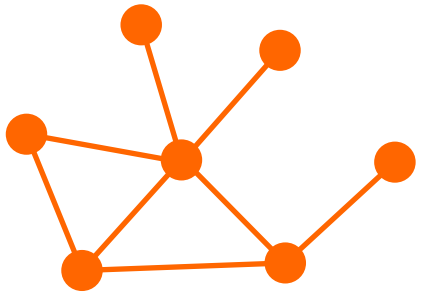
The quest for consistency: What's wrong with the nodes of functional brain networks?

Onerva Korhonen

26.2.2019

What's wrong with the nodes of functional brain networks?

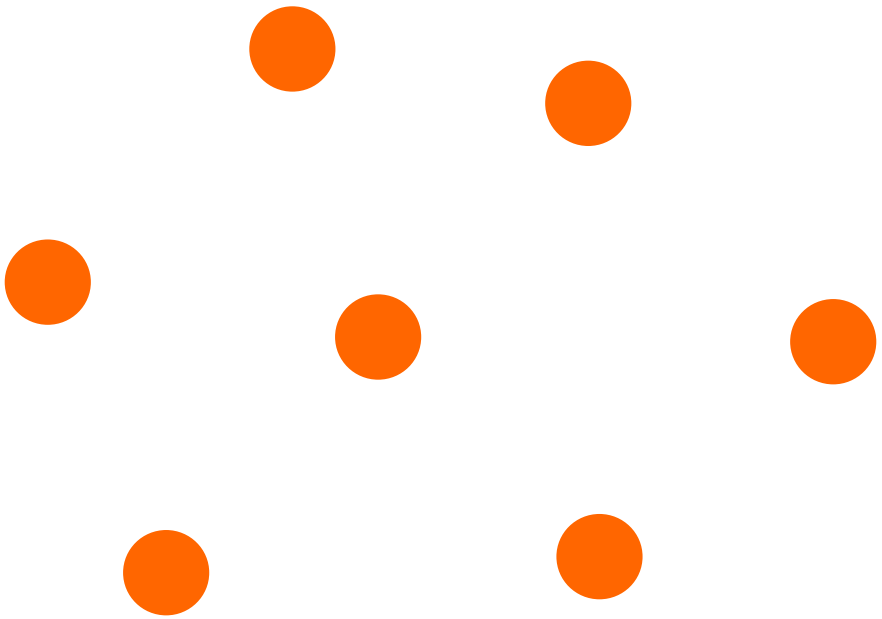
What's wrong with the nodes of functional brain networks?



Networks: what and why?

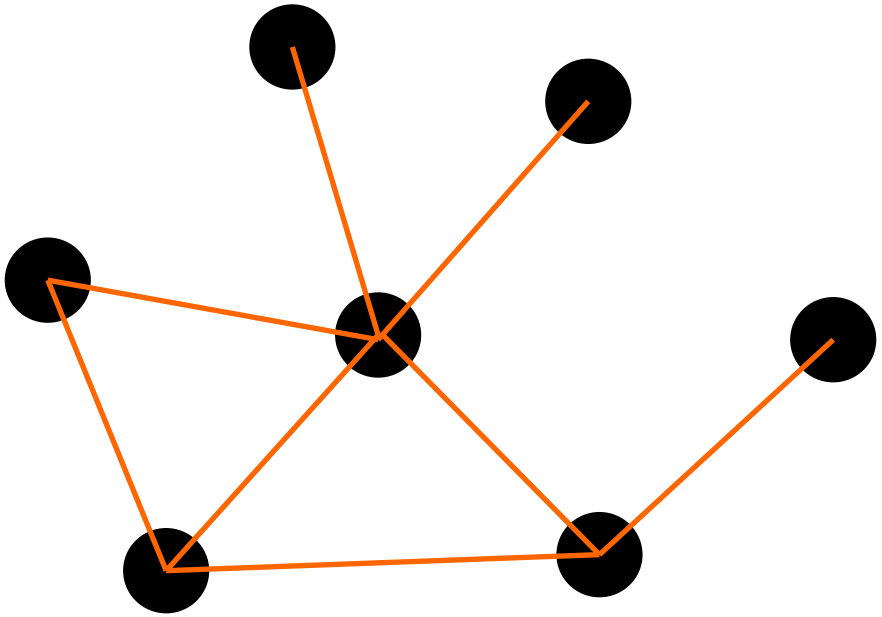
- **Network:** a model of connections and interactions
  - Internet, public transport, social networks

Networks: what and why?



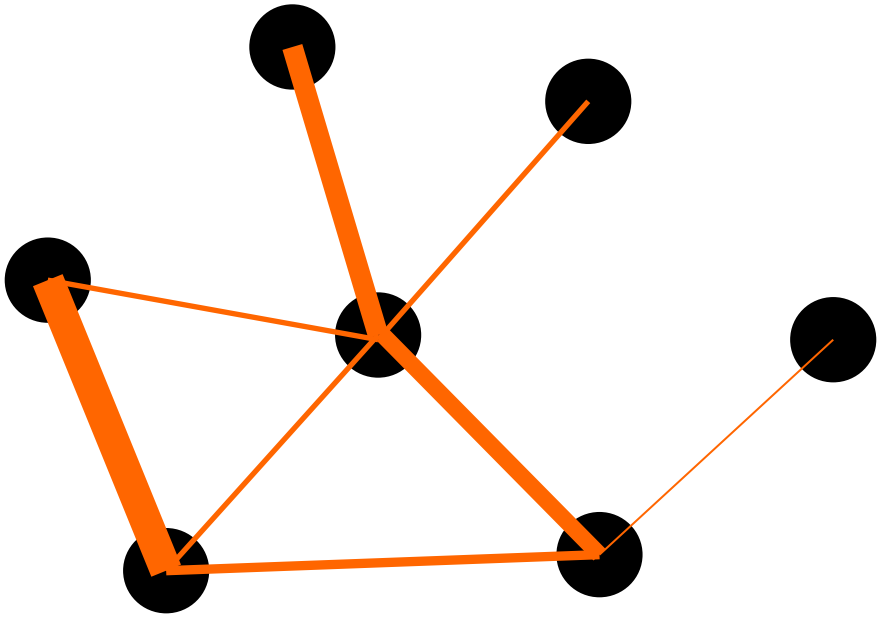
- **Network:** a model of connections and interactions
  - Internet, public transport, social networks
- **Nodes:** network's basic elements
  - Web pages, stops, people

Networks: what and why?



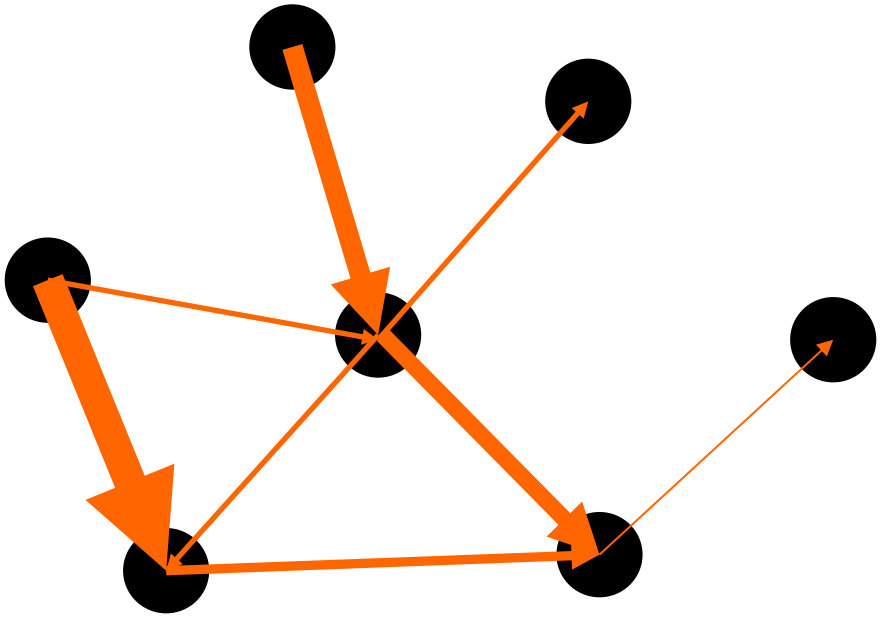
- **Network:** a model of connections and interactions
  - Internet, public transport, social networks
- **Nodes:** network's basic elements
  - Web pages, stops, people
- **Links:** connections between nodes
  - Web links, transport lines, social relationships

Networks: what and why?



- **Network:** a model of connections and interactions
  - Internet, public transport, social networks
- **Nodes:** network's basic elements
  - Web pages, stops, people
- **Links:** connections between nodes
  - Web links, transport lines, social relationships
  - Weights?

Networks: what and why?

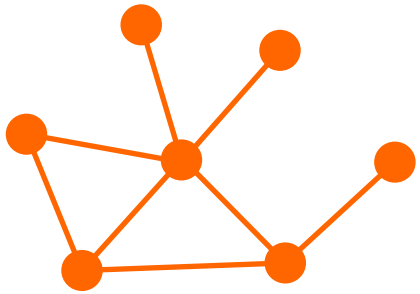


- **Network:** a model of connections and interactions
  - Internet, public transport, social networks
- **Nodes:** network's basic elements
  - Web pages, stops, people
- **Links:** connections between nodes
  - Web links, transport lines, social relationships
  - Weights?
  - Direction?

What's wrong with the nodes of functional brain networks?

Brain networks:

- Model for interactions in the brain



Brain networks

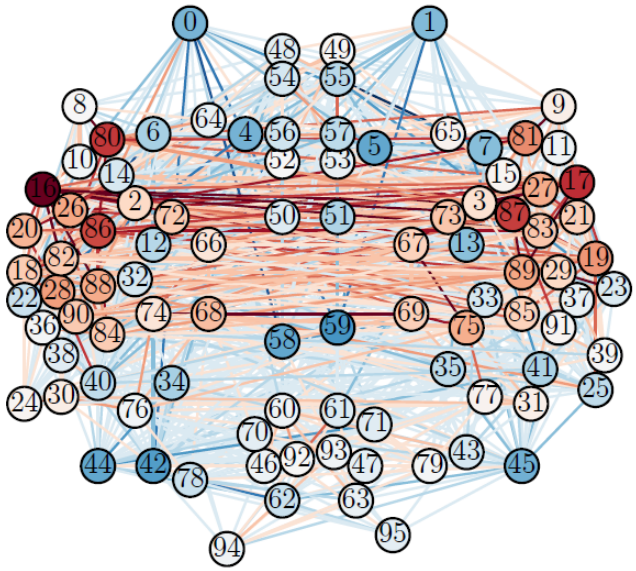


Fig: Alakörkkö *et al.* 2017, *European Journal of Neuroscience*

- Brain: a system of neural interactions
- Network: a natural model for the brain
- Different brain networks:
  - Structural: anatomic connections
  - Functional: temporal coactivation
  - Effective: causality

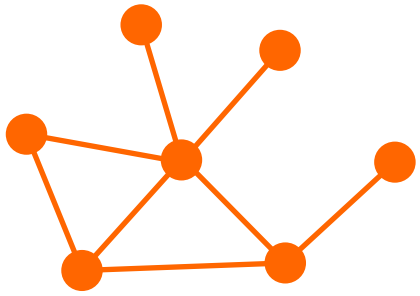
What's wrong with the nodes of functional brain networks?

