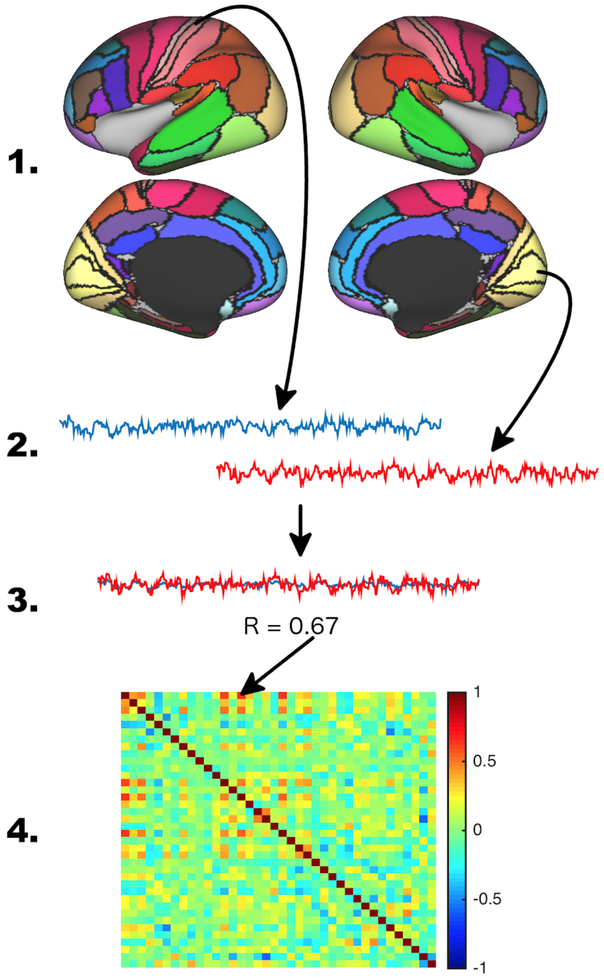
Network modeling analysis

- Resting state preprocessing
- Node definition and edge calculation
- Group analysis and challenges
- Comparison of resting state methods

Node-based methods



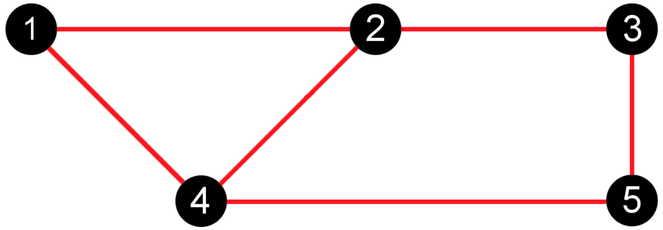
Node definition

Timeseries extraction

Edge calculation

Network matrix

Group analysis



Bijsterbosch et al (2017)

Node definition

Node nomenclature

Node = fundamental processing unit

Parcel = node derived from a brain parcellation

Region of interest (ROI) = node in different contexts (seed-based correlation/ task analysis)

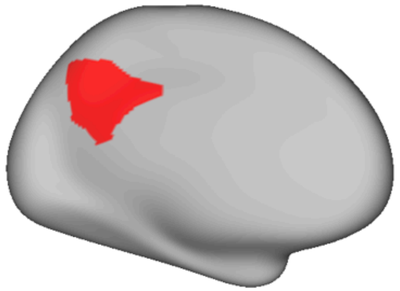
Cortical Area = region of cortex distinct from neighboring cortex in function, cytoarchitecture, connectivity, or topographic organization

Network = collection of things

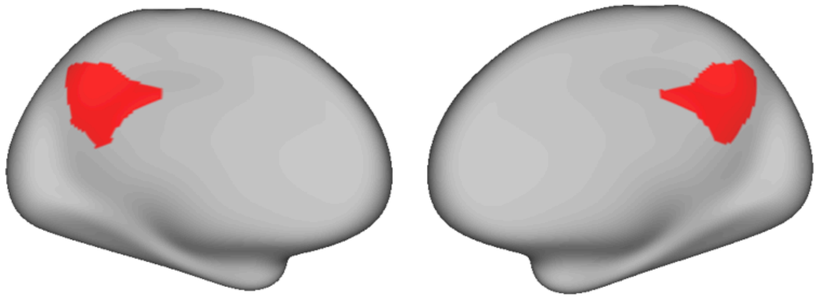
1. All nodes and edges of the brain ("network neuroscience")
2. A subset of inter-connected nodes (modules)
3. Macroscale systems of the brain (resting state networks; RSNs)

