AoN Brainhack
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What is a functional connectivity?

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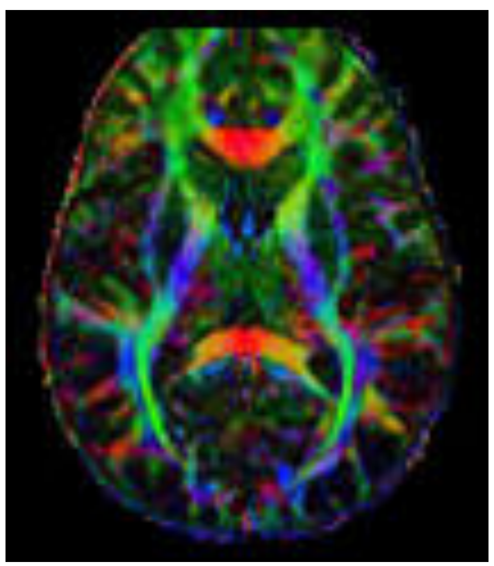
Warsaw, November 18th 2017

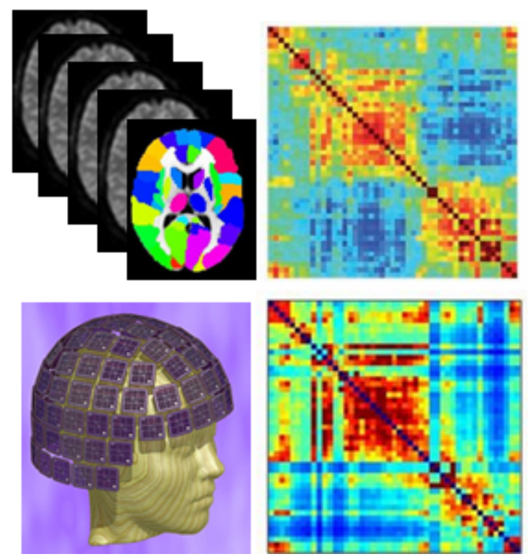
Plan of the presentation

[0] what is functional connectivity?
[1] correlation vs causation
[2] Pearson’s correlation vs partial correlation
[3] infomation-theoretical measures of functional connectivity
[4] time domain vs frequency domain
[5] static vs dynamic functional connectivity
[6] hierarchical models of functional connectivity
[7] multiple body interactions
[8] traps in functional connectivity research
[9] functional connectivity vs prediction studies

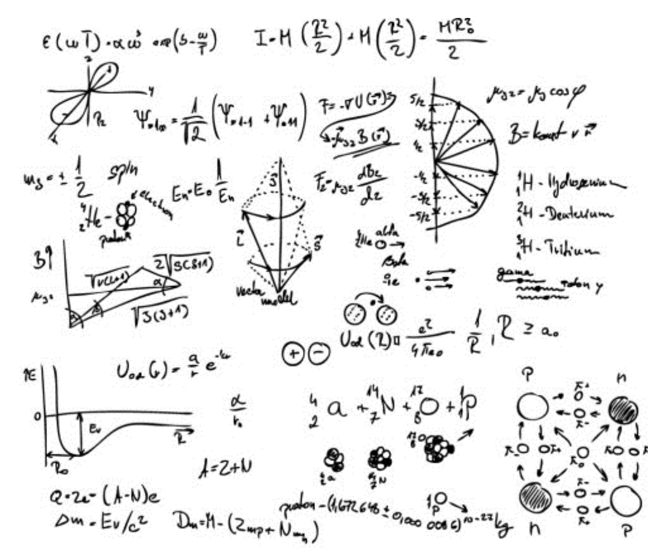
The concept of functional connectivity comes from brain research



anatomical connectivity



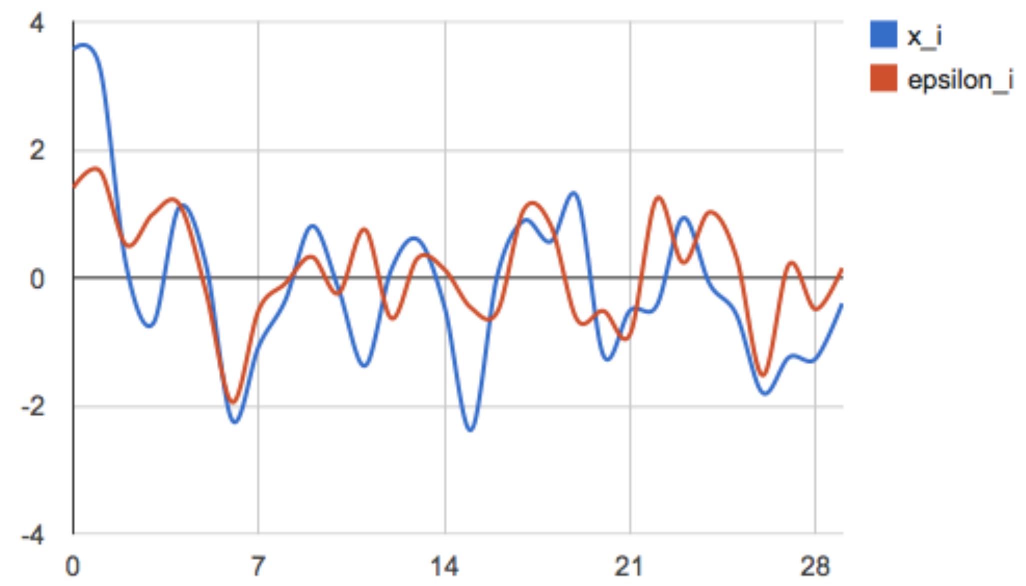
functional connectivity



effective connectivity

But what is the functional connectivity, on the conceptual level?

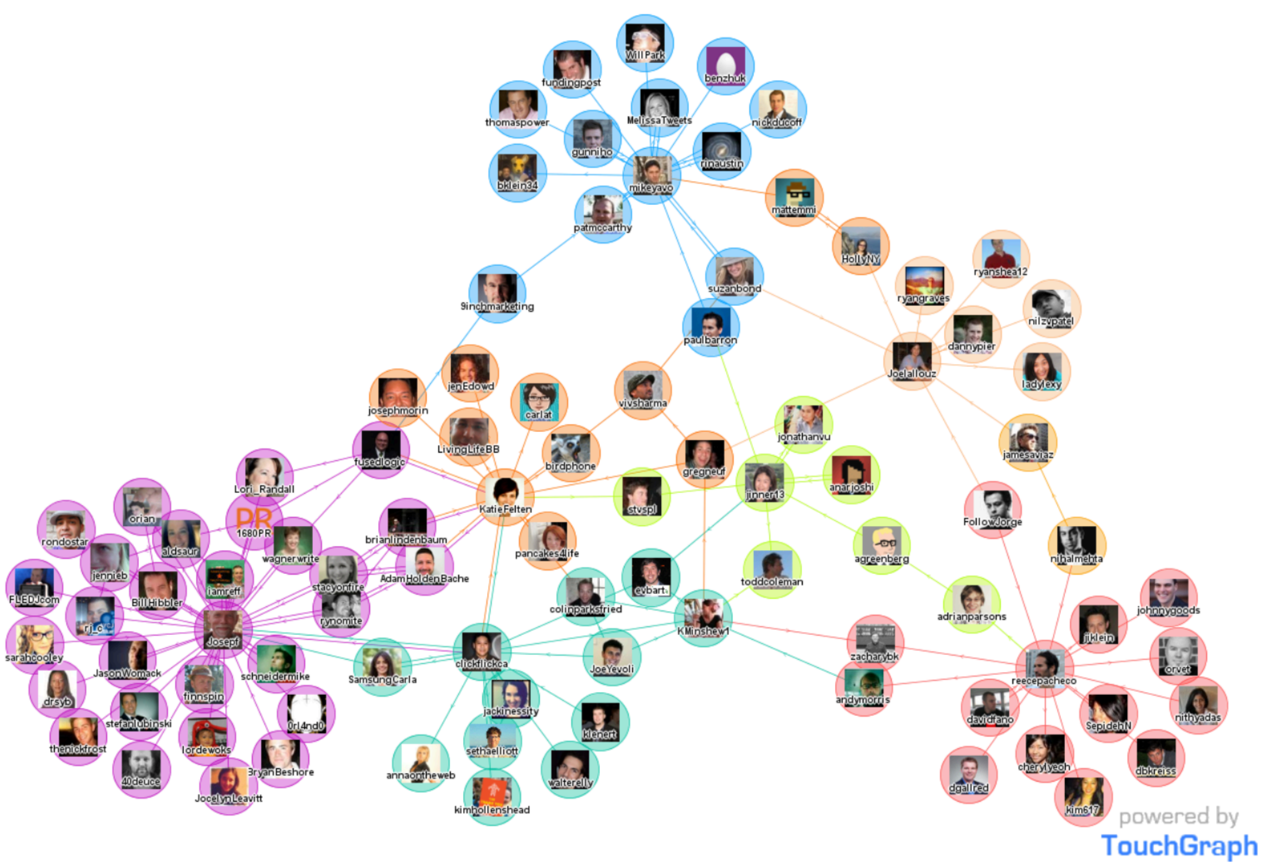
- functional connectivity = *association* between two variables
- assumption: if two variables correlate, they are a part of the same process



