# **Small-world networks and epilepsy**: Graph theoretical analysis of intracerebrally recorded mesial temporal lobe seizures

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# Epilepsy

- Abnormal neuronal activity in the brain affecting mental and physical functions
- Many kinds of symptoms
  - lose consciousness
  - involuntary motions
  - unusual feelings or sensations
- Seizures are Unforeseen, unpredictable
- Common pragnosis: abnormal synchronization of neurons (may be due to illness, lack of oxygen, brain injury, etc...)

# Epilepsy

- Apart from changes in levels of synchronization, transition to seizure state may also be characterized by changes in spatial/functional organization and may be studied with graph theory

# Overview

- **Hypothesis**: functional neuronal networks during temporal lobe seizures change in configuration before and during seizures
- **Method**: Apply synchronization and graph analysis to EEG recordings
- **Goal**: Analysis of neuronal networks during seizures may provide insight into seizure genesis and development

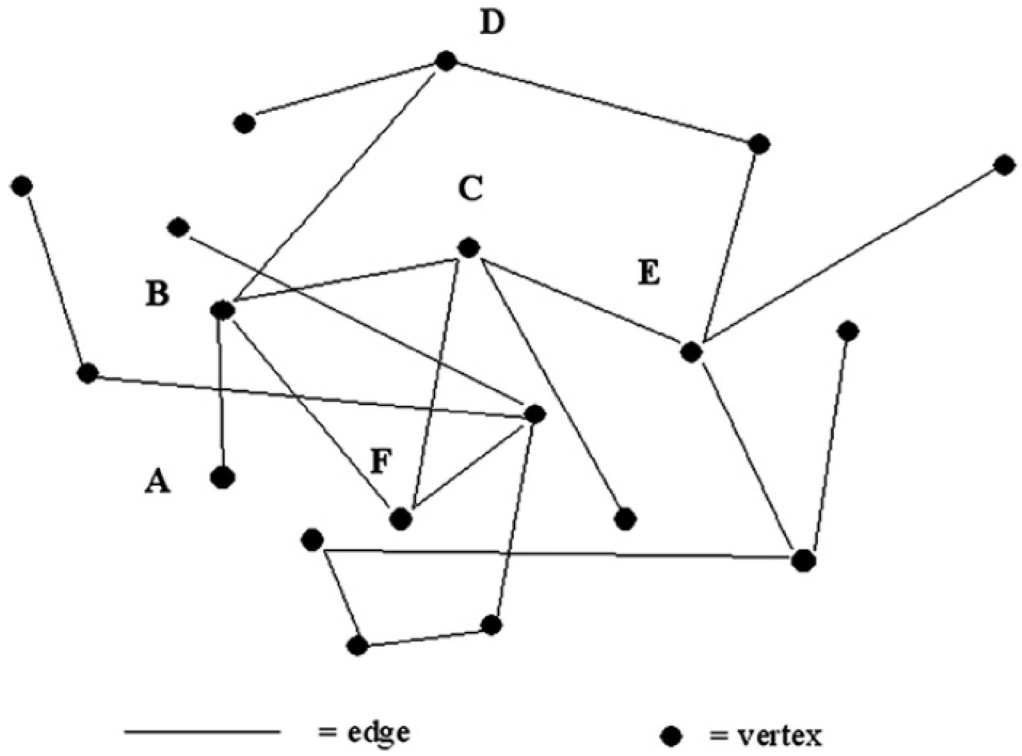
# Graph analysis

- G=(V,E)
- *deg*(G)=**k**, average *deg*(v∈V)
- *Characteristic path length (**L**)* = overall integration / connectivity
  - Mean of all shortest paths
- *Clustering coefficient (**C**)* = local strucutre / connectedness
  - How many neighbors of a vertex are neighbors of each other?
  - Mean of all clustering coefficients

