EEG source Imaging

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www.electrical-neuroimaging.ch

Basic Definitions :

- general inverse problem as a remote sensing problem.
- the source localization inverse problem
- difficulties associated to inverse problems: ill posed inverse problems (e.g. $y=x^2$.)
- a priori information as a way to regularize an ill posed inverse problems

Overview of Inverse Solutions: biophysical constrains

Two basic principles before start applying inverse solutions.

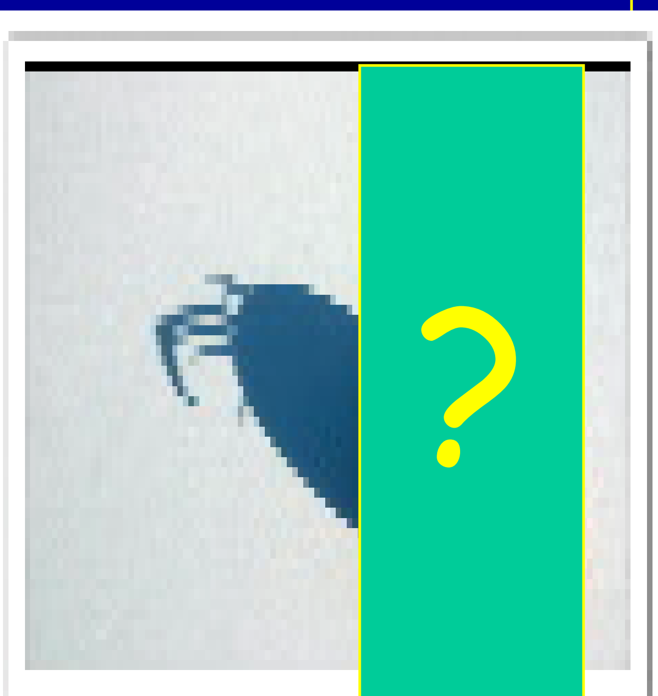
Factors that can distort the inverse solution estimates

Robust methods for the analysis of EEG /MEG sources

*"In any special doctrine of nature there can be only as much *proper* science as there is *mathematics* therein" I.Kant

Inverse Problem Definition

- Determination of an unknown magnitude (cause) through the use of indirect measurements (effect) related to it. "Remote Sensing"



Unknown magnitude characterizing an object or a process (size, composition)

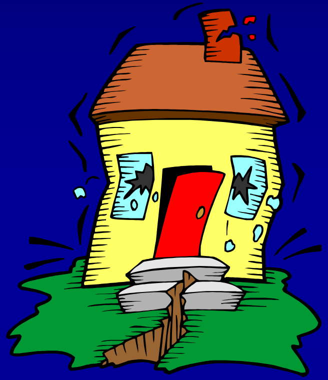
Data or measurements: contains incomplete information about the object/process

A priori information

Inverse problems are everywhere

Gas Prospection

Earthquake prediction



Weather forecasting

Mathematics

Interpolation
Derivation
etc

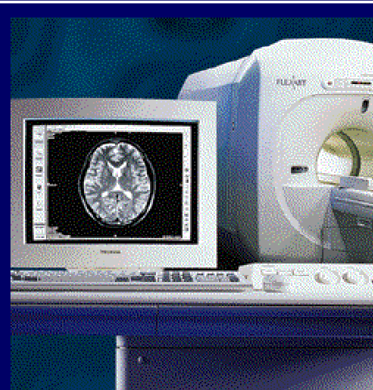
Inverse Problems
Medicine?

Non-invasive Functional Human Brain Mapping

Hemodynamic Methods

PET / SPECT

fMRI



Electromagnetic Methods

MEG

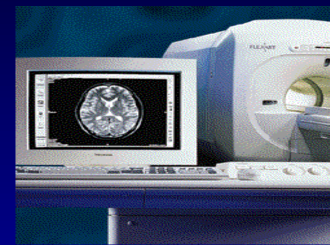
EEG

Remote sensing inverse problem

(external measuremets) ⟺ Mathematical relationship ⟺ (activity inside the BRAIN)

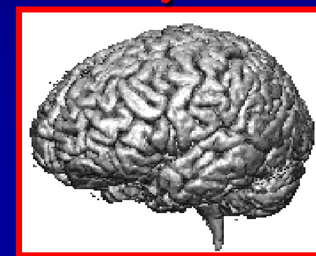
Before the inverse problem…

Recording of
EEG
(60 or more)

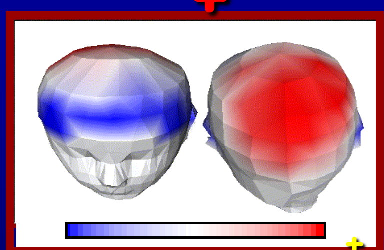


Recording of the
Anatomical
MRI

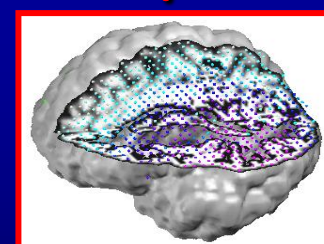
Recording of the
3D-positions
Of the electrodes



Brain
segmentation

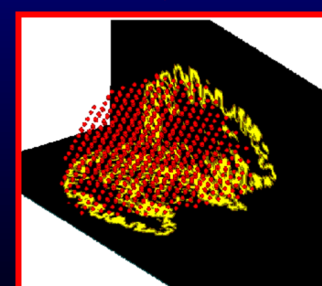


Mapping of the
electric field



Definition
of the
gray matter

$V = L\ J$



Definition of the
solution space
within the
gray matter

Compute L using geometry and
conductivities with BEM, FEM.

The electromagnetic inverse problem

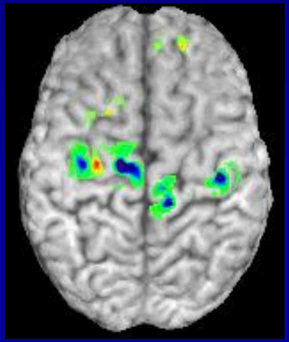
Set of currents J

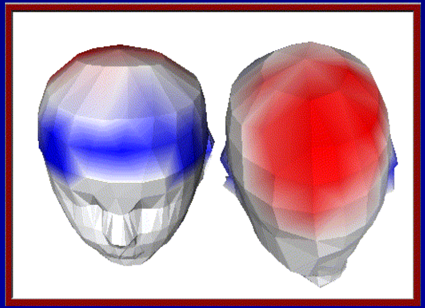
L

(J,V)

Set of maps V

Unknown
Magnitude,
Cause
Domain





Data,
Effect
Image

Function or Operator: LJ=V or L(J)=V

Relation one-to-one (e.g. dipoles)
many-to-one (e.g. distributed source)

defined by 3 elements:
(Domain, Image, Function)

Difficulties associated to inverse problems

- Definition of well posed and ill posed problems
- Examples with function $y=x^2$
- Regularization: the “treatment” for ill posed problems

Well-posed Inverse Problems

1) The solution exists

2) The solution is unique

3) The solution depends continuously on the data (*)

Otherwise it is ill-posed.

