High resolution functional networks measured with MEG

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Large-scale Networks in fMRI

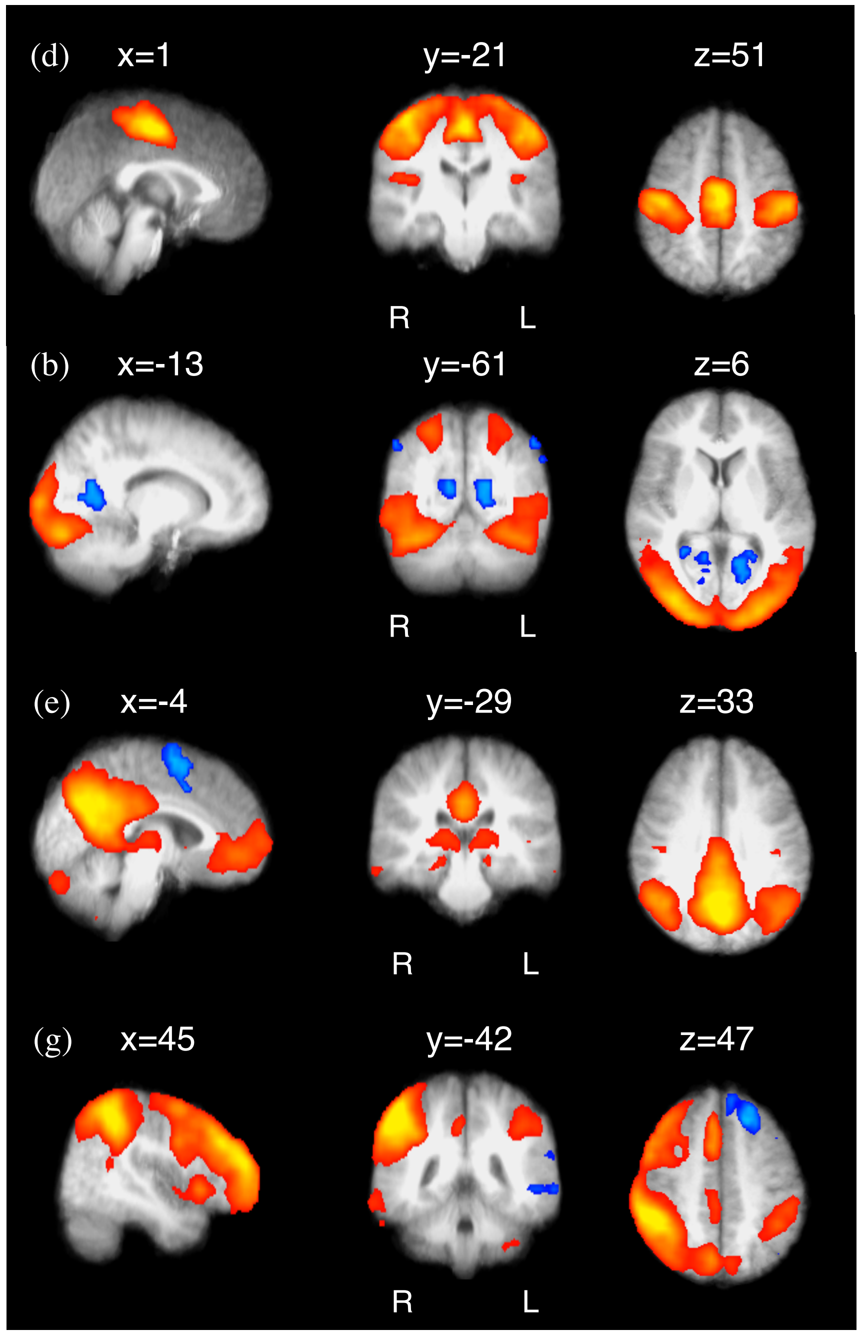
Resting state networks (RSNs)

sensori-motor

visual

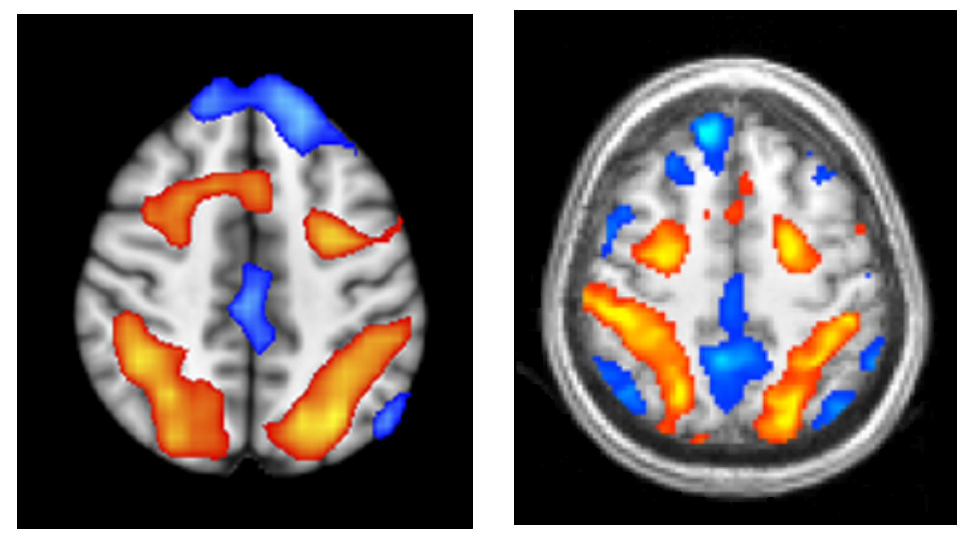
default mode

right fronto-parietal



Beckmann, Phil Trans Roy Soc B, 2005

The same networks are recruited in task and rest



task rest

Smith et al., PNAS, 2009

Large-scale Networks in MEG?

- What is happening at **faster** time-scales?
- What are the specific neuronal **interactions**?

Large-scale Networks in MEG?

- What is happening at **faster** time-scales?
- What are the specific neuronal **interactions**?

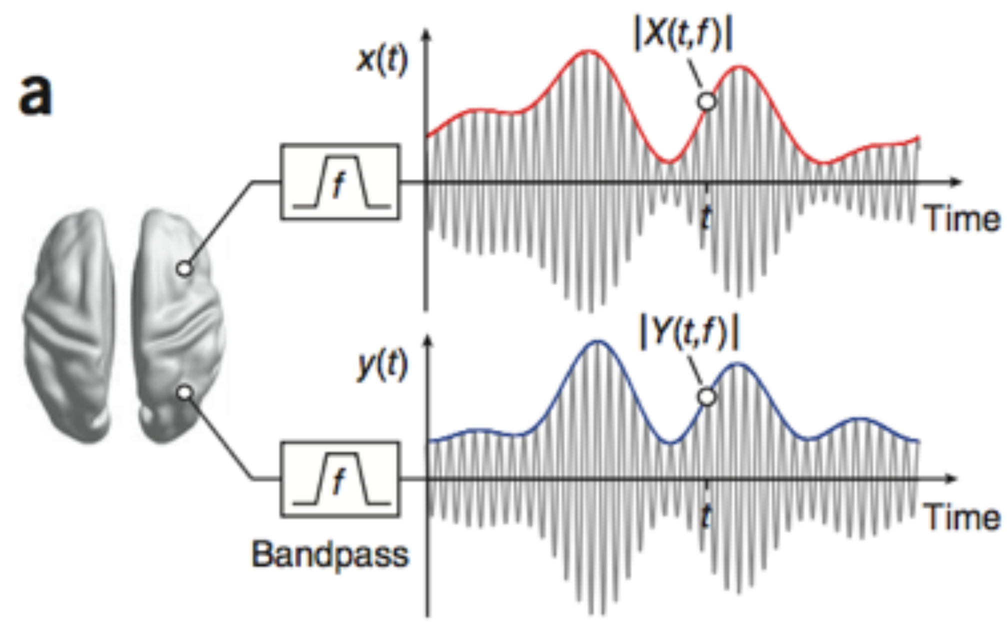
- Can we use MEG to answer these questions?
    - excellent temporal res (millisecs)
    - good spatial res
    - non-invasive

MEG: what functional connectivity (FC) measure should we use?

- Can NOT use raw zero-lag correlation as we do in fMRI (due to conduction delays)
- Need to use measures that are robust to non-zero lags

e.g. **Amplitude Coupling**

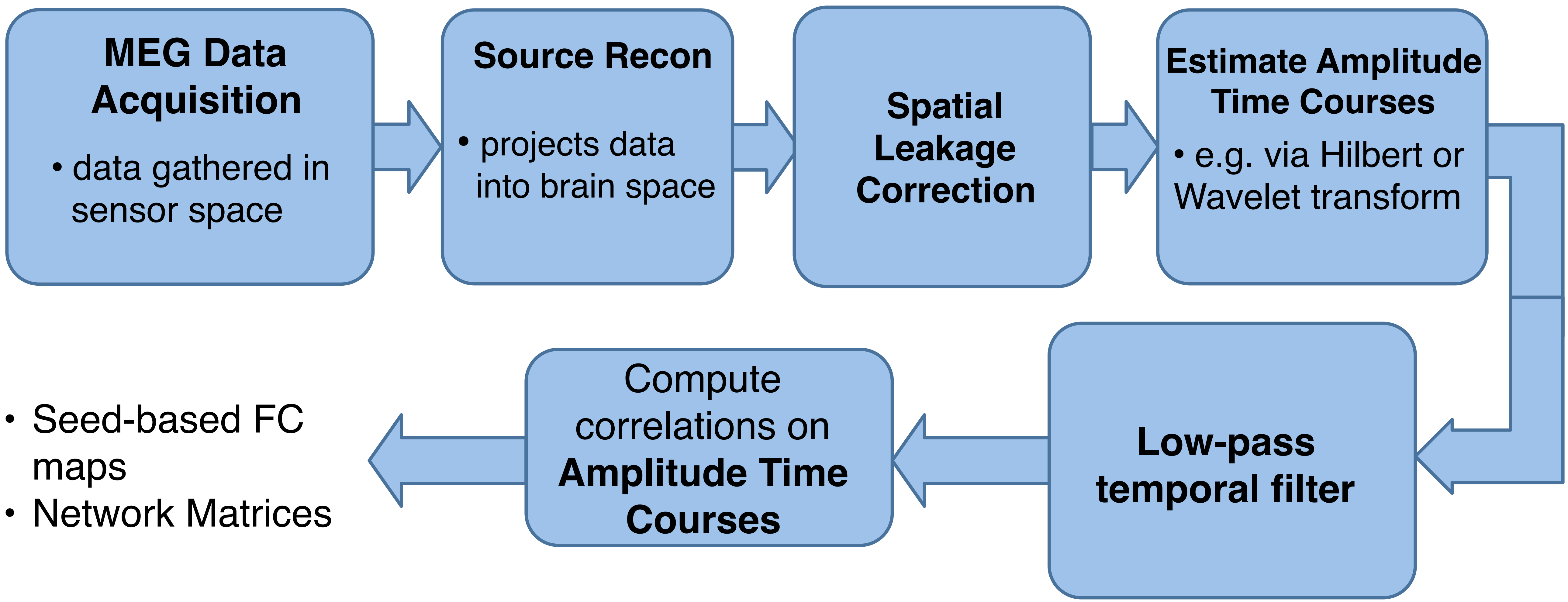
- Detects if the amplitude (or power or envelope) time courses in particular frequency bands are correlated



Hipp et al.; Nat Neuro (2012)

Brookes et al.; Neuroimage (2013)

MEG FC: Amplitude Coupling

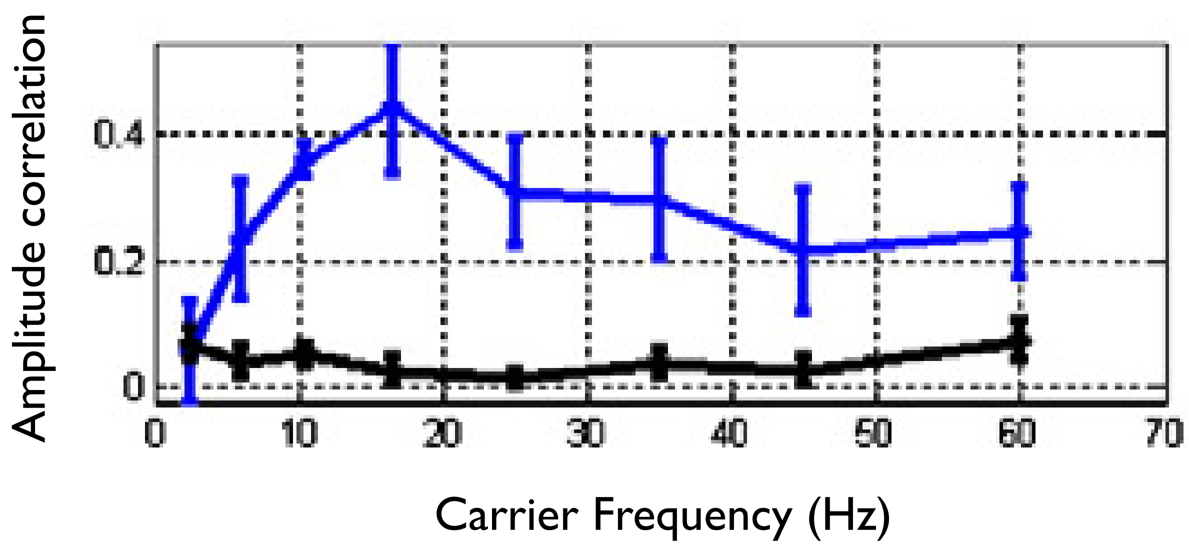


Hipp et al.; Nat Neuro (2012)

Brookes et al.; Neuroimage (2013)

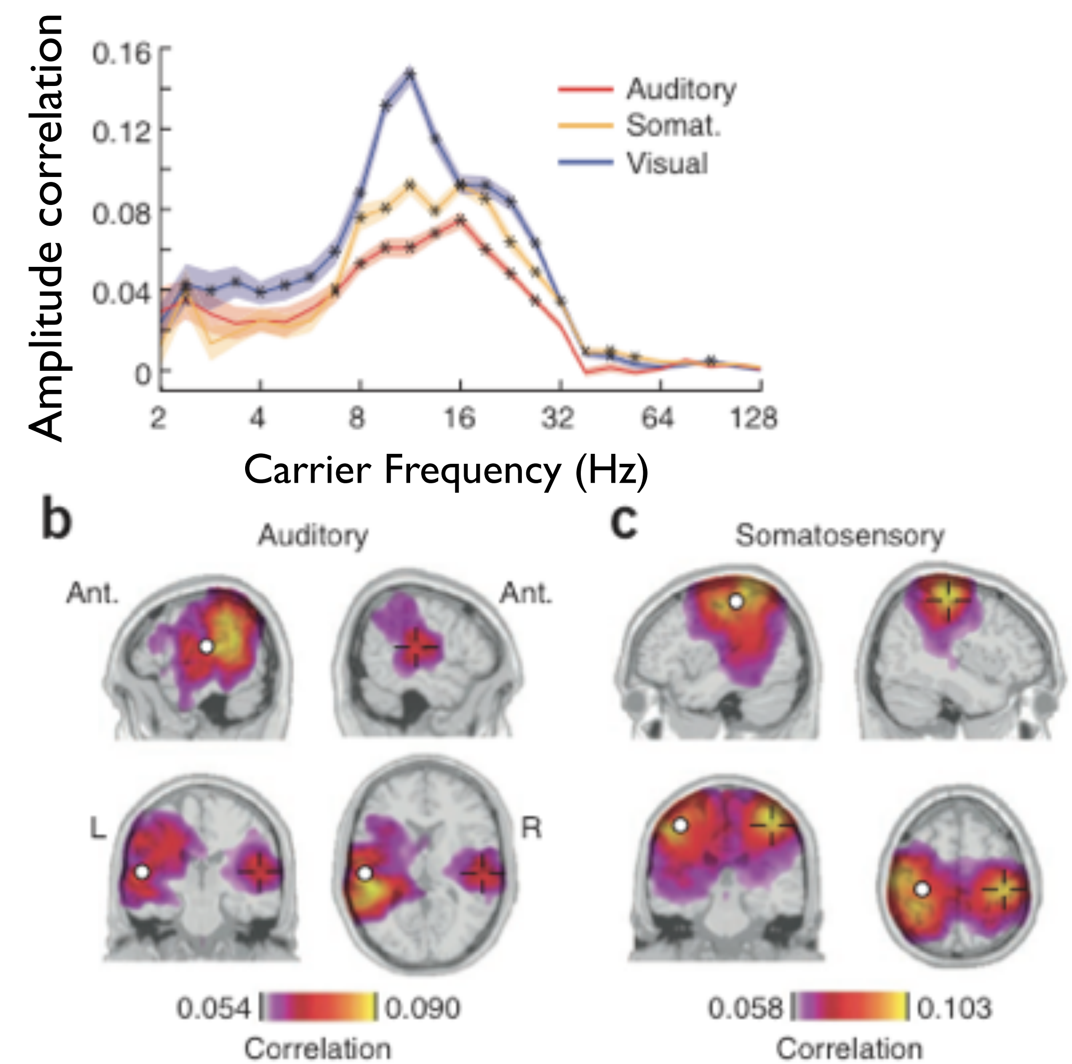
MEG FC: Amplitude Coupling

- Resting state data



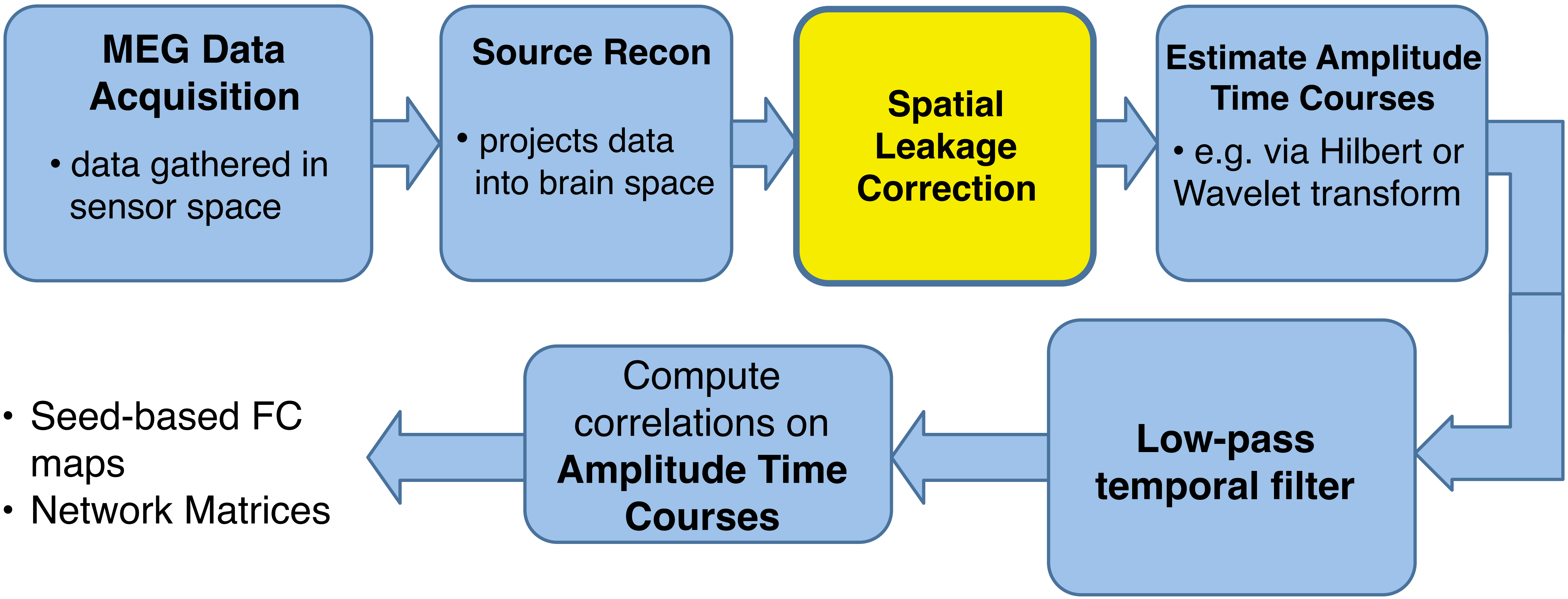
Significant beta band ***amplitude correlation*** between the left and right motor cortices

