Oscillatory responses and functional connectivity

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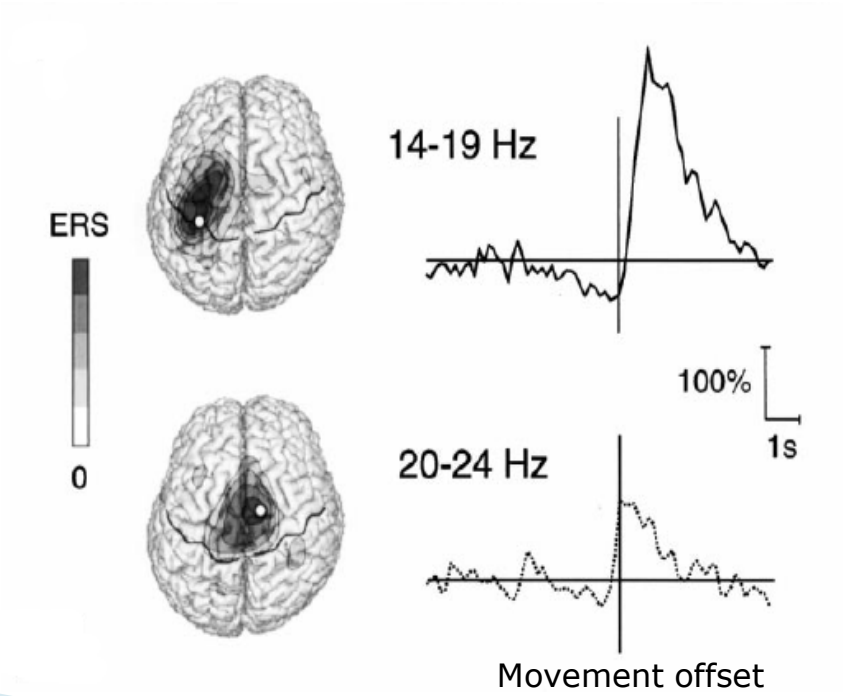
Contents

- Modulation of rhythmic/oscillatory activity in the brain
  - induced (non-phase-locked frequency specific) activity
- Rhythmic/oscillatory (frequency specific) interactions
  - Functional/effective connectivity
- Cortical level analysis of both rhythmic activity and connectivity
  - Primarily with beamforming techniques

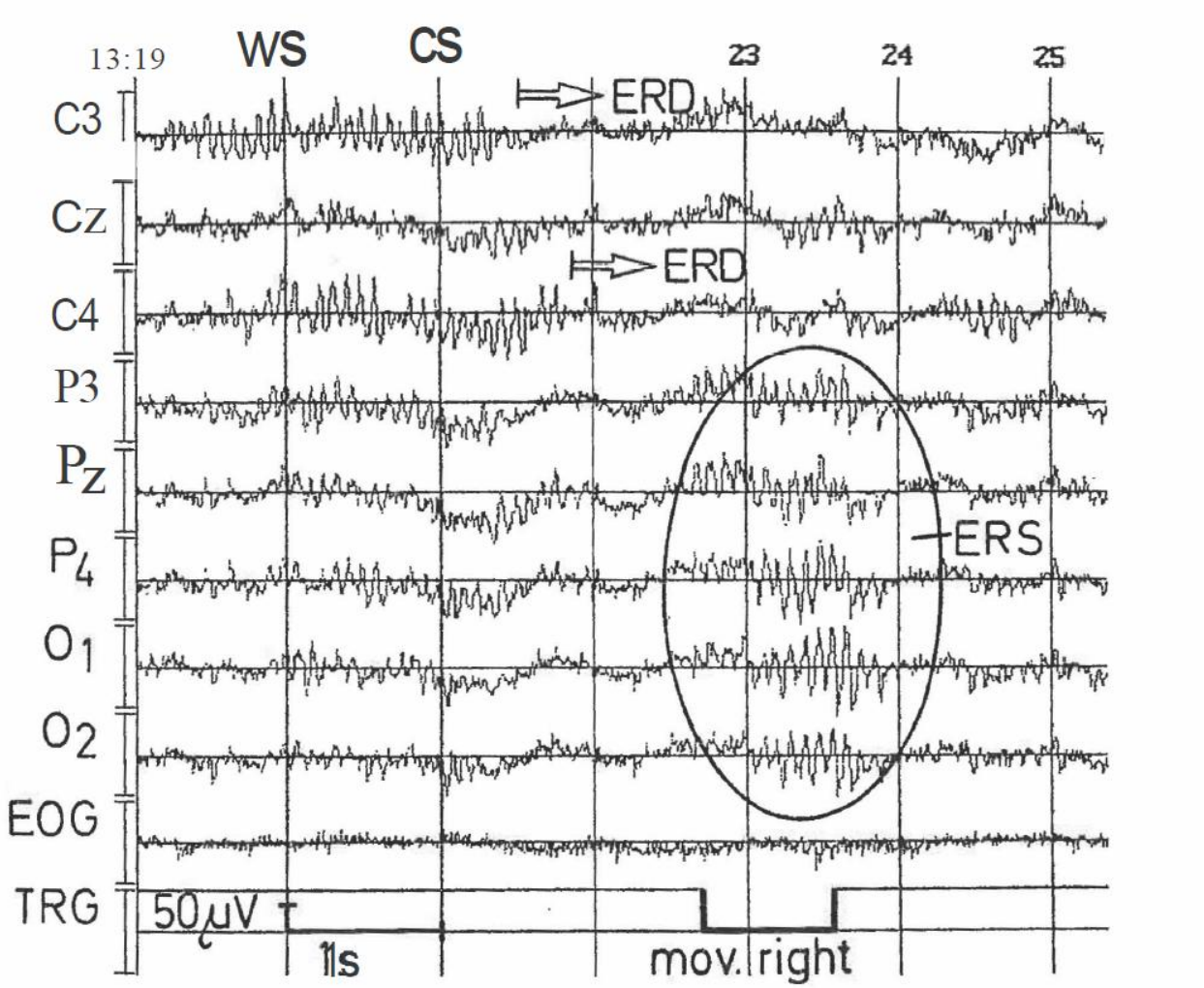
Modulation of rhythmic activity

- Stimuli and tasks can transiently modulate level of rhythmic activity
  - Both suppression and enhancement



Pfurtscheller Neurosci Lett 2000

Rhythmic modulation in raw data



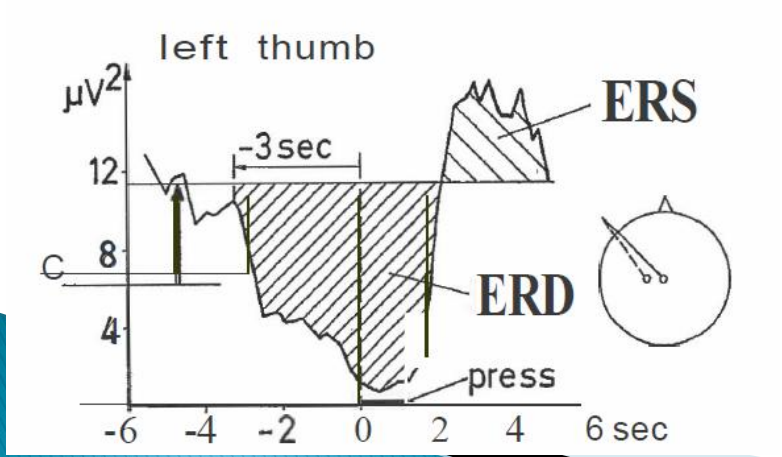
Pfurtscheller EEG Clin Neuro1992

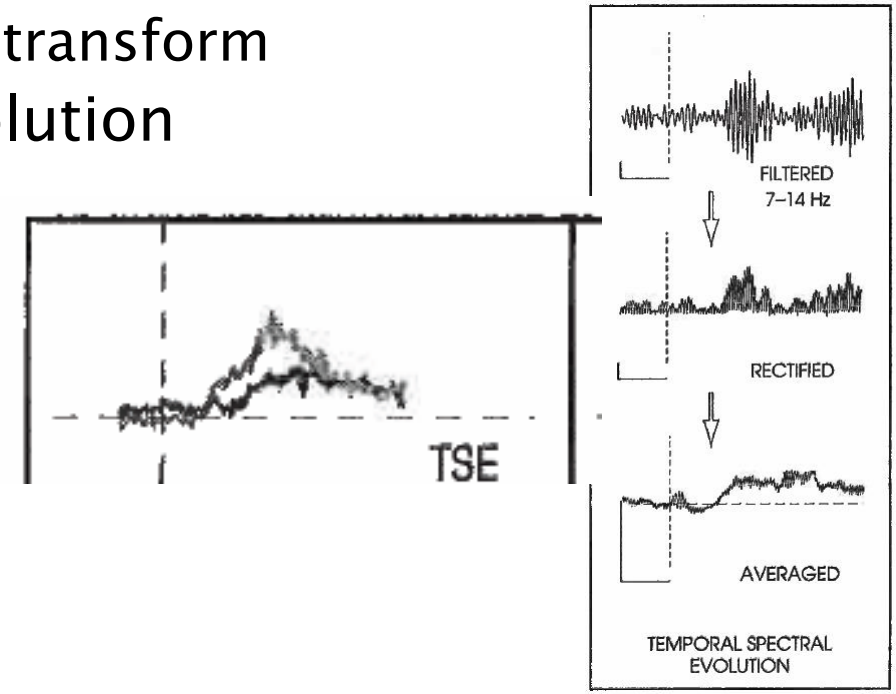
Spectral analysis (estimation) techniques

- Filtering-based techniques
- Short-time/term Fast Fourier Transform (SFFT)
- Wavelet transform

Filtering-based approaches

- Time-series filtered to *a priori* defined bands
- Amplitude/power estimation per trial
  - Event-related synchronization/de-synchronization
    - Squared signal/hilbert transform
  - Temporal-spectral evolution
    - Rectification
- Averaging

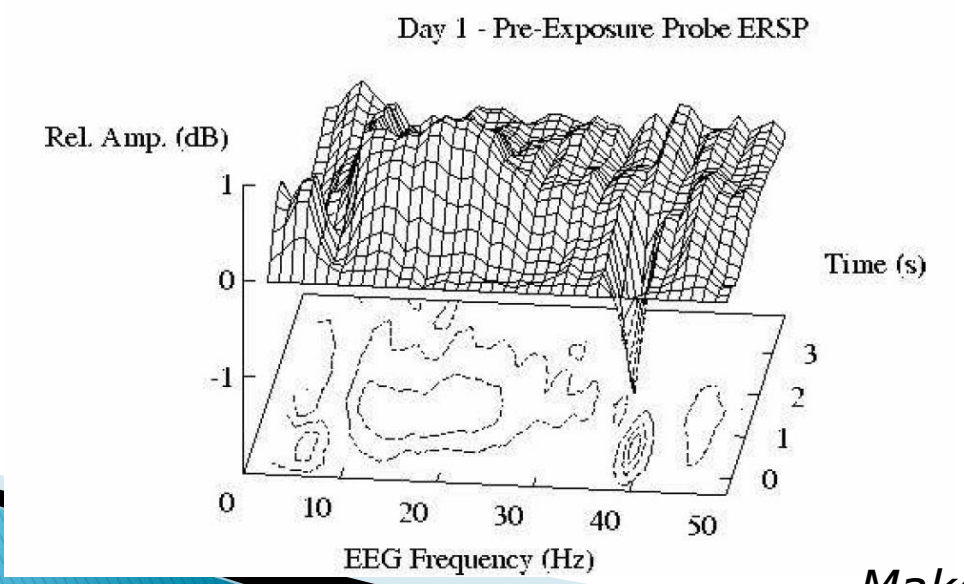




Pfurtscheller Elec Clin Neuro1992
Salmelin & Hari Neuroscience 1994

SFFT

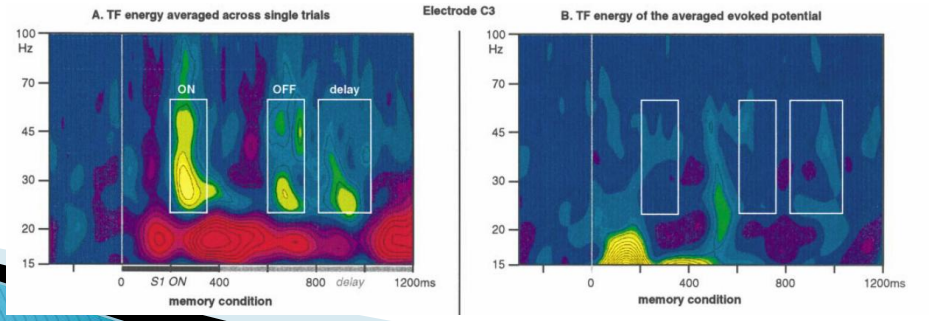
- Event-related spectral pertubation (ERSP)
  - Short FFT segments (e.g. 256 samples) with large (e.g. 75%) overlap
  - Segments windowed and averaged across trials
  - At typical sampling frequencies and trial lengths, spectral estimates at ~5-20 time instances



Makeig EEG Clin Neuro 1993

Wavelets

- Time-frequency representation (TFR)
  - Convolution of trial time-series with wavelets (=a bank of filters)
    - de-trending before convolution
  - Complex data, absolute squared values for power
  - Averaging
- Length of convolution window depends on frequency band
  - Better compromise between time and frequency resolutions than with SFFT

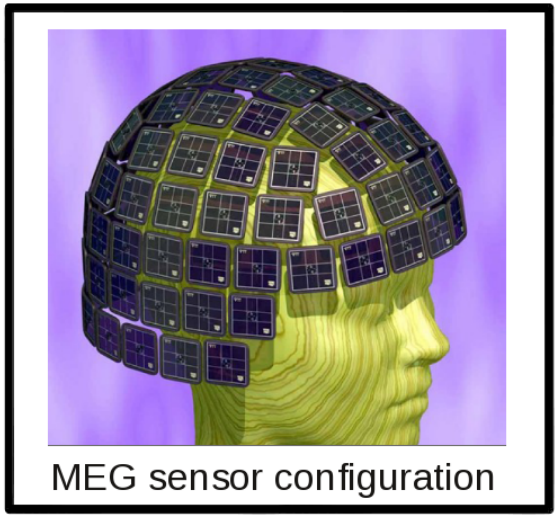


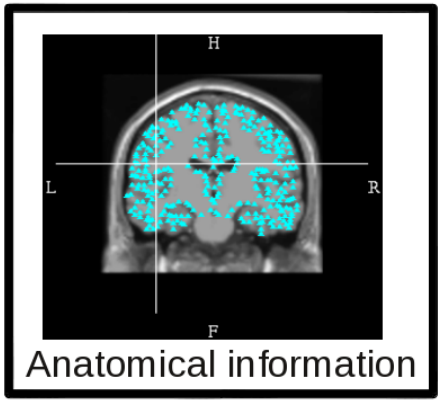
Tallon-Baudry J Neurosci 1998

Cortical level analysis of rhythmic activity

- Continuous data
  - Sequential dipole-modeling (sECD)
  - Frequency domain minimum current estimate (MCE_{FD})
  - Beamforming
    - Dynamic Imaging of Coherent Sources (DICS)
- Event-related data
  - Minimun Norm Estimate (MNE)
  - Beamforming
    - event-related Dynamic Imaging of Coherent sources (erDICS)

Cortical-level MEG



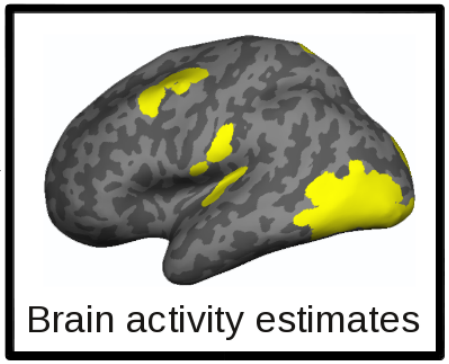


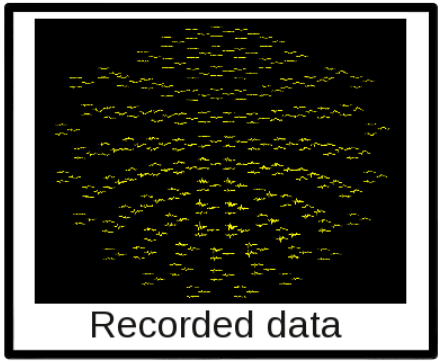
Forward solution

$$\min_{A}[AC(f)A^T + \alpha\|A\|^2] \quad with \quad AL(r) = 1$$

Mathematical constraints

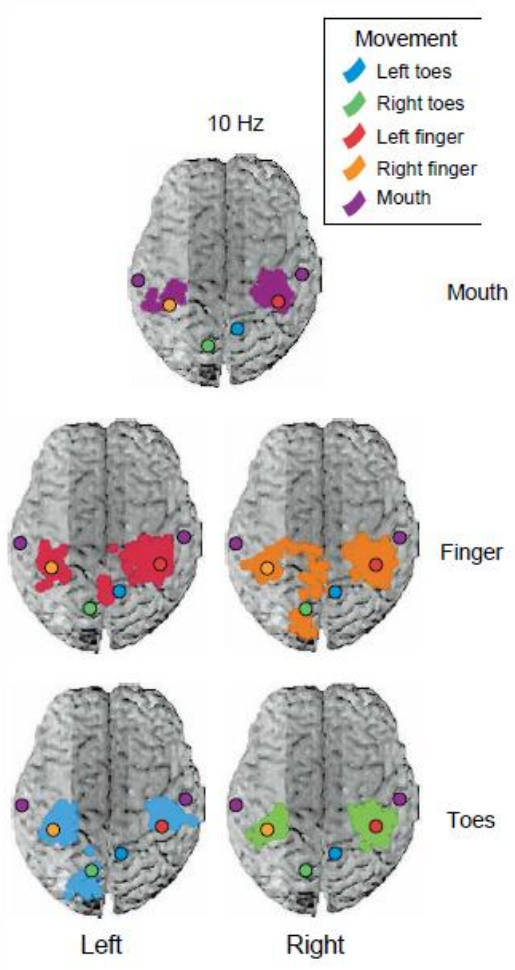
Inverse solution





Sequential dipole modeling

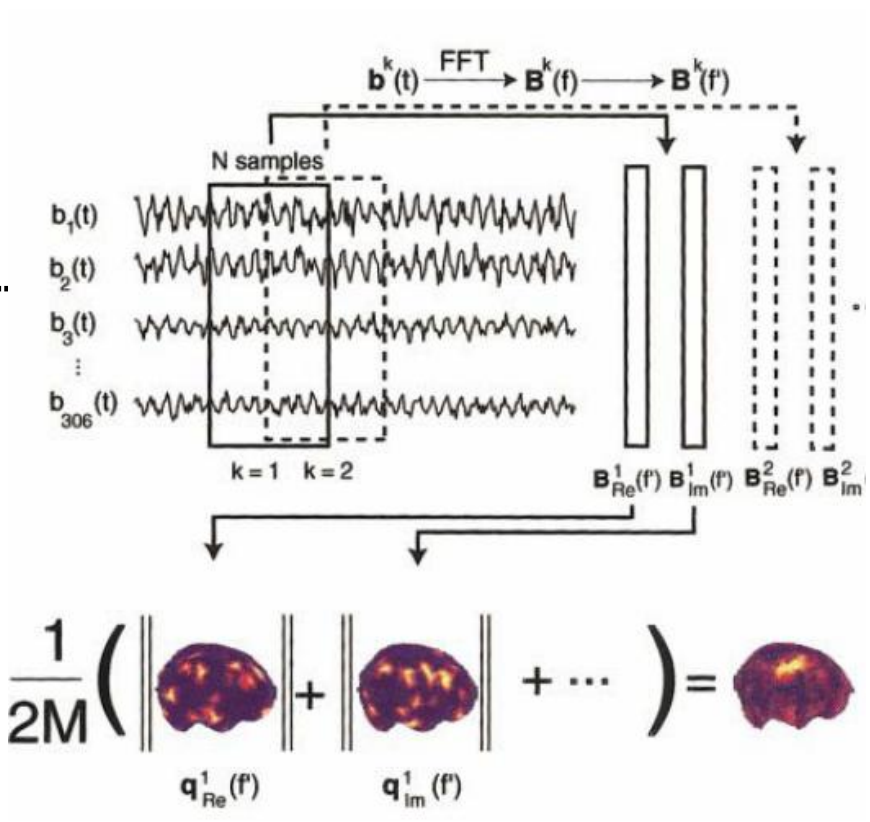
- Filtering the signal to a selected band (e.g. 8–13Hz)
- Sequential dipole modeling at e.g. every 10 ms
  - Sensor selection, goodness-of-fit
- Clustering/dipole density



Hari & Salmelin TINS 1997

Frequency domain minimum current estimate

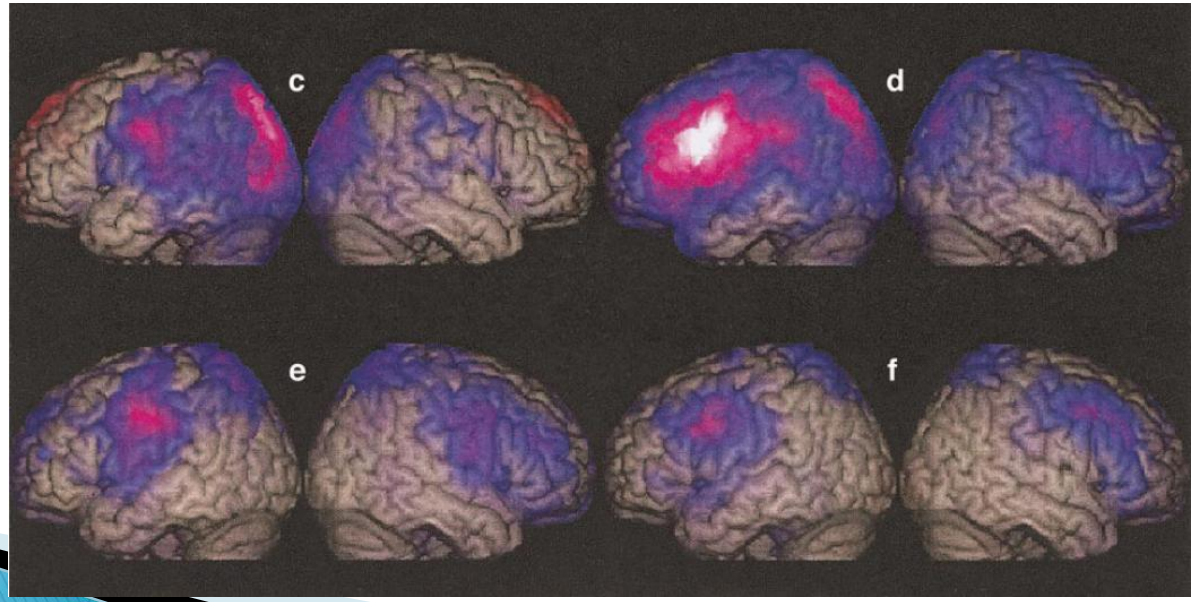
- Windowing
- DFT
- MCE on the real and imaginary part of DF
  - Per window
  - absolute value after MCE
- Averaging



Jensen & Vanni Neuroimage 2002

Beamforming, option #1

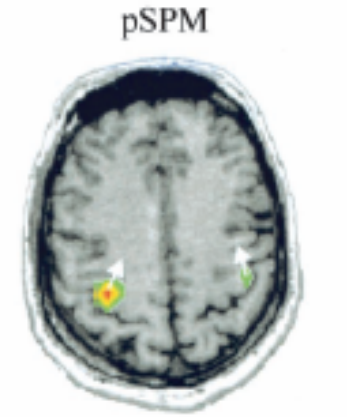
- E.g. synthetic aperture magnetometry
- Estimation of time-series at cortical-level (virtual electrodes)
- Computation of spectral estimates for estimated time-series



Singh et al Neuroimage 2002

Beamforming, option #2:Dynamic Imaging of Coherent Sources

- Transformation of the MEG signals into frequency domain at sensor-level
  - Transformation close to Welch's modified periodogram method
    - Cross combinations between all MEG sensors
    - Cross spectral density (CSD) matrix obtained
- Direct computation of power at cortical level from the CSD
  - No need for time-series estimation at virtual channels

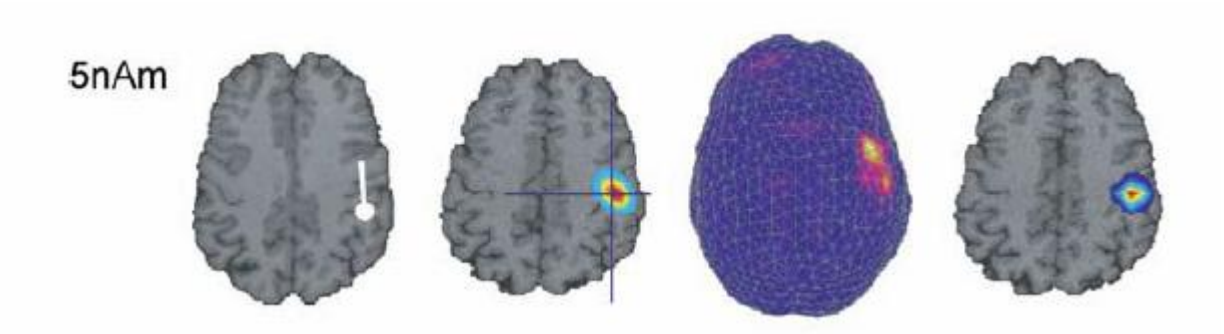


Gross et al PNAS 2001

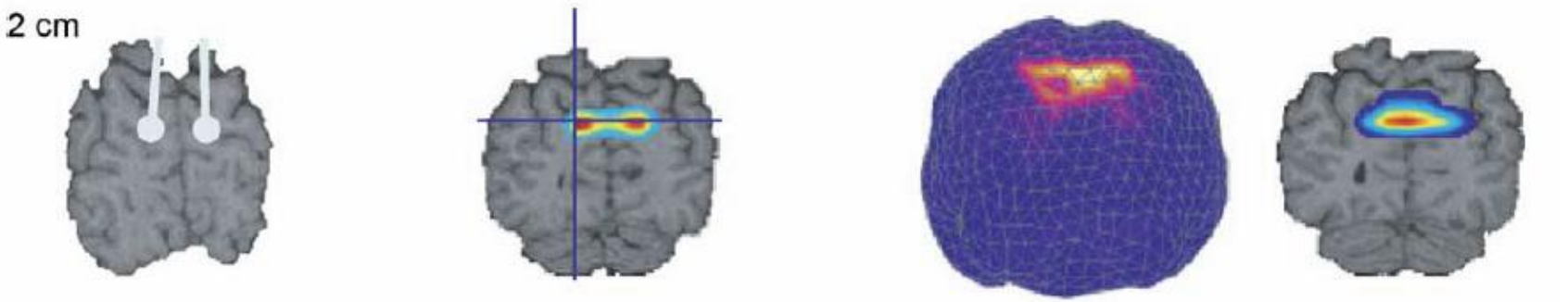
Welch's averaged, modified periodogram

- Prior to DFT
  - data divided into partially overlapping segments
  - windowing functions applied to reduce spectral leakage
- Variance and effects from random noise reduced due to the averaging
- Lowered spectral resolution

Differences (?) between source localization approahces



A single source

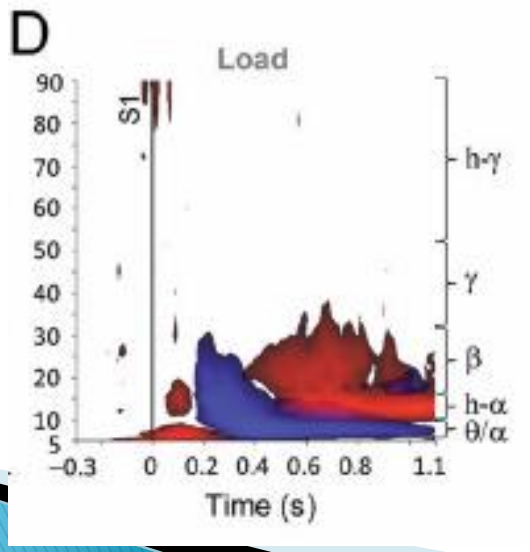


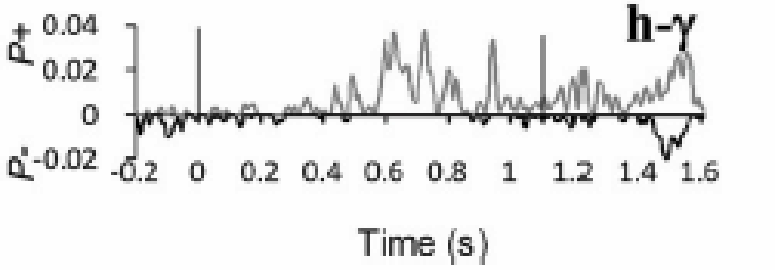
2 close-by sources

Liljeström et al Neuroimage 2005

Minimum norm estimate

- Inversion of sensor-signals into cortical space
  - Raw time-series inversion
    - Analysis of oscillatory activity for estimated time-series
  - Filtered/wavelet-transformed data inversion
    - More specific weighting of the inversion

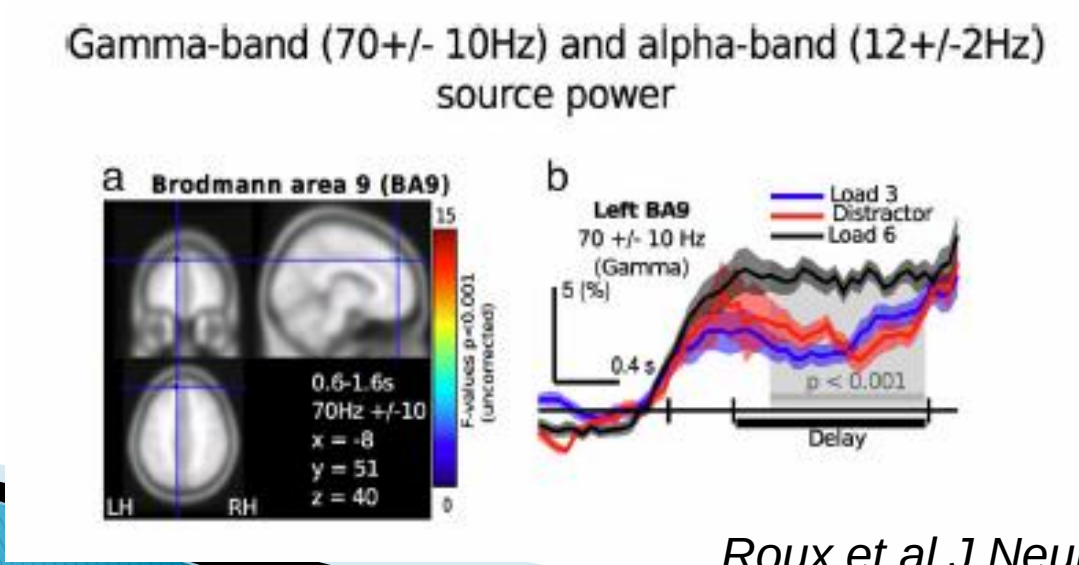




Palva et al J Neurosci 2011

Beamforming, option #1

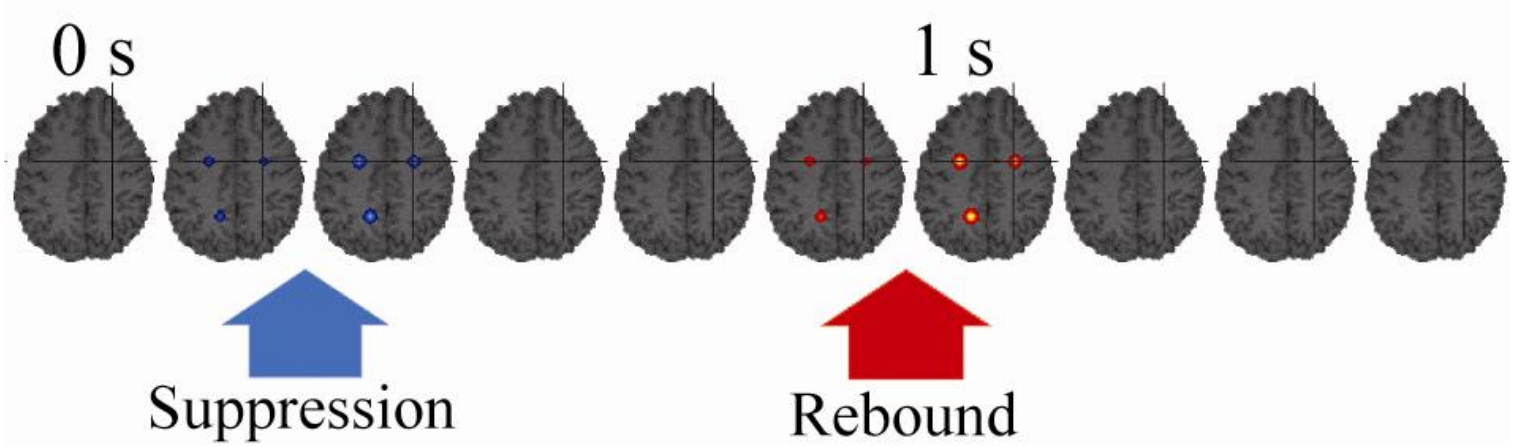
- Estimation of time-series at cortical-level (virtual electrodes)
  - E.g. with DICS CSD as the basis for weighting the sensor-level data
- Computation of spectral estimates/filtering using the obtained time-series



Roux et al J Neurosci 2012

Beamforming, option # 2: event-related DICS (erDICS)

- Cross spectral density matrix as a function of time (wavelets)
- Direct estimation of oscillatory dynamics at cortical level (without time-series estimation)



Laaksonen et al Neuroimage 2008

Statistical evaluation of the results

- Distribution of modulation of oscillatory activity not necessarily normal
  - Non-parametric statistics
- Large dimensionality of time-frequency-spatial data
  - Correction for multiple comparisons
    - Permutation statistics
      - Individual and group-level
- Variability of the data across multiple dimensions
  - Individual- vs. group-level analysis?
    - Systematicity of individual-level results (?)

Maris et al J Neurosci Methods 2007

Rhythmic interactions

- Rhythmic/oscillatory (frequency specific) interactions
- Cognitive functions are thought to build on connectivity within large-scale neuronal networks
  - Synchrony over multiple frequency bands most likely mechanism of large-scale integration *(Varela et al Nat Rev Neurosci 2001)*
- Both coactivation and causality measures used for estimation of interactions
  - Functional/effective connectivity

Coactivation measures

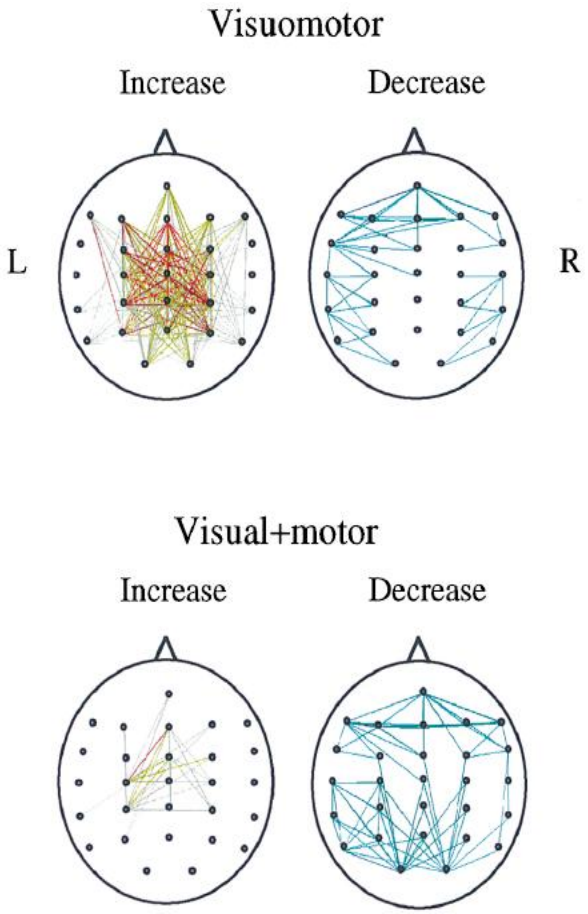
- Coherence: cross-spectral density normalized with power spectral densities
  - Co-occurrence of oscillations, amplitude dependent
- Phase locking (PLV/PLS): estimation of phase difference constancy in event-related paradigms
  - Estimation of phase
- Synchronization index (SI): estimation of preferred phase difference
  - Applicable to continuous tasks
  - Estimation of phase

Causality measures

- Directionality index (DI): estimation of uni- versus bi-directionality from instantaneous phases
  - Estimation of phase
- Granger causality: quantification of predictability of one time series using information contained in another series
  - Based on autoregressive models
  - Directed transfer function (DTF), Partial directed coherence (PDC)
- *Imaginary part of coherence, phase-lag index*
- *Modeling-based approaches (Dynamic Causal Modeling)*

Functional coupling (coactivation)

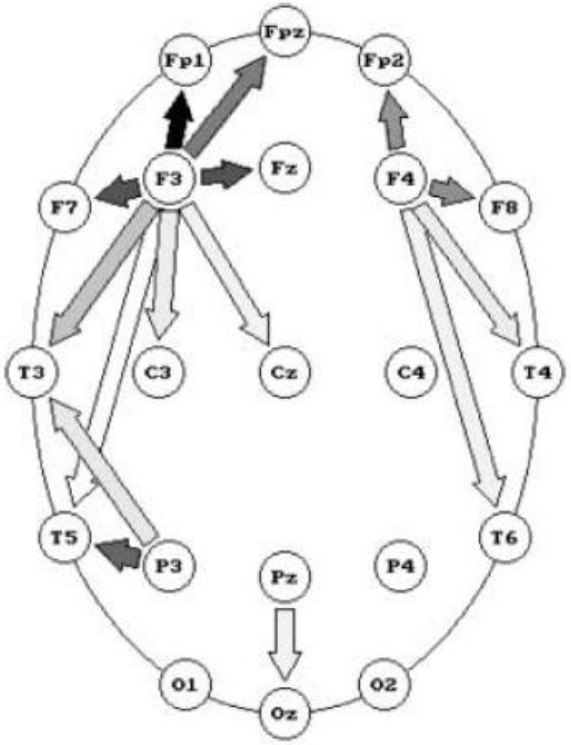
- Changes in coherence and/or phase coupling between tasks
  - Or vs. rest



Classen et al J Neurophysiol 1998

Effective coupling (causality)

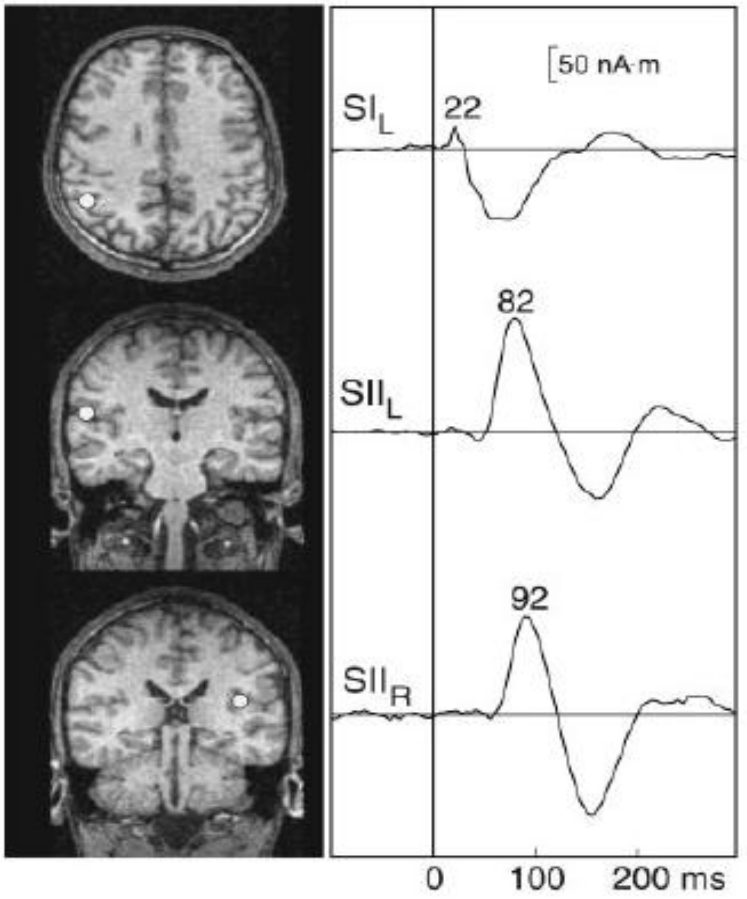
- Directed influence between pre-defined sets of areas (or at the sensor level)
  - Prediction of one time series based on information contained in another



Kaminski et al Biol Cybern 2001

Phase-locking at sensor-level

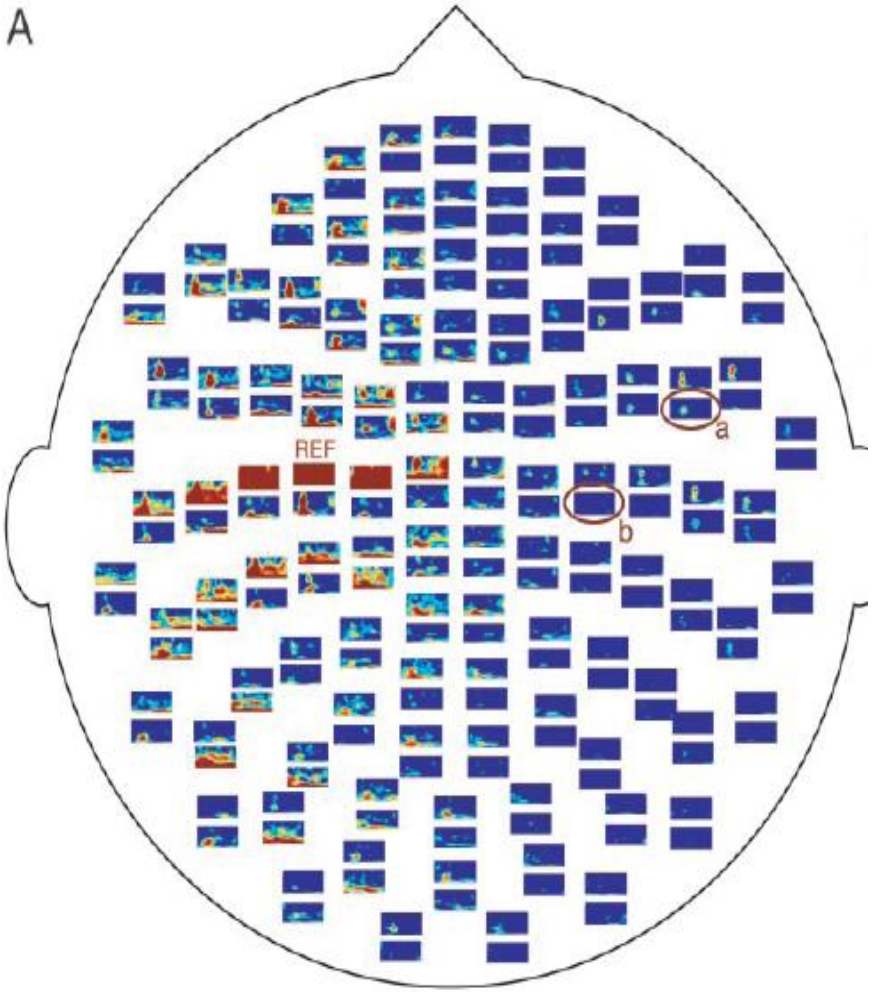
- Unilateral median nerve stimulation
  - SI & SII localization using standard dipole modelling
  - Sensor that showed the strongest 15- to 25-Hz oscillations 50-150 ms after stimulus taken as reference (SI)



Simões et al, PNAS 2003

Localization of phase-locked pairs

- The channel with the strongest evoked response in the SII region, and orthogonal to the reference channel selected to represent the SII area

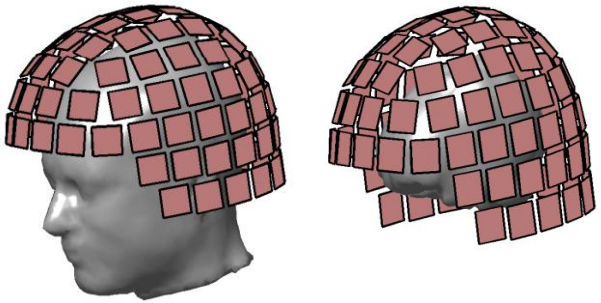


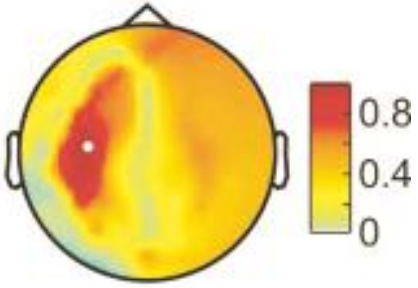
Simões et al, PNAS 2003

Field spread in MEG

- Field spread leads to a wide-spread representation of any source at the sensors
  - Multiple sensors detect the same activity
    - Spurious interactions
- Field spread not completely abolished in source space
  - Spurious interactions particularly in locations that show no real activity

Field spread in MEG



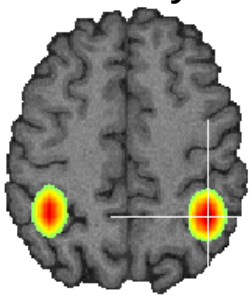


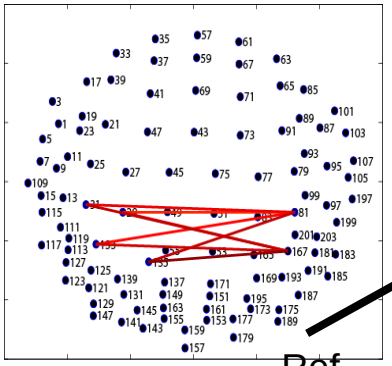
No correlated activity!

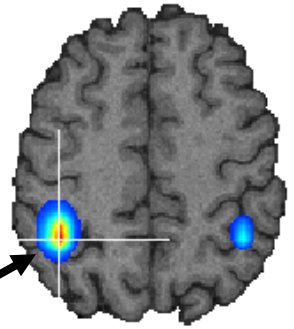
Activity

Interactions

Two sources

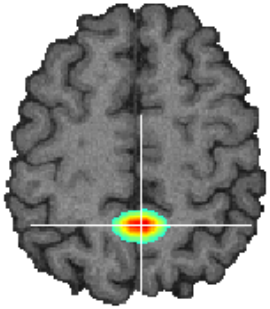


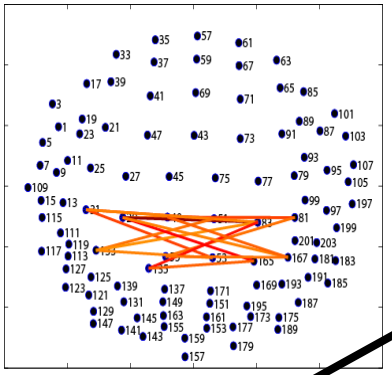


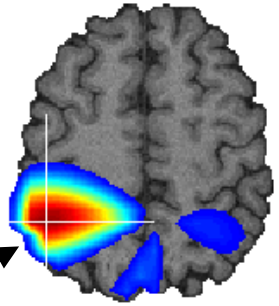


Ref

One source







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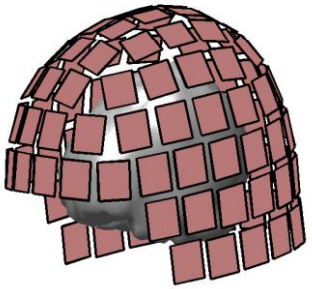
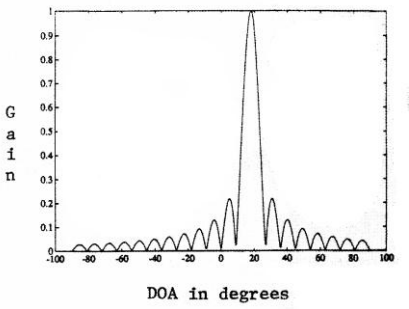
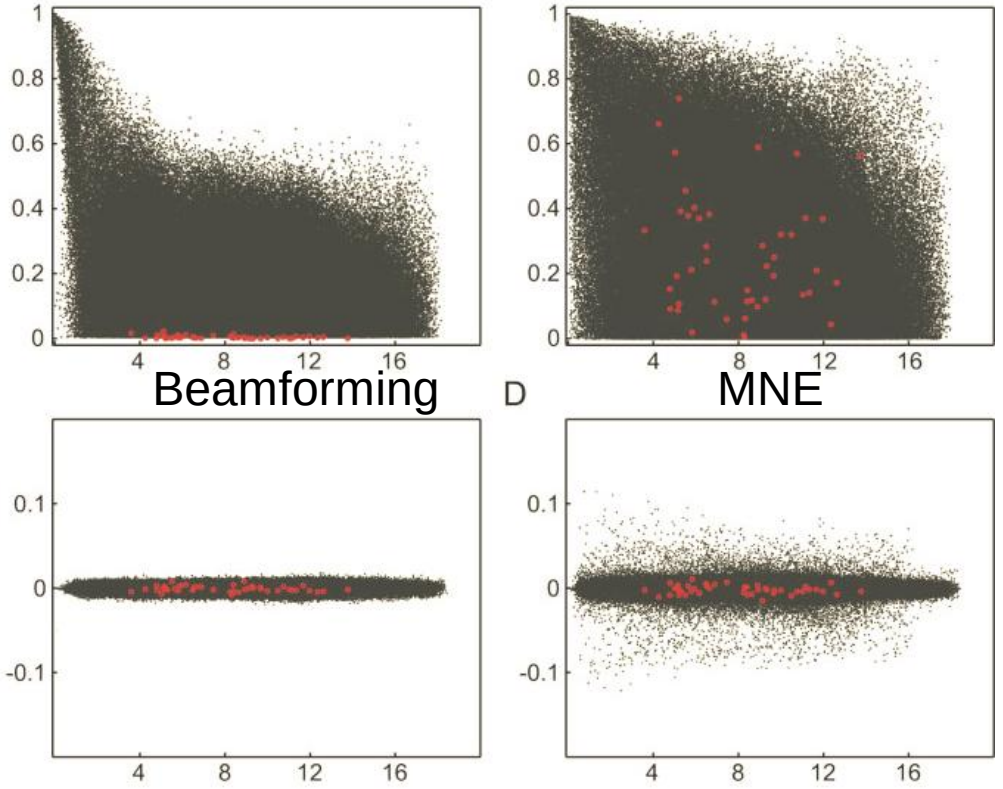
Field spread/spatial leakage





Leakage between spatial filters



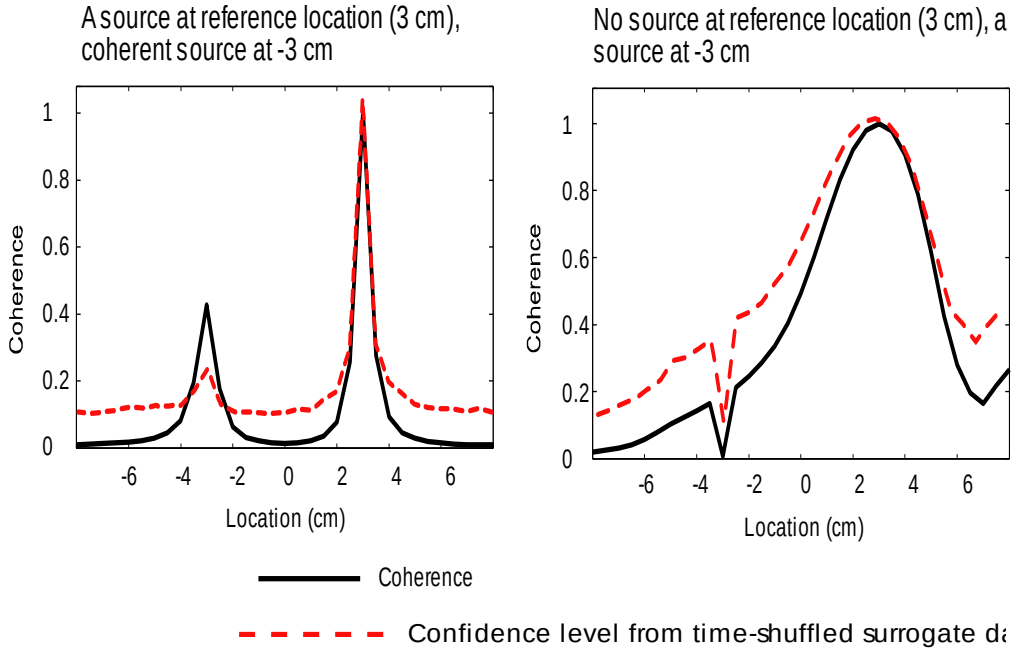
Power matched contrast

Van Veen and Buckley IEEE ASSP Magazine 1988

Schoffelen and Gross HBM 2009

Significance of coupling

- Testing via surrogate data
  - Random shuffling: if time-series properties are identical (leakage), correlation remains



Kujala et al Neuroimage 2008

Thoughts related to field spread

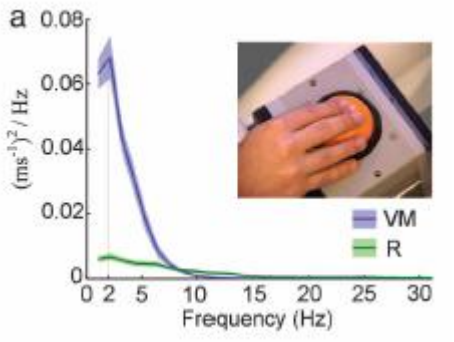
- Artefactual/spurious interactions
  - Non-directed measures
    - Can one then use them at all?
      - Stable patterns of cortical interactions
      - Field spread really problematic
  - Directed measures, elimination of instantaneous leakage
    - Elimination->suppression
    - Added assumptions and complexity
      - Less robust and repeatable
    - Physiological validity?

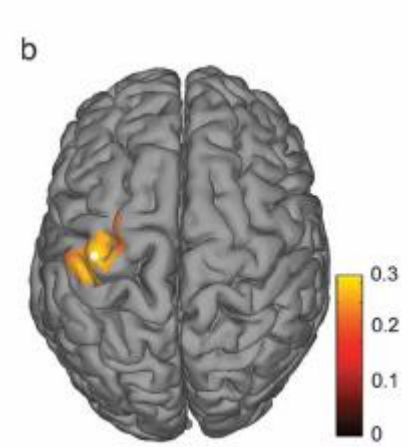
Imaging interacting networks

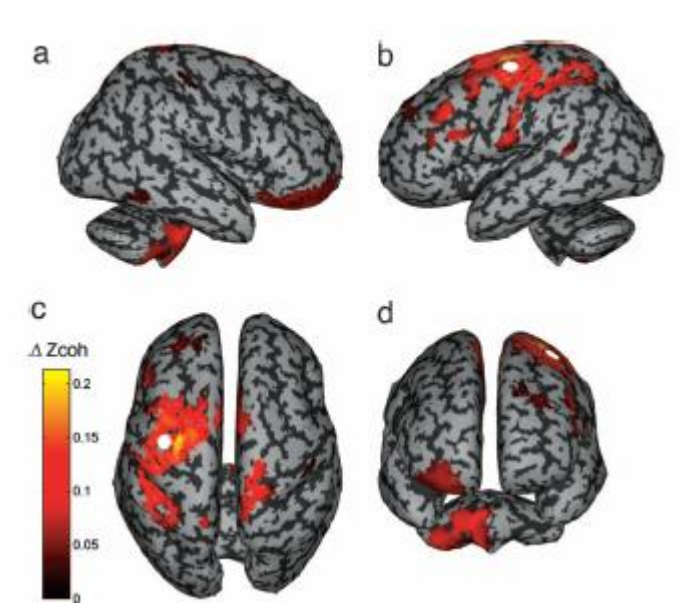
- Predefined regions of interest *(Astolfi et al Clin Neurophysiol 2005, Babiloni et al Neuroimage 2005)*
- Localizing areas via activity measures
  - Localization based on evoked responses *(Ioannides et al Hum Brain Mapp 2000)*
  - Localization of areas active at tag-frequecy *(David et al Neuroimage 2003, Cosmelli et al Neuroimage 2004)*
    - Modeling interactions in activated networks (Friston Neuroimage 2003)
- Imaging directly via cortico-cortical coherence
  - Beamforming *(Gross et al PNAS 2001)*
  - Minimum norm estimates *(Jerbi et al PNAS 2007)*

Minimum norm estimates

- Estimation of trial timeseries
- Estimation of interaction metrics



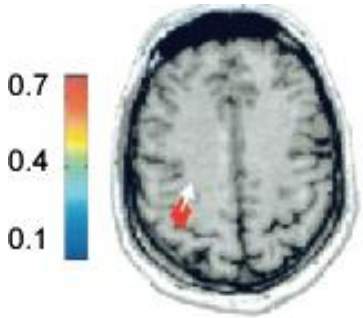




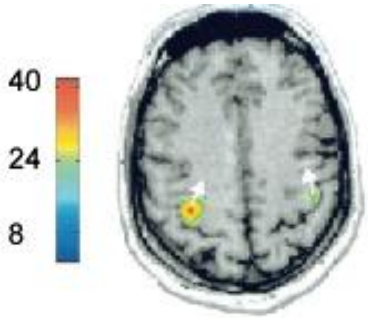
Jerbi et al PNAS 2007

Dynamic Imaging of Coherent Sources

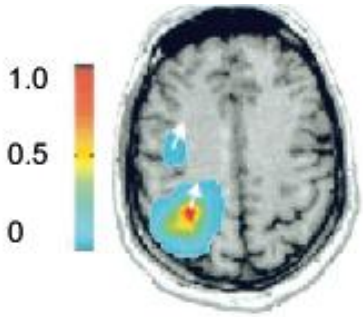
- Frequency domain transformation at sensor-level
  - Direct estimation of oscillatory dynamics at cortical level possible (without time-series estimation)
- Imaging of oscillatory power and coherence in continuous tasks
  - Estimation of time-courses of activity for phase-coupling/causality analysis



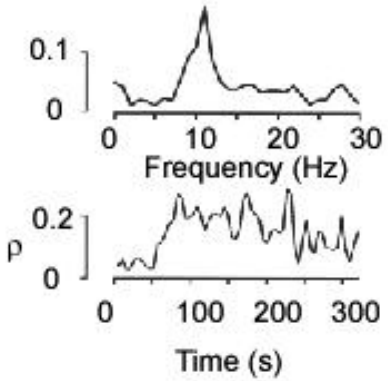
EMG-MEG



Rhythmic activity



Cortico-cortical coherence

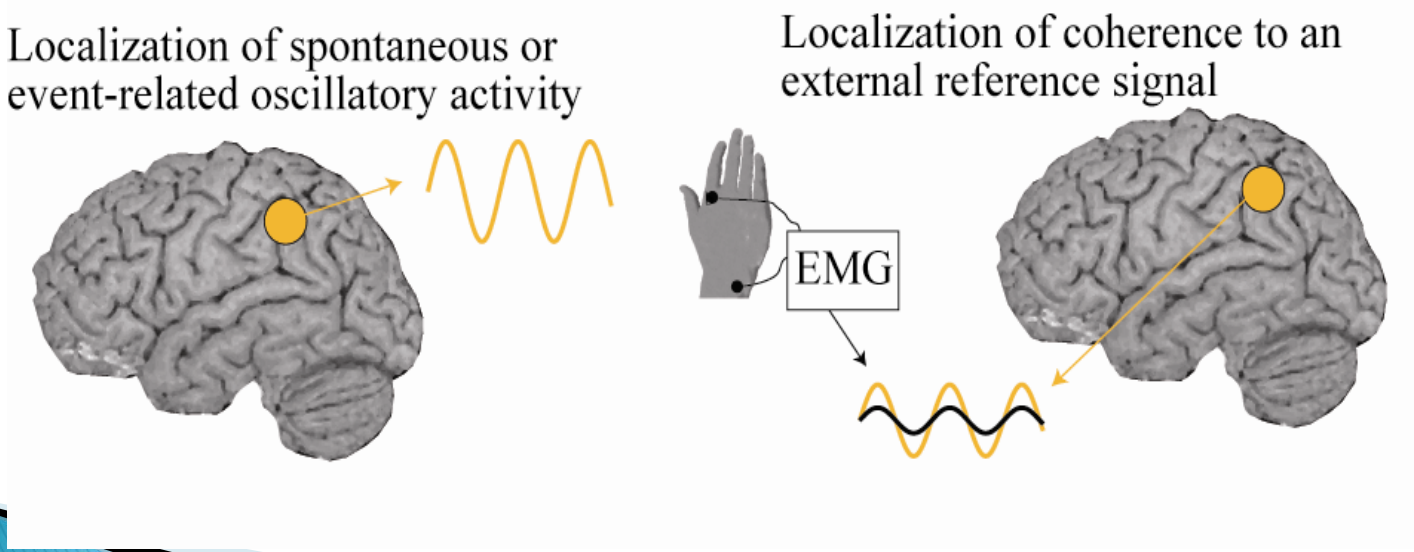


Coherence and phase-coupling

Gross et al PNAS 2001

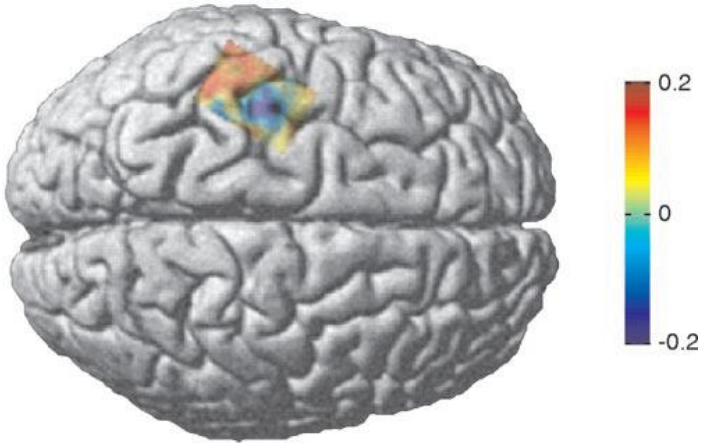
Identification of cortical reference areas

- Cortical reference area beneficial for cortico-cortical imaging of coherence
- Identifiable via
  - External reference signals
  - Rhythmic activity



Interactions during finger movement

- Right index finger movement task
- Contralateral M1 coherent with EMG-signal
- Separation of M1/S1 with directionality index (DI)

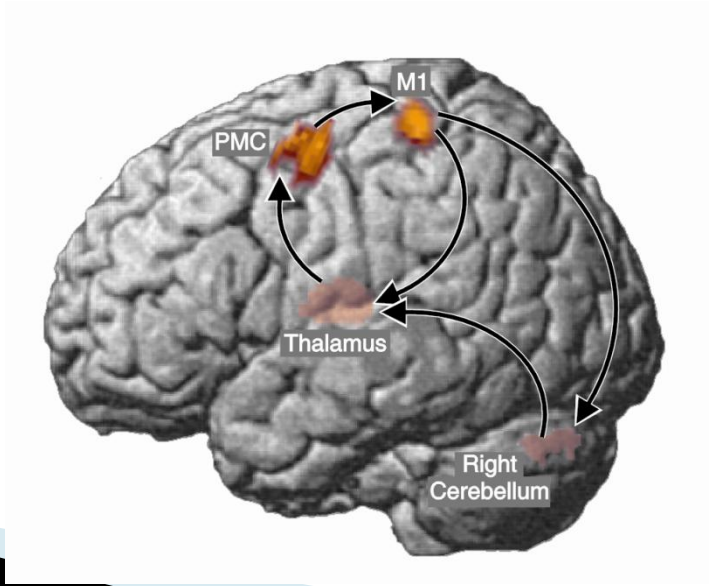


Separation of efferent and afferent components

Gross et al PNAS 2002

Imaging of networks from M1

- Cortico-cortical coherence between M1 and all other brain regions
  - Group-level statistics
- Connectivity characterization with phase-coupling (SI) and causal measures (DI)



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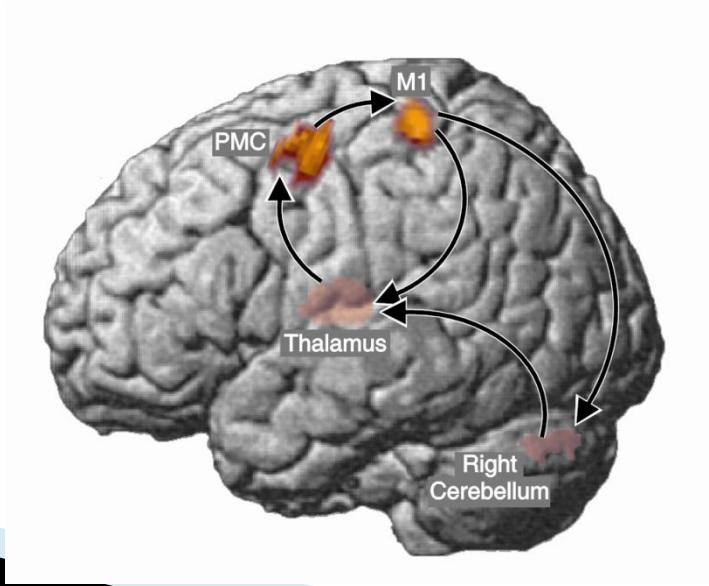
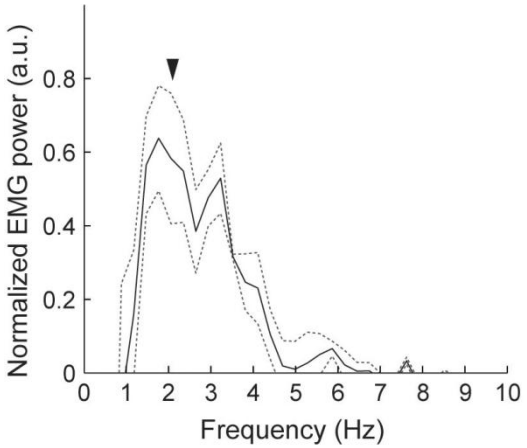


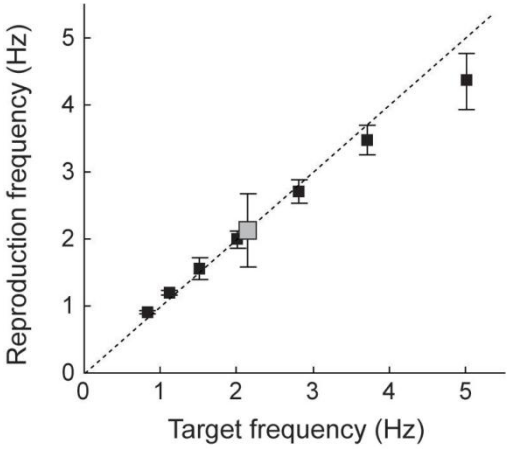
Butz et al J Physiol Paris 2006, Pollok et al Exp Brain Res 2006, J Cogn Neurosci 2007

Coherence and spontaneous rhythmicity

- Preferred/spontaneous rates observed in various motor behaviors
  - Human speech displays several rhythmic features
- Spontanous speech rates and their relationship with cortico-muscular coherence?



Rhythmicity in spontaneous speech

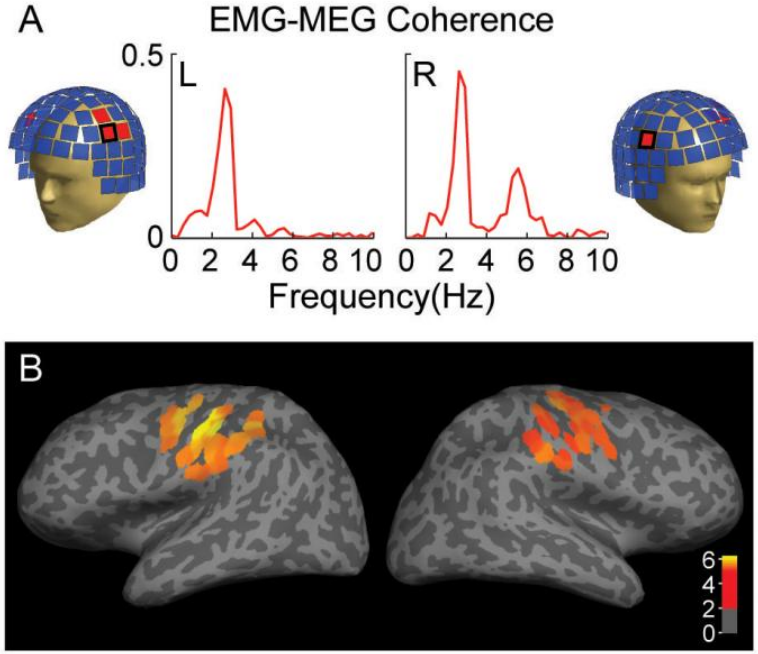


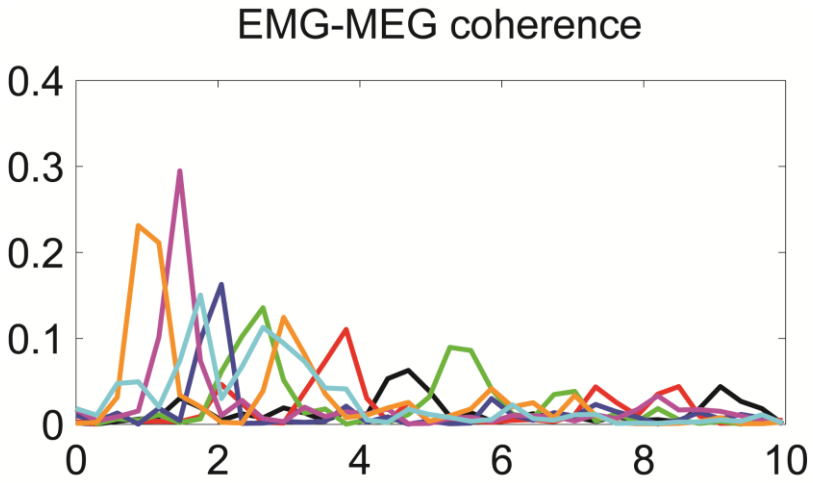
Task: Experimentally controlled syllable production

Ruspantini et al J Neurosci 2012

Cortico-muscular coherence

- Identification of mouth motor area
- Coherence at the fundamental and 1st harmonic frequency of syllable production

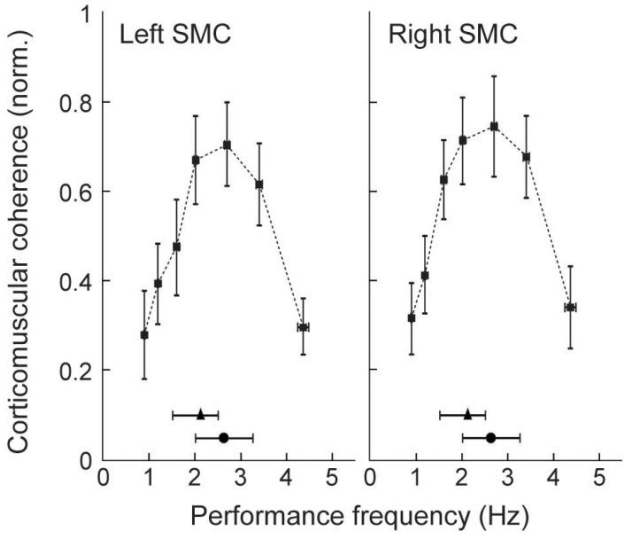


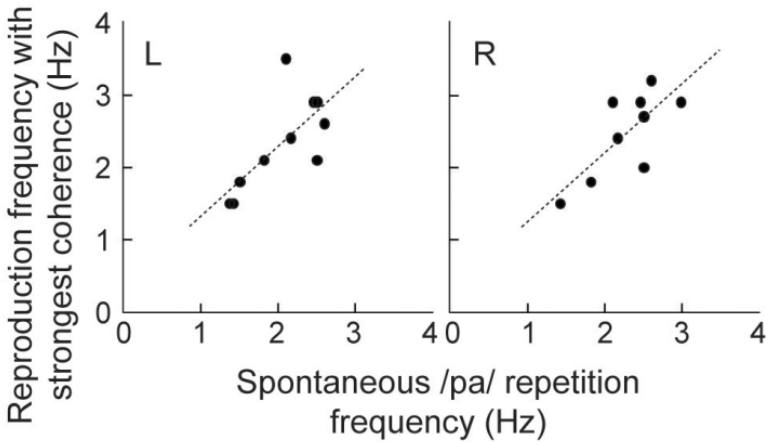


Ruspantini et al J Neurosci 2012

Tuning of coherence

- Maximal coherence at central rates
- Rate showing maximal coherence correlates with individual spontaneous rate

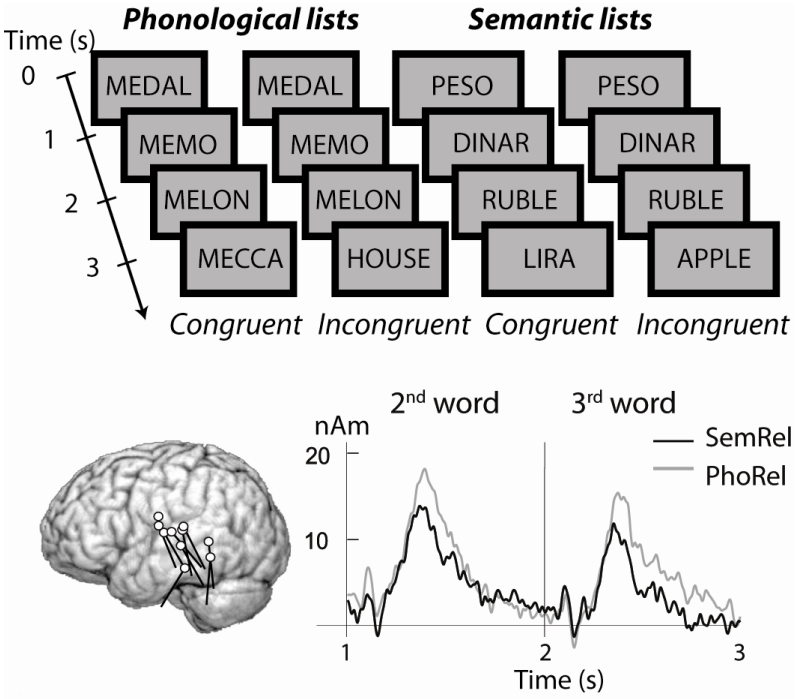




Ruspantini et al J Neurosci 2012

Modulation of cortico-cortical connectivity during priming

- Task: Visual semantic and phonological priming
  - Link between cortical interactions and decrease in activation (and increased efficiency)?
  - Starting from the left STC



Vartiainen et al, J Neurosci 2009
Kujala et al, Cereb Cortex 2012

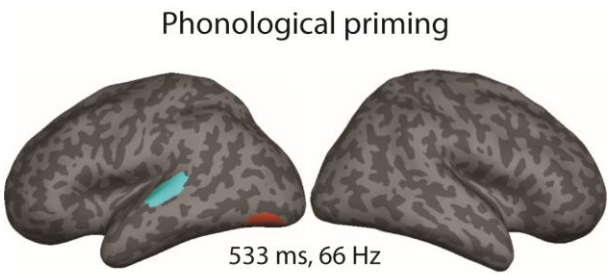
Analysis procedure

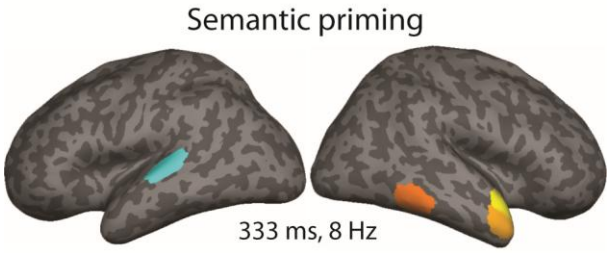
- Step 1: Identification of time-frequency windows of interest at sensor-level
- Step 2: Identification of cortical areas underlying the sensor-level effects (also pruning)
- Step 3: Characterization with Granger Causality

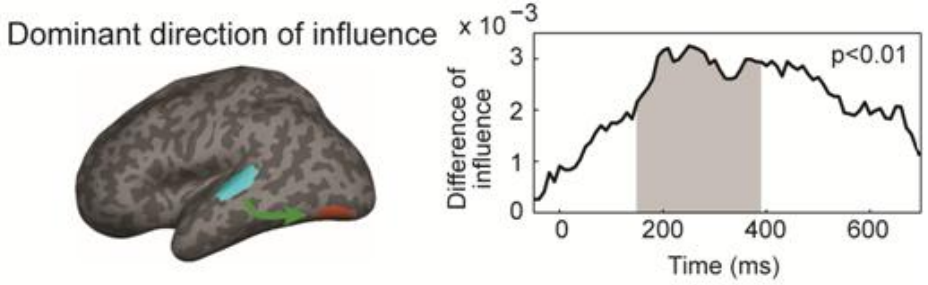
Kujala et al, Cereb Cortex 2012

Event-related interactions

- Spatio-temporo-spectral dissociation of semantic and phonological priming
- Differential role of STS

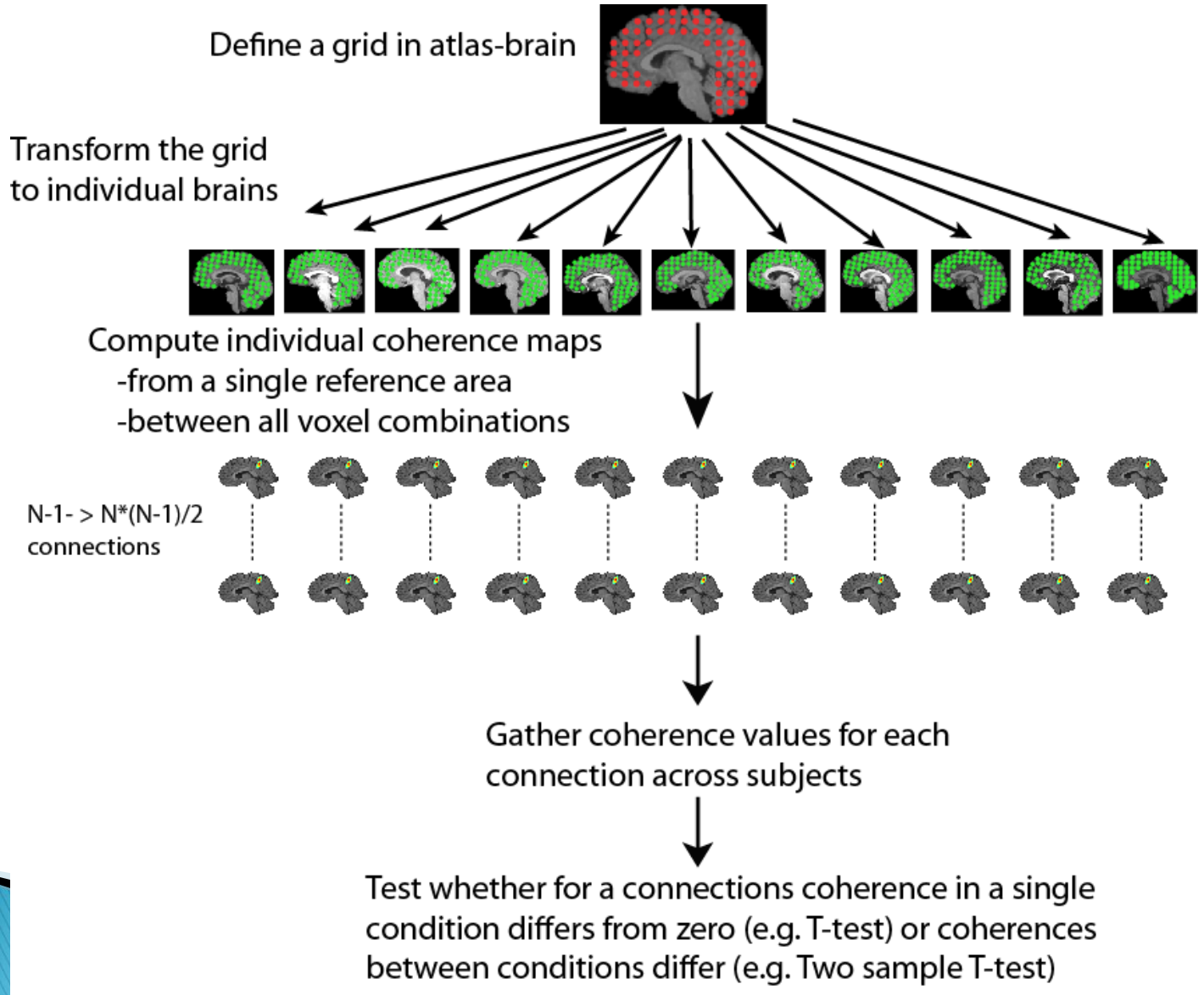






Kujala et al, Cereb Cortex 2012

All-to all connectivity



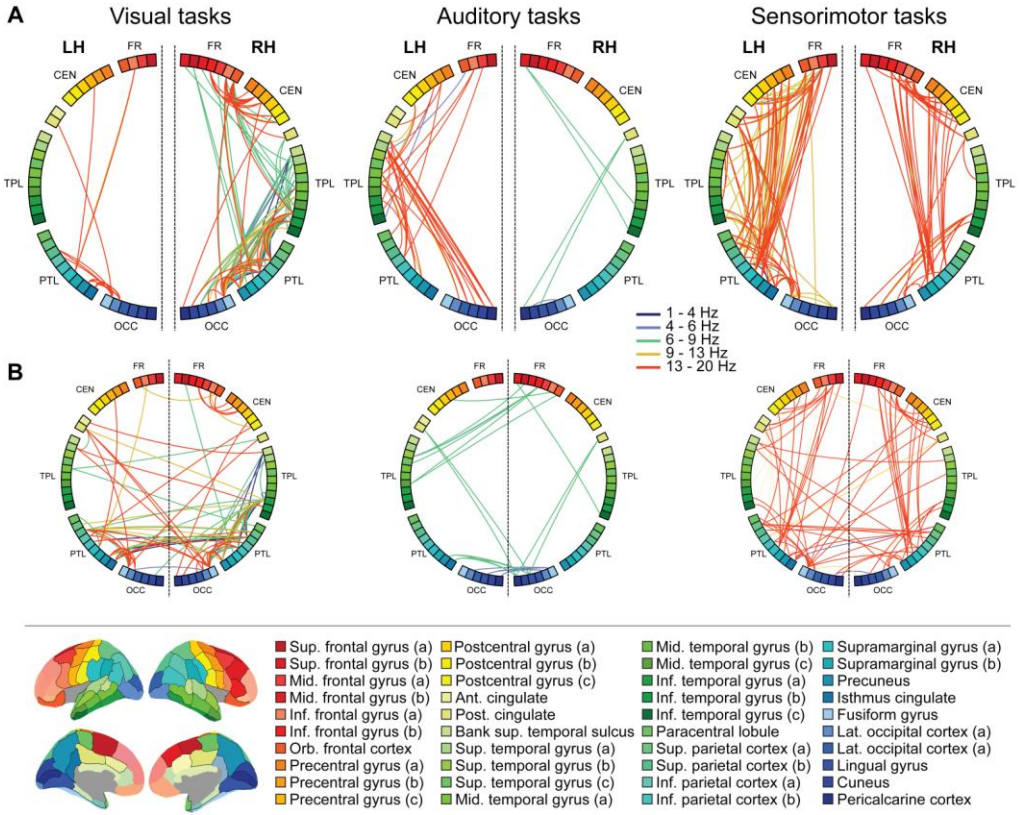
Connectivity across behavioral modalities

- Calculation of coherence between all voxel combinations (~3000000 connections)
- Group-level statistics

Saarinen et al, submitted

Modulation of large-scale network structures

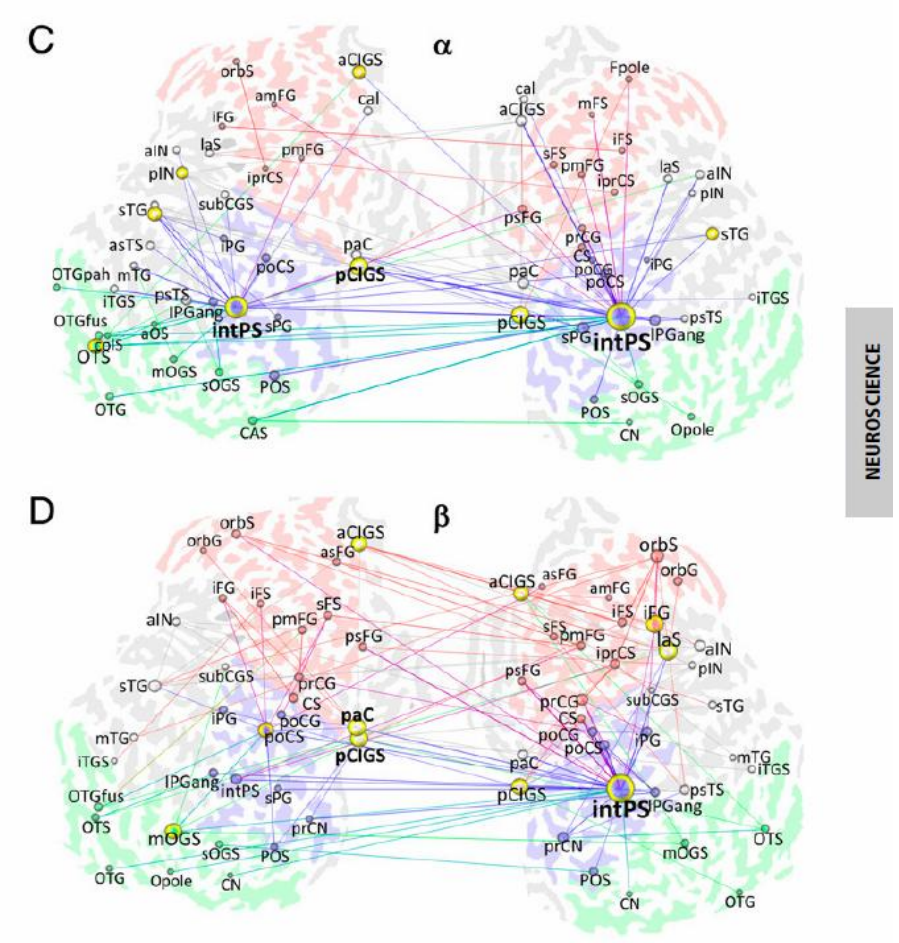
- Parecellation of cortex into larger regions
- Evaluation of mean coherence between regions



Saarinen et al, submitted

Connectivity via direct parcellation

- Estimation of mean time-series for each region
- Computation and evaluation of connectivity using these ~100 time-series

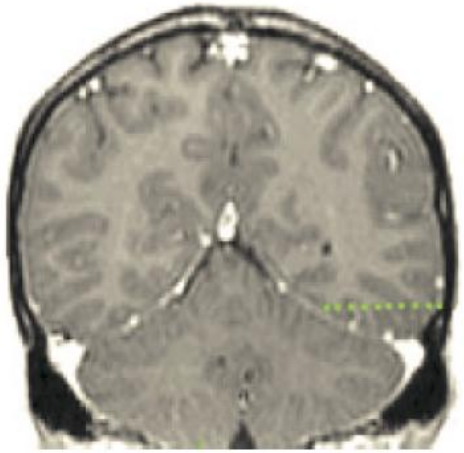


NEUROSCIENCE

Palva et al PNAS 2010

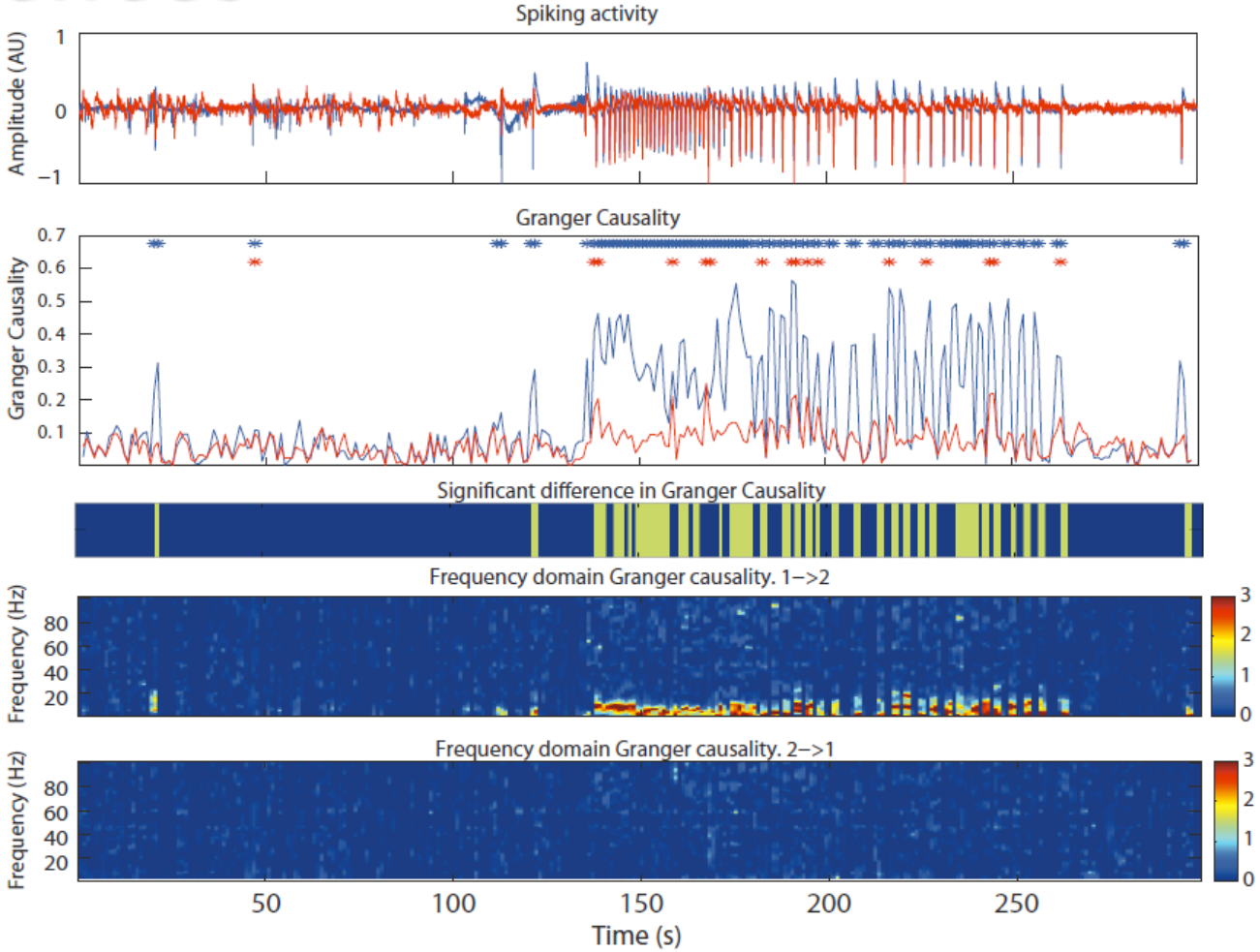
All-to-all connectivity with directed measures

- Identification of epileptogenic networks with Granger Causality
  - Automatic identification of seizure onset zone
  - Stereotactic in-depth electrodes (SEEG)
  - Bi-variate Granger Causalty (*Seth 2010 J Neurosci Methods*)



Kujala et al in preparation

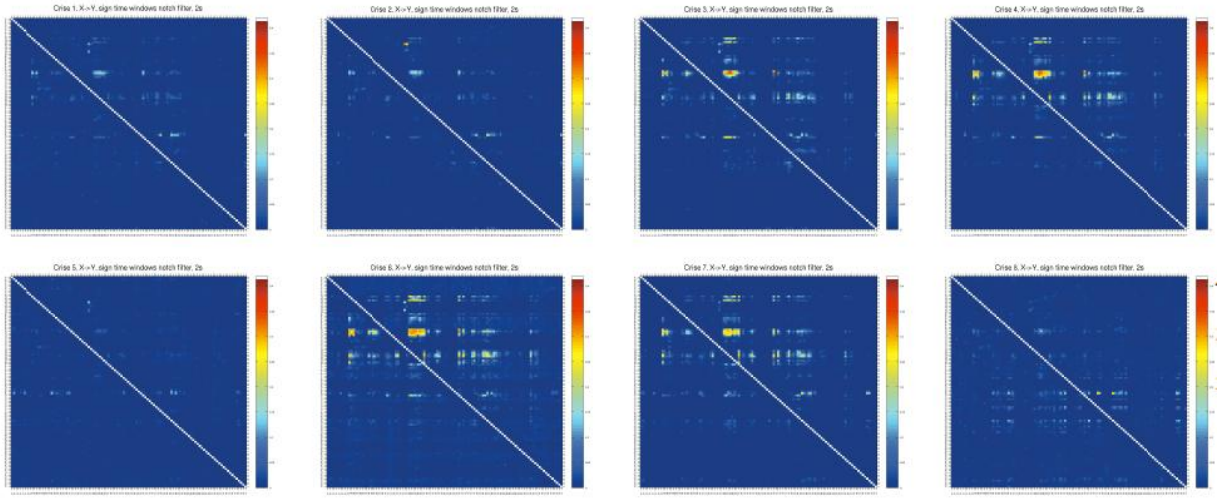
Co-incident spiking and causal influences



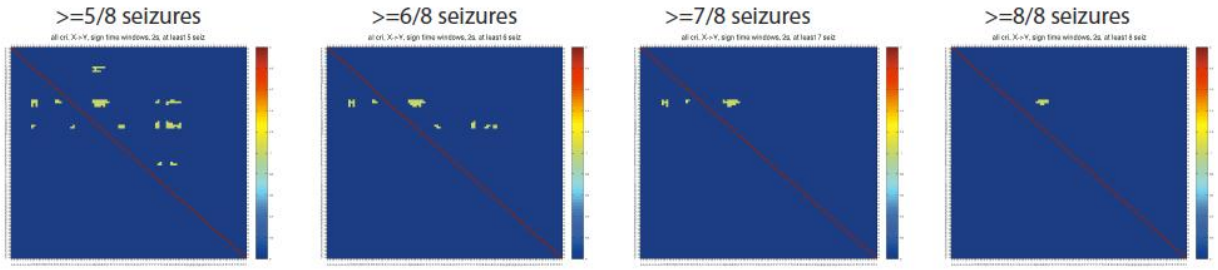
-> Prominent causality during the ictal phase

Kujala et al in preparation

GC patterns across electrodes



% of significant GC across electrode-pairs and seizures

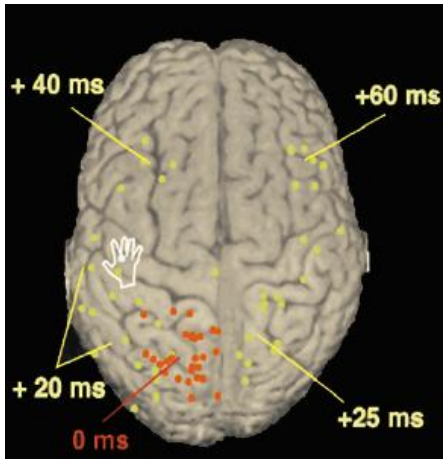


Causality in at least N/8 seizures

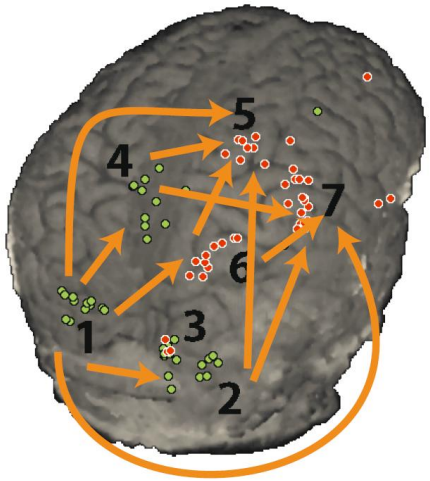
Kujala et al in preparation

Epileptogenic networks with MEG

- Estimation of cortical-level time-series with broad-band beamforming (DICS)
- Detection of most prominent driving and receiving brain areas during seizure



Dipole modeling



Granger Causality

Summary, oscillatory responses

- Various spectral estimation techniques for event-related activity/responses
- Various approaches for estimating cortical-level correlates
- Statistical evaluation

Summary, interactions

- Possible to image rhythmic interactions in MEG
  - Problems with field spread
- Identification of areas via
  - External reference signals (~=EMG)
    - possible to start from cortico-cortical coherence
- Possible to study all-to-all connectivity as well
- Evaluation of both validity and statistical significance of the findings
- Interesting and physiologically relevant measure of behavior!

Discussion

- Correspondence between brain areas identified as nodes in network analysis and areas showing task-specific activation
  - Rhythmic activity ≠ rhythmic interactions (?)
- How valid is coherence (or any other metric) as a measure for identifying areas?
  - Phase and cross-frequency coupling, causality?
- Individual vs. group level analysis, i.e., spatio-spectro-temporal variability vs. statistical power?

Matlab exercise

- Characterization of cortico-cortical connectivity
  - Spurious vs. valid coherence in simulated data