Audition: cognitive neuroscience and experimental design in MEG

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Plan:

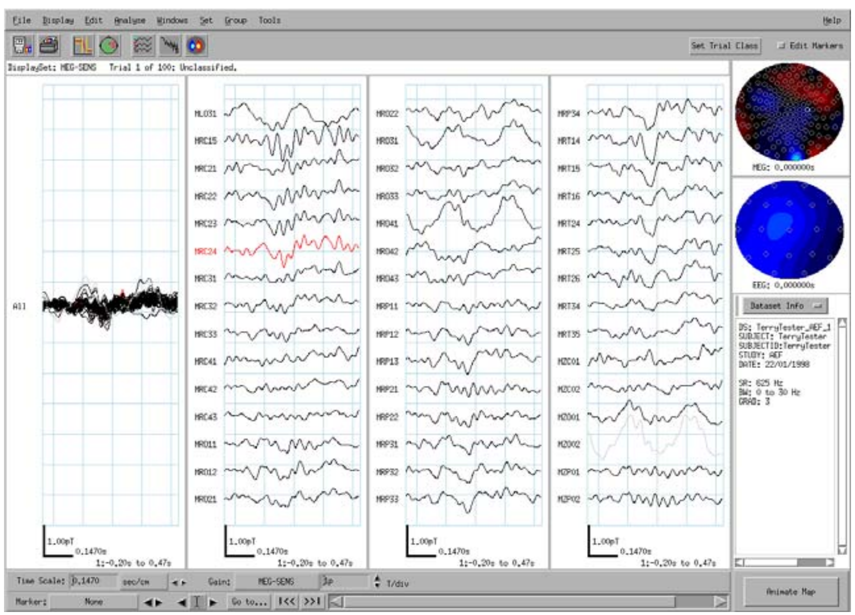
- Review of MEG sources
- Issues in design of auditory MEG experiments
- Review of auditory MEG data
- Source Localisation

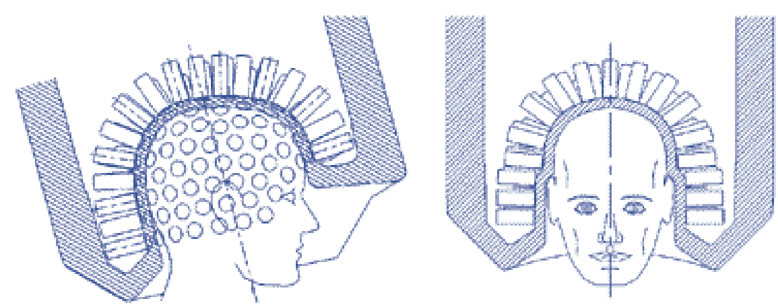
  Dipole modelling

  Distributed source modelling

MagnetoEncephaloGraphy (MEG)

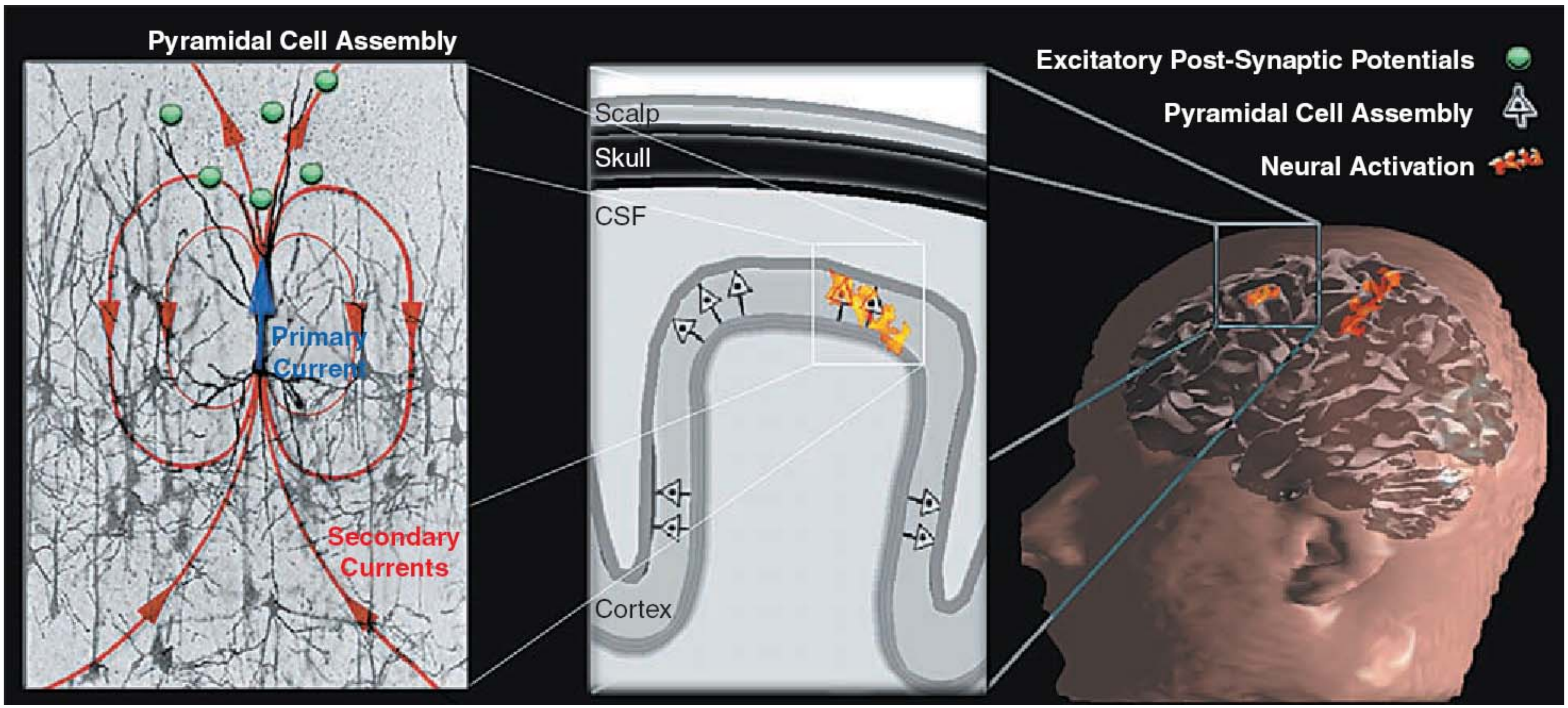
- Measurement of tiny magnetic fields outside the head generated by electrical activity within the head
- Functional Imaging technique
- Direct measure of neuronal activity (ms TR)
- Modern MEG scanners are equipped with ~ 300 channels





