Techniques to Estimate Brain Connectivity from Measurements with Low Spatial Resolution

1. What is coherence?
2. The problem of volume conduction
3. Recent developments

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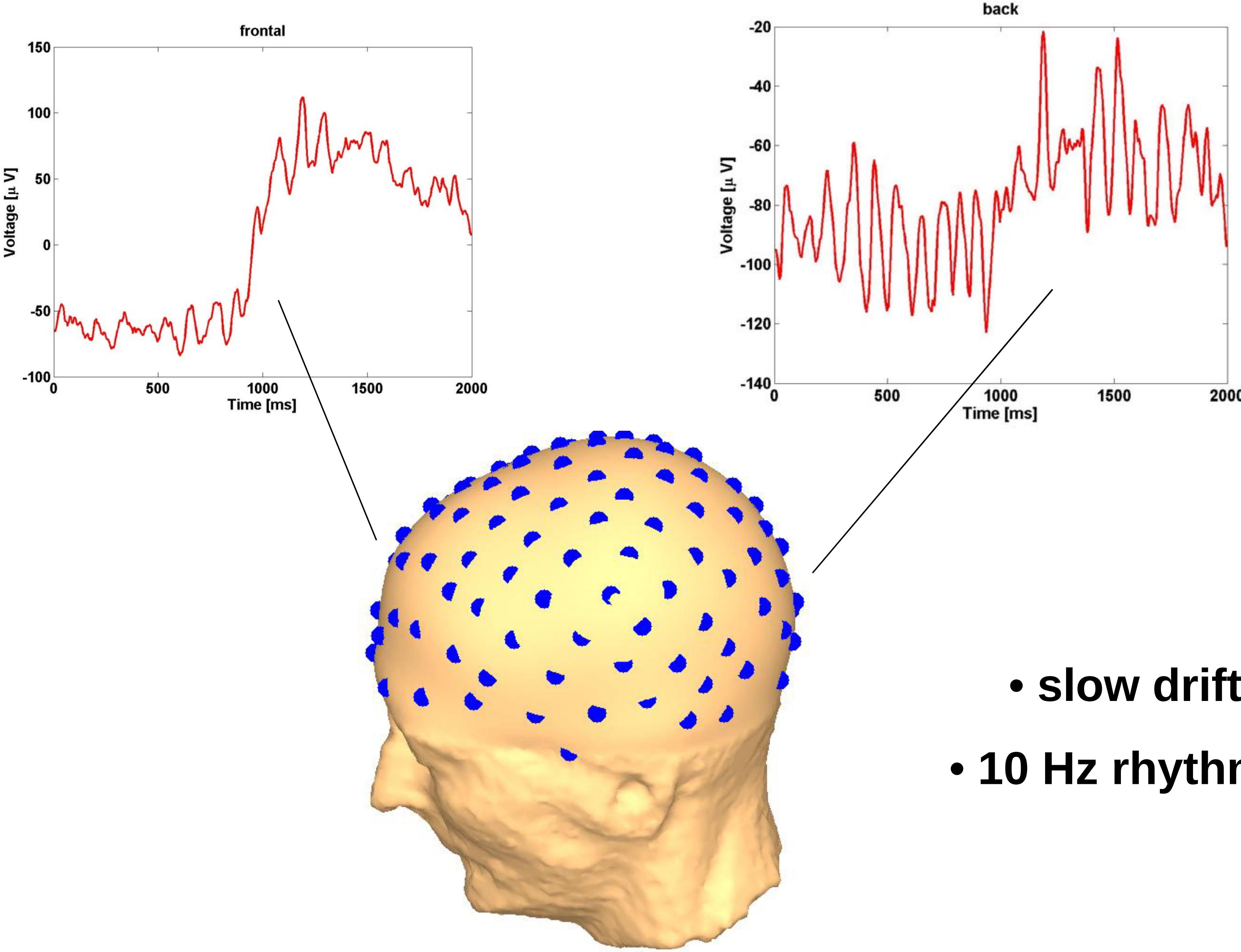
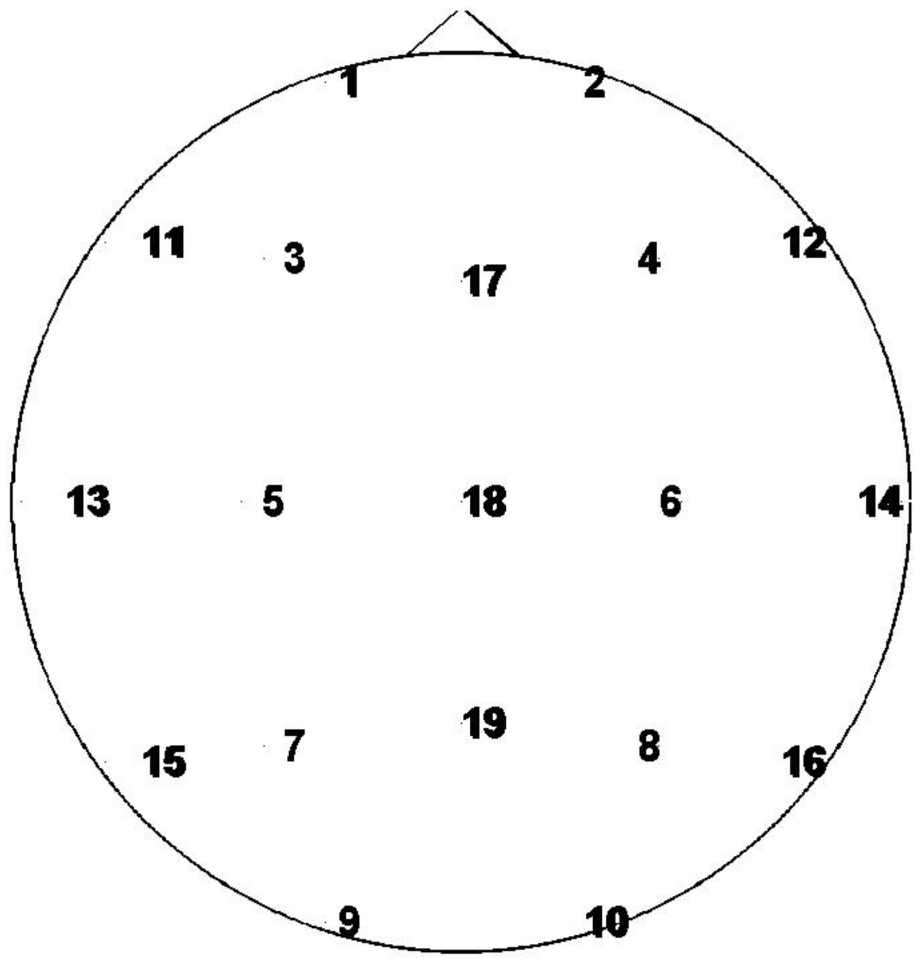
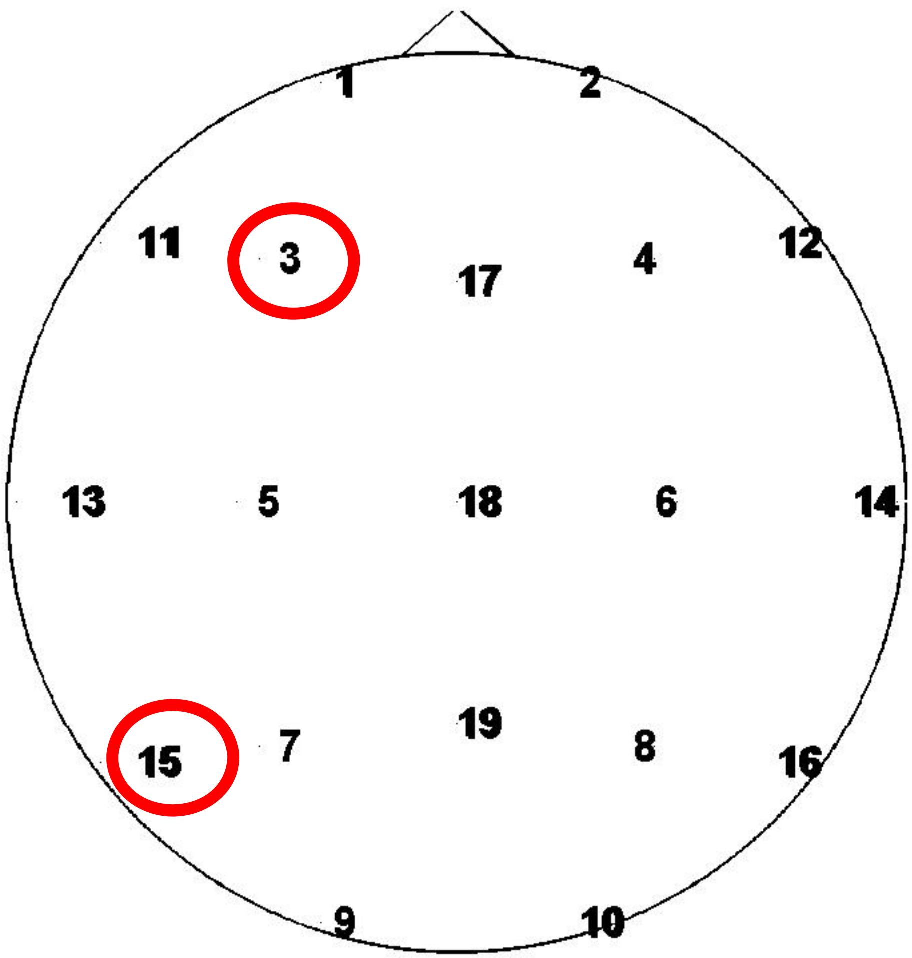


- **slow drifts**
- **10 Hz rhythm**

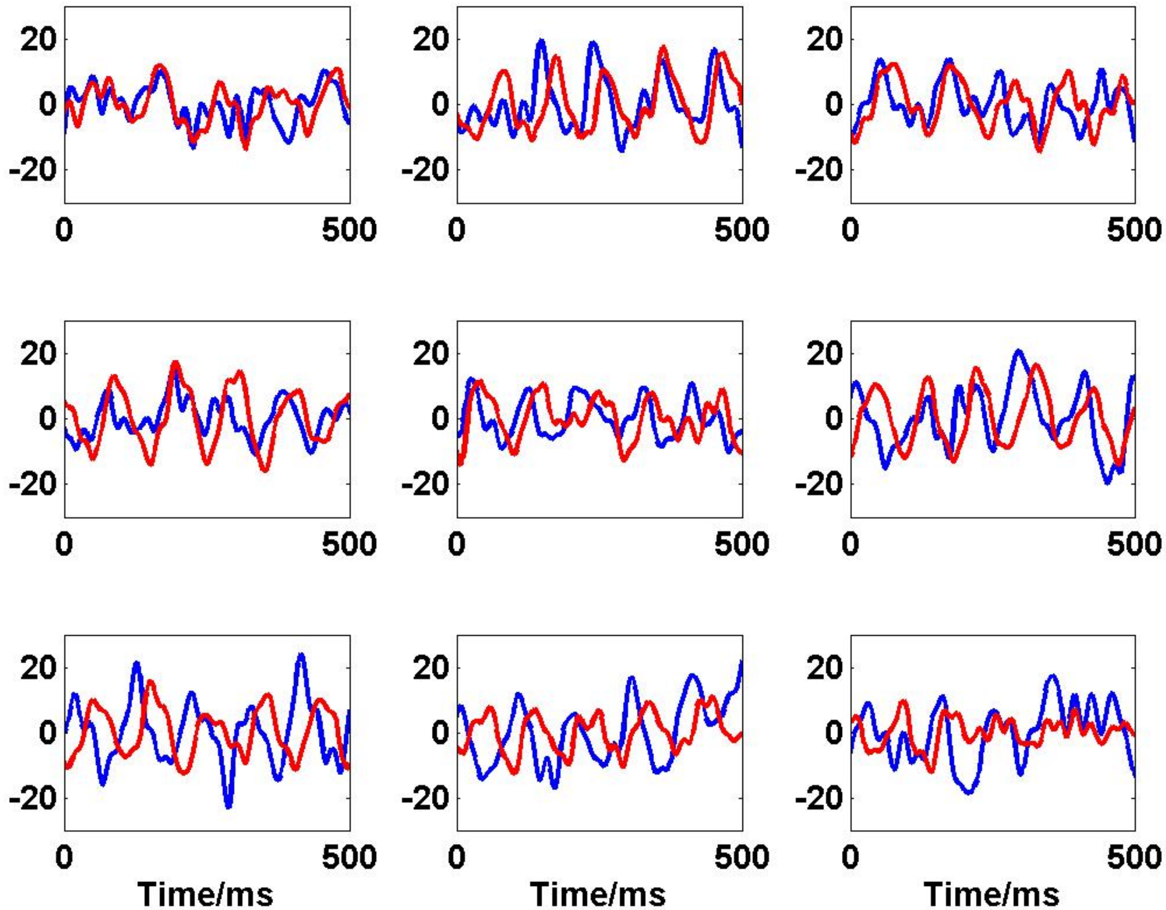
EEG sensor configuration



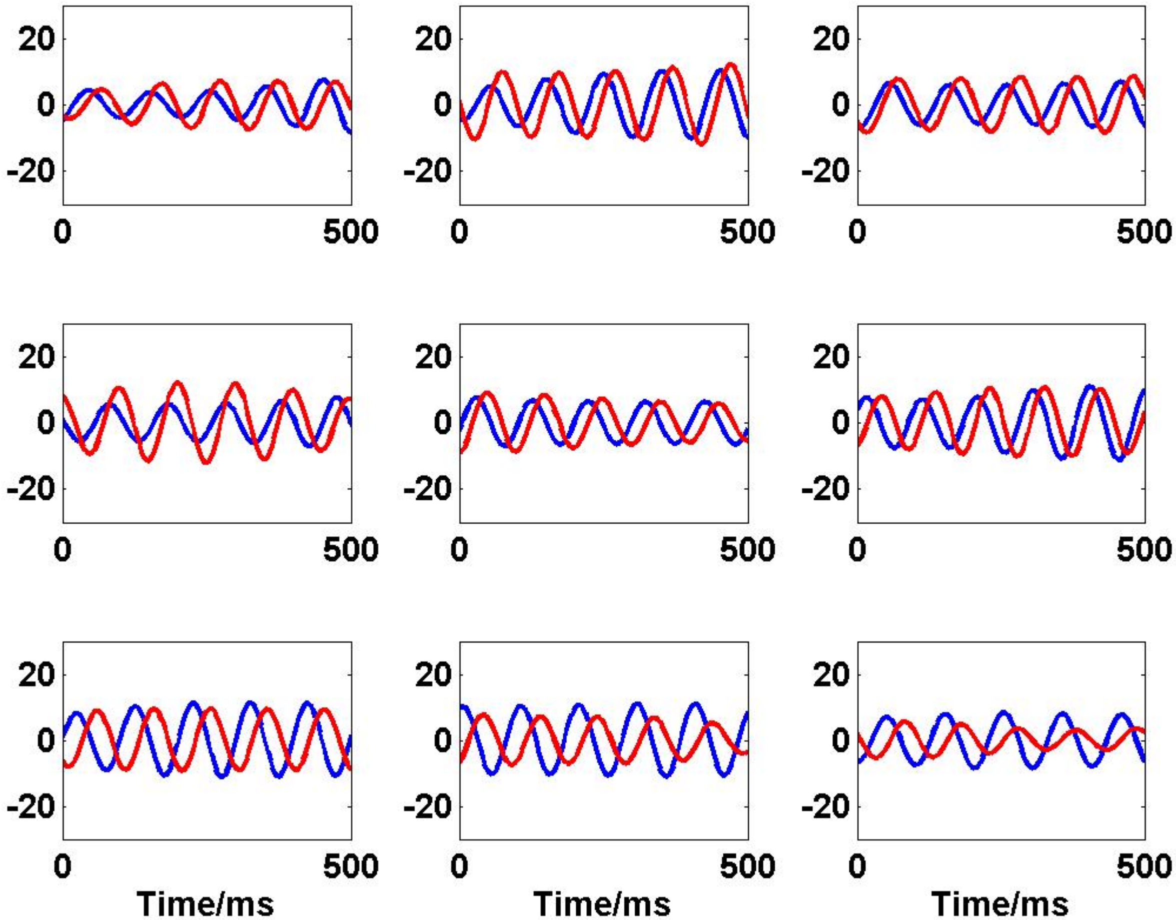
EEG sensor configuration

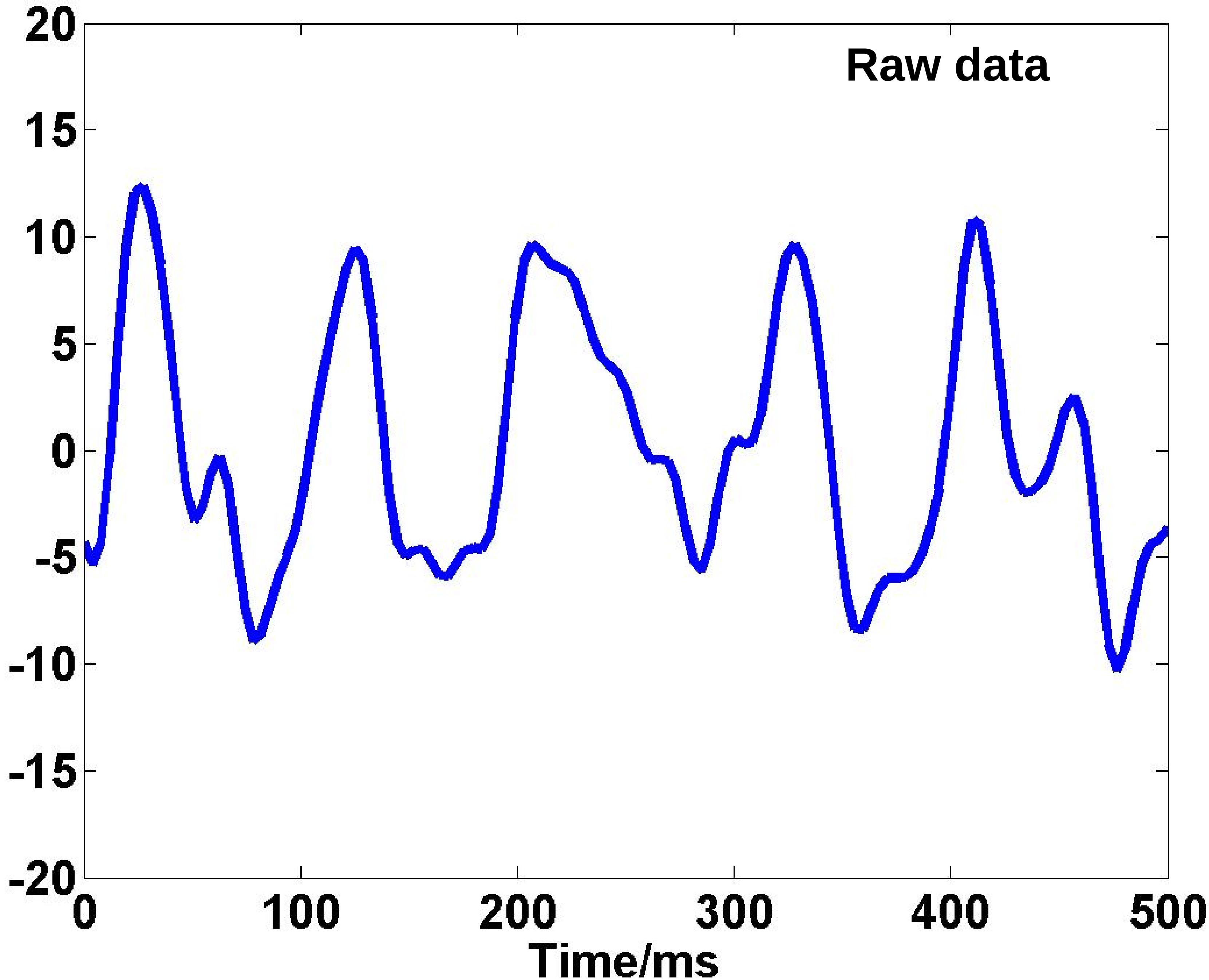


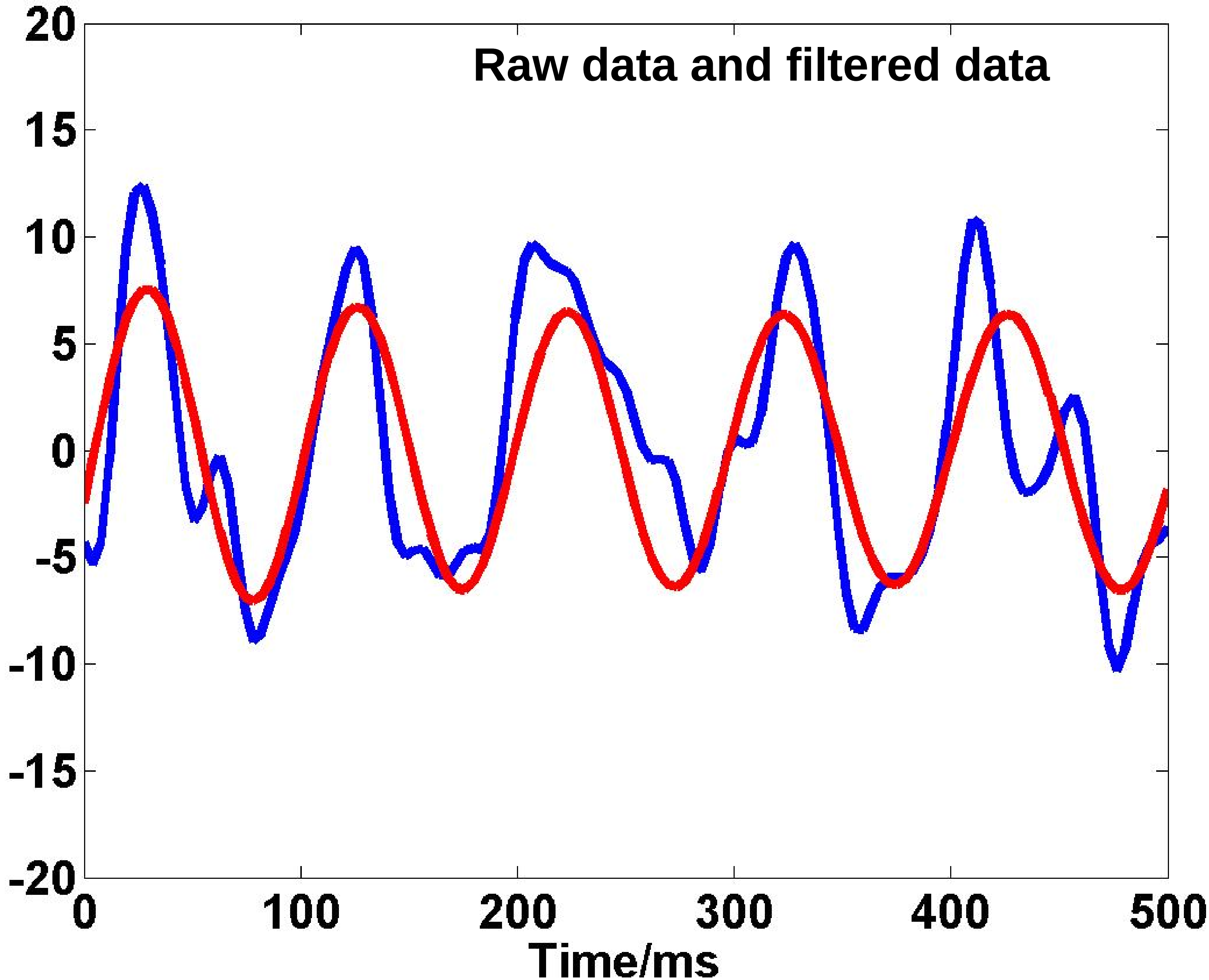
Unfiltered data in two channels for various trials



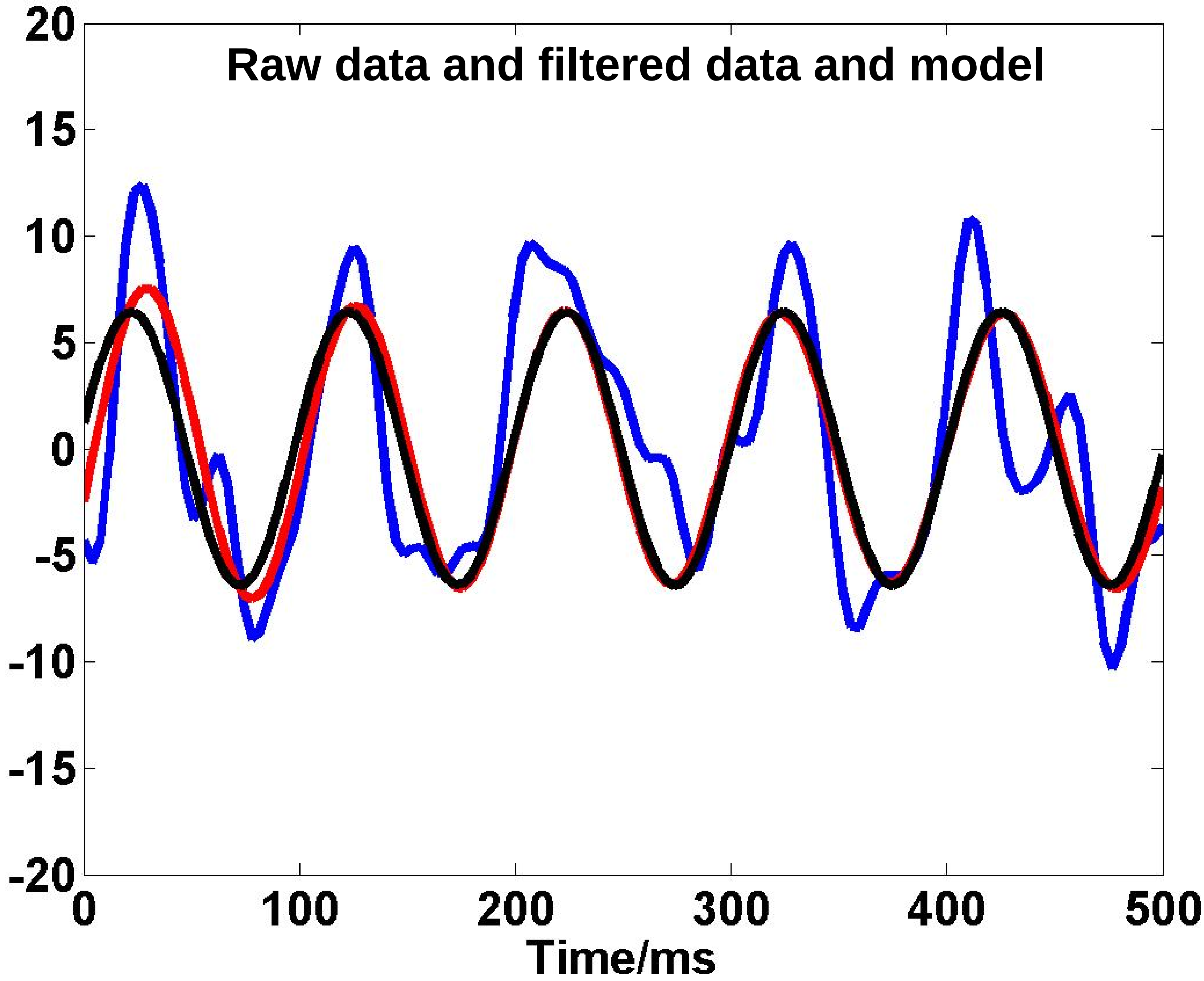
Filtered data in two channels for various trials



