How not to construct functional brain networks

Onerva Korhonen

NIMEG Group Meeting

5.10.2022

Aalto University
School of Science

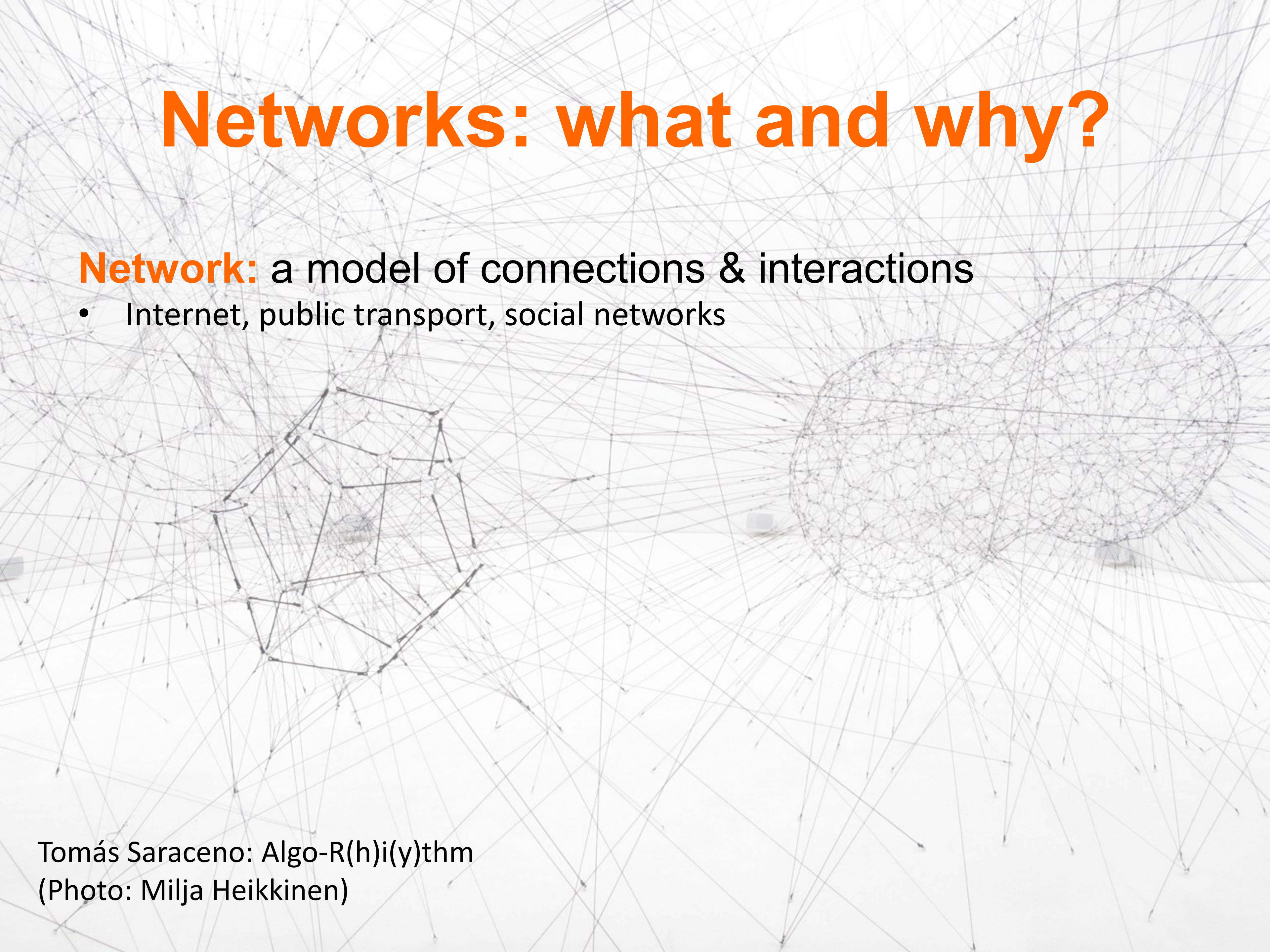
SUOMEN AKATEMIA
FINLANDS AKADEMI
ACADEMY OF FINLAND

Slides: https://github.com/onerva-korhonen/presentations/blob/master/nimeg_051022.pdf

Networks: what and why?

Network: a model of connections & interactions

- Internet, public transport, social networks



Tomás Saraceno: Algo-R(h)i(y)thm
(Photo: Milja Heikkinen)

Networks: what and why?

Network: a model of connections & interactions

- Internet, public transport, social networks

Nodes: network's basic elements

- Web pages, stops, people

Tomás Saraceno: Algo-R(h)i(y)thm
(Photo: Milja Heikkinen)

Networks: what and why?

Network: a model of connections & 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

Tomás Saraceno: Algo-R(h)i(y)thm
(Photo: Milja Heikkinen)

Networks: what and why?

Network: a model of connections & 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?

Tomás Saraceno: Algo-R(h)i(y)thm
(Photo: Milja Heikkinen)

Networks: what and why?

Network: a model of connections & interactions

- Internet, public transport, social networks

Nodes: network's basic elements

- Web pages, stops, people

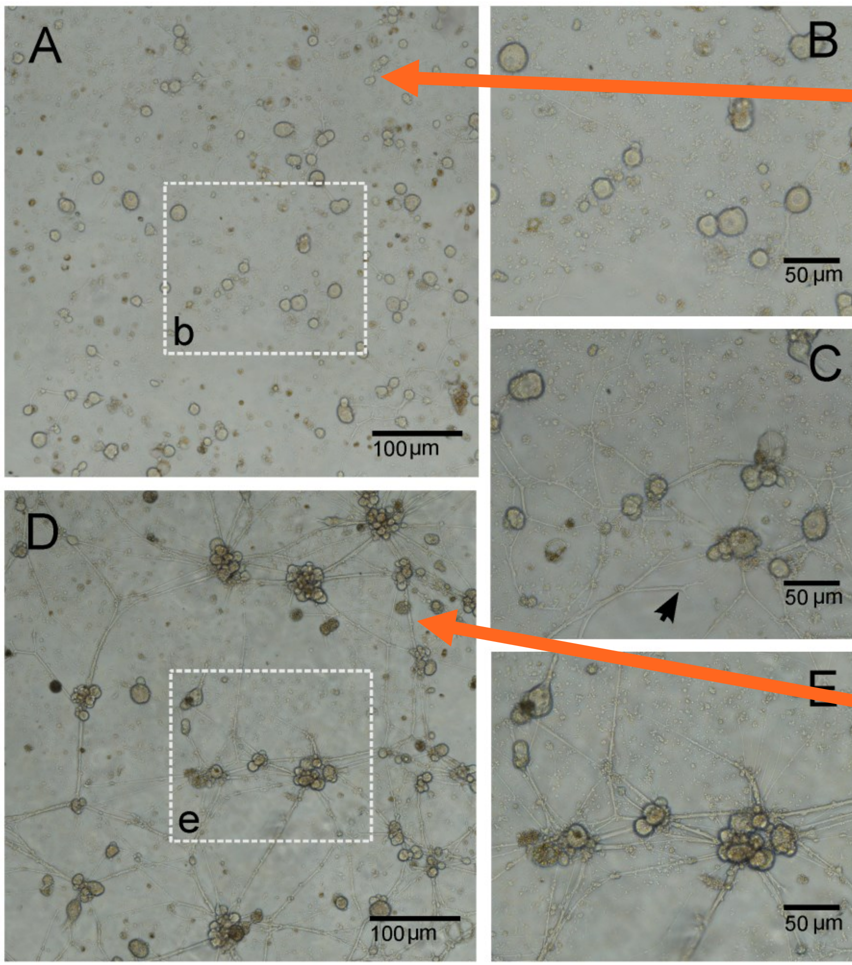
Links: connections between nodes

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

Tomás Saraceno: Algo-R(h)i(y)thm
(Photo: Milja Heikkinen)

Why is the brain a network?

