



Brain networks: Why, what, how – and how not?

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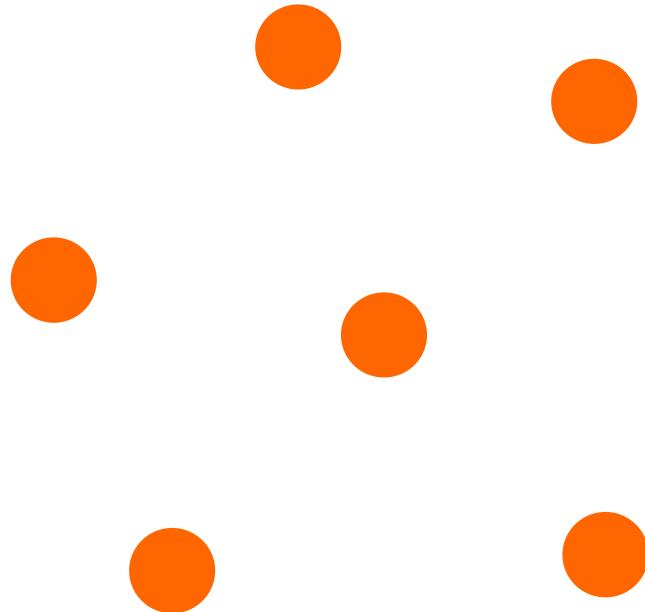
25.5.2020

Slides: <https://github.com/onerva-korhonen/presentations/blob/master/upsala-250520.pdf>

Networks: what and why?

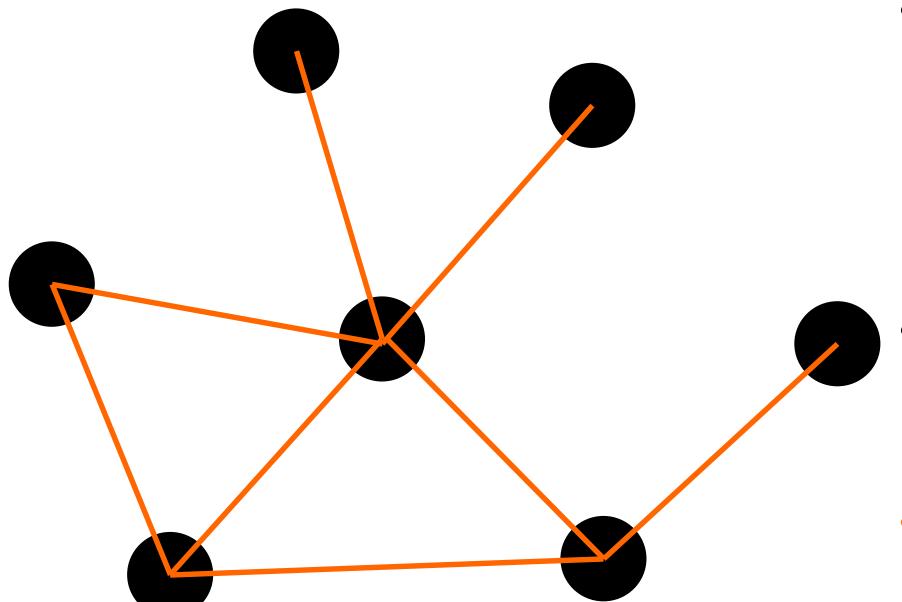
- **Network:** a model of connections and interactions
 - Internet, public transport, social networks

Networks: what and why?



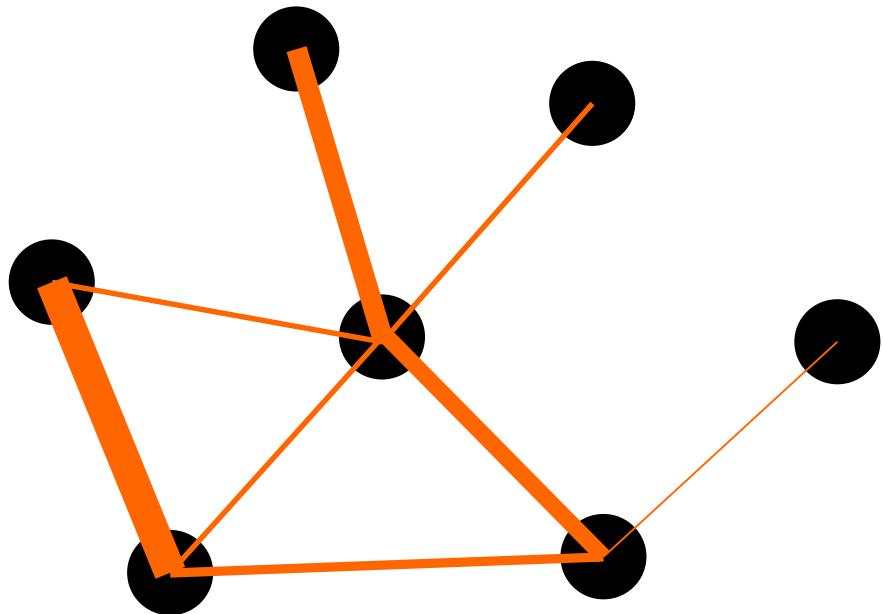
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- **Nodes:** network's basic elements
 - Web pages, stops, people

Networks: what and why?



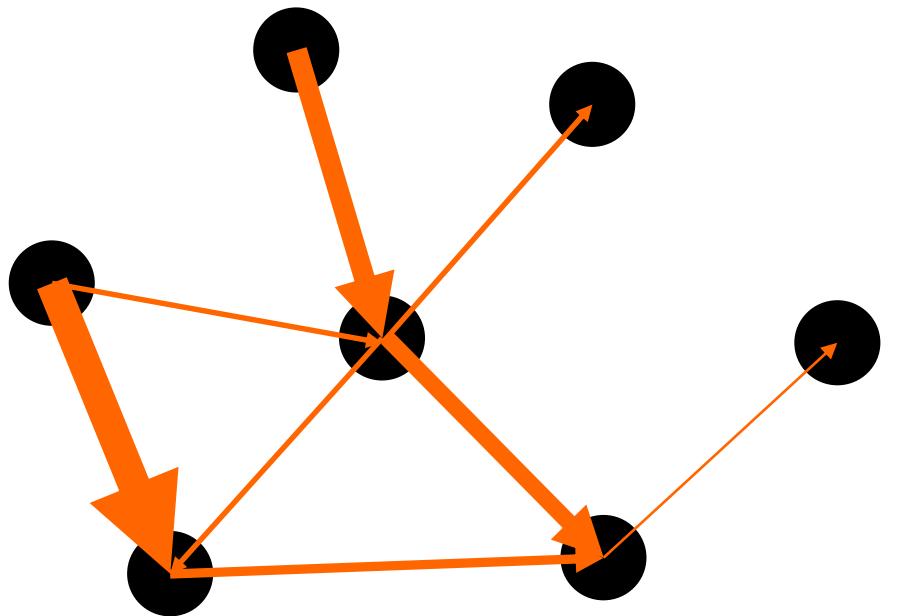
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Networks: what and why?



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 - Weights?

Networks: what and why?

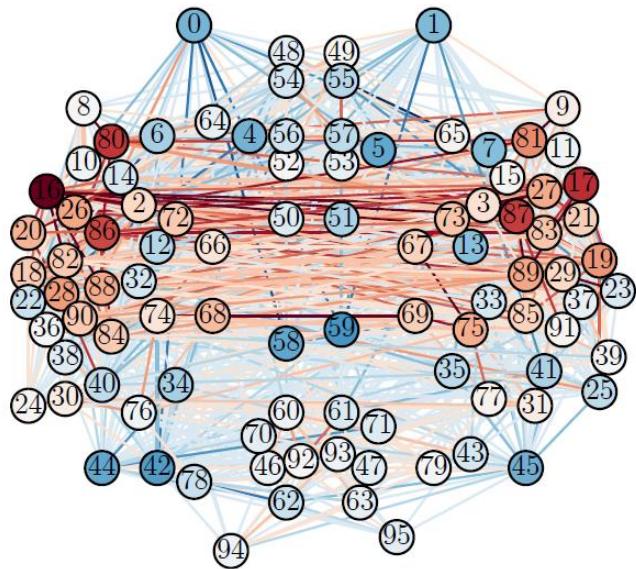


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 - Web links, transport lines, social relationships
 - Weights?
 - Direction?

Brain networks: Why?

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?

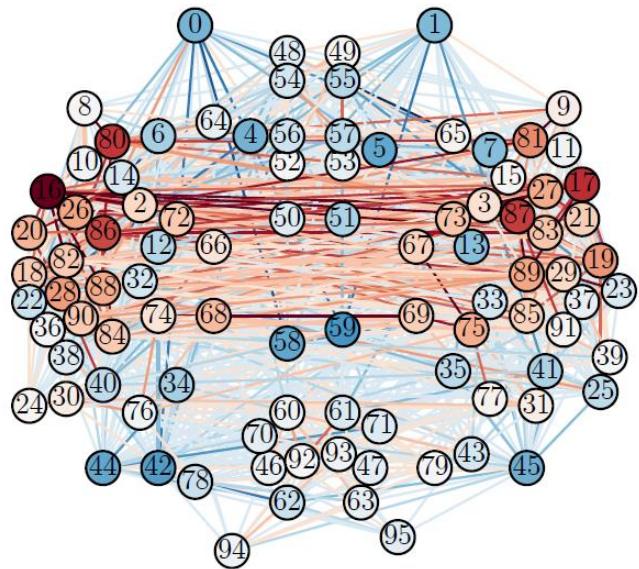
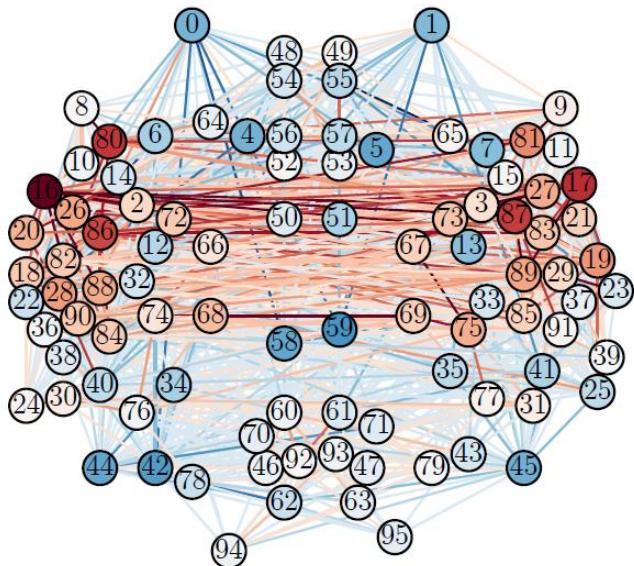


Fig: Alakörkkö et al. 2017,
European Journal of Neuroscience

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

Why is the brain a network?

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

Brain networks: What?

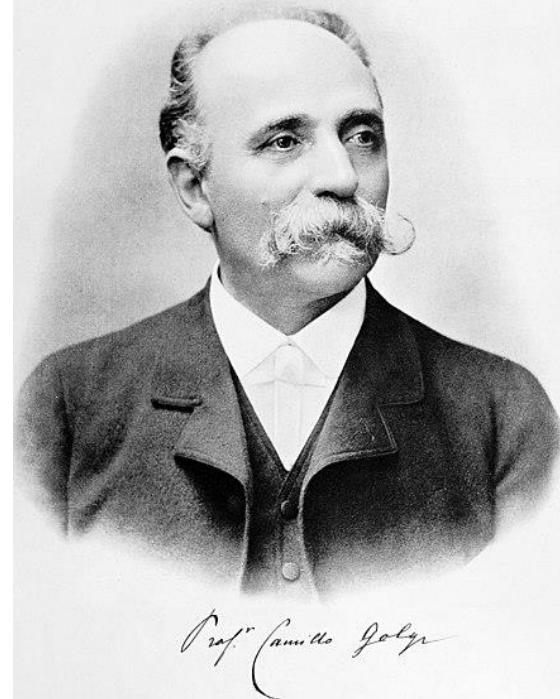
Brain networks: some history

Fig: Wikipedia Commons, public domain



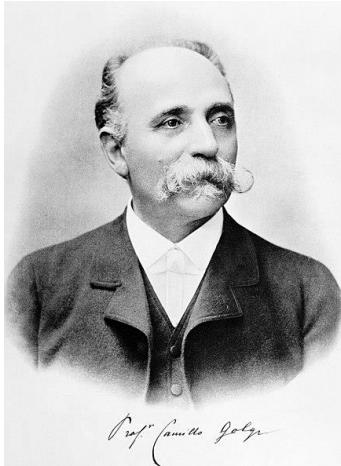
Joseph von Gerlach (1820-1896)

