Connectomics and Graph Theory

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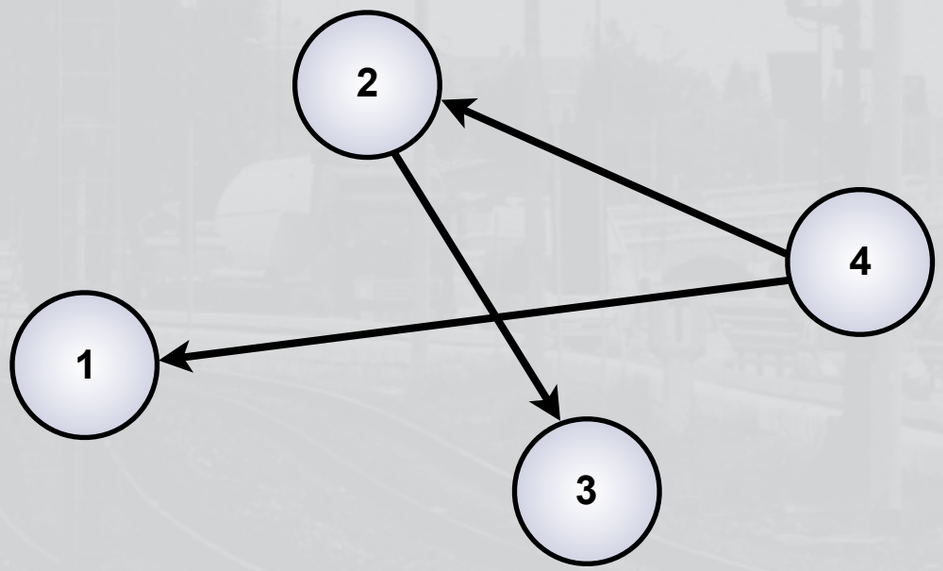
Photo by José Martín Ramírez Carrasco
https://www.behance.net/martini_rc

Overview

- What is a graph?
- Real problems as graph problems
- Graphs in neuroscience and neuroimaging
- Representing brain connectivity using graphs
- Advantages and limitations of this approach
- Robustness of *in vivo* connectomes
- The importance of subnetworks
- Combining information from multiple modalities
- Future work

Graphs

- A highly abstract representation of a set of vertices connected by edges
- Edges may be directed or undirected, and may have associated weights or costs
- A natural representation of connected systems
- Theoretically very well characterised
- Broad range of applications



The bridges of Königsberg

- Vertices are pieces of land; edges are bridges
- Can you walk around the town crossing every bridge once?
- Note: multiple links between two vertices make this a “multigraph”

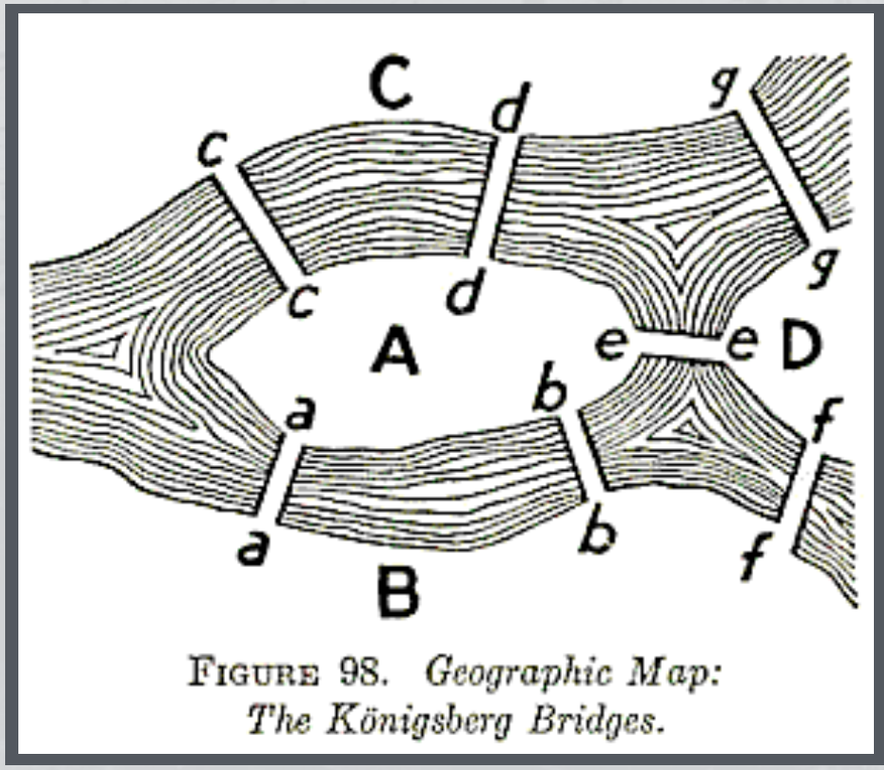
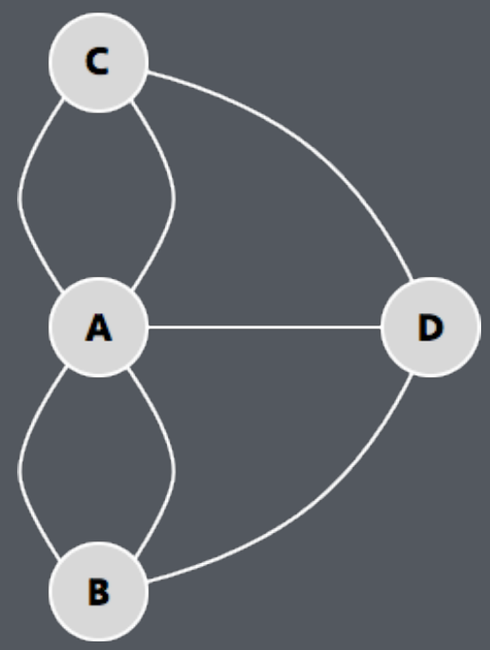


