Time Series

and the brain

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Center for Mind/Brain Sciences (CIMeC) at University of Trento

2015
STARTING GRANT: Semantic Memory in the brain
(Scott Fairhall)

2014
CONSOLIDATOR GRANT: Trust in Economics (Neurobiological bases)
(Giorgio Coriclli)

2013
STARTING GRANT: MApping the Deprived VIsual System
(Olivier Collignon)

2012
STARTING GRANT: Construction of perceptual space-time
(David Melcher)

2011
ADVANCED GRANT: Predisposed mechanisms for social orienting: A comparative neuro-cognitive approach 2011 (Giorgio Vallortigara)

STARTING GRANT: Brain-state dependent perception: finding the windows to consciousness
(Nathan Weisz)

STARTING GRANT: Compositional Operations in Semantic Space
(Marco Baroni)

2010
STARTING GRANT: How the brain codes the past to predict the future
(Uri Hasson)

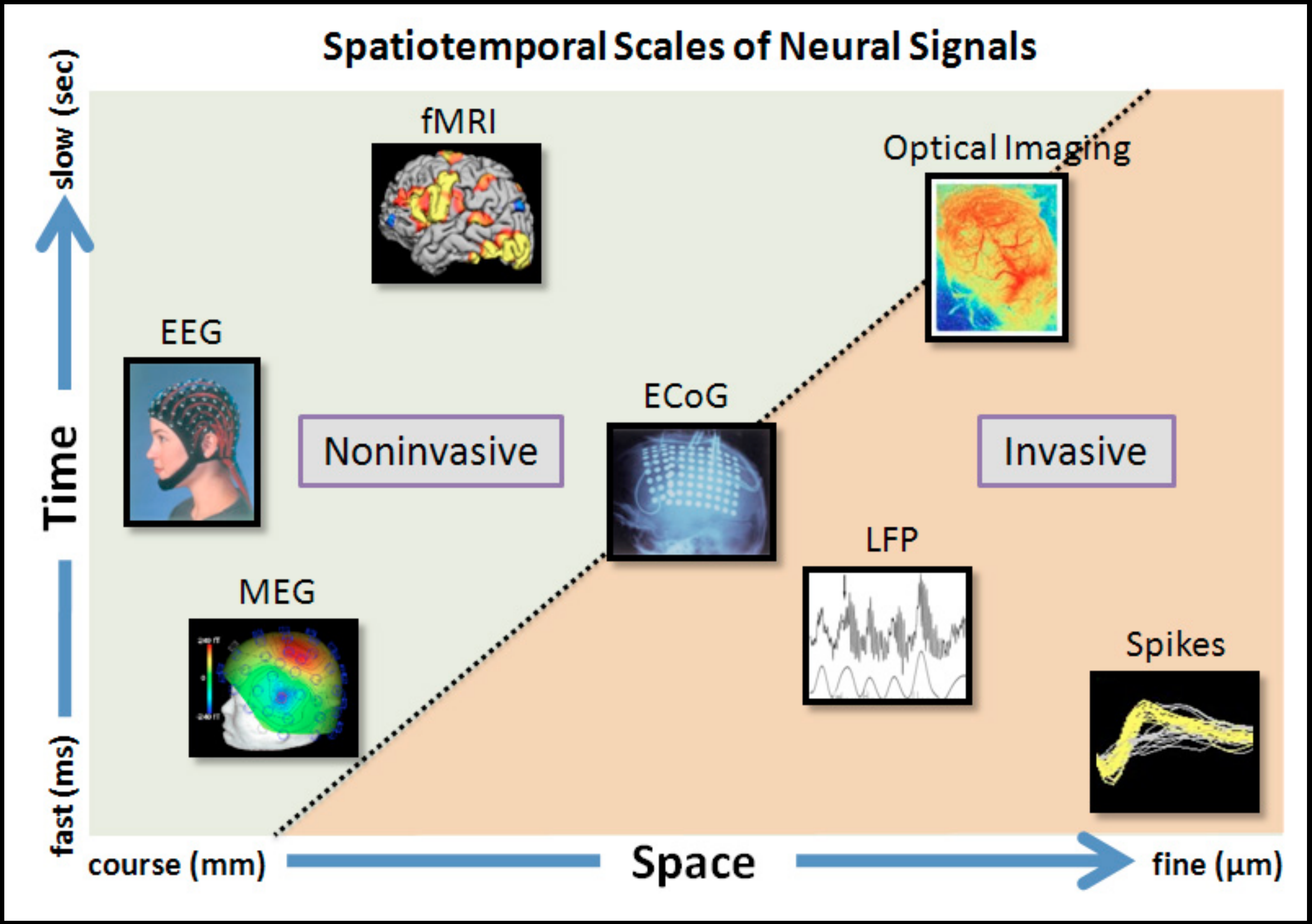
Overview

1. Preliminary notes
2. Methods for time series acquisition
3. Time series during rest - Slow-frequency processes vs. fast dynamics
4. Stationary networks
5. Dynamics networks
6. Ongoing issues

Preliminary notes

Things we do with time

1. On the level of single time series:
    a. Typical frequency-domain analyses (power spectra, power in low frequency)
    b. ICA
    c. Time-domain analysis (entropy and variants, dynamic systems approaches: self-similarity, fractal features, embedding dimensions, Hurst exponent)
    d. Peak analysis
    e. Temporal motifs
2. On the level of multiple time series
    a. Pairwise correlations (functional connectivity)
    b. Causality analyses (Granger, dynamic causal models, structural equation models, psychophysiological interactions)
    c. Network-based analysis (topology, partition structure)
    d. Spatiotemporal ICA
    e. Dynamic connectivity



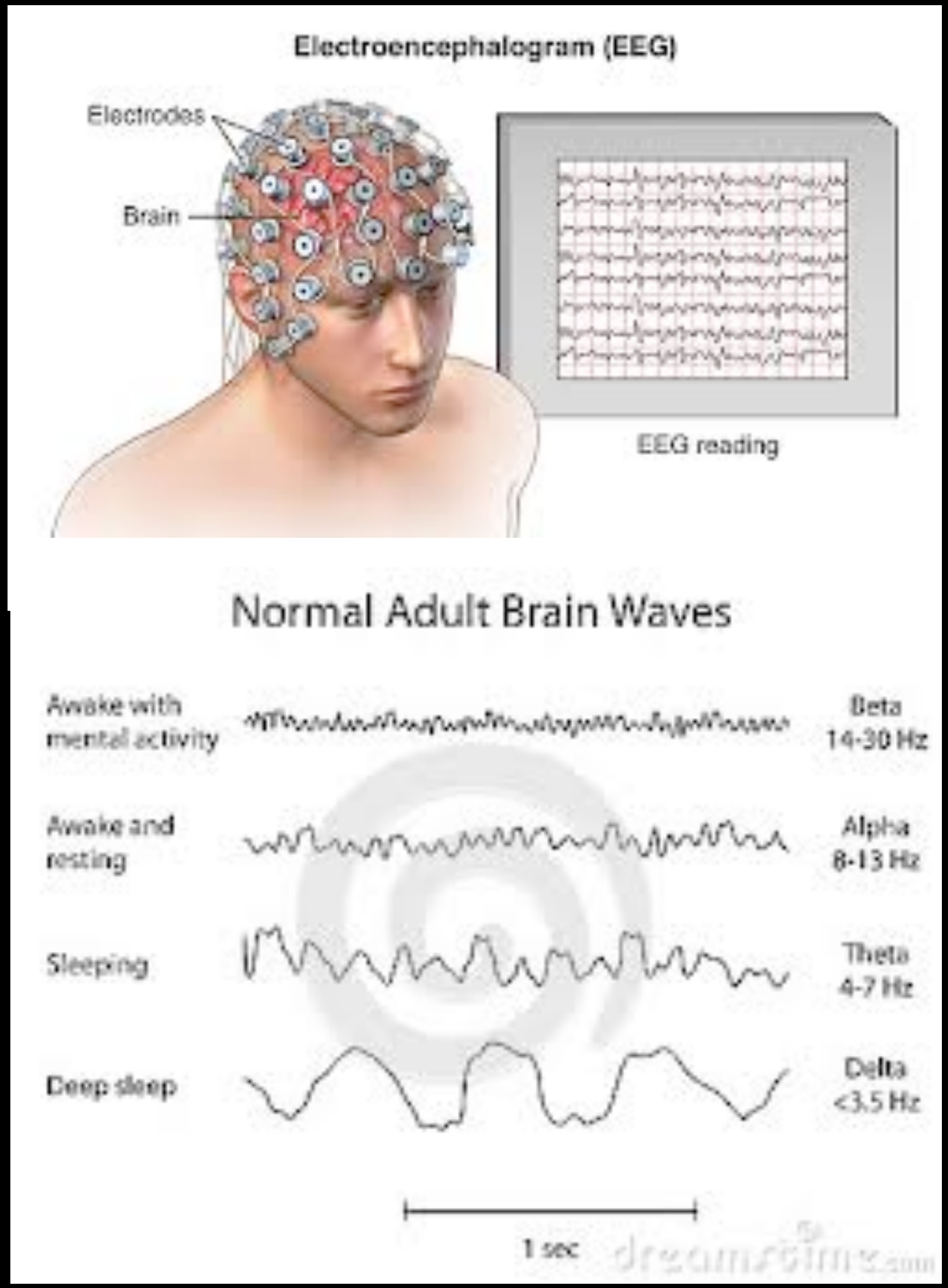
Space and Time

Electroencephalography, Magnetoencephalography, Electrocorticography, functional MRI

EEG

- Measures spontaneous or induced electrical activity manifested as synchronous activity of multiple neurons

- Rapid sampling rate

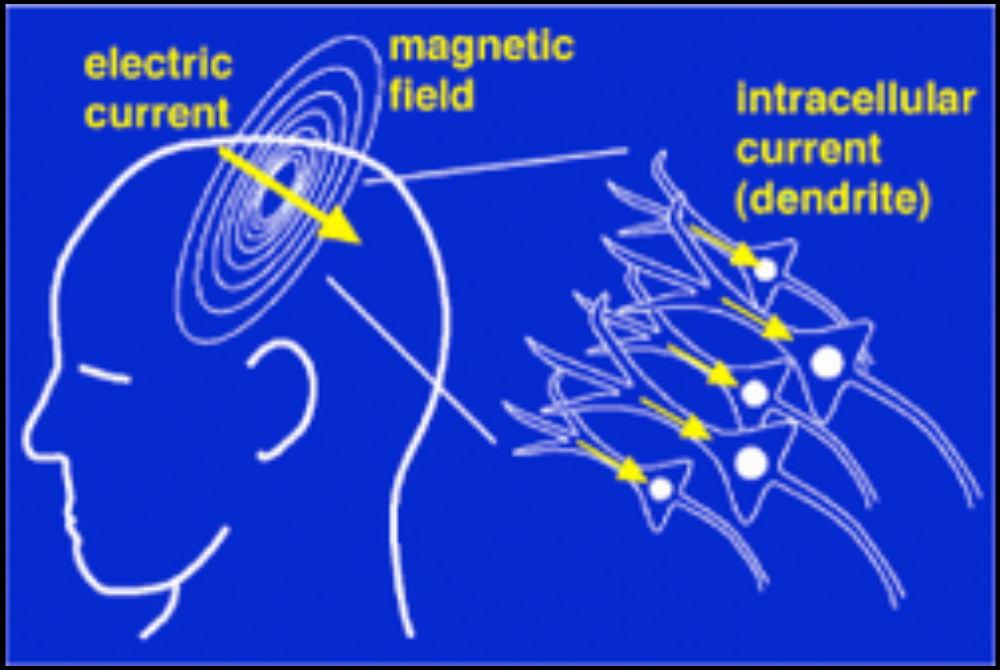


MEG

- Measures changes in magnetic field around the head

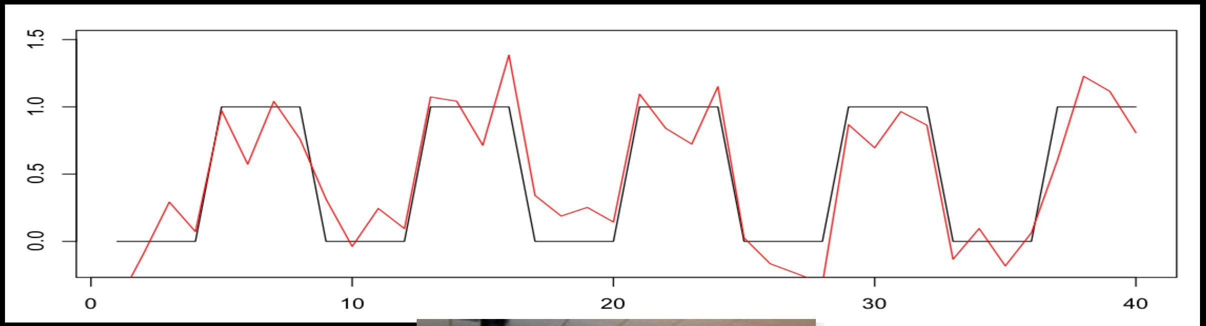
- Rapid sampling rate

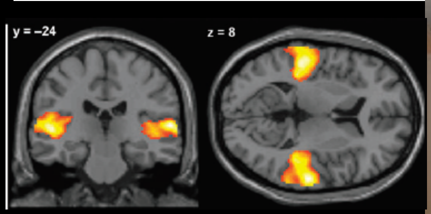
- sensitive to radial dipoles and less sensitive than EEG to deep sources of activity

