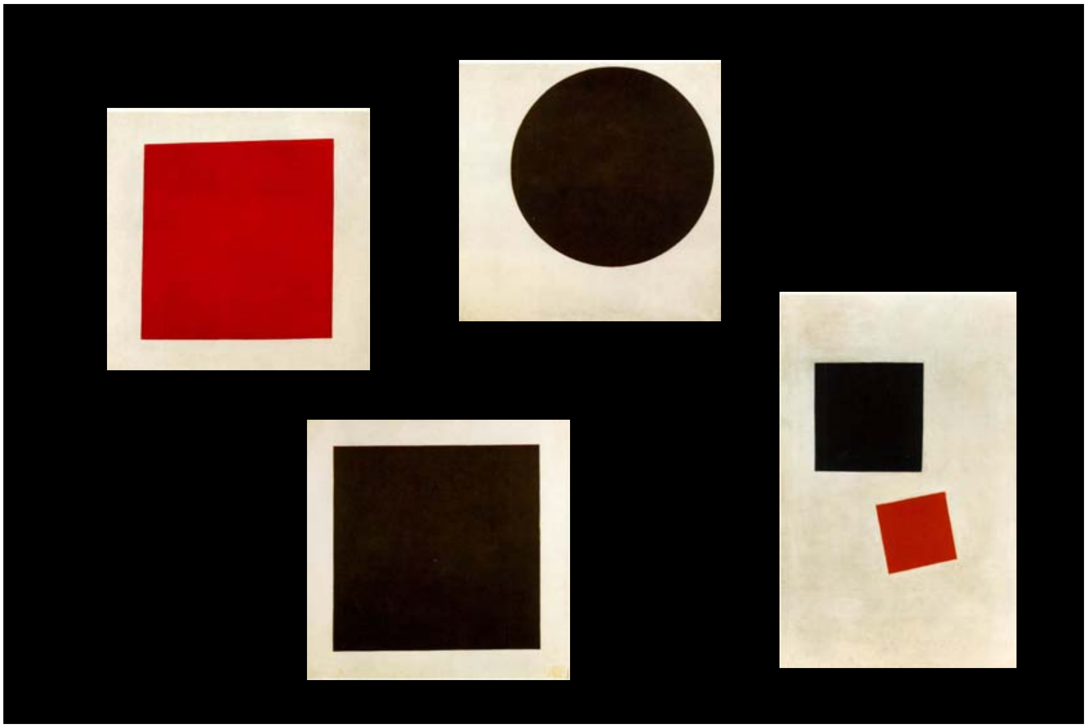


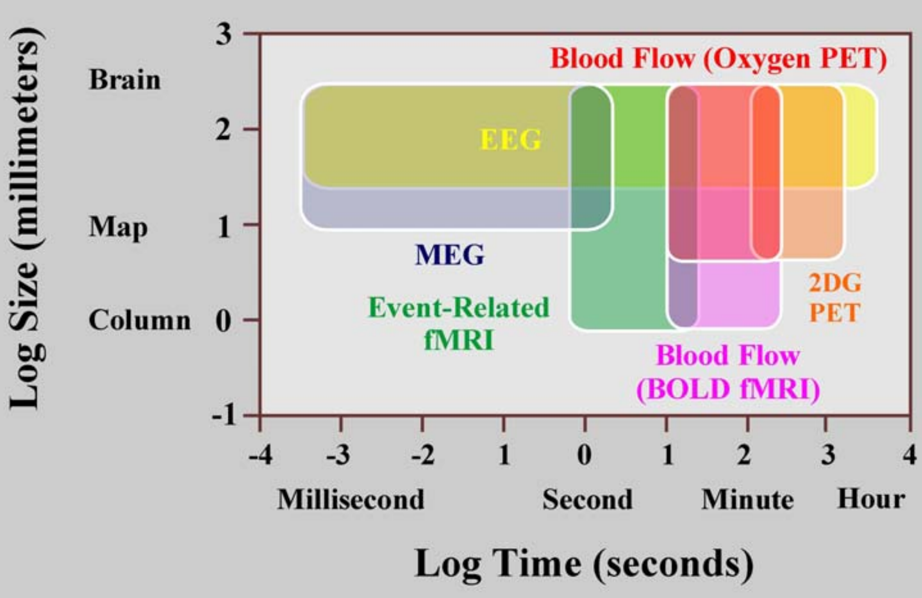
Consilience

"…when an induction, obtained from one class of facts, coincides with an induction, obtained from another different class."

William Whewell, 1840, quoted by
Edward. O. Wilson, 1998

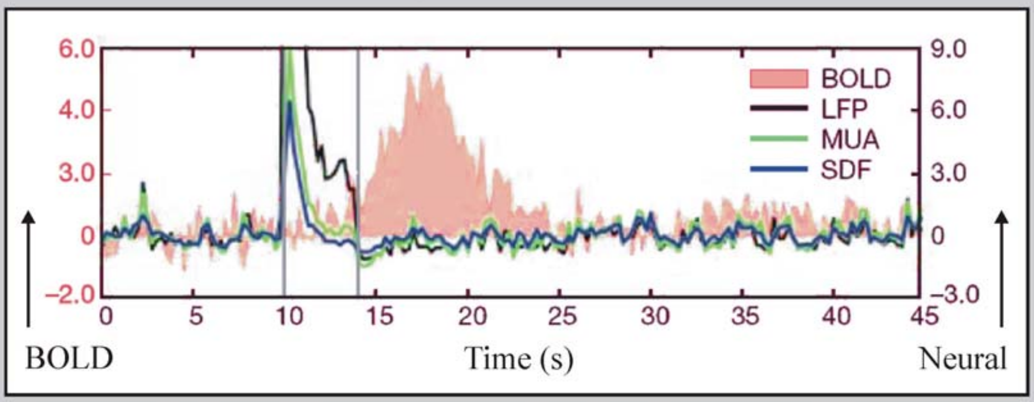
Physiology of the Human Brain

- **Timing:** electric and magnetic recordings can provide precise timing of events occurring in different parts of the brain.
- **Location:** hemodynamic recordings (e.g. fMRI) can localize areas of activation during cerebral processing.

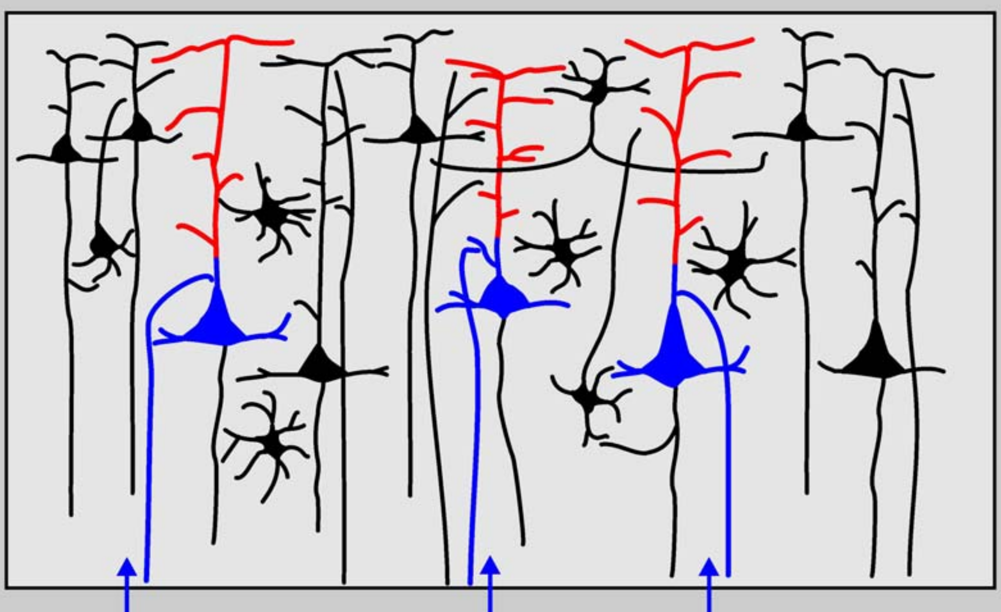


Relations between BOLD fMRI and Neural Activity

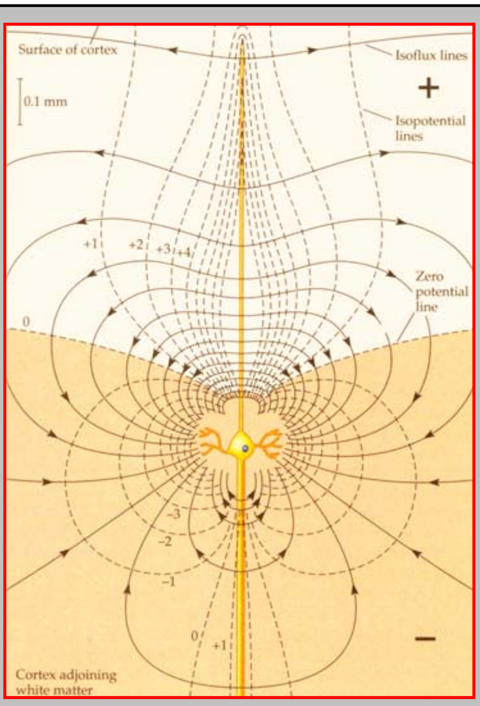
Logothetis et al., 2001



Changes in the blood flow begin about 2 s after the neural activity. Impulse response peaks about 5 seconds after it begins and lasts for 15-20 s. BOLD response can be predicted by convolving the Local Field Potential (LFP) with the Hemodynamic Impulse Response. Multiple Unit Activity (MUA) and Spike Density Function (SDF) measure neuronal activation.



Activation of specific afferents

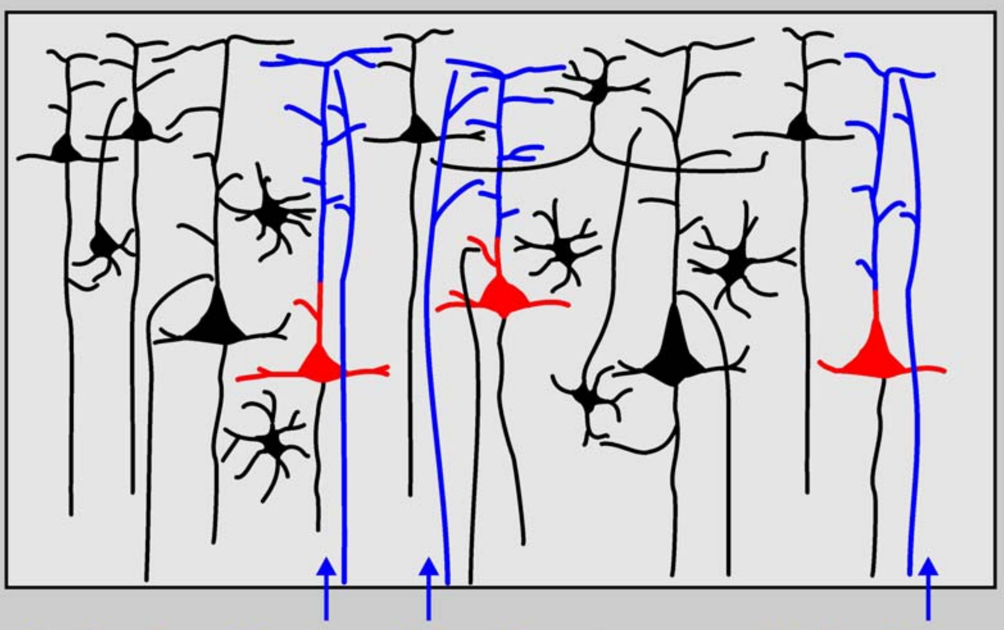


Synaptic depolarization on the cell body causes positive ions to flow from the extra-cellular space into the neuron – setting up a current “sink.”

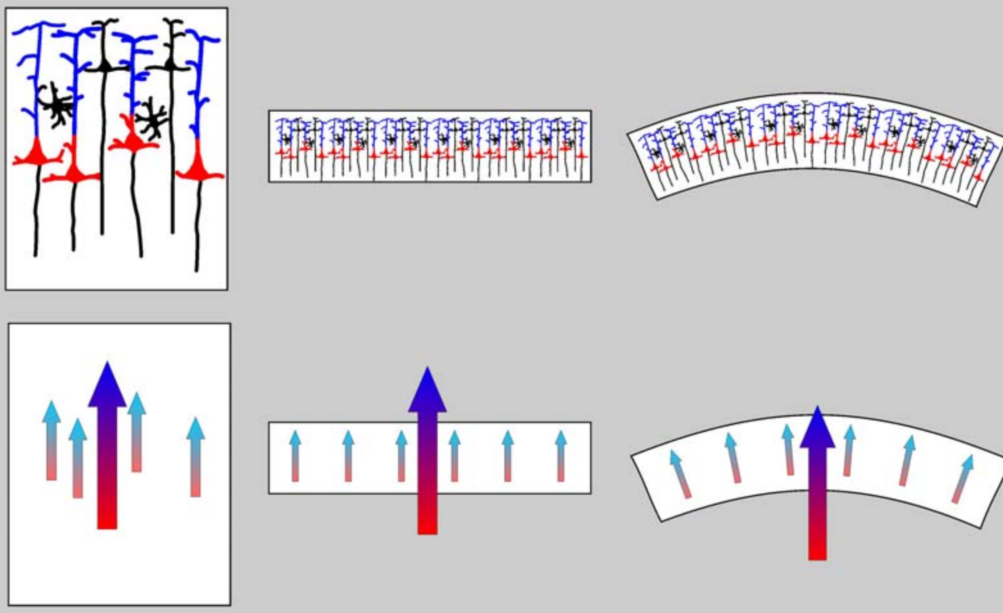
Extracelllular current flows from surface toward the sink. Electrodes on the surface record a positive potential. Near the soma they record a negative potential.

Intracellular current flows in the reverse direction. This is what determines the magnetic recording.