Fig: Wikipedia Commons, public domain



Camillo Golgi (1843-1926)

Brain networks: some history



The *reticulum* theory:

- The brain tissue = a continuous network, *reticulum*
- First attempts to map the nervous networks of animals
- Problem: no neurons = no nodes

Brain networks: some history

Fig: Wikipedia Commons, public domain

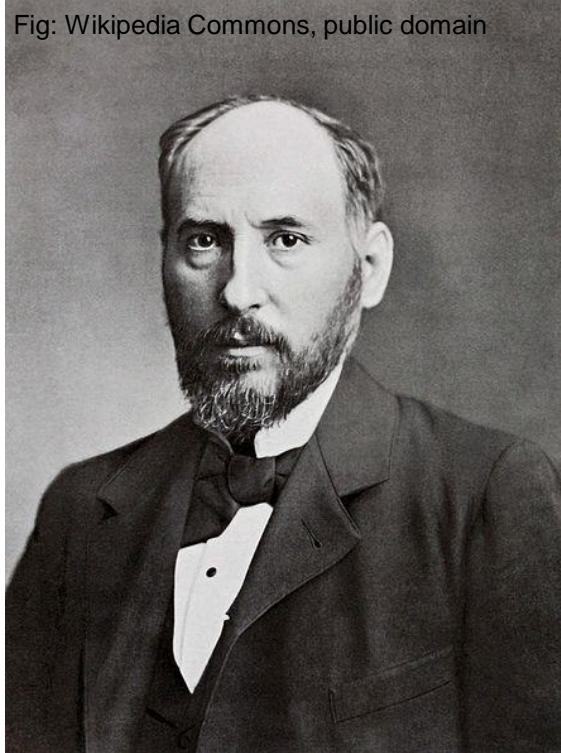


Fig: Wikipedia Commons, public domain

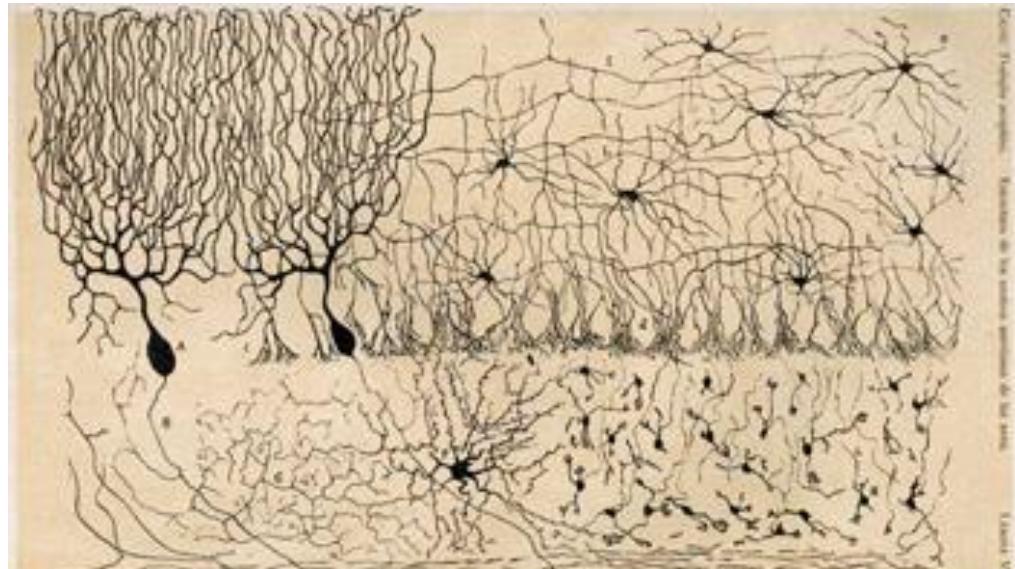


Photo: Milja Heikkinen

Santiago Ramón y Cajal (1852-1934)

- The brain = a collection of neurons



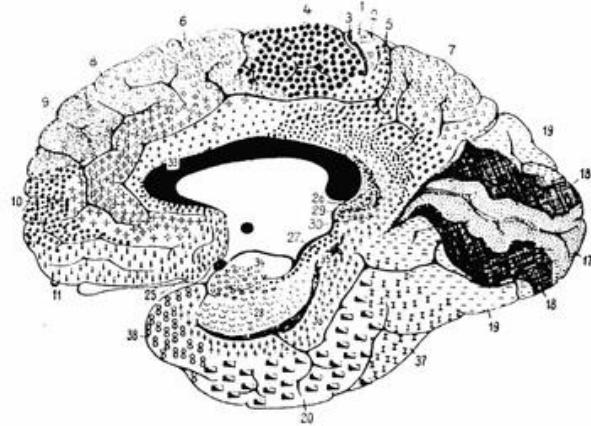
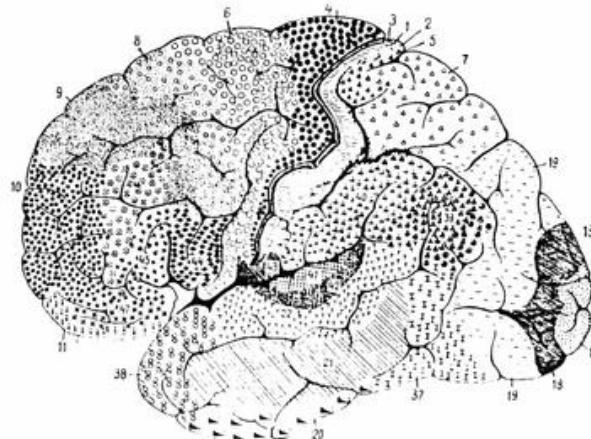
Brain networks: some history



Korbinian Brodmann (1868-1918)

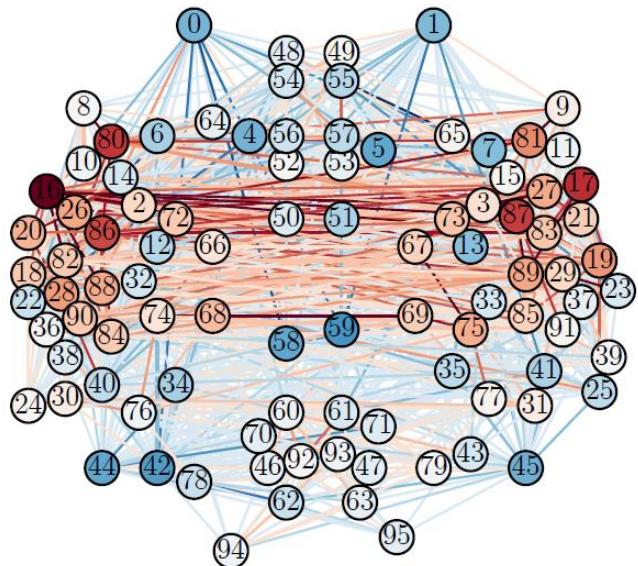
- Brain areas have different cells
- Different cells = different tasks
=> specialized brain areas

Fig: Wikipedia Commons, public domain



Brain networks: some history

Renaissance of brain networks:

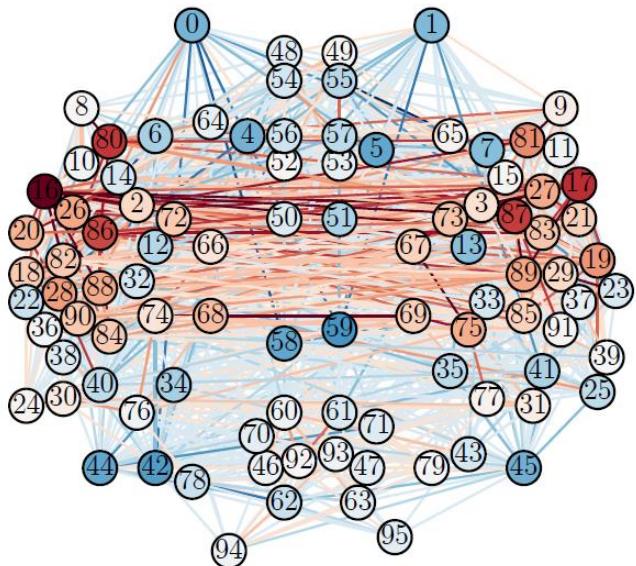


- The neural network of *C. elegans* (White et al. 1986)
- First mappings of human brain networks in 1990s
- **Connectome, connectomics** = network of structural connections (Hagmann 2005, Sporns et al. 2005)
- **Network neuroscience** = neuroscience with network tools (Muldoon & Bassett 2016, Bassett & Sporns 2017)

Network neuroscience

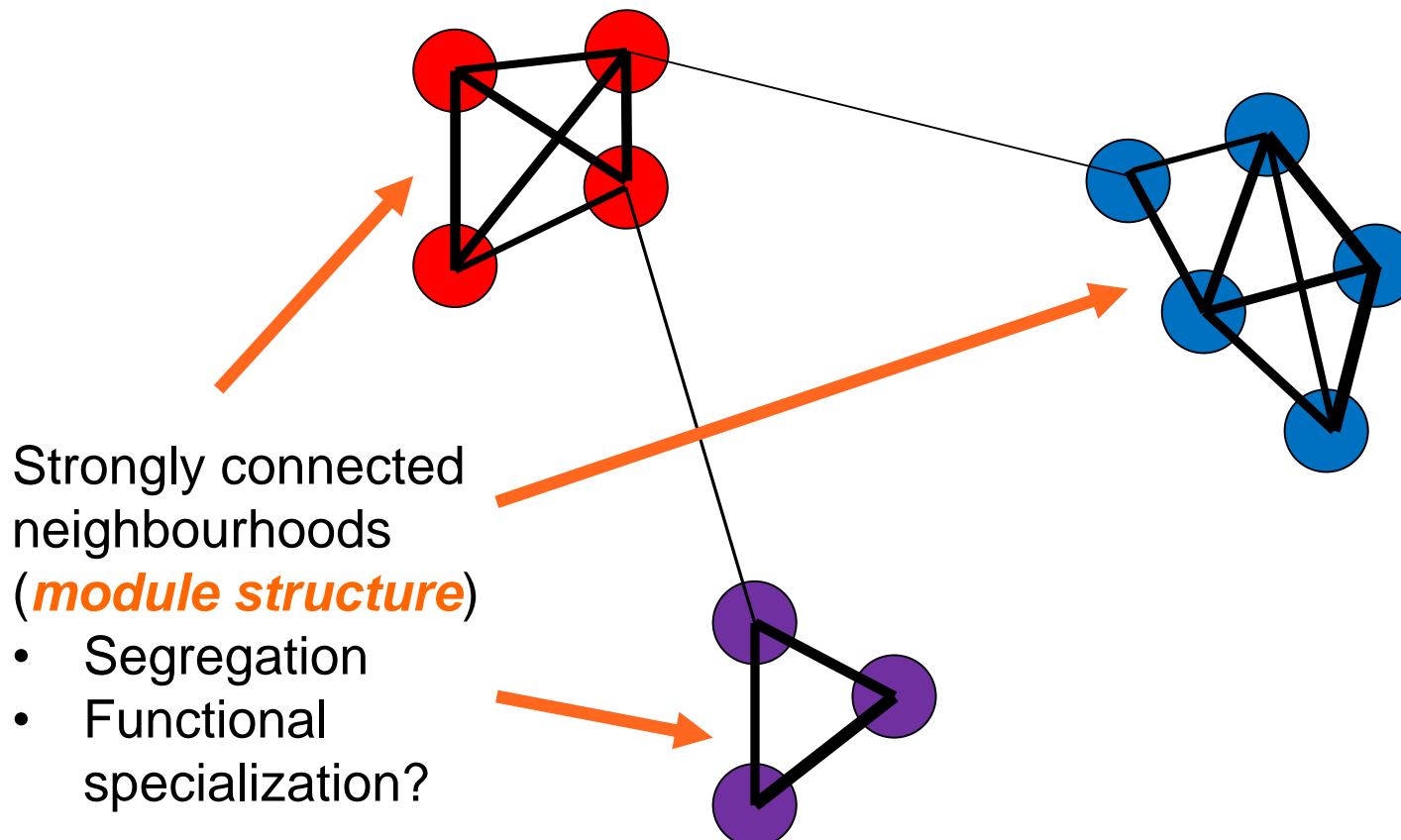
- Network neuroscience = applying network tools on the brain
- Two aims:
 1. Understand the healthy brain
 2. Find causes of diseases
- Broad scales:
 - Molecule – neuron – brain area – human
 - Milliseconds – years
- Different brain networks:
 - **Structural:** anatomic connections
 - **Functional:**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