Functional brain networks:

- Links = coactivation
- From fMRI data

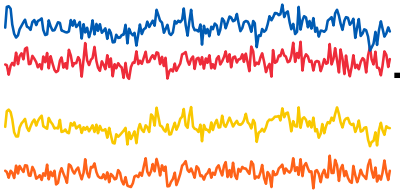
Brain networks:

- Model for interactions in the brain



Node definition

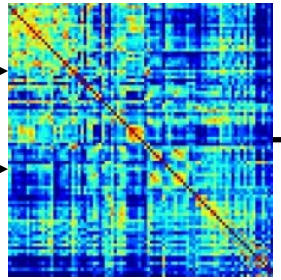
fMRI BOLD signal



Preprocessing

Coarse-graining

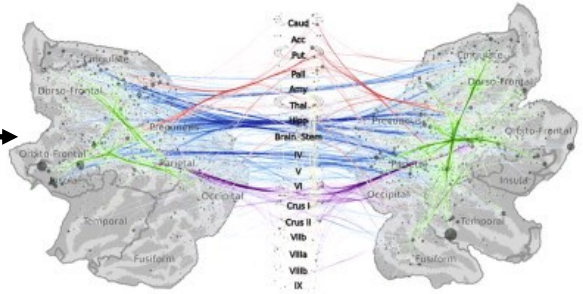
Correlation matrix



Link definition

Thresholding

Functional brain network



Network from Nummenmaa et al. 2014, *NeuroImage*

What's wrong with the nodes of functional brain networks?

Nodes:

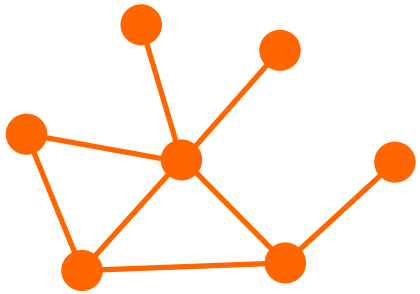
- Regions of Interest (ROIs) or voxels?

Functional brain networks:

- Links = coactivation
- From fMRI data

Brain networks:

- Model for interactions in the brain



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*

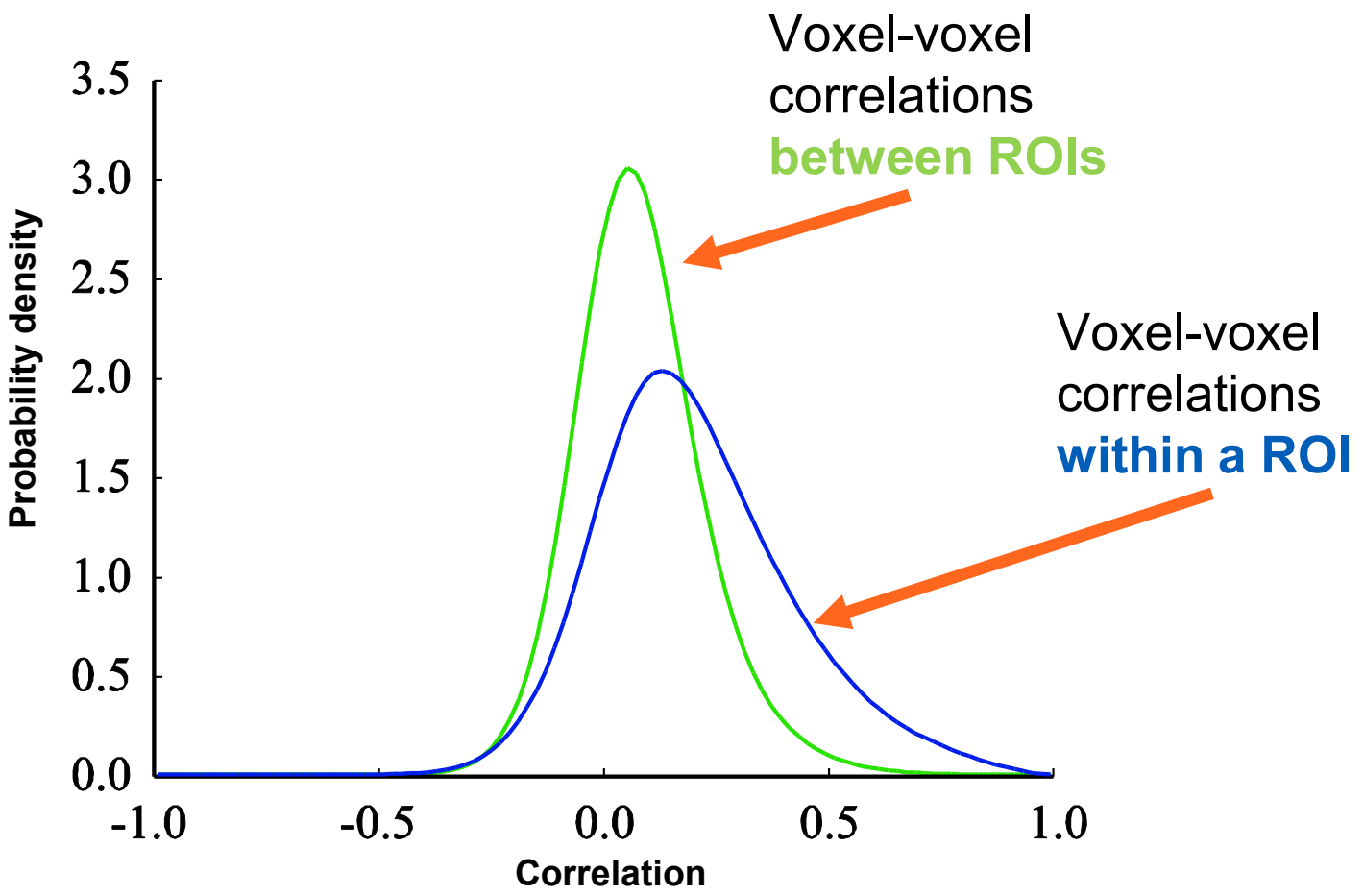
Research questions

- 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?



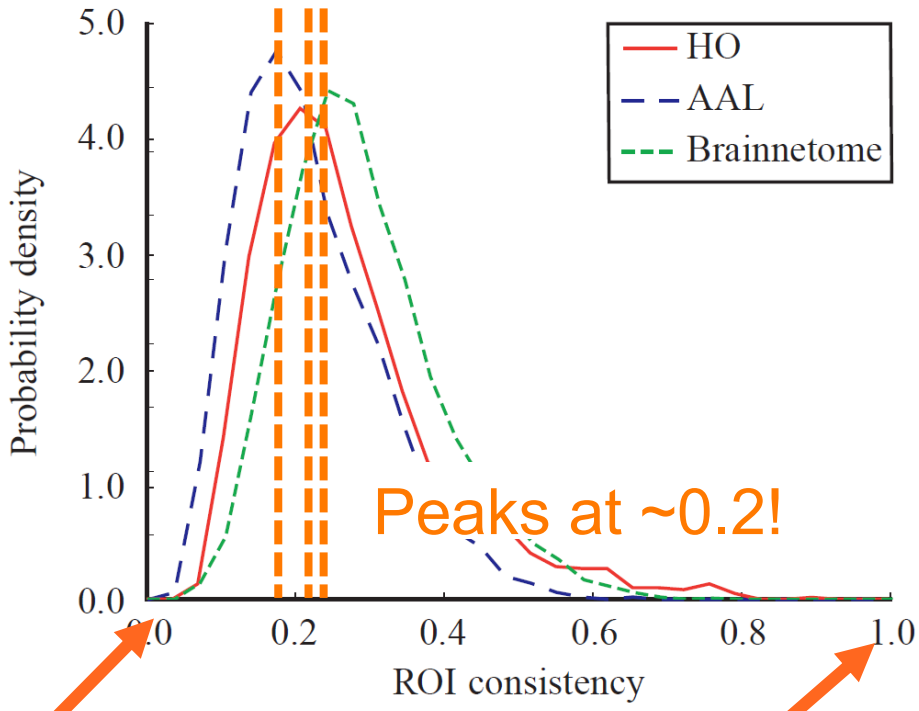
How homogeneous are ROIs?

- **Spatial consistency**

= measure of functional homogeneity:

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

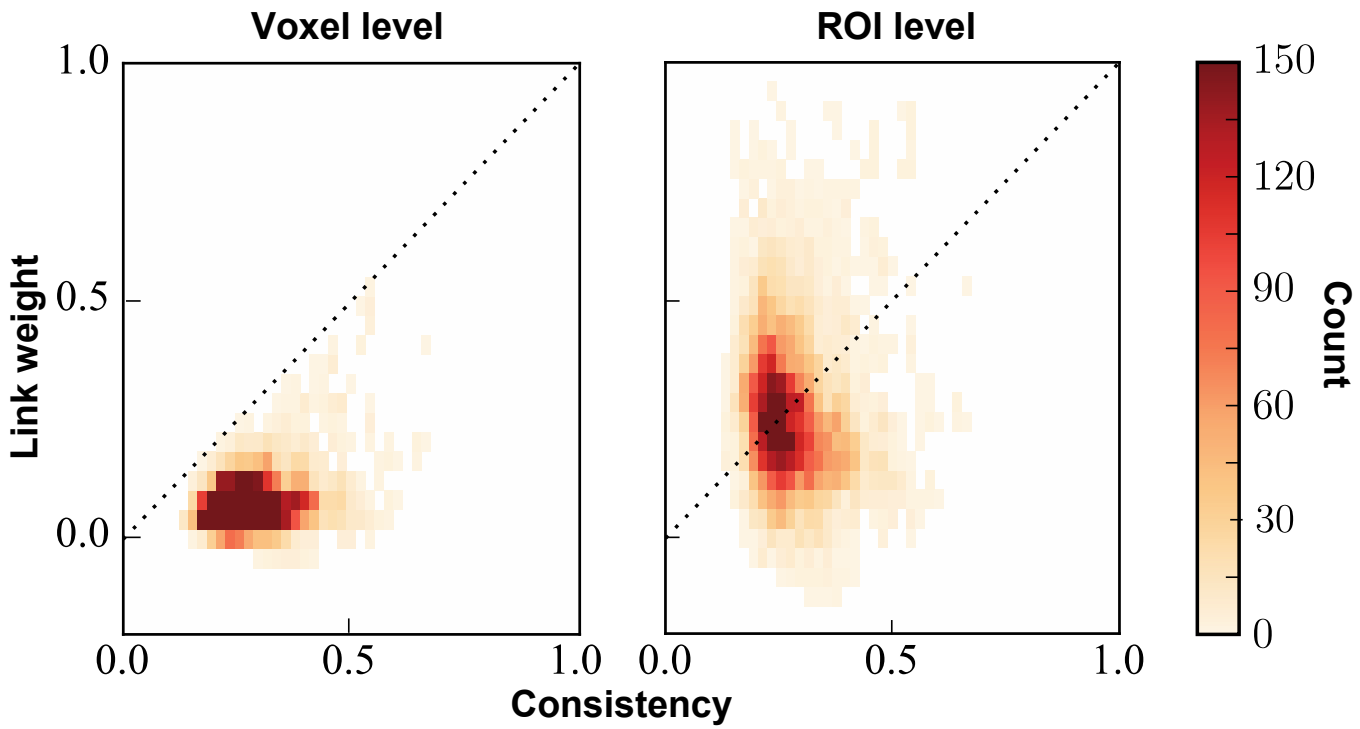
- Straightforward to calculate
- Easy to interpret



