Are Epileptic Seizures Condensed Sleep?

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Causality, Information Transfer and Dynamical Networks, June 2014

Motivation for this study:

There is apparently a strong interrelation between sleep and epileptic seizures

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Sleep disruption and sleep deprivation predispose seizures even in clinically healthy subjects (Dinner, 2002; Rajna and Veres, 1993)

Excessive daytime sleepiness, sleep maintenance insomnia, and obstructive sleep apnea are 2 to 3 times more common in people with epilepsy than in the general population, especially when seizures are poorly controlled.
(Cortesi et al. 1999, Batista et al. 2007, Maganti et al. 2006, Khatami et al. 2006)

Abnormalities in the sleep architecture in patients with epilepsy (especially for TLE) (Manni et al. 1990, Touchon et al. 1991, Grigg-Damberger et al. 2012):
(1) reduced time spent in rapid eye movement (REM) sleep;
(2) prolonged REM latency;
(3) increased wake after sleep onset resulting in reduced total sleep time and sleep efficiency;
(4) increased number of arousals, awakenings, and stage shifts, even in the absence of seizures during the night

Seizures occur predominantly in a drowsy state (Bazil and Walczak, 1997; Crespel et al., 1998; Foldvary-Schaefer and Grigg-Damberger, 2006)

Motivation for this study:

Cortical lesions are a frequent cause for seizures, but may also impair sleep (Gottselig et al., 2002)

Seizures during wakefulness are often followed or even seem to induce so-called post-ictal sleep.

The same neuronal circuits appear to produce sleep oscillations and epileptiform activity, namely Thalamo-cortical circuits, and also Hippocampal circuits. (Beenhakker and Huguenard, 2009). -> spike waves as hypersynchronous sleep spindels? (Huguenard Mc Cormick 2007, McCormick Bal 1997)

Motivation for this study:

These complex interrelations between sleep and epilepsy may be due to common underlying neurophysiological processes!

Metodology:

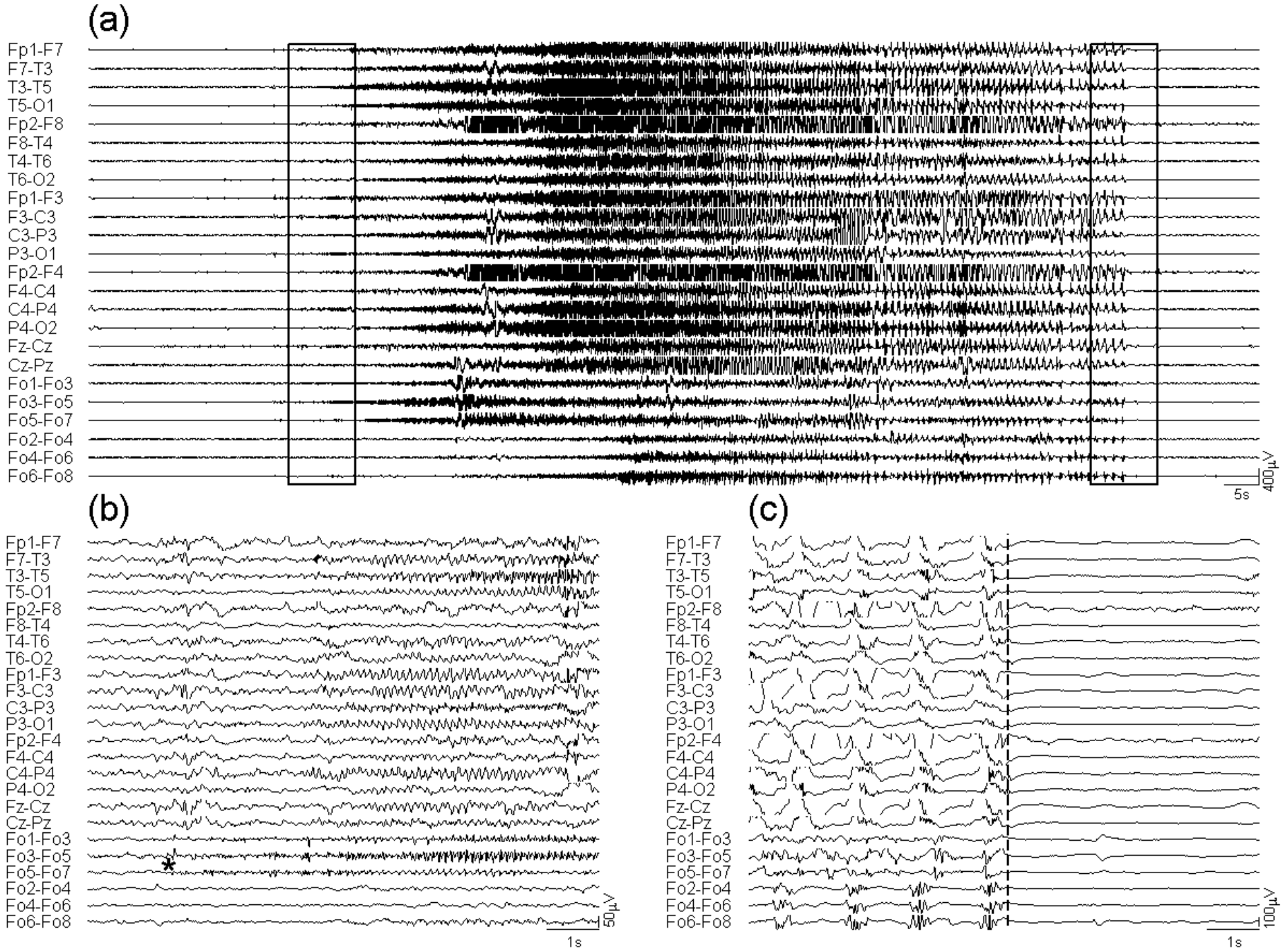
We focus on the dynamical evolution of the spatial interrelations of brain activity, viz. the dynamics of the functional network.

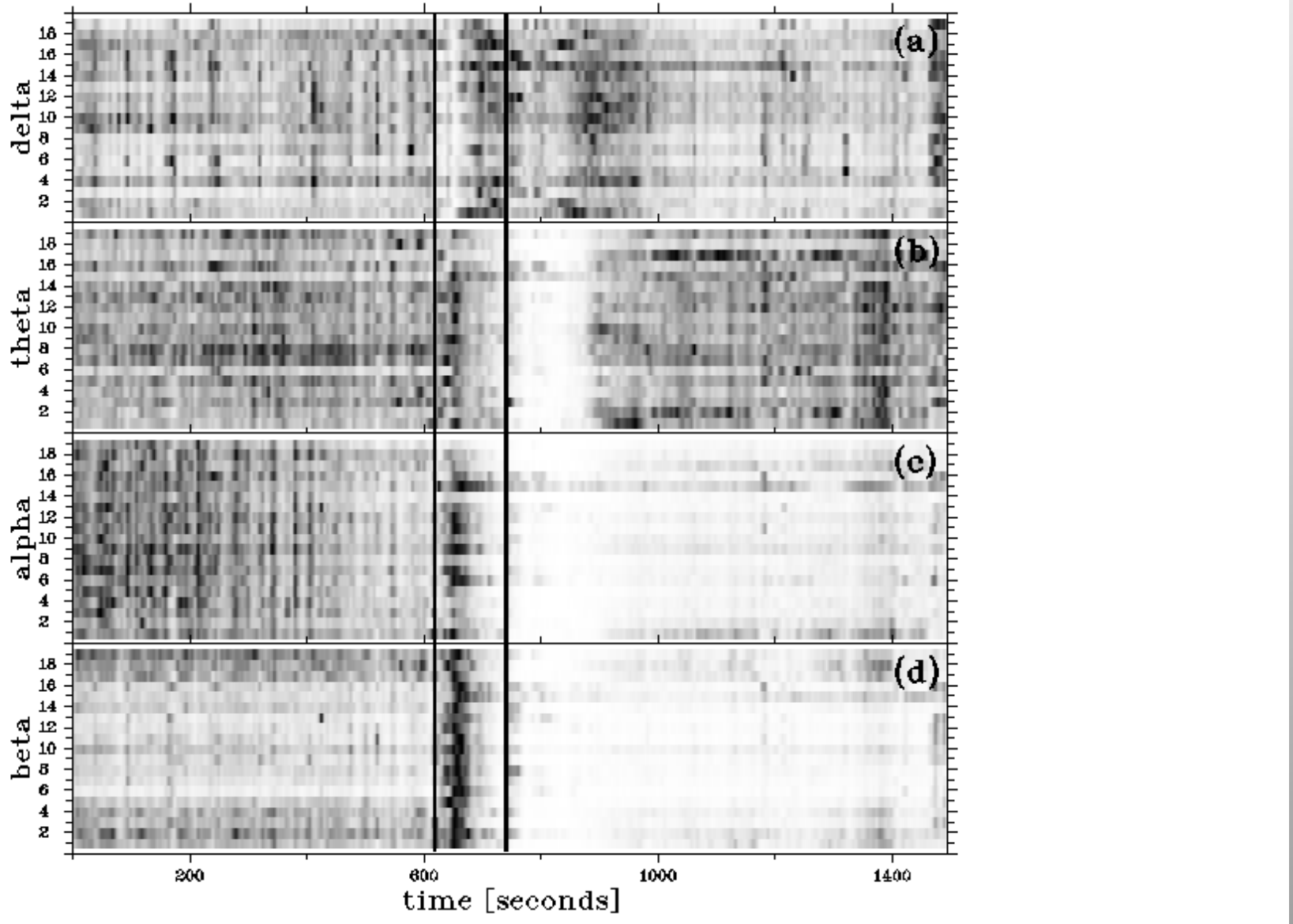
Part 1: Power spectra and graph theoretical analysis

EEG data:

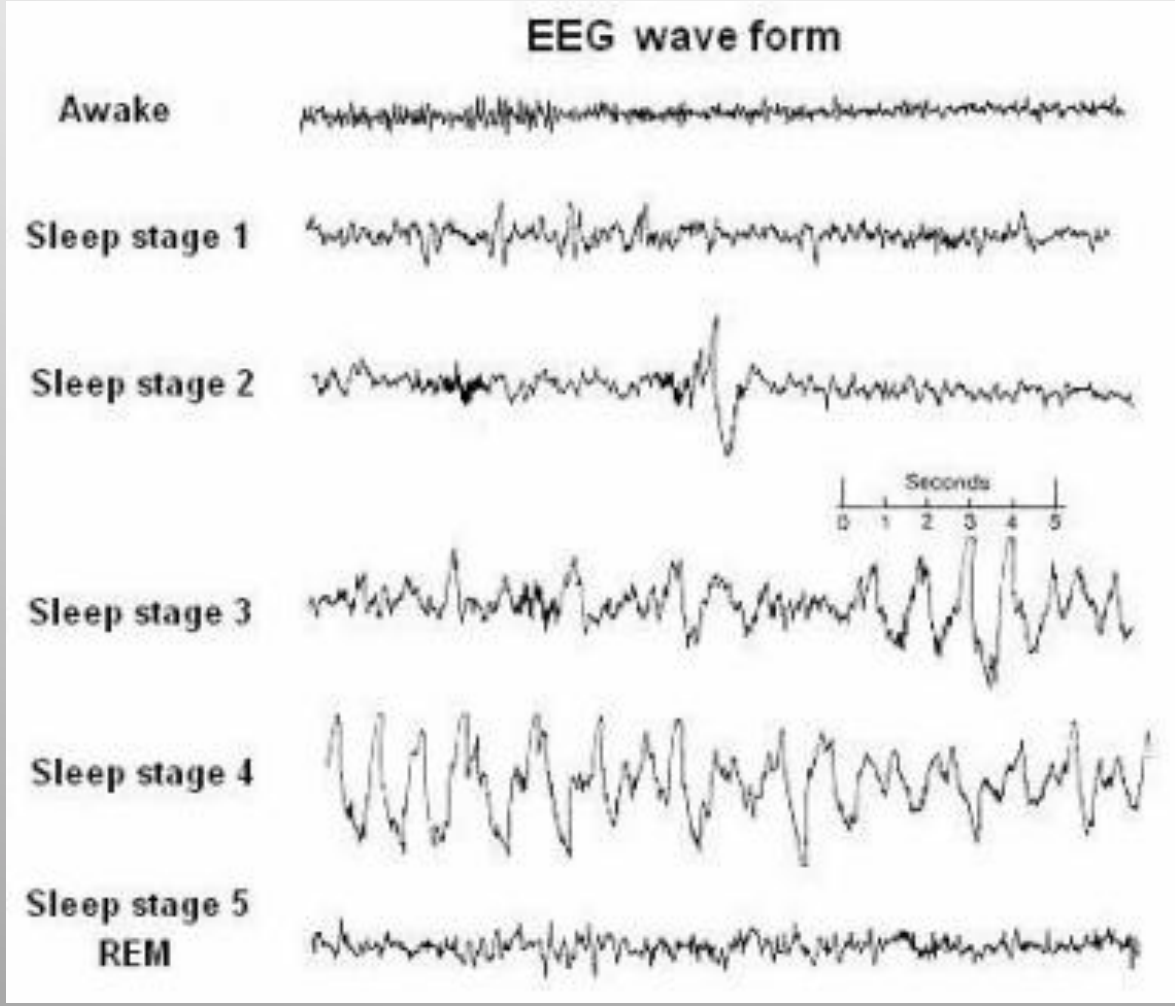
Ten patients suffering from focal onset pharmaco-resistant epilepsy
six females; mean age (SD) 26 8 years; range 17–45 years
In total we analyzed 20 EEG-recordings of a peri-ictal transition.

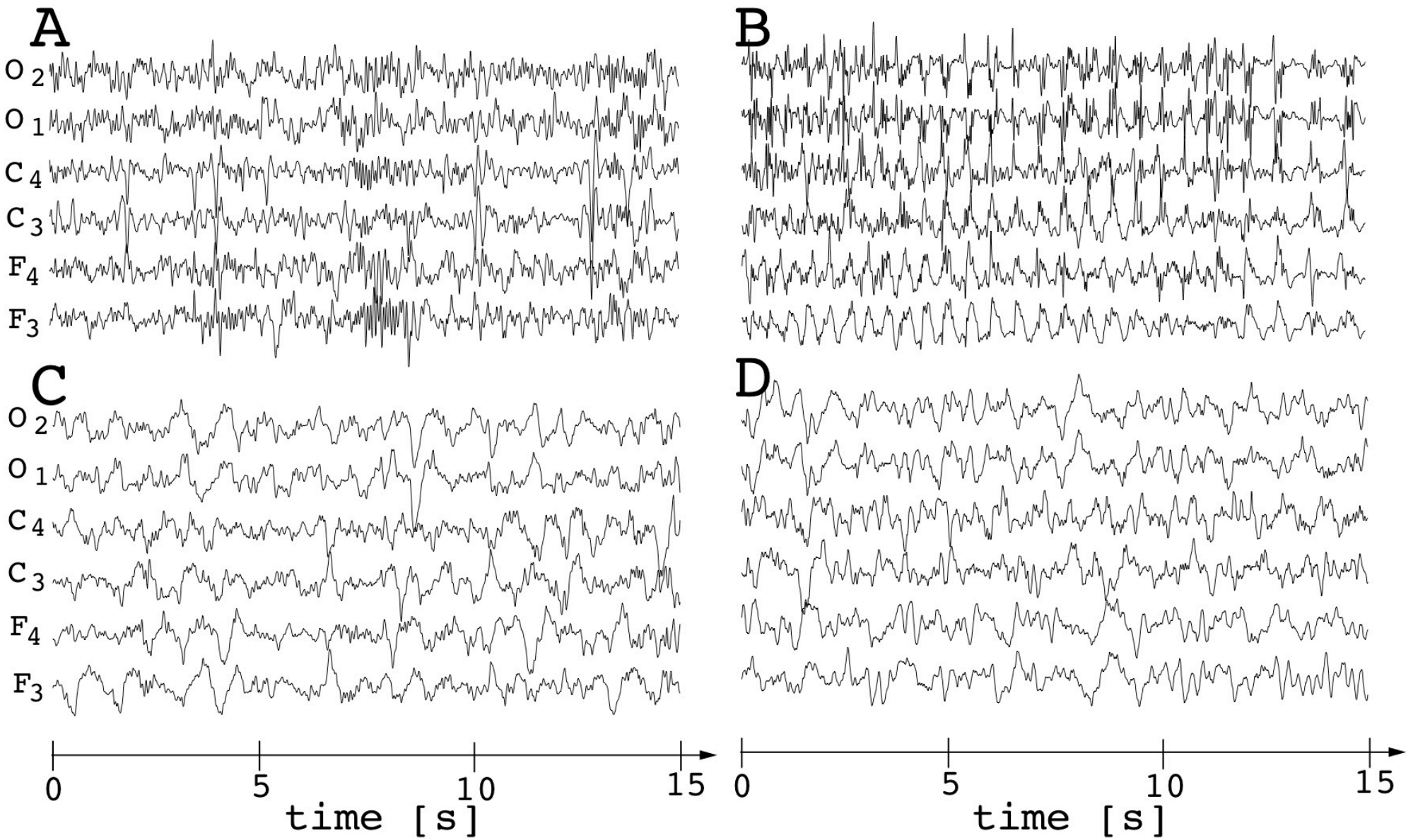
12 volunteers taking no medication, eight females; mean age (SD)
23 9 years; range 17–46 years.


