Measuring Connectivity with RS-FMRI

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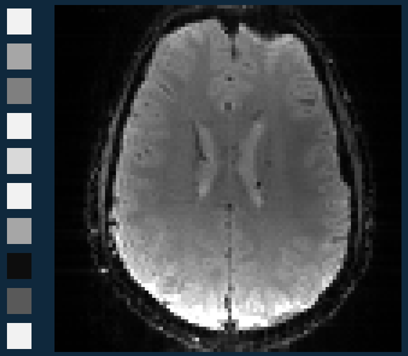
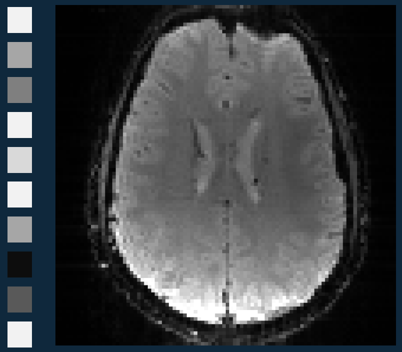
LINEAR MODELS IN FMRI

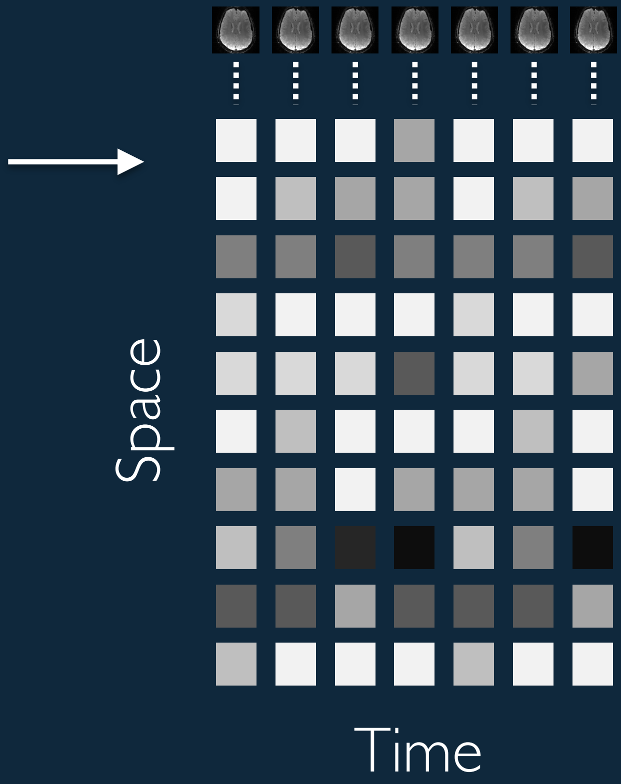
Data as a Space-Time Matrix



Time point 1



Time point 2



Signal characteristics, are important, not structure

Spatial Dimensions: 64x64x48 ~ 10^5

Temporal Dimensions: ~ 10^2

Linear Models

Paired spatial and temporal "components"

Consistent mathematical framework

$$Y = \beta \cdot X$$

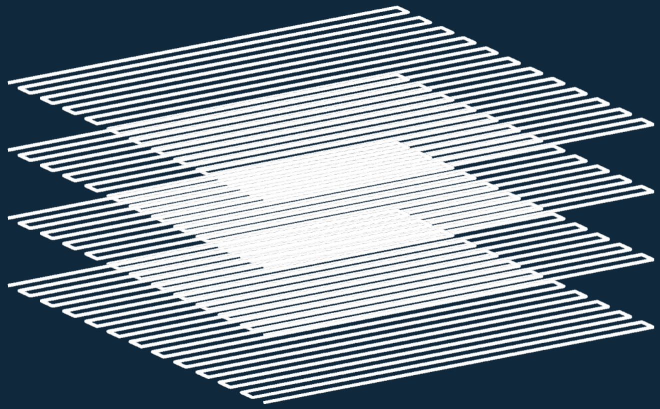
Data — Spatial Maps — Time-Courses

ACQUISITION & PRE-PROCESSING

Typical Acquisition Parameters

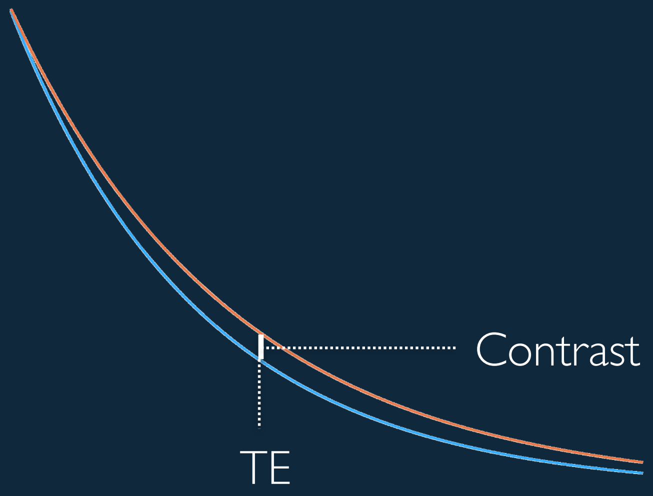
	Typically:
Acquisition Type	Single-shot, gradient-echo

Multi-slice EPI



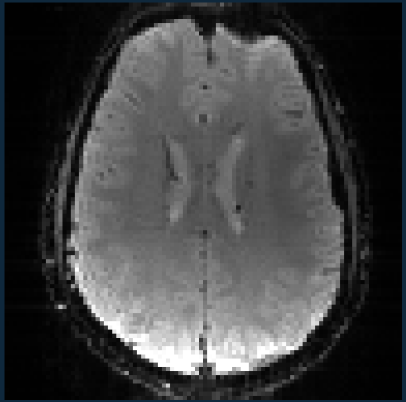
Typical Acquisition Parameters

	Typically:
Acquisition Type	Single-shot, gradient-echo
Contrast	T2* - BOLD

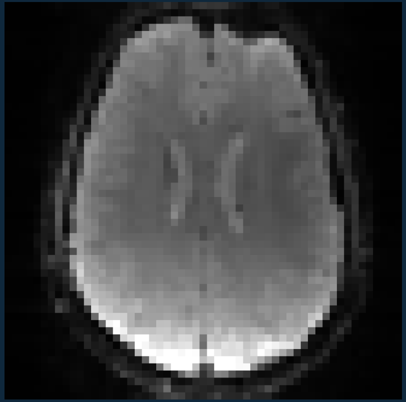


Typical Acquisition Parameters

	Typically:
Acquisition Type	Single-shot, gradient-echo
Contrast	T2* - BOLD
Spatial Resolution	2.0 ~ 3.5 mm



2.0 mm



3.5 mm

Typical Acquisition Parameters

	Typically:
Acquisition Type	Single-shot, gradient-echo
Contrast	T2* - BOLD
Spatial Resolution	2.0 ~ 3.5 mm
Temporal Resolution	1 ~ 3 seconds
Duration	5 ~ 15 minutes

0.16 – 0.5 Hz sampling

100 ~ 1000 time points

Typical Acquisition Parameters

	Typically:
Acquisition Type	Single-shot, gradient-echo
Contrast	T2* - BOLD
Spatial Resolution	2.0 ~ 3.5 mm
Temporal Resolution	1 ~ 3 seconds
Duration	5 ~ 15 minutes
Condition	Eyes open – "think of nothing"

Data Pre-Processing

Geometry	Filtering
Brain Extraction	Spatial Smoothing
Motion Correction	Temporal Filtering
Distortion Correction	Nuisance Regression
Registration	Global Signal Regression*

*Murphy & Fox, "Towards a consensus regarding global signal regression for resting state functional connectivity MRI", NeuroImage 2016

STATIC FUNCTIONAL CONNECTIVITY

Static Functional Connectivity

Functional Connectivity:

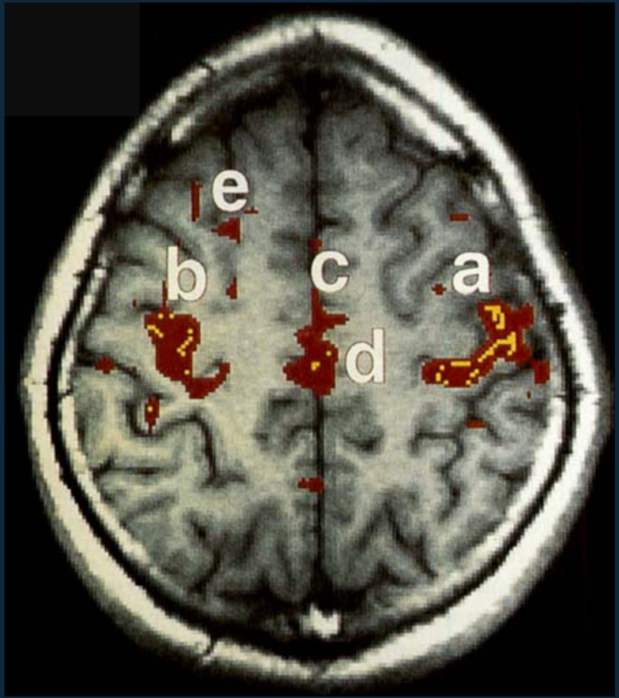
Strength of connectivity
Un-directed

Fixed connectivity pattern over time

1. SEED CONNECTIVITY

Seed-Based Correlation

Connectivity as a pattern matching problem



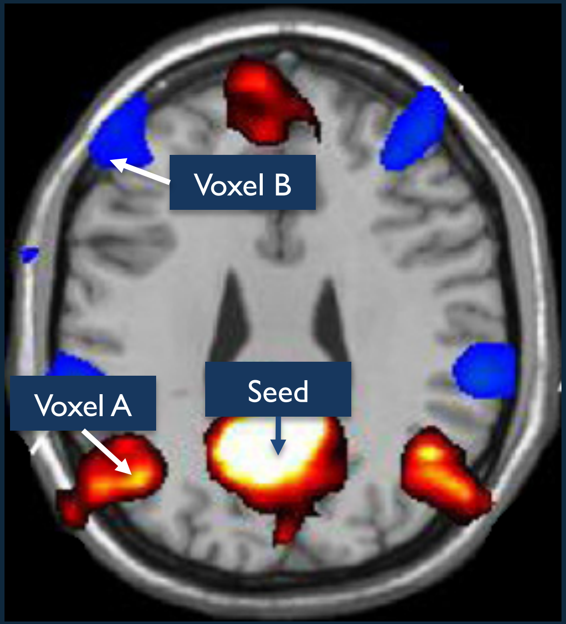
Biswal et al., *MRM* 1995

Connectivity Metric: Temporal Correlation

Seed

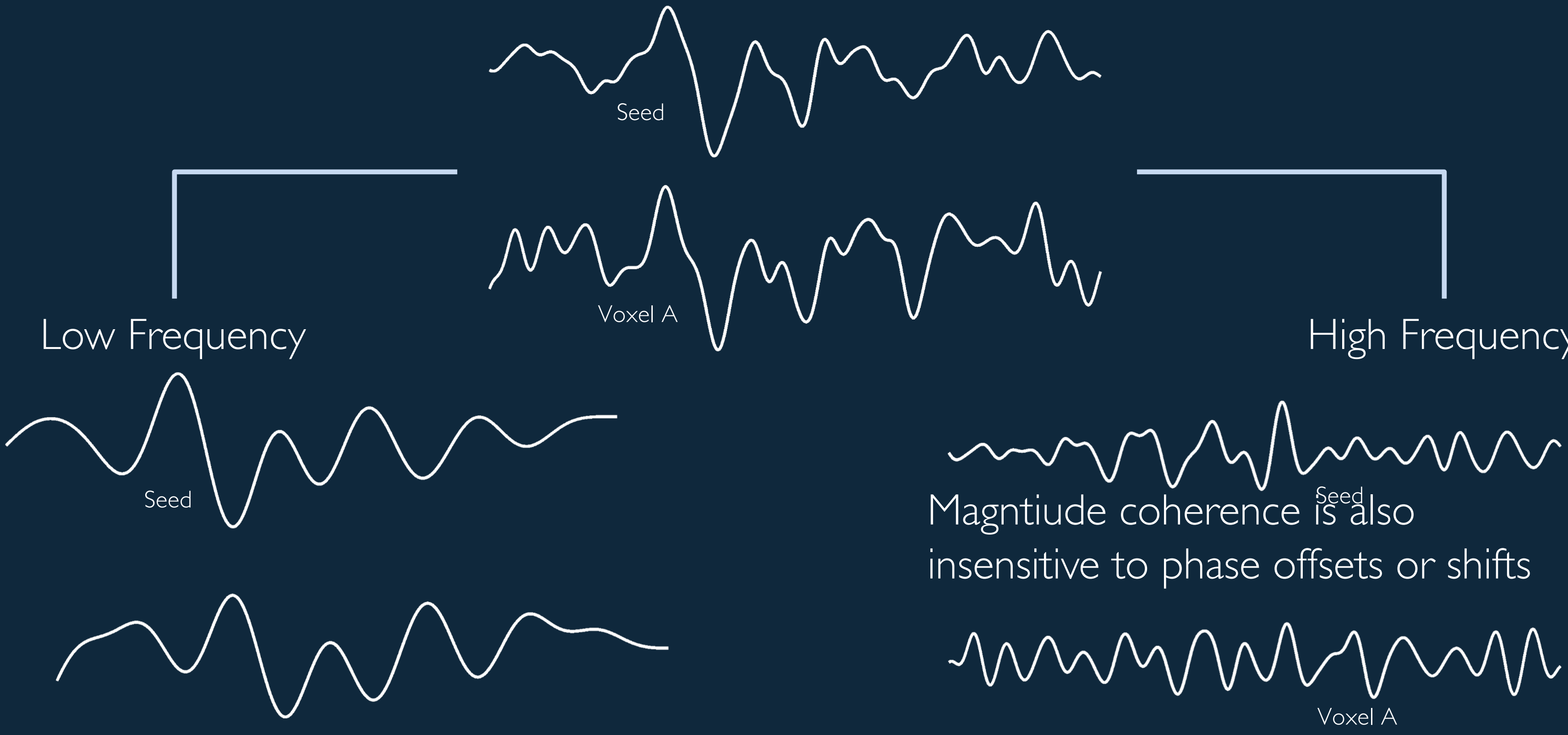
Voxel A
$r = 0.74$
high, positive connectivity