FIGURE 98. *Geographic Map: The Königsberg Bridges.*

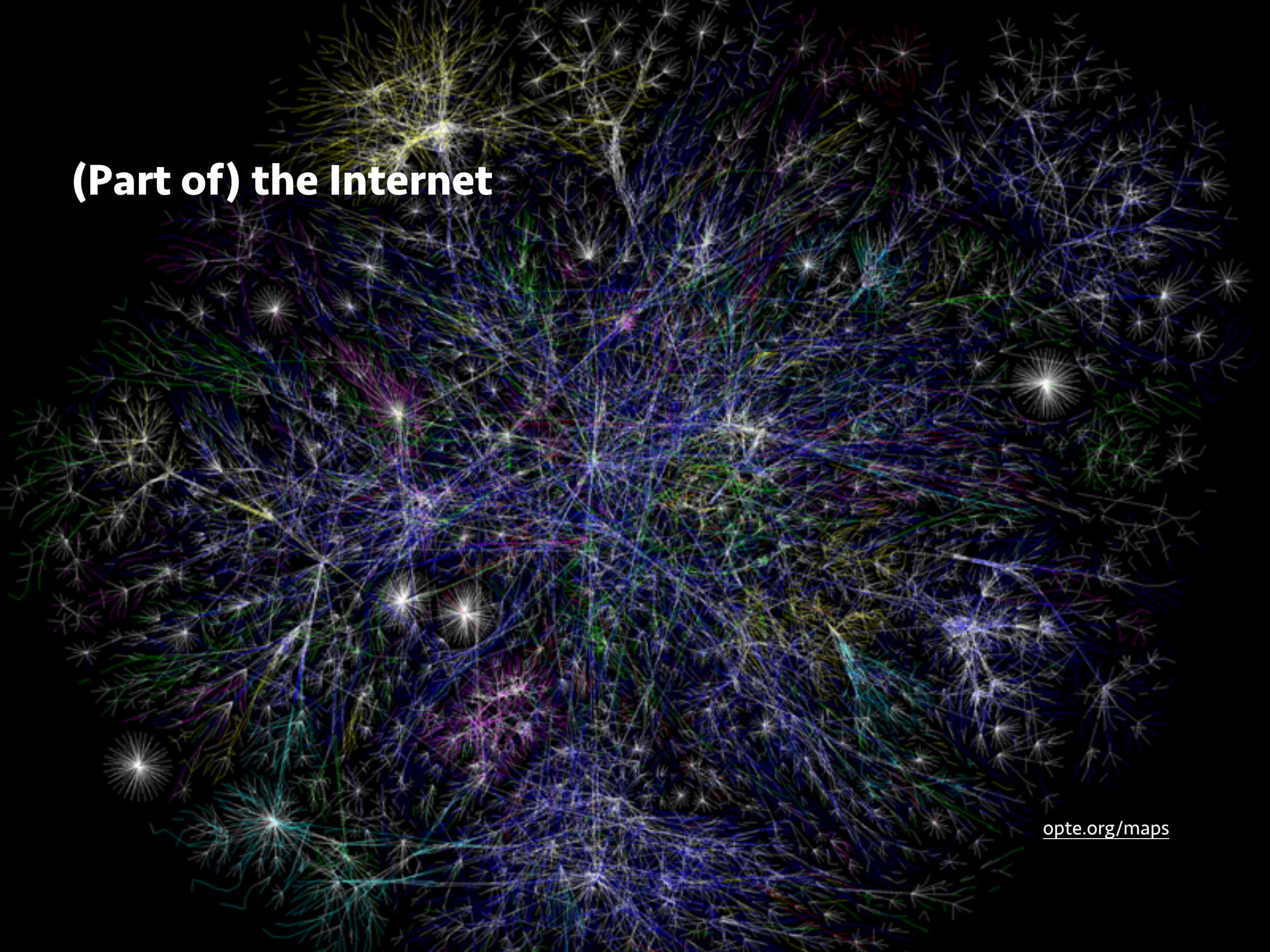


	A	B	C	D
A		2	2	1
B	2			1
C	2			1
D	1	1	1	

A more modern graph problem

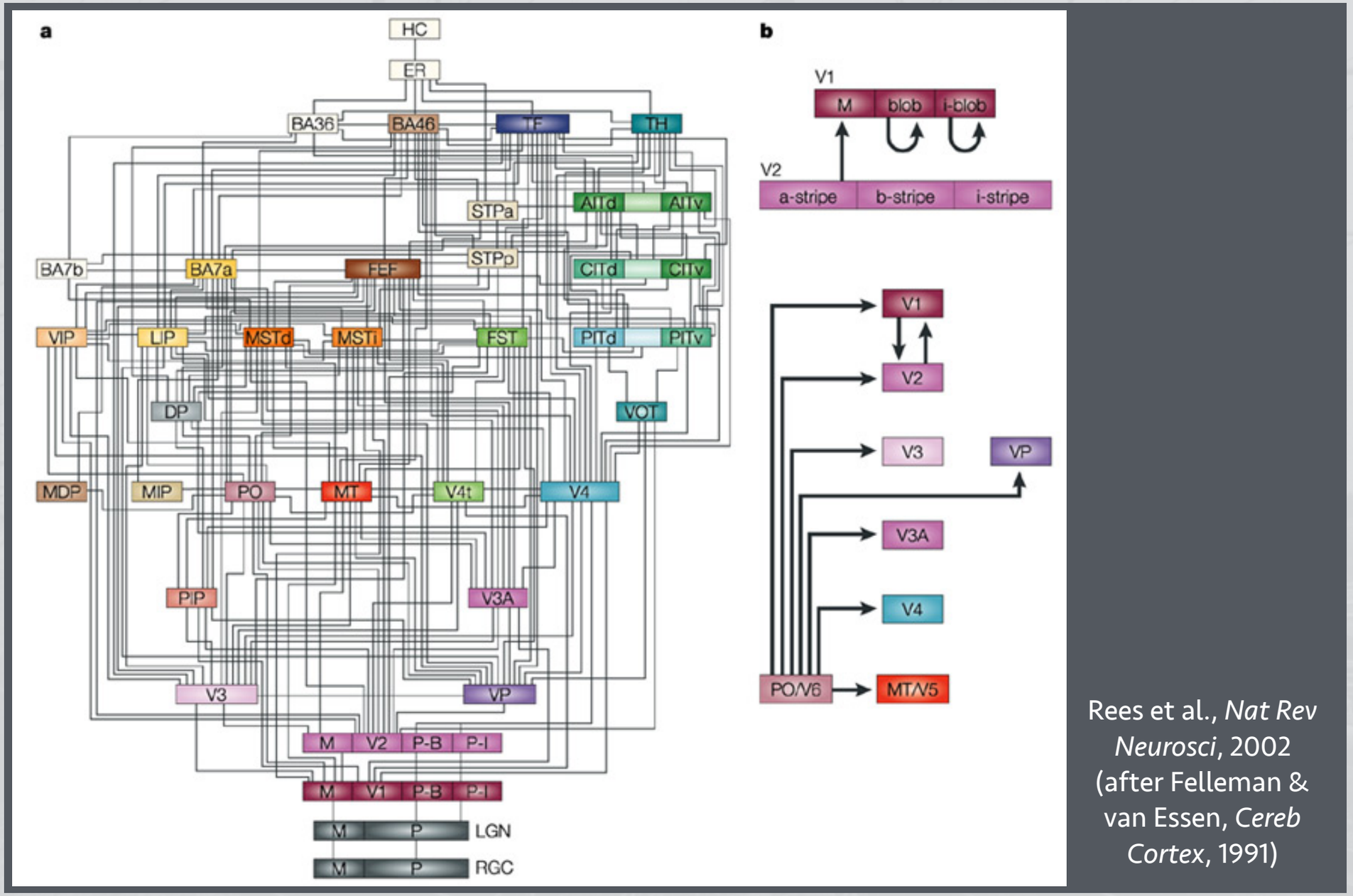
- Travel times as edge costs

(Part of) the Internet



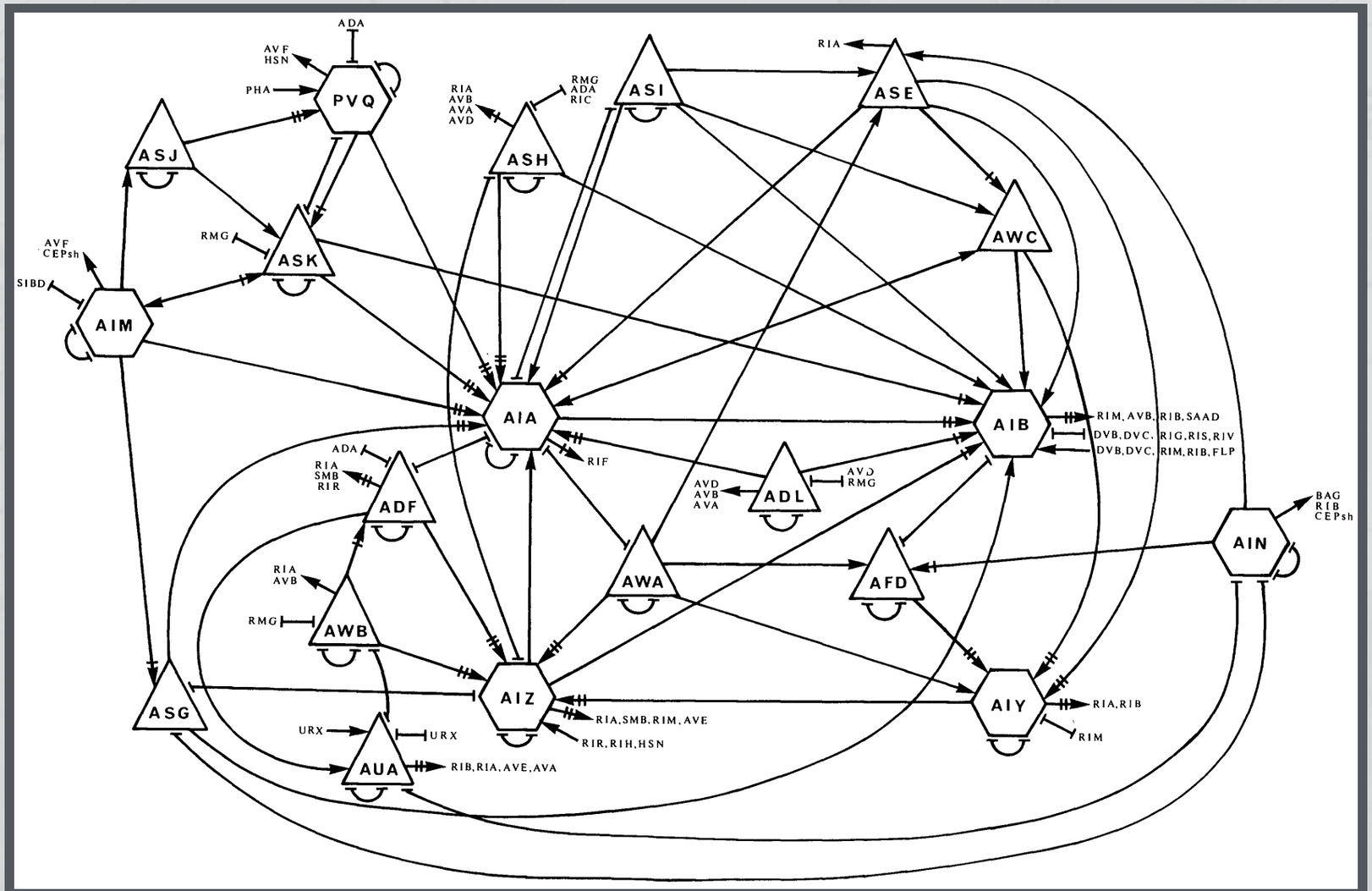
opte.org/maps

Connectivity and the brain



Rees et al., *Nat Rev Neurosci*, 2002 (after Felleman & van Essen, *Cereb Cortex*, 1991)

The “connectome”



White et al., *Philos Trans Roy Soc B*, 1986

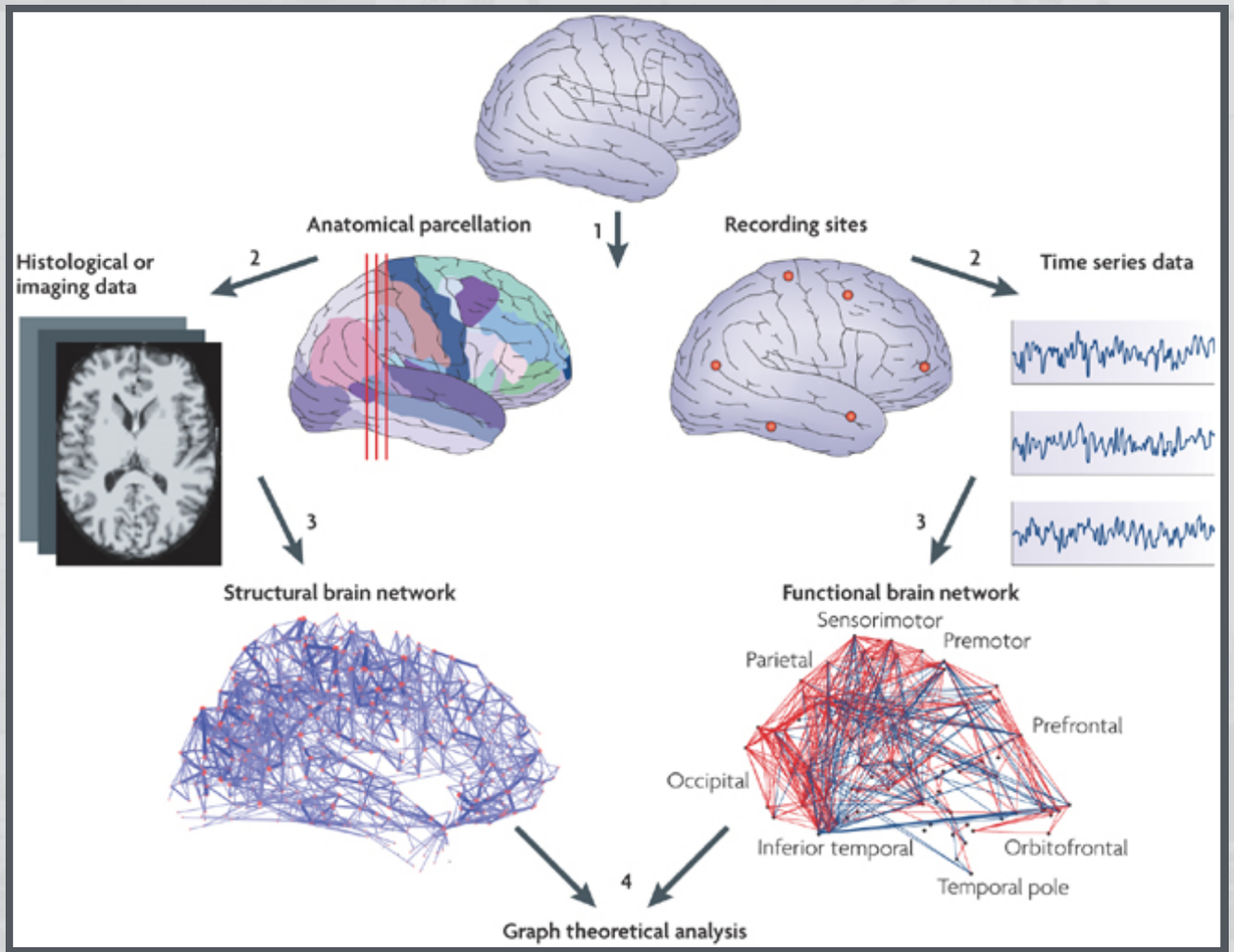
- Circuitry of the nematode nervous system is fully mapped out

Connection and disconnection

- Development of the brain's connectivity continues for years after birth
- Differences in connectivity patterns may underlie some of the variability in intelligence and cognitive information processing
- Disconnection between brain regions thought to be a key factor in age-related cognitive decline
- Many neurological diseases are also thought to be associated with loss of connectivity (disconnection syndromes)
- Preserving connectivity is extremely important to ensure an optimal outcome after brain surgery
- Neuroimaging offers the chance to study connectivity *in vivo*
- Information can come from structural or functional MRI, EEG, MEG, etc.

