



**BRAIN RESEARCH
IMAGING CENTRE**
Edinburgh

MULTIMODAL IMAGING AND THE NEURAL BASIS OF EEG AND FMRI

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OVERVIEW

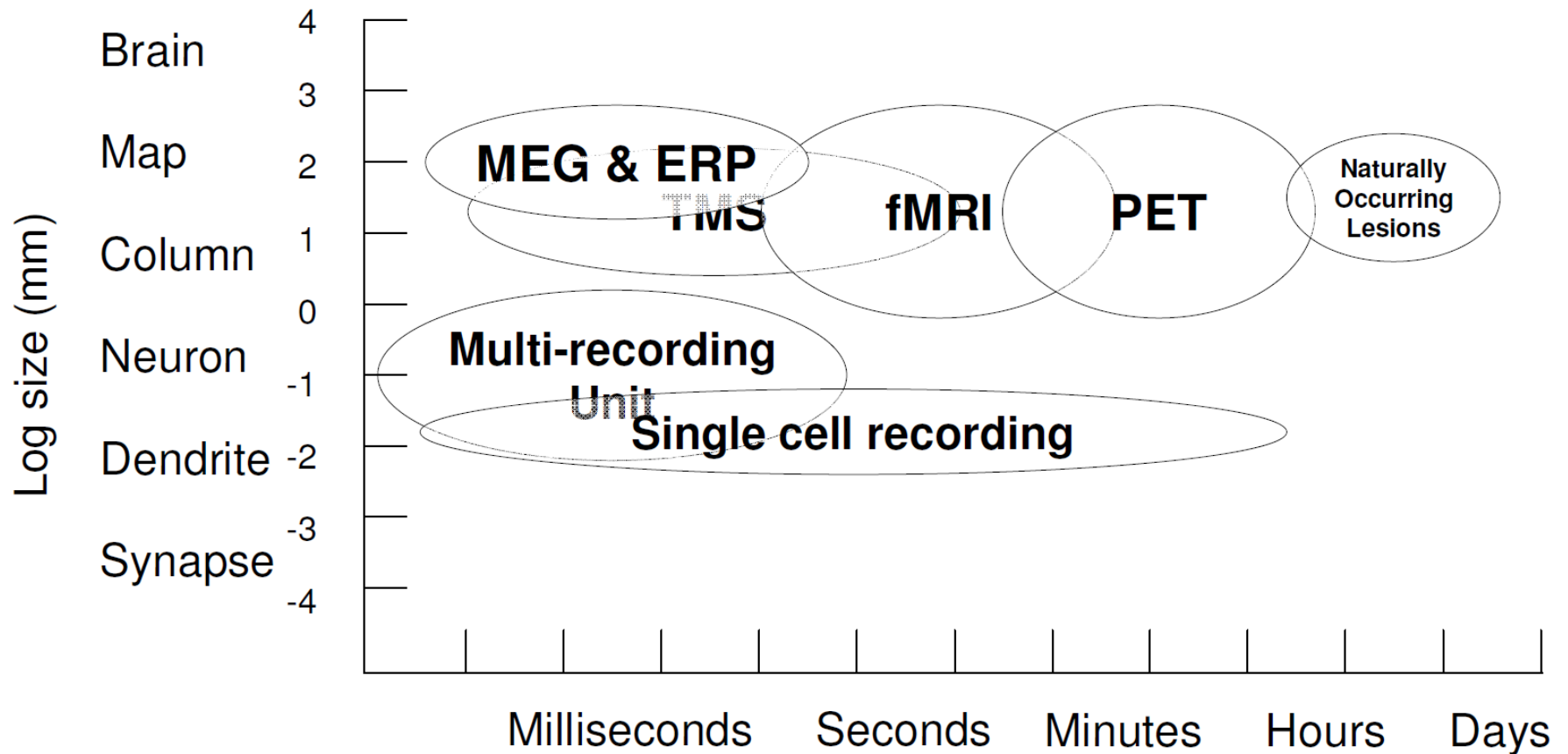
- EEG-fMRI as multimodal functional imaging
- EEG recordings
- fMRI BOLD
- Challenges in multimodal recording
- Does it correlates?





EEG-FMRI AS MULTIMODAL FUNCTIONAL IMAGING

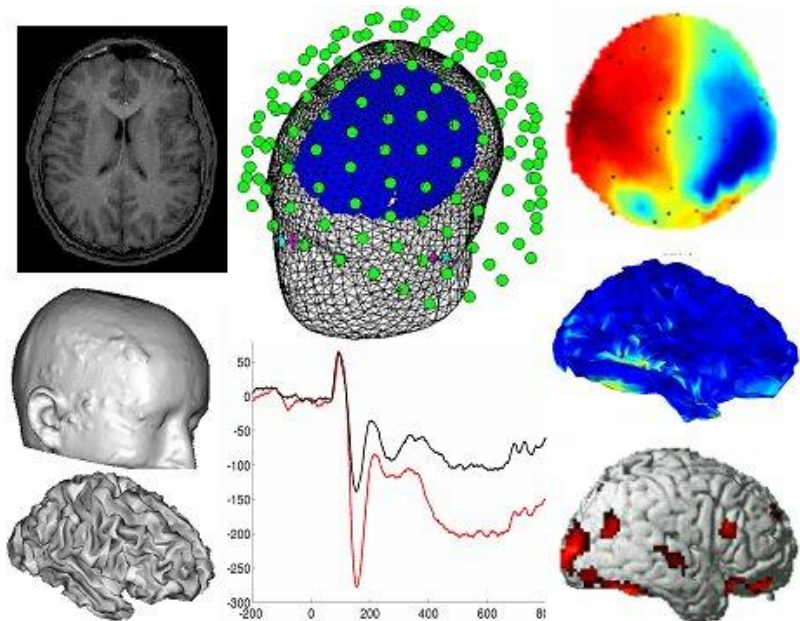
WHY COMBINING?



WHY COMBINING?



<http://fmri.uib.no/>



<http://bmet.wikia.com/wiki/Electroencephalography>

WHY COMBINING?

- EEG correlated functional MRI is designed to capture the electrophysiological and haemodynamic manifestations of brain activity.
- Although, EEG and fMRI can be recorded in the same subjects at different time, multimodal imaging refers essentially to their synchronous recording.
- EEG–fMRI emerged from the field of epilepsy imaging with the need for non-invasive imaging of the epileptic focus.



WHY COMBINING?

- Synchronous recording eliminates potential intersession bias - eliminating the effects of habituation, learning, attention, fatigue, anxiety, etc.
- The restricted space available in the scanner bore, the position of the experiment subject during the simultaneous recording (supine rather than sitting upright) and the loud noise caused by the MRI gradient system are all factors altering the experimental effects.
- Study of spontaneous (paradigm-free) brain activity, such as natural variations in EEG background (alpha rhythm), wakefulness, or activity during resting state
- EEG–fMRI is one strategy that can ascribe the timeline of brain activity in relation to cognitive processing, thanks to the high temporal resolution of EEG, and also specify the role of distinct events or oscillation patterns in combination with reliable information about the neuroanatomical structures involved, thanks to fMRI.