Brain: 10^{11} neurons, 10^{14} synapses



Day 3 after separating neurons: axon bundles start to grow

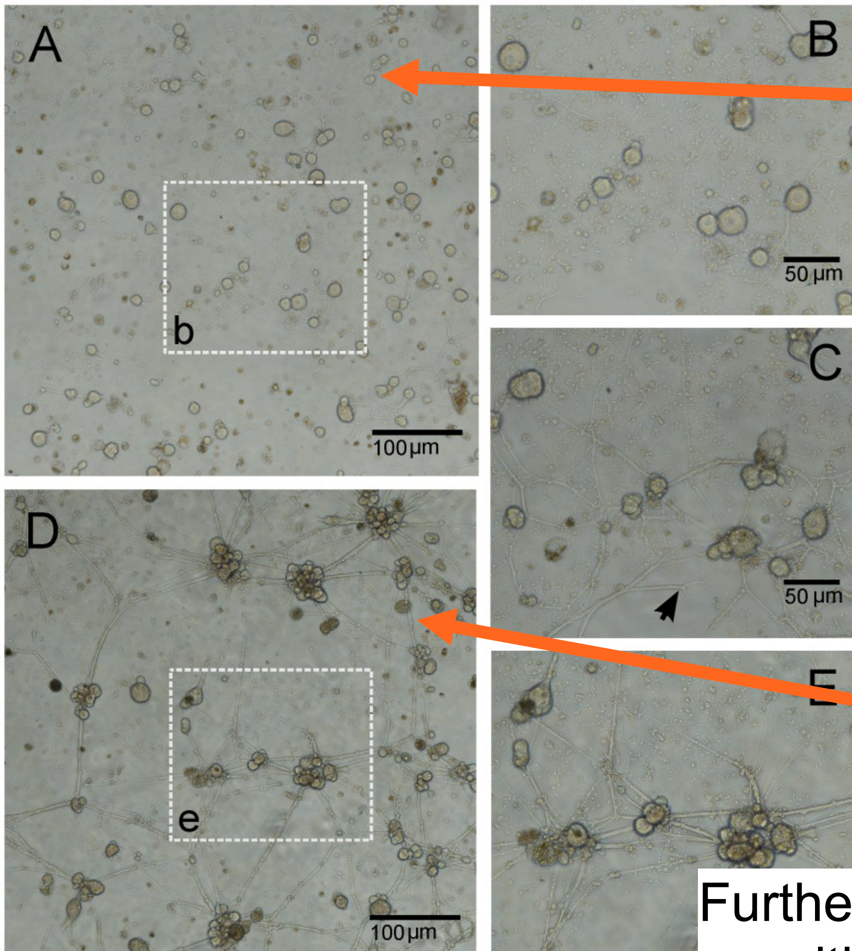
Day 6: non-connected neurons start to die

Day 12: a complex network of connected neurons

Fig: de Santos-Sierra et al. 2014, published under CC BY 4.0

Why is the brain a network?

Brain: 10^{11} neurons, 10^{14} synapses



Day 3 after separating neurons: axon bundles start to grow

Day 6: non-connected neurons start to die

Day 12: a complex network of connected neurons

Fig: de Santos-Sierra et al. 2014, published under CC BY 4

Further evidence from functional neuroimaging: cognitive tasks require co-activation of brain areas

Network neuroscience

(Bassett & Muldoon 2016, Bassett & Sporns 2017)

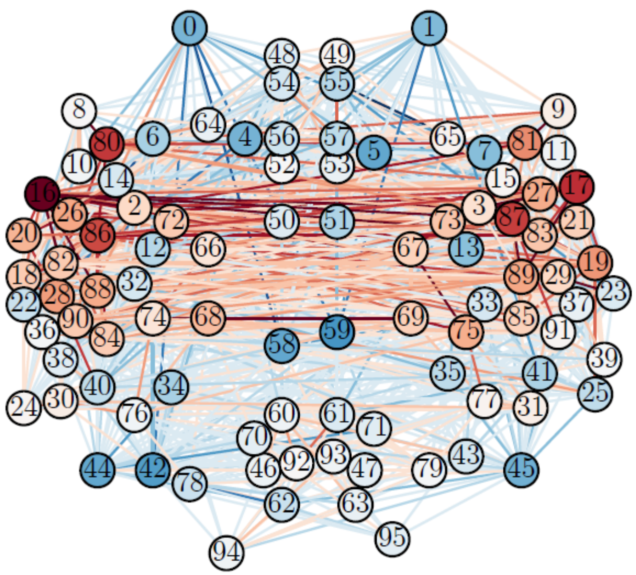


Fig: Alakörkkö *et al*. 2017, *European Journal of Neuroscience*

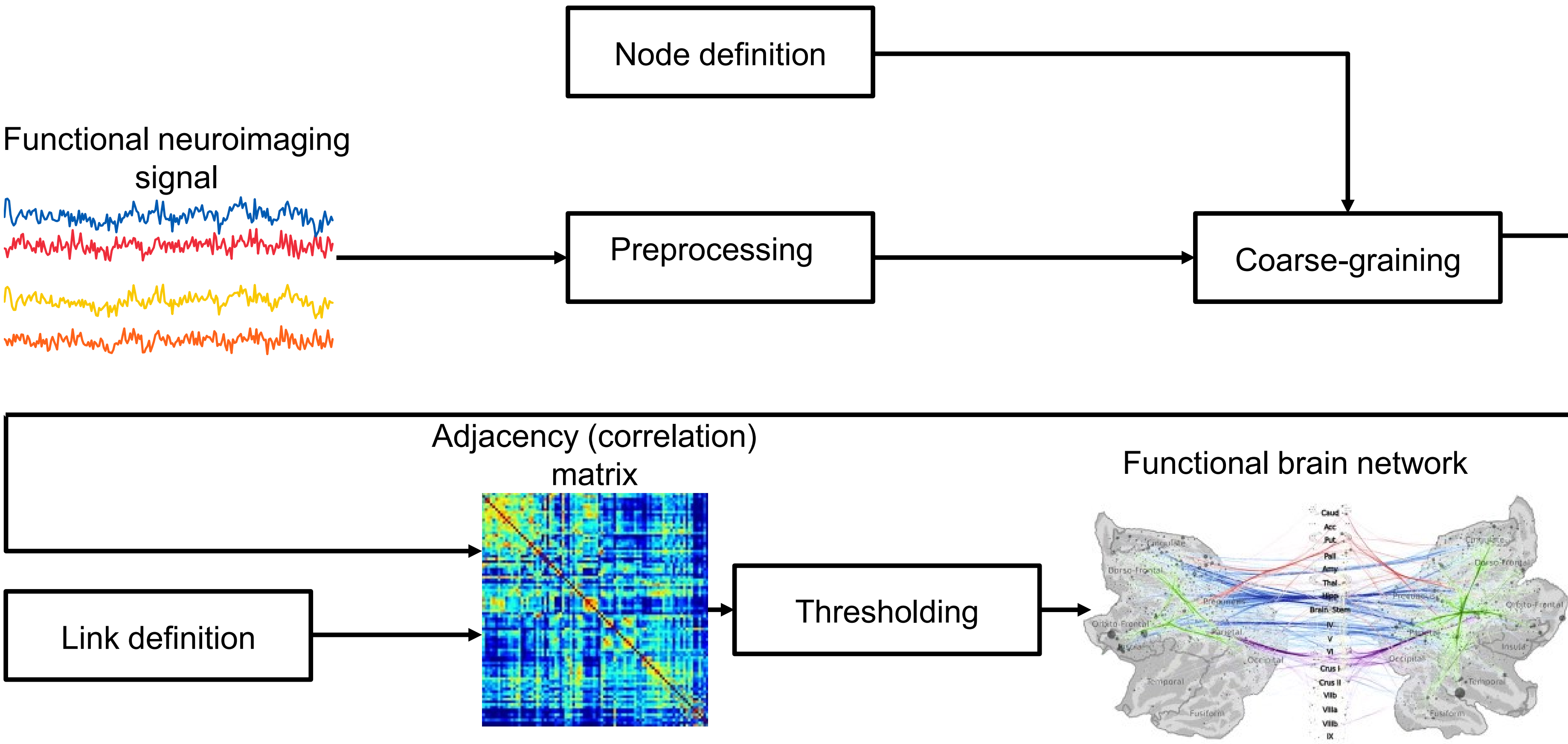
- Network neuroscience = applying network tools on the brain