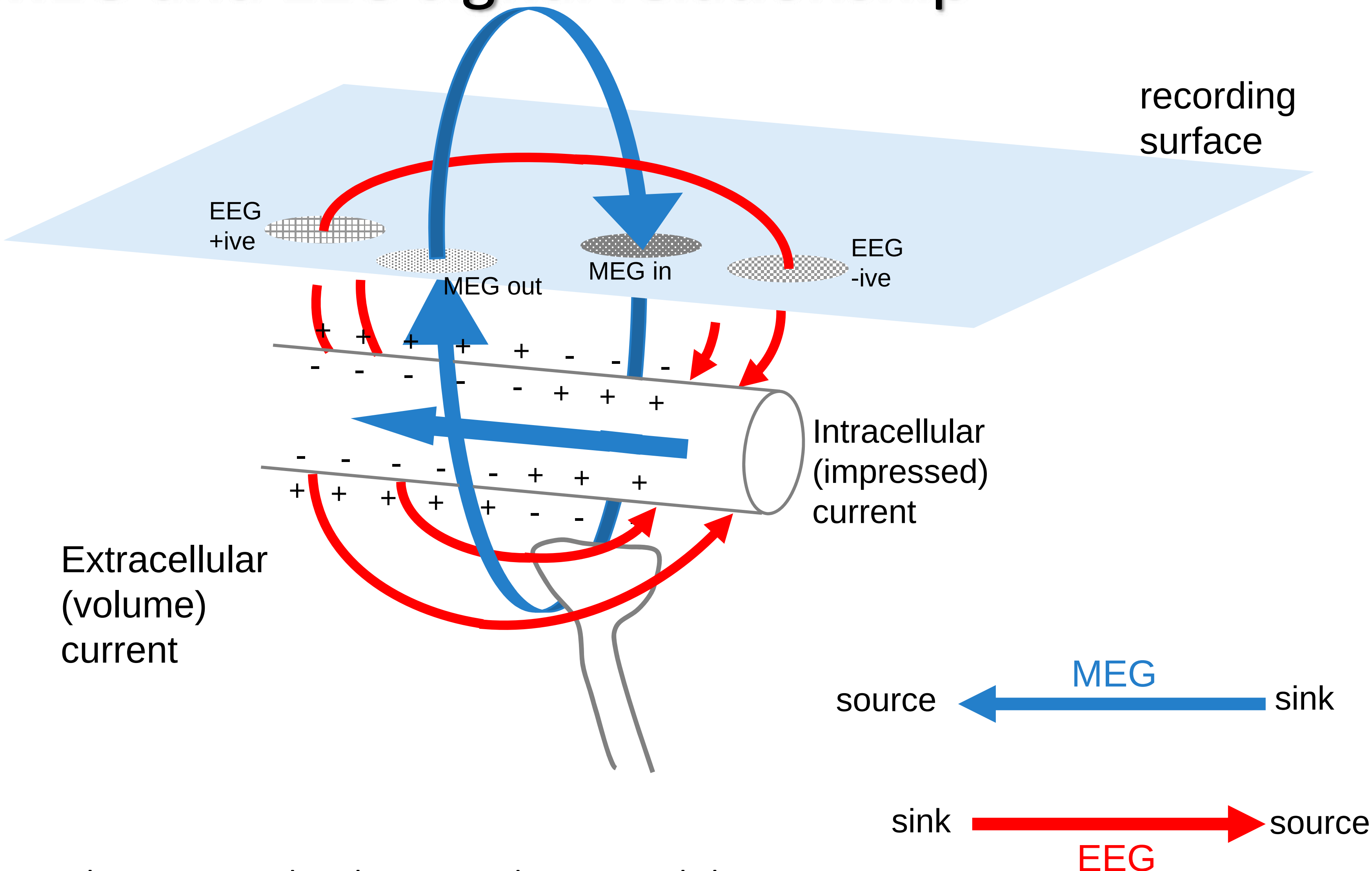
The source of MEG signals: A reminder…

- Spatial and temporal summation of around 100,000 neurons
- The electrical current associated with neuronal activity is known as the ‘primary current’



Sylvain Baillet, J.C. Mosher, R.M. Leahy (2001) Electromagnetic Brain Mapping. IEEE Signal Processing Magazine, Volume 18(6), page 14-30.

MEG and EEG signal relationship



- Dipoles associated with MEG and EEG signals have opposite source-sink orientations;
- Magnetic fields are orthogonal to electric potentials;

ISSUES FOR THE DESIGN OF AUDITORY MEG EXPERIMENTS

Stimulus Types

The auditory system encodes variety of sounds with complex spectro-temporal patterns (speech, music etc.)
Changing variables make them hard to control

Clicks, Tones and noise are used to enable greater experimental control

How do sound features (intensity, pitch etc) modify brain activity?

Stimulus Delivery

Challenge is to deliver sounds without perturbing the natural magnetic field

Conventional headphones are unsuitable

E-A-R TONE System

Tube-phones – Sound is delivered as electrical signal to transducers placed away from the MEG sensors. Using foam ear plugs attenuates the ambient accoustic noise

Monaural vs Binaural Stimulation

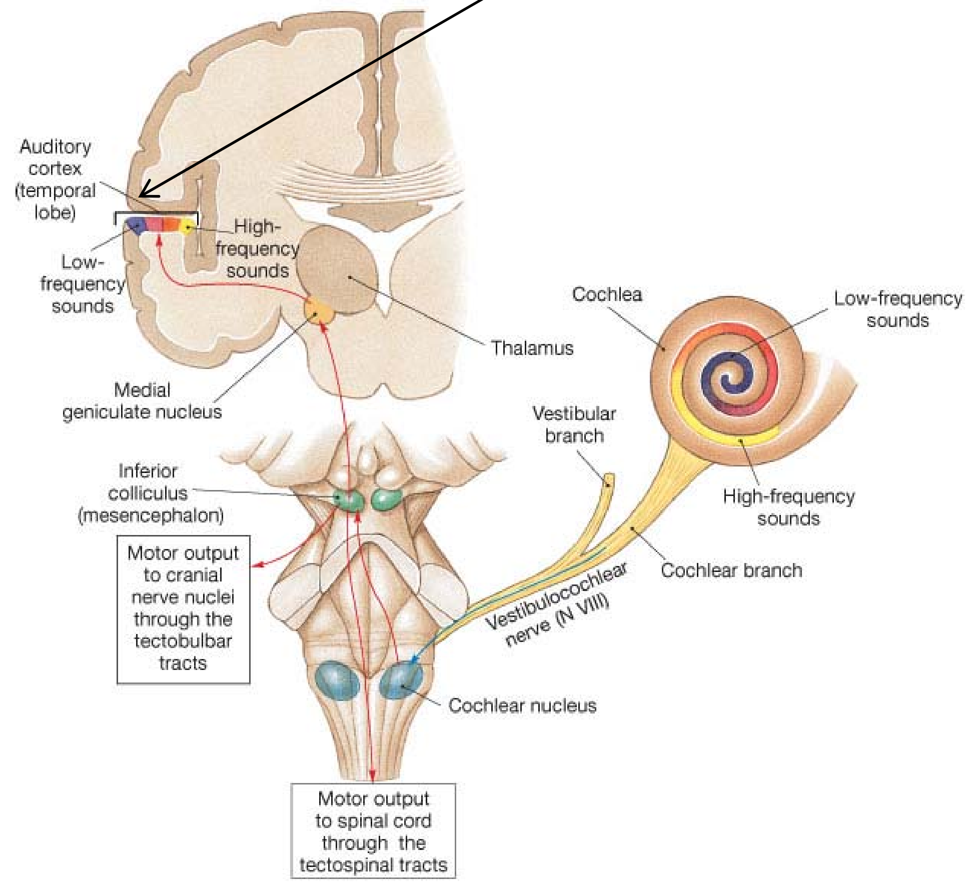
Multiple sources complicate identification of sources
Stronger response in the contralateral hemisphere

Tonotopic organisation

Monaural – Reduces the number of sources with large response amplitude

• Beneficial for certain types of analysis, dipoles and beamformers

Binaural – Hemispheric asymmetries, dichotic listening



Other design issues...

- **The length of recordings**

Spatial resolution of MEG is dependent on head movement which must be minimised. Experiment length is limited to (~ 20min)

Discomfort increases head movement, introduces artefacts (muscle activity) in the data

The length of stimuli (and experiment) influenced by need for sufficient Signal-to-Noise ratio – averaging trials (~ 50 per condition)

- **Task performance**

Task performance affects quality of the data.

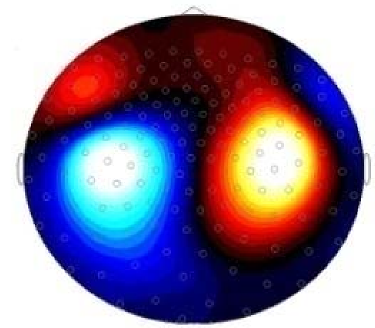
Passive listening to sounds
No task (visual fixation) = hard to stay alert. Can cause head movement and artefacts data
Eyes-closed = alpha activity
Attention to task modulates certain components of the evoked response (P3m)

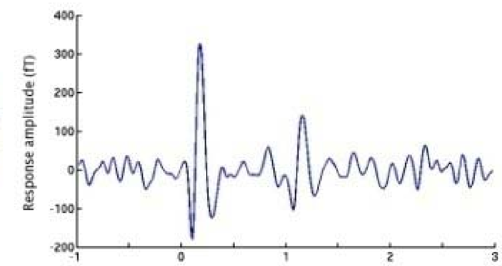
Silent movies (subtitled), reduce boredom and possibility of head- movement
But not ideal where behavioural responses are needed (attention/response to sound).