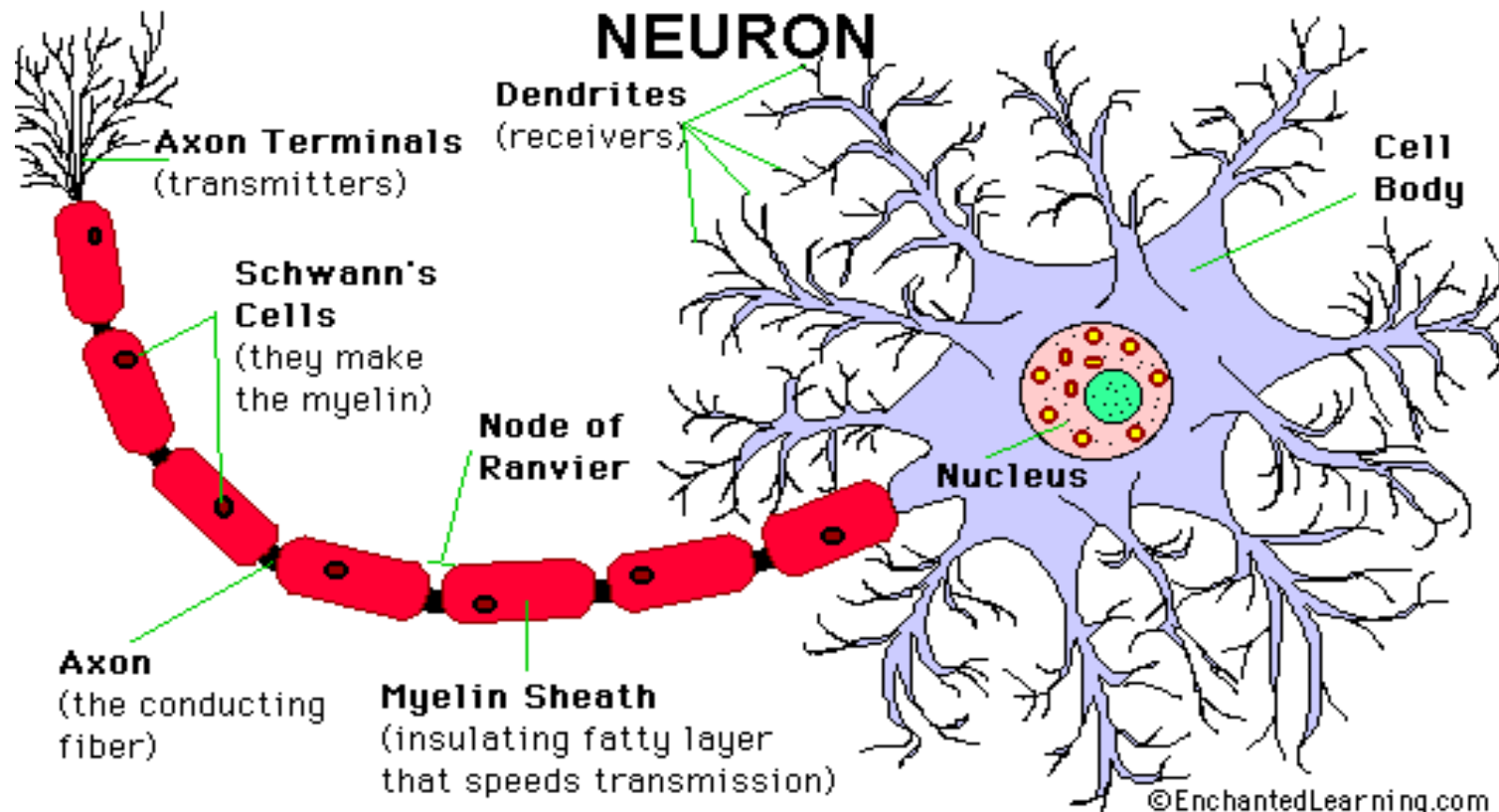


EEG RECORDINGS

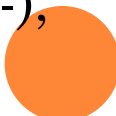
Back to basic (neurophysiology)
Neural recordings (LFP / EEG)

Back to basic

- Neuron have dendrites (inputs) and 1 axon (output)



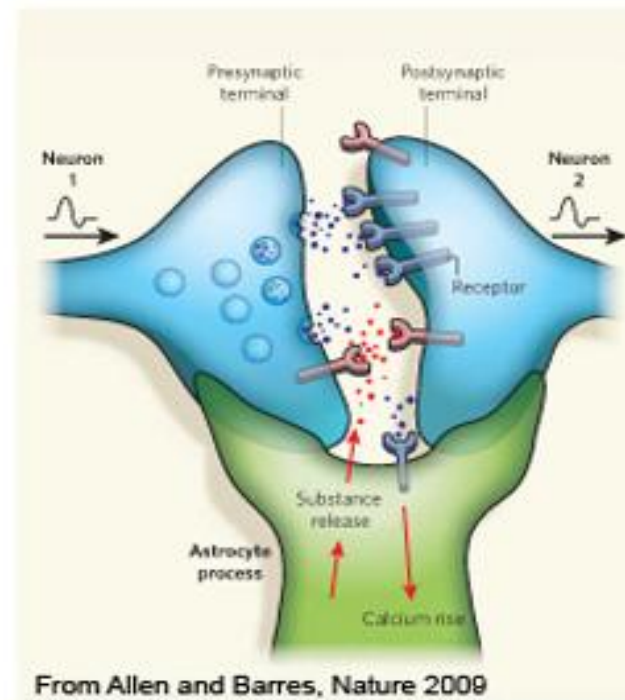
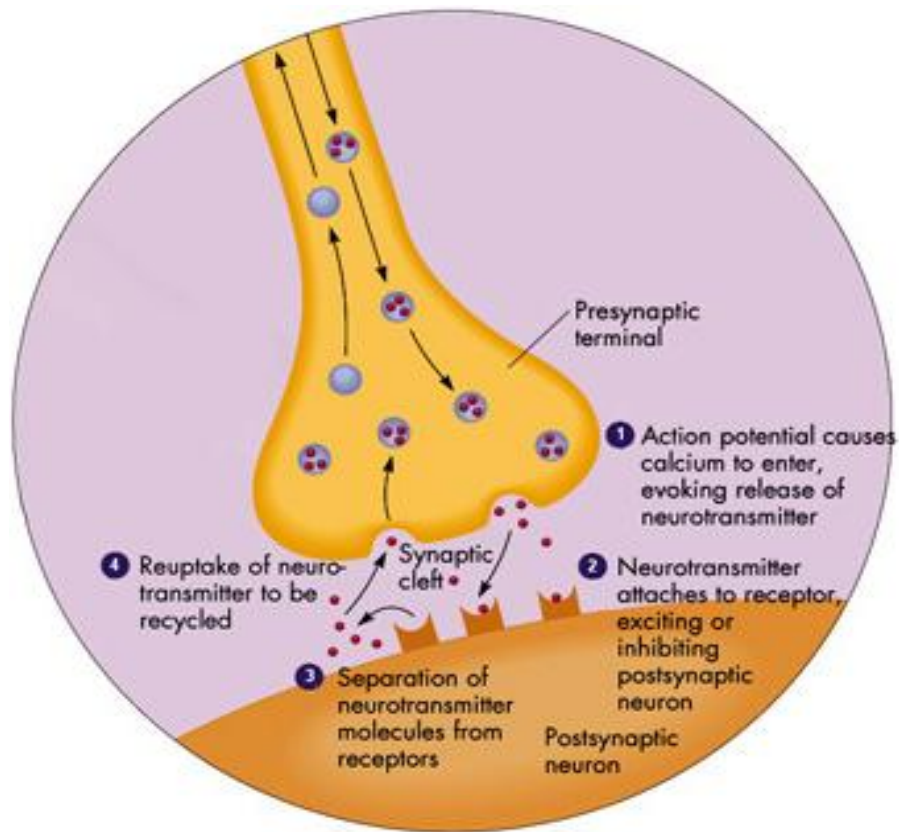
Back to basic

- Neuronal membranes are 10nm-thick liquid-crystal bilayer of phospholipids that preserve differences between the intra and extracellular environments.
 - Neuronal membranes have ion channels letting molecule to diffuse and also have selective pumps (e.g. the sodium-potassium pump forces 3Na^+ out of the cell and picks up 2K^+ into the cell on the return trip) causing a **concentration gradient**.
 - Because ions have electrical charge, the concentration gradient creates an **electrical potential** (about -70 millivolt) between the inside and the outside of the cell.
 - Neurotransmitter leads to the opening of **ions channels** through which some ions, such as sodium (Na^+), chloride (Cl^-), potassium (K^+) and calcium (Ca^{2+}) will diffuse.
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Back to basic

