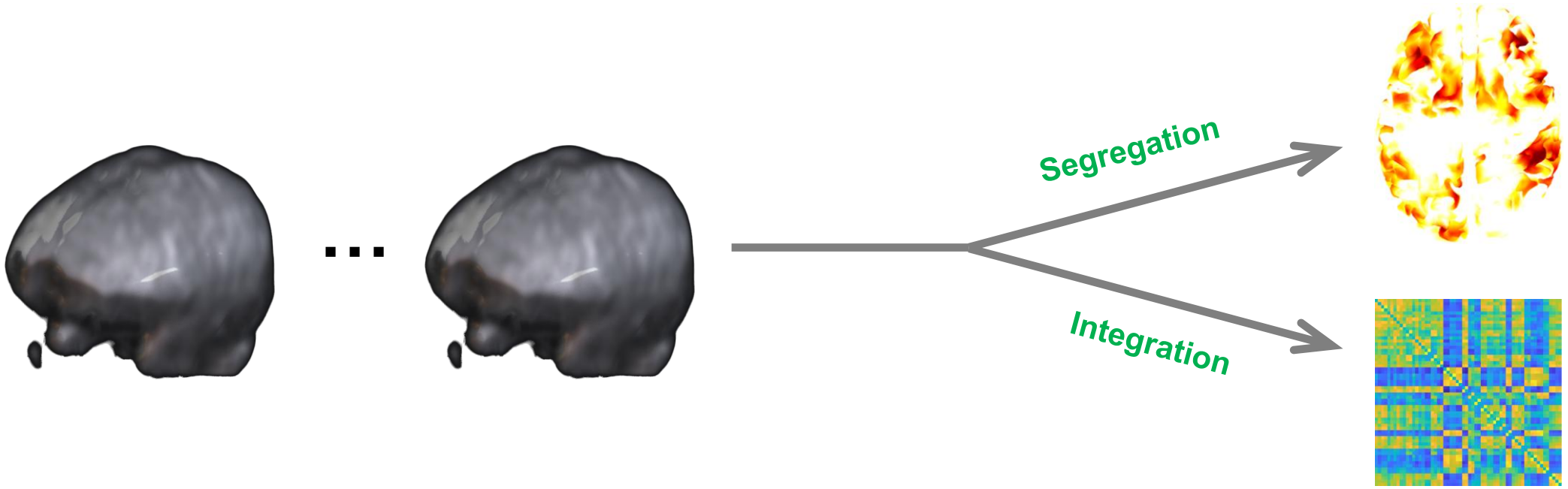
Medical/Bio Research Topics Ⅰ: Week 06 (8 April 2025)

Functional MRI (2):
Data Processing Methods

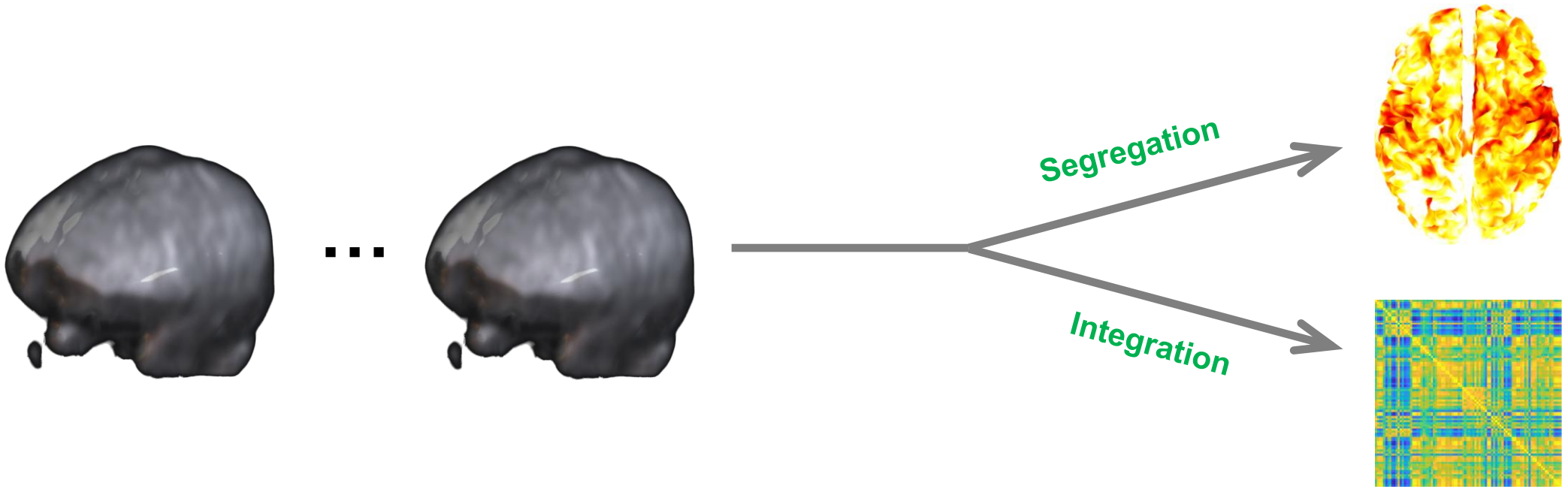
기능 자기공명영상 (2):
데이터 처리 방법

Brain Mapping with Functional MRI (fMRI)

- Task-based fMRI

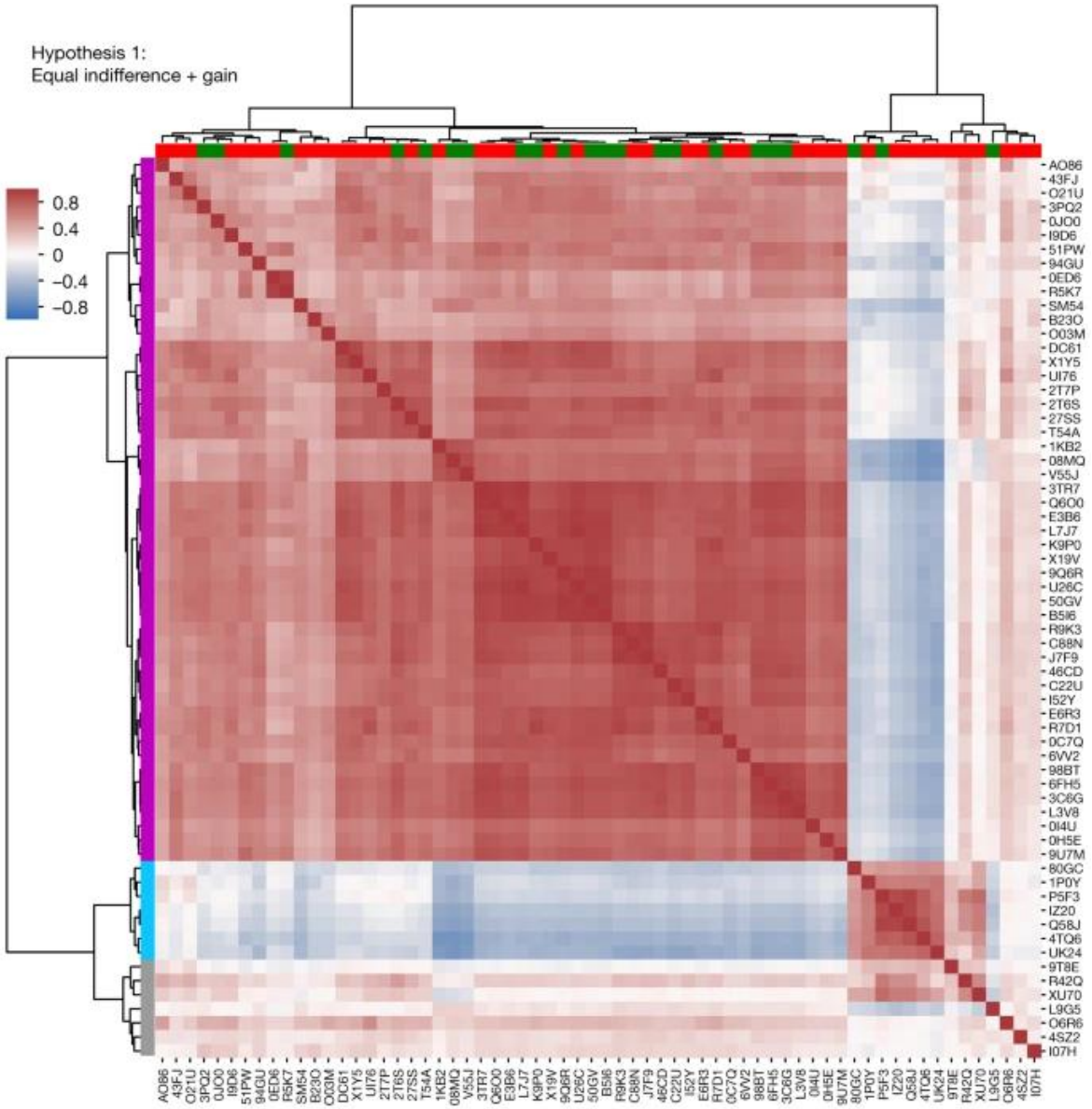


- Resting state fMRI



Analytical Variability in fMRI

- Variability of reported results [Botvinik-Nezer et al, 2020]
  - Resulted from different analysis pipelines
  - As strong factors, spatial smoothness, software package used, and methods of multiple test correction



[Botvinik-Nezer et al, 2020]

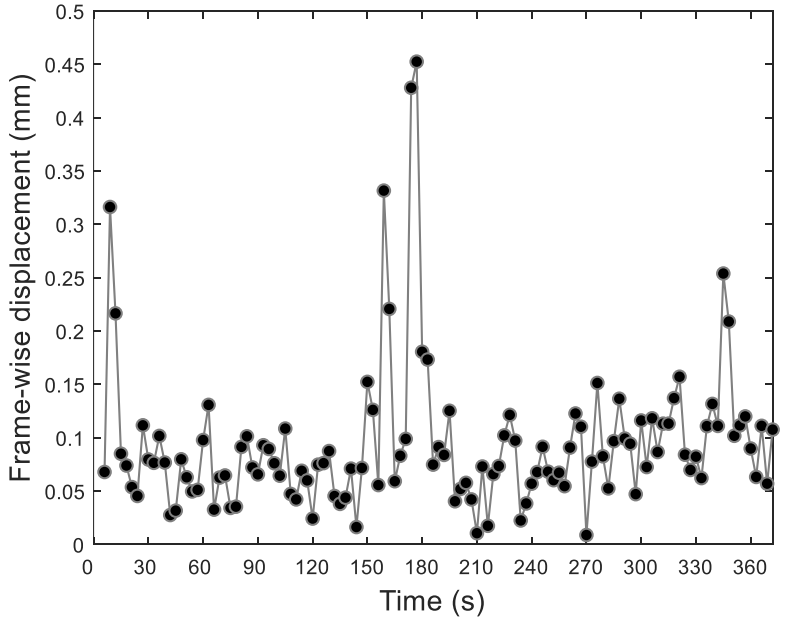
Analytical Variability in Whole Brain Statistical Results

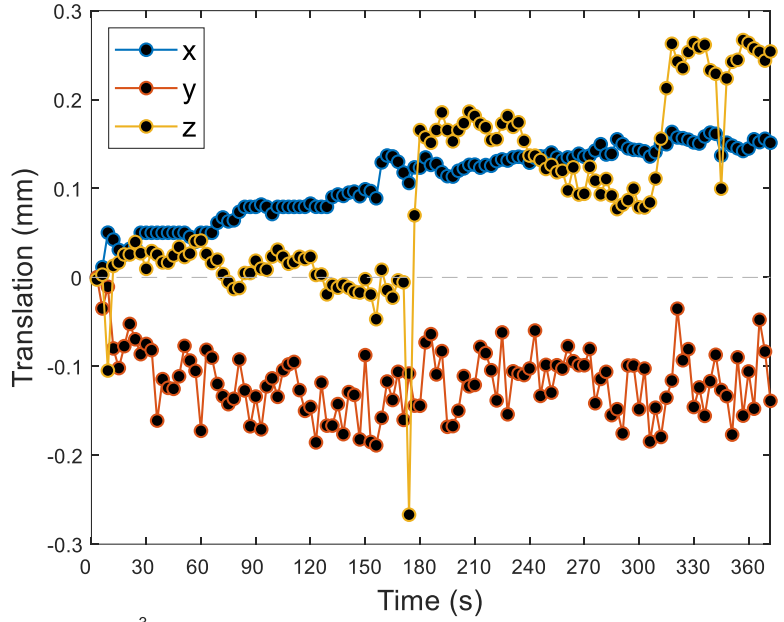
Preprocessing

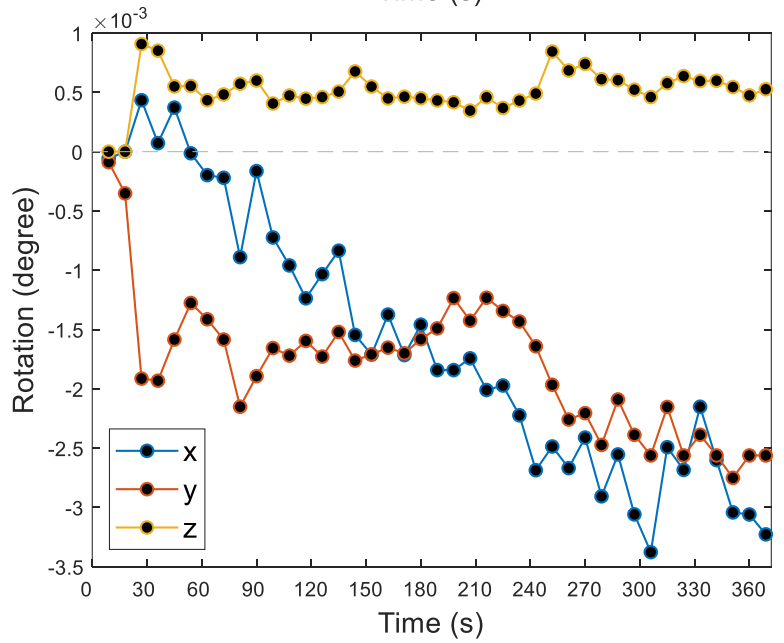
- Numerous steps to clean and standardize fMRI data before modeling and statistical analysis based on the extraction of signals that are faithful to underlying neuronal activity
  - Identifies nuisance (non-neuronal) sources of variability and reduces their effect on fMRI data
  - Addresses particular imaging artifacts and the anatomical localization of signals

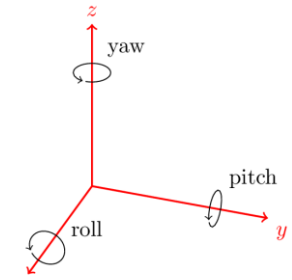
- After preprocessing, it is assumed that fMRI signals are anatomically localized in terms of coordinates
  - Correction for unwanted variation
    - Difference in slice timing
    - Head motion
    - Inhomogeneity (small local inhomogeneities in the magnetic field based on differences in magnetic susceptibility between adjacent tissues or materials (such as air and brain tissue))-induced distortion
  - Normalization
  - Smoothing