Eickhoff et al (2018)

Node characteristics



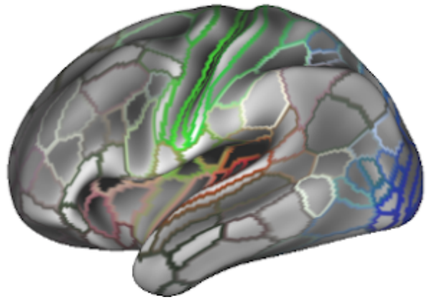
Contiguous = intuitive and consistent with cortical areas



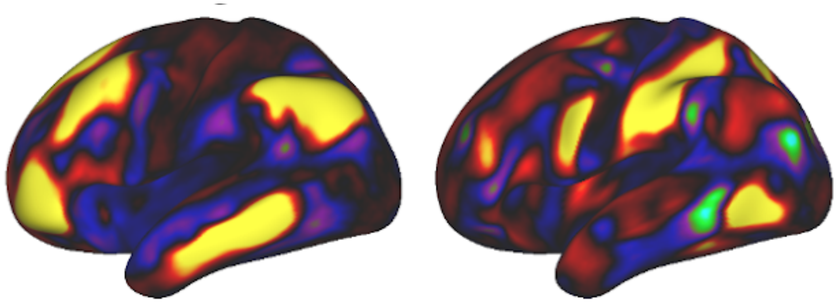
Non-contiguous = fits with hemispherical symmetry and hierarchical structure

Bijsterbosch et al (2017)

Node characteristics



Binary (hard parcellation) = intuitive for graph representations and interpretation



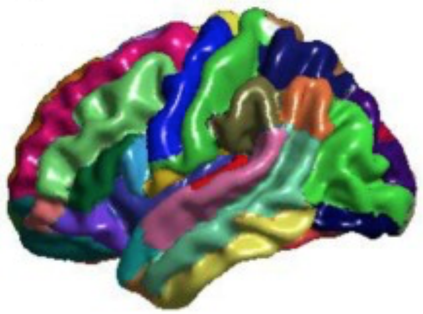
Weighted (soft parcellation) = fits with complex brain organization and allows for measurement error and physiological limits (HRF)

Bijsterbosch et al (2017), Glasser et al (2016)

Node definition

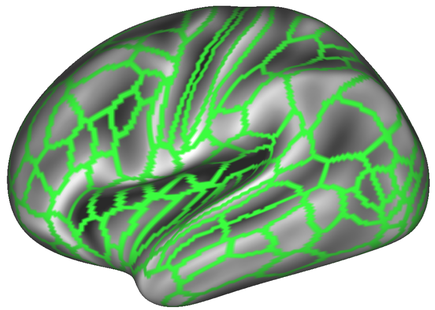
Anatomical atlases

- Harvard-Oxford/ AAL
- Avoid if possible because typically based on small number of subjects and not a good estimation of functional boundaries



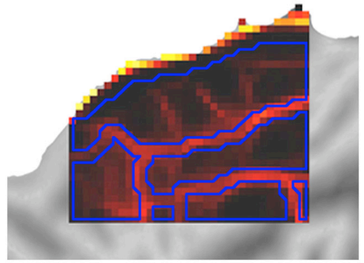
Functional atlases

- Yeo 2011/ Glasser 2016
- Many good functional atlases available, though few comparison studies
- How to map onto individuals is very important



Data-driven parcellation

- ICA/ Clustering/ Gradients
- Estimate parcellation from the same dataset used for further analyses
- How to map group parcellation onto individuals very important

