Functional Brain Imaging with MEG (Magnetoencephalography), EEG (Electroencephalography) and sEEG (Stereotaxic EEG)

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Functional neuroimaging

It's the study of the **brain activity** through **functional imaging devices**



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Brain anatomy



Source: Gray's anatomy (public domain)

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Relation between location and function?



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Relation between location and function?



From the eye to the cortex



Left (resp. right) visual field is projected to the right (resp. left) hemisphere in the primary visual cortex (VI)

VI stands in the occipital region around the **calcarine fissure**

Source: adapted from http:// homepage.psy.utexas.edu/homepage/Class/ Psy308/ Salinas/Vision/Vision.html).

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Relation between location and function?



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Electrophysiology: Origin of the signals

Brain anatomy



Source: dartmouth.edu

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APS (action potentials) & PSPS (post-synaptic potentials)



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APS (action potentials) & PSPS (post-synaptic potentials)



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APS (action potentials) & PSPS (post-synaptic potentials)



Action potentials:

fields diminish too rapidly to sum

Postsynaptic currents:

fields diminish gradually

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Neurons as current generators

Large cortical pyramidal cells organized in macro-assemblies with their **dendrites normally oriented to the local cortical surface**



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Neurons as current generators



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EEG & MEG systems



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MEG sensors



Magnetometer

- General magnetic fields
- Very sensitive overall, **noisy**

Planar Gradiometer

- Focal magnetic fields
- Most sensitive to fields directly underneath



Axial Gradiometer

-Focal magnetic fields

- Most sensitive to fields directly underneath it

Magnetic shielding



Hence the importance of shielding...

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Magnetic shielding

Magnetically Shielded Room (MSR)



3-ply µ-metal room



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A machine (Neromag vectorview)



No Magnet Quiet Machine makes no noise Participant can sit or lay down Can record 128 EEG simultaneously



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sEEG systems



Intracranial electrodes; 5 to 15 contacts per electrode Around 10 electrodes are implanted





Stereotaxic Implantation

sEEG systems



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Interictal discharges involving multiple regions (a network)

Seizure onset

[Schwartz et al Epilepsy Res 2011]

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Sample EEG measurements

EEG: • \approx 100 sensors

MEG : • \approx 150 to 300 sensors

Sampling between 250 and 1000 Hz

High temporal resolution but what about spatial resolution?

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At each time instant EEG sensors measure a potential field

Remark: Such a smooth potential field confirms the presence of current generators within the head

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MEG topography exhibits also a dipolar field but MEG has a **better spatial resolution**

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M/EEG Measurements: Notation

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What can you do with M/EEG?

I. Cognitive studies

- Which areas are activated during a given cognitive task? When are they active? What is common in a population of subjects?
- 2. Therapy (Epilepsy)
 - Where is the location of the origin of epileptic seizures?
 - Will my patient be able to talk if I remove this area of the cortex?
- 3. Brain computer interfaces (BCI)
 - How to extract in real time the signal of interest from EEG measurements in order to control a computer?

Source: life.com

Source: nih.gov

Data acquisition examples

Earphones

Also: Button Pads Button Gloves Manual Tapper

Stimulus delivered by E-Prime, PsychToolBox, etc.

Presentation Screen (moved to front!)

Electrical Stimulator

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Data acquisition examples

MEG/EEG

evoked responses

What are the challenges?

Signal Extraction:

Signal processing, Denoising, Artifact rejection, Single trial analysis.

Forward problem:

Maxwell Equations, Numerical solvers, Finite and Boundary Element Method (BEM & FEM), Image Segmentation and meshing for head modeling.

Inverse problem:

Deconvolution problem, III-posed problem, Requires efficient solvers to use different priors.

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Raw continuous data

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Time frame: 10 seconds

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Time frame: 10 seconds

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Artifact correction

- SSP PCA correction
- Signal space projections
- Empty room correction
- Independent component analysis (ICA)
To get clean data...