Auditory MEG Data

Evoked vs Induced MEG Data

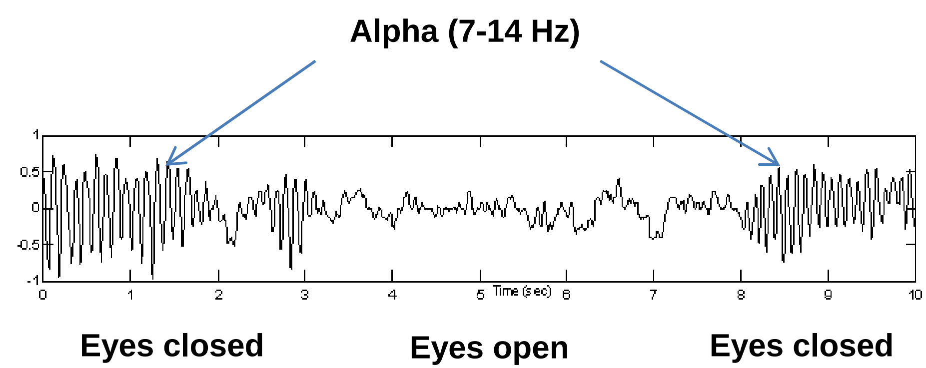
In a typical MEG experiment, data will contain **stimulus-evoked** and **stimulus-induced** brain activity





Evoked response: transient deflection in response to a sensory input

- Phase-locked to the onset of the stimulus
- Fixed latency
- Requires averaging single trials



Induced response: modulation of the ongoing brain activity due to an external event

- Time-locked to the onset of the stimulus
- Variable latency
- Does not "average in"

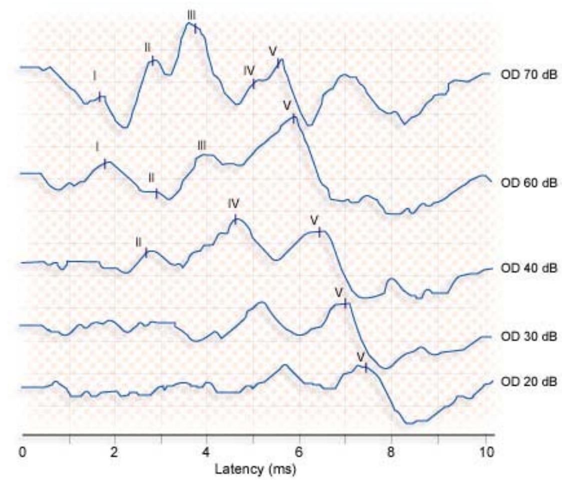
Characterised by a change in spectral power of the response within a specific frequency band

Auditory Evoked Field (AEF)

An **evoked field** is a transient energy onset response**,** synchronized to an external sensory event with different components.

- **<u>Exogenous Evoked Fields</u>** - characteristics (latency, amplitude, field distribution) depend on the ***sensory*** modality employed, and that are relatively **independent of mental set.**

Auditory Brainstem Responses (ABRs)
(Difficult to measure with MEG)
Middle-latency responses (MLRs) (~10-50 ms)
N1m (~ 100ms)
P2m (~ 200ms)



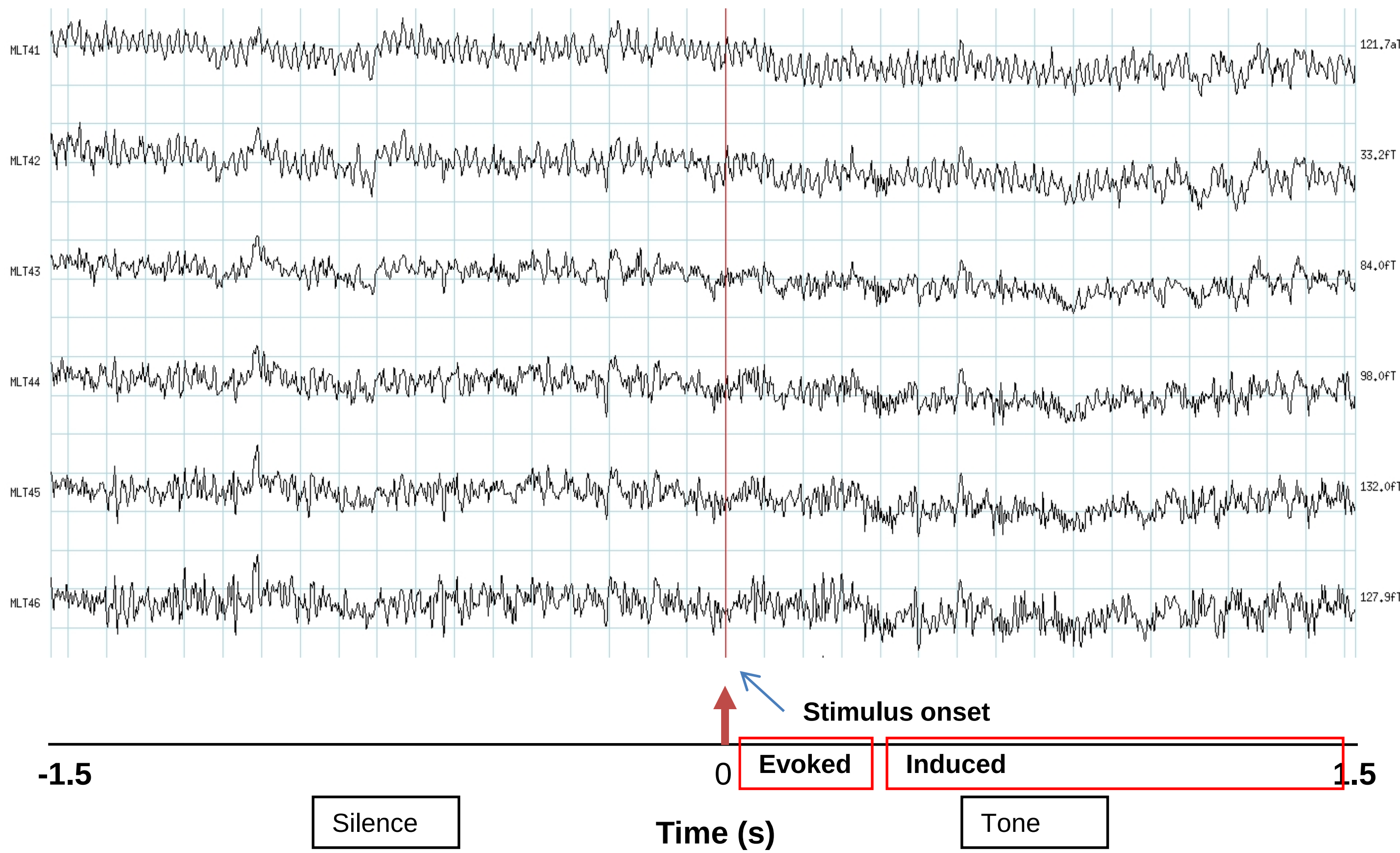
- **<u>Endogenous (Cognitive) Evoked fields</u>** - characteristics are relatively independent of the sensory modality employed, but **depend on mental set.**

P3m (~ 300ms)

Raw Auditory MEG Data

Showing…
Single Trial

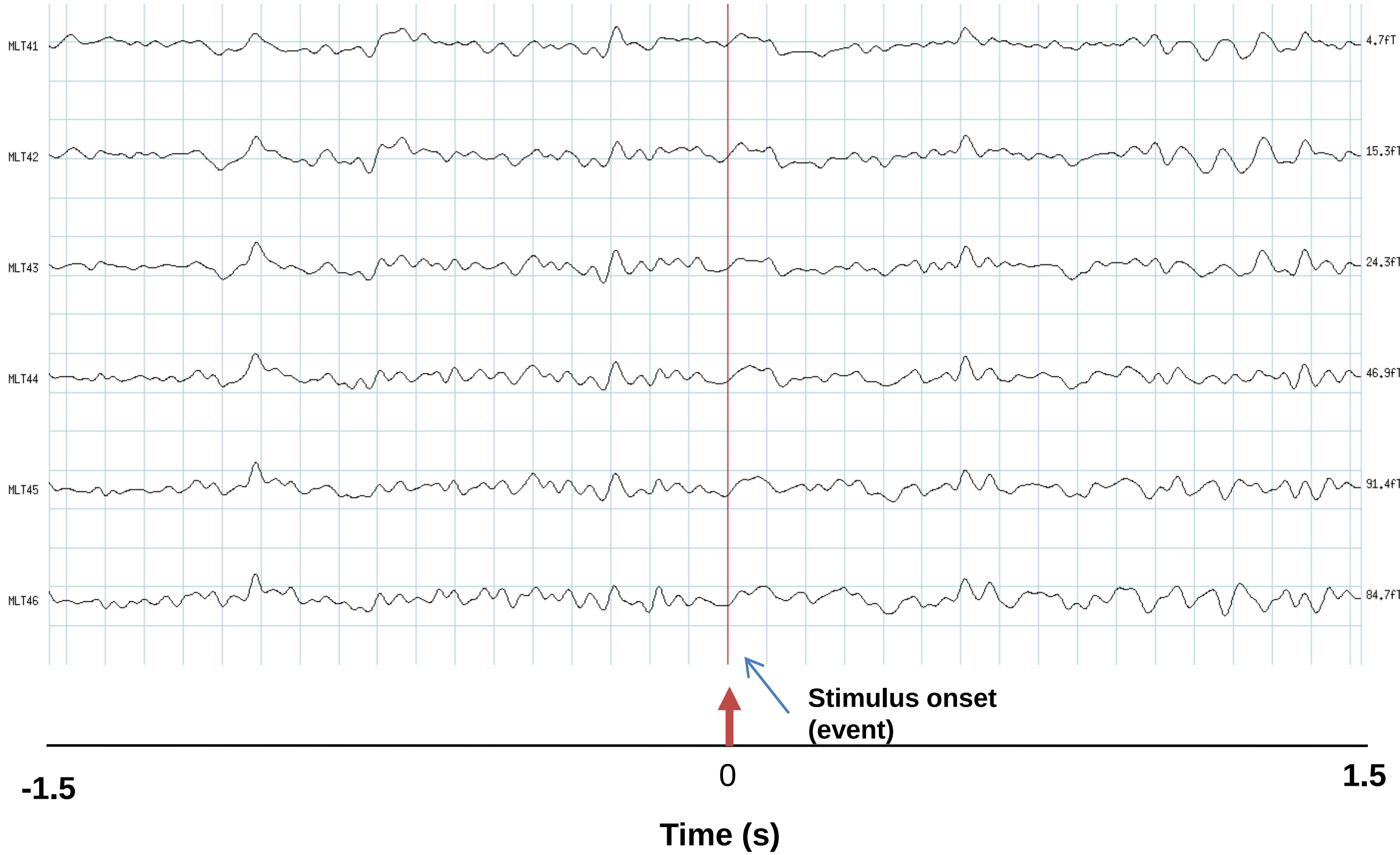
6 Channels over the left temporal lobe



Stimulus: pure tone at 3.5 kHz

Right ear stimulation at 60dB
100 repetitions (trials)

