Data Science meets Neuroscience: Towards a Better Understanding of the Epileptic Process

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Epilepsy

- affects over 50 million people worldwide one of the most common neurological disorders
- predisposition to epileptic seizures
- for $\approx 30\,\%$ of patients no adequate seizure control

  $\rightarrow$ strong need for novel therapies

traditional concept: *epileptic focus*

- circumscribed area of brain
- critical amount of neurons $\rightarrow$ epileptic seizure

emerging concept: *epileptic network*

- dynamics in any part affects all other parts
- seizure proneness in any part influenced by dynamics in whole network

Structural brain networks

- **small-scale**:
  nodes $\rightarrow$ single neurons
  edges $\rightarrow$ synapses

  desirable, but hard (impossible?) to access
- **large-scale**:
  nodes $\rightarrow$ brain regions
  edges $\rightarrow$ fiber bundles

  high-res. magnetic resonance imaging (MRI),
  diffusion tensor imaging (DTI), ...

Functional brain networks

- **small-scale**:
  nodes $\rightarrow$ single neuron dynamics
  edges $\rightarrow$ synaptic (other) interactions

  emerging technologies
- **large-scale**:
  nodes $\rightarrow$ sensors (dynamics of networks of neuron networks)
  edges $\rightarrow$ interactions, time series analysis

  (invasive) electroencephalography (iEEG/EEG),
  magnetoencephalography (MEG), functional MRI (fMRI), ...

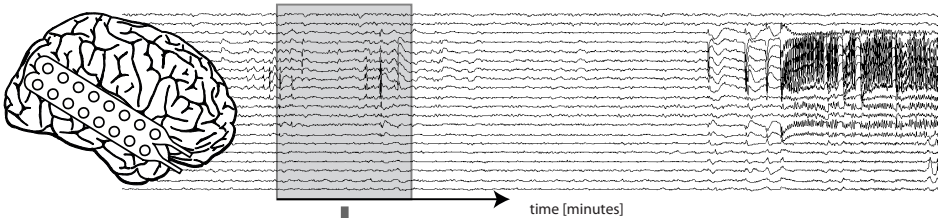
Inferring networks from iEEG data

- node $\leftrightarrow$ electrode contact
- edge $\leftrightarrow$ interaction between nodes
  which properties of interaction needed?
  - strength
  - direction
  - delay
  - ?

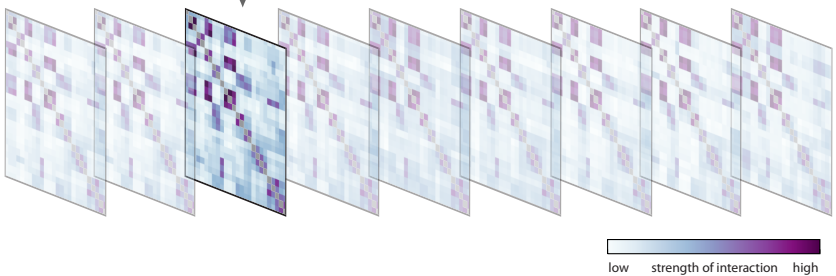
  estimated with suitable measure based on
  - amplitude
  - phase
  - state space
  - information theory
  - ?

Inferring networks from iEEG data

1. Recording



2. Estimation of interaction



Inferring interaction properties with information theory

Strength of interaction

Order parameter $\gamma \in [0, 1]$ with

$$\gamma := \frac{1}{N_\eta} \sum_{\eta=1}^{N_\eta} S_X(\omega_\eta) S_Y(\omega_\eta)$$

with in-step changing tendency

$$S_X(\omega_\eta) = \begin{cases} +1 & \text{if } H(\omega_\eta) < H(\omega_{\eta-1}) \\ -1 & \text{else.} \end{cases}$$

Direction of interaction

Directionality index $T \in (-\infty, \infty)$ with

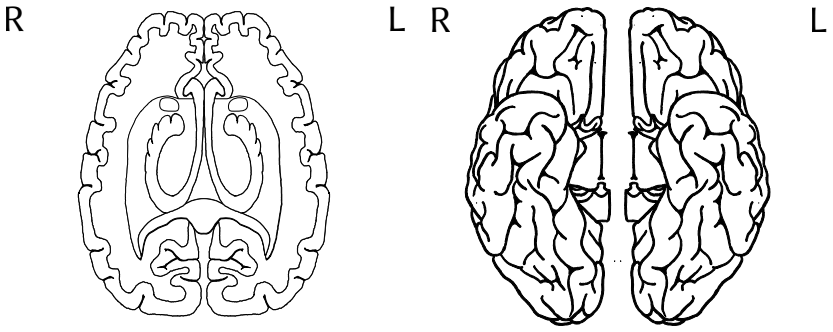
$$T = T_{X \to Y} - T_{Y \to X}$$

with Symbolic Transfer Entropy

$$T_{Y \to X} = \sum_{x_i, x_{i-1}, y_{i-1}} p(x_i, x_{i-1}, y_{i-1}) \log_2 \frac{p(x_i \mid x_{i-1}, y_{i-1})}{p(x_i \mid x_{i-1})}$$