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



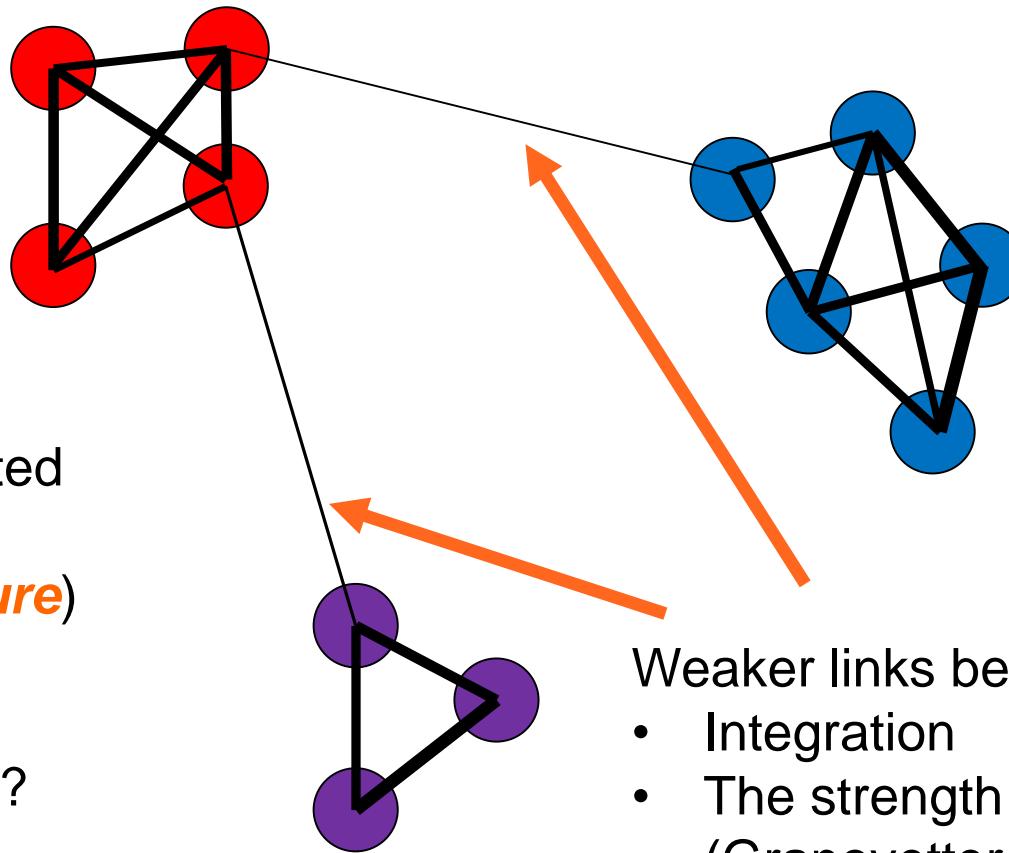
What do brain networks look like?

Segregation-integration (Sporns 2013):



What do brain networks look like?

Segregation-integration (Sporns 2013):



Strongly connected
neighbourhoods
(**module structure**)

- Segregation
- Functional specialization?

Weaker links between modules

- Integration
- The strength of weak ties
(Granovetter 1973)

What do brain networks look like?

Segregation-integration (Sporns 2013):

Most network links are short (= inside module)

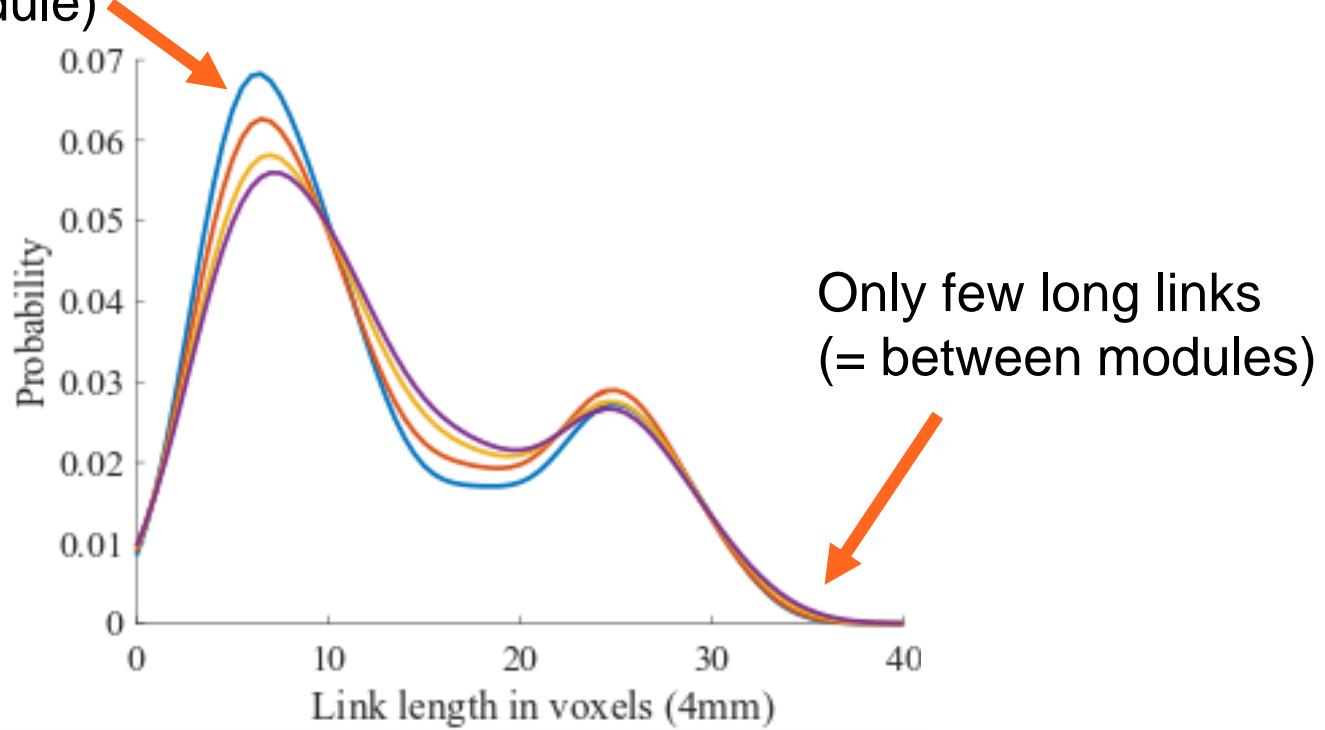


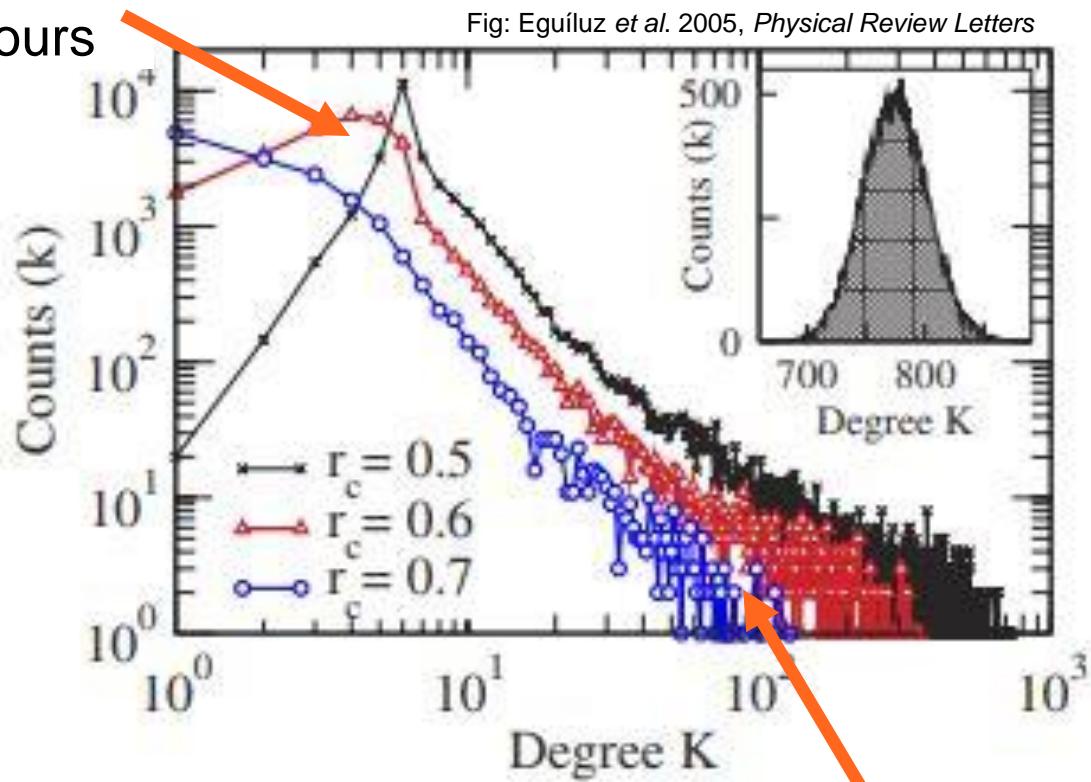
Fig: Alakorkkó *et al.* 2017, *European Journal of Neuroscience*

What do brain networks look like?

Scale-freeness (Eguíluz et al. 2005)

Most nodes have few neighbours

Fig: Eguíluz et al. 2005, *Physical Review Letters*

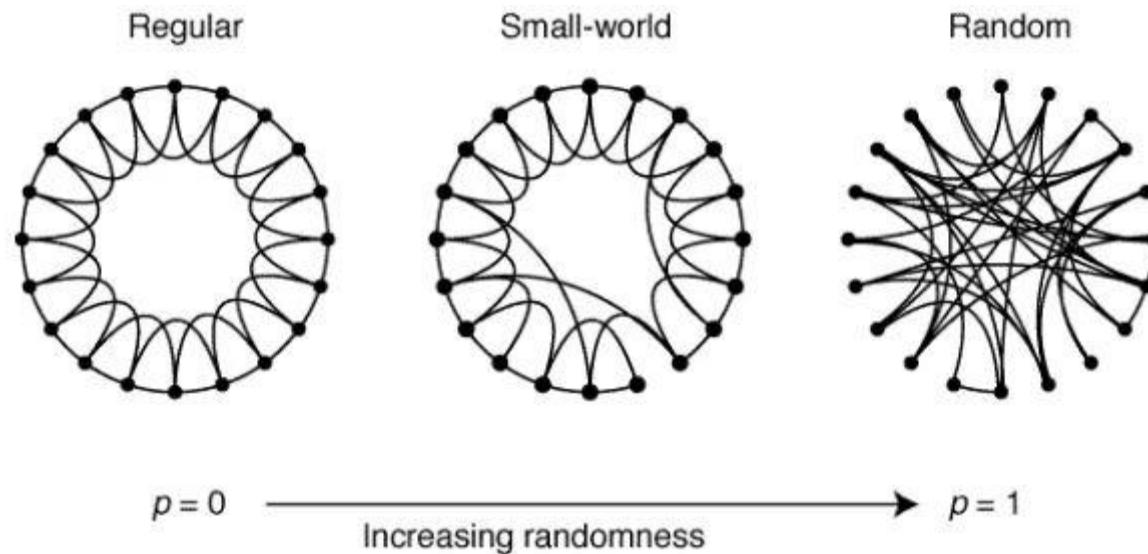


Some nodes (**hubs**) with lots of neighbours
• Hubs connect to each other (**rich-clubs**)

What do brain networks look like?

Small-worldness (Watts & Strogatz 1998,
Sporns & Zwi 2004)

Fig: Watts & Strogatz. 1998, *Nature*



Compared to random:

- High clustering ("friends of my friends are my friends")
- Short paths

What do brain networks look like?

Small-worldness (Watts & Strogatz 1998,
Sporns & Zwi 2004)

But is the brain really a small world? (Papo et al. 2016)

- Data collection and preprocessing?
- Measuring small-worldness?
- Interpretation?
- A fundamental organization principle or a consequence of limited space?



Compared to random:

- High clustering ("friends of my friends are my friends")
- Short paths

What do brain networks look like?

One never looks at the same brain network twice! (Heraclitus, feat. O. Korhonen)

Brain networks change:

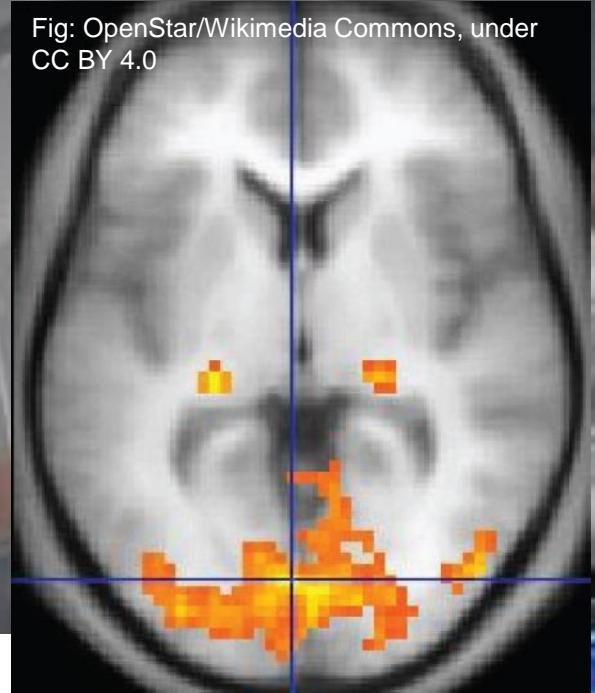
- Spontaneously over time
- Between cognitive tasks
- With age
- Between health and disease (e.g. Alzheimer's disease, Parkinson's disease, Autism Spectrum Disorders, epilepsy)

Brain networks: How?