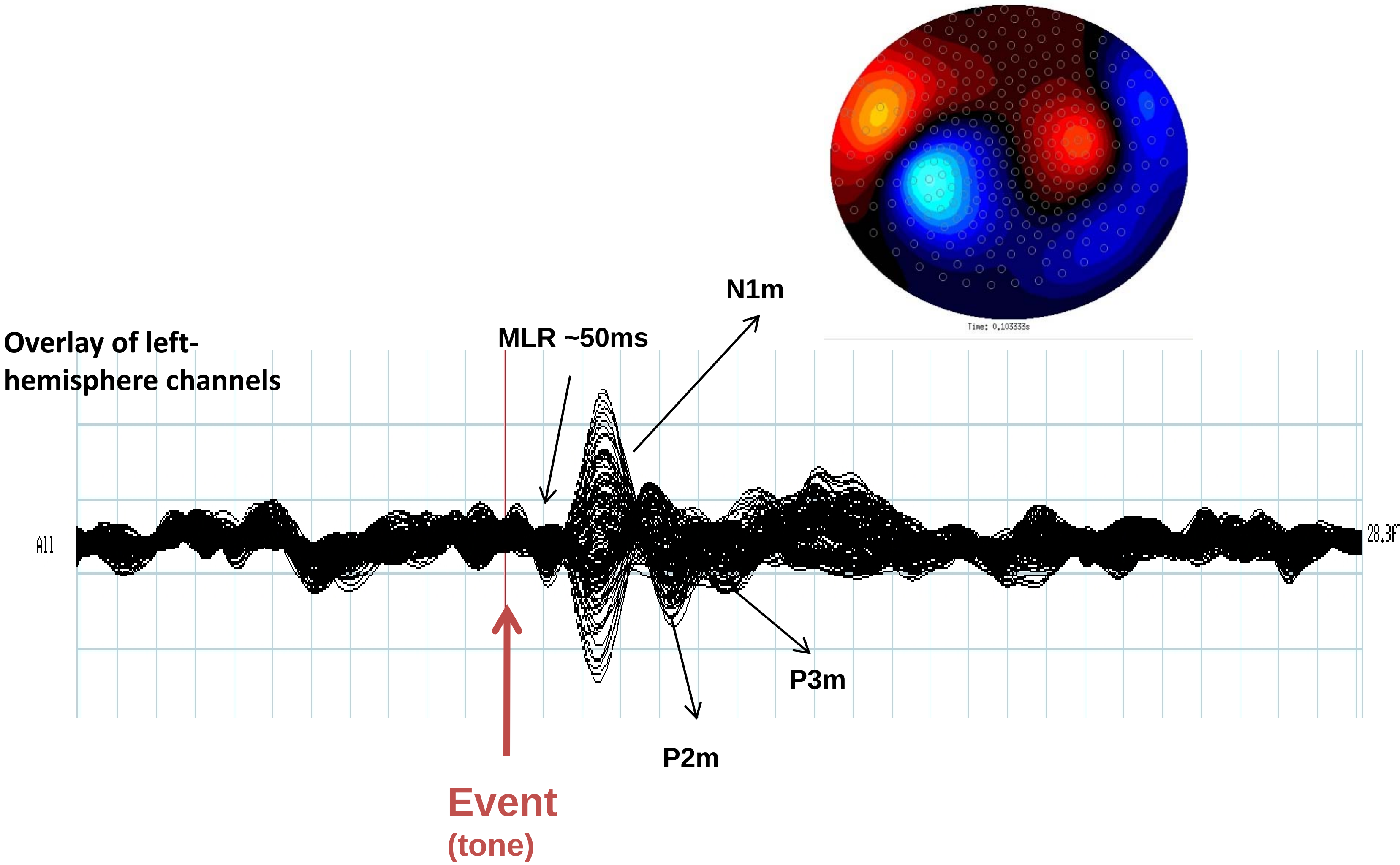
Filtered Auditory MEG Data



The signal-to-noise ratio (SNR) is still not high enough to reveal the stimulus evoked response

Averaged Auditory Evoked Field (AEF)

Averaging (100 trials): Improvement of the SNR with the square root of the number of trials averaged



The N100m

The main emphasis in AEF studies has been on the N1m response

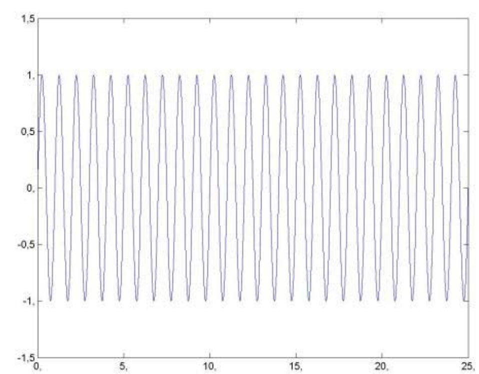
- Early MEG studies indicated that N1m was generated within the sylvian fissure in the upper surface of the temporal lobe (Hari et al., 1980; Elberling et al., 1980)

- Contralateral N1m has larger amplitude & is ~5-10ms earlier than ipsilateral N1m

- More recent studies show that multiple areas are involved including the A1 and the planum temporale (Lutkenhoner and Steinstrater, 1998)

The latency and amplitude of the N1m is modulated by stimulus parameters

For example, in the case of sinusoidal pure tones:

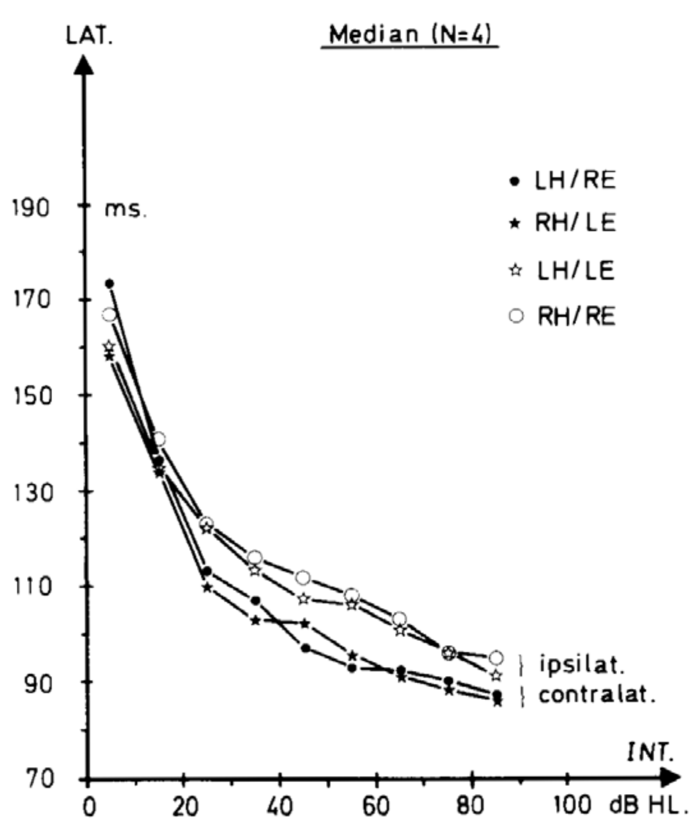


- The higher the frequency, the shorter the latency of N1m (Woods et. al., 1993)

