EEG/MEG 1:

Measurement, Pre-Processing and Data Reviewing

Olaf Hauk

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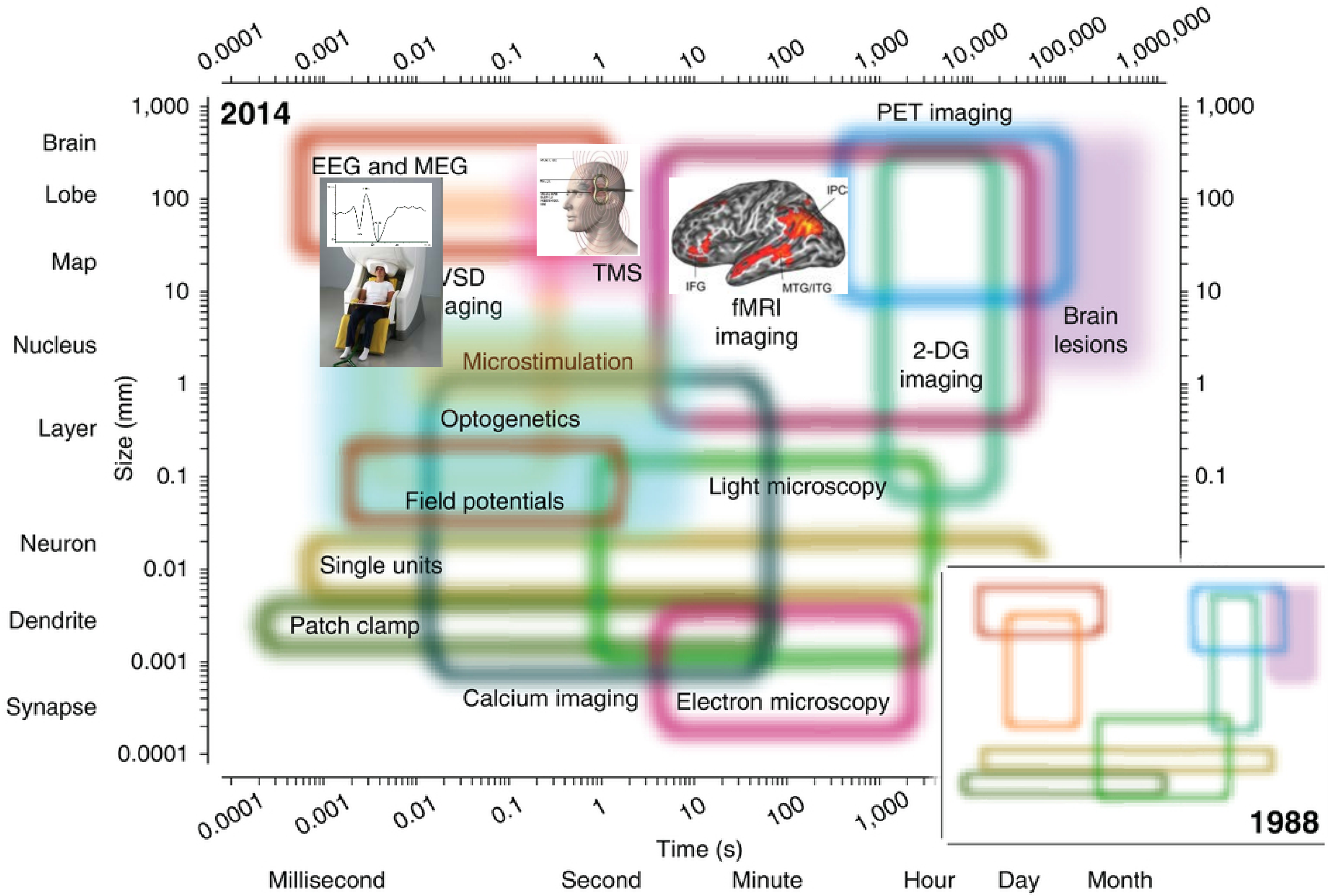
Introduction to Neuroimaging Methods, 5.2.2024

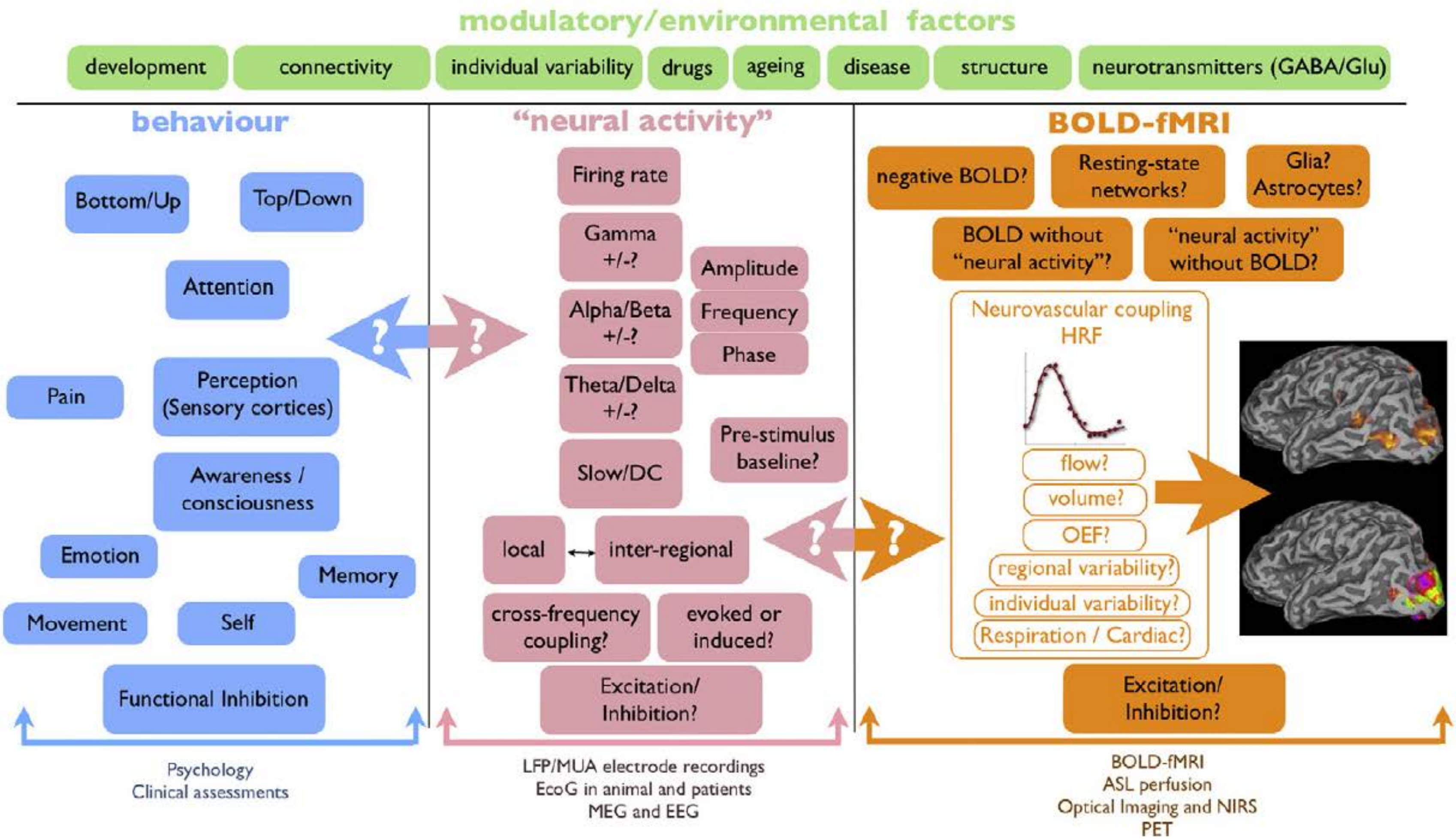
Neuroimaging Methods Vary With Respect To Spatial and Temporal Resolution

(and their invasiveness, physiology, etc.)



Seijnowki, Churchland, Movshon, Nat Nsc 2014

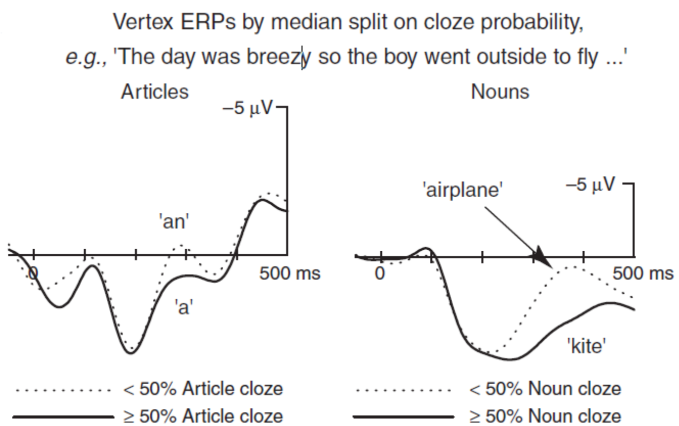
Which "Neural Activity" Do You Mean?



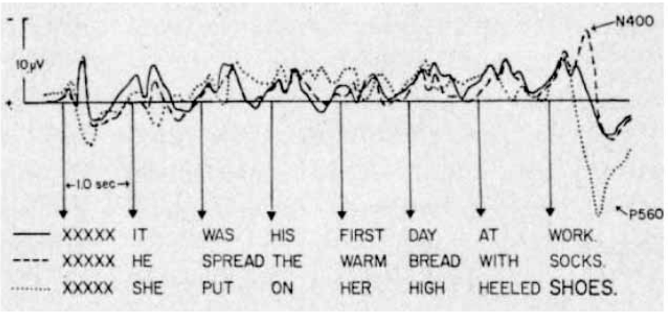
Singh, NI 2012

EEG/MEG "Activity" Can Be Analysed In A Number Of Ways, e.g.

Event-Related Potentials

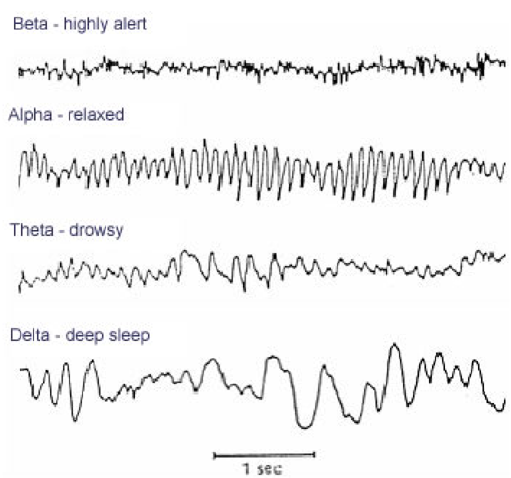


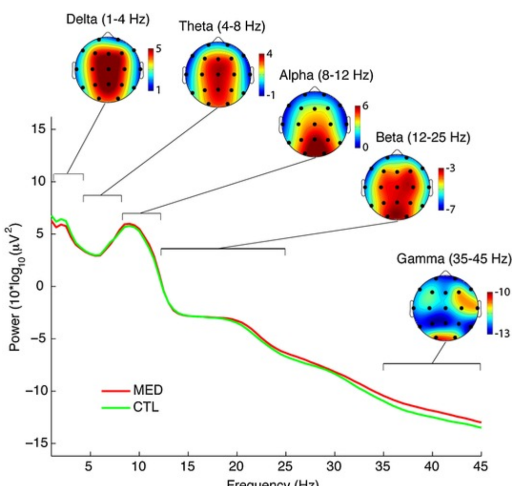
deLong, Urbach, Kutas, Nat Nsc 2005



Kutas&Hillyard, Science 1980

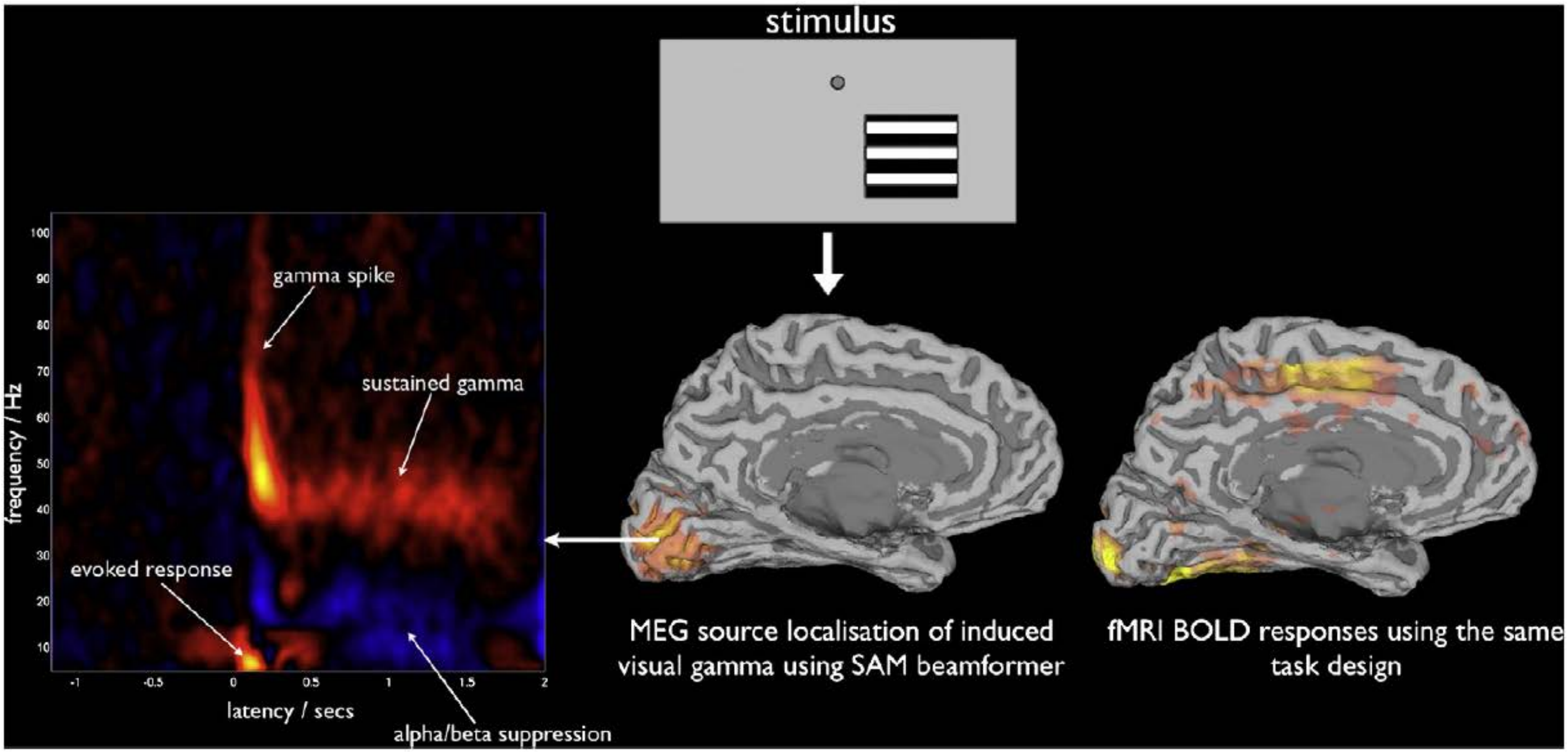
Brain "Rhythms"/"Oscillations"





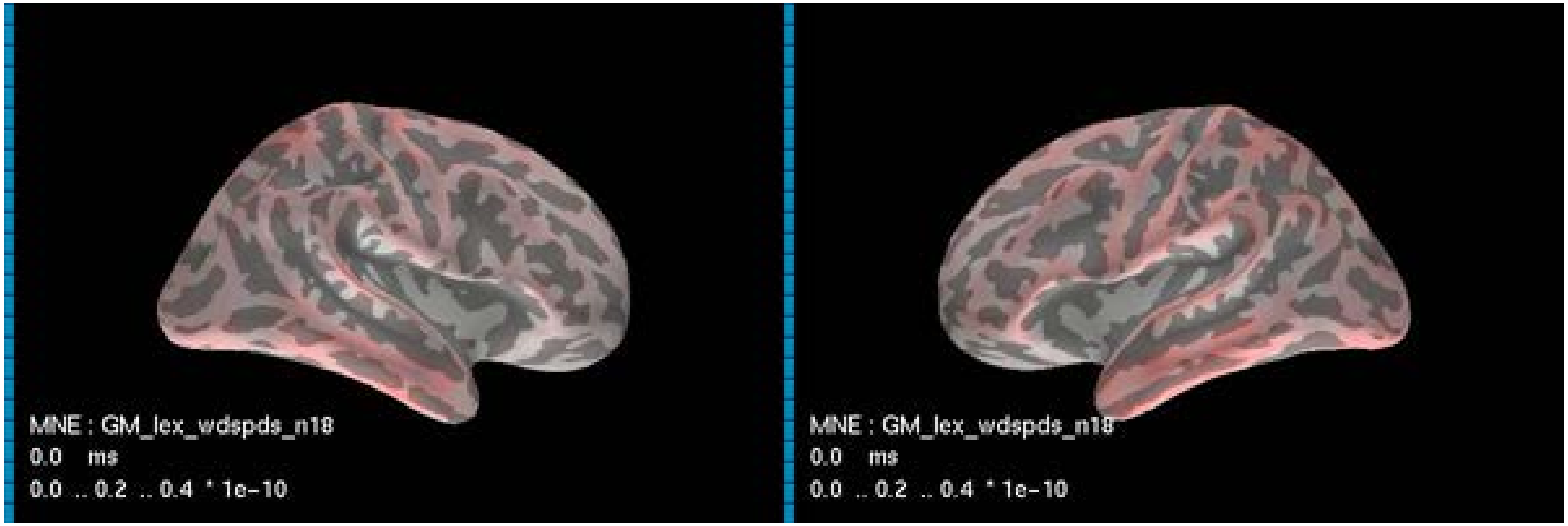
http://link.springer.com/article/10.1007%2Fs10339-009-0352-1/

Which "Neural Activity" Do You Mean?



