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

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13.5.2024

Slides:
github.com/onerva-korhonen/presentations/blob/master/brainnet_stockholm_130524.pdf

Networks: what and why?

Network: a model of connections & interactions

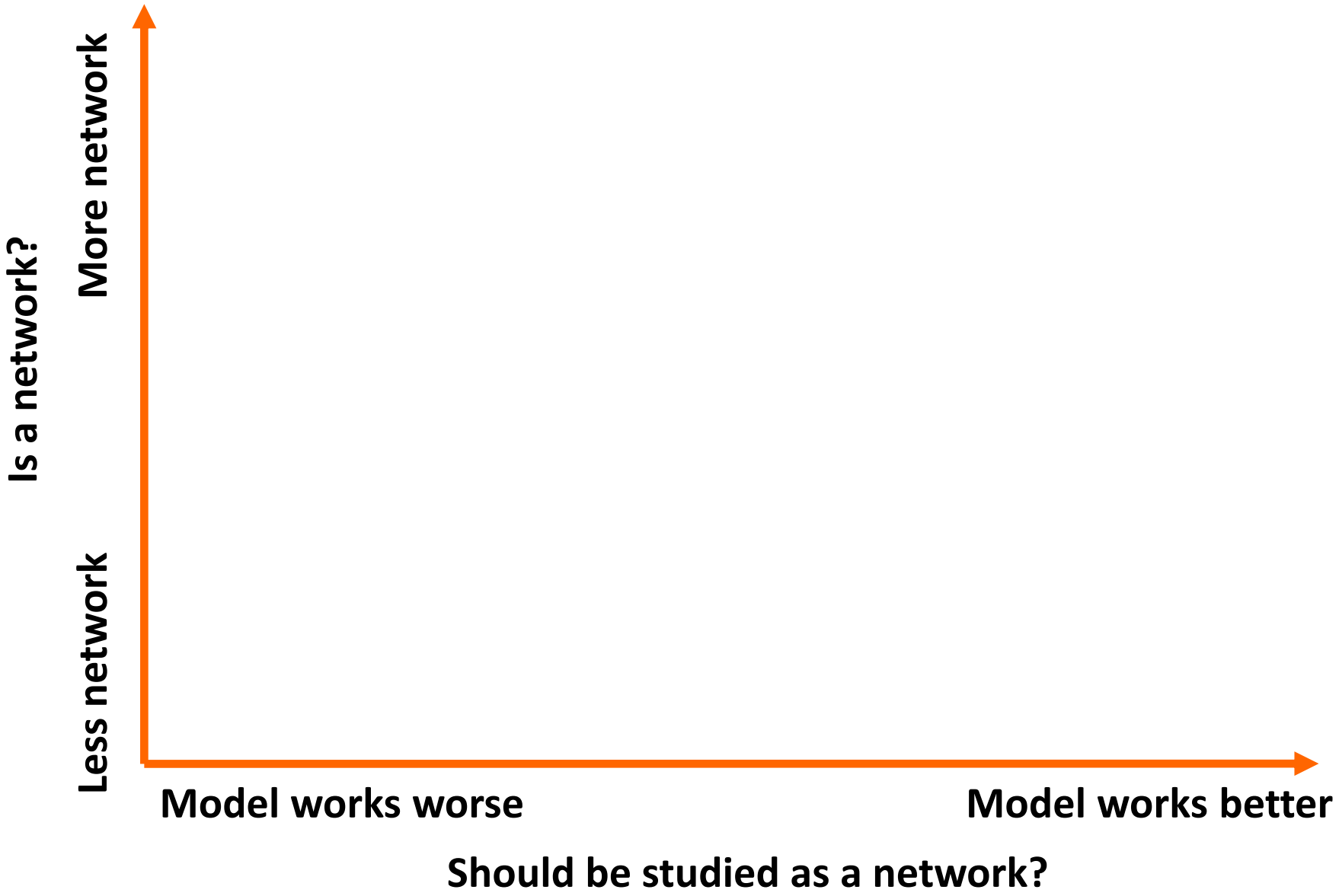
Nodes: network's basic elements

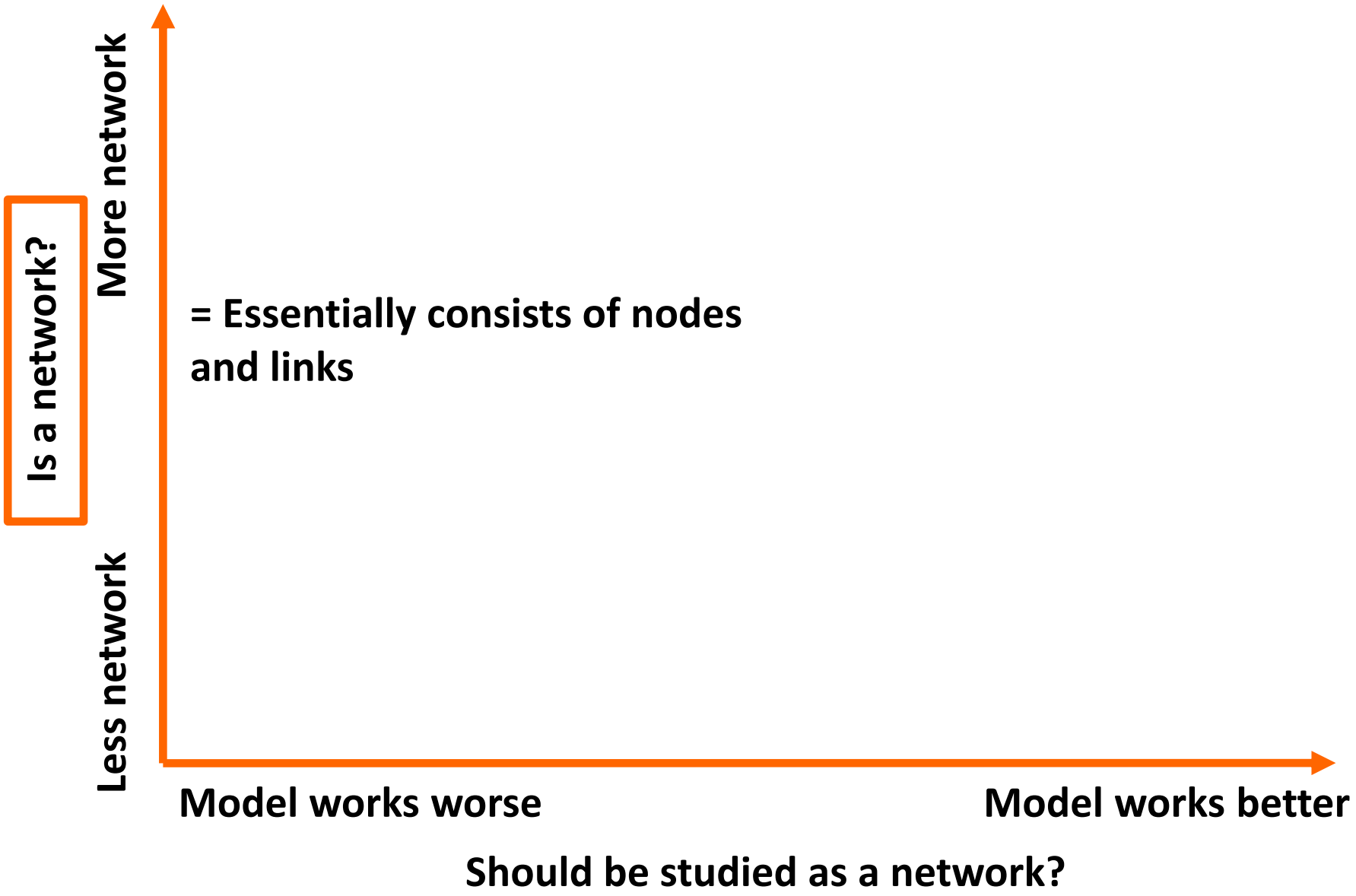
Links: connections between nodes

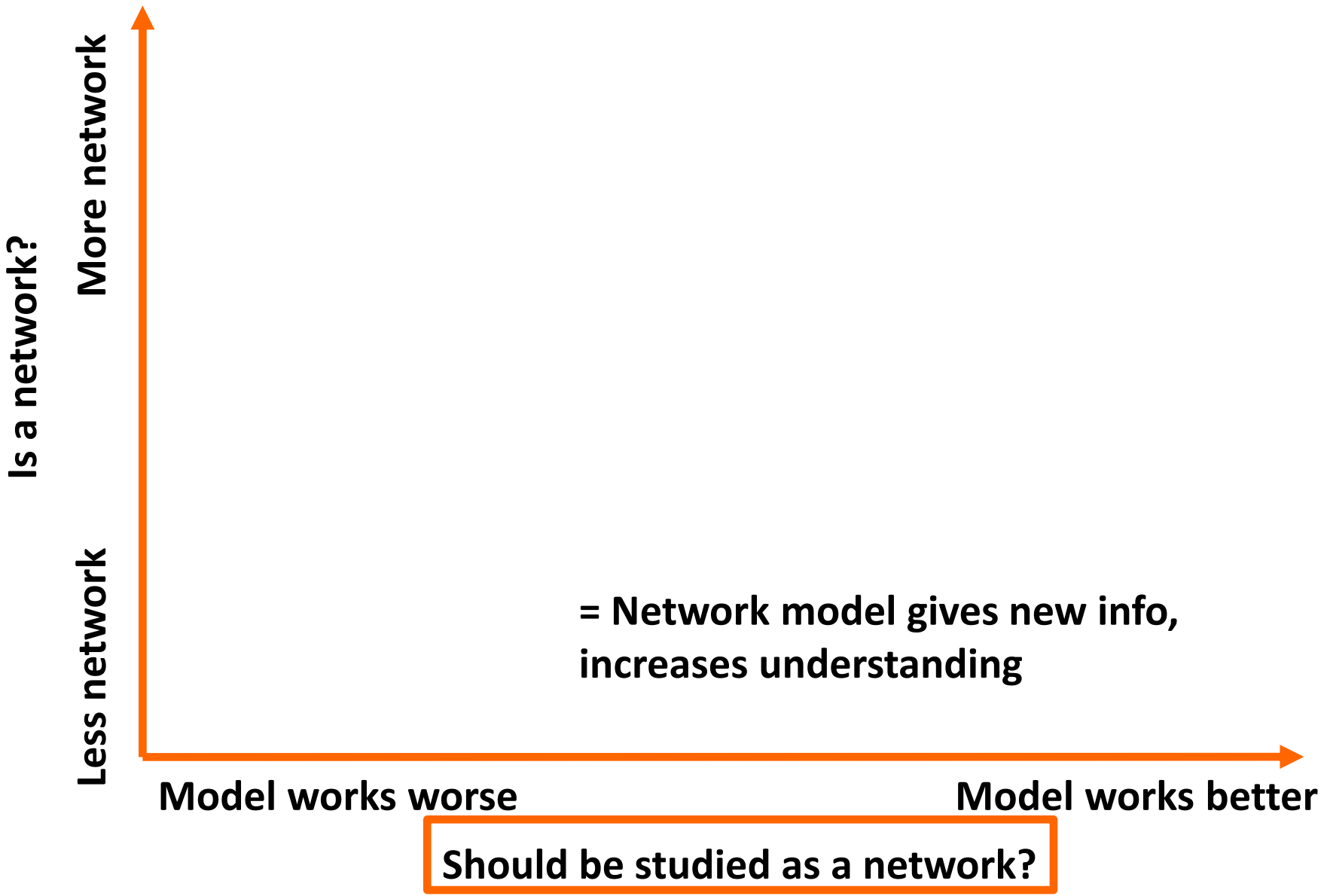
- Weights?
- Direction?

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