Jacques Hadamard (1865-1963)

-Sur les problèmes aux dérivées partielles et leur signification physique. *Bull. Univ. of Princeton*, pages 49-52, 1902.

* Only present in the electromagnetic inverse problem if the number of sensors is “too high”

Inverse Problem Solution: Existence

Domain: { All positive and negative Real numbers }
Image: { All positive and negative Real numbers }

Law $\quad y = f(x) = x^2$

Inverse problem for $f(x)=-25$:

Find x such that square of $x=-25$

Has no solution → Ill posed

Inverse Problem Solution: Uniqueness

Domain: { All positive and negative Real numbers }
Restricted Image: { All positive Real numbers }

Law $y = f(x) = x^2$

Then $f(5)=f(-5)=25$ is many-to-one

Inverse problem for $f(x)=25$:

Find x such that square of $x=25$

The solution is not unique: 5 or –5? → Ill posed

Inverse Problem Solution : Regularization I

Restricted Domain: {All positive Real numbers }
Restricted Image: { All positive Real numbers }

Law $y = f(x) = x^2$ *Nature cannot be changed!!*

Then f(5)=25 is one-to-one

Inverse problem for f (x)=25 :

Find x such that square of x=25

Has a unique solution: 5 → Well posed

Inverse Problem Solution : Regularization II

•Converts irregular or ill posed problems into
Regular, well posed problems

•Determined by the a priori or additional information that tailor
or mold the solution and or the data space.

-Related to our preferences and\or our free will to select a solution:

Note: A priori information producing a well posed problem is no necessarily a physiologically meaningful solution.

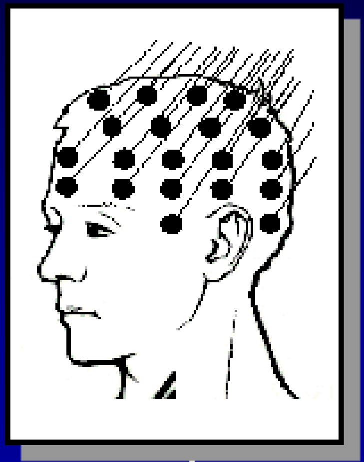
e.g. solutions with minimum energy (sources only near to the sensors) or maximum smoothness (no activity at all near the sensors) are unlikely to exist in the brain.

Example of multiples sources generating the same potential map

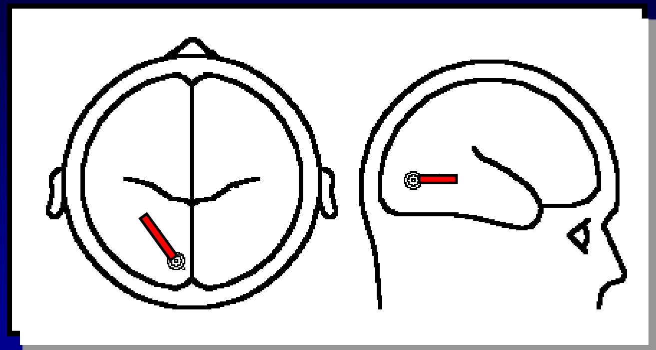
Using a realistic head model and realistic electrode configuration.

In E:\Curso_EEG_IP\curso_CHUV\mira11.lm

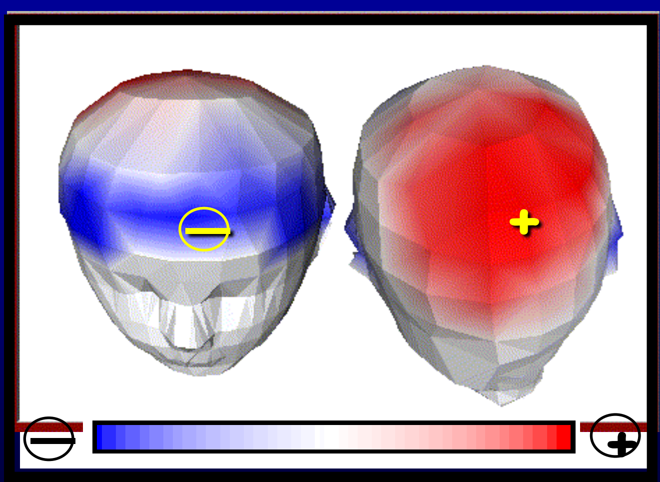
Solutions of the inverse problem obtained by restriction of the source space



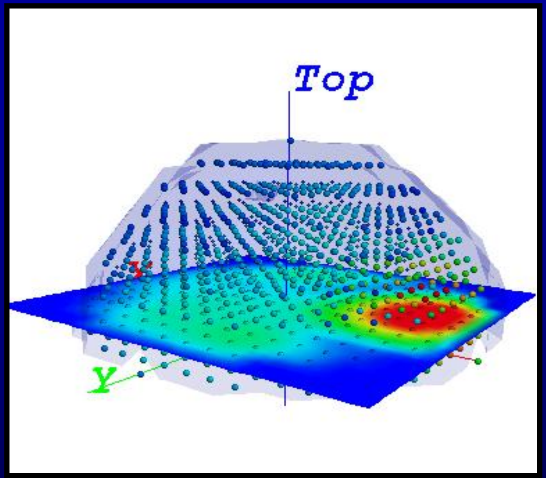
Search for one or a few equivalent dipoles



Number of dipoles must be known



Calculation of a 3D current distribution



A priori assumptions have to be correct (e.g. minimal norm, solution structure)

Common errors in source localization

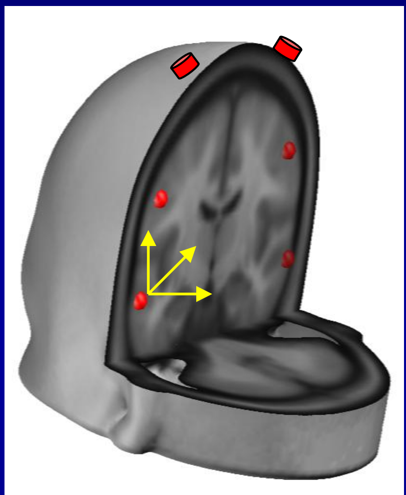
- Since MySolution is computed for each voxel separately (e.g. Beamformers) then it has no influence from "the others". (check resolution kernels and you will see)

- If MySolution (e.g. sLORETA) has Zero Dipole Localization then it estimates correctly any combination of single sources. (check the superposition of the spread functions as in the example that follows).

