MRC Cognition and Brain Sciences Unit
75th ANNIVERSARY 1944 - 2019
UNIVERSITY OF CAMBRIDGE

EEG/MEG 1:

Measurement, Pre-Processing and Data Reviewing

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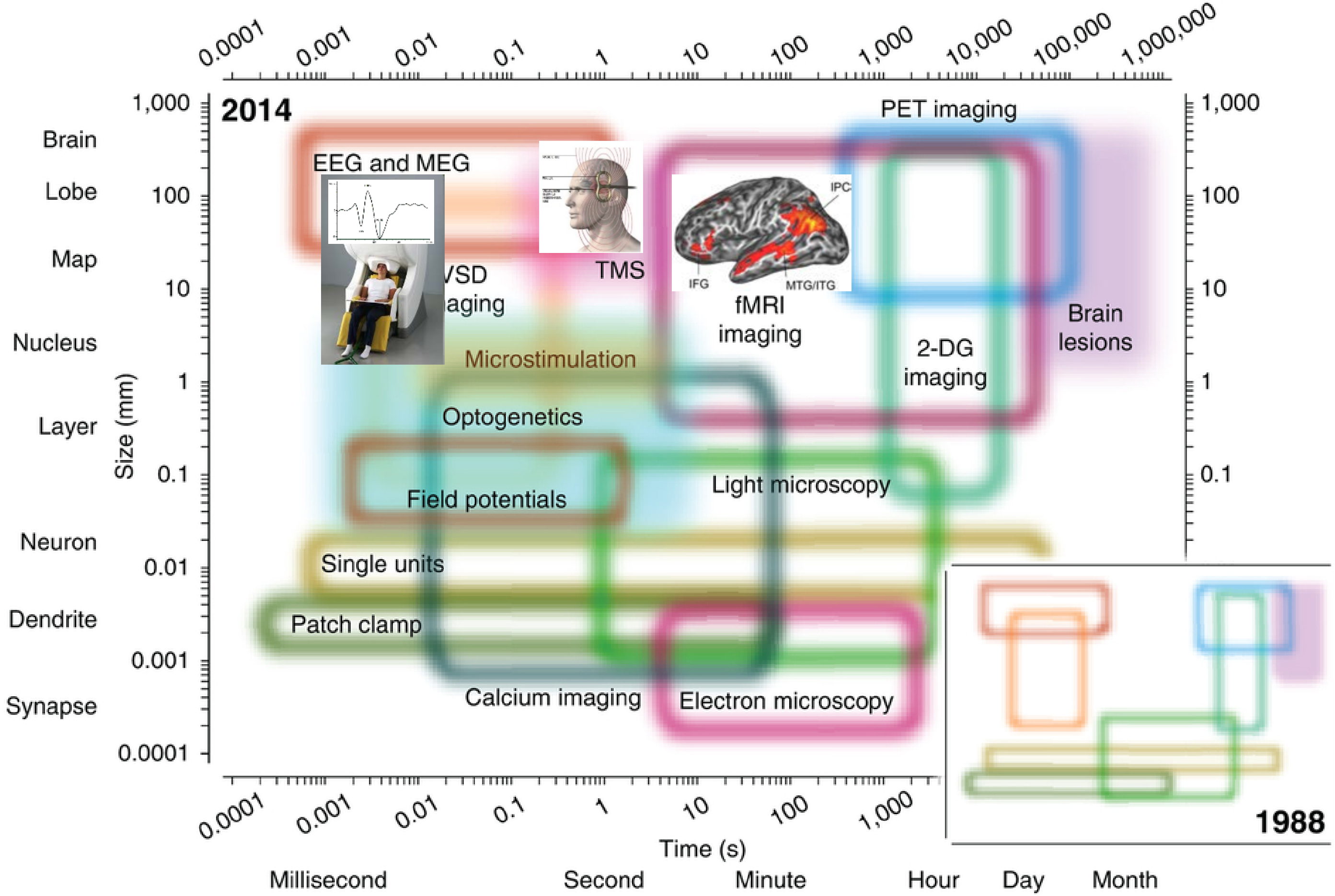
Introduction to Neuroimaging Methods, 25.1.2021

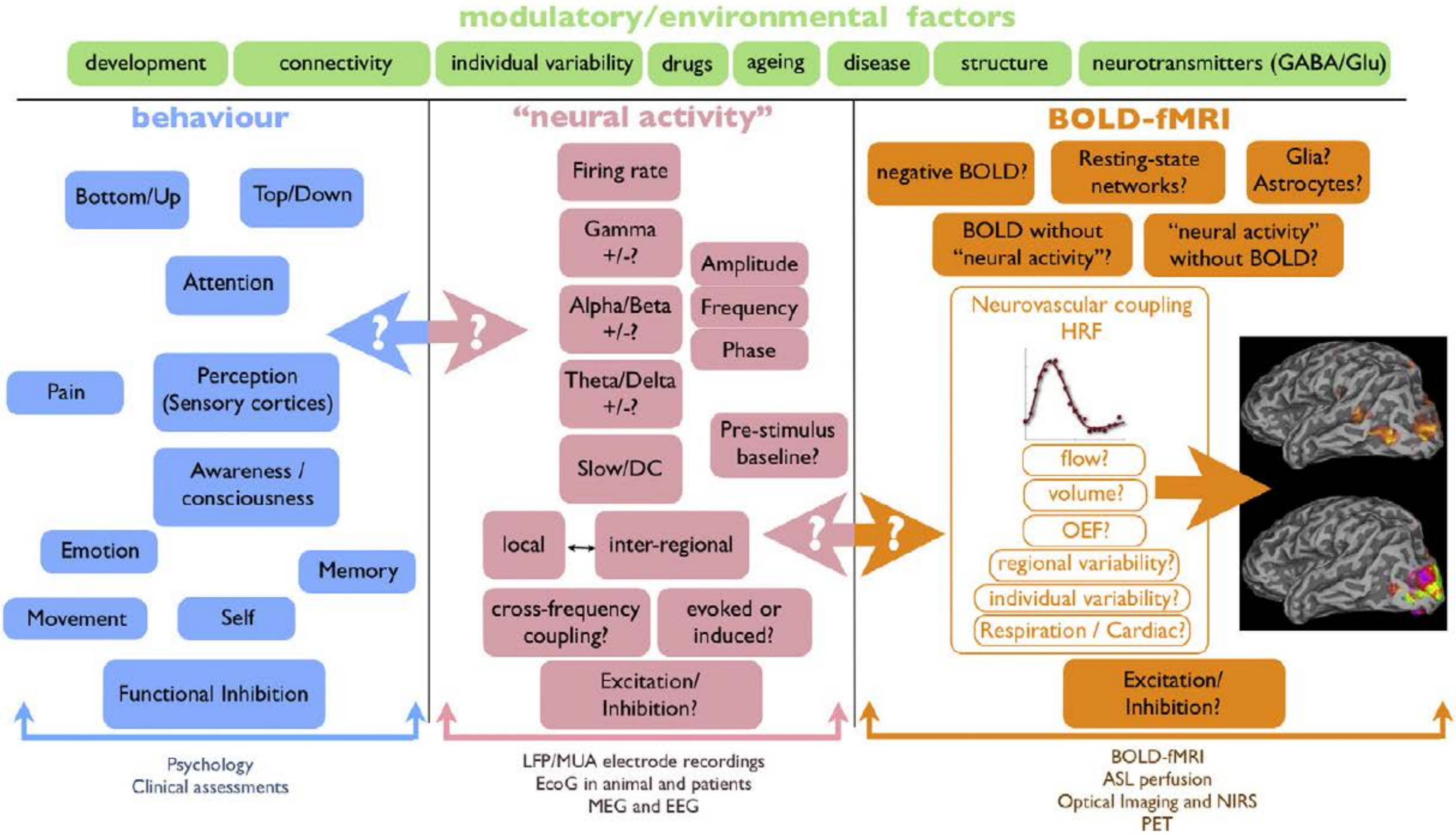
Neuroimaging Methods Vary With Respect To Spatial and Temporal Resolution

(and their invasiveness, physiology, etc.)



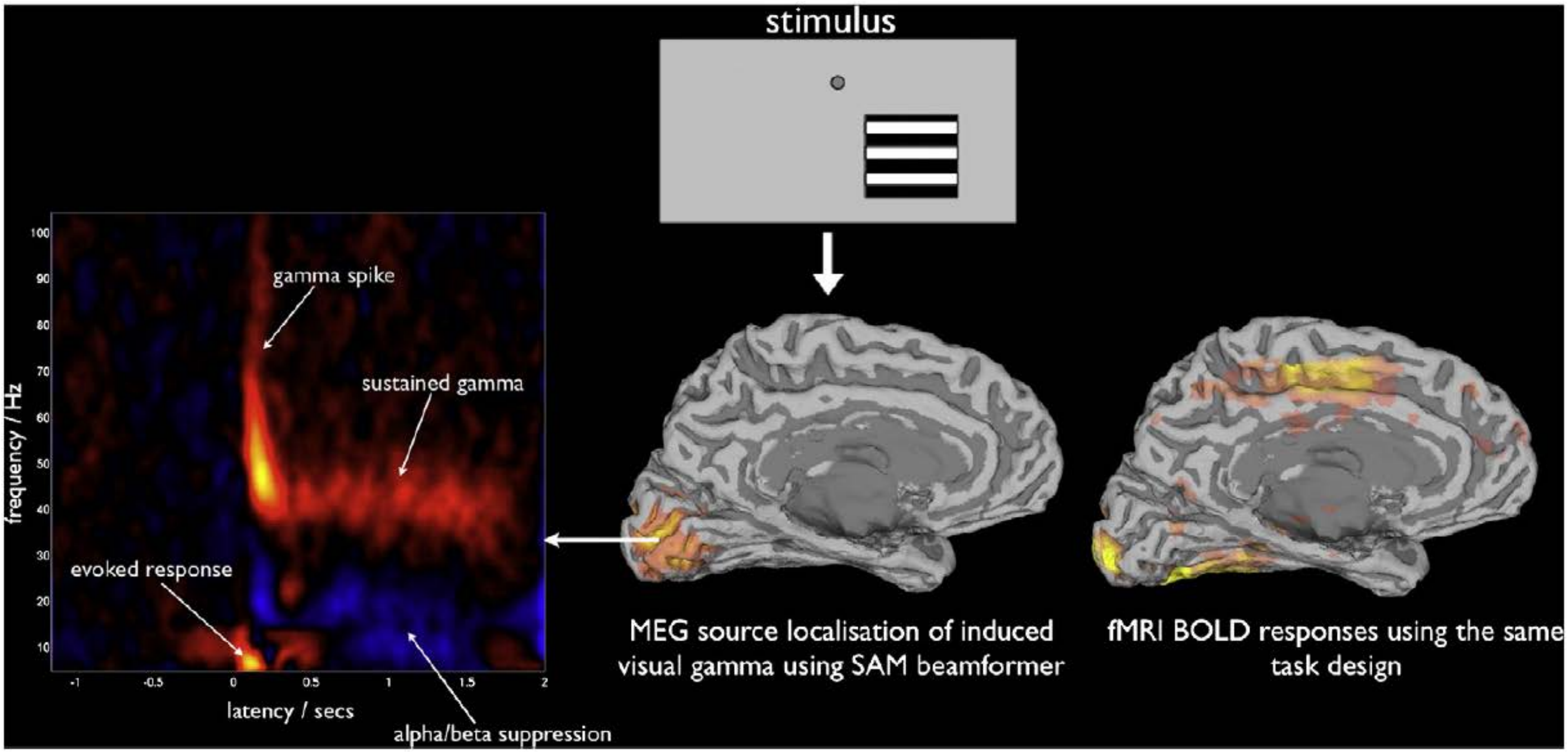
Seijnowki, Churchland, Movshon, Nat Nsc 2014

Which "Neural Activity" Do You Mean?



Singh, NI 2012

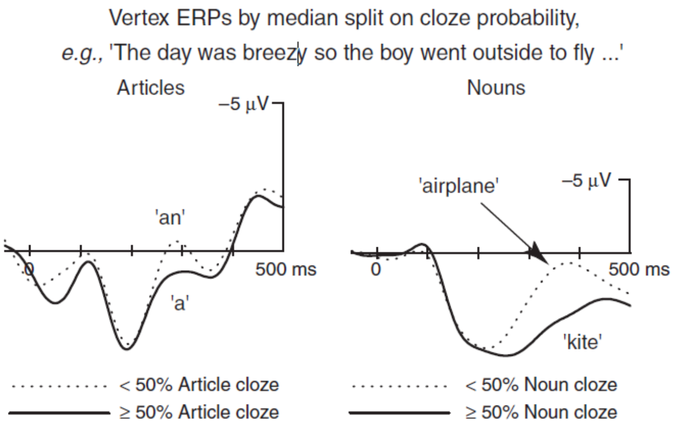
Which “Neural Activity” Do You Mean?