Frame-wise displacement

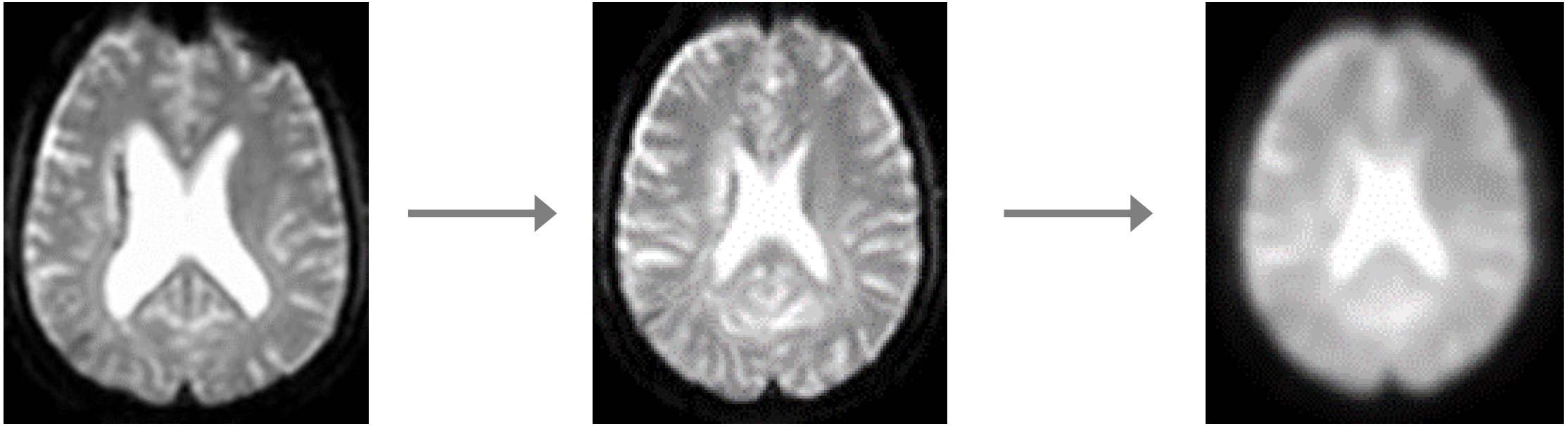








Estimated Head Motion



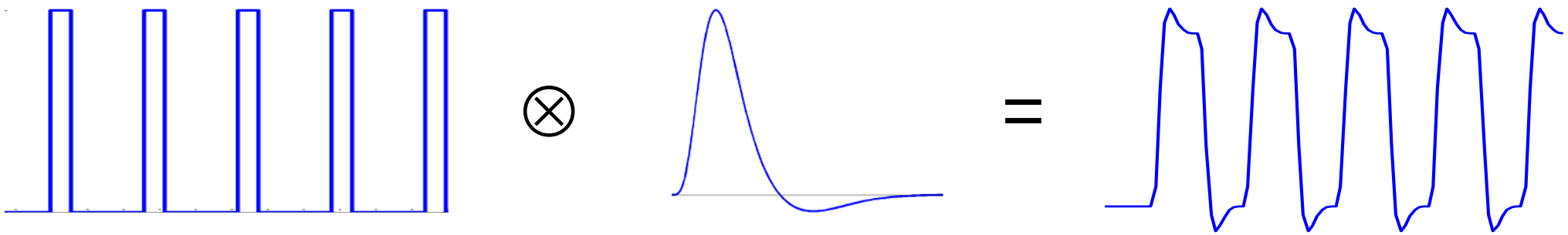
Normalization

Smoothing

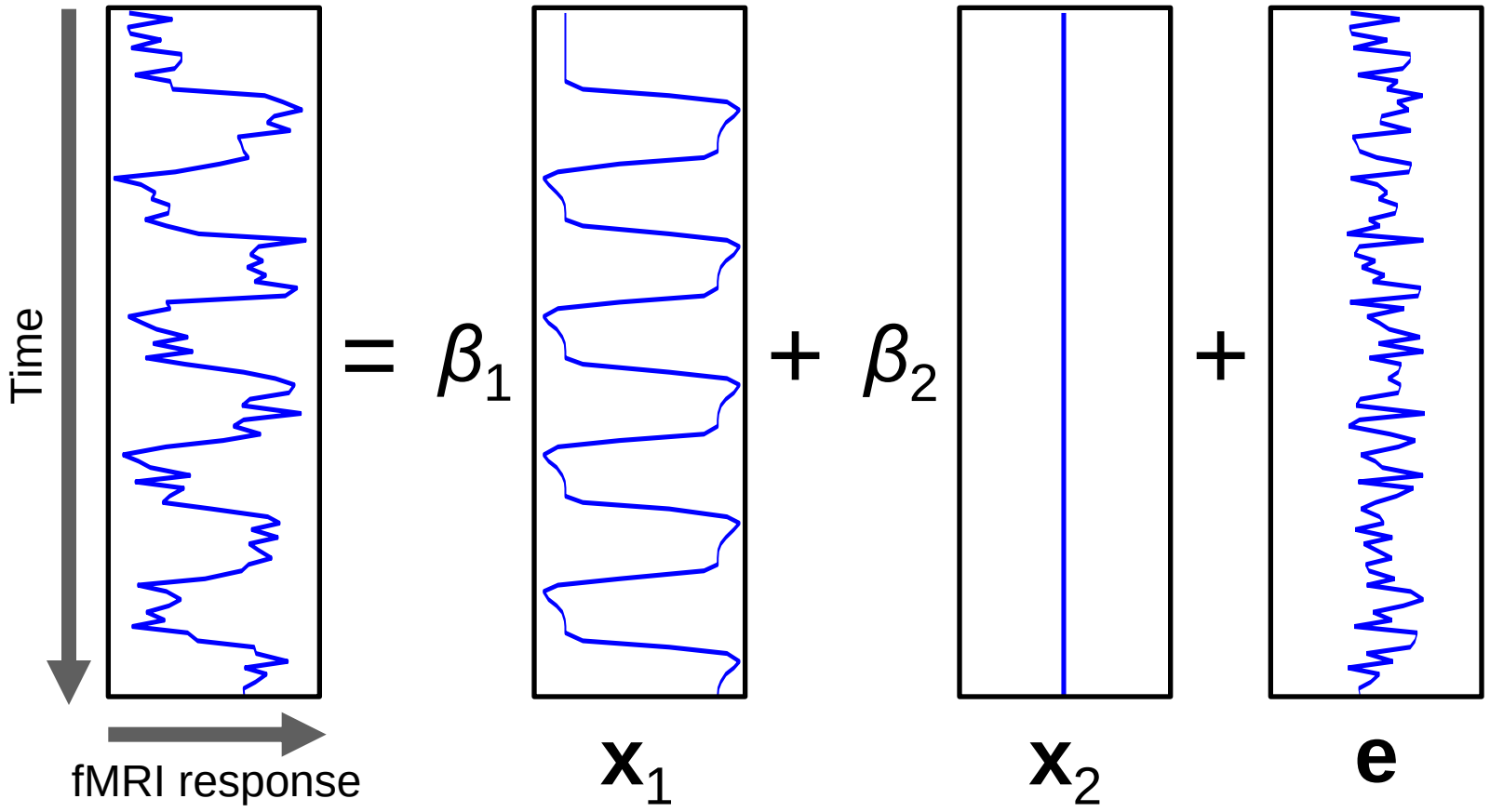
Normalization and Smoothing

Task-based fMRI: Segregation Analysis

- Mass univariate statistical analysis
- General linear model: $\boldsymbol{y} = \boldsymbol{X\beta} + \boldsymbol{e}$
  - Observed fMRI time series ~ predicted fMRI time series + nuisance variables + error
  - $\boldsymbol{y}$: observed fMRI time series
  - $\boldsymbol{X}$: design matrix
  - $\boldsymbol{\beta}$: parameter estimate
  - $\boldsymbol{e}$: error



fMRI Time Series Prediction Using Experimental Timing

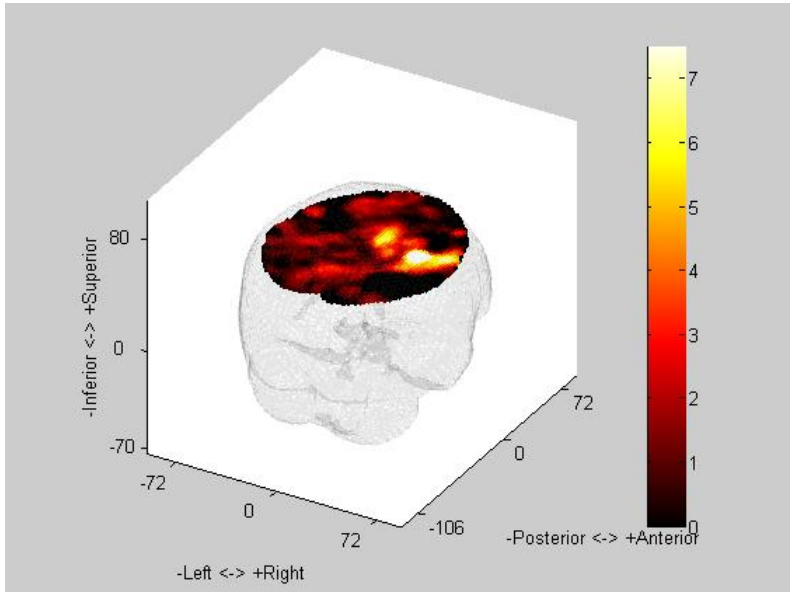


$$\boldsymbol{y = X\beta + e = x_1\beta_1 + x_2\beta_2 + e}$$

General Linear Model for Functional Segregation Analysis in Task-based fMRI

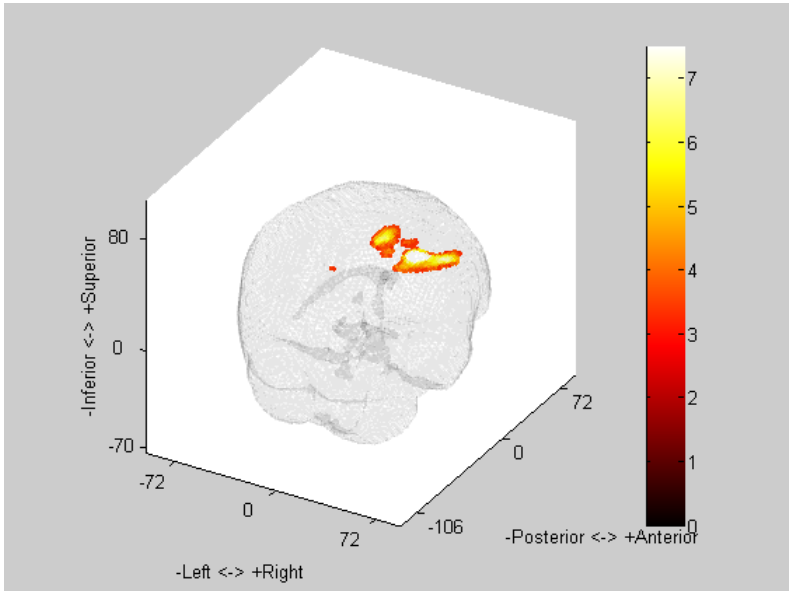
- Search of local brain activity
  - By statistical inferences under the null-hypothesis that predicted fMRI time series are no closer to observed fMRI time series than expected by chance
  - Requires correction for multiple tests

_t_ map



Thresholding
at a significance level

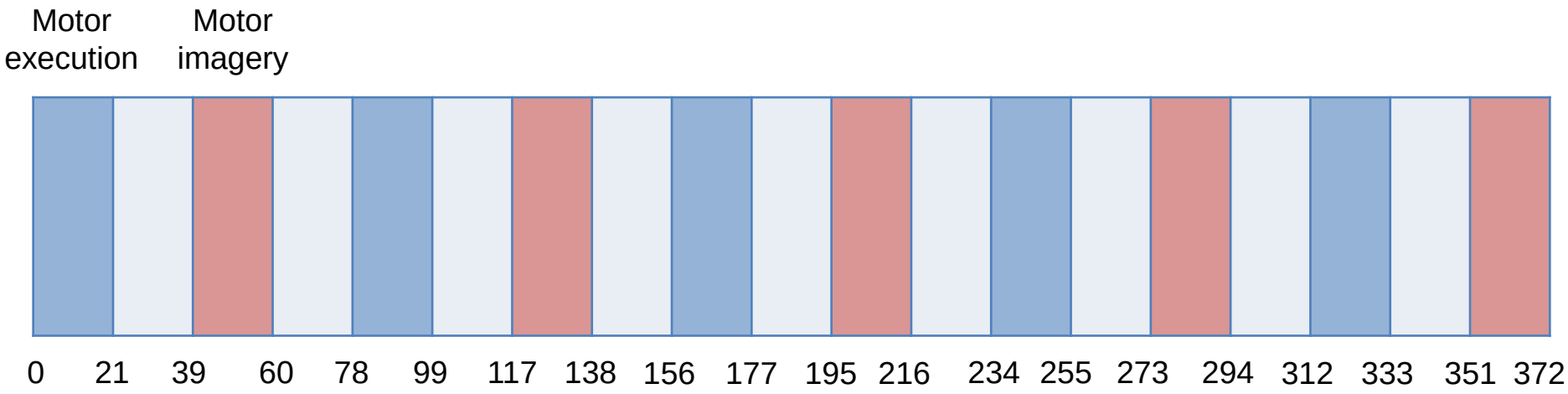
Thresholded _t_ map



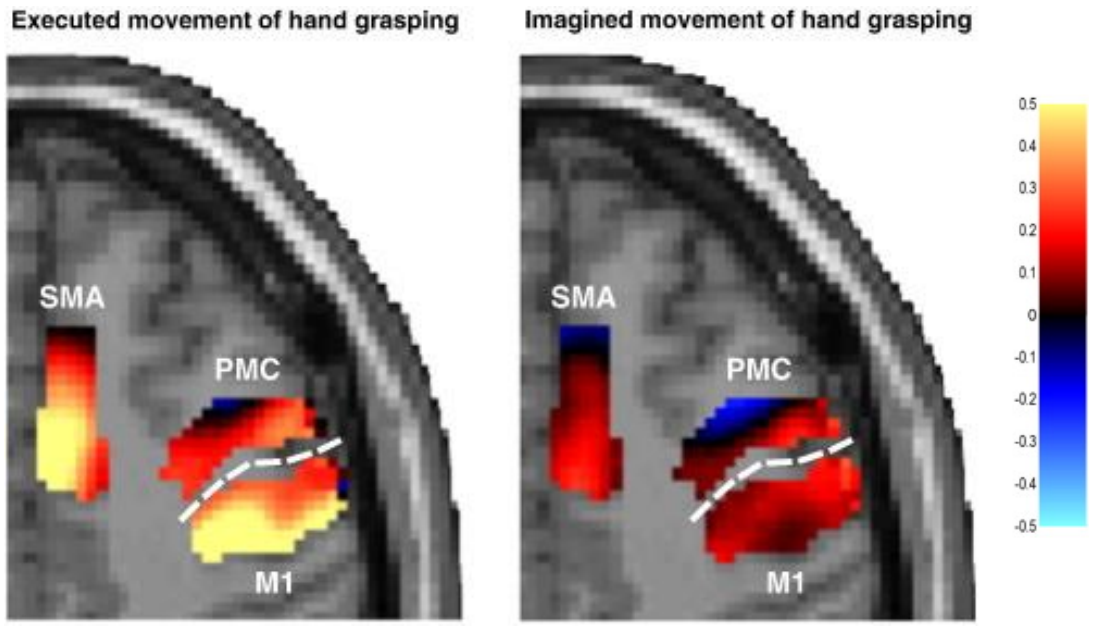
$$t = \frac{c^T \hat{\beta}}{\sqrt{\mathrm{var}(e)\, c^T (X^T X)^{-1} c}}$$