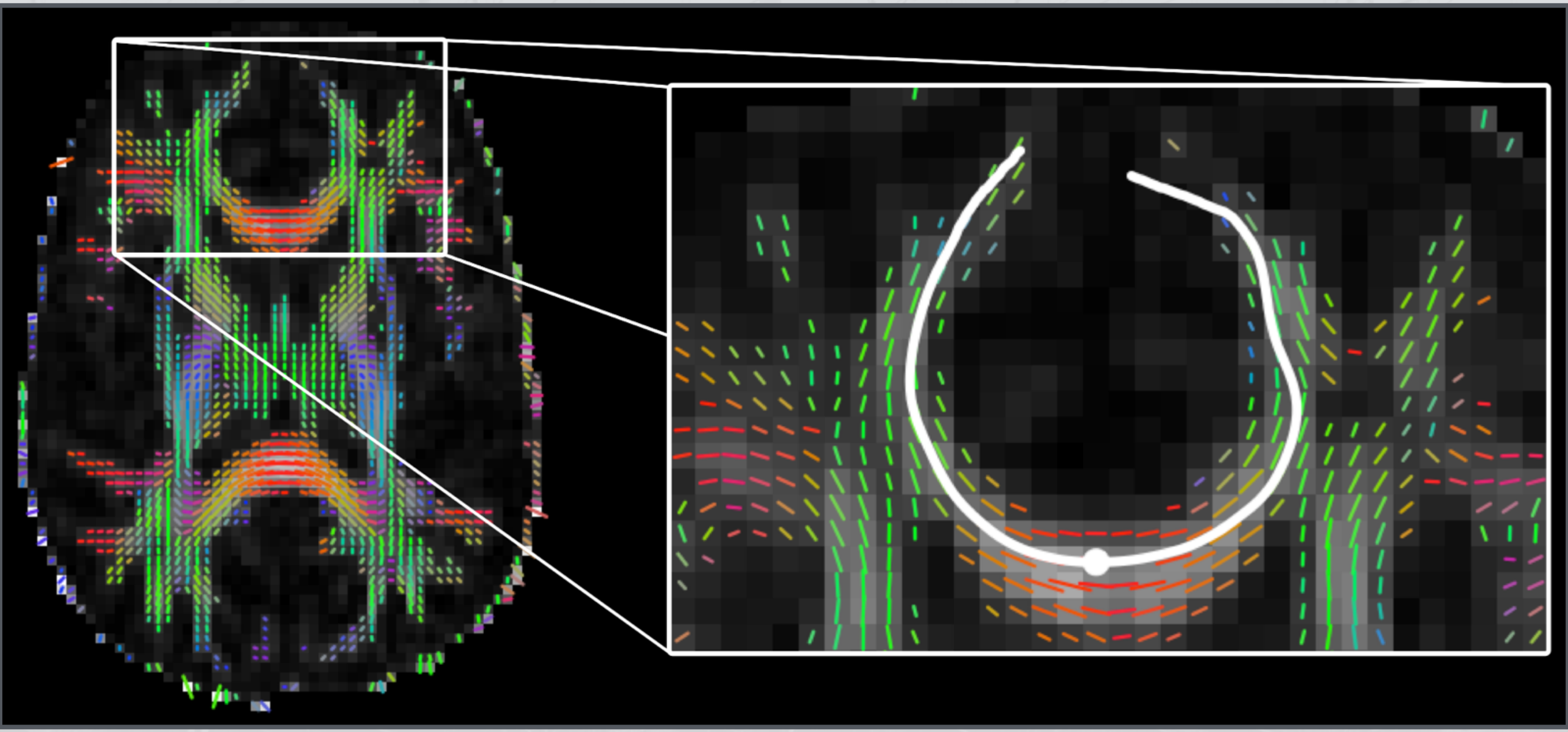
Definitions of connectivity

- **Structural connectivity**: the physical axon bundles connecting brain regions together
- **Functional connectivity**: associations between neural activity in spatially remote regions of grey matter
- **Effective connectivity**: patterns of influence by some neural systems over others