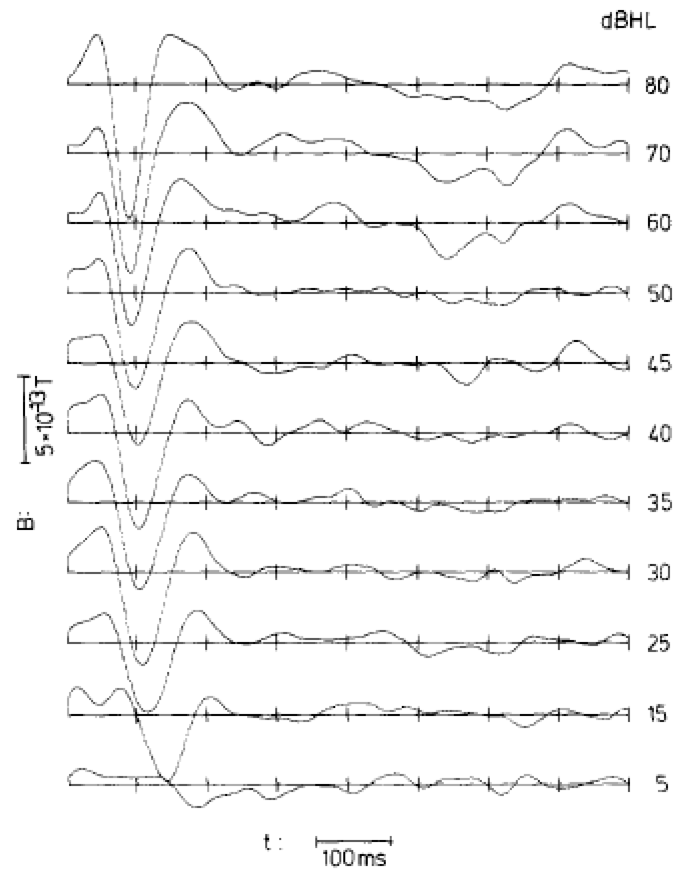
- The louder sounds the shorter the latency and the higher the amplitude of N1m (Elberling et al., 1981)

- Inter-stimulus Interval – The shorter the ISI, the smaller the amplitude

The Effect of Stimulus Intensity



Elberling et al., 1981



Bak et al., 1985

Cortical Tonotopy based on the N100m

The tonotopic organisation of the cochlea is maintained throughout the auditory system.

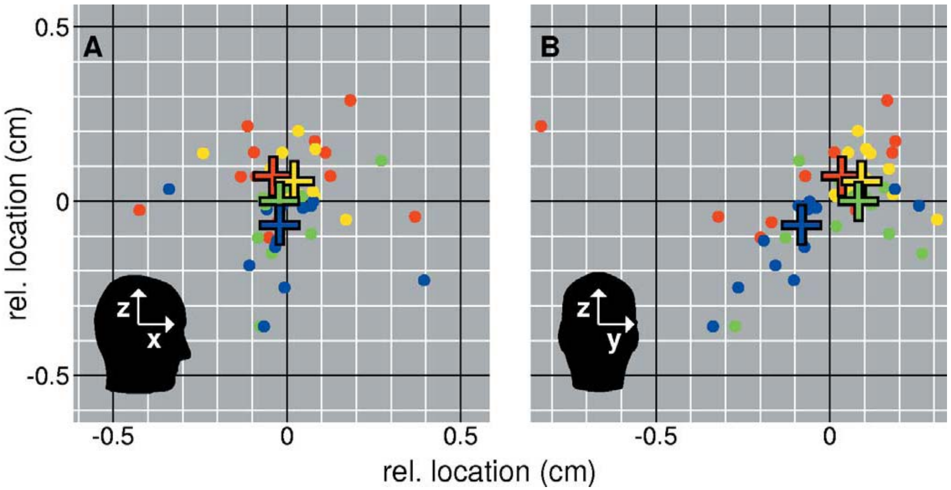
Can AEFs, particularly N100m, reveal tonotopic organisation in the cortex? Lots of contradictory results....

Elberling et al. (1982) found that ECD for N1 in response to a 500Hz tone was more anterior than for a 4000Hz tone; 1000 Hz in between.

Others found no shift in location (Arlinger et al., 1982; Tuomisto et al., 1983; Pelizzone et al., 1985)

Lutkenhoner et al. (2003)
N1m does not arise from a tonotopically organised source in the auditory cortex.

- **High inter-individual variability**
- **Multiple tonotopic cortical sources**

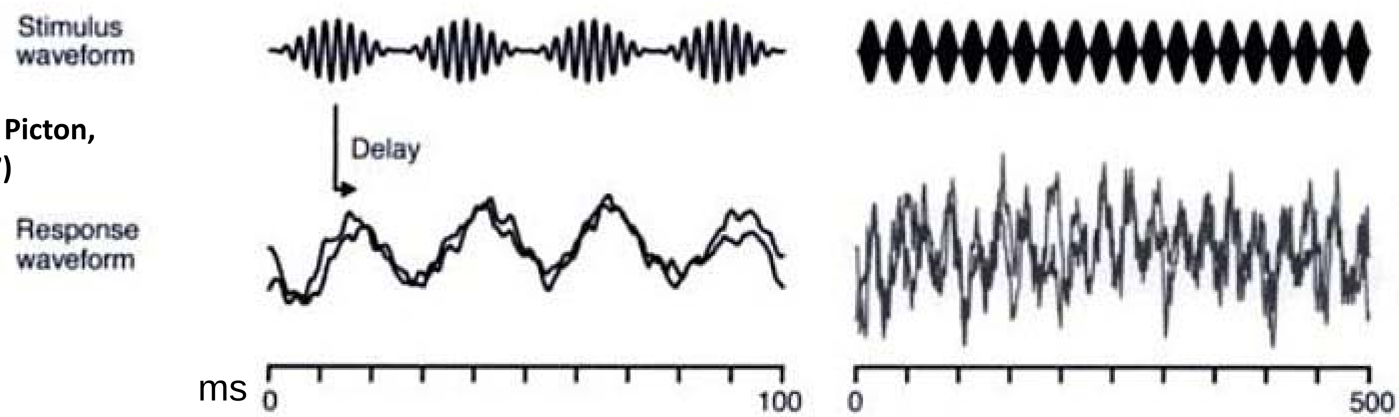


RED 250Hz YELLOW 500Hz GREEN 1000Hz BLUE 2000Hz

The Auditory Steady State Response (ASSR)

- The ASSR is an electrophysiological response to rapid auditory stimuli (Galambos et al. 1981)
- Sinusoidal response evoked by periodic trains of transient auditory stimuli (click, tones etc.)
- Maximum amplitudes to pulses presented at 40Hz
- Can be generated by rapid modulation of pure tone amplitude (AM) or frequency (FM).
- Signal intensity can be as high as 120 dB HL

From Picton, (2007)



400Hz tone, AM at 40Hz

Slower modulation rates (< 60 Hz) = Cortical regions
Faster modulation rates (> 60 Hz) = Brainstem

Source localisation for MEG Data

Estimating the neuronal sources

The Inverse Problem

- Estimating the source and distribution of the primary currents from the magnetic field measurements outside the head.
- Not enough information:
  - ***Ill-posed problem – solution is non-unique***

There are physical and mathematical reasons for this non-uniqueness:

- Not all current sources generate a magnetic field (radial component).
- There are more possible sources than there are measurement devices.

Therefore, the solution of MEG/EEG inverse problem is not possible from the measured data alone

a priori assumptions: Information about cortical currents that will reduce the solution to a unique one.

Estimating the neuronal sources

To solve the inverse problem, we need:

- Model of the head (volume conductor);
- Model of the source (Equivalent Current Dipole);

The Forward Problem

Predicting the extracranial field patterns produced by current dipole sources inside the head given the conductor geometry of the surrounding medium.

The Forward Solution is unique; there is only one magnetic field distribution that is possible from the given current distribution (Helmholtz, 1853).

If the primary source and the surrounding conductivity distribution are known, the potential/field can be calculated from Maxwell's equations.

MEG: the head can be modelled using homogenous sphere(s) therefore the solution is very simple.

EEG: Requires a realistic head model to account for anisotropy. More complicated due to irregular head shape and is more computationally intensive.