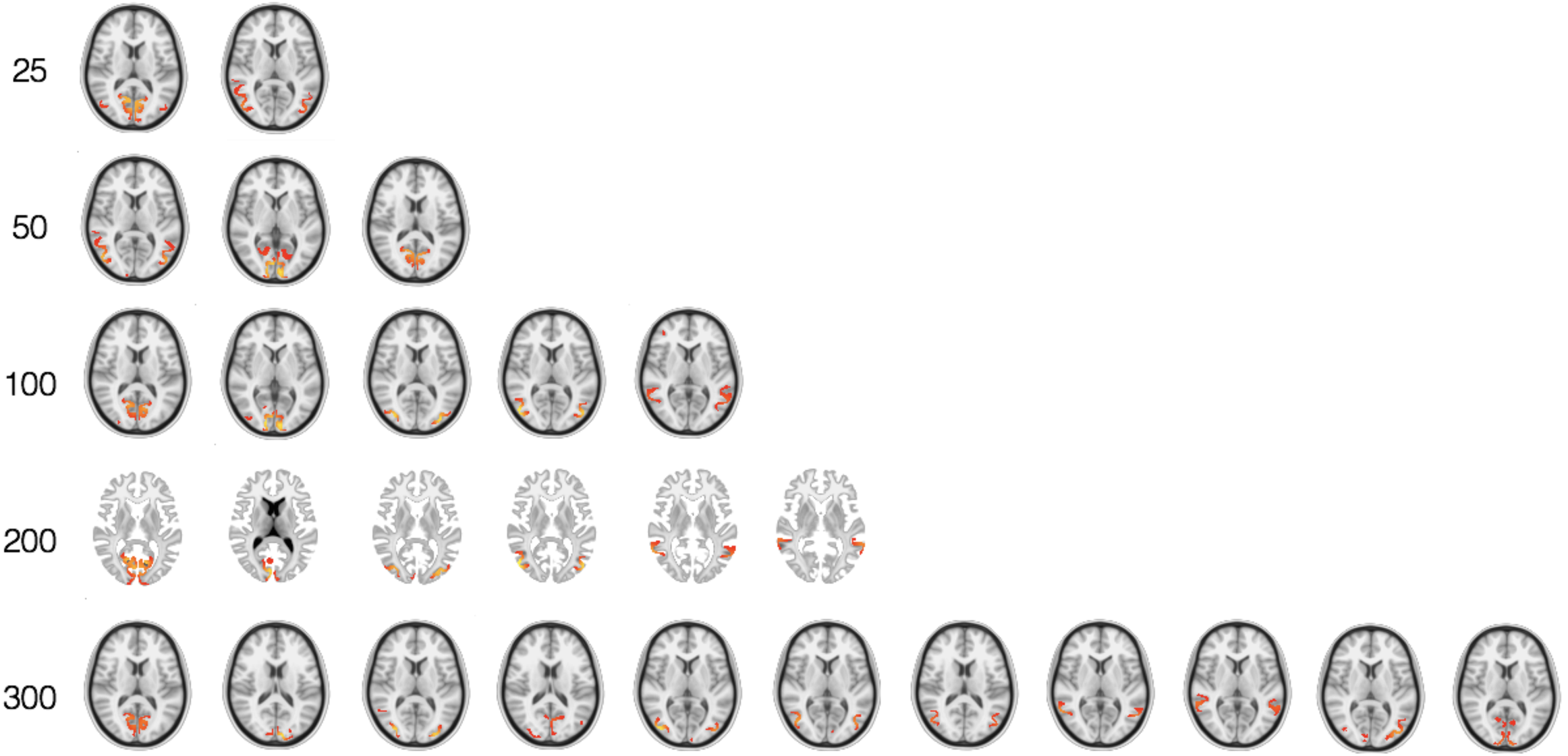


Tzourio-Mazoyer et al (2002), *Yeo et al (2011)*, *Glasser et al (2016)*, *Cohen et al (2008)*

Your own versus literature

Functional atlas	Data-driven paracellation
Many good quality atlases available in literature	Use your own data to estimate your nodes
Easy to interpret and relate to other findings	Interpretation and comparison to the literature can be hard
May not be optimally matched your (patient) data	Best representation of the organization in your data

ICA for parcellation



Timeseries extraction

Hard parcellation:

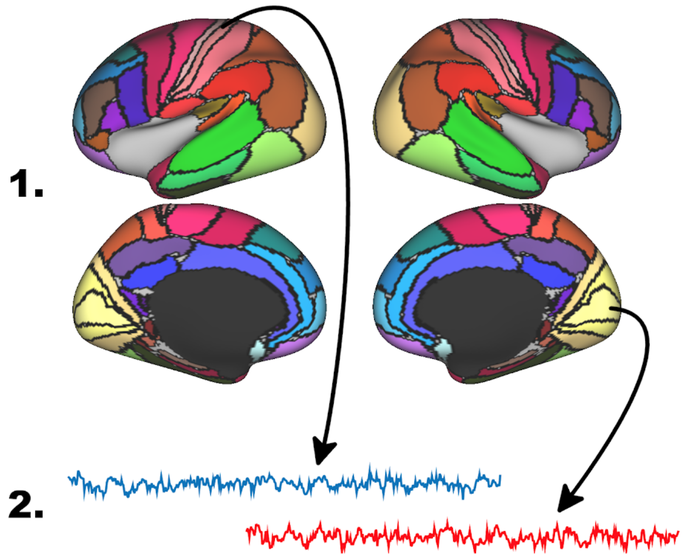
- Masking (mean timeseries)
- Eigen timeseries (PCA)
- Using multilayer classifier

