***Elaboration di Immagini - Laurea in Bioinformatica***

*Prof. G. Menegaz*

# EEG SIGNAL PROCESSING

## *3. Electrical Source Imaging*

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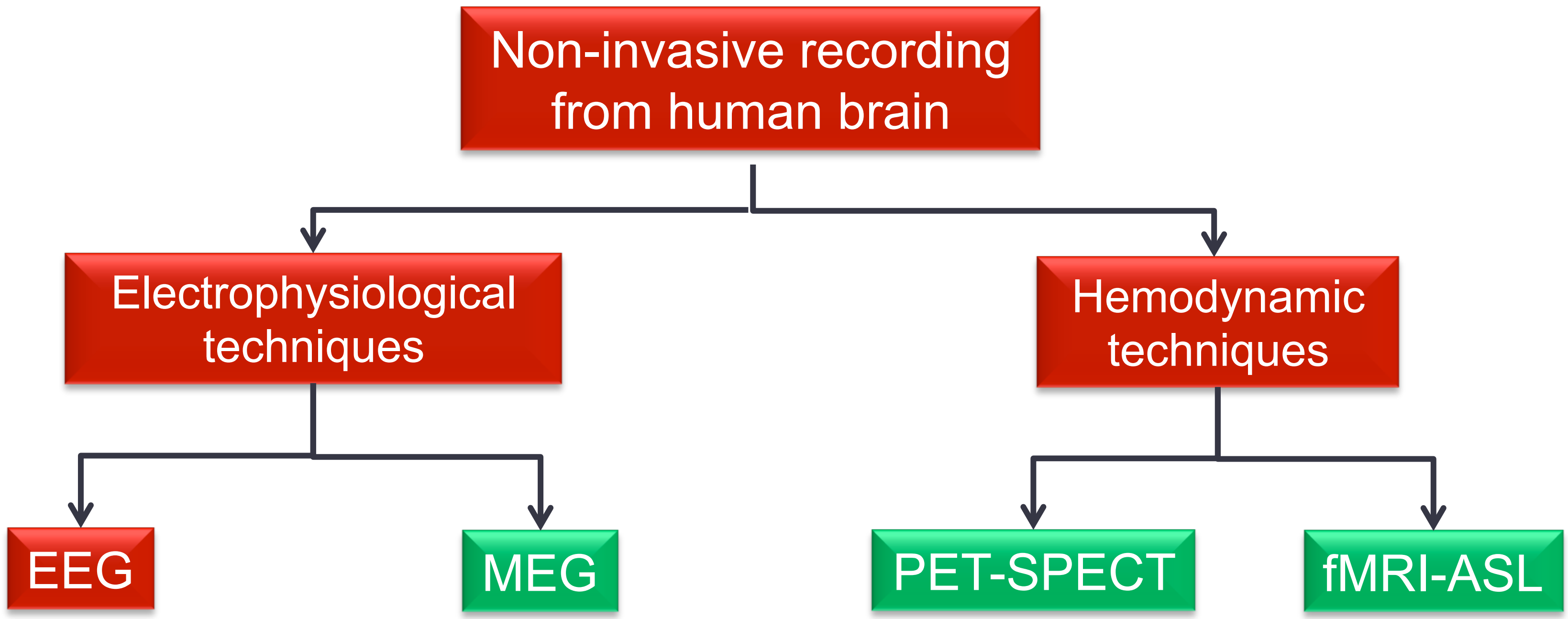
31/04/2017

# Measuring Neural Activity

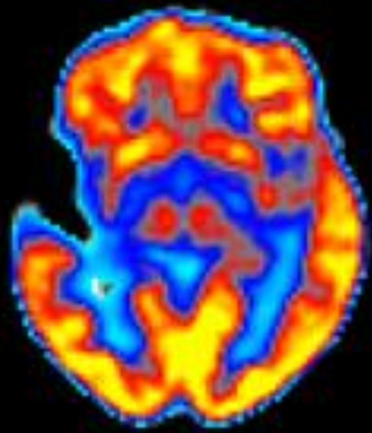



Poor spatial resolution
(about 1 cm)
Excellent temporal resolution
(< 1 ms)

Excellent spatial resolution
(about 1-2 mm)
Poor temporal resolution
(about 1 s)

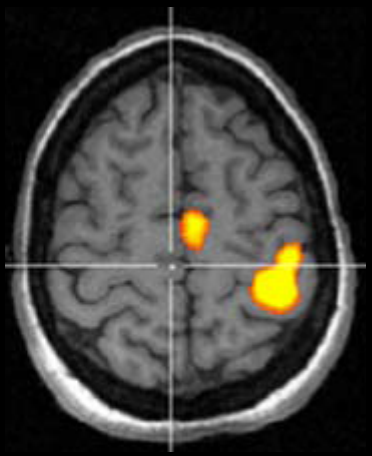
# Non-invasive imaging techniques

## Measuring hemodynamic activity

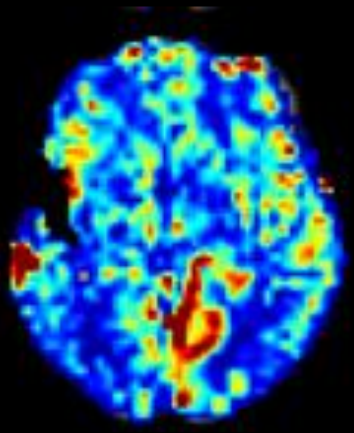


PET
(positron emission tomography)

SPECT
(single photon emission computed tomography)



fMRI
(functional magnetic resonance imaging)

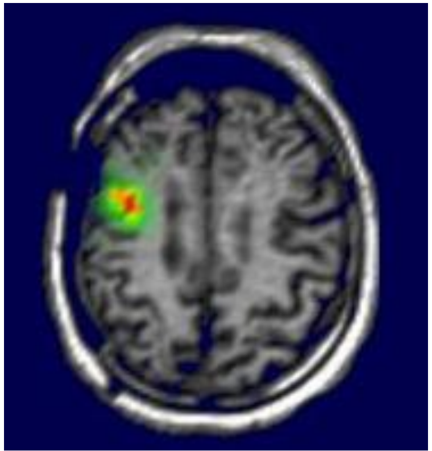


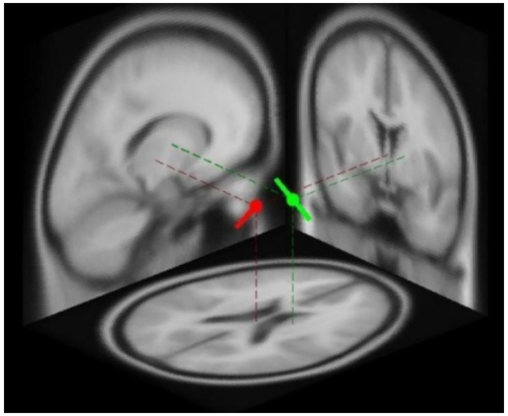
ASL
(arterial spin labellng)

# Non-invasive imaging techniques

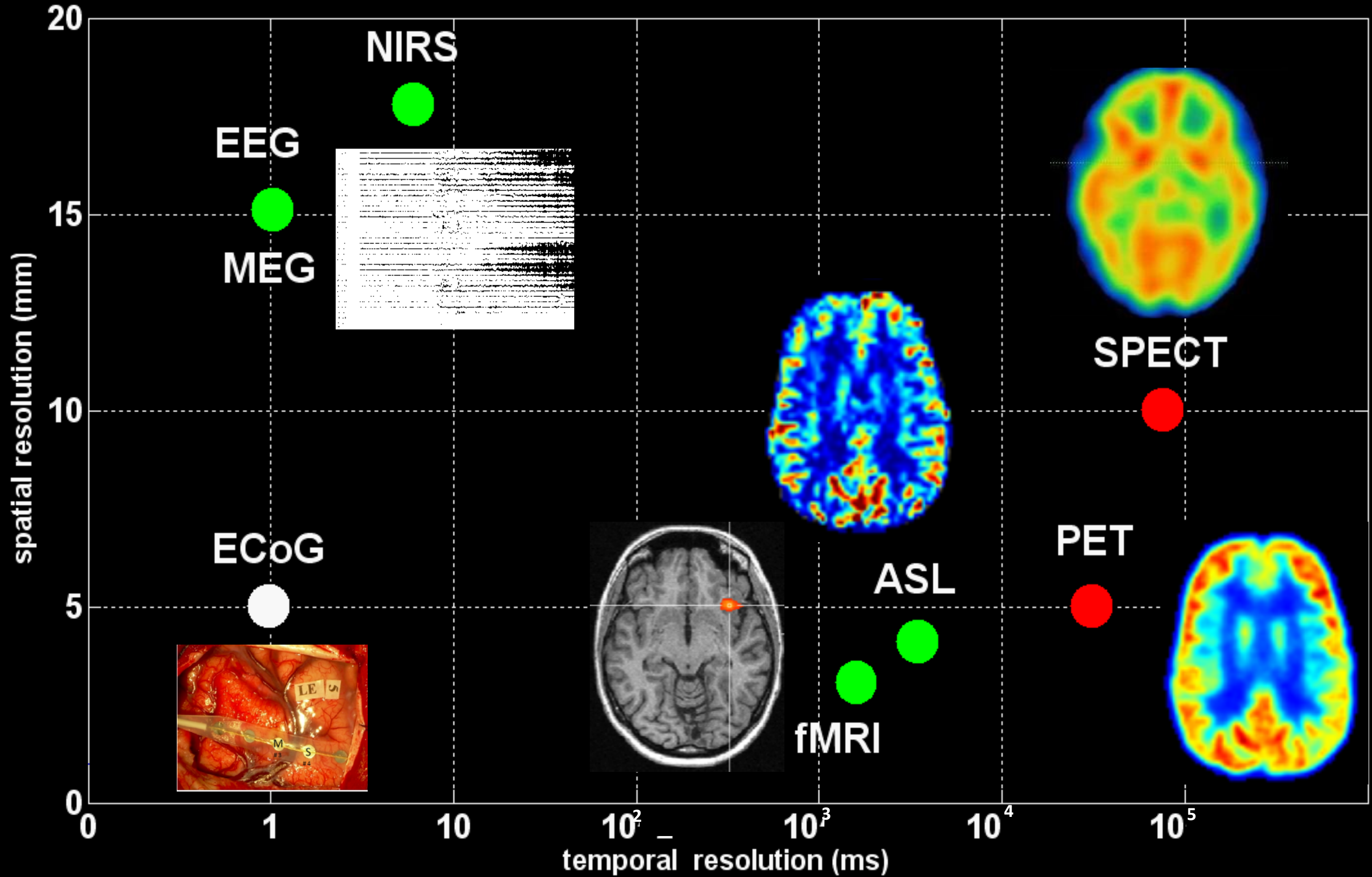


Imaging techniques



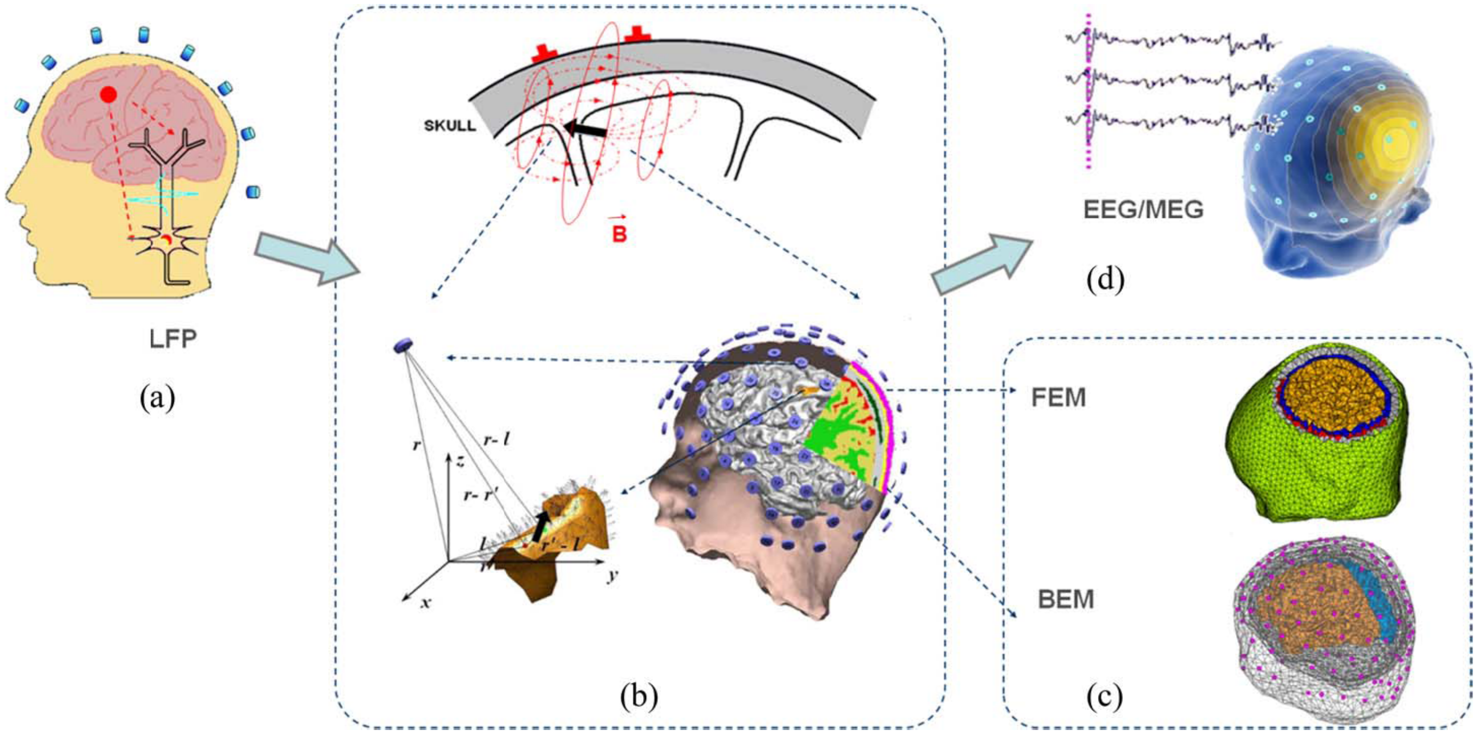


# Temporal and Spatial resolution



# Electrical Source Imaging

# Electrophysiological imaging of brain activity




EEG/MEG signals are mainly generated from synchronized activation of cortical pyramidal neurons located within the cortical gray matter.