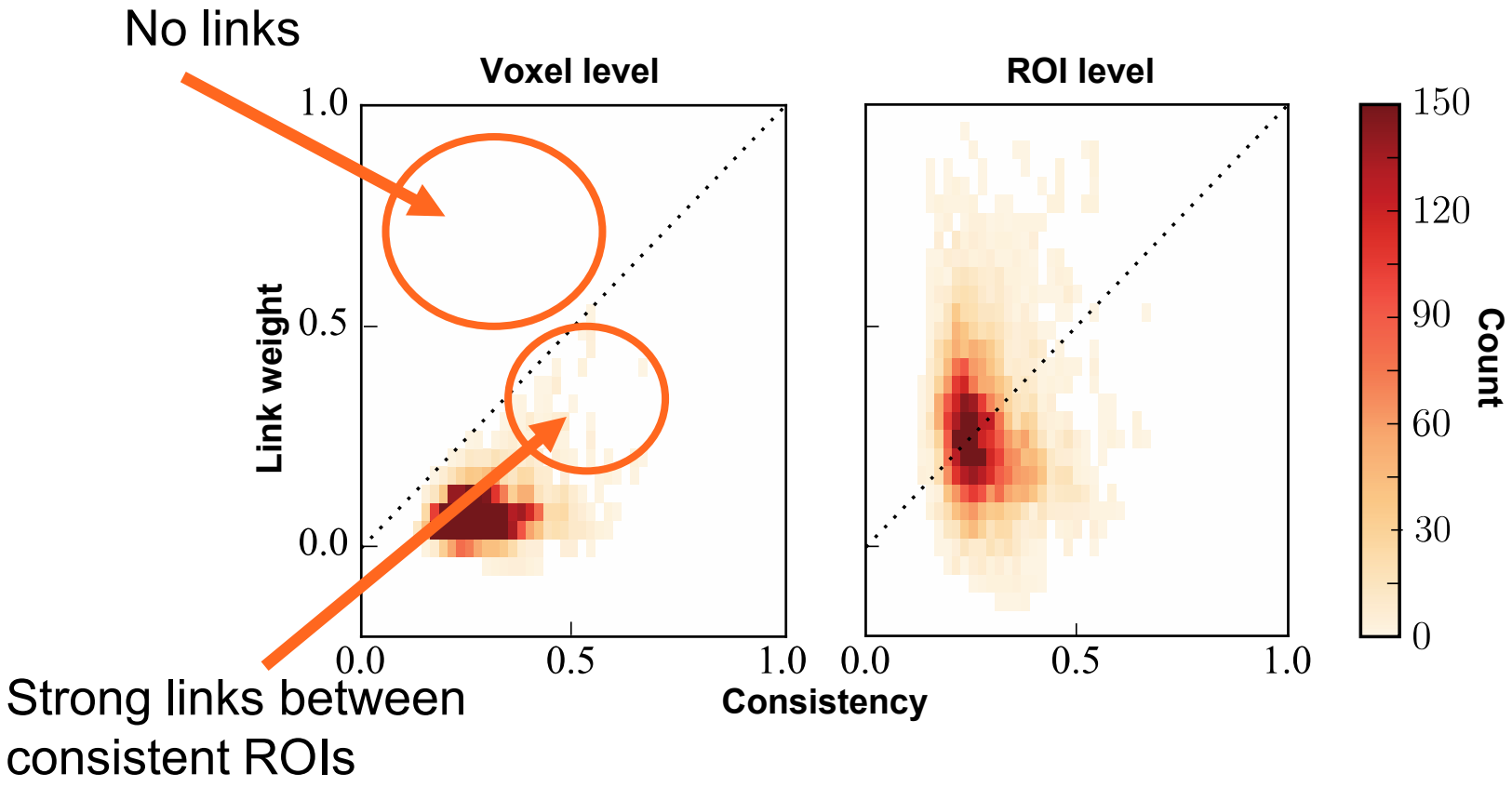
Lack of homogeneity

Perfect homogeneity

Does consistency predict connectivity?

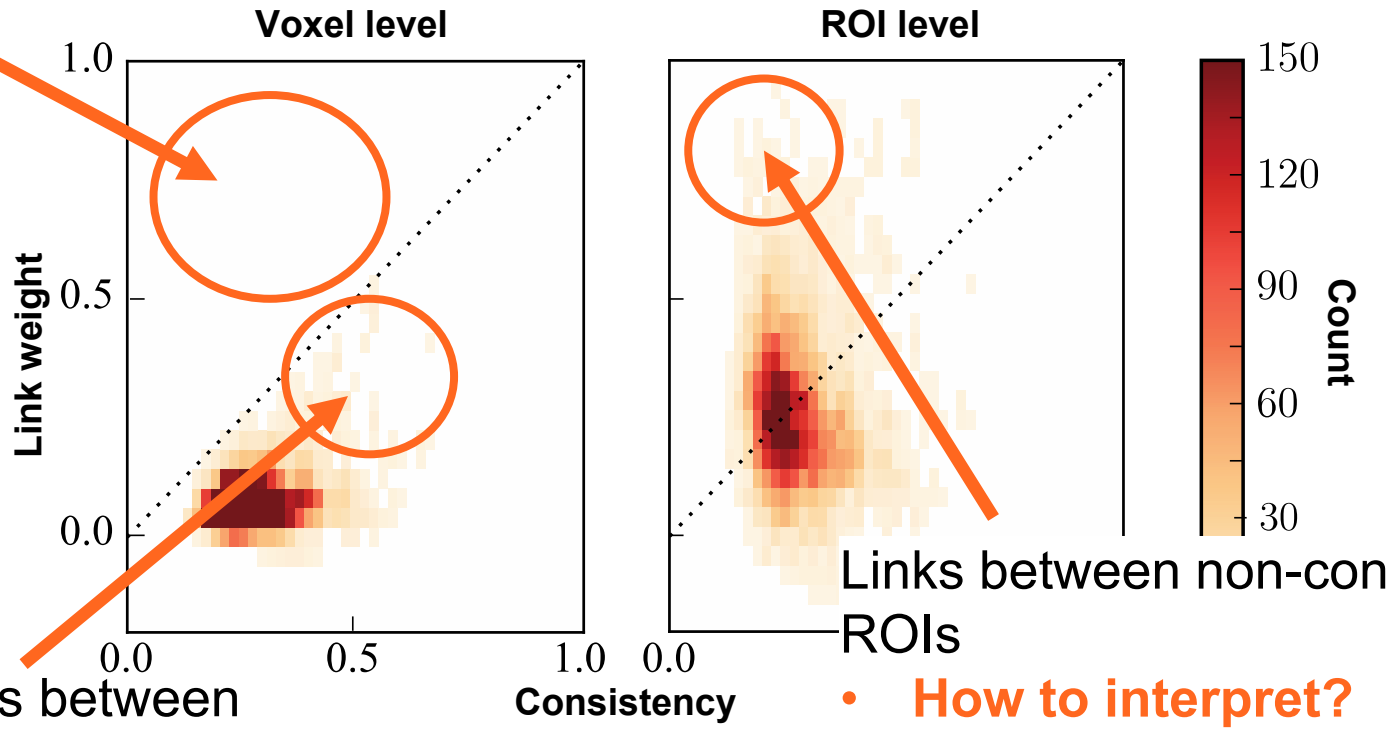


Does consistency predict connectivity?



Does consistency predict connectivity?

No links

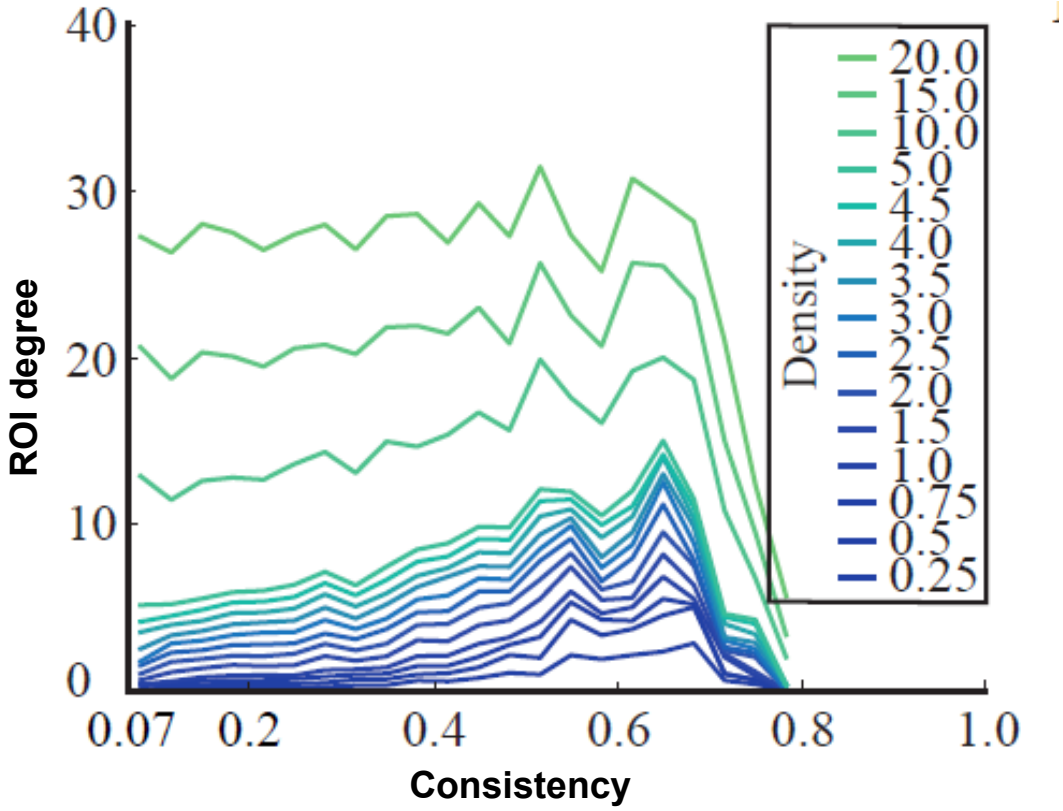


Strong links between consistent ROIs

Links between non-consistent ROIs

- **How to interpret?**

Does consistency tell about ROI's functional role?



