Jyväskylä Summer School 2013

COM7: Electromagnetic Signals from The Human Brain: Fundamentals and Analysis (TIEJ659)

Neurophysiological basis of MEG/EEG

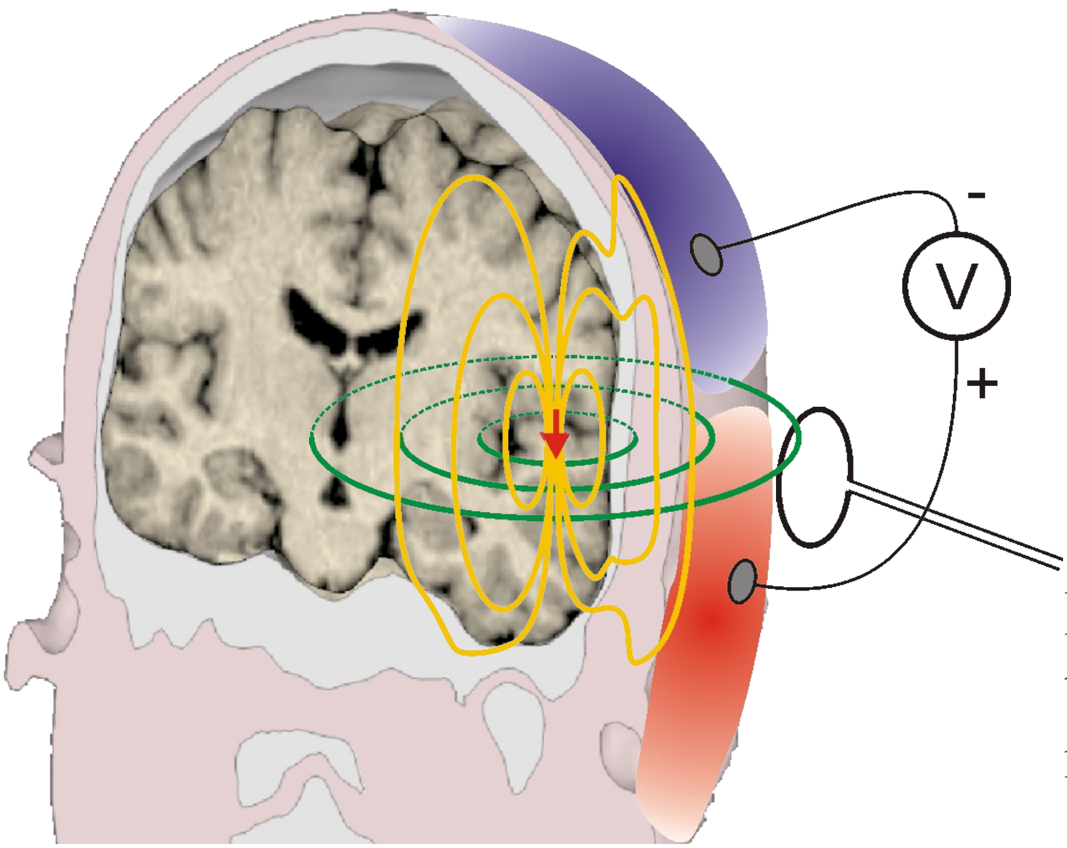
Lauri Parkkonen

Dept. Biomedical Engineering
and Computational Science
Aalto University
Lauri.Parkkonen@aalto.fi

Elekta Oy
Helsinki, Finland
Lauri.Parkkonen@elekta.com

MEG/EEG signals

Cellular currents in an
active neuron population...



... give rise to extracranial electric potentials and magnetic fields

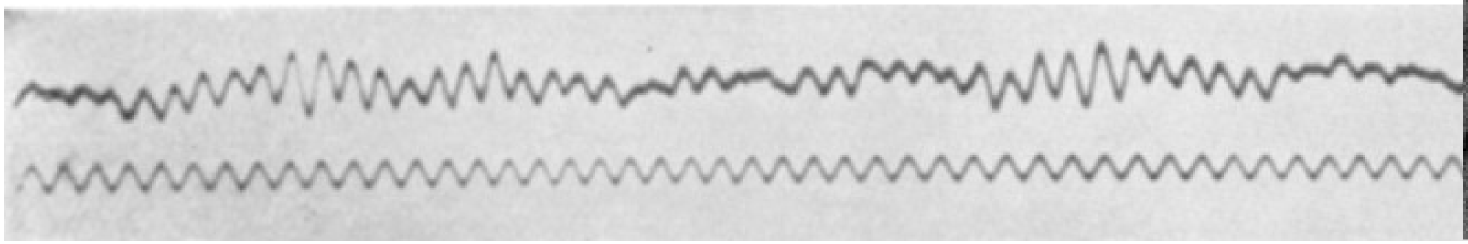
EEG = measuring the potential differences on the scalp

MEG = measuring the extracranial magnetic fields

MEG and EEG are different views of the same neural sources

The first EEG measurement

- Hans Berger recorded the first human EEG (alpha waves) in 1924



Upper trace: Human EEG
Lower trace: 10-Hz timing signal

The first MEG measurement

- MEG became practical only after the SQUID (superconducting quantum interference device) sensor was invented
- David Cohen made the first MEG measurement with a SQUID in 1972 at MIT

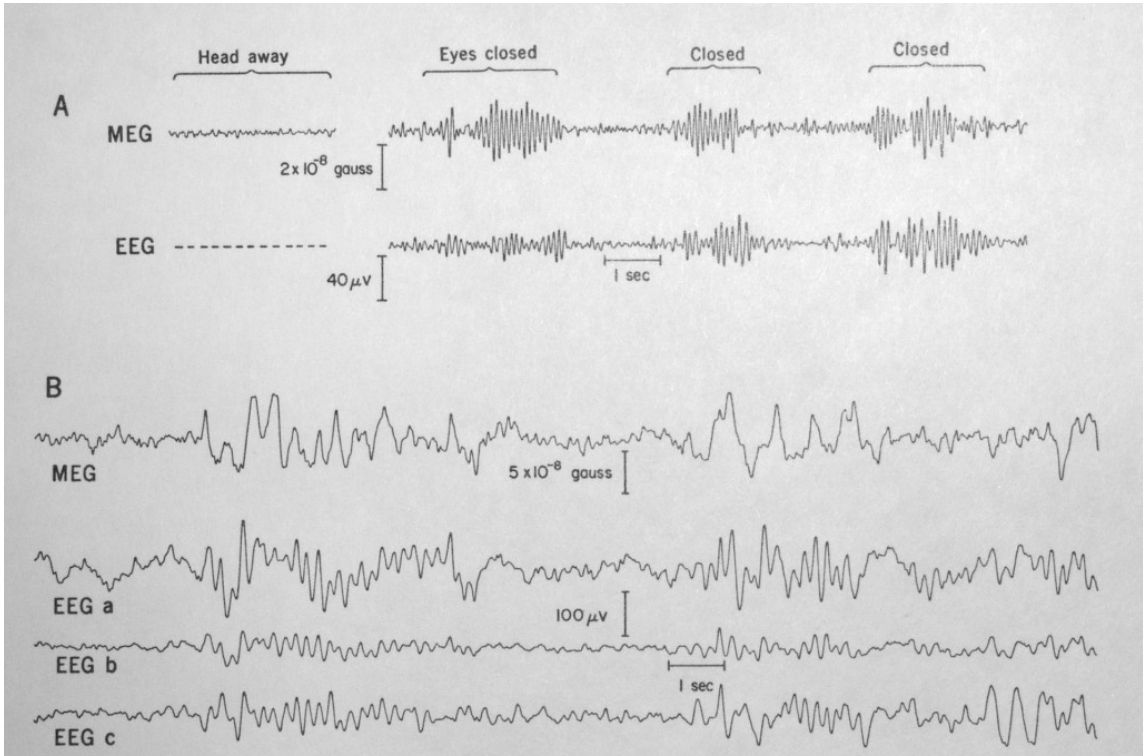
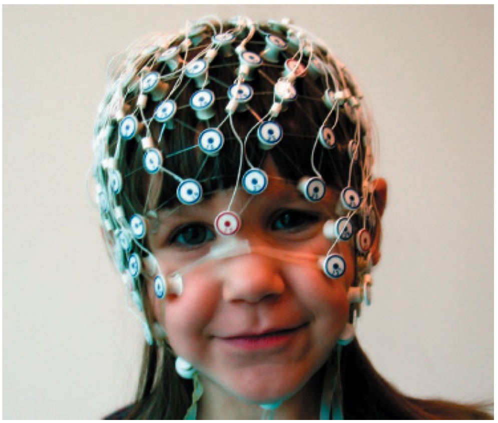
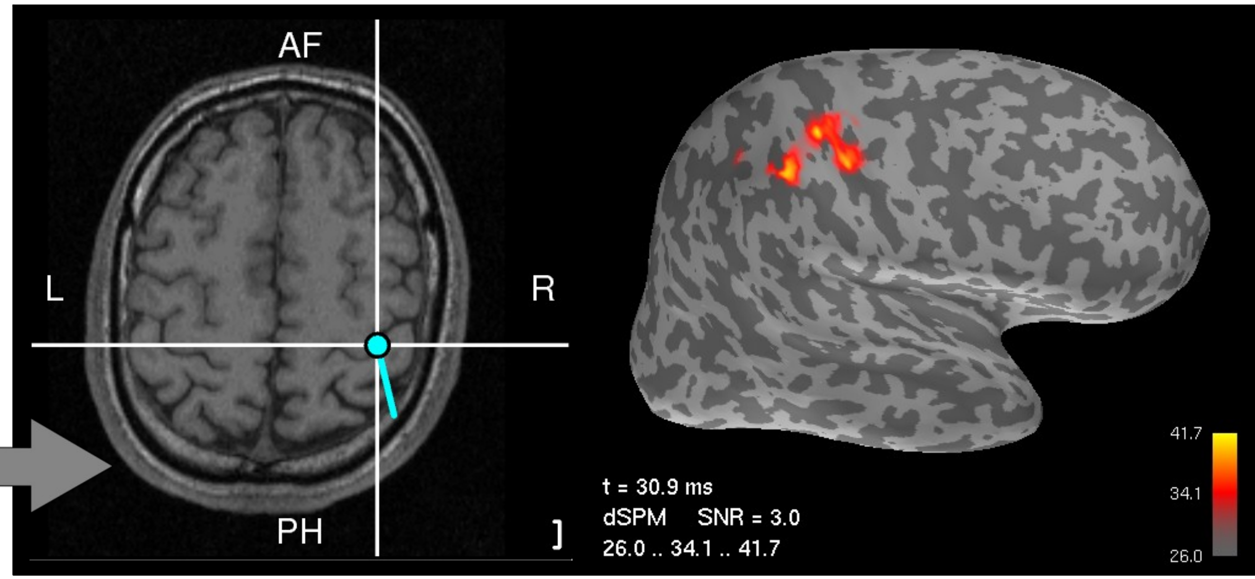


Fig. 2. Simultaneous MEG and EEG recordings. (A) Alpha rhythm from the brain of a normal subject, clearly seen in both MEG and EEG. The magnetometer was located at the left occipital region, as were the bipolar set of EEG leads. The bandwidth on both channels was 4 to 15 hz. (B) Large events, induced by hyperventilating, from

Cohen, Science 1972

Modern EEG and MEG





- Localization of brain activity (source modelling
- Applications
  - Epilepsy diagnostics
  - Pre-surgical mapping
  - Neuroscientific research

MEG+video recording of an epileptic seizure

Courtesy of Dr. R. Paetau, Helsinki Univ. Central Hospital

MEG is expensive... why bother?

Measured quantity

- MEG/EEG: Electromagnetic fields due neural currents
- fMRI: Hemodynamics modulated by neural activity

Temporal resolution

- MEG & EEG (~1 ms) << fMRI (~1 s)

Spatial resolution

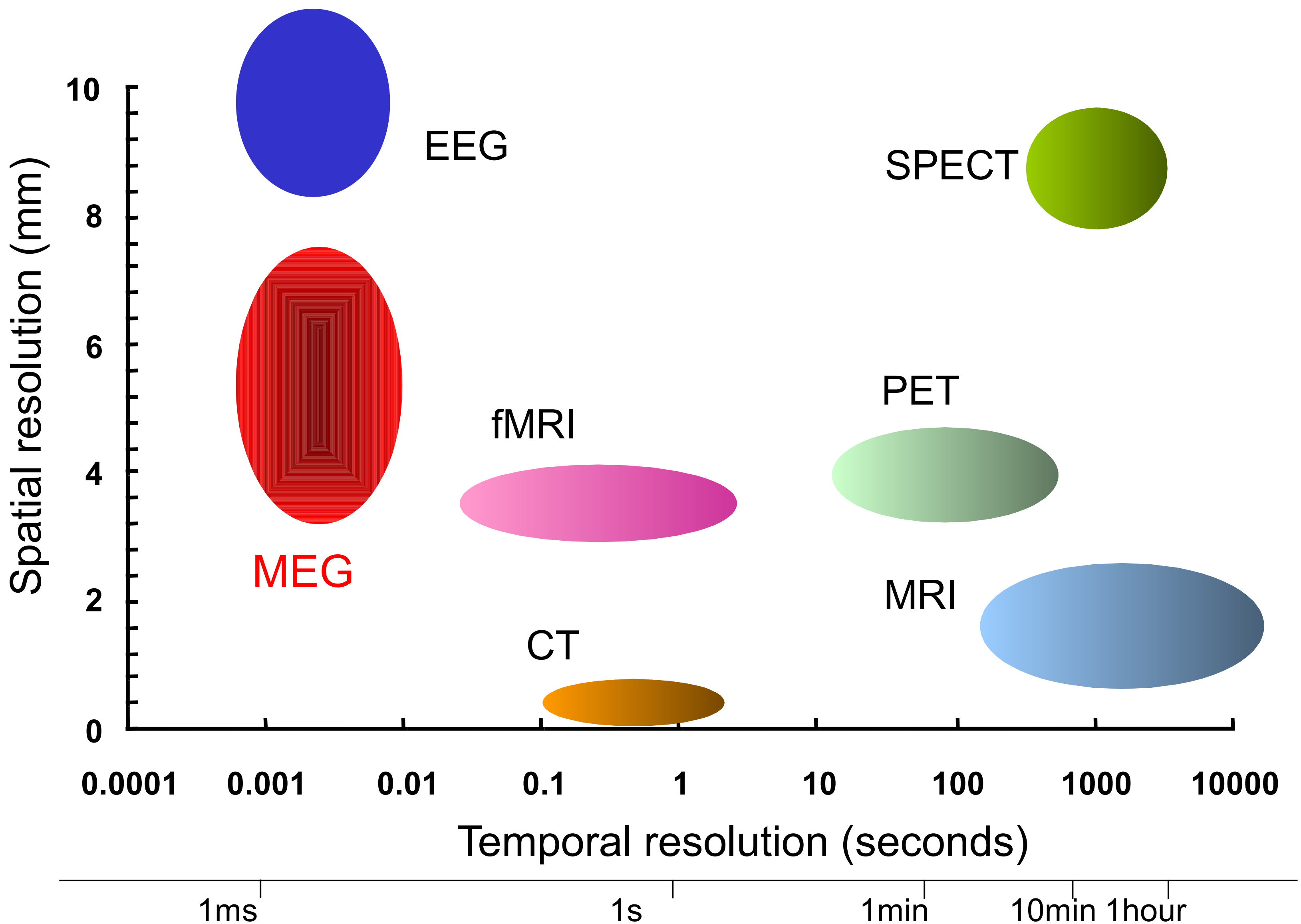
- fMRI (~1 mm) < MEG (~1 cm) < EEG (~few cm)