Not all that glitters is a network



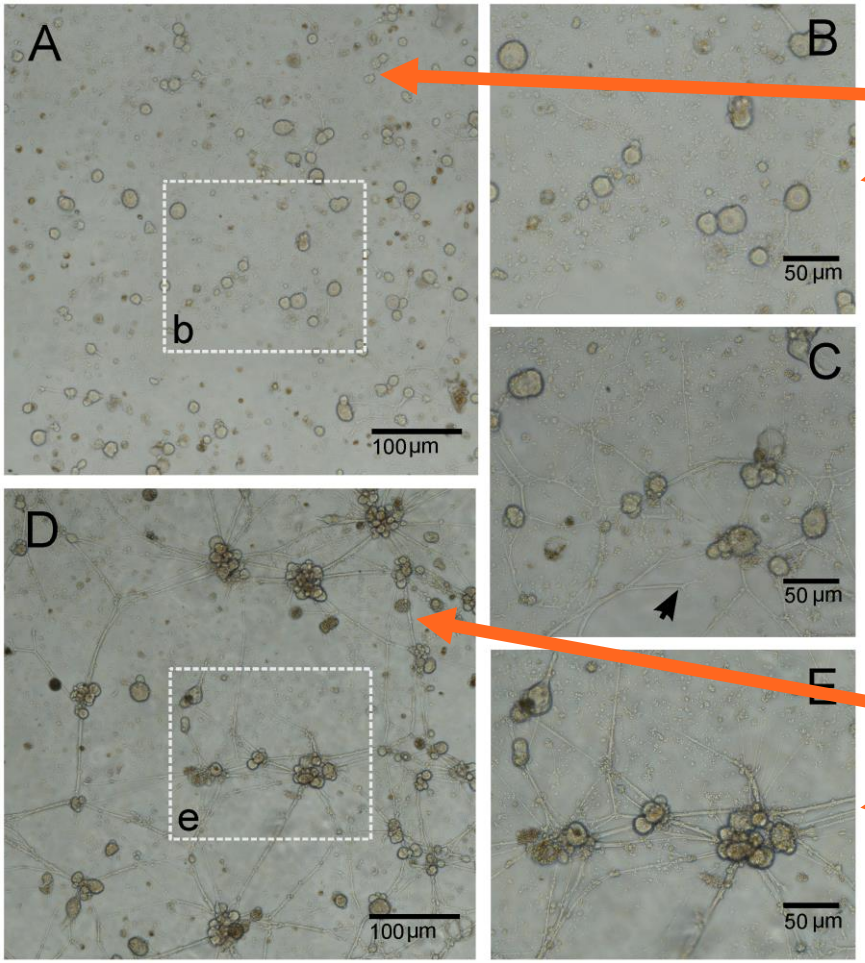

Is a network?
More network
Less network
= Essentially consists of nodes and links
Model works worse
Model works better
Should be studied as a network?


Is a network?
More network
Less network
= Network model gives new info,
increases understanding
Model works worse
Model works better
Should be studied as a network?

Brain networks: Why?

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

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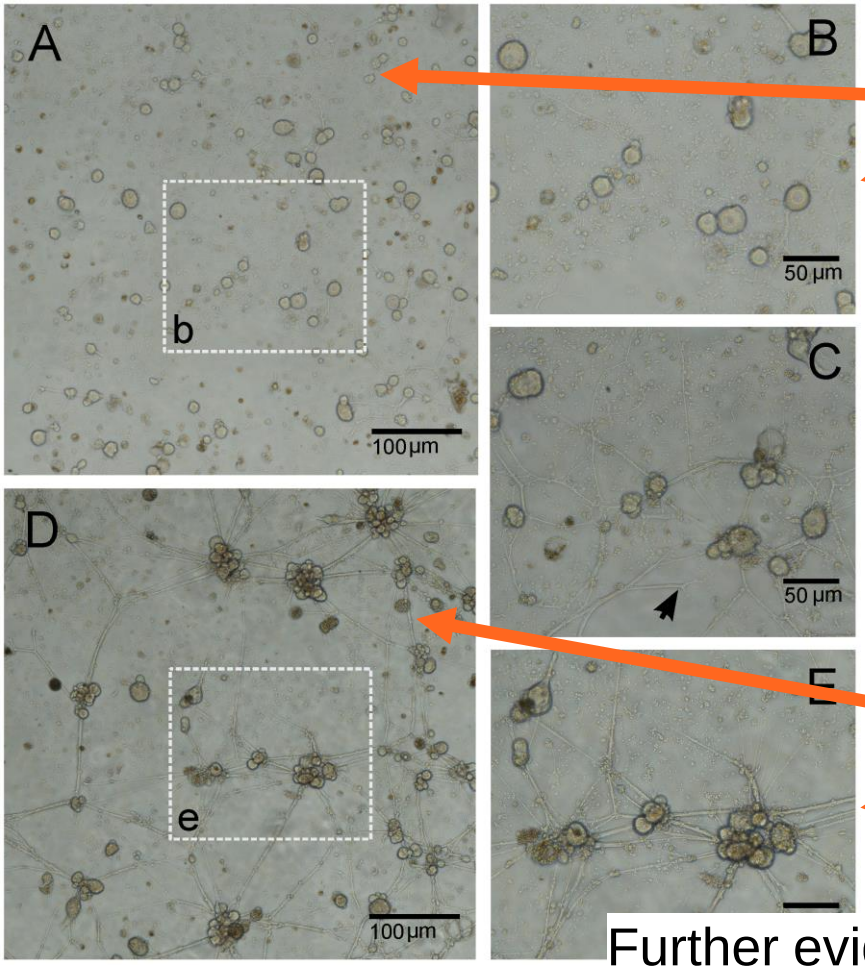