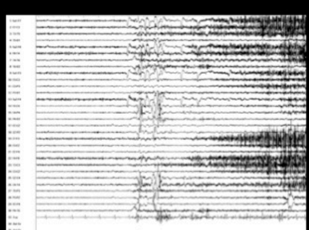
When pyramidal neurons are excited, the synaptic currents flowing across the cell membranes induce local excitatory postsynaptic potentials as well as magnetic fluxes, which collectively form the sources for EEG and MEG, respectively. When cortical neurons in columnar vicinity are in synchronized activation, the synaptic current flow, at a macroscopic level, approximates a **current dipole** located on cortical surface and oriented perpendicular to the local cortical surface.

The configuration (e.g. **location, magnitude, and orientation**) of such current dipole can be related with EEG or MEG signals through the modeling of head volume conduction.

He et al., IEEE Transaction on Biomedical Engineering, 2011

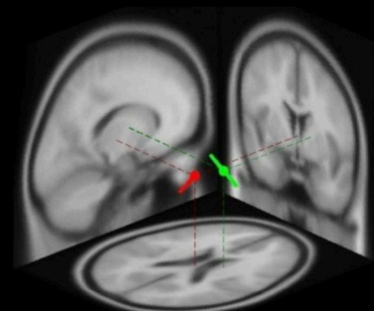
# Electrical Source Imaging (ESI)

Scalp
electric field



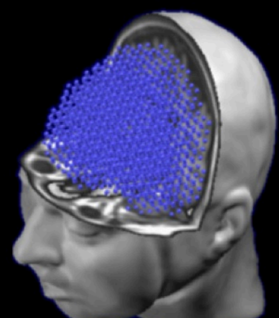
## SOURCE MODEL

Dipole



ECD assumes the underlying neuronal sources to be focal

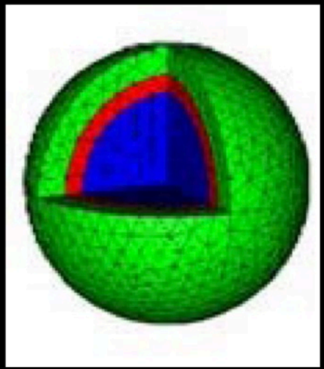
Distributed



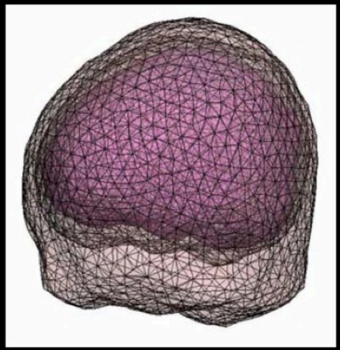
The 3D grid of solution points is considered as a possible location of a brain activity source

## HEAD MODEL

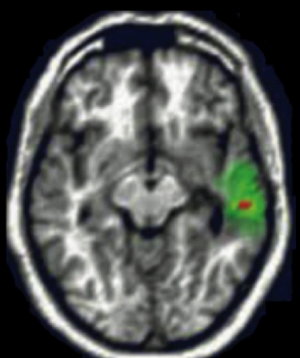
Spherical



Realistic



Source



*Pascual-Marqui et al., 1994*
*Michel et al., 2004*

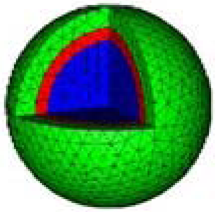
# Electrical Source Imaging (ESI)

Electrophysiological source imaging (ESI) is a model-based approach for imaging electrical sources associated with brain activation from noninvasive EEG or MEG measurements.

ESI entails:

1) **forward modeling** of brain sources and head volume conduction to establish a linear source-to-measurement relationship.
2) **inverse imaging** of brain electrical sources from measured EEG, via various strategies, most commonly dipole localization and distributed source imaging.

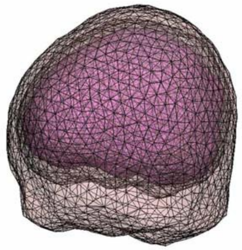
# Head models



1. **Sphere-shaped head models**
   (uniform conductivity) → computationally efficient

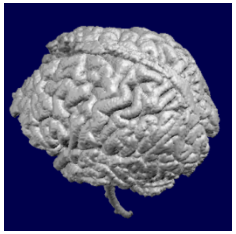
2. **Realistic Head Model:** these numerical models allow incorporating the realistic geometry of the head and brain after reconstruction of the anatomical structure from individual or standardized MRI data sets.

**Boundary Element Method (BEM):** gathers a more realistic shape of brain compartments of isotropic and homogeneous conductivities by using closed triangle meshes



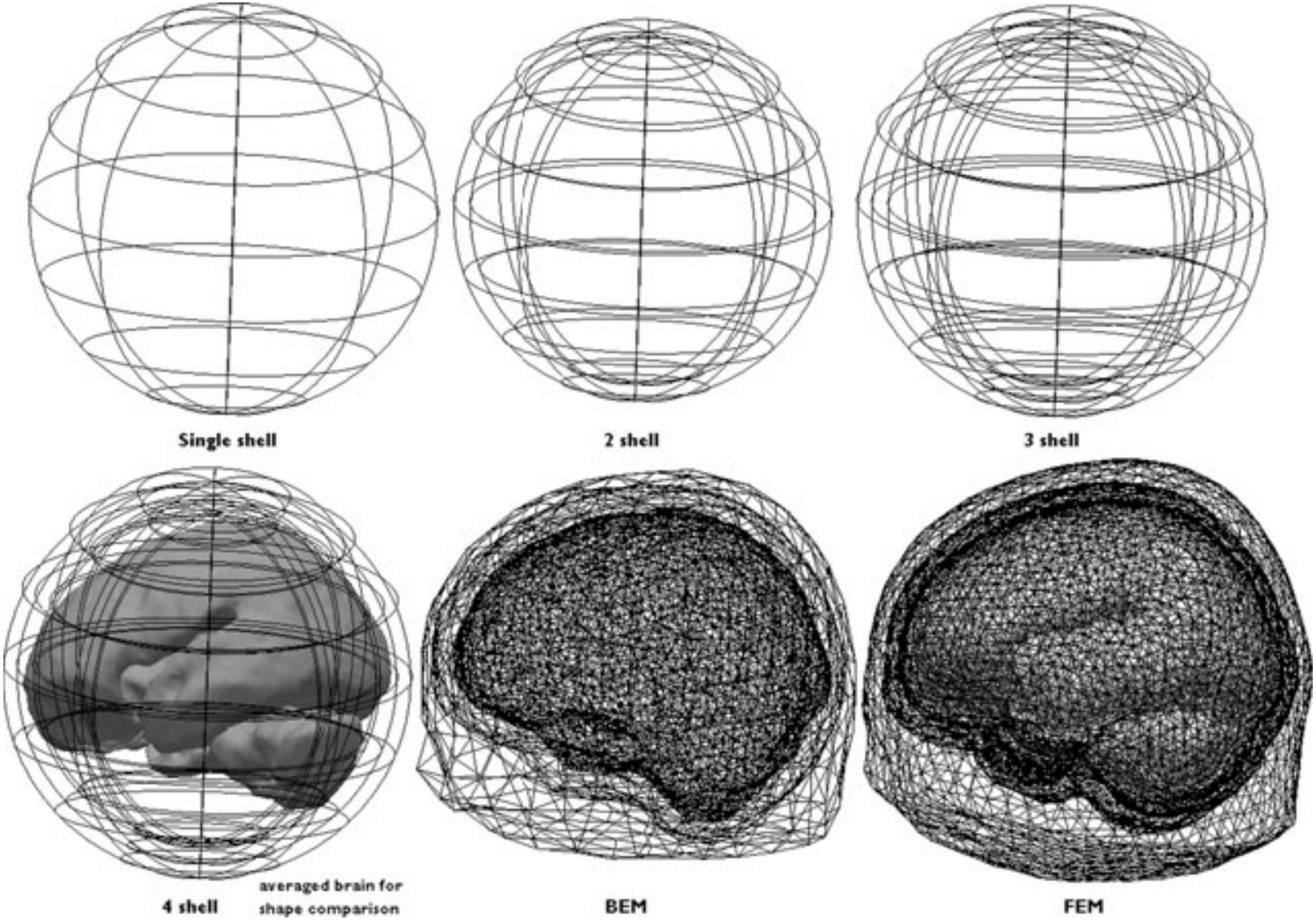
Meijs et al., 1987

**Finite-Element Method (FEM):** allow better accuracy than the BEM because they allow a better representation of the cortical structures



Bertrand et al., 1991, Awada et al., 1997

# Head models




**Realistic shape – (BEM isotropic, FEM anisotropic)**

Plummer et al., Epilepsia, 2008

# Forward Problem

EEG forward problem describes the distribution of electric potentials for given source locations, orientations, and signals. The relationship between EEG signals ( $\Phi$ ) and cortical current source dipoles (J) can be represented by a linear system:

?

$$\Phi = \mathbf{KJ} + c1$$

measured scalp potentials (EEG)

lead field matrix (describes how a unit dipole of a certain location and orientation is related to the EEG)

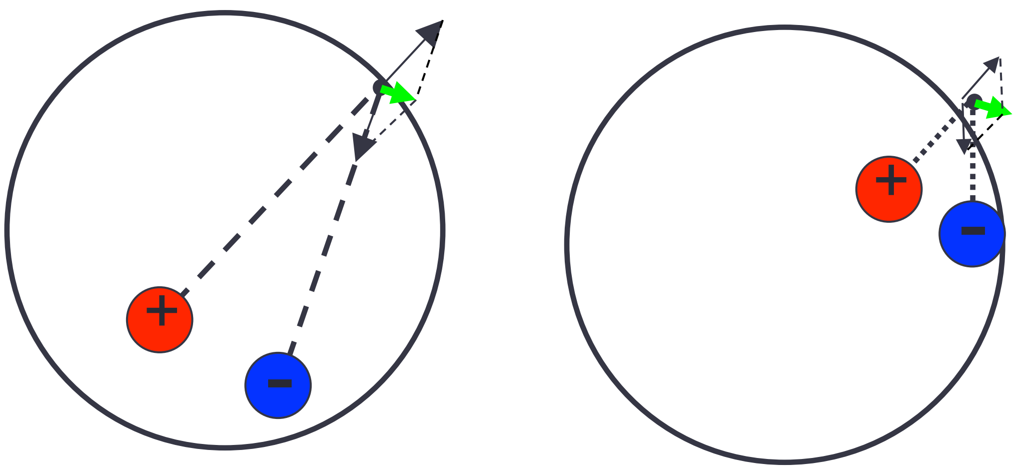
current density

# Inverse Problem

The inverse problem is used to convert measured electric potentials (EEG) into current densities of the sources.