ICA (soft parcellation):

- Dual regression/ back projection

Alternative:

- Hierarchical estimation of group & subject
- e.g. PROFUMO

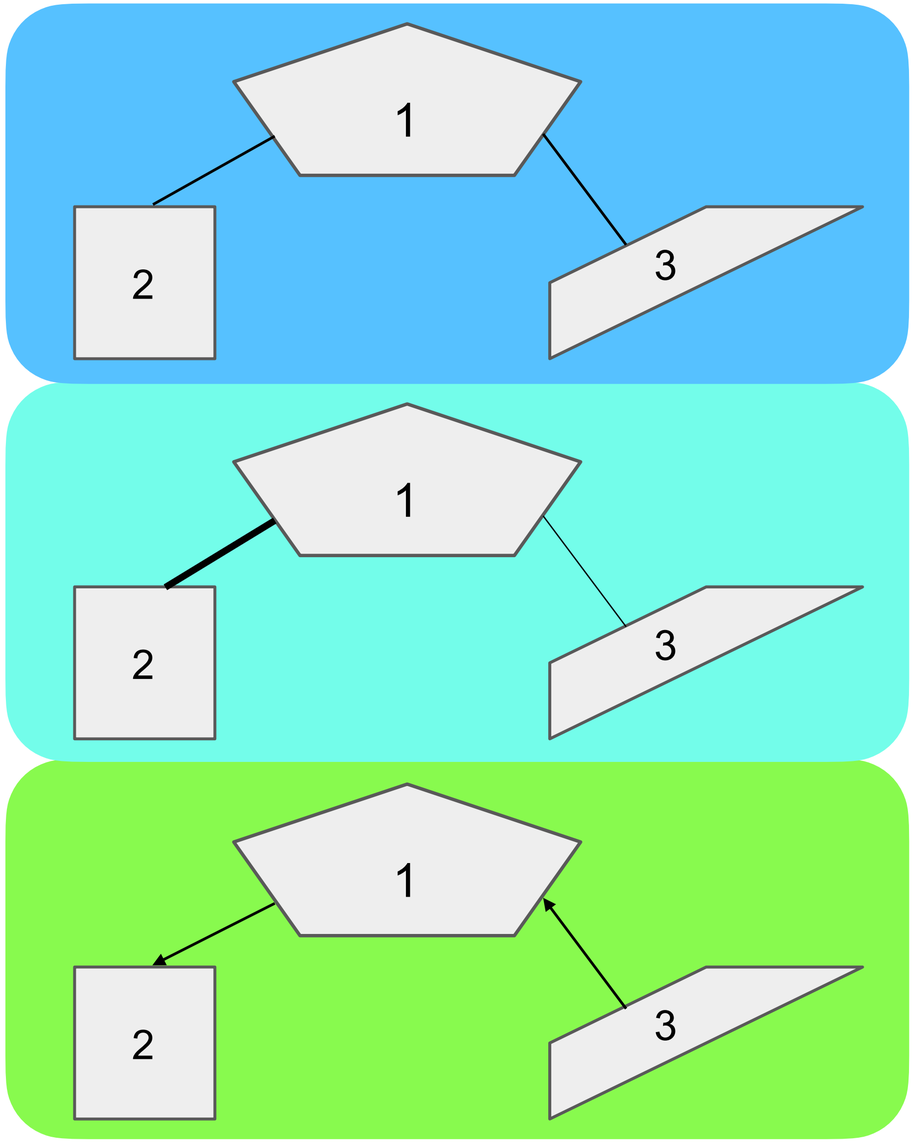


Hacker et al (2013), Nickerson et al (2017), Calhoun et al (2001), Harrison et al (2020), Bijsterbosch et al (2017)