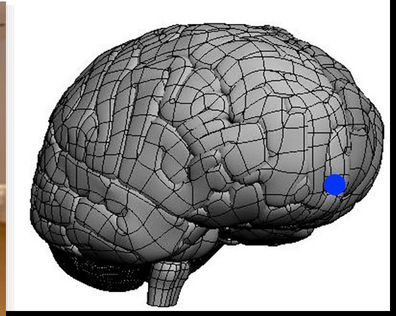


FMRI

- Measures changes in local oxygen content within gray matter
- Scale of ~ 2mm^3; temporal resolution ~ 1Hz
- Equally sensitive to activity across the brain (with few exceptions)
- fluctuations ~ 1% from background “noise”







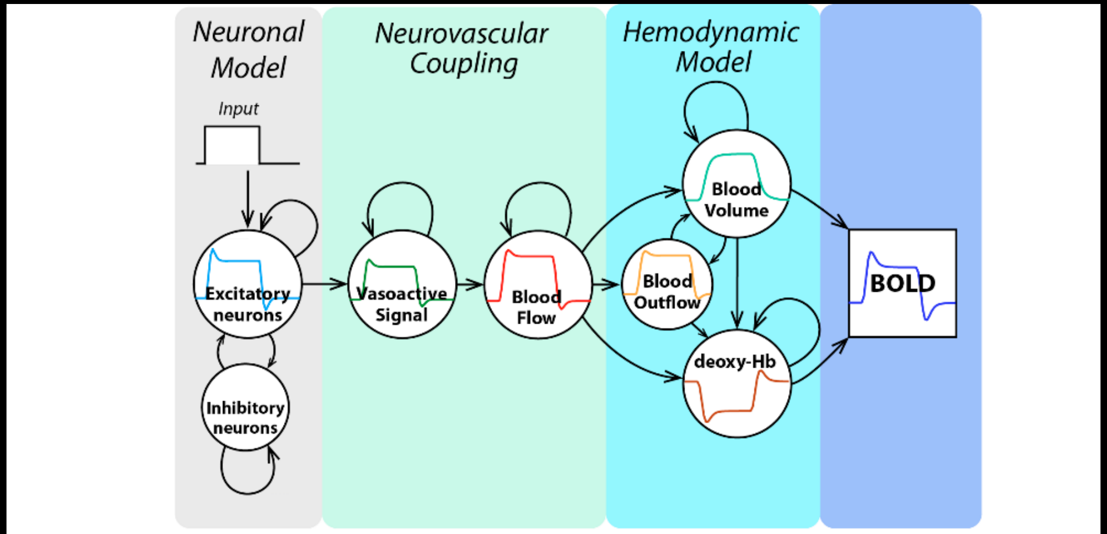


Figure 1. Schematic illustration of physiological variables and their interactions assumed in P-DCM.

A never-resting human brain

- The human brain continuously consumes energy. The brain accounts for 20% of energy consumption during rest, and surprisingly, actual cognitive activity appears to increase that by no more than 5%

- In the last 10 years, there is a massive effort to understand the nature of this intrinsic activity

- Guiding premise: the brain is not reactive, but maintains ordered modes of operation during rest via rhythmic synchronization (Buzsaki and Draguhn 2004)

- A dominant framework for understanding this endogenous activity is in terms of networks operating while the brain is at rest (Resting State Networks; RSNs)

The RSN paradigm

- Defining a network via seed
- reveal map of brain areas functioning in synchrony

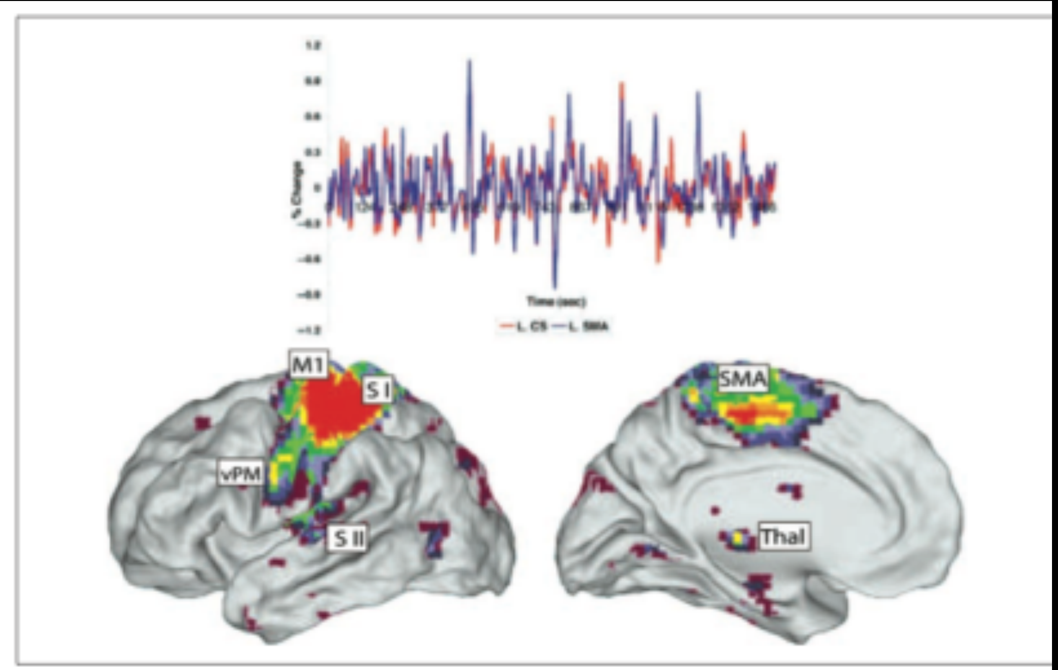


Figure 1. Temporal correlation of spontaneous BOLD signal fluctuations between brain regions of similar functionality. The figure shows the how the time course of the BOLD signal extracted from the left central sulcus (primary motor cortex, M1) is significantly correlated with time courses from other regions including primary sensory cortex (S1), second sensory cortex (S2), SMA, ventral premotor cortex (vPM), putamen, thalamus (thal), and cerebellum, all regions commonly recruited during motor actions. Regions that activate jointly seem to maintain a high level of spontaneous correlation at rest. The inset shows the high correlation over about 30 minutes between signal time courses in central sulcus and SMA.

The RSN paradigm

- Not just motor network
- Some patio-temporal ICAs suggest 1000s of networks

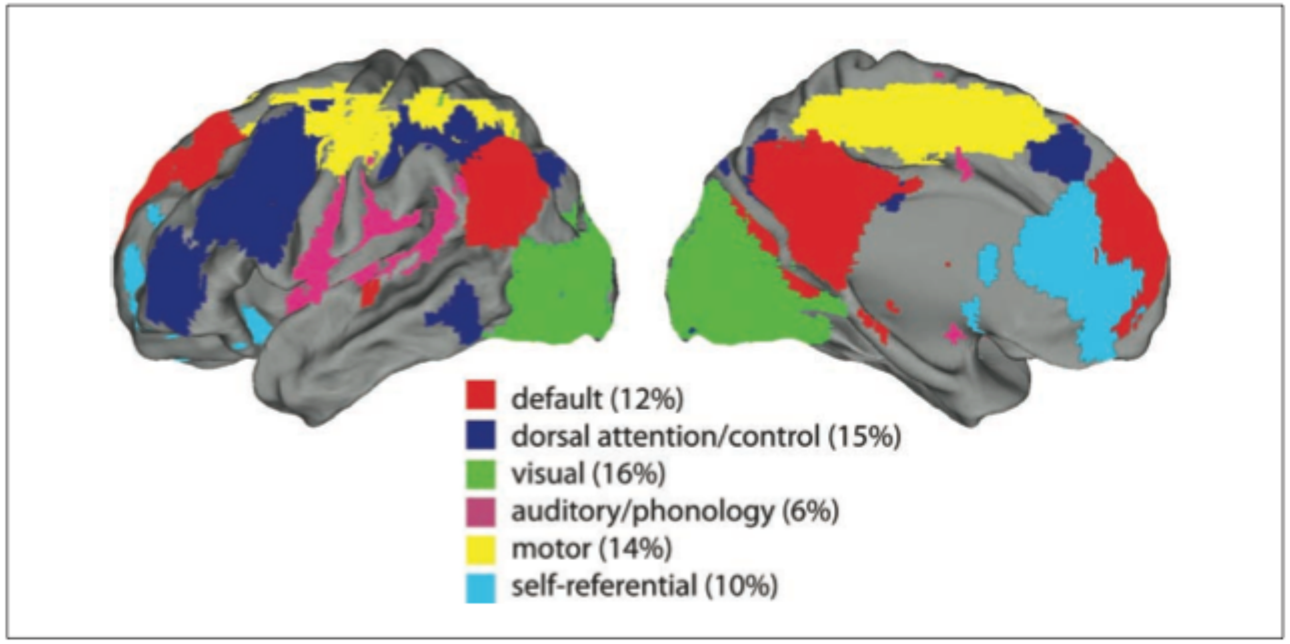
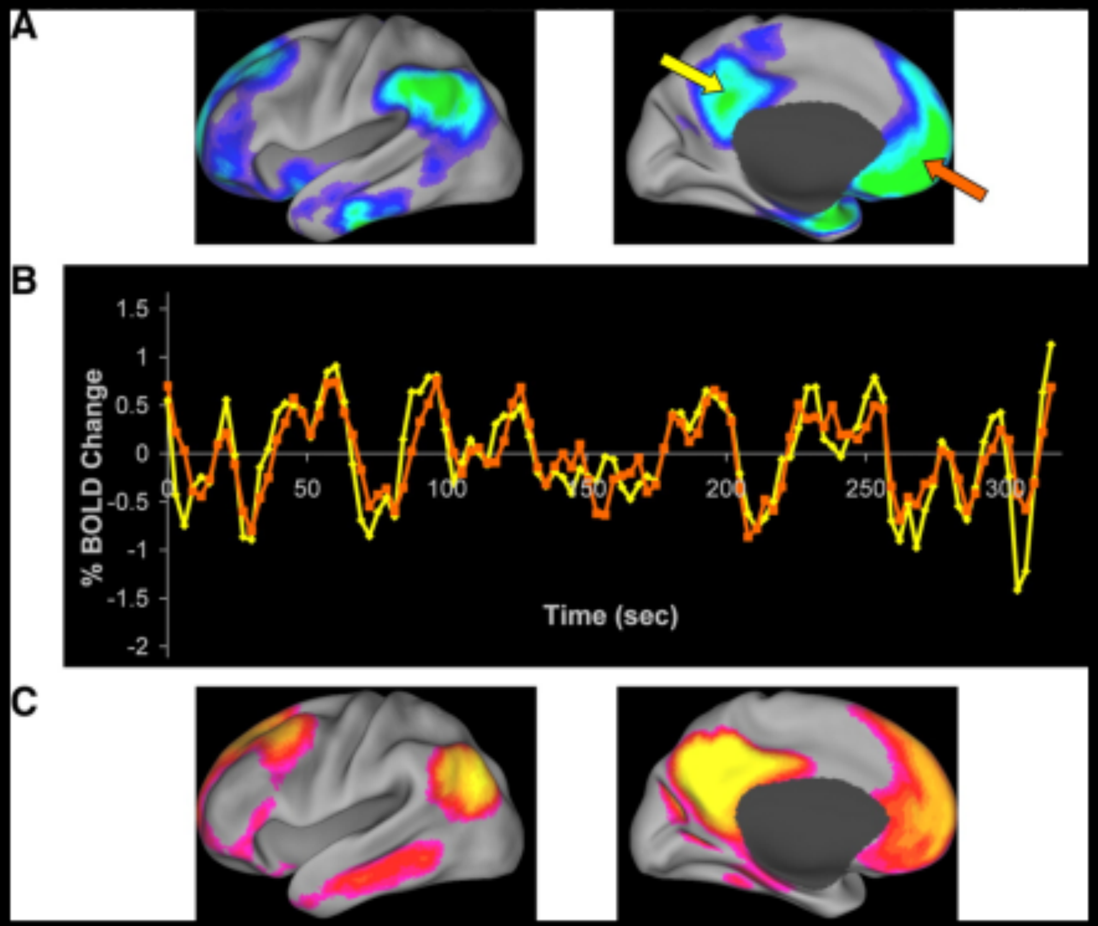


Figure 2. Different identified resting state networks (RSN) onto the same atlas brain covering about 66% of the total brain volume. These RSN are somato-motor, visual occipital and auditory temporal, and several associative networks covering fronto-temporal-parietal cortices (dorsal attention, default, language, and control).

The RSN paradigm

- One network — the Default Mode Network — has received much attention



Fox, Michael D., et al. "The human brain is intrinsically organized into dynamic, anticorrelated functional networks." Proceedings of the National Academy of Sciences of the United States of America 102.27 (2005): 9673-9678.