Voxel B
$r = -0.15$
low, negative connectivity



Chang et al., *NeuroImage* 2010

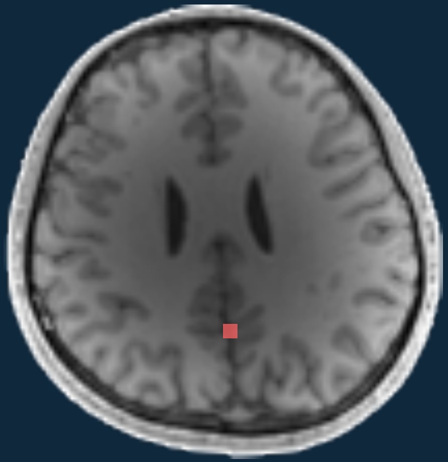
Connectivity Metric: Coherence



Magntiude coherence is also insensitive to phase offsets or shifts

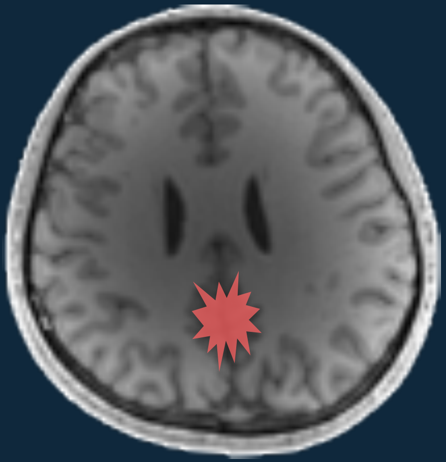
Defining Seeds – ROI size

Single Voxels



Regions of Interest

Geometric

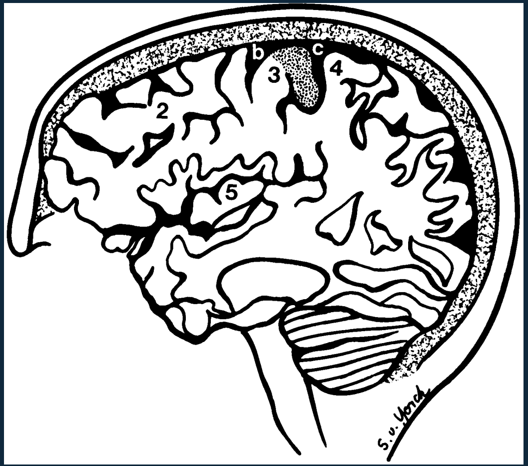


Data-Driven

Defining Seeds - Sources

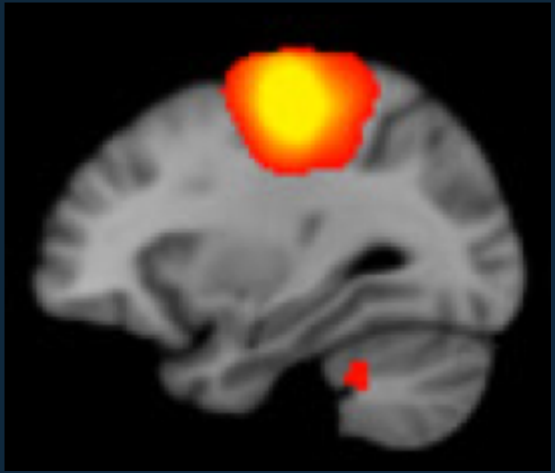
a priori

Structural



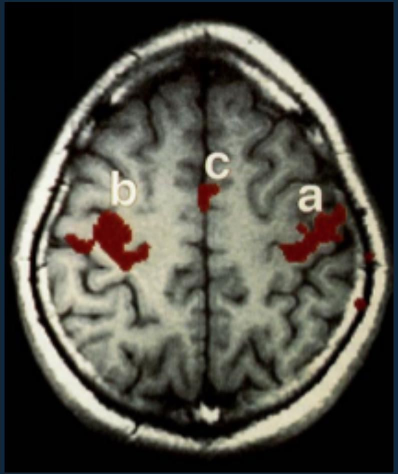
Yousry et al., *Brain* 1997

Functional



Smith et al., *PNAS* 2009

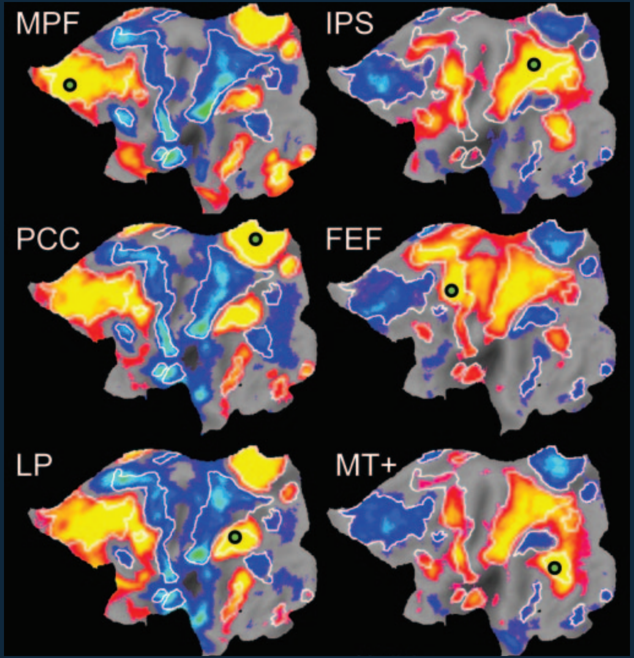
Localizer Experiment



Biswal et al., *MRM* 1995

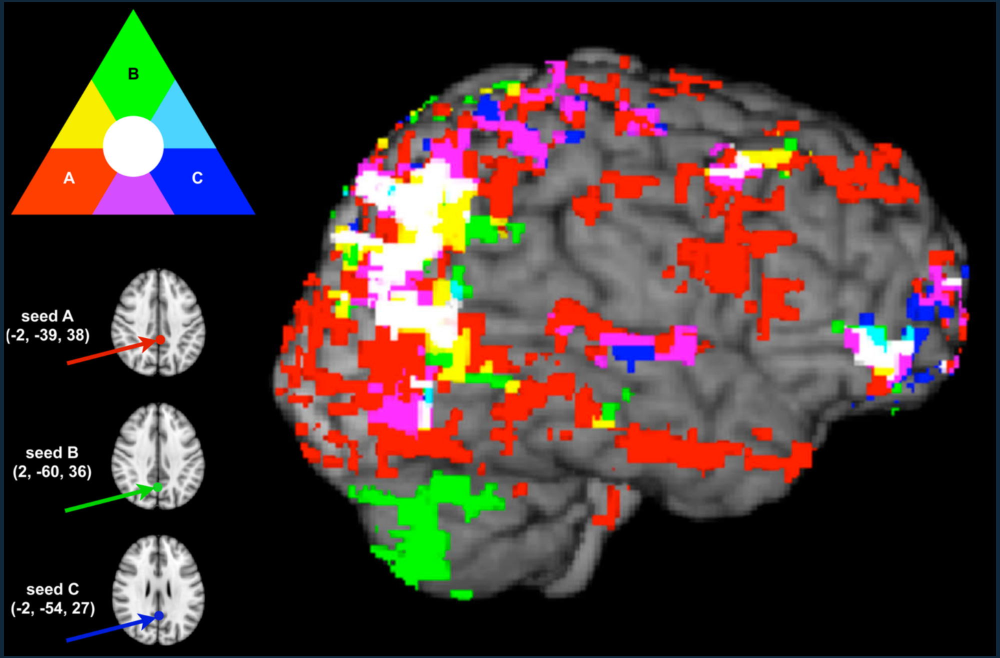
Different Seeds, Different Connectivity

Task Negative   Task Positive



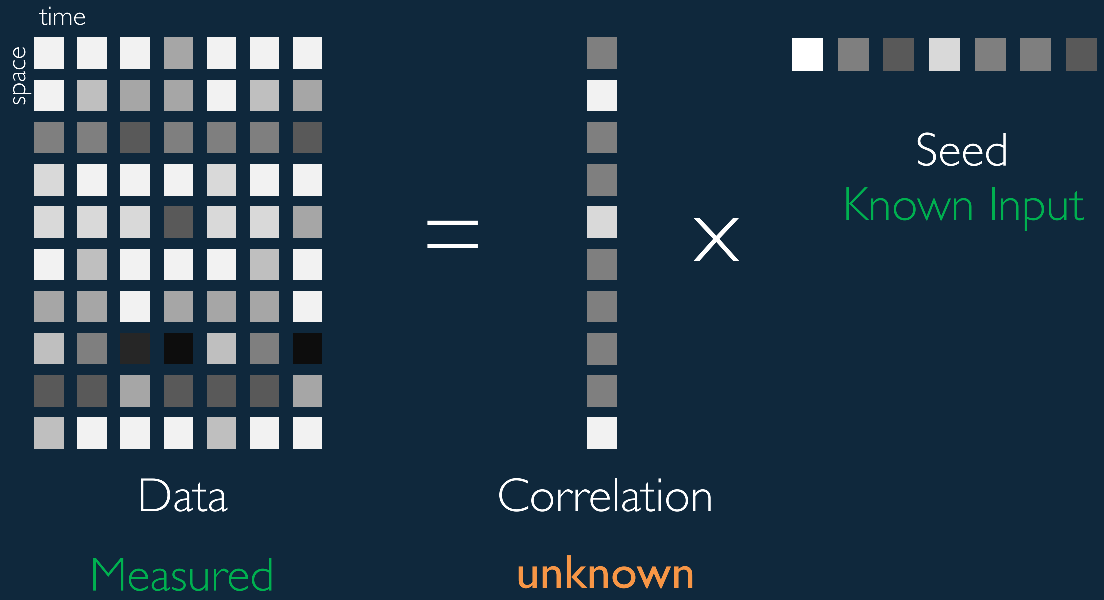
Fox et al., *PNAS* 2005

Default Mode Network



Cole et al., *Front Sys Neurosci* 2010

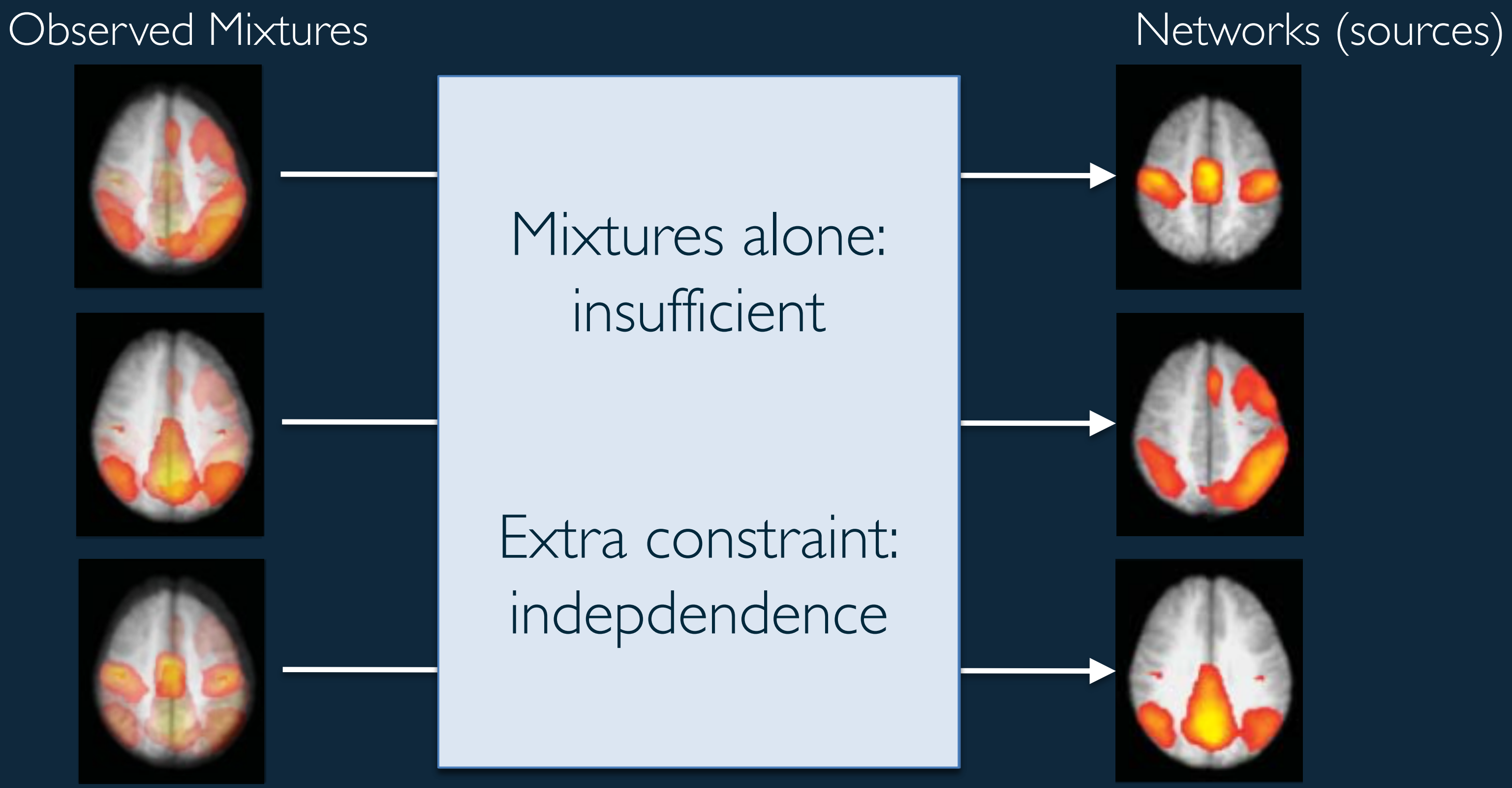
Seed-Based Correlation: Linear Model



Seed-correlation is a linear model

2. SPATIAL ICA

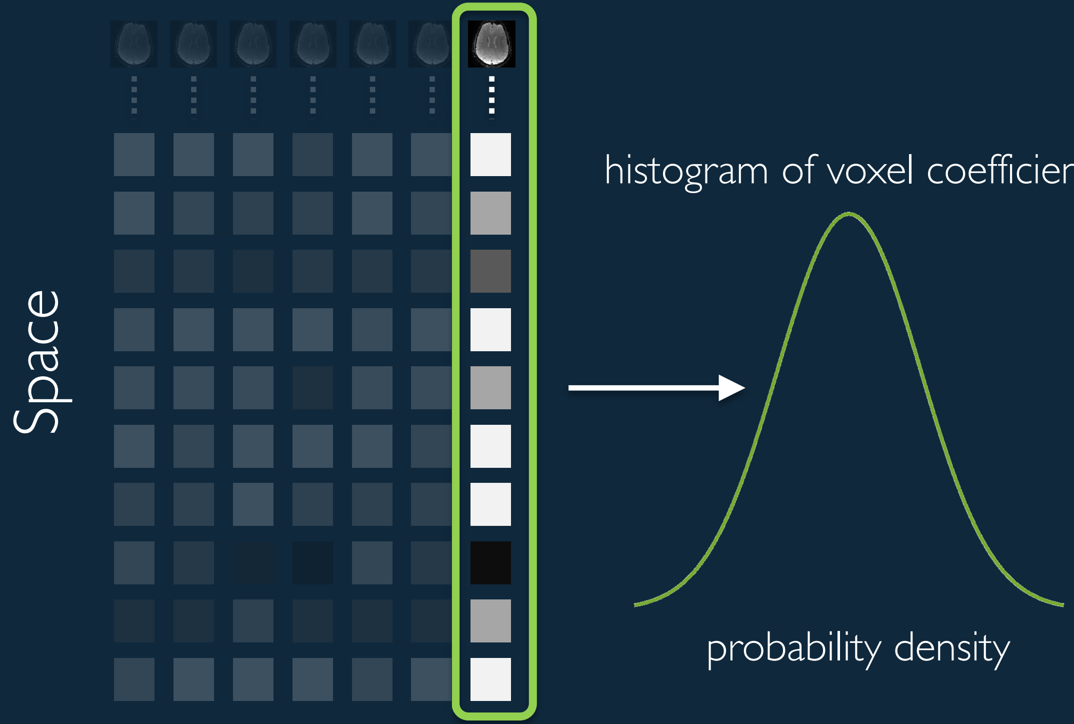
Spatial Independent Component Analysis



Spatial ICA Statistical Model

Spatial networks are *independent*

Assessed with probability distributions

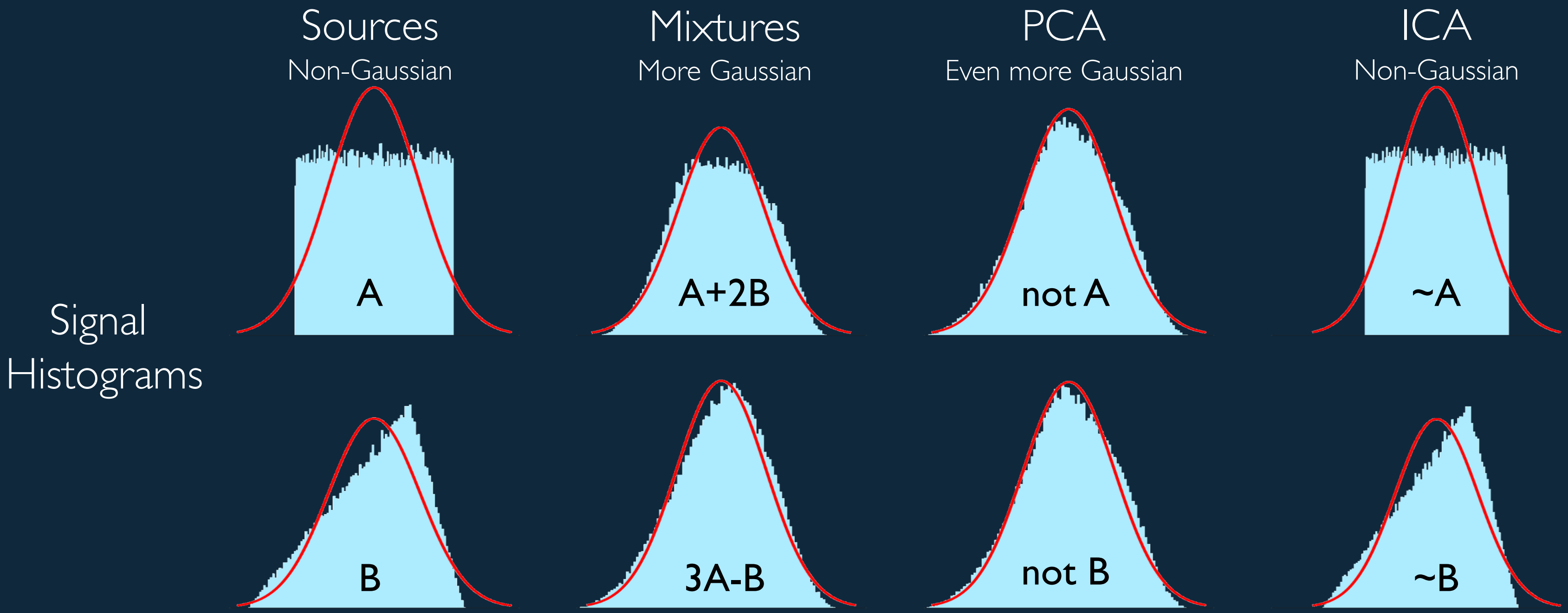


Non-Gaussianity – Central Limit Theorem

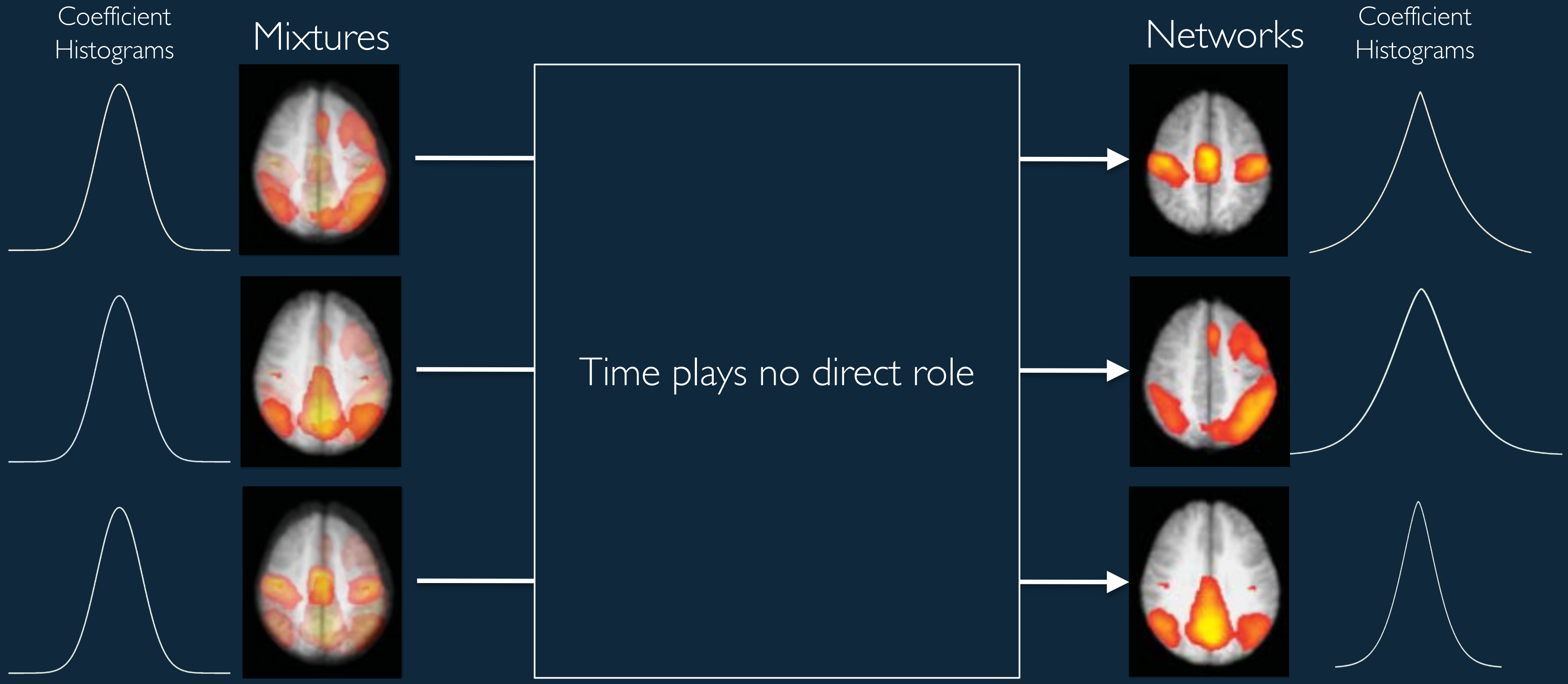
FastICA – Non-Gaussianity
Hyvarinen et al., *IEEE-TNN* 1999

