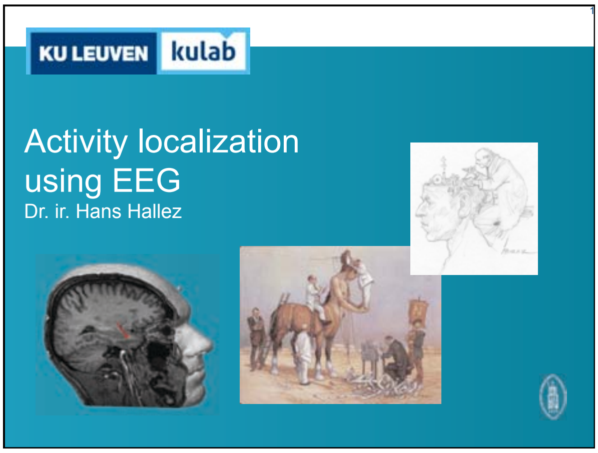
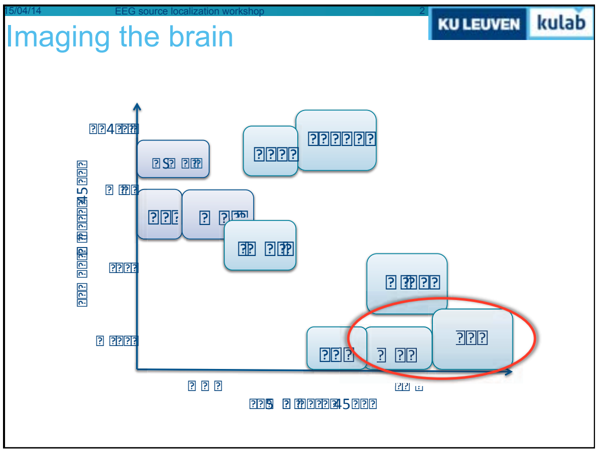
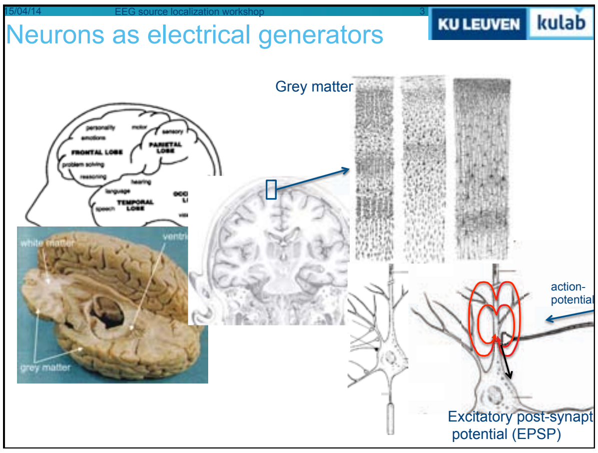
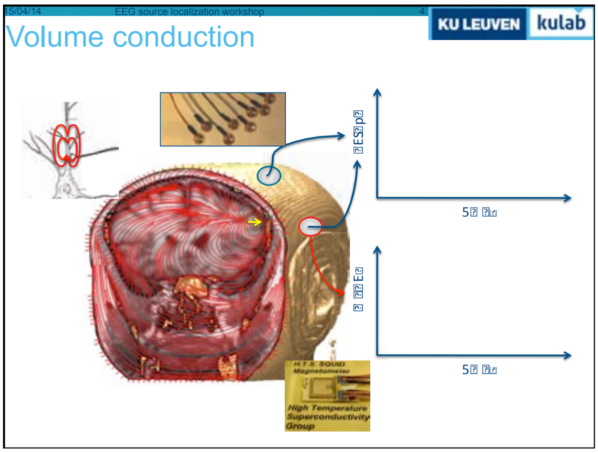
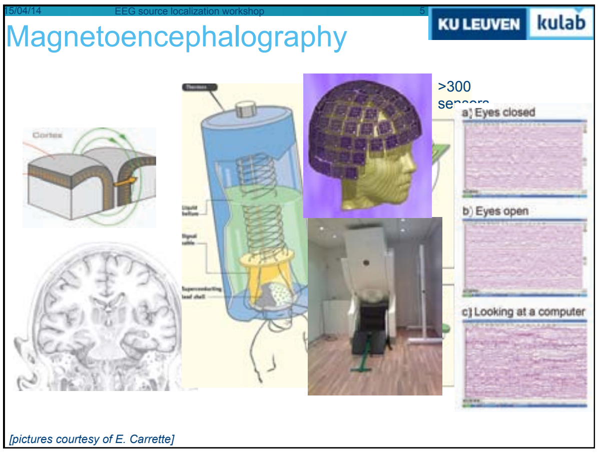
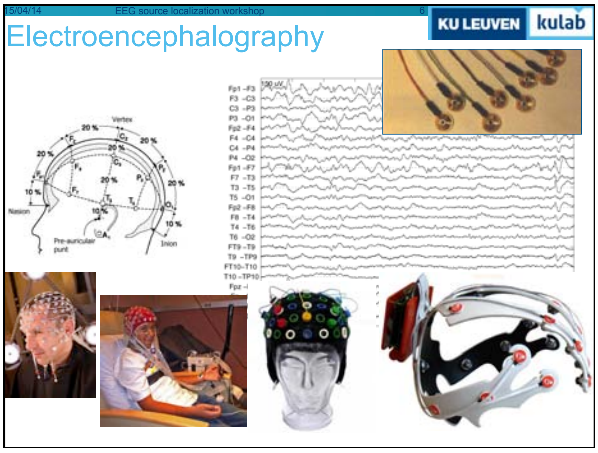

KU LEUVEN kulab
Activity localization using EEG
Dr. ir. Hans Hallez

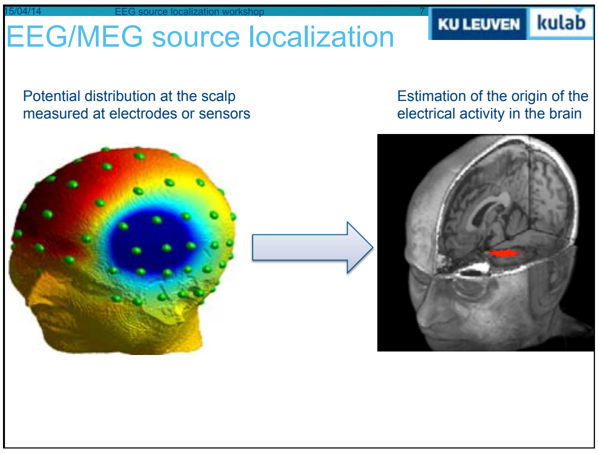

15/04/14
EEG source localization workshop
2
KU LEUVEN kulab
Imaging the brain


15/04/14
EEG source localization workshop
3
KU LEUVEN kulab
Neurons as electrical generators
Grey matter
white matter
grey matter
action-potentia
Excitatory post-synapt
potential (EPSP)