Signal-to-noise ratio

- In raw data, comparable among MEG, EEG and fMRI

The niche of MEG: direct measurement of neuronal activity with high temporal resolution and decent spatial resolution

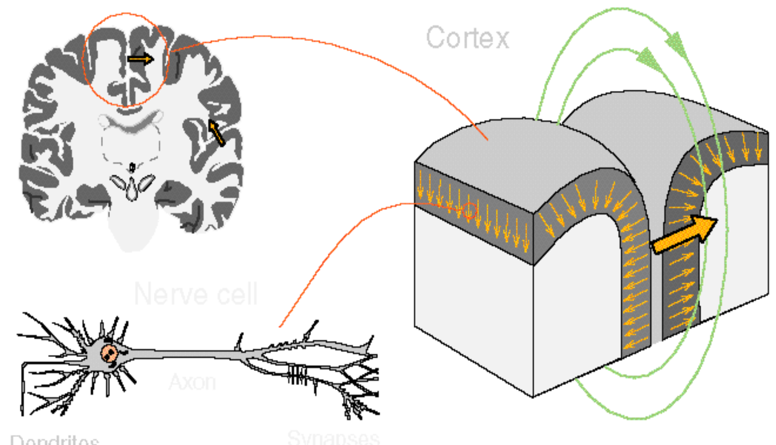
Comparison of brain imaging methods



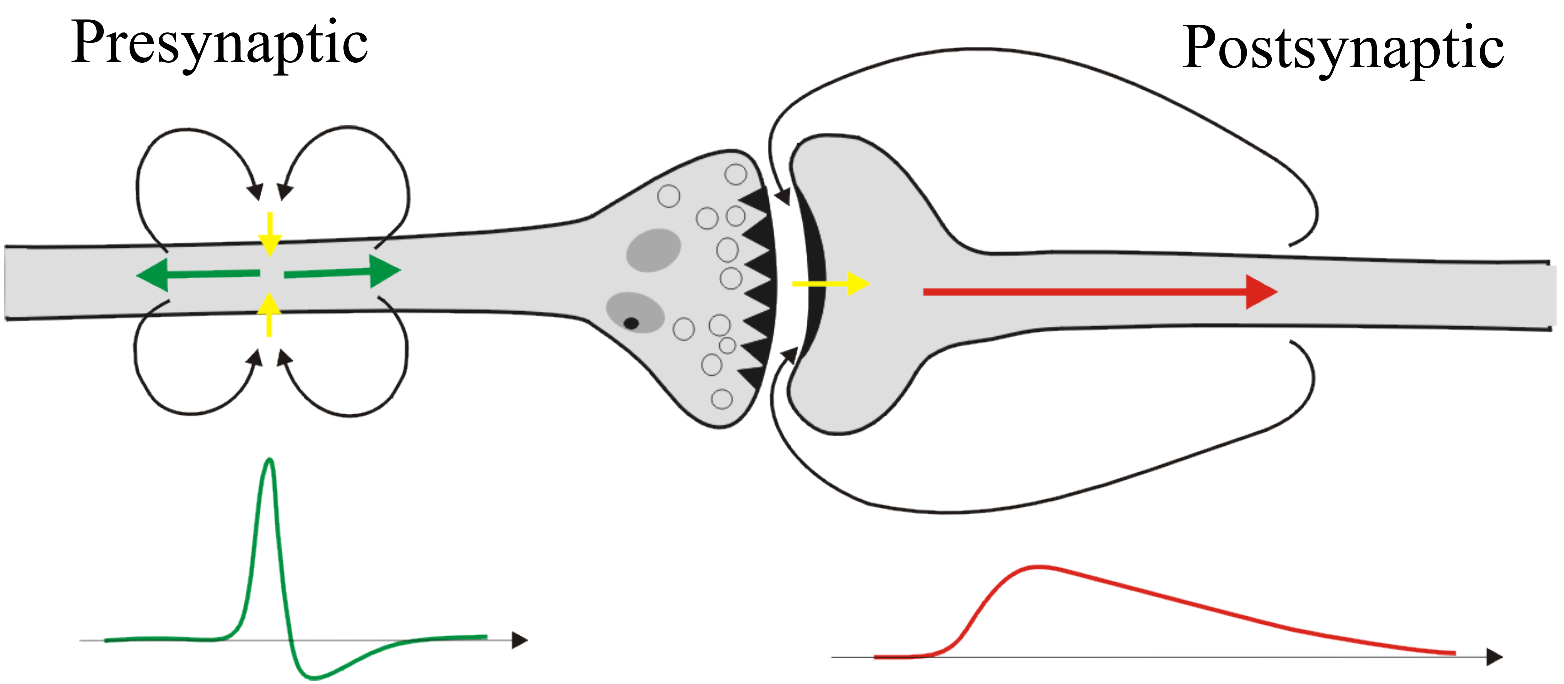
Outline

- Genesis and nature of MEG signals
- Instrumentation for MEG
- MEG data analysis
- (More) examples of neuroscience studies with MEG

The genesis & nature of MEG signals

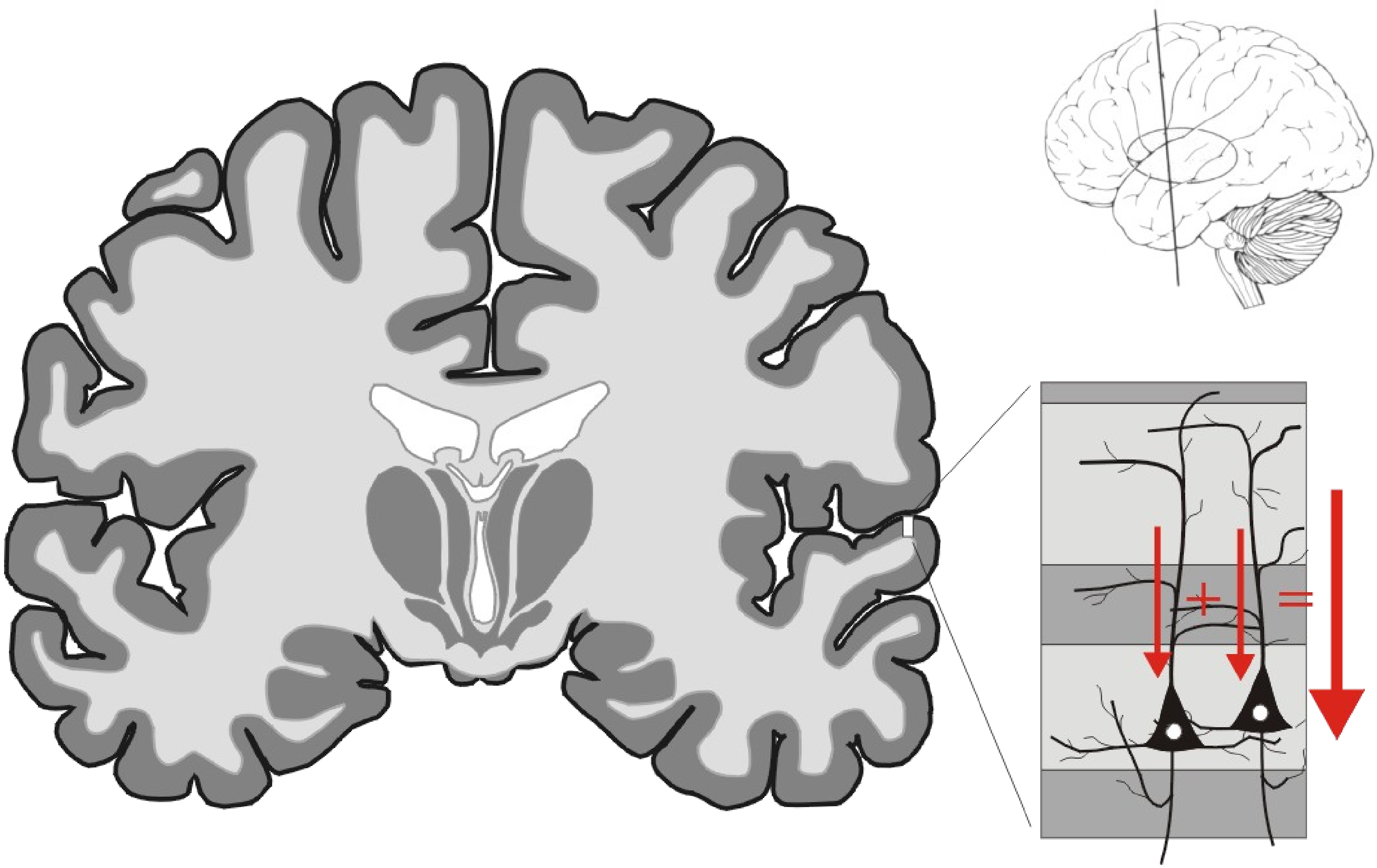


Currents in axons and dendrites



- Action potentials:
  - Fast: no/little temporal summation
  - Cancellation: fields diminish rapidly
- Postsynaptic currents:
  - Slow: temporal summation
  - dipolar currents
  - **the main source of MEG&EEG!**

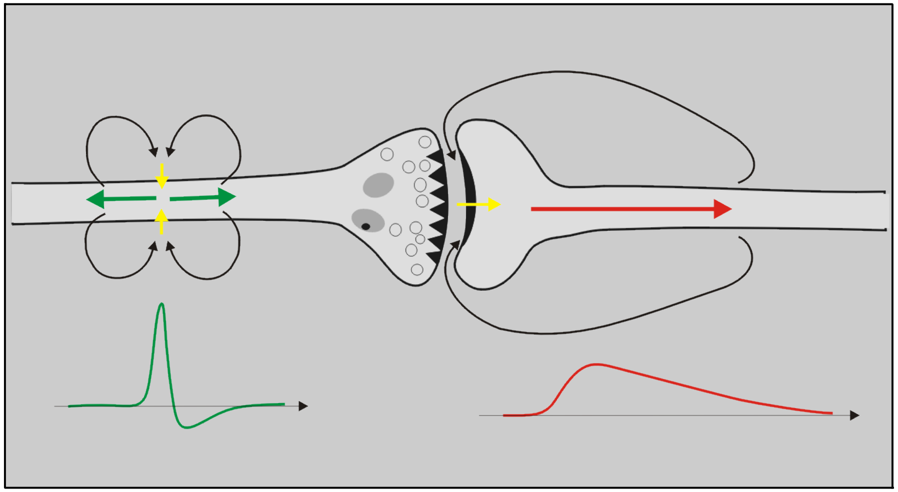
Spatial summation: Parallel dendrites



Pyramidal cells: parallel orientation => spatial summation

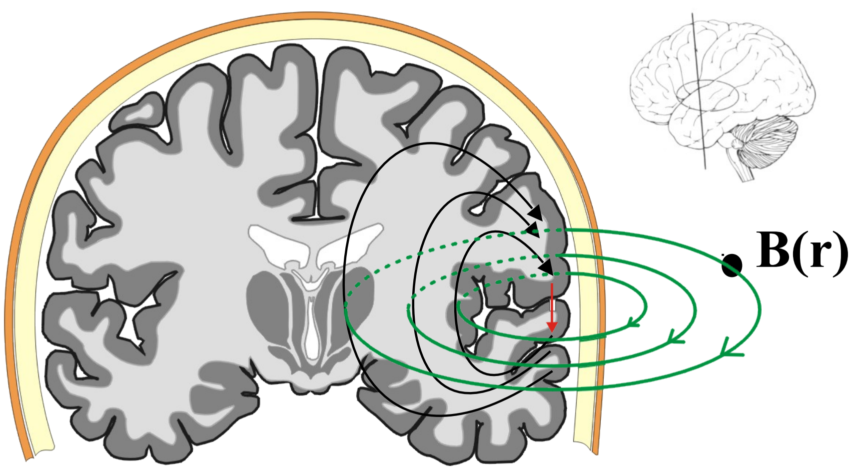
Neural currents

- Impressed currents $\mathbf{J}_i(\mathbf{r})$
  - due to electrochemical gradients and open ion channels across the cell membrane
- Primary currents $\mathbf{J}_p(\mathbf{r})$
  - due to impressed currents
  - currents inside dendrites and axons
  - decay with distance from the synapse
- Volume currents $\mathbf{J}_v(\mathbf{r})$
  - due to primary currents
  - passive, ohmic current flow



Neural currents and fields

- All currents generate a magnetic field!
- Skull is a poor conductor => it distorts and blurs electric signals **but not magnetic!**



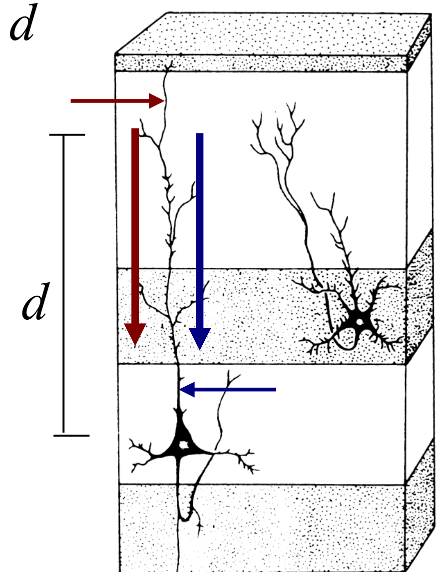
- The primary currents are directly related to the neural activation, thus, we would like to estimate them based on the measured MEG/EEG signals.

MEG/EEG signal strength

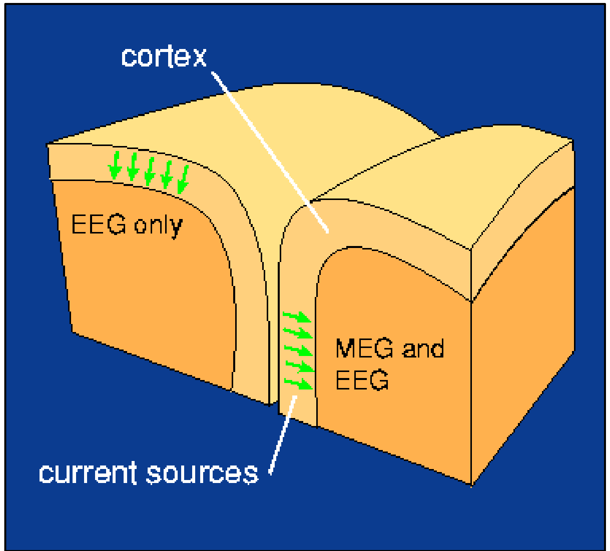
- **Synaptic input**
  - excitatory or inhibitory
  - synapses at apical dendrites or close to the cell body
- **Degree of synchronization**
  - Within a cortical patch, ~1% of neurons signalling synchronously with a stimulus produce > 80% of the signal [*Hari 1990*]
- **Orientation of the primary current**
  - in a **perfectly spherical conductor**, radial currents do not produce net **magnetic** field outside of the conductor
  - EEG sees both radial and tangential currents

Dipole moment = current · distance

$$Q = I \cdot d$$

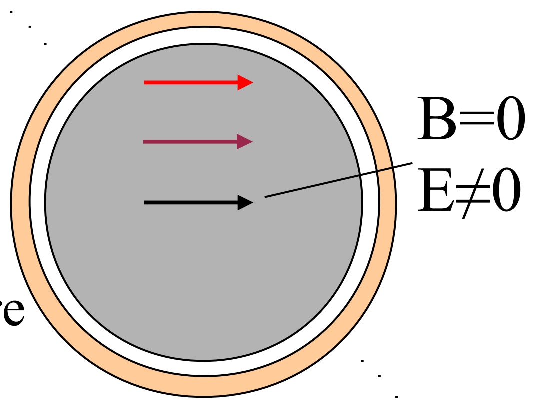


Adapted from Kandel et al.