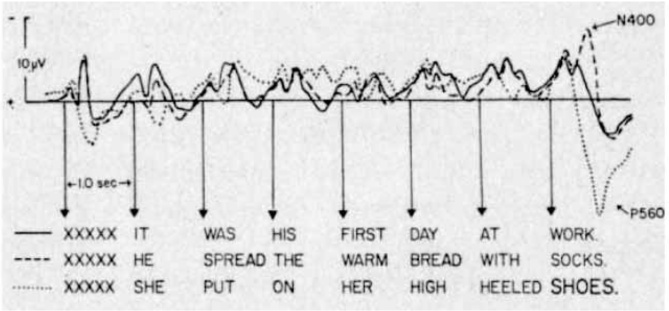
Singh, NI 2012

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

Event-Related Potentials

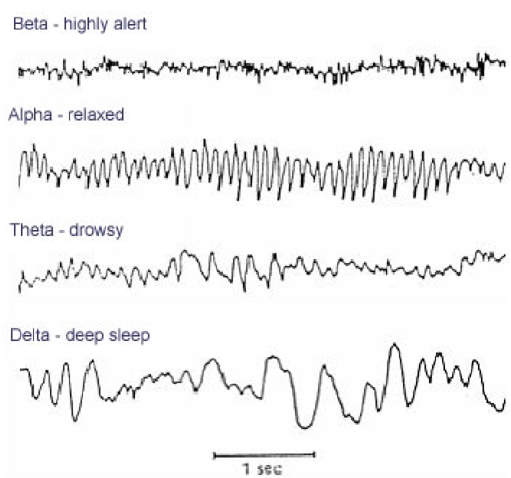


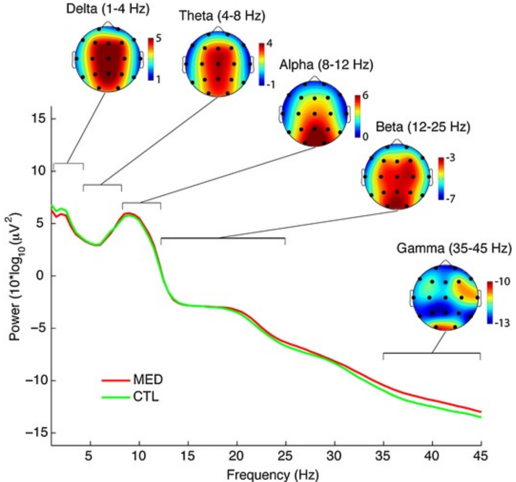
deLong, Urbach, Kutas, Nat Nsc 2005



Kutas&Hillyard, Science 1980

Brain "Rhythms"/"Oscillations"

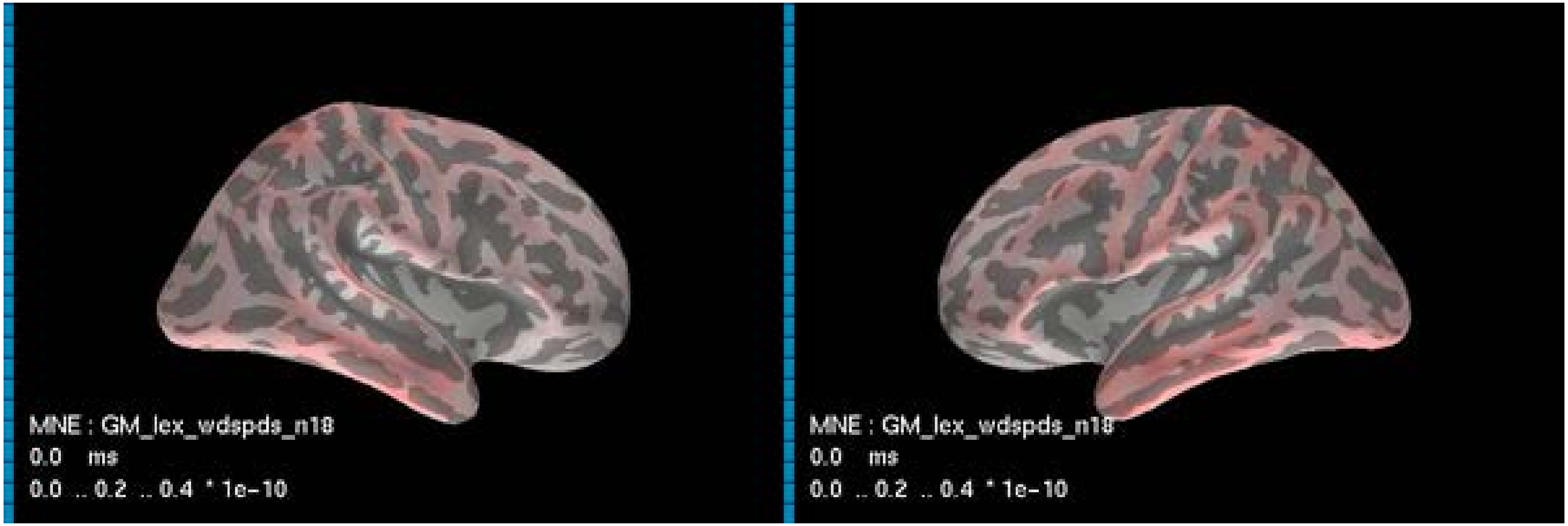




http://link.springer.com/article/10.1007%2Fs10339-009-0352-1/

What We Really Want:
Spatio-Temporal Brain Activity

(Movies rather than pictures)



EEG/MEG Literature

Books:

- Supek & Aine: "Magnetoencephalography (2^{nd})", 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.

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

A Brief History Of Bioelectromagnetism

Ancient Egypt, 2750 BC:

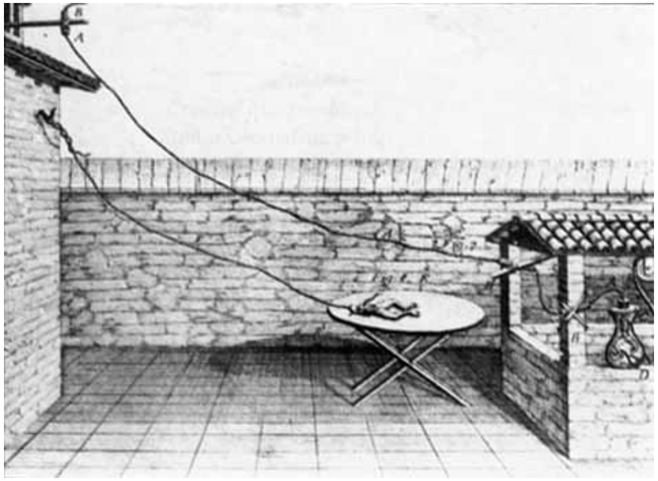
Electric Fish ("Thunderer of the Nile")
Some Roman writers mention electric shocks as an ailment for headaches (~ 0 AC)...

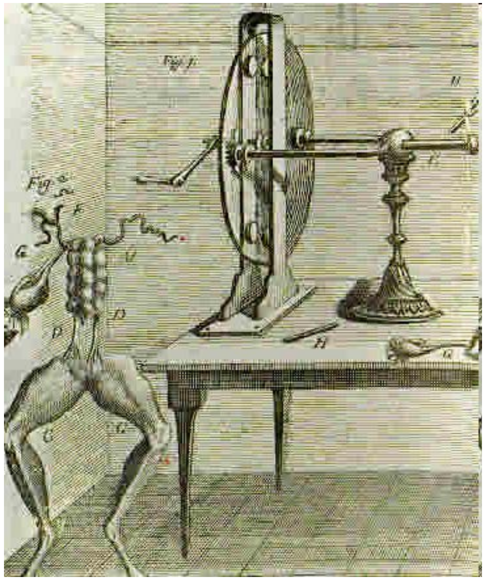
Ancient Greece, 600 BC:

Thales describes static electricity "electron"

Early Science

1771
Luigi Galvani, Bologna
“animal electricity”



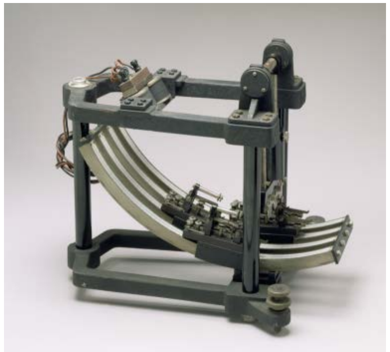


In 1803:
“On the first application of the process to the face, the jaws of the deceased criminal began to quiver, and the adjoining muscles were horribly contorted, and one eye was actually opened. …
Mr Pass, the beadle of the Surgeons’ Company, who was officially present during this experiment, was 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/