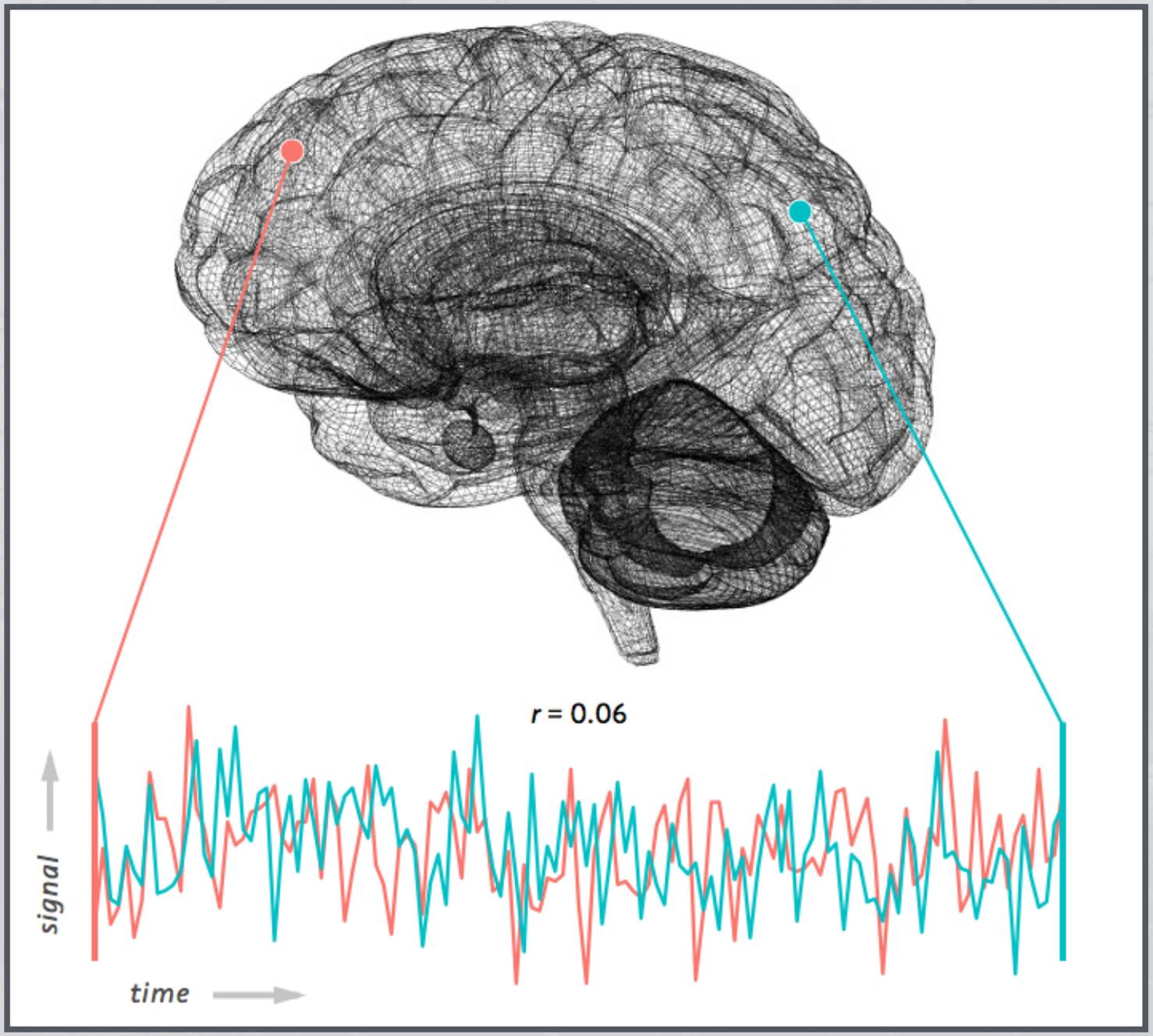


Bullmore & Sporns, *Nat Rev Neurosci*, 2009

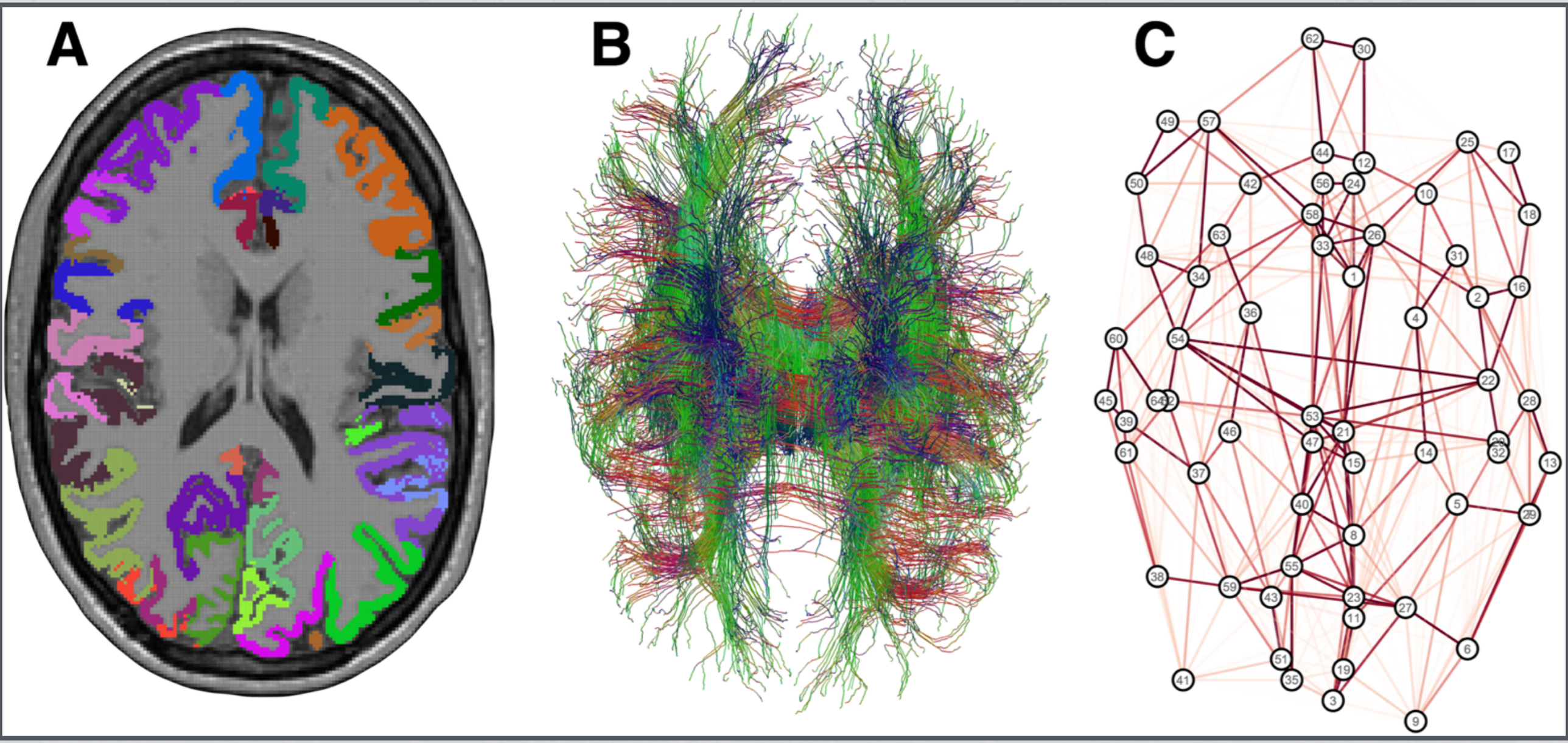
Structural connectivity: tractography



Functional connectivity: correlated time-courses



In vivo connectomics



Graph characteristics

- A range of measures have been developed in graph theory to describe characteristics of graphs and their vertices
- Connection density: the proportion of all possible edges which are present in the graph (cost)
- Average path length: the mean shortest path length between pairs of vertices (efficiency)
- Betweenness centrality: the number of shortest paths between other vertices which pass through a particular vertex (hubs)

Clinical and cognitive relationships

- Epilepsy patients show increased path lengths in cortical thickness networks (Bernhardt et al., *Cereb Cortex*, 2011)
- Changes to hubs and clustering properties of networks based on grey matter volume in patients with schizophrenia (Bassett et al., *J Neurosci*, 2008)
- Path length in functional networks related to intelligence (Langer et al., *Hum Brain Mapp*, 2011)
- Tractography-based structural network efficiency related to cognitive abilities in old age (Wen et al., *J Neurosci*, 2011)

Scope and limitations

- A graph can be created using any measure of association between brain regions of interest…
- … but an association does not necessarily correspond to a direct connection
- Establishing direction of connections is challenging
- Abstract nature of graph makes systematic errors in underlying data invisible
- All the caveats of any preprocessing steps apply
- Choice of regions to use as vertices matters (cf. Zalesky et al., *NeuroImage*, 2010), but is usually arbitrary
- Substantial methodological variation in the literature

Some questions

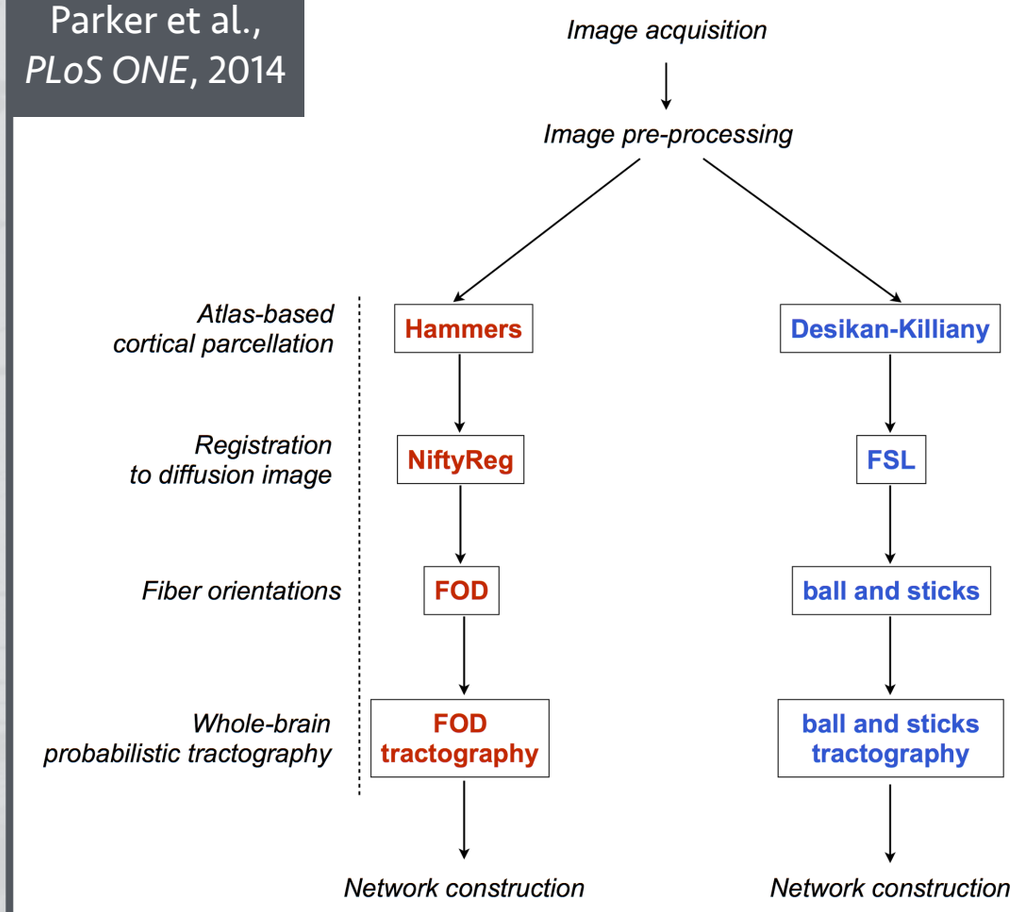
- How robust are reconstructed connectomes?
- How can one identify important subnetworks without strong prior expectations?
- To what extent does structure predict function?
- How should one combine information from different modalities?