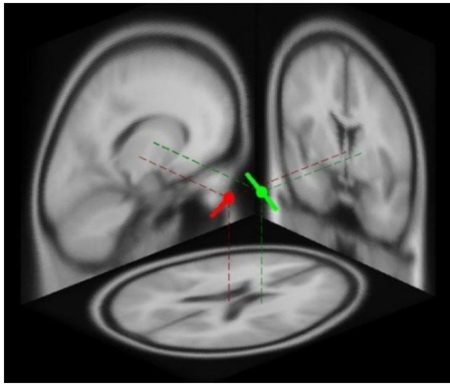
The inverse problem is ill-posed because an infinity of different source configurations can produce the same EEG scalp distribution

Nurez and Srinivasan, 2006

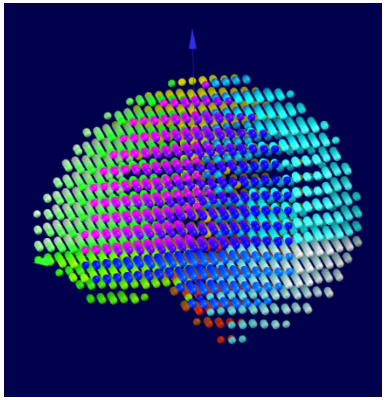



Scherg and Von Cramon, 1985, Liu et al., 1998, Babiloni et al., 2003, Michel et al., 2004

# Inverse solutions



1. **DISCRETE**
   **Equivalent current dipole (ECD) approach**
   where the signals are assumed to be generated by few focal sources.



2. **DISTRIBUTED**
   **Linear distributed (LD) approaches**
   which consider that the dipoles are regularly distributed in cerebral volume according to a 3D grid and where all possible source locations are considered simultaneously.

# Inverse Problem → Inverse solutions

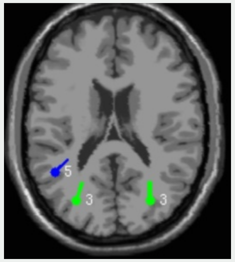
## Equivalent current dipole approach

ECD assumes the underlying neuronal sources to be focal

Number of sources < number of sensors
OVERDETERMINED PROBLEM

The lead field matrix has more rows (number of sensors) than columns (number of sources)

Source model and source waveforms



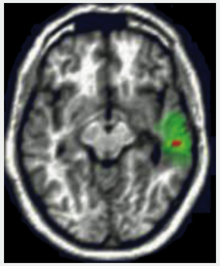
## Linear distributed

The 3D grid of solution points is considered as a possible location of a brain activity source

Number of sources >> number of sensors
UNDERDETERMINED PROBLEM

The lead field matrix has more columns than rows

3D volume image for each time point



# Equivalent current dipole

**Parameter Estimates**

To determine the best location of the sources, the squared error between the surface electric potential map generated by dipoles using a certain forward model and the actual measured potential map is calculated.

**Methods**

- Dipole fitting methods [Scherg, 1990]
- linear constrained minimum variance (LCMV) beamformers [Van Veen et al., 1997]
- the multiple signal classification (MUSIC) [Mosher and Leahy, 1998]
- …

**Limitations**

ECD models have some limits in estimating in advance the number of dipoles and localizing extended sources.

The center of mass of the cortical activity is localized, but the distribution and the extension of the activity remain to be determined [He et al., 2011].

# Linear distributed approches

The estimation of the dipole source configuration **J** is provided by the solution of the linear system:

?

$$\mathbf{\Phi} = \mathrm{K}\mathbf{J} + c\mathbf{1}$$

$\mathbf{\Phi} \in R^{N_E \times 1}$ with $\mathbf{\Phi} = (\Phi_1, \Phi_2, \ldots, \Phi_{N_E})^T$ : is a $N_E \times 1$ known matrix of measurements of scalp electric potential differences

$N_E$: number of electrodes

$\mathbf{1} \in R^{N_E \times 1}$ : is a vector of ones

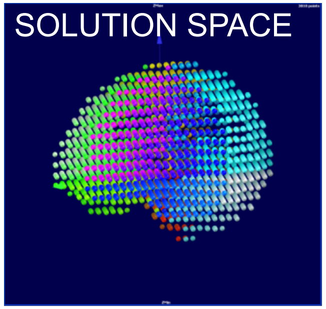
$\mathbf{J} \in R^{(3N_V \times 1)}$ : matrix of current densities at $N_V$ points within the brain volume

c : accounts for the physical nature of electric potential

$\mathrm{K} \in R^{N_E \times (3N_V)}$ : transfer matrix or lead field matrix

$$\mathrm{K} = \begin{pmatrix} \mathbf{k}_{1,1}^T & \mathbf{k}_{1,2}^T & \cdots & \mathbf{k}_{1,N_V}^T \\ \mathbf{k}_{2,1}^T & \mathbf{k}_{2,2}^T & \cdots & \mathbf{k}_{2,N_V}^T \\ \cdots & & & \\ \mathbf{k}_{N_E,1}^T & \mathbf{k}_{N_E,2}^T & \cdots & \mathbf{k}_{N_E,N_V}^T \end{pmatrix}$$

$\mathbf{k}_{e,v} \in R^{3\times 1}$ : are determined by all proprieties of the head, i.e. geometry and conductivity profile.




Pascual-Marqui, Seikihara, Brandeis and Michel, Electrical Neuroimaging

# Particular inverse solutions

## Minimum norm least square (MN) solution

$$\min_{\mathbf{J},c} \Psi \quad \text{with} \quad \Psi = \left\| \Phi - \mathbf{KJ} - c\mathbf{1} \right\|^2 + \lambda \mathbf{J}^T \mathbf{J}$$

[Hamalainen and Ilmoniemi, 1984]

Solution: $\hat{\mathbf{J}} = \mathbf{T}\Phi$ with $\mathbf{T} = \mathbf{K}^T \mathbf{H} (\mathbf{HKK}^T \mathbf{H} + \lambda \mathbf{H})^+$

$\mathbf{H} = \mathbf{I} - \frac{1}{N_E} \mathbf{1}\mathbf{1}^T$ : denotes the $N_E$x$N_E$ average reference operator

λ : Tikhonov regularization parameter

"+" denotes the Moore–Penrose generalized inverse

$\mathbf{I}$ : $N_E$x$N_E$ identity matrix

$\mathbf{1}$ : Nx1 matrix comprised of ones

$N_E$ : number of electrodes

Minimum norm solutions favors superficial sources and misplaces deep sources

## Weighted minimum-norm least squares (WMN) solution

$$\min_{\mathbf{J},c} \Psi_D \quad \text{with} \quad \Psi_D = \left\| \Phi - \mathbf{KJ} - c\mathbf{1} \right\|^2 + \lambda \mathbf{J}^T \mathbf{DJ}$$

[Pascual-Marqui et al., 1994, Gorodnitsky et al., 1995, Grave de Peralta and Gonzalez, 1998]

Solution: $\hat{\mathbf{J}}_D = \mathbf{T}_D \Phi$ with $\mathbf{T}_D = \mathbf{D}^{-1} \mathbf{K}^T \mathbf{H} (\mathbf{HKD}^{-1} \mathbf{K}^T \mathbf{H} + \lambda \mathbf{H})^+$

D is used to "re-weight" the solution, i.e. to incorporate some prior knowledge about the spatial distribution of the source activity

# Particular inverse solutions

## Low-resolution electromagnetic tomography algorithm (LORETA)

$$\min_{\mathbf{J},c} \Psi_W \quad \text{with} \quad \Psi_W = \left\| \Phi - \mathbf{KJ} - c\mathbf{1} \right\|^2 + \lambda \mathbf{J}^T W \mathbf{J}$$

[Pascual-Marqui et al., 1994, 1999]

Solution: $\hat{\mathbf{J}}_W = \mathbf{T}_W \Phi$ with $\mathbf{T}_W = \mathbf{W}^{-1}\mathbf{K}^T\mathbf{H}(\mathbf{HKW}^{-1}\mathbf{K}^T\mathbf{H} + \lambda\mathbf{H})^+$

$$\mathbf{J}^T\mathbf{WJ} = \sum_v \left\| \mathbf{j}_v - AveNeighb(\mathbf{j}_v) \right\|^2$$

$AveNeighb$ : average of current densities in the immediate neighborhood of point v, excluding point v

LORETA minimizes the squared norm of the Laplacian of the weighted 3D current-density vector field. It incorporates the ”smoothness assumption” selecting the inverse solution of the measured data with the smoothest distribution in space.

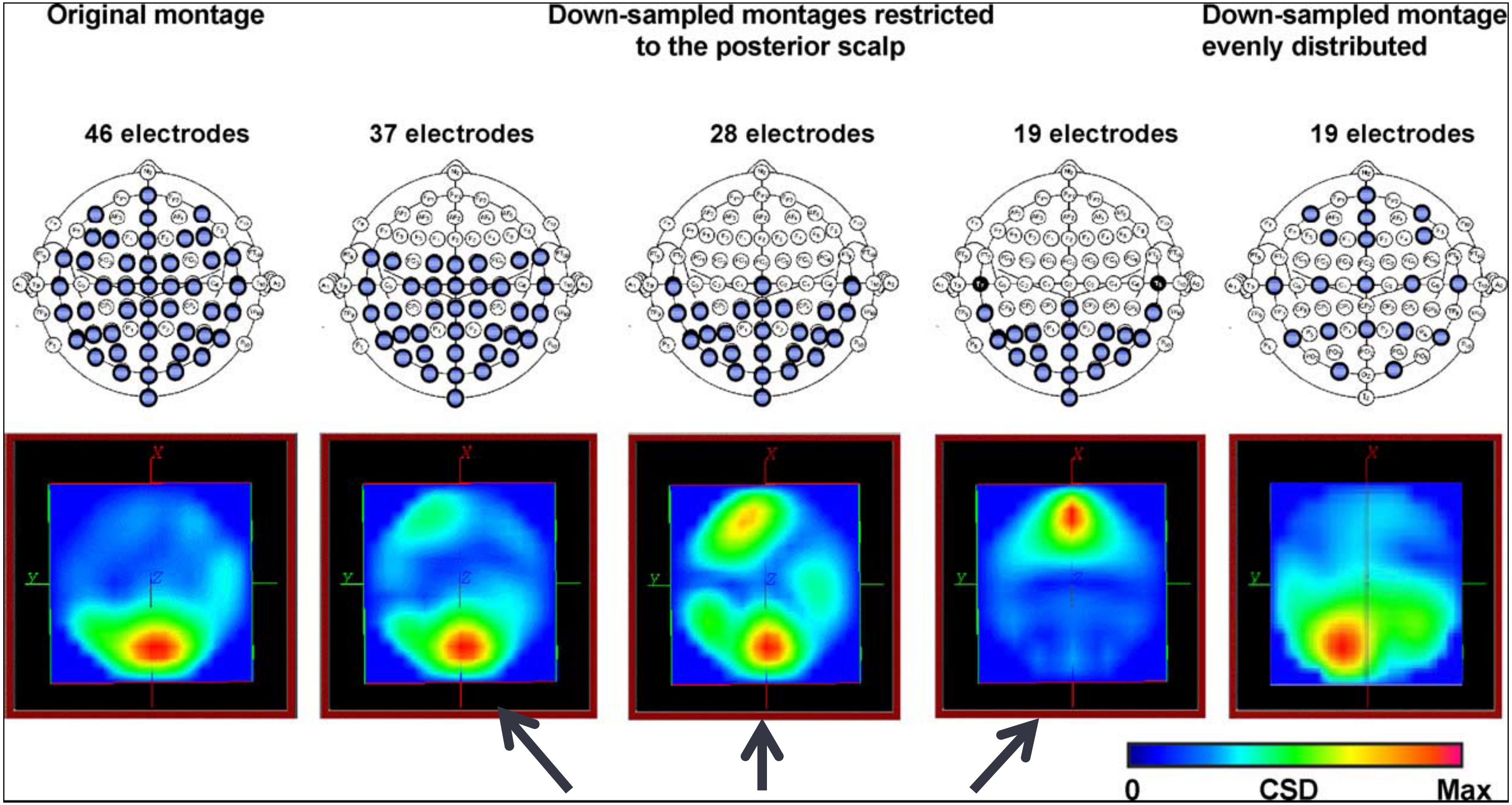
## Local Autoregressive Average (LAURA)

$$\mathbf{J}^T\mathbf{W}_{Laura}\mathbf{J} = \sum_v \left\| \mathbf{j}_v - WeightedAveNeighb(\mathbf{j}_v) \right\|^2$$

[Grave de Peralta and Gonzalez, 2002]

The estimated activity at one point depends on the activity at neighboring points according to electromagnetic laws (i.e. the strength of the source declines with the inverse of the squared distance of the potential field).