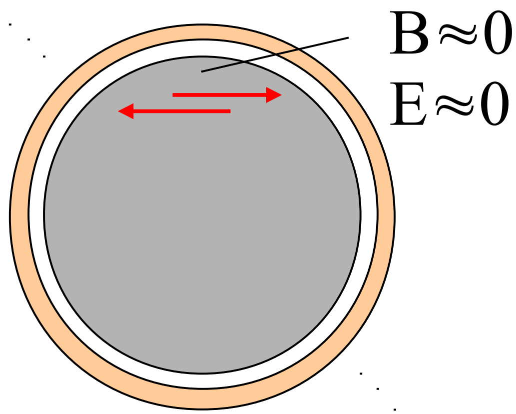


MEG/EEG signal strength

- Depth
  - more attenuation the deeper the primary current
  - no **magnetic** signal from the center of a conducting sphere

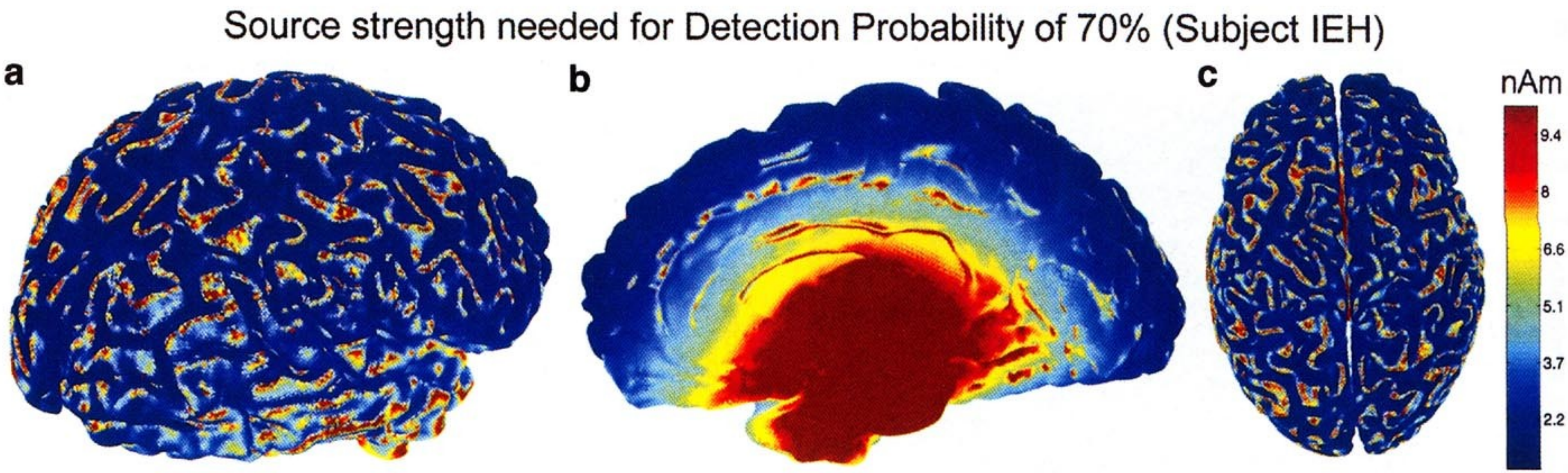


- Cancellation by near-by sources
  - close-by activations with simultaneous, opposing currents decrease the signal



What do we then see with MEG?

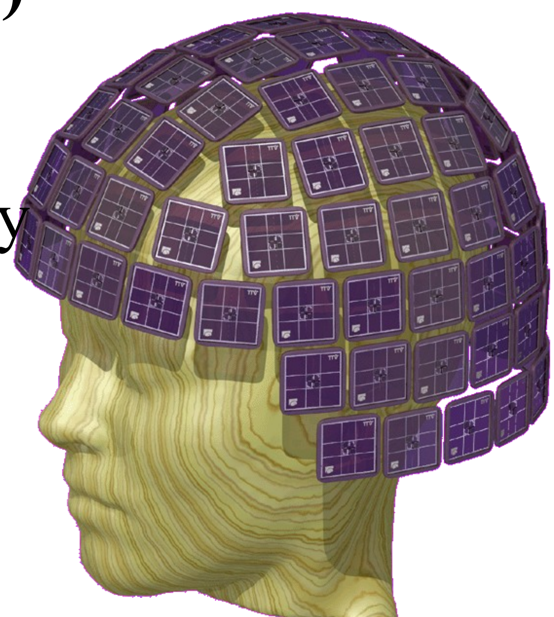
- Almost all of the cortex with fissural activity emphasized



Hillebrand & Barnes, 2002

MEG experiment

Stimuli (if any)
- auditory
- visual
- somatosensory
- olfactory
- pain
- ...



MEG/EEG
- evoked responses
- induced responses
- changes in brain connectivity

Task
- attend or ignore
- detect and react
- imagine
- observe/imitate
- ...

Behavioral responses
- limb/finger movement
- eye gaze
- speech
- ...

MEG data analysis

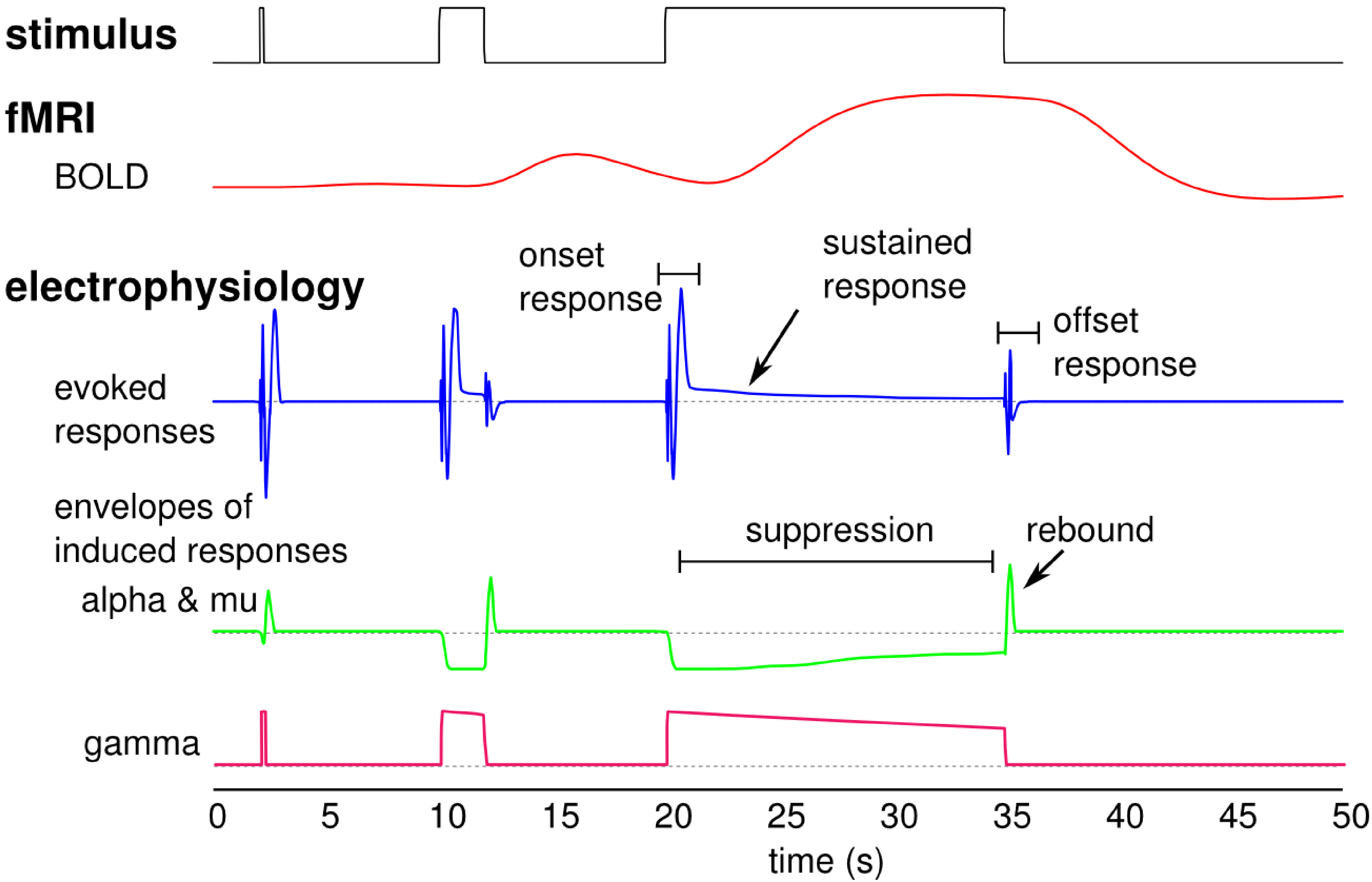
MEG/EEG measurement

Signal processing
Improve signal-to-noise ratio of the signal components of interest, e.g., by averaging trials and by filtering.

Source modelling
Estimate the primary current distribution (or its statistic) given the MEG/EEG data.

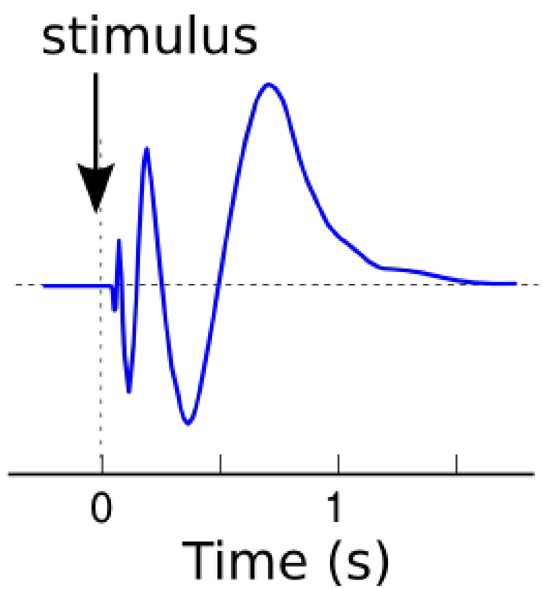
Visualization
Superimpose the source estimate on the anatomical MR image

MEG/EEG and fMRI-BOLD responses

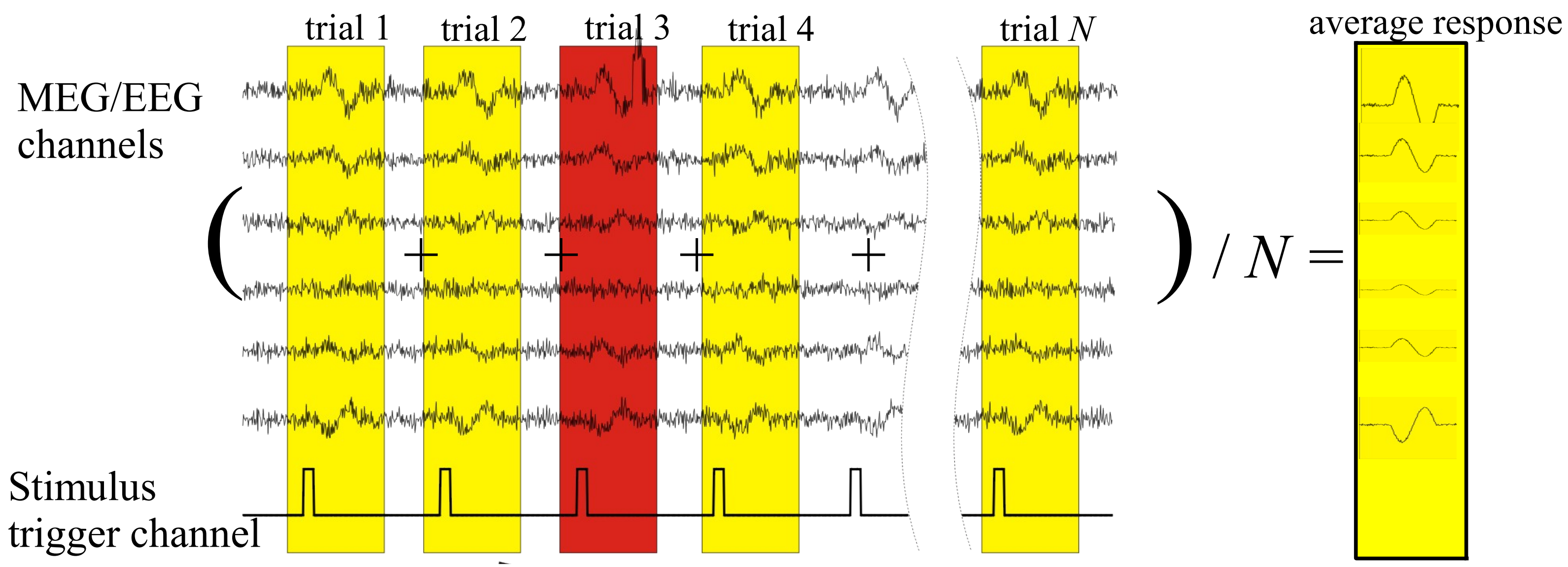


Evoked responses

- Stimulus typically elicits a sequence of transient *responses*, each comprising one or more *components*
- Earliest responses automatic, later responses susceptible to cognitive manipulations
- With increasing latency, responses typically get longer-lasting and larger in amplitude
- Naming of the responses: N (for EEG vertex negative), P (for EEG vertex positive) followed by the nominal approximate latency in milliseconds
  - For example, with auditory word stimuli: Brainstem waves I–VII, N17, P50, N100, P200, P300, N400
  - Suffix 'm' to emphasize a magnetic response, e.g., N100m



Evoked responses: Averaging

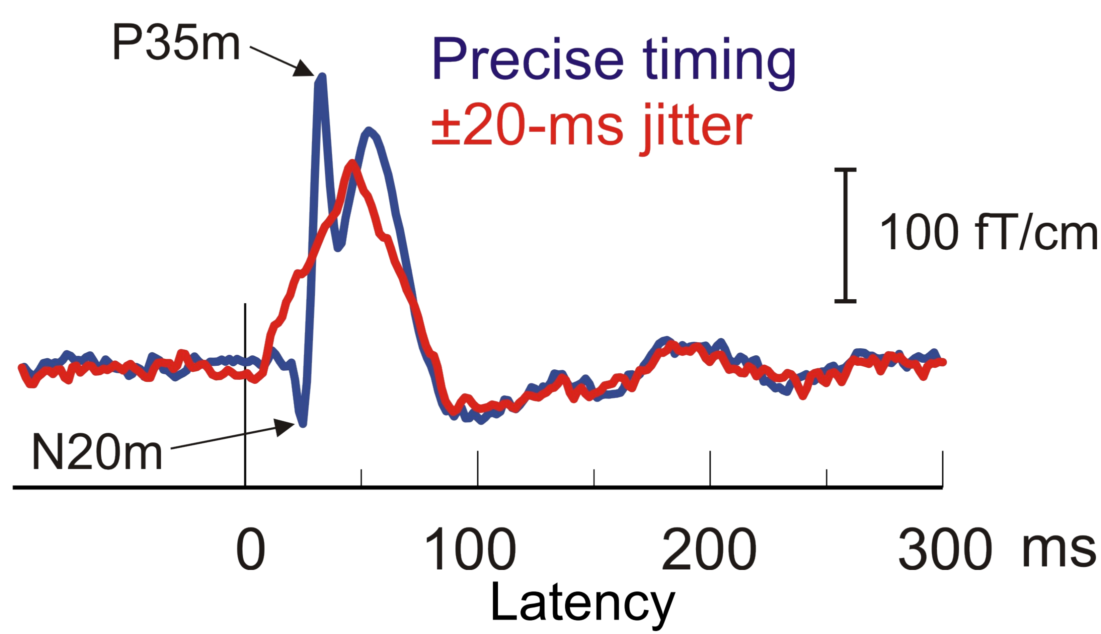


- Signal model: stimulus-locked activity + uncorrelated noise
- Signal recovery: stimulus-locked time-domain averaging
- SNR ~ sqrt(number of trials)
- Linear operation: Order interchangeable with other linear operations