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



Functional networks: EEG & MEG

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

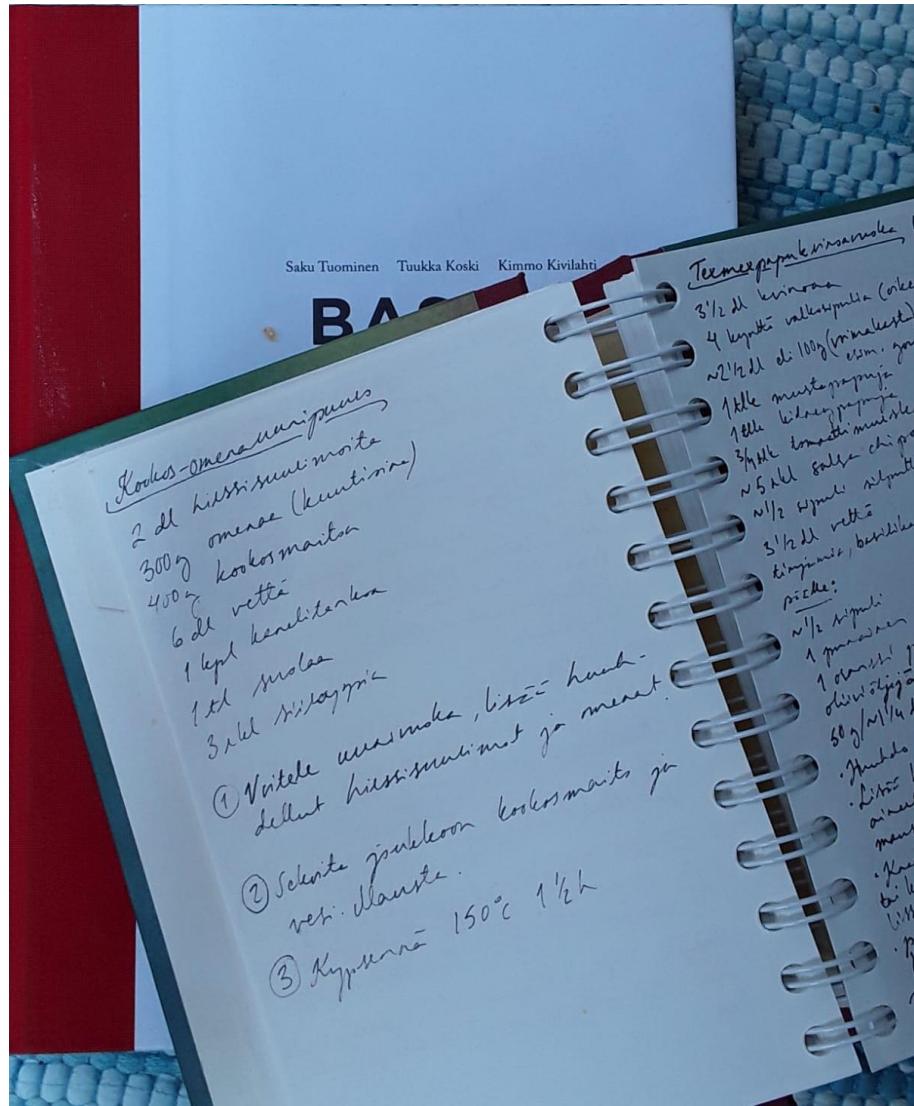


Fig: Wikimedia Commons, public domain



- 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

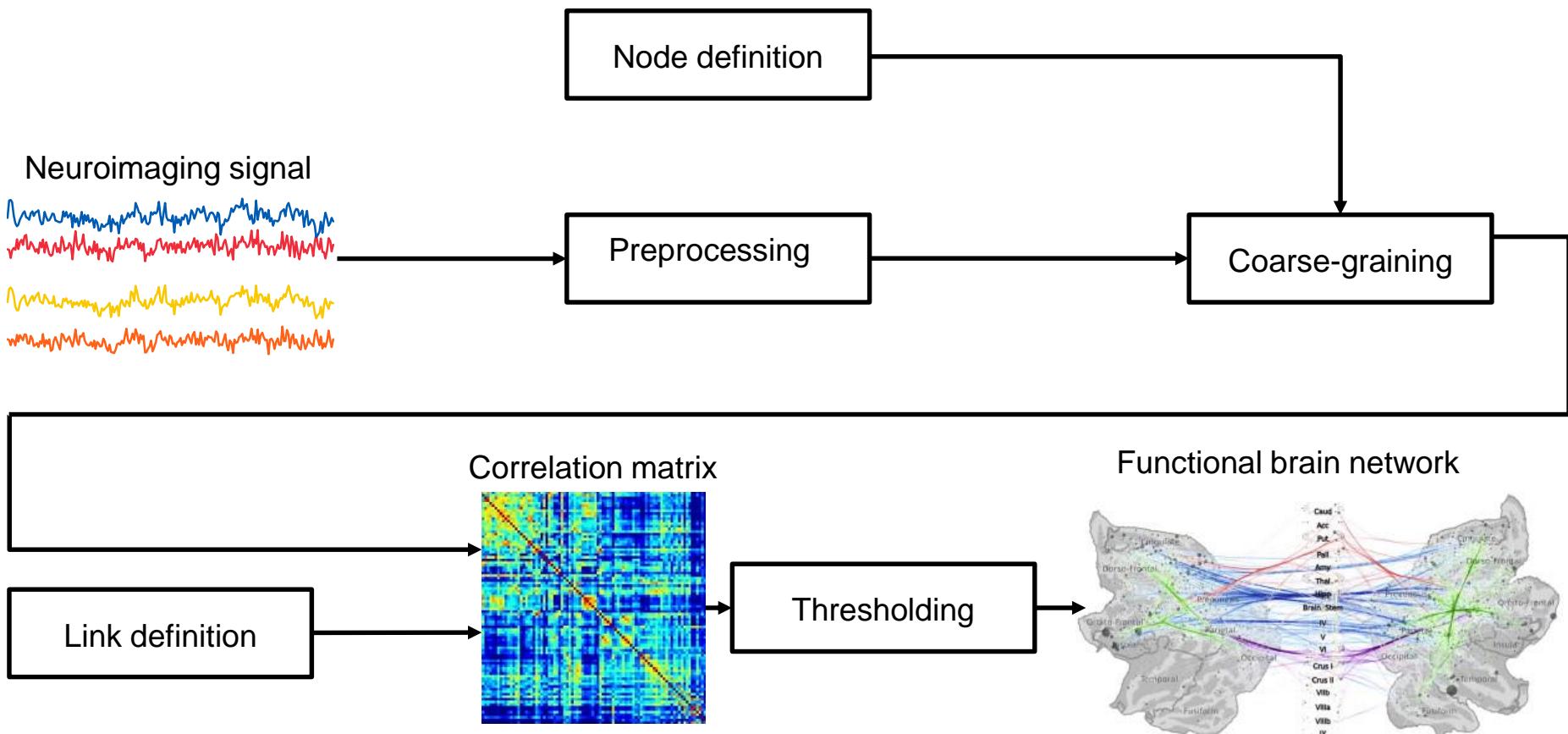
Functional networks: how-to?



A simple recipe:
weighted networks from time series

1. Define nodes
(each one with a time series)
2. Define link weights
(measures of similarity between time series)
3. Define threshold,
discard sub-threshold links

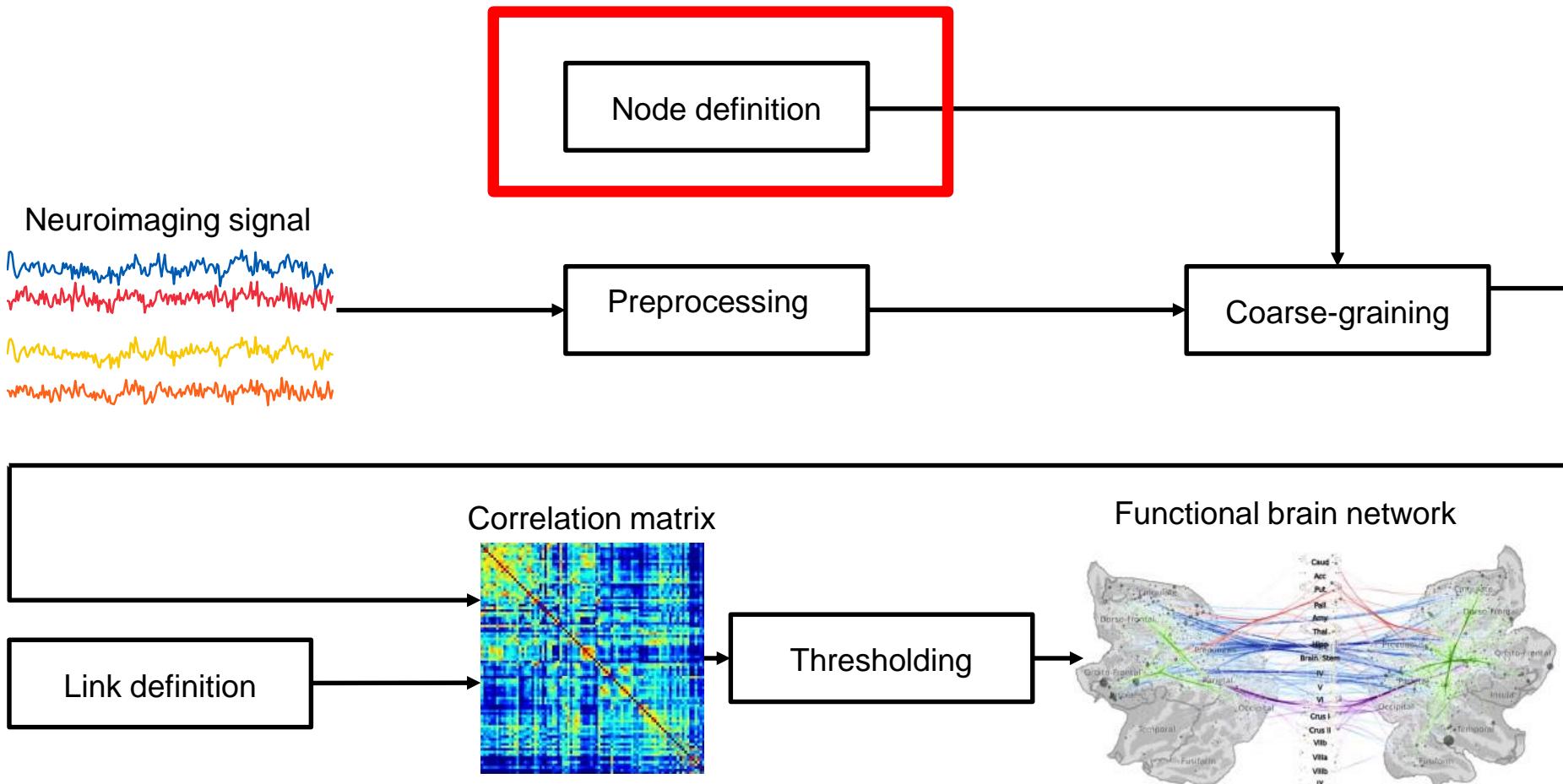
Functional networks: how-to?



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

Brain networks: How not?

Functional networks: how-to?



