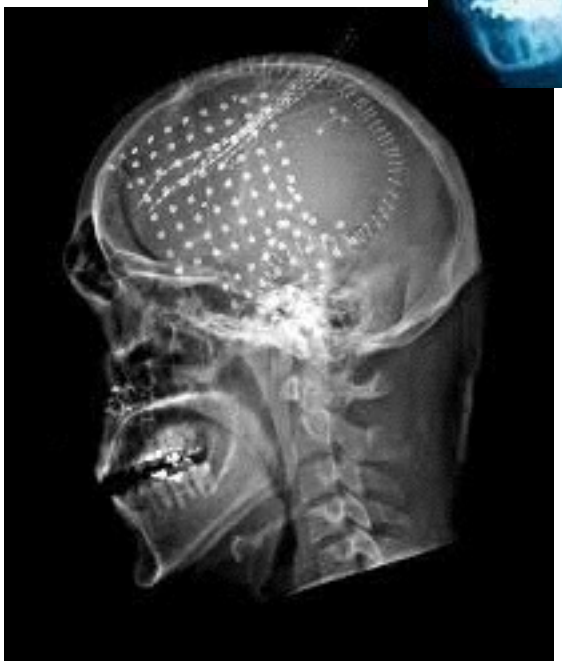
- deep brain

recording-stimulation

- deep brain
- subdural

recording-stimulation

- deep brain
- subdural
- trans-cranial



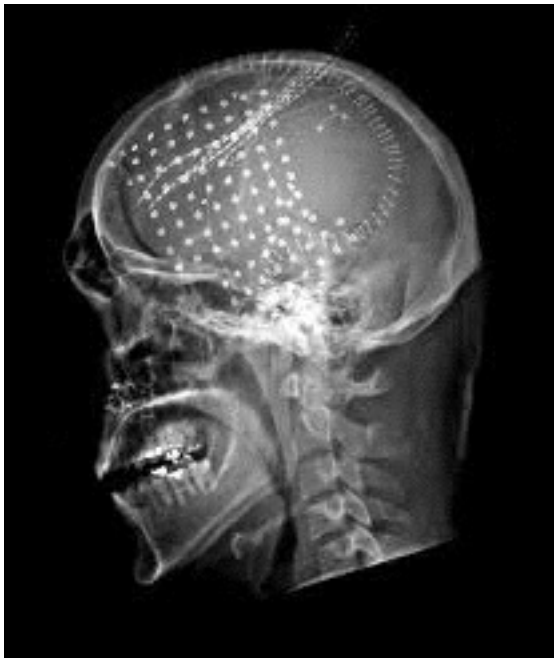
recording-stimulation

- deep brain
- subdural
- trans-cranial

tradeoff: invasive versus effective
micro versus macro

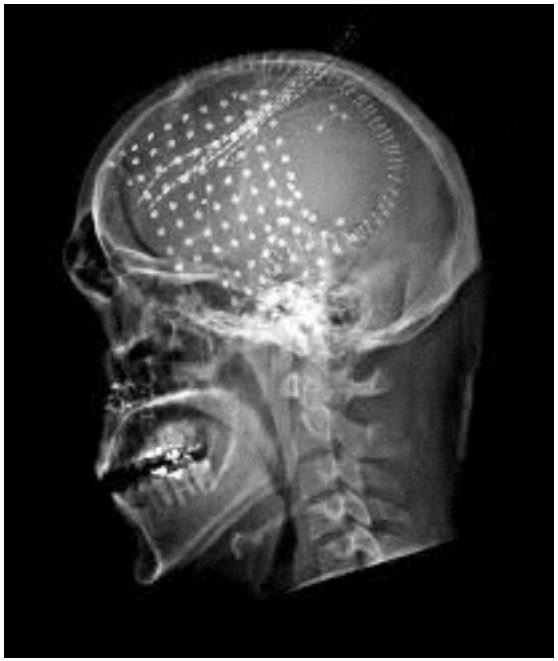
our methodology

- deep brain
- subdural
- trans-cranial



today's application

- subdural recording
  - identify epileptic zone



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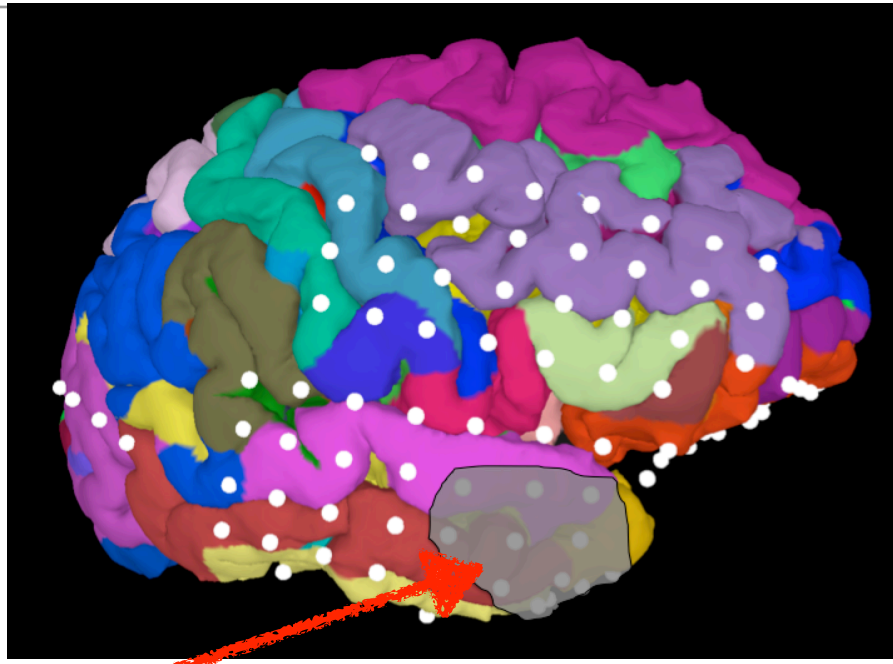
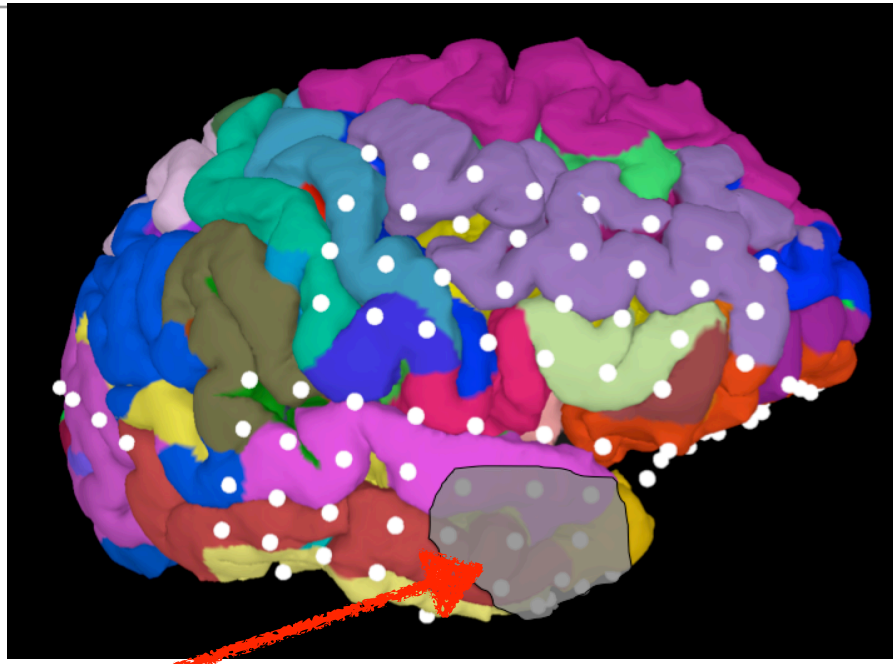
  - resection!



epileptic zone

potential application

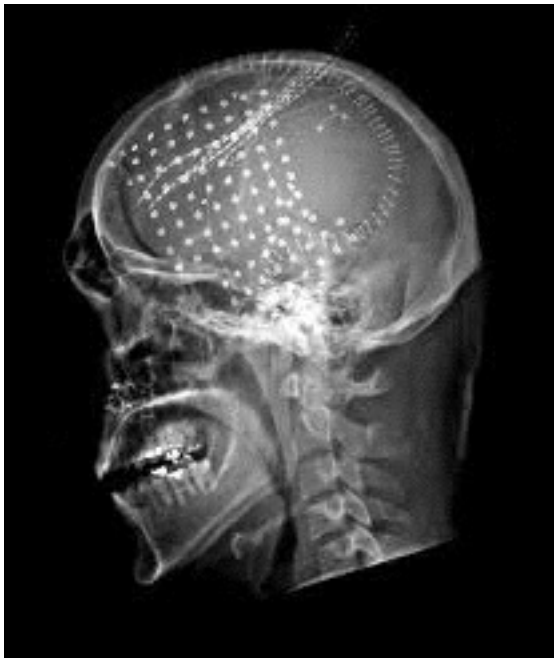
- subdural stimulation



epileptic zone

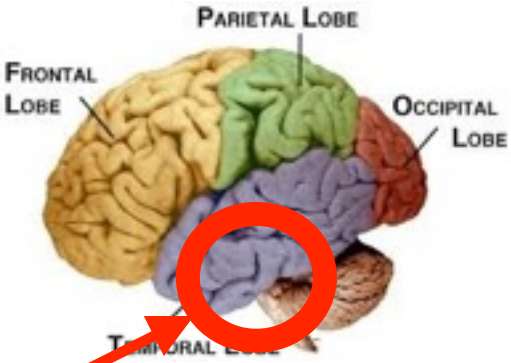
subdural recording and modulation

- electro-cortico-graphy (ECoG)
  - subdural
  - 154 channels (electrodes)

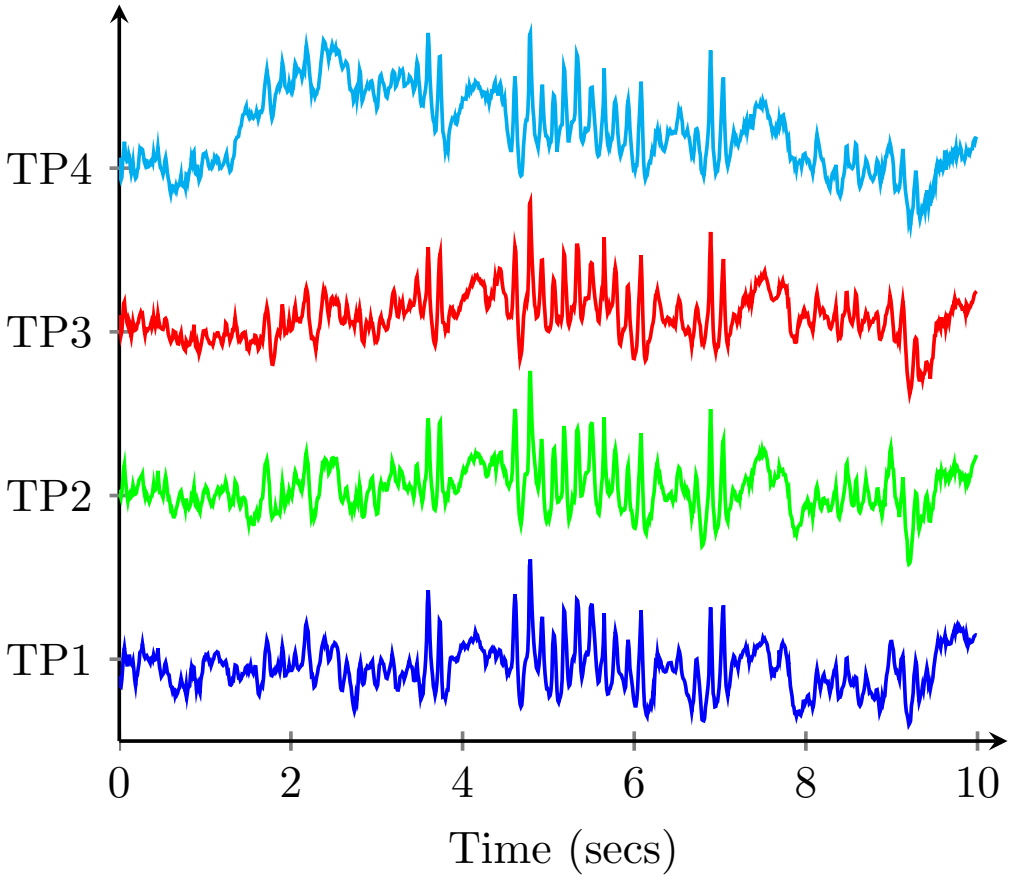


recording

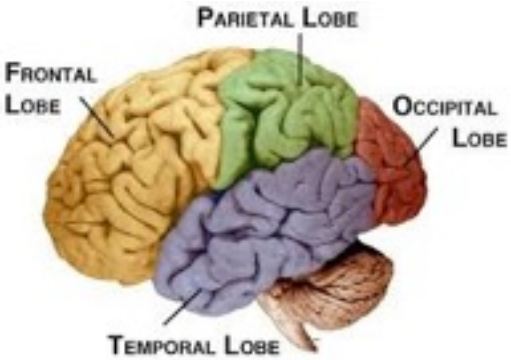
- electro-cortico-graphy (ECoG)
  - subdural
  - 154 channels (electrodes)
- recording



