Origin of Functional measurements

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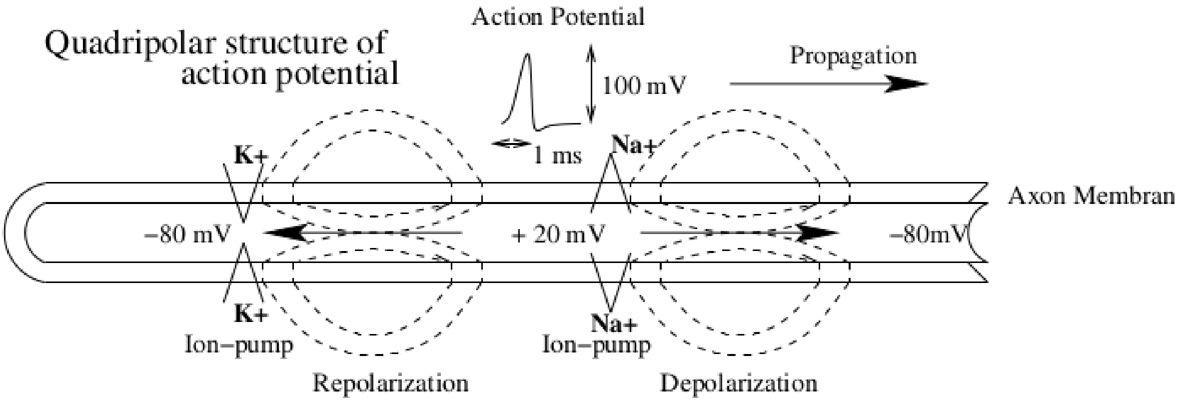
Application of ML to MRI, electrophysiology and brain computer interfaces

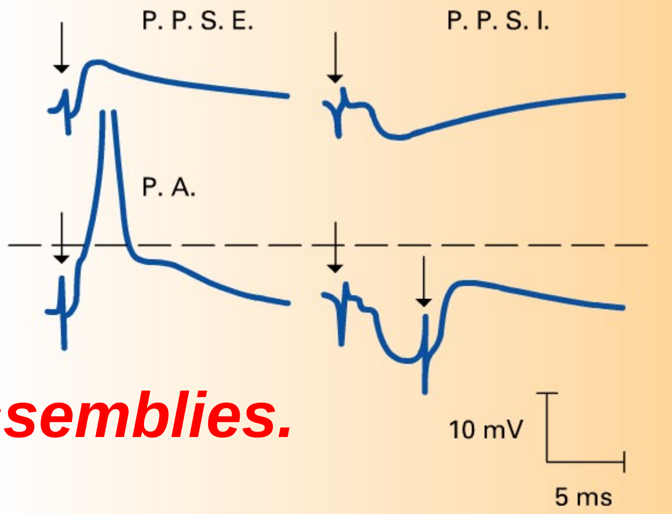
Neural current sources

- Action potentials (AP): strong and short, quadrupolar → faster decrease with distance ($1/r^3$).



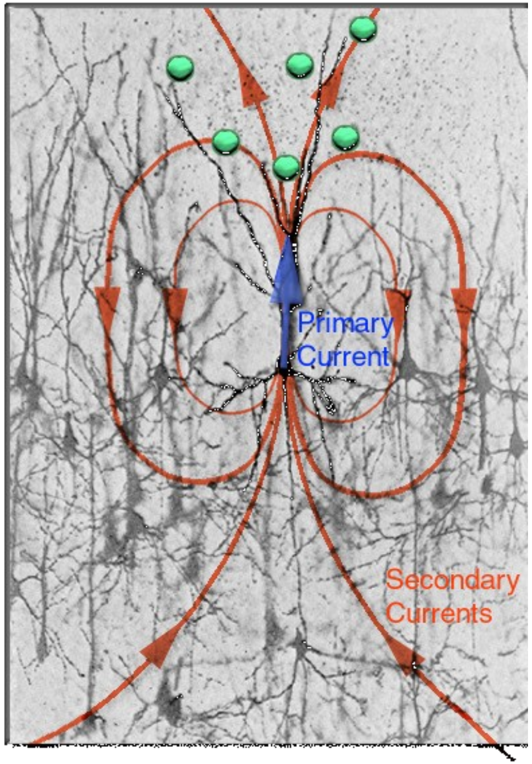
The ion exchanges corresponding to action potentials.

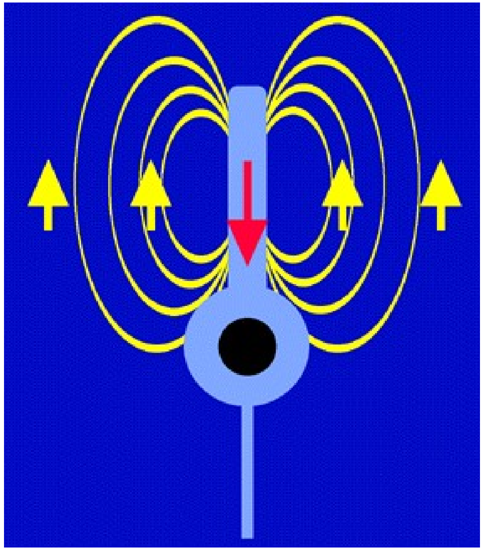
- Postsynaptic potentials (PSP):
  Weaker, but wider and slower and bipolar.
  →***Superposition in synchronized neural assemblies.***
  →***Weaker decrease with distance ($1/r^2$).***