Day 3 after separating neurons: axon bundles start to grow

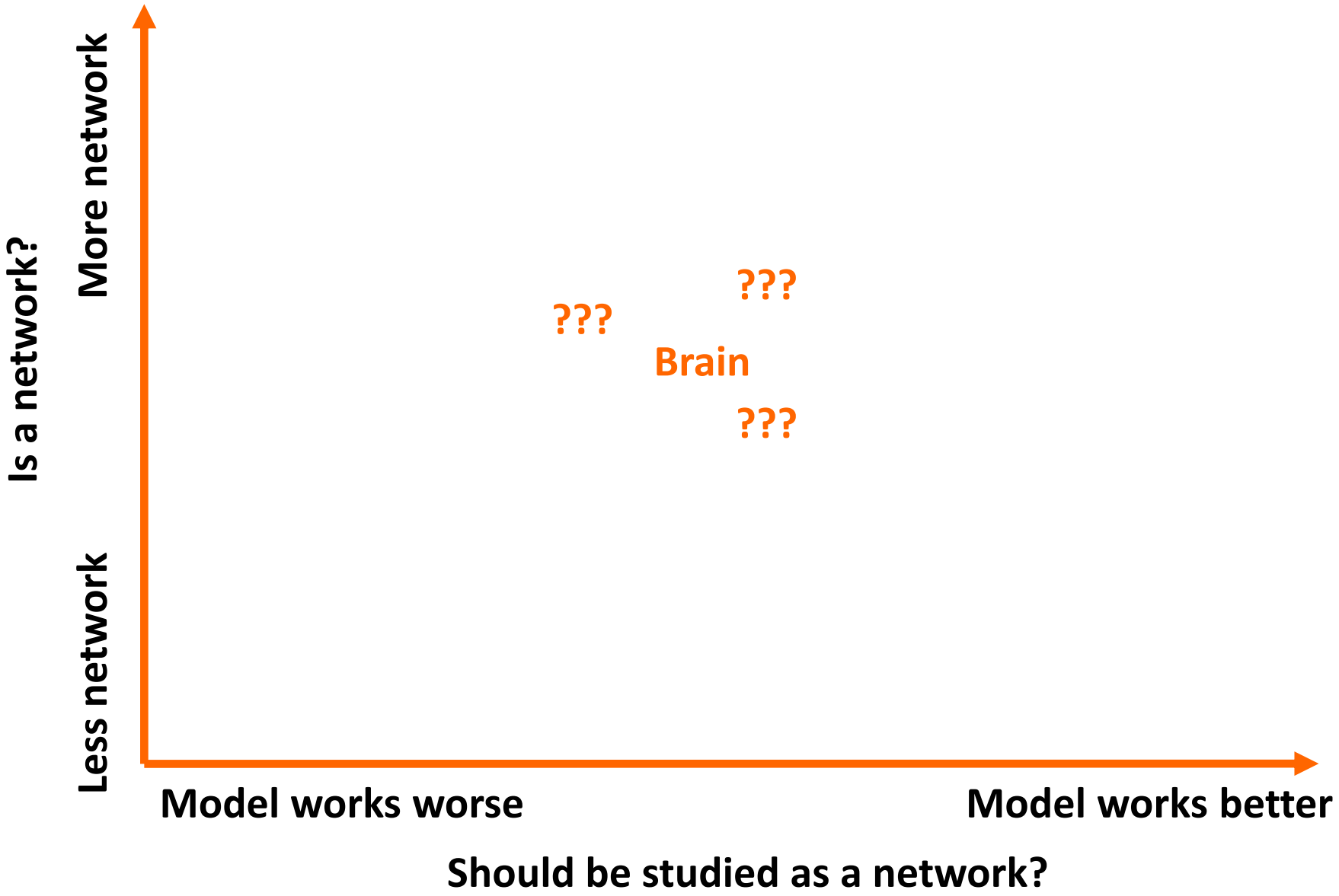
Day 6: non-connected neurons start to die

Day 12: a complex network of connected neurons

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

Fig: de Santos-Sierra et al. 2014. Emergence of sm
anatomical networks in self-organizing clustered ne
PLOS One 9(1): e85828, published under CC BY 4.0

Brain networks: What?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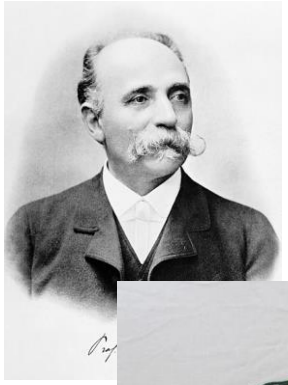
Figs: Wikimedia Commons, public domain



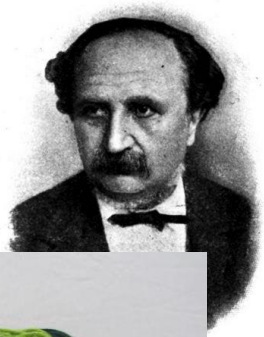


Photo: Milja Heikkinen

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Brain

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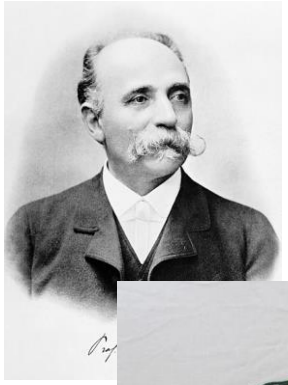

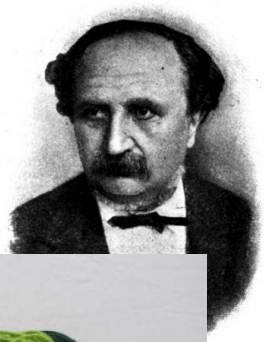

Photo: Milja Heikkinen

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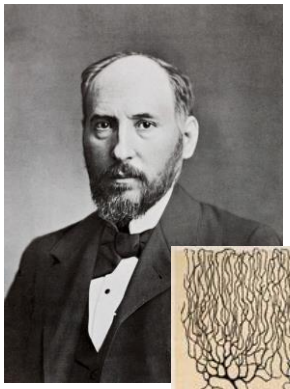

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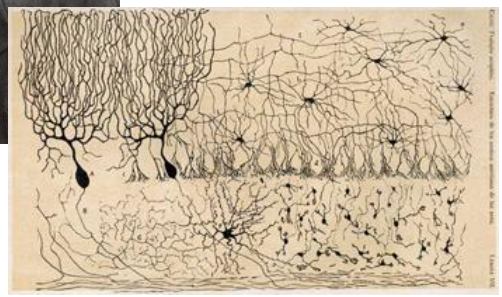

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Brain

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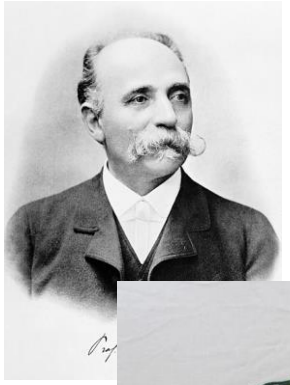

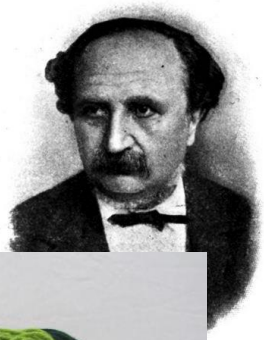

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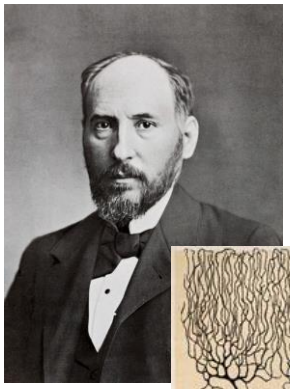