Evoked responses: Timing/synchronization matters

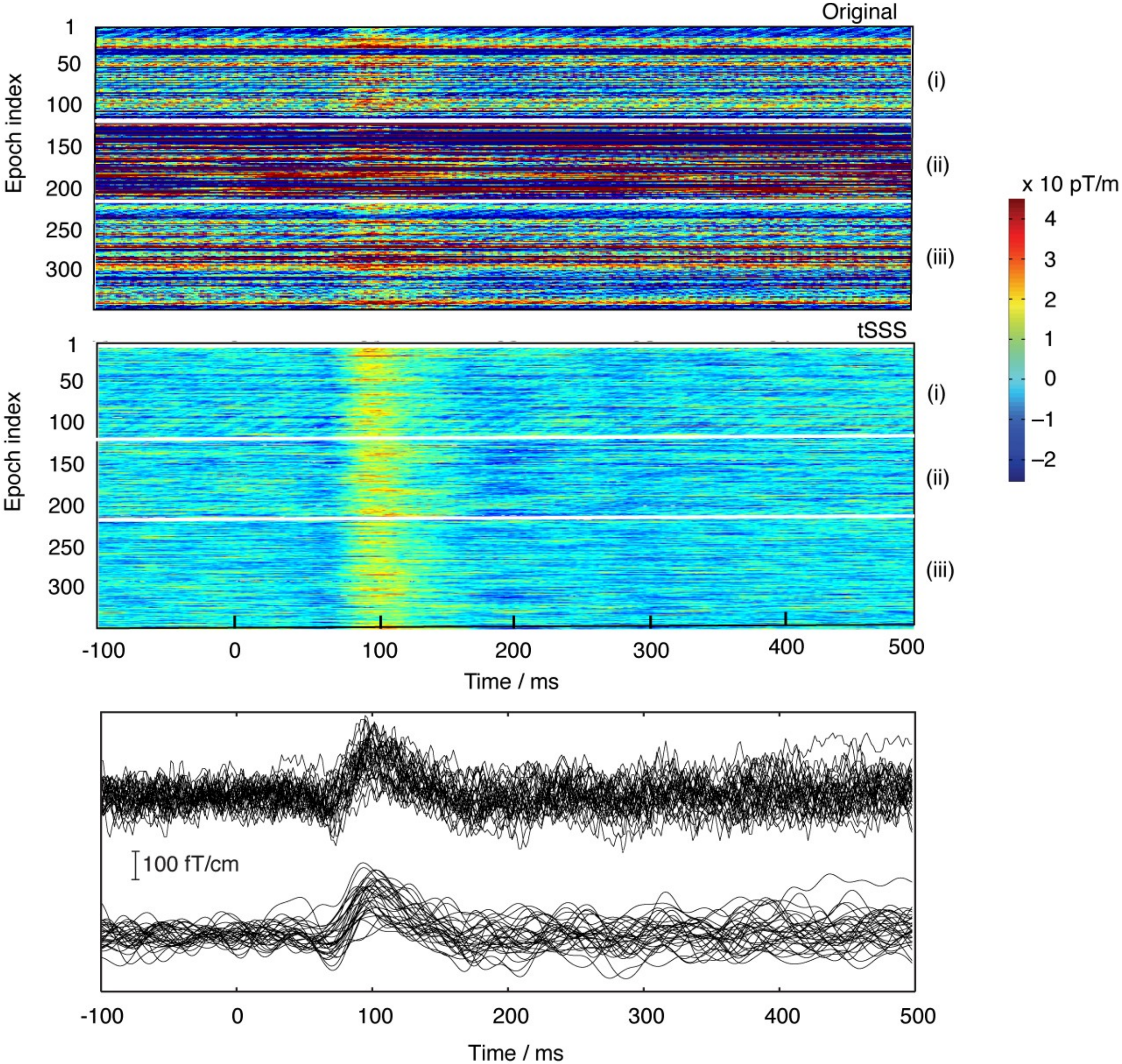
- Sloppy stimulus timing (jitter) yields smeared average MEG/EEG responses.
- Physiological jitter produces similar effects.
- Single-trial analysis may reveal physiological trial-to-trial variation in amplitude and latency

Somatosensory evoked fields



Evoked responses: Single trial

Auditory evoked fields, no averaging

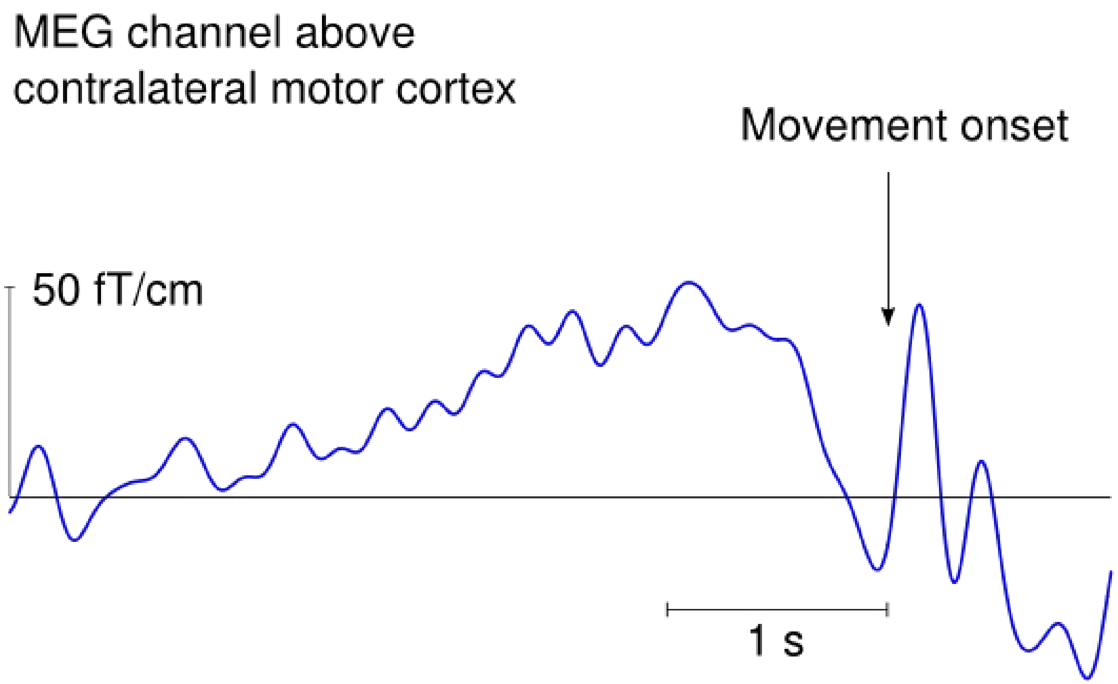


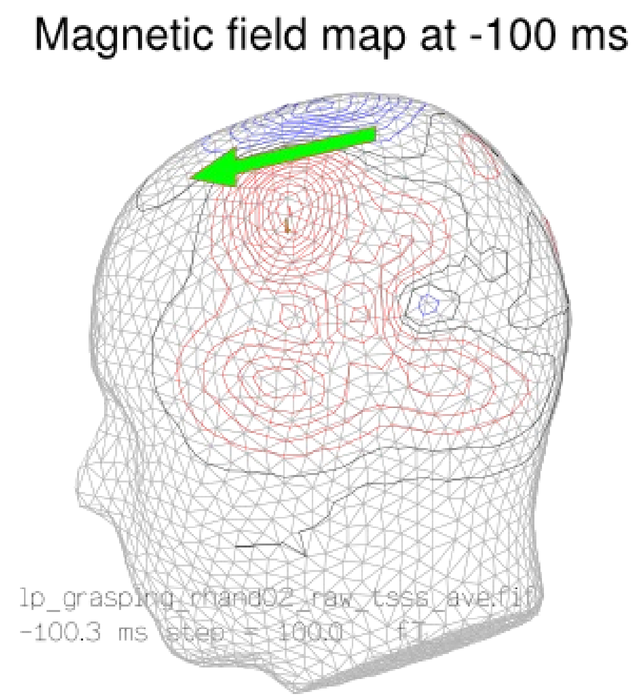
Taulu and Hari (2009) Hum. Brain Mapp.

Evoked responses: Low frequencies

- Self-paced movements give rise to Bereitschaft (readiness) potentials and fields detectable seconds prior to the movement

Self-paced grasping movements with the right hand,
EMG-triggered averaging ($N = 93$),
pass-band DC – 5 Hz

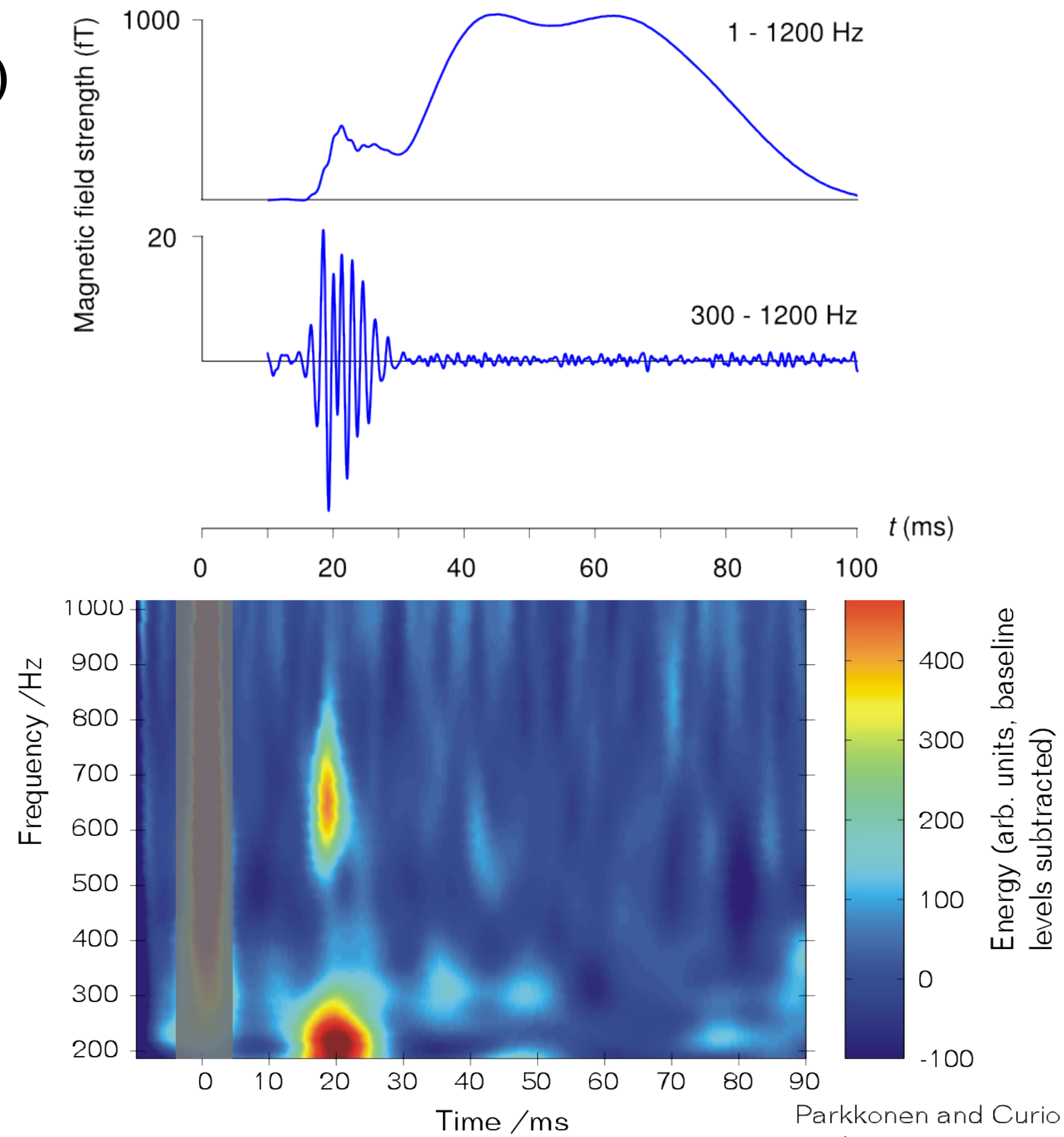




Parkkonen, unpubl.

Evoked responses: High frequencies

- High-frequency oscillations (~600 Hz) in response to electric median nerve stimulation
- Partly axonal activity