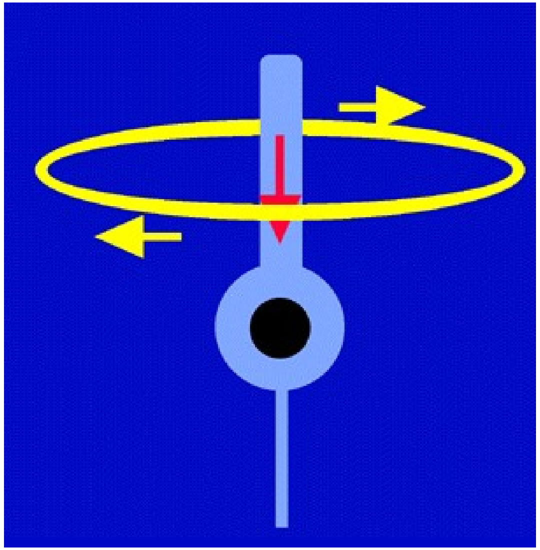
Neural current sources

- EEG/MEG directly measure PSP currents after propagation.
- Sources modeled as dipoles.





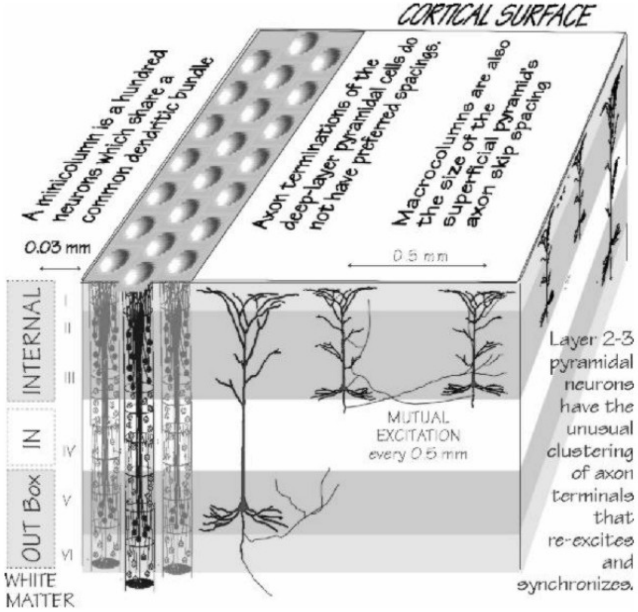
Electrical current flow lines

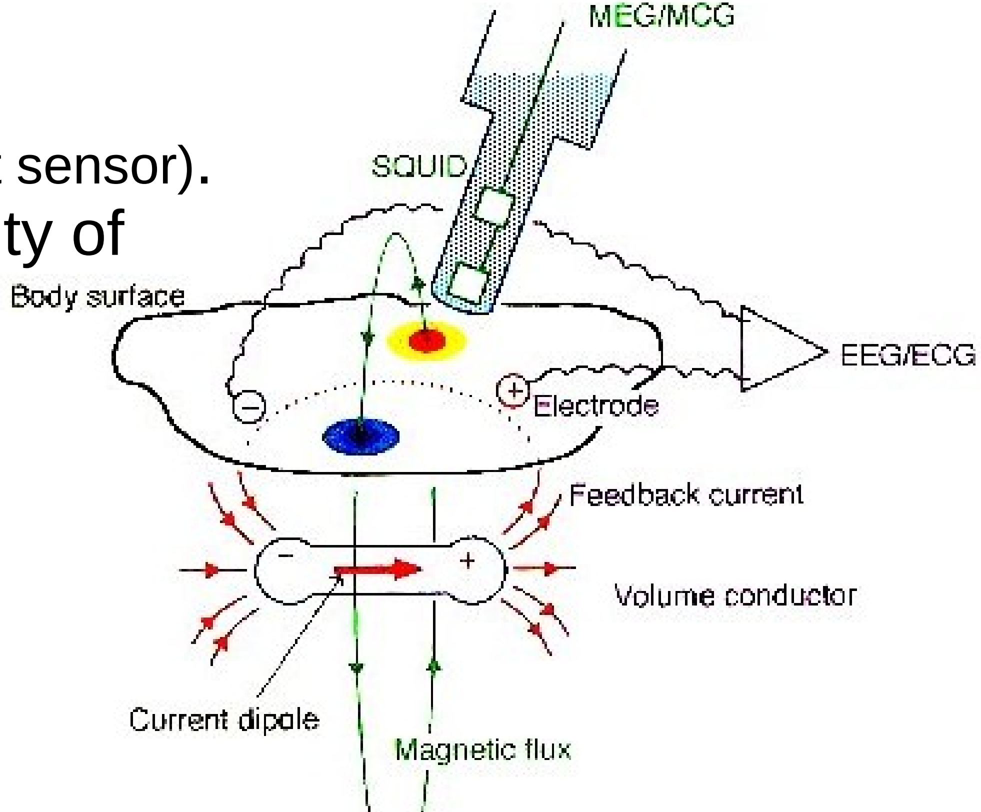


Magnetic field flow lines

EEG/MEG measurements

- A dipole is about 20fAm
  → too small to measure (10nAm at sensor).
- Synchronized and coherent activity of millions of pyramidal neurons.





EEG: From 1 to 100mV.
MEG: About 100 fT.

Goals

Source localisation: Compute sources from measurements.

To do that we will “compare” measurements with

Simulated / predicted values for these measurements.

Forward model: Predict sensor values from sources…

So this is called an inverse problem.

These inverse problems are known to be ill-posed:

- Non existence.
- Non uniqueness.
- Non continuity.