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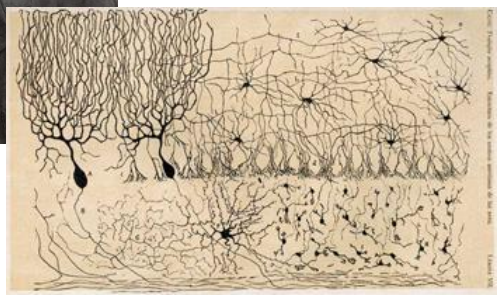

Figs: Wikimedia Commons, public domain

Brain

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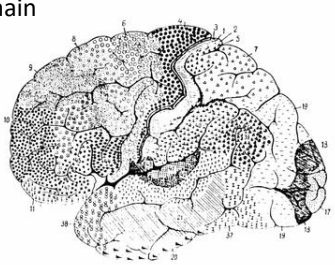

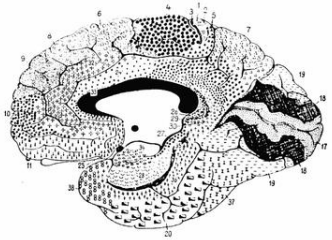

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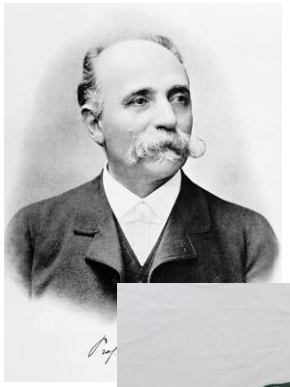

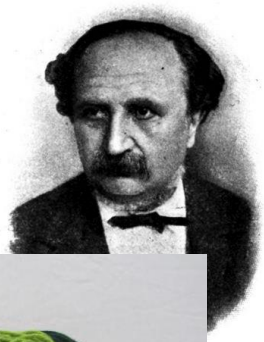

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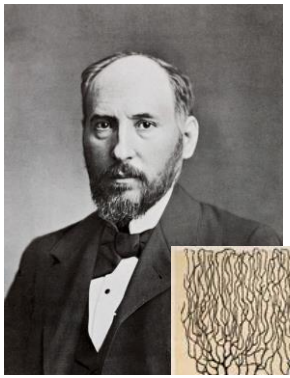

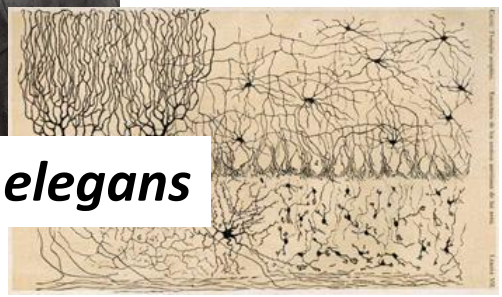

Figs: Wikimedia Commons, public domain

White et al. 1986: *C. elegans*

Brain

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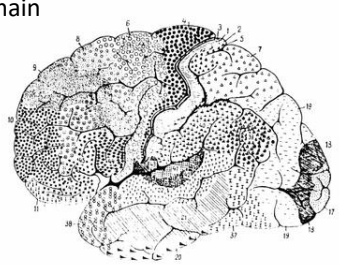

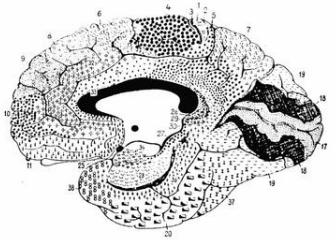

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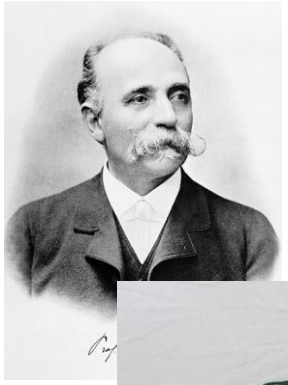

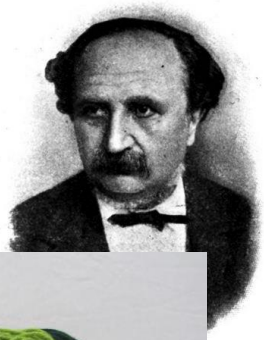

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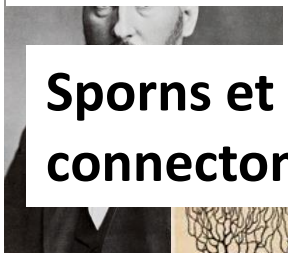
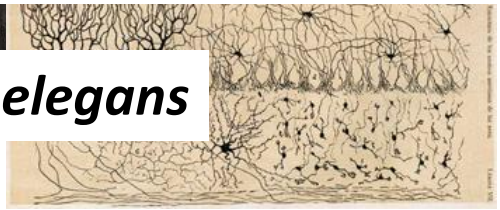
Bassett & Muldoon 2016, Bassett & Sporns 2017: network neuroscience



Sporns et al. 2005, Hagmann 2005: connectomics, connectome



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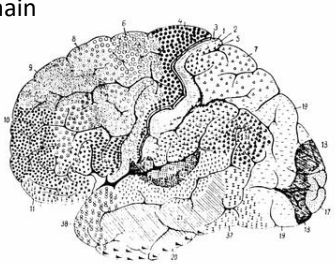
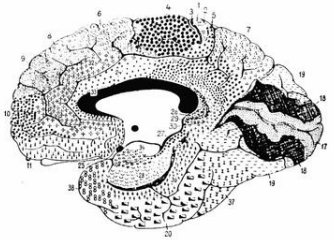




Is a network?

More network

Less network

Model works wors

Model works better

Should be studied as a network?

Network neuroscience

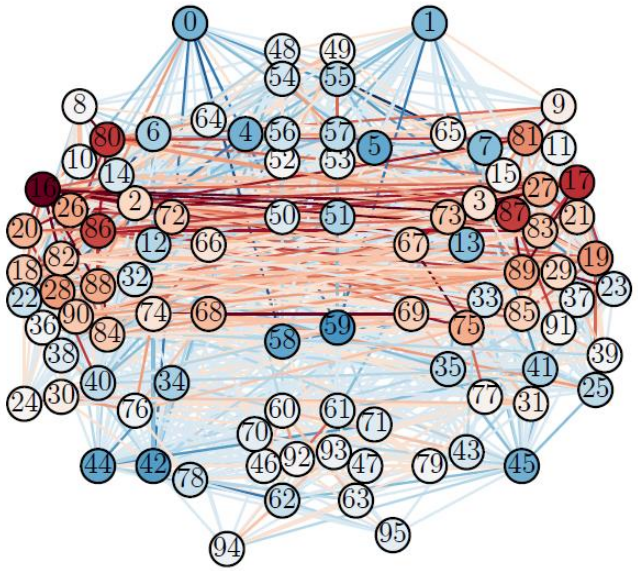
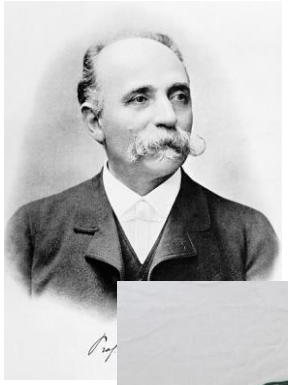
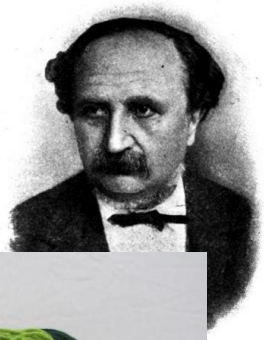


Fig: Alakörkkö *et al.* 2017, *European Journal of Neuroscience*

- 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: anatomical connections
  - **Functional**: temporal coactivation
  - Effective: causality

Figs: Wikimedia Commons, public domain





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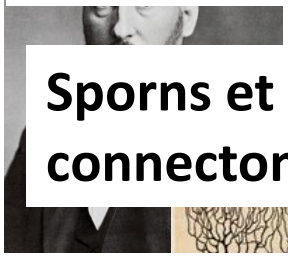
Bassett & Muldoon 2016, Bassett & Sporns 2017: network neuroscience



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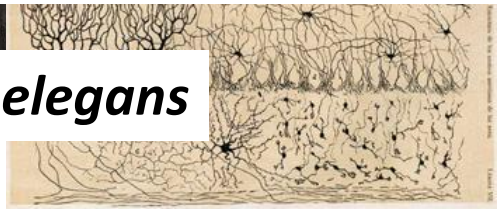

Figs: Wikimedia Commons, public domain

Brain

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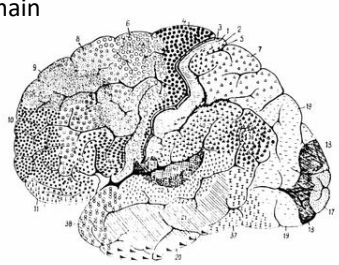
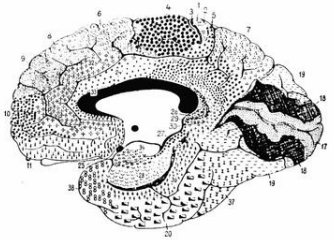




Is a network?