Model of the source

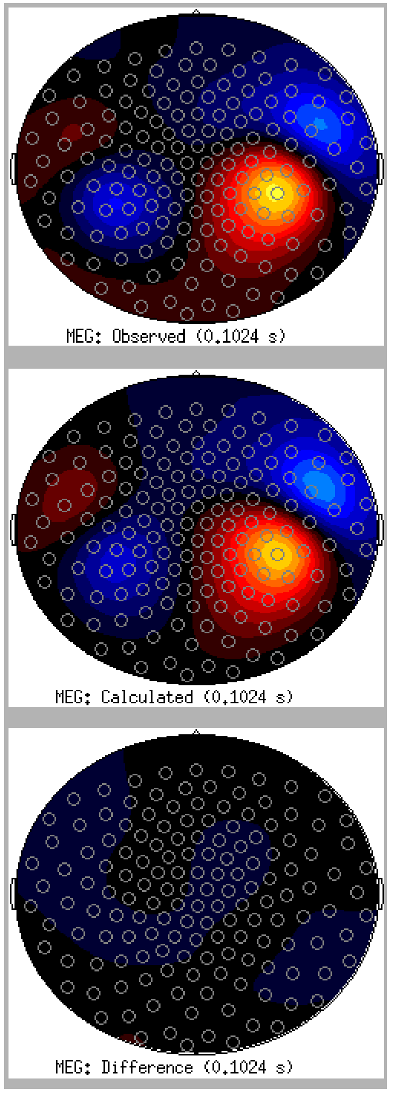
The simplest source model is the Equivalent Current Dipole (ECD) analysis;

A pair of opposite forces with –ve and +ve poles.

Current dipole in a homogenous sphere model has 6 params:

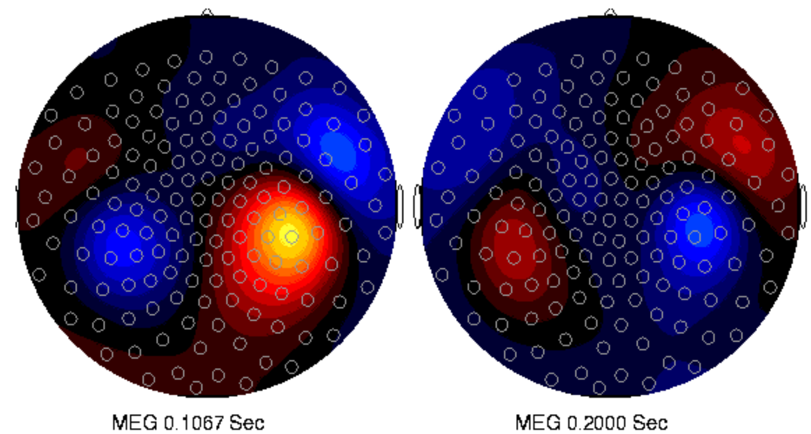
- 3 define its position (x, y, z)
- 2 define its tangential orientation (azimuth and declination)
- 1 defines its strength

The source is obtained by reducing the difference between the measured and the predicted signals; residual; goodness-of-fit.

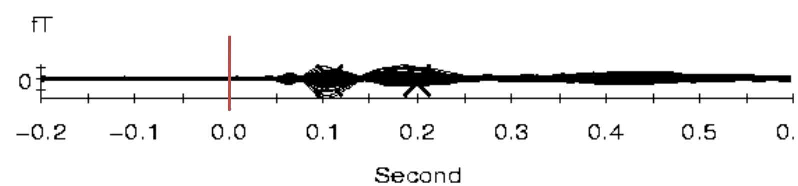


Conventional MEG paradigm

- Present a tone to one ear
- Record the MEG for a few hundred milliseconds e.g. 800ms (an *epoch*).

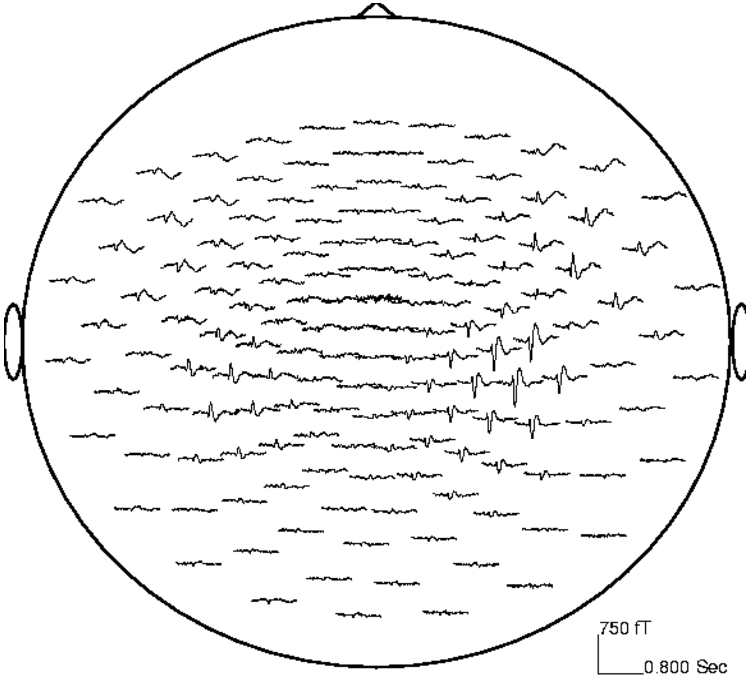


- Average hundreds (200) of epochs to increase SNR.



- Pick a time (latency) with a peak response.
- Test the assumption that an observed field pattern is statistically indistinguishable from a pattern that would be produced by an ECD.

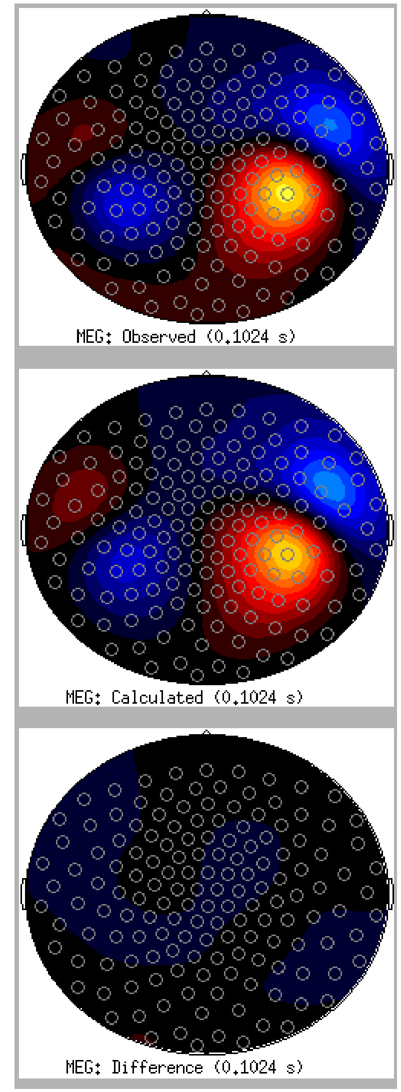
Modeling the average auditory evoked field



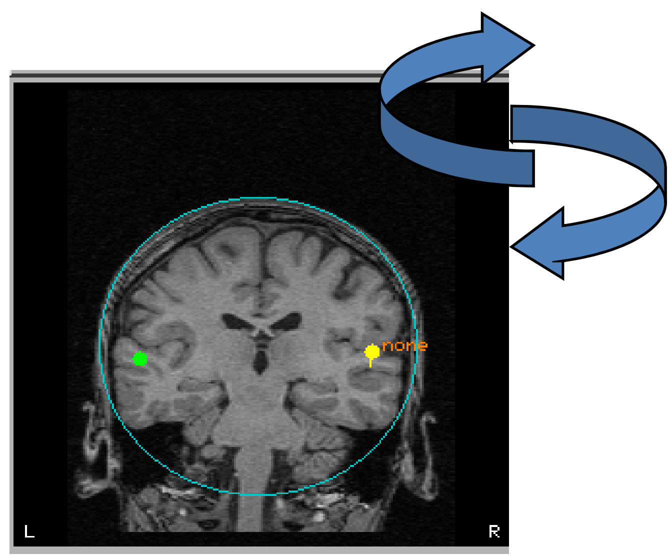
Peak at t=100ms;
Fit a dipole to this latency

Measured field

Modeled field



Average field
–100ms to 400ms post-stimulus



Problems with dipole modelling

- Requires averaging of many short epochs assuming that relevant neural events are both time and phase locked to a sensory stimulus (fixed latency) – ok for sensory processing.
- If the neural response to stimulus ‘jitters’ (ms) from trial to trial the power in the averaged response will be significantly reduced – not useful for studying induced activity - namely cognitive processes.
- The time-invariance assumption makes it difficult to do more cognitive experiments.
- User-dependent. Number of sources, latencies, and starting guess.
- Modeled solutions become less robust as they become more complex. More dipoles, more starting guesses, more sensitive to noise.

Distributed source models

Assume that the sources are distributed within a volume or surface (the source space) and then to use various estimation techniques to find out the most likely source distribution.

Distributed source-modeling techniques may provide reasonable estimates of complex source configurations without having to resort to complicated dipole fitting strategies.

