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

Onerva Korhonen

Twitter: @OnervaKorhonen

5.6.2019

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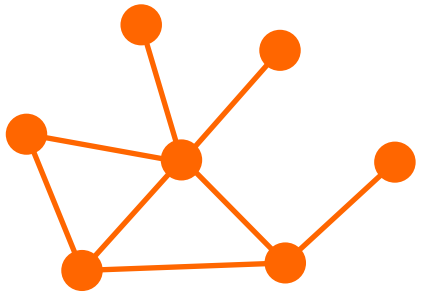

Networks: what and why?

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

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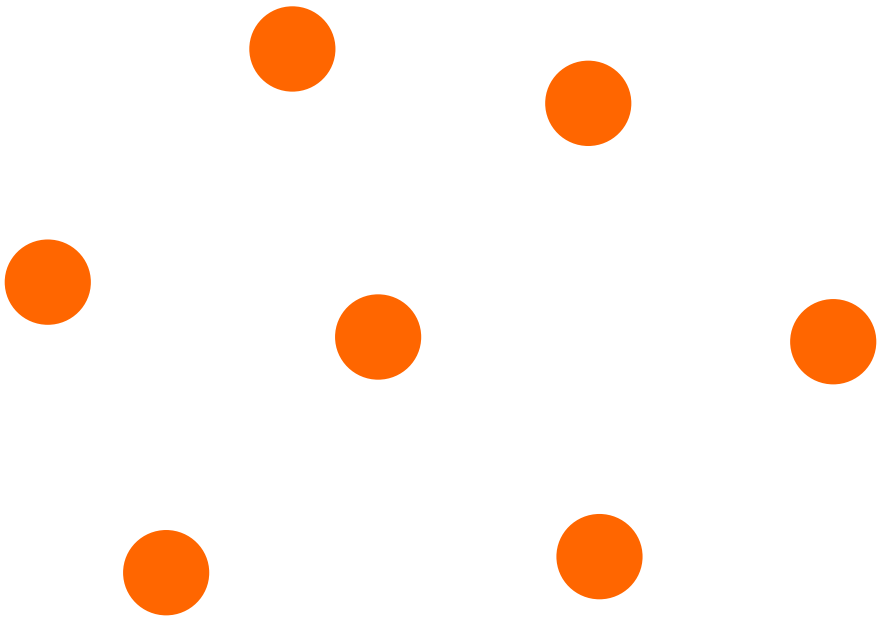

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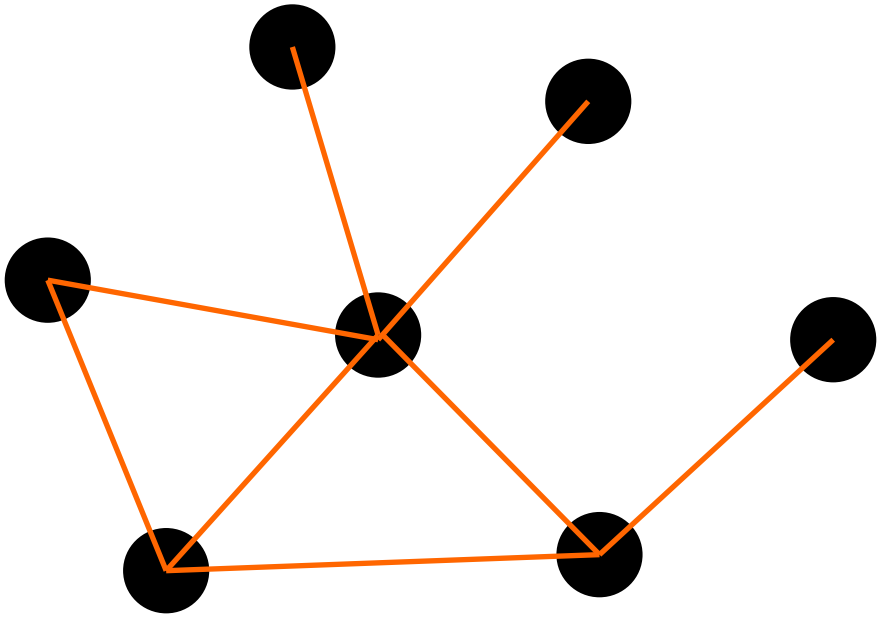

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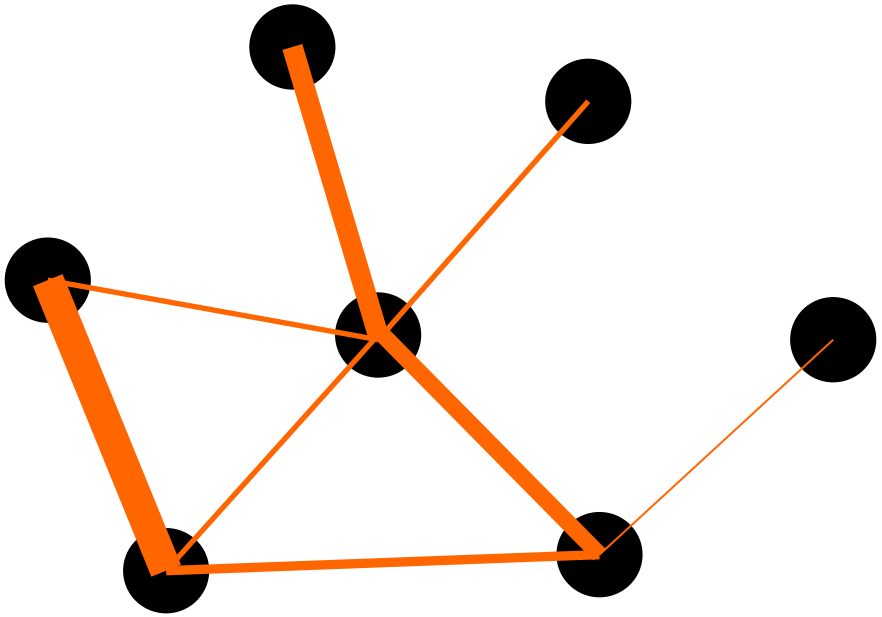

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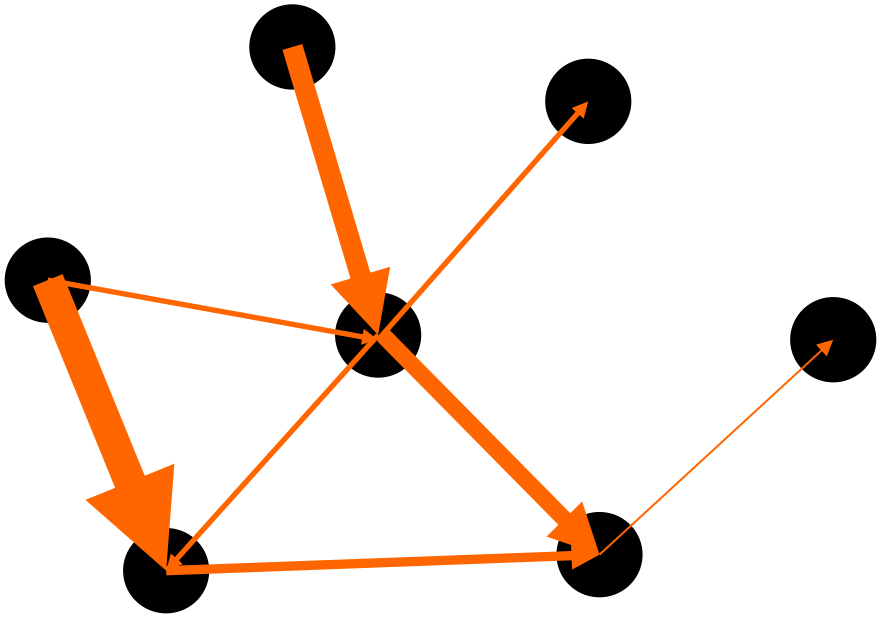

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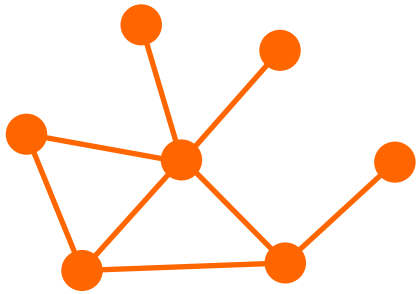
  - Weights?
  - Direction?

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

Brain networks:

- Model for interactions in the brain



Why is the brain a network?