More network

Less network

how to define nodes/links?

structure/function?

correlation = causation?

Model works wors

Model works better

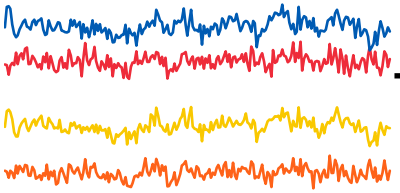
Should be studied as a network?

Brain networks: How?

Functional networks: how-to?

Node definition

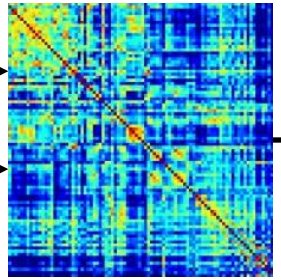
Func neuroimaging signal



Preprocessing

Coarse-graining

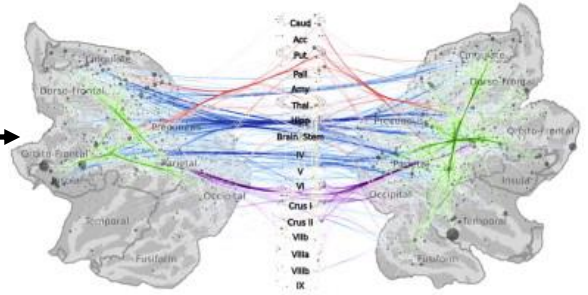
Similarity matrix



Link definition

Thresholding

Functional brain network



Network from Nummenmaa et al. 2014, by permission

One never looks at the same network twice

Heraclitus, feat. O. Korhonen

Traditionally: static brain networks

- For func brain networks, correlations calculated over the whole time series

However, the brain needs to respond to changing stimuli

=> Natural assumption: brain networks change in time

Changes reported:

- Spontaneously over time, between tasks, with age, between health and disease
- In both links and nodes
- For review: Iraji et al. 2019, Korhonen et al. 2021 (section 3.4)

Brain networks: How not?

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

More on this:

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

ROIs:

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

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

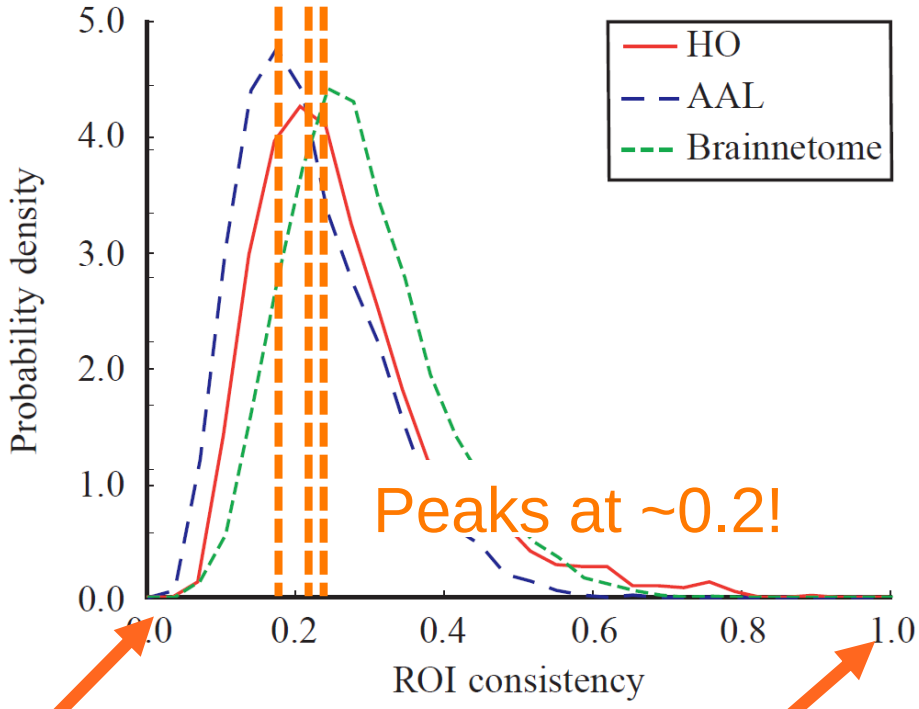
Violent?

How homogeneous are ROIs?

Spatial consistency
= measure of functional homogeneity:

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

Fig: Korhonen et al. 2017



Lack of homogeneity

Perfect homogeneity

ROIs have rich internal connectivity structure

High spatial consistency

Low spatial consistency

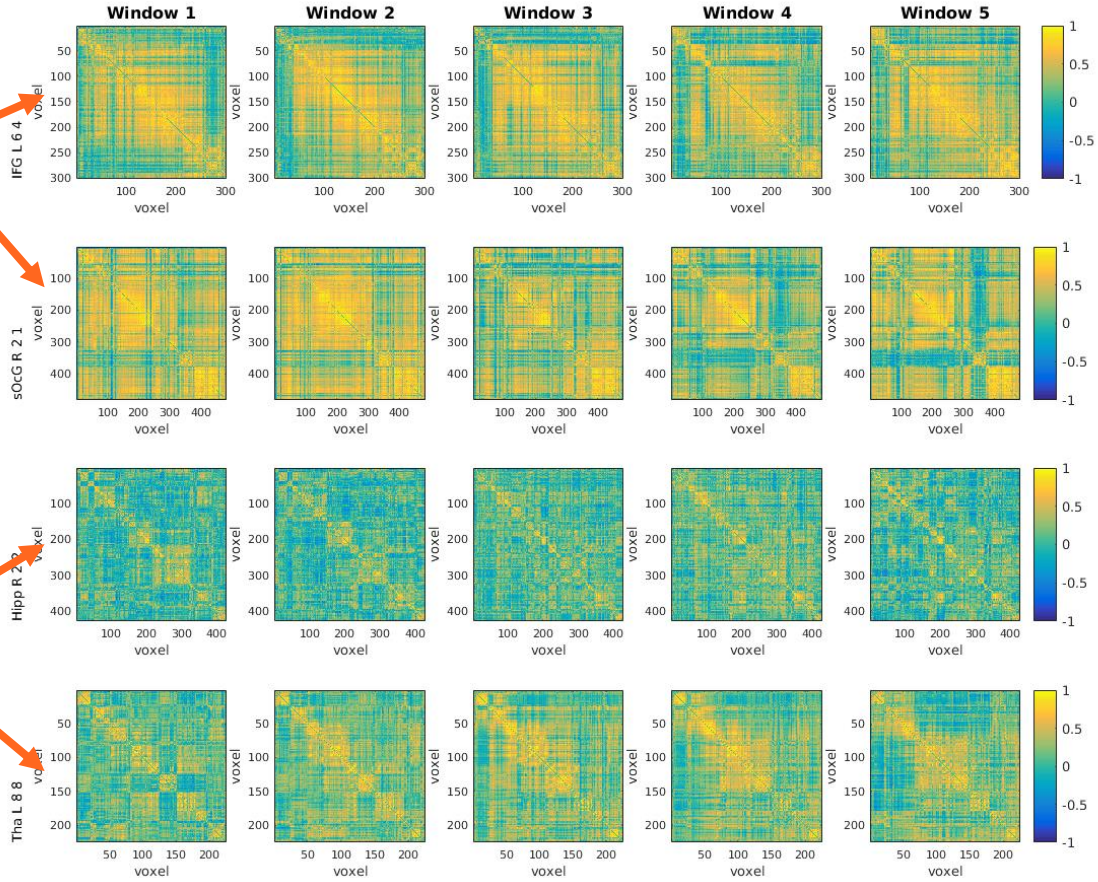


Fig: Ryyppö et al. 2018

ROIs have rich internal connectivity structure

High spatial consistency

Low spatial consistency

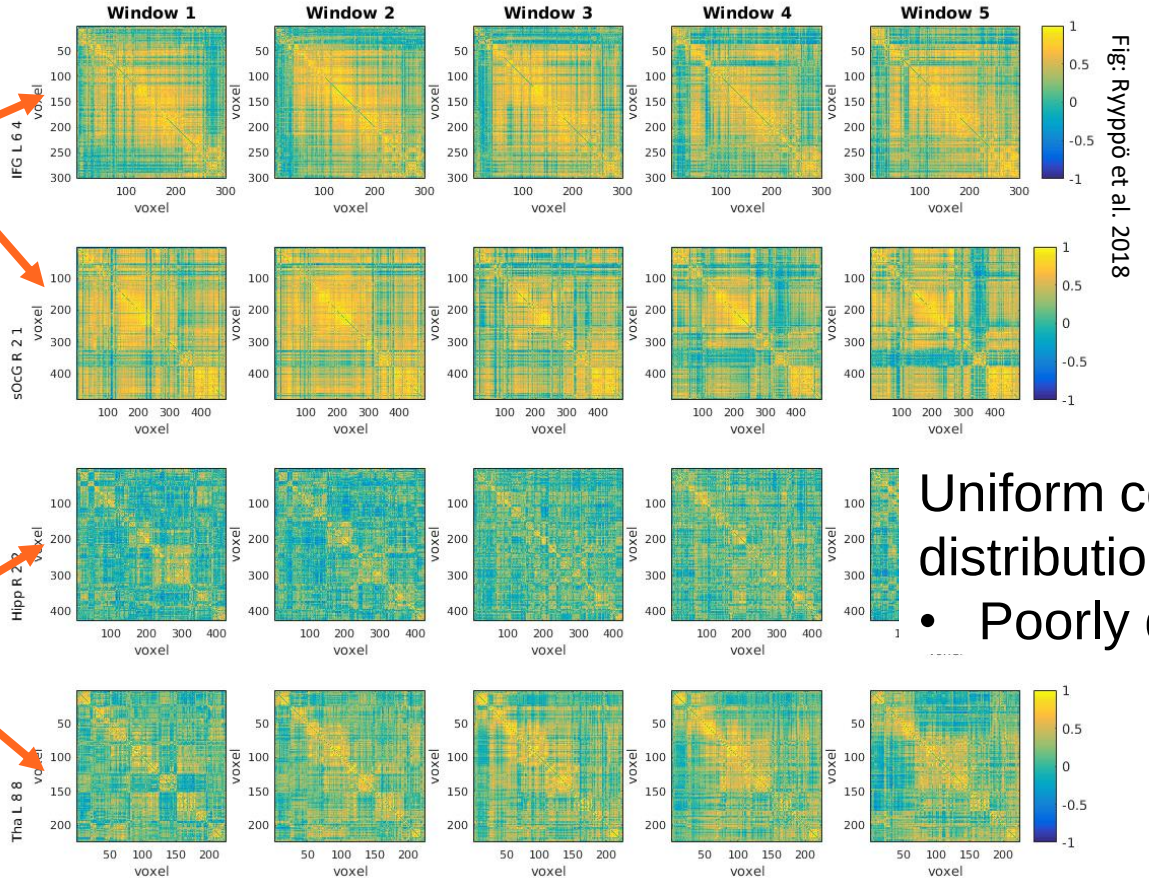


Fig: Ryyppö et al. 2018

Uniform correlation distribution

- Poorly defined ROI?

ROIs have rich internal connectivity structure

High spatial consistency

Low spatial consistency

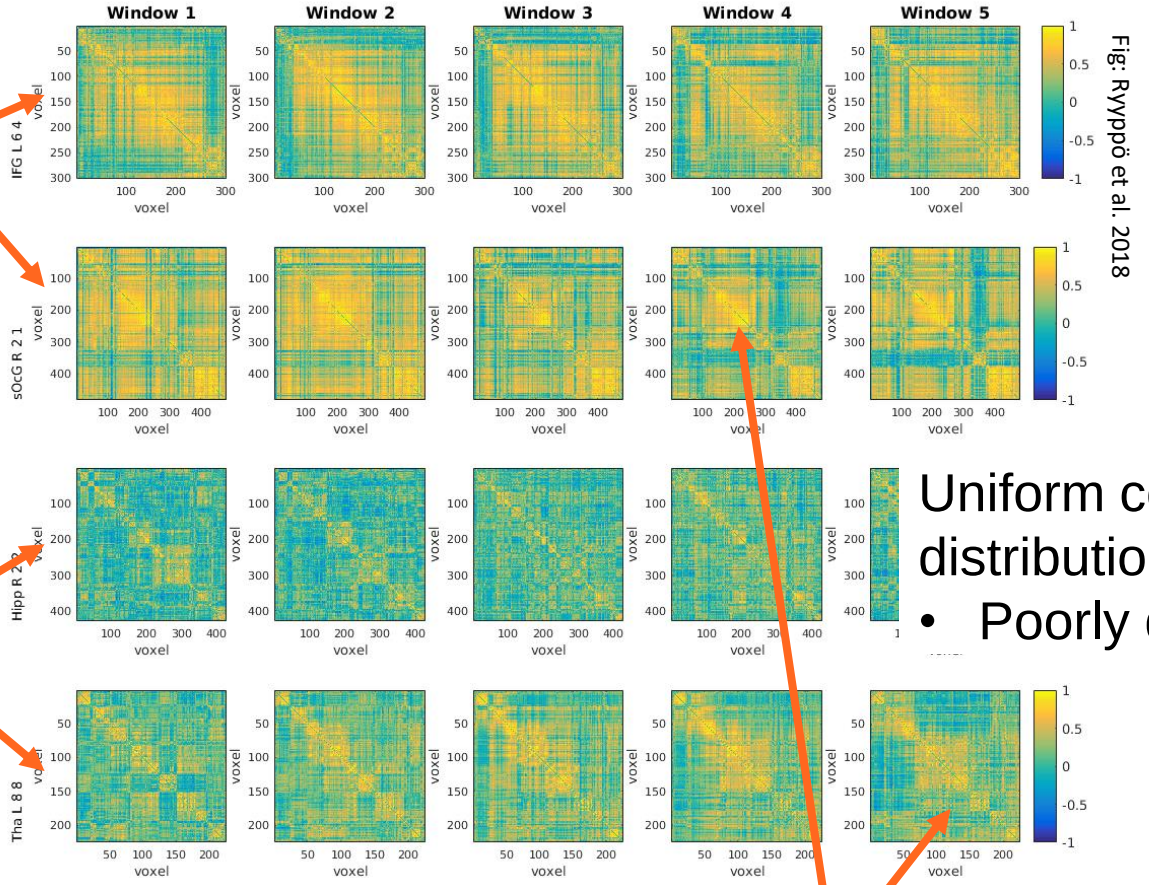


Fig: Ryyppö et al. 2018

Uniform correlation distribution

- Poorly defined ROI?

Intra-ROI modules

- Activation?
- Network topology?