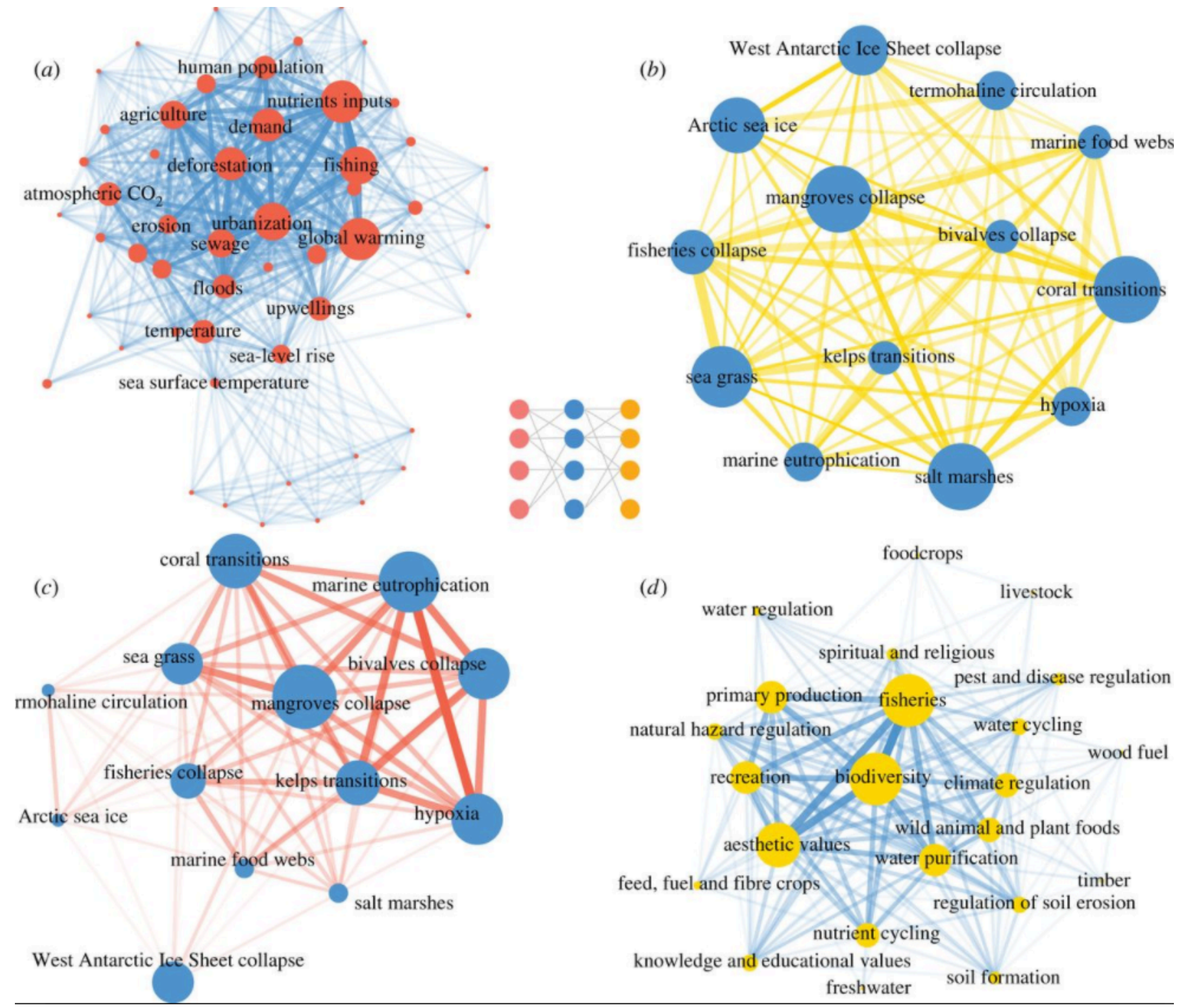
- there is no *official* definition of functional connectivity

In what other areas of natural sciences can we define functional connectivity?

- in any area where we have networks of interacting nodes



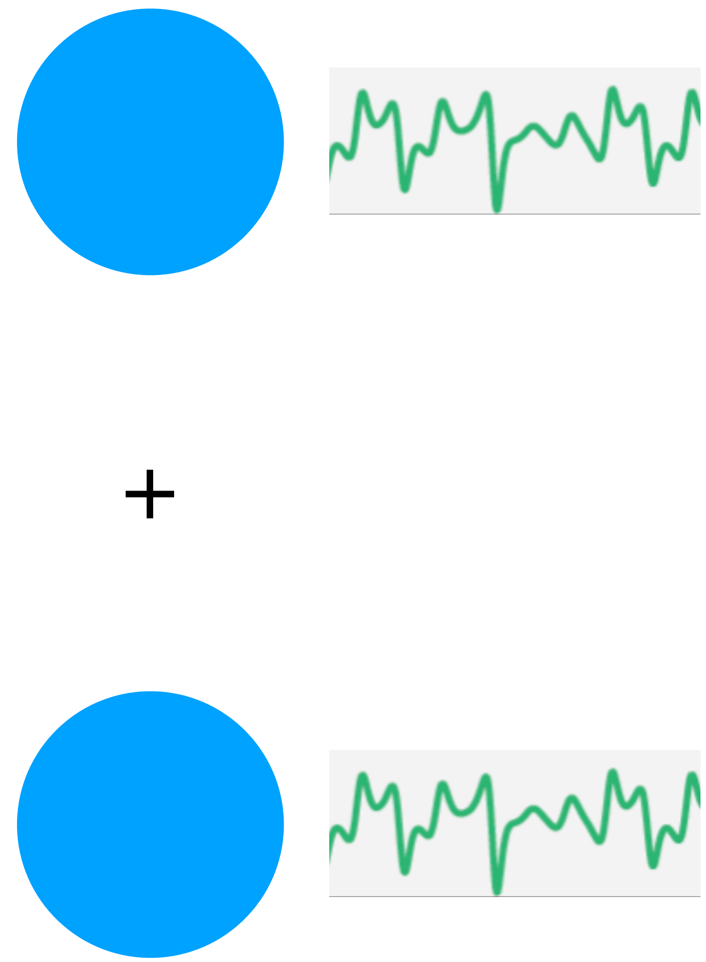
social networks



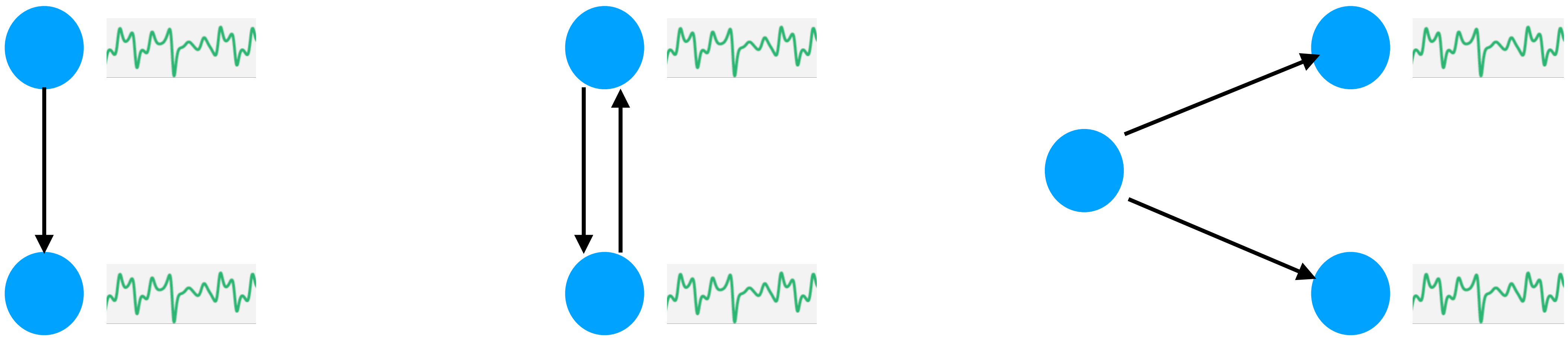
marine ecosystems

Rocha et al. (2014) Marine regime shifts: drivers and impacts on ecosystems services. *Philosophical Transactions of the Royal Society B*