Brookes et al., Neuroimage, (2011)



Hipp et al. 2012 (Nat Neuro)

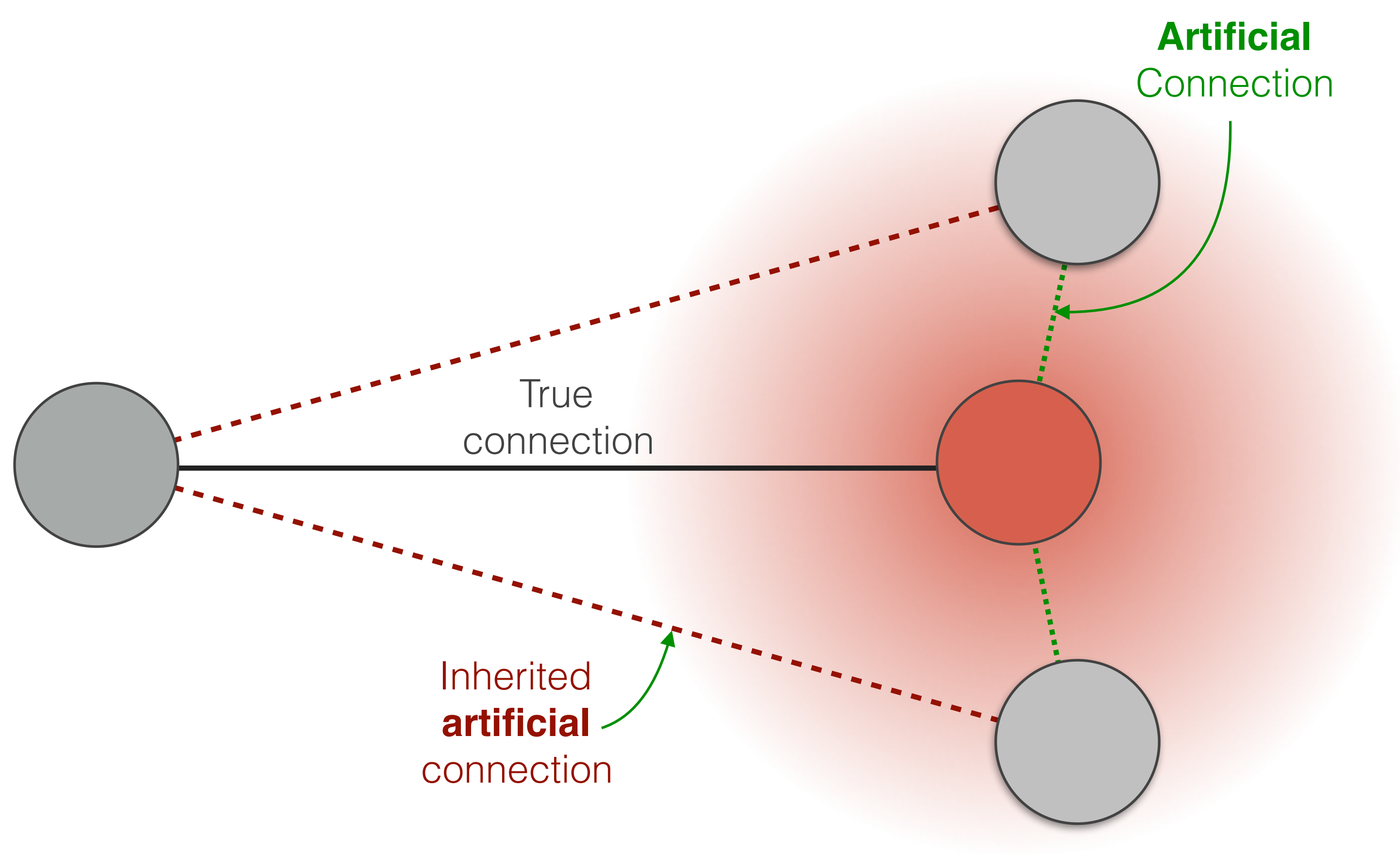
MEG FC: Amplitude Coupling



- Seed-based FC maps
- Network Matrices

Spatial Leakage

Uncertainties in the source reconstruction induce zero-lag spatial correlations in source space



SOLUTION: remove all zero-lag correlations

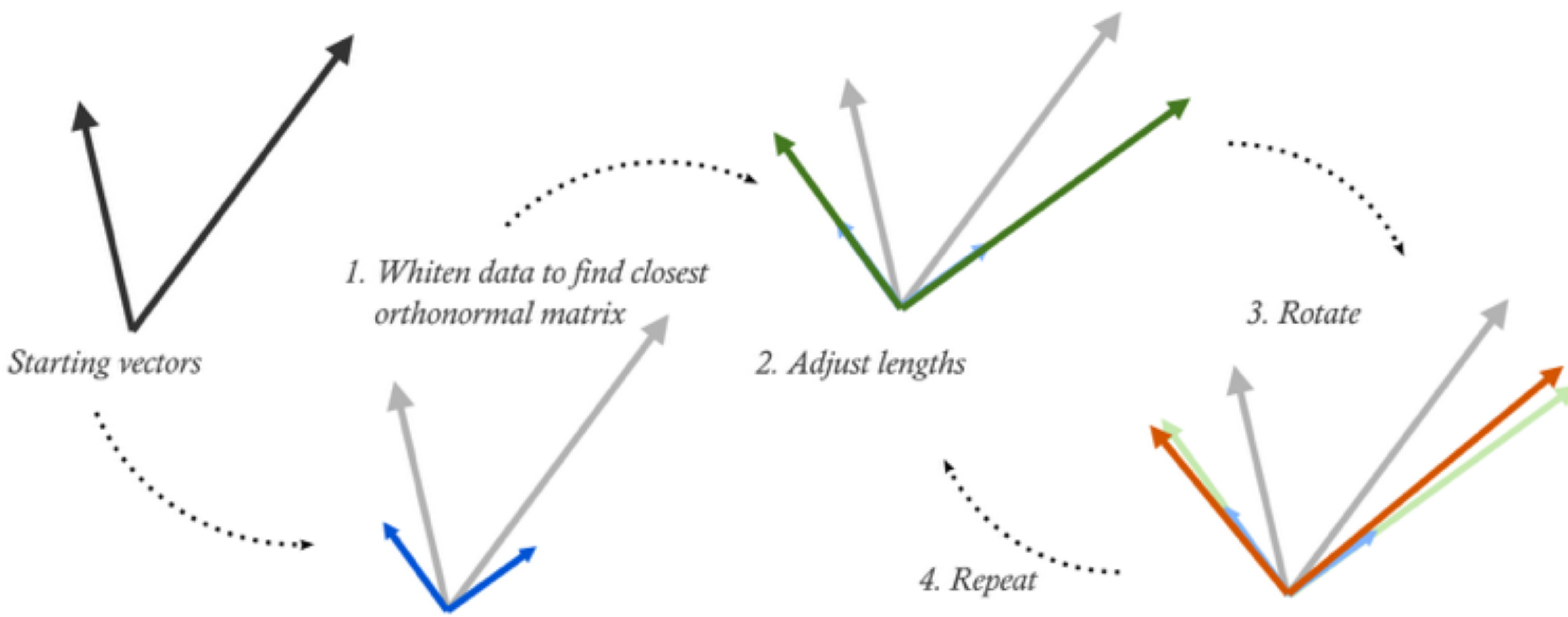
- Orthogonalise **pairs** of raw time courses (regress one out of the other) **before** computing amplitude time courses

Hipp et al.; Nat Neuro (2012)

Brookes et al. ; Neuroimage (2013)

Multi-region spatial leakage correction

Can perform a **multi-region** orthogonalisation in one shot:



- finds the closest set of orthogonal vectors to the original timecourses
- any subsequent multi-variate analysis (e.g. regularised partial correlation) is possible

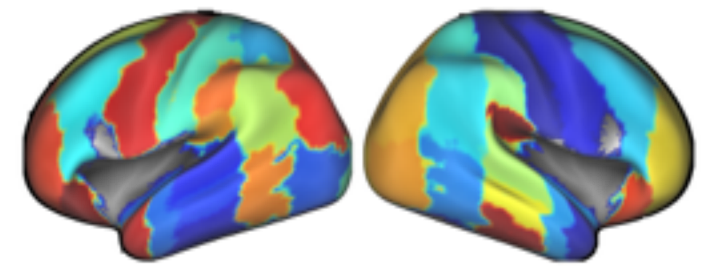
Colclough,…,Woolrich; Neuroimage, 2015

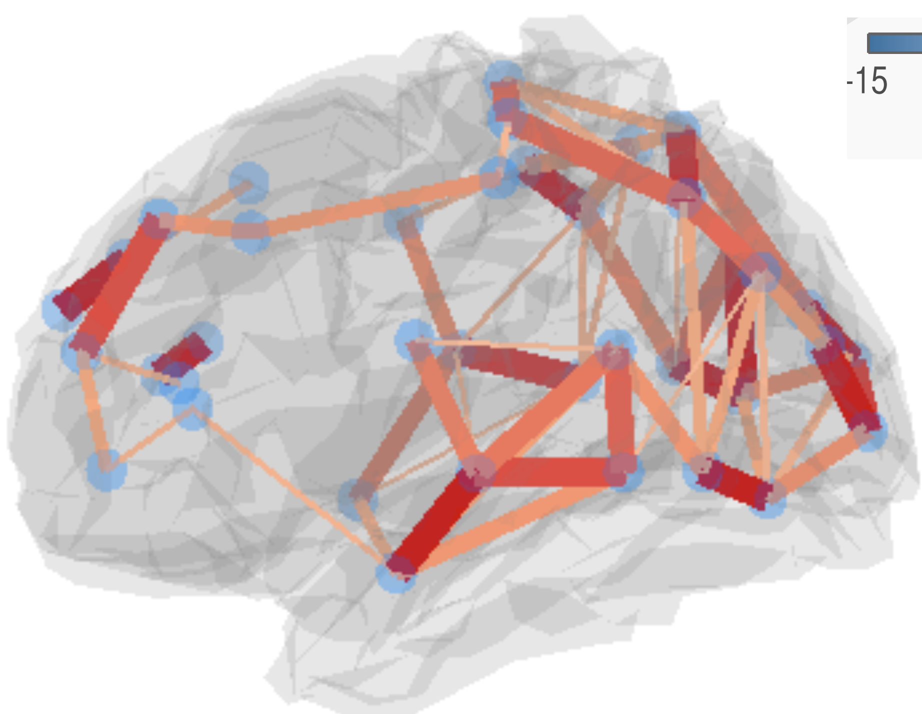
Network matrices from resting MEG

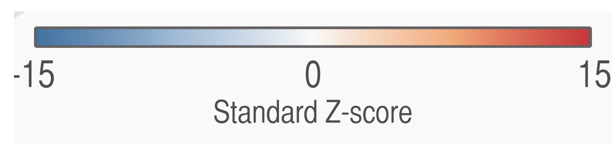
8 subjects' eyes open resting-state data

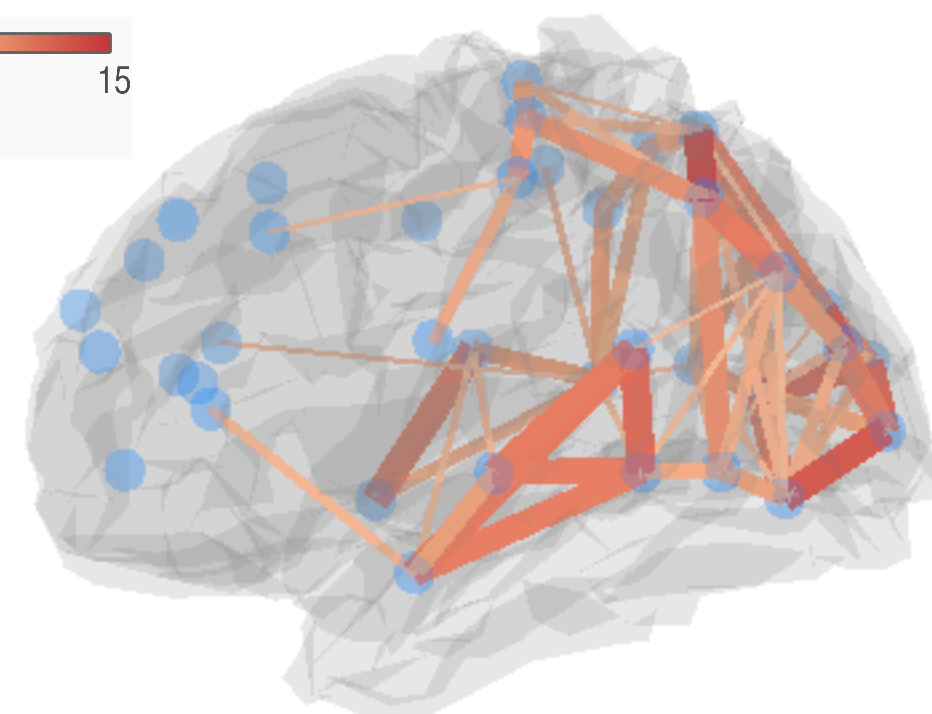
- alpha band (8-12 Hz) amplitude time-courses
- compute regularised partial correlation network matrices
  - thresholded at 5% FDR
- reveals a strongly inter-connected visual network

38 cortical regions









No Spatial Leakage Correction

Multivariate Spatial Leakage Correction

Colclough, Smith … Woolrich; Neuroimage (2015)