- Two aims:
  1. Understand the healthy brain
  2. Find causes of diseases

- Broad scales:
  - Molecule – neuron – brain area – human
  - Milliseconds – years

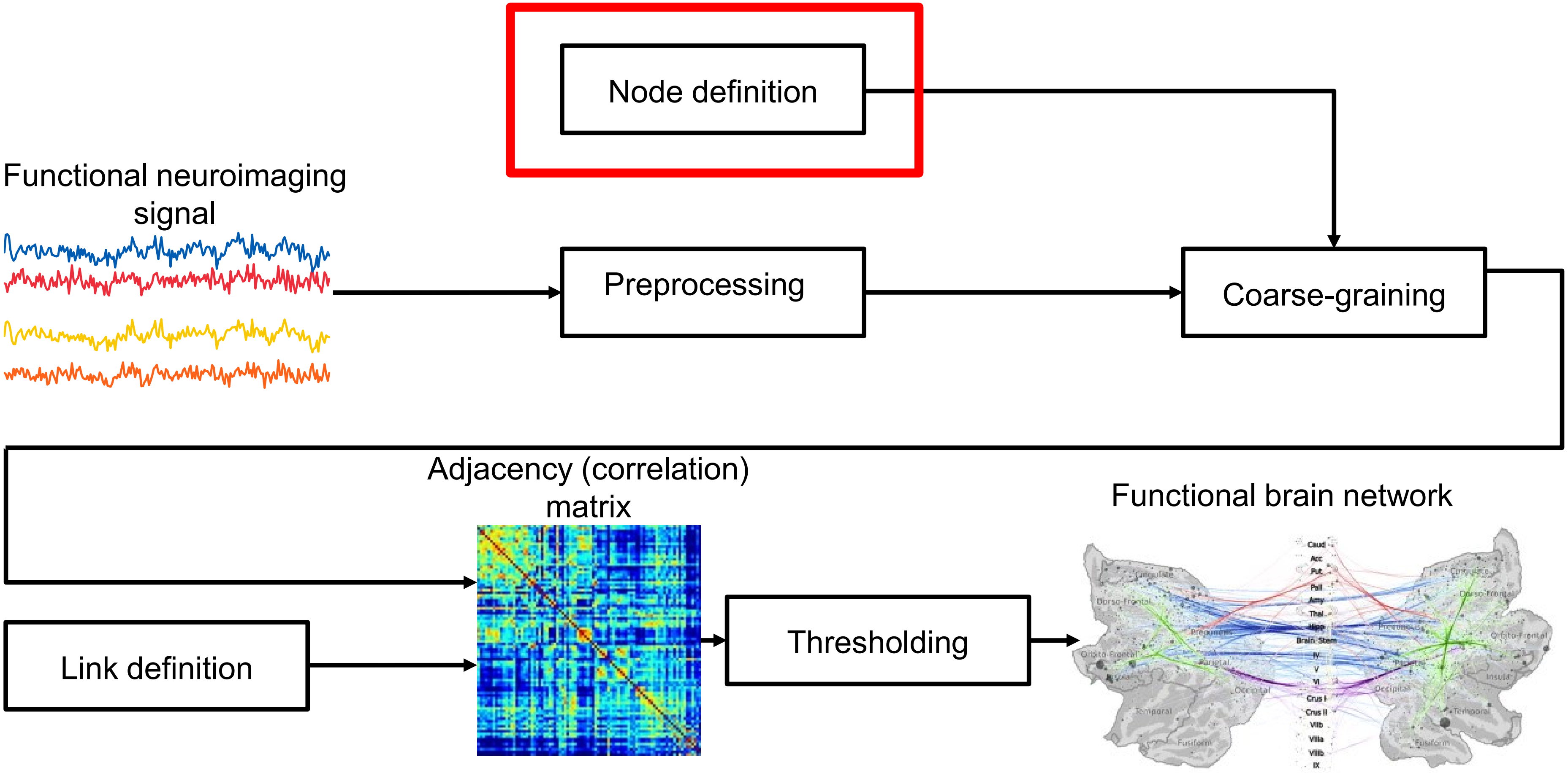
- Different brain networks:
  - Structural: anatomic connections
  - ***Functional:*** temporal coactivation
  - Effective: causality

Functional brain networks: how-to?



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

Functional brain networks: how-to?



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

The problem of node definition

No natural candidates above the scale of neurons

=> huge variation in node definition

- Number of nodes: from < 100 to 10^5

Node definition affects network properties (e.g. Wang et al. 2009)

Common strategies (for a review, Korhonen et al. 2021, section 3.2):

- 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 are similar)?
- ROI time series to represent voxel dynamics:

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

Violent?