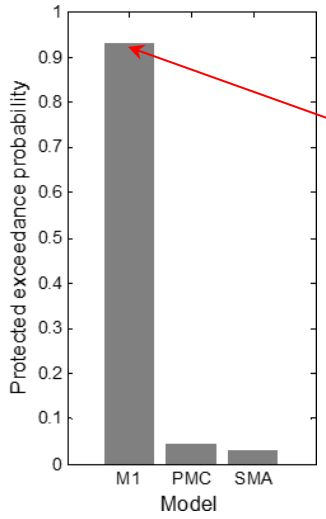
Search for Local Brain Activity by Statistical Inferences

[Task-based fMRI: Segregation Analysis]

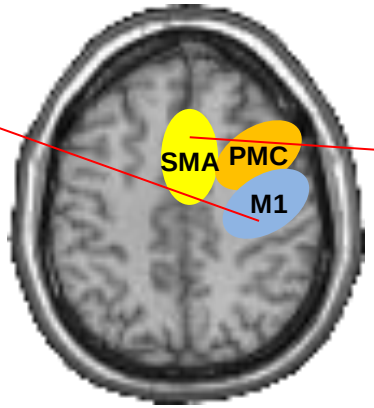


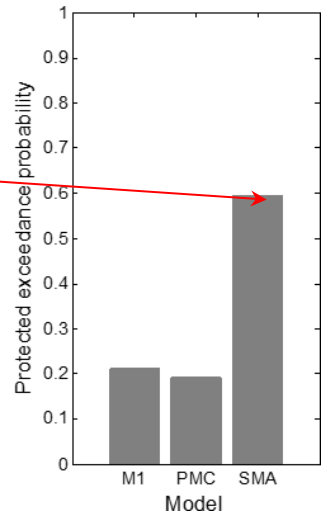
- 124 scans (372 seconds)
- Tasks
  - Motor execution
  - Motor imagery





Motor execution

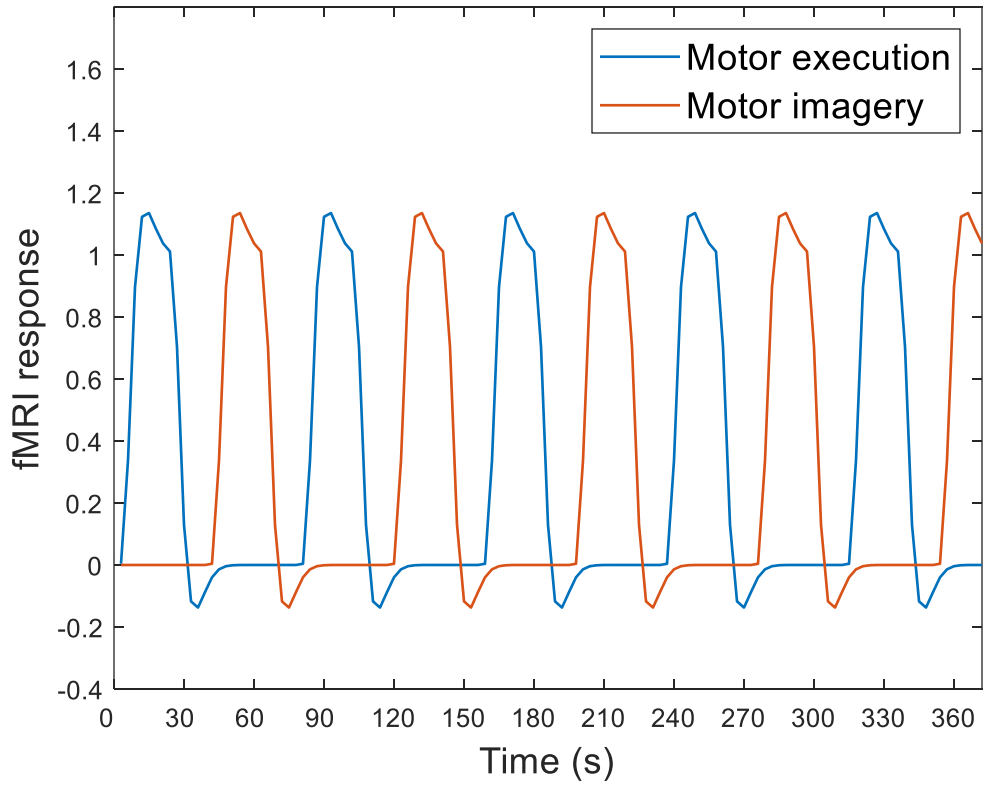




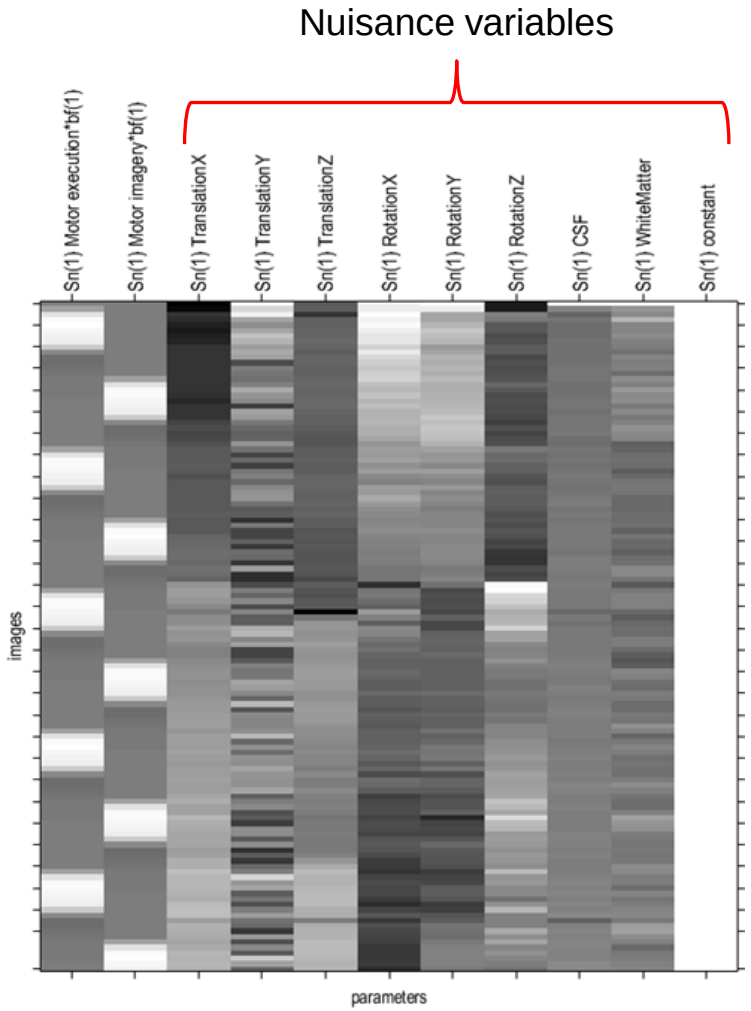
Motor imagery

[Park et al., 2015]

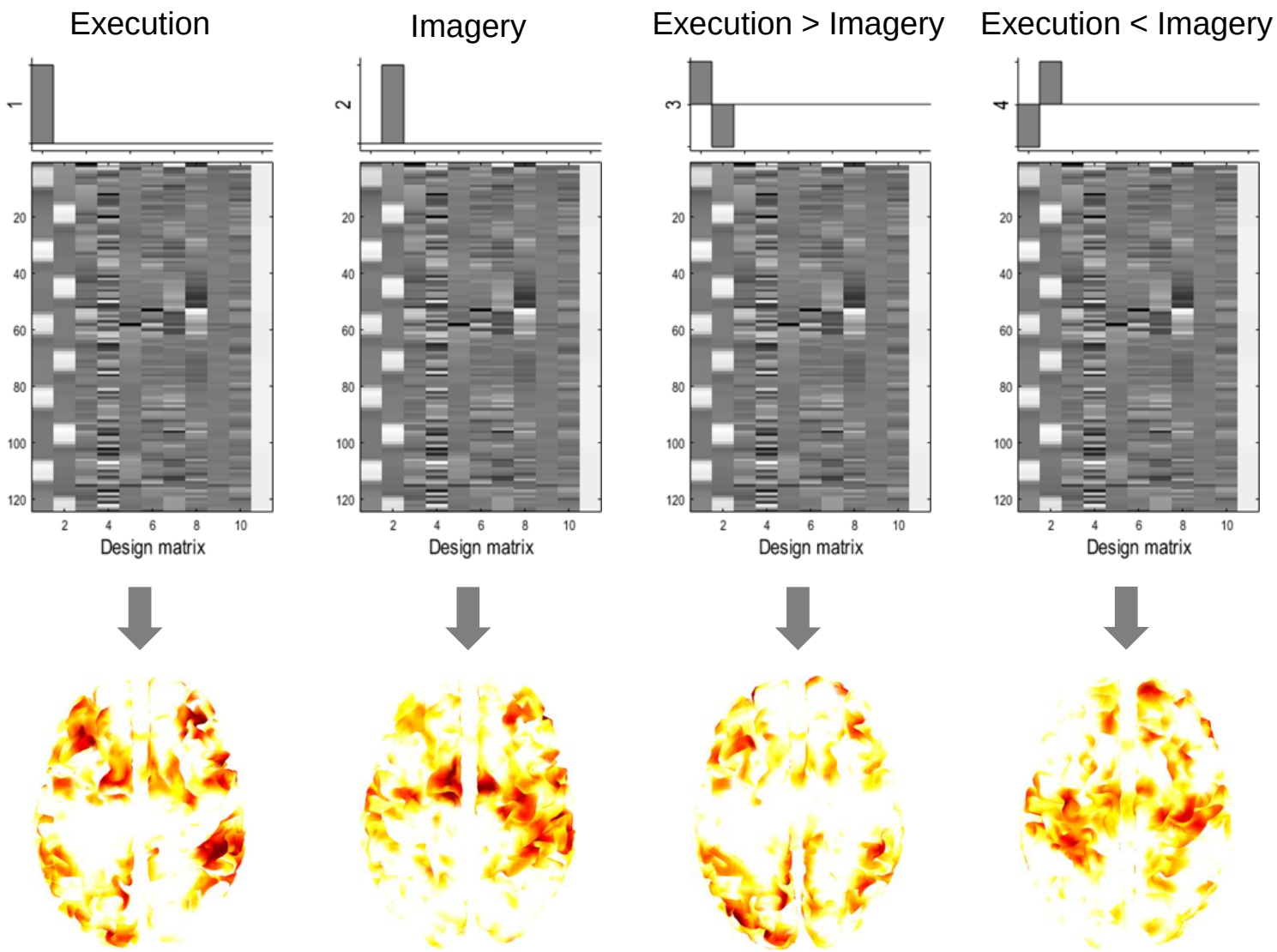
Motor Execution vs Motor Imagery



Predicted fMRI Time Series



Design matrix



Activity during a task

Activity difference between tasks

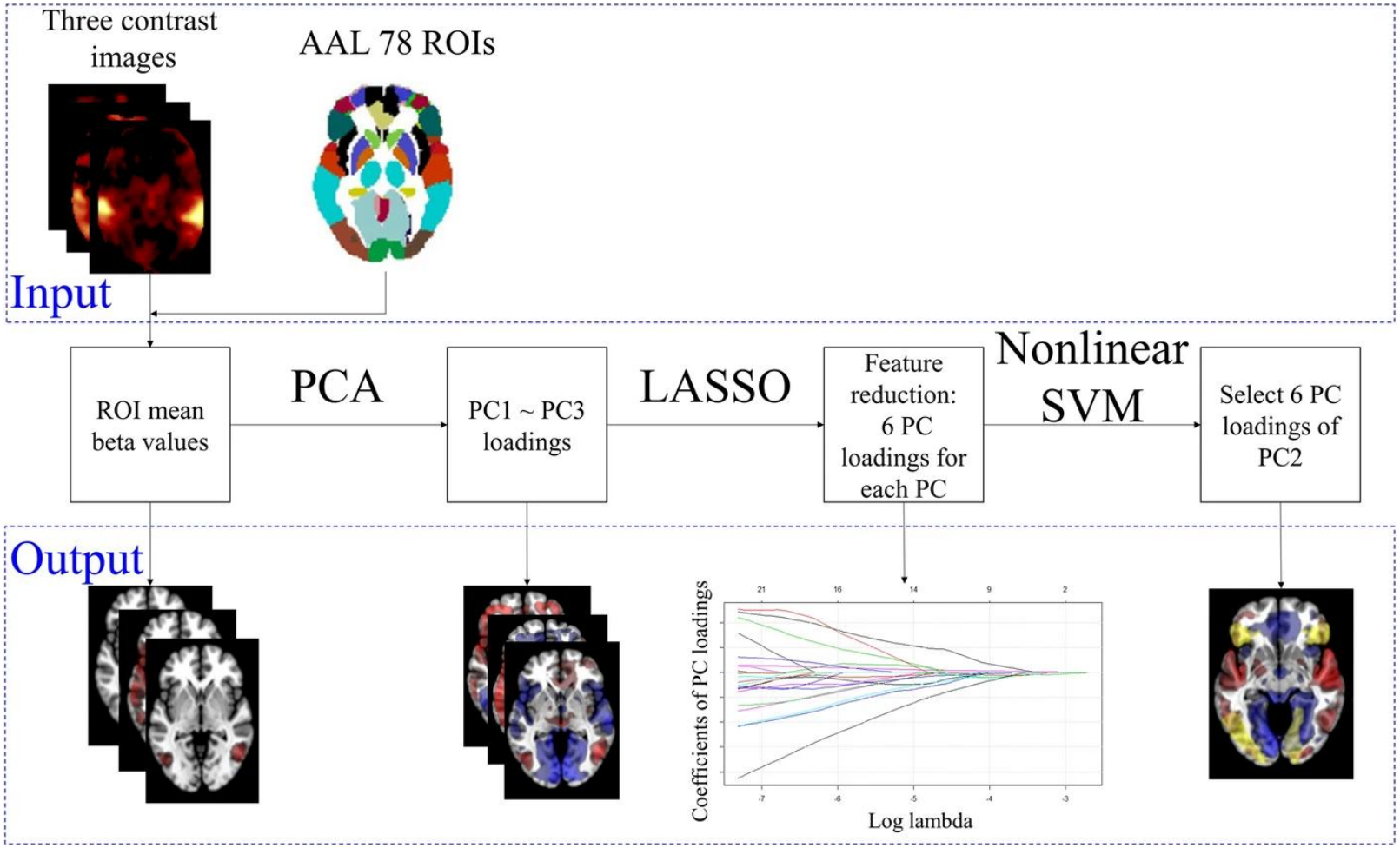
- Input to machine learning models
  - Table of voxel-wise or area-wise activity values