Example Application: Heritability of MEG connectomes

Human Connectome Project twin rest data

MZ

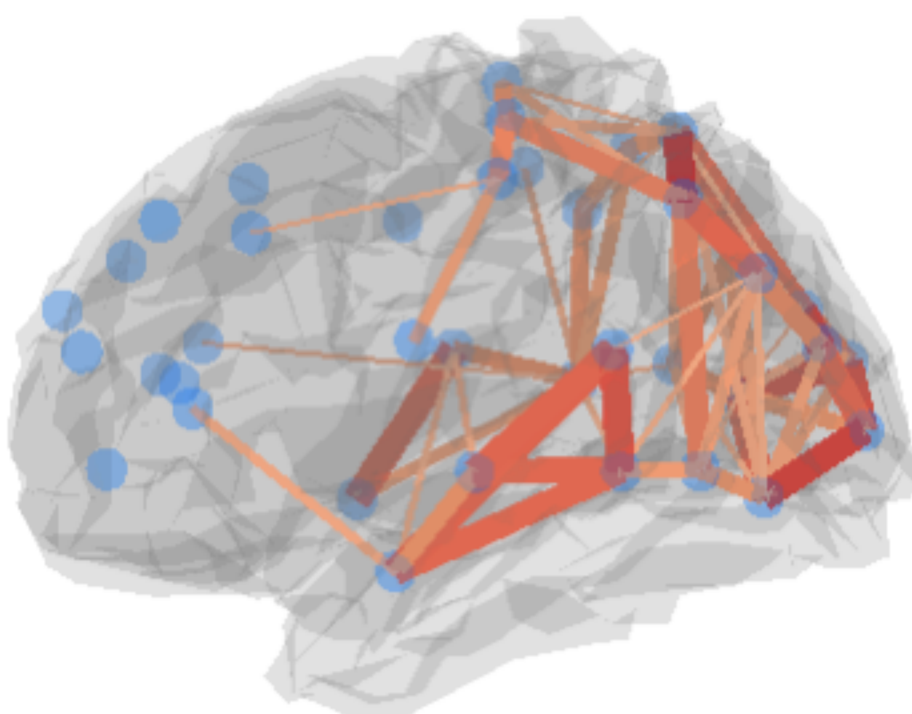
DZ

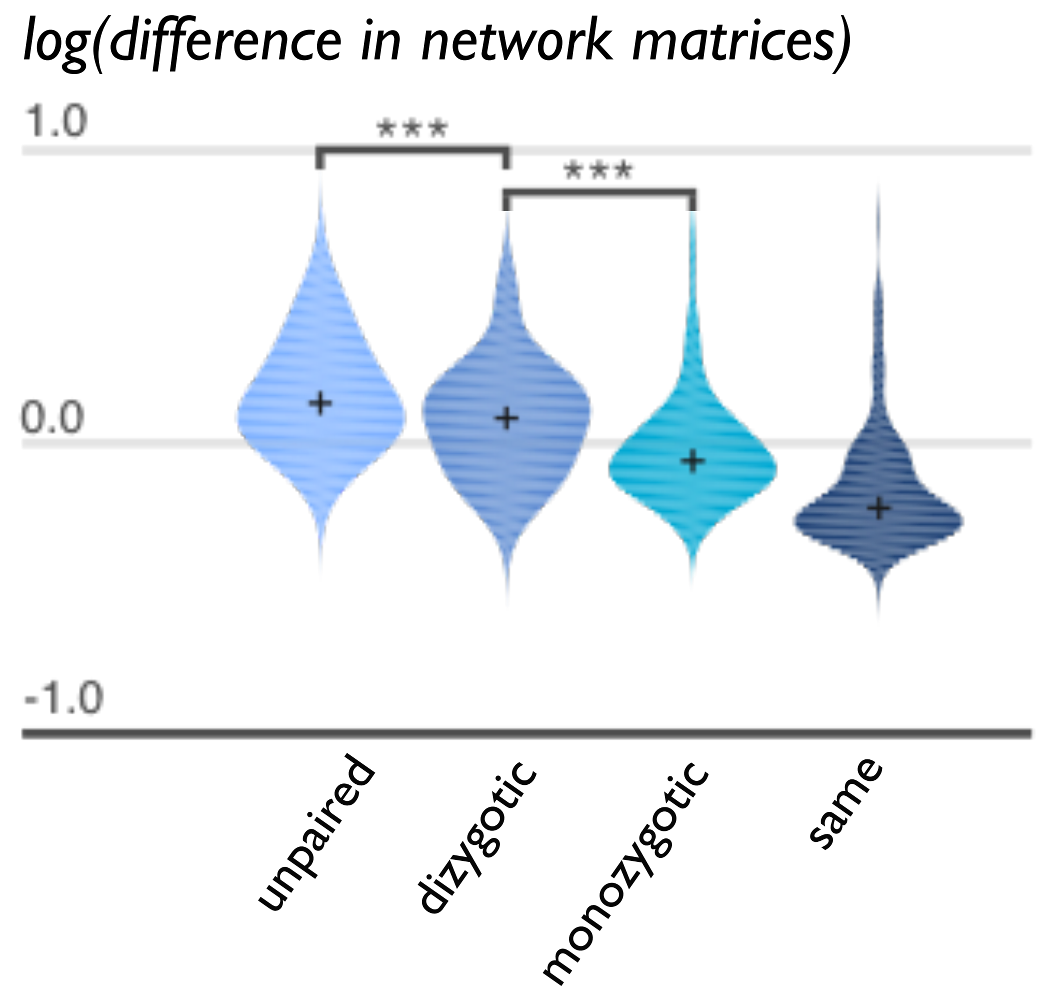
Colclough, Smith … Woolrich; In submission

Example Application: Heritability of MEG connectomes

Human Connectome Project twin rest data

MEG - alpha band amplitude correlations (61 subjects)

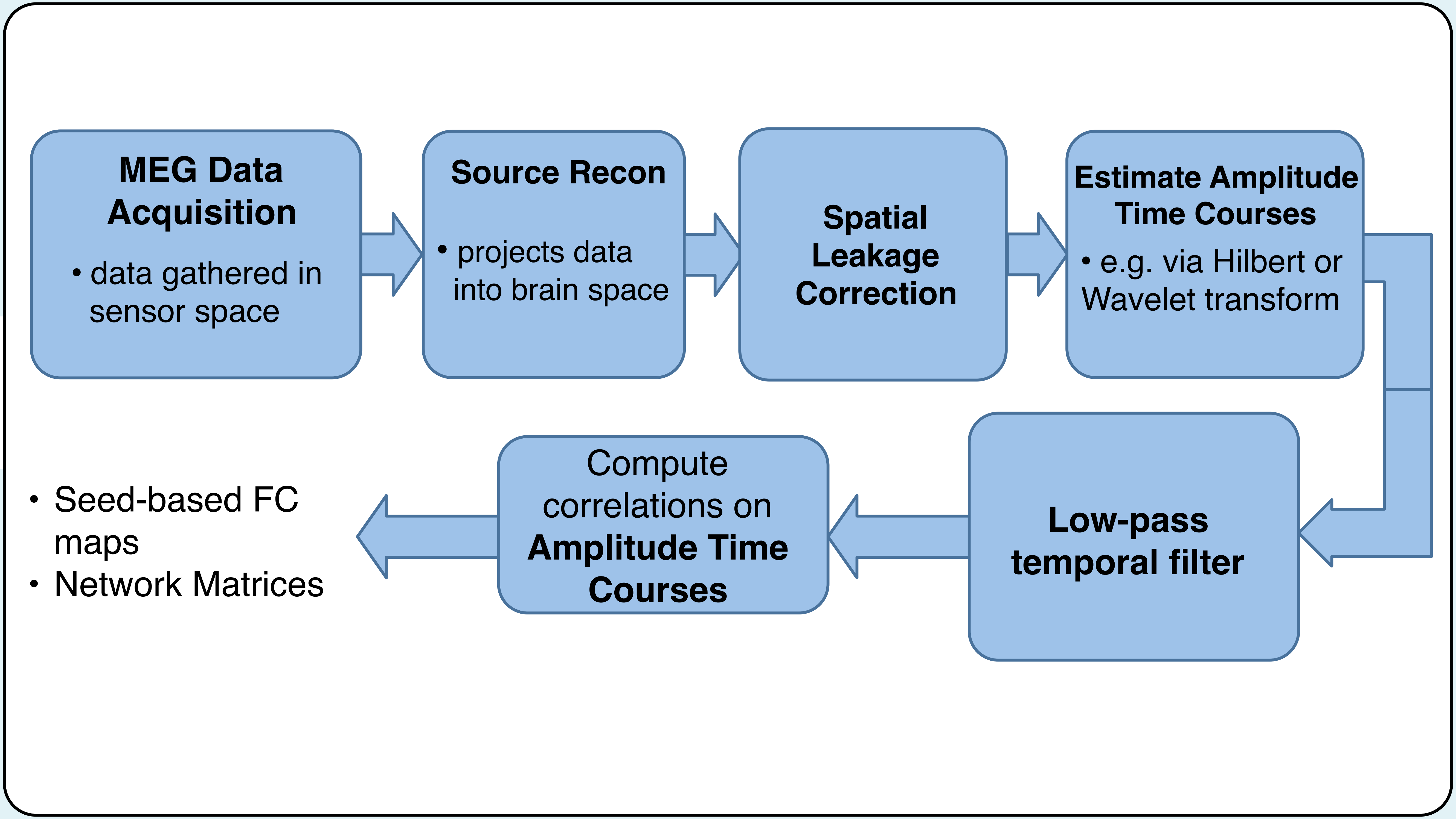




- Mean edge heritability: 33% (p = 0.01)
- Shared genetics outweigh shared environment (p = 0.02)

Colclough, Smith … Woolrich; In submission

MEG Resting State Networks?



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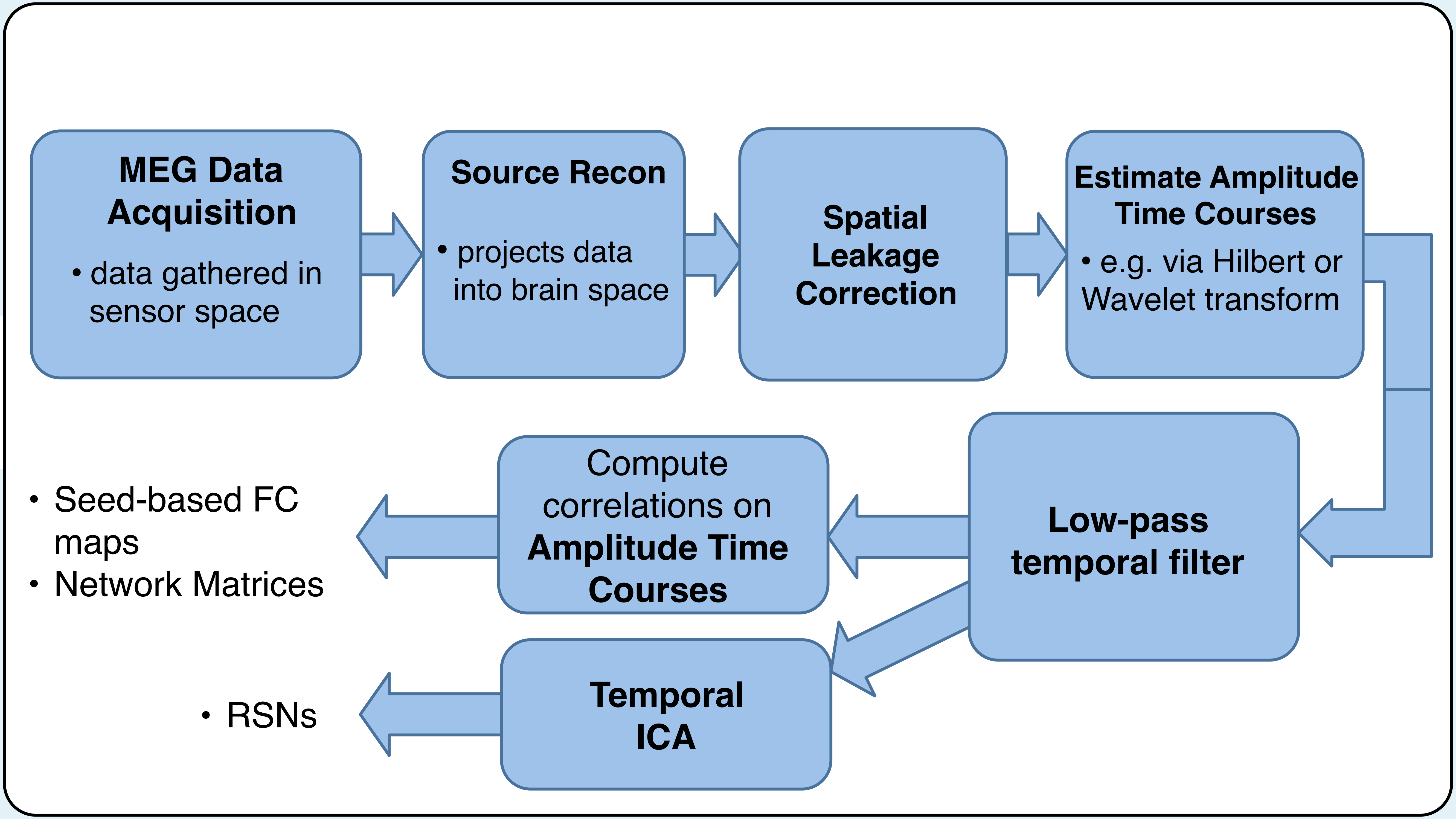
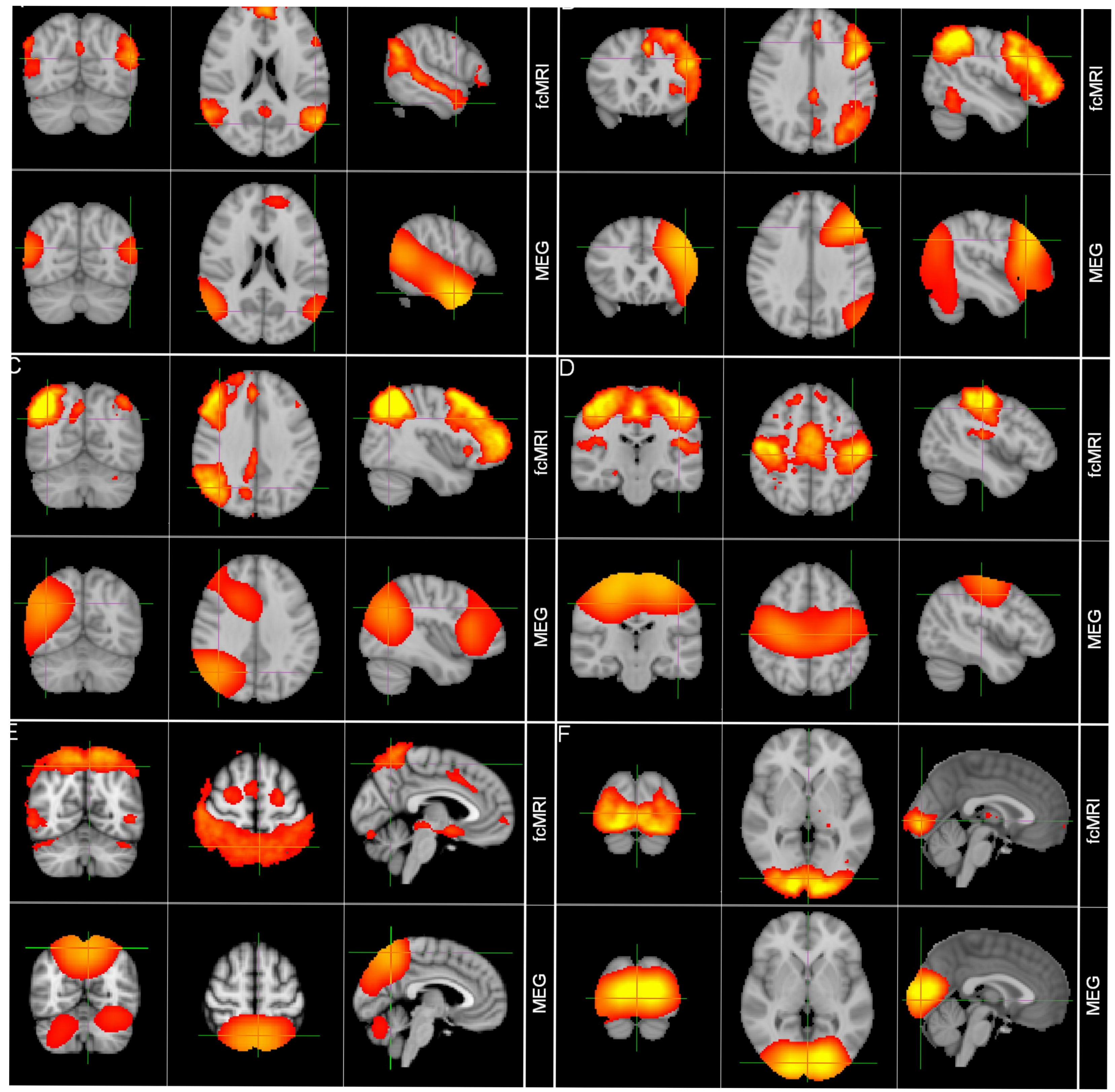


MEG RSNs

- RSNs found in MEG data using temporal ICA
- Eyes open, 10 subjects
- Good correspondence with fMRI ICA networks
- Found in beta band (except for DMN in the alpha band)



Brookes,…, Morris; PNAS (2011)

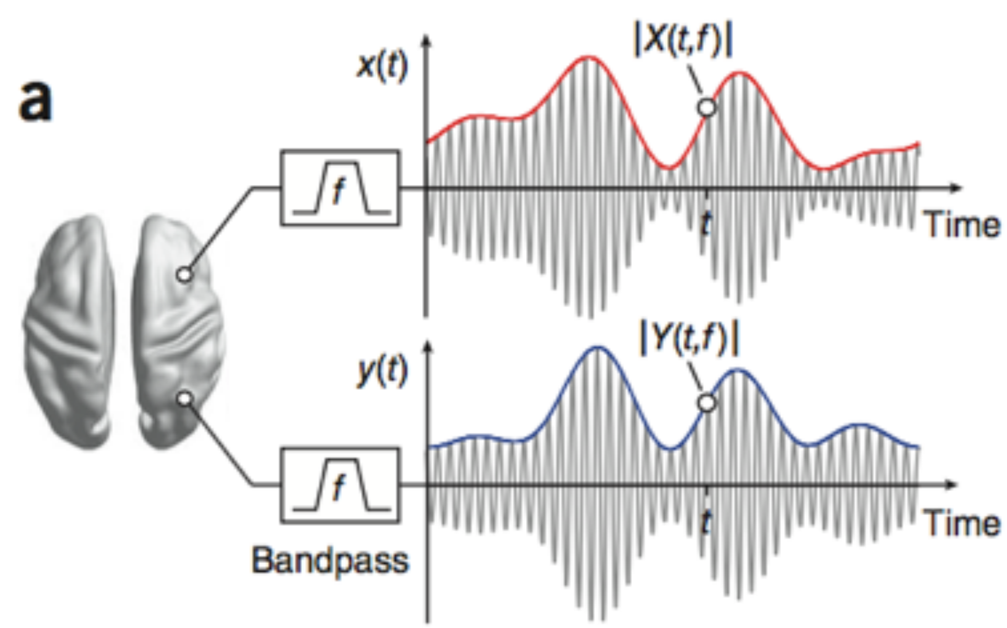
MEG: what FC measure should we use?

- Can NOT use raw zero-lag correlation as we do in fMRI (due to conduction delays)

- Need to use measures that are robust to non-zero lags

e.g. **Amplitude Coupling**

- Detects if the amplitude (or power or envelope) time courses in particular frequency bands are correlated



Hipp et al.; Nat Neuro (2012)

Brookes et al.; Neuroimage (2013)

MEG: what FC measure should we use?