Edge estimation

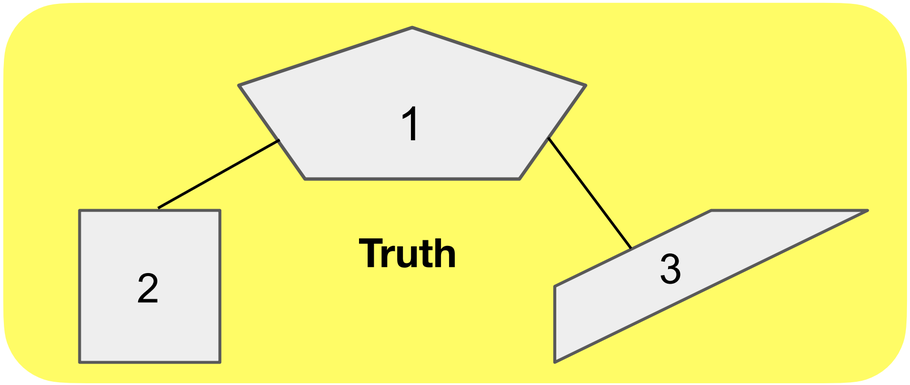
Edge calculation

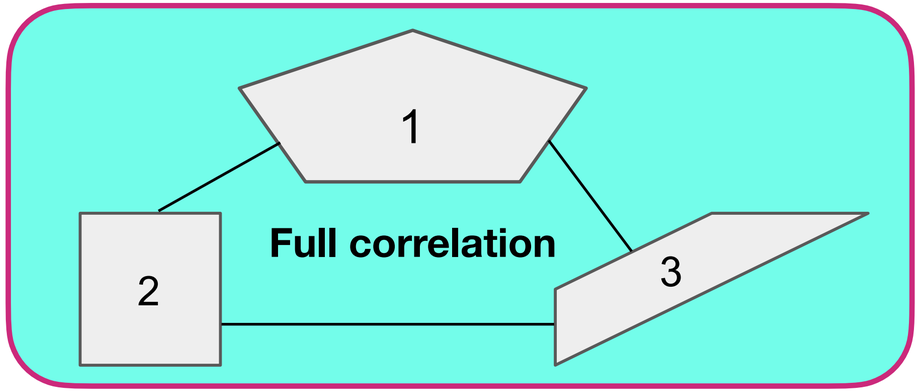
- Presence/ absence of edges
- Strength of edges
- Directionality of edges



Direct versus indirect connections

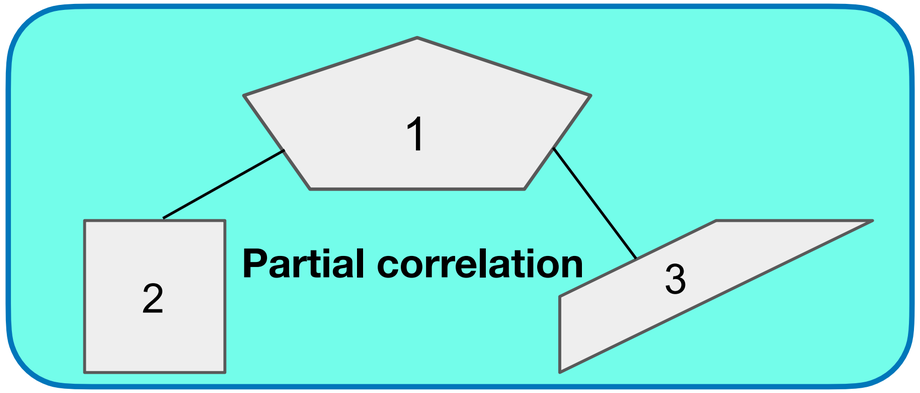
- Correlation between 2 and 3 will exist
- Therefore full correlation will incorrectly estimate connection 2-3
- 2-3 is an indirect connection