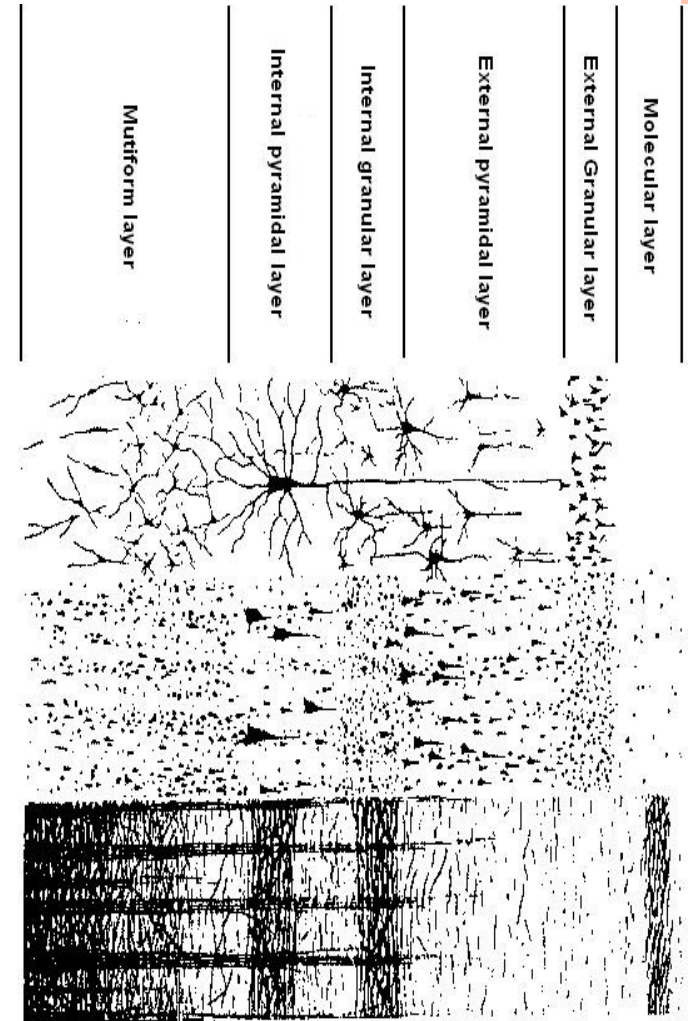
- Neuron communicate via synapses. The release of neurotransmitters interact with postsynaptic membrane receptors that gate ion channels.
- For example, the glutamate (the most common neurotransmitter ~90%) opens postsynaptic Na^+ channels. The influx of Na^+ decreases the electrical potential at the channels location. This local **depolarization** is referred to as an **excitatory postsynaptic potential (EPSP)**.
- Other neurotransmitters show, on the opposite, inhibitory effects. For example, the GABA (gamma aminobutyric acid) interacts with receptors to open Cl^- and K^+ channels. The influx of Cl^- or efflux of K^+ results in an increase in the resting potential at the channels location. This local **hyperpolarization** is referred to as an **inhibitory postsynaptic potential (IPSP)**.

Back to basic

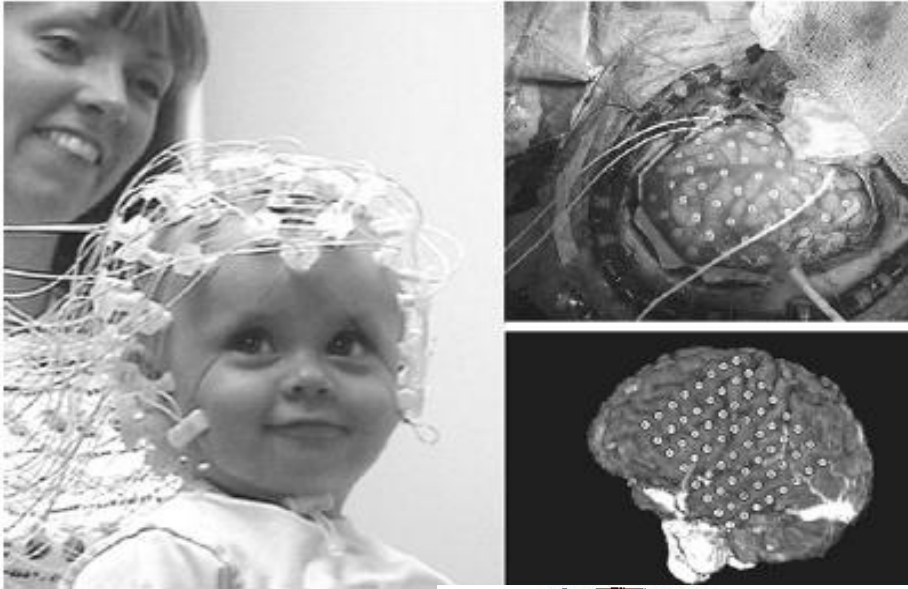


Neural recordings

- A nanoelectrode located on the cortex record **local field potentials**, i.e. the sum of extracellular potentials elicited by the synchronous firing of neurons.
- LFP polarity changes because it can 'see' EPSPs arriving at the surface layers i.e. positive charges are 'leaving' and thus record a negative potential, whereas a deep electrode would see positive charges 'approaching' and thus record a positive potential and vice versa when EPSP arrive to the deep layers. Note polarities are reversed for IPSP.

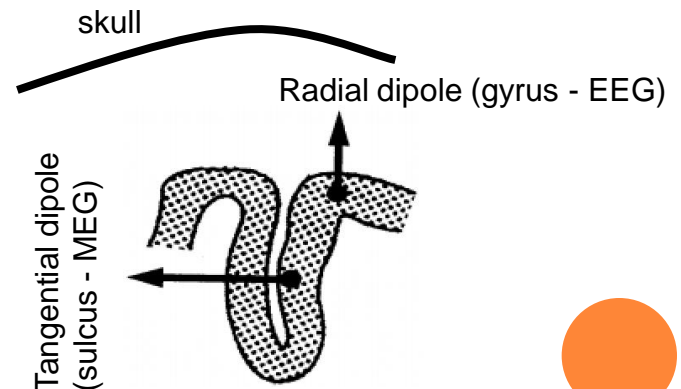
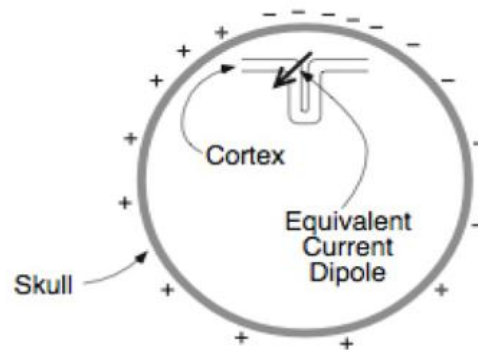
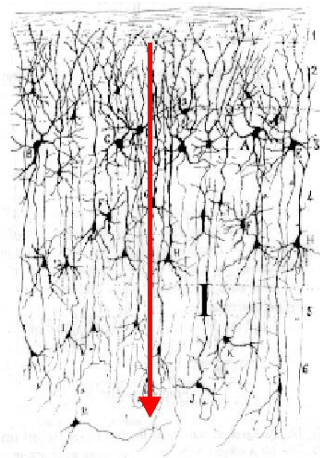


EEG



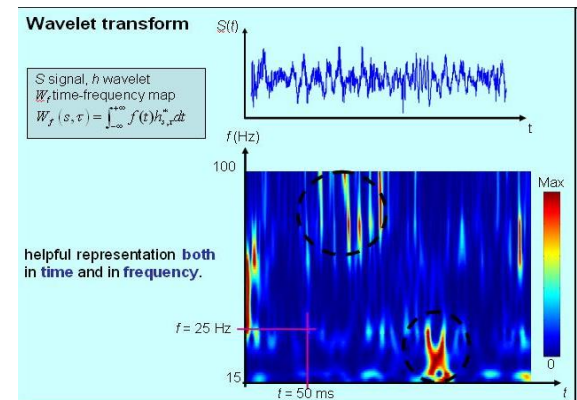
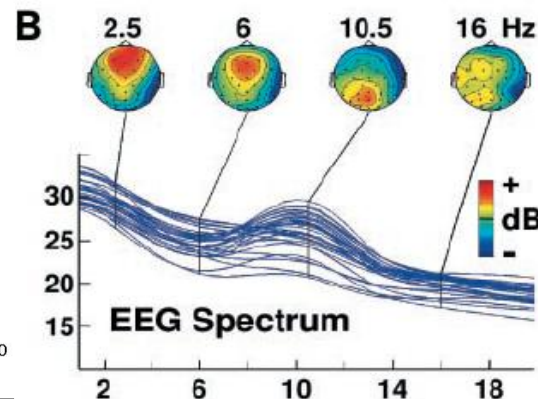
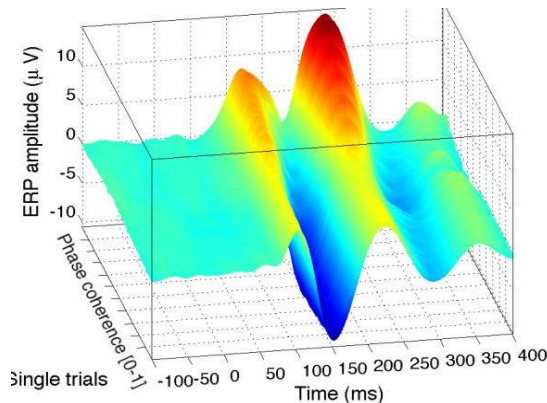
EEG

- EEG recordings correspond to the summed post-synaptic potentials and thus reflect LFP
- It necessitates the synchronized firing of neurons which aligned, so as to be able to see an equivalent current dipole (need volumes of about $2.5 \times 3\text{mm}$ whilst a macro-column is about $10\text{-}100\text{nAm}$ ($10^5 - 10^6$ neurons)).
- EEG captures mainly radial activity, that is activity located on gyri



EEG

- The signal is thus composed of time-series recorded at multiple electrodes, or inferred on sources (where it comes from)
- Data processing can therefore be done in the time domain (ERP), frequency domain (Power) or Time-frequency domain (ERSP).