(a)
Fp1-F7
F7-T3
T3-T5
T5-O1
Fp2-F8
F8-T4
T4-T6
T6-O2
Fp1-F3
F3-C3
C3-P3
P3-O1
Fp2-F4
F4-C4
C4-P4
P4-O2
Fz-Cz
Cz-Pz
Fo1-Fo3
Fo3-Fo5
Fo5-Fo7
Fo2-Fo4
Fo4-Fo6
Fo6-Fo8
400μV
5s
(b)
Fp1-F7
F7-T3
T3-T5
T5-O1
Fp2-F8
F8-T4
T4-T6
T6-O2
Fp1-F3
F3-C3
C3-P3
P3-O1
Fp2-F4
F4-C4
C4-P4
P4-O2
Fz-Cz
Cz-Pz
Fo1-Fo3
Fo3-Fo5
Fo5-Fo7
Fo2-Fo4
Fo4-Fo6
Fo6-Fo8
*
50μV
1s
(c)
Fp1-F7
F7-T3
T3-T5
T5-O1
Fp2-F8
F8-T4
T4-T6
T6-O2
Fp1-F3
F3-C3
C3-P3
P3-O1
Fp2-F4
F4-C4
C4-P4
P4-O2
Fz-Cz
Cz-Pz
Fo1-Fo3
Fo3-Fo5
Fo5-Fo7
Fo2-Fo4
Fo4-Fo6
Fo6-Fo8
100μV
1s


(a)
(b)
(c)
(d)
delta
theta
alpha
beta
18
16
14
12
10
8
6
4
2
200
600
1000
1400
time [seconds]

Typical EEG for different sleep stages





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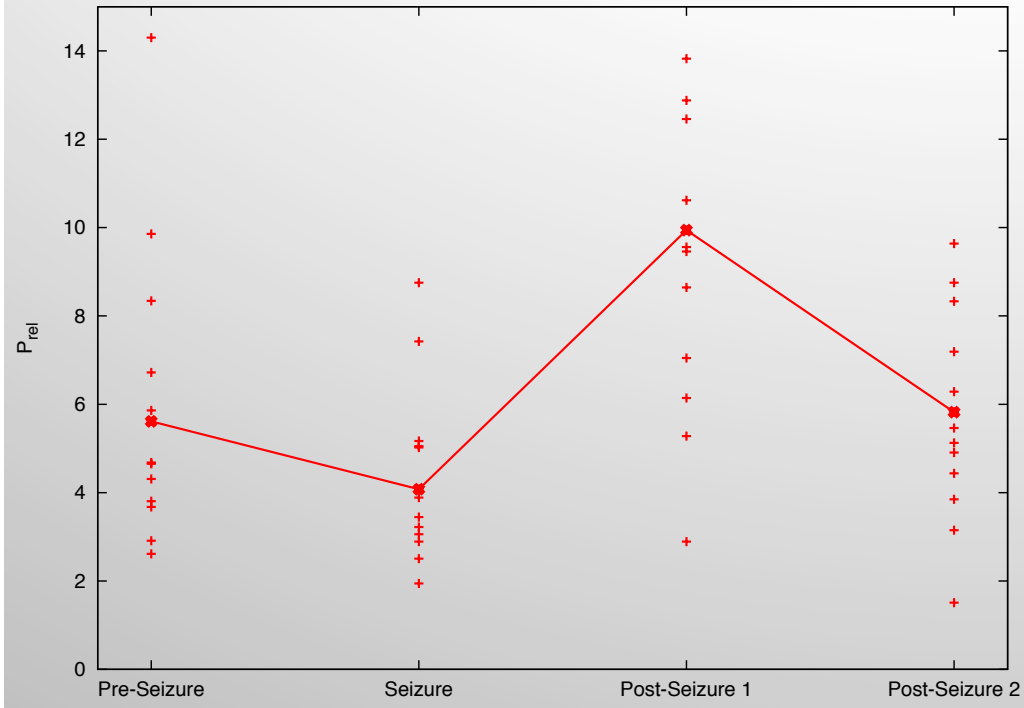
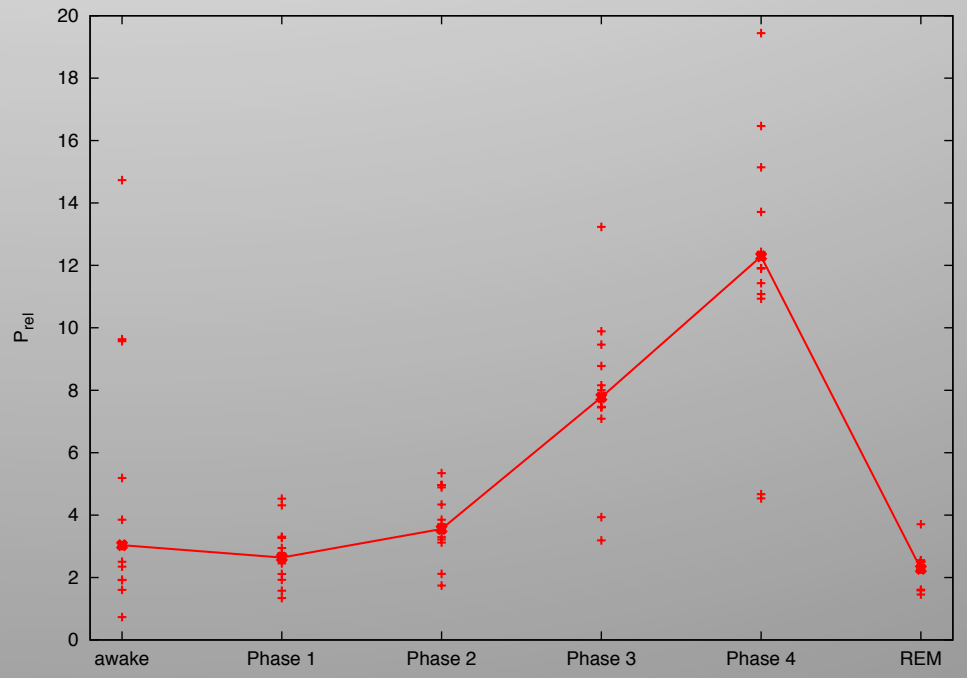


Relative Power

$$P_{rel} = P_{\delta} / P_{\theta+\alpha+\beta}$$



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Zero-Lag Cross-Correlation Matrix:

$$C_{ij}(\tau) = \int_{-\infty}^{\infty} X_i(t) X_j(t+\tau) dt$$

We do not have continuous, infinitely long EEG recordings

$$\tilde{X}_i(k) = \frac{X_i(k) - \overline{X}}{\sigma_i} \qquad k = 1, \ldots, T \qquad i = 1, \ldots, M$$

$$C_{ij} = \frac{1}{T} \sum_{k=1}^{T} \tilde{X}_i(k) \tilde{X}_j(k)$$

Do these modification lead to erroneous estimates?

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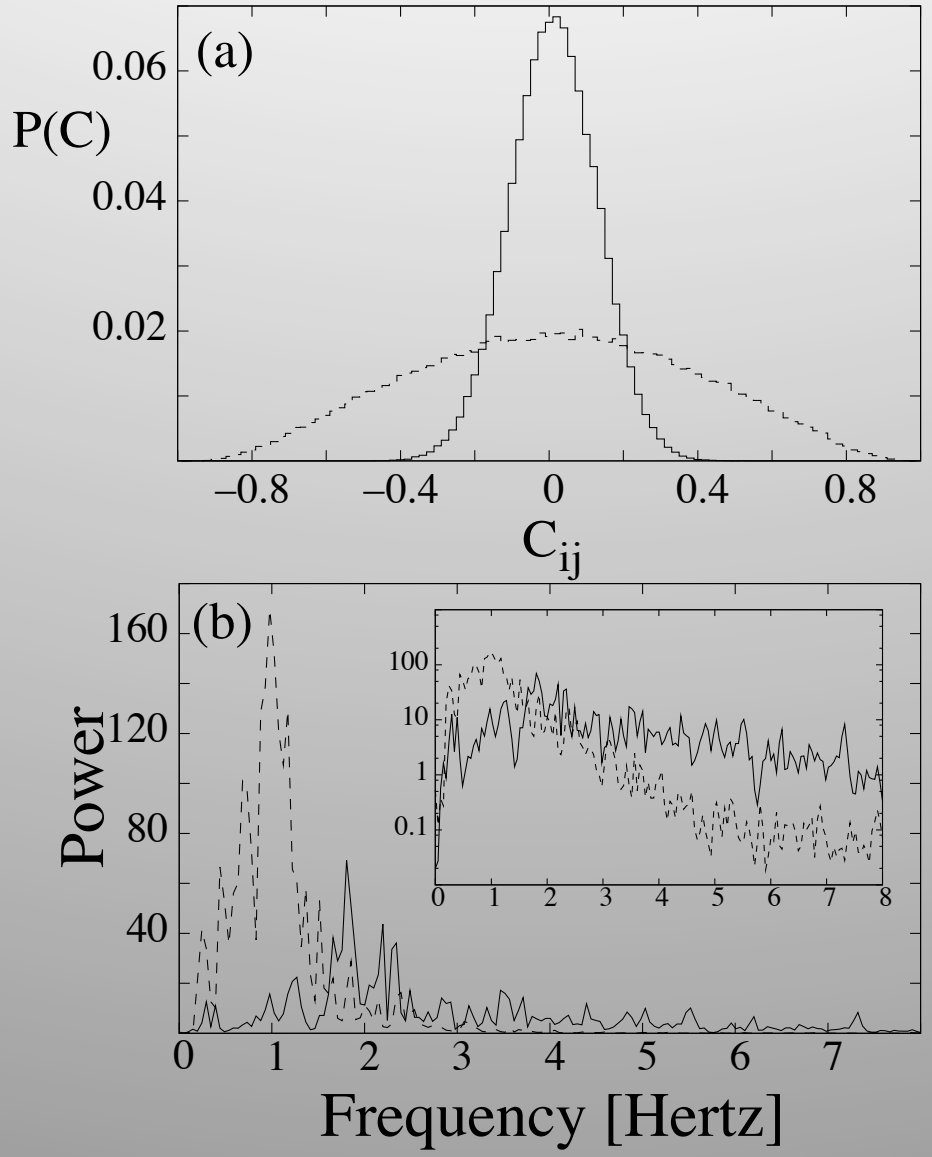
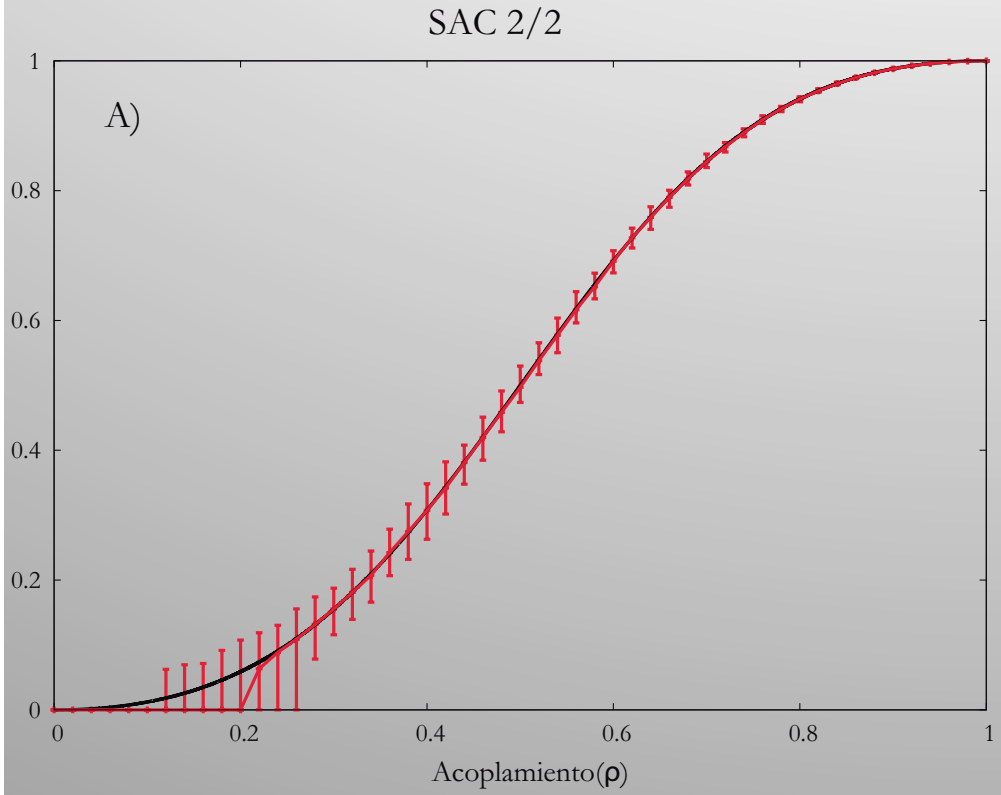
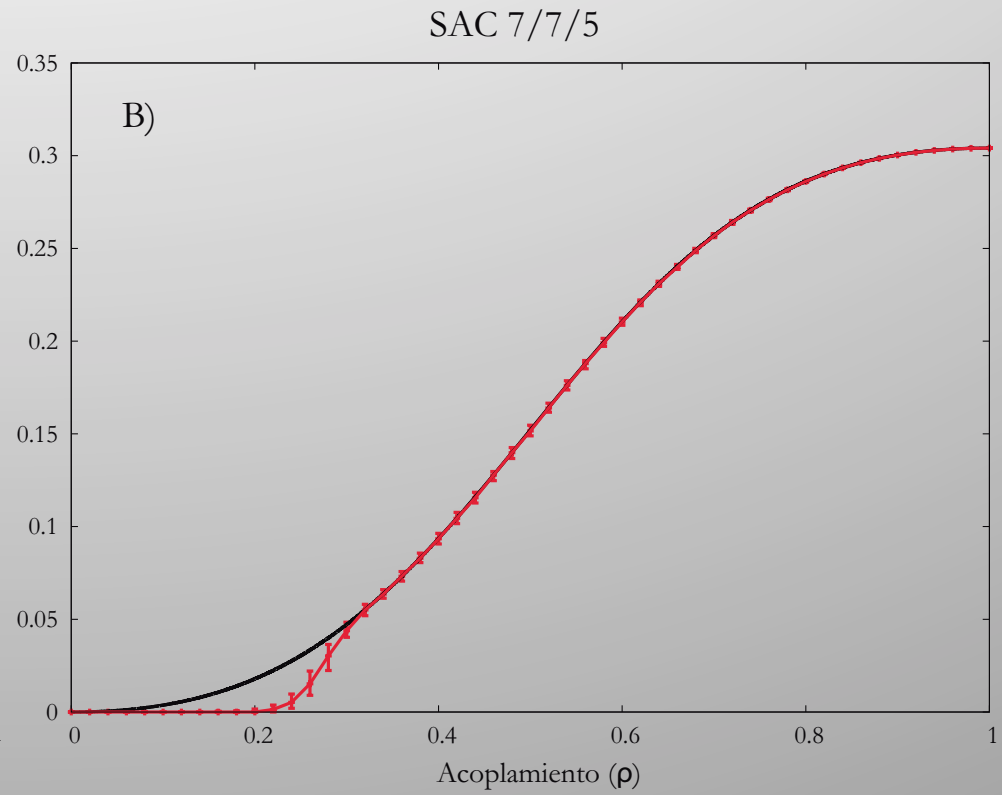
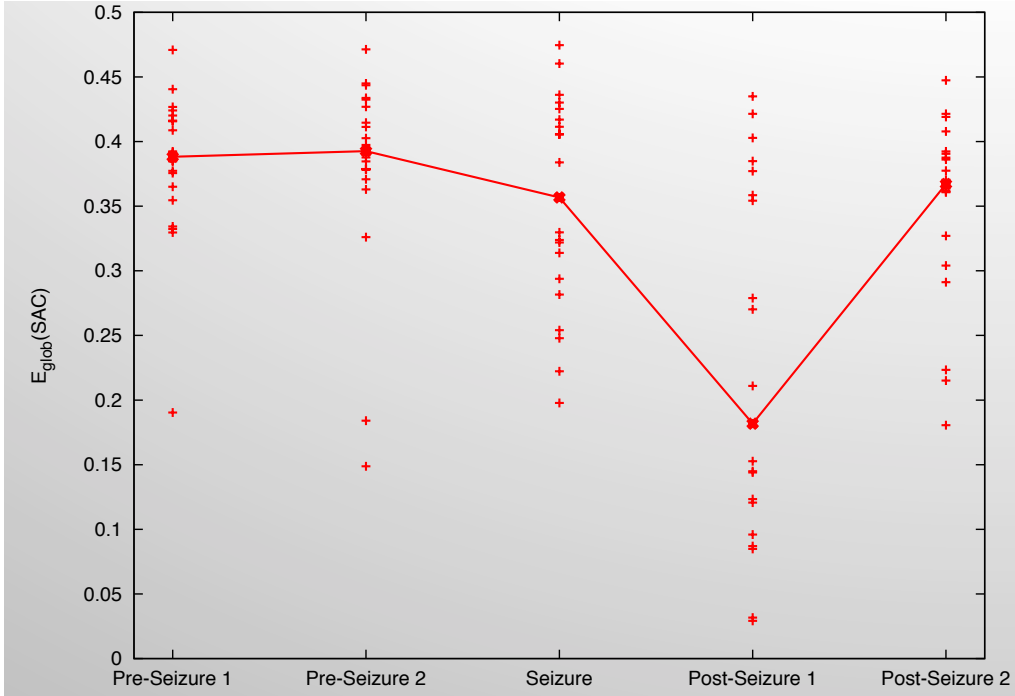


We proposed a practical solution for the problem of the so called "random Correlations"!

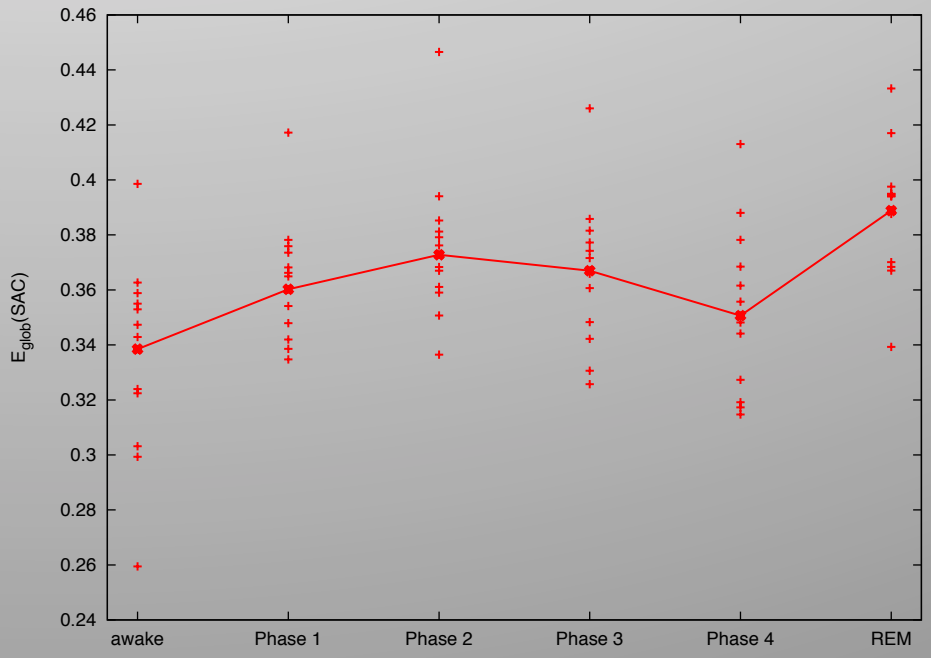




A.O. Marín García, et al. Neural Network, 2013



Global Efficiency



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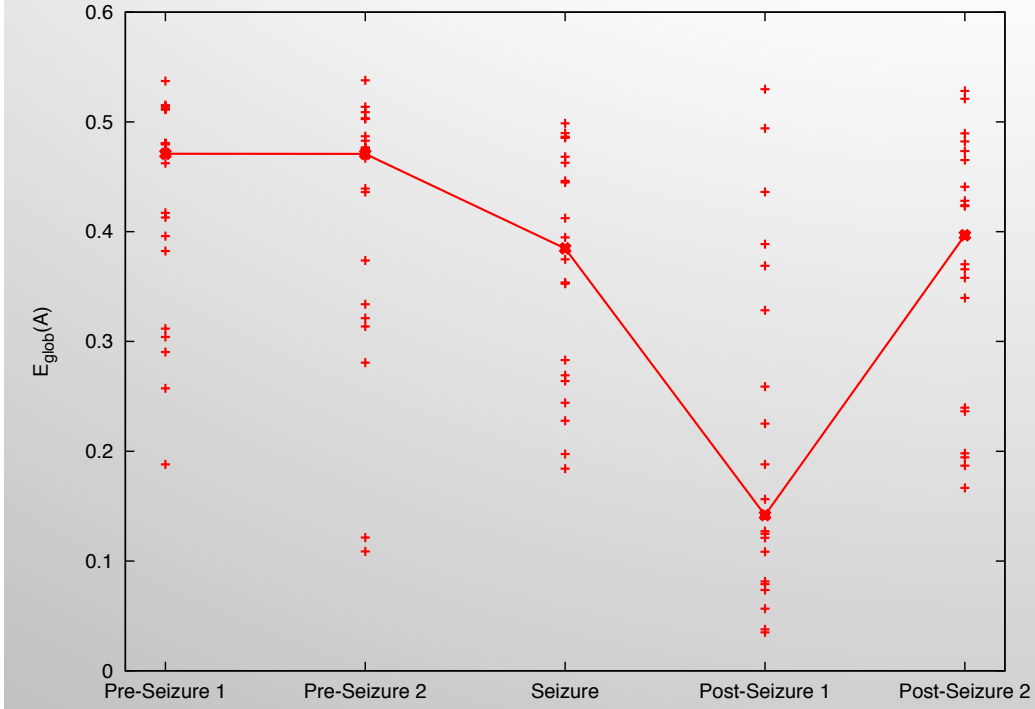
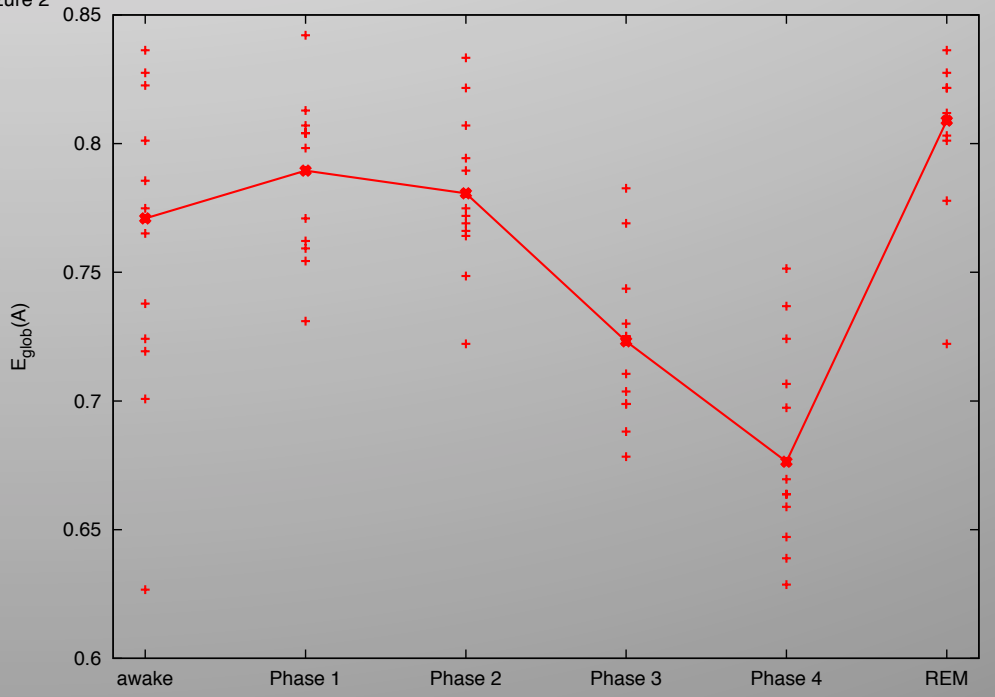