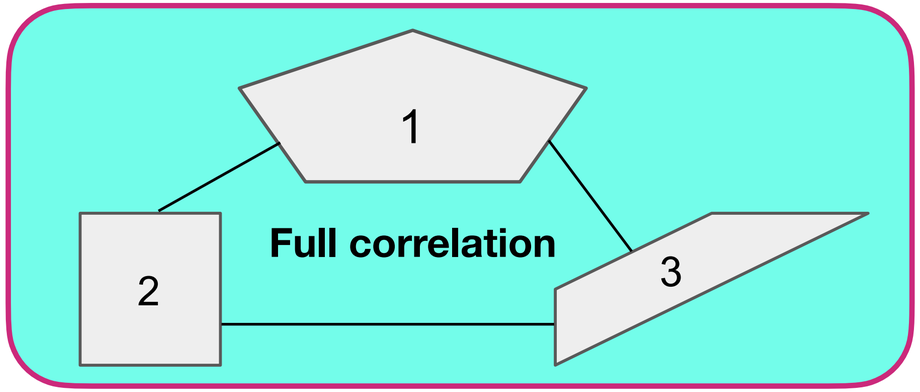




Partial correlation

- Before correlating 2 and 3, first regress 1 out of both (“orthogonalise wrt 1”)
  - If 2 and 3 are still correlated, a direct connection exists
- More generally, first regress all other nodes’ timecourses out of the pair in question
  - Equivalent to the inverse covariance matrix