General advice: Ask those authors to provide you the resolution matrix and you will see that their claims do not hold

Resolution matrix: use

2 electrodes



4 solution Points or voxels

4 * 3 voxels ➔12 by 12

7th row =X component at 3thrd point

1	0.48	0.94	0.48	-0.84	-0.75	-0.67	-0.86	-0.93	-0.10	-0.93	0.16
0.48	1	0.74	0.99	-0.87	-0.94	-0.97	-0.85	-0.13	0.81	-0.14	0.94
0.94	0.74	1	0.75	-0.97	-0.92	-0.88	-0.98	-0.75	0.23	-0.76	0.48
0.48	0.99	0.75	1	-0.87	-0.94	-0.97	-0.85	-0.14	0.81	-0.15	0.94
-0.84	-0.87	-0.97	-0.87	1	0.98	0.96	0.99	0.60	-0.43	0.61	-0.66
-0.7	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	99	0.98	0.46	-0.57	0.47	-0.77
-0.67	-0.97	-0.88	-0.97	0.96	0.99	1	0.95	0.36	-0.66	0.37	-0.83
-0.86	-0.85	-0.98	-0.85	0.99	0.98	0.95	1	0.62	-0.40	0.63	-0.63
-0.93	-0.13	-0.75	-0.14	0.60	0.46	0.36	0.62	1	0.45	0.99	0.20
-0.10	0.81	0.23	0.81	-0.43	-0.57	-0.66	-0.40	0.45	1	0.44	0.96
-0.93	-0.14	-0.76	-0.15	0.61	0.47	0.37	0.63	0.99	0.44	1	0.19
0.16	0.94	0.48	0.94	-0.66	-0.77	-0.83	-0.63	0.20	0.96	0.19	1

Resolution matrix: abuse

- Ho: If a method G reconstructs correctly the single sources (e.g. Zero Dipole Localization error) then G reconstructs correctly any combination of sources.
- Reconstruction of sources 1 and 12 is correct when they are alone, i.e.:

1	0.48	0.94	0.48	-0.84	-0.75	-0.67	-0.86	-0.93	-0.10	-0.93	0.16
0.16	0.94	0.48	0.94	-0.66	-0.77	-0.83	-0.63	0.20	0.96	0.19	1

But the reconstruction of 1 and 12 simultaneously yields:

1.16	1.42	1.42	1.43	-1.50	-1.52	-1.51	-1.50	-0.72	0.86	-0.74	1.16

Then Ho is false, i.e, the zero DLE is indeed a trivial property (see ANA inverse solution) unable to predict the performance of an inverse solution for simultaneously active sources

Examples of Inverse Solutions proposed in the literature

obtained by mathematical restrictions of the sources

Linear:

- **Minimum Norm**
- **Weighted Minimum Norm**
- **LORETA**
- **PROMS**
- **Backus & Gilbert**
- **WROP**

Non-Linear:

- **Equivalent Dipoles**
- **BESA**
- **MFT**
- **FOCUSS**
- **CURRY**
- **EMTT**
- **Beamformers (SAM)**

Biophysical Constraints : Electra source model with LAURA regularization.

Sensible a priori information : EPIFOCUS or ANA for concentrated sources

Maxwell equations (time domain)

$$\nabla \circ \boldsymbol{E} = \rho / \varepsilon \qquad (1')$$

$$\nabla \times \boldsymbol{E} = -\partial \boldsymbol{B} / \partial t \qquad (2')$$

$$\nabla \circ \boldsymbol{B} = 0 \qquad (3')$$

$$\nabla \times \boldsymbol{B} = \mu(\boldsymbol{J} + \varepsilon \partial\ \boldsymbol{E} / \partial t) \qquad (4')$$

E and B are the electric and magnetic fields completely and uniquely defined by their rotor (∇x), their divergence (∇°) and a boundary condition.
J is the total current density vector,
ε and μ stand for physical properties of the media, and
ρ is a (charge or current) density.

Maxwell equations :quasi-static approximation

$$\nabla \circ \boldsymbol{E} = \rho / \varepsilon \qquad (1)$$

$$\nabla \times \boldsymbol{E} = 0 \Leftrightarrow \boldsymbol{E} = -\nabla V \qquad (2)$$

$$\nabla \circ \boldsymbol{B} = 0 \Leftrightarrow \boldsymbol{B} = \nabla \times \boldsymbol{A} \qquad (3)$$

$$\nabla \times \boldsymbol{B} = \mu \boldsymbol{J} \Rightarrow \nabla \circ \boldsymbol{J} = 0 \qquad (4)$$

For frequencies < 1000 Hz (Plonsey and Heppner 1967):

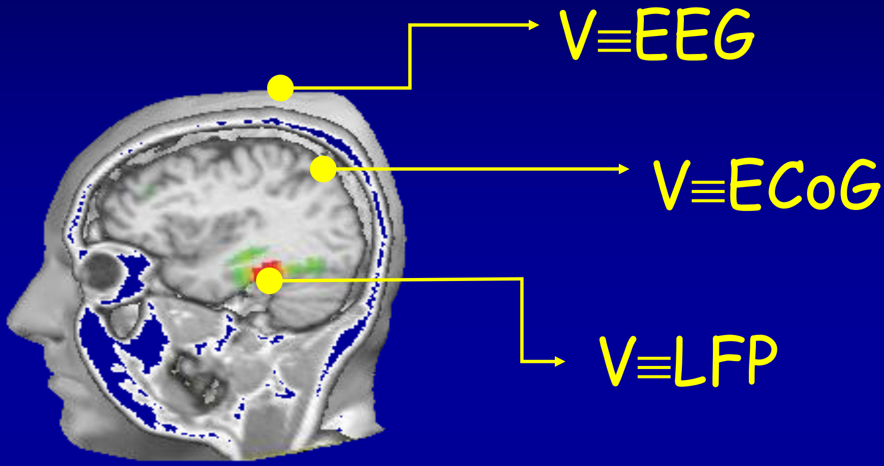
- Electric and Magnetic fields are independent.
- Instantaneous propagation to the sensors (no memory process)

Quasi stationary => Irrotational sources (ELECTRA)

experimental and theoretical evidences

> geometries considered were simple ones. What I have shown here is that, in fact, the fields measured do not even arise from $\bar{J}^i$, but rather from secondary sources only. These secondary sources, in turn, depend on both the electrical field and the interfaces, and hence are related to $\nabla \cdot \bar{J}^i$ and the geometry. So both electric and magnetic

Plonsey, R. In: Biophysical Journal, Vol 39, 309-312, Copyright © 1982 by Biophysical