# Effect of the electrode distribution on the estimation of the source



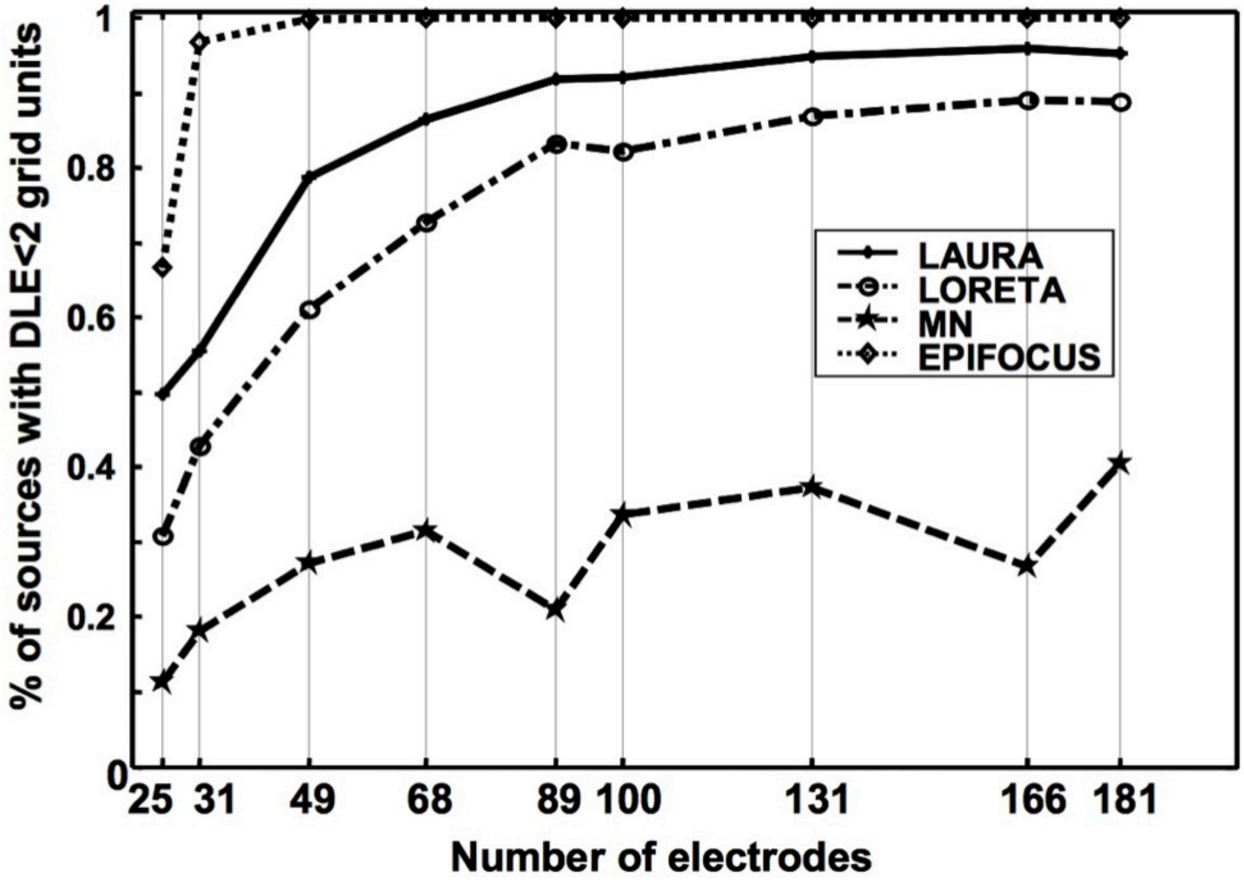

**LORETA, visual EP**

**→ Occipital activation**

Frontal electrodes excluded

Michel et al., Clinical Neurophysiol 2004

# Effect of the number of electrodes on source localization




Michel et al., Clinical Neurophysiol 2004

# Electrical Source Imaging:
# clinical applications

# Electrical Source Imaging: clinical applications

Identification of spontaneous EEG activity:

1. **Interictal activity** of epileptic patients
2. **Brain rhythm** in resting state (e.g. alpha rhythm)
3. **Sleep waves** (spindle)

And evoked:

4. **Evoked potential (EP)**

# Electrical Source Imaging: clinical applications

Identification of spontaneous EEG activity:

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3. **Sleep waves** (spindle)

And evoked:

4. **Evoked potential (EP)**

# Drug resistant focal epilepsy

The feature of partial seizures is the presence of abnormal electrical activity that originates from an epileptic foci.

Seizures prevent healthy development and may cause brain damage.

**Treatment**

35% of focal epilepsy patients do not respond to medication, and must undergo surgical resection of the epileptic focal points.

Surgery requires accurate localization of the foci.

# Candidate for epilepsy surgery

- Persistent seizures despite appropriate pharmacological treatment
- Impairment of quality of life due to ongoing seizures

**STANDARD PRESURGICAL WORKUP (Patient selection)**

clinical history
standard EEG
long-term video EEG
MRI
Neuropsychological evaluation

**NON INVASIVE IMAGING METHODS**

HIGH-DENSITY EEG MEG
PET, SPECT, ASL
EEG-fMRI

**INVASIVE EXAMINATIONS**

Stereo EEG

**SURGICAL DECISION**

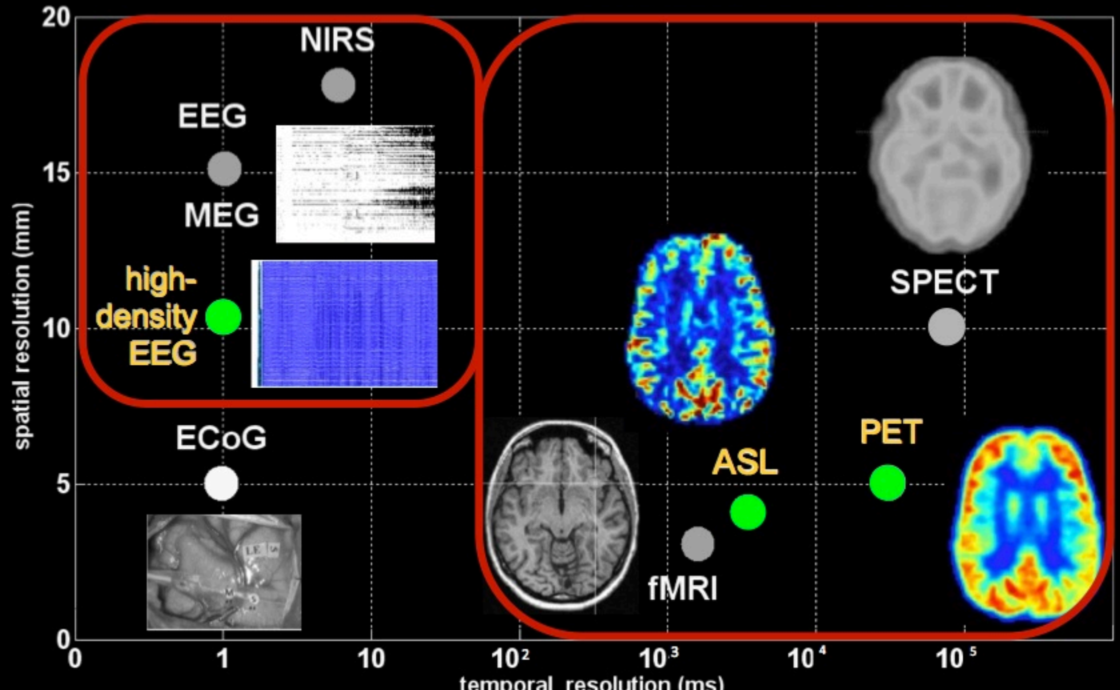
**They do not always provide the localizing accuracy required for surgical planning**

# Candidate for epilepsy surgery

- Standard presurgical workup does not always provide the localizing accuracy and precision required for surgical planning

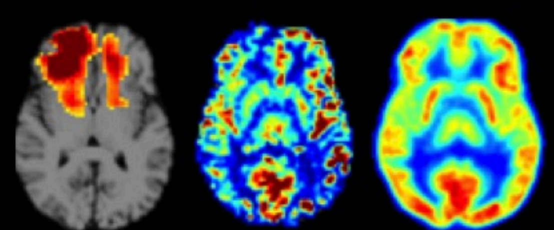
- Non-invasive imaging methods are useful to correctly identify the activity before the surgery treatment

## NON-INVASIVE IMAGING TECHNIQUES IN EPILEPSY




## MULTIMODAL APPROACH

Each bears limitations that can be partly overcome by combining their results!



*Bagshaw et al., 2006; Brodbeck et al., 2010; Groening et al., 2009; Storti et al., 2012; Vulliemoz et al., 2010ab*