Singh, NI 2012

What We Really Want:
Spatio-Temporal Brain Activity
(Movies rather than pictures)



EEG/MEG Literature

Books:

- Supek & Aine: “Magnetoencephalography (2nd)”, Springer 2019
- Ilmoniemi & Sarvas: Brain Signals – Physics and Mathematics of MEG and EEG”, MIT 2019
- Hari R, Puce A. “MEG-EEG Primer”. Oxford University Press 2017.
- Sekihara & Nagarajan: “Electromagnetic Brain Imaging”, Springer 2015.
- Cohen, Mike X; “Analyzing Neural Time Series Data”; MIT Press 2014.
- Hansen, Kringelbach, Salmelin: “MEG: An Introduction to Methods”, OUP 2010.
- Sekihara & Nagarajan: “Adaptive Spatial Filters For Electromagnetic Brain Imaging”. Springer 2008.
- SJ Luck: “An Introduction to The Event-Related Potential Technique”, MIT 2005.
- TC Handy: “Event-Related Potentials”, MIT 2004.
- http://imaging.mrc-cbu.cam.ac.uk/meg/IntroEEGMEG

Guidelines for MEG and EEG research:

- Gross et al., “Good practice for conducting and reporting MEG research.“, Neuroimage 2013.
- Picton et al., “Guidelines for using human event-related potentials to study cognition: recording standards and publication criteria.“, Psychophysiology 2000.

Demos of some open software packages:
https://www.frontiersin.org/research-topics/5158/from-raw-megeeg-to-publication-how-to-perform-megeeg-group-analysis-with-free-academic-software

Plus software tutorials, online talks, etc. etc.
Plus specialised papers etc. etc.

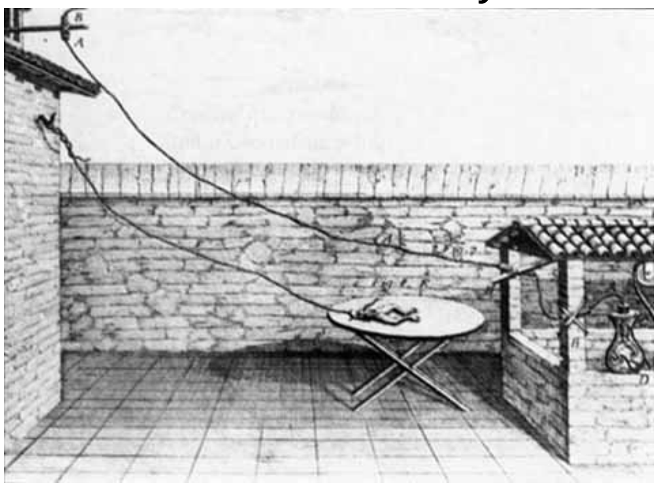
A Brief History Of Bioelectromagnetism

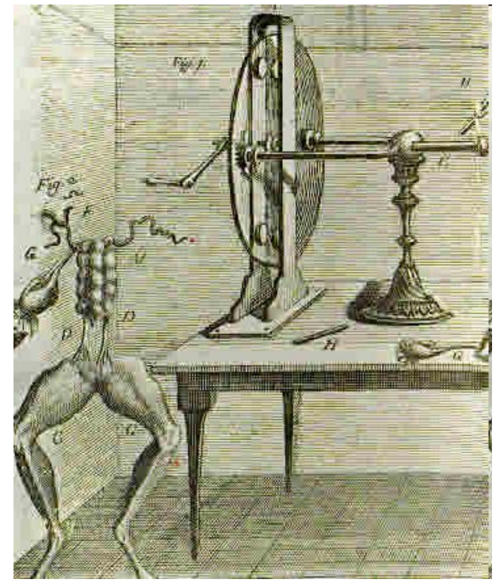
Ancient Egypt, 2750 BC:
Electric Fish ("Thunderer of the Nile")
Some Roman writers mention electric shocks as an ailment for headaches (~ 0 AC)...

Ancient Greece, 600 BC:
Thales describes static electricity
"electron"

Early Science

1771
Luigi Galvani, Bologna
"animal electricity"

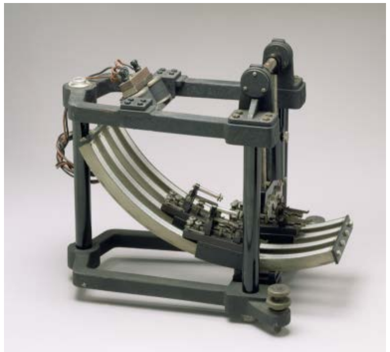




In 1803:
"On the first application of the process to the face, the jaws of the deceased criminal began to quiver, and the adjoining muscles were horribly contorted, and one eye was actually opened. …
Mr Pass, the beadle of the Surgeons' Company, who was officially present during this experiment, was so alarmed that he died of fright soon after his return home."
http://www.executedtoday.com/2009/01/18/1803-george-foster-giovanni-aldini-galvanic-reanimation/

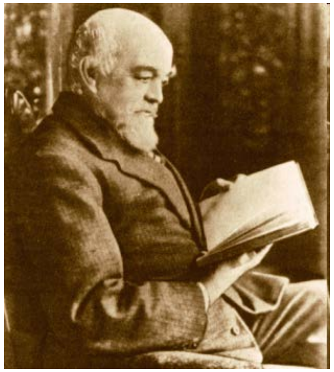
Early Electrophysiology

1842: Du Bois-Reymond, Berlin
nerve action potentials neurons



1852: Helmholtz, Berlin
speed of action potentials in frogs neurons

1875: Richard Caton, Liverpool
first “ECoG” from animals



http://www.sciencemuseum.org.uk/broughttolife/objects/display.aspx?id=4360

Early EEG

MRC
Cognition and Brain Sciences Unit

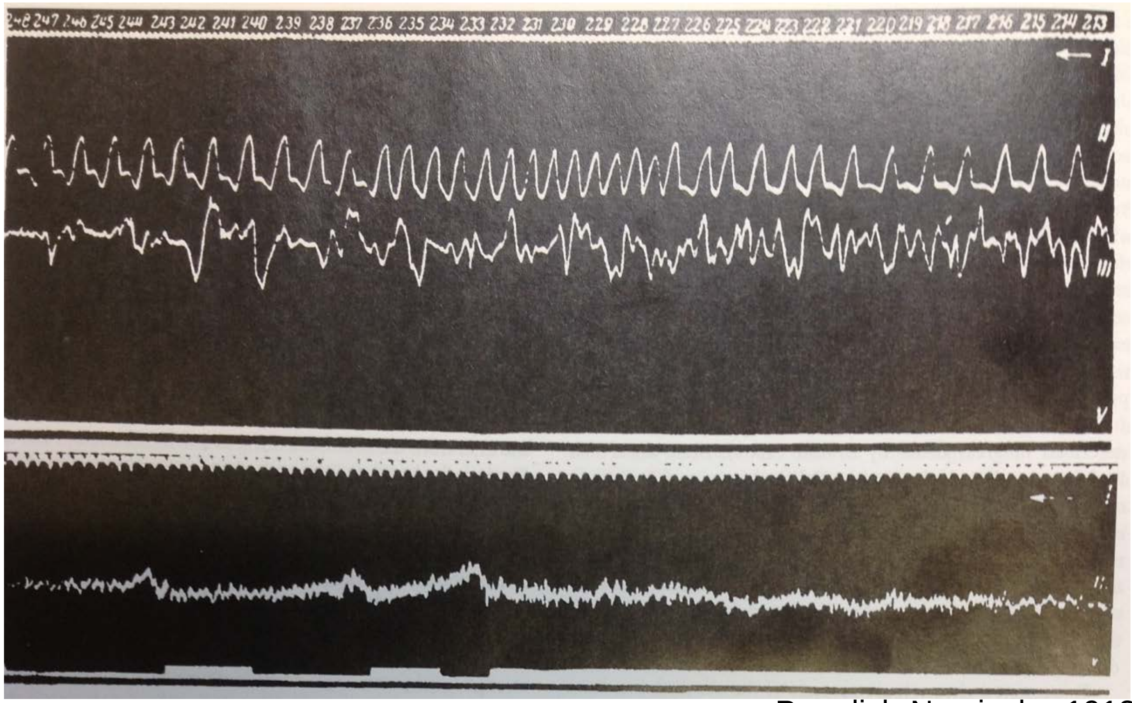
Time marker

Artery pulsation

Brain potential

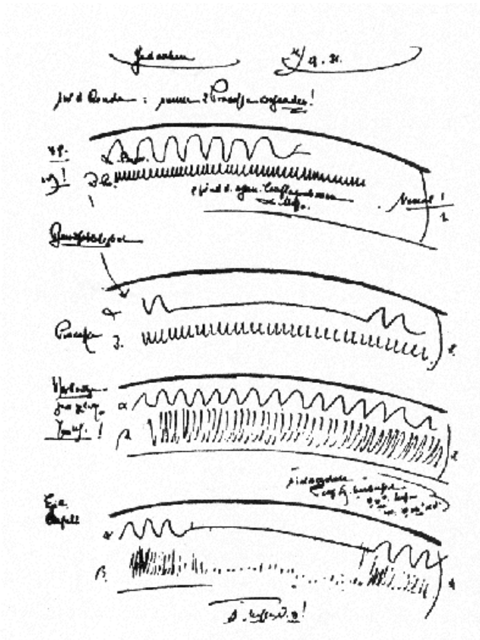
Response to sciatic nerve stimulation

Stimulation signal



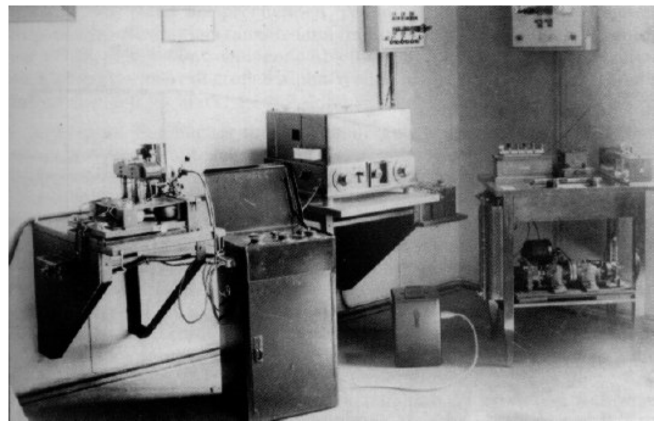
Pravdich-Neminsky, 1913

Early EEG

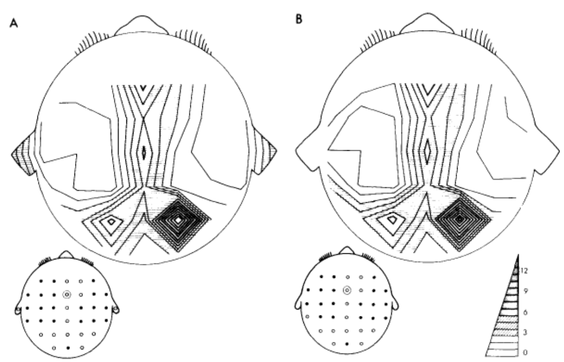


Hans Berger, Jena 1924

First Fourier Analysis of EEG: Berger&Dietsch 1931



1969/70: 32/48-channel EEG, “generators”



Lehmann, 1971

Early ERPs

A summation technique for detecting small signals in a large irregular background. By G. D. Dawson. *Neurological Research Unit, Medical Research Council, National Hospital, Queen Square, London, W.C.* 1

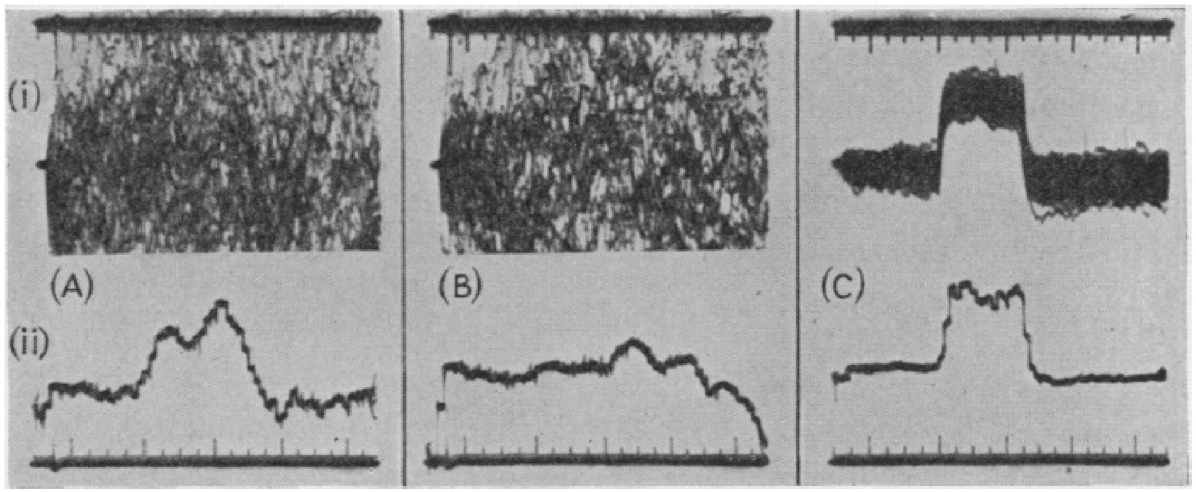


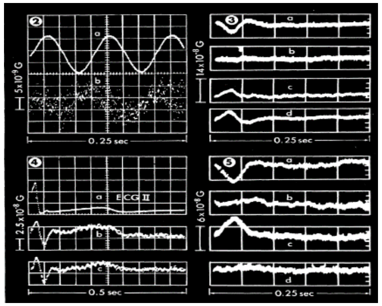
Fig. 1. An experiment to detect cerebral responses when the left ulnar nerve was stimulated at the wrist once per second. The upper line of traces shows sets of 55 records superimposed and the lower line the averages of these given by the machine. In A, from the contralateral scalp, there was one electrode on the midline and one over the right central sulcus. In B, from the ipsilateral scalp, the record was taken from the same midline electrode and one over the left central sulcus. In C is shown the result of making the electrode over the central sulcus positive to that on the midline by 5 μV. The largest spikes in the time scales show intervals of 20 msec., and the stimulus was applied 5 msec. after the start of each sweep.