EEG SUMMARY

- EEG recordings are done via electrodes at the surface of the scalp and capture millisecond electrical events.
- EEG recordings reflect LFP, thus showing the summed post-synaptic potentials – but the polarity is meaningless (does not reflect EPSP or IPSP)
- EEG electrodes can only ‘see’ particular types of dipoles (mainly gyrus activity) and necessitate the synchronization of large assemblies with a bias toward pyramidal neurons.
- Information can be gathered in the spatial and frequency domains





fMRI BOLD

- The fMRI signal and measurement
- The BOLD signal
- Neural activity vs. BOLD response

THE FMRI SIGNAL

- Using MRI technology to measure a surrogate of neural activity, i.e. changes in blood flow (Ogawa et al., PNAS 1990)



Belliveau et al. 1991

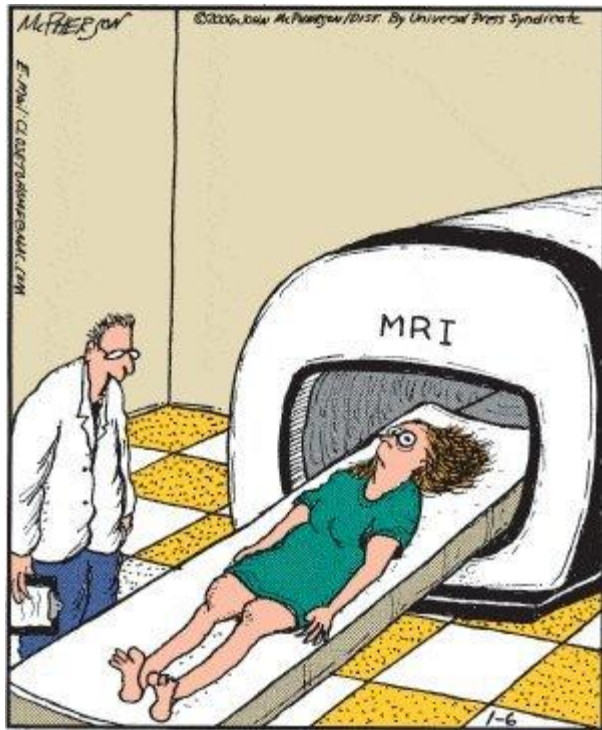


WHAT CAN WE MEASURE?

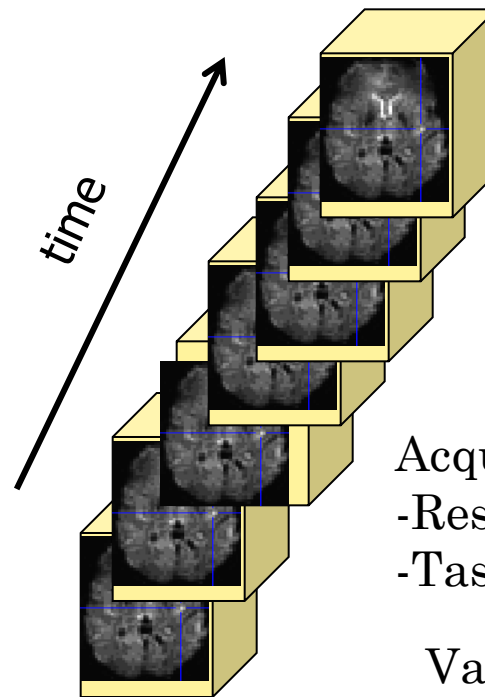
- *functional segregation* and *functional integration*.
- Functional segregation = the specialization of brain regions for some aspect(s) of a function.
- Functional integration = the study of connected processes. Methods for functional integration can be broadly divided into functional connectivity (~ finding statistical patterns) and effective connectivity (~ model how regions interacts).



FMRI IN PRACTICE



"OK, Mrs. Dunn. We'll slide you in there, scan your brain, and see if we can find out why you've been having these spells of claustrophobia."

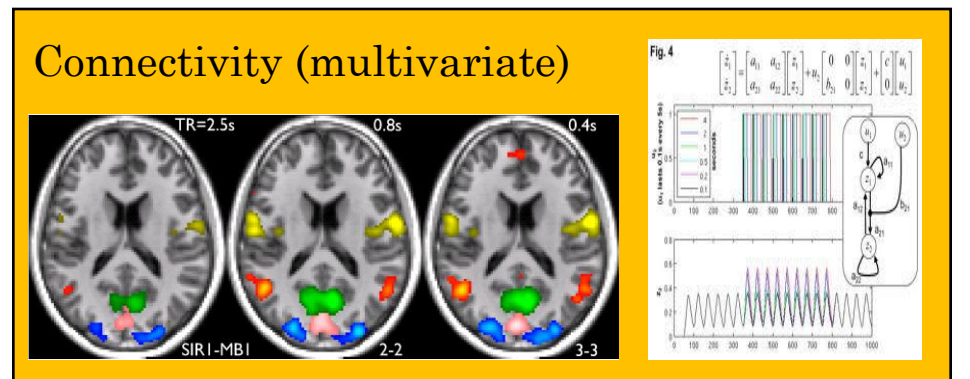
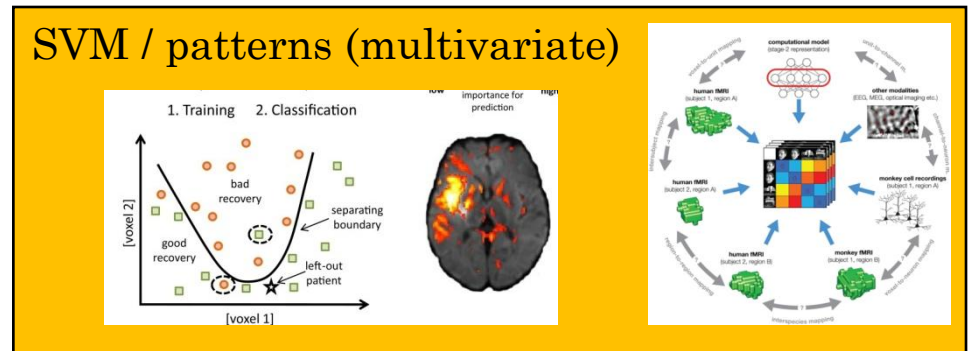
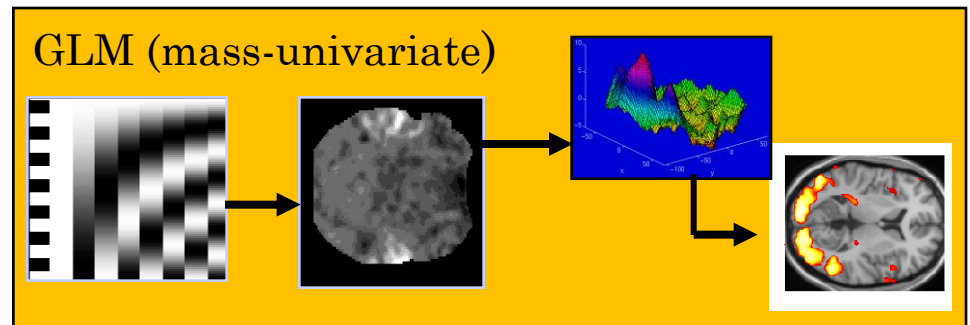
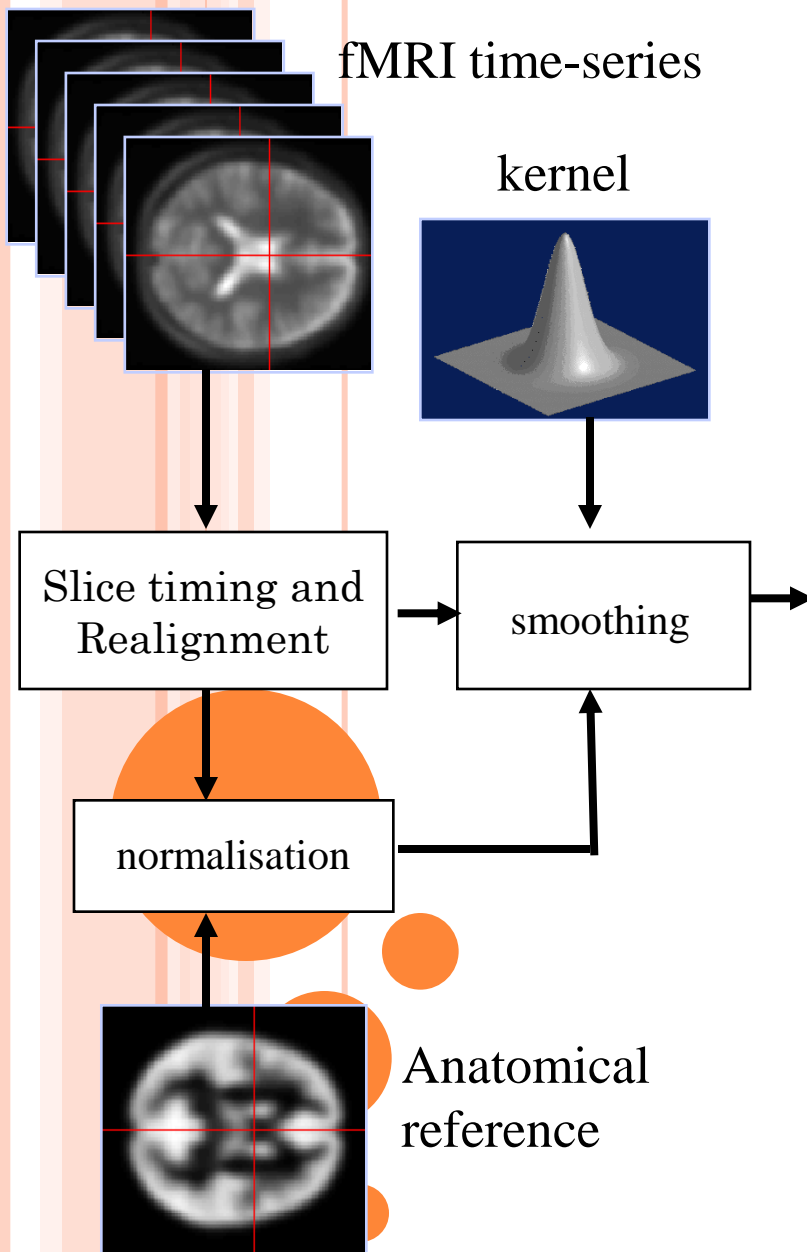