The RSN paradigm

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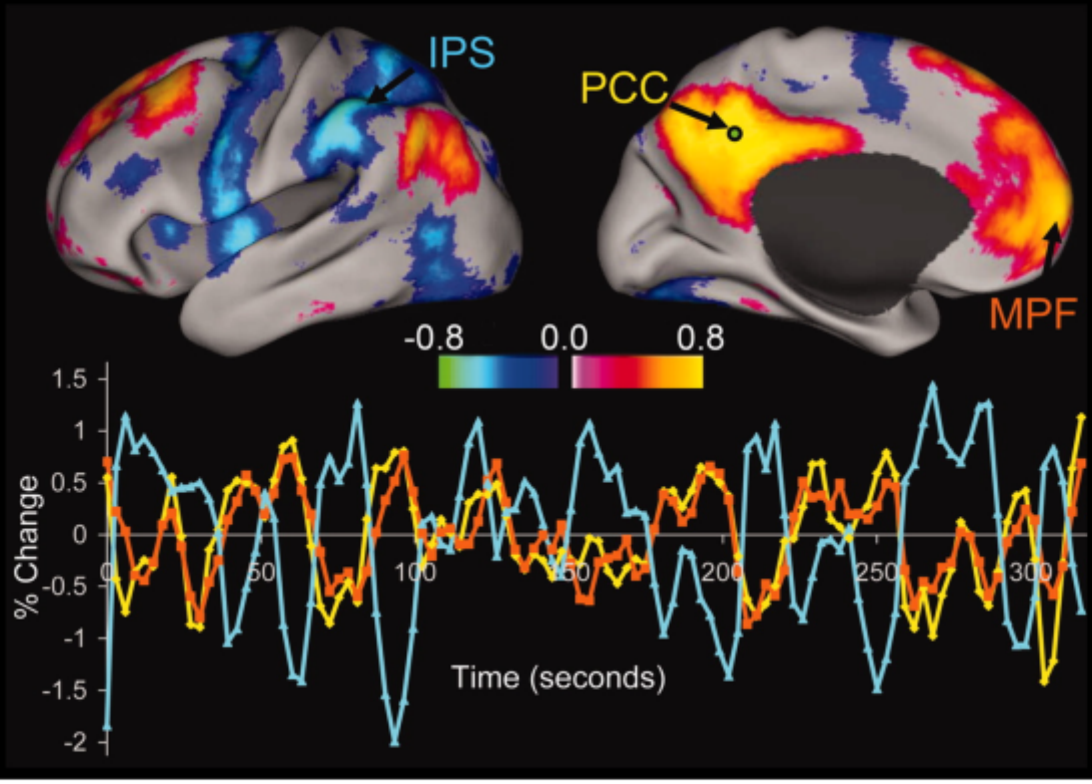


Fox M D et al. PNAS 2005;102:9673-9678

Fox, Michael D., et al. "The human brain is intrinsically organized into dynamic, anticorrelated functional networks." Proceedings of the National Academy of Sciences of the United States of America 102.27 (2005): 9673-9678.

The RSN paradigm

Robinson, Simon, et al. "A resting state network in the motor control circuit of the basal ganglia." BMC neuroscience 10.1 (2009): 1.

- Most spectral power is in low to very-low frequencies
- Dominant networks often show a peak between .01 and .05 Hz (20-100sec)
- The HRF is a filter

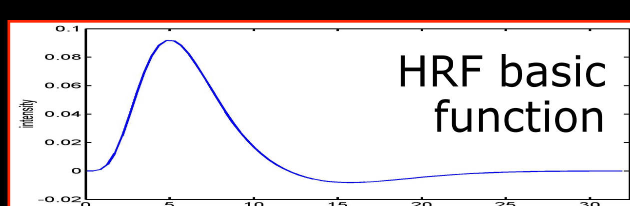
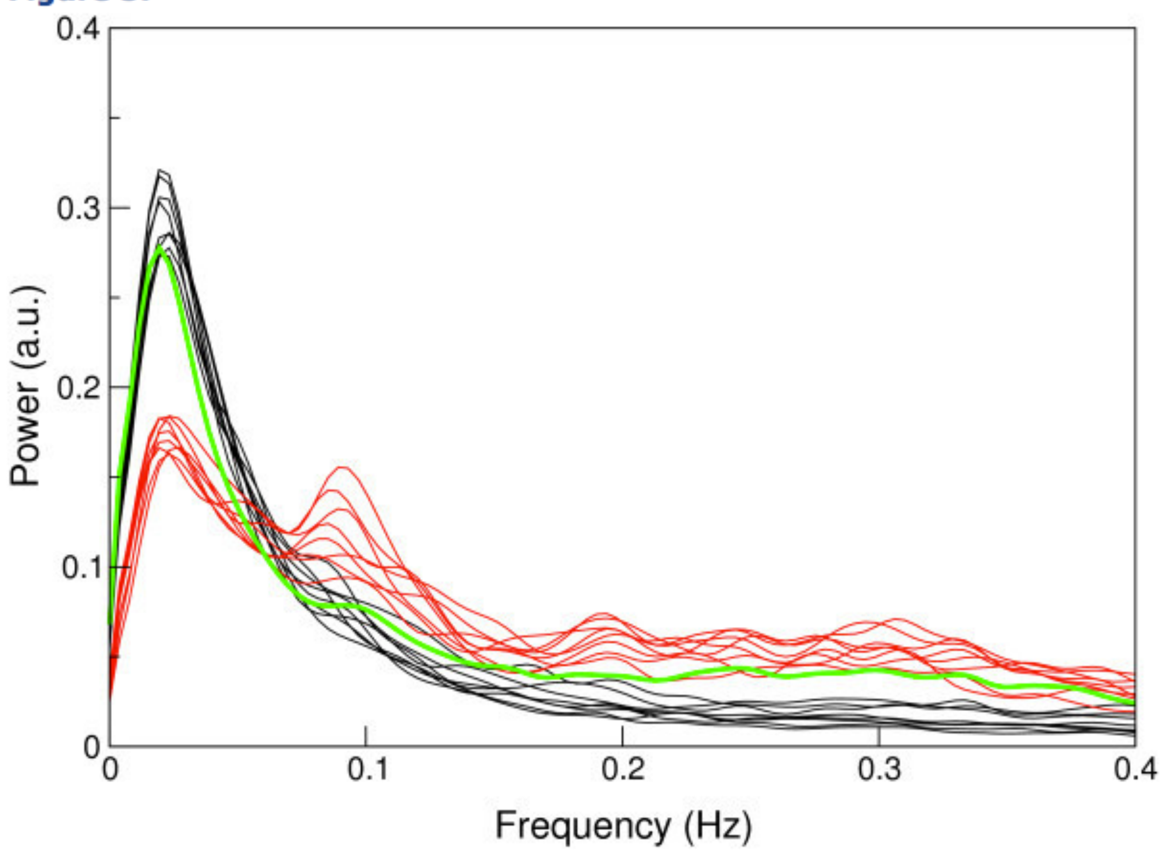


Figure 5.



Comparison of the mean spectral distribution of the basal ganglia RSN component over subjects (green) with the spectral distributions of documented RSNs (black) and physiological components (red).

Robinson *et al. BMC Neuroscience* 2009 **10**:137 doi:10.1186/1471-2202-10-137

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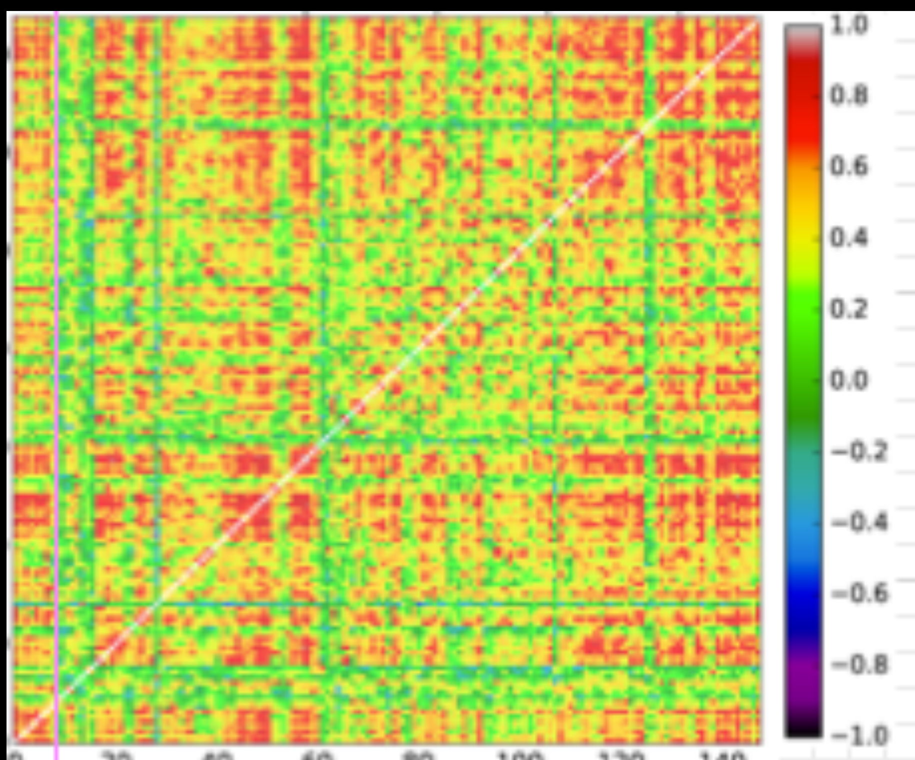
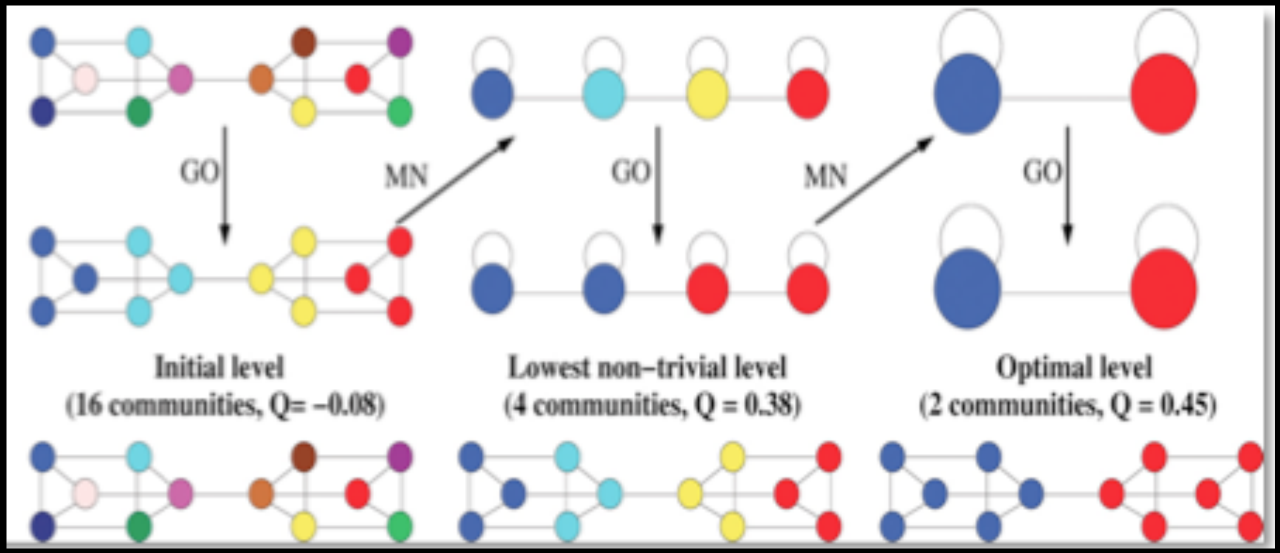
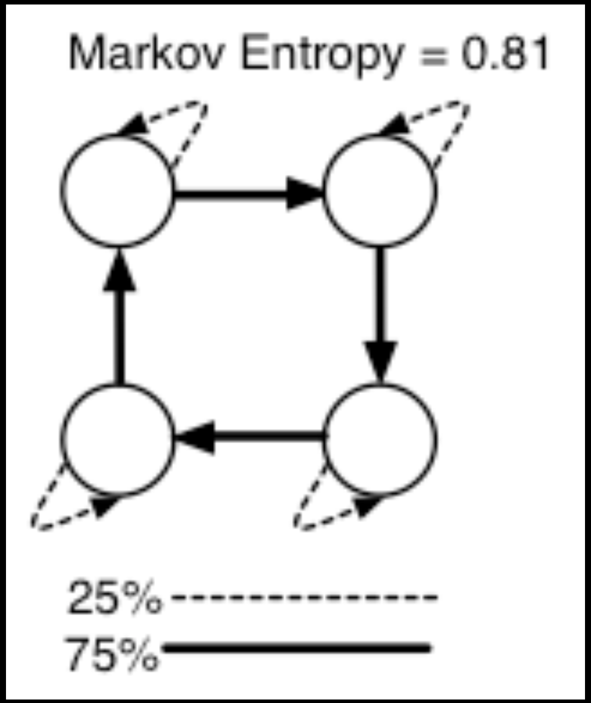
The Network paradigm