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
- For each ROI, we build “closest neighborhoods” (35 strongest links of ROI)

Measures

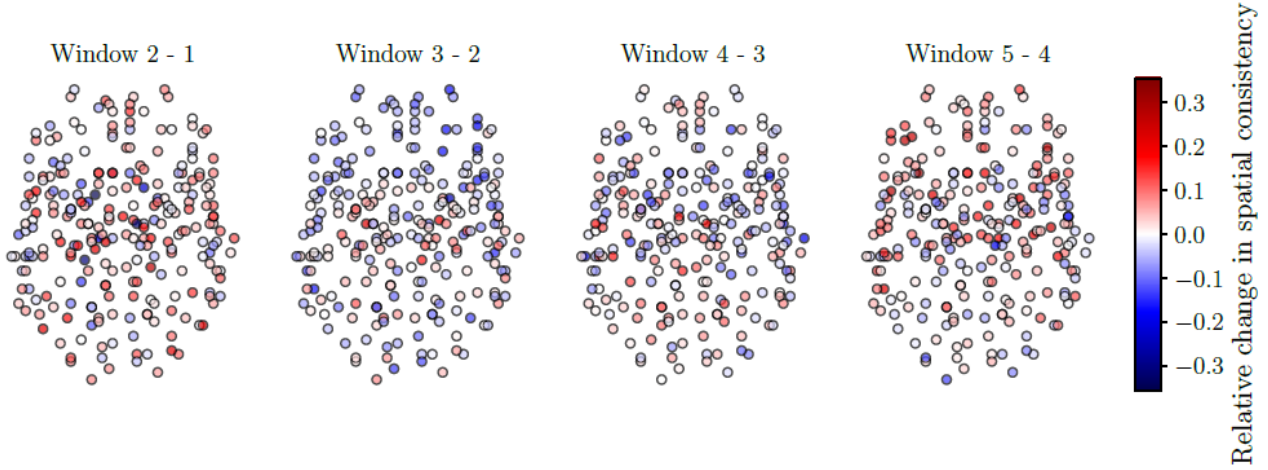
- Spatial consistency φ_{spat}: functional homogeneity of ROI
- Spatiotemporal consistency: time-dependence of φ_{spat}

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

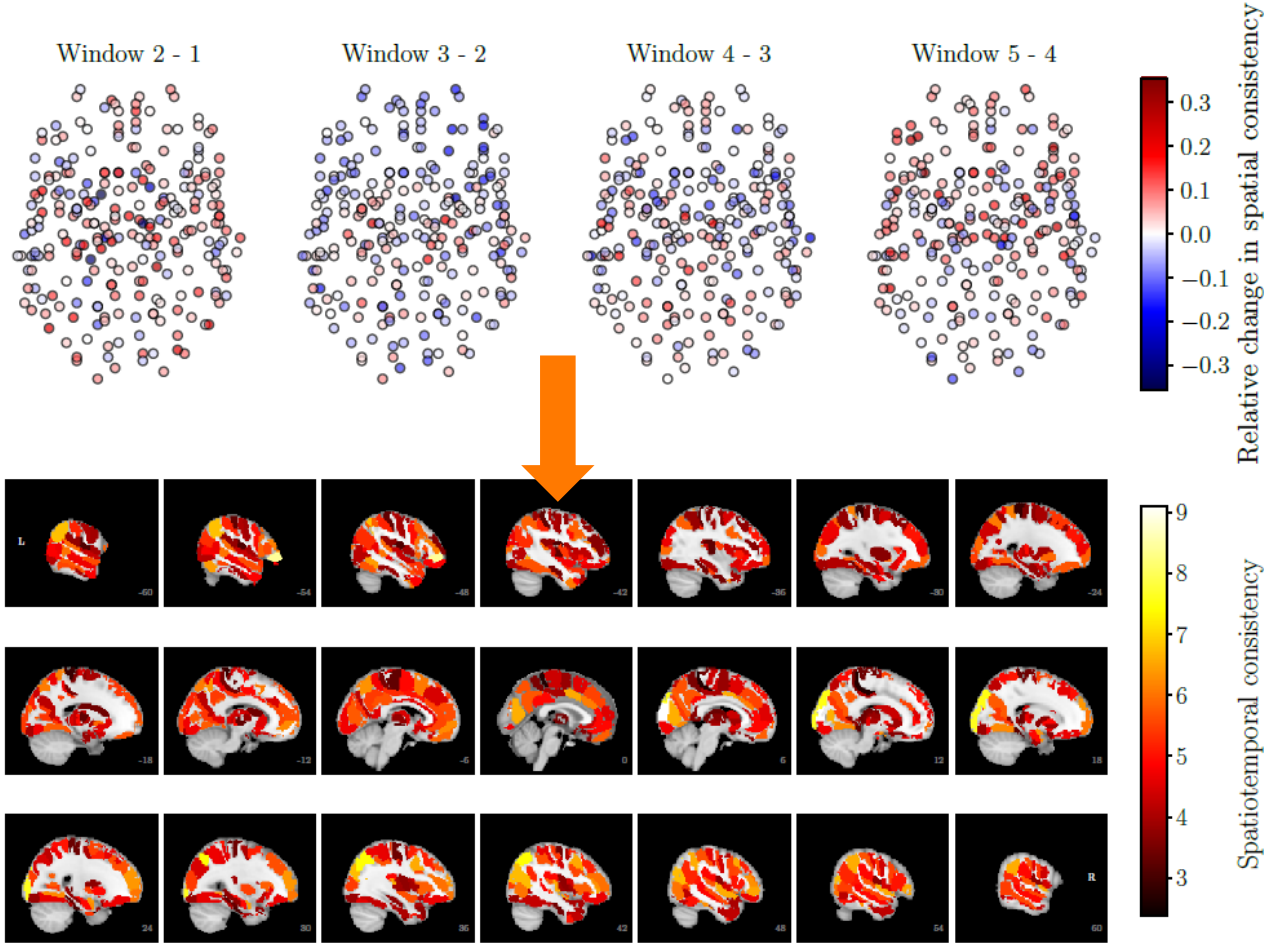
- Network turnover: changes in local network structure