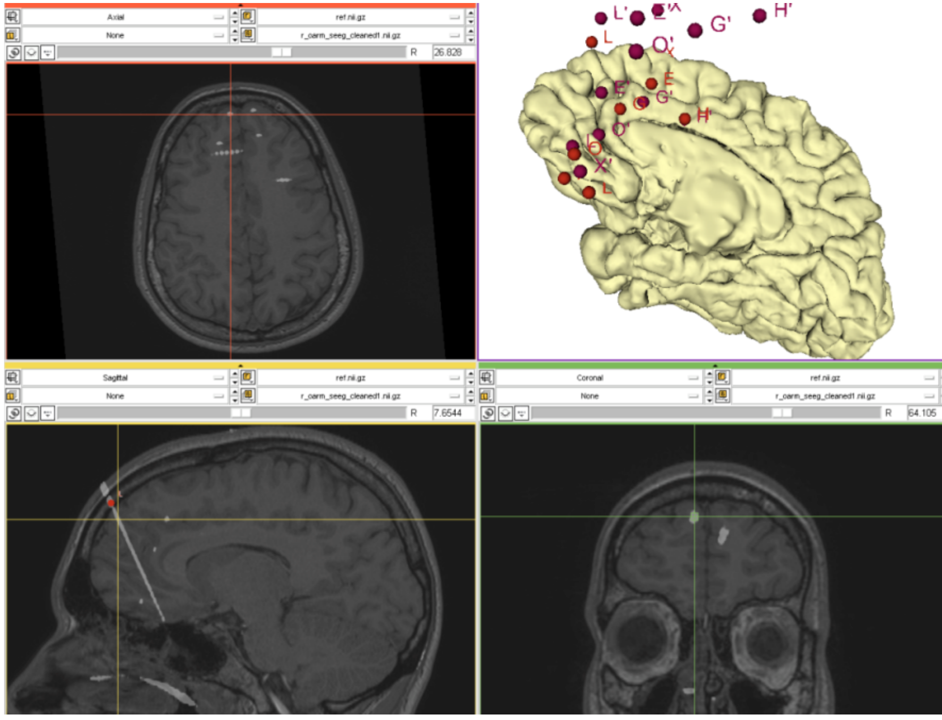
# Invasive examinations

**Stereo EEG**

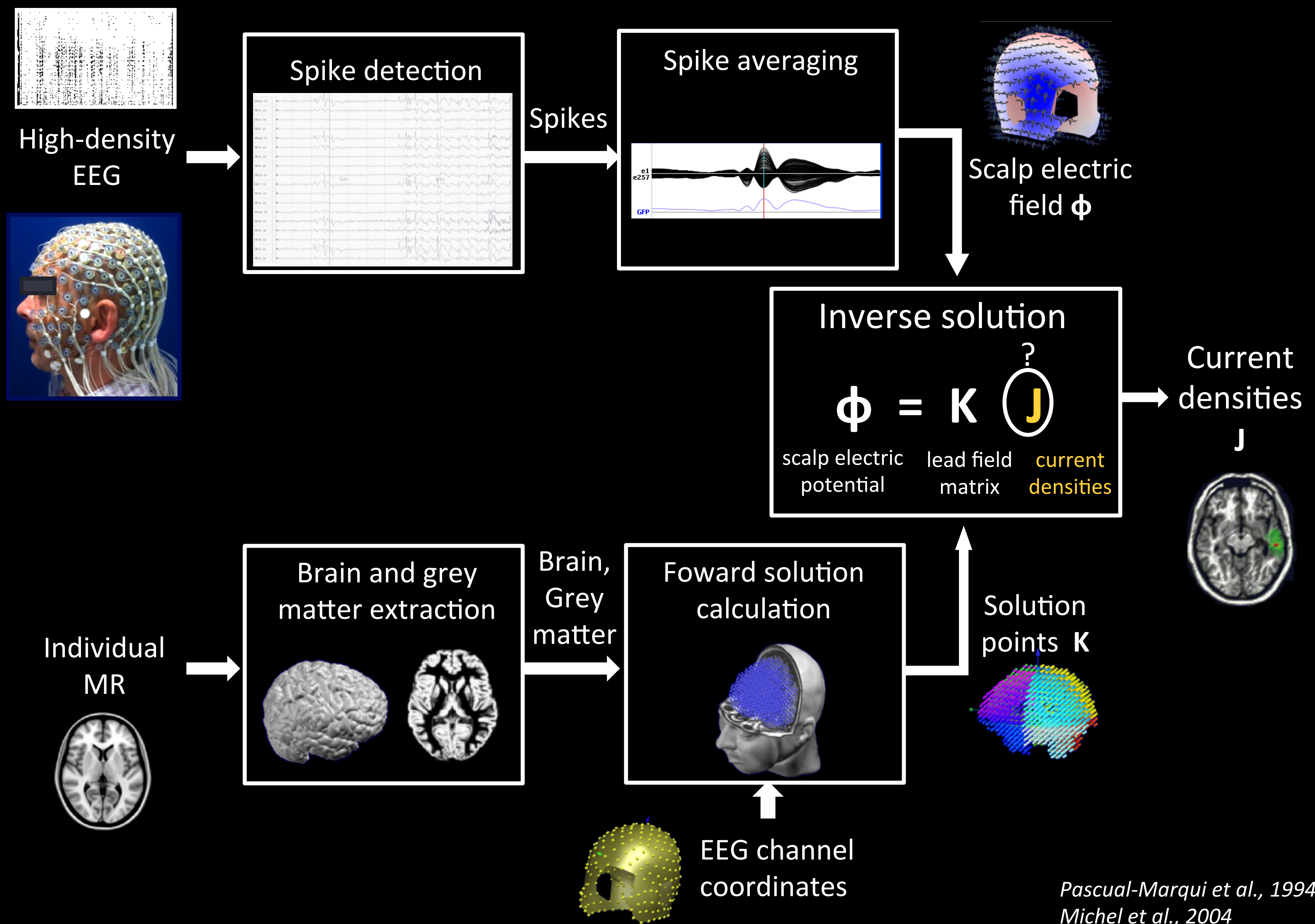
Intracerebral electrodes are implanted into the selected brain area to record the electrical activity during epileptic seizures, thus contributing to define with accuracy the boundaries of the epileptogenic zone, i.e. the area of brain generating the seizures which should be eventually surgically resected to achieve freedom from epileptic attacks.

- The implantation of intracerebral electrodes is carried out on the basis of non-invasive examinations.

- It is used in patients with epilepsy not responding to drug treatment, and who are potential candidates to receive brain surgery in order to control seizures.

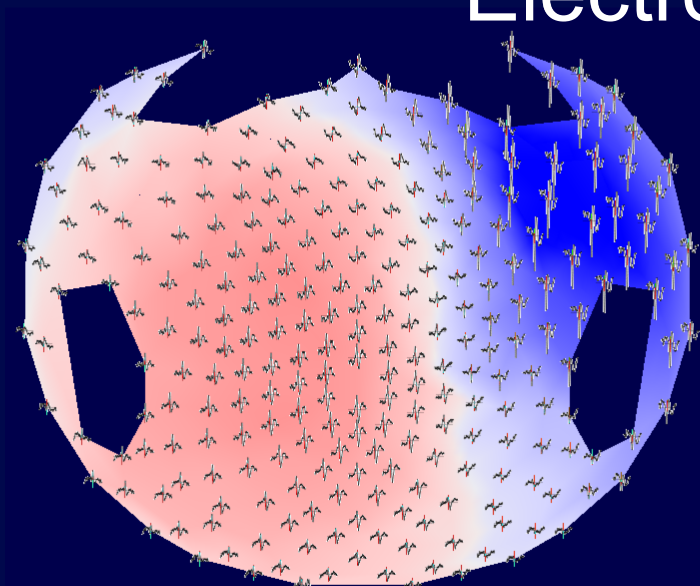


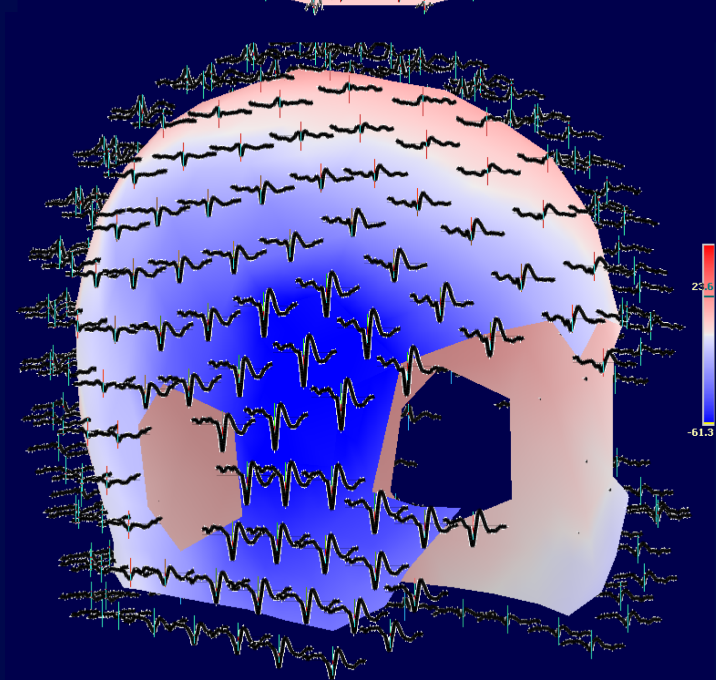
# High-density EEG and ESI

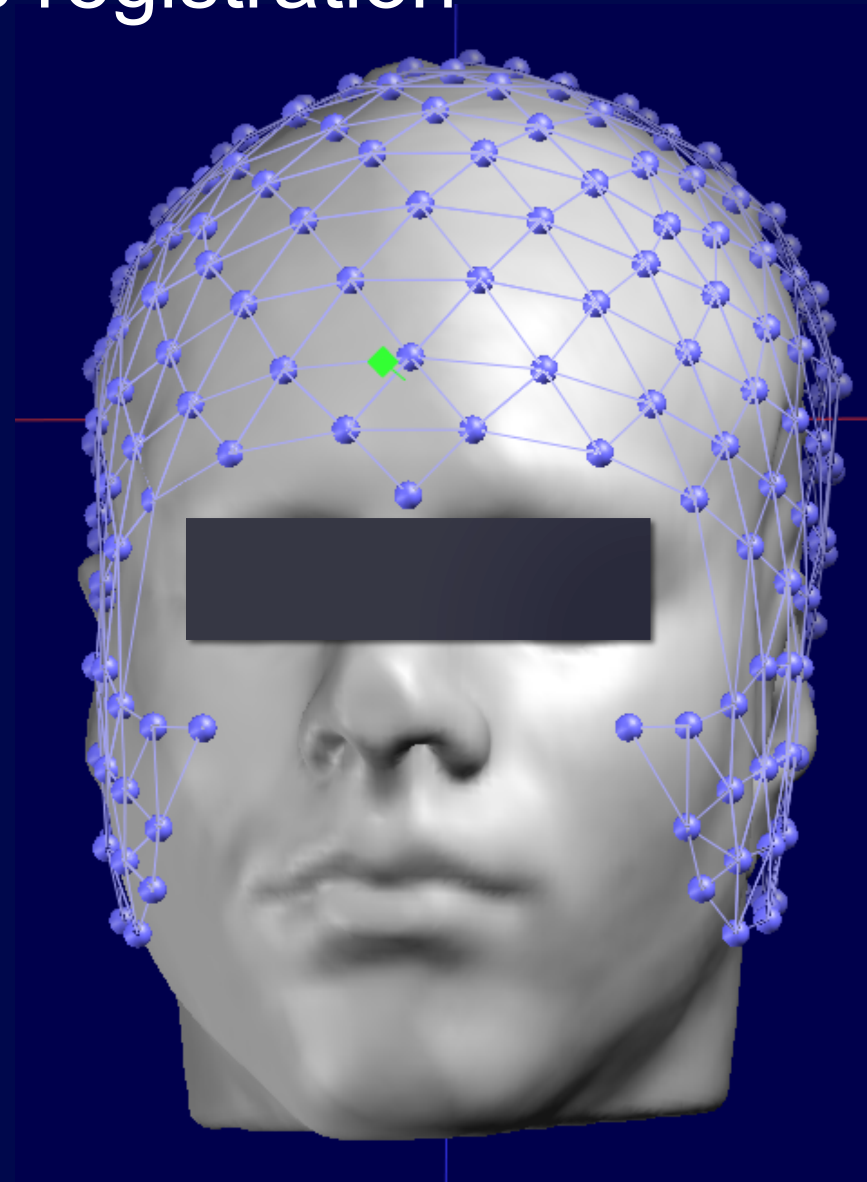



*Pascual-Marqui et al., 1994*
*Michel et al., 2004*

# Electrodes registration

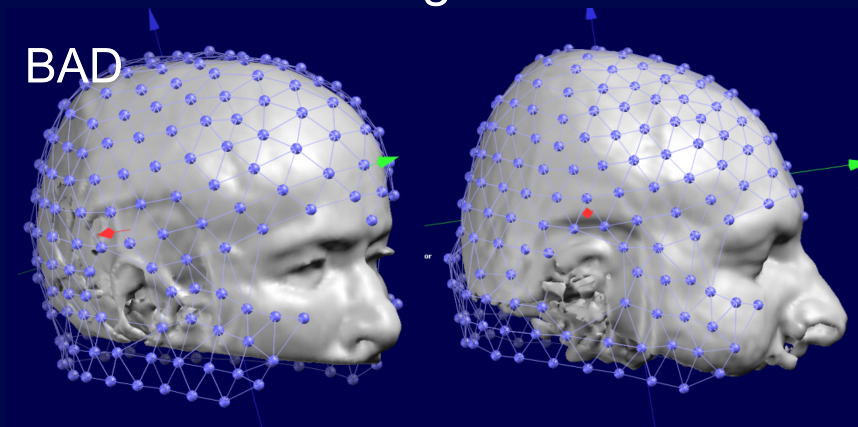


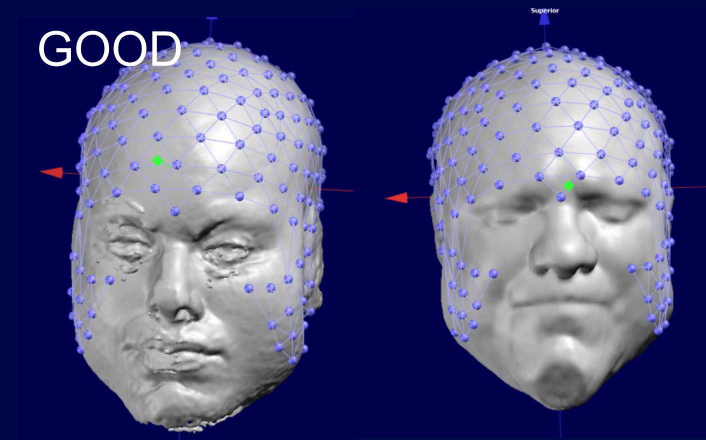


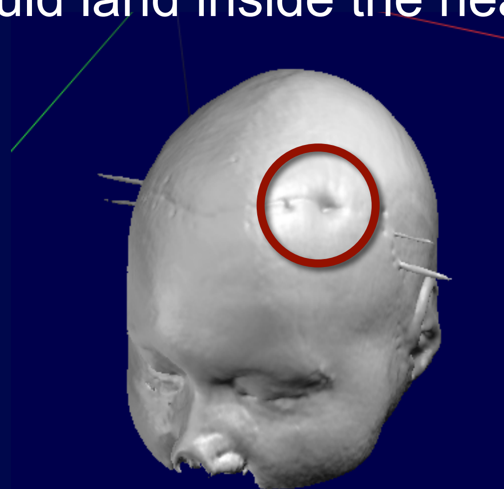
# Electrodes registration : practical issues