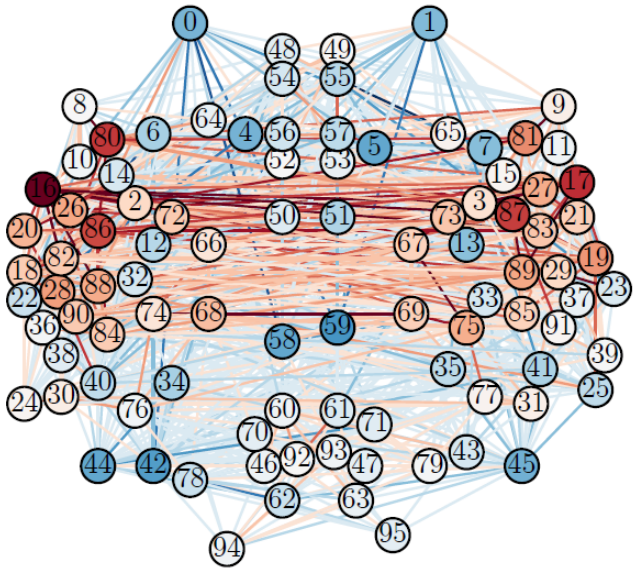


Fig: Alakörkkö *et al.* 2017, *European Journal of Neuroscience*

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

Network neuroscience

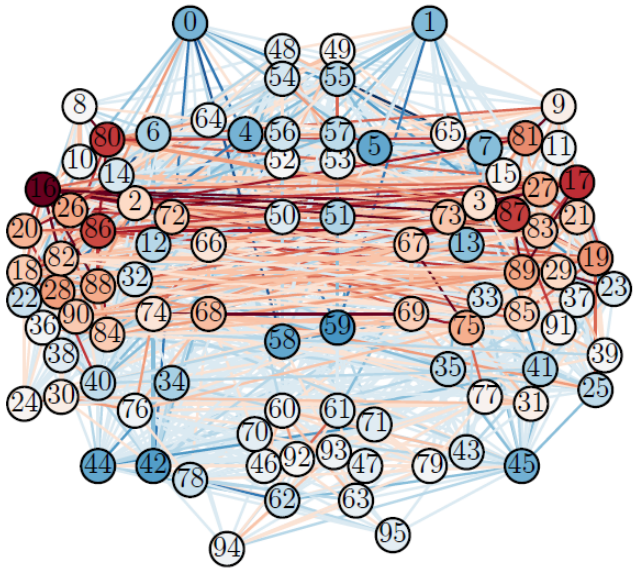


Fig: Alakörkkö *et al.* 2017, *European Journal of Neuroscience*

- Network neuroscience = 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

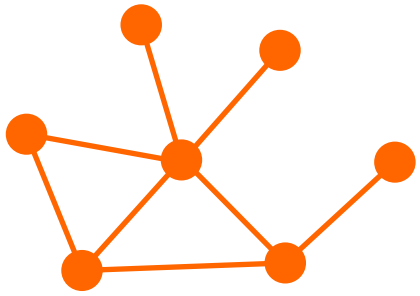
What's wrong with the nodes of functional brain networks?

Functional brain networks:

- Links = coactivation
- From fMRI data

Brain networks:

- Model for interactions in the brain



Functional magnetic resonance imaging (= fMRI)

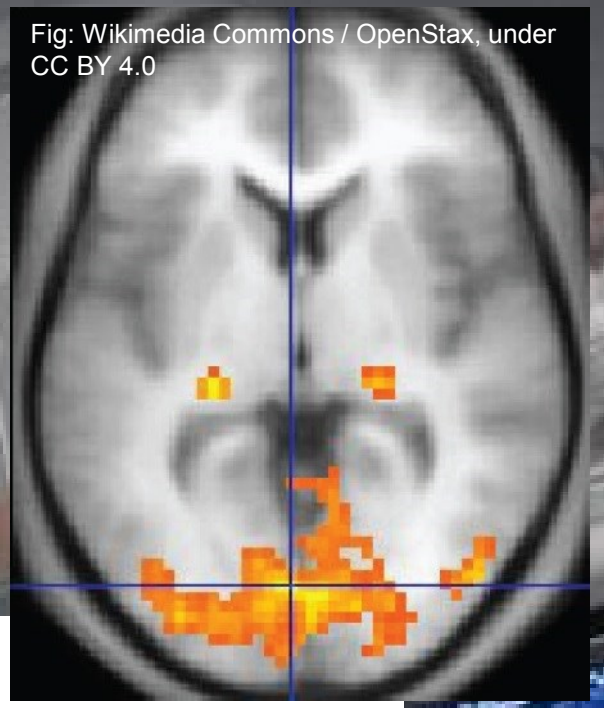


Fig: Wikimedia Commons / OpenStax, under CC BY 4.0

- Based on magnetic properties of haemoglobin
- fMRI uses two magnetic fields:
  1. A strong static field aligns haemoglobin molecule spins
  2. A short pulse disturbes the alignment
- After the pulse, spins return to equilibrium, emitting a radio wave
- Different waves from oxygen-rich and oxygen-poor heamoglobin
  => **oxygen-rich areas localized**
- Brain function requires oxygen
  => **high oxygen level = high activity**
- Measurement unit = voxel

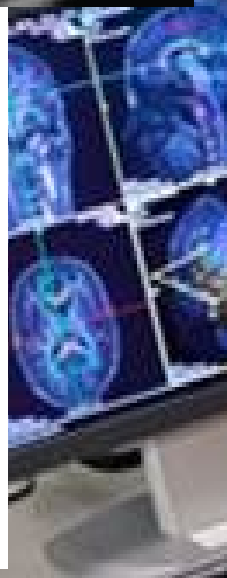


Fig: Aalto Magnetic Imaging (AMI Center), by parmission

fMRI vs MEG/EEG

fMRI

- Connection between oxygen and activation not fully known

MEG/EEG

- A direct measure of brain activity

fMRI vs MEG/EEG

fMRI

- Connection between oxygen and activation not fully known
- Measured in anatomical space

MEG/EEG

- A direct measure of brain activity
- Measured in sensor space => inverse transform needed

fMRI vs MEG/EEG

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- Very high spatial resolution (~mm)

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fMRI vs MEG/EEG

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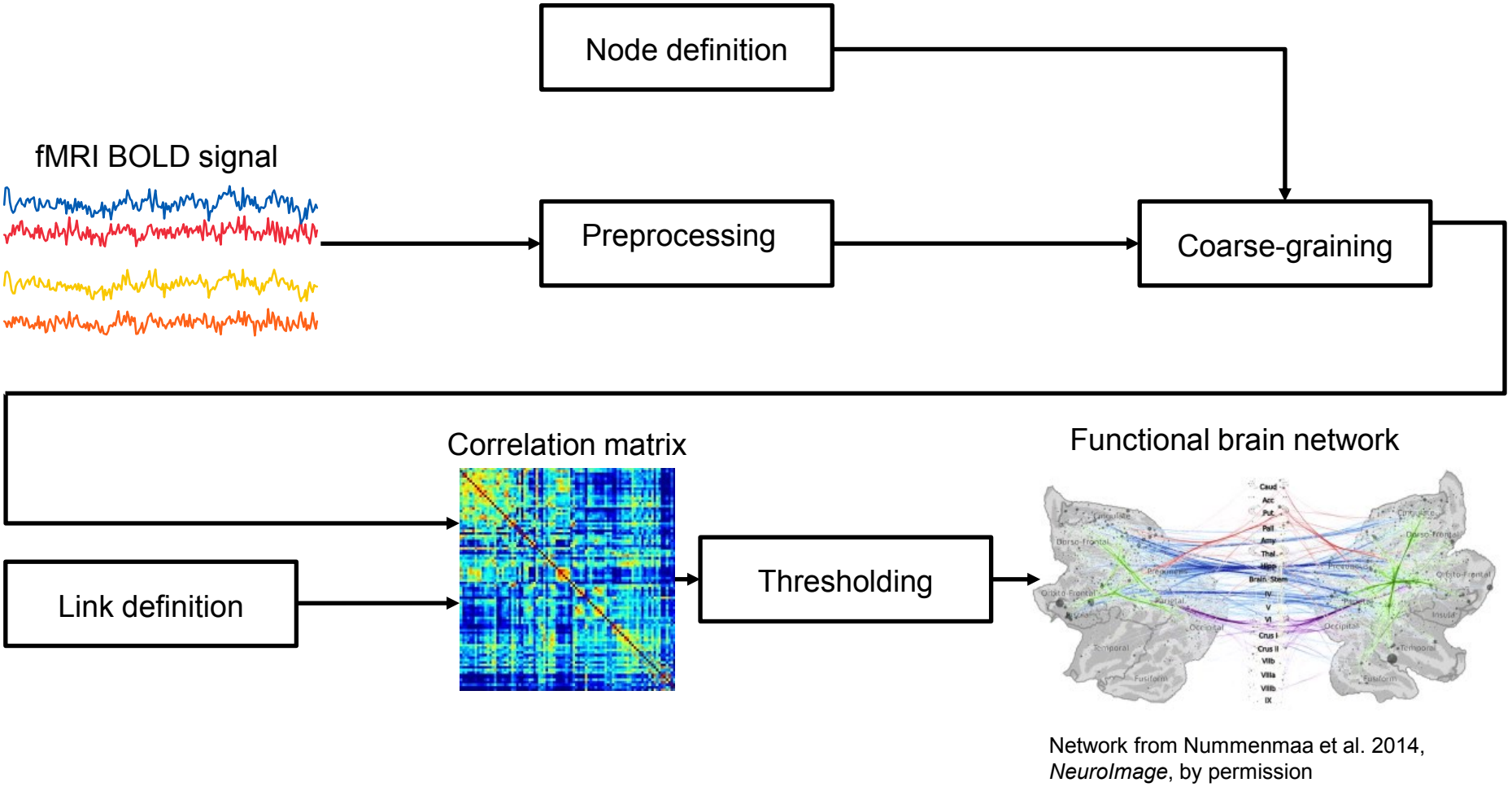
fMRI and MEG/EEG are **complementary methods** (although so far difficult to measure at the same time)

Functional brain networks: how-to?