$$\delta_{network}(I) = 1 - \mu_t^{Jaccard}(I)$$

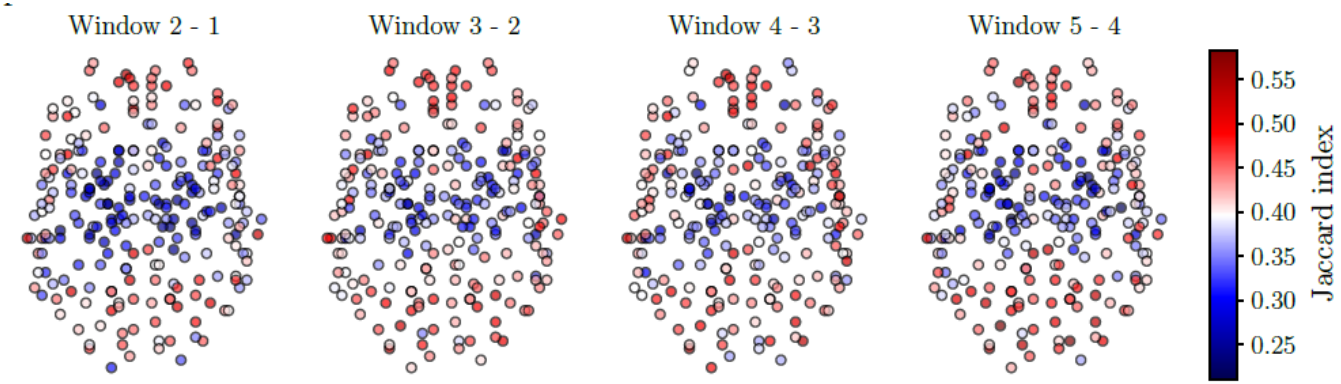
Spatial consistency changes in time



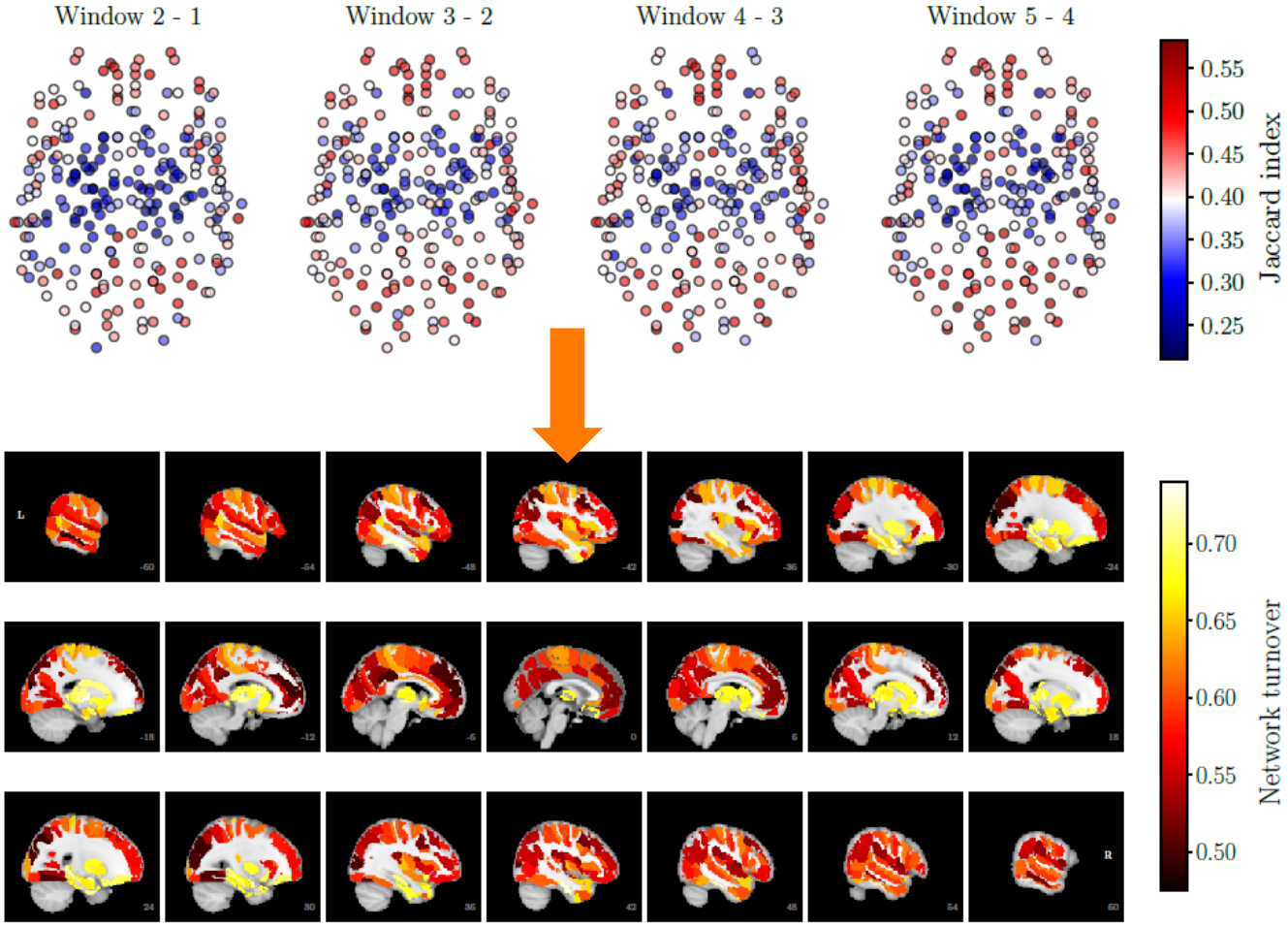
Spatial consistency changes in time



Turnover in network neighborhoods



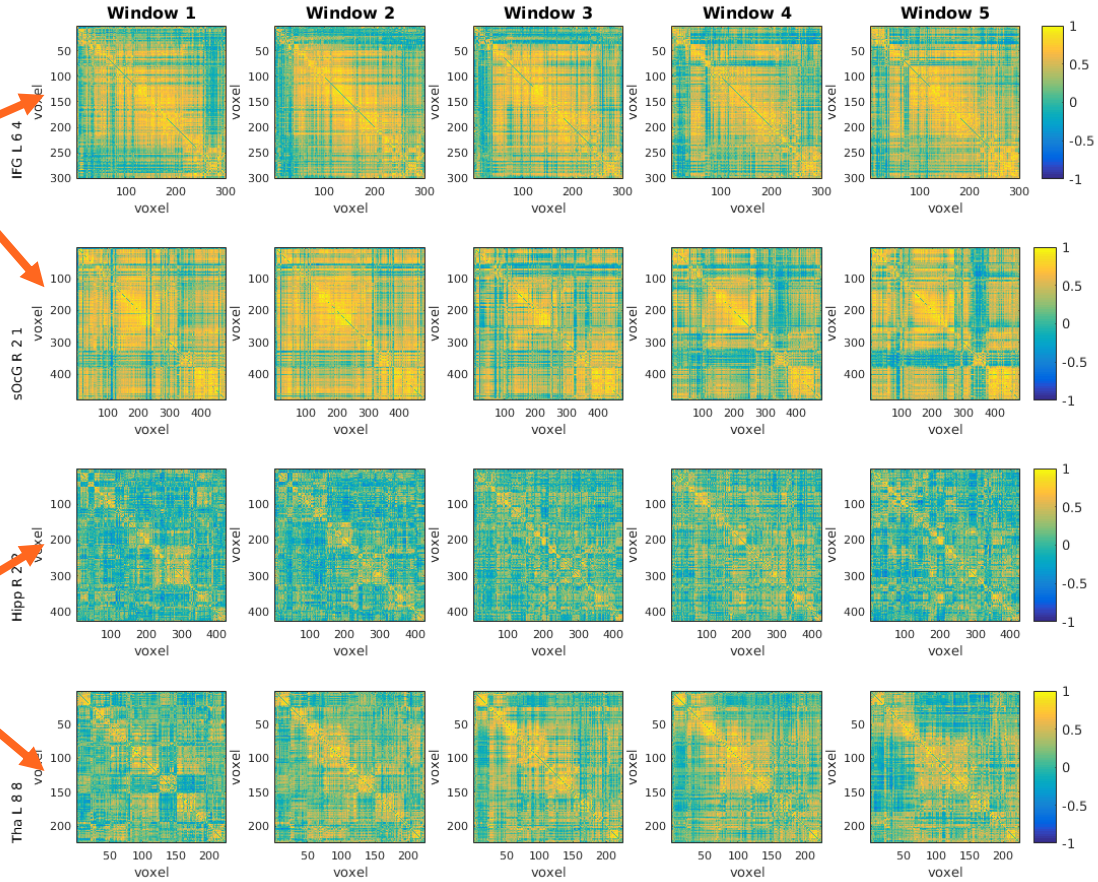
Turnover in network neighborhoods



ROIs have rich internal connectivity structure

High spatial consistency

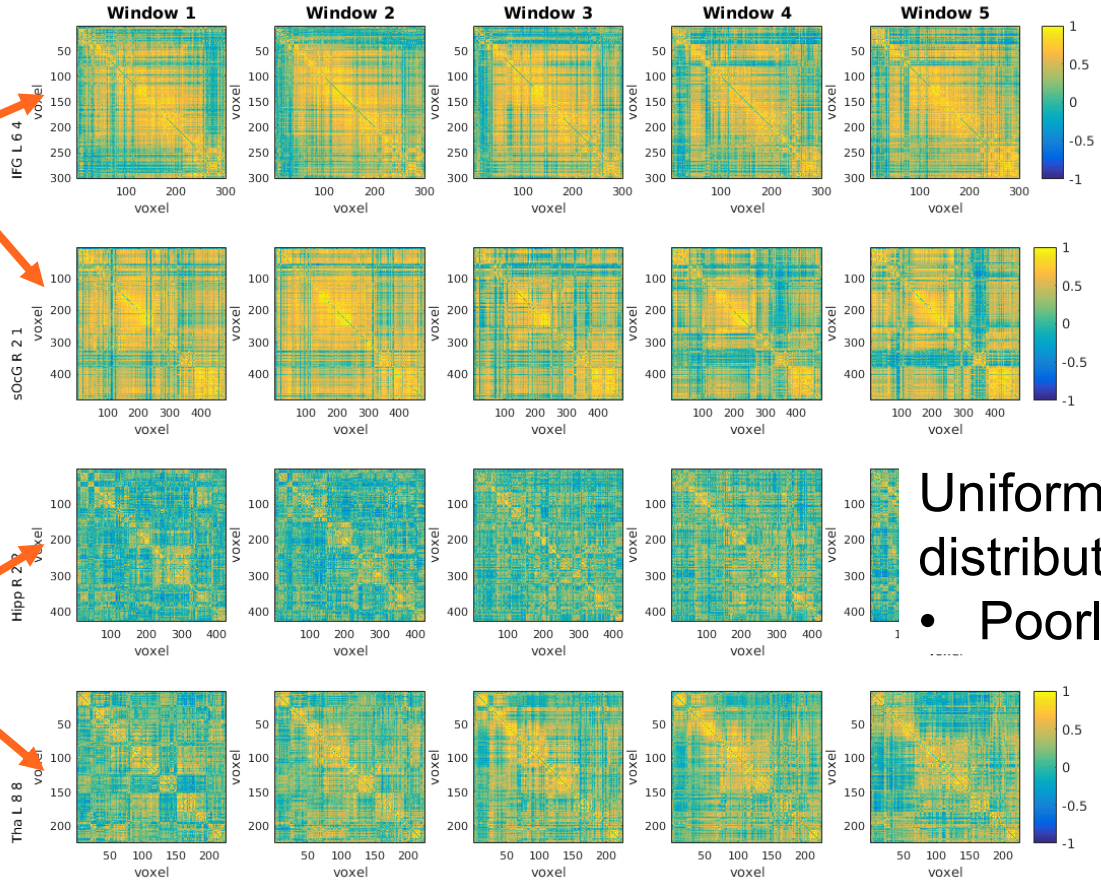
Low spatial consistency



ROIs have rich internal connectivity structure

High spatial consistency

Low spatial consistency



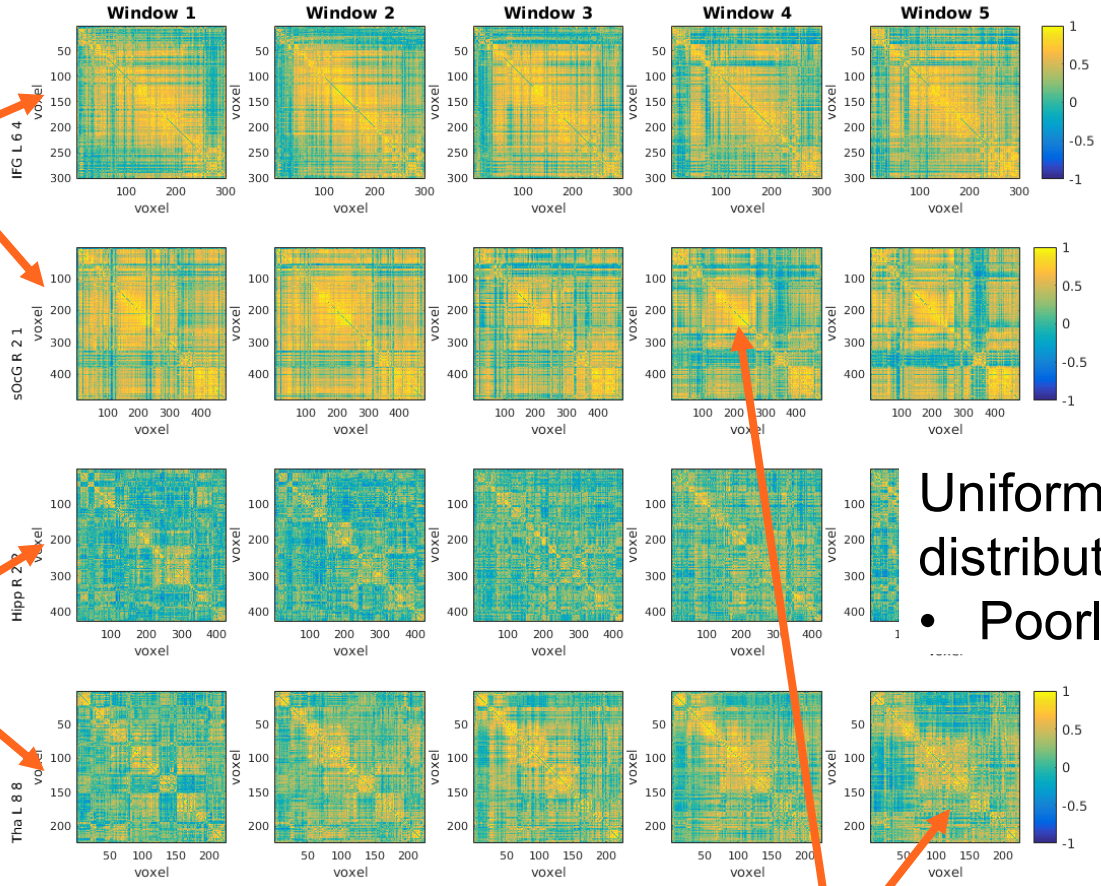
Uniform correlation distribution

- 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?