15/04/14
EEG source localization workshop
4
KU LEUVEN kulab
Volume conduction


5/04/14
EEG source localization workshop
KU LEUVEN
kulab
Magnetoencephalography
>300
a) Eyes closed
b) Eyes open
c) Looking at a computer
[pictures courtesy of E. Carrette]


5/04/14
EEG source localization workshop
KU LEUVEN
kulab
Electroencephalography


5/04/14
EEG source localization workshop
7
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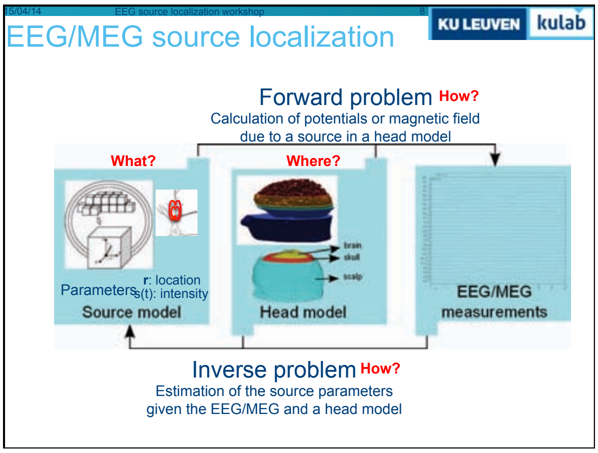
EEG/MEG source localization
Potential distribution at the scalp measured at electrodes or sensors
Estimation of the origin of the electrical activity in the brain


5/04/14
EEG source localization workshop
8
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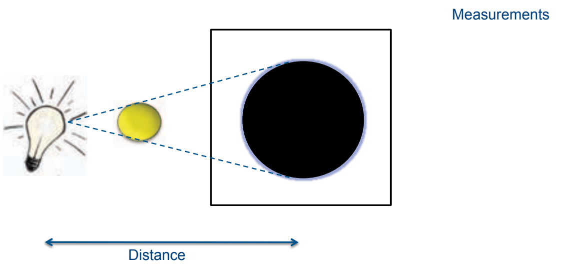
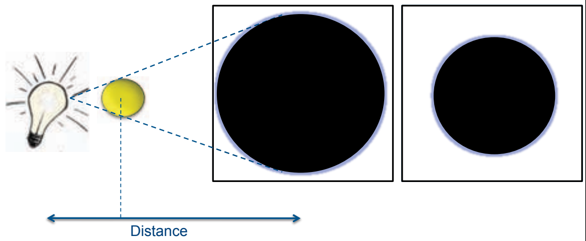
EEG/MEG source localization
Forward problem How?
Calculation of potentials or magnetic field due to a source in a head model
What?
Where?
Parameters
r: location
s(t): intensity
Source model
brain
skull
scalp
Head model
EEG/MEG measurements
Inverse problem How?
Estimation of the source parameters given the EEG/MEG and a head model

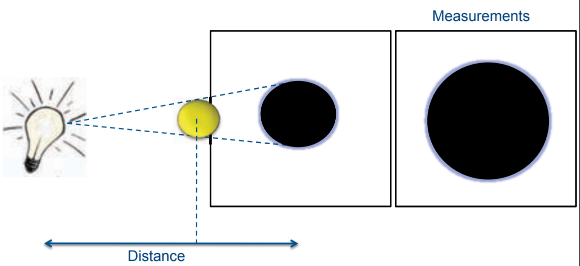
An similar problem



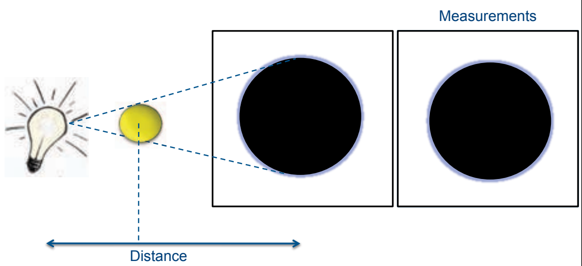
An similar problem

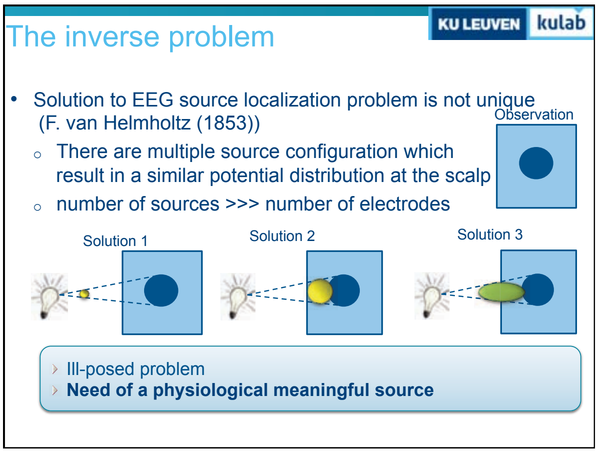


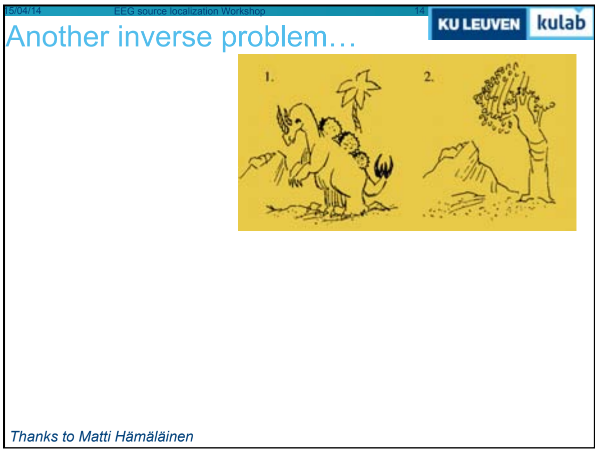
An similar problem

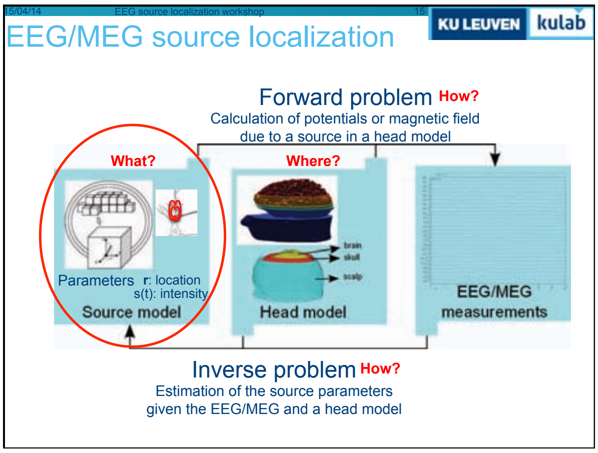


An similar problem




The inverse problem
KU LEUVEN kulab
Solution to EEG source localization problem is not unique (F. van Helmholtz (1853))
There are multiple source configuration which result in a similar potential distribution at the scalp
number of sources >>> number of electrodes
Observation
Solution 1
Solution 2
Solution 3
Ill-posed problem
Need of a physiological meaningful source