Forward model:

Predicting sensor values from sources….

- Start from physics.
- Establish computational models of electric/magnetic propagation on the head.
- Pinpoint some theoretical properties and difficulties:
    - Silent sources.
    - Nested sphere geometries.
- Various models of increasing complexity.
    - Nested closed surfaces.
        - Surfacic methods.
        - Volumic methods.

Some maths/physics...

Reminder on differential operators (1)

Let (x, y, z) denote the canonical basis of $\mathbb{R}^3$.

The *nabla* operator is $\nabla = \begin{pmatrix} \partial_x \\ \partial_y \\ \partial_z \end{pmatrix}$ This is just a notation.

The *gradient* of a scalar field $a(x, y, z)$ is $\nabla a = \begin{pmatrix} \partial a/\partial x \\ \partial a/\partial y \\ \partial a/\partial z \end{pmatrix}$.

The *divergence* of a vector field $\mathbf{b} = \begin{pmatrix} b_x \\ b_y \\ b_z \end{pmatrix}$ is the scalar field

$$\nabla \cdot \mathbf{b} = \frac{\partial b_x}{\partial x} + \frac{\partial b_y}{\partial y} + \frac{\partial b_z}{\partial z}$$

The *Laplacian* is $\Delta a = \nabla \cdot \nabla a = \dfrac{\partial^2 a}{\partial x^2} + \dfrac{\partial^2 a}{\partial y^2} + \dfrac{\partial^2 a}{\partial z^2}$

Reminder on differential operators (2)

The *curl* of vector field $\mathbf{b}$ is

$$\nabla \times \mathbf{b} = \begin{pmatrix} \partial a_y/\partial z - \partial a_z/\partial y \\ \partial a_z/\partial x - \partial a_x/\partial z \\ \partial a_x/\partial y - \partial a_y/\partial x \end{pmatrix}.$$

Product rule for the gradient

$$\nabla(a\, b) = a\, \nabla b + b \nabla a$$

Product of a scalar and a vector

$$\nabla \cdot (a\, \mathbf{b}) = a\, \nabla \cdot \mathbf{b} + \mathbf{b} \cdot \nabla a$$

$$\nabla \times (a\, \mathbf{b}) = a\, \nabla \times \mathbf{b} + \nabla a \times \mathbf{b}$$

Vector dot product

$$\nabla(\mathbf{a} \cdot \mathbf{b}) = (\mathbf{a} \cdot \nabla)\mathbf{b} + (\mathbf{b} \cdot \nabla)\mathbf{a} + \mathbf{a} \times (\nabla \times \mathbf{b}) + \mathbf{b} \times (\nabla \times \mathbf{a})$$

Vector cross product

$$\nabla \cdot (\mathbf{a} \times \mathbf{b}) = \mathbf{b} \cdot (\nabla \times \mathbf{a}) - \mathbf{a} \cdot (\nabla \times \mathbf{b})$$

$$\nabla \times (\mathbf{a} \times \mathbf{b}) = \mathbf{a}(\nabla \cdot \mathbf{b}) - \mathbf{b}(\nabla \cdot \mathbf{a}) + (\mathbf{b} \cdot \nabla)\mathbf{a} - (\mathbf{a} \cdot \nabla)\mathbf{b}$$

Important properties:

$$\nabla \times \nabla a = 0$$

$$\nabla \cdot (\nabla \times \mathbf{b}) = 0$$

$$\nabla \times \nabla \times \mathbf{b} = \nabla(\nabla \cdot \mathbf{b}) - \Delta \mathbf{b}$$

Electrical current propagation

- Maxwell equations

Name	Differential form
Gauss's law	$\nabla \cdot \mathbf{E} = \frac{\rho}{\varepsilon_0}$
Gauss's law for magnetism	$\nabla \cdot \mathbf{B} = 0$
Faraday's law	$\nabla \times \mathbf{E} = -\frac{\partial \mathbf{B}}{\partial t}$
Ampère's circuital law	$\nabla \times \mathbf{B} = \mu_0 \left(\mathbf{J} + \varepsilon_0 \frac{\partial \mathbf{E}}{\partial t} \right)$

- **E** electric field.
- **B** magnetic field.
- **J** electric current sources.
- ρ charge density.
- t time.

$\varepsilon_0 = 8.85\, 10^{-12} kg^{-1} m^{-3} A^2 s^4$, $\mu_0 = 4\pi 10^{-7} kg\, m\, A^{-2} s^{-2}$, $\varepsilon_0 \mu_0 c^2 = 1$.
$\mathbf{E}$ is expressed in $V\, m^{-1}$, $\mathbf{B}$ in T (tesla), $\mathbf{J}$ in $A\, m^{-2}$ and ρ in $C\, m^{-3}$.

Electric current sources **J**

- Two components
  - Volumic ohmic currents $\sigma \mathbf{E}$.
  - Polarization currents $\frac{\partial \mathbf{P}}{\partial t}$.

$$\mathbf{J} = \sigma \mathbf{E} + \frac{\partial \mathbf{P}}{\partial t}$$

$$\nabla \times \mathbf{B} = \mu_0 \left(\sigma \mathbf{E} + \varepsilon \frac{\partial \mathbf{E}}{\partial t} \right)$$

- **P** = $(\varepsilon-\varepsilon_0)$ **E** : polarization vector.
- ε: Permitivity of the medium.
- σ: Conductivity.

Electrical current propagation

- Quasistatic approximation
  → time derivatives can be neglected.