- Can NOT use raw zero-lag correlation as we do in fMRI (due to conduction delays)

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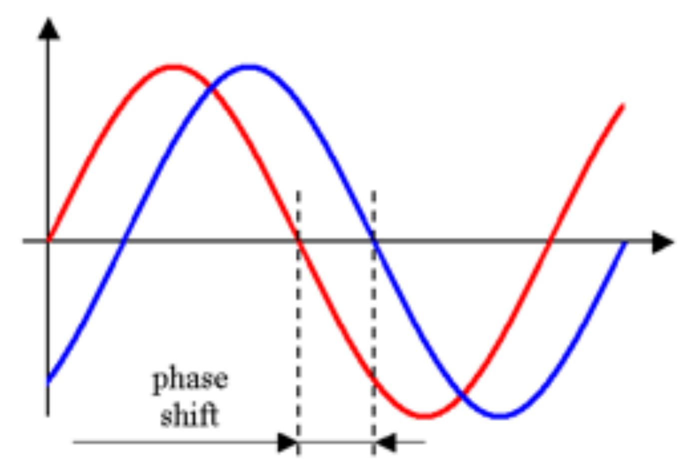
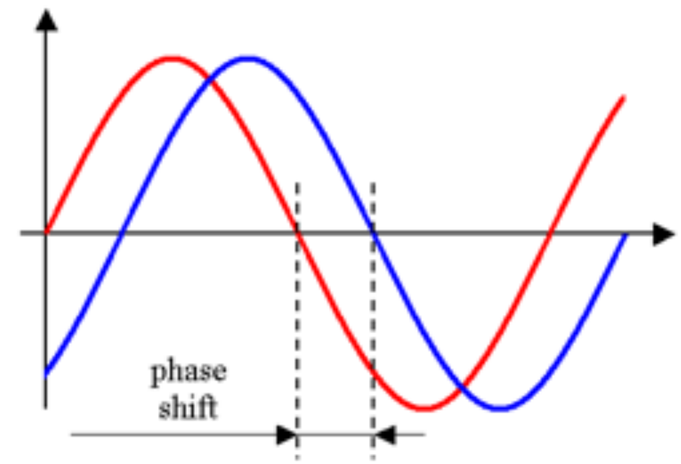
- Phase coupling measures
  - Detect consistent phase differences between brain signals



Phase Coupling Measures

- Detect consistent phase differences between brain signals



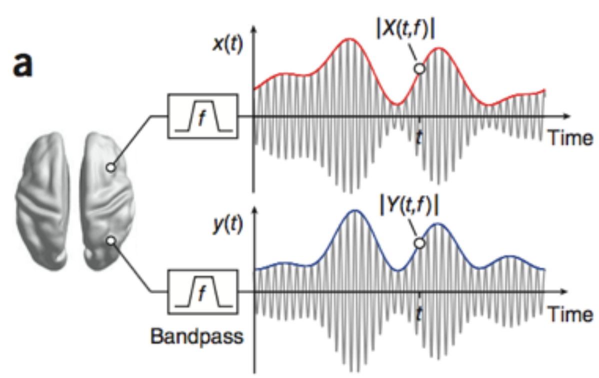
Spectral Methods
- estimated via multi-tapers or MAR models
- need to choose sensible taper size or model order

Phase Estimation Methods
- phase estimated on band-pass filtered data
- need to choose sensible freq bands

	Spatial Leakage Correction?	Partial?
Coherence	No	No
Imaginary coherence	Yes	No
Partial coherence	No	Yes
Phase Locking Value (PLV)	No	No
Phase Locking Index (PLI)	Yes	No

Colclough et al., How reliable are MEG resting-state connectivity metrics? Neuroimage, 2016

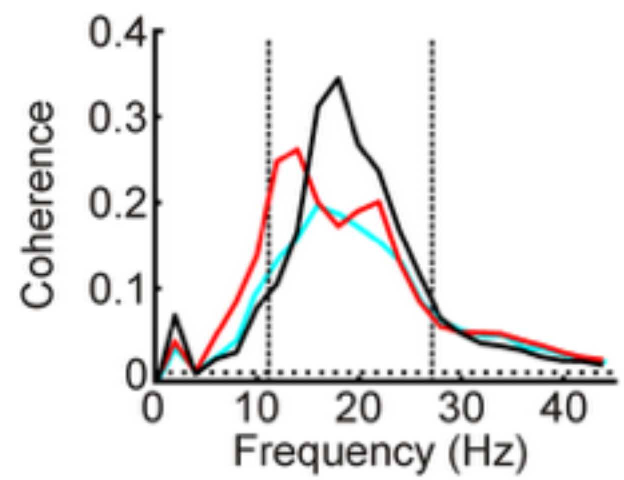
MEG: what FC measure should we use?



Amplitude Coupling

Envelope Correlation

Envelope Partial Correlation



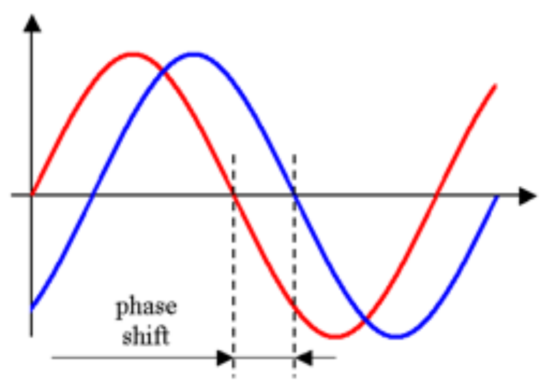
Phase coupling: spectral methods

Coherence

Partial Coherence

PDC

Marzetti et al, NI, 2013



Phase coupling: phase estimation methods

PLV

PLI

PSI

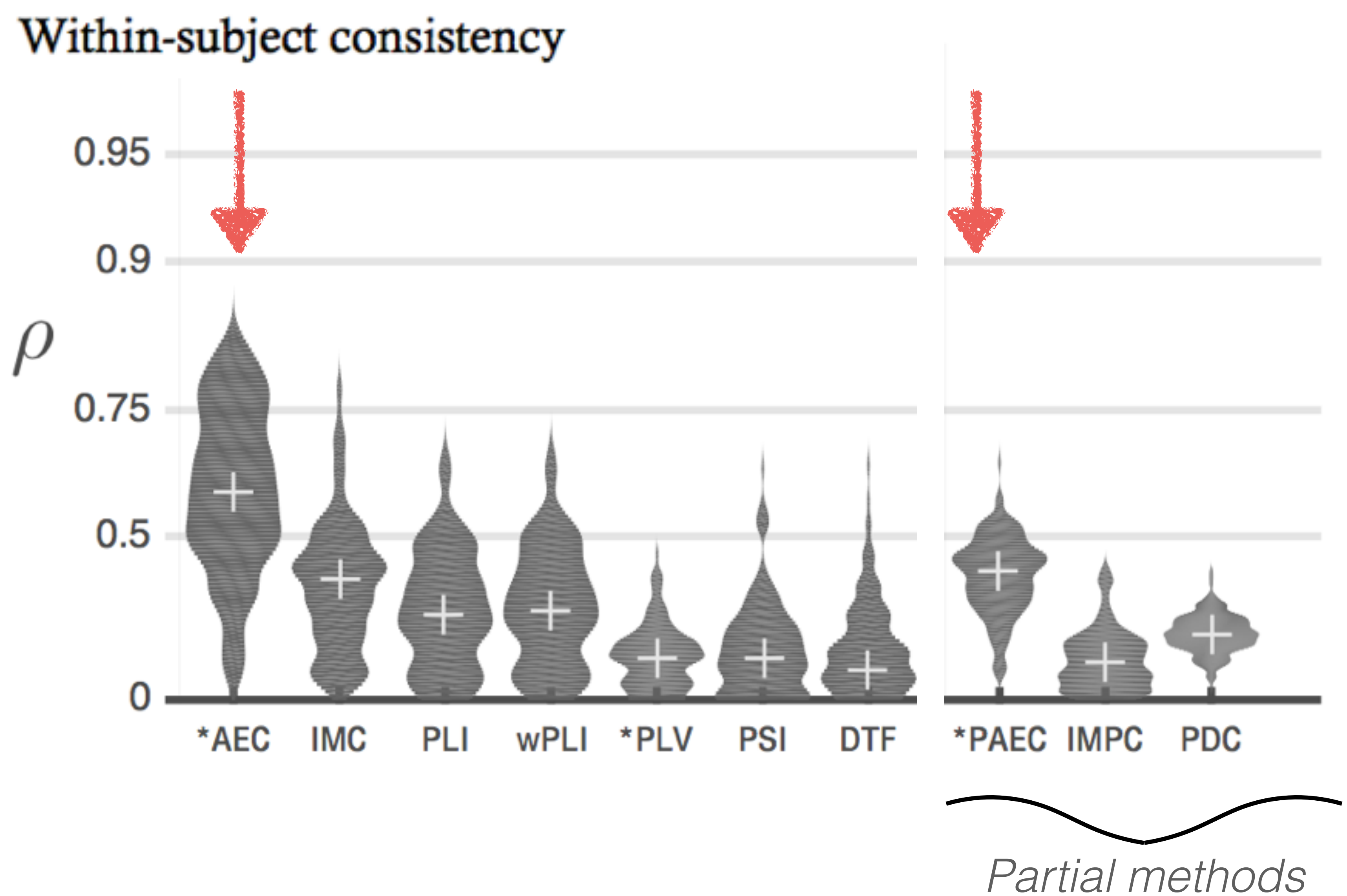
wPLI

Ewald et al, Biomed Tech, 2013

It depends on the context!

MEG: what FC measure in the resting state?

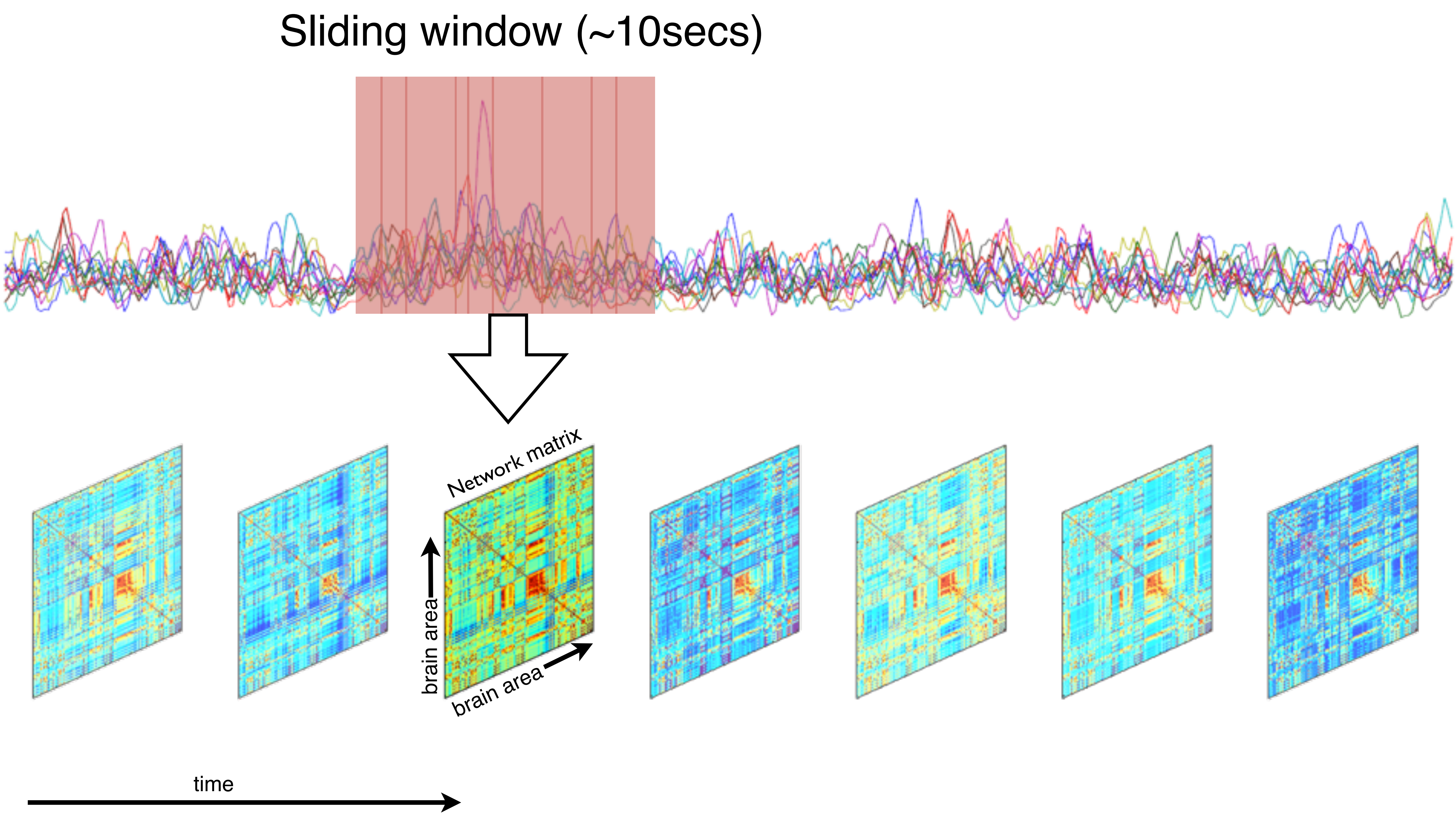
- **Resting-state** data from Human Connectome Project, 61 subjects with 3 sessions each
- Most consistent is amplitude correlations with spatial leakage correction (*AEC)



Colclough et al., How reliable are MEG resting-state connectivity metrics? Neuroimage, 2016

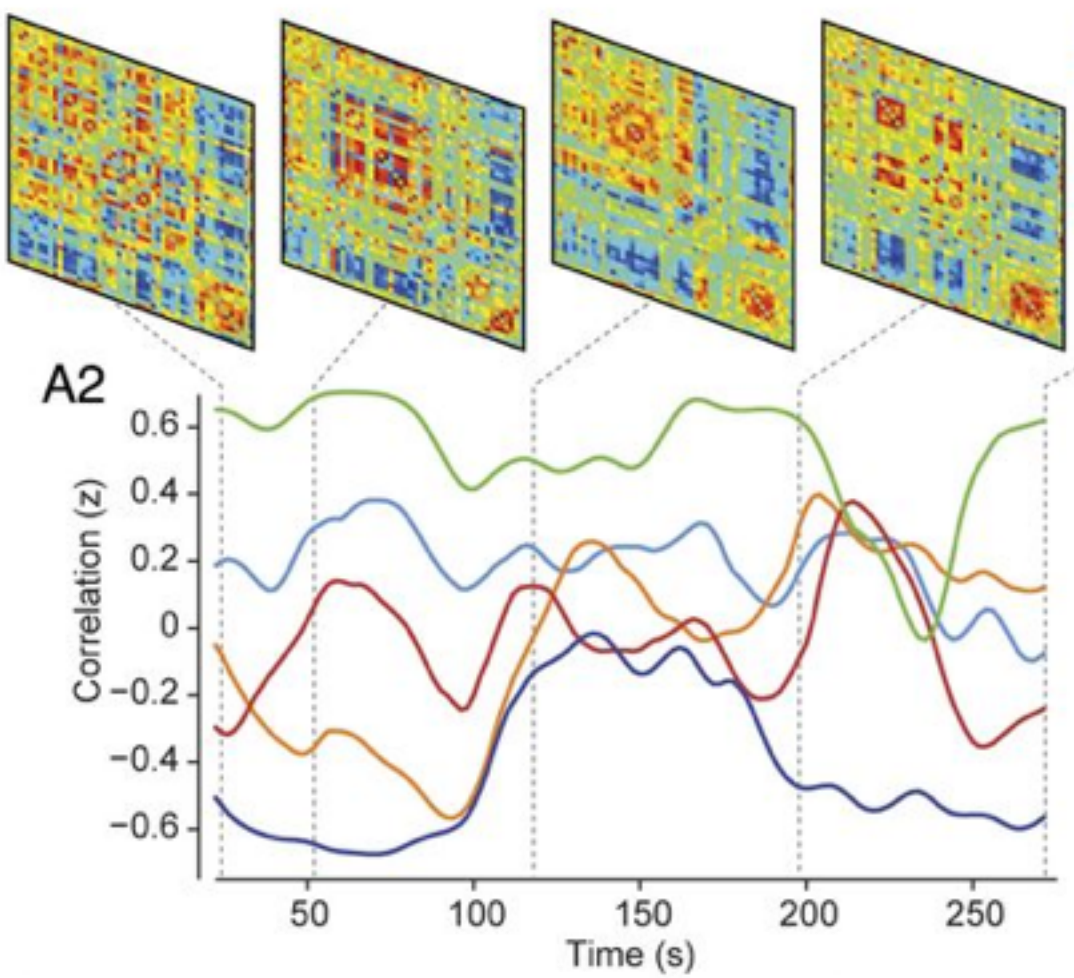
Time-varying functional connectivity

Compute ***sliding window*** correlation network matrices



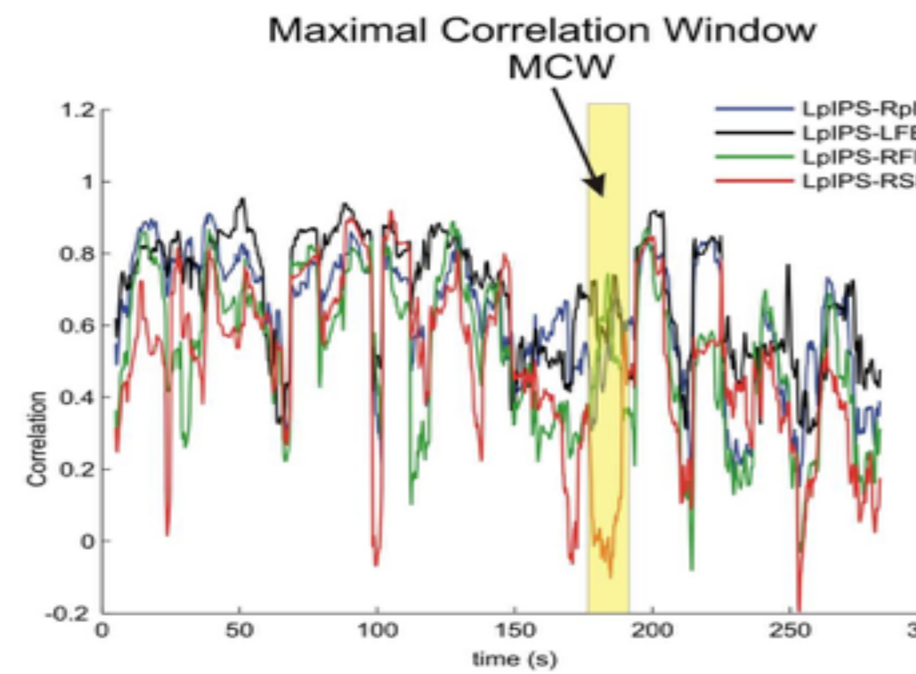
Non-stationary functional connectivity

Sliding window FC in fMRI:



Allen et al. (Cerebral Cortex 2012)

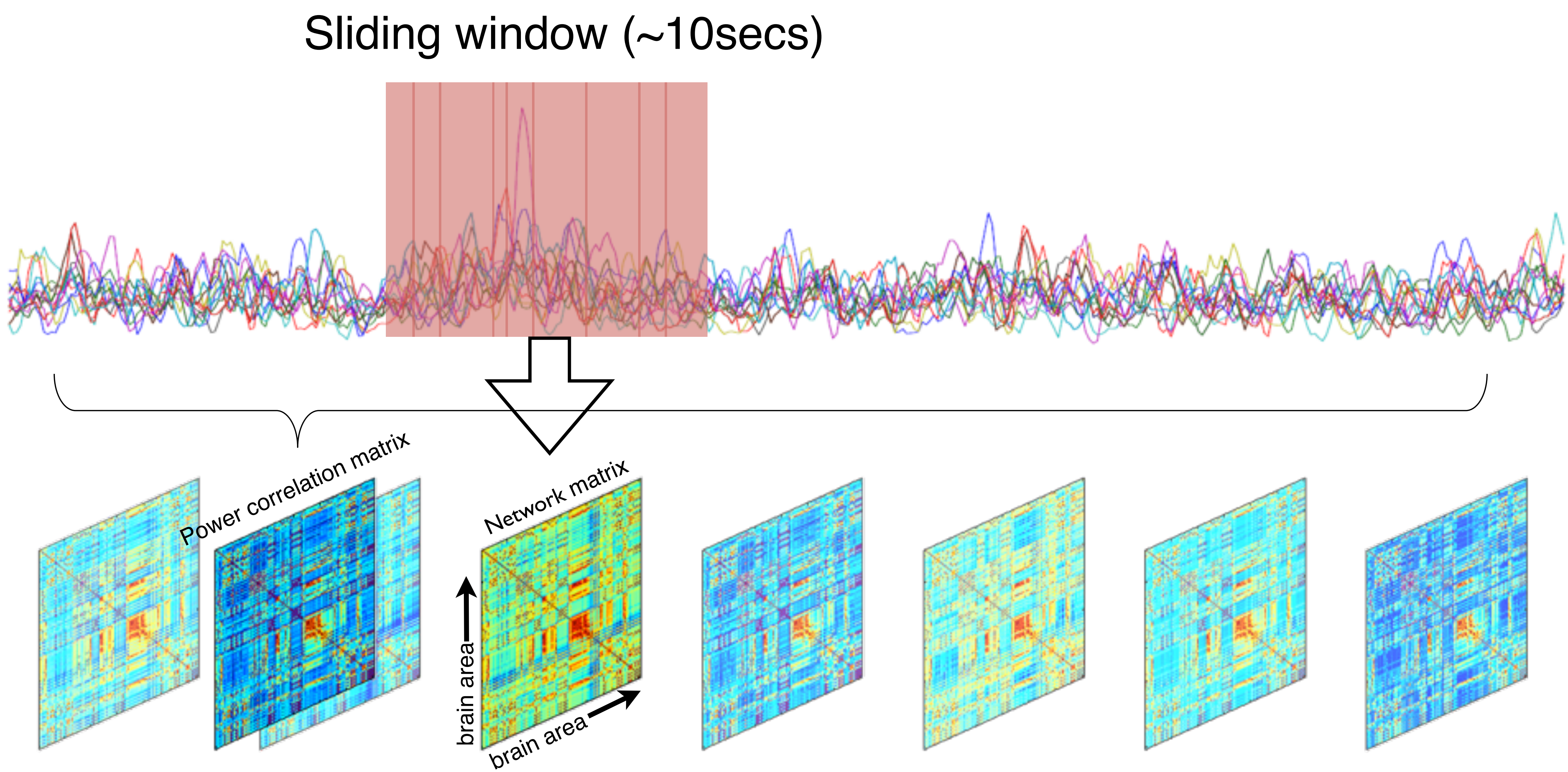
Sliding window FC in MEG:



de Pasquale et al. (PNAS 2010)

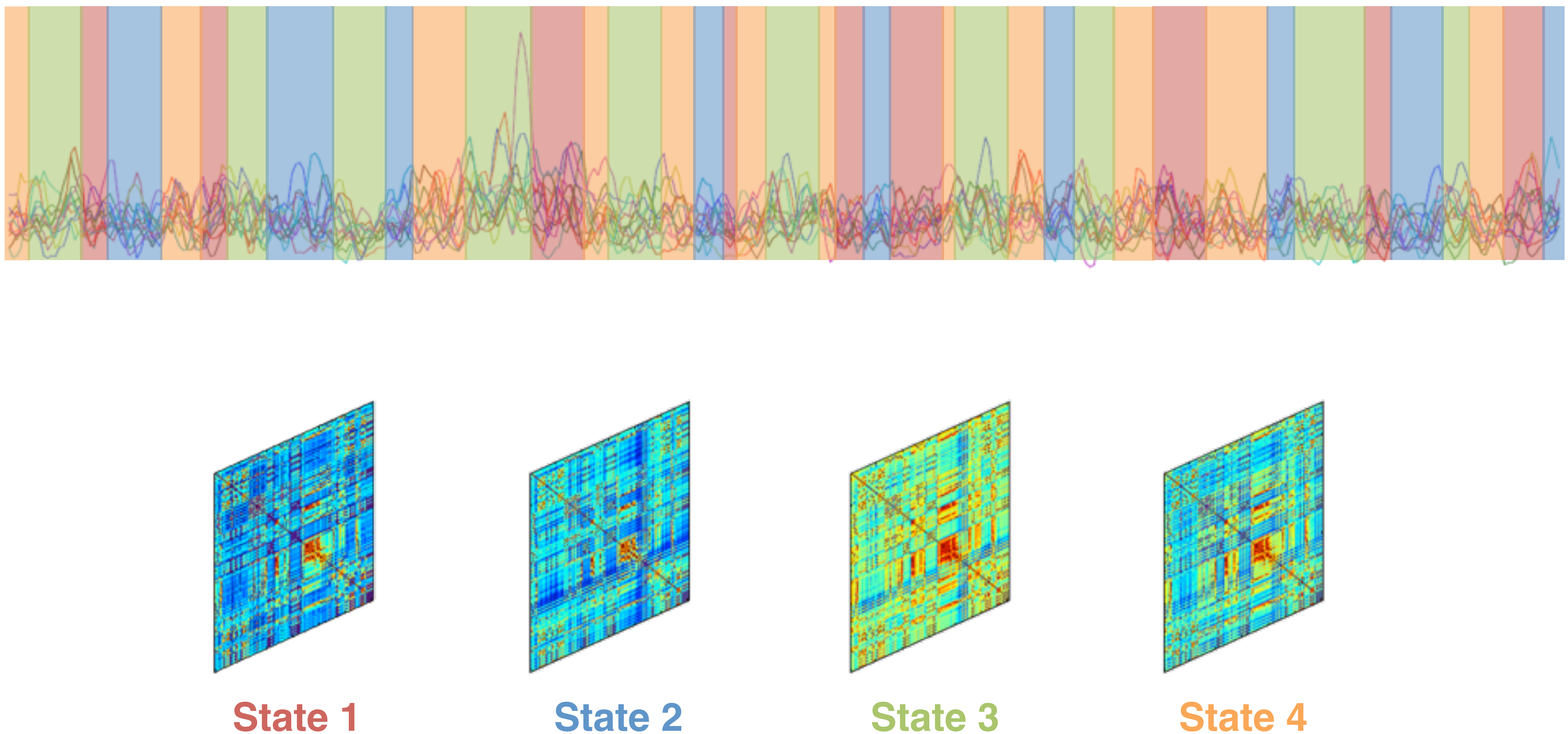
Time-varying functional connectivity

BUT: Sliding window correlation requires time window of sufficient length:



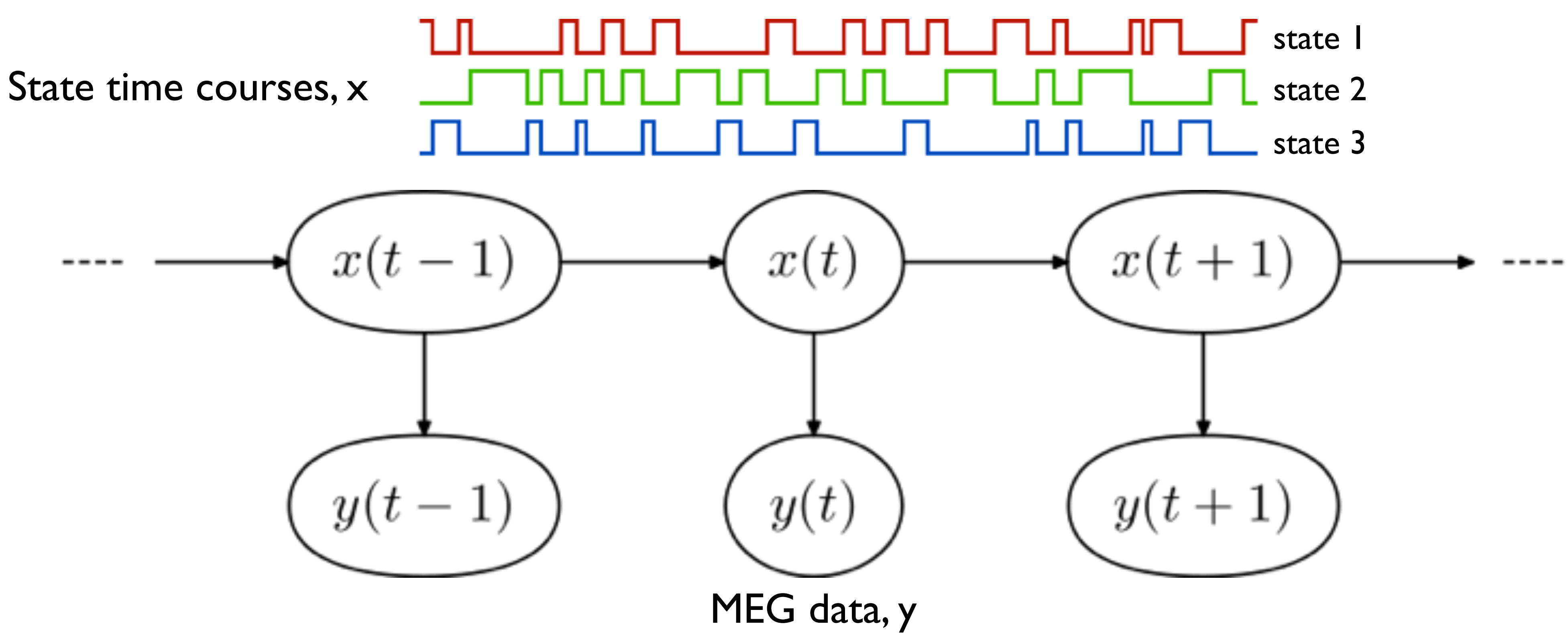
Time-varying functional connectivity

Instead pool data over disjoint time periods:



Hidden Markov Model (HMM)

- Generative model, consisting of:
  - state time courses, x - indicating which state the system is in at each time point



Baker,…,Woolrich; eLife (2014)

Hidden Markov Model (HMM)

- Generative model, consisting of:
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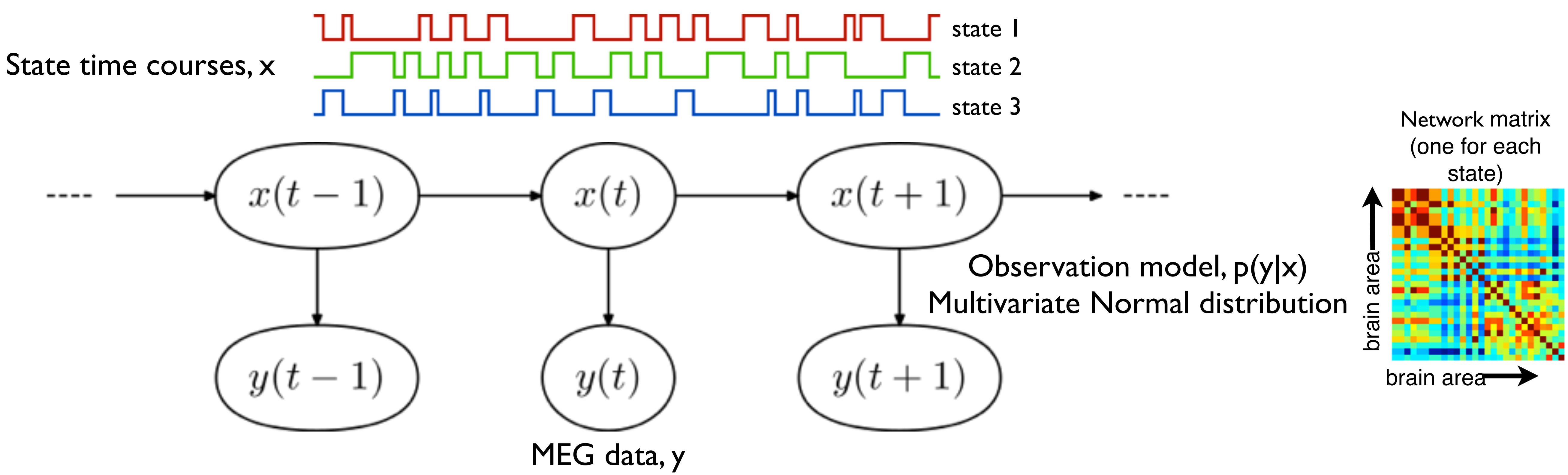

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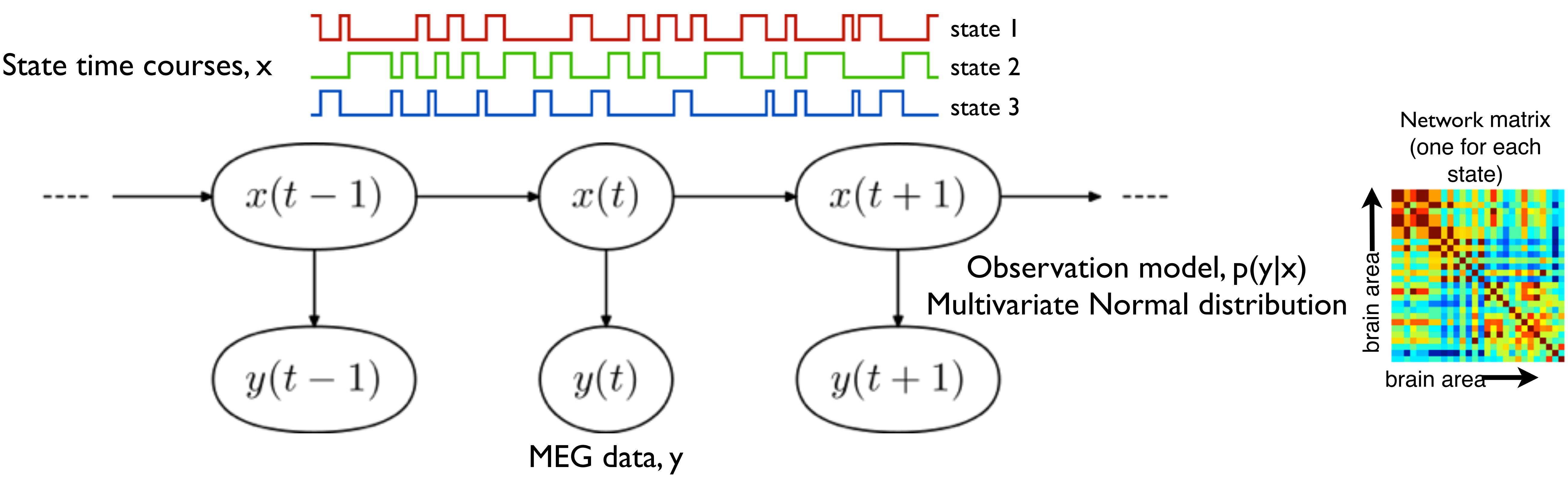


- Variational Bayes inference

Baker,…,Woolrich; eLife (2014)

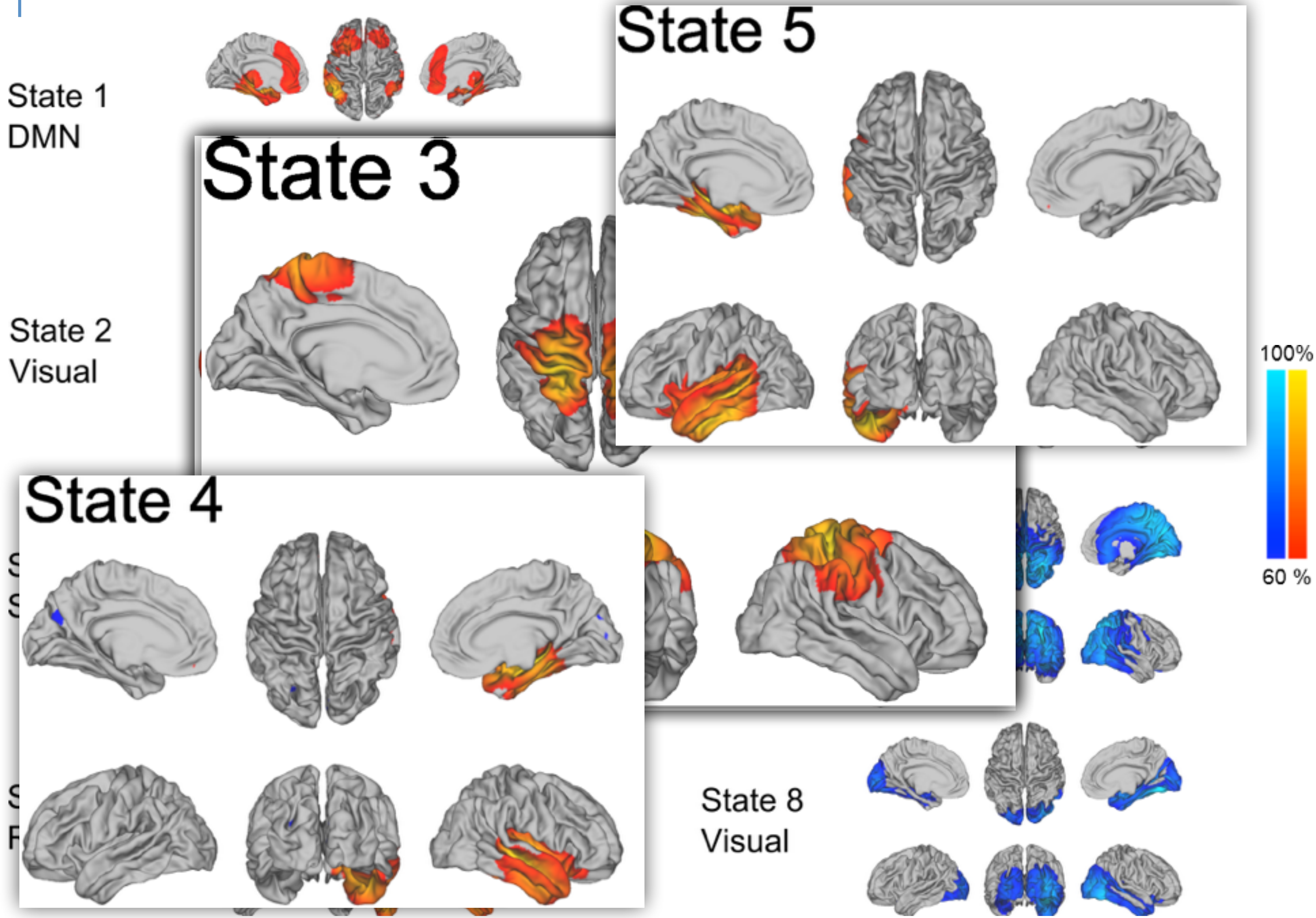
HMM on MEG resting state data

- Can we use the HMM to infer ***transient brain states*** from resting MEG data?
  - Resting state data acquired with CTF 275 channel MEG system
  - 9 subjects, 10 minutes eyes open
  - Projection to source space using beamforming
  - HMM run on amplitude time courses (4 – 30 Hz)

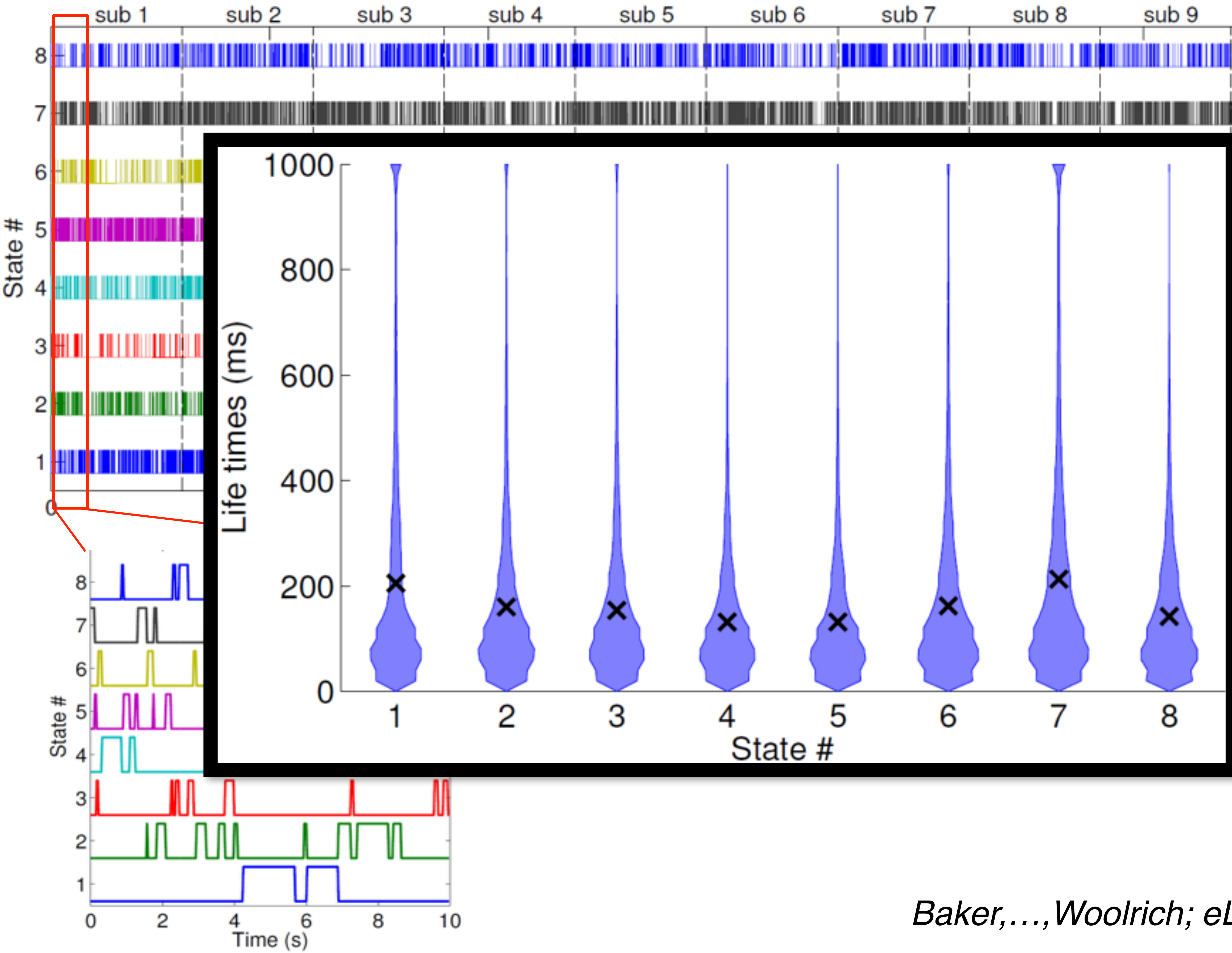
Baker,…,Woolrich; eLife (2014)

HMM on MEG resting state data

Baker,…,Woolrich; eLife (2014)

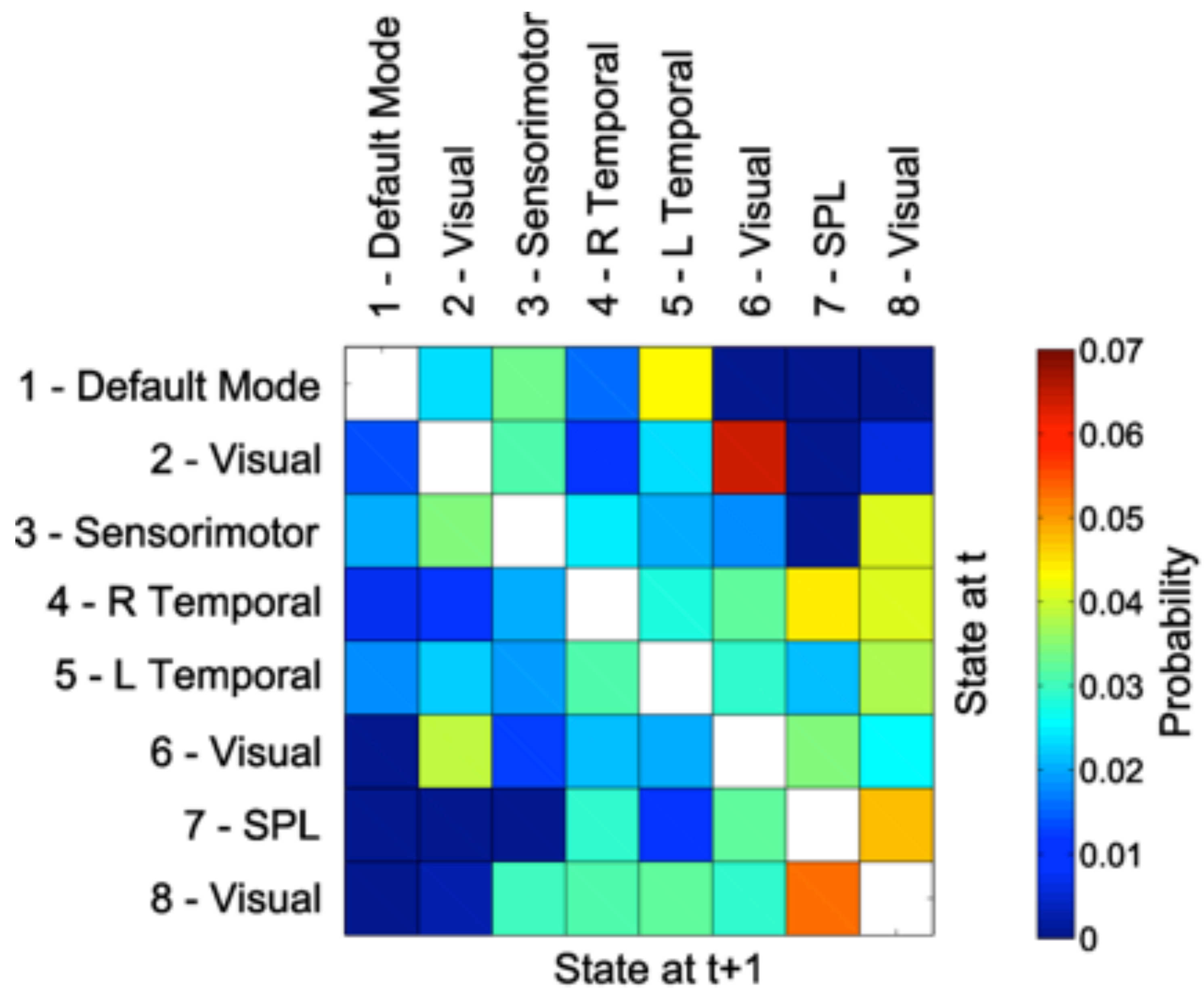


State time courses



Baker,…,Woolrich; eLife (2014)

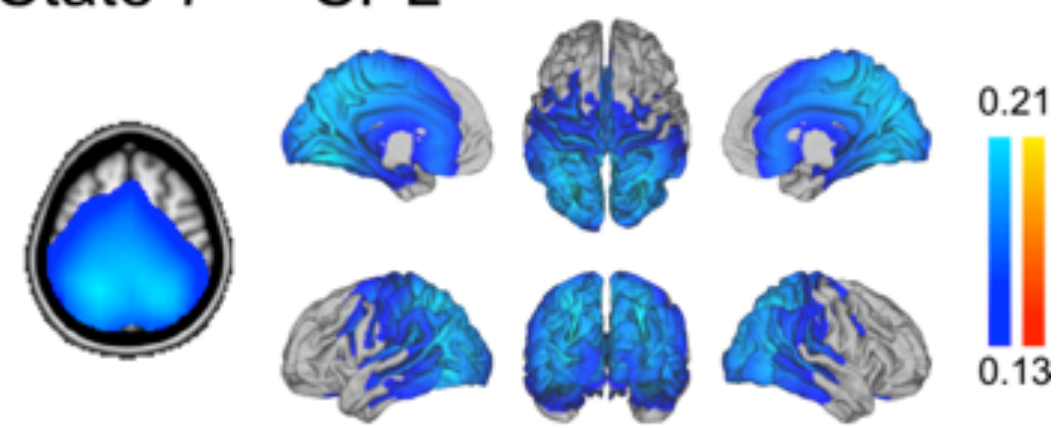
State Transition Probabilities



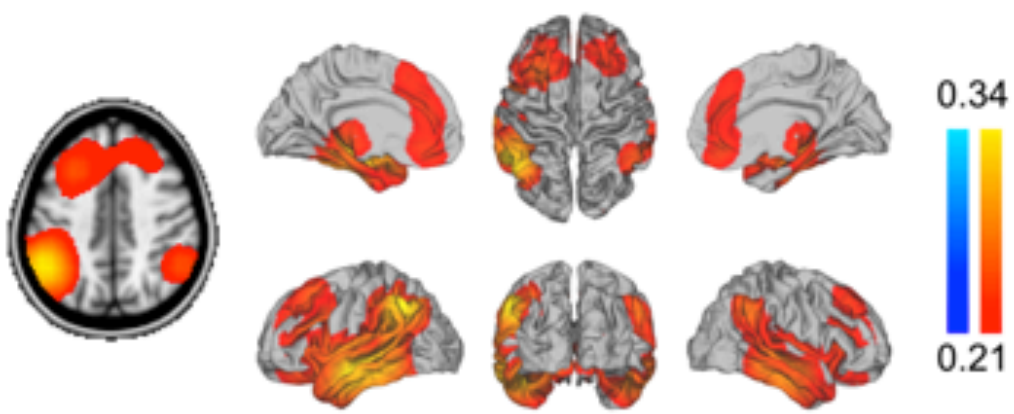
Baker,…,Woolrich; eLife (2014)

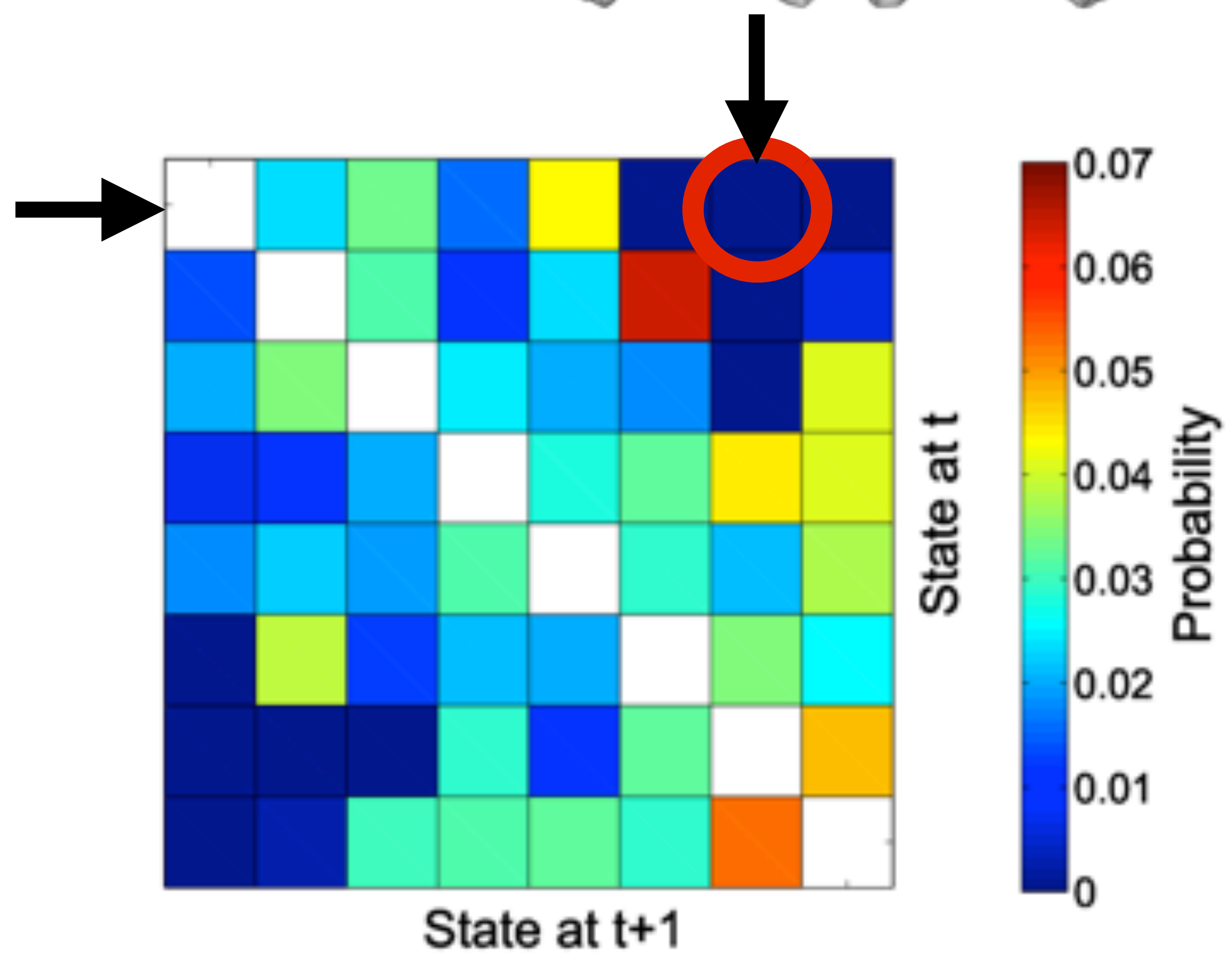
State Transition Probabilities

State 7 - SPL



State 1 - Default Mode



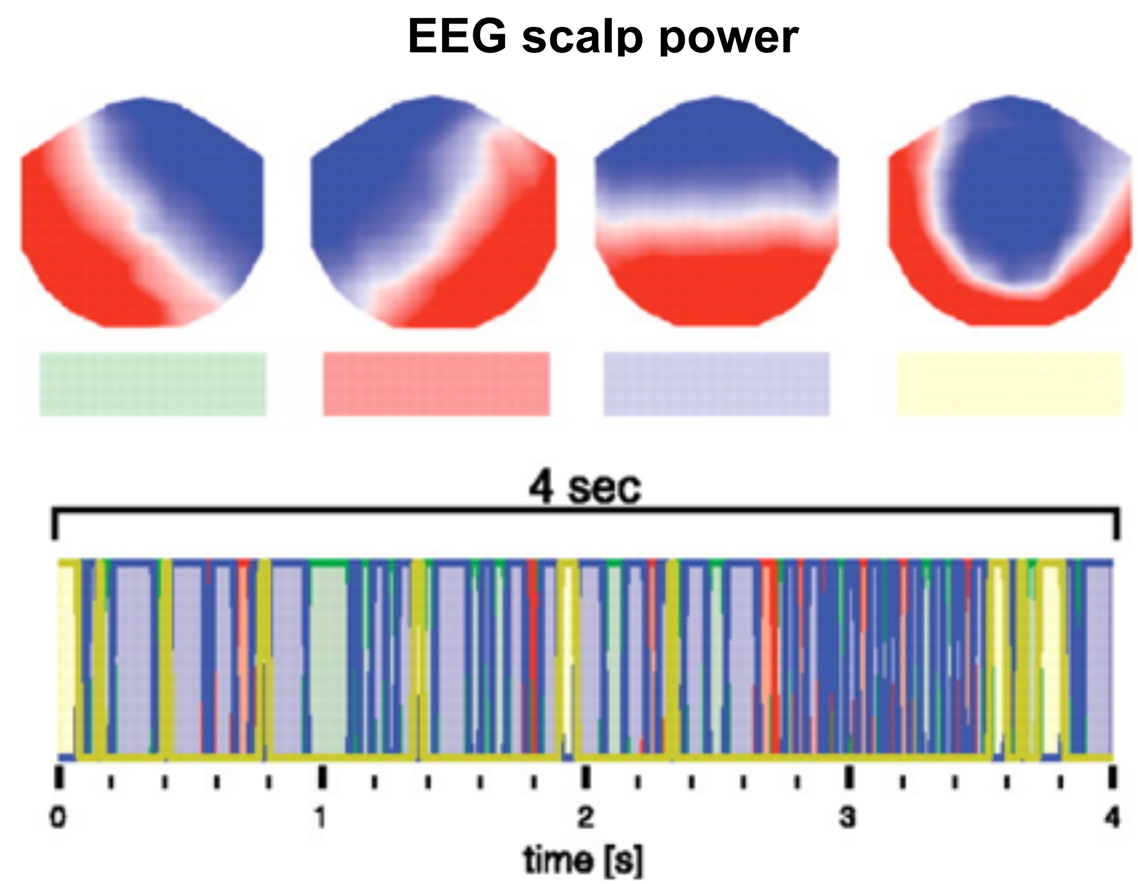


DAN/DMN anticorrelation in fMRI (Fox et al., PNAS, 2005)?