Dawson, Proceedings of the Physiological Society, 1951

First MEG: Pre-SQUID age

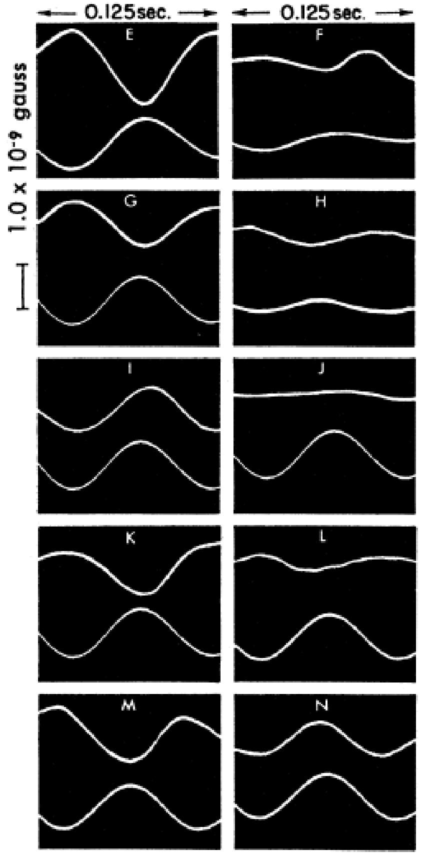
MEG pioneers MIT

MCG, 1967/(63)



Cohen, Science 1967

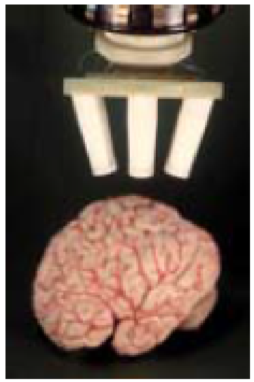
MEG, 1968

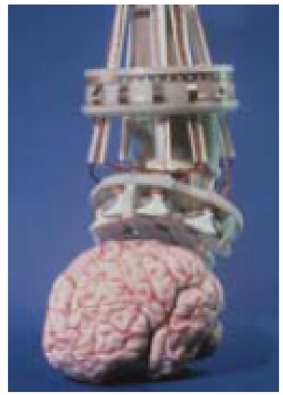


Cohen, Science 1968

Alpha Rhythm

The Fast Evolution of MEG





1983
by HUT
4 channels
30 mm in diameter
(coverage: 7 cm^2)
Axial

1986
by HUT
7 channels
93 mm in diameter
(coverage: 68 cm^2)
Axial

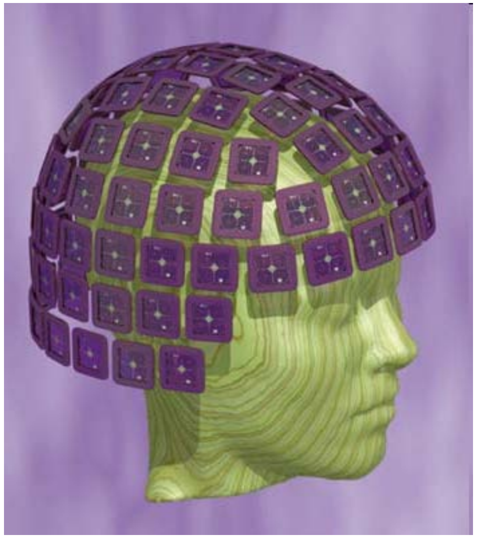
1989
by HUT
24 channels
125 mm in diameter
(coverage: 123 cm^2)
Planar

1991
by Neuromag
122 channels
whole head
(coverage: 1100 cm^2)
Planar
12 Deliveries

1997
by Neuromag
306 channels
whole head
(coverage: 1220 cm^2)
Planar & Magnetometers

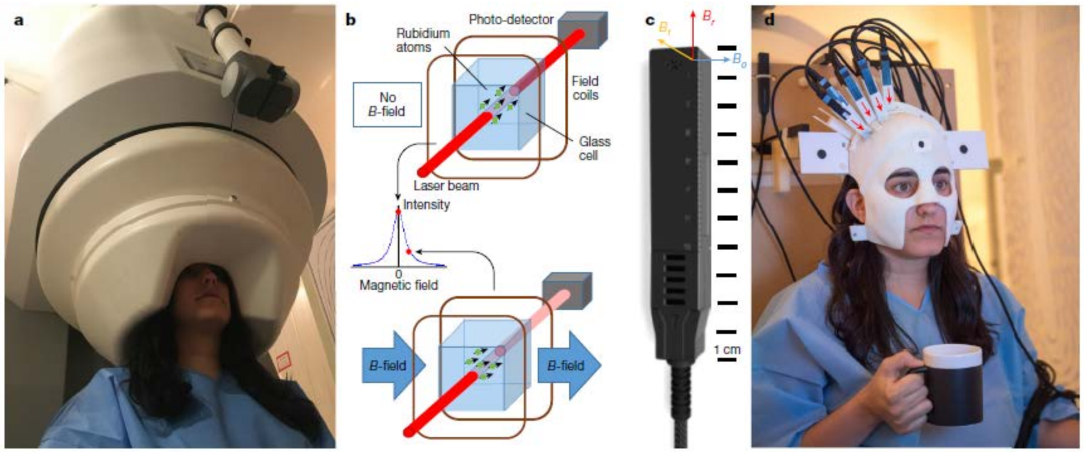
MEG – The Present

e.g. MEGIN Triux System
306 MEG sensors (102 magnetometers, 204 gradiometers)
64 EEG electrodes

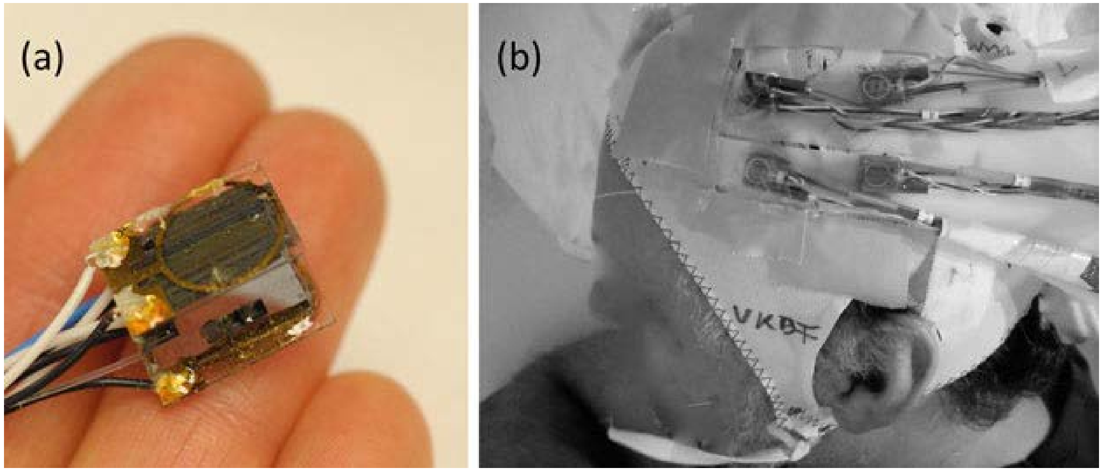


MEG – The (Near) Future

On-Scalp Optically Pumped Magnetometers



https://twitter.com/wellcometrust/status/976534659436703744 Boto et al., Nature 2018

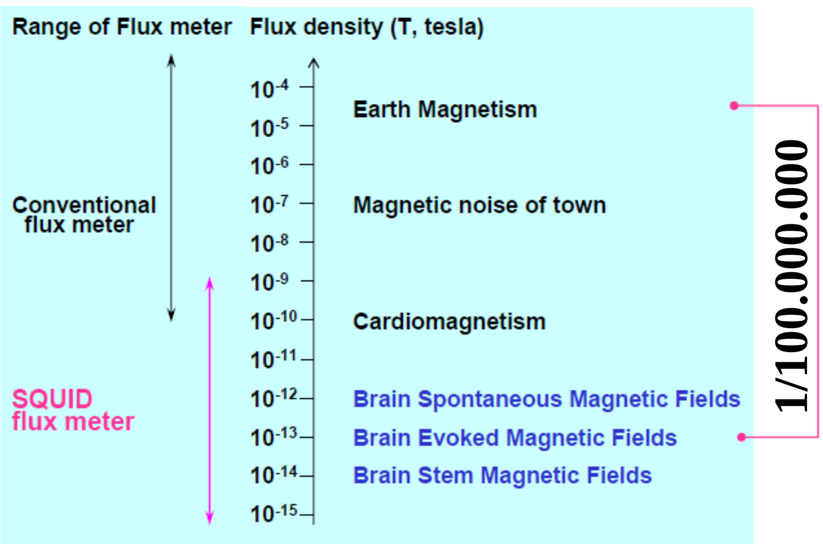


Knappe, Sander, Trahms, chapter in "Magnetoencephalography" by Supek & Aine (edts)

The Measurement Of EEG/MEG Signals

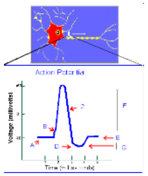
What EEG/MEG Are Measuring

Magnetoencephalography (MEG)



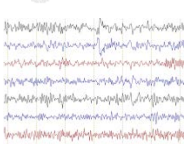
Electroencephalography (EEG)

Household Batteries
~ 1-12 V



Cell Membrane Potentials
~ 70 mV

ECG:
~ 1mV

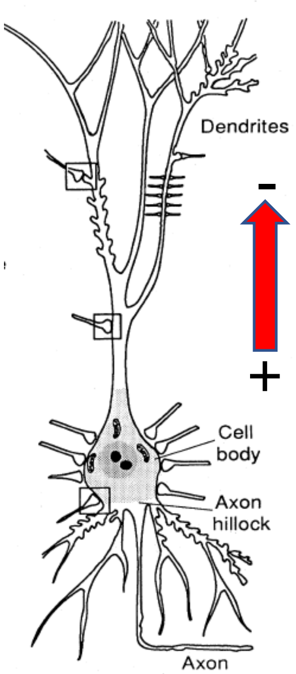


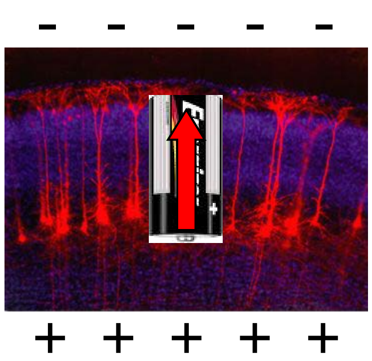
Raw EEG: ~ 30 µV
Eye blinks: > 100 µV

ERPs: ~ 0-10 µV

Main Generators of Electrical Activity in the Brain

- **Apical dendrites of pyramidal cells**
- **NOT action potentials** (too short-lived and quadrupolar)
- **EEG/MEG: same generators, different sensitivity**





Dipolar currents

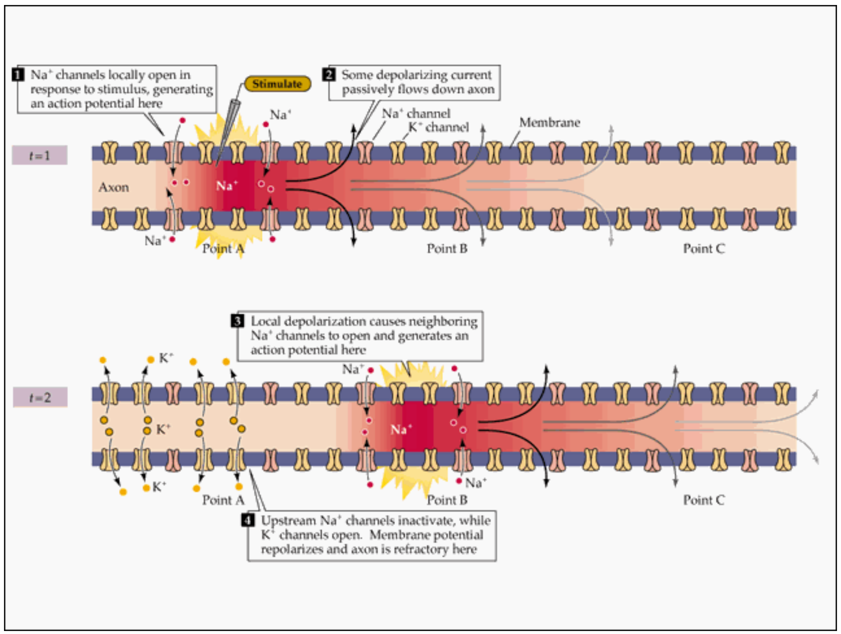
- ~ 1 Million synapses needed to activate simultaneously
- Luckily: ~10000 cells per mm^2, ~ 1000 synapses per cell

=> several mm^2 can produce measurable signal

MRC Cognition and Brain Sciences Unit

EEG/MEG Are Mostly Insensitive To Action Potentials

Action potentials are caused by active cellular mechanisms,
not passive “Ohmic” currents.
(Very different speeds)



http://www.arts.uwaterloo.ca/~bfleming/psych261/lec4se21.htm

Action potentials are quadupolar

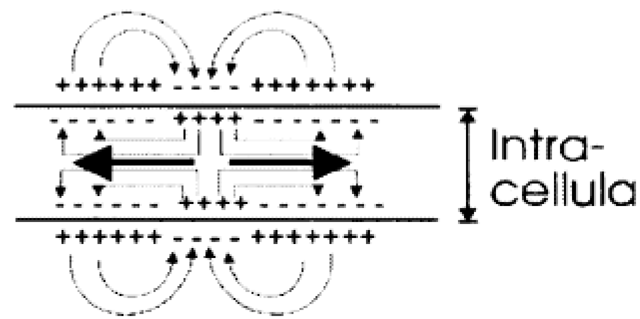


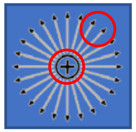
Figure I.1: *Schematic representation of an action potential*
Wieringa thesis, http://www.medcat.nl/megeeg/chap1.htm

Currents due to action potentials are very short-lived and asynchronous as well as “quadrupolar” (i.e. two opposing dipoles).

The Physics of EEG/MEG:
Quasi-Static Approximations of Maxwell's Equations

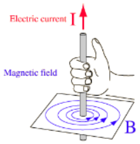
- The summed electric flux around a close surface is proportional to the total electric charge enclosed within this surface (Gauss's Law)

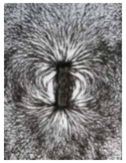
$$\nabla \cdot \boldsymbol{E} = \frac{\rho}{\varepsilon_0} = 0 \; (for\ dipoles)$$



- *Magnetic field lines are closed (Gauss's Law for magnetism)*

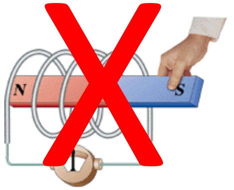
$$\nabla \cdot \boldsymbol{B} = 0$$





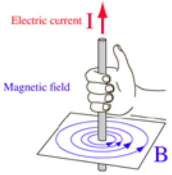
- *We do not consider any inductive effects (Faraday's Law):*

$$\nabla \times \boldsymbol{E} = 0$$



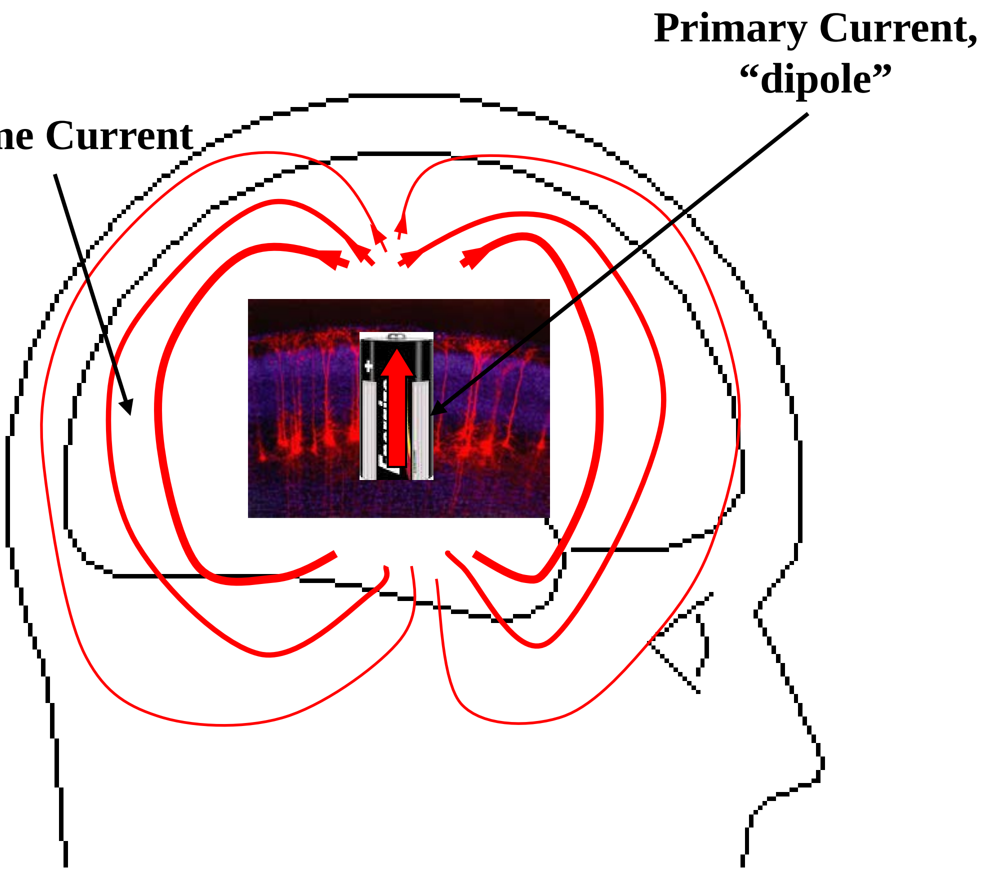
- *Magnetic fields are only caused by static currents (Ampere's Law):*

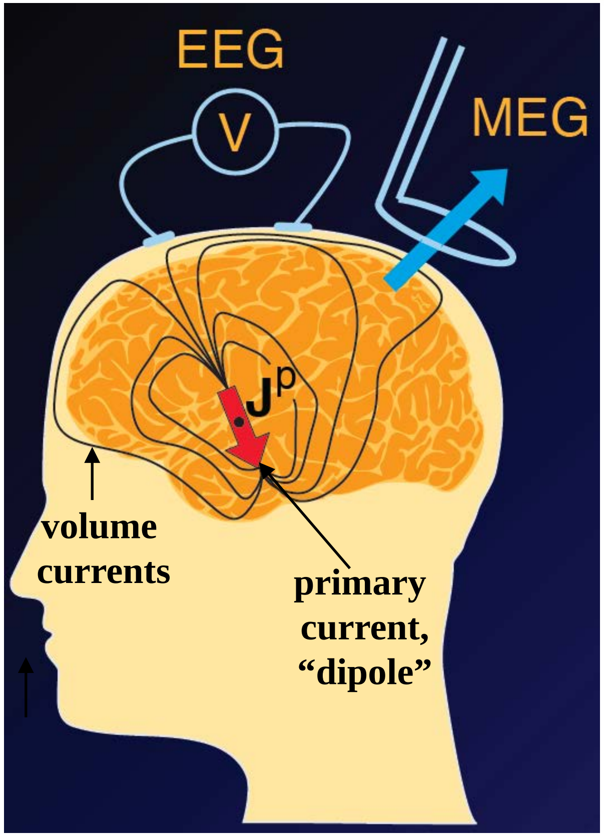
$$\nabla \times \boldsymbol{B} = \mu_0 \mathbf{J}$$



The relationship between EEG/MEG measurements and their brain sources is instantaneous (no "waves").

