

Multimodal Static and Dynamic Connectomes

Mark Woolrich
University of Oxford



Oxford centre for Human Brain Activity



Centre for FMRI of the Brain

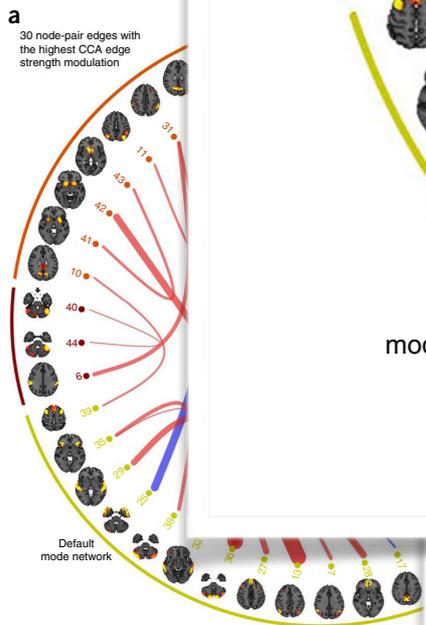
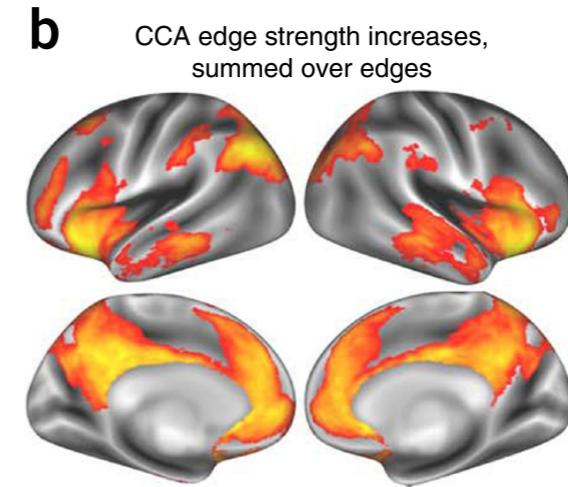
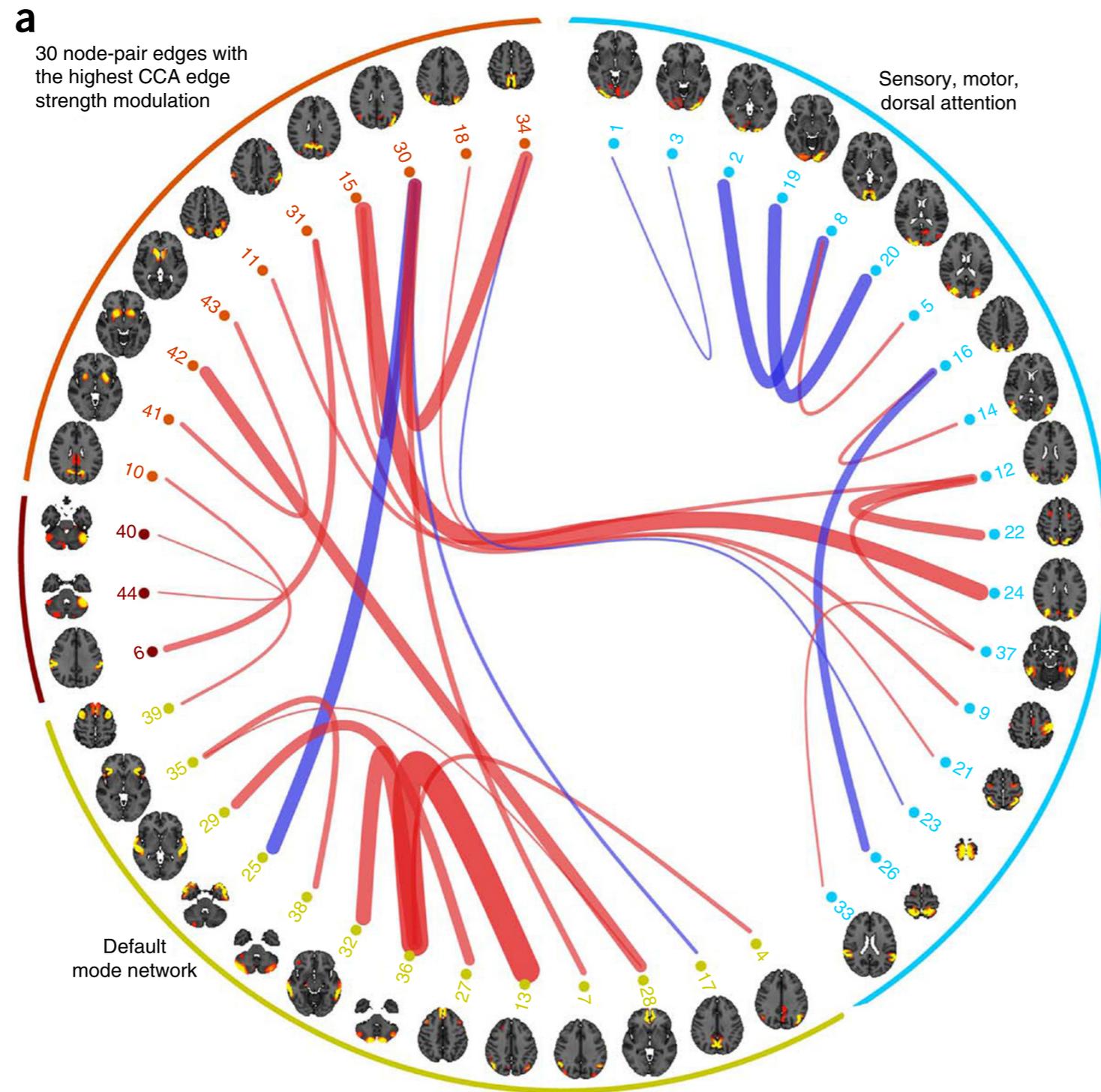


Overview

- **Static Connectomes**
 - Individual parcel variability
 - Electrophysiological connectomes
- **Dynamic Brain Networks**
 - Going beyond sliding window with Hidden Markov Models

Human Connectome Project resting state fMRI data (~1000 subjects)

SM Smith et al (2015) Nature Neuroscience

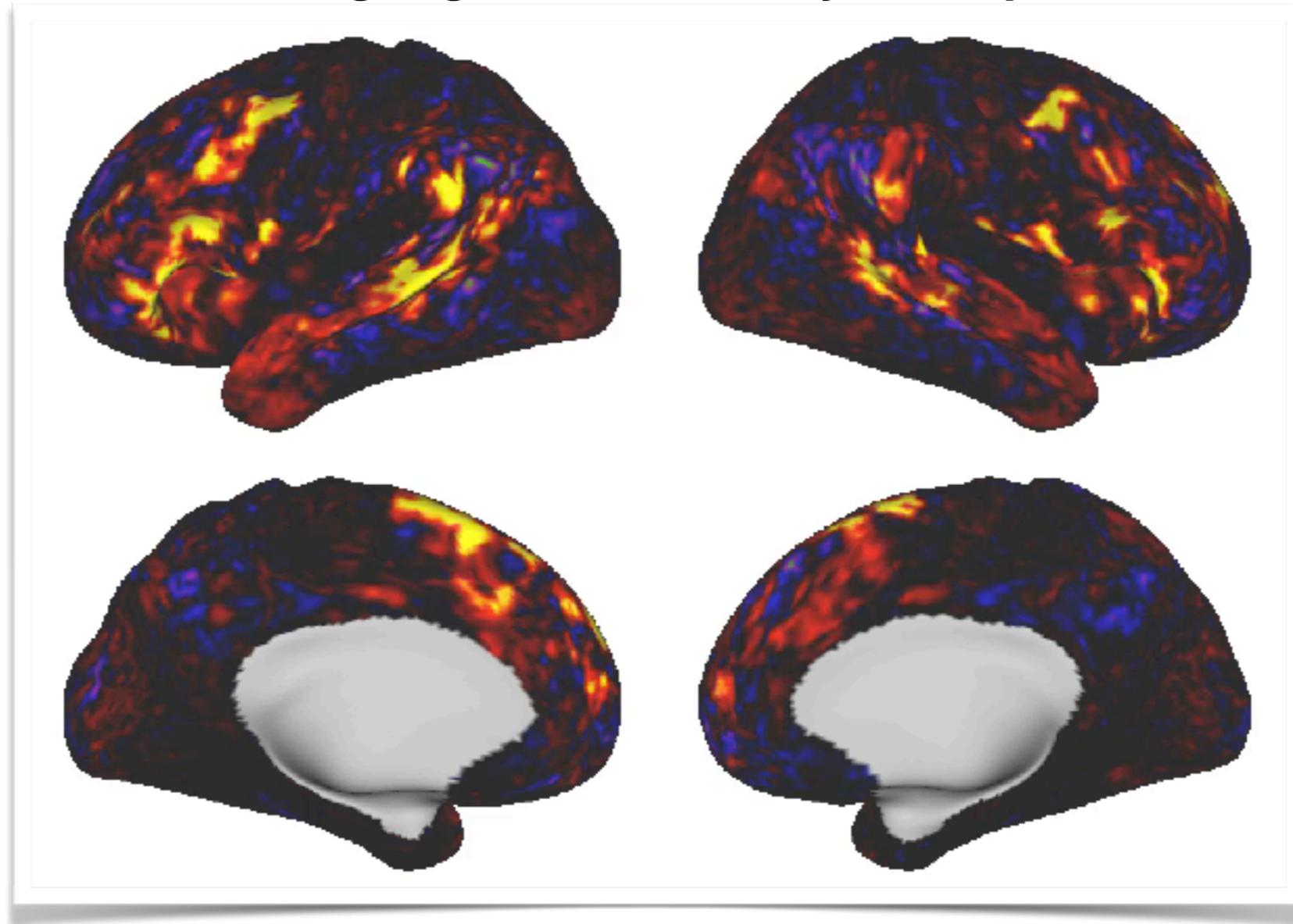


-0.36 | **Nega** | Positive test for THC (cannabis)
 Fluid intelligence (number of skipped responses)

responses)
 counting of \$200)
 ed
 t
 st (true positives)
 test (specificity)
 counting of \$40,000)
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 rse)
 weekdays with any tobacco in last week
 on continuous performance test (false positives)
 positive test for THC (cannabis)
 gence (number of skipped responses)

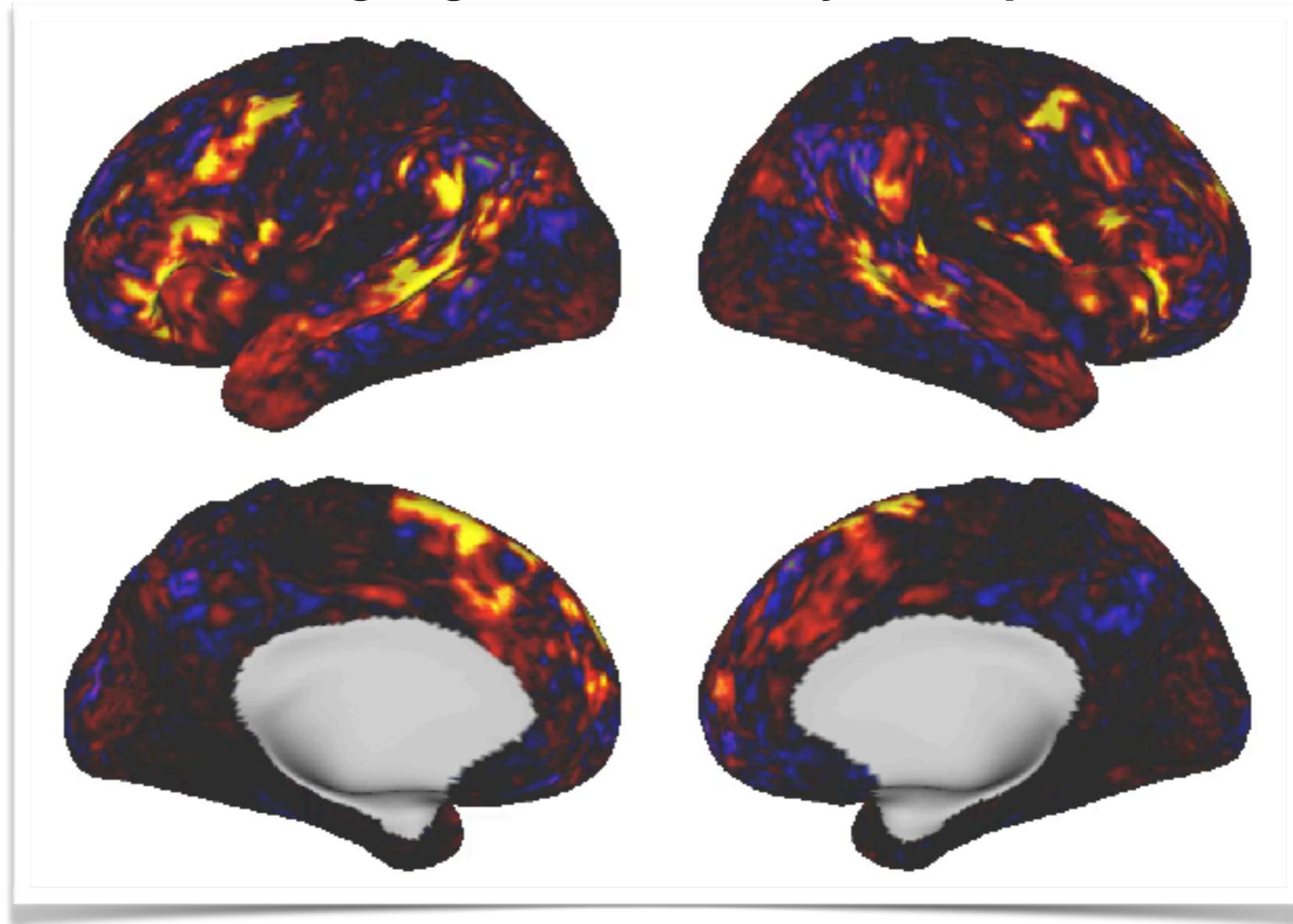
But what about individual variability?

Language network subject maps



But what about individual variability?

Language network subject maps



- Individual variability in spatial maps/parcellations can translate into apparent changes in functional connectivity

But what about individual variability?

- Two step procedure:

1. Predefine or estimate group atlas



2. Estimate how individuals vary from the group atlas

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2. Estimate how individuals vary from the group atlas

- All-in-one:

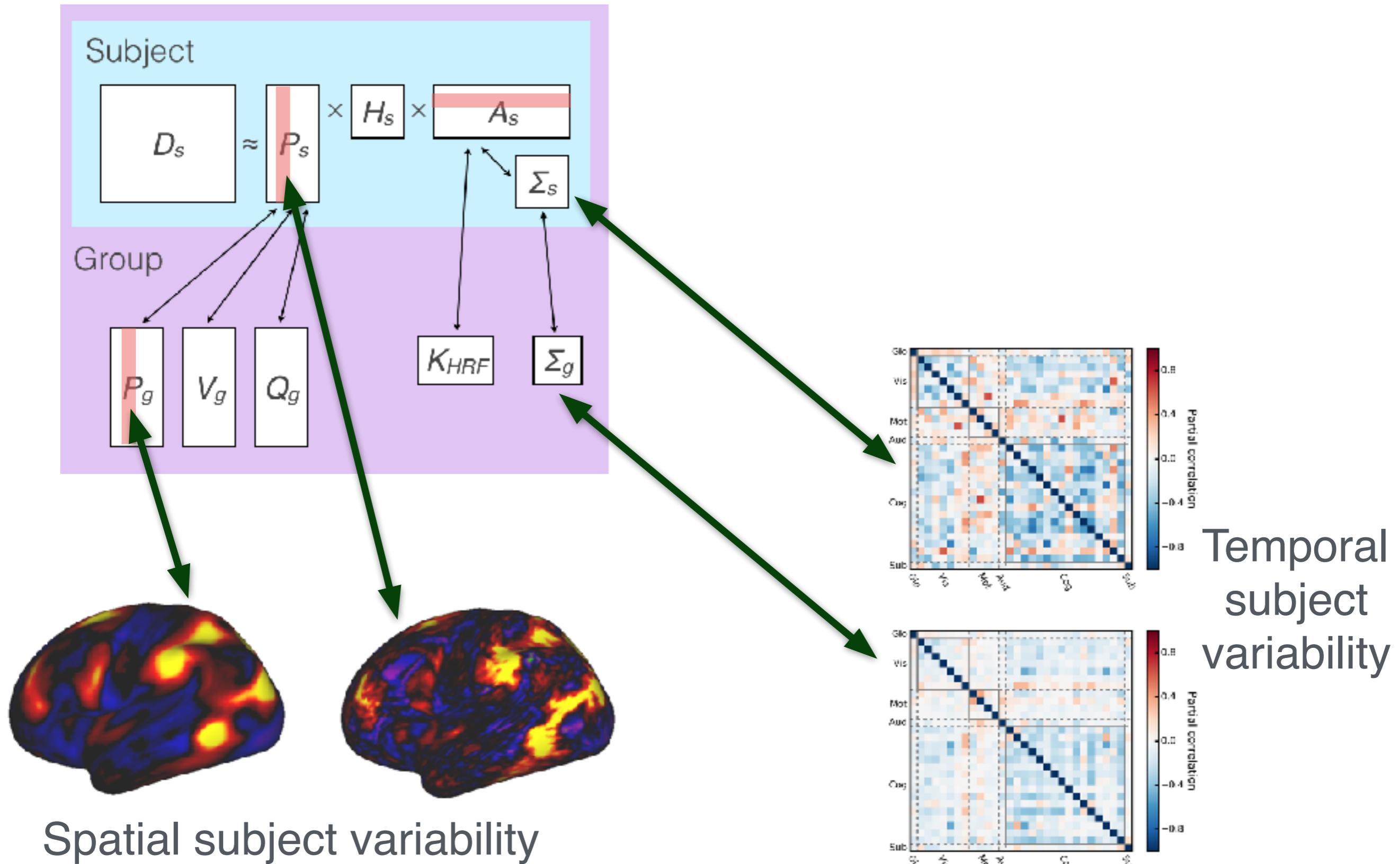
Estimate a group atlas



Estimate how individuals vary from the group atlas

ProFuMo

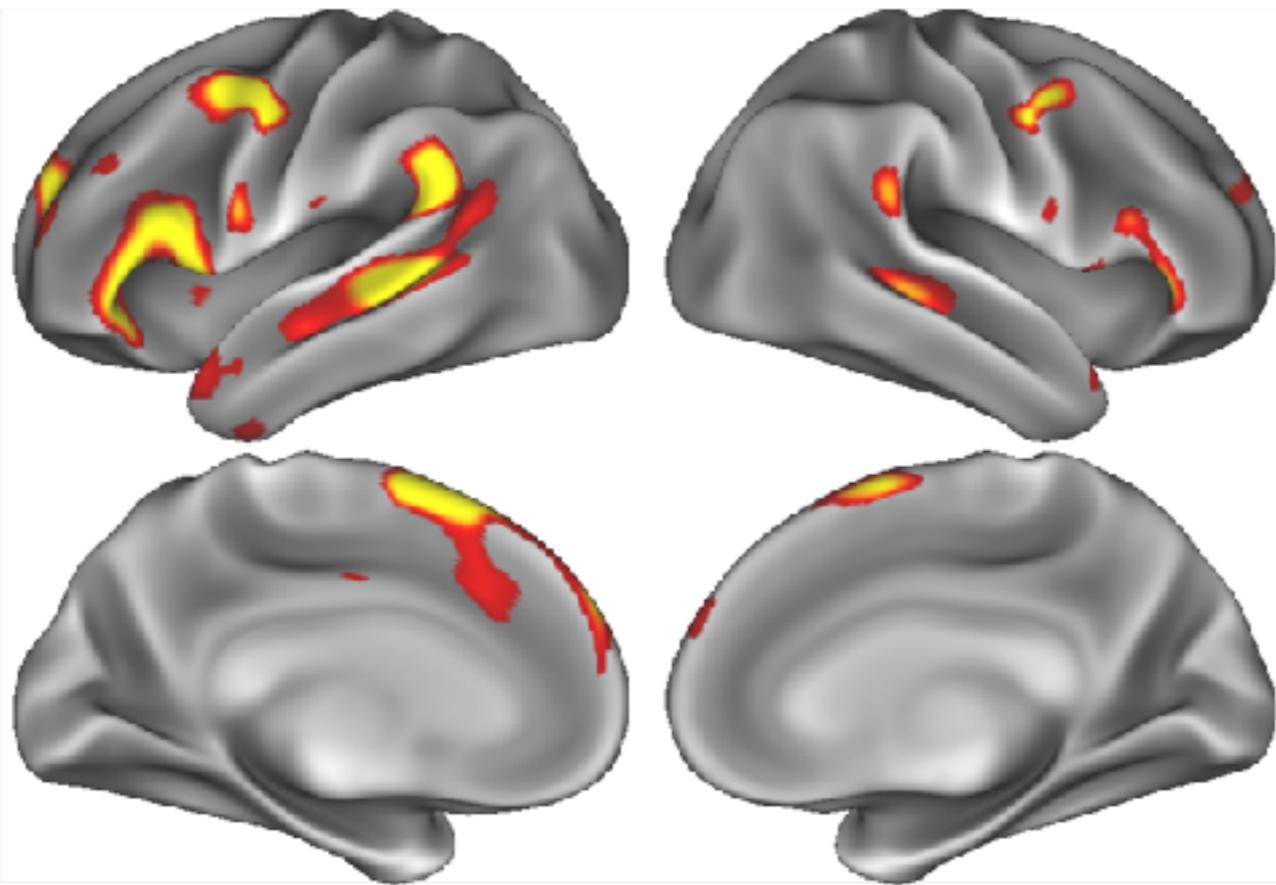
Harrison et al. Large-scale Probabilistic Functional Modes from resting state fMRI, Neuroimage 2015



ProFuMo

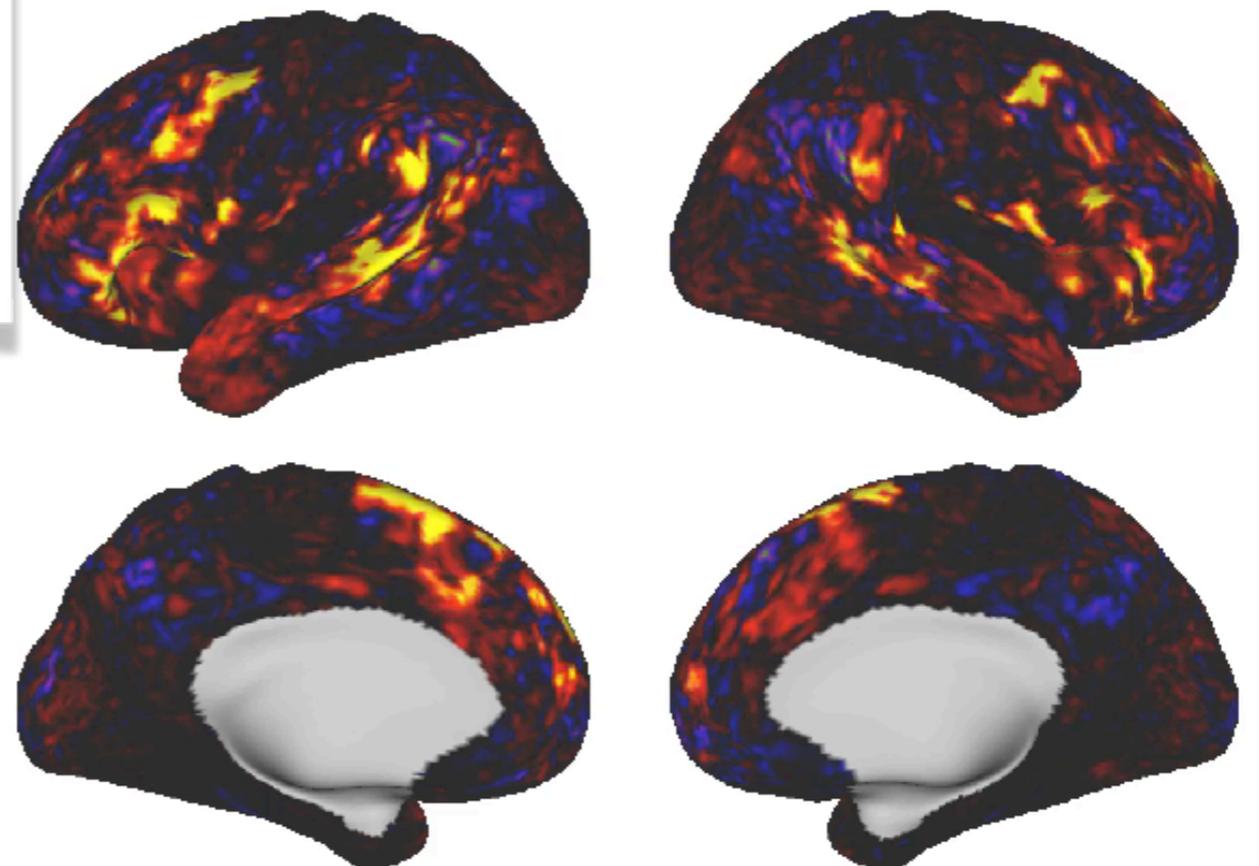
Harrison et al. Large-scale Probabilistic Functional Modes from resting state fMRI., Neuroimage 2015