1. Electrodes floating in the air below the MRI cut



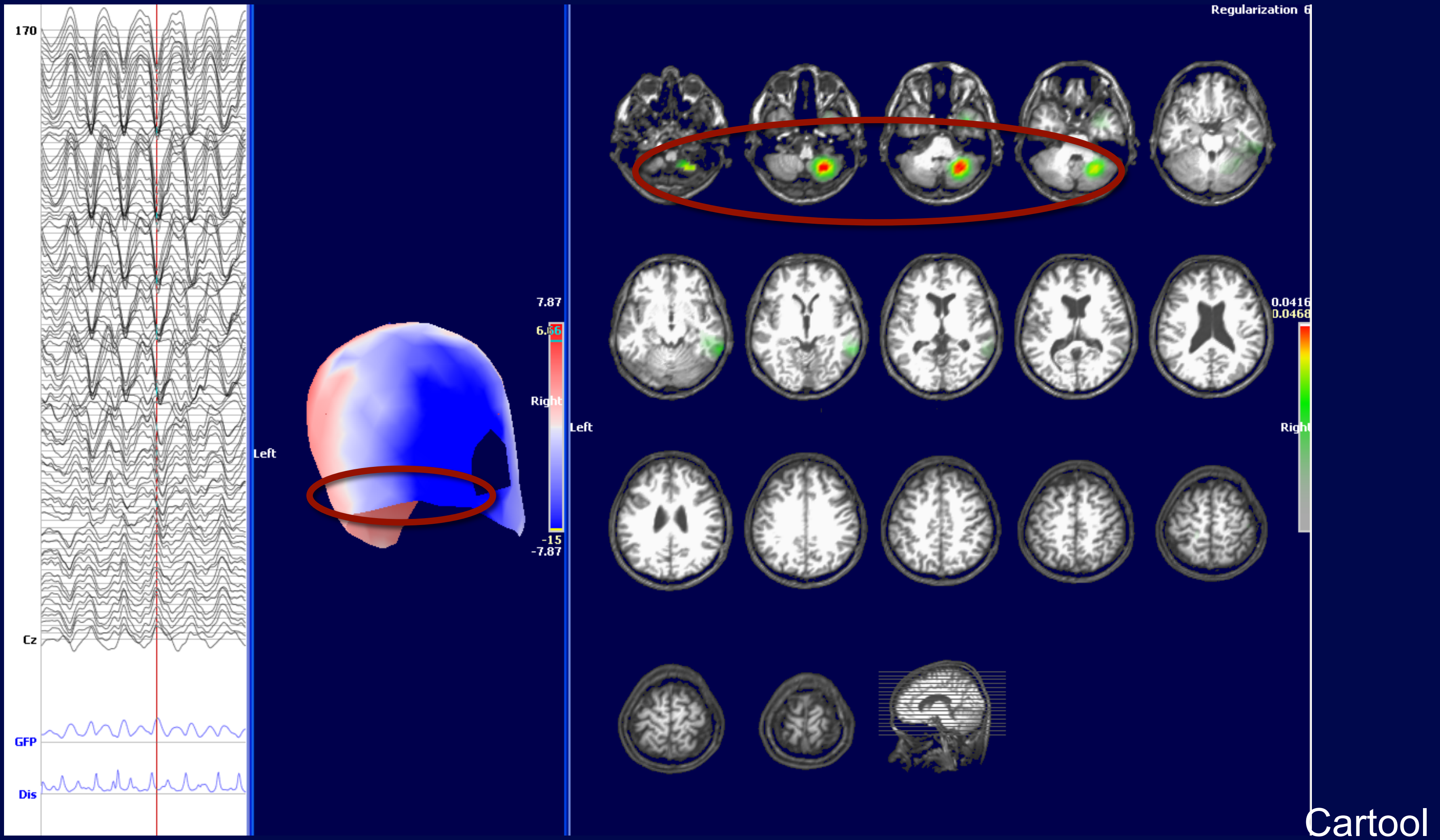

2. Registering electrodes to a corrupted MRI (irregular surface) → some electrodes could land inside the head



Cartool

# MRI (brain and grey matter extraction): issues

3. Skull-stripped brain should contain grey and white matters and void of cerebellum



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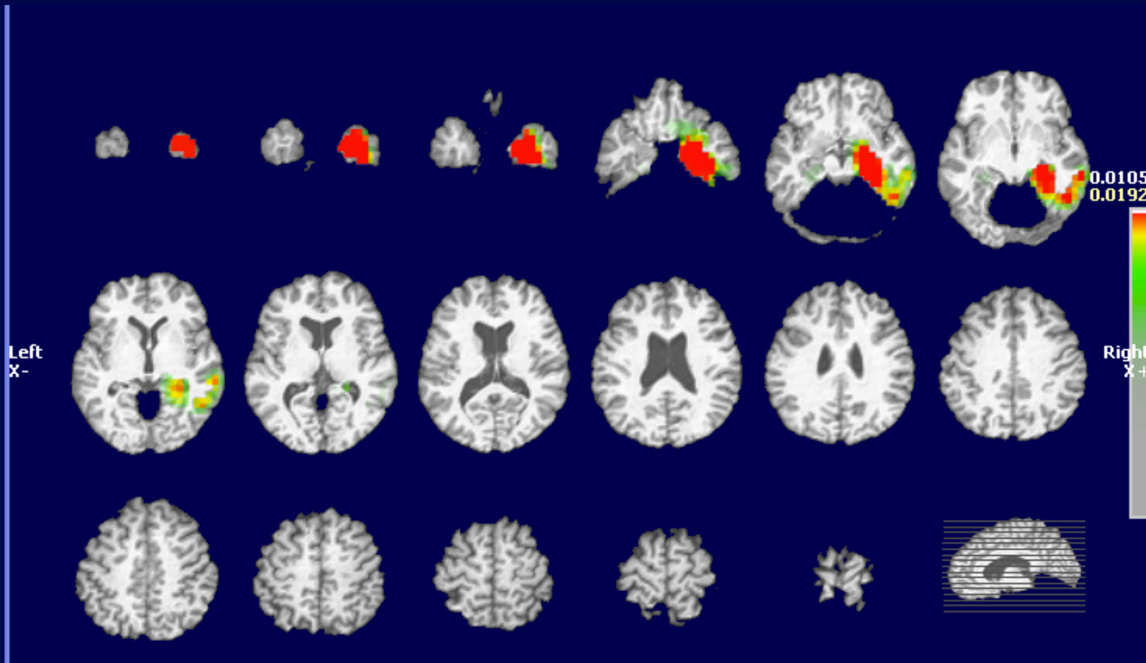
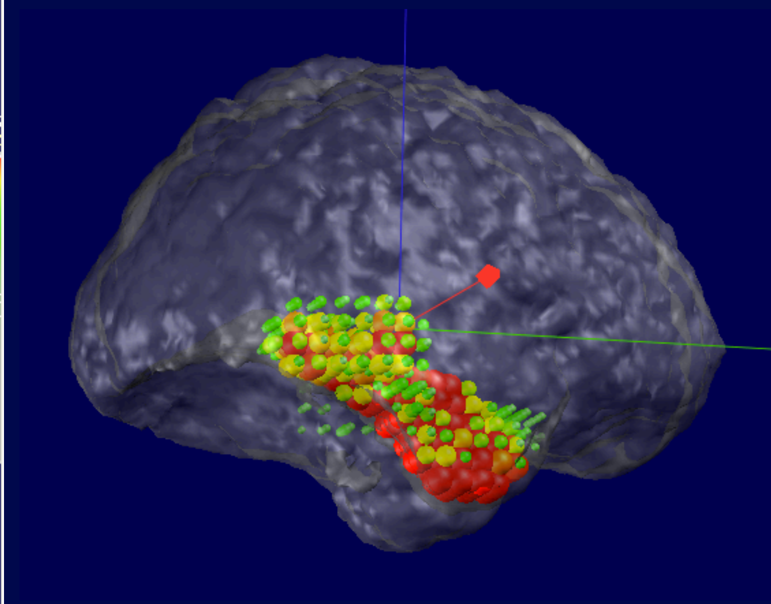
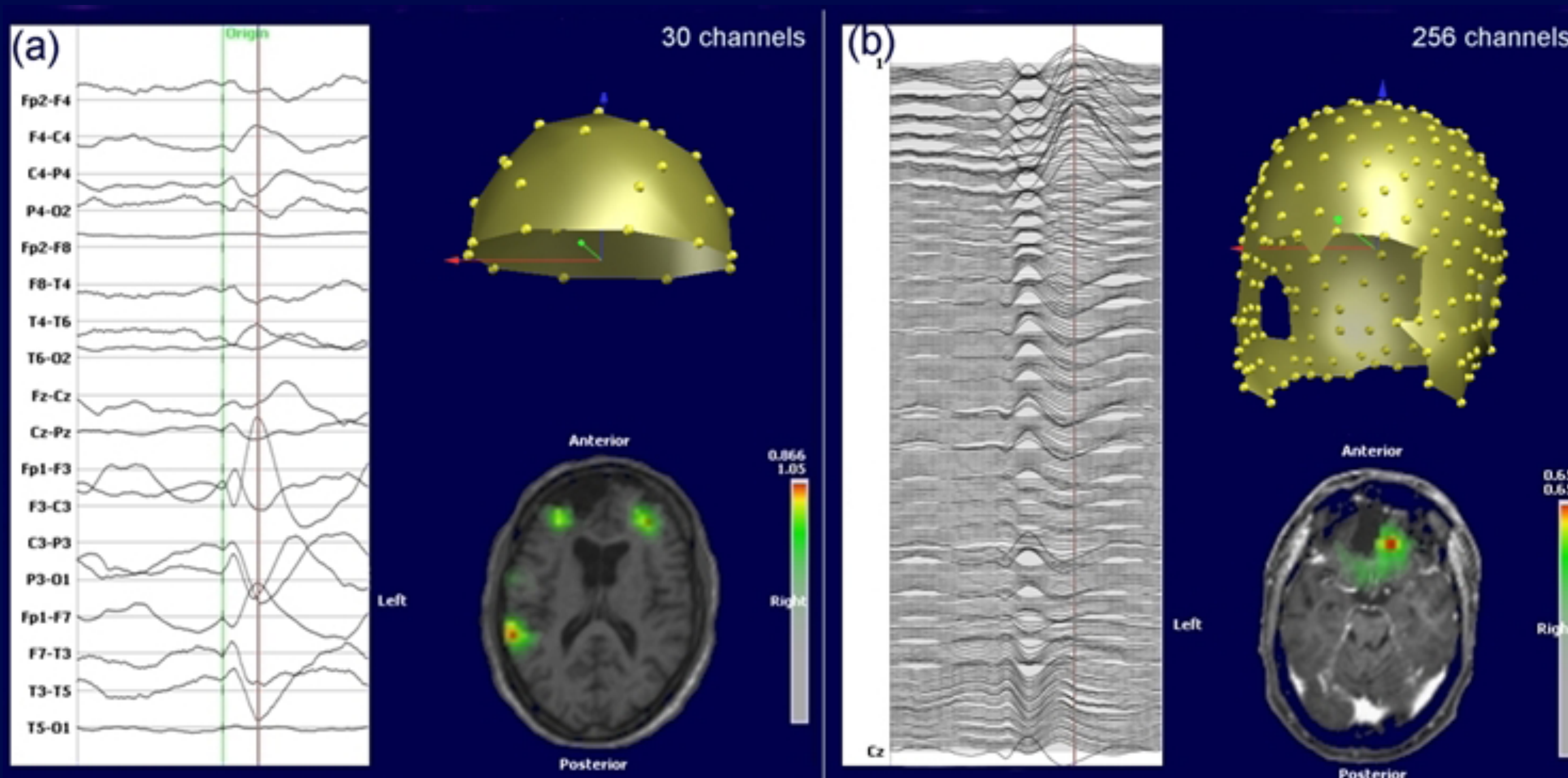