Probabilistic ICA
Beckmann et al., *IEEE-TMI* 2004

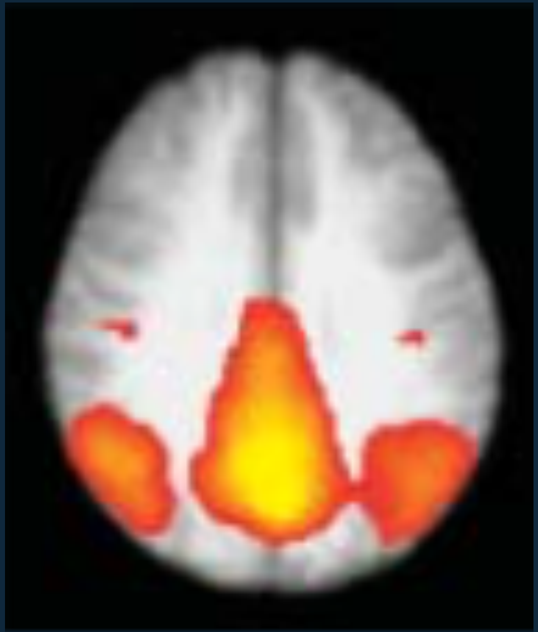
InfoMax – Mutual Information
Bell et al., *Neural Comp* 1995

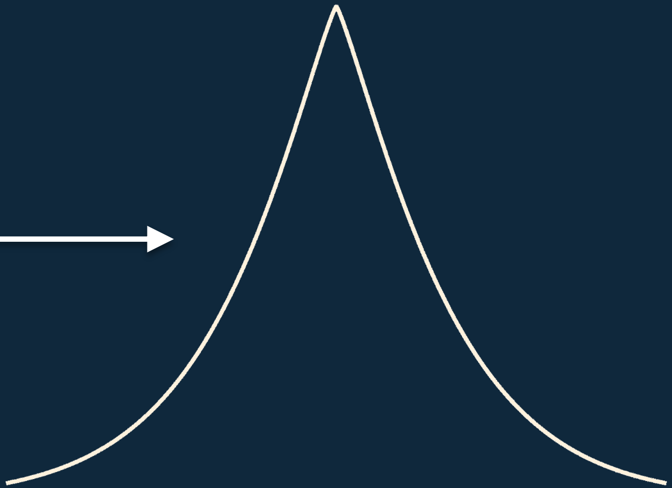


Spatial Independent Component Analysis



Spatial ICA "Connectivity"





These voxels are implicitly "connected" because the spatial coefficients produce a maximally non-Gaussian histogram

Connectivity Comparison

Spatial Information

Spatial ICA

Spatial coefficient distributions

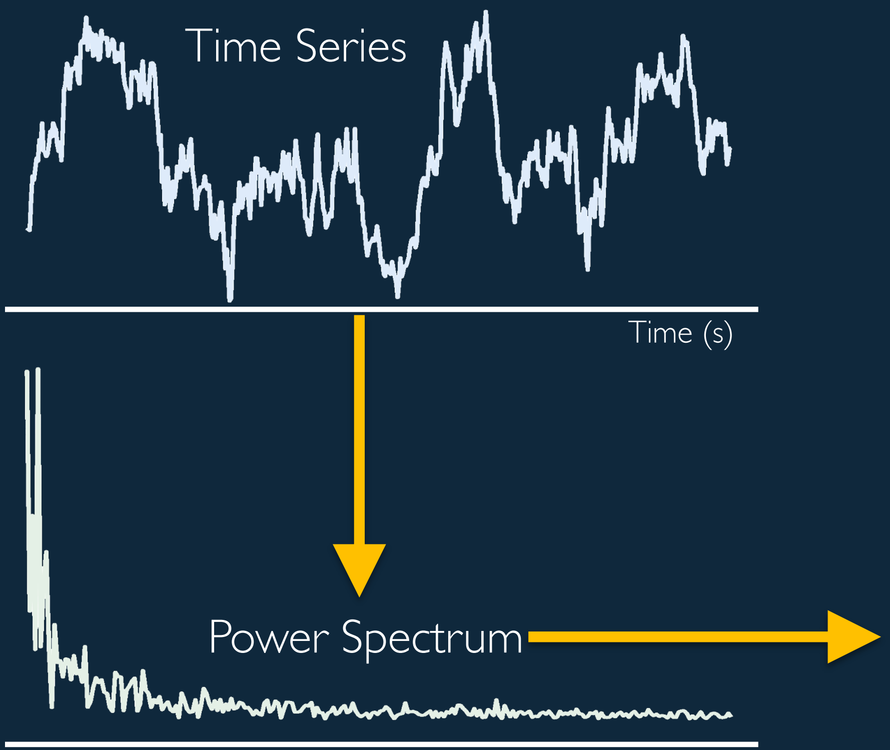
Seed Correlation

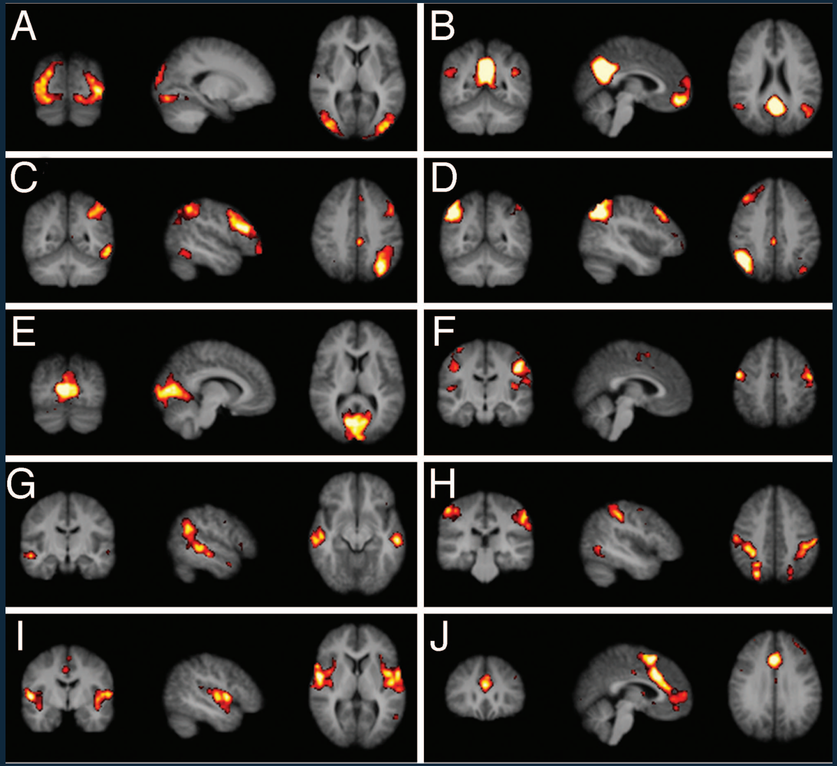
Seed size, location

Temporal correlations

Temporal Information

Space x Frequency

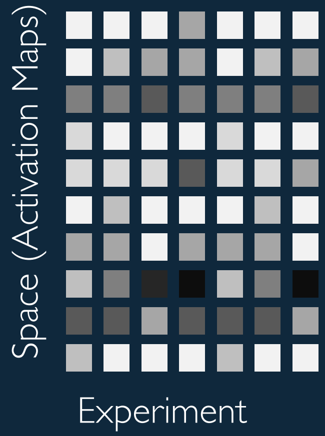


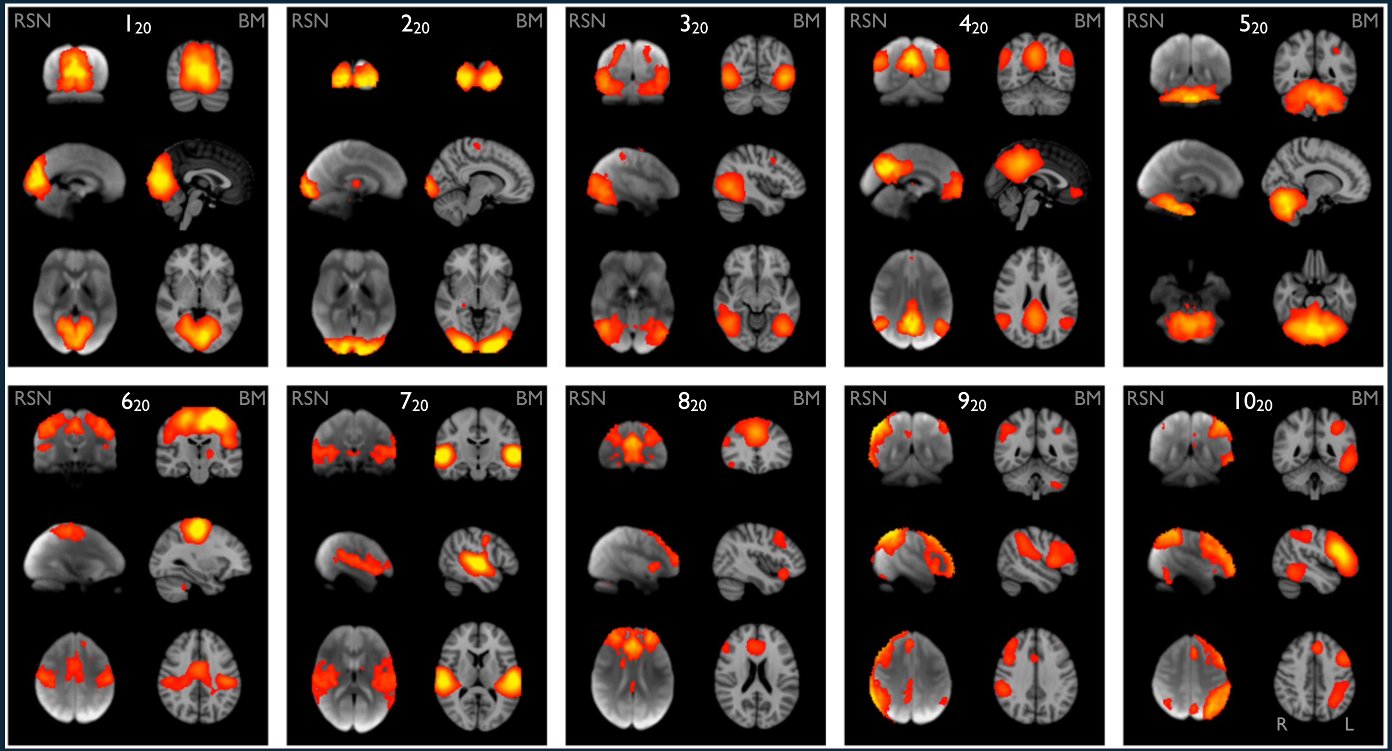


Damoiseaux et al., *PNAS* 2006

Space x Experiment

BM (BrainMap)