Language network group map



HCP resting state fMRI data

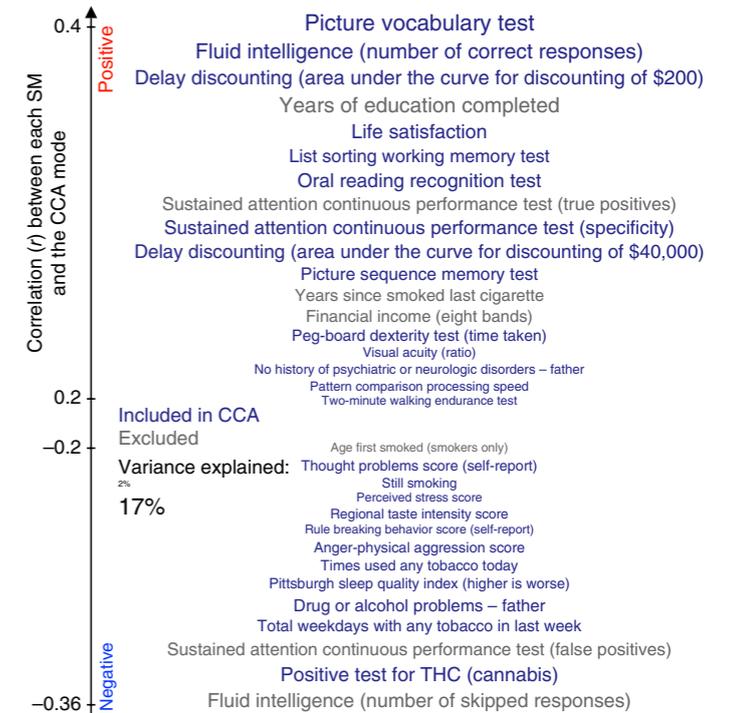
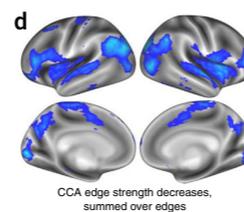
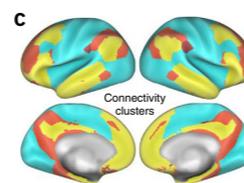
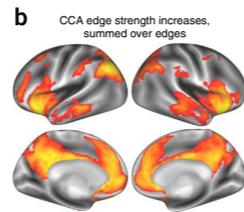
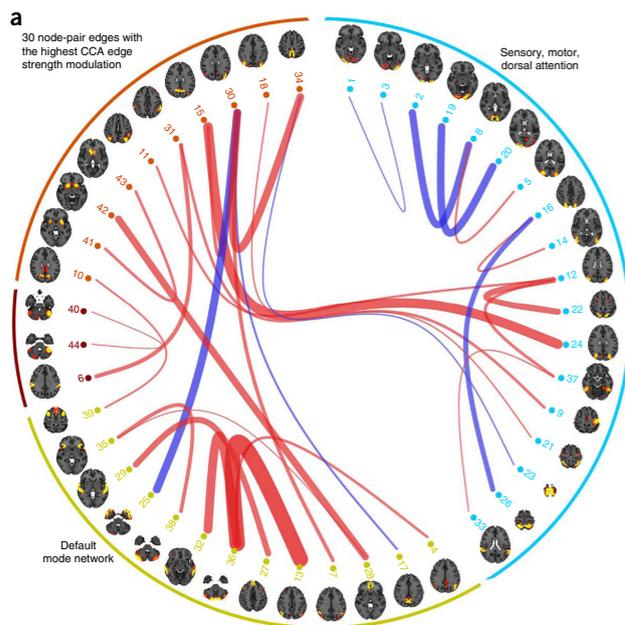
Language network subject maps



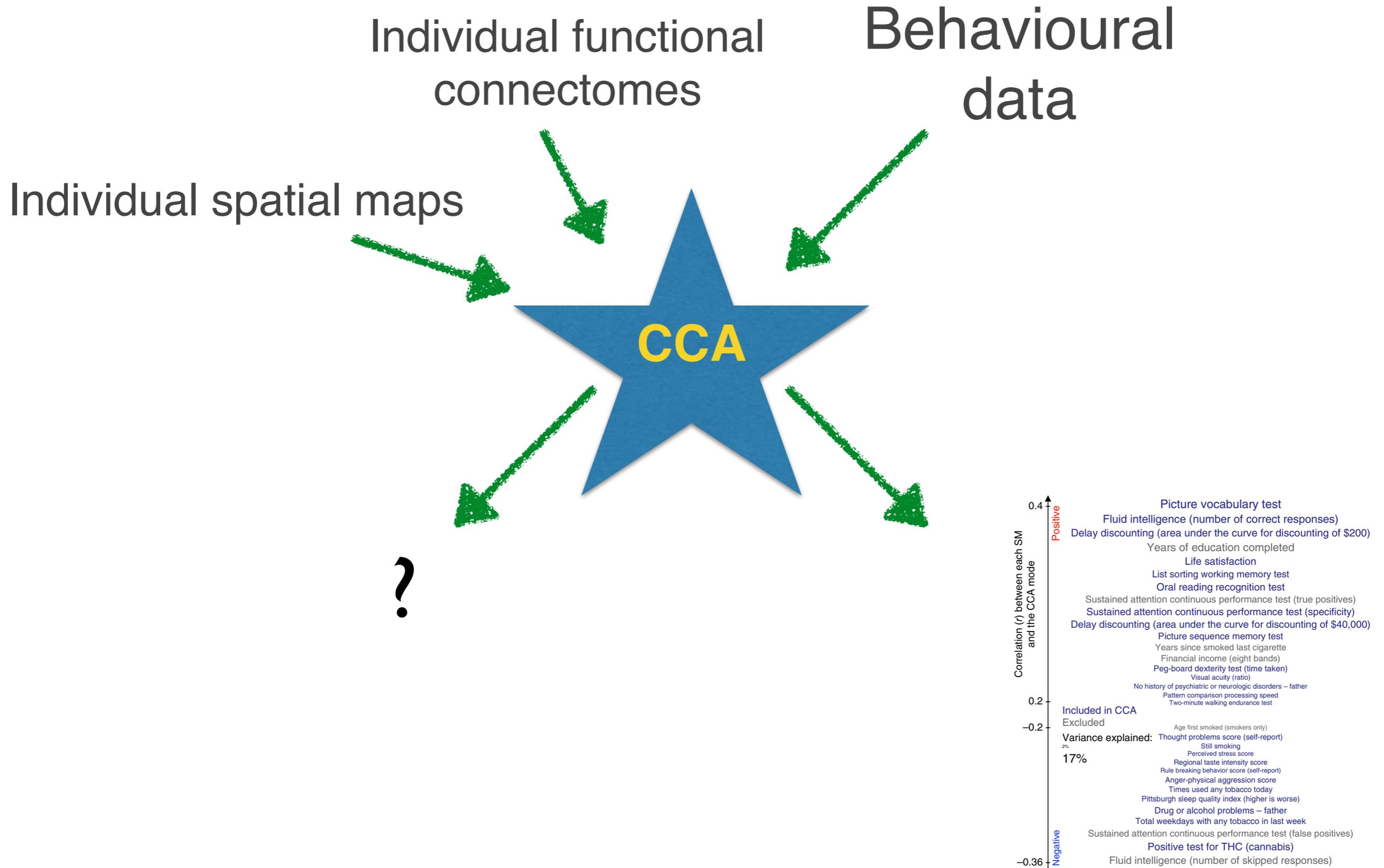
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Functional connectome

Behavioural data



Human Connectome Project resting state fMRI data (~1000 subjects)
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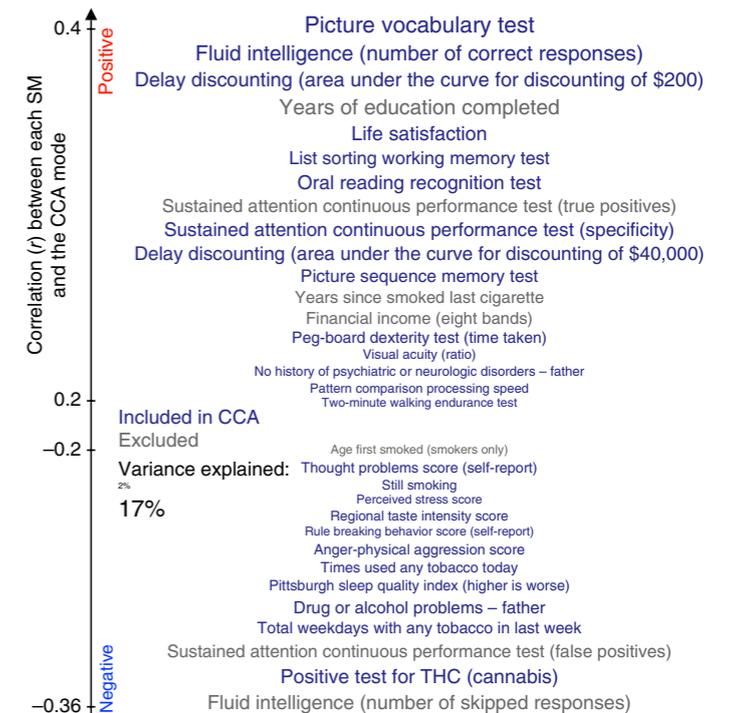
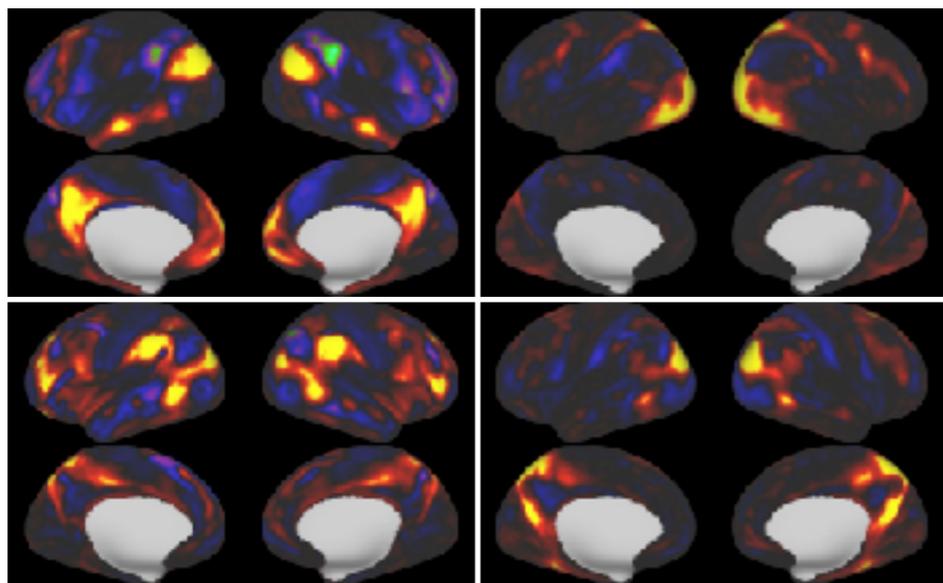
Individual variability in spatial maps dominates! *Harrison et al. Abstract #1890* *Bijsterbosch et al. Abstract #4020*

Individual functional connectomes

Behavioural data

Individual spatial maps

CCA

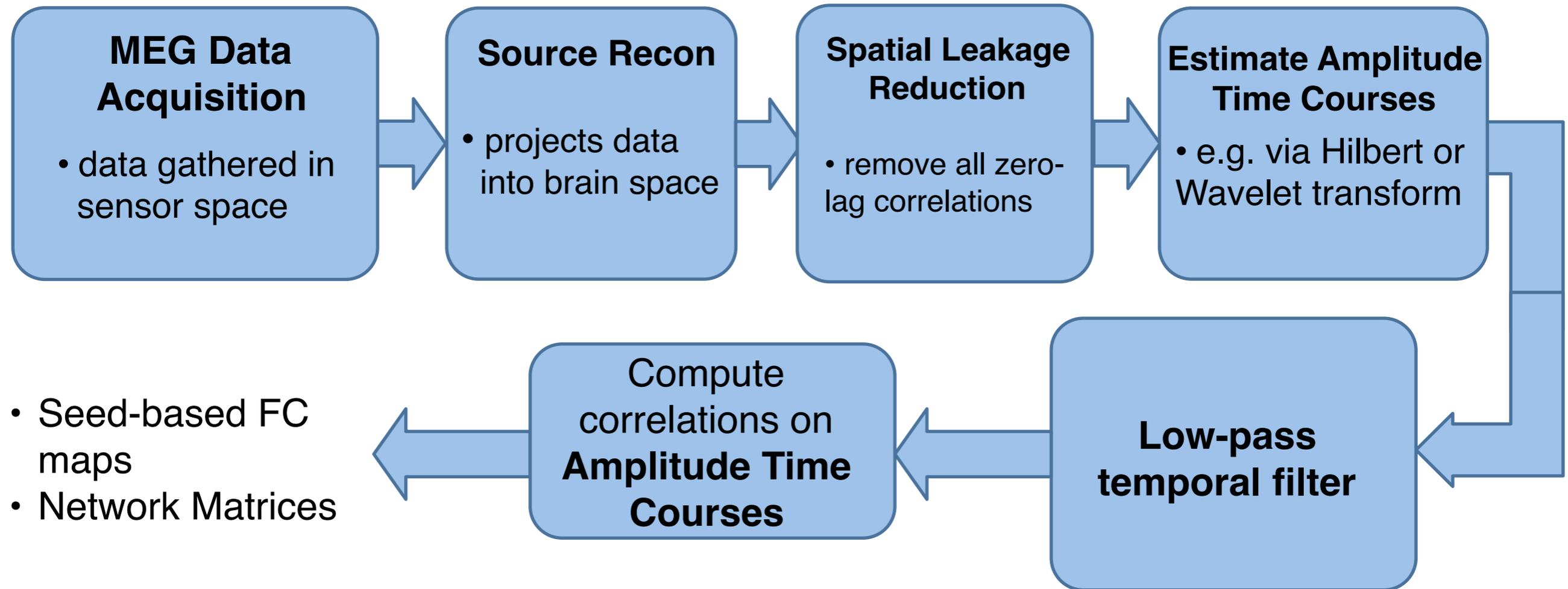


Large-scale Networks in M/EEG?

- What is happening at **faster** time-scales?
- What are the specific neuronal **interactions**?
- Can we use MEG to answer these questions?
 - excellent temporal res (milliseconds)
 - good spatial res
 - non-invasive



MEG: Amplitude Coupling

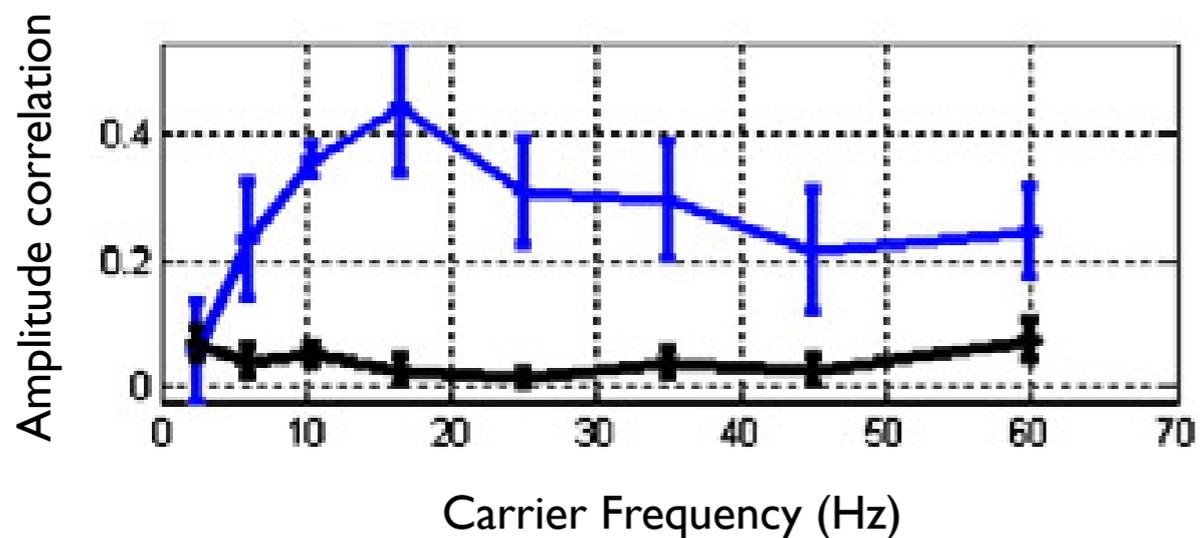


Hipp et al.; Nat Neuro (2012)

Brookes et al.; Neuroimage (2013)

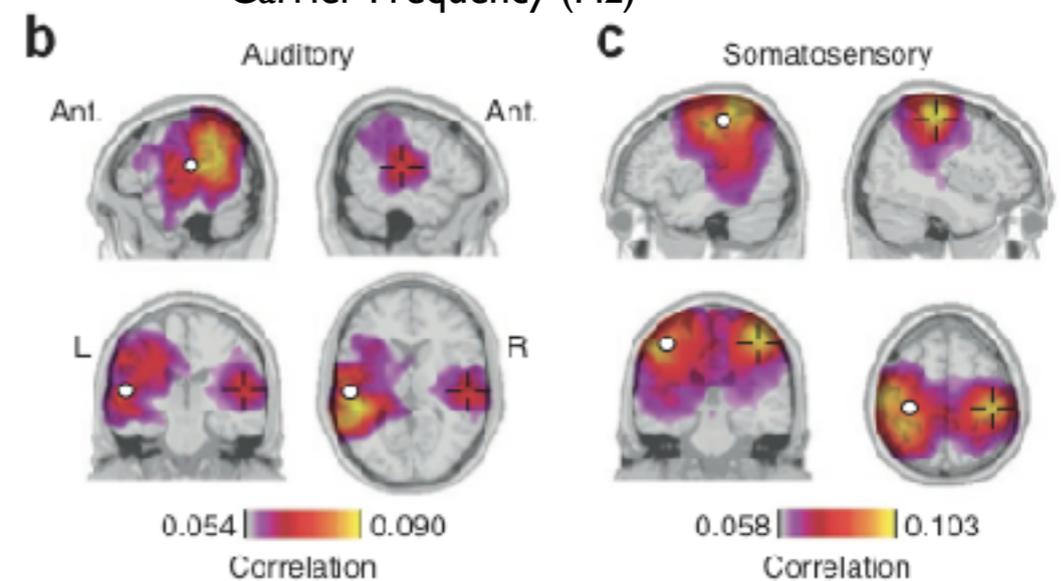
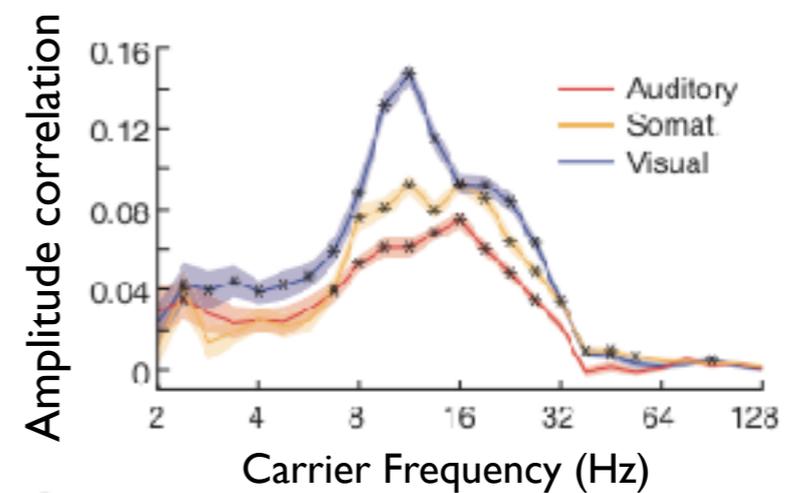
MEG: Amplitude Coupling

- Resting state data



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

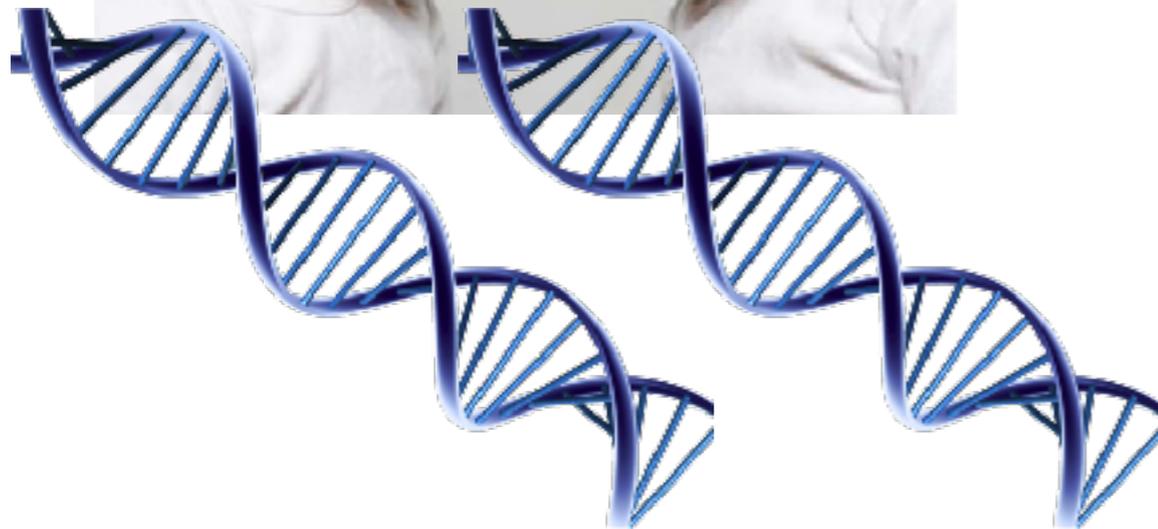
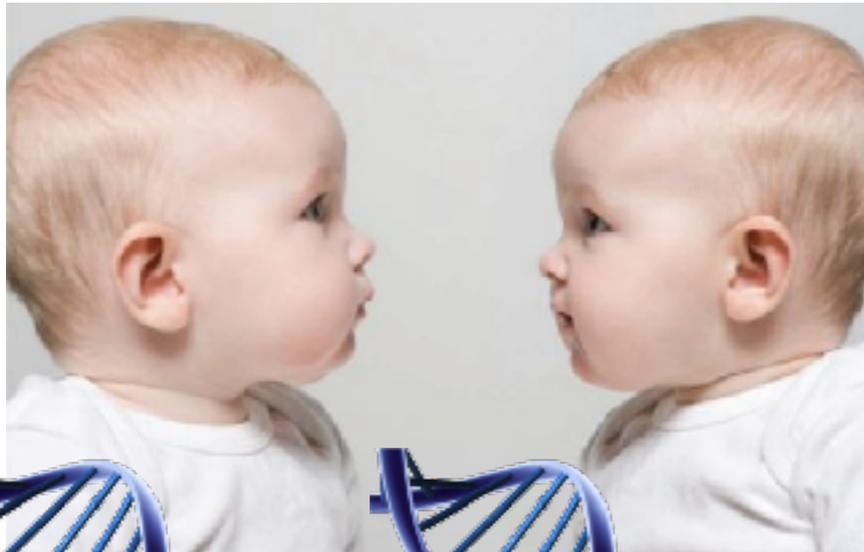
Brookes et al., Neuroimage, (2011)



