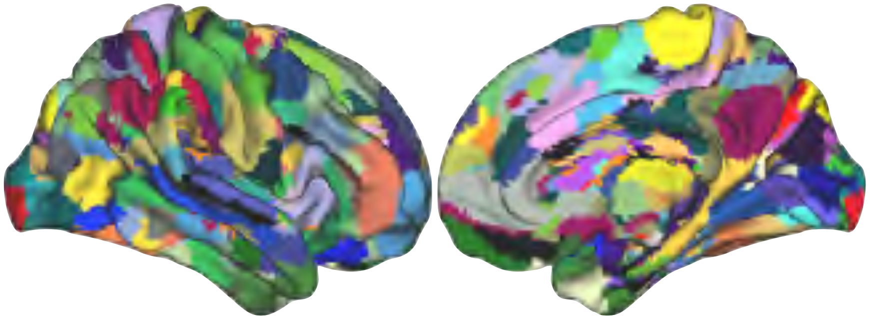
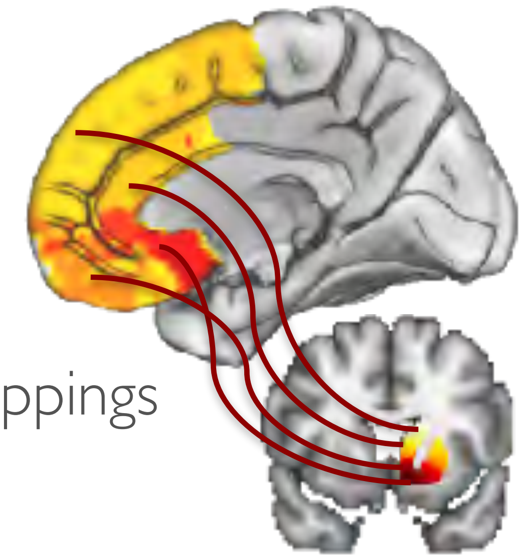
ICP & Congrads … etc.

Christian F. Beckmann

Overview



Connectivity based
parcellations



Connectopic mappings

…etc (MELODIC / FLICA)

Instantaneous Connectivity Parcellations

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

Functional parcellation using time courses of instantaneous connectivity

Erik S.B. van Oort [a,*], Maarten Mennes [a], Tobias Navarro Schröder [a,c], Vinod J. Kumar [d], Nestor I. Zaragoza Jimenez [a,e], Wolfgang Grodd [d], Christian F. Doeller [a,c], Christian F. Beckmann [a,b,f]

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[b] *Radboud University Medical Centre, Department of Cognitive Neuroscience, Nijmegen, The Netherlands*
[c] *Kavli Institute for Systems Neuroscience and Centre for the Biology of Memory, Norwegian University of Science and Technology, NTNU, 7491 Trondheim, Norway*
[d] *Max Planck Institute for Biological Cybernetics, Tübingen, Germany*
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A R T I C L E I N F O

Keywords:
Parcellation
Resting state
FMRI
Motor cortex
Thalamus
Subcortex
Entorhinal cortex

A B S T R A C T

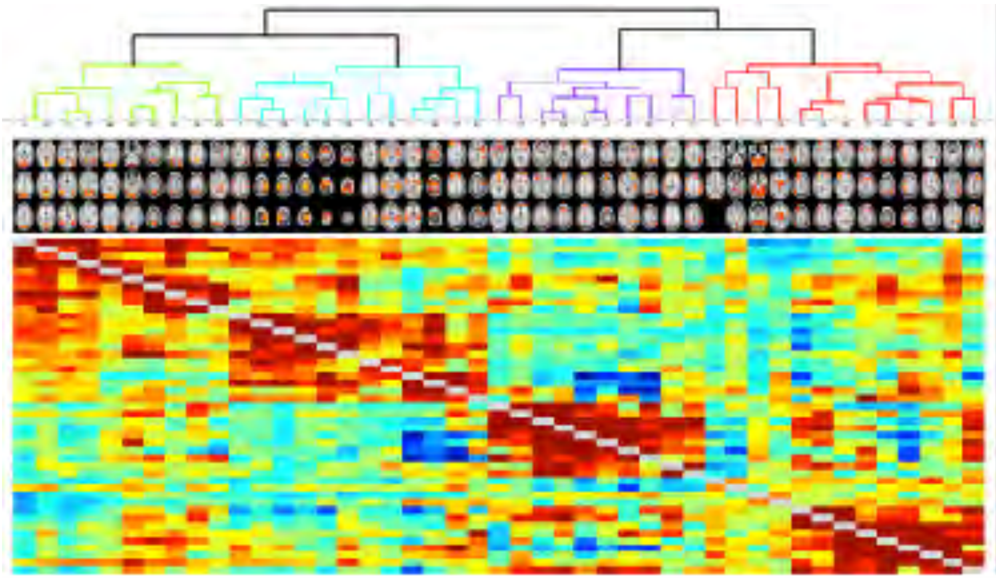
Functional neuroimaging studies have led to understanding the brain as a collection of spatially segregated functional networks. It is thought that each of these networks is in turn composed of a set of distinct sub-regions that together support each network's function. Considering the sub-regions to be an essential part of the brain's functional architecture, several strategies have been put forward that aim at identifying the functional sub-units of the brain by means of functional parcellations. Current parcellation strategies typically employ a bottom-up strategy, creating a parcellation by clustering smaller units. We propose a novel top-down parcellation strategy, using time courses of instantaneous connectivity to subdivide an initial region of interest into sub-regions. We use split-half reproducibility to choose the optimal number of sub-regions.

We apply our Instantaneous Connectivity Parcellation (ICP) strategy on high-quality resting-state FMRI data, and demonstrate the ability to generate parcellations for thalamus, entorhinal cortex, motor cortex, and subcortex including brainstem and striatum. We evaluate the subdivisions against available cytoarchitecture maps to show that our parcellation strategy recovers biologically valid subdivisions that adhere to known cytoarchitectural features.

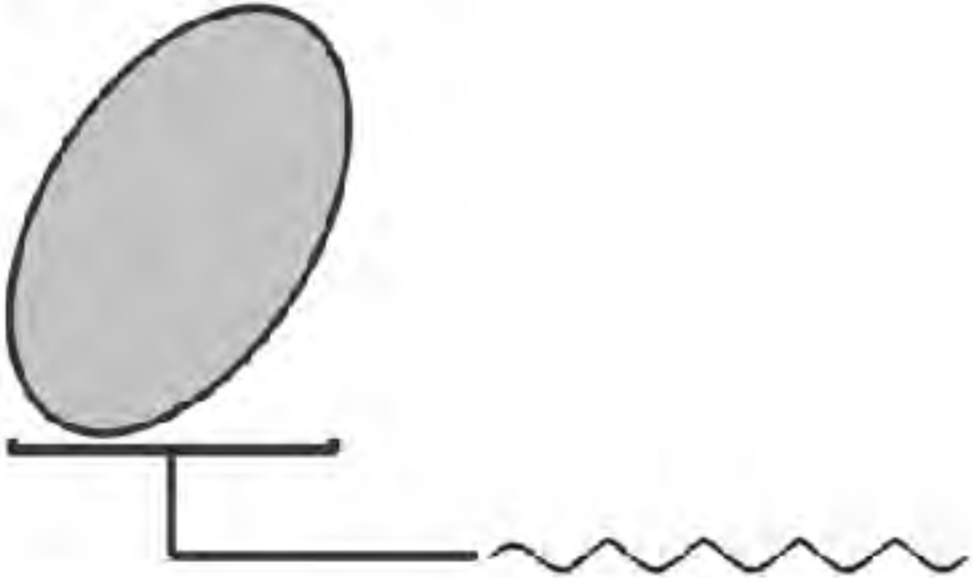
van Oort et al. (2017) Functional Parcellation using time courses of instantaneous connectivity. NeuroImage 170:31-40.

‘Bottom-up’ parcellations

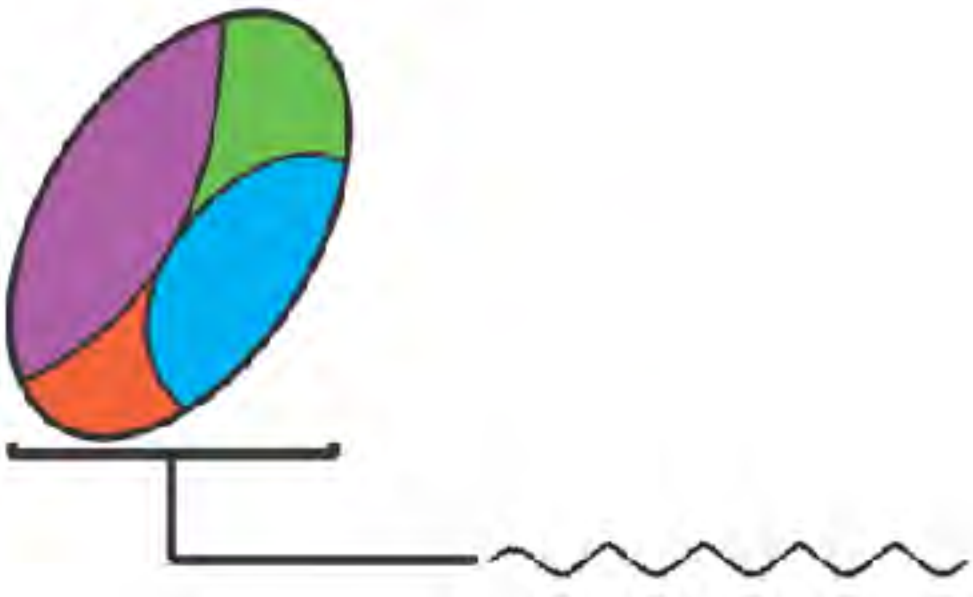
- *Lack of biological validity*
- Choice of scale is arbitrary
- Chosen scale might be too high for the data, enforcing splits that do not reflect underlying differences in function / connectivity
- Solution: Top-down parcellation.
  - Need to understand how systems break into subcomponents