Smith et al., *PNAS* 2009

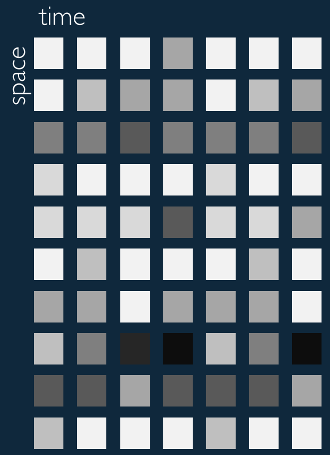
ICA Linear Model

GLM

Measured

unknown

Known Input



=

Spatial Maps
(Sources)

×

Time Courses
(Source Mixtures)

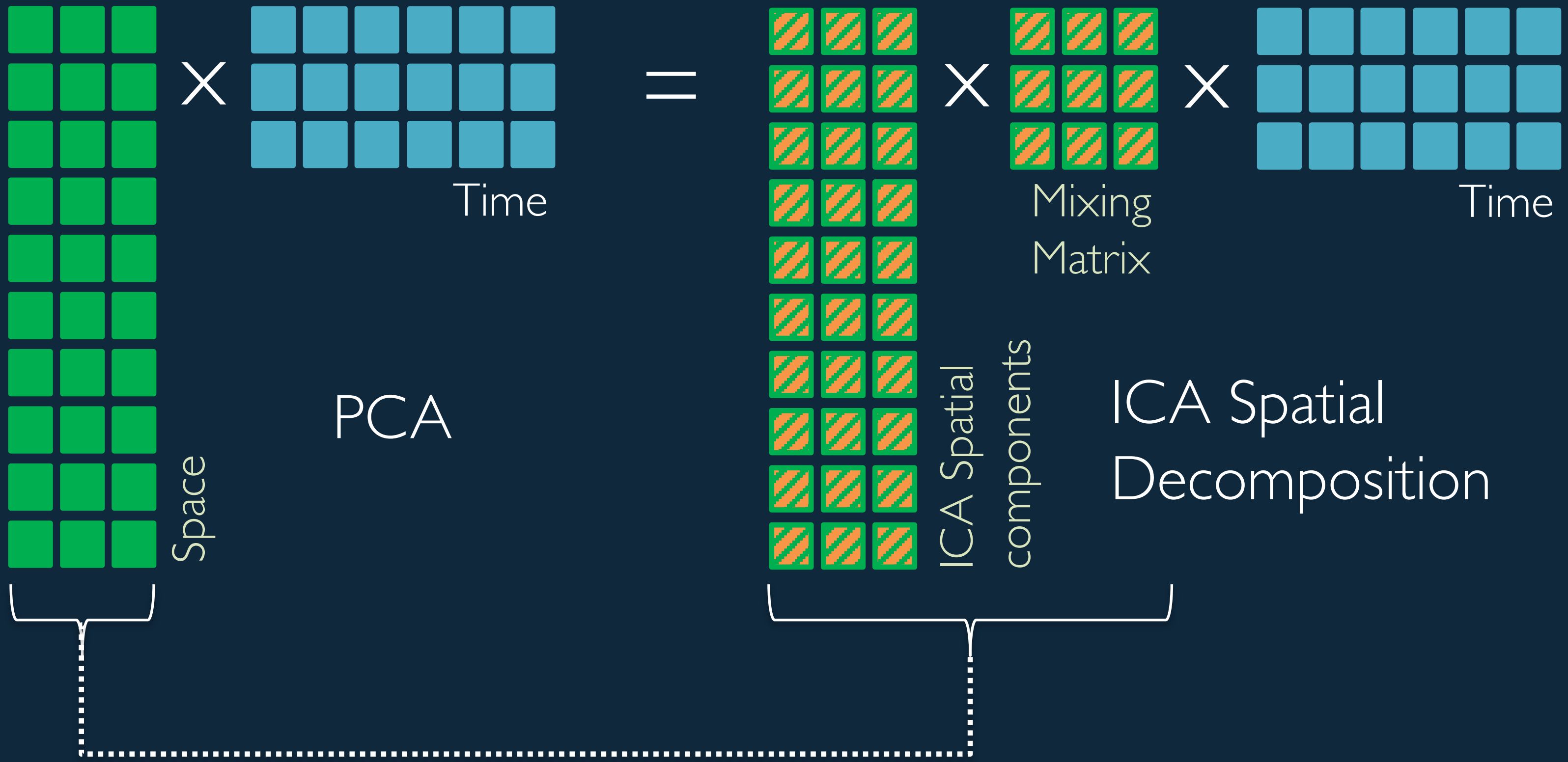
ICA

Measured

unknown

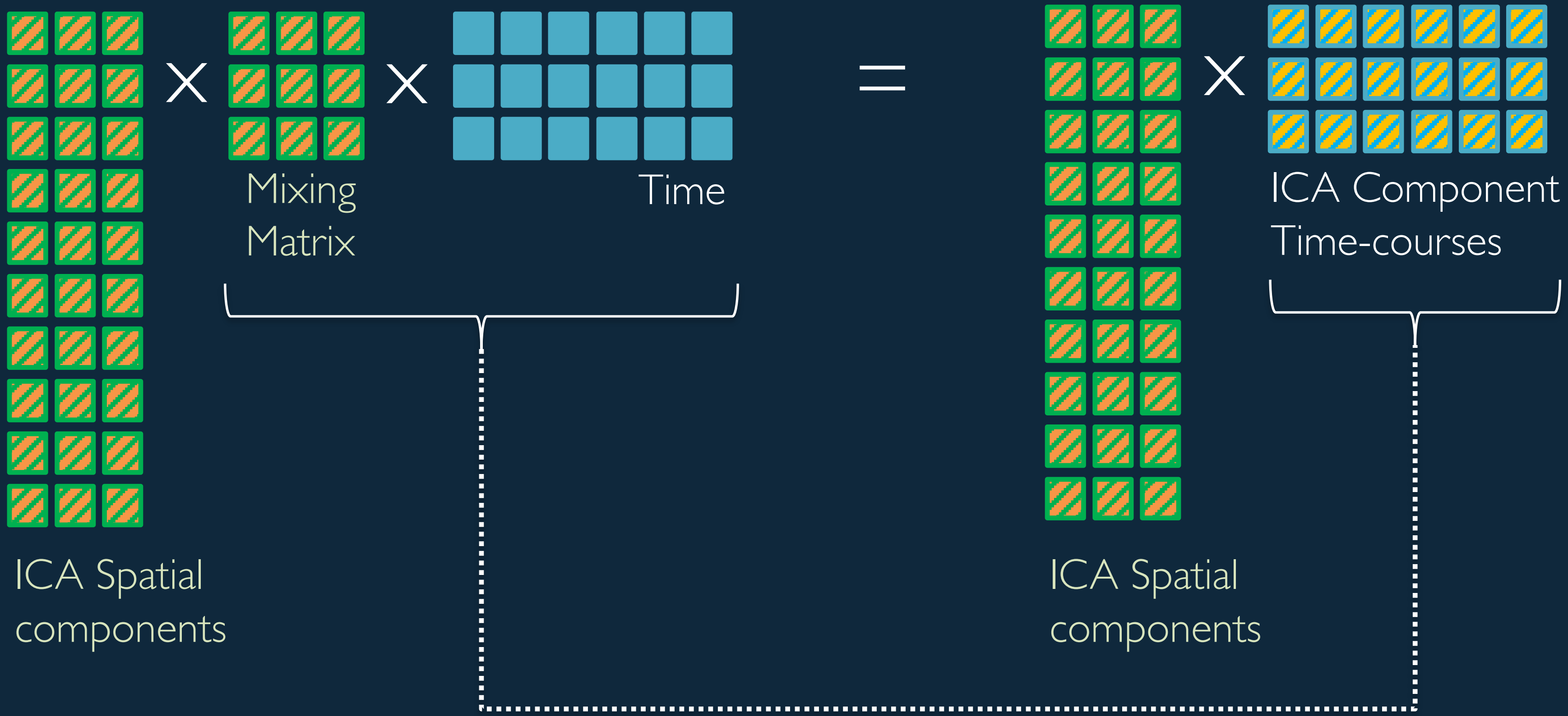
unknown

PCA Pre-processing



ICA Spatial
Decomposition

ICA Time-Courses



ICA Spatial and Temporal dimensions

Temporal Dimensions: ~ 10^2

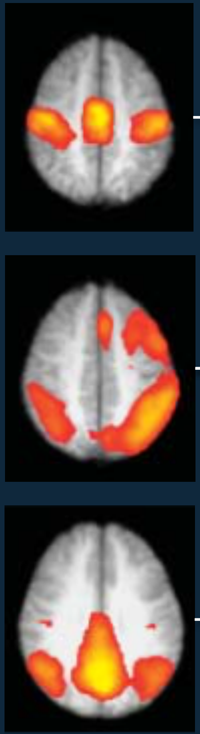
300 time-points

Gaussian or not?

Spatial Dimensions: 64x64x48 ~ 10^5

200,000 voxels

ICA – Inputs and Dimensionality



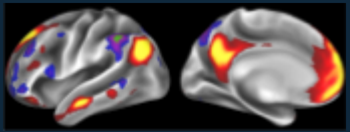
Multiple networks simultaneously from a single decomposition

Very little user input (model free)

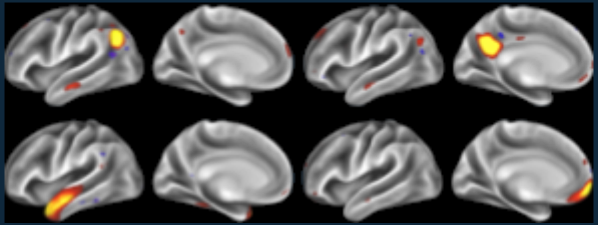
ICA takes a dimensionality (number of networks) input parameter

- *a priori*
- maximising model evidence
- model complexity metrics: AIC/BIC/MDL

Smith et al., *Trends Cog Sci* 2013



Low Dimensionality



High Dimensionality

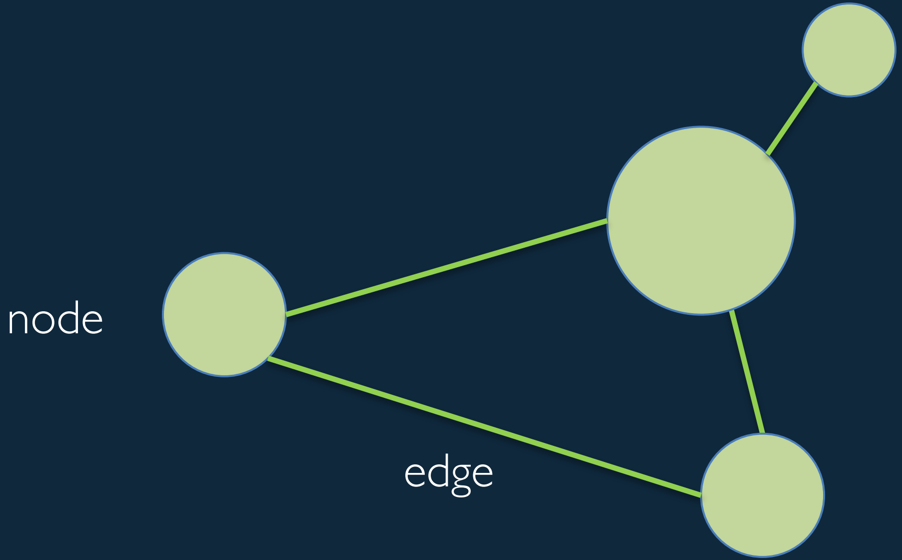
3. GRAPH METHODS

What are Graphs?

Nodes

Some spatial location
A "parcel"

What are Graphs?