temporopolar



recording



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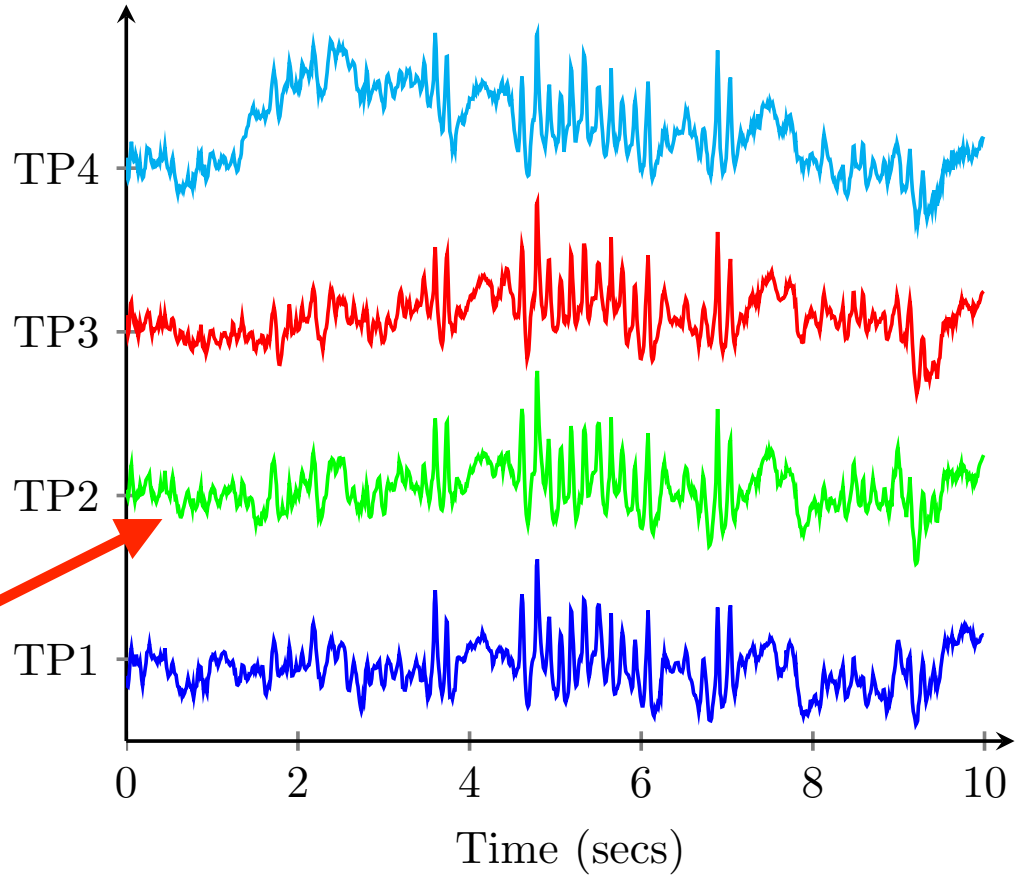
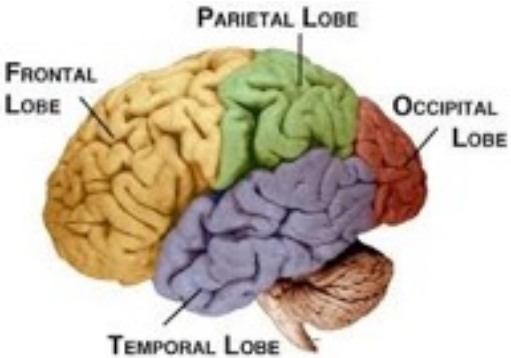


these are not spikes

recording



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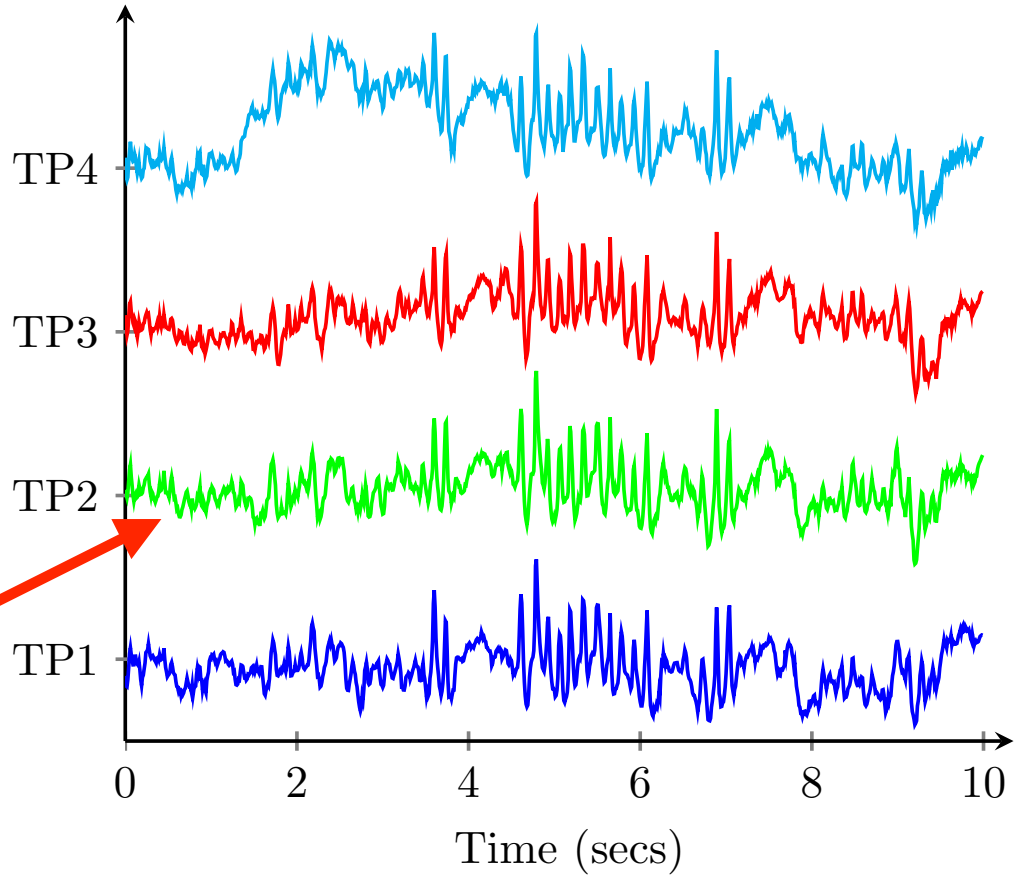
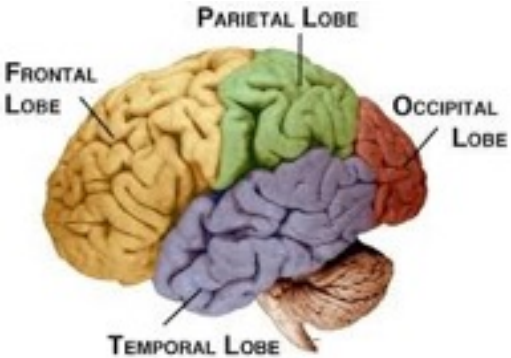


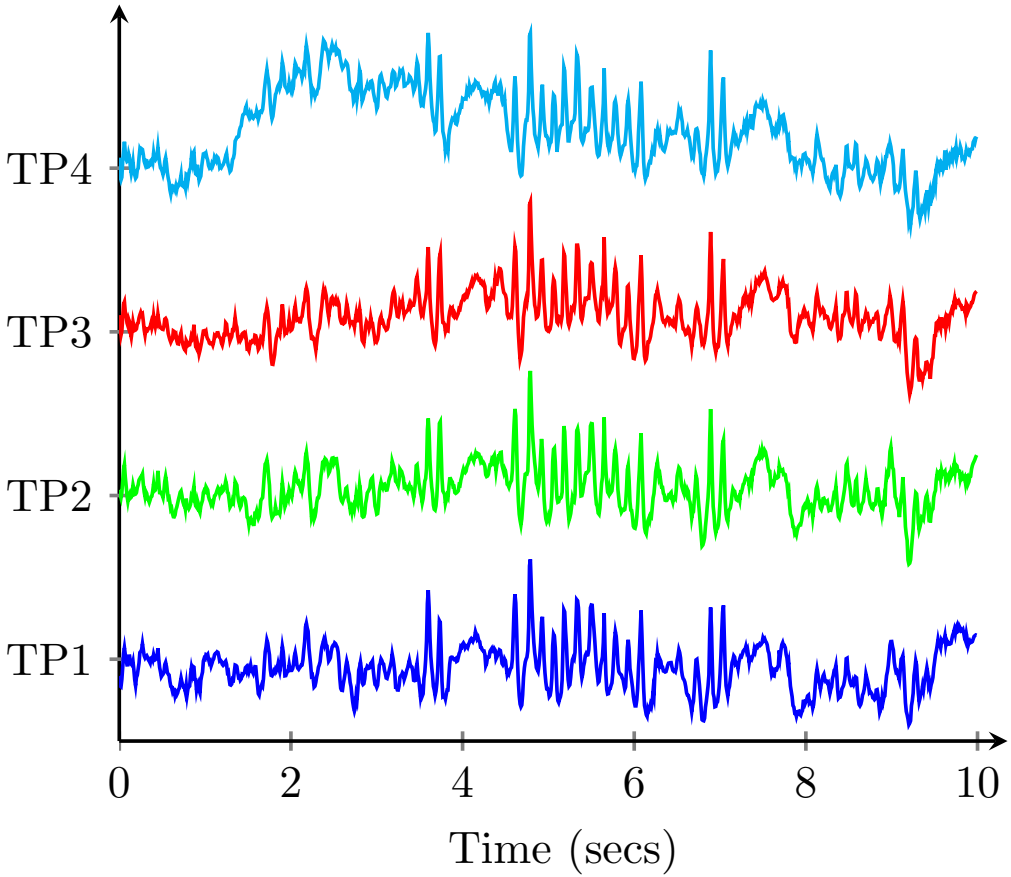
these are not spikes

local field potentials

recording

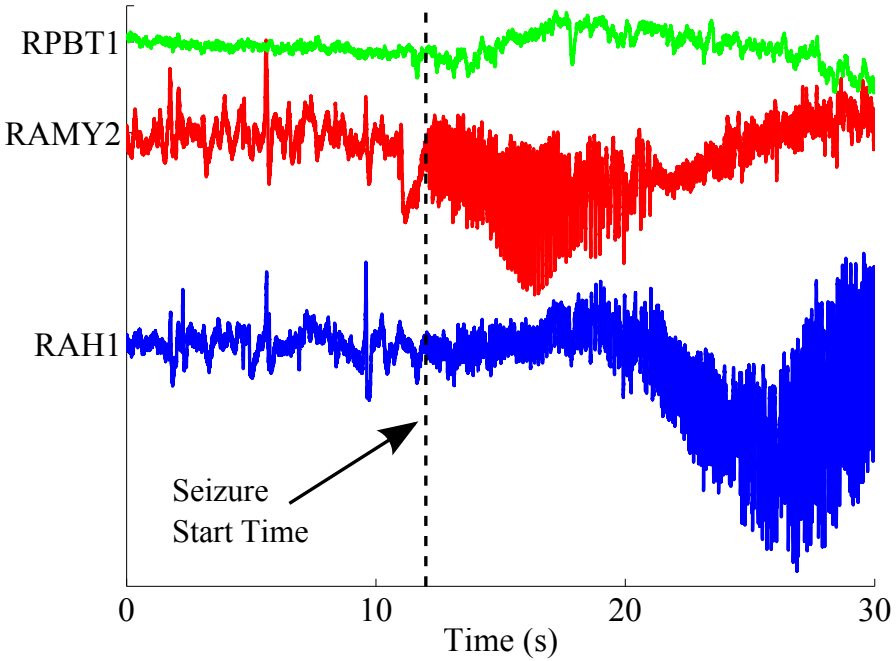


- electro-cortico-graphy (ECoG)
  - subdural
  - 154 channels (electrodes)
- recording
- stimulation?