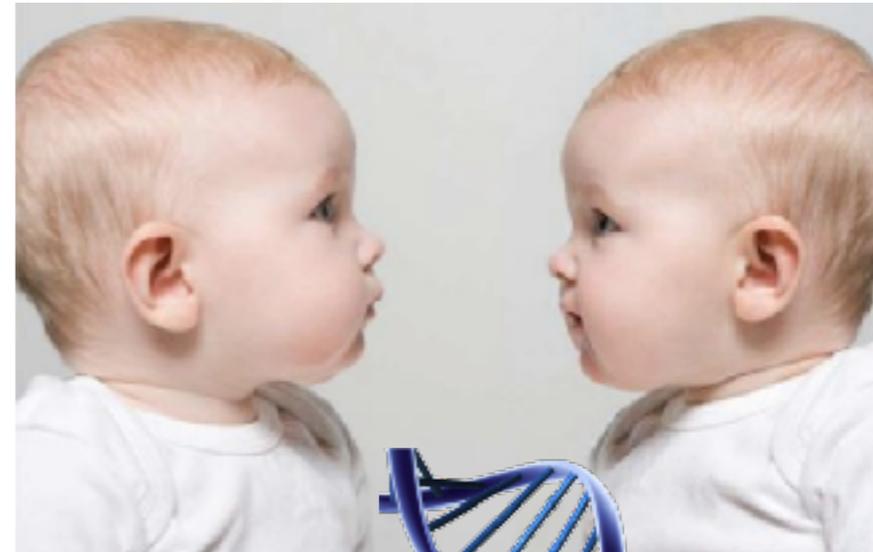
Hipp et al. 2012 (Nat Neuro)

Example Application: Heritability of connectomes

Human Connectome Project twin rest data



MZ



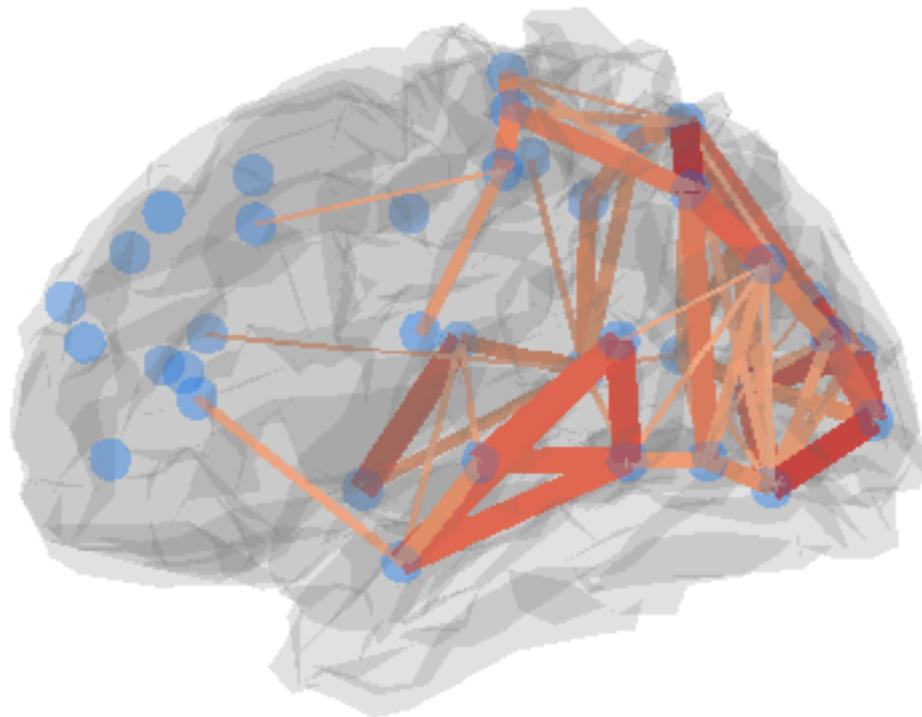
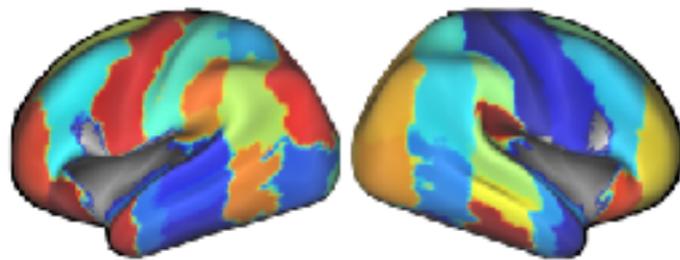
DZ

Example Application: Heritability of connectomes

Human Connectome Project twin rest data

MEG - alpha band amplitude correlations (~ 100 subjects)

38 cortical regions

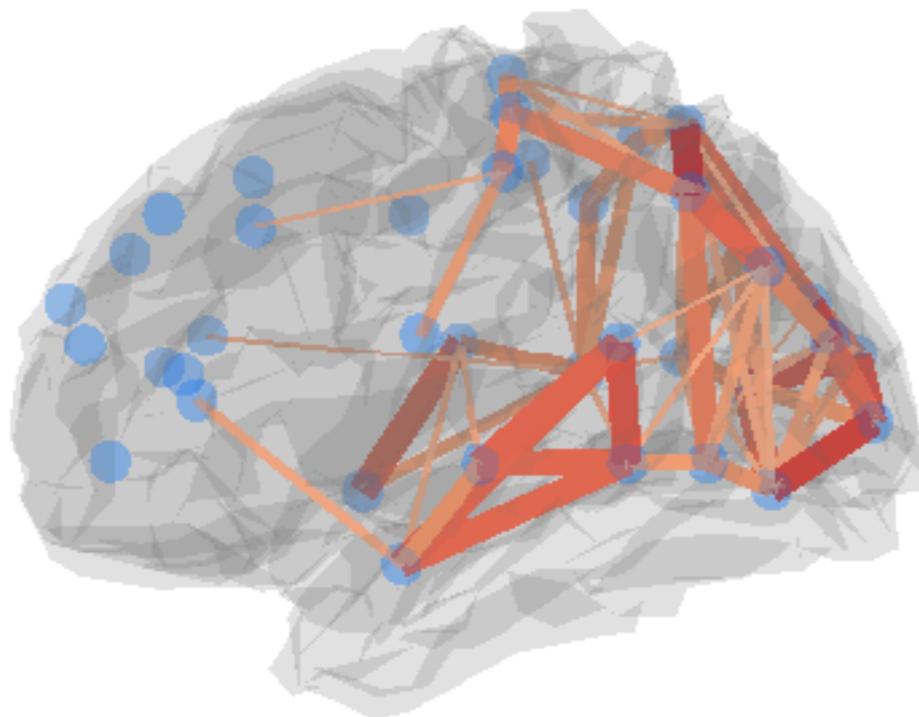
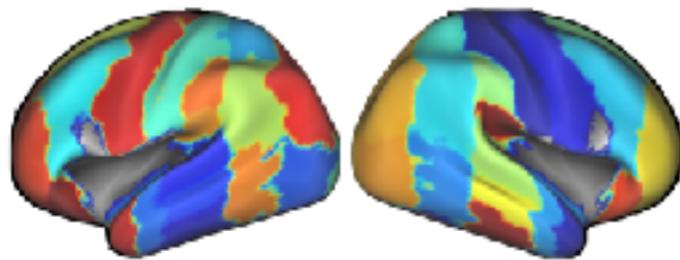


Example Application: Heritability of connectomes

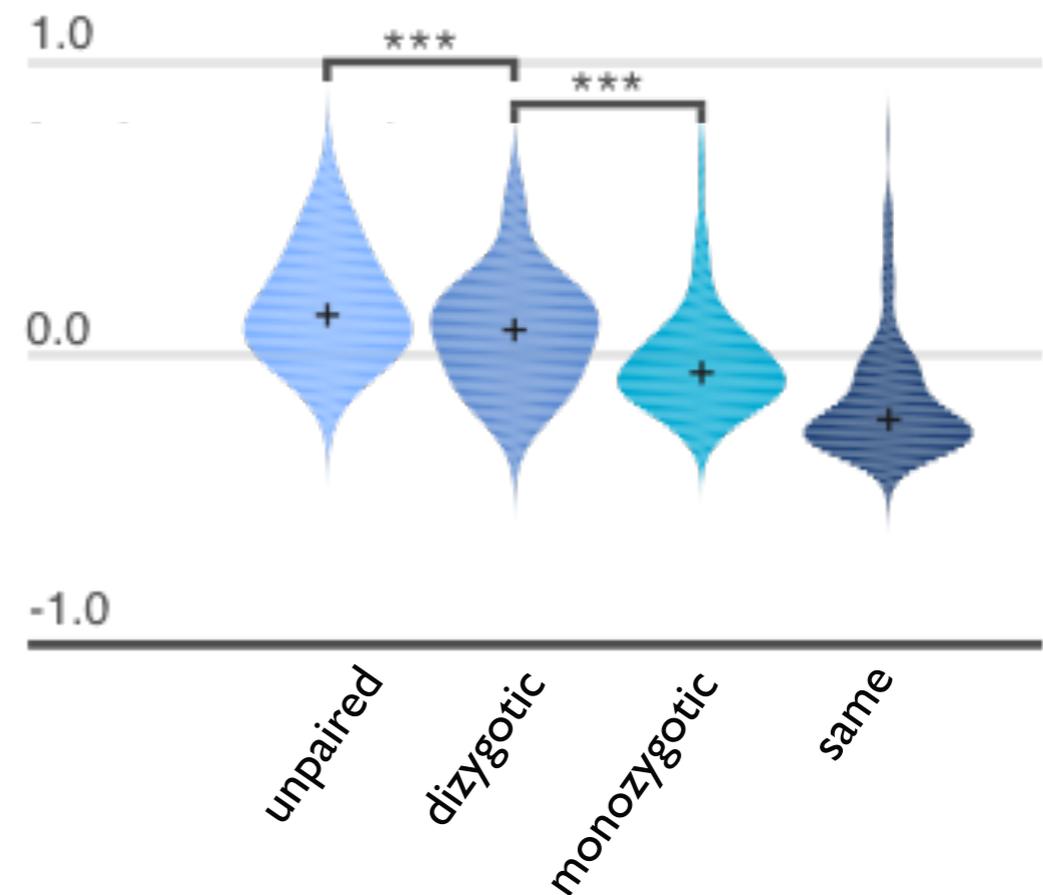
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MEG - alpha band amplitude correlations (~100 subjects)

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log(difference in network matrices)



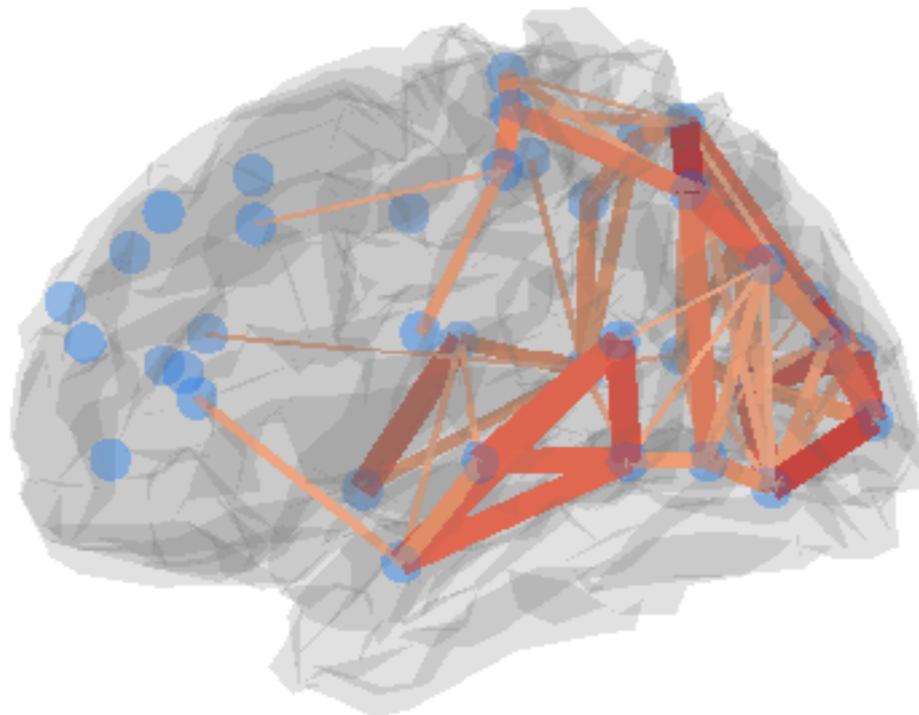
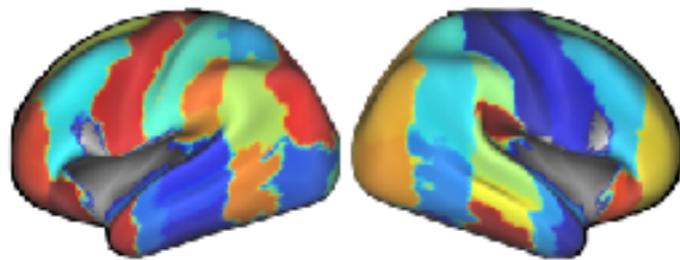
- Mean edge heritability: 33% ($p = 0.01$)

Example Application: Heritability of connectomes

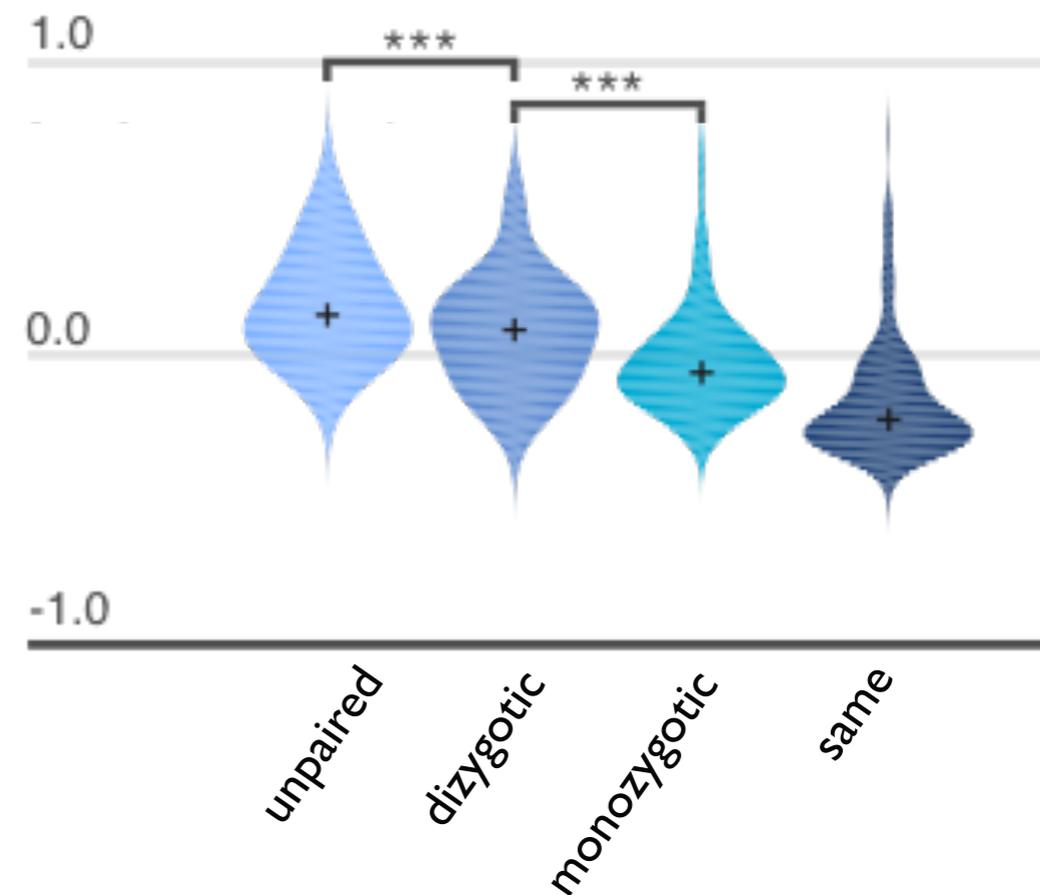
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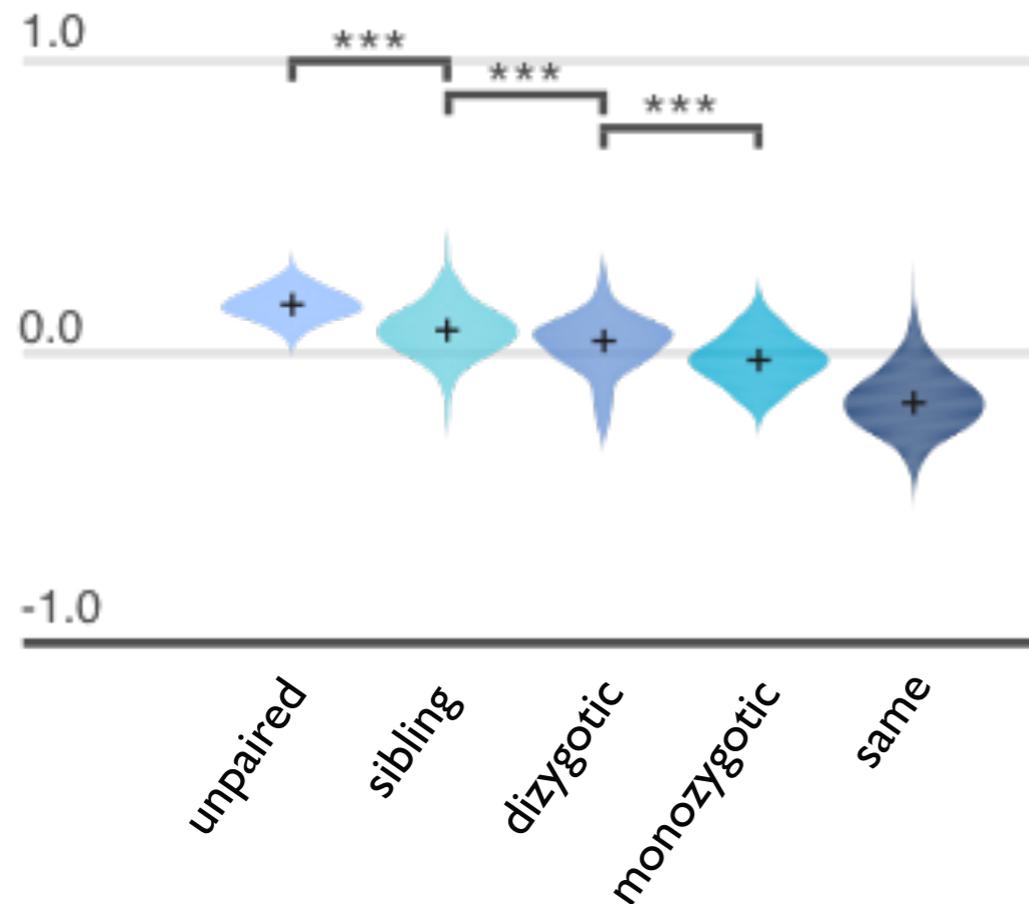
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- Shared genetics outweigh shared environment ($p = 0.02$)

Example Application: Heritability of connectomes

Human Connectome Project twin rest data

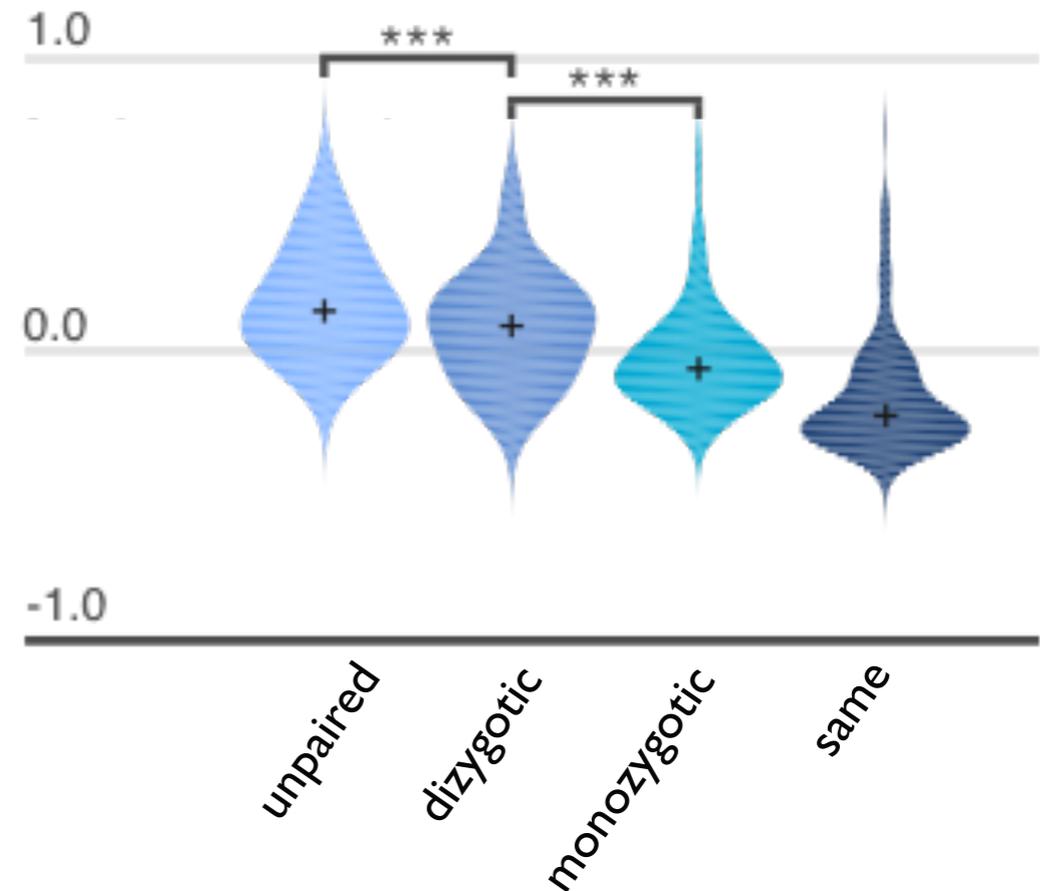
fMRI (~1000 subjects)

log(difference in network matrices)



MEG - alpha band (~100 subjects)

log(difference in network matrices)

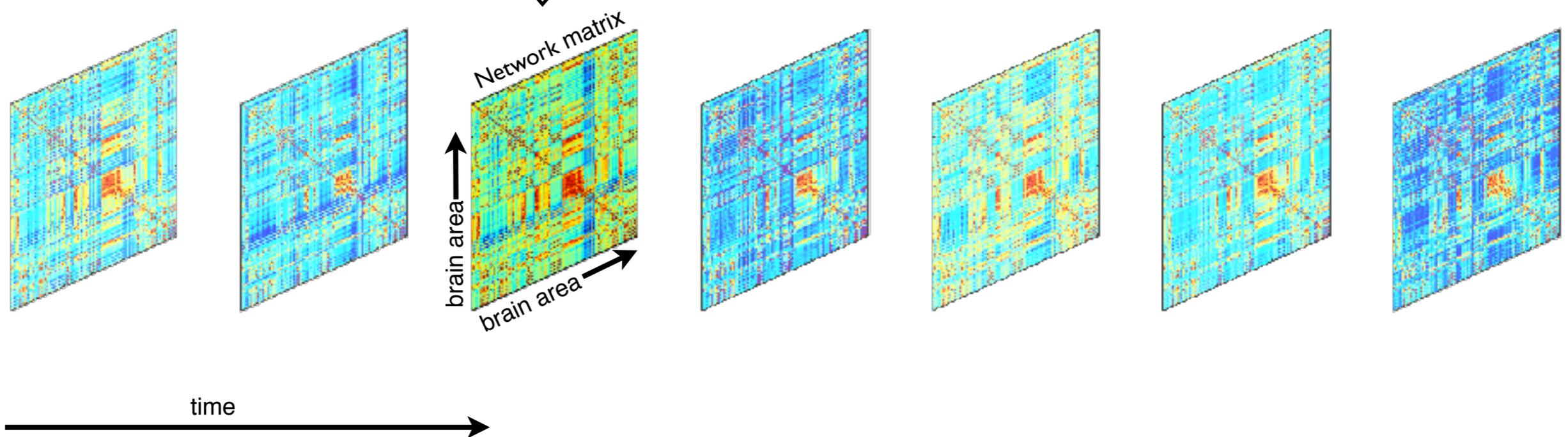
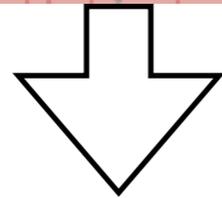
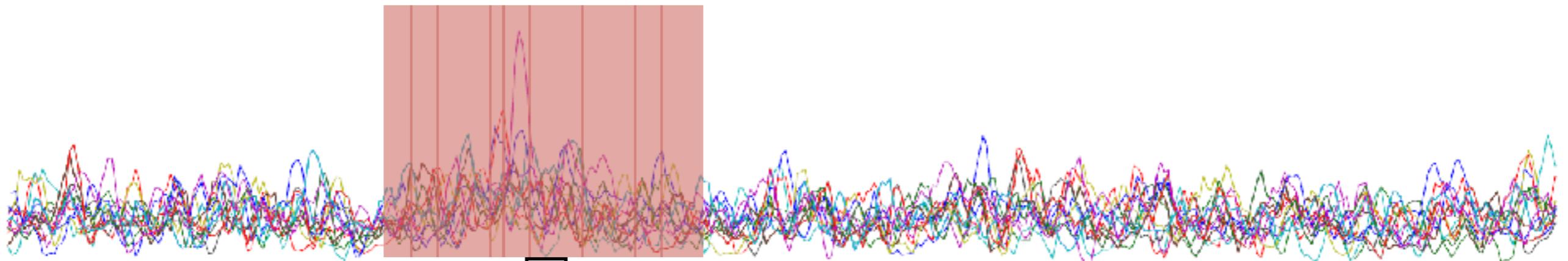