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

The problem of node definition

- No natural candidates above the neuronal scale
- Node selection affects network properties (e.g. Wang et al. 2009)
- Some commonly used nodes:
 - voxels/vertices
 - random clumps of voxels/vertices
 - Regions of Interest (**ROIs**): collections of voxels/vertices

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*

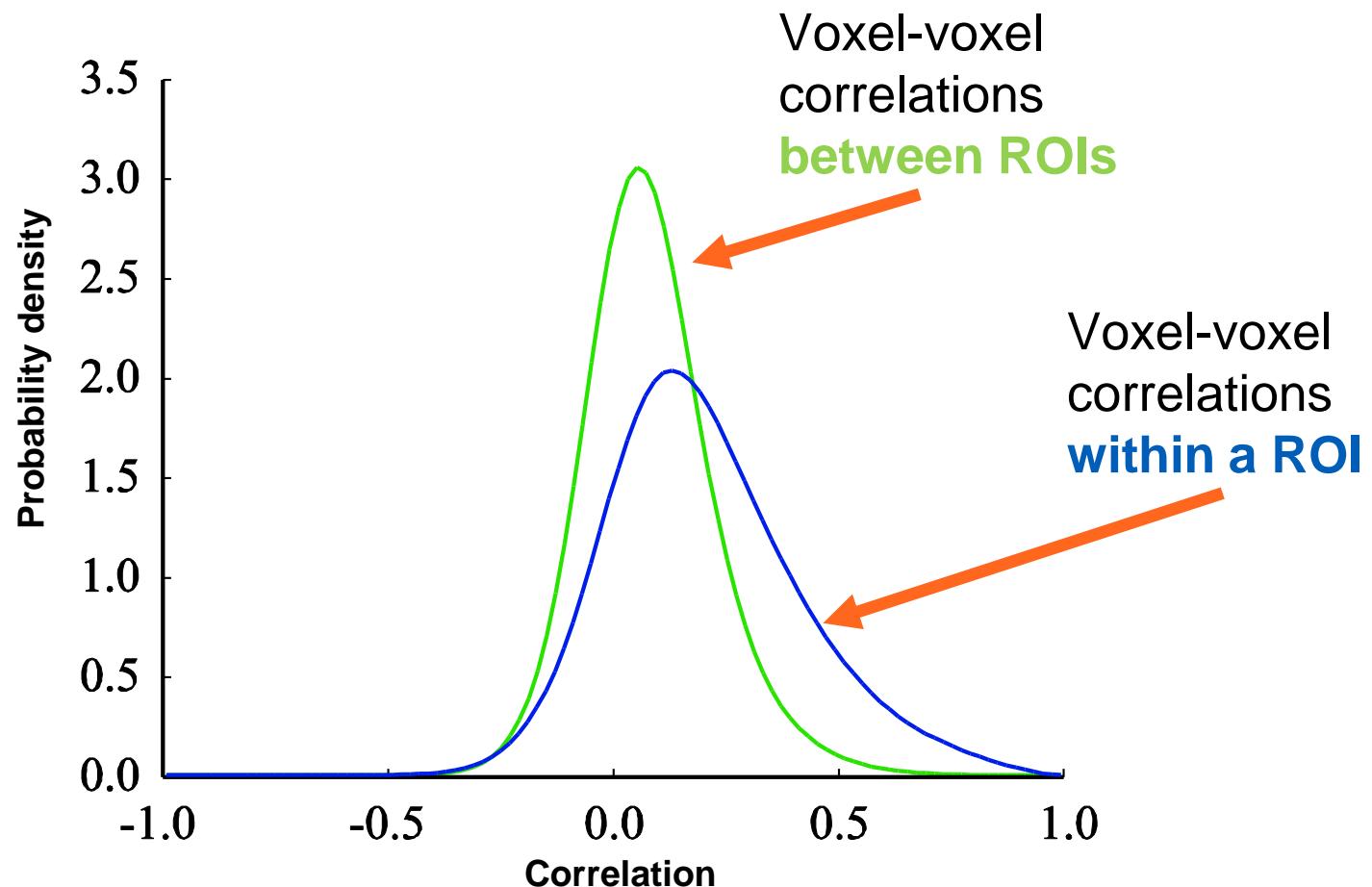
Research questions

- 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?



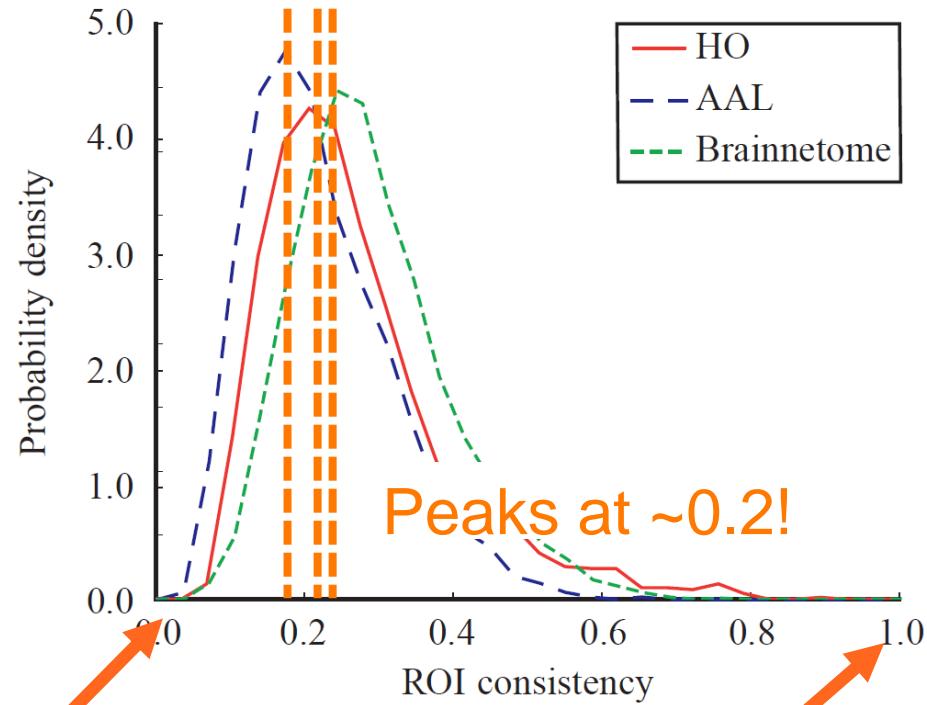
How homogeneous are ROIs?

- **Spatial consistency**

= measure of functional homogeneity:

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

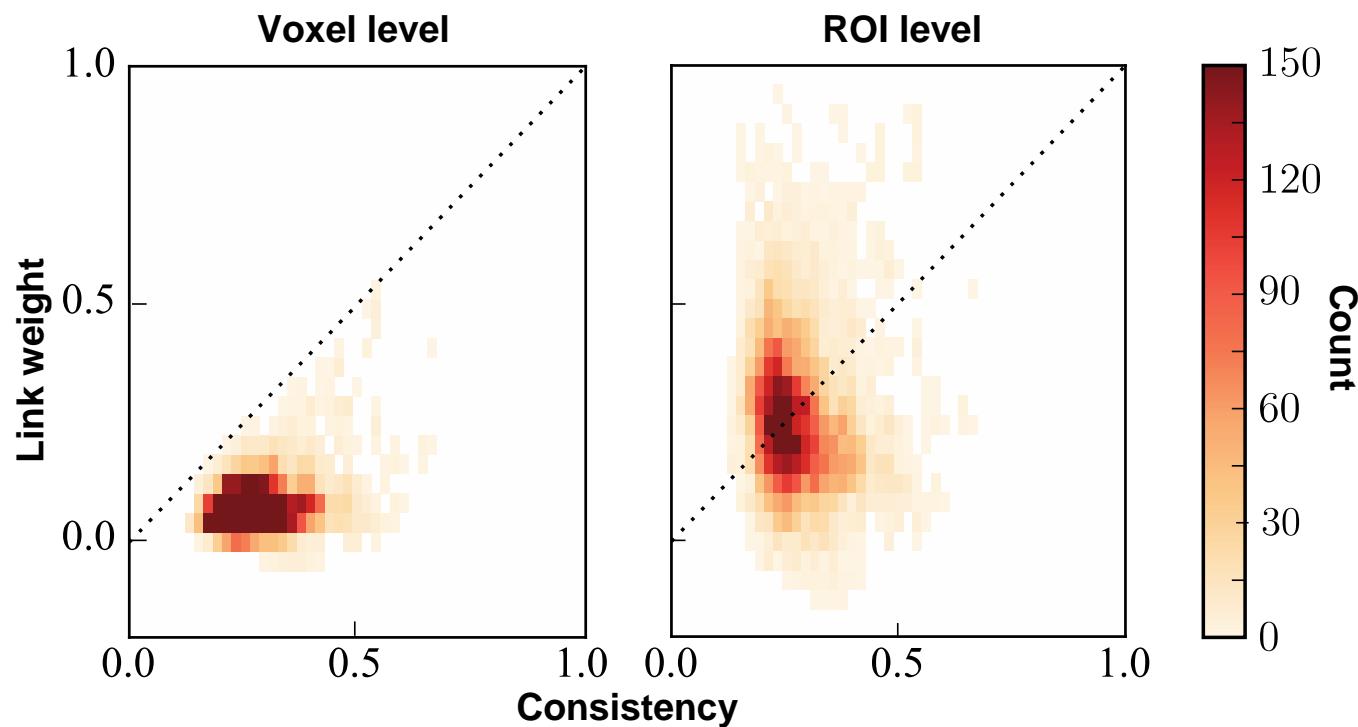
- Straightforward to calculate
- Easy to interpret



Lack of
homogeneity

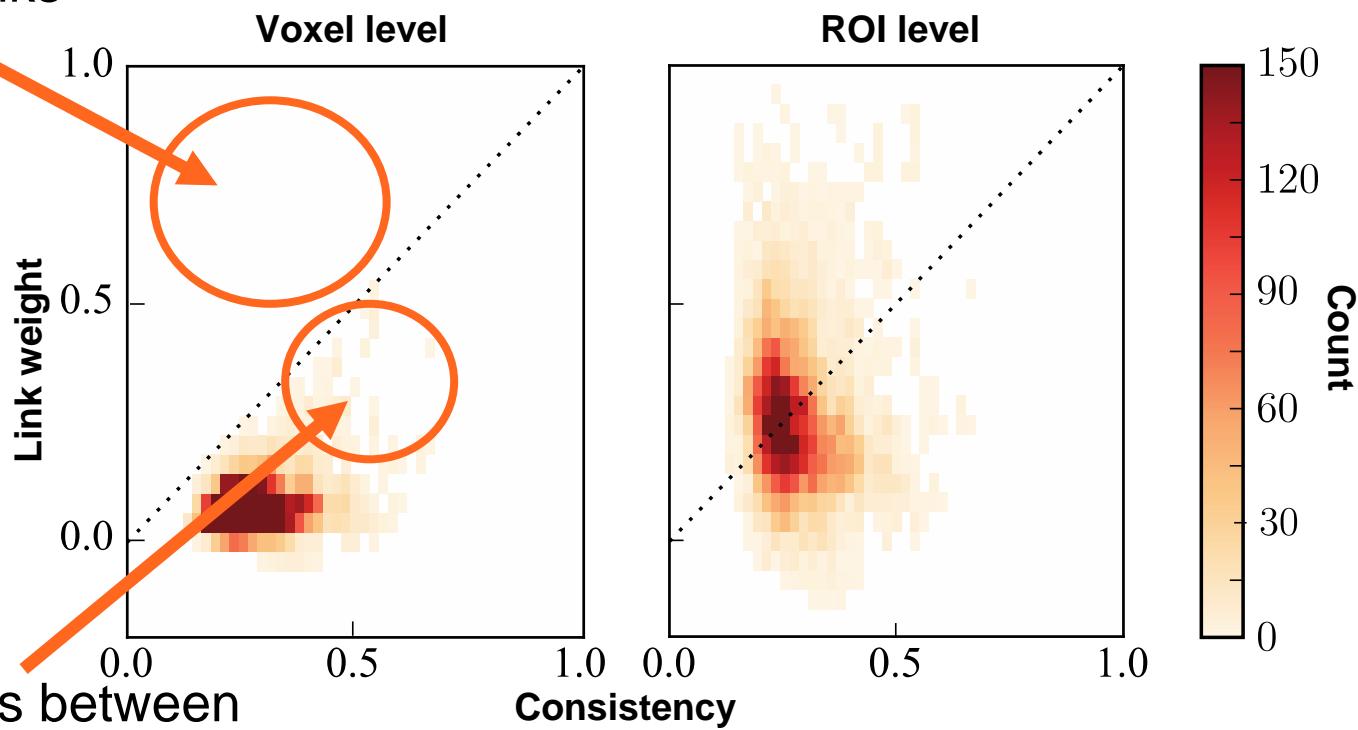
Perfect
homogeneity

Does consistency predict connectivity?



Does consistency predict connectivity?