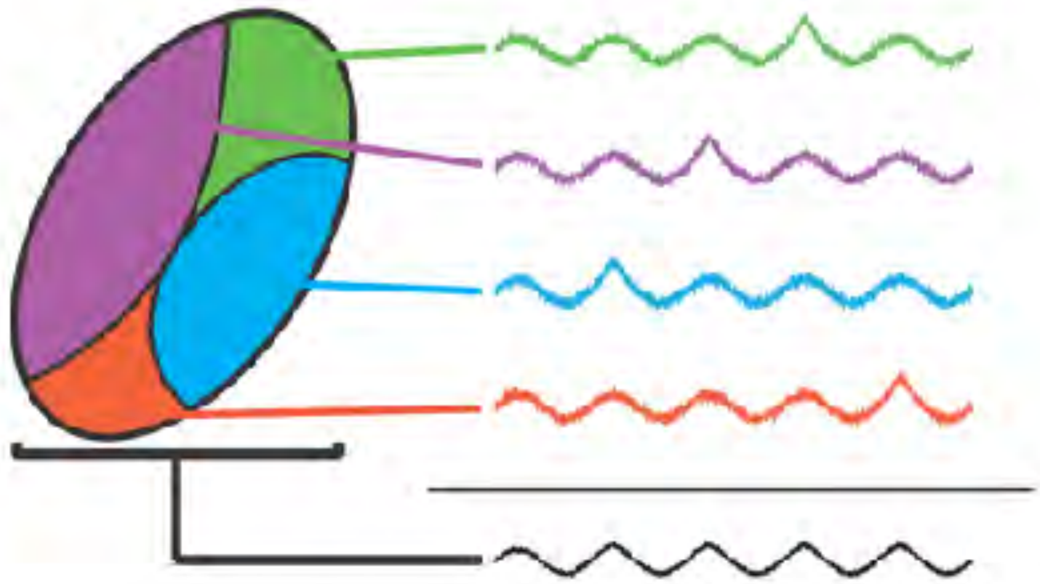
‘Top-down’ parcellations



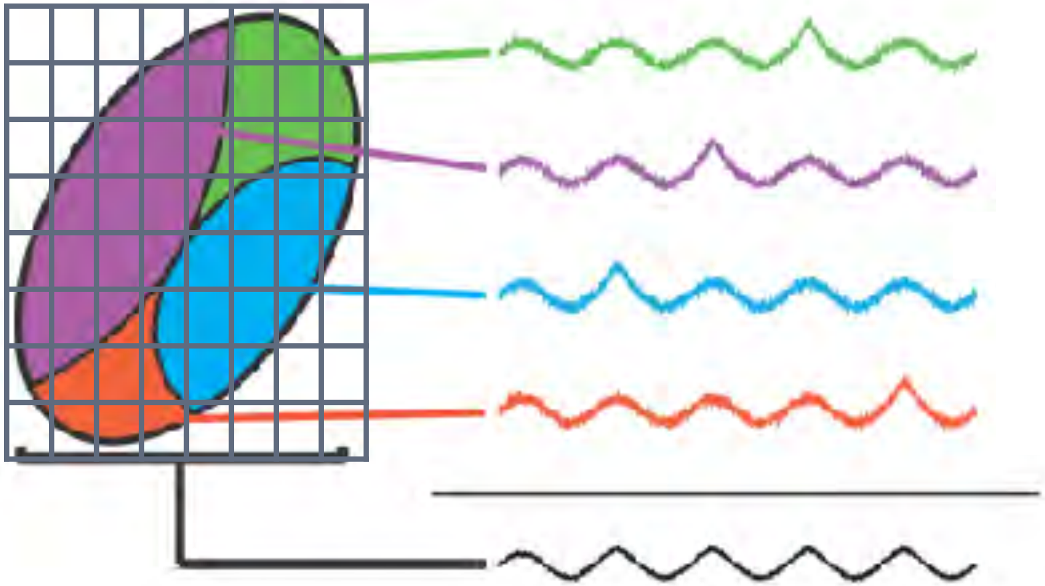
‘Top-down’ parcellations



‘Top-down’ parcellations



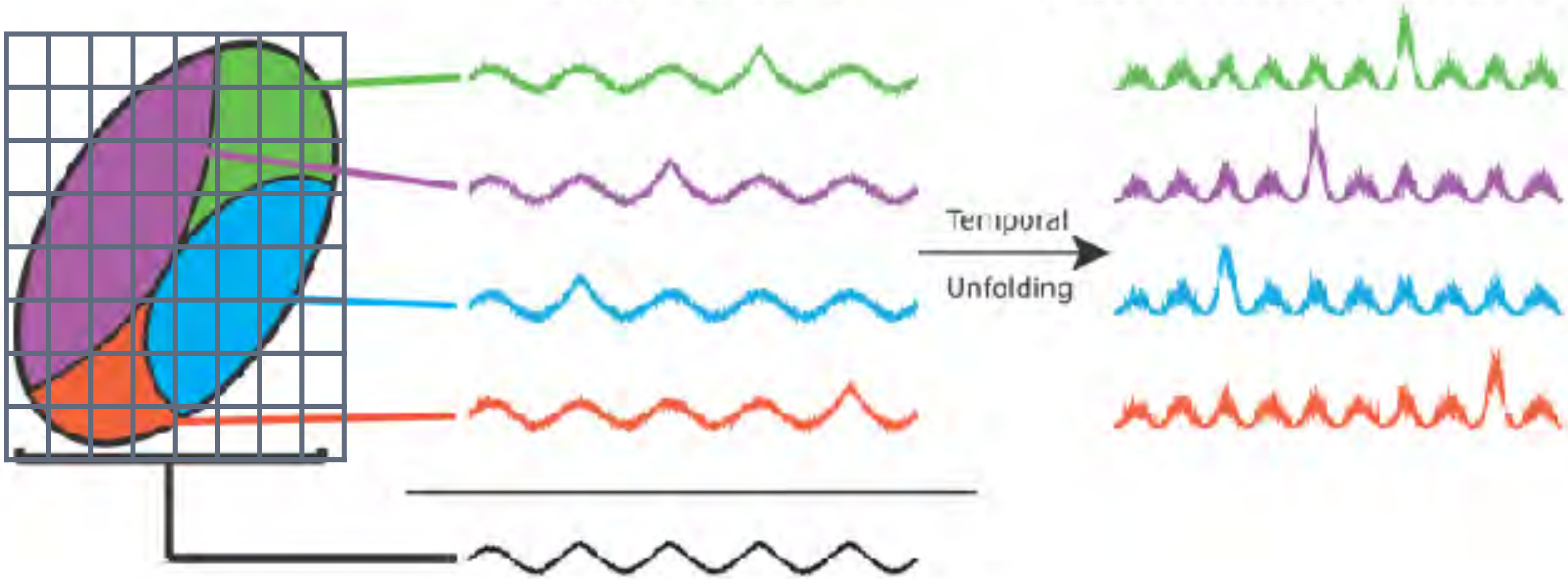
‘Top-down’ parcellations



$$\rho_{x,y} = \frac{1}{T}\sum_{n=1}^{T} x(n)y(n)$$

some measure of ‘connectivity’… PC, say

‘Top-down’ parcellations

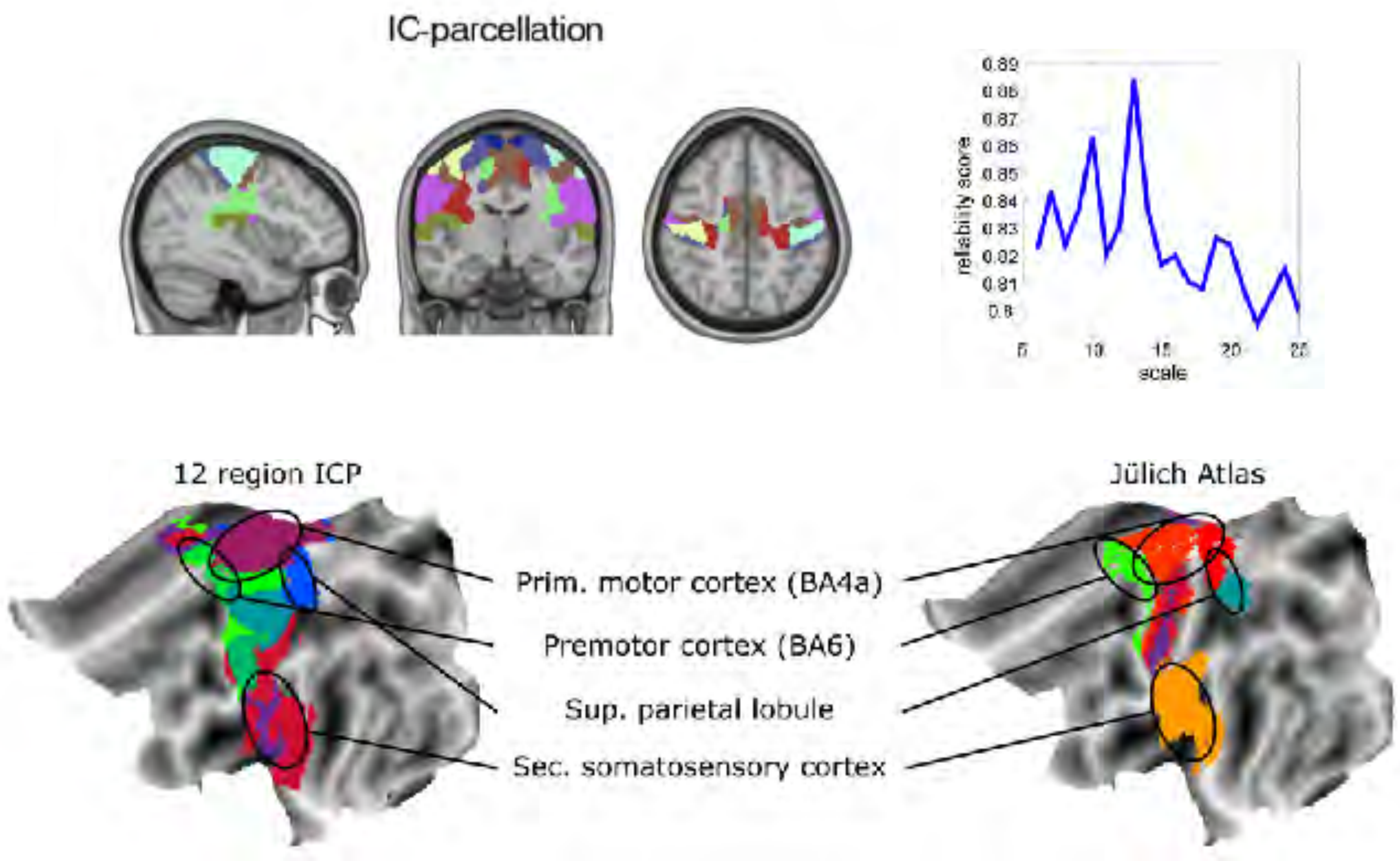


$$\rho_{x,y} = \cancel{\frac{1}{T}\sum_{n=1}^{T}} x(n)y(n)$$

some measure of ‘connectivity’… PC, say

Instantaneous Connectivity: reflect how much a given time point contributes to the final measure of ‘connectivity’:
Pearson Correlation -> Shur product

Example: ICP in the motor system

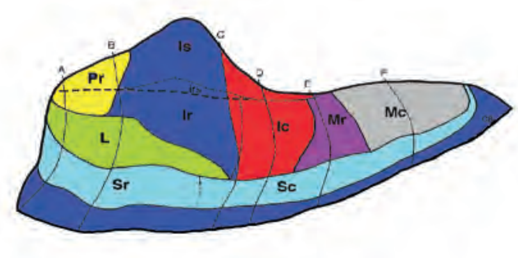


Van Oort, Mennes … Beckmann
NeuroImage 2017

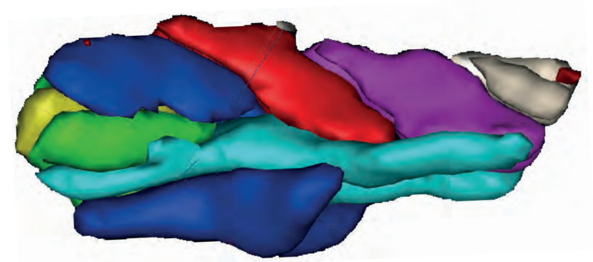
Example: ICP in subcortex

Entorhinal cortex

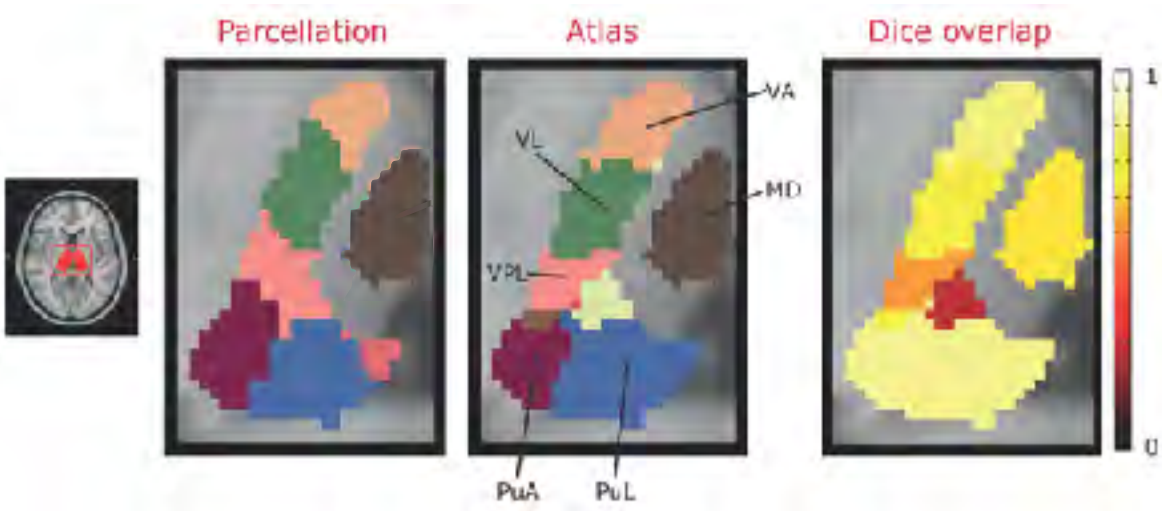
Histological Atlas
Krimer et al 1997



In-vivo t-fMRI
ICP



Thalamus

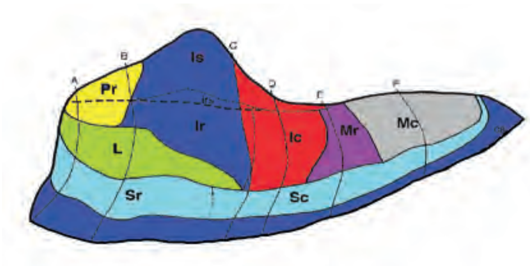


Van Oort, Mennes … Beckmann
NeuroImage 2017

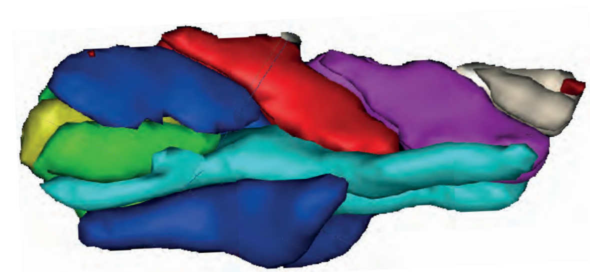
Example: ICP in subcortex

Entorhinal cortex

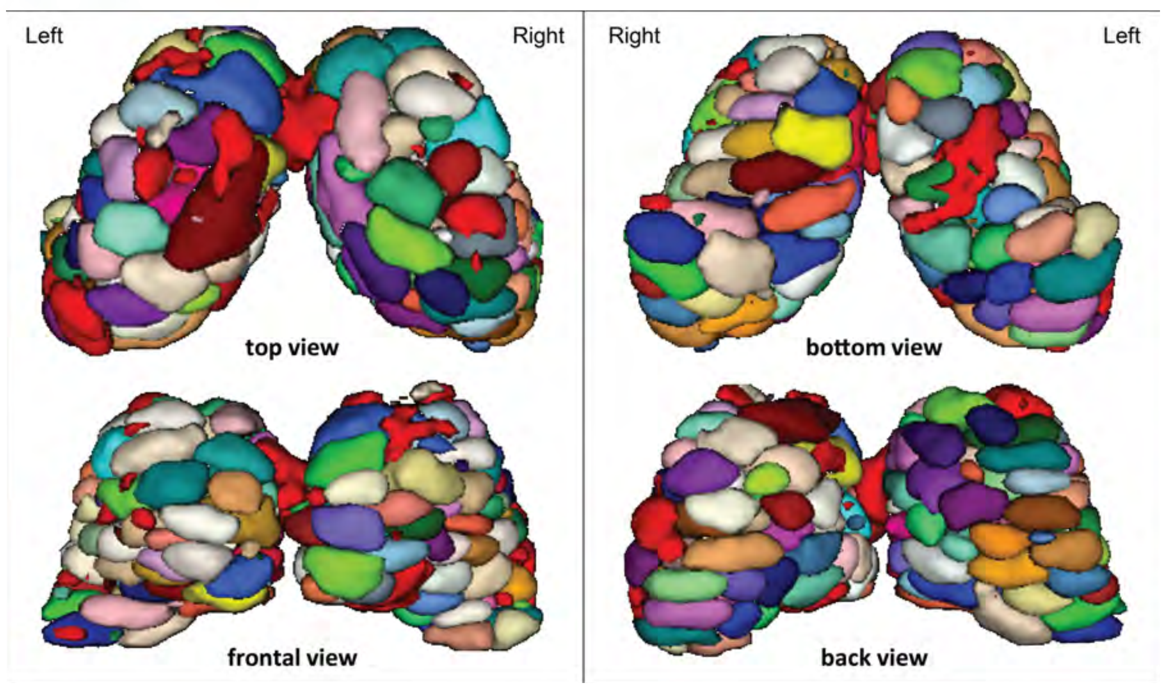
Histological Atlas
Krimer et al 1997



In-vivo t-fMRI
ICP

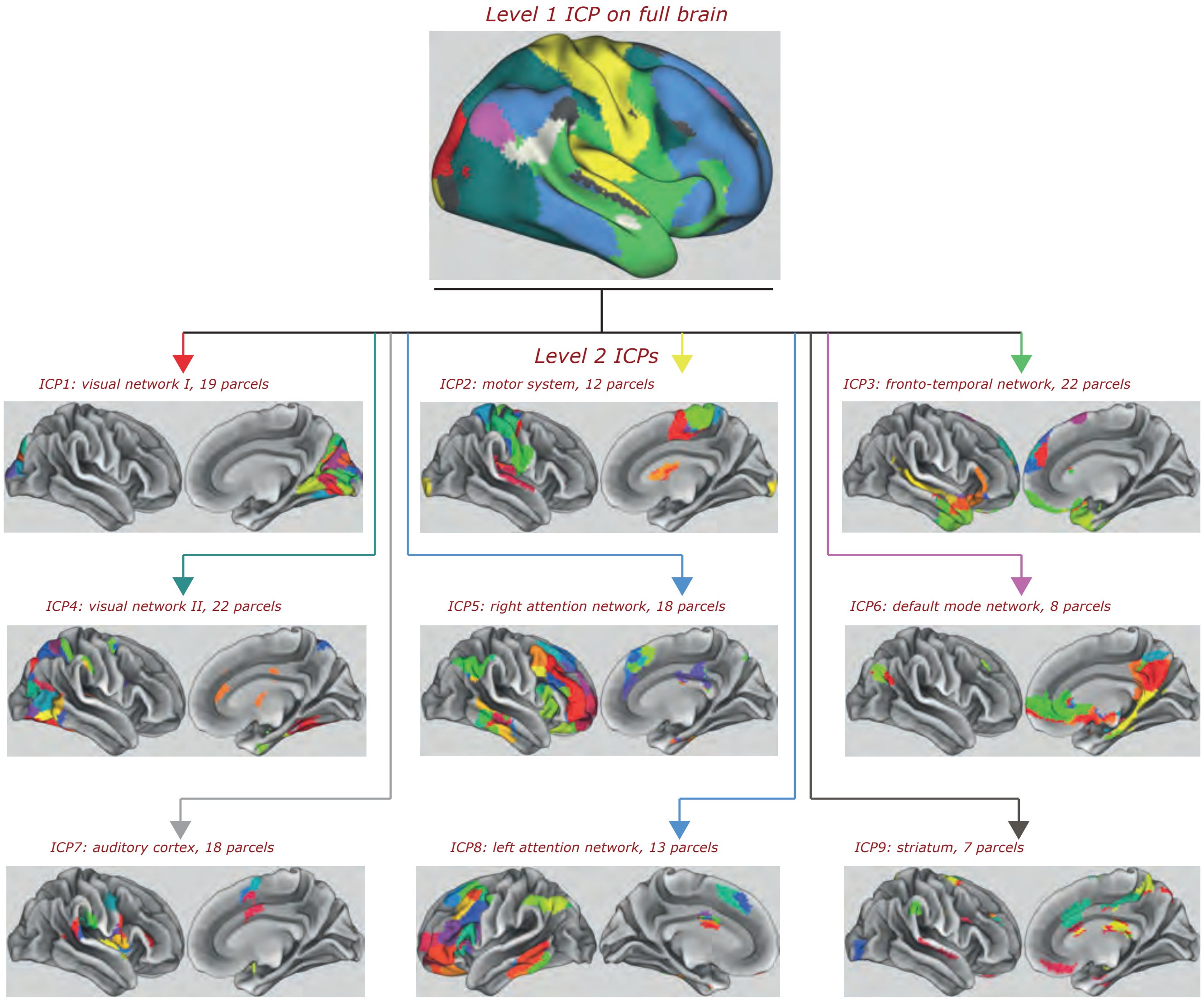


Thalamus



See poster 2725!
Kumar et al.