Features →

Samples ↓

	Voxel or Area 1 activity	Voxel or Area 2 activity	Voxel or Area 3 activity	…
Subject 1	-	-	-	-
Subject 2	-	-	-	-
Subject 3	-	-	-	-
⋮	-	-	-	-

  - Brain activity map

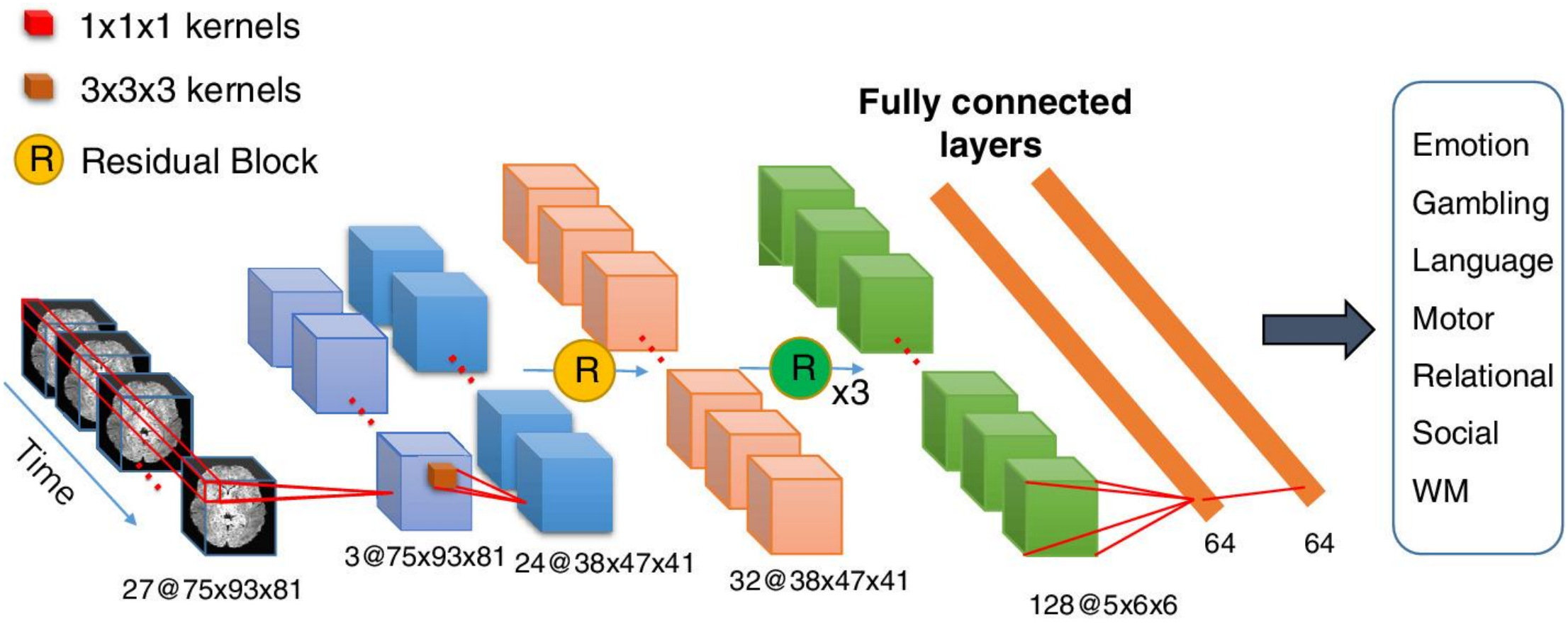


[Lee et al., 2021]

Application of Traditional Machine Learning to Brain Activity Features

Automated Task State Decoding

- Uses deep learning algorithms to automatically decode and predict specific task states or stimuli from task-based fMRI data
- Learns to identify the distinctive patterns of neural activity associated with each task state of the brain



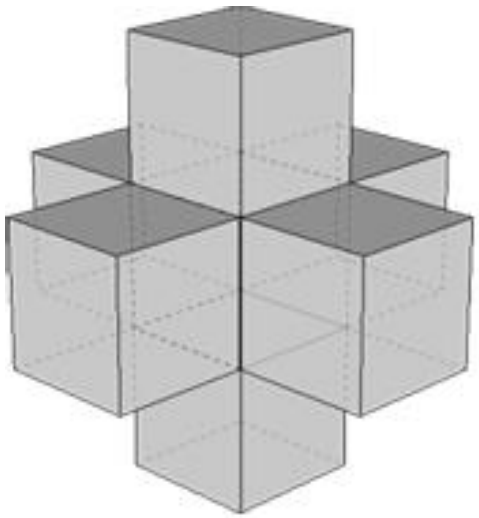
[Wang et al., 2019]

Task State Decoding from Task-based fMRI Data

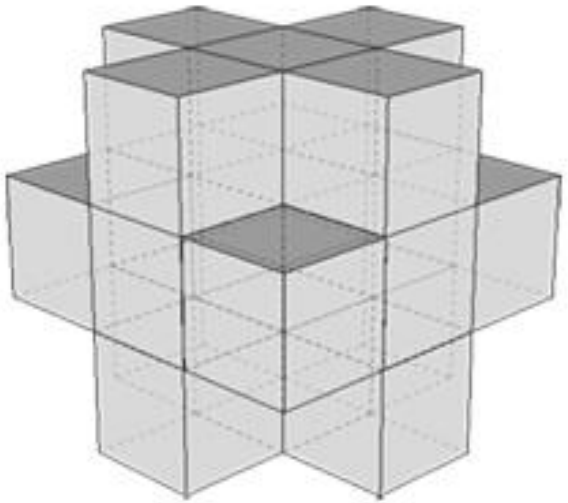
Resting State fMRI: Segregation Analysis

- Regional homogeneity [Zang et al., 2004]
  - Synchronization of time series between a given voxel and its neighbors
    - Neighbors: *K* nearest neighbors
    - Synchronization: Kendall's coefficient of concordance (KCC)

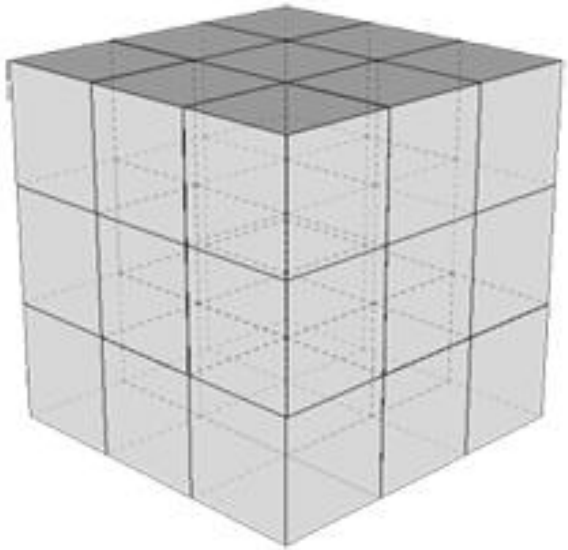
$$\mathrm{KCC} = \frac{\sum_{i=1}^{n} R_i^2 - n(\overline{R})^2}{\frac{1}{12}K^2(n^3 - n)} = 12\frac{\sum_{i=1}^{n}(\overline{R}_i)^2}{(n^3 - n)} - 3\frac{(n+1)}{(n-1)}$$



Faces
(7 voxels)



Faces + Edges
(19 voxels)

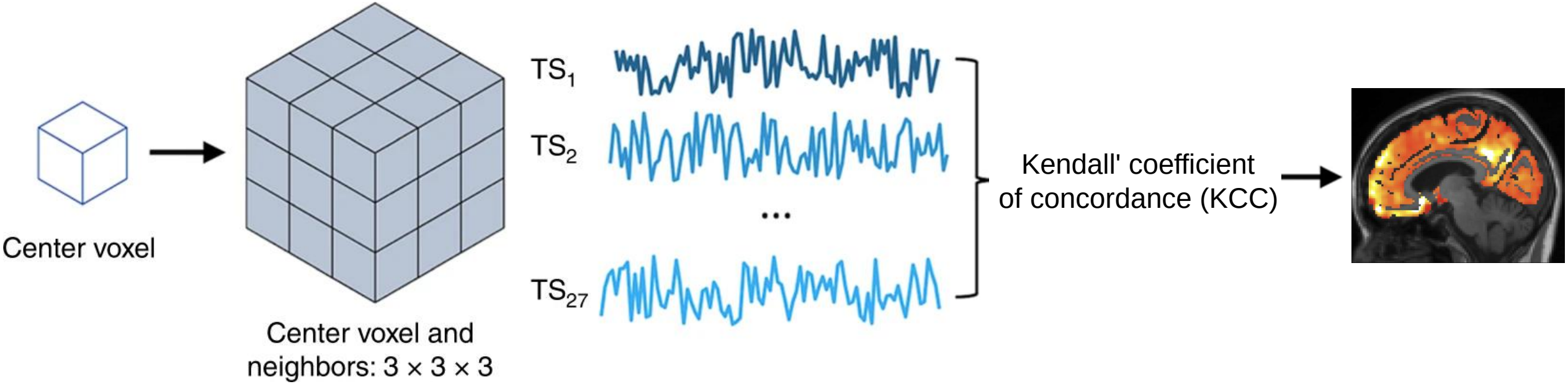


Faces + Edges + Corners
(27 voxels)

[https://fcp-indi.github.io/docs/latest/user/reho]

Different Definitions of Nearest Neighbors

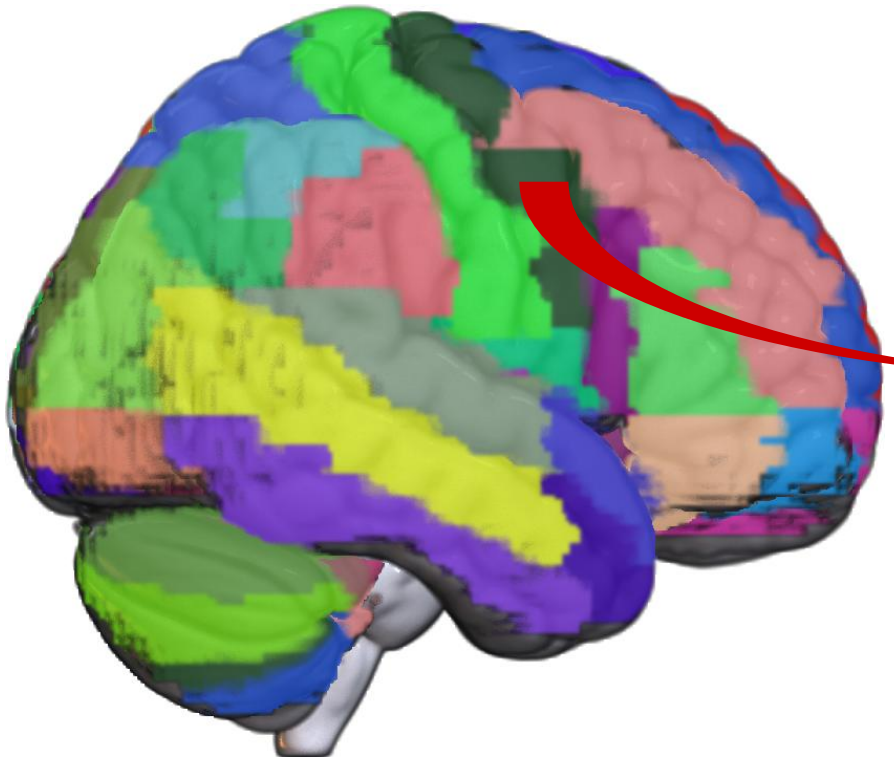
- Based on the hypothesis that intrinsic brain activity is manifested by clusters of voxels rather than single voxels
- Requires no pre-defined voxel or area
- Provides information about the local activity of areas throughout the brain

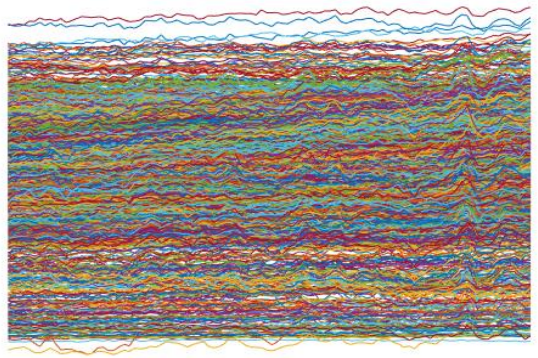


[Harrison et al., 2019]

Regional Homogeneity

- Seed-based correlation [Biswal et al., 1995]
  - Synchronization of time series between a seed and all other voxels in the brain
    - Seed: pre-defined voxel or area
    - Synchronization: statistical association, particularly correlation
  - Based on the hypothesis that brain areas with similar activity patterns are likely to be communicating and sharing information
  - Often used to explore a set of brain areas that share similar patterns of activity

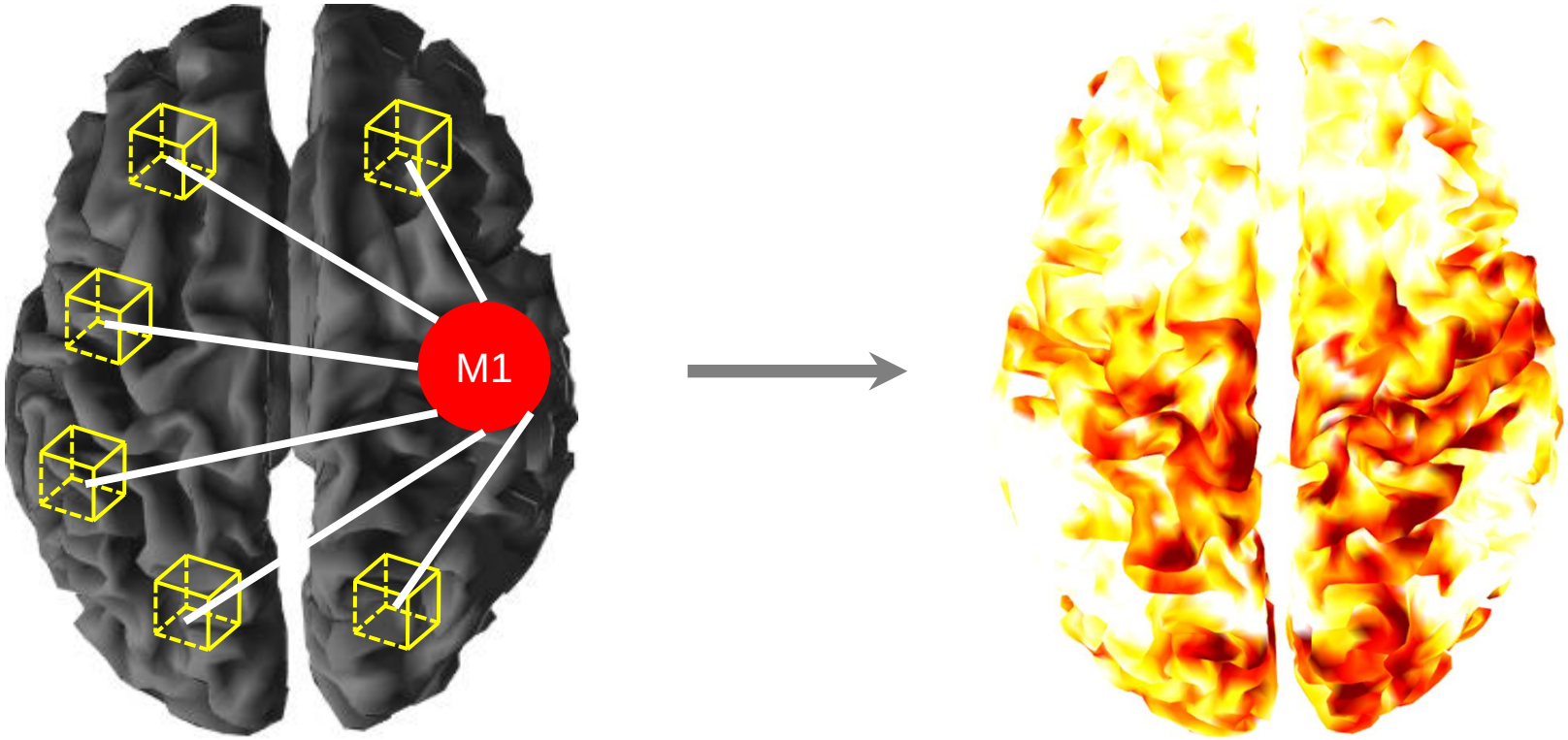




Representative fMRI time series

fMRI time seirs
from multiple voxels

Extraction of fMRI Time Series from a Seed (Primary Motor Cortex)