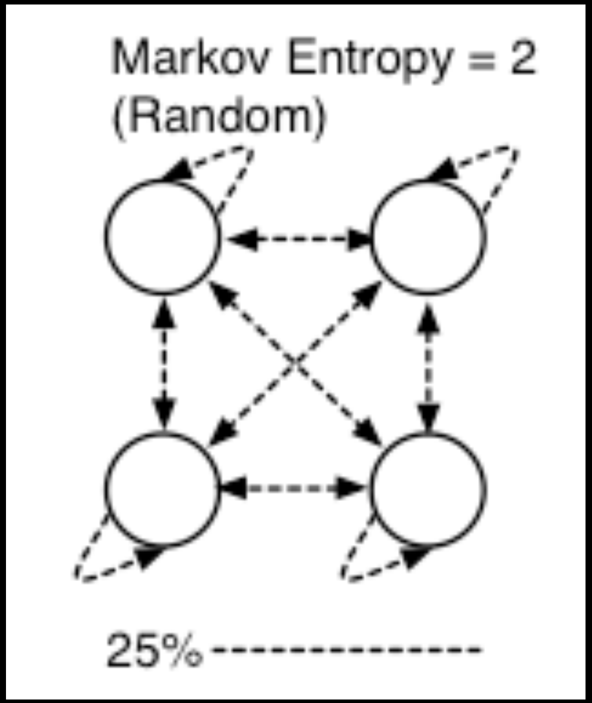


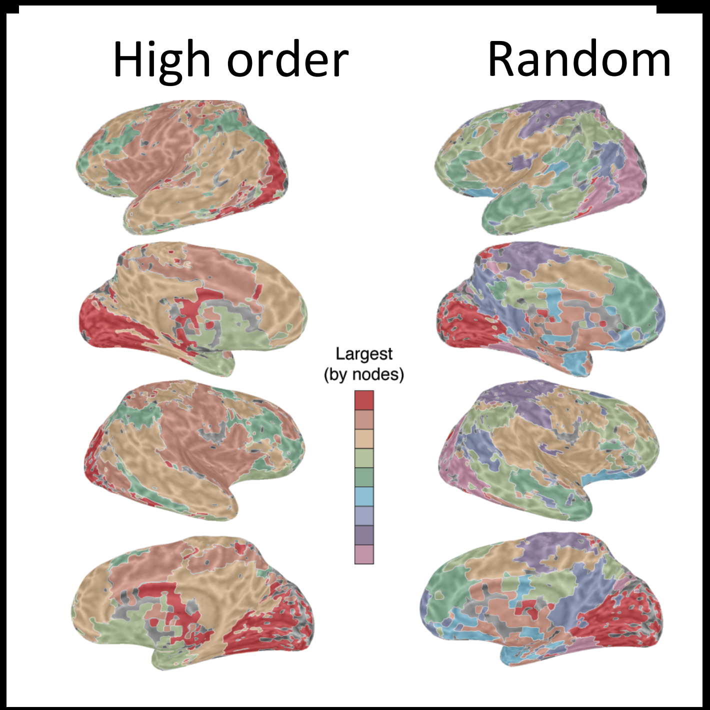


Blondel, Vincent D., et al. "Fast unfolding of communities in large networks." Journal of statistical mechanics: theory and experiment 2008.10 (2008): P10008.

The Network paradigm







Andric, Michael, and Uri Hasson. "Global features of functional brain networks change with contextual disorder." Neuroimage 117 (2015): 103-113.

Fast, non-oscillatory dynamics

<u>Local Peaks</u>

- 70 sec of movie viewing (Skipper et al., 2009)
- Local minima and maxima in a time series (ventral premotor) were identified
- Peaks tend to occur with gestures when gestures are meaningful, but this match does not hold when the movie is accompanied by non-meaningful gestures
- Figure shows 13 peaks in 70sec.

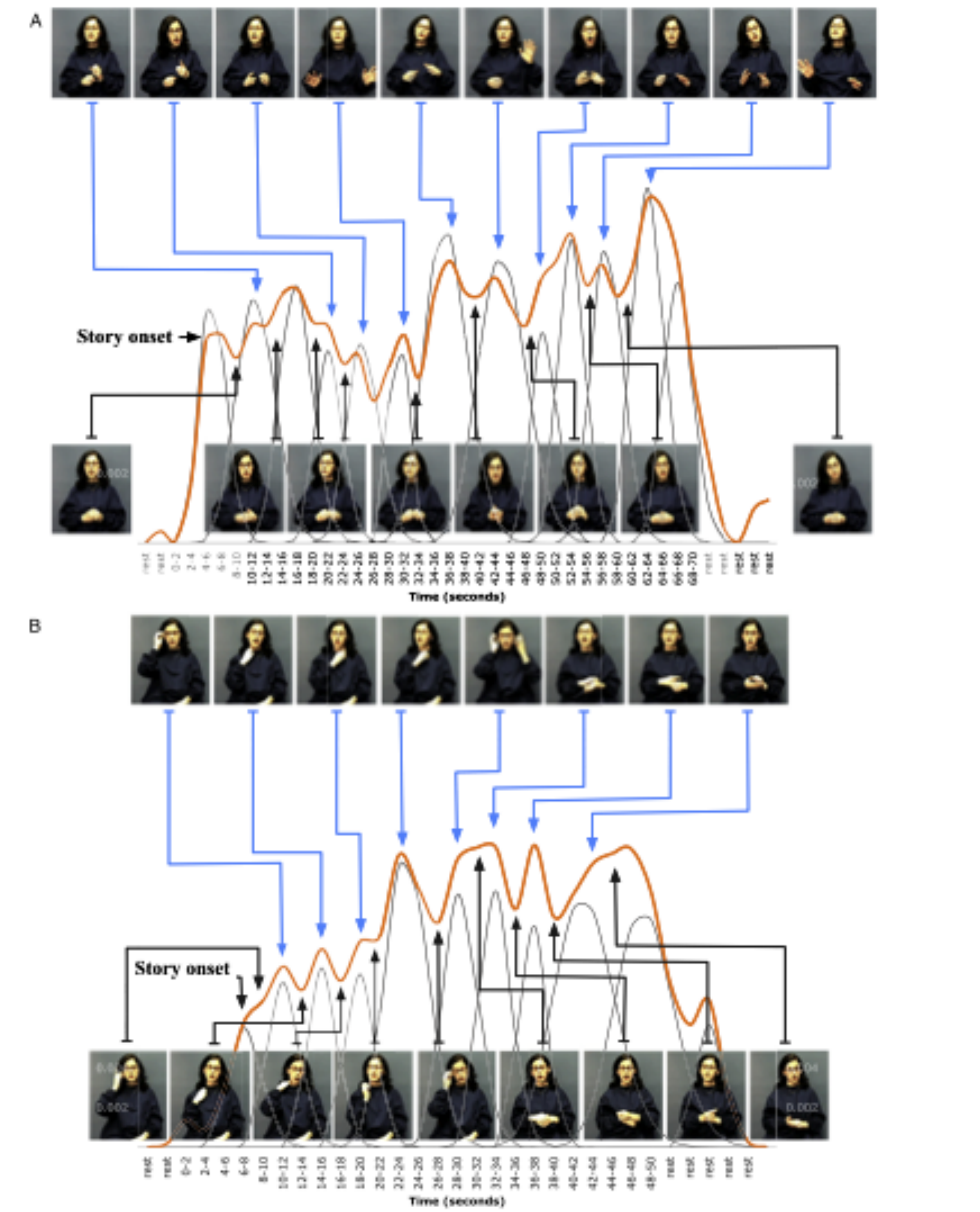


Figure 1. Peak and Valley Analysis of the Gesture or Self-Adaptor Conditions

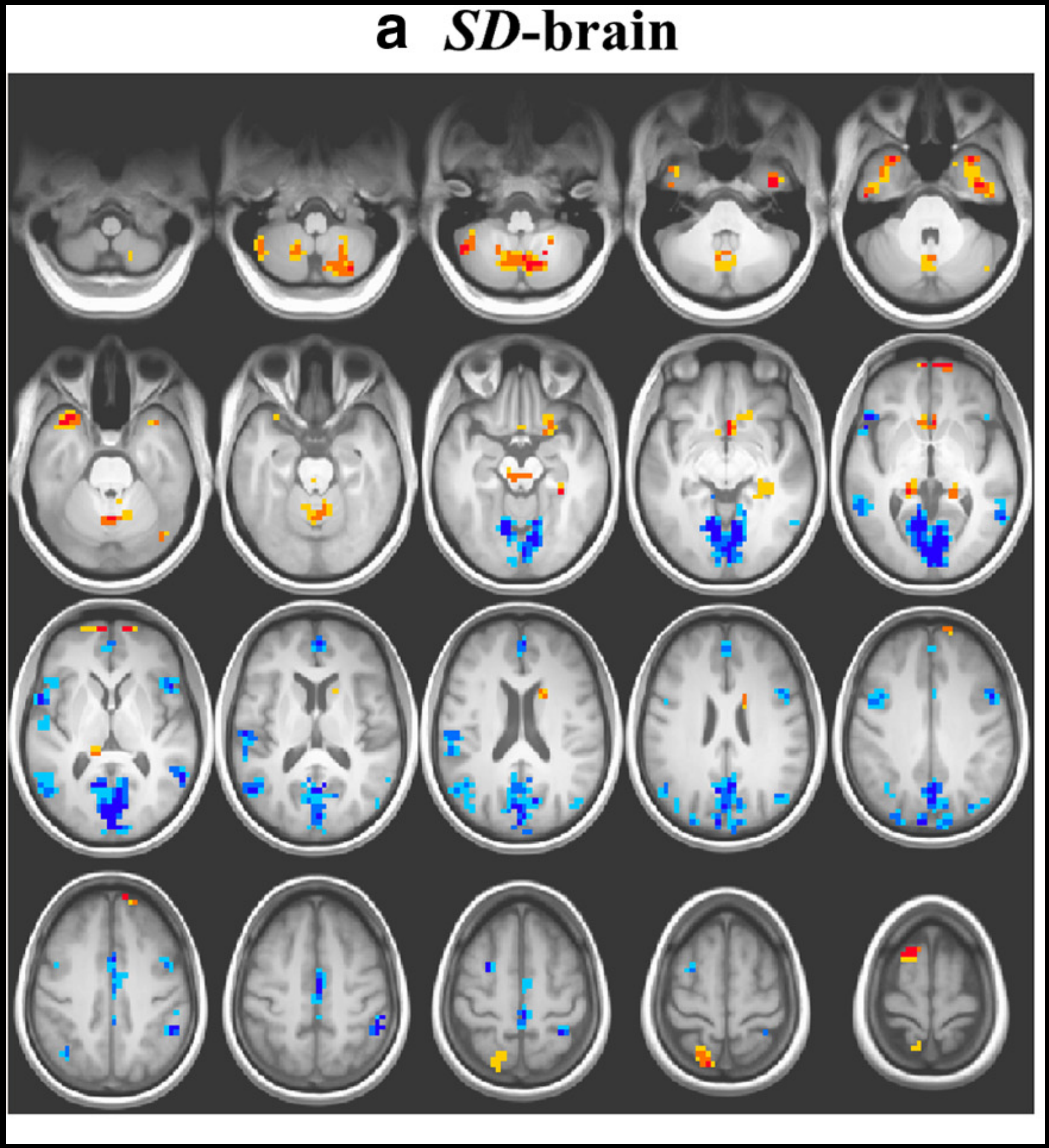
Peaks and valleys associated with the brain's response to the (A) Gesture and (B) Self-Adaptor conditions in ventral pre- and primary motor cortex (PMv; see Figure S2). Frames from the movies associated with peaks are on the top row, and frames associated with valleys are on the bottom. The orange line is the brain's response. Gray lines are the gamma functions fit at each peak in the response that were used to determine which aspects of the stimulus resulted in peaks and valleys (see text). Note that in the Gesture condition (A), cospeech gestures are associated with peaks and hands-at-rest are associated with valleys. In contrast, in the Self-Adaptor condition (B), self-adaptor movements are associated with both peaks and valleys.

Skipper, Jeremy I., et al. "Gestures orchestrate brain networks for language understanding." Current Biology 19.8 (2009): 661-667.

Fast, non-oscillatory dynamics

Standard deviation

- Garrett et al. (2010). Short 20sec epochs of between-task rest epochs contain meaningful variance. Standard deviation in these epochs correlated with chronological age

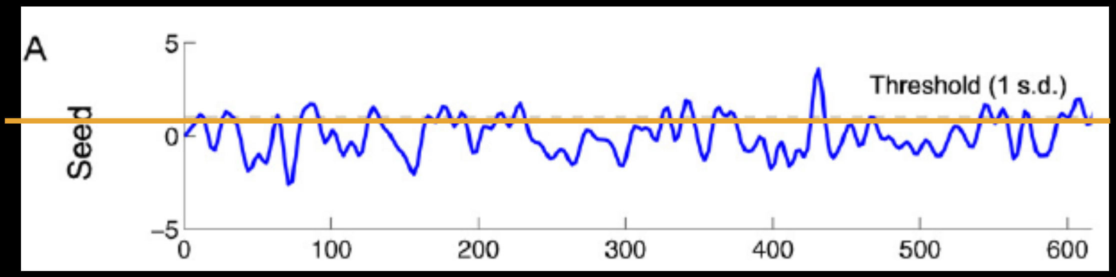


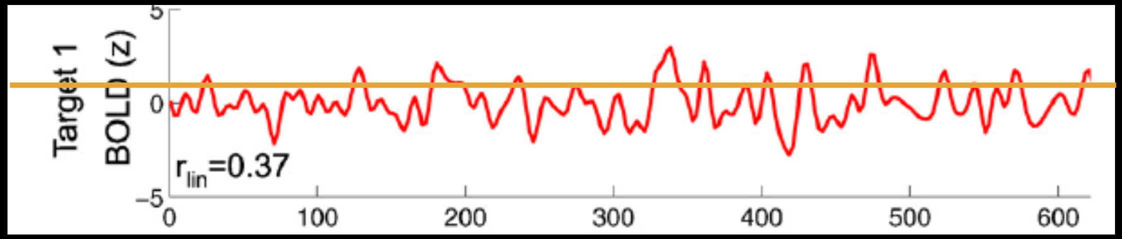
Garrett, Douglas D., et al. "Blood oxygen level-dependent signal variability is more than just noise." The Journal of Neuroscience 30.14 (2010): 4914-4921.

