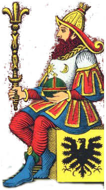
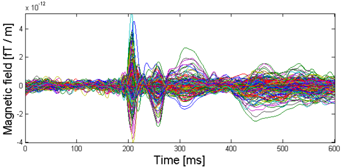
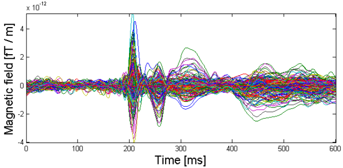
Two applications of mathematics to neuroscience

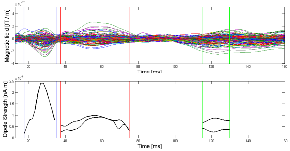
Dipartimento di Matematica, Università degli Studi di Genova.
Gruppo MIDA, Methods for Image and Data Analysis

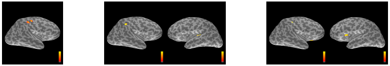



x 10^-12
Magnetic field [fT / m]
Time [ms]

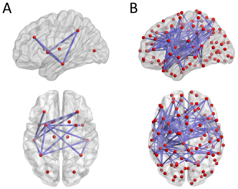


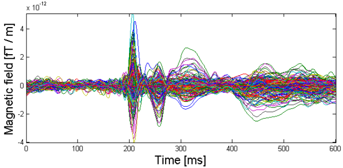
Inverse Problem: reconstruct brain activity from recorded data.





Brain connectivity: quantify the correlation between distant brain areas.





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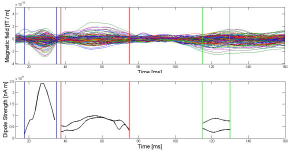
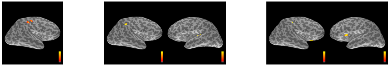
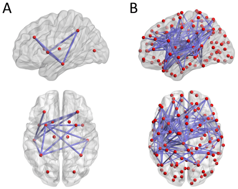




Functional segregation: each brain region/neural assembly has a specialized function.

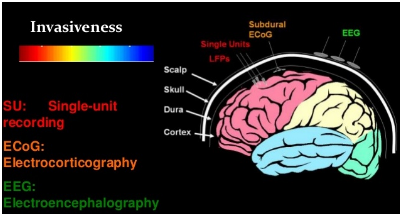
Brain connectivity: quantify the correlation between distant brain areas.



Functional integration: brain activity consists in the coordinate activation of a very large number of neural assemblies distributed across different cortical areas.

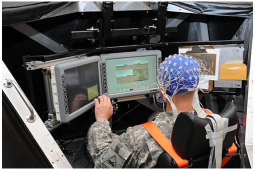
Brain Computer Interface

A brain-computer interface (BCI), is a direct communication pathway between the brain and an external device.



From invasive BCI

To non-invasive BCI



Brain connectivity

Definition

Structural connectivity:
delineation and assessment of white matter fiber tracts within the brain.

Modalities: Magnetic Resonance Imaging, Diffusion Tensor Imaging.

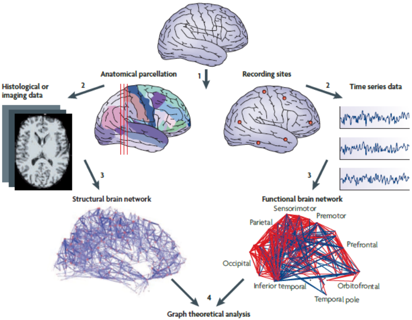
Functional connectivity:
analysis of the temporal correlation among the activity of distant brain regions.
(Region A and B are interacting?)
Effective connectivity:
what is the direction of this correlation?
(Region A is causal to region B or viceversa?)

Modalities: EEG, MEG, PET, fMRI.

A basic approach

E. Bullmore, O. Sporns (2009).

Complex brain network: graph theoretical analysis of structural and functional systems.



Step 1: Define the network nodes (source–space vs sensor–space). For each node k we will have a time serie $X_k(t)$.

Step 2: Estimate a continuous measure of interaction between nodes.

Step 3: Generate an association matrix and/or a binary *adjacency matrix* by compiling all pairwise associations between nodes

Step 4: Calculate the network parameters of interest in this graphical model.

