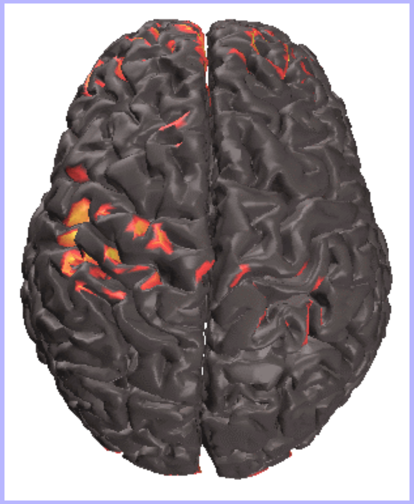
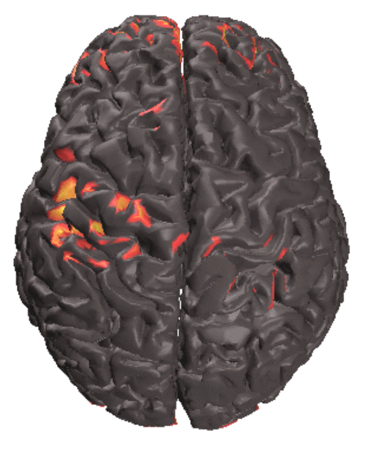


MEG/EEG Network Dynamics in Cognitive Neuroscience

Gregory V. Simpson, Ph.D.

Collaborators



DNL - UC San Francisco

Dynamic Neuroimaging Laboratory (DNL)

- Corby Dale
- Darren Weber
- Tracy Luks
- Anthony Kaveh
- Morgan Hough
- Alex Wu
- Brian Shulman
- Tim Rankin

– Steve Bressler (FAU)
– Richard Leahy (USC)
– Felix Darvas (UW)
– Dimitrios Pantazis (MIT)
– Tom Nichols (UMich)
– Gregor Rainer (Max Planck)
– Robert Zatorre (MNI)
– Sylvain Baillet (CNRS Paris)
– Scott Makeig (UCSD)
– John George (LANL)
– Randy McIntosh (Rotman, Toronto)
– Jeremy Caplan (Rotman)
– John Foxe (AECOM)
– Michael Worden (Brown)
– [Keith Worsley (MNI)]

Overview

EEG/MEG

Timing information relevant to multiple functional scales:

- Intracortical
- Intercortical
- Sub-second cognitive operations

Spectral Information:

- Functional tags associated with different oscillatory frequencies.
- Cross-Frequency Coupling.
- Oscillatory signals used in measuring connectivity.

Cortical – Cortical Connectivity, Timing and Spectral properties.

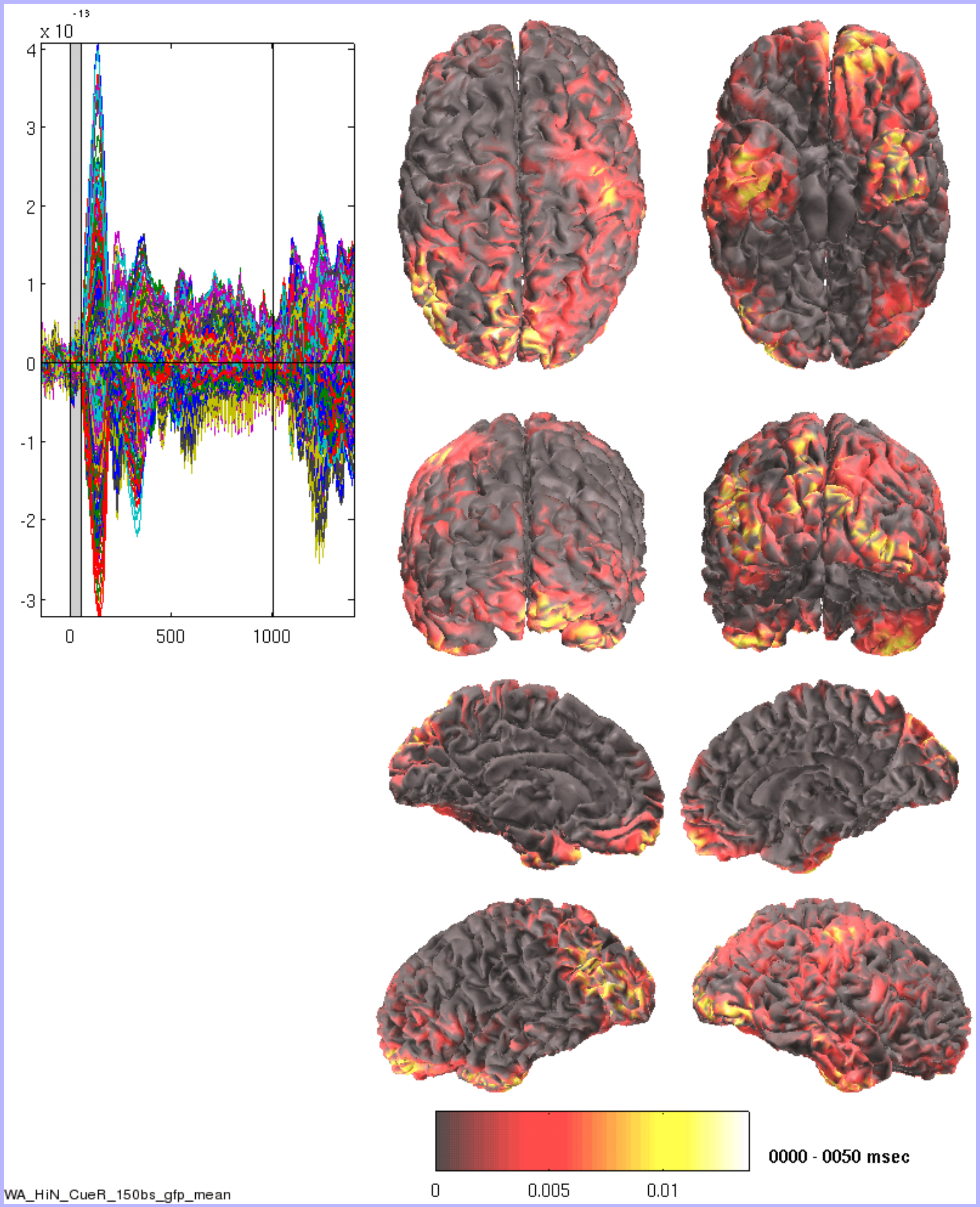
- Timing of interactions between regions in a network.
- Sub-second changes in networks during cognition.
- Long range cortical-cortical interactions and changes in local intracortical synchronization.
- Spectral specificity.

Large-scale cortical networks as the bases of cognition.

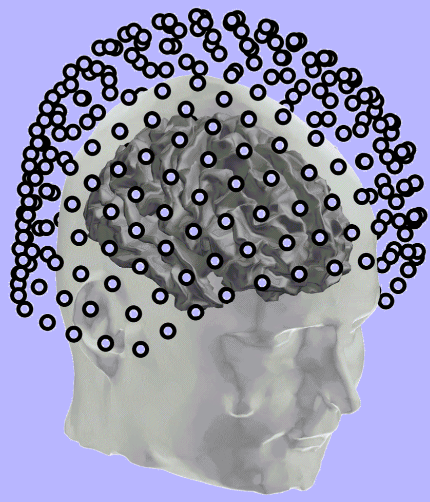
Multiple cortical regions are activated during higher order cognition (frontal, parietal, sensory). The cortical configurations of active systems vary at a sub-second timescale commensurate with the timing of component cognitive operations.

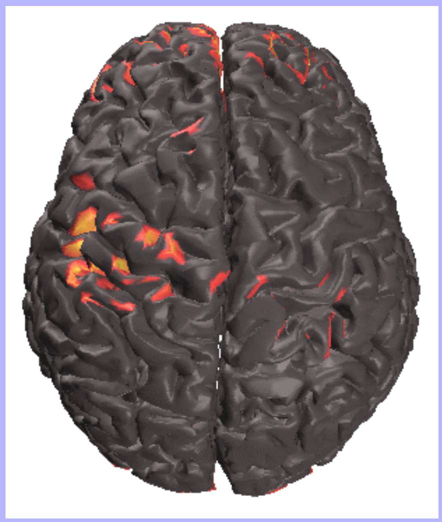
These cortical systems suggest functional networks, and there is growing evidence of interactions between regions to support the notion of functional networks.

These images reflect just one of at least five different electrophysiological signatures of activity. Extremely rich datasets.



Inverse Problem/Brain Source Imaging





Magnitude at every time point during the epoch.

Brain Source Imaging

The inverse problem: information from sensors - solve for location and strength of currents ("sources") in the cortex that produce the sensor data.

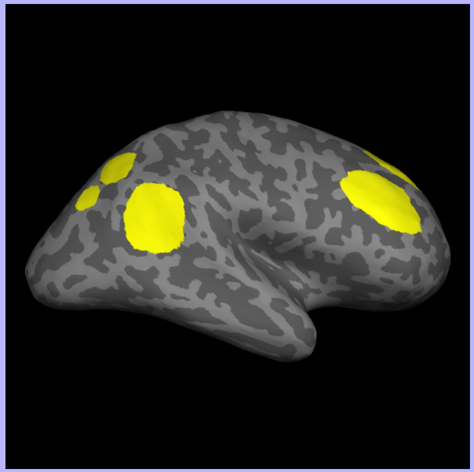
Categories of methods:

- Cortically constrained minimum norm provides current at each cortical patch.
- Beamformers.
- ICA approach.
- Spatiotemporal Dipoles (single or few focal sources)

Spatial Resolution/Accuracy

Point-spread function:

• PSF varies somewhat for each cortical region.
• can be measured for any region and used to identify magnitude and extent of spread to neighboring regions of interest.



Differentiating activity in neighboring regions:

Activity in regions that are close together (relative to their point-spread) can still be resolved if there are differences in timing and/or magnitude differences across conditions.

Assigning activity to a region:

Blurred images limit localization (1-3 cm). Consequently, precise localization of location and extent of activity is limited.

Types of signals: Event Related Potentials/Fields (ERP/ERF) & Oscillatory Activity

ERP/ERF:
Stimulus-locked recording of each stimulus trial and signal averaging across trials. Improves signal to noise, also reduces signals that are stimulus evoked, but not phase locked across trials.

Oscillatory Activity (differentiation in the frequency domain):
Time series, whether stimulus evoked or ongoing, can be decomposed into multiple frequency bands.

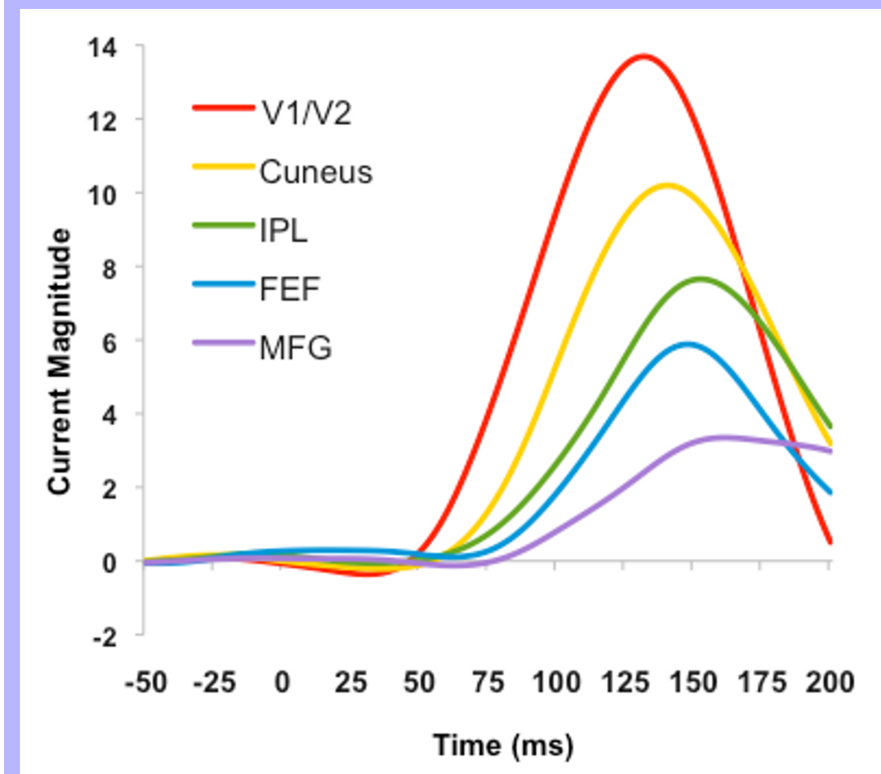
Different frequency bands are being associated with different functional roles.

Temporal and Spectral: The timing of magnitude changes in different oscillatory frequencies can be extracted.

Functional relevance of high temporal resolution

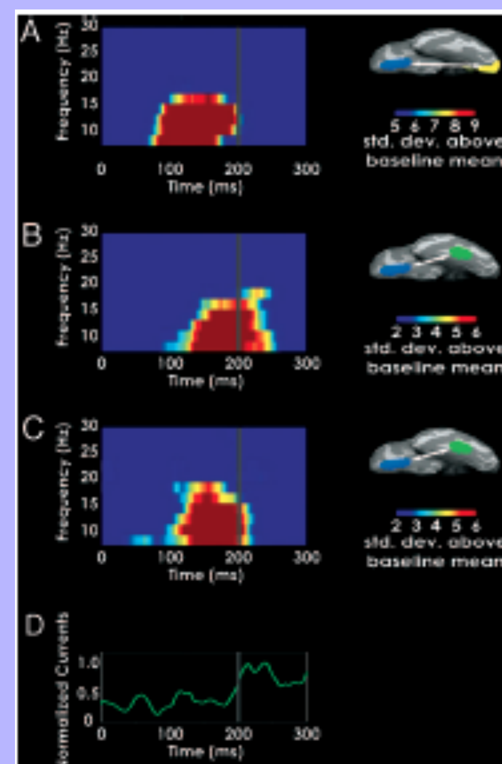
Sufficient to identify sequential flow of activity from one cortical region to another.

Sufficient to measure a cognitive operation in <100 msec. (bottom-up to top-down)



Simpson et., J Neurosci in press

OFC to Fusiform – Successful Object Recog.



Bar et al., PNAS 2006

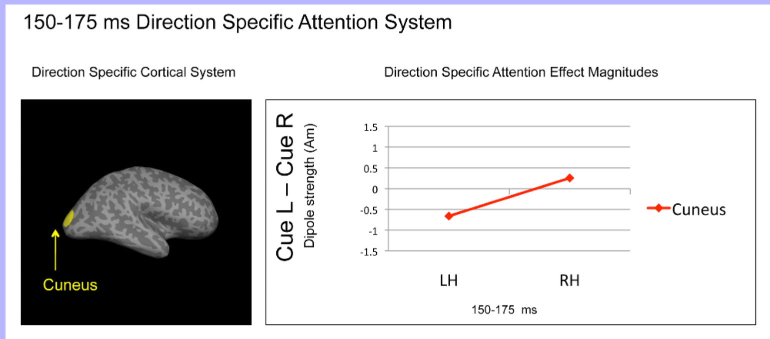
Timing: Network dynamics support functional specificity:

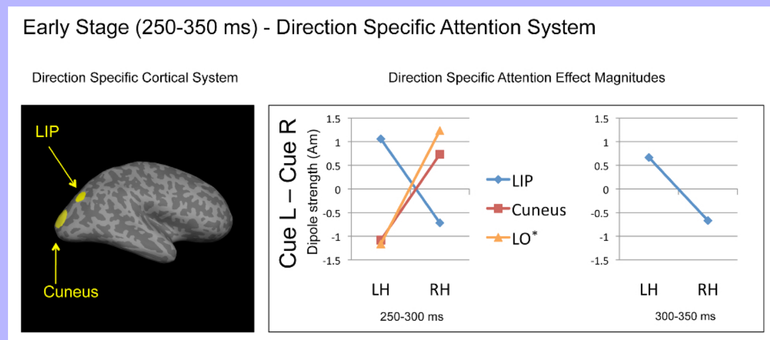
Co-Activation of different sets of cortical regions at different sub-second processing stages.

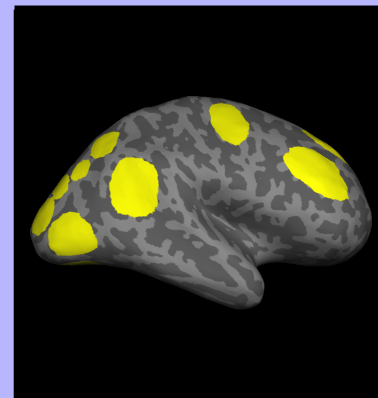
"Network" in the sense of regions that are co-active for a specific cognitive function and a specific processing stage (i.e. without cortical-cortical connectivity measures).

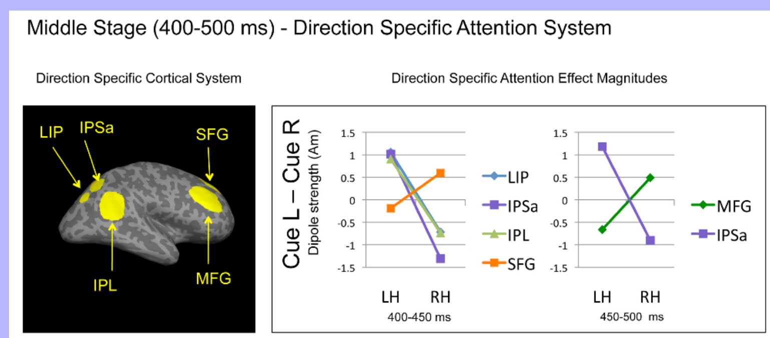
Example: deployment of visual spatial attention

Anatomically Distinct Cortical Systems Underlie Each Stage of Attentional Deployment



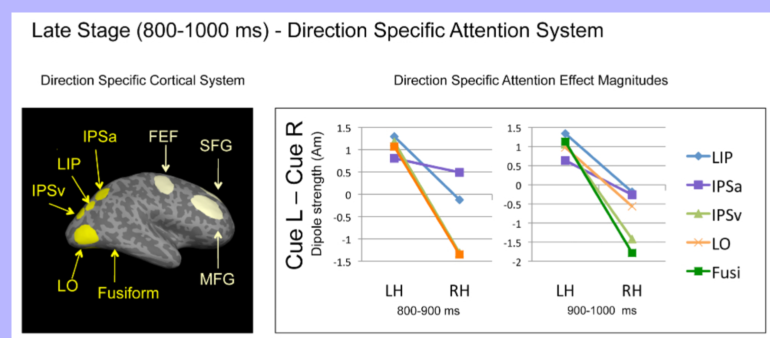



One system or multiple systems?



Fundamental organizational concept:

That different cortical networks can form dynamically at sub-second stages of cognitive processes.

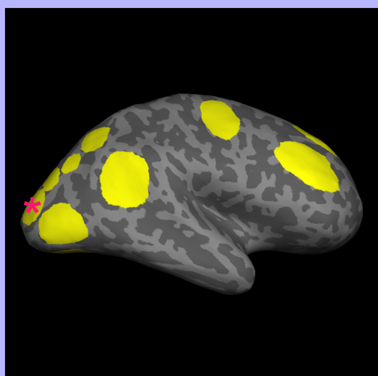


A cortical region can participate in multiple functional roles by working in concert with different cortical systems.

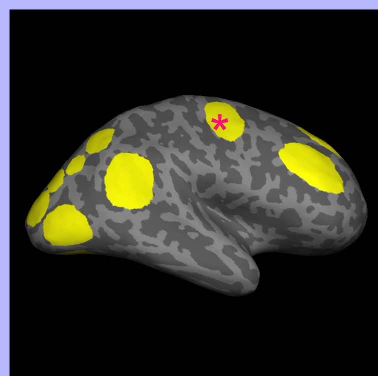
Simpson et al., J. Neurosci in press

Temporal Resolution: At each stage of attentional deployment a different brain region influences subsequent performance.

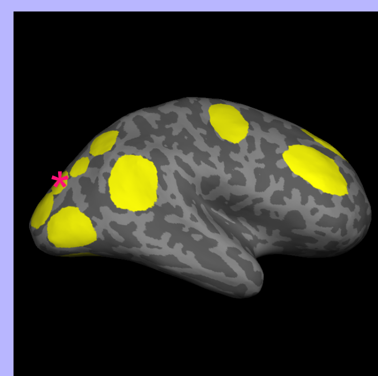
Cuneus (150 ms.)



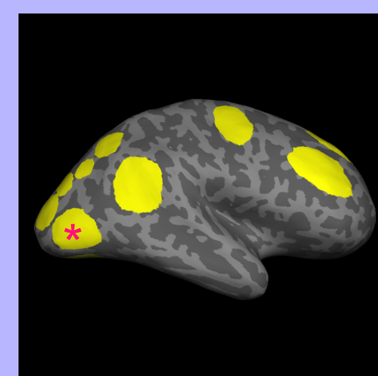
FEF (250 ms)



IPSv (400 ms.)



LO (800 ms.)



Adopted from Simpson et al., 2011

Oscillatory Brain Activity:

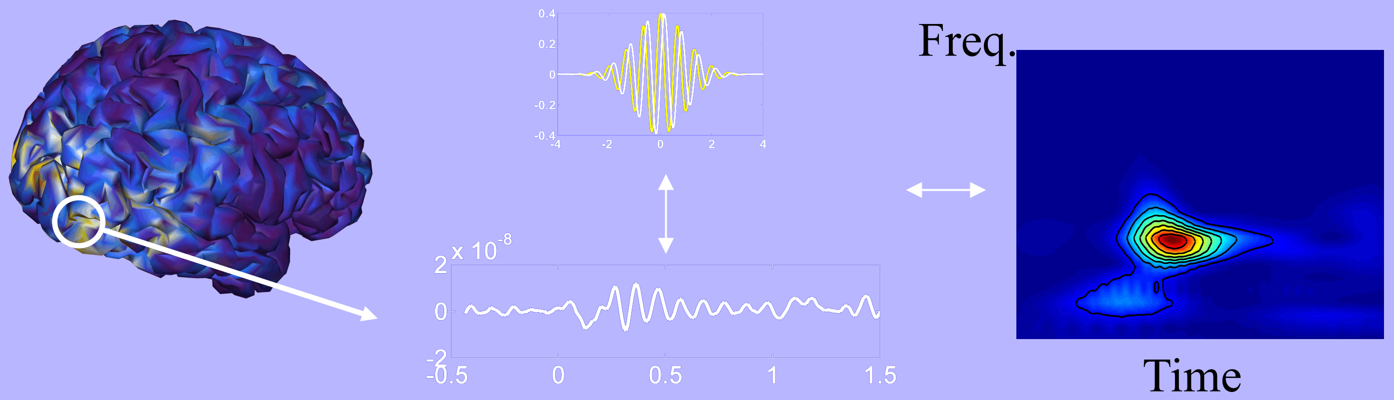
- Synchronization across many neural scales.
  - Neuronal ensembles to intercortical interactions
- Coordination of information and processing.
  - From grouping of unit activity to coordination between distant/functionally related regions.
- Associated with sensorimotor/cognitive function.

Oscillatory Brain Activity

Several frequency bands may be associated with different functional roles.

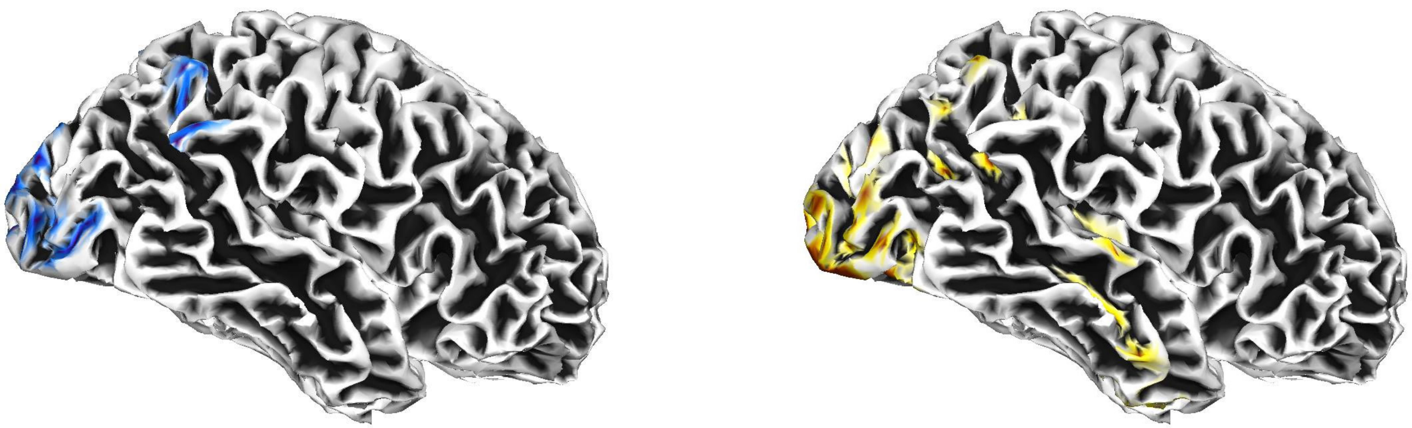
- Theta (4-7 Hz)
- Low Alpha (8-10 Hz); High Alpha (11-14 Hz)
- Low Beta (15-25 Hz); High Beta (25-35 Hz)
- Low Gamma (35-70 Hz) High Gamma (70-120 Hz)

Complex Morlet Wavelet Expansion



Cognitive operations can involve multiple frequency bands in the same cortical regions.

Attention specific modulation of visual regions



Alpha (11-14Hz) Gamma (30-50Hz)

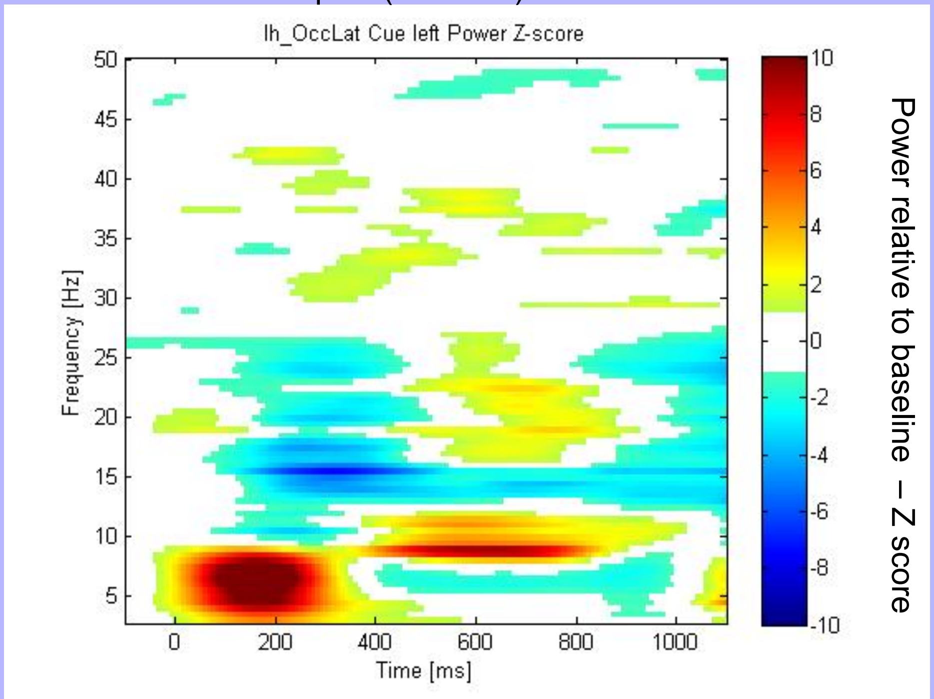
Attending to the left simultaneously decreases Alpha and increases Gamma in the right hemisphere cortical representations of the attended location.

Pantazis et al., 2005

Spectral specificity and temporal organization

• Attentional modulation occurs in multiple frequency bands.
• There are distinct temporal windows on a sub-second time scale commensurate with cognitive operations.
• Different frequencies are modulated at different stages of processing.

Lat. Occipital (left hemi) – Attend Left



Attention specific changes in local neuronal synchronization (power) – Lateral Occipital cortex (LO).

Dynamics support differentiation of functional roles

Timing of Attentional Modulation of Alpha

PARIETAL REGIONS

SPL: early transient, shifting.

IPS: early onset and late, diminishing.

TPJ: late onset, diminishing.

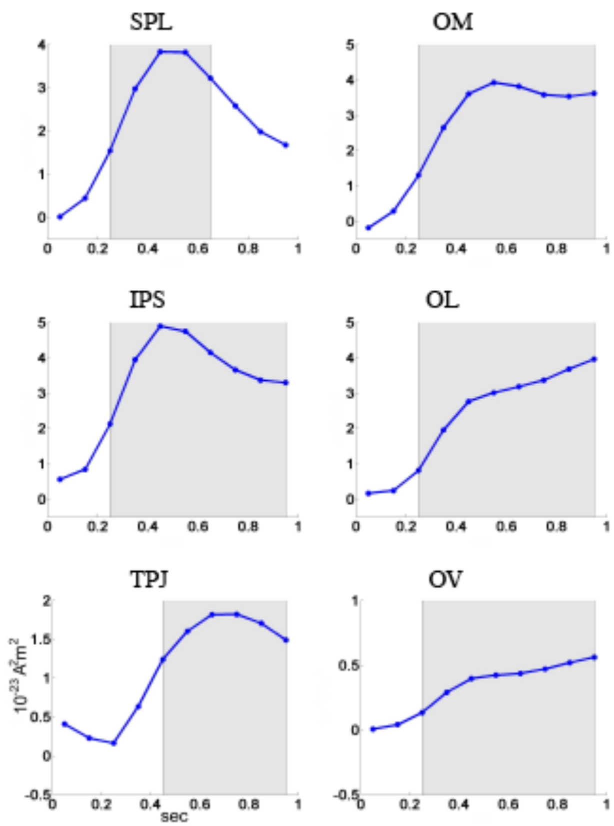


Fig. 11. Temporal dynamics of the ispilateral vs. contralateral statistic S^{STF} during 0-1 sec at 6 cortical regions. Shaded areas indicate significance after multiplicity correction using a false discovery rate procedure.

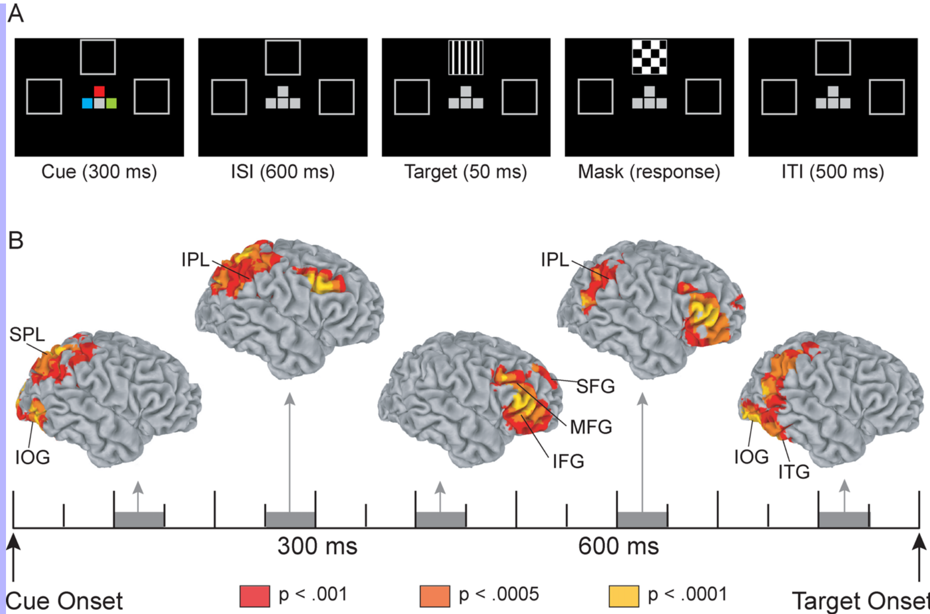
OCCIPTAL REGIONS

All areas: Early onset, sustained, and increasing until S2 arrival.

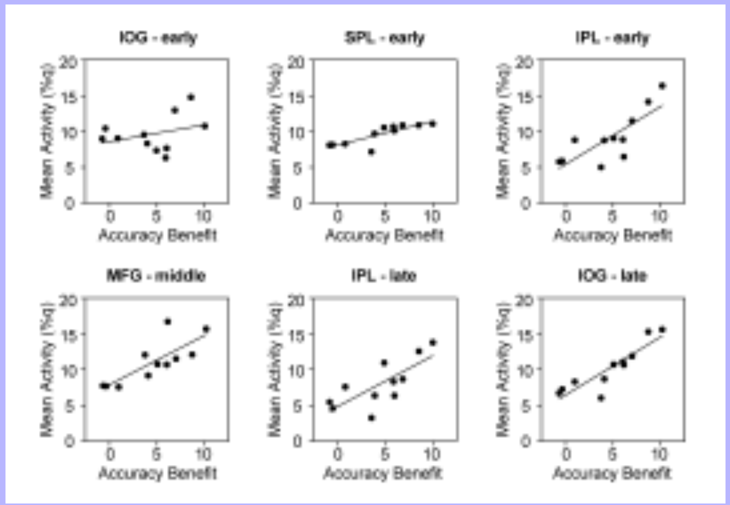
OV also has attentional modulation of Gamma 750-1000

Pantazis et al., 2009

Timing at the level of cognitive operations



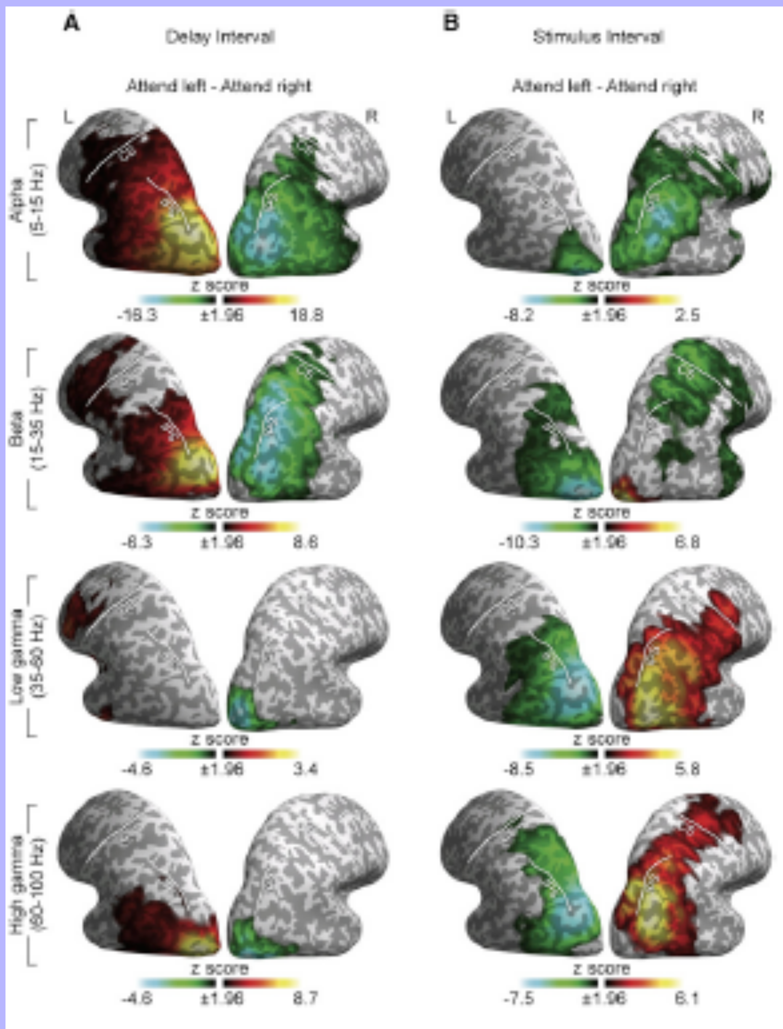
Sequential cortical systems underlying visual attentional modulation of Theta



Magnitude of Theta modulation predicts performance.

Green & McDonald, PLoS 2008

Cortical Spectral Specificity: A dimension of functional organization. Different cortical systems are active in different frequency bands and these systems are task dependent.



Different cortical distribution of direction specific attention activity in different frequency bands.

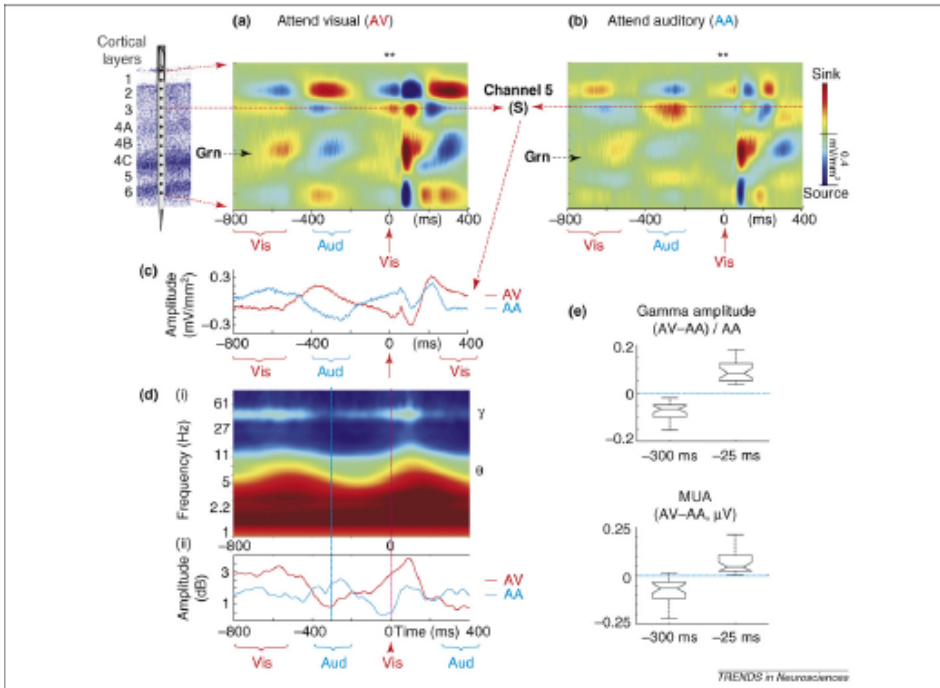
From Siegel et al., Neuron 2008

Direct Relation to Animal Models

Oscillatory field potentials can be measured together with unit activity in animal cortex to provide a bridge between the human recordings and the detailed neural information provided in animal recordings.

Interactions of different frequencies as mechanisms of intracortical and intercortical functional organization.

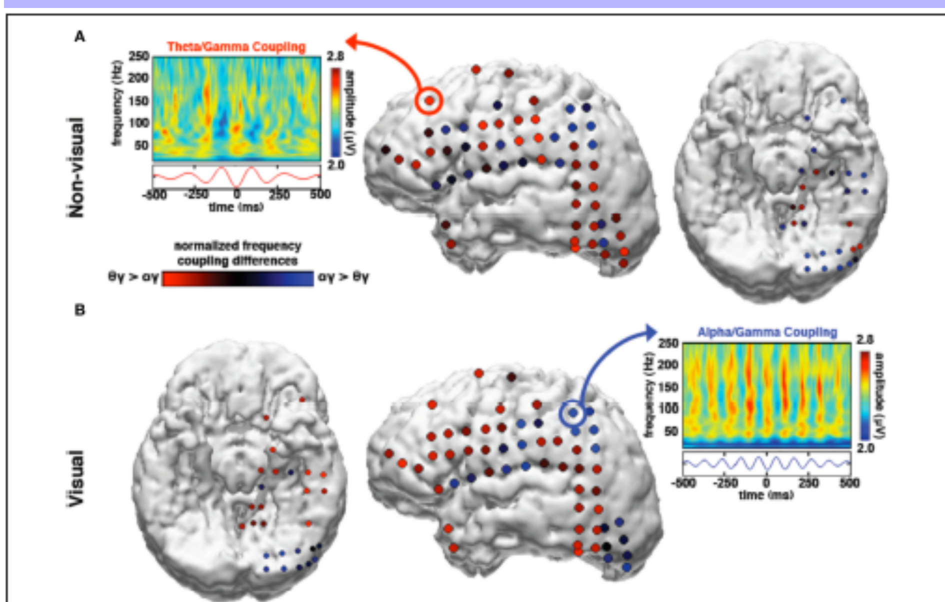
- Cross frequency coupling
- Hierarchy of frequencies
- Entrainment of modulating frequencies
- Dependency on timing of functional operations



Intracortical – multiple frequencies. Support from laminar recordings within cortex (see also e.g. Lee, Simpson et al., Neuron 2005; Gregoriou et al., 2009)

“Hierarchy” – cross frequency coupling; low modulating higher frequencies.

Schroeder & Lakatos, TINS 2008



Intracortical modulation of gamma at two different slower rhythms, Theta and Alpha.
Cortical and/or task specificity.

Canolty & Knight, TICS 2010

Measures of cortical-cortical interactions

• **Coherence:** caveat - increased power in either region can appear as increased coherence.

• **DICS:** useful for identifying regions that are co-active to use as ROIs for follow-up analyses with phase locking or Granger measures. *Gross et., PNAS 2001*

• **Phase Locking:** measure of synchronization between regions that can provide phase difference information that can be converted to latency differences and assessed with respect to expected conduction time between regions - can indirectly support directional influence. *Lachaux et al., 2000*

• **Directional measures**, e.g. Granger Causality, Mutual information: Provide measures in support of a directional influence (e.g. from Region A to Region B). *Brovelli et al., PNAS 2006*

• **Caveat:** “Third-party” (common) inputs. When testing for interaction between Regions A and B, there may be a third or common source of input from Region C.

Cortical-Cortical interaction measures and point spread issues:

If the two regions being tested for phase locking are so close that activity in one region can contribute substantially to the activity assigned to the other region, then there is the danger of measuring phase locking between the same signal at both locations.

How to assess:

<u>Phase locking values are very large (approaching 1) and not time varying.</u>

<u>Phase Difference is 0 or 180 degree</u>.

Principles of Dynamic Brain Network Operation

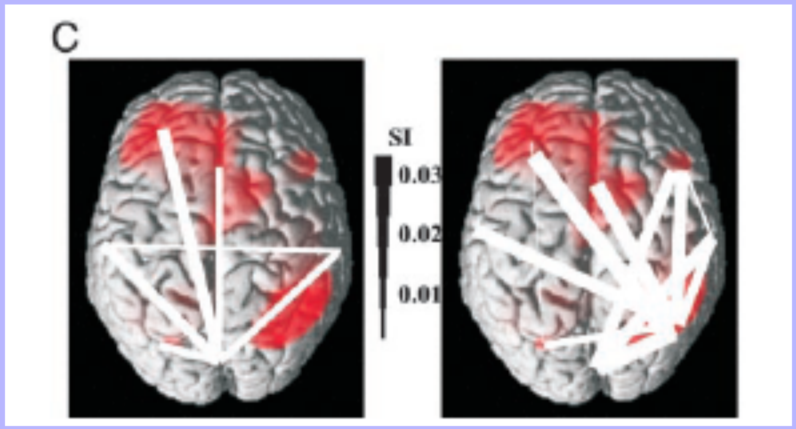
Subset of Basic Examples:

- A cortical node (A) can utilize oscillatory activity to interact with another node (B) at a common frequency.
- The interactions between cortical nodes A and B can occur in a uni-directional mode (A-to-B) or bi-directional mode (A-to-B and B-to-A) at different sub-second intervals.
- Cortical nodes can interact in the bi-directional mode by having one direction (A-to-B) coded in one frequency band (e.g. alpha) and the other direction (B-to-A) coded in another frequency (e.g. beta).
- A node can exert a nonlinear modulating influence at one frequency on the oscillatory activity at another node occurring at another frequency. For example: the level of gamma activity in area B can be modulated over time at a theta frequency by area A.
- Oscillatory activity at one frequency at node A can be nonlinearly coupled to oscillatory activity at another frequency at node B.
- A cortical node can interact with multiple other cortical nodes at the same time to form a distributed functional network.
- A cortical node can actively participate in more than one functional network <u>at the same time</u>, by virtue of the oscillatory frequencies it operates in. For example: node A can interact with nodes B, C, and D at one frequency (e.g. alpha), and also with nodes G, H and I at another frequency (e.g. theta).
- Functional networks can change in a fraction of a second. Coupled with the above principles this enables models with both parallel and rapid serial processes over the course of cognitive processing.

Simpson & Bressler

Specificity of Cortical Networks for Cognitive Processes

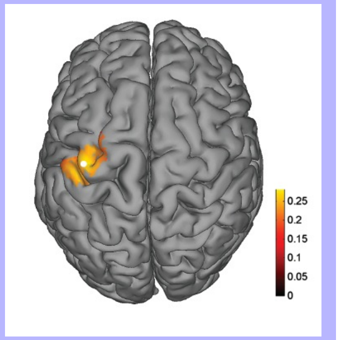
Attentional Blink Task

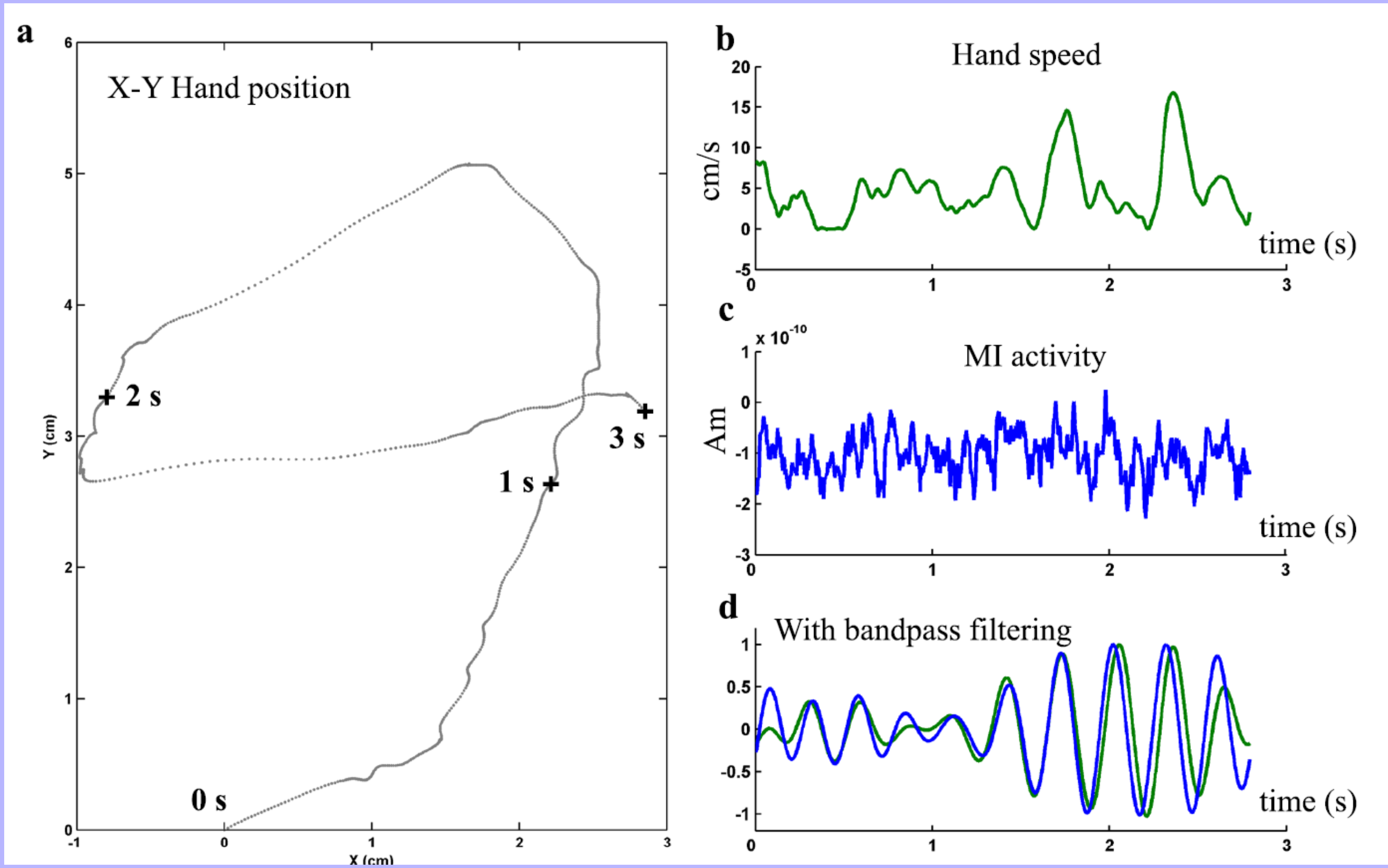


Stimulus Network   Target Network

Strength of synchronization between regions; Gross et al., PNAS 2004

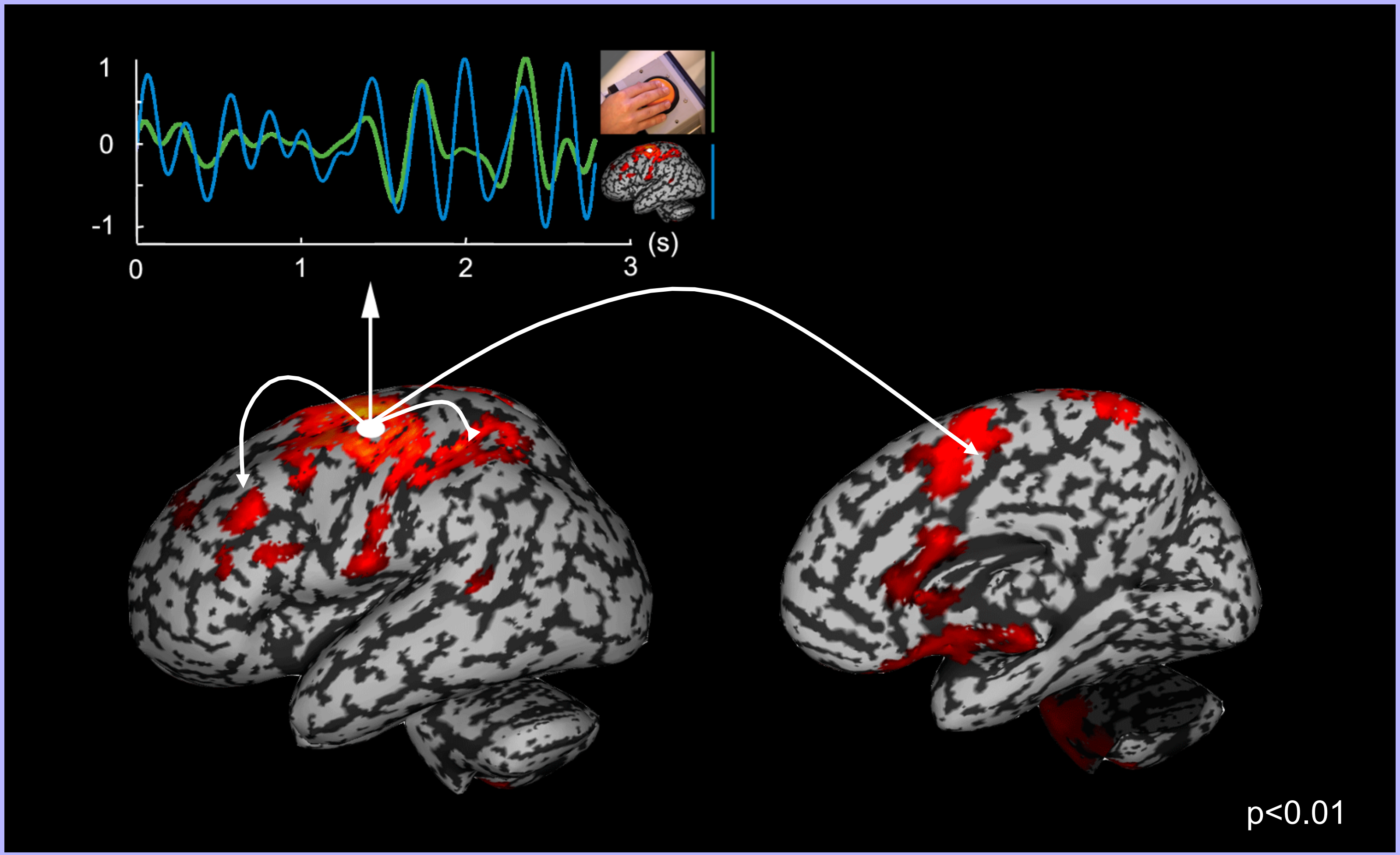
Brain activity coherent with hand speed





(Jerbi et al., PNAS, 2007)

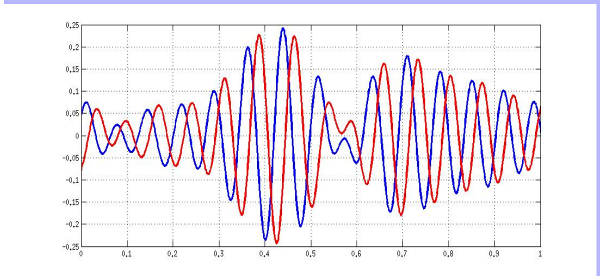
Network in coherence with activity in primary motor cortex



(Jerbi et al., PNAS, 2007)

Note: medial PFC – interplay self-action/change in external visual

Inferred direction with Phase Delay.



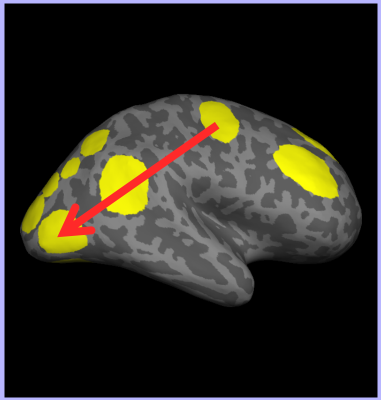
•Translate the the phase delay for a specific frequency into time (msec):

- Area A precedes Area B by X msec.

• Is X consistent with the physiological conduction time from A to B?

• If so, then this can provide indirect support for direction.

• If there are additional frequencies that show phase locking, and the delays for these are also consistent with A precedes B by X msec., then this adds support.



FCx top-down interaction with VCx.

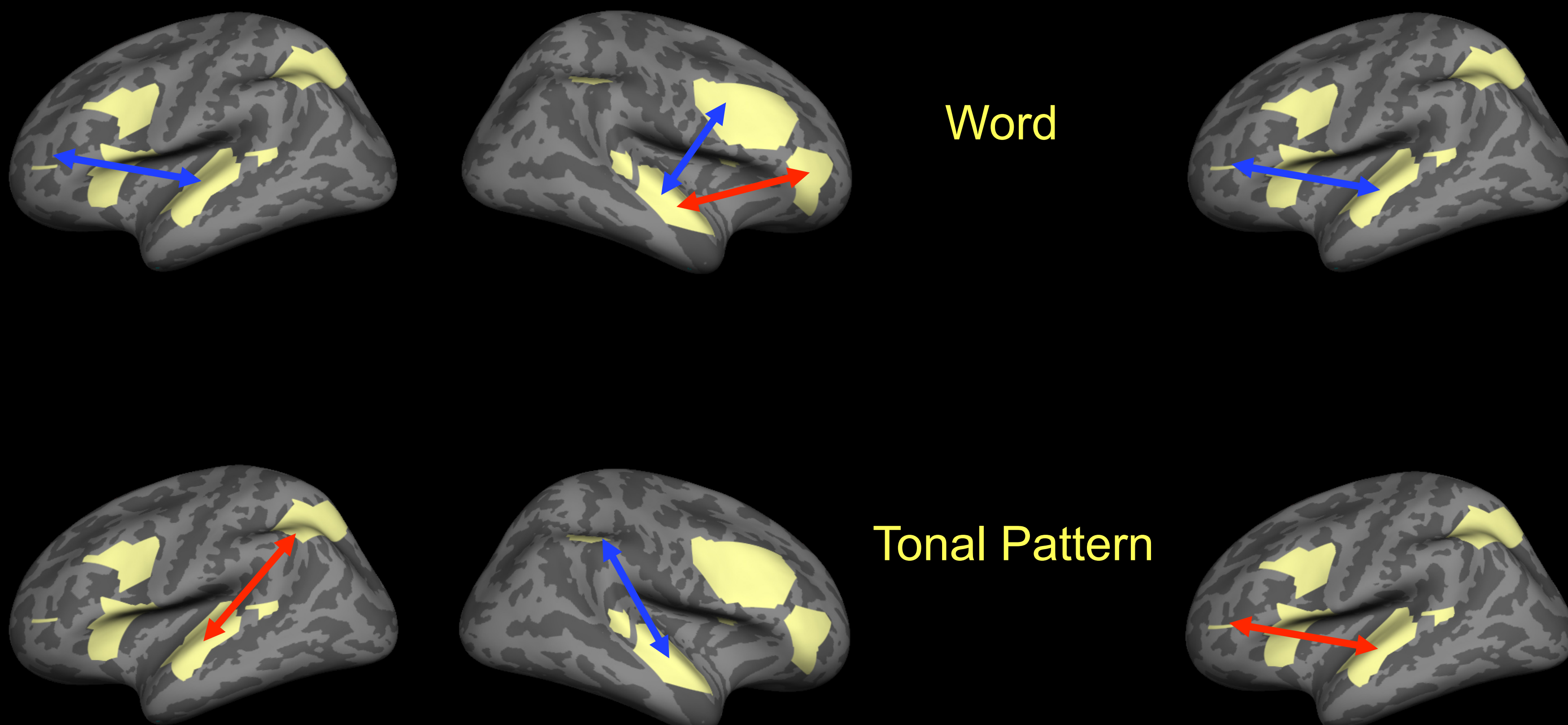
- Increased phase-locking in Theta (4 Hz) between FCx and VCx.
- Phase delay = 36 degrees → 25 msec.
- Support for communication from FCx to VCx.

See Gregoriou et al., Science 2009; primate FEF-V4

Network Specificity: Task, Accuracy and RT

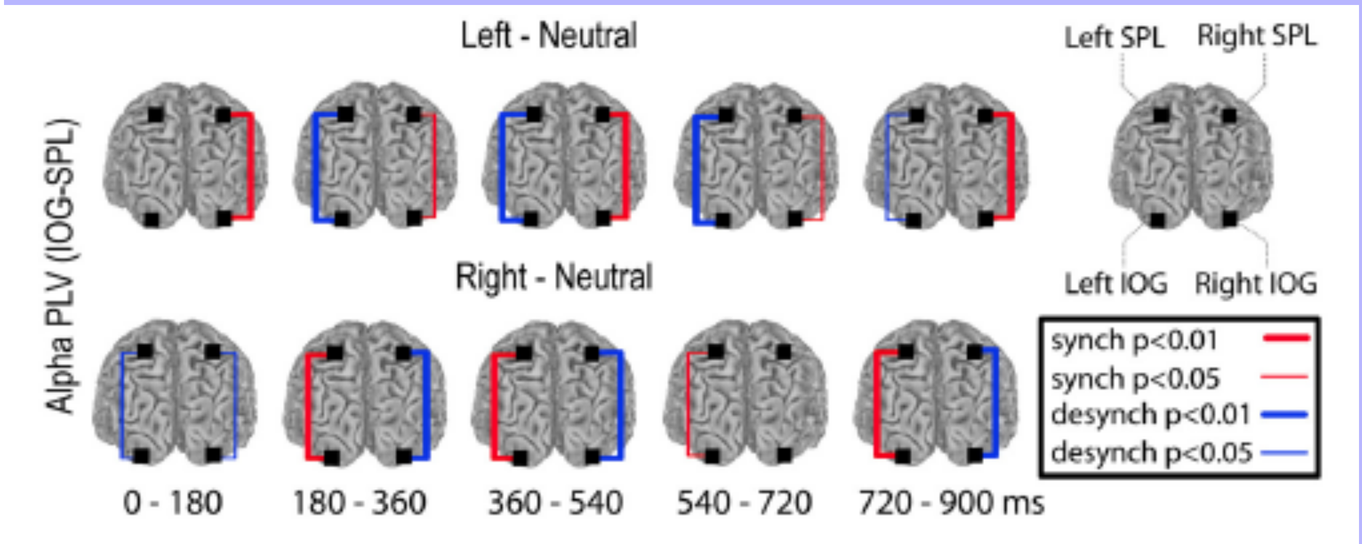
Accuracy

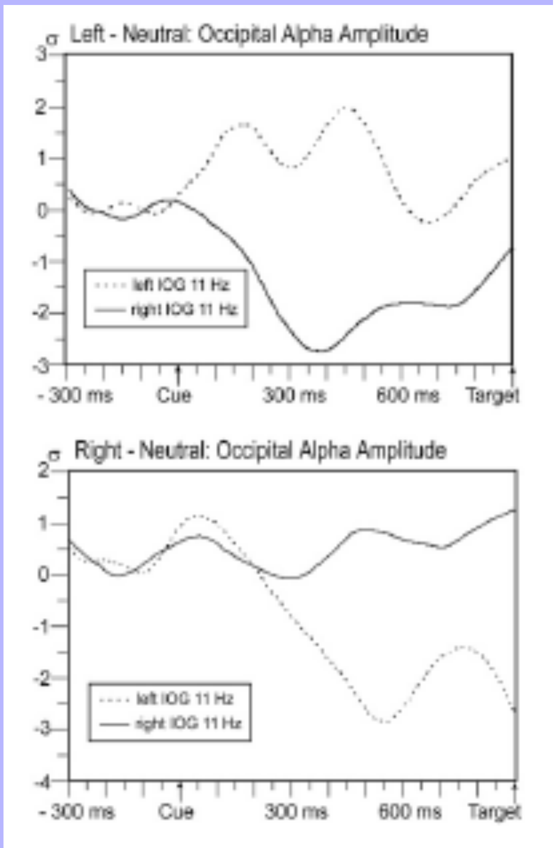
Reaction Time



Simpson et al., 2009 CNS

Intra and Inter-Cortical synchronizations in the same frequency





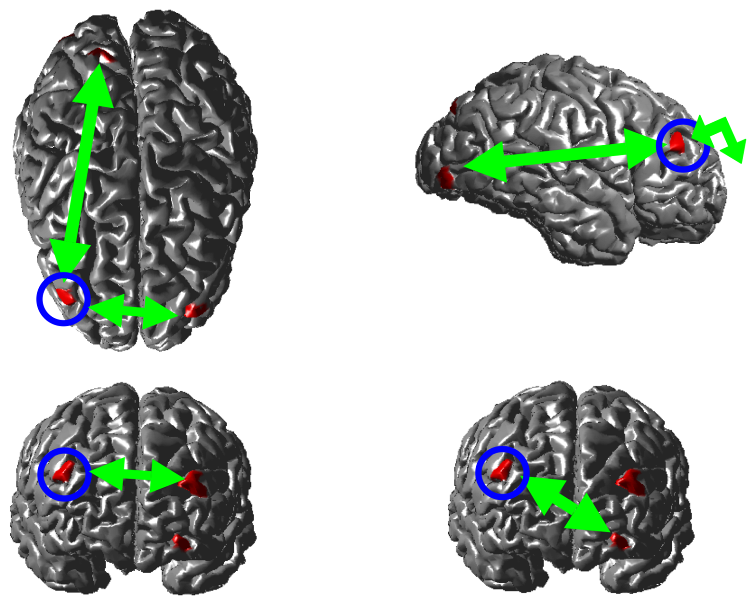
Decreased intra-cortical synchronization with increased intercortical synchronization in alpha band.

Doesburg et al., Brain Research 2009

A cortical region can participate in multiple, functionally distinct networks at the same time by interacting in different oscillatory frequencies.

Cortical "Multi-Networking"

Right DorsoLateral Prefrontal Cortex (blue circle) forms two functionally distinct cortical networks at the same time by synchronizing activity with other cortical regions in two different frequency bands during a visual attention task.

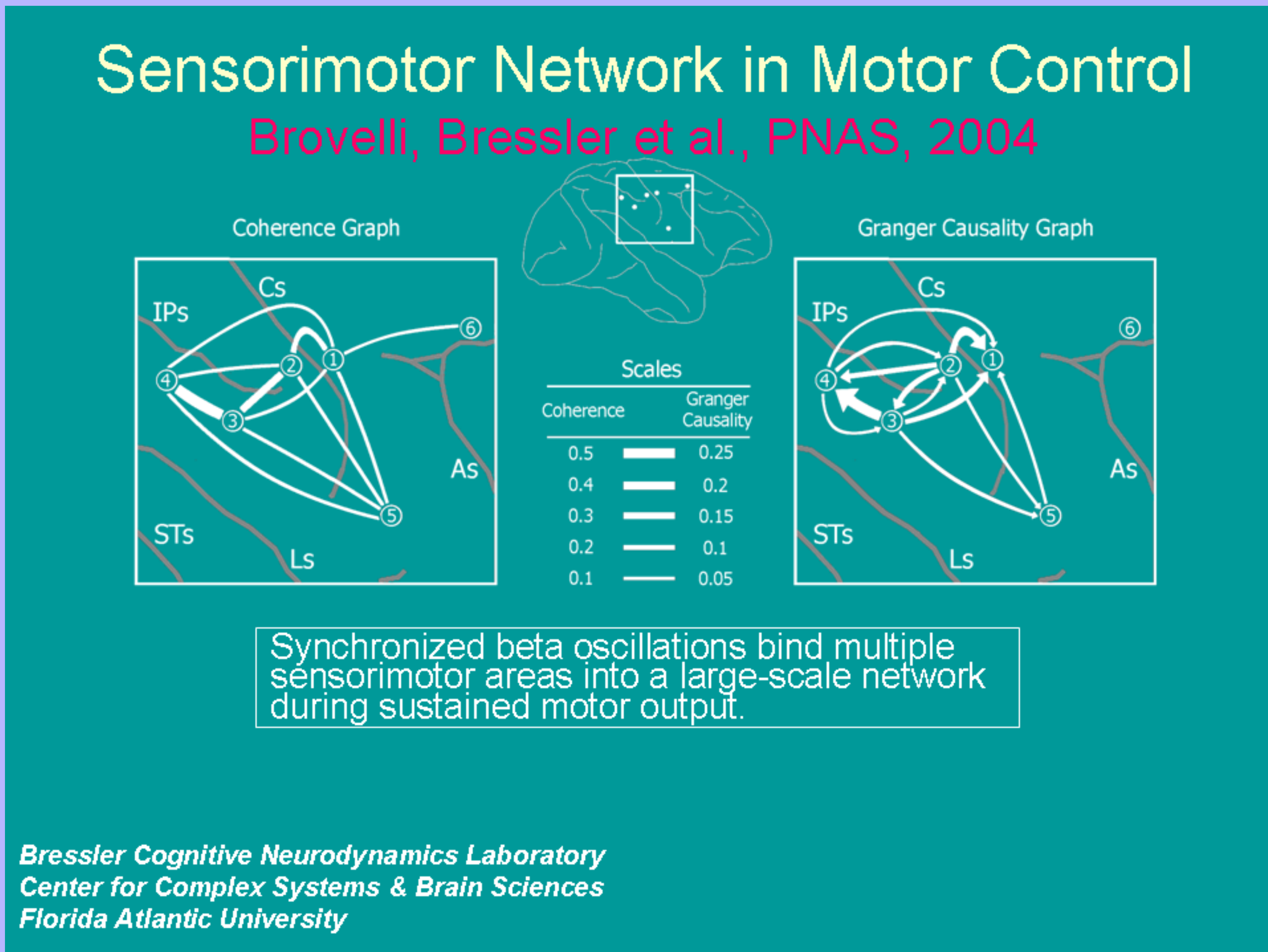


Alpha Network
Parietal and DorsoLateral Prefrontal

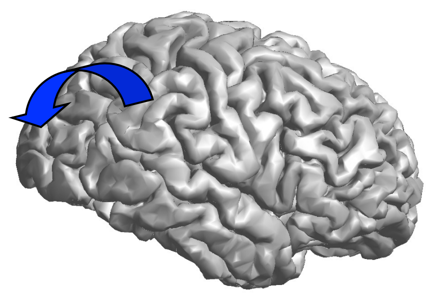
Theta Network
Occipital and Ventral Prefrontal

Darvas, Simpson, Bressler

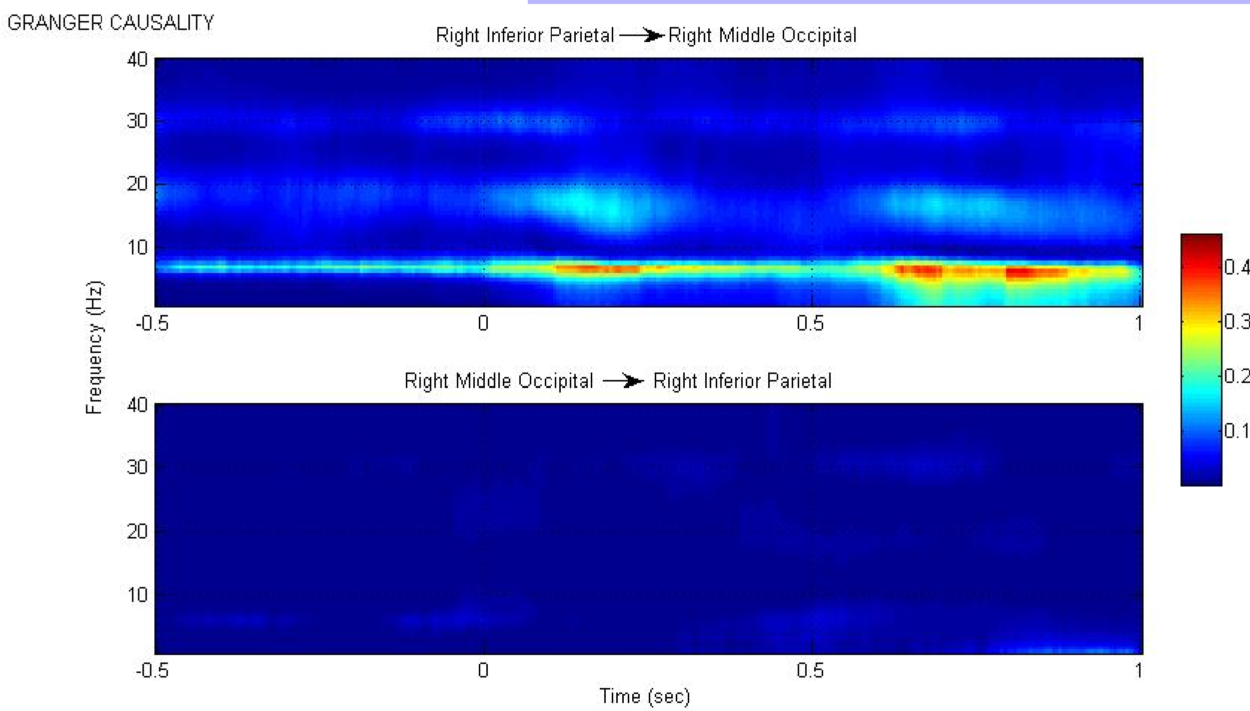
Granger Causality: analysis of electrophysiological data



Functional Connectivity
Granger Causality: Uni-Directional Cortical Interaction

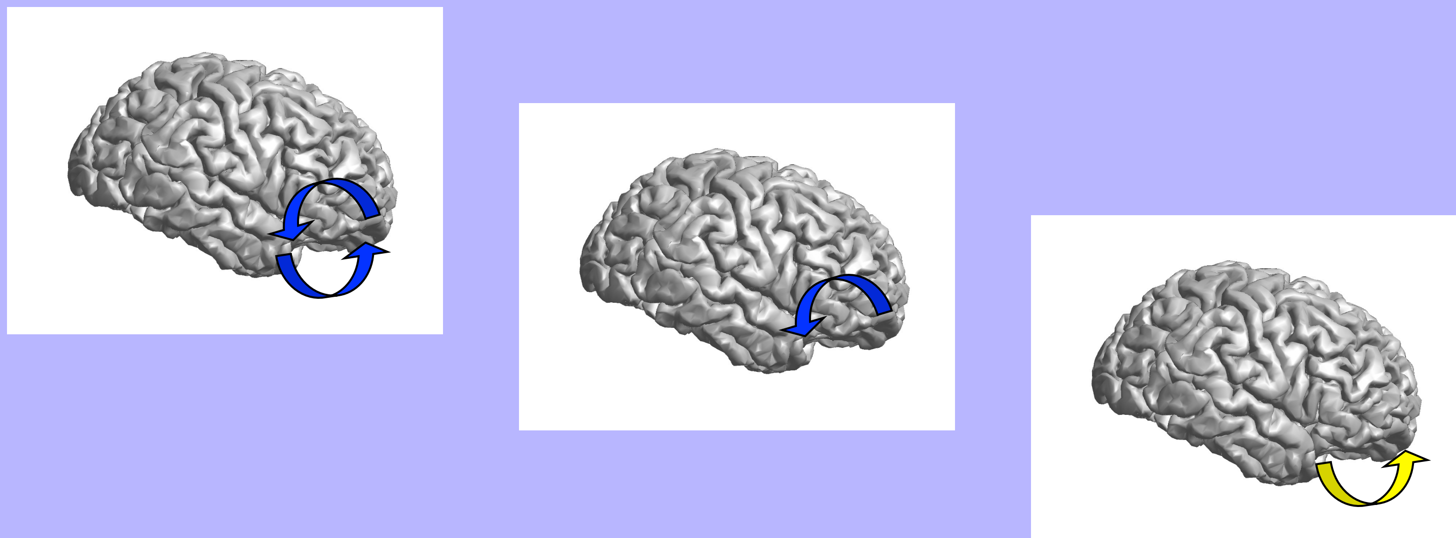


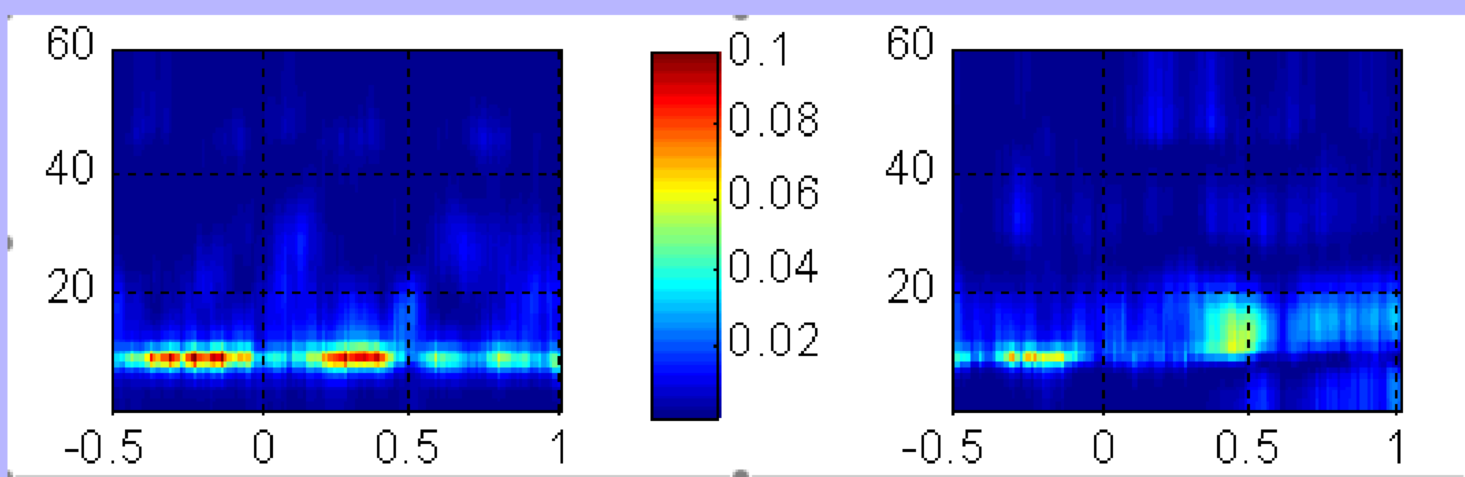
Top-Down Control
Without Bottom-Up Counterpart
Parietal to Occipital (Alpha).



Functional Interactions

Granger Causality combined with spectral and temporal specificity differentiate multiple types of interactions



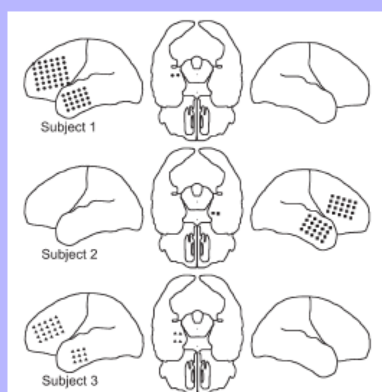


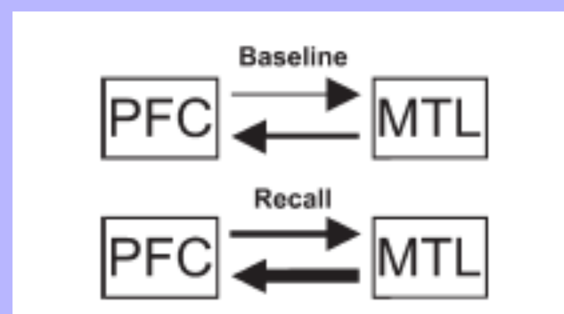
Frontal -> Temporal
(Top-Down)

Temporal -> Frontal
(Bottom-Up)

Identifying nature of cortical interactions underlying memory retrieval (free recall task).

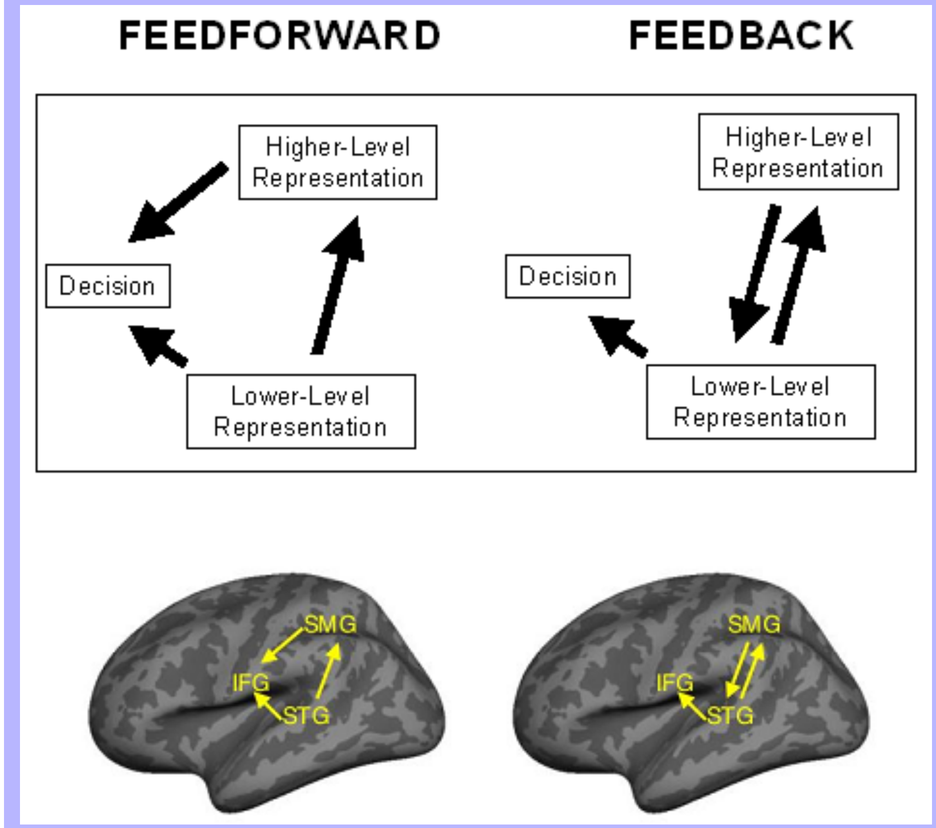
Granger analyses applied to Theta activity





Andersen et al., Cerebral Cortex 2010

Neural Causation:
Lexical Influences on Speech Perception

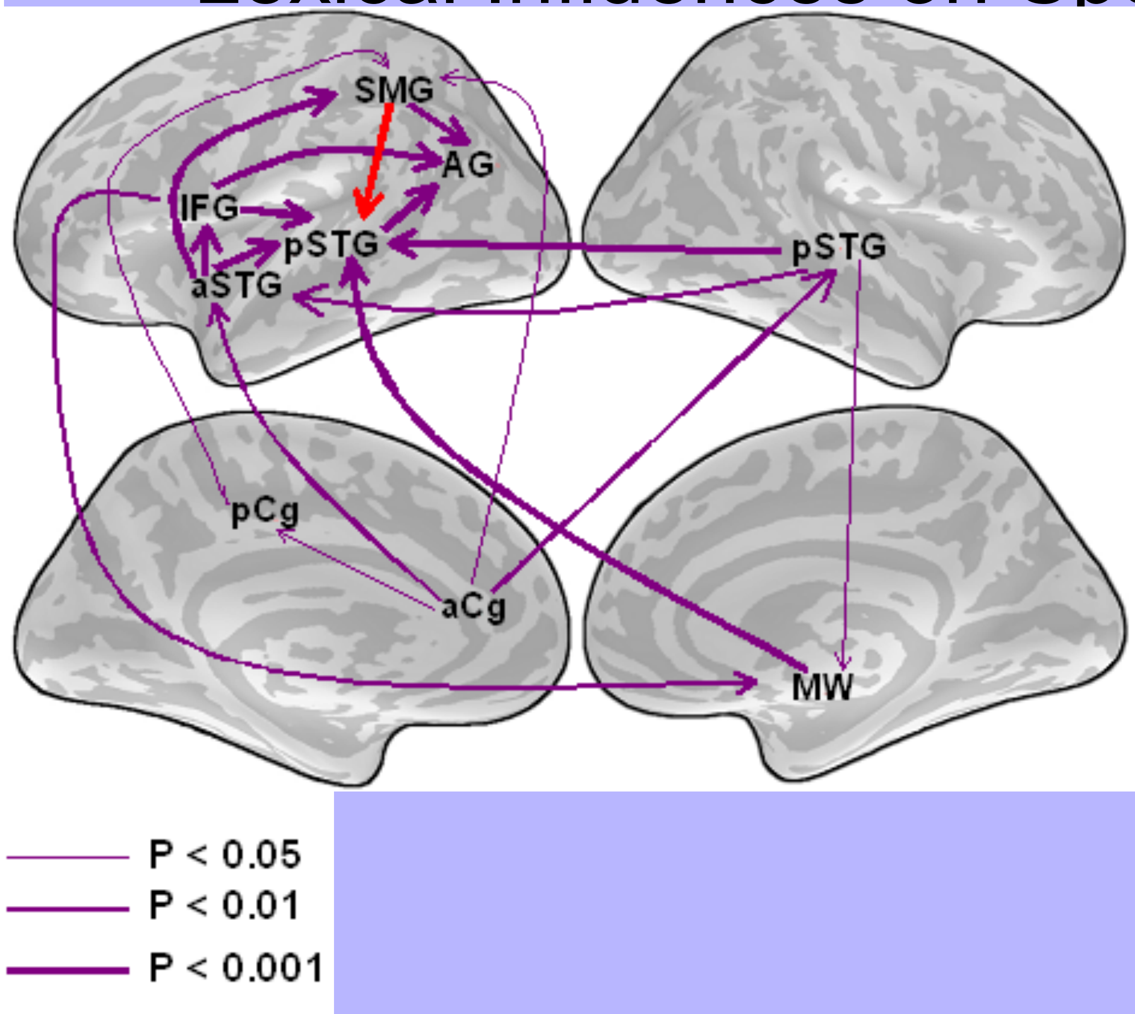


- Ganong effect: perception of ambiguous speech sounds affected by context
  - *shandal – sandal*
  - *shampoo – sampoo*

- Interaction of lexical and phonetic processes:
  – Top-down (feedback) model
  vs.
  – Feedforward model

Gow, Segawa, Ahlfors & Lin, *NeuroImage,* 2008

Neural Causation: Lexical Influences on Speech Perception



- ROIs:
  - phase synchrony with left pSTG in 40 Hz gamma band at 280-480 ms
- Granger causality:
  - top-down lexical influence (left SMG) on phonetic processing (left pSTG)

Gow, Segawa, Ahlfors & Lin, *NeuroImage,* 2008

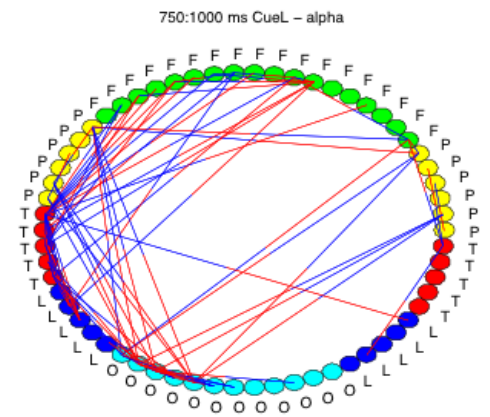
Granger Causality

• One frequency band.
• One time window.

• Multiple Brain Regions Interact

•Top-Down
•Bottom-Up
•Bi-Directional
•Divergence
•Convergence

•Strength not indicated



Dynamic Network Complexity

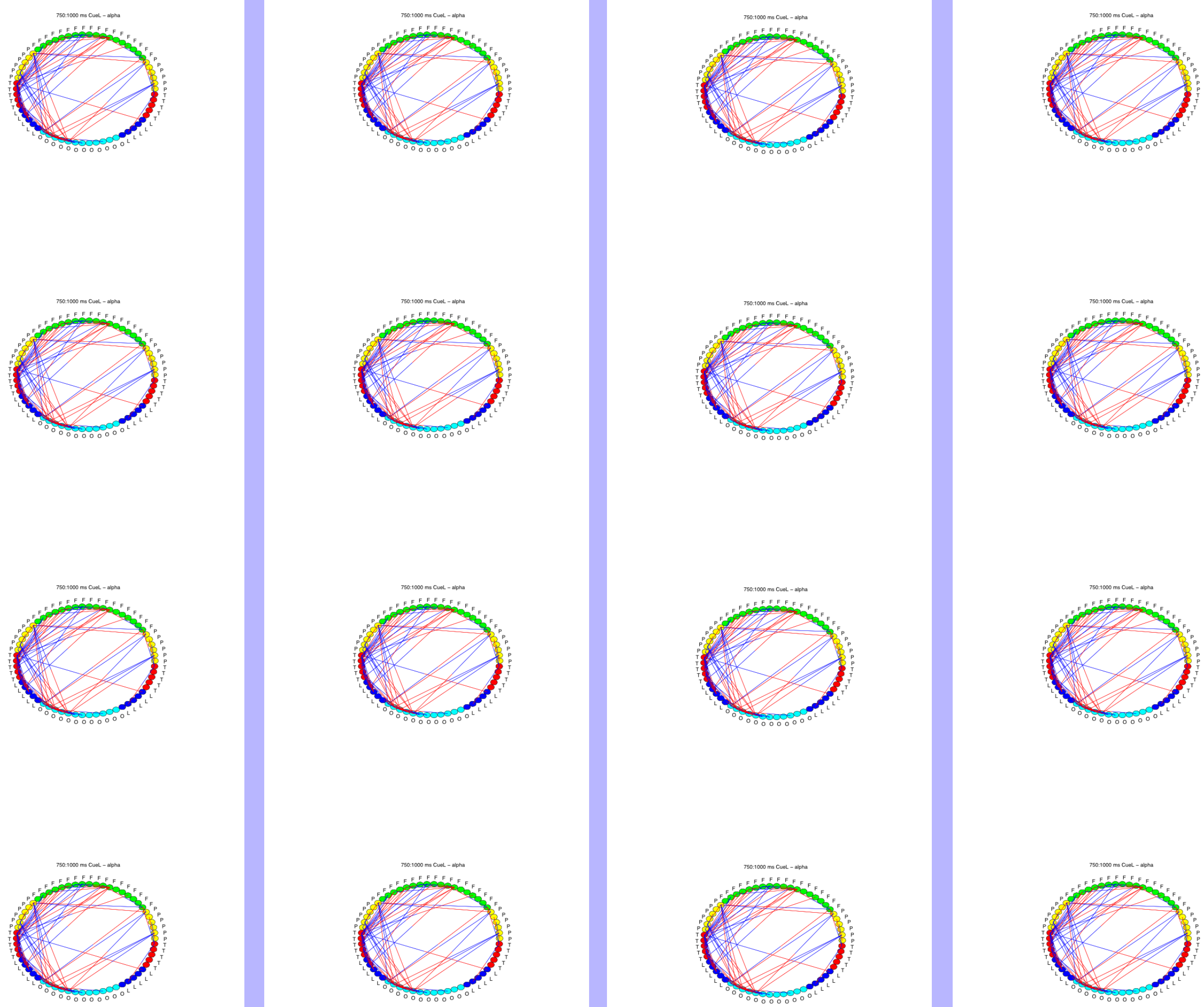
Frequency

Theta

Alpha

Beta

Gamma



Time Windows