Acquisition of time-series

- Resting state (~8 min)
- Task (from 5min to ?)

Various constraints

- Stay still
- No metal
- Expe. designs



fMRI results are statistics

THE BOLD SIGNAL

- After a sensorial stimulation (or event after 'auto-stimulation', e.g. mental imagery), there is an increased neuronal activity in some part(s) of the brain. This increased neuronal activity elicits an increase in oxygen and glucose consumption supplied by the vascular system.
- The MRI signal measured in functional imaging is usually a signal that measures changes in the microvasculature oxygenation. More precisely, it deals with venous oxygenation (oxygenation in arteries is always 90-100%)
- The relationship between venous oxygenation and the MR signal strength corresponds to images called Blood Oxygenation Level Dependent (BOLD).




THE BOLD SIGNAL

- In 1936, Linus Pauling discovered that the hemoglobin molecule has magnetic properties that differ depending upon whether or not it is bound to oxygen. The oxygenated hemoglobine (Hb) is diamagnetic as it has no unpaired electron and no magnetic moment. In contrast, the deoxyhemoglobin (dHd) is paramagnetic as it has unpaired electron and magnetic moment.
- Thus, because blood deoxygenation affects magnetic susceptibility, MR pulses used in fMRI should show more signal for blood with oxygen (Hd) and less signal for blood deoxygenated (dHb)!! but I've just said that we look at the venous system, i.e. where we have dHb – How can we have more signal?

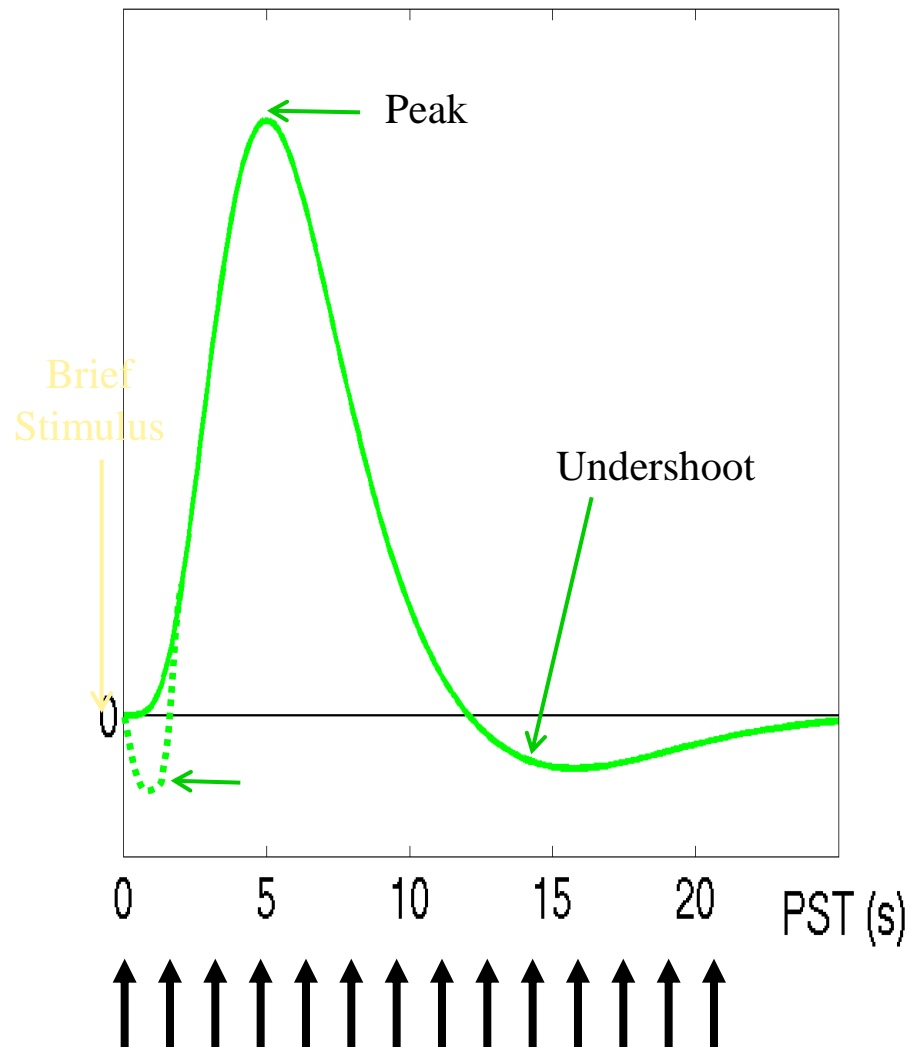


THE BOLD SIGNAL

- PET studies using $\text{H}_2\text{O}_{15}^*$ and FDG^* have shown that the regional cerebral blood flow (rCBF) and the regional cerebral metabolic rate (rCMR) increase during activation phases (neuronal stimulation). However, rCBF and rCMR are not completely coupled. During activations, the rCMRO_2 increase of 5% but the rCBF increase of 29% (Fox & Raichle, 1986).
 - **This hyper-perfusion (McIntyre, et al. 2003) is the basis of the BOLD contrast.** At rest, the oxygen level is around 95% in the arterial system and around 60-80% in the venous system (Bandettini, 1999). During activation, the oxygen level increases up to 90% in the venous system → less perturbation of local magnetic field
- 

THE BOLD SIGNAL

- The BOLD signal increases about 2 sec after the neural activity, it then reaches a plateau at about 5 – 8 sec. It will plateau if the neural activity continues. Once the neural activity stops, the signal returns to baseline 8 to 11 sec later. Finally, a transient change referred to as the undershoot can be observed.