More on this:

- Korhonen et al. 2017
- Ryyppö et al. 2018

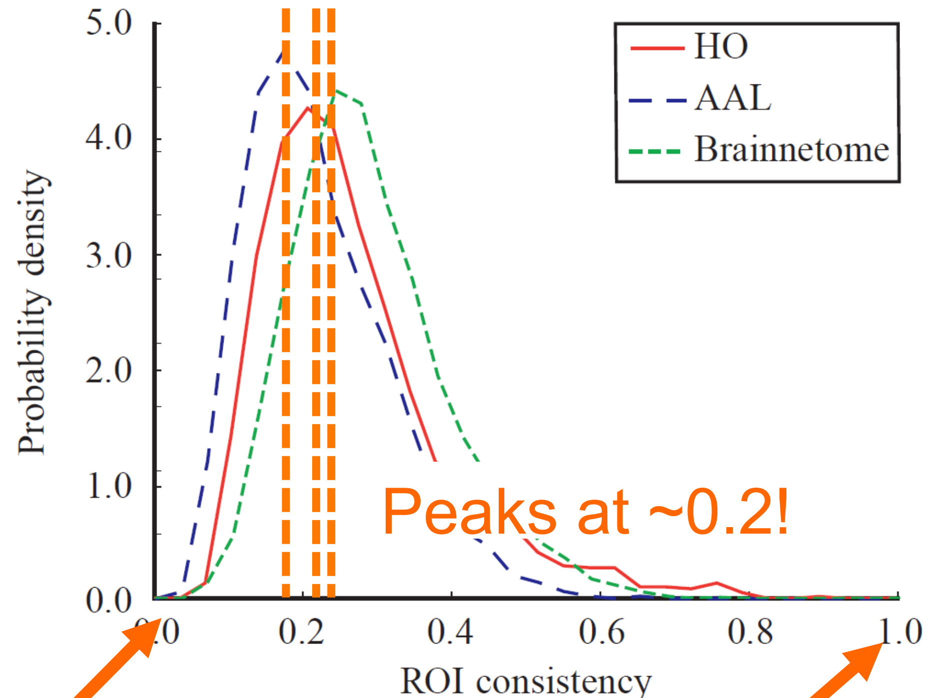
How homogeneous are ROIs?

Korhonen et al., 2017. *Network Neuroscience*

- ***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

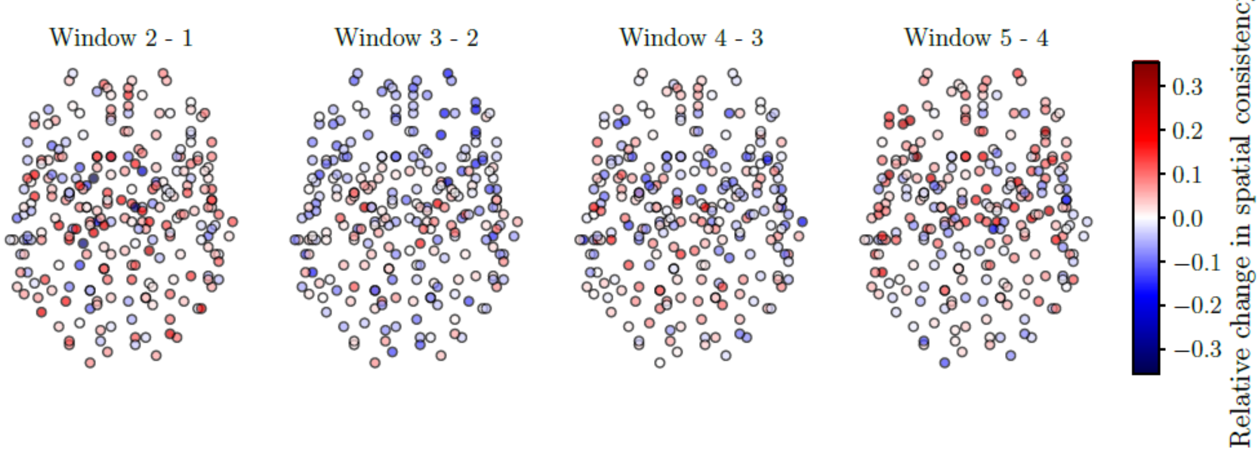


Lack of homogeneity

Perfect homogeneity

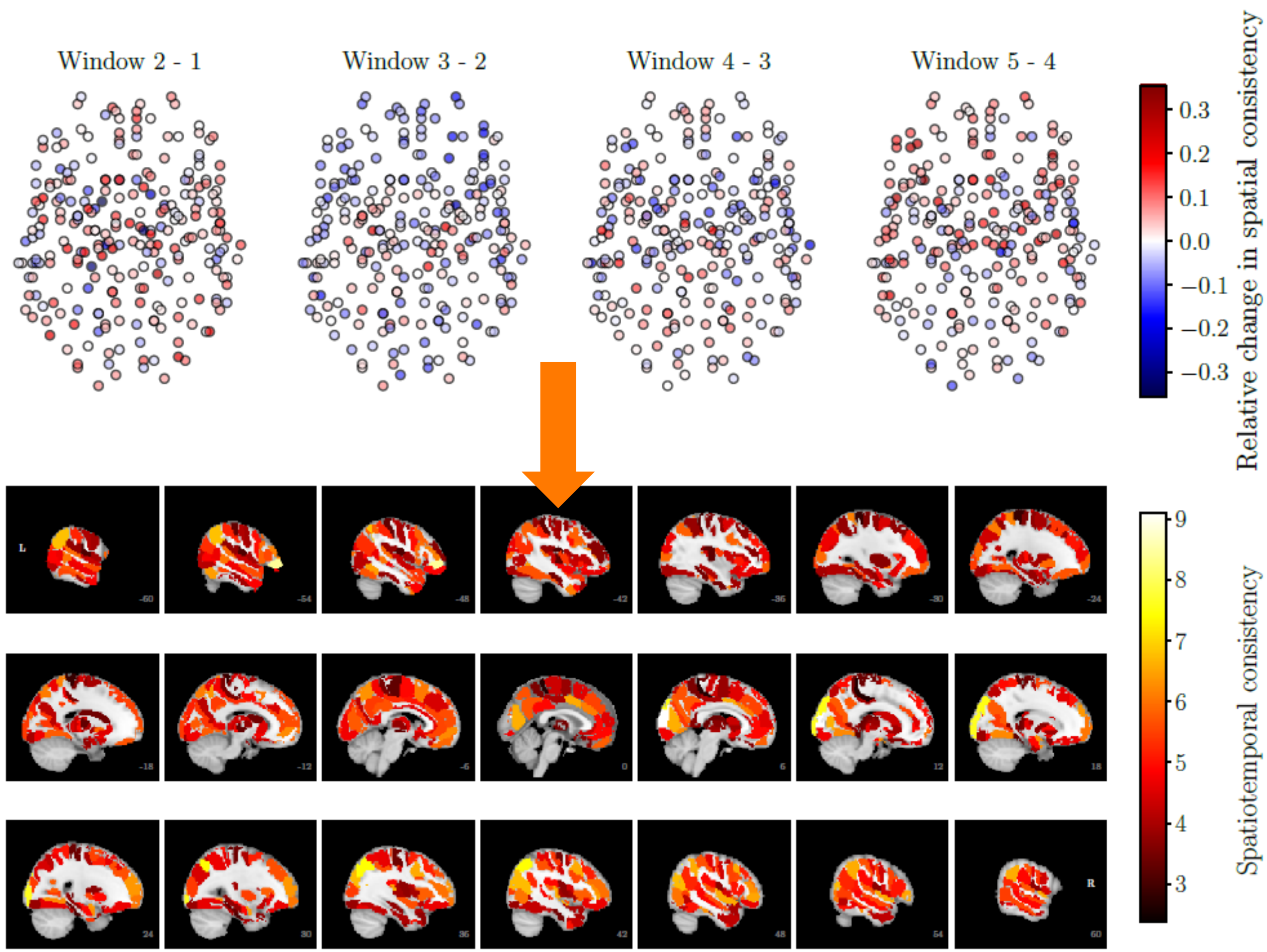
- Correlates with ROI size & connectivity