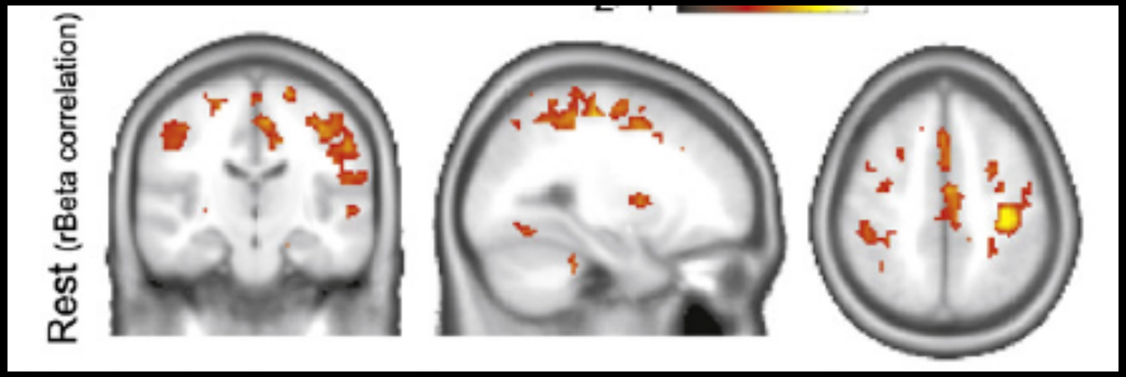
Fast, non-oscillatory dynamics

<u>Phasic events (I)</u>

- Tagliazucchi et al (2010)
- Obtain time series from a certain region (a seed); note 'peaks'
- Tests if there are brain areas showing peaks at the same time and that have the same shape as seed-region peaks
- Find: premotor systems bilaterally peak at similar times





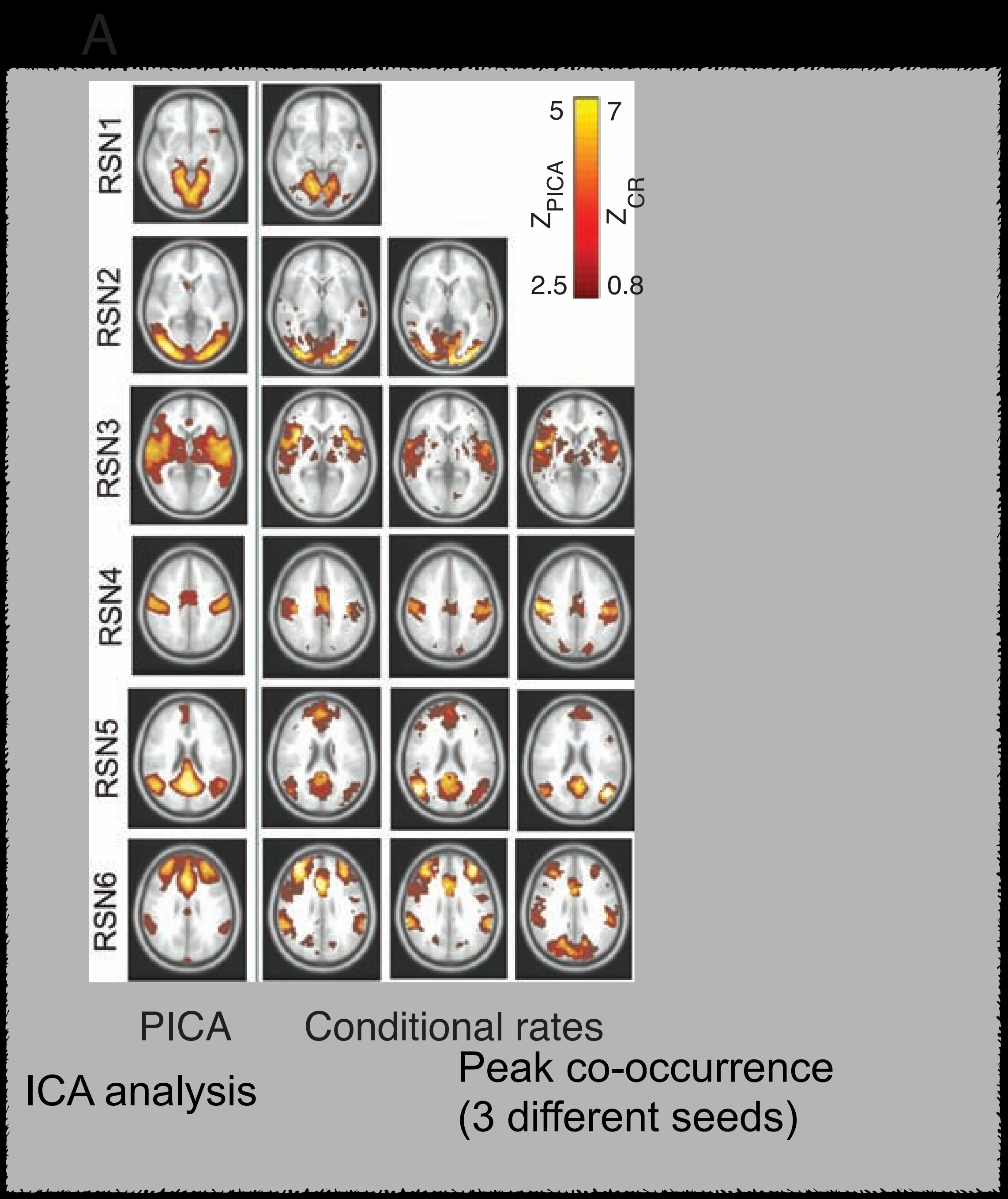


Tagliazucchi, Enzo, et al. "Spontaneous BOLD event triggered averages for estimating functional connectivity at resting state." Neuroscience letters 488.2 (2011): 158-163.

Fast, non-oscillatory dynamics

Phasic events (I)

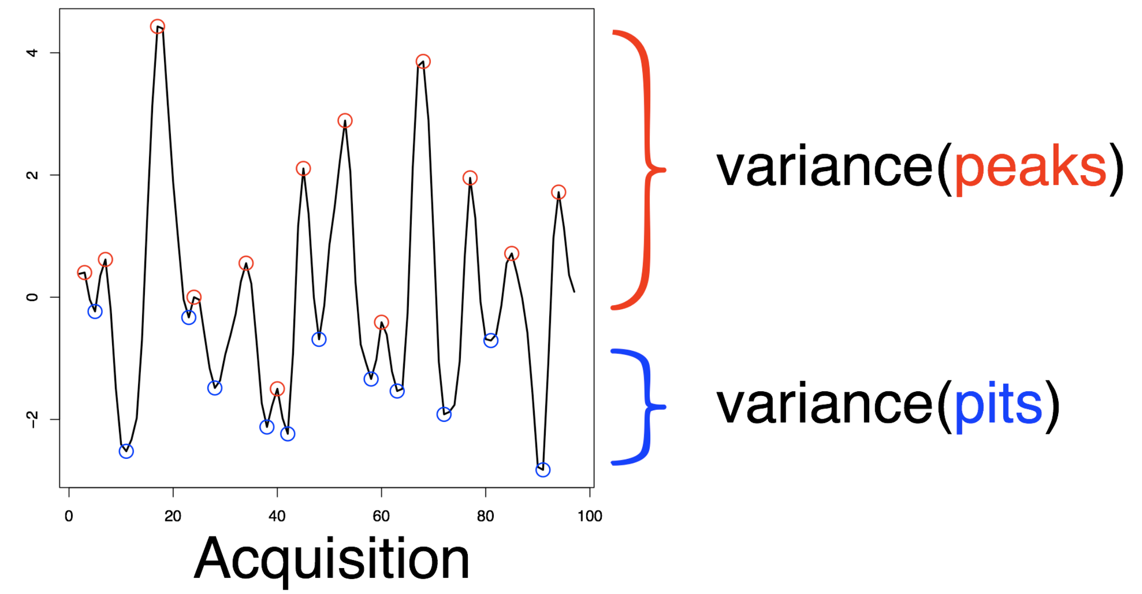
- Tagliazucchi et al (2012)
- The method identifies many well defined RSNs
- 3 (!) points are sufficient to obtain the networks; 5 points already provides high correlation with PCA results.
- Compression ratio of 95%



Fast, non-oscillatory dynamics

Amplitude Variance Asymmetry: basics

- Allows identification of ceiling and floor mode patterns
- Does not index randomness (well behaved and random can have no AVA)
  - Differs from measures of disorder tracking entropy
  - Differs from measures that will return the same value for a time series 'y' and the time series '-1*y'
  - Is not logically correlated with the variance of the time series (consider increasing amplitude of sine wave)



B

Amplitude Variance Asymmetry test per voxel:

Null Hypothesis: Voxel Ratio (VR) = $\sigma^2(\text{peaks})/\sigma^2(\text{pits}) = 1$

Group-level test: $\text{Mean}(\log(VR_1), \log(VR_2)...\log(VR_n)) \neq 1$

Single-participant test: Levene's $W > F(df_a, df_b)$

$df_a = 1;$

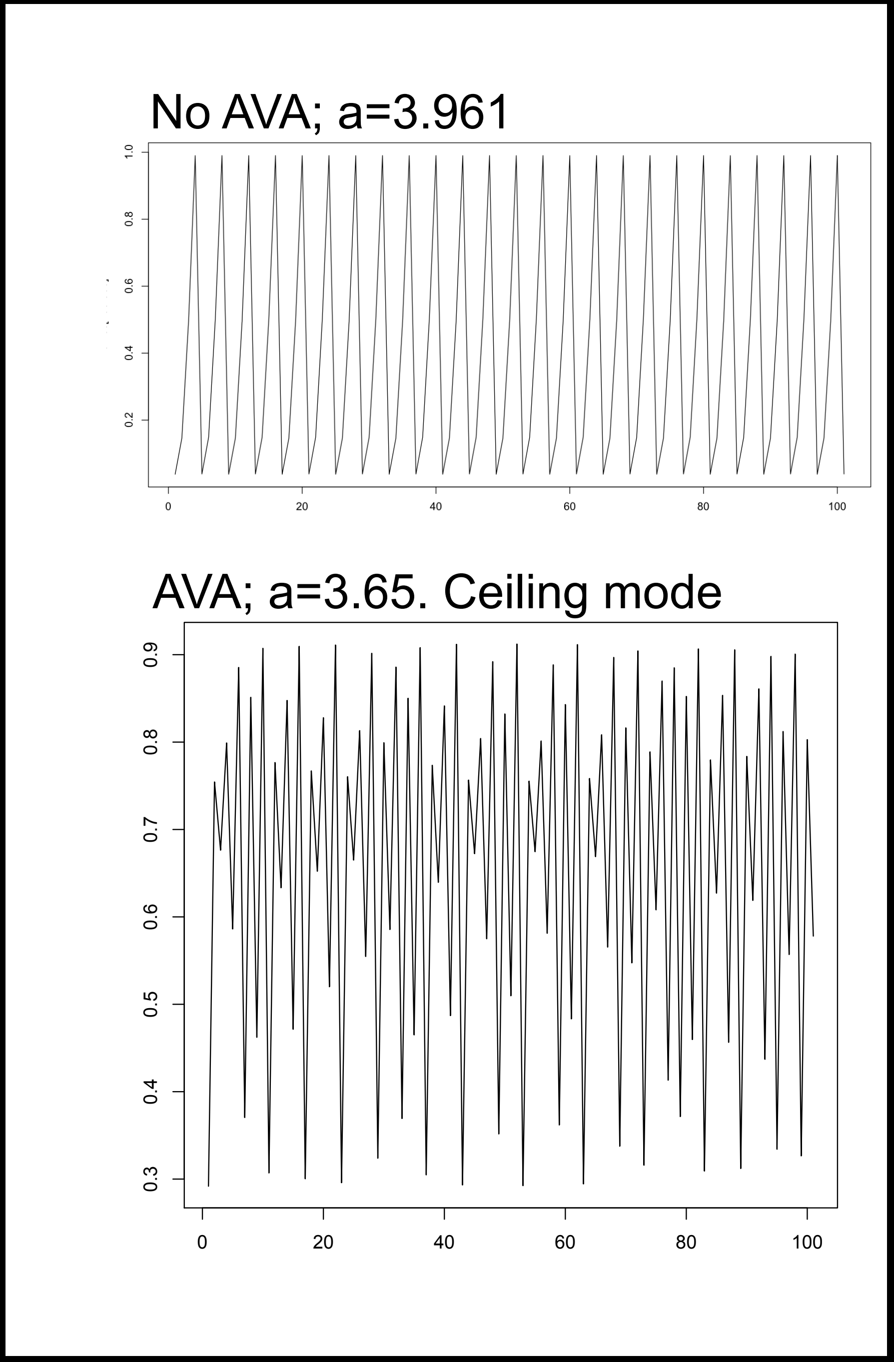
$df_b = N(\text{peaks}) + N(\text{pits}) - 1.$

Davis, Ben, et al. "Functional and developmental significance of amplitude variance asymmetry in the BOLD resting-state signal." Cerebral Cortex (2013): bhs416.