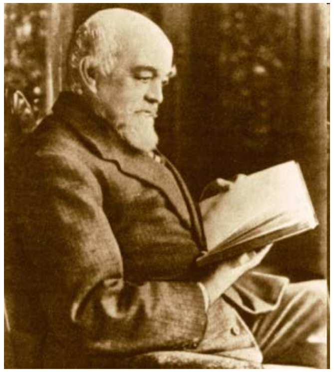
Early Electrophysiology

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

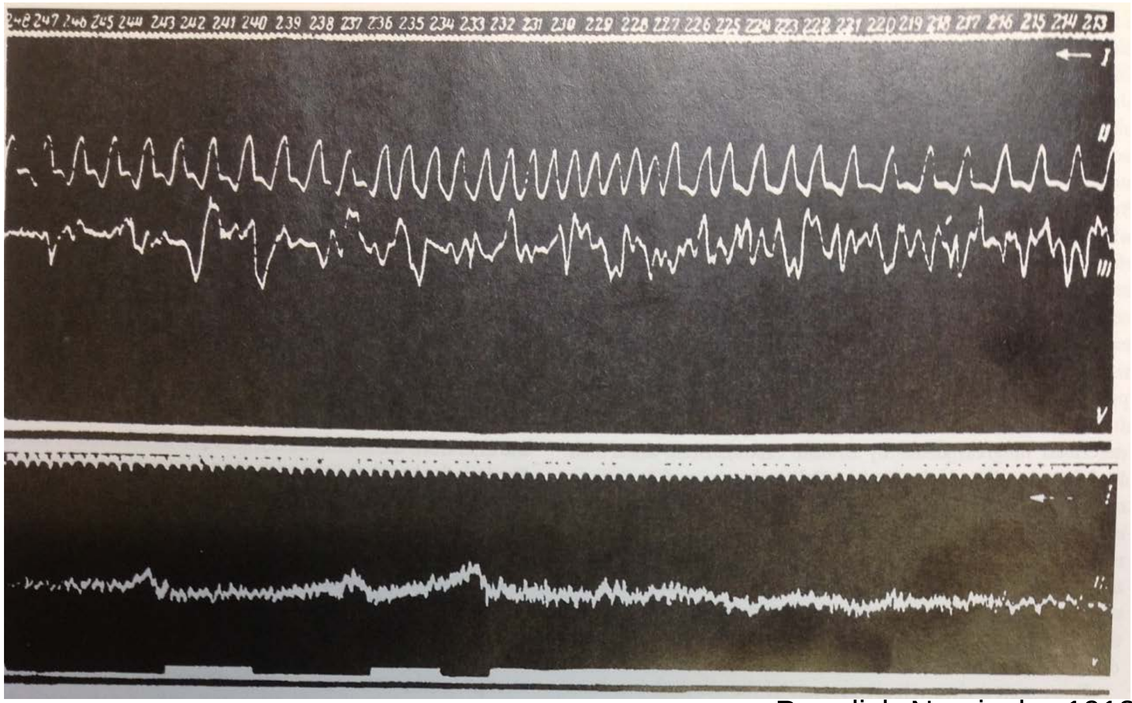
Time marker

Artery pulsation

Brain potential

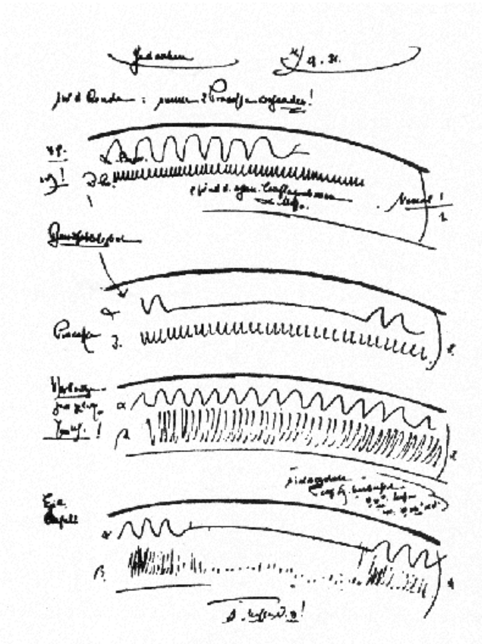
Response to sciatic nerve stimulation

Stimulation signal



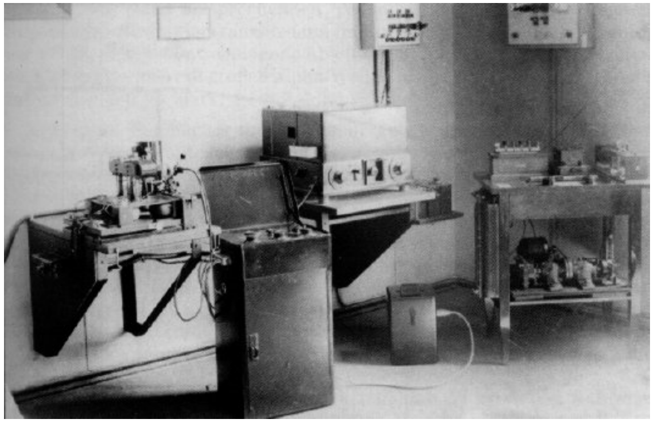
Pravdich-Neminsky, 1913

Early EEG

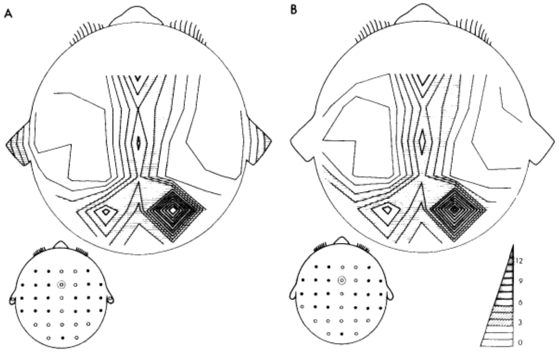


Hans Berger, Jena 1924

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

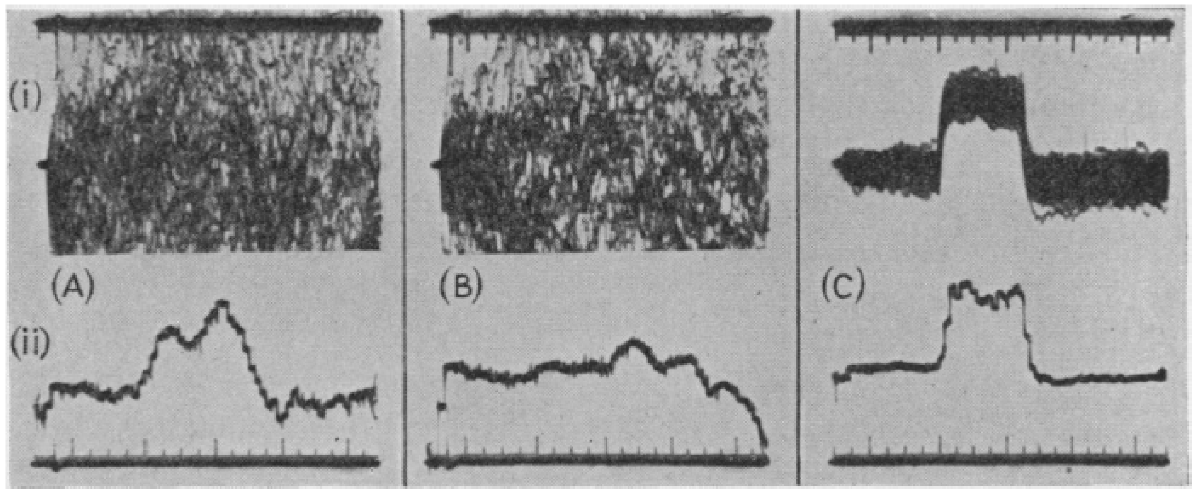


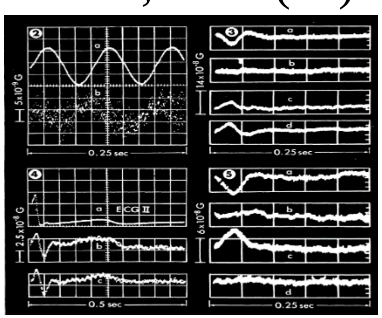
Fig. 1. An experiment to detect cerebral responses when the left ulnar nerve was stimulated at the wrist once per second. The upper line of traces shows sets of 55 records superimposed and the lower line the averages of these given by the machine. In A, from the contralateral scalp, there was one electrode 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

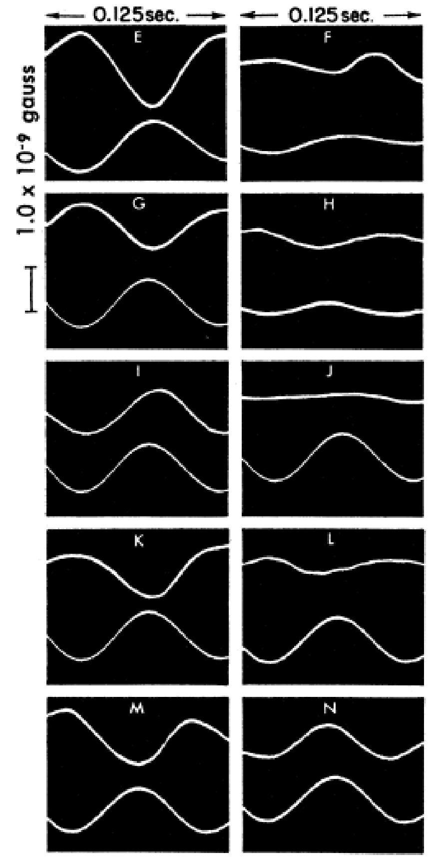
MEG pioneers MIT

MCG, 1967/(63)



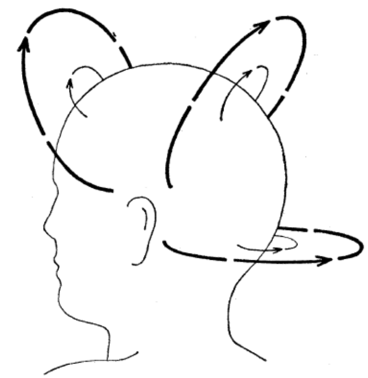
Cohen, Science 1967

MEG, 1968



Cohen, Science 1968

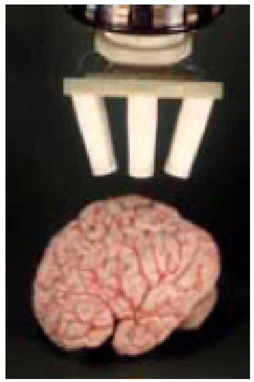
Alpha Rhythm



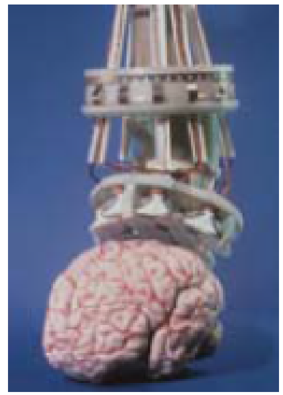
MRC
Cognition and Brain Sciences Unit

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



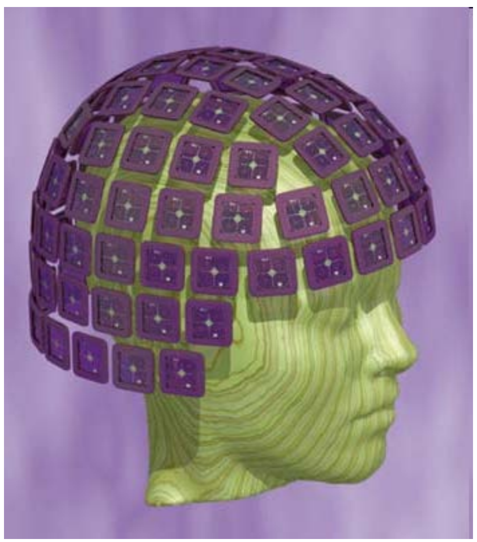
1989
by HUT
24 channels
125 mm in diameter
(coverage: 123 cm^2)
Planar

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

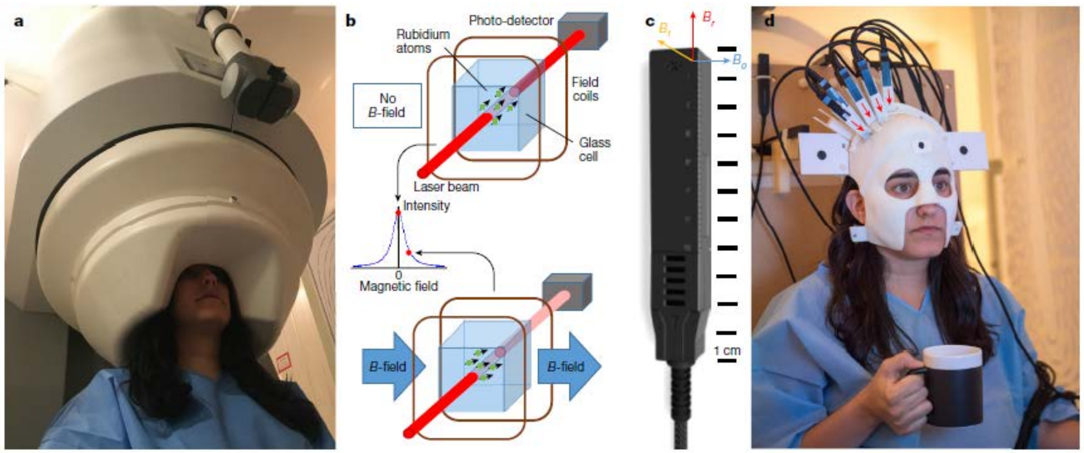
MEG – The Present

e.g. MEGIN Triux System
306 MEG sensors (102 magnetometers, 204 gradiometers)
Up to 120 EEG electrodes (70 typically used)

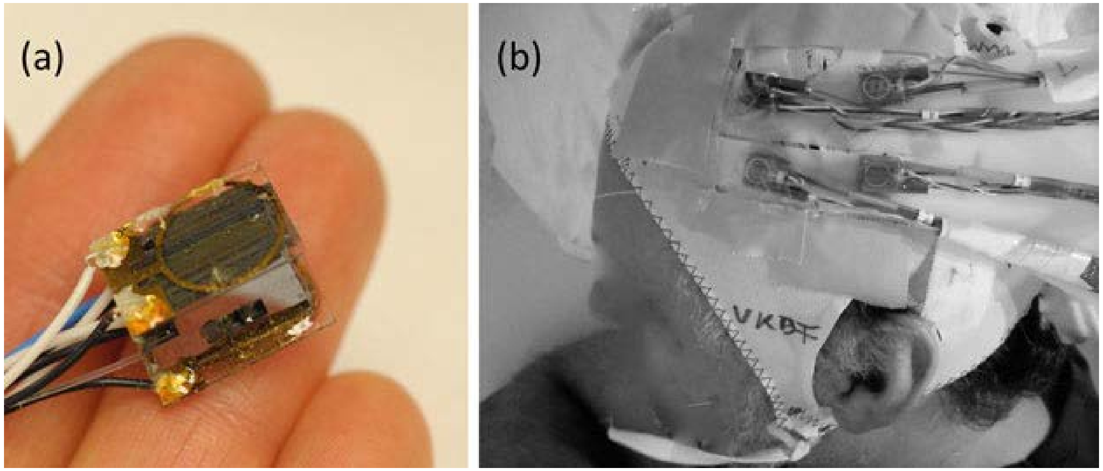


MEG – The (Near) Future

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)

Warning Signals

"Danilevsky (1852-1939) … finished his thesis entitled 'Investigations into the Physiology of the Brain' (1877). … He published an extensive textbook of human physiology in 1915. … He saw his high hopes unfulfilled as far as the spontaneous electrical activity of the brain was concerned.
… He was not the only EEG researcher with shattered hopes in the field of psychophysiology".
From: Niedermeyer and Schomer, 2011

"The mistakes in electroencephalography can fairly be attributed to ignorance of the theory underlying either the behaviour of the material or the equipment used to study it."
W.G. Walter & G. Parr (1950).

"Inappropriate computer methods are worse than no computer methods at all."
Nunez&Srinivasan, 2006, Electric Fields of the Brain, p. 91

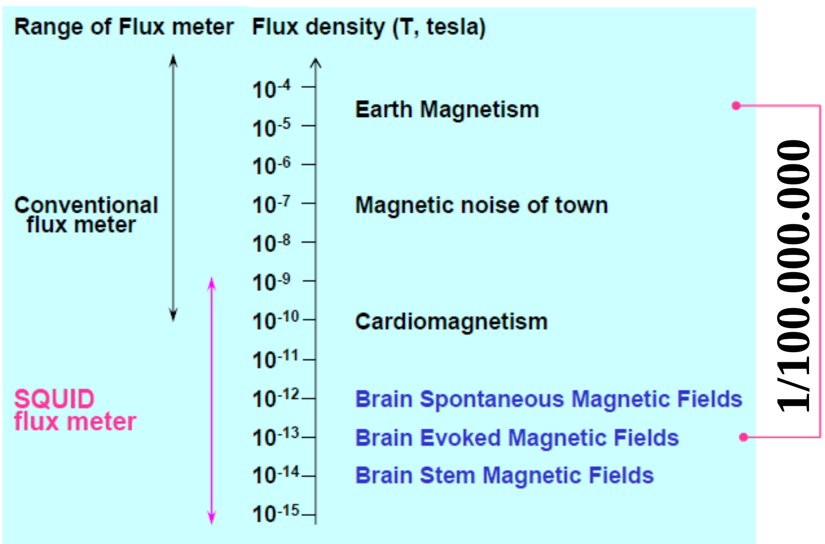
"No matter how enmeshed a commander becomes in the elaboration of his own thoughts, it is sometimes necessary to take the enemy into account."
Winston Churchill

"It is not enough to set tasks; we must also solve the problem of the methods for carrying them out.
… Unless the problem of method is solved, talk about the task is useless."
Mao Zedong, Quotations

The Measurement Of EEG/MEG Signals

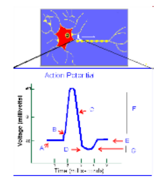
What EEG/MEG Are Measuring

Magnetoencephalography (MEG)



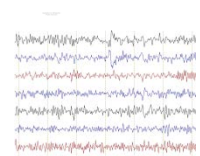
Electroencephalography (EEG)