Another inverse problem…
KU LEUVEN kulab
1.
2.
Thanks to Matti Hämäläinen


EEG/MEG source localization
KU LEUVEN kulab
Forward problem How?
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Parameters r: location s(t): intensity
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brain
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scalp
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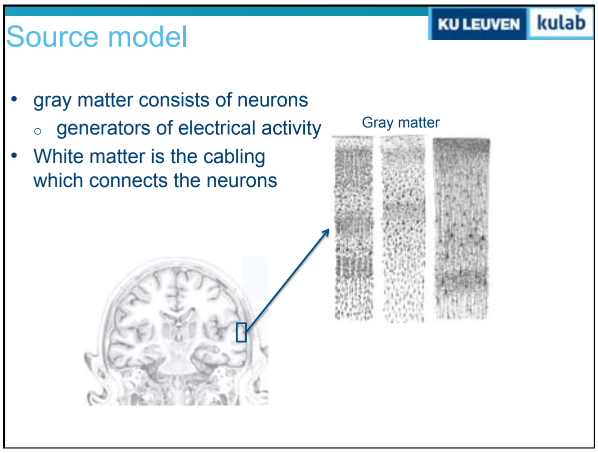
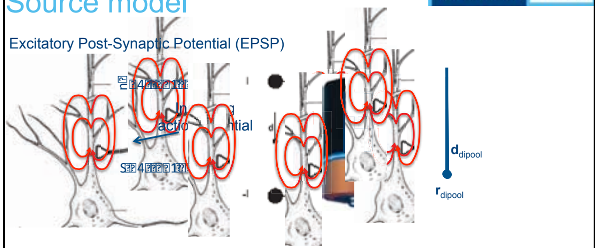

Source model
KU LEUVEN kulab
gray matter consists of neurons
generators of electrical activity
White matter is the cabling which connects the neurons
Gray matter

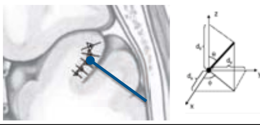
Source model

Excitatory Post-Synaptic Potential (EPSP)



Microscopic current due to 1 EPSP : **5.10^{-5} nA**

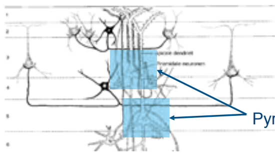
Macroscopic current measured: **50 nA** equivalent to a cortical patch of **5.5×5.5 mm²**



6 parameters
- Location **r** (x,y,z)
- Orientation : θ,φ
- Intensity : s

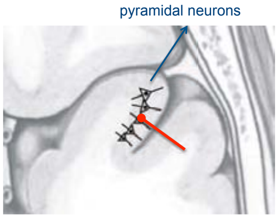
Source model : generators of EEG

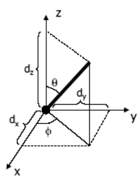
- Superposition of large group of synchronously activated neurons required to produce measurable potentials at the scalp
- Pyramidal neurons
  - Long apical dendrites oriented in parallel, perpendicular to the cortex
  - Are believed to be the main EEG generators



Source model

- Measurable signal created by
  - superposition of currents in a group pyramidal neurons (5 mm x 5 mm patch of gray matter)
  - Modeled by a current dipole

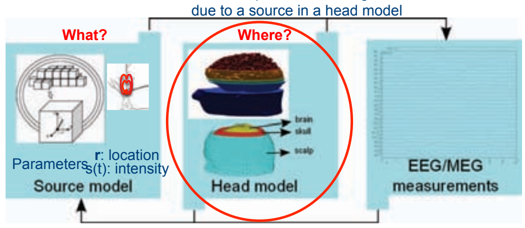




position : *x, y, z*
orientation : *θ, φ*
magnitude : *I*

EEG/MEG source localization

Forward problem How?
Calculation of potentials or magnetic field due to a source in a head model

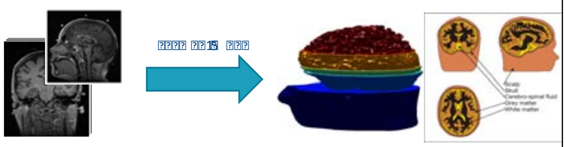


Inverse problem How?
Estimation of the source parameters given the EEG/MEG and a head model

Volume conductor modeling

- Simplified spherical head models
  - Easy solution for forward problem

- Realistic head models



- Conductivities?

Head model

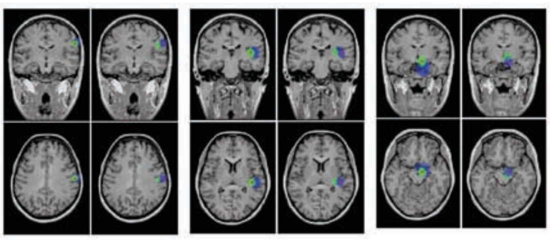
- Conductivities
  - Values (S/m)

compartments	Geddes & Baker (1967)	Oostendorp (2000)	Gonçalves (2003)	Guttierrez (2004)	Lai (2005)
scalp	0.43	0.22	0.33	0.749	0.33
skull	0.0060.013	0.015	0.0081	0.012	0.0132
cerebro-spinal fluid	-	-	-	1.79	-
brain	0.120.48	0.22	0.33	0.313	0.33
$\sigma_{scalp}/\sigma_{skull}$	80	15	42	26	25

  - Patient dependent
  - Time dependent

Head model

- Conductivities
  - Brain-to-skull conductivity ratio (80 vs 25)

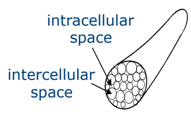


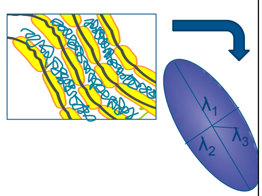
128 electrodes

[Wang et al, Biomedical Research International, 2013]

Head model

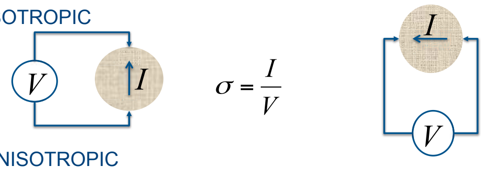
- Incorporation of anisotropic conductivities
  - For simplicity, often isotropic conductivities are used
  - In reality some tissues are anistropic
- Diffusion tensor imaging
  - determination of the orientation of white matter fiber bundles
  - Conductivities