stimulation (modulation)

- protocol
  - depress the influence of one population of neurons on another
  - temporally precise low frequency stimulation of selected electrodes
    - triggered by markers



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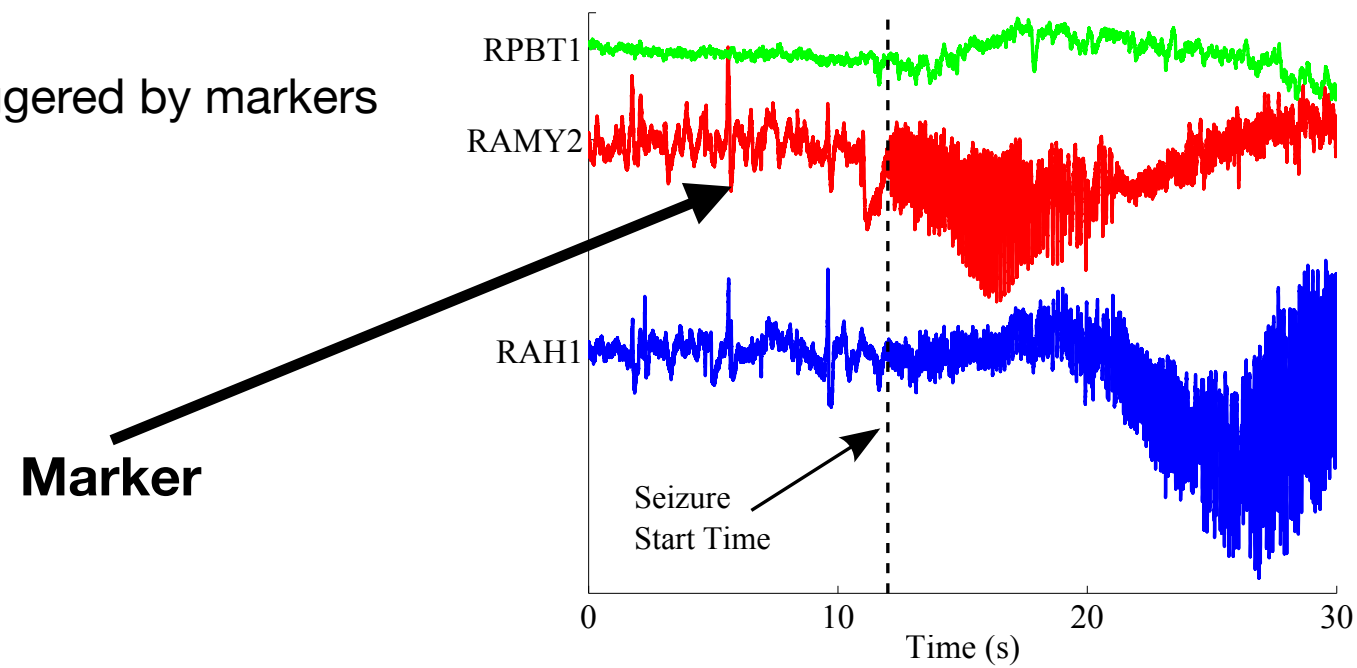

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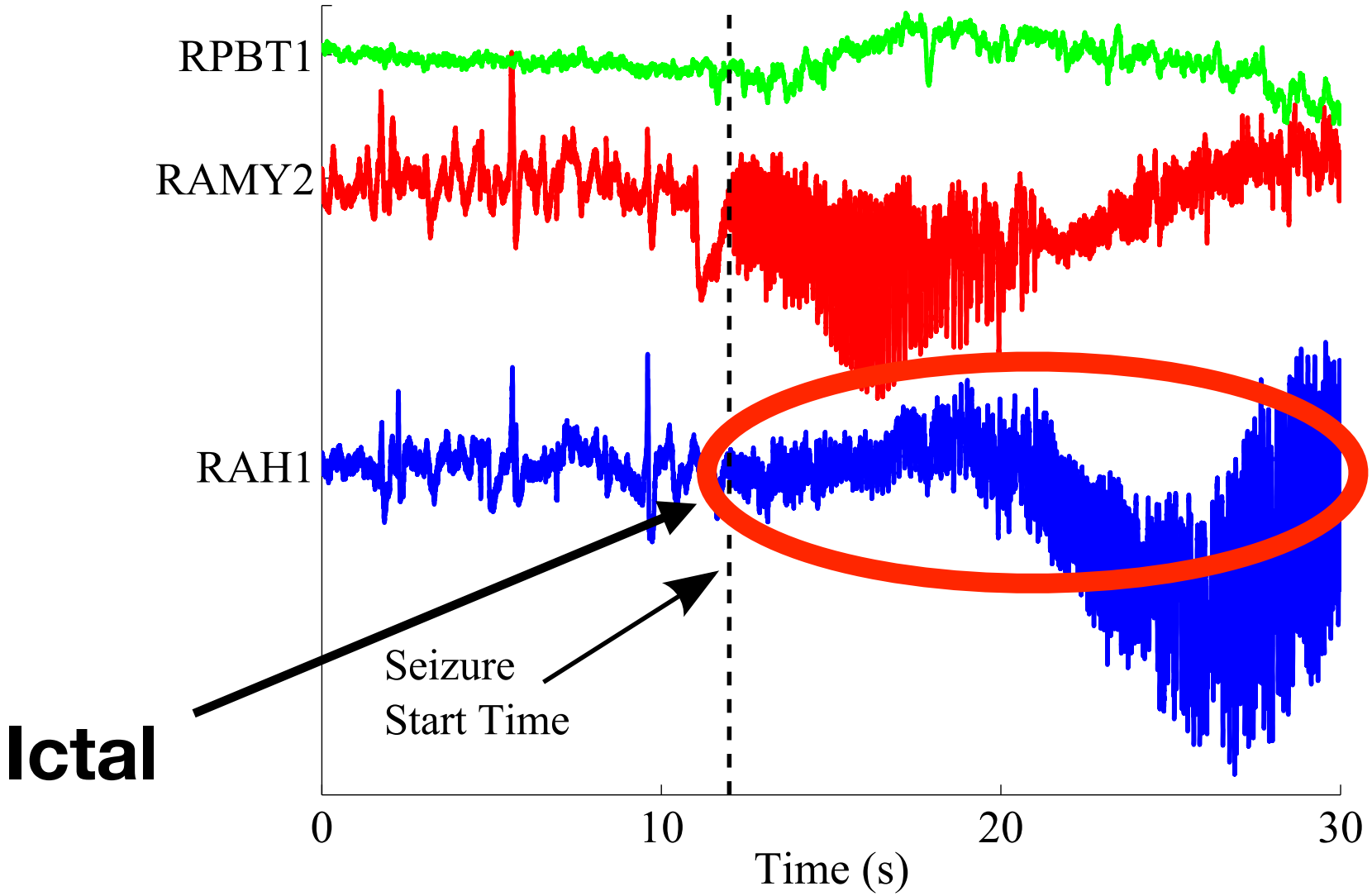

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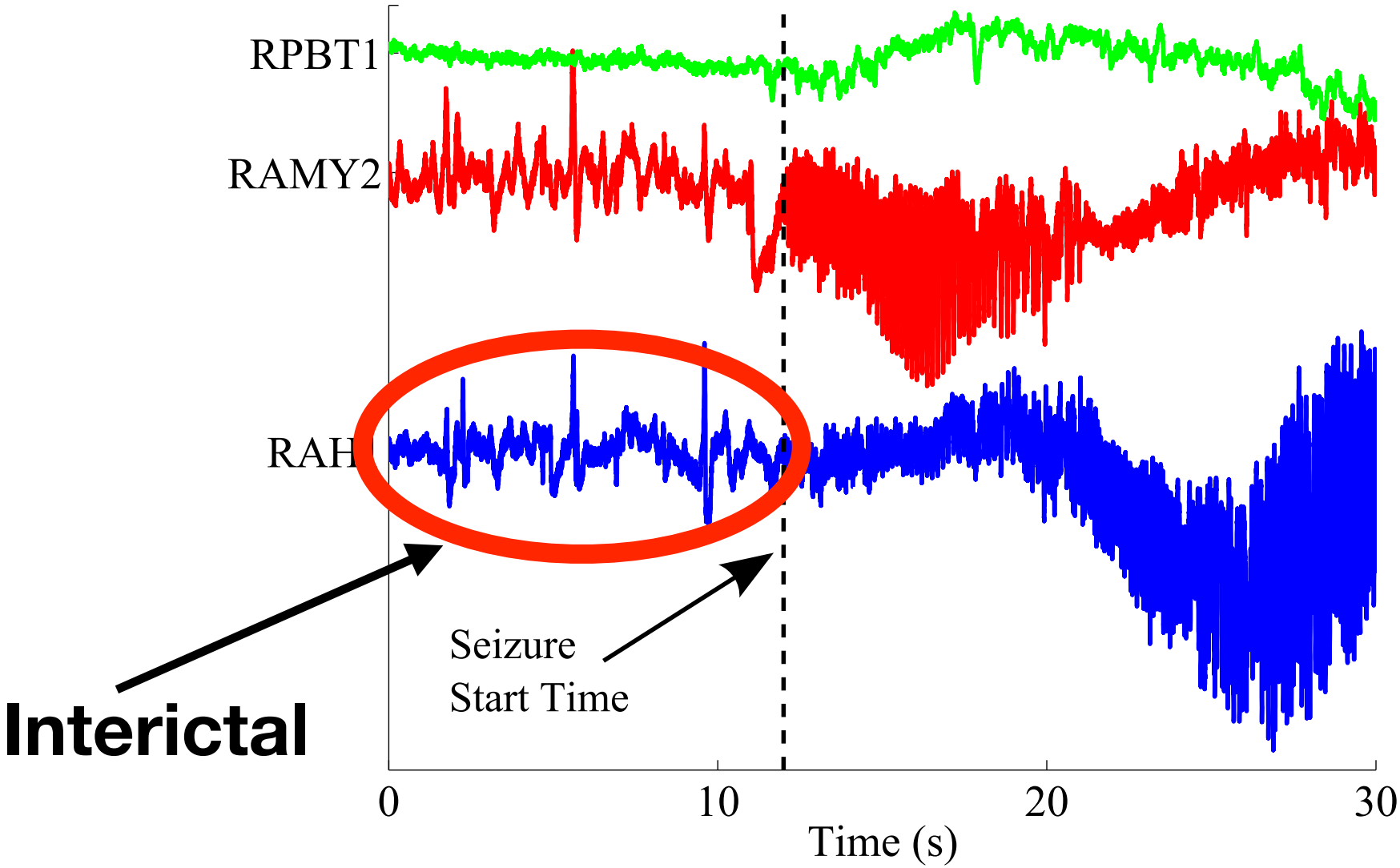

stimulation (modulation)

- protocol
  - depress the influence of one population of neurons on another
  - temporally precise low frequency stimulation of selected electrodes
    - triggered by markers
  - performance metric
    - reduction in the number of interictal spikes

stimulation (modulation)