Seed-based Correlation for the Primary Motor Cortex

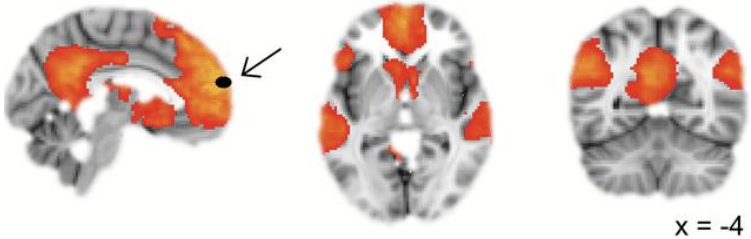
Left middle temporal gyrus

x = -44 y = -66 z = 46

Right middle temporal gyrus

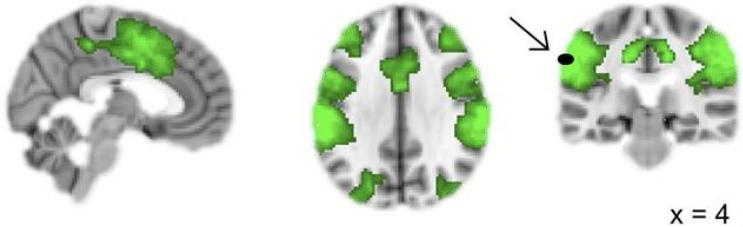
x = -52 y = -64 z = 22

Left medial frontal gyrus



x = -4 y = -58 z = 2

Left supramarginal gyrus

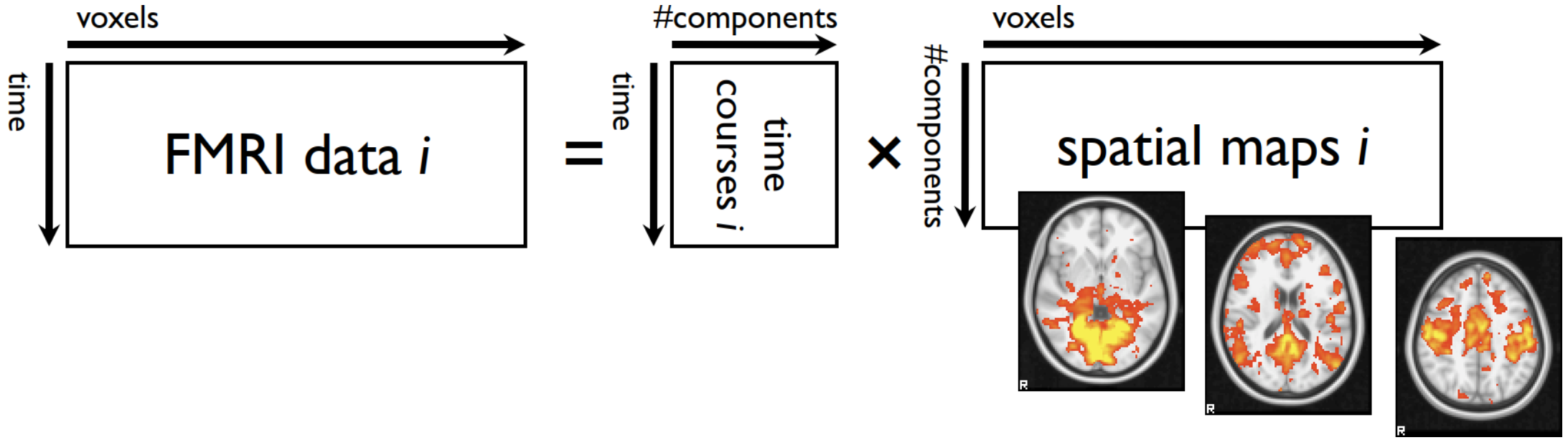


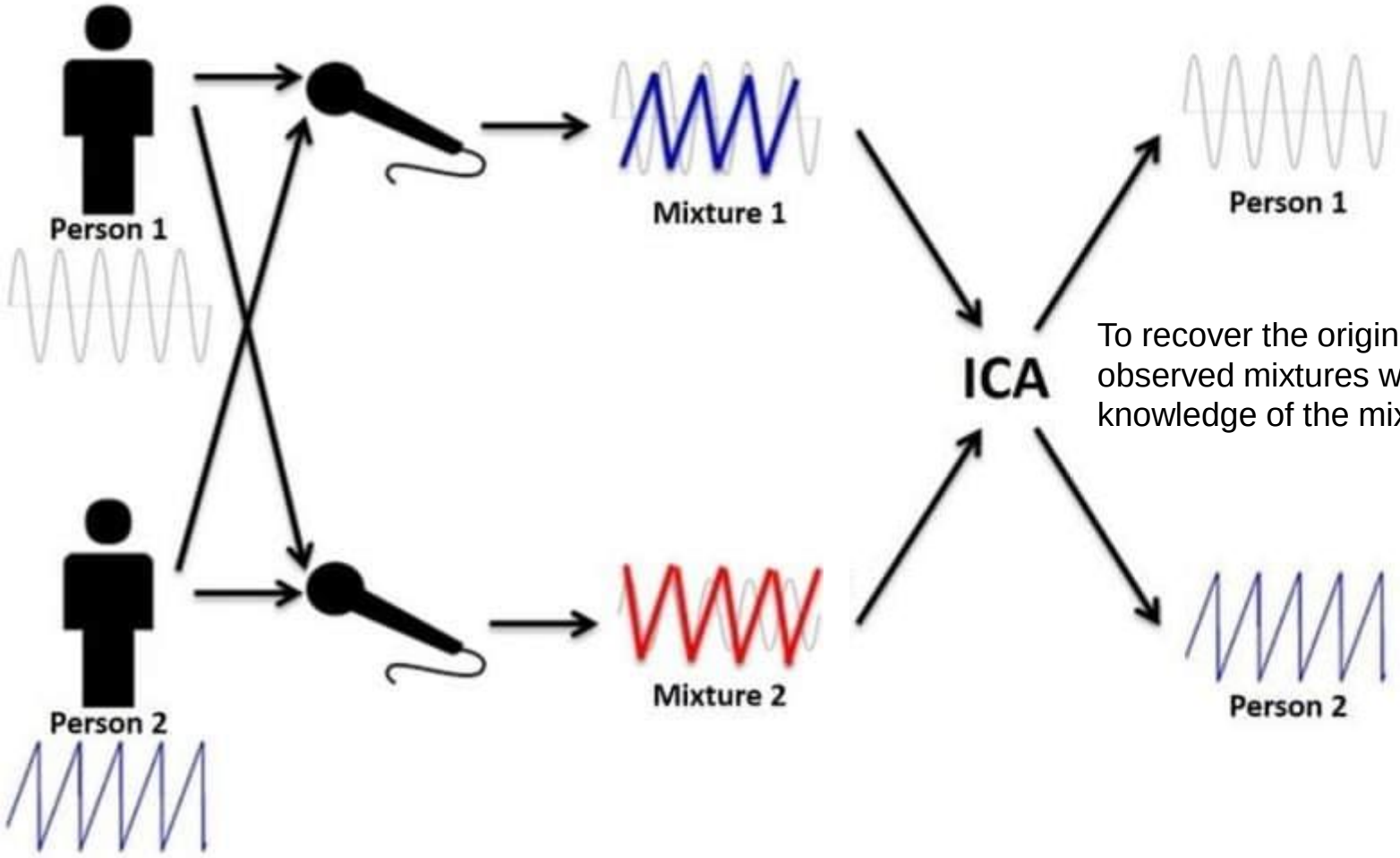
x = 4 y = -28 z = 32

[Cousijn et al., 2014]

Time Series Synchronization Explored by Correlation with Different Seeds

- Independent component
  - Statistical source or factor that independent component analysis (ICA) aims to extract from multivariate data
    - Spatial map and its time course separated from fMRI data
  - Based on the hypothesis that the observed data are linear mixtures of the unknown independent components

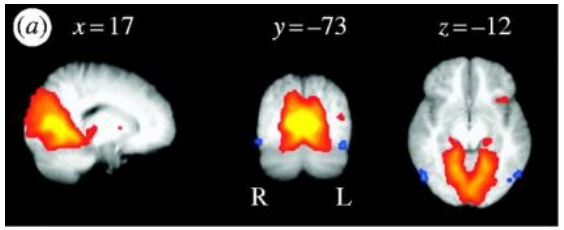




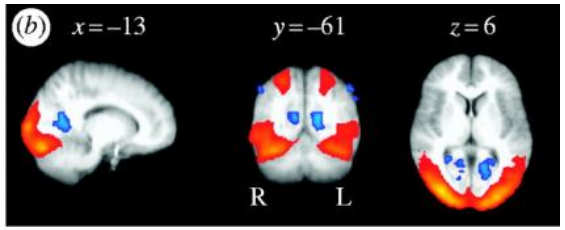
To recover the original signals from the observed mixtures without having prior knowledge of the mixing process

[https://vocal.com/blind-signal-separation/independent-component-analysis/]

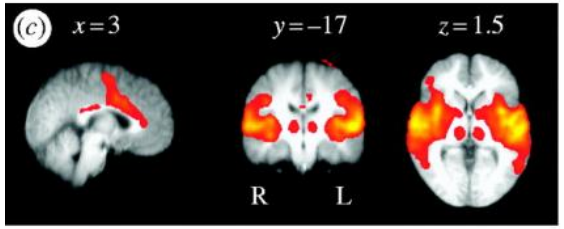
Independent Component Analysis for the Cocktail Party Problem



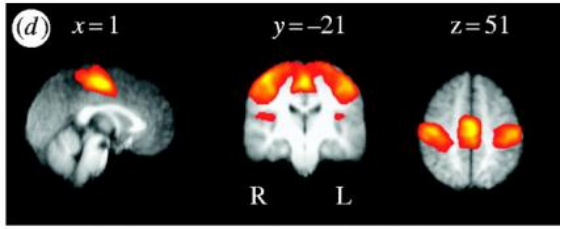
Medial visual cortical areas



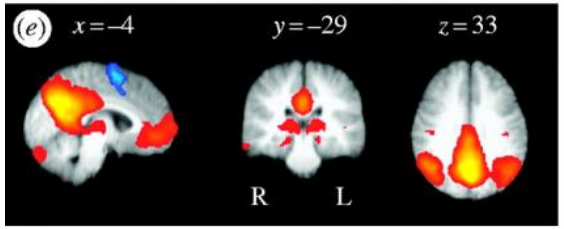
Lateral visual cortical areas



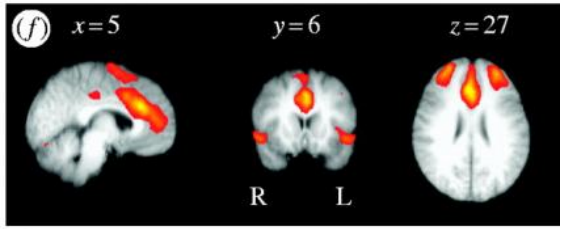
Auditory system



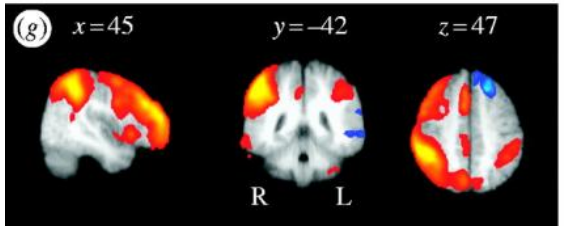
Sensory–motor system



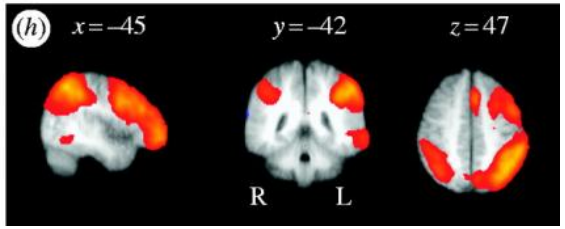
Visuo-spatial system



Executive control



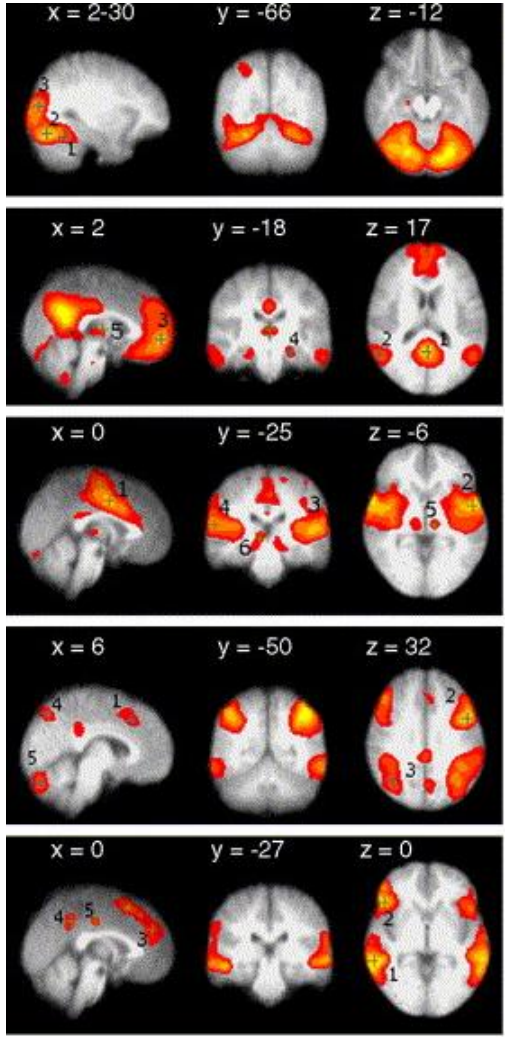
Right dorsal visual stream



Left dorsal visual stream

[Beckmann et al., 2005]

Time Series Synchronization Explored by Independent Component Analysis (1)