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Time frame: 10 seconds

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Source localisation with M/EEG: The forward and inverse problems

Forward problem: Objective

Predict what is the Electric Potential or the Magnetic Field produced by a current generator outside of the head



How to do it?

- Find from **Maxwell equations** the equations adapted to the problem.
- Define a model for the current generators (e.g., sources modeled by equivalent current dipoles).
- Solve numerically the differential equations obtained for a real anatomy obtained by MRI.



Maxwell Equations with **quasi-static** approximation

$$\begin{cases} \nabla \times \vec{E} = 0 \\ \nabla \cdot \vec{B} = 0 \\ \nabla \times \vec{B} = \mu_0 \vec{J} \\ \nabla \cdot \vec{E} = \frac{\rho}{\epsilon_0} \end{cases}$$

Remark: quasi-static implies no temporal derivatives and no propagation delay

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Maxwell



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Maxwell

Potential equation (relation between the potential and the sources):

$$\nabla \cdot \nabla \times \vec{B} = 0 \Rightarrow \nabla \cdot (\vec{J}_s + \vec{J}_c) = 0$$

$$\Rightarrow \nabla \cdot \vec{J}_p = \nabla \cdot (\sigma \nabla V) \qquad Poisson Equation$$

Magnetic field equation:

Remark: Relation with Kirchoff's law

$$\vec{B} = rac{\mu_0}{4\pi} \int \vec{J}(r') imes rac{r-r'}{\|r-r'\|^3} dr'$$

 $\Rightarrow \vec{B} = \vec{B}_0 - \frac{\mu_0}{4\pi} \int \sigma \nabla V \times \frac{r - r'}{\|r - r'\|^3} dr'$

Biot and Savart's law

Observations:

- $\bullet\,B$ is obtained after V
- B decreases in I/R²
- B is due both to primary currents and volume currents

where
$$\vec{B}_0 = \frac{\mu_0}{4\pi} \int \vec{J}_p \times \frac{r - r'}{\|r - r'\|^3} dr'$$

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Head models

Requires to model the properties of the different tissues: skin, skull, brain etc.

Hypothesis: The conductivities are **piecewise constant**



Realistic models



[Geselowitz 67, De Munck 92, Kybic et al. 2005]

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Head models

Requires to model the properties of the different tissues: skin, skull, brain etc.

Hypothesis: The conductivities are **piecewise constant**

Sphere models

Analytical solutions fast to compute but very **coarse** head model (esp. for EEG)

Realistic models

Boundary element method (BEM), i.e., numerical solver with approximate solution.

EEG : [Berg et al. 94, De Munck 93, Zhang 95] MEG : [Sarvas 87]

[Geselowitz 67, De Munck 92, Kybic et al. 2005]

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The M/EEG inverse problem

Inverse problem: Objective

Find the current generators that produced the M/EEG measurements



Inverse problem approaches

- Dipole fitting
- Scanning methods
- Distributed models

Dipole fitting



The equivalent of triangulation

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Dipole fitting: procedure



Median Nerve Dipole Fitting Results









7 sensors







92 sensors



99.7%



84.6%







99.2%



97.6%



97.6%





85.8%



85.8%



Time course of SEF



Distributed models



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Distributed source framework

M = GX + E

Linear forward model, i.e.,

M is the sum of the contributions of all the sources (Superposition principle)

- $\mathbf{M} \in \mathbb{R}^{d_m imes d_t}$: M/EEG Measurements $\mathbf{X} \in \mathbb{R}^{d_x imes d_t}$: Source amplitudes (Unknowns) $\mathbf{G} \in \mathbb{R}^{d_m imes d_x}$: Leadfield (or Gain) matrix
- $\mathbf{E} \in \mathbb{R}^{d_m imes d_t}$:additive noise



Scanning methods

$\mathbf{M} = \mathbf{G}\mathbf{X} + \mathbf{E}$

Scanning : One source at a time i.e. one column of G at a time

Idea: Find how well it can explain the data while trying to cancel what can come from other sources