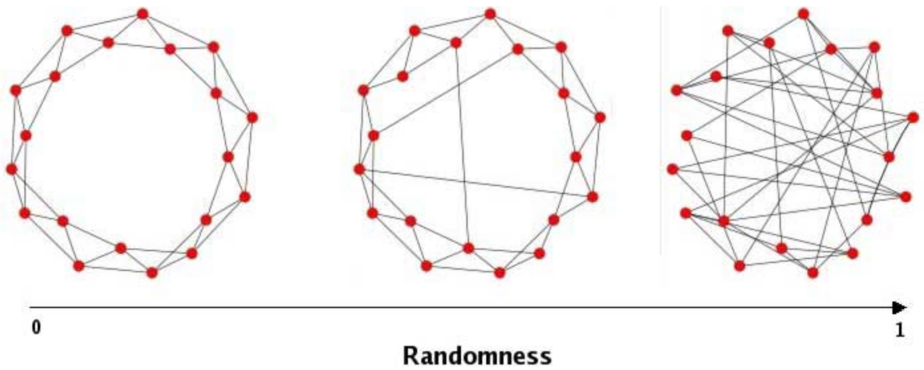
# Clustering coefficient – example

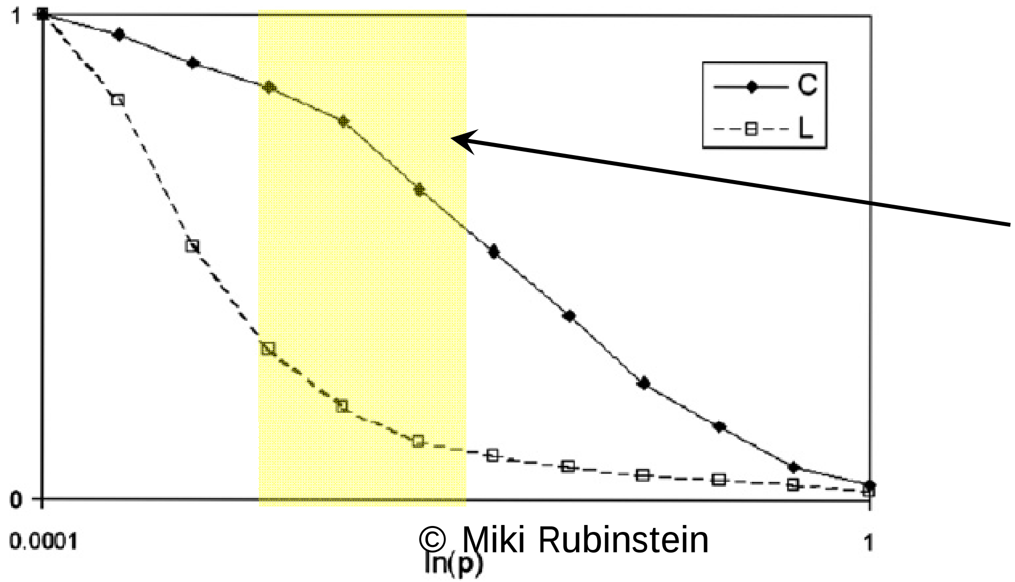
- vertex B:
  - Determine B's neighbors: A,C,D,F
  - Determine how many edges exist between the neighbors: 1 (C,F)
  - 4 Neighbors → 6 possible connections.

    In general: k(k-1)/2
- ➔ C(B)=1/6



# Graph analysis [Watts, Strognaz 1998]

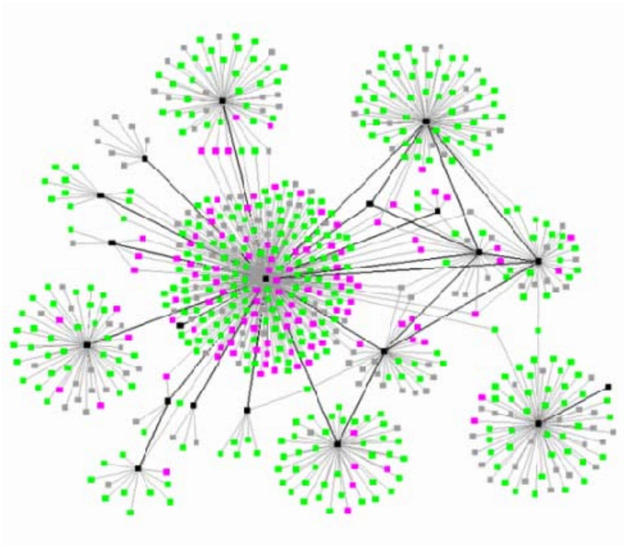



“Small-world”

# Small-world networks

- High C, relatively short L
- Appropriate models for social networks, internet, Kevin Bacon game...



- Neuronal networks
  - May be optimal for synchronizing neuronal activity between brain regions [Lago-Fernandez et al., 2000; Barahona and Pecora, 2002]

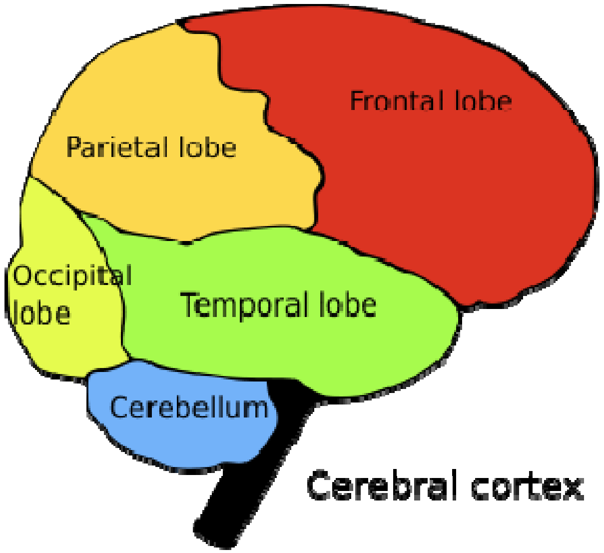
# Related work

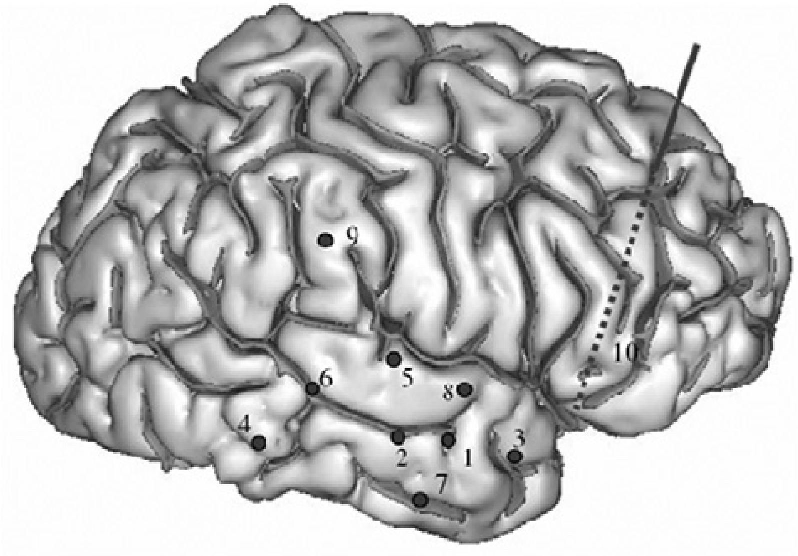
- Graph analysis of fMRI, EEG showed a small network configuration [S*porns et al., 2000; Stam, 2004; Salvador et al., 2005; Achard et al., 2006; Stam et al., 2007; Micheloyannis et al., 2006a*]