Visual cortical areas

Visuospatial and executive system

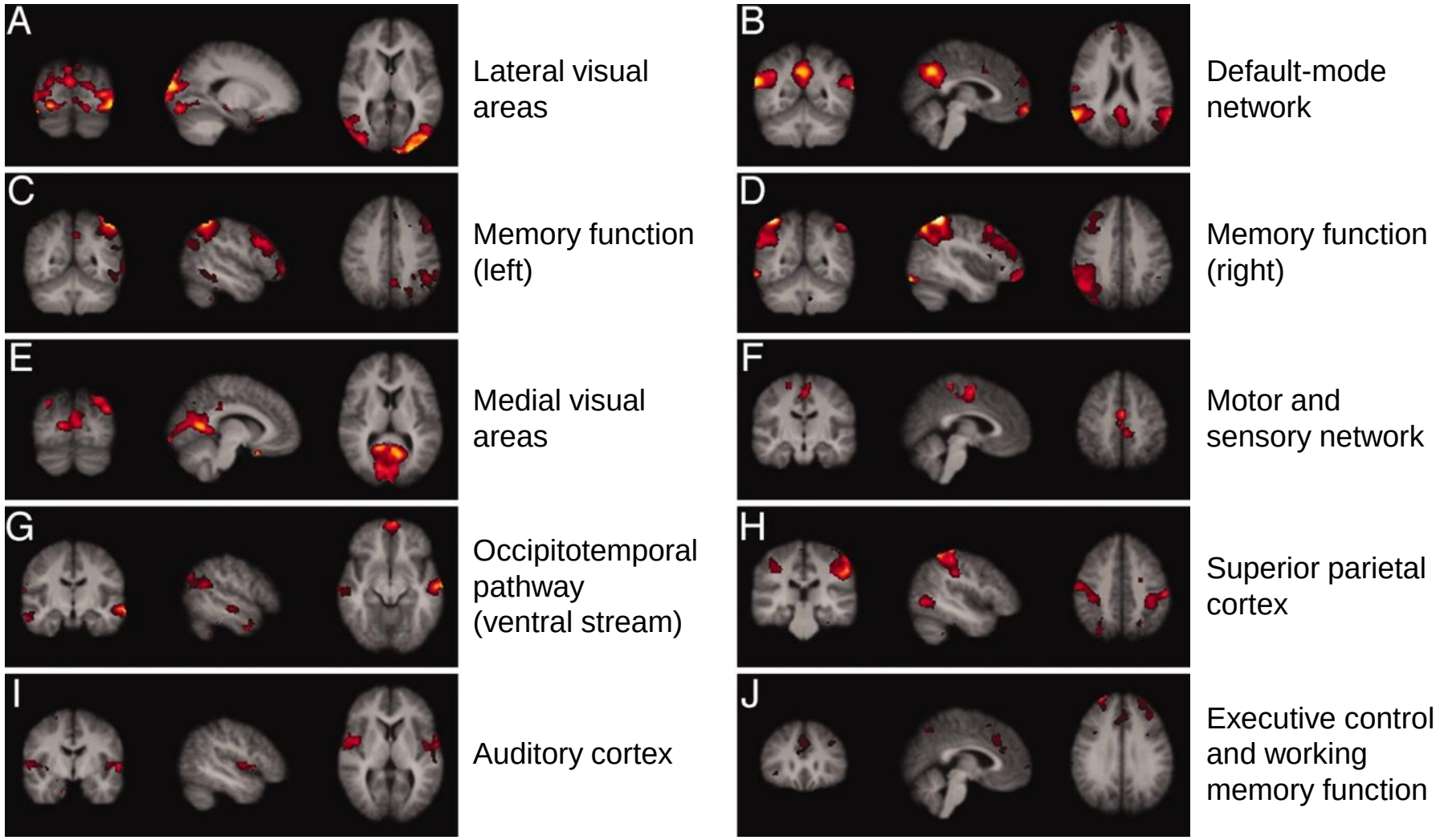
Sensory and auditory system

Dorsal pathway

Ventral pathway

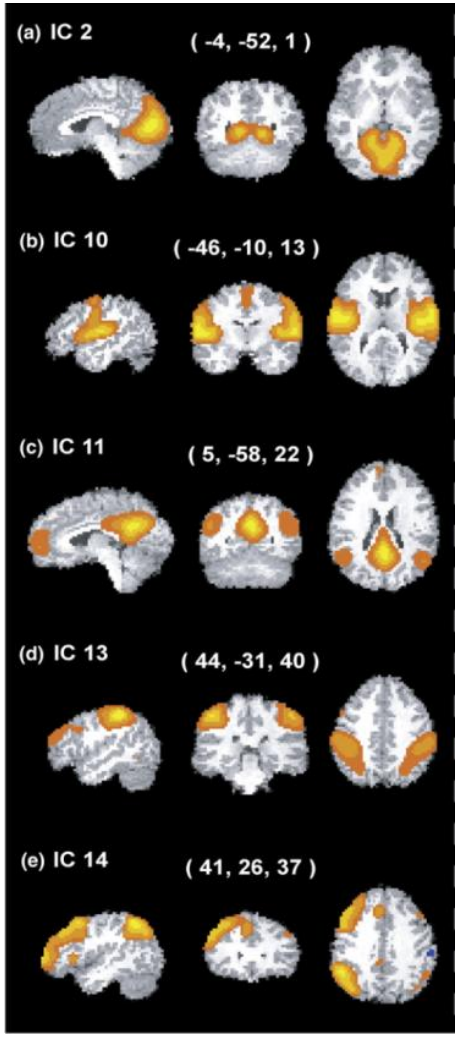
[De Luca et al., 2006]

Time Series Synchronization Explored by Independent Component Analysis (2)



[Damoiseaux et al., 2006]

Time Series Synchronization Explored by Independent Component Analysis (3)



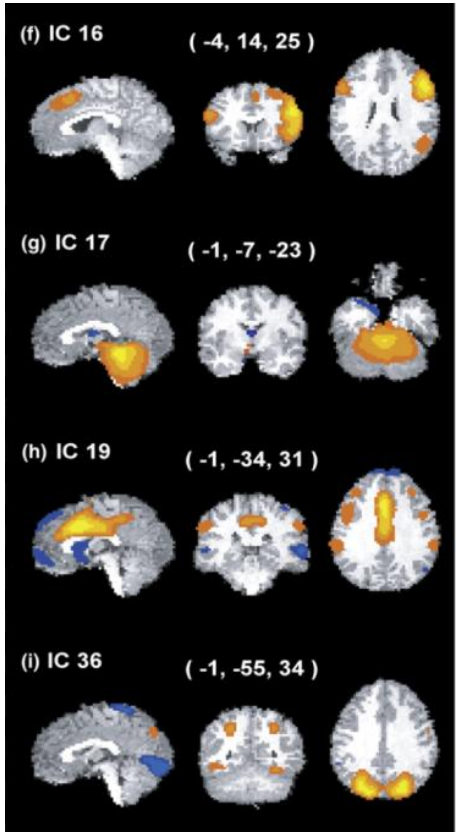
Medial occipital cortices

Bilateral temporal cortices and ACC

PCC, ACC, and bilateral inferior parietal cortex (default-mode network)

Bilateral motor areas

Right medial and lateral frontal cortices and parietal cortex



Left medial and lateral frontal cortices and parietal cortex

Cerebellum

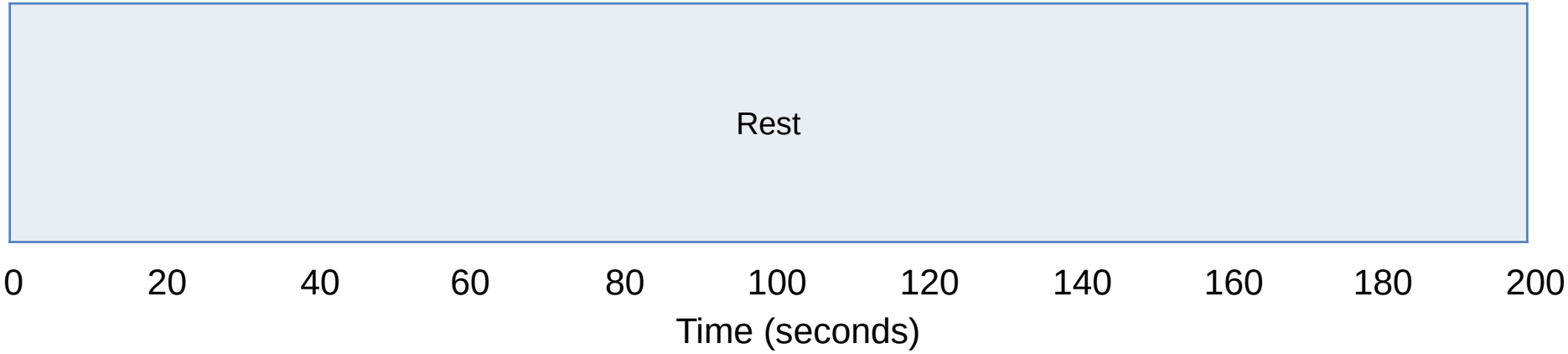
Medial frontal/ACC, bilateral DLPFC, bilateral temporal cortex and striatum

Bilateral lateral occipital cortices

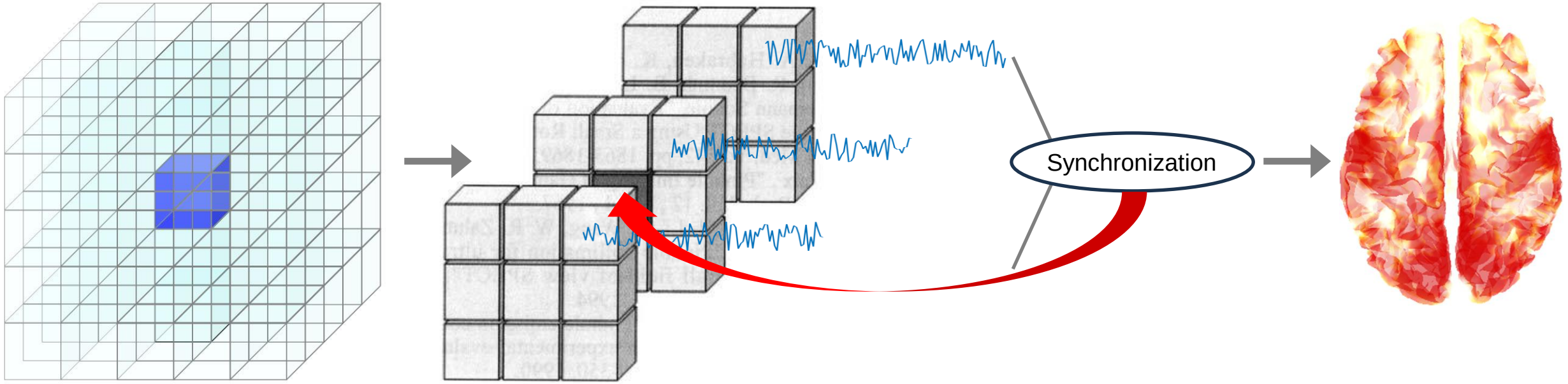
[Chen et al., 2008]

Time Series Synchronization Explored by Independent Component Analysis (4)

[Resting State fMRI: Segregation Analysis]



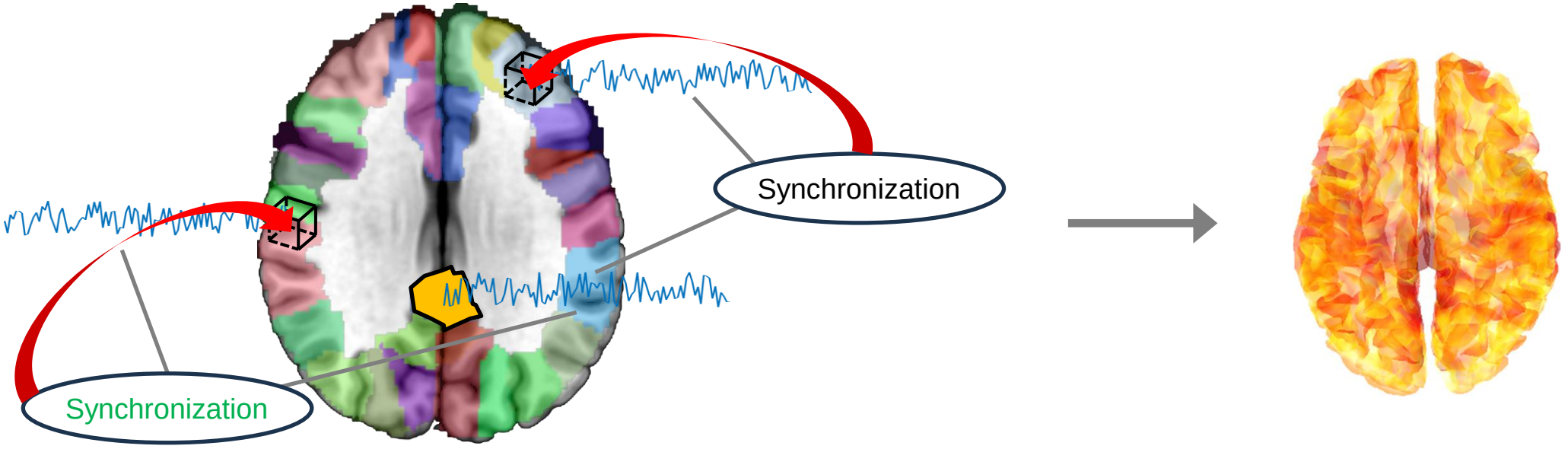
– 100 scans (200 seconds)



Centre voxel

Nearest neighbours

Regional Homogeneity



Seed: posterior cingulate gyrus

Correlation with the Posterior Cingulate Gyrus: Default Mode Network

[Statistical Analysis of Resting State fMRI]

