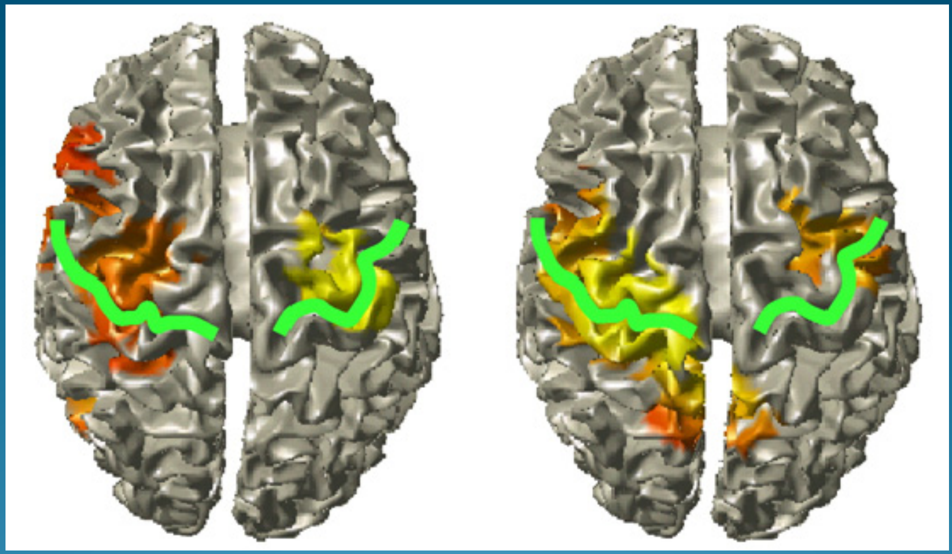
MEG: Magnetic Source Imaging of Brain Function



Tim Bardouille

February 17th, 2011

Talking Points

MEG

• offers an advantageous combination of spatial and temporal resolution

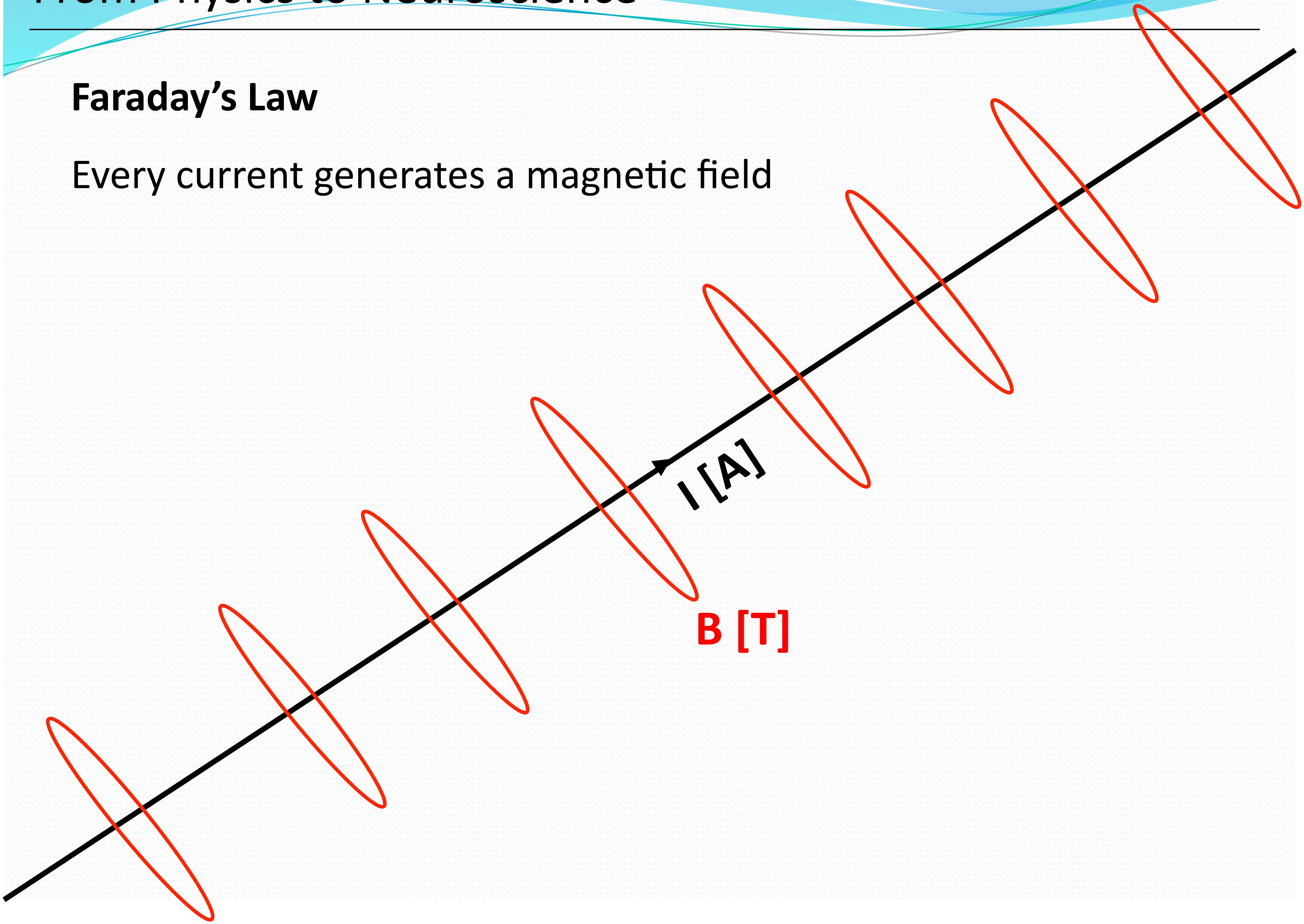
• is well-suited to imaging functional connectivity in the brain

• challenges (opportunities?) are:

- large data structures
- multiple types of responses
- source localisation in a spherical geometry

Faraday's Law

Every current generates a magnetic field



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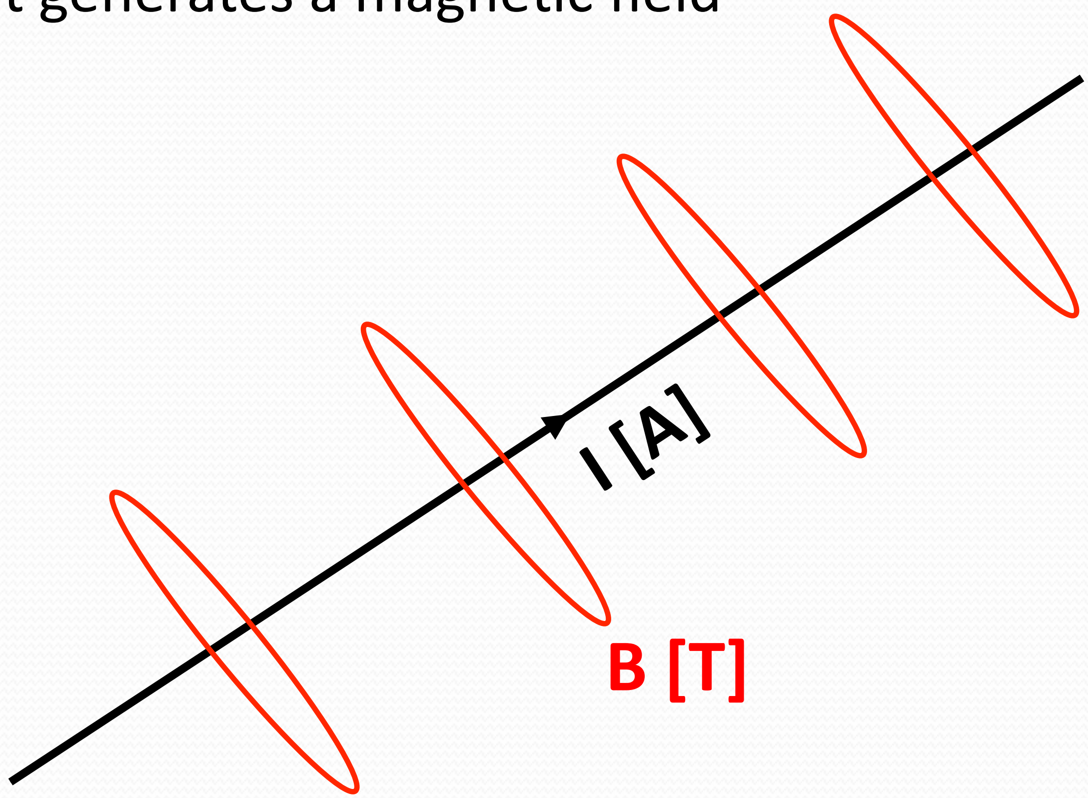

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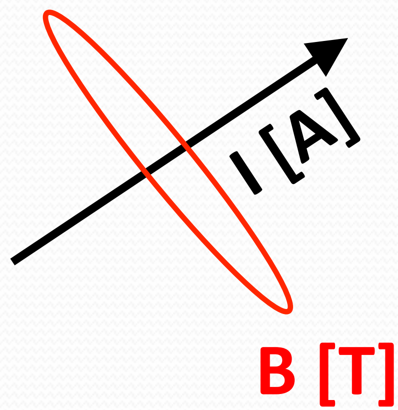
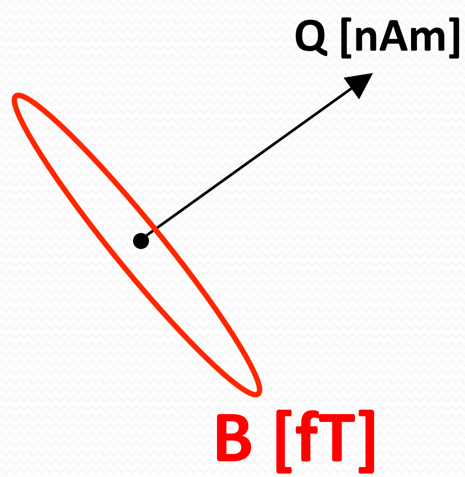


A Current Dipole

Current flow over distance, as distance approaches zero



Q and **B** are vectors: magnitude and orientation

From Physics to Neuroscience

A Current Dipole

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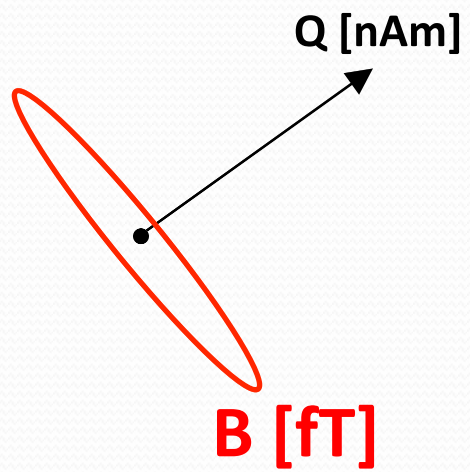

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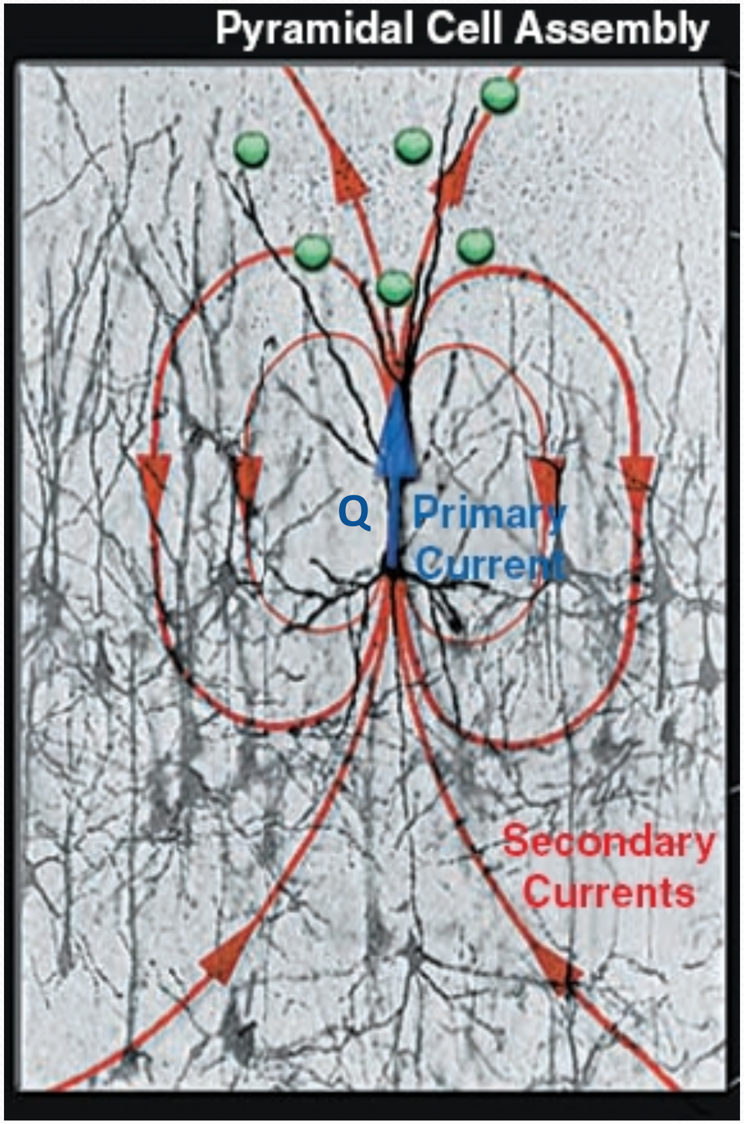
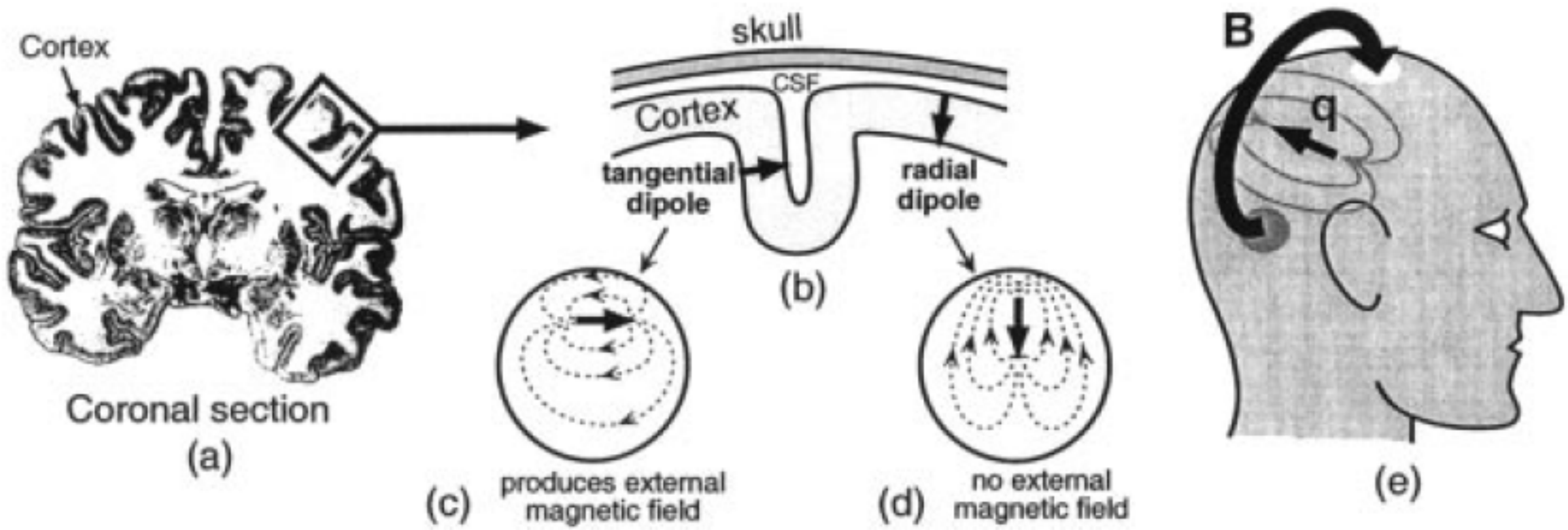


(Baillet et al., 2001)

Neuroimaging With MEG

Synchronous neural firing generates tiny magnetic fields



(Vrba, Robinson, 2001)

How do we detect these small fields?

Neuroimaging With MEG

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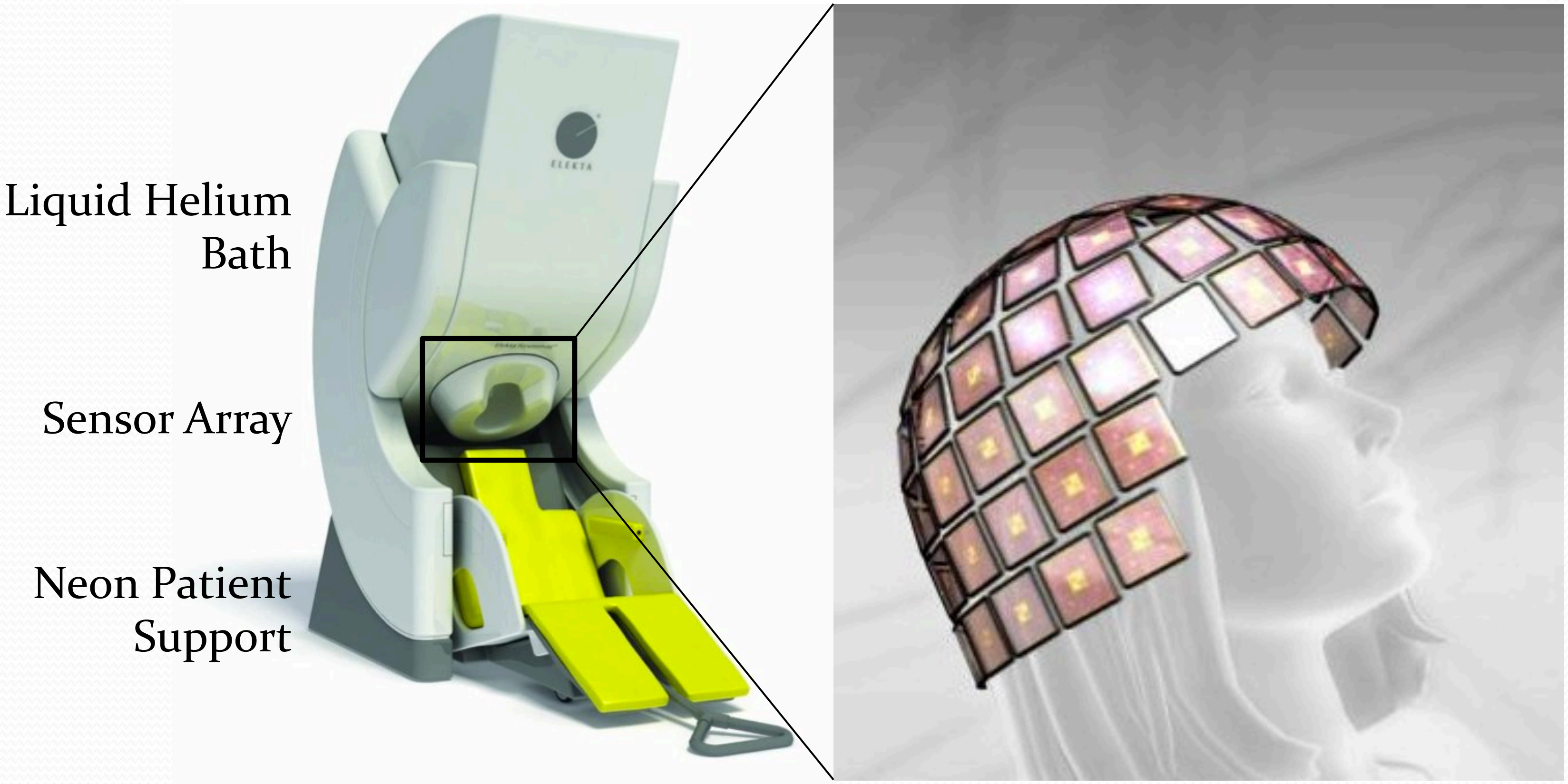

Whole head mapping of magnetic field strength outside the head over time allows us to interpolate when and where synchronised neural activity occurs

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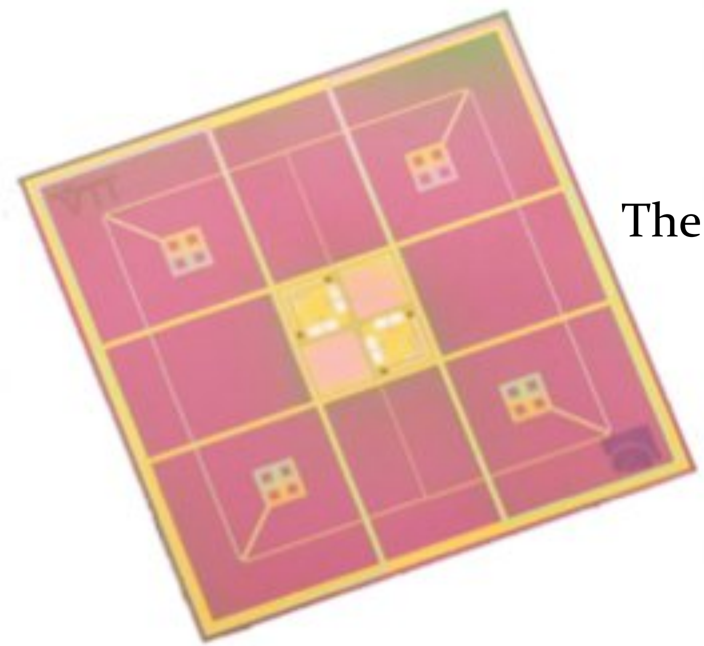


The “Elekta” MEG Sensor

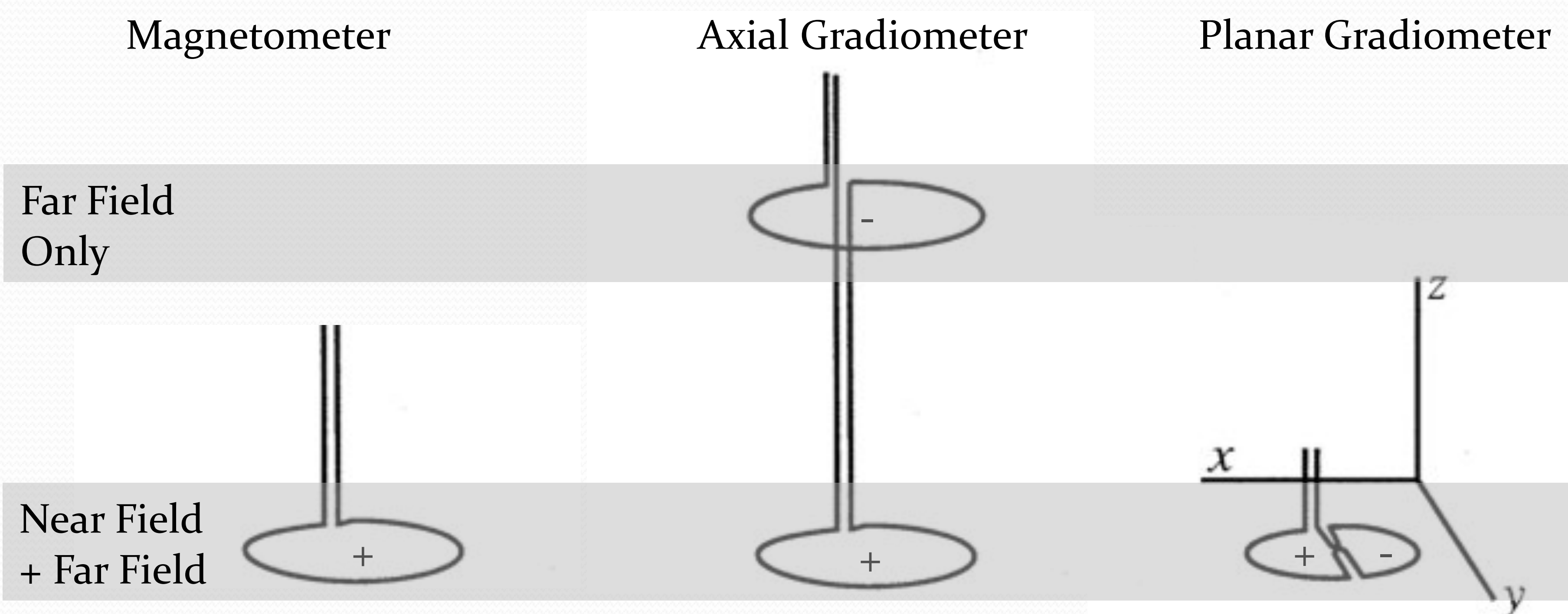
Whole head mapping of magnetic field strength outside the head over time allows us to interpolate when and where synchronised neural activity occurs

Neuroimaging With MEG

Combining Flux Transformers and SQUIDs

<u>Flux Transformers</u>
"Transform" magnetic "flux"into current (Right Hand Rule)

Types of flux transformers:



(Hamalainen, 1993)

MEG field topography will be different for each gradiometer type!!!

Neuroimaging With MEG

Combining Flux Transformers and SQUIDs

<u>Super Conducting QUantum Interference Device</u>

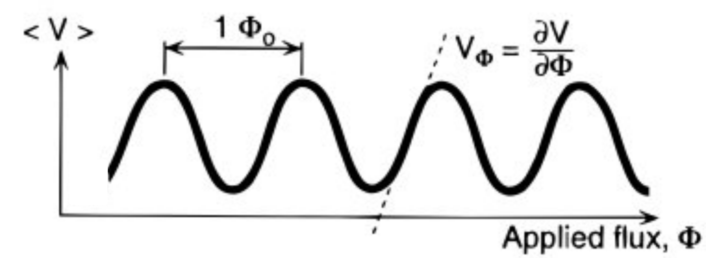
• requirement: all components are superconducting (T = -269 °C)

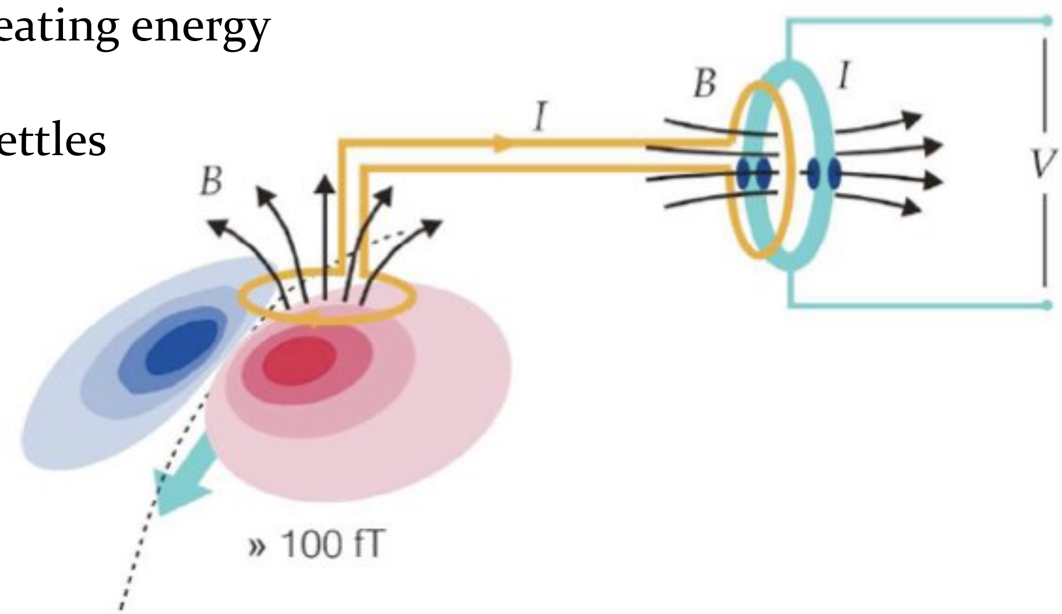
• energy in the SQUID sits in a "quantum well"

• flux transformer converts B field to current

• current is induced on the SQUID creating energy

• Voltage is measured as the SQUID settles





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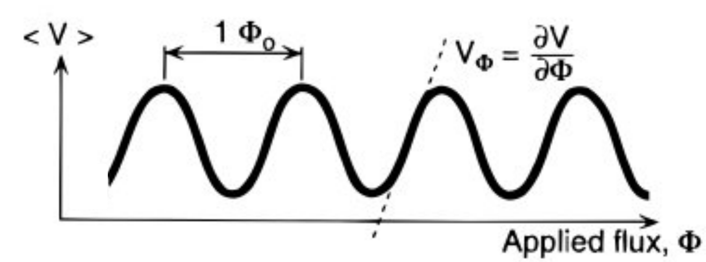
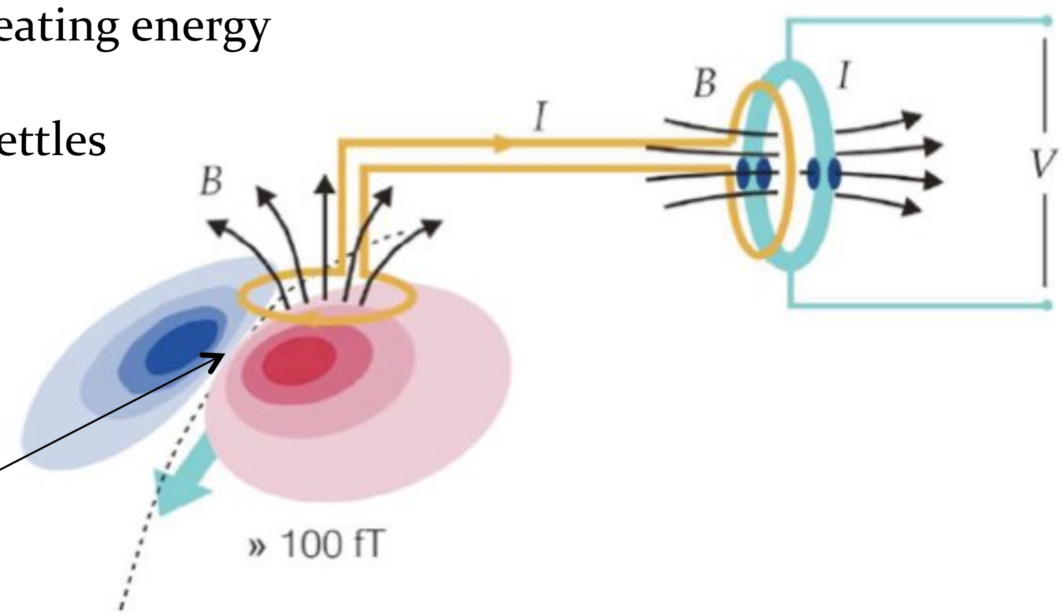




Note: Planar gradiometer is maximal here

Neuroimaging With MEG

MEG vs EEG

MEG:

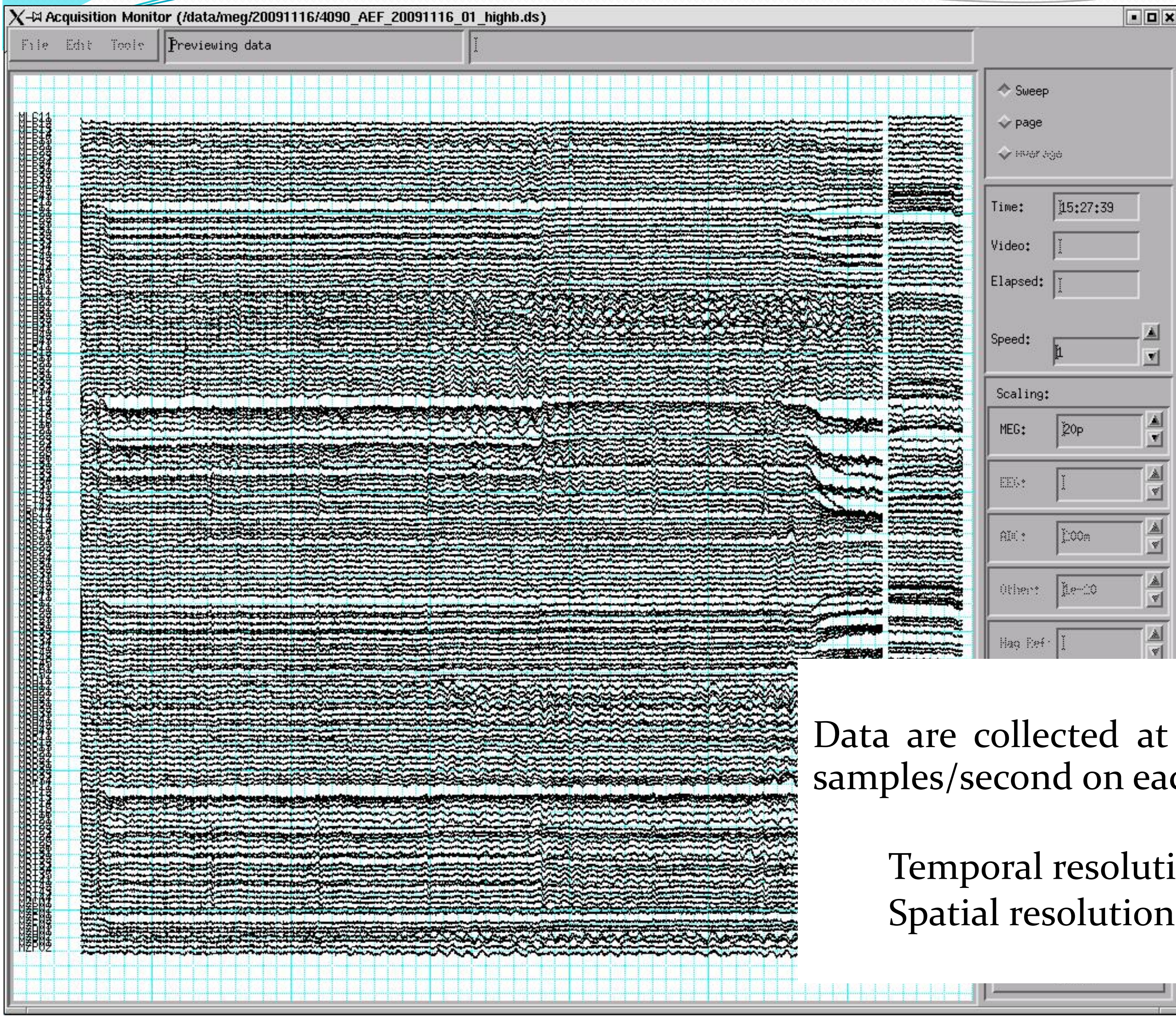
- is undistorted by intervening tissues and scalp
- is relatively insensitive to deep sources and radial sources
- has higher effective resolution
- has quicker setup
- records from 150-300 sensors
- can provide complimentary information to EEG (often recorded simultaneously)
- about 10X more expensive

MEG vs. fMRI

MEG:

- is a more direct measure of neural activity (BOLD is neurovascular)
- offers much higher temporal resolution (ms vs s)
- has poorer spatial resolution
- about the same price
- offers no structural imaging capability

A Needle In A Haystack



Data are collected at rates up to 2500 samples/second on each sensor.

Temporal resolution: ~1 ms
Spatial resolution: ~ 1-5 mm

A Needle In A Haystack

The magnetic fields of interest ***(SIGNAL)*** are buried in other magnetic fields ***(NOISE):***

THE SIGNAL

• synchronous neuronal firing (0.1 – 1 million neurons)

10-100 x 10^{-15} T (fT)

THE NOISE

•environmental source of noise (i.e. power lines, elevators, cars, etc.)

10^{-9} T (nT)

• magnetic artifacts generated by the body (i.e. eye, muscle, etc.)

10^{-12} T (pT)

• brain signals in which we're not interested ("brain noise")

10-100 x 10^{-15} T (fT)

• intrinsic sensor (SQUID) noise

10^{-15} T (fT)

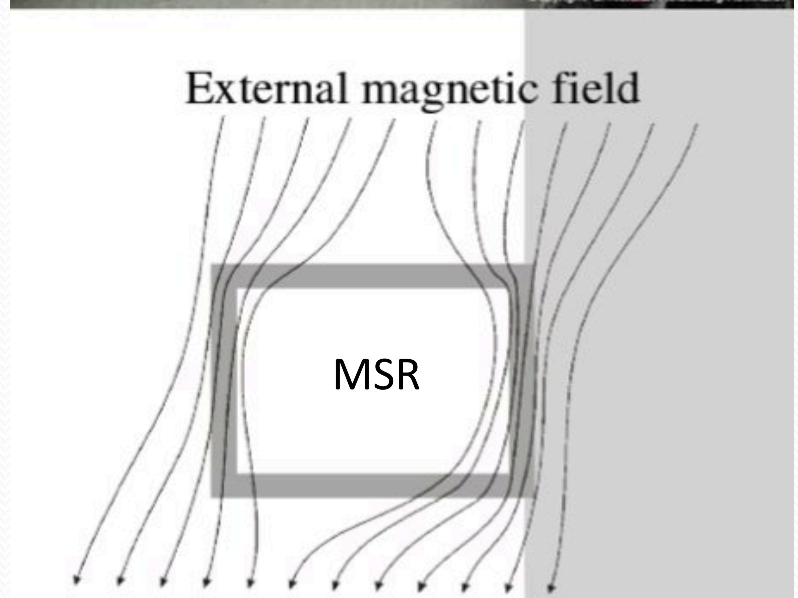
GOAL OF DATA ANALYSIS: Improve the Signal-to-Noise Ratio (SNR)

A Needle In A Haystack

The magnetic fields of interest ***(SIGNAL)*** are buried in other magnetic fields ***(NOISE):***

Properties of Magnetic Noise

- environmental noise occurs far from the MEG
    - so … use a magnetically shielded room (MSR)
    - or … model it out (SSS)



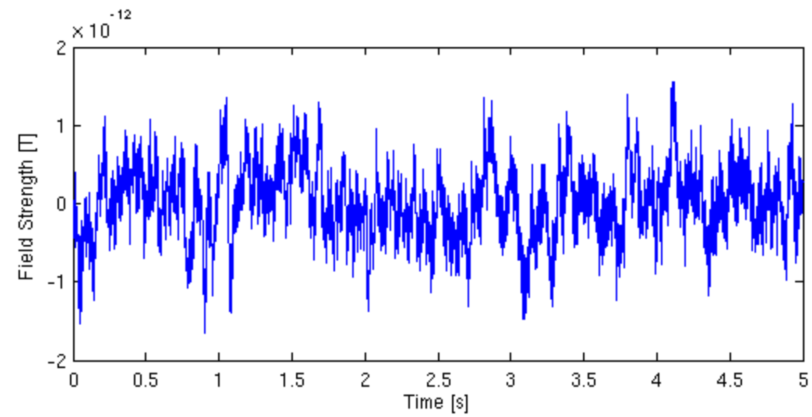
A Needle In A Haystack

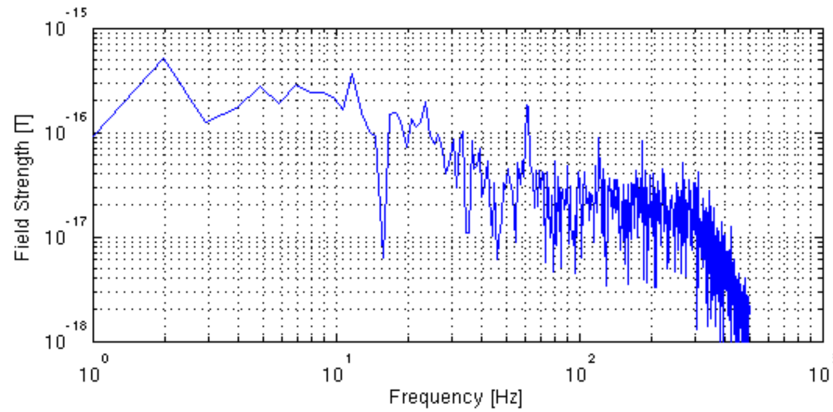
The magnetic fields of interest ***(SIGNAL)*** are buried in other magnetic fields ***(NOISE):***

Properties of Magnetic Noise

• covers the entire frequency spectrum while neuromagnetic activity is 0-100 Hz

• so … filter it out





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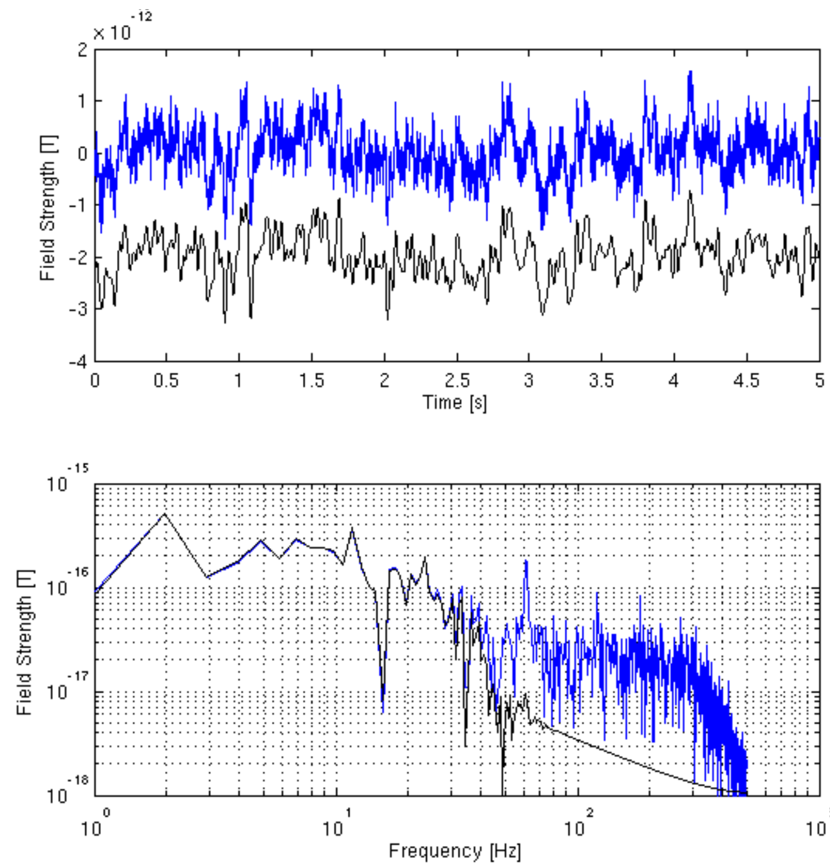

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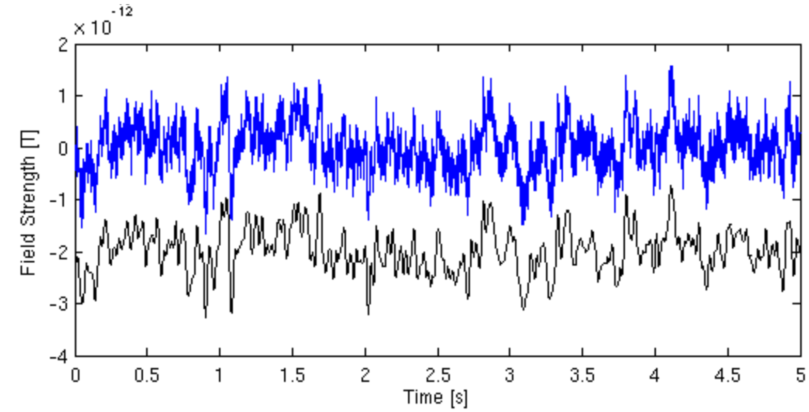
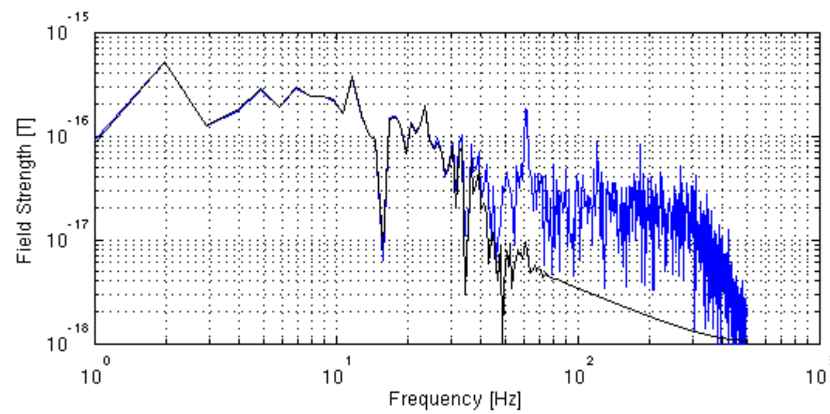


- generally **not temporally correlated** with stimulation or behaviour
    - so … correlate it out
    - This is event-related analysis



- generally **not temporally correlated** with other neural populations
    - so … correlate it out
    - This is functional connectivity analysis

A Needle In A Haystack

Enough noise!!!
What about the signal???

The magnetic fields of interest ***(SIGNAL)*** are buried in other magnetic fields ***(NOISE):***

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• covers the entire frequency spectrum while neuromagnetic activity is 0-100 Hz
  • so … filter it out

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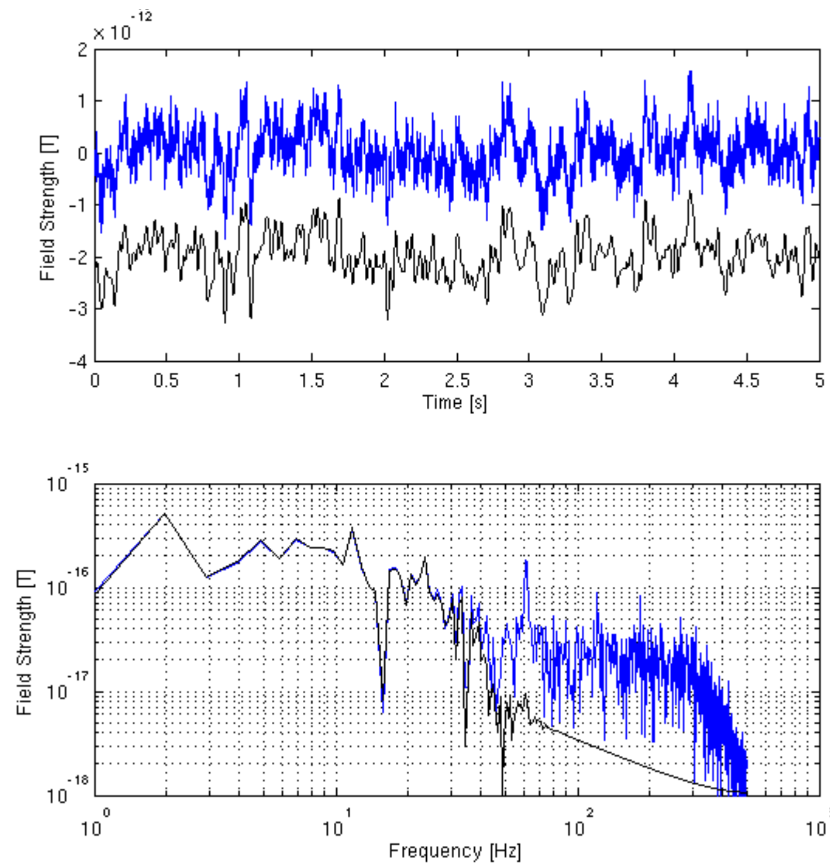

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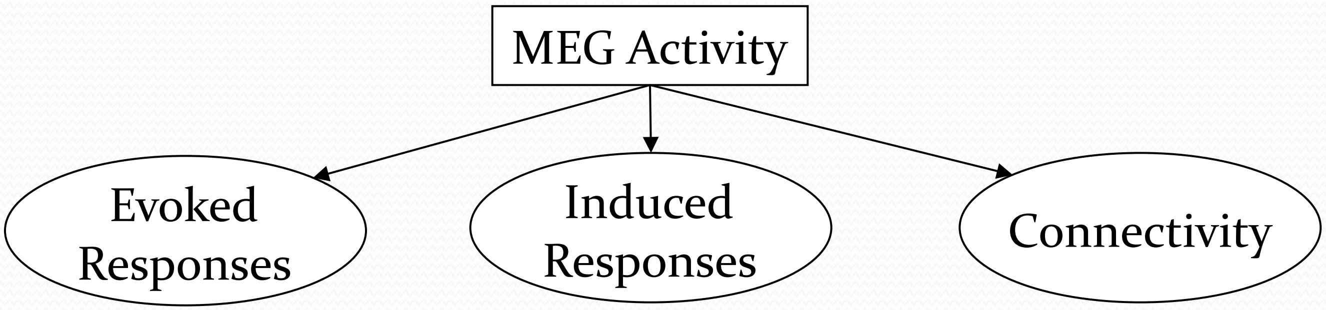


What types of brain signals do we measure with MEG?

“Evoked” activity

- synchronous neural firing that occurs at a consistent latency with respect to a stimulus or event

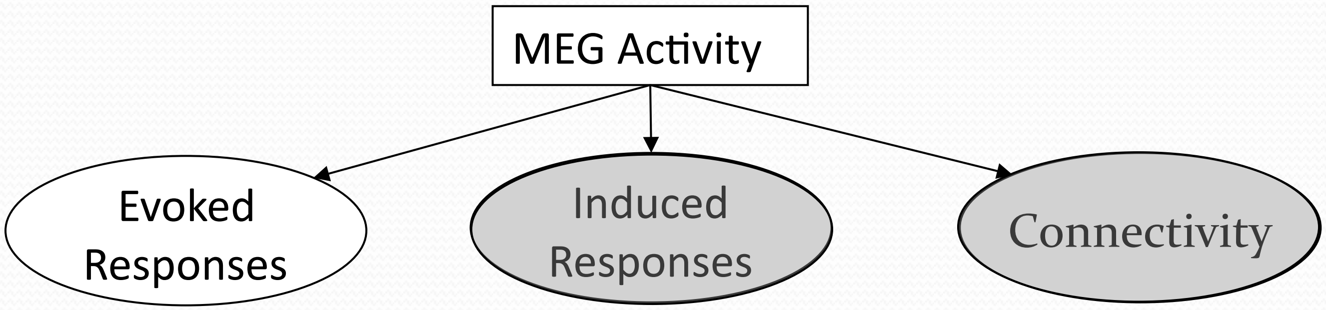
“Induced” activity

- changes in the strength of ongoing neural rhythms

“Connectivity”

- synchrony between neural rhythms in spatially separated neuronal populations

Finding Evoked Responses



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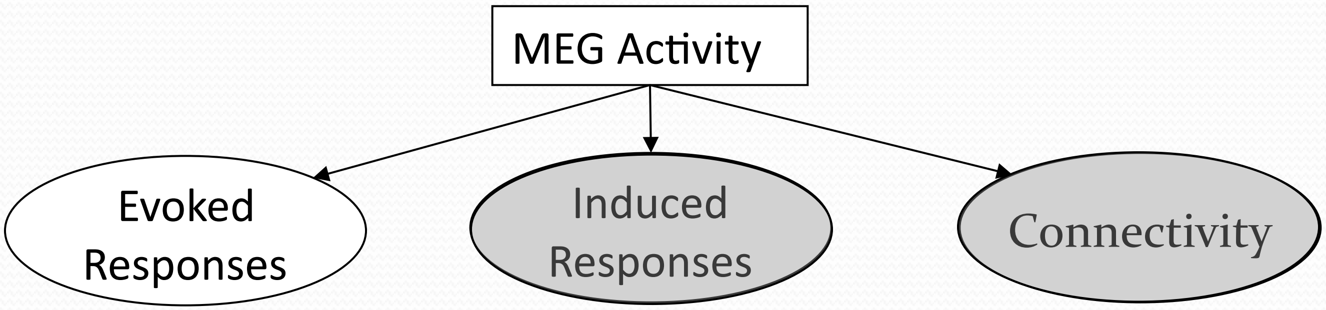


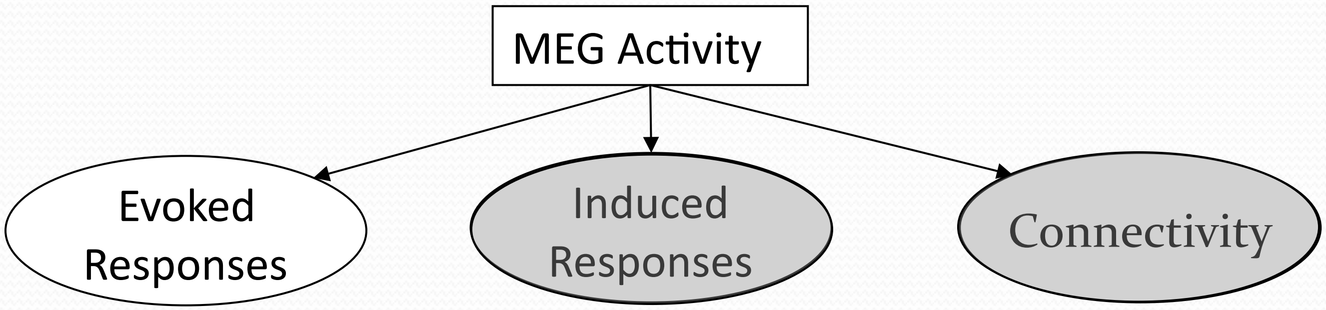
Characteristics of an Evoked Neuromagnetic Signal

- occur inside the helmet
- relatively slow (< 100 Hz, usually < 40 Hz)
- strong temporal correlation with stimulation or behaviour

Characteristics of a Magnetic Noise

- generally occur outside the helmet
- covers the entire noise spectrum
- generally no temporally correlation with stimulation or behaviour

Finding Evoked Responses



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MSR/SSS

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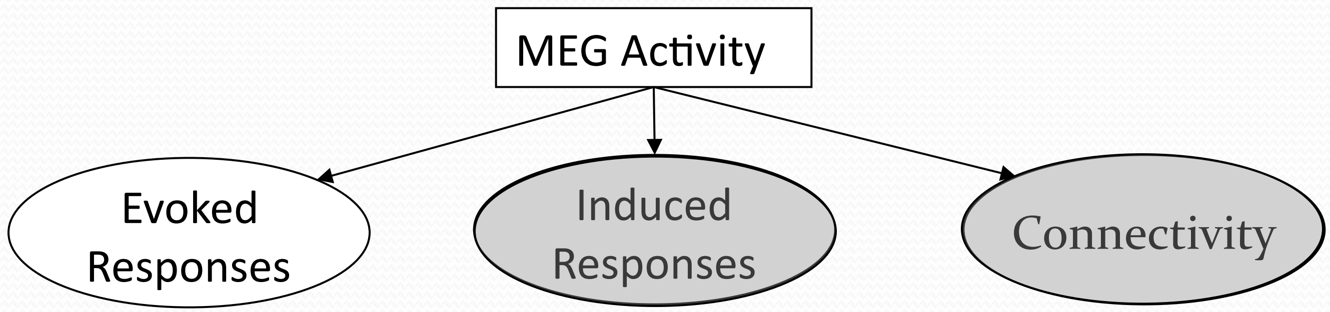

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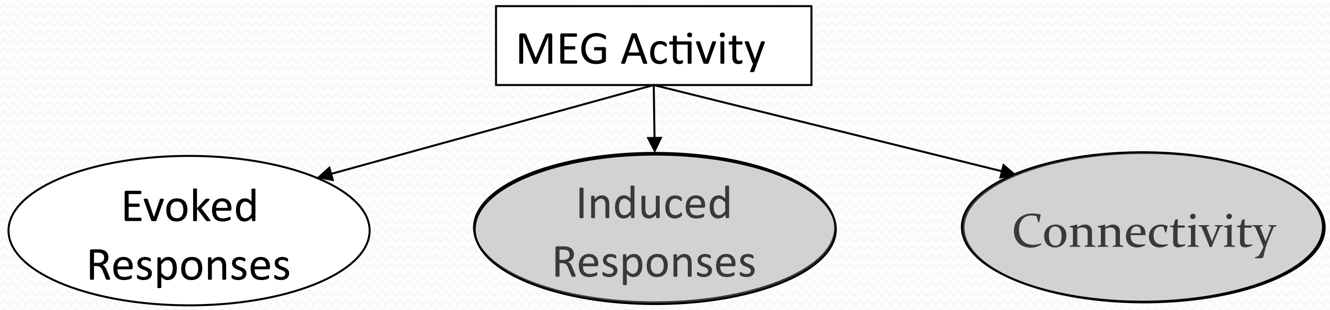

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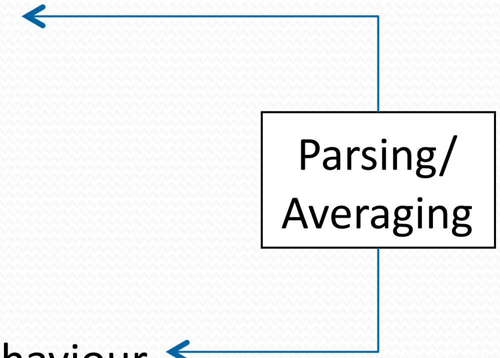
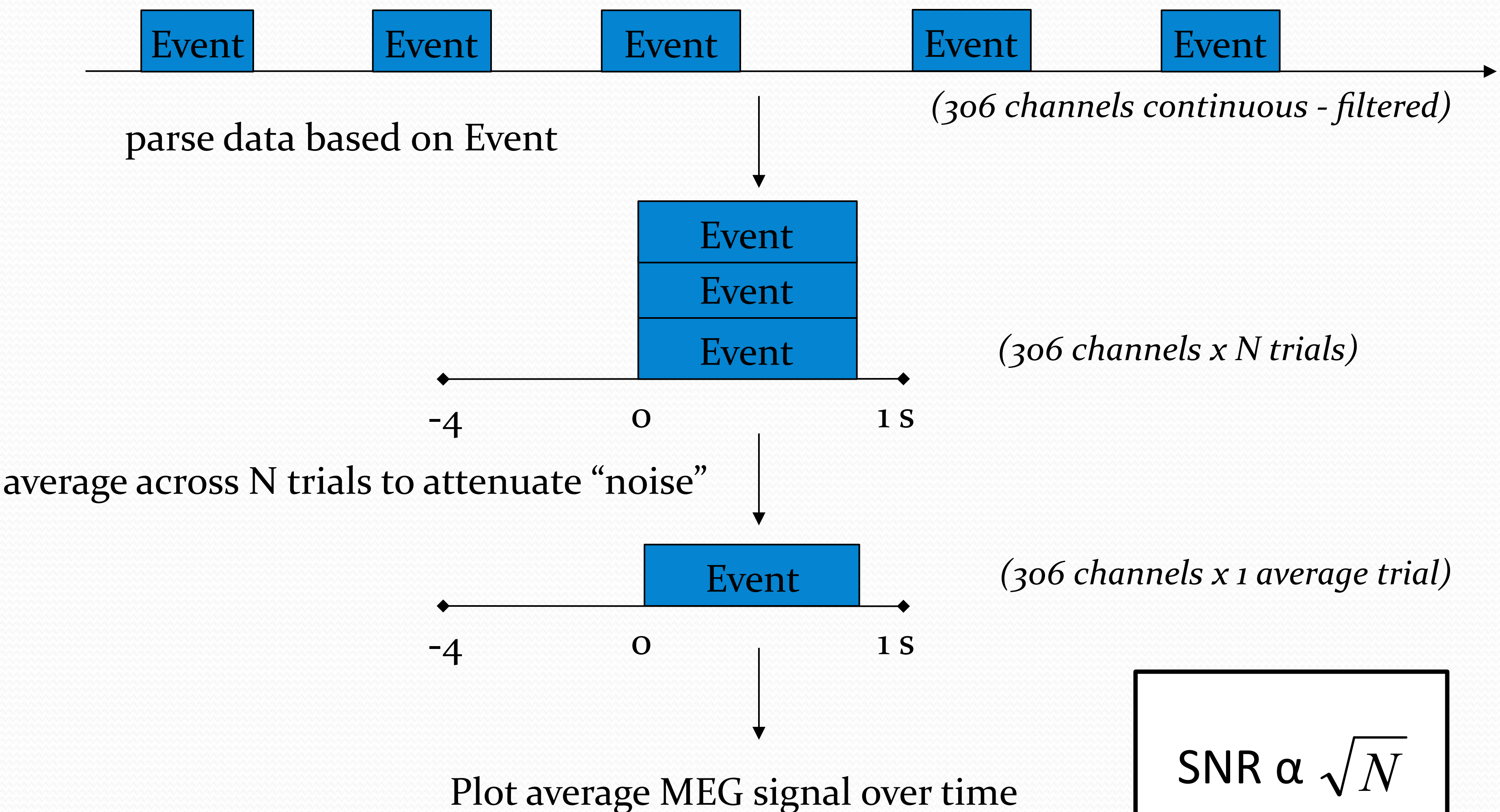


Finding Evoked Responses

MEG Data are Synchronised to Events, then Averaged

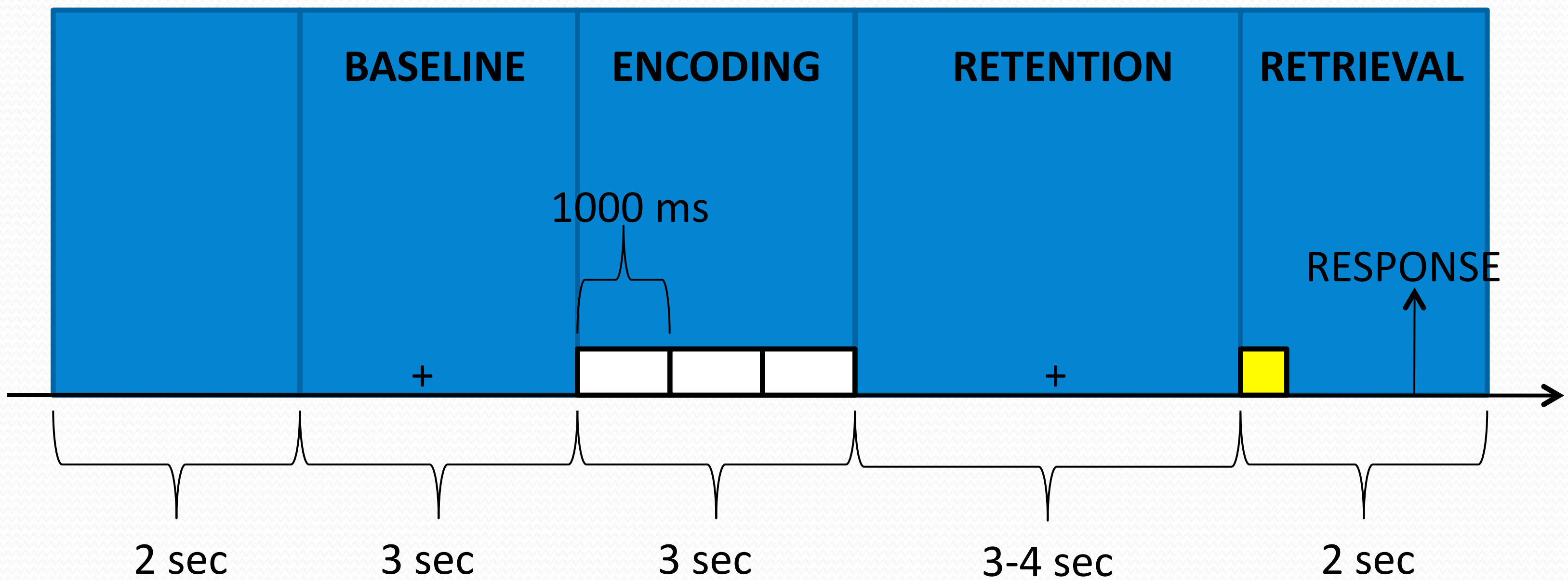


SNR $\alpha \sqrt{N}$

Example: Language Lateralisation

Where and When Does Language-Related Processing Occur in the Cortex?

- subjects see a list of 3 intact ("nameable") or scrambled images
- after a wait interval (3-4 s), an image is presented
- subject responds to indicate if fourth image is "new" or "old"
- condition order is random



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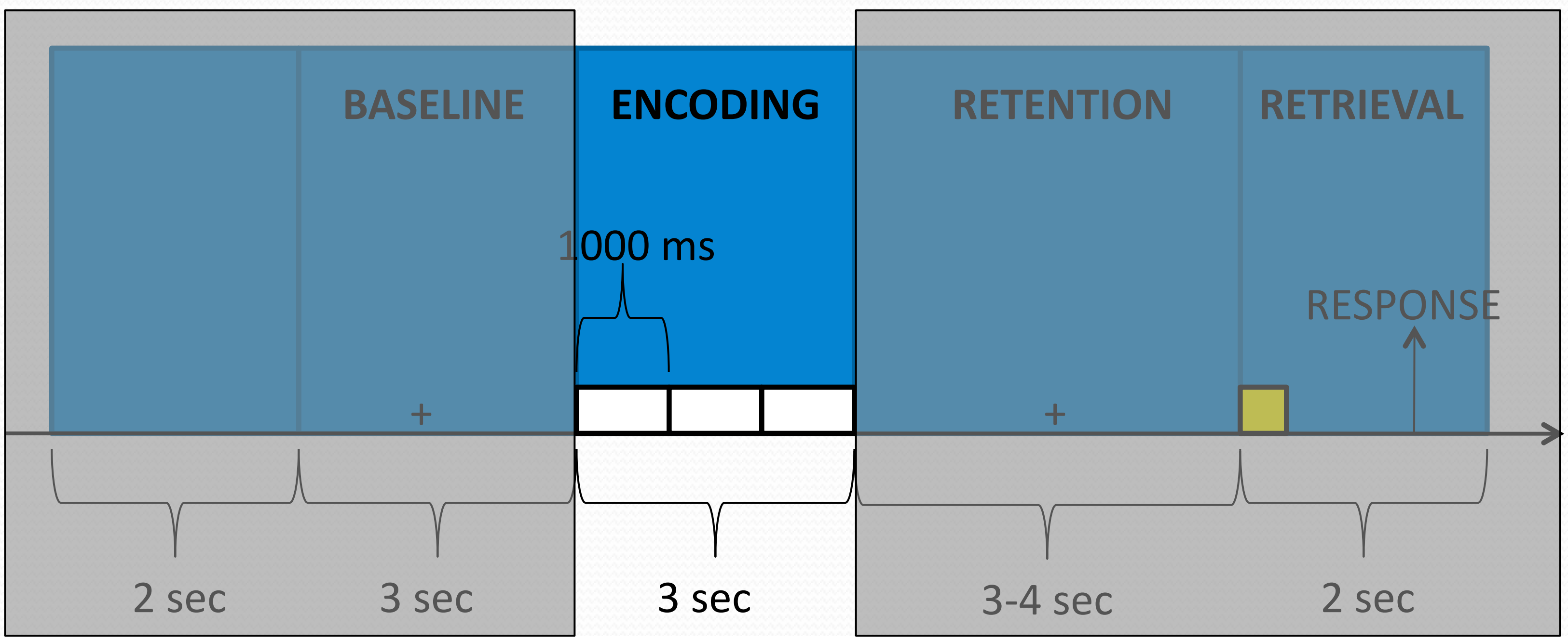
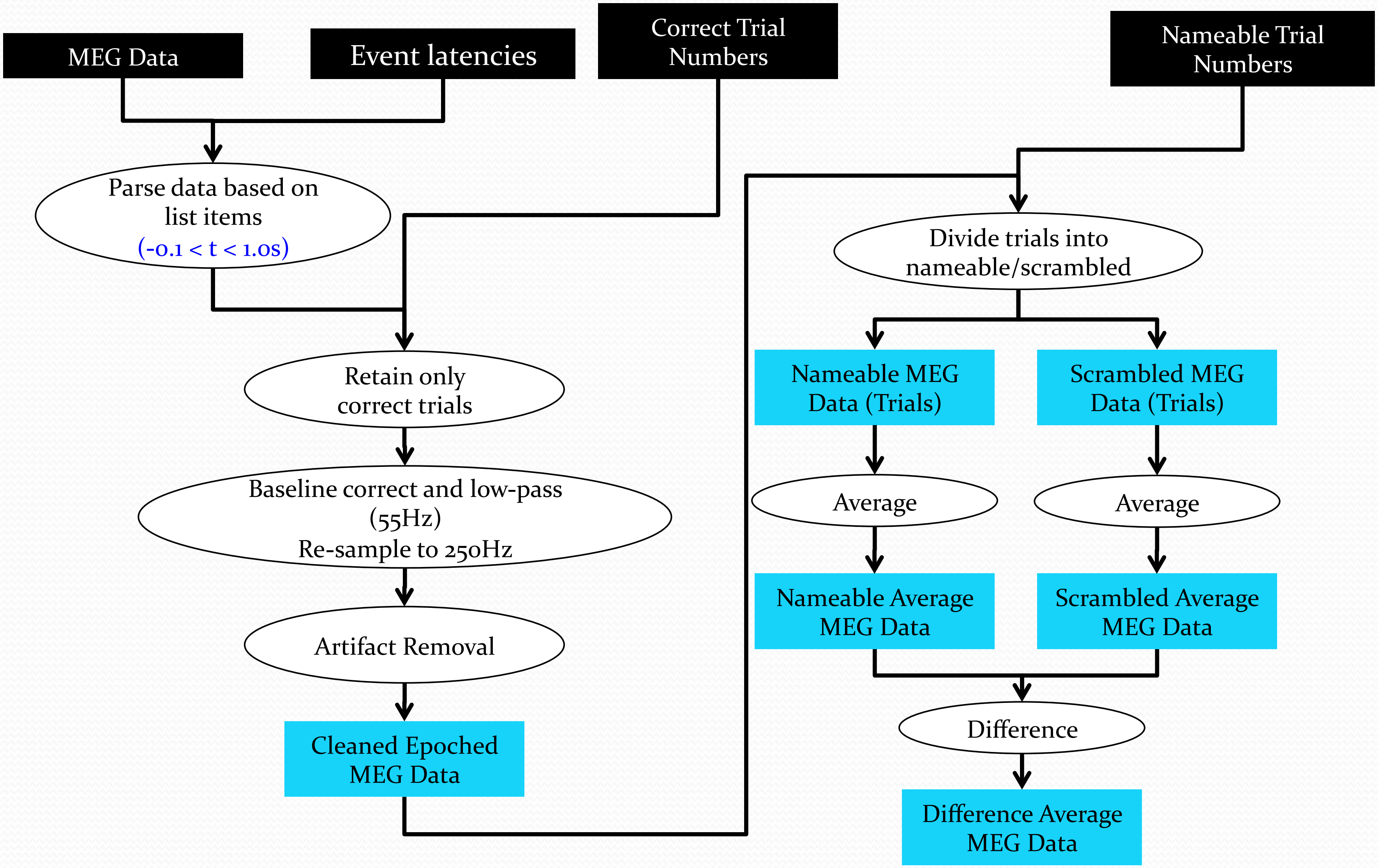


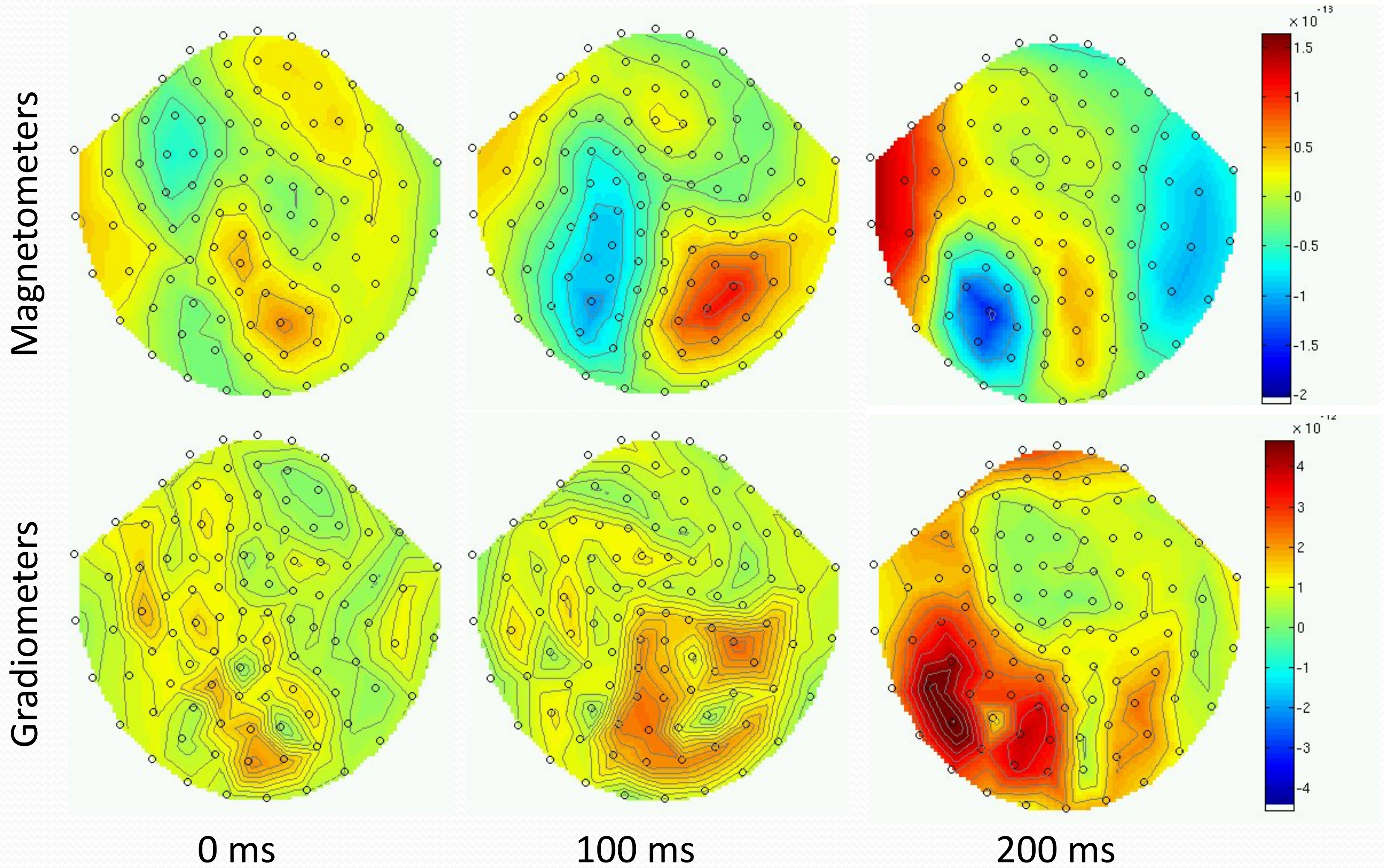
Example: Language Lateralisation

Data Analysis: Language-Related Evoked Response



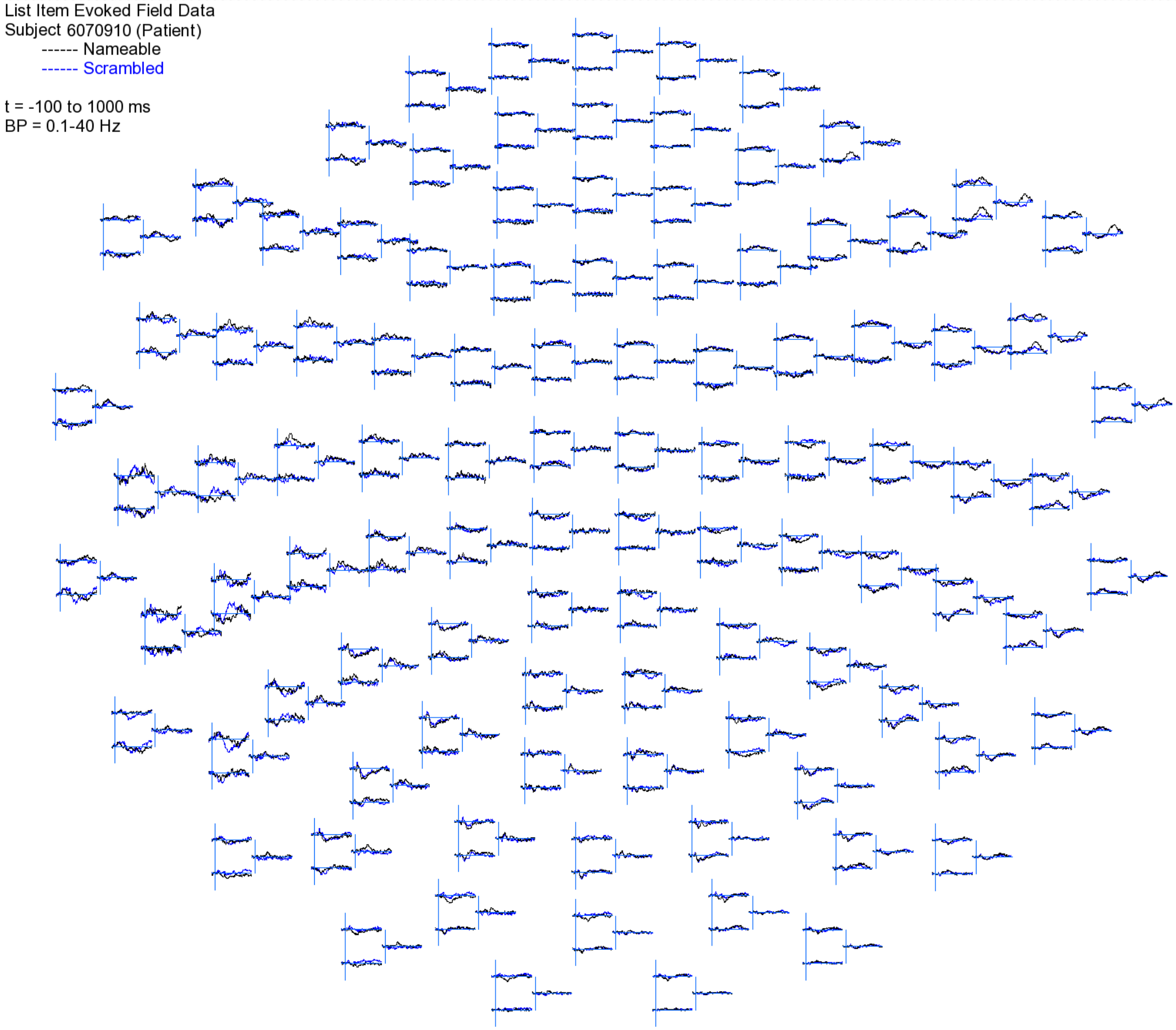
Example: Language Lateralisation

Averaged MEG Data for Nameable List Objects Shows Left Lateralized Activation



Example: Language Lateralisation

Language-Related Differences are Consistently Evident in the Left Hemisphere



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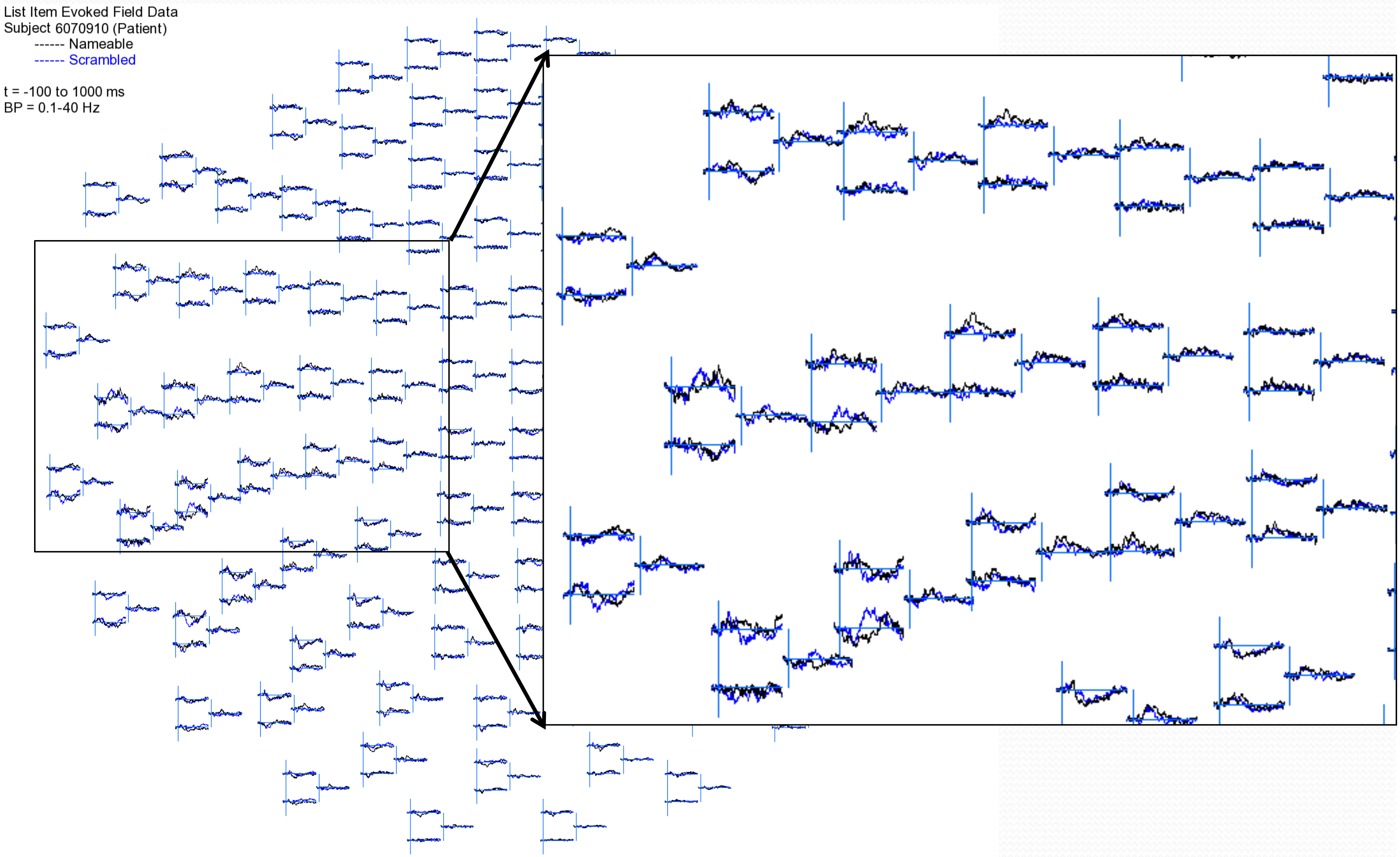

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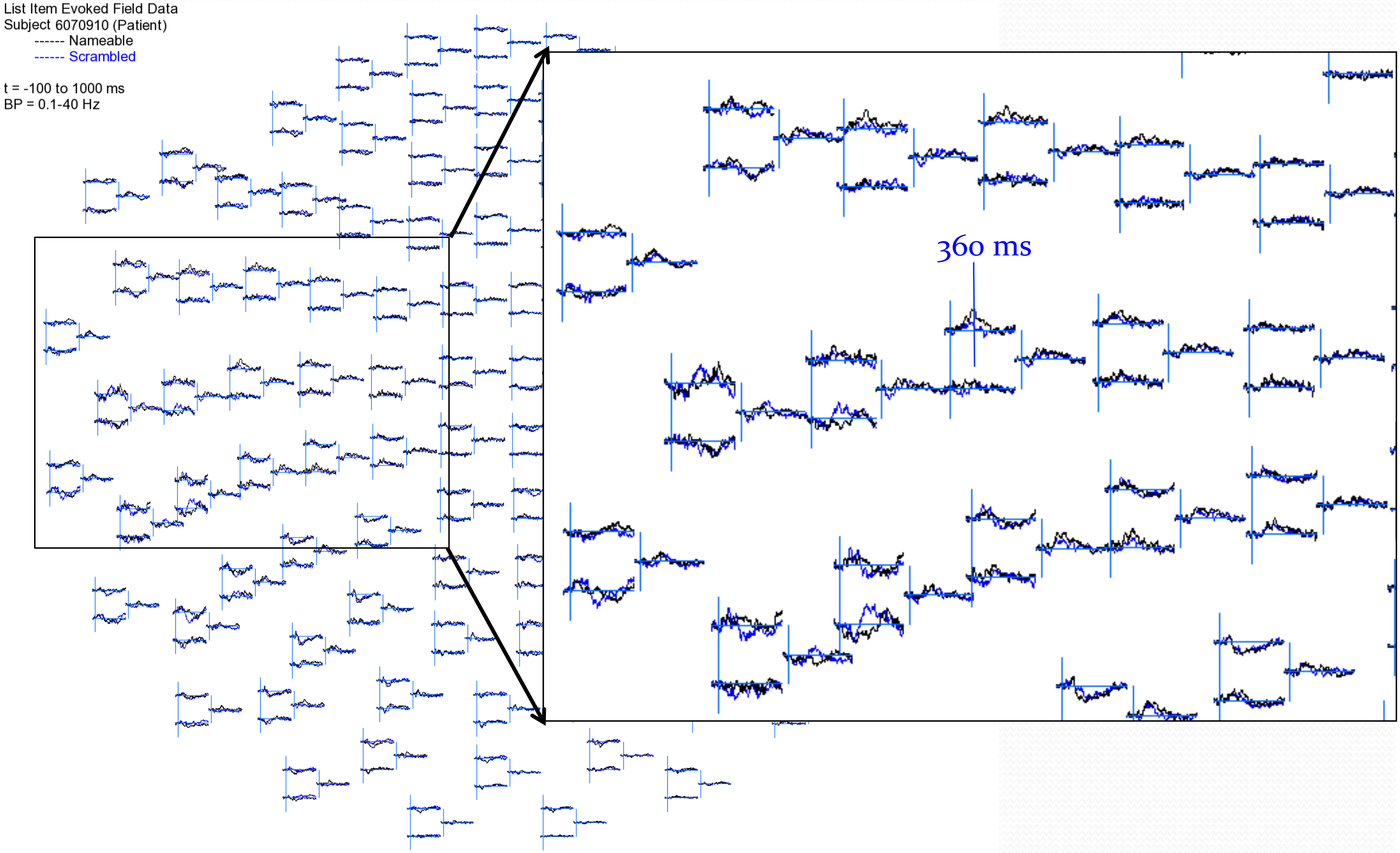
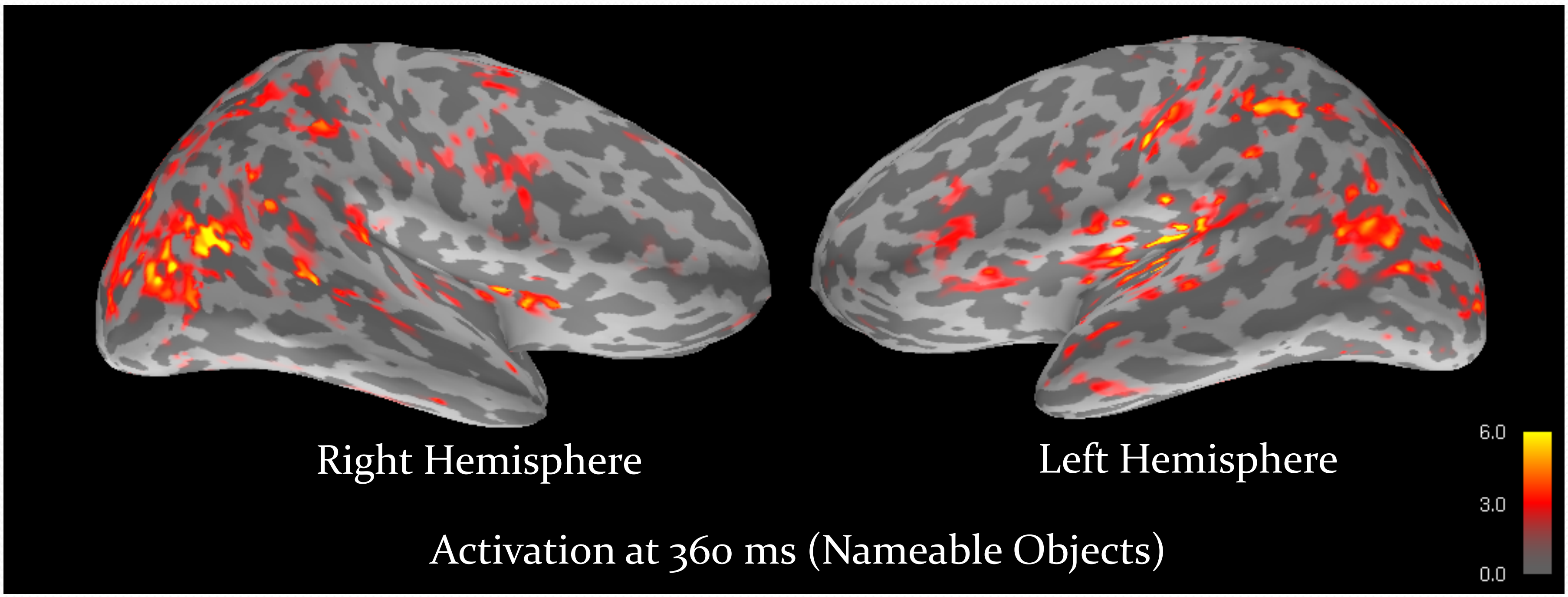


Example: Language Lateralisation

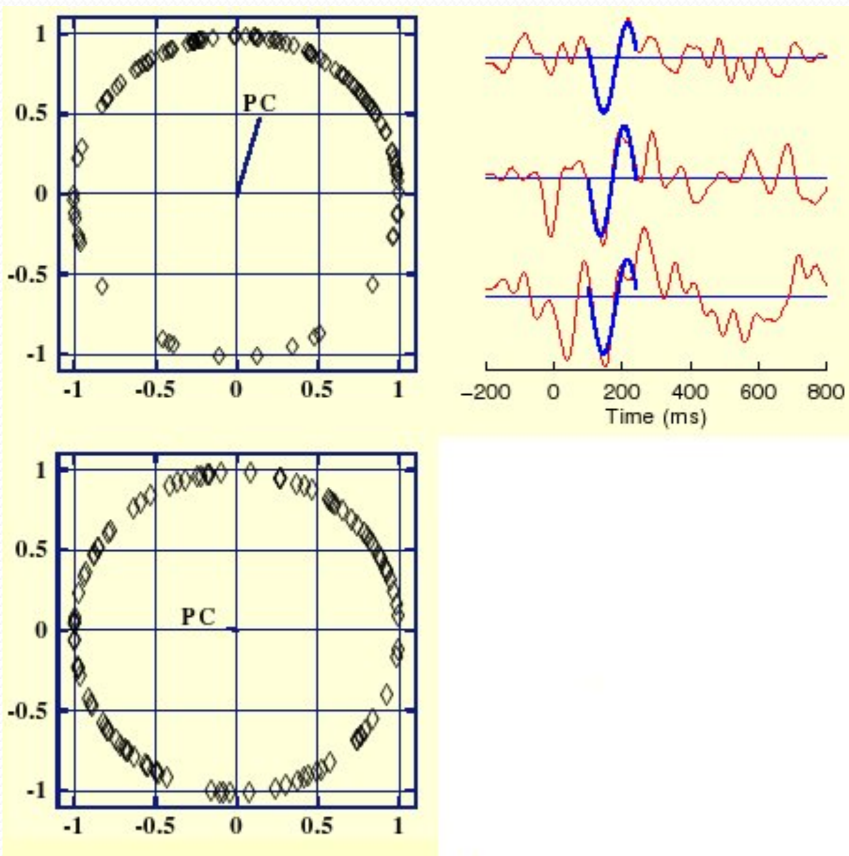
Source Modelling with Minimum Norm Estimation (MNE) shows Left Lateralised Language-Related Evoked Responses (360 ms)



An Alternate Evoked Response Finder

Inter-Trial Coherence (ITC)

- a normalised (0…1) measure of synchronisation of phase across trials for a given signal
- How consistent is the signal phase across trials?
- Evoked responses, by definition, have high ITC



$$\bar{R} = \frac{1}{N}\left(C^2 + iS^2\right)$$

$$\text{where } C = \sum_{n=1}^{N} \cos\varphi_n, S = \sum_{n=1}^{N} \sin\varphi_n$$

$$\left|\bar{R}\right| = \text{magnitude of "phase locking"}$$

$$\varphi\left(\bar{R}\right) = \text{ mean phase of evoked response}$$

$$p\left(\bar{R}, N\right)$$

(Stapells et al., EEG Clin Neurophysiol, 1987)

Example: Somatosensory Steady-State Response

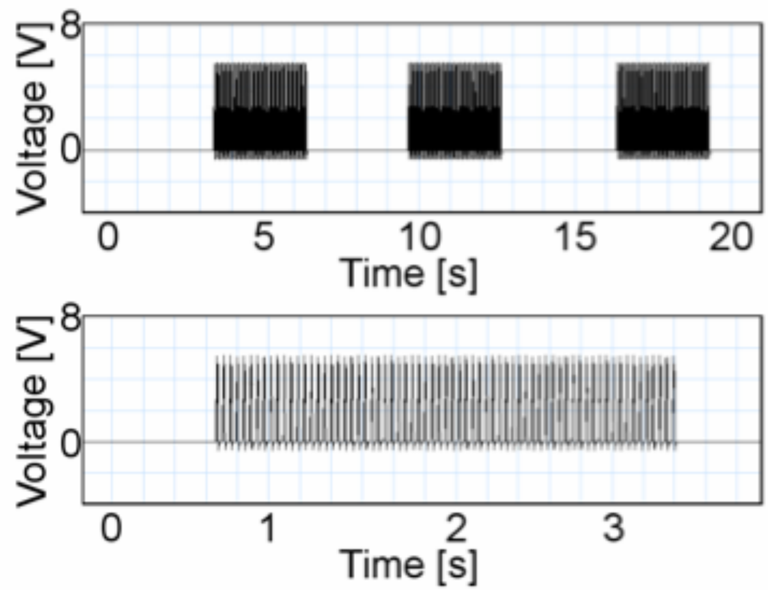
<u>Steady-State Somatosensory Stimulation</u>

• steady-state stimulation of the right index finger pad at 23 Hz

• MEG, EMG (right 1DI) and somatosensory stimulator driving signal will be recorded

• 23 Hz pulse trains will be applied for 3 seconds with a randomised inter-stimulus interval (ISI) of 3-5 seconds

• the subject watches a movie with subtitles

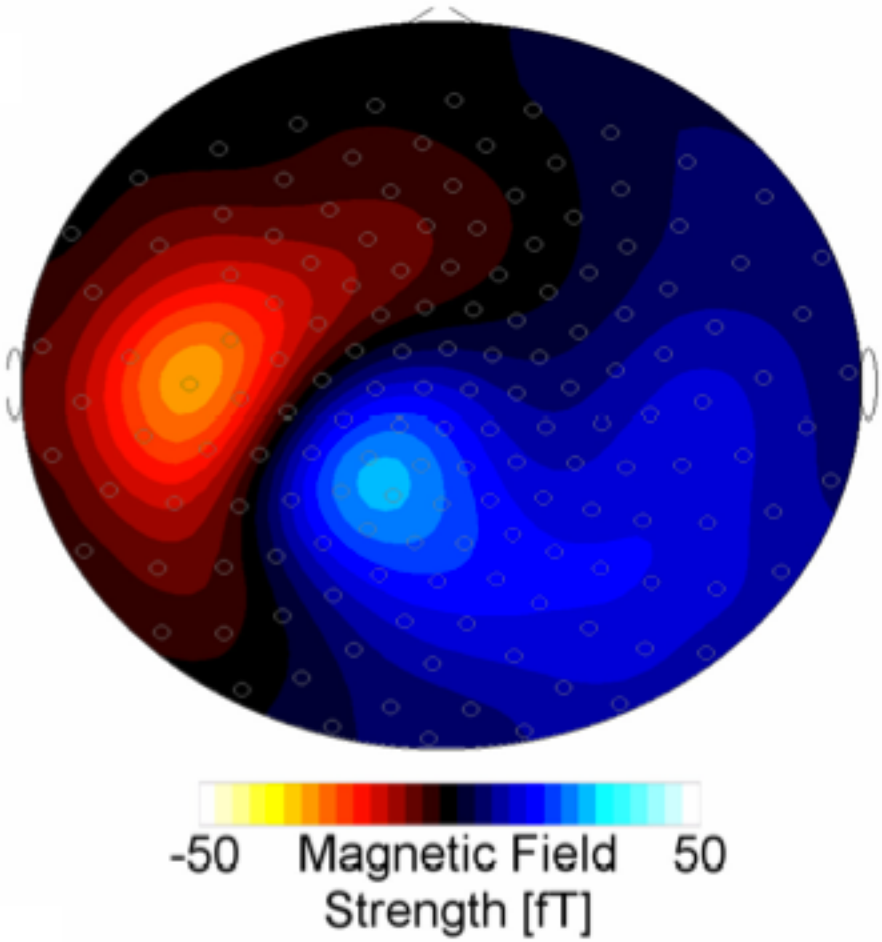


Onset asynchrony = 6-8 seconds / onset

10 minute data collection => 600 s / 7.5 s/onset = 80 epochs

Example: Somatosensory Steady-State Response

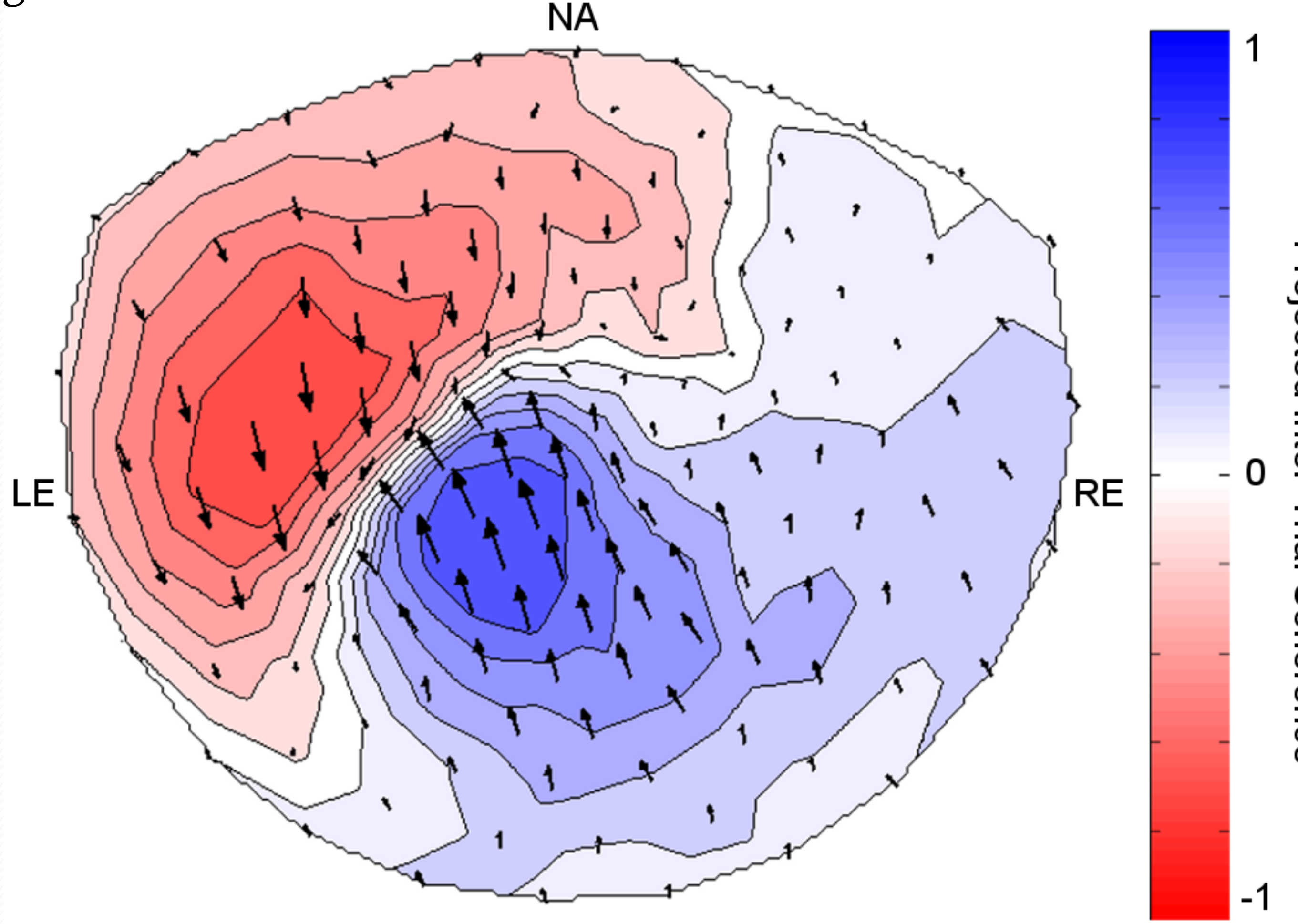
Steady-state evoked field is strongest at contralateral MEG sensors



(Bardouille, Ross, NeuroImage, 2008)

Example: Somatosensory Steady-State Response

Inter-trial coherence is also strongest at contralateral MEG sensors. Mean phase varies from a single value.



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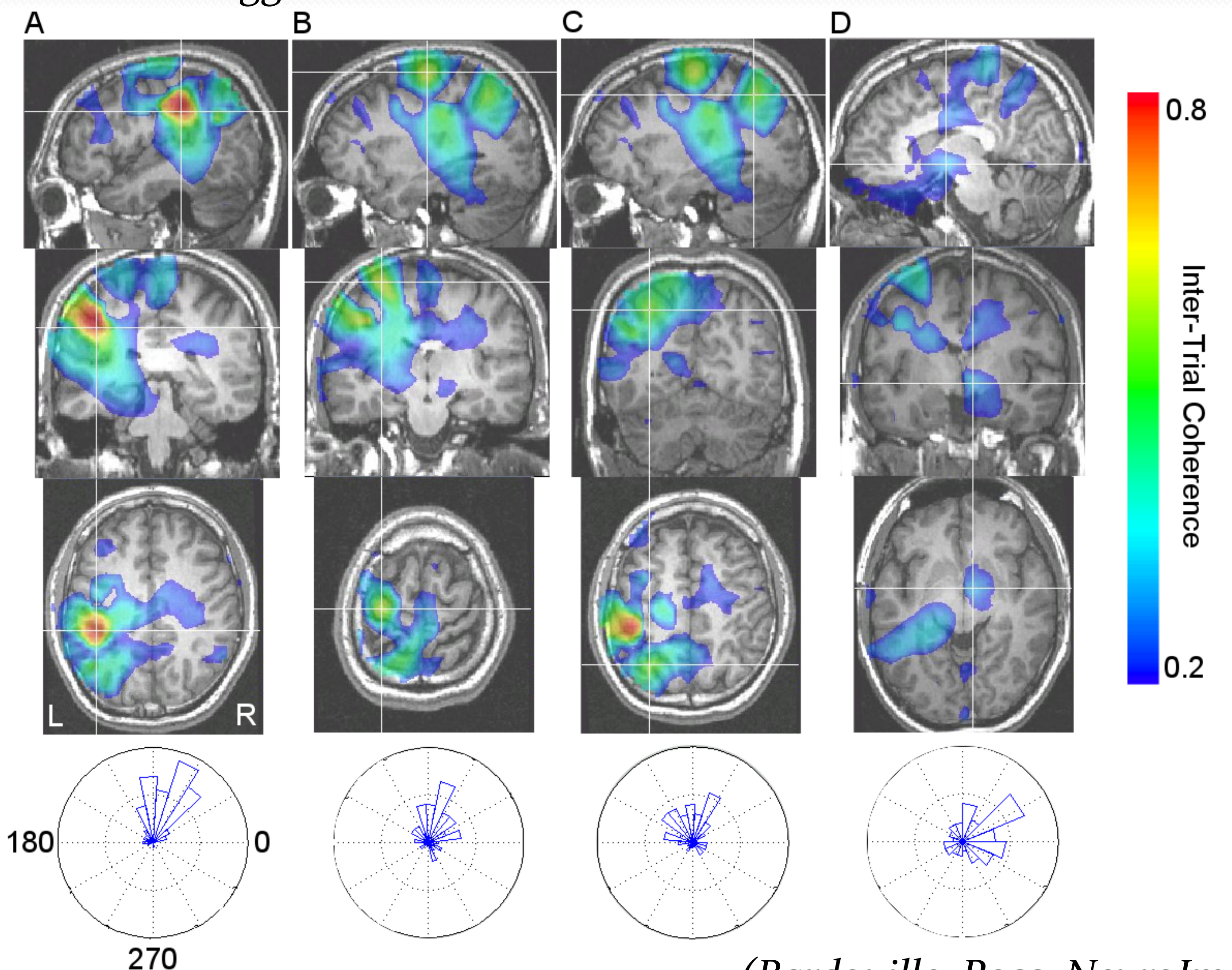
Example: Somatosensory Steady-State Response

Inter-trial coherence identifies multiple brain areas activated by finger vibration at different phases. This suggests a network involved in somatosensation.



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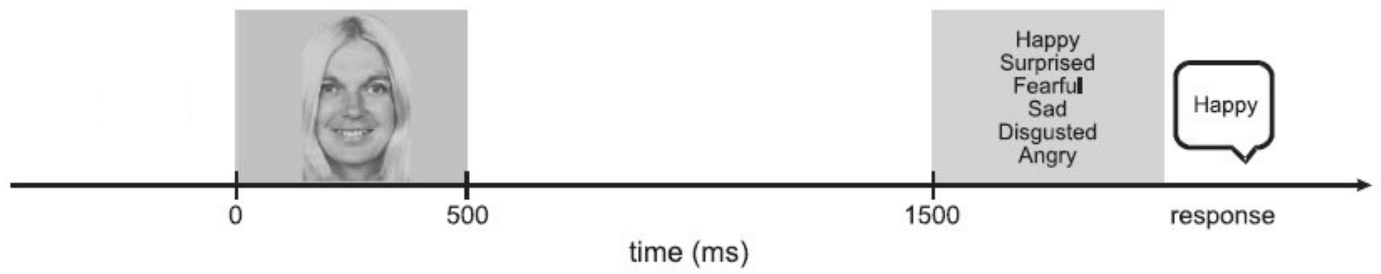
Connectivity and Schizophrenia

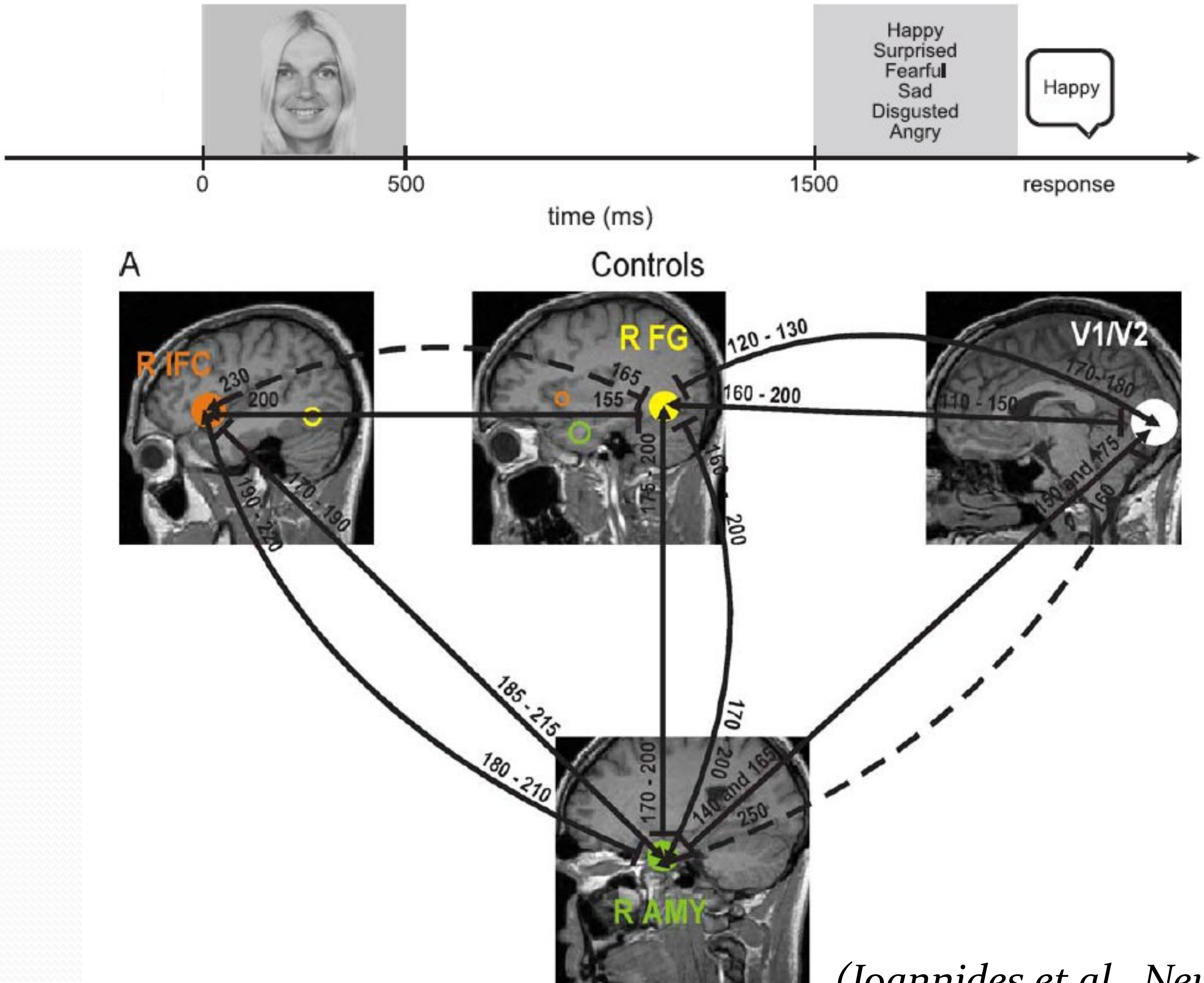
Evaluating Emotional Faces



(Ioannides et al.. NeuroImage 2004)

Connectivity and Schizophrenia

Mutual Information Identifies Connectivity Between V1/V2 – Fusiform Gyrus – Inferior Frontal Cortex – Amygdala During Emotion Recognition



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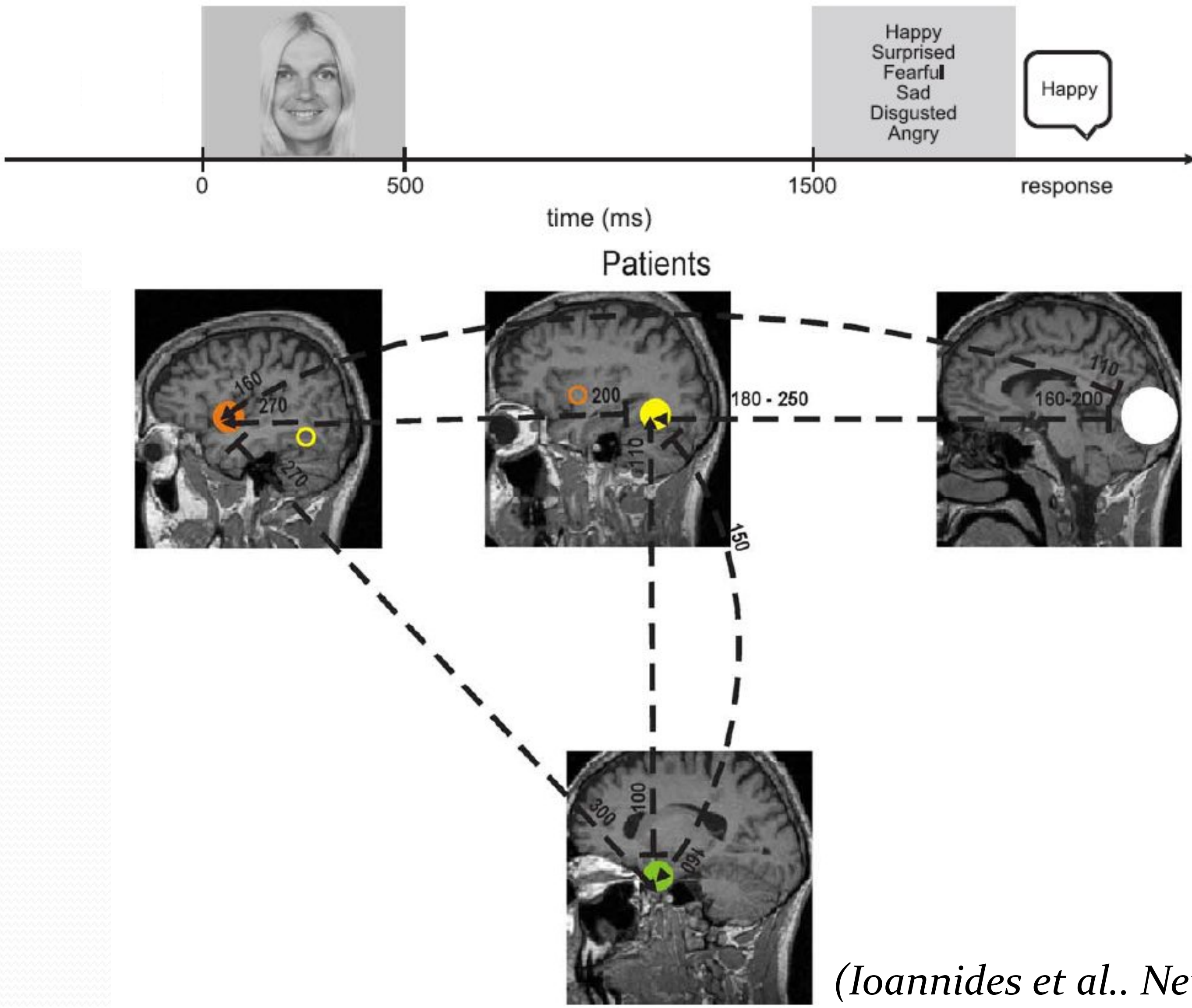
Connectivity and Schizophrenia

Connectivity Is Reduced During Emotion Recognition in Persons with Schizophrenia



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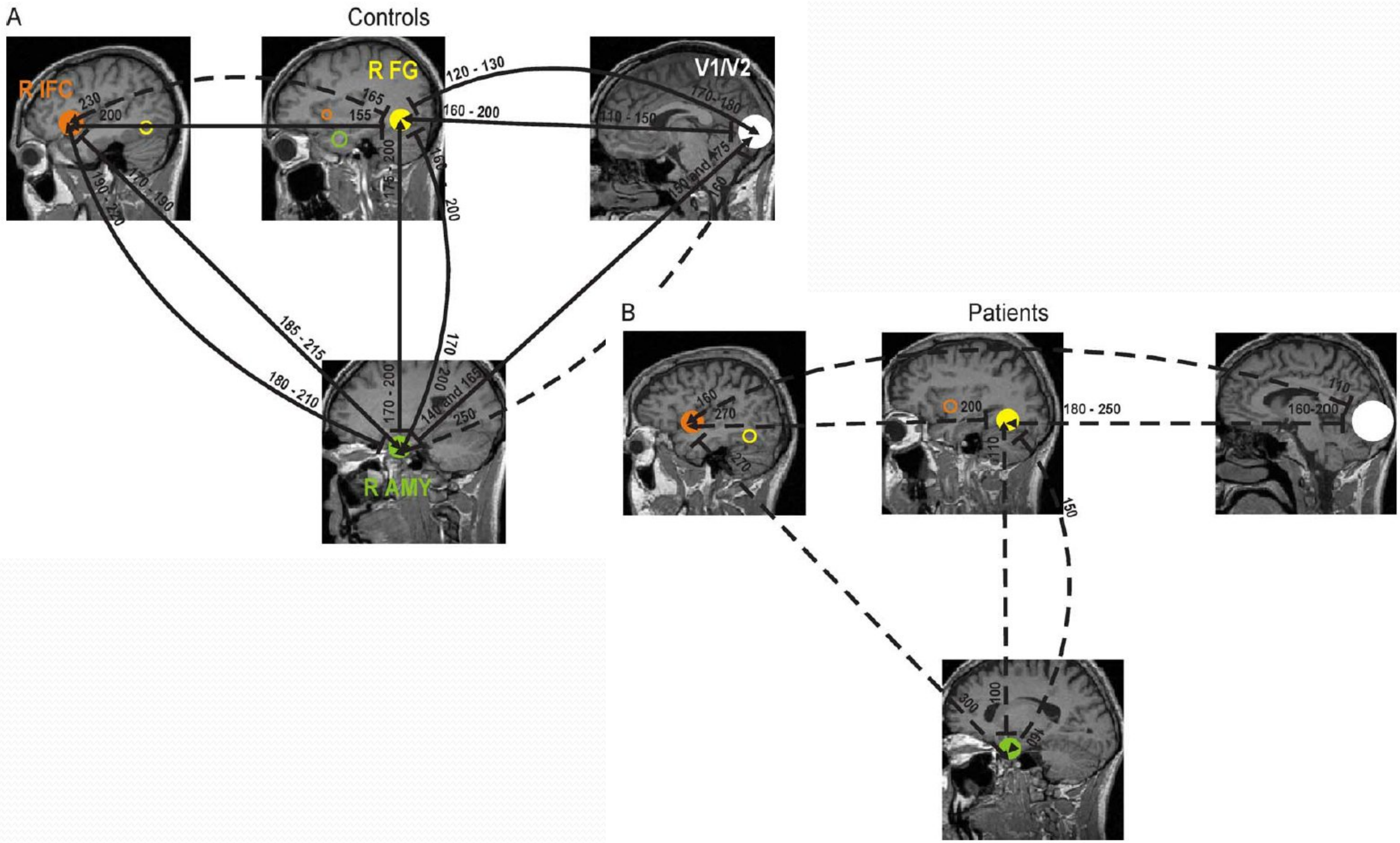
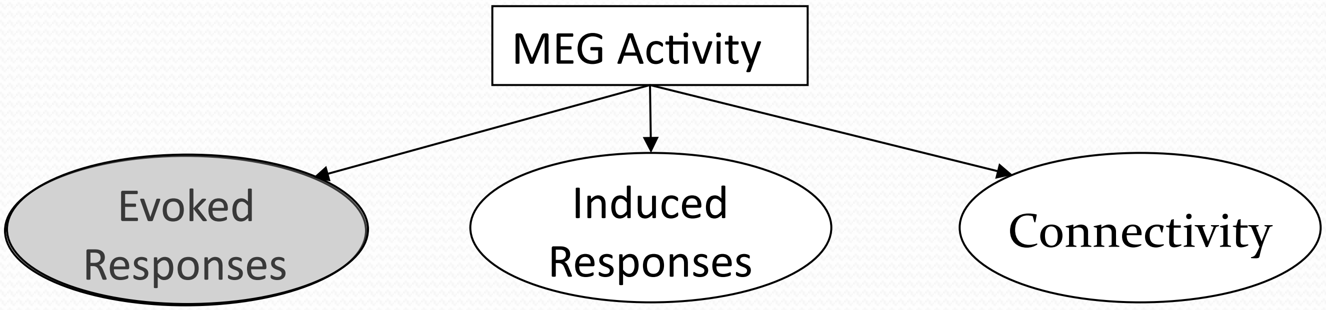


(Ioannides et al.. NeuroImage 2004)

Neural Oscillations and Functional Connectivity



What types of brain signals do we measure with MEG?

"Evoked" activity

- synchronous neural firing that occurs at a consistent latency with respect to a stimulus or event

"Induced" activity

- changes in the strength of ongoing neural rhythms

"Connectivity"

- synchrony between neural rhythms in spatially separated neuronal populations

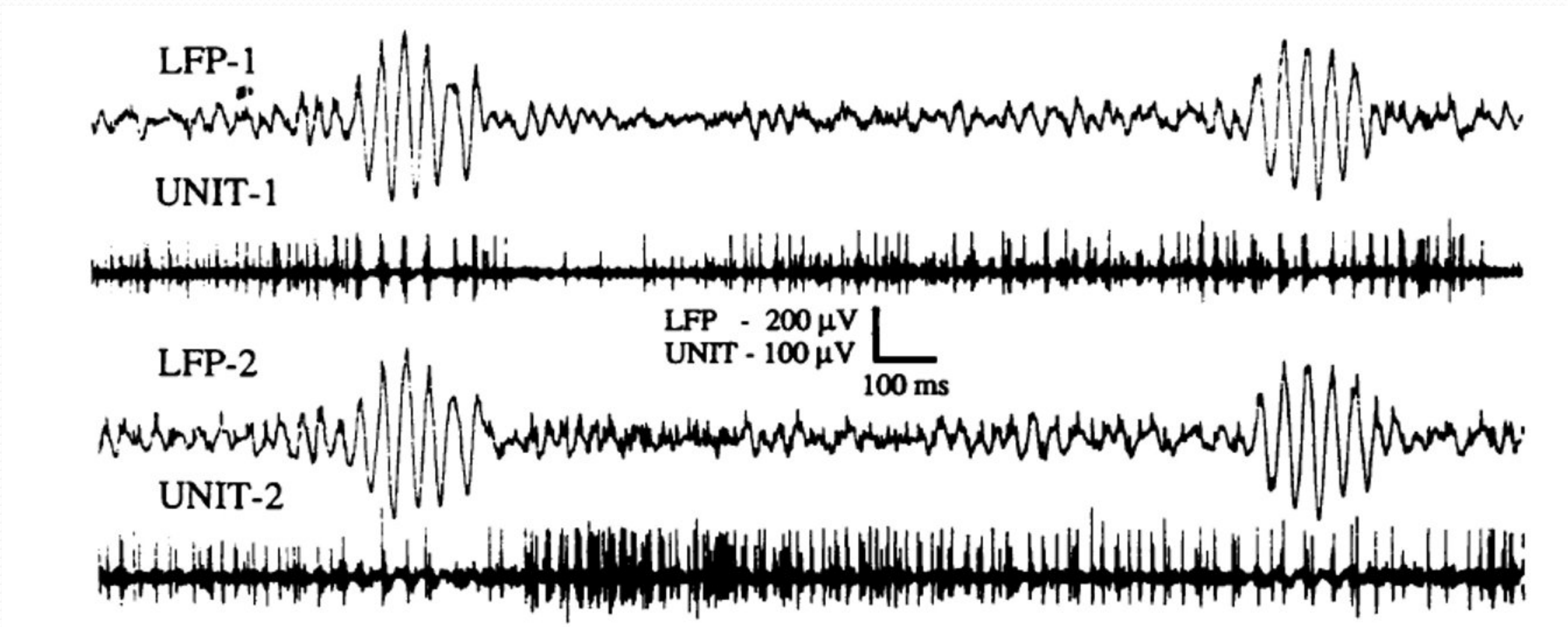
Neural Oscillations and Functional Connectivity

Cortical Oscillations (Rhythms)

• bursts of oscillatory activity found in neuroelectric/magnetic recordings

• indicative of rhythmic firing in the underlying population of neurons

• likely caused by sub-threshold oscillations of neuronal membrane potentials



(Murthy, Fetz, 1992)

Neural Oscillations and Functional Connectivity

Cortical Oscillations (Rhythms)

• bursts of oscillatory activity found in neuroelectric/magnetic recordings

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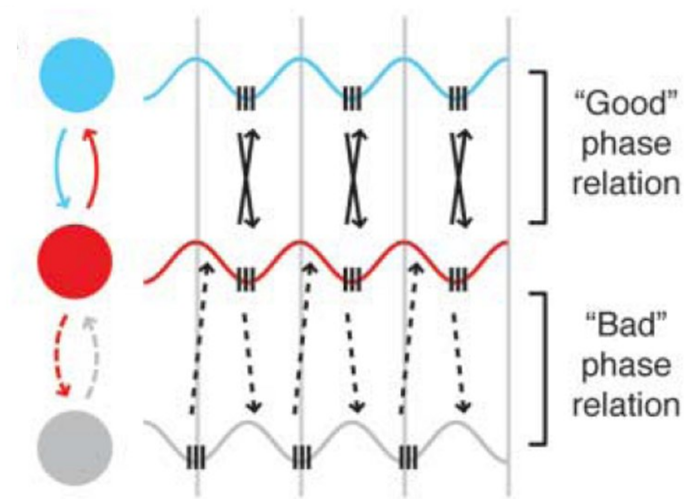
Why is this interesting?

• cortical rhythms are a major component of brain activity in general

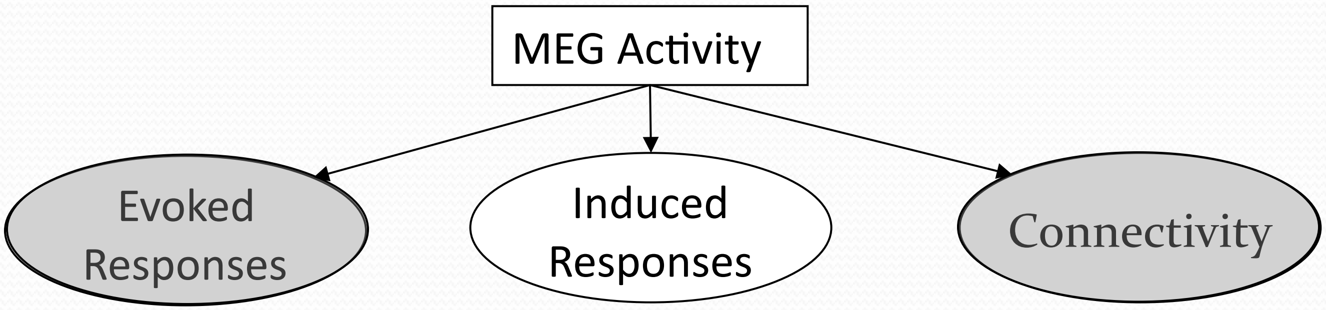
• changes in cortical rhythms have functional significance

• synchrony in rhythms between neuronal groups may facilitate communication



(Womelsdorf et al., Science, 2007)

Finding Induced Responses



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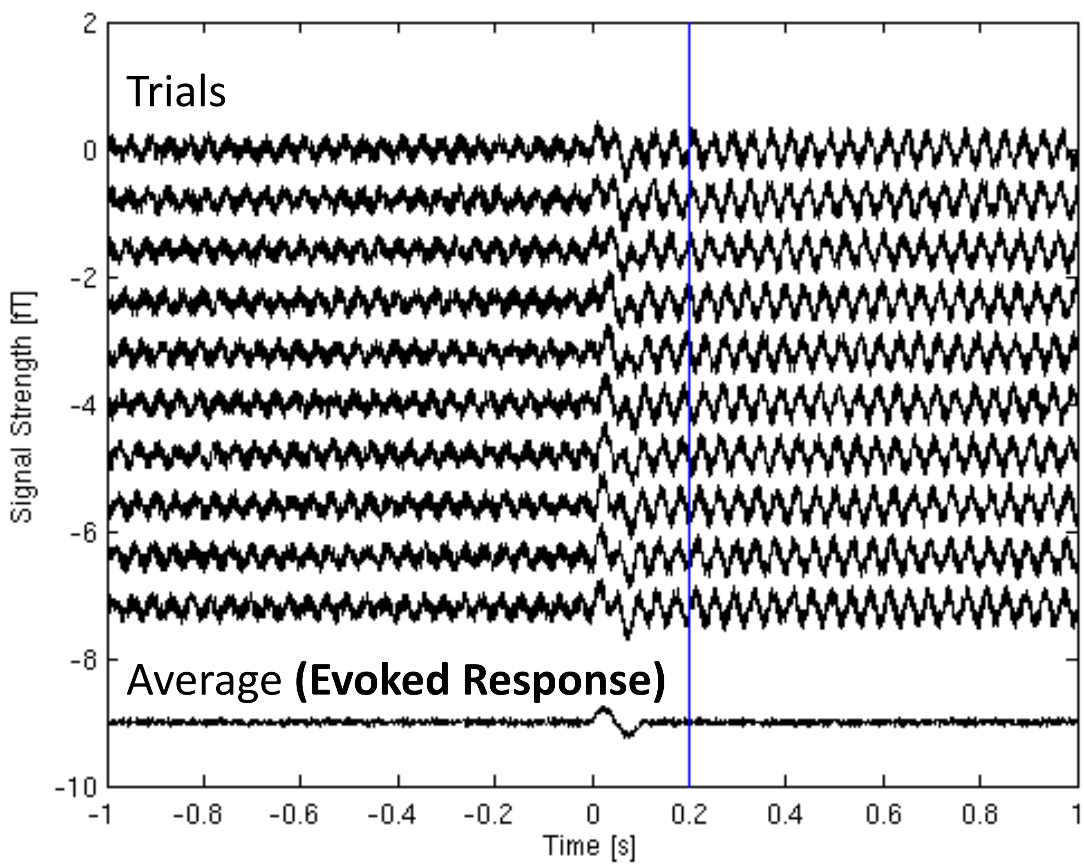
Finding Induced Responses

Evoked and Induced Activity

10 x 2 second trials @ 1250 Hz sample rate

1 cycle of 10 Hz at t = 0 s

ongoing 20 Hz signal (from 0.1 to 0.2 fT at t = 0 s)



Neuroimaging With MEG

Evoked and Induced Activity

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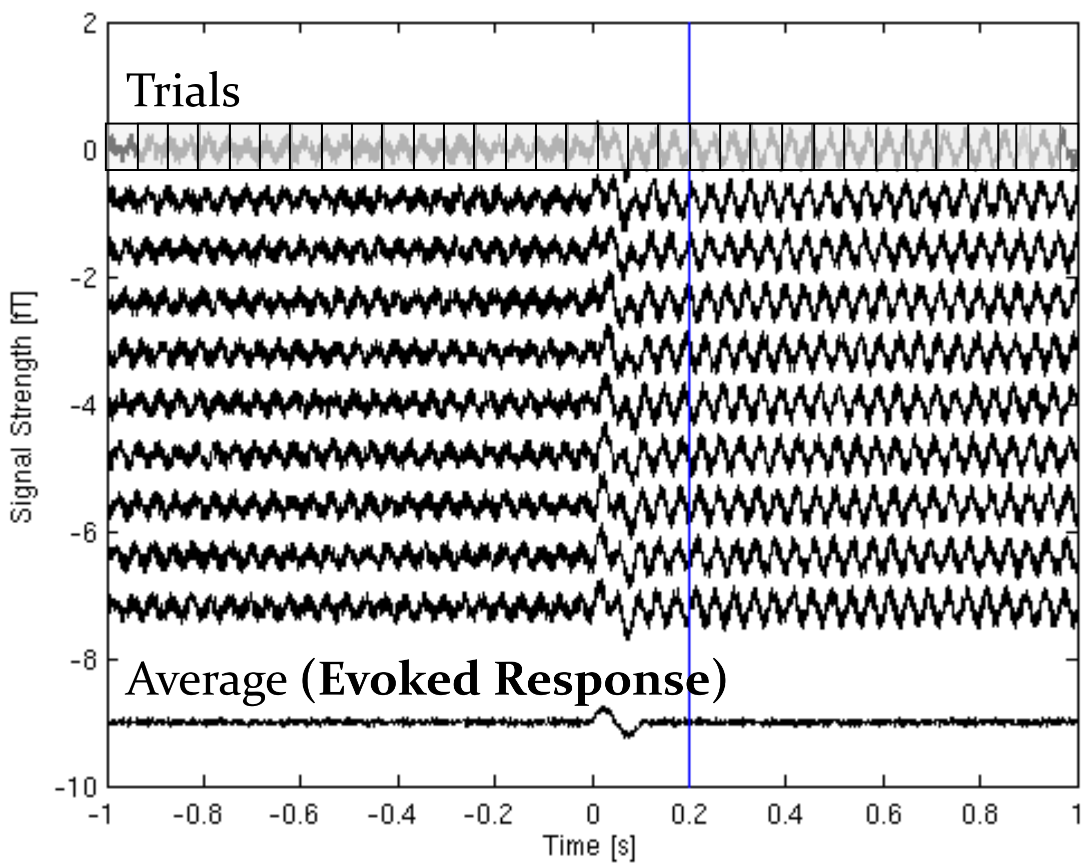

Induced Response

1. Calculate power spectrum for each segment
2. Average power spectra across trials
3. Plot average power spectrum over time

Finding Induced Responses

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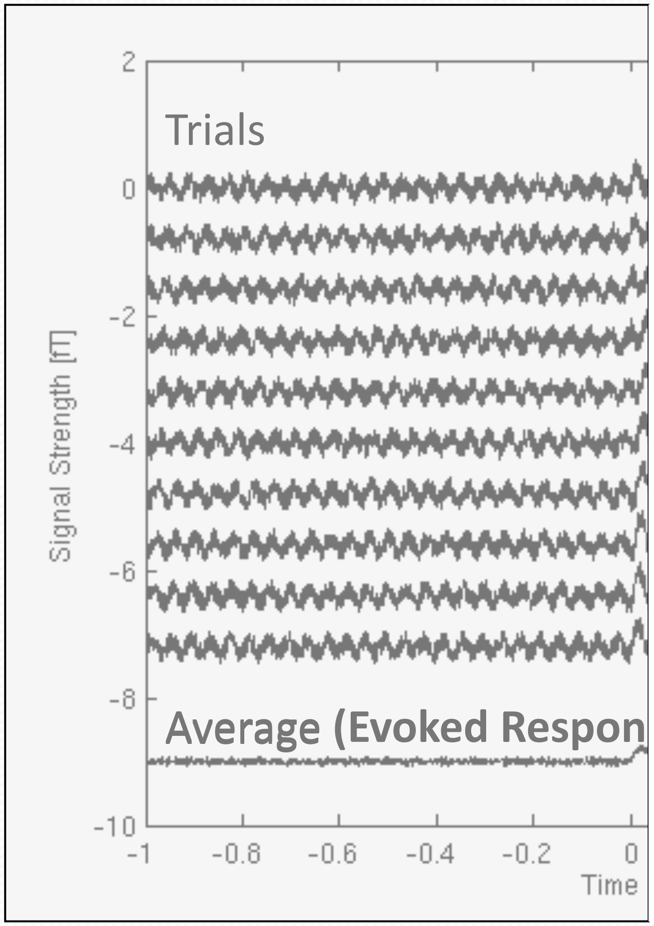
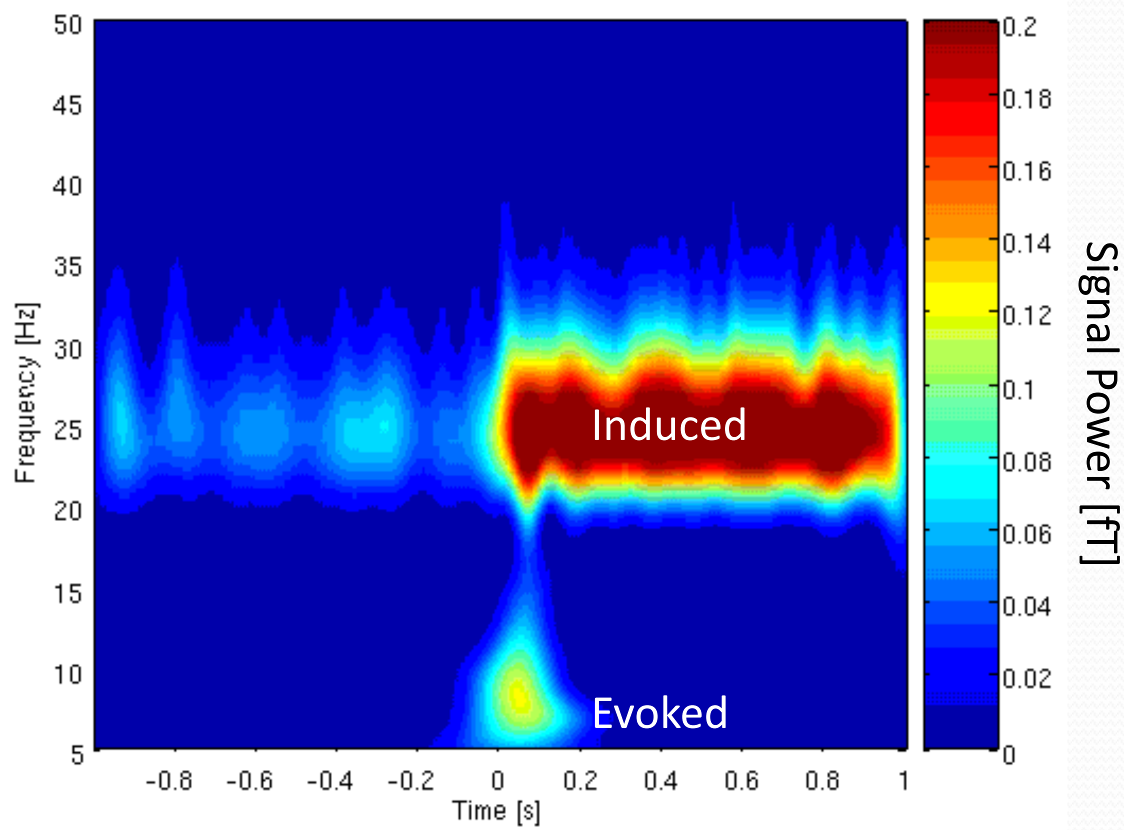


Single Trial Time-Frequency Response



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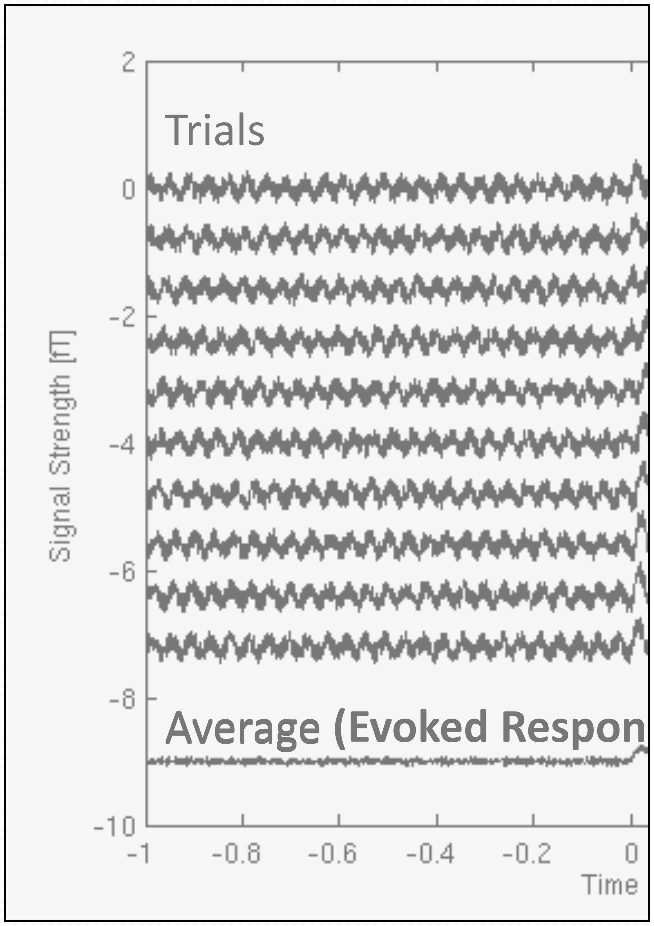

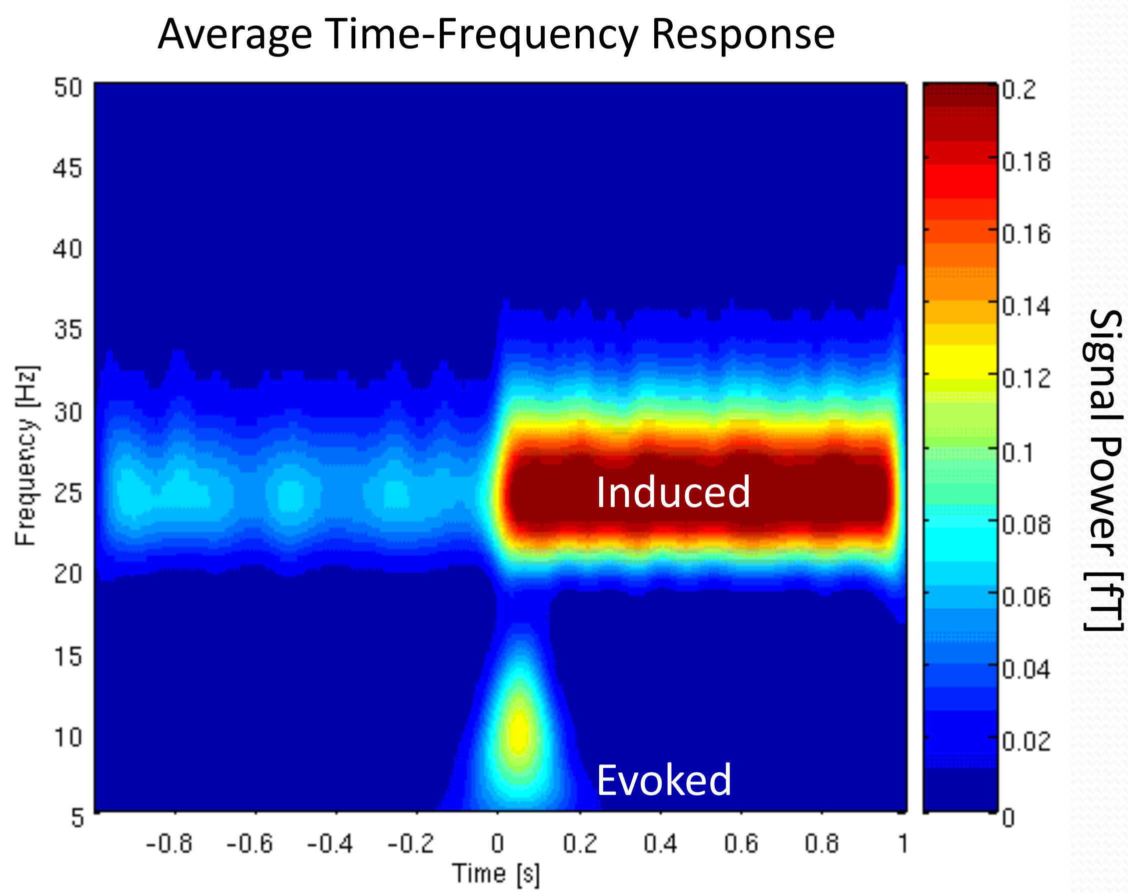

Finding Induced Responses

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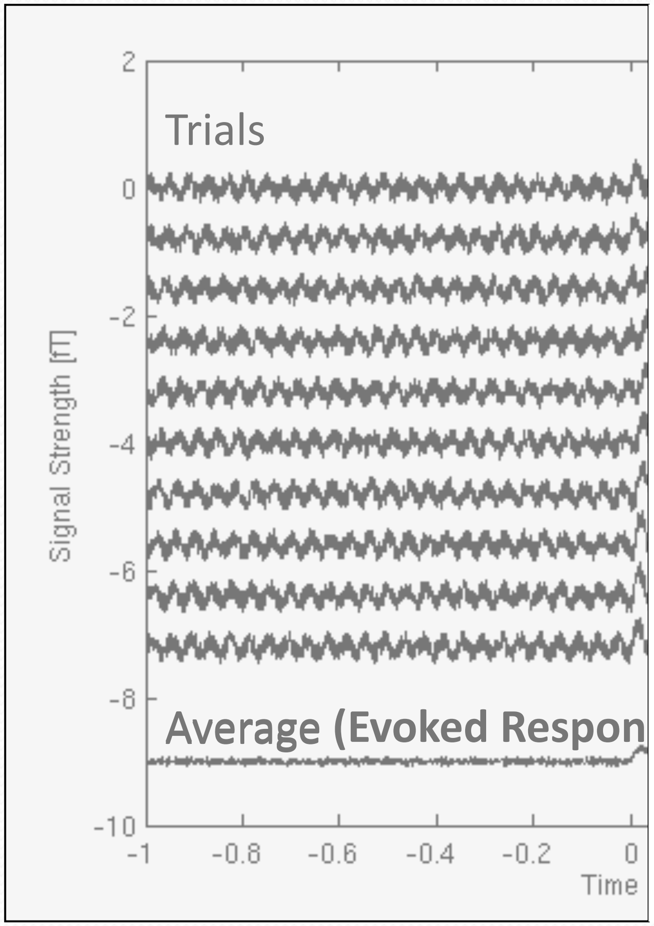
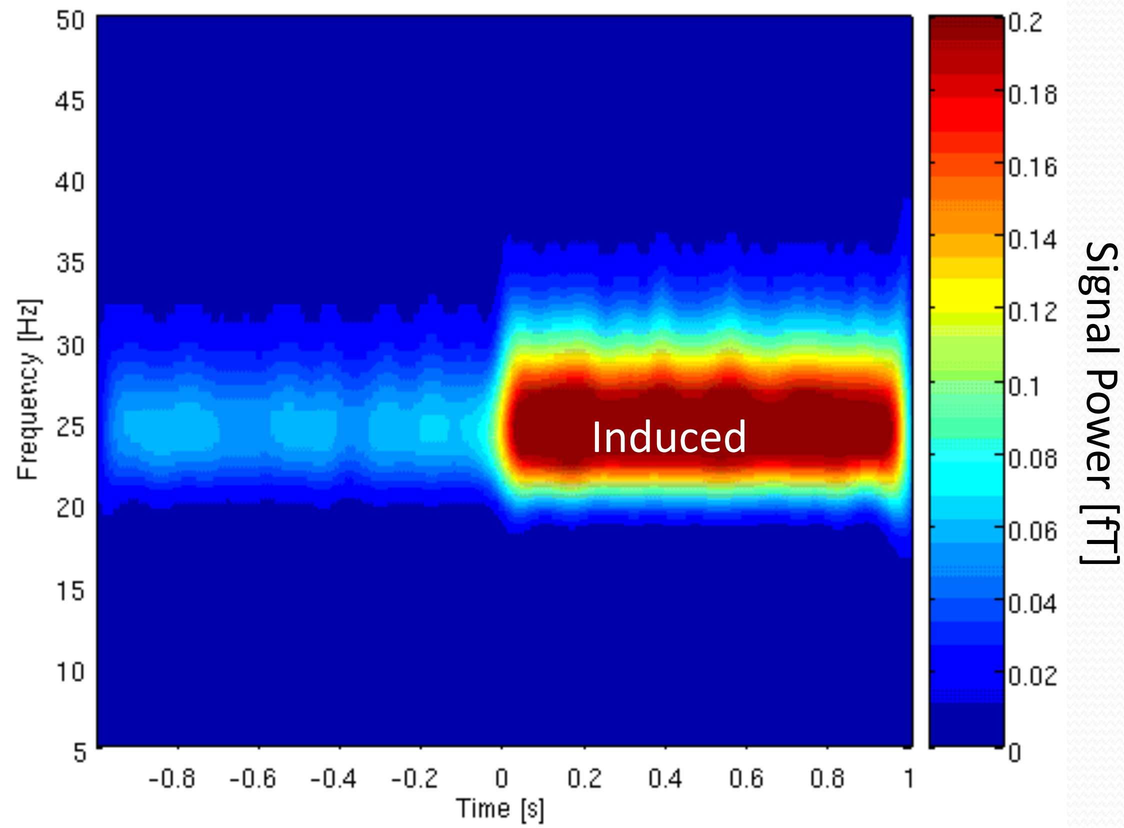
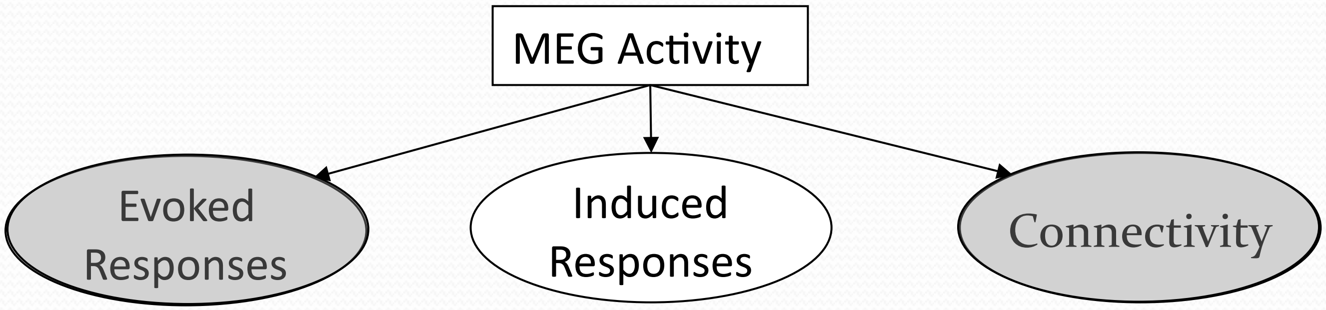


Induced Time-Frequency Response



Finding Induced Responses



<u>Characteristics of an Induced Neuromagnetic Signal</u>

- occur inside the helmet
- occurs in a specific frequency band (α, β, θ, δ, γ, …)
- weak temporal correlation with stimulation or behaviour

<u>Characteristics of a Magnetic Noise</u>

- generally occur outside the helmet
- covers the entire noise spectrum
- generally no temporally correlation with stimulation or behaviour

Finding Induced Responses

MEG Data are Synchronised to Events, then Averaged

Event Event Event Event Event

(306 channels continuous)

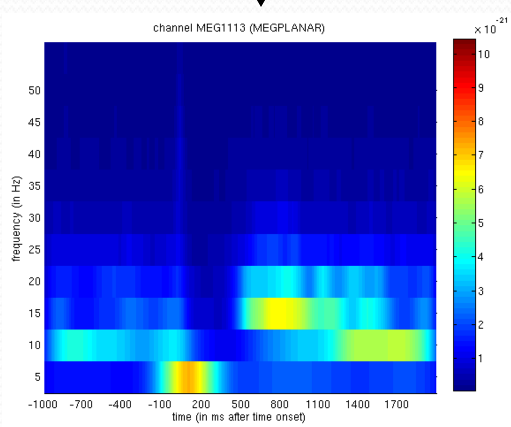
parse data based on Event

Event
Event
Event

(306 channels x 100 trials)

-2 0 2 s

Generate average TFRs



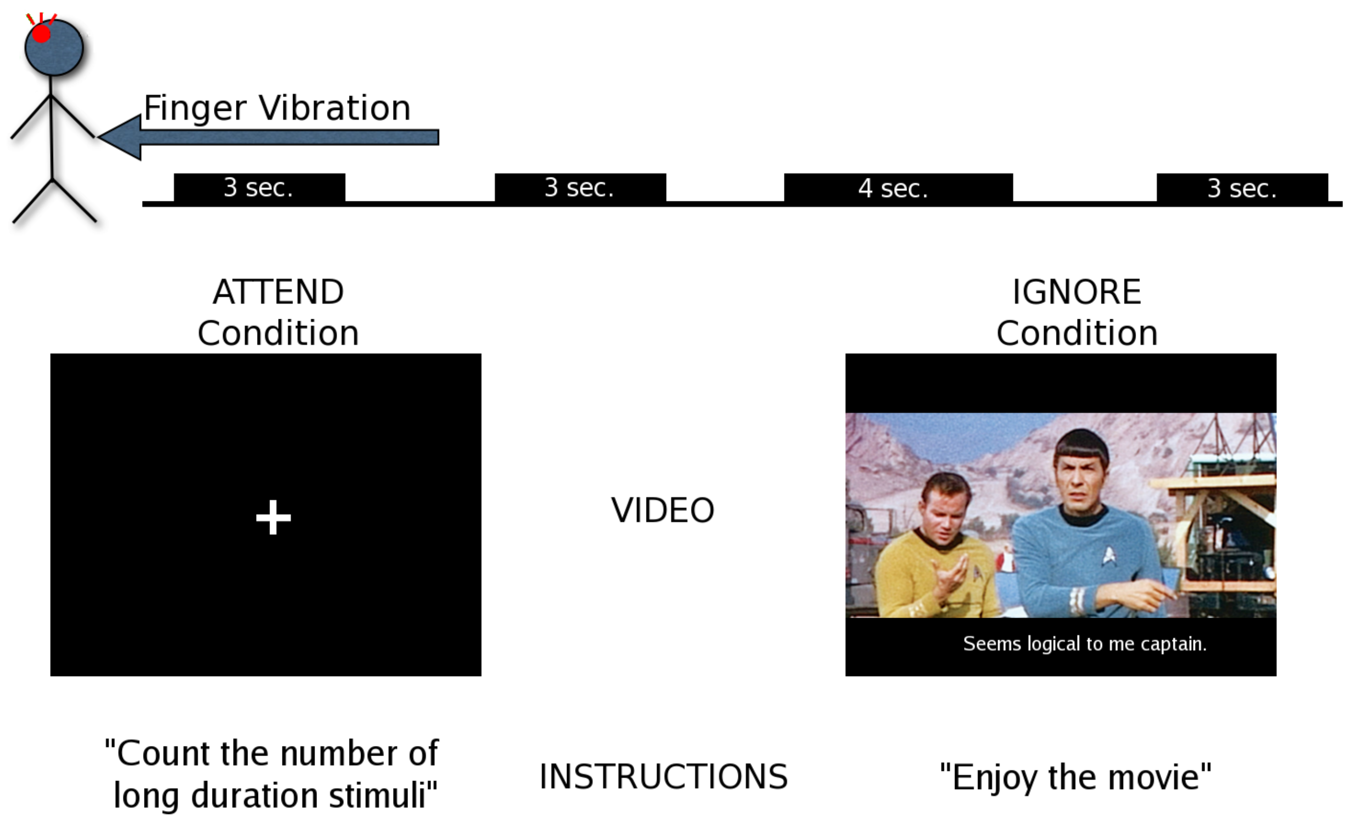
Baseline Correction

$$\Delta P(t,f) = \frac{P(t,f) - \overline{P}(t_{baseline},f)}{\overline{P}(t_{baseline},f)} \cdot 100\%$$

(306 channels x 1 trials
x 32 frequency bin)

Finger Vibration and Attention

How Does Focused Attention Change Responses to Finger Vibration?



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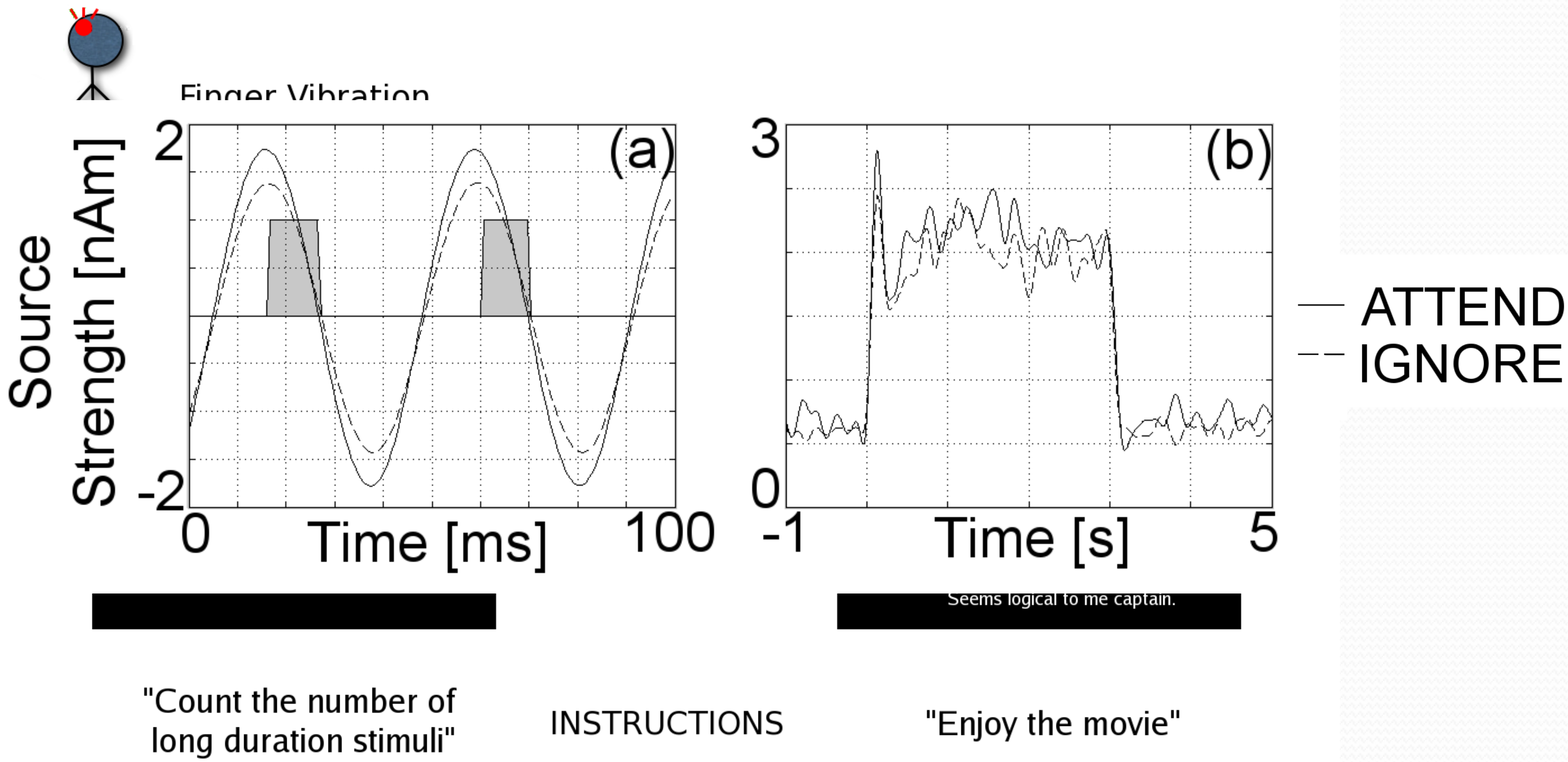

The steady-state response in contralateral SI gets 10% bigger.

(Bardouille et al., Eur J Neurosci, 2010)

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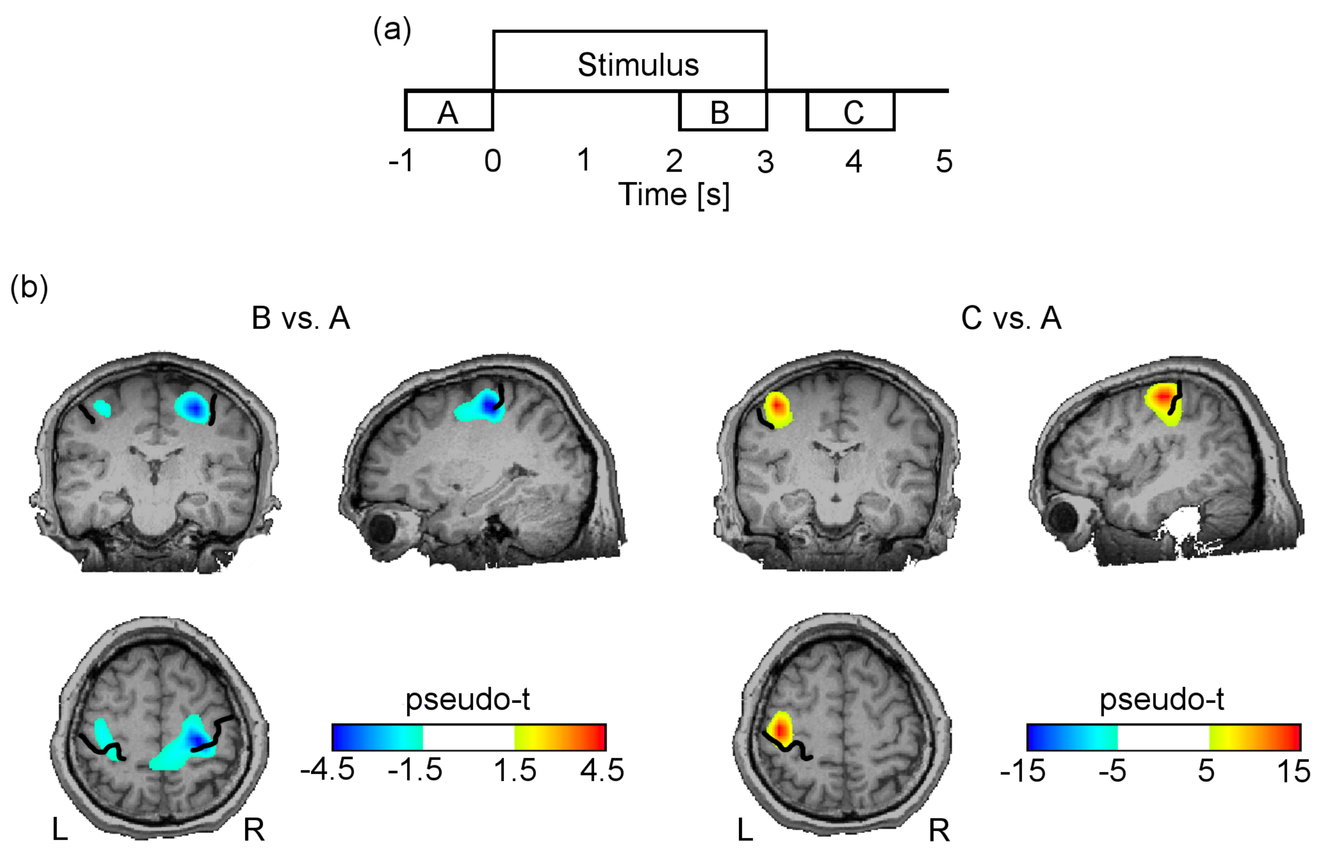

In the attend condition, changes in beta (15-30 Hz) power occur bilaterally in SI and MI

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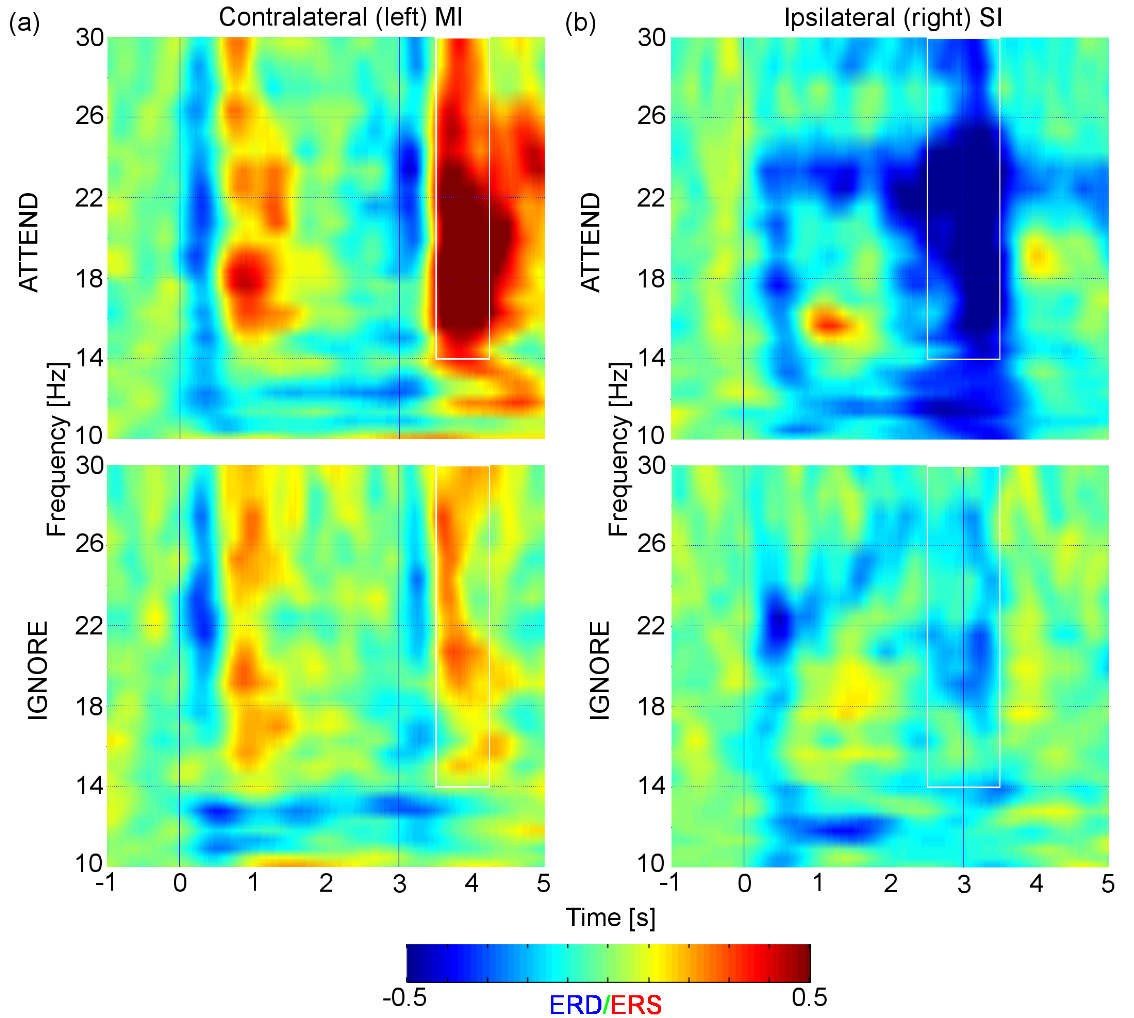

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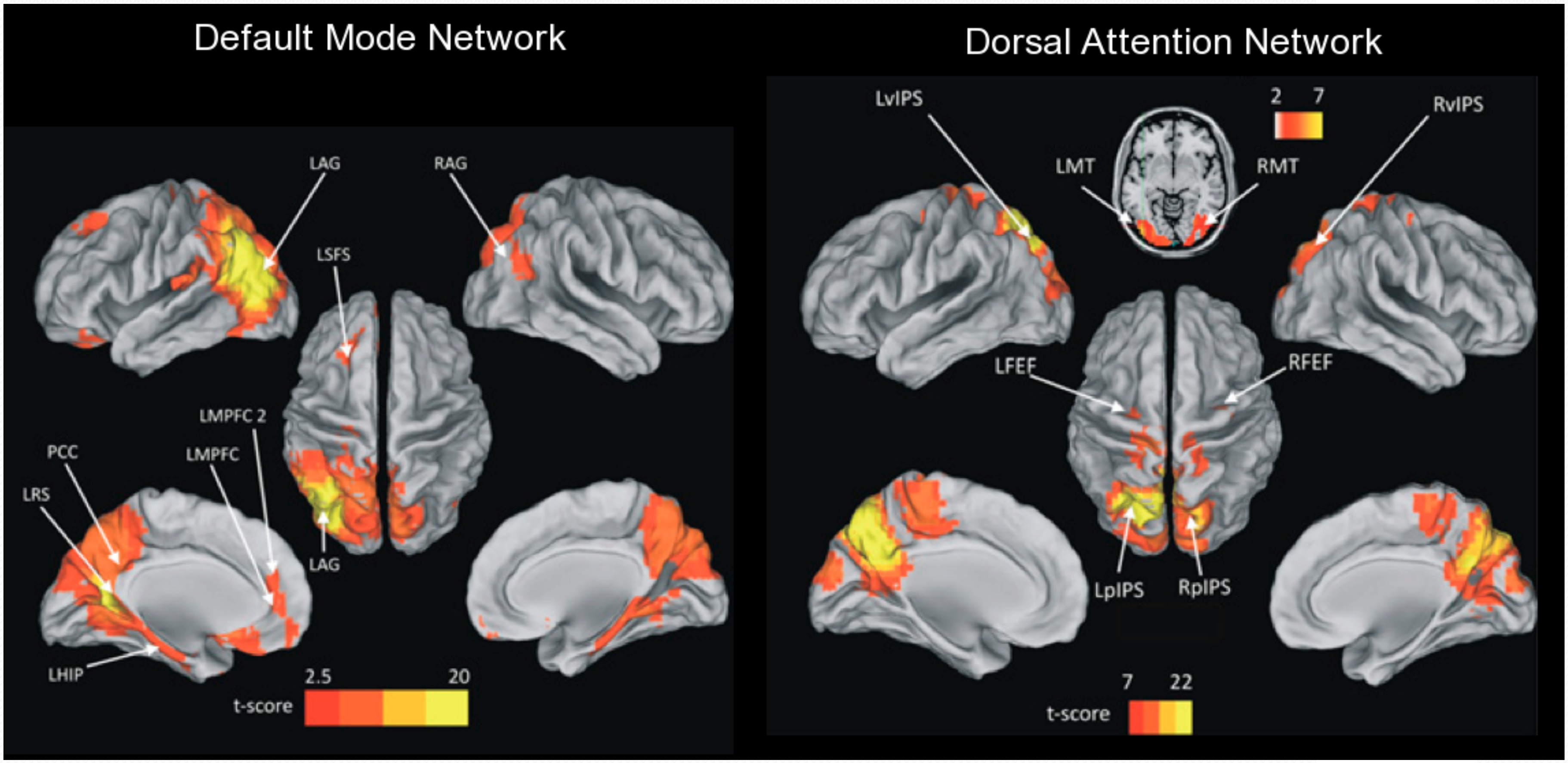
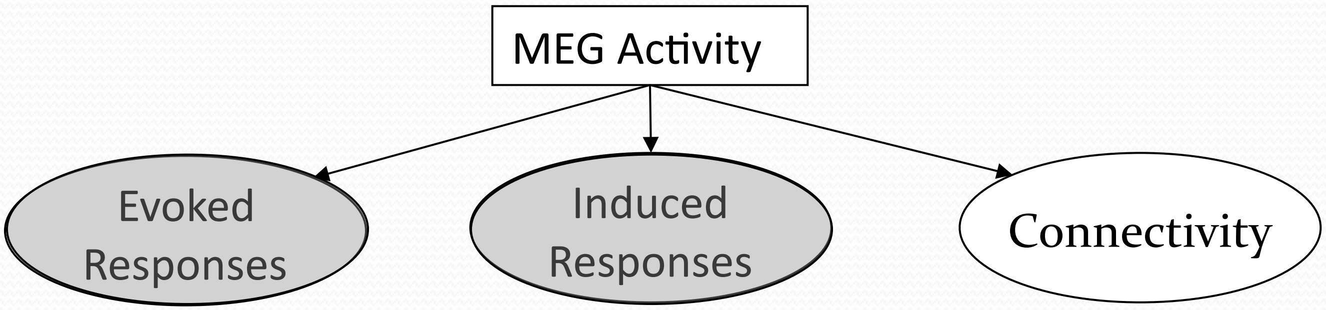
Resting-State Networks and MEG

Concurrent changes in cortical oscillations occur even at rest



(de Pasquale et al., PNAS, 2010)

Coherence and Functional Connectivity



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Coherence and Functional Connectivity

Coherence is:

- a normalised measure of the phase consistency between two signals as a function of frequency
- bound between 0 and 1
- high for synchronized oscillators (i.e. communicating neural populations)
- phase of coherence defines the mean phase difference (i.e. lag)
- measured with respect to another signal (not an event)

Cross - Spectral Density

$$G_n^{xy}(f) = F_n(x(t), f) \cdot F_n^*(y(t), f)$$

where F = Fourier transform

Mean Cross - Spectral Density

$$\overline{G}_n^{xy}(f) = \frac{1}{N}\sum_{n=1}^{N} G_n^{xy}(f)$$

Coherence

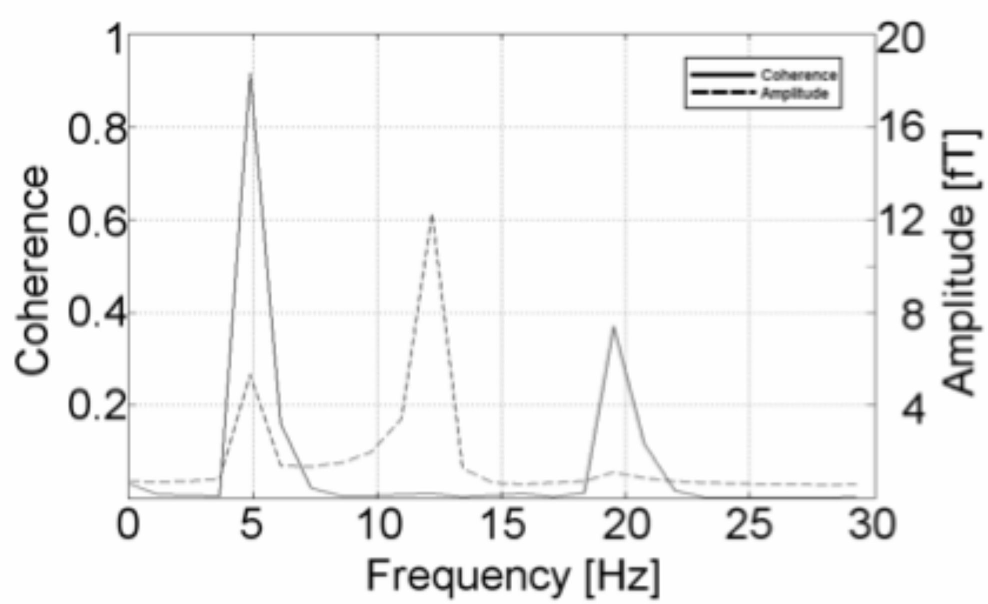
$$C^{xy}(f) = \frac{\overline{G}_n^{xy}(f)}{\sqrt{\overline{G}_n^{xx}(f)\,\overline{G}_n^{yy}(f)}}$$

Coherence and Functional Connectivity

Example

- 450 1-second epochs
- 2 signals containing 3 sinusoids plus white noise

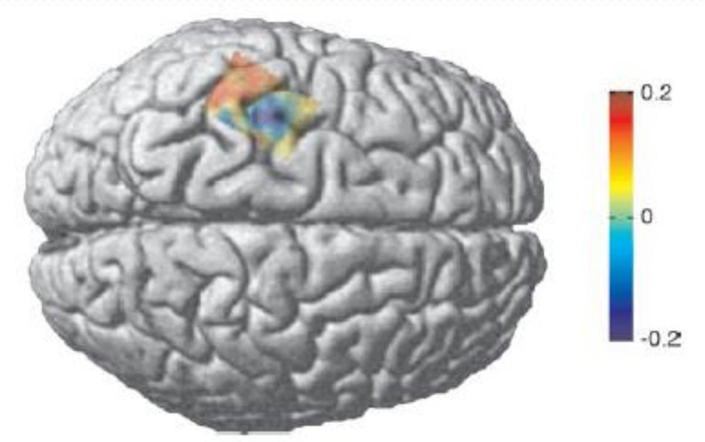
	Frequency	Amplitude	$\Delta\phi$ [°]
Moderate amplitude and synchrony	5 Hz	5 fT	± 18
Large amplitude, no synchrony	12 Hz	12 fT	± 180
Small amplitude, complete synchrony	20 Hz	1 fT	± 0



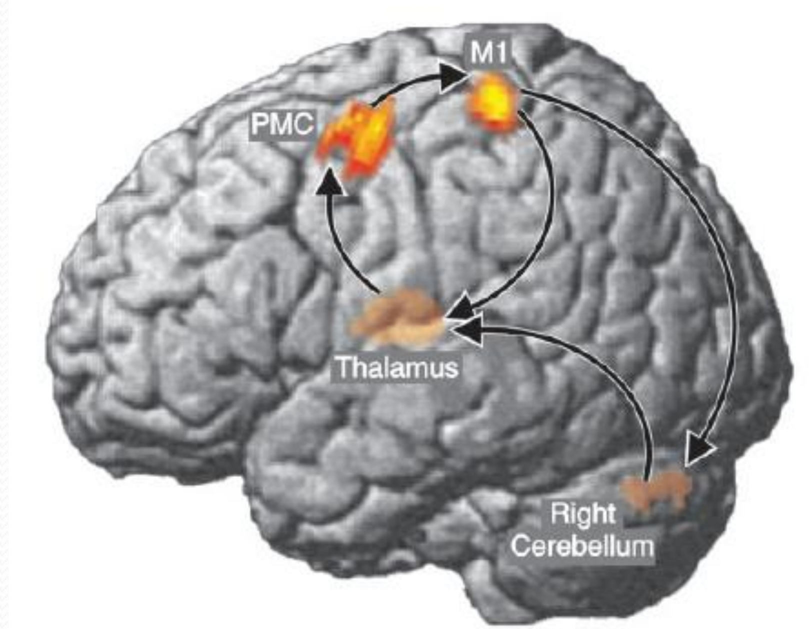
Coherence and Functional Connectivity

Coherence can identify a cerebello-thalamo-cortical network associated with slow, precise finger movements

Synchronized with Muscle (6-9 Hz)

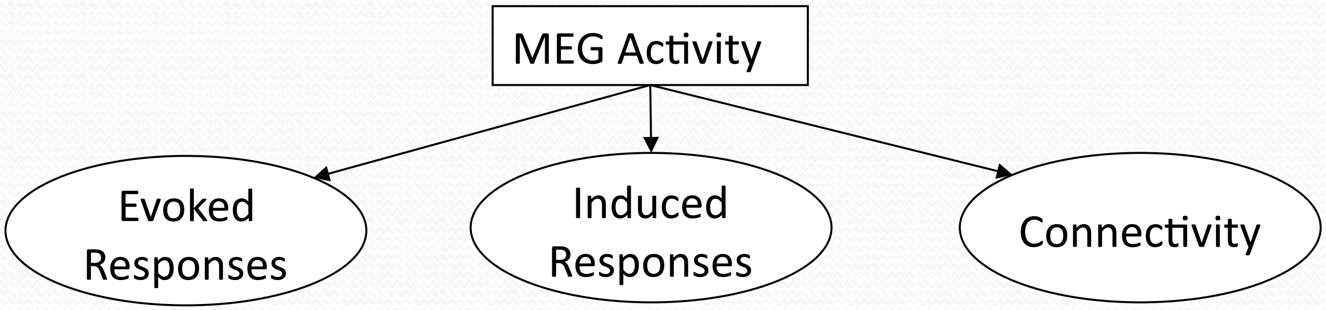


Synchronized with Motor cortex (6-9 Hz)



(Gross et al, PNAS, 2001)

Summary



<u>Neuromagnetic Activity</u>

Tells us about:

- synchronization of neural activity that is phase-locked to an event
  - ✓ neural firing temporally correlated to an event
- changes in ongoing neural activity related to an event
  - ✓ neural inhibition or excitation depending on the frequency
- synchronization between the neuromagnetic activity and the muscle
  - ✓ functional connectivity / binding

✓ Is a powerful method for imaging the brain as a dynamic system