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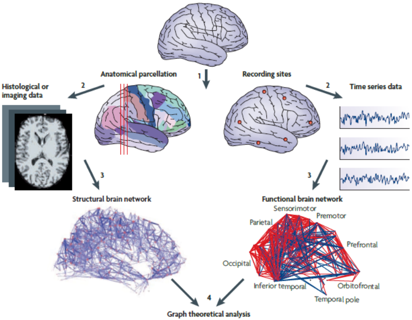

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Measure of association between nodes

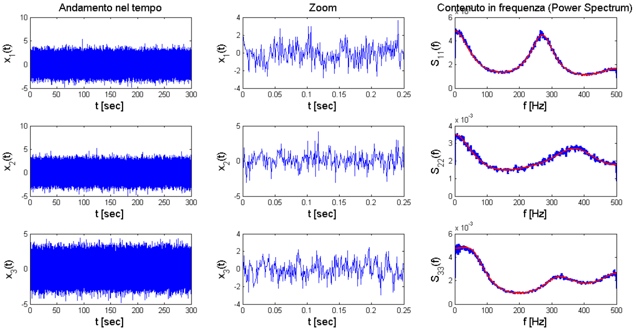
INPUT: N time-series

$$\{x_1(t), \ldots, x_N(t)\}_{t=1}^{T}.$$

usually normalized so to have

- zero mean,
- unit variance.

Example:



$$\begin{pmatrix} x_1(t) \\ x_2(t) \\ x_3(t) \end{pmatrix} = \sum_{k=1}^{K} \begin{pmatrix} B_{11}(k) & 0 & 0 \\ B_{21}(k) & B_{22}(k) & 0 \\ 0 & 0 & B_{33}(k) \end{pmatrix} \begin{pmatrix} x_1(t-k) \\ x_2(t-k) \\ x_3(t-k) \end{pmatrix} + \begin{pmatrix} \epsilon_1(t) \\ \epsilon_2(t) \\ \epsilon_2(t) \end{pmatrix}.$$

Granger causality (Effective connectivity)

Definition of causality by Wiener (1956): given two simultaneously measured signals, if the first signal can be predicted better by incorporating the past information from the second signal than using only the information from its own past, than the second signal can be called causal to the first one.

STEP 1: Construction of the AutoRegressive models

- univariate

$$x(t) = \sum_{k=1}^{p} a_{xk} x(t-k) + u_x \qquad y(t) = \sum_{k=1}^{p} a_{yk} y(t-k) + u_y$$

- bivariate

$$x(t) = \sum_{k=1}^{p} a_{xyk} x(t-k) + \sum_{k=1}^{p} b_{xyk} y(t-k) + u_{xy}$$

$$y(t) = \sum_{k=1}^{p} a_{yxk} x(t-k) + \sum_{k=1}^{p} b_{yxk} y(t-k) + u_{yx}$$

u_x, u_y, u_{xy}, u_{yx} uncertainties or residual noises associated with the model.

Granger causality (Effective connectivity)

STEP 2: to analyze if $y(t)$ is causal to $x(t)$ the variance of the corresponding univariate and bivariate processes are computed:

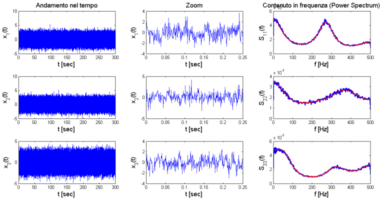
$$x(t) = \sum_{k=1}^{p} a_{xk} x(t-k) + u_x \Rightarrow V_{X|X_-} := Var(u_x)$$

$$x(t) = \sum_{k=1}^{p} a_{xyk} x(t-k) + \sum_{k=1}^{p} b_{xyk} y(t-k) + u_{xy} \Rightarrow V_{X|X_-,Y_-} := Var(u_{xy}).$$

Then

$$\boxed{G_{Y\to X} := \ln\left(\frac{V_{X|X_-}}{V_{X|X_-,Y_-}}\right)}$$

Example:



Granger Causality:

$$\begin{pmatrix} NaN & 0.0317 & 0.0000 \\ 0.0000 & NaN & 0.0000 \\ 0.0000 & 0.0000 & NaN \end{pmatrix}$$

Coherence (functional connectivity)