Spatial consistency changes in time



Ryyppö et al., 2018. *Network Neuroscience*

Spatial consistency changes in time



Ryyppö et al., 2018. *Network Neuroscience*

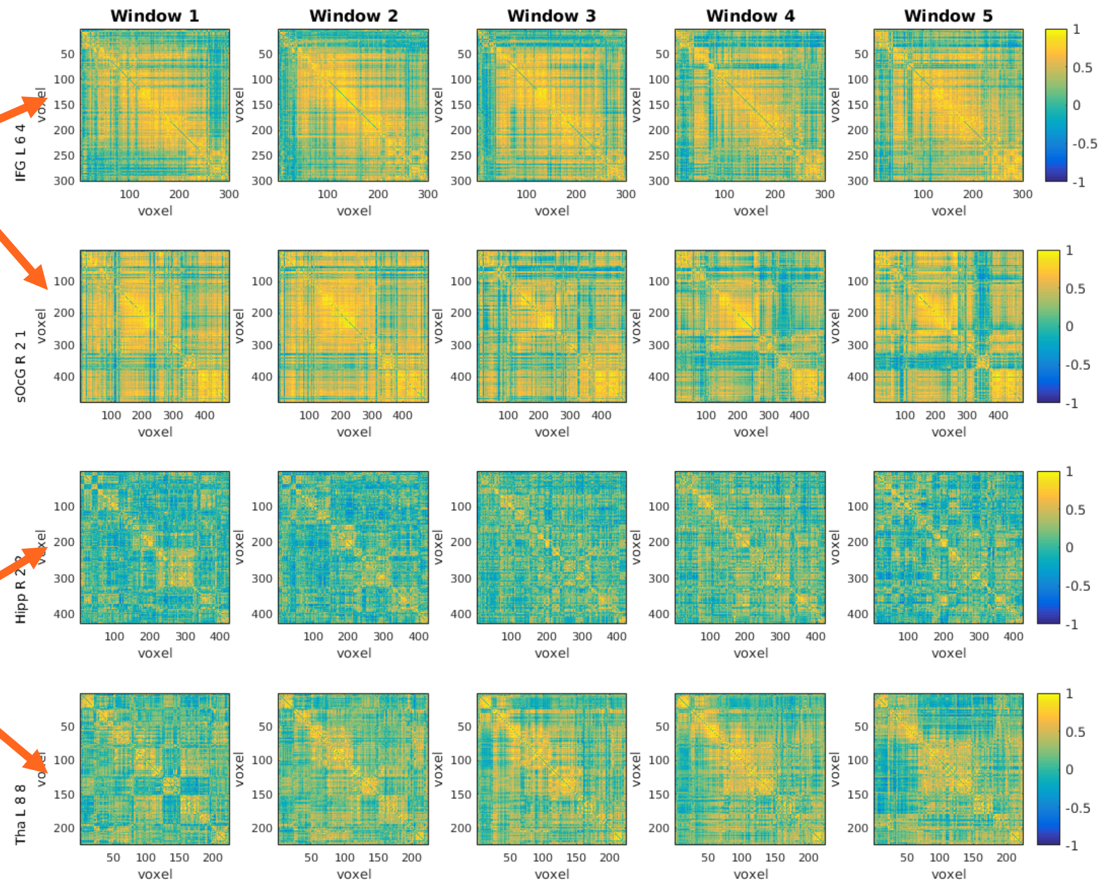
Spatiotemporal consistency

= stability of spat. consistency

ROIs have rich internal connectivity structure

High spatial consistency

Low spatial consistency

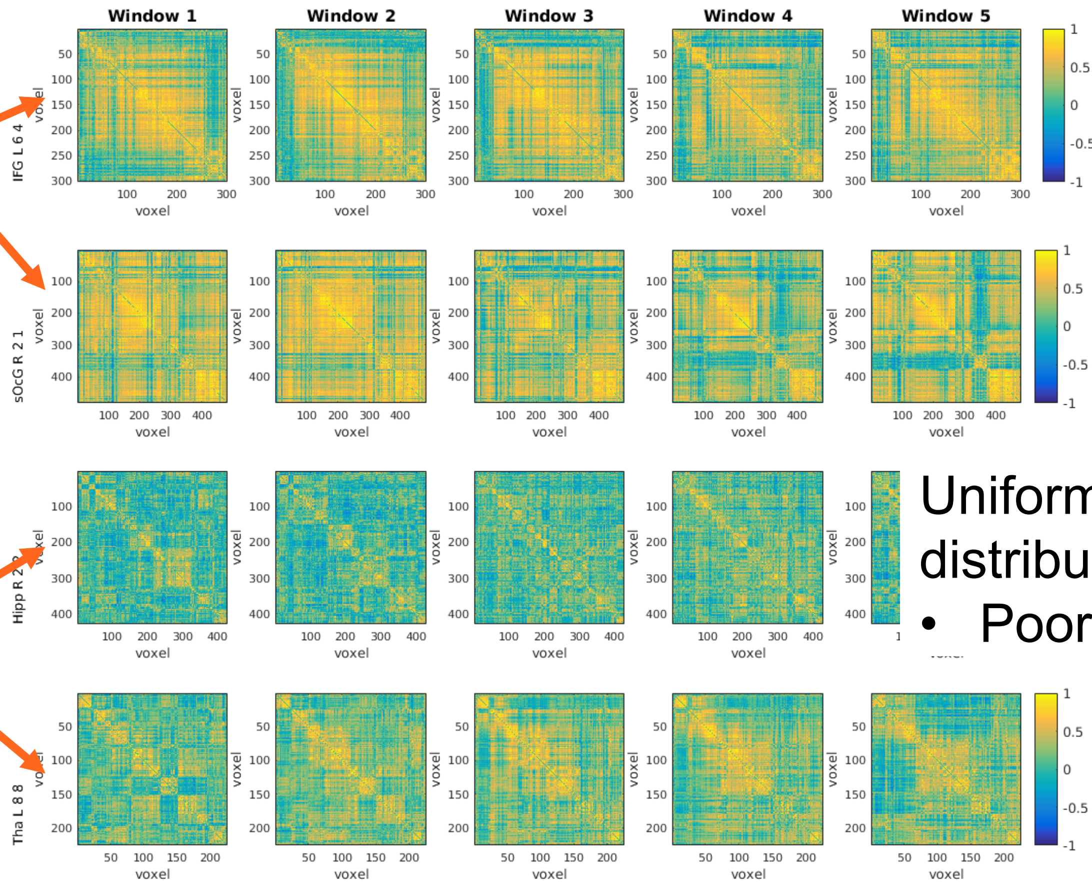


Ryyppö et al., 2018. *Network Neuroscience*

ROIs have rich internal connectivity structure

High spatial consistency

Low spatial consistency



Uniform correlation distribution

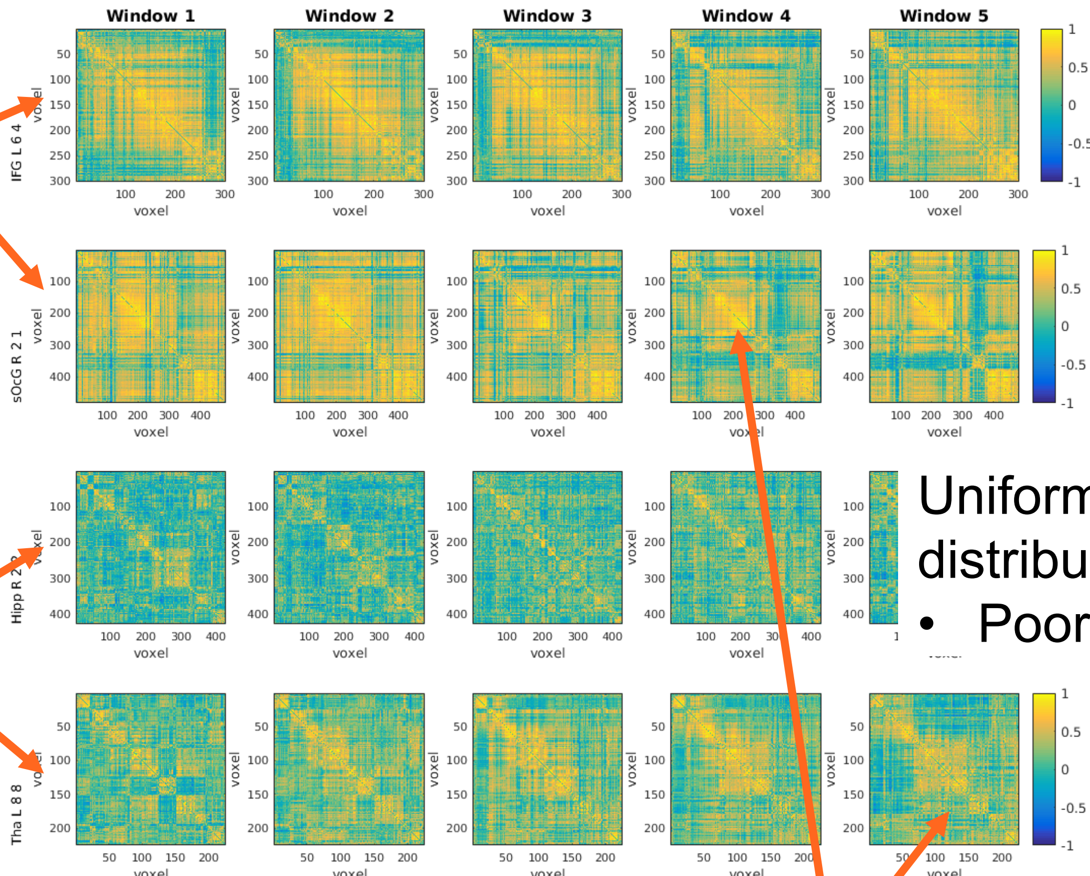
- Poorly defined ROI?

Ryyppö et al., 2018. *Network Neuroscience*

ROIs have rich internal connectivity structure

High spatial consistency

Low spatial consistency