Common methods: beamformers (LCMV) and MUSIC



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M = GX+E : An ill-posed problem



Linear problem with more unknowns than the number of equations: it's ill-posed => Use prior

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Inverse problem framework

An optimization problem:

$$\begin{split} \mathbf{X}^* &= \arg\min \|\mathbf{M} - \mathbf{G}\mathbf{X}\|_F^2 + \lambda \phi(\mathbf{X}), \lambda > 0 \\ \mathbf{X} & \mathsf{Data fit} & \mathsf{Prior} \ (\mathsf{penalization}) \\ \lambda &: \mathsf{Trade-off between the data fit and the prior} \end{split}$$

where $\|\mathbf{A}\|_F = \mathbf{tr}(\mathbf{A}^T\mathbf{A})$

 $\phi(\mathbf{X})$ Measures the complexity of X, it's the prior.

Examples for $\phi(\mathbf{X}) : \ell_1, \ \ell_2, \ \ell_p \text{ with } p \ge 1, \text{ entropy } \dots$

Remark: If $\phi(\mathbf{X})$ is strictly convex we have a unique minimizer (sufficient but not a necessary condition)

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Definition: Convex function



$$f(\theta x + (1 - \theta)y) \le \theta f(x) + (1 - \theta)f(y)$$

for all $0 \le \theta \le 1$

is strictly convex iff

$$f(\theta x + (1 - \theta)y) < \theta f(x) + (1 - \theta)f(y)$$

for all $0 < \theta < 1$

Remark: The presentation is restricted to functions defined on \mathbb{R}^n

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Inverse problem

Optimization problem:

- Data fit is **quadratic** hence **convex**
- If $\phi(\mathbf{X})$ is **convex**, then it's a **convex** optimization problem

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Smooth or non-smooth

• Smooth:

- L2 (regularized Leastsquares, Tikhonov)
- Entropy based methods
- etc.
- Non-smooth:
 - LI $\phi(\mathbf{X}) = \|\mathbf{X}\|_1 = \sum |x_i|$

 $\phi($

• Total-Variation

$$\phi(\mathbf{X}) = \|\mathbf{X}\|_1 = \sum_{i,j} |x_{ij}|$$
$$\mathbf{X}) = TV(\mathbf{X}) = \|\nabla_{surf} \mathbf{X}\|$$

 $\phi(\mathbf{X}) = \|\mathbf{X}\|_2^2 = \sum x_{ij}^2$

• etc.

LI vs L2 norms on combined M/EEG data

Activation in left-auditory cortex L1 result L2 result

$\phi(\mathbf{X})$ with M/EEG data: L2

Simple L2 (Tikhonov):

$\mathbf{X}^* = \underset{\mathbf{X}}{\operatorname{arg\,min}} \mathbf{E}(\mathbf{X}) = \underset{\mathbf{X}}{\operatorname{arg\,min}} \|\mathbf{M} - \mathbf{G}\mathbf{X}\|_F^2 + \lambda \|\mathbf{X}\|_F^2, \lambda > 0$



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Quiz: Complexity and Computing times

- Complexity of matrix multiplication
 - GX with $G \in \mathbb{R}^{d_m \times d_x}$ and $X \in \mathbb{R}^{d_x \times d_t}$
- Complexity of matrix inversion

 $(G^T G + \lambda I)^{-1}$

- Resolution of a linear system: Ax = b (when A is sparse or dense)
- Resolution of many linear system:

$$Ax_i = b_i, i = 1, ..., d_n$$

L2 a.k.a. Minimum Norm Estimates (MNE)

$$\phi(\mathbf{X}) = \|\mathbf{W}\mathbf{X}\|_{F}^{2} = \sum_{i,j} w_{i}^{2} x_{ij}^{2} = \|\mathbf{X}\|_{\boldsymbol{\Sigma},2}^{2}$$
$$\mathbf{W}^{2} = \mathbf{\Sigma} \text{ source covariance}$$