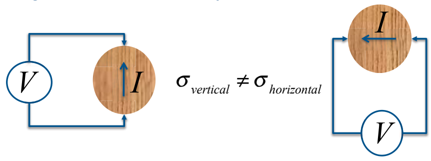
Head model

- ISOTROPIC



$$\sigma = \frac{I}{V}$$

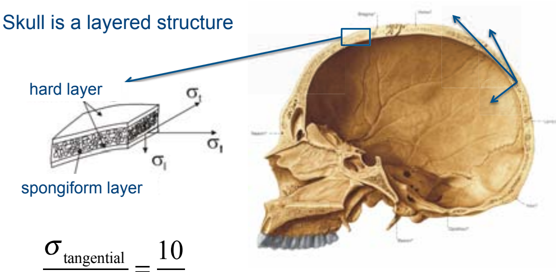
- ANISOTROPIC
  - Magnitude of conductivity is direction-dependant



$$\sigma_{vertical} \neq \sigma_{horizontal}$$

Head model

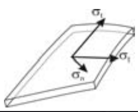
- Skull is a layered structure



$$\frac{\sigma_{\text{tangential}}}{\sigma_{\text{normal}}} = \frac{10}{1}$$

Head model

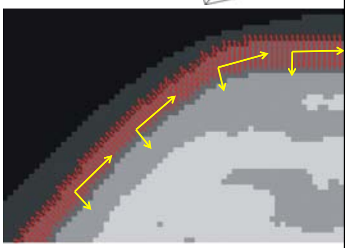
- In each voxel of the skull
  - Determine the normal direction onto the skull
  - Define the tensor



$$\Sigma_{local} = \begin{bmatrix} \sigma_n & 0 & 0 \\ 0 & \sigma_t & 0 \\ 0 & 0 & \sigma_t \end{bmatrix}$$

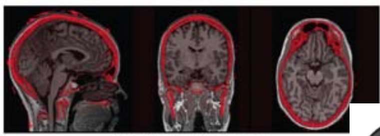
  - Transform the tensor to global coordinate system

$$\Sigma_{global} = \mathbf{T} \cdot \begin{bmatrix} \sigma_n & 0 & 0 \\ 0 & \sigma_t & 0 \\ 0 & 0 & \sigma_t \end{bmatrix} \cdot \mathbf{T}^T$$

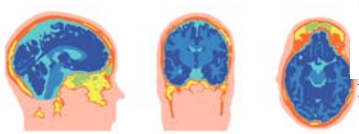


Head model

- Increasing spatial resolution in medical imaging scanners allows us to model very detailed

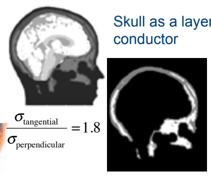


(a) MR with overlaid CT image in red.



(b) Segmented reference head model.

Skull as a layered conductor

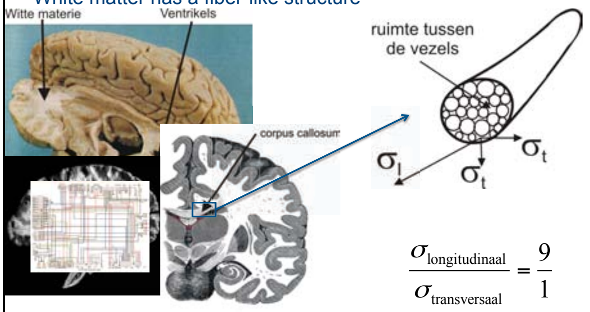


$$\frac{\sigma_{\text{tangential}}}{\sigma_{\text{perpendicular}}} = 1.8$$

[Montes et al., 2013, Brain Topography]

Head model

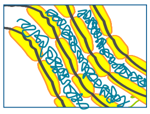
- White matter has a fiber-like structure

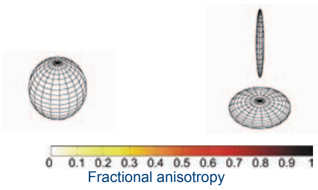


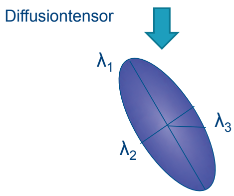
$$\frac{\sigma_{\text{longitudinaal}}}{\sigma_{\text{transversaal}}} = \frac{9}{1}$$

Head model

- Ordinary MR image contains no information on the white matter fiber tracts
- Diffusion weighted images measure diffusion of watter in different directions

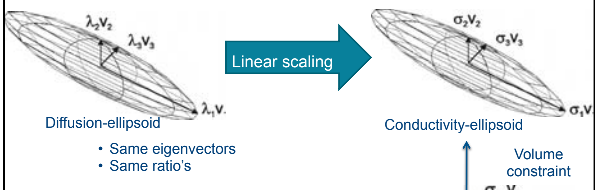






Head model

- From diffusion tensor to conductivity tensor

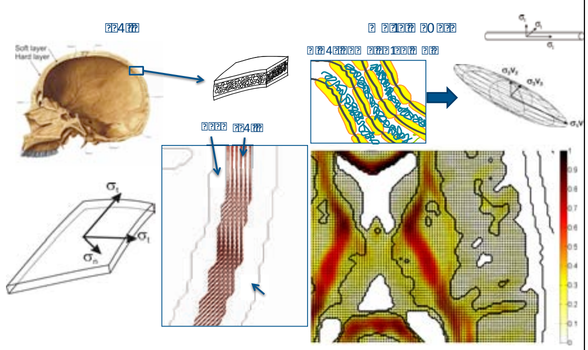


- Same eigenvectors
- Same ratio's

$$\frac{\lambda_1}{\sigma_1} = \frac{\lambda_2}{\sigma_2} = \frac{\lambda_3}{\sigma_3} = c$$

$$\sigma_{iso} = 0.33\, S/m$$

Head model



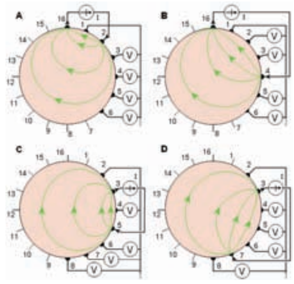
Head model

- How far do we need to go?
  - Complete 3D model
    - Incorporation of anisotropic conductivities
    - Incorporation of defects

- MR-image can be used directly in the segmentation proces

Headmodel

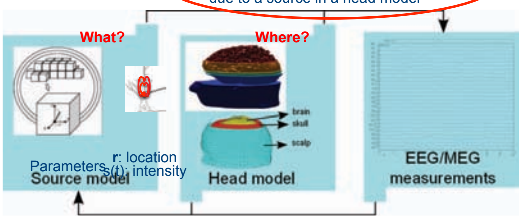
- Determining conductivities with Electrical Impedance Tomography



Good to detect changes in conductivity
But still very difficult to measure an absolute value

