Master Mathématiques Vision Apprentissage

Functional neuroimaging & Brain-Computer Interfaces

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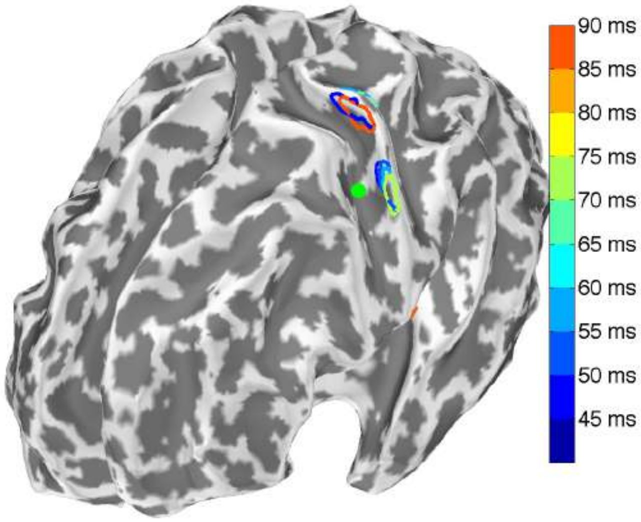
PARIETAL team

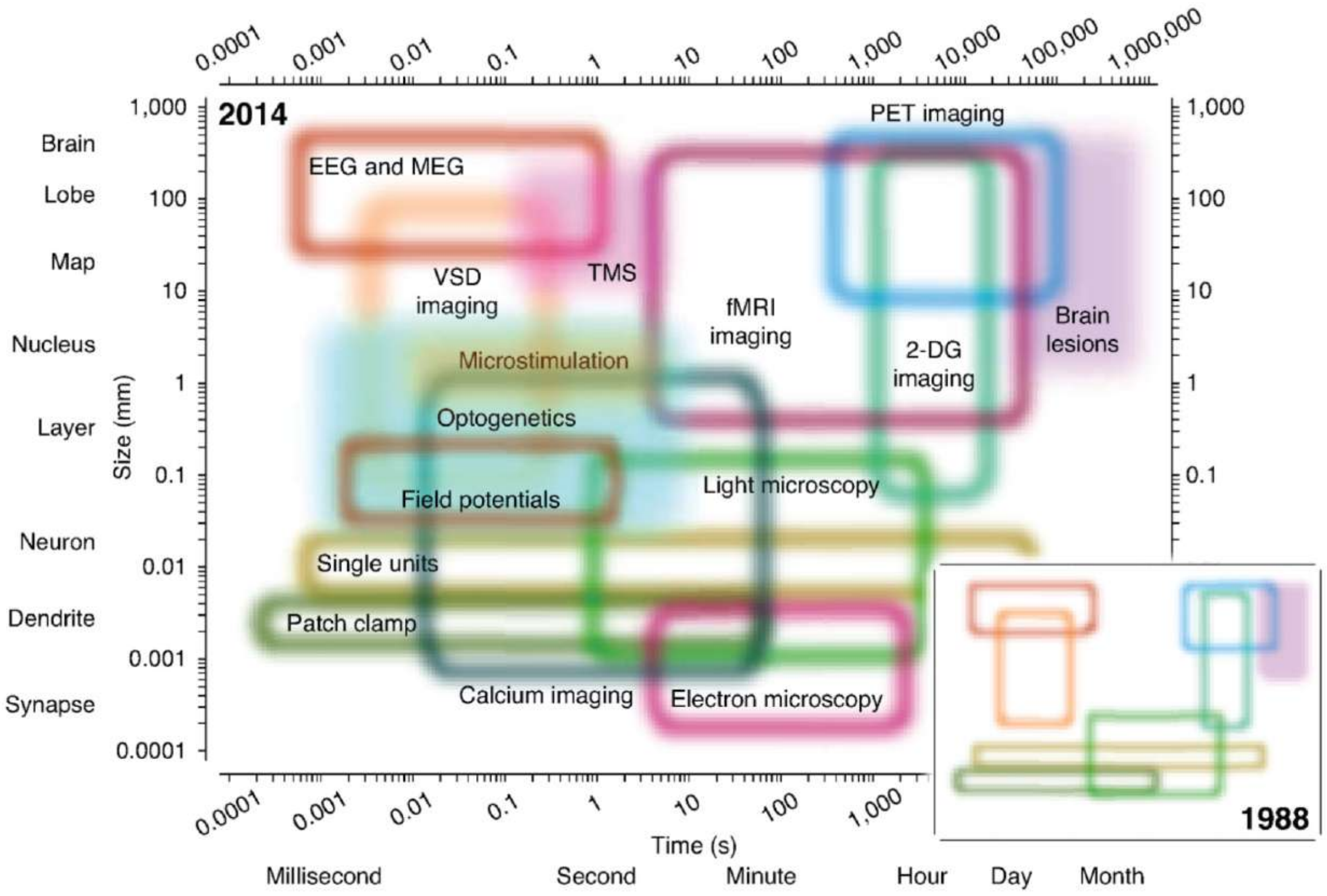
Developping tools to understand brain functioning

Biology ⟷ Physics



Mathematics ⟷ Algorithms

Neuroimaging tools



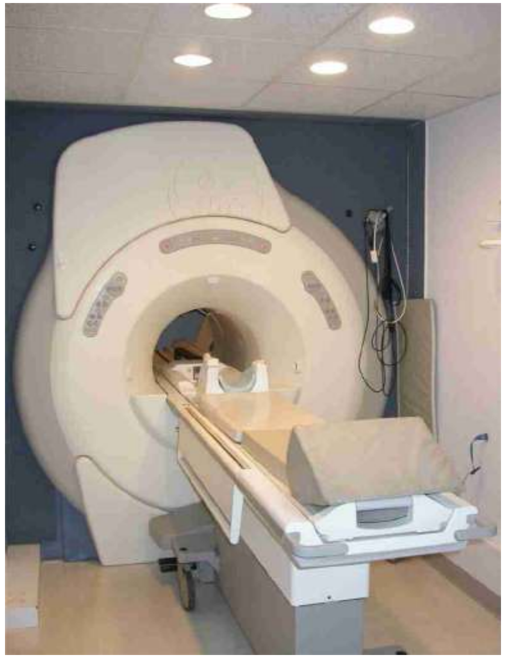
Adapted from (Sejnowski et al., Nature Neuroscience, 2014)

Brain imagery and electromagnetism

- Passive electromagnetism
  - Electroencephalography – EEG
  - Magnetoencephalography – MEG

- Active electromagnetism
  - Anatomical MRI
  - Functional MRI
  - Diffusion MRI

Temporal resolution

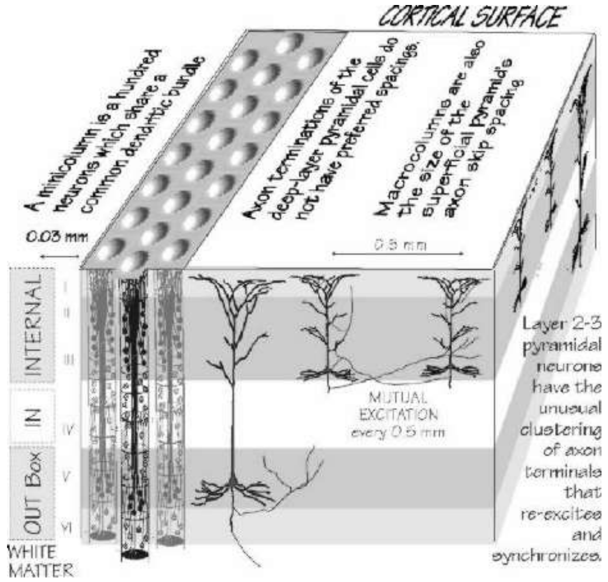


Spatial resolution

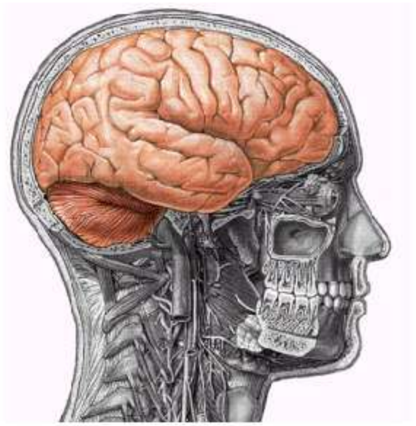
Challenges related to these modalities

- Finding the activity (When? Where?)
  - Clinical perspectives (neurodegenerative diseases)
  - Cognitive sciences (brain functioning)

- Modelling
  - Sources
  - Interactions between brain areas
  - Relationships between modalities

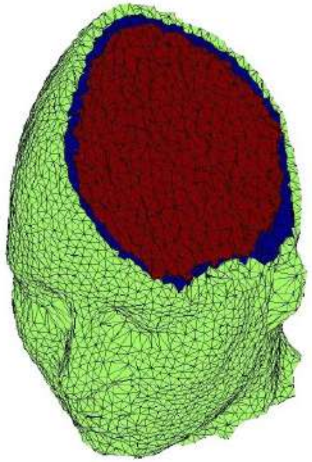


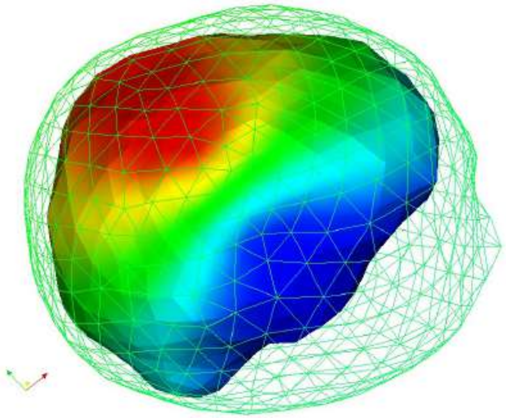
- Applications
  - Brain-computer interfaces
  - Brain reading

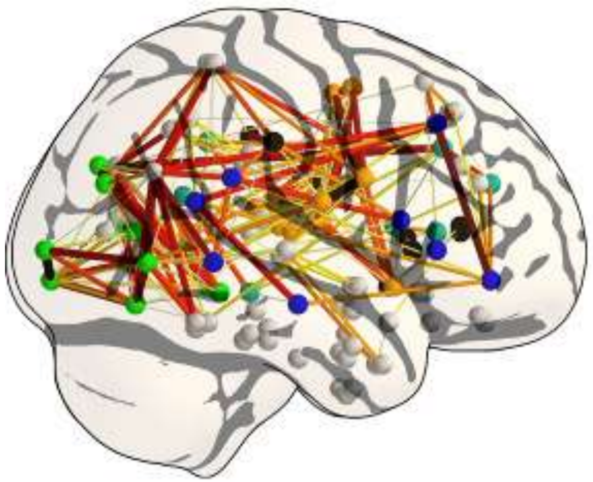


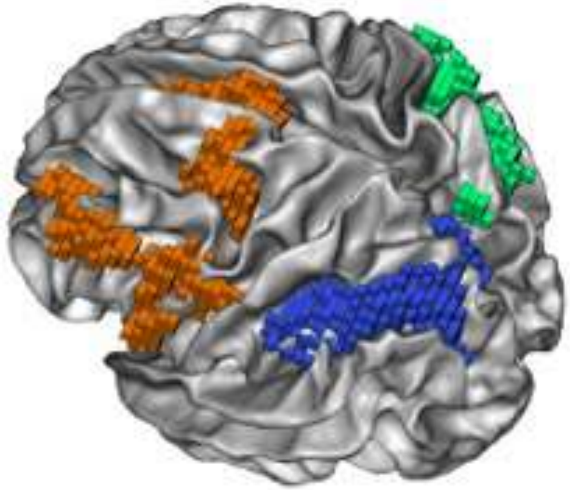
Techniques

- Numerical resolution
  - Direct/inverse problem
  - Data analysis (denoising, advanced methods)
  - Machine learning
- Statistics
  - Discrimination between the activity of interest and background activity
  - Significance of the results









Themes of the module

- Notions of biology and biophysics
- Notions of electromagnetism
- Finite elements (surface and volumes)
- Source localization
- Inverse problems
- Networks
- Optimization
- Statistics, hypothesis tests
- Brain-Computer Interfaces
- Classification, features selection

Objectives of the module

- M/EEG
  - Knowing the origin of M/EEG signals
  - Building a pipeline to preprocess and analyze M/EEG data
  - Building a pipeline to apply machine learning approaches on M/EEG data
  - Interpreting results
- Functional neuroimaging
  - Knowing the origin of fMRI data
  - Manipulating statistical inference on multi-subject fMRI data
  - Classifying fMRI data
  - Interpreting results

Outline

- Magnetoencephalography and electroencephalography (M.-C. Corsi) – 18/01 → 08/02
- Functional neuroimaging (B. Thirion) – 15/02 → **28/03**
- Room 2E29

Outline

- Magnetoencephalography and electroencephalography (M.-C. Corsi) – 18/01 → 08/02
  - **M/EEG data: where it all begins!** - 18/01 – 9:30-12:30AM
  - **Estimating the sources of M/EEG activity** – w/ Théo Papadopoulo (Inria, Sophia-Antipolis) - 25/01 – 9:30-12:30AM
  - **How to further explore M/EEG data to answer scientific questions?** – 01/02 – 9:30-12:30AM
  - **How to use real-time M/EEG data for clinical purpose?** – 08/02 – 9:30-12:30AM **@ Paris Brain Institute!** (+visit of the neuroimaging platform)

Outline

- Magnetoencephalography and electroencephalography (M.-C. Corsi) – 18/01 → 08/02
- Functional neuroimaging (B. Thirion) – 15/02 → **28/03**
  - **fMRI data modelling** – 15/02 – 9:30-12:30AM
  - **Statistical inference for brain imaging** – **29/02** – 9:30-12:30AM
  - **Statistical methods for functional brain connectivity mapping** – **21/03** – 9:30-12:30AM
  - **Classification and machine learning techniques for fMRI data analysis** – **28/03** – 9:30-12:30AM