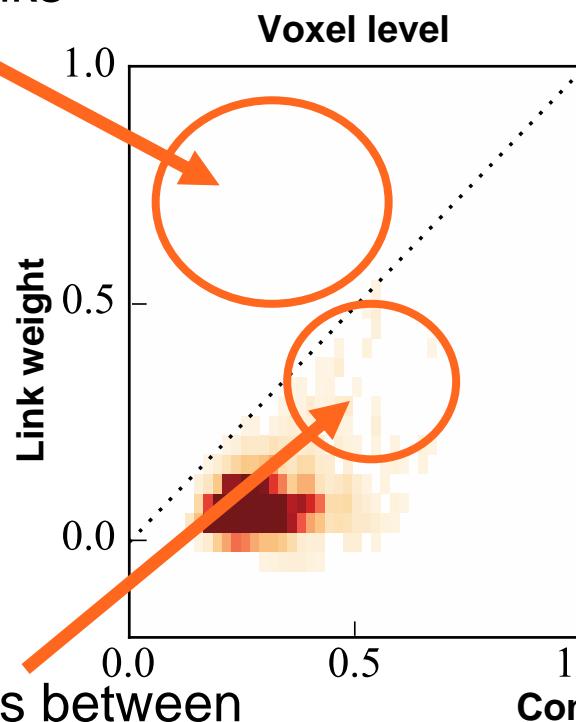
No links



Strong links between
consistent ROIs

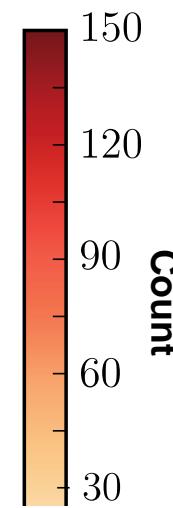
Does consistency predict connectivity?

No links



Voxel level

ROI level

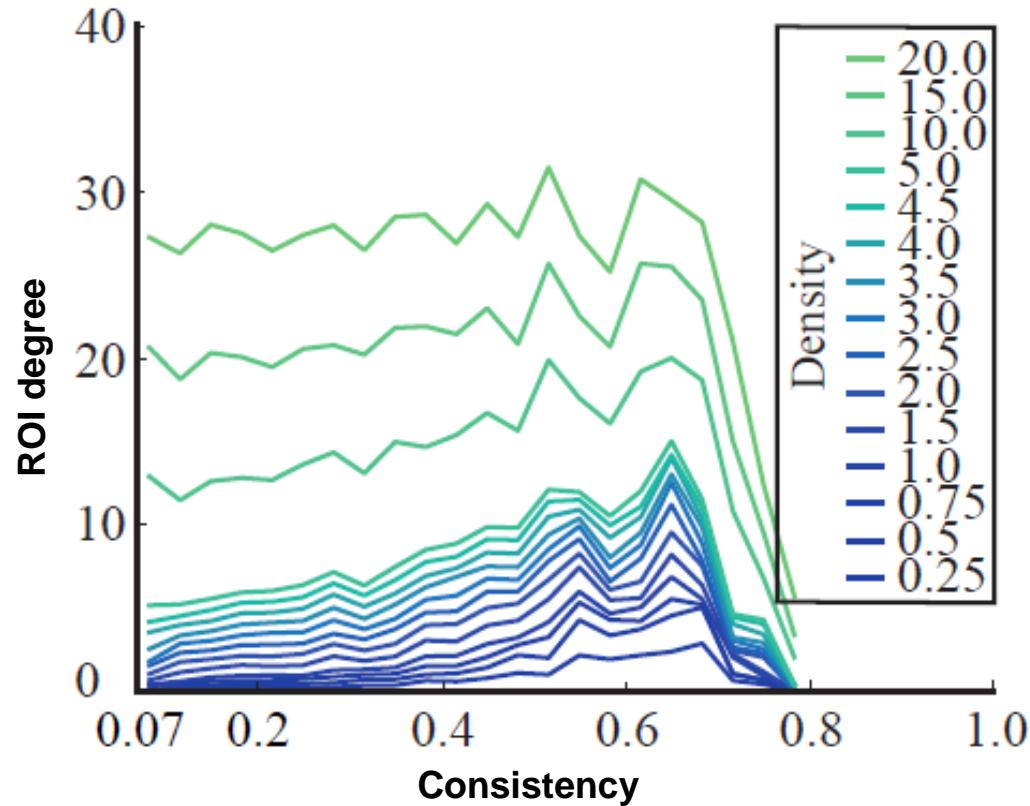


Count

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

Ryppö, 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 listening (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

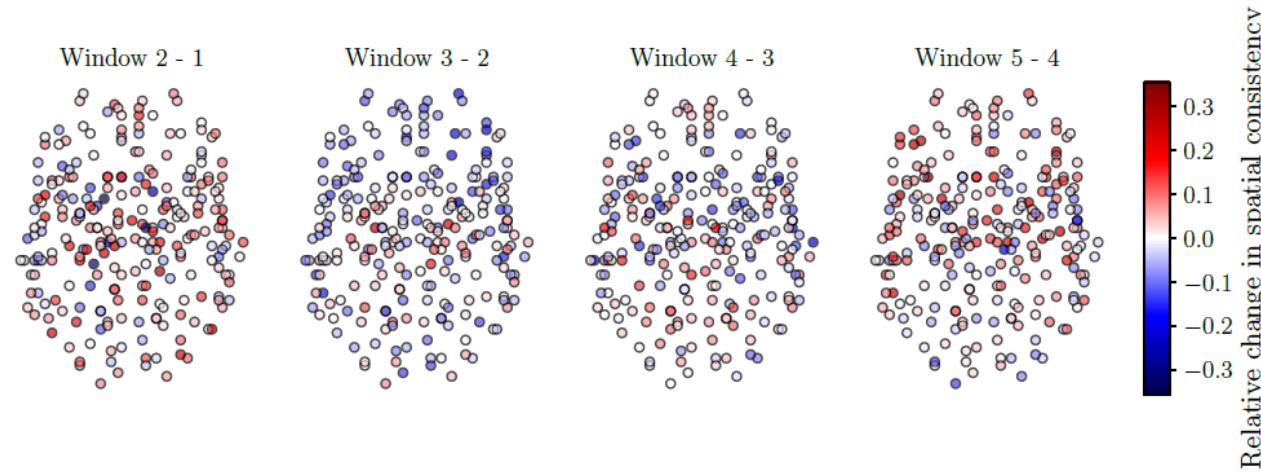
- Spatial consistency φ_{spat} : functional homogeneity of ROI
- Spatiotemporal consistency: time-dependence of φ_{spat}

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

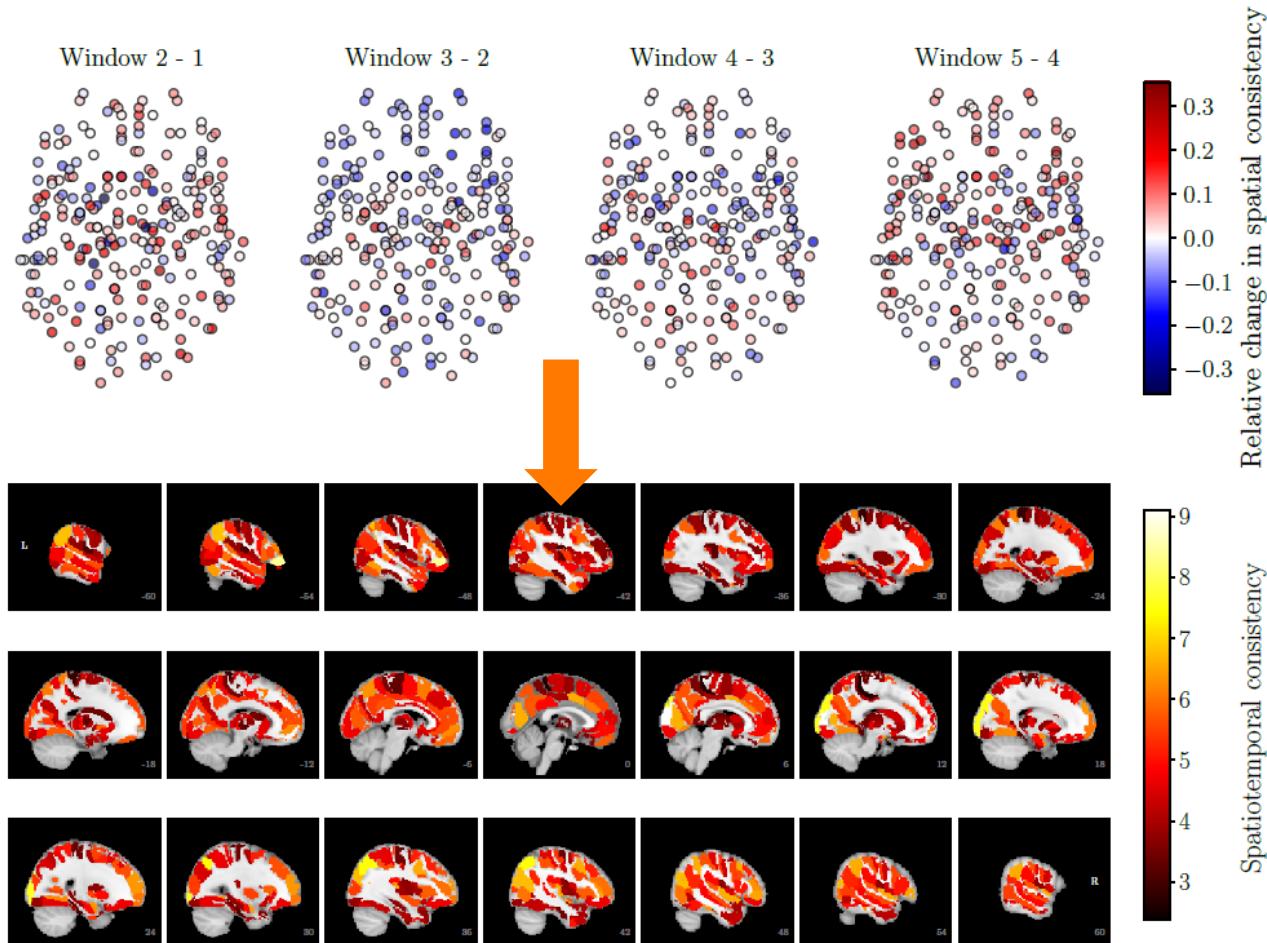
- Network turnover: changes in local network structure