Hierarchical functional atlas of the human brain



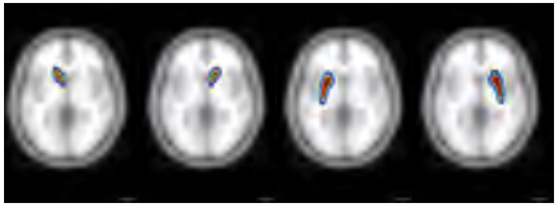
Van Oort et al, in preparation

Example: Dopamine Transporter SPECT data

Comparison of canonical ROIs vs rfMRI network-derived basis functions

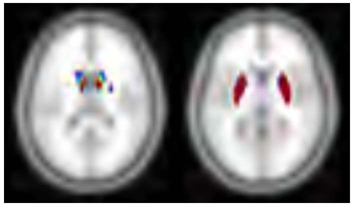
Anatomically-informed BF: Harvard-Oxford Atlas Prob Maps

n=4

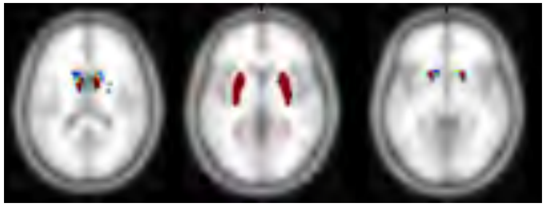


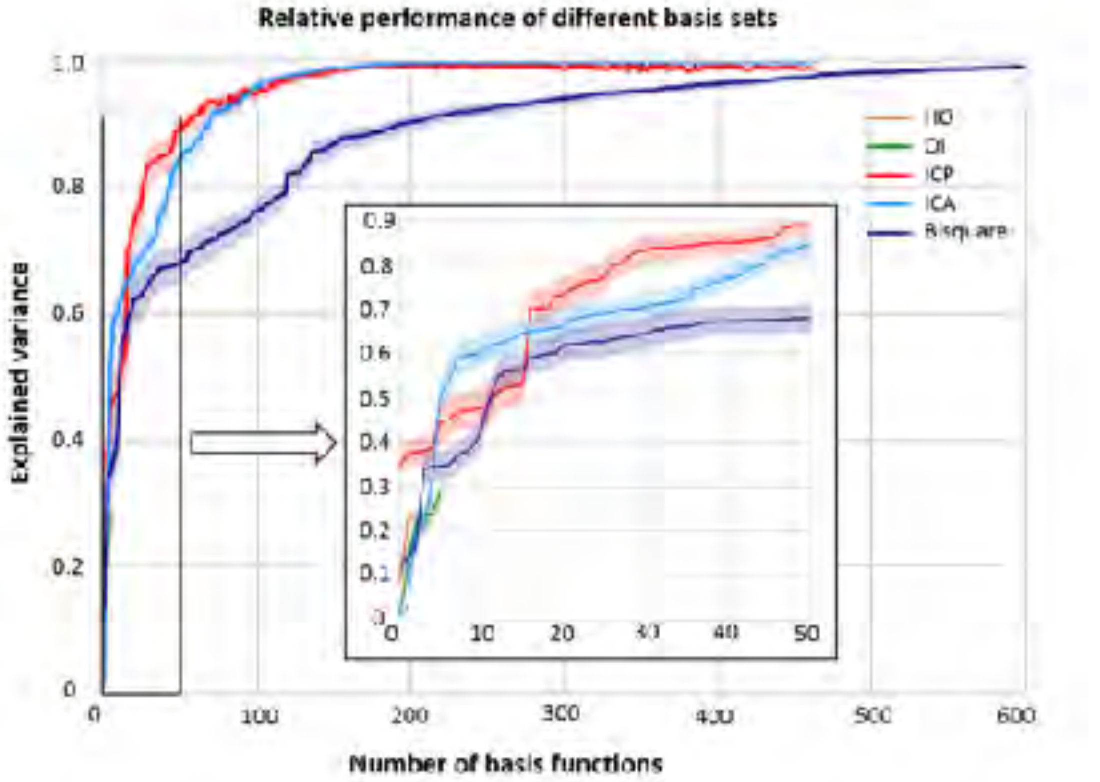
Functionally-informed BF: ICP Prob Maps

n=2



n=3





Huerta et al, NeuroImage 2017

ICP - Instantaneous Connectivity Parcellations

- Implemented in FSL MELODIC
- C++ code-base (ships with every install of FSL)
- command-line option for single-subject and group level analysis
- Automatic dim. estimation
- released in a next version of FSL

www.fmrib.ox.ac.uk/fsl

Connectopic mapping

Topographic organisation as a critical feature of biological information processing

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

Connectopic mapping with resting-state fMRI

Koen V. Haak [a,b,*], Andre F. Marquand [a,b,d], Christian F. Beckmann [a,b,c]

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[b] Department of Cognitive Neuroscience, Radboud University Medical Centre, Nijmegen, 6500 HB, The Netherlands
[c] Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (FMRIB), University of Oxford, Oxford, OX3 9DU, United Kingdom
[d] Department of Neuroimaging, Centre for Neuroimaging Sciences, Institute of Psychiatry, King's College London, De Crespigny Park, London, SE5 8AF, United Kingdom

A R T I C L E I N F O

Keywords:
Resting-state fMRI
Functional connectivity
Topographic maps
Manifold learning
Spatial statistics

A B S T R A C T

Brain regions are often topographically connected: nearby locations within one brain area connect with nearby locations in another area. Mapping these connection topographies, or 'connectopies' in short, is crucial for understanding how information is processed in the brain. Here, we propose principled, fully data-driven methods for mapping connectopies using functional magnetic resonance imaging (fMRI) data acquired at rest by combining spectral embedding of voxel-wise connectivity 'fingerprints' with a novel approach to spatial statistical inference. We apply the approach in human primary motor and visual cortex, and show that it can trace biologically plausible, overlapping connectopies in individual subjects that follow these regions' somatotopic and retinotopic maps. As a generic mechanism to perform inference over connectopies, the new spatial statistics approach enables rigorous statistical testing of hypotheses regarding the fine-grained spatial profile of functional connectivity and whether that profile is different between subjects or between experimental conditions. The combined framework offers a fundamental alternative to existing approaches to investigating functional connectivity in the brain, from voxel- or seed-pair wise characterizations of functional association, towards a full, multivariate characterization of spatial topography.

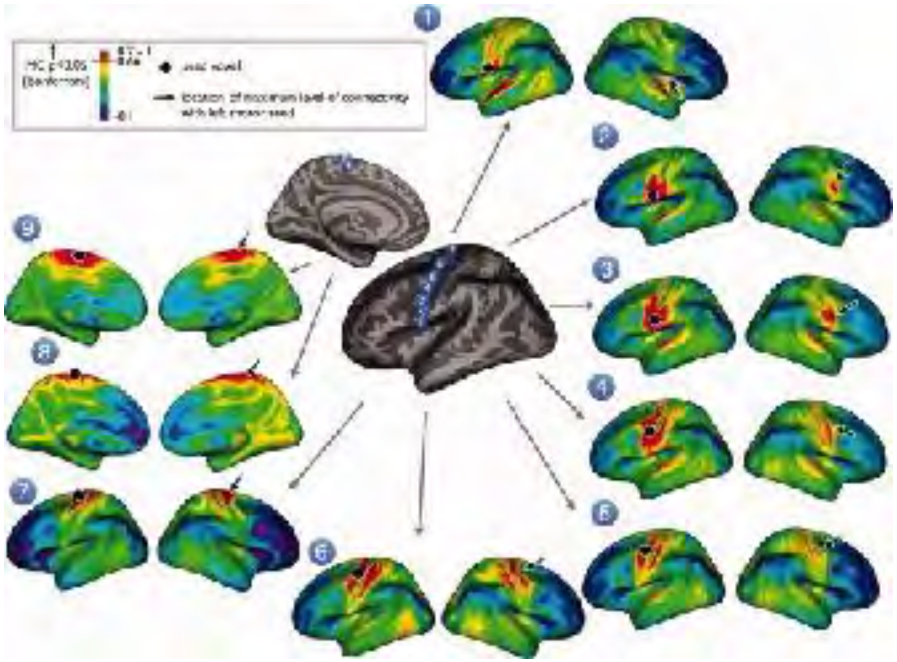
1. Introduction

An important open question in systems neuroscience is how the

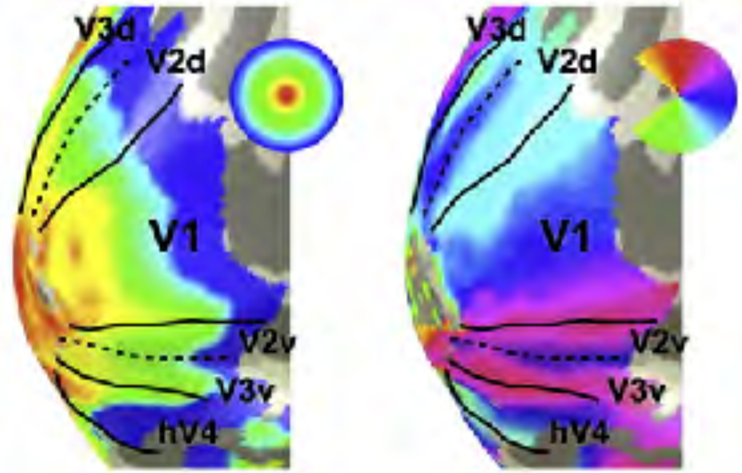
characterize the brain into parcels of homogeneous connectivity (Smith, 2012; Smith et al., 2013b; Power et al., 2014), while viable analysis methods for mapping these fine-grained patterns of connectivity are

Haak KV, Marquand AF, Beckmann CF (2017) Connectopic mapping with resting-state fMRI. NeuroImage 170:83-94.

Beyond ROIs: from Connectivity to Connectopy



van den Heuvel & Hulshof Pol, 2010



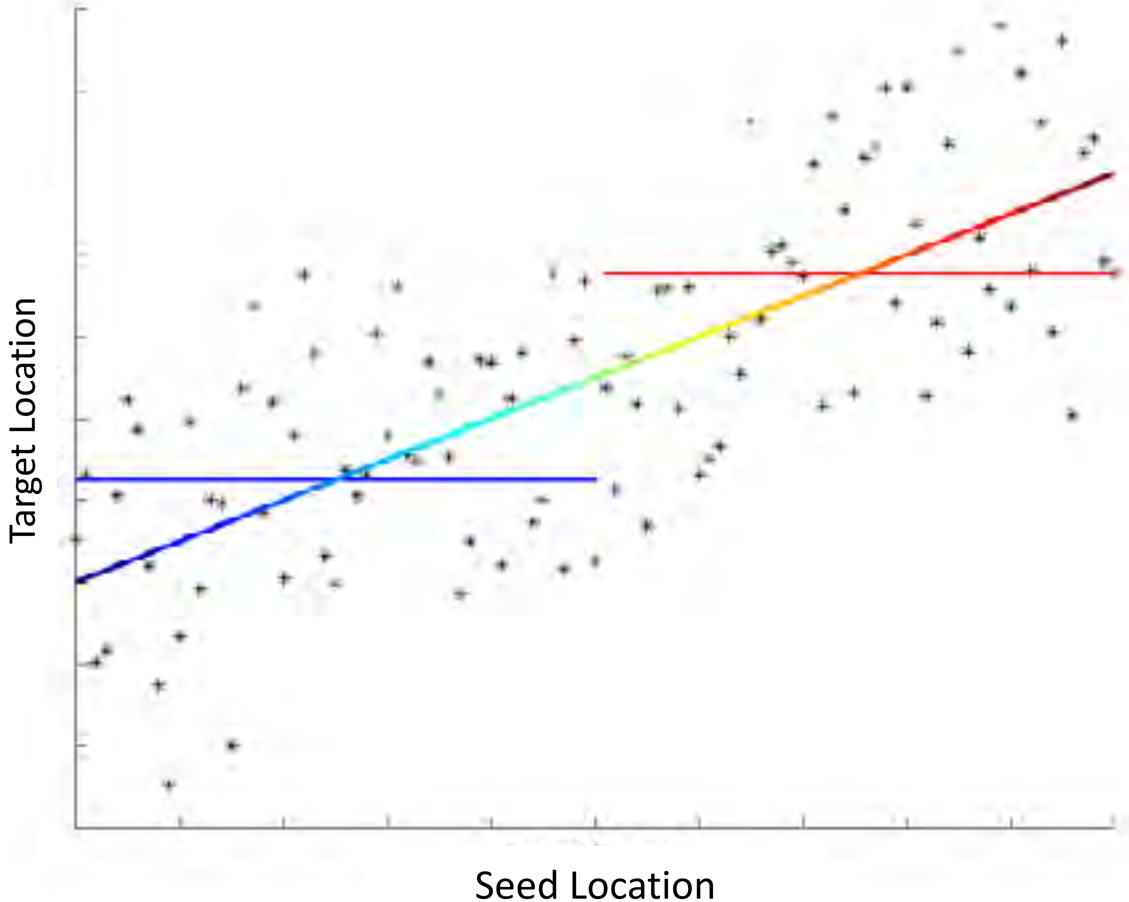
Haak et al., 2012

Functional organisation:

- much of cortex known to be topographically organised
  'functional variation'

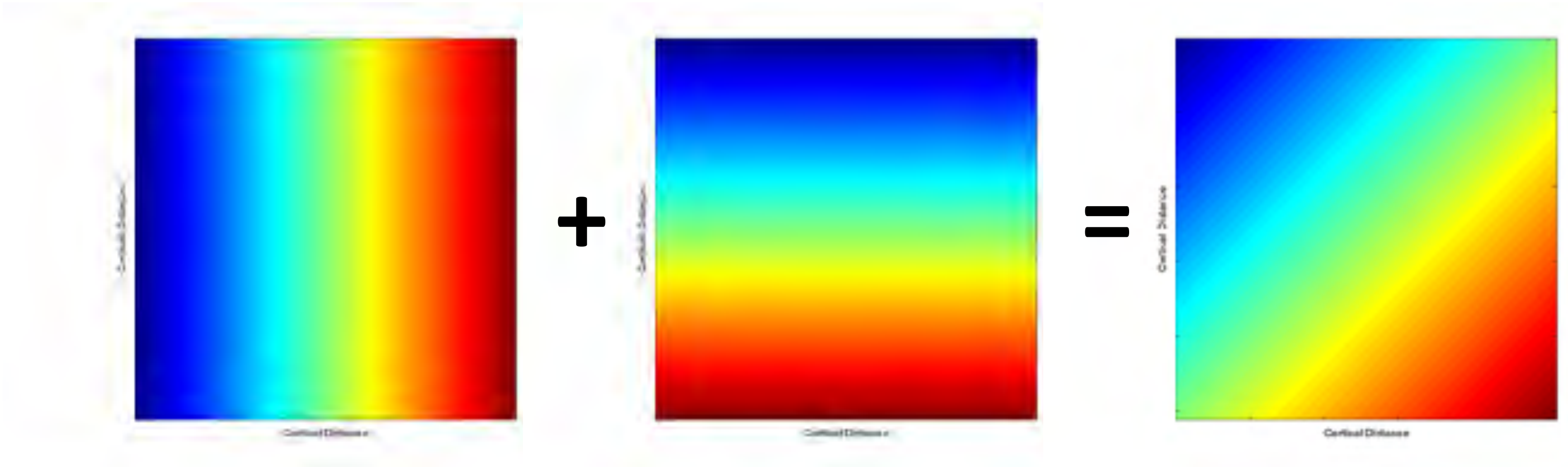
- overlapping modes of organisation
  'functional multiplicity'

Clusters or gradients?



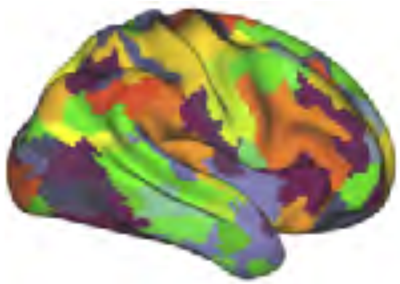
In the **presence of gradients**, spurious clusters may be detected with high reproducibility & replicability

Clusters or gradients?

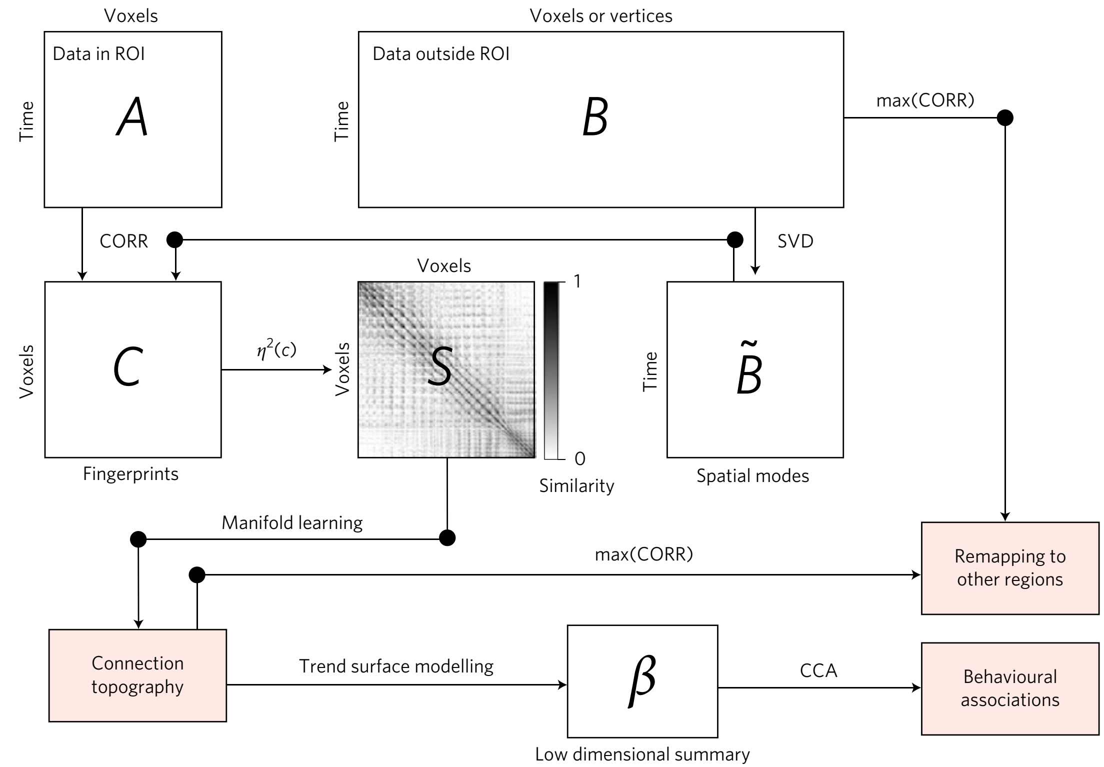


In the **presence of overlapping gradients**, ‘wrong’ clusters may be detected with high reproducibility & replicability