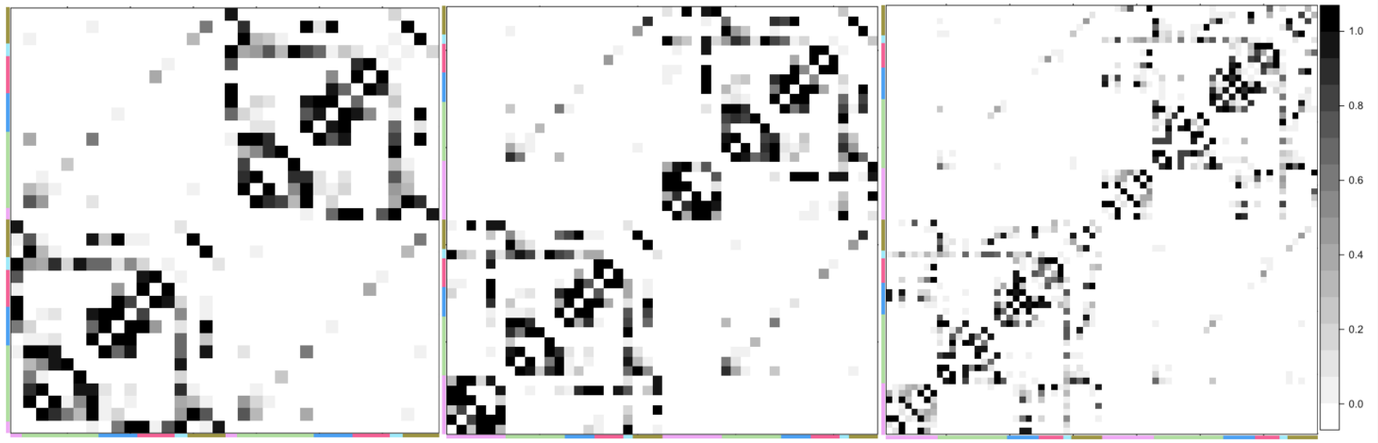
Robustness

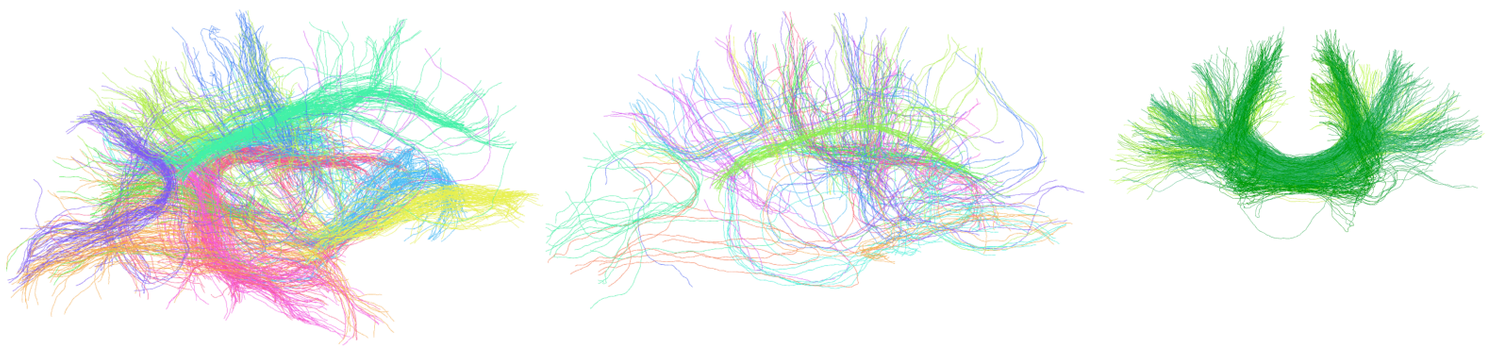
- There is little consistency in the processes used to reconstruct connectomes
- Different pipelines may result in different results and therefore conclusions
- We need confidence in the robustness of the result if we want to make reliable scientific inferences

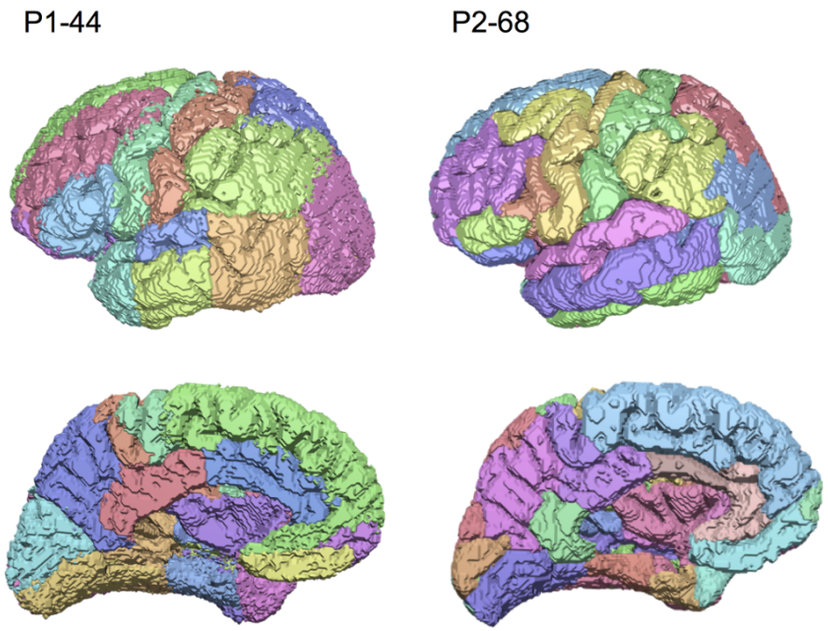
Robust connections across data processing pipelines