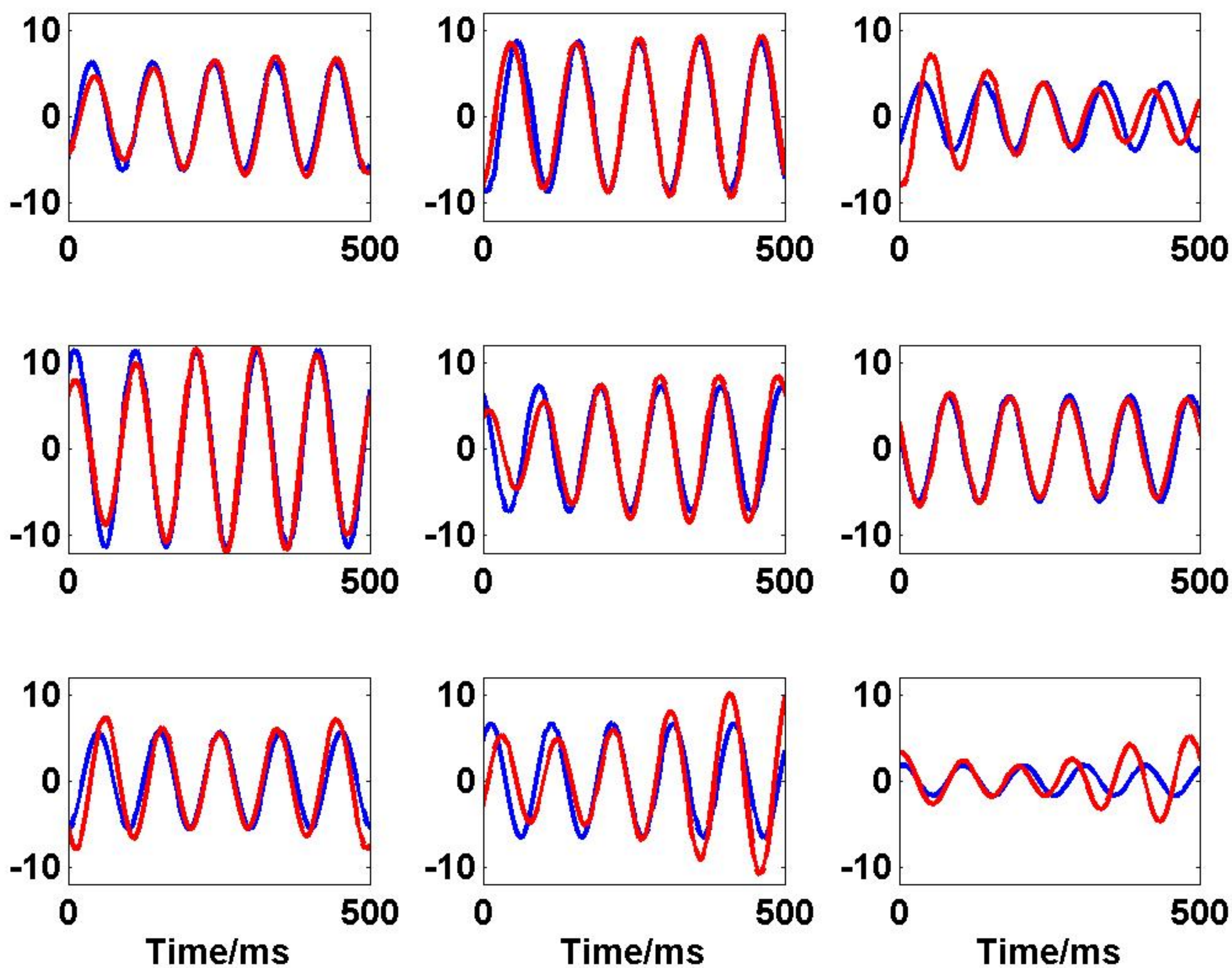

Raw data
20
15
10
5
0
-5
-10
-15
-20
0
100
200
300
400
500
Time/ms

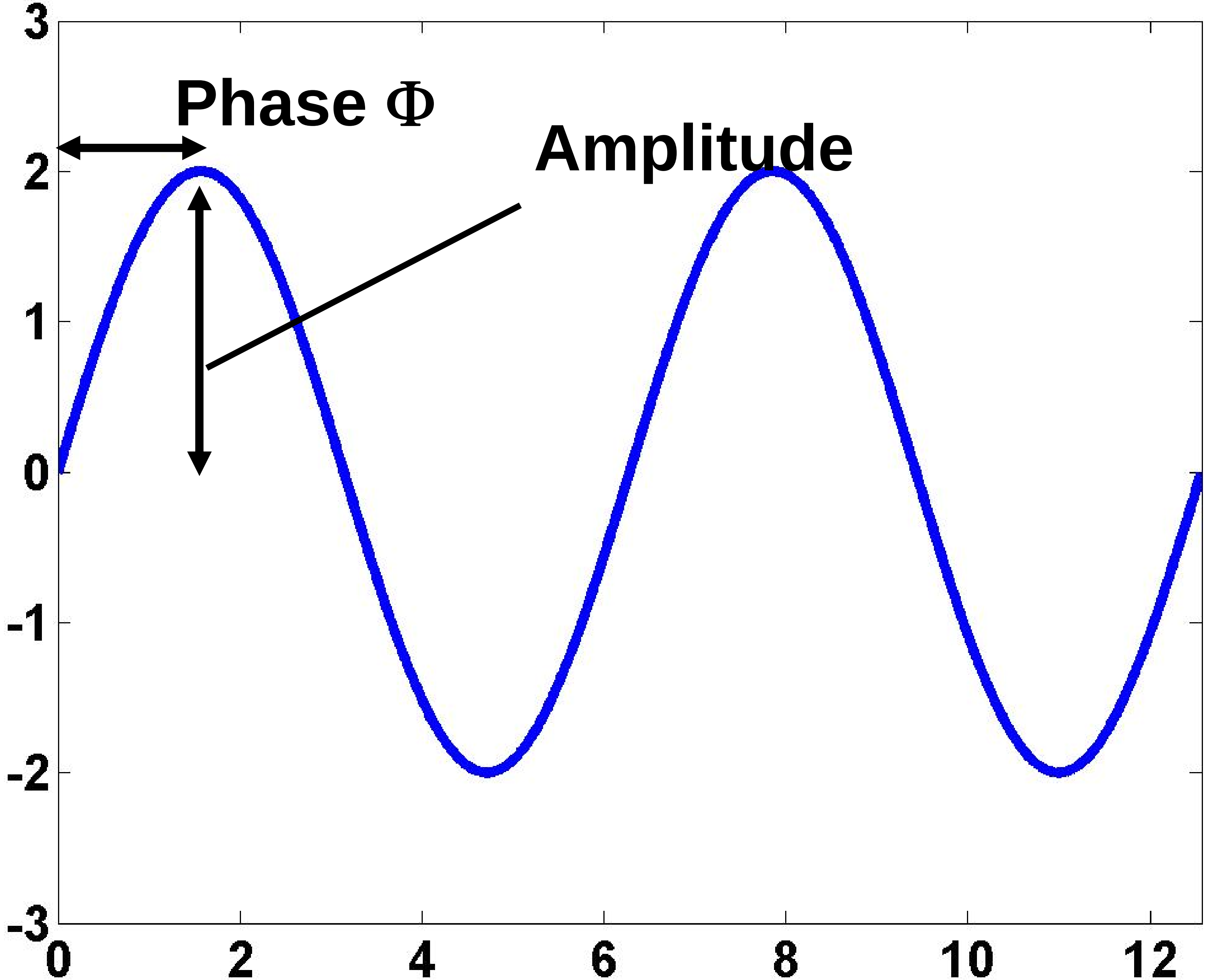


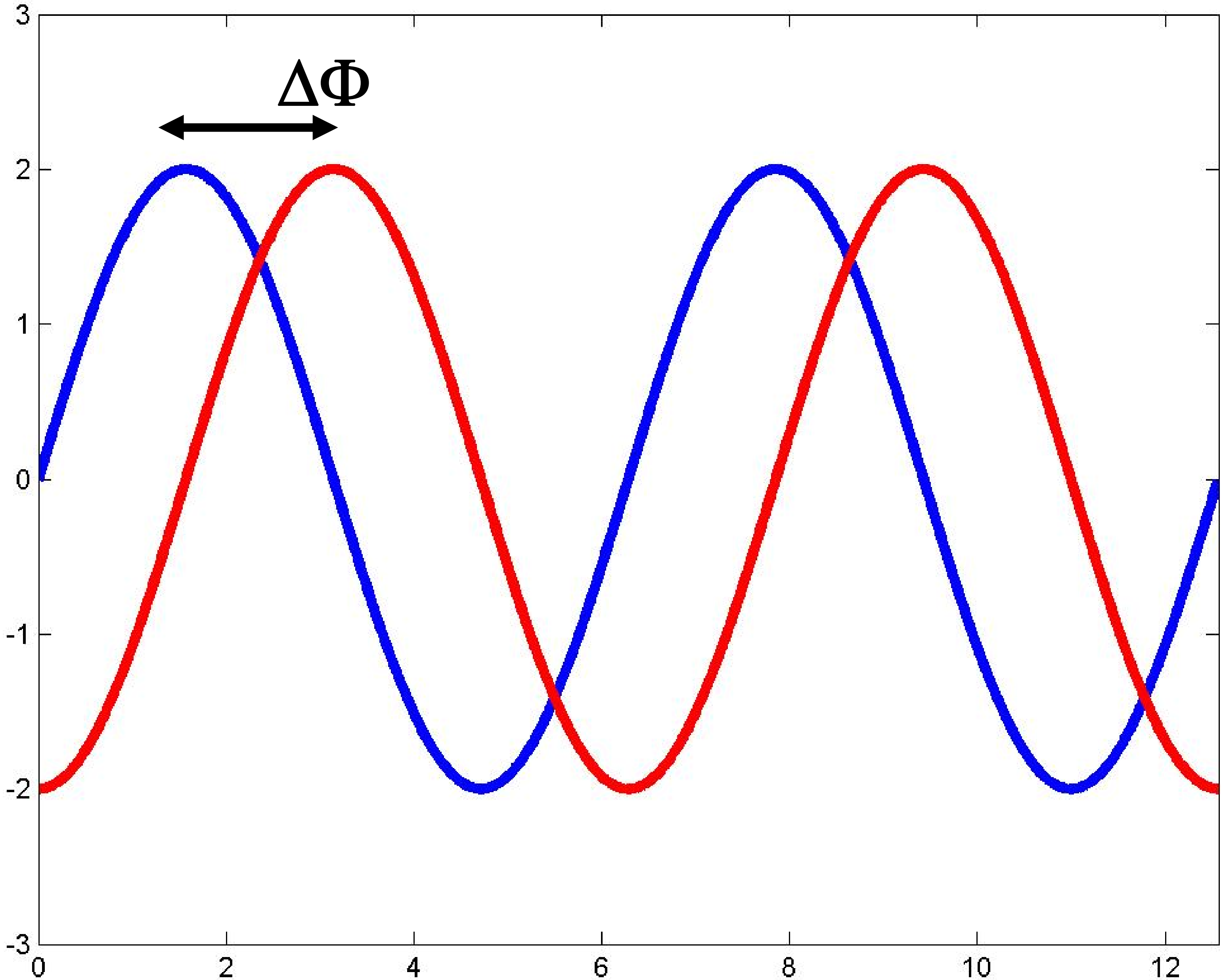
Raw data and filtered data
20
15
10
5
0
-5
-10
-15
-20
0
100
200
300
400
500
Time/ms


Raw data and filtered data and model
20
15
10
5
0
-5
-10
-15
-20
0
100
200
300
400
500
Time/ms

