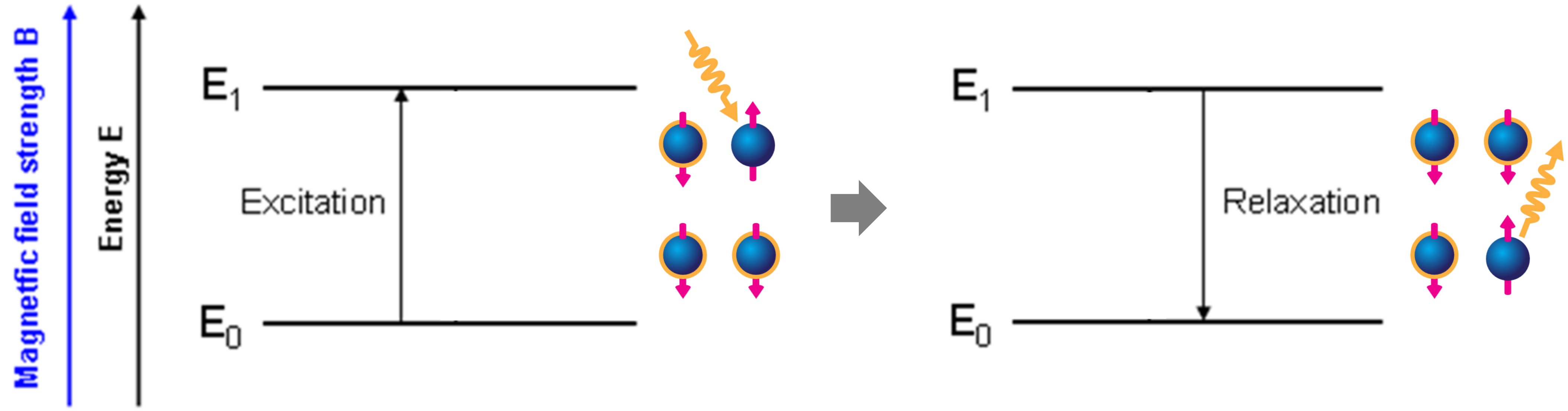
Medical/Bio Research Topics Ⅱ: Week 03 (19.09.2025)