Leads to a **closed form solution** (matrix multiplication):

$$\mathbf{X}^* = \mathbf{\Sigma}^{-1} \mathbf{G}^T (\mathbf{G} \mathbf{\Sigma}^{-1} \mathbf{G}^T + \lambda \mathbf{Id})^{-1} \mathbf{M}$$

[Tikhonov et al. 77, Wang et al. 92, Hämäläinen et al. 94]

L2 a.k.a. Minimum Norm Estimates (MNE)

$$\phi(\mathbf{X}) = \|\mathbf{W}\mathbf{X}\|_F^2 = \sum_{i,j} w_i^2 x_{ij}^2 = \|\mathbf{X}\|_{\mathbf{\Sigma},2}^2$$

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[Tikhonov et al. 77, Wang et al. 92, Hämäläinen et al. 94]

Remarks:

- MNE is known as Ridge regression in statistics.
- **Really fast** to compute (SVD of **G**), hence very much used in the field.

• In practice, it's **much more complicated** (whitening data, correcting artifacts, channels with different SNRs, setting λ based on SNR, loose orientation, ...) **THM:** A lot of domain knowledge to make it work

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How do I set the regularization parameter?

The L-curve



[Hansen 92]

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A naïve but efficient approach

Compute the SVD (Singular Value Decomposition) of G: $\mathbf{G} = \mathbf{U}\mathbf{S}\mathbf{V}^T$ with $\mathbf{U}\mathbf{U}^T = \mathbf{U}^T\mathbf{U} = \mathbf{I}$ $\mathbf{V}\mathbf{V}^T = \mathbf{V}^T\mathbf{V} = \mathbf{I}$ S diagonal + zeros



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A naïve but efficient approach

Compute the SVD (Singular Value Decomposition) of G:

$$G = USV^T$$

with $\mathbf{U}\mathbf{U}^{T} = \mathbf{U}^{T}\mathbf{U} = \mathbf{I}$ $\mathbf{V}\mathbf{V}^{T} = \mathbf{V}^{T}\mathbf{V} = \mathbf{I}$ S diagonal + zeros

Replace the SVD in: $\begin{aligned} \mathbf{X}^* &= \mathbf{G}^T (\mathbf{G}\mathbf{G}^T + \lambda \mathbf{I})^{-1} \mathbf{M} \\ \mathbf{X}^* &= \mathbf{G}^T (\mathbf{U}\mathbf{S}^2\mathbf{U}^T + \lambda \mathbf{I})^{-1} \mathbf{M} \\ &= \mathbf{G}^T (\mathbf{U}(\mathbf{S}^2 + \lambda \mathbf{I})\mathbf{U}^T)^{-1} \mathbf{M} \\ &= \mathbf{G}^T \mathbf{U} (\mathbf{S}^2 + \lambda \mathbf{I})^{-1} \mathbf{U}^T \mathbf{M} \\ &= \mathbf{V}\mathbf{S} (\mathbf{S}^2 + \lambda \mathbf{I})^{-1} \mathbf{U}^T \mathbf{M} \end{aligned}$

 λ compares to the squared singular values of G Take λ as a percentage of the max singular value

http://youtu.be/Uxr5Pz7JPrs



time=0.00 ms

Alexandre Gramfort, Telecom ParisTech, CEA/Neurospin

Beyond L2 priors

$\phi(\mathbf{X})$ with M/EEG data: LI

LI priors a.k.a. Minimum current estimate (MCE) :

$$\phi(\mathbf{X}) = \|\mathbf{X}\|_1 = \sum |x_i| \quad \text{with} \ d_t = 1$$

i [Matsuura et al. 95] $\phi(\mathbf{X})$ is convex, non differentiable and has no closed form solution.

Remarks:

- It's the **LASSO** problem in the Machine Learning community [Tibshirani 96]
- It's the **Basis Pursuit** problem in Signal Processing [Chen Donoho Saunders 99]
- Matsuura uses linear programming but other algorithms exist, e.g., LARS [Efron 2004], Homotopy [Osborne 2000], coordinate descent, IRLS, proximal iterations etc.

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Iterative Least Squares (IRLS)

Idea:
$$\|\mathbf{X}^*\|_1 = \sum_i |x_i^*| = \sum_i \frac{(x_i^*)^2}{w_i} = \|\mathbf{X}^*\|_{w,2}$$
 when $w_i = |x_i^*|$

$$\lim_{\substack{\mathbf{x} \\ \mathbf{x} \\ \mathbf{x}$$



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Iterative Least Squares (IRLS)

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$\phi(\mathbf{X})$ with M/EEG data: L2 I

$$\phi(\mathbf{X}) = \|\mathbf{X}\|_{21} = \sum_{i} \sqrt{\sum_{t} |x_{i,t}|^2}$$

2-level mixed-norm



[Ou et al. Neuroimage 2009]

- It introduces temporal structure in the prior
- It guarantees that the active sources are the same over time



Remark : It is known as Group Lasso in Machine Learning & «joint feature selection»

[Yuan et al. 2006, Obozinski 2009 ...]

L21 with loose orientation

$$\phi(\mathbf{X}) = \|\mathbf{X}\|_{21} = \sum_{i} \sqrt{\sum_{t} |x_{i,t}^{normal}|^2 + \rho |x_{i,t}^{tang1}|^2 + \rho |x_{i,t}^{tang2}|^2}$$





custom but still a 2-level THM: you need custom sparse mixed-norm solvers adapted to M/EEG

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But... the brain is not stationary

L21 like any other sparse solver available today it imposes the sources to be the same over the entire time interval



Challenge:

How do you promote sparse solutions with non-stationary sources?

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back to M = G X + E



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$M = GZ\Phi + E$



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Time-frequency (TF) prior

The classical approach [MNE, dSPM, sLORETA]:

$$\hat{\mathbf{X}} = \arg\min_{\mathbf{X}} \frac{\|\mathbf{M} - \mathbf{G}\mathbf{X}\|_{F}^{2} + \lambda\phi(\mathbf{X})}{\text{data fit}}, \ \lambda > 0$$

we propose:

- $\hat{\mathbf{Z}} = \arg\min_{\mathbf{Z}} \|\mathbf{M} \mathbf{G}\mathbf{Z}\boldsymbol{\Phi}^{\mathcal{H}}\|_{F}^{2} + \lambda\phi(\mathbf{Z}), \text{ then } \hat{\mathbf{X}} = \hat{\mathbf{Z}}\boldsymbol{\Phi}^{\mathcal{H}}$
- Φ : is a **TF dictionary** of Gabor atoms
- $\boldsymbol{Z}: \textbf{coefficients}$ of the $\textbf{TF}\ \textbf{transform}$ of the sources

Advantage: localization in space, time and frequency in one step

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Why does it make sense?

and why a sparse prior shall work ?



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Time frequency dictionaries

discrete version of the complex Gabor transform = short time fourier transform (STFT)

- It is **invertible**
- It is **translation invariant**

(not like classical dyadic wavelets)

- It can capture **non-stationary signals** (not like FFT) (It is classically used in M/EEG on sensor measurements)
- It is **relatively fast** to compute

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What is a good prior on Z?

MEG Auditory data

Protocol: 50 epochs of auditory tones in left ear (305 MEG, 59 EEG channels)



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MEG Visual data



Protocol: 50 epochs of visual flash in left hemi-field (305 MEG, 59 EEG channels)





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time=133.99 ms							
0.100	0.229	0.357	0.486	0.614	0.743	0.871	1.00





Conclusion

To sum up

• MEG and EEG measure the electrical activity of local

assemblies of neurons (post-synaptic potentials)

- Can be used for: clinical applications (epilepsy, sleep), cognitive studies or BCI
- Acquisitions: physics
- Forward problem: image (segmentation), maths (PDE, numerical solvers)
- Inverse problem: statistics, optimization, signal processing