Household Batteries
~ 1-12 V



Cell Membrane Potentials
~ 70 mV

ECG:
~ 1mV

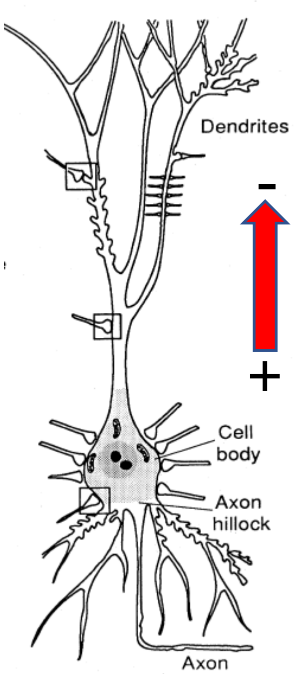


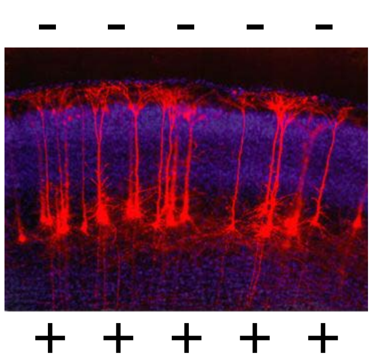
Raw EEG: ~ 30 µV
Eye blinks: > 100 µV

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**





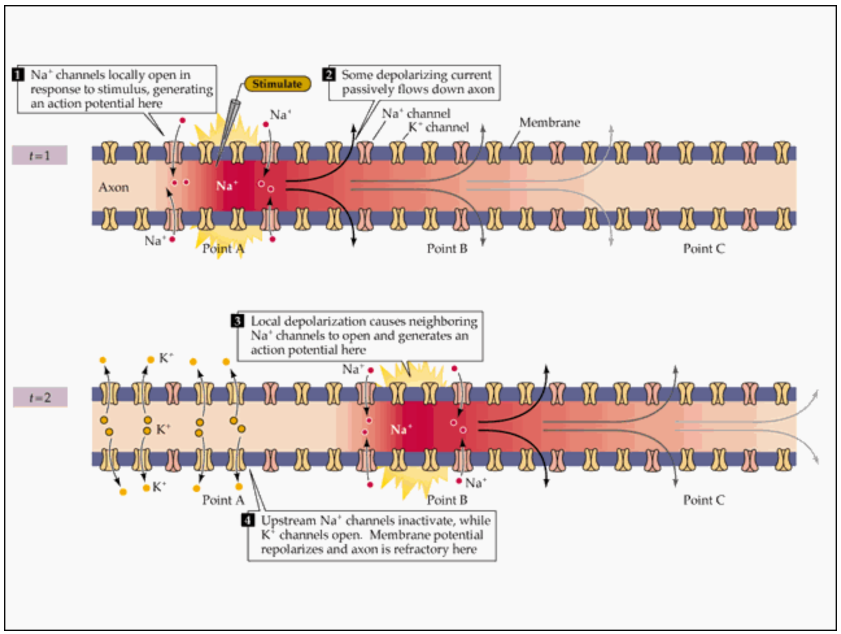
Dipolar currents

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

=> several mm^2 can produce measurable signal

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

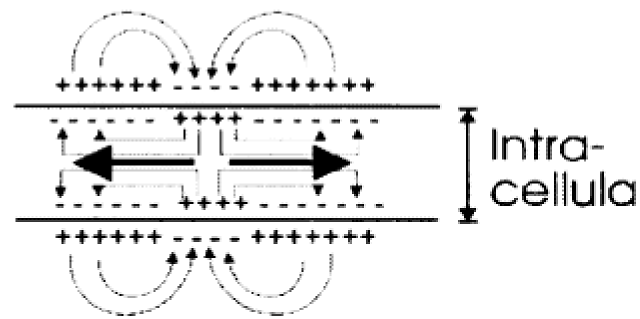


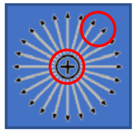
Figure I.1: *Schematic representation of an action potential*
Wieringa thesis, http://www.medcat.nl/megeeg/chap1.htm

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

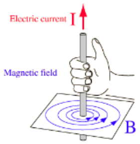
- The summed electric flux around a close surface is proportional to the total electric charge enclosed within this surface (Gauss's Law)

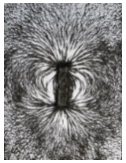
$$\nabla \cdot \boldsymbol{E} = \frac{\rho}{\varepsilon_0} = 0 \; (for\ dipoles)$$



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

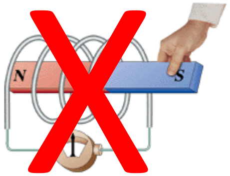
$$\nabla \cdot \boldsymbol{B} = 0$$





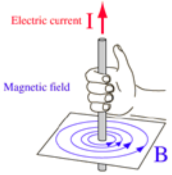
- *We do not consider any inductive effects (Faraday's Law):*

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



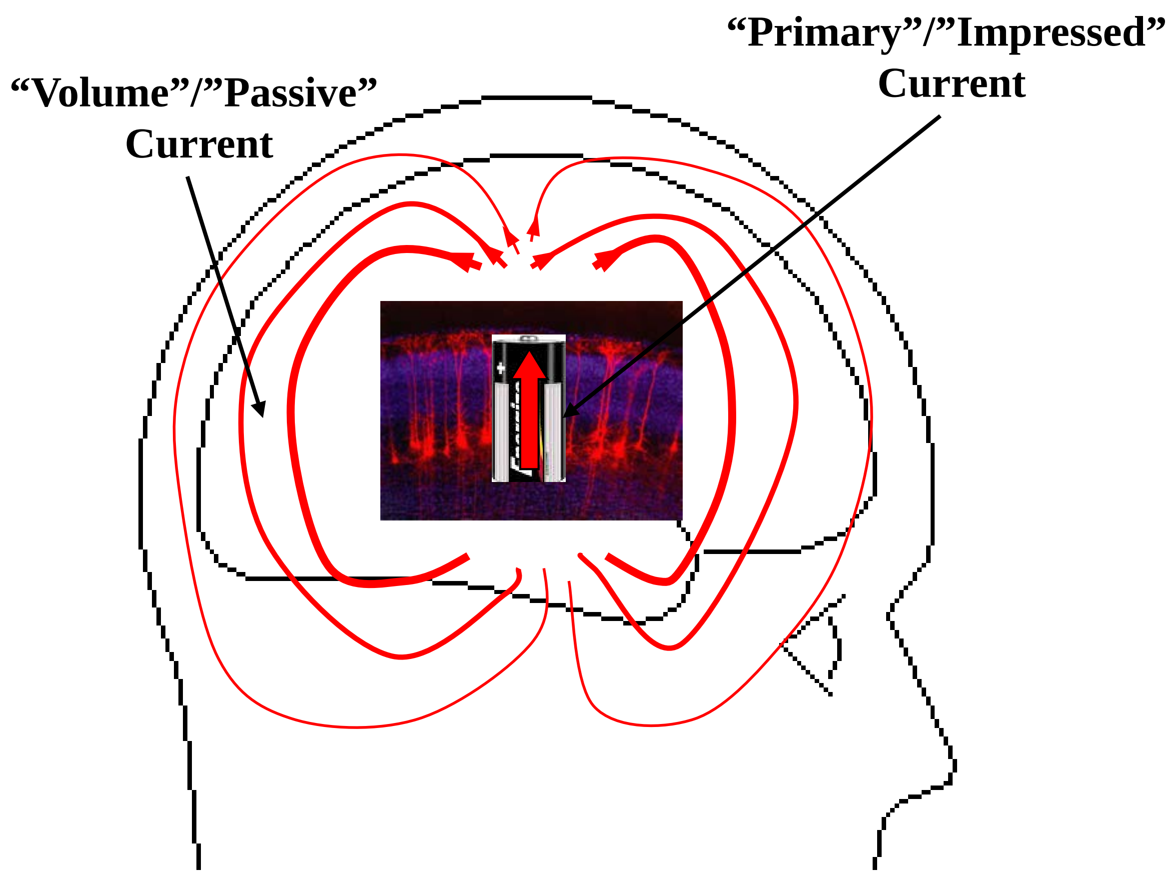
- *Magnetic fields are only caused by static currents (Ampere's Law):*

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

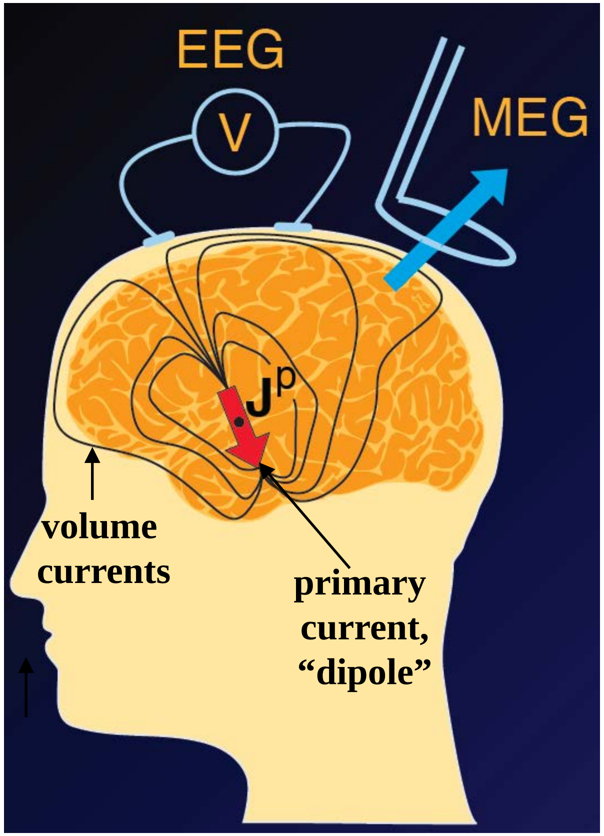


The relationship between EEG/MEG measurements and their brain sources is instantaneous (no "waves").

Current Flow in the Head



EEG/MEG Measurements



Volume currents affect both EEG and MEG –

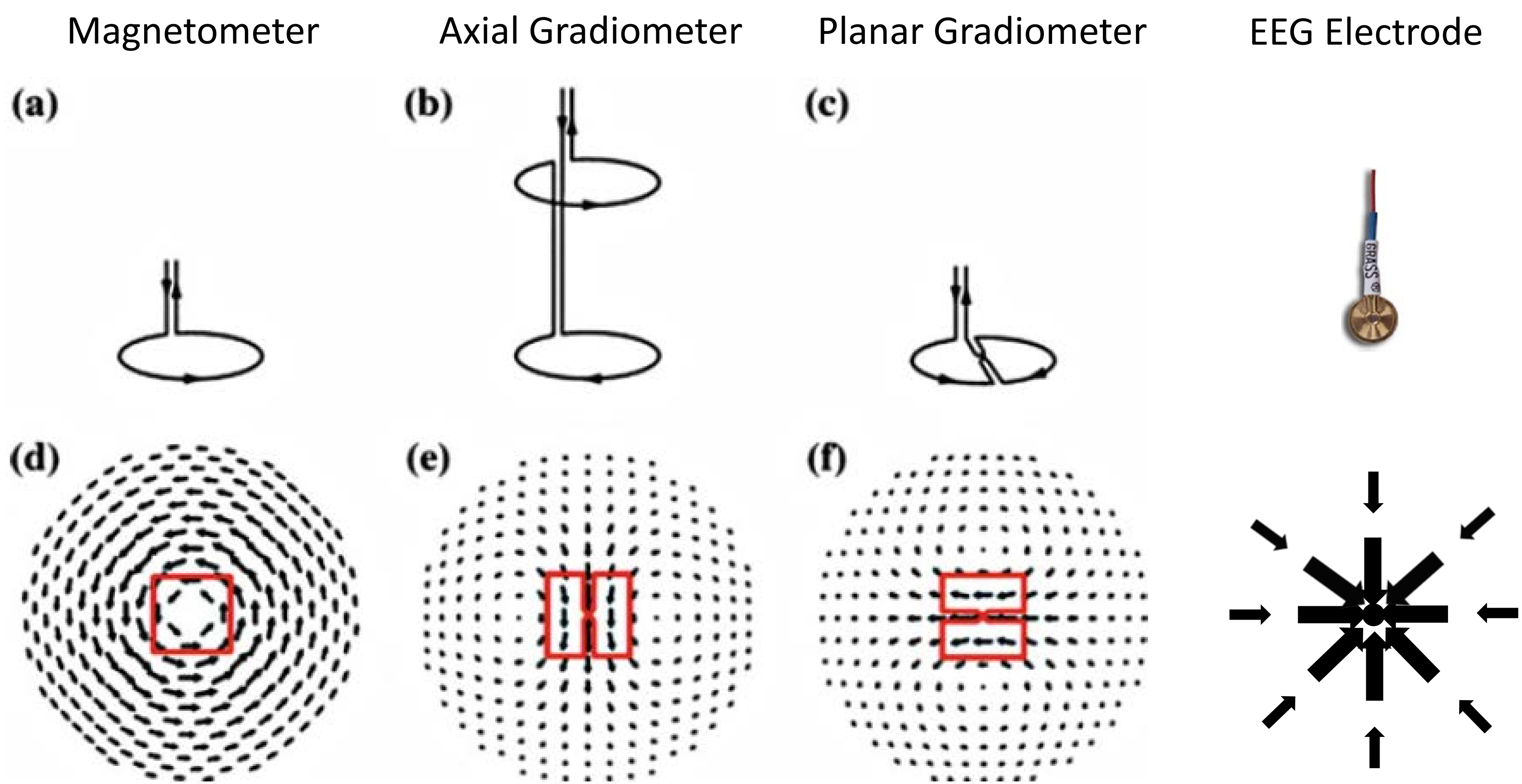
but EEG more than MEG

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

Different Sensors and their Sensitivities (Leadfields)

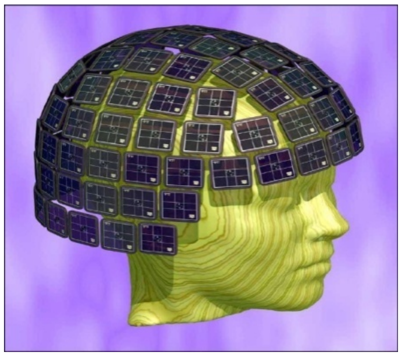
Leadfields are "sensitivity profiles" of individual sensors.