- relationship between the small-world phenomenon and epilepsy suggested by model studies [Netoff et al. 2004, Perch et al. 2005]
  - the start of the bursting phase showed drop of C – a more random architecture

- Never tested with seizure recordings

# EEG signal (see details in the paper)



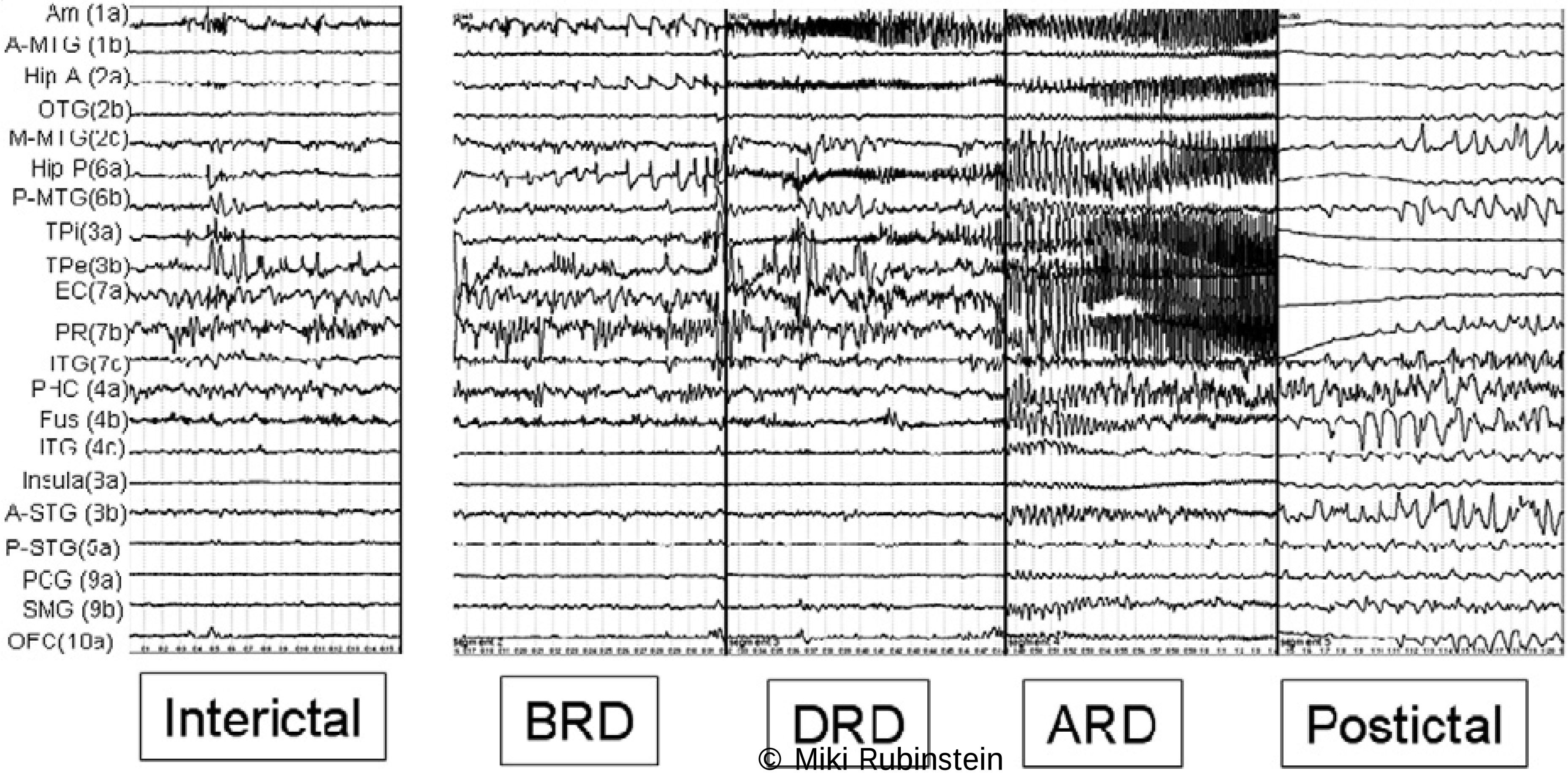




- 10 – Electrode exploring the orbitofrontal cortex: cognitive processes such as decision-making and expectation

# EEG signal

- 7 patients
- Total 21 brain regions (per patient)
- 5 epochs of interest (16s each) [Bartolomei et al., 2004]
  - Interictal - normal brain activity
  - Before Rapid Discharges (BRD) – before seizure start
  - During Rapid Discharges (DRD) – early ictal
  - After Rapid Discharges (ARD) – late ictal
  - Postictal – brain recovery from seizure

