The quest for consistency: How to *not* construct functional brain networks

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3.6.2020

Slides: https://github.com/onerva-korhonen/presentations/blob/master/wins-030620.pdf

Why is the brain a network?

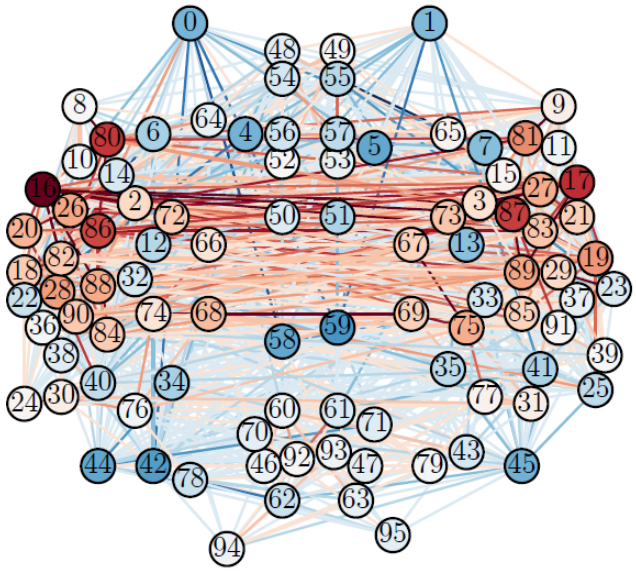
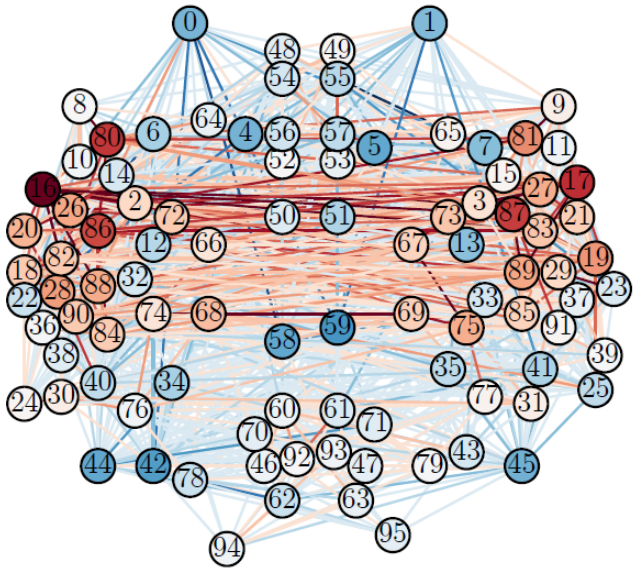


Fig: Alakörkkö *et al.* 2017, *European Journal of Neuroscience*

- Brain = a system of neurons
  - Separated neurons tend to reconnect

Why is the brain a network?



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- Axon bundles connect brain areas

Why is the brain a network?

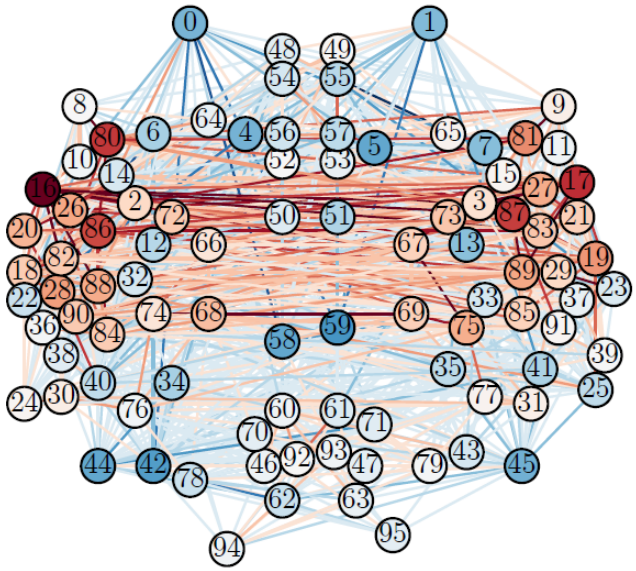


Fig: Alakörkkö *et al.* 2017, *European Journal of Neuroscience*

- Brain = a system of neurons
  - Separated neurons tend to reconnect
- Axon bundles connect brain areas
- Cognitive tasks require collaboration of brain areas

Network neuroscience

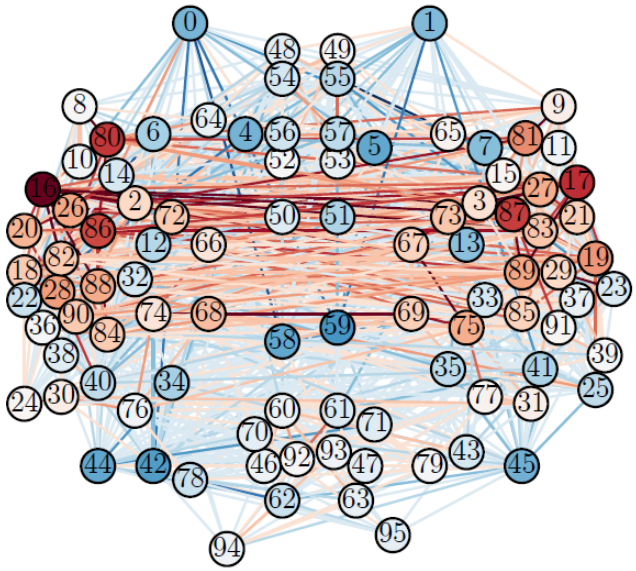


Fig: Alakörkkö *et al.* 2017, *European Journal of Neuroscience*

- Network neuroscience (Muldoon & Bassett 2016, Bassett & Sporns 2017) = applying network tools on the brain
- Two aims:
  1. Understand the healthy brain
  2. Find causes of diseases
- Broad scales:
  - Molecule – neuron – brain area – human
  - Milliseconds – years
- Different brain networks:
  - Structural: anatomic connections
  - Functional: temporal coactivation
  - Effective: causality

Functional networks: fMRI

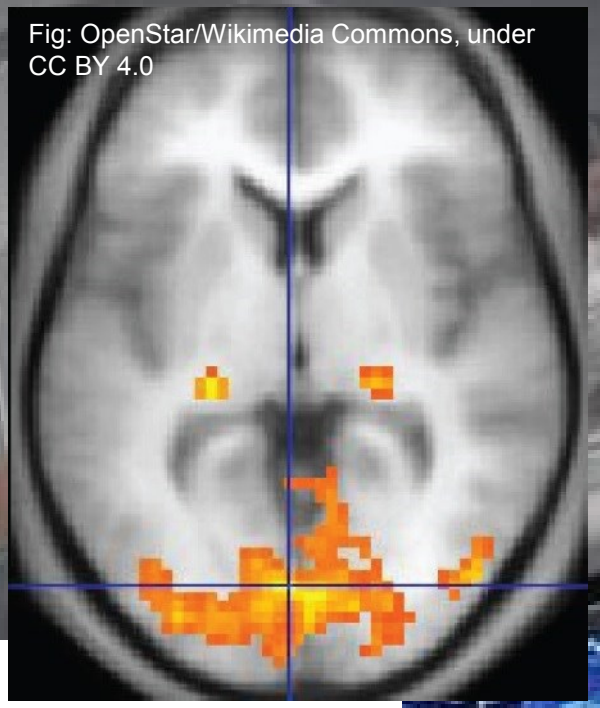


Fig: OpenStar/Wikimedia Commons, under CC BY 4.0

- Based on magnetic properties of haemoglobin
- Oxygen-rich and oxygen-poor haemoglobin behave differently in a (strong) magnetic field
  => **oxygen-rich areas localized**
- Brain function requires oxygen
  => **high oxygen level = high activity**
- Measurement unit = voxel