Name	Differential form
Gauss's law	$\nabla \cdot \mathbf{E} = \frac{\rho}{\varepsilon_0}$
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- **E** electric field.
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Poisson equation

From Maxwell-Ampere $\nabla \times \mathbf{B} = \mu_0 \mathbf{J}$ we deduce $\nabla \cdot \mathbf{J} = 0 \,. \quad (1)$

$$\nabla \times \mathbf{E} = 0 \quad \Longrightarrow \quad \boxed{\mathbf{E} = -\nabla \boxed{V}\,.}$$

This is the so-called potential, which is defined up to a constant.V

We divide the current density $\mathbf{J}$ into two components:

$$\underline{\mathbf{J} = -\sigma\nabla V + \mathbf{J}^{\mathrm{p}}}.$$

primary current

Ohmic or *return* current $\sigma\mathbf{E}$

Plugging this expression of J in (1) gives: $\boxed{\nabla \cdot (\sigma \nabla V) = \nabla \cdot \mathbf{J}^{\mathrm{p}}\,.}$

Biot-Savart Law

From Maxwell-Ampere $\nabla \times \mathbf{B} = \mu_0 \mathbf{J}$

$$\mathbf{B} = \frac{\mu_0}{4\pi} \int \mathbf{J}(\mathbf{r}') \times \frac{\mathbf{r} - \mathbf{r}'}{\|\mathbf{r} - \mathbf{r}'\|^3} d\mathbf{r}' \ .$$

It is easy to show that B does not depend on conductivity in an infinite and homogeneous medium.

Alternate formulation:

$$\mathbf{B} = \mathbf{B}_0 - \frac{\mu_0}{4\pi} \int \sigma \nabla' V(\mathbf{r}') \times \frac{\mathbf{r} - \mathbf{r}'}{\|\mathbf{r} - \mathbf{r}'\|^3} d\mathbf{r}' \ ,$$

$$\mathbf{B}_0 = \frac{\mu_0}{4\pi} \int \mathbf{J}^{\mathrm{p}}(\mathbf{r}') \times \frac{\mathbf{r} - \mathbf{r}'}{\|\mathbf{r} - \mathbf{r}'\|^3} d\mathbf{r}' \ .$$

Silent sources

There are configurations of non-null sources that give null measurements at sensors.

Examples are:

- $\nabla \cdot \mathbf{J}^{\mathrm{p}} = 0$, which can happen if $\mathbf{J}_{\mathbf{p}} = \nabla \times \mathbf{b}$ for any vector field $\mathbf{b}$.
  $\implies$ The potential $\mathbf{V}$ is constant everywhere (but $\mathbf{B}$ varies).
- Radially oriented sources for MEG in spherical geometry (but there is EEG signal).
- Equally distributed sources on a closed smooth surface (Both EEG and EEG are zero outside of the surface and constant inside it).

Forward models…

From equations to models

- Equations depend on some physical quantities: sources $\mathbf{J}^{\mathrm{p}}$ and conductivities σ.
- Conductivities depend on the tissues $\Longrightarrow$ geometry.
- Methods will depend on how we take into account of this geometry.
- *Realistic geometries are provided by MR images.*

Forward models

- **Analytic methods**
  - simple geometry (nested spheres),
  - very often used for MEG in practise.
- **Surface methods**
  - conductivity assumed piecewise constant.
- **Volume methods**
  - conductivity (scalar/tensor) defined at each voxel.

From previous equations.

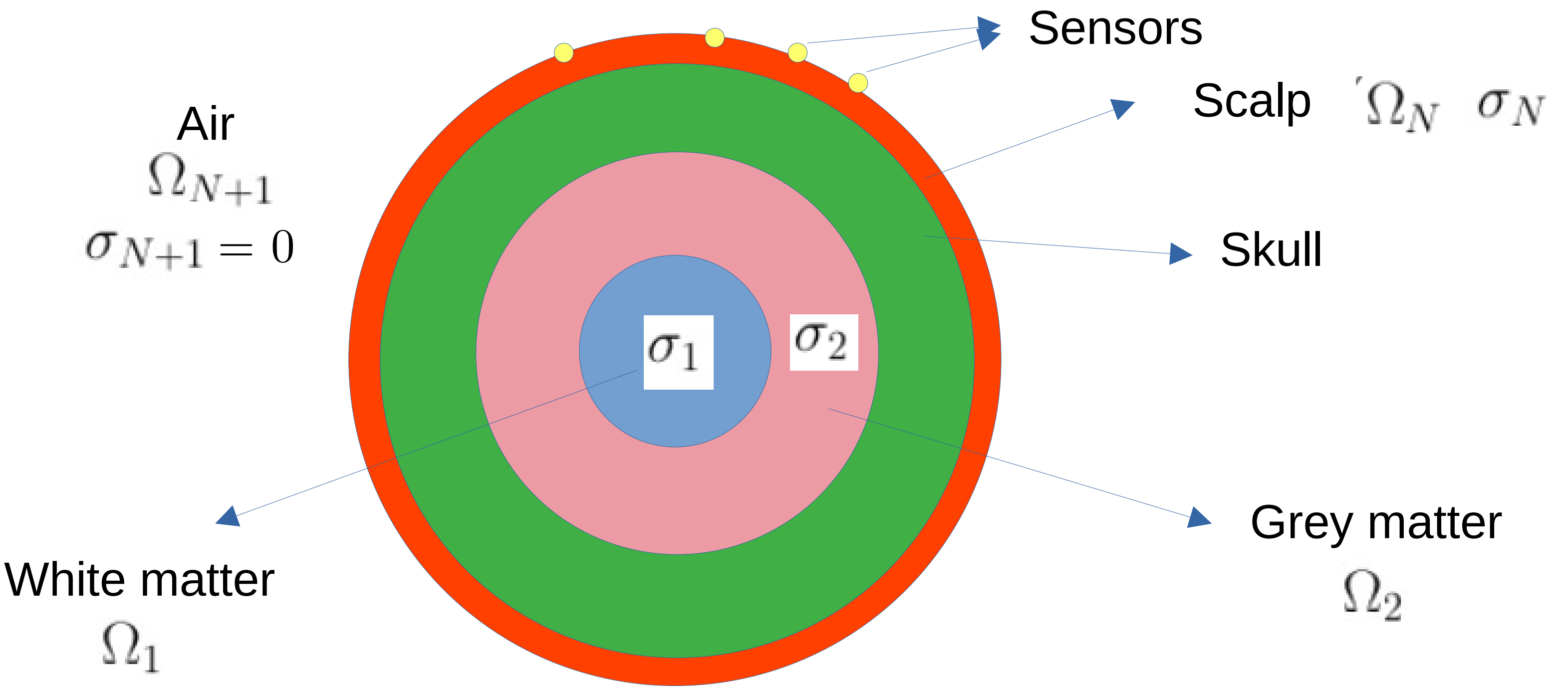
- **Discretization:** BEM or FEM, P0 or P1, ...