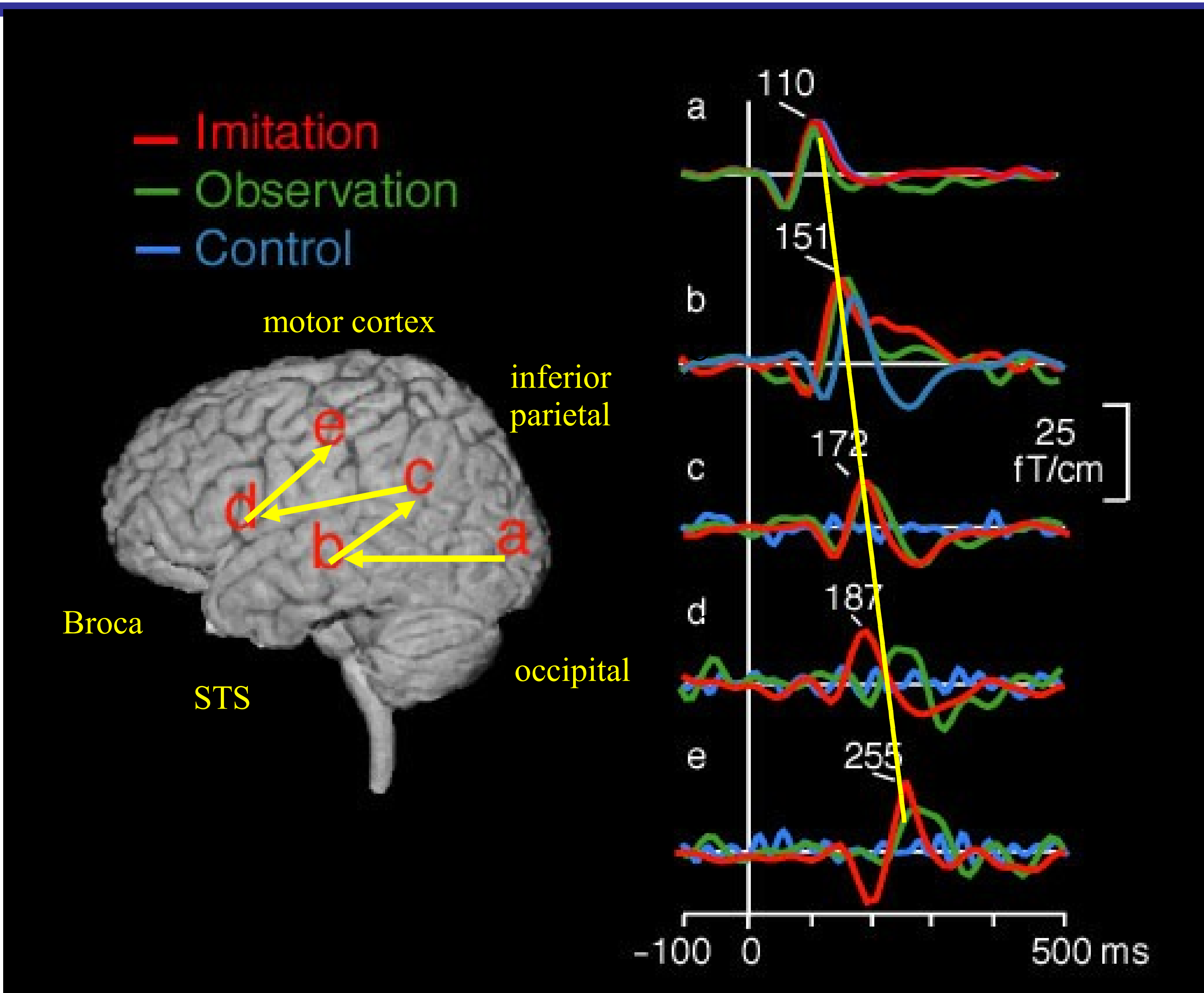


Parkkonen and Curio, work in progress

Evoked responses, an example: Viewing and imitating lip forms

Nishitani & Hari 2002

Evoked responses: Imitation of lip forms



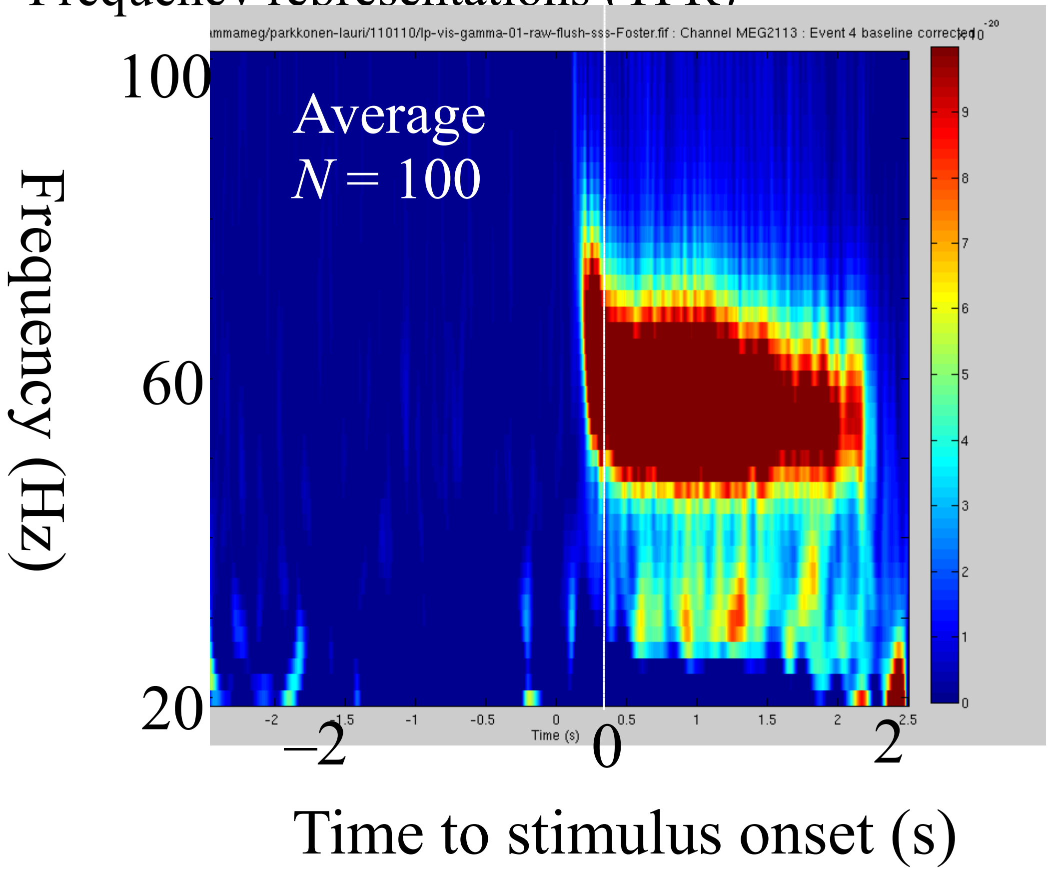
Nishitani & Hari, Neuron 2002

Induced responses

- Stimulus/task modulates the amplitude of an oscillatory signal
- The oscillation is **not** phase-locked to the stimulus
  - Trial averaging destroys the response rather than improves the SNR unless phase information is removed

Induced responses (cont'd)

- Constructive averaging only by destroying the phase information
- Estimation of instantaneous energy or power using wavelets or Hilbert transformation. Subsequent averaging.
  - Time–Frequency representations (TFR)

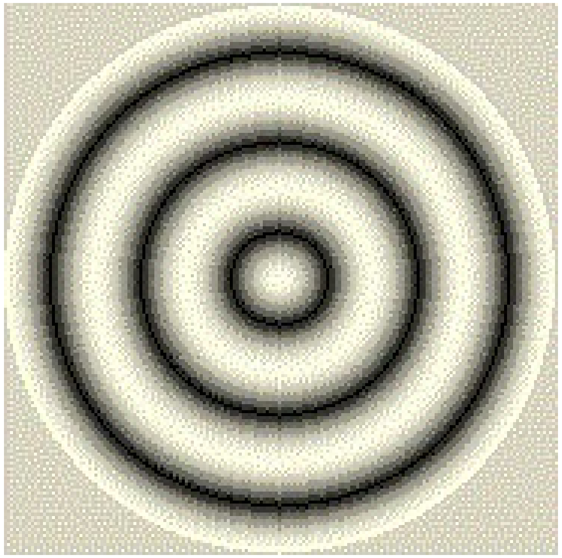


Induced gamma-band responses

- Experiment

  Visual stimulus; inward-moving circular gratings whose contraction speed changed at a random latency. Trial duration 1.5–2.0 s.

  Attention task; subjects had to detect and report a speed change [Hoogenboom et al. 2006]



- Measurements

  Elekta Neuromag 306-channel MEG system

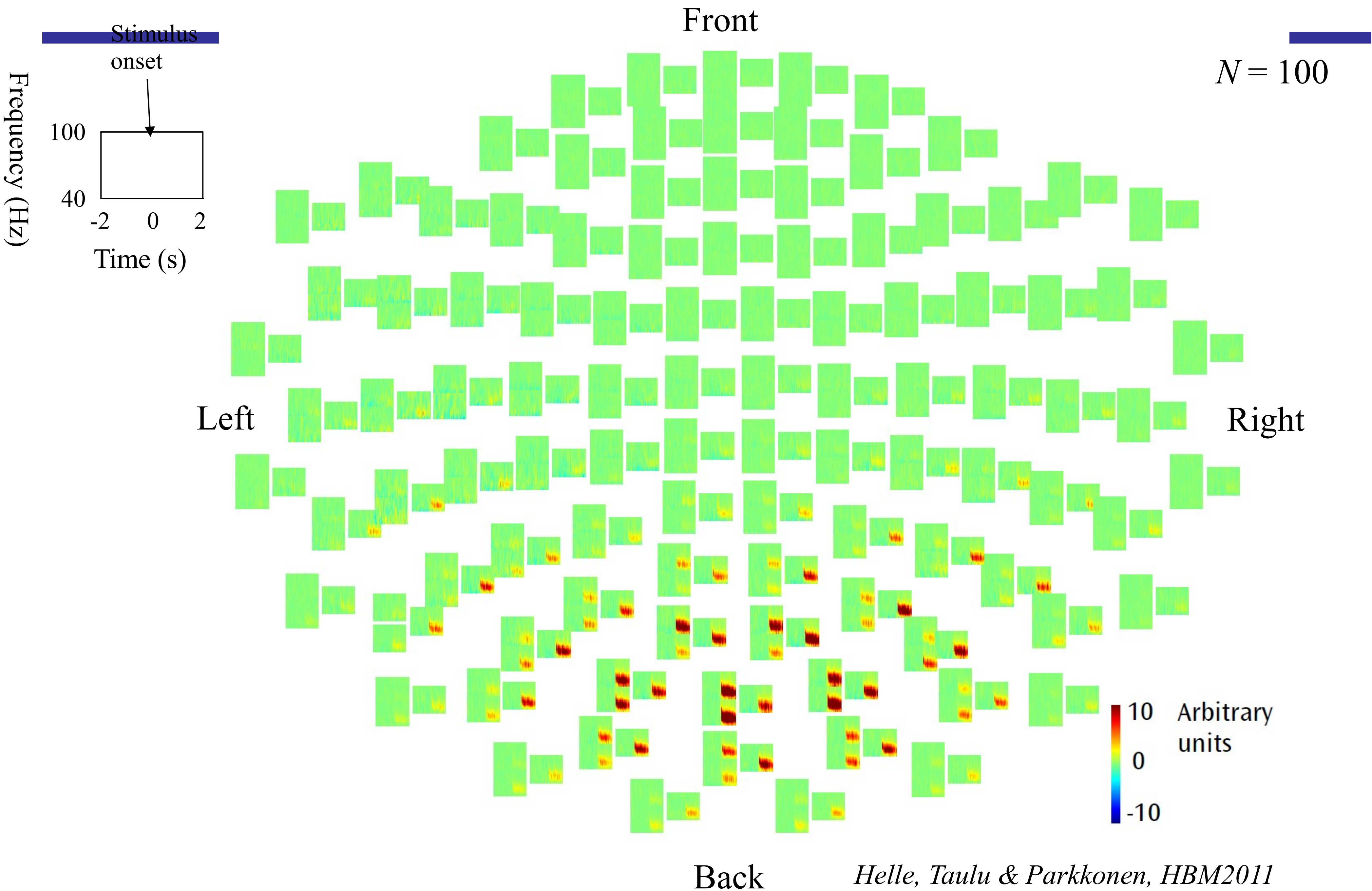
  Two subjects, 400 trials per subject in four blocks

- Analysis

  Wavelet-based extraction of instantaneous amplitude in time–frequency space

  Source modelling with beamformer; localization and computation of “virtual electrode” signals

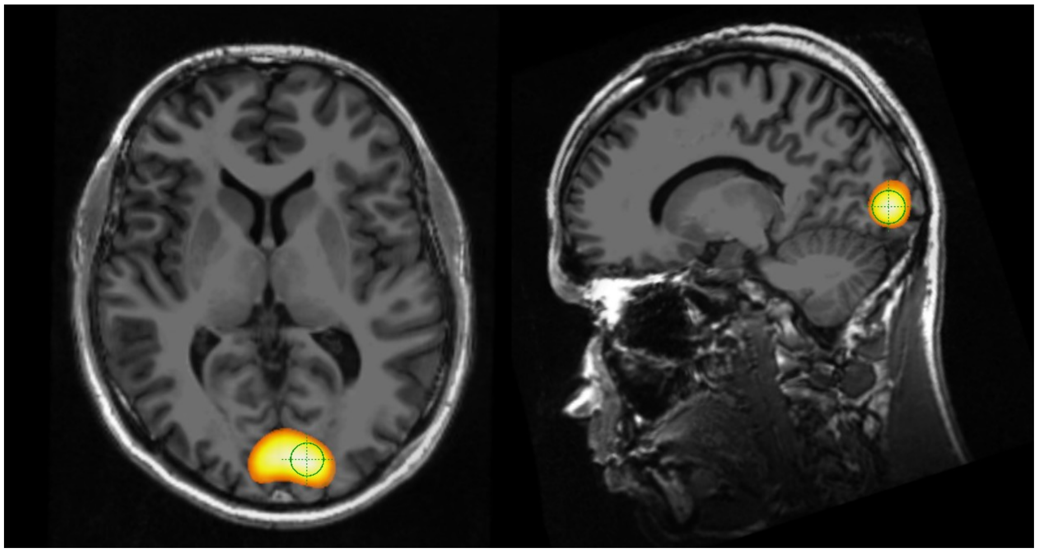
Induced gamma-band responses



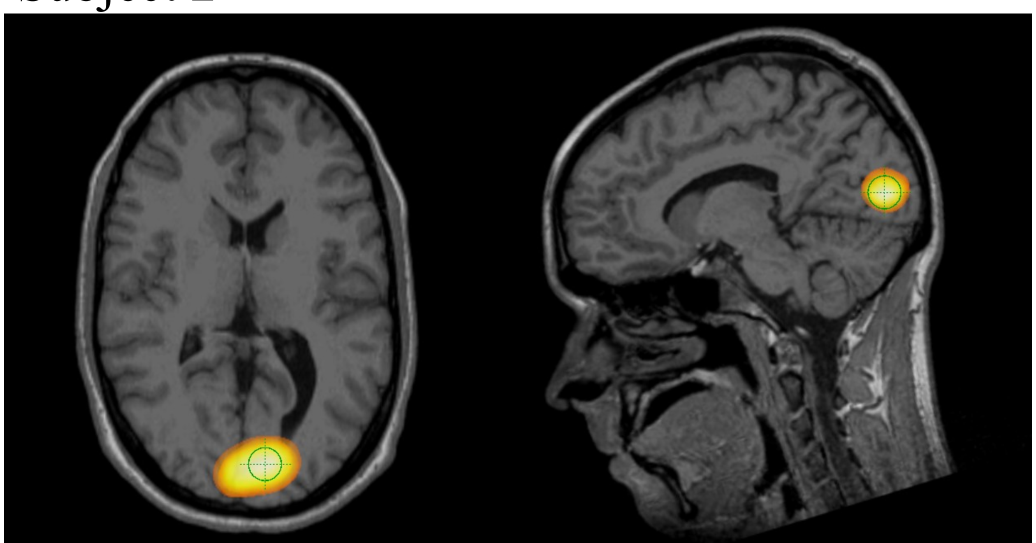
Helle, Taulu & Parkkonen, HBM2011

Gamma-band responses: Neural sources

Subject 1



Subject 2



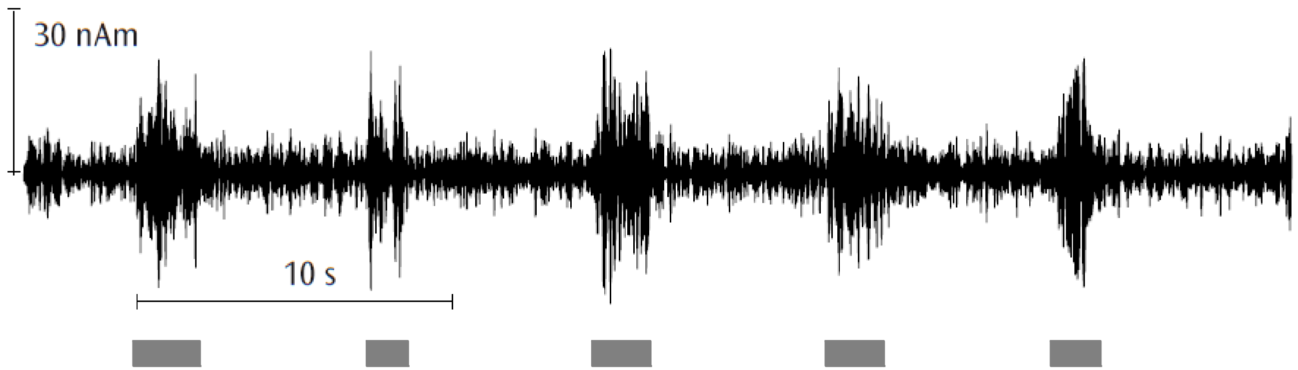
Beamforming

- Filtering to 55–80 Hz
- Dual-state construct (baseline vs. active)
- Scanning of the entire cranial volume