Baker,…,Woolrich; eLife (2014)

Relationship to EEG microstates?

- Do the HMM states represent source space counterparts of EEG microstates?



Van De Ville et al. PNAS (2010)

- Quasi-stable topographies of EEG power over the scalp that remain stable for periods of ~100 ms

- EEG microstates correlate with BOLD RSNs

  (e.g. Musso et al. 2010, Britz et al., 2010, Yuan et al. 2012)

A different HMM observation model

- Multivariate Normal (MVN) observation model requires use of amplitude time courses
  - what about working with raw time courses?
    - e.g. can we then find time-varying phase locking?
- Instead: Multivariate autoregressive model (MAR) per HMM state
  - captures different multi-region spectral properties for each state
  - e.g. PSD or coherence

MAR model: $$x_t = \sum_{i=1}^{p} W_i x_{t-i} + e_t$$

Vidaurre et al., Neuroimage, 2016

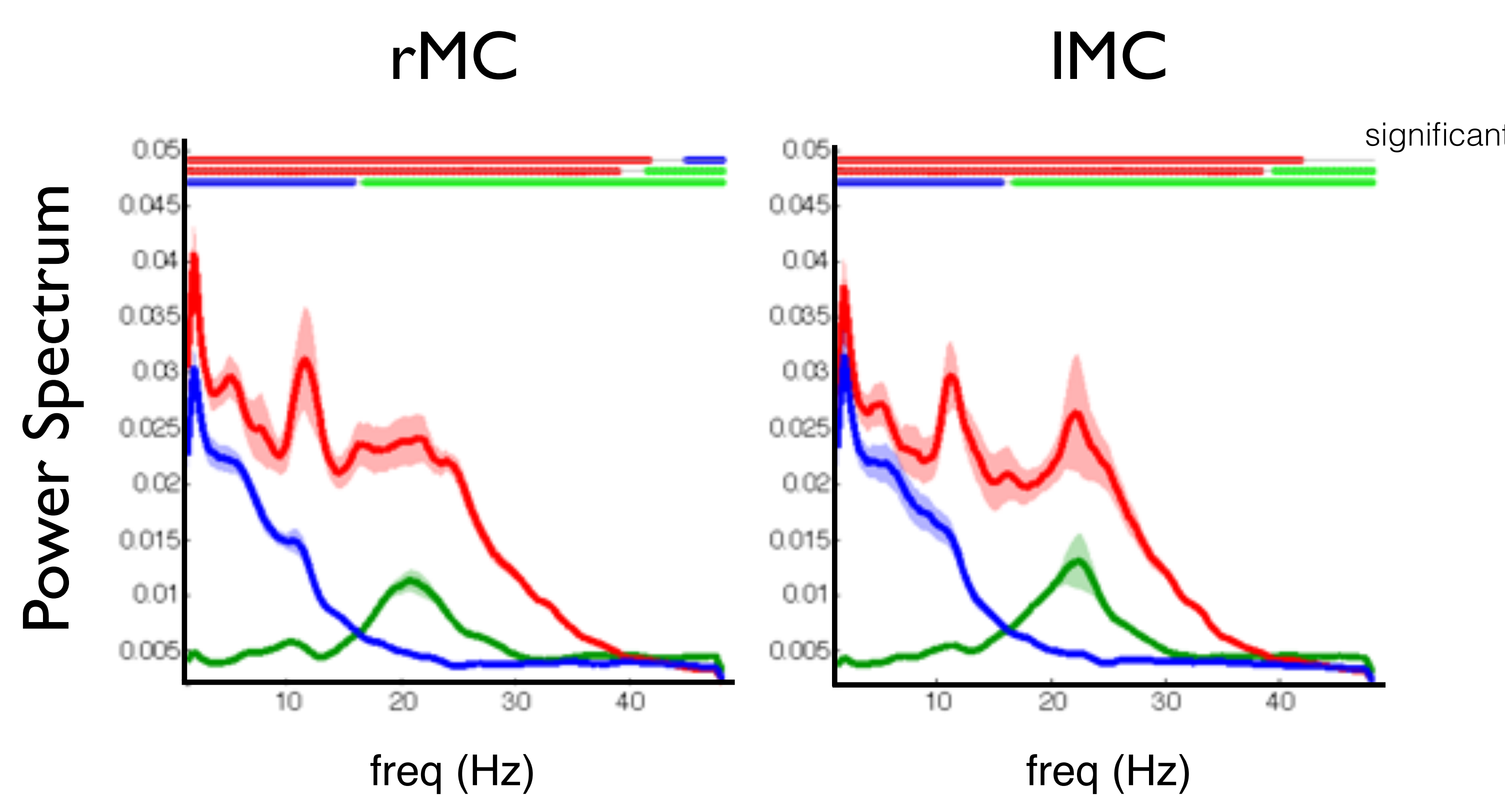
Are brain states modulated by task?

- Self-paced finger tapping task
  - 2 left/right MC parcels
  - 3 HMM states
  - 8 subjects
  - raw time-courses (1-50 Hz)
  - HMM with MAR observation model
- Do we see task-related HMM states?

(Note: HMM is run with **no** knowledge of task timings)

Motor task: spectral properties

Spectral properties of each HMM state

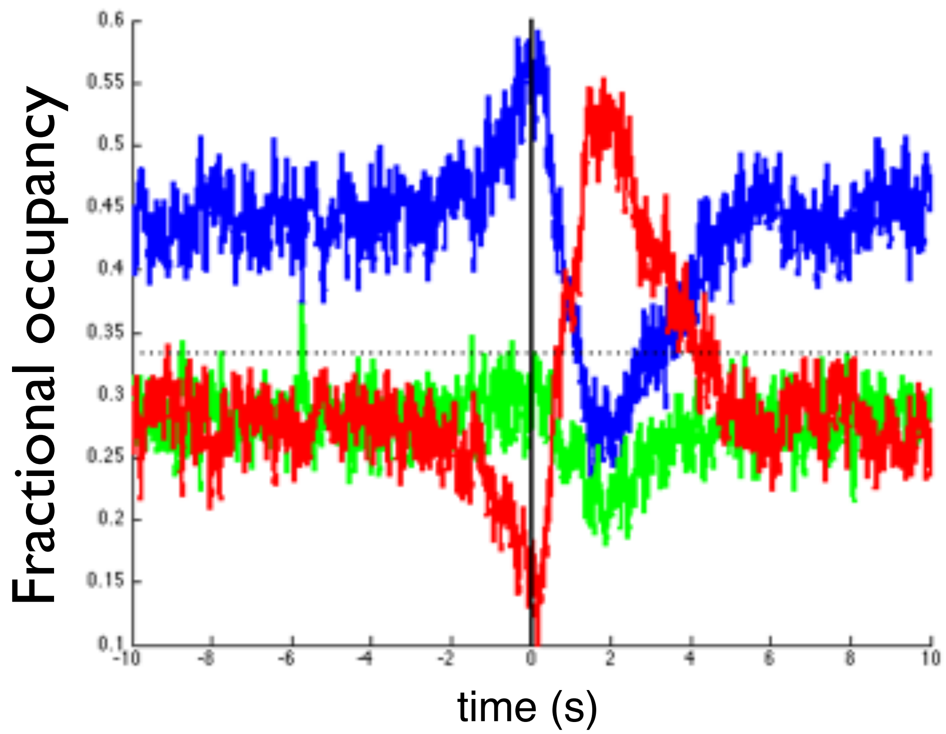


- significant state-dependent (time-varying) power spectra

Vidaurre et al., Neuroimage, 2016

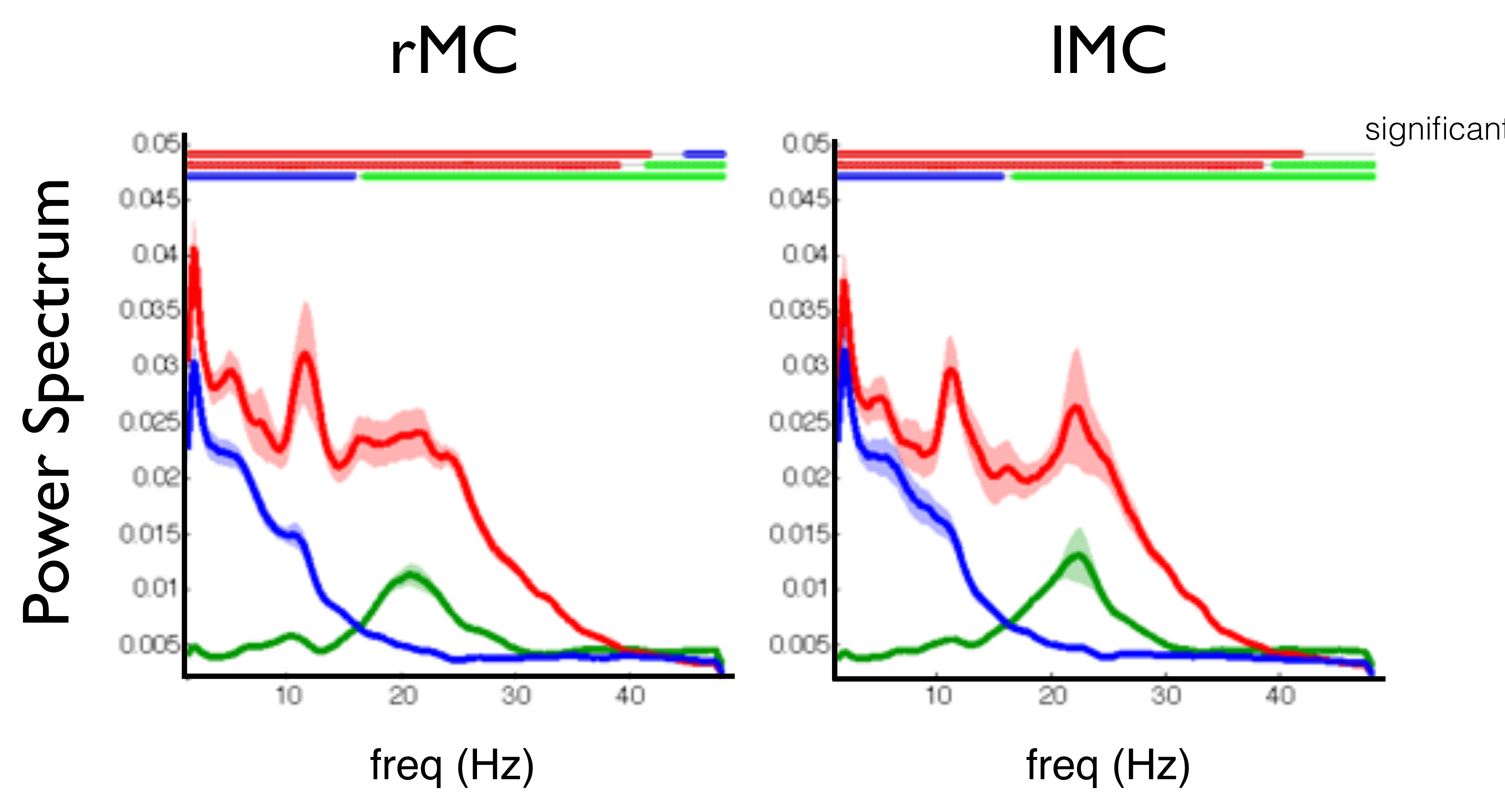
Motor task: spectral properties

HMM state time-courses



Finger-tap (beta suppression)
Post-finger-tap (beta rebound)
Baseline

Spectral properties of each HMM state



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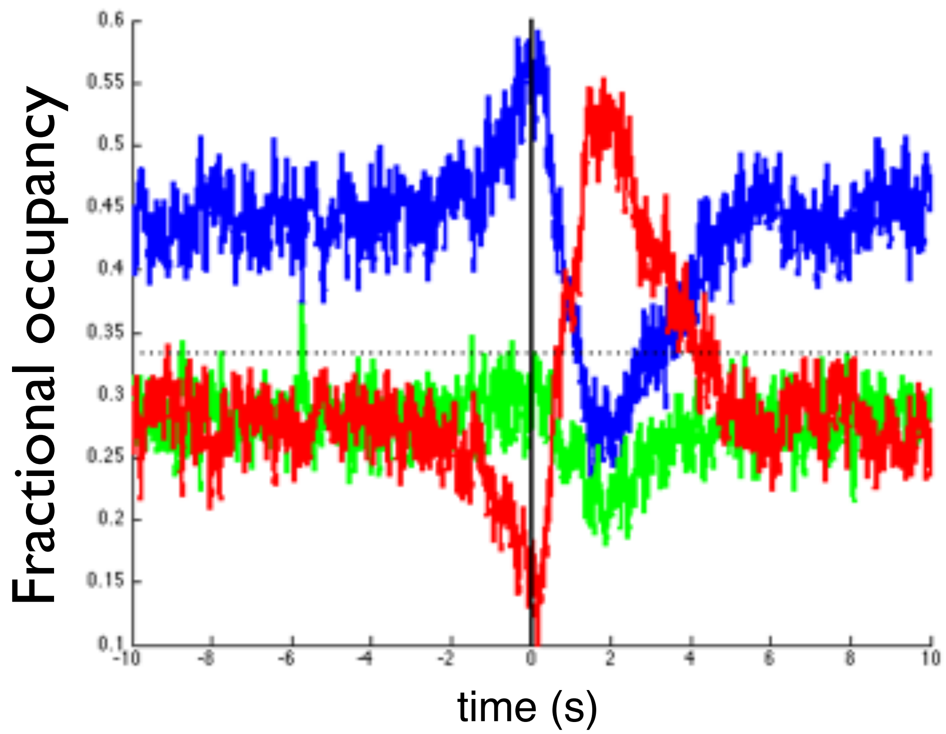
Vidaurre et al., Neuroimage, 2016