- protocol
  - depress the influence of one population of neurons on another
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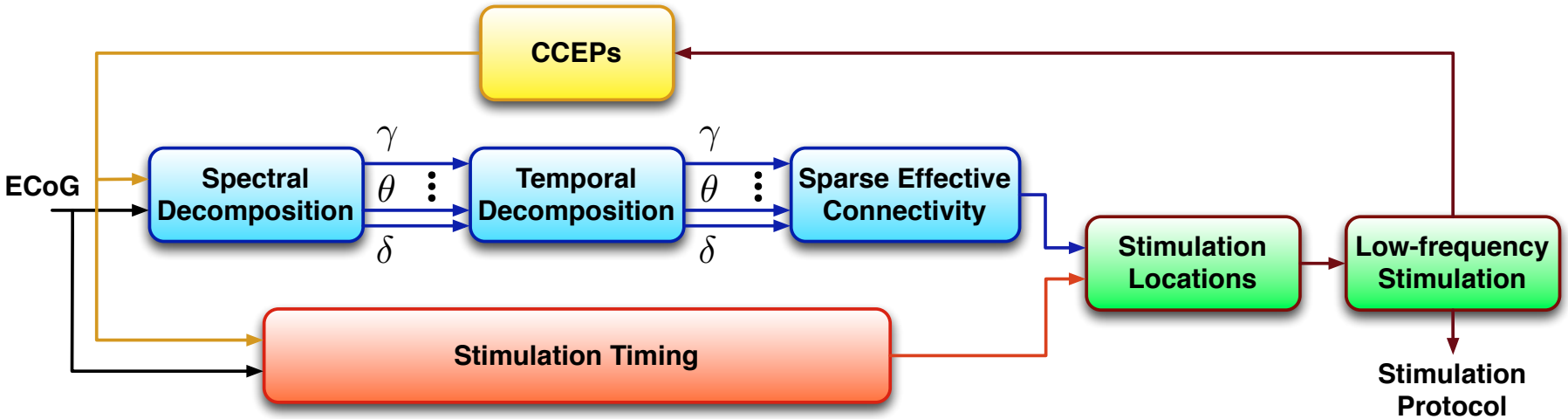
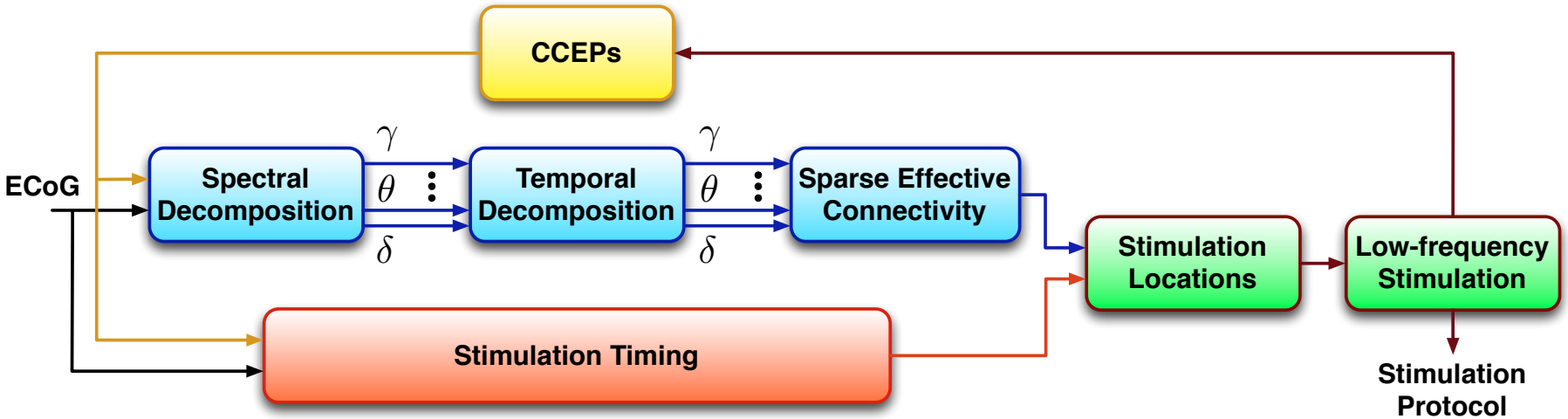


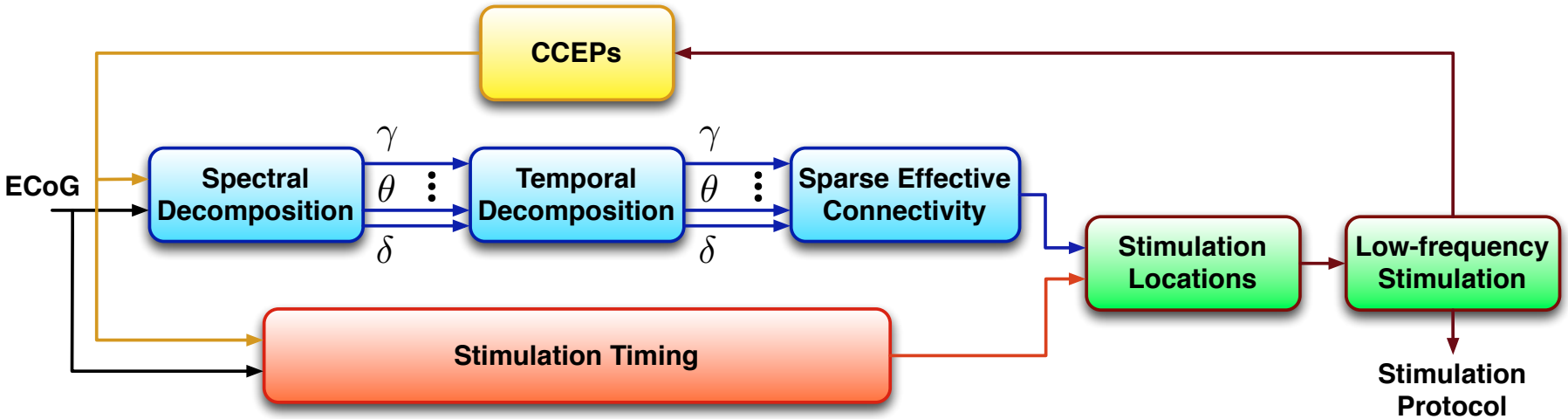
research agenda

- temporally precise low frequency stimulation of selected electrodes



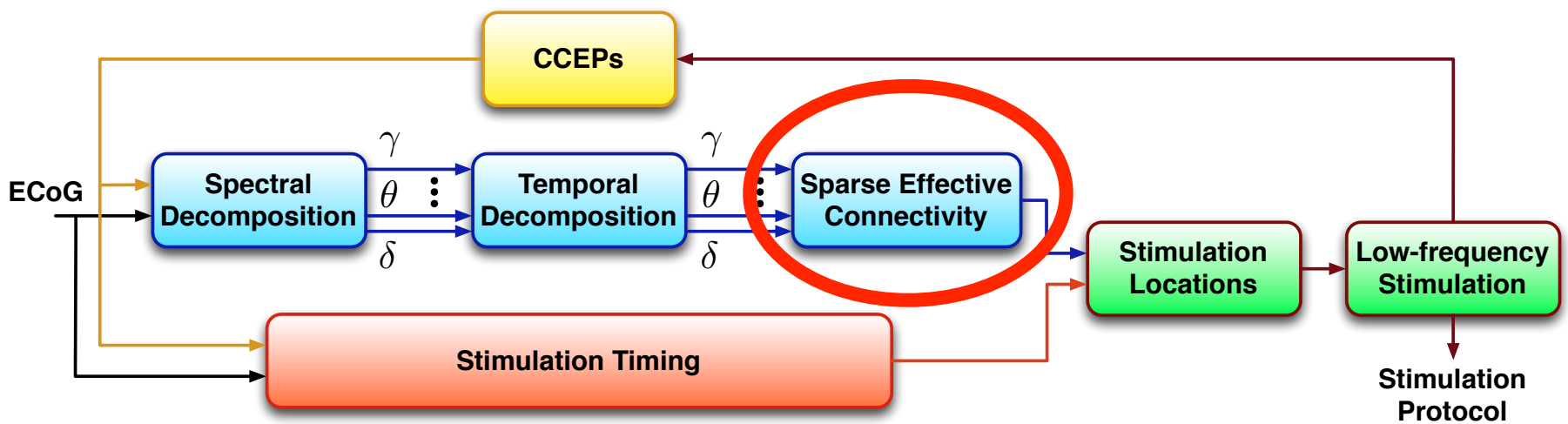
research agenda

- temporally precise low frequency stimulation of selected electrodes
- develop a model and protocols
- build the system
- clinical trial

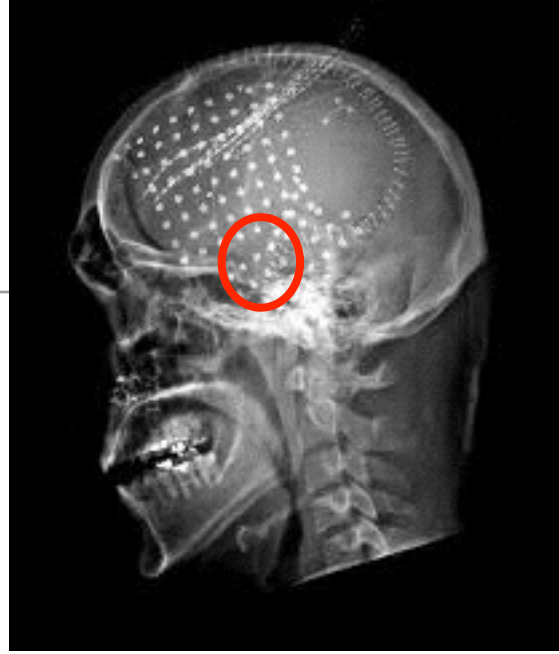


today's talk

- develop
  - sparse effective connectivity graph



modeling of the recordings



- time series of length N
- d channels

$$\mathbf{X}_1^N = (\mathbf{x}_1, \mathbf{x}_2, \cdots, \mathbf{x}_N)$$

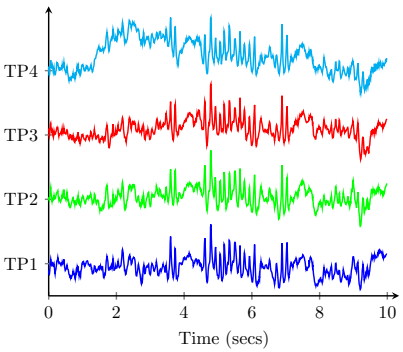
$$\mathbf{x}_n = [x_n(1), x_n(2), \cdots, x_n(d)]^T \in \Re^d \ \forall n$$

modeling

- time series of length N
- d channels

these are not spikes

local field potentials



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modeling

- time series of length N——hours and hours of observations
- d channels——154

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modeling

- time series of length N——hours and hours of observations
- d channels——154

exploit natural sparsity

modeling

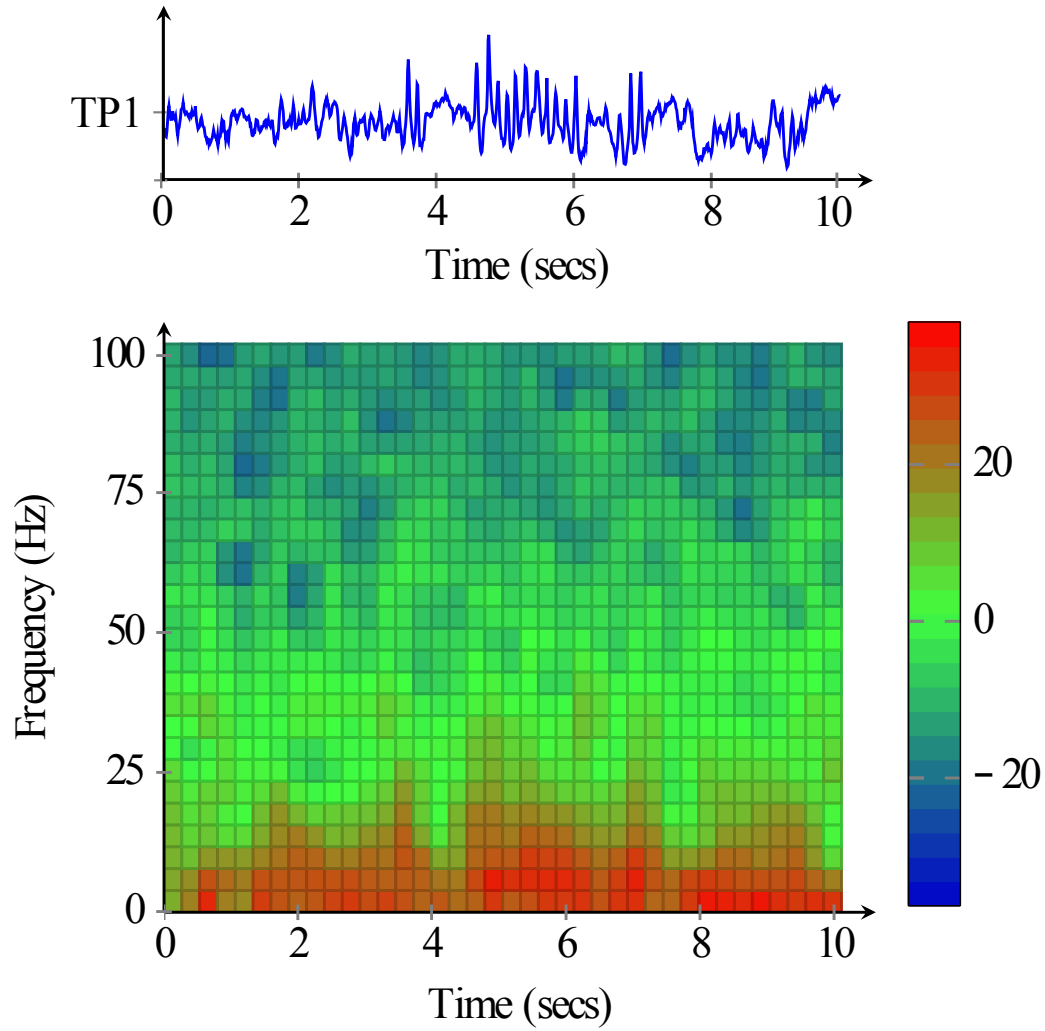
- time series of length N——hours and hours of observations
- d channels——154

exploit natural sparsity

spectral? temporal? spatial?