Input: $x_i(t), x_j(t)$

Step 1: Compute the fourier Transform:

$$x_i(f) = A_i(f)e^{i\phi_i(f)} \qquad x_j(f) = A_j(f)e^{i\phi_j(f)}$$

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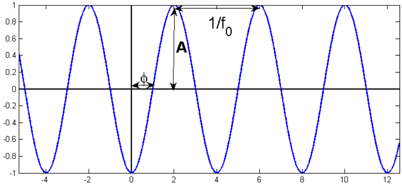

$$x(t) = A\ sin\left(2\pi f_0(t - \phi)\right)$$

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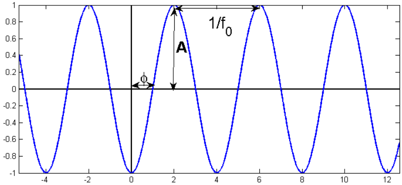

$$x(t) = A\ sin\,(2\pi f_0(t-\phi))$$

$$\Downarrow$$

$$x(f) = A/2e^{i\pi(2*\phi+\frac{pi}{2})}\,(\delta(f-f_0)+\delta(f-f_0))$$

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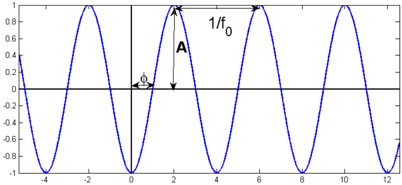

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Coherence (functional connectivity)

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Step 1: Compute the fourier Transform:

$$x_i(f) = A_i(f)e^{i\phi_i(f)} \qquad x_j(f) = A_j(f)e^{i\phi_j(f)}$$

Step 2: Compute the cross-spectrum:

$$S_{ij}(f) =< x_i(f)x_j^*(f) >=< A_iA_je^{i(\phi_i-\phi_j)} >$$

Coherence (functional connectivity)

Input: $x_i(t), x_j(t)$

Step 1: Compute the fourier Transform:

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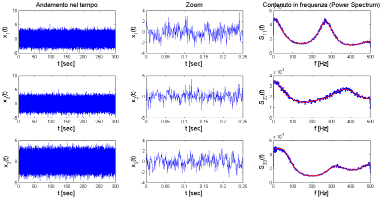
Step 2: Compute the cross-spectrum:

$$S_{ij}(f) = < x_i(f)x_j^*(f) > = < A_iA_je^{i(\phi_i-\phi_j)} >$$

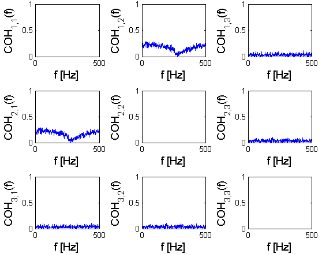
Step 3: Normalize to obtain Coherence:

$$\begin{aligned} COH_{ij}(f) &= \frac{|S_{ij}(f)|}{\sqrt{S_{ii}(f)S_{jj}(f)}} \\ &= \frac{< A_iA_je^{i(\phi_i-\phi_j)} >}{\sqrt{< A_i^2 >< A_j^2 >}} \end{aligned}$$

Example:



Coherence:



Granger Causality:

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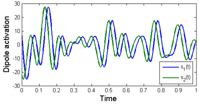
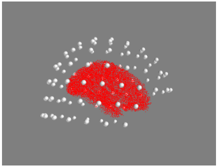
Purposes:

1. test and compare the temporal resolution of different connectivity measures.

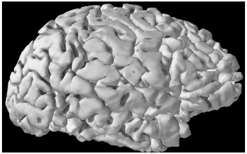
Step1: *Signals-theory level*



Step2: Sensor level

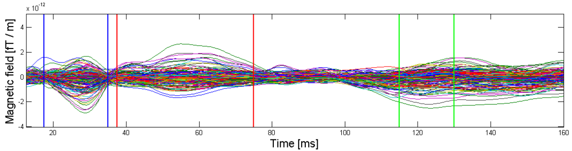


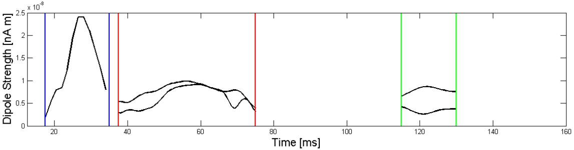
Step3: Source-Space level

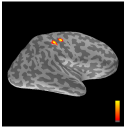


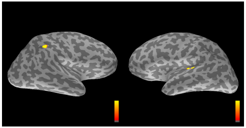
2. quantify the impact of *inverse algorithm* on this temporal resolution.