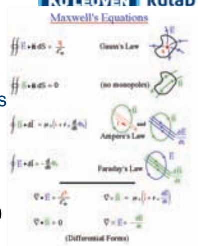
EEG/MEG source localization

Forward problem **How?**
Calculation of potentials or magnetic field due to a source in a head model



Inverse problem **How?**
Estimation of the source parameters given the EEG/MEG and a head model

Forward problem



- Calculation of the electrode potentials given the head model, electrode positions and the source
- Quasi-static approach

$$\nabla \cdot (\sigma(x,y,z) \cdot \nabla V(x,y,z)) = \nabla \cdot \mathbf{J}(x,y,z)$$

Geometry
Electrode positions
Dipole parameters
Conductivities

Potential at the electrodes

Forward Problem

- Head model
  - Spherical head models
    - Analytical solution
    - Fast, but not realistic

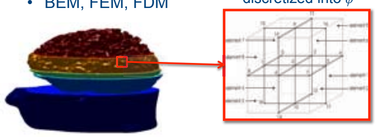
$$V(\mathbf{r}_{elec}, \mathbf{d}, \mathbf{r}_s) = \frac{d}{4\pi\sigma_4 r_4^2} \sum_{n=1}^{\infty} \frac{2n+1}{n} \left(\frac{r_{dip}}{r_4}\right)^{n-1} (f_n n \cos\alpha P_n(\cos\gamma) + g_n \cos\beta \sin\alpha P_n^1(\cos\gamma))$$

  - Realistic head models
    - Numerical solutions
    - BEM, FEM, FDM

Potentials V are discretized into φ

$$\left(\sum_{n=1}^{18} A_n\right)\varphi_0 - \sum_{n=1}^{18} A_n \varphi_n = \delta I_{ijk} - \delta I_{i'j'k'}$$

$$A\Phi = I$$

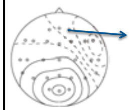


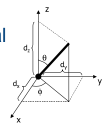
Linear system of equations of > 5 million equations

[Hallez et al., Physics in Medicine and Biology 2005]

Forward Problem : spatio-temporal model

- Linearity of the Maxwell equations
  - A dipole can be seen as 3 dipoles with orthogonal orientation along X, Y and Z-axis





Potential due to projection of dipole onto Z-axis

$$v_{el} = v_x + v_y + v_z$$

$$= L_x d_x + L_y d_y + L_z d_z$$

Potential at electrode due to a unitary dipole along Z-axis

$$= \begin{bmatrix} L_x & L_y & L_z \end{bmatrix} \begin{bmatrix} d_x \\ d_y \\ d_z \end{bmatrix}$$

$$= \begin{bmatrix} L_x & L_y & L_z \end{bmatrix} \begin{bmatrix} e_x \\ e_y \\ e_z \end{bmatrix} s$$

Contribution to the potential due to a dipole along each direction

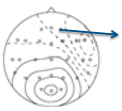
Position dependent

Orientation of a unitary dipole (=dipole with magnitude equal to 1)

Intensity of the dipole (magnitude)

Forward Problem : spatio-temporal model

- Linearity of the Maxwell equations



$$v_{el}(t) = L(\mathbf{r}_d, \mathbf{r}_{el})\mathbf{e}_d s(t) = a(\mathbf{r}_d, \mathbf{r}_{el}, \mathbf{e}_d) s(t)$$

Intensity

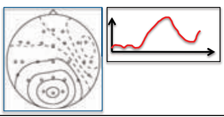
Lead-fieldmatrix non-linear wrt dipole location

orientation

Contribution of a unitary dipole

Topography = potential distribution at the scalp on *p* electrodes

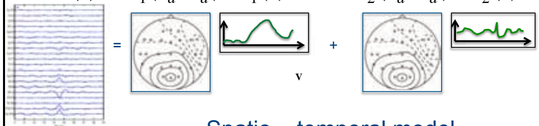
$$\mathbf{v}(t) = \begin{bmatrix} v_{el,1}(t) \\ \vdots \\ v_{el,p}(t) \end{bmatrix} = \begin{bmatrix} a(\mathbf{r}_d, \mathbf{r}_{el,1}, \mathbf{e}_d) \\ \vdots \\ a(\mathbf{r}_d, \mathbf{r}_{el,p}, \mathbf{e}_d) \end{bmatrix} s(t) = \mathbf{a}(\mathbf{r}_d, \mathbf{e}_d) \cdot s(t)$$



Forward Problem : spatio-temporal model

- Linearity of the Maxwell equations

$$\mathbf{v}(t) = \mathbf{a}_1(\mathbf{r}_d, \mathbf{e}_d) \cdot s_1(t) + \mathbf{a}_2(\mathbf{r}_d, \mathbf{e}_d) \cdot s_2(t) + \ldots$$



Spatio – temporal model

$$\mathbf{V} = \begin{bmatrix} \mathbf{a}_1(\mathbf{r}_d, \mathbf{e}_d) & \ldots & \mathbf{a}_p(\mathbf{r}_d, \mathbf{e}_d) \end{bmatrix} \begin{bmatrix} \mathbf{s}_1(t) \\ \vdots \\ \mathbf{s}_p(t) \end{bmatrix} = \mathbf{A}\mathbf{S}^T$$

Topographies

Source signals

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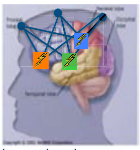
Decomposition methods

Spatio – temporal model

$$\mathbf{V} = \left[\mathbf{a}_1(\mathbf{r}_d, \mathbf{e}_d) \;\; \dots \;\; \mathbf{a}_p(\mathbf{r}_d, \mathbf{e}_d)\right] \begin{bmatrix} \mathbf{s}_1(t) \\ \vdots \\ \mathbf{s}_p(t) \end{bmatrix} = \mathbf{A}\mathbf{S}^T$$

Topographies

Source signals



Decomposition by *p* dipole sources

How to determine these:
See inverse problem

- Neurophysiological basis
- Model-driven: controllable

- Model driven : many a priori known parameters
- Number of sources

- Decomposition by *m* signal sources
- Based on properties of time series
  - Blind source separation
  - PCA, ICA, CCA

- Data-driven : no need for a complicated head model
- Few parameters

- Largely dependent on the data
- Sources should be stationary

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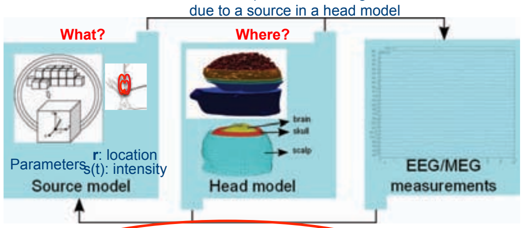
EEG/MEG source localization

Forward problem **How?**

Calculation of potentials or magnetic field due to a source in a head model



Inverse problem **How?**

Estimation of the source parameters given the EEG/MEG and a head model

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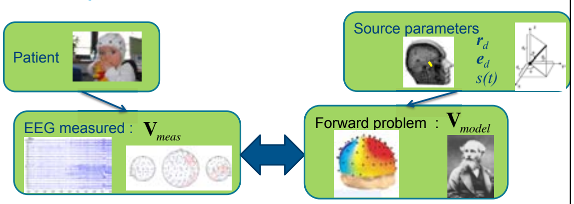
Inverse problem



Estimation of the parameters by means of minimization of a cost function

$$RE = \left\| \mathbf{V}_{meas} - \mathbf{V}_{model} \right\|$$

Spatio-temporal model

$$= \left\| \mathbf{V}_{meas} - \mathbf{A}\mathbf{S}^T \right\|$$

? Number of sources ?