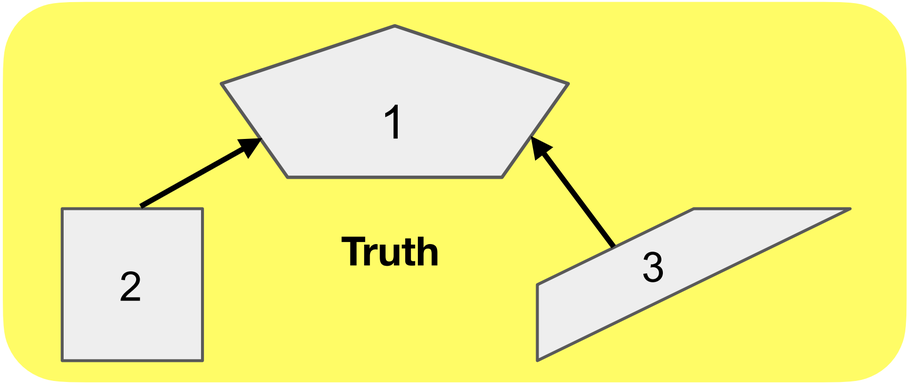


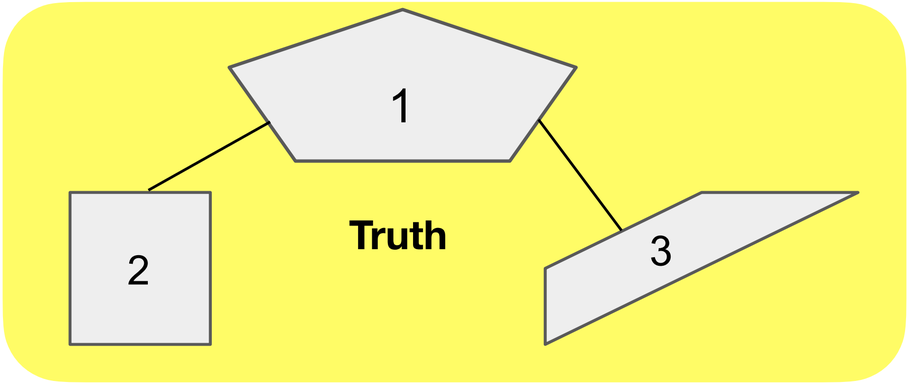


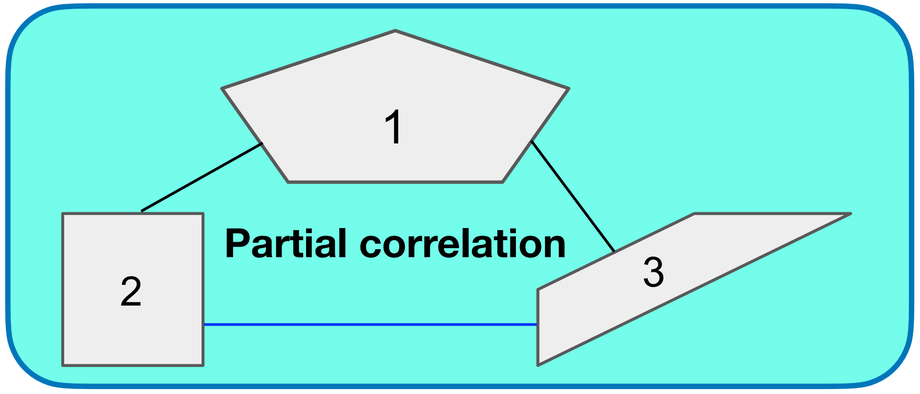
Regularisation

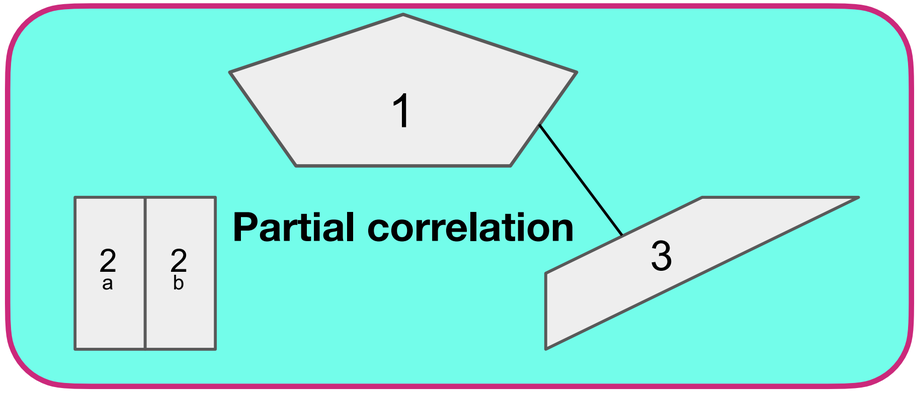
- Urgh! If you have 200 nodes and 100 timepoints, this is impossible!
- A problem of DoF - need large #timepoints - #nodes
- When inverting a “rank-deficient” matrix it is common to aid this with some mathematical conditioning, e.g. force it to be sparse (force low values that are poorly estimated to zero)
- Regularised partial correlation (such as ICOV, Ridge)
- But still important to maximise temporal degrees of freedom

Need to carefully define nodes







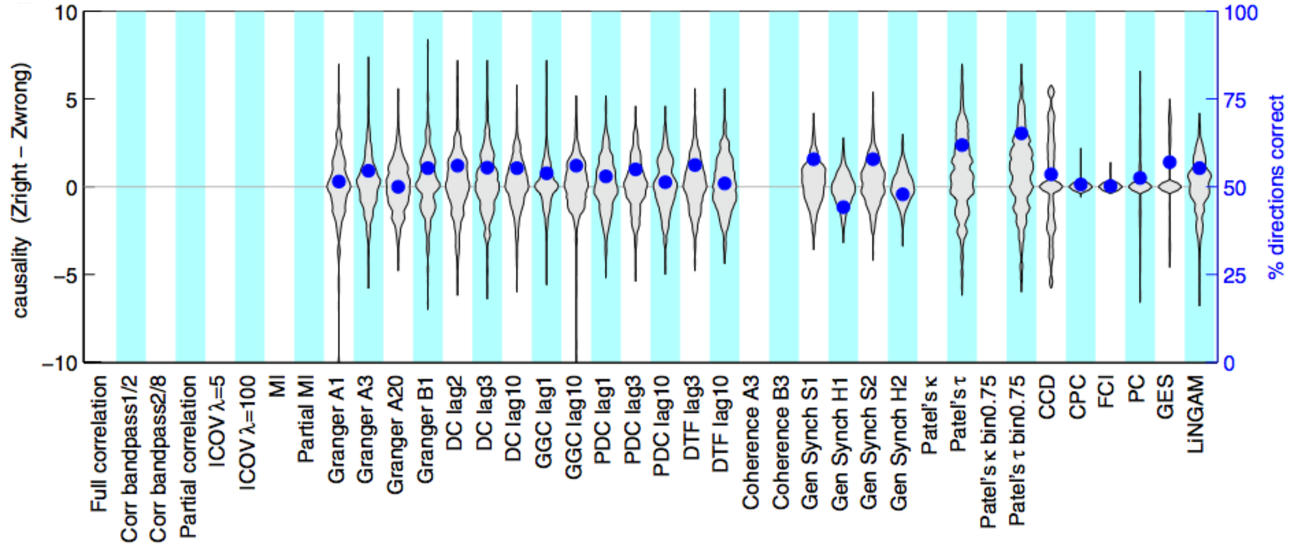


Berkson's paradox = false positive (2-3)

Over-splitting = false negative (1-2)

Directionality of edges

- Directionality is hard to estimate in BOLD data
- Don’t use lag-based methods such as Granger causality
- Perhaps directionality is oversimplistic view of neural connectivity (particularly in resting-state)?



Smith et al (2011)

Resources

- FSL mailing list
- Book (Amazon/ OUP)
- All references on the bottom of slides contain ‘clickable’ links