- Regional homogeneity ~

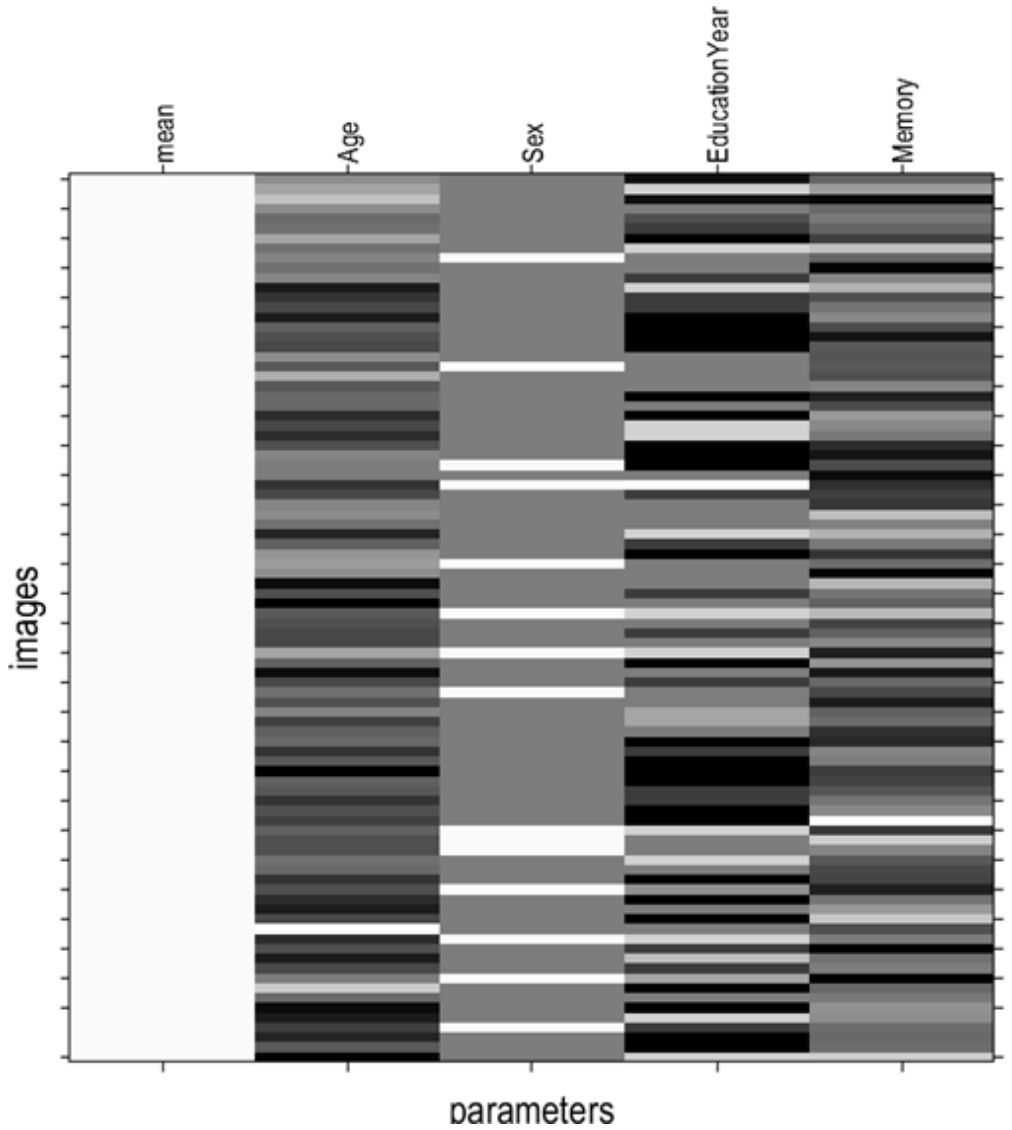
  Age +

  Sex +

  Education year +

  Memory performance

Design matrix



Output

Regression

Positive correlation

Negative correlation

- Correlation with the posterior cingulate gyrus ~

  Age +

  Sex +

  Education year +

  Memory performance

Output

Regression

Positive correlaton

Negative correlation

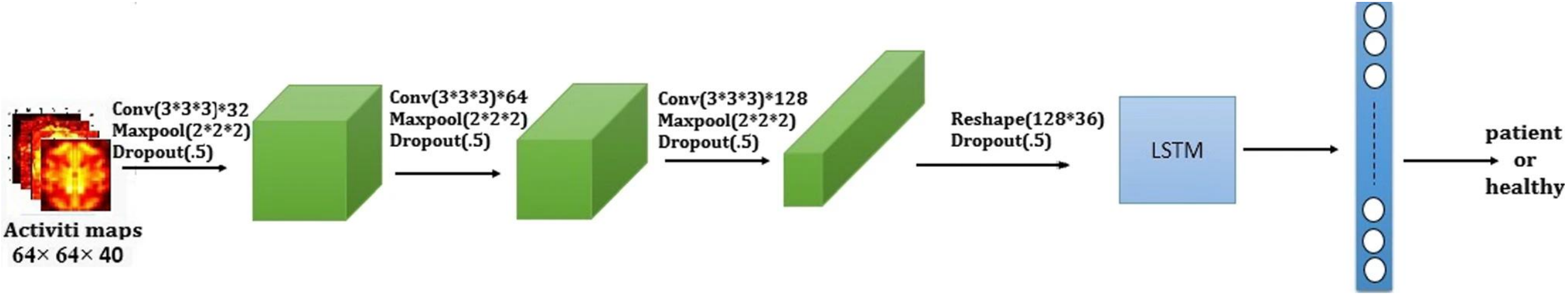
- Input to machine learning models
  - Table of voxel-wise or area-wise synchronization (regional homogeneity, seed-based correlation, or independent component) values

Features →

Samples ↓

	Voxel or Area 1 synchronization	Voxel or Area 2 synchronization	Voxel or Area 3 synchronization	…
Subject 1	-	-	-	-
Subject 2	-	-	-	-
Subject 3	-	-	-	-
⋮	-	-	-	-

  - Time series synchronization (regional homogeneity, seed-based correlation, or independent component) map

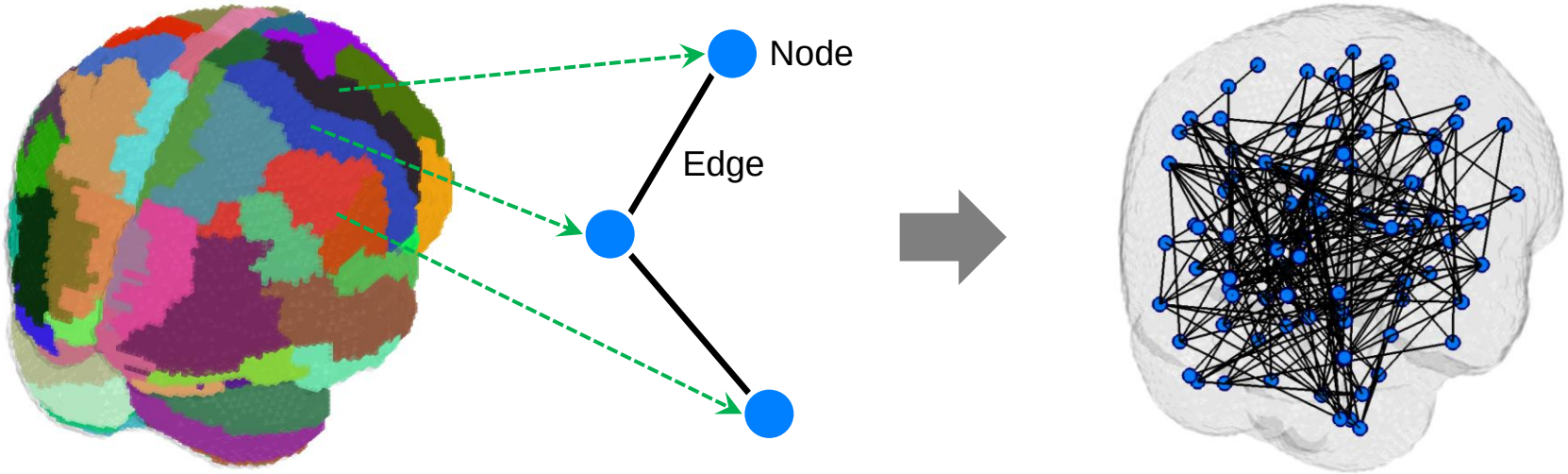


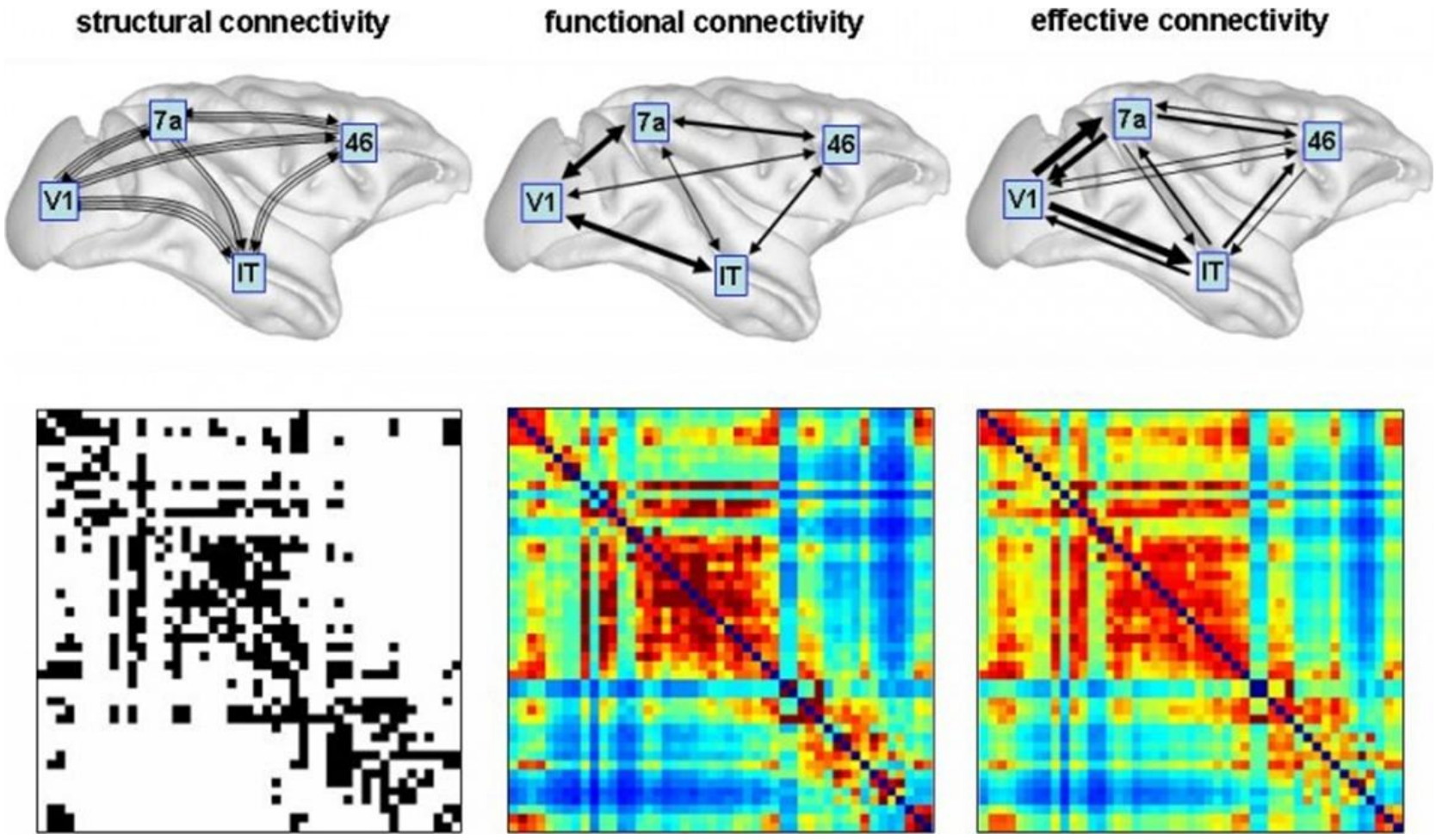
[Ghanbari et al., 2022]

Application of Deep Learning to Time Series Synchronization Maps

Resting State fMRI: Integration Analysis

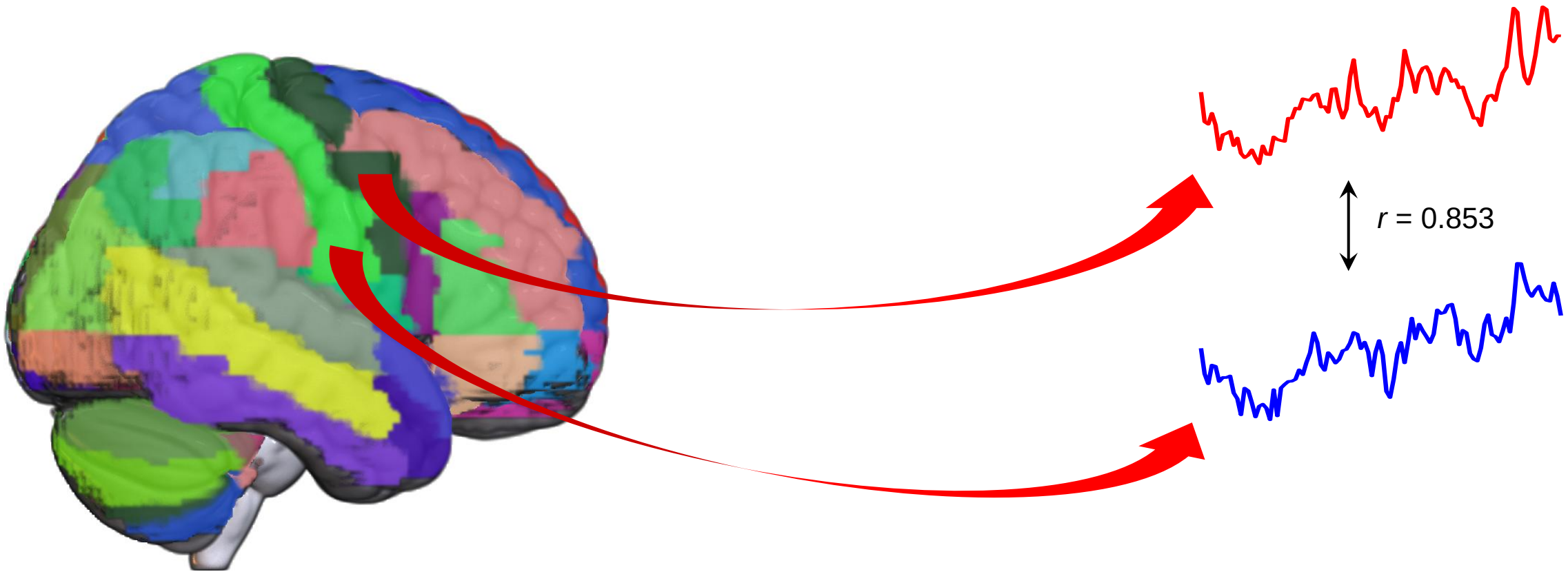
- Network
  - Set of nodes and edges
    - Nodes: pre-defined areas
    - Edges: connectivity (correlation or causality) between areas



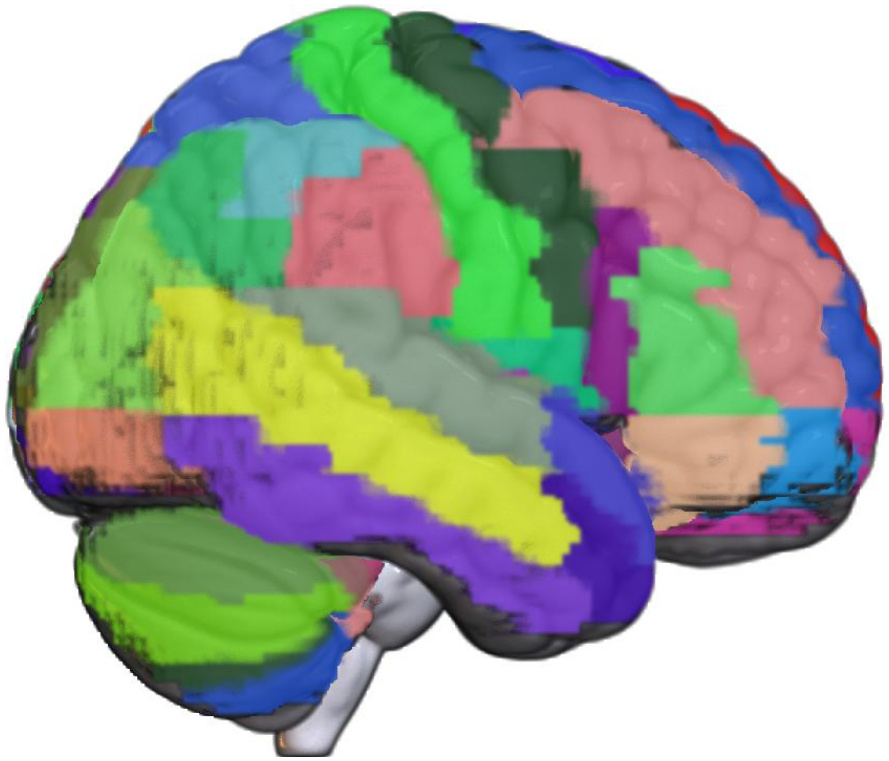


[Honey et al., 2007]