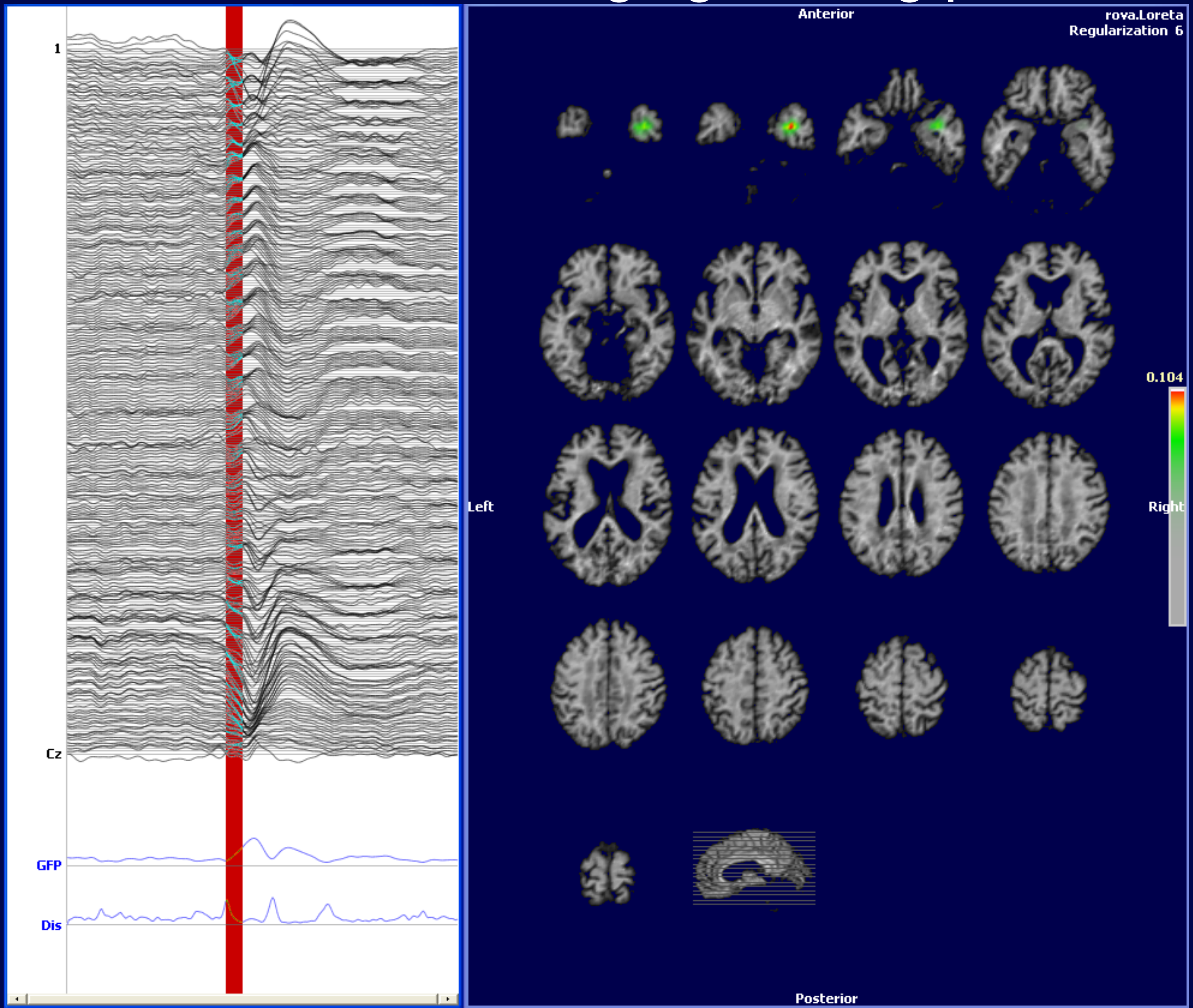
Cartool

# Effect of the number of electrodes on the estimation of the source

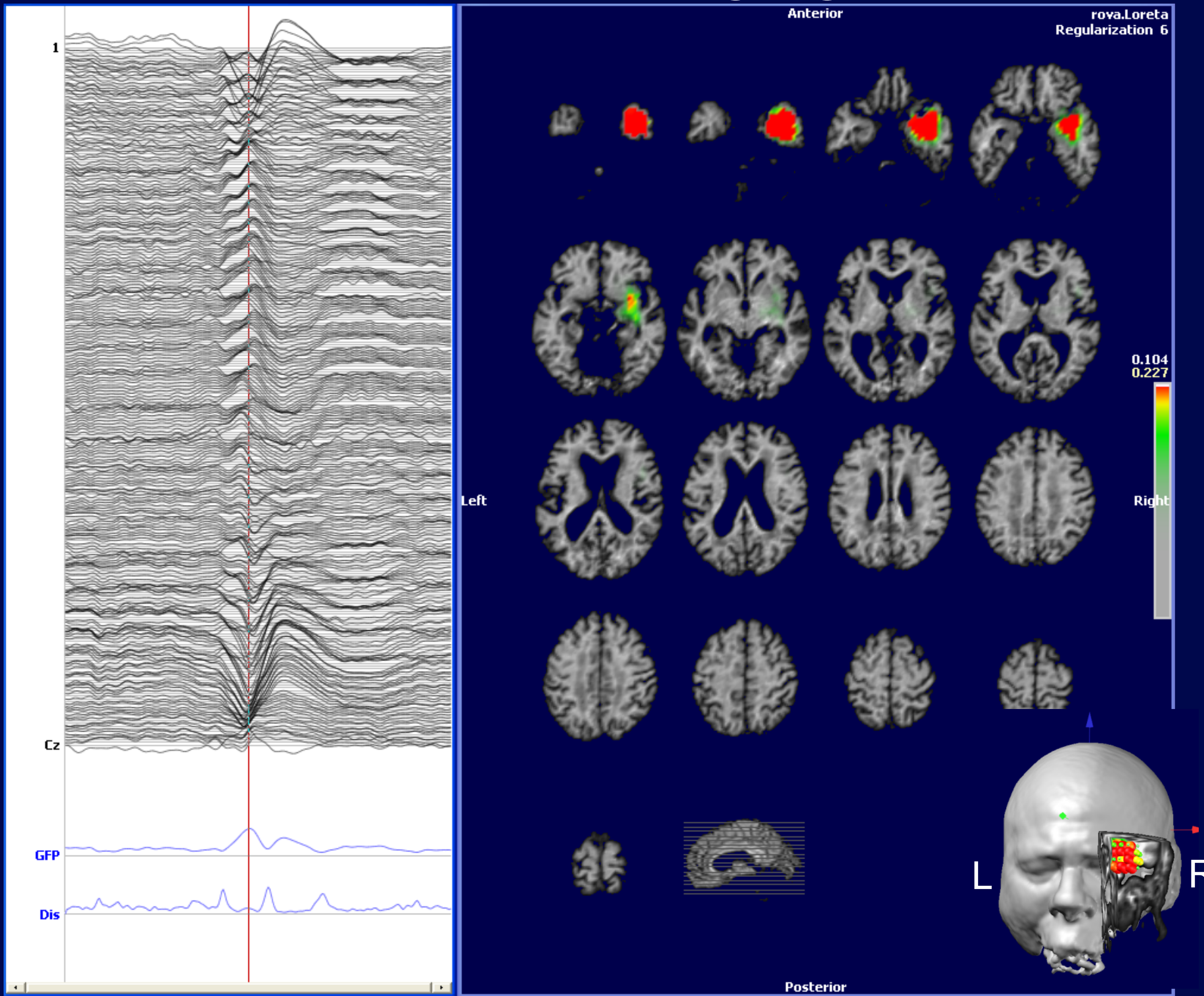



The source localization can be biased by a low number of electrodes [Michel et al., 2004] → increasing the number of electrodes the localization can be improved.

# Electrical source imaging – rising phase

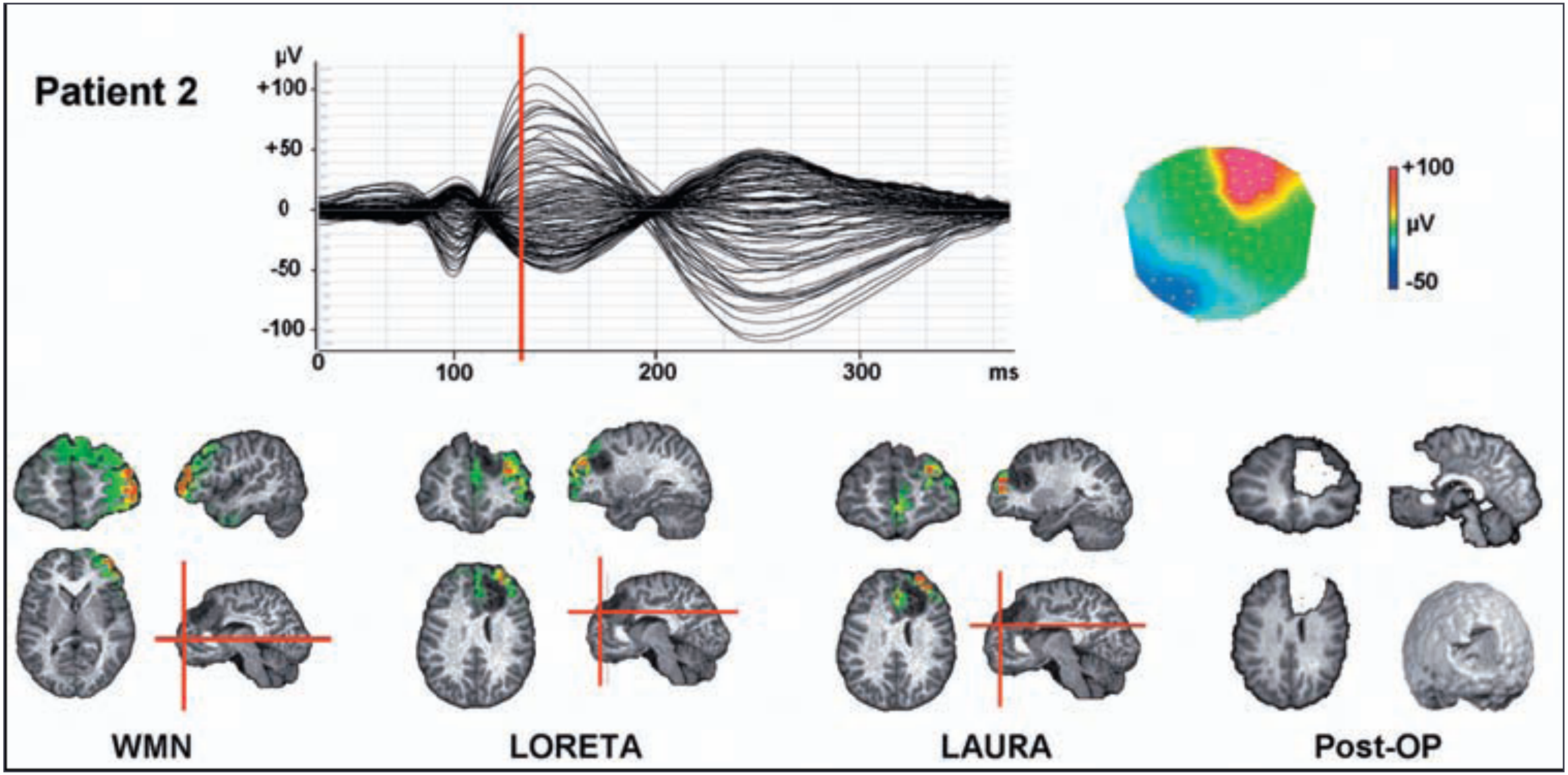


# Electrical source imaging – peak



# ESI and Clinical Validation

Differences between inverse solution algorithms and the post-surgical MRI




Michel et al., Electrical Neuroimaging, 2009

# Electrical Source Imaging: clinical applications

Identification of spontaneous EEG activity:

1. **Interictal activity** of epileptic patients
2. **Brain rhythm** in resting state (e.g. alpha rhythm)
3. **Sleep waves** (spindle)

And evoked:

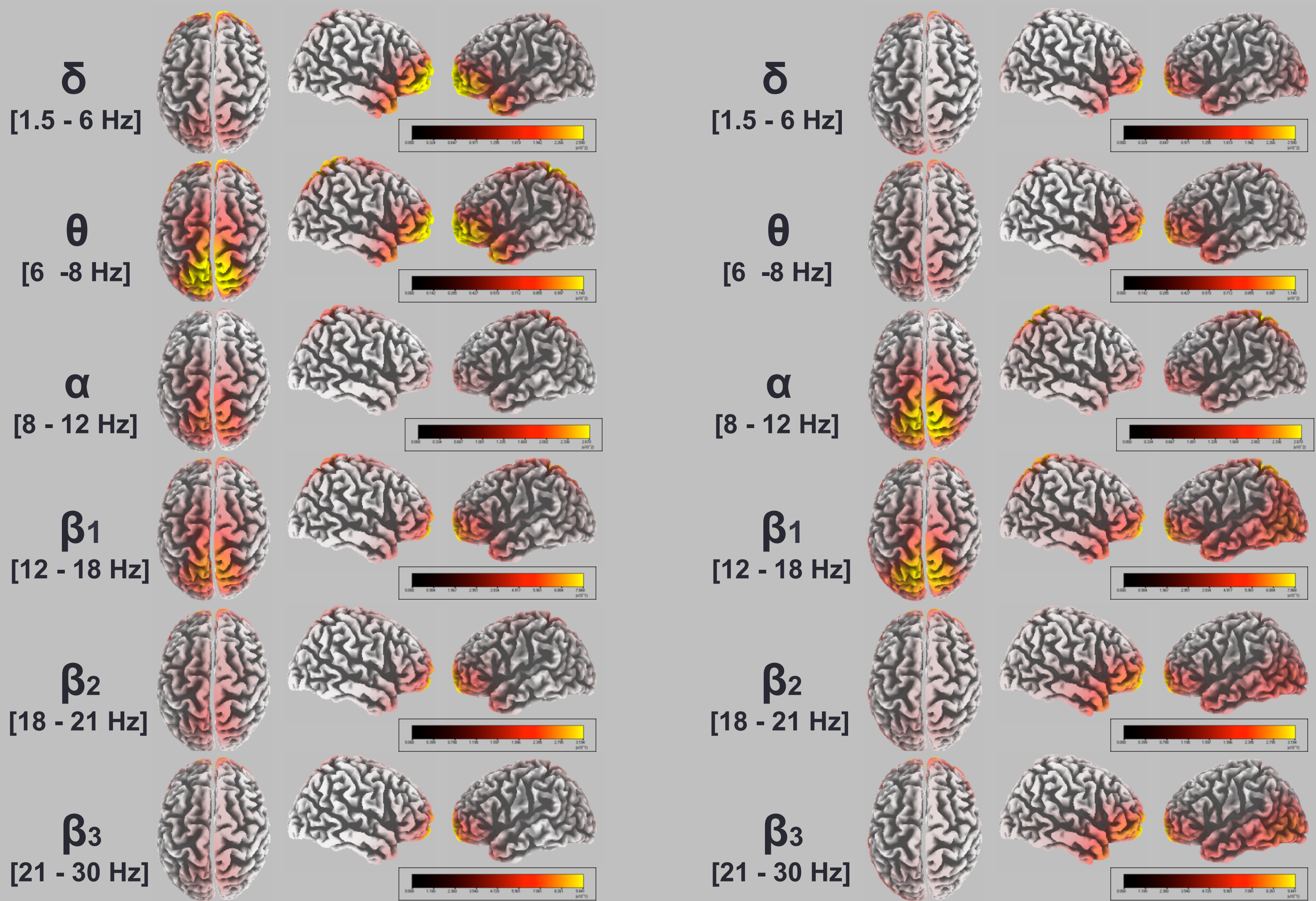
4. **Evoked potential (EP)**

# Electrical Source Imaging of Alpha Rhythm

Scalp EEG activity shows oscillations at a variety of frequencies. Several of these oscillations have characteristic frequency ranges, spatial distributions and are associated with different states of brain functioning (e.g. waking and the various sleep stages).
These oscillations represent synchronized activity over a network of neurons.