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Dynamic Connectomes

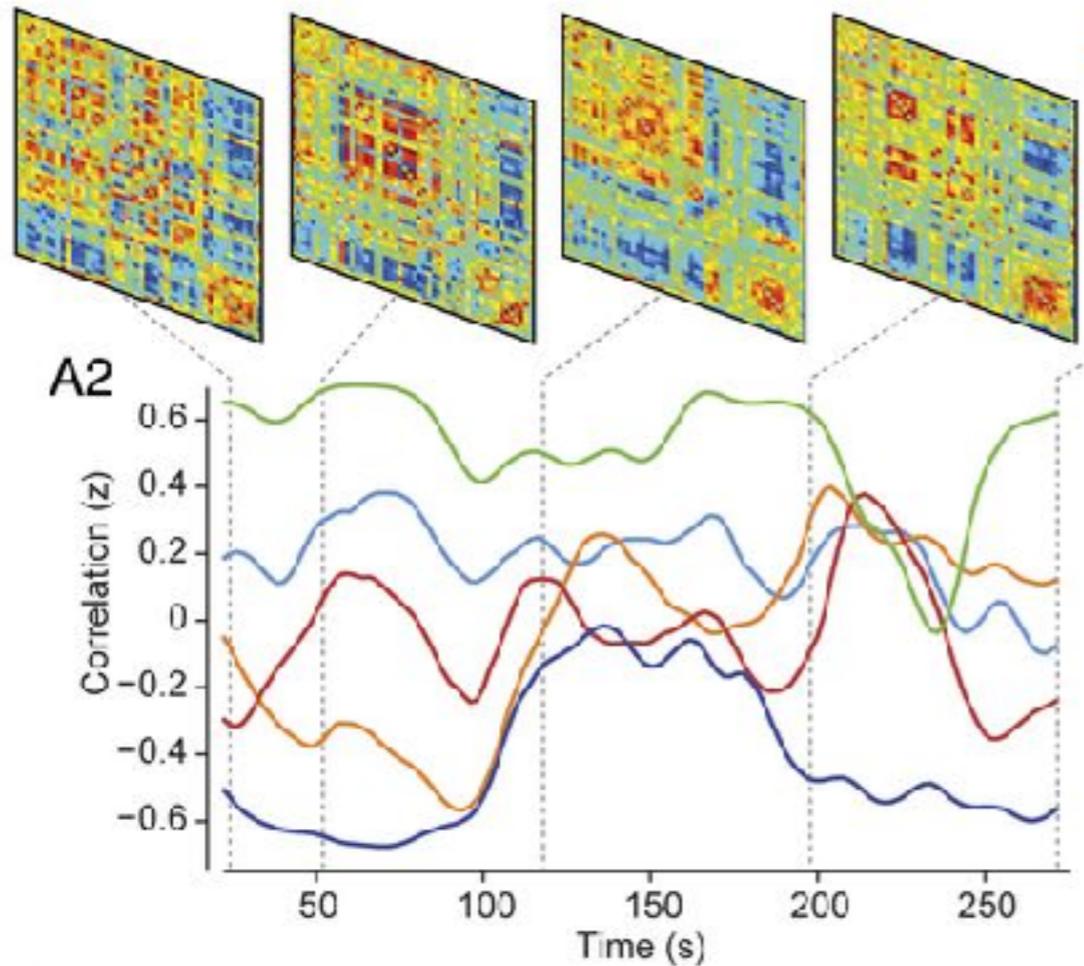
Compute *sliding window* correlation network matrices

Sliding window (~10secs)

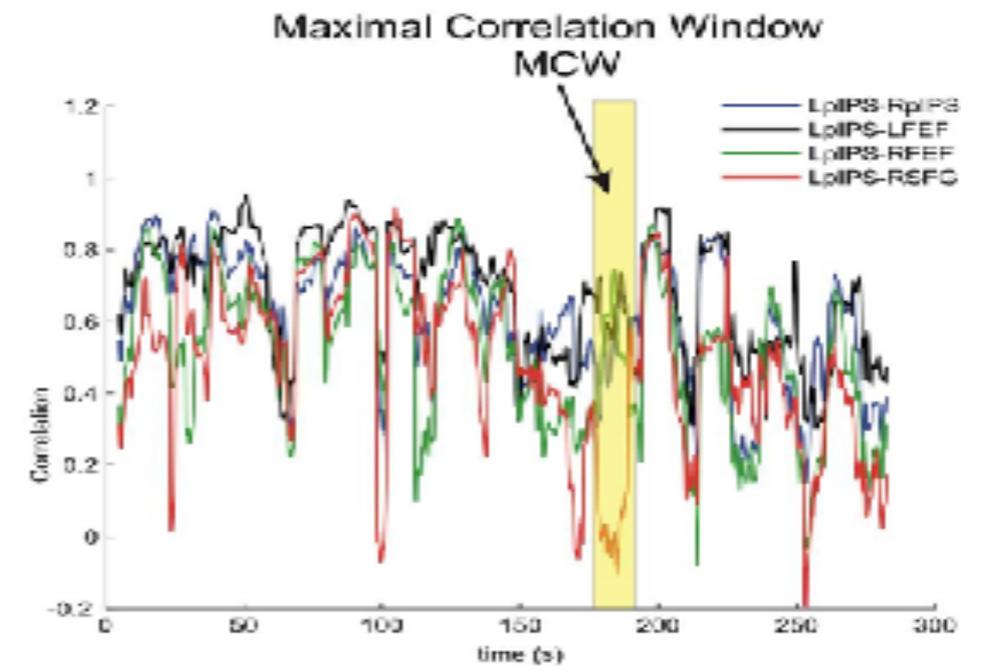


Non-stationary functional connectivity

Sliding window FC in fMRI:



Sliding window FC in MEG:



de Pasquale et al. (PNAS 2010)

Allen et al. (Cerebral Cortex 2012)

Issues with sliding windows

How to choose the width of the window?

- too short - unreliable estimation
- too long - misses quick changes

NeuroImage 147 (2016) 212–216

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/yrimp



Can sliding-window correlations reveal dynamic functional connectivity in resting-state fMRI?

R. Hindriks^{a,*}, M.H. Adhikari^a, Y. Murayama^d, M. Ganzetti^{b,c}, D. Mantini^{b,c}, N.K. Logothetis^d, G. Deco^{a,c}

^a Center for Brain and Cognitive Computational Neurosciences Group, Department of Information and Communication Technologies (Instituto Tecnológico de Informática), Basque Country, Spain

^b Department of Medical Sciences and Technology, IIR, Zurich, Switzerland

^c Department of Experimental Psychology, University of Oxford, Oxford, England

^d Department of Psychology and Cognitive Processes, Max Planck Institute for Biological Cybernetics, Tübingen, Germany

* Corresponding author. E-mail: rahindri@tecnico.ulisboa.pt (R.H.).



ORIGINAL ARTICLE

On the Stability of BOLD fMRI Correlations

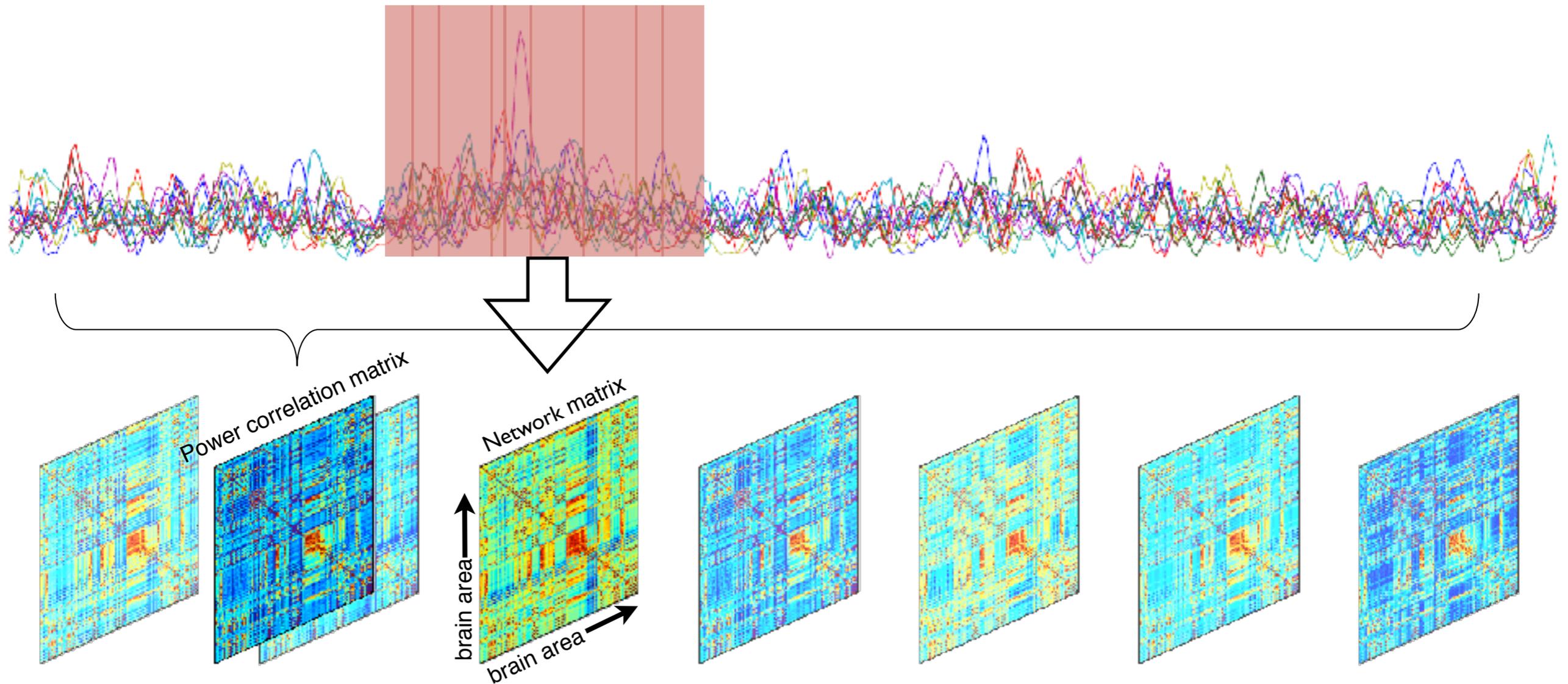
Timothy O. Laumann¹, Abraham Z. Snyder^{1,2}, Anish Mitra², Evan M. Gordon^{3,4}, Caterina Gratton¹, Babatunde Adeyemo¹, Adrian W. Gilmore⁵, Steven M. Nelson^{3,4}, Jeff J. Berg⁵, Deanna J. Greene^{2,6}, John E. McCarthy⁷, Enzo Tagliazucchi^{8,9}, Helmut Laufs^{9,10}, Bradley L. Schlaggar^{1,2,6,11,12}, Nico U. F. Dosenbach¹, and Steven E. Petersen^{1,2,5,12}

Cerebral CORTEX

Dynamic Connectomes

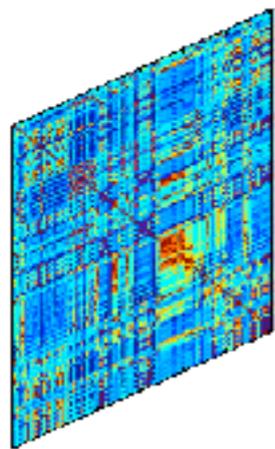
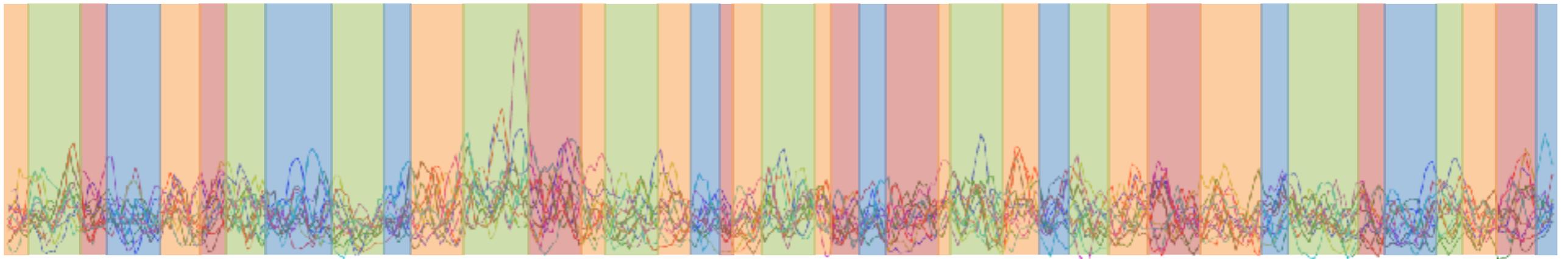
Time-varying FC as short-lived brain states:

Sliding window (~2-10secs in MEG, ~30-60secs in fMRI)

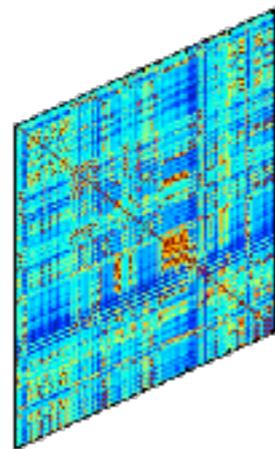


Dynamic Connectomes

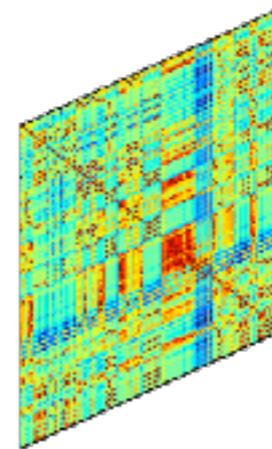
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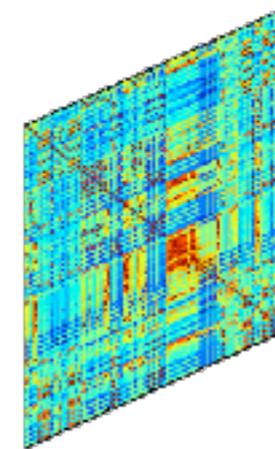
State 1



State 2



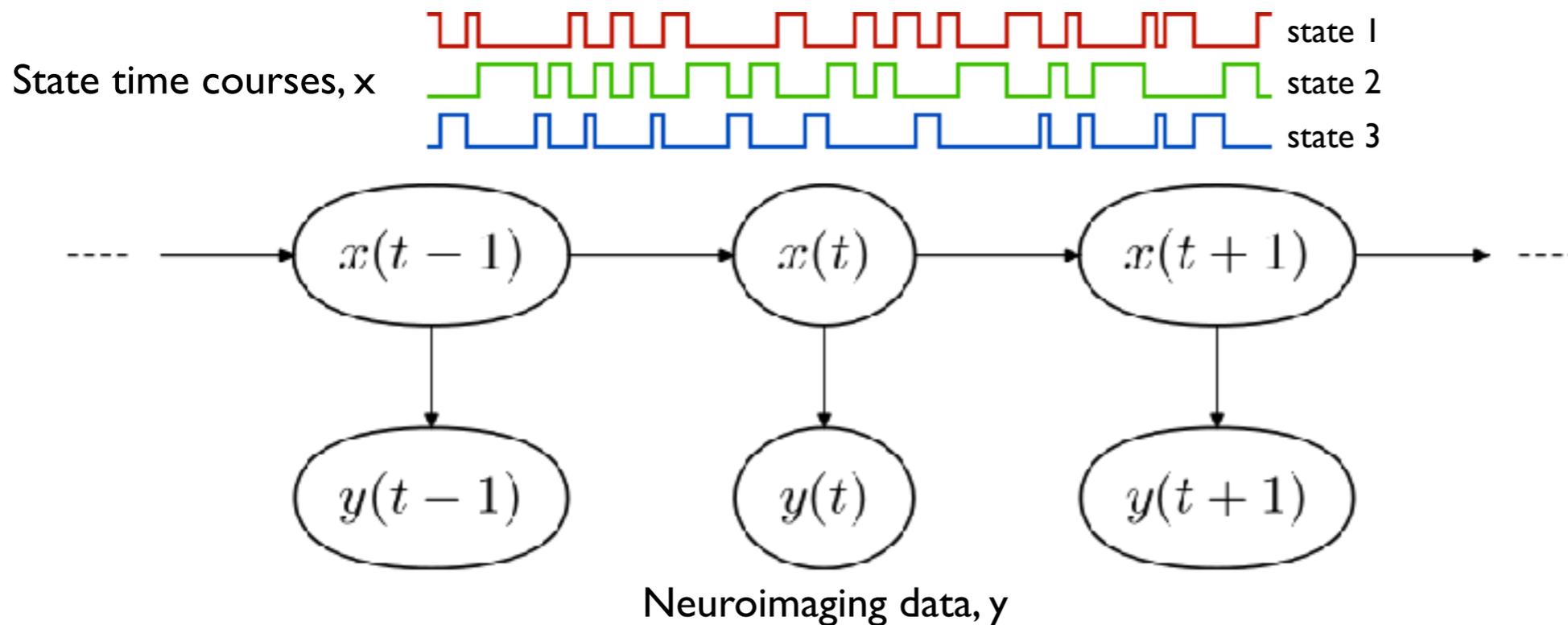
State 3



State 4

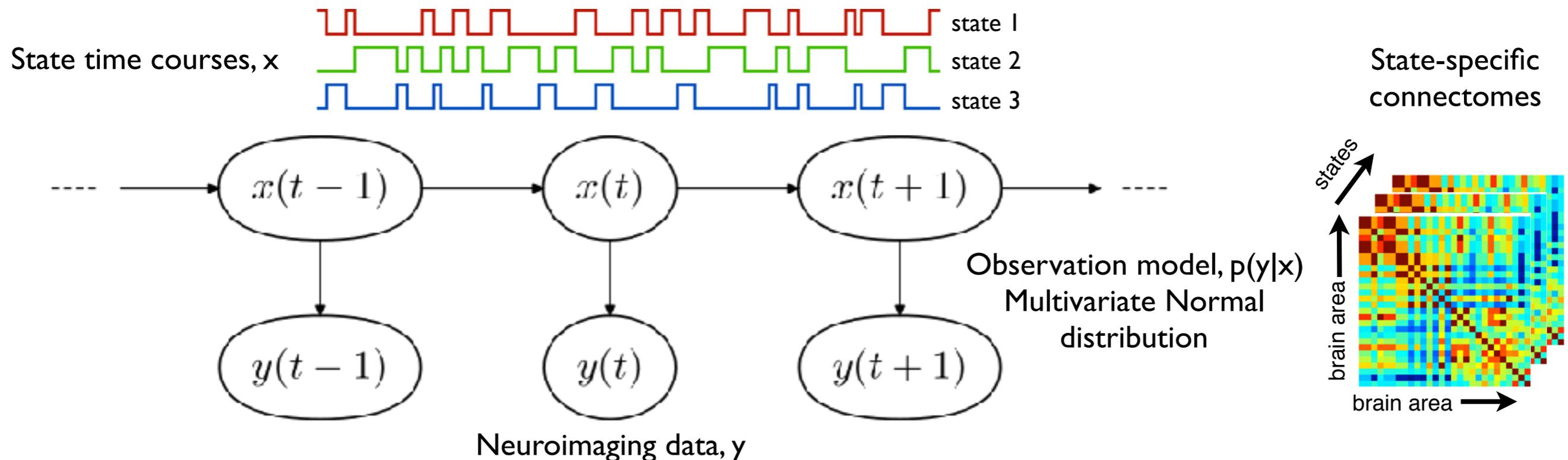
Hidden Markov Model (HMM)

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



Hidden Markov Model (HMM)

- Generative model, consisting of:
 - state time courses, x - indicating which state the system is in at each time point
 - observation model - which predicts the data, y , for a given state



Hidden Markov Model

<https://github.com/OHBA-analysis/HMM-MAR>



EEG



fMRI



MEG



Intracranial recordings



Hidden Markov Model

<https://github.com/OHBA-analysis/HMM-MAR>



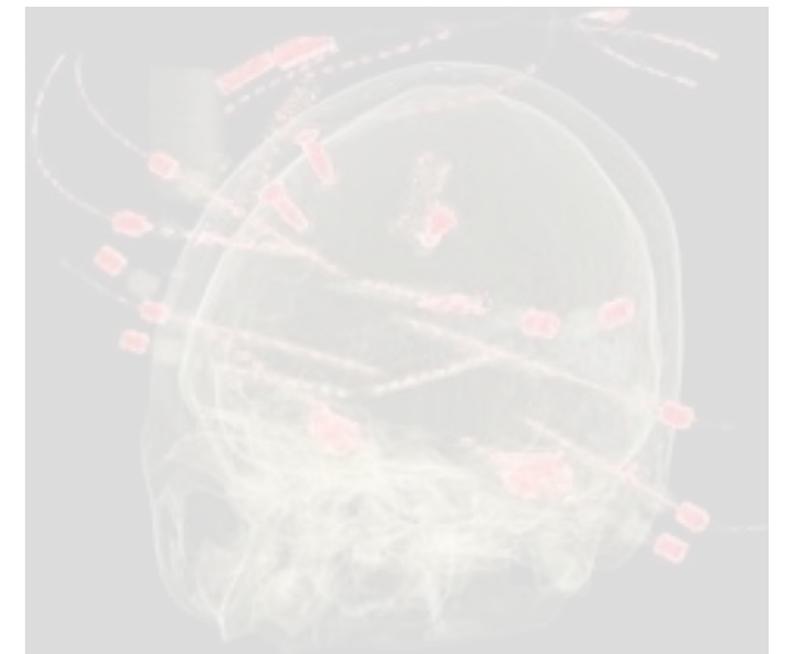
EEG



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HMM on resting fMRI data

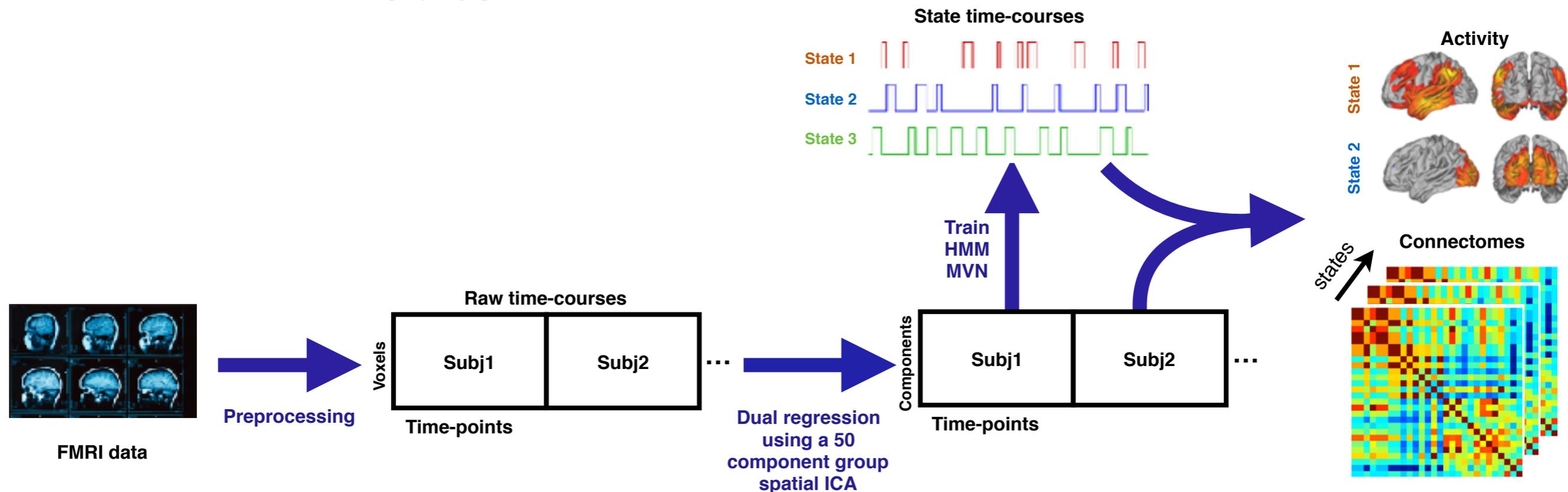
- Can we use the HMM to infer *dynamic networks in resting fMRI* data?
- What is the nature of the dynamics?