We need fast multiple acquisitions
= time series of 3D volumes

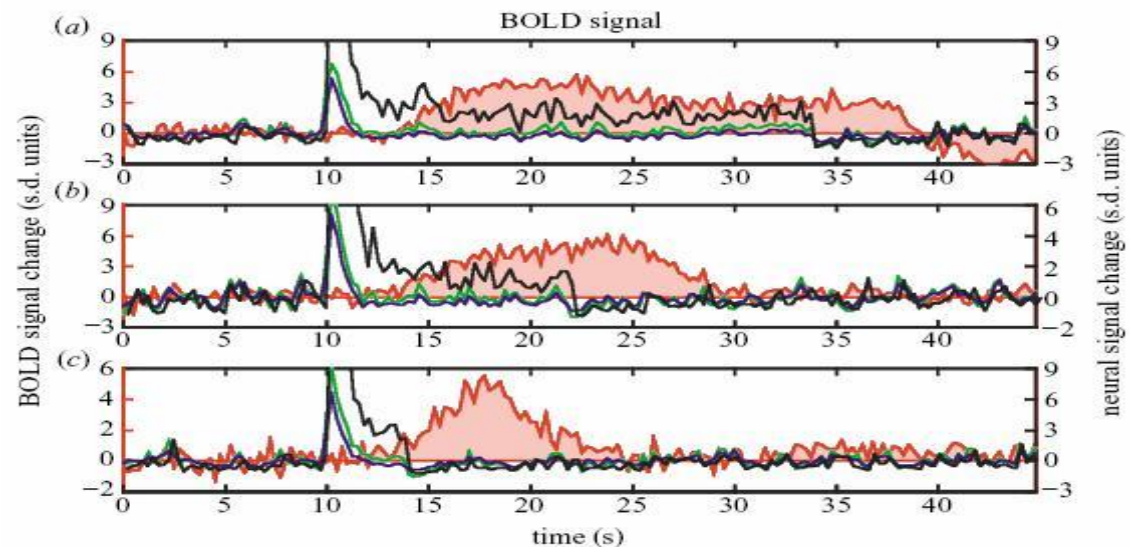
NEURAL ACTIVITY VS. BOLD RESPONSE

- The BOLD signal reflects the firing of neural populations such as a strong correlation exists between the BOLD amplitude and local field potentials data (Logothetis, 2001)

24 sec stimulation

12 sec stimulation

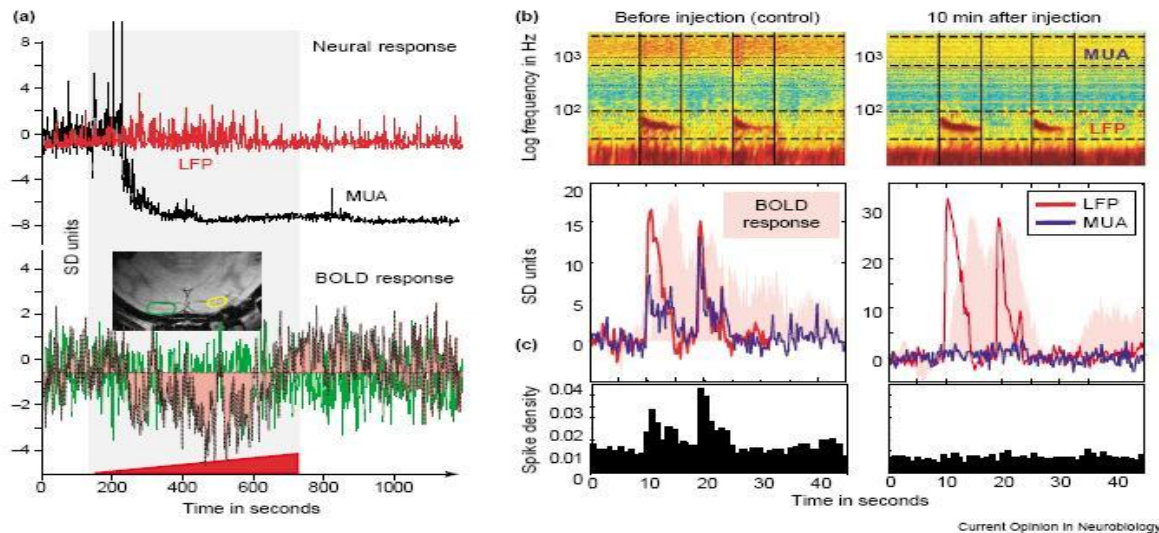
4 sec stimulation



- This means that BOLD is more related to synaptic activity than neural activity per se (i.e. the interplay of EPSP and IPSP)

NEURAL ACTIVITY VS. BOLD RESPONSE

- The relationship between neural spiking and BOLD signal is NOT straightforward because it reflects synaptic activity, which means one cannot really say if the BOLD signal relates to a neural excitation or inhibition.



Serotonin (5HT) is injected during 10min (red) during a visual stimulation. Soon after injection, the multiunit activity decreases (inhibition) but both LFP and BOLD are clearly above baseline (Logothetis 2003).

The BOLD signal reflects mainly the input and local processing of neural information



FMRI SUMMARY

- The BOLD is mostly correlated with extra-cellular recordings – e.g. the BOLD correlates better with LFP (an aggregate signal associated with perisynaptic events and is biased toward pyramidal neurons) than spiking activity (individualized axonal responses).
- This implies that the BOLD reflects the synaptic activity = input and local processing of information (excitations and inhibitions alike)
- The BOLD is however more inclusive than LFP by being also sensitive to long range feedback and neuro-modulatory processes.





CHALLENGES IN MULTIMODAL RECORDING

- Safety
- fMRI artefacts
- EEG artefacts
-

SAFETY

- The MRI static magnetic field is always on. The strength of the magnetic is nowadays of 3Tesla 60.000x stronger than the earth's magnetic field of .00005T → need to use special EEG systems which are non magnetic (but still conduct electrical current!)



<http://mrimetaldetector.com/blog/>



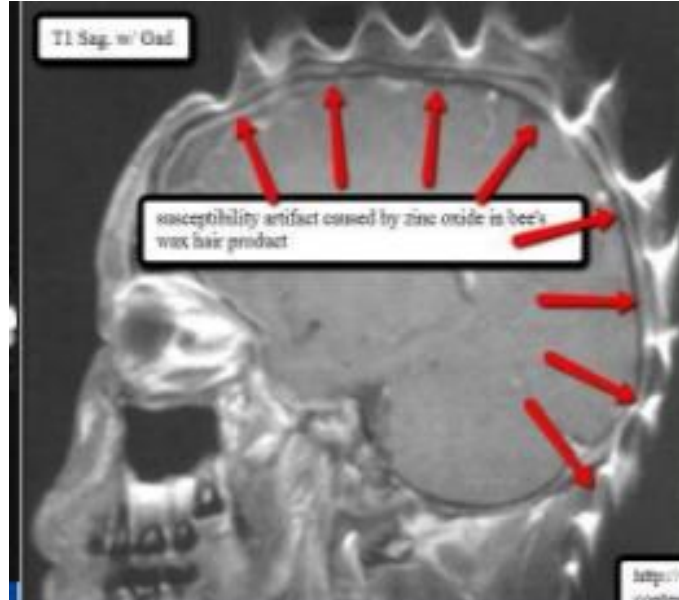
SAFETY

- During MRI, small magnetic gradient fields are continuously turned on and off allowing to make protons to oscillate at different frequencies and phases
- Following Faraday's Law, the RF field also induces currents into an electrically conductive object
- The energy is transmitted to the electrode leads and dissipated at the points of highest thermal resistance: the contact point between the electrode pin and the scalp