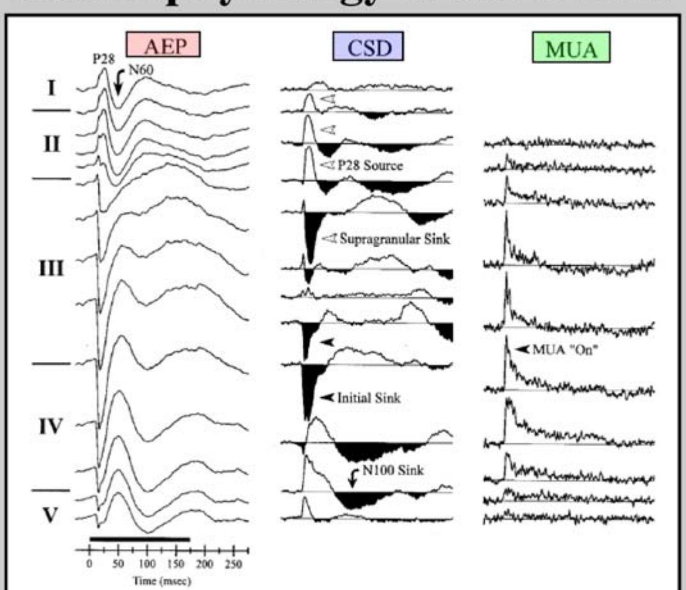
Huettel et al, 2004 from Creutzfeldt, 1974



Activation of nonspecific afferents or association fibers



Electrophysiology of the Cortex

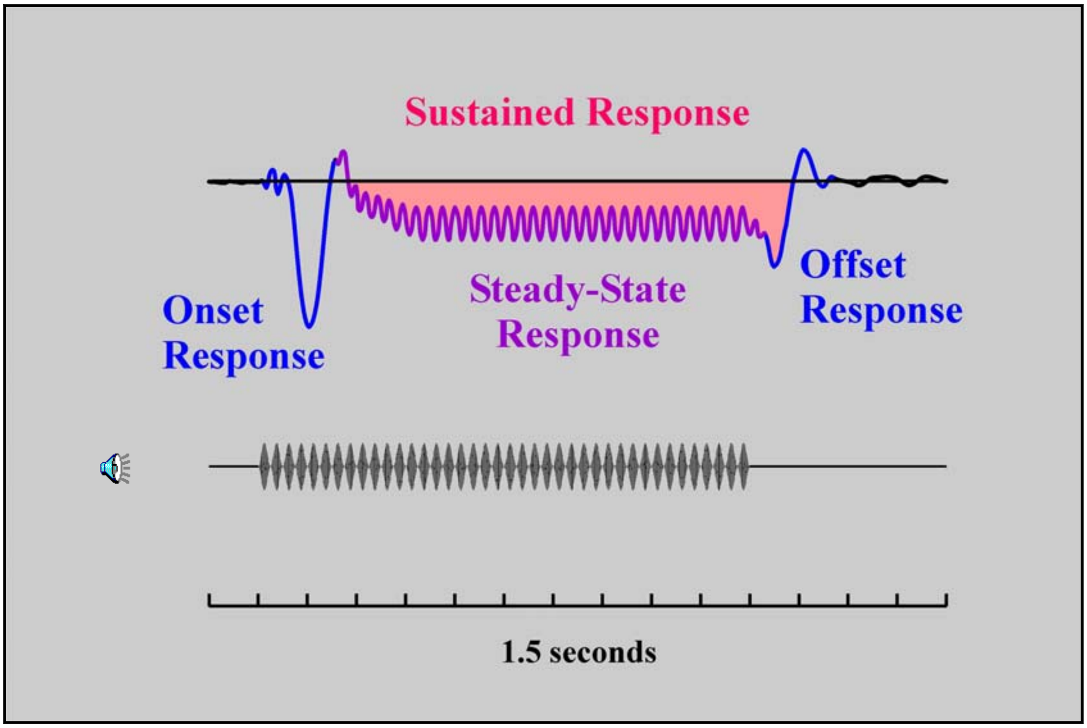


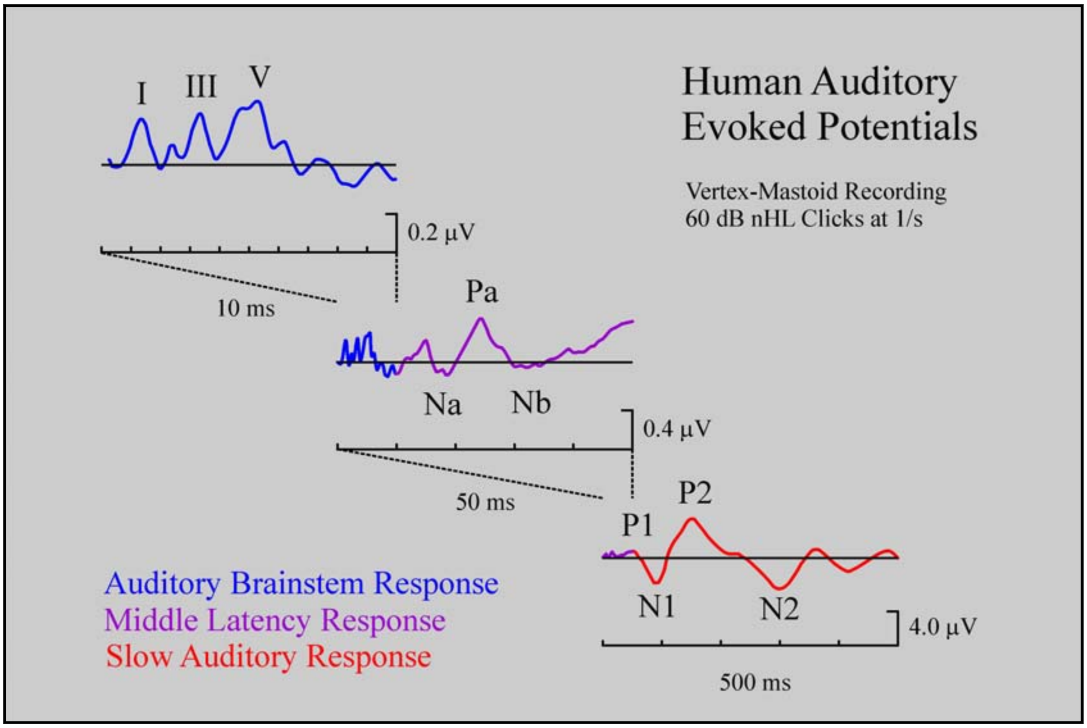
Fishman et al., 1999

Localized synaptic activity causes sources and sinks in the extracellular fluid (measured with current source density).

These generate field potentials that vary with how the current flows in the cortex.

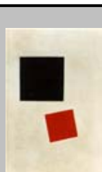
If synaptic activity causes sufficient depolarization, action potentials result (unit activity)


Sustained Response
Onset
Response
Steady-State
Response
Offset
Response
1.5 seconds


Human Auditory
Evoked Potentials
Vertex-Mastoid Recording
60 dB nHL Clicks at 1/s
I
III
V
0.2 µV
10 ms
Pa
Na
Nb
0.4 µV
50 ms
P1
P2
N1
N2
4.0 µV
500 ms
Auditory Brainstem Response
Middle Latency Response
Slow Auditory Response

Time

- You will never understand how it works unless you know its timing. A major characteristic of causality is time (**post hoc ergo propter hoc**).
- MEG and EEG will not give the complete timing of cerebral processes. For example, they may only show when something begins or ends.



Electric and Magnetic Recordings

- **Electric:** Activation of neurons generate currents in the extra-cellular spaces. These currents set up potential fields in the head that can be recorded by electrodes attached to the scalp.
- **Magnetic:** Intracellular currents generate magnetic fields that can be recorded by super-conducting quantum interference devices close to the scalp

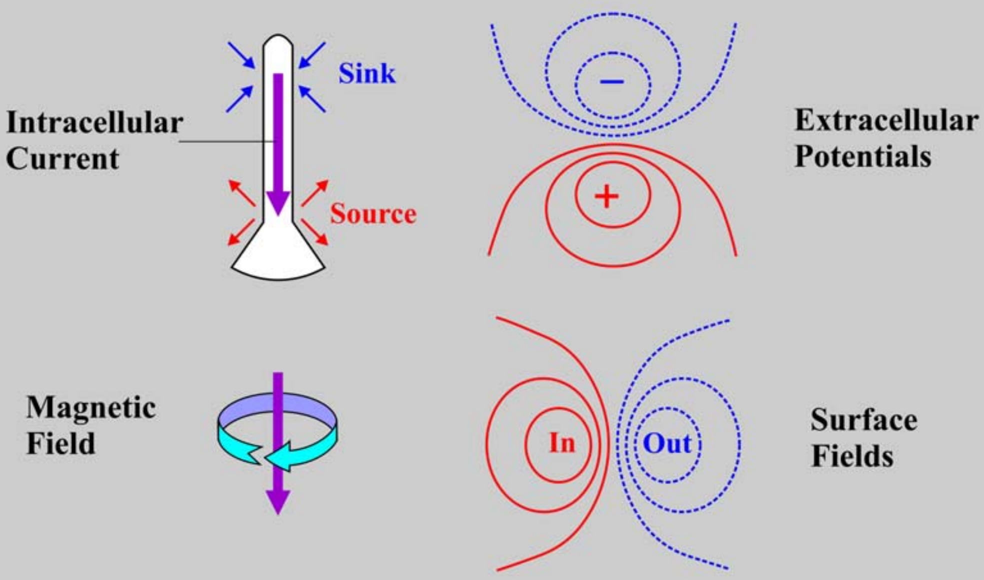
Recordings

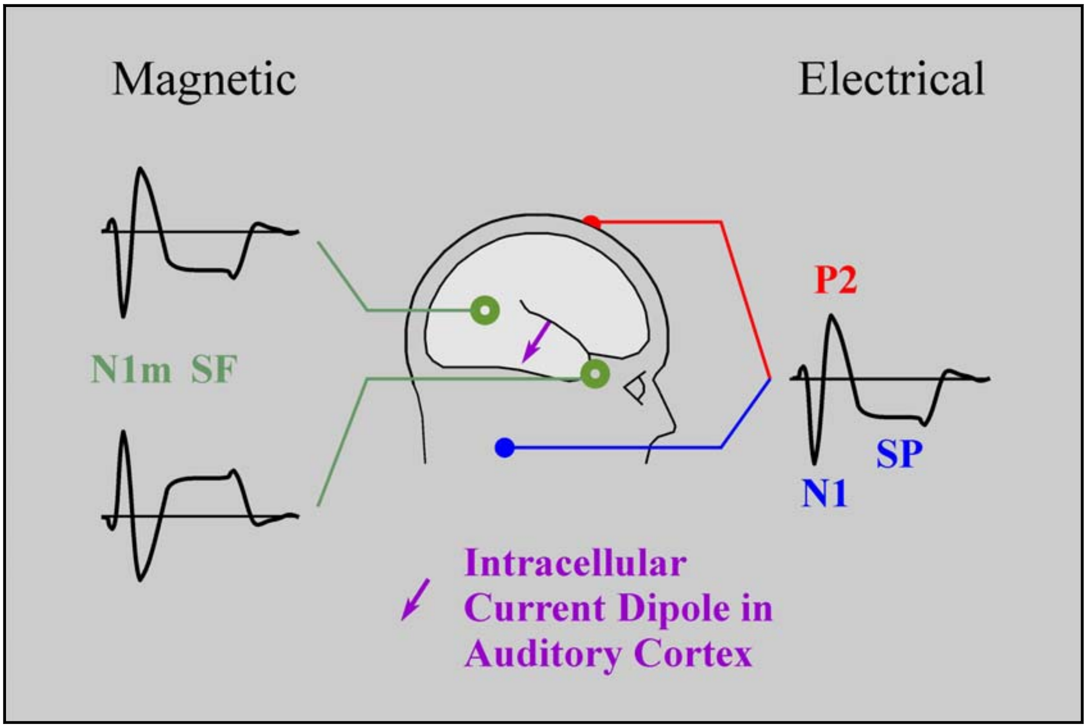
Electric | **Magnetic**

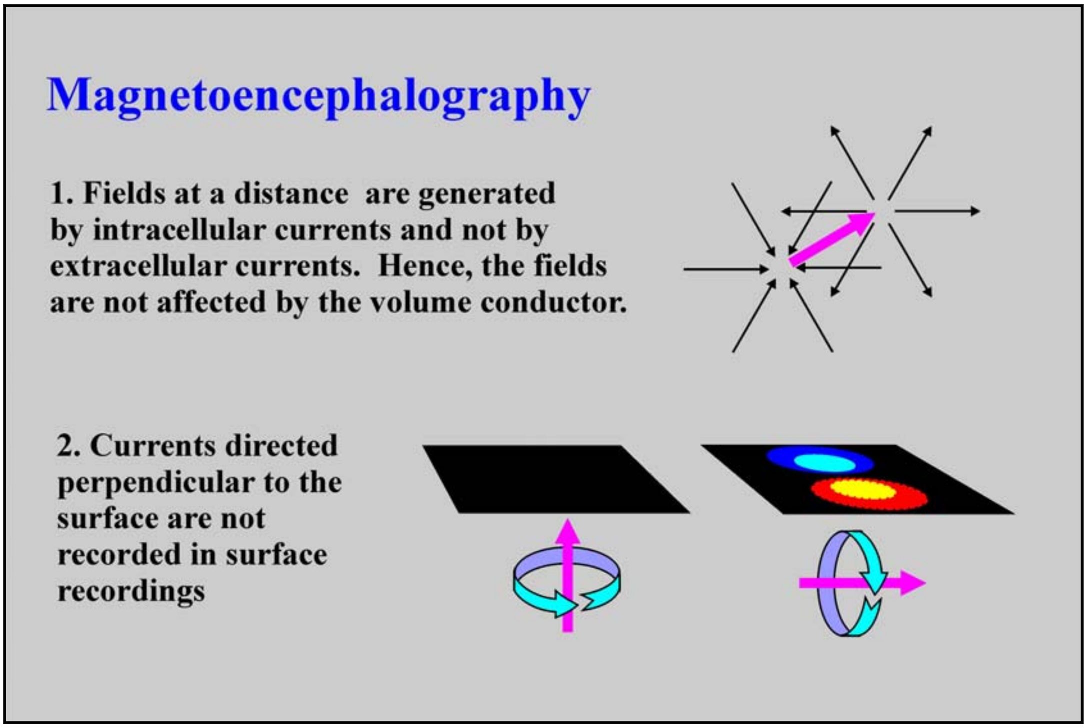
Electrode preparation
Volume Conductor Effects

Movement
Magnetic Noise

Non-Cerebral Artifacts




Magnetic
Electrical
N1m SF
P2
SP
N1
Intracellular
Current Dipole in
Auditory Cortex