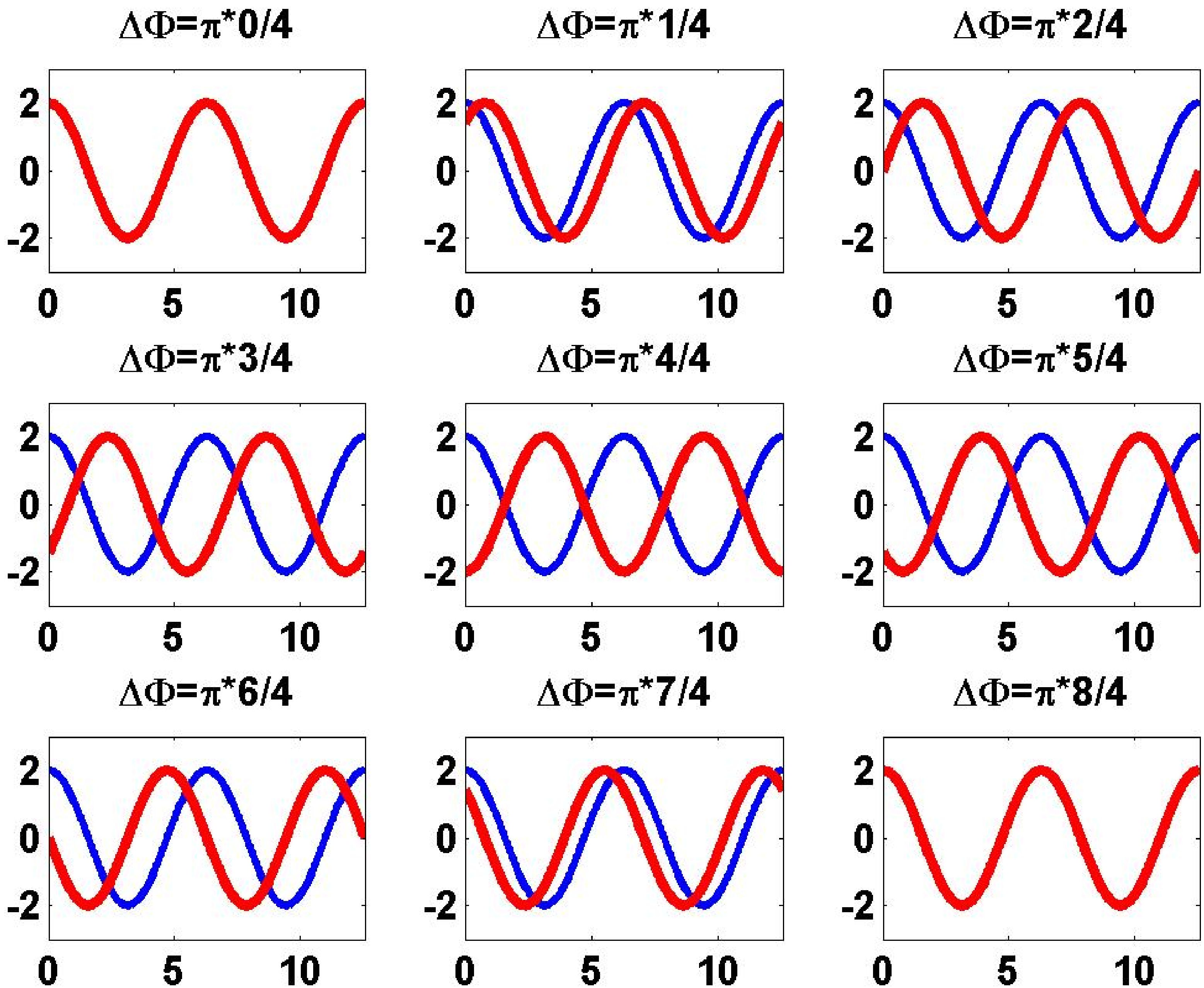
Filtered Data vs. Model

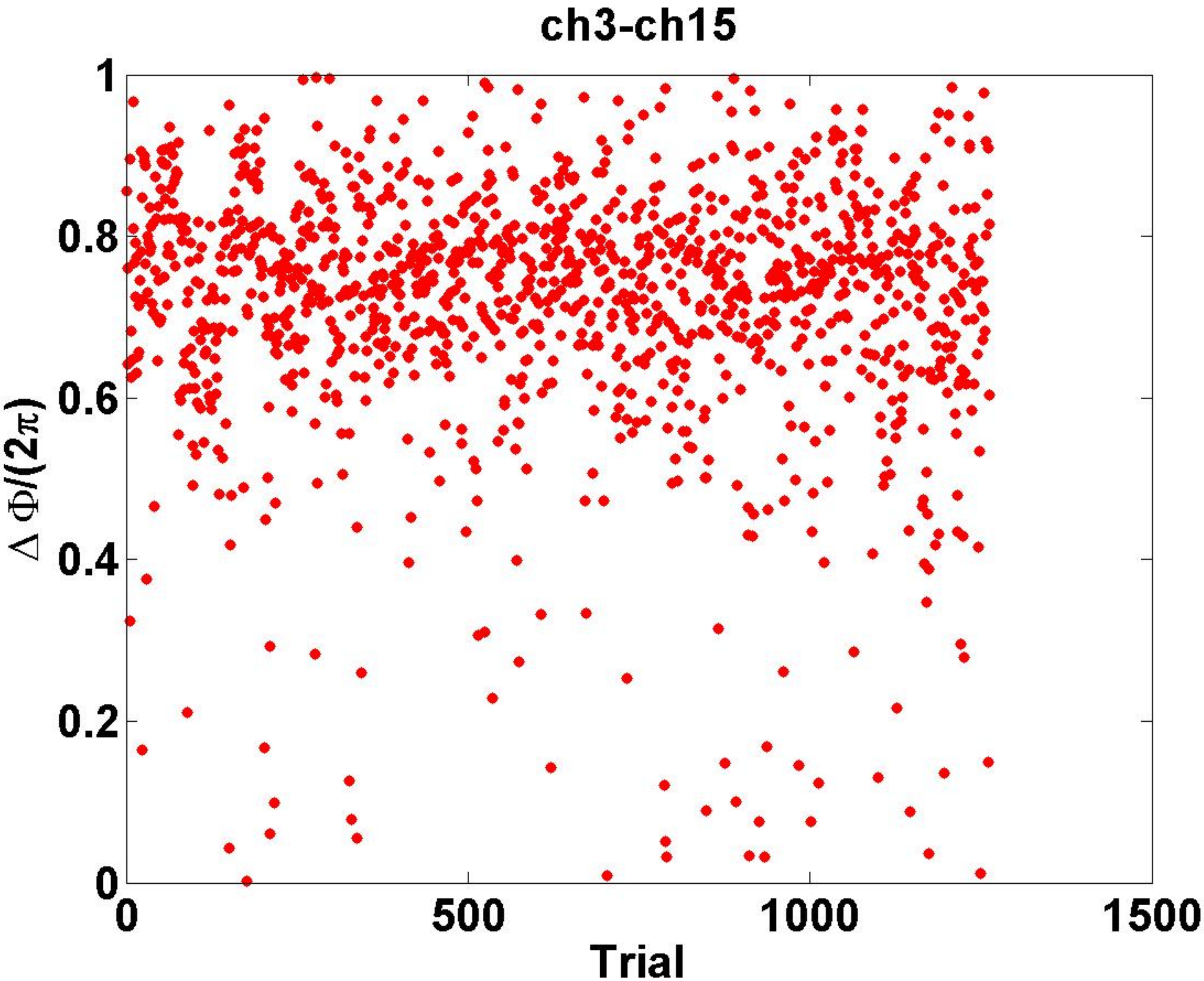


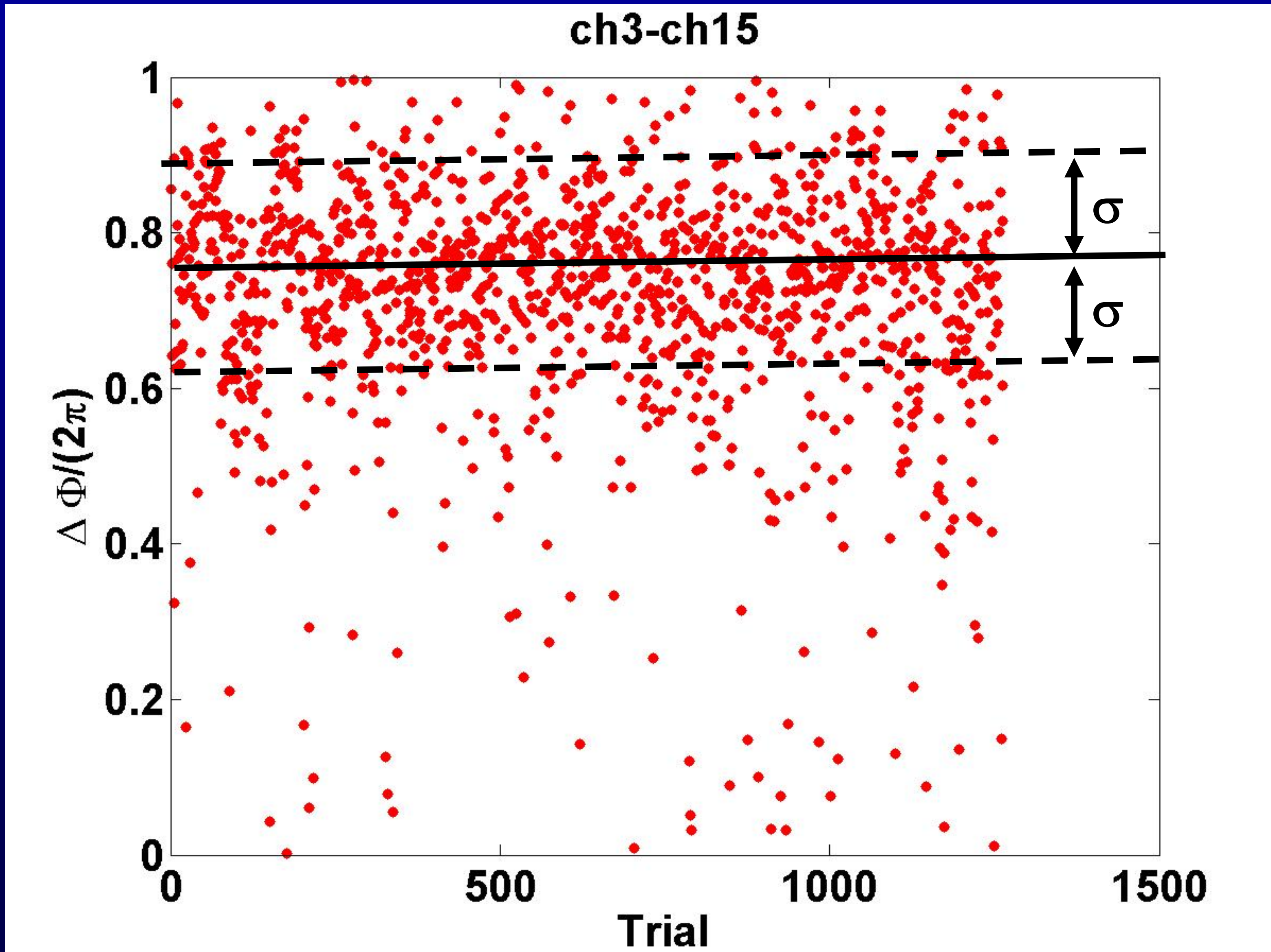

Phase Φ
Amplitude
3
2
1
0
-1
-2
-3
0
2
4
6
8
10
12

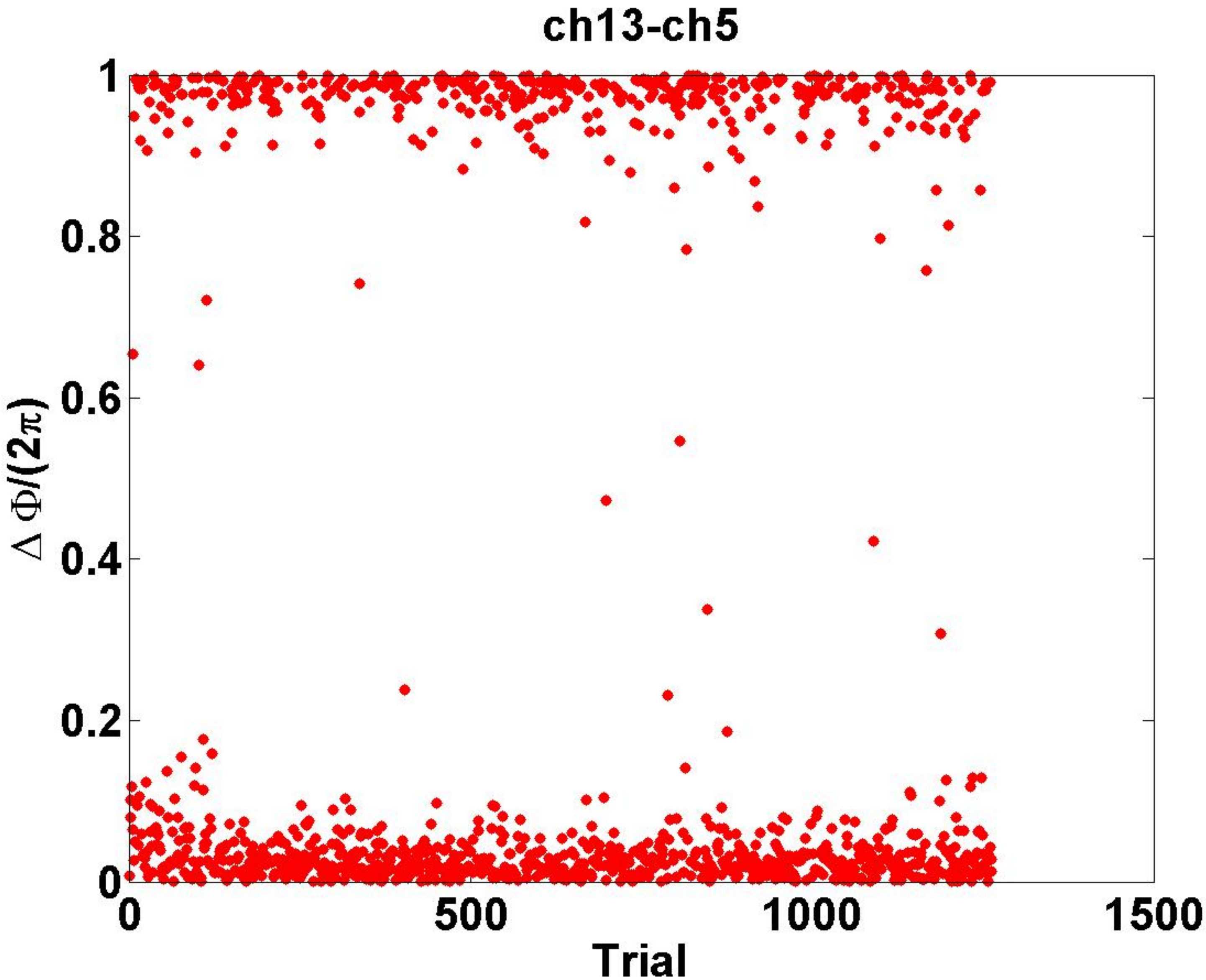


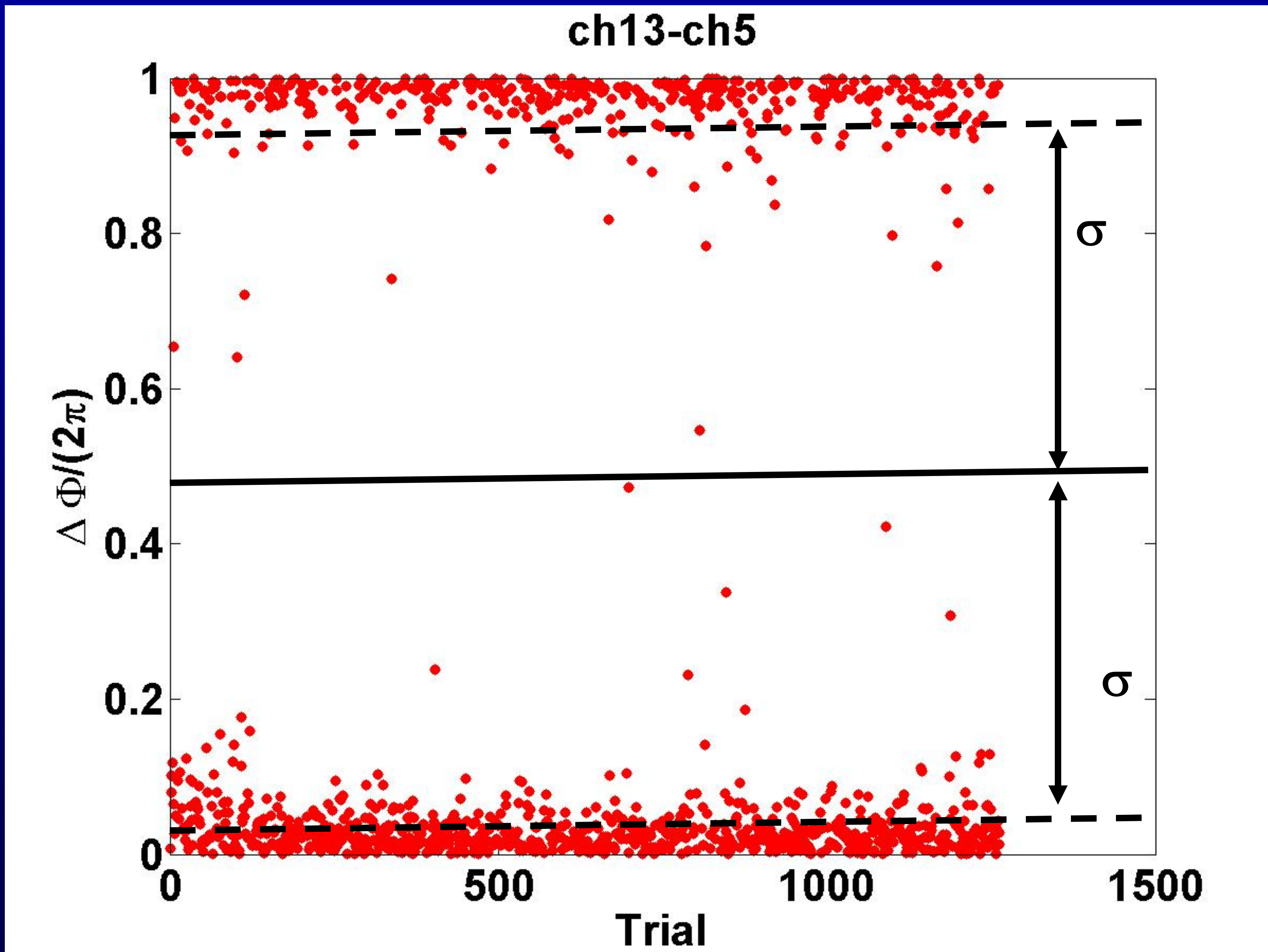
ΔΦ
3
2
1
0
-1
-2
-3
0
2
4
6
8
10
12


ΔΦ=π*0/4
ΔΦ=π*1/4
ΔΦ=π*2/4
ΔΦ=π*3/4
ΔΦ=π*4/4
ΔΦ=π*5/4
ΔΦ=π*6/4
ΔΦ=π*7/4
ΔΦ=π*8/4
2
0
-2
0
5
10

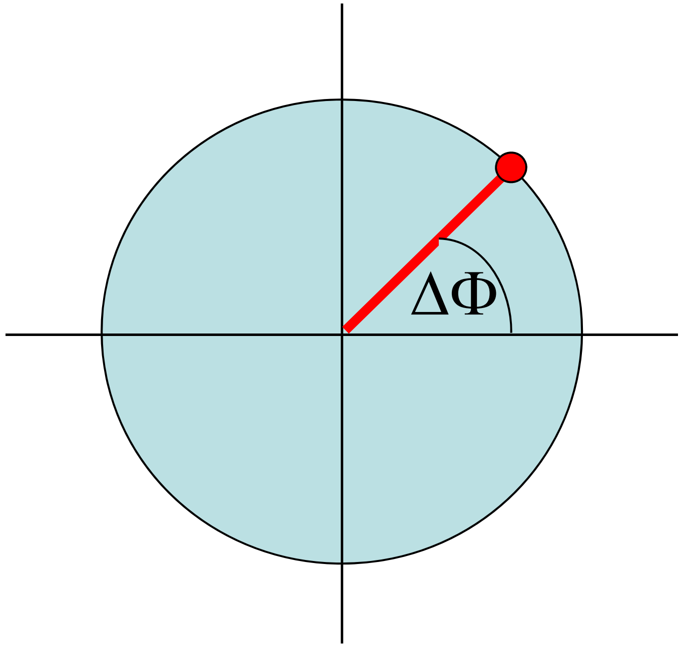

ch3-ch15
1
0.8
0.6
0.4
0.2
0
0
500
1000
1500
Trial
Δ Φ/(2π)


ch3-ch15
Δ Φ/(2π)
Trial
σ
σ
0
0.2
0.4
0.6
0.8
1
0
500
1000
1500


ch13-ch5
1
0.8
0.6
0.4
0.2
0
0
500
1000
1500
Trial
Δ Φ/(2π)



ch13-ch5
Δ Φ/(2π)
Trial
σ
σ
0
0.2
0.4
0.6
0.8
1
0
500
1000
1500

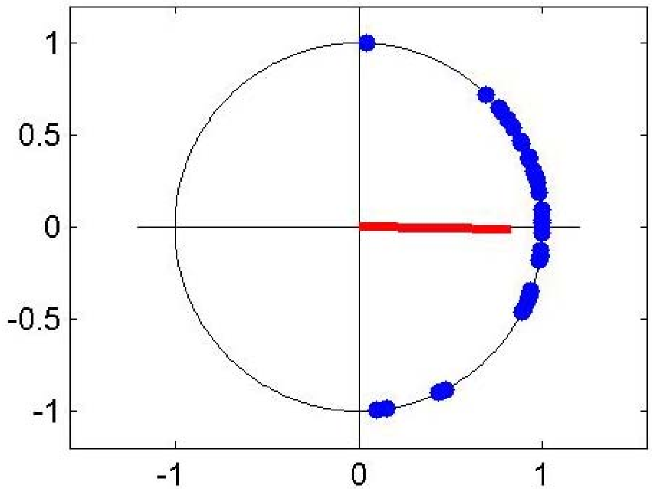


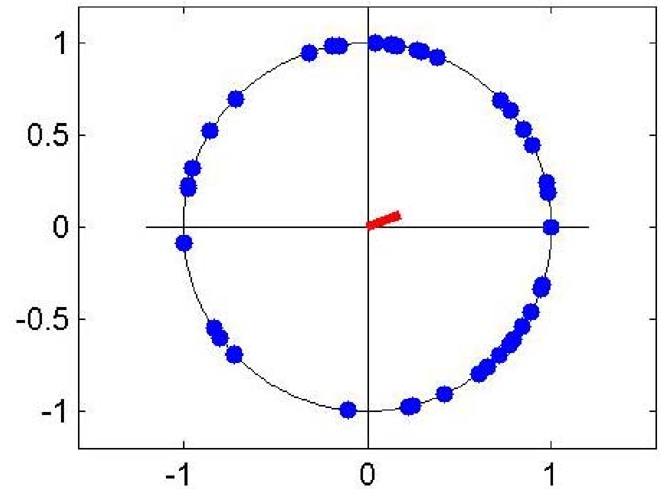
real valued

$$\begin{pmatrix} \cos(\Delta\Phi) \\ \sin(\Delta\Phi) \end{pmatrix}$$

complex valued

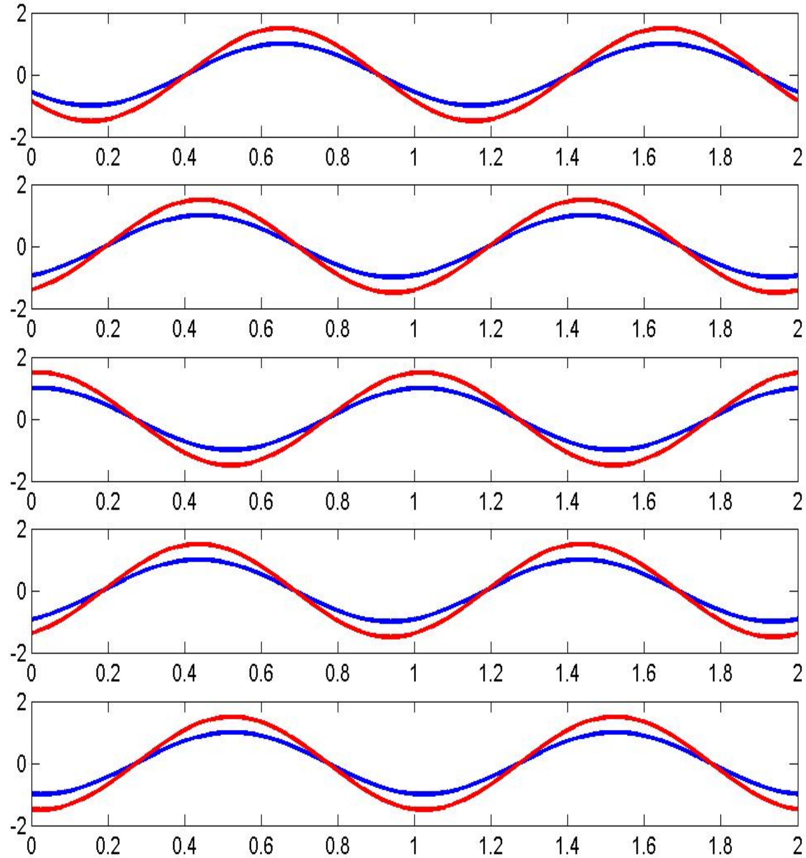
$$\exp(i\Delta\Phi)$$



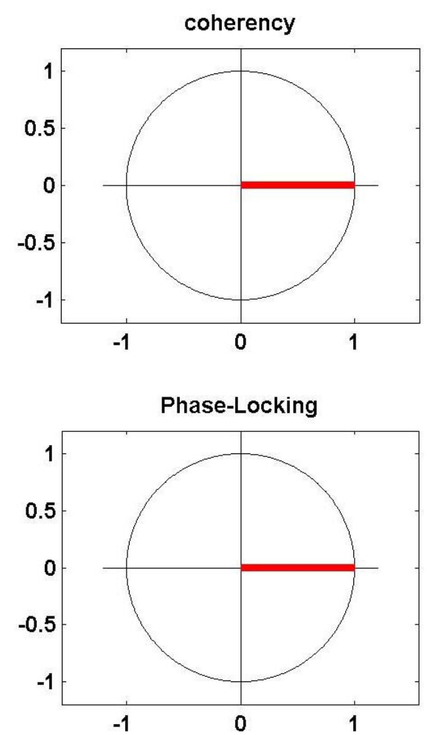


Phase Locking: $$PL = \left| \frac{1}{K} \sum_k \exp(i(\Phi_{1k} - \Phi_{2k})) \right|$$

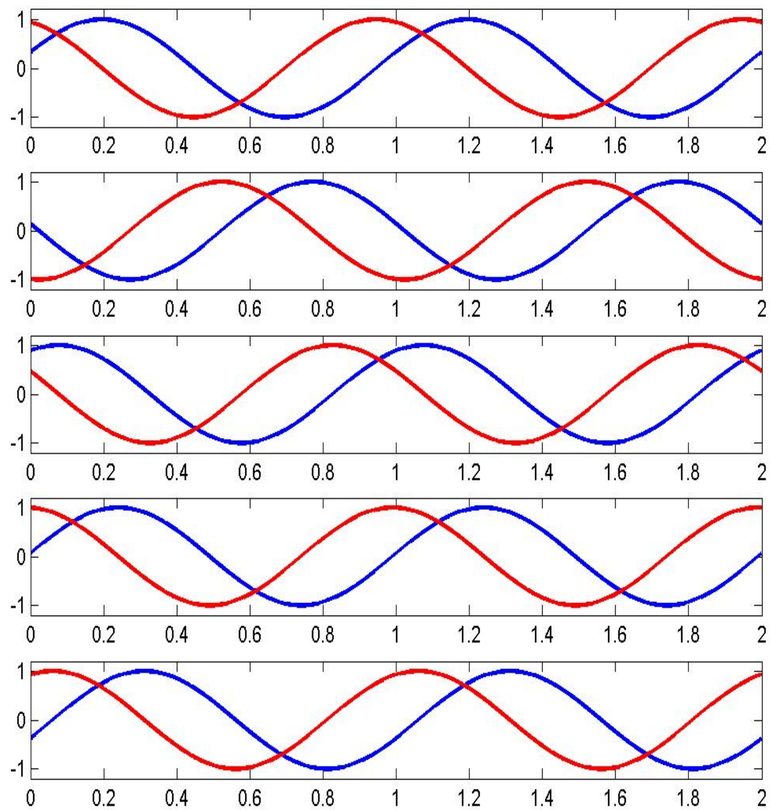
Coherence: $$C = \frac{\frac{1}{K}\sum_k r_{1k} r_{2k} \exp(i(\Phi_{1k} - \Phi_{2k}))}{\left(\frac{1}{K}\sum_k r_{1k}^2 \frac{1}{K}\sum_k r_{2k}^2\right)^{1/2}} = \frac{\left\langle z_1 z_2^* \right\rangle}{\sqrt{\left\langle \left|z_1\right|^2 \right\rangle}\sqrt{\left\langle \left|z_2\right|^2 \right\rangle}}$$



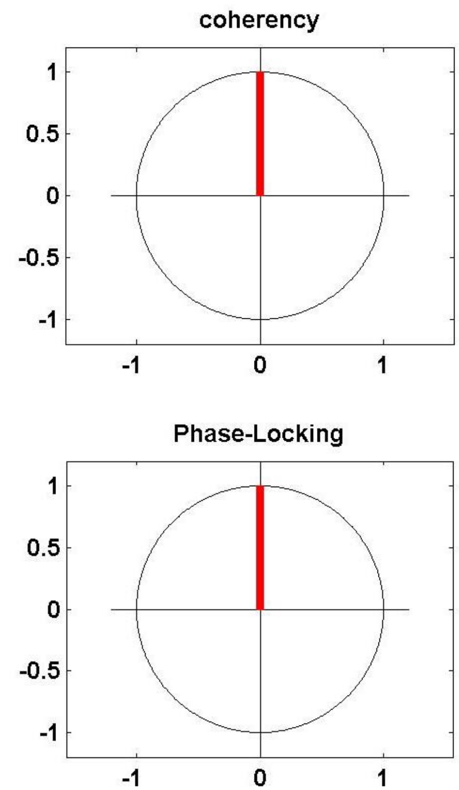
2
0
-2
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
2



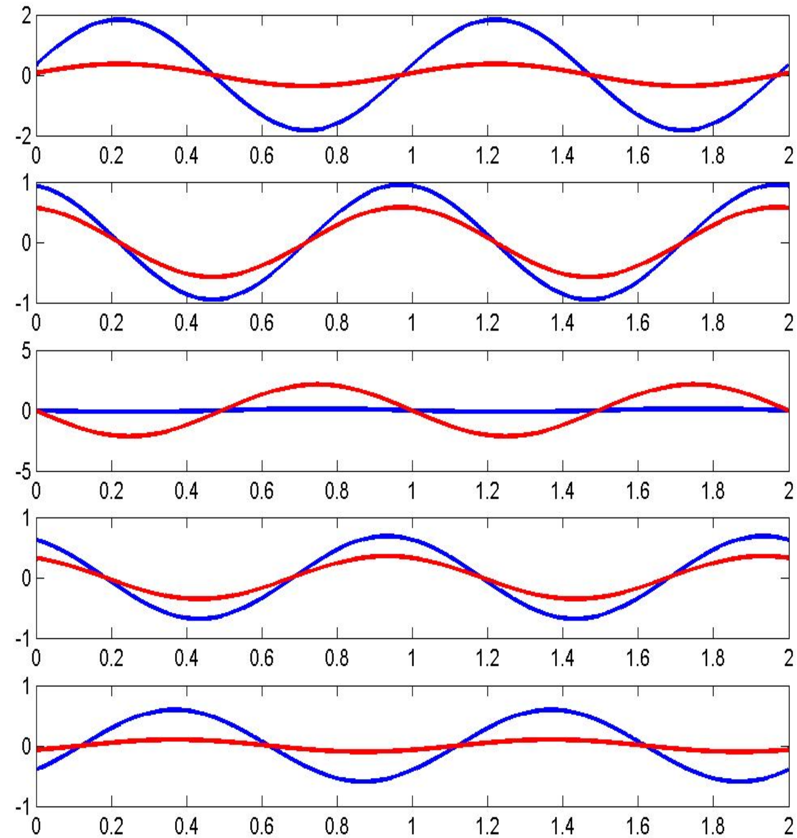
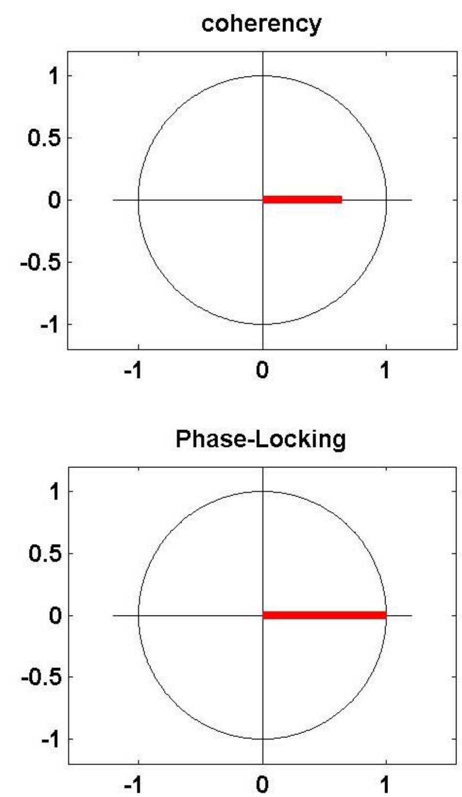
coherency
1
0.5
0
-0.5
-1
-1
0
1
Phase-Locking



1
0
-1
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
2



coherency
Phase-Locking
1
0.5
0
-0.5
-1
-1
0
1



coherency
Phase-Locking

2. The problem of volume conduction:

Data:

$$z_i(f,k)$$

Channel

Frequency

Epoch

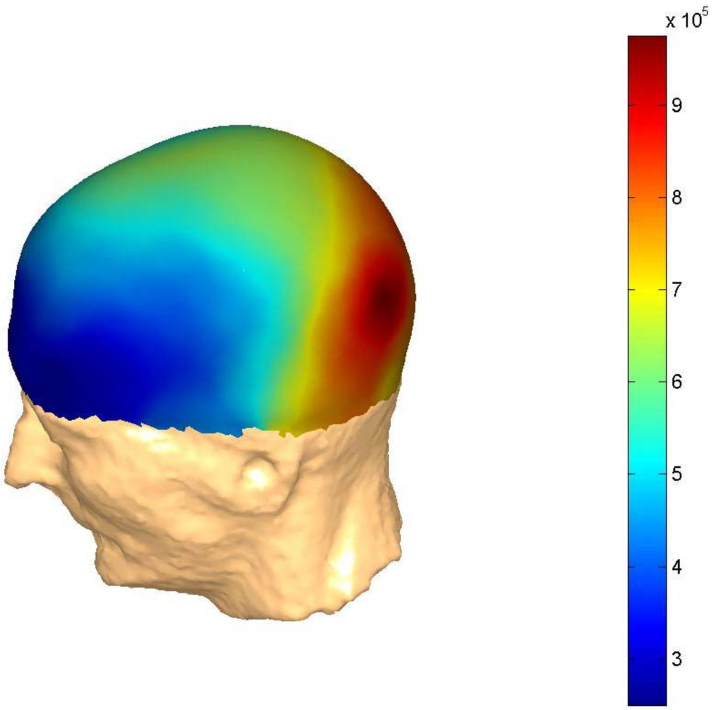
Cross-spectrum:

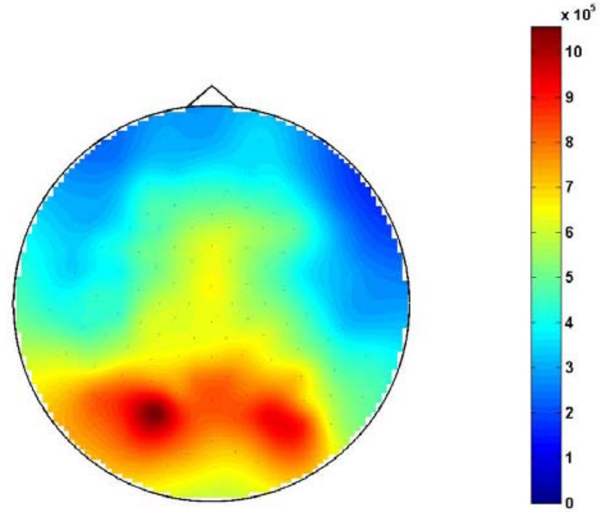
$$S_{ij}(f) = \frac{1}{K}\sum_{k=1}^{K} z_i(f,k) z_j^*(f,k)$$

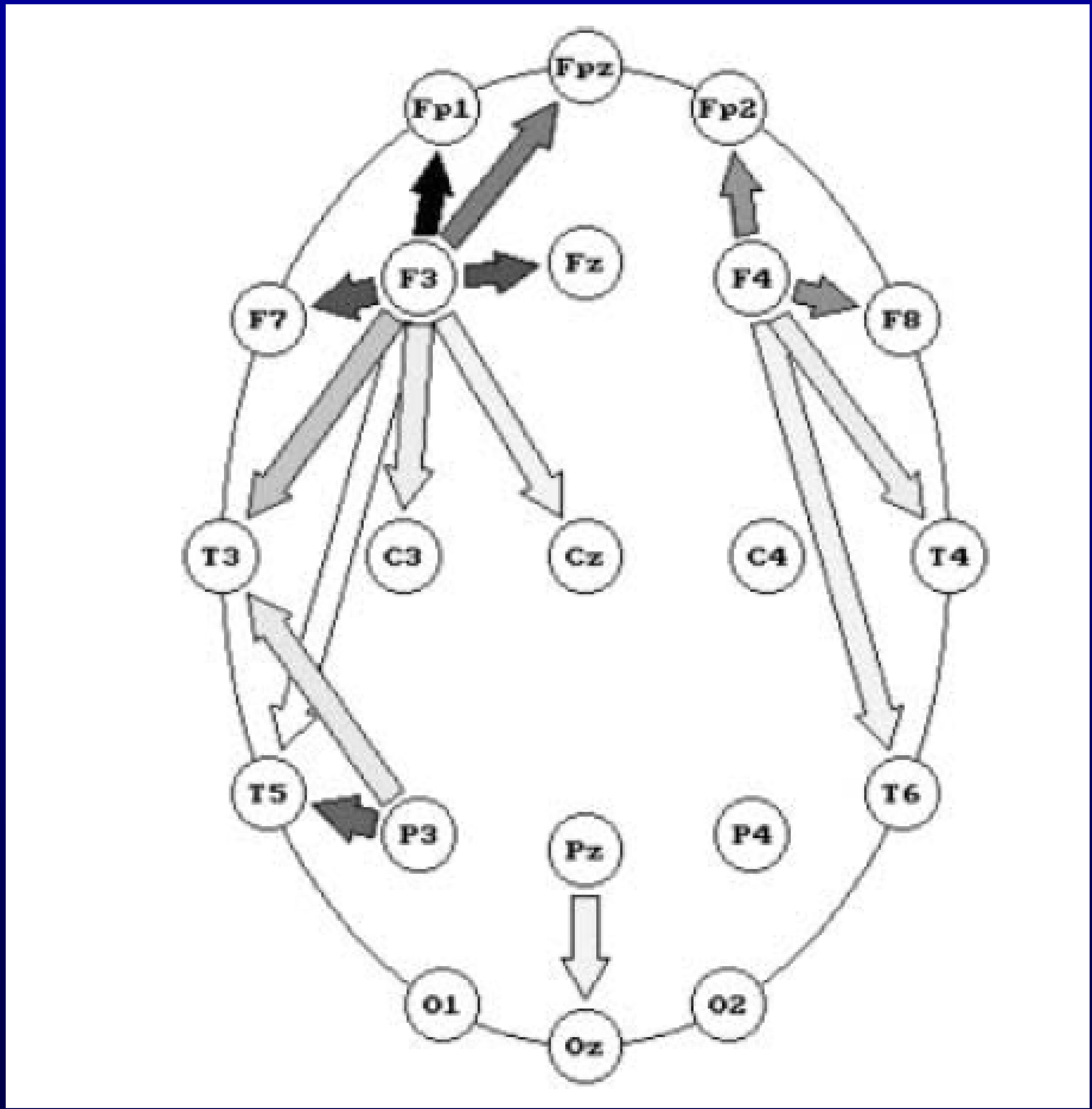
Coherency:

$$C_{ij}(f) = \frac{S_{ij}(f)}{\sqrt{S_{ii}(f) S_{jj}(f)}}$$

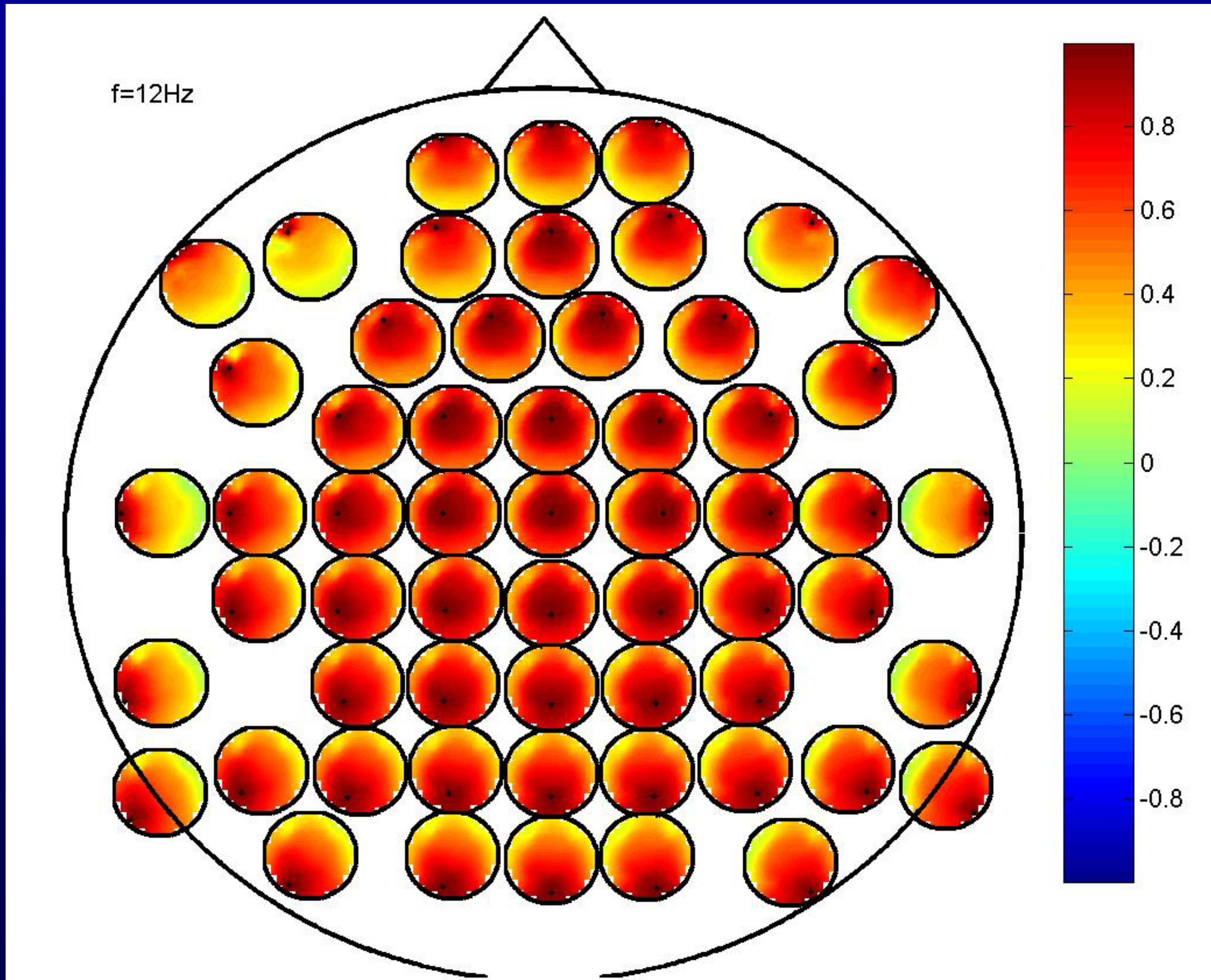
Power at 10 Hz



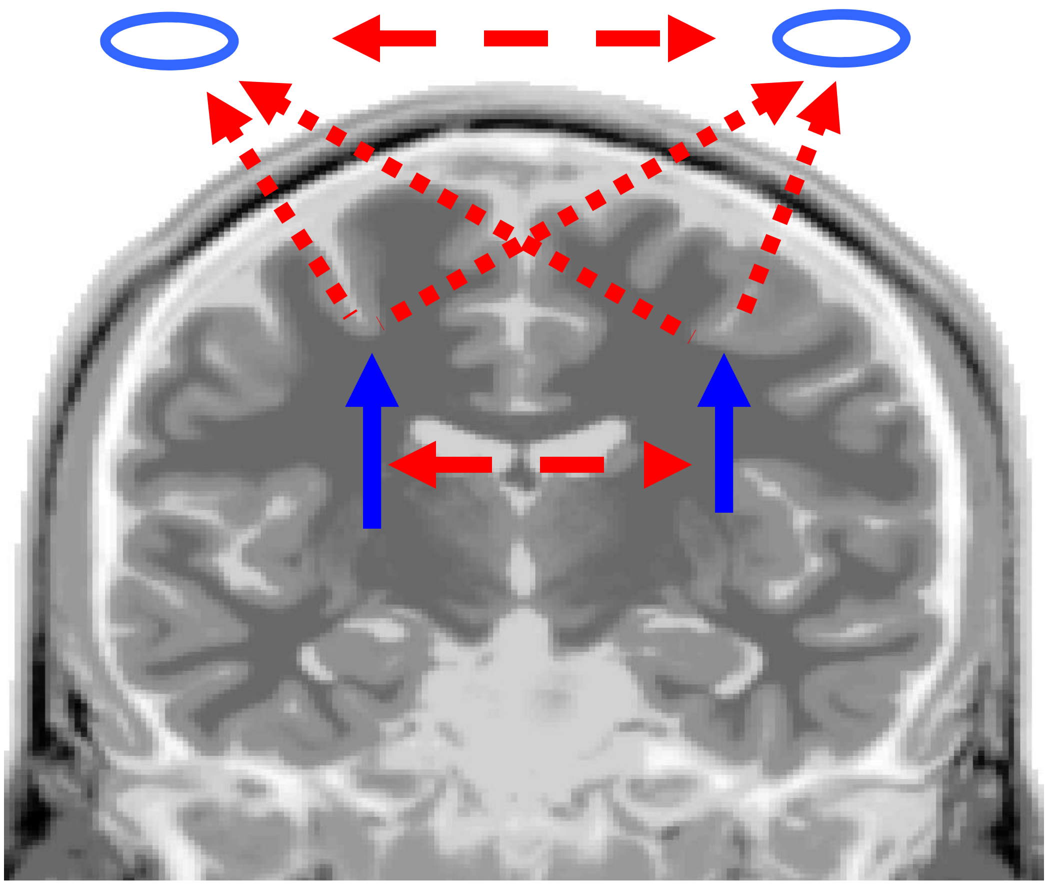



Fpz
Fp1
Fp2
F3
Fz
F4
F7
F8
T3
C3
Cz
C4
T4
T5
P3
Pz
P4
T6
O1
Oz
O2

Rest Coherence

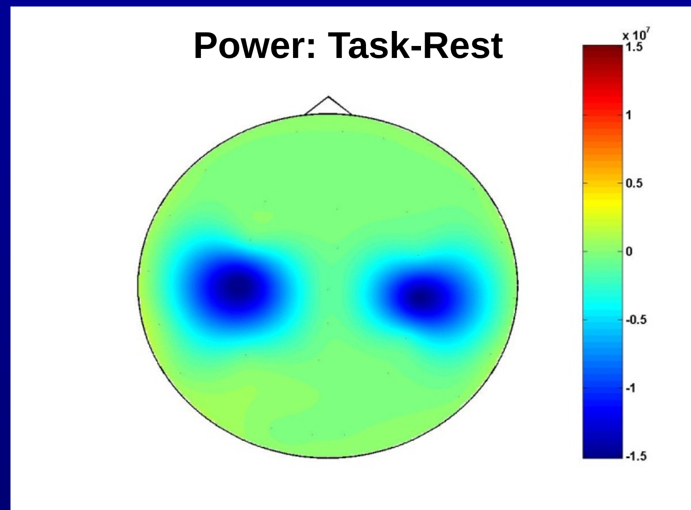


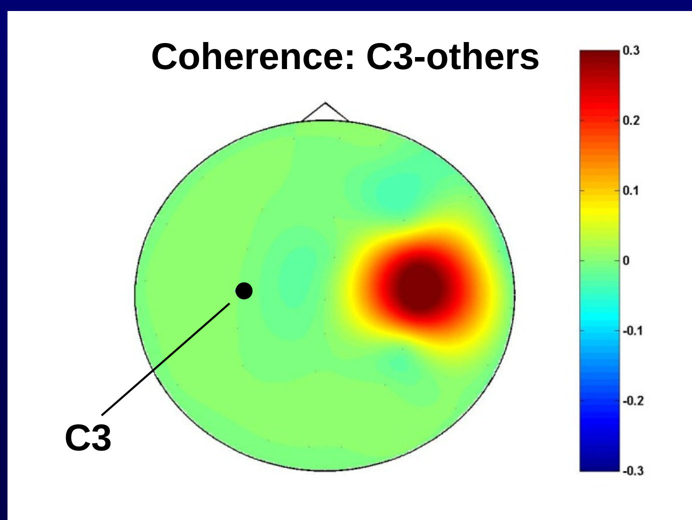
The Problem of volume conduction

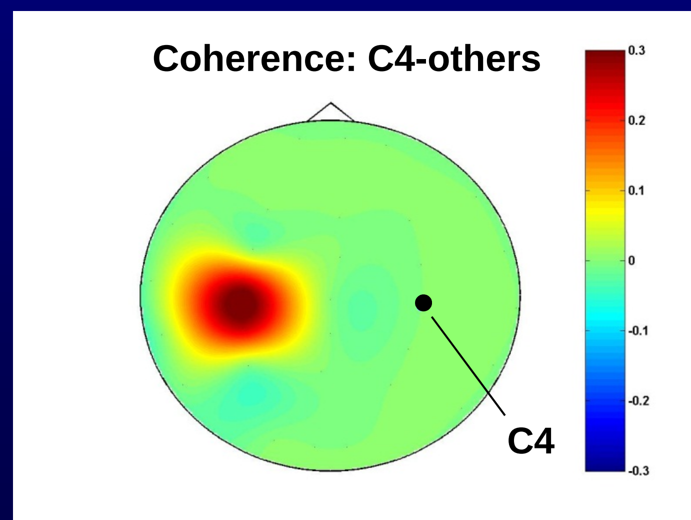


EEG-simulation of ERD (two sources)

Rest: Real background + simulated dipoles
Task: Real background







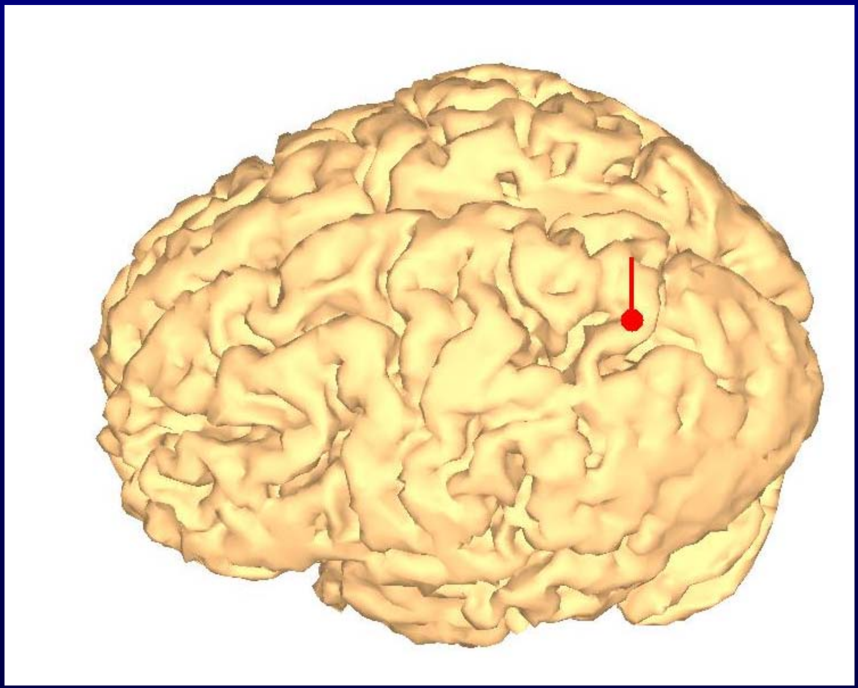
Fake!! Sources were indepent!!

EEG-simulation of ERD (1 source)

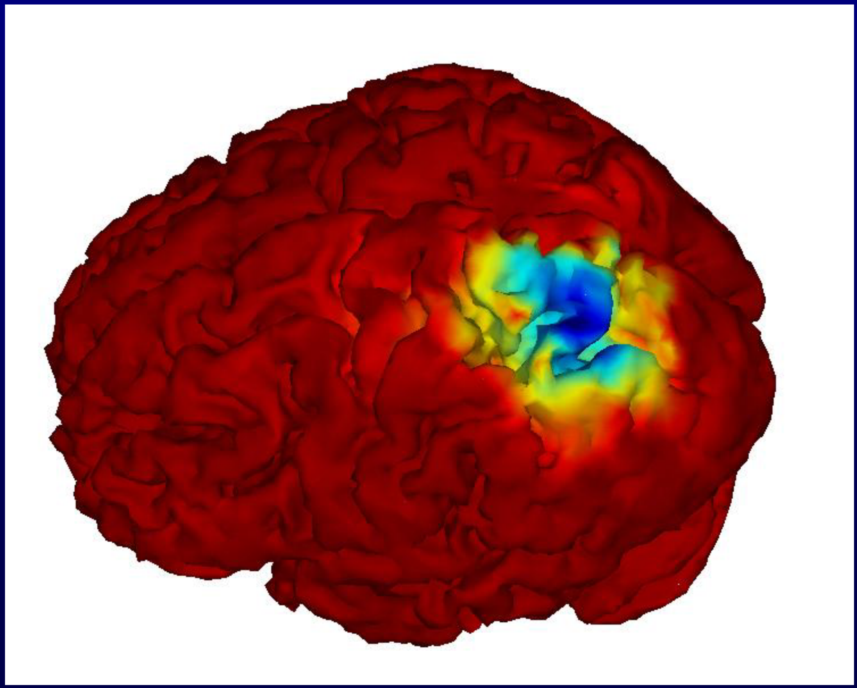
Rest: Real background + simulated dipole
Task: Real background