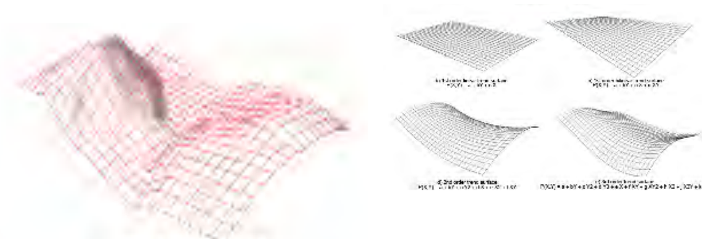
CONGRADS: connectopic mapping



From hard to ‘soft’ parcellations



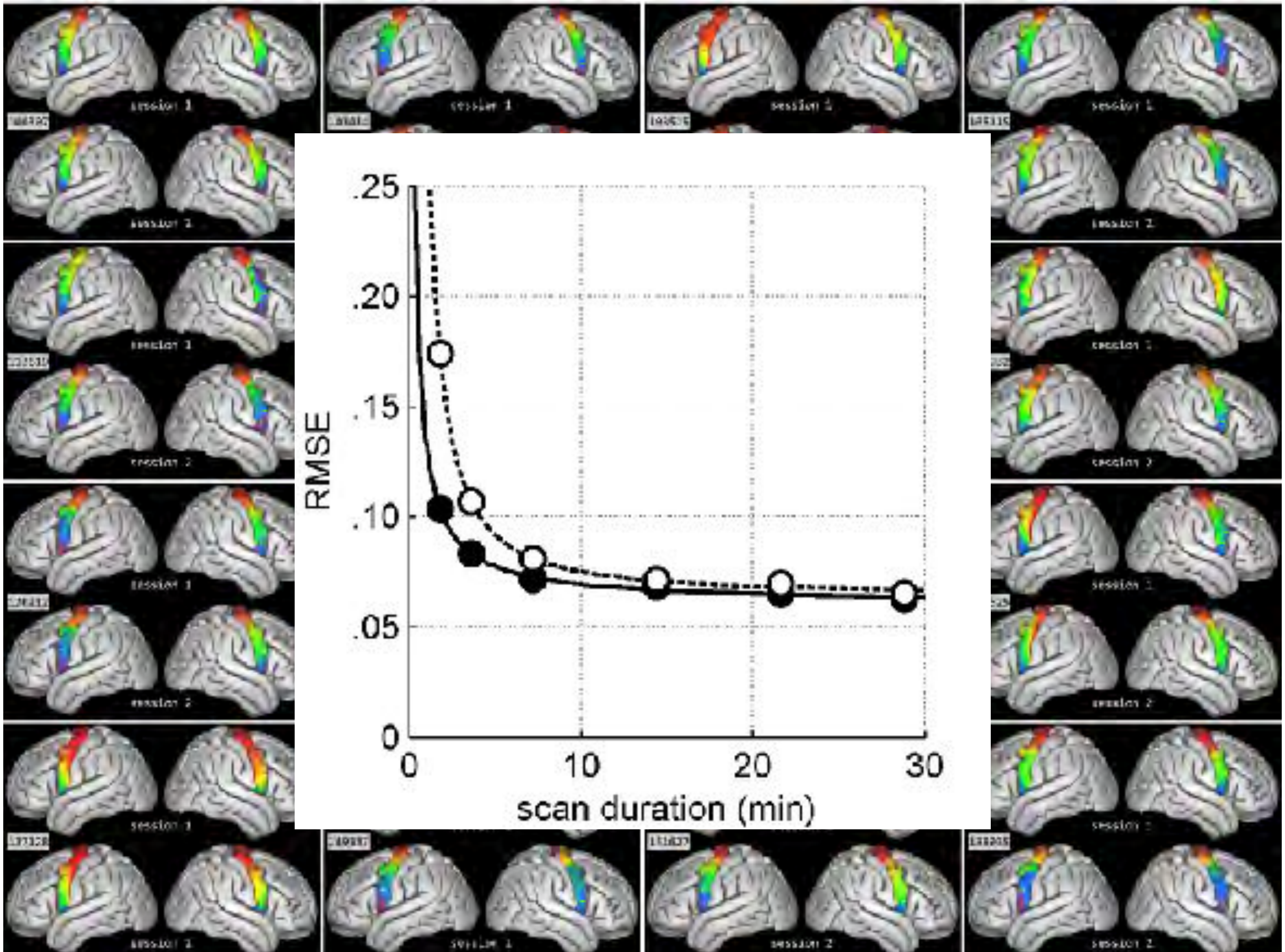
Connectopic maps



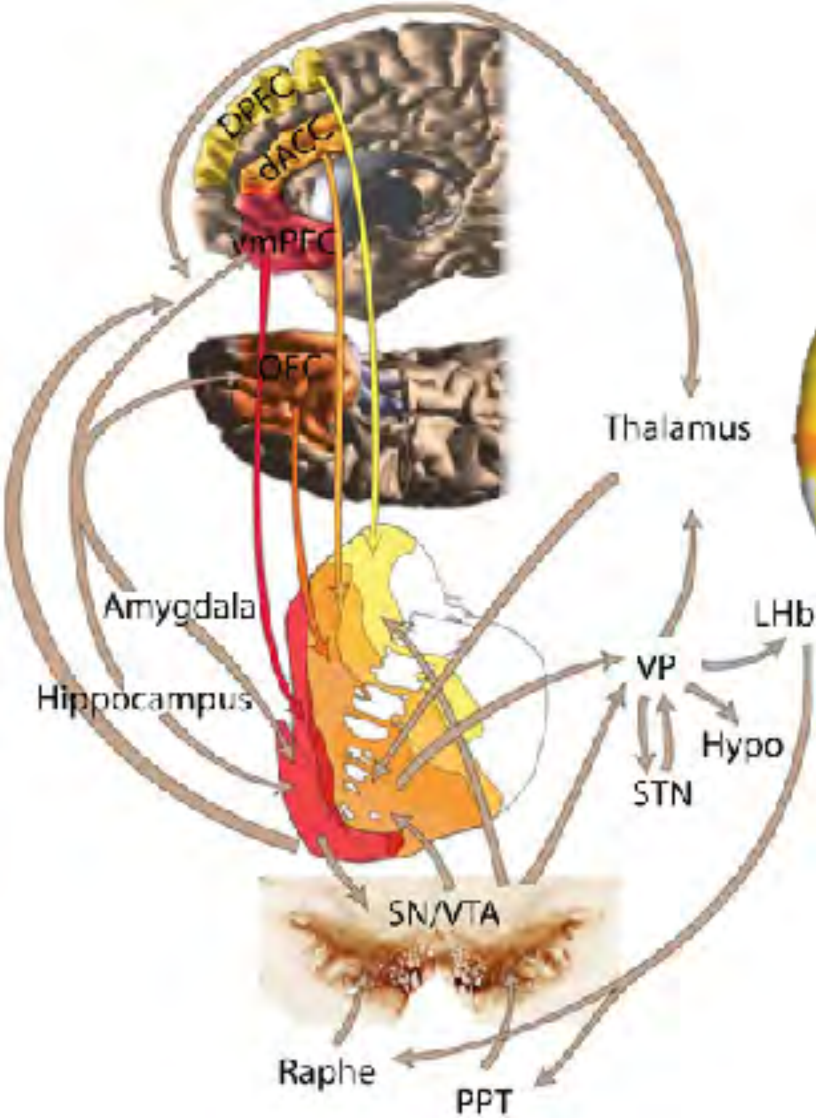
Trend-surfaces

Haak, Marquand & Beckmann, NeuroImage 2017

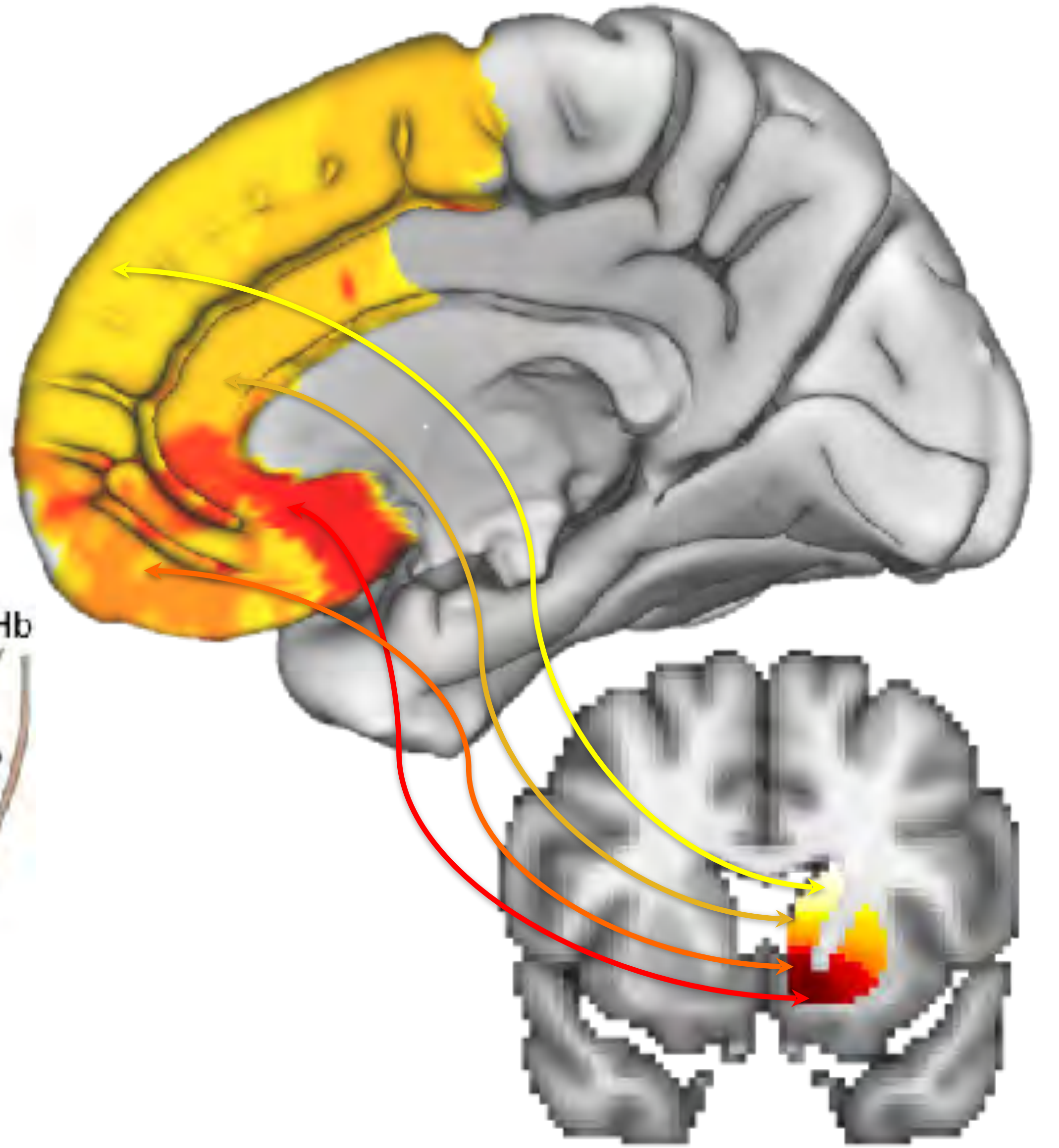
Reproducibility across sessions and subjects



Systems Neuroscience: mapping mechanisms



Haber & Knutson, 2010

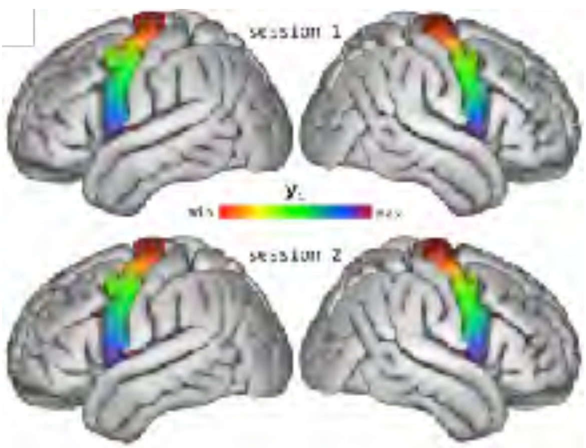


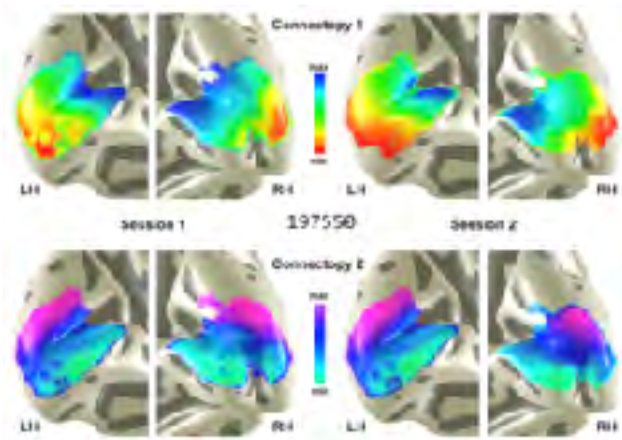
Marquand et al. 2017

Congrads:

Connectivity gradients / connectopic maps in ROIs including Trend Surface Modeling

https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/OtherSoftware





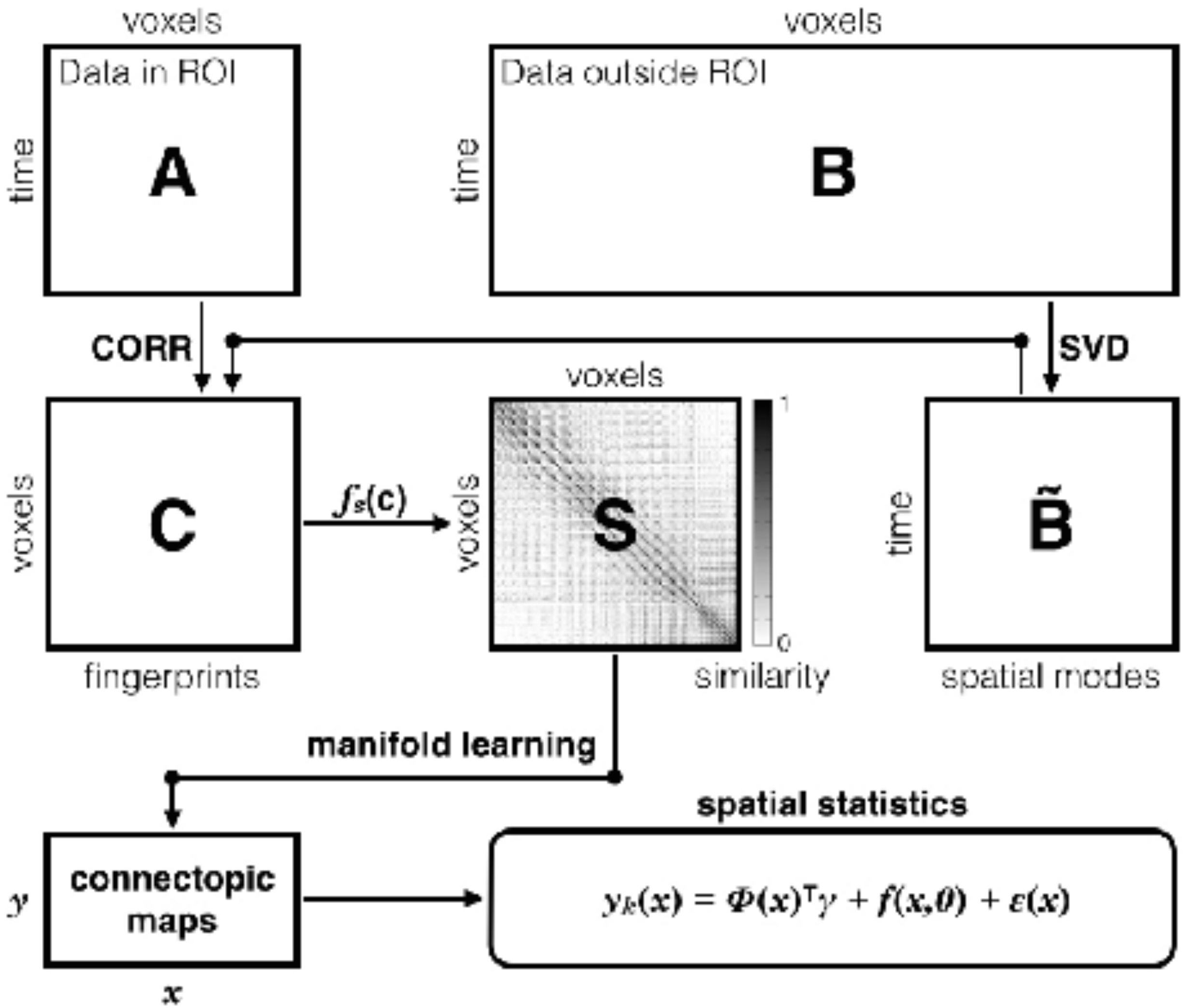
Congrads:

Connectivity gradients / connectopic maps in ROIs including Trend Surface Modeling

https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/OtherSoftware

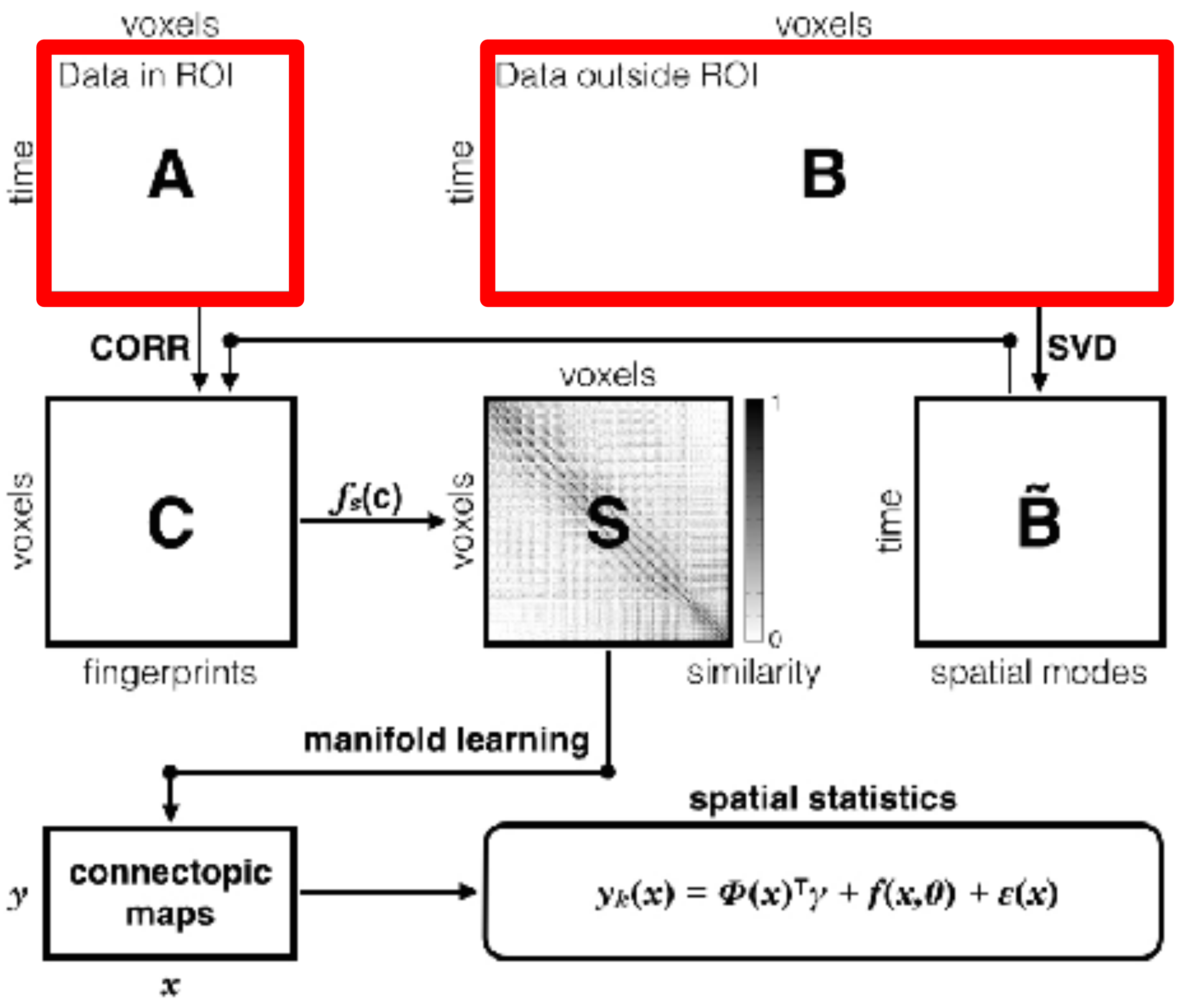
Package contents:

```
- congrads       [wrapper shell script]
- conmap.py      [connectectopic mapping code]
- trendsurf.py   [trend surface modeling code]
- bayesreg.py    [Bayesian regression for TSM]
- README         [basic usage info and notes]
```

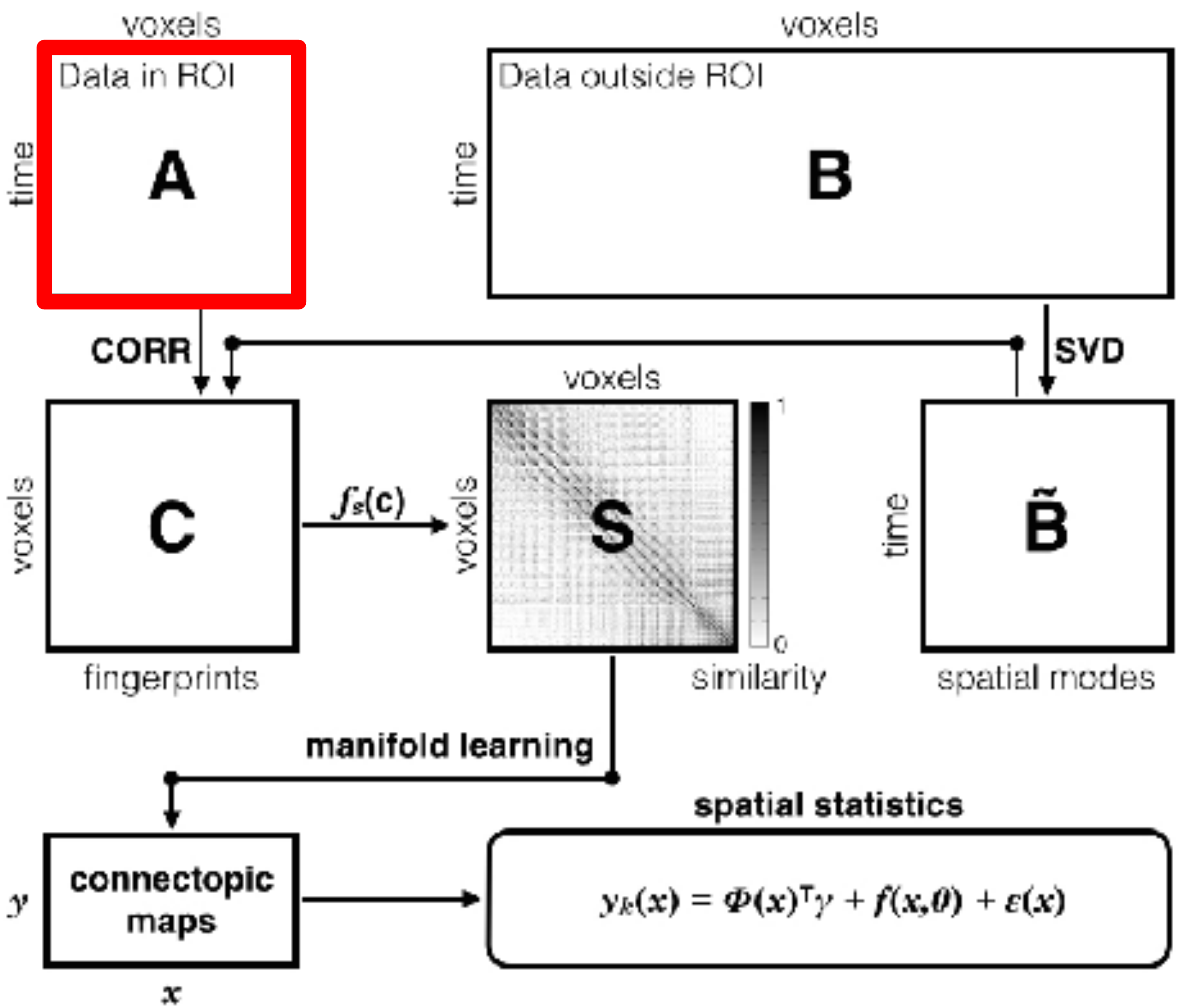


Haak KV, Marquand AF, Beckmann CF (2017) Connectopic mapping with resting-state fMRI. NeuroImage 170:83-94.