Parker et al., *PLoS ONE*, 2014



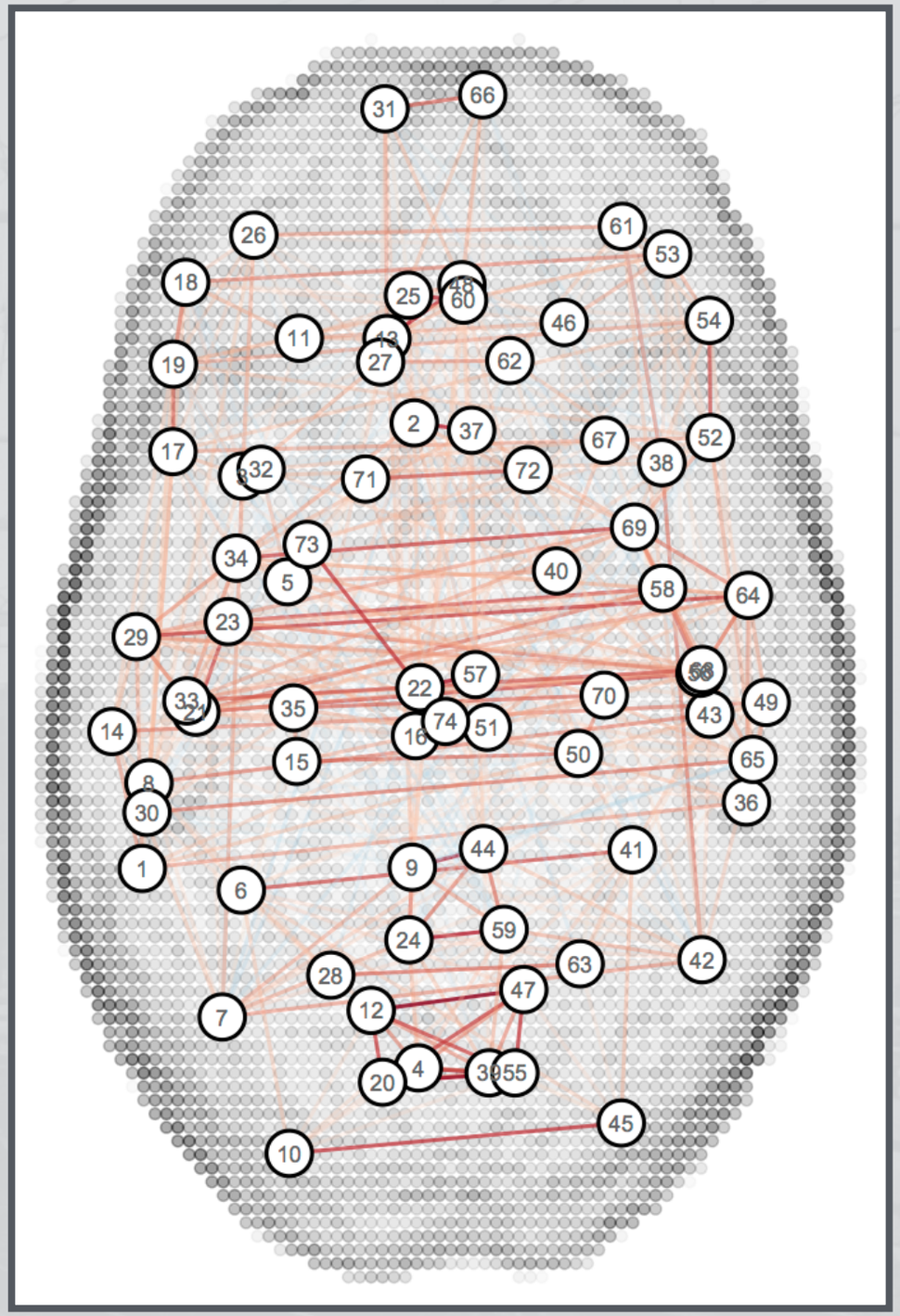




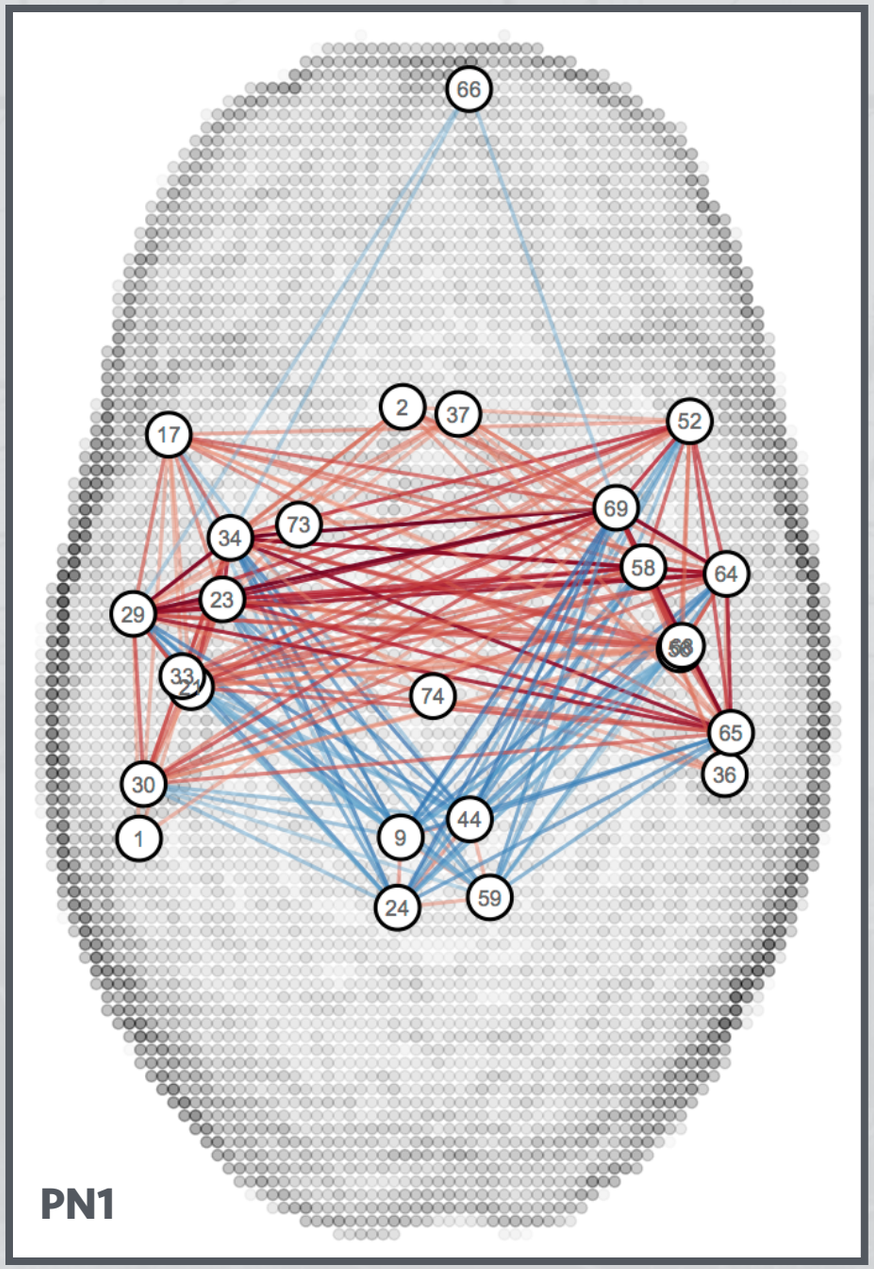


The whole connectome?

- Connectome-level analysis is now becoming common
- Graph theory can be used to describe network topology
- But it is reasonable to assume that the whole network is not involved in any given task
- Therefore development and disease processes may not show up as global topology changes
- Strategy: partition or decompose network into interesting subnetworks