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

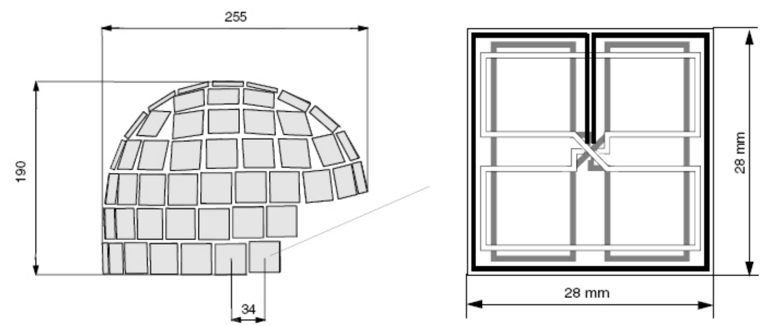
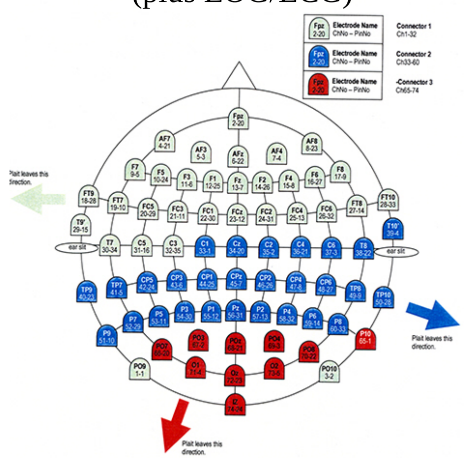


Figure 1.6. (left) Detector array, side view. Average distance between sensor elements : 34,6 mm. (right) Triple sensor detector unit.

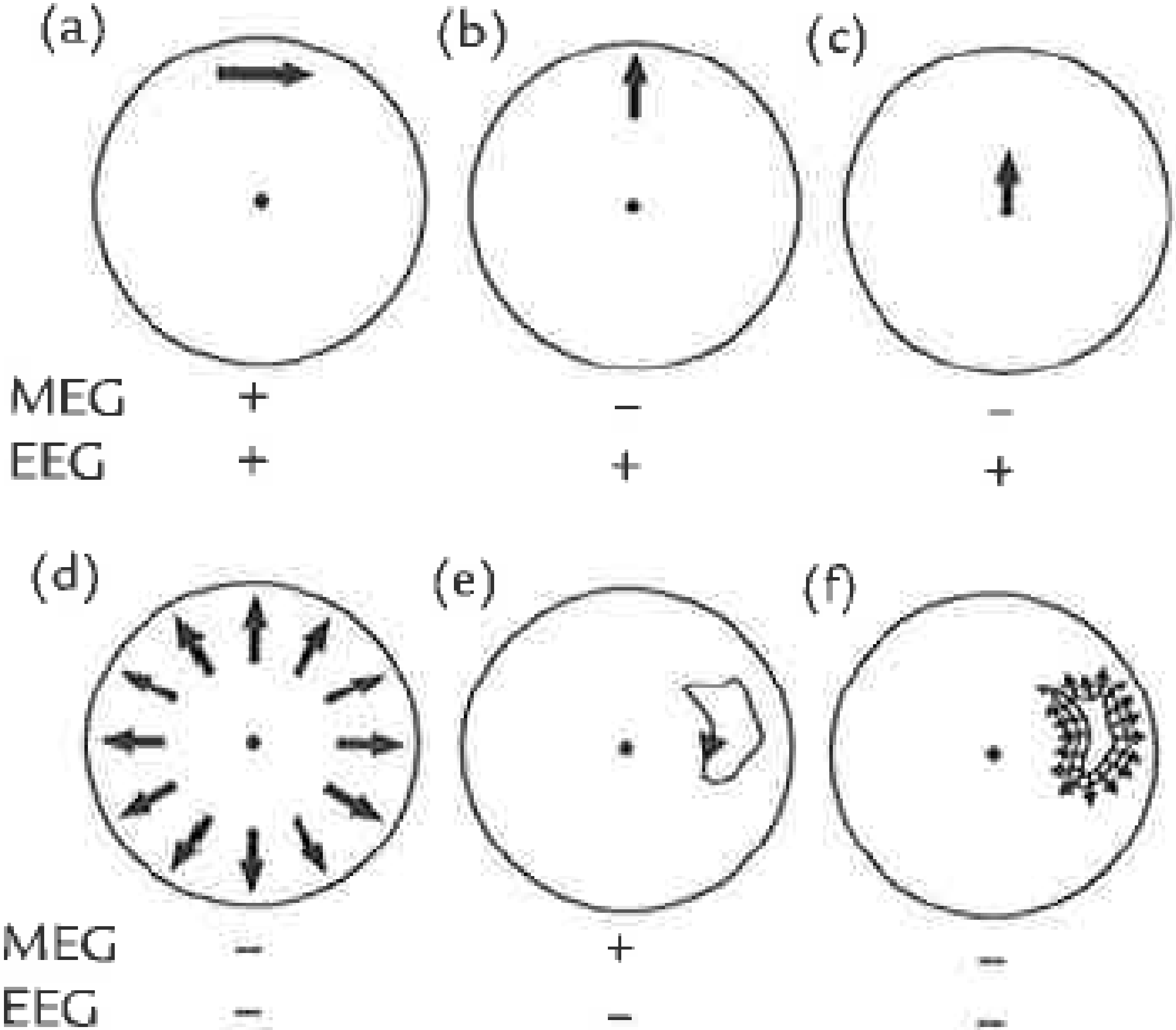
64 EEG electrodes

(plus EOG/ECG)



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

EEG and MEG Are Differentially Sensitive To Radial and Tangential Sources



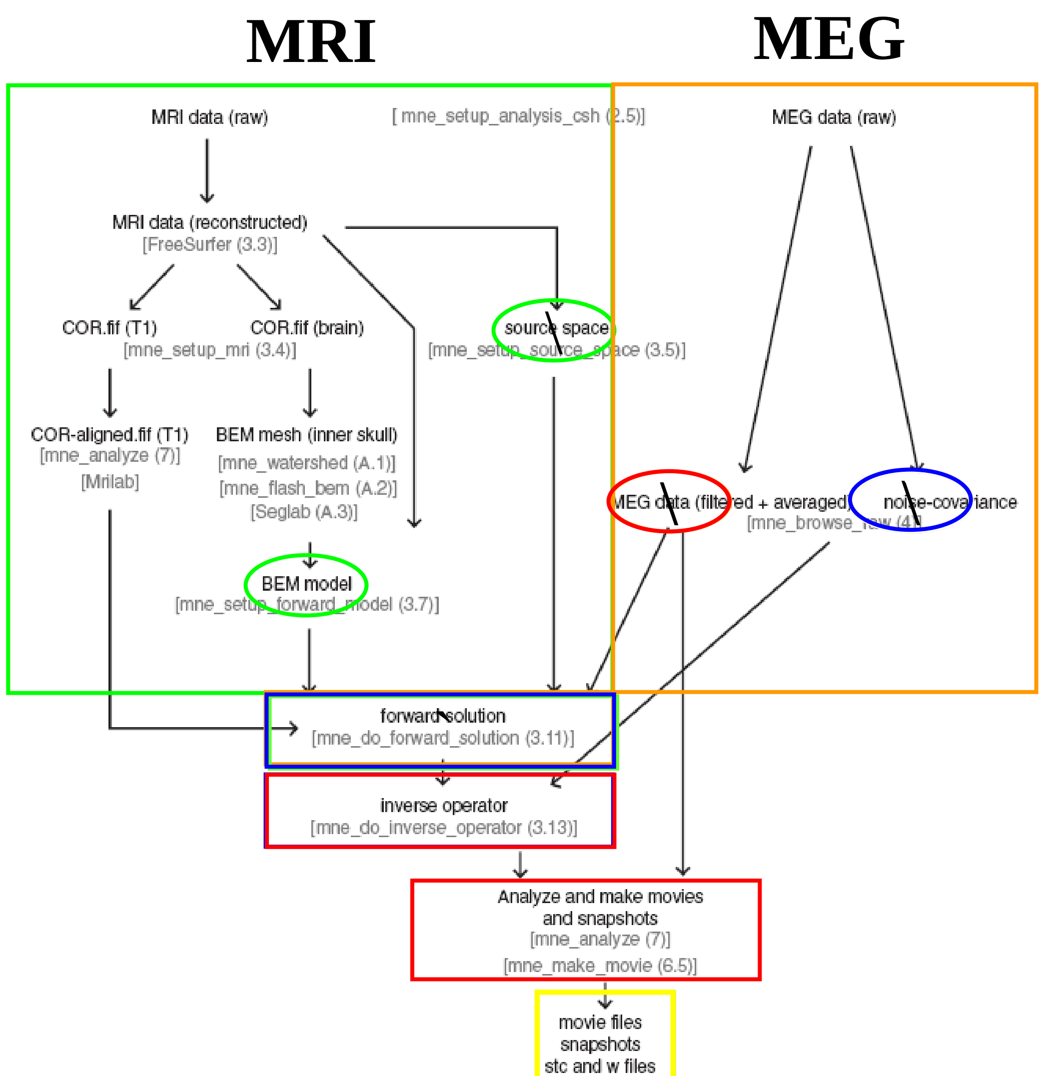
MEG is relatively insensitive to radial currents, and therefore also to deep currents.

Some complex source distributions may not produce EEG or MEG signals.

MEG-EEG Primer, Hari & Puce, OUP 2017

Data Pre-Processing

Typical EEG/MEG Analysis Pipeline



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

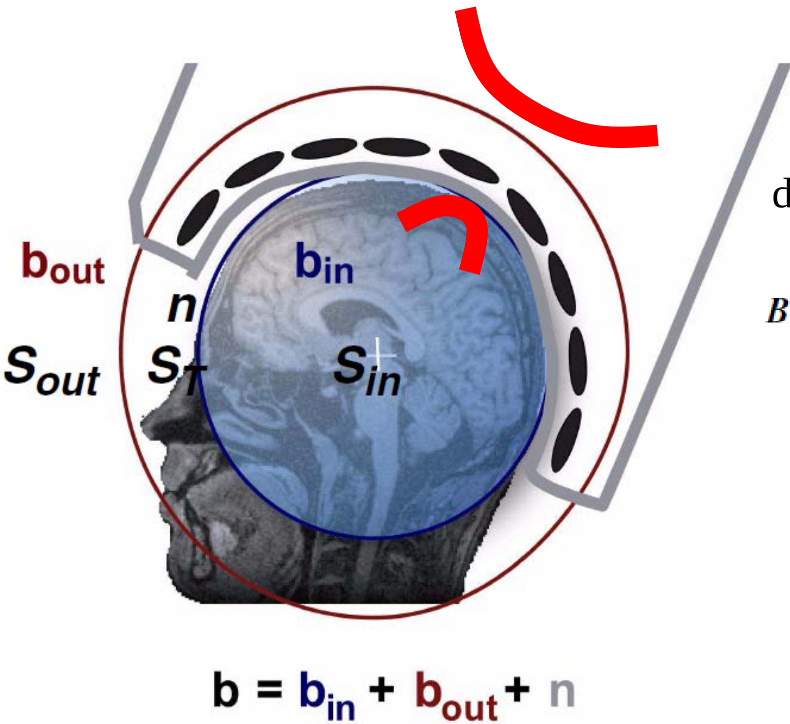
Wisdoms:

"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)**:**

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

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

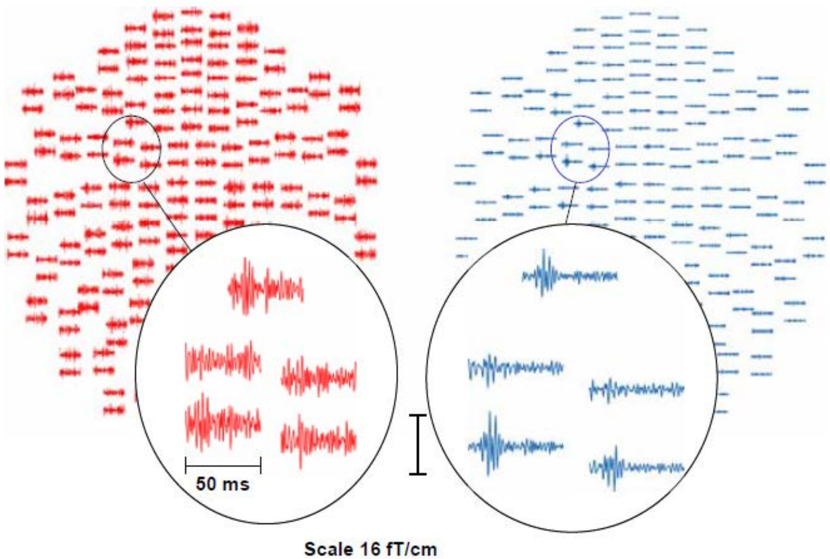
$$\omega_{nm}(\theta, \varphi) = n Y_{nm} e_r + \frac{\partial Y_{nm}}{\partial \theta} e_\theta + \frac{im Y_{nm}}{\sin\theta} e_\varphi,$$

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

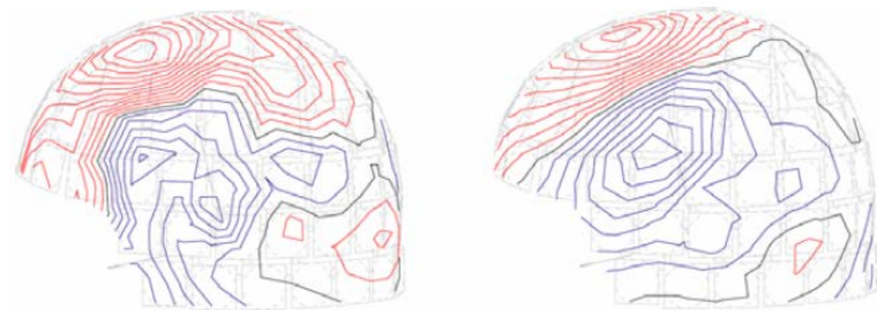
Elekta Neuromag

Maxfilter

Without With



Without With



Original Field Map

SSS Reconstructed Field Map

Latency 20 ms
Q = 2 nAm

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.