Current Flow in the Head





http://www.nmr.mgh.harvard.edu/meg/pdfs/talks/

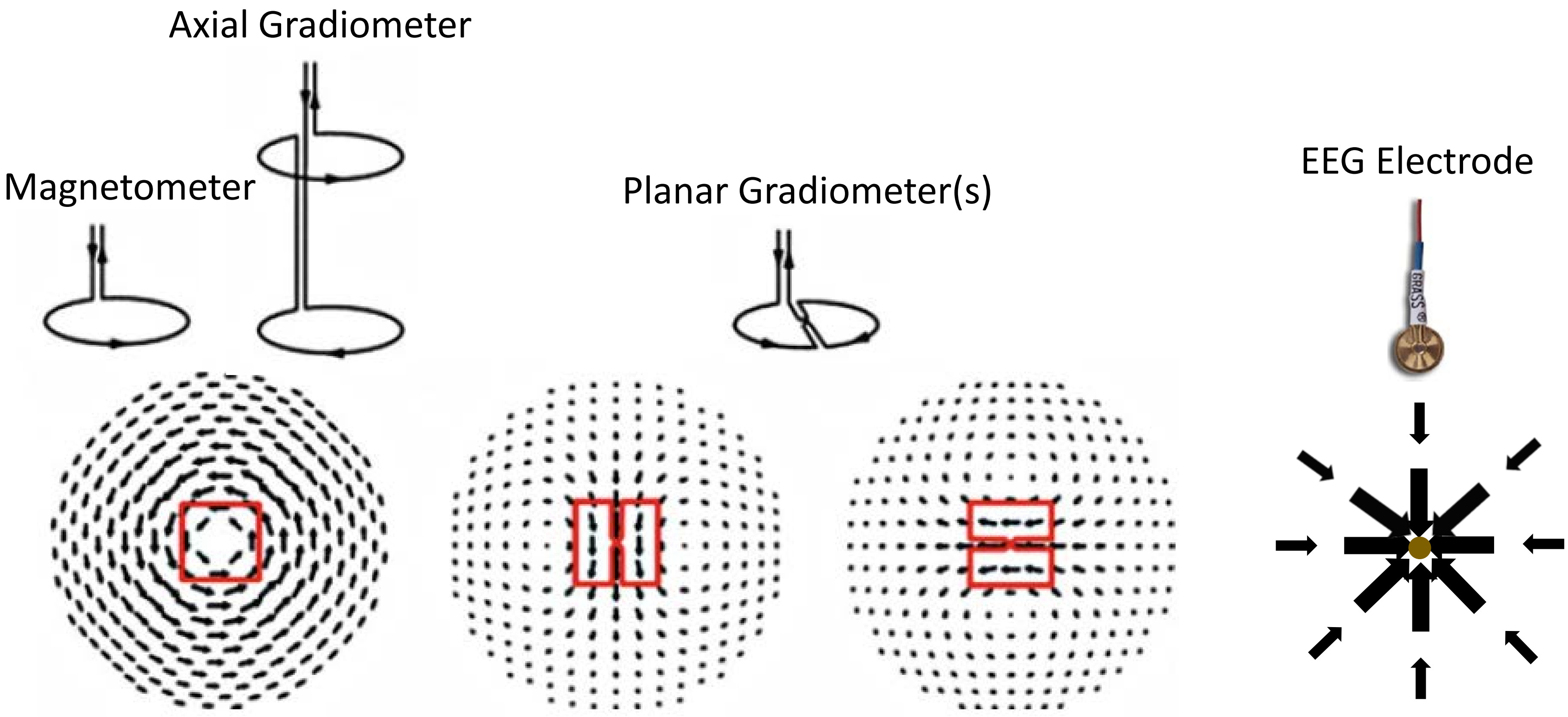
Volume currents affect both EEG and MEG –

but EEG more than MEG

Different Sensors and their Sensitivities (Leadfields)

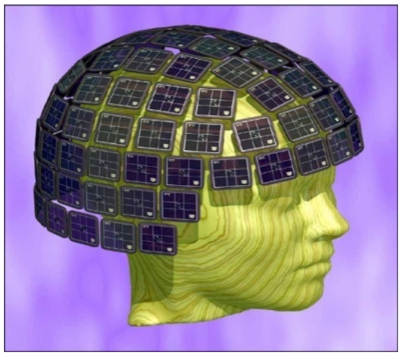
Leadfields are "sensitivity profiles" of individual sensors.

Each sensor is maximally sensitive to sources oriented along the arrows, and insensitive to sources perpendicular to the arrows.



The MEGIN Triux Neo System At CBU

306 channels in 102 locations



1 magnetometer and 2 planar gradiometers at each location

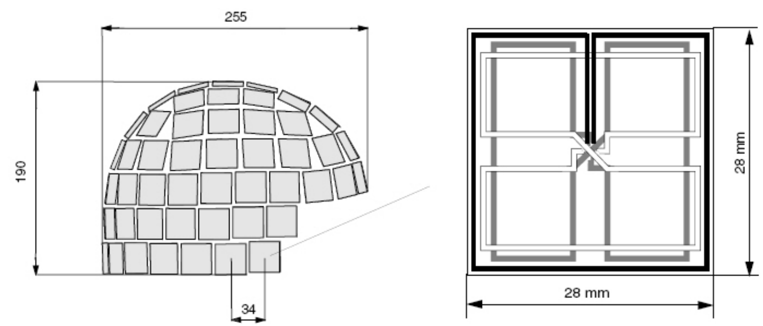
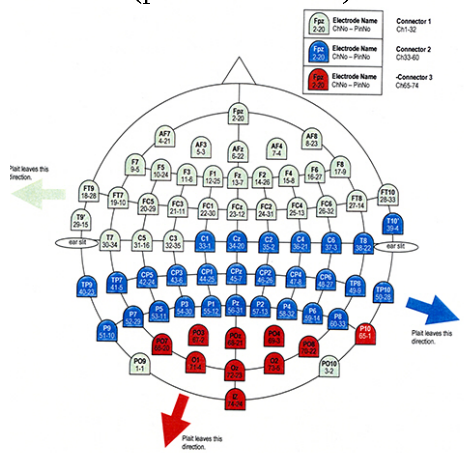


Figure 1.6. (left) Detector array, side view. Average distance between sensor elements : 34,6 mm. (right) Triple sensor detector unit.

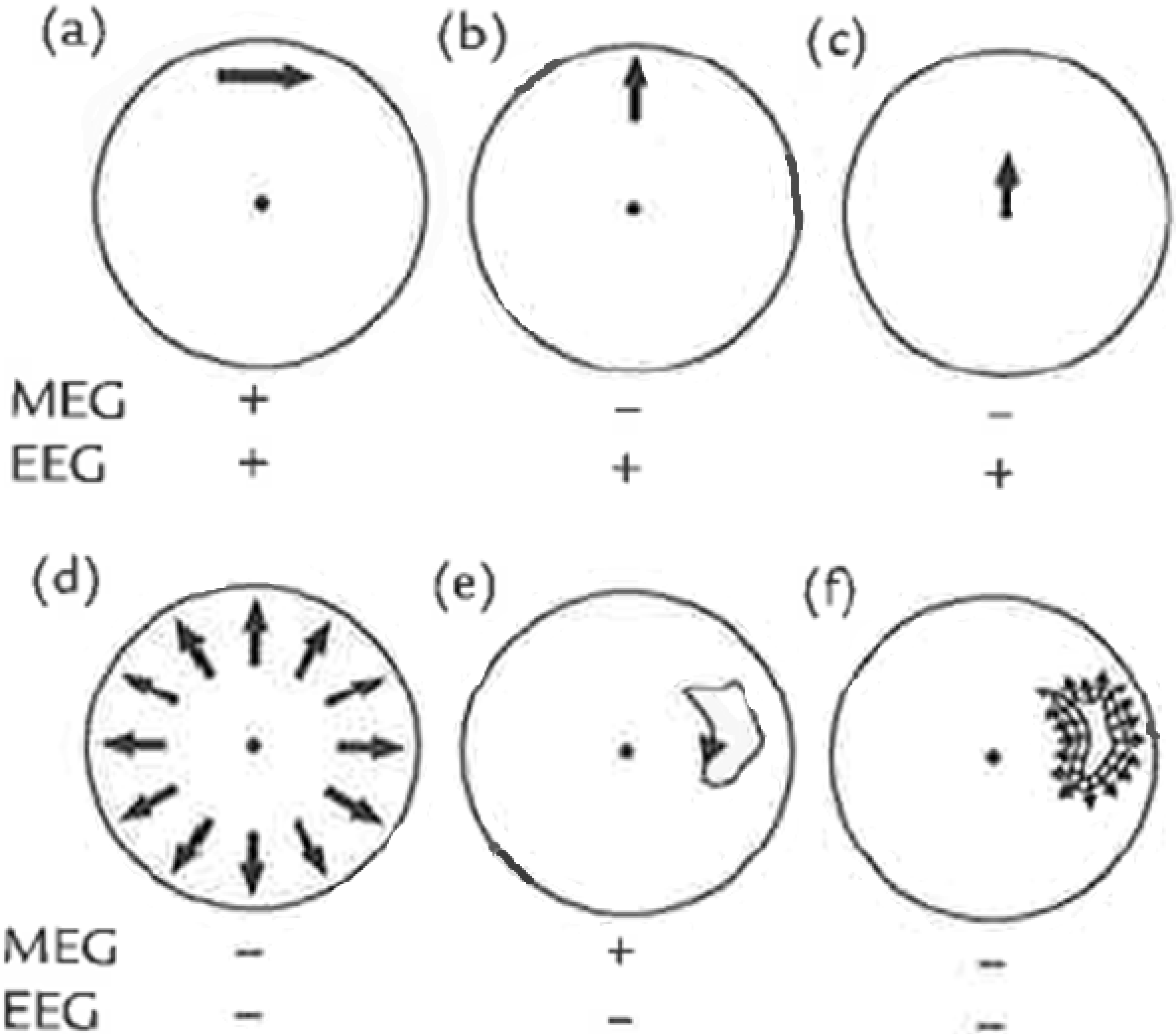
64 EEG electrodes

(plus EOG/ECG)



http://imaging.mrc-cbu.cam.ac.uk/meg/VectorviewDescription

EEG and MEG Are Differentially Sensitive To Radial and Tangential Sources



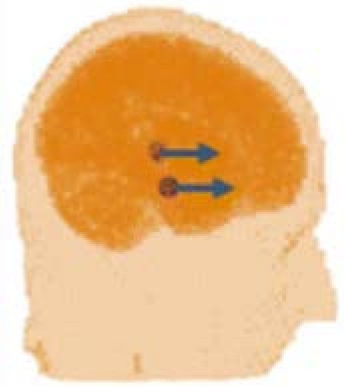
MEG is relatively insensitive to radial sources, and therefore also to deep sources.

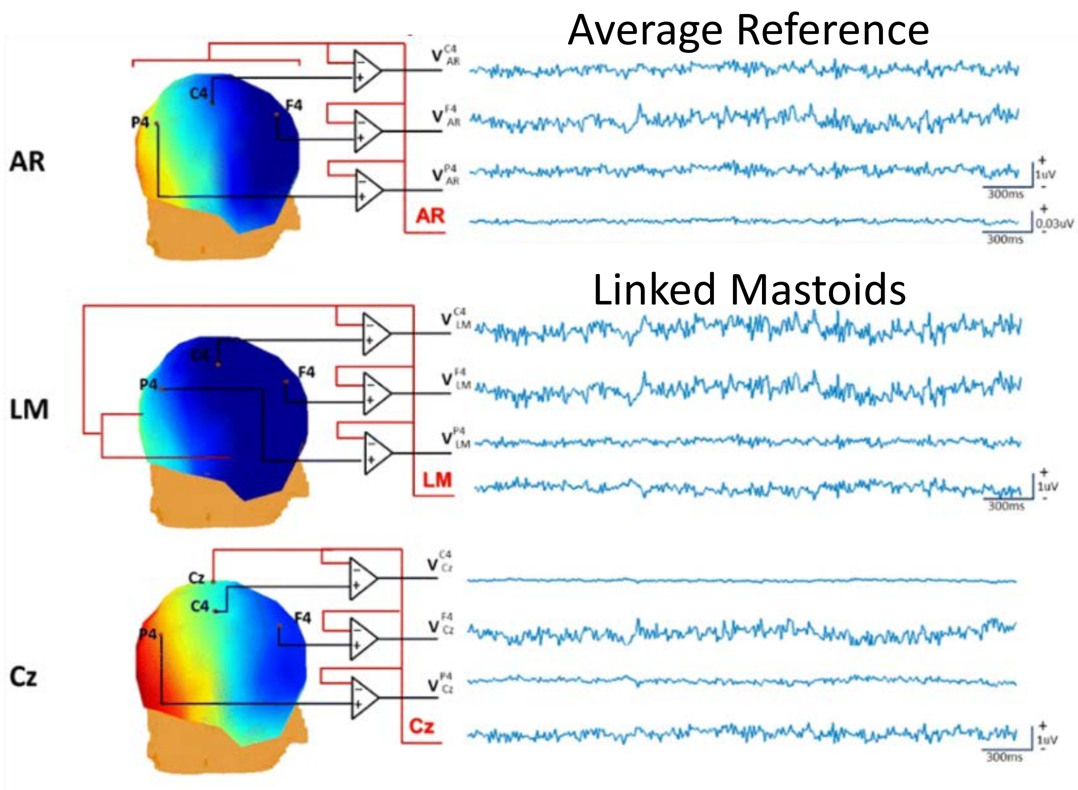
Some complex source distributions may not produce either EEG or MEG signals (“invisible”, “null space”).

MEG-EEG Primer, Hari & Puce, OUP 2017

EEG only: Choice of reference site

Data from
two simulated dipoles



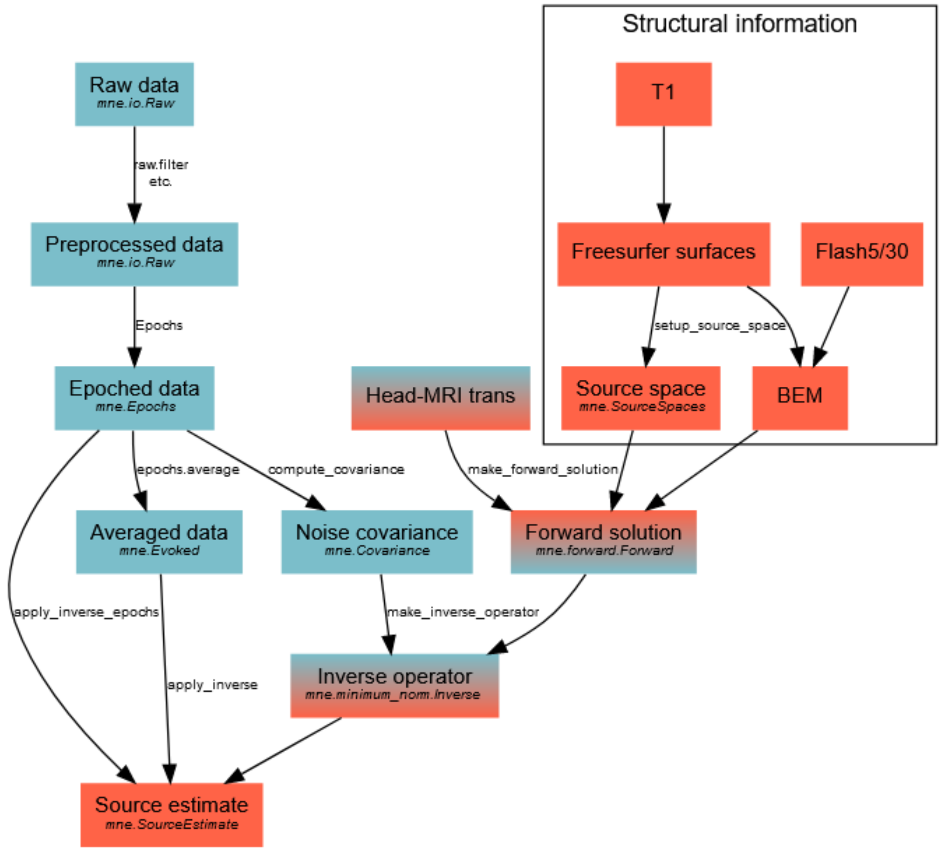


The choice of reference changes time course and topography. For high-density recordings (> 65 channels), average reference is recommended.
Note: Source estimates do not depend on the reference.