Inverse using beamformer (DICS) on cortex

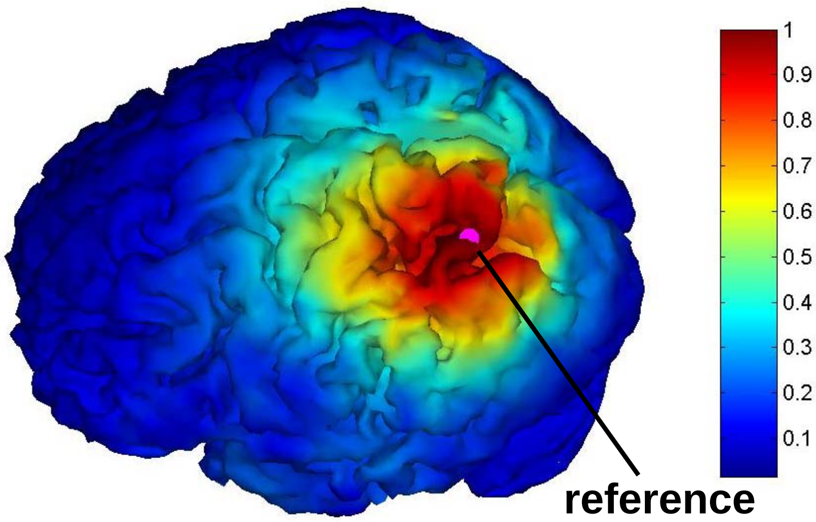
Simulated dipole



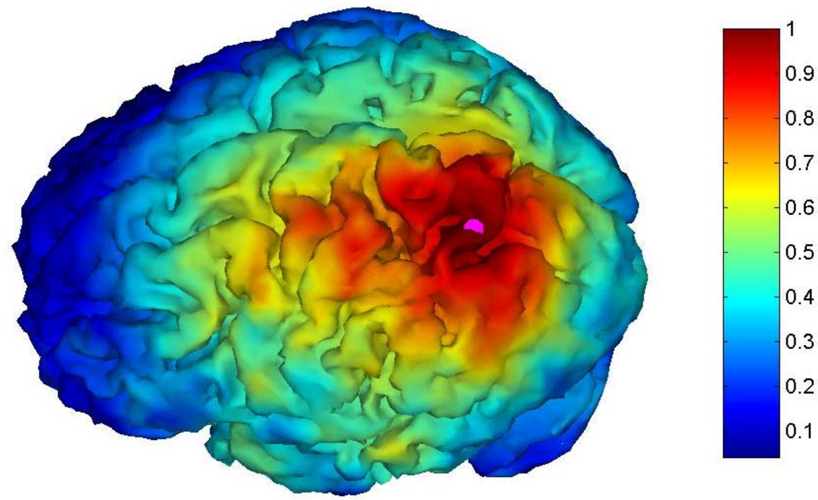
Estimated power ratio: Task/Rest



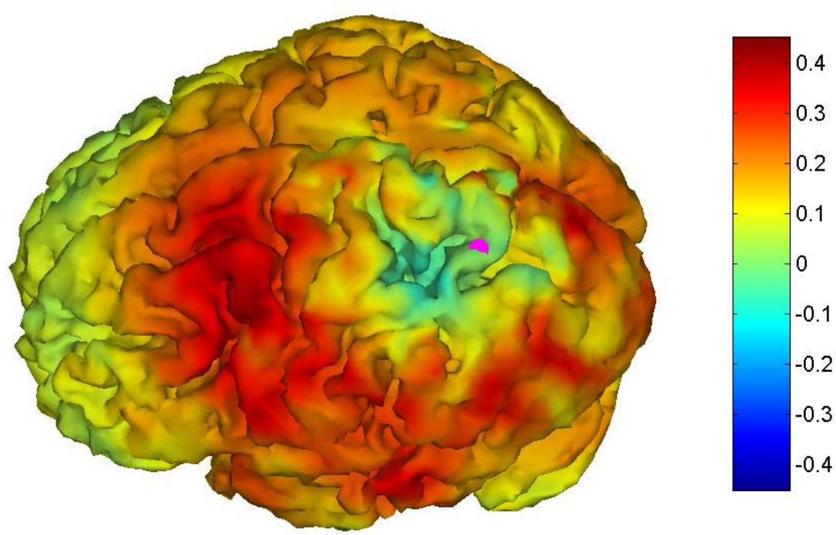
Coh., signal+background



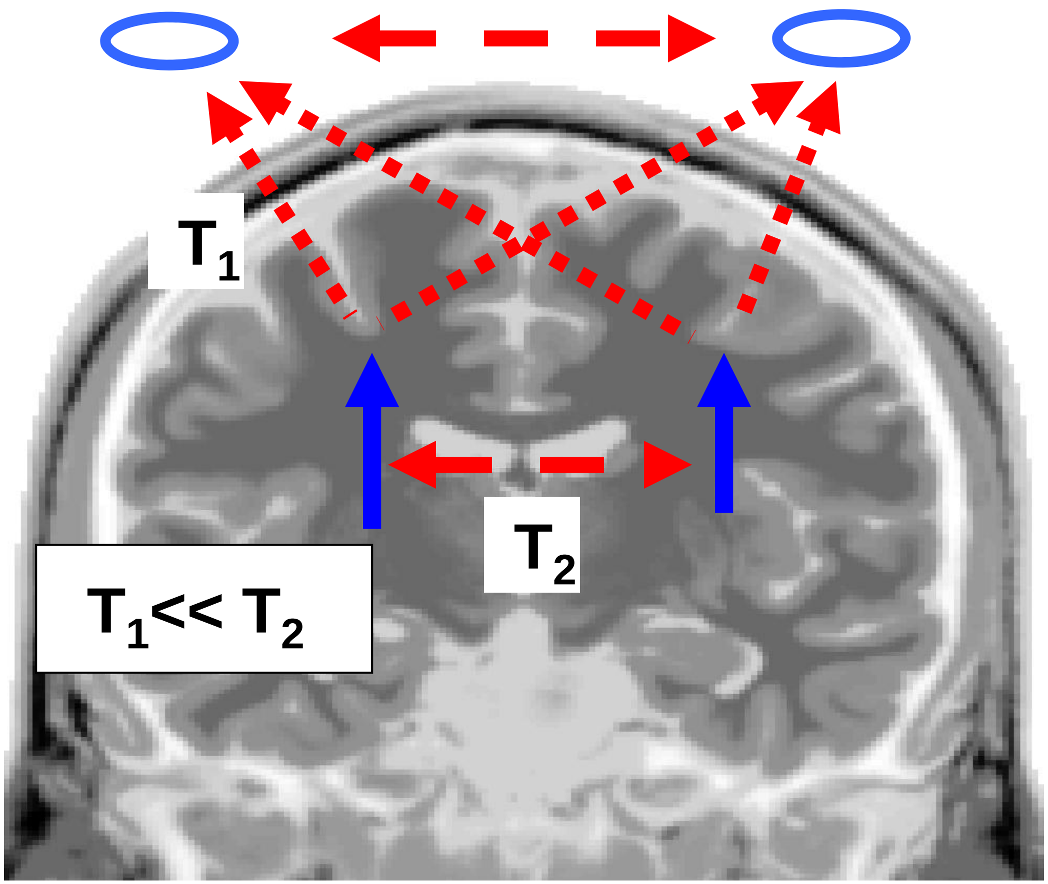
Coh., background

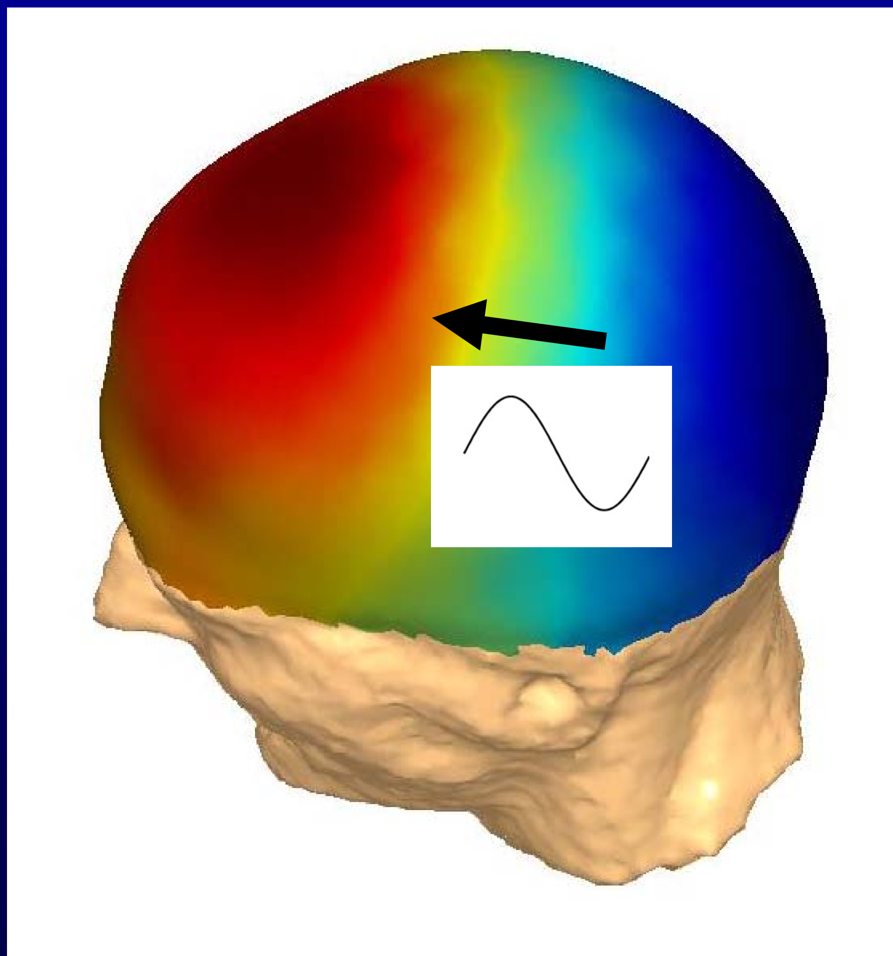


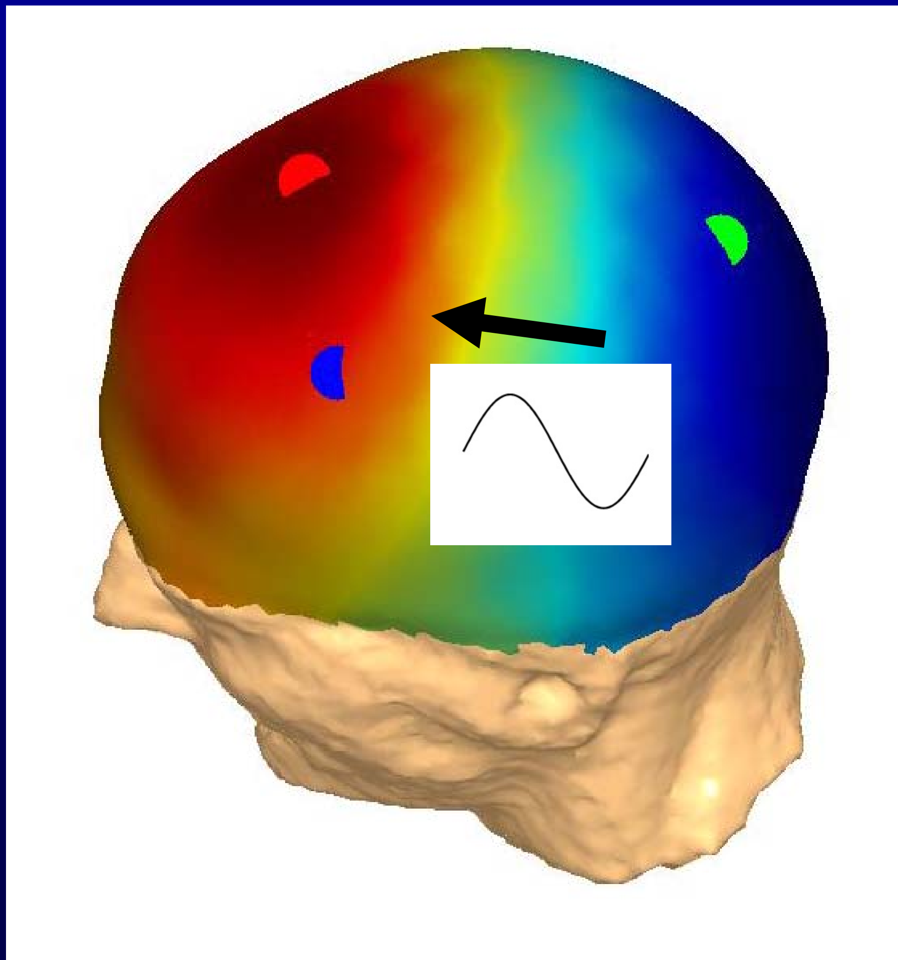
Coh., difference

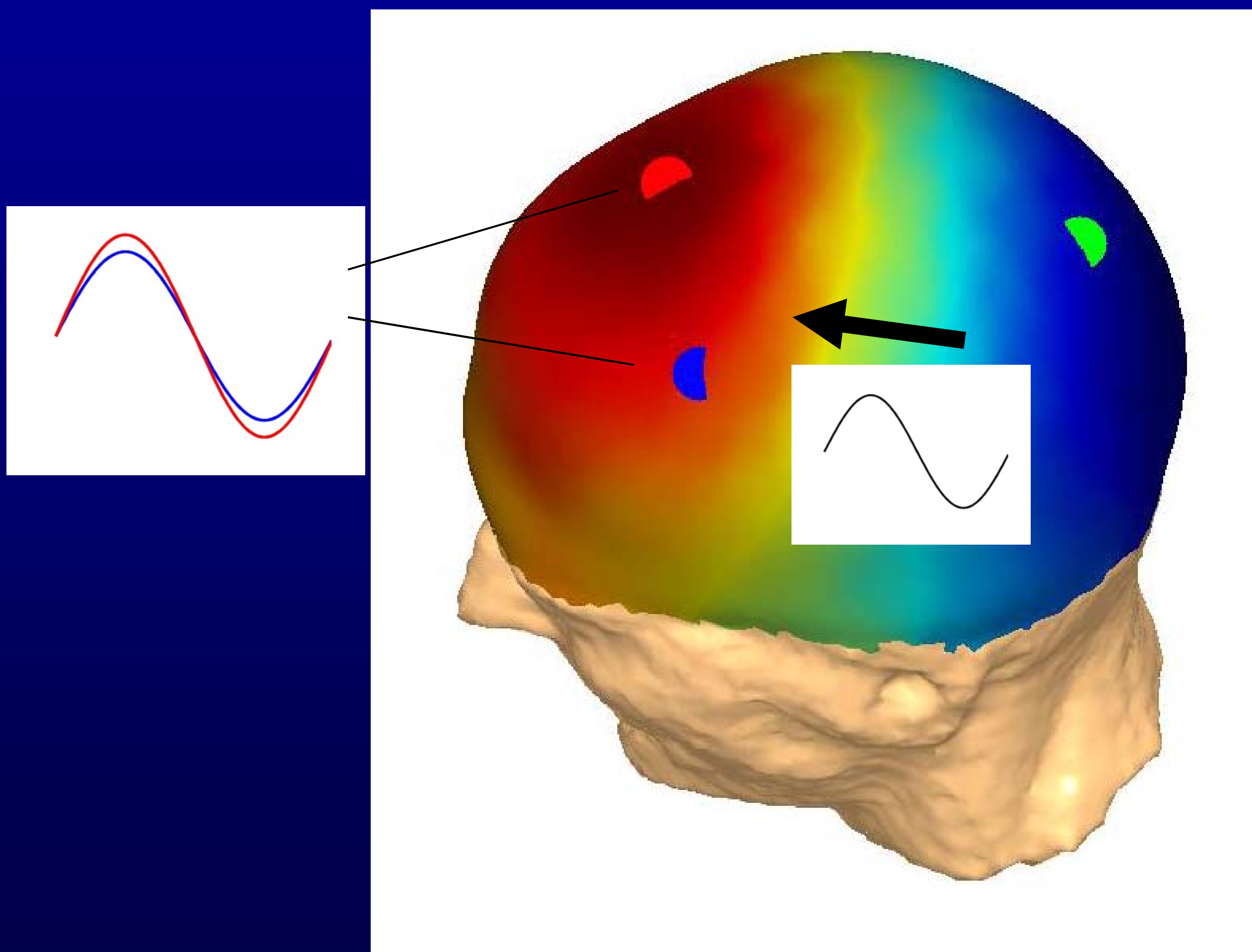


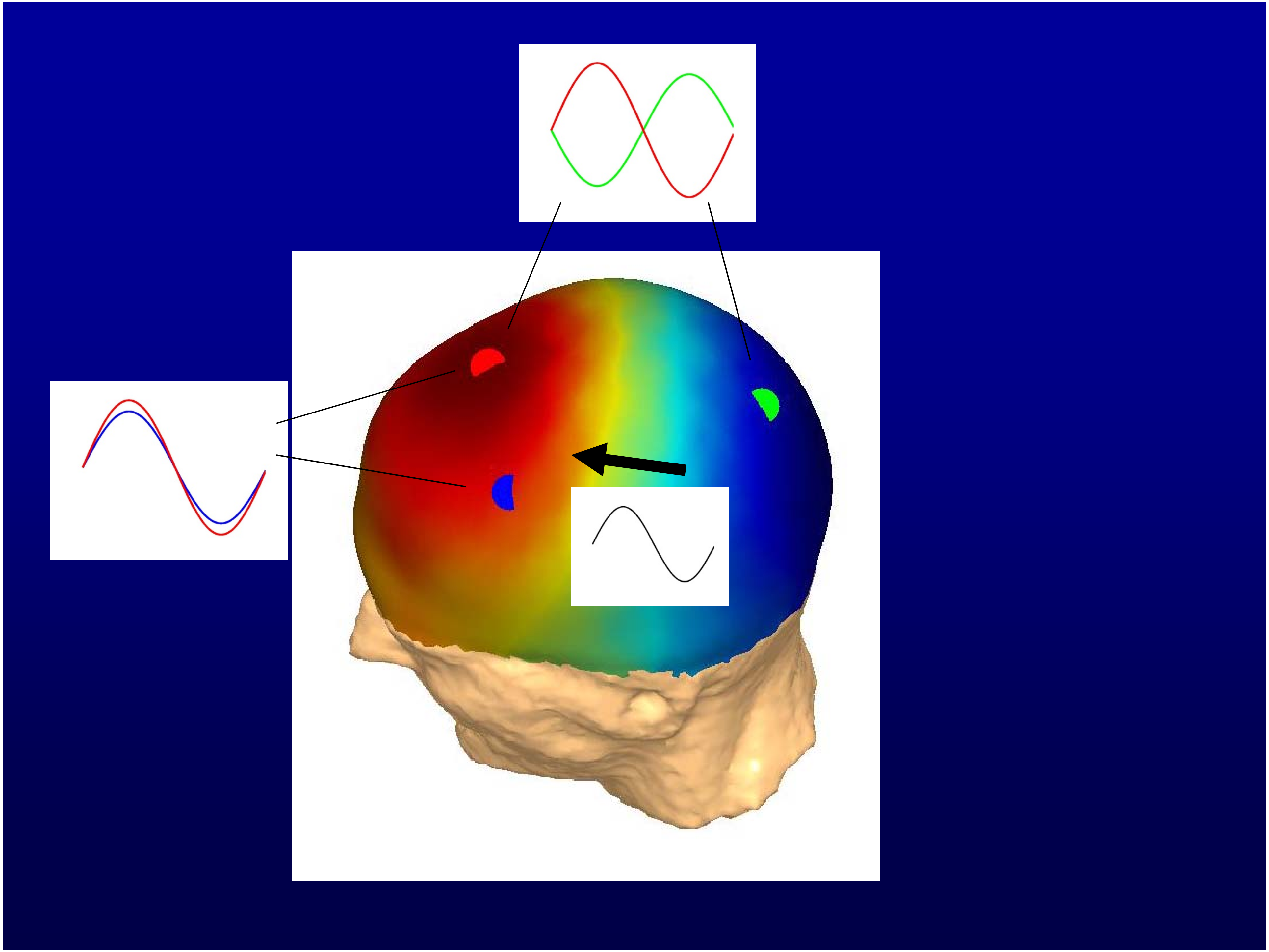
The role of the imaginary part of coherency

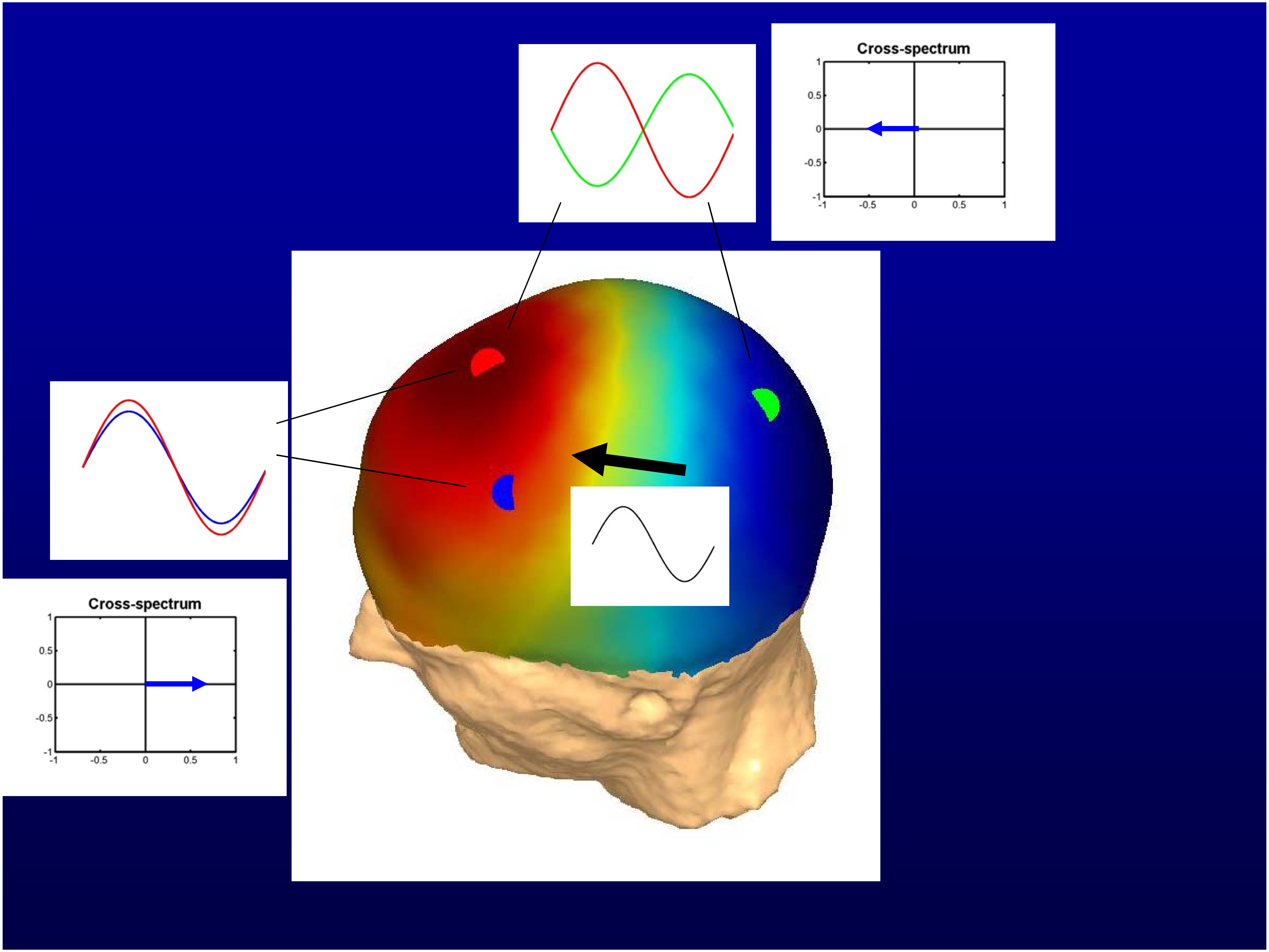










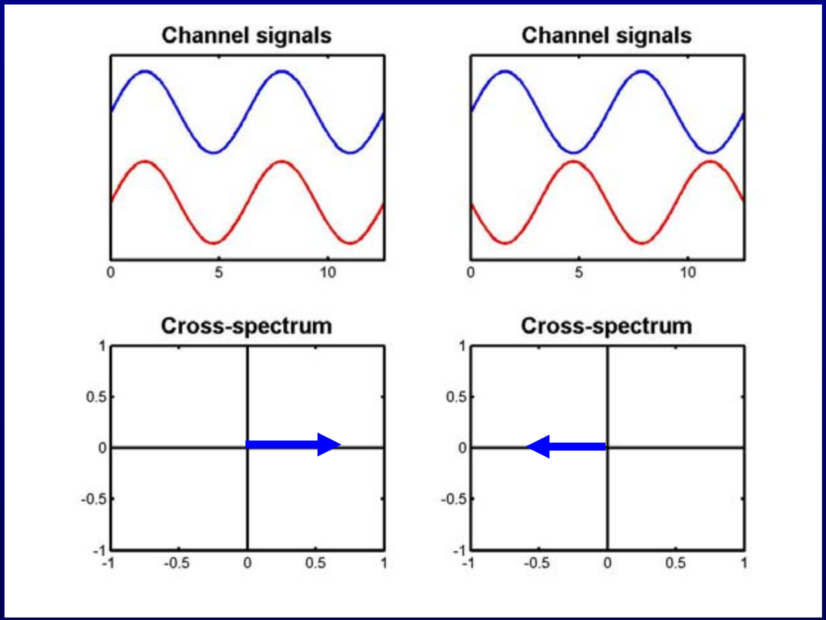


Cross-spectrum
1
0.5
0
-0.5
-1
-1
-0.5
0
0.5
1
Cross-spectrum
1
0.5
0
-0.5
-1
-1
-0.5
0
0.5
1

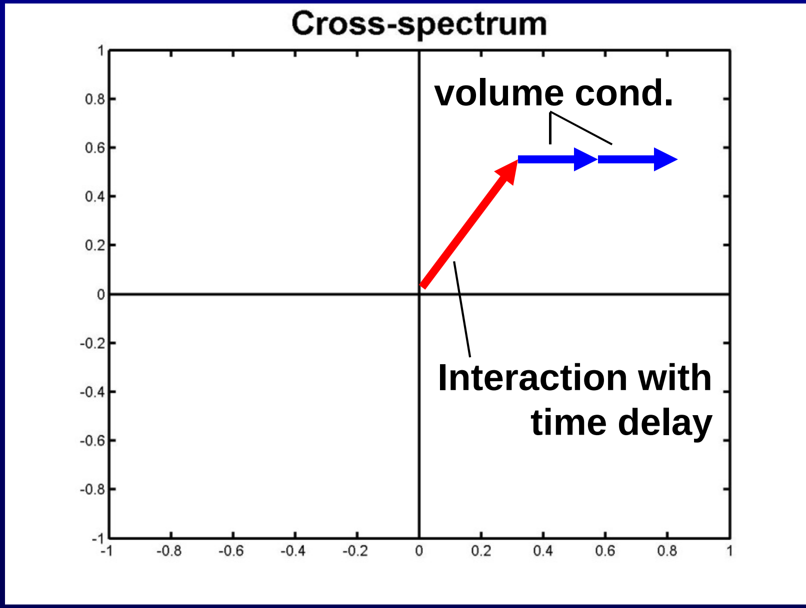
Observation:

Independent sources do not contribute to the imaginary part of the cross-spectrum

1 (non-interacting) source

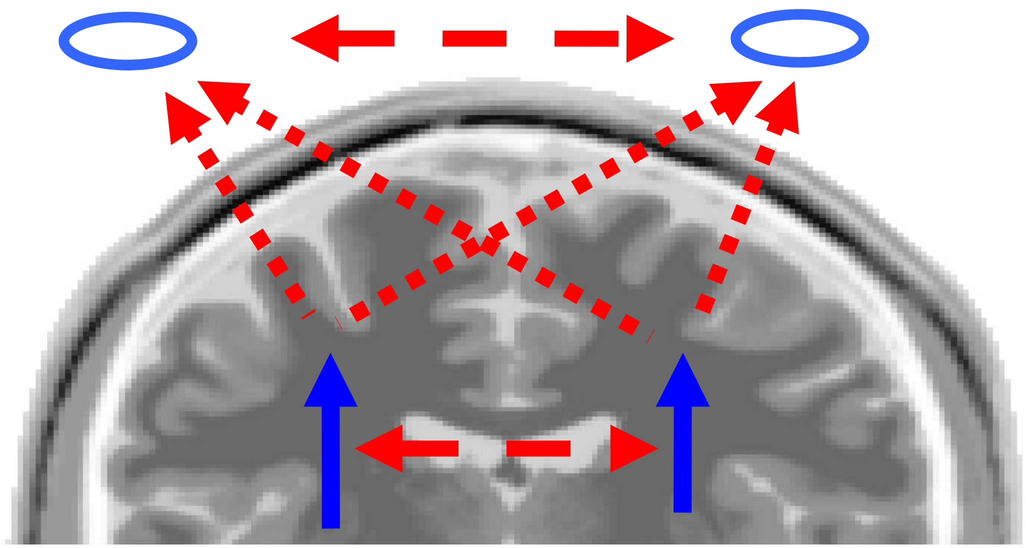


Many sources



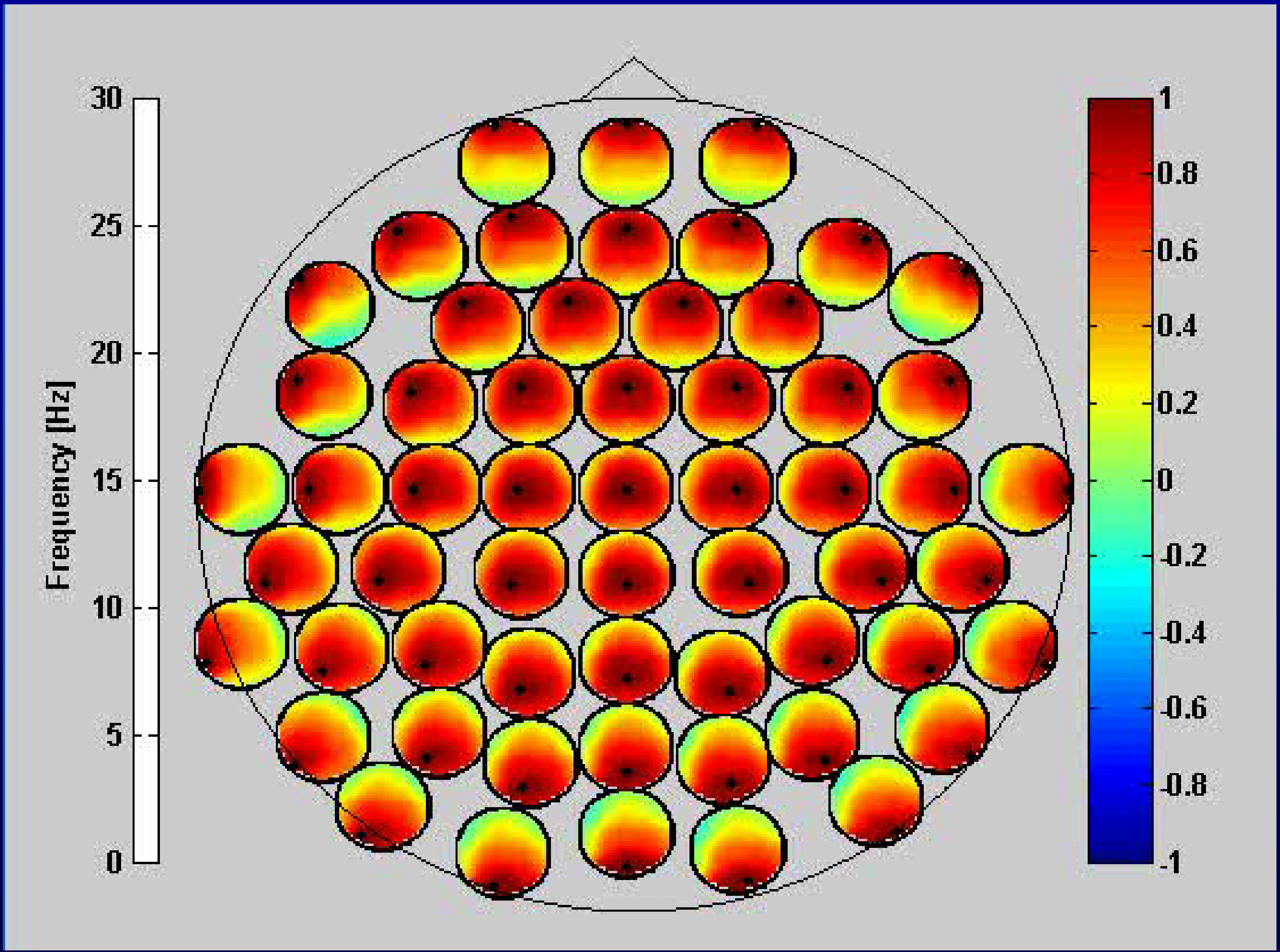
Independent sources do not contribute to the imaginary part of the cross-spectrum

$$S_{12}(f) = \mathrm{Re}(S_{12}(f)) + i\,\mathrm{Im}(S_{12}(f))$$

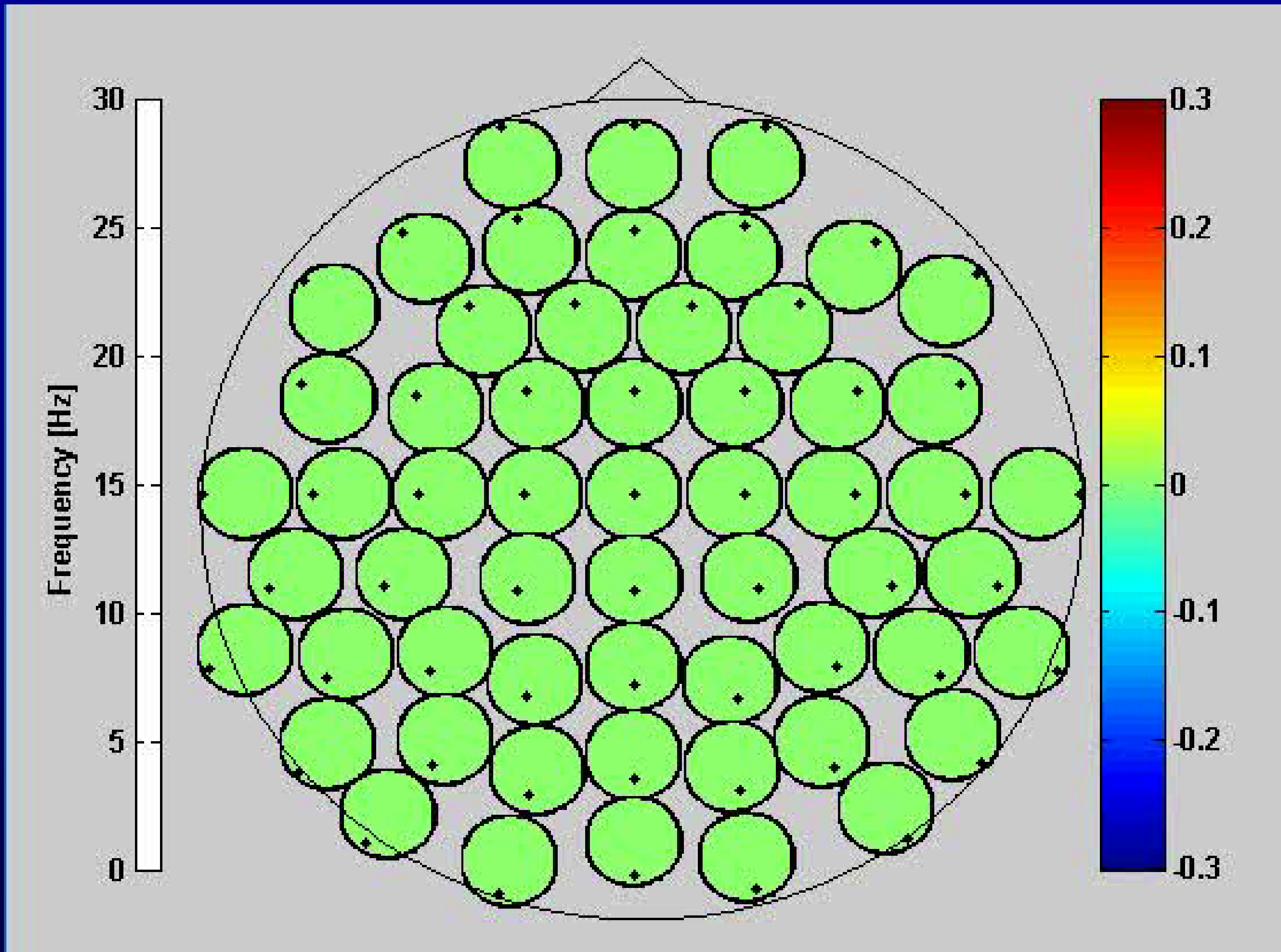


$$S = L \begin{pmatrix} P_1 & 0 & \cdots & 0 \\ 0 & P_2 & \cdots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \cdots & P_M \end{pmatrix} L^T$$

Real part of coherency = correlation at given frequency

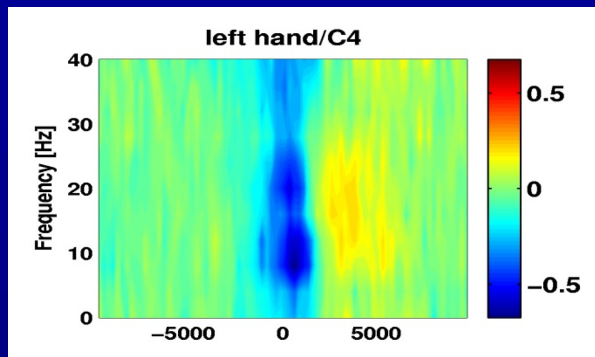


Imaginary part of coherency

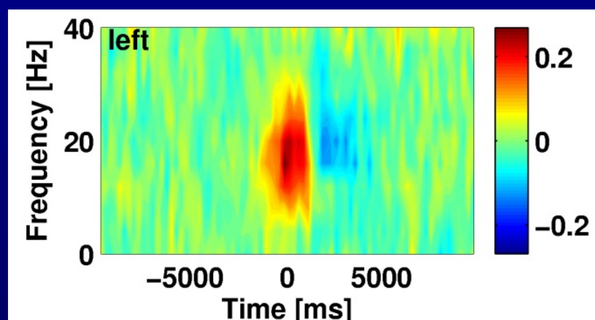


Selfpaced movement, C3-C4 relationships

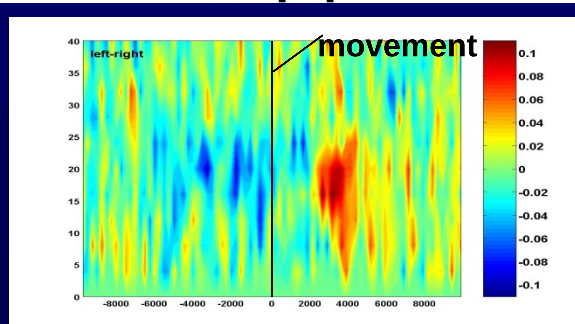
Power



Coherence



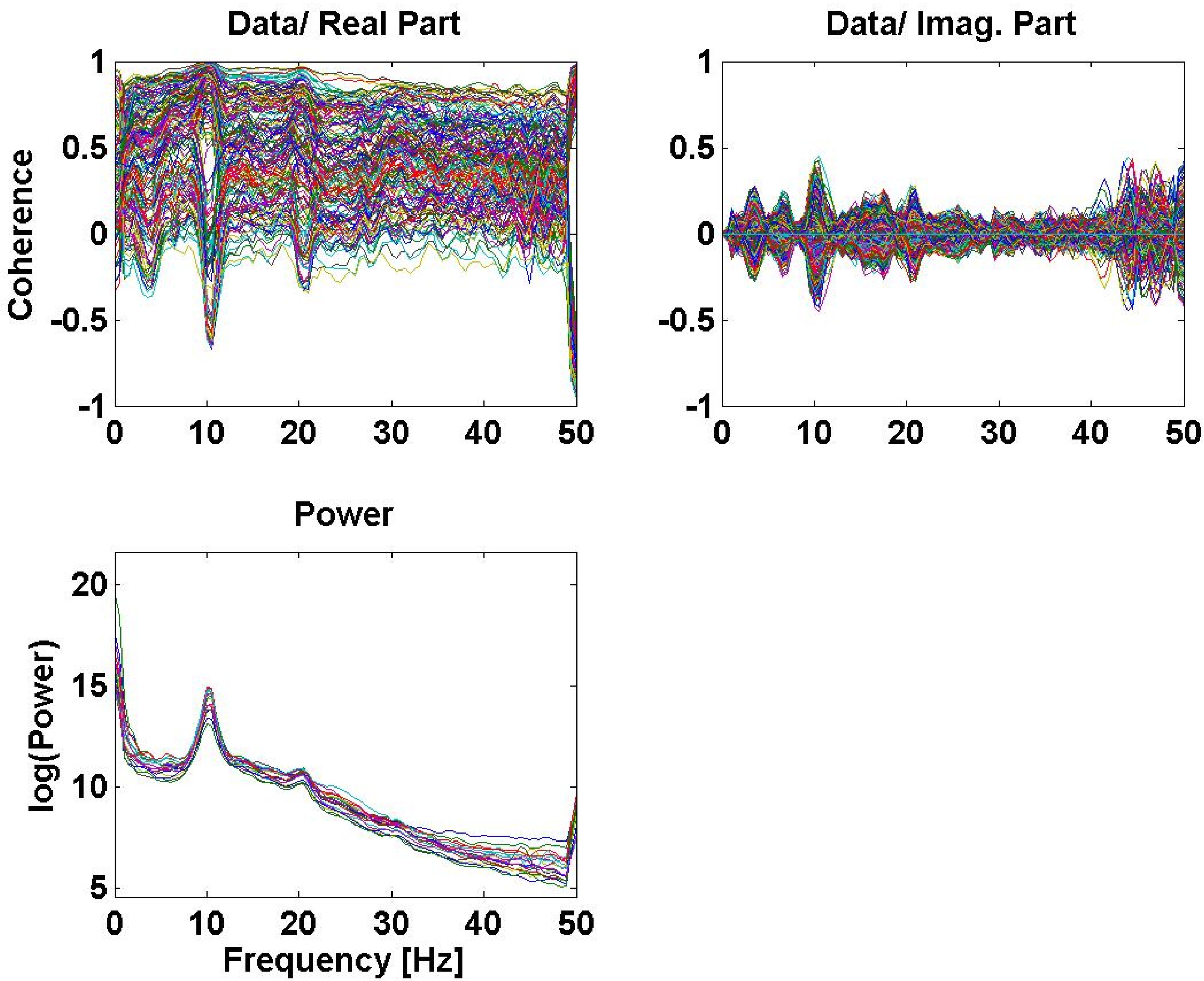
Imaginary coherency



Observations:

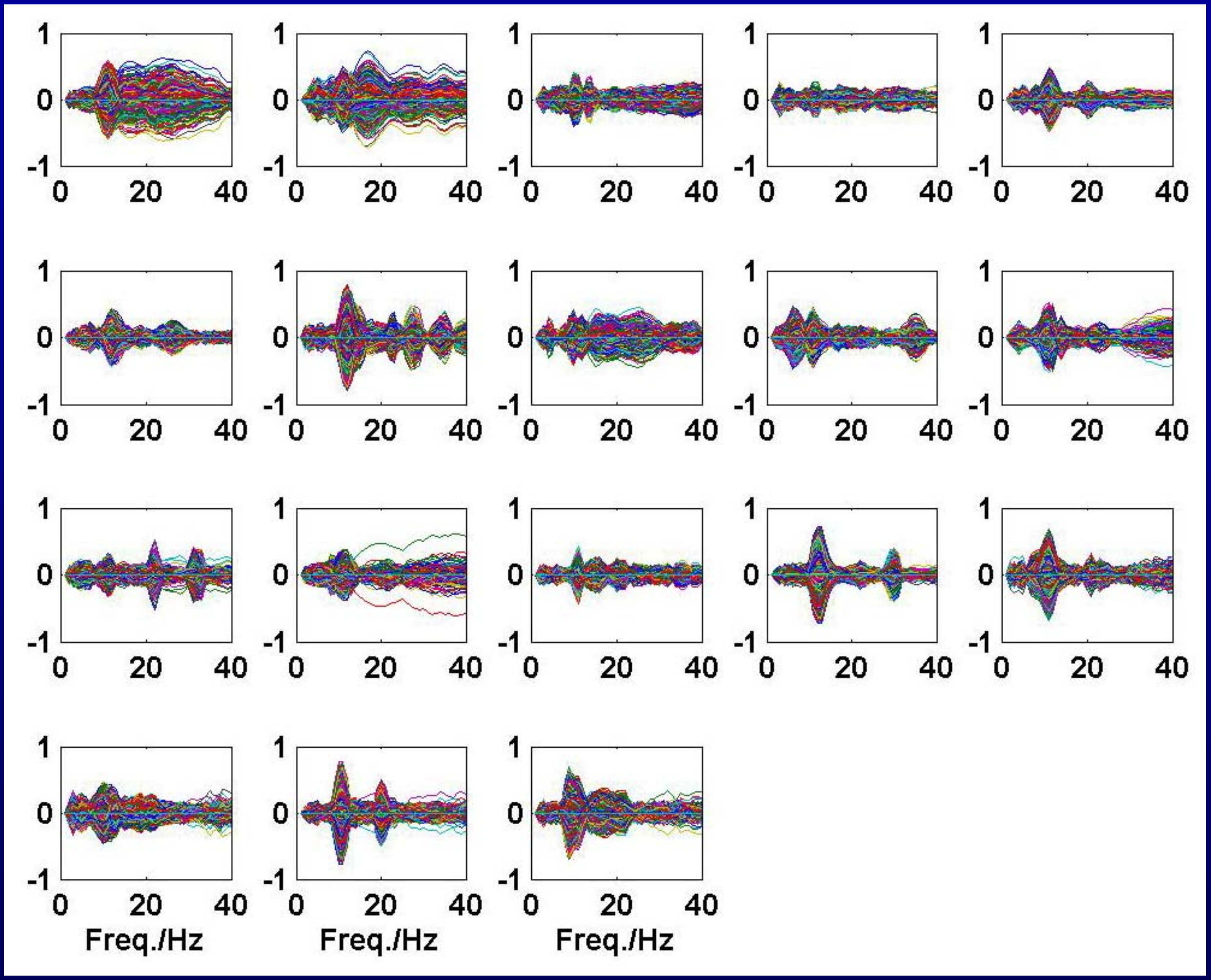
- coherence follows power
- imaginary part has onset 5 secs before movement
- imaginary part not related to power

Nolte, et.al., Clinic. Neurophys., 2004

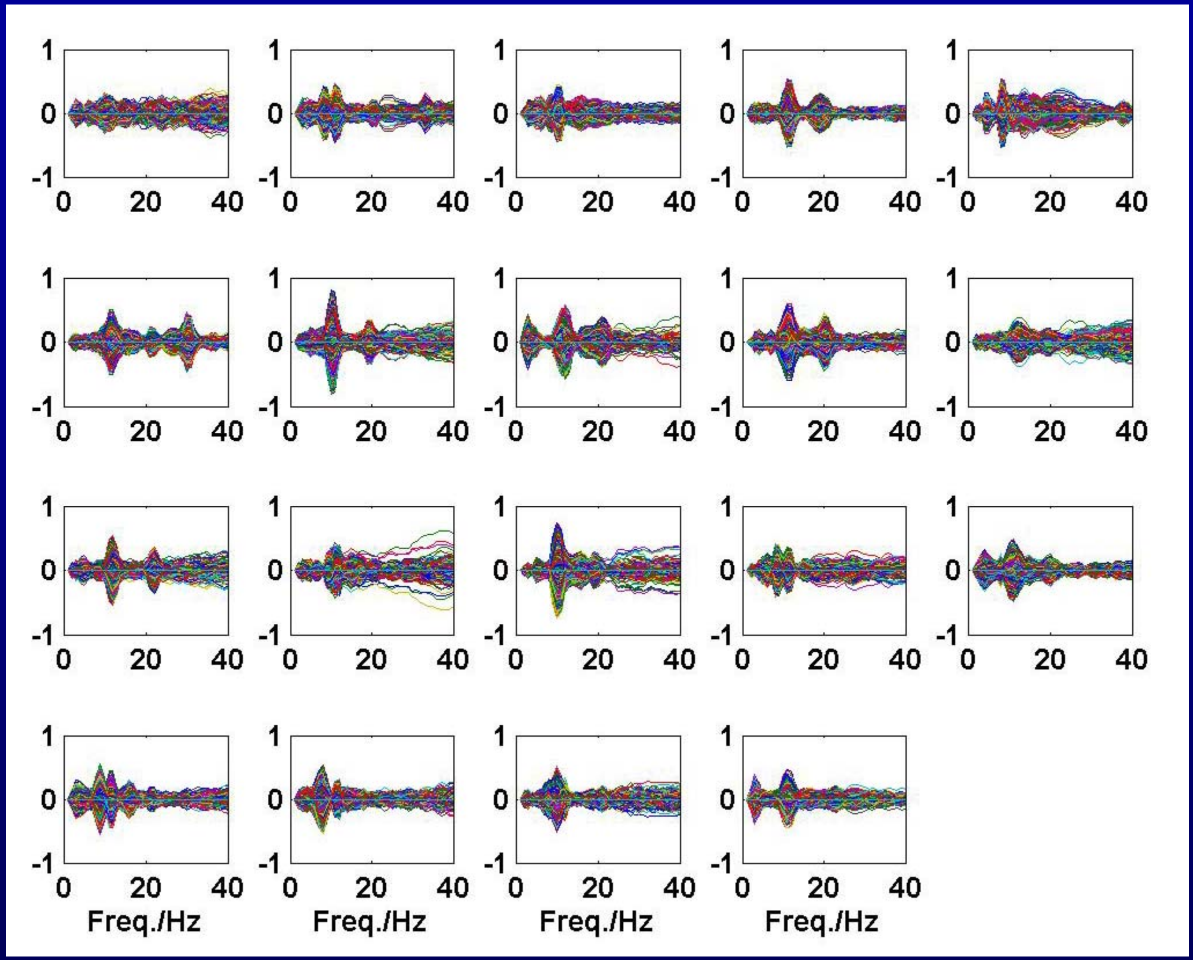


Data/ Real Part
Coherence
1
0.5
0
-0.5
-1
0
10
20
30
40
50
Data/ Imag. Part
1
0.5
0
-0.5
-1
0
10
20
30
40
50
Power
log(Power)
20
15
10
5
0
10
20
30
40
50
Frequency [Hz]

Normal subjects, eyes closed, ImCoh



Schizophrenic patients, eyes closed, ImCoh



- Huge variability across subjects
- Schizophrenics more regular than controls??

Methods based on imaginary parts of cross-spectra

- **Decomposition into subspaces ('PISA')**
- **Decomposition of source distributions ('MOCA')**
- **Causality ('PSI')**

1. Surrogate Data

Preserve everything except quantity of interest

- **Create data from *non-interacting* sources**
- **As close to actual data as possible**

Here: Use Independent Component Analysis (ICA) to construct surrogate data

Shahbazi et. al., Biomag 2010

Surrogate Data to test for artefacts of volume conduction

Data $\vec{x}(t) = \left(x_1(t), \ldots, x_n(t)\right)$

1. Demix with ICA $\qquad \vec{s}(t) = W\vec{x}(t)$

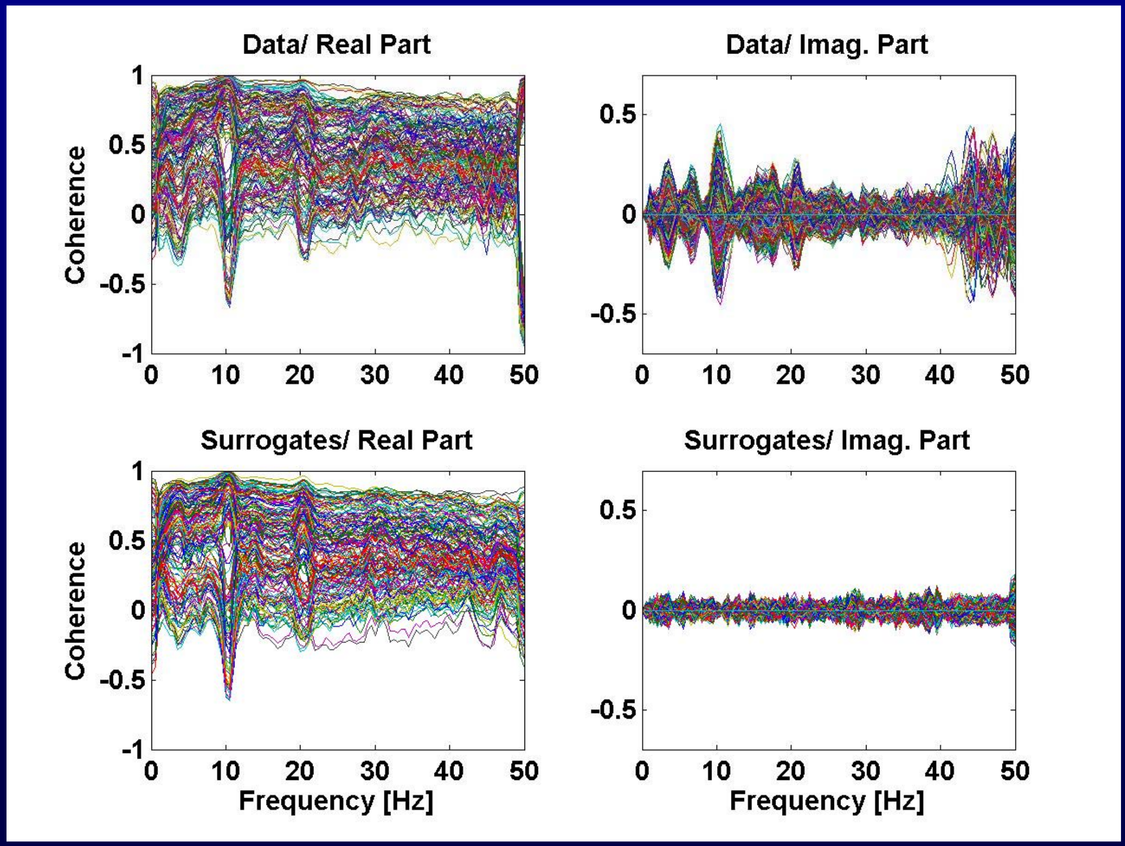
2. Delay i.th component by (i - 1) * T

$$v_1(t) = s_1(t)$$
$$v_2(t) = s_2(t+T)$$
$$v_3(t) = s_3(t+2T)$$
$$\vdots$$

3. Remix $\qquad \vec{\mathrm{x}}_{\mathrm{surr}}(t) = W^{-1}\vec{v}(t)$

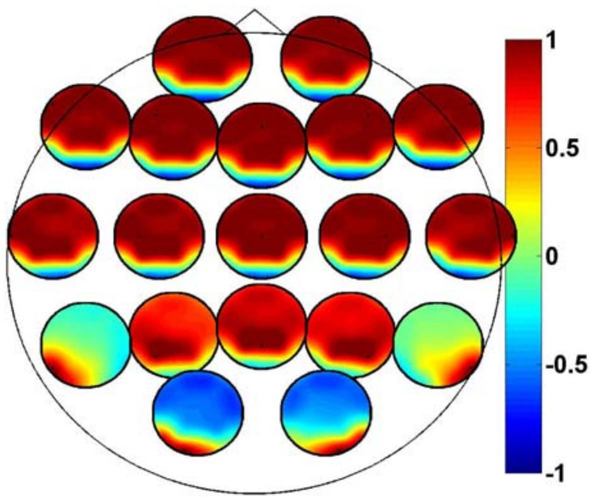
Cross-spectrum $$S_{ij}(f) = \left\langle z_i(f) z_j^*(f) \right\rangle$$

Coherence $$C_{ij}(f) = \frac{S_{ij}(f)}{\left(S_{ii}(f) S_{jj}(f)\right)^{1/2}}$$

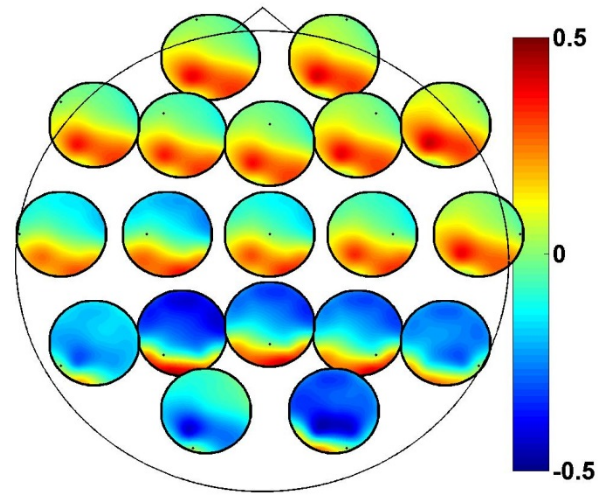


Coherence at 10Hz

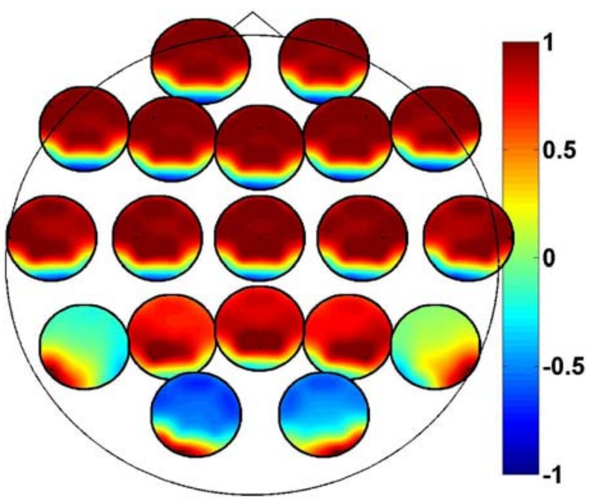
Data, Real Part



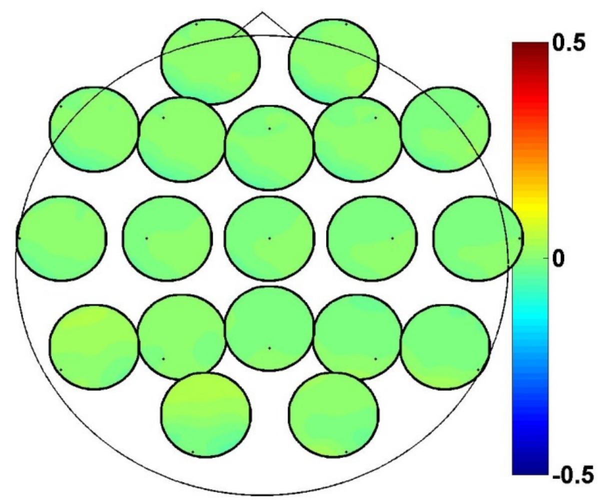
Data, Imag. Part



Surro, Real Part

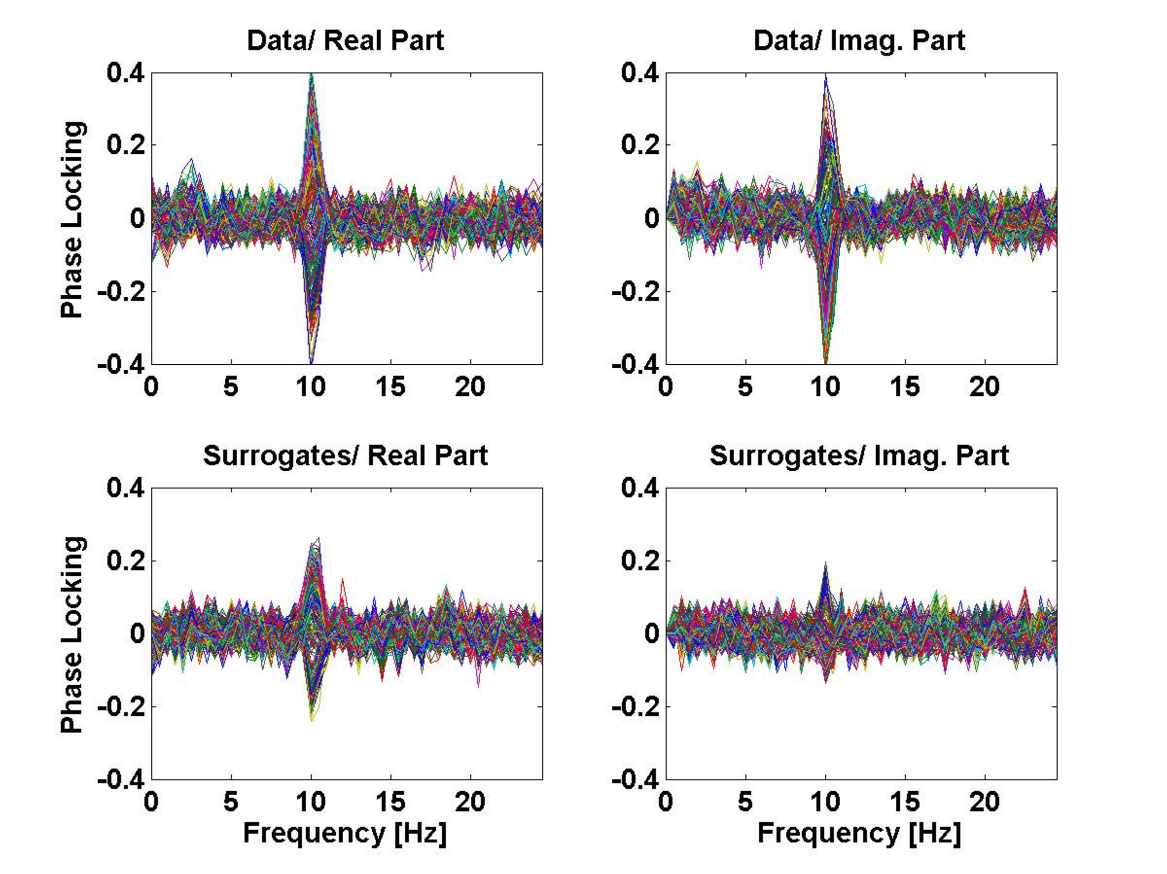


Surro, Imag. Part



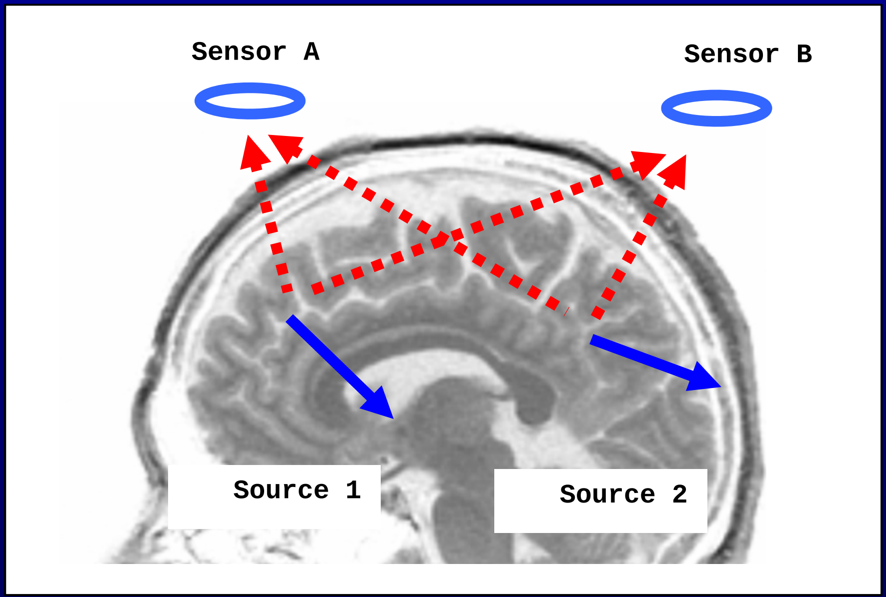
1:2 Phase Locking

$$PL_{ij}(f) = \left\langle \exp\left(i\left(2\Phi_i(f) - \Phi_j(2f)\right)\right)\right\rangle$$



2. Source orientation
(inverse here with eLORETA)

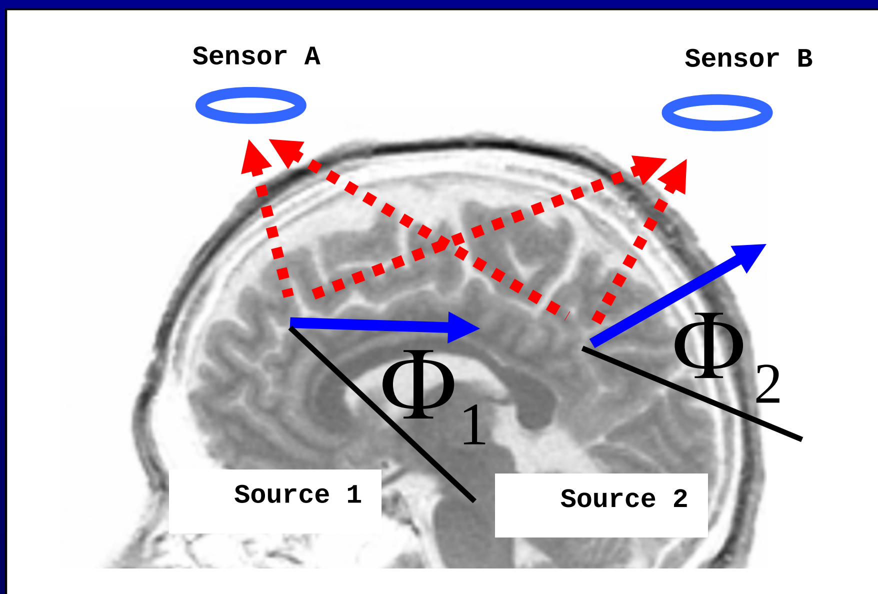
1. Fixe source direction to maximize power
2. Calculate connectivity measure

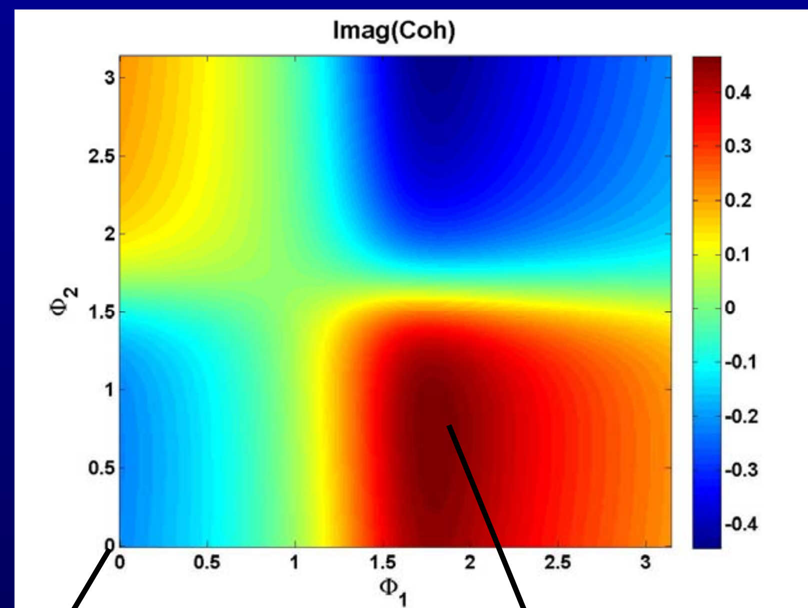


Problems

1. Interacting sources don‘t have to be strong
2. Poor spatial resolution -> short range interactions like volume conduction -> long range bias