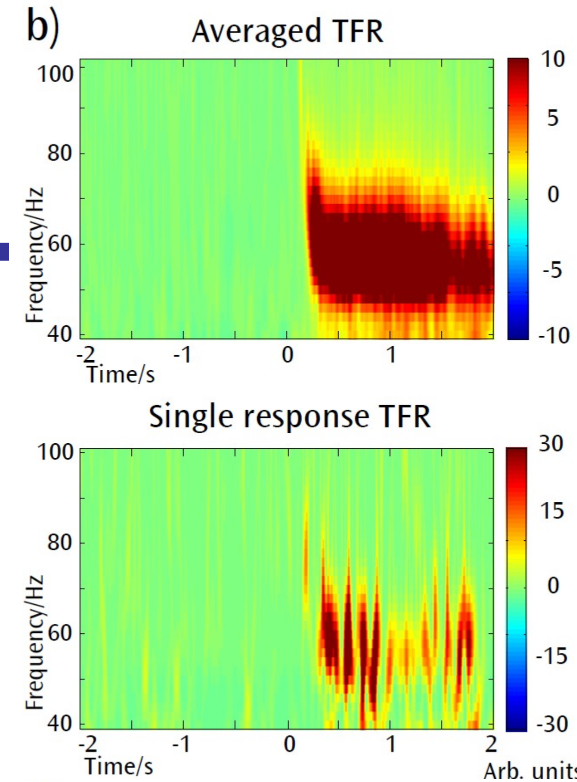
Helle, Taulu & Parkkonen, HBM2011

Gamma-band responses: Source signals

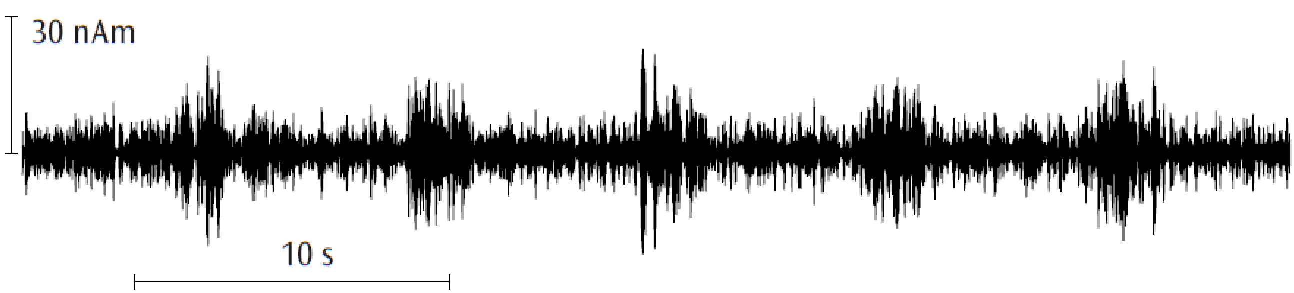
Subject 1

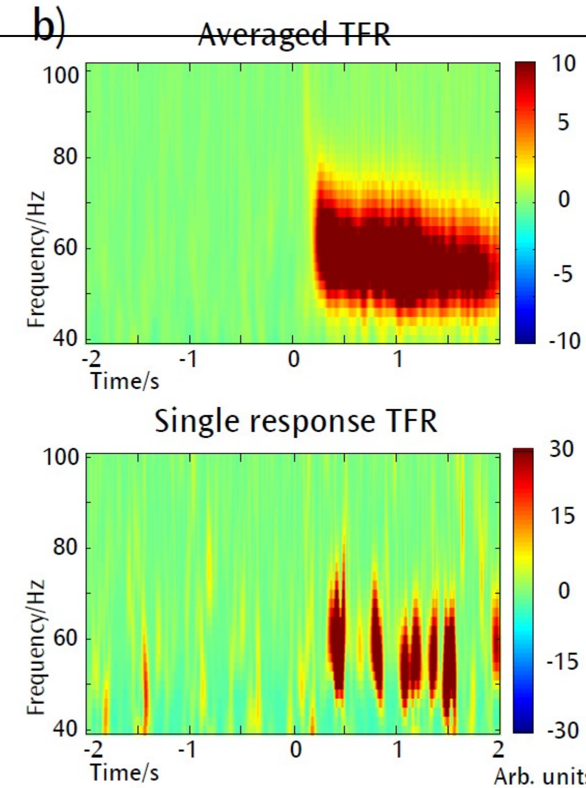


Single stimulus presentations



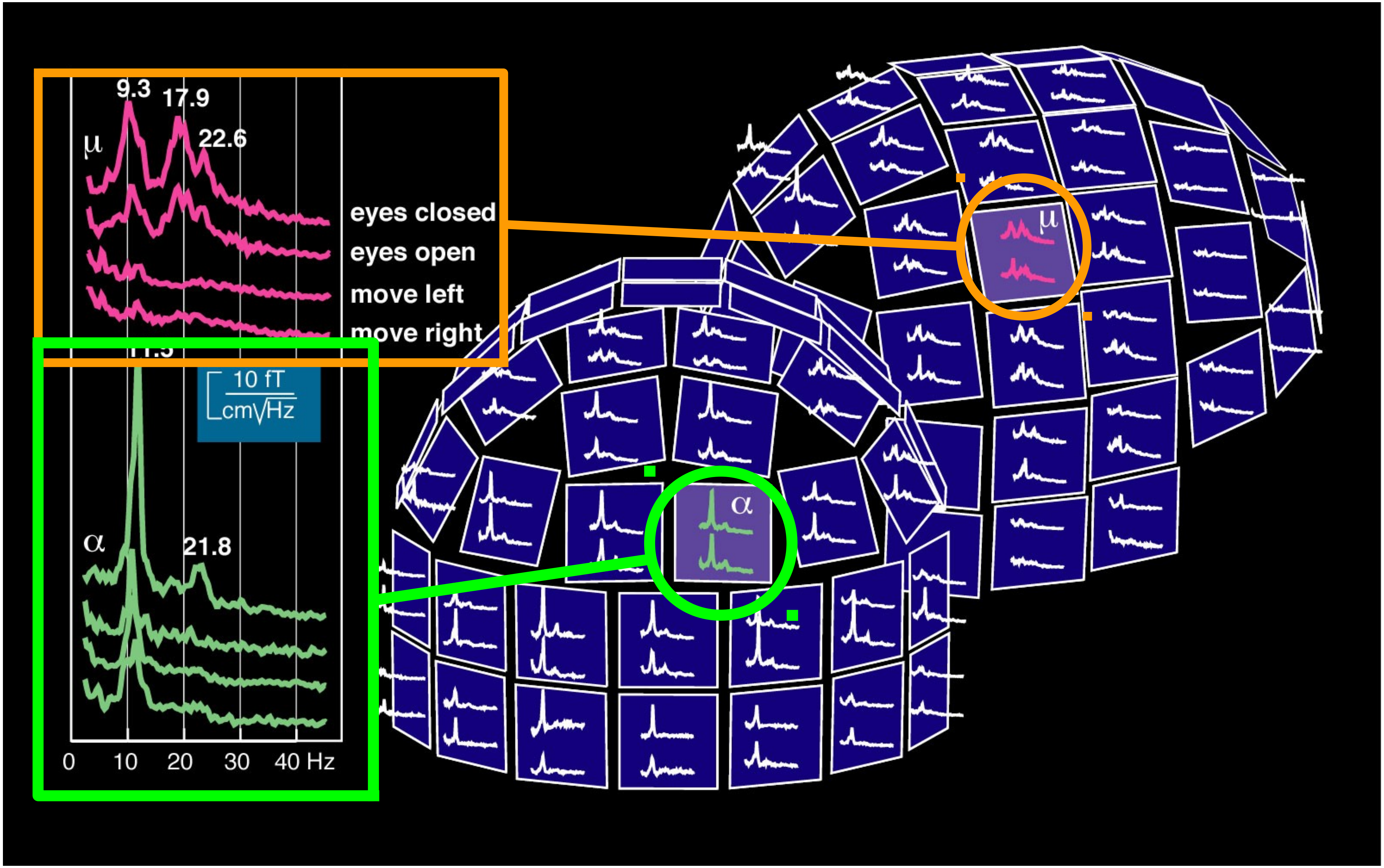
Subject 2





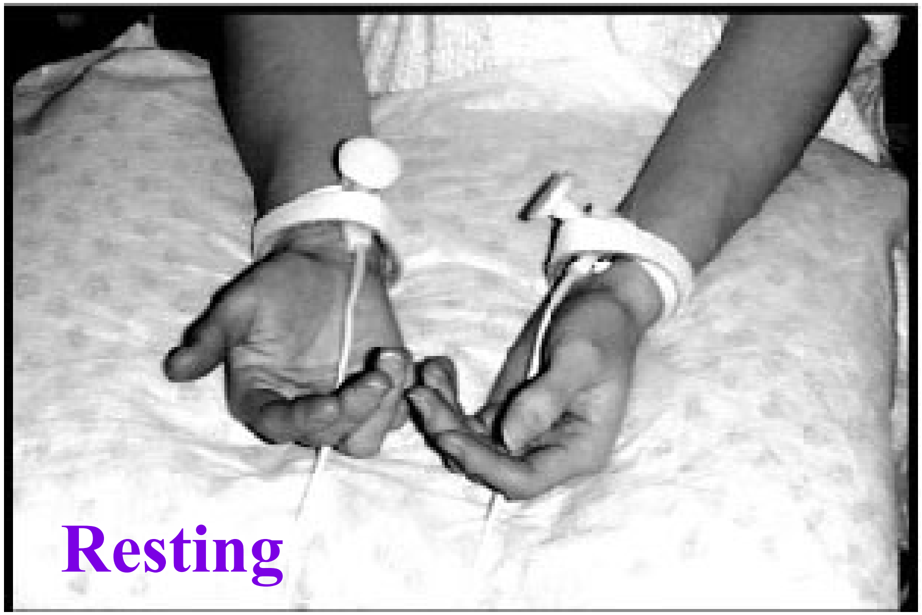
Helle, Taulu & Parkkonen, HBM2011

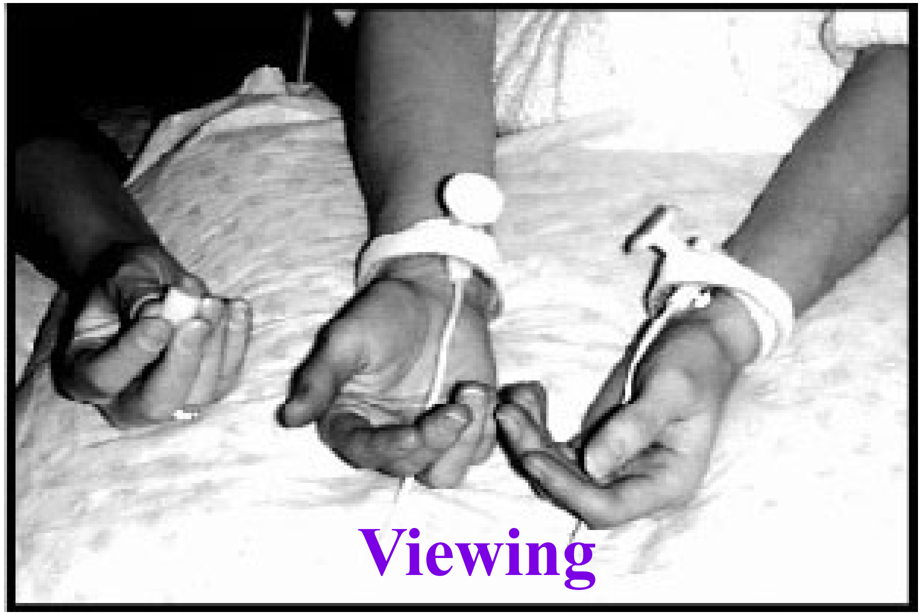
The well-known brain rhythms



Slide courtesy of R. Hari

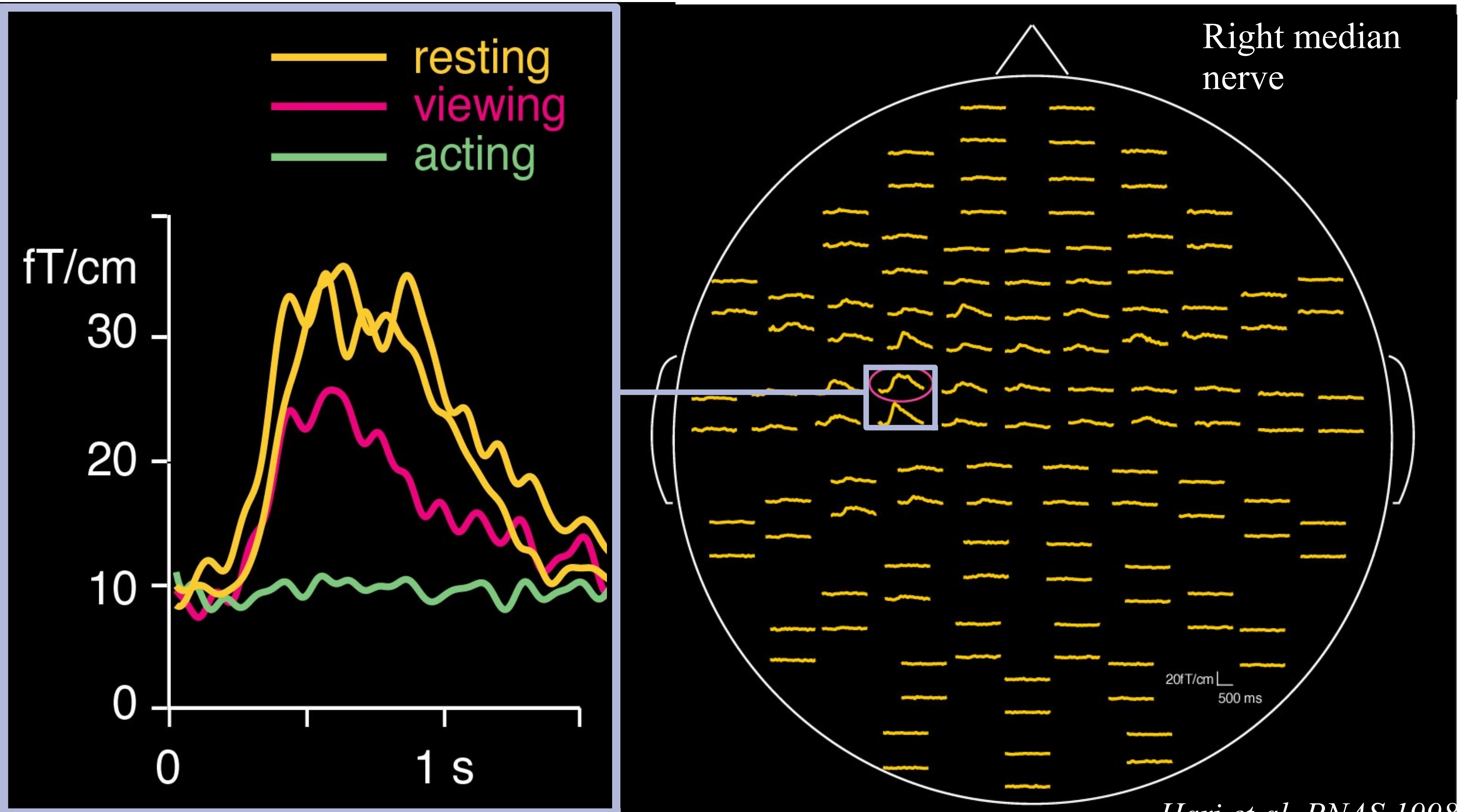
Induced responses: Action viewing





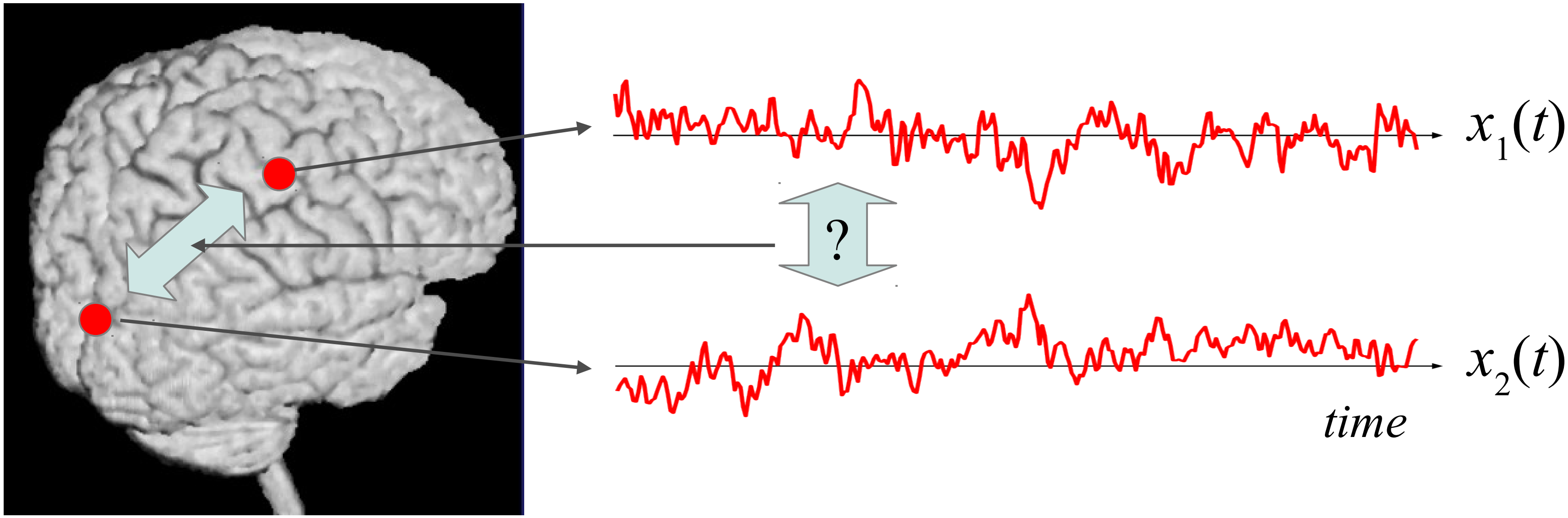
Induced responses: Action viewing

20-Hz level after the median nerve stimulus



Hari et al. PNAS 1998

Functional connectivity



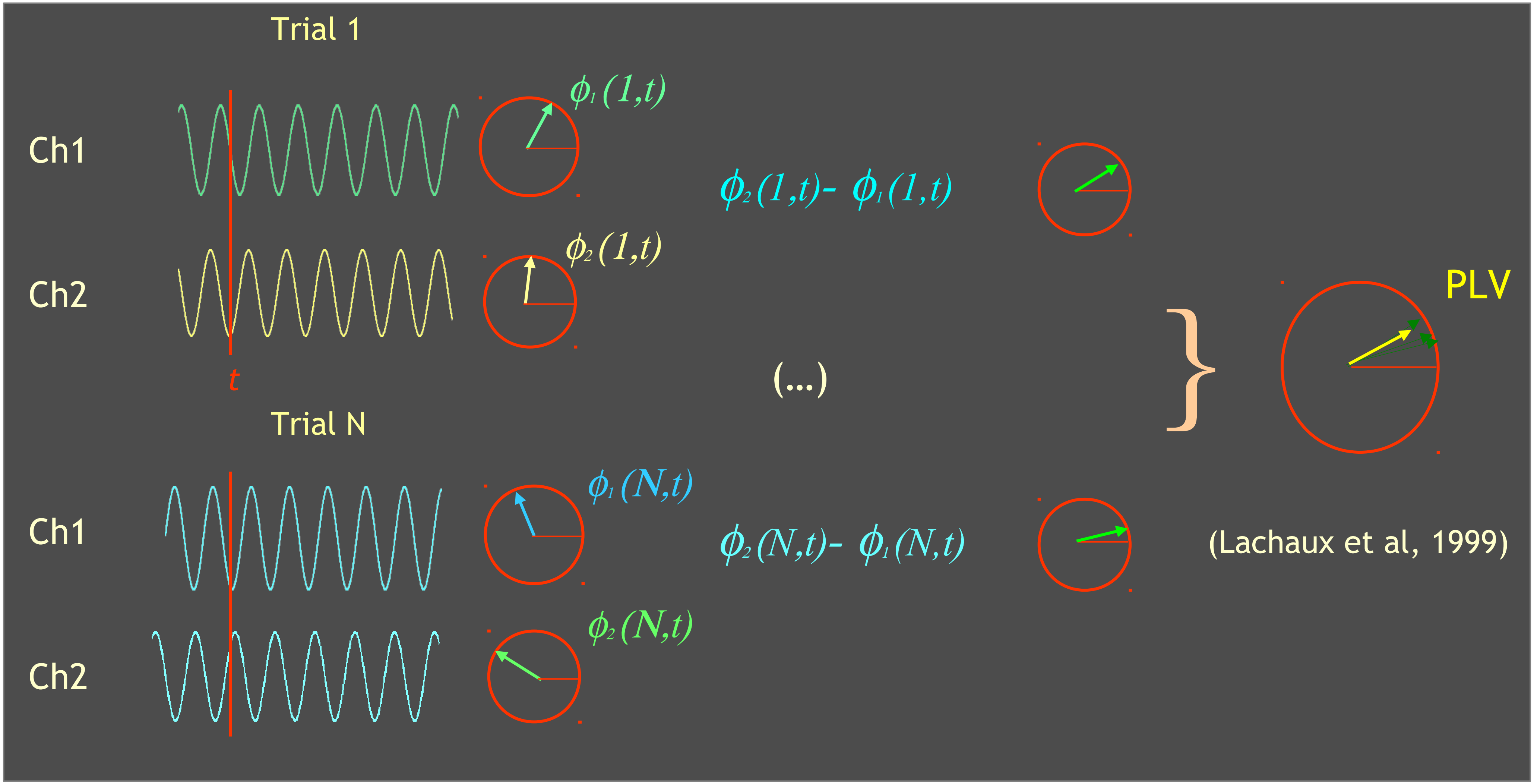
A statistical dependence of the activities of two cortical regions. Indicates information flow between those regions.