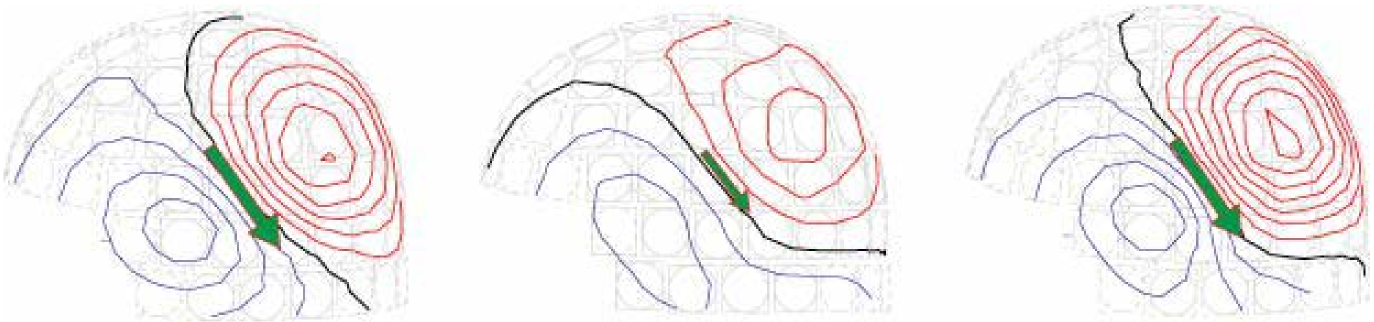
Compensation of disturbances caused by head movements ("-movecomp")
By extracting head position indicator (HPI) signals applied continuously during a measurement, the data transformation capability is utilized to estimate the corresponding MEG signals in a static reference head position.