Fast, non-oscillatory dynamics

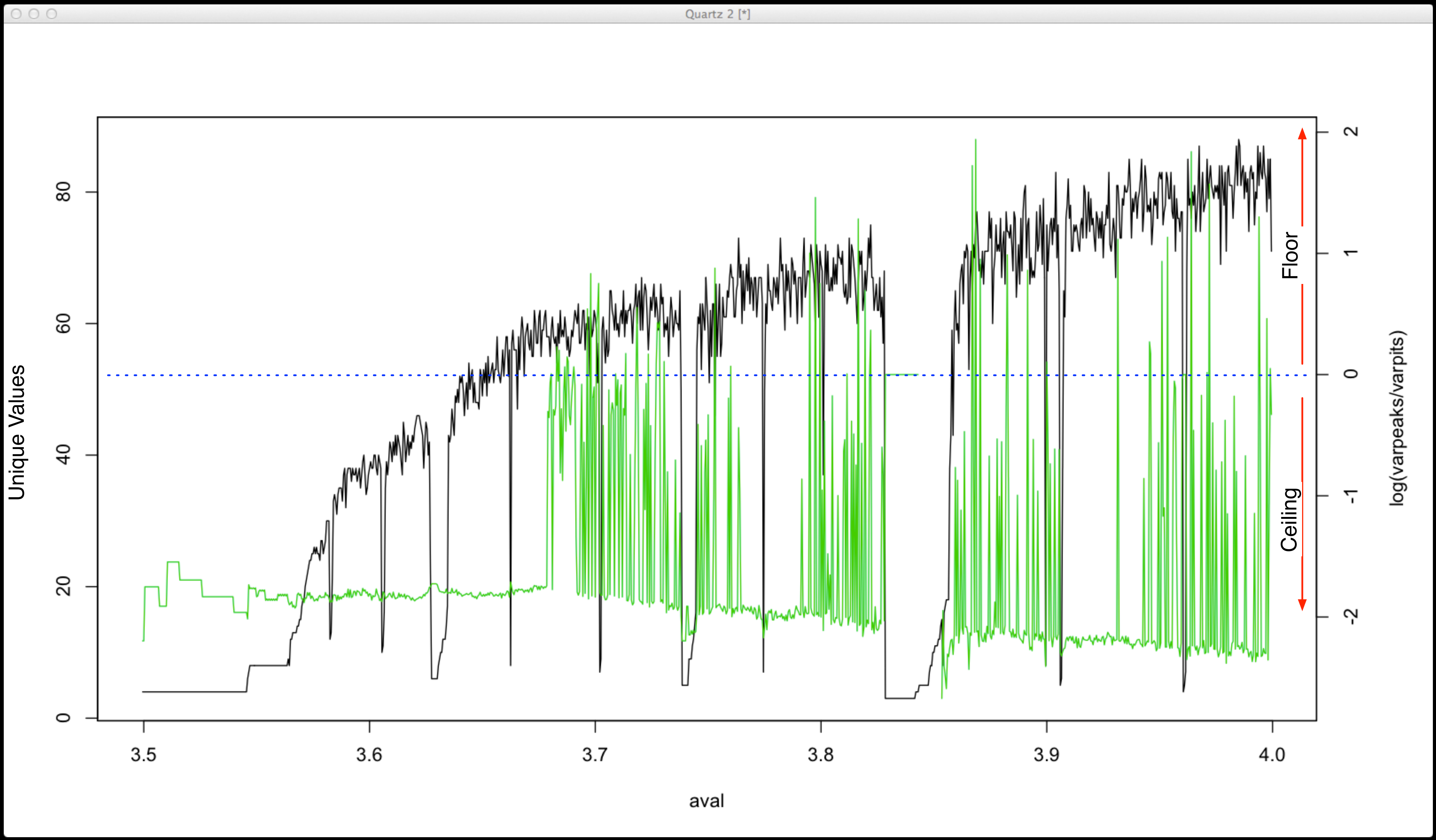
<u>Amplitude Variance Asymmetry: occurring in dynamic systems</u>

- f(x)= a x (1- x) { with 3 < a < 4}
- Simulate 20K element series per each value of a; grab the final 10K, calculate AVA and plot against number of discrete values in the series



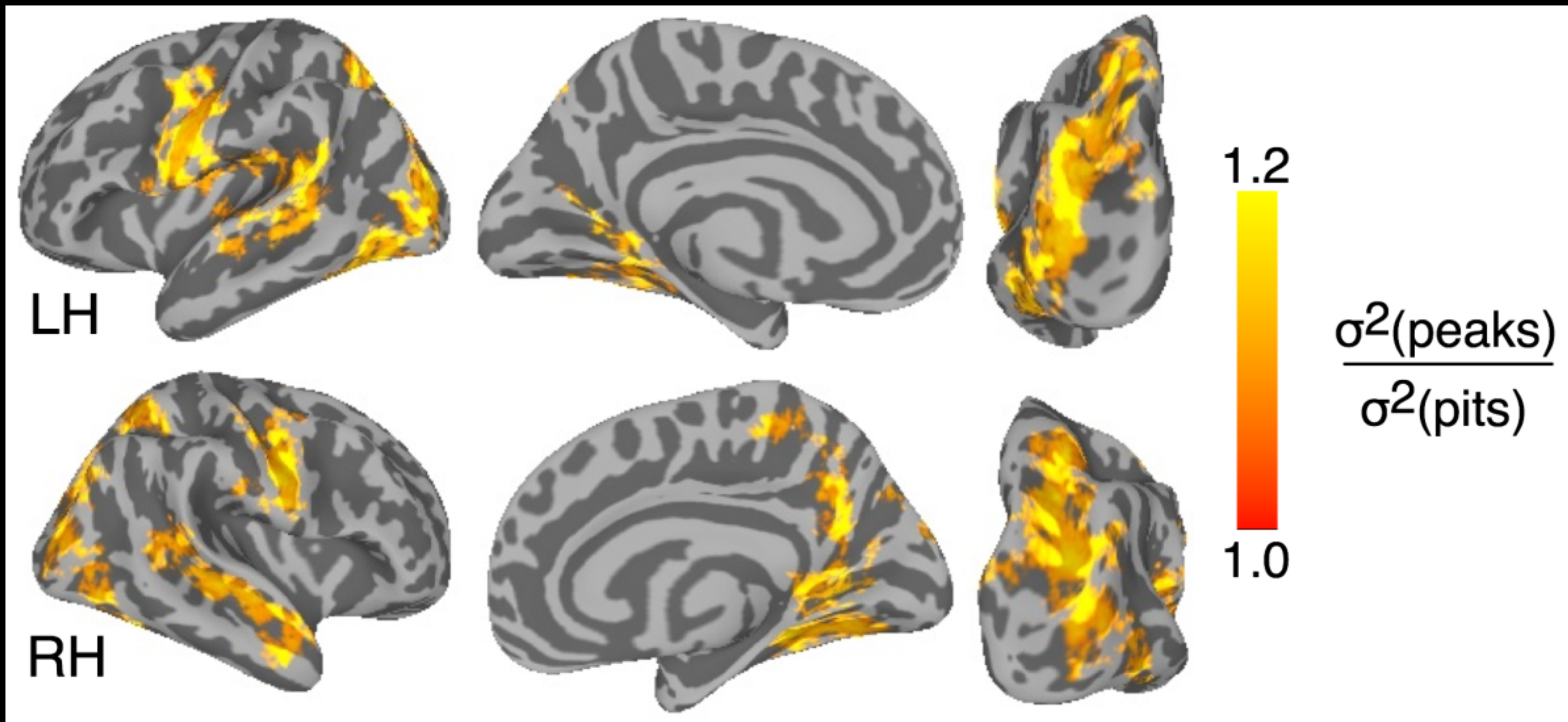
Fast, non-oscillatory dynamics

Amplitude Variance Asymmetry: occurring in dynamic systems



Fast, non-oscillatory dynamics

Amplitude Variance Asymmetry: In the brain



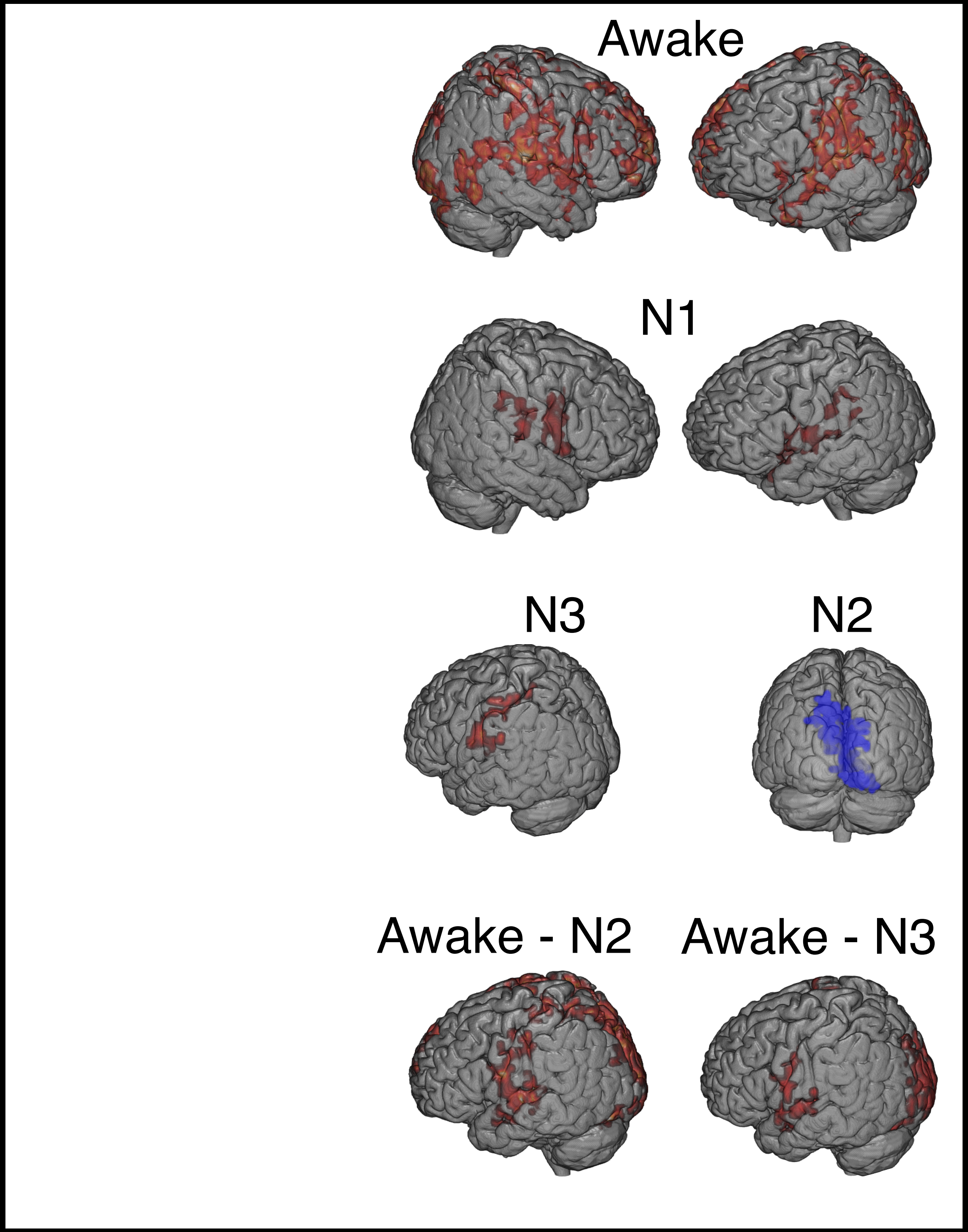
Davis, Ben, et al. "Functional and developmental significance of amplitude variance asymmetry in the BOLD resting-state signal." Cerebral Cortex (2013): bhs416.