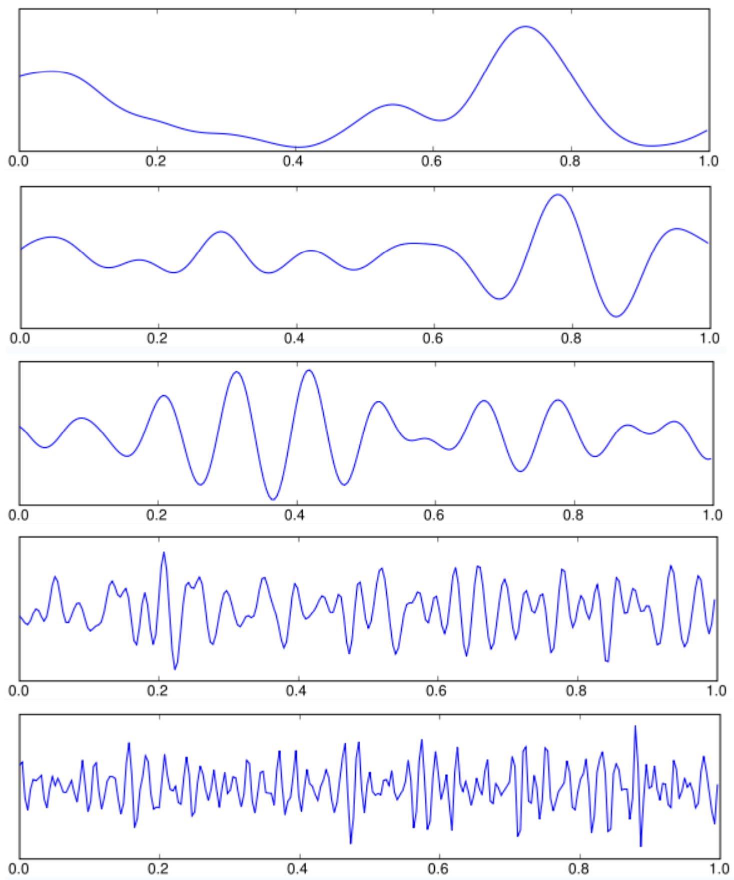
# EEG signal



Am (1a)
A-MTG (1b)
Hip A (2a)
OTG(2b)
M-MTG(2c)
Hip P(6a)
P-MTG(6b)
TPi(3a)
TPe(3b)
EC(7a)
PR(7b)
ITG(7c)
PHC (4a)
Fus (4b)
ITG (4c)
Insula(3a)
A-STG (3b)
P-STG(5a)
PCG (9a)
SMG (9b)
OFC(10a)
Interictal
BRD
DRD
ARD
Postictal

# EEG signal - wave patterns

- Broad band (1-48 Hz)
- delta (1–4 Hz): slow wave sleep
- theta (4–8 Hz): drowsiness, arousal, meditation
- alpha (8–13 Hz): closing eyes, relaxation
- beta (13–30 Hz): active, busy , anxious thinking
- gamma (30–48 Hz): motor functions



# Synchronization Likelihood (SL)

## [Stam, van Dijk, 2002]

- Input: time series $X=x_i$, $Y=y_i$, $i=1..N$
- [*Rulkov et al., 1995*] Synchronization is said to exist between systems X, Y if exists F 1-1 and continuous such that $Y=F(X)$

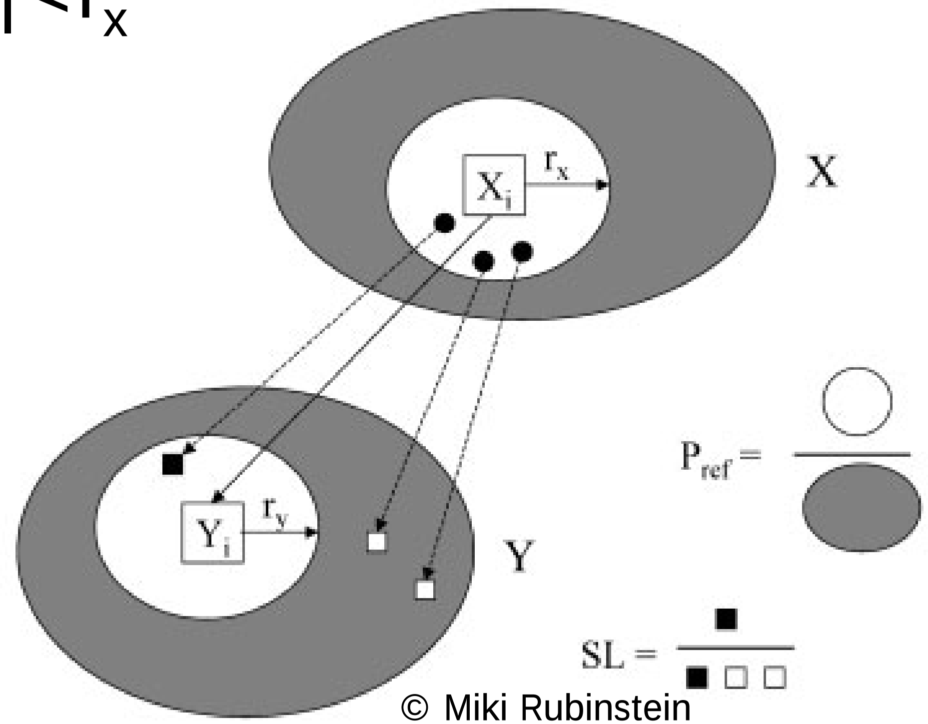
- *Time-delay embedding* [Takens, 1981]:

$$X_i = (x_i, x_{i+L}, x_{i+2\times L}, x_{i+3\times L}, \ldots, x_{i+(m-1)\times L})$$

- L=time lag, m<<N, N-(mxL) vectors in 'state space'
- [*Takens, 1981*] For sufficiently large m, state space vectors correspond to the *attractor* of the underlying system

# Synchronization Likelihood (SL)

- SL expresses the probability that Yi and Yj will be almost identical ($|Yi-Yj|<r_y$), given that $|Xi-Xj|<r_x$