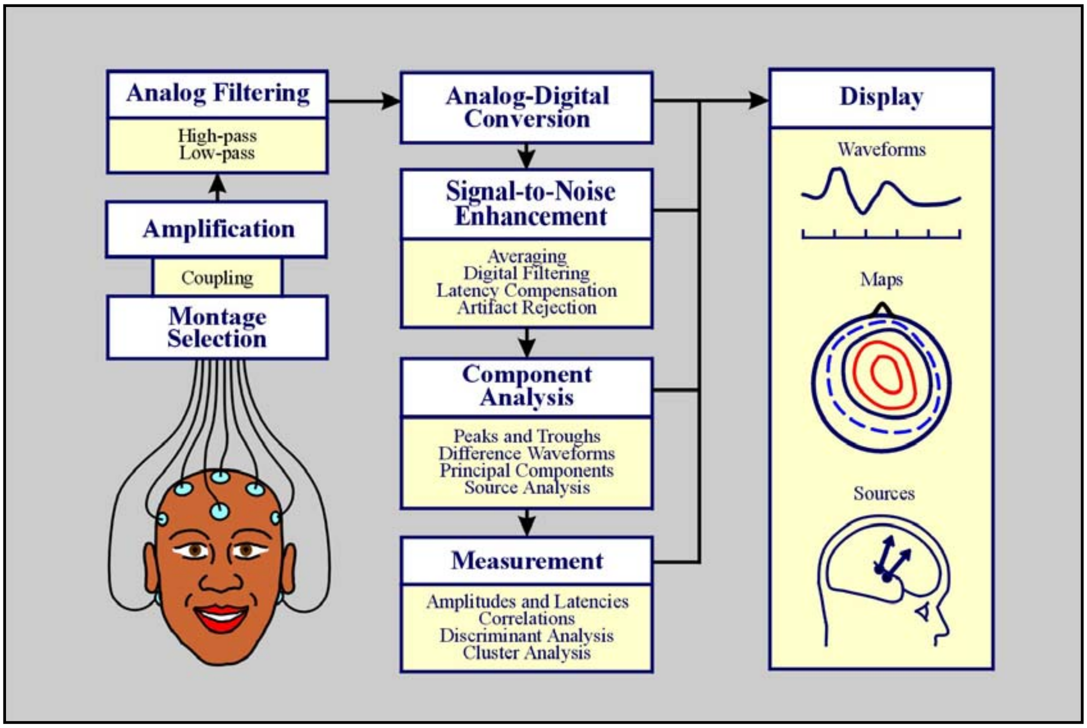

Magnetoencephalography
1. Fields at a distance are generated by intracellular currents and not by extracellular currents. Hence, the fields are not affected by the volume conductor.
2. Currents directed perpendicular to the surface are not recorded in surface recordings

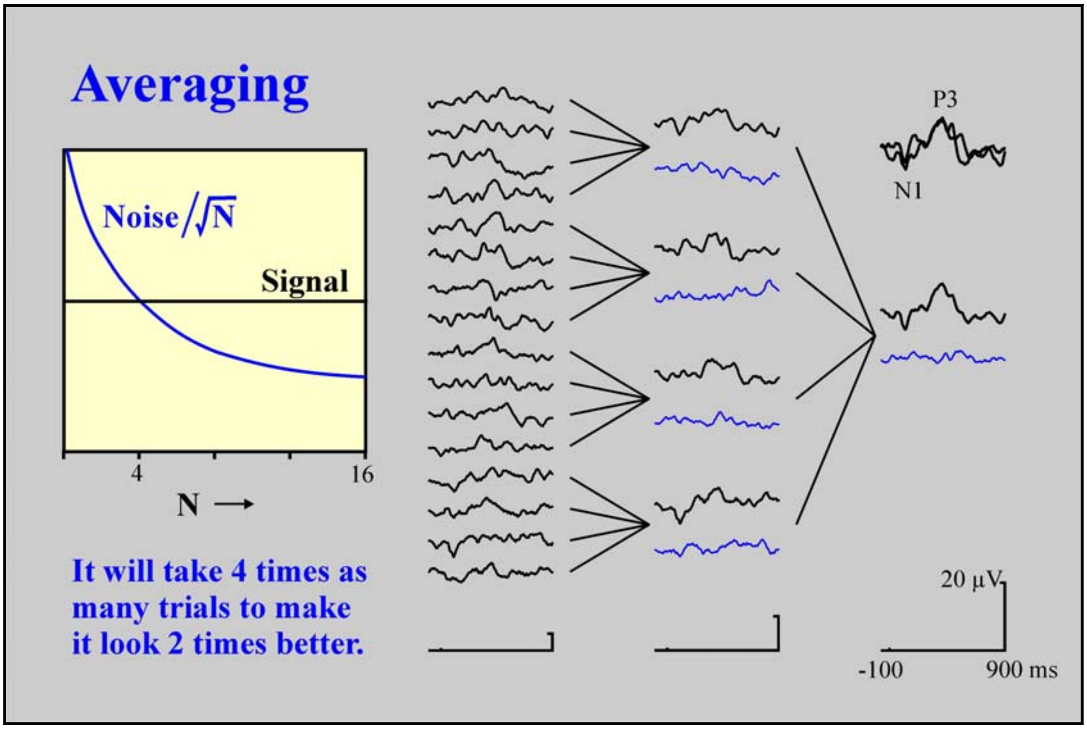
Magnetic Attractions

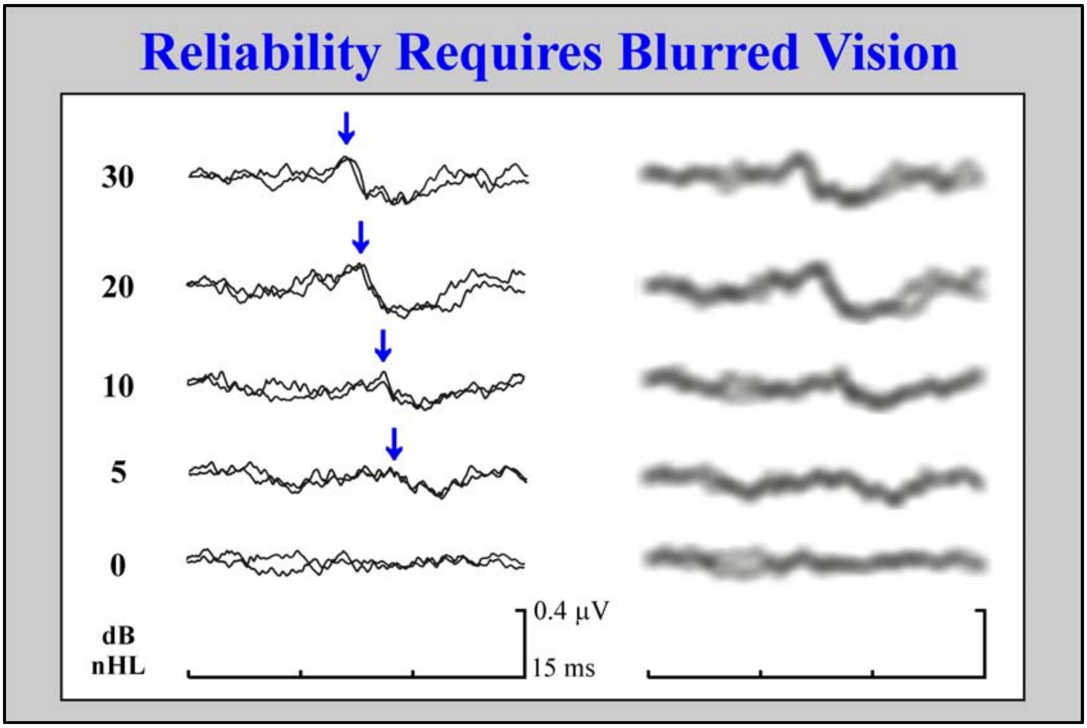
- Magnetic fields are unaffected by the volume conductor and the sources are therefore more accurately localized than with electrical fields.
- Magnetic sensors do not have to be attached to the scalp. However, there are problems of movement.
- By looking only at tangential sources, the MEG gives a simpler view of intracerebral activity.

Detecting Signals in Noise

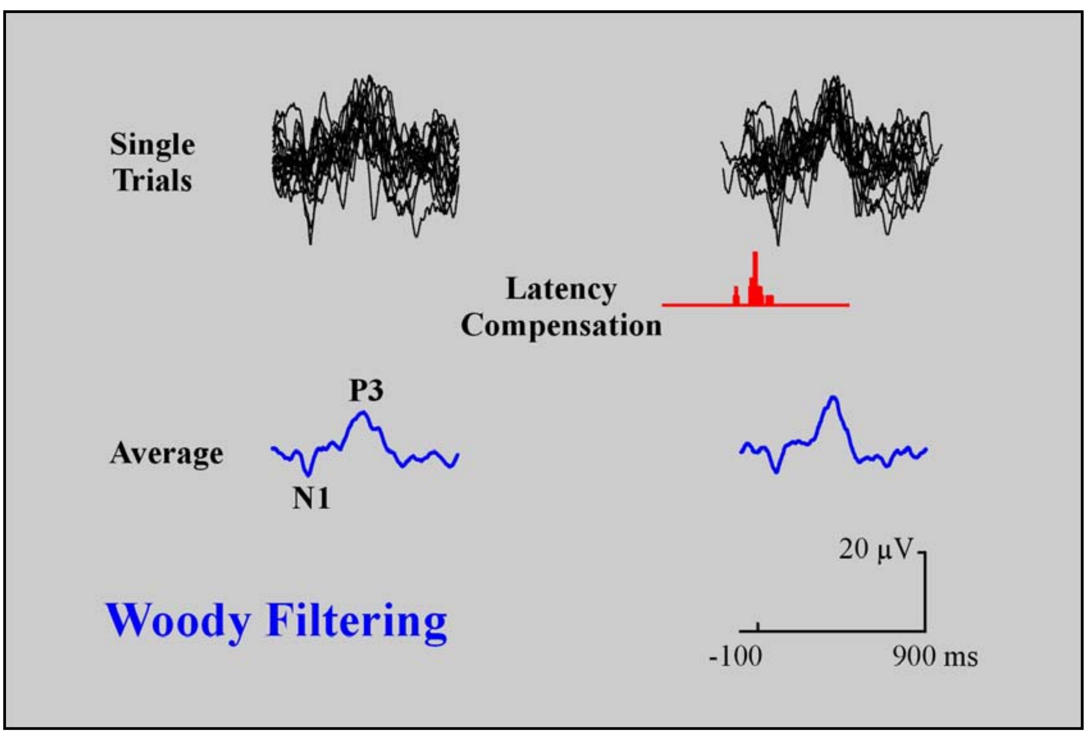
- **Averaging:** activity that is not time-locked to an event will be reduced by the square-root of the number of trials combined.
- **Filtering:** an optimal filter reduces the activity in inverse proportion to the signal-to-noise ratio at any frequency.
- **Correlation:** can measure similarity between a template and the recorded activity at different latencies


Analog Filtering
High-pass
Low-pass
Amplification
Coupling
Montage Selection
Analog-Digital Conversion
Signal-to-Noise Enhancement
Averaging
Digital Filtering
Latency Compensation
Artifact Rejection
Component Analysis
Peaks and Troughs
Difference Waveforms
Principal Components
Source Analysis
Measurement
Amplitudes and Latencies
Correlations
Discriminant Analysis
Cluster Analysis
Display
Waveforms
Maps
Sources

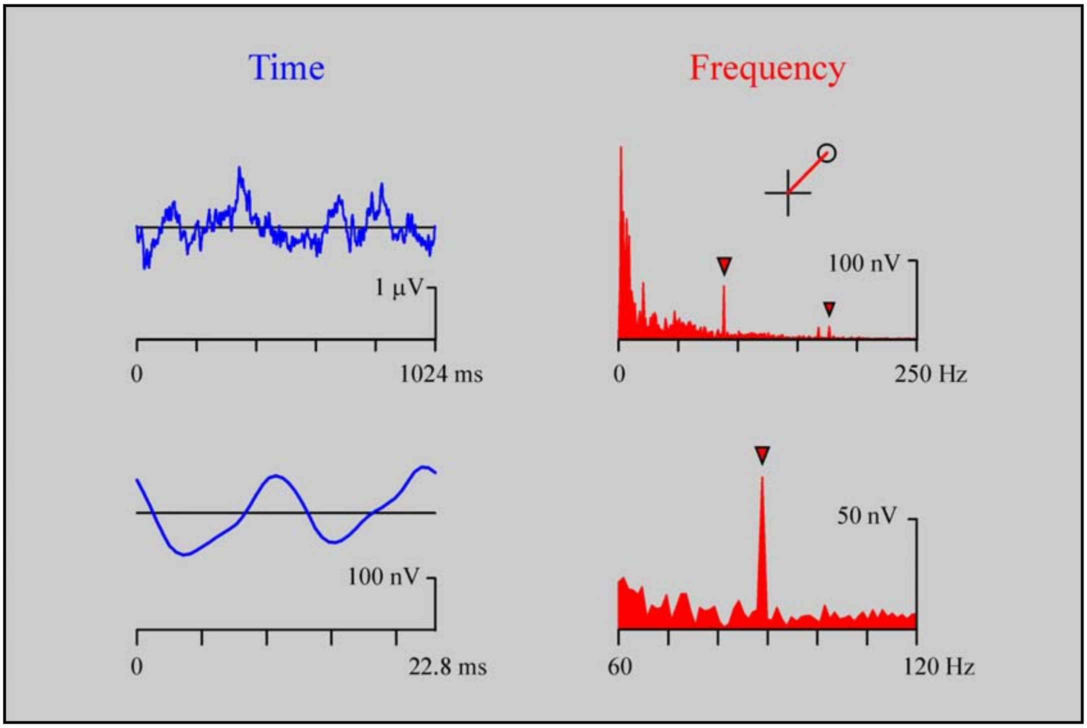

Averaging
Noise/√N
Signal
4
16
N →
It will take 4 times as many trials to make it look 2 times better.
P3
N1
20 µV
-100
900 ms



Reliability Requires Blurred Vision
30
20
10
5
0
dB
nHL
0.4 µV
15 ms



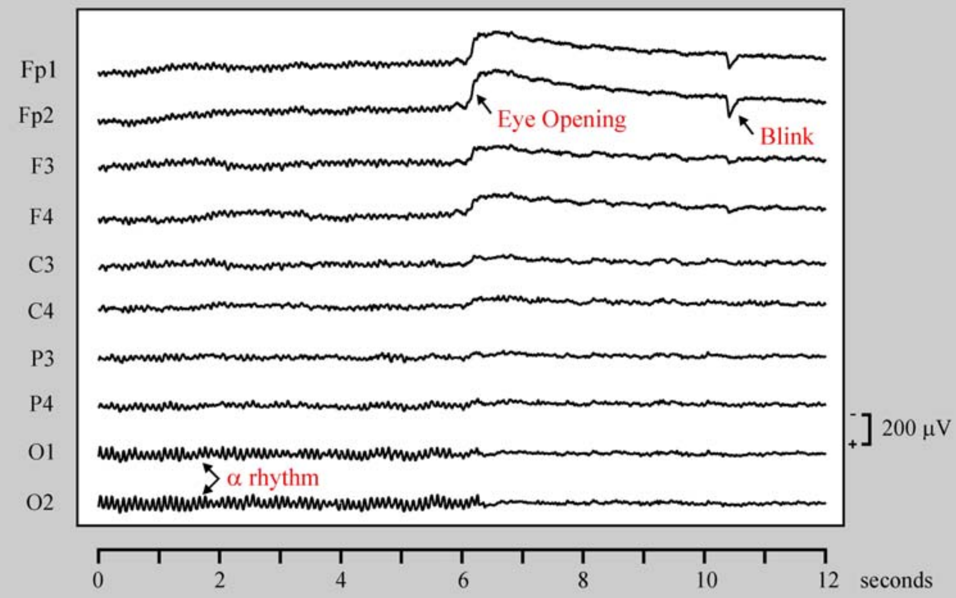
Single
Trials
Latency
Compensation
P3
Average
N1
20 µV
-100
900 ms
Woody Filtering