Poisson Equation

$$V(r) = \int_V \nabla \cdot J^p(r_v) G(r, r_v)$$

$$J^p = \nabla\phi + \nabla \times \mathbf{A} + \nabla H$$

$$V(r) = \int_V G\nabla \cdot \nabla\phi + \cancel{\int_V G\nabla \cdot \nabla \times \mathbf{A} + \int_V G\nabla \cdot \nabla H}$$

$$\nabla \cdot (\sigma \nabla V) = \nabla \cdot J^p$$

$$J^p = \nabla\phi$$

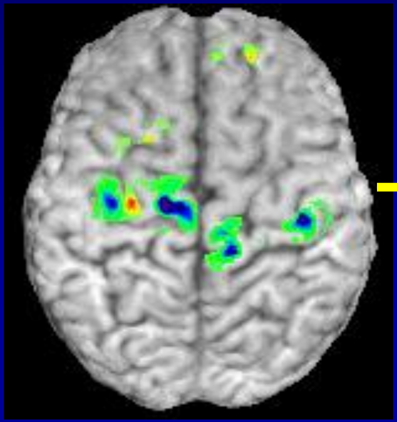
$$\sigma \Delta V = \Delta\phi$$

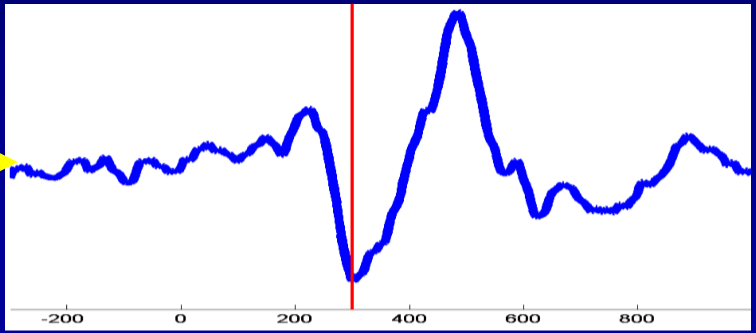
V and Φ have proportional sources and sinks

Irrotational sources ➔ No vorticity, it does not form vortices

ELECTRA

(biophysical constraint: irrotational source model)





No dipoles
But
potentials

Main Properties

•Non invasive estimation of local field potentials as measured by intracranial electrodes.

•Characterizes Real sources of the EEG (irrotational sources) under the quasi-stationary assumption.

•Reduces the number of unknowns to one third (higher resolution).

• Changes the resolution kernels (!!)

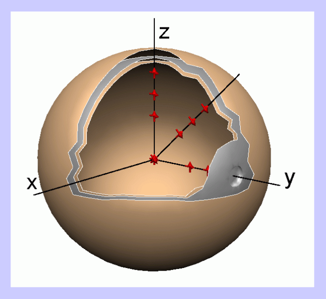
•Same sources and sinks than the measured potential V

A unique solution is obtained on the basis of biophysical laws governing propagation of fields within tissues (LAURA regularization).

Constraint for unique solution:

The potential or the currents decay as a function of a power of the distance similar to well known theoretical fields ➔ Local autoregressive average (LAURA)

Physical laws about: propagation of electrostatic fields in physical media



Grave et al., Human Brain Mapping, 1997, 1999, 2000
Grave et al., IEEE Trans Biomed Eng 1998,
Grave et al., Neuroimage 2004

Two basic principles before start applying inverse solutions

P1➔ While the EEG/MEG activity measured at the scalp certainly contain (we do not know how much) information about the EEG/MEG sources, scalp maps DO NOT indicate the location of the sources.

P2➔ If the maxima of the scalp activity is attained at a given surface location (e.g. at the occipital sensors) you CANNOT be surprised IF the SLA produces a maximum near to that sensor (e.g. at the occipital region of the brain).

P1 and P2 also apply to measures derived from the EEG or the estimated sources, that is, if a T-test between two conditions show occipital differences in the EEG then you cannot blame the inverse solution if, contrary to your personal expectancies, the T-test on the inverse solution also identifies occipital voxels.

Factors that can distort the inverse solution estimates

- Base line correction: change electrodes values independently

  Solution: avoid it before computing sources

- Grand mean averages: different latencies for different subjects (phasic or phase resetting EP model?)

  Solution: use single subjects instead

- Artificial maps: created from EEG data preprocessing as EEG segments with low silhouette values

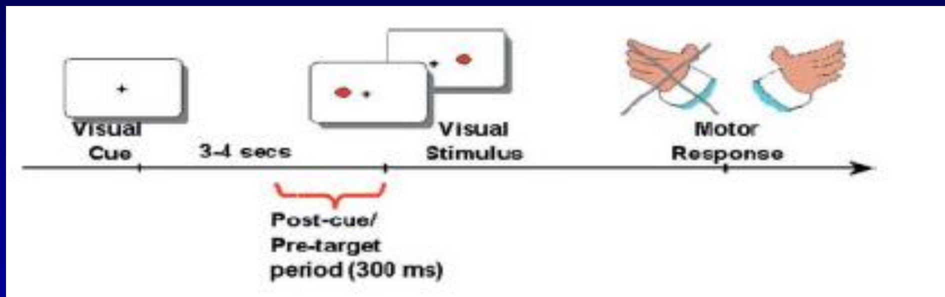
  Solution: use a cluster evaluation technique to select the maps

The true baseline response is flat.

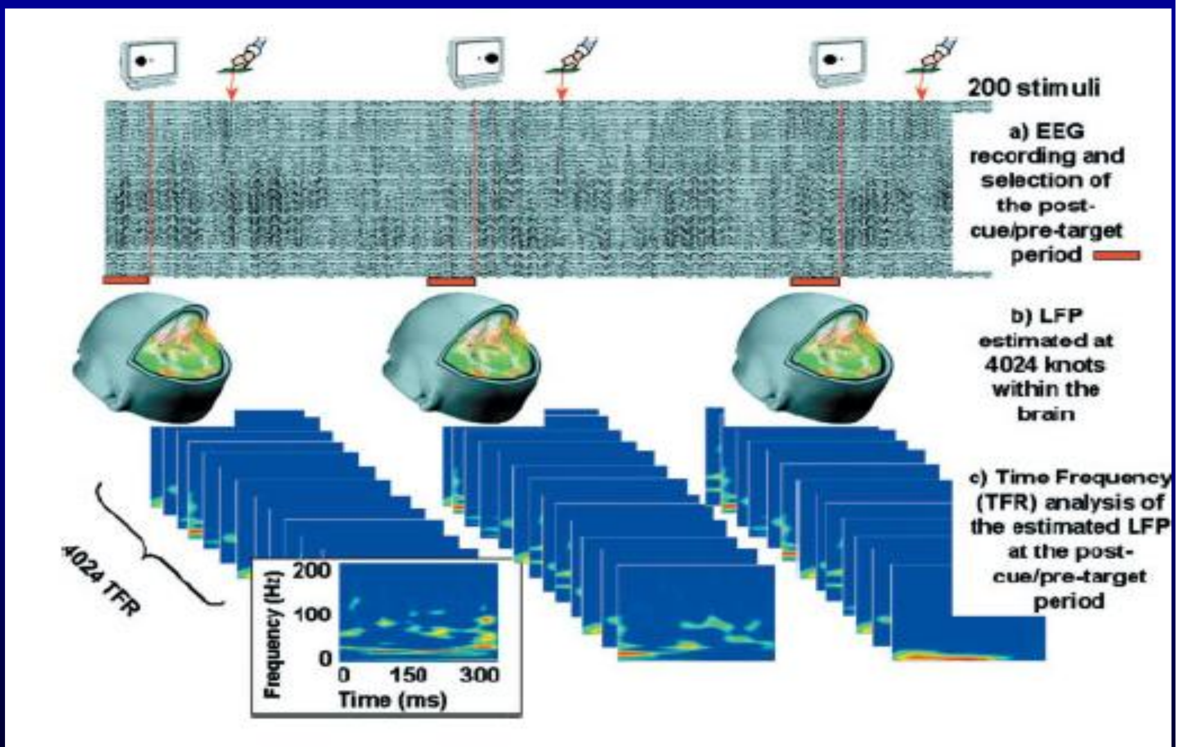
True or False?