# Synchronization Likelihood (SL)

- $r_x$ ($r_y$) is chosen such that the likelihood that two randomly chosen vectors X (Y) will be closer than $r_x$ ($r_y$) equals $P_{ref}$

$$C_r = \frac{1}{N^2}\sum_{i=1}^{N-1}\sum_{j=i+1}^{N}\theta(r - |X_i - X_j|)$$

- $\theta(X)=0$ if $X>=0$, $\theta(X)=1$ if $X<0$

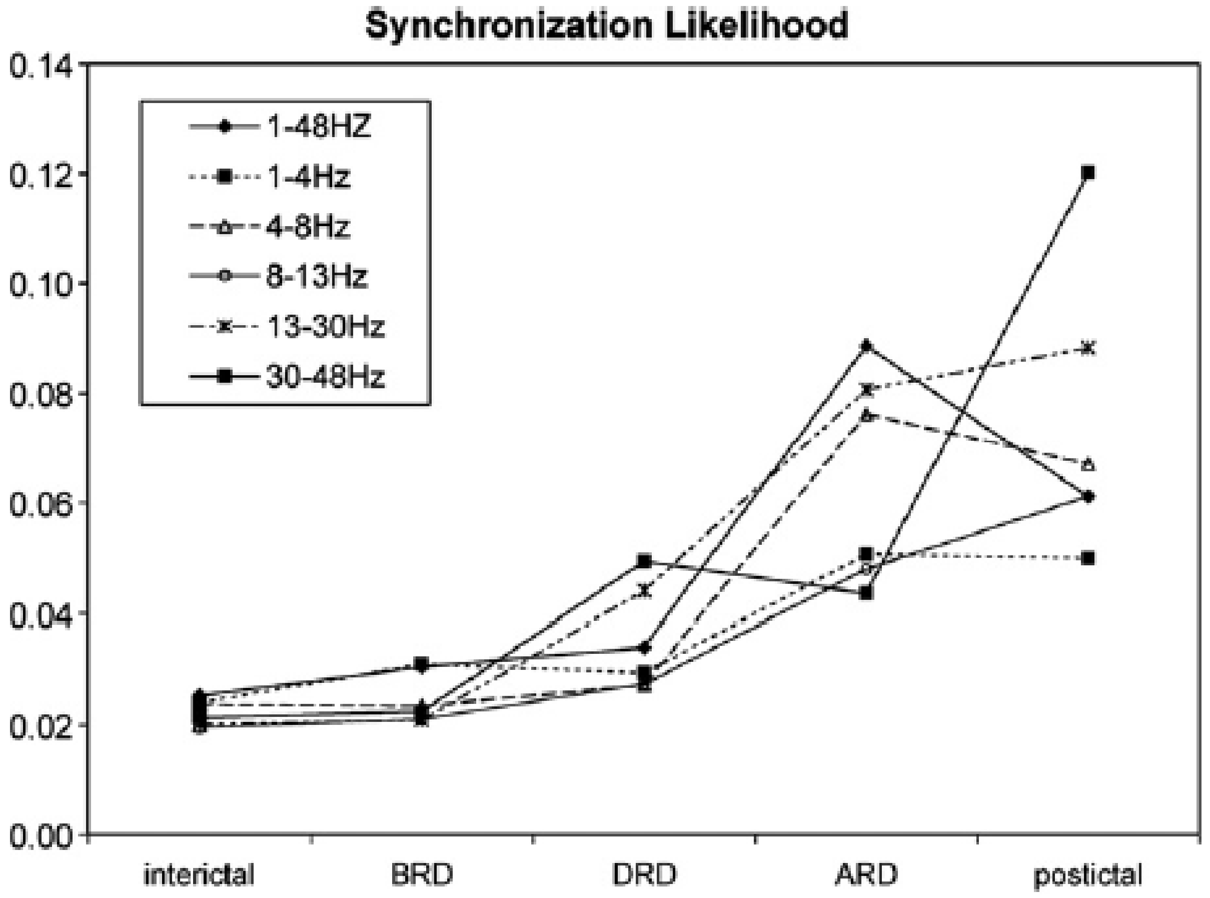
$$SL = \frac{1}{N'}\sum_{i}\sum_{j}\theta(r_y - |Y_i - Y_j|)$$

# Synchronization Likelihood (SL)

- Perfect synchronization → SL=1

  Independent → SL will equal the likelihood that random vectors $Y_i$, $Y_j$ are closer than $r_y = P_{ref}$
- Symmetric: $SL_{XY}=SL_{YX}$
- Sensitive to linear and nonlinear dependencies
- Output: 21x21 matrix for each EEG epoch (per frequency band)

# Synchronization Likelihood (SL)



# Changes in synchronization

- Each epoch compared to interictal state
- Significant ($p<0.05$) increase in all bands ARD, postictal periods
- Increase in BRD period only significant in the delta band (1–4 Hz)
- Increase in DRD period only significant in alpha (8–13 Hz), beta (13–30 Hz) and delta bands