2. Source orientation
(inverse here with eLORETA)

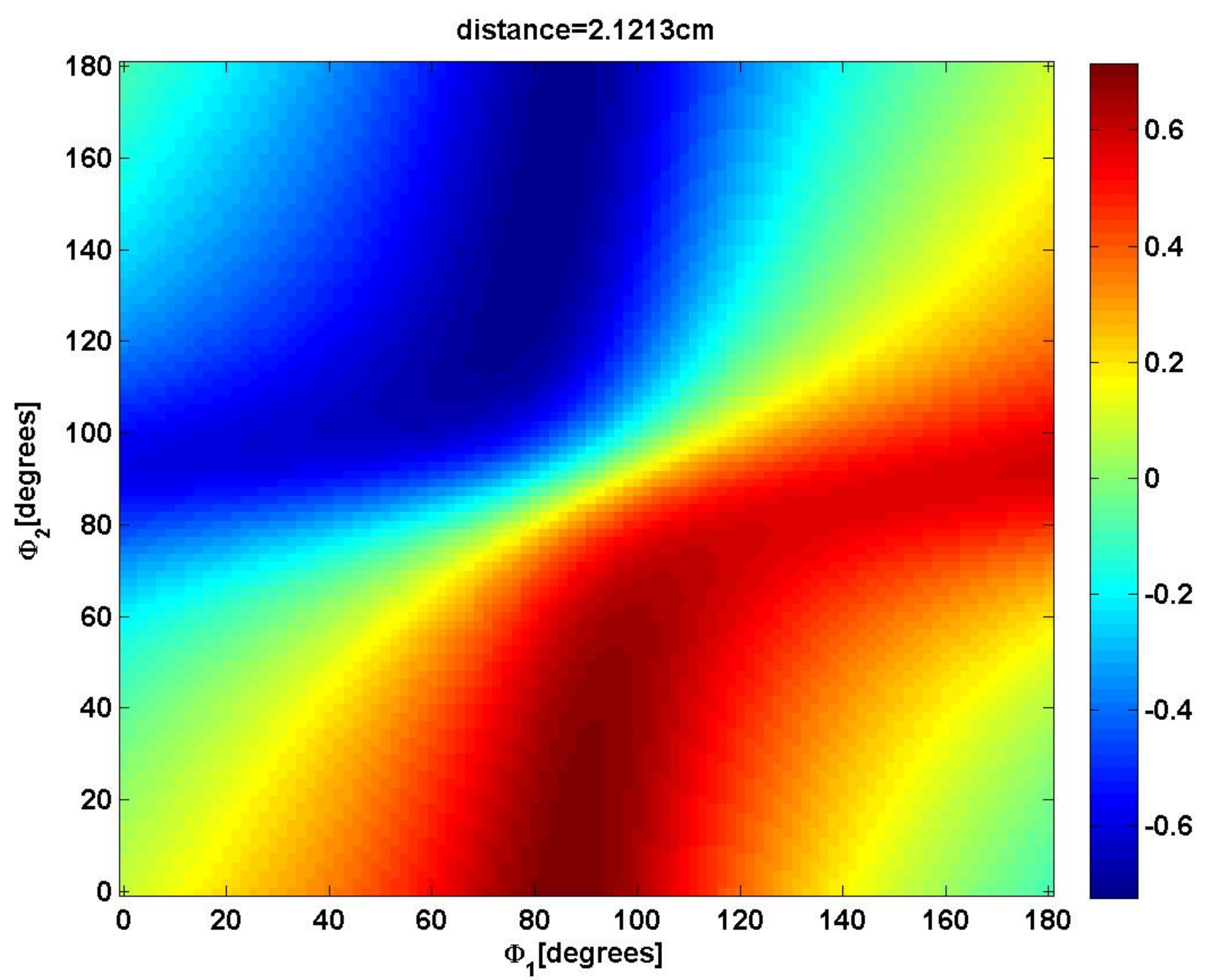


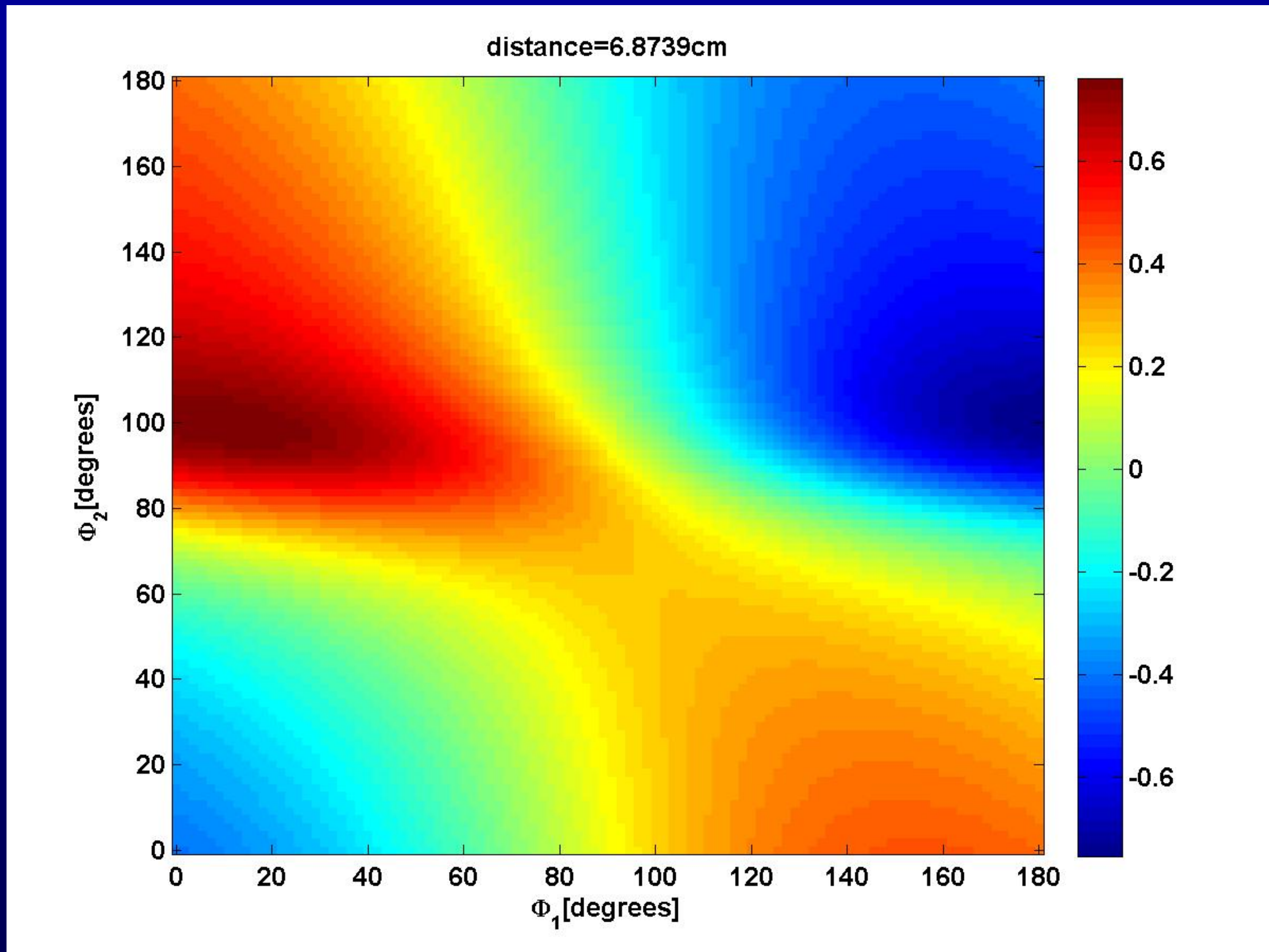


Fixed orientation **Maximal interaction**

For each voxel pair: select orientation which maximizes imaginary coherence.

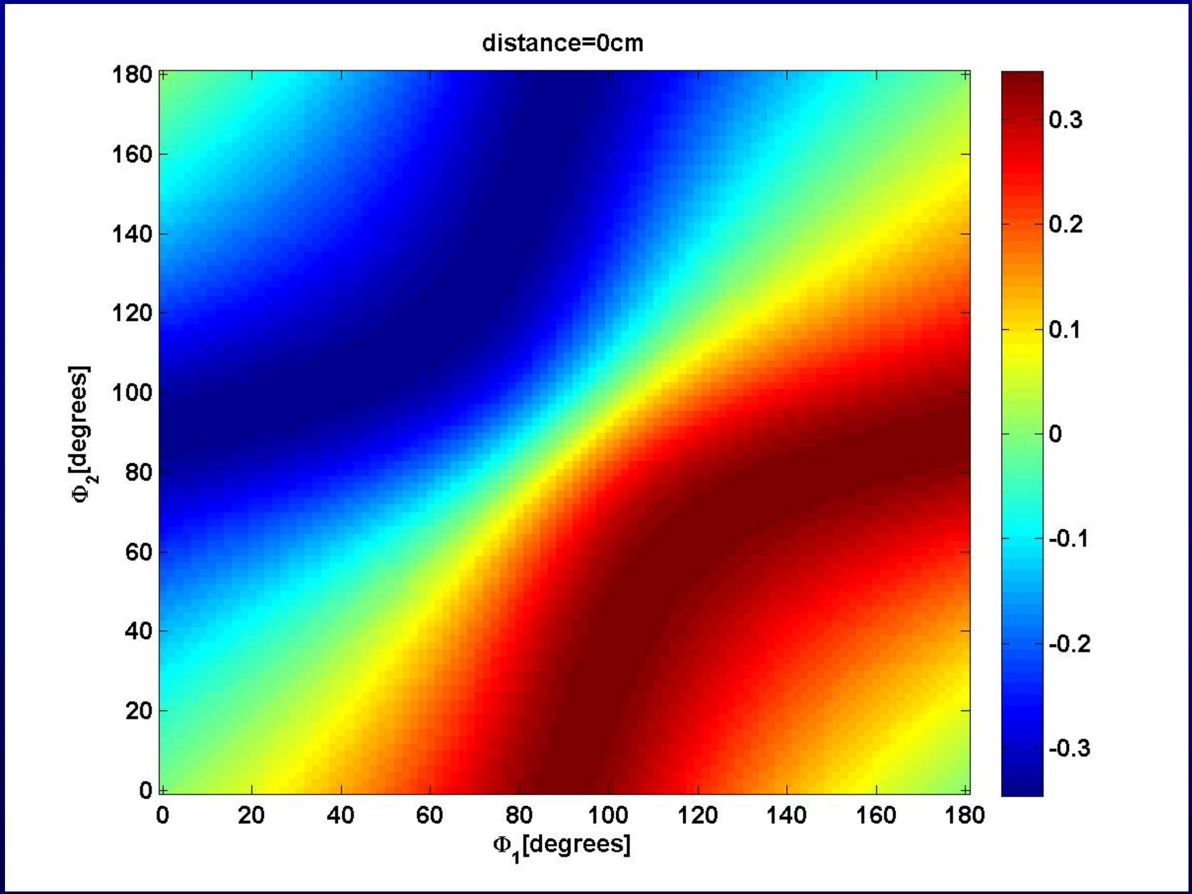
Ewald et. al., Neuroimage, 2012; Shahbazi et. al., Comput. and math. methods in medicine, *2012*


distance=2.1213cm
0
20
40
60
80
100
120
140
160
180
Φ_1[degrees]
Φ_2[degrees]
0.6
0.4
0.2
0
-0.2
-0.4
-0.6

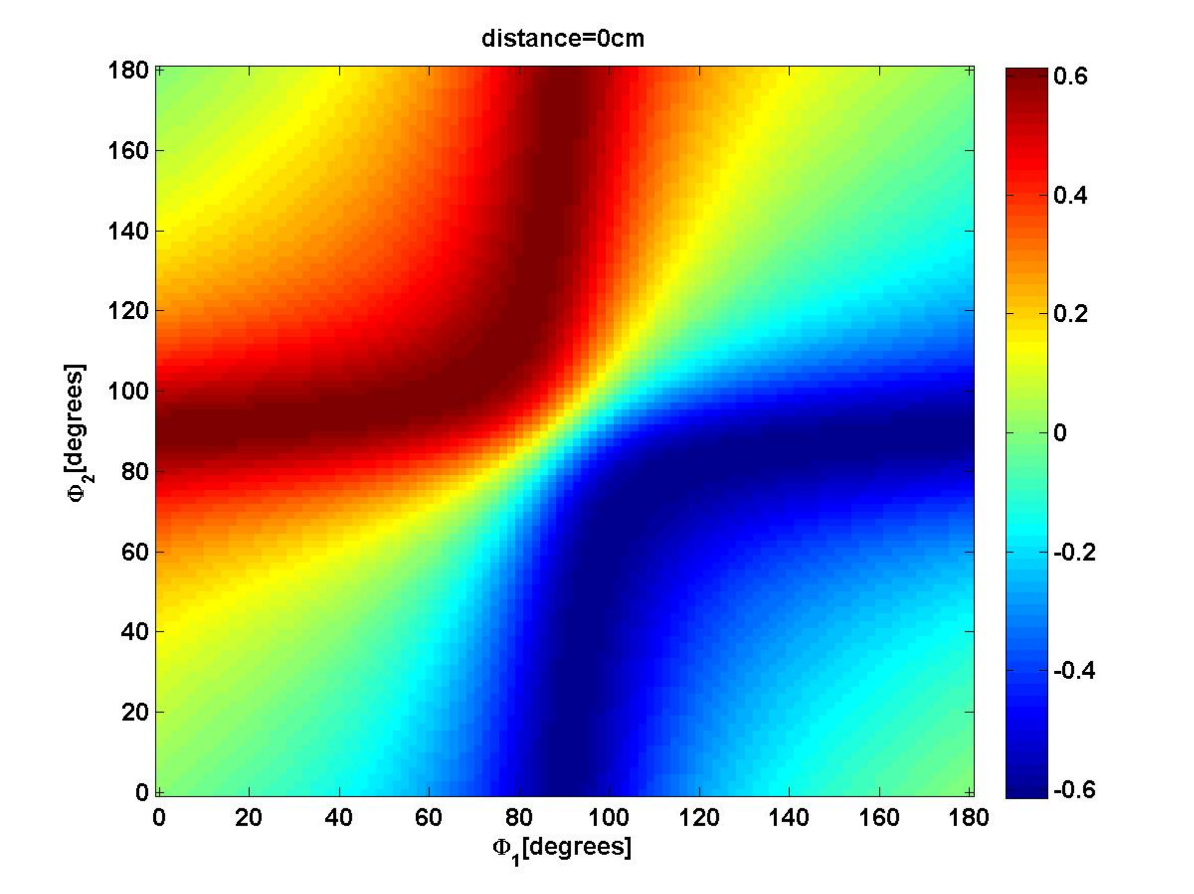


distance=6.8739cm
180
160
140
120
100
80
60
40
20
0
Φ_2[degrees]
0
20
40
60
80
100
120
140
160
180
Φ_1[degrees]
0.6
0.4
0.2
0
-0.2
-0.4
-0.6

Local Interactions: a voxel interacts with itself (rotating dipole)

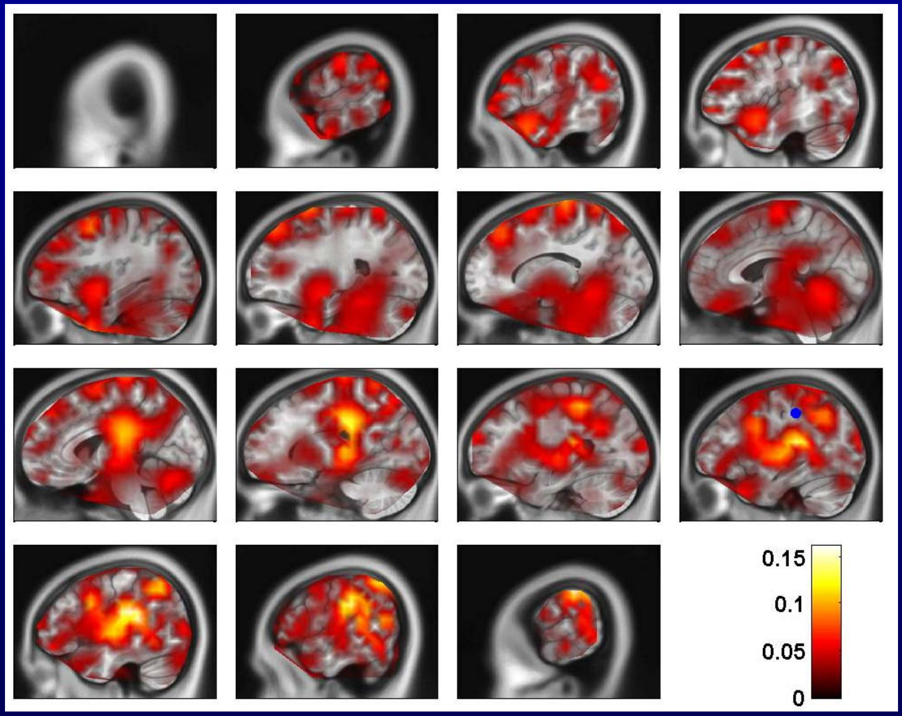


Local Interactions: a voxel interacts with itself (rotating dipole)

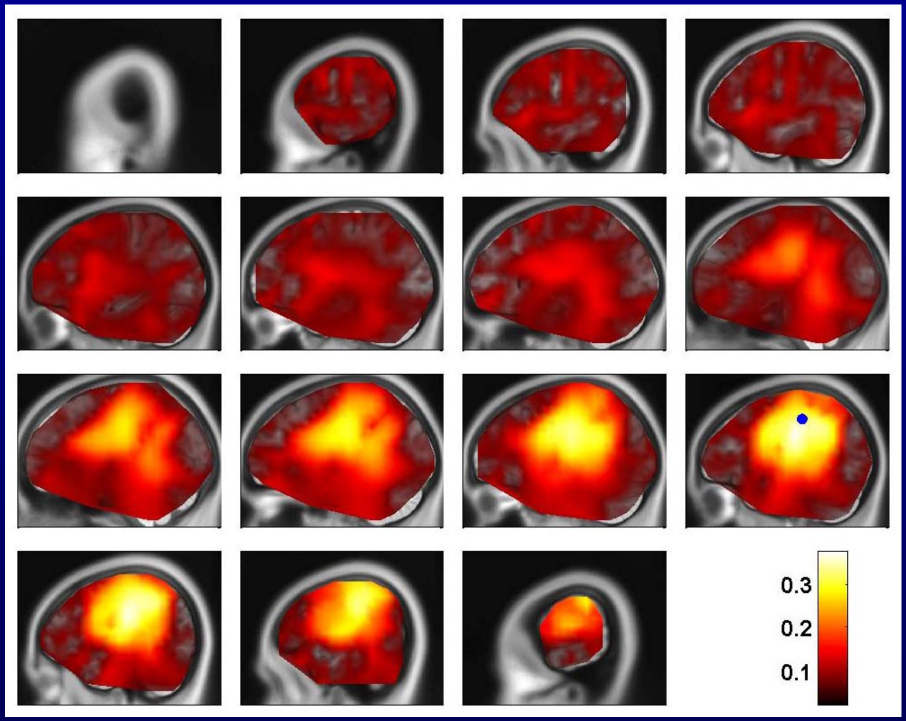


Beta rhythm, resting state, MEG, normal subject

Fixed Dipole orientation

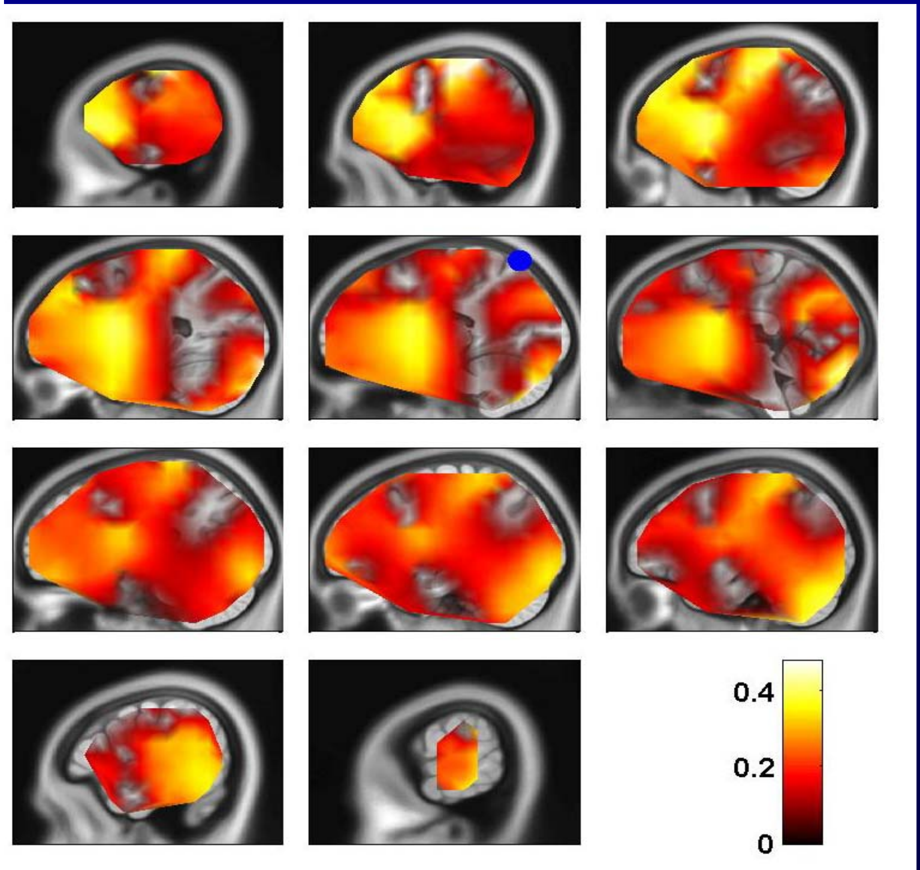


Variable Dipole orientation

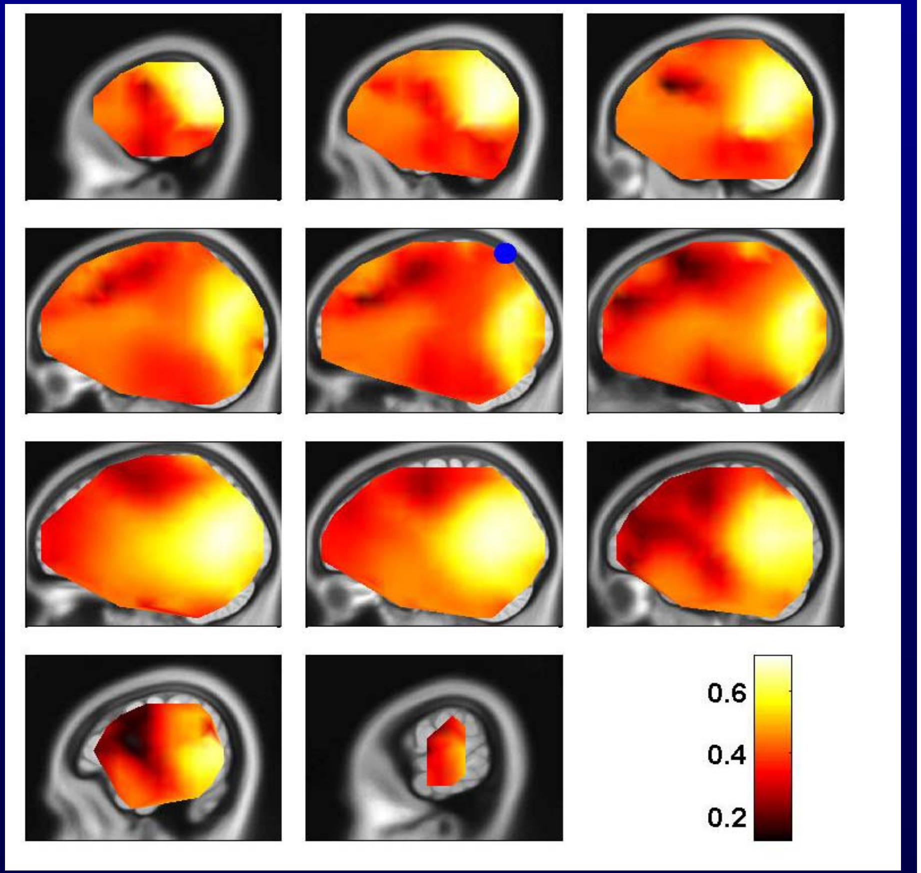


Alpha rhythm, resting state, EEG, normal subject

Fixed Dipole orientation

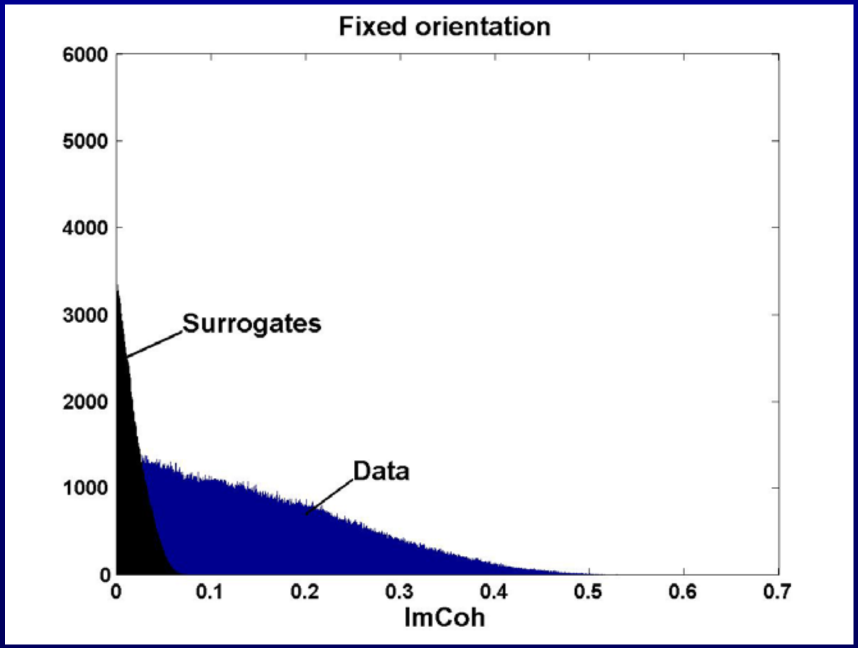


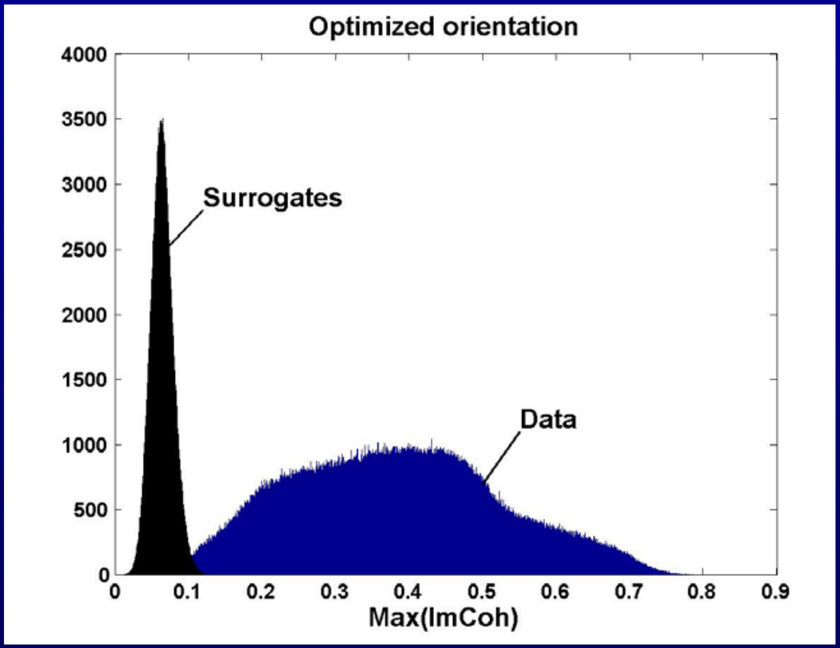
Variable Dipole orientation



Alpha rhythm, resting state, EEG, normal subject

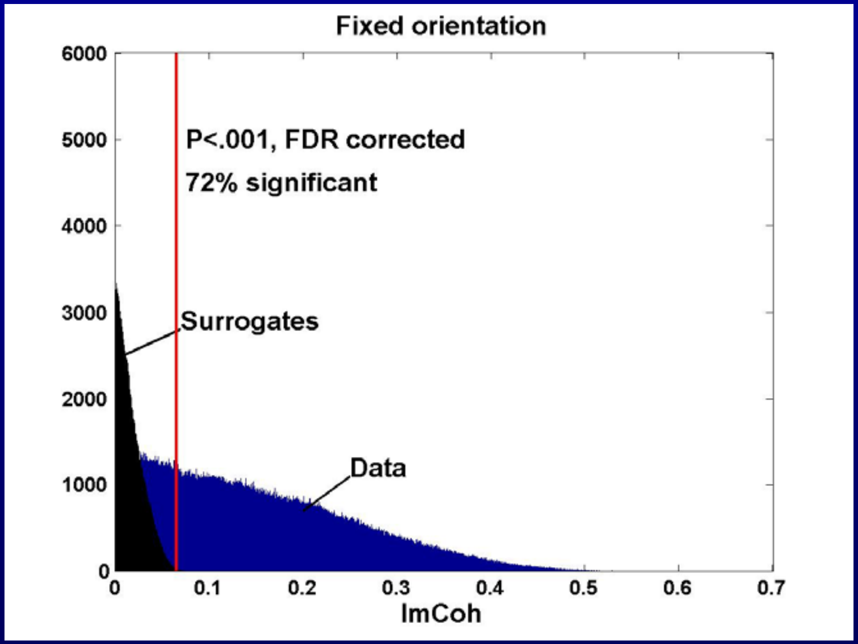
Histograms for all connections (5000 x 5000)