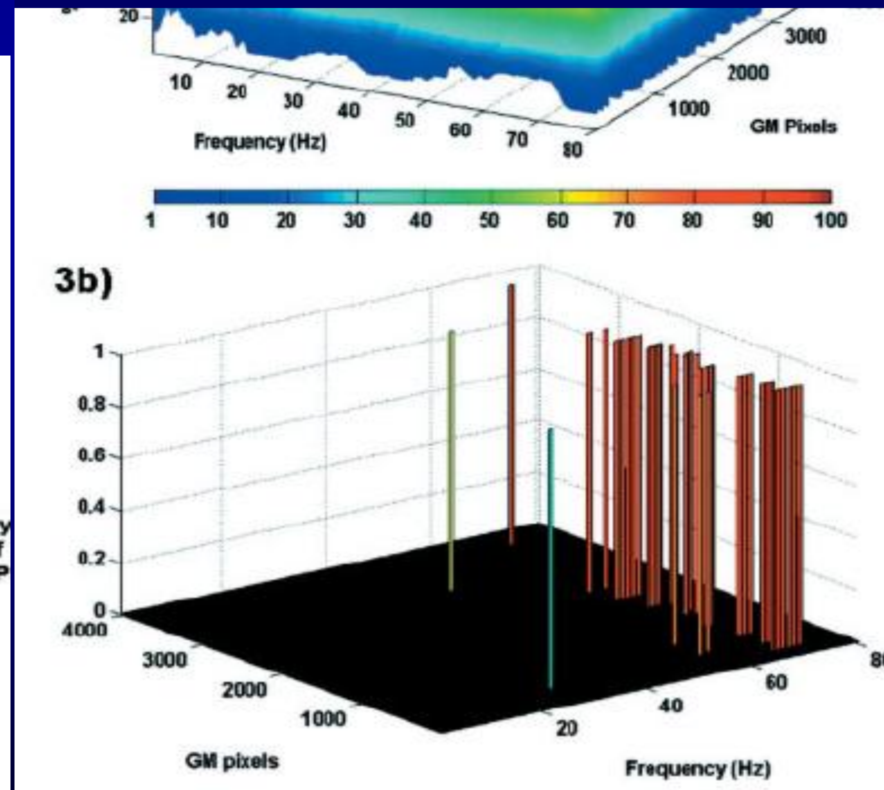
Prediction of Response Speed by Pre-stimulus

High-Frequency (Gamma Band) Oscillations



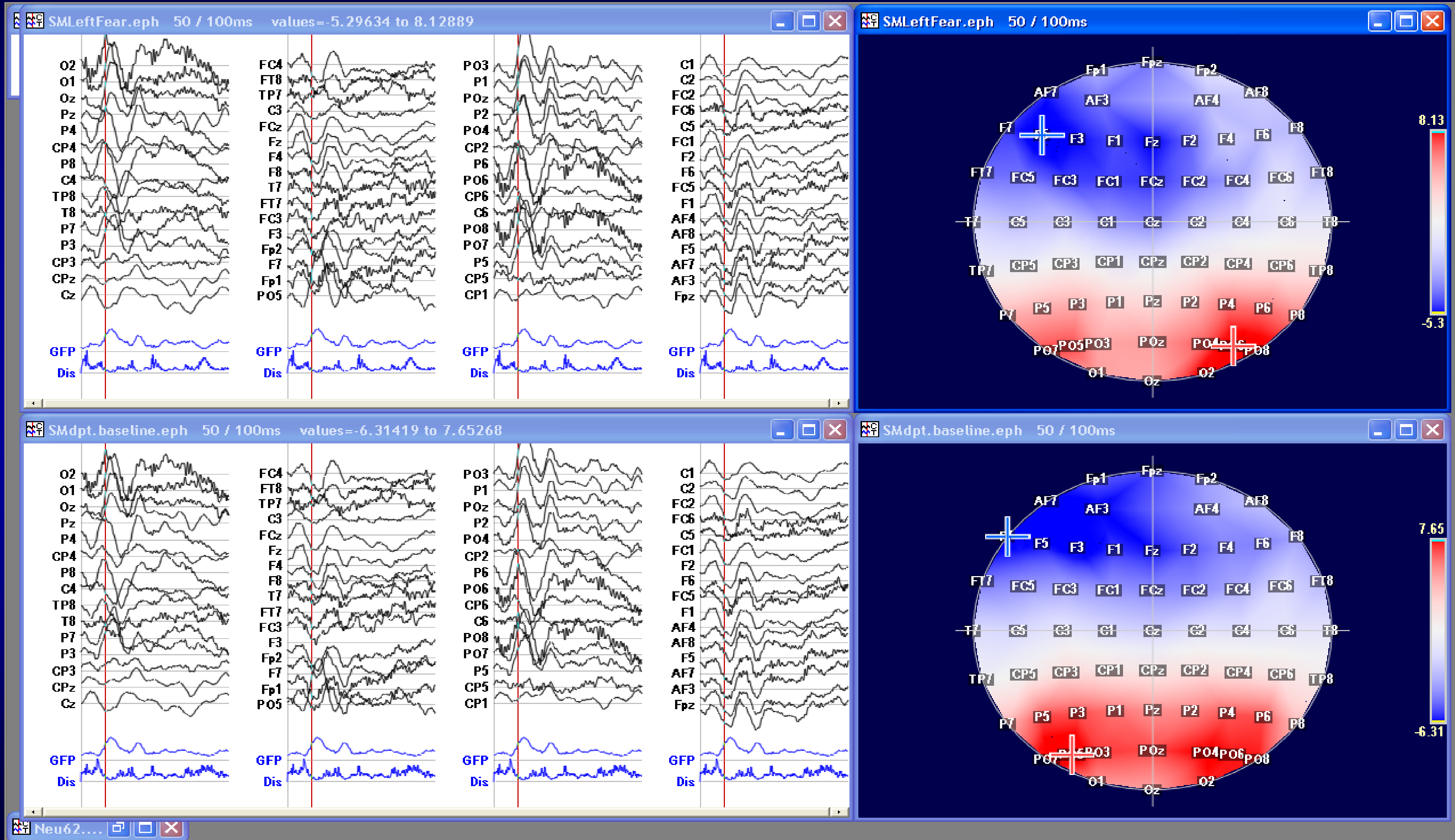
Early Gamma Oscillations Decreases Reaction Time





