EEG/MEG 3:

Functional Connectivity Analysis

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Brain Connectivity

Structural/Anatomical Connectivity:
Hardware links between brain regions
(e.g. DWI/DTI).

Functional Connectivity:
Statistical dependencies of activation between brain regions
(e.g. correlation, or spectral measures such as phase-locking and coherence).

Effective Connectivity:
Causal interactions of activation between brain regions
(Granger Causality, Dynamic Causal Modelling).

For example:
http://journal.frontiersin.org/article/10.3389/fnsys.2015.00175/full
http://www.sciencedirect.com/science/article/pii/S0165027012000817
http://www.ncbi.nlm.nih.gov/pubmed/21477655
http://online.liebertpub.com/doi/abs/10.1089/brain.2011.0008

Taxonomy Of Popular Functional Connectivity Methods

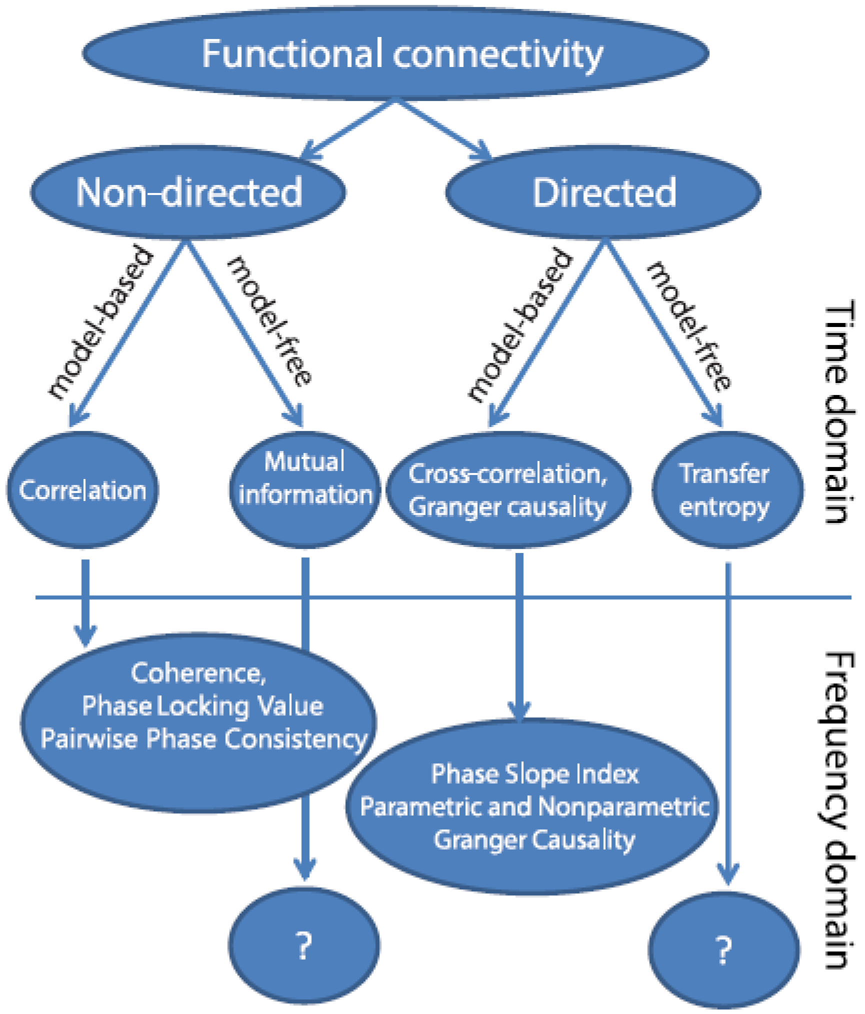
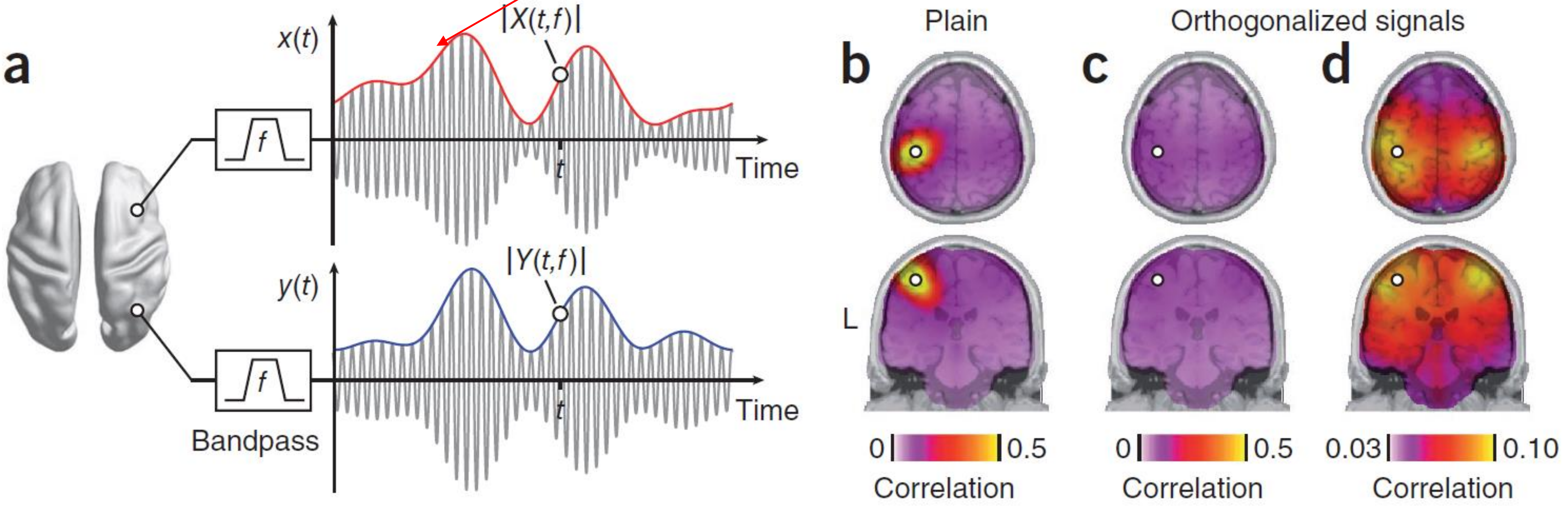


FIGURE 1 | A taxonomy of popular methods for quantifying functional connectivity.

Bastos & Schoeffelen, Front Syst Nsc 2016
https://www.frontiersin.org/articles/10.3389/fnsys.2015.00175/full

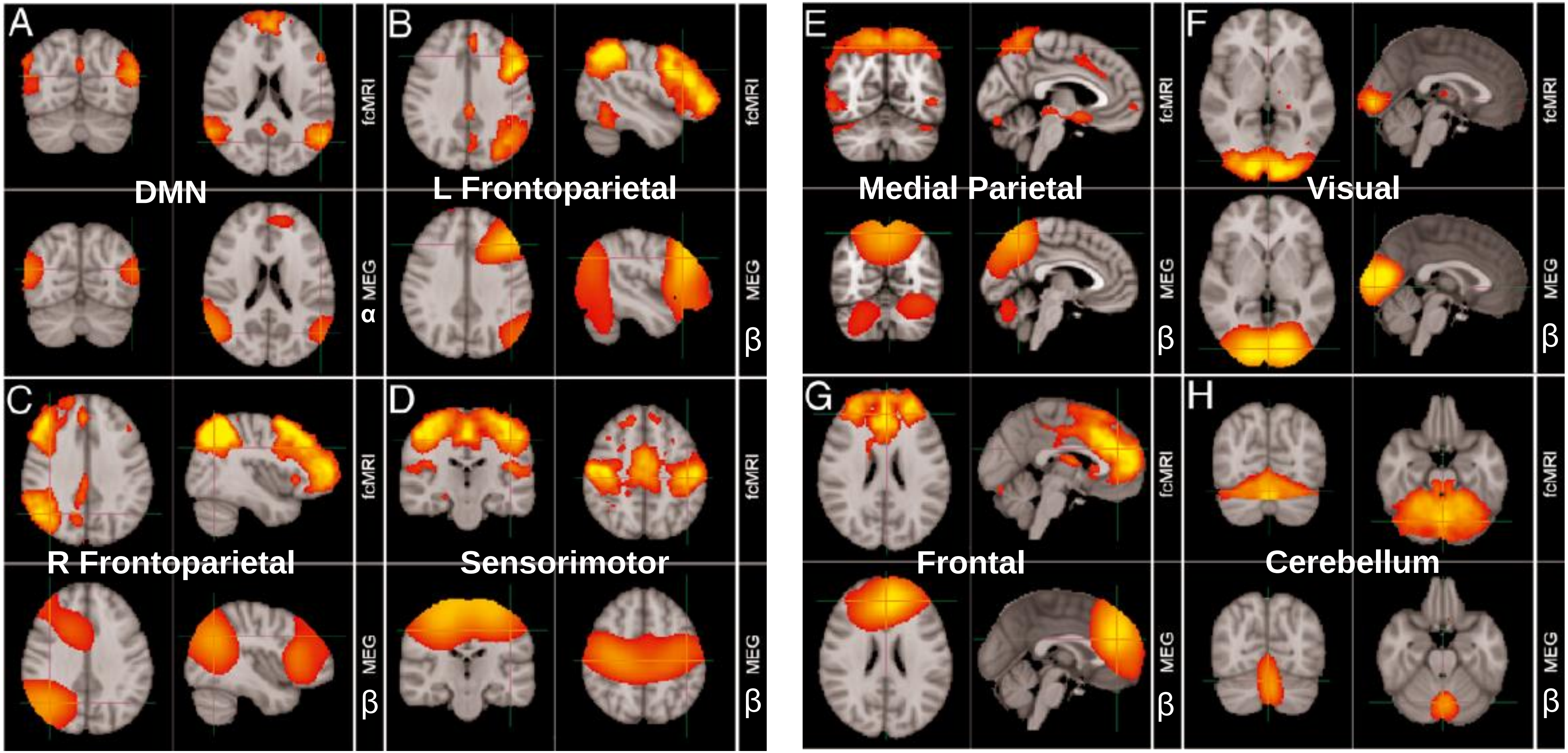
Functional Connectivity of Resting State Activity

(“Hilbert”) Envelope for a frequency band



Hipp et al., Nat Nsc 2012, https://www.nature.com/articles/nn.3101

Functional Connectivity of Resting State Activity



Brooks et al., PNAS 2011, https://www.pnas.org/doi/10.1073/pnas.1112685108

Spectral Connectivity – “Synchronisation”

Neuron
Perspective

Rhythms for Cognition: Communication through Coherence

Pascal Fries[1,2,*]

https://www.sciencedirect.com/science/article/pii/S0896627315008235

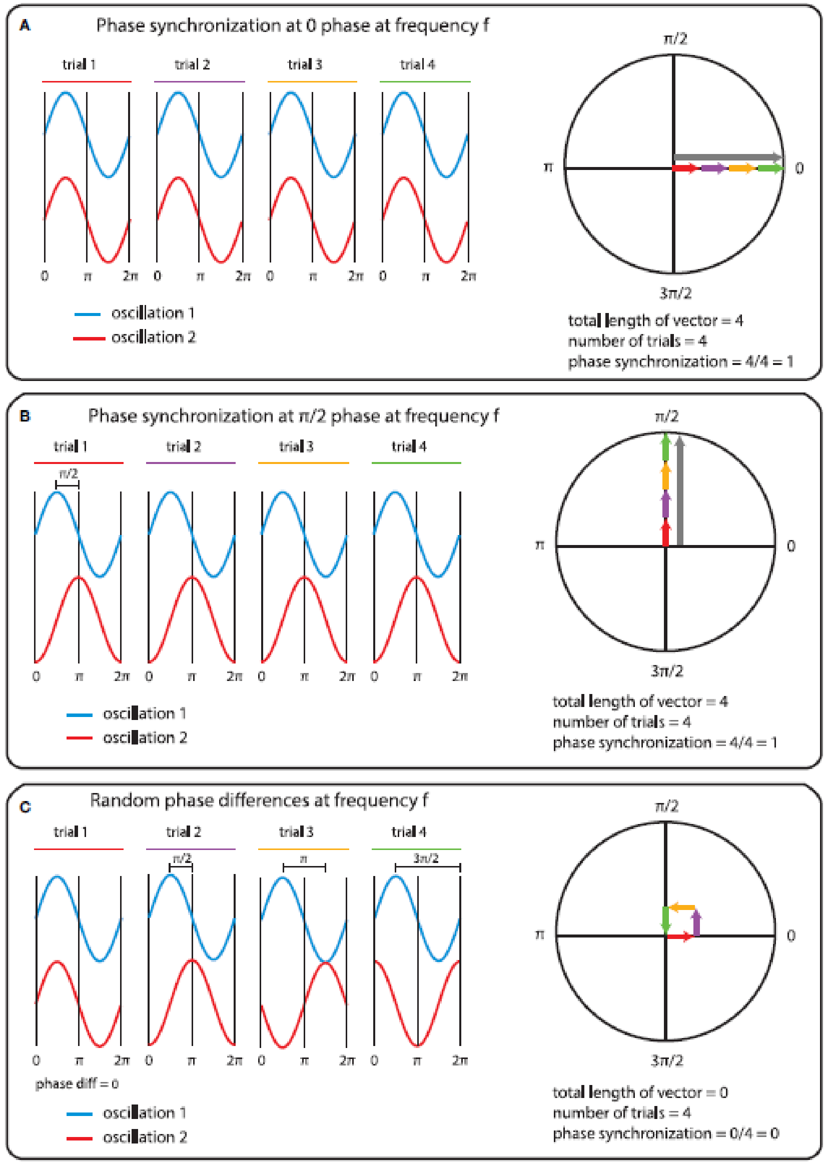
Spectral fingerprints of large-scale neuronal interactions

Markus Siegel[1], Tobias H. Donner[2]* and Andreas K. Engel[3]*

https://www.nature.com/articles/nrn3137

Coupled Oscillators: https://www.youtube.com/watch?v=T58lGKREubo

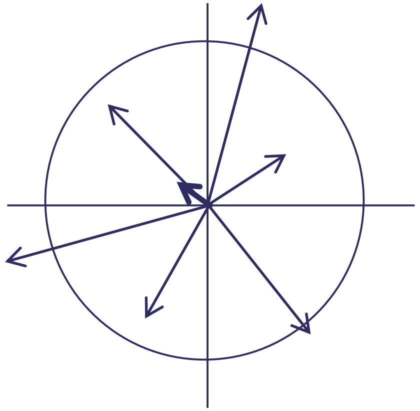
Phase-Locking – Use Only Phase, Ignore Amplitude



e.g., Bastos & Schoeffelen, Front Syst Nsc 2016, Fig. 3
https://www.frontiersin.org/articles/10.3389/fnsys.2015.00175/full

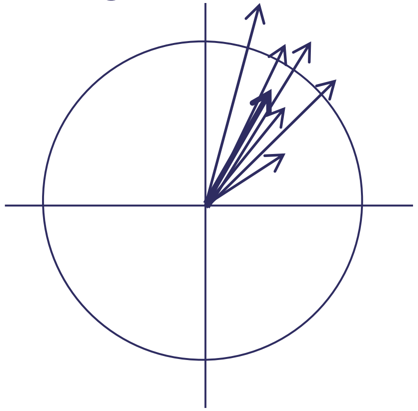
(Magnitude-Squared) Coherence

Low Coherence



Every vector represents the amplitude and phase difference of one trial.

High Coherence



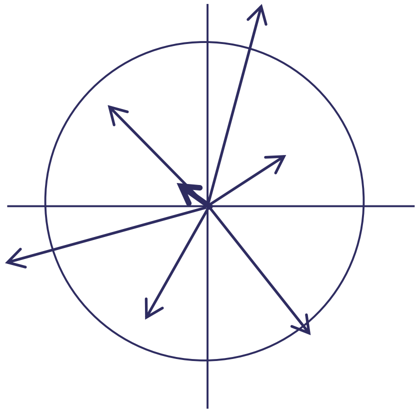
Coherence takes amplitude as well as phase consistency into account.
It can be interpreted as “amplitude-weighted phase-locking value”, i.e. trials with low amplitudes are given lower weight than those with higher amplitudes.

If one signal is a time-shifted and re-scaled version of another signal, then their Coherence is 1.
If two signals are random and independent of each other, then their Coherence is 0.

e.g., Bastos & Schoeffelen, Front Syst Nsc 2016
https://www.frontiersin.org/articles/10.3389/fnsys.2015.00175/full

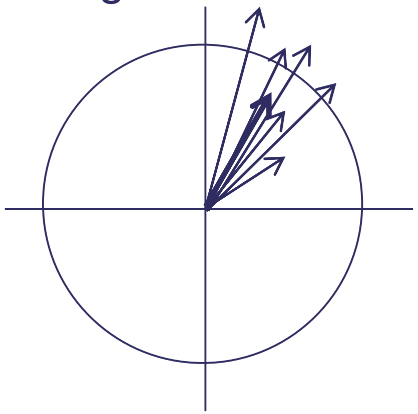
Phase-Locking vs Coherence

Low Coherence

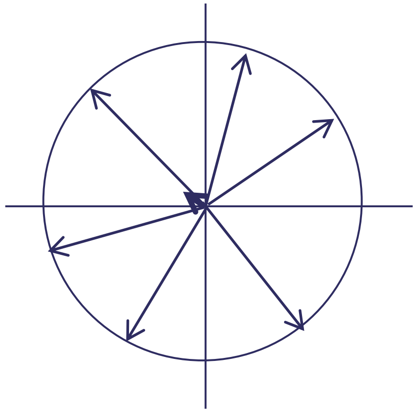


Every vector represents the amplitude and phase difference of one trial.

High Coherence

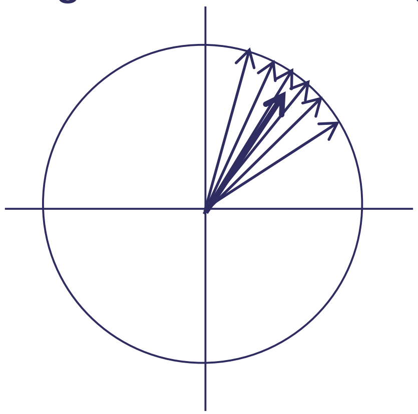


Low Phase-Locking



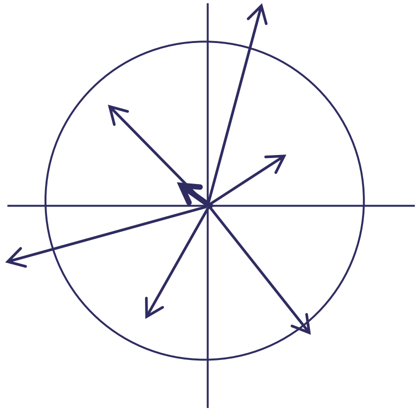
We are not interested in amplitude, and normalise all vectors to unit length. The average vectors measure the phase-consistency across signals (phase-locking value, PLV).

High Phase-Locking

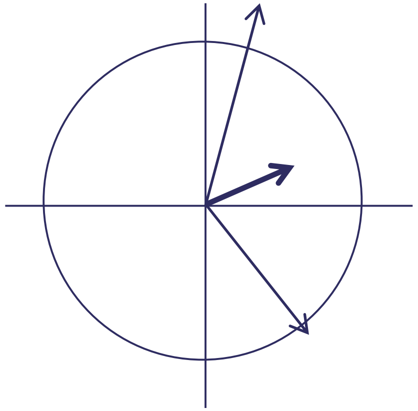


Sample Size and SNR Bias

More trials



Fewer trials



Many connectivity metrics are positively biased (e.g. Coherence with values between 0 and 1), i.e. one gets positive values even in the presence of pure noise.
Importantly, the metric depends on the number of trials.
⇒ Plot metric for baseline data and different trials counts in your own data
⇒ Equalise trials counts between conditions
⇒ Baseline correction

This effect is relatively small for ~>50 trials:

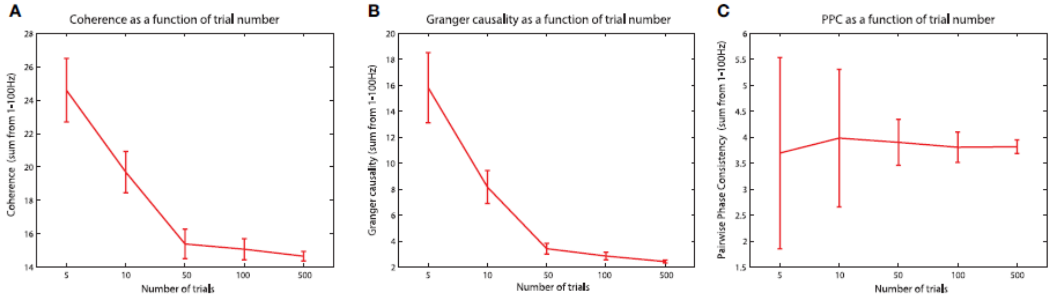
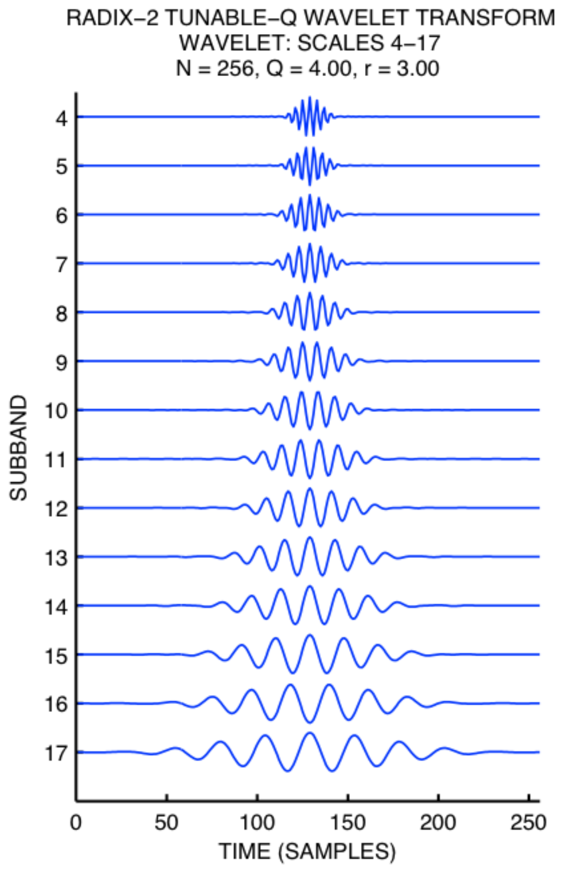


FIGURE 10 | Sample size bias for coherence and Granger causality estimates. (A–C) For each respective metric, simulations based on 5, 10, 50, 100, and 500 trials were run, and coherence **(A)**, Granger causality **(B)**, and PPC **(C)** were calculated. Each panel reflects the average ± 1 standard deviation across 100 realizations.

Bastos & Schoeffelen, Front Syst Nsc 2016
https://www.frontiersin.org/articles/10.3389/fnsys.2015.00175/full

Time-Resolved Connectivity

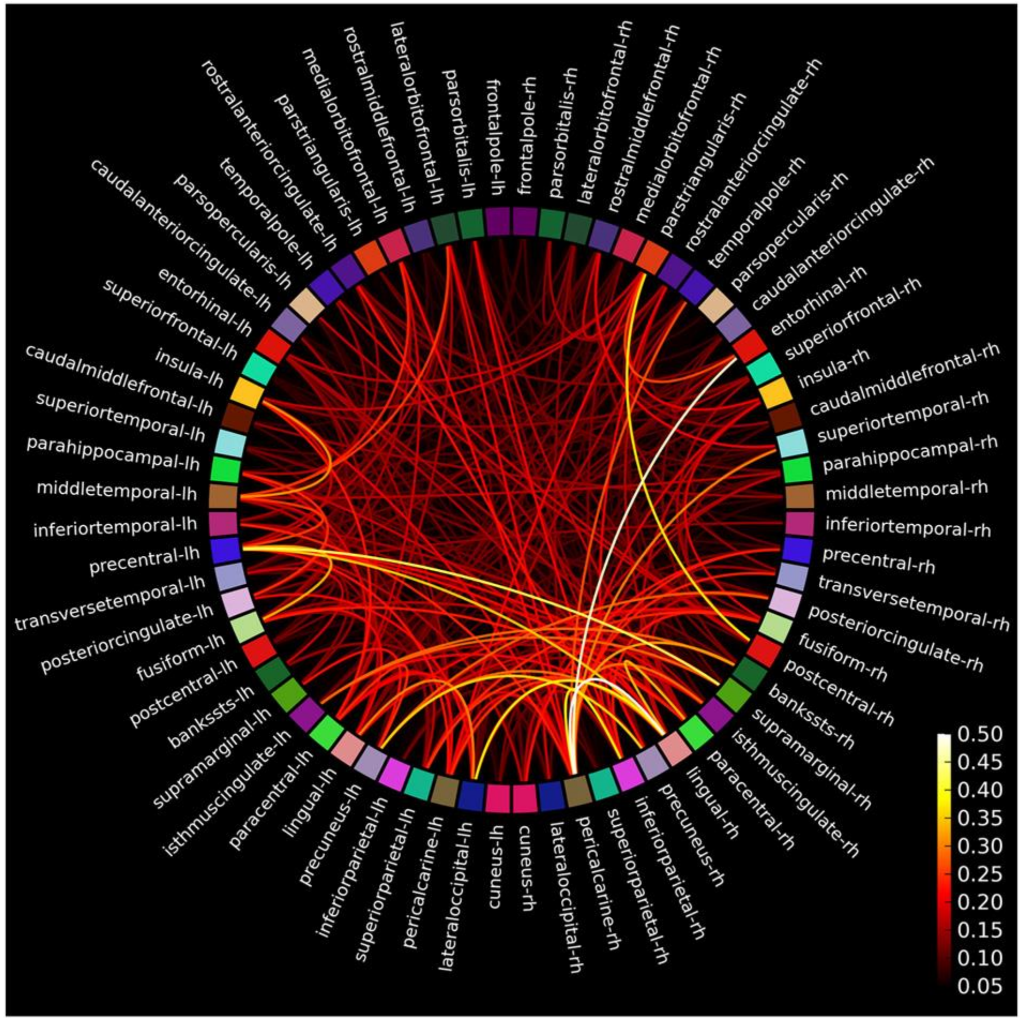
Spectral connectivity measures can be computed for separate time windows, or they can be computed continuously using wavelets or Hilbert transform (subject to general trade-off between frequency and time resolution).



Temporal resolution decreases as frequency decreases

(wavelets are getting “broader”)

Bivariate Functional Connectivity Is Relatively Easy To Compute - And Therefore Suitable For Exploratory “All-To-All” Analyses



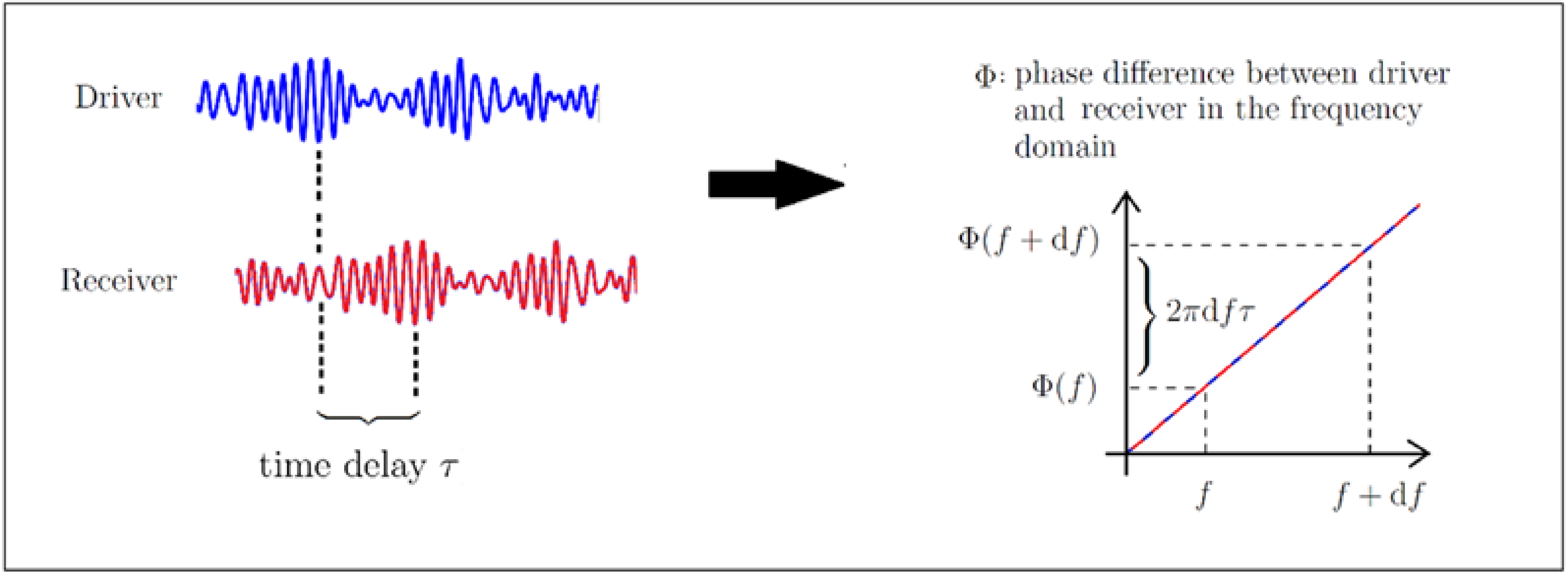
Gramfort et al., NI 2014
https://www.sciencedirect.com/science/article/pii/S1053811913010501

Directed Functional Connectivity

Phase-Slope Index (PSI):

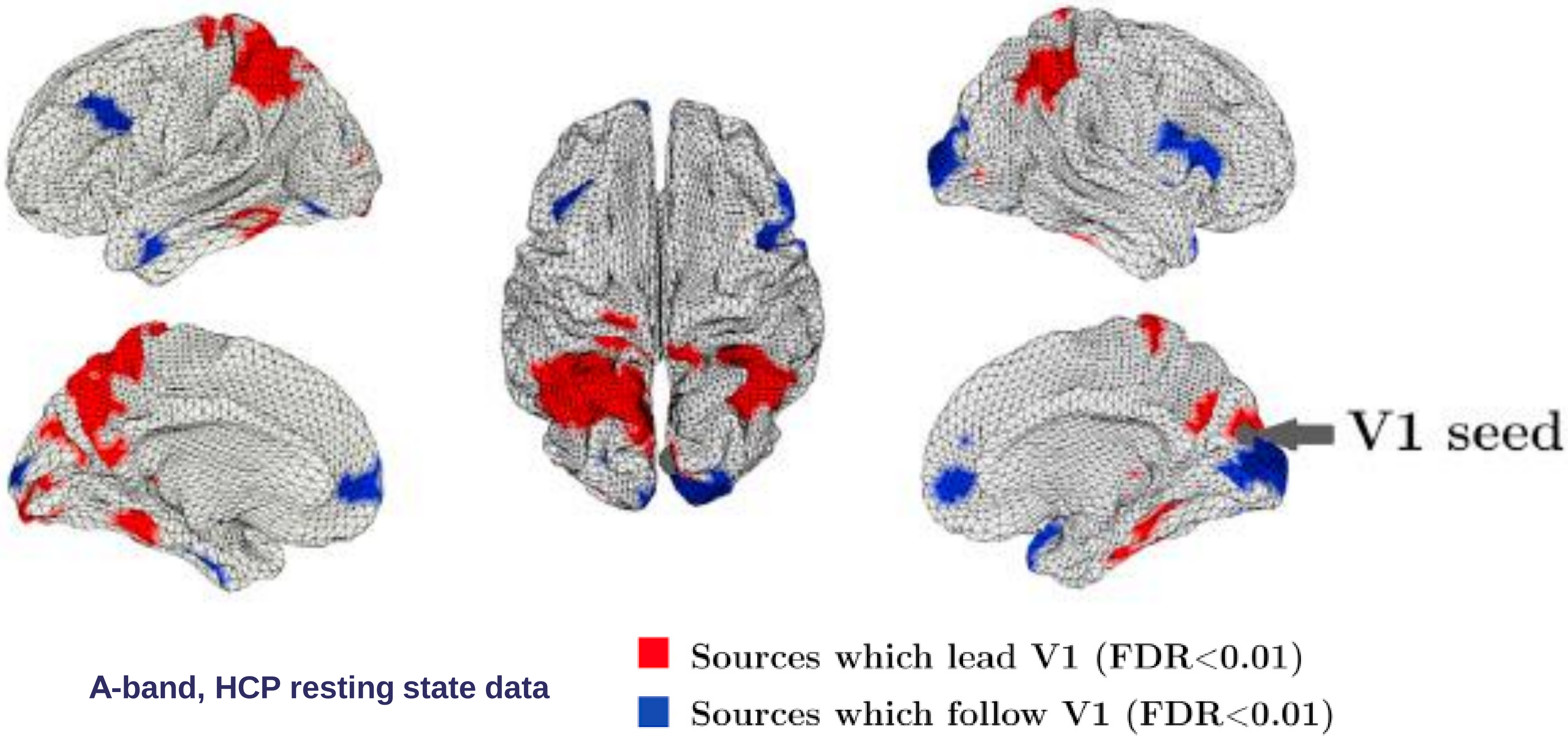
For signals with a stable time delay, the phase in the frequency domain should depend linearly on frequency

Nolte et al, Phys Rev Let 2008, http://doc.ml.tu-berlin.de/causality/
Basti et al., NI 2018, https://www.sciencedirect.com/science/article/pii/S1053811918301897
Bastos & Schoeffelen, Front Syst Nsc 2016, https://www.frontiersin.org/articles/10.3389/fnsys.2015.00175/full



Basti et al., J Serb Soc Comp Mech 2017
https://www.scopus.com/record/display.uri?eid=2-s2.0-85044605749&origin=inward

Phase Slope Index (PSI)



A-band, HCP resting state data

Basti et al., Neuroimage 2018
https://www.sciencedirect.com/science/article/pii/S1053811918301897

Directed Functional Connectivity

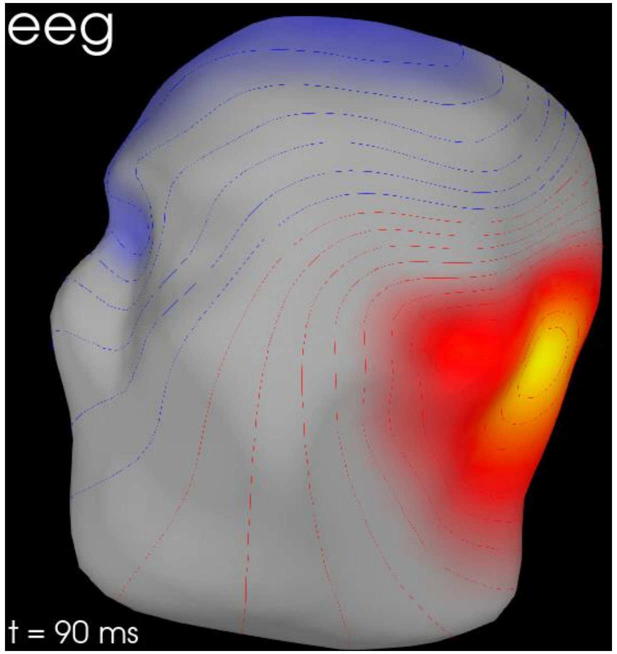
Auto-regressive models, Granger Causality:
…in the time domain:
Predict the future of a signal based on the past of its own and other signals

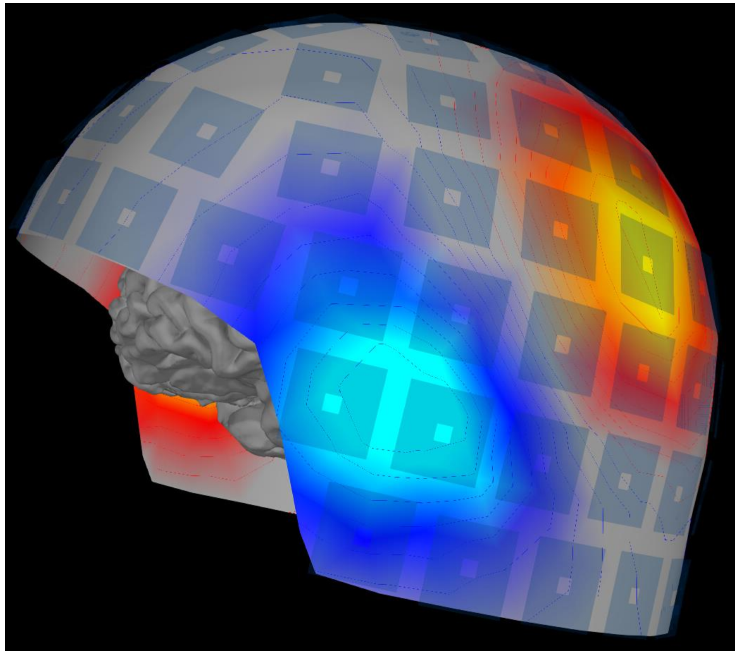
…in the frequency domain:
- Partial Directed Coherence
- Directed Transfer Function

Bastos & Schoeffelen, Front Syst Nsc 2016, https://www.frontiersin.org/articles/10.3389/fnsys.2015.00175/full
Greenblatt et al., J Nsc Meth 2012, https://www.sciencedirect.com/science/article/pii/S0165027012000817
Haufe et al. NI 2013, https://www.sciencedirect.com/science/article/pii/S1053811912009469

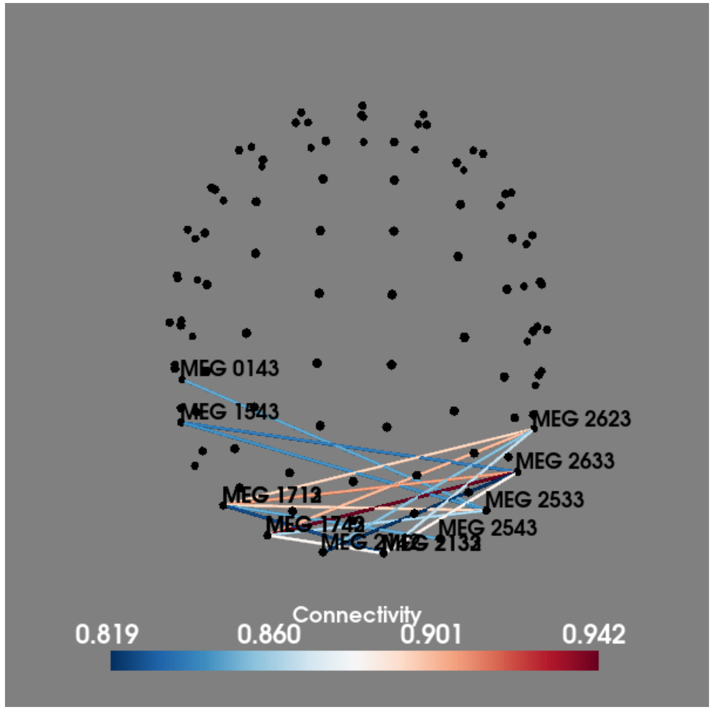
“Connectivity” in sensor space is hard to interpret due to volume conduction

Tone to right ear



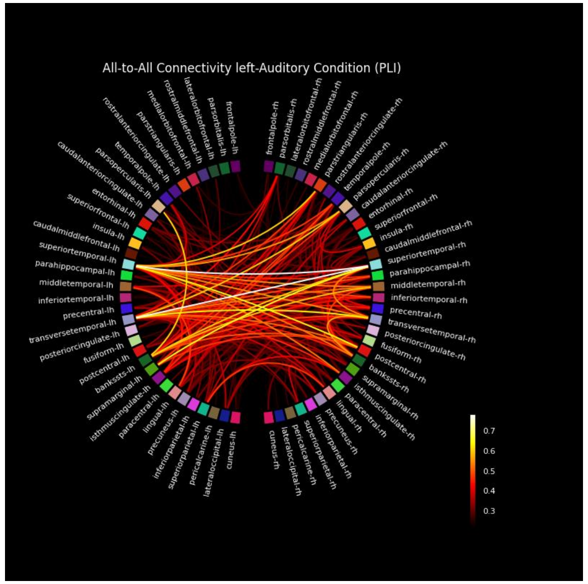


All-to-all “connectivity” for visual evoked response in sensor space

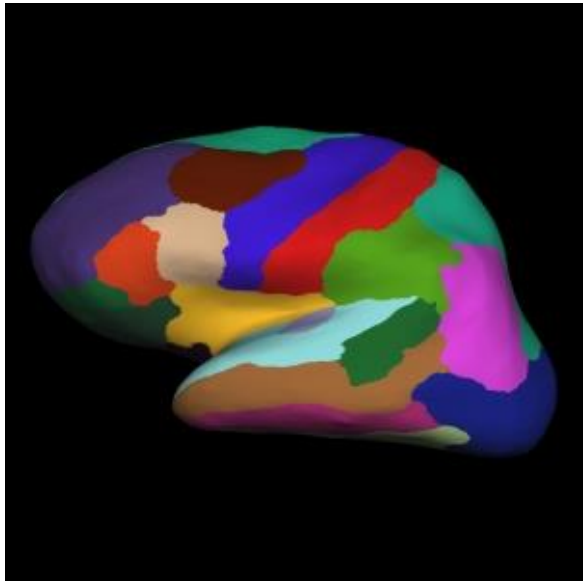


https://mne.tools/mne-connectivity/stable/auto_examples/sensor_connectivity.html

Connectivity in source space is limited by leakage



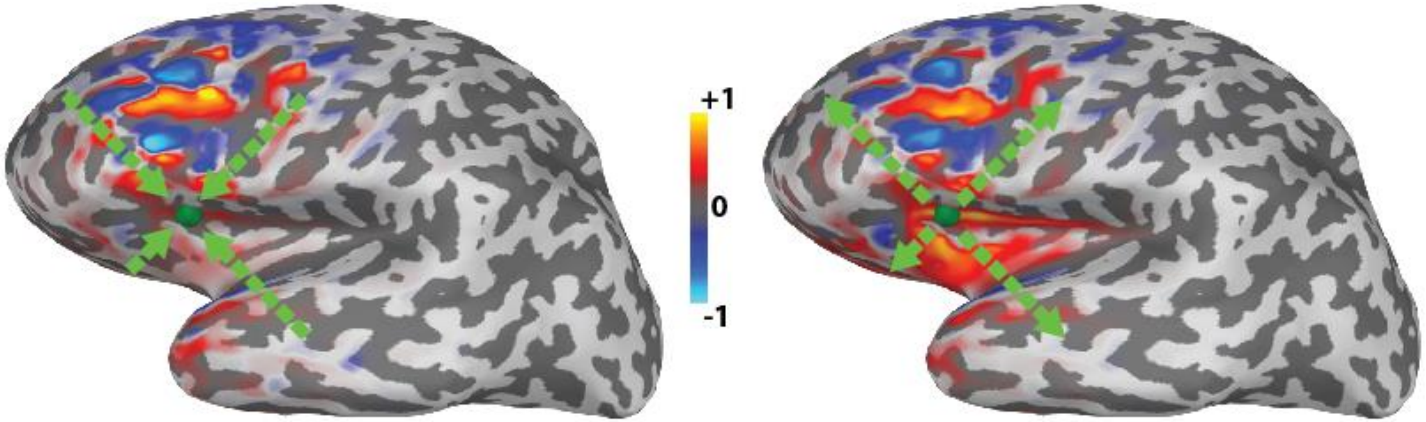
https://mne.tools/mne-connectivity/stable/auto_examples/mne_inverse_label_connectivity.html



https://surfer.nmr.mgh.harvard.edu/fswiki/CorticalParcellation

Cross-Talk Function CTF

Point-Spread Function PSF



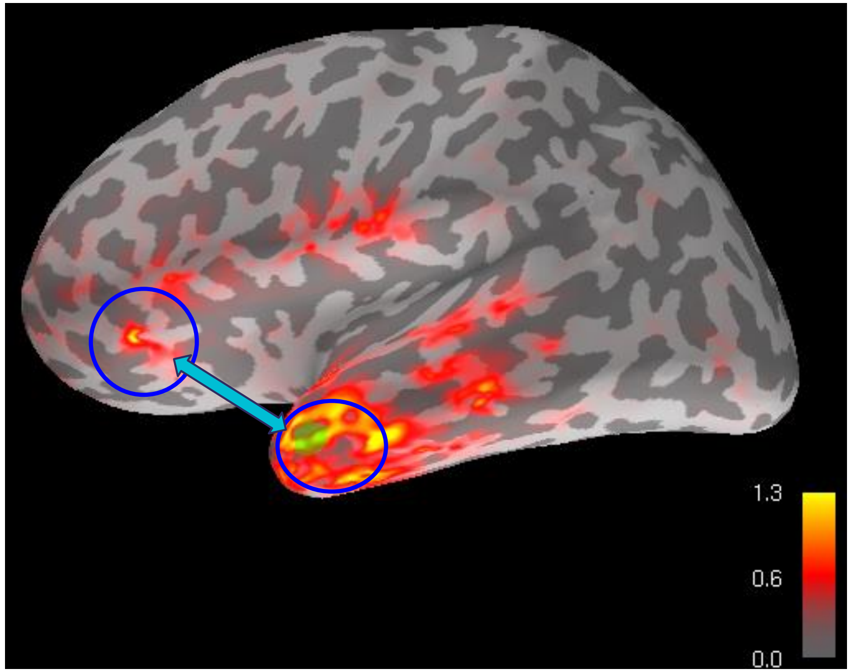
How other sources may affect the estimate for this source

How this source affects estimates for other sources

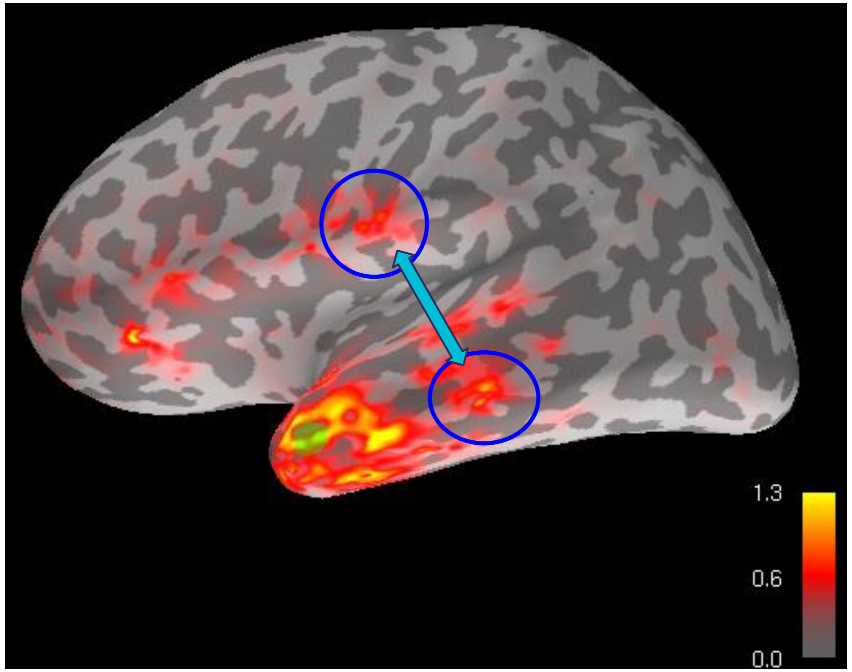
e.g. Hauk, Stenroos, Treder, Neuroimage 2022, https://www.sciencedirect.com/science/article/pii/S1053811922002993

The effect of leakage on (zero-lag) connectivity

Connectivity between two regions may reflect cross-talk from one of the regions



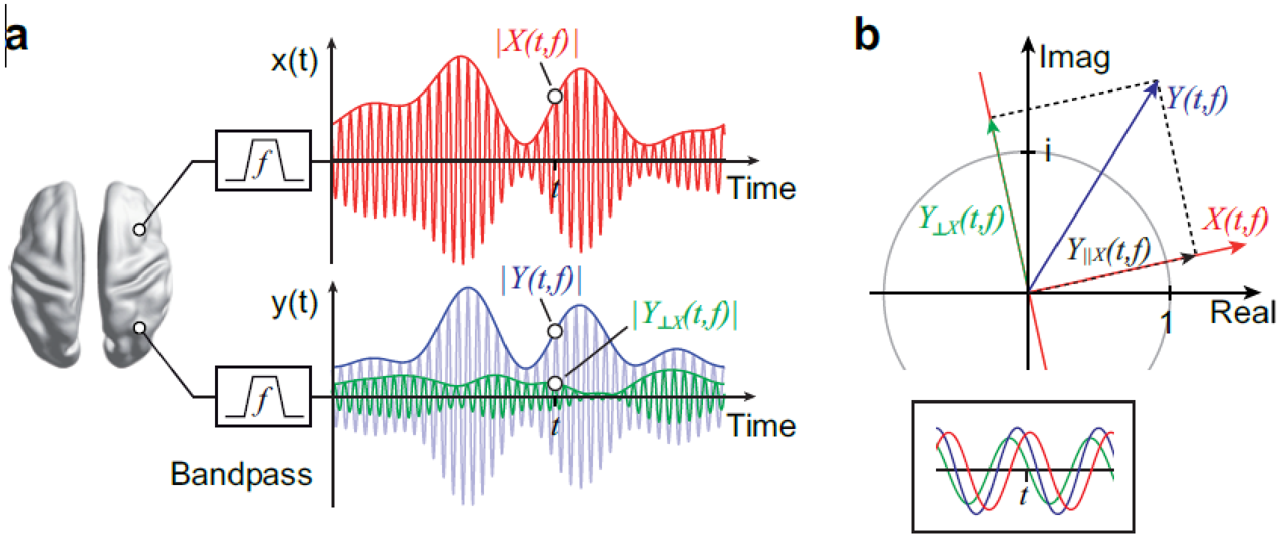
Connectivity between two regions may reflect cross-talk from a third region



One Possibility: Remove Zero-Lag Connectivity

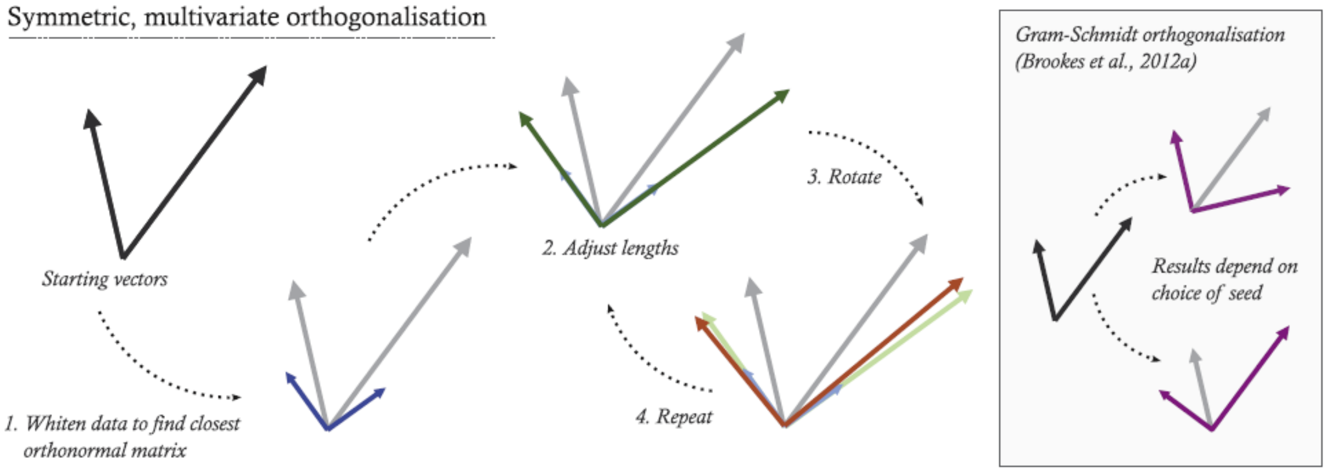
Orthogonalisation of time courses, Partial regression

Bivariate:



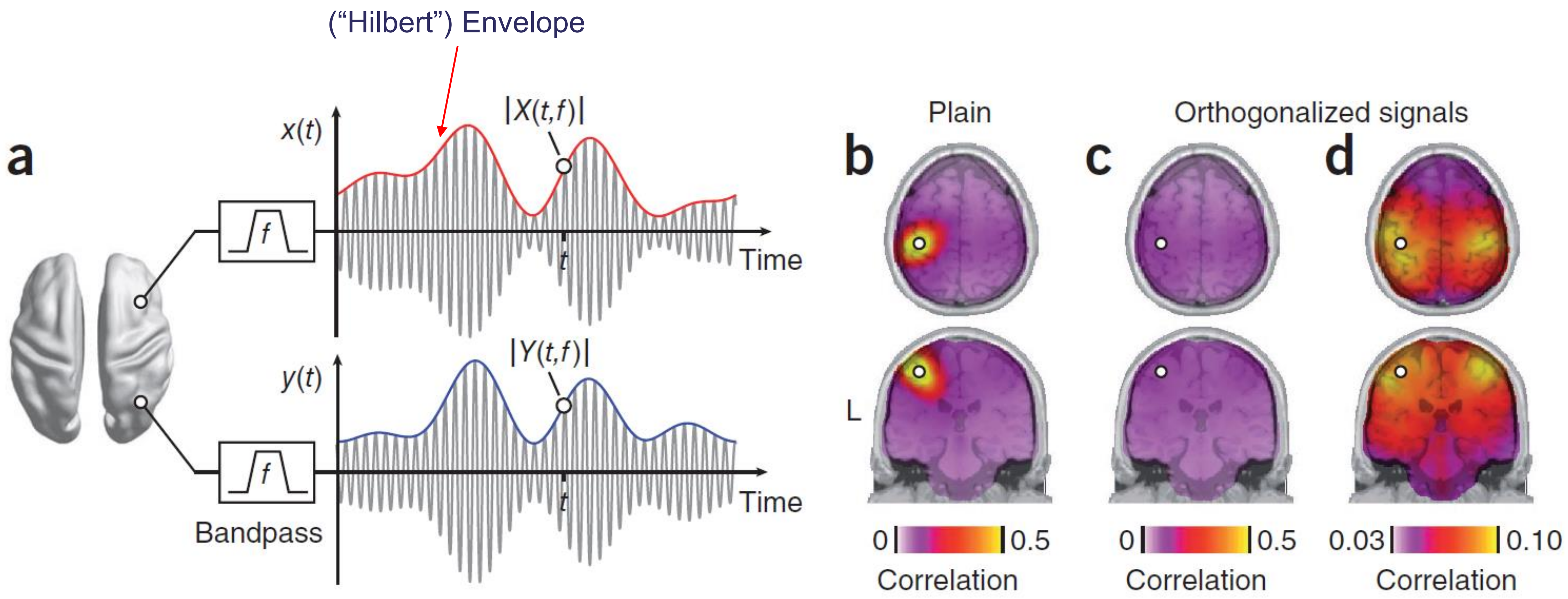
Hipp et al., Nat Nsc 2012, https://www.nature.com/articles/nn.3101

Multivariate:



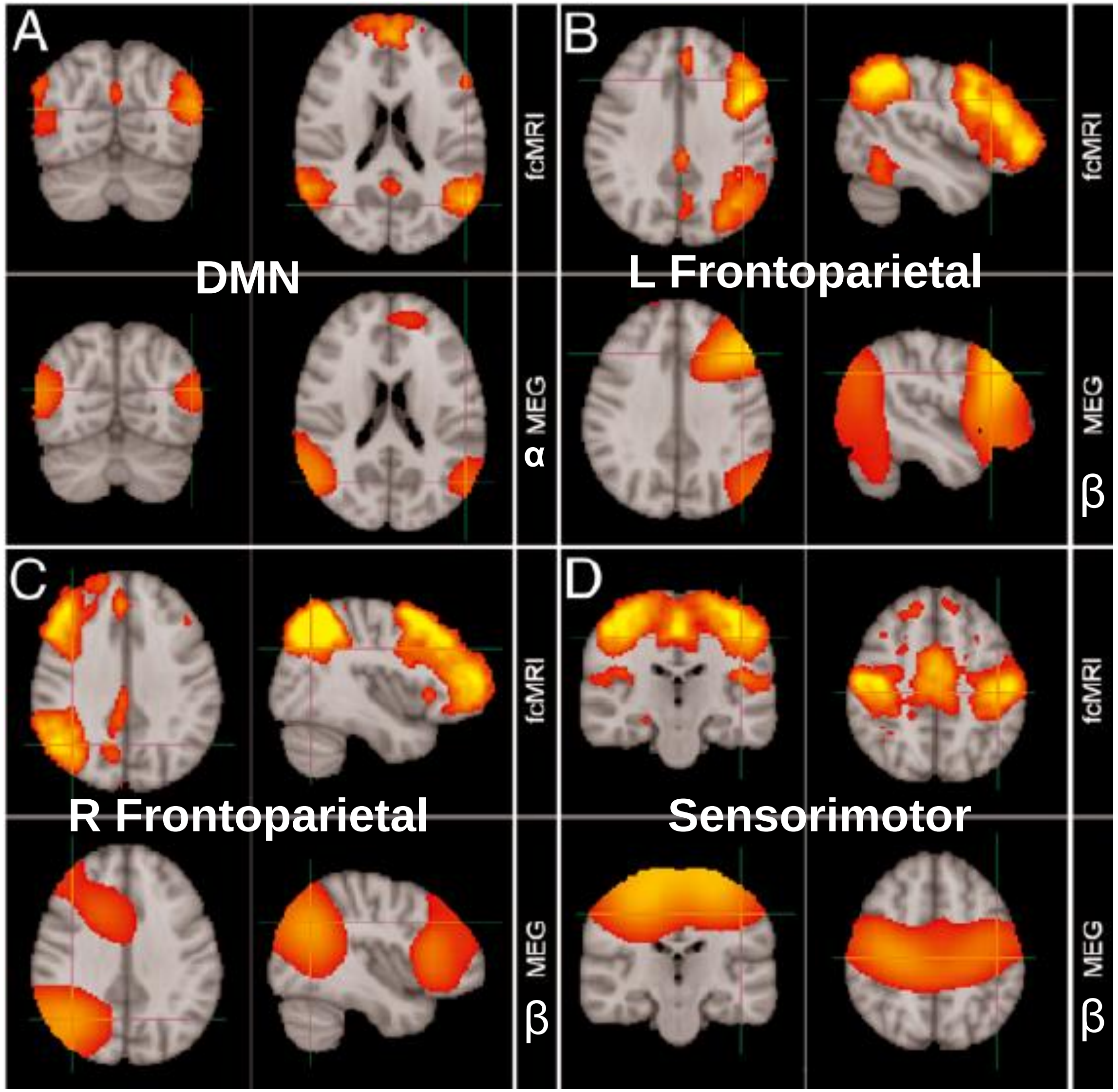
Colclough et al., NI 2015, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4528074/

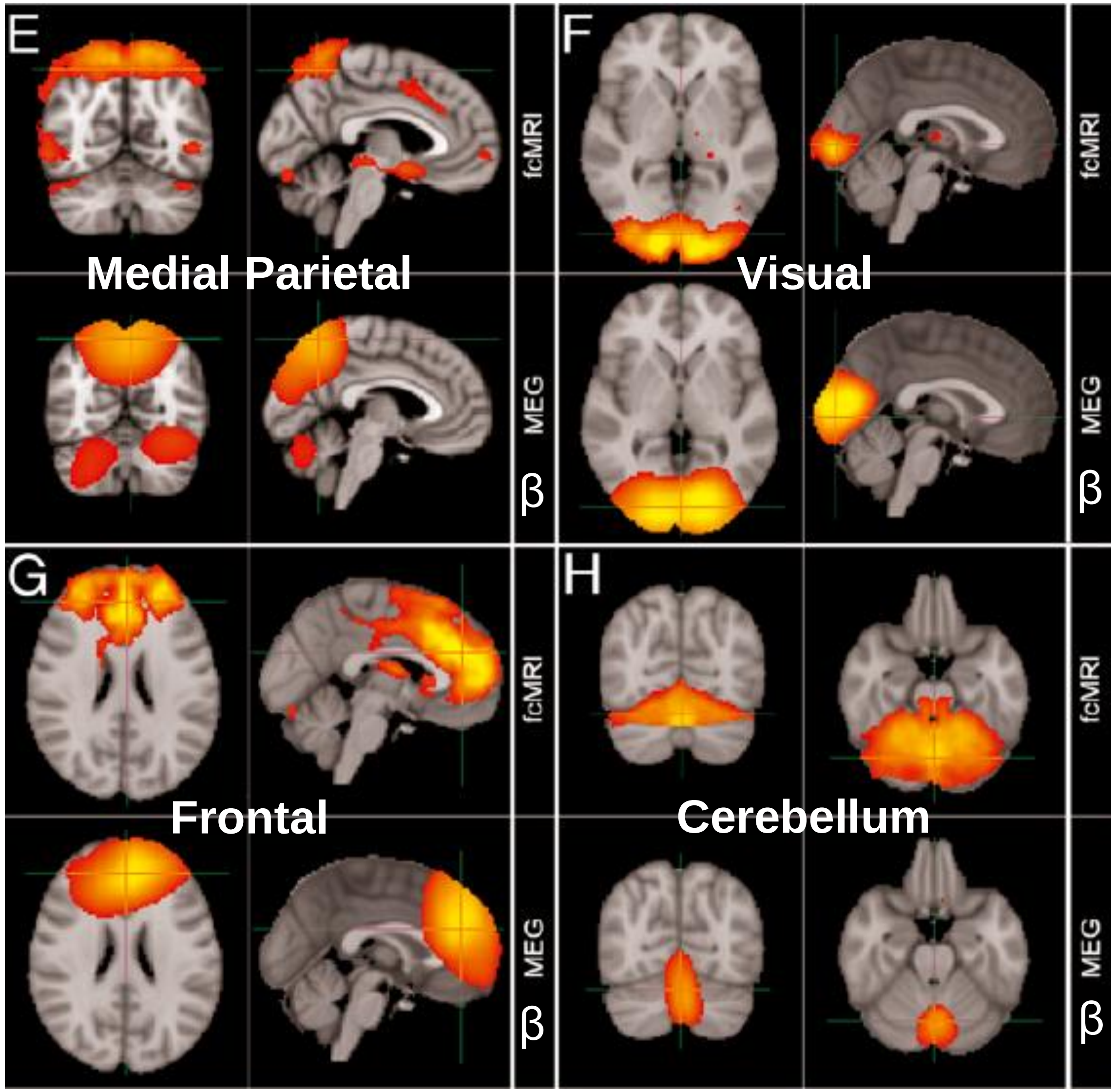
Functional Connectivity of Resting State Activity



Hipp et al., Nat Nsc 2012, https://www.nature.com/articles/nn.3101

Functional Connectivity of Resting State Activity





Brooks et al., PNAS 2011, https://www.pnas.org/doi/10.1073/pnas.1112685108

Another Possibility: Ignore “Zero-Lag” Connectivity

E.g.: Imaginary Part of Coherency

In spectral connectivity measures like Coherence, only use the imaginary part of the signal, which is unaffected by zero-lag connectivity (phase differences of zero are only represented in the real part).

Nolte et al., Clin Neurophysiol 2004, https://www.sciencedirect.com/science/article/pii/S1388245704001993
Ewald et al., NI 2012, https://pubmed.ncbi.nlm.nih.gov/22178298/
Pascqual-Marqui, arXiv 2007a and 2007b, https://arxiv.org/abs/0706.1776, https://arxiv.org/abs/0711.1455

Note: “Non-zero-lag methods” may also ignore true zero-lag connectivity, e.g. for bilateral sources – one may through out the child with the bath water.

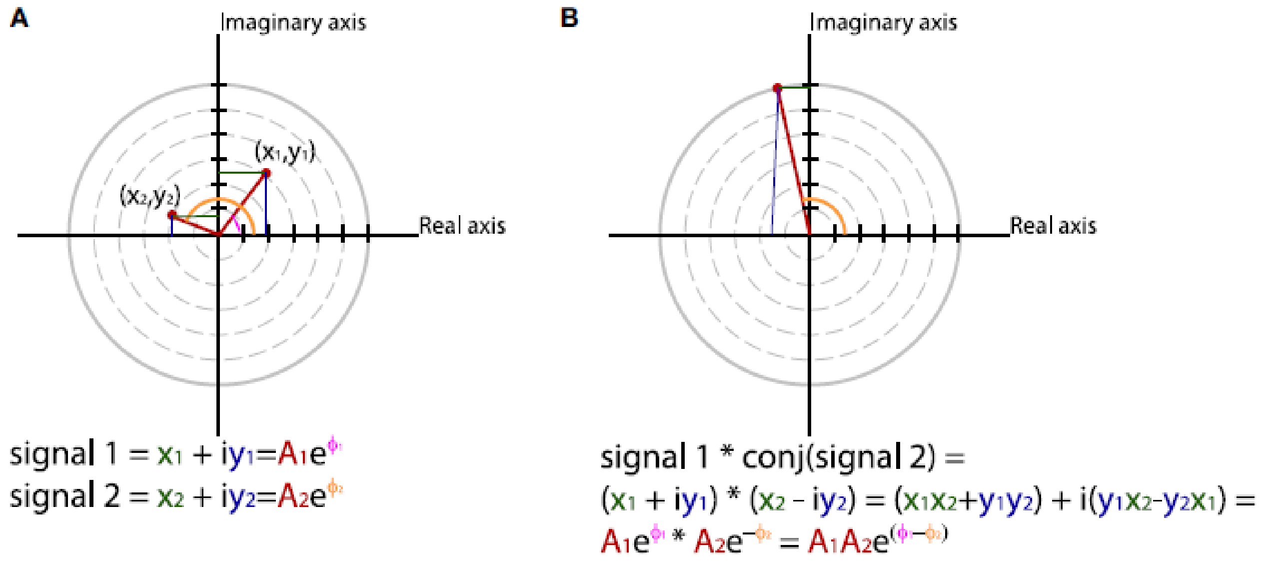


FIGURE 2 | Using polar coordinates and complex numbers to represent signals in the frequency domain. (A) The phase and amplitude of two signals. **(B)** The cross-spectrum between signal 1 and 2, which corresponds to multiplying the amplitudes of the two signals and subtracting their phases.

Bastos & Schoeffelen, Front Syst Nsc 2016, https://www.frontiersin.org/articles/10.3389/fnsys.2015.00175/full

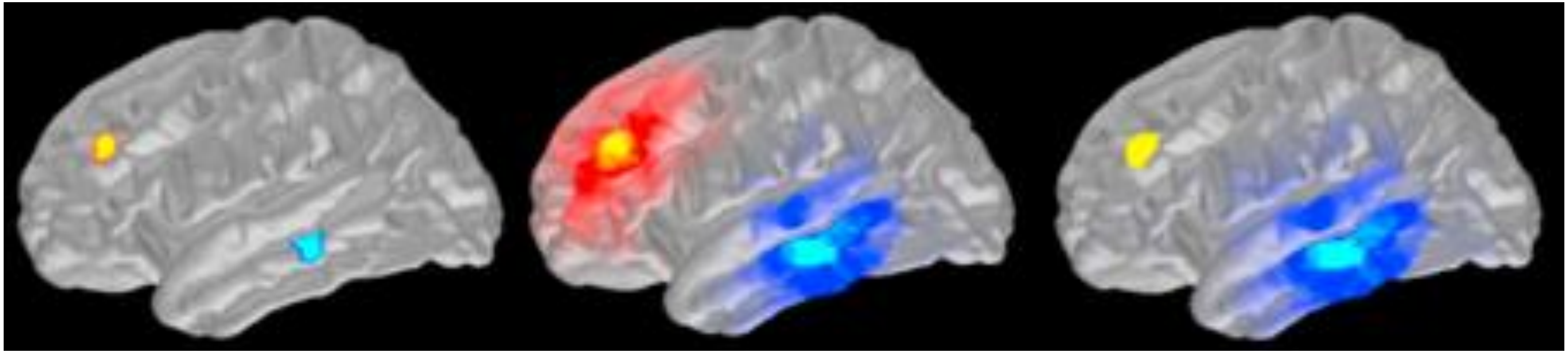
Removing zero-lag effects does not remove leakage altogether

The inverse problem still exists

True non-zero-lag connectivity

Zero-lag measures

Non-zero-lag measures



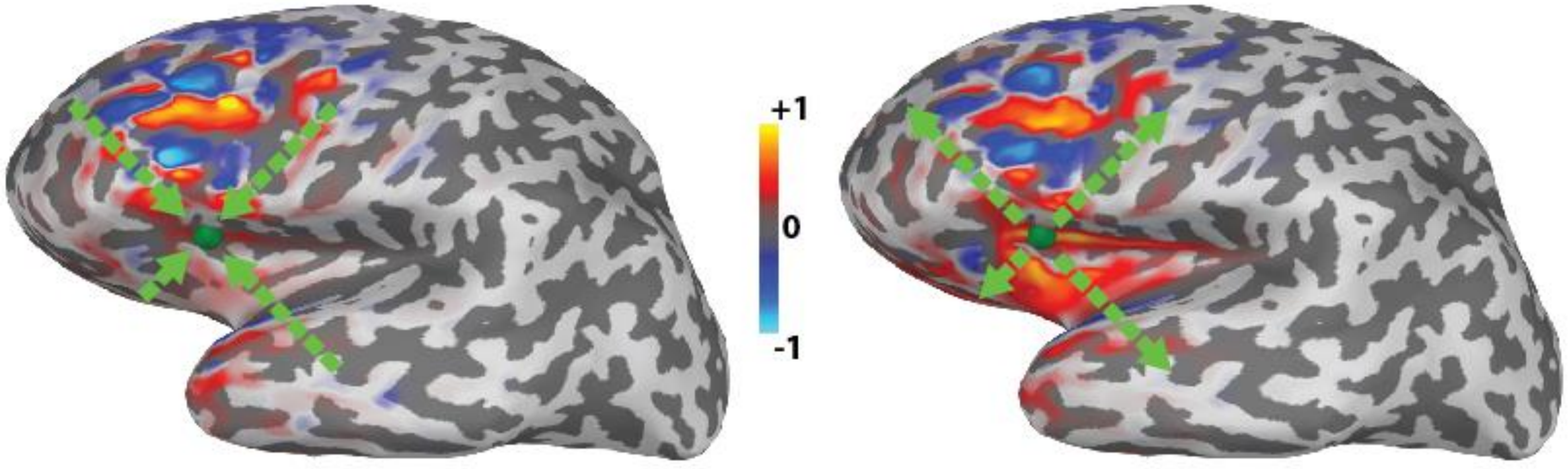
Farahibozorg, Henson, Hauk; NI 2018; https://pubmed.ncbi.nlm.nih.gov/28893608/
Also: Palva et al.; NI 2018; https://www.sciencedirect.com/science/article/pii/S1053811918301290?via%3Dihub

Spatial Resolution / Leakage:

Point-Spread and Cross-Talk

Cross-Talk Function
(CTF)

Point-Spread Function
(PSF)



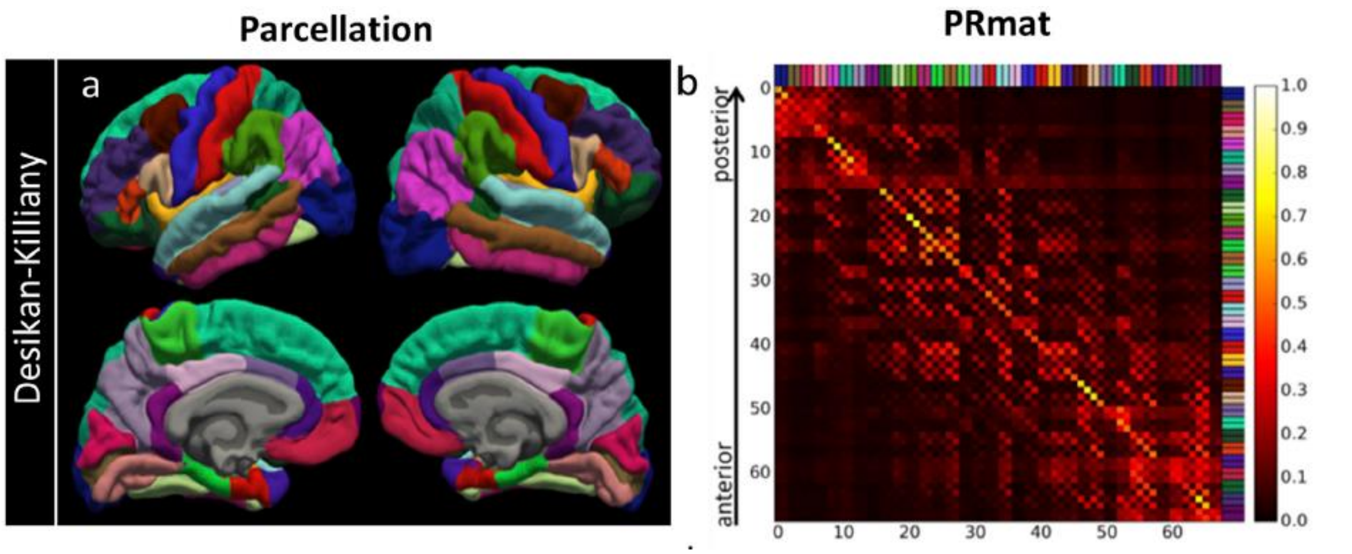
How other sources may affect the estimate for this source

How this source affects estimates for other sources

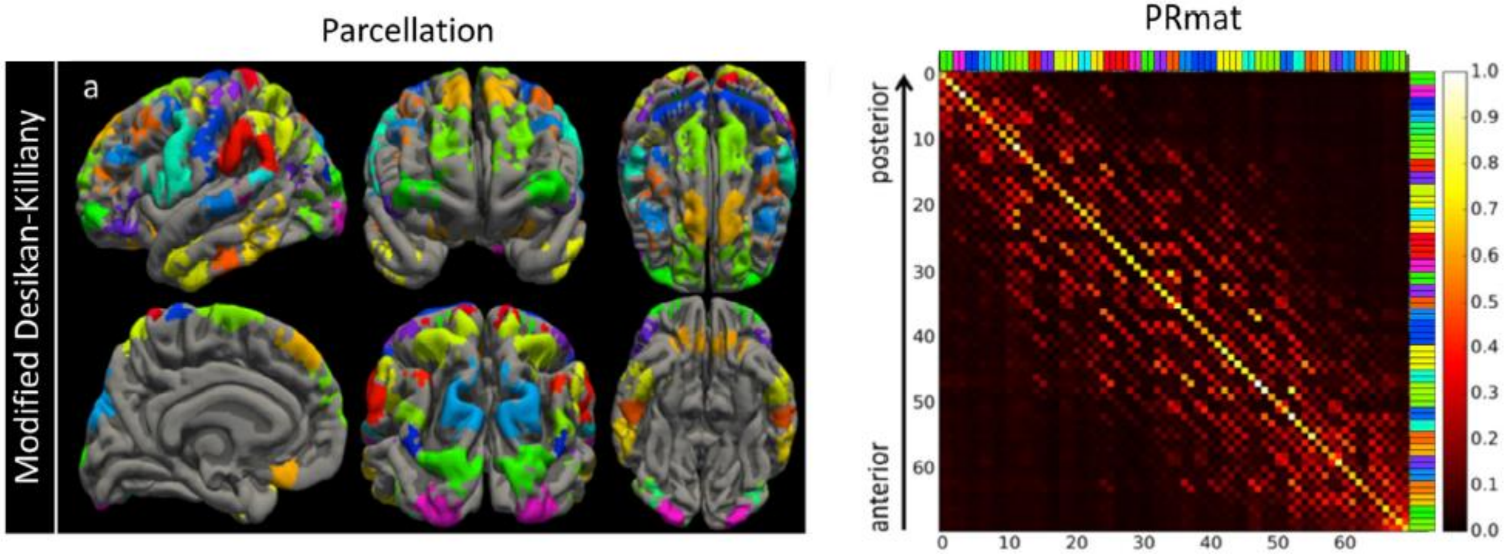
Hauk, Stenroos, Treder, Neuroimage 2022
https://www.sciencedirect.com/science/article/pii/S1053811922002993

Adaptive cortical parcellation based on resolution matrix

Original Parcellation

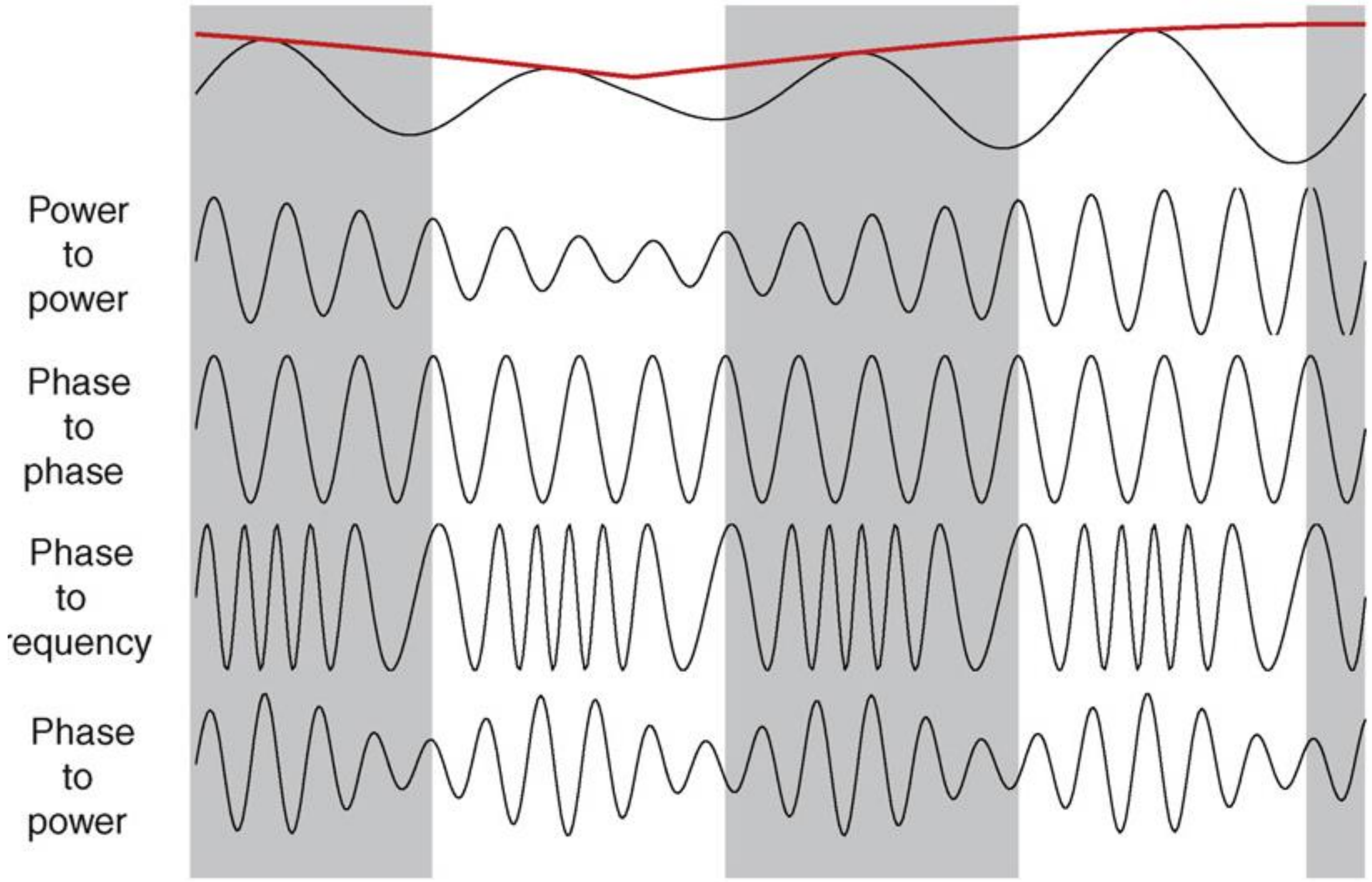


Modified Parcellation



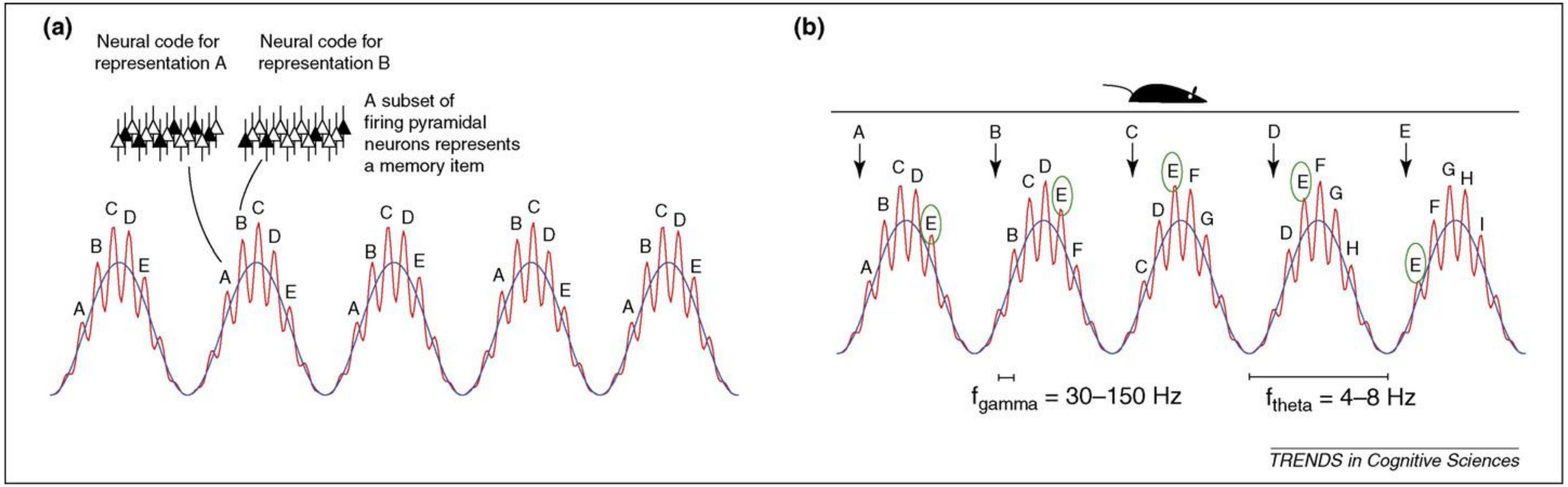
Farahibozorg/Henson/Hauk NI 2018, https://pubmed.ncbi.nlm.nih.gov/28893608/
Also: Wang et al.; NI 2018; https://www.sciencedirect.com/science/article/pii/S1053811918300569

Cross-Frequency Coupling



Jensen & Colgin, TICS 2007

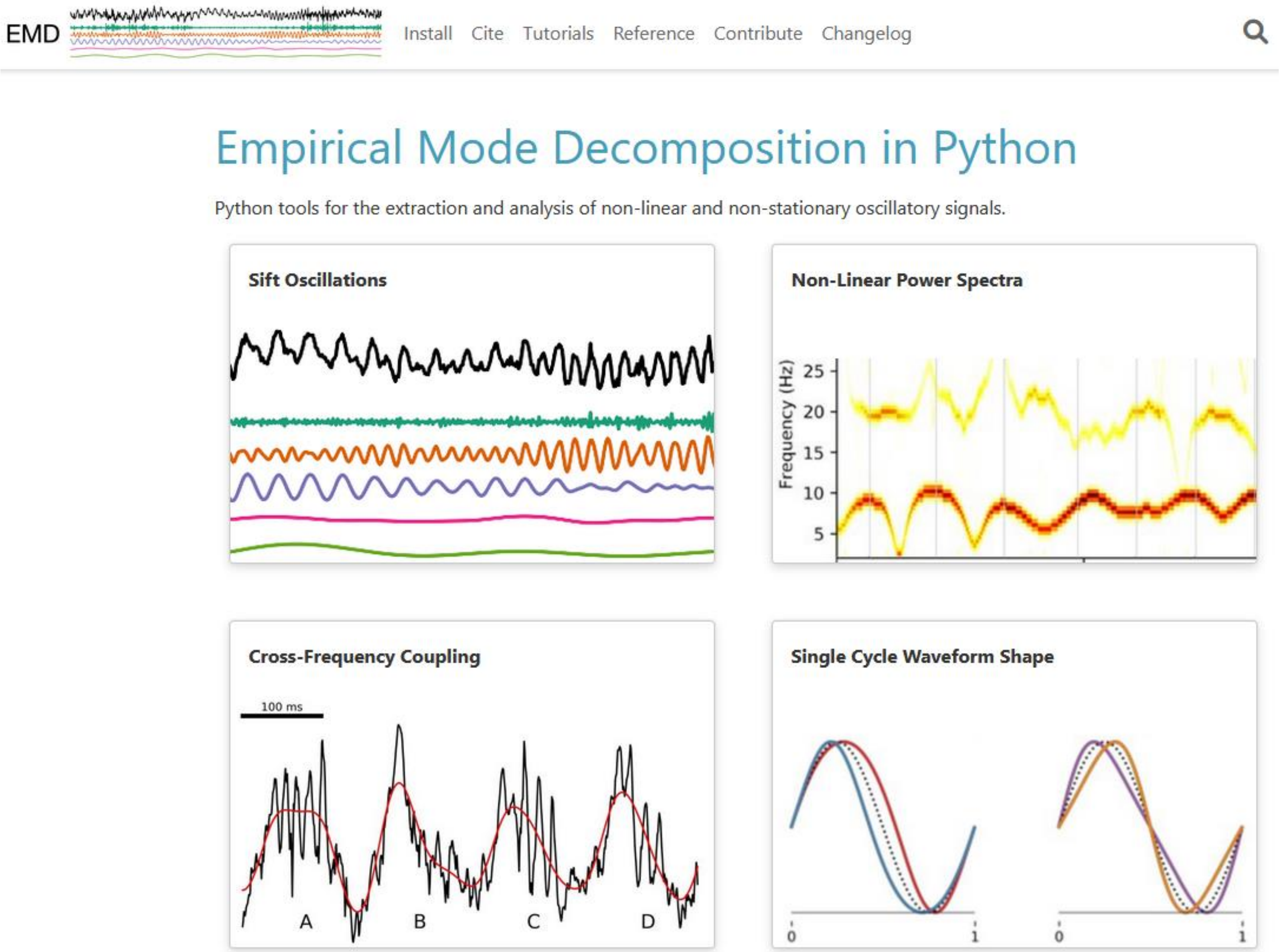
For Example: Theta-Gamma Coupling



Jensen & Colgin, TICS 2007

Figure 2. Models proposing computational roles for cross-frequency interactions between theta and gamma oscillations by means of phase coding. (a) In a model for working memory, individual memory representations are activated repeatedly in every theta cycle [10] (reviewed in Ref. [11]). Each memory representation is represented by a subset of neurons in the network firing synchronously. Because different representations are activated in different gamma cycles, the gamma rhythm serves to keep the individual memories segmented in time. The number of gamma cycles per theta cycle determines the span of the working memory. (b) A model accounting for theta phase precession in rats. As a rat advances through an environment, positional information is passed to the hippocampus. This activates the respective place cell representations, which provokes the prospective recall of upcoming positions. In each theta cycle, time-compressed sequences are recalled: one representation per gamma cycle. Consider the firing of a cell participating in representation E. As the rat advances, this cell fires earlier in the theta cycle, thus accounting for phase precession. According to this scheme, the number of gamma cycles per theta cycle is related quantitatively to the phase precession [13].

Python Toolbox for Cross-Frequency Coupling and more



https://emd.readthedocs.io/en/stable/index.html

More Python Toolboxes:

bycycle - cycle-by-cycle analysis of neural oscillations

repo status Active | pypi v1.1.0 | build passing | codecov 95% | license Apache License, 2.0 | python 3.6 | 3.7 | 3.8 | 3.9 | 3.10 | 3.11 | publication 10.1152/jn.00273.2019

ByCycle is a module for analyzing neural oscillations in a cycle-by-cycle approach.

Overview

`bycycle` is a tool for quantifying features of neural oscillations in the time domain, as opposed to the frequency domain, using a cycle-by-cycle approach. Rather than applying narrowband filters and other methods that use a sinusoidal basis, this approach segments a recording into individual cycles and directly measures each of their properties including amplitude, period, and symmetry.

This is most advantageous for analyzing the waveform shape properties of neural oscillations. It may also provide advantages for studying traditional amplitude and frequency effects, as well. Using cycle properties can also be used for burst detection.

A full description of the method and approach is available in the paper below.

https://bycycle-tools.github.io/bycycle/

FOOOF - fitting oscillations & one over f

repo status Active | pypi v1.1.0 | build passing | codecov 98% | license Apache License, 2.0 | python 3.6 | 3.7 | 3.8 | 3.9 | 3.10 | 3.11 | paper nn10.1038

FOOOF is a fast, efficient, and physiologically-informed tool to parameterize neural power spectra.

Overview

The power spectrum model conceives of a model of the power spectrum as a combination of two distinct functional processes:

- An aperiodic component, reflecting 1/f like characteristics, with
- A variable number of periodic components (putative oscillations), as peaks rising above the aperiodic component

This model driven approach can be used to measure periodic and aperiodic properties of electrophysiological data, including EEG, MEG, ECoG and LFP data.

The benefit of fitting a model in order to measure putative oscillations, is that peaks in the power spectrum are characterized in terms of their specific center frequency, power and bandwidth without requiring predefining specific bands of interest and controlling for the aperiodic component. The model also returns a measure of this aperiodic components of the signal, allowing for measuring and comparison of 1/f-like components of the signal within and between subjects.

https://fooof-tools.github.io/fooof/

Non-Spectral and Effective Connectivity

Granger Causality: Is one time series useful to predict another?
$x(t)$ Granger-causes $y(t)$ if past values of $x(t)$ add information to past values of $y(t)$ for predicting future values of $y(t)$.

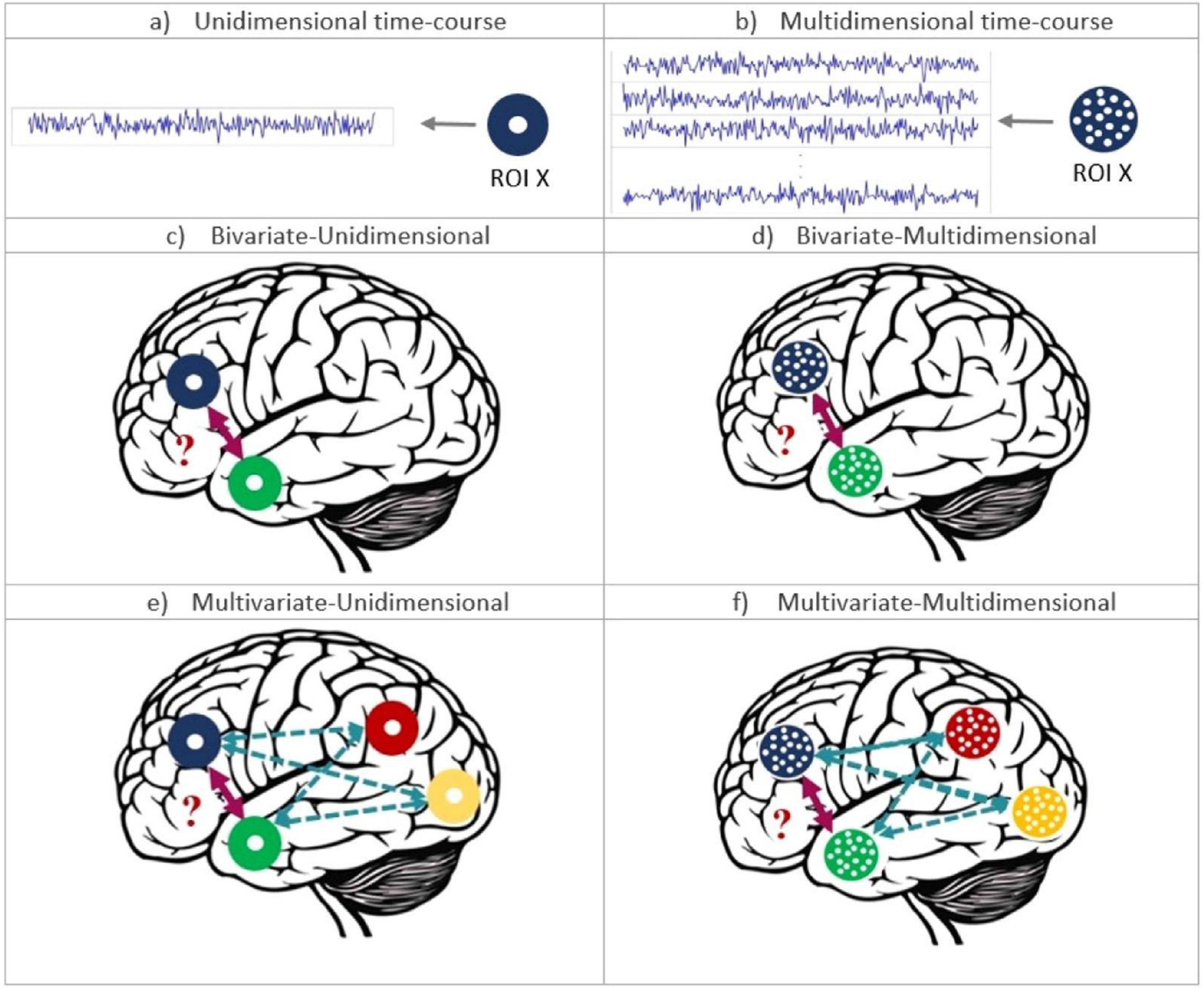
http://www.scholarpedia.org/article/Granger_causality
Multivariate Granger Toolbox: http://www.sussex.ac.uk/sackler/mvgc/
http://journal.frontiersin.org/article/10.3389/fnsys.2015.00175/full

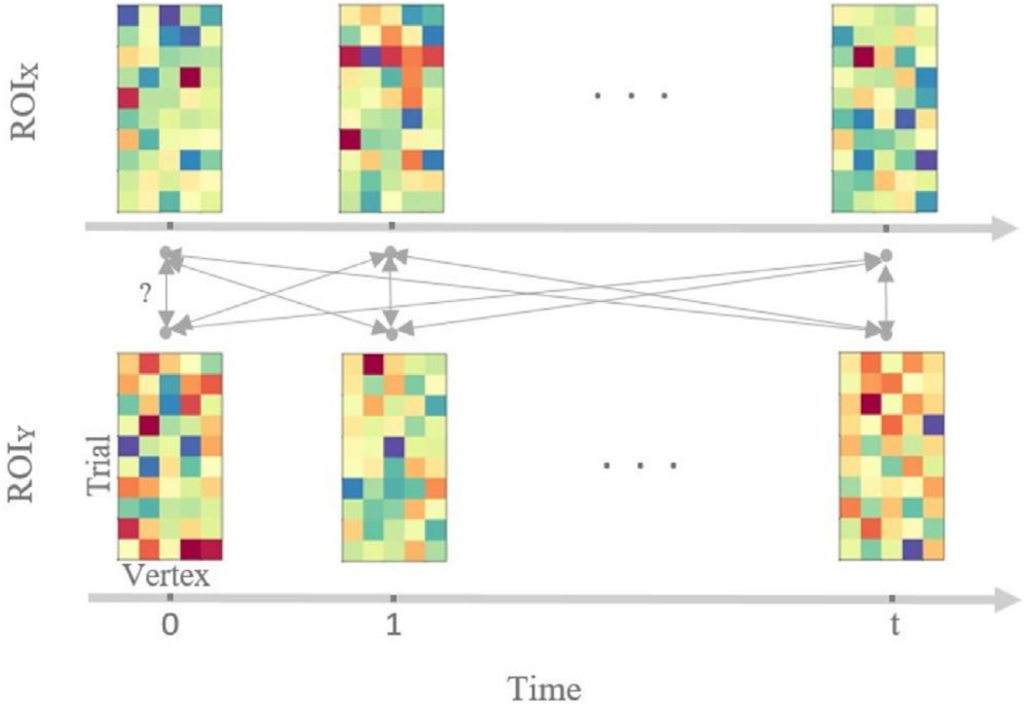
Structural Equation Modelling (SEM):
Models covariance structure of brain activation across brain regions (e.g. “path analysis”).

Dynamic Causal Modelling (DCM):
Models brain dynamics across regions as differential equations, in combination with Bayesian parameter/model estimation.

http://www.scholarpedia.org/article/Dynamic_causal_modeling

Multi-Variate and Multi-Dimensional Connectivity





Rahimi et al., NI 2022, https://pubmed.ncbi.nlm.nih.gov/36813063/
Also:
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Thank you