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

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

Nodes:

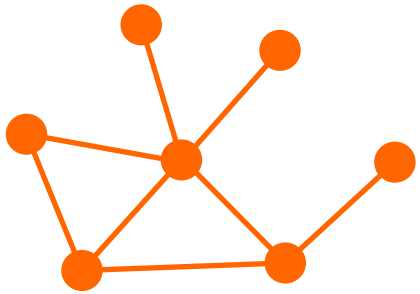
- No natural candidates above the neuronal scale
- Node selection affects network properties
- Regions of Interest (ROIs) or voxels?

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*

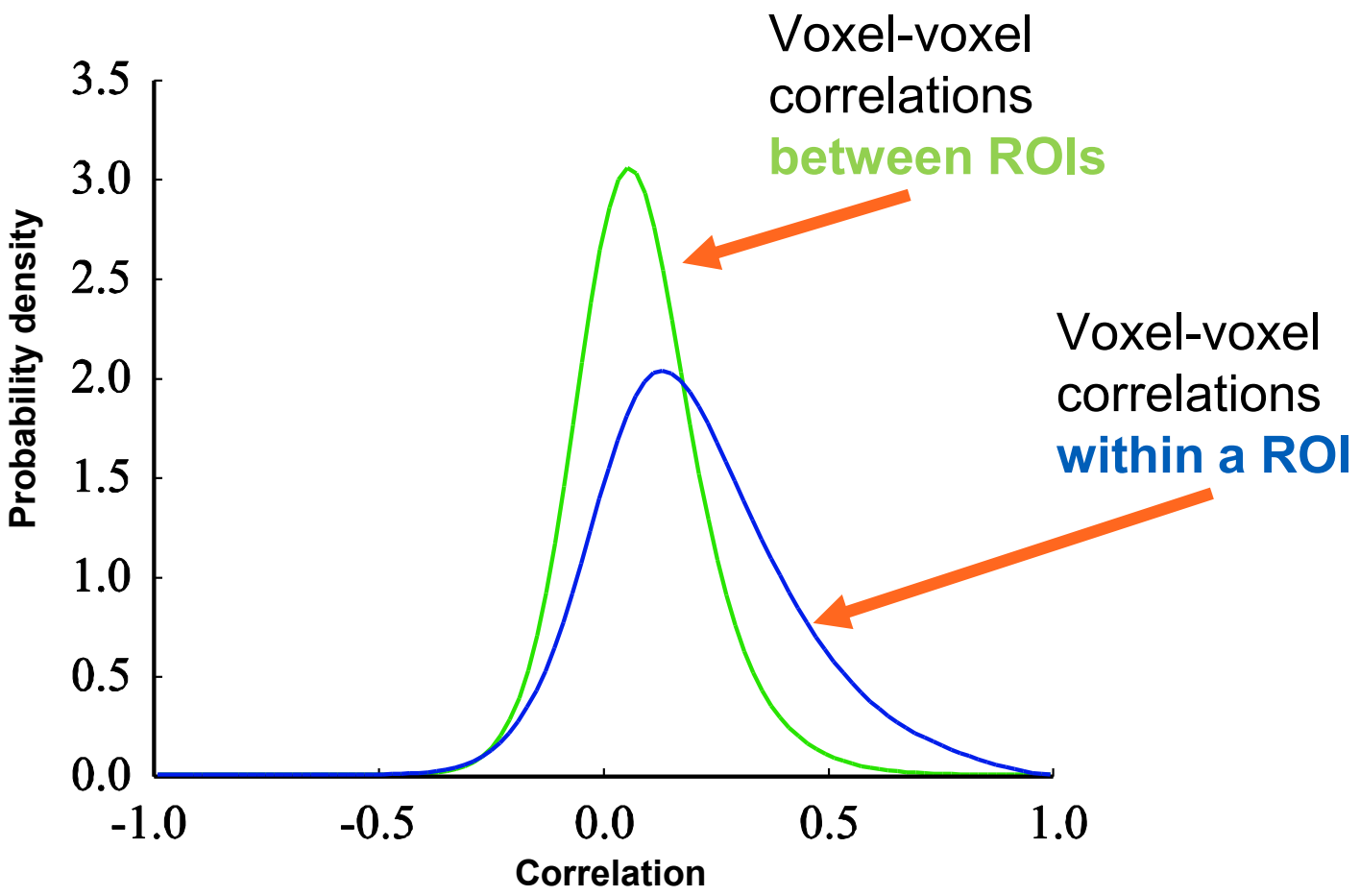
Research questions

- 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?



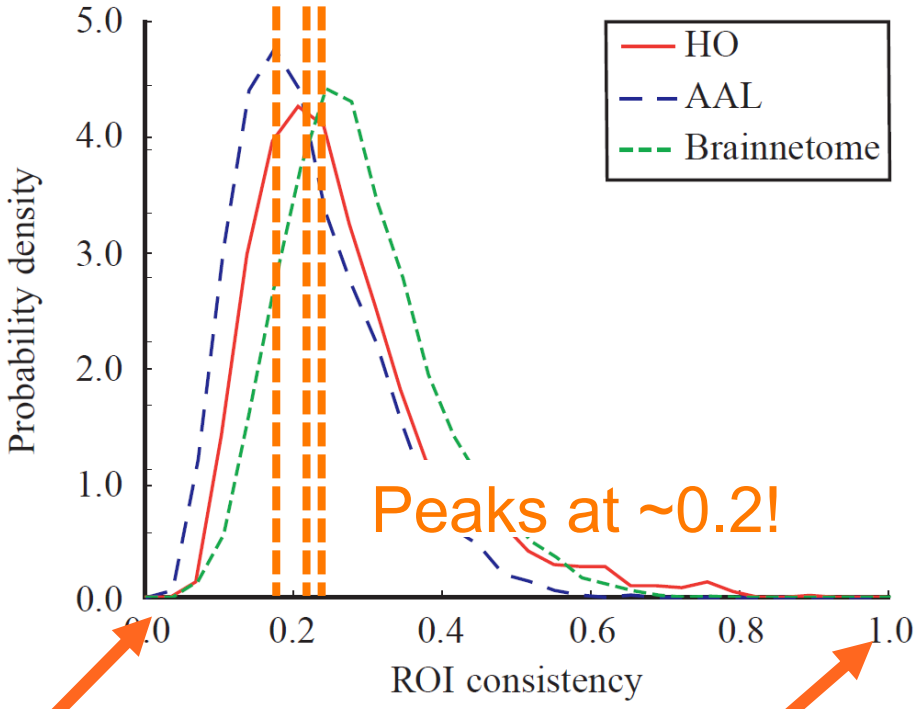
How homogeneous are ROIs?