Gonzalez et al. 2005, Human Brain Mapping 24:50-58

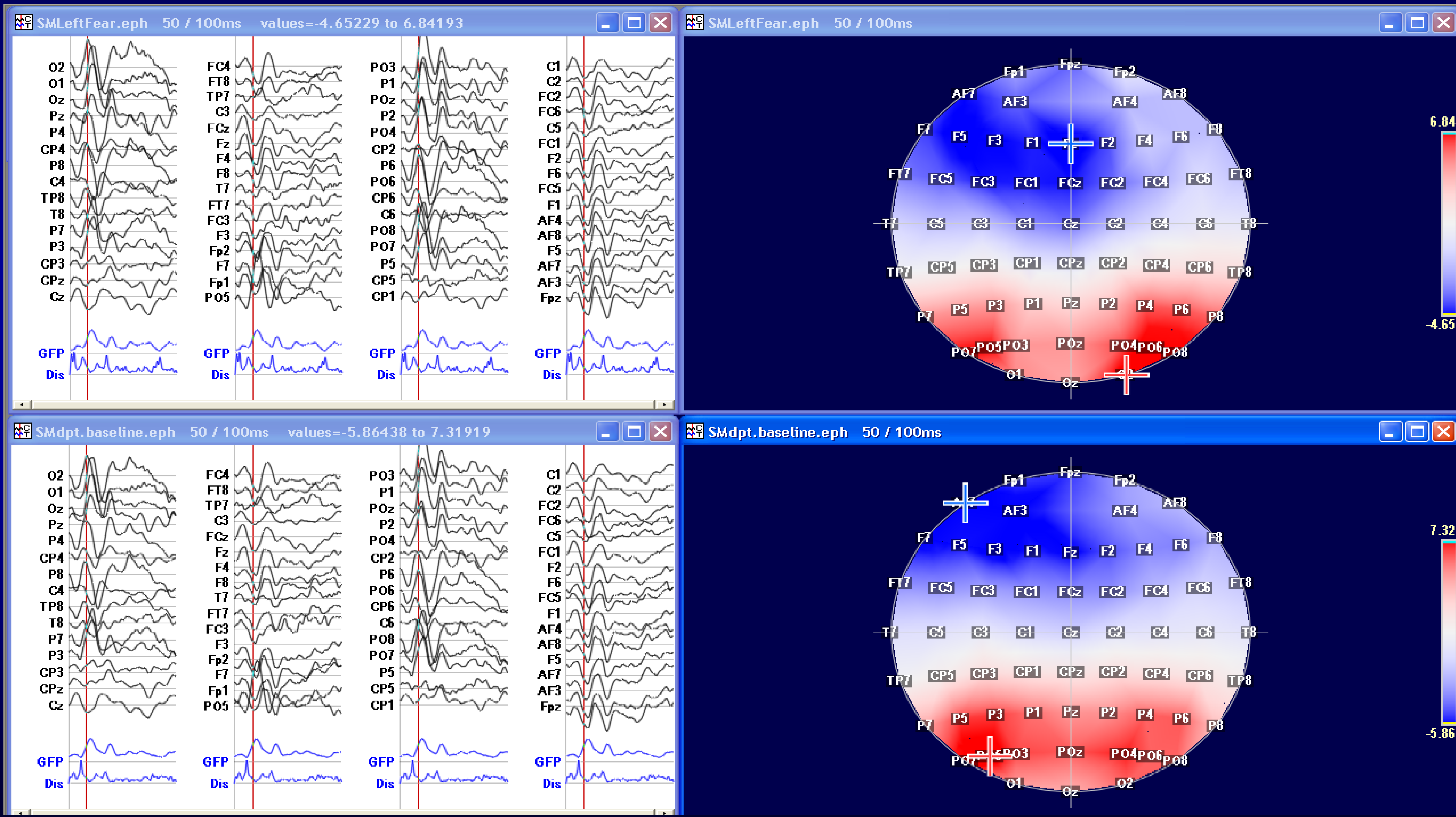
Baseline correction Effects (P100)