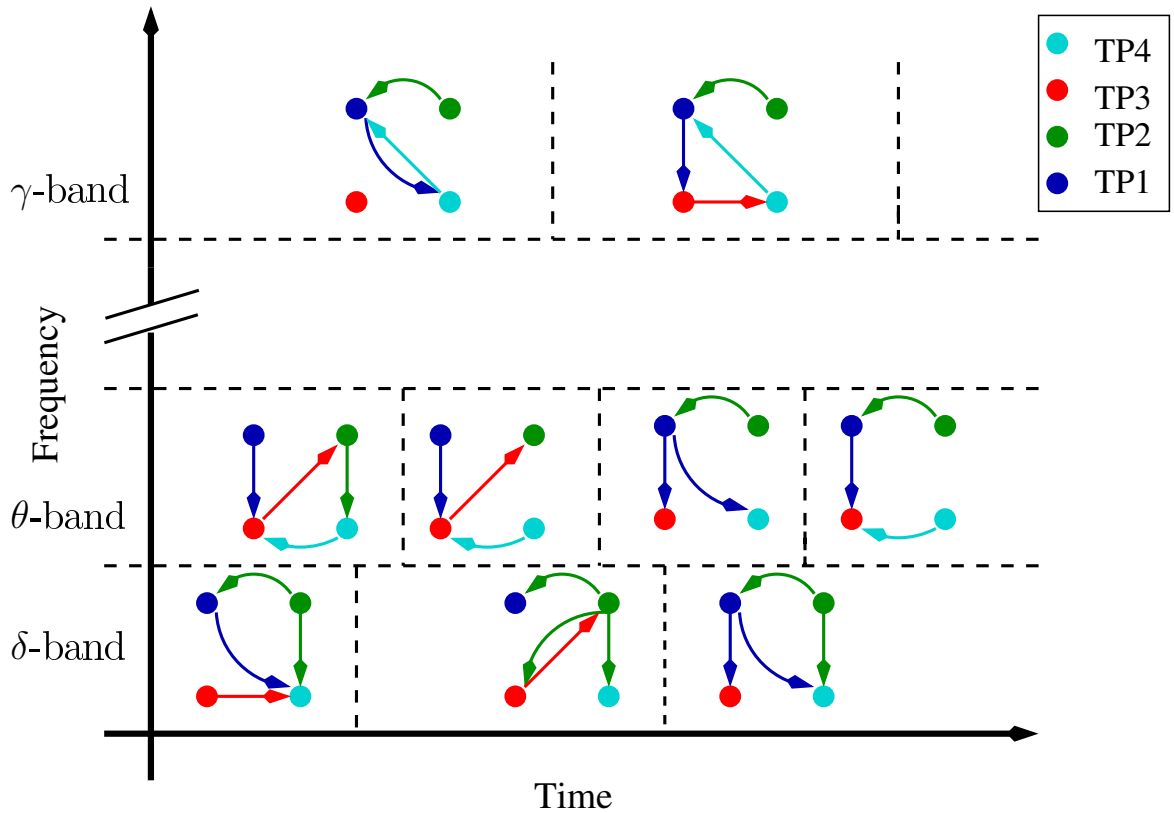
spectral decomposition

- time-frequency analysis
  - 0.1-4 Hz δ band
  - 4-8 Hz θ band
  - 8-14 α band
  - 14-30 β band
  - > 30 γ band



spatial connectivity

- graphical model
  - connectivity
  - causality



spatial connectivity

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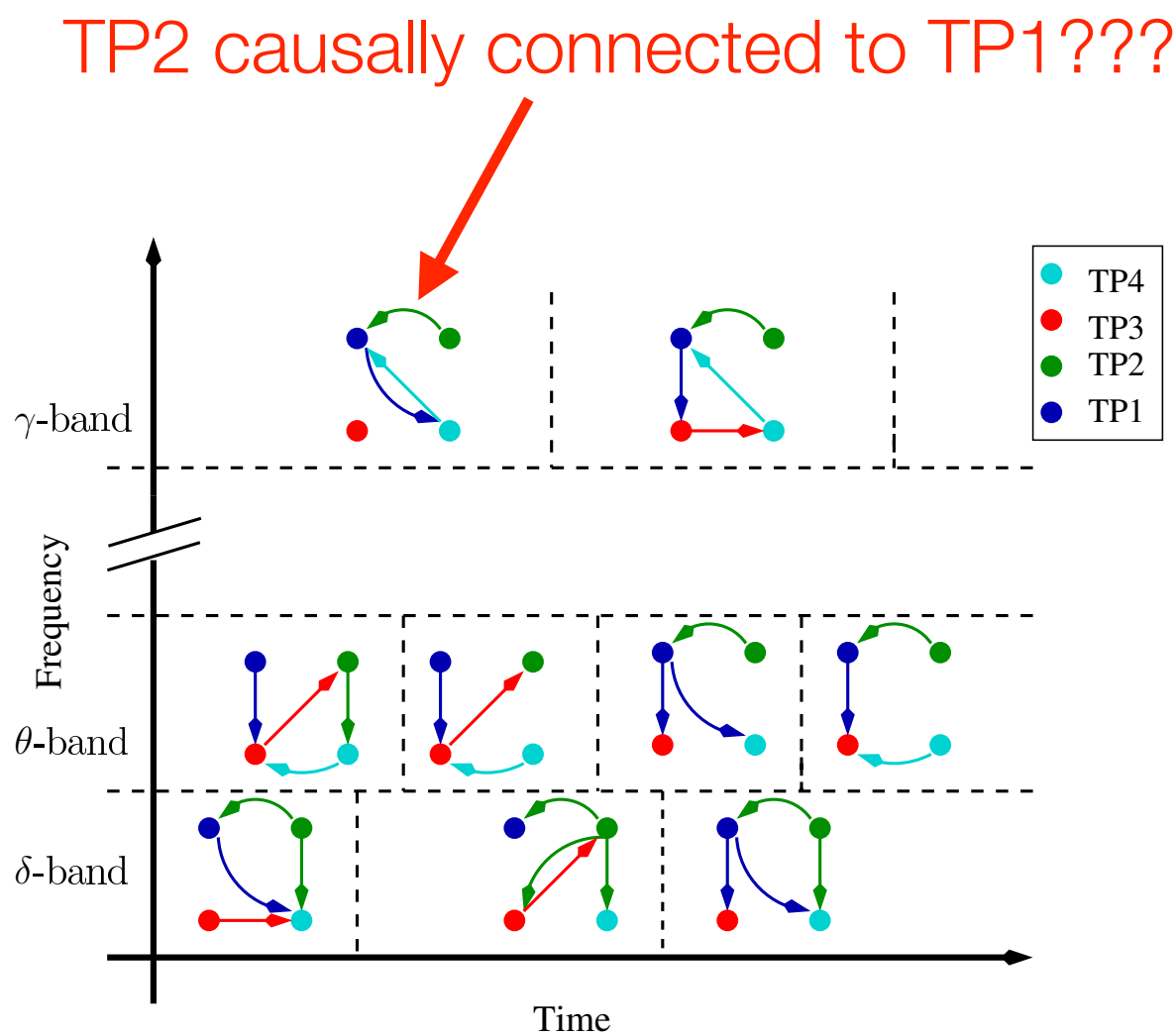


causality

- one time series forecasting another
    - economics
    - transportation
    - …

causality

- one time series forecasting another
    - economics
    - transportation
    - ...
        - Norbert Wiener (1956)
        - Clive Granger (1969)
        - Hans Marko (1973)
        - James Massey (1990)
        - Kramer (1998)

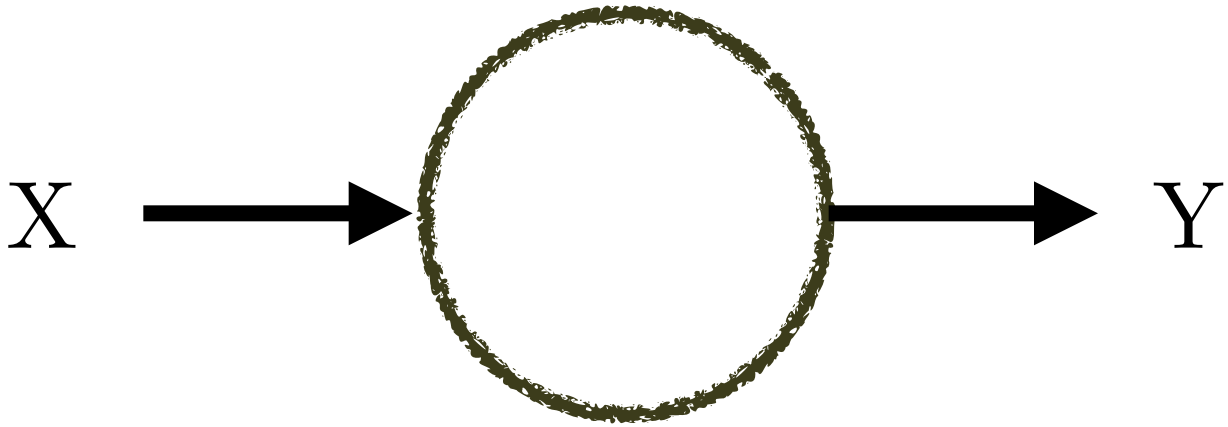
a little background

a little background

- mutual information

$$I(X;Y) = \int f_{XY} \log \frac{f_{XY}}{f_X f_Y}$$

- average information about **X** provided by **Y**



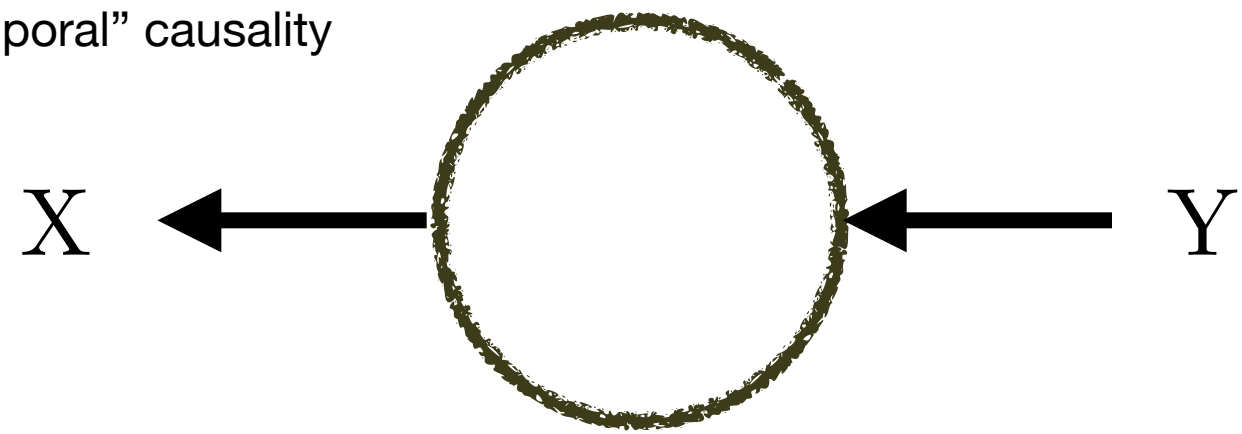
a little background

- mutual information

$$I(X;Y) = \int f_{XY} \log \frac{f_{XY}}{f_X f_Y}$$

- not directional

- no “temporal” causality



a little background

- directed information and causality

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

- directional

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

a little background

- mutual information of time series

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

- causality?

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a little background

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- causality?

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

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

a little background

- directed information of time series

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

- where

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

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

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

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

4 examples

example 1

$$Y_n = X_n + z_n$$

- with i.i.d.

$$X_n \sim \text{Gaussian}(0, \sigma_X^2)$$

$$z_n \sim \text{Gaussian}(0, \sigma_z^2)$$

example 1

independent

$$Y_n = X_n + z_n$$

- with i.i.d.