$$A\,X = B$$

Structure	Unknowns	Source term
Δ_σ	$V, \partial_{\mathbf{n}} V$	$f(\mathbf{J}^{\mathrm{p}})$

Spherical models

The head is modeled as a set of concentric spheres with homogeneous tissue between any two spheres.



Parameters are the radii of the spheres and the conductivities.

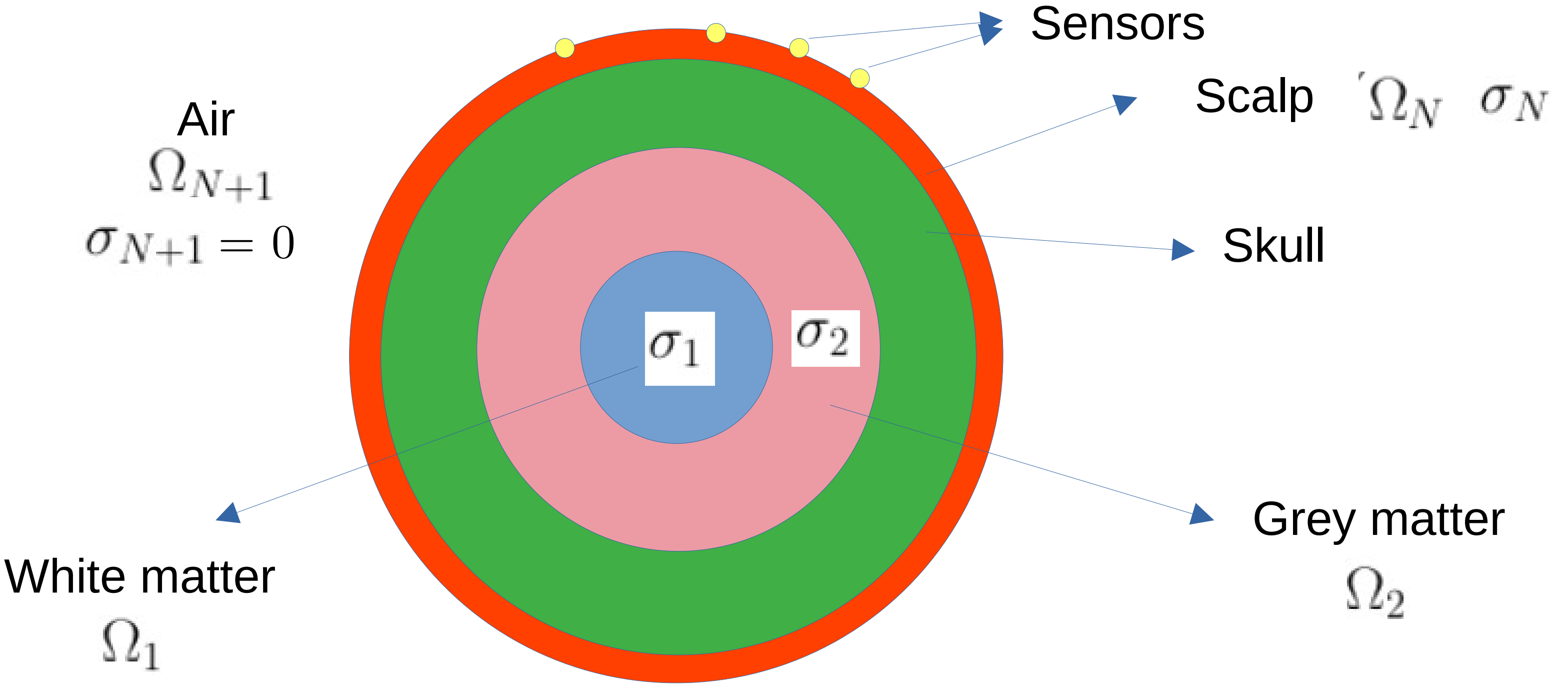
$\Downarrow$

With these parameters, it is possible to compute values at sensors analytically.

Each tissue has an homogeneous constant and isotropic conductivity.