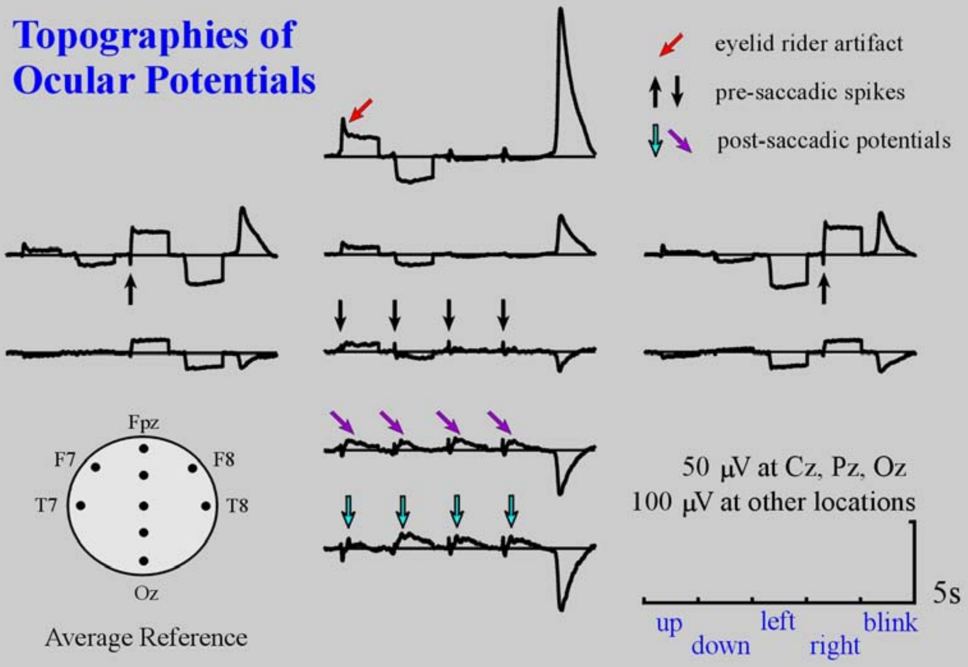
Non-Cerebral Artifacts

- **Prevention**: instruct subject how not to generate the artifacts ("Do not move your eyes"), or how to decrease them ("Relax")
- **Averaging:** artifacts that are randomly related to the stimuli or responses can be decreased by averaging
- **Rejection**: identify when artifacts are present and eliminate those trials from further analysis.
- **Compensation**: measure the artifact, estimate how much it contributes to the recordings, and subtract that estimation away

Human Electroencephalogram



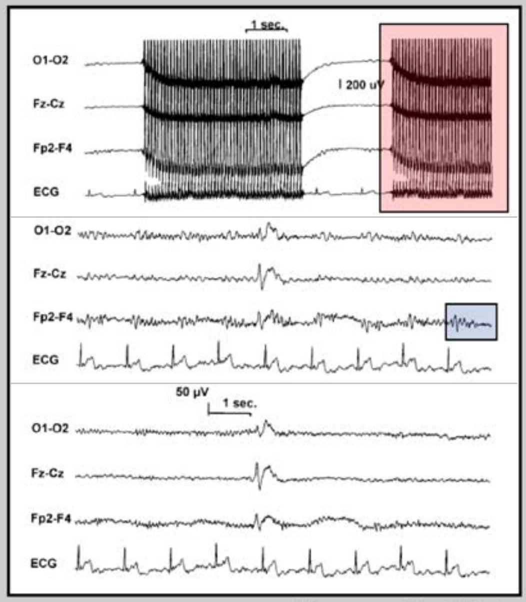
Topographies of Ocular Potentials



Recording EEG during fMRI

Imaging artifact is time-locked to the timing triggers of echo-planar imaging. Averaging the artifact gives a signal that can then be subtracted from the EEG. Filtering also helps since EEG is lower in frequency than the imaging artifact.

Movement in the magnetic field causes current to flow in the EEG electrode circuits. This can occur with head movement and also with the pulse (ballisto-cardiogram). Averaging on the ECG can be used to remove the latter. Averaging on a movement transducer can be used to remove both.

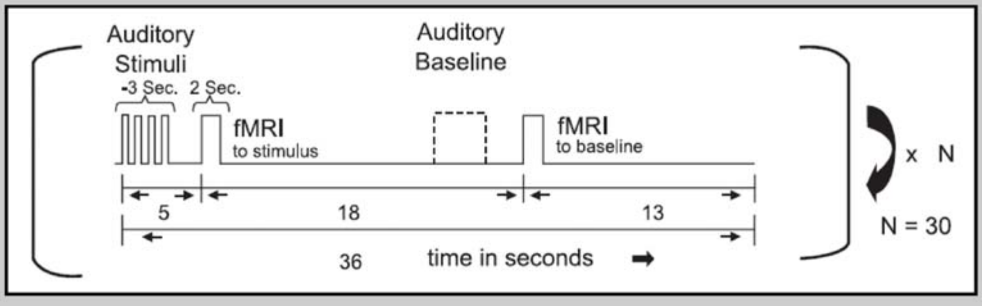


Allen et al., 2000

Paradigms for fMRI and ERP Recordings

Stimulus rates for event-related fMRI are necessarily slower than those used in recording ERPs. This can lead to differences in attention - it is hard to maintain attention when stimuli come very slowly. Also many ERP effects are rate-dependent (e.g. the P300 amplitude).

When auditory stimuli are used, one must worry about the masking effects of the acoustic noise caused by the imaging. One approach to this is to use a sparse sampling protocol (e.g. Scarff et al., 2004):

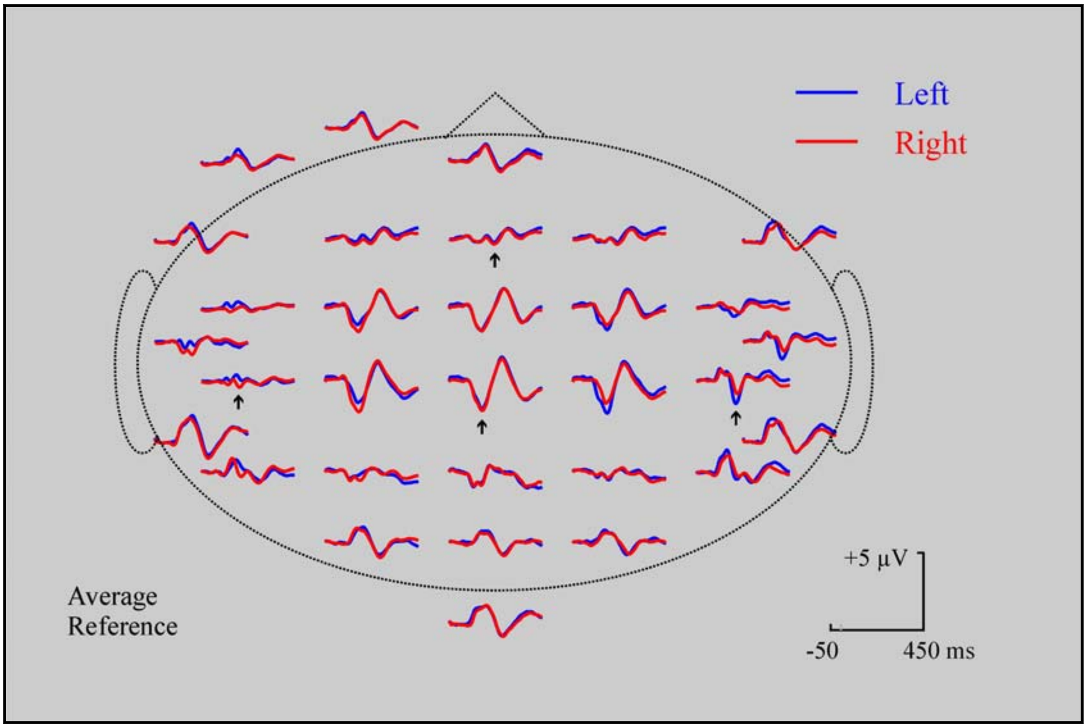


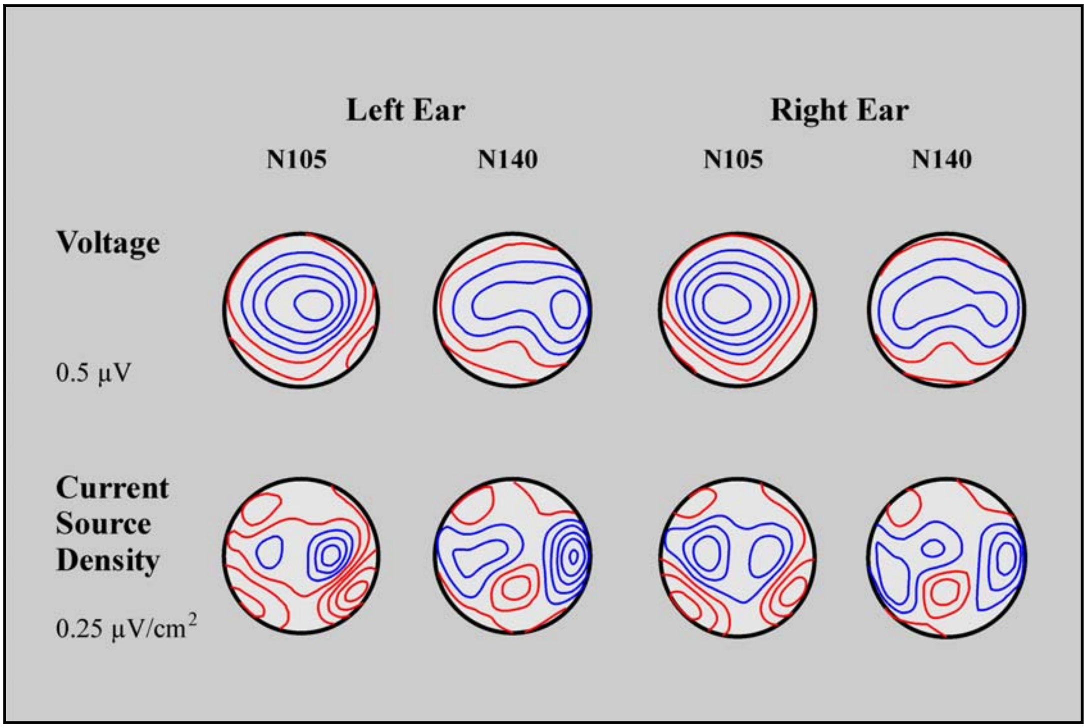
Taking Time

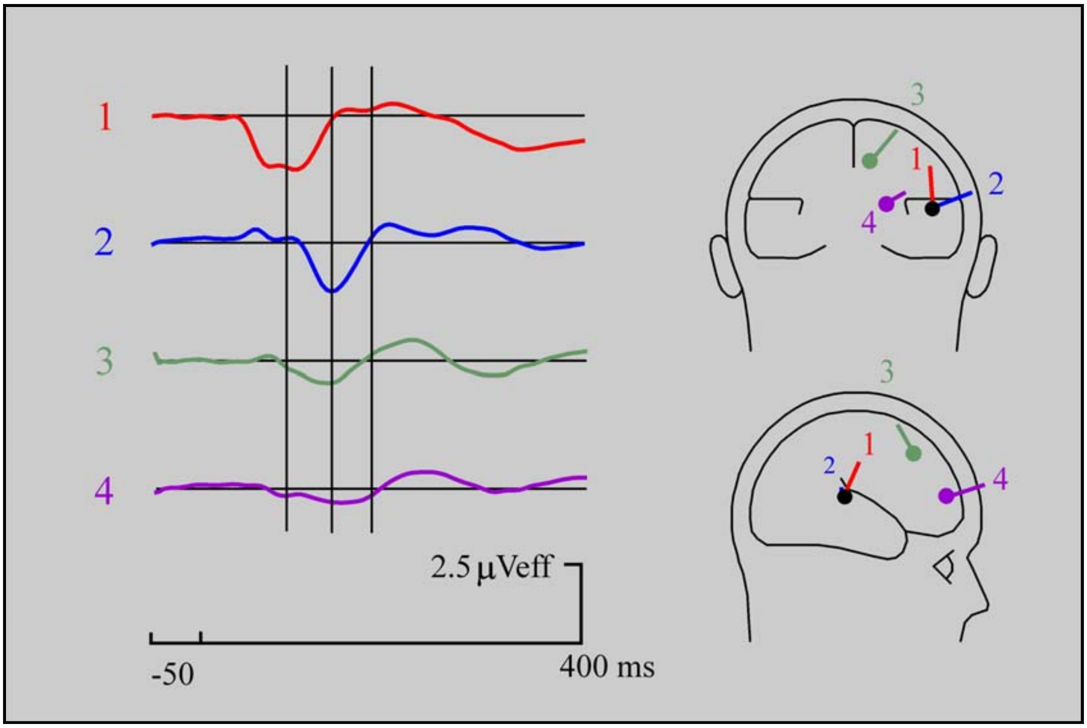
- MEG and EEG signals are obscured in background noise. Time must be taken to distinguish the signals from the noise.
- Experimental designs in MEG or EEG will involve far more trials than conditions or subjects. This is different from simple behavioural studies using reaction time (or fMRI studies using BOLD).

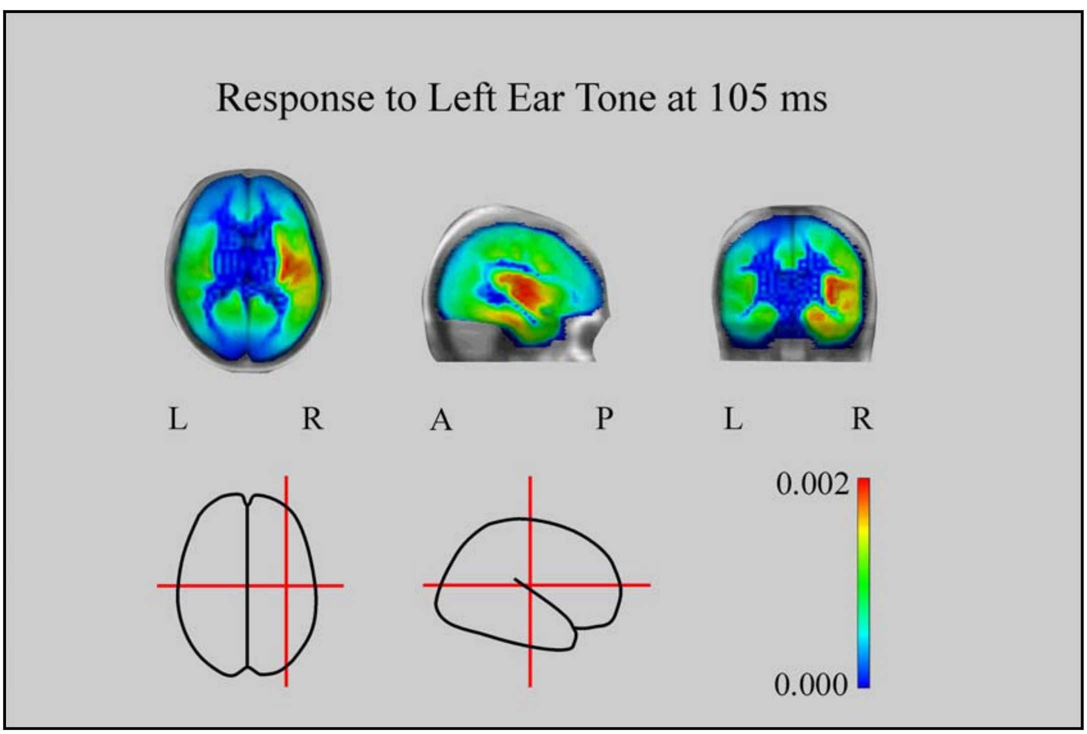
Types of Source Analysis

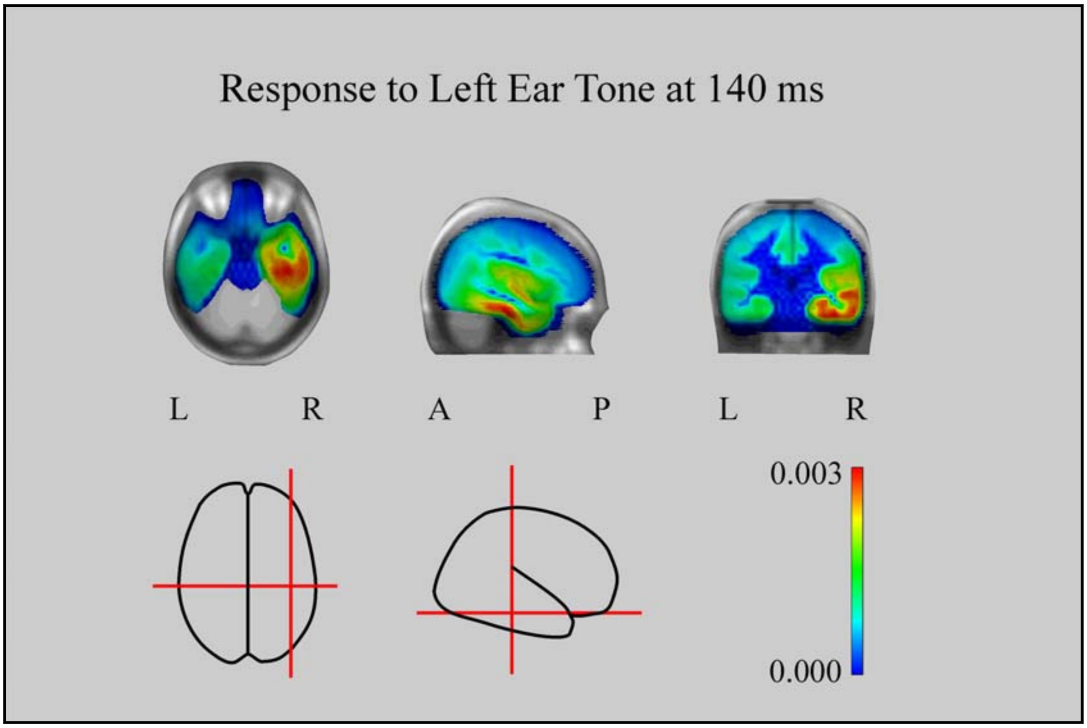
- **Discrete:** sources are a small number of point dipoles, each representing the activity of a region of the brain - e.g., Brain Electric Source Analysis (BESA)
- **Distributed:** source currents occur throughout the brain with the constraint that they have minimum total current or change in current - e.g., Low-Resolution Electromagnetic Tomography

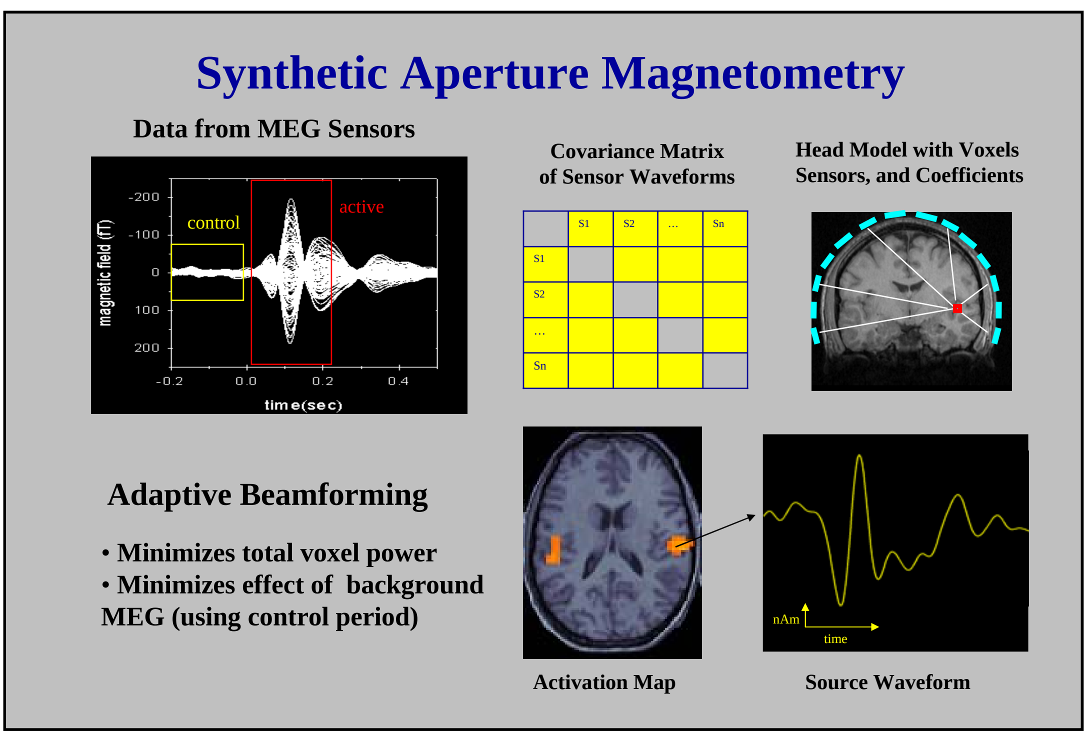

Left
Right
Average
Reference
+5 µV
-50
450 ms


Left Ear
Right Ear
N105
N140
N105
N140
Voltage
0.5 µV
Current
Source
Density
0.25 µV/cm2


1
2
3
4
2.5 µVeff
-50
400 ms
3
1
2
4
3
1
2
4


Response to Left Ear Tone at 105 ms
L
R
A
P
L
R
0.002
0.000


Response to Left Ear Tone at 140 ms
L
R
A
P
L
R
0.003
0.000


Synthetic Aperture Magnetometry
Data from MEG Sensors
magnetic field (fT)
-200
-100
0
100
200
control
active
-0.2
0.0
0.2
0.4
time(sec)
Covariance Matrix
of Sensor Waveforms
S1
S2
…
Sn
Head Model with Voxels
Sensors, and Coefficients
Adaptive Beamforming
• Minimizes total voxel power
• Minimizes effect of background MEG (using control period)
nAm
time
Activation Map
Source Waveform

Start:

Human Brain
The Movie

Herdman Productions

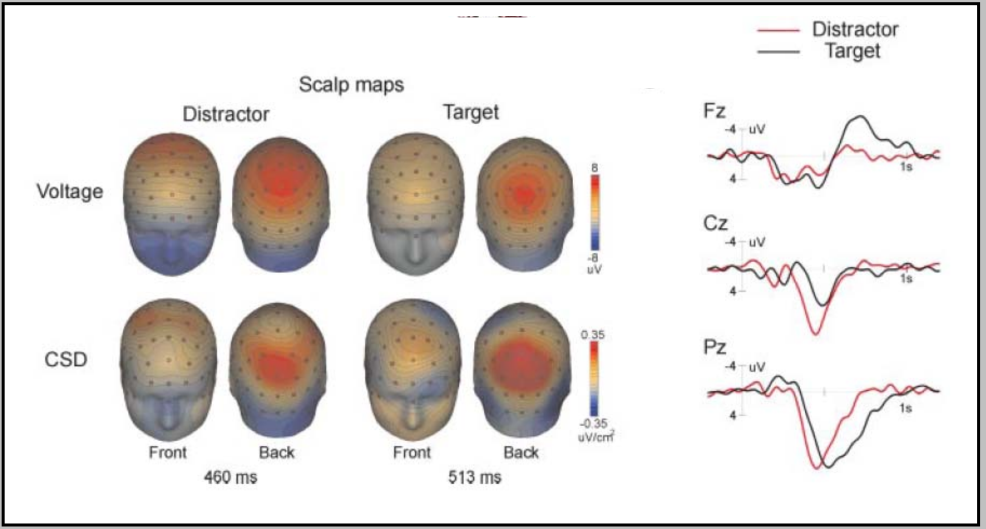
Desperately Seeking Sources

- The inverse problem has no unique solution, but only best guesses. Constraints are necessary.
- Even when not perfect, source waveforms are a better representation of what is happening than sensor waveforms.

Combining fMRI and ERP

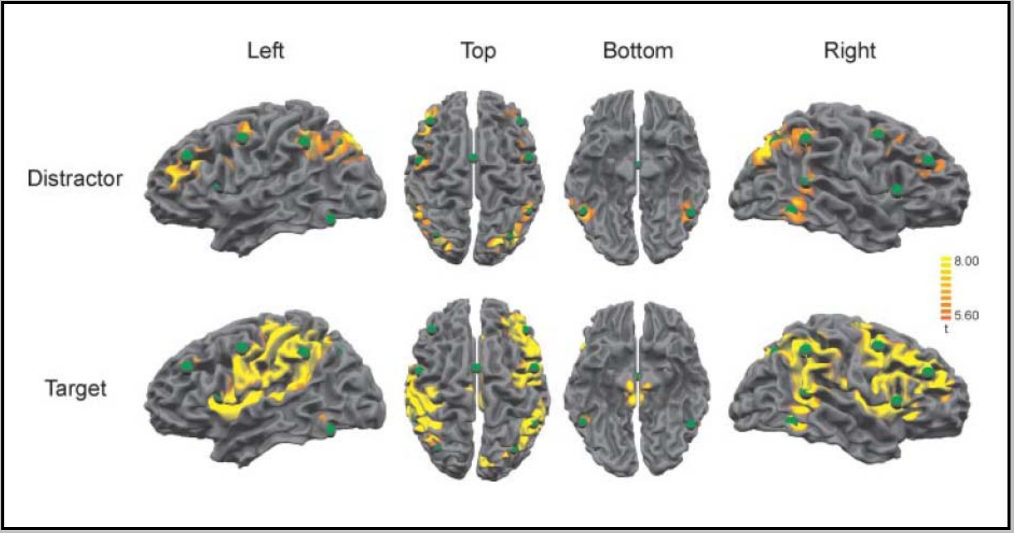
- **Seeding sources:** dipoles for a discrete source analysis are located at regions that show activation on the fMRI
- **Biasing sources:** a distributed source analysis is weighted so that sources where there is fMRI activation are enhanced

Seeding Sources

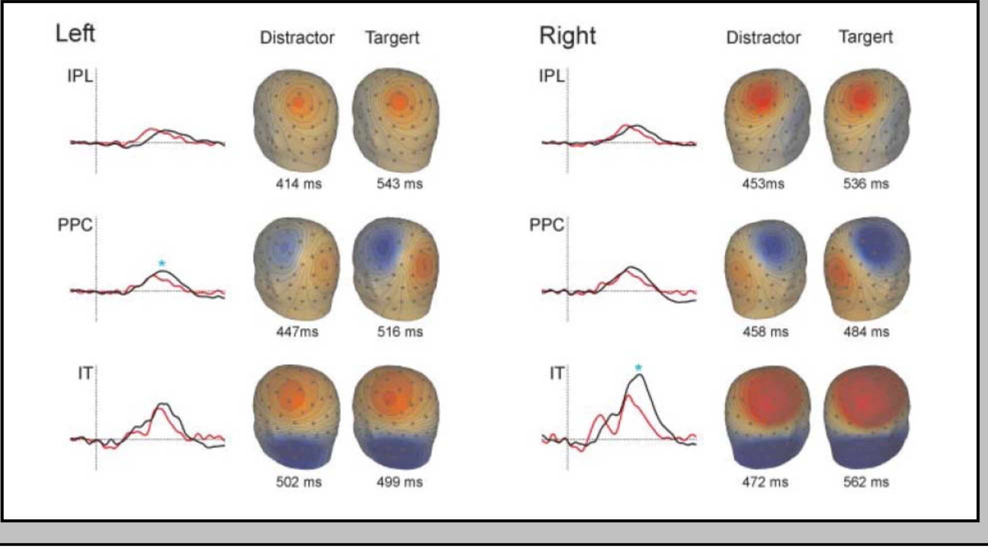


Bledowski et al, J Neurosci, 24:9353-9360, 2004

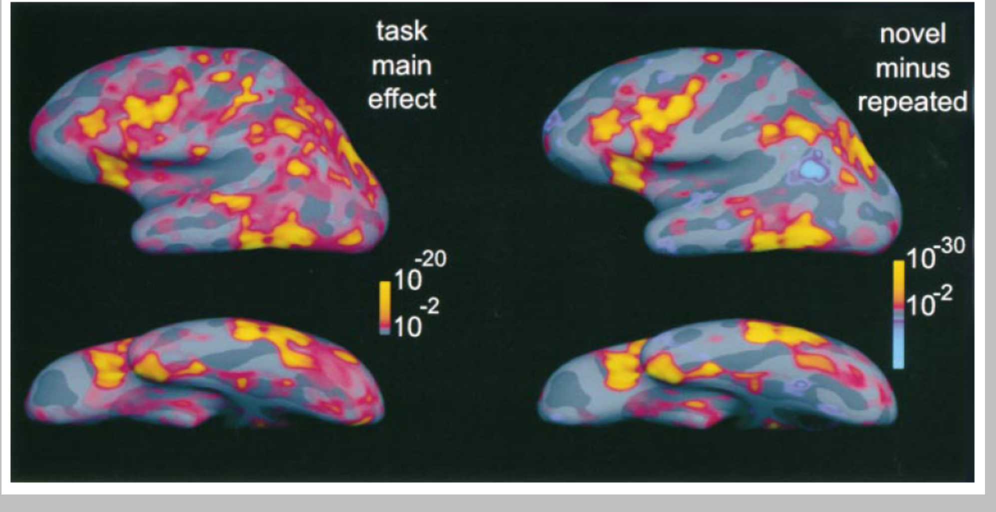
Regional sources (three orthogonal dipoles) are located in regions showing fMRI activation:



The Inferior Parietal Lobe, Posterior Parietal Cortex and Inferior Temporal Cortex all contribute to the P3b wave.

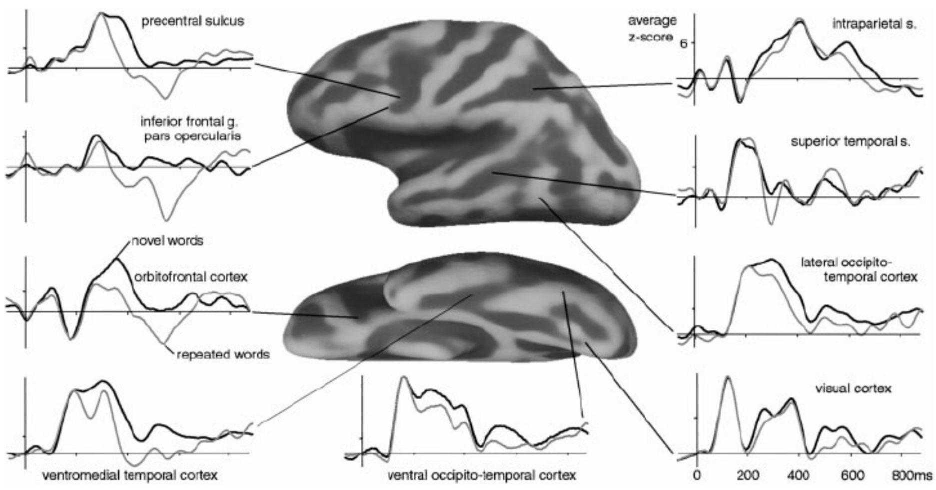


Biasing Sources



Dale et al., Neuron, 26:55-67, 2000

Spreading activation of multiple cortical areas, frontal areas being particularly active during novel stimuli



Issues in ERP-fMRI Relations

Co-registration

Simultaneous recordings

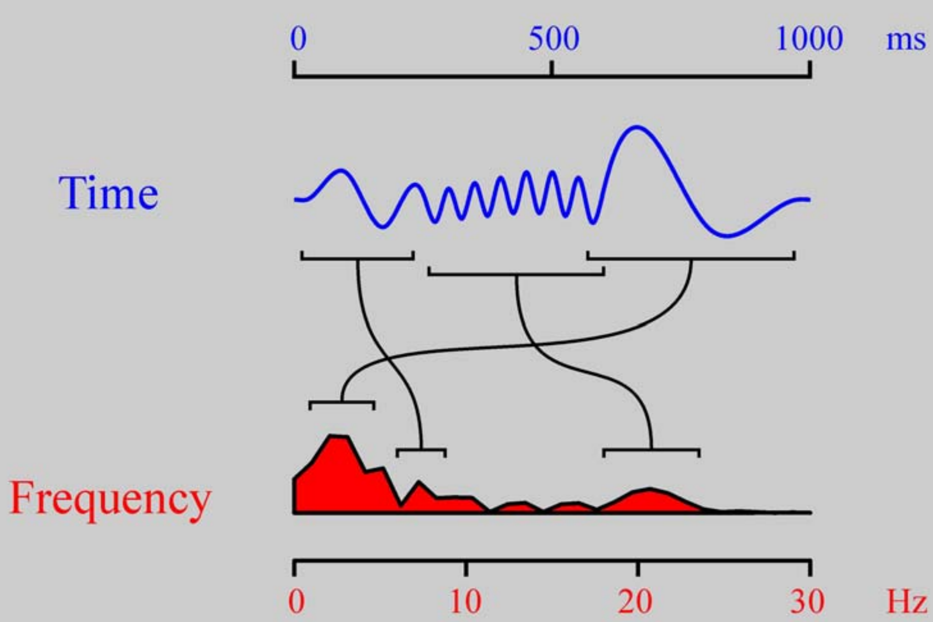
Electromagnetic sources may not change blood flow

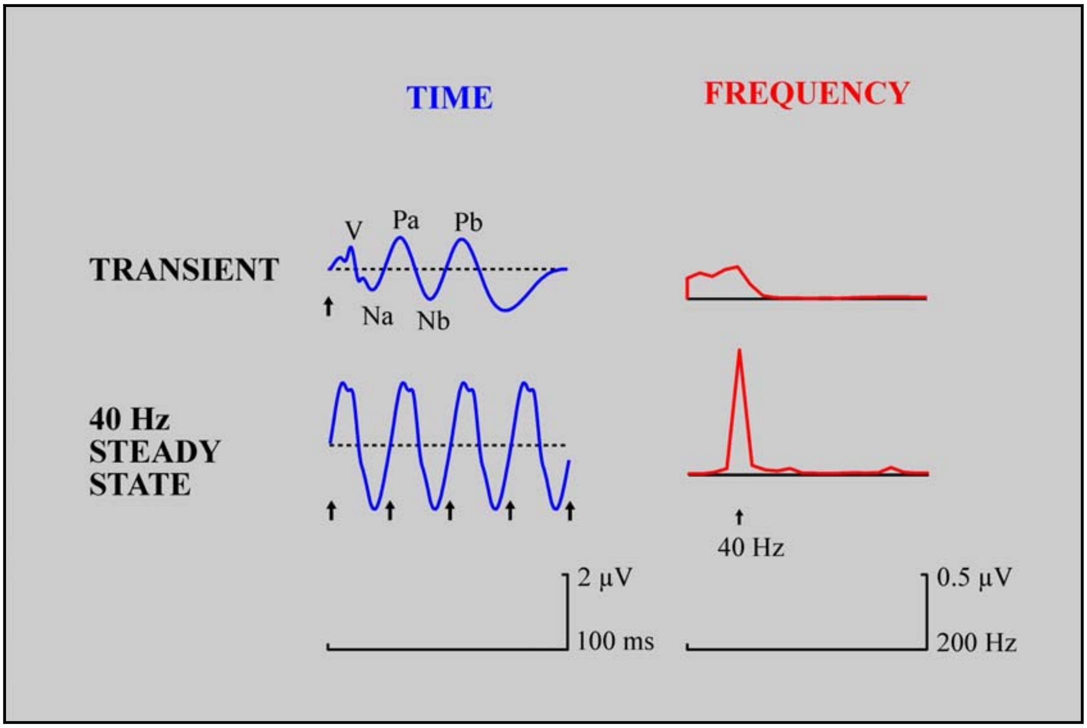
Active areas may not generate electromagnetic fields at a distance

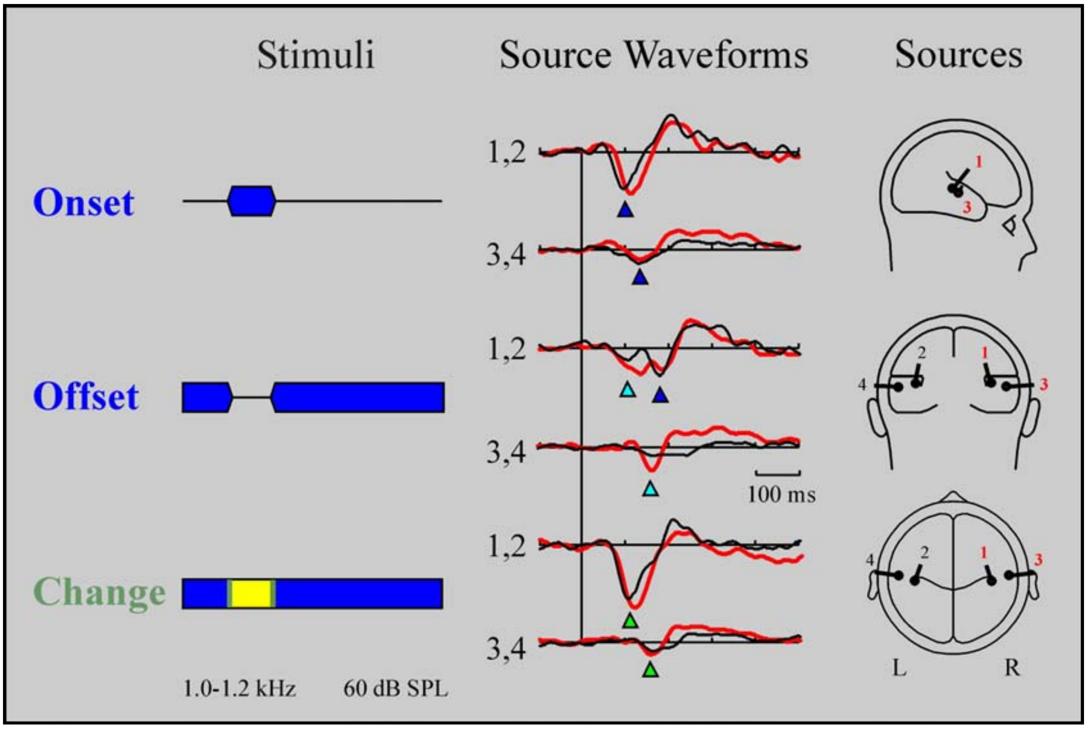
Relation between source currents or blood flow and neuronal activation not clear

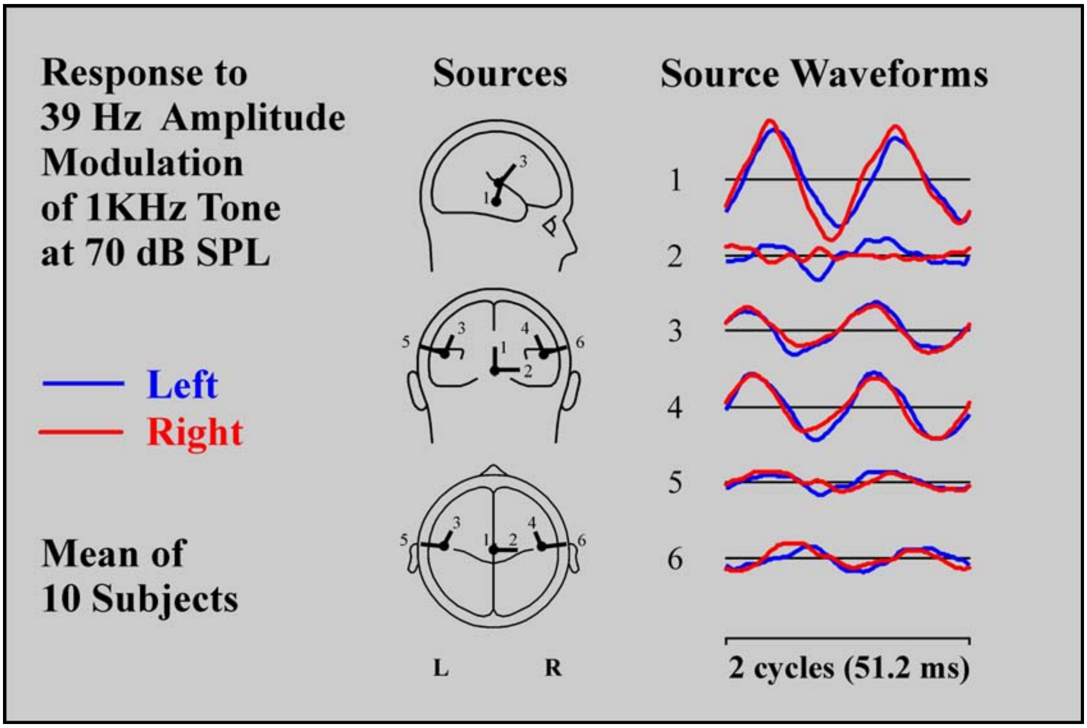
Evoked Potentials

- **Transient:** evoked by infrequent and irregular stimuli; change their frequency components through the duration of the response, and with stimulus repetition.
- **Steady-State:** evoked by periodic stimulation; constituent frequency components maintain a stable amplitude and phase through the duration of the response



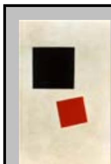

TIME
FREQUENCY
TRANSIENT
V
Pa
Pb
Na
Nb
40 Hz
STEADY
STATE
40 Hz
2 µV
100 ms
0.5 µV
200 Hz


Stimuli
Source Waveforms
Sources
Onset
Offset
Change
1,2
3,4
1,2
3,4
1,2
3,4
100 ms
1.0-1.2 kHz
60 dB SPL
L
R



Time and Frequency

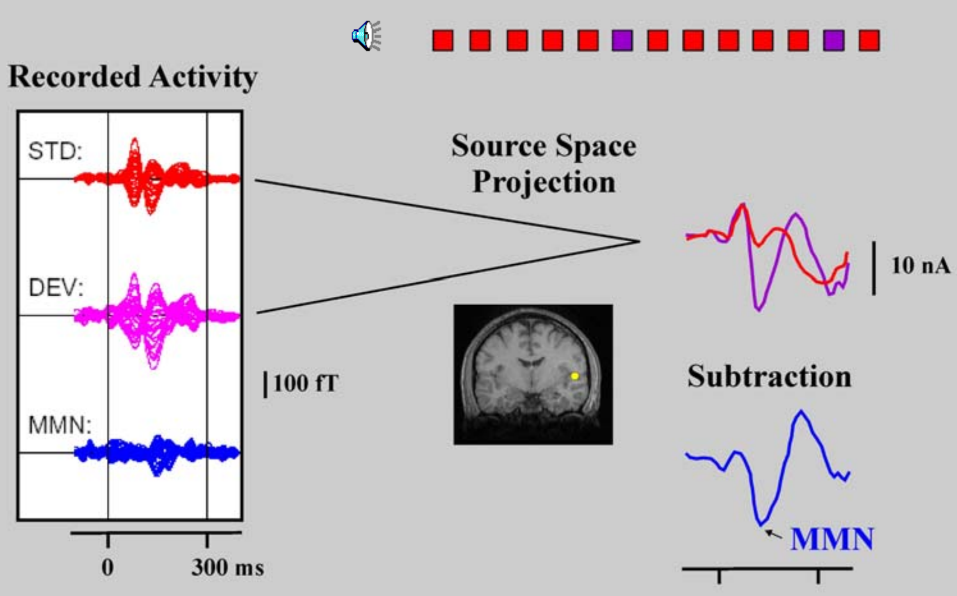
- Transient responses are best viewed in the time domain, and can give information about when things change in cerebral processing
- Steady-state responses are best viewed in the frequency domain, and can be objectively evaluated.



Determining the Components

- **Difference-Waveforms:** evaluates a process present in one recording but not the other.
- **Principal Component Analysis:** determines what contribute most to the variance of a data set
- **Independent Component Analysis:** determines components with independent temporal waveforms.
- **Partial Least Squares:** provides components that are directly related to the experimental manipulations (Lobaugh et al., Psychophysiology, 38: 217-230, 2001.)

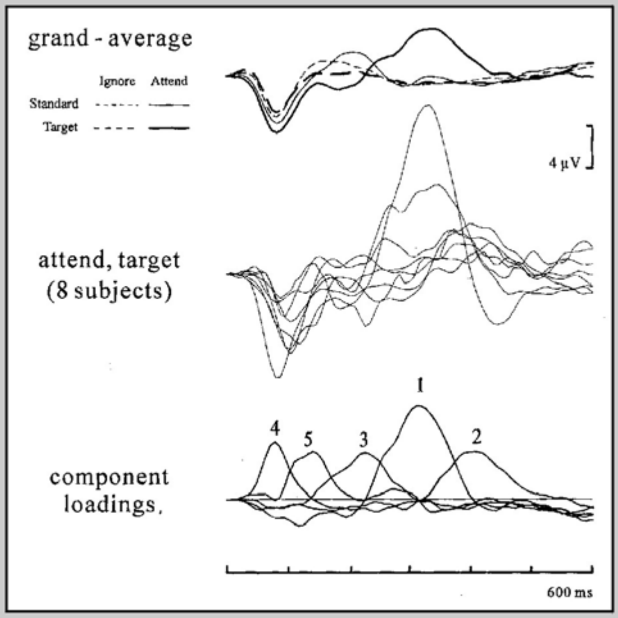
Analysis of the Mismatch Negativity



Principal Component Analysis

Component 1 - P3 wave
Component 2 - P3 in some subjects
Component 3 - MMN
Component 4 - N1 in one subject
Component 5 - N1 wave

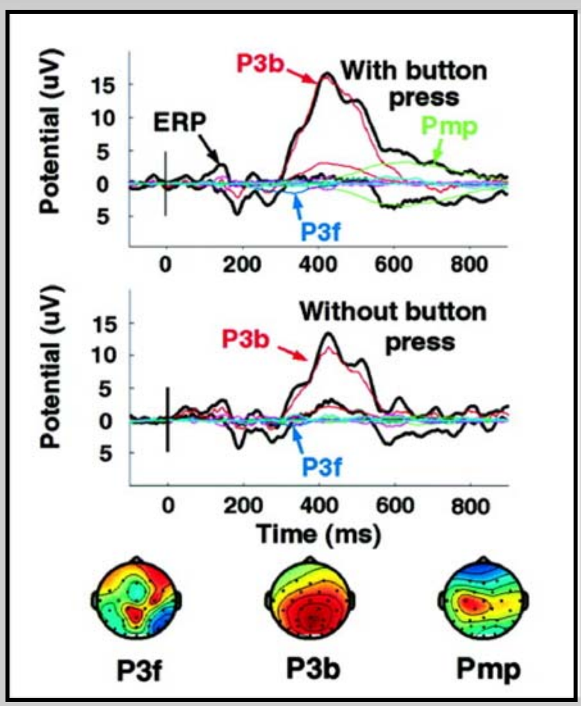
Limitations - assumes latency consistency of component across subjects and conditions



Independent Component Analysis

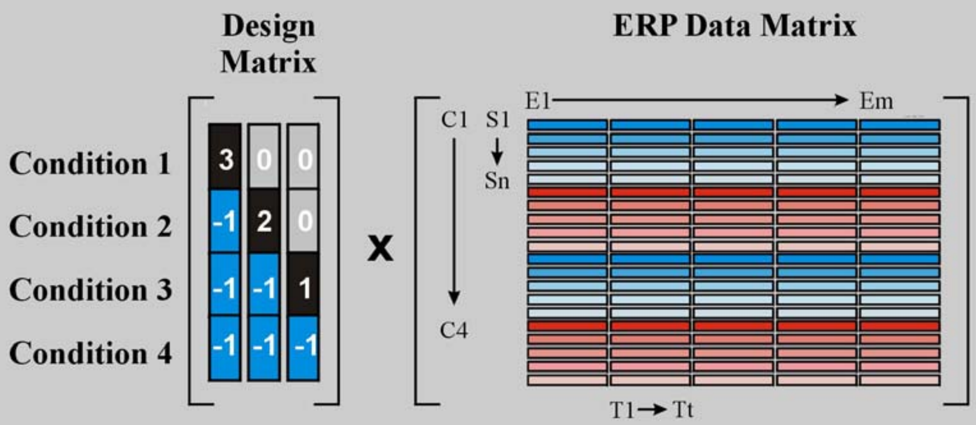
Subject responds to occasional targets by pressing button with right index finger, or simply notes the occurrence of the target without any motor response.

Makeig et al., 1999
J. Neurosci. 19:2665-80



Partial Least Squares Analysis of ERP Data

Computes a least squares fit of a covariance matrix between a design matrix and the data matrix. It is like a principal component analysis except that the solutions are constrained to that part of the covariance structure attributable to the experimental manipulations.



Deconstructing Waveforms

- Any component analysis should ultimately refer to activities in sets of neurons and not to abstract effects.
- Most component analyses cannot handle differences in time between conditions
- Most component analyses do not distinguish signal from noise.

Spontaneous EEG

- **EEG Rhythms**: generally due to the synchronization of neurons at a rate determined either by pacemaker circuits or by feedback loops.
- **Desynchronization**: of slow rhythms such as the occipital alpha rhythm or the central mu rhythm, may be caused by increased neuronal activation
- **Synchronization:** of faster rhythms such as the gamma rhythms, may relate to perceptual processes like binding.

Human EEG

Spontaneous Activity

delta	<4 Hz
theta	4-8
alpha	8-13
beta	13-35
gamma	35-80

Event-Related Activity

lambda, V-waves, K-complexes
evoked potentials
emitted potentials
desynchronization
induced activity

Specific Rhythms

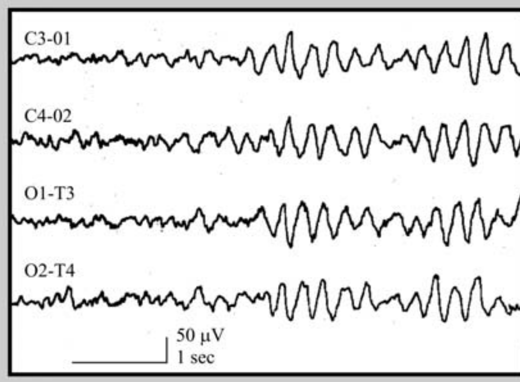
alpha	occipital
mu	central
sigma	sleep spindles
kappa	temporal

hedonic hypersynchrony

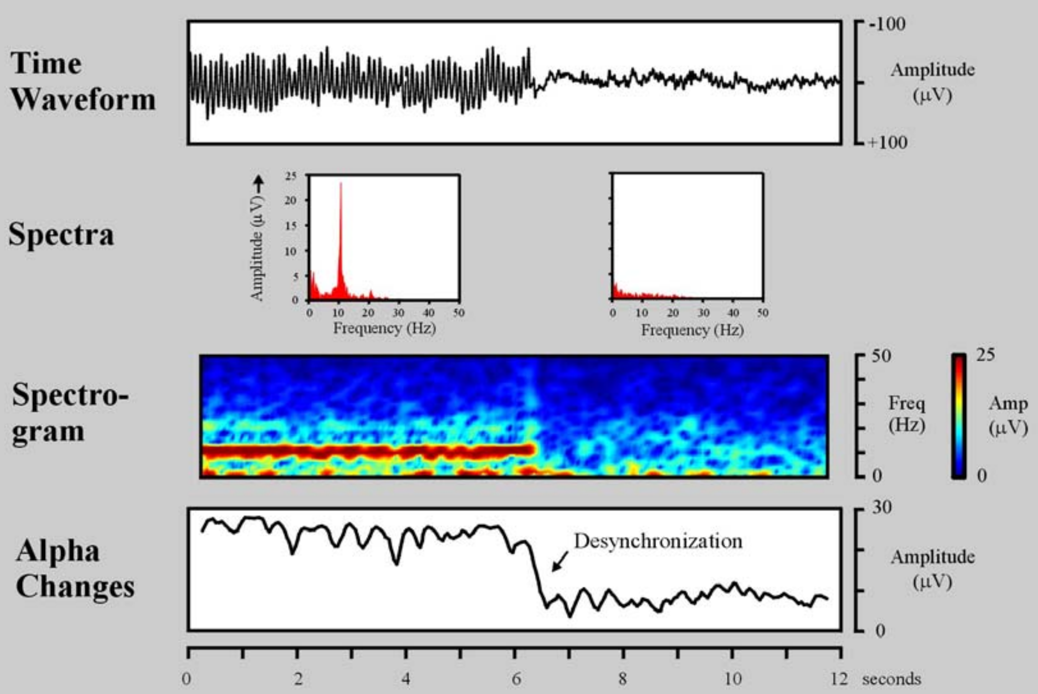
Artifacts

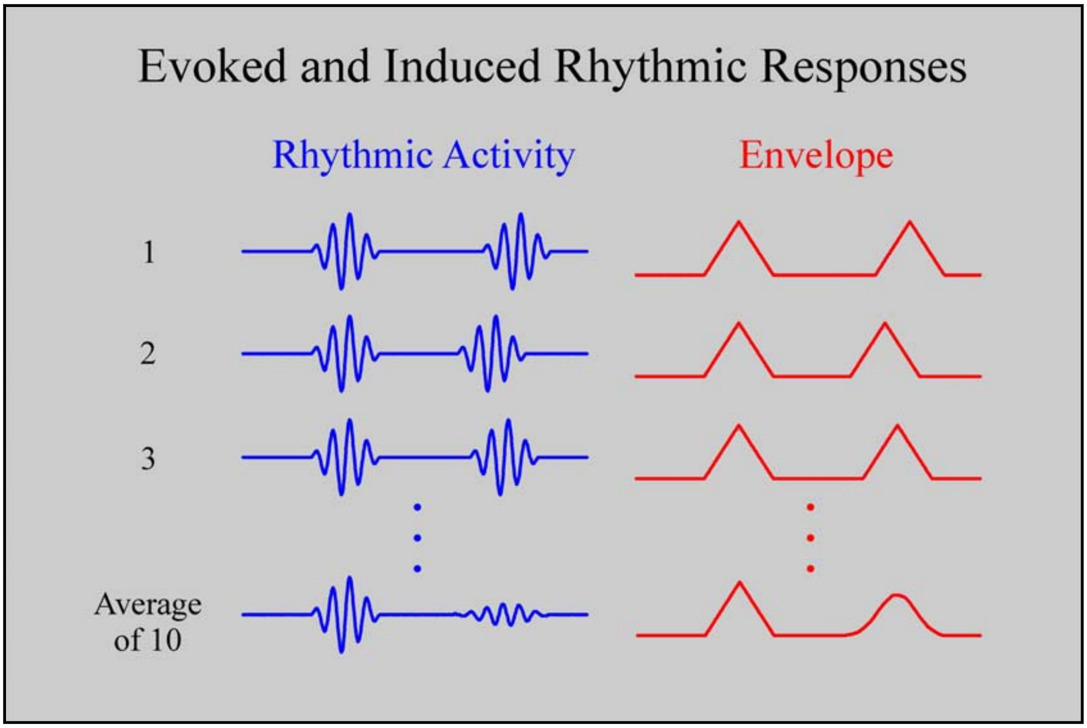
eyes	line noise
muscle	video monitors
skin	earphones
tongue	electrical stimuli

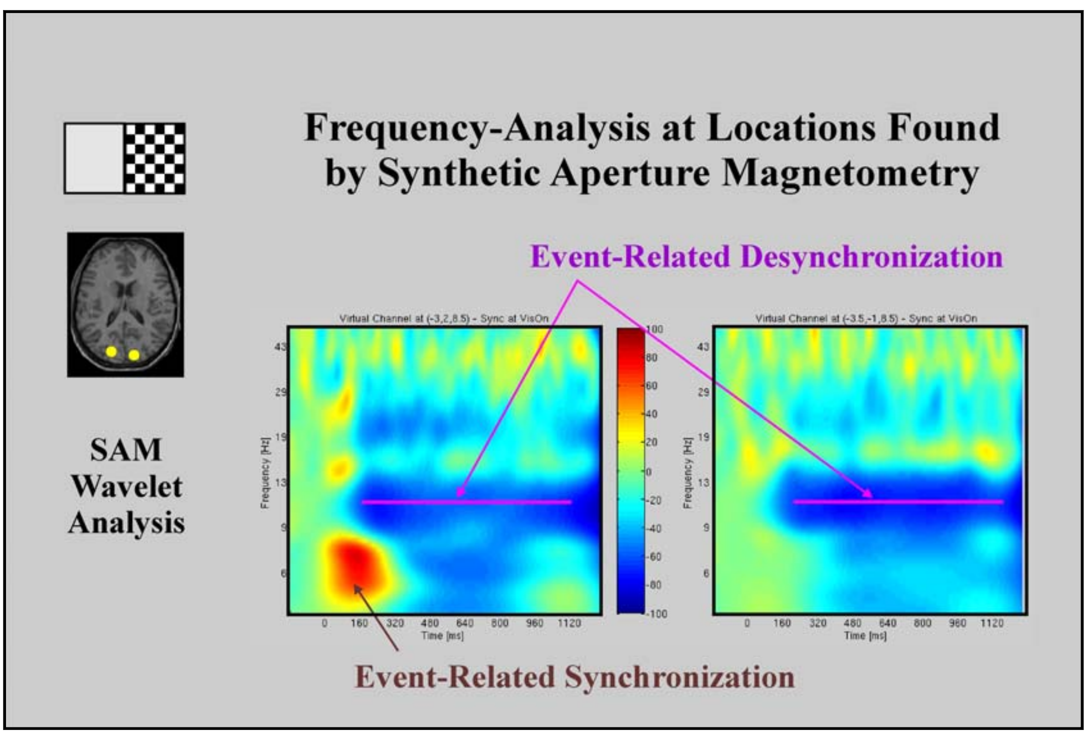
Hedonic Hypersynchrony

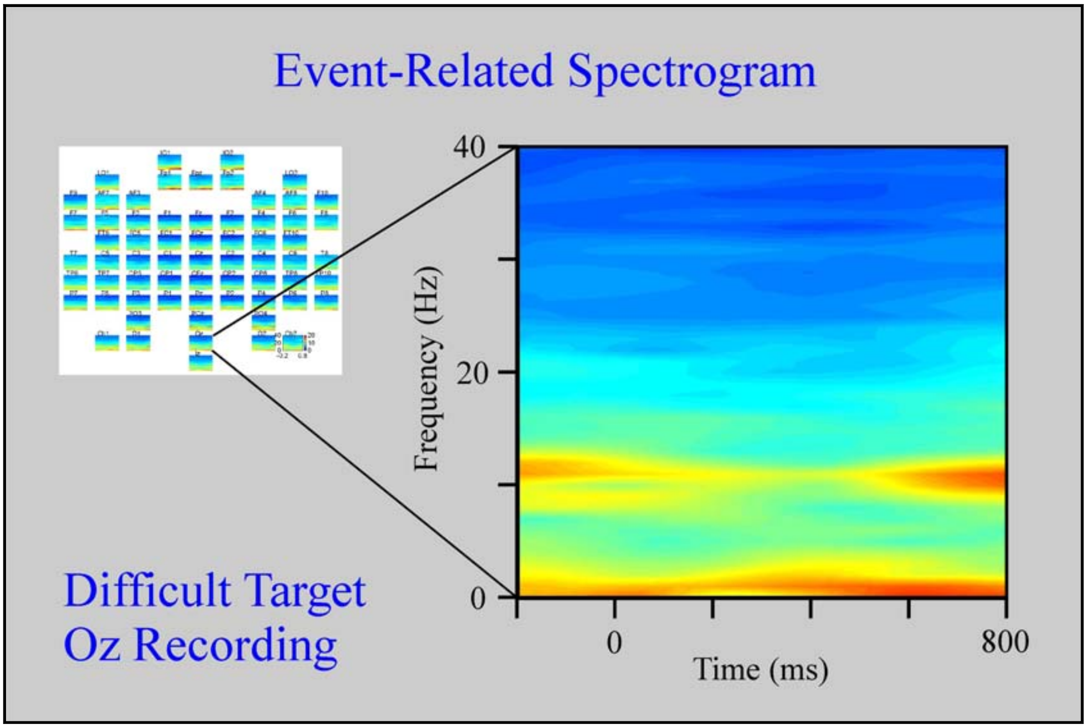


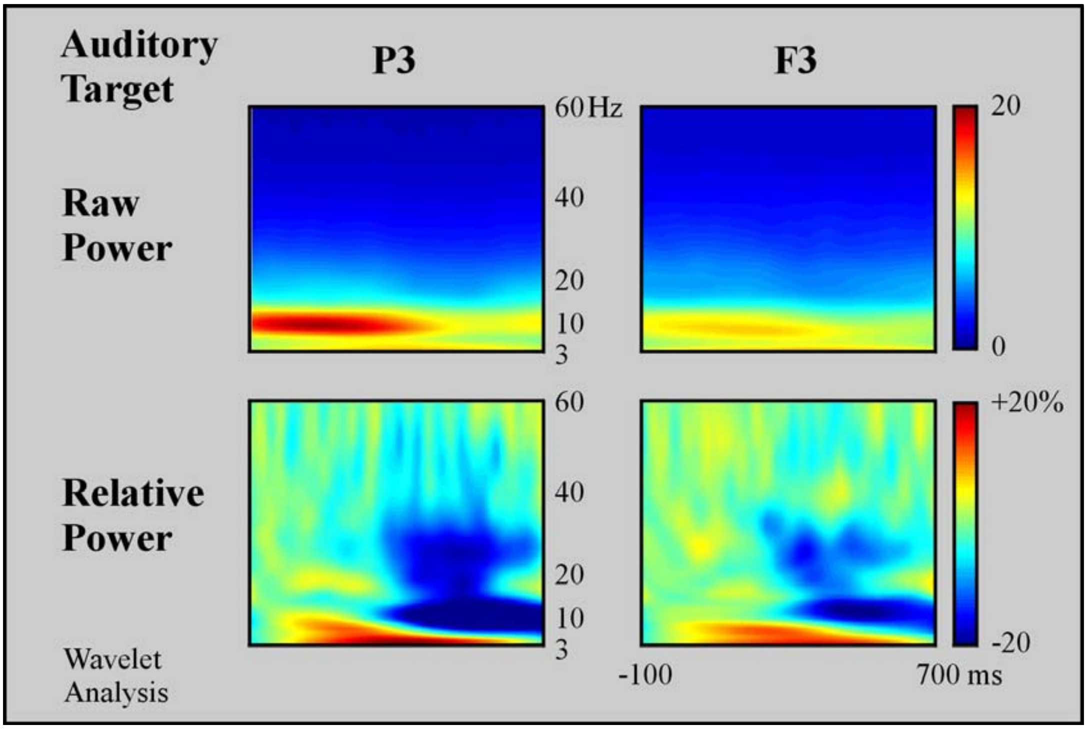
R. L. Maulsby, Electroenceph. Clin. Neurophysiol., 31:157-165, 1971

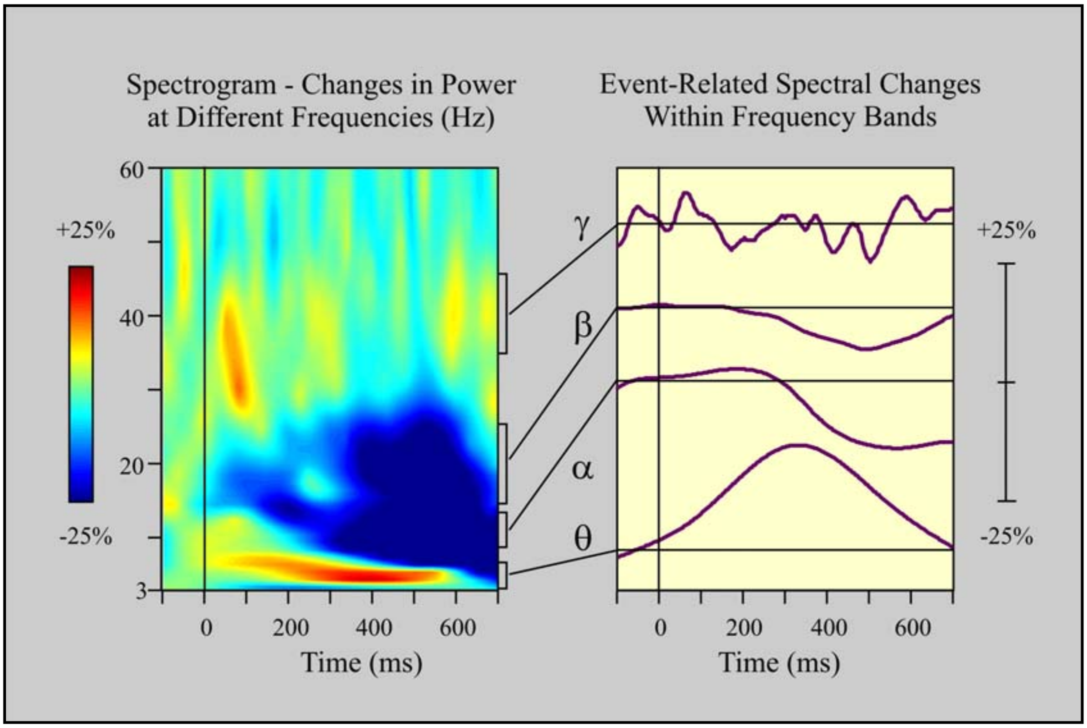


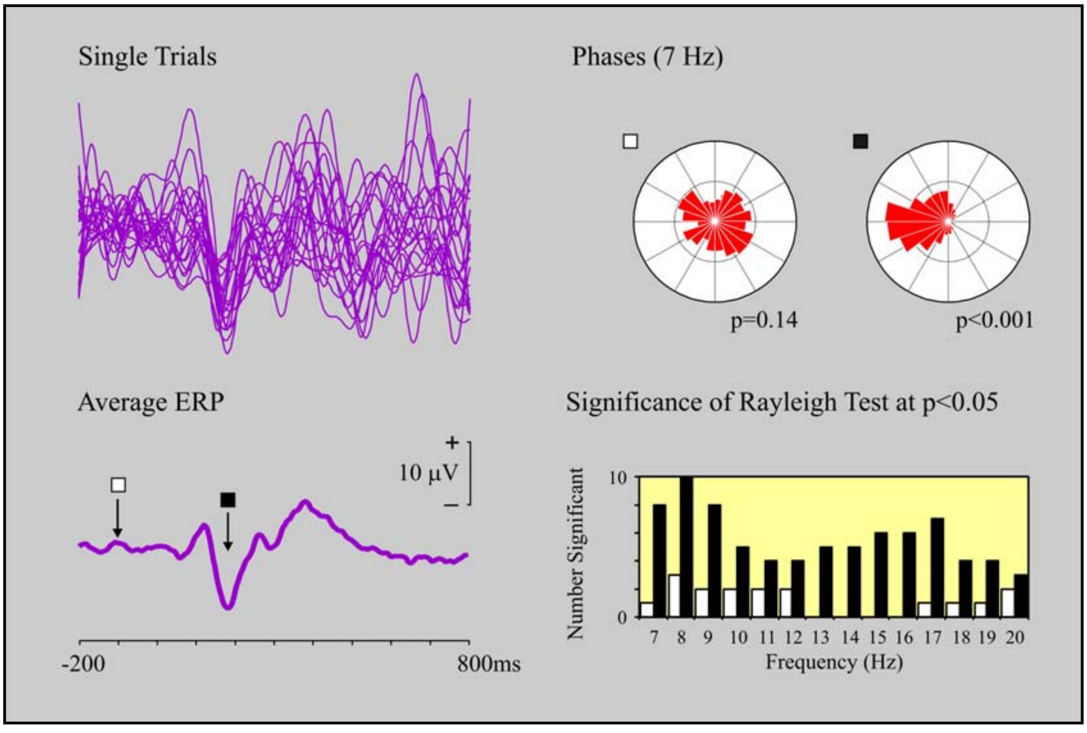

Evoked and Induced Rhythmic Responses
Rhythmic Activity
Envelope
1
2
3
Average of 10


Frequency-Analysis at Locations Found by Synthetic Aperture Magnetometry
SAM Wavelet Analysis
Event-Related Desynchronization
Frequency [Hz]
Time [ms]
Event-Related Synchronization


Event-Related Spectrogram
40
20
0
Frequency (Hz)
0
800
Time (ms)
Difficult Target
Oz Recording


Auditory
Target
P3
F3
Raw
Power
60 Hz
40
20
10
3
20
0
Relative
Power
60
40
20
10
3
+20%
-20
-100
700 ms
Wavelet
Analysis


Spectrogram - Changes in Power at Different Frequencies (Hz)
Event-Related Spectral Changes Within Frequency Bands
60
40
20
3
+25%
-25%
γ
β
α
θ
0
200
400
600
Time (ms)
+25%
-25%


Single Trials
Phases (7 Hz)
p=0.14
p<0.001
Average ERP
10 μV
+
–
-200
800ms
Significance of Rayleigh Test at p<0.05
Number Significant
10
0
7 8 9 10 11 12 13 14 15 16 17 18 19 20
Frequency (Hz)

Rhythms of the Brain

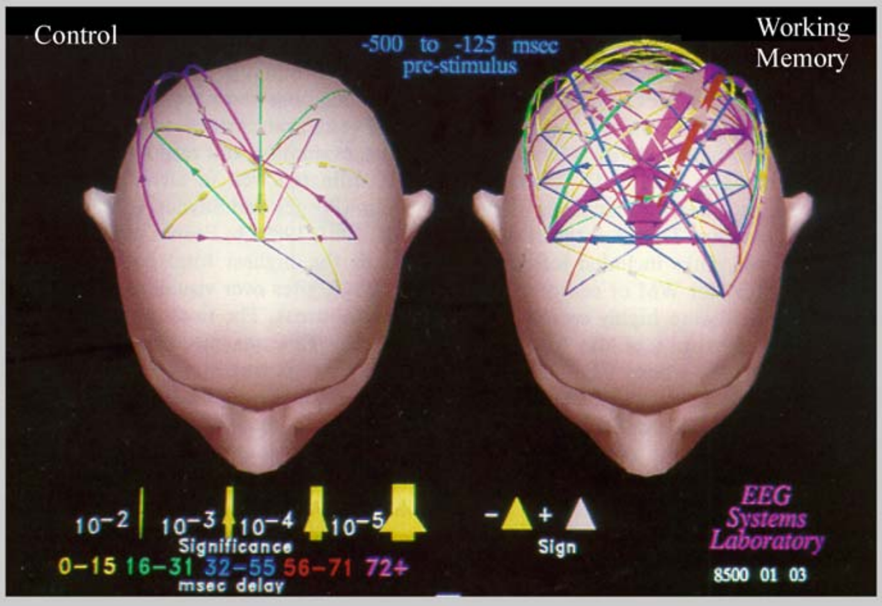
- The background EEG/MEG is not just noise but is important to information processing.
- Relations between the background EEG/MEG and the event-related potentials or fields can best be explained by the idea that they share generators.

Information Transfer

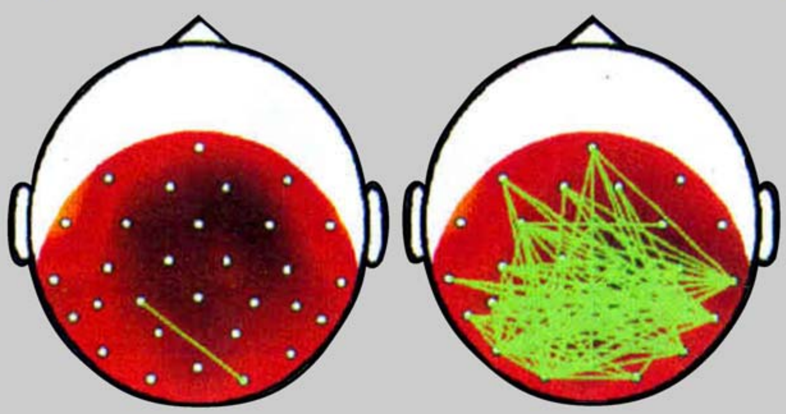
- **Correlational Analyses**: how well activity in one region is related to activity in another region, can be performed in either time or frequency domain.
- **Limitations:** need to consider the volume-conducted field spread from one region to another; problems of using a vector-variable.

Gevins and Cutillo, Electroenceph Clin Neurophysiol 1993, 87:128-143

Cross-covariance of time waveforms



Perception's shadow: long-distance synchronization of human brain activity

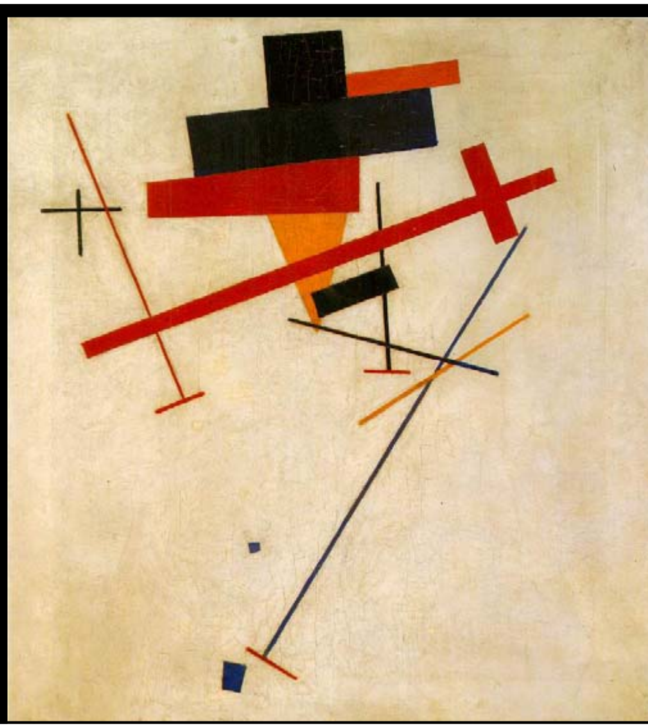


Rodriguez et al., 1999
Nature, 397:430-433

Synchronization of gamma activity when face recognized

Information Transfer

- MEG/EEG timing can give a direction to the transfer.
- Ultimately, one will need to study correlations between source rather than sensor waveforms.
- Temporal coding of the MEG/MEG signal (e.g. onset response more than sustained response) is problematical.



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