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example 1

$$Y_n = X_n + z_n$$

- then

$$I(Y \to X) = I(X \to Y) = I(X;Y) = \frac{1}{2}\log(1 + \frac{\sigma_X^2}{\sigma_z^2})$$

example 2

$$Y_n = X_{n-1} + z_n$$

- with i.i.d.

$$X_n \sim \text{Gaussian}(0, \sigma_X^2)$$

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example 2

independent

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example 2

$$Y_n = X_{n-1} + z_n$$

- then

$$I(X \to Y) = \frac{1}{2}\log(1 + \frac{\sigma_X^2}{\sigma_z^2})$$

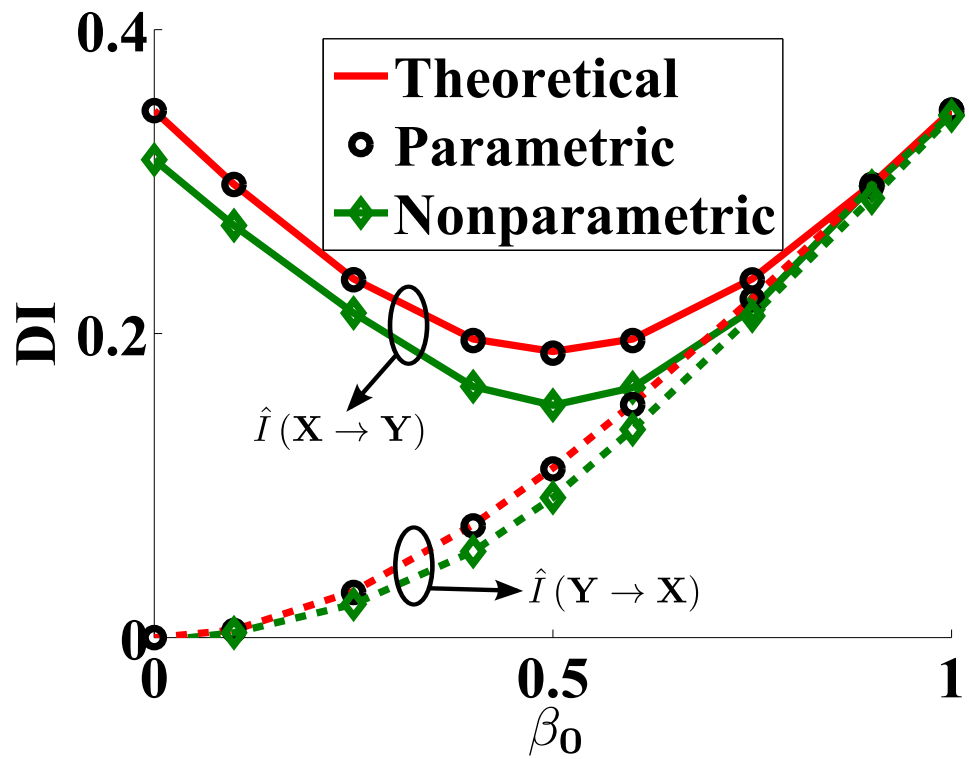
$$I(Y \to X) = 0$$

$$X_n \sim \text{Gaussian}(0, \sigma_X^2)$$
$$z_n \sim \text{Gaussian}(0, \sigma_z^2)$$

example 3= 1+2

- linear autoregressive

$$Y_n = \beta_0 X_n + (1 - \beta_0) X_{n-1} + z_n$$



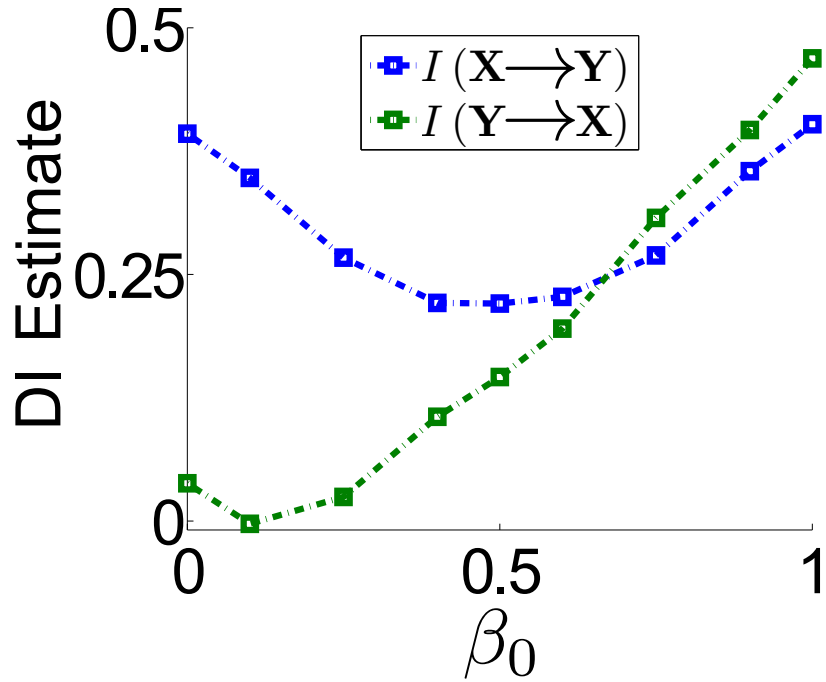
$$X_n \sim \text{Gaussian}(0, \sigma_X^2)$$
$$z_n \sim \text{Gaussian}(0, \sigma_z^2)$$

example 4

- nonlinear

$$Y_n = \beta_0 X_n^2 + (1 - \beta_0) X_{n-1}^2 + z_n$$

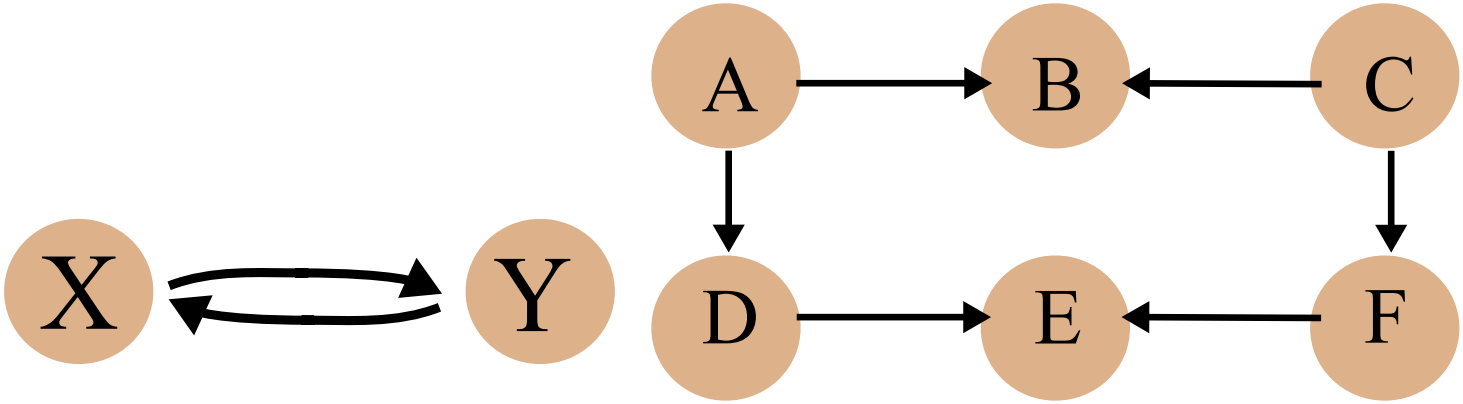
- estimates
  - non parametric
  - data driven



directed information for a network

- example

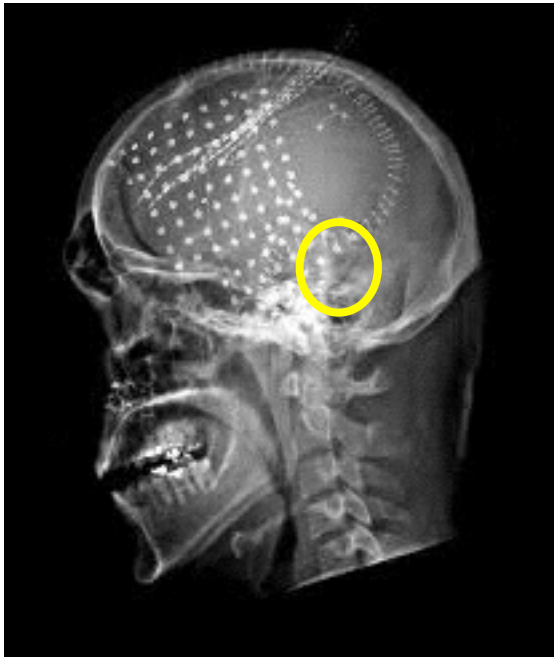
$$I(B \to D|A) = 0$$



(a) Two Node Causal Network (b) Six Node Causal Network

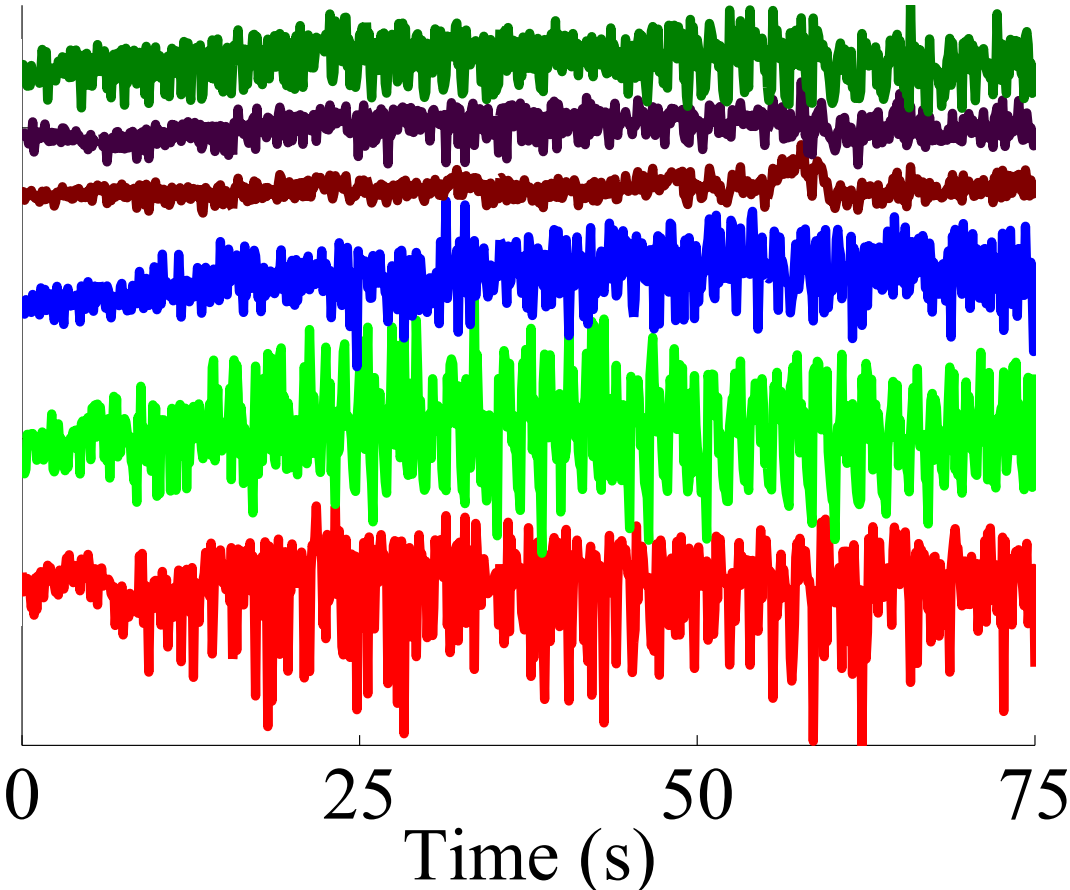
back to real data!

- subdural recording from epileptic patients
  - 151 channels
  - sampling rate 1KHz



back to real data!