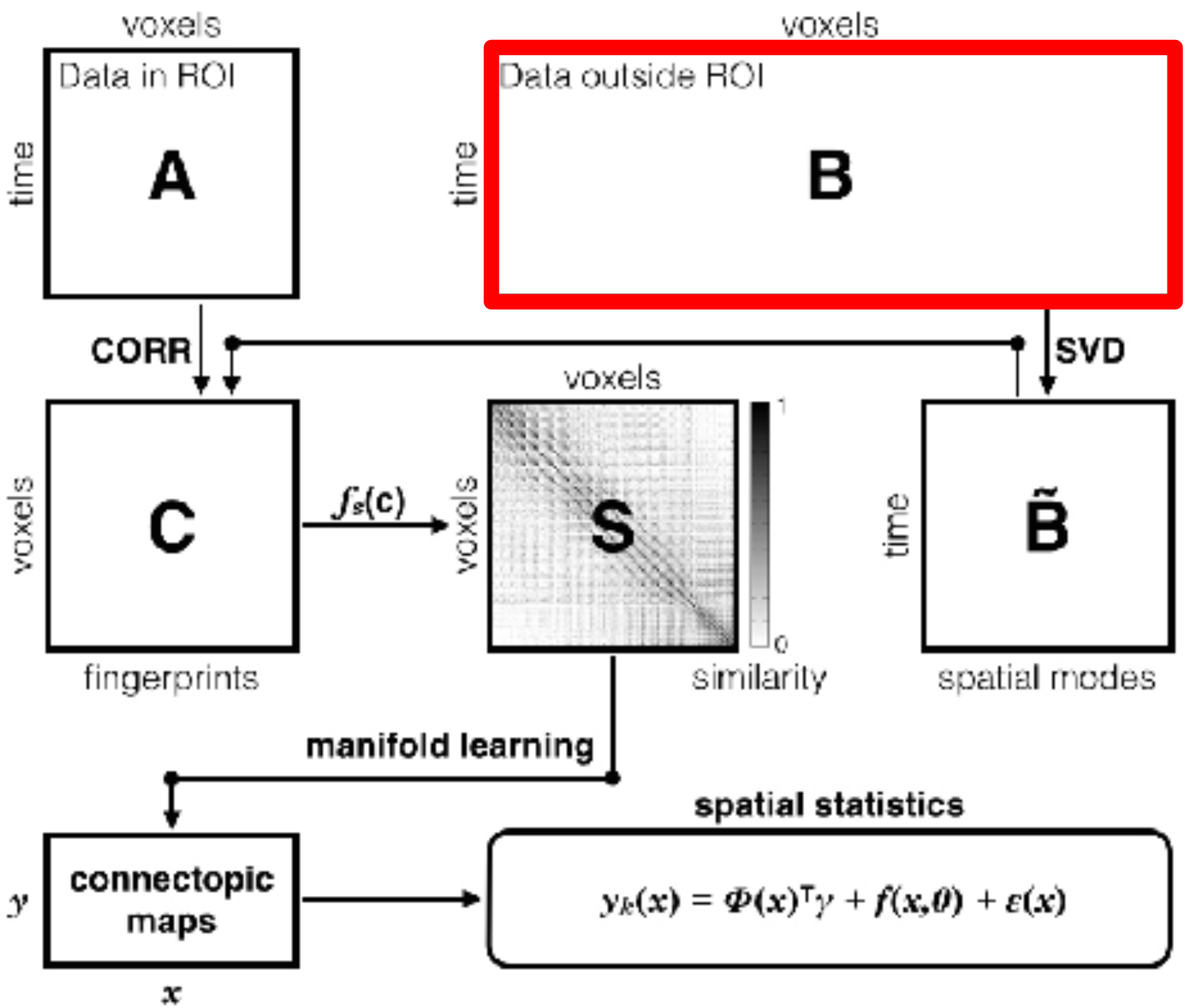
```
Usage:
./congrads -i <input> -r <roi> -m <mask> -o <out> [options]

Compulsory arguments:
    -i           input file name [4D image]
    -r           region-of-interest [3D binary image]
    -m           mask [3D binary image]
    -o           path to output directory


Optional arguments:
    -n <int>     number of connectopic maps [default=1]
    -s           save eta-squared matrix
    -z           normalise output maps to range [0-1]
    -p           project connectopic maps into mask
    -f <int>     fit spatial model of order <int>
    -F <int>     fit spatial model of order <int>
                 to pre-estimated connectopic map(s)
                 compulsory arguments: -i -r -o
```