Yao et al., Brain Topography 2019

Data Pre-Processing

Typical EEG/MEG Analysis Pipeline



https://mne.tools/stable/overview/cookbook.html

Data Pre-Processing - Artefacts

Artefacts

Artefacts can be

- **non-physiological,** i.e. from outside the body (sensor-intrinsic noise, line noise, moving objects, vibrations)
  => Maxfilter (SSS), Frequency-Filtering, SSP, PCA/ICA

- **Physiological but non-brain**, e.g. eye movements, muscles
  => SSP, PCA/ICA, H/L-Filtering

- **Physiological from the brain,** i.e. brain sources that are not of interest or not included in your source model
  => choose appropriate source estimation, regularisation

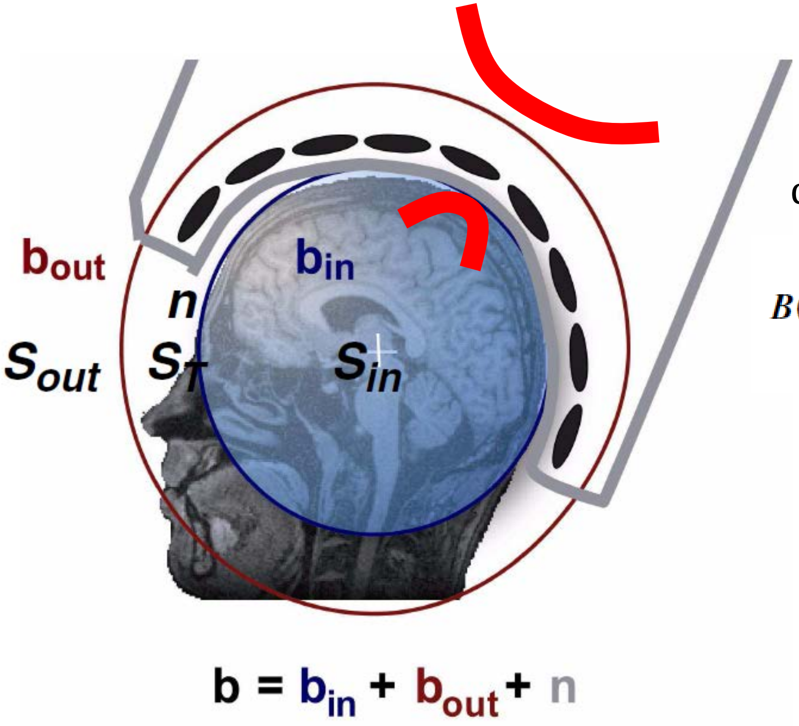
Wisdoms:

"Some people's signal is other people's noise."

Unfortunately, you cannot just choose what's signals and what's noise.

It's always better to avoid artefacts than to correct them.

Maxfilter – Suppressing Signals From Distant Sources



The mathematical basis of Maxfilter:

decomposition of magnetic field into spherical harmonics

$$B(r) = -\mu_o \sum_{n=1}^{\infty} \sum_{m=-n}^{n} \alpha_{nm} \frac{\nu_{nm}(\theta, \varphi)}{r^{n+2}} - \mu_o \sum_{n=1}^{\infty} \sum_{m=-n}^{n} \beta_{nm} r^{n-1} \omega_{nm}(\theta, \varphi).$$

$$\nu_{nm}(\theta, \varphi) = -(n+1) Y_{nm} e_r + \frac{\partial Y_{nm}}{\partial \theta} e_\theta + \frac{im Y_{nm}}{\sin\theta} e_\varphi,$$

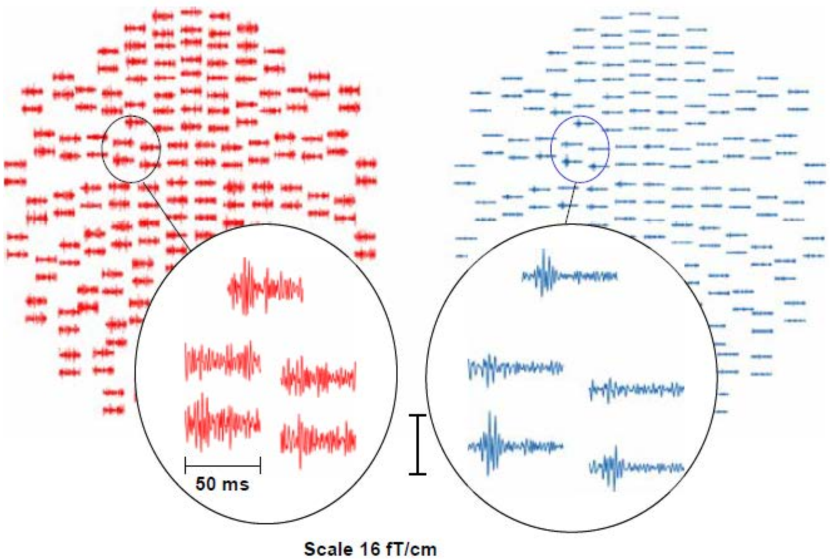
$$\omega_{nm}(\theta, \varphi) = n Y_{nm} e_r + \frac{\partial Y_{nm}}{\partial \theta} e_\theta + \frac{im Y_{nm}}{\sin\theta} e_\varphi,$$

The measured magnetic field distribution is decomposed into “inside” (the helmet) and “outside” components, and the outside components are removed.

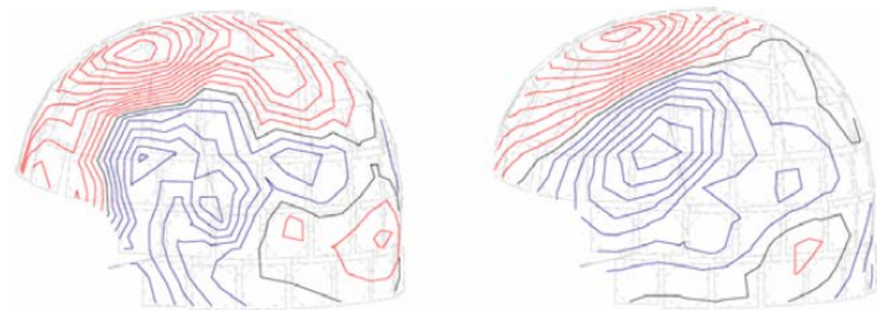
Taulu & Kajola, Journal of Applied Physics 2005

Maxfilter

Without With



Without With



Original Field Map

SSS Reconstructed Field Map

Latency 20 ms
Q = 2 nAm

Taulu & Kajola, Journal of Applied Physics 2005

Maxfilter

http://imaging.mrc-cbu.cam.ac.uk/meg/Maxfilter_V2.2

Software shielding (Signal Space Separation, SSS)
By subtracting the outer SSS components from measured signals, the program suppresses artifacts from distance sources.

Automated detection of bad channels
By comparing the reconstructed sum with measured signals, the program can automatically detect if there are MEG channels with bad data that need to be excluded from Maxwell-filtering.

Spatio-temporal suppression of artifacts ("-st")
By correlation the time courses of SSS artefact components with the cleaned signal, the program can identify and suppress further artefacts that arise close to the sensor array.

Notch Filter to remove 50Hz line noise.

Transformation of MEG data between different head positions ("-trans")
By transforming the inner components into harmonic amplitudes (i.e. virtual channels), MEG signals in a different head position can be estimated easily.

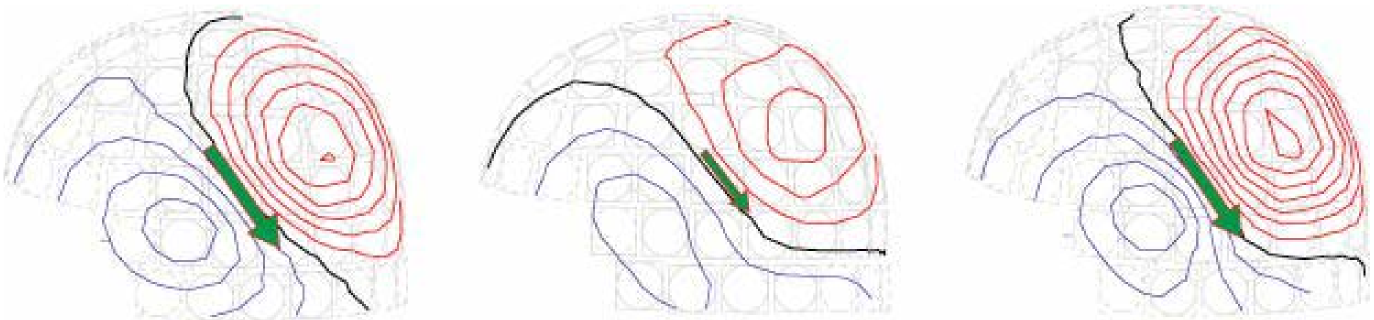
Compensation of disturbances caused by head movements ("-movecomp")
By extracting head position indicator (HPI) signals applied continuously during a measurement, the data transformation capability is utilized to estimate the corresponding MEG signals in a static reference head position.

Maxfilter – Movement Compensation

Head movement is tracked continuously (well, every 200 ms) via HPI (Head Position Indicator) coils.

We can take Maxfilter parameters from any time point t,
and estimate the MEG signals at sensor positions of time point t_0.

This compensates – to some degree – for spatial variation caused by head movements.



Stable subject

Moving subject,
No compensation

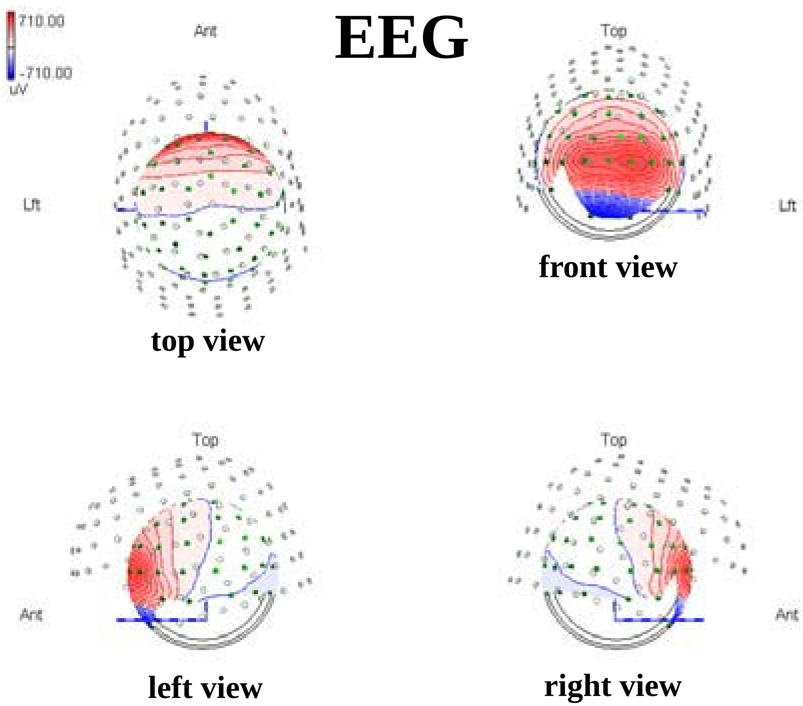
Moving subject,
with compensation

Elekta Neuromag

Common Artefacts: Eye Blinks

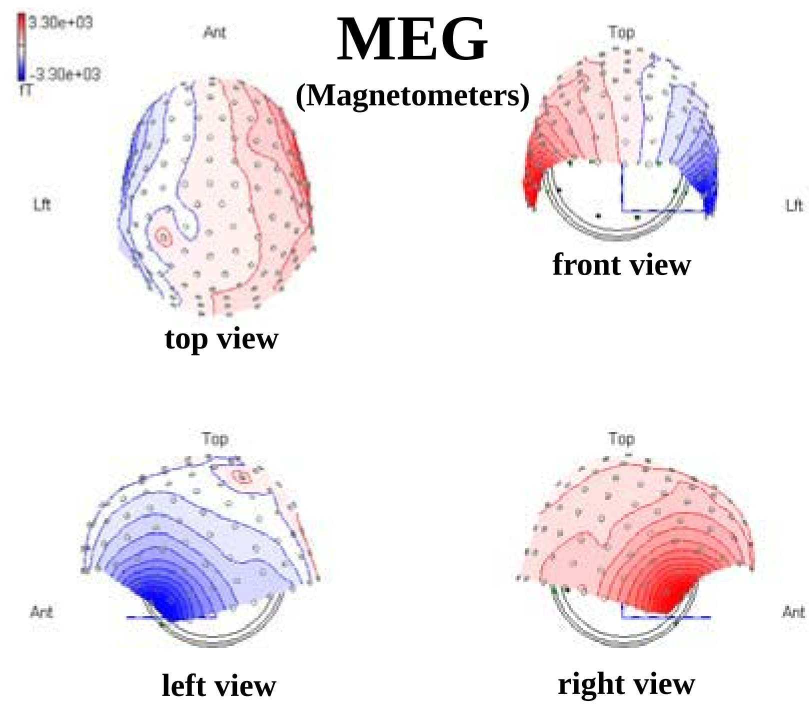
Affects EEG and MEG

EEG



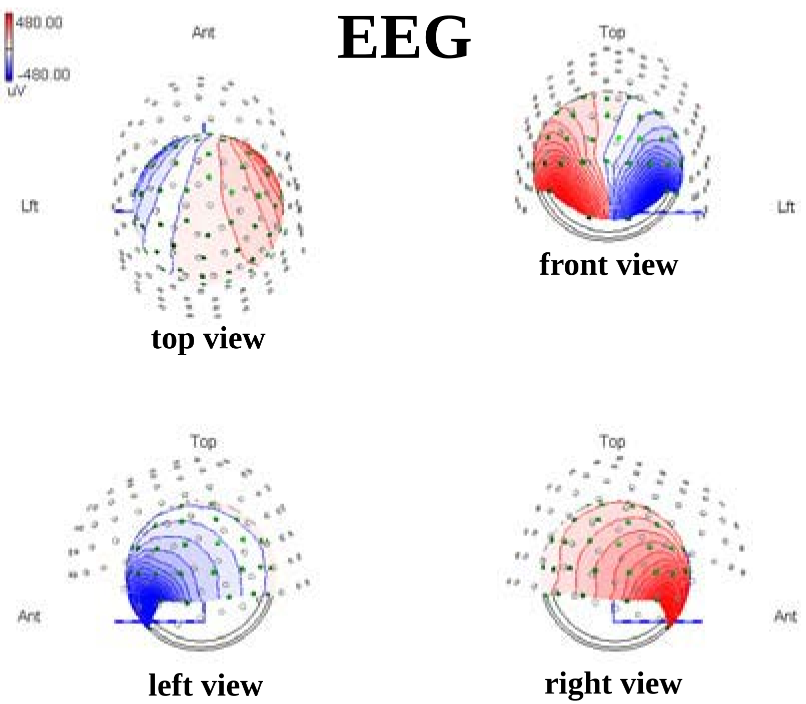
MEG

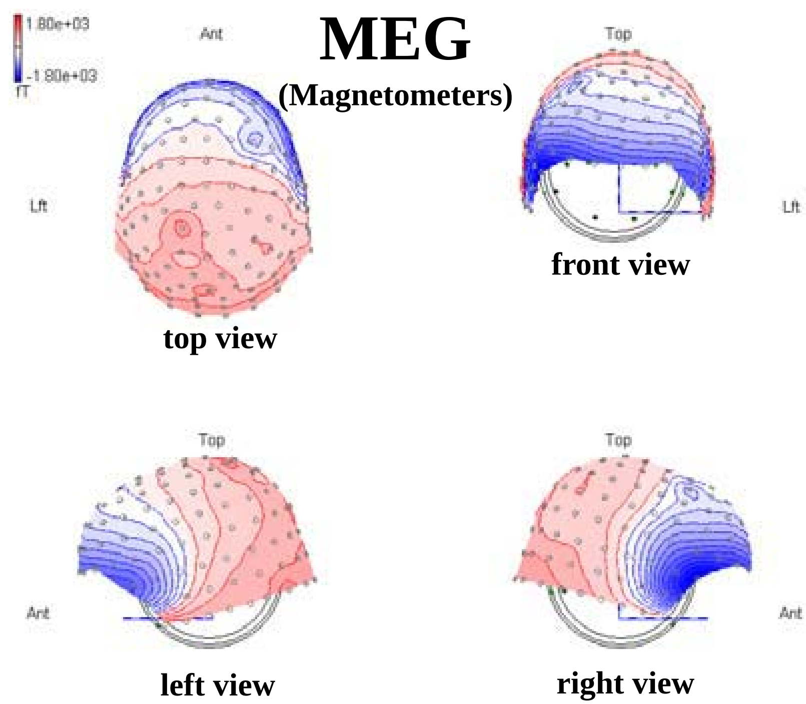
(Magnetometers)