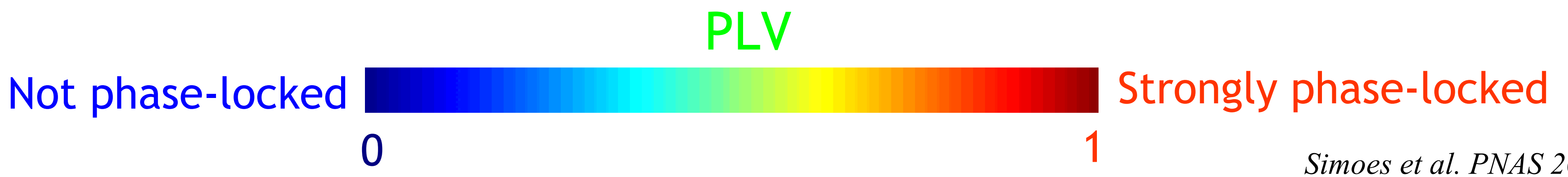
In MEG, x_1 and x_2 can be the time series of two MEG sensors or two cortical sources.

Dependence can be quantified in several ways: Correlation (with lag), coherence, phase locking, mutual information, ...

Direction of the information flow can also be estimated: Granger causality, ...

Functional connectivity: Phase-locking value (PLV)



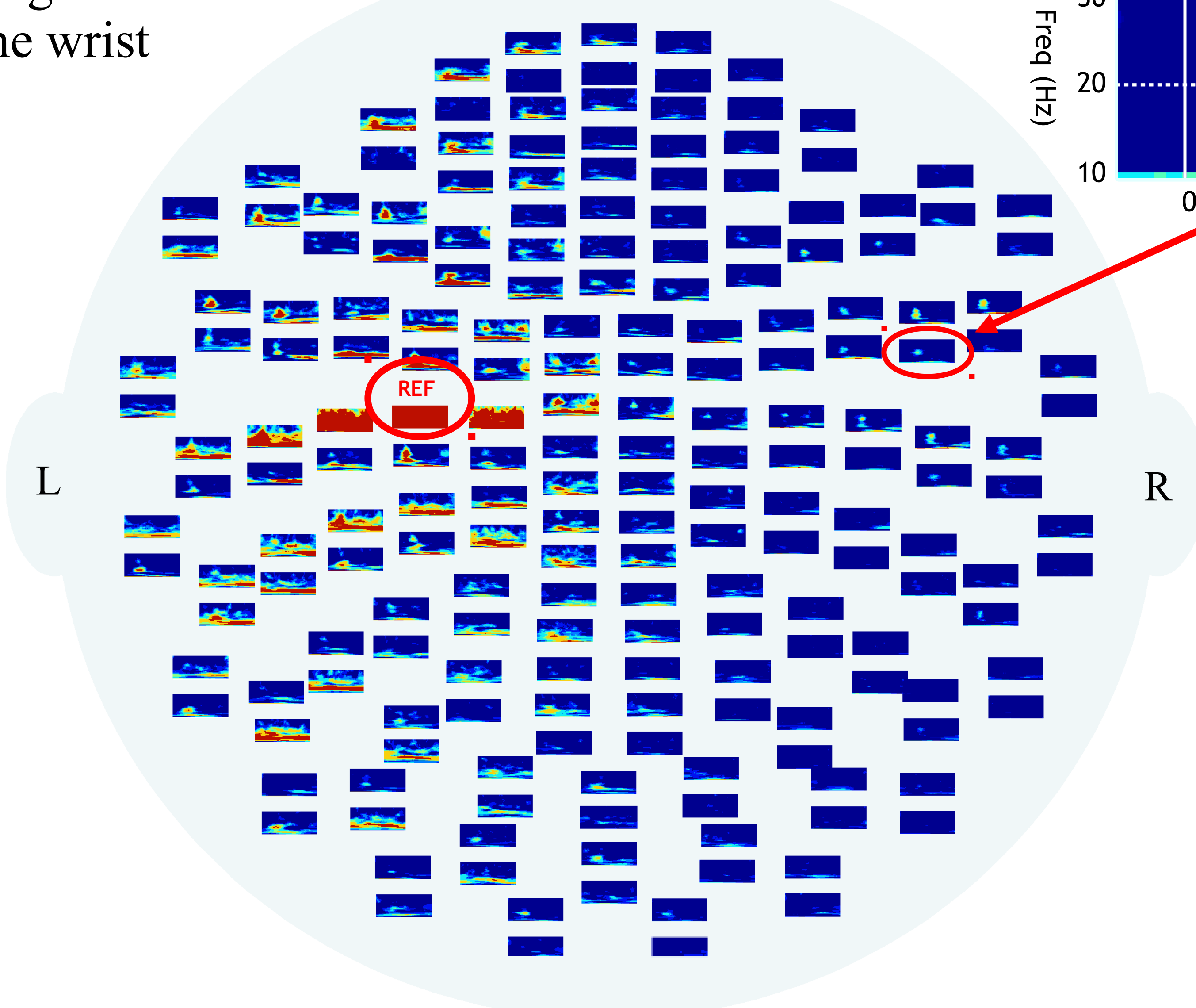


Simoes et al. PNAS 2003

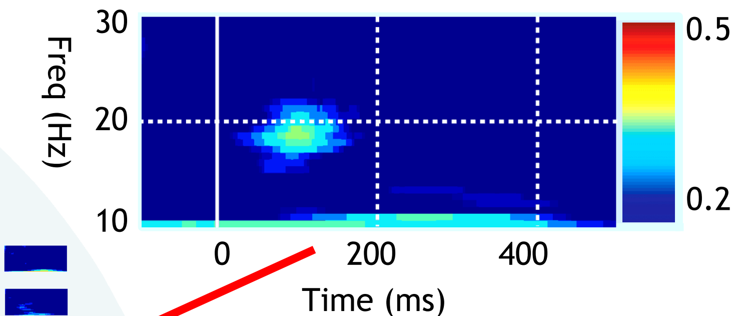
Connectivity: Phase locking between first and second somatosensory cortices

Electric stimulation of the right median nerve at the wrist

Phase-locking values (PLV)



Left SI *vs.* Right SII

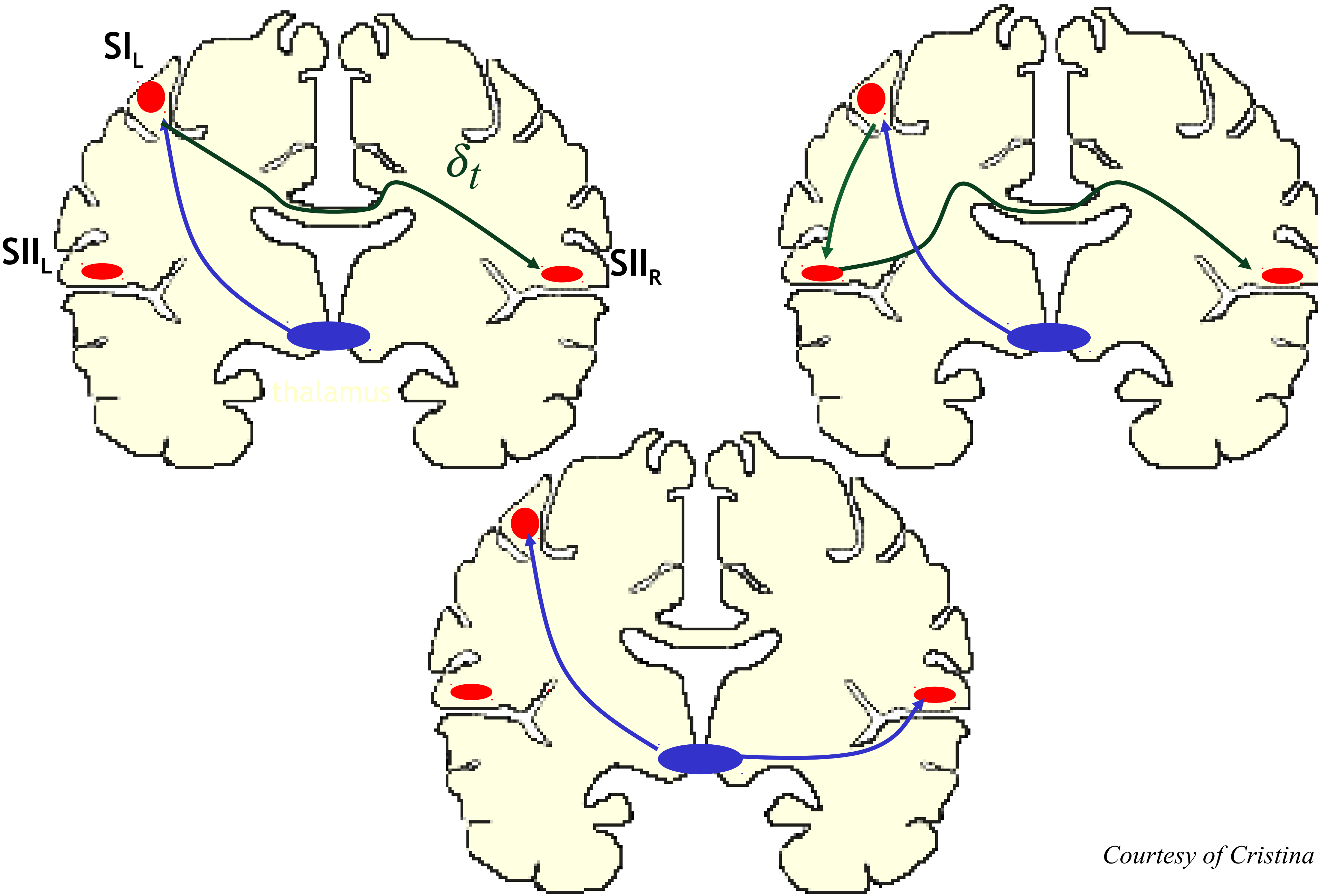


Statistical testing using surrogate data (permuting the trials of the REF sensor) to get the null distribution.

$p < 0.05$

Simoes et al. PNAS 2003

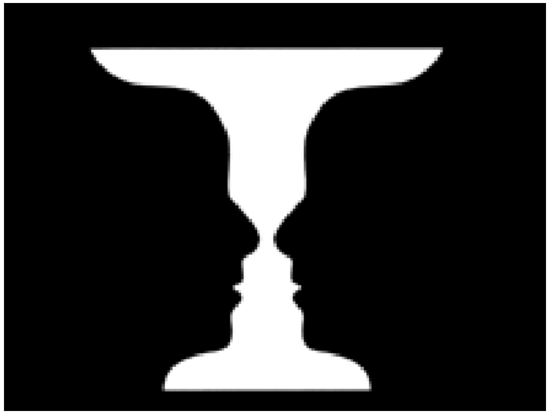
Interpreting connectivity: Do not forget the possibility of latent/hidden sources



Courtesy of Cristina Simoes

Tagged stimuli: Studying bistable perception with MEG

- Ambiguous figures often evoke alternating percepts (perceptual bistability)

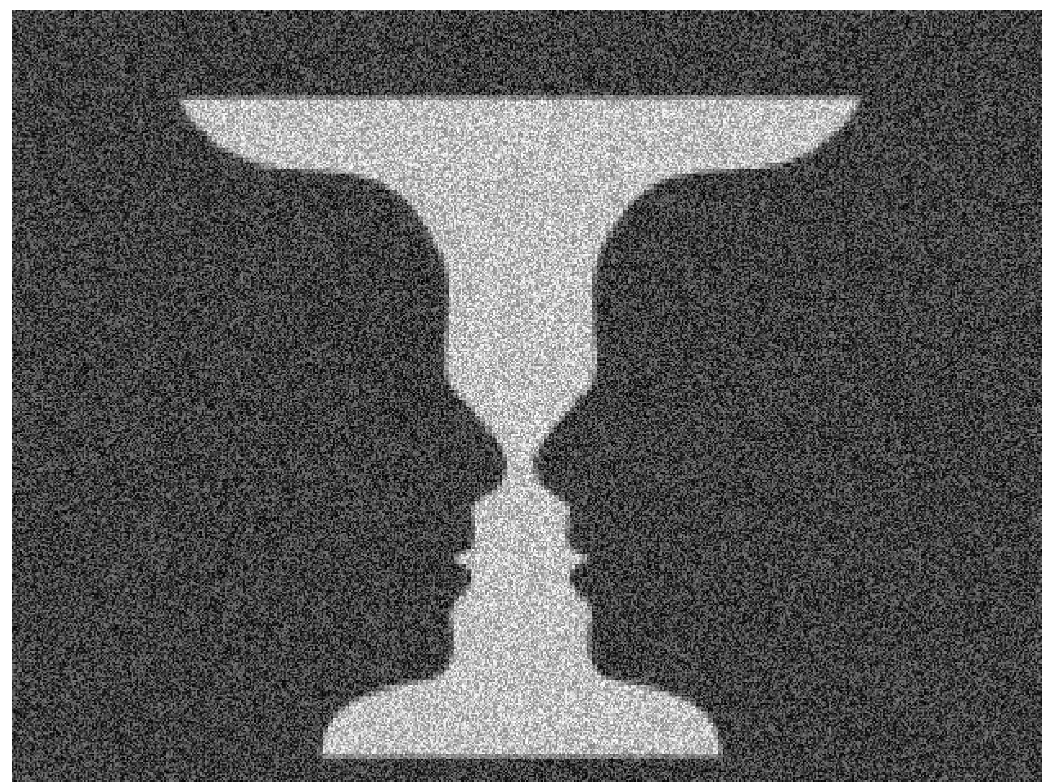


- Physical stimulus invariant but perception changes
- How do the “brain states” of the two percepts differ?

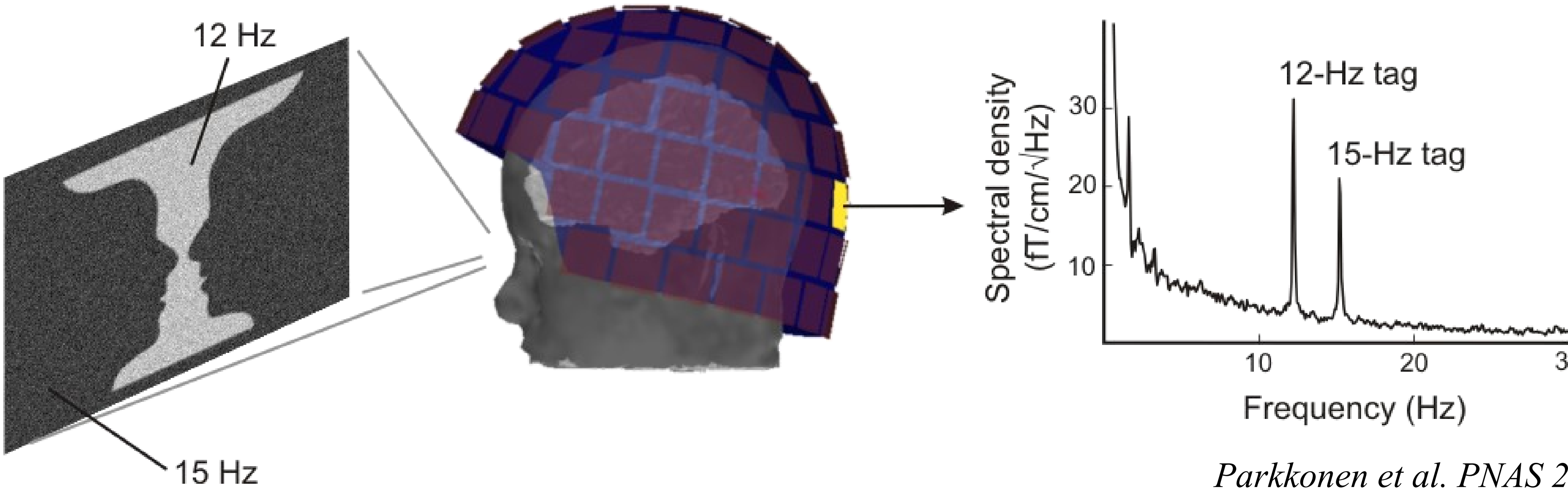
Bistable vision: Stimulus

- Rubin's face-vase figure with superimposed dynamic tag signals
- Tags: Random noise patterns updated at:
  - 12 Hz for the vase region
  - 15 Hz for the faces

A slow-motion illustration



Bistable vision: Experiment



Parkkonen et al. PNAS 2008

- Do the tag-related signals modulate with the percept?
- MEG experiment:
  - fixate between the “noses”
  - report the percept with the right index finger
  - 10-min recording

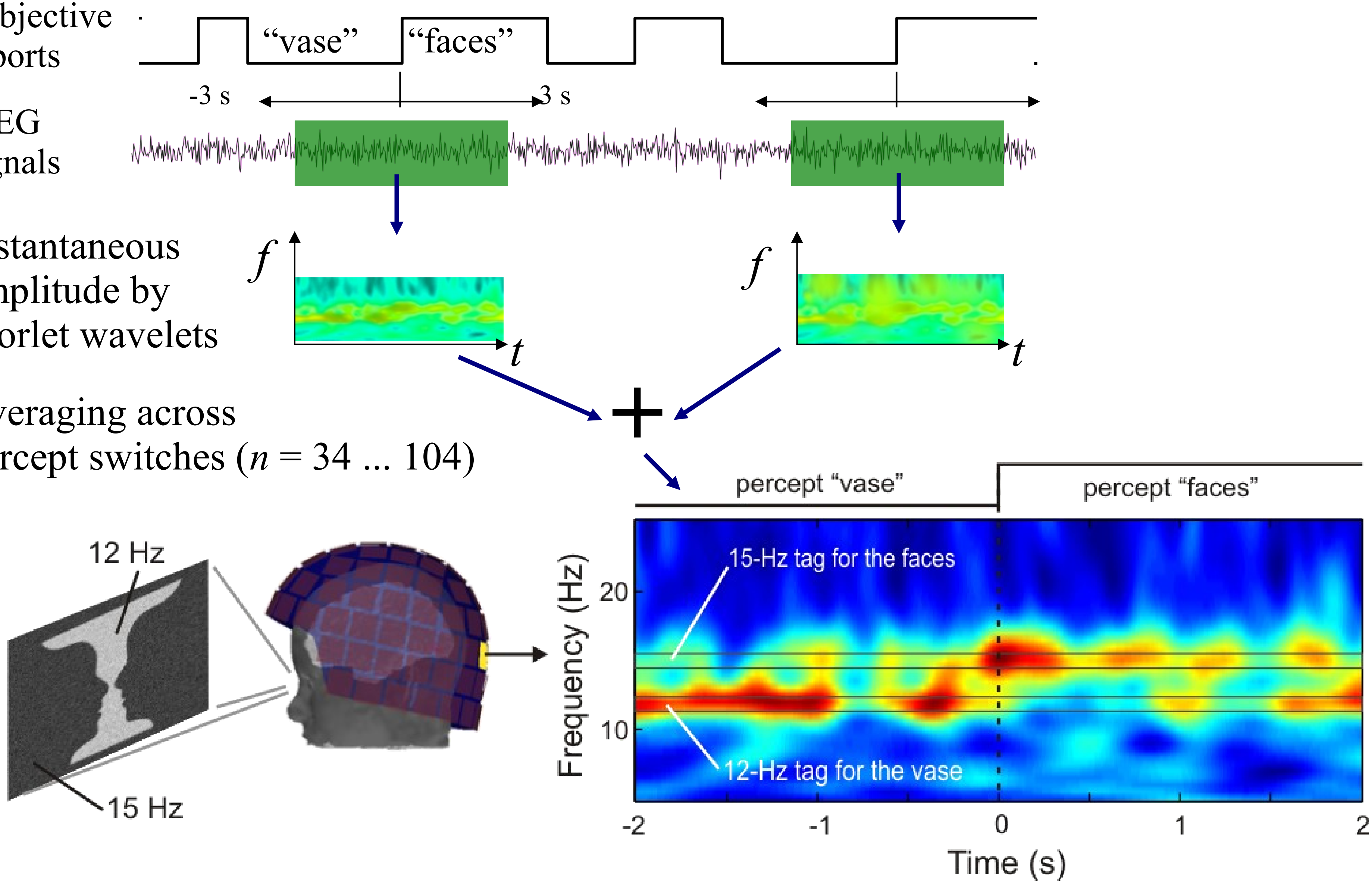
Dynamics of the tag signals

Subjective reports

MEG signals

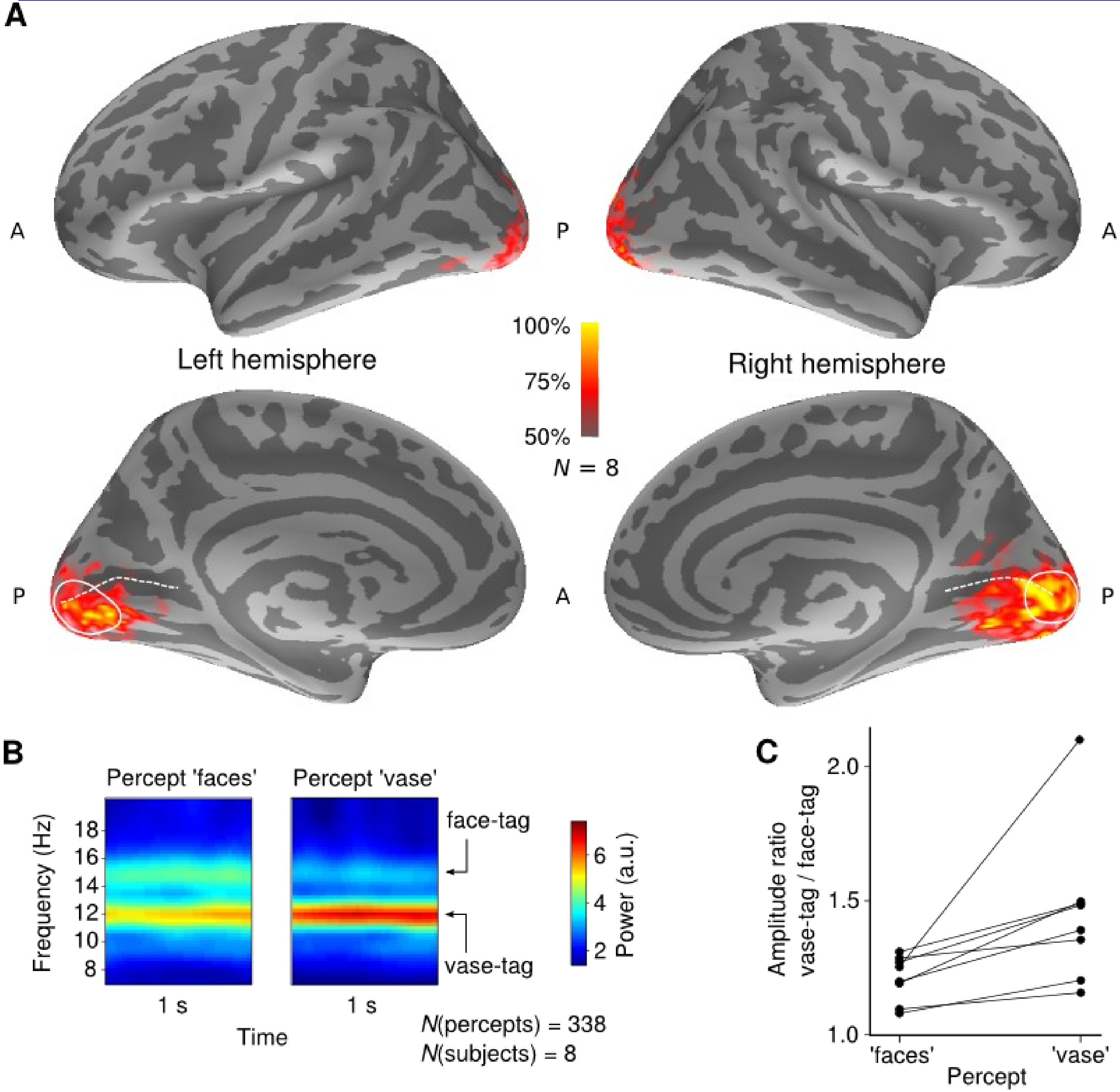
Instantaneous amplitude by Morlet wavelets

Averaging across percept switches (n = 34 ... 104)



Parkkonen et al. PNAS 2008

Cortical signal sources



Parkkonen et al. PNAS 2008

Bistable perception: Discussion

- Perceptual bistability is manifested in the activity of the early visual cortices
- The observed modulation is most likely a top-down effect that accentuates the “object part” of the visual field and suppresses the background, cf. figure–ground segregation.
- Early visual areas contribute directly to visual awareness and conscious vision.

Conclusions

- MEG and EEG excel in studies that require high temporal resolution
- Ideal applications: Tracking cortical activation sequences and functional connectivity at short time scales
- MEG generally allows better localization than EEG
- MEG/EEG data can be looked at in many ways
  - Evoked responses: transients to, e.g., changes in sensory input
  - Induced responses: changes in the amplitude of ongoing neural oscillations
  - Functional connectivity changes
  - Responses to tagged stimuli