- High (~mm) spatial resolution, low (~s) temporal resolution

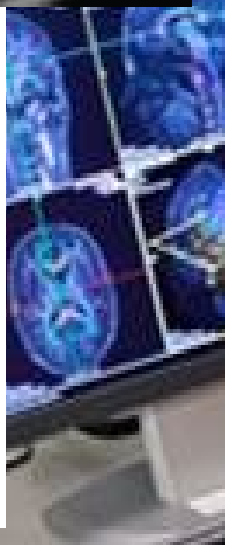


Fig: Aalto Magnetic Imaging (AMI Center), by permission

Functional networks: EEG & MEG

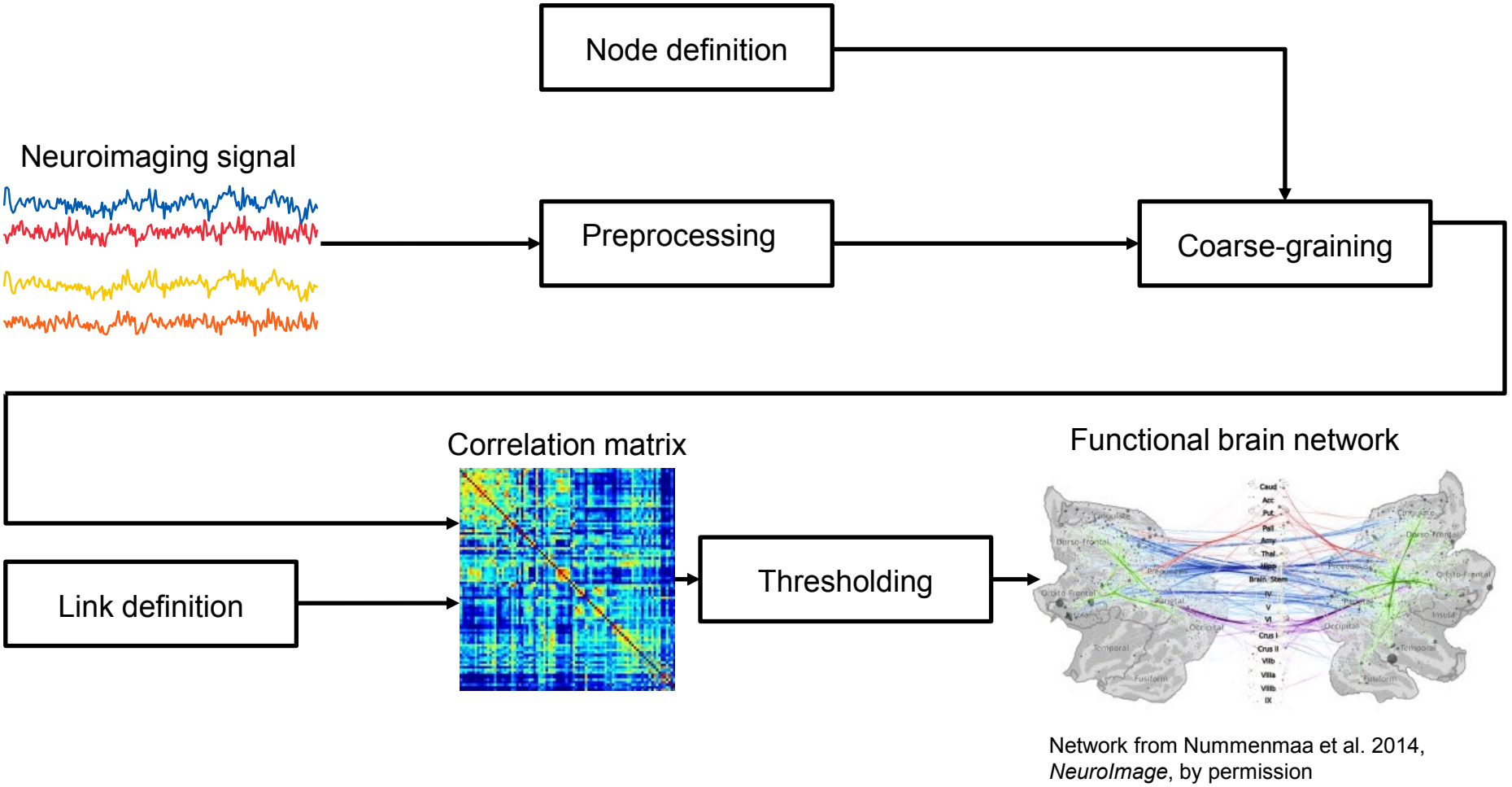

Fig: Chris Hope/Wikimedia Commons, under CC BY 2.0


Fig: Wikimedia Commons, public domain

- Neurons interact electrically
- EEG: the electrical field of the brain
- MEG: the magnetic field of the brain
- Inverse model: time series of brain surface vertices

- Excellent (~ms) temporal resolution, lower spatial resolution

Functional networks: how-to?

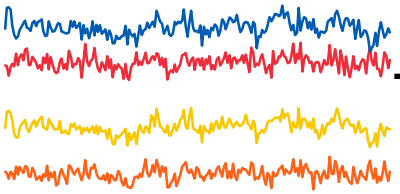


Network from Nummenmaa et al. 2014, *NeuroImage*, by permission

Functional networks: how-to?

Node definition

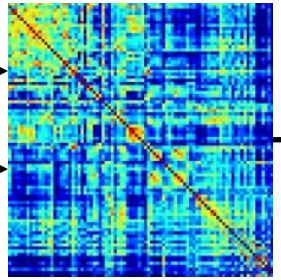
Neuroimaging signal



Preprocessing

Coarse-graining

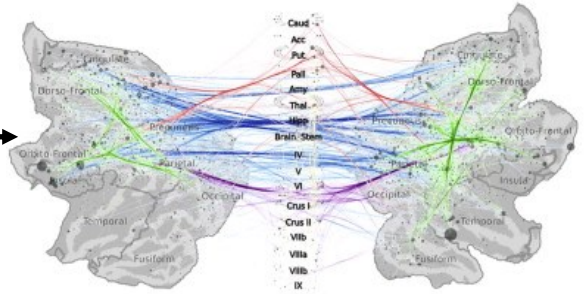
Correlation matrix



Link definition

Thresholding

Functional brain network



Network from Nummenmaa et al. 2014, *NeuroImage*, by permission

Voxels vs ROIs

Voxels:

- fMRI imaging resolution
- noisy signals?
- ~10.000 nodes
- large computational load

ROIs:

- collections of voxels
- defined by anatomy, function, connectivity, …
- homogeneous (= all voxels have same dynamics)?
- ROI time series to represent voxel dynamics:

$$X_I = \frac{1}{N_I} \sum_{i \in I} x_i$$

Violent?

Consistency of Regions of Interest as nodes of fMRI functional brain networks

Korhonen, O., Saarimäki, H., Glerean, E., Sams, M., & Saramäki, J. 2017. *Network Neuroscience*

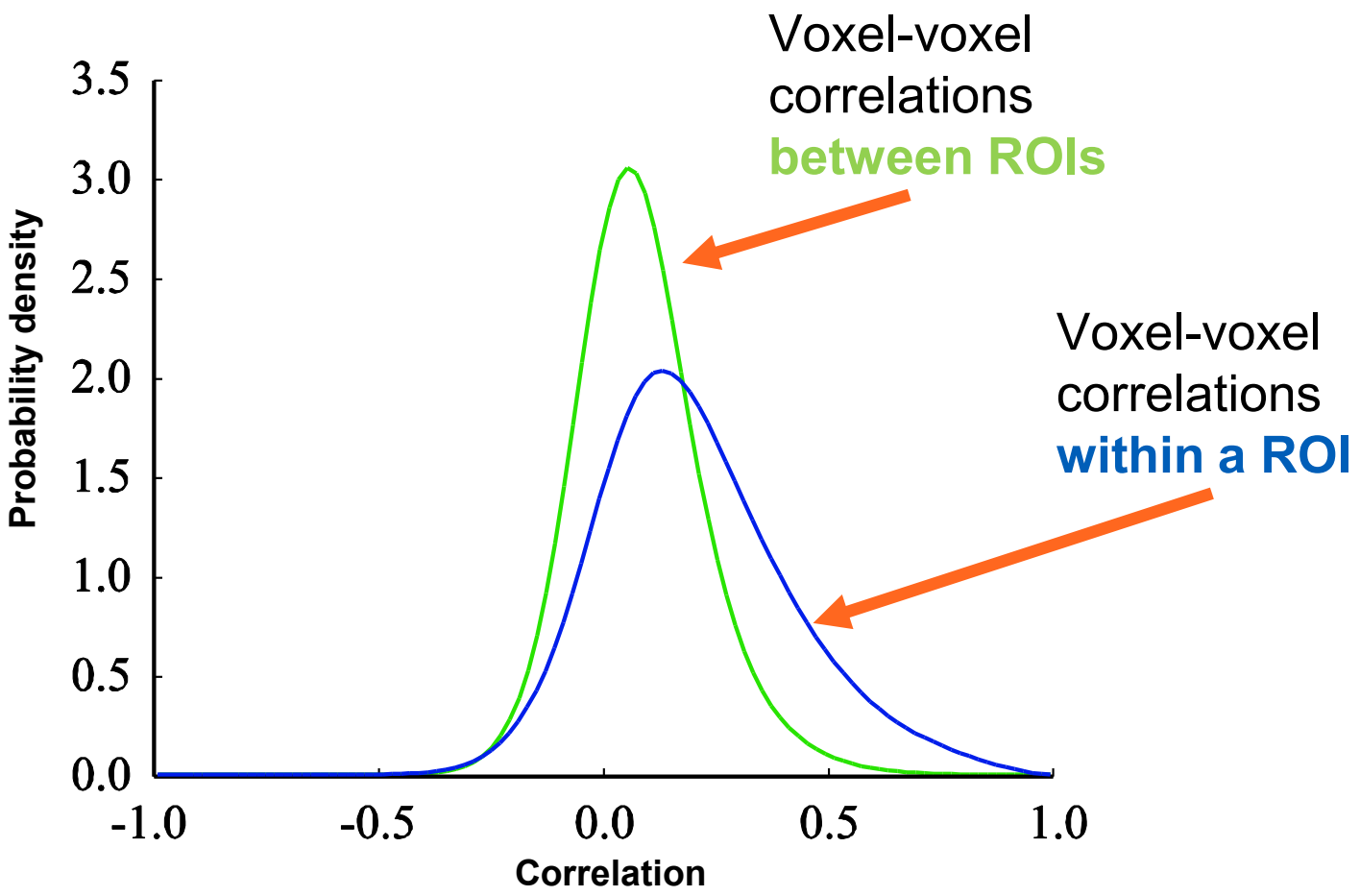
Research questions

- What should nodes of brain networks depict?
  - ROIs or voxels?
- Are ROIs functionally homogeneous?