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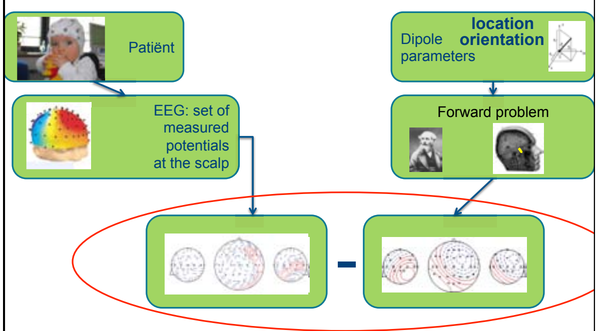
Inverse problem



Changing location and orientation parameters until a minimal difference is reached

Inverse problem

- Fit a model to a set of measurements
  - potential values calculated by a model versus measured at the patient
- Minimalization of a cost function

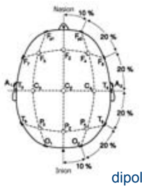
$$RRE = \frac{\left\| \mathbf{V}_{\text{measured}} - \mathbf{V}_{\text{model}} \right\|}{\left\| \mathbf{V}_{measured} \right\|}$$

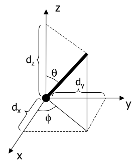
- Potentials
  - non-linear relation w.r.t. dipole location
  - linear relation w.r.t. orientation and intensity

Inverse problem

- Single dipole
  - What we want is dipole that results in measured potentials

$$\mathbf{L}(\hat{\mathbf{r}}) \cdot \hat{\mathbf{d}} = \mathbf{V}_{measured}$$





dipole has 6 parameters

  - Linear system of equations
    - number of dipole parameters << number of measurements
    - Problem is overdetermined
    - There is no solution to the problem => best fit of the solution

$$RRE = \frac{\left\| \mathbf{V}_{\text{measured}} - \mathbf{L}(\mathbf{r}) \cdot \mathbf{d} \right\|}{\left\| \mathbf{V}_{measured} \right\|}$$

Inverse problem

- Single dipole
  - Estimation in least squares sense
    - non-linear estimation through Nelder-Mead simplex, Levenberg Marquardt methods
  - Simplification
    - Sub-optimal solution

Nx3 3x1 Nx1 N : number of electrodes

$$\mathbf{L}(\mathbf{r}) \cdot \mathbf{d} = \mathbf{V}_{measured}$$

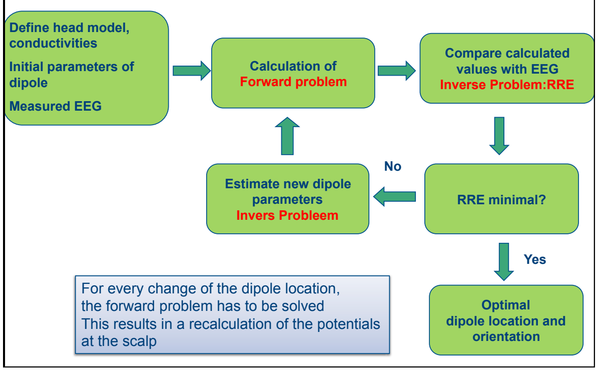
$$\mathbf{d}_{opt} = \mathbf{L}^{+}(\mathbf{r}) \cdot \mathbf{V}_{measured}$$ Pseudo-inverse of a matrix

- The costfunction becomes

$$RRE = \frac{\left\| \mathbf{V}_{\text{measured}} - \mathbf{L}(\mathbf{r}) \cdot \mathbf{d} \right\|}{\left\| \mathbf{V}_{measured} \right\|} = \frac{\left\| \mathbf{V}_{\text{measured}} - \mathbf{L}(\mathbf{r}) \cdot \mathbf{L}^{+}(\mathbf{r}) \cdot \mathbf{V}_{measured} \right\|}{\left\| \mathbf{V}_{measured} \right\|}$$

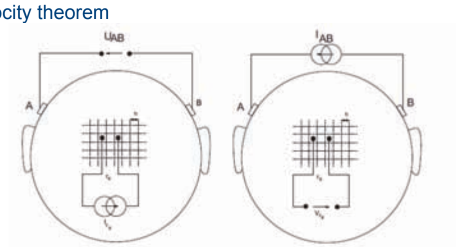
Only 3 paramters (location) need to be estimated instead of 6.

Inverse problem



Inverse problem

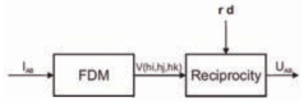
- Reciprocity theorem



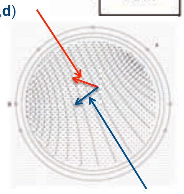
$$U_{AB} I_{AB} = V_{r_x} I_{r_x}$$

Invers probleem

- Reciprocity theorem
  - Electrode pair as a current source and sink



dipool (**r**,**d**)



Electric field = $\nabla V(\mathbf{r})$

1. Calulcate forward problem using lead as a current source and sink
2. N-1 leads if there are N electrodes
3. The potential due to a arbitrary dipole can then be written as

$$U_{AB}(\mathbf{r},\mathbf{d}) = \frac{\mathbf{d}^T \cdot \nabla V(\mathbf{r})}{I_{AB}}$$

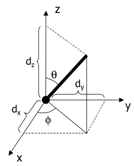
Invers probleem

- Reciprocity
  - Solving the invers problem can be accelerated significantly
  - < 1 sec
  - But, the leadfields (=electric field due to a current source and sink at electrode positions) should be calculated before hand

Inverse problem

- Multiple dipoles
  - What we want is a number of dipoles that result in measured potentials

$$\mathbf{L}(\mathbf{r}_1)\cdot\mathbf{d}_1 + \mathbf{L}(\mathbf{r}_2)\cdot\mathbf{d}_2 + \mathbf{L}(\mathbf{r}_3)\cdot\mathbf{d}_3 + \ldots = \mathbf{V}_{measured}$$