Fearful faces. 200 ms baseline, Identical processing otherwise

Effect on inverse solutions

Low pass (<30Hz) filtering effects



Factors that can distort the inverse solution estimates

- Base line correction: change electrodes values independently

  Solution: avoid it before computing sources

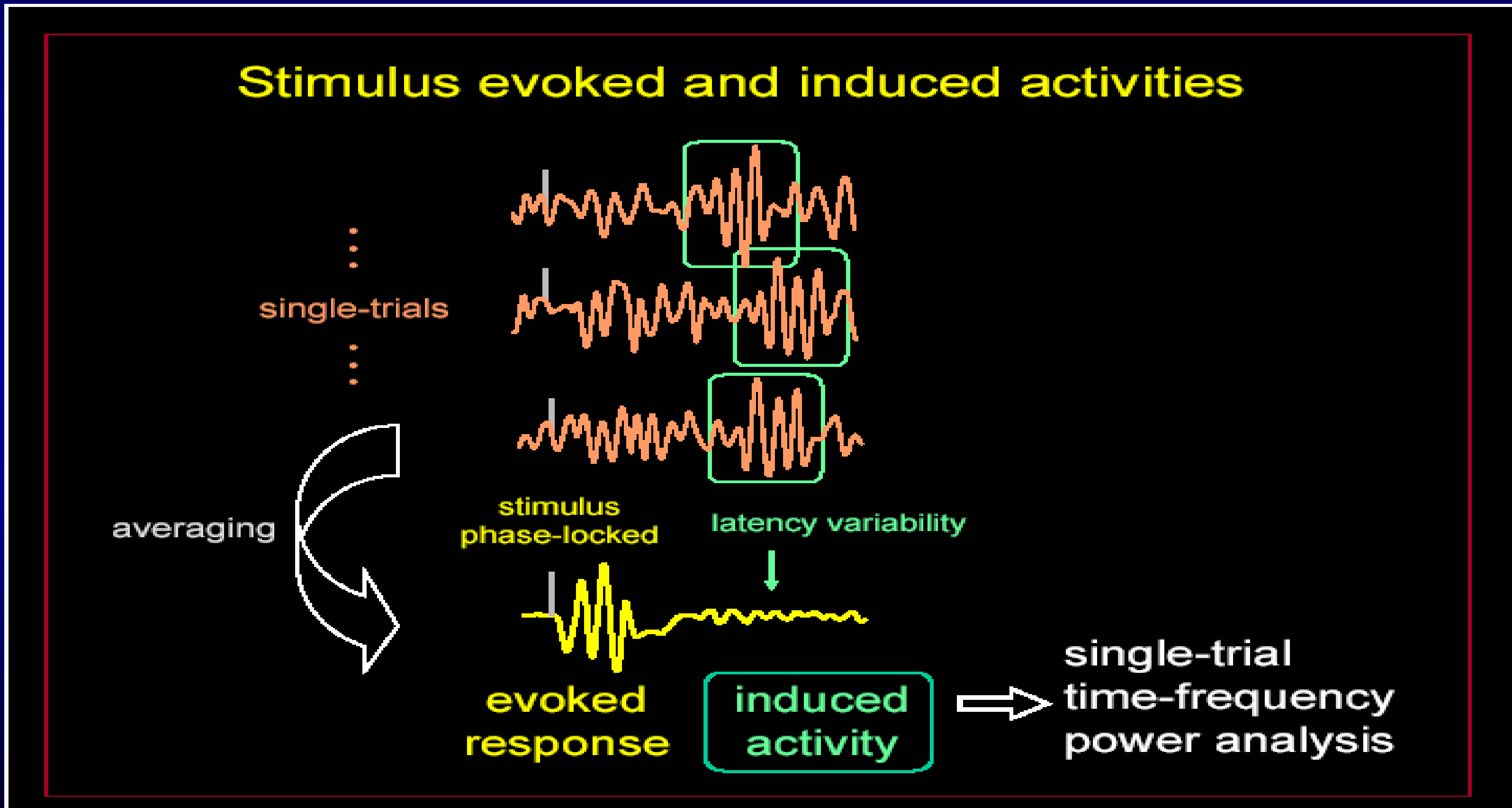
- Grand mean averages: different latencies for different subjects (phasic or phase resetting EP model?)

  Solution: use single subjects (single trials !) instead

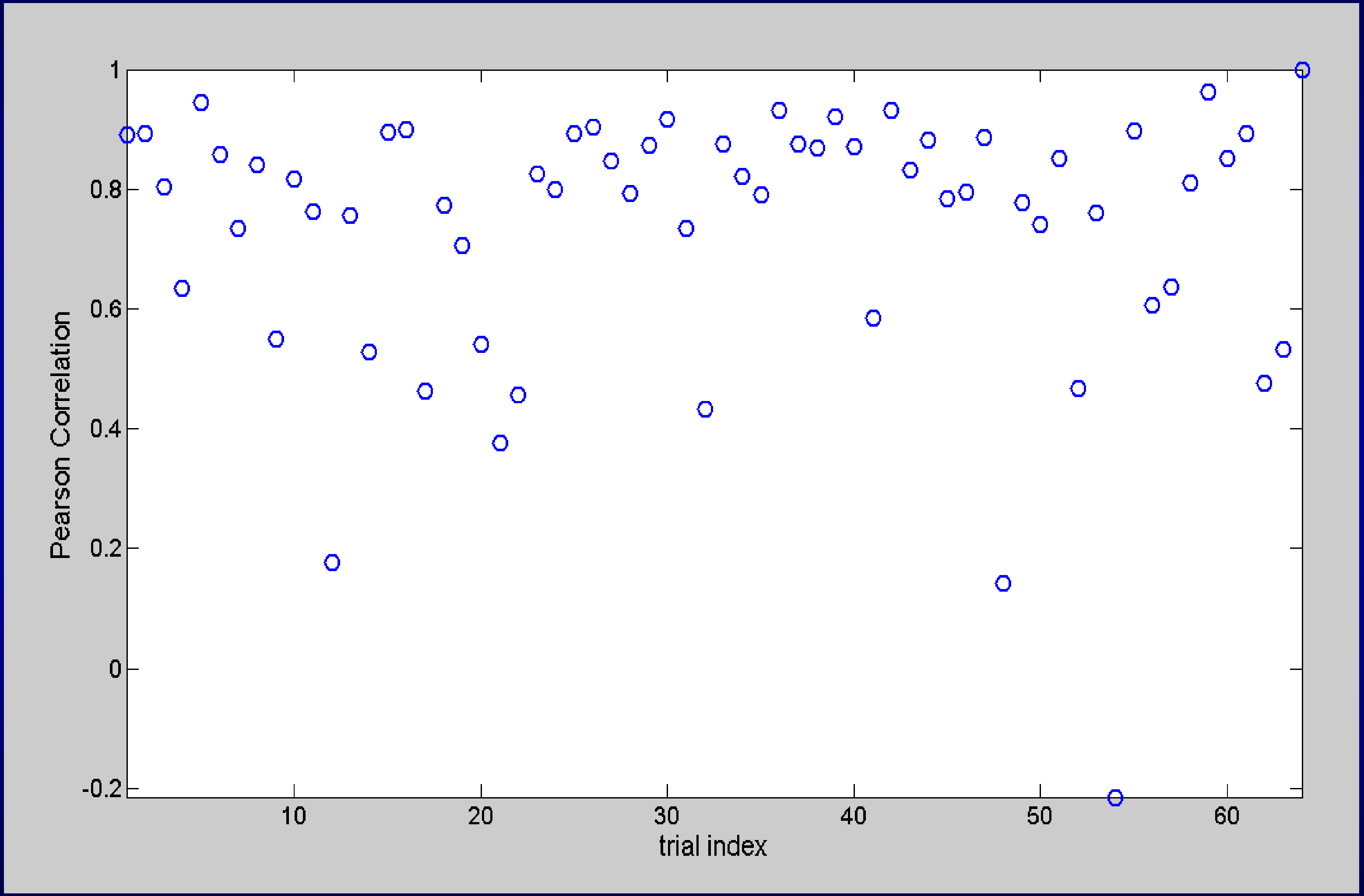
- Artificial maps: created from EEG data preprocessing as EEG segments with low silhouette values

  Solution: use a cluster evaluation technique to select the maps

Oscillations might cancel out in the mean



Is the mean map (P100) present on single trials?