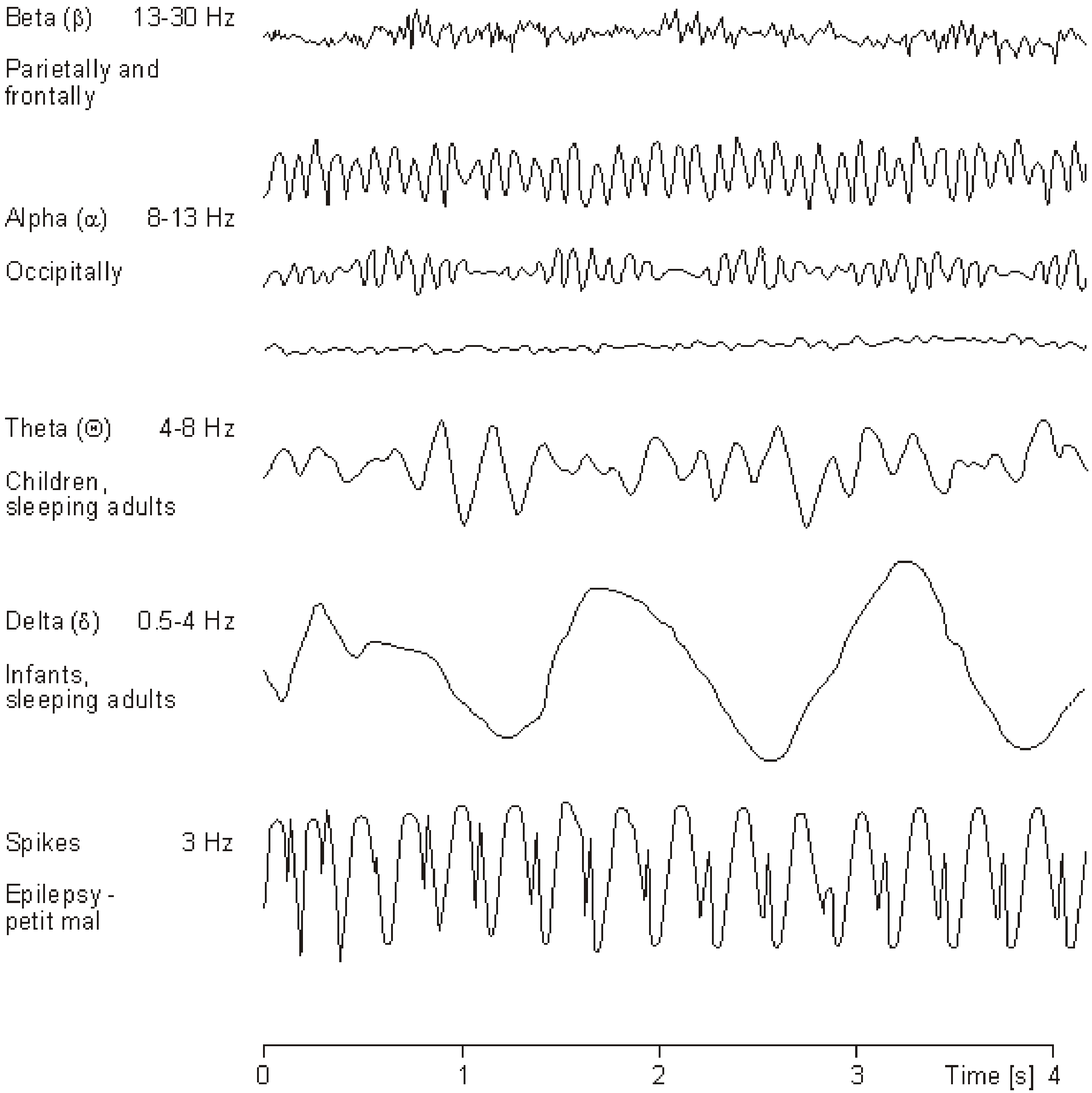
Examples

Minimum norm – Chooses the solution with minimum power
LORETA – neuronal activity is spatially smooth
SAM – no two neuronal sources are perfectly correlated
ICA, PCA, SSS, FOCUSS, VARETA, MUSIC, DICS,…. and many more pretty names

MEG/EEG Recorded brain activity

Functionally significant frequency bands of the brain

An ideal method not only localises with accuracy, but reveals induced activity in terms of task-related increase or decrease in power in different frequency bands across the entire brain



Some common techniques

<u>Minimum Norm Estimation (Hamalainen and Ilmoniemi, 1984; 1994)</u>

- Estimates the distribution and strength of thousands of dipoles on a 3D grid
- Selects the one with minimal current density within the brain
- Mathematically, it estimates the 3D source distribution with the smallest least square norm that fit the actual data

<u>LORETA (Pasqual Marqui et al., 1994; 1999)</u> Low Resolution Brain Electromagnetic Tomography

- Estimates current density distribution in 3D Talairach space
- Activity has maximum similarity (i.e., maximum synchronization), in terms of orientation and strength, between neighboring neuronal populations (represented by adjacent voxels).
- "Smoothness Assumption": for each voxel the current density should be as close as possible to the average current density of the neighbouring voxels

<u>Beamformers (Van Veen et al., 1997; Hillebrand et al., 2005)</u> Synthetic Aperture Magnetometry (SAM)

- Spatial filter approach that doesn't rely on averaging - elaborate noise cancellation
- Works with lower signal-to-noise ratio - Requires fewer repetition of stimulus – No signal averaging, robust to jitter.
- Ideal for studying induced (vs evoked) brain activity
- Assumes fewer sources than sensors which are independent
- Output is 3D image of source activity

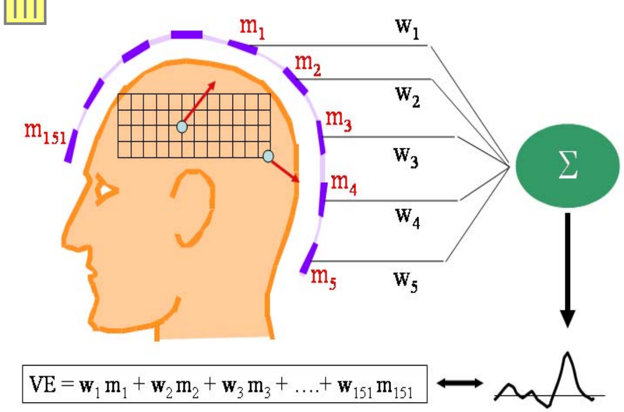
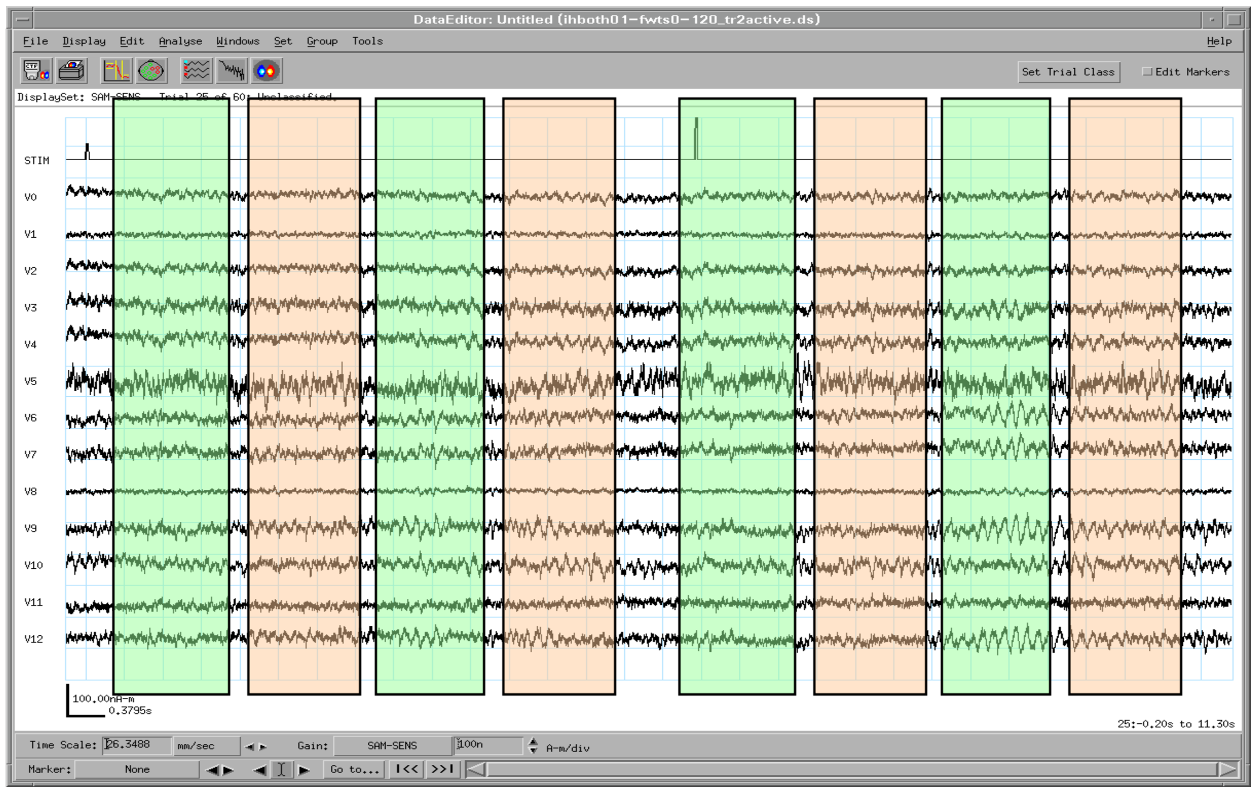


Figure courtesy of Dr. D. Cheyne, University of Toronto (modified)

- Set of weights for each voxel (spatial filter);
- Output is weighted sum of all measurements;
- Reconstructed waveform VE;
- Can be regarded source space signal.