Example I: Strength and direction of interaction between brain regions

Functional modules:



EEG Data	
multi-channel invasive EEG recordings	200 Hz sampling rate
recording duration: 7.8 days	0.1 Hz to 70 Hz band-pass filter
number of seizure: 12	16 bit A/D Converter

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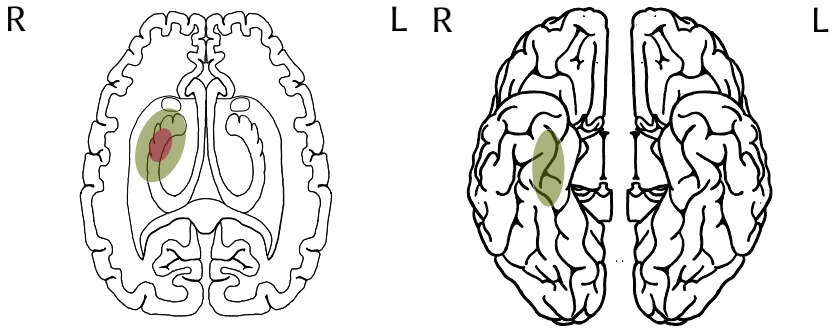

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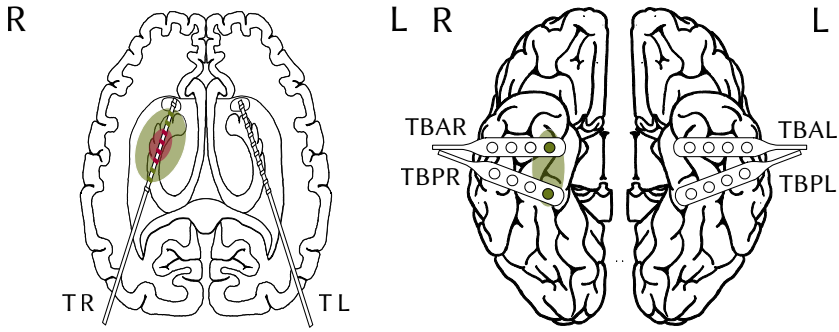

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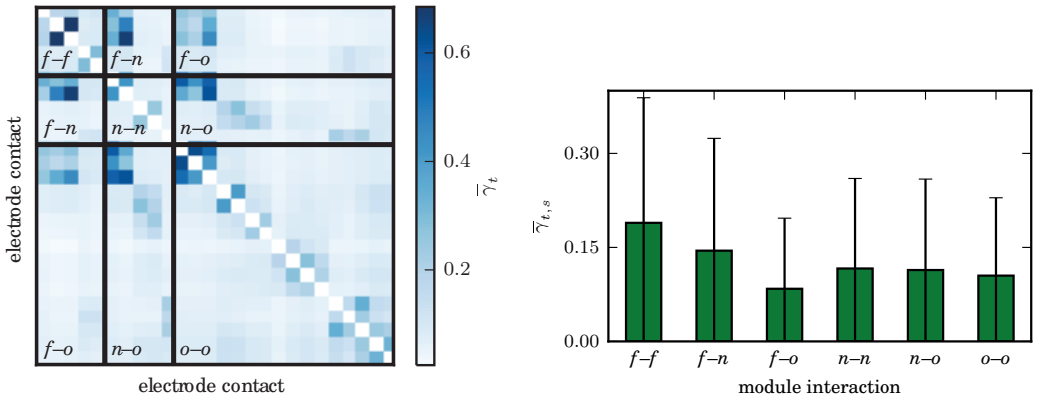
Example I: Strength and direction of interaction between brain regions

Temporal average of strength of interactions

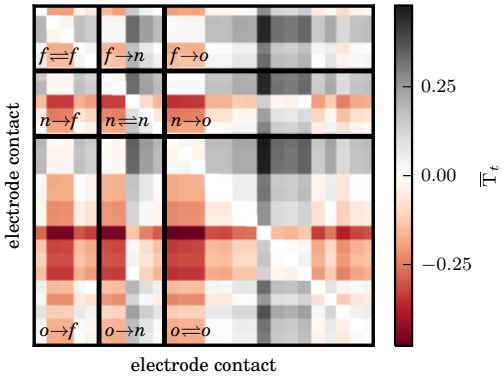


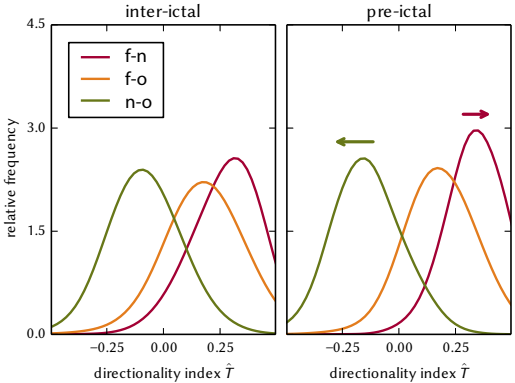
→ Can we identify brain region through their interaction properties?