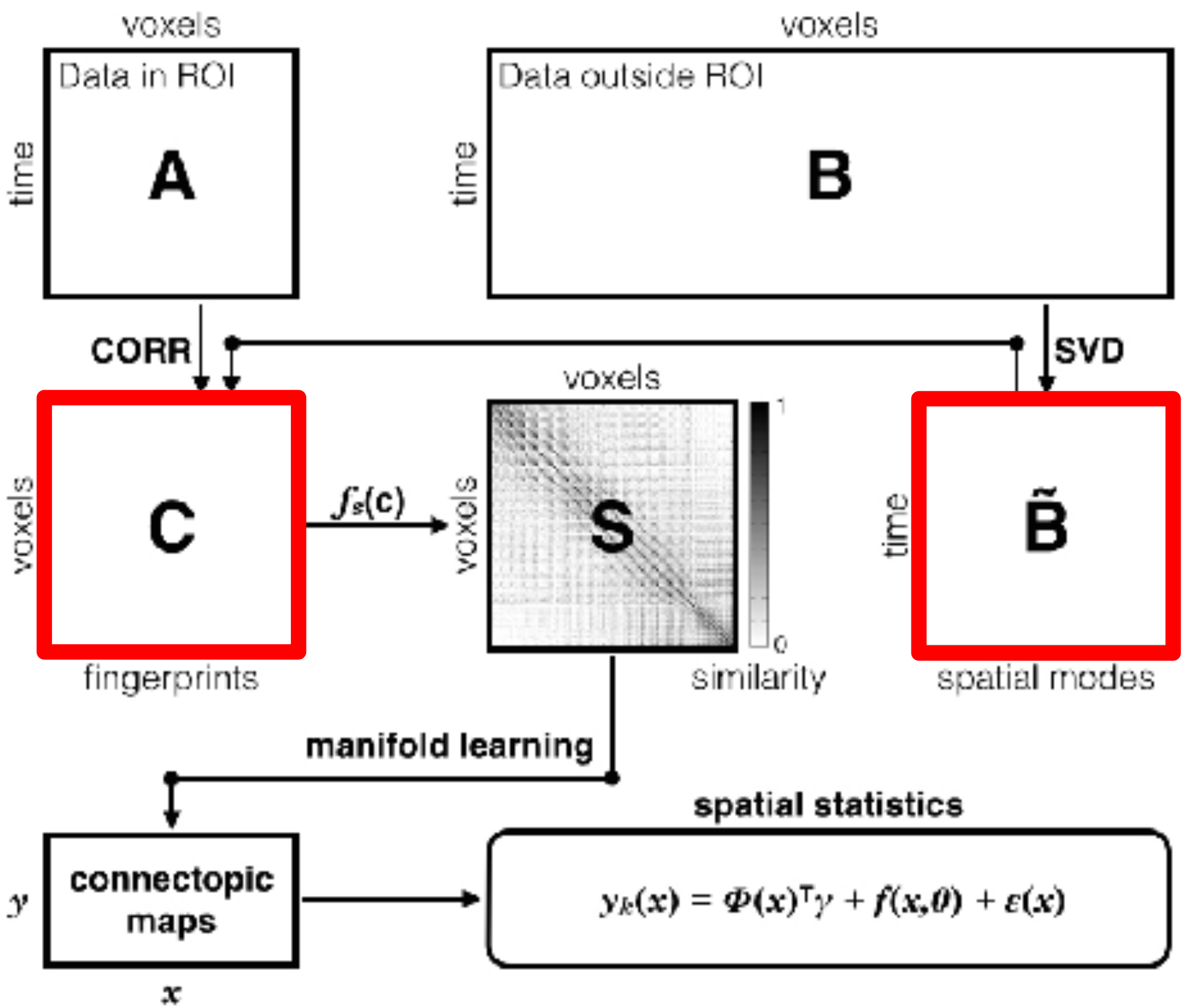
`-i <input> specifies input data`



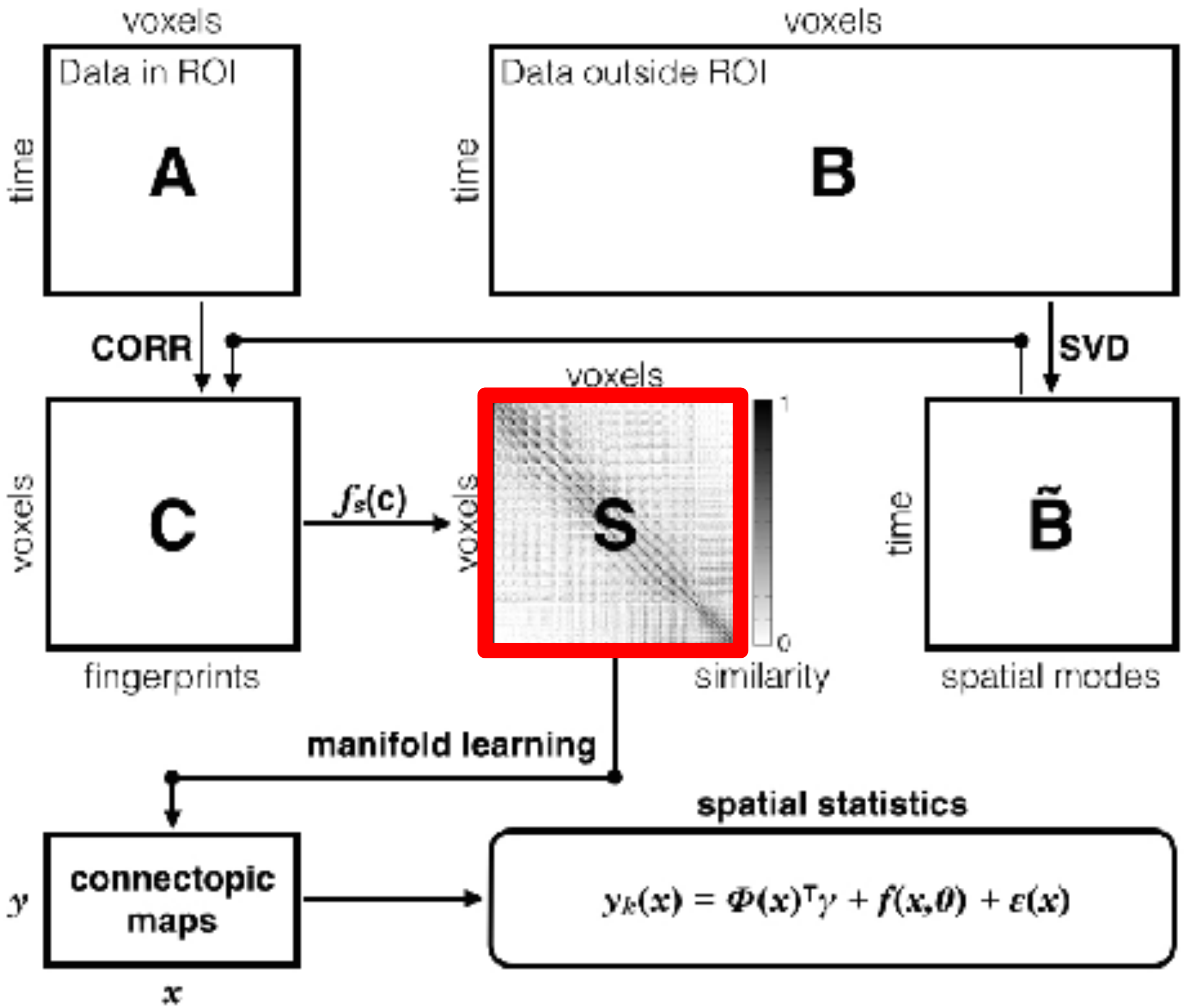
-r <roi> specifies data in ROI



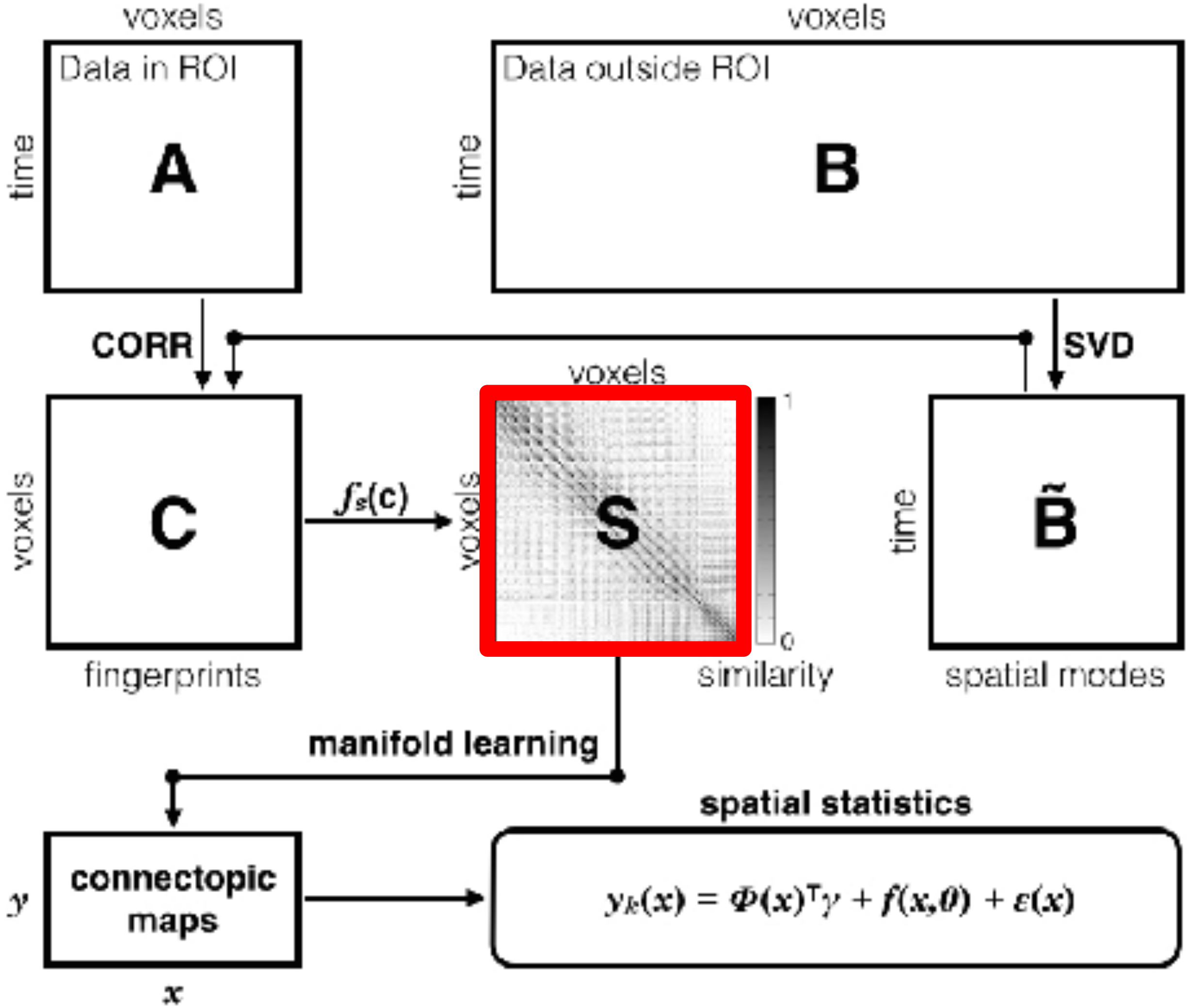
-m <mask> specifies data outside ROI



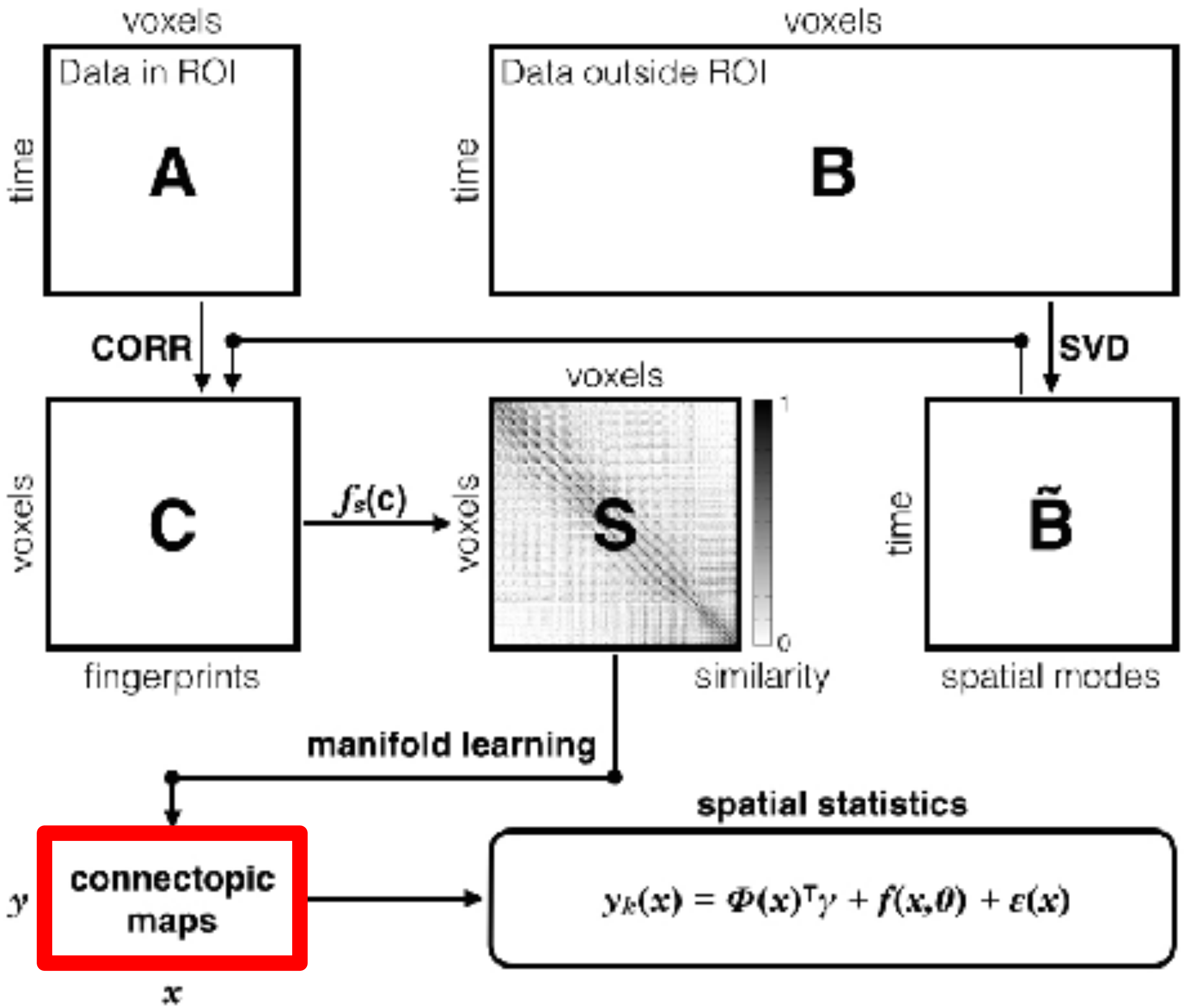
Connectivity Fingerprinting



Similarity among voxel-wise fingerprints

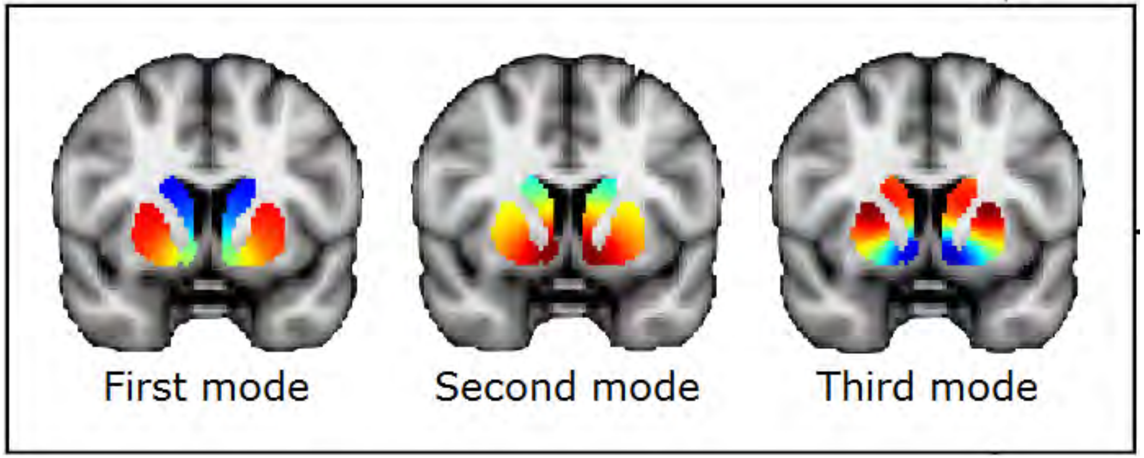



```
./congrads -i <input1> -i <input2> ...
```



-n <int> specifies number of maps

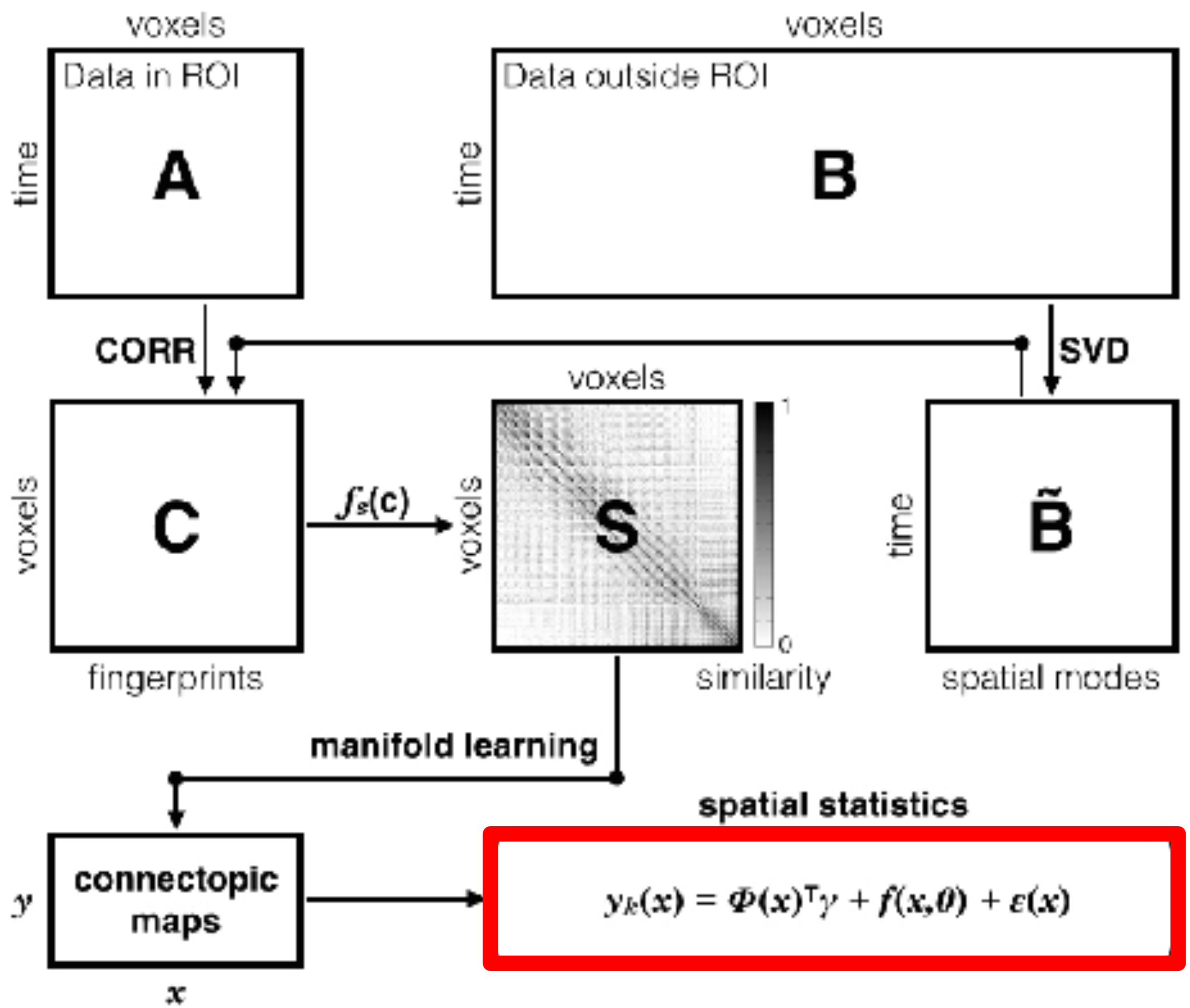
Multiple overlapping modes of organisation in human striatum



`-n <int> specifies number of maps`

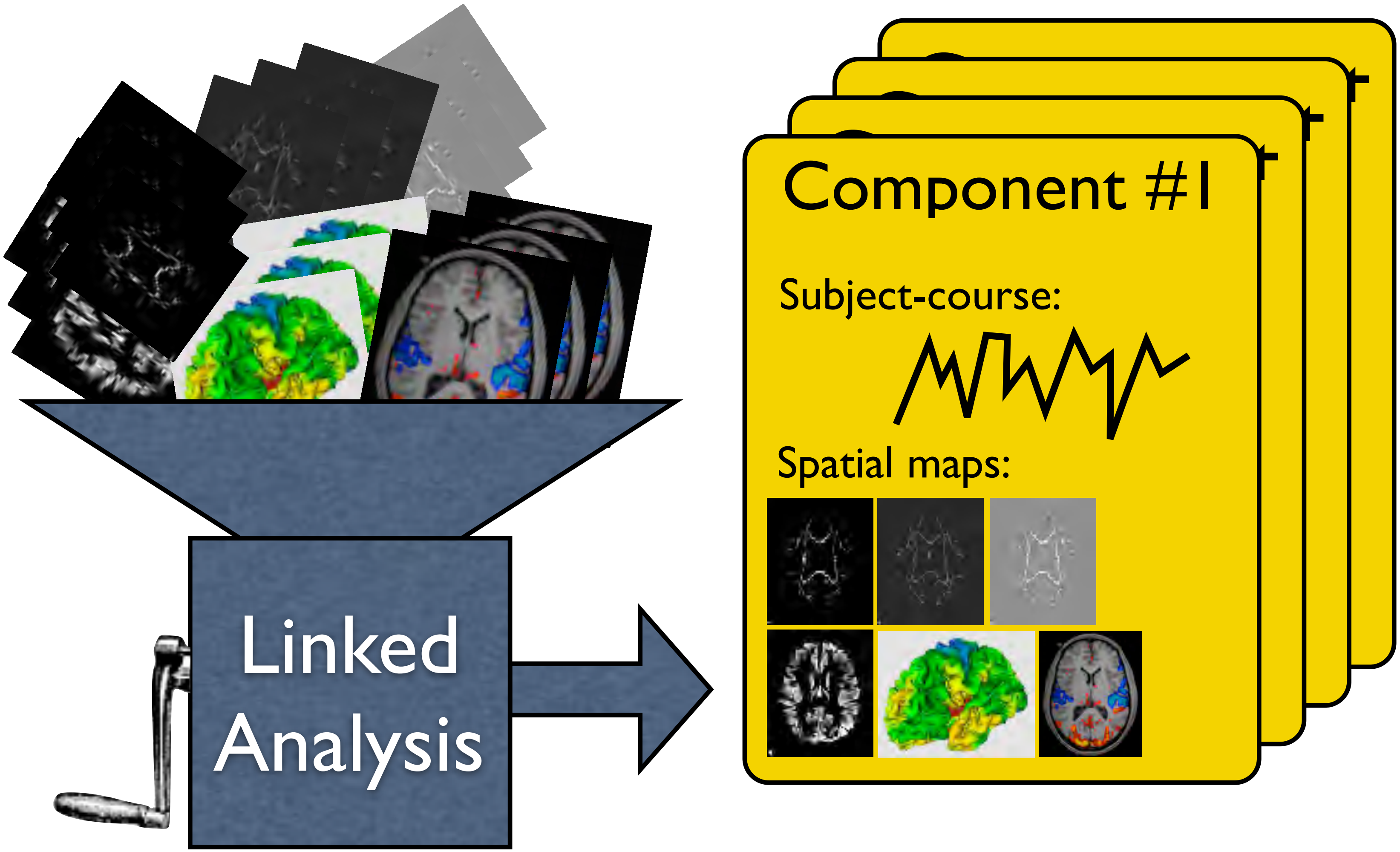
Marianne Oldehinkel

–see poster 2409!