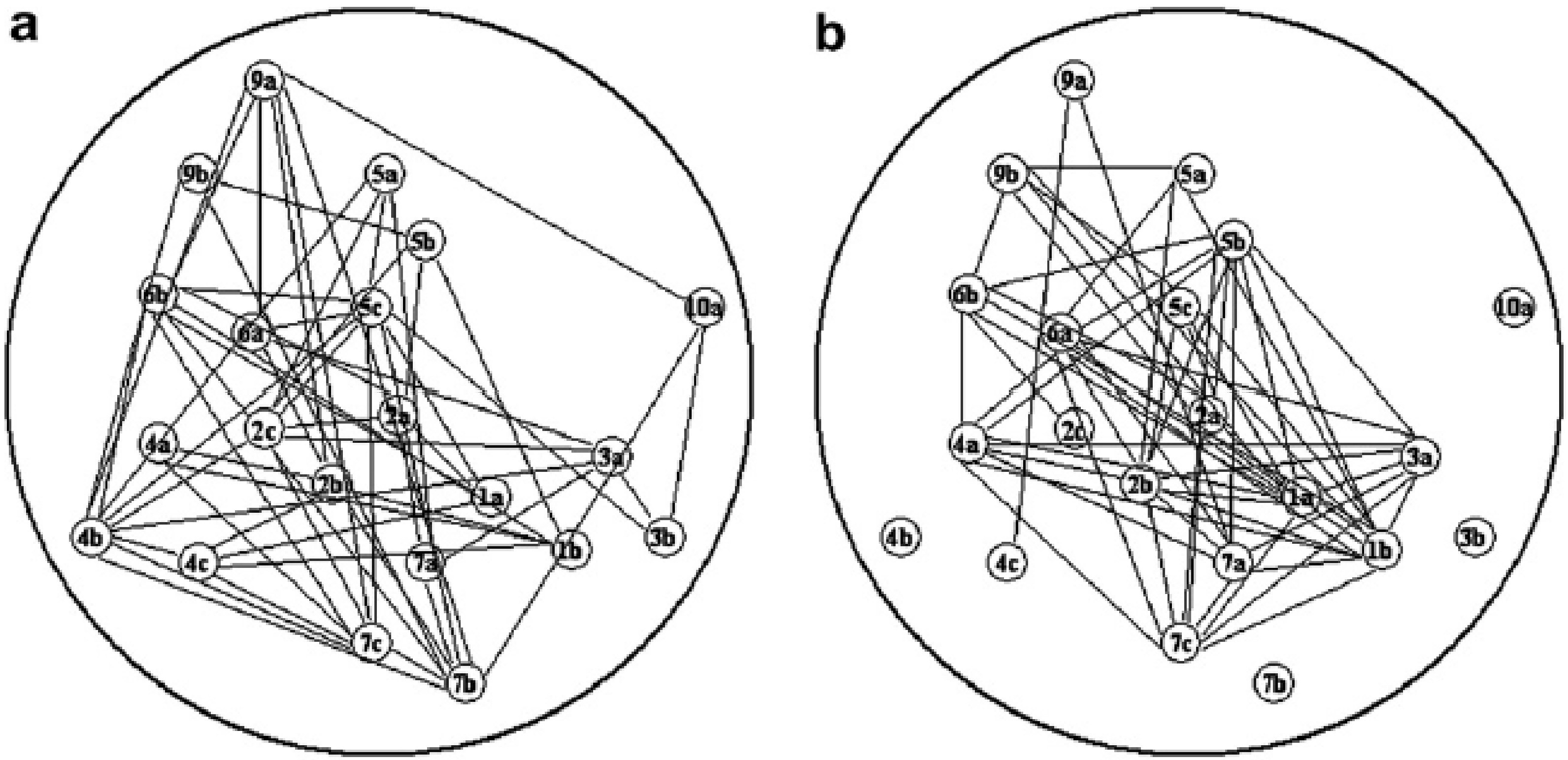
# Computing C and L

- V(G) = EEG channels
- E(G) = SL values larger than some threshold t

- Note: need to counteract synchronization differences between epochs!

- [stam et al. 2007] Start with t=0 and iteratively increase (decreasing *deg*(G)) until required degree is reached – graphs for all epochs will have same number of edges!
- K=6 was used