HMM on resting fMRI data

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 - Resting state (eyes open) ***Human Connectome Project*** fMRI data
 - ~1000 subjects (1hr each) - HMM on BIG data (stochastic learning)
Vidaurre et al., Under Revision, Neuroimage SI “Dynamic Brain Networks”
 - 12 HMM states

HMM on resting fMRI data

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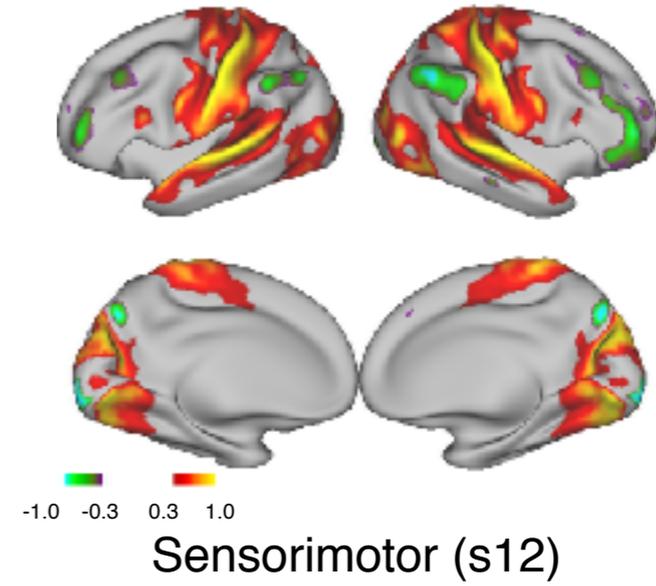
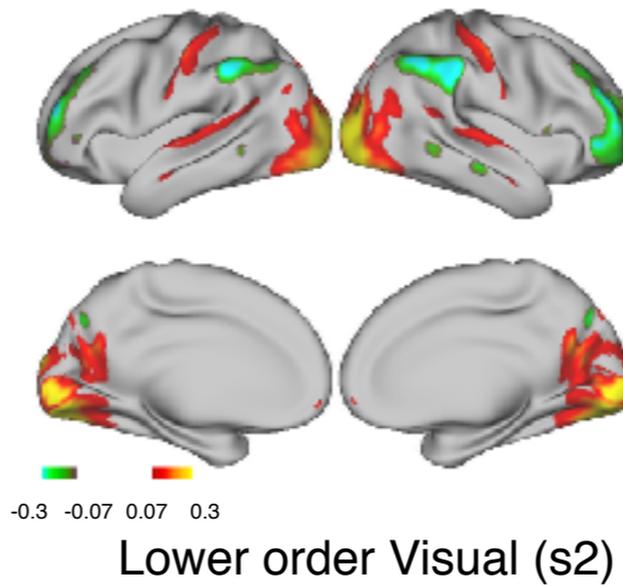
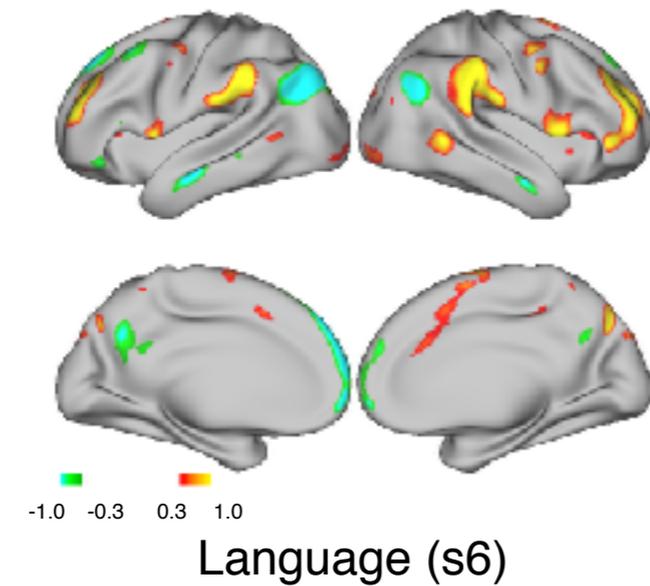
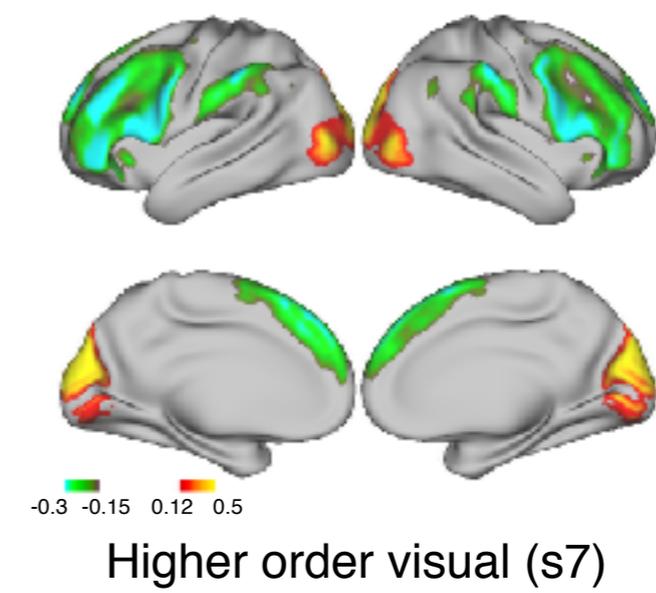
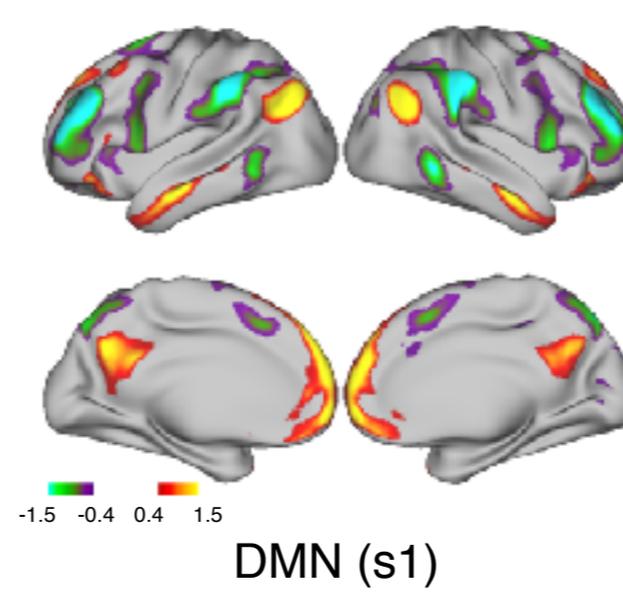
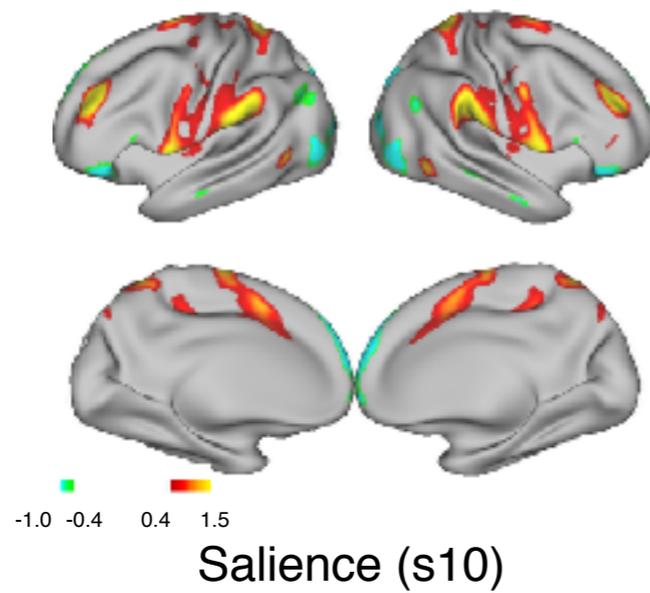


Vidaurre et al., Poster #3955: talk on Wed 10:43am
Vidaurre et al., Under Revision

FMRI HMM state spatial maps

Vidaurre et al., Poster #3955: talk on Wed 10:43am

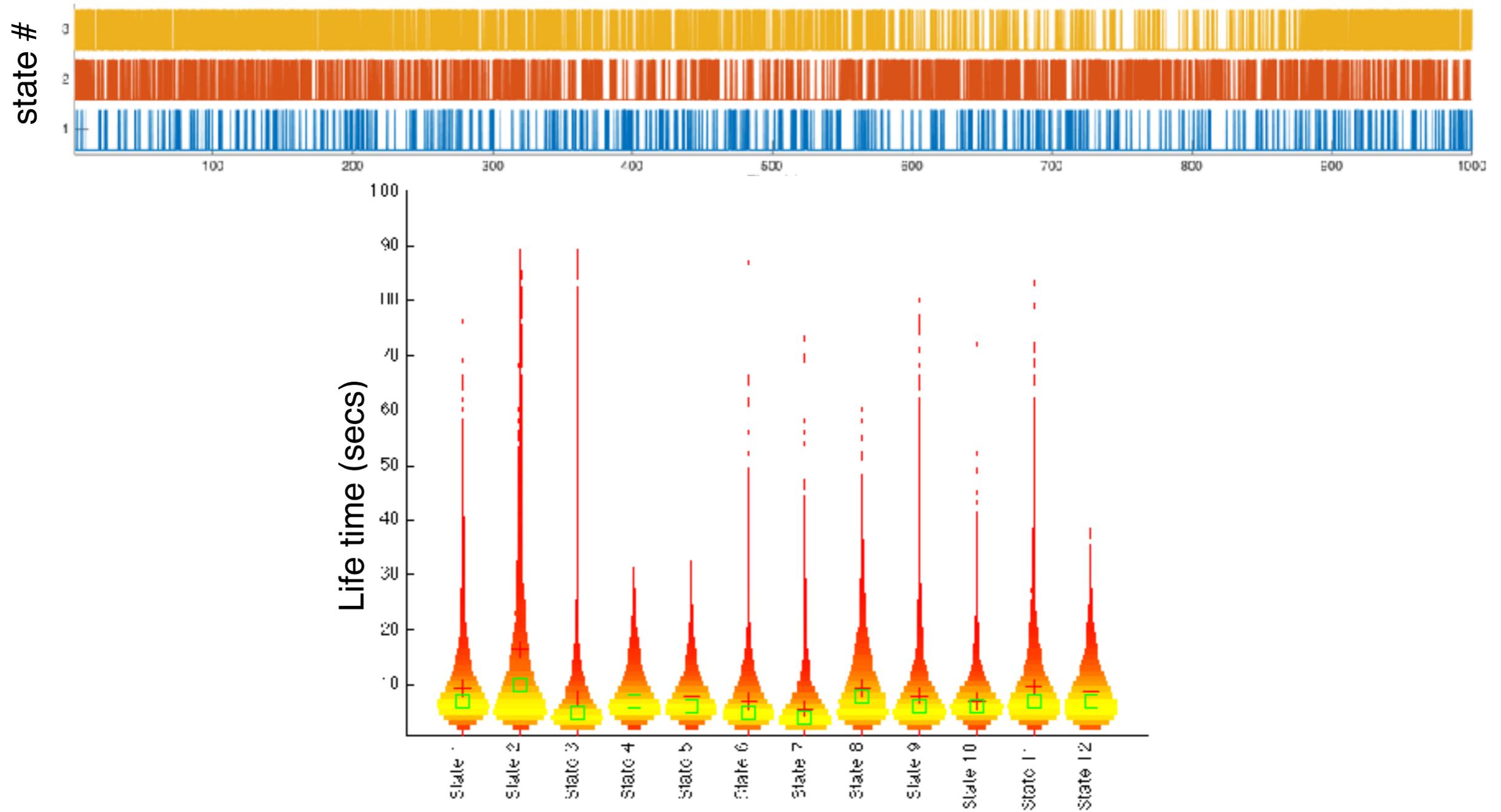
Vidaurre et al., Under Revision



FMRI HMM state dynamics

Vidaurre et al., Poster #3955: talk on Wed 10:43am

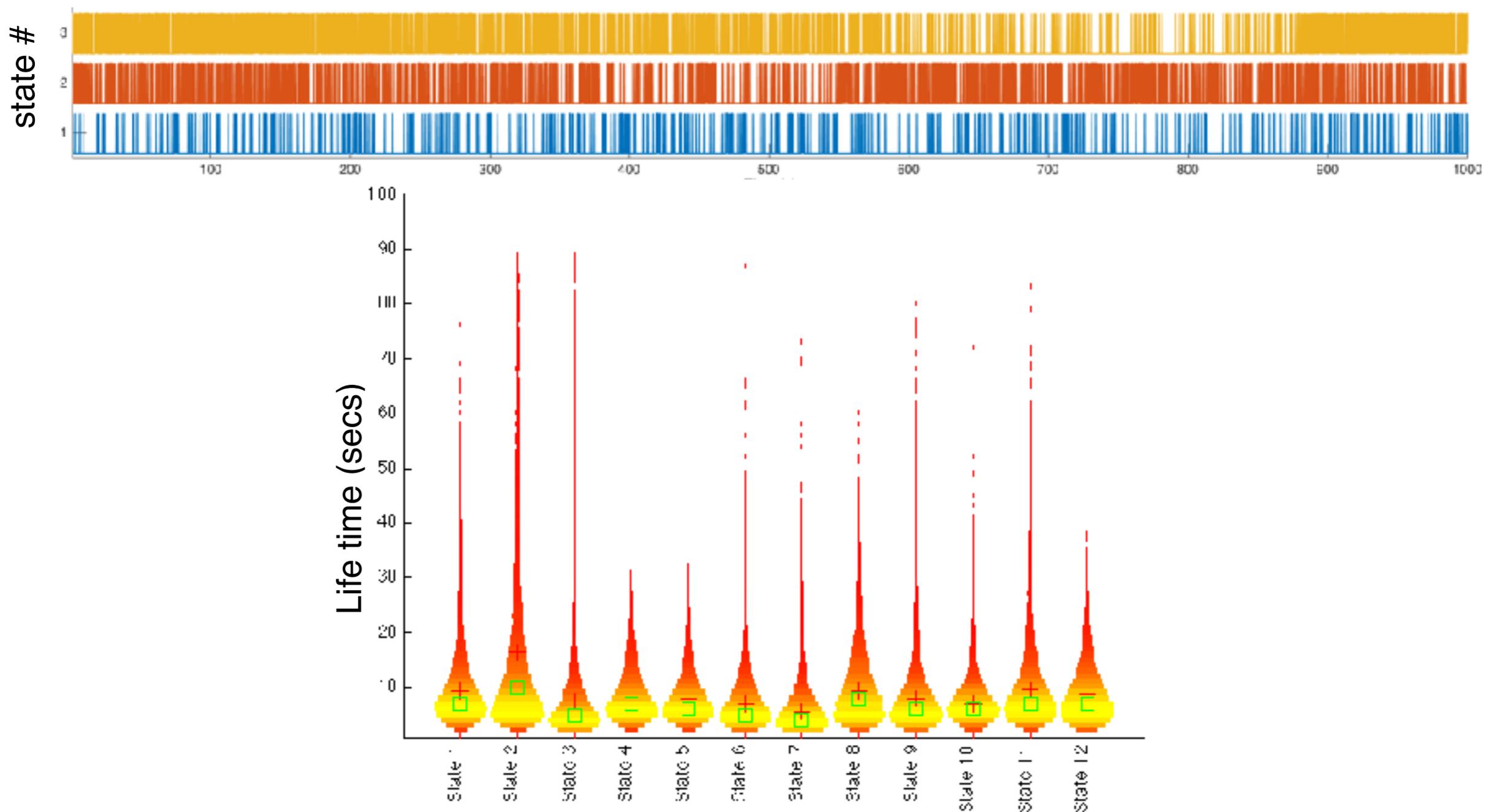
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FMRI HMM state dynamics

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Vidaurre et al., Under Revision



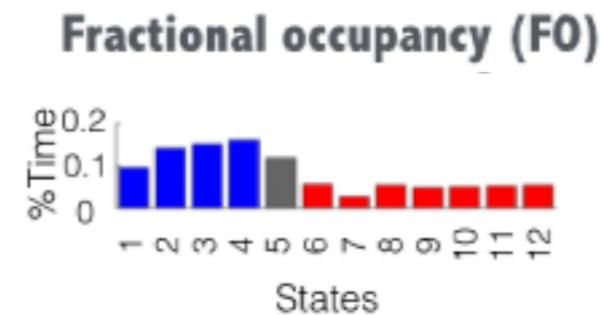
Is there hierarchical temporal structure in the state time courses?

Is there hierarchical temporal structure?

- in the rate of occurrence brain states?

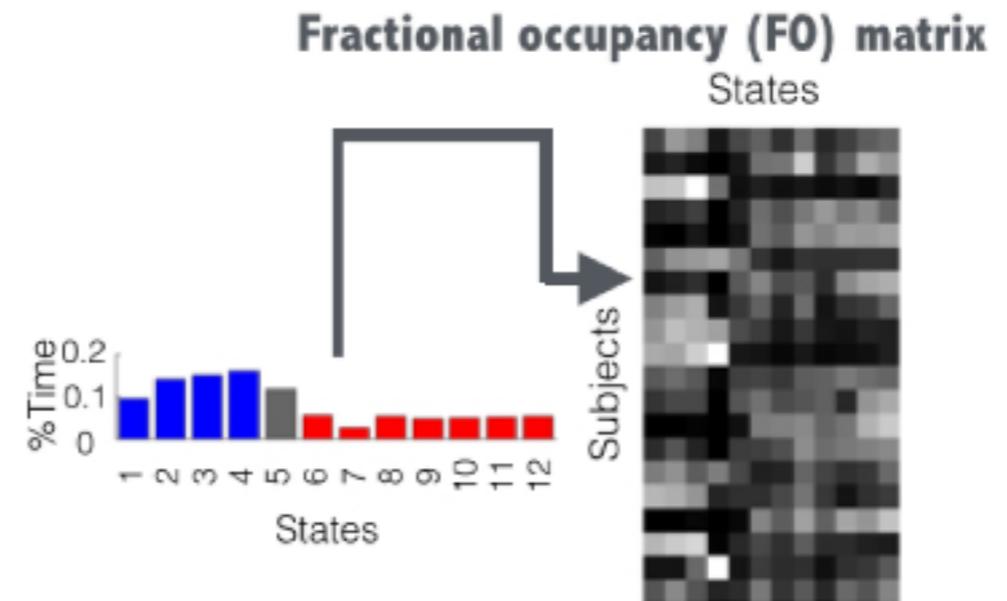
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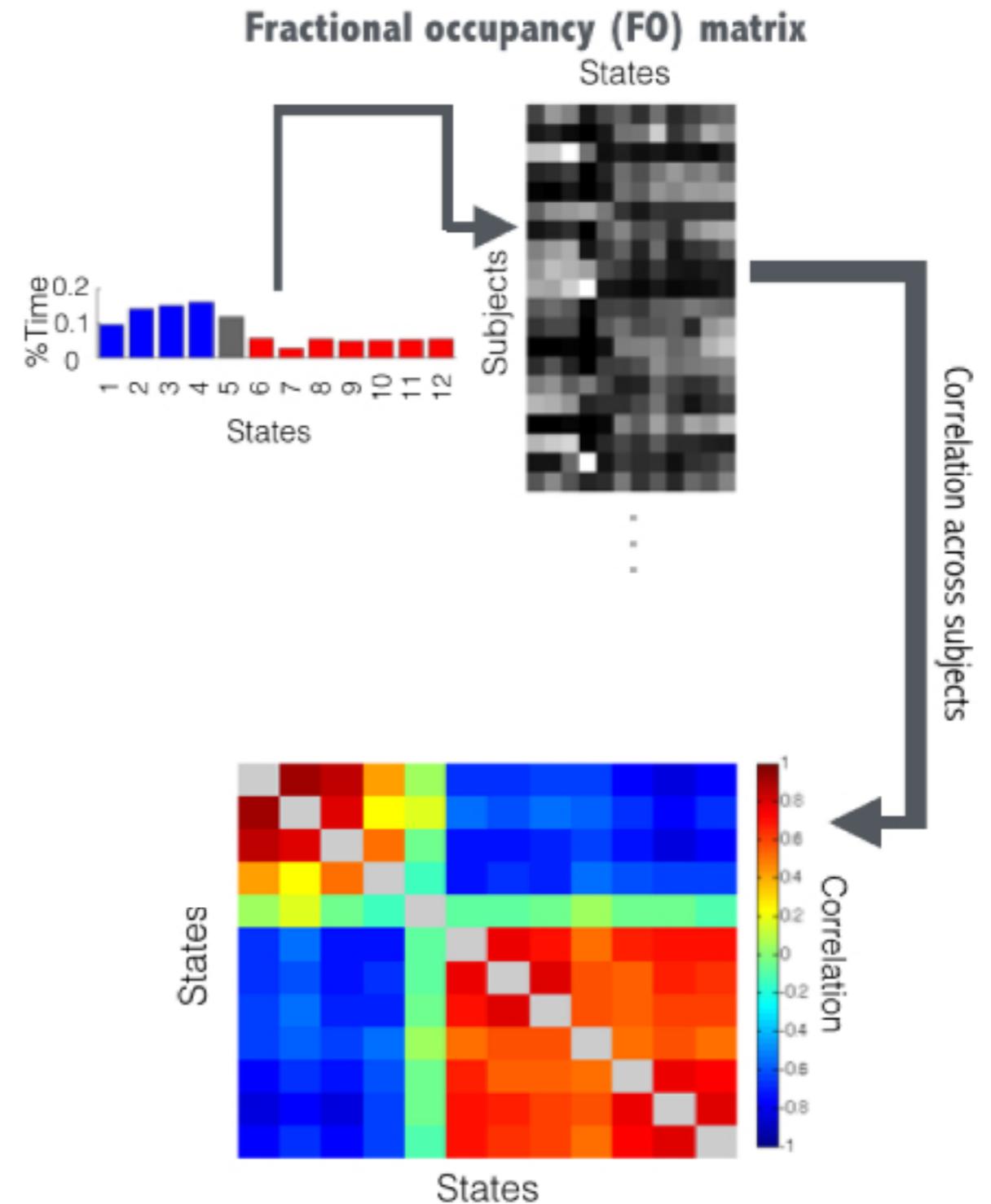
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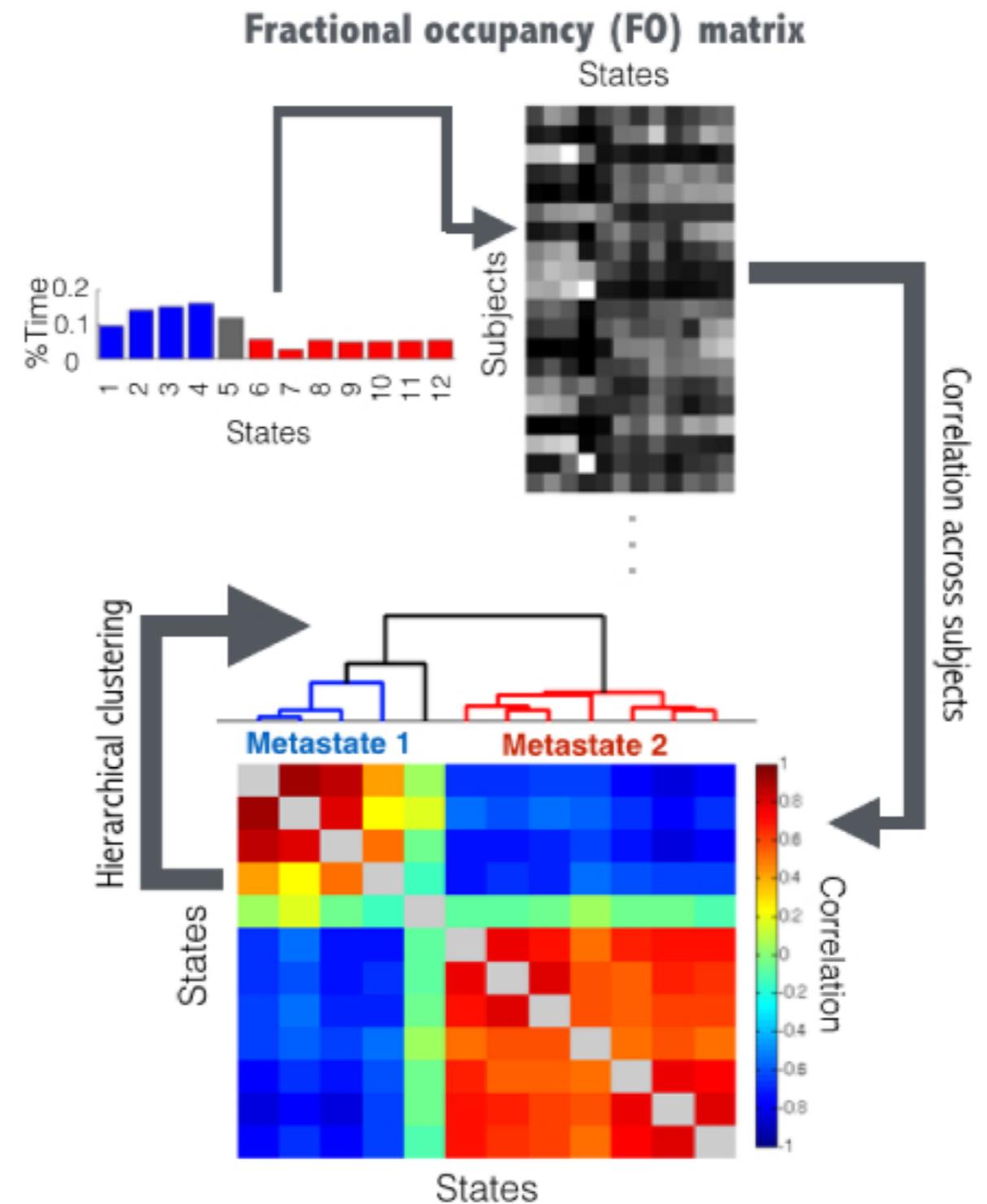
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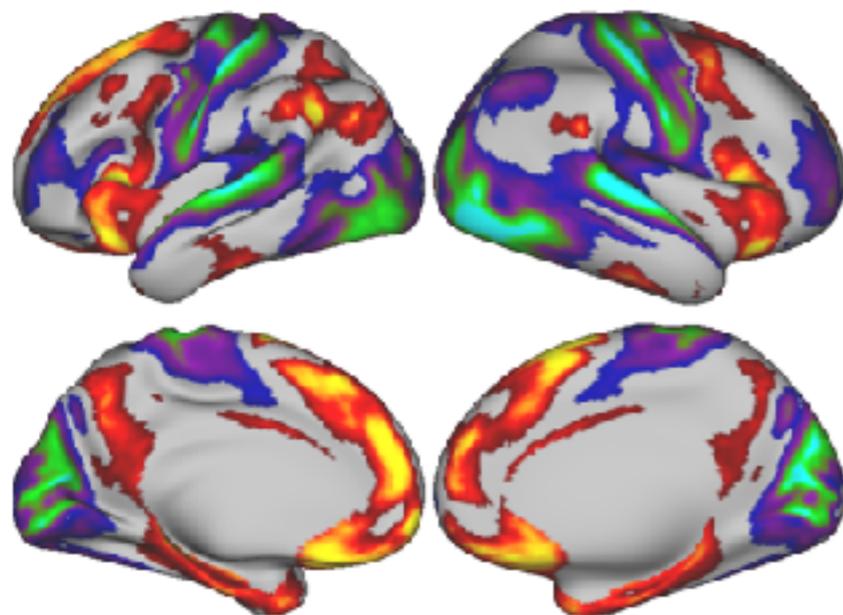
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Is there hierarchical temporal structure?