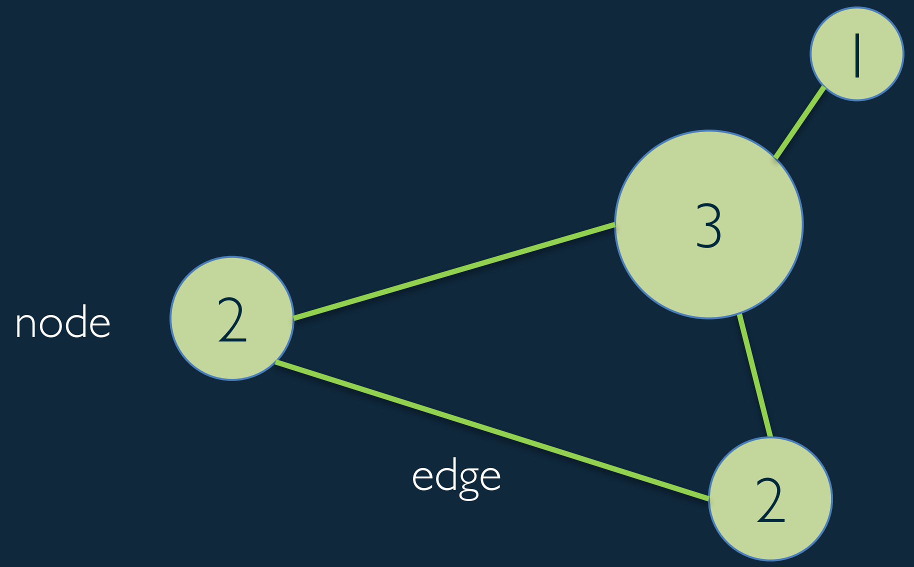
Nodes

Some spatial location
A "parcel"

Edges

Relationship between nodes
Defined by some connectivity metric
Function connectivity → undirected edges

What are Graphs?



Nodes

Some spatial location
A "parcel"

Edges

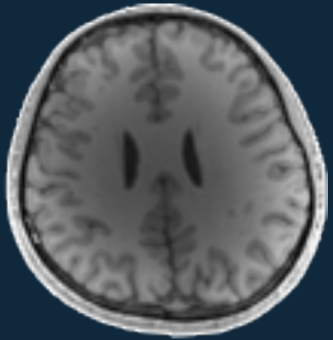
Relationship between nodes
Defined by some connectivity metric
Function connectivity → undirected edges

Degree

Number of connections a node has

Defining Nodes: Parcellation

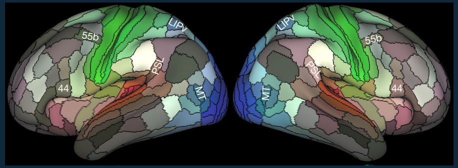
Voxels



Clustering

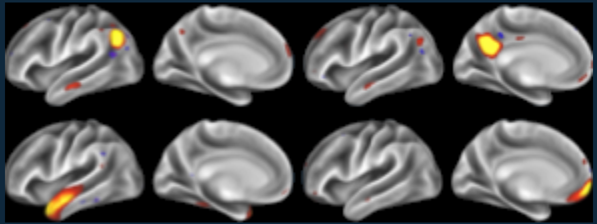
Craddock et al., *Human Brain Mapping* 2012

Multi-Modal



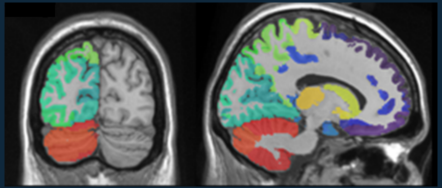
Glasser et al., *Nature* 2016

ICA



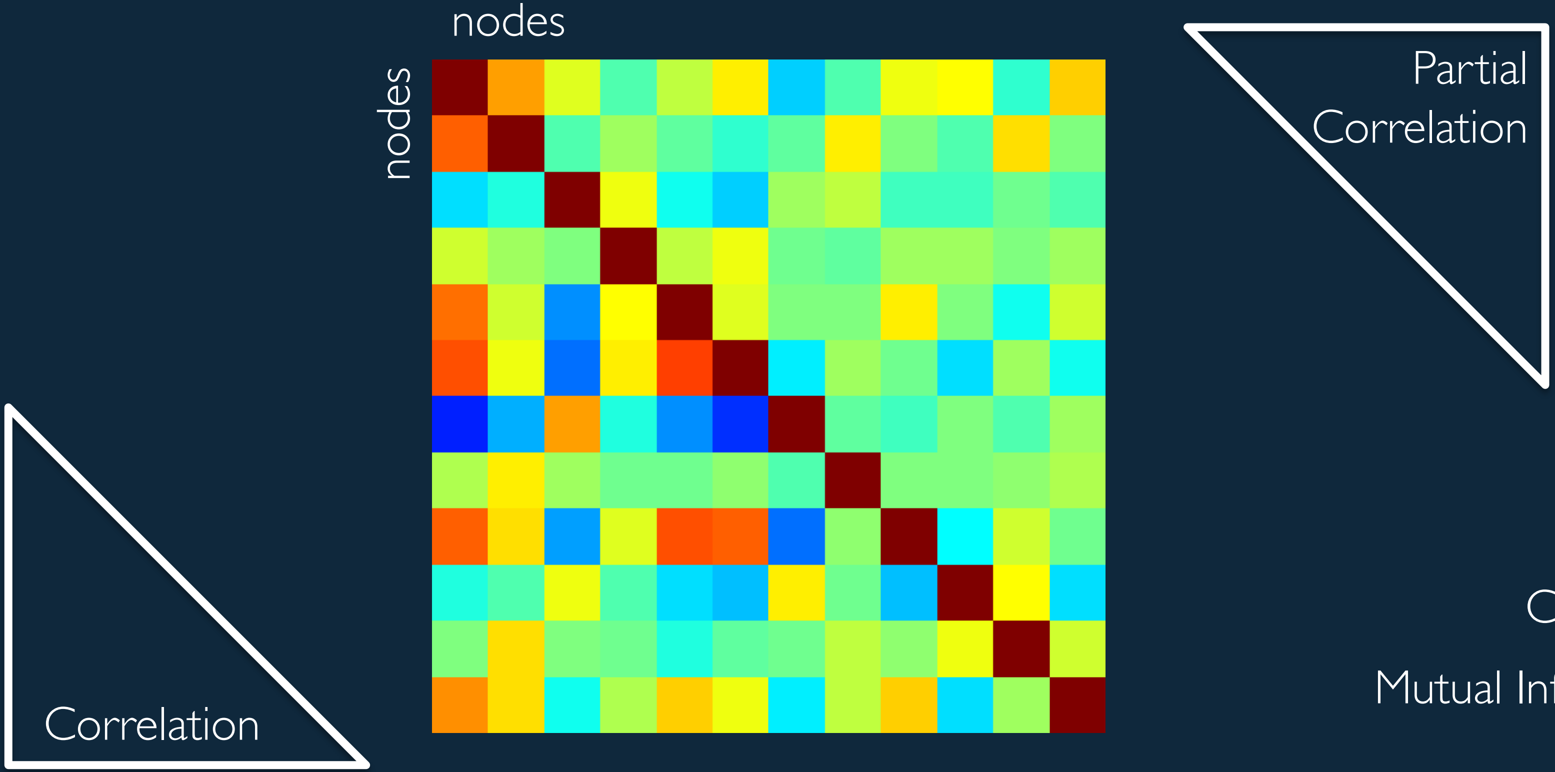
Smith et al., *Trends in Cognitive Neuroscience* 2013