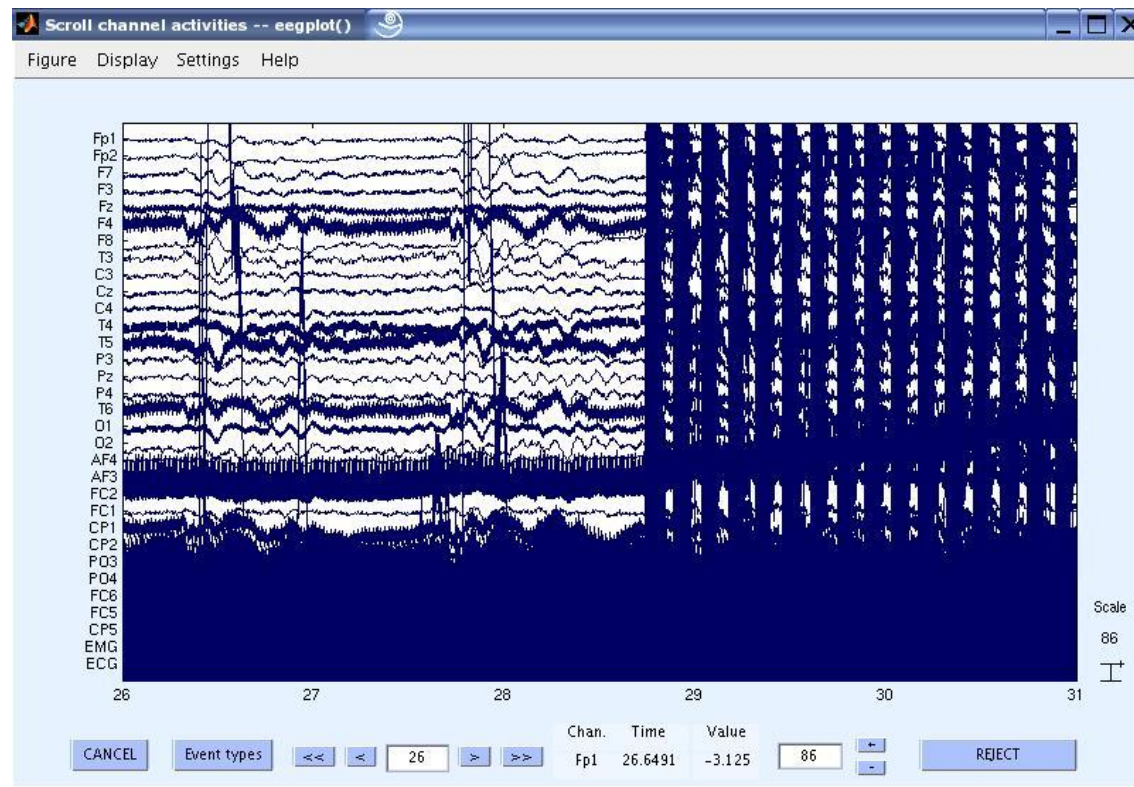
MRI ARTEFACTS

- The introduction of magnetic object distort the magnetic field
- Vibrations of elements inside the scanner also affect the signal



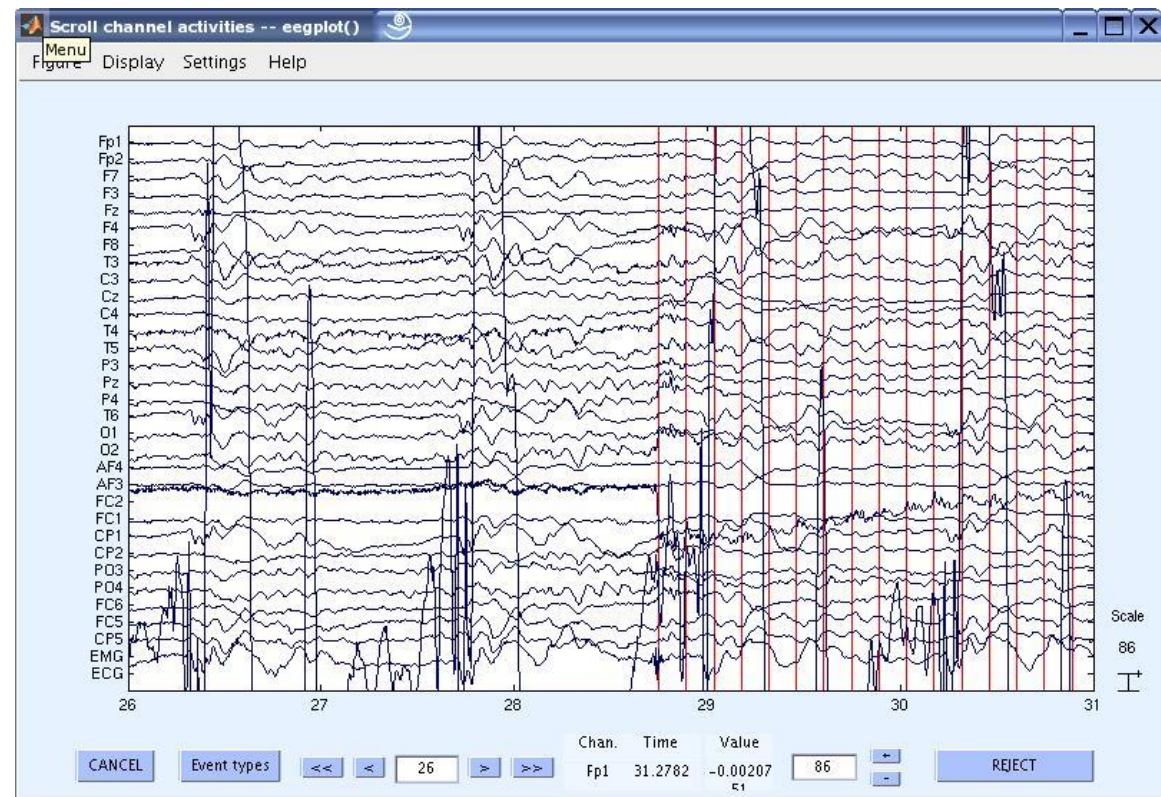
EEG ARTEFACTS

- Gradients fields induce electrical signals way stronger than the EEG signal



EEG ARTEFACTS

- Below this is the ballistocardiogram artefact (the hearth signal)



<http://fsl.fmrib.ox.ac.uk/eeglab/fmribplugin>



DOES IT CORRELATES?

BOLD vs. ERP

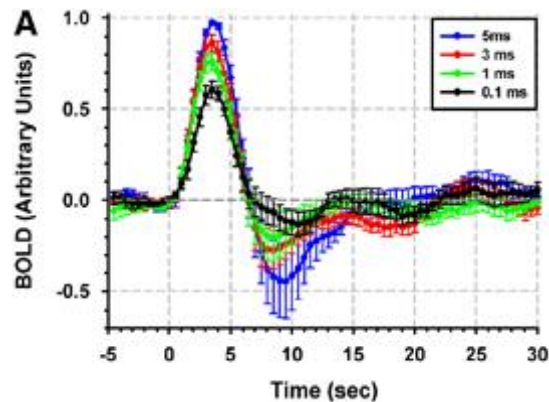
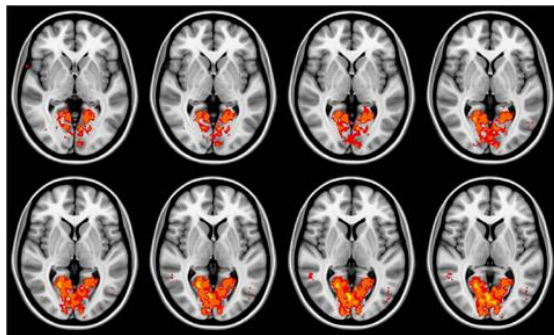
- EEG–fMRI has mainly been used as a special form of fMRI. In most applications, EEG is used as either an epoch categorisation device or as a supplier of potential explanatory variables for the BOLD model.
- Correlation BOLD and ERP sometimes observed .. and sometimes not, in particular different components can correlates differently because they can reflect the combination of multiple sources.



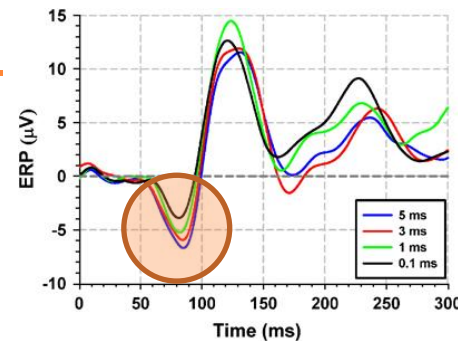
BOLD vs. ERP

- Yesilyurt et al. (2010): simple light emitting diodes flashing at different durations.