- subdural recording from epileptic patient P1
  - 151 channels
  - sampling rate 1KHz
- approach
  - model based
  - data driven



model based

- nonlinear
- linear
    - moving average autoregressive
- Gaussian

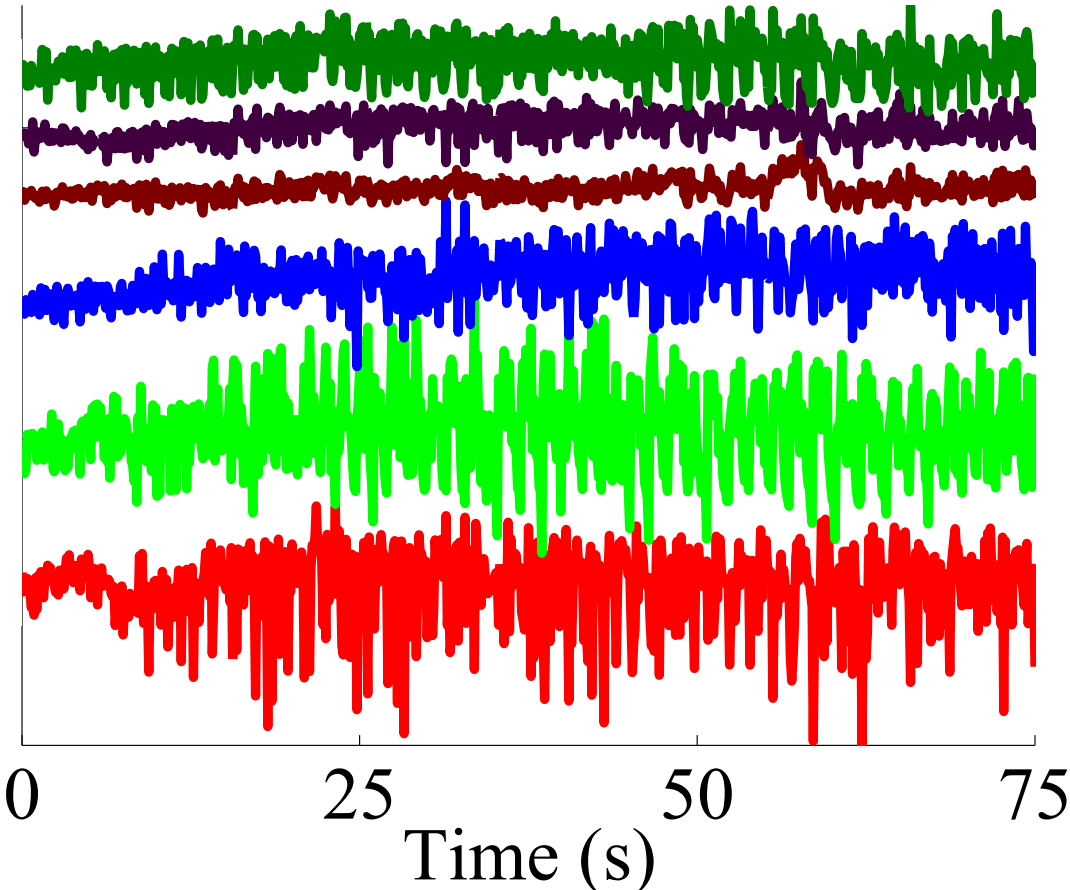
data driven

- non-parametric

back to real data!

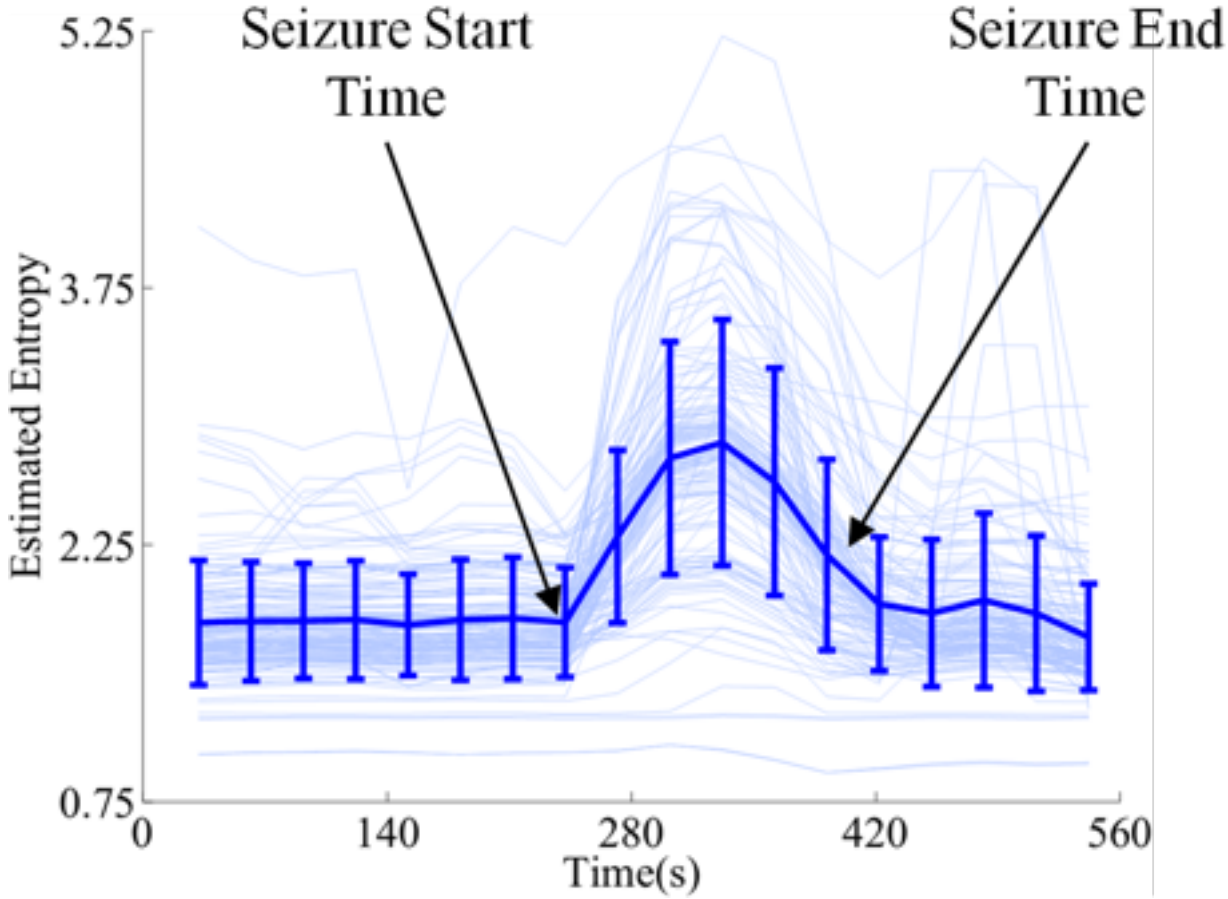
- seizure onset zone

- seizure



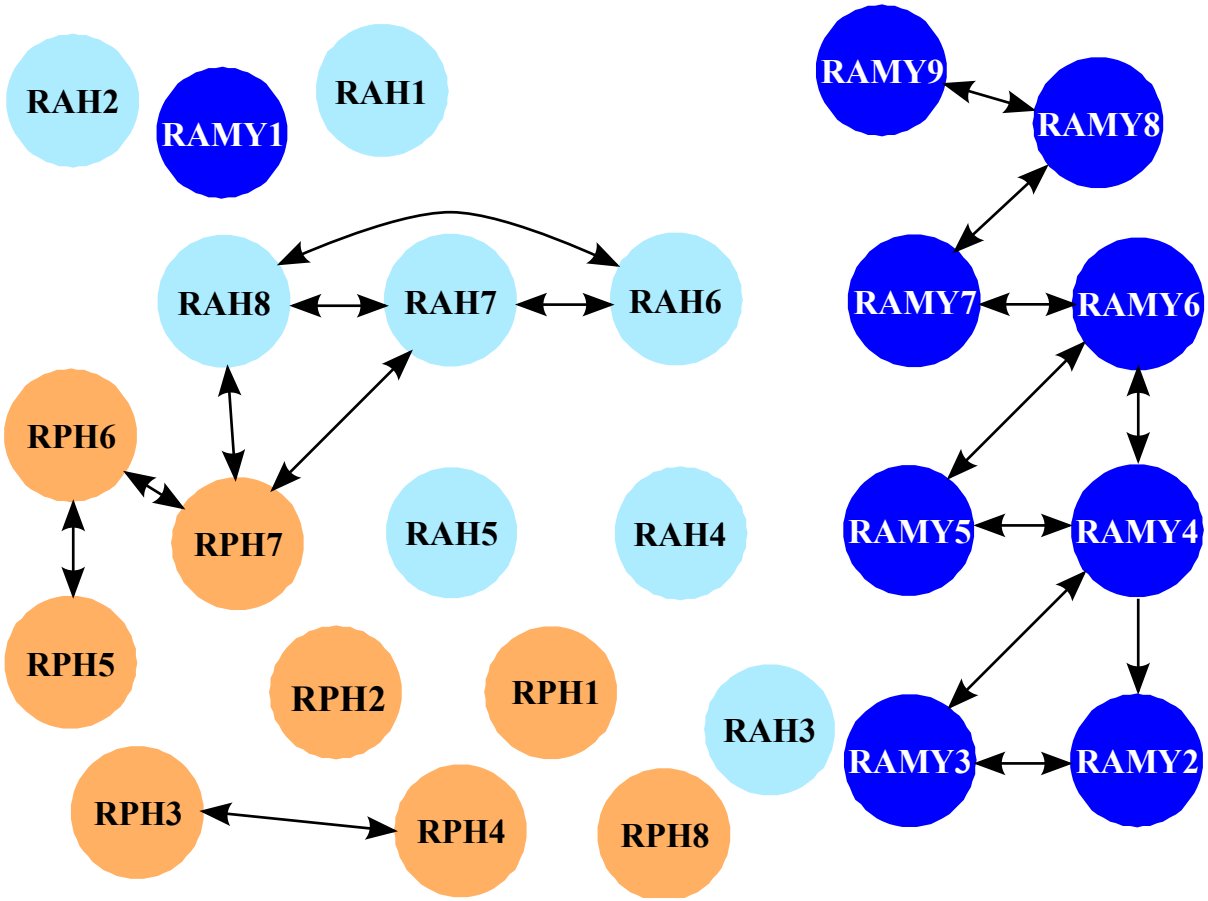
back to real data!

- 151 channels
- seizure
  - temporal focus



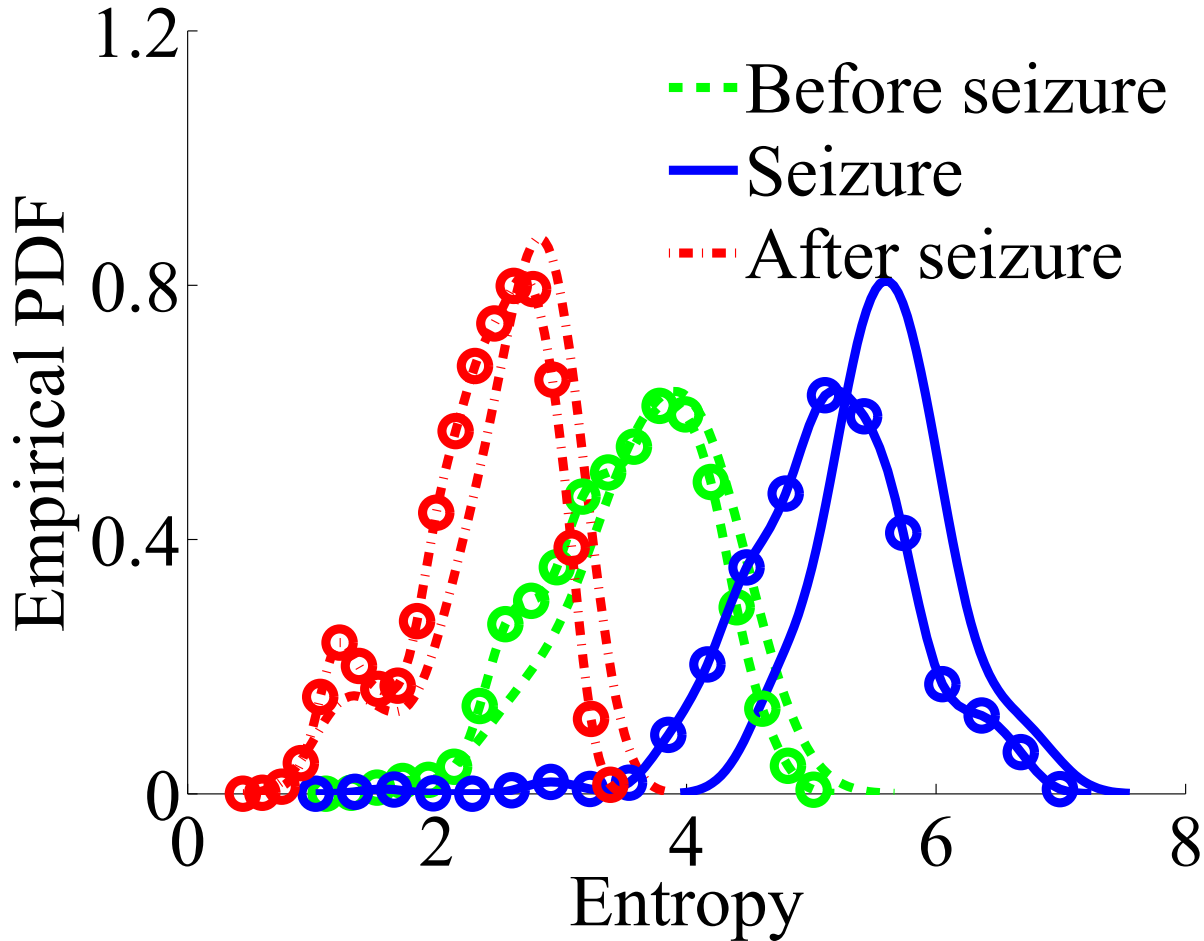
seizure onset zone

- directed information
- spatial focus
  - prior
  - during
  - post seizure



back to real data!