Ryyppö et al., 2018. *Network Neuroscience*

Uniform correlation distribution

- Poorly defined ROI?

Intra-ROI modules

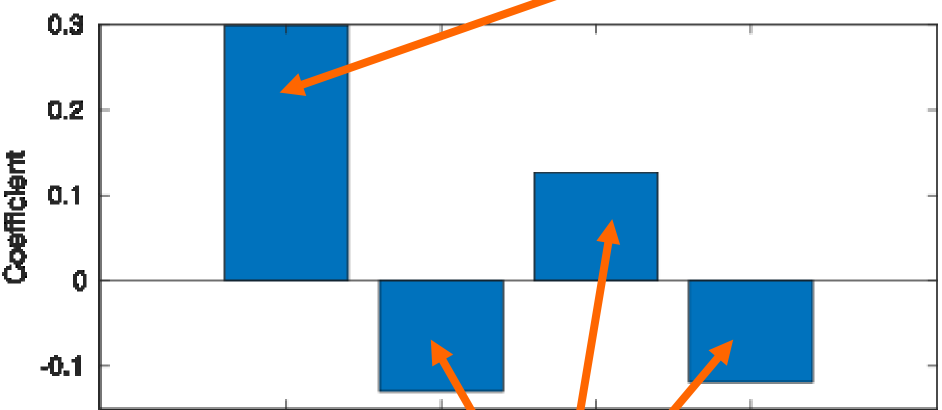
- Network topology?

Consistency predicts topology

Hub vs non-hub:
Accuracy:
Training 60.39%
Test 60.23%
(> Random 50.03%)

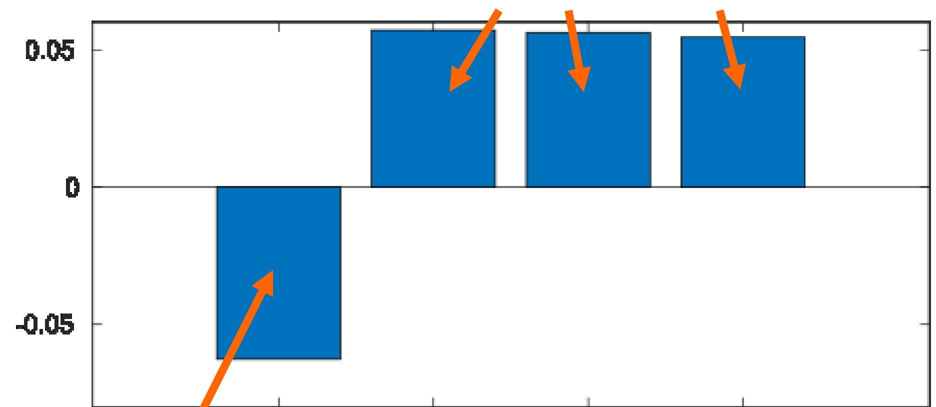
Provincial vs connector hub
Accuracy:
Training 53.23%
Test 52.57%
(> Random 50.38%)

φ_{spat} predicts hubness



Hubs have lower internal density, high φ_{st}, and uniform in-ROI correlations

φ_{spat}, varying correlations, and φ_{st} predict provincial role

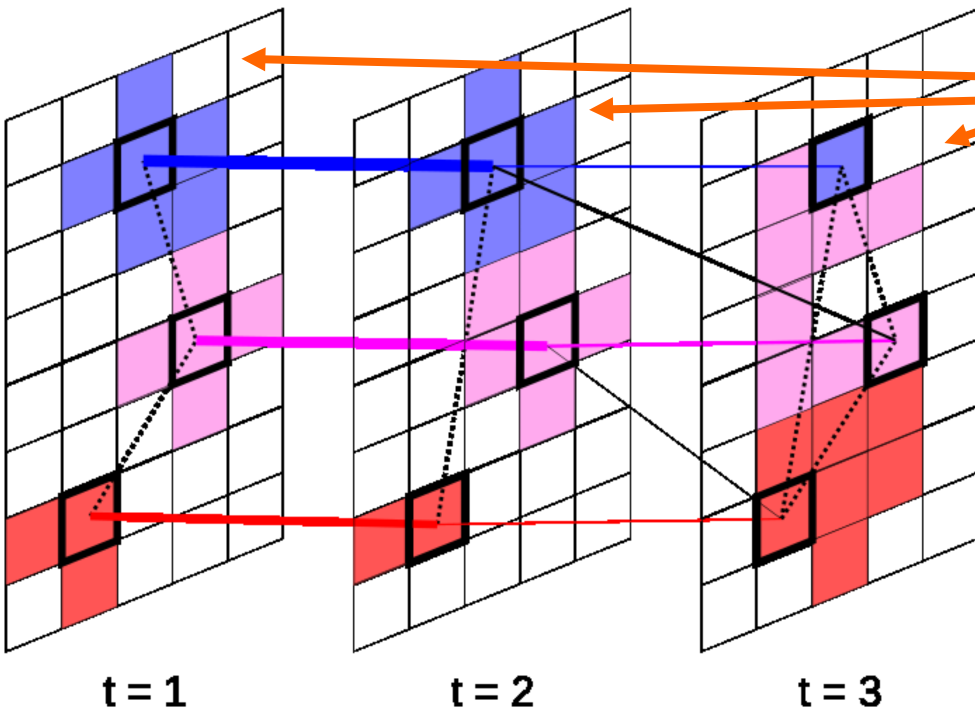


Low internal density = connector hub

Possible solution: time-dependent nodes

(On-going, with T. Nurmi, M. Hakonen, I. Jääskeläinen & M. Kivelä)