Correlation vs causation



Correlation vs causation



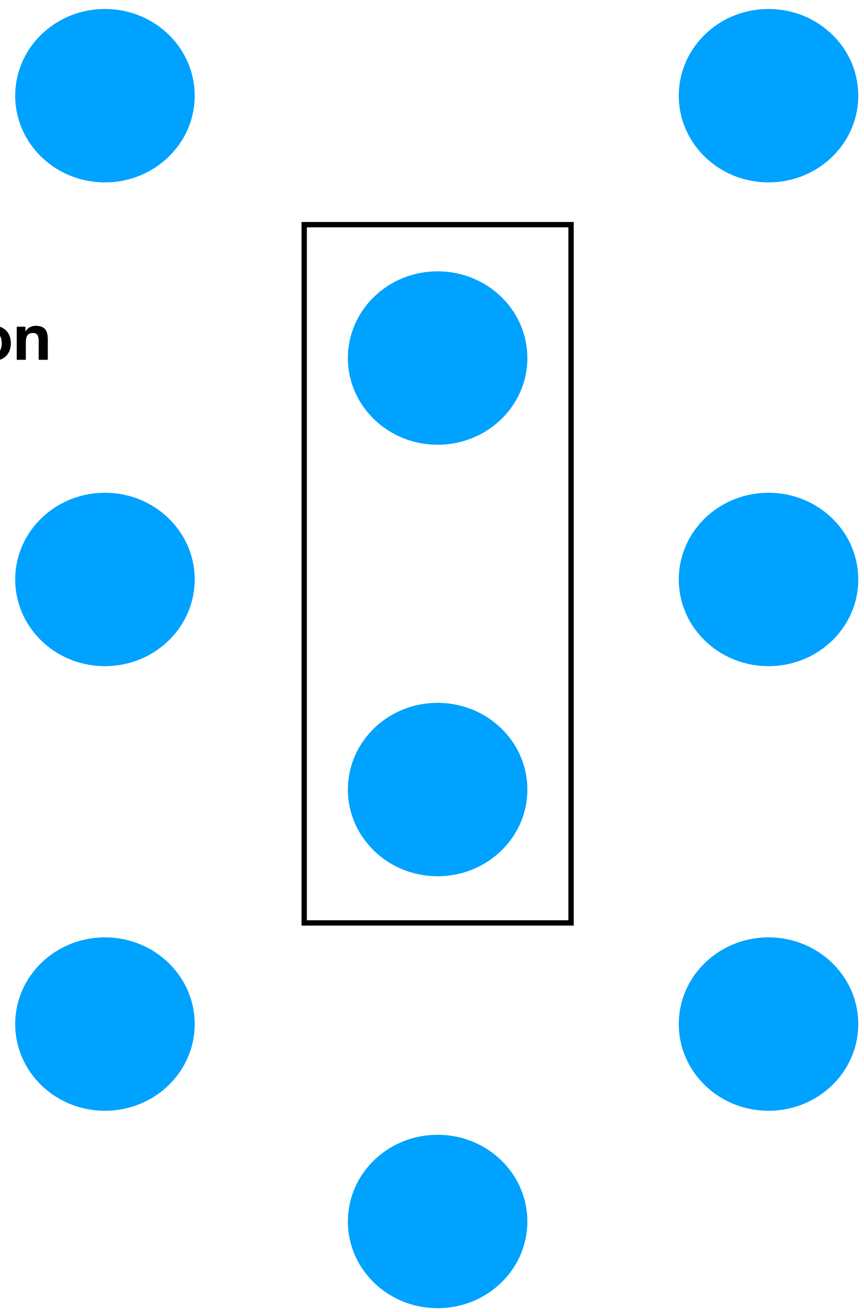
example: polio epidemy in 1950-1960

source: Freakonomics movie

How to *operationalize* the functional connectivity?

Pearson’s correlation vs partial correlation

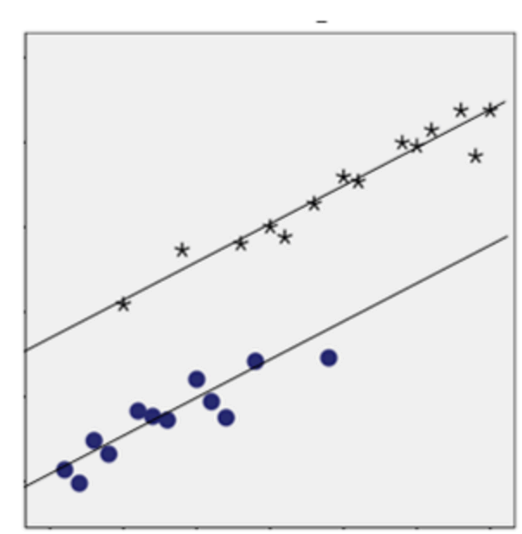
picture with
linear interaction



Pearson’s correlation (Pearson’s r)

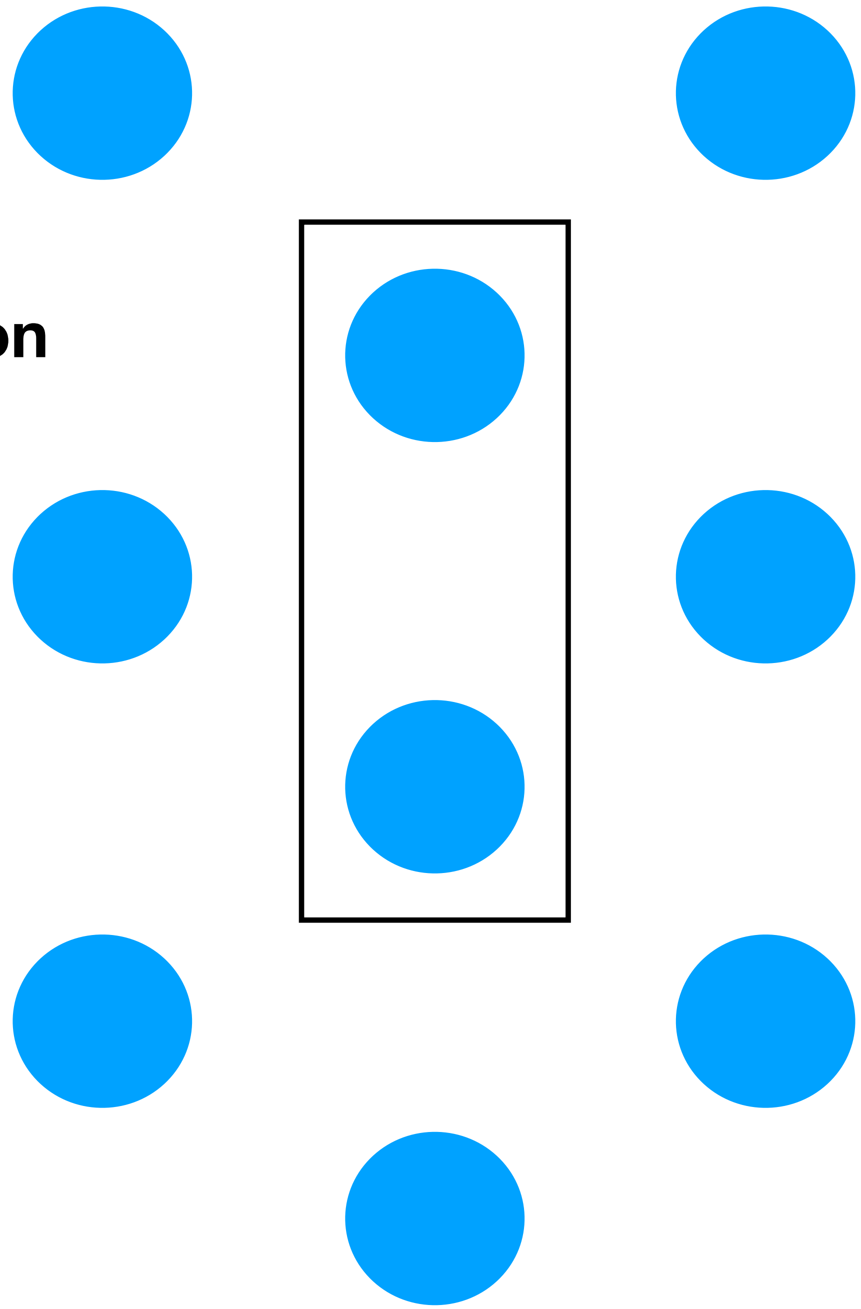
a pairwise measure of association
which treats the pair of nodes
as an isolated system