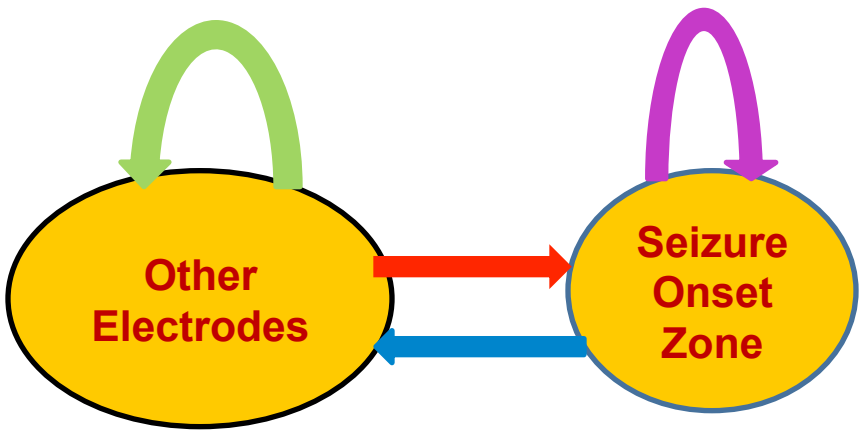
- epileptic zone
  - 25 channels
  - coarse temporal focus

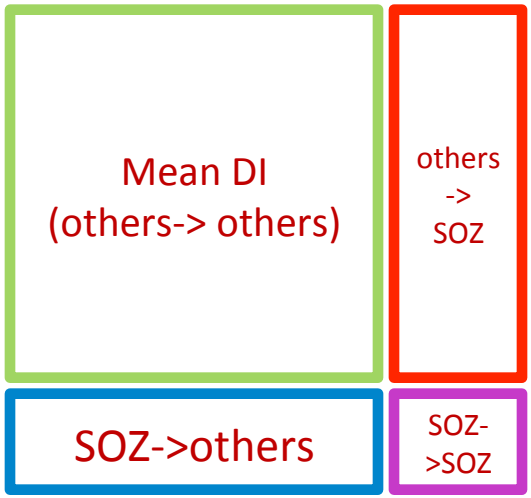


epileptic zone

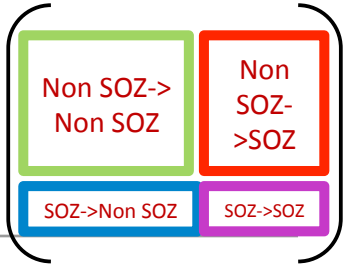
- focused on the epileptic zone
- temporally (coarse) focused on seizure
- causality!

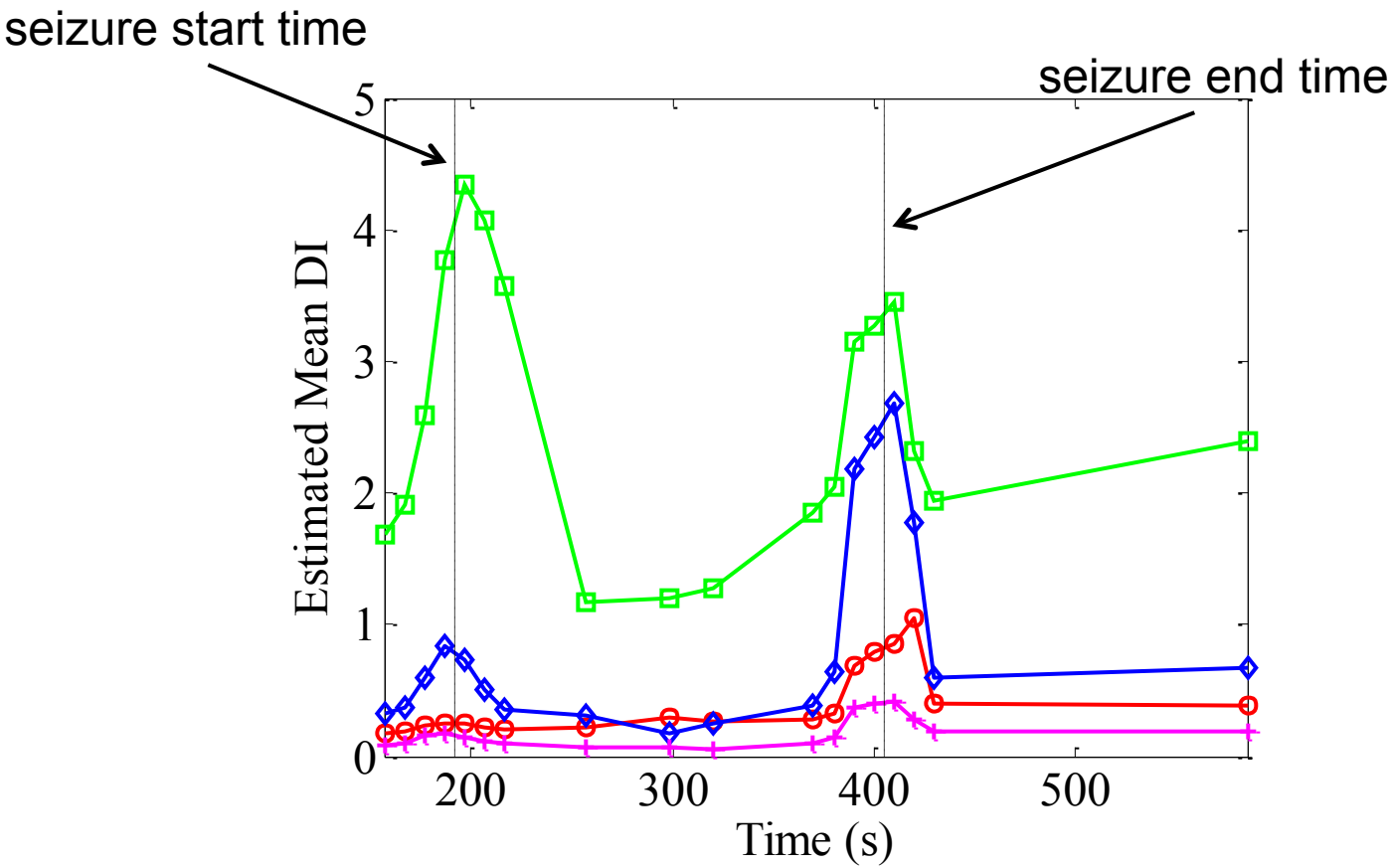
seizure onset zone





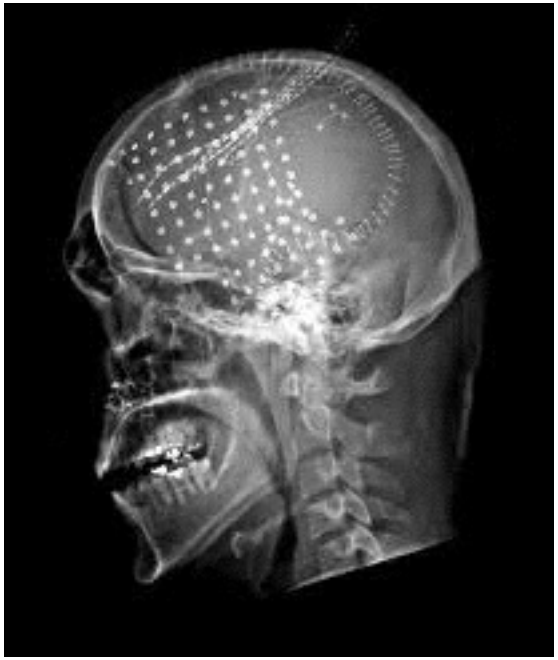
dynamic causal connectivity





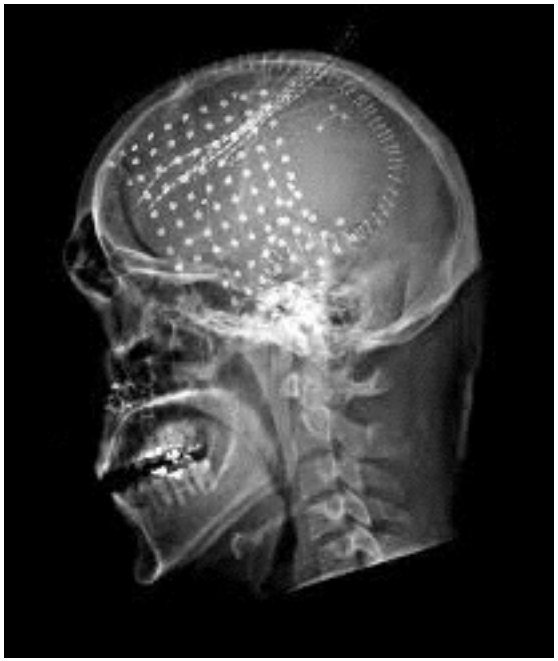
a few thoughts

- clear goals
- numerous open questions
- tremendous amount of data
- great tools



final thoughts

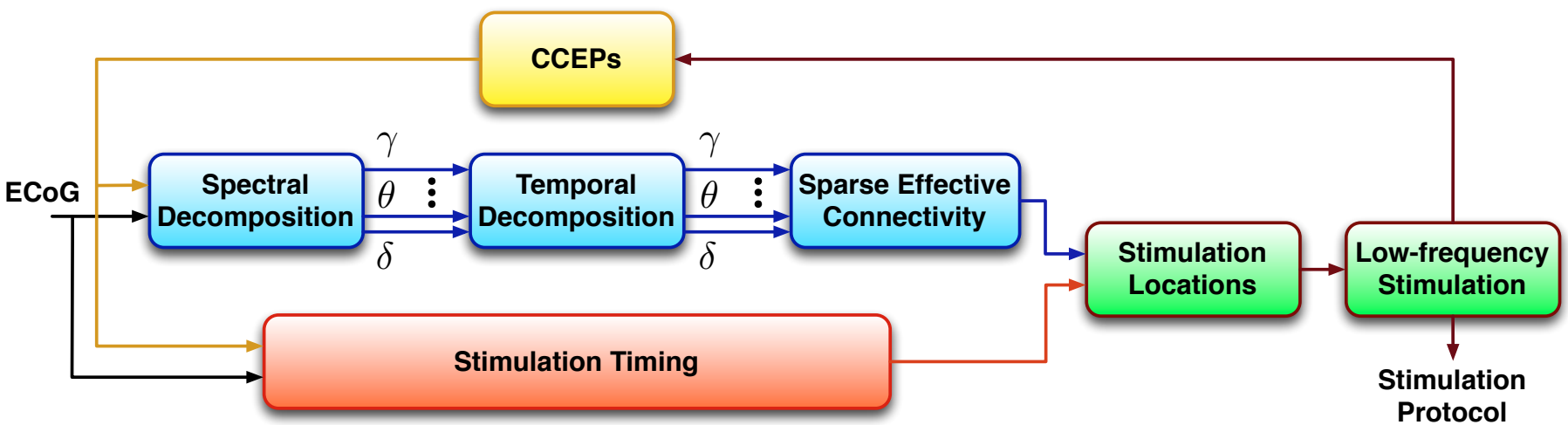
- closed loop stimulation
  - markers
    - spectral
    - temporal
      - prediction
      - fine
    - spatial



final thoughts

- closed loop stimulation
  - markers
  - real time

low frequency stimulation to depress the excitable state



final thoughts

- develop protocols
    - temporal markers
    - directed connectivity
- build the system
- clinical trial !!!!!