Methods

- Two sets of resting-state fMRI data:
  - 13 in-house subjects
  - 28 subjects from ABIDE I initiative
- 215 time points (~6 min)
- ROIs from three atlases:
  - HO: anatomical
  - AAL: anatomical
  - Brainnetome: connectivity-based
- Connectivity investigated at voxel and ROI levels

How correlated are voxels of a ROI?



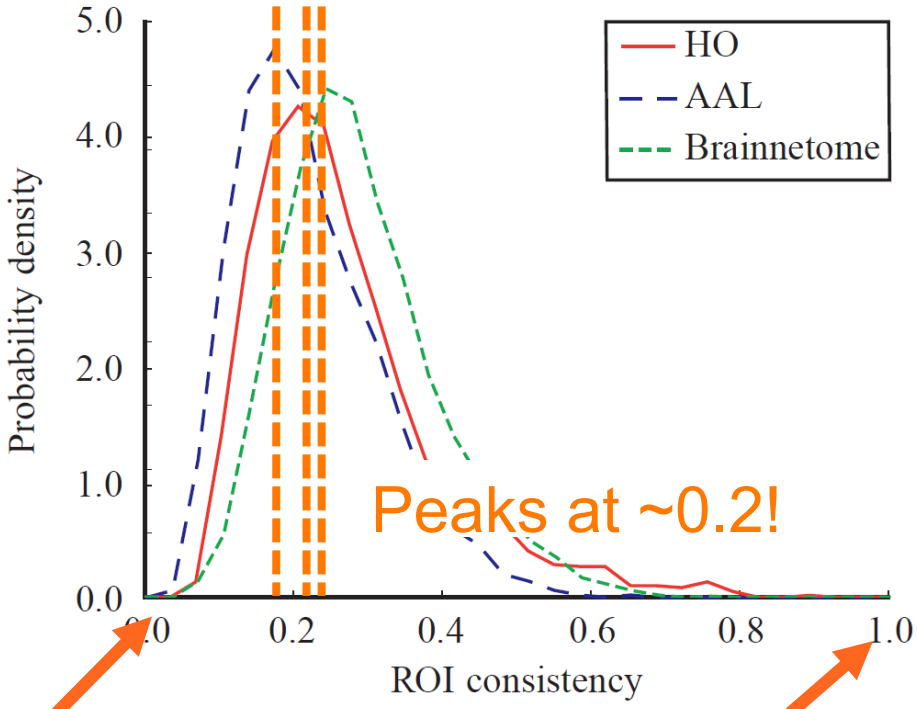
How homogeneous are ROIs?

- **Spatial consistency**

= measure of functional homogeneity:

$$\varphi_{spat}(I) = \frac{1}{N_I(N_I - 1)} \sum_{i,i' \in I} C(x_i, x_{i'})$$

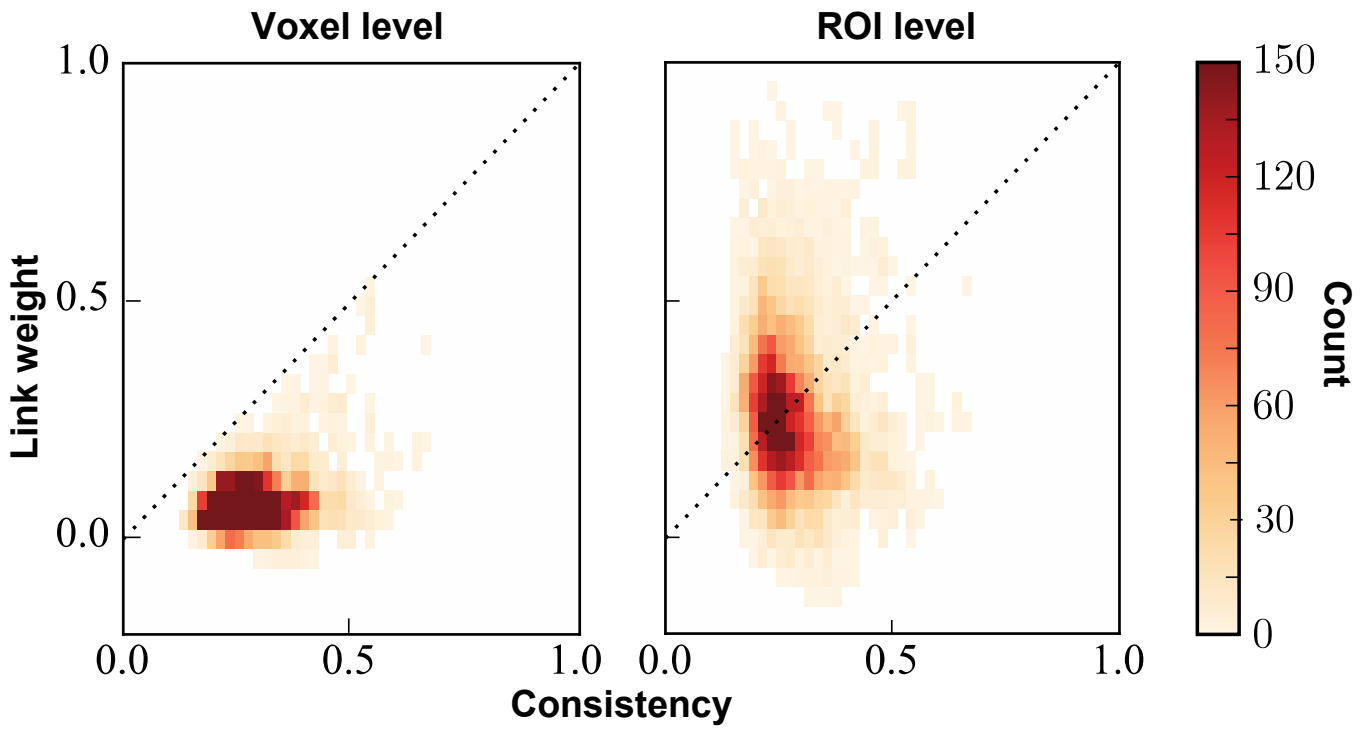
- Straightforward to calculate
- Easy to interpret



Lack of homogeneity

Perfect homogeneity

Does consistency predict connectivity?