- **Spatial consistency**

= measure of functional homogeneity:

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

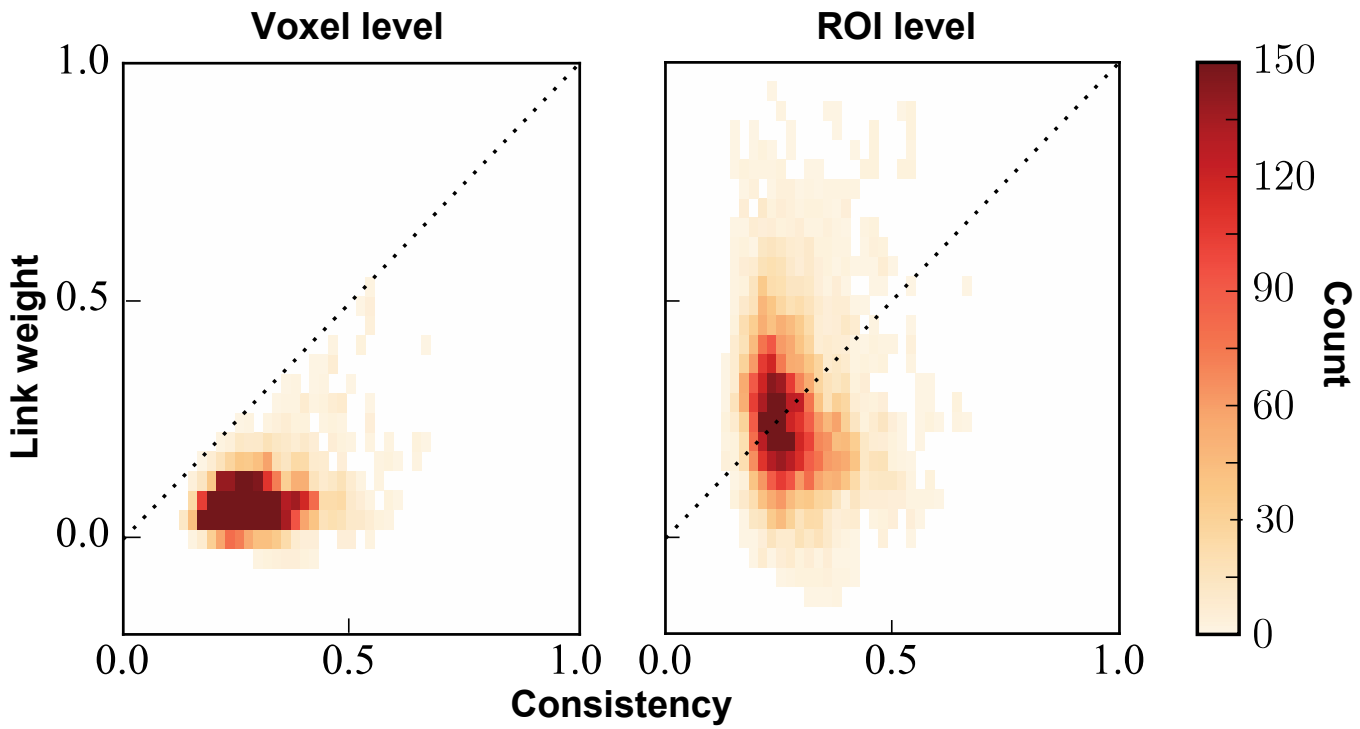
- Straightforward to calculate
- Easy to interpret



Lack of homogeneity

Perfect homogeneity

Does consistency predict connectivity?



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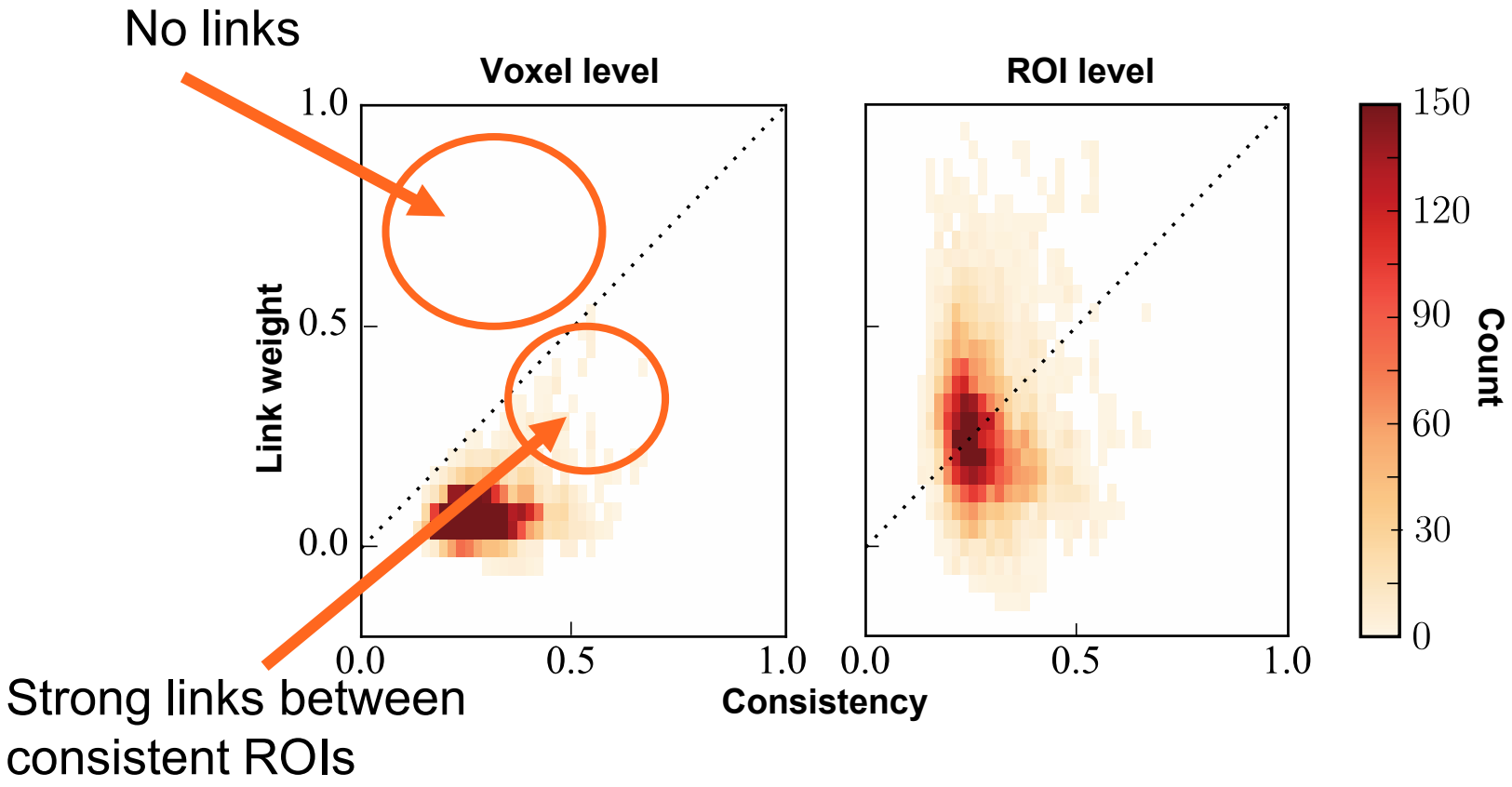