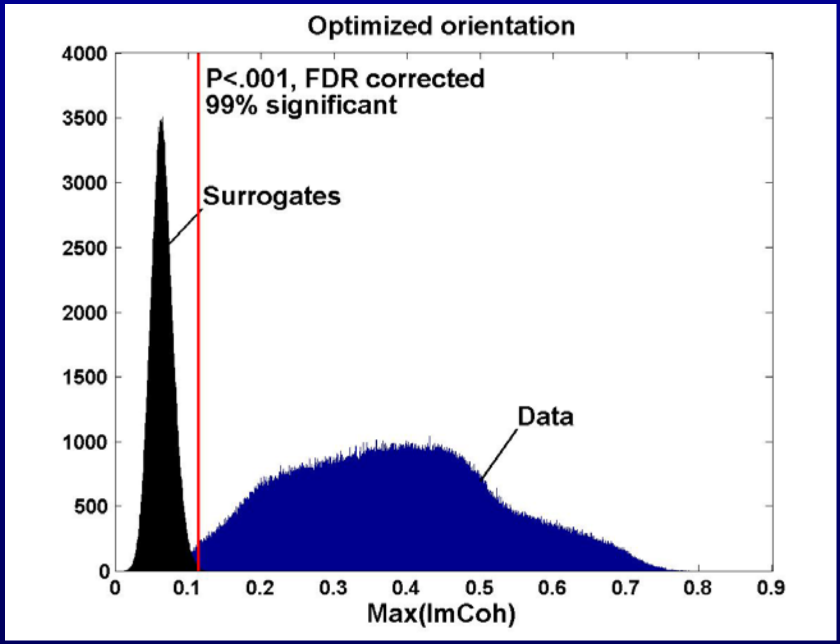




Alpha rhythm, resting state, EEG, normal subject

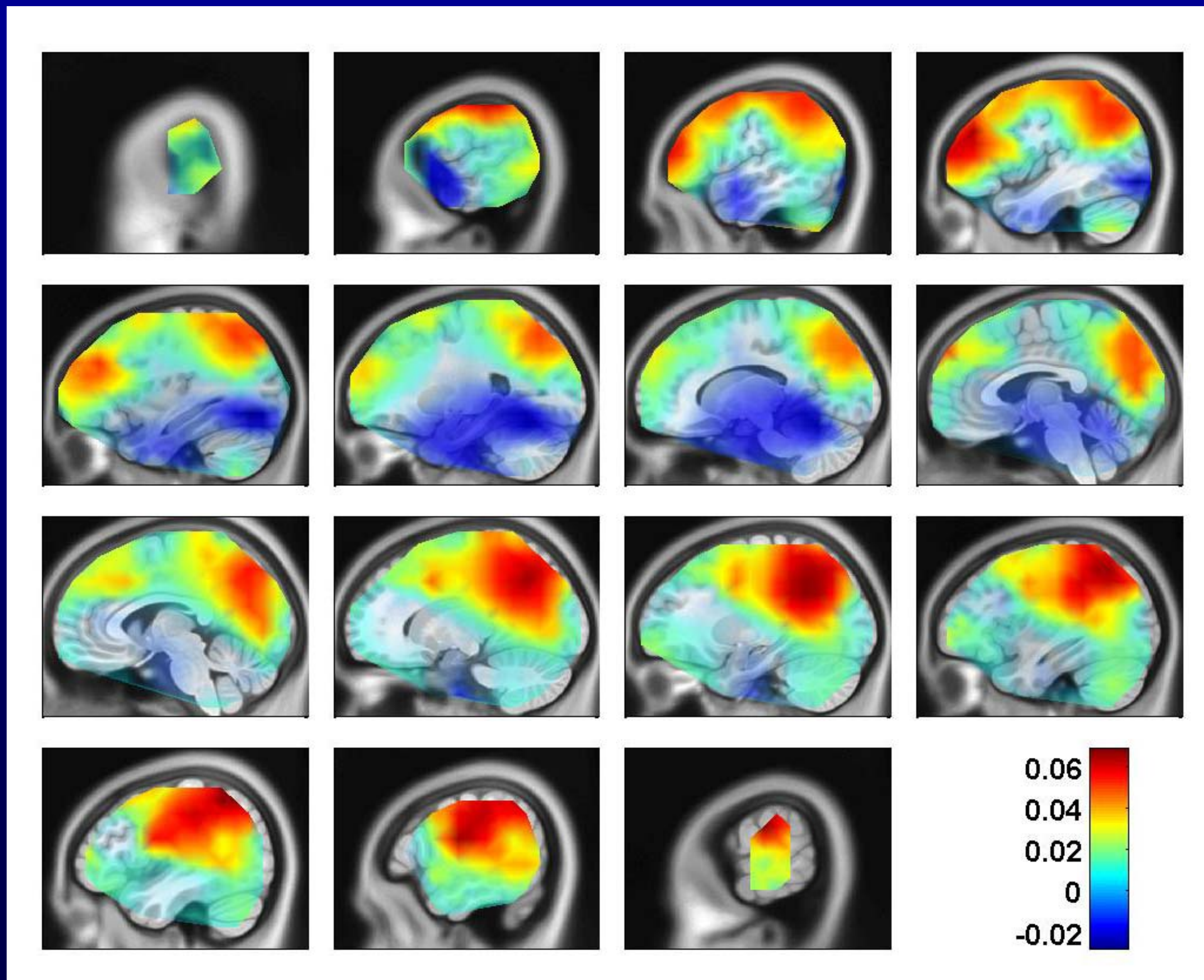
Histograms for all connections (5000 x 5000)



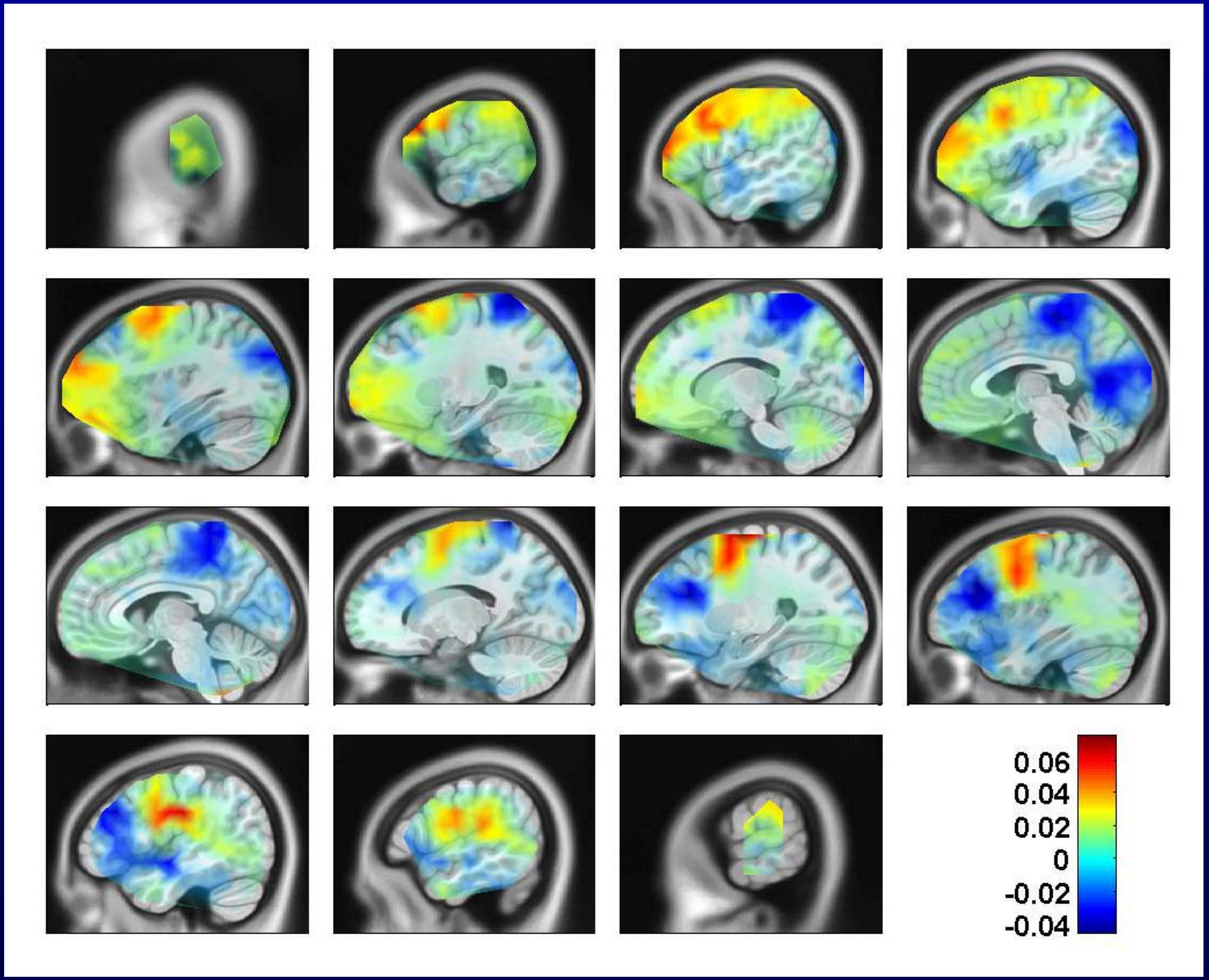


- **Everything appears to be connected with everything**
- **Graph measures based on significance useless**

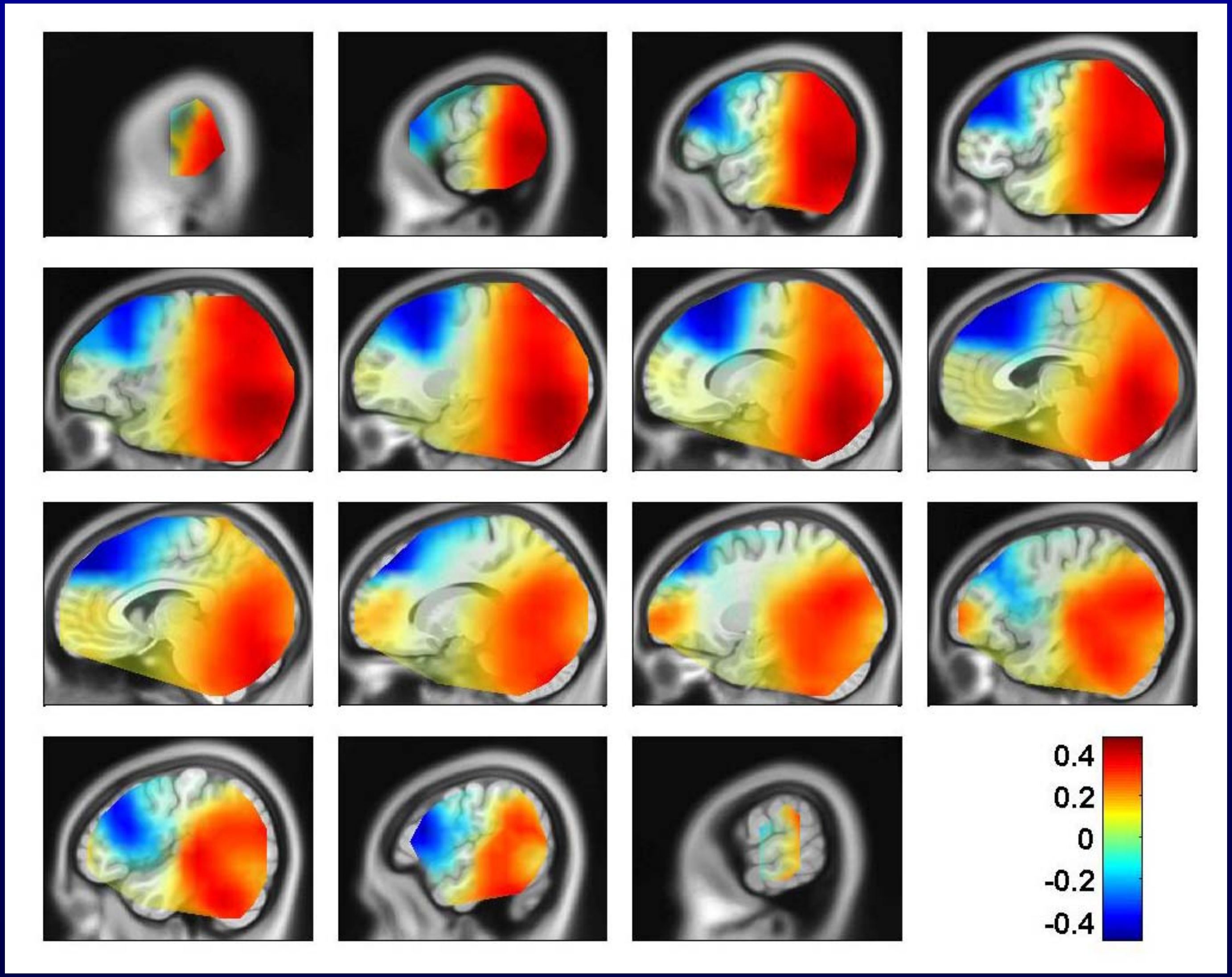
Grand average, 19 Patients-18 Controls
Variable orientation, mean interaction for each voxel



Grand average, 19 Patients-18 Controls
Fixed orientation, mean interaction for each voxel



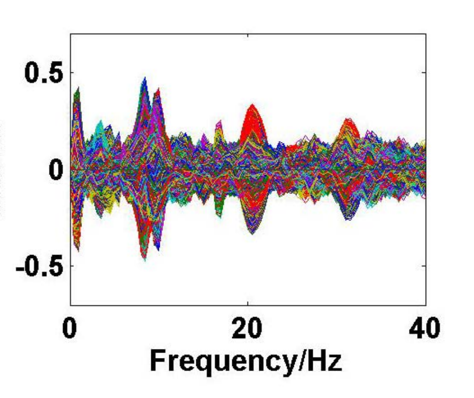
Grand average, 19 Patients-18 Controls
Normalized power difference: (P1-P2)/(P1+P2)



3. Nonlinear measures robust to mixing artefacts

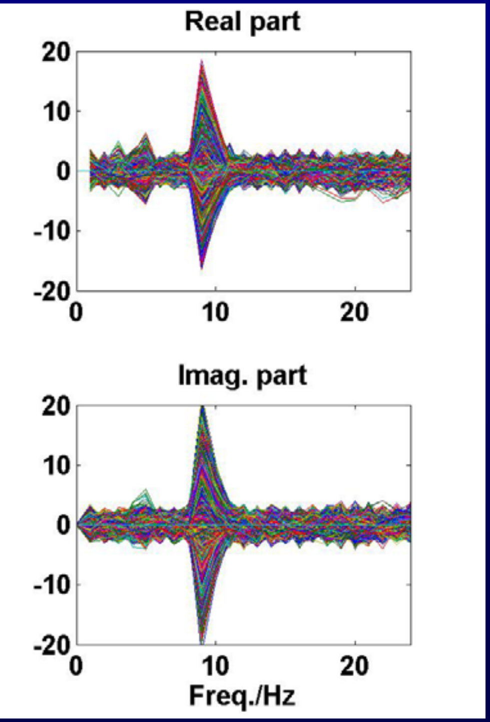
2nd order:
Imaginary part of cross-spectrum:

$$iS_{ij}^{anti}(f) = \left\langle z_i(f) z_j^*(f) \right\rangle - \left\langle z_j(f) z_i^*(f) \right\rangle$$



3rd order:
antisymmetric part of cross-bispectrum:

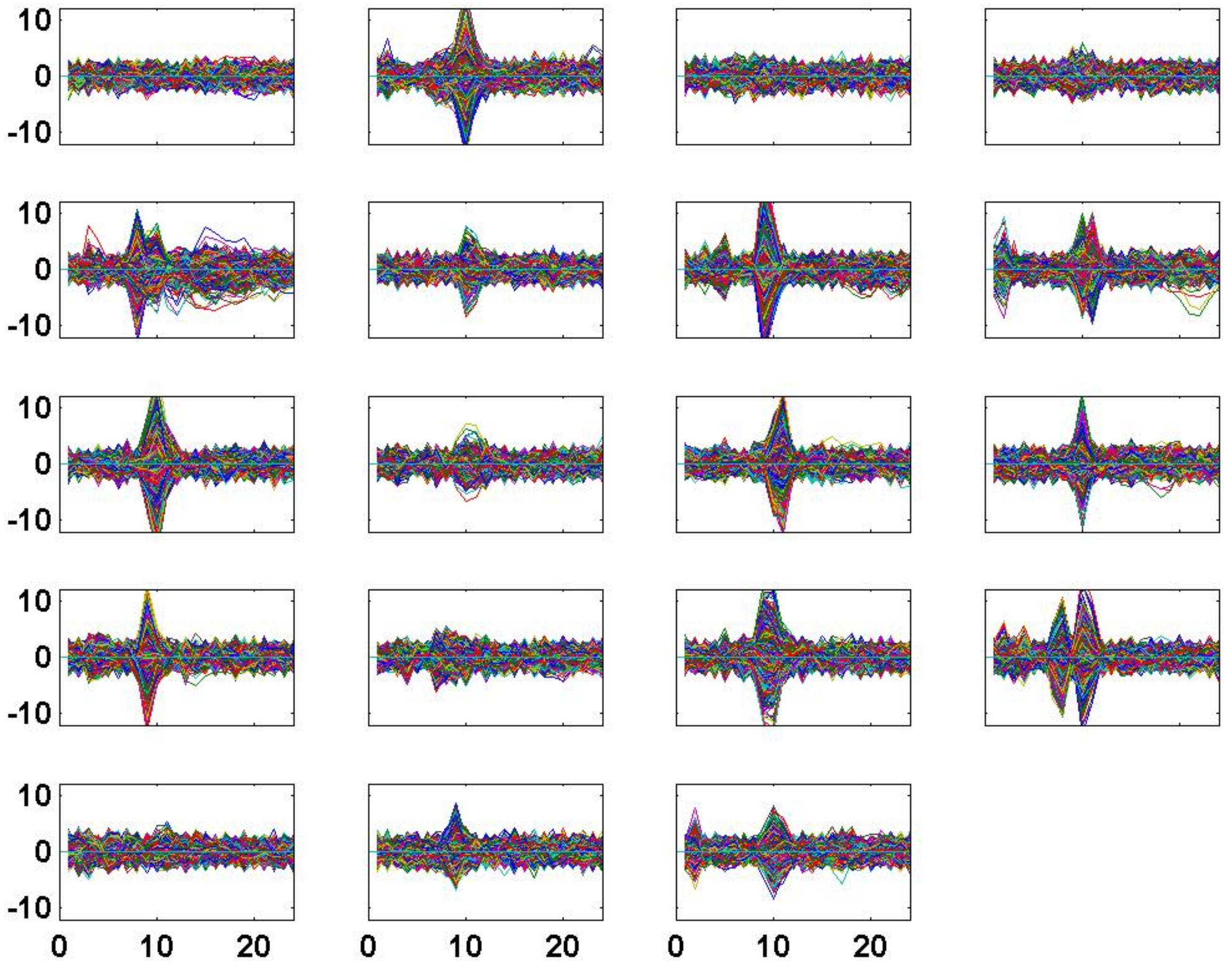
$$B_{ij}^{anti}(f) = \left\langle z_i(f) z_i(f) z_j^*(2f) \right\rangle - \left\langle z_j(f) z_i(f) z_i^*(2f) \right\rangle$$

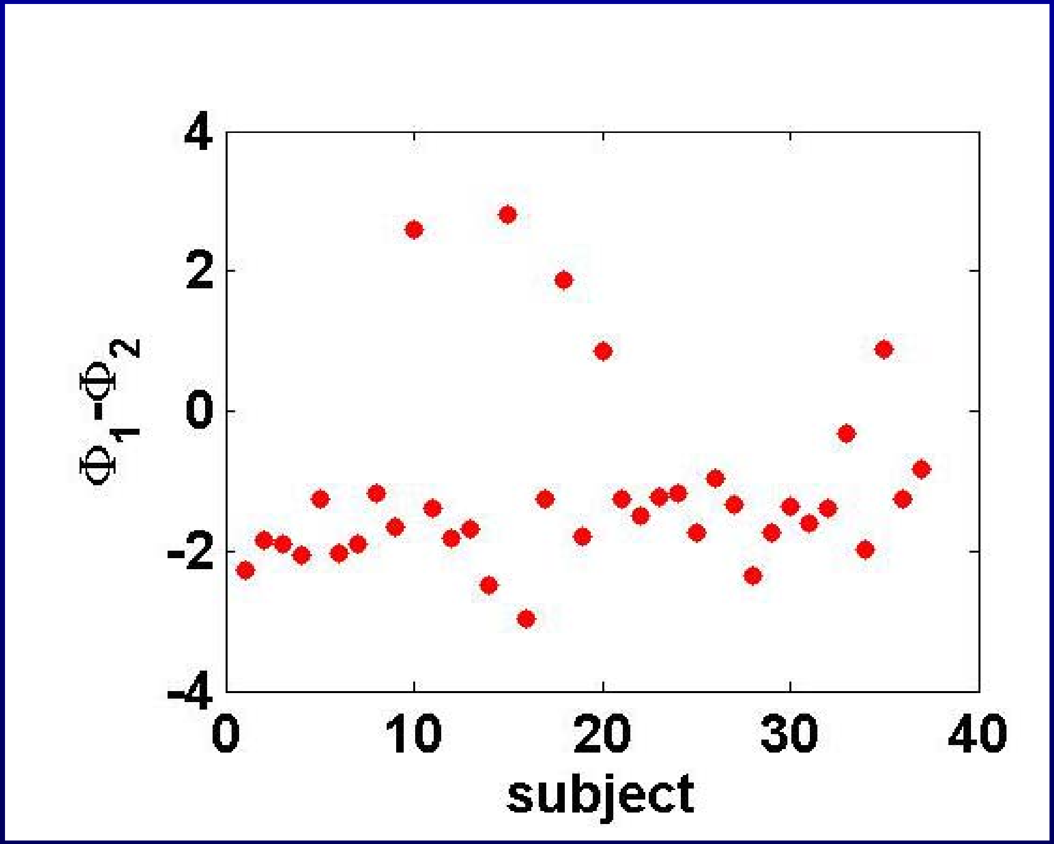


Nonlinear measure is complex valued
and results are less rich across frequencies

Chella et. al., in preparation

Antisymmetric parts of bispectra (real part), schizophrenics, eyes closed





Can one explain this with a model?

Remarks on nonlinear measures of interaction robust to artefacts of volume conduction

1. Observable but weak signals
2. Allows deeper insight into dynamics
3. Beyond third order???

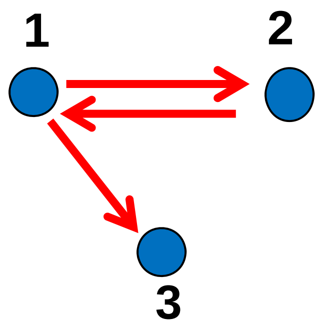
Antisymmetrization of 4.th order moments? No!
This is an open question.

Summary on new stuff

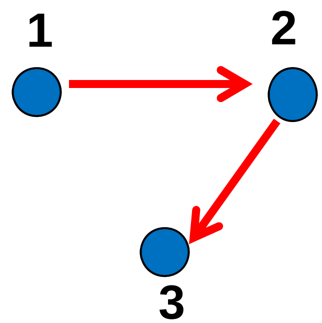
1. **Surrogate Data control for artifacts of volume conduction**
2. **Choose source orientation according to interaction**
3. **Nonlinear Measures are interesting but weak**

Biomag 2014, Halifax, Causality Challenge

- **Given: 1000 simulated data sets, 3 channels, random dynamical systems + additive noise, Matlab code is available**
- **Task: Estimate all direct causal connections**



$$\begin{pmatrix} 0 & 1 & 1 \\ 1 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$



$$\begin{pmatrix} 0 & 1 & 0 \\ 0 & 0 & 1 \\ 0 & 0 & 0 \end{pmatrix}$$

Counting:

+1 point for each correct detection

-3 points for each false detection

Thanks to

Mark Hallett

Ou Bai

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