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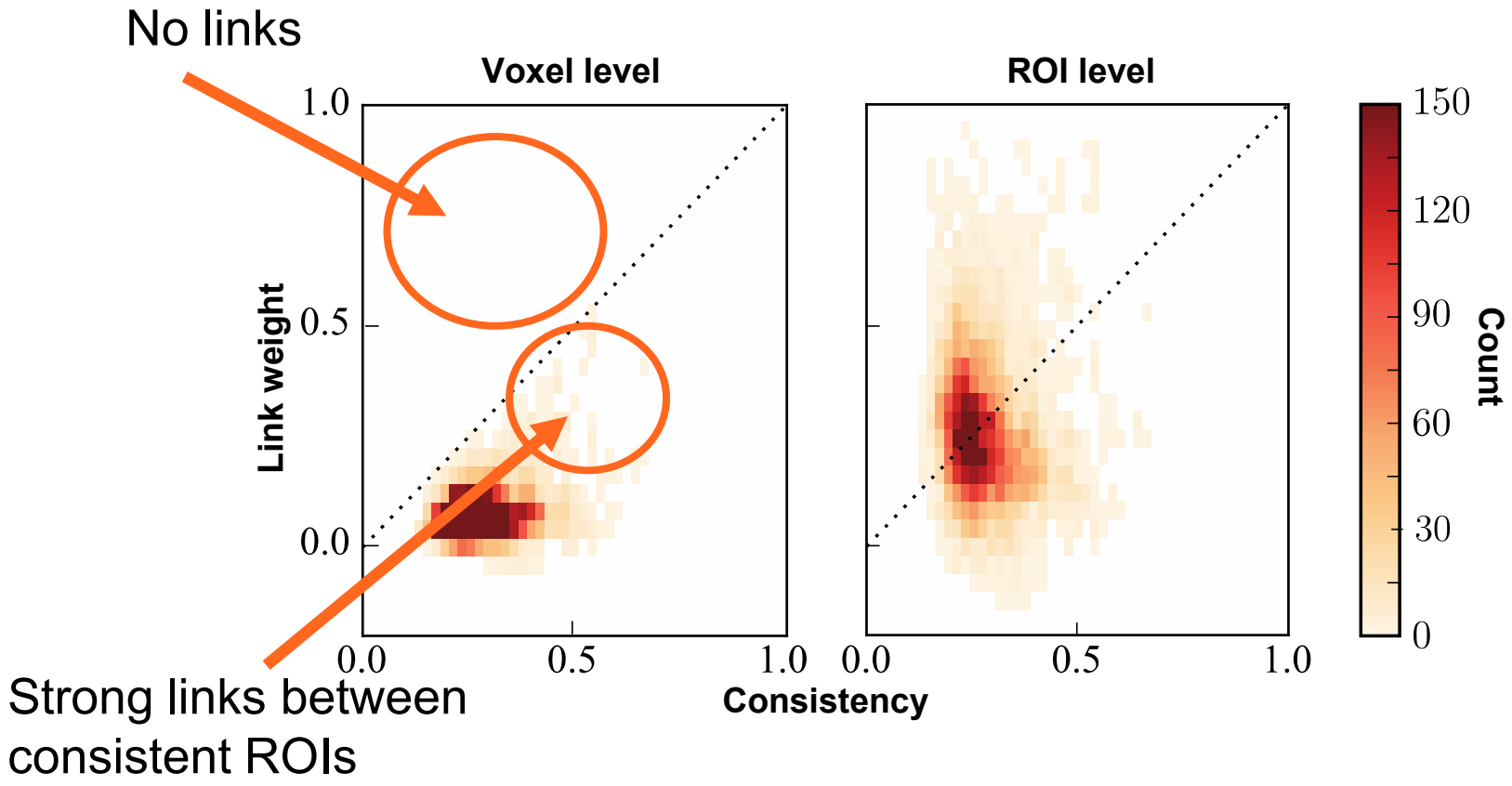

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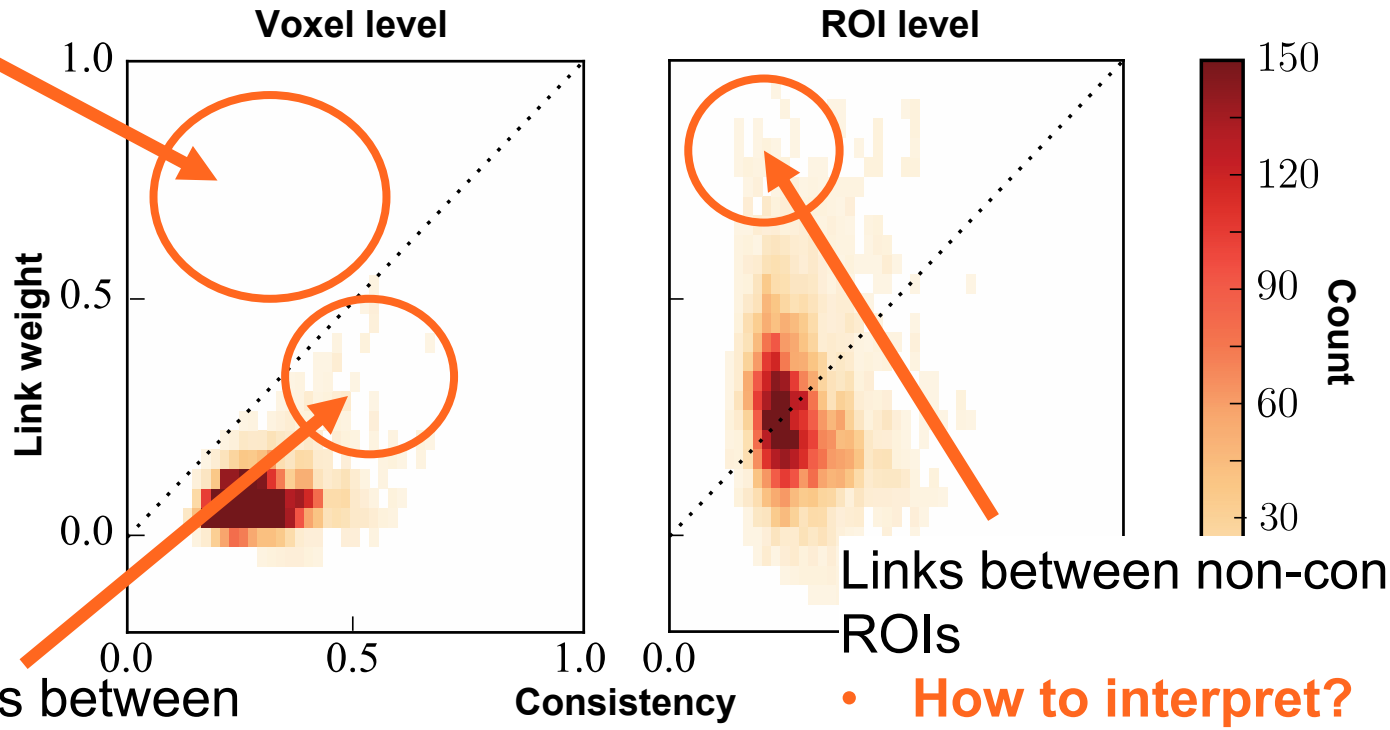


- **How to interpret?**

Conclusions

- ROIs are not always functionally homogeneous

- Strong ROI-level correlations between low-consistency ROIs may be spurious

- Does a low spatial consistency tell about

  a) A bad ROI definition

  b) High noise level

  c) Inactivity of the ROI?

Regions of Interest as nodes of dynamic functional brain networks

Ryyppö. E., Glerean, E., Brattico, E., Saramäki, J., & **Korhonen, O.** 2018, *Network Neuroscience*

Research questions

- ROIs as nodes of dynamic brain networks?
- Temporal behaviour of spatial consistency?

Methods

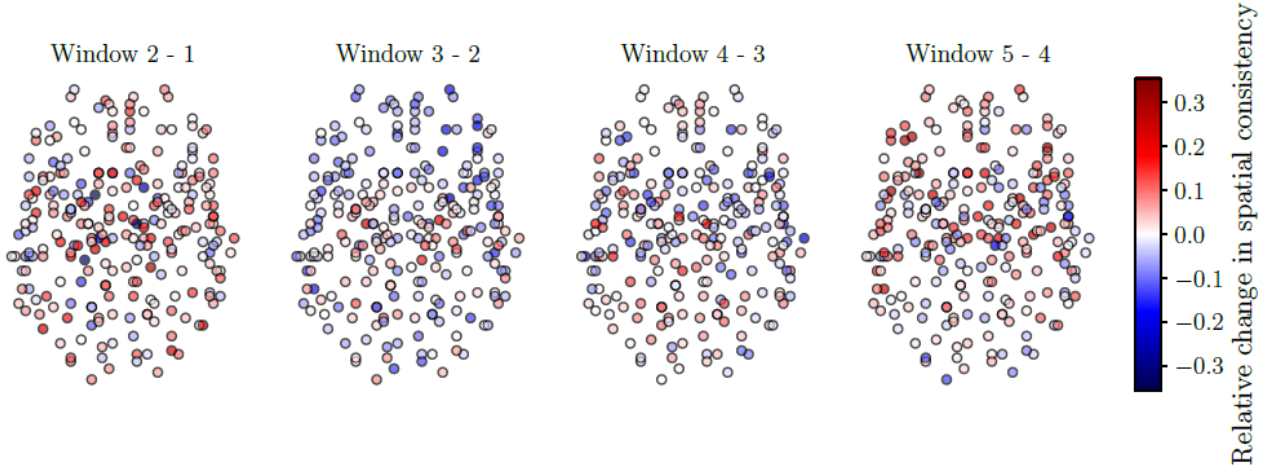
- Two sets of fMRI data:
  - Music listenig (13 subjects)
  - Resting-state (28 subjects)
- ROIs:
  - Brainnetome
  - HO
  - AAL
- Time windows: 80 samples (160s), 50% overlap

Measures

- Spatial consistency φ_{spat}: functional homogeneity of ROI
- Spatiotemporal consistency: time-dependence of φ_{spat}

$$\varphi_{st}(I) = \frac{N_t(N_t - 1)}{2\sum_{t<t'} \frac{|\varphi_{spat}(I,t) - \varphi_{spat}(I,t')|}{\varphi_{spat}(I,t)}}$$