Pearson’s r is parametric and assumes
linear relationship between variables



Pearson’s correlation vs partial correlation

picture with linear interaction



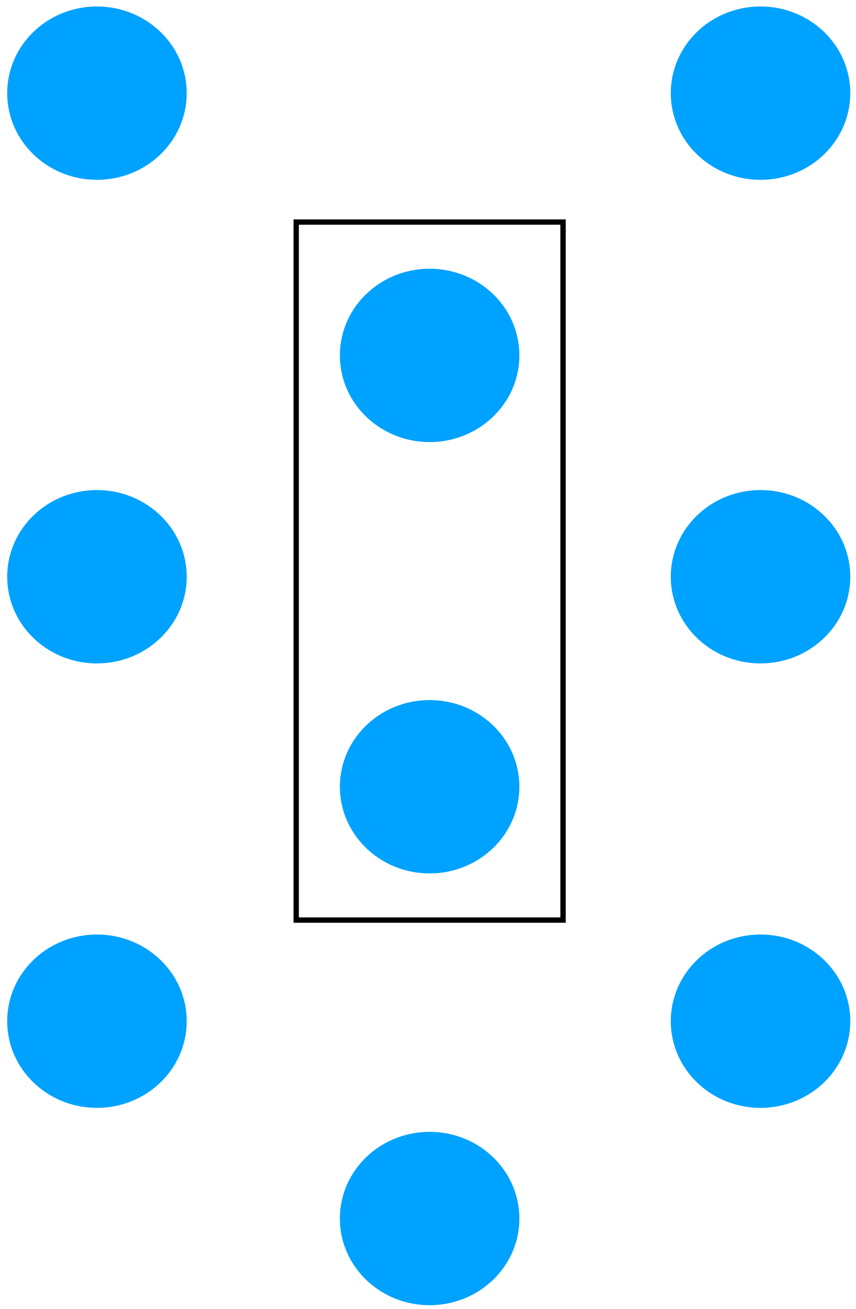
[1] one standard way of computing Pearson’s r:

$$\rho_{X,Y} = \frac{\mathrm{cov}(X,Y)}{\sigma_X \sigma_Y}$$

σ - standard deviation

[2] many ways of computing confidence intervals

Pearson’s correlation vs partial correlation



[2] many ways of computing confidence intervals:

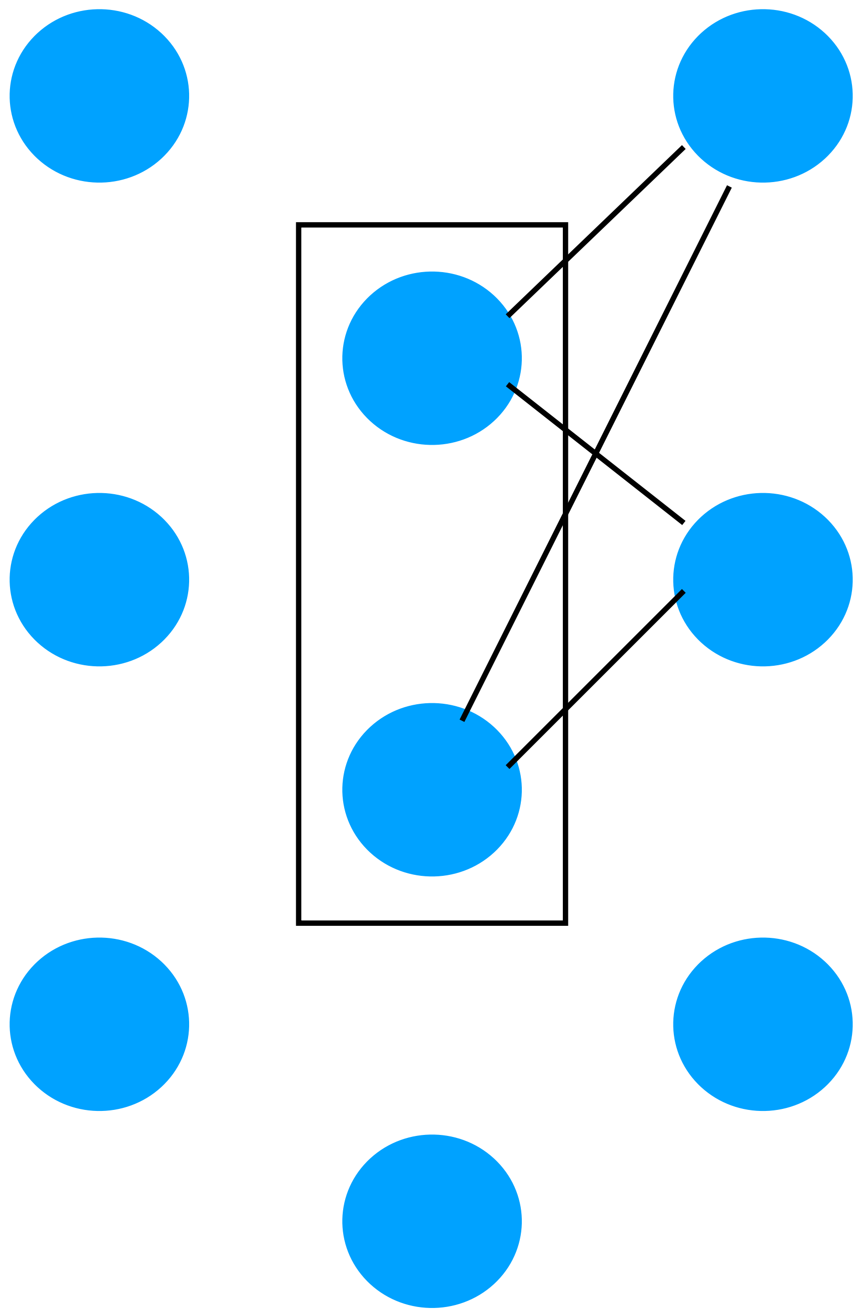
[a] with use of t-statistic (MATLAB):

The p-value is computed by transforming the correlation to create a *t* statistic having N-2 degrees of freedom, where N is the number of rows of X.
The confidence bounds are based on an asymptotic normal distribution of 0.5*log((1+R)/(1-R)), with an approximate variance equal to 1/(N-3)

[b] with use of Z-statistic:

Since the sampling distribution of Pearson's r is not normally distributed, Pearson's r is converted to Fisher's z' and the confidence interval is computed using Fisher's z'. The values of Fisher's z' in the confidence interval are then converted back to Pearson's r’s

Pearson's correlation vs partial correlation

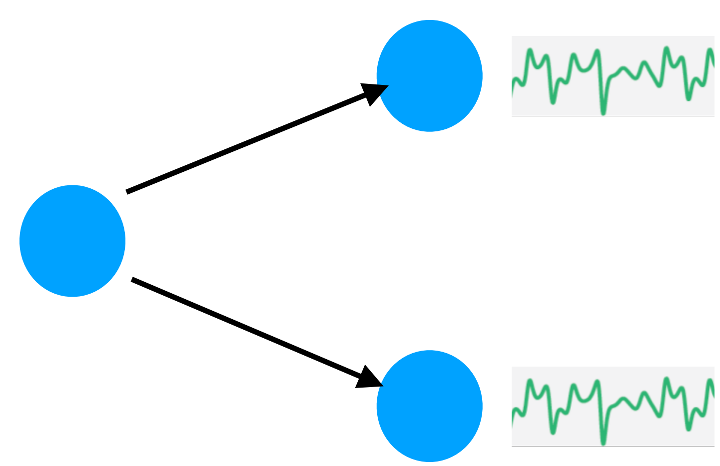


Partial correlation:

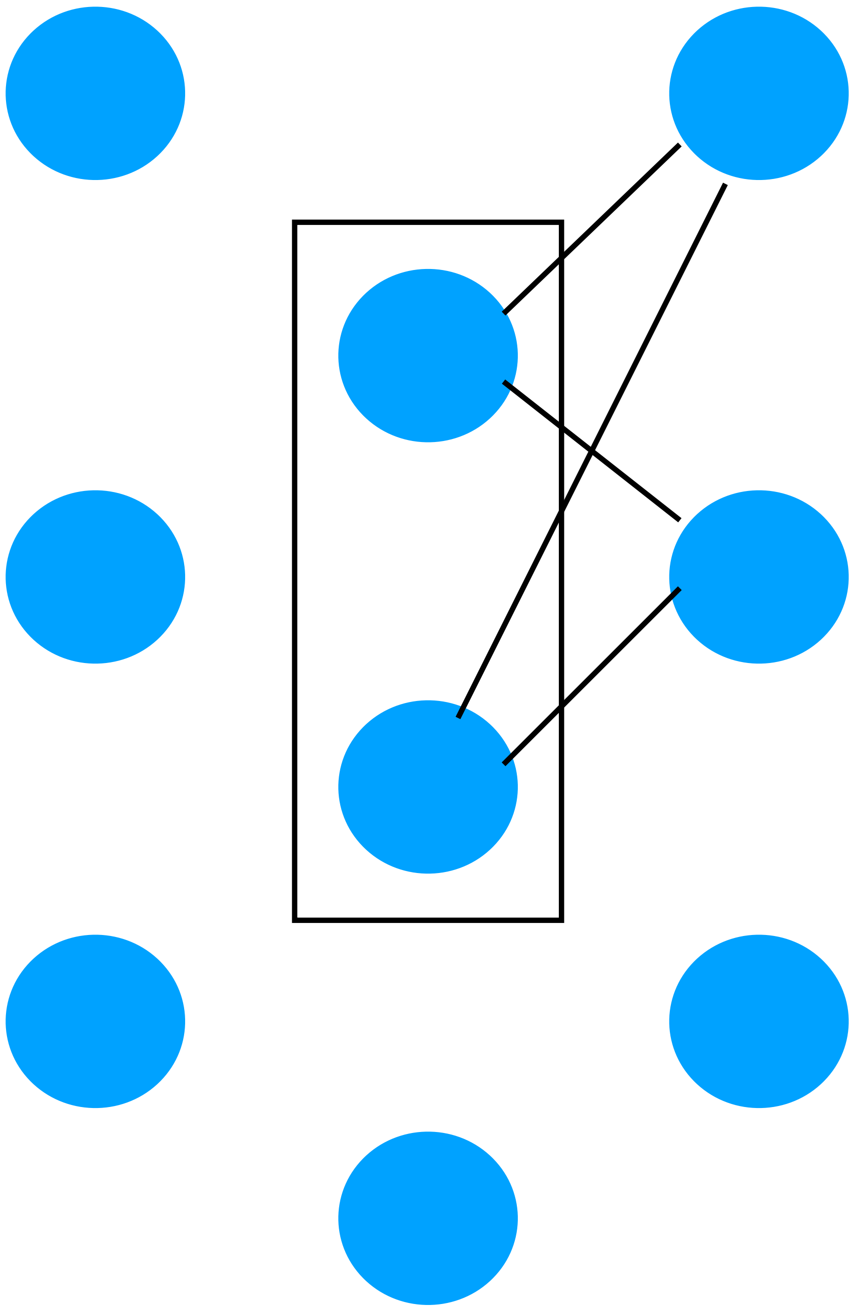
takes into account other nodes in the network

'first, regress the influence of other nodes in the network and isolate the two nodes, and then compute the Pearson's correlation between the two nodes'

many ways to compute partial correlation!



Pearson's correlation vs partial correlation



Partial correlation can be computed in multiple ways. Two most popular ways:

[1] via Ordinary Least-Square Regression:

$$\mathbf{w}_X^* = \arg\min_{\mathbf{w}} \left\{ \sum_{i=1}^{N} (x_i - \langle \mathbf{w}, \mathbf{z}_i \rangle)^2 \right\}$$

$$\mathbf{w}_Y^* = \arg\min_{\mathbf{w}} \left\{ \sum_{i=1}^{N} (y_i - \langle \mathbf{w}, \mathbf{z}_i \rangle)^2 \right\}$$

The residuals are then:

$$e_{X,i} = x_i - \langle \mathbf{w}_X^*, \mathbf{z}_i \rangle$$

$$e_{Y,i} = y_i - \langle \mathbf{w}_Y^*, \mathbf{z}_i \rangle$$

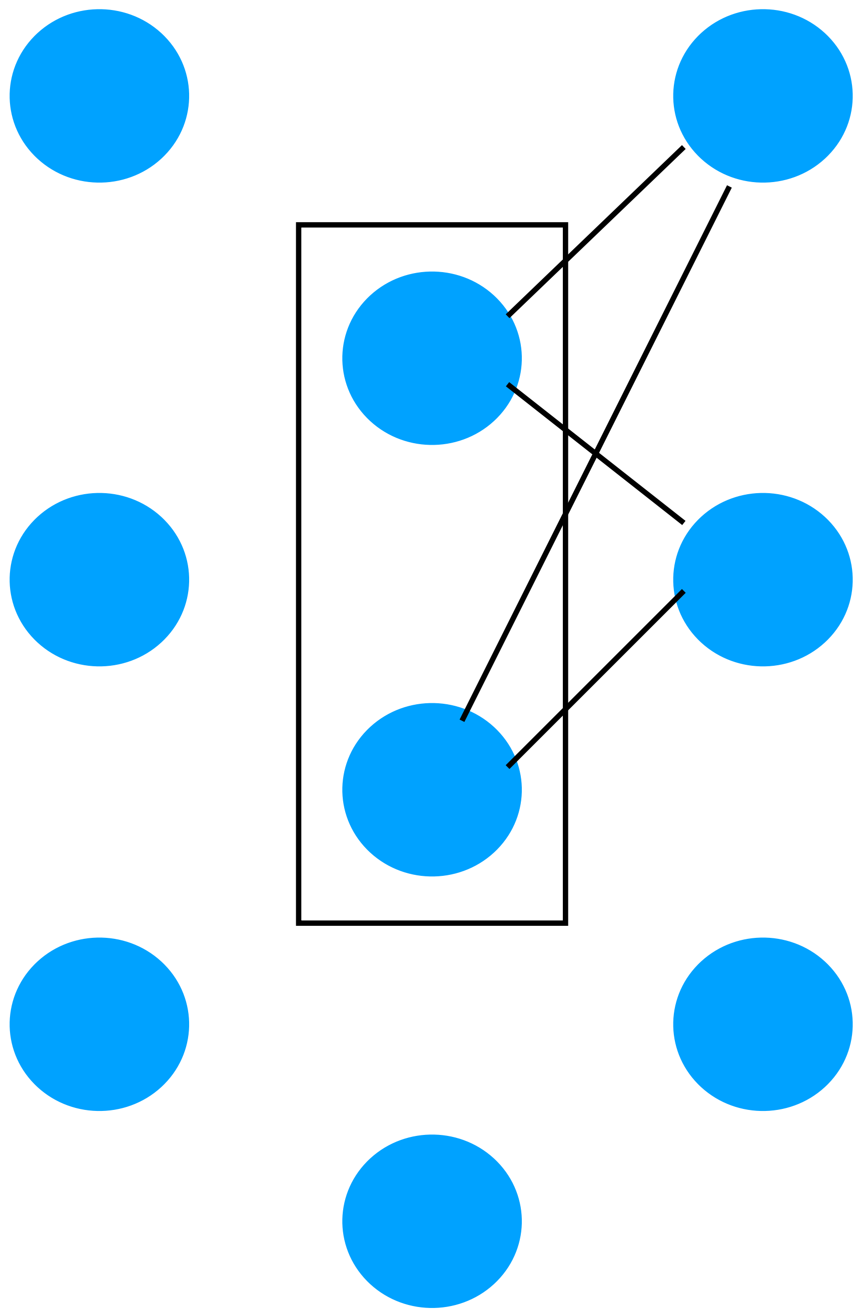
+ Pearson's correlation on the residuals

[2] through inverse covariance:

$$\rho_{ij\cdot} = \frac{\mathbb{C}_{ij}^{-1}}{\sqrt{\mathbb{C}_{ii}^{-1}\mathbb{C}_{jj}^{-1}}}$$

(estimation recommended for large networks)

Pearson’s correlation vs partial correlation



Many ways of computing
confidence intervals for inverse covariance:

[1] through permutation testing

[2] through mixture modeling
(Bielczyk & Walocha et al, 2017)

Information-theoretical measures of functional connectivity

Mutual information:

$$I(X;Y) = \sum_{x,y} P_{XY}(x,y) \log \frac{P_{XY}(x,y)}{P_X(x)P_Y(y)}$$

Pxy - joint probability for X and Y
Px, Py - marginals:

$$P_X(x) = \sum_{y} P_{XY}(x,y)$$

This definition works for discrete variables.