Atlas



Bohland et al., *PLoS One* 2009

Defining Edge Strengths

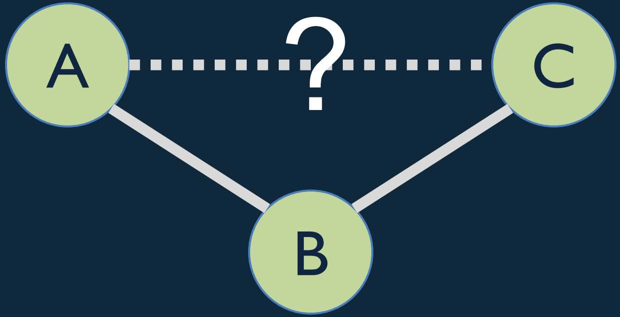


Coherence

Mutual Information

Patel's κ

Partial Correlation



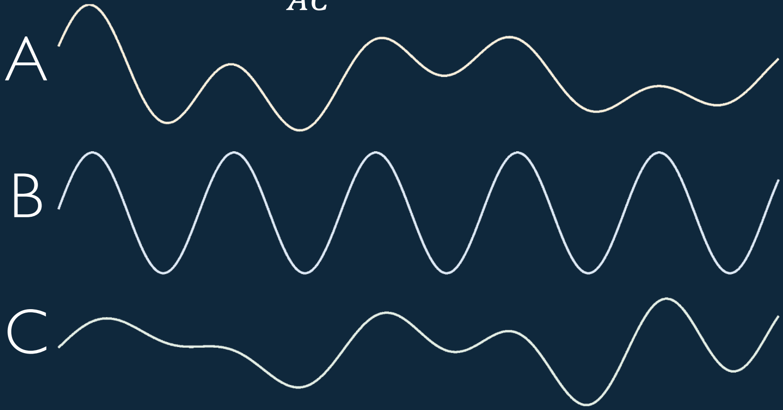
Full Correlation

A→C strong connectivity

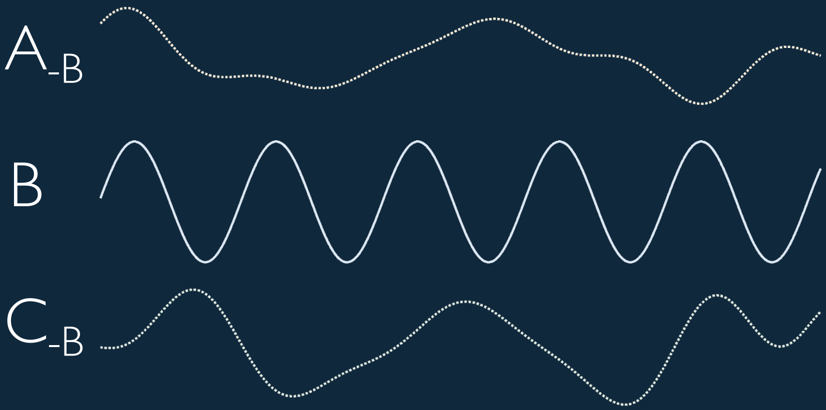
Partial Correlation

A→C weak connectivity

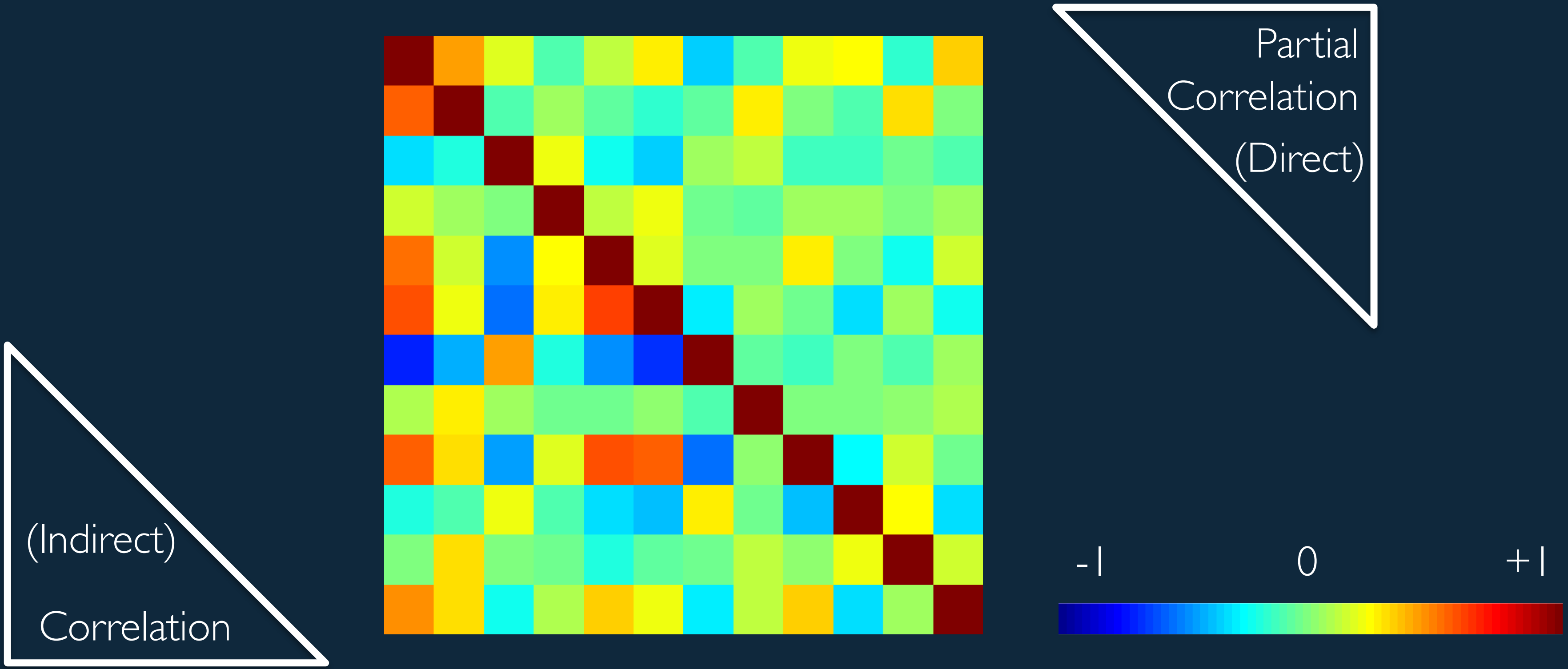
$$r_{AC}^{full} = 0.58$$



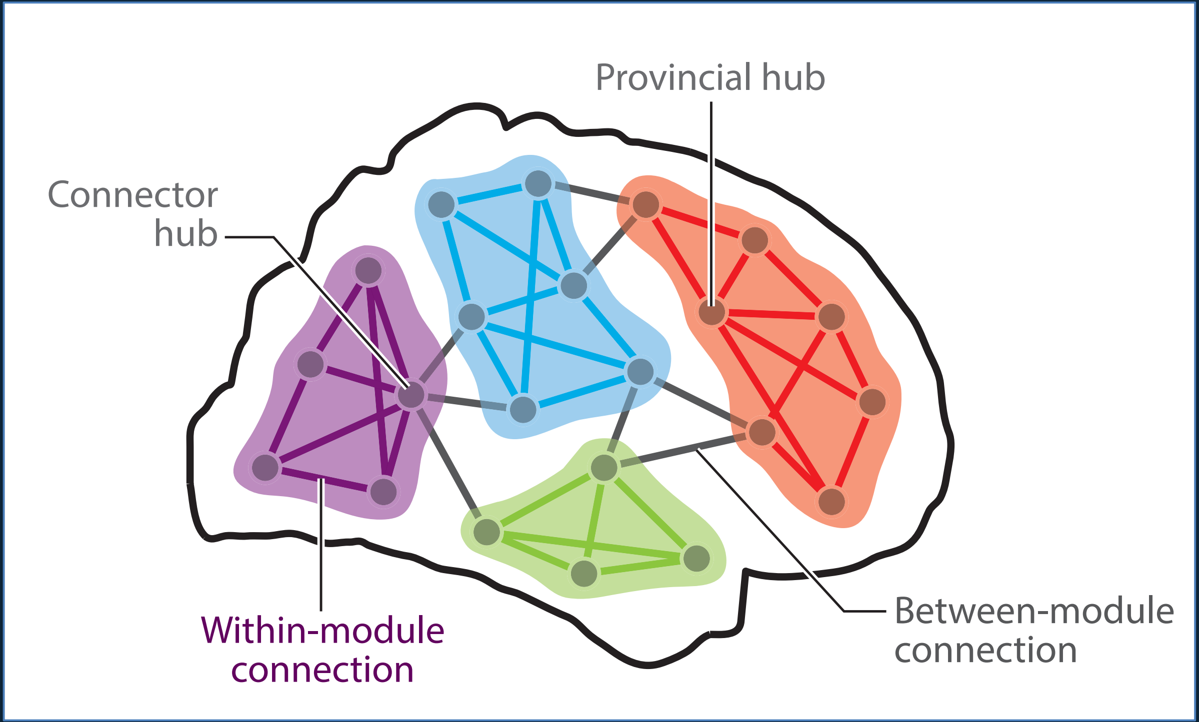
$$r_{AC}^{partial} = 0.21$$



Partial Correlation Network Matrix



Network Features - Hubs

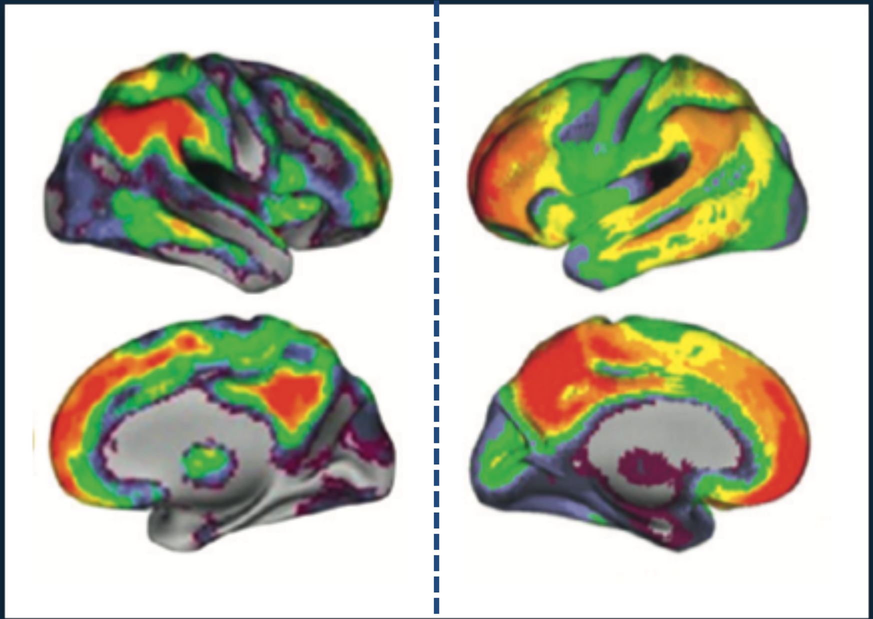


Sporns et al., *Ann Rev Psych* 2016

Network Features – Hubs and Centrality

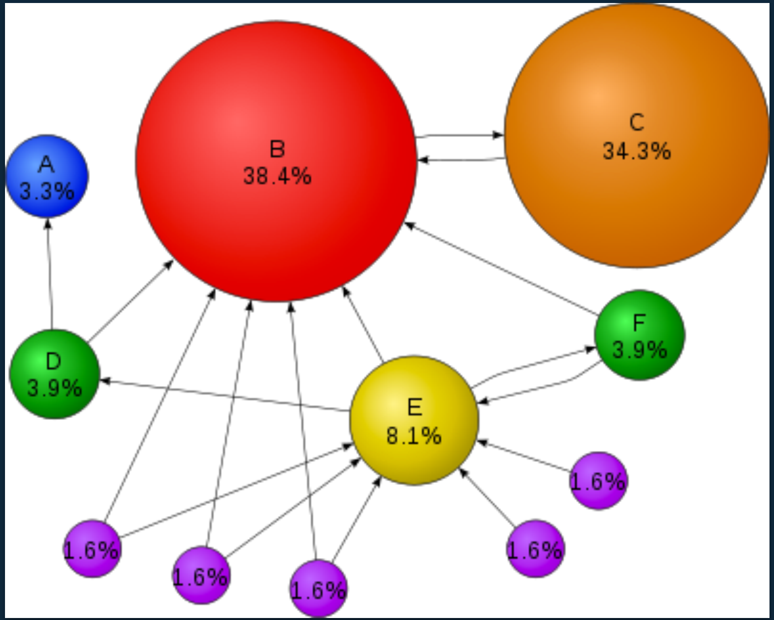
Functional Connectivity Hubs

Alzheimer's Aβ Deposition



van den Heuvel, *Trends in Cog Sci* 2013

Google PageRank Centrality

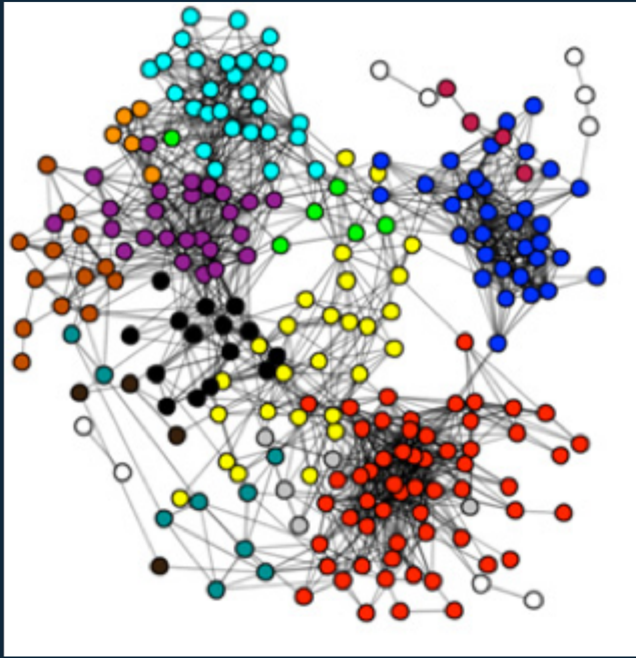


courtesy of Wikipedia

Network Features - Communities

Community/Subgraph/Module Detection

network efficiency



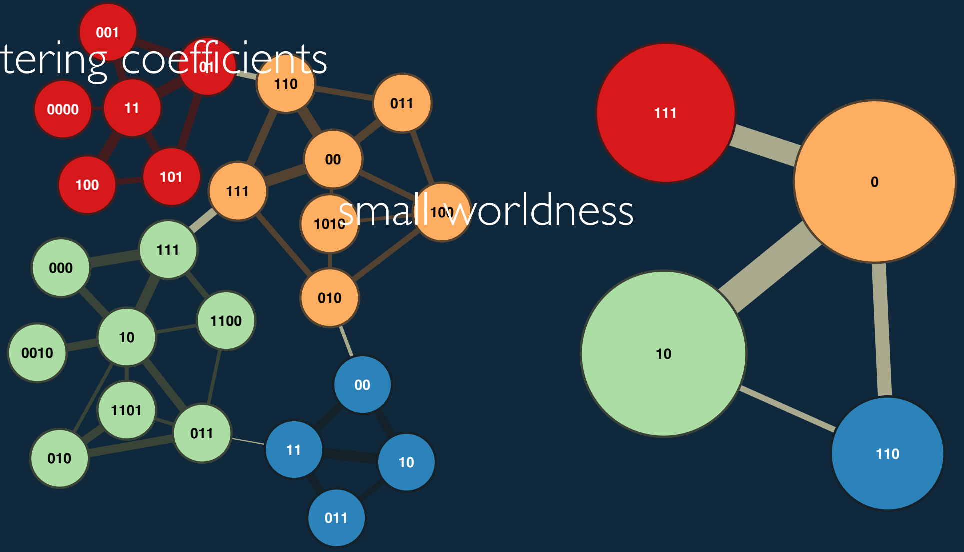
Power et al., *Neuron* 2011

InfoMap

Rosvall et al., *PNAS* 2008

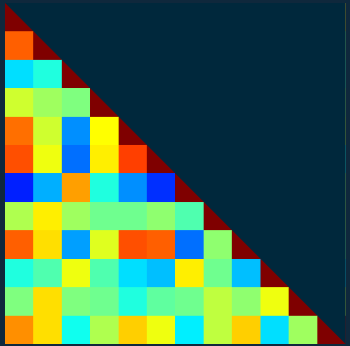
clustering coefficients

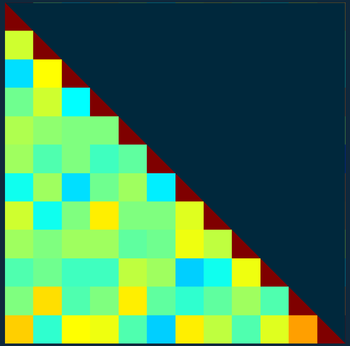
small worldness

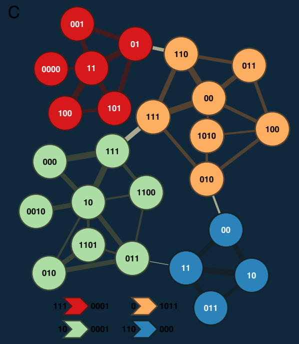


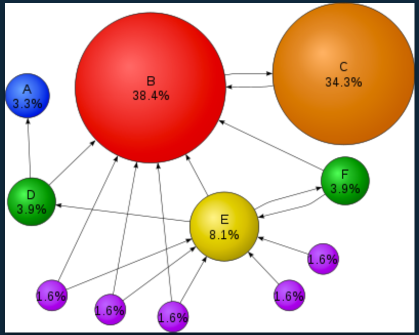
Graph Analysis – Many Choices

Node Definition / Parcellation	Edge Metric	Feature Extraction









Connectivity Comparison

Spatial Information

Spatial ICA
Spatial coefficient distributions

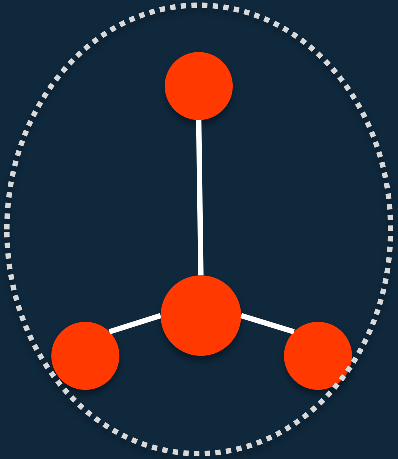
Graph Methods
Parcellations
Edge metrics