Spatial consistency changes in time



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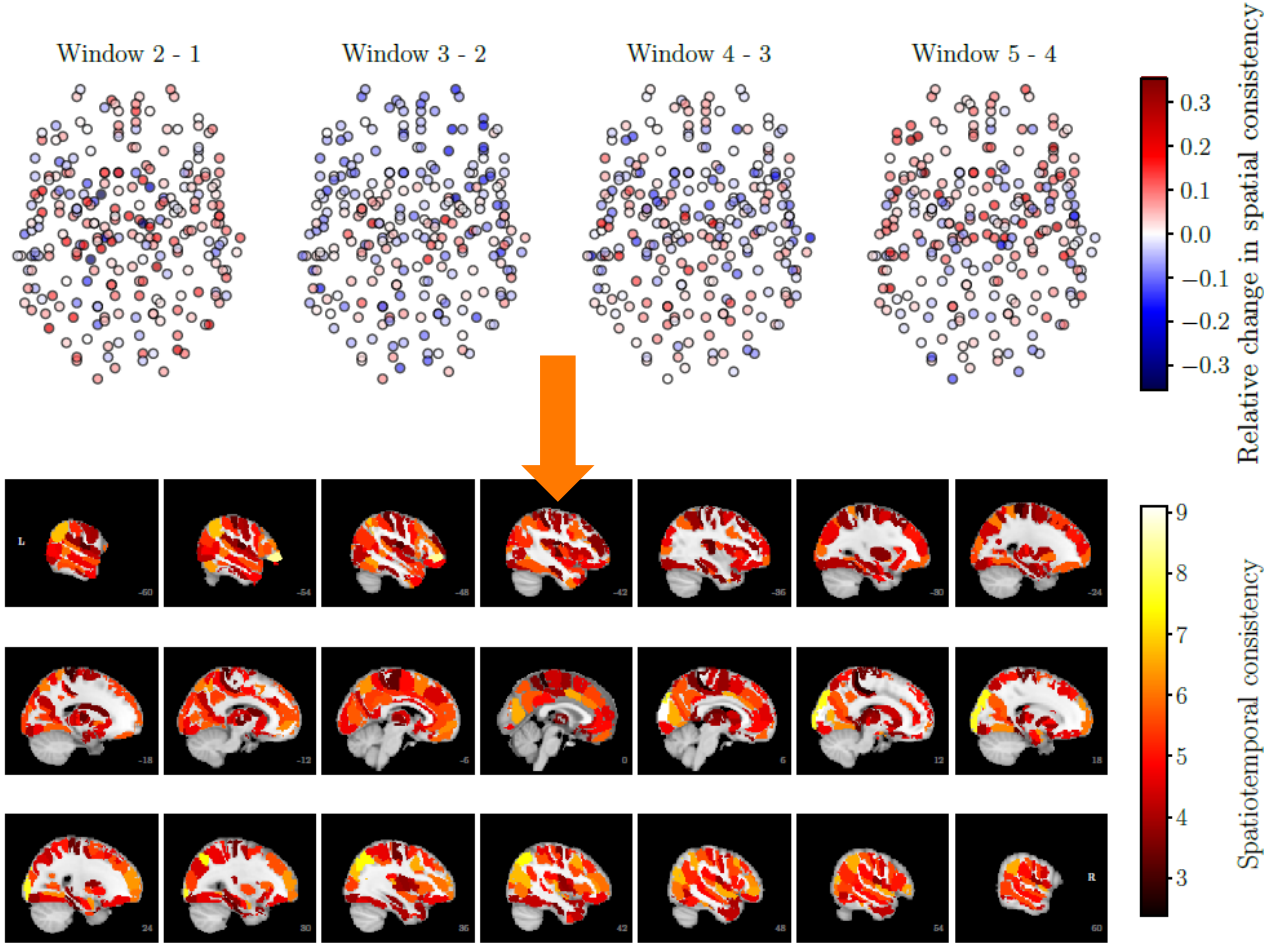
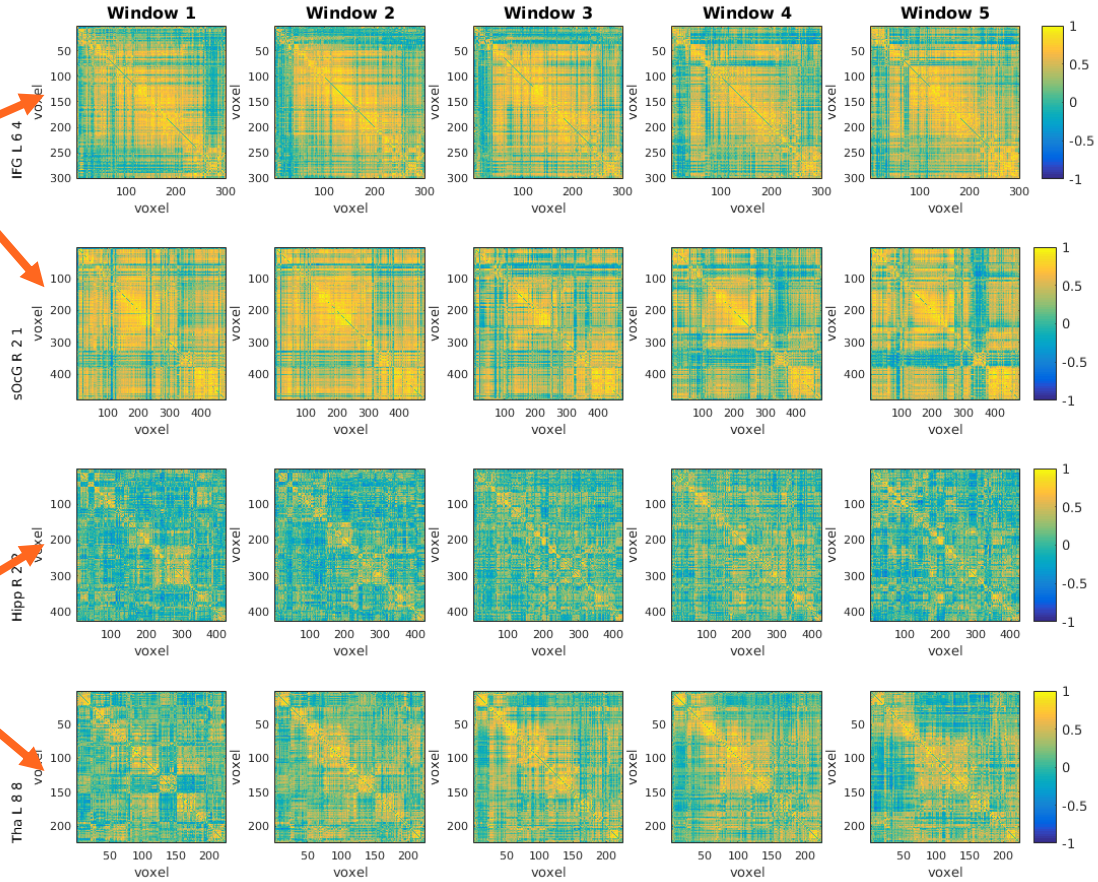