Information-theoretical measures of functional connectivity

add the note about histograms

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This definition works for discrete variables.

The difference between correlation and mutual information

Pearson's correlation measures the *linear* relationship (Pearson's correlation) between two variables, X and Y.

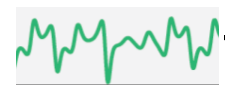
Mutual information is more general and measures the reduction of uncertainty in Y after observing X. Therefore, MI can measure non-monotonic relationships and other more complicated relationships.

Time domain vs frequency domain

poor time resolution
no oscillatory patterns

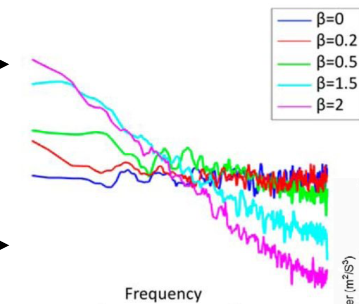
X(t)

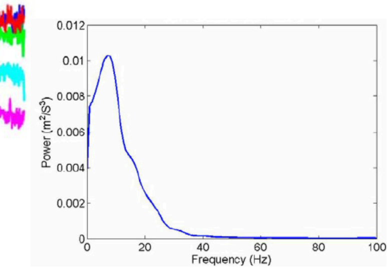
Y(t)



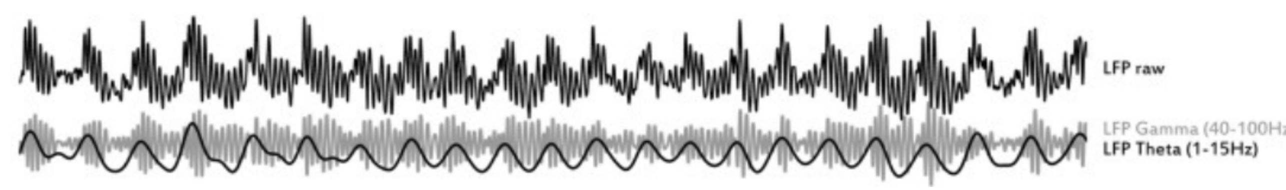
X(t)

Y(t)





power spectrum



Correlation

> Pearson’s correlation

> partial correlation

Coherence

> phase-phase coupling

> phase-amplitude coupling

> amplitude-amplitude coupling

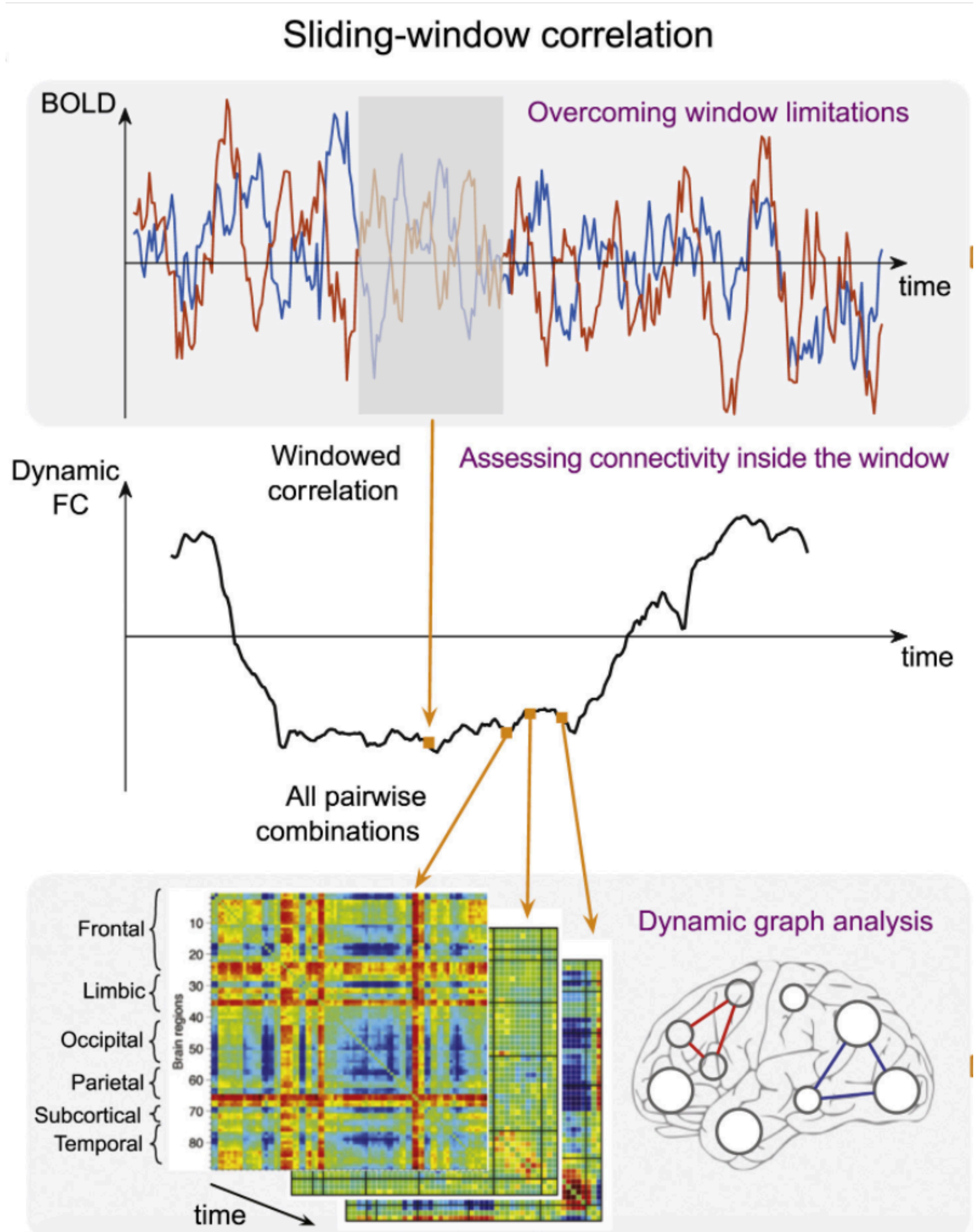
time domain

frequency domain

Static vs dynamic functional connectivity

analysis of the temporal patterns in functional connectivity with use of a *sliding window* (Sakoğlu et al, 2010)