Seed Correlation
Seed size, location
Temporal correlations

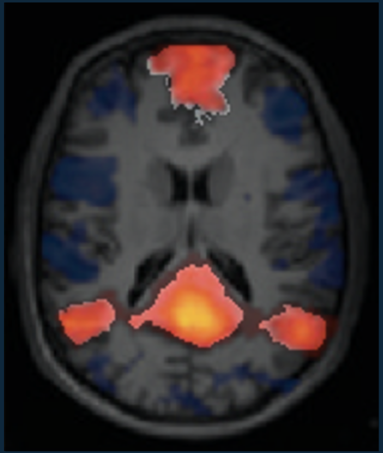
Temporal Information

Connectivity Comparison

Default Mode Network



Seed Correlation (PCC)



Uddin et al., HBM 2009

Spatial ICA

De Luca et al., NeuroImage 2006

Subgraph Detection (red)

Power et al., *Neuron* 2011

DYNAMIC FUNCTIONAL CONNECTIVITY

Dynamic Connectivity

Changing connectivity profiles over time

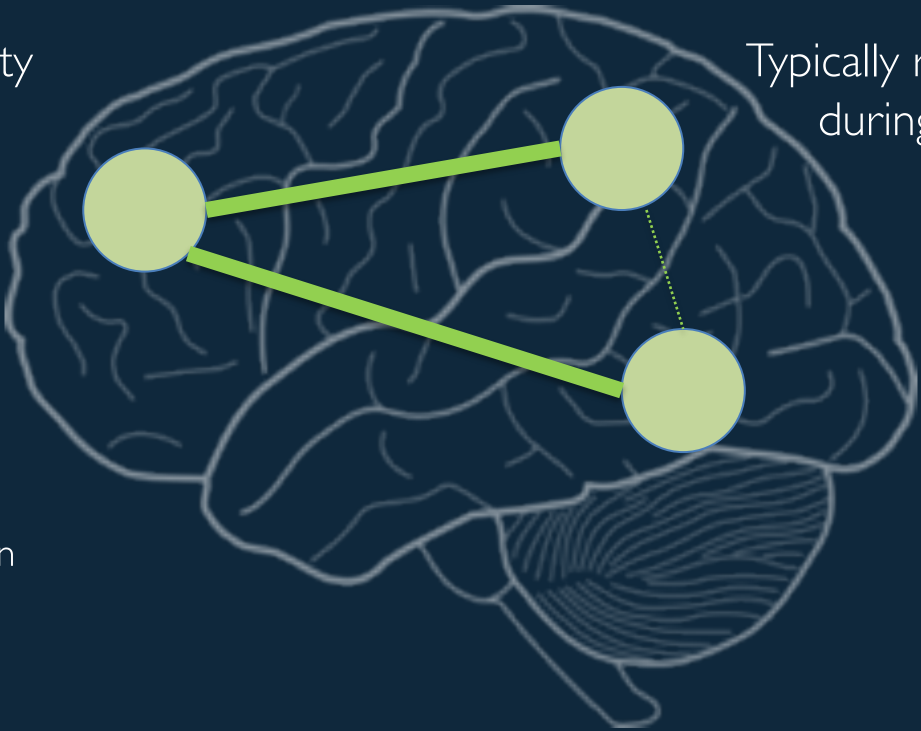
Dynamic Connectivity

Changing connectivity profiles over time

Typically refers to changes during a scan or experiment

Dynamic Connectivity

Changing connectivity profiles over time



Typically refers to changes during a scan or experiment

Changes in :

- internal "state"
- top-down modulation
- attention
- learning
- etc

Dynamic Connectivity

Changing connectivity profiles over time

Typically refers to changes during a scan or experiment

Changes in :

- internal "state"
- top-down modulation
- attention
- learning
- etc

Sliding Window Correlation

Chang et al., *NeuroImage* 2010

Temporal Independent Component Analysis

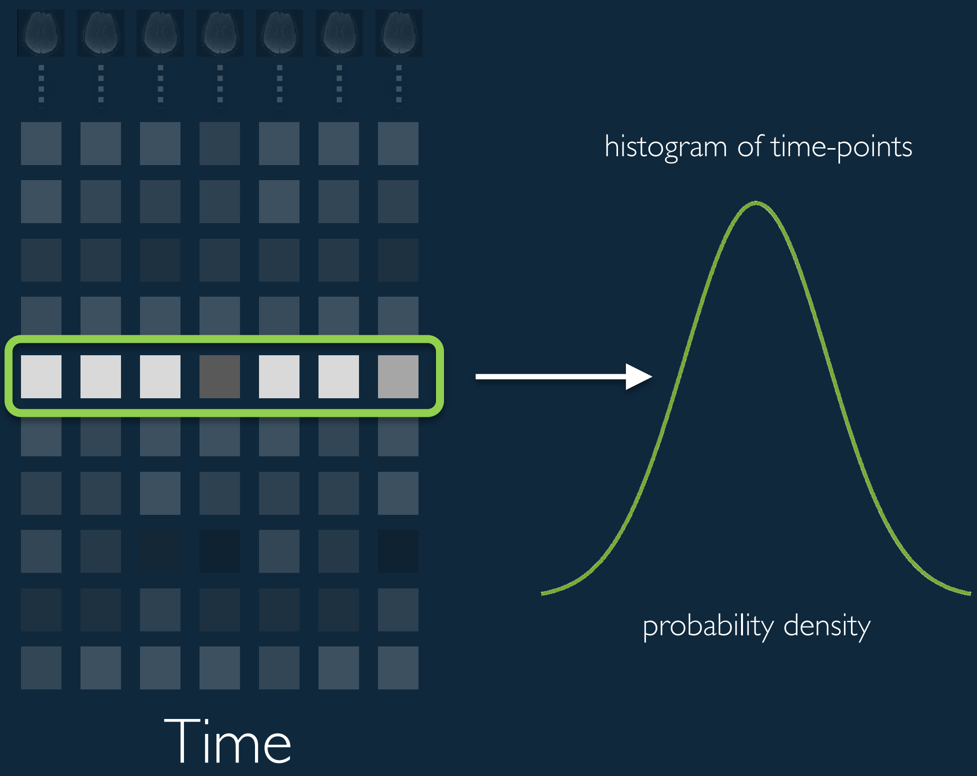
Time-courses are *independent*

Functional Integration:

Spatial ICA –
spatially non-overlapping

Temporal ICA –
spatially overlapping

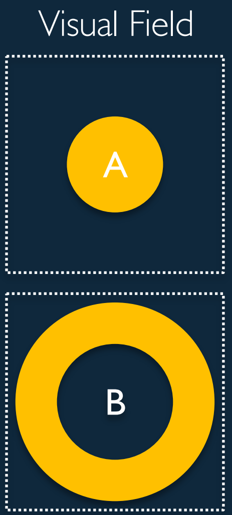
Accounts for temporal
non-stationarity in correlation models

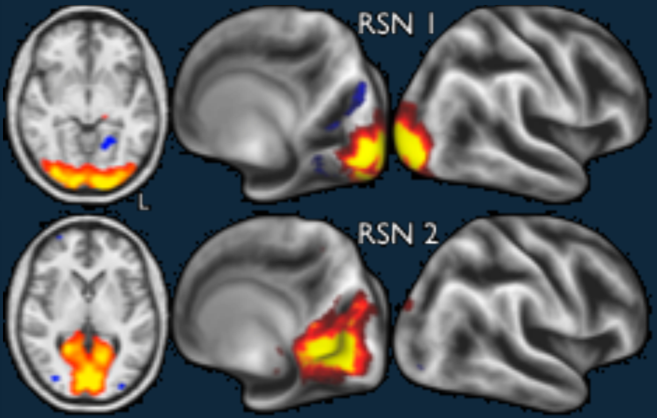


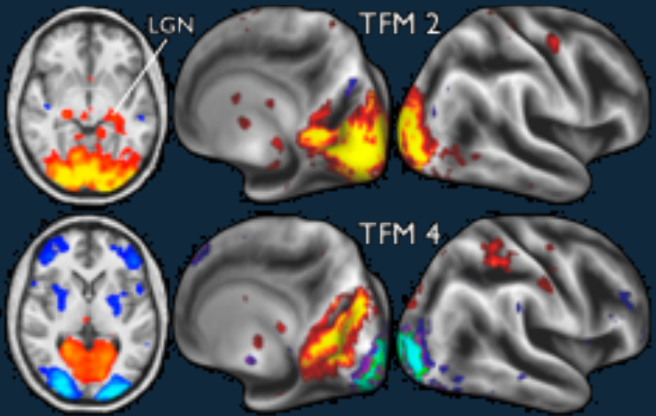
Spatial vs Temporal Decompositions

RSN: Spatial ICA

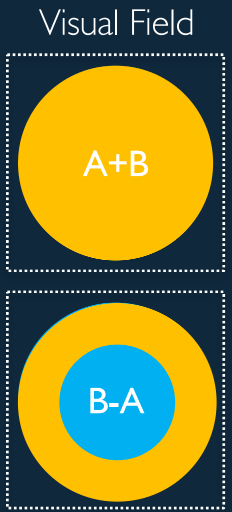
TFM: Temporal ICA







Smith et al., *PNAS* 2012



Spatially non-overlapping

Spatially overlapping

Temporal Dimensionality

Temporal Dimensions: ~ 10^2

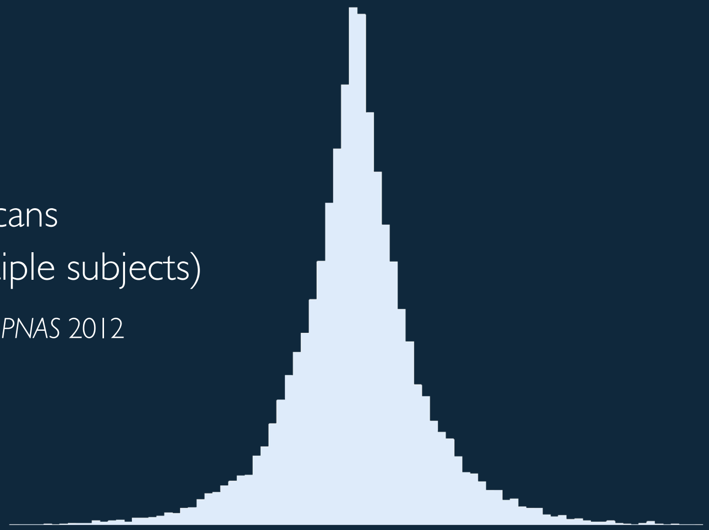
300 time-points

36×10 minute scans

(SMS-EPI, multiple subjects)

Smith et al., *PNAS* 2012

Temporal Dimensions ~ 10^4



24,000 time-points

SUMMARY

Summary

- Not an exhaustive list of connectivity methods!
- Many different methods and metrics for quantifying connectivity
  - Using information across space, time, or some combination
- Connectivity in RS-FMRI shows remarkably robust structures
- But outputs reflect constraints, assumptions and models used