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Degree maps



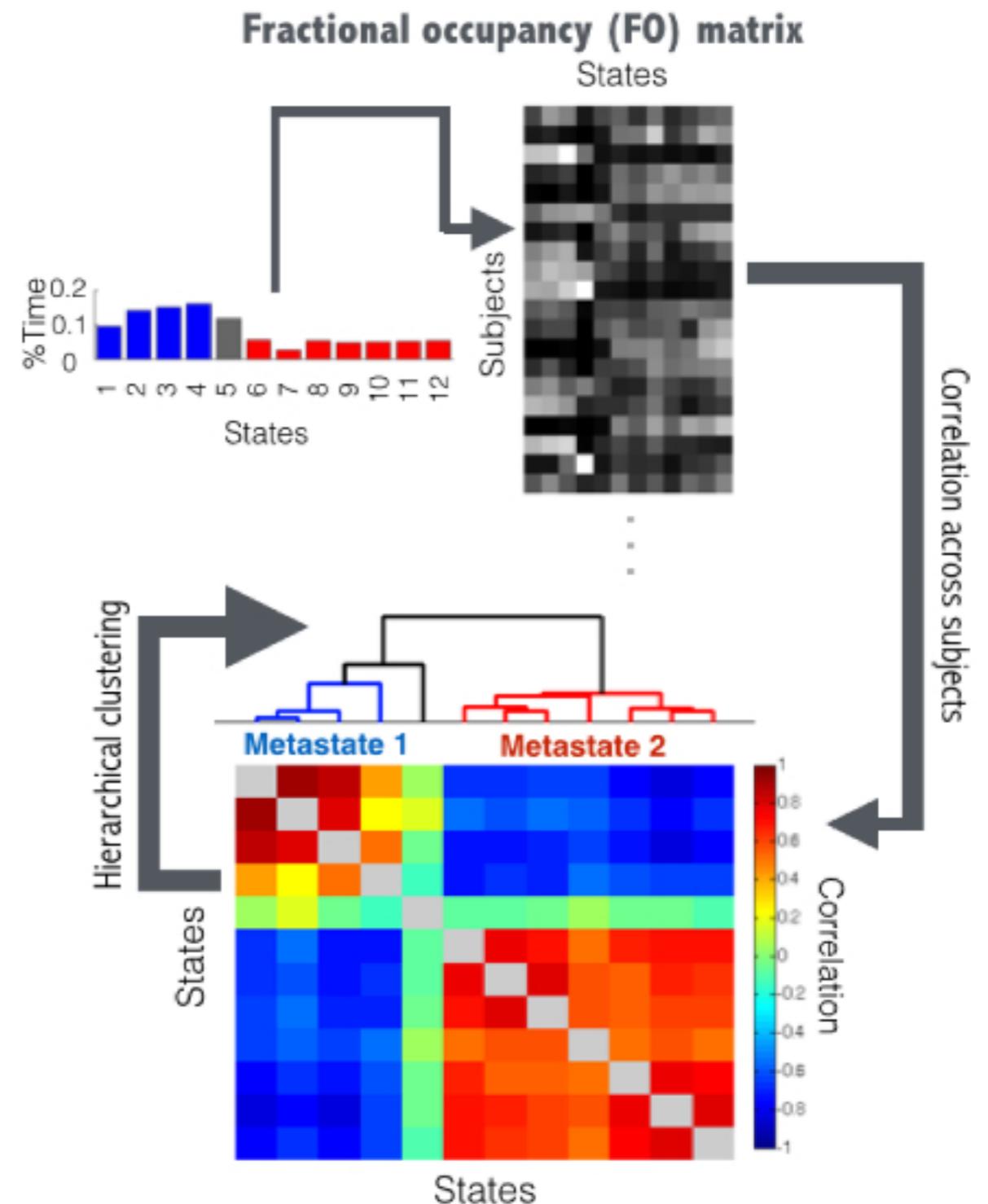
Metastate 2

Metastate 1



Cognitive

Sensory/motor



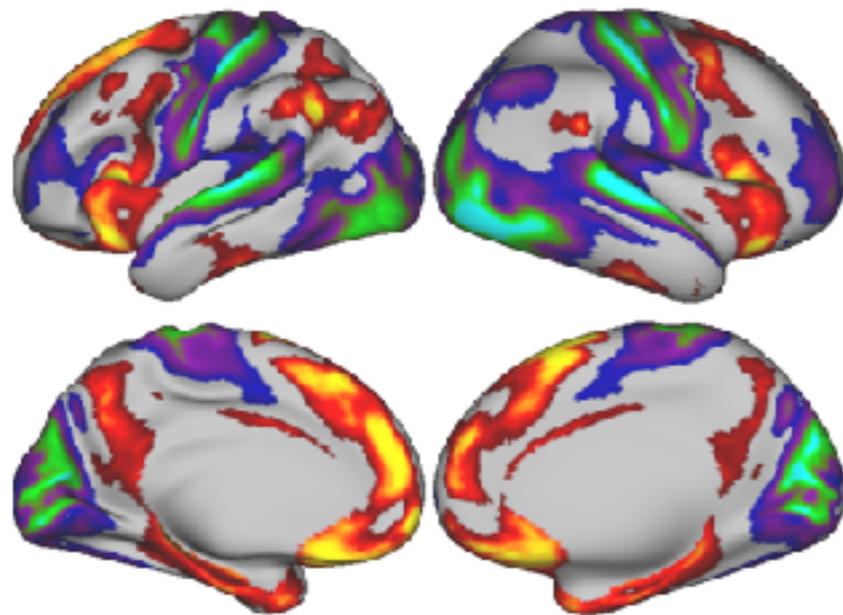
Is there hierarchical temporal structure?

- in the sequencing of brain states?

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Degree map



Metastate 2

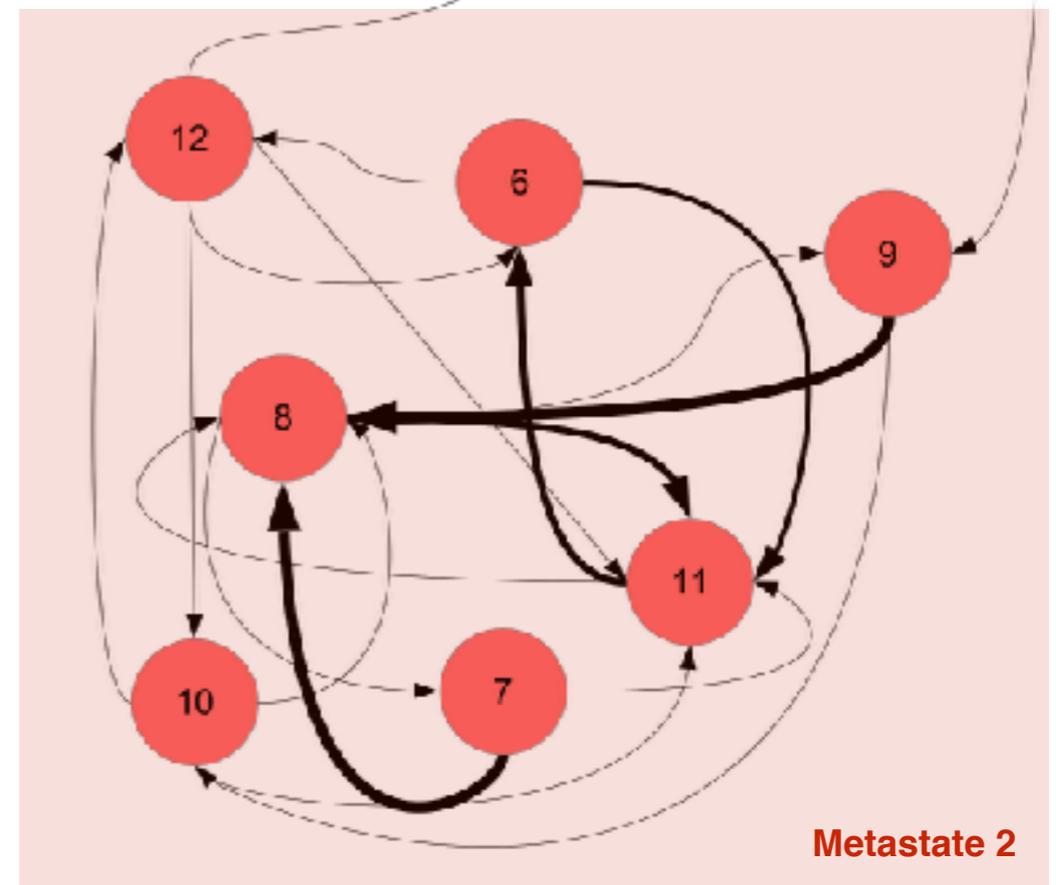
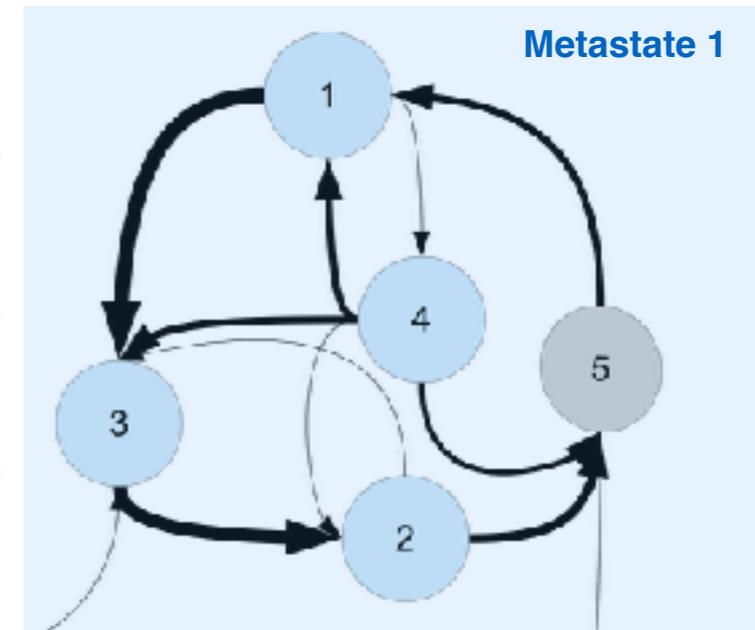
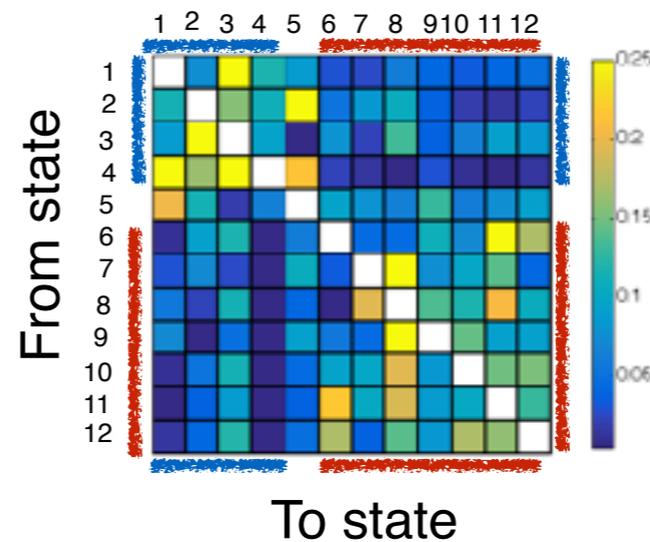
Metastate 1



Cognitive

Sensory/motor

Transition probabilities between the states



Hidden Markov Model

<https://github.com/OHBA-analysis/HMM-MAR>



EEG



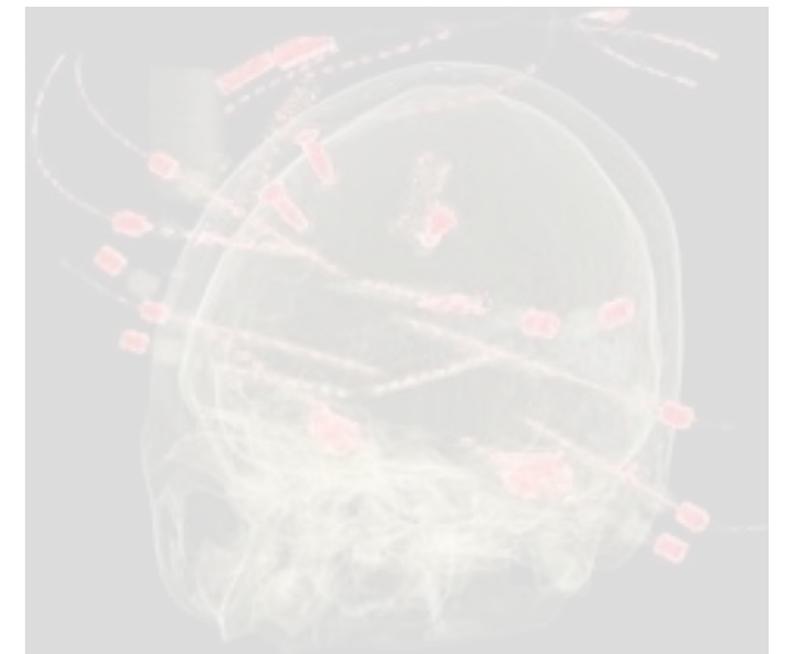
fMRI



MEG



HMM



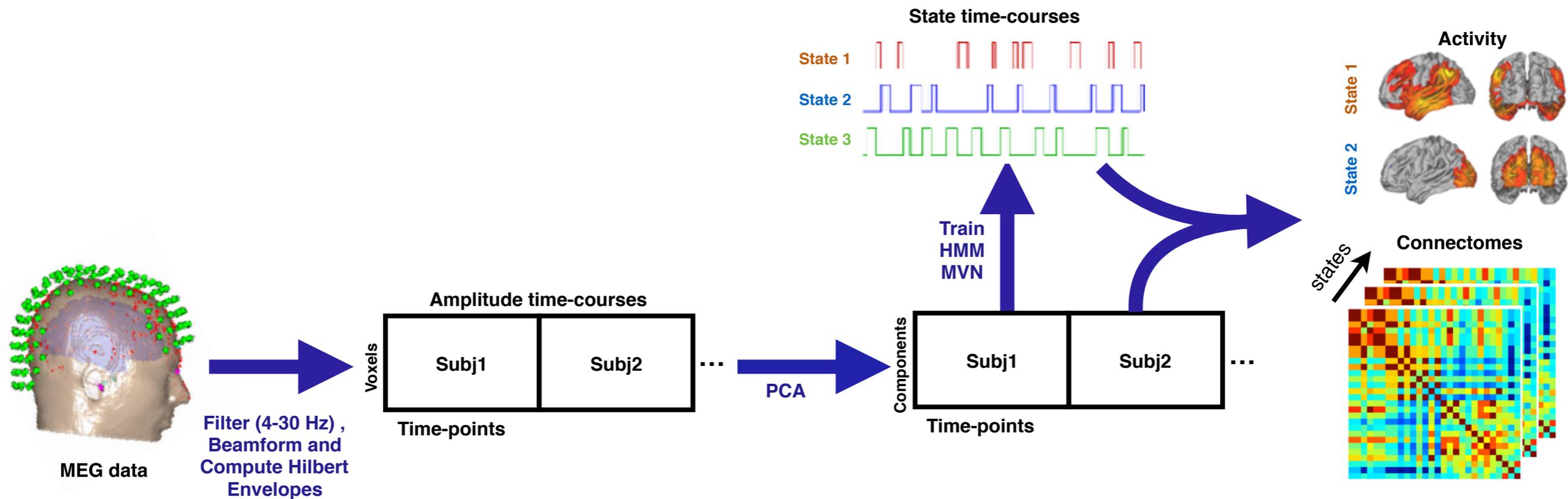
Intracranial
recordings

Hidden Markov Model (HMM)

- Can we use the HMM to infer ***dynamic networks in resting MEG*** data?
- How fast are the dynamics?
 - Resting state (eyes open) CTF MEG data
 - 9 subjects (10 minutes each)
 - 8 HMM states

Hidden Markov Model (HMM)

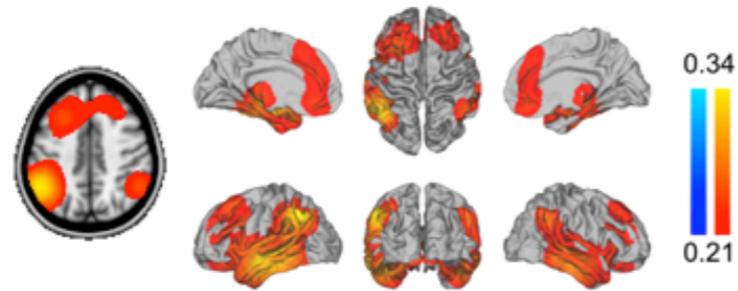
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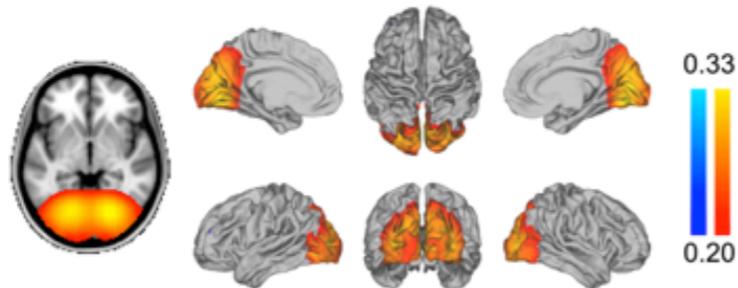
Brain Network Dynamics

HMM reveals MEG resting state networks that switch on fast sub-second timescales (~ 100 ms)

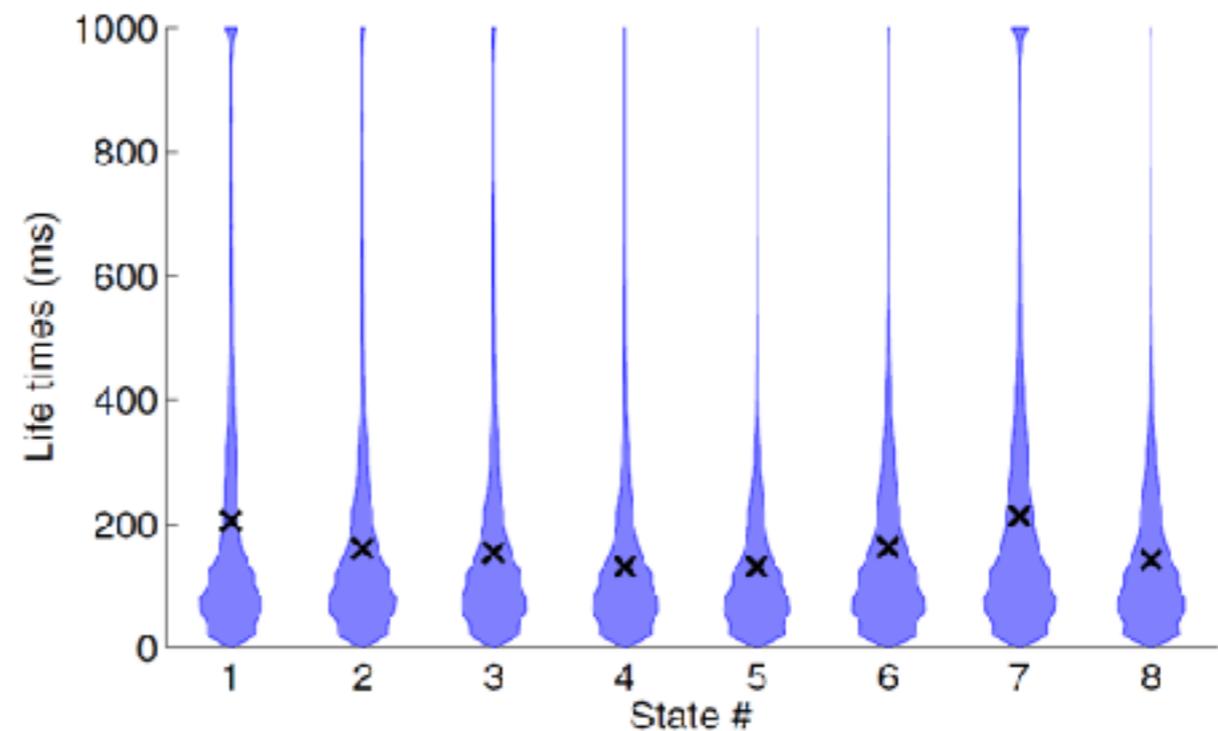
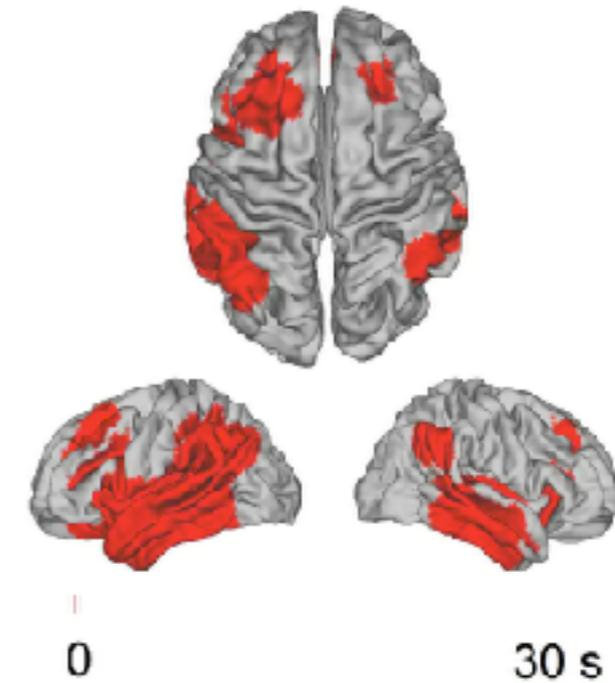
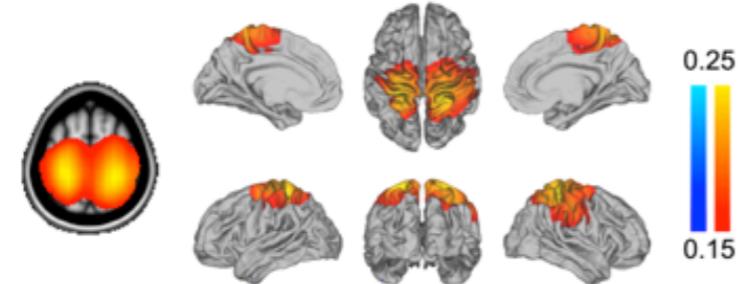
State 1 - Default Mode



State 2 - Visual



State 3 - Sensorimotor



Baker, ..., Woolrich; eLife (2014)

MEG: Time Delay Embedded HMM (TIDEH)

- What about running HMM on raw resting MEG data?
 - Are there transient states of distinct **phase coupling**?