chronnectome

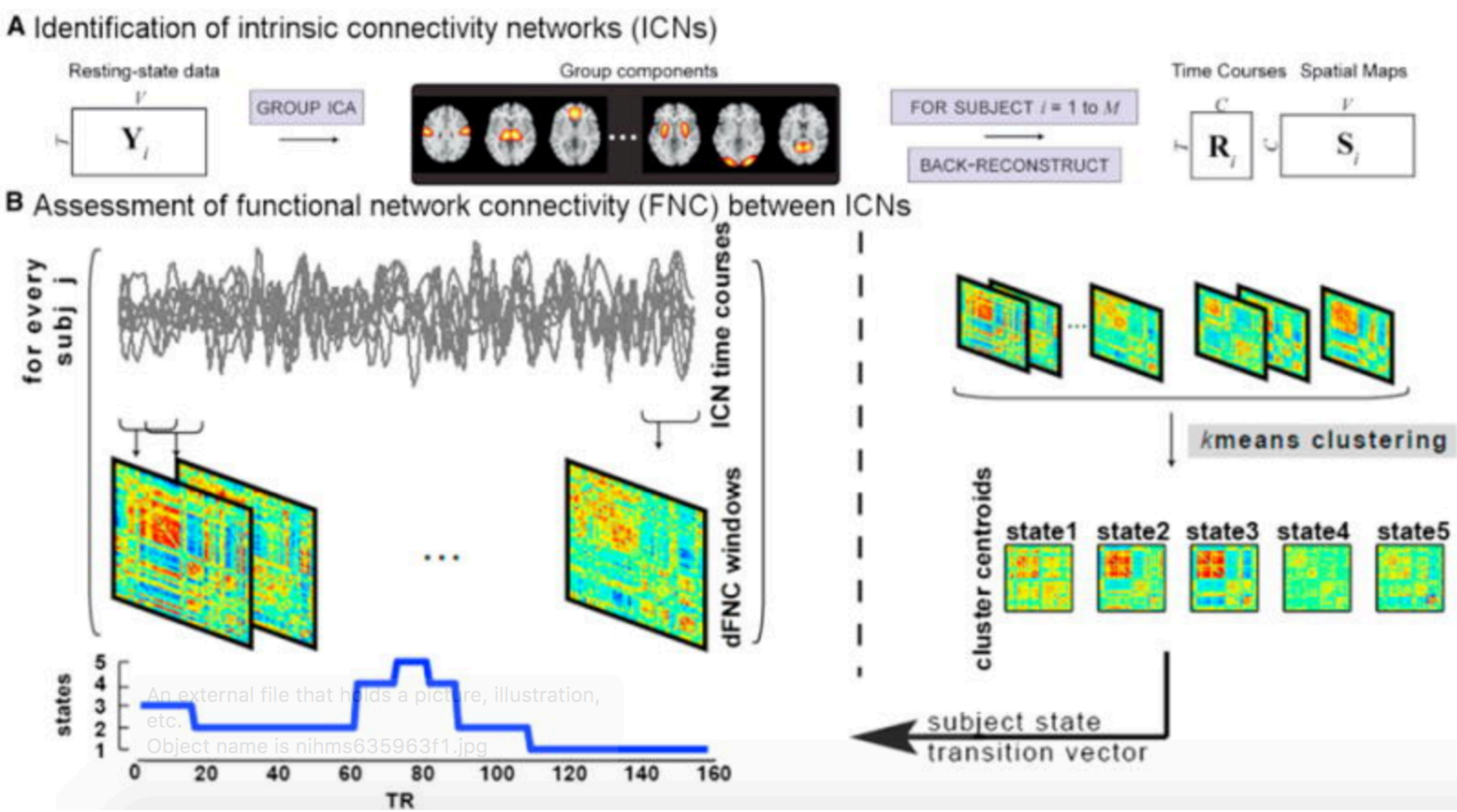


used primarily in fMRI research, see a review paper:

http://www.sciencedirect.com/science/article/pii/S1053811916307881

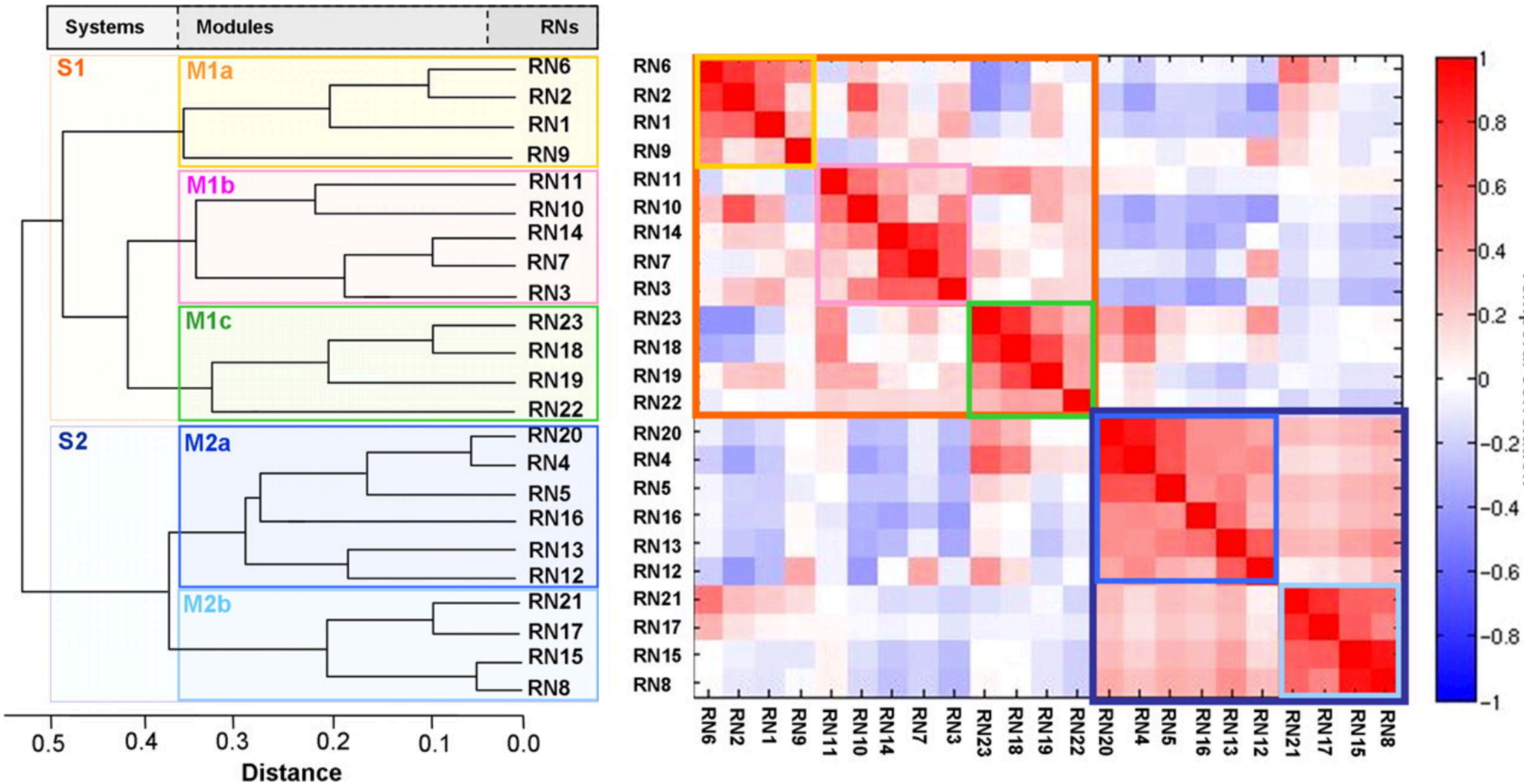
Static vs dynamic functional connectivity

A 'Chronnectome' idea:



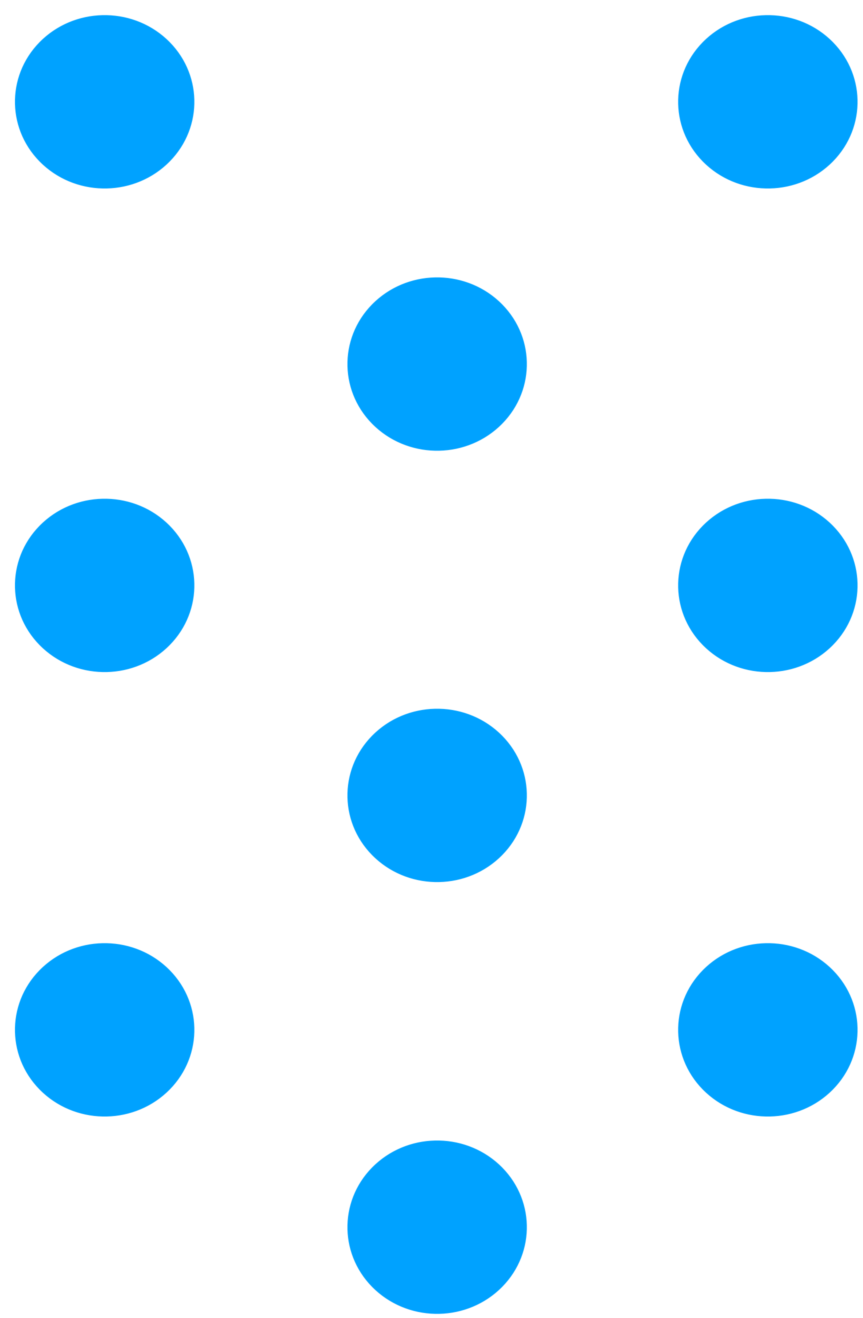
Calhoun et al. (2014)

Hierarchical models of functional connectivity

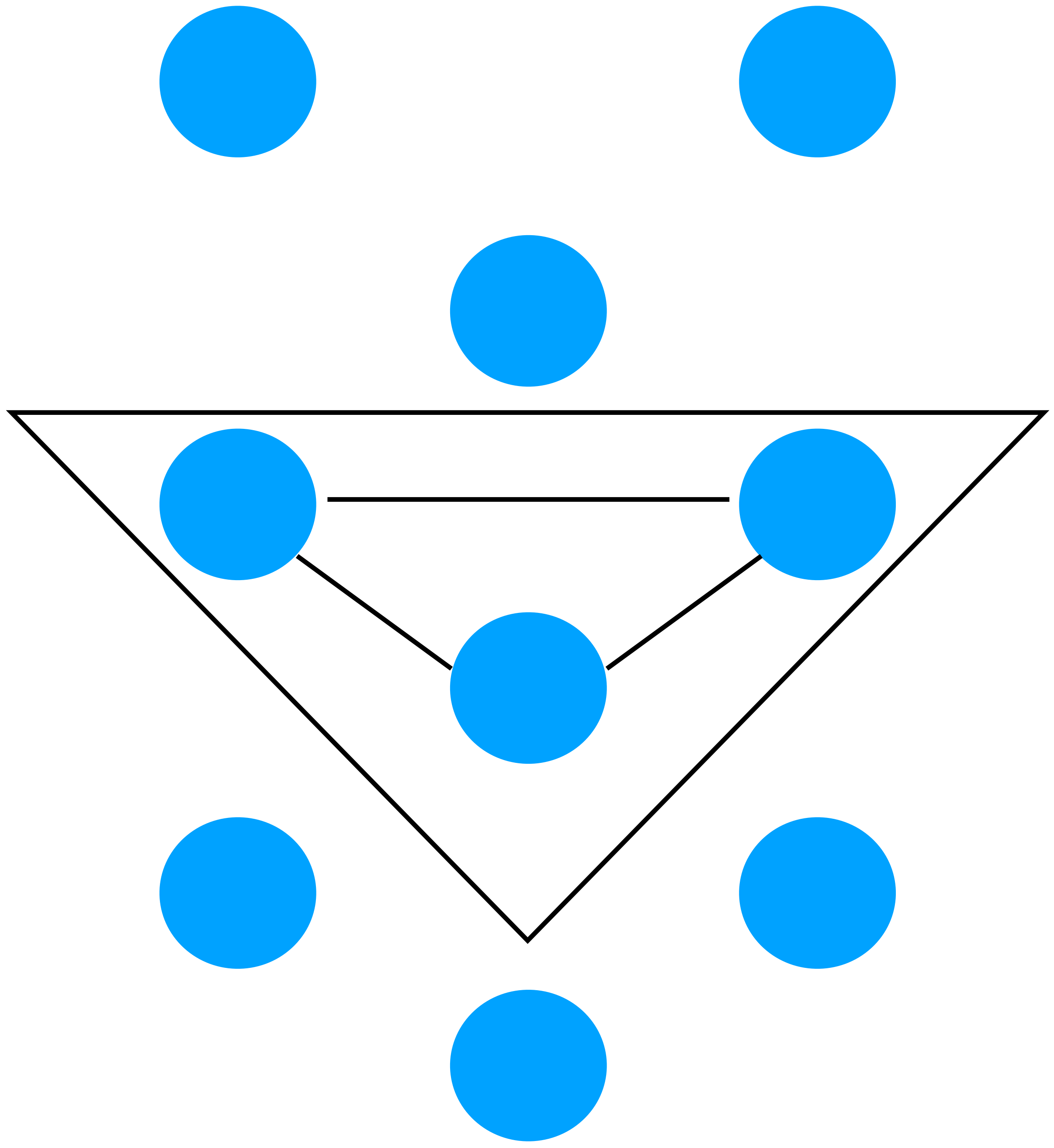


Doucet et al., Journal of Neurophysiology 2011

Multiple body interactions



Multiple body interactions



Pearson's r for two nodes:

$$\frac{\mathrm{E}\{(X-\mu_X)(Y-\mu_Y)\}}{\sqrt{\mathrm{Var}(X)\mathrm{Var}(Y)}}$$

Pearson's r for three nodes:

$$\frac{\mathrm{E}\{(X-\mu_X)(Y-\mu_Y)(Z-\mu_Z)\}}{\sqrt{\mathrm{Var}(X)\mathrm{Var}(Y)\mathrm{Var}(Z)}}$$

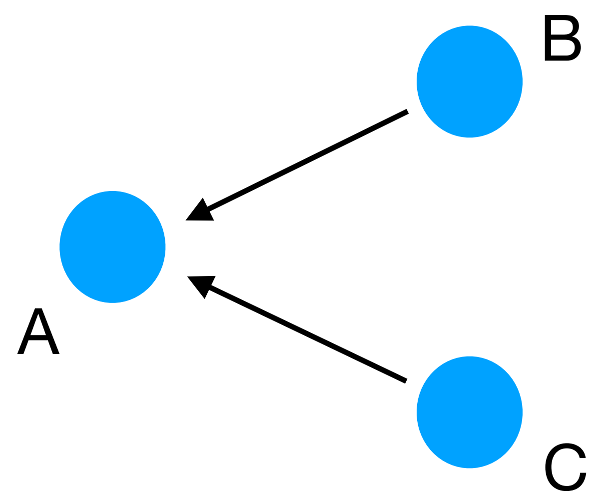
Most common traps in functional connectivity research

[1]
- Pearson’s correlation can result in networks denser than the true underlying connectivity
- partial correlation can result in networks sparser than the true underlying connectivity

<u>Conclusion:</u> it is a good idea in general to compare compute both of them as the truth is somewhere in between

[2] the multiple comparisons problem

[3] Berkson’s paradox



happens when calculating partial correlation with use of Ordinary Least Squares regression for two unrelated sources with a common sink

regressing time series A from B and C induces a *spurious negative correlation* between B and C

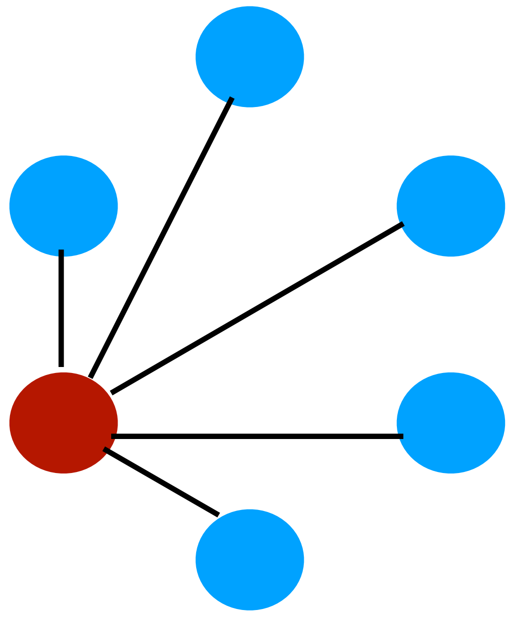
Food for thought:
Functional connectivity research vs prediction studies

<u>functional connectivity:</u>
do the two variables correlate?

<u>prediction study:</u>
you can predict a value of one variable from a value of another variable
(usually because these two variables correlate)

Linear Discriminant Analysis finds coefficients a_i such that:

$$v = \sum a_i v_i$$



<u>Conclusion</u>: these two research problems are mathematically close to each other

<u>A research question</u>:
How about applying Linear Discriminant Analysis to do a functional connectivity research?
Can the activity in one node of the network be predicted from activity in other nodes in the network?

Datasets we will be working on in this project

[1] Human Connectome Project fMRI datasets
[2] MyConnectome Project multimodal datasets
[3] open datasets on weather / stock exchange / social networks

…the list to be updated

The team that prepared the pipeline for this project

ONLINE BRAIN INTENSIVE

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Thank you for your attention!