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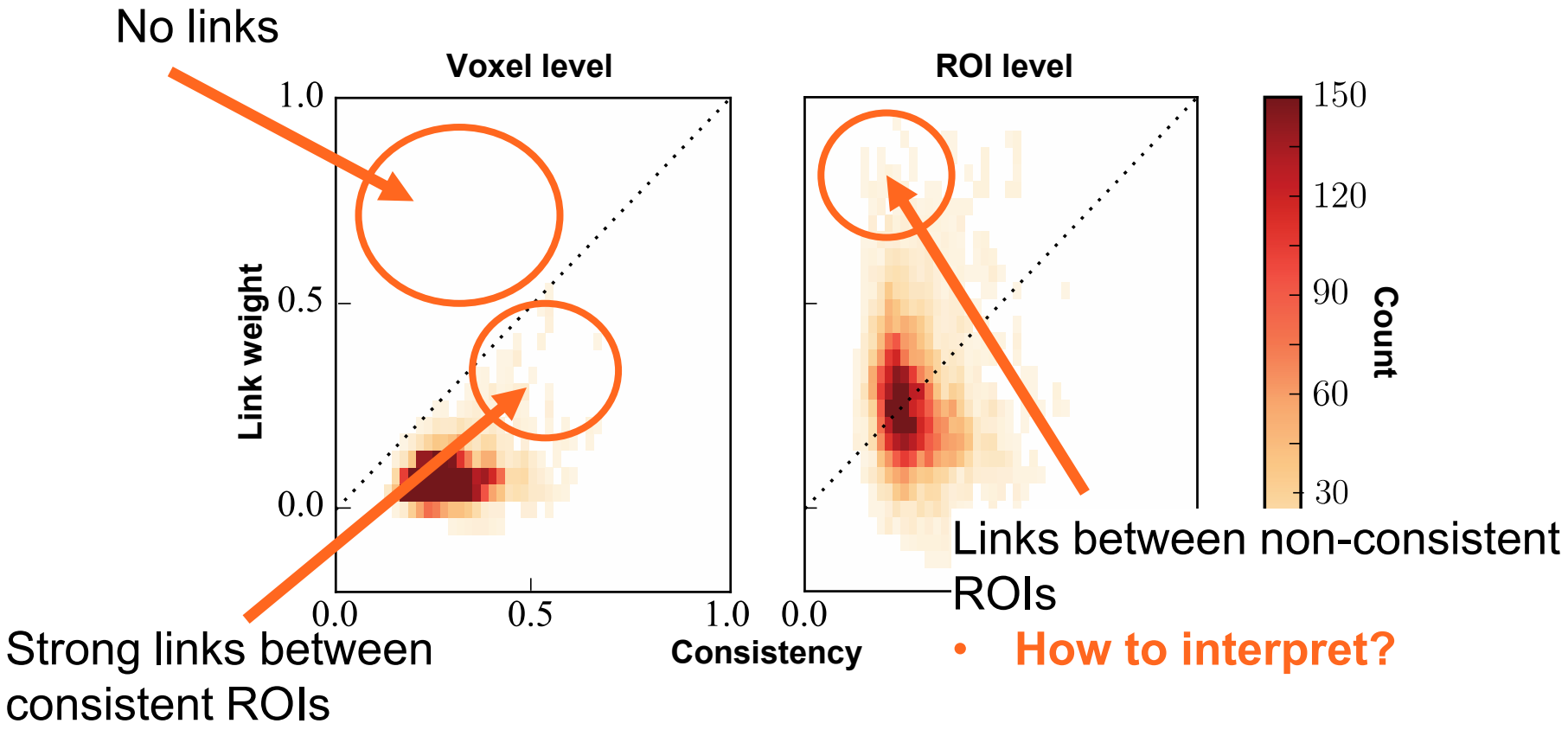
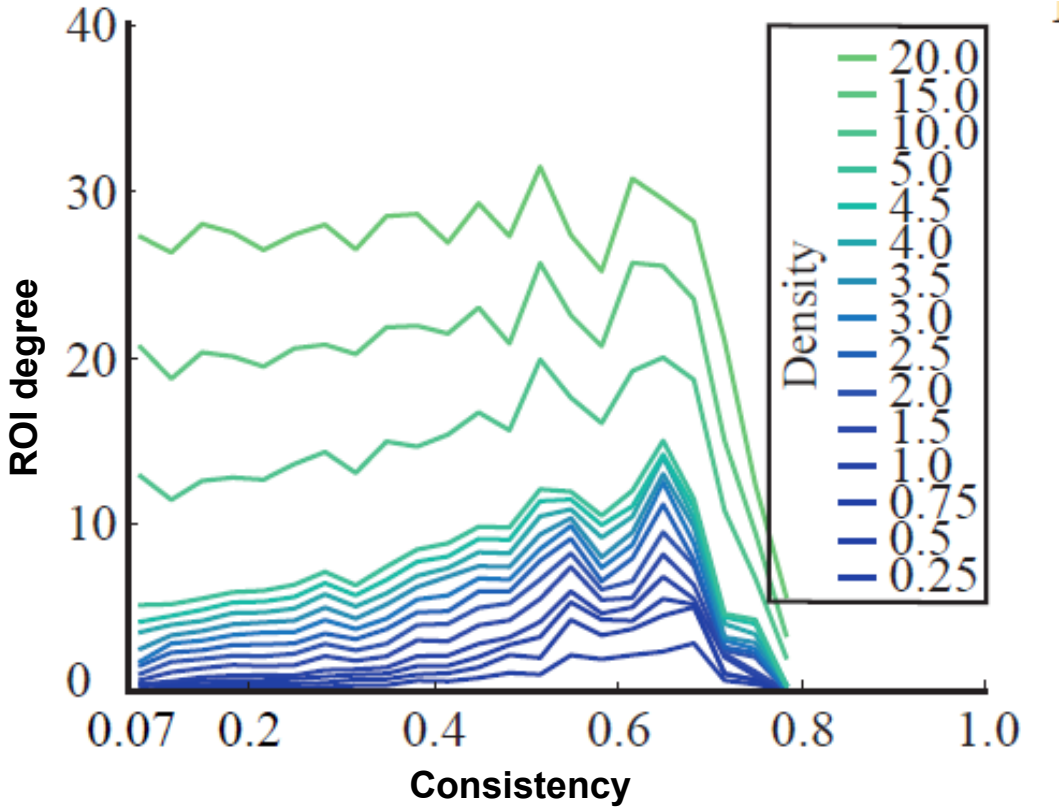


- **How to interpret?**

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

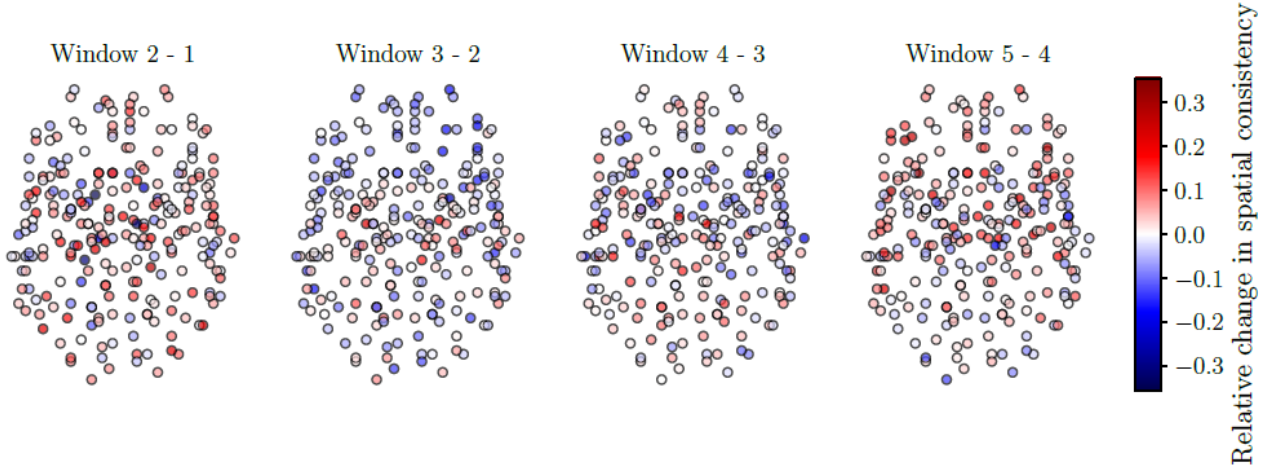
- Spatial consistency φ_{spat}: functional homogeneity of ROI
- Spatiotemporal consistency: time-dependence of φ_{spat}