Principal networks



PN1

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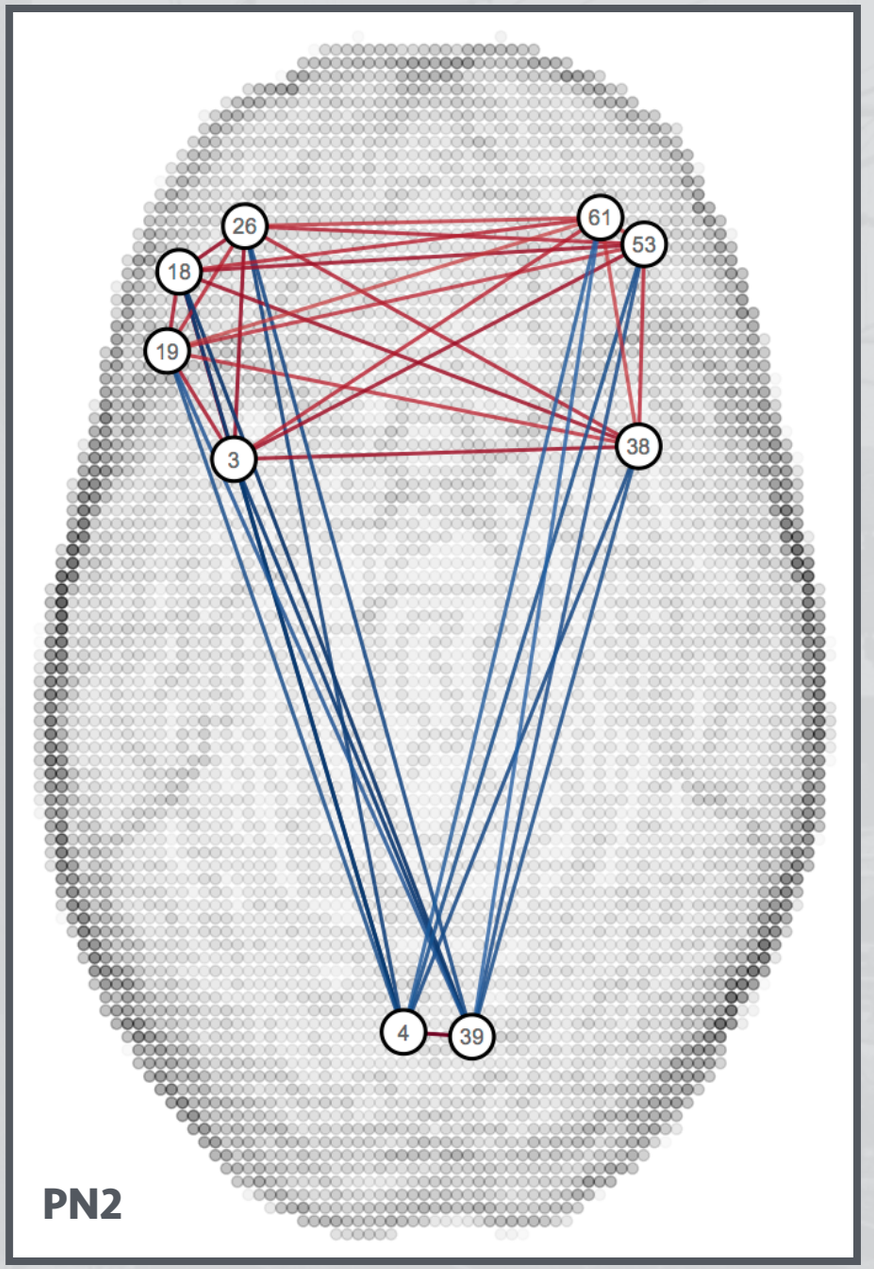

PN2

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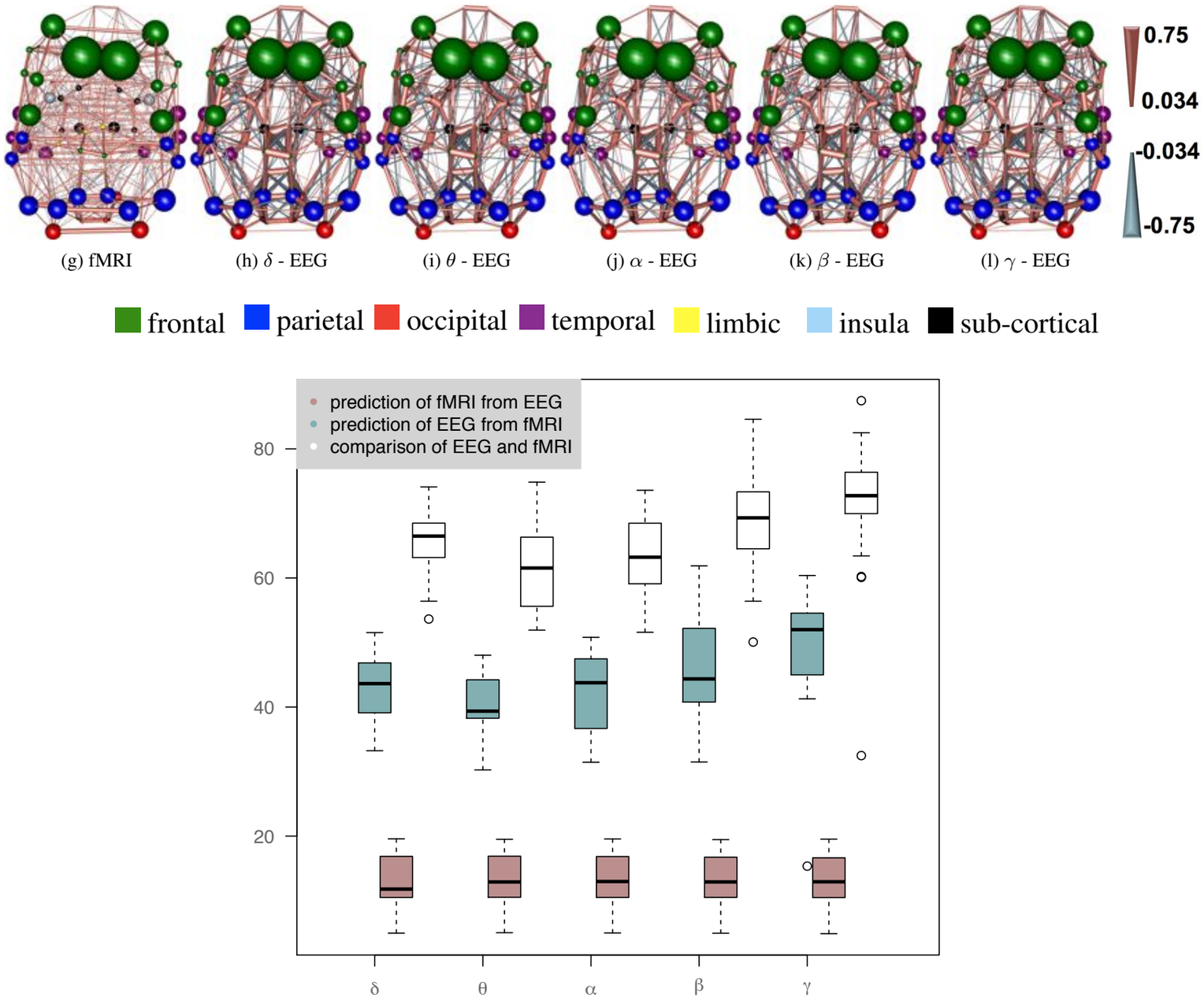
cf. Clayden et al., *PLoS ONE*, 2013

Between-modality prediction

- Given a connectome from one modality, can we predict another?
- Are some measures of connectivity better than others for this purpose?
- What information is most useful for the prediction?

Inter-modal functional connectivity



Deligianni et al., *Front Neurosci*, 2014

Structural vs functional

- Structural and functional connectivity are conceptually different…
- … but are underpinned by the same systems
- There should be substantial commonality
- Graph approaches allow the two to be represented similarly…
- … but patterns of connectivity often differ in important ways
- Functional connectivity is often found to be more variable than structural connectivity
- Combining the two effectively remains an elusive goal for now

Areas of current and future interest

- Joint modelling of structural and functional connectivity
- Characterisation of population variability in connectivity patterns
- Integration of prior knowledge into connectome analysis
- Specialisation of image analysis approaches for sensitivity in particular diseases
- One-versus-many approaches for identifying abnormalities in individual patients

Thanks

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