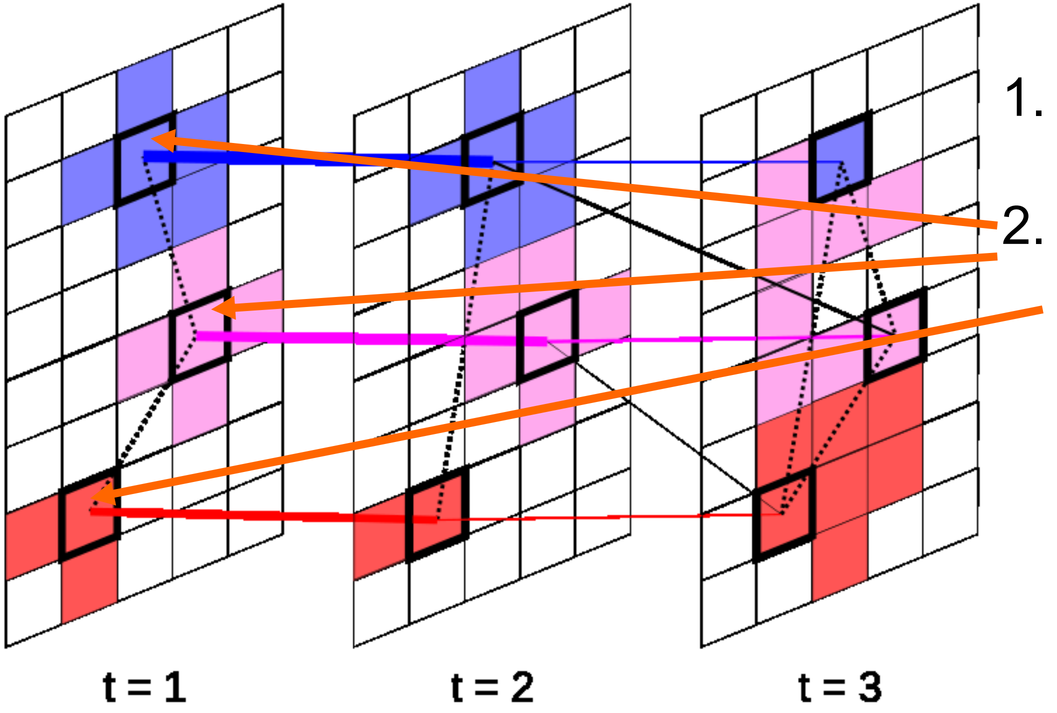
Based on multilayer networks (= different connections in the same network), for review: Kivelä et al. 2014



1. Layers = time windows

Possible solution: time-dependent nodes

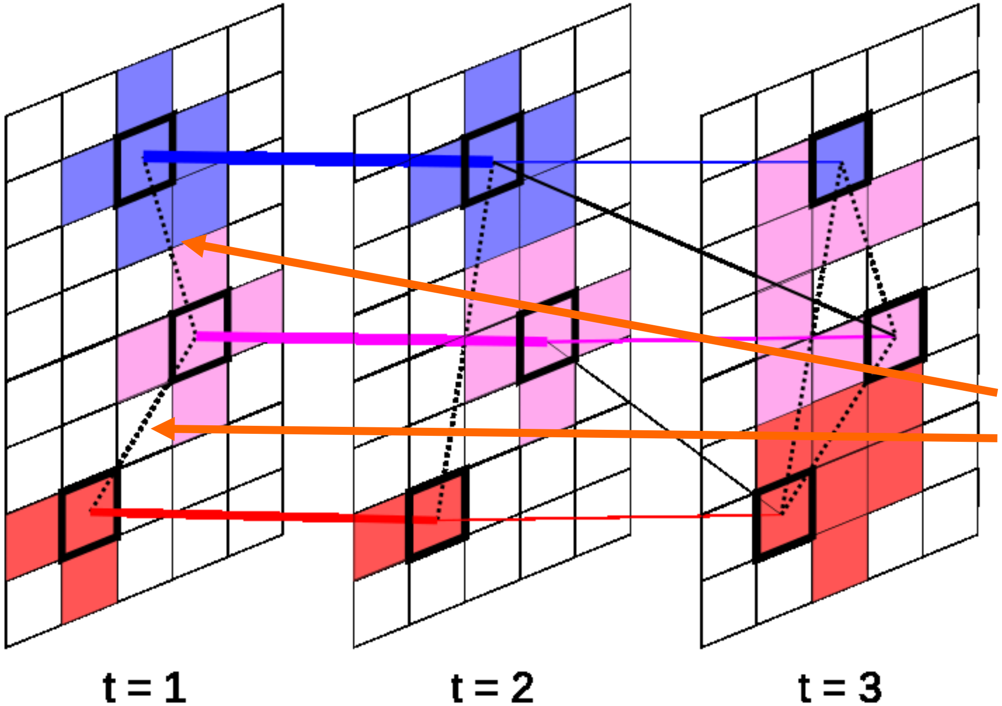
Based on multilayer networks (= different connections in the same network), for review: Kivelä et al. 2014