Internal connectivity and topological roles of nodes in functional brain networks

Ryyppö. E, Saramäki, J., & **Korhonen, O.**
Work in progress

Research questions

- Functional meaning of internal connectivity?
- Do internal connectivity and functional homogeneity predict ROIs' topological roles (= Hub or non-hub? Bridge-builder or provincial hub?)?

Methods

- Free music listening fMRI data (see above)
- ROIs: Brainnetome
- Links:
  - Pearson correlation coefficient between voxels
  - Thresholded to 0.01%
  - Link between ROIs = number of links between ROIs' voxels
- Predictors:
  - Spatial consistency φ_{spat}
  - Spatiotemporal consistency φ_{st}
  - SD of correlations inside ROI: broadness of correlation distribution
  - Self-link weight: number of voxel-level links inside the ROI
  - Relative self-link weight: normalized by ROI size
  - ROI size

Topological roles*

- Communities detected with Louvain algorithm
- Within-module strength: how connected node *i* is in its own module *s*?

$$z_i = \frac{\kappa_i - \bar{\kappa}_s}{\sigma_{\kappa_s}}$$

$$\kappa_i = \sum_{i' \in s} A(i, i')$$

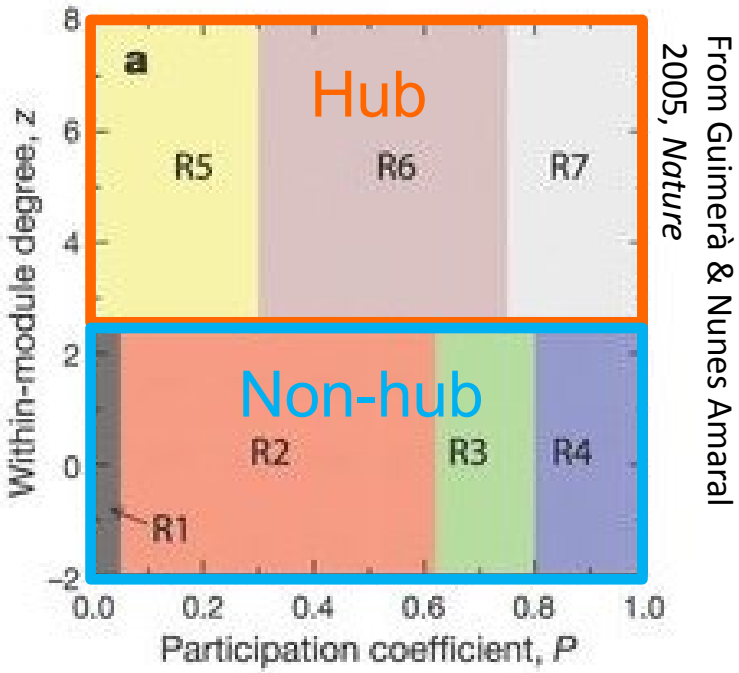
- Participation coefficient: how distributed are node *i*'s connections among modules?

$$P_i = 1 - \sum_s \left(\frac{\kappa_{is}}{k_i} \right)^2$$

* According to Guimerà & Nunes Amaral 2005, *Nature*

Prediction tasks

1) Hub vs non-hub: logistic ridge regression

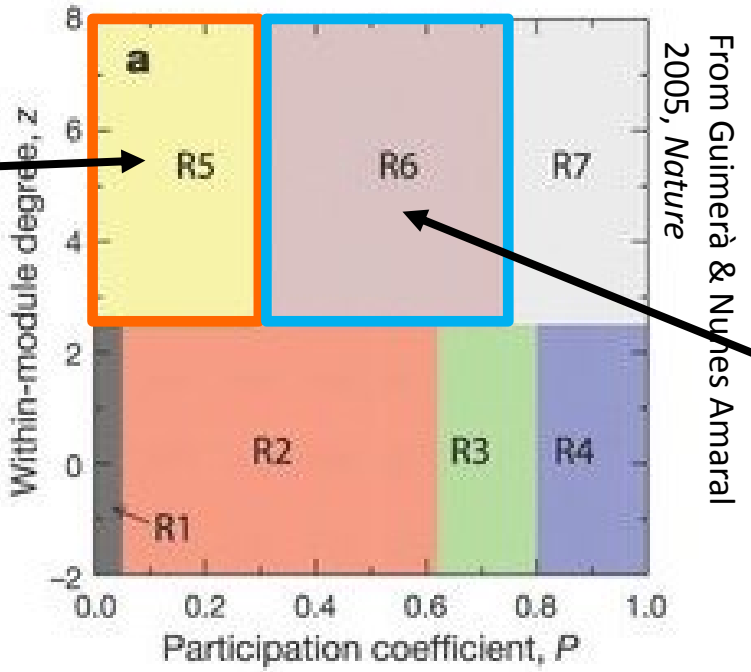


From Guimerà & Nunes Amaral 2005, *Nature*

Prediction tasks

2) Provincial vs connector hub: logistic ridge regression

Provincial

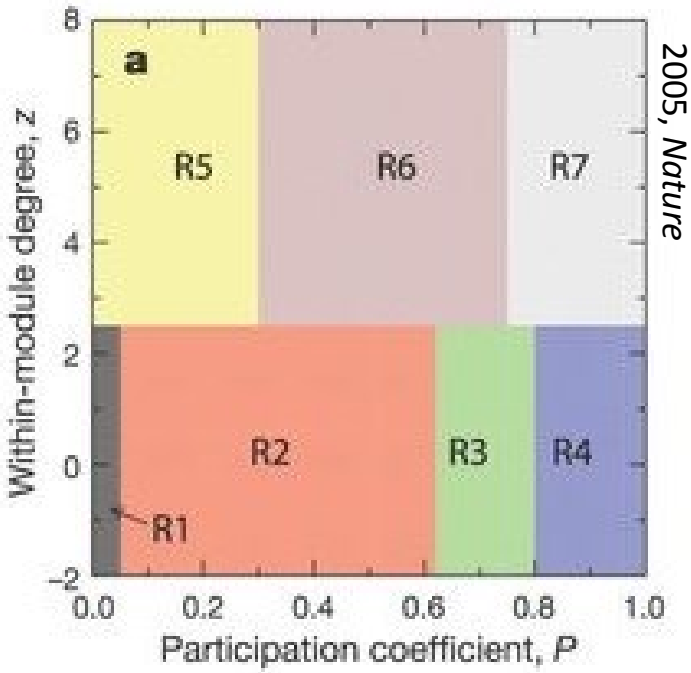


From Guimerà & Nunes Amaral 2005, *Nature*

Connector

Prediction tasks

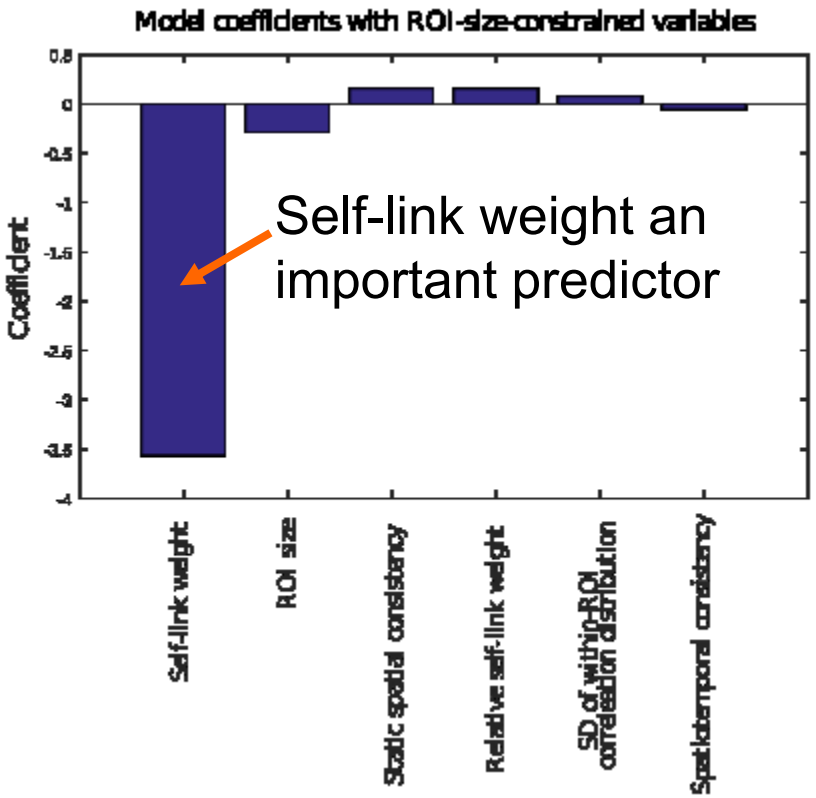
3) Multi-role classification: linear discriminant model