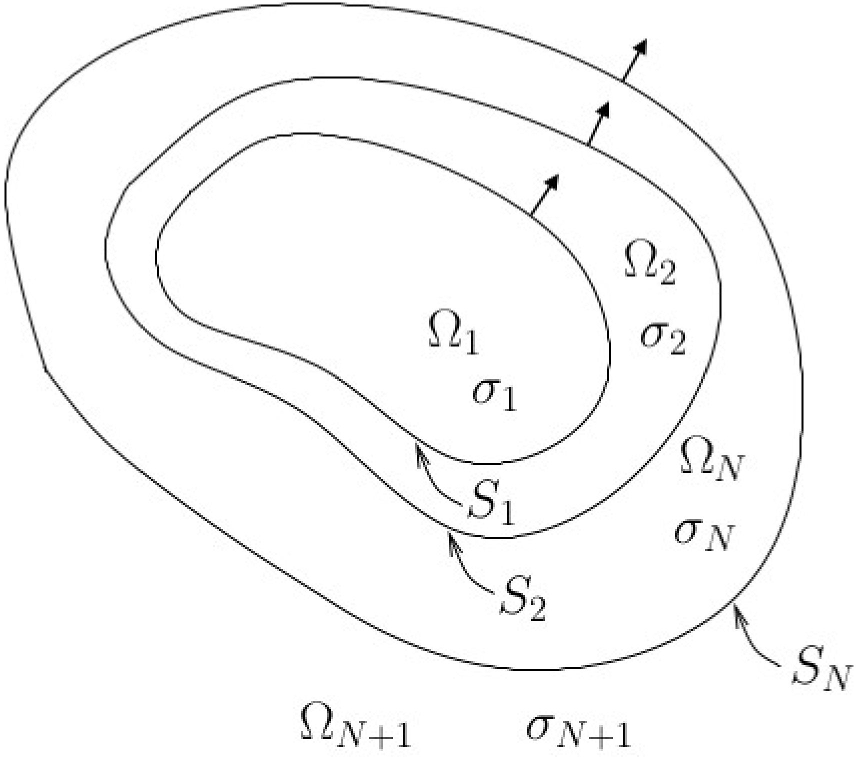
Spherical models

The head is modeled as a set of concentric spheres with homogeneous tissue between any two spheres.



With these specific models, it is possible to show that the magnetic field $\mathbf{B}$ does not depend on conductivity (only $\mathbf{B}_0$ is non-zero) and on radial components of sources.

Semi-realistic model



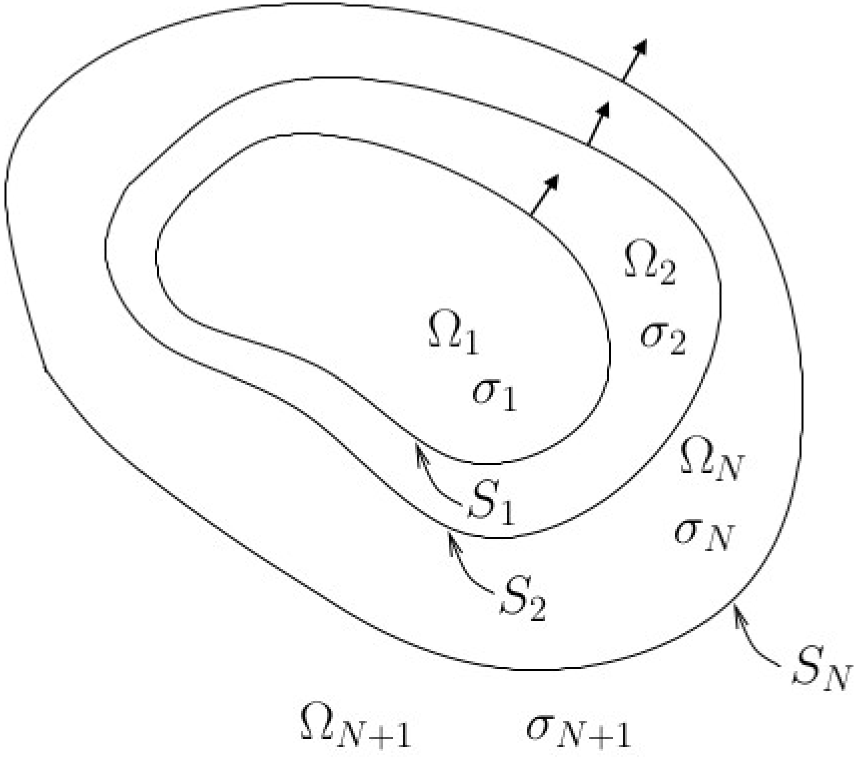
A generalization of concentric spheres which allow to change the shape of the interfaces between tissues.

Conductivities are still constant homogeneous and isotropic within each tissue.

There is no longer an analytic solution, but there are continuous surface equations that need to be solved.

Discretization gives a linear system
$\Longrightarrow$ Surface methods
(Boundary Element Methods - BEM).

Realistic model



A generalization of concentric spheres which allow to change the shape of the interfaces between tissues.

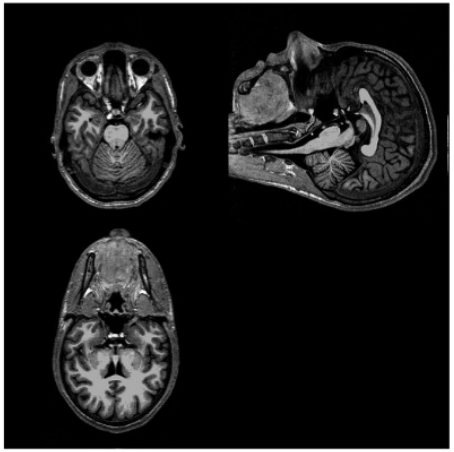
Conductivities are no longer constant homogeneous and isotropic within each tissue (they can change at each point).