1. Layers = time windows
2. ROIs optimized inside layers for maximal homogeneity (voxel-level clustering)

Possible solution: time-dependent nodes

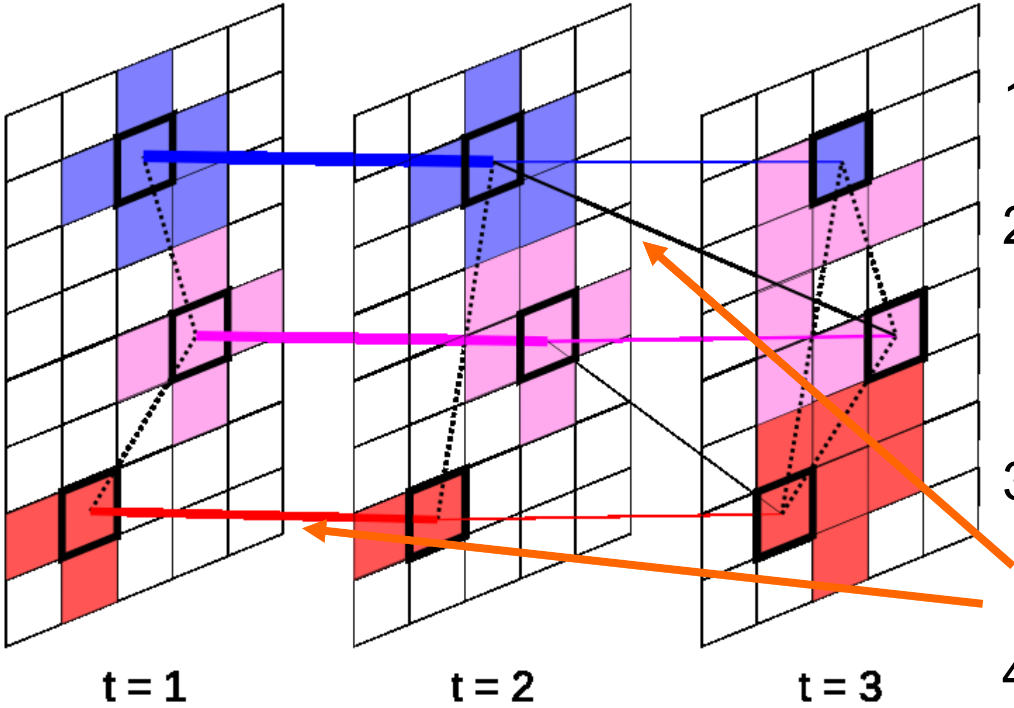
Based on multilayer networks (= different connections in the same network), for review: Kivelä et al. 2014



1. Layers = time windows
2. ROIs optimized inside layers for maximal homogeneity (voxel-level clustering)
3. Intralayer links = Pearson correlation

Possible solution: time-dependent nodes

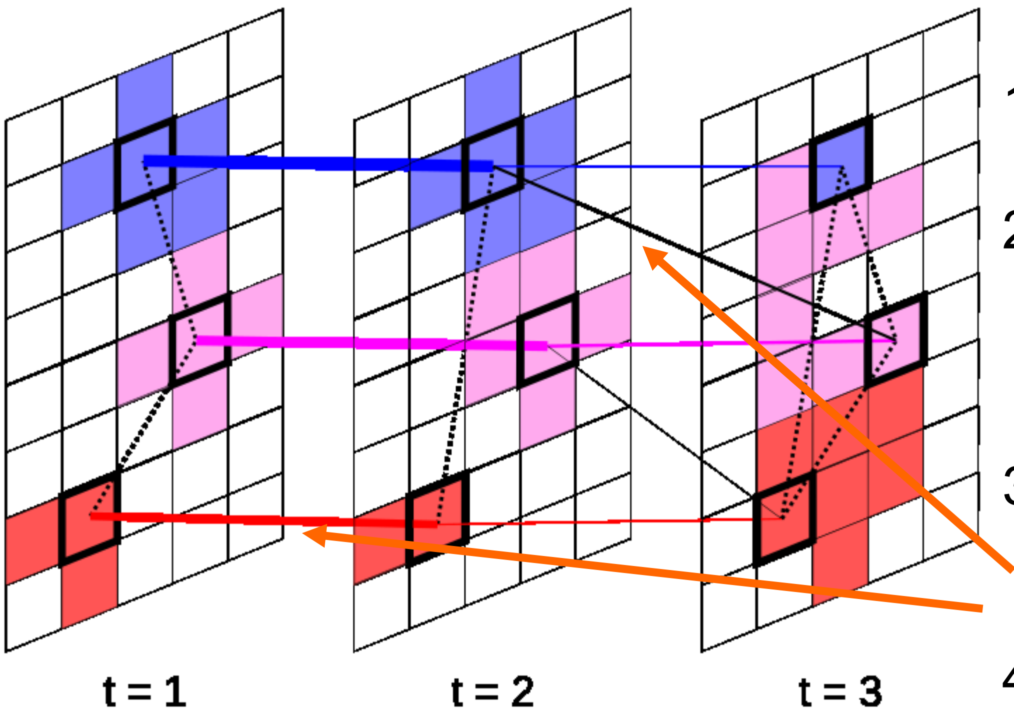
Based on multilayer networks (= different connections in the same network), for review: Kivelä et al. 2014



1. Layers = time windows
2. ROIs optimized inside layers for maximal homogeneity (voxel-level clustering)
3. Intralayer links = Pearson correlation
4. Interlayer links = spatial overlap

Possible solution: time-dependent nodes

Based on multilayer networks (= different connections in the same network), for review: Kivelä et al. 2014



1. Layers = time windows
2. ROIs optimized inside layers for maximal homogeneity (voxel-level clustering)
3. Intralayer links = Pearson correlation
4. Interlayer links = spatial overlap

Questions:

- How do ROIs change over time? Splitting, merging, disappearing?
- State changes?
- What about Alzheimer's disease?

Conclusions

- It's not trivial to construct a functional brain network
  - Node definition?
  - Not covered today: preprocessing, space, thresholding, link definition, multilayers in multiple-person neuroscience?
  - **Know your methods!**
- Currently used nodes functionally inhomogeneous
  - Data lost in averaging
  - Can we trust observed 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

Alakörkkö, T., Saarimäki, H., Glerean, E., Saramäki, J., & Korhonen, O. 2017. Effects of spatial smoothing on functional brain networks. *European Journal of Neuroscience* 46(9).

Bassett, D. S. & Sporns, O. 2017. Network Neuroscience. *Nature Neuroscience* 20(3).

de Santos-Sierra, D., Sendiña-Nadal, I., Leyva, I., Almendral, J. A., Anava, S., Ayali, A., Papo, D., & Boccaletti, S. 2014. Emergence of small-world anatomical networks in self-organizing clustered neuronal cultures. *PLoS One* 9(1): e85828.

Kivelä, M., Arenas, A., Barthelemy, M., Gleeson, J. P., Moreno, Y., & Porter, M. A. 2014. Multilayer networks. *Journal of Complex Networks* 2(3).

Korhonen, O., Saarimäki, H., Glerean, E., Sams, M., & Saramäki, J. 2017. Consistency of Regions of Interest as nodes of fMRI functional brain networks. *Network Neuroscience* 1(3).

Korhonen, O., Zanin, M., Papo, D., 2021. Principles and open questions in functional brain network reconstruction. *Human Brain Mapping* 42(11).

Muldoon, S. F. & Bassett, D. S. 2016. Network and multilayer network approaches to understanding human brain dynamics. *Philosophy of Science* 82(5).

Nummenmaa, L., Saarimäki, H., Glerean, E., Gostopoulos, A., Jääskeläinen, I. P., Hari, R., & Sams, M. 2014. Emotional speech synchronizes brains across listeners and engages large-scale dynamic brain networks. *NeuroImage* 102.

Ryyppö, E., Glerean, E., Brattico, E., Saramäki, J., & Korhonen, O. 2018. Regions of Interest as nodes of dynamic functional brain networks. *Network Neuroscience* 2(4)

Wang, J., Wang, L., Zang, Y., Yang, H., Tang, H., Gong, Q., … He, Y. 2009. Parcellation-dependent small-world brain functional networks: A resting-state fMRI study. *Human Brain Mapping* 30(5).

Thank you!

Questions, comments?

onerva.korhonen@gmail.com

onervakorhonen.wordpress.com
Twitter: @OnervaKorhonen

Slides: https://github.com/onerva-korhonen/presentations/blob/master/nimeg_051022.pdf