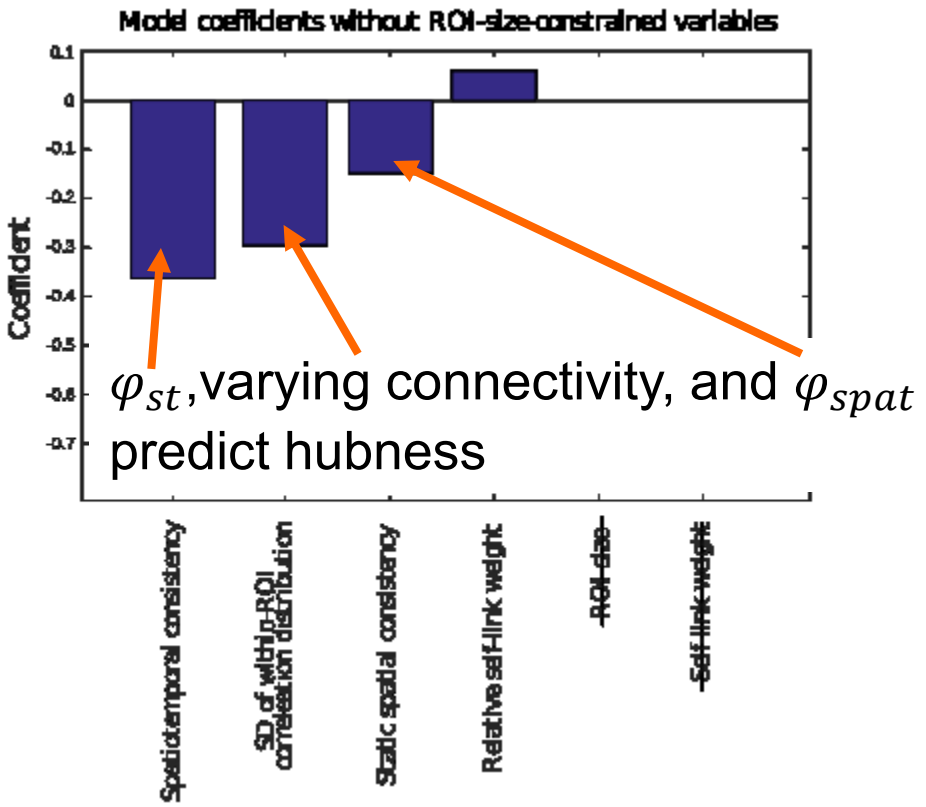
From Guimerà & Nunes Amaral 2005, *Nature*

Results: Hub vs non-hub

Accuracy:
Training 74.43%
Test 74.07%
(> Random 55.01%)

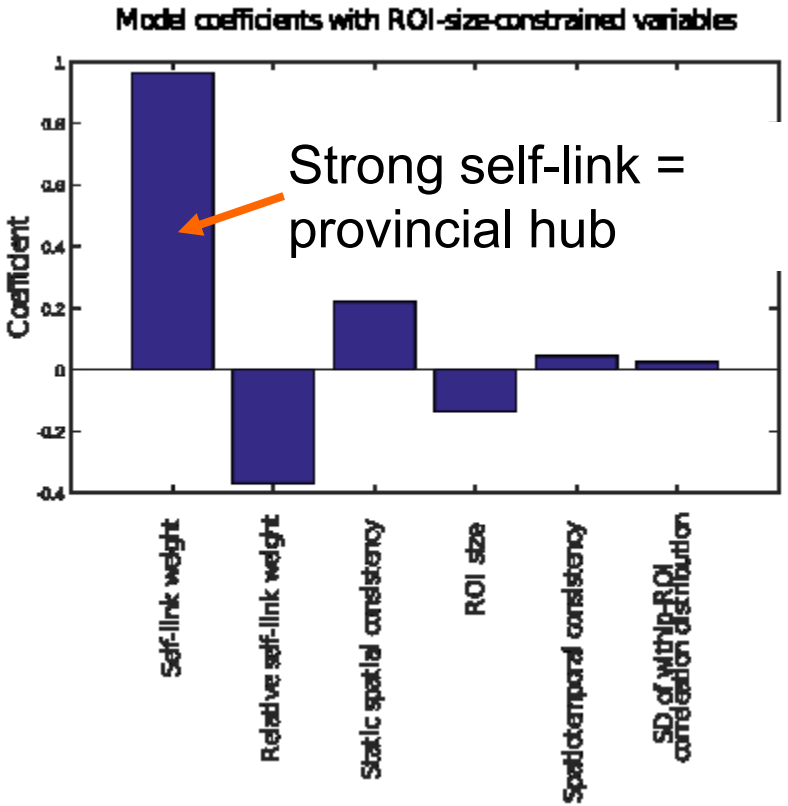


Accuracy:
Training 64.22%
Test 62.31%
(> Random 55.01%)

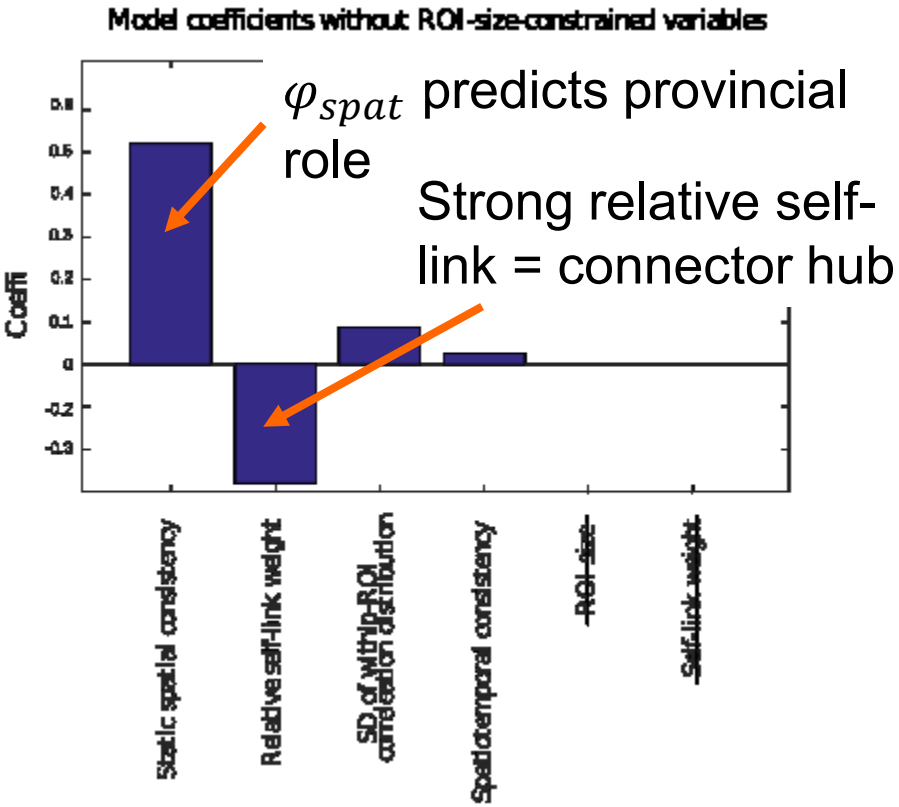


Results: Provincial vs connector hub

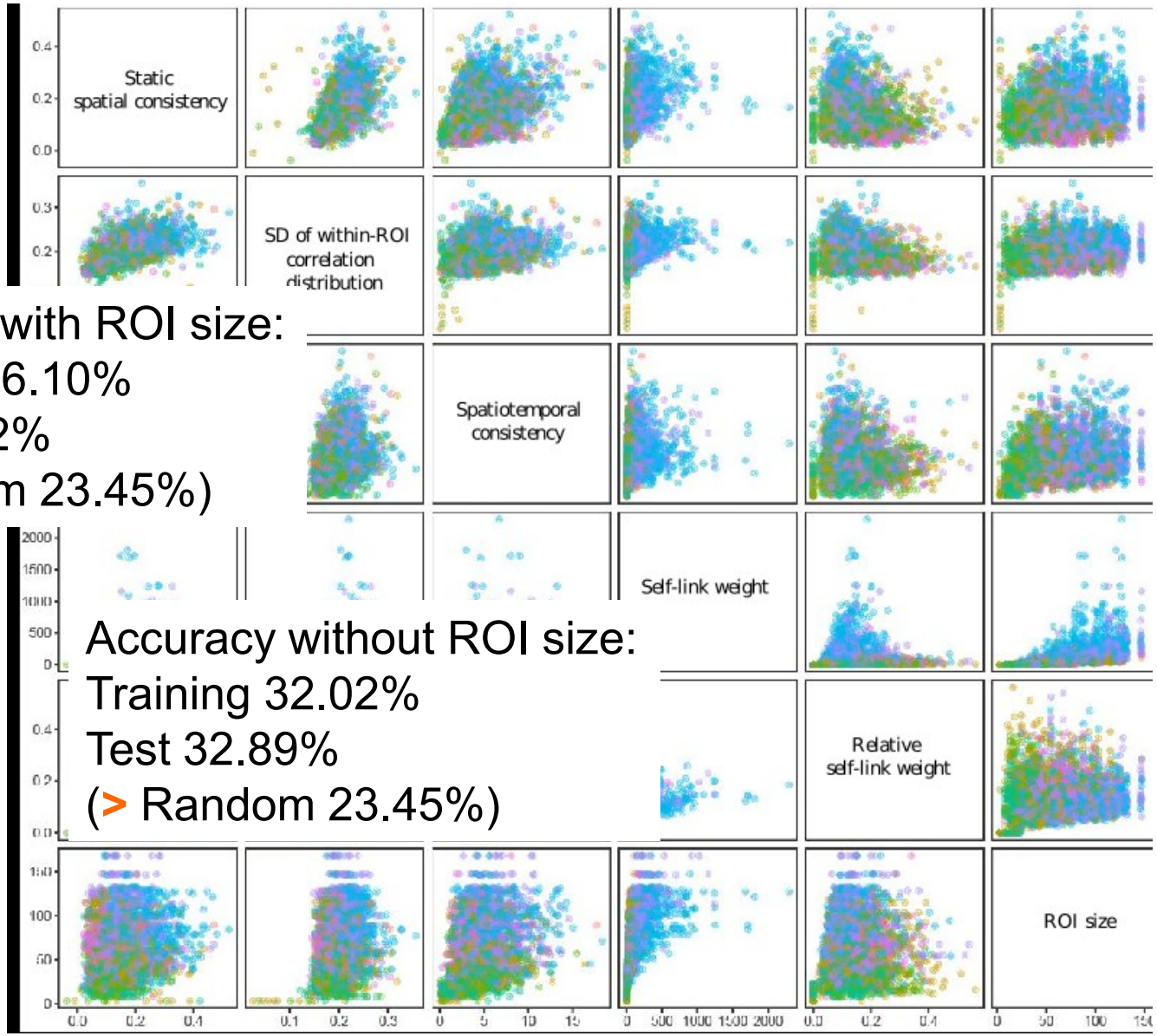
Accuracy:
Training 67.47%
Test 66.54%
(> Random 50.20%)