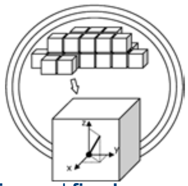
dipole has 6 parameters

  - Linear system of equations
    - number of dipole parameters is now even more than number of measurements
    - Becomes less determined
    - There is no solution to the problem => best fit of the solution

$$RRE = \frac{\left\| \mathbf{V}_{measured} - \mathbf{L}(\mathbf{r}_1)\cdot\mathbf{d}_1 - \mathbf{L}(\mathbf{r}_2)\cdot\mathbf{d}_2 - \mathbf{L}(\mathbf{r}_3)\cdot\mathbf{d}_3 - \ldots \right\|}{\left\| \mathbf{V}_{measured} \right\|}$$

Suboptimal solution does not hold!
Very difficult to find a global minimum of the RRE…

Inverse problem

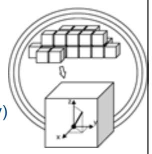


- Distributed source models

$$\underset{Nxp\ \ pxt}{\mathbf{AS}^T} = \mathbf{V}_{measured}$$

  - N: number of electrodes, p: number of dipoles, t: number of time samples
  - Each dipole in a voxel has a **fixed position** and **fixed orientation** and a **variable intensity**
  - Many parameters (10000+) and few measurements
- Highly underdetermined
  - number of parameters >> number of measurements
  - Infinite number of solutions

Inverse problem



- Distributed source models
  - Minimum norm solution where
    - Choose the solution with minimal norm (least energy)

$$\text{minimize}\|\mathbf{S}\|\text{with respect to } \mathbf{AS}^T = \mathbf{V}_{measured}$$

    - Solution

Pseudo-inverse

$$\mathbf{S}^T = \mathbf{A}^+\mathbf{V}_{measured} \qquad \mathbf{A}^+ = \mathbf{A}^T(\mathbf{AA}^T)^{-1}$$

  - Weighted minimum norm solution
    - Least energy with respect to a weighting factor (e.g. fMRI activity)

$$\text{minimize}\|\mathbf{WS}\|\text{with respect to } \mathbf{AS}^T = \mathbf{V}_{measured}$$

$$\mathbf{S}^T = \left(\mathbf{W}^T\mathbf{W}\right)^{-1}\mathbf{A}^T(\mathbf{A}(\mathbf{W}^T\mathbf{W})^{-1}\mathbf{A}^T)^{-1}\mathbf{V}_{measured}$$

[Grech et al., 2008, Journal of NeuroEngineering and Rehabilitation]

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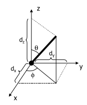
Inverse problem

$$RE = \left\|\mathbf{V}_{meas} - \mathbf{AS}^T\right\|$$

Assumption : Within the EEG time frame there is only one source

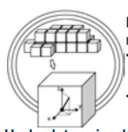


Single dipole model
- Location
- Orientation
- Intensity

Overdetermined system
- #parameters (=6 or 3) < #electrodes

Least squares solution
- Best fit of the model onto the measurements
- Time consuming

Assumption : there are many sources



Distributed source model
- ≈ 10000 dipoles distributed of grey matter
- Intensity

Underdetermined system (ill-posed)
- #parameters > #electrodes

Minimum norm solution
- Fast
- Regularization

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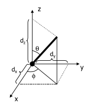
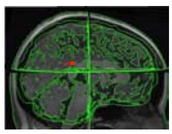
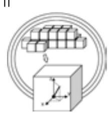
Inverse problem

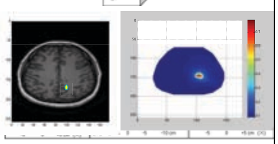
$$RE = \left\|\mathbf{V}_{meas} - \mathbf{AS}^T\right\|$$





Parametric solution



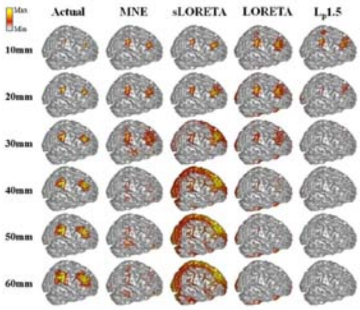


Imaging solution
MNE, (s)LORETA, FOCUSS
beamformers

MUSIC, RAP – MUSIC, POP – MUSIC
Multiple dipole localization (2 – 6 dipoles)

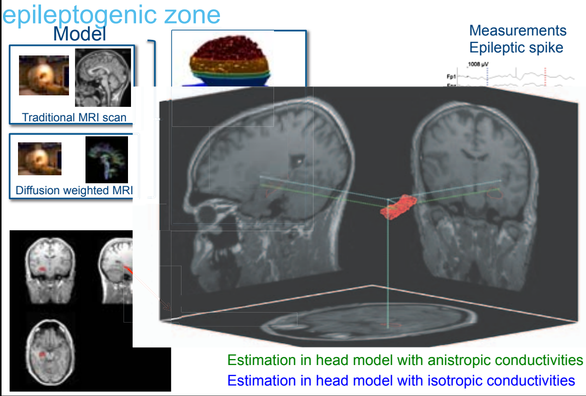
Inverse problem

- EEG imaging
  - Various ways to to perform imaging



[Cho et al, 2011, Brain Topography]

Application: Localization of the epileptogenic zone

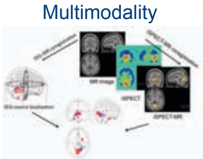


Estimation in head model with anistropic conductivities

Estimation in head model with isotropic conductivities

Examples and trends

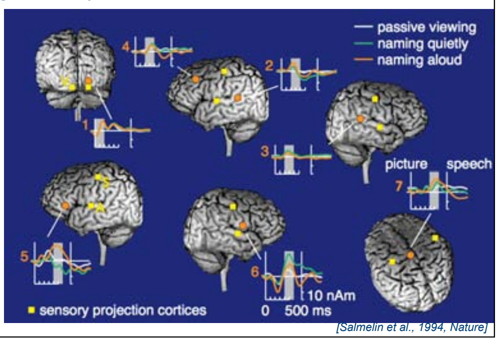
Multimodality



Connectivity

EEG source tracking

- Tracking of activity



[Salmelin et al., 1994, Nature]

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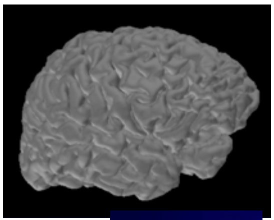
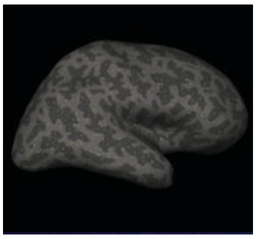
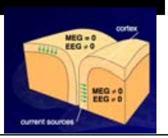
Inflated brain

- Inflation of the cortex to reveal sulci







Constrain dipole orientation in the sulci

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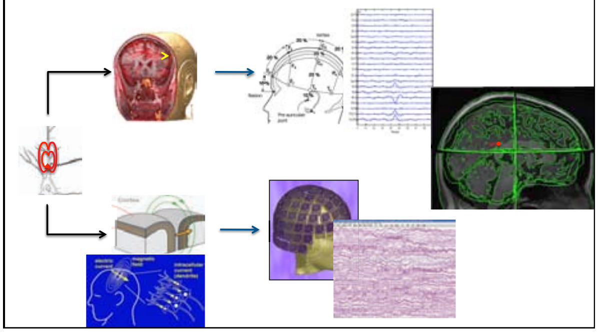
Simultaneous EEG/MEG source localization

- EEG and MEG are generated by the same neuronal activity



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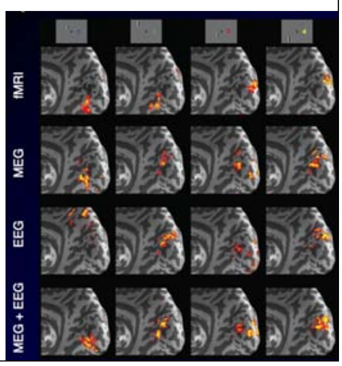
Simultaneous EEG/MEG source localization

- Comparison EEG/MEG/fMRI



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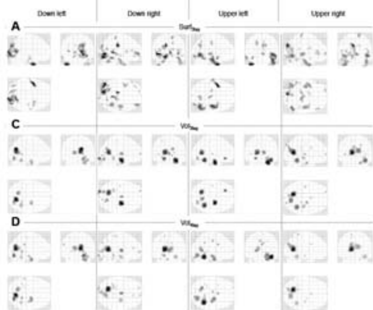
Surface meshes vs volumetric

- Volumetric mesh results in more localized source

Surface mesh

Three-layered Volumetric mesh

Four-layered Volumetric mesh



[Strobbe et al. 2014, submitted]

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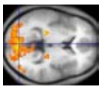
Multimodal integration of EEG source localization

- Use functional imaging to improve spatial resolution of EEG source localization
  - Also provides timing information of the functional activation
  - A priori information of EEG source localization

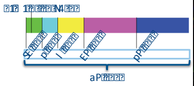
Use functional MRI and EEG

Preprocessing :
MR artefact
BCG artefact



Use ictal SPECT for localization op epileptic seizures

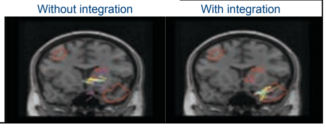
Time information of sources



Ictal SPECT

Without integration

With integration



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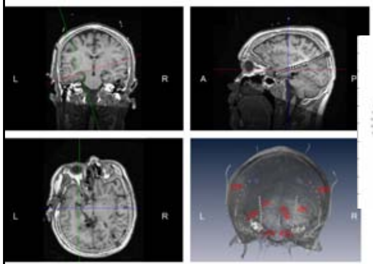
Connectivity analysis

Functional connectivity
propagation pattern of information flow between signals



Use of functional connectivity in to **accurately estimate to onset zone** of an epileptic seizure

Correlation with structural connectivity from fibretracking

[van Mierlo et al. 2010, Neuroimage]

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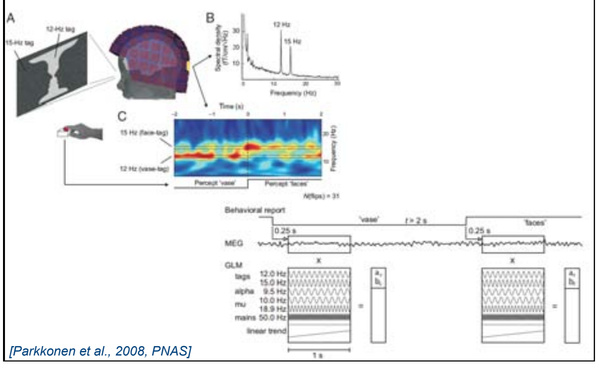
Example: ambiguous scene perception



[Parkkonen et al., 2008, PNAS]

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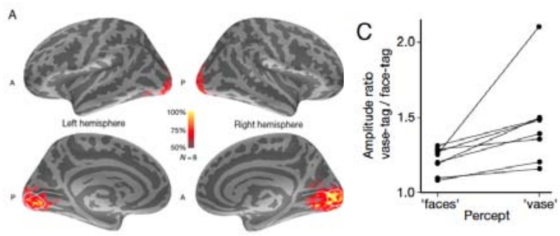
Example: ambiguous scene perception



[Parkkonen et al., 2008, PNAS]

Complex source models

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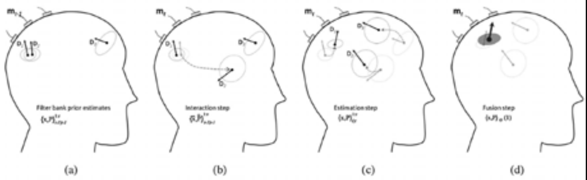
- Using adequate assumptions, complex source models can be derived using the “simple” dipole model



[Antelis J. et al., 2013, Journal of Neuroscience Methods]

Advanced hardware

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- Taking the EEG system outside the examination room

Conclusion

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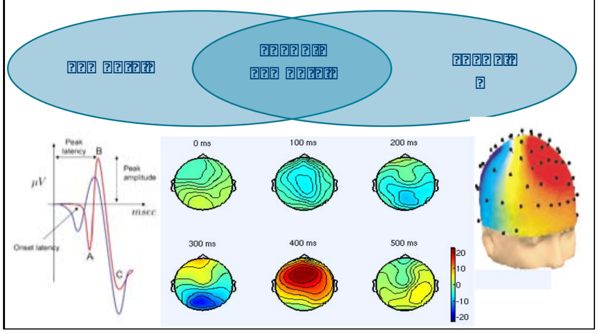
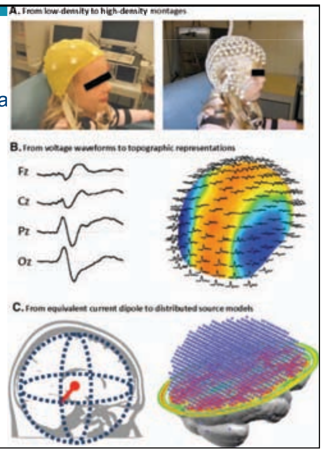
- EEG processing has to be considered in time as wel in space



Conclusion

- Evolution towards more data



[Christophe Michel, 2012, NeuroImage]

Conclusions

- EEG and MEG can be used to investigate the electrophysiological activations in the brain
  - Adequate model (source, head model)
  - Link with anatomy
  - Spatio-temporal models
- Trends
  - Big Data
    - How to process all these data?
  - Combination of multiple modalities
    - to increase the resolution
    - to exploit the time information

Thank you for your attention