Information & contacts

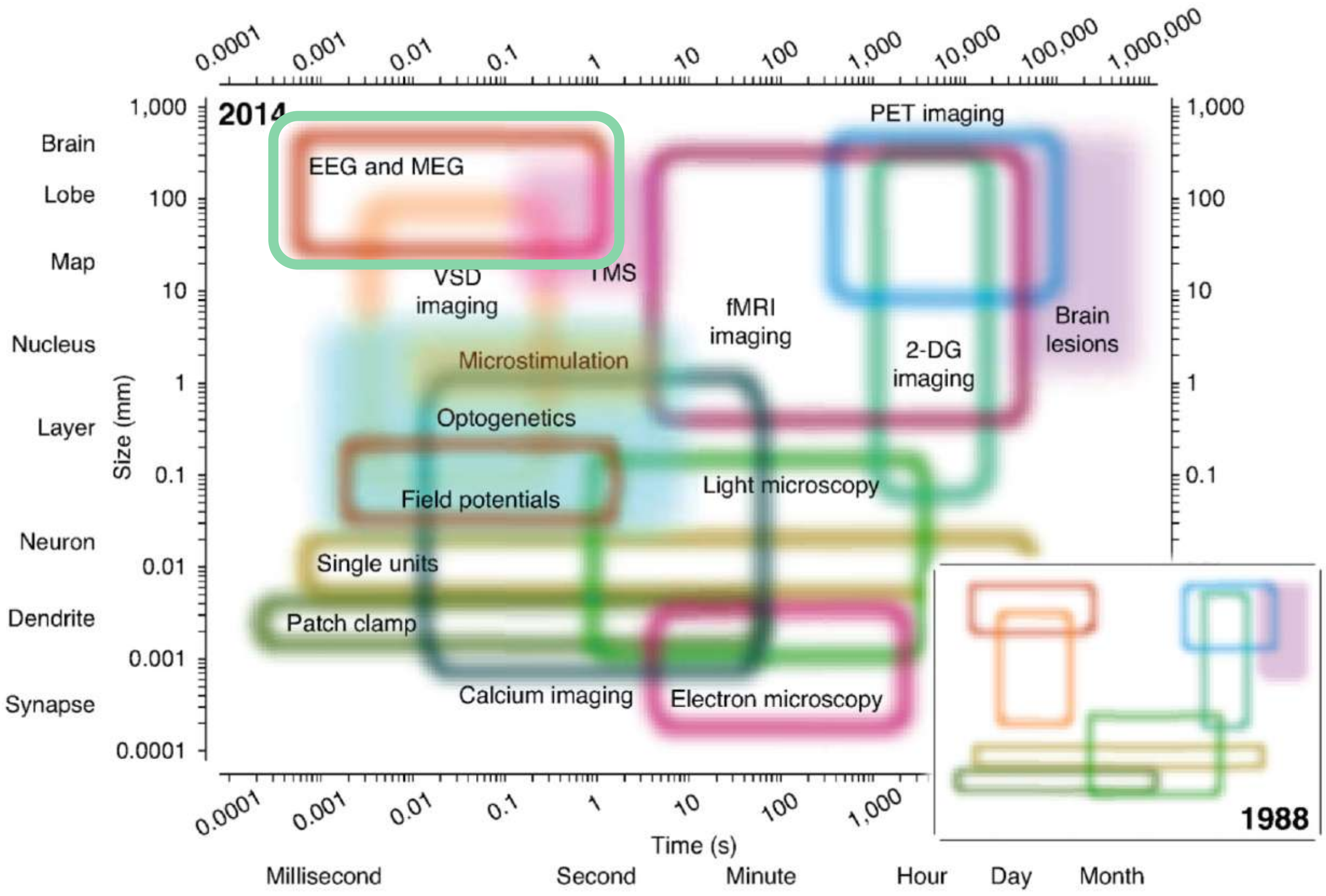
- Webpage dedicated to the module (updated w/slides):
  https://project.inria.fr/mvabrainfunctionalimaging/

- For any question related to the module
  - mva-meeg@inria.fr (mailing-list gathering the registered students and the co-lead)

- Co-lead contact info for specific questions
  - fMRI – Bertrand Thirion (Saclay) – bertrand.thirion@inria.fr
  - M/EEG – Marie-Constance Corsi (Paris) – marie-constance.corsi@inria.fr

GENERALITIES – M/EEG PART

M/EEG and other modalities



Adapted from (Sejnowski et al., Nature Neuroscience, 2014)

Objectives of the M/EEG part

- Knowing the origin of M/EEG signals
- Being familiar with the steps that constitute an experimental protocol
- Understanding the pro & cons when building a processing pipeline
- Being able
  - To build a pipeline to apply machine learning approaches on M/EEG data
  - To interpret results of an analysis

Outline

- Magnetoencephalography and electroencephalography (M.-C. Corsi) – 18/01 → 08/02
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Exam

- Format: Practical work in python & open questions
- Estimated time to complete it: 2 hours
- Probably sent after the third lesson (Feb 1st)
- Deadline: **February 22nd** to avoid overlapping with the exam associated to fMRI & the internship

Any question?

LESSON 1 – M/EEG DATA: WHERE IT ALL BEGINS!

Outline

- Basic principles of biophysics
- Data acquisition: What? How?
- Data analysis – main steps

BASIC PRINCIPLES OF BIOPHYSICS

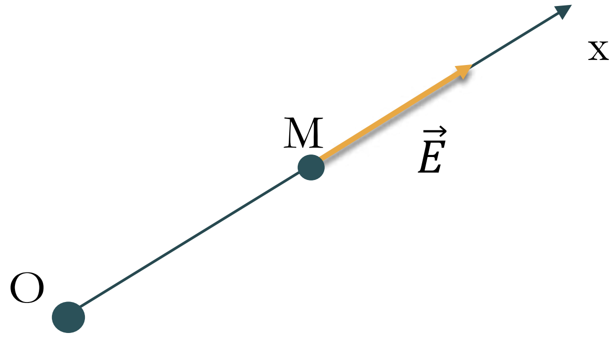
Questions addressed in this section

- Electro & magnetostatic
  - What is a potential, an electric current, a magnetic field?
  - Magnetostatic: Biot & Savart law
- Where do the M/EEG signals come from?
  - Neurotransmitter & electrochemistry
  - Synaptic current, actional potential, & volumic current

- Field: zone where a gravitational/electrical/magnetic force acts on any object
- Electrical charge
  - fundamental propriety of matter that respects the conservation principle
  - "sign" convention by B. Franklin: 1.6×10^{-19} C
- Electric field $\vec{E}$
  - $\vec{E} = \frac{1}{q}\,\vec{F_e}$
  - In the vacuum: sum of the electric fields produced by each charge.

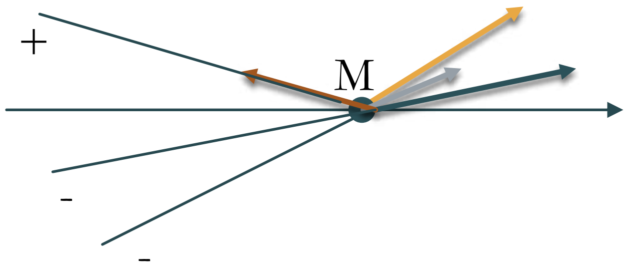
ἤλεκτρον - Amber

- Field $\vec{E}$ created by a charge q



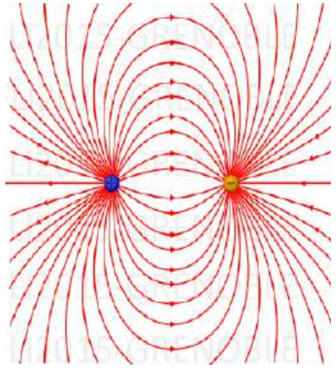
$$\vec{E} = \frac{q_1}{4\pi\varepsilon_0 \|OM^2\|} \cdot \frac{\overrightarrow{OM}}{OM}$$

- An ensemble of charges

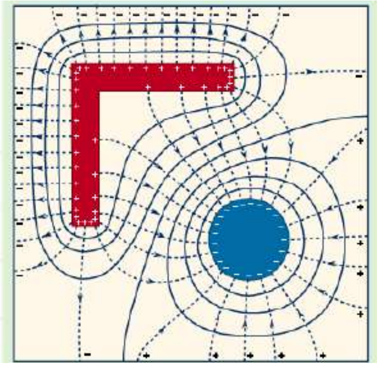


Sum of vectors

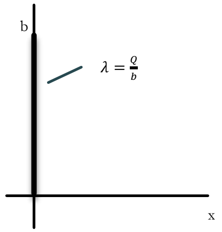
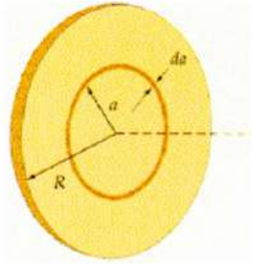
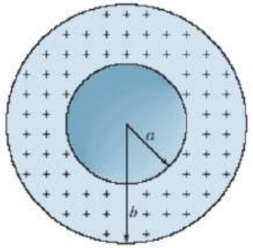
- Dipole of charge



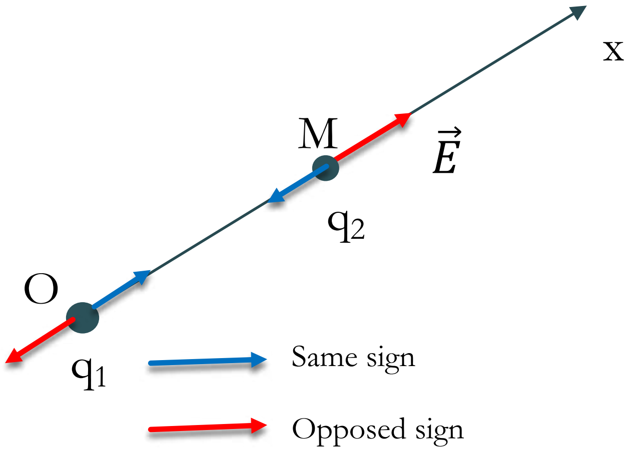
- Density of charges

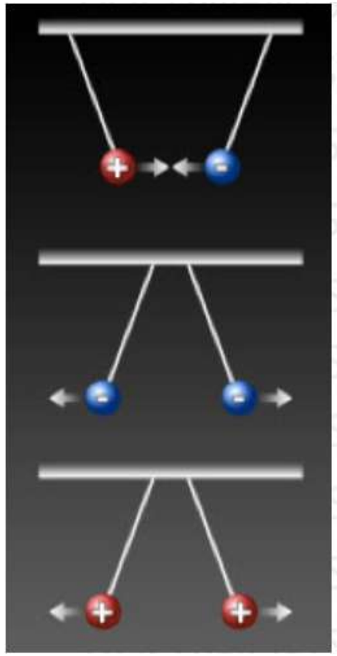


Electrostatic – density of charges

	Linear	Surface	Volume
Representation			
Density of charge	l or r_l (C/m)	S or r_s (C/m2)	R or r_v (C/m3)
Computation	$Q = \int \lambda\, dS = \int \lambda\, dy$	$Q = \iint \sigma\, d\sigma = \iint \sigma r\, dr d\varphi$	$Q = \iiint \rho dV = \iiint \rho R^3 sin$

- Coulomb's law





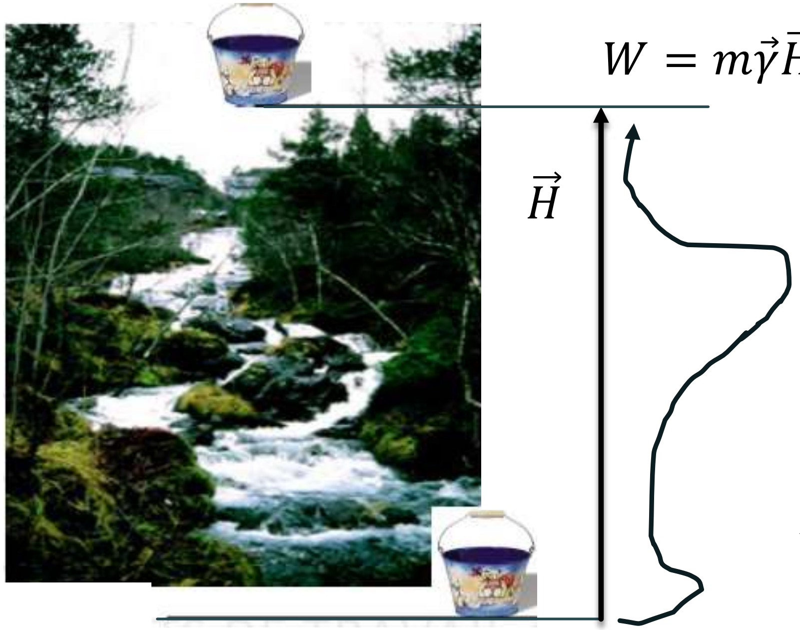
$$\vec{F} = \frac{q_1 q_2}{4\pi\varepsilon_0 \|OM^2\|} \cdot \frac{\overrightarrow{OM}}{OM}$$

$$\vec{F} = q_2 \vec{E}$$

By convention, in the International System:

$$\frac{1}{4\pi\varepsilon_0} = 9.10^9$$

- Electrical potential



$W = m\vec{\gamma}\vec{H}$

Gravitational field

Gravitational potential

Hydraulic potential energy

Electrostatic

- Electrical potential

$$V = \frac{\sum \Delta j}{q}$$

$$V = \frac{\int_{infinity\ of\ the\ space}^{considered\ point} \Delta j}{q}$$

$$V = \frac{\int_{infinity\ of\ the\ space}^{considered\ point} \vec{E}\,(x)\,dx}{q}$$

$$U(a,b) = V(a) - V(b)$$

Potential always defined up to a constant (infinity of the space)