Dickten et al. *(in preparation)*.

Example I: Strength and direction of interaction between brain regions

Temporal average of direction of interaction





→ Is prediction of seizures feasible?

Lehnertz and Dickten *Phil. Trans. R. Soc. A* (2015).

Example II

Importance of brain regions during epileptic seizures

- Which brain regions are important for epileptic seizures?
- Before, during, after the seizure?
- Is the focus most important?
- What does *important* mean for network nodes?

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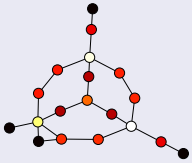
- What does *important* mean for network nodes?
  $\Rightarrow$ concept from graph theory: *centralities*

Estimating importance of brain regions

Betweenness centrality

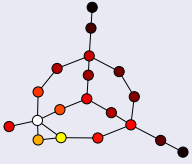


$$C^B(n) = \frac{2}{(N-1)(N-2)} \sum_{h \neq n \neq m}^{N} \frac{\eta_{hm}(n)}{\eta_{hm}},$$

- η_{hm}: number of all shortest paths between the nodes h and m
- $\eta_{hm}(n)$: number of these paths running through node n

based on concept of shortest paths between pairs of nodes

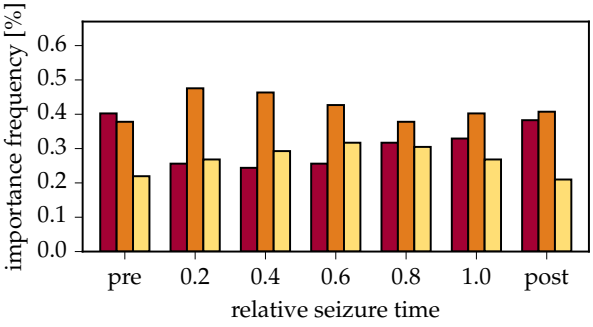
Eigenvector centrality

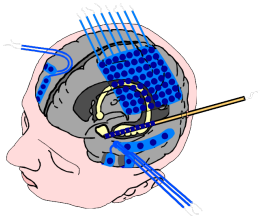


$$C^E(n) = v_n \text{ with } \sum_{i=1}^{n} A_{ij} v_j = \lambda_{\max} v_i$$

iterative approach: nodes are central, if they are connected with other central nodes

Which brain region is important for epileptic seizures?





Functional modules

- focus
- neigborhood
- remote

as indicated by eigenvector centrality C^E

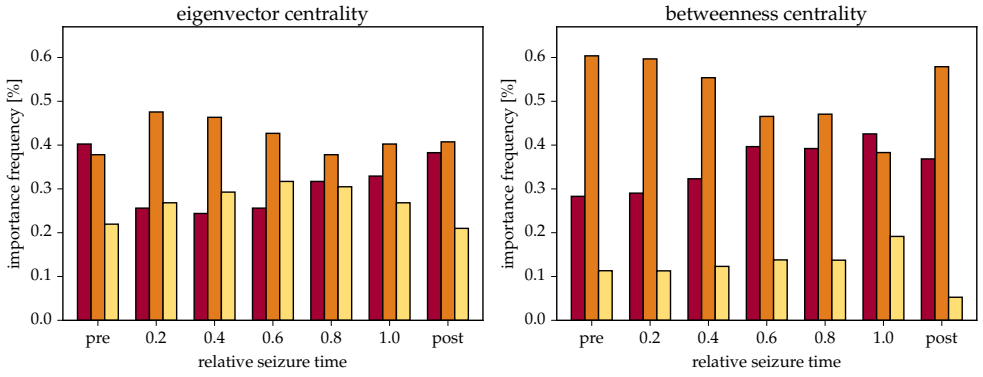
using correlation ρ for network inference

EEG Data

82 multi-channel invasive EEG recordings
from 52 patients (20 woman, 32 men)
number of electrode contacts: mean 66 (range 26–124)
recording duration: mean 455 s (range 112 s to 1702 s)
seizure duration: mean 120.1 s (range 33.8 s to 395.8 s)

200 Hz sampling rate
0.1 Hz to 70 Hz band-pass filter
16 bit A/D Converter
recording montage: unipolar

Impact of different centrality indices



Geier et al. *Seizure* 2015

Conclusion

Better understanding of the epileptic process?

- neighborhood of the focus important for seizure generation
- focus plays secondary role
- neighborhood steers the epileptic process?
- treatmeant and seizure control
  - resection of neighborhood?
  - modification of functional brain network?

Influencing factors

- spatial and temporal sampling, missing observations
- choice of properties of interaction
- choice of measure of interaction
- ...