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

- Network turnover: changes in local network structure

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

Spatial consistency changes in time



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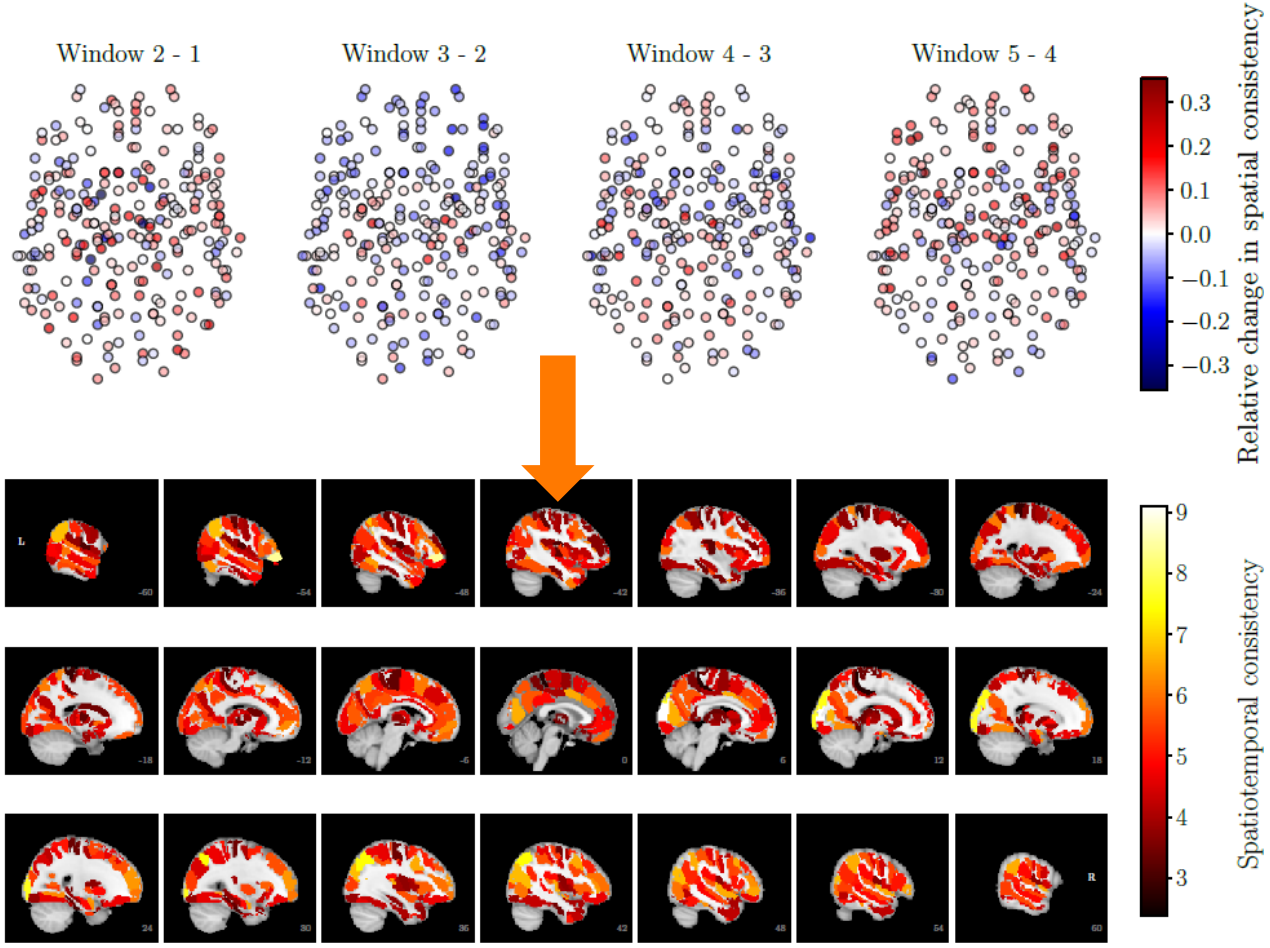
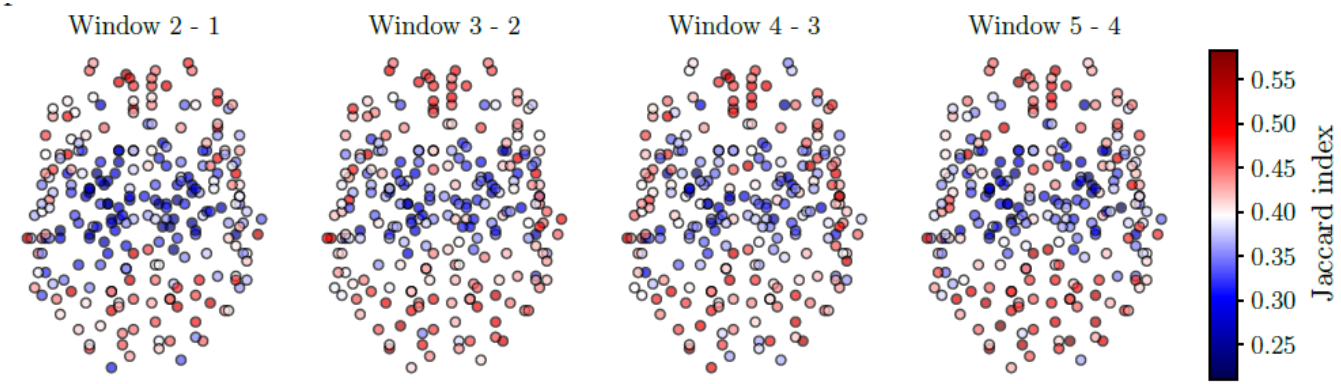


Turnover in network neighborhoods



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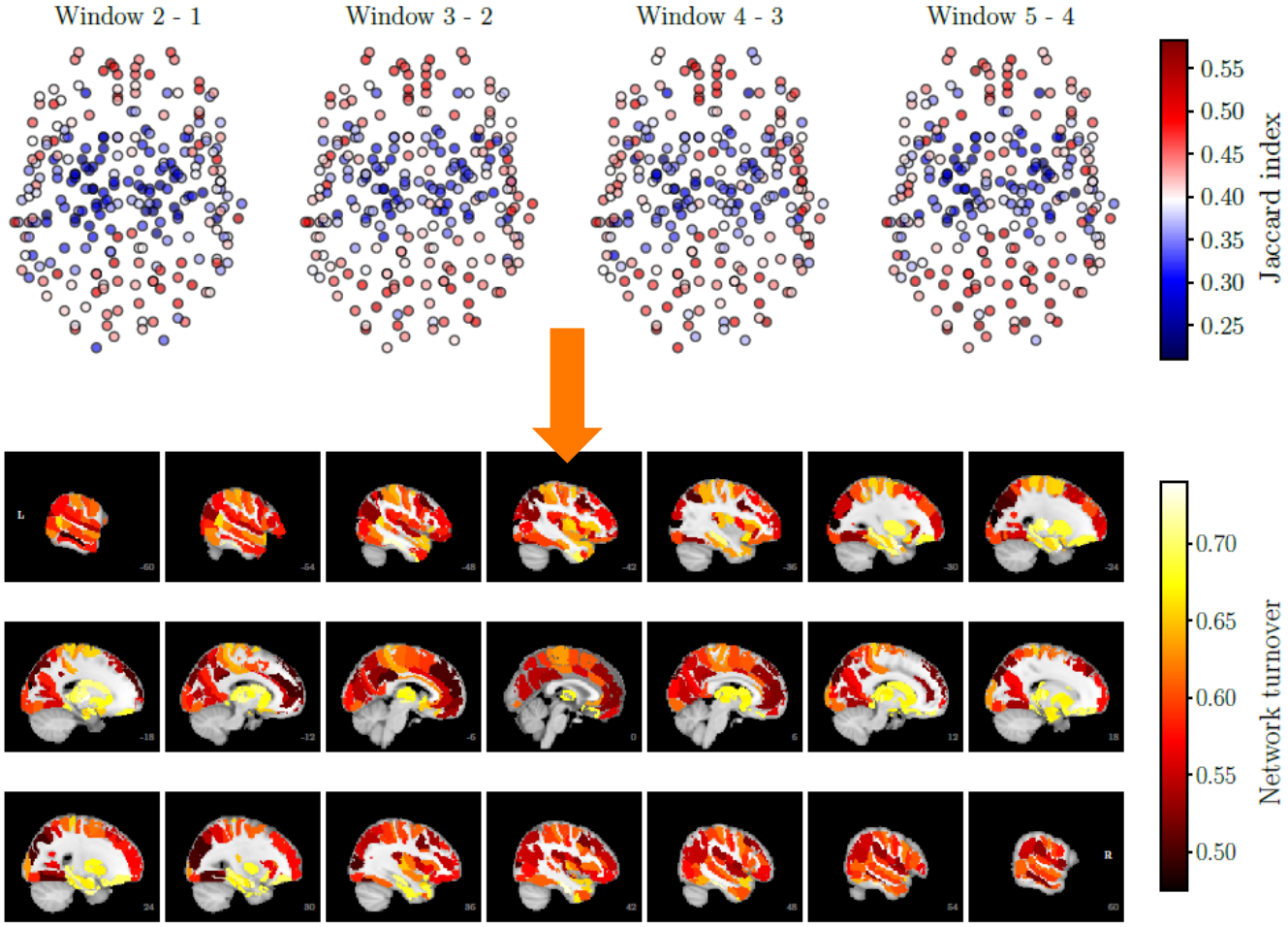
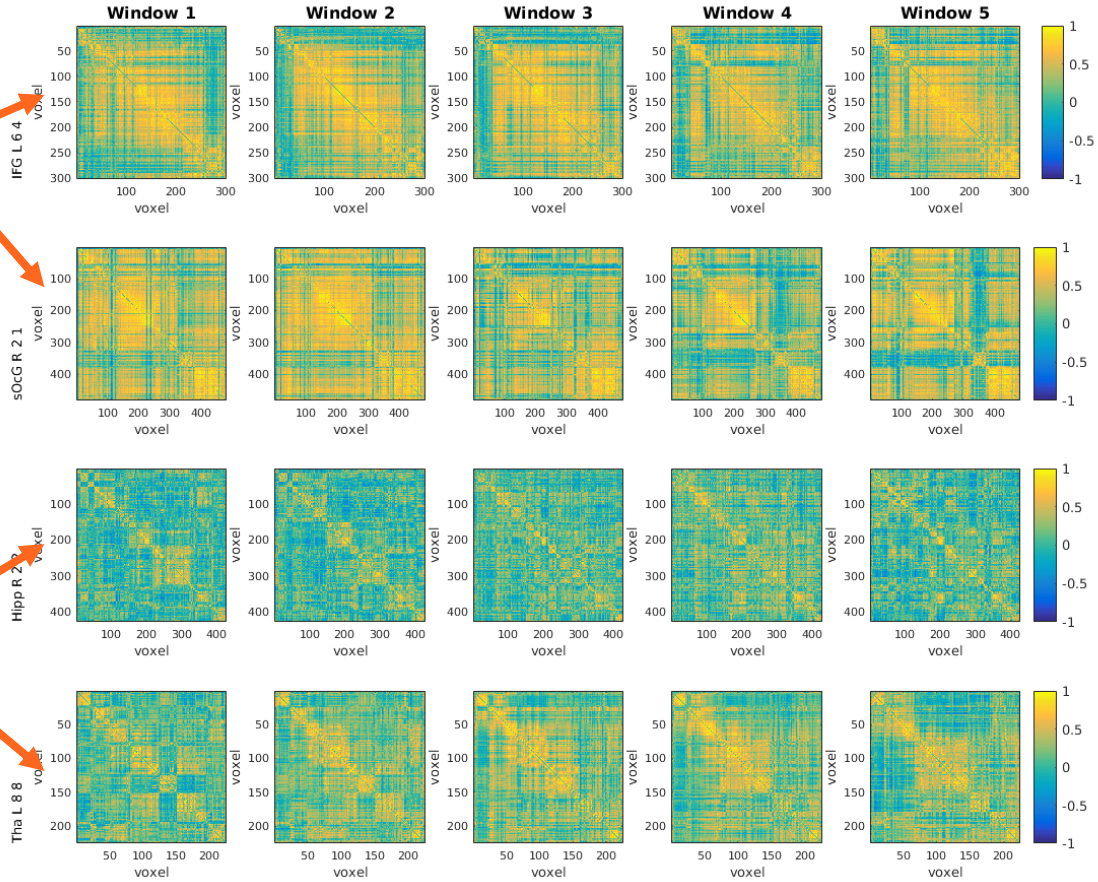