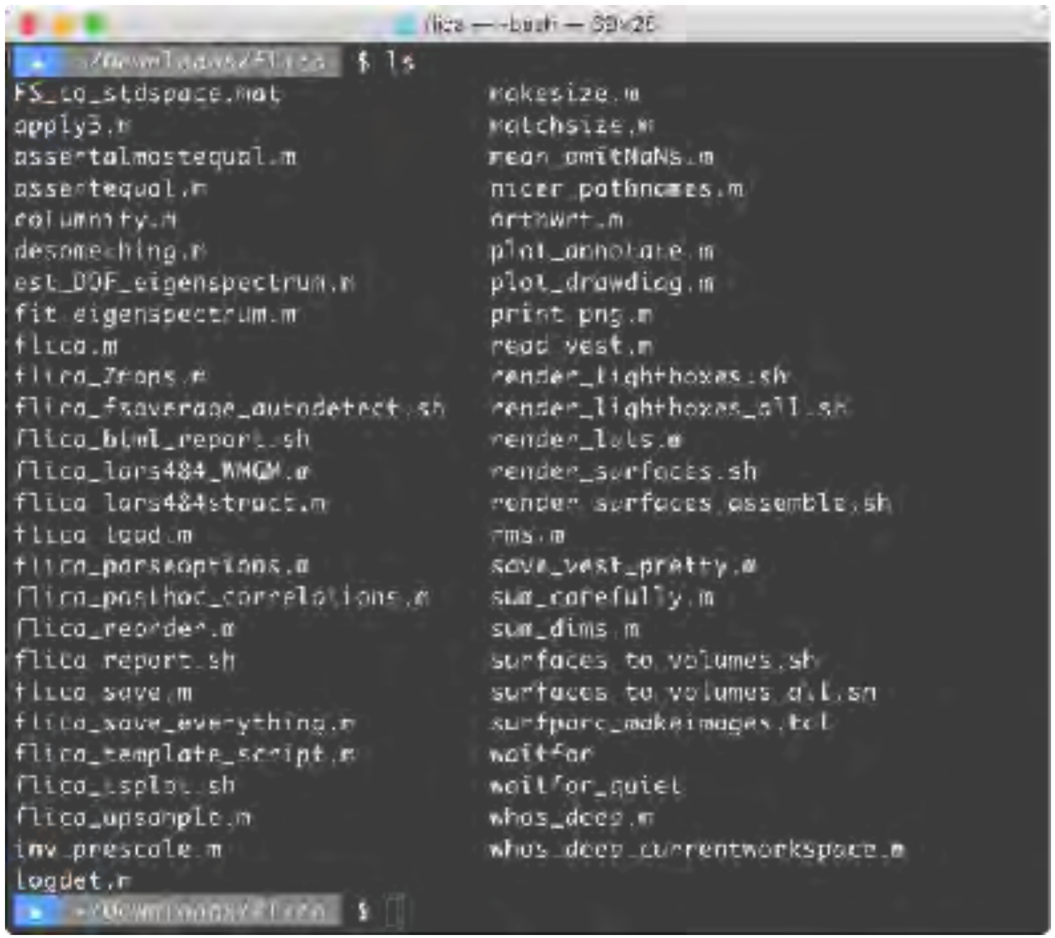
-f fit trend surface model of order <int>

...etc: FLICA (linked ICA)



…etc: FLICA (linked ICA)

– Current: mix of Shell and MATLAB scripts .sh and .m



…etc: FLICA (linked ICA)

- NEW: python

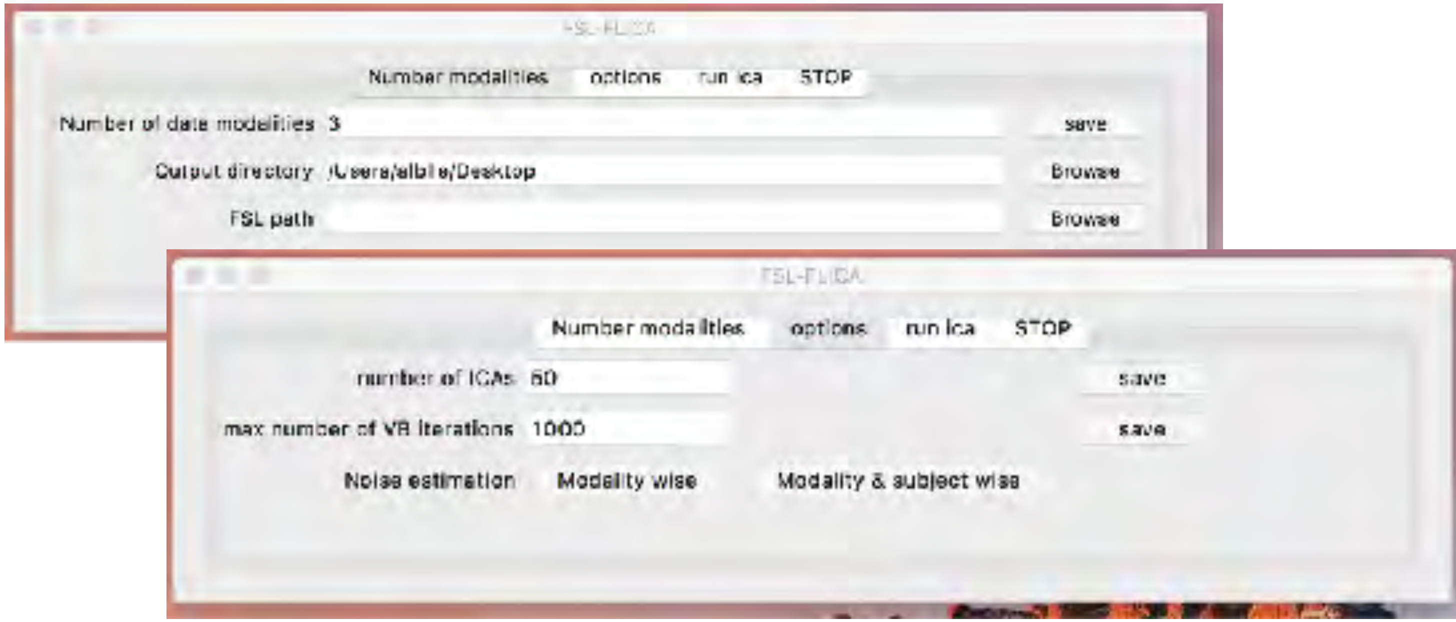
- Variety of source models

- allow new different input modalities (not necessarily brain images), e.g.
  - partial correlation matrices of functional data
  - behavioural measures
  - EEG ERP statistics
  - automatic dimensionality estimation

Alberto Llera

…etc: FLICA (linked ICA)

– GUI



– it will be available as part of the next FSL release.

– If you can not wait, contact Alberto Llera (poster 1954) a.llera@donders.ru.nl

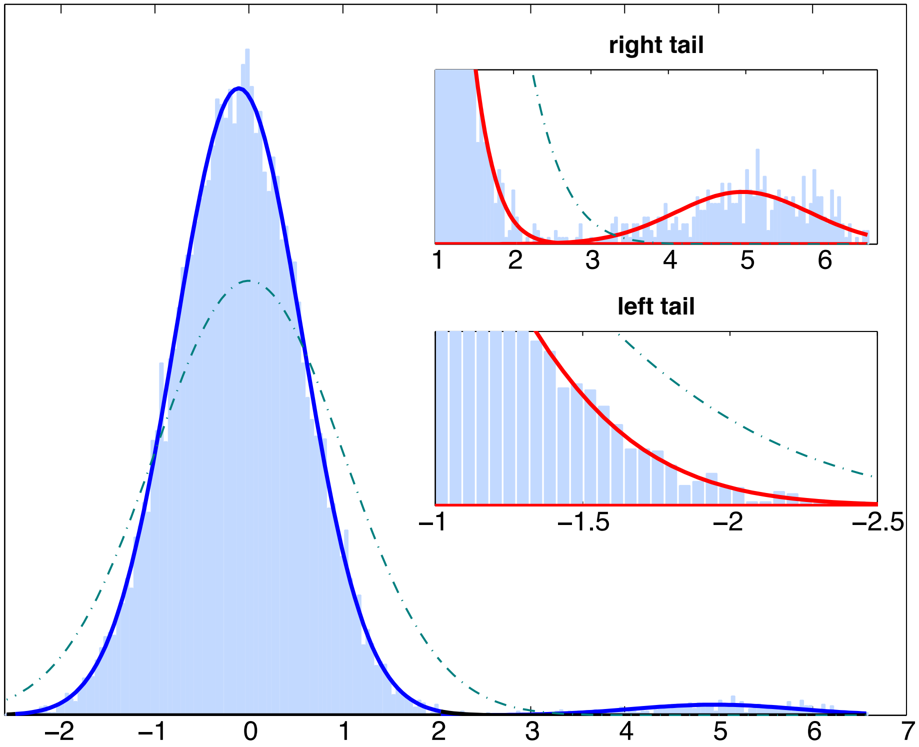
...etc: MELODIC Mixture Modelling

–classical null-hypothesis testing is invalid

–after estimation, the spatial maps are a projection of data on to the 'unmixing matrix'

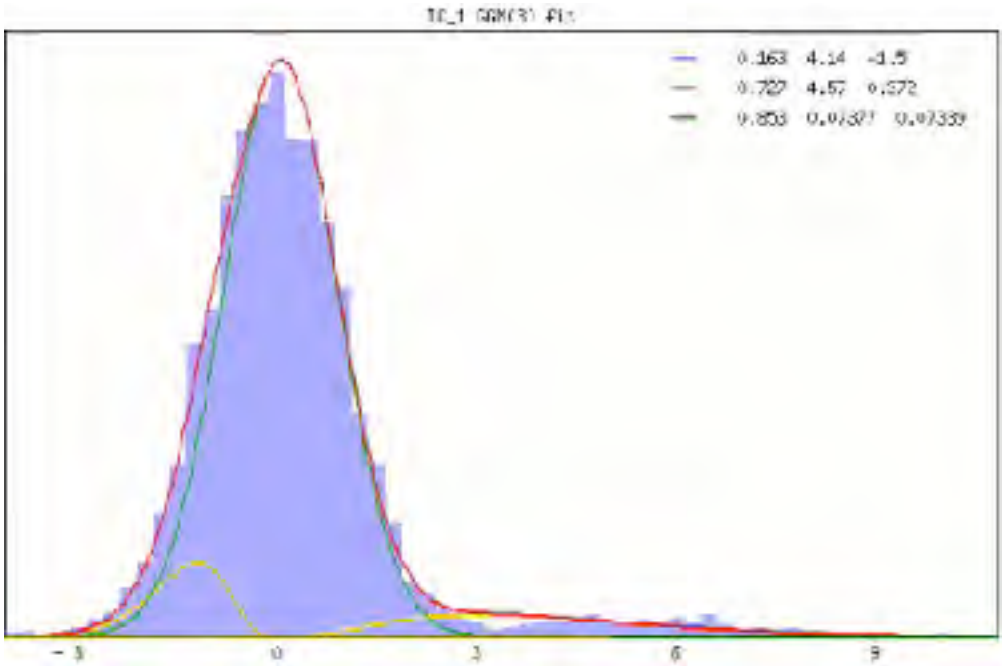
–data is assumed to be a linear combination of signals and noise

–the distribution of the estimated spatial maps is a mixture distribution!



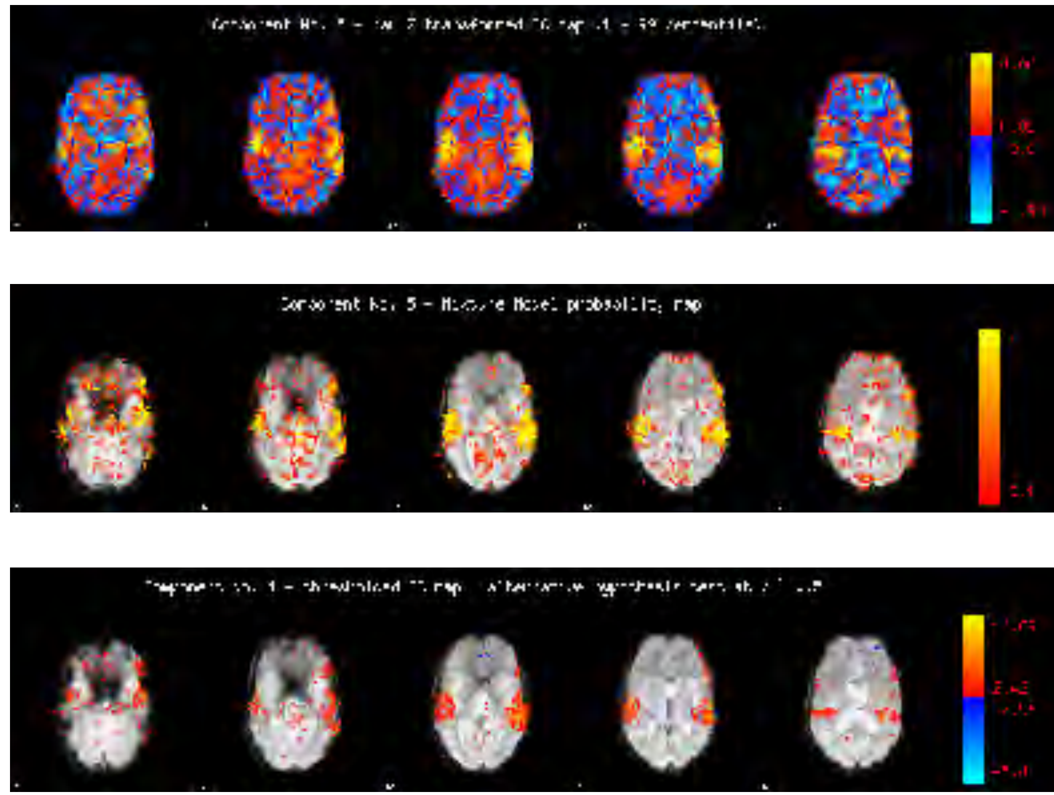
Alternative Hypothesis Testing (AHT)

- use Gaussian/Gamma mixture model fitted to the histogram of intensity values (using EM)



Alternative Hypothesis Testing (AHT)

- use Gaussian/Gamma mixture model fitted to the histogram of intensity values (using EM)
- Alternative hypothesis thresholding: ratio of probability under the non-null relative to total probability at each voxel



Alternative Hypothesis Testing (AHT)

- use Gaussian/Gamma mixture model fitted to the histogram of intensity values (using EM)
- Alternative hypothesis thresholding: ratio of probability under the non-null relative to total probability at each voxel
- **Local FDR** implemented in FSL-MELODIC as command-line option

  `—mmthresh=0.05d`