Max Correlation coefficients between single trials (period 80-120 ms) and mean P100 map (t-test measures correlation ≠ zero)

Factors that can distort the inverse solution estimates

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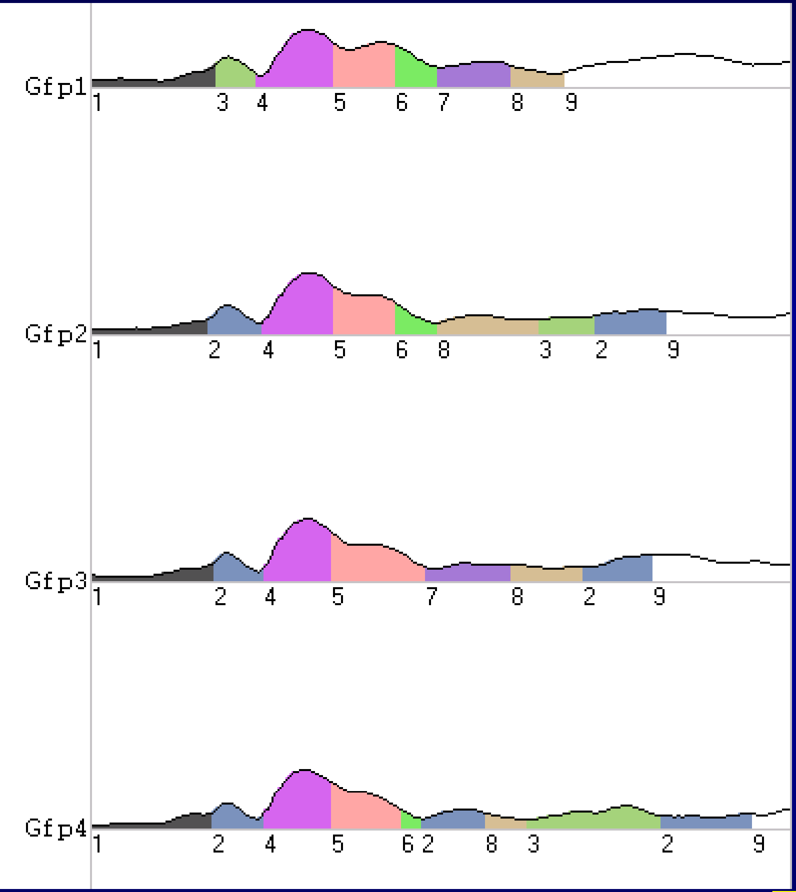
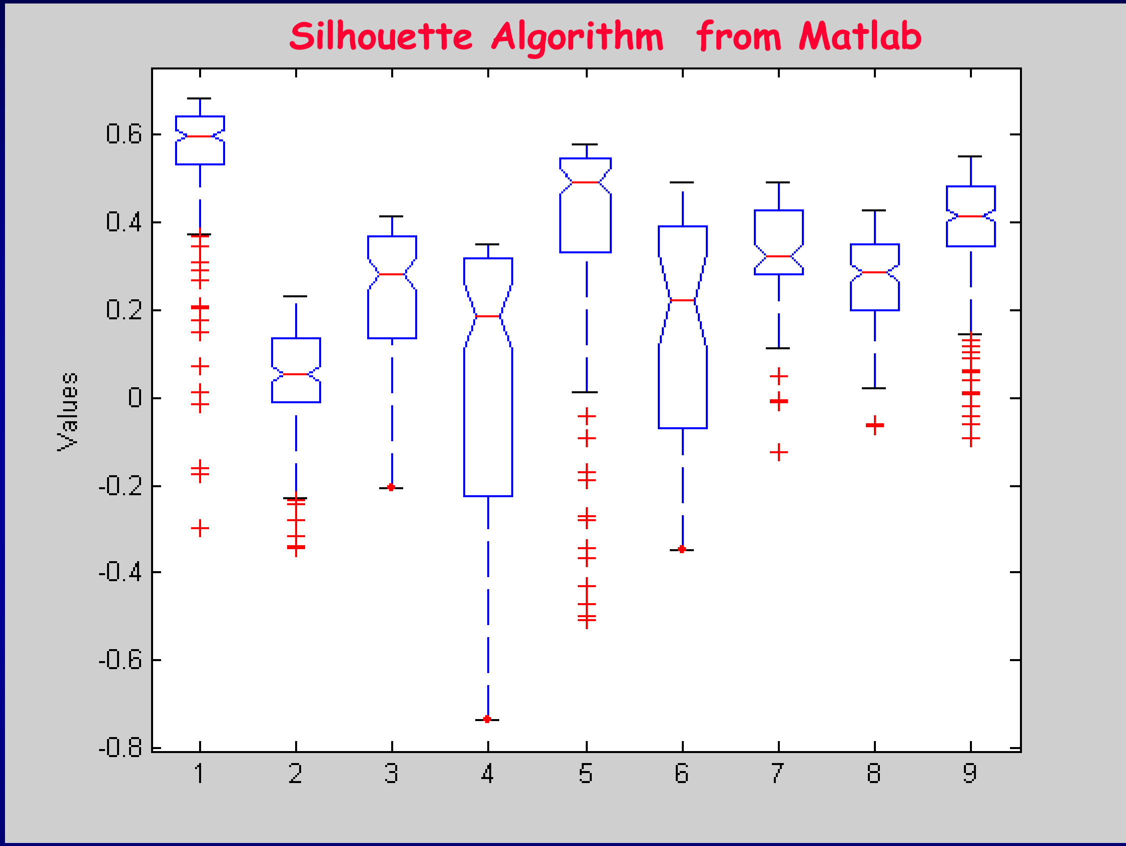
Selecting the maps with cluster evaluation techniques





Segments obtained with Cartool for the 4 grand means of 10 subjects in 4 conditions.

- Lower than 0.25 ➔ No substantial structure found
- Close to zero ➔ maps can be in any other cluster as well.
- Negative values ➔ maps incorrectly classified

Maps with negative values are present in all segments. To solve this avoid suboptimal algorithms (e.g. K-means).

Robust methods for the analysis of EEG /MEG sources

-) Avoid the use of source distributions obtained from a single map, whatever you have been told about the localization method or the method used to obtain the map.
- 2) Use source models reducing the inverse problem to scalar fields. Give preference to physically sound transformations like ELECTRA.
- 3) Use measures based on the temporal information of the brain activity. For example power spectrum densities, or measures that are independent of scale factor of the signals like correlation coefficients, etc.
- 4) Use contrasts between conditions or against a pre-stimulus to reduce systematic ghost and lost sources effects.
- 5) Use correlations between measures derived from the time course of the brain pixels and other behavioral or physiological measurements (e.g. reaction time in Human Brain Mapping 24:50-58 2005).