The localization of EEG rhythms in normal subjects, without any paradigm (attention, visual and auditory stimuli) are obtained from the EEG signal filtered for specific frequency bands.

# Electrical Source Imaging of Brain Rhythms



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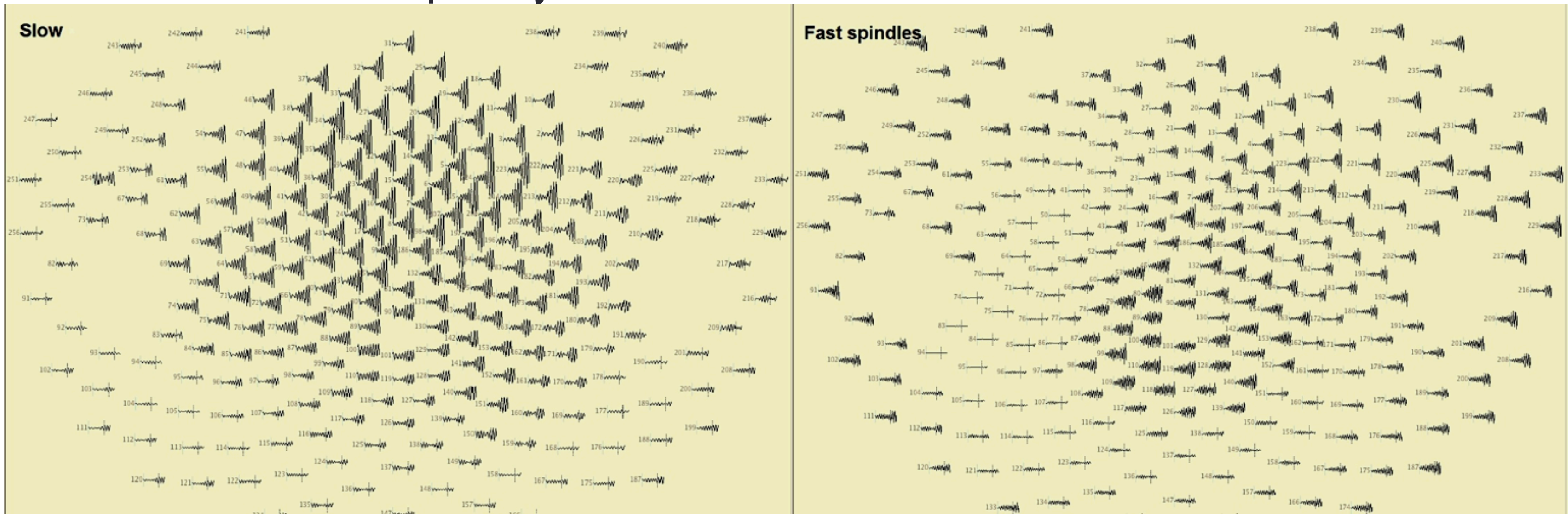
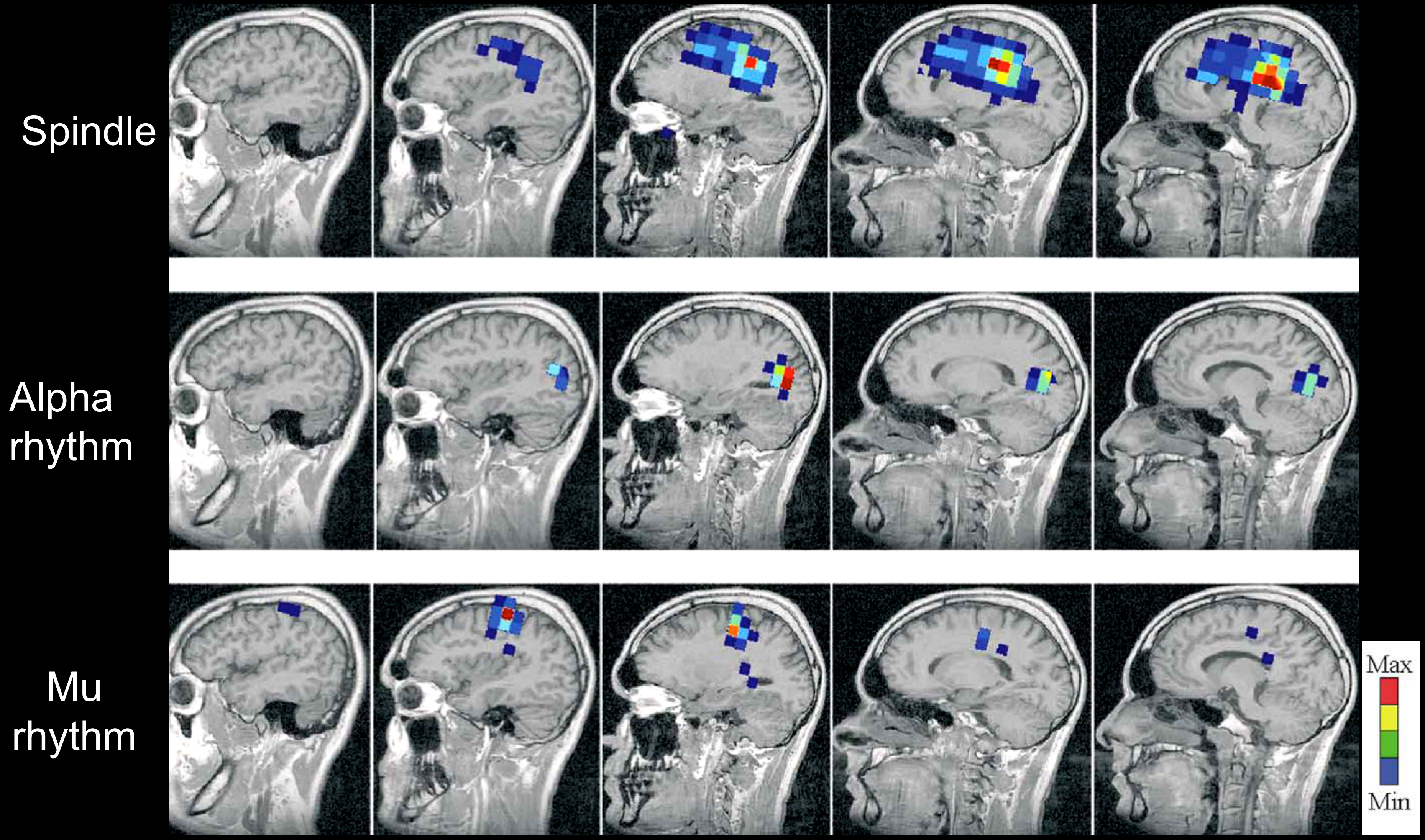
# Sleep

| Stage | Frequency (Hz) | Amplitude (micro Volts) | Waveform type |
|---|---|---|---|
| awake | 15-50 | <50 | |
| pre-sleep | 8-12 | 50 | alpha rhthym |
| 1 | 4-8 | 50-100 | theta |
| 2 | 4-15 | 50-150 | splindle waves |
| 3 | 2-4 | 100-150 | spindle waves and slow waves |
| 4 | 0.5-2 | 100-200 | slow waves and delta waves |
| REM | 15-30 | <50 | |

A **sleep spindle** is a burst of oscillatory brain activity visible on an EEG that occurs during stage 2 sleep. Sleep spindles are bursts of waxing and waning oscillations in the frequency of 10 to 15 Hz and last from 0.5 to 2 s.



# Electrical Source Imaging of Brain Rhythm




Manshanden et al., Clin Neurophysiol 2002

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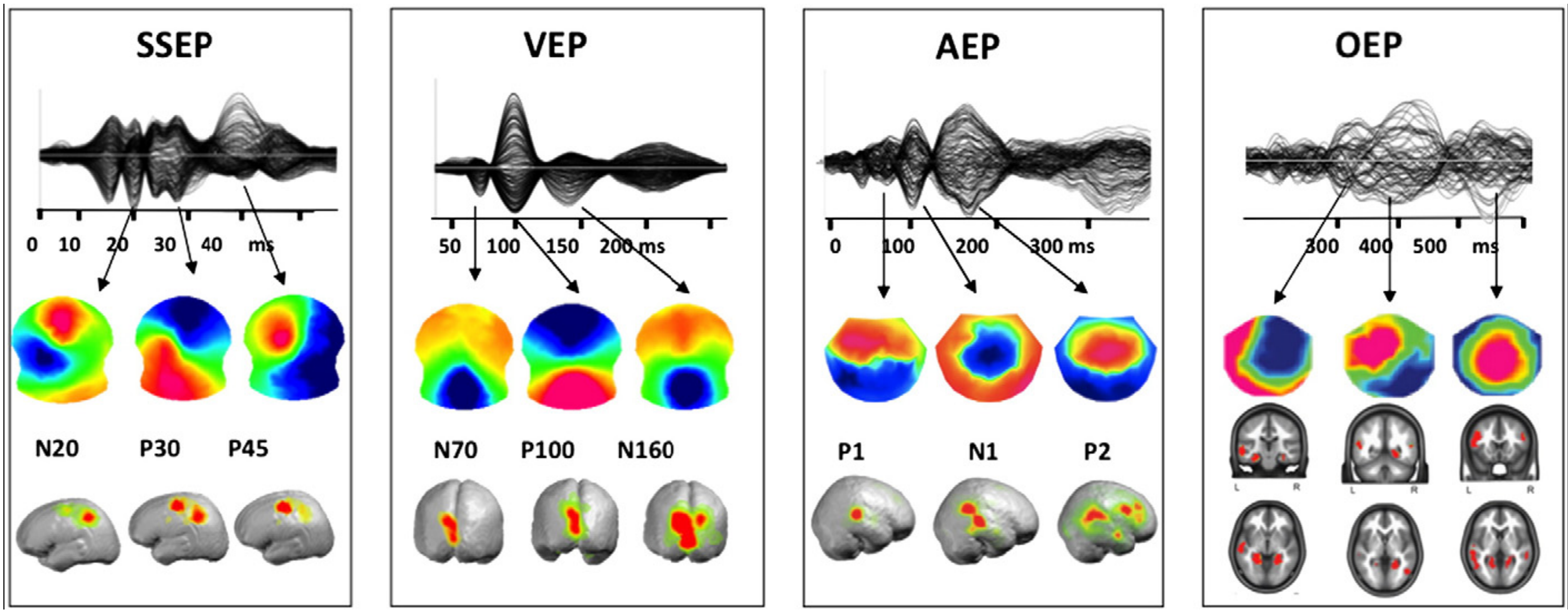
# Electrical Source Imaging of EP

256-channel somatosensory evoked potential (SSEP) after right median nerve stimulation

256-channel visual evoked potential (VEP) after full-field checkerboard reversal.

192-channel auditory evoked potential (AEP) after short tones.

64-channel olfactory evoked potential after unilateral nostril stimulation with hydrogen sulfide.




Lascano et al., J. Clin. Neurophysiol 2009