# Computing C and L



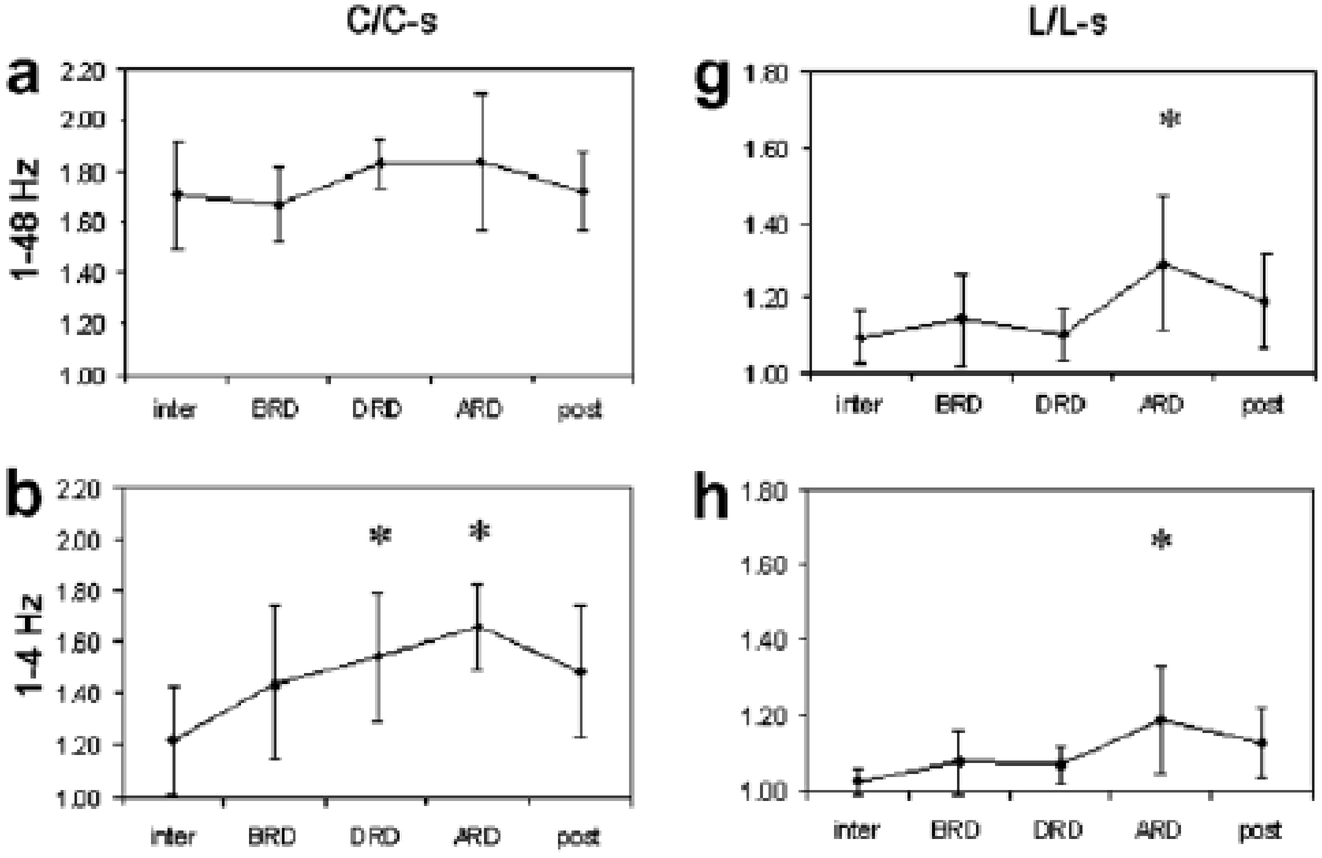

Interictal 8-13 Hz

Ictal (ARD) 8-13 Hz

# Computing C and L

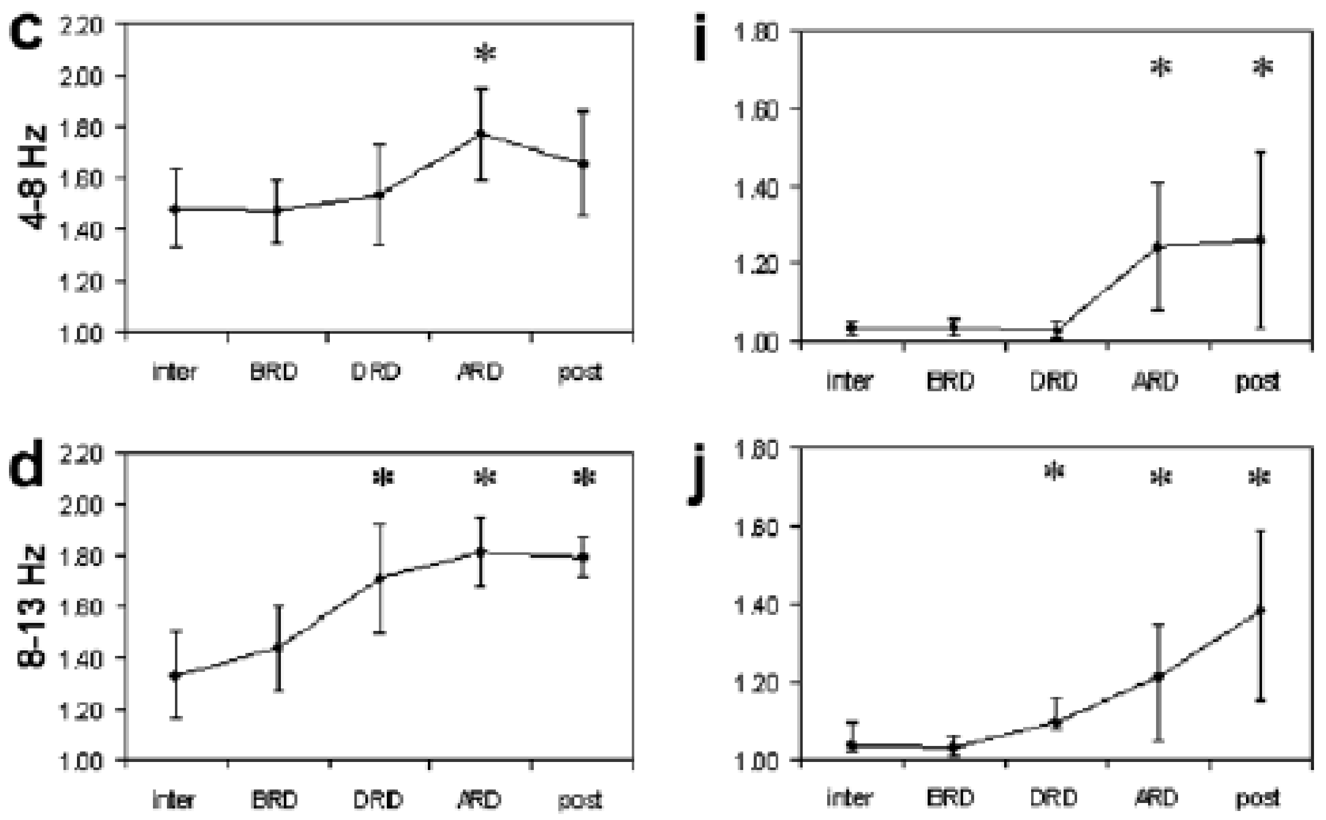
- 20 random networks are generated for each epoch and mean C-s, L-s are computed [Sporns and Zwi, 2004] (degree distributions are maintained)
- C/C-s and L/L-s is used