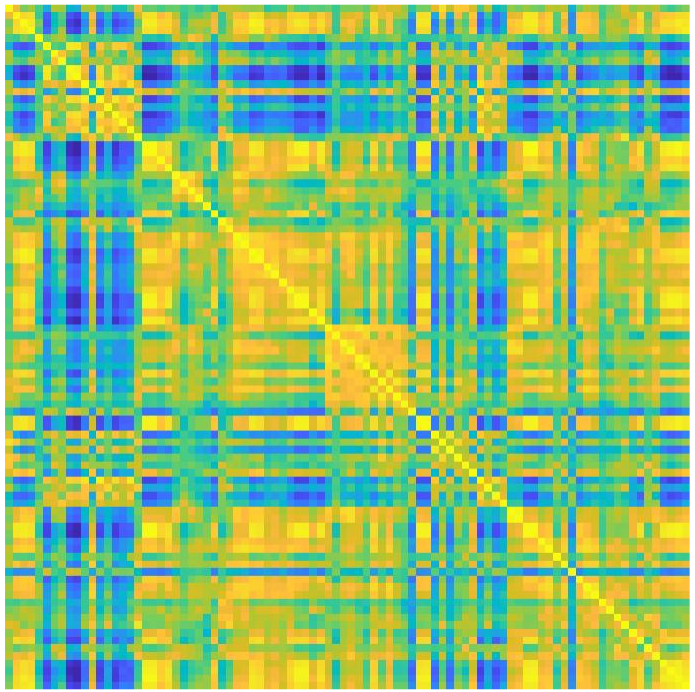
Modes of Brain Connectivity



Pair-wise Correlation of Time Series



Time series correlation



Functional Network or Connectome

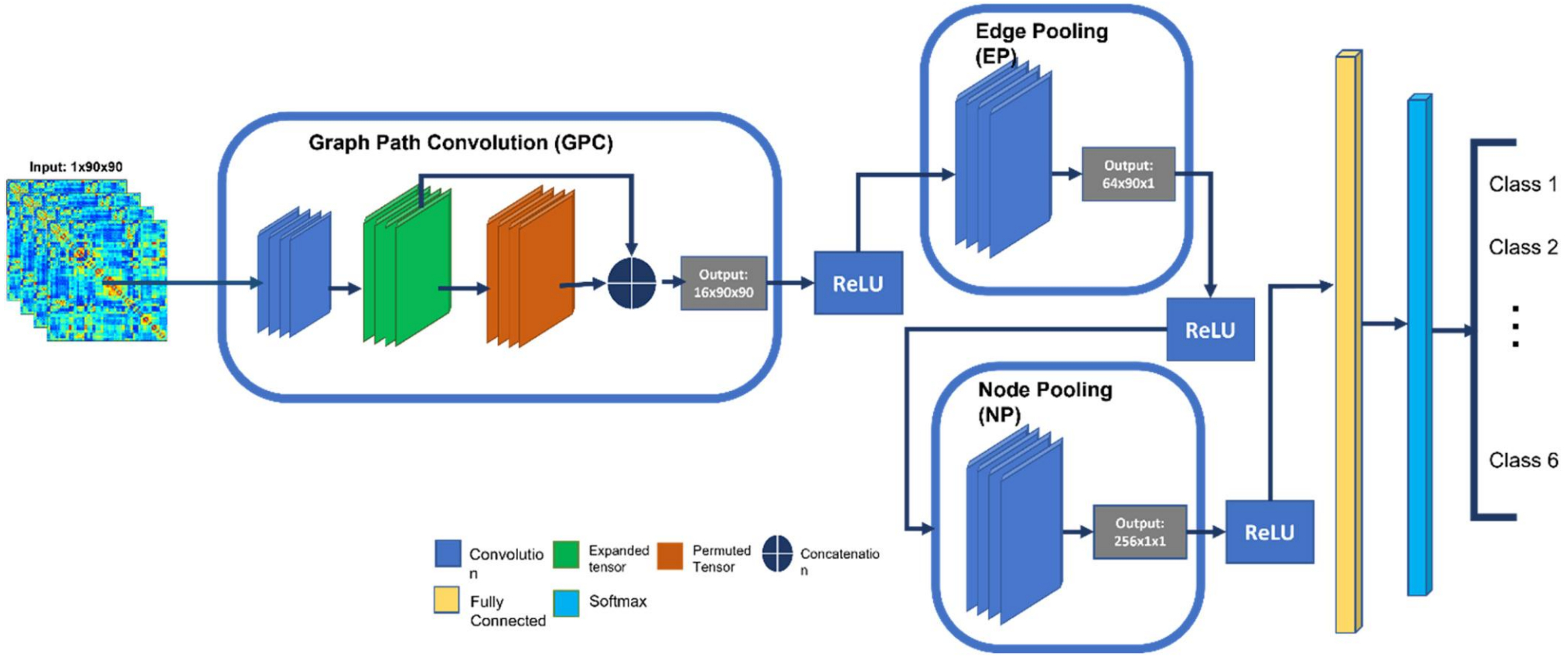
- Input to machine learning models
  - Table of area-to-area connectivity (correlation or causality) values

Features →

Samples ↓

	Areas 1 – 2 connectivity	Areas 1 – 3 connectivity	Areas 1 – 4 connectivity	…
Subject 1	-	-	-	-
Subject 2	-	-	-	-
Subject 3	-	-	-	-
⋮	-	-	-	-

  - Functional network map

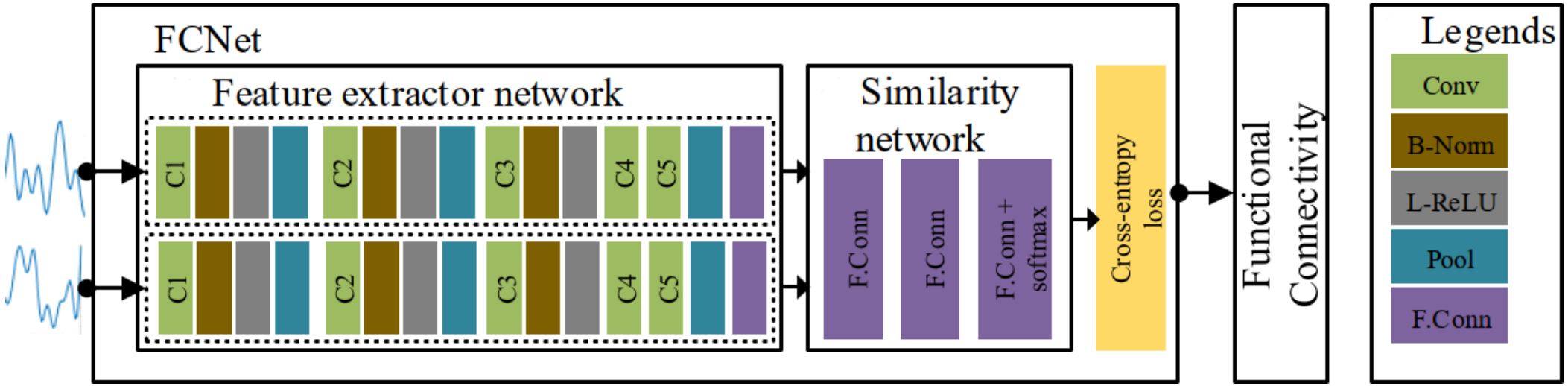


[Alorf et al., 2022]

Application of Deep Learning to Functional Network Maps

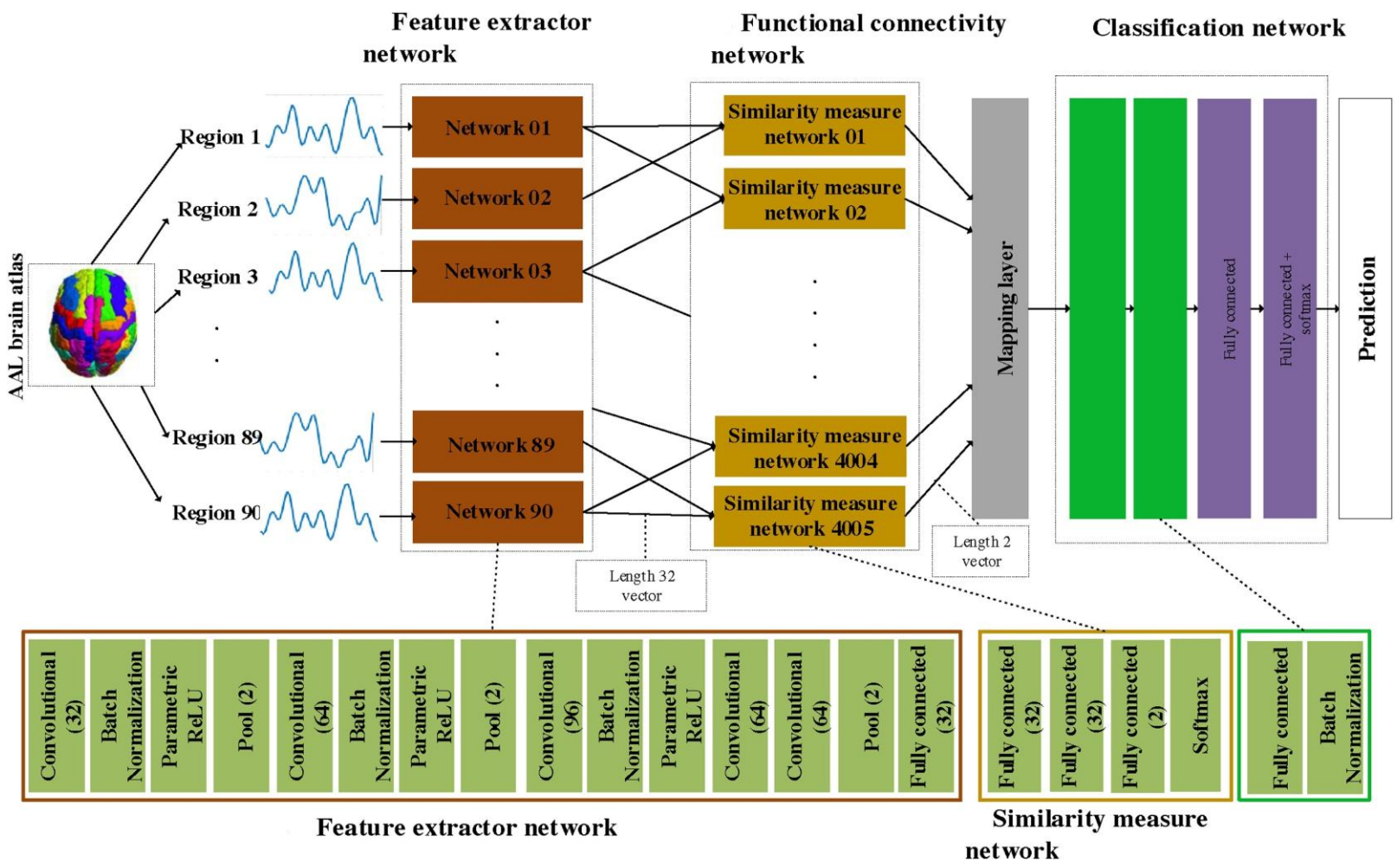
Automated Functional Connectivity Extraction

- Applies deep learning algorithms to identify functional relationships between brain areas
- Employs neural networks to separate signal from noise in connectivity data



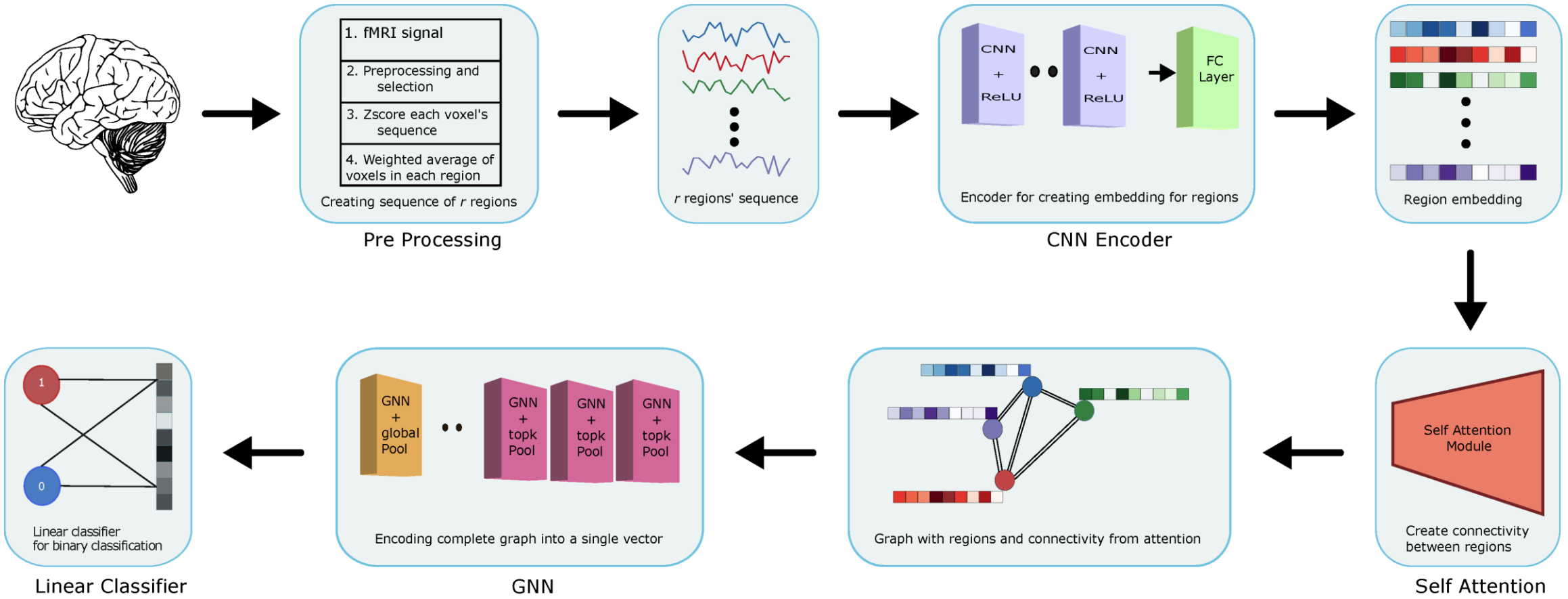
[Riaz et al., 2017]

FCNet: Functional Connectivity Extraction



[Riaz et al., 2020]

DeepFMRI: Functional Connectivity Extraction



[Mahmood et al., 2021]

BrainGNN: Functional Connectivity Extraction