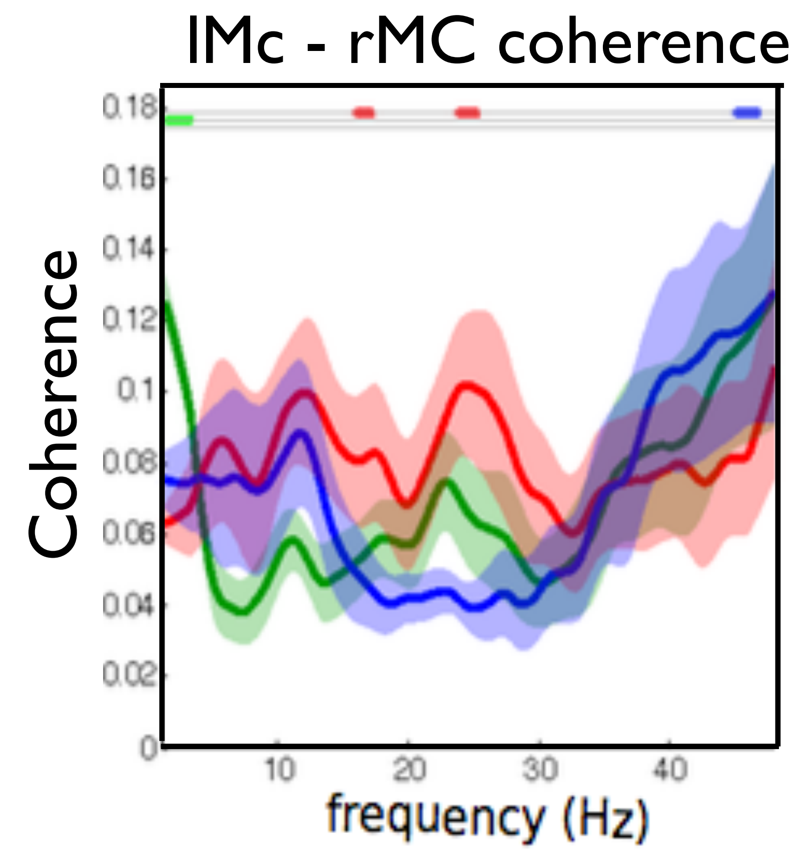
Motor task: spectral properties

HMM state time-courses



Finger-tap (beta suppression)
Post-finger-tap (beta rebound)
Baseline

Cross-Spectral properties of each HMM state



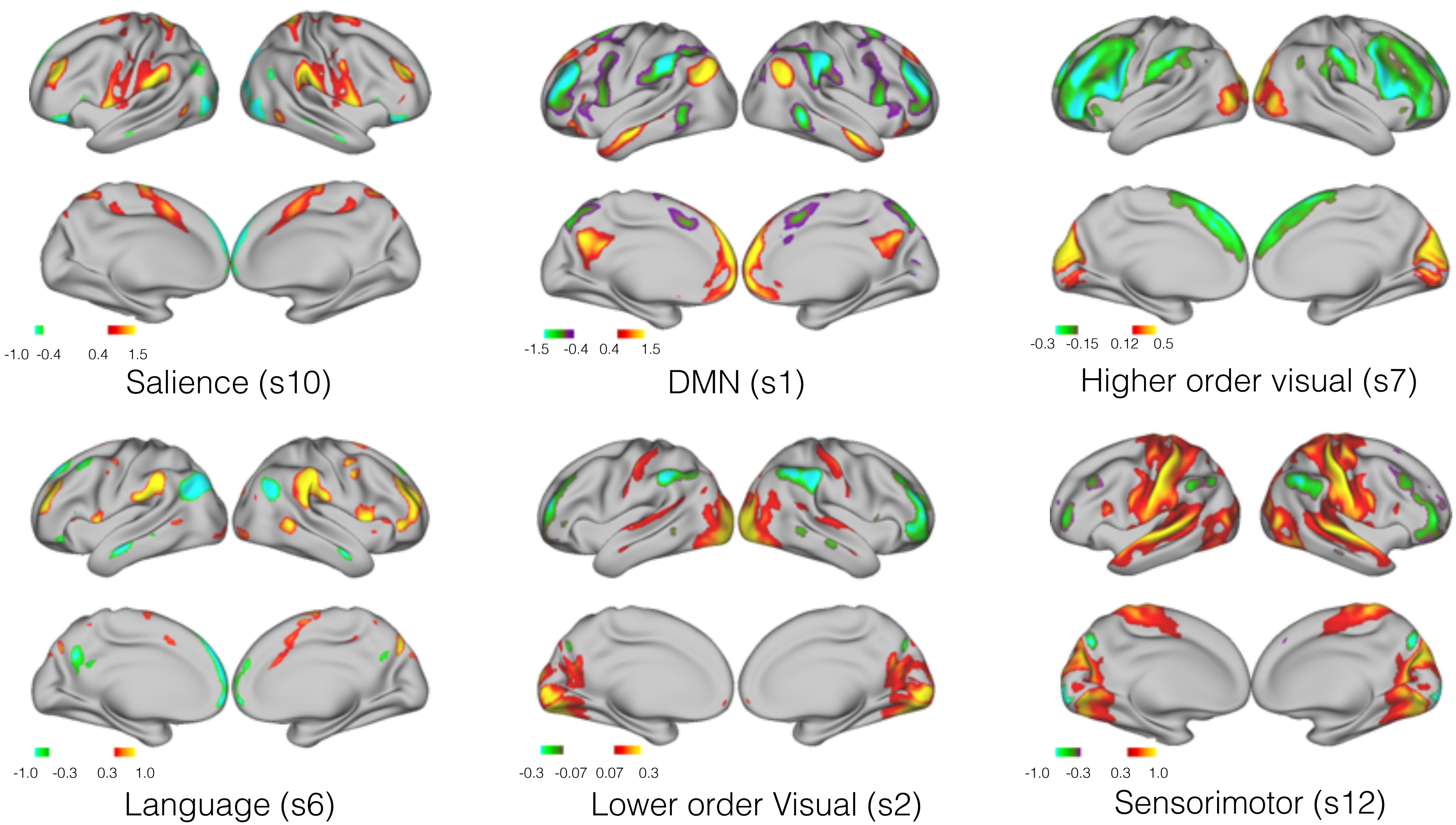
- significant state dependent (time-varying) coherence (phase locking)

Vidaurre et al., Neuroimage, 2016

HMM on resting fMRI data

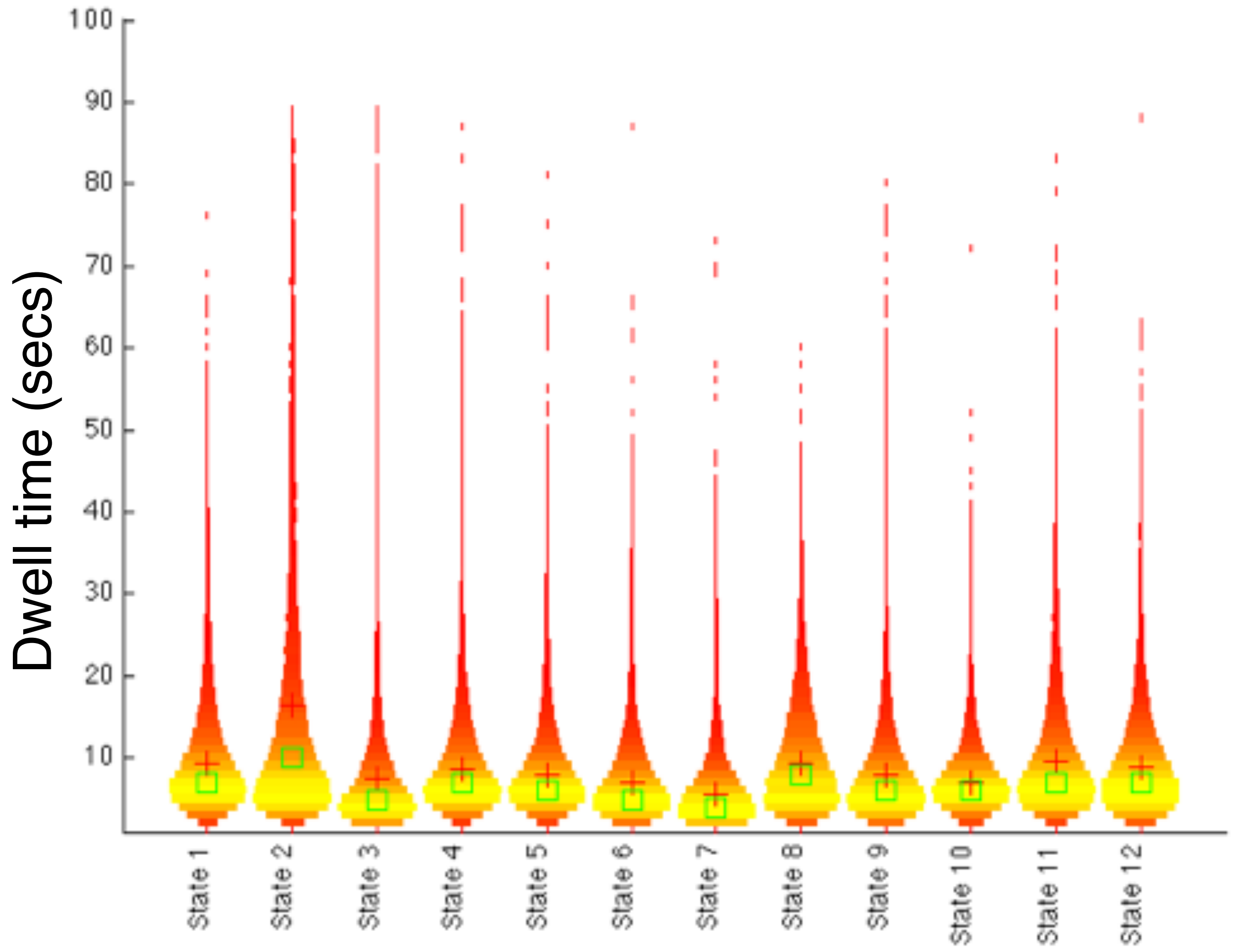
Diego Vidaurre et al., In preparation

- HMM on fMRI data
- HMM on BIG data (stochastic learning)
    - e.g. HCP resting fMRI (~1000 subjects):



HMM on resting fMRI data

Diego Vidaurre et al., In preparation



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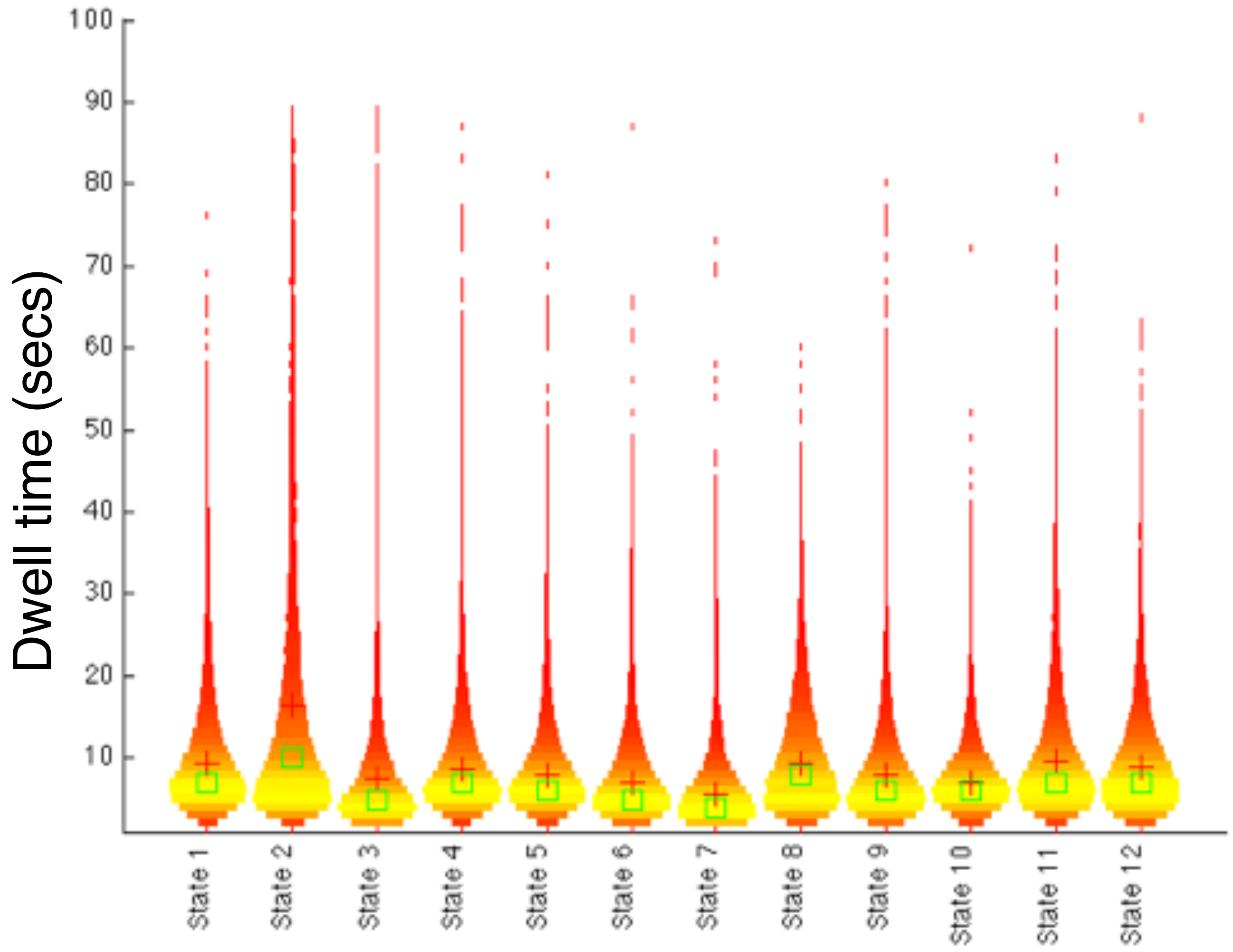
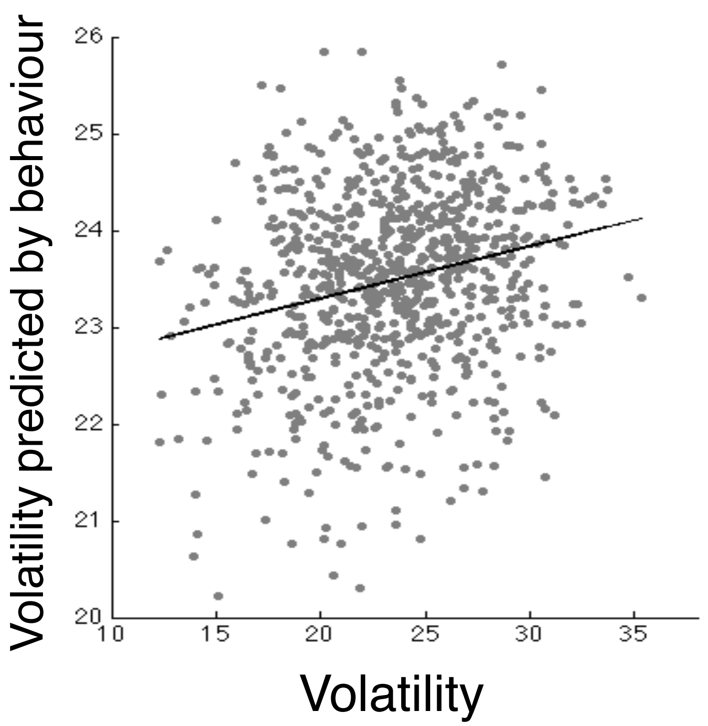
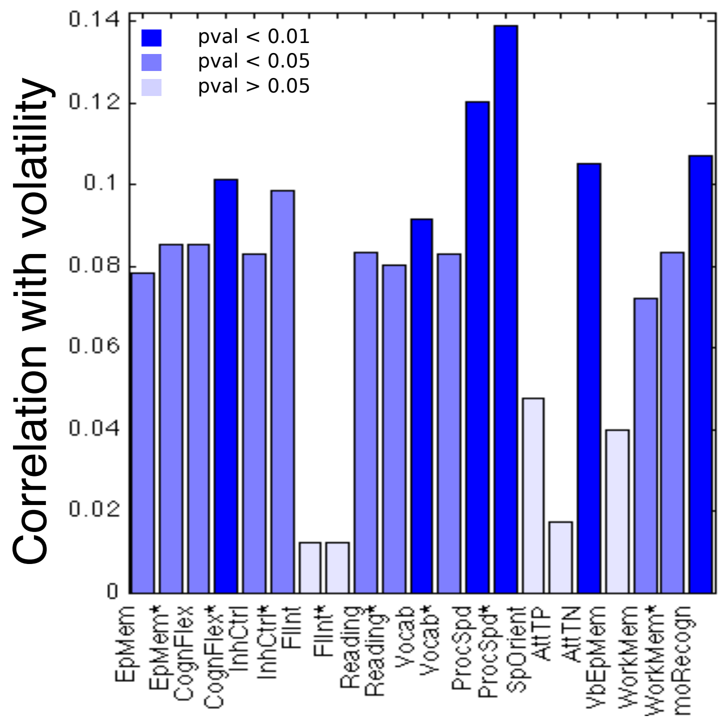


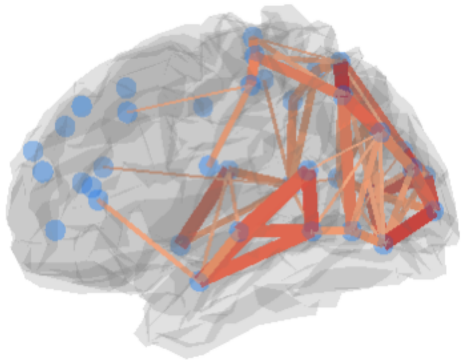
- Speed of state switching ("volatility") predicts behaviour



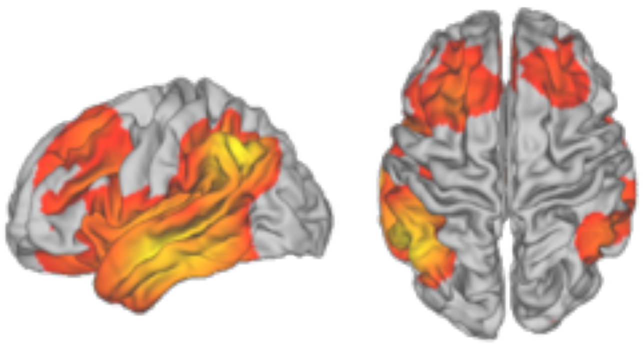


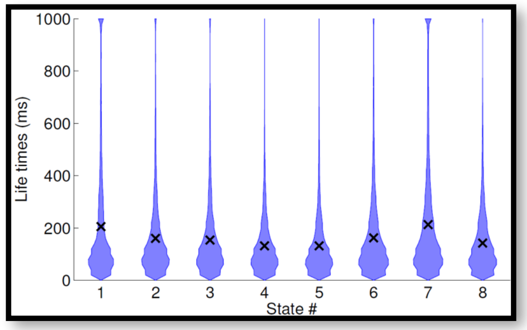
Summary

- MEG functional connectomes can be computed using correlation between **power** time-courses
  - phase-locking measures are less sensitive (in resting state data)
  - beware spatial leakage!

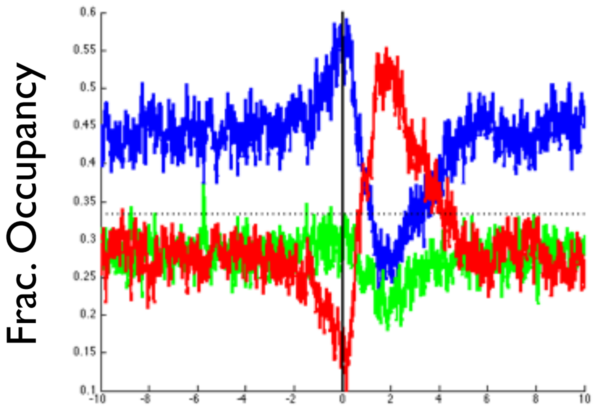


- MEG and HMM can identify brain states switch on **~100ms time-scales**, much faster than previously shown





- The occurrence of brain states predicts **task** state and **behavioural traits**



- Further reading:

"Magnetoencephalography: From Signals to Dynamic Cortical Networks"
edited by Supek and Aine

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