# Results



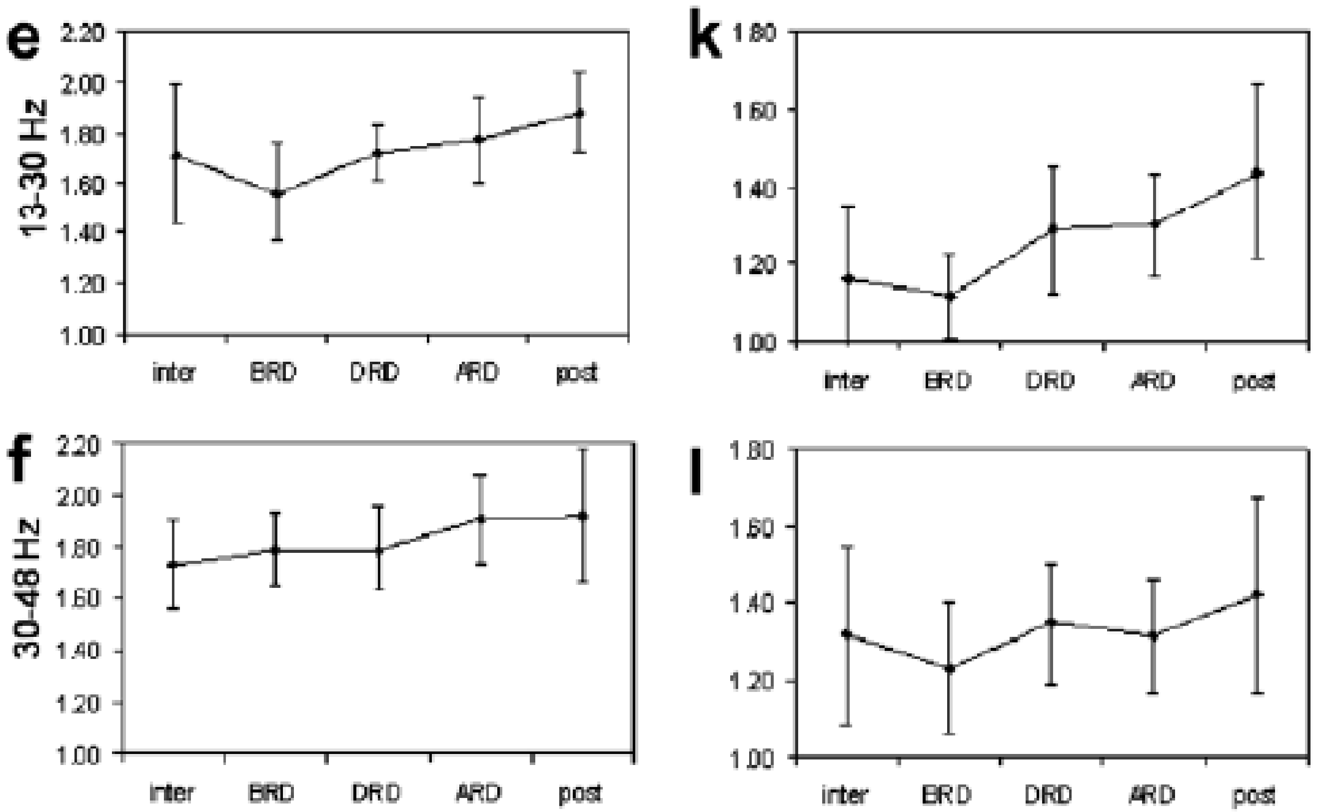

*significant ($p < 0.05$).

# Results



c
4-8 Hz
2.20
2.00
1.80
1.60
1.40
1.20
1.00
inter
BRD
DRD
ARD
post
i
1.80
1.60
1.40
1.20
1.00
inter
BRD
DRD
ARD
post
d
8-13 Hz
2.20
2.00
1.80
1.60
1.40
1.20
1.00
inter
BRD
DRD
ARD
post
j
1.80
1.60
1.40
1.20
1.00
inter
BRD
DRD
ARD
post

# Results



e
13-30 Hz
2.20
2.00
1.80
1.60
1.40
1.20
1.00
inter
BRD
DRD
ARD
post
k
1.80
1.60
1.40
1.20
1.00
inter
BRD
DRD
ARD
post
f
30-48 Hz
2.20
2.00
1.80
1.60
1.40
1.20
1.00
inter
BRD
DRD
ARD
post
l
1.80
1.60
1.40
1.20
1.00
inter
BRD
DRD
ARD
post

# Changes in topology

- Broadband, beta, gamma did not generally show significant changes in C/C-s, L/L-s
- Alpha band significantly higher ictally and postictally
- Most obvious change in lower frequency bands (1-13 Hz)

Results interictal epoch versus the other periods

| *p*-values: | BRD | | DRD | | ARD | | Postictal | |
|---|---|---|---|---|---|---|---|---|
| Frequency band (Hz) | *C*/*C*-s | *L*/*L*-s | *C*/*C*-s | *L*/*L*-s | *C*/*C*-s | *L*/*L*-s | *C*/*C*-s | *L*/*L*-s |
| 1–48 | – | – | – | – | – | .043 | – | – |
| 1–4 | – | – | .043 | – | .028 | .046 | – | – |
| 4–8 | – | – | – | – | .043 | .018 | – | .043 |
| 8–13 | – | – | .018 | .028 | .018 | .018 | .018 | .018 |
| 13–30 | – | – | – | – | – | – | – | – |
| 30–48 | – | – | – | – | – | – | – | – |

*Abbreviations*. BRD, before rapid discharges; DRD, during rapid discharges; ARD, after rapid discharges; *C*/*C*-s, clustering coefficient; *L*/*L*-s, path length.
–, not significant.

# summary

- “First work where small-world characteristics are studied in intracerebral EEG recordings of temporal lobe seizures”
- Significant Increase in synchronization between seizure periods and normal brain activity
- Increase in C in the lower frequency bands (1–13 Hz), and an increase in L during and after the seizure compared to the interictal recordings
- Since C/C-s and L/L-s increased significantly during seizure, it seems that the interictal network had a more random configuration
- The increase of L/L-s was significant but rather small - more compatible with small-world than ordered configuration
- Postictal state also disclosed changes in network configuration

# My (not so educated) opinion

- Incorporating synchronization and graph analysis seems interesting
- Collection of previously suggested methods
- 7 patients (one problematic)
- Comparing all channels, using all bands
- Underlying (physical) brain topology

# Thank You !

# Interesting references


- Watts DJ, Strogatz SH. Collective dynamics of 'small-world' networks. Nature 1998;393(6684):440–2.
- Stam CJ, van Dijk BW. Synchronization likelihood: an unbiased measure of generalized synchronization in mulitvariate data sets. Physica D2002;163:236–51.
- Takens F. Detecting strange attractors in turbulence. Lecture in mathematics 1981(898):366–81.
- Stam CJ, Jones BF, Nolte G, Breakspear M, Scheltens P. Small-World Networks and Functional Connectivity in Alzheimer's Disease. Cereb Cortex 2007;17(1):92–9.