ROIs have rich internal connectivity structure

High spatial consistency

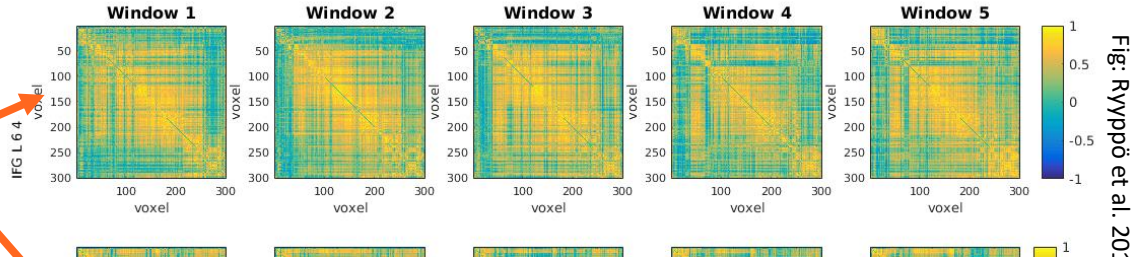
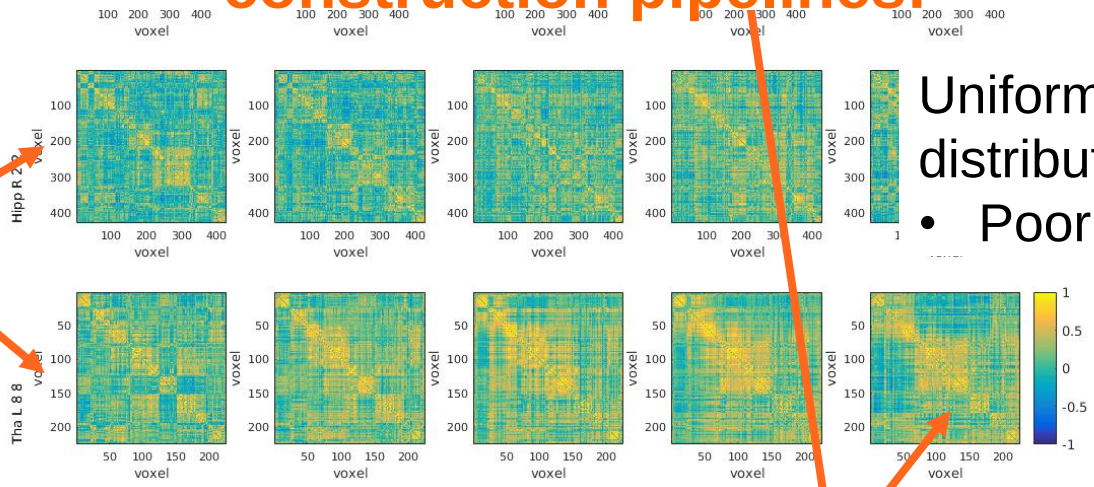


Fig: Ryyppö et al. 20

Ignored by (most) current network construction pipelines!

Low spatial consistency



Uniform correlation distribution

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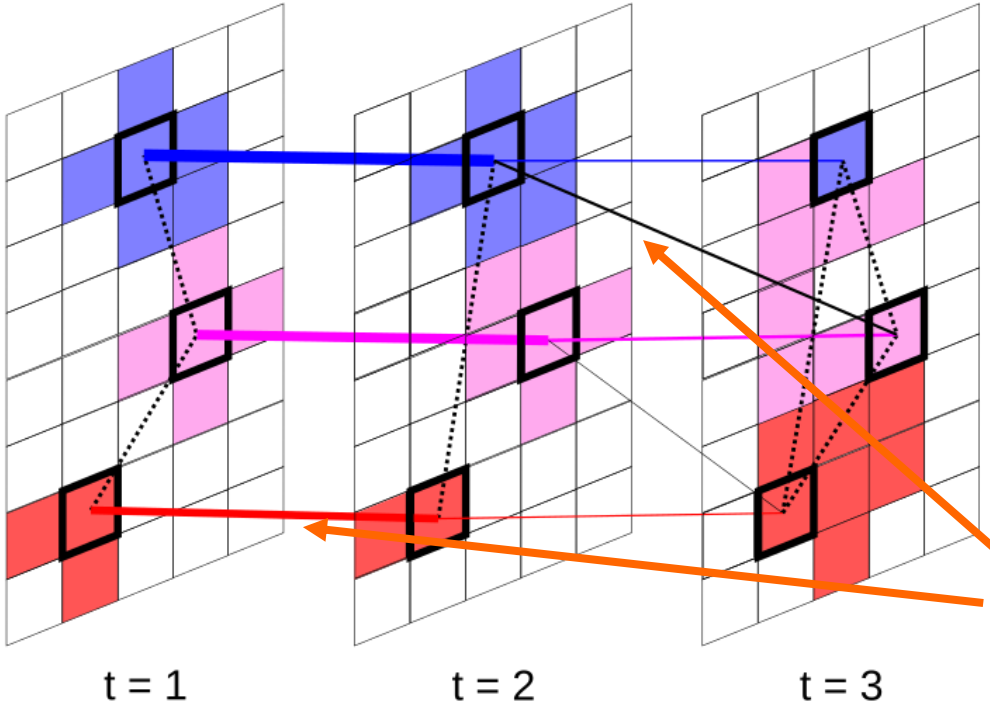
Intra-ROI modules

- Activation?
- Network topology?

Possible solution: time-dependent nodes

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

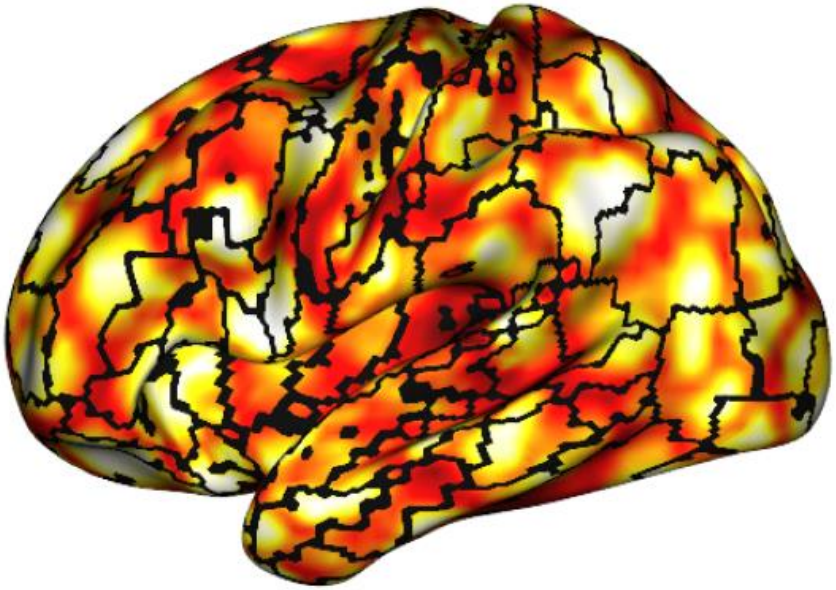
Based on multilayer networks (= different connections in the same network), for review: Kivelä et al. 2014



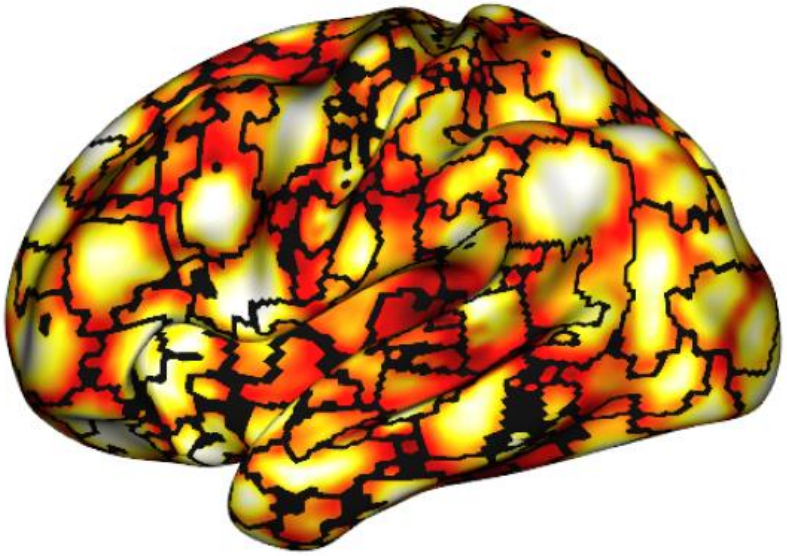
1. Layers = time windows
2. ROIs optimized inside layers for maximal homogeneity (voxel-level clustering)
3. Intralayer links = Pearson correlation
4. Interlayer links = spatial overlap

Possible solution: time-dependent nodes

- Simulated data: spherical ROIs, similarity to centroid decays Gaussially with distance
- Background: Regional Homogeneity (= average similarity to neighbours), white = higher similarity