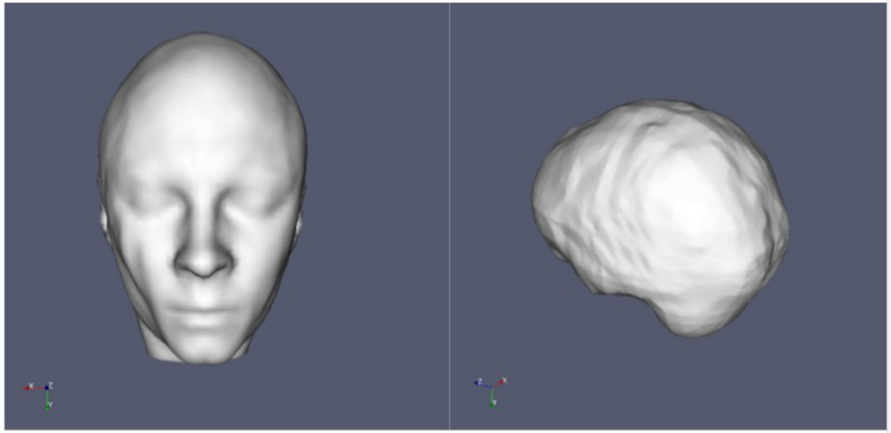
There is no longer an analytic solution, but there are continuous volumic equations that need to be solved.

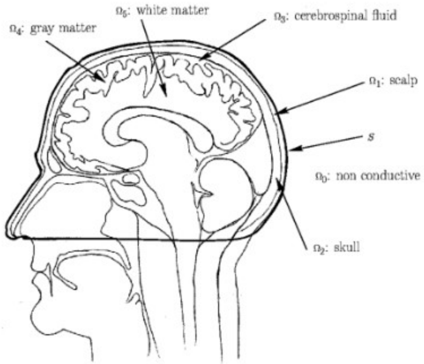
Discretization gives a linear system
$\Longrightarrow$ Volumic methods
(Finite Element Methods - FEM).

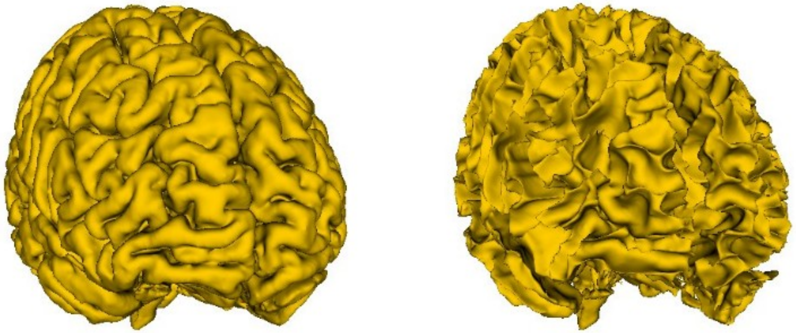
Tissue modelling

Needed for semi-realistic and realistic methods







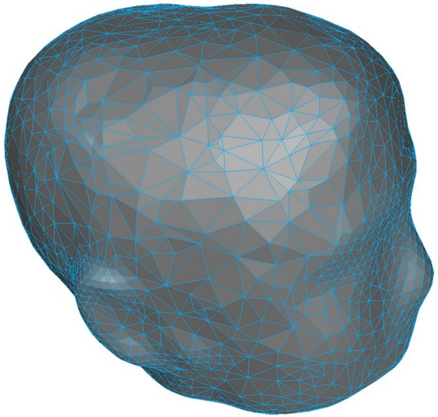


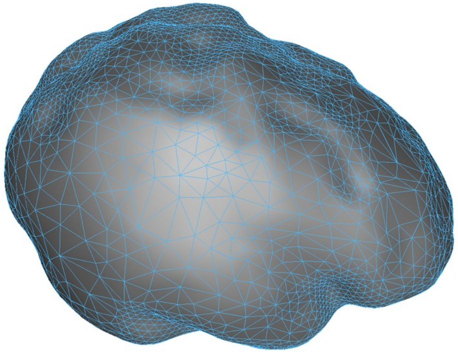
Discretization

Continuous models involve continuous quantities:

- Geometric models.
- Physical quantities (e.g. potential or magnetic field).

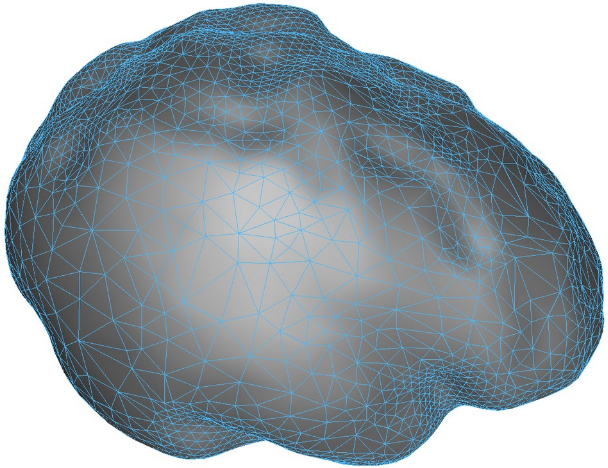
Those quantities need to be discretized in order to get a computational model $\Longrightarrow$ meshes (surfacic or volumic).

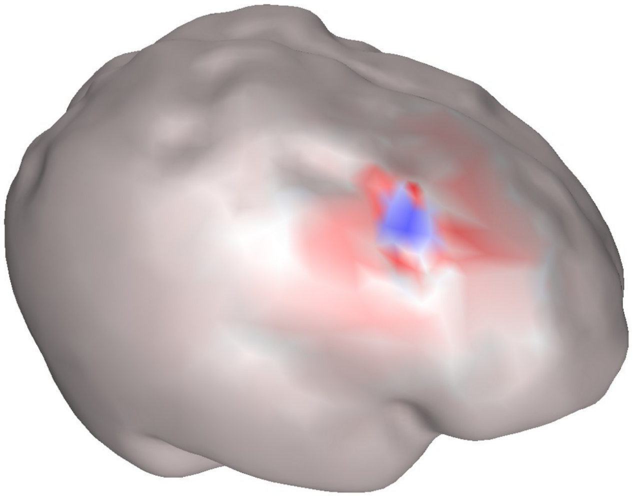




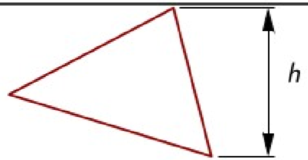
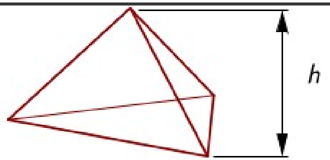
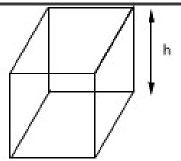
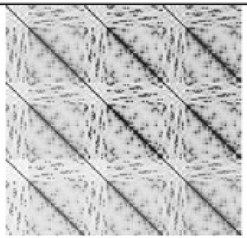
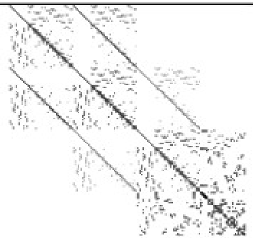
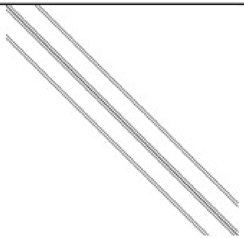
Physical quantities

- Discretization inherited from geometry.
- Discrete → Continuous through interpolation.





Discretization

Boundary Elements	Finite Elements	Implicit Finite Elements
piecewise constant	arbitrary	arbitrary
surface	volume	volume
		
$N = O(h^{-2}), \quad 10^5 \sim 10^6$	$N = O(h^{-3}), \quad 10^7 \sim 10^8$	$N = O(h^{-3}), \quad 10^7 \sim 10^8$
 126×126, full	 156×156, **sparse** (8%)	 **sparse,banded** (1.5%)
symmetric	symmetric positive	symmetric positive
GMRES, QMR, ...	conjugate gradient	conjugate gradient
FMM, multiscale	multilevel	multigrid

Computing the Forward model

Realistic and semi-realistic models.

- **Discretization:** BEM or FEM, P0 or P1, ...

$$AX = B$$

Structure Δ_σ

Unknowns $V, \partial_{\mathbf{n}} V$

Source term $f(\mathbf{J}^{\mathrm{p}})$

- C : Number of EEG sensors.
- S: Size of the discretization of the source space.

We solve for $\mathbf{V}$ in all the volume of the head, and just keep values at sensors. Because the problem is linear in $\mathbf{J_p}$, we can do that for every source (or source component) independently.

For each source (or source component), we collect values at sensors in a matrix:

$$\mathbf{V}_s = \mathbf{G}\ \mathbf{J_p}$$

Vector of potential at sensors of size C.

Vector describing the sources of size S.

Leadfield (or gain) matrix C x S.

Computing the Forward model

Realistic and semi-realistic models.

- **Discretization:** BEM or FEM, P0 or P1, . . .

$$AX = B$$

Structure	Unknowns	Source term
Δ_σ	$V, \partial_{\mathbf{n}} V$	$f(\mathbf{J}^{\mathrm{p}})$

- C’ : Number of MEG sensors.
- S: Size of the discretization of the source space.

We solve for $\mathbf{B}$ in all the volume of the head, and just keep values at sensors. Because the problem is linear in $\mathbf{J_p}$, we can do that for every source (or source component) independently.

A very similar leadfield matrix can be constructed for the magnetic field.

$$\mathbf{B}_{\mathrm{s}} = \mathbf{G}_{\mathbf{B}}\ \mathbf{J}_{\mathbf{p}}$$

Vector of magnetic field at sensors of size C’.

Vector describing the sources of size S.

Leadfield (or gain) matrix C’ x S.

Computing the Forward model

Realistic and semi-realistic models.

For each source (or source component), we have two gain matrices:

Vector of potential at sensors of size C.

$$\mathbf{V}_s = \mathbf{G}\ \mathbf{J}_\mathbf{p}$$

Vector describing the sources of size S.

$\boxed{\text{Leadfield (or gain) matrix C x S.}}$

Vector of magnetic field at sensors of size C'.

$$\mathbf{B}_s = \mathbf{G}_\mathbf{B}\ \mathbf{J}_\mathbf{p}$$

Vector describing the sources of size S.

$\boxed{\text{Leadfield (or gain) matrix C' x S.}}$

- C : Number of EEG sensors.
- C': Number of MEG sensors.
- S: Size of the discretization of the source space.

These equation are for a single time instant but can be easily extended to handle time windows (replace $\mathbf{V}_s$, $\mathbf{B}_s$ and $\mathbf{J}_\mathbf{p}$ by matrices which second dimension is T (size of the time window). $\mathbf{G}$ and $\mathbf{G}_\mathbf{B}$ are unchanged.