Functional MRI: Basic Principles and Data Processing Methods

기능 자기공명영상: 기본 원리 및 데이터 처리 방법

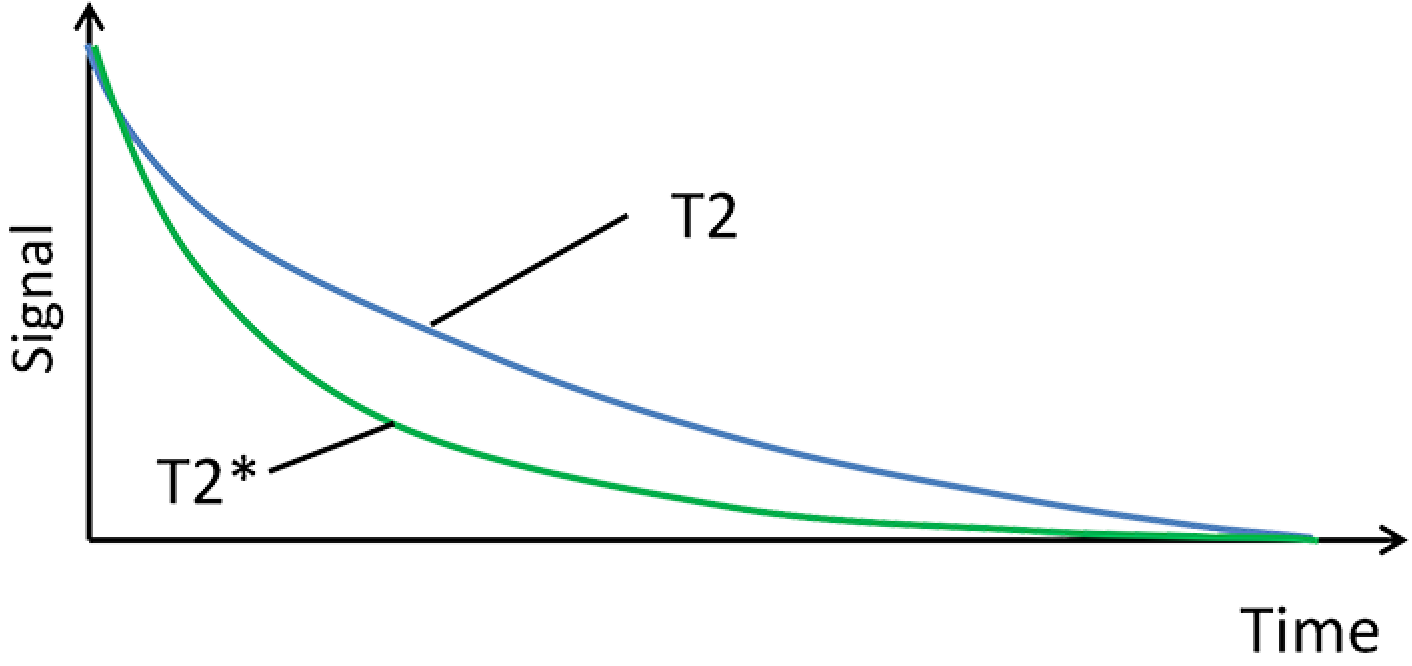
MRI Principles

- Medical application of nuclear magnetic resonance (NMR)
  - Generates different contrasts between tissues based on the relaxation properties of hydrogen nuclei therein



- MRI contrast types
  - T1-weighted contrast
    - Primarily uses a spin-echo or a gradient-echo sequence
    - With short Echo Time (TE) and short Repetition Time (TR) to maximize T1 contrast and minimize T2 effects
  - T2-weighted contrast
    - Primarily uses a spin-echo sequence
    - With long TE to allow for T2 decay and long TR to minimize T1 effects
  - T2* (T2 star)-weighted contrast
    - Typically uses a gradient echo echo-planar imaging (EPI) sequence
    - With medium to long TE to maximize sensitivity to T2* effects and short to medium TR to allow for rapid sampling of the signal while maintaining adequate signal-to-noise ratio

- T2* contrast
  - Combines true T2 decay and magnetic field inhomogeneity effects
    - T2* relaxation is sensitive to both spin-spin interactions (like T2) and local magnetic field inhomogeneities, causing faster dephasing of spins and shortening T2*
  - T2* sensitivity to local magnetic field inhomogeneities in and around blood vessels forms the foundation of the blood-oxygen-level dependent (BOLD) effect in functional MRI (fMRI)
    - Allows for rapid image acquisition (essential for temporal resolution)
    - Provides good contrast for detecting BOLD signal changes
    - Enables whole-brain coverage in reasonable scan times



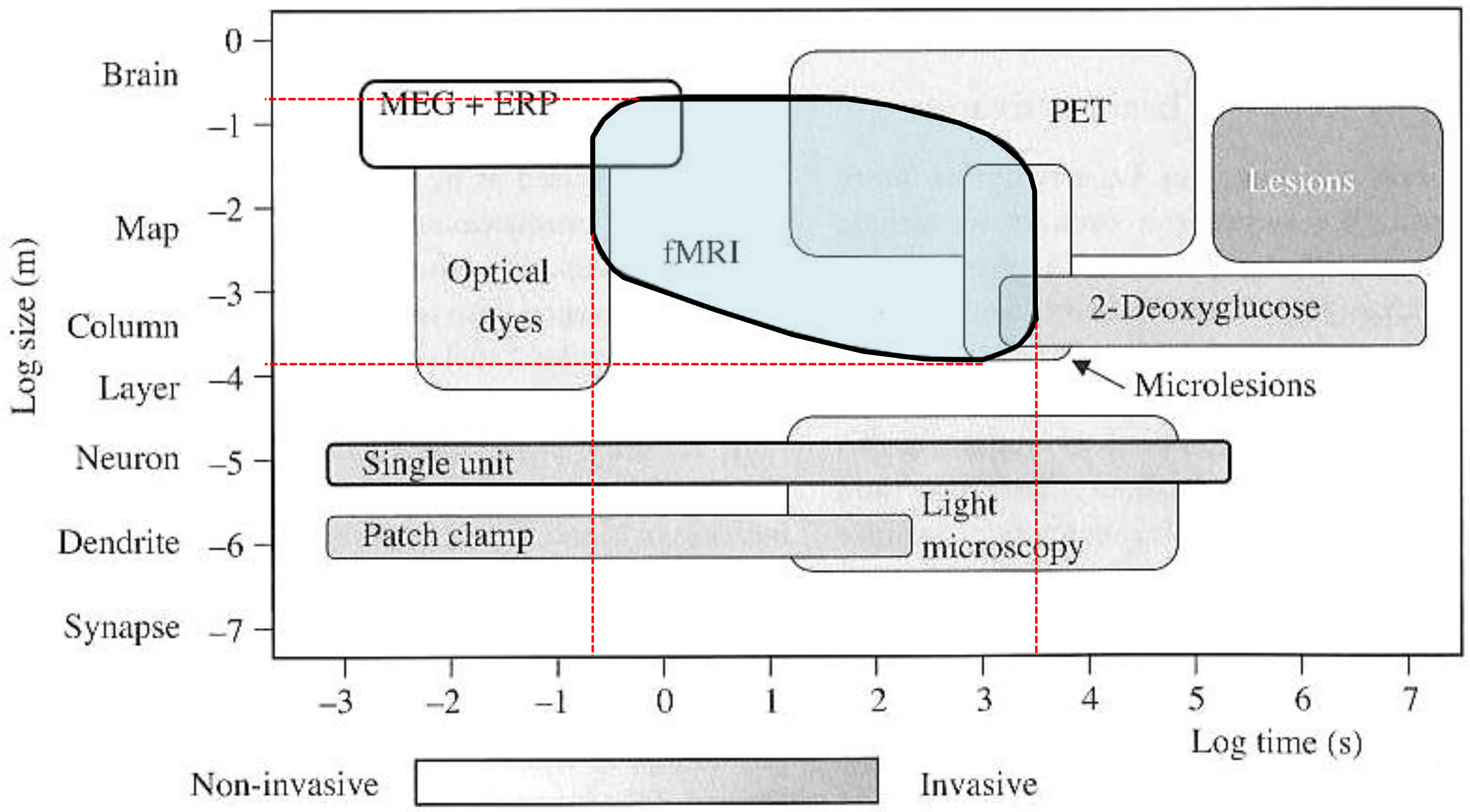
[https://www.radiologycafe.com/frcr-physics-notes/mr-imaging/t1-and-t2-signal/]