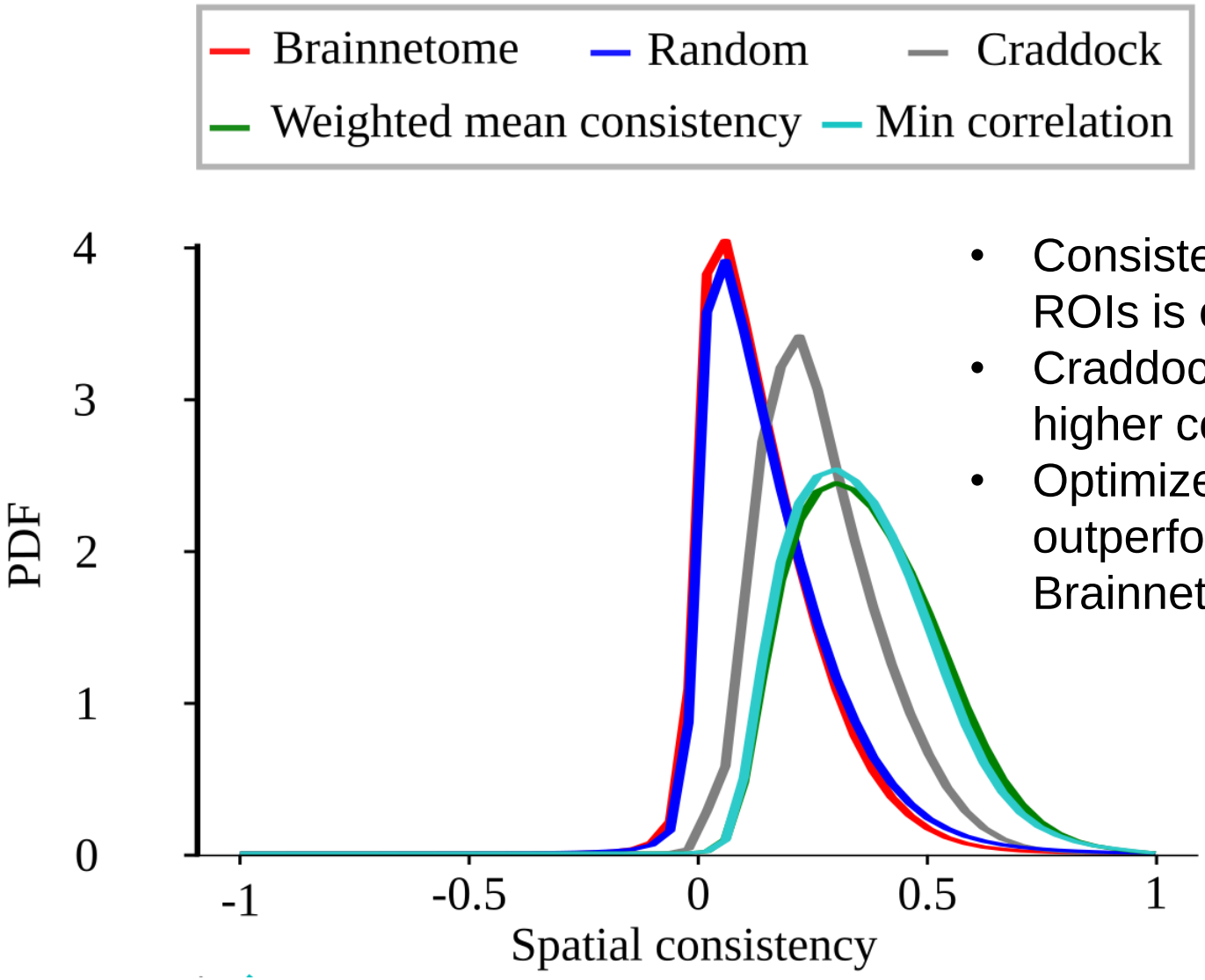


Brainnetome



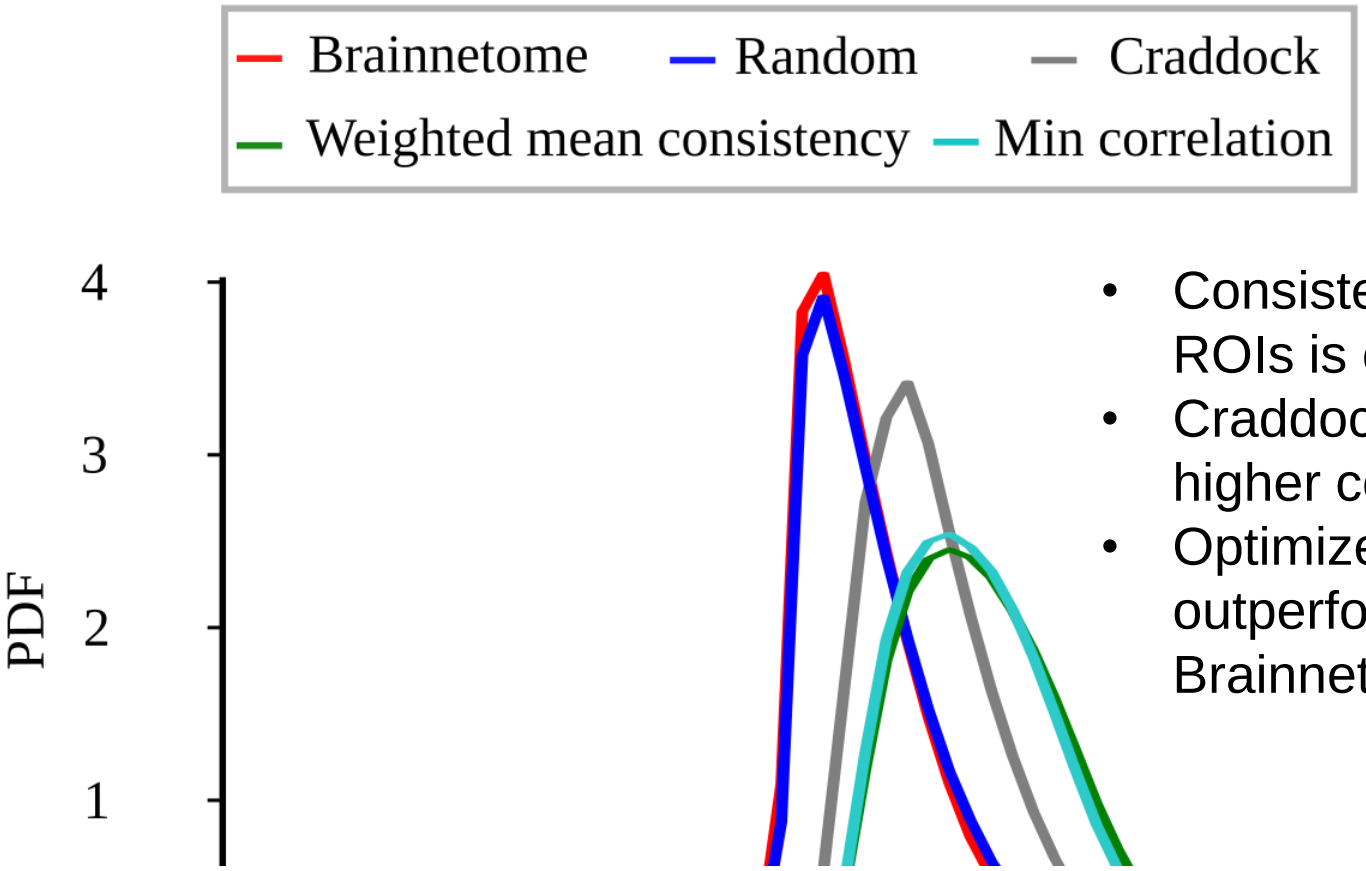
Optimized

Possible solution: time-dependent nodes



- Consistency of Brainnetome ROIs is close to random
- Craddock algorithm yields higher consistency
- Optimized approaches outperform both Brainnetome and Craddock

Possible solution: time-dependent nodes



- Consistency of Brainnetome ROIs is close to random
- Craddock algorithm yields higher consistency
- Optimized approaches outperform both Brainnetome and Craddock

Questions:

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

Conclusions

- Network theory helps to understand the (human) brain
- Not all that glitters is a network – is the (human) brain?
- Network construction is not trivial
  - Node definition?
  - Not covered today: preprocessing, link definition, thresholding?
  - ➢ **Know your methods!**
- Brain networks change in time
  - Traditionally, network dynamics are ignored
  - Including time opens new horizons
  - Example: time-dependent nodes

➢ **Needed: critical thinking & discussion**

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Thank you!

Questions, comments?

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Slides: github.com/onerva-korhonen/presentations/blob/master/brainnet_stockholm_130524.pdf