ROIs have rich internal connectivity structure

High spatial consistency

Low spatial consistency



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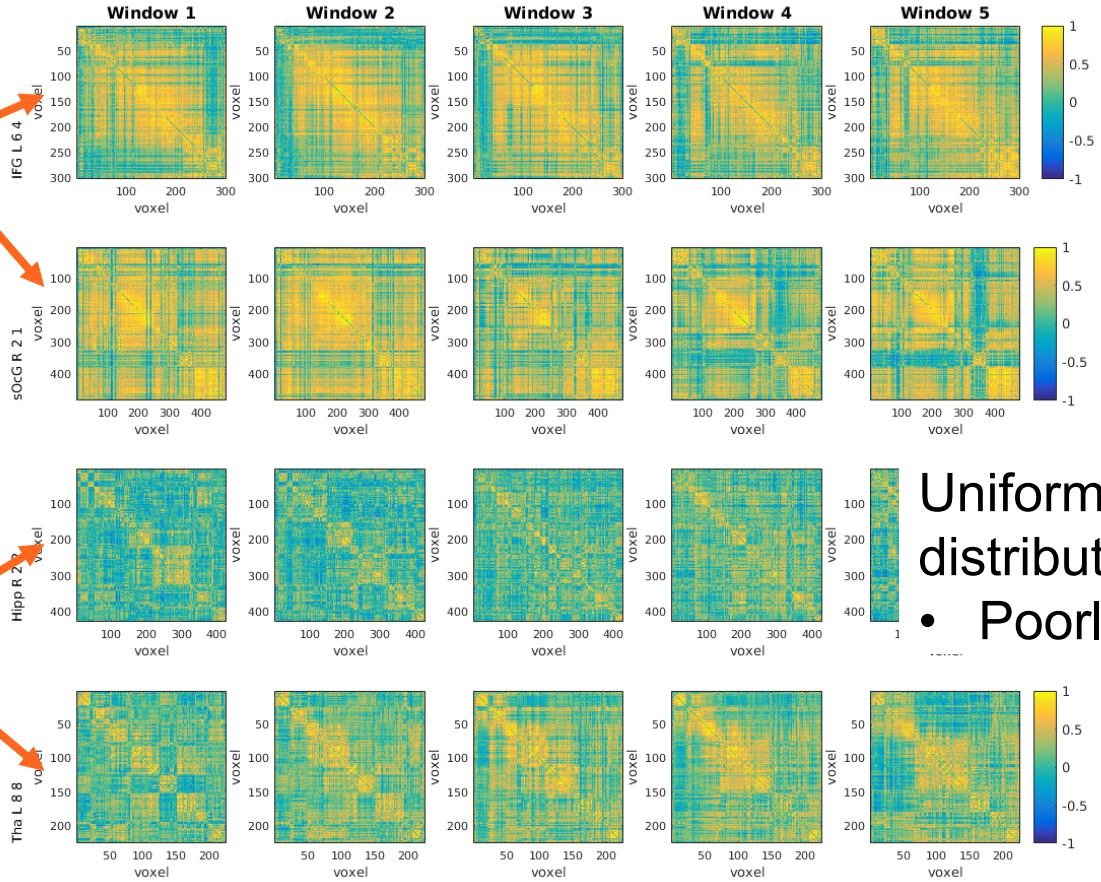


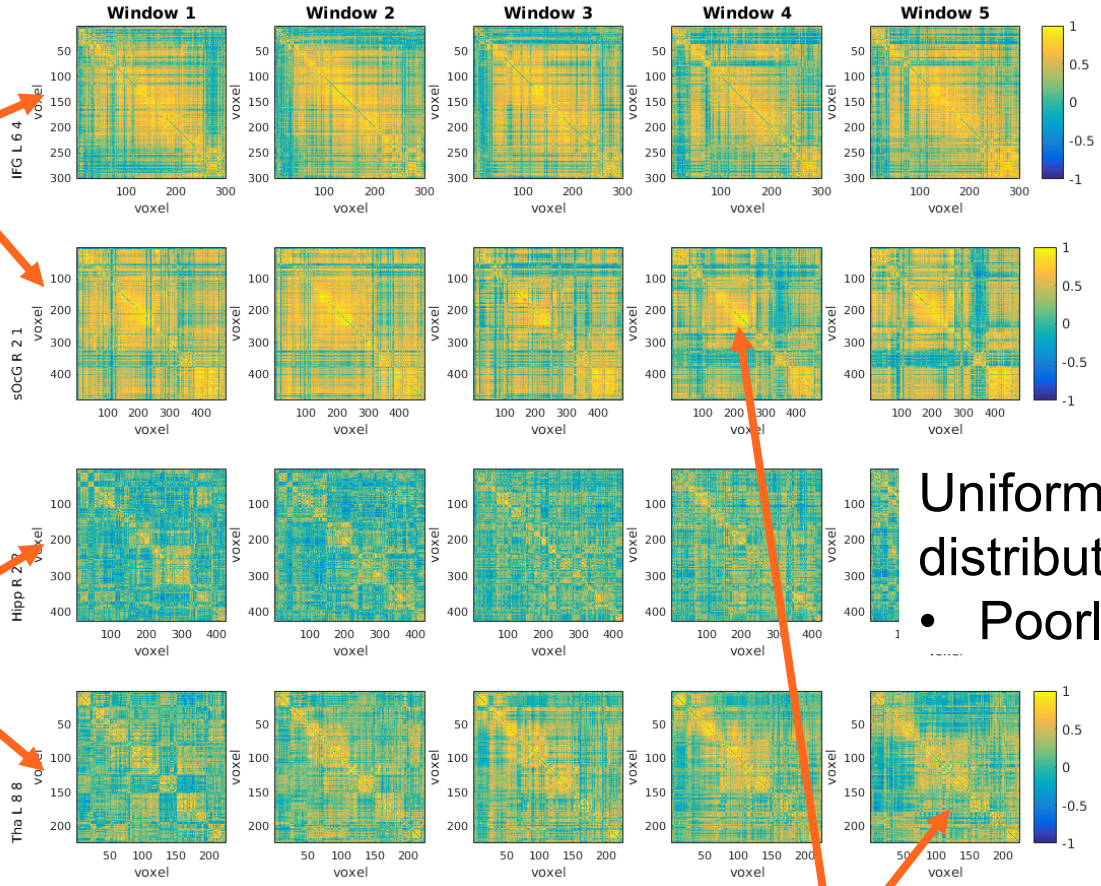
Uniform correlation distribution

- Poorly defined ROI?

ROIs have rich internal connectivity structure

High spatial consistency

Low spatial consistency



Uniform correlation distribution

- Poorly defined ROI?

Intra-ROI modules

- Network topology?

Conclusions

- Spatial consistency changes in time
  - Reflects activation?
- ROIs have time-dependent internal structure
  - Relates to network topology?
- Do brain networks have stable nodes?

On-going work: Internal connectivity and topological roles of nodes in functional brain networks

with Elisa Ryyppö, Ana Triana & Jari Saramäki

Research questions

- Why does consistency change in time?
- Is consistency connected to network structure?

Methods

- Two sets of fMRI data:
  - Music listenig (13 subjects)
  - Resting-state (28 subjects)
- ROIs: Brainnetome
  - Subject's native space
  - Standard space
- Two link definition approaches
  - Pearson correlation
  - Coarse-graining (Kujala et al. 2016)

Predictors

- ROI size: number of voxels
- 5 measures of internal connectivity:
  - Spatial consistency φ_{spat} : functional homogeneity of ROI
  - Spatiotemporal consistency φ_{st} : time-dependence of φ_{spat}
  - SD of correlations inside ROI: broadness of correlation distribution
  - Self-link weight: number of voxel-level links inside the ROI
  - Internal density: normalized by ROI size

Topological roles

- Global hubness (Klimm et al. 2014):
  - How central the node is?

$$h_i = \frac{s_i - \langle s_R \rangle}{\sigma_R}$$

- Connectorness:
  - Does the node build bridges?