Accuracy:
Training 61.26%
Test 60.85%
(> Random 50.20%)



Results: Multi-role classification



Accuracy with ROI size:
Training 36.10%
Test 38.12%
(> Random 23.45%)

Accuracy without ROI size:
Training 32.02%
Test 32.89%
(> Random 23.45%)

Conclusions

- Internal connectivity measures predict topological roles

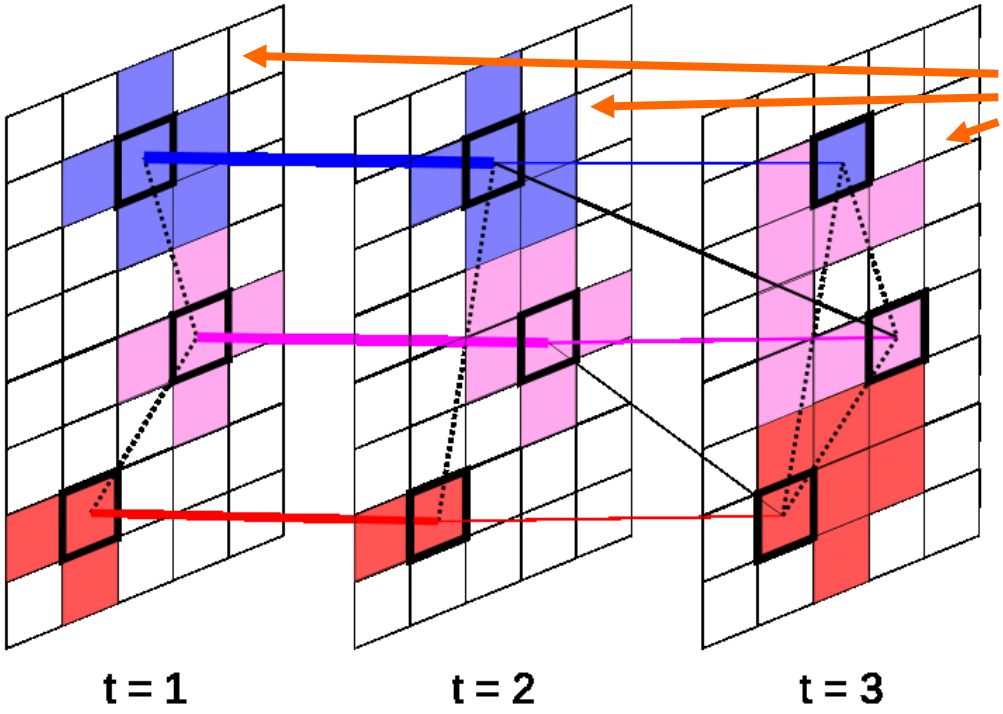
  ⇒Varying homogeneity not a technical flaw!
- Often ROI time series = average of voxel time series

  ⇒ Low homogeneity = lost data

  ⇒ Flexible nodes needed
- Next:
  - Topological roles without Louvain
  - Neuroscientific interpretation
  - Network model with flexible nodes

Network model with flexible nodes

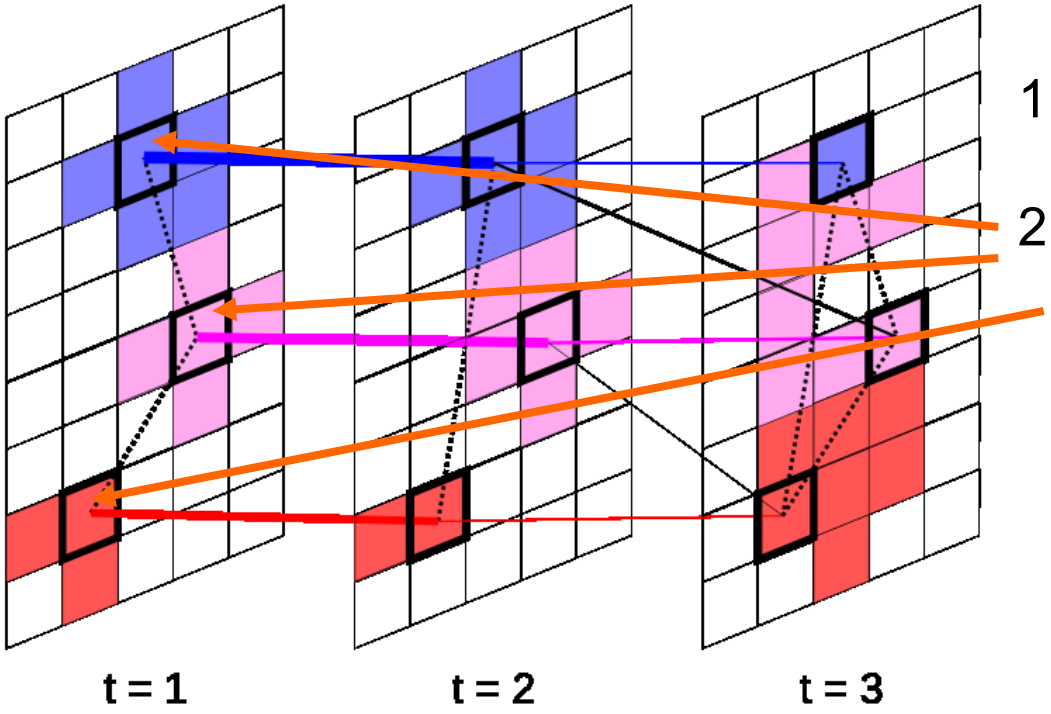
- Based on multilayer networks (= different connections in the same network)



1. Layers = time windows

Network model with flexible nodes

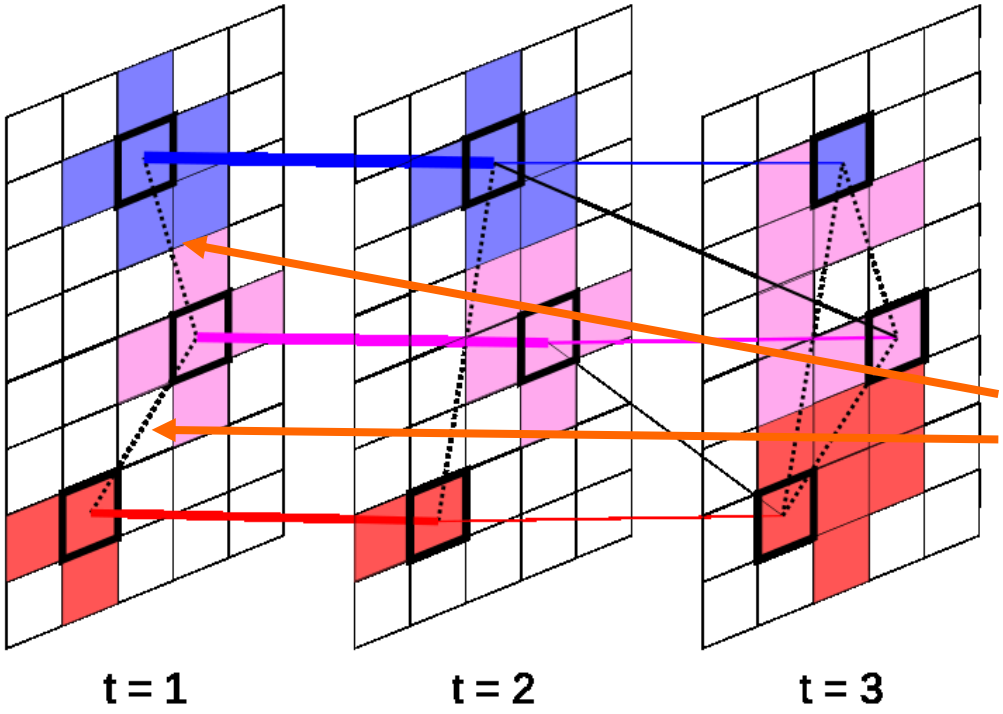
- Based on multilayer networks (= different connections in the same network)



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

Network model with flexible nodes

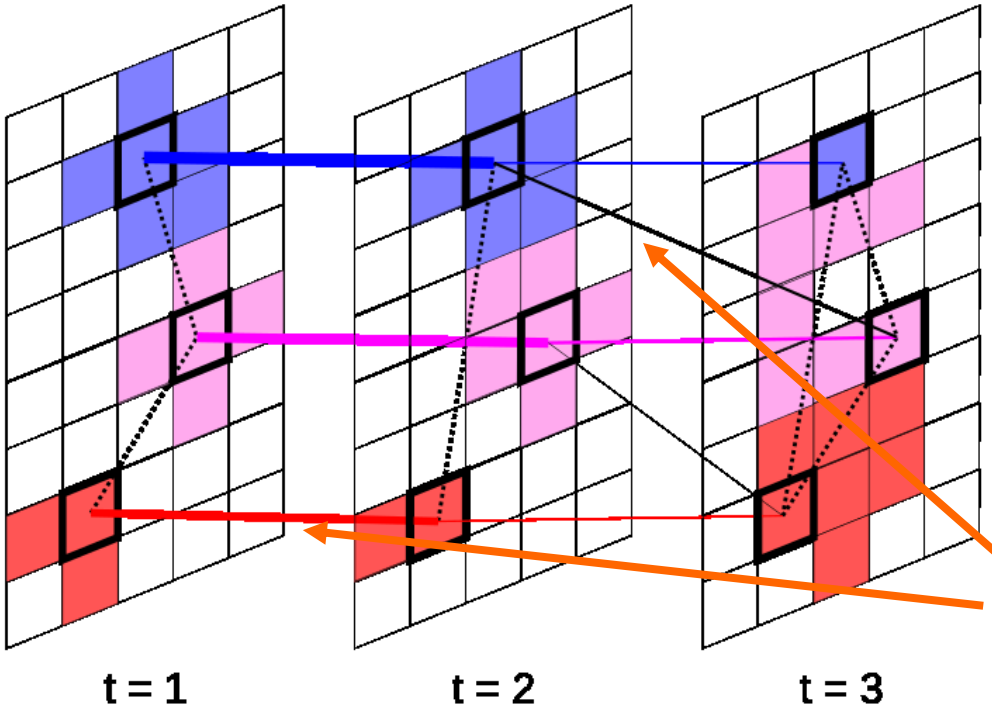
- Based on multilayer networks (= different connections in the same network)



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

Network model with flexible nodes

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



1. Layers = time windows
2. ROIs optimized inside layers for maximal consistency
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?
  - Homogeneity predicts topology
- Low homogeneity isn't a technical flaw

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

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

Thank you!

Questions, comments?

onerva.korhonen@gmail.com

onervakorhonen.wordpress.com
Twitter: @OnervaKorhonen