ROIs have rich internal connectivity structure

High spatial consistency

Low spatial consistency



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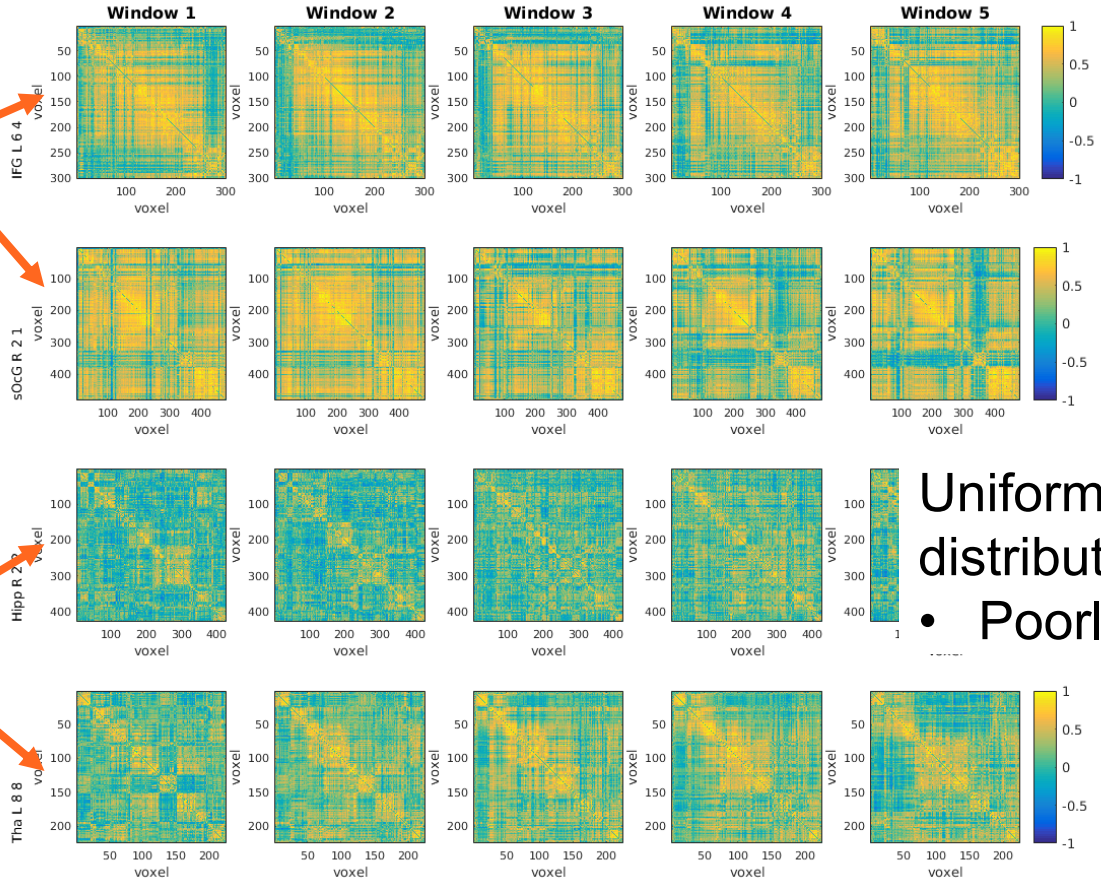

Uniform correlation distribution

- Poorly defined ROI?

ROIs have rich internal connectivity structure

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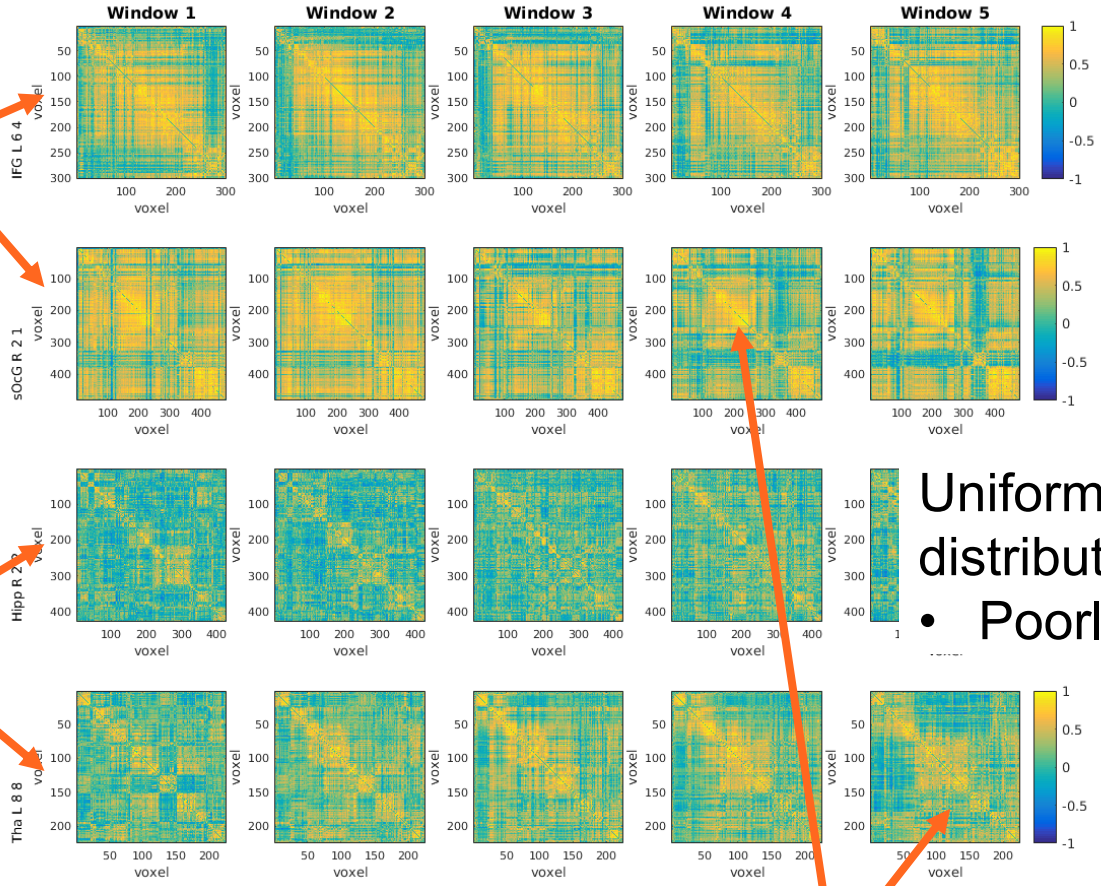


Uniform correlation distribution

- Poorly defined ROI?

Intra-ROI modules

- Network topology?