Fast, non-oscillatory dynamics

<u>Amplitude Variance Asymmetry: during sleep</u>

- N1: transitional sleep; associated with loss of posterior alpha
- N2, N3: Non REM sleep
- N3: slow wave

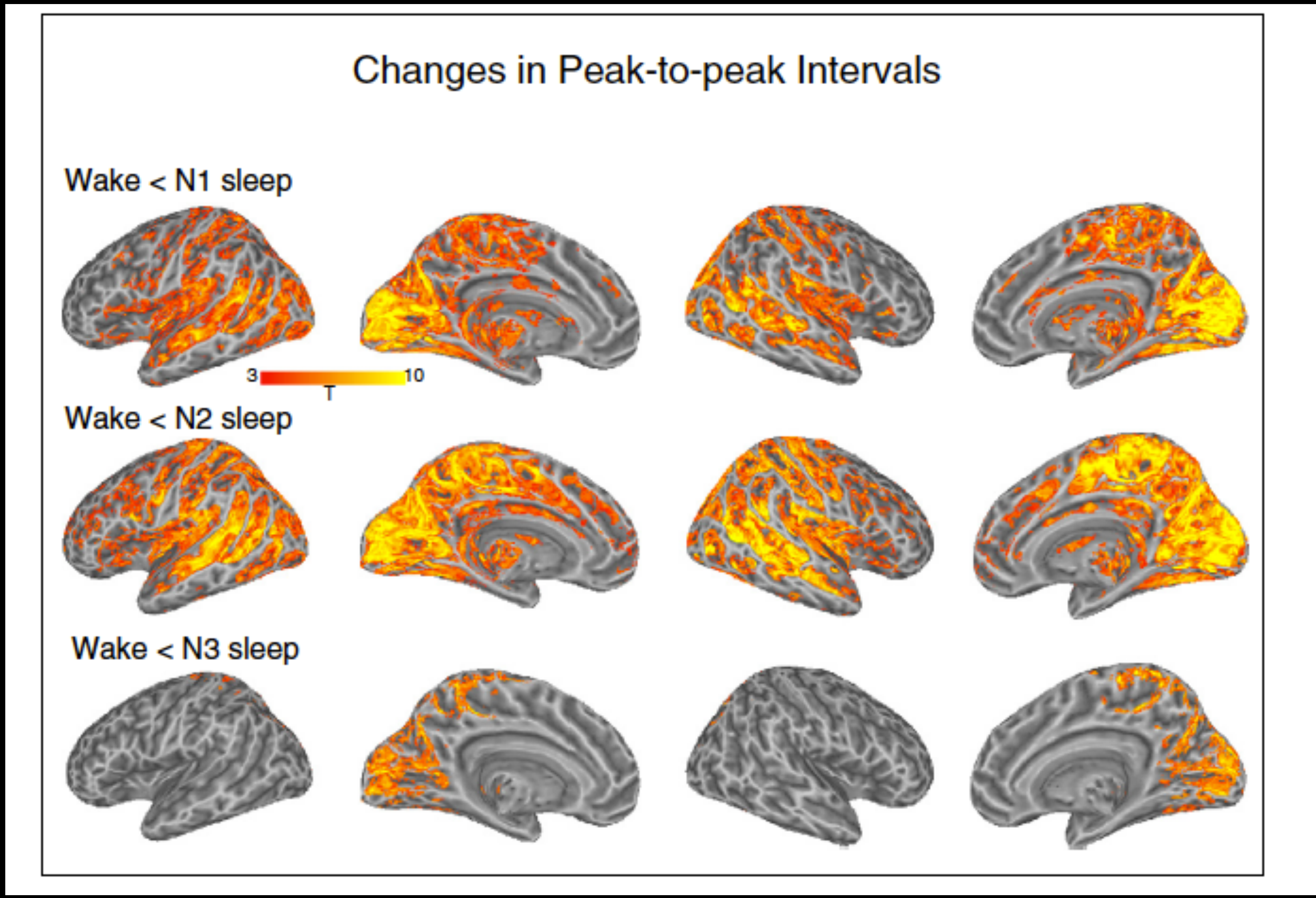
Davis, Ben, et al. "Progression to deep sleep is characterized by changes to BOLD dynamics in sensory cortices." NeuroImage 130 (2016): 293-305.



Fast, non-oscillatory dynamics

Amplitude Variance Asymmetry: during sleep

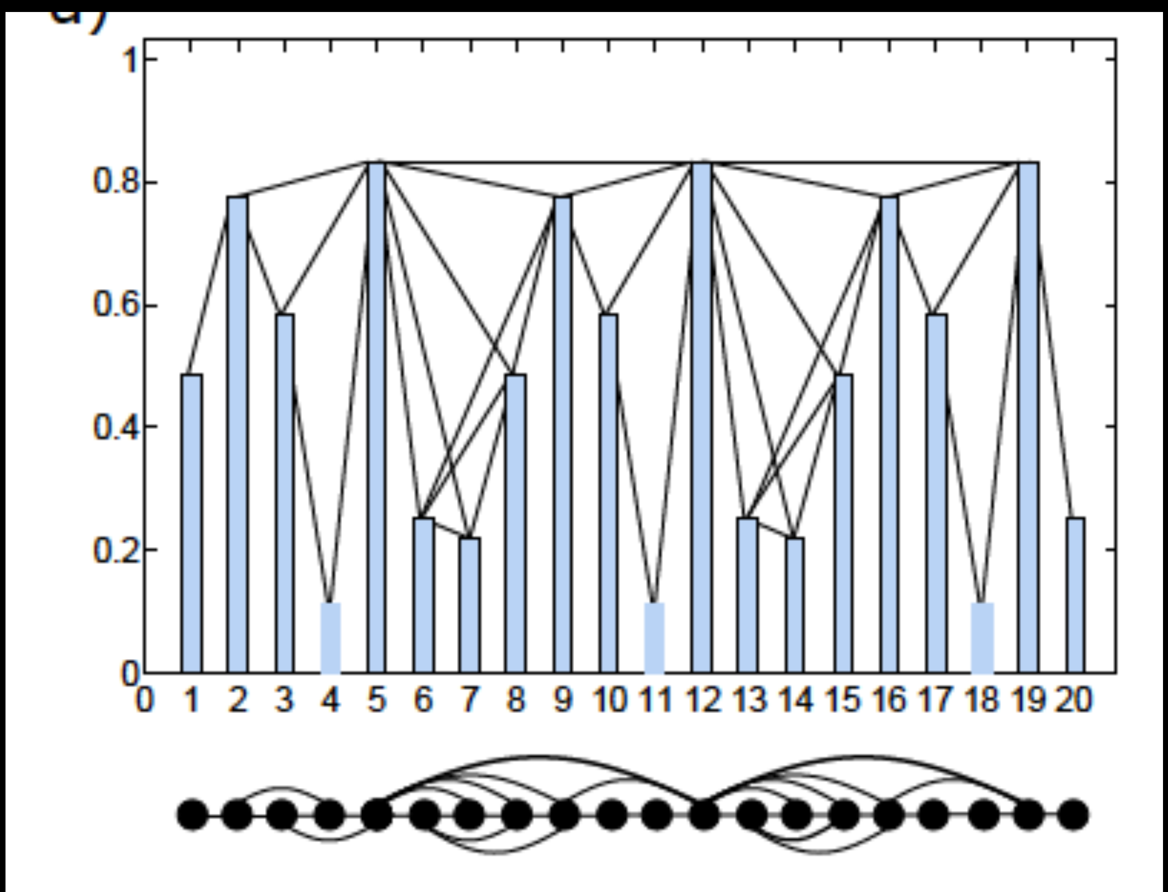
- Peak-to-peak intervals shorter during wakefulness
- Contain more information than AVA

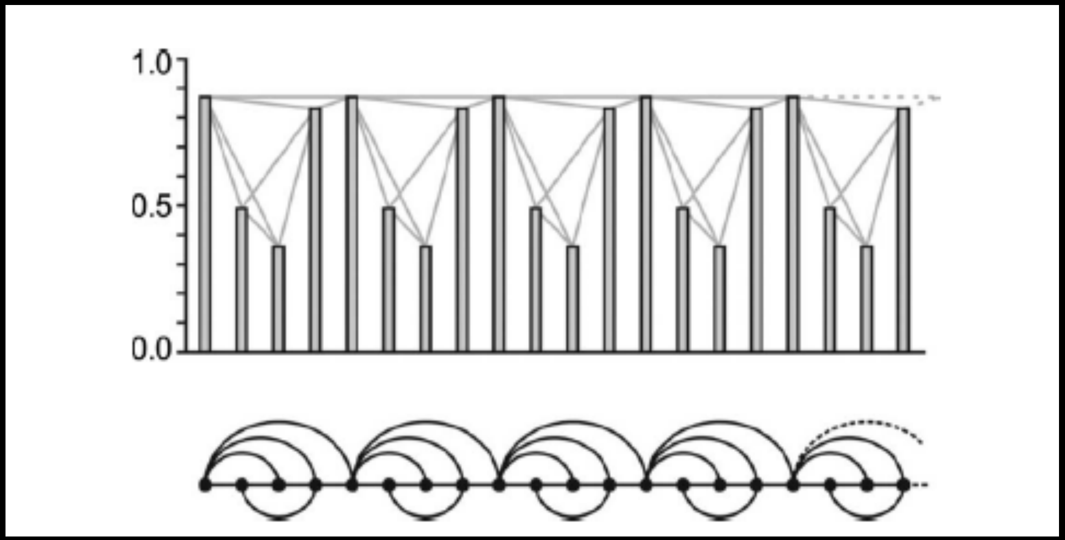


Davis, Ben, et al. "Progression to deep sleep is characterized by changes to BOLD dynamics in sensory cortices." NeuroImage 130 (2016): 293-305.

Fast, non-oscillatory dynamics

Amplitude Variance Asymmetry:
moving on





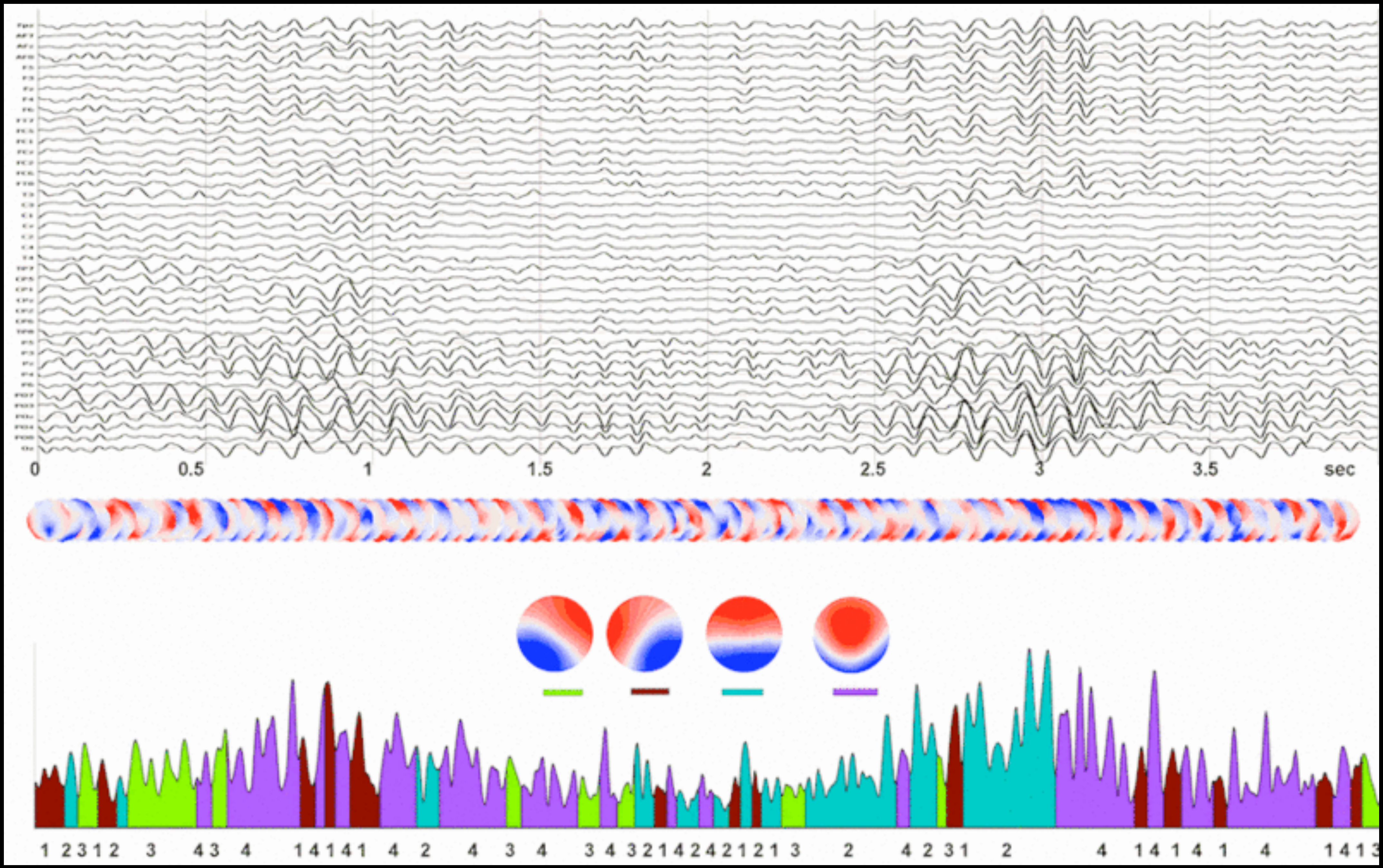
Lacasa, Lucas, et al. "From time series to complex networks: The visibility graph." Proceedings of the National Academy of Sciences 105.13 (2008): 4972-4975.

Lacasa 2009; visibility graphs

Micro states and Motifs

- Spatio-temporal building blocks of continuous activity (Britz et al., 2010)
- State: configuration of spatial activity that holds for some time.
- Spatio-temporal clustering identifies states

Britz, Juliane, Dimitri Van De Ville, and Christoph M. Michel. "BOLD correlates of EEG topography reveal rapid resting-state network dynamics." Neuroimage 52.4 (2010): 1162-1170.


0
0.5
1
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3
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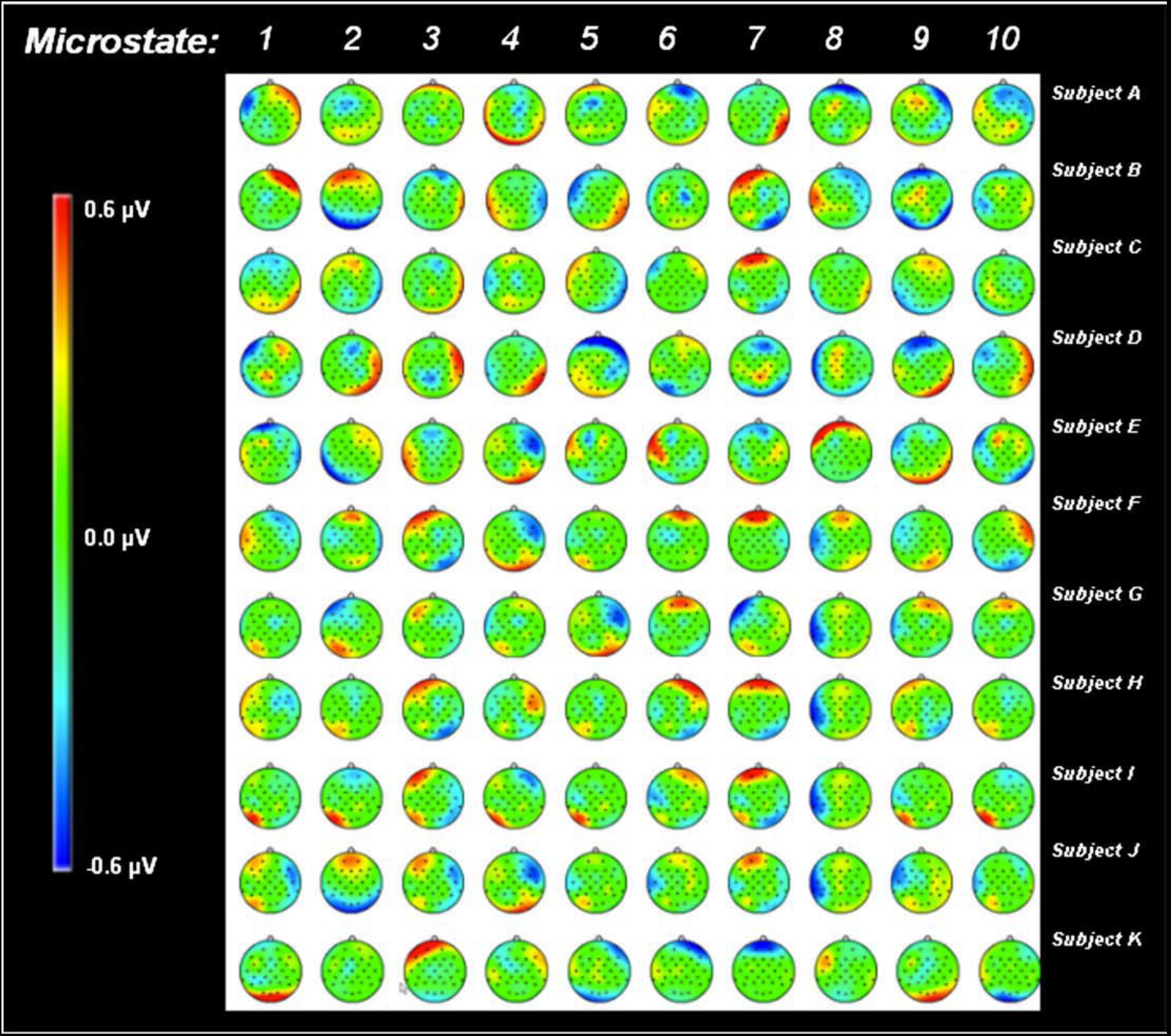
sec
1 2 3 1 2 3 4 3 4 1 4 1 4 1 4 2 4 3 4 3 4 3 2 1 4 2 4 2 1 2 1 3 2 4 2 3 1 2 4 1 4 1 4 1 4 1 4 1 3

4sec EEG map


Microstate:
1
2
3
4
5
6
7
8
9
10
0.6 µV
0.0 µV
-0.6 µV
Subject A
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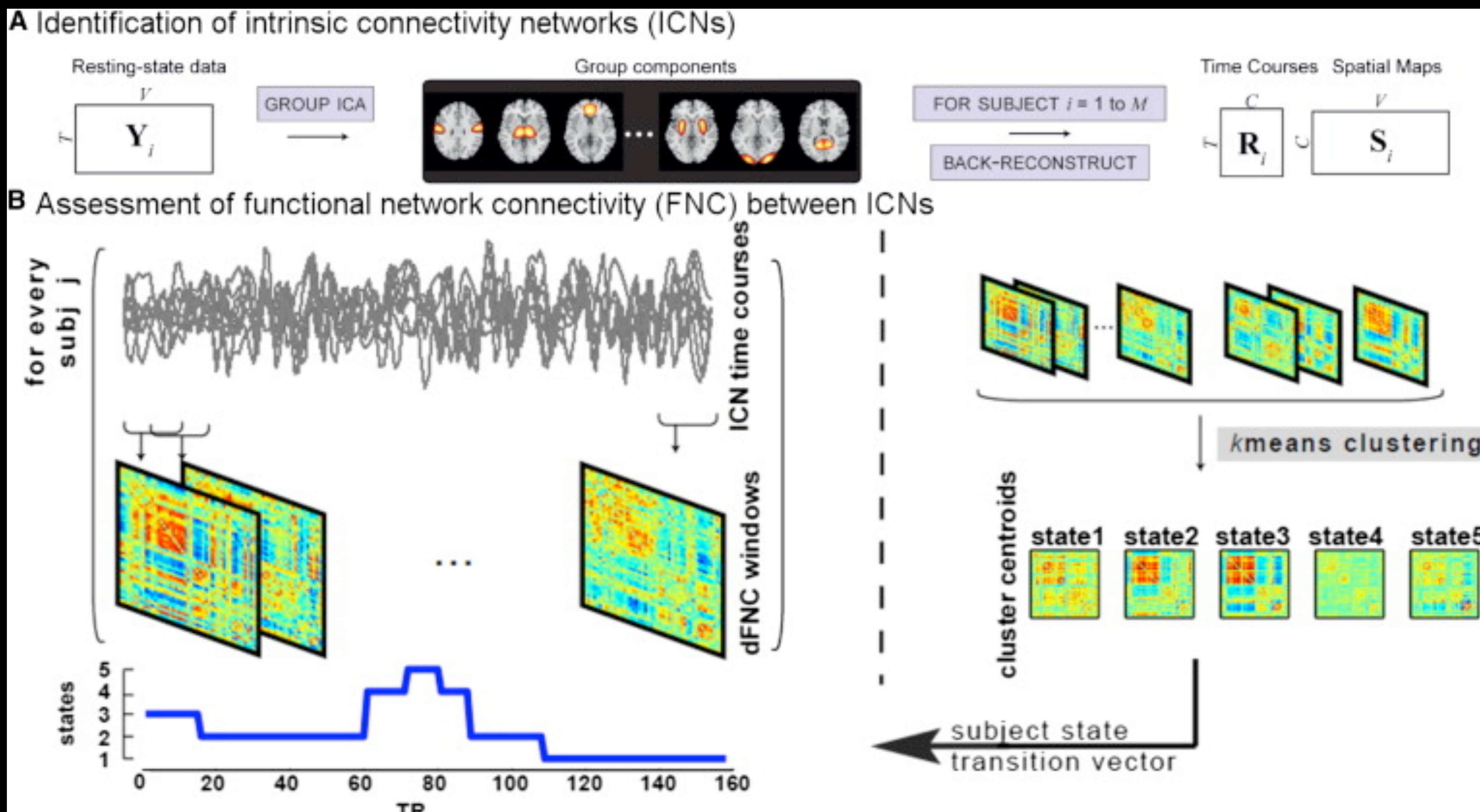
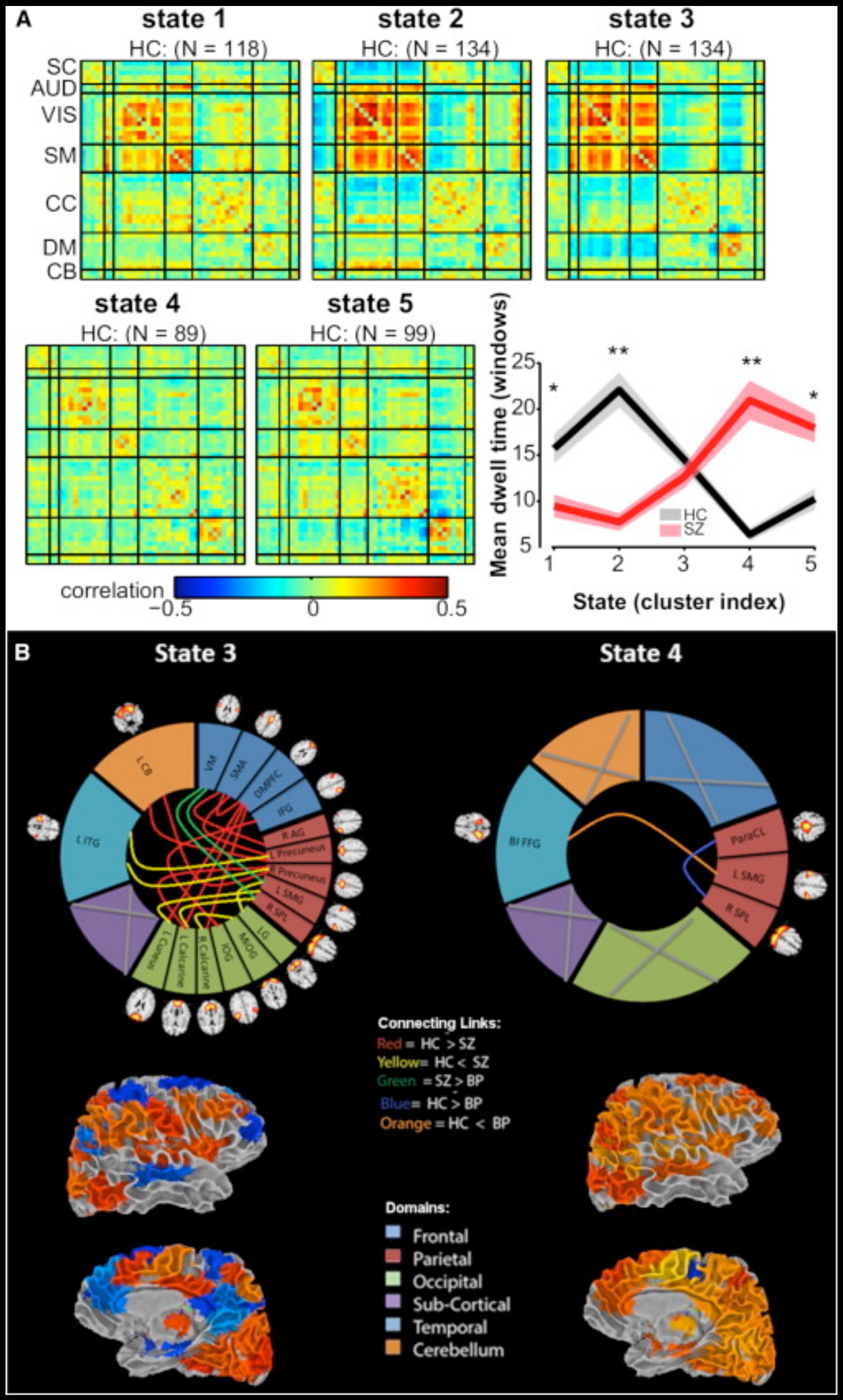
Subject C
Subject D
Subject E
Subject F
Subject G
Subject H
Subject I
Subject J
Subject K

Time-dependent networks in fMRI: chronnectome



Calhoun et al., 2015 Motifs in connectivity of eigenvectors

Time-dependent networks in fMRI: chronnectome



- Schizophrenics spend longer in state 4 (less connected state)

Calhoun et al., 2015

What next

- 1. There *are* technologies within neuroinformatics for storing and sharing neuroimaging data —> limited to files and metadata. There is not work that can be done on the time series directly as stored in any sort of database that allows searches
- 2. Identification of repeated patterns; approximate searches will be important! Allows us to verify whether to psychological states or populations that may manifest slight but systematic differences in manifestation of a pattern. Motif discovery will become central.
- 3. Real-Time MEG, fMRI – what is the person thinking about? What finger/hand would he want to move? Did this activity tend to precede an error/hand moving in the last session ("*show me all time windows that, in this session, followed the current pattern*").
- 4. Adapting to multivariate data – extend for purposes of search and classification.
- 5. How do we merge approaches? Isax indexing depends on domain knowledge (length of time series you will search for). Can the 'time series' indexed in the database reflect fluctuations in these features.
- 6. From time series to local source. local peak fitting