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

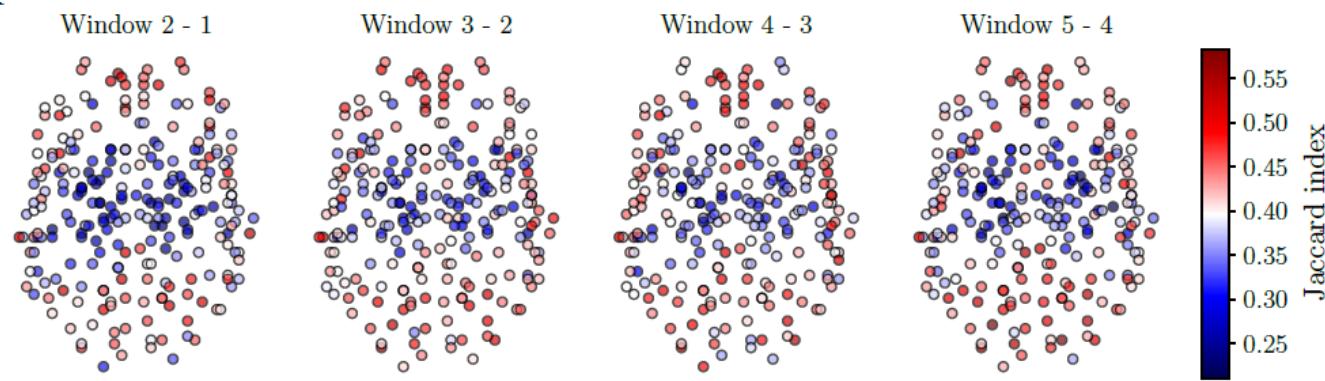
Spatial consistency changes in time



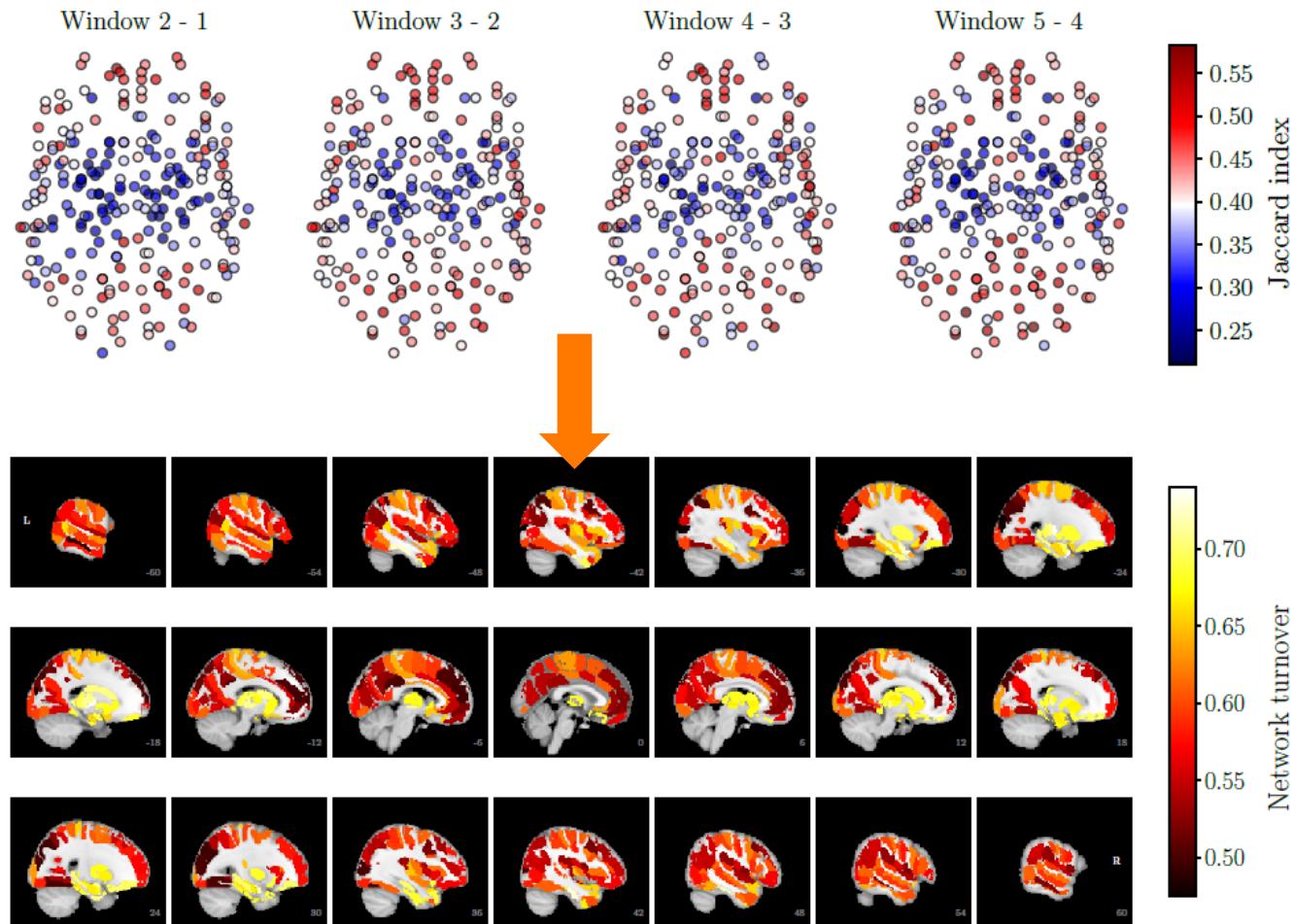
Spatial consistency changes in time



Turnover in network neighborhoods

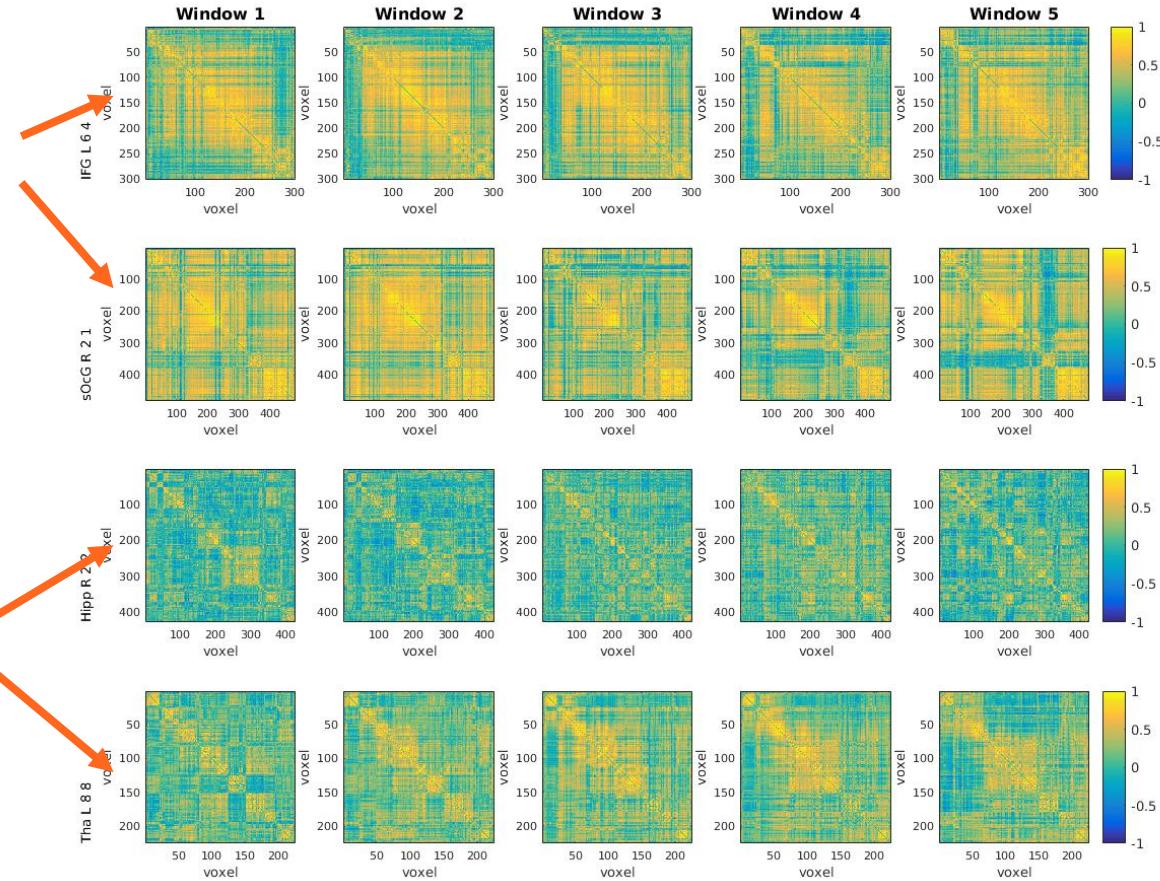


Turnover in network neighborhoods



ROIs have rich internal connectivity structure

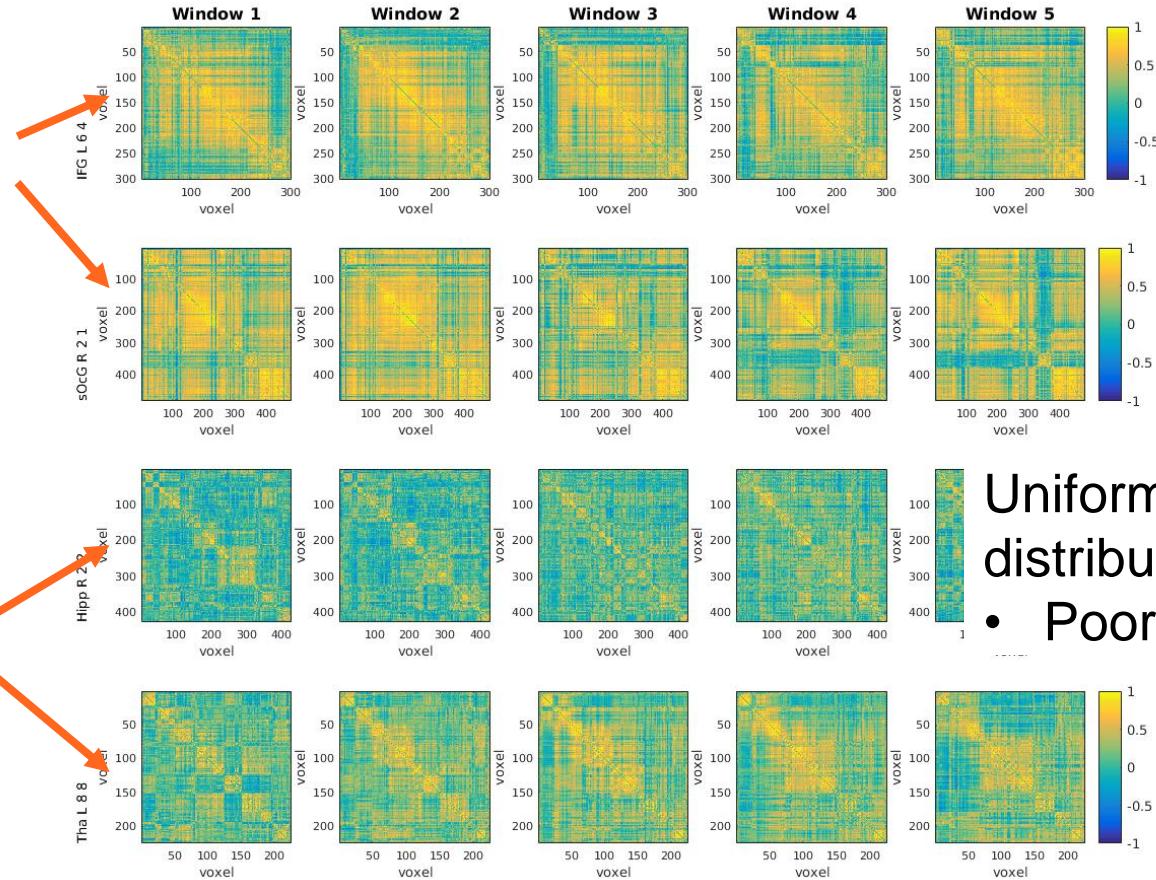
High spatial consistency



Low spatial consistency

ROIs have rich internal connectivity structure

High spatial consistency



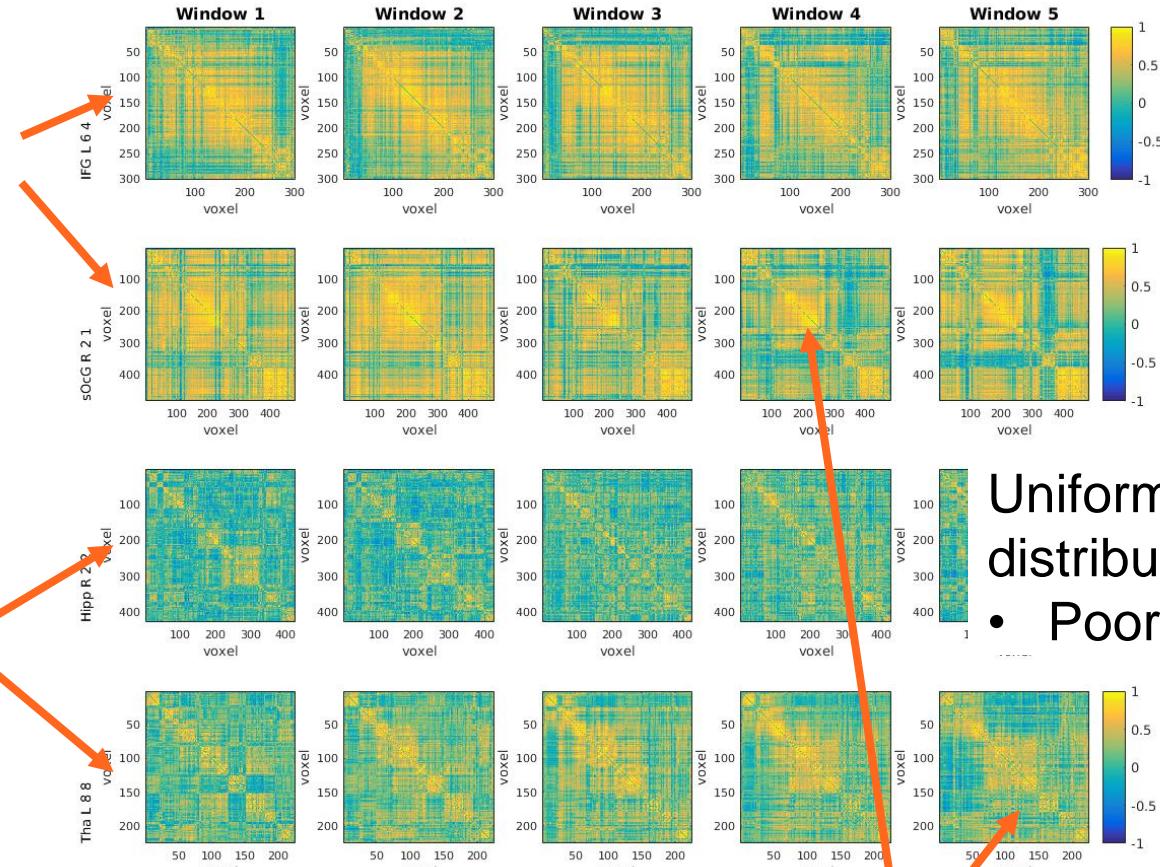
Low spatial consistency

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

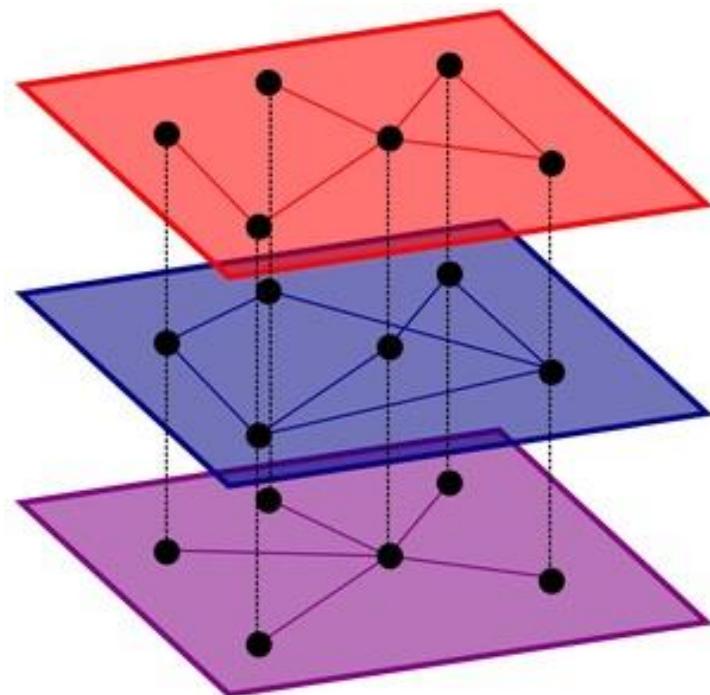
- Spatial consistency changes in time
 - Reflects activation?
- ROIs have time-dependent internal structure
 - Relates to network topology?
- Do brain networks have stable nodes?