“Communication through neuronal coherence”, Fries et al., TICS, 2005

MEG: Time Delay Embedded HMM (TIDEH)

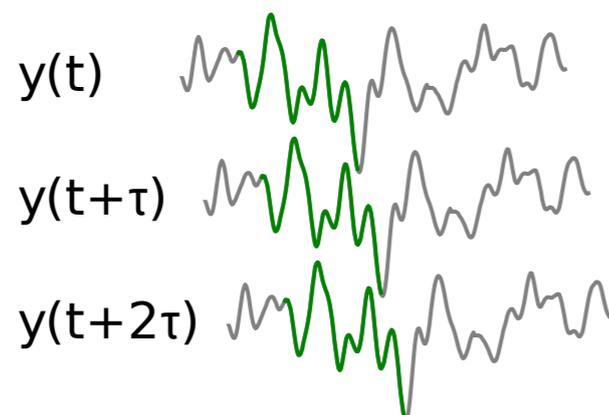
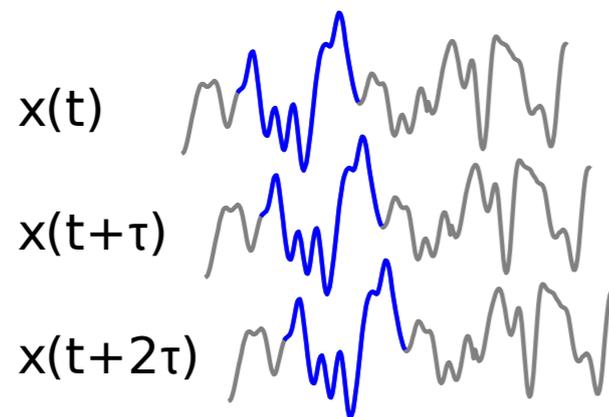
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- Use time delay embedding with HMM

time delay embedding



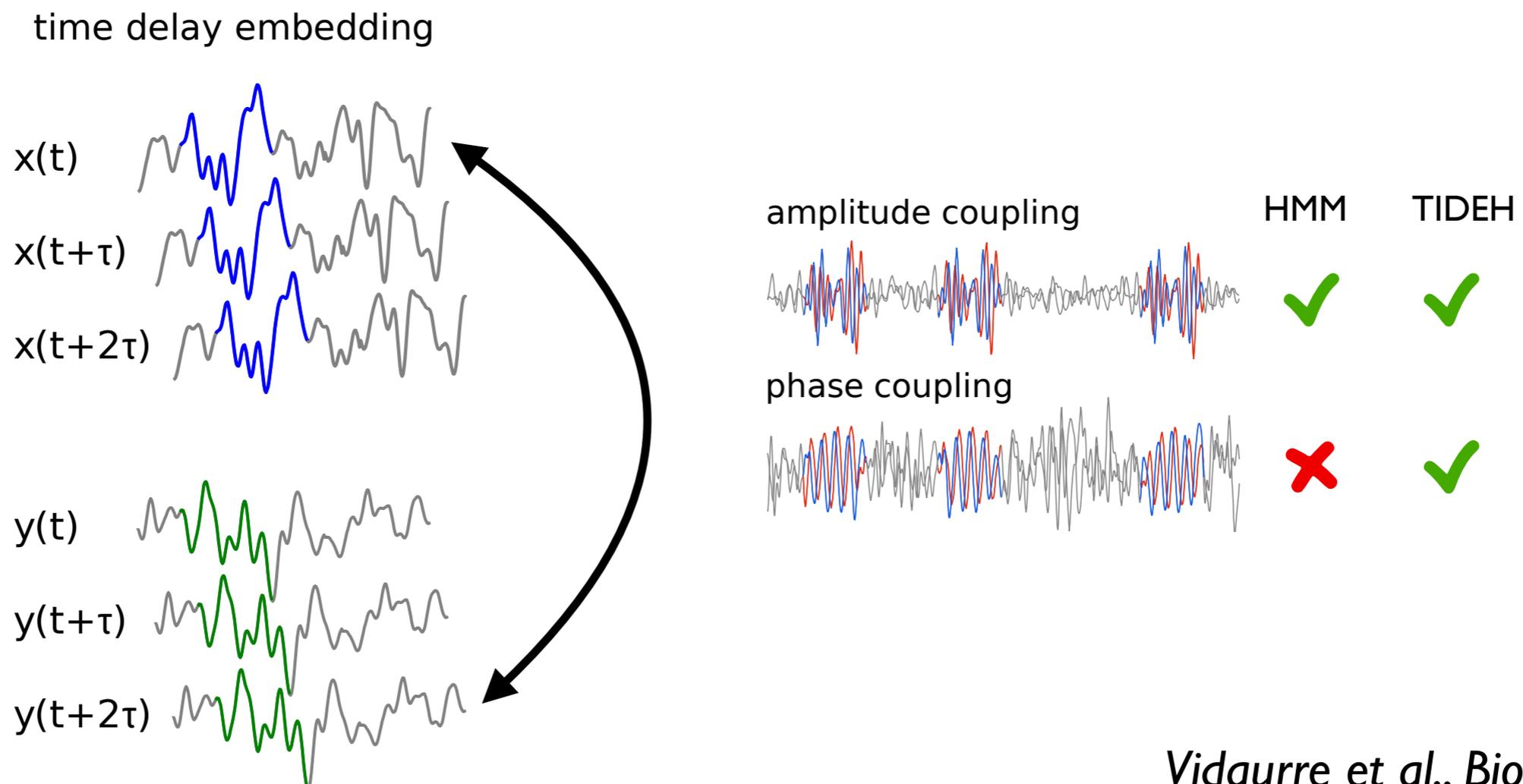
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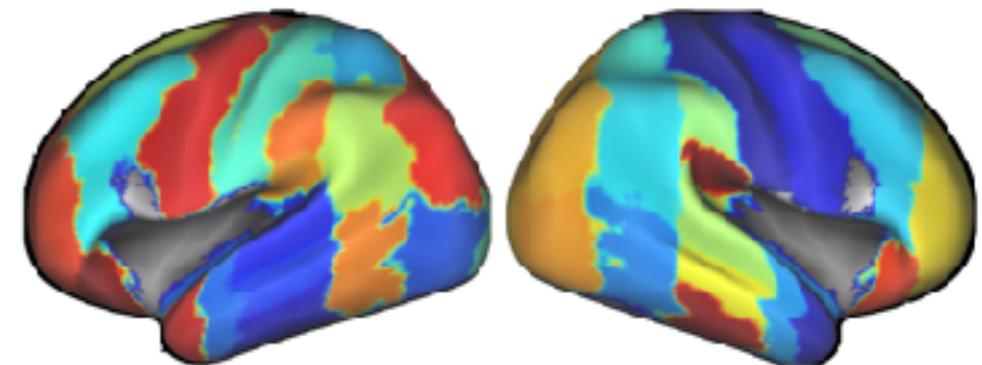
“Communication through neuronal coherence”, Fries et al., TICS, 2005

- Use time delay embedding with HMM



MEG: Time Delay Embedded HMM (TIDEH)

- Are there fast transient brain states of distinct ***phase locking*** in the resting state?
- Time embedded HMM on:
 - Resting state (eyes open) CTF MEG
 - 51 subjects (6 mins each)
 - 38 node parcellation
 - 1-45Hz raw time courses
 - 8 HMM states

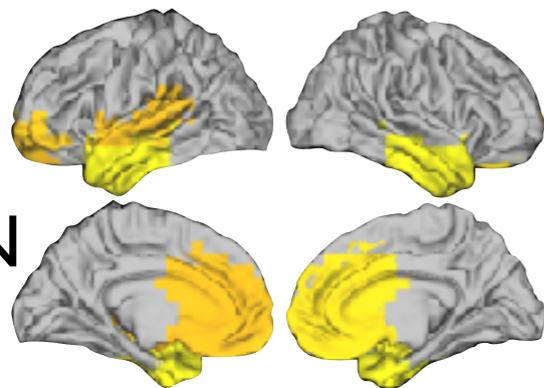


Rel. Amplitude
(1-30Hz)

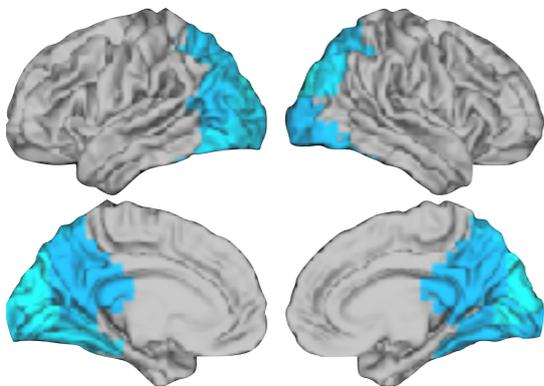
Rel. Amplitude
(1-30Hz)

Vidaurre et al., BioRxiv, 2017
Poster #1892

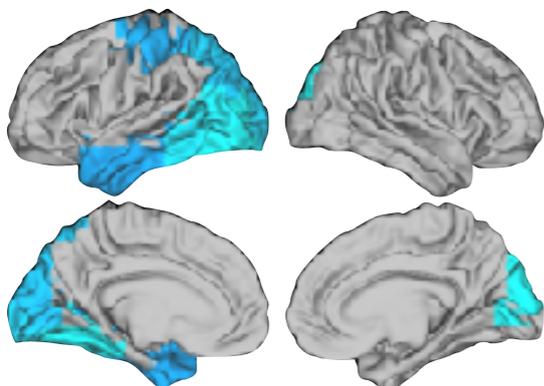
S1
aDMN



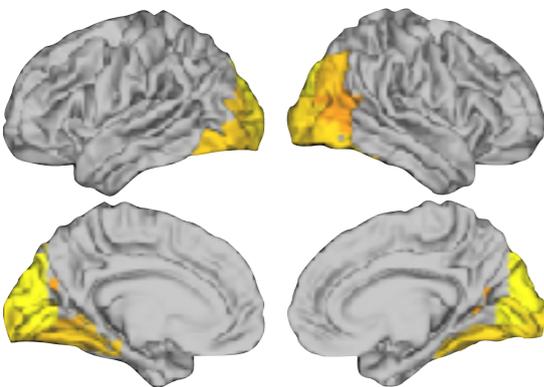
S2
Vis



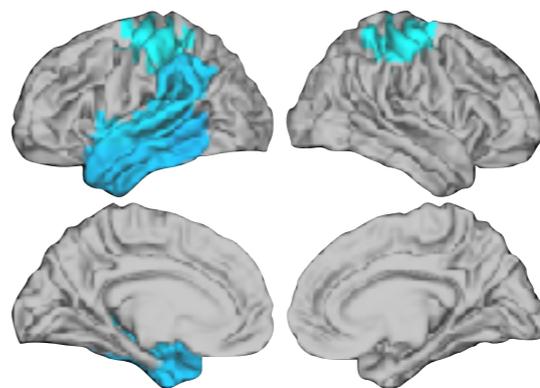
S3



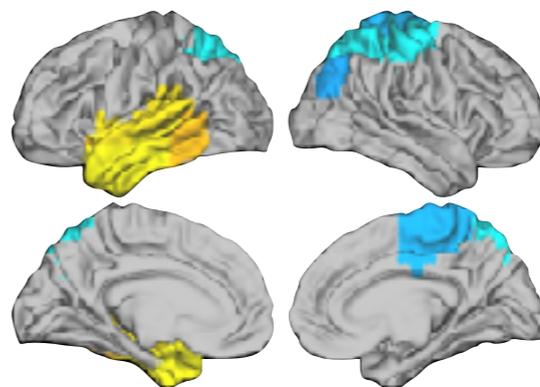
S4
Vis



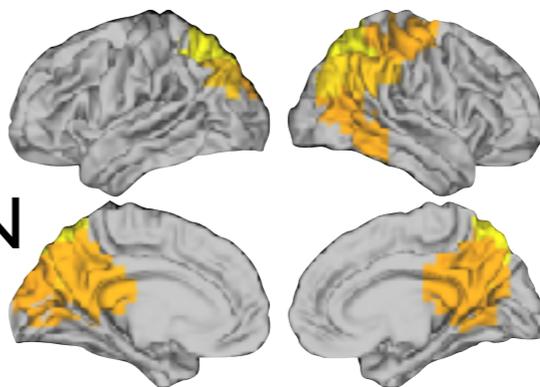
S5
Mot



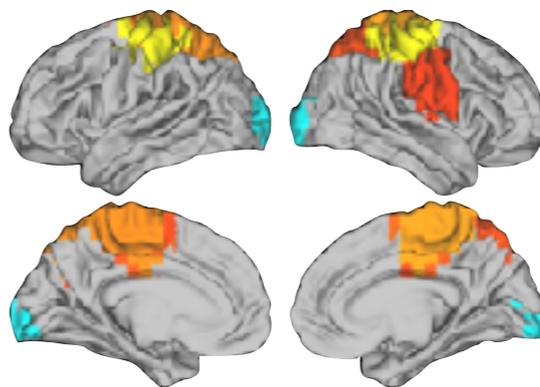
S6



S7
pDMN



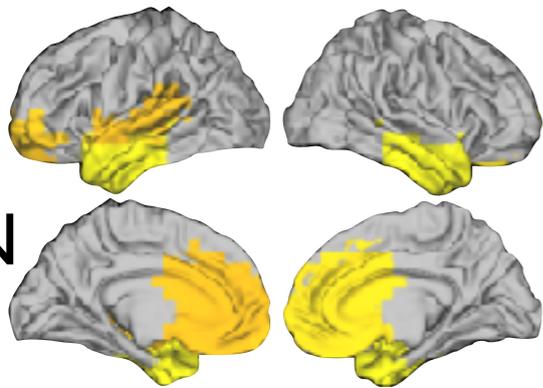
S8
Mot



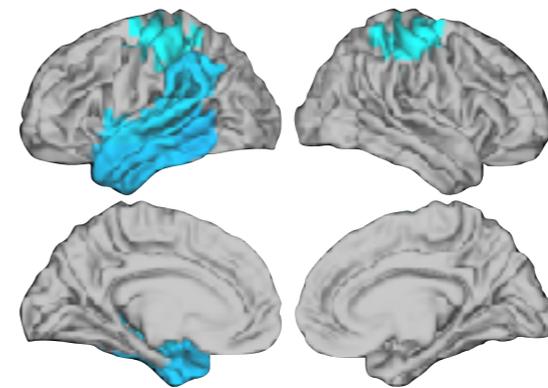
Rel. Amplitude
(1-30Hz)

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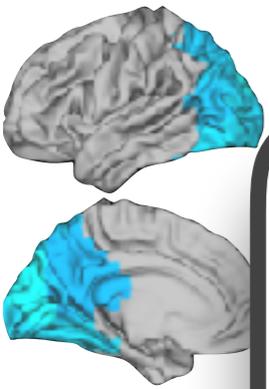
S1
aDMN



S5
Mot

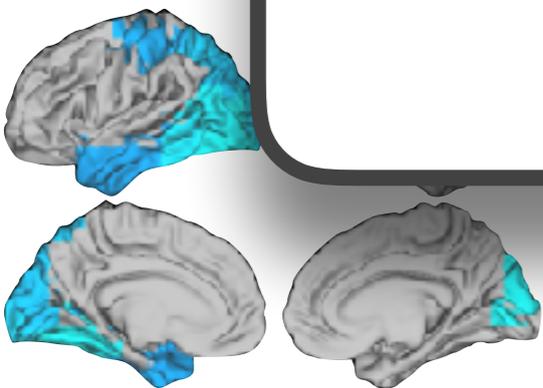


S2
Vis

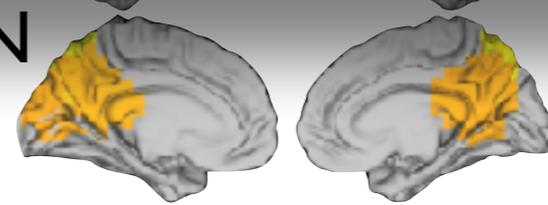


Do the state visits represent transient events of distinct phase-coupling?

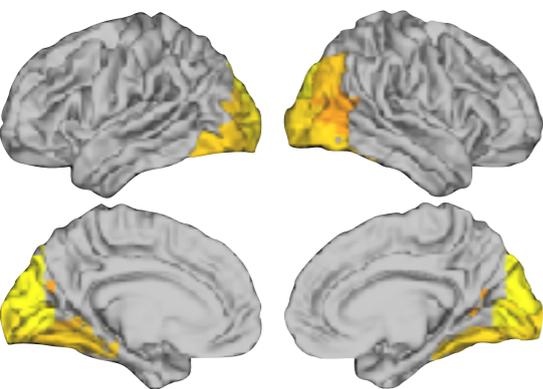
S3



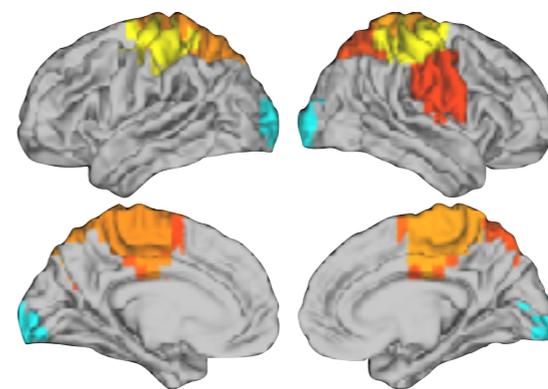
pDMN



S4
Vis



S8
Mot



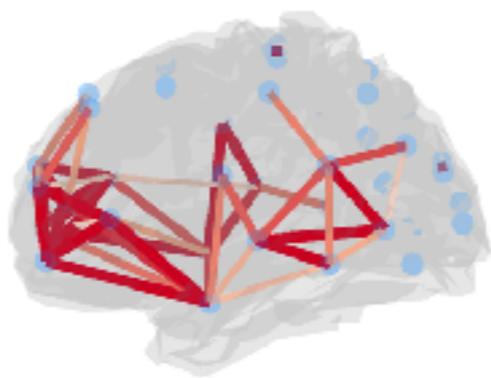
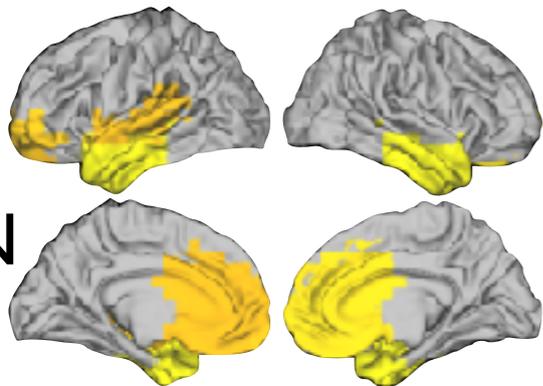
Rel. Amplitude
(1-30Hz)

Coherence
(1-30Hz)

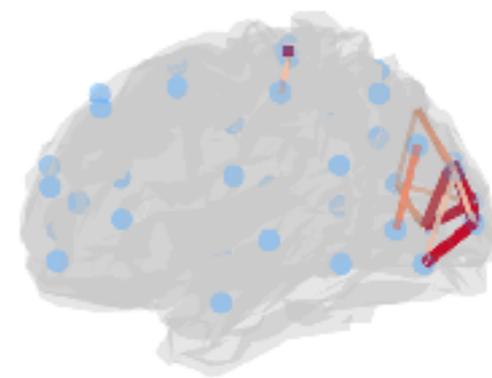
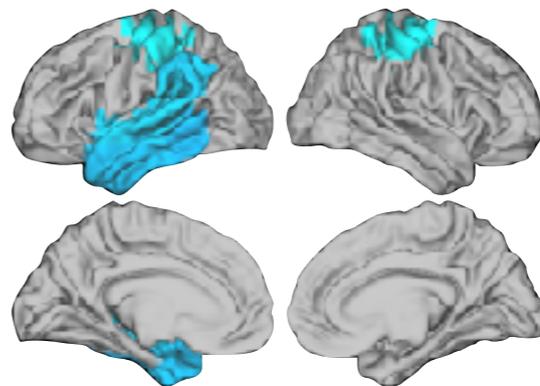
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Coherence
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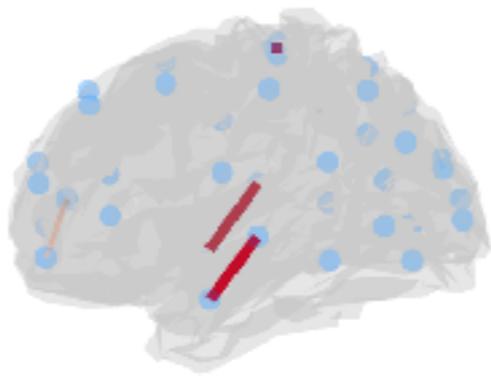
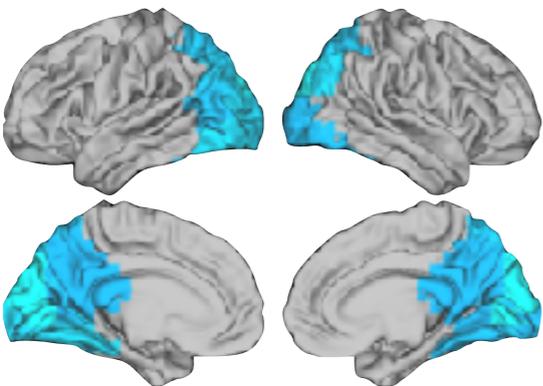
S1
aDMN



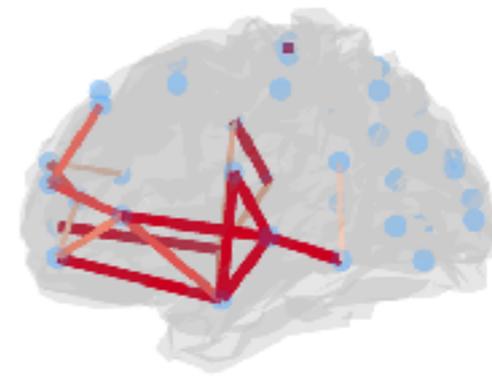
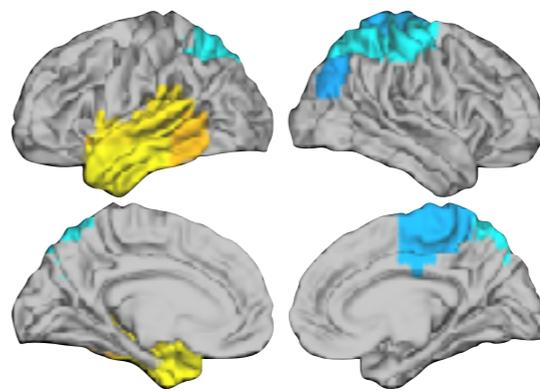
S5
Mot