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

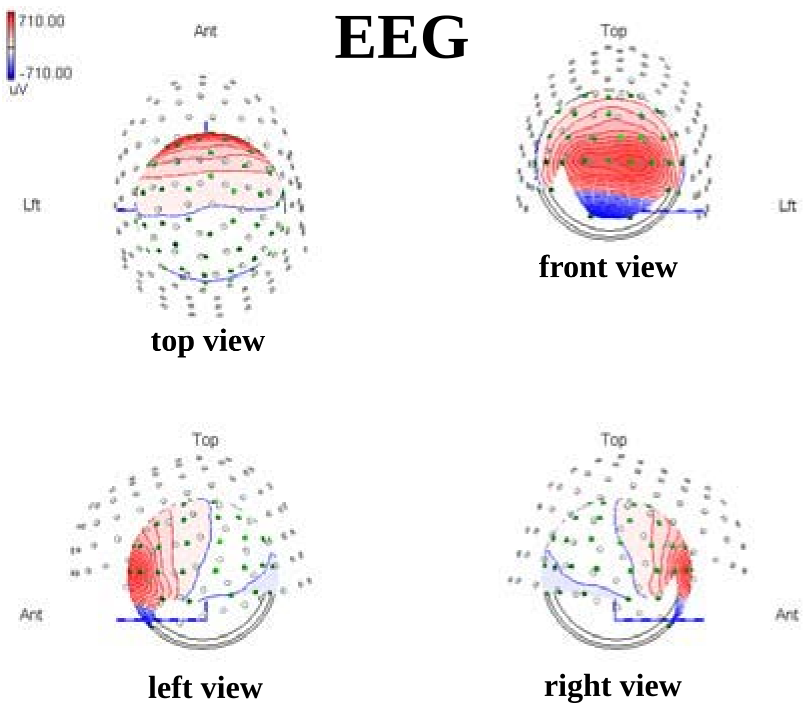
Moving subject, No compensation

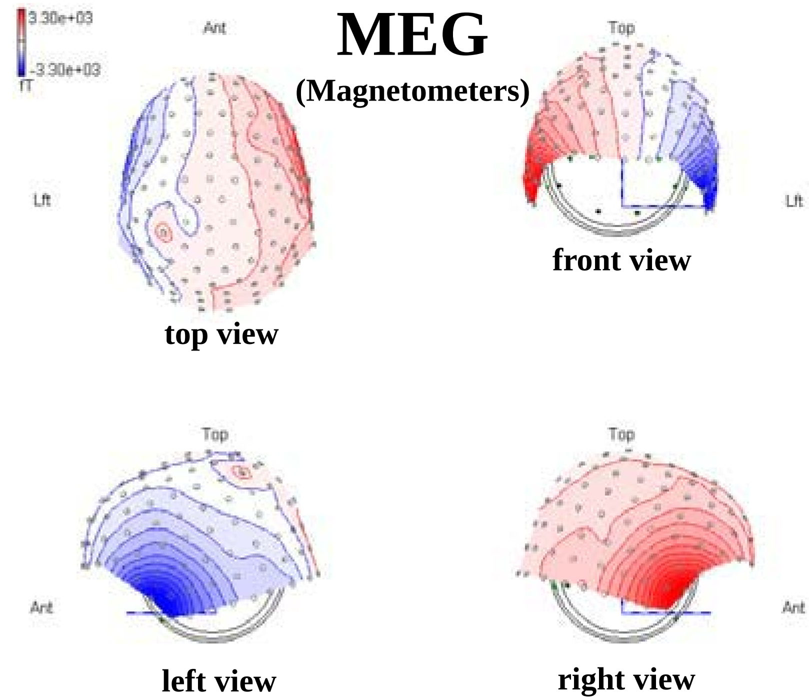
Moving subject, with compensation

Elekta Neuromag

Common Artefacts: Eye Blinks

Affects EEG and MEG

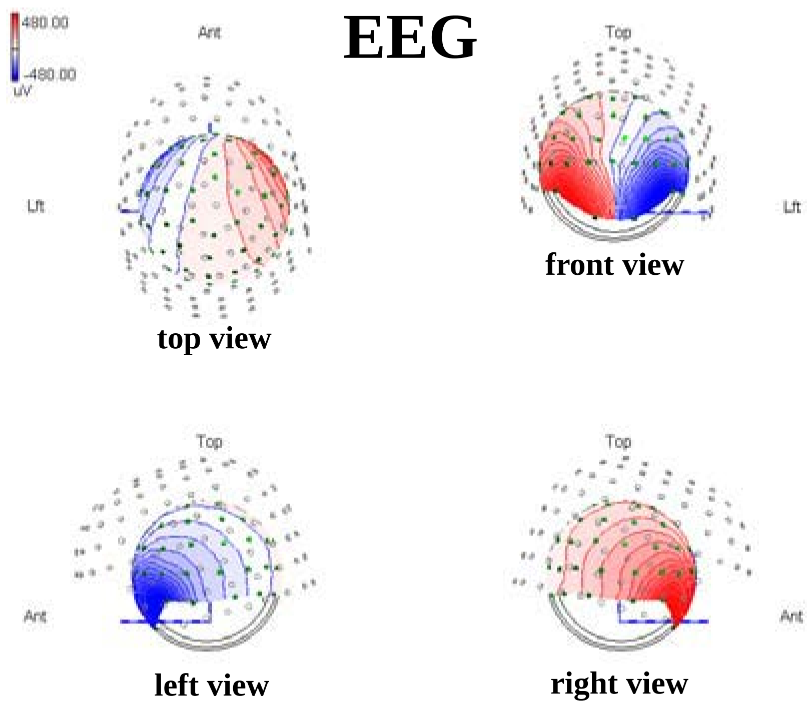


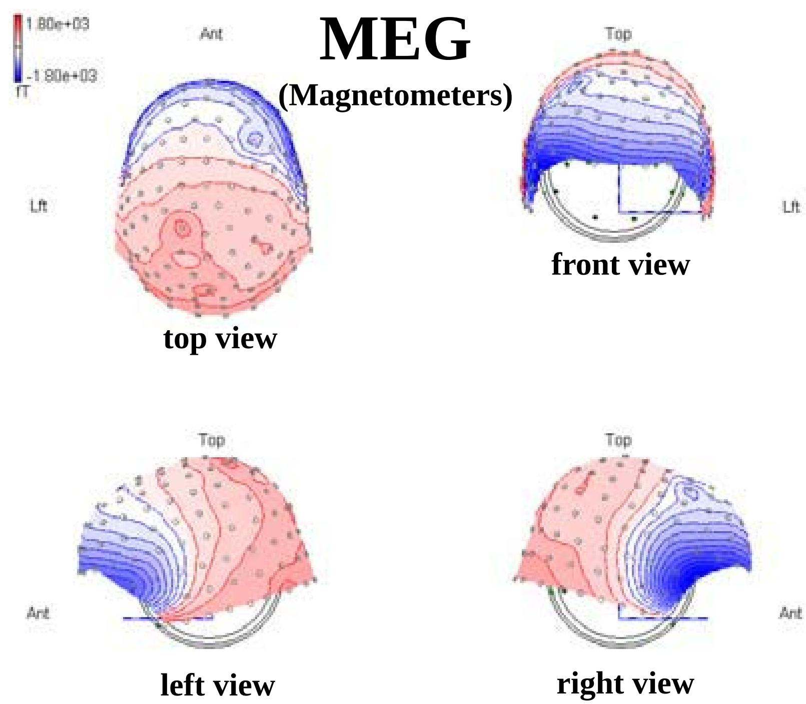


MRC
Cognition and Brain Sciences Unit

Common Artefacts: Eye Movement to the Right

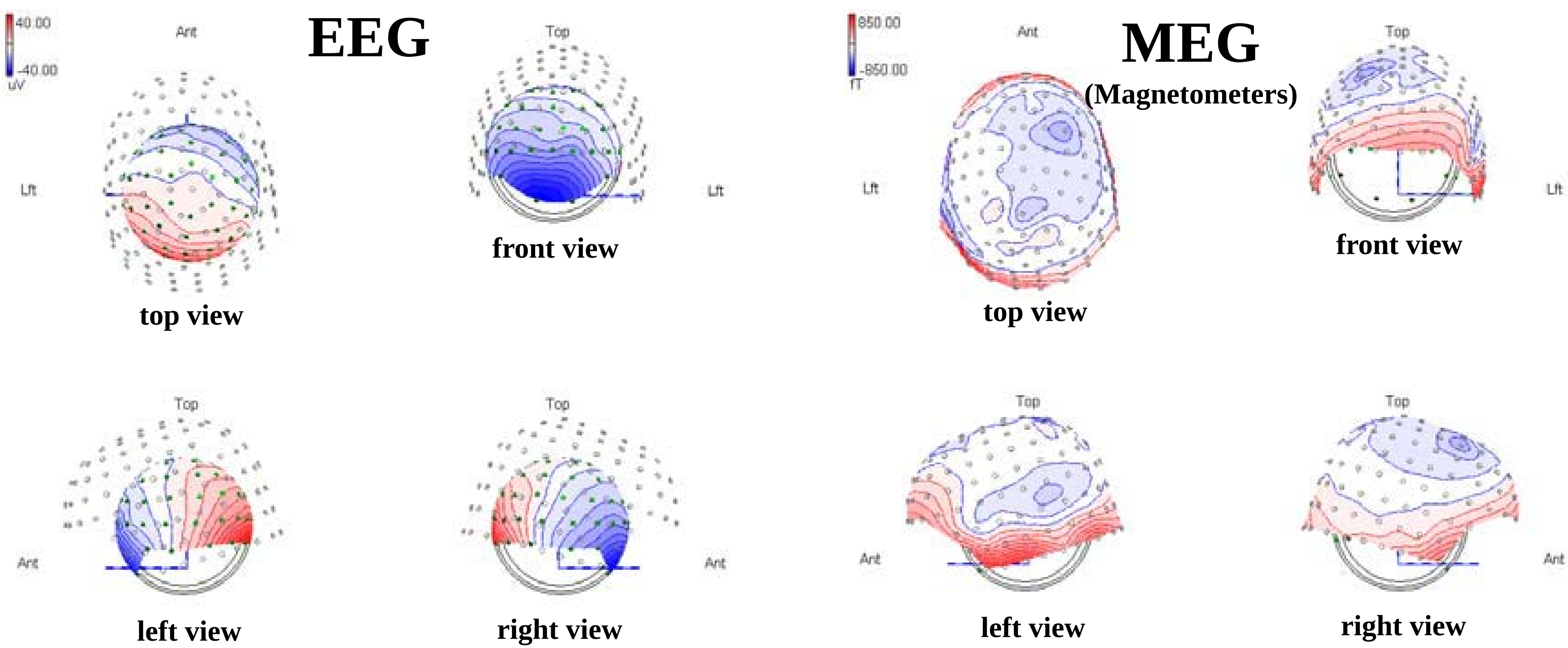
Affects EEG and MEG





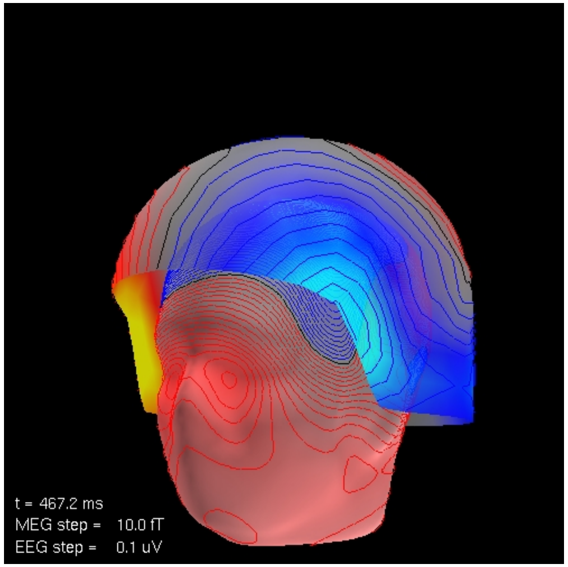
Common Artefacts: Heart Beat

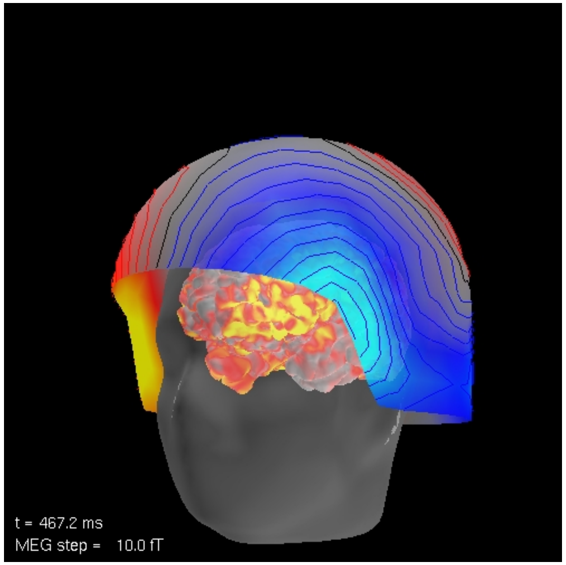
Affects EEG and MEG



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.

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 **N.**

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

D = a***N** + **Signal**

You only analyse **Signal.**

This works well with eye-movement and blink artefacts.

Note:

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

PCA and SVD

• Decompose data into **orthogonal** components $\mathbf{T}_1$, $\mathbf{T}_2$, etc. (topographies or time courses), i.e. data $\mathbf{D} = a*\mathbf{T}_1 + b*\mathbf{T}_2 + \ldots$

• Find the components you don't like (e.g. correlate highly with EOG and ECG, or components that explain little variance).

• Reconstitute your data only with the "good" components,

e.g. $\mathbf{D} = a*\mathbf{T}_1 + c*\mathbf{T}_3 + \ldots$ if component 2 reflects eye blinks.

Also:

• Components have an order according to the variance they explain (e.g. var($\mathbf{T}_1$)>var($\mathbf{T}_2$)>…)

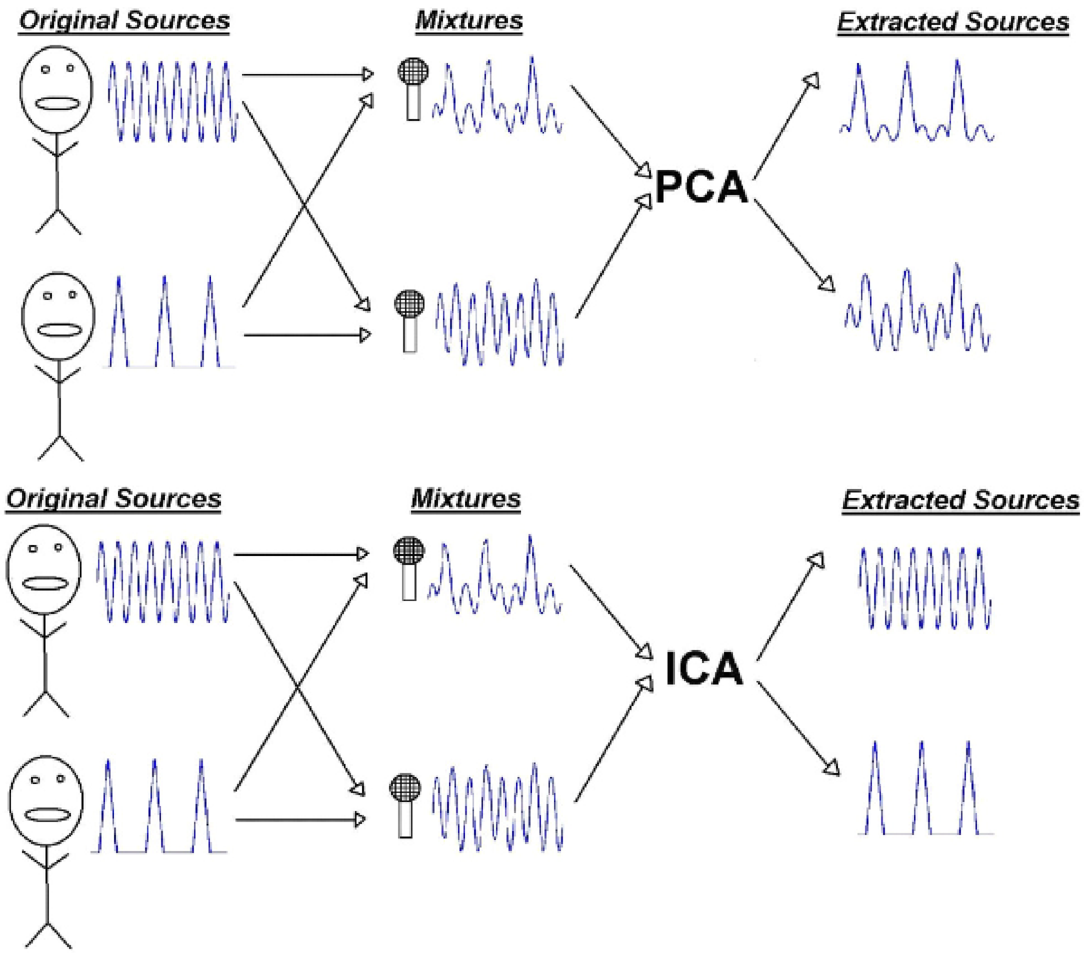
• Can be used to determine the number of independent components (according to specified criteria)

• Relatively fast (try svd() or princomp() in Matlab).

•**Unfortunately: Orthogonality and variance ordering is not physiologically plausible.**

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 for example to remove eye movement and heart beat artefacts.

Data Pre-Processing – Frequency Filtering

Filtering and Downsampling

- Choose a “convenient” sampling rate with respect to processing speed and storage (usually 250 Hz to 500 Hz ok).
- In our MEG we have to sample at 1000 Hz during acquisition because of head position indicator (HPI) signals.
- Downsampling can lead to “aliasing” if the data are not filtered appropriately (Nyquist theorem).
- Filtering can reduce (possibly remove) some artefacts such as sensor noise, muscle artefacts, line noise.

Specialised reading (also check books on previous slide):

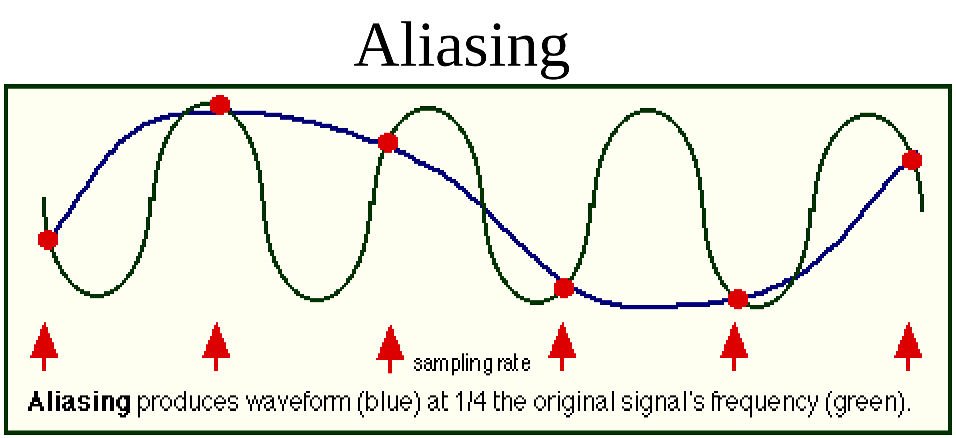
Widmann et al., Journal of Neuroscience Methods 2015, https://www.sciencedirect.com/science/article/pii/S0165027014002866.

Filtering

- The optimal filter strongly depends on your specific data and questions.
- General rule: Filter as much as necessary, but as little as possible.
- Filtering changes the timecourse of your signals: Low-pass filters smooth the data, high-pass filters attenuate slow activity
- (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/).

Aliasing

- Downsampling can lead to “aliasing” if the data are not filtered appropriately (Nyquist theorem).

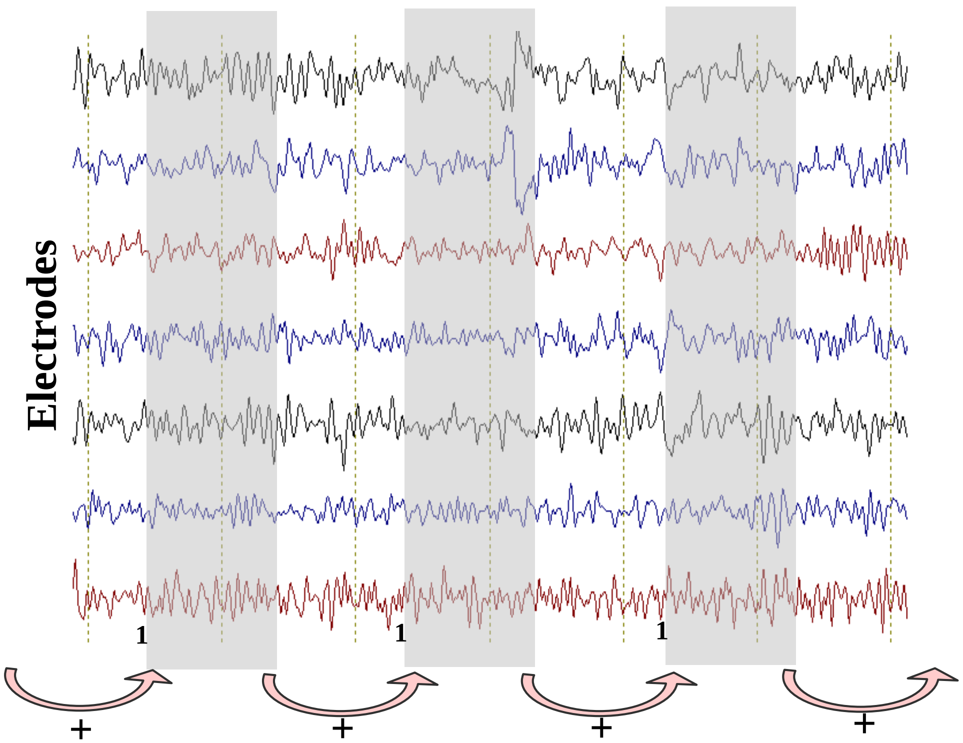


Also watch:
https://www.youtube.com/watch?v=R-IVw8OKjvQ
Thanks to Alessandro.