$$b_i = \frac{\sum_{l_{ij} > l_t} A_{ij}}{\sum A_{ij}}$$

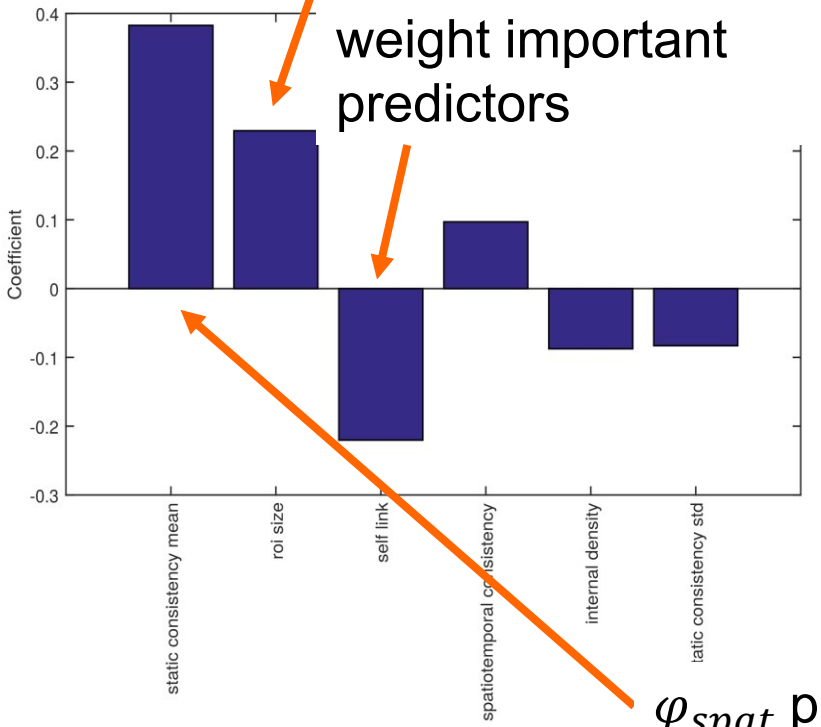
- Prediction with logistic regression

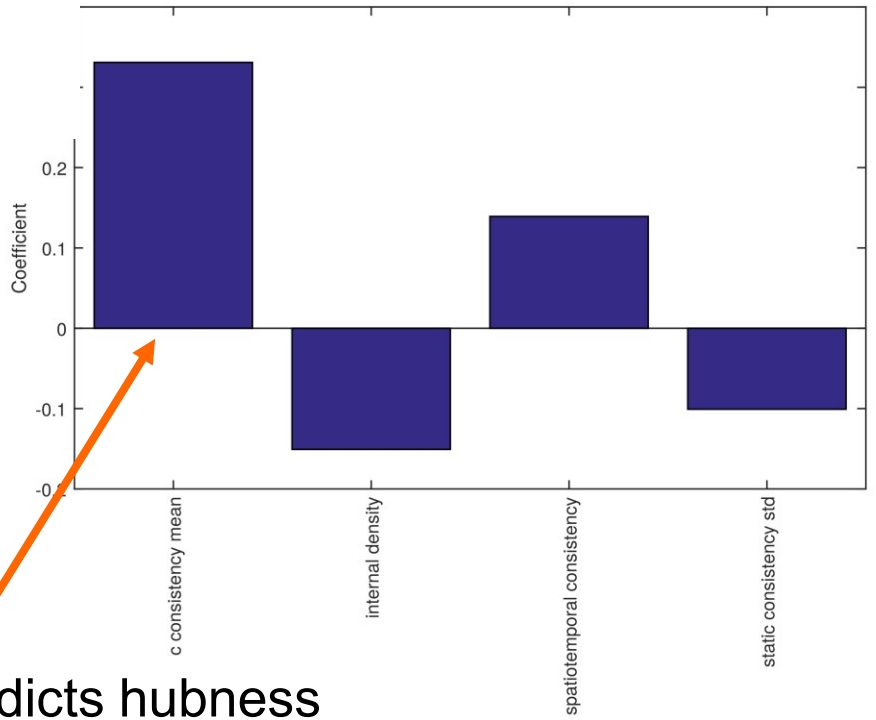
Results: Hub vs non-hub

Accuracy:
Training 61.65%
Test 60.10%
(> Random 50.03%)

Accuracy:
Training 60.75%
Test 59.96%
(> Random 50.03%)

ROI size and self-link weight important predictors

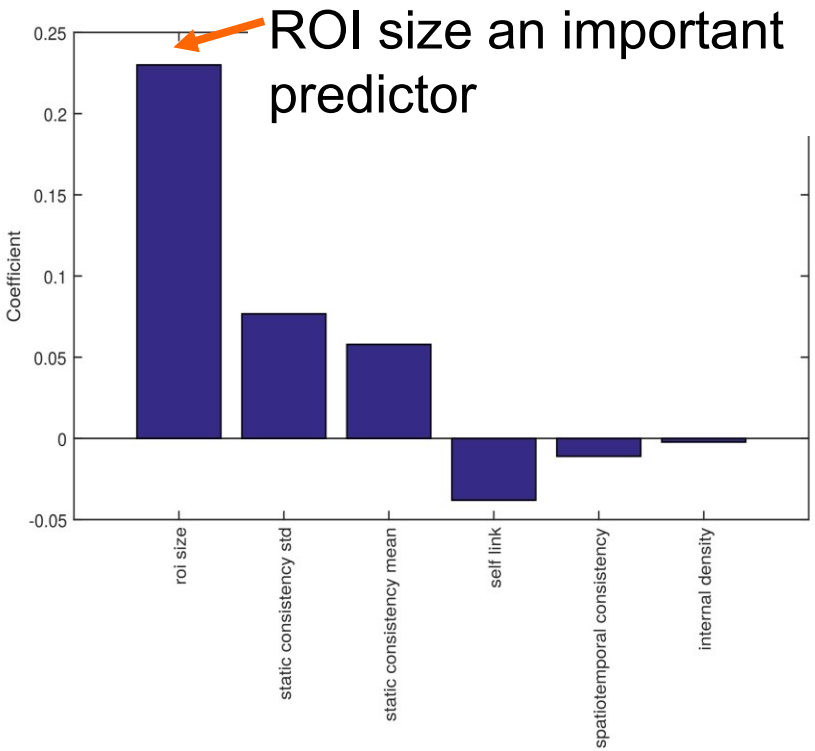




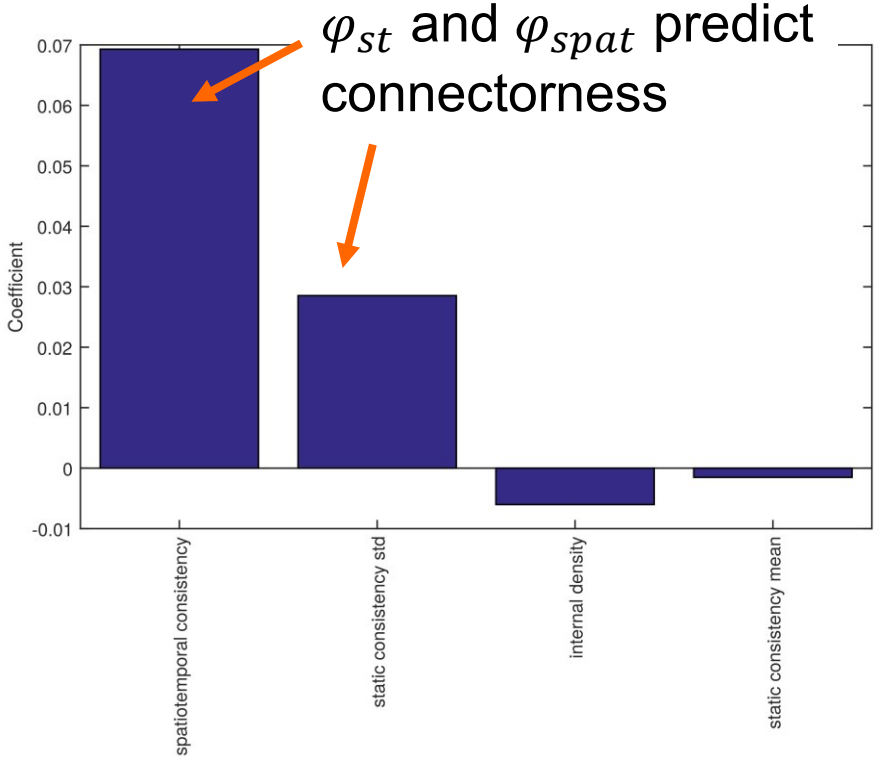
φ_{spat} predicts hubness

Results: Connector vs non-connector

Accuracy:
Training 57.82%
Test 55.97%
(> Random 50.38%)



Accuracy:
Training 52.80%
Test 52.17%
(> Random 50.38%)



Conclusions

- Internal connectivity measures predict topological roles

  $\Rightarrow$Varying homogeneity not a technical flaw!

- ROI time series = average of voxel time series

  $\Rightarrow$ Low homogeneity = lost data

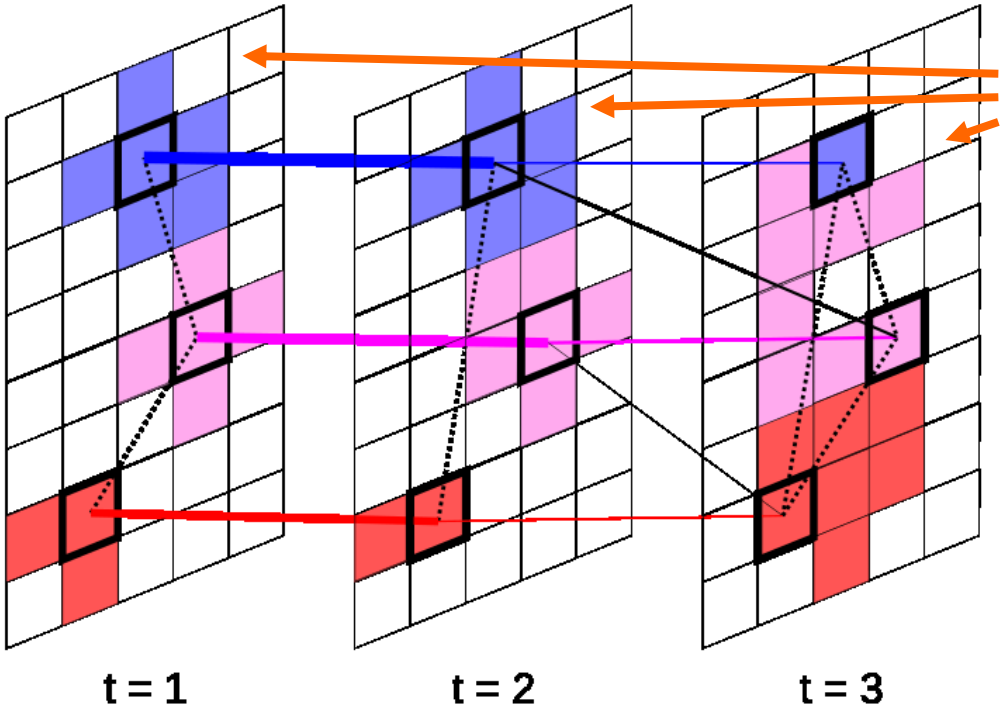
  $\Rightarrow$ Flexible nodes needed

On-going work: Multilayer brain networks with flexible nodes

with Tarmo Nurmi, Maria Hakonen, Iiro Jääskeläinen & Mikko Kivelä

Network model with flexible nodes

- Based on multilayer networks (= different connections in the same network)