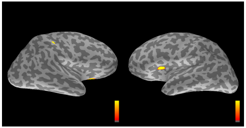
The Electro/Magnetoencephalography (MEEG) Inverse Problem


x 10^-12
Magnetic field [fT / m]
4
2
0
-2
-4
20
40
60
80
100
120
140
160
Time [ms]


x 10^-8
Dipole Strength [nA m]
2.5
2
1.5
1
0.5
0
20
40
60
80
100
120
140
160
Time [ms]

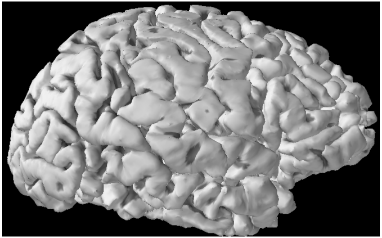






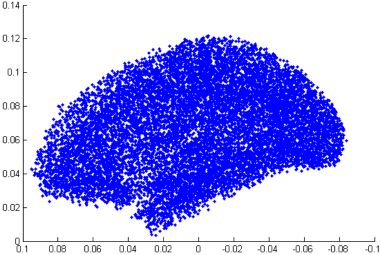
From Magnetic Resonance

$$\Omega \in \mathbb{R}^3$$



To source-space

$$\{r(c)\}_{c=1,\ldots,N_c}$$



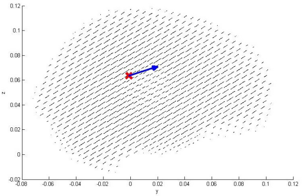
Static Multi–Dipolar Model with Time–Varying Moments

Single dipole:

$$q\,\delta\,(r - r(c))$$

where

- q dipole moment
- $r(c)$ dipole position.
  Points of a brain–grid $\{r(c)\}_{c=1}^{N_c}$



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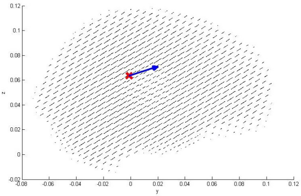

At each time–point t the neural currents are approximated with

$$\sum_{k=1}^{d} q_t^{(k)}\delta\left(r - r(c^{(k)})\right)$$

where $d \leq D_{\max}$ is the number of active dipoles.

Data: the magnetic field recorded by the N_s sensors at N_t time–points

$$\mathbf{y} = (y_1, \cdots, y_{N_t}) \in \mathbb{R}^{N_s \ N_t}$$

Unknown: number of dipoles and their parameters

$$\begin{aligned} \mathbf{x} &= (d, \mathbf{c}, \mathbf{q}) \\ &= \left(d, c^{(1)}, \ldots, c^{(d)}, q_1^{(1)}, \ldots q_1^{(d)}, \ldots, q_{N_t}^{(1)}, \ldots, q_{N_t}^{(d)}\right) \end{aligned}$$

From Biot-Savart equation (conditionally linear model):

$$\mathbf{y} = G(d, \mathbf{c})\mathbf{q} + \mathbf{e}$$

where

- $G(d, \mathbf{c})$ is the *leadfield matrix*
- $\mathbf{e}$ is the noise affecting the measurements.

Bayesian Approach to Inverse Problems

Data, unknown and noise are modeled with random variables.
The aim becomes to approximate the posterior pdf $\pi(\mathbf{x}|\mathbf{y})$.

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From Bayes theorem:

$$\pi(\mathbf{x}|\mathbf{y}) = \frac{\pi(\mathbf{x})\pi(\mathbf{y}|\mathbf{x})}{\pi(\mathbf{y})}$$

where

- $\pi(\mathbf{x})$ is the prior pdf:
  embodies all information about the unknowns available before the data are recorded;
- $\pi(\mathbf{y}|\mathbf{x})$ is the likelihood function:
  embodies the forward problem and the noise model.
- $\pi(\mathbf{y})$ is a normalizing constant.

Let's go to MatLab.