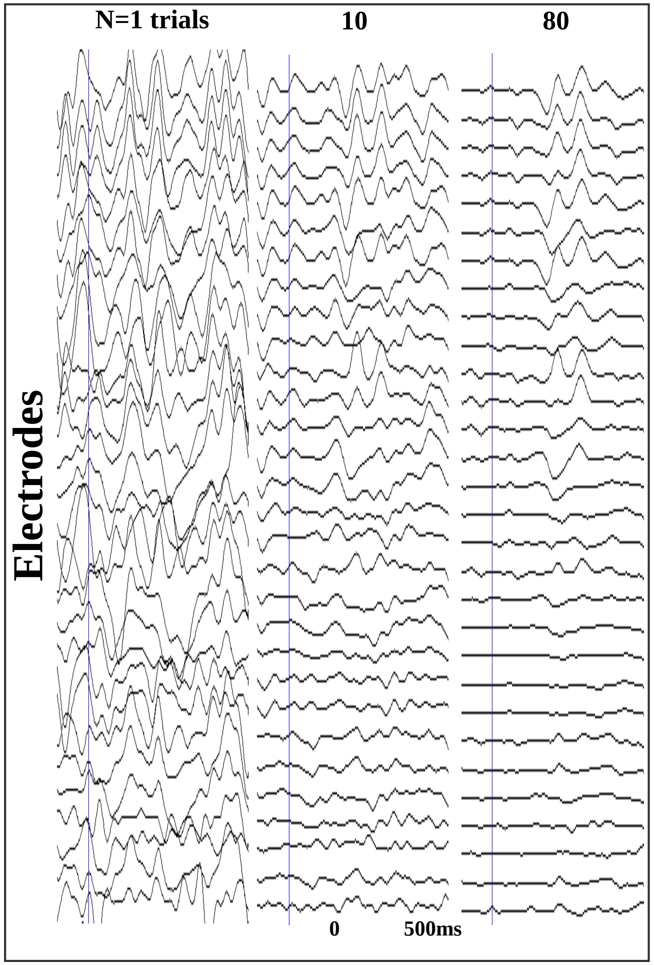
Evoked Responses
Event-Related Potentials and Fields (ERPs and ERFs)

Data Averaging

Continuous “raw” data:



Averaged data:



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

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).

Artefact Rejection

Usually, epochs are excluded from averaging when their data exceed some maximum-minimum criterion.

Make sure "chronically bad channels" are excluded from this procedure
(or there won't be any data left to average).

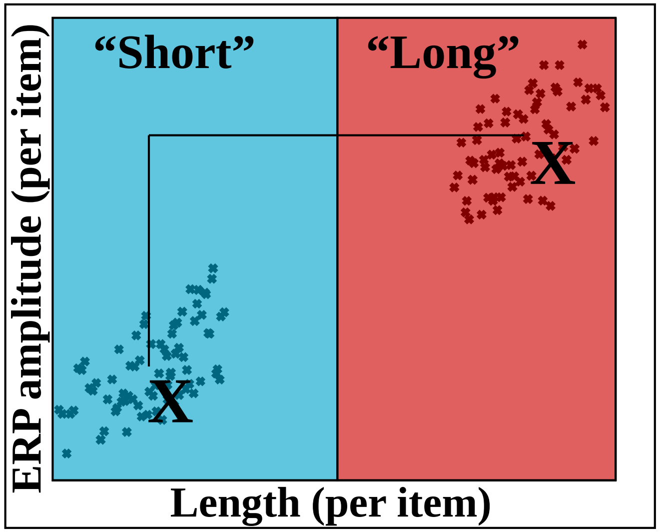
Prior to any procedure that combines signals across channels, such as average reference, SSP or ICA, bad channels should be removed
(or signals from bad channels may be projected into the good ones).

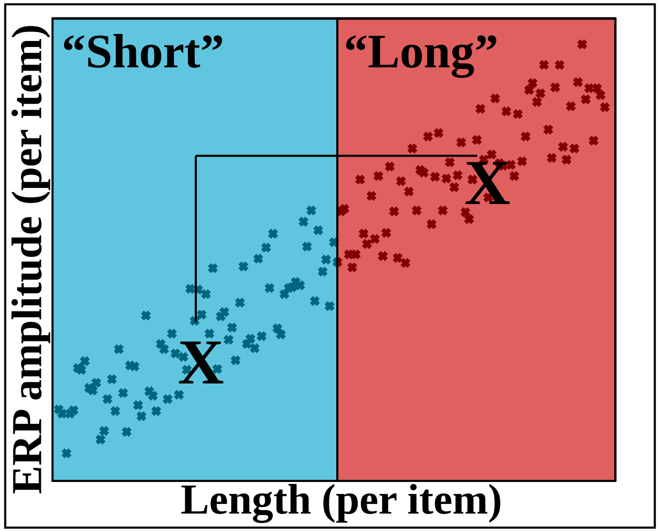
Appropriate filtering and artefact correction (e.g. ICA) should be applied beforehand
(but don't feel too safe: artefacts may slip through).

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

Parametric vs Factorial Designs

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

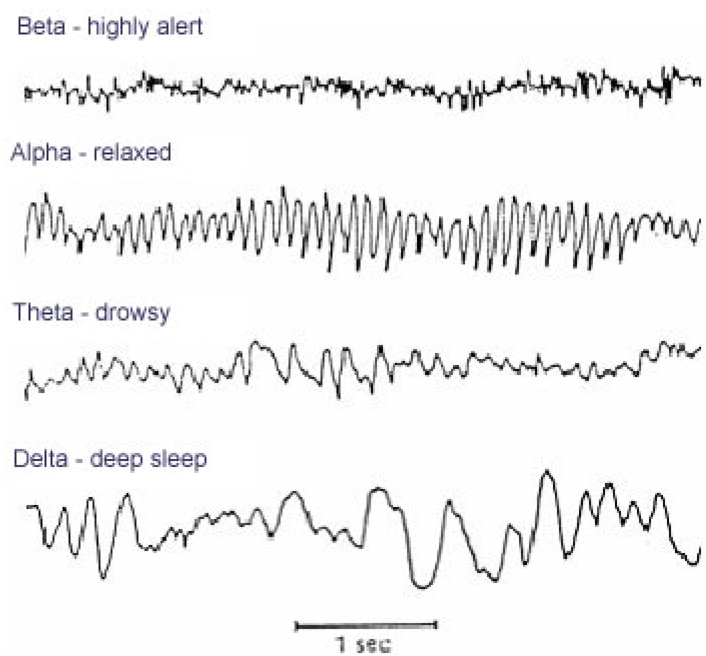


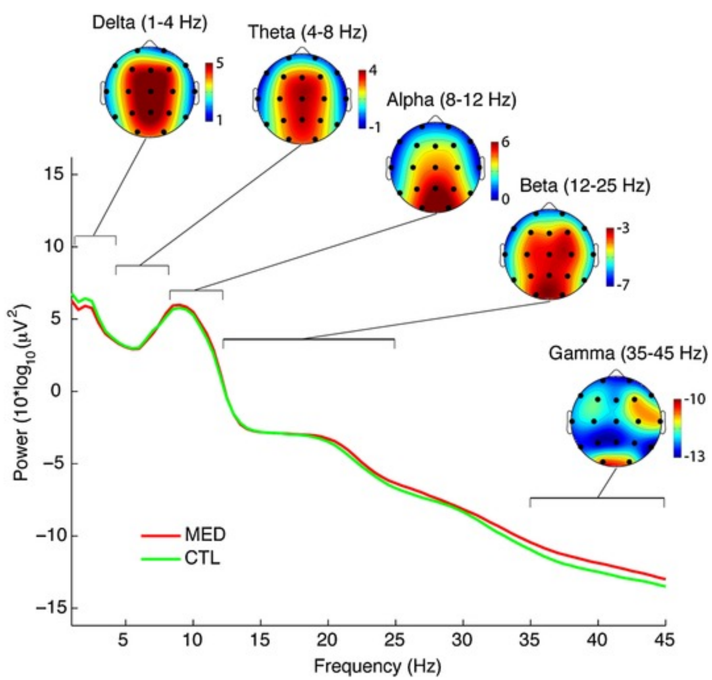


Smith & Kutas, Psychophysiol 2015a
Hauk et al., Neuroimage 2006

"Brain Rhythms" and "Oscillations"

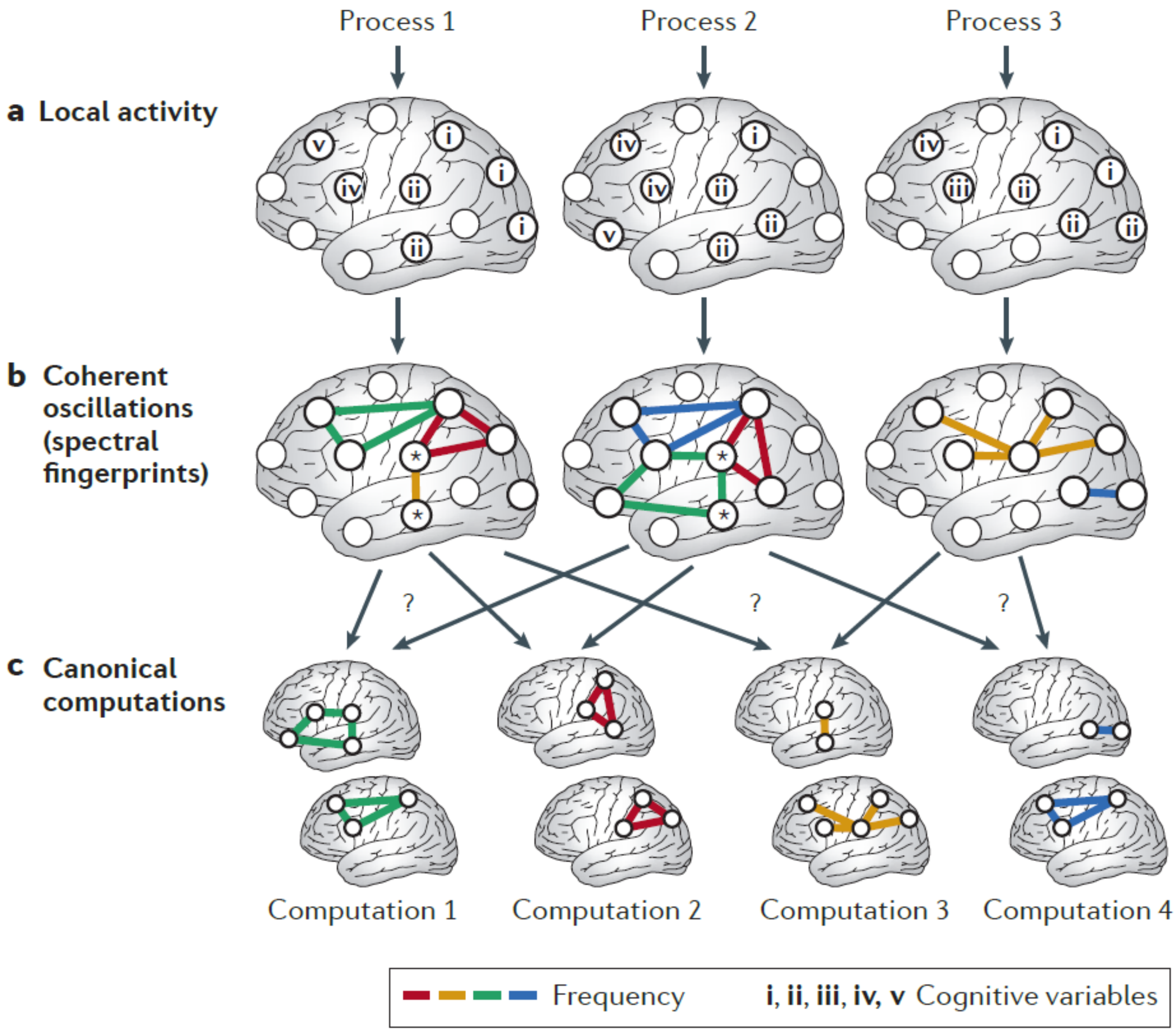
Time course and topography may differ among different frequency bands
(and may depend on task, environment, subject group etc.)





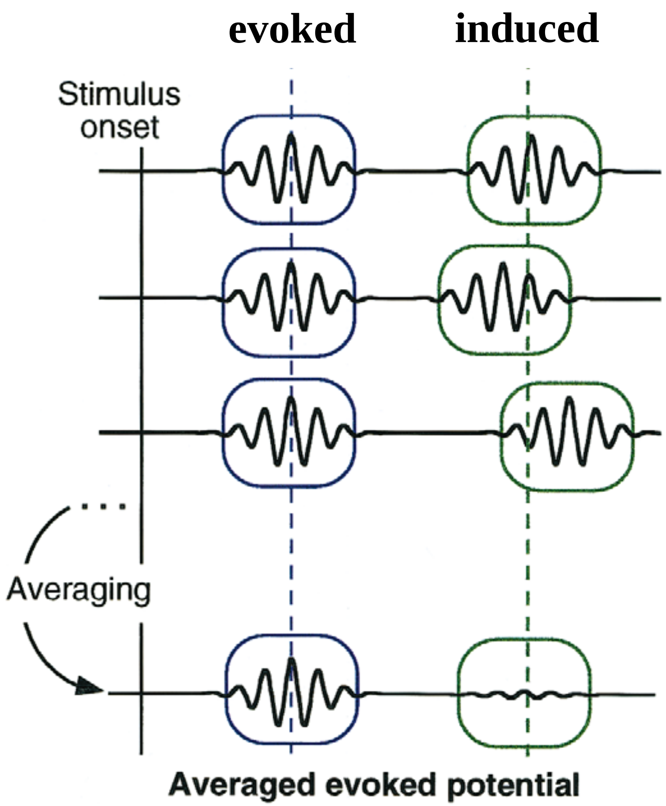
http://link.springer.com/article/10.1007%2Fs10339-009-0352-1/

"Brain Rhythms" and "Oscillations"



Siegel et al., Nat Nsc 2012

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.