Global Efficiency estimated from the adjacency matrix (pure structure effects)



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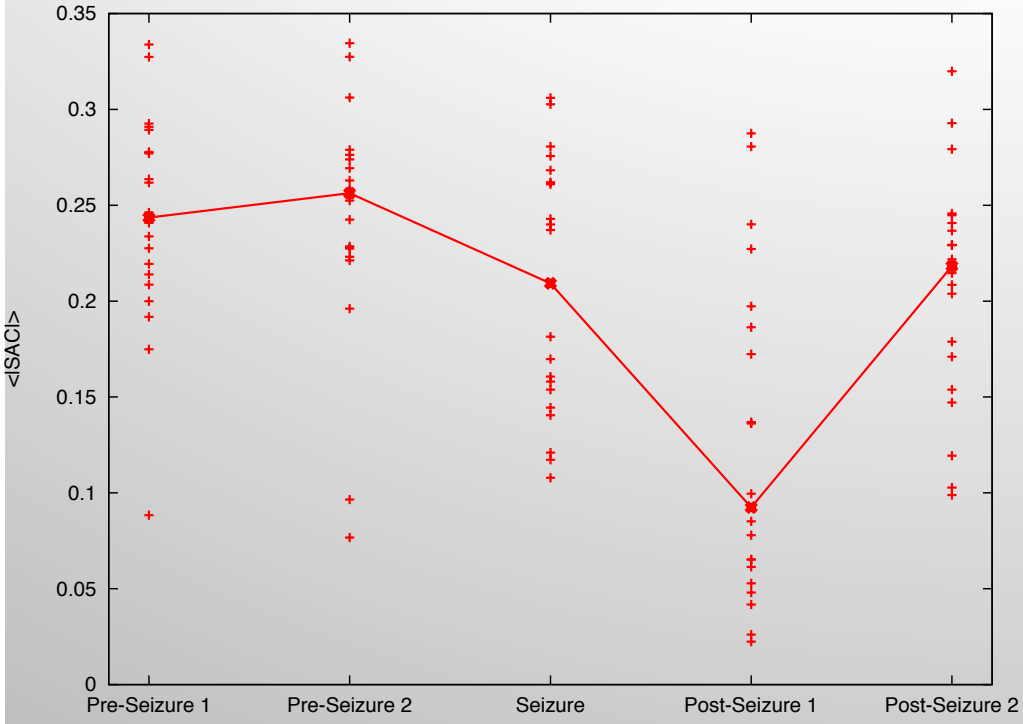
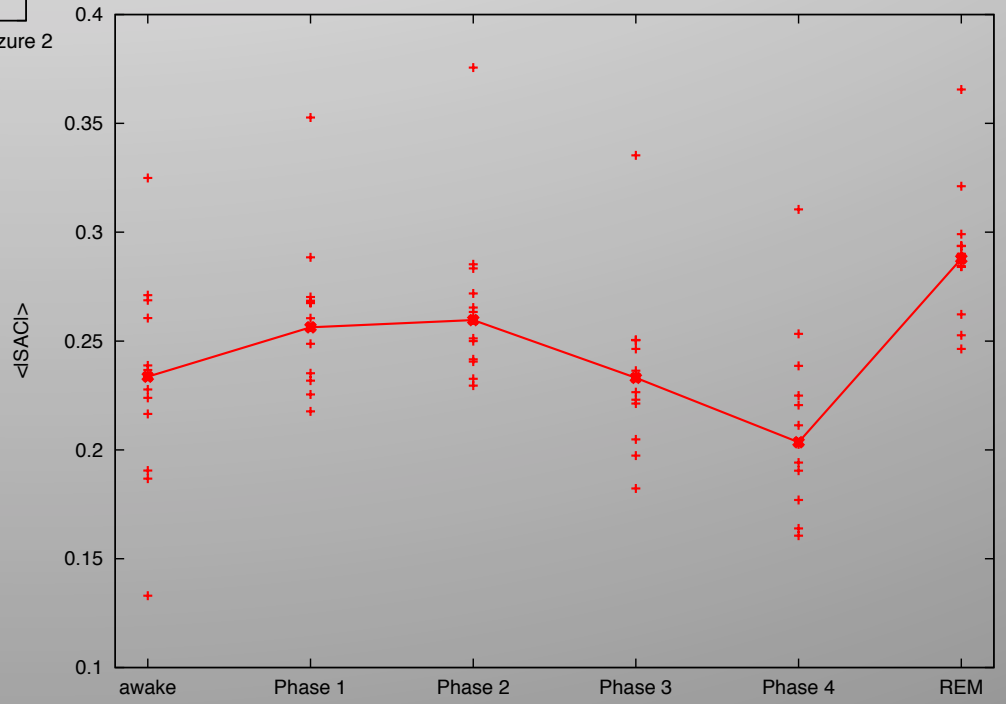
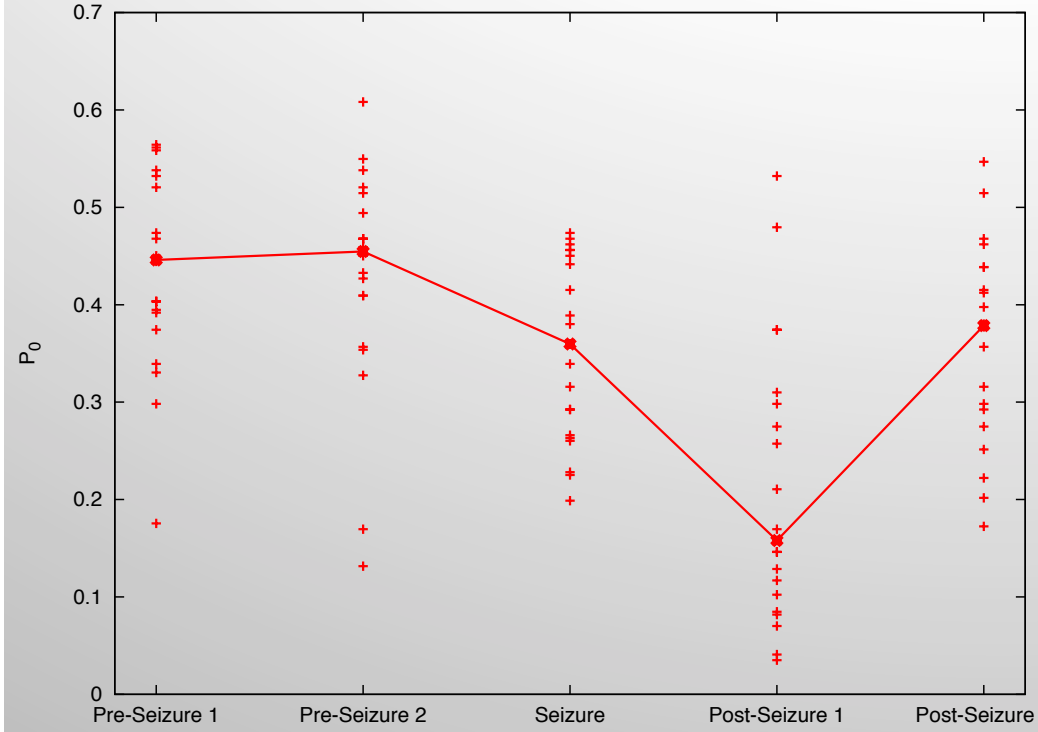
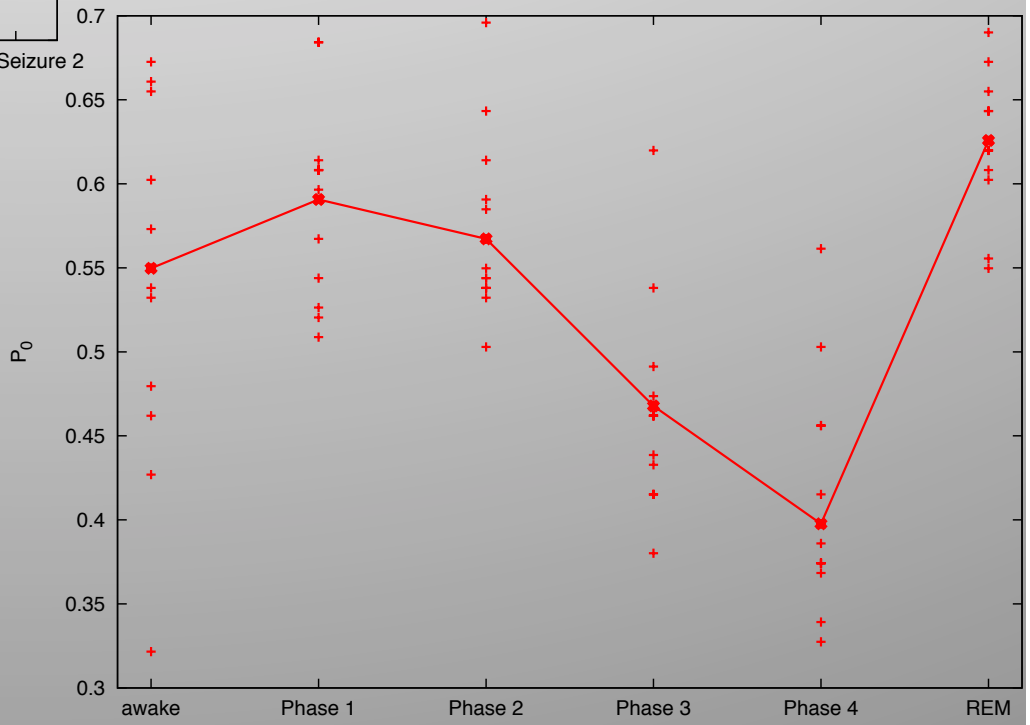
Average Correlation

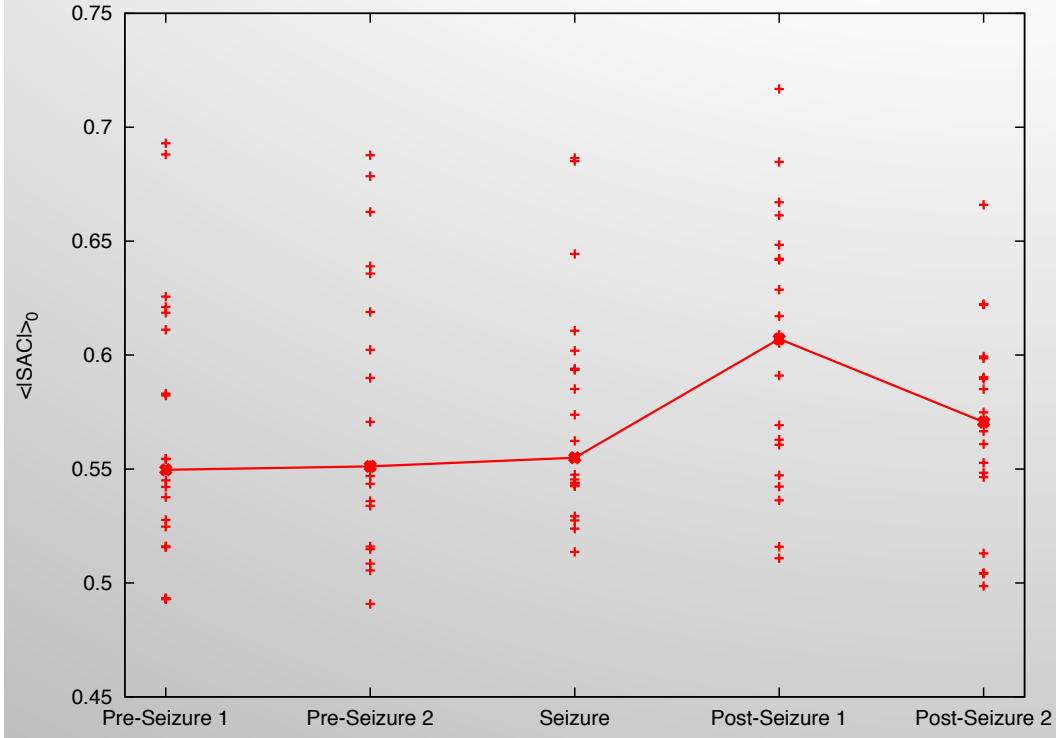




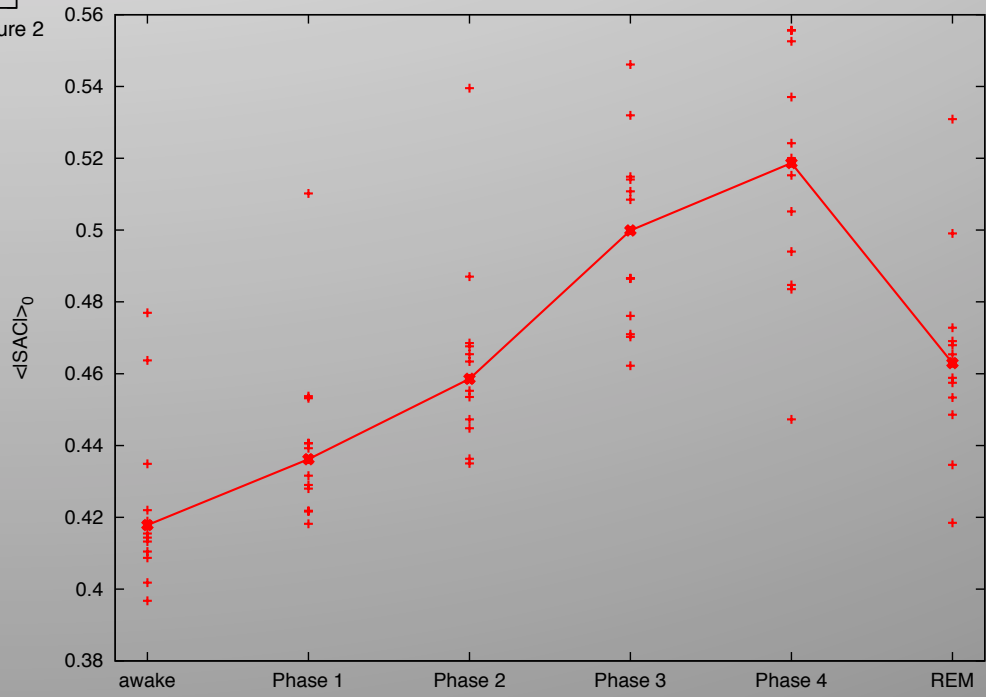
Density of the connectivity matrix







Average taken over nonzero matrix elements



- Similar changes of the brain rhythms occur during sleep cycles and the peri-ictal transition
- Large amplitude, irregular slow-wave activity was emphasized to possibly contribute to loss of consciousness
- A strong disconnection occurs during slow wave activity, which leads to a significant reduction of the global efficiency and the average correlation strength
- The surviving interrelations are strengthened/only the strongest survive
- It seems that the functional network measured upon the scalp segregates such that strong interrelations are established within the fragments.
- It has been shown that an early loss of consciousness was correlated with the degree of thalamo-cortical synchrony in patients with mesial temporal lobe seizures (Guye et al., 2006)
- These circuits are supposed to be responsible for large amplitude slow wave activity (Beenhakker and Huguenard, 2009)

Part 2: Stationary pattern and deviations from it

Problems:

(1) Noisy

(2) Influence of the EEG-reference

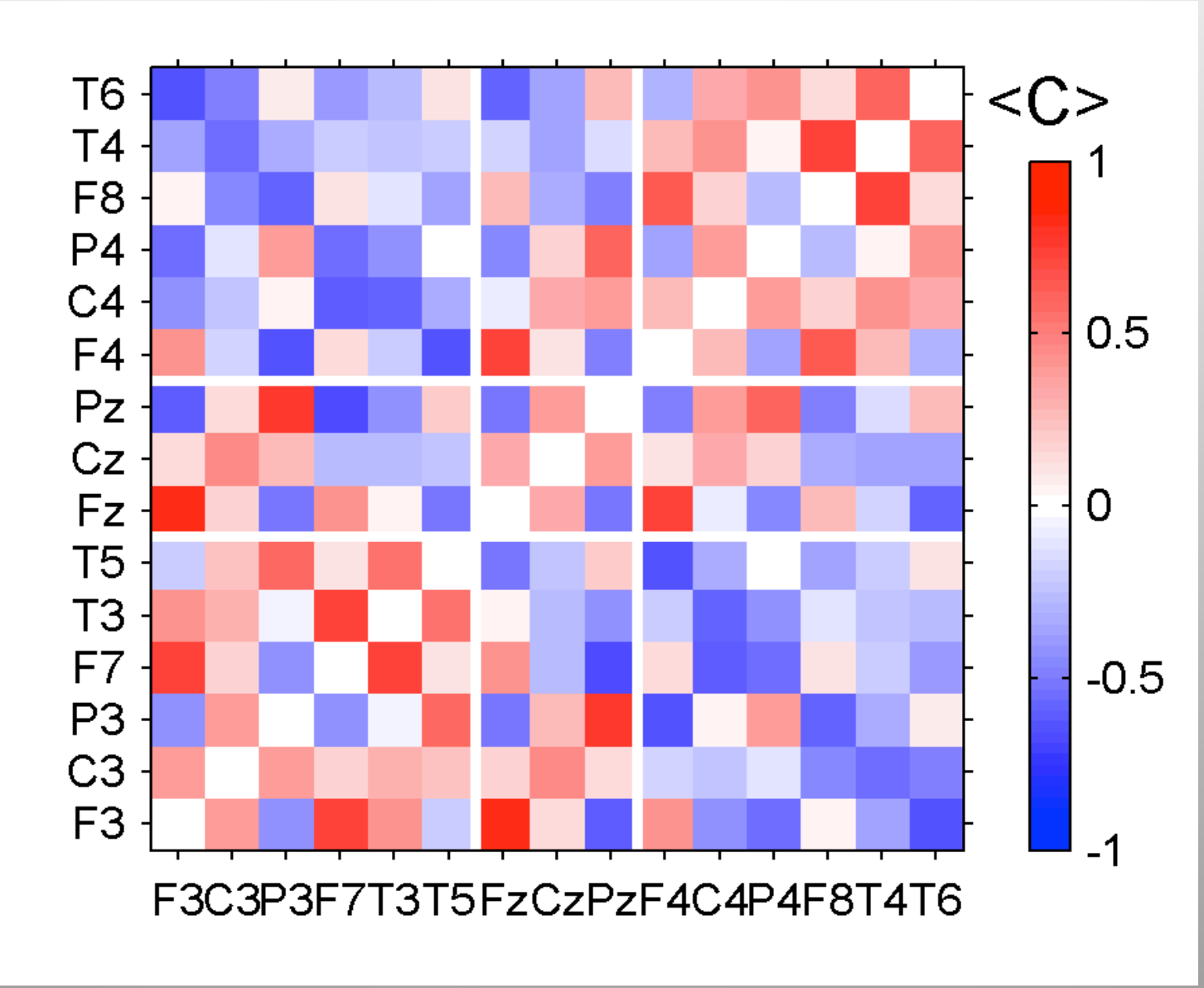
(3) Problem of volume conduction

(4) Highly non-stationary

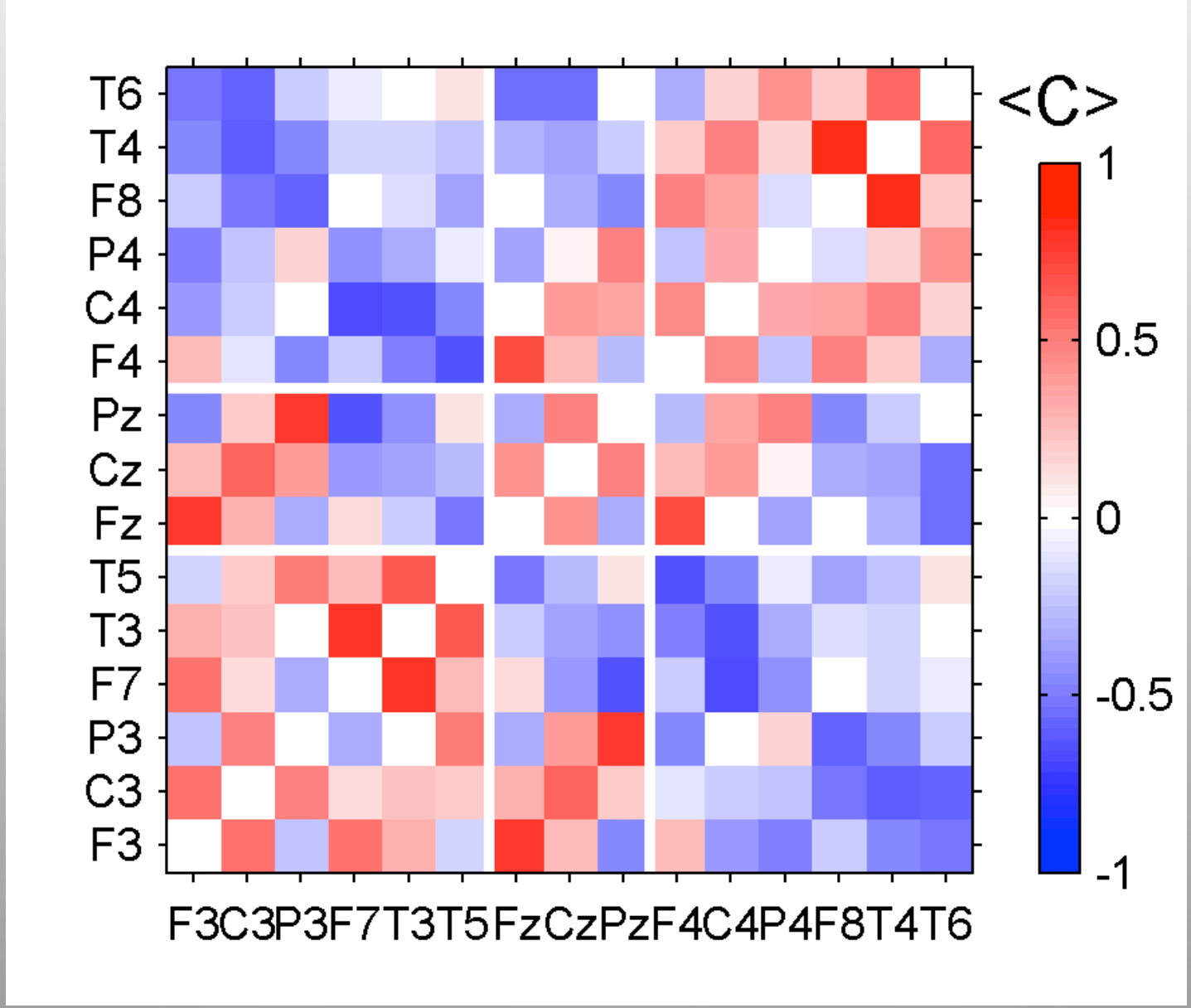
Correlations are not positive definite.

Makes it sense to calculate averages over large, non-stationary data segments?

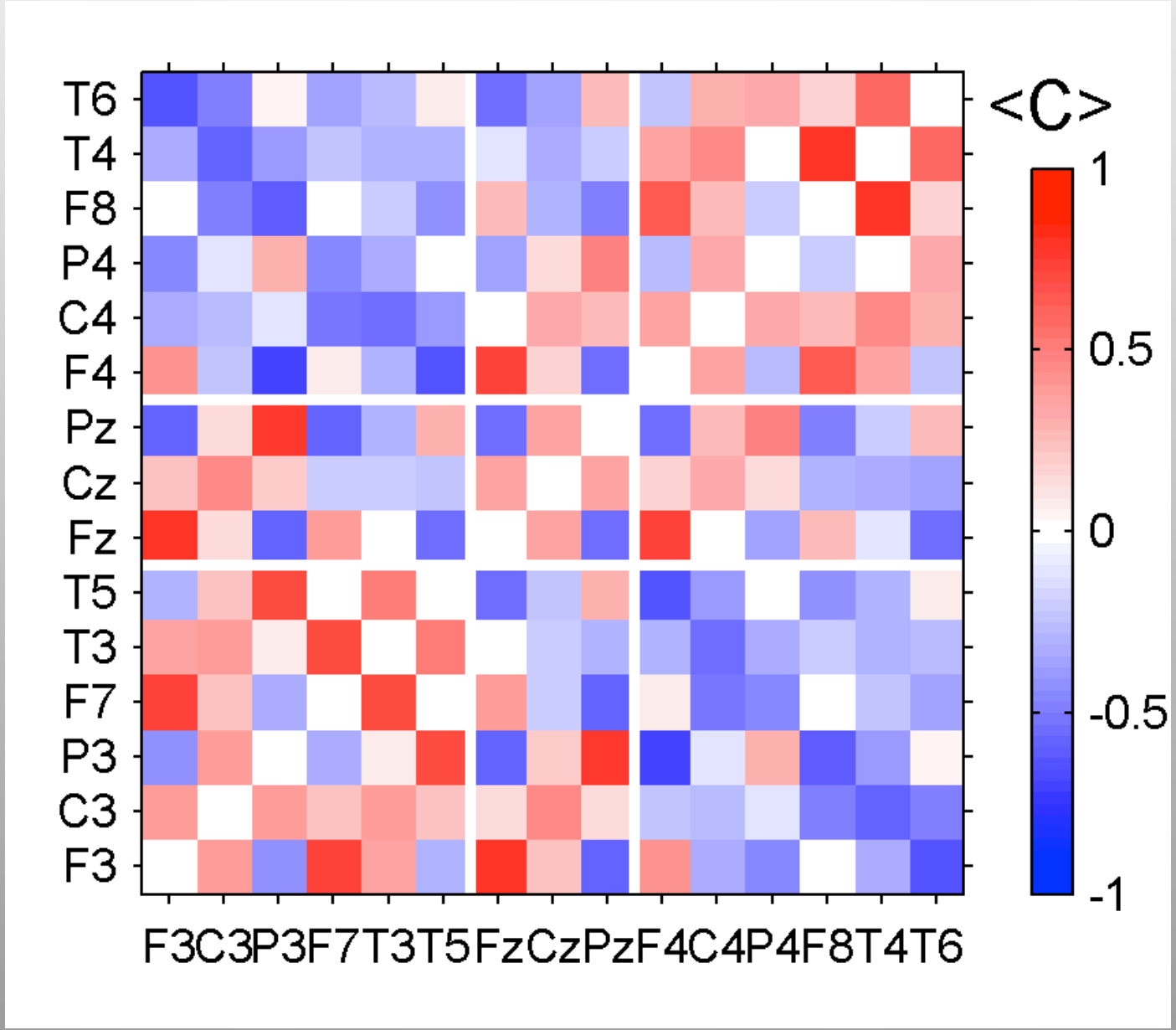
Average over a 2 minutes interval just before seizure onset

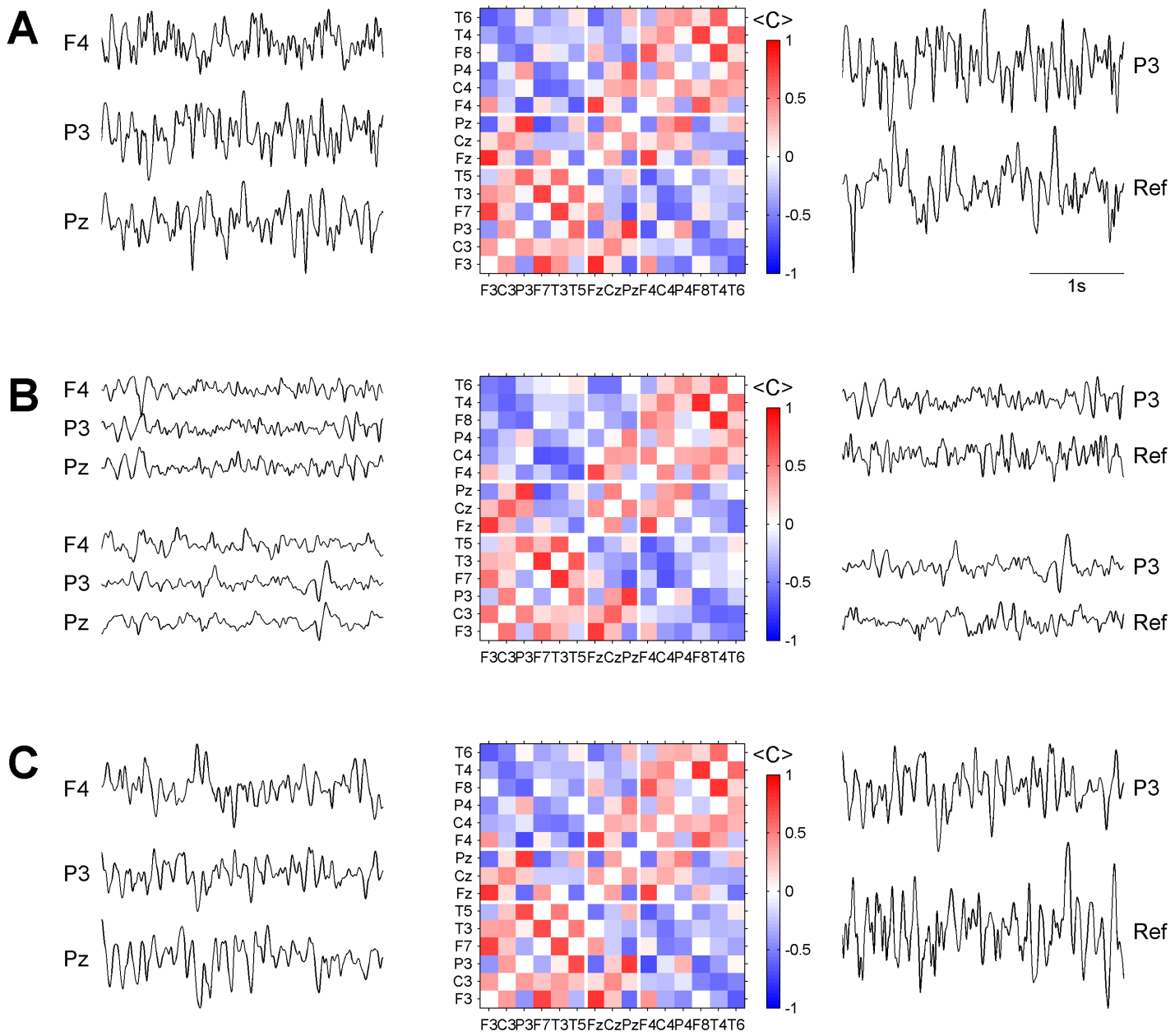


Average over the seizure interval



Average over a 2 minutes interval just at seizure offset




A
F4
P3
Pz
T6
T4
F8
P4
C4
F4
Pz
Cz
Fz
T5
T3
F7
P3
C3
F3
F3C3P3F7T3T5FzCzPzF4C4P4F8T4T6
<C>
1
0.5
0
-0.5
-1
P3
Ref
1s
B
F4
P3
Pz
F4
P3
Pz
T6
T4
F8
P4
C4
F4
Pz
Cz
Fz
T5
T3
F7
P3
C3
F3
F3C3P3F7T3T5FzCzPzF4C4P4F8T4T6
<C>
1
0.5
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-0.5
-1
P3
Ref
P3
Ref
C
F4
P3
Pz
T6
T4
F8
P4
C4
F4
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Cz
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T5
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F3
F3C3P3F7T3T5FzCzPzF4C4P4F8T4T6
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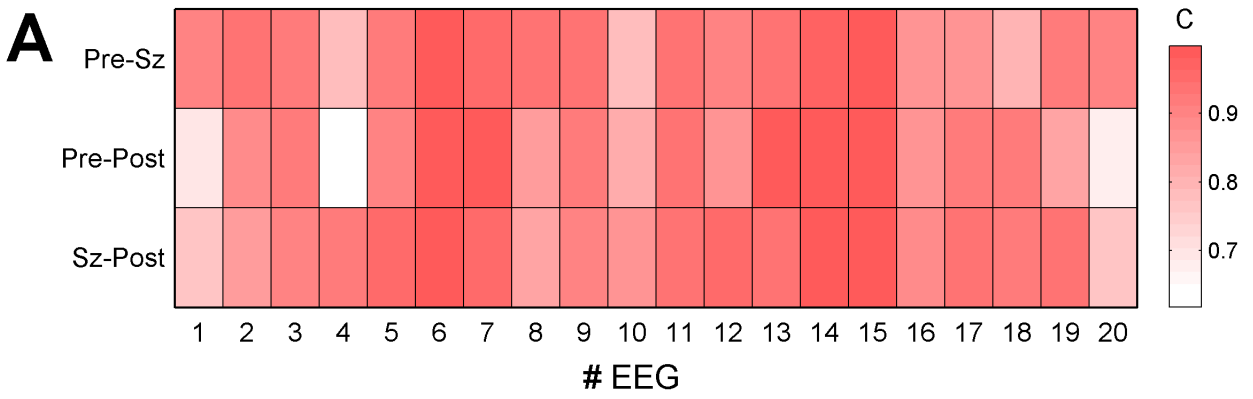
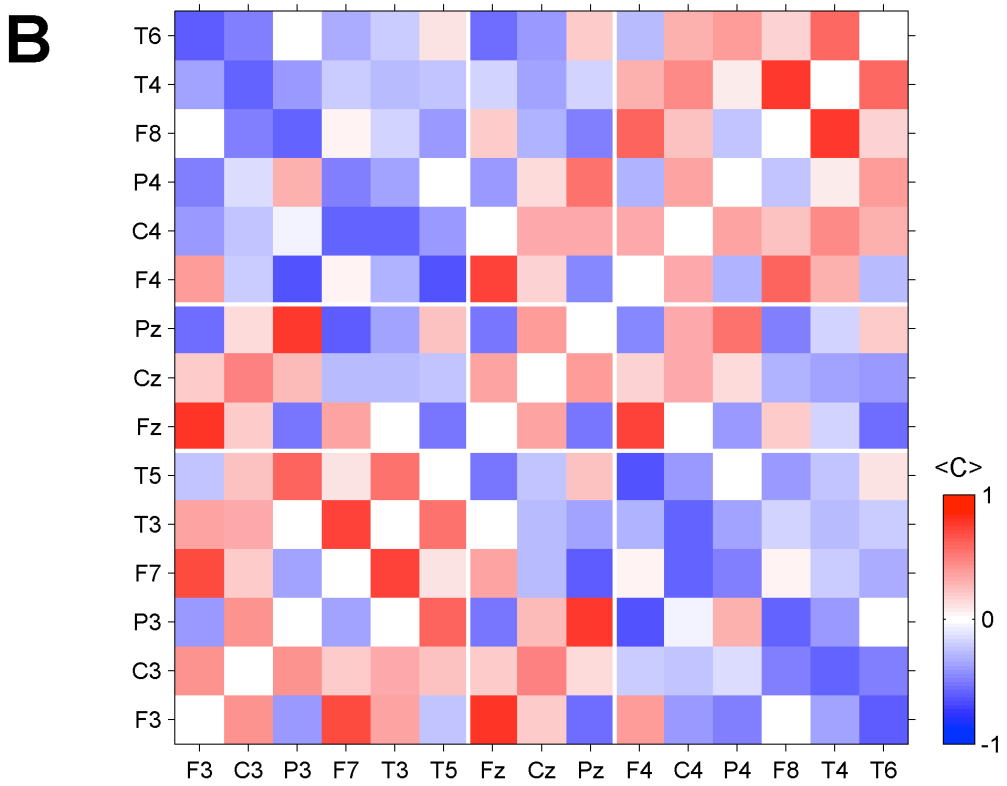
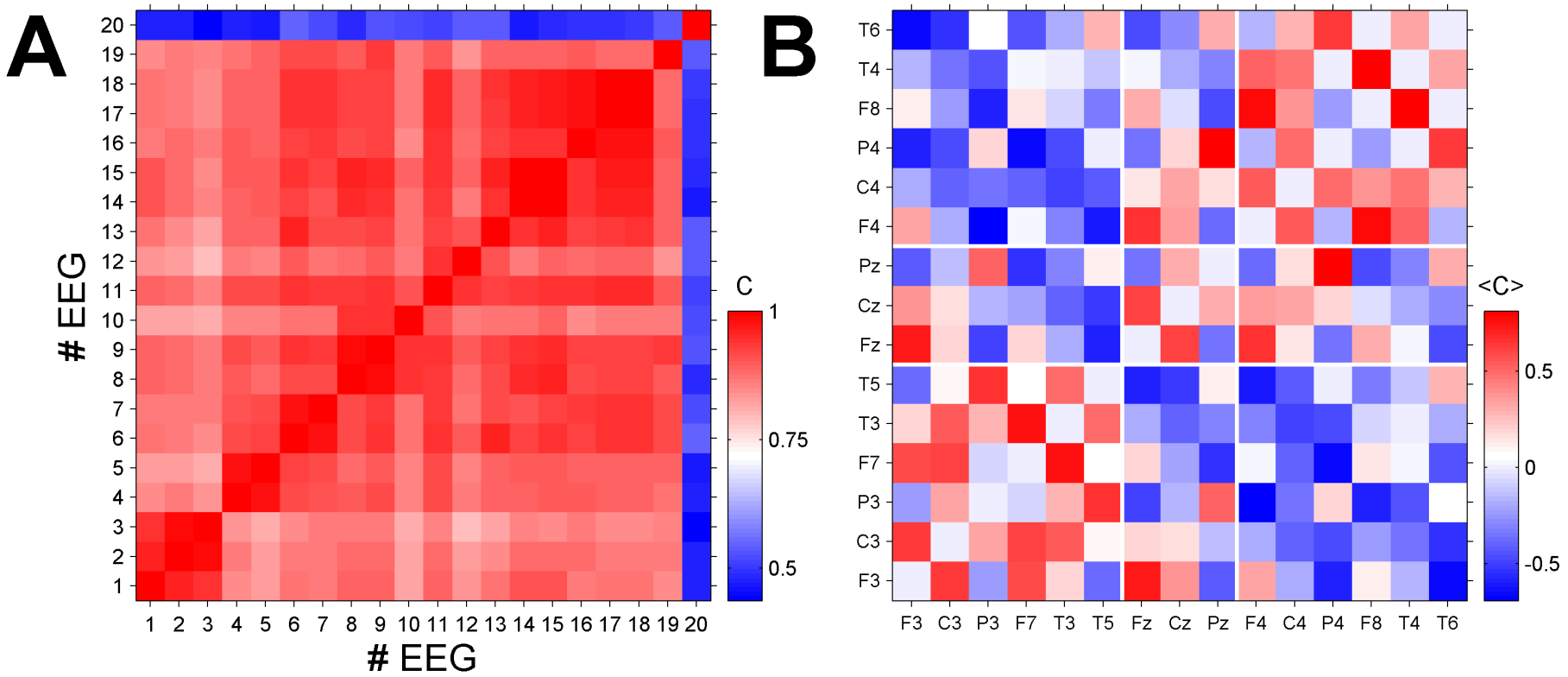

A
Pre-Sz
Pre-Post
Sz-Post
C
0.9
0.8
0.7
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
EEG

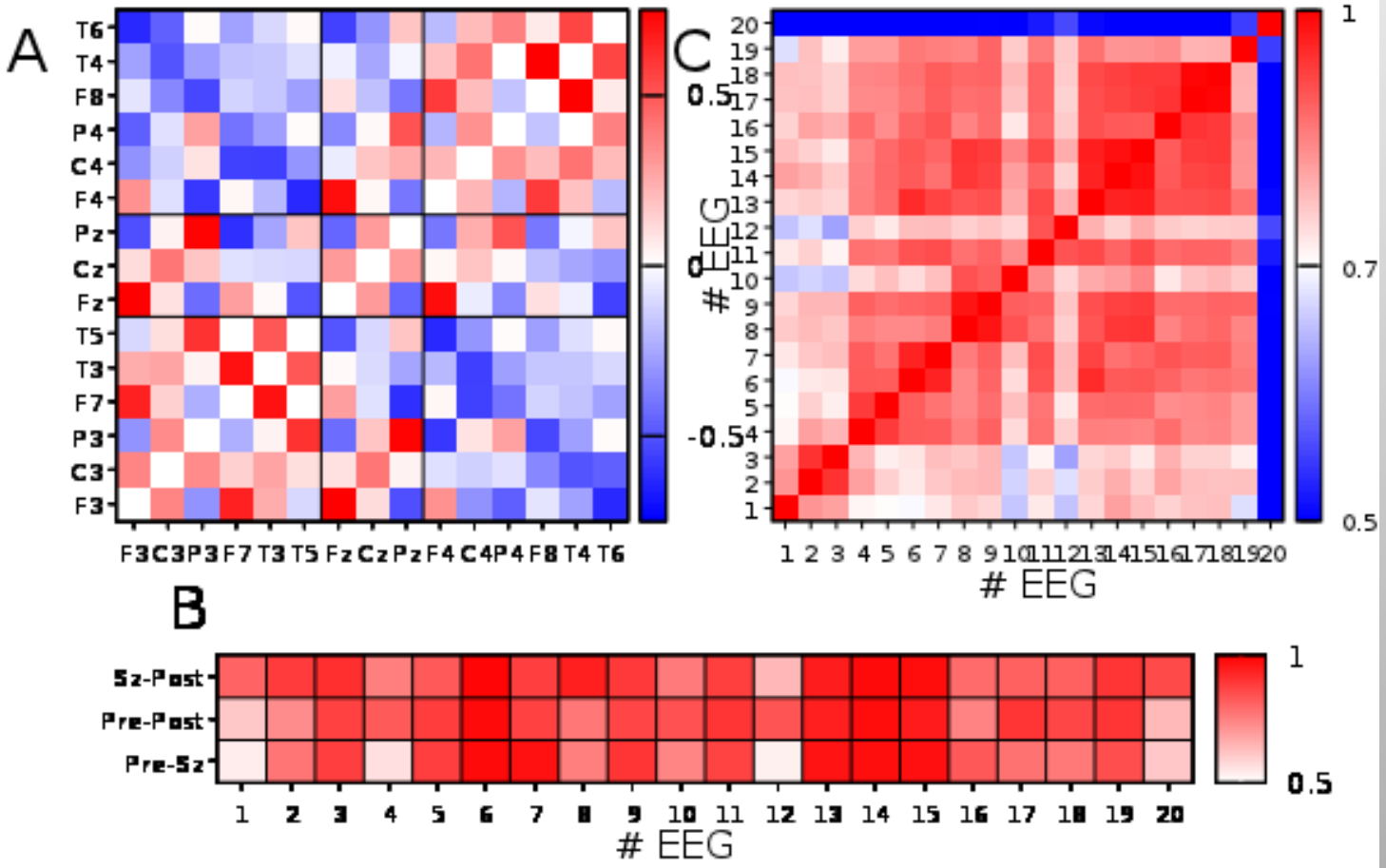

B
T6
T4
F8
P4
C4
F4
Pz
Cz
Fz
T5
T3
F7
P3
C3
F3
F3 C3 P3 F7 T3 T5 Fz Cz Pz F4 C4 P4 F8 T4 T6
<C>
1
0
-1

Comparison of the peri-ictal averages of the 20 EEG recordings

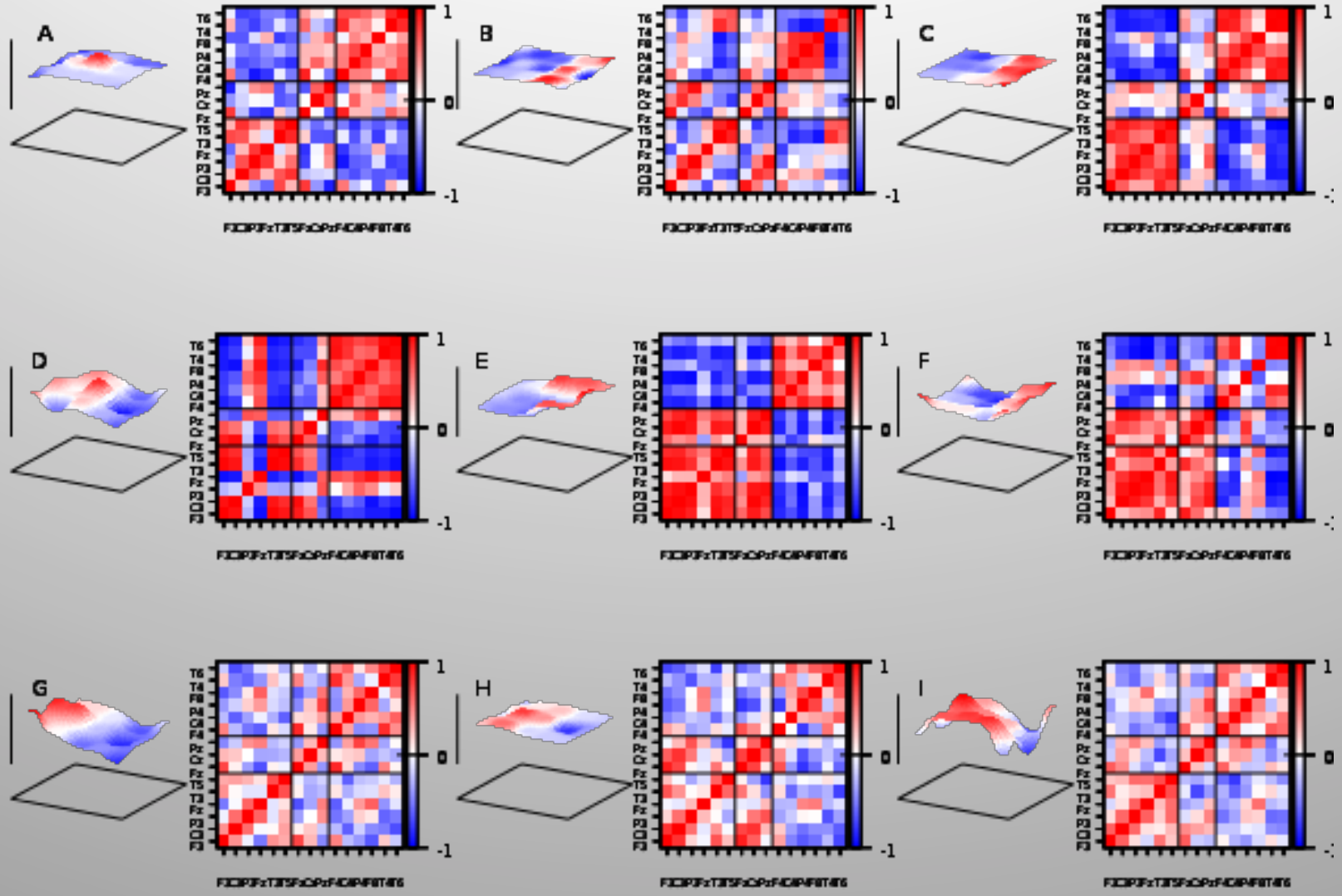


Is that simply a trivial volume conduction effect?

We checked for that by estimating maximum lag correlations, excluding those matrix elements where maximum correlations are found for zero lag.



We also calculated weighted phase lag indexes and got similar results



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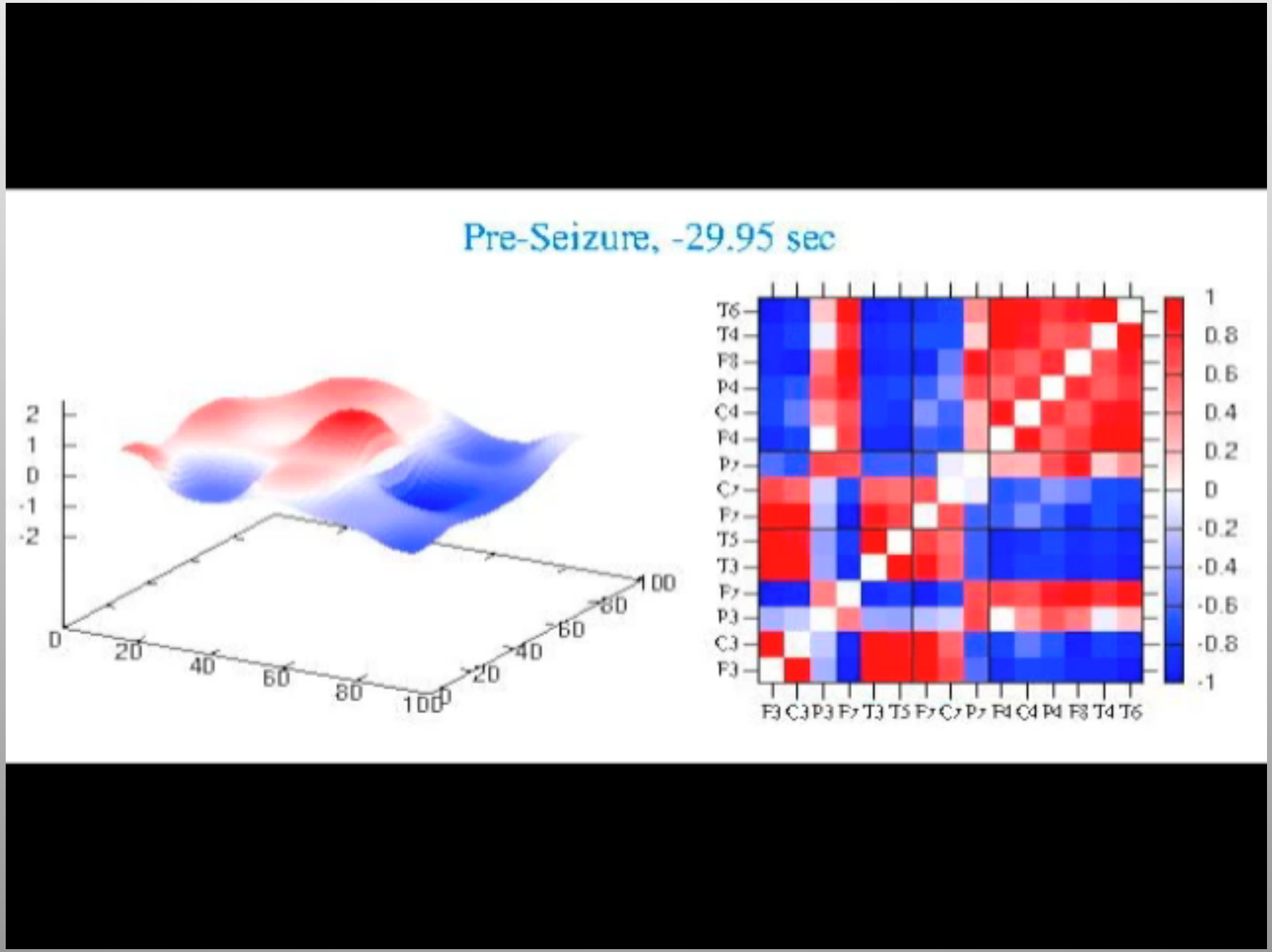
Pre-Seizure, -29.95 sec
2
1
0
-1
-2
0
20
40
60
80
100
0
20
40
60
80
100
T6
T4
F8
P4
C4
F4
Pz
Cz
Fz
T5
T3
Fp
P3
C3
F3
F3 C3 P3 Fz T3 T5 Fp Cz Pz F4 C4 P4 F8 T4 T6
1
0.8
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
-1

Is this pronounced stationary correlation pattern a manifestation of the pathology?

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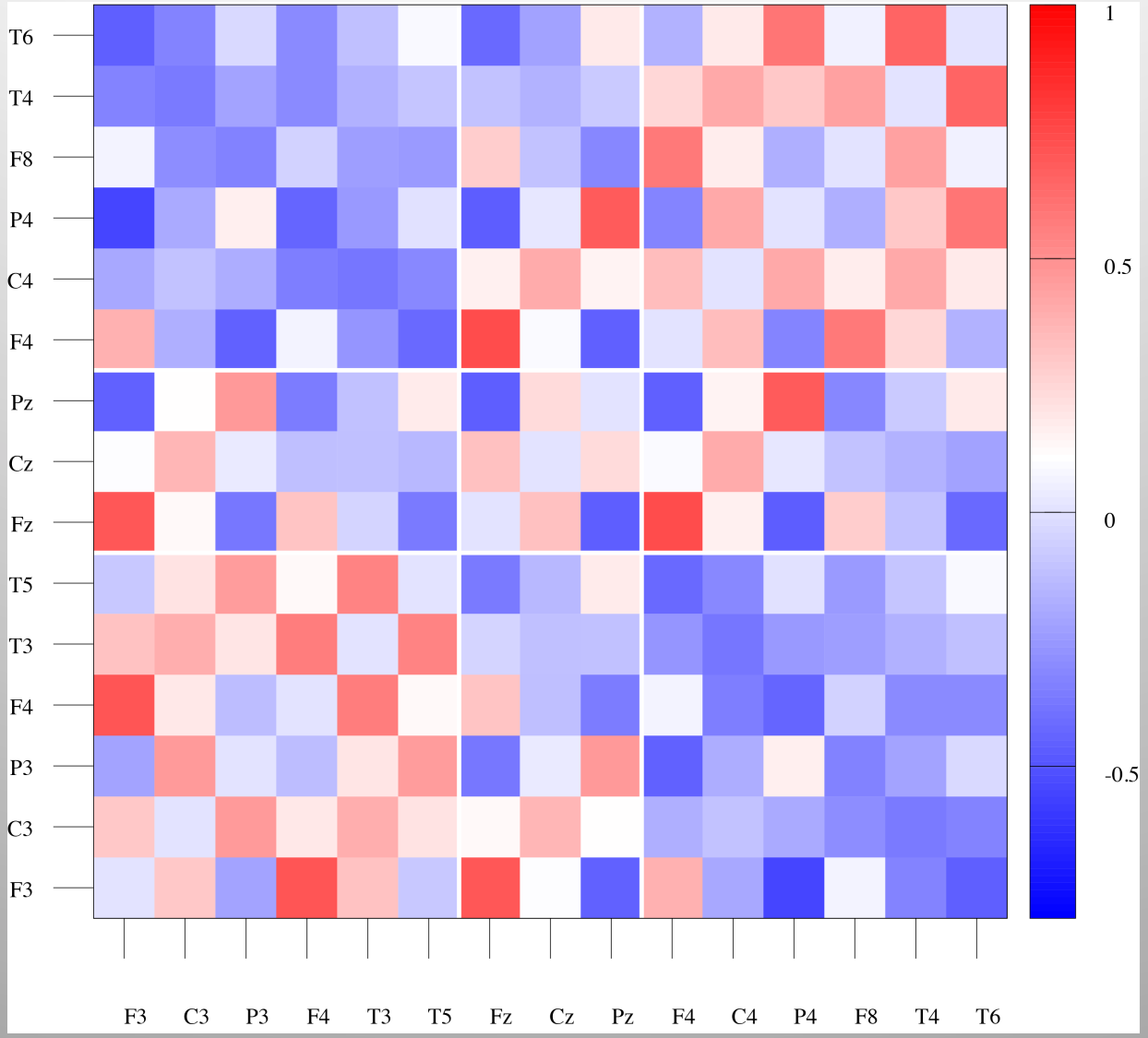
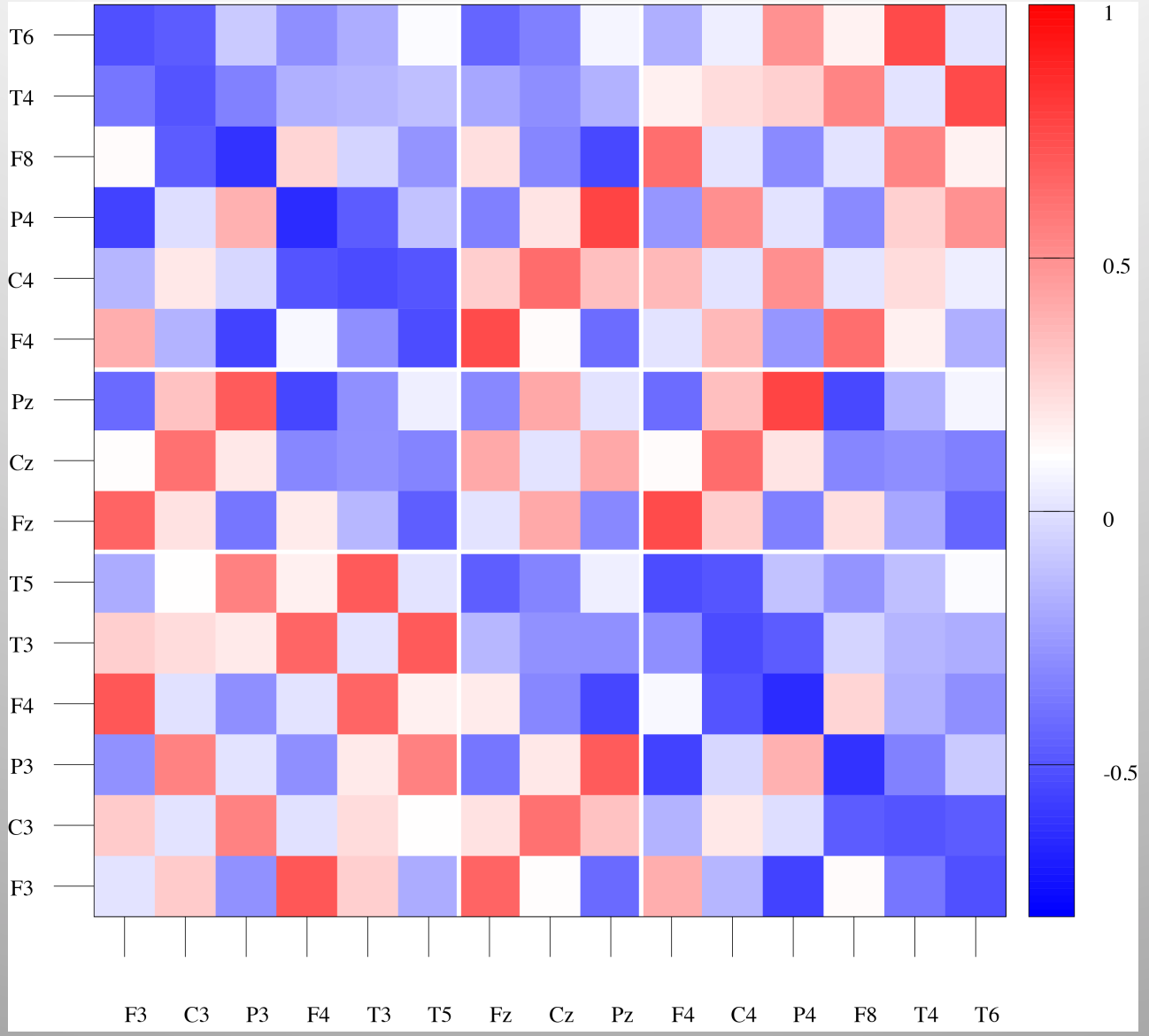
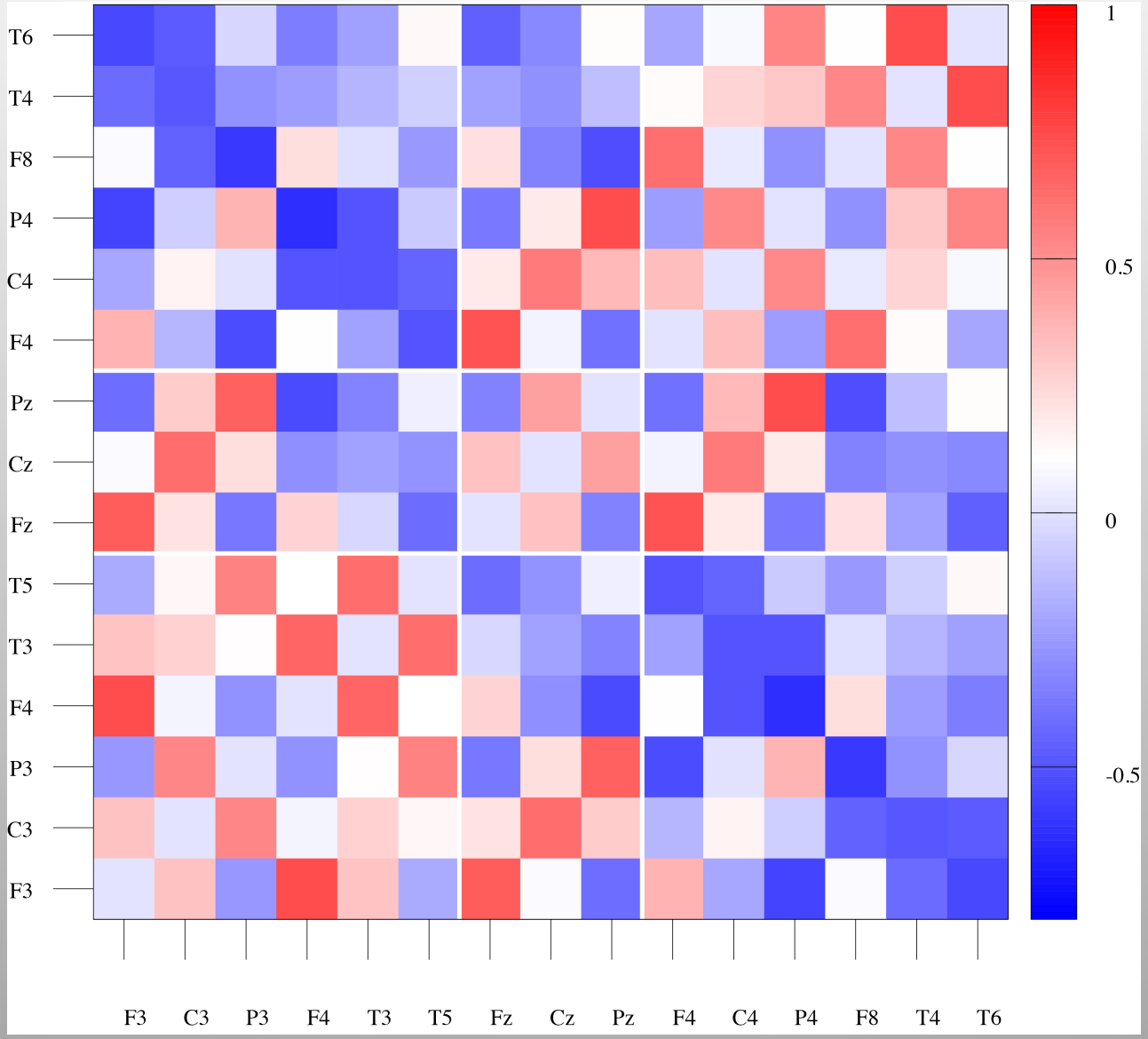
Lets turn to the sleep data of healthy subjects



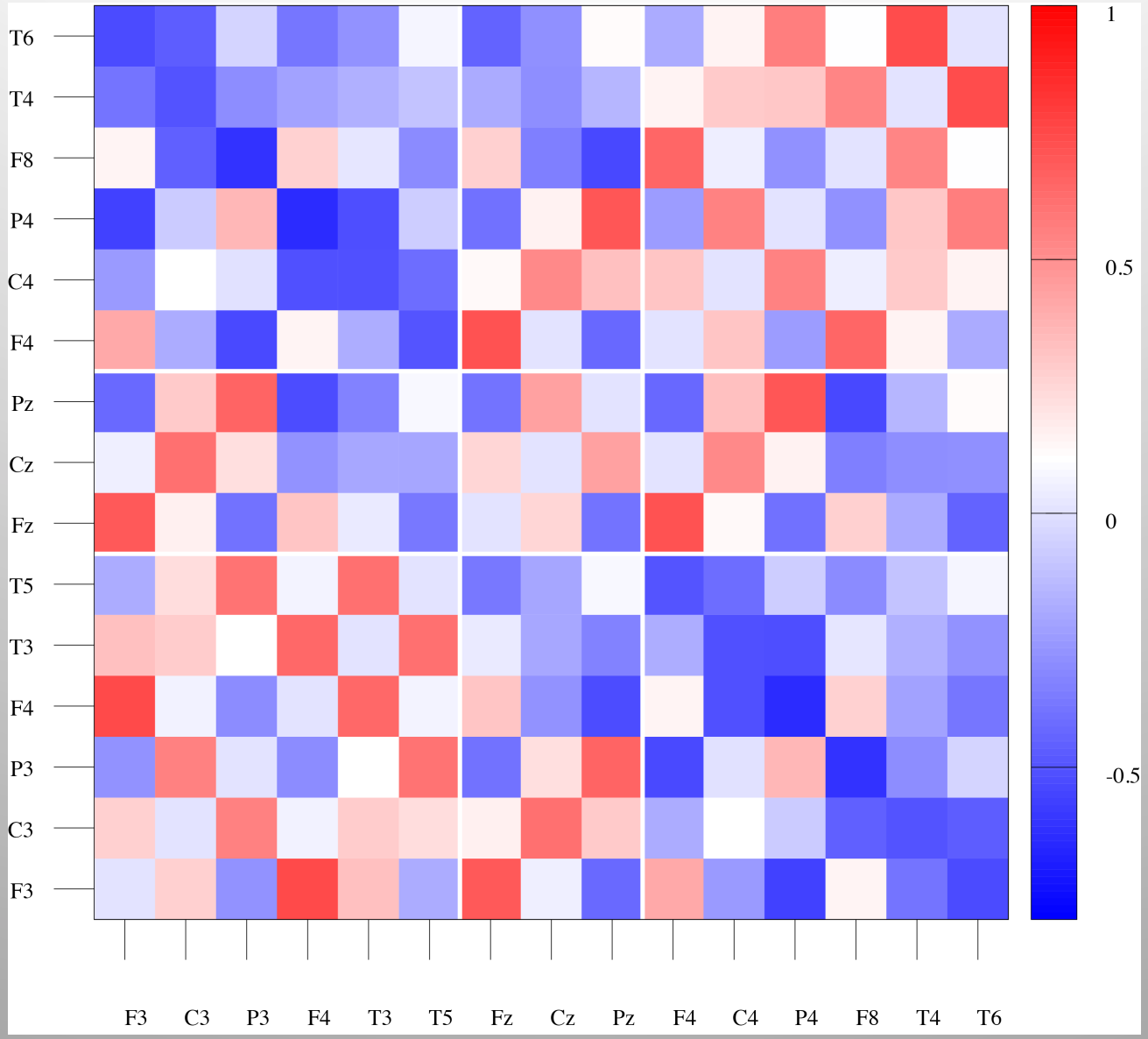
Subject 1, Awake



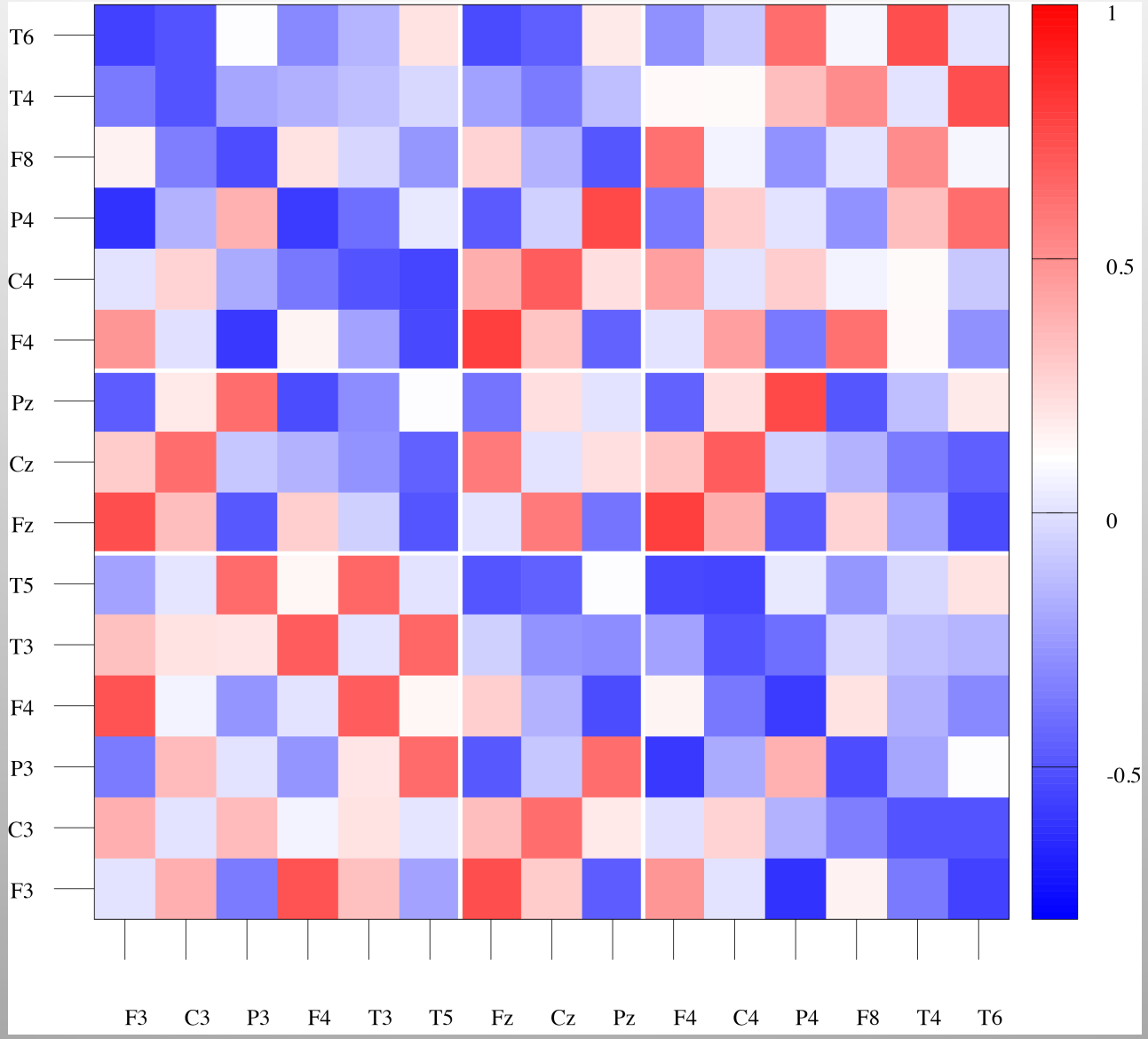
Subject 1, Stage 2



Subject 1, Stage 3

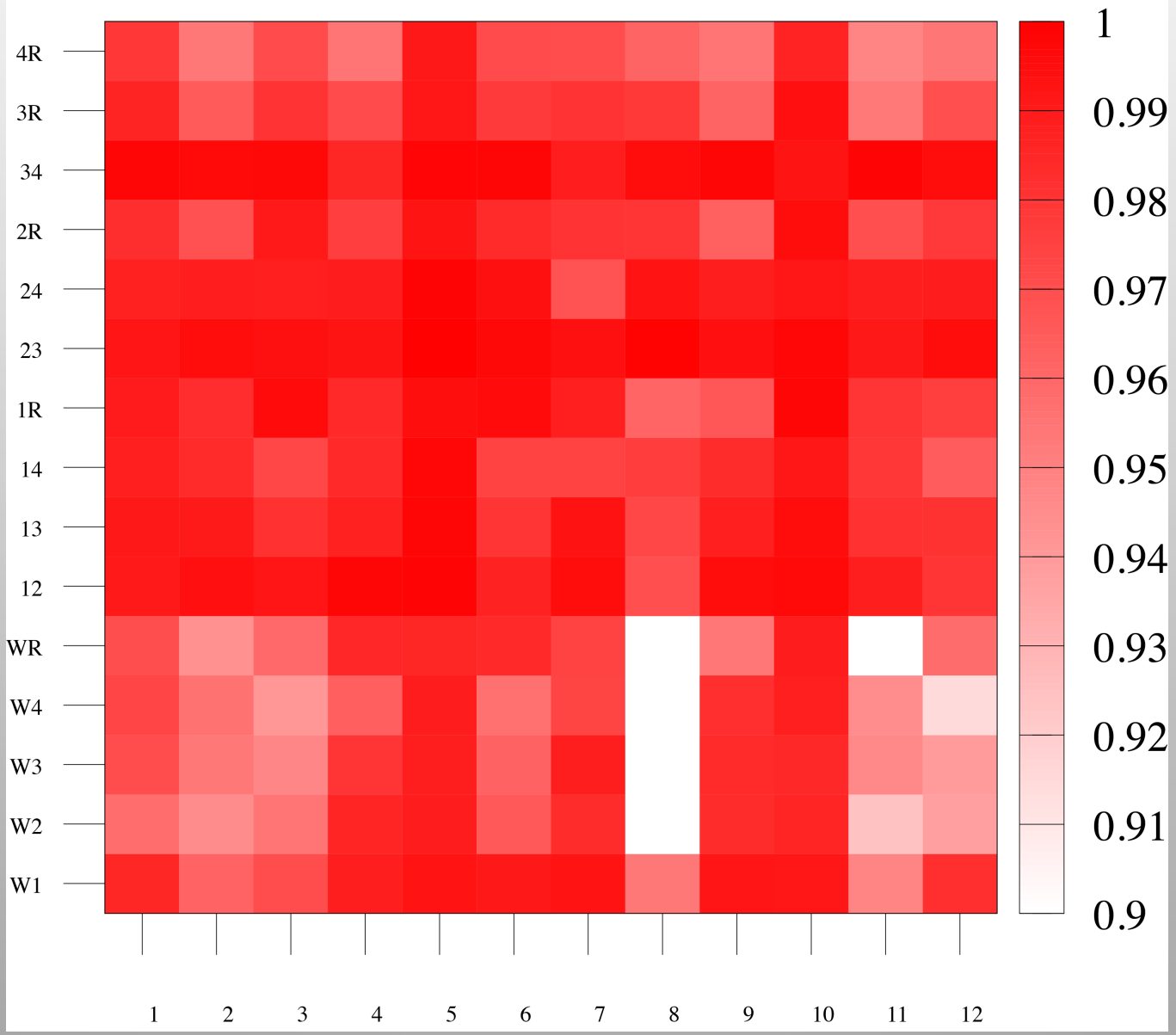


Subject 1, Stage 4

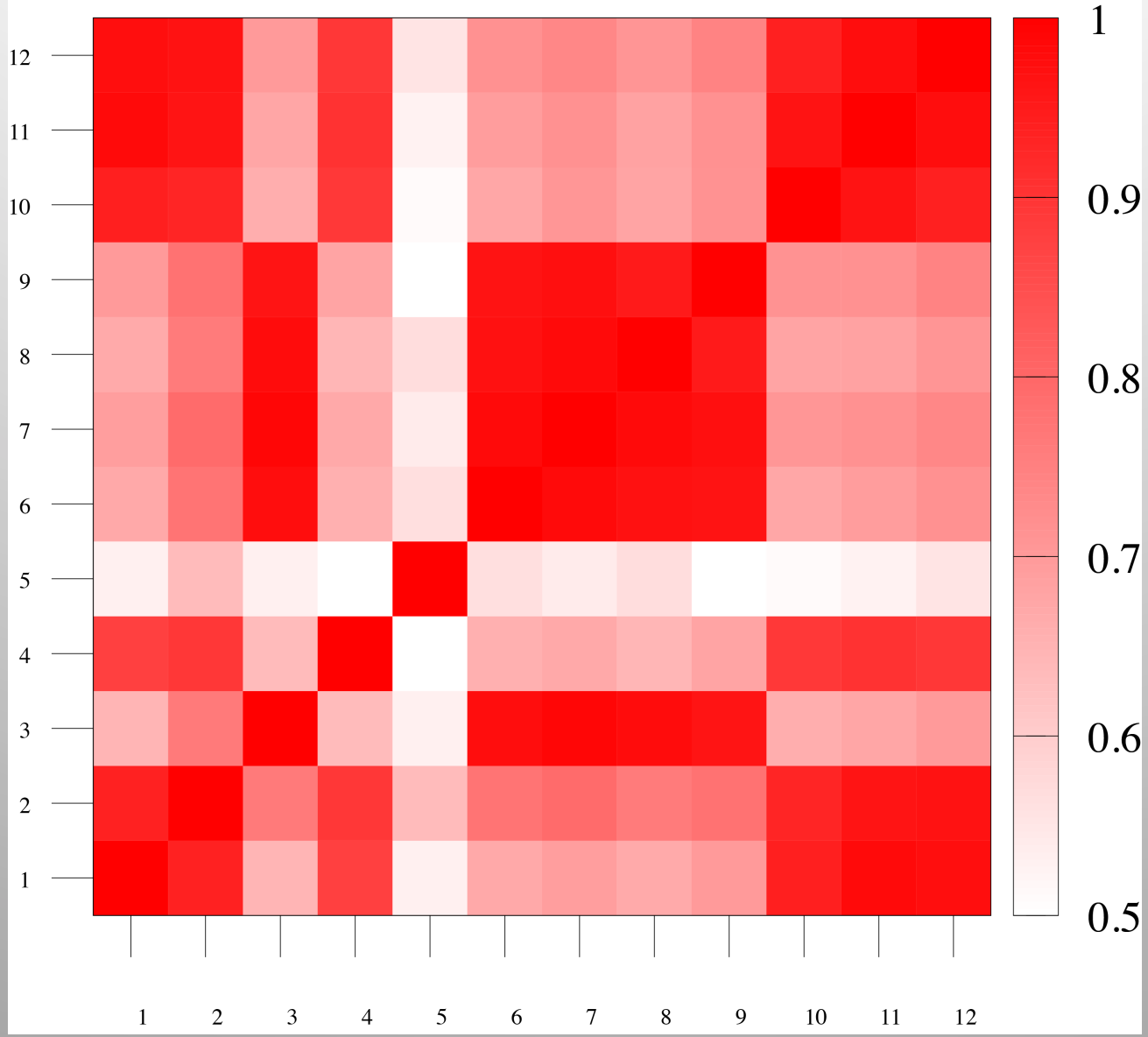


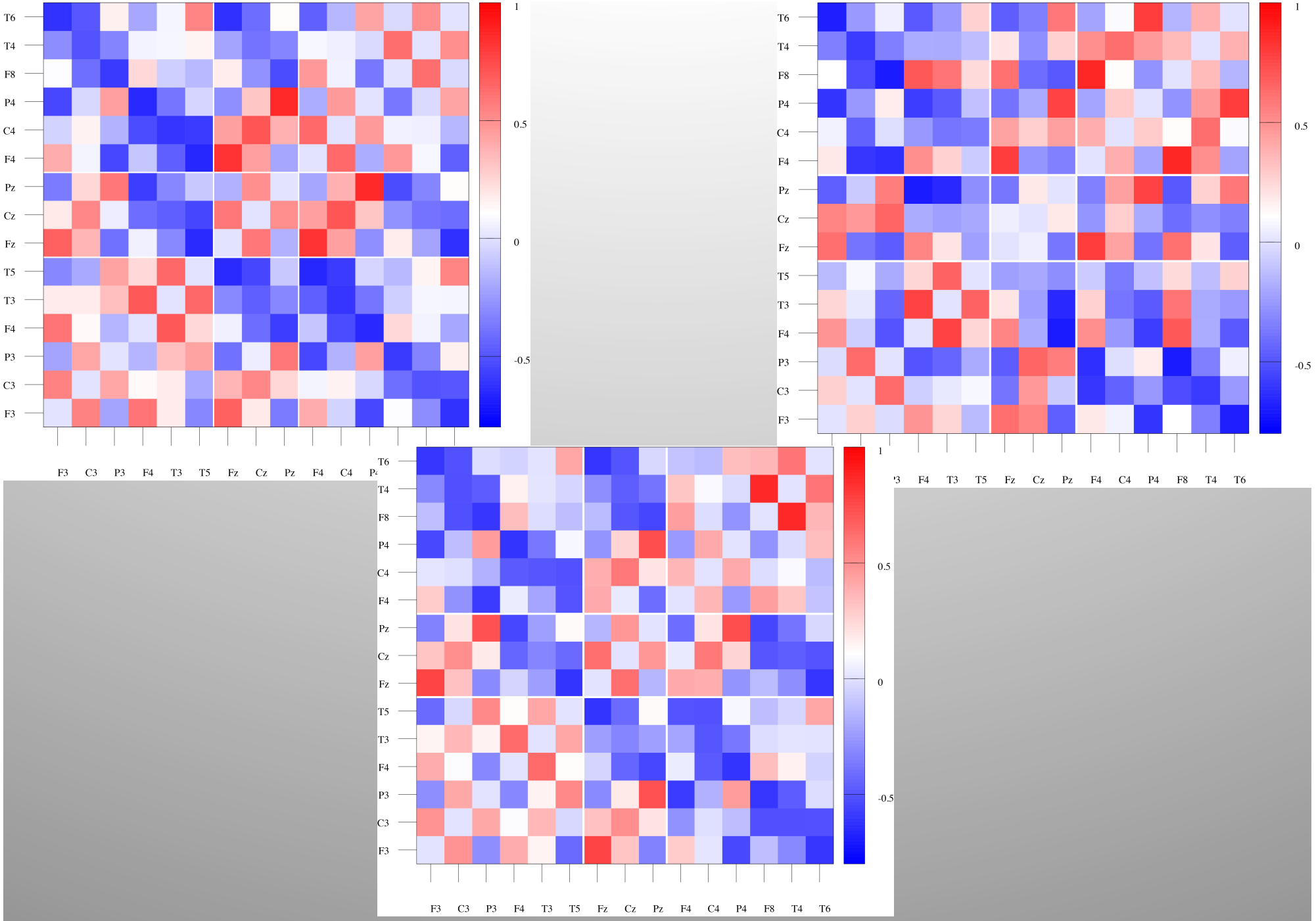
Subject 1, REM

Banda de Frecuencia U



Banda de Frecuencia U





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According to our findings it seems that the “attractor” of electrical brain activity is a kind of limit cycle (and not a fix-point of zero activity).

The temporal evolution of the brain activity manifests itself via transient deformations of this kind of dynamical “ground state”.

Such a standing wave phenomenon may provide an efficient and fast coordination of local functional networks, viz. the integration of local information processing may occur via a globally correlated state

Effective and fast triggering of different, maybe distant local circuits can be moderated by such a globally collective state.

The interplay between functional segregation and information integration may occur in this picture via bottom up or top down processes.

Deformations of the oscillation pattern might be generated locally, when a perturbation restricted to a certain brain region might propagate over the whole scalp (bottom up).

It is also conceivable that multiple local distortions get suppressed by globally collective oscillations (top down).

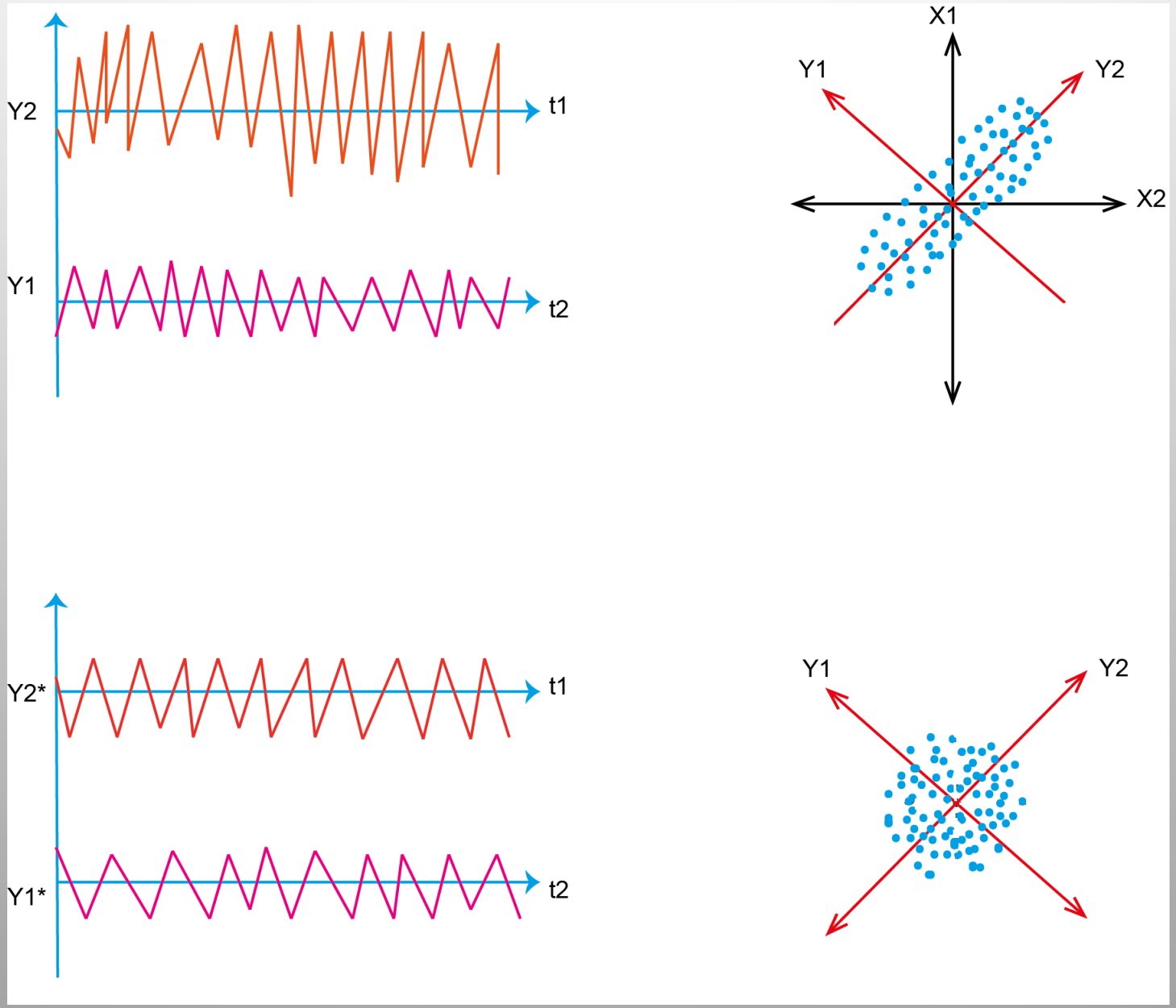
Dynamics = departures from the “dynamical ground state”, viz. deviations from the stationary correlation pattern.

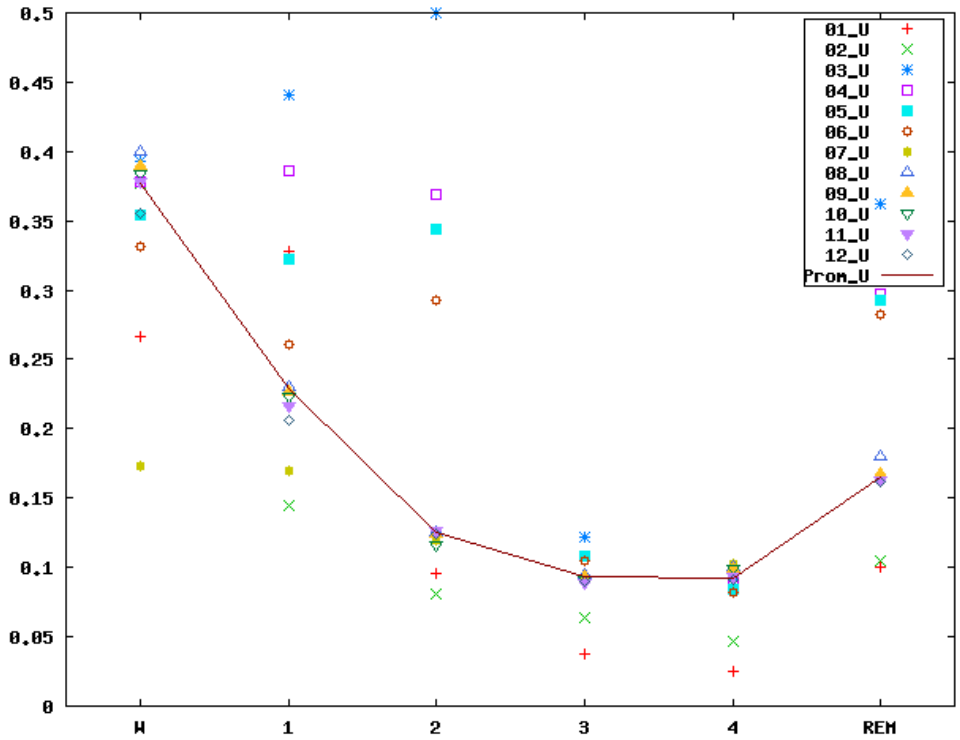
Here we follow two strategies:

$$D_{ij}^{(1)}(t) = SAC_{ij}(t) - < C >$$

$$\hat{Y} = \hat{D}\hat{X}$$

$$D_{ij}^{(2)}(t) = SAC_{ij}^{y}(t)$$


Y2
t1
Y1
t2
X1
Y1
Y2
X2
Y2*
t1
Y1*
t2
Y1
Y2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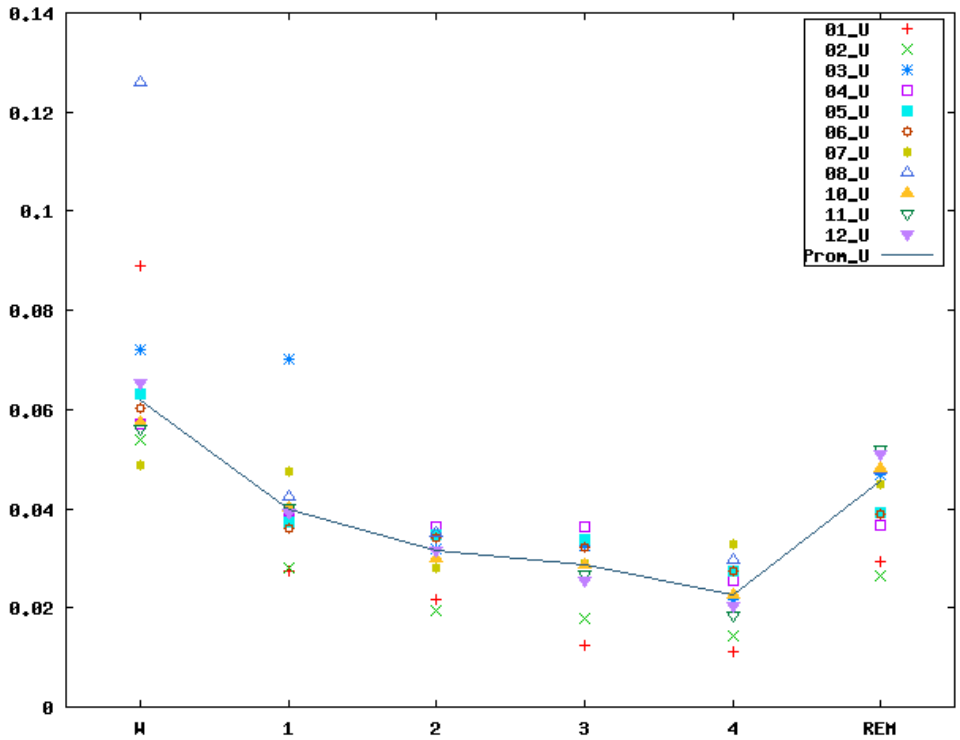
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
W
1
2
3
4
REM
01_U
02_U
03_U
04_U
05_U
06_U
07_U
08_U
09_U
10_U
11_U
12_U
Prom_U


0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
W
1
2
3
4
REM
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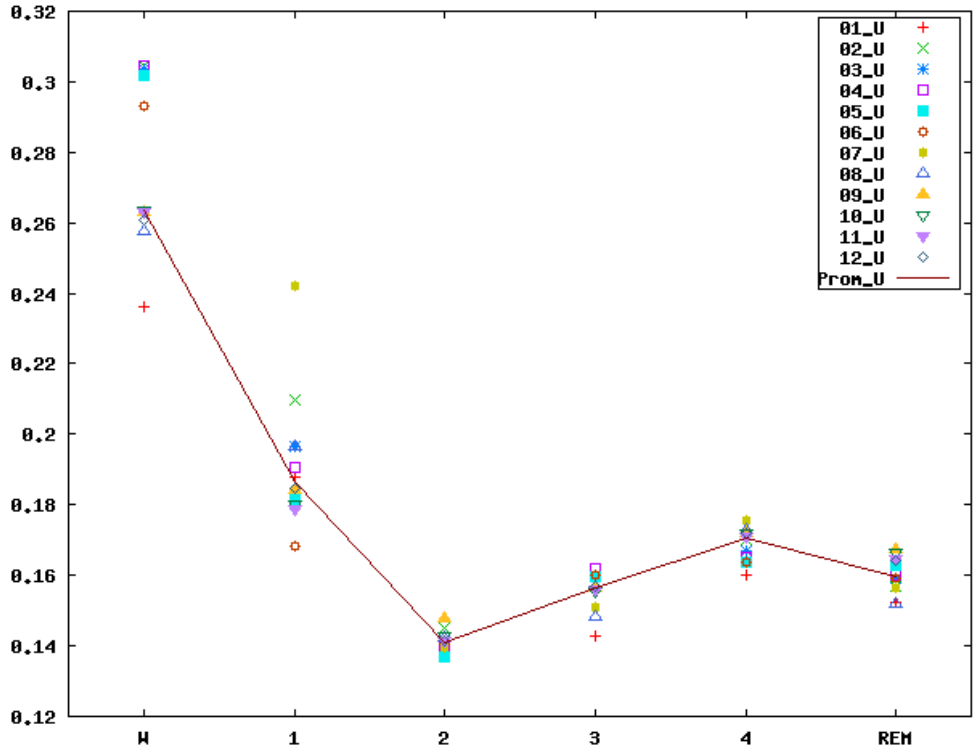
02_U
03_U
04_U
05_U
06_U
07_U
08_U
10_U
11_U
12_U
Prom_U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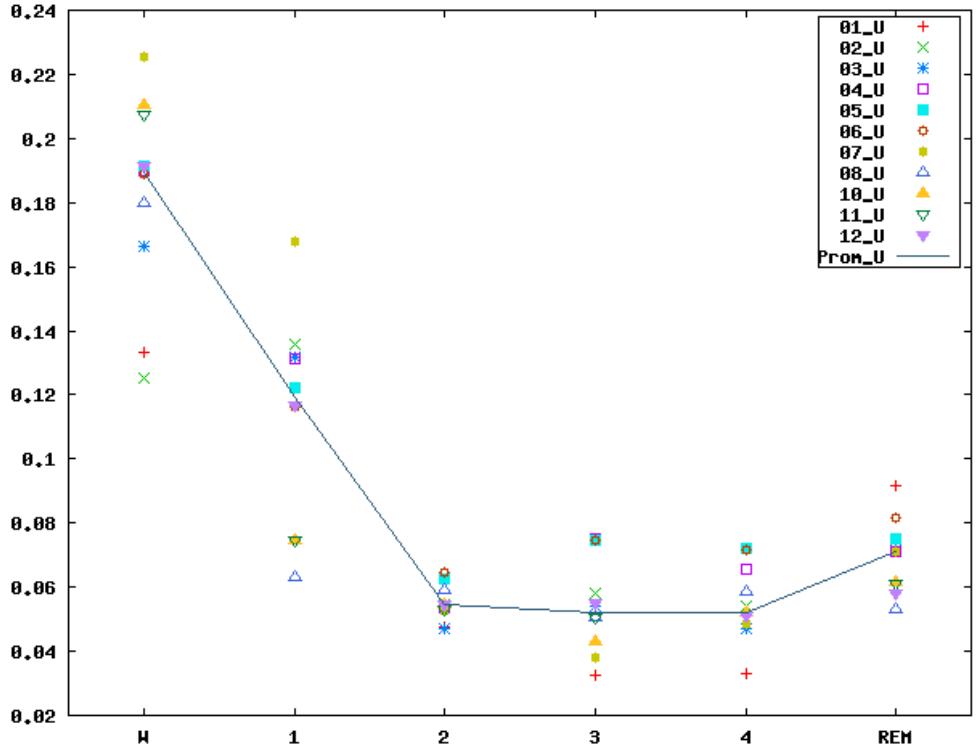
0.22
0.2
0.18
0.16
0.14
0.12
W
1
2
3
4
REM
01_U
02_U
03_U
04_U
05_U
06_U
07_U
08_U
09_U
10_U
11_U
12_U
Prom_U


0.24
0.22
0.2
0.18
0.16
0.14
0.12
0.1
0.08
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0.02
W
1
2
3
4
REM
01_U
02_U
03_U
04_U
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10_U
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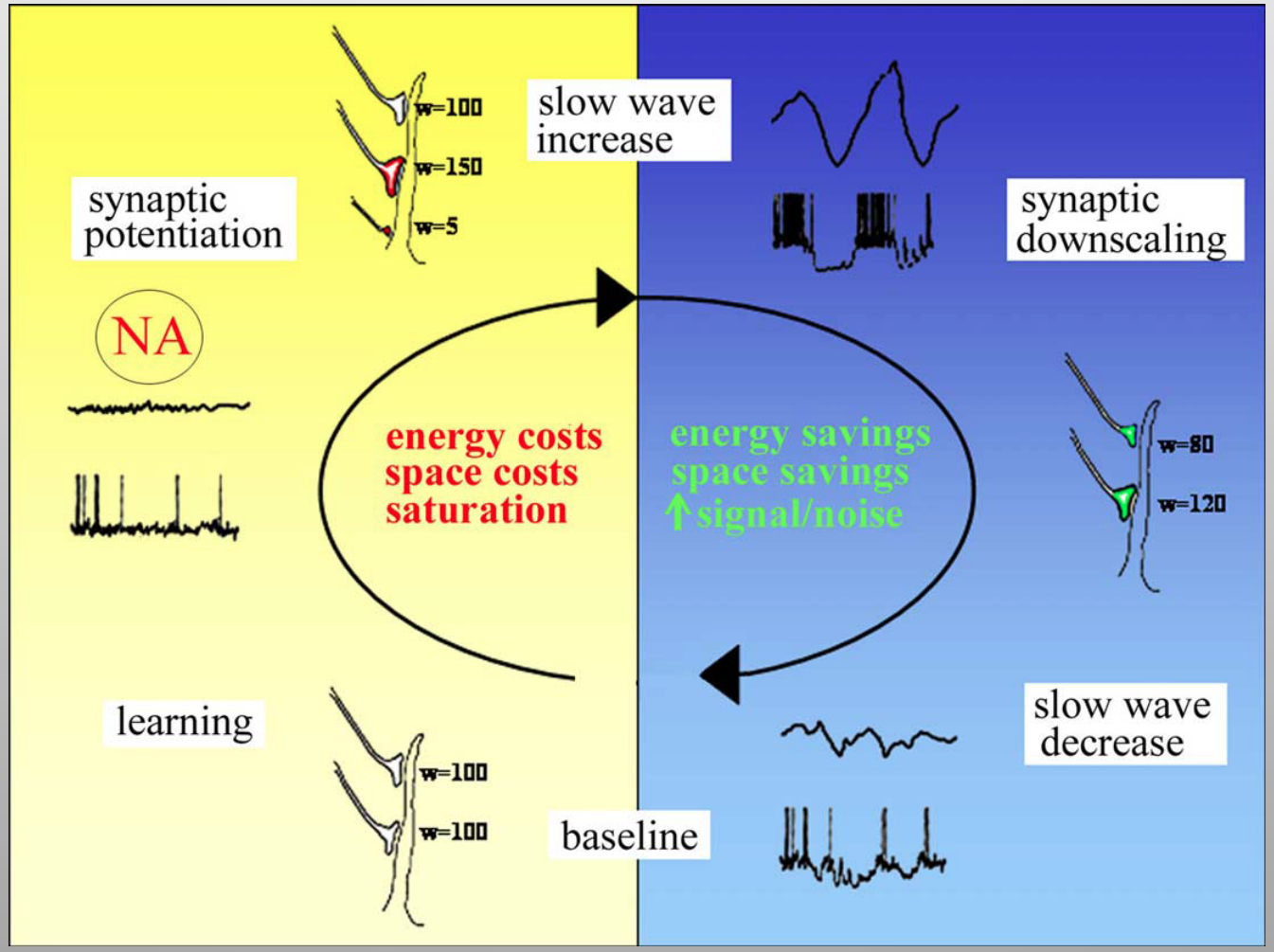
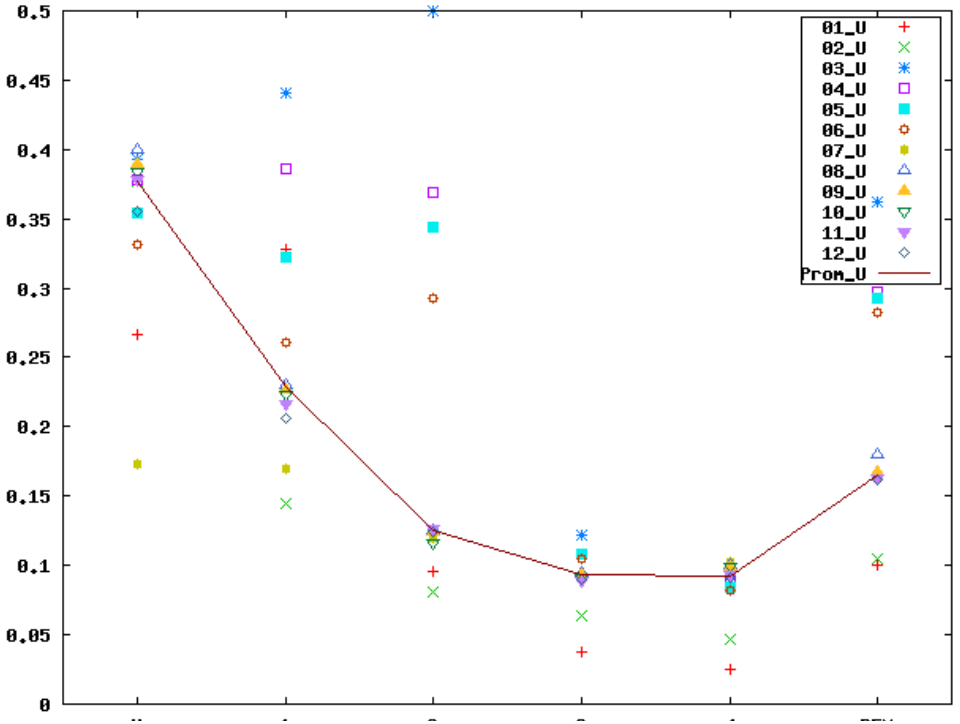
Prom_U

Tononi Cirelli, Sleep Medicine Reviews 10, 2006, 49-62

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02_U
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04_U
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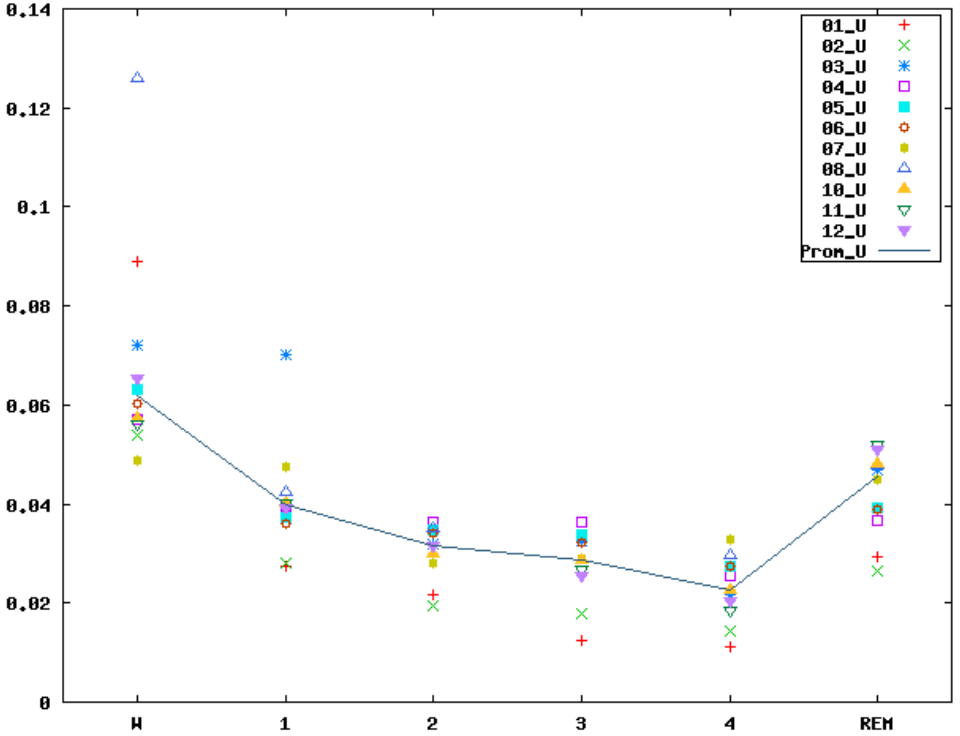
07_U
08_U
09_U
10_U
11_U
12_U
Prom_U


01_U
02_U
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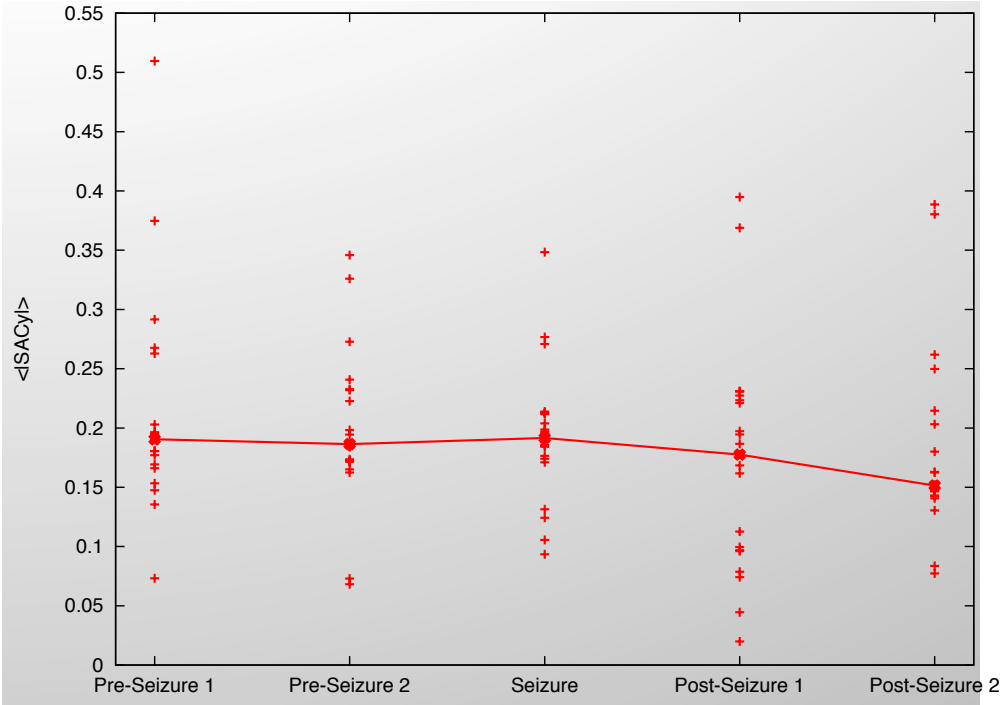
Prom_U
W
1
2
3
4
REM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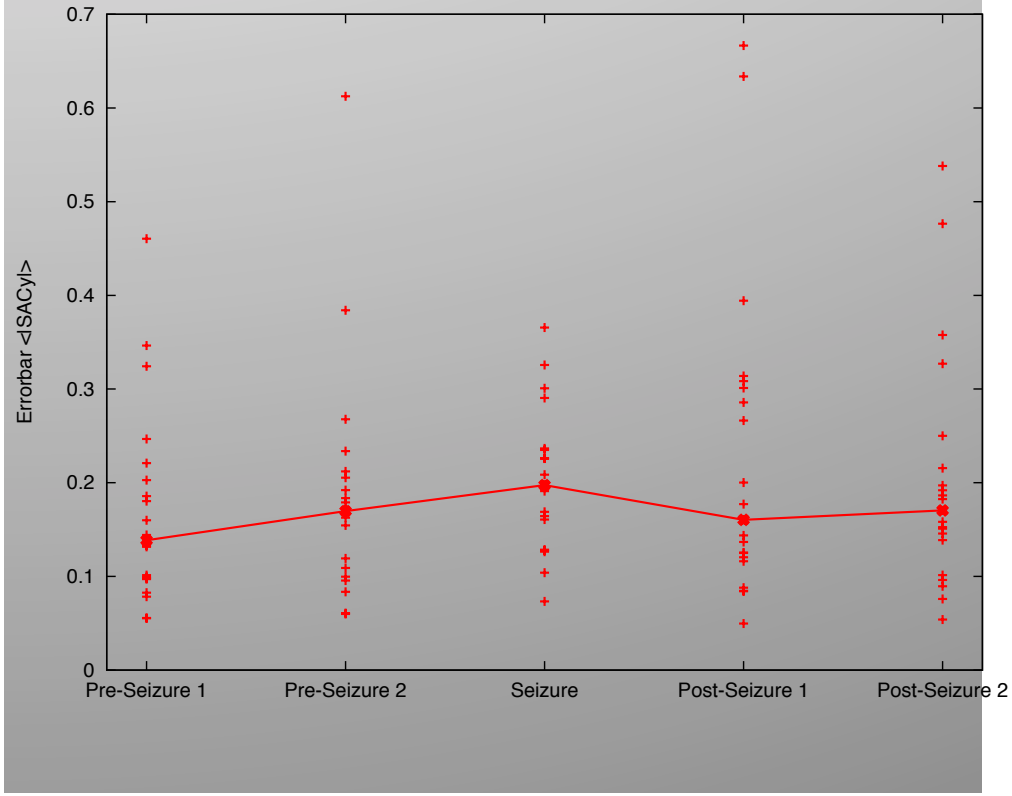
Pre-Seizure 2
Seizure
Post-Seizure 1
Post-Seizure 2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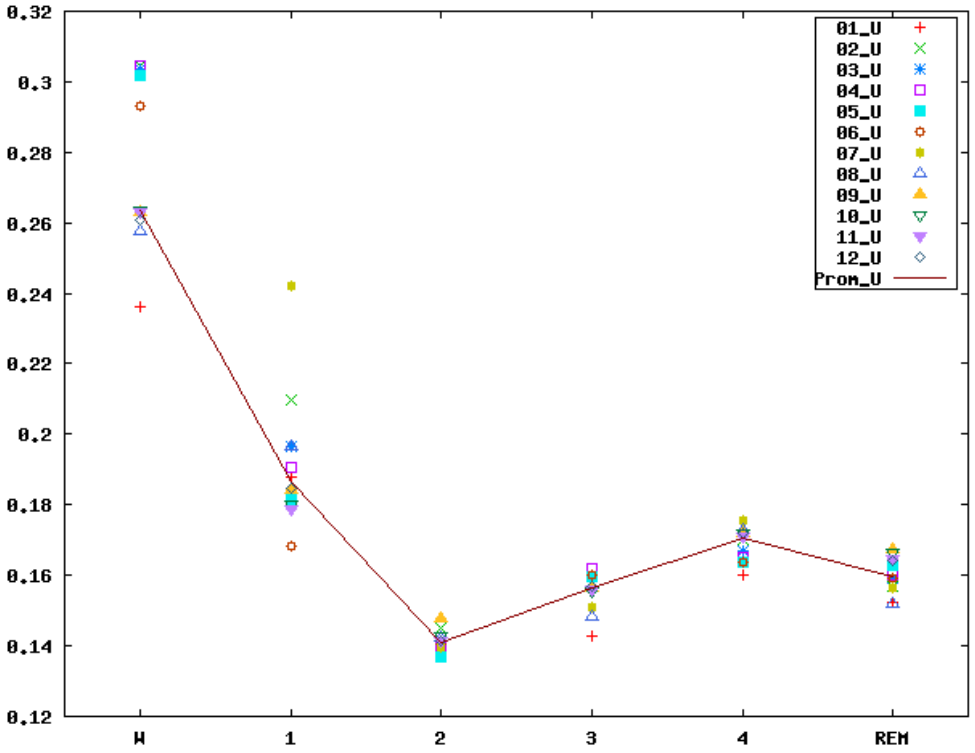
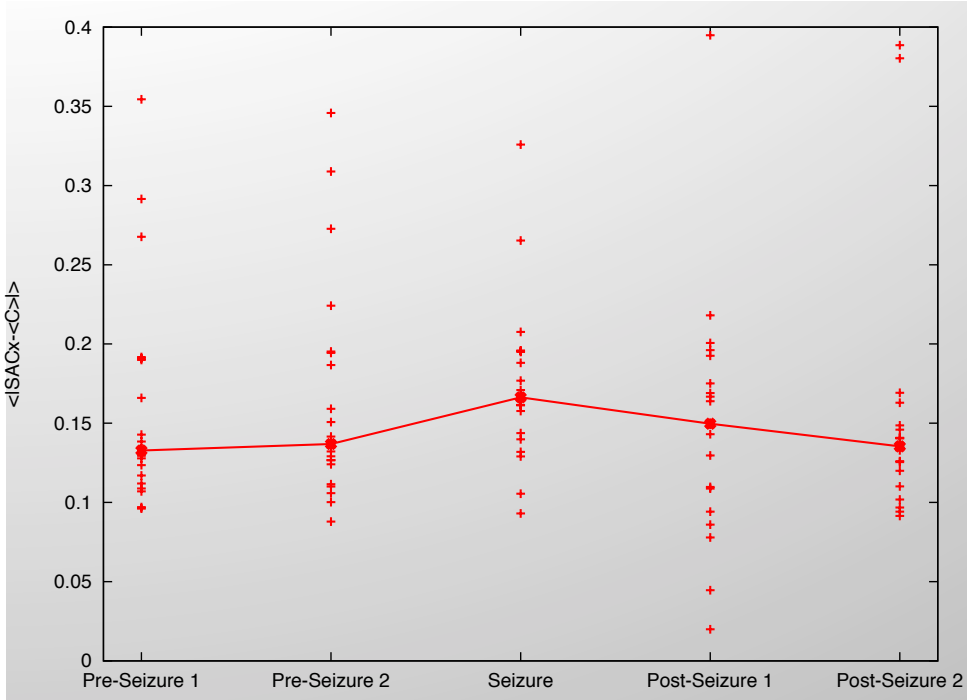
Pre-Seizure 1
Pre-Seizure 2
Seizure
Post-Seizure 1
Post-Seizure 2


01_U
02_U
03_U
04_U
05_U
06_U
07_U
08_U
09_U
10_U
11_U
12_U
Prom_U
0.32
0.3
0.28
0.26
0.24
0.22
0.2
0.18
0.16
0.14
0.12
W
1
2
3
4
REM


<|SACx-<C>|>
0.4
0.35
0.3
0.25
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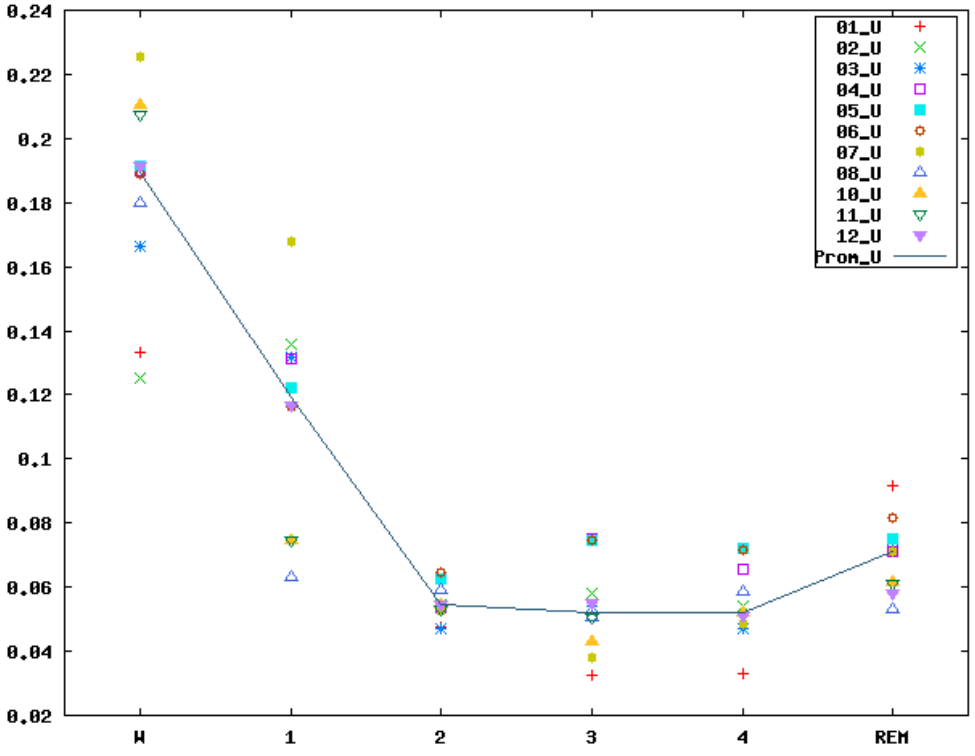
0.15
0.1
0.05
0
Pre-Seizure 1
Pre-Seizure 2
Seizure
Post-Seizure 1
Post-Seizure 2


01_U
02_U
03_U
04_U
05_U
06_U
07_U
08_U
10_U
11_U
12_U
Prom_U
0.24
0.22
0.2
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0.12
0.1
0.08
0.06
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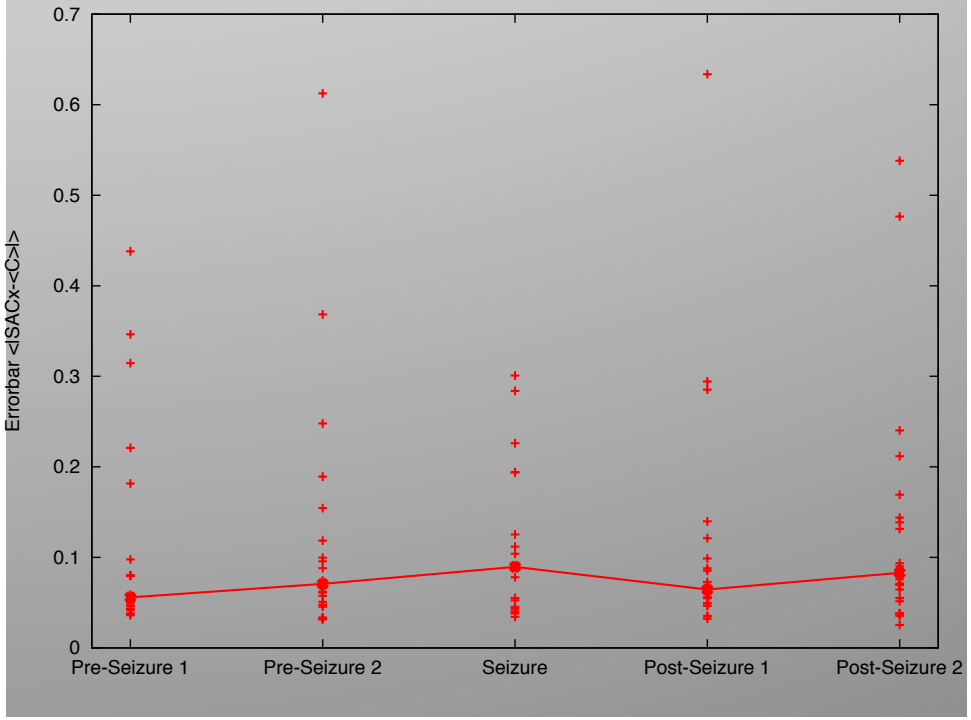
0.02
W
1
2
3
4
REM


Errorbar <|SACx-<C>|>
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0.5
0.4
0.3
0.2
0.1
0
Pre-Seizure 1
Pre-Seizure 2
Seizure
Post-Seizure 1
Post-Seizure 2

Are epileptic seizures condensed sleep???

I'm very grateful to all of the collaborators !!!

And I thank you very much for paying attention!!!!