Conclusions

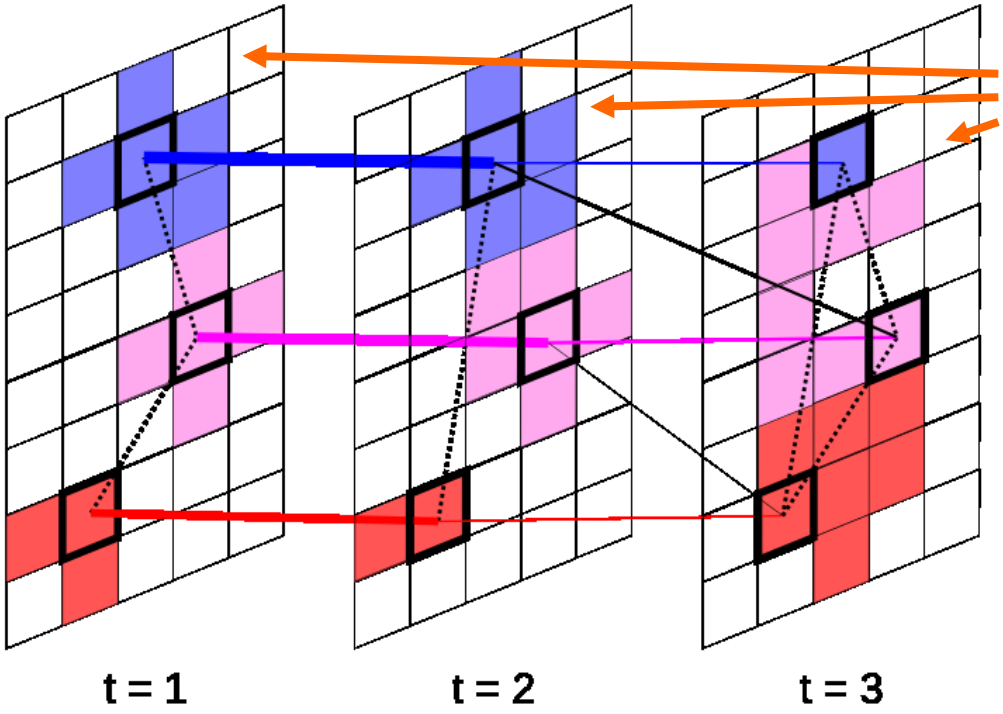
- Spatial consistency changes in time
  - Reflects activation?
- ROIs have time-dependent internal structure
  - Relates to network topology?
- Do brain networks have stable nodes?

On-going work: 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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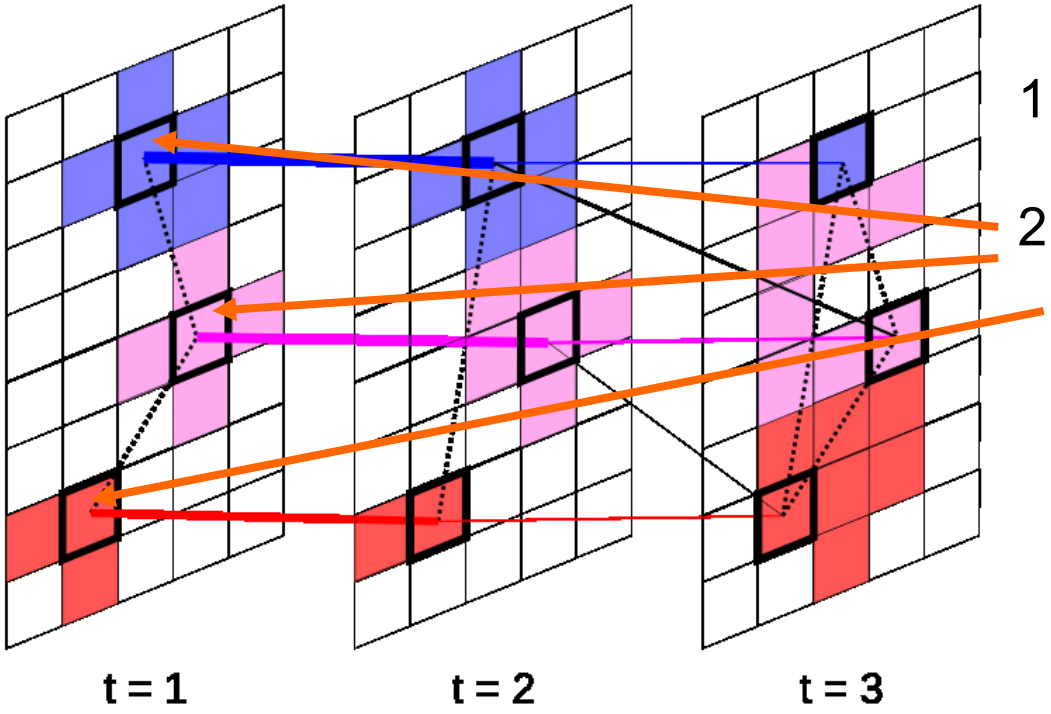

1. Layers = time windows
2. ROIs optimized inside layers for maximal consistency

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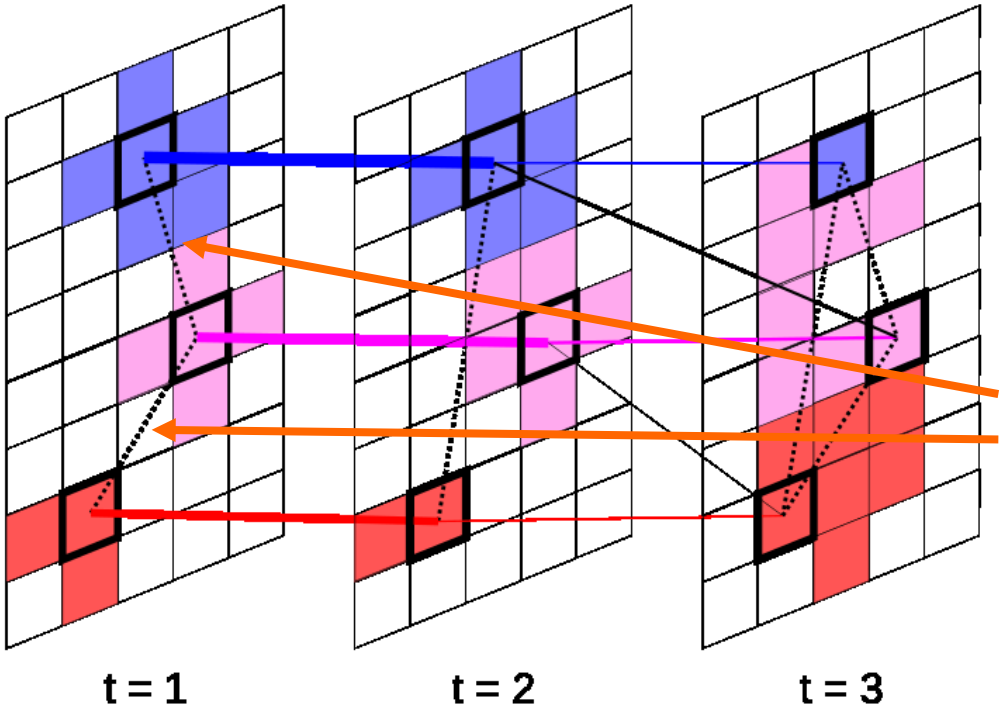

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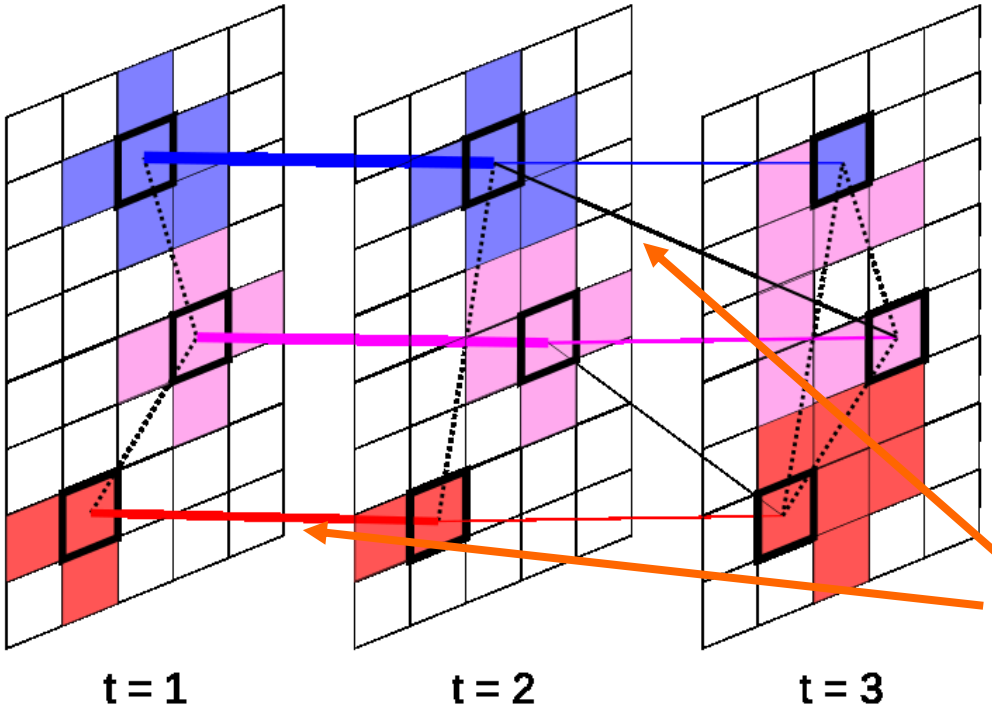

1. Layers = time windows
2. ROIs optimized inside layers for maximal consistency
3. Interlayer links = Pearson correlation
4. Intralayer links = spatial overlap

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?
- 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