On-going work: Multilayer brain networks with flexible nodes

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

Network model with flexible nodes

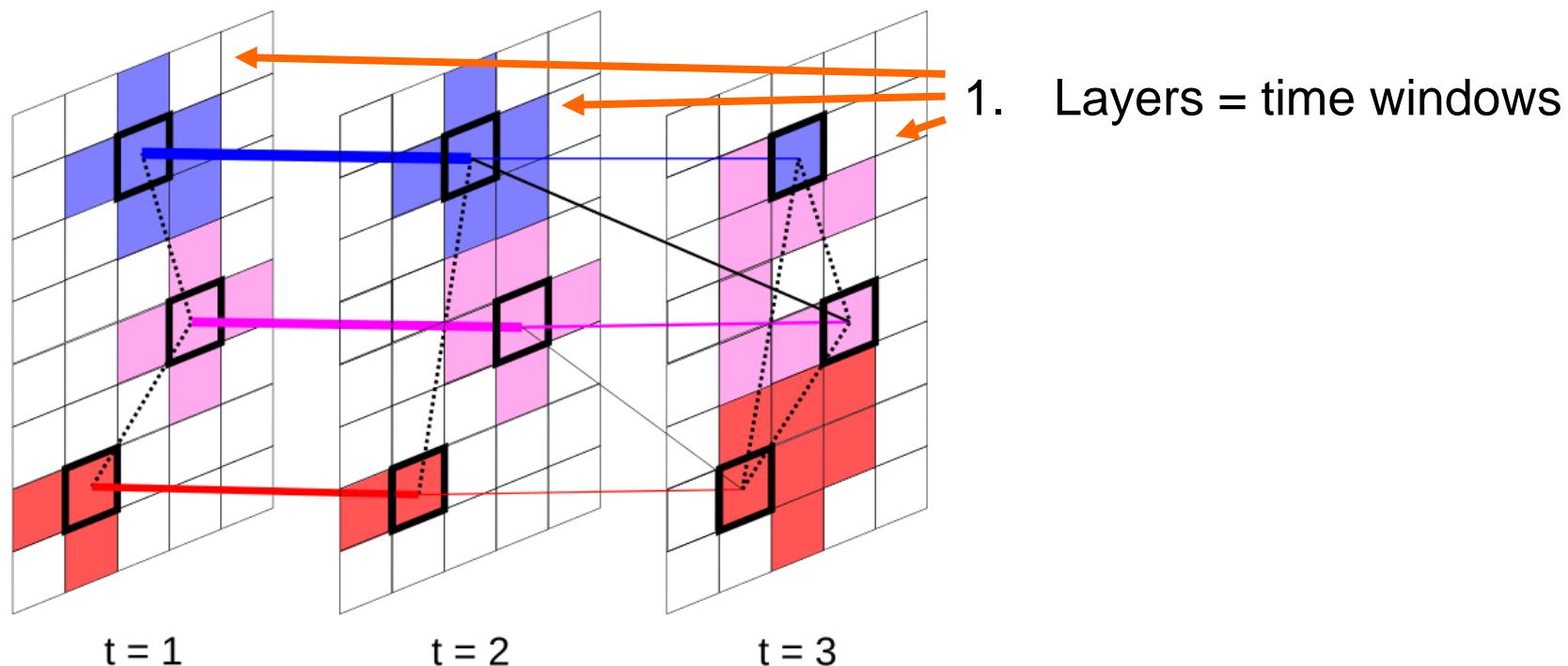
- Based on *multilayer networks* (e.g. Kivelä et al. 2014):



- Different connections in a single network
- Each connection type on its own layer
- Interpretation of inter-layer connections?
- Typical examples: social networks, transport, ...

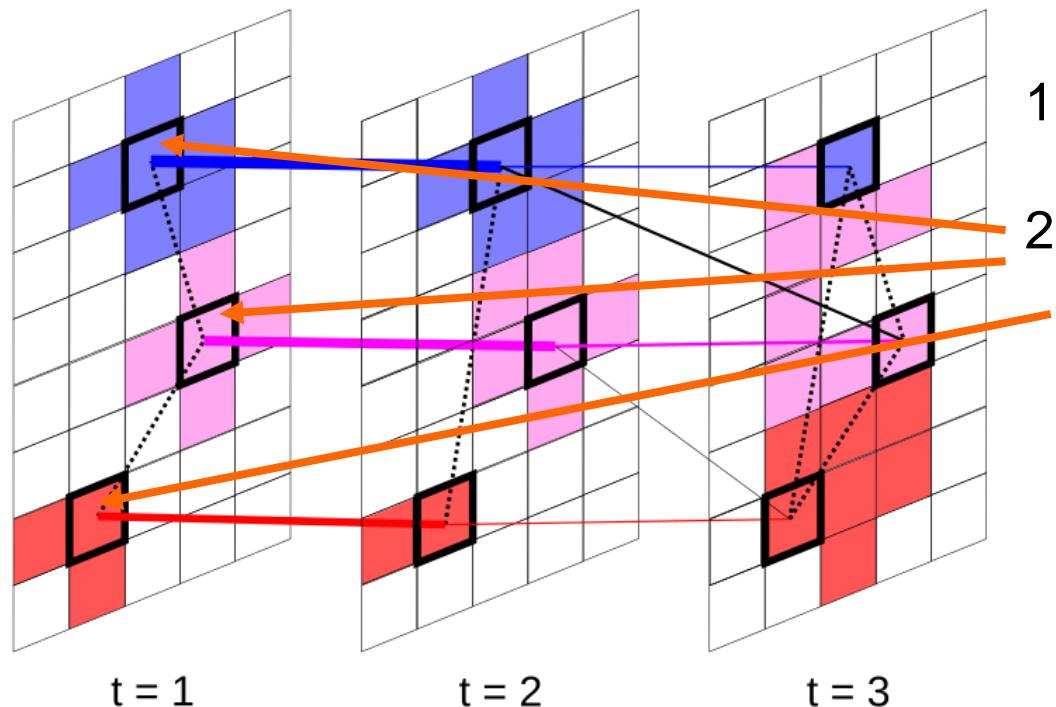
Network model with flexible nodes

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



Network model with flexible nodes

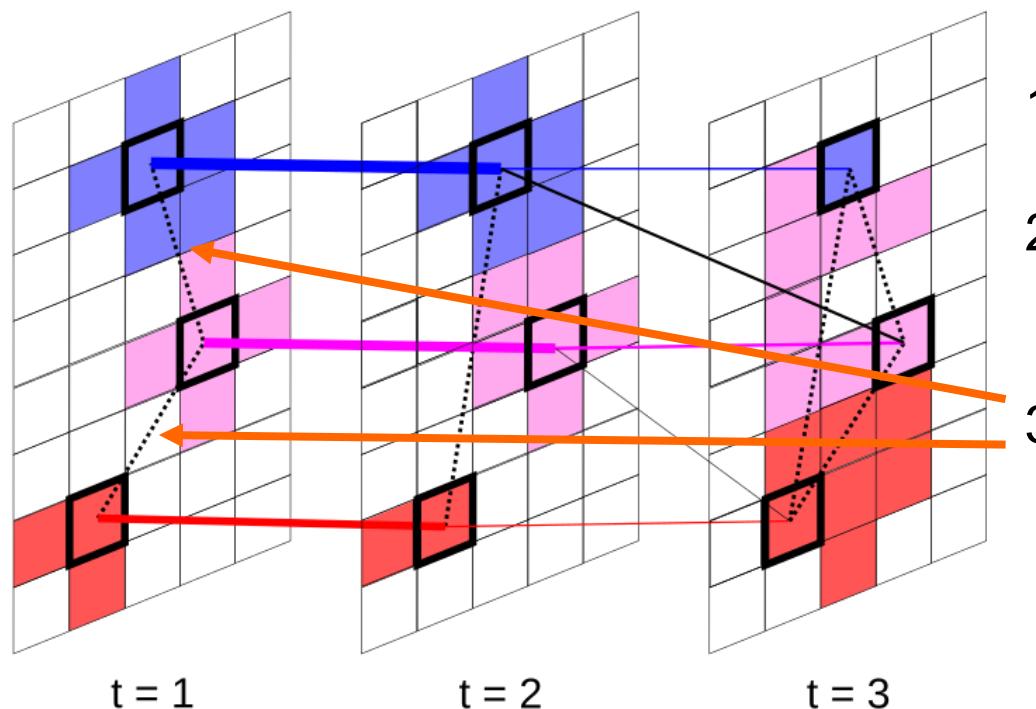
- Based on multilayer networks (= different connections in the same network)



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

Network model with flexible nodes

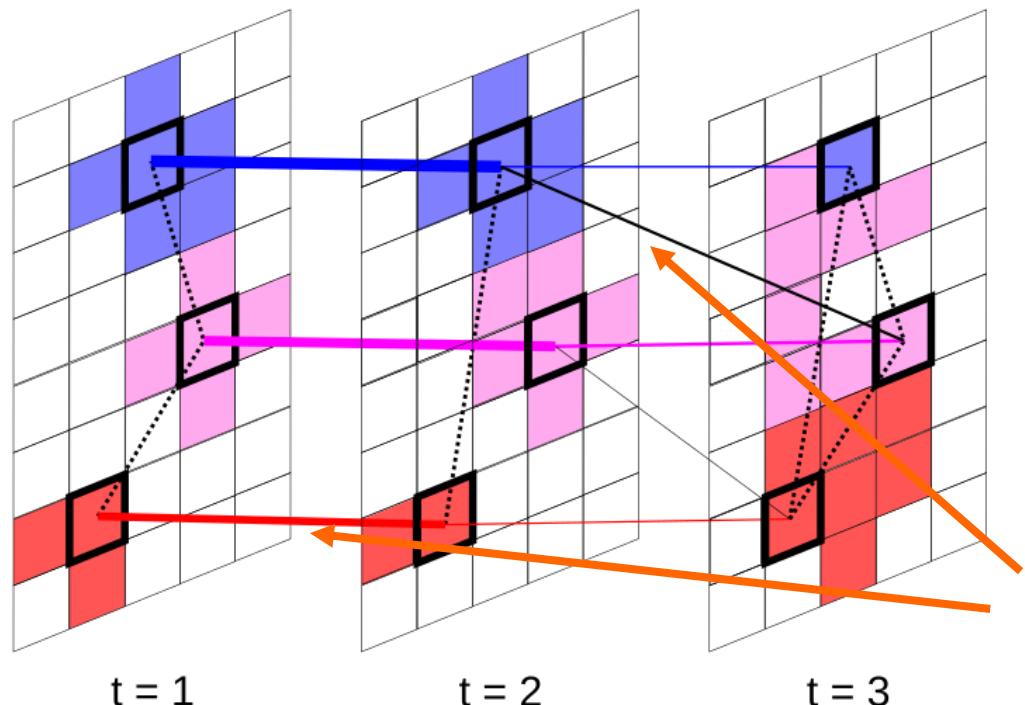
- Based on multilayer networks (= different connections in the same network)



1. Layers = time windows
2. ROIs optimized inside layers for maximal homogeneity
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 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
 - ⇒ Can't be fixed by new static nodes
 - ⇒ **Flexible nodes needed!**

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Thank you!

Questions, comments?

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Twitter: @OnervaKorhonen

Slides: <https://github.com/onerva-korhonen/presentations/blob/master/upsala-250520.pdf>