Common Artefacts: Eye Movement to the Right

Affects EEG and MEG

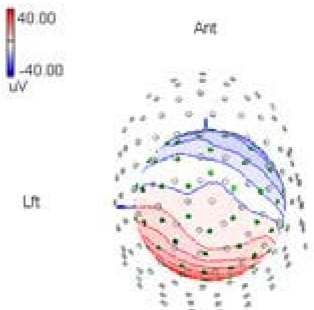




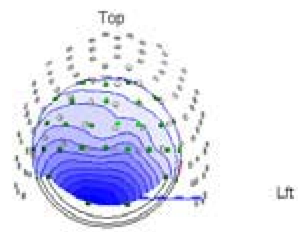
Common Artefacts: Heart Beat

Affects EEG and MEG

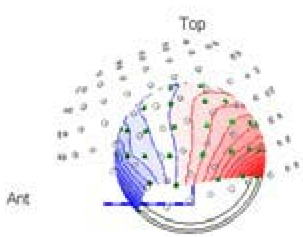
EEG



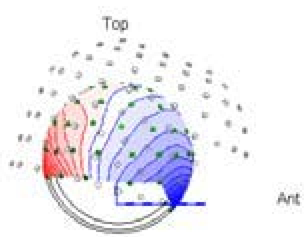
top view



front view

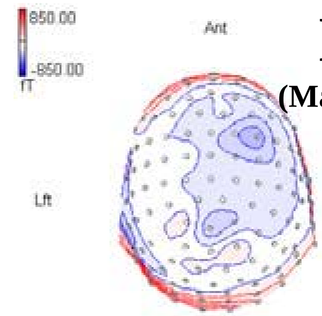


left view

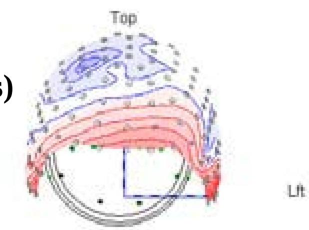


right view

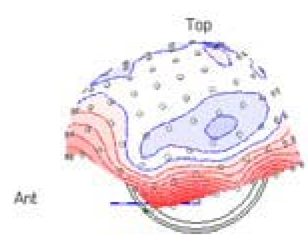
MEG
(Magnetometers)



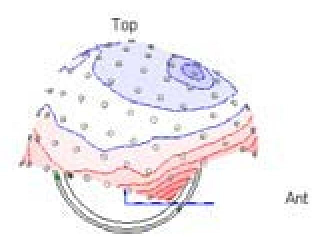
top view



front view



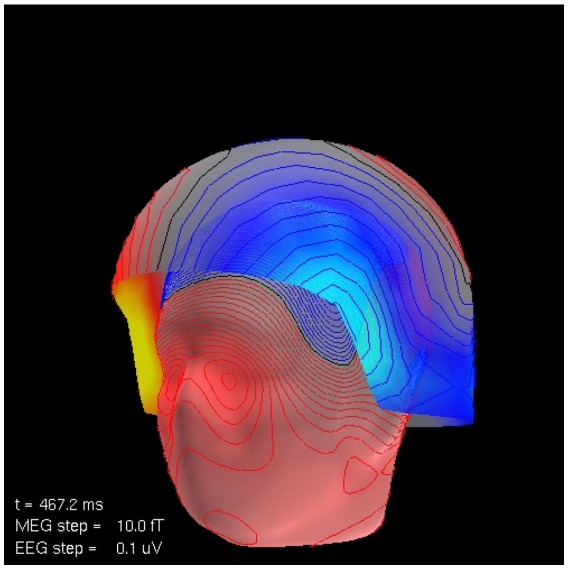
left view

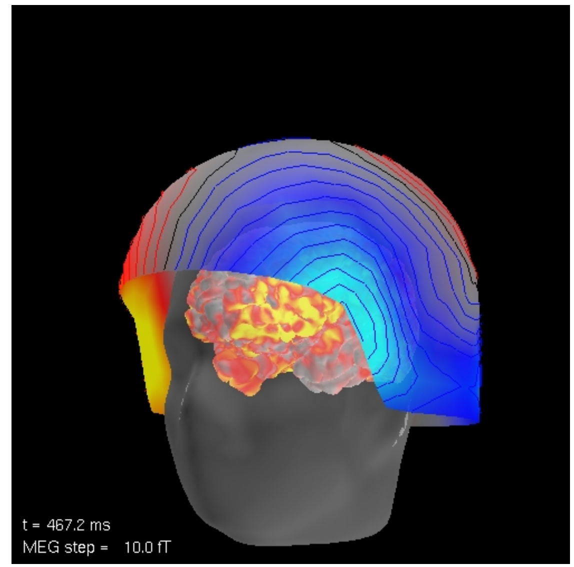


right view

Artefacts in EEG and MEG
Will End Up in Source Space

Example: Eye Blink





This will affect all source estimation methods.
=> Get rid of your artefacts beforehand,
especially when they may vary systematically with your variables of interest.

Separating Signal and Noise Components

If signal and noise have characteristic topographies, several methods can be applied to remove (some) noise or extract signals:

- SSP: Signal Space Projection (needs pre-defined topographies)

The following often go under the term “blind source separation”, because the topographies are not pre-defined, and found by the methods themselves (under certain assumptions):

- PCA: Principal Component Analysis
- SVD: Singular Value Decomposition
- ICA: Independent Component Analysis

Signal Space Projection (SSP)

You know the artefact topography **A** and regress it out of your data.

You decompose your data **D**, such that

D = a***A** + **Signal**

You only analyse **Signal.**

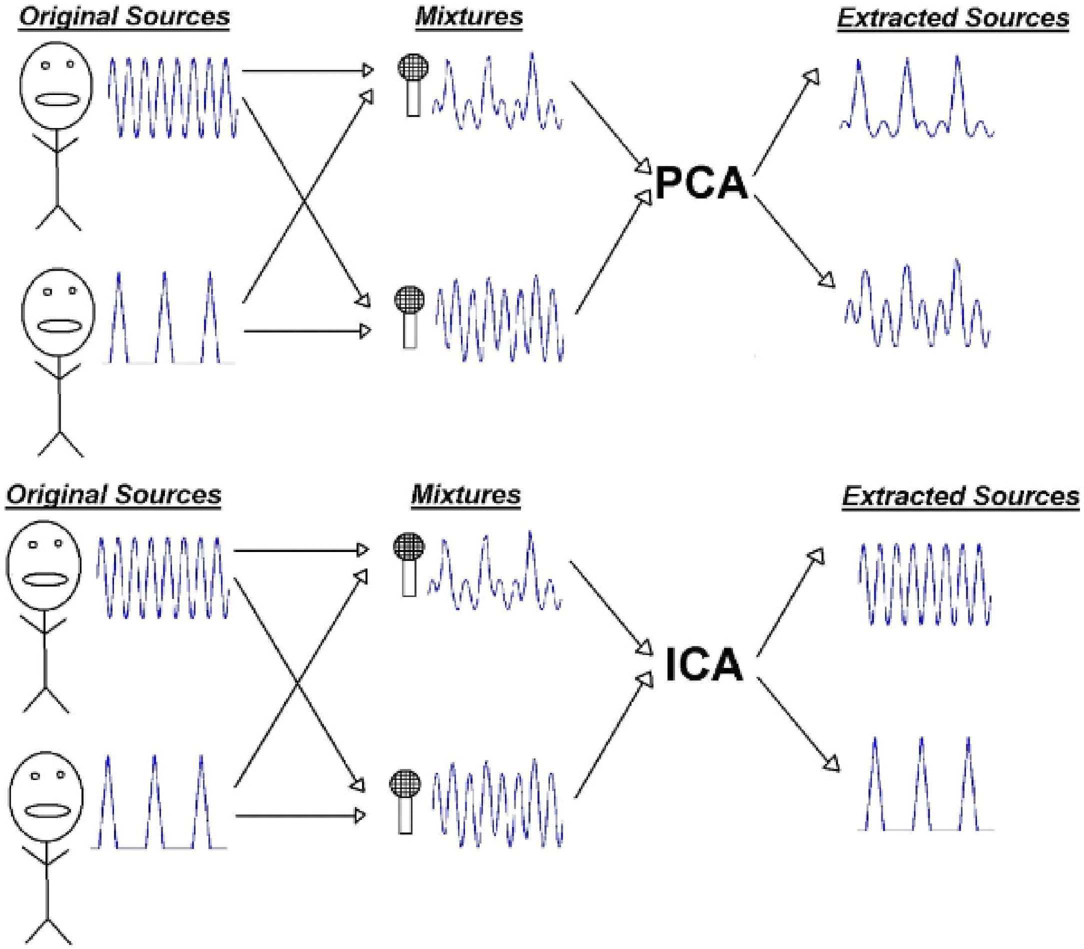
This works well with eye-movement and blink artefacts.

Note:

Brain signals whose topographies are highly correlated with **A** will also be removed or attenuated.

Independent Component Analysis

Example: (De-)mixing of sources in the cocktail party effect



http://www.tqmp.org/Content/vol06-1/p031/p031.pdf

Independent Component Analysis

Basic idea is similar to PCA and SVD:

Decompose data into components $\mathbf{T}_1$, $\mathbf{T}_2$, etc. (topographies or time courses),

i.e. data $\mathbf{D} = a*\mathbf{T}_1 + b*\mathbf{T}_2 + \ldots$

But:

- ICA does not produce orthogonal components, and does not assume Gaussianity of signals.
- There are number of ICA algorithms available that have been optimised for EEG/MEG data.

  They usually work well to remove eye movement and heart beat artefacts.
- Check what type of artefacts are relevant to you – if there aren't any you may not need ICA.

Data Pre-Processing
Frequency and Time-Domain Filtering

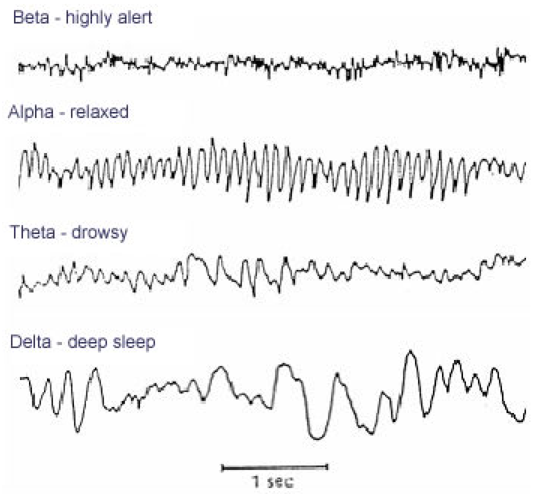
MRC

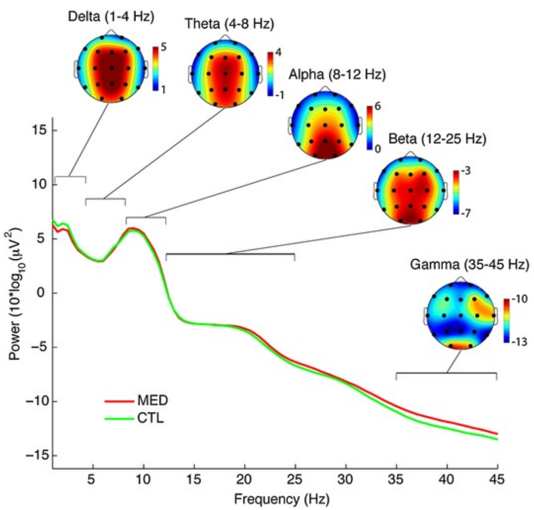
Cognition and Brain Sciences Unit

Frequency Spectrum of EEG Data

Time course and topography may differ among different frequency bands

(and may depend on task, environment, subject group etc.)

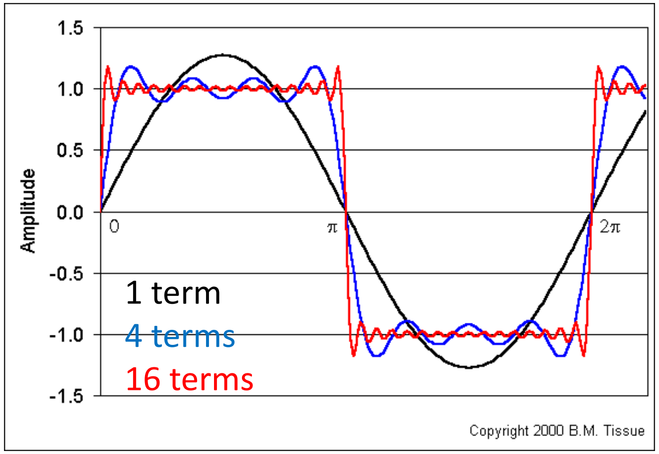




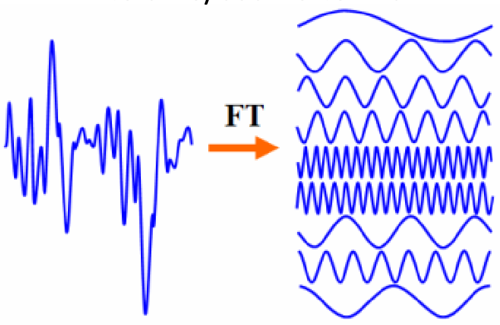
Cahn et al., Cogn Proc 2010,
http://link.springer.com/article/10.1007%2Fs10339-009-0352-1/

Time-Domain Signals Can Be Represented in the Frequency Domain - and Vice Versa

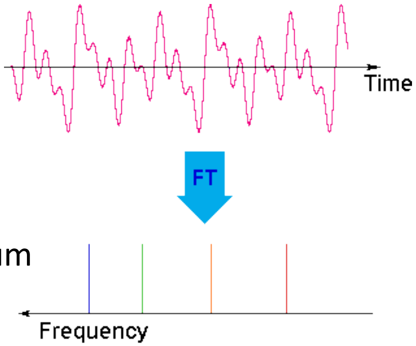
Approximating a step function with Fourier terms



Decomposing signals into sine/cosine terms



Frequency Spectrum



Basic Principals of Frequency Filtering

If you signals of interest and artefacts occur in separate frequency bands:

- Decompose your signal into its frequency spectrum
- Remove the part of the frequency spectrum that represents artefacts
- Recompose your time domain signal from the remaining frequency spectrum

Examples:

- Line Noise from electrical equipment (50 or 60 Hz): Notch filter
- Muscle artefacts are commonly high frequency (> 30 Hz): Low-pass filter

Basic Principals of Frequency Filtering

Filtering changes the time course of your data. Thus:

“Filter as much as necessary but as little as possible.”

Common types of filters:

“High-pass”: Lets higher frequencies pass, suppressses lower frequencies (incl. “detrending”)

“Low-pass”: Lets lower frequencies pass, removes higher frequencies

“Band-pass”: Lets frequencies within a frequency band pass, suppresses frequencies above and below the band

“Notch” filter: A very sharp band-pass filter, e.g. for 50 or 60 Hz line noise

(e.g. Cheveigen & Nelken, Neuron 2019, https://www.sciencedirect.com/science/article/pii/S0896627319301746), Widmann et al., Journal of Neuroscience Methods 2015, https://www.sciencedirect.com/science/article/pii/S0165027014002866, Tanner et al., Psychophysiology 2016, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4506207/).