The Beamformer



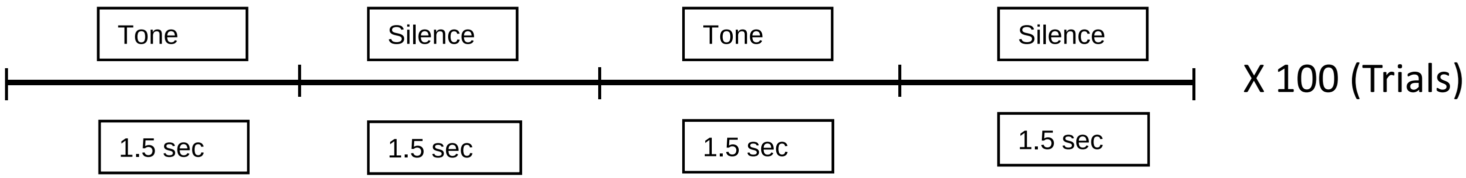
Active

Passive

Entire data can be divided into Active and passive segments. SAM constructs an SPM in each pre-defined frequency band, which measures the difference in signal power between Active and Passive.

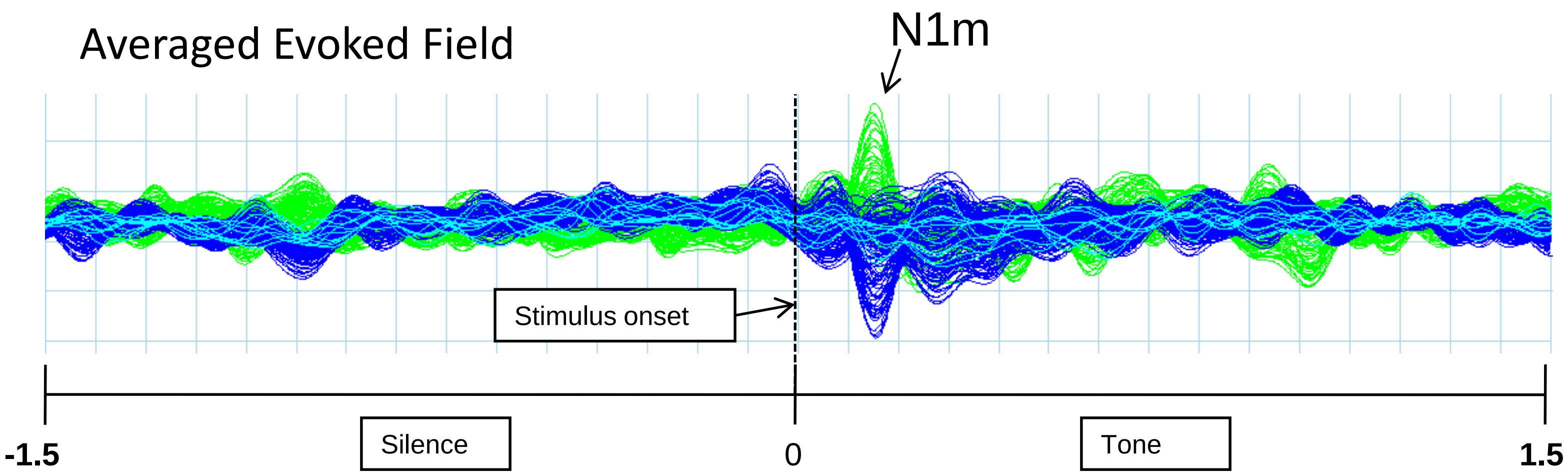
Example

How is ongoing brain activity modulated in response to a pure tone



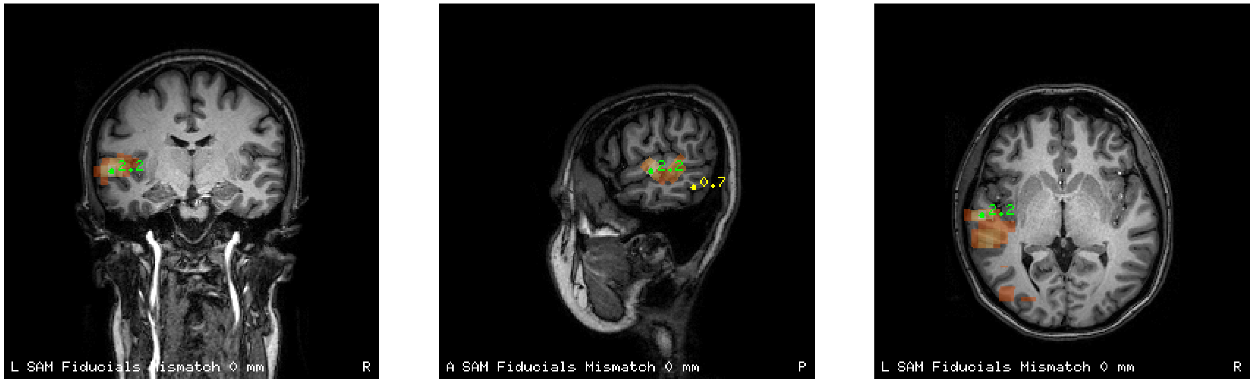
Pure tone: 3500Hz @ 60dB; monaural (right ear)

Averaged Evoked Field



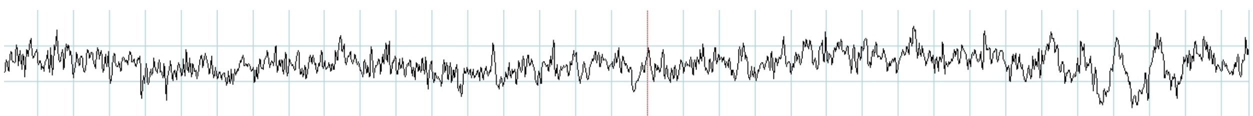
The question is how does brain activity change after the evoked response?

Beamfomer analysis is performed on the RAW MEG data using 1 second before and after stimulus onset.

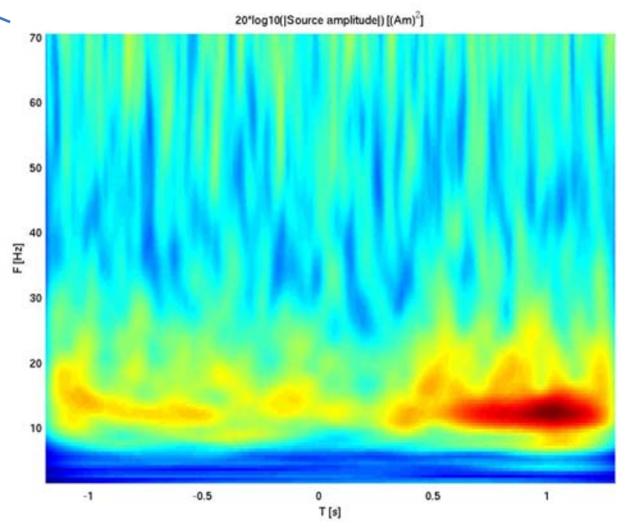


Analysis in the 0-80 Hz band;

Power Increase



VE for the location of peak activity



Time-Frequency analysis reveals an increase in power around 12Hz, sustained for 1 second post-stimulus onset

Which localisation technique to chose?

Depends on the:

- type of experiment (primary sensory/motor function vs. cognitive function)
- type of response that is measured (time- and phase-locked evoked response vs. time-locked induced oscillatory responses)
- prior knowledge about the neuronal sources (many sources vs. few sources; correlated sources vs. uncorrelated sources)

Useful references:

Elberling C, Bak C, Koefoed B, Lebech J, Saermark K. (1981) Auditory magnetic fields from the human cortex: Influence of stimulus intensity. Scandinavian Audiology;10:203–207.

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Pascual-Marqui RM, Michel C, and Lehman D. (*1994*) "Low resolution electromagnetic tomography: A new method for localizing electrical activity in the brain," *Int. J. Psychophysiol., vol. 18, pp. 49-65.*

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