1. Layers = time windows

Network model with flexible nodes

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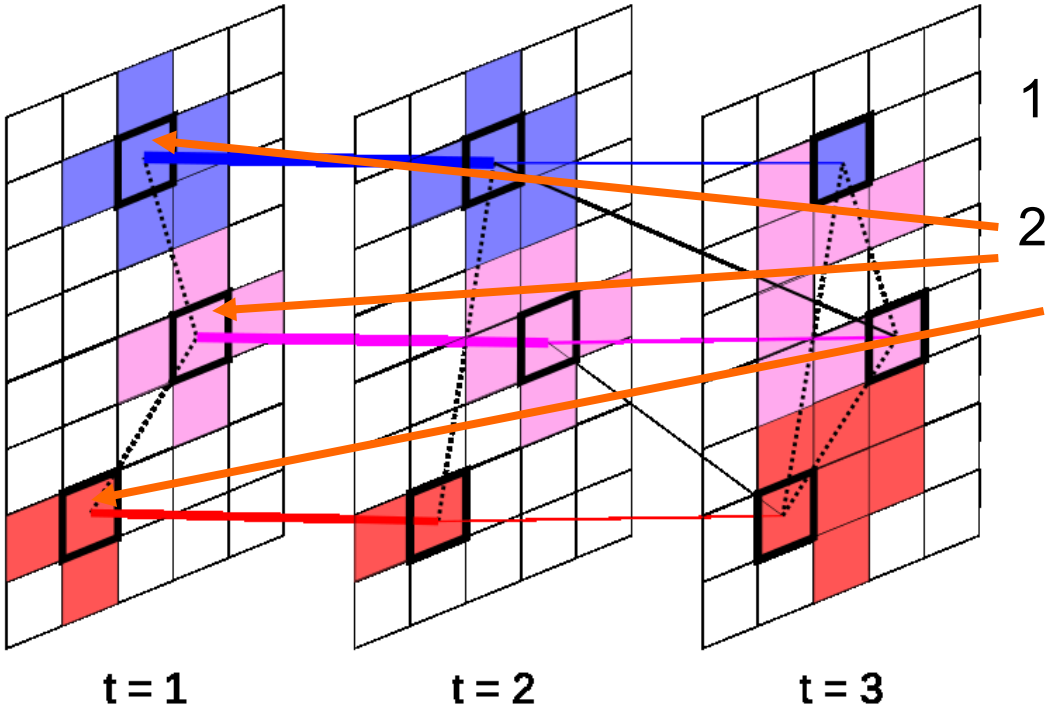

1. Layers = time windows
2. ROIs optimized inside layers for maximal homogeneity

Network model with flexible nodes

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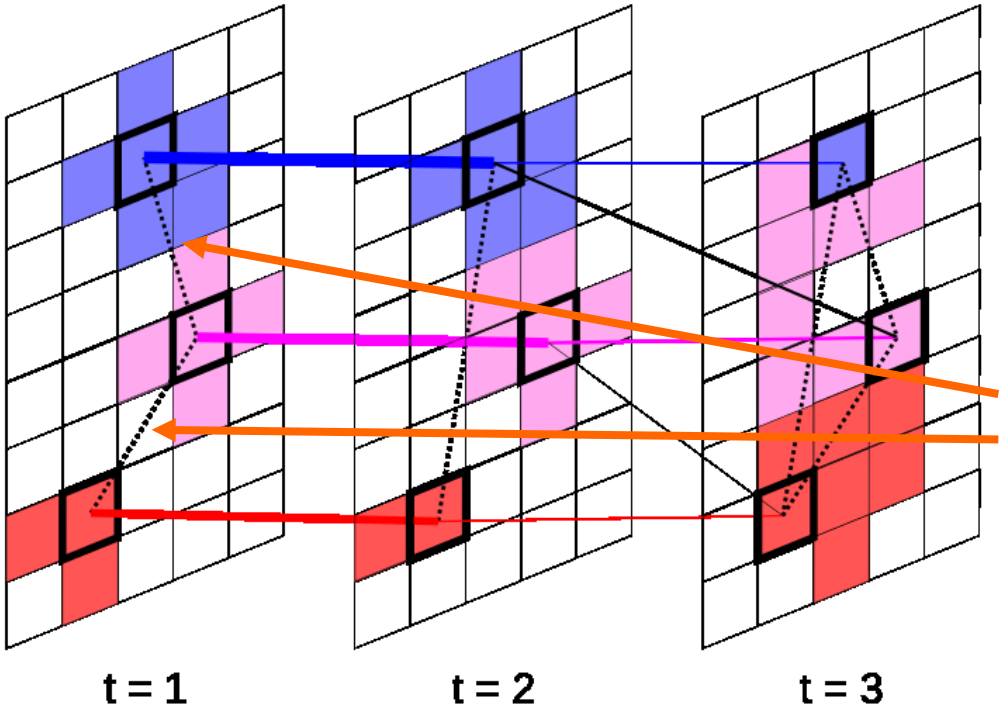

1. Layers = time windows
2. ROIs optimized inside layers for maximal homogeneity
3. Interlayer links = Pearson correlation

Network model with flexible nodes

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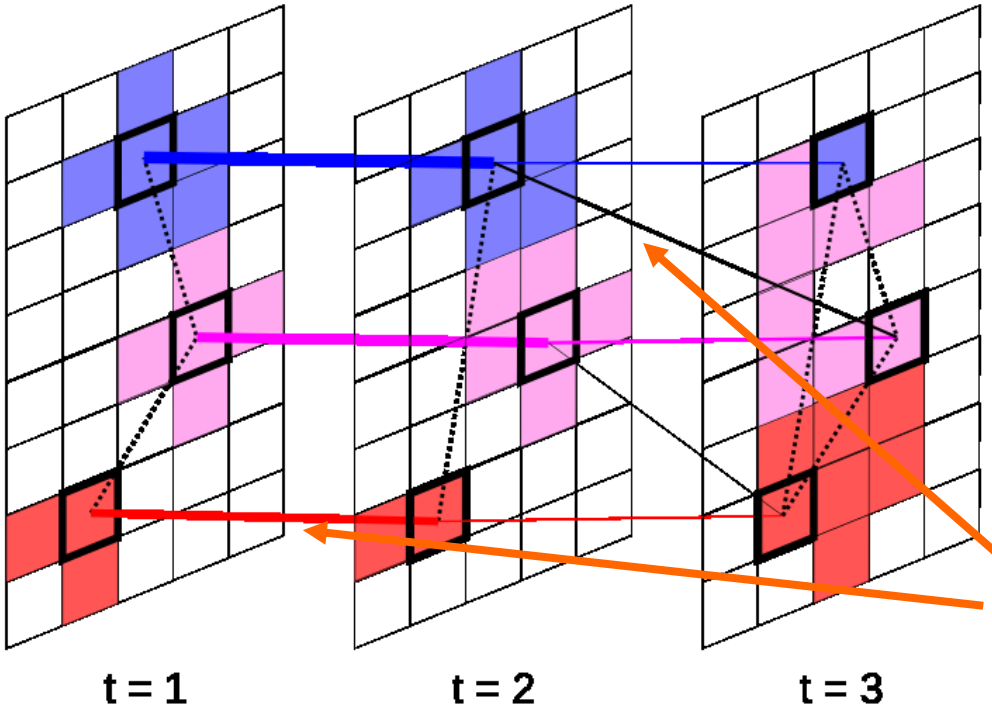

1. Layers = time windows
2. ROIs optimized inside layers for maximal homogeneity
3. Interlayer links = Pearson correlation
4. Intralayer links = spatial overlap

General conclusions

- It's not trivial to construct a functional brain network
  - **Know your methods!**
- Currently used nodes are not functionally homogeneous
  - Data lost in averaging
  - Risk of spurious connectivity?
- Homogeneity changes in time
  - Changes relate to function?
- Low homogeneity isn't a technical flaw

$\Rightarrow$ Can't be fixed by new static nodes

$\Rightarrow$ **Flexible nodes needed!**

References

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Thank you!

Questions, comments?

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Slides: https://github.com/onerva-korhonen/presentations/blob/master/wins-030620.pdf