Quicker T2* Decay than T2 Decay

fMRI

- MRI technique primarily for measuring brain activity indirectly through the coupling between hemodynamics (changes in blood flow, blood volume, and blood oxygenation) and neuronal activity
  - Creates a movie that non-invasively reveals details of events over time in the brain
- Applications of fMRI
  - Brain function analysis

- Spatially within millimeters
- Temporally within a window of a few seconds



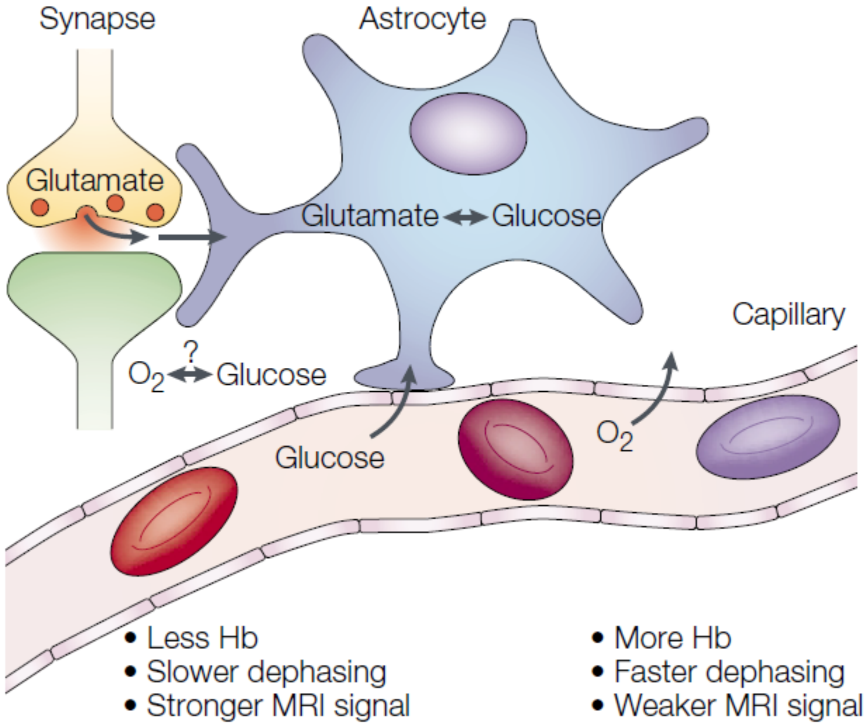
[Adapted from Churchland and Sejnowski, 1988]

fMRI in Comparison with Other Neuroscience Methods