=> measurement of a difference of potential U

Consequence for EEG

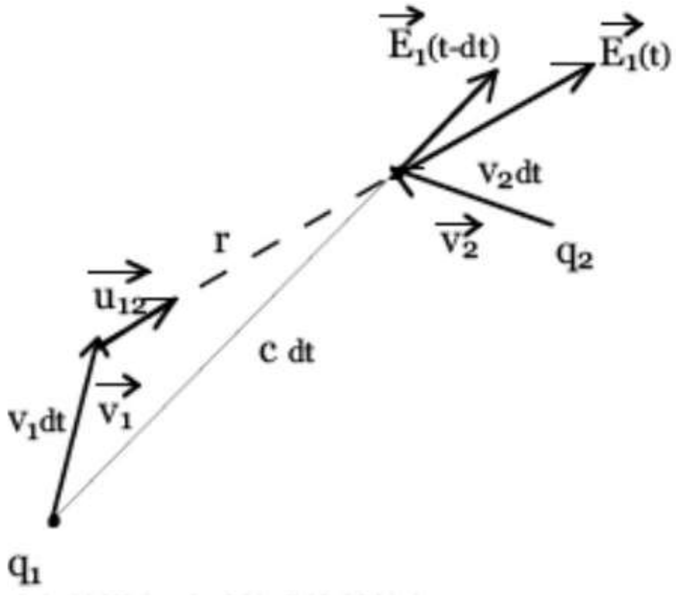
- Need of a "potential reference" (arbitrary location)
- Comparison of measurements made with the same reference compulsory
- Mono/bi-polar montages

- Electrical potential – 3D generalization (vacuum)

$$V(x_2, y_2, z_2) = \frac{1}{4\pi\varepsilon_0} \iiint \frac{\rho(x_1,y_1,z_1)}{r_{12}} dx_1 dy_1 dz_1$$

With ρ the density of charges in point 1 and $\overrightarrow{r_{12}} = \overrightarrow{r_2} - \overrightarrow{r_1}$

$$\vec{E} = -\vec{\nabla}V$$



BUT

- $\vec{E}$ does not explain the trajectory of q_2, is there some supplementary force?
- Delay in the electrostatic effects
- The electrical effects cannot result from only the electrostatic field

Magnetic field

- Exact formulation of the force

$$\vec{F} = q\vec{E} + q\vec{v} \wedge \vec{B}$$

- Magnetic force: « correction » to the Coulomb force -> magnetic field $\vec{H}$

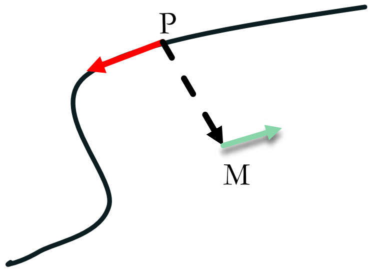
- In the vacuum: the magnetic induction $\vec{B}$ (μ_0 is the permeability of a vacuum)

$$\vec{B} = \mu_0\vec{H}$$

Biot & Savart law

- Magnetic field (in Tesla) created by the crossing of an intensity current I in a linear circuit

$$\overrightarrow{B(M)} = \frac{\mu_0}{4\pi}\int \frac{I\overrightarrow{dl} \wedge (\overrightarrow{PM})}{\left|\overrightarrow{PM}\right|^3}$$

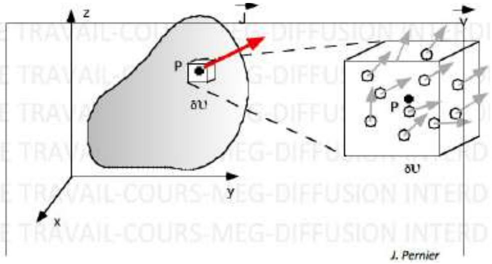


- Generalization e.g. ions:

$$\overrightarrow{B(M)} = \frac{\mu_0}{4\pi}\frac{q\vec{v} \wedge (\overrightarrow{PM})}{\left|\overrightarrow{PM}\right|^3}$$

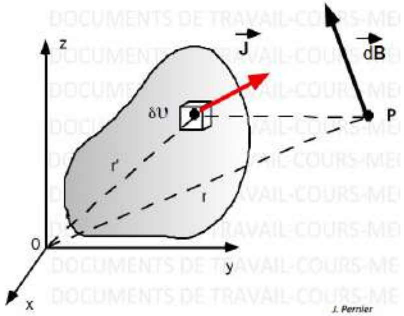
- Magnetic induction:

$$\overrightarrow{B(M)} = \frac{\mu_0}{4\pi}\sum_{i=1}^{N} \frac{q_i\vec{v_i} \wedge (\overrightarrow{P_iM})}{\left|\overrightarrow{P_iM}\right|^3}$$

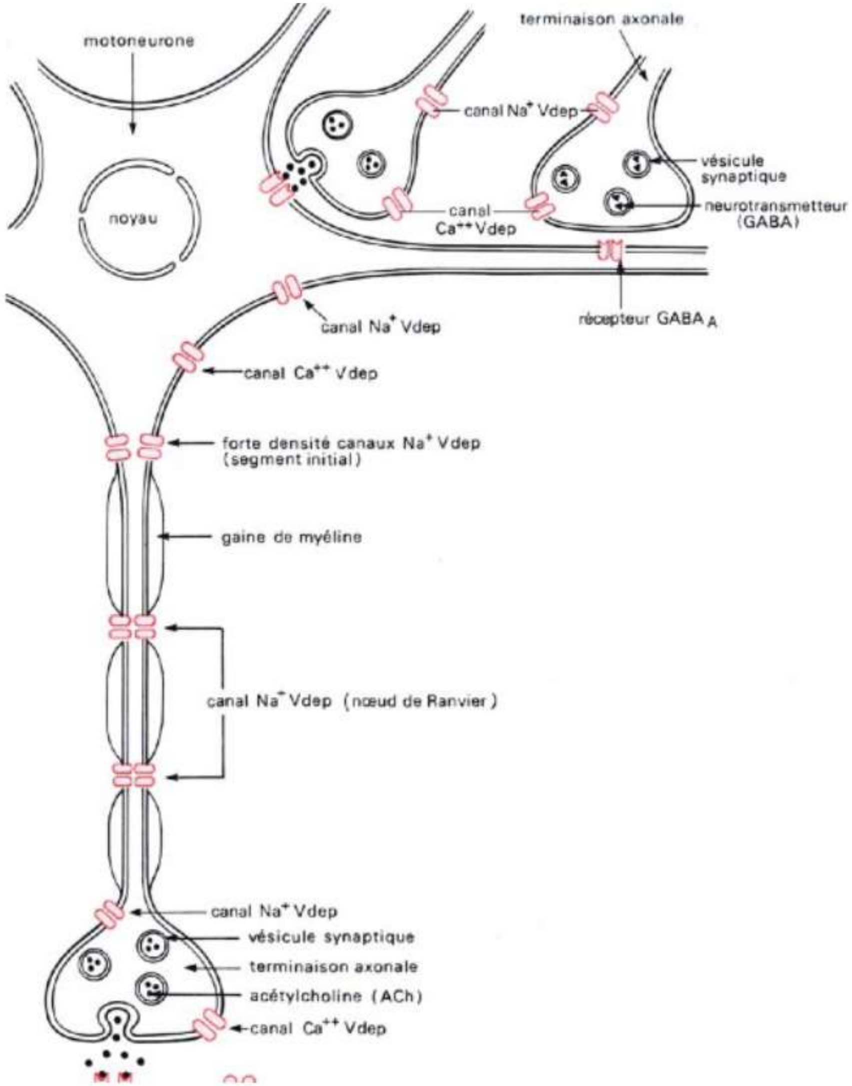


- Magnetic induction created by a current distribution

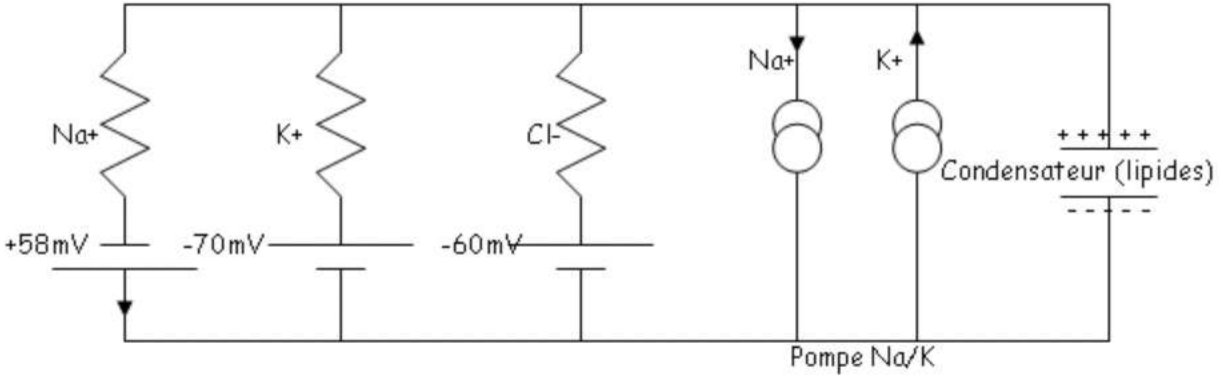
$$\overrightarrow{B(r)} = \frac{\mu_0}{4\pi}\iiint_v \overrightarrow{J(r')} \wedge \frac{\vec{r} - \overrightarrow{r'}}{\left|\vec{r} - \overrightarrow{r'}\right|^3} dv$$



Let's move to the neurons…



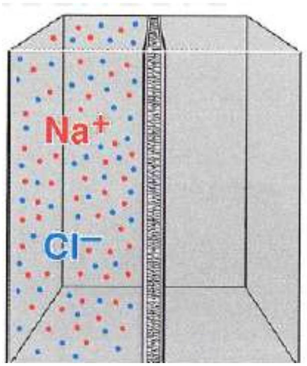
Adapted from Neurobiologie cellulaire, C. Hammond



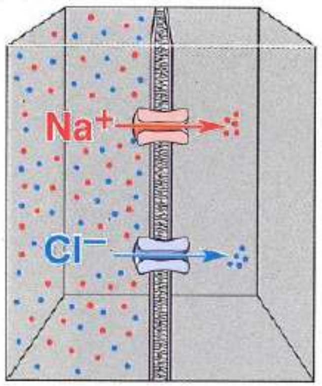
Adapted from Biophyics classes, C. Delpuech

Movement of ions – diffusion effect

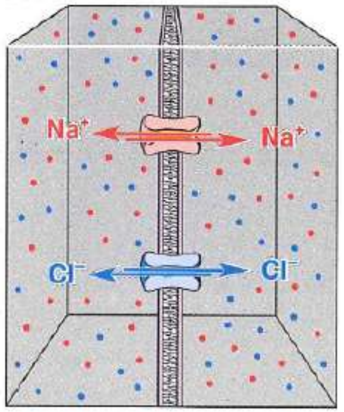
- State 1 – boxes separated with a phospholipid membrane



- State 2 – two channels protein are open to enable movements in both ways



- State 3 – after a while the ionic concentrations are the same in the two boxes



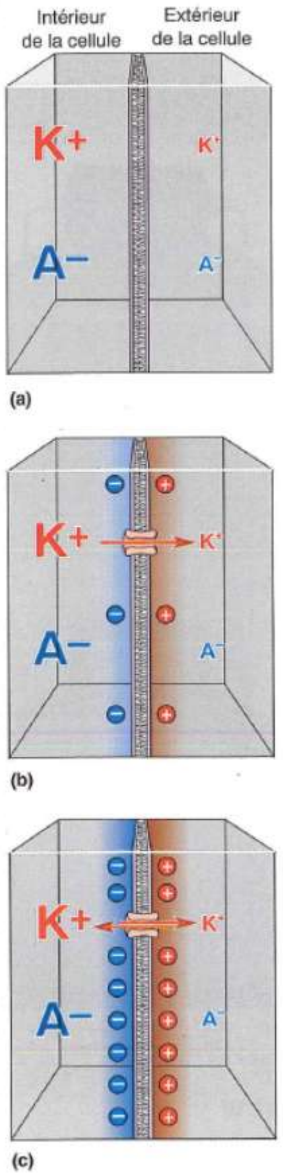
Equilibrium potentials

- Case a - 2 boxes separated with a phospholipid membran. Here different ionic concentrations between the two boxes

- Case b – Insertion of one channel protein – K+ ions can freely circulate but not the anions

- Case c – after a while, the electrical interaction force applied to K+ is stronger.

The ionic potential is the difference of potentials that compensates the ionic concentration gradient



Neuron – equilibrium at the membrane

- Nernst equation to compute the equilibrium potential of a given ion:

$$E(ion) = \frac{RT}{ZF}\ln(\frac{[ion]_{ext}}{[ion]_{int}})$$

R: universal gas constant

T: temperature, in kelvins

Z: ion valence

F: Faraday constant, the magnitude of charge (in coulombs) per mole of ions, $F = 96485.3321233100184 \text{ C mol}^{-1}$

$[\text{ion}]_{\text{ext}}$= extracellular concentration

$[\text{ion}]_{\text{int}}$= intracellular concentration

- Transposition of the Ohm's law (U=RI) to an electrochemical gradient

$$I(ion) = g(ion)(E_m - E_{ion})$$

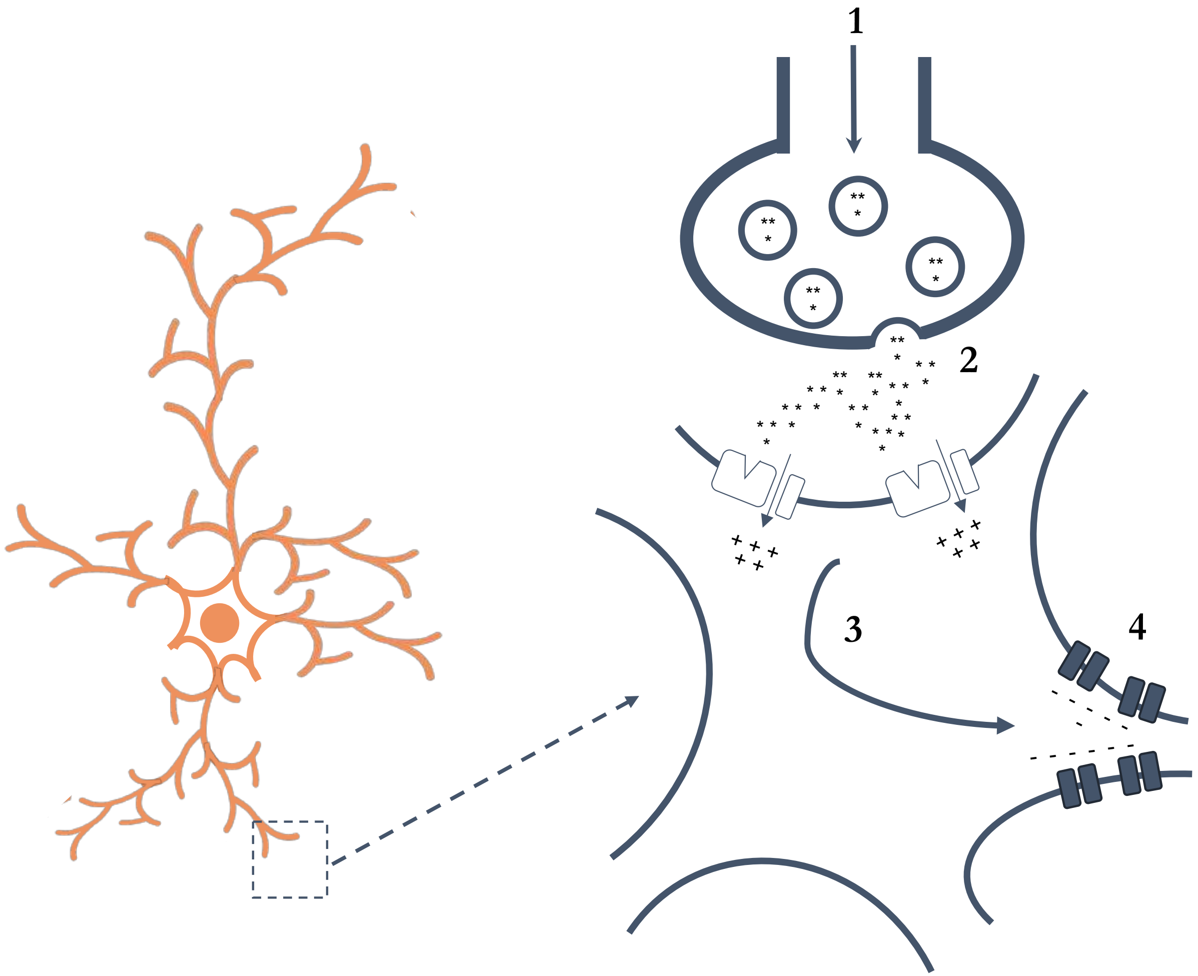
Ionic current

Membrane conductance for the ion (1/R)

Membrane potential (measured)

Equilibrium potential of the considered ion

Origins of M/EEG signals



1 – An action potential (AP) arrives at a synaptic cleft

2 – Transmission of chemical information via neurotransmitters

3 – Creation of post-synaptic potentials (PSPs) and local currents

4 – Creation of a current sink & propagation until the cell body to generate a current source

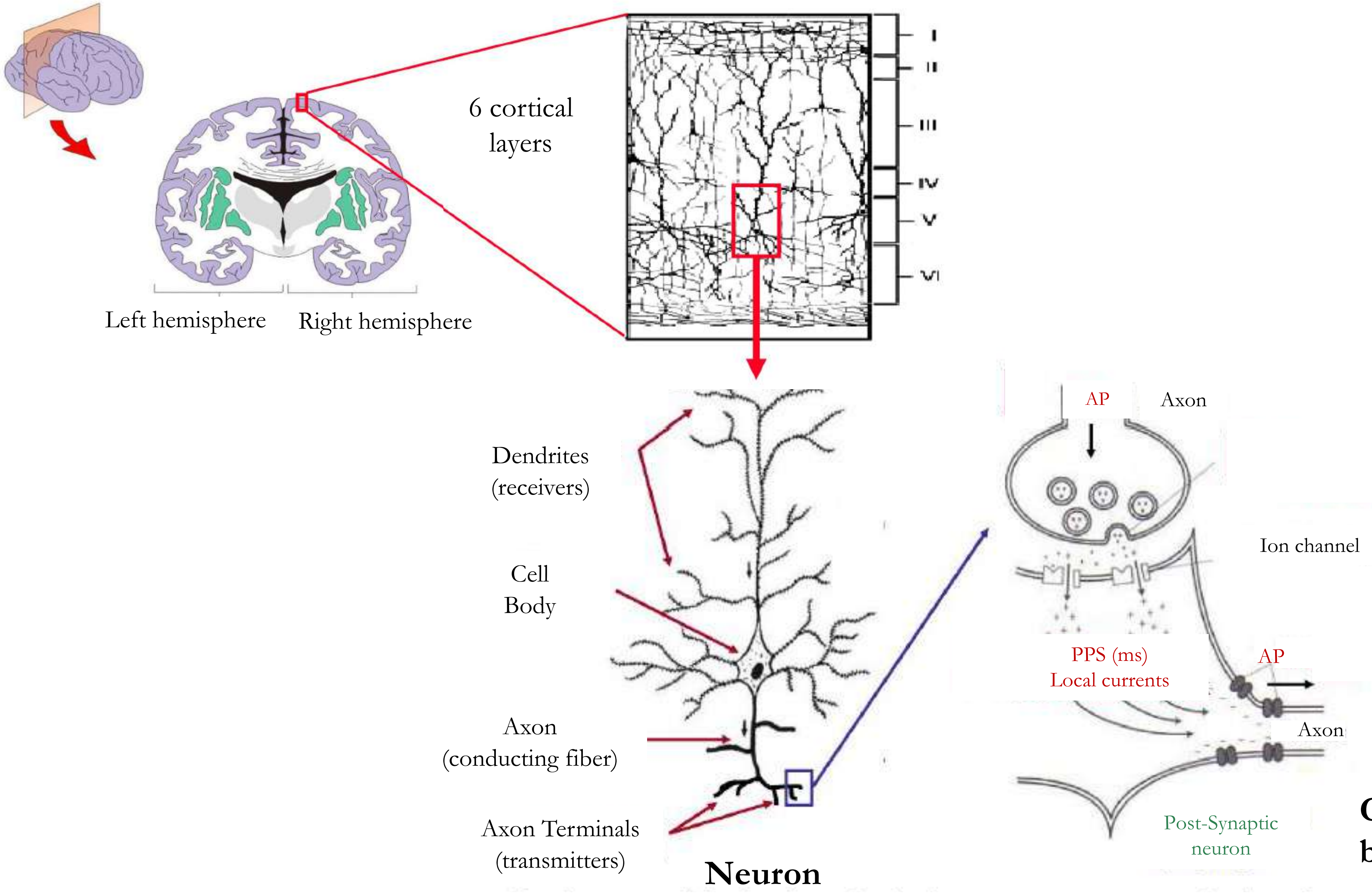
Origins of M/EEG signals

	Action potential (AP)	Post-synaptic potential (PSP)
Changes of the generated field with the distance	Fast decrease	Slower decrease
Duration	Short (<5ms)	Longer (tens of ms)

Advantage towards the distance between sources and the scalp

More advantageous to the temporal synchronization of the activity of a large number of neurons, necessary to be captured by M/EEG

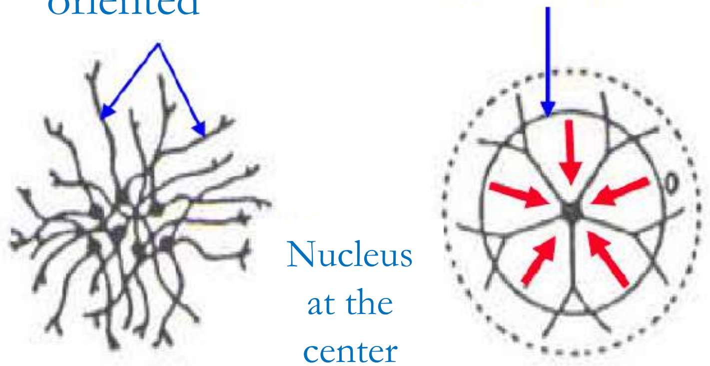
Origins of M/EEG signals



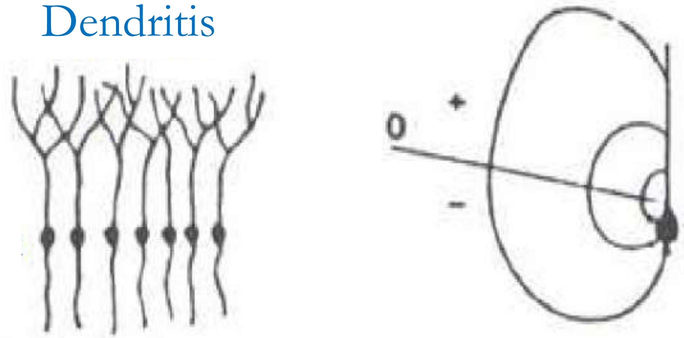
AP: Action Potential
NT: Neurotransmitters
PSP: Post-Synaptic Potentials

Communication between neurons

Origins of M/EEG signals

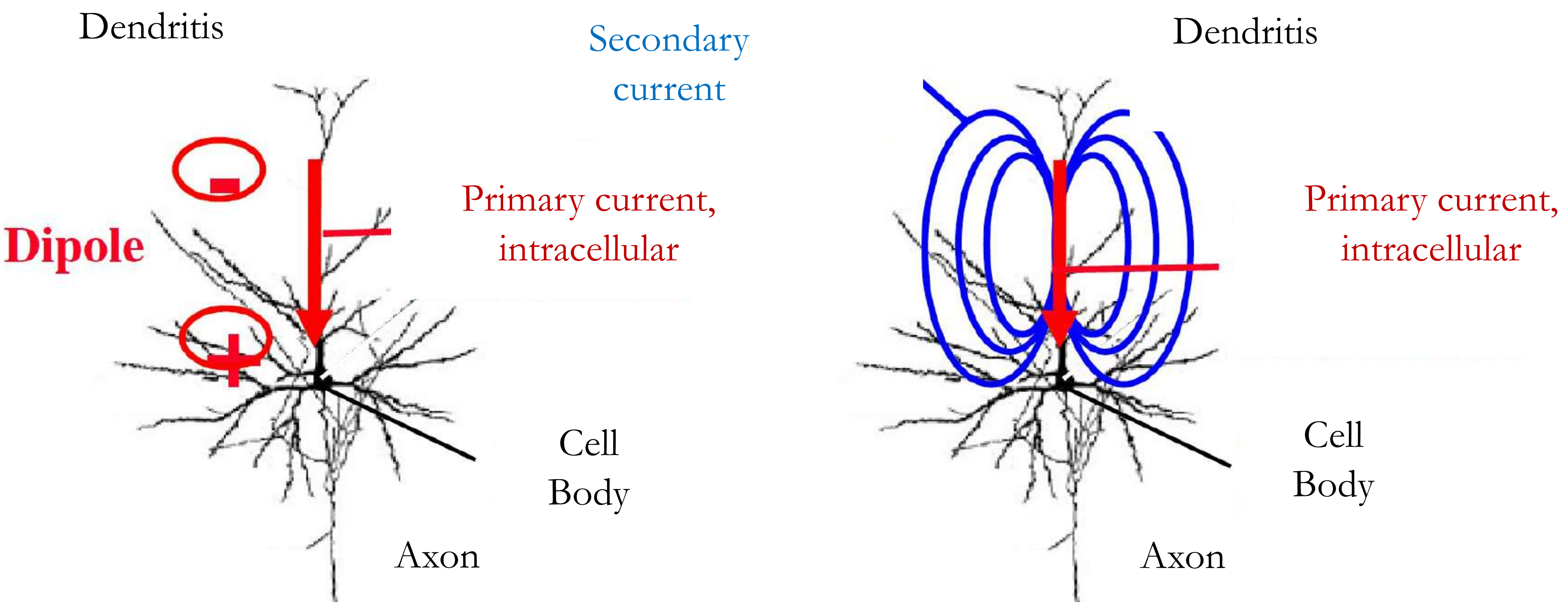


Closed configuration



Open configuration

Adapted from Cerveau et psychologie, O. Houdé et al, Puf Ed., 2002



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Origins of M/EEG signals

EEG

- Surface recordings of the **changes in electrical potential**
  - Mostly induced by **primary/extracellular currents**

MEG

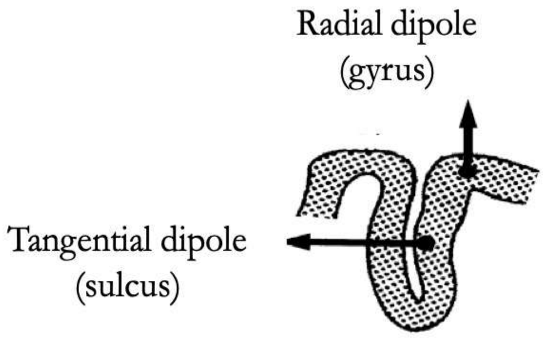
- Surface recordings of the **changes in magnetical field**
  - Linked to **secondary/intracellular currents**

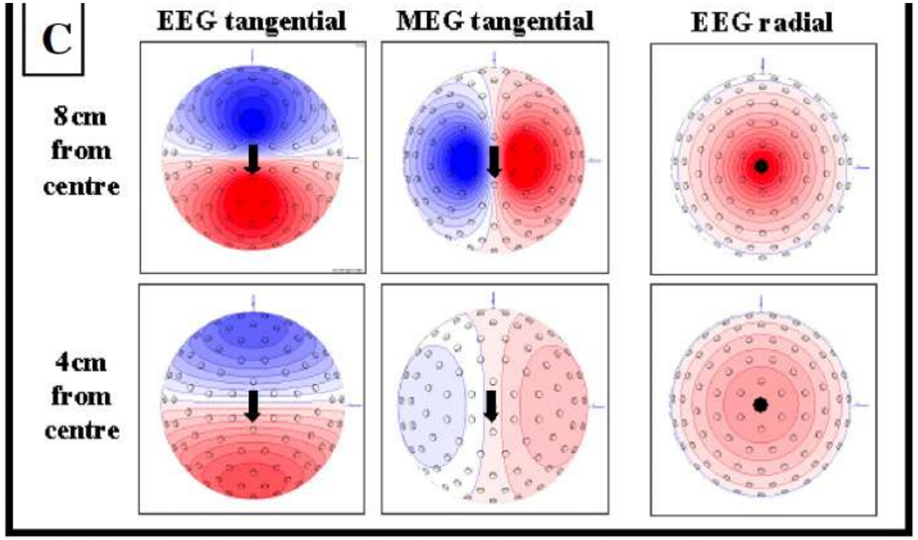
Result from the **sum of the unitary activity of large populations of synchronous neurons**

Origins of M/EEG signals

EEG

MEG





Cognitive and Brain Sciences Unts (MRC)

Origins of M/EEG signals

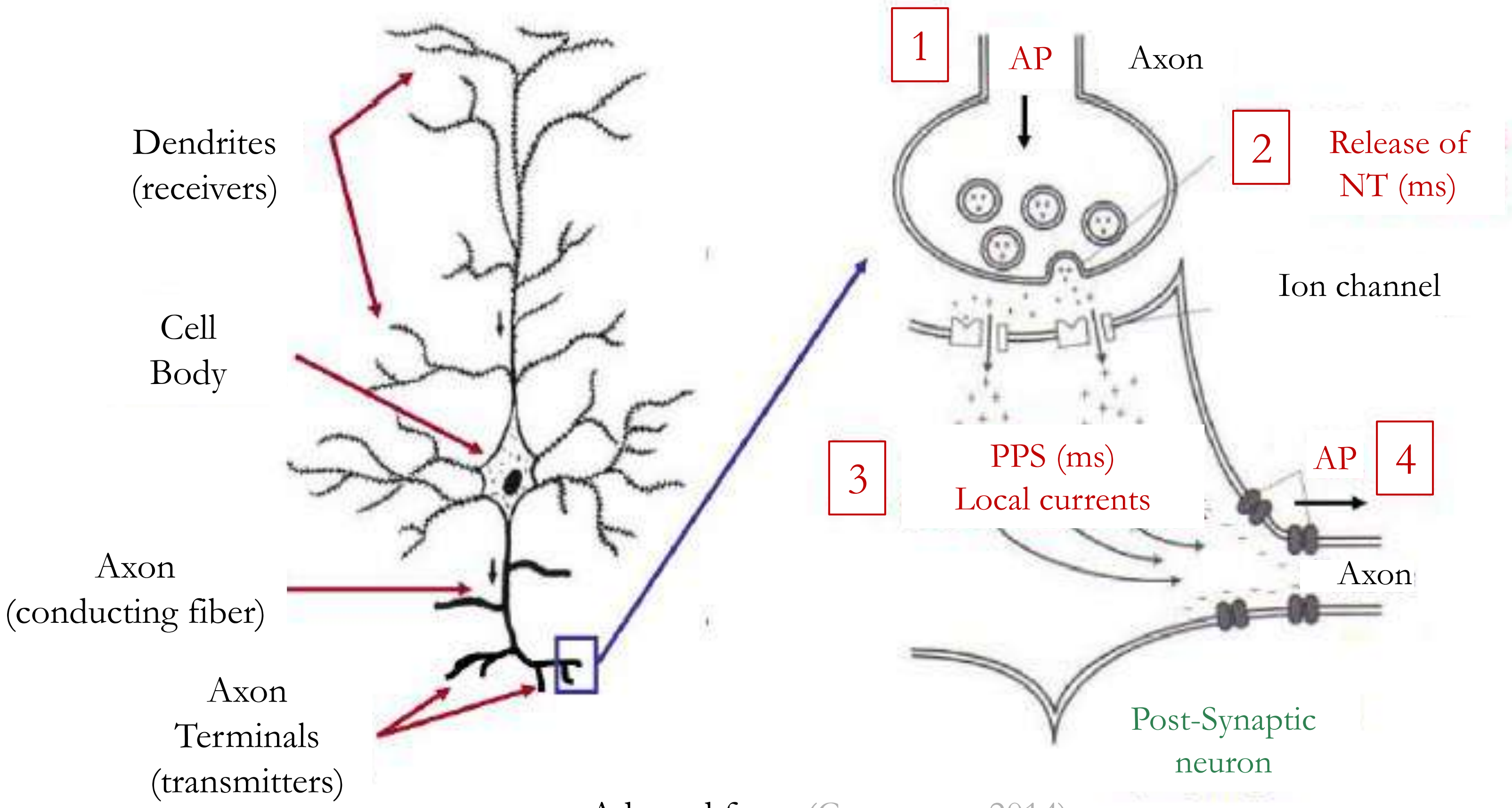
EEG

- Surface recordings of the **changes in electrical potential**
  - Mostly induced by **primary/extracellular currents**
    - Sensitive to **radial (+) & tangential currents**

MEG

- Surface recordings of the **changes in magnetical field**
  - Linked to **secondary/intracellular currents**
    - Senstive to **tangential currents**

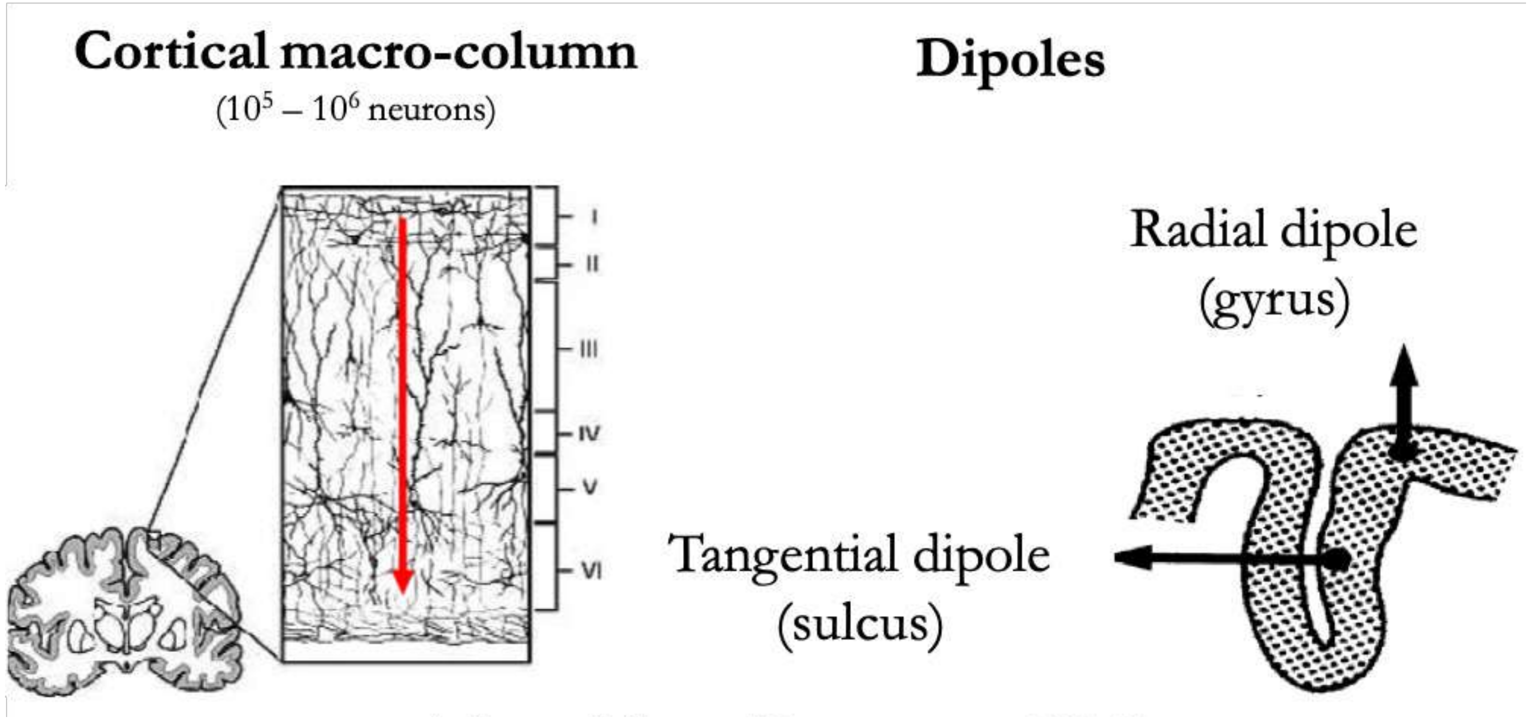
Part 1 – take-home message



Adapted from (Campagne, 2014)

AP: Action Potential
NT: Neurotransmitters
PSP: Post-Synaptic Potentials

M/EEG signals come from **post-synaptic potentials**



Adapted from (Campagne, 2014)

E/MEG signals result from the **spatial & temporal sum** of the activity at the level of a **large population** of synchronous neurons

DATA ACQUISITION

WHAT? HOW^2?

Questions addressed in this section

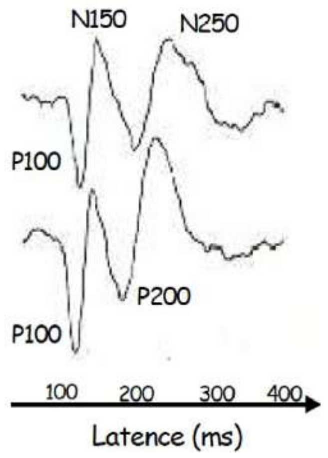
- What do we record with M/EEG?
  - Evoked responses
  - Oscillatory activity

- How do we record M/EEG data?
  - EEG instrumentation
  - MEG instrumentation

- What differ EEG signals with MEG signals?

Nomenclature: the latency, the amplitude, the shape and the polarity

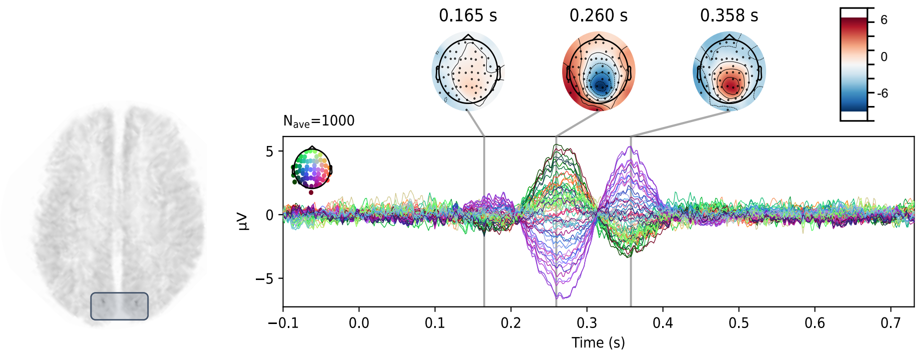
- Nxxx: one negative wave @ xxx ms (EEG)
- Pxxx: one positive wave @ xxx ms (EEG)
- Mxxx: one wave @ xxx ms (MEG)



Adapted from [Campagne, 2014]

Components

- Early components (exogenous): related to stimulus characteristics
- Late components (endogenous): related to the task, to the subject's stat



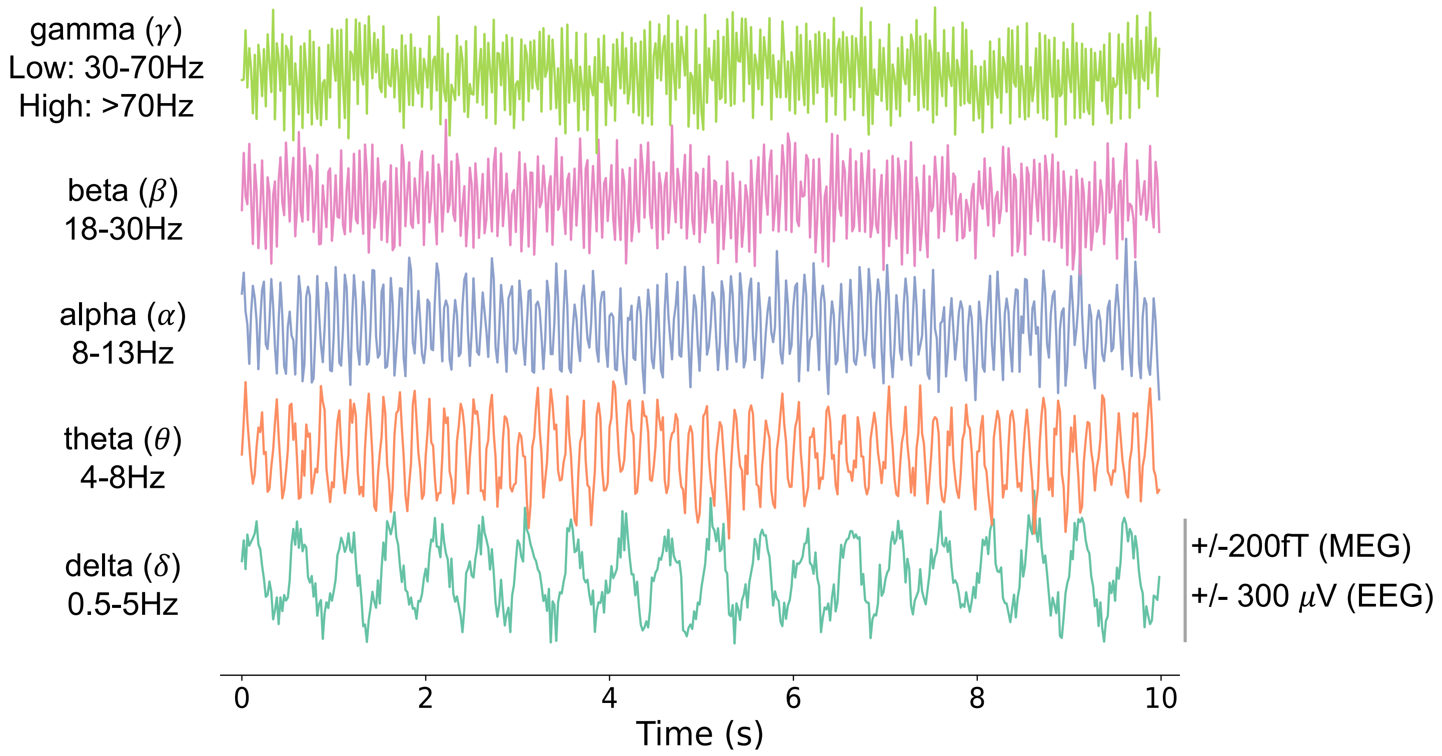
Adapted from [Corsi, 2023]

BCI application: P300 Speller

Oscillatory activity

Spontaneous activity, characteristics:

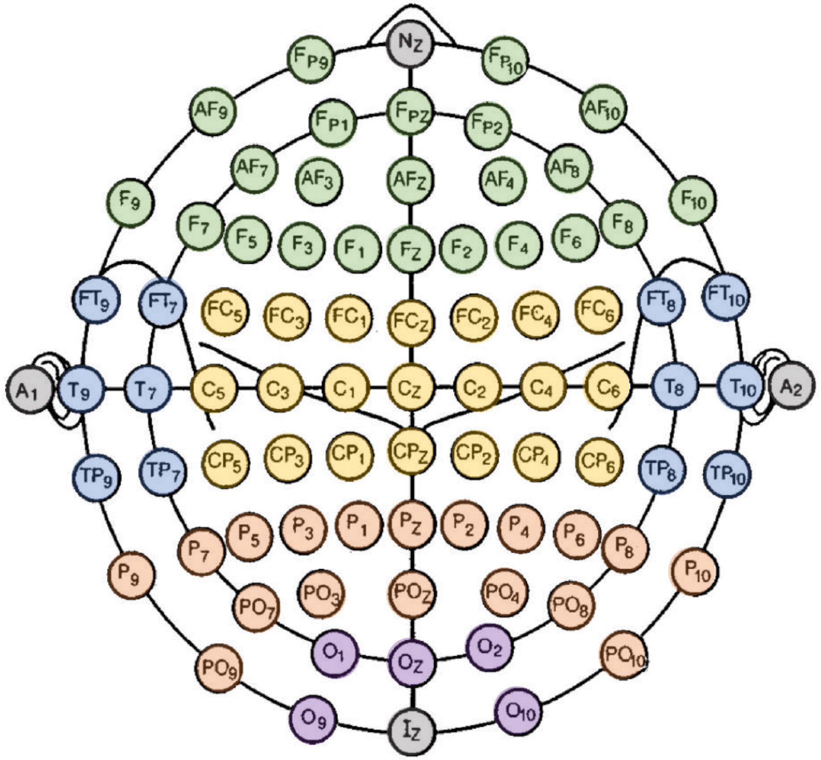
- Frequency
- Amplitude
- Shape
- Localization
- Psychopsychological context
- Duration
- Vanishing



Adapted from [Corsi, 2023]

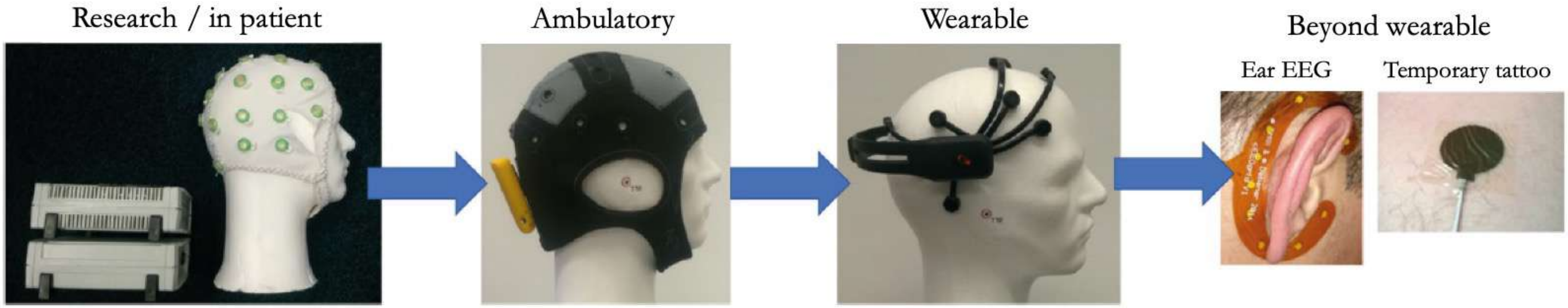
BCI application: motor-imagery based BCI

EEG instrumentation



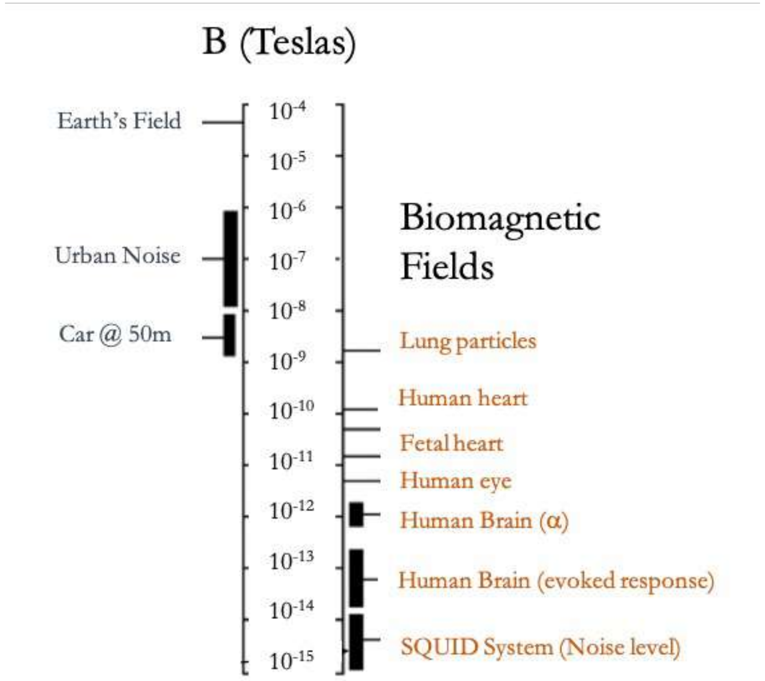
Adapted from (Corsi, 2023)

EEG instrumentation

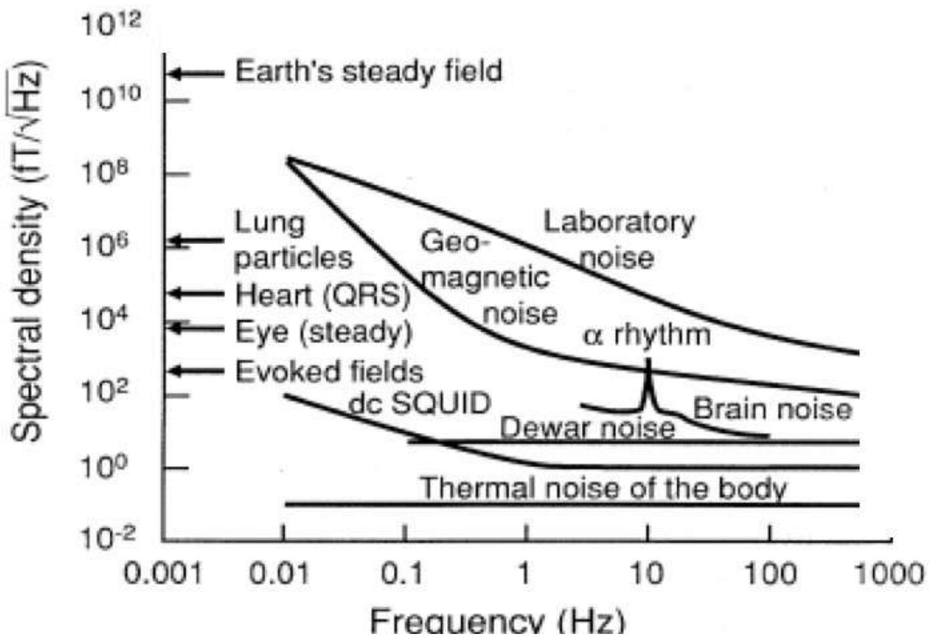


Overview of the evolution of EEG modalities, adapted from (Casson, 2019)

MEG instrumentation



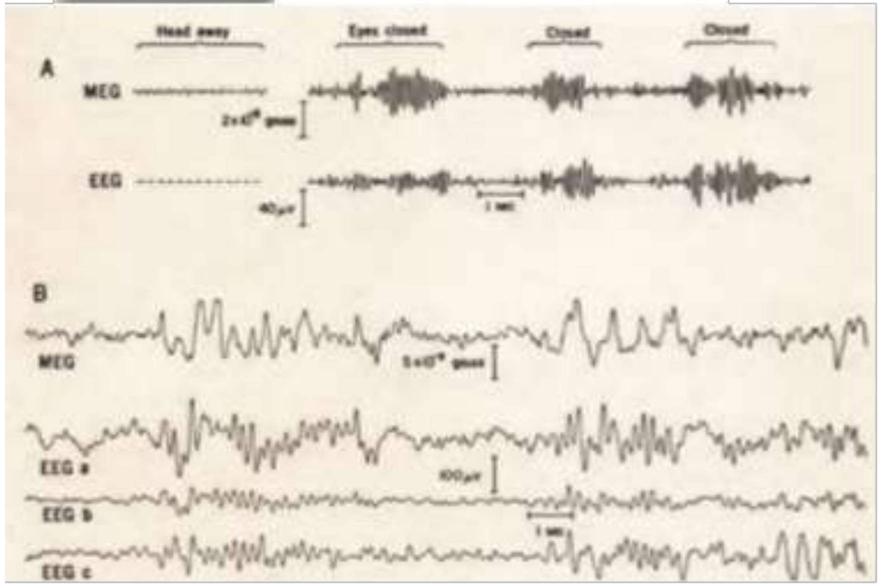
Adapted from (Garnero, 2011)



Adapted from (Hämäläinen et al, 1993)

MEG instrumentation

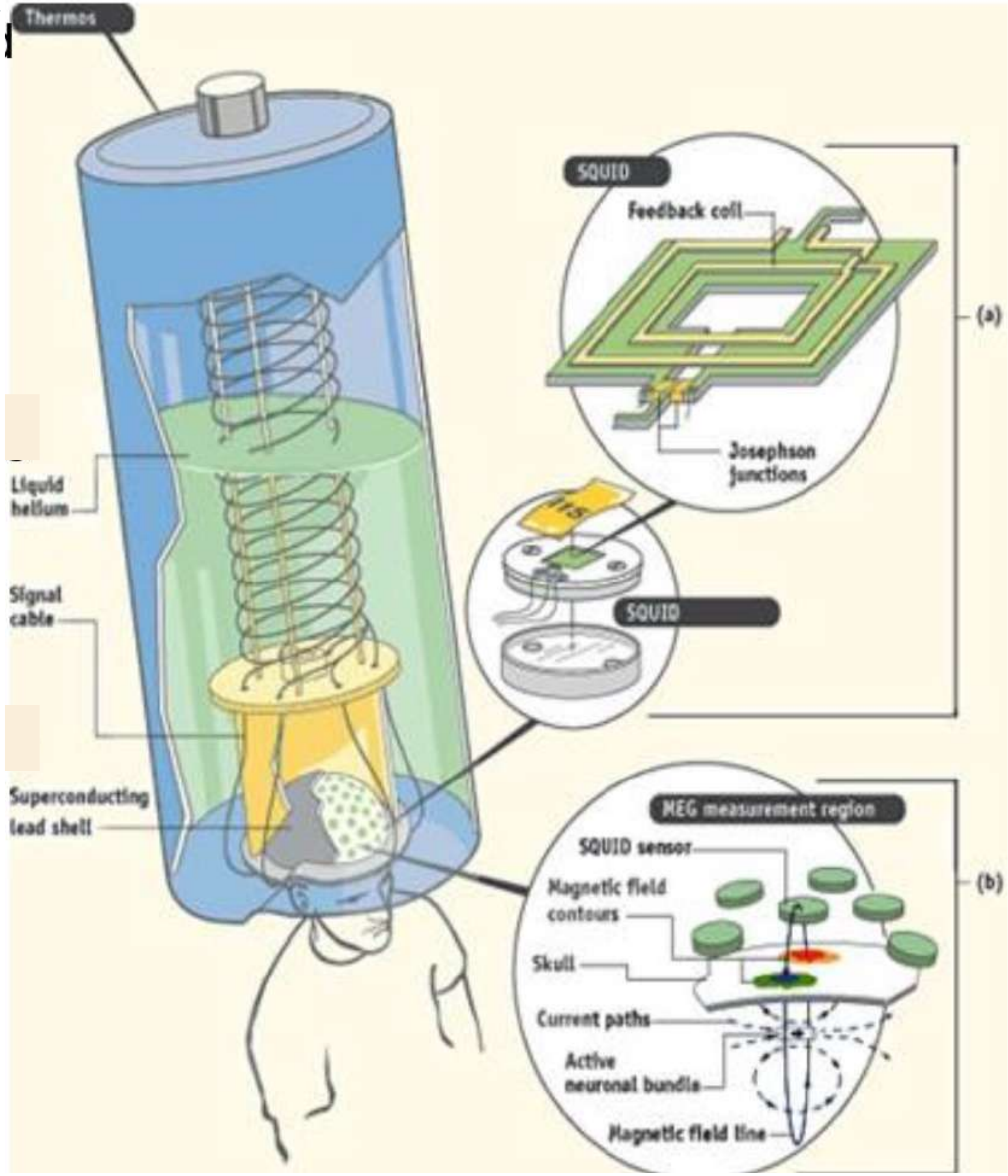
David Cohen



Registration obtained in 1971

1st MEG device

MEG instrumentation

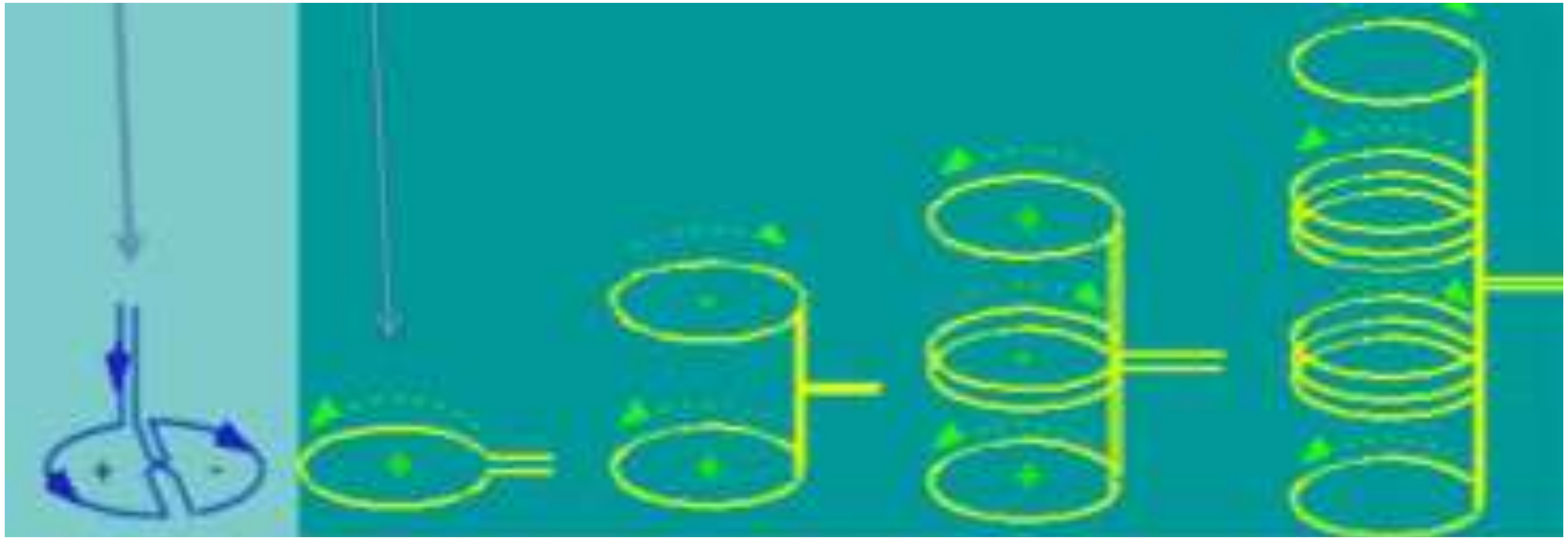


MEG instrumentation

Axial gradiometer (hardware)

Planar gradiometer

Magnetometer



1st order

2nd order

3rd order

Not sensitive to uniform fields

Not sensitive to uniform gradient fields

Not sensitive to uniform second derivate of fields

Magnetometers & gradiometers – more sensitive around the sensor

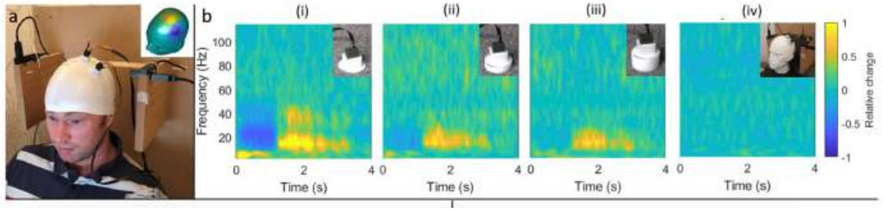
Planar gradiometers – more sensitive to sources under the sensor (directional)

MEG instrumentation

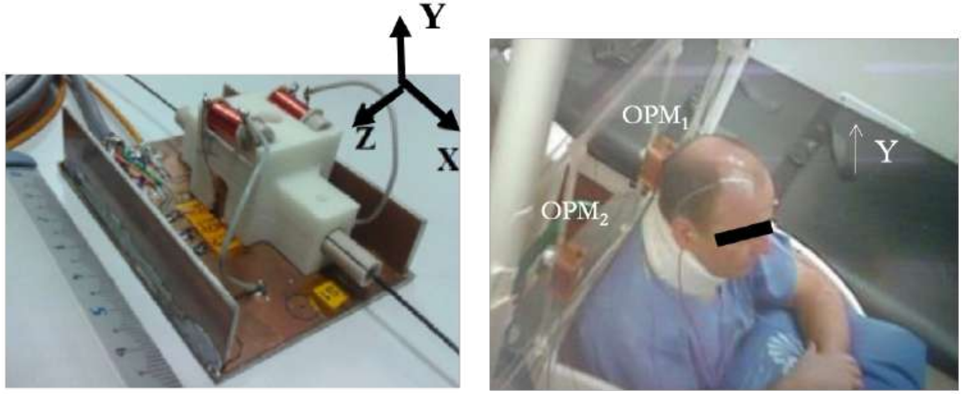
Current MEG device

QuSpin first prototype
(Shah et al, 2013)

Wearable system
(Boto et al, 2018)



Simultaneous M/EEG measurements with Gen-2 OPM
(Boto et al, 2019)



^{4}He OPM & experimental setup adapted from (Labyt*, Corsi* et al, 2019)

M/EEG experiment, main steps

Adapted from [Corsi, 2023]

Take-home message

	MEG	EEG
Measurement	Magnetic field, + intracellular currents	Difference of electric potentials, + extracellular currents
Spatial resolution	1 cm	2-3 cm
Temporal resolution	1 ms or less	
Avantages	- Absolute values - Less affected by bone - Focal	- Portable - Cost
Drawbacks	- Financial & mechanical constraints - Sensitive to physiological artifacts	- Need of a reference - Affected by bone - Diffuse - Sensitive to physiological artifacts

DATA ANALYSIS

THE MAIN STEPS (OFFLINE)

Questions addressed in this section

- M/EEG signals
  - What are the main artifacts observed with M/EEG signals?
- M/EEG signal processing
  - How to remove artifacts?
- What are the dos/don’ts when processing M/EEG signals?

Preliminary remarks

Plethora of methods to preprocess and analyze your data but before everything :

- Have a look to your data

- Take the time to consider different preprocessing pipelines instead of applying one blindly
  - Each method has its pros/cons
  - Some of them can **alter** your signal (filters)
  - It strongly depends on the quality of your dataset
  - It depends on the **purpose of your study**

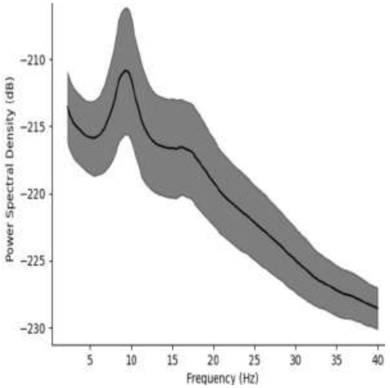
Main steps

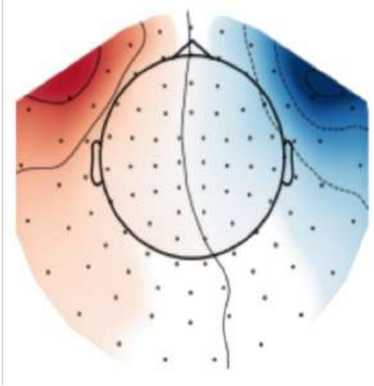
Data inspection

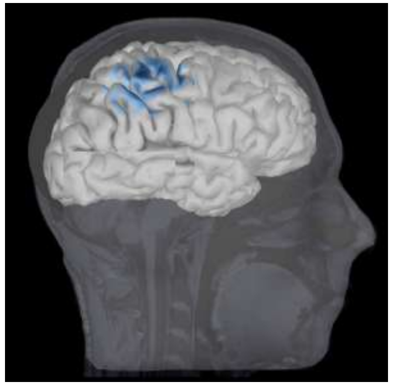
Artifacts removal

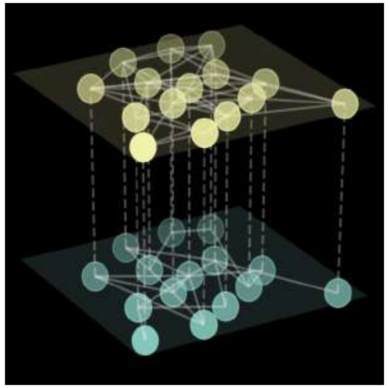
Source reconstruction

Advanced analysis



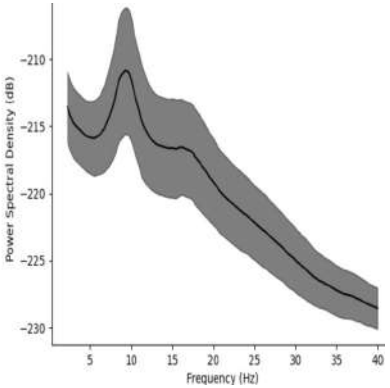


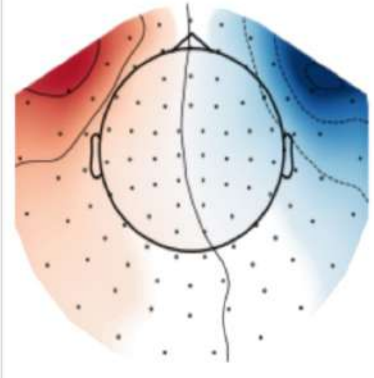


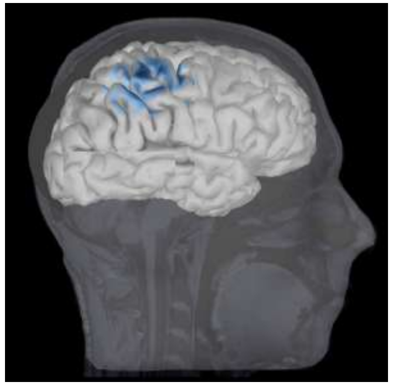


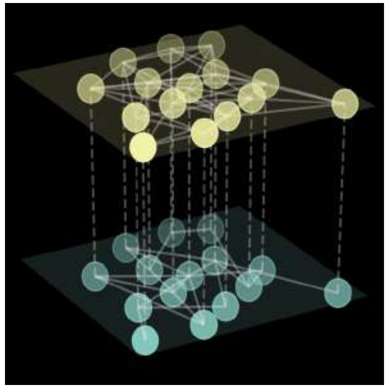
Main steps

Data inspection → Artifacts removal → Source reconstruction → Advanced analysis









The most crucial steps – addressed here

See next week w/ T. Papadopoulo

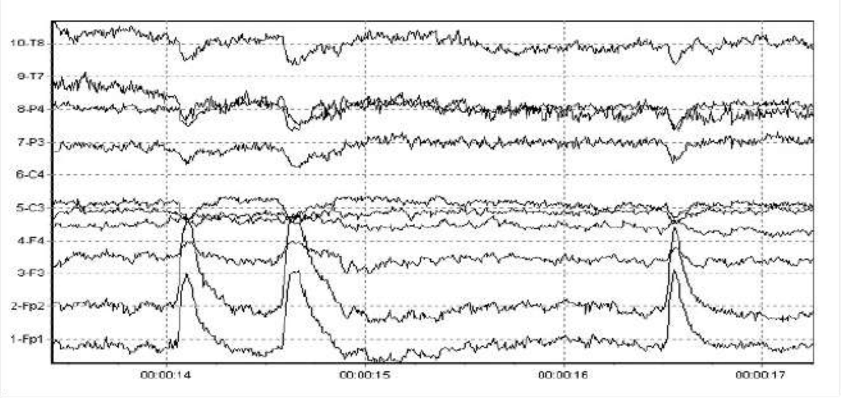
Data inspection

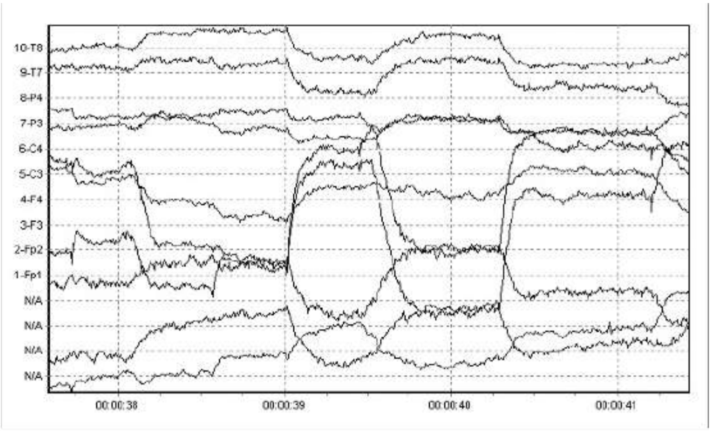
- Questions
  - What kind of artifacts do I have ?
  - Do they present a pattern ?
  - Do they affect one/several channels ?
  - How long do they last ?

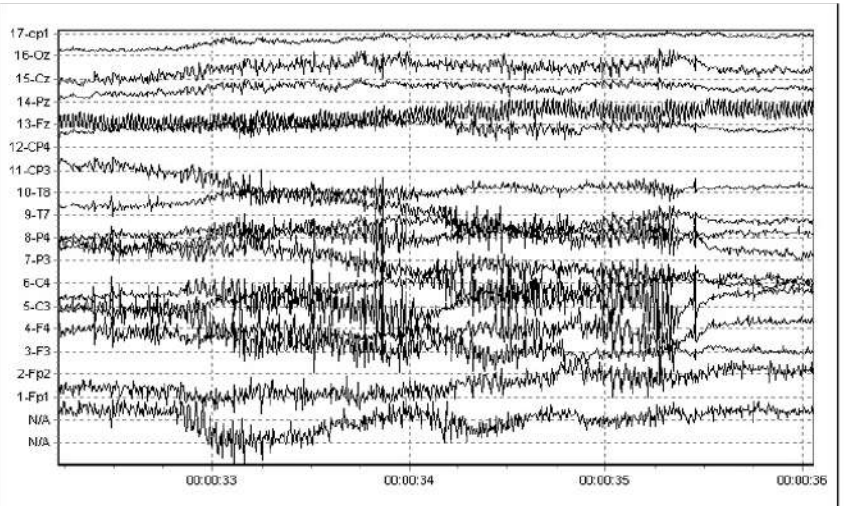
- Tools to address them
  - Timeseries
  - Power spectra
  - Use of biosignals/triggers to detect events

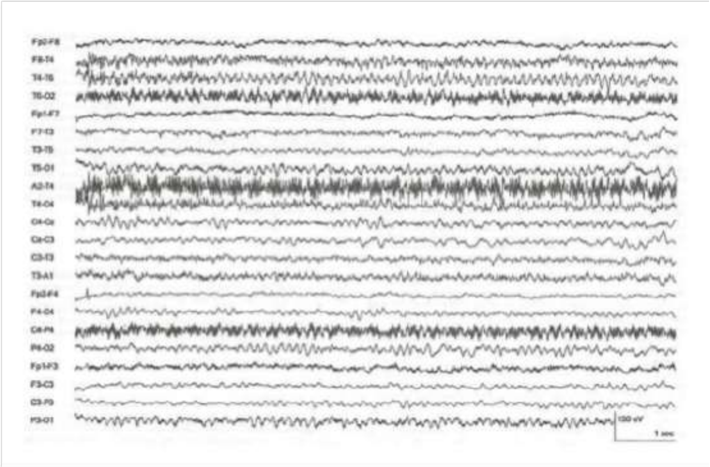
Artifacts removal – what methods?

Depends on the type of artifacts & your problematic to be addressed







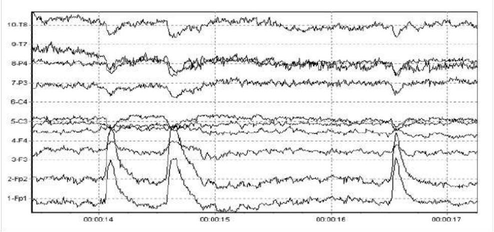


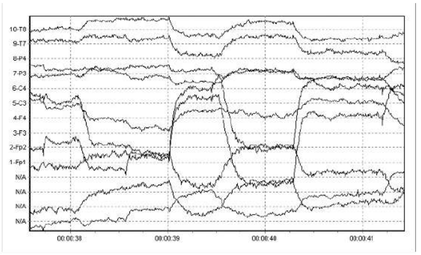
Artifacts removal – what methods?

Depends on the type of artifacts & your problematic to be addressed

- Powerline & need to study activity in the gamma band

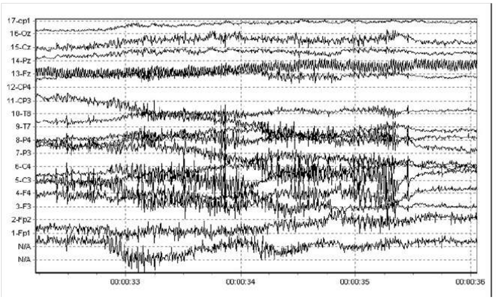
⇒ Notch filter @ 50Hz

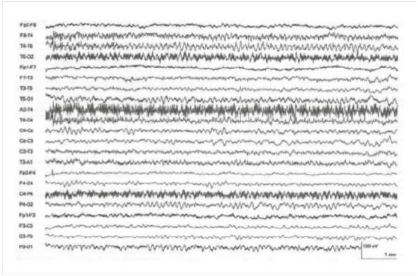




- Clear patterns (blinks, saccades, cardiac activity)

⇒ Independent component analysis & use of biosignals





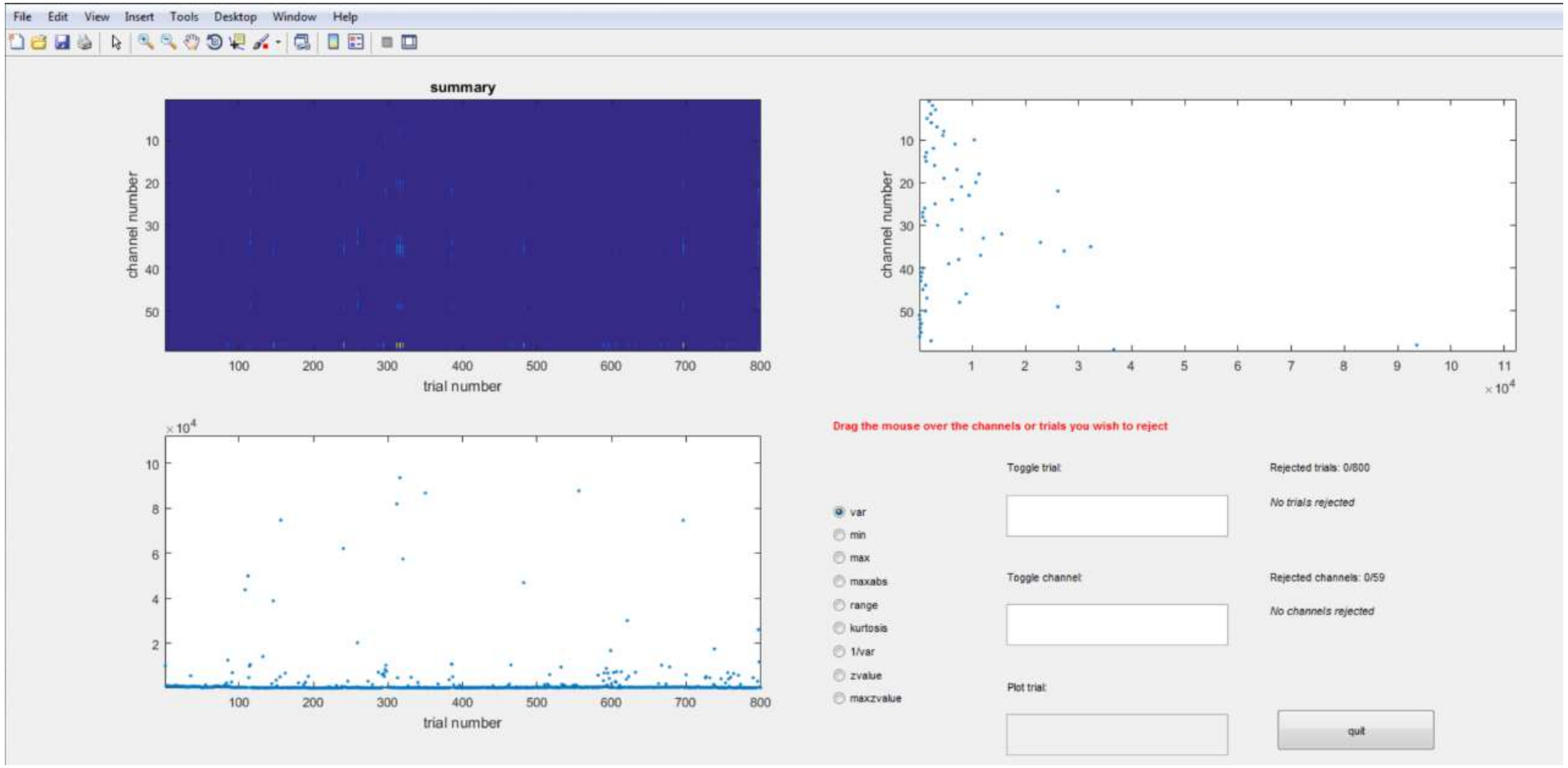
- A broken channel

⇒ Interpolation (depends on the location though)

Artifacts removal – quality check

Do not underestimate this step to assess the efficacy of your pipeline!

- Timeseries & power spectra before vs after
- Identify suited judgement criteria: variance, zscore…



Matlab

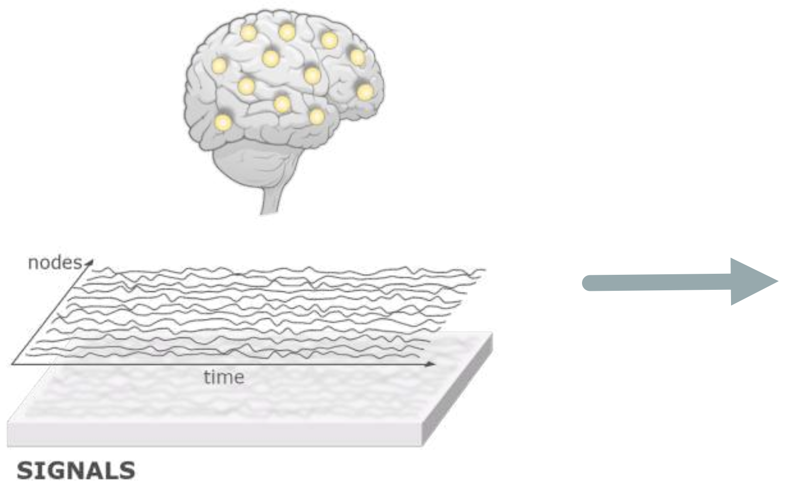
Python

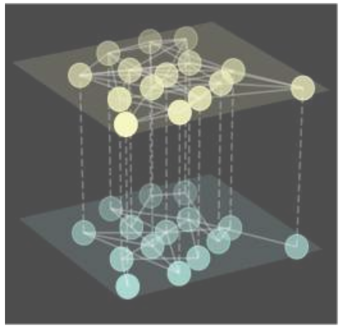
All of them provides tips and tutorials to guide you in the analysis of your dataset!

Take home messages

Before applying any filter/method:

- During the experiment, take notes
- Take the time to inspect your data!
- Construct (and test!) a suited pipeline with QC





To go further…

- Tools for M/EEG data analysis – with many tutorials
  - Python: MNE-Python
  - Matlab: Brainstorm, Fieldtrip

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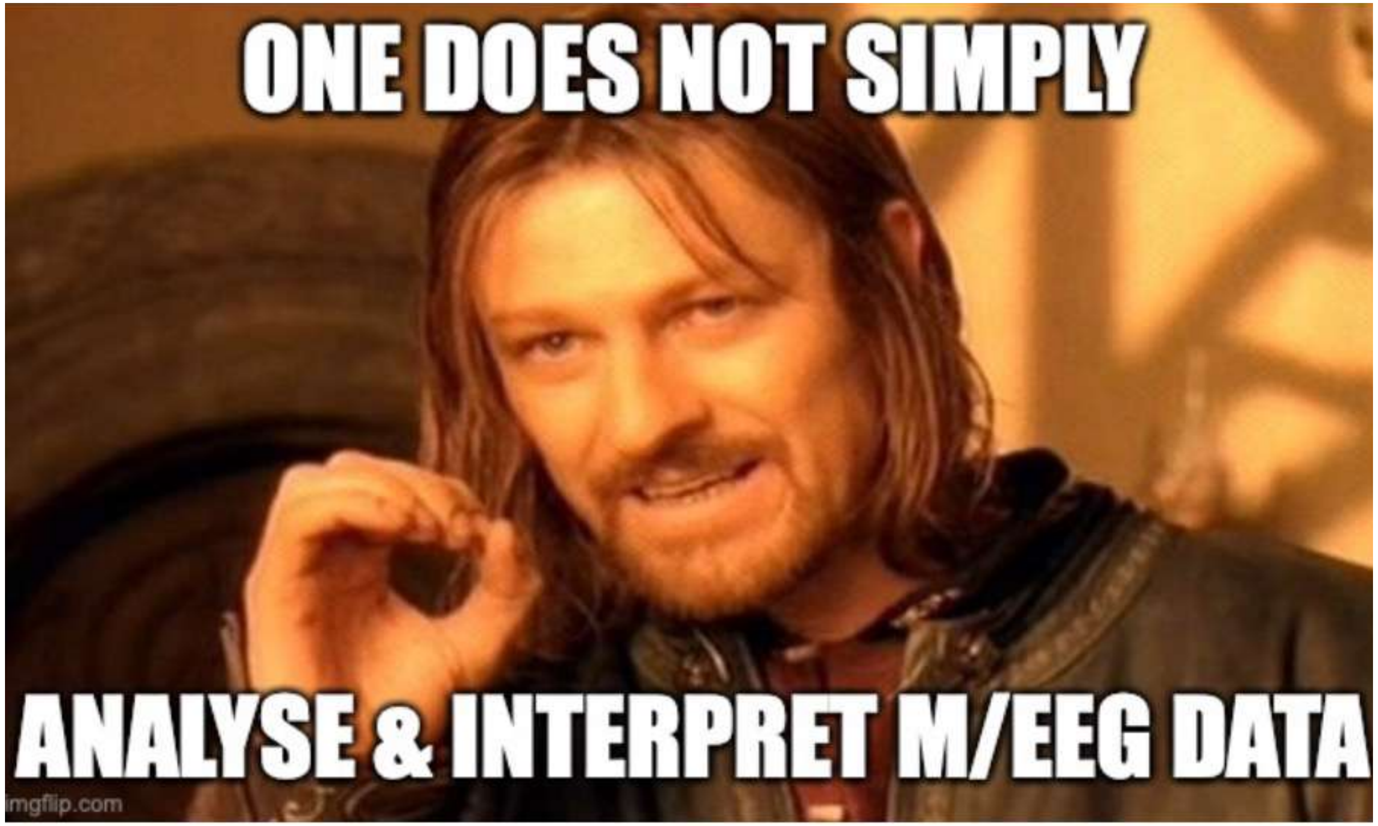
- Tools for M/EEG data analysis – with many tutorials
  - Python: MNE-Python
  - Matlab: Brainstorm, Fieldtrip

- M/EEG
  - Chapter book (open access)
    - Origins of the signals,
    - M/EEG experiments,
    - Data analysis,
    - Features extraction & selection,
    - Brain disorders

To go further…

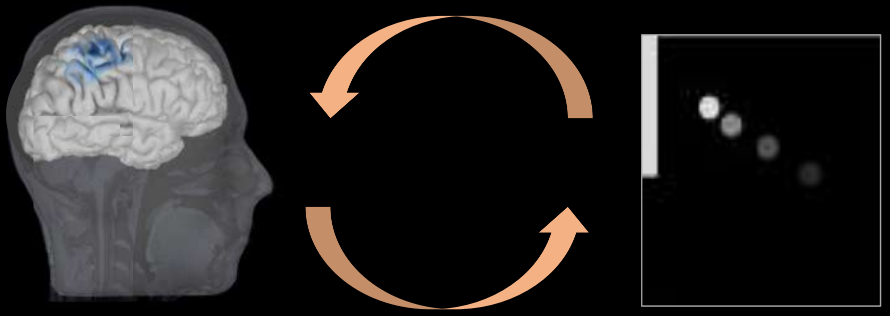
- Tools for M/EEG data analysis – with many tutorials
  - Python: MNE-Python
  - Matlab: Brainstorm, Fieldtrip

- M/EEG
  - Chapter book (open access)
  - Github repo
    - E/MEG data visualization,
    - Data extraction (ERD/S),
    - Classification



Let's see together an example!

Lesson 1: ✓



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