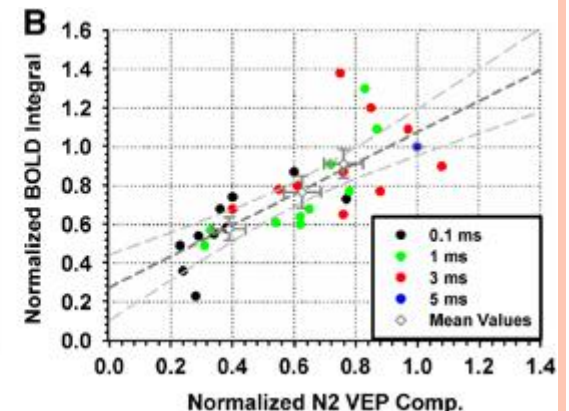
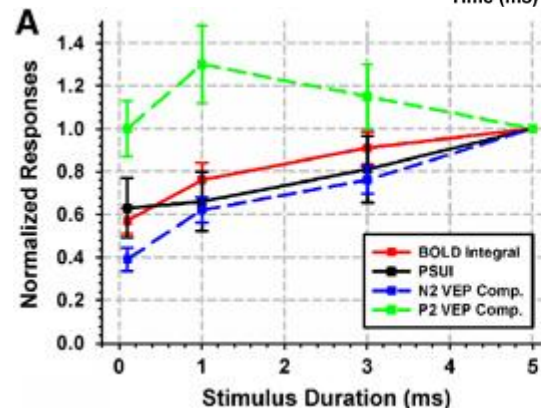
fMRI



EEG

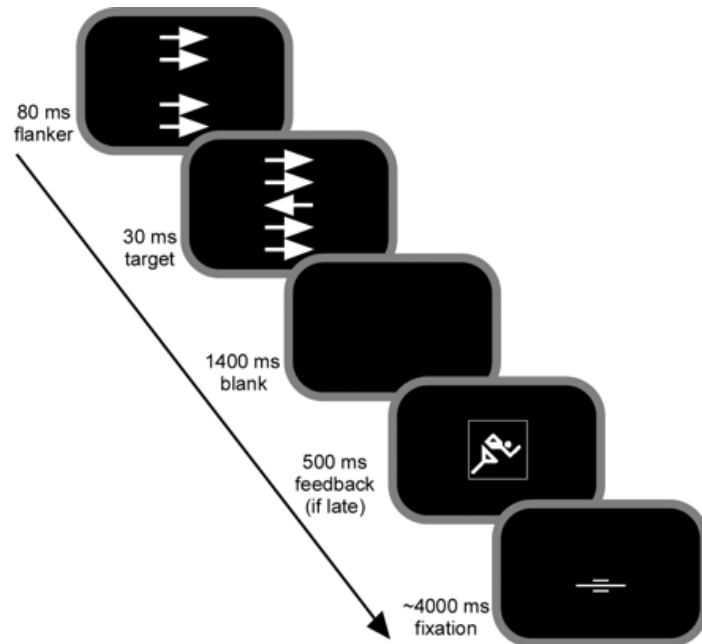


$$R^2 \sim 0.6$$

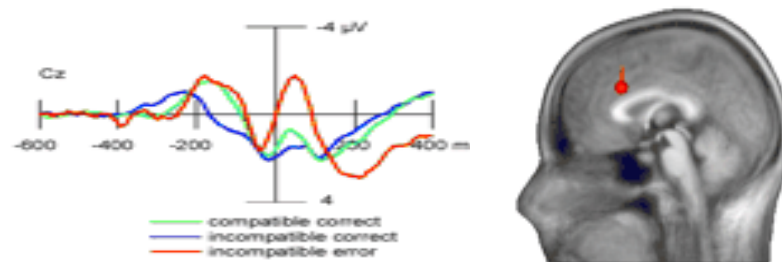


BOLD vs. ERP

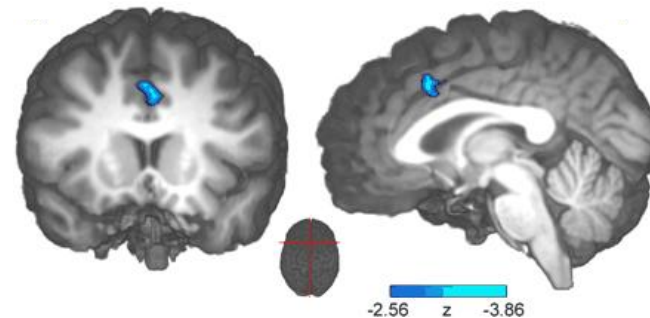
- EEG can be used to inform fMRI
- Debener et al. (2005): speeded flanker task / conflict monitoring



ICA Component and source location



fMRI activation = f(ICA trial variations)



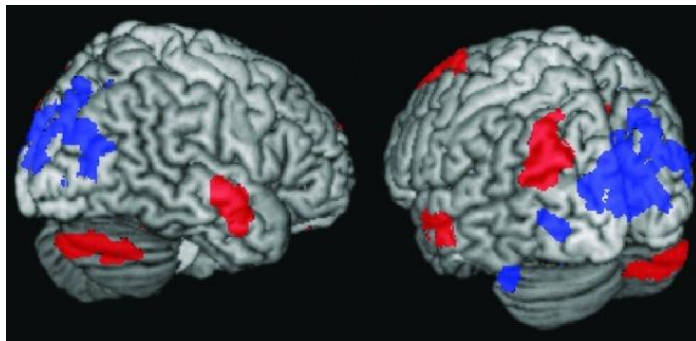
BOLD vs. EEG POWER

- ERP are very short duration, and do not consume as much energy as long lasting oscillations. Indeed, it has been shown strong correlation between EEG power and BOLD.
- The spontaneous BOLD activity (resting state) in different brain areas is linked to distinct EEG frequency bands.

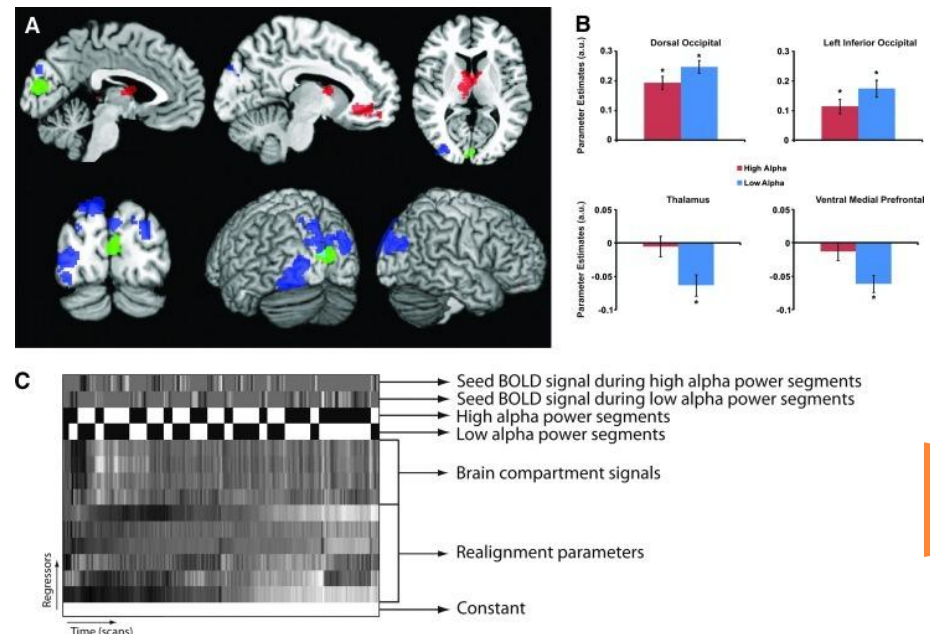


BOLD vs. EEG POWER

- Scheeringa et al (2012) show for instance that when alpha power increases (as e.g. now as you are getting sleepy), BOLD connectivity between V1 and occipital brain regions decreases and that the negative relation of the visual cortex with the ventral-medial prefrontal cortex is reduced (= enhanced functional inhibition during a higher alpha activity?).



Positive & Negative correlation with alpha power





SOME REFERENCES

Books

- EEG: **Luck (2005)**. An Introduction to the Event-Related Potential Technique. MIT Press
- fMRI: **Huettel et al. (2009)**. Functional Magnetic Resonance Imaging. Sinauer Associates.
- EEG-fMRI: **Ullsperger, M & Debener, S. (2010)**. Simultaneous EEG and fMRI: Recording, Analysis, and Application. Oxford University Press.

Articles

- Yesilyurt et al. (2010). *JCBF*, 30, 449-458
- Debener et al. (2005). *J. Neurosc*, 25, 11730-11737
- Scheeringa et al (2012). *Brain Connect*. 2, 254-64
- See also: Mullinger et al. (2013) Best Current Practice for Obtaining High Quality EEG Data During Simultaneous fMRI. *J. Vis. Exp.* (76) <http://www.jove.com/video/50283/best-current-practice-for-obtaining-high-quality-eeg-data-during>