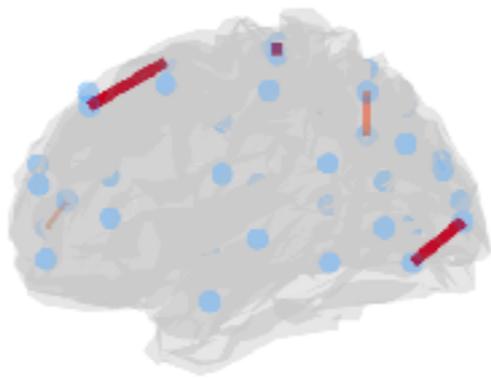
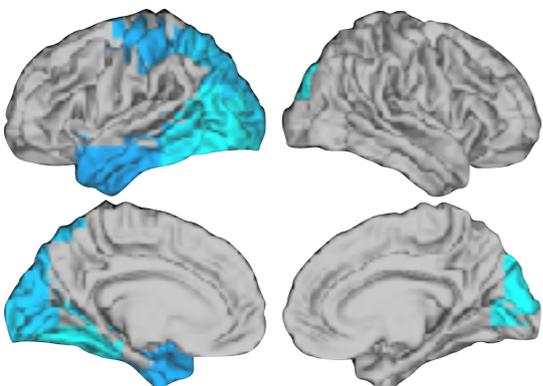
S2
Vis



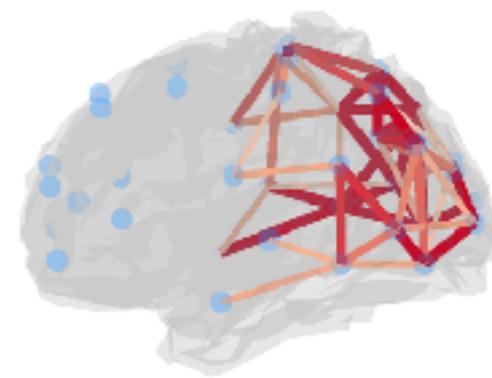
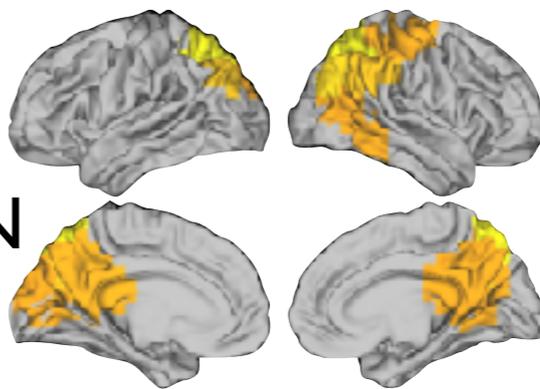
S6



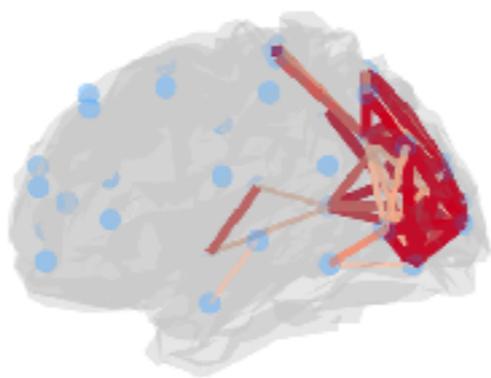
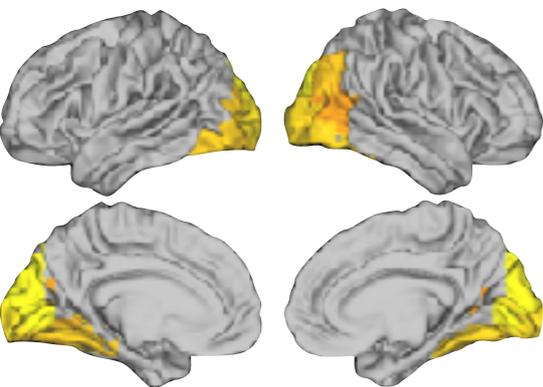
S3



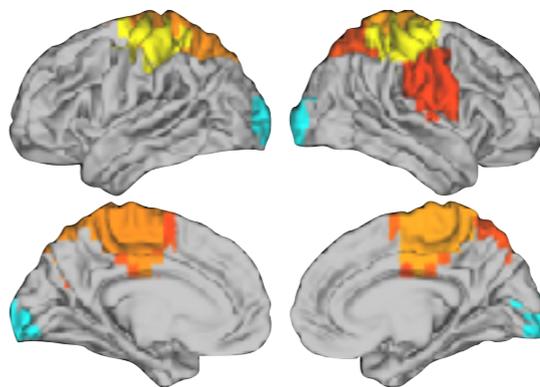
S7
pDMN



S4
Vis



S8
Mot

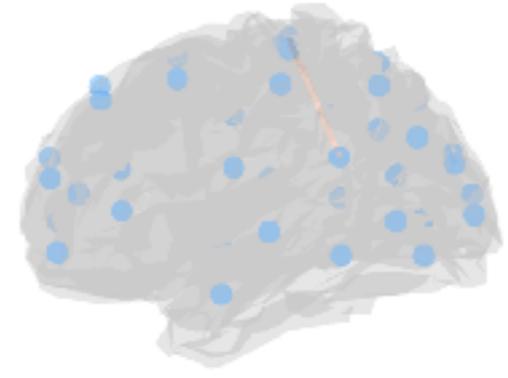
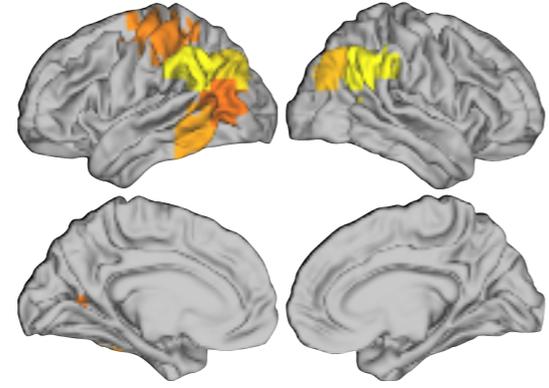
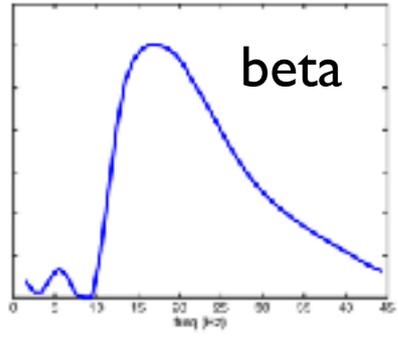
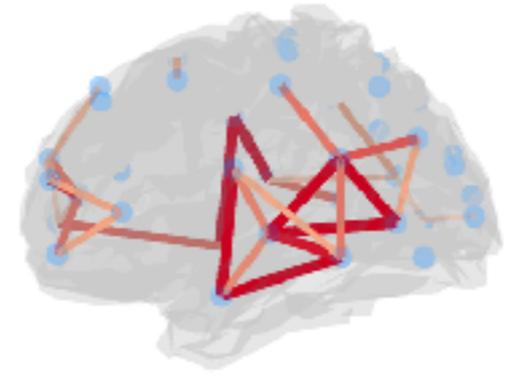
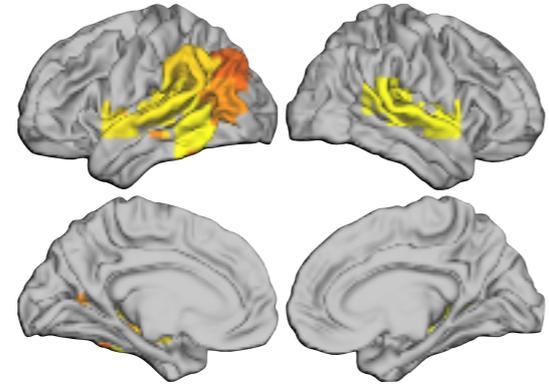
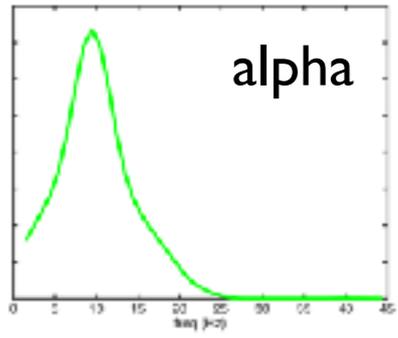
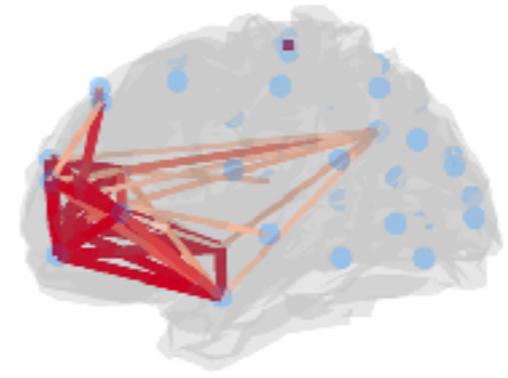
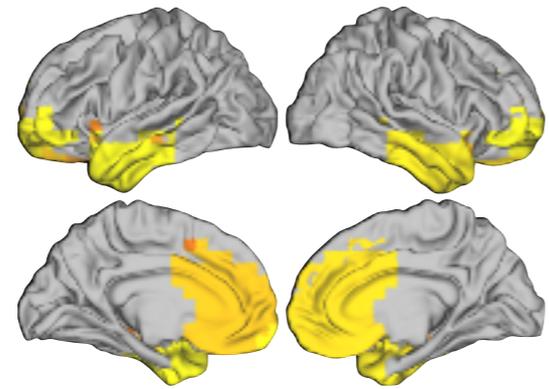
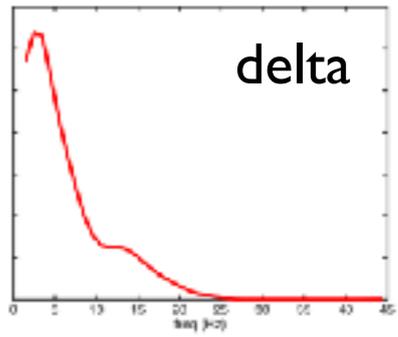
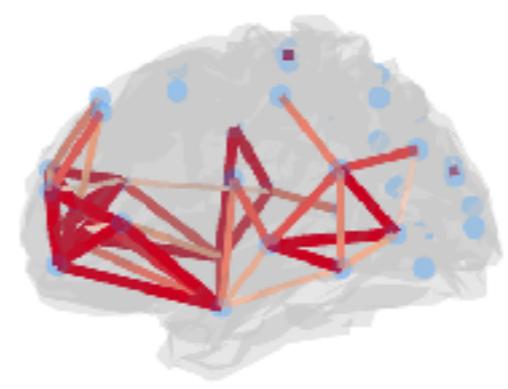
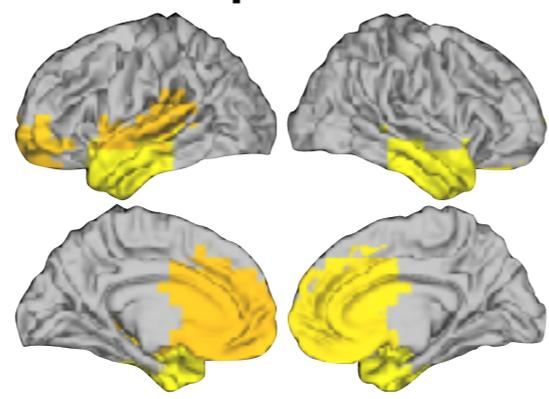


S1 - anterior DMN

Amplitude

Coherence

wideband
1-30Hz



S1 - anterior DMN

S7 - posterior DMN

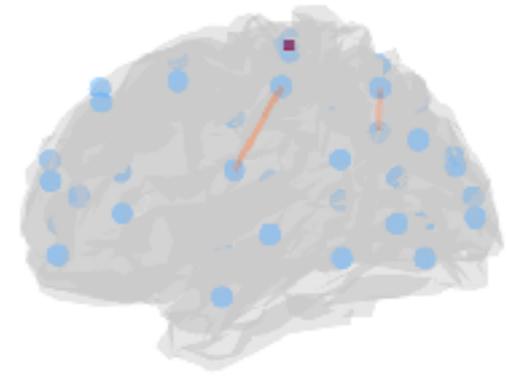
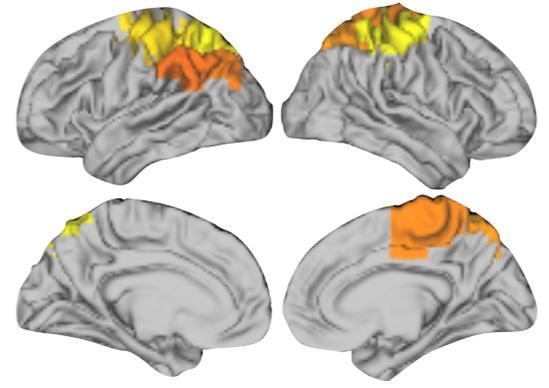
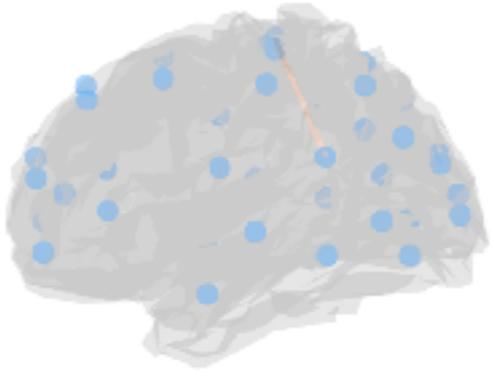
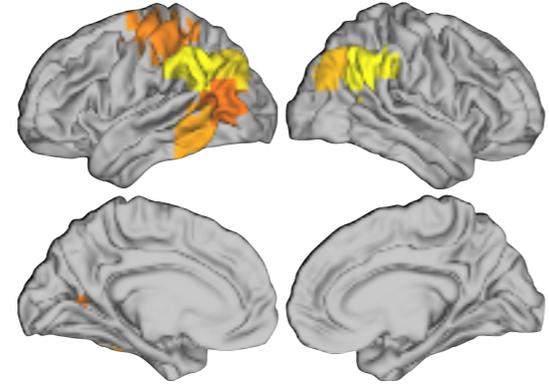
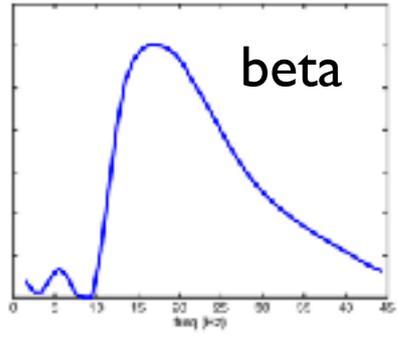
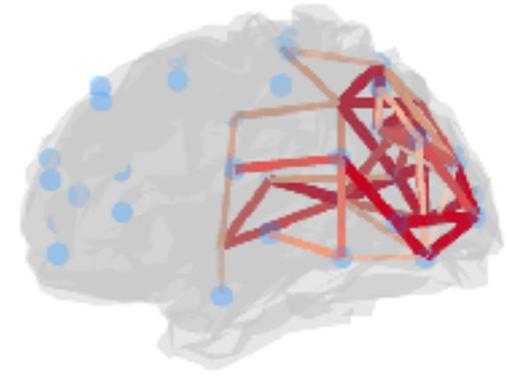
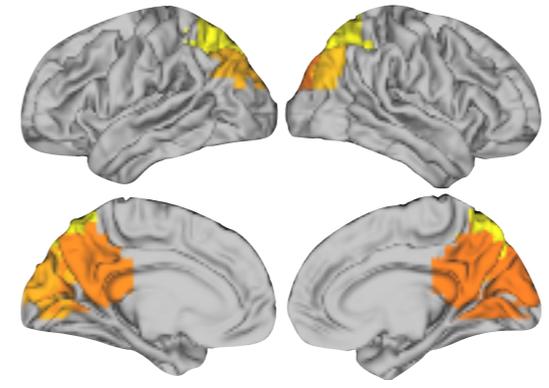
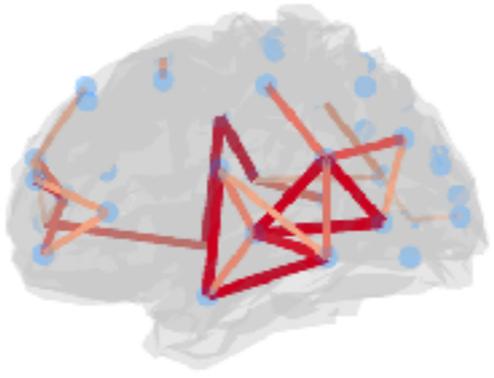
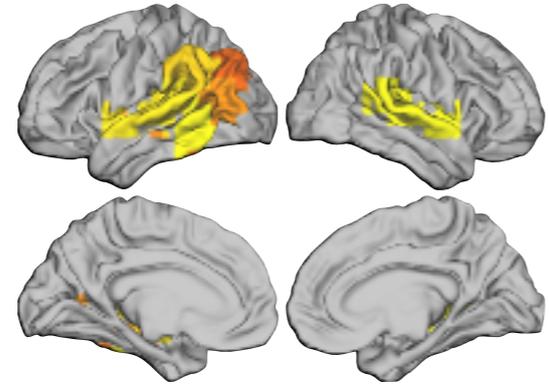
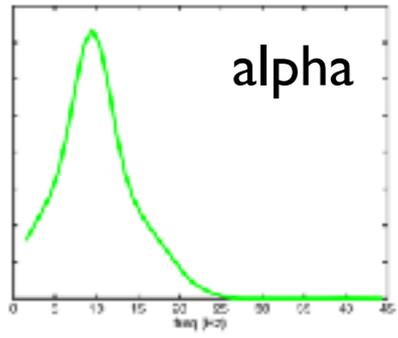
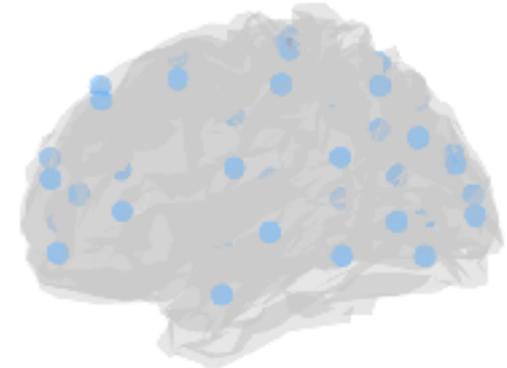
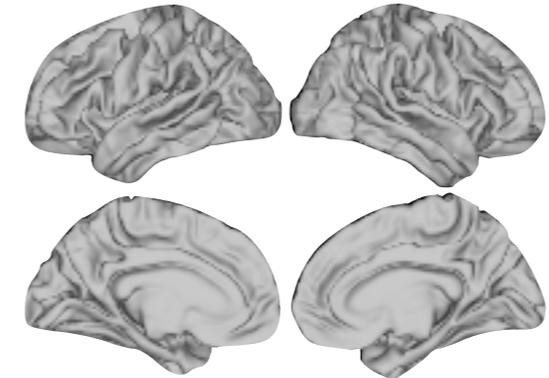
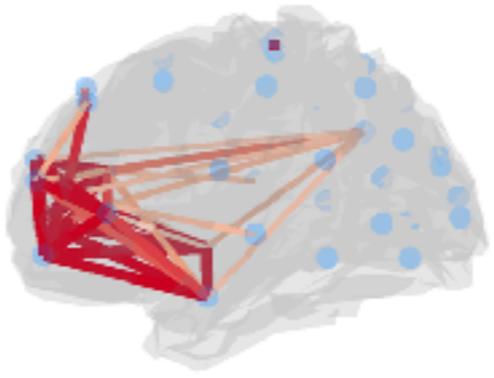
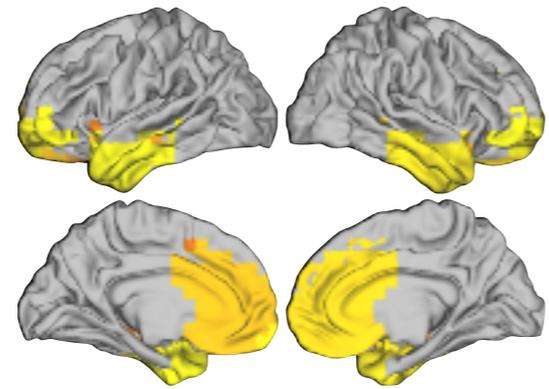
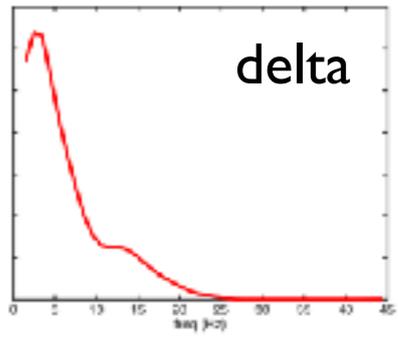
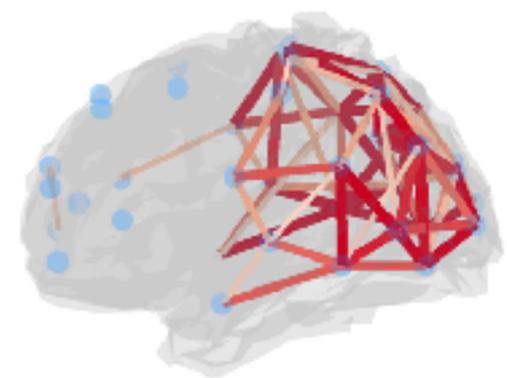
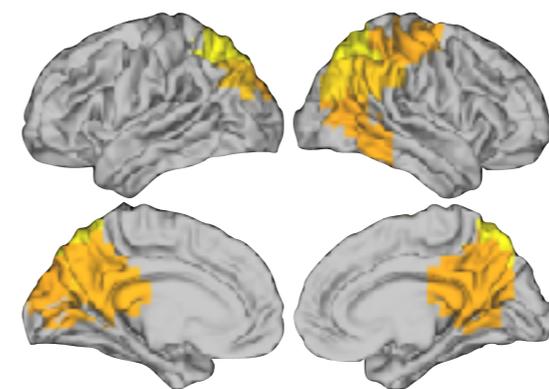
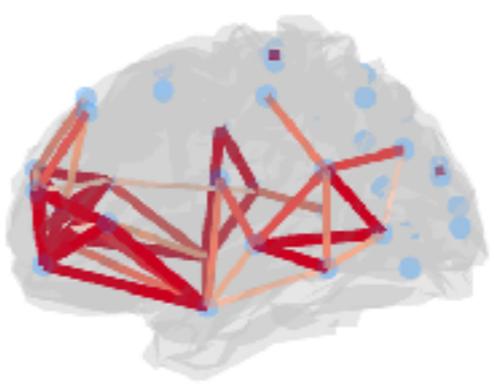
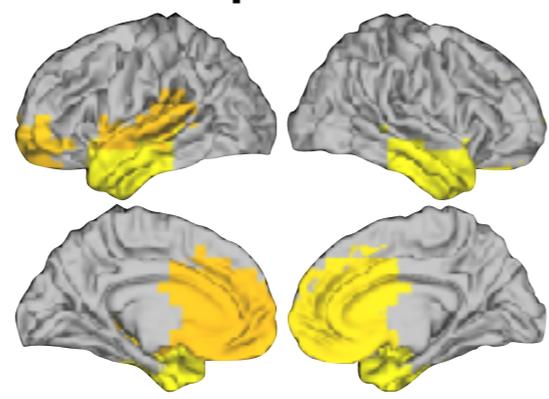
Amplitude

Coherence

Amplitude

Coherence

wideband
1-30Hz



Summary

- **Static connectomes** can be computed using fMRI raw correlations and MEG amplitude correlations
 - Beware spatial misalignments over subjects!
- **Dynamic connectomes** can be computed across modalities using Hidden Markov Modelling (HMM), e.g.:
 - Hierarchical temporal organisation of networks in resting **fMRI**
 - Dynamics of large-scale phase coupling in resting-state **MEG**

Acknowledgements



NIH Human Connectome Project

MRC MEG UK Partnership

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