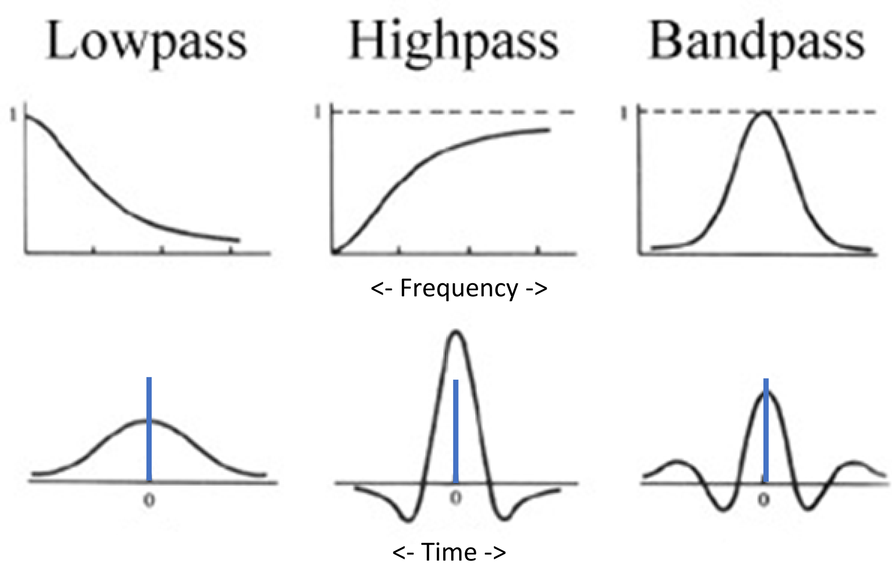
Basic Principals of Frequency Filtering

Time-domain and frequency-domain filtering are two sides of the same coin:

One type of frequency-domain filtering corresponds to one type of time-domain filtering.

Frequency domain

Time domain

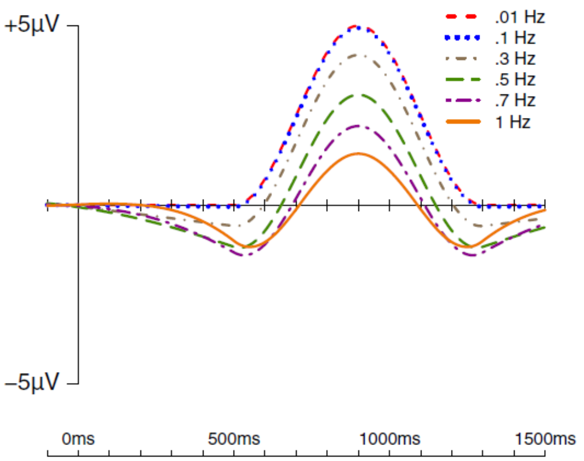


https://uk.mathworks.com/matlabcentral/fileexchange/51155-time-domain-filtering-vs-frequency-domain-filtering-in-images

Filtering can affect both signal and artefact

High-pass filtering:

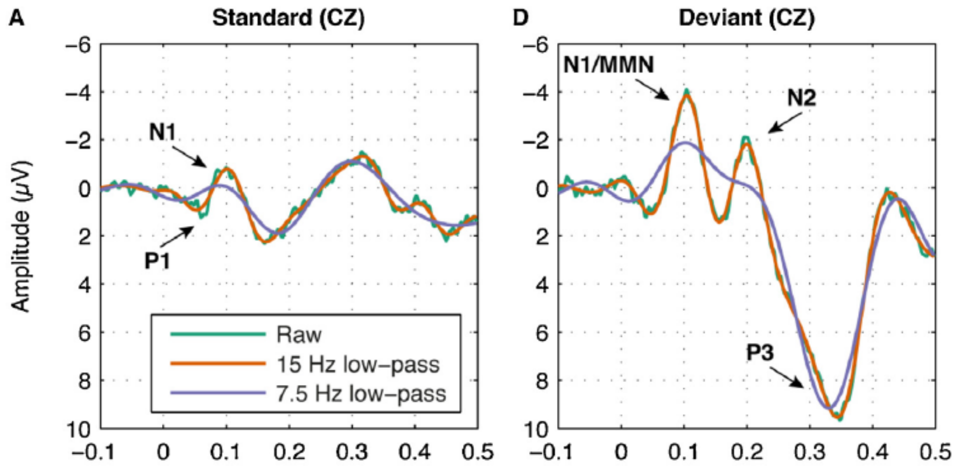
"(linear/polynomial) Detrending"
"Removing slow drifts"



Tanner et al., Psychophysiology 2016,
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4506207

Low-pass filtering:

"Smoothing"

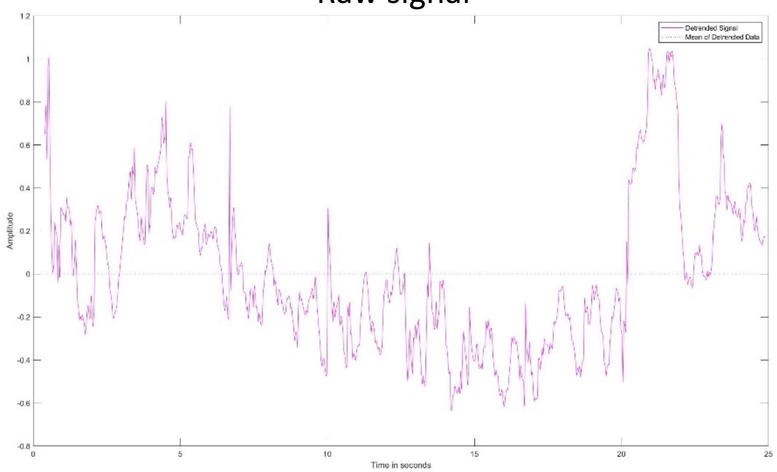


Widmann et al., Journal of Neuroscience Methods 2015,
https://www.sciencedirect.com/science/article/pii/S0165027014002866

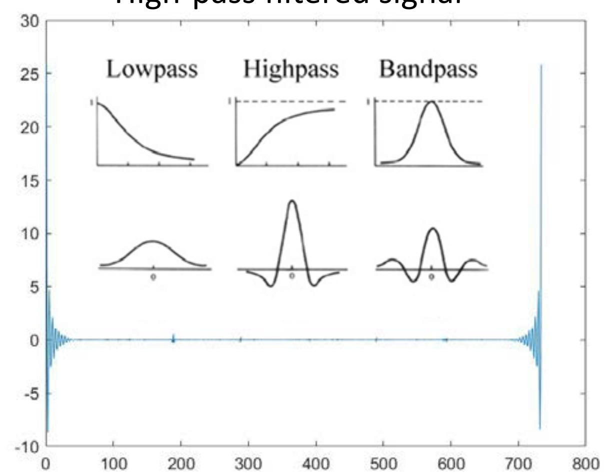
Edge Artefacts of Filters

- Filtering artefacts occur at signal discontinuities, e.g. at the beginning and the end of the data.
- Thus, filter the “longest possible data segment”, ideally the raw data as early as possible.
- If you have to filter epochs, consider filtering longer epochs than you actually need.
- Be careful with “effects” close to the border of epochs.

Raw signal



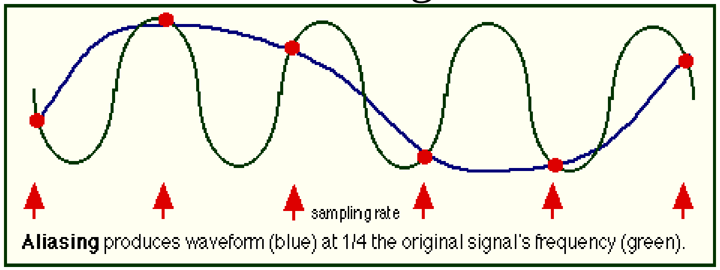
High-pass filtered signal



Filtering and Downsampling: "Aliasing"

- Downsampling can lead to "aliasing" if the data are not filtered appropriately (Nyquist theorem): Filter at least below half of the sampling frequency before downsampling.

Aliasing



Also watch:
https://www.youtube.com/watch?v=R-IVw8OKjvQ
Thanks to Alessandro.

Evoked Responses
Event-Related Potentials and Fields (ERPs and ERFs)

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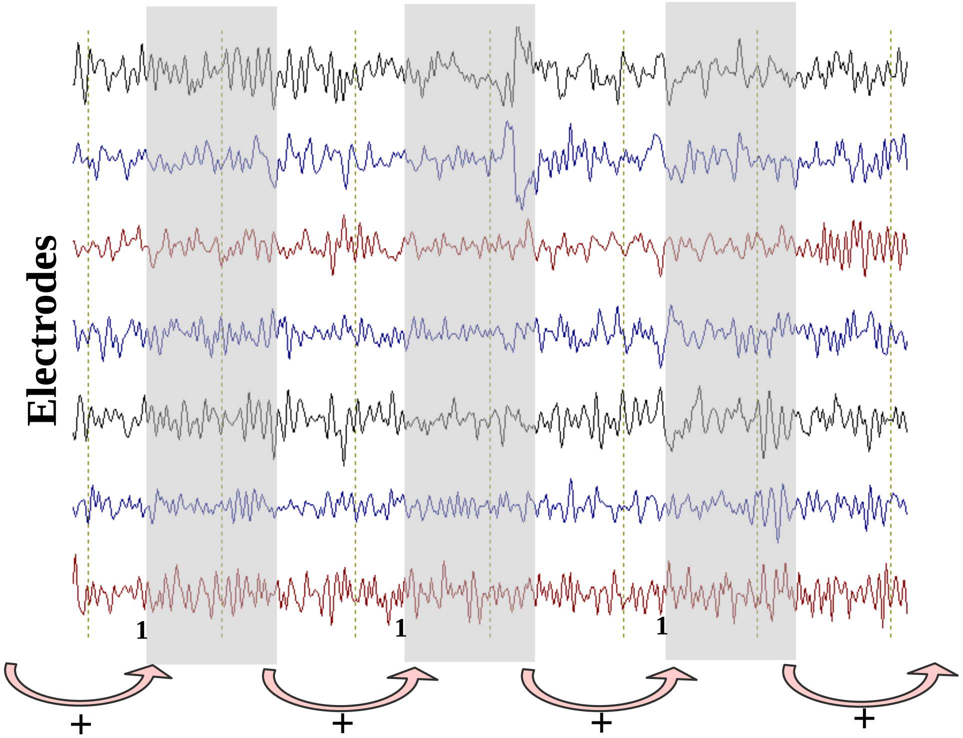
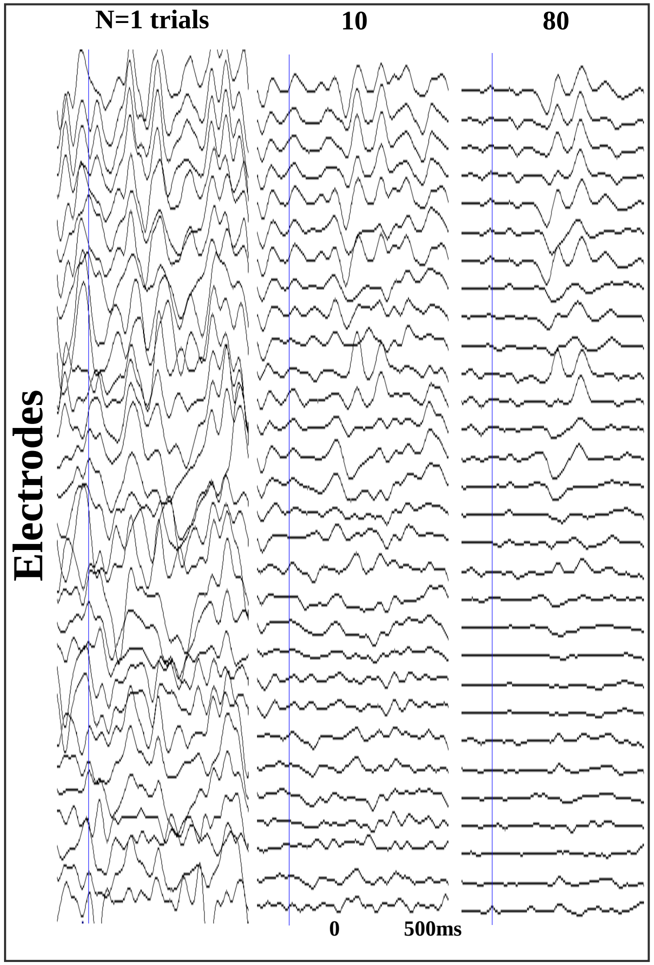
Cognition and Brain Sciences Unit

Data Averaging

Continuous "raw" data:

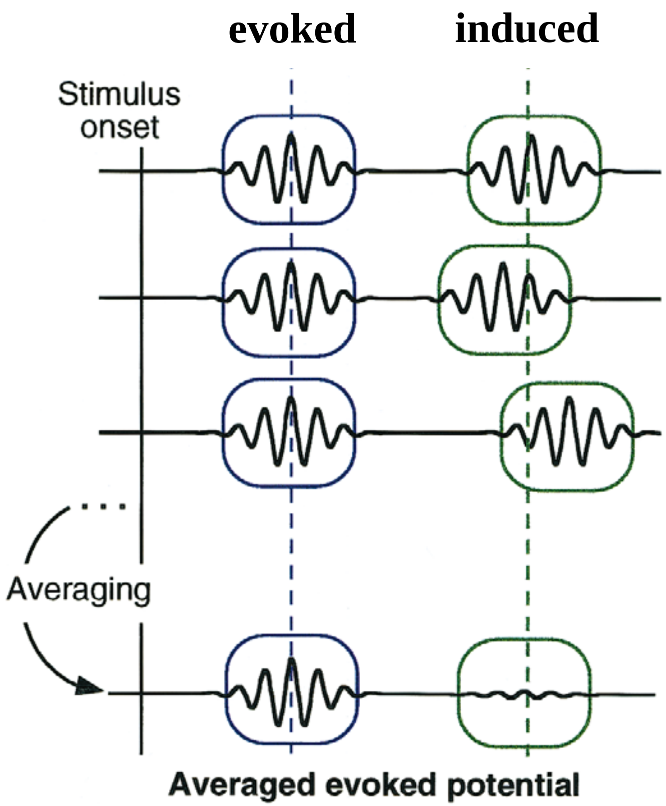


Averaged data:



http://imaging.mrc-cbu.cam.ac.uk/meg/IntroEEGMEG

Evoked and Induced Activity



Tallon-Baudry & Bertrand, TICS 1999

Temporal jitter across trials has a larger effect on higher frequencies, and they are more likely to be attenuated by averaging.

Data Averaging

The necessary number of trials depends on effect size, noise, variability across participants, your stats etc. –
the more the better if feasible.

For random noise, variance goes down with n, and standard deviation with sqrt(n).

For “one-off” artefacts, amplitude in the average goes down with n.

“Robust Averaging” procedures exist (e.g. in SPM) that weigh epochs with an estimate of their reliability (e.g. distance to mean).

Steps For Artefact Correction and Rejection

1) **Remove “chronically bad channels”** as early as possible (you can interpolate them, but see * below). They are usually identified by visual inspection.

2) Apply **spatial artefact correction**, usually ICA. Check the ICA component to make sure they capture relevant artefacts (e.g. eye blinks and heart beats).

3) Apply appropriate **frequency-/time-domain filtering**. This will depend on your specific questions – “as much as necessary, as little as possible”.

4) If averaging epochs (for ERPs, ERFs), use appropriate **artefact rejection thresholds**. Check how many epochs get rejected. If excessive, check for bad channels or systematic artefacts (eye blinks, movements).

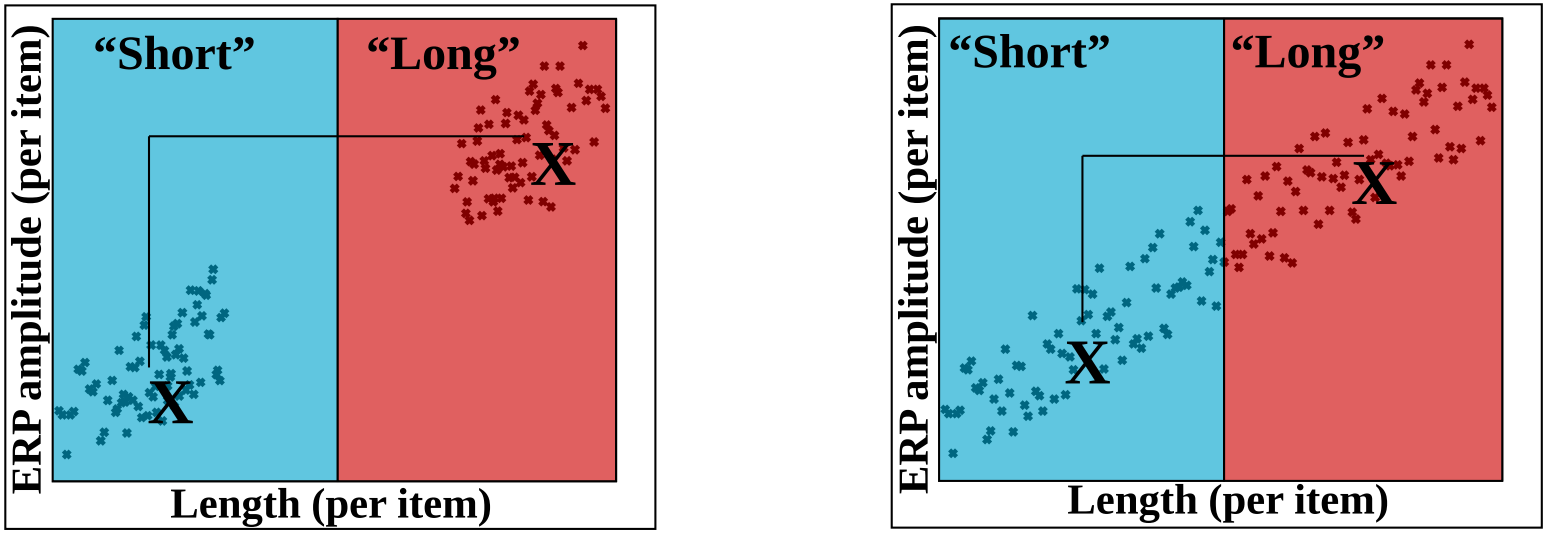
5) The proof of the pudding is in the eating: **Check data quality** by visual inspection, compute SNRs, etc.

* Interpolation does not recover information. It is not necessary if you don’t combine data across subjects in sensor space.

P.S.: There are artefact rejection methods that try to save as much data (channels, epochs) as possible, e.g. https://autoreject.github.io/stable/index.html.

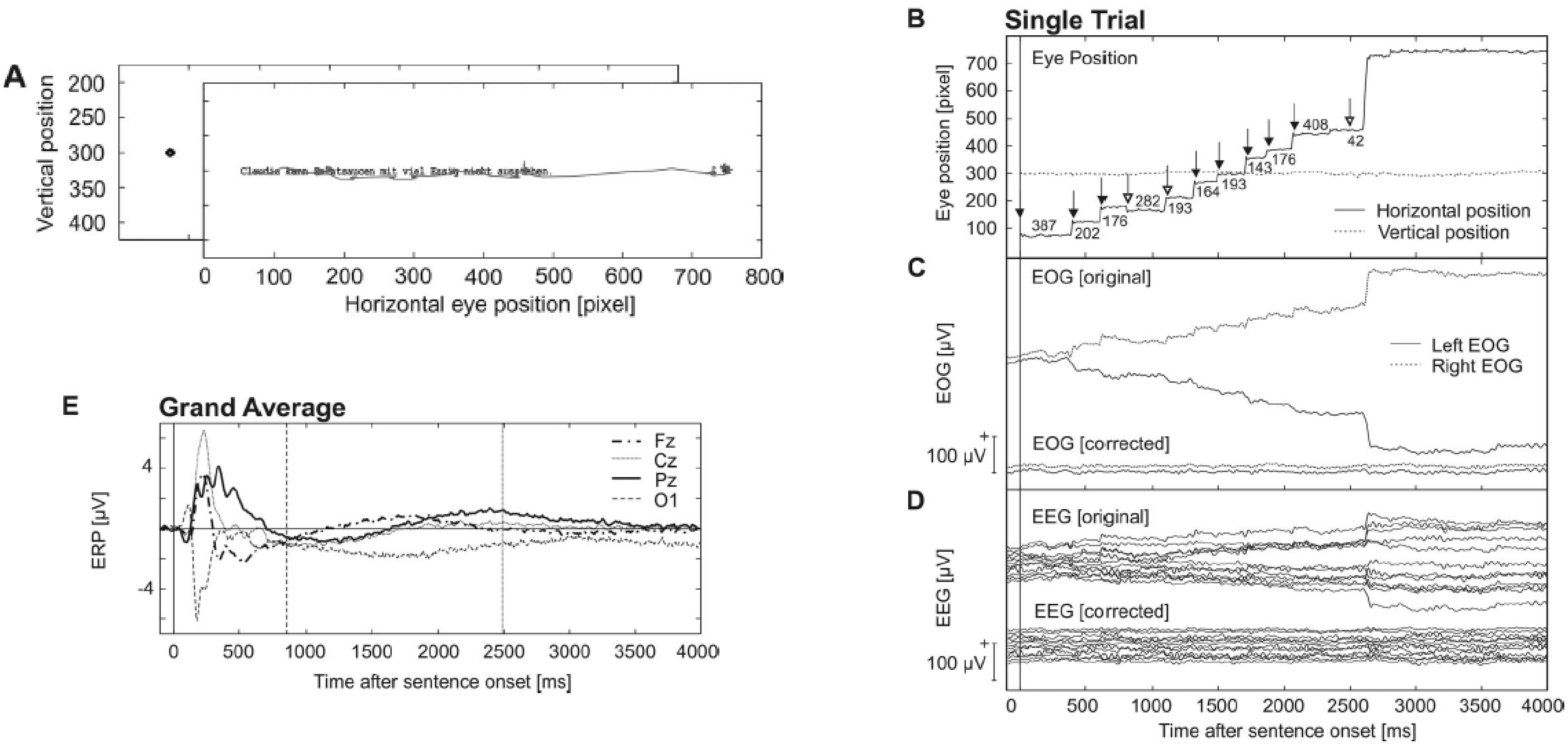
Parametric vs Factorial Designs

Consider parametric analysis/GLM if stimulus variables are continuous.
(still less common in EEG/MEG than in fMRI analysis)



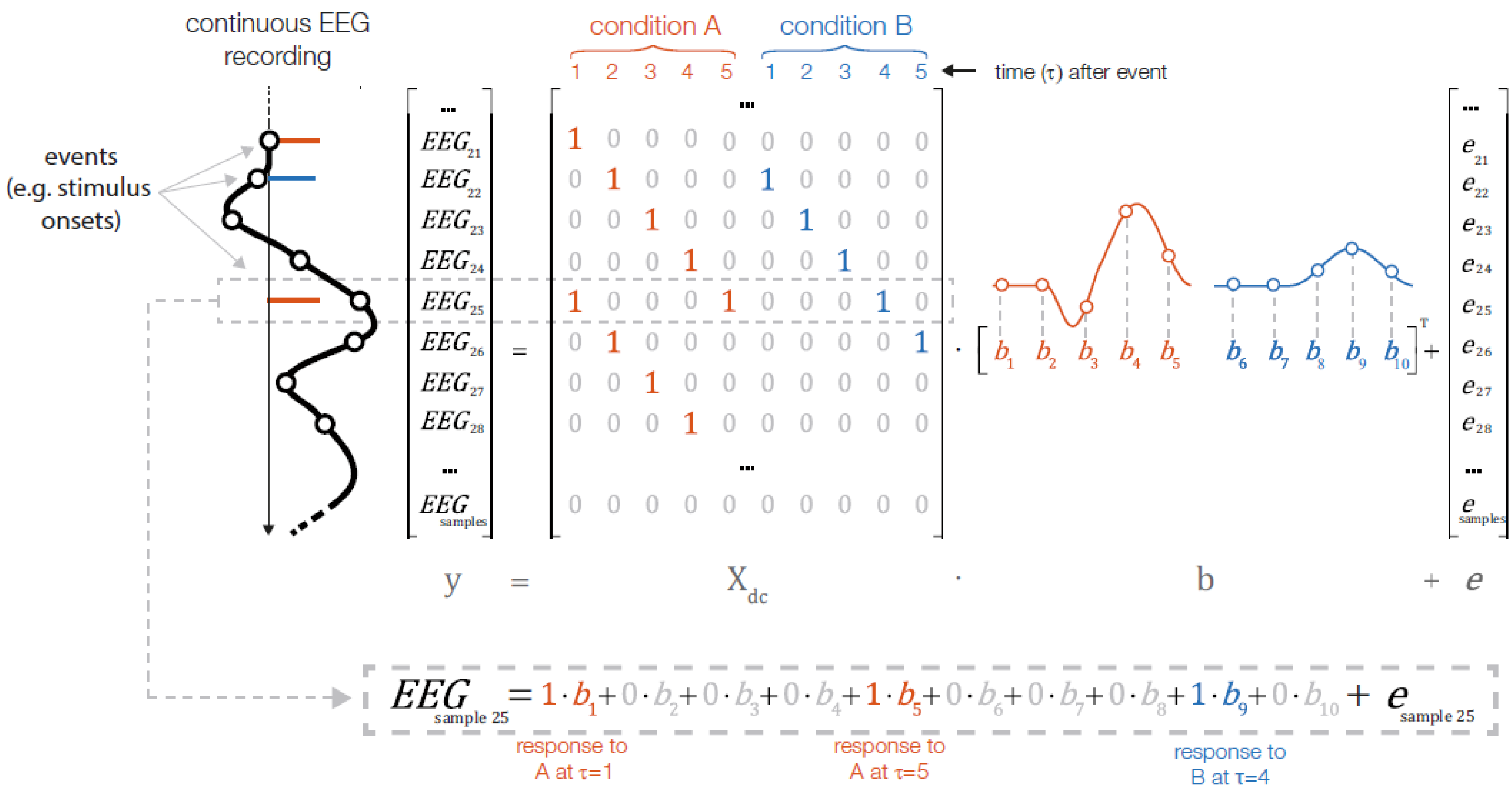
Smith & Kutas, Psychophysiol 2015a
Hauk et al., Neuroimage 2006

Naturalistic Paradigms: EEG with eye movements



Dimigen, JEP-G 2011, https://pubmed.ncbi.nlm.nih.gov/21744985/

Deconvolution of EEG signals – UNFOLD toolbox

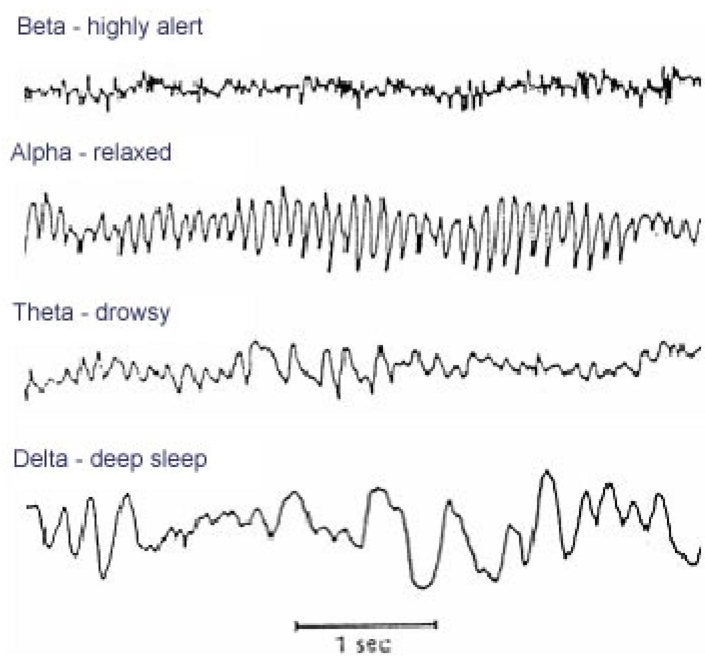


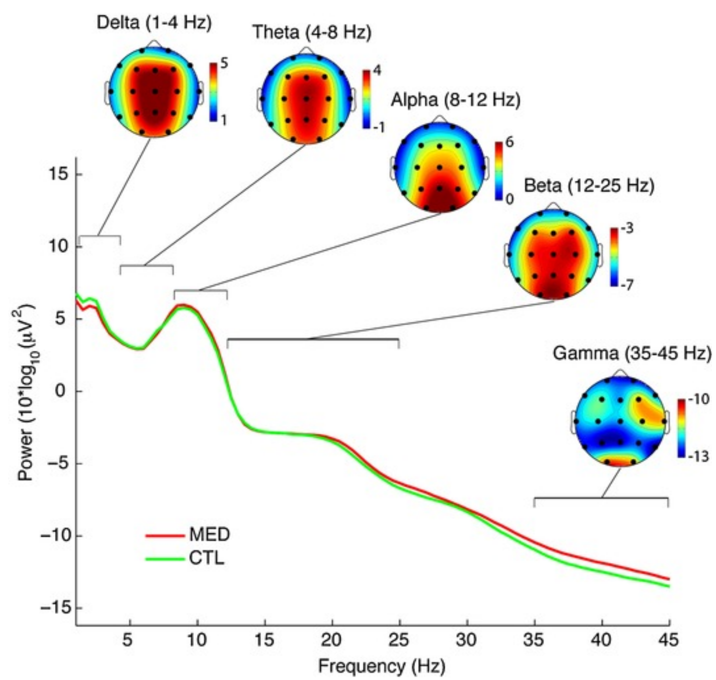
Ehinger & Dimigen, PeerJ 2019, https://www.unfoldtoolbox.org

“Brain Rhythms” and “Oscillations”

Time course and topography may differ among different frequency bands

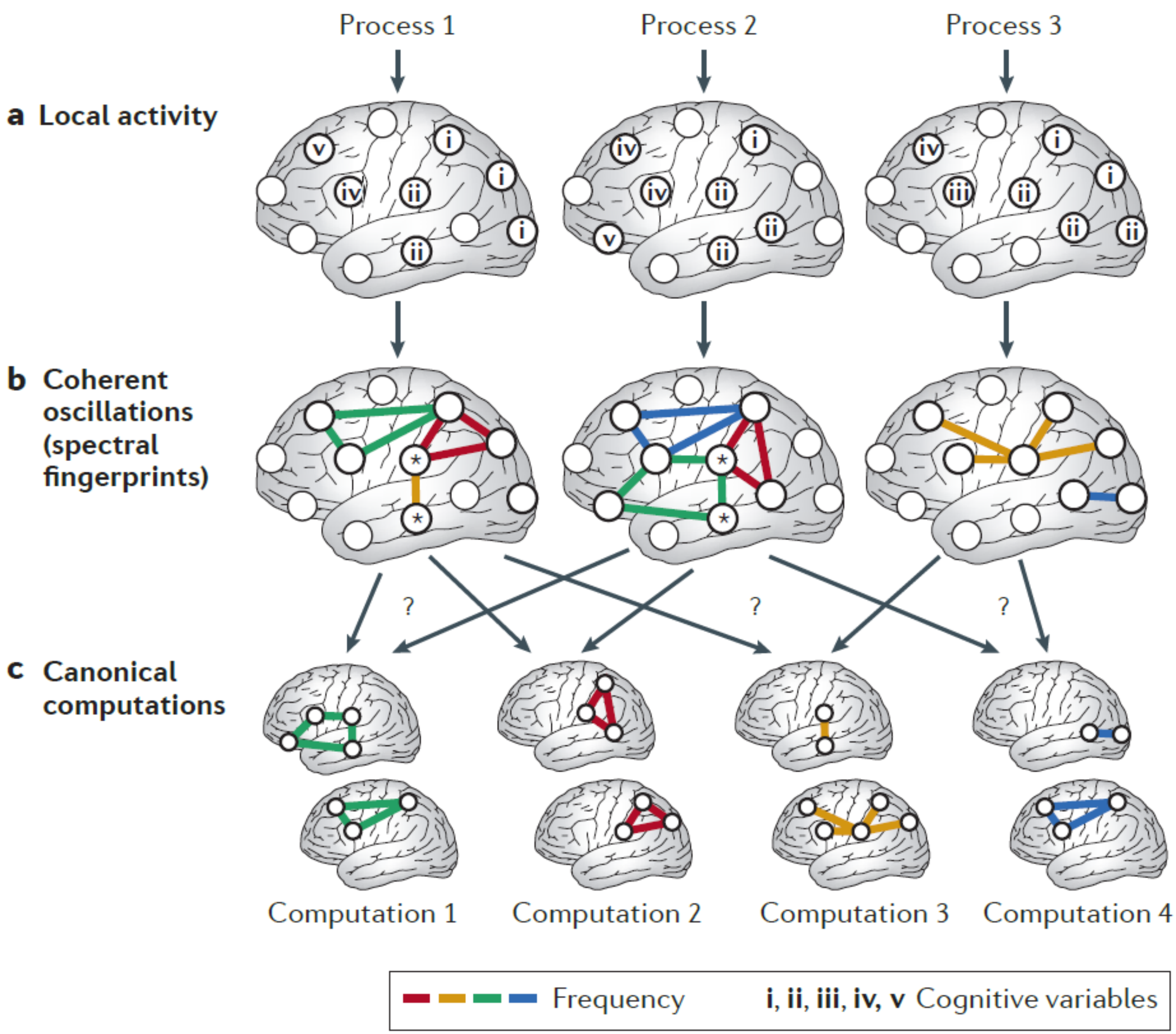
(and may depend on task, environment, subject group etc.)





http://link.springer.com/article/10.1007%2Fs10339-009-0352-1/

Brain Rhythms, Oscillations, Connectivity



Siegel et al., Nat Nsc 2012

How To Do It

There are quite a few **open-source** options, see e.g.:
http://www.biomagcentral.org/resources/tools.html

Special Issue:

"From raw MEG/EEG to publication: how to perform MEG/EEG group analysis with free academic software"

https://www.frontiersin.org/research-topics/5158/from-raw-megeeg-to-publication-how-to-perform-megeeg-group-analysis-with-free-academic-software#articles

Resources:

Biomag Central: http://www.biomagcentral.org/

MEG-UK website: https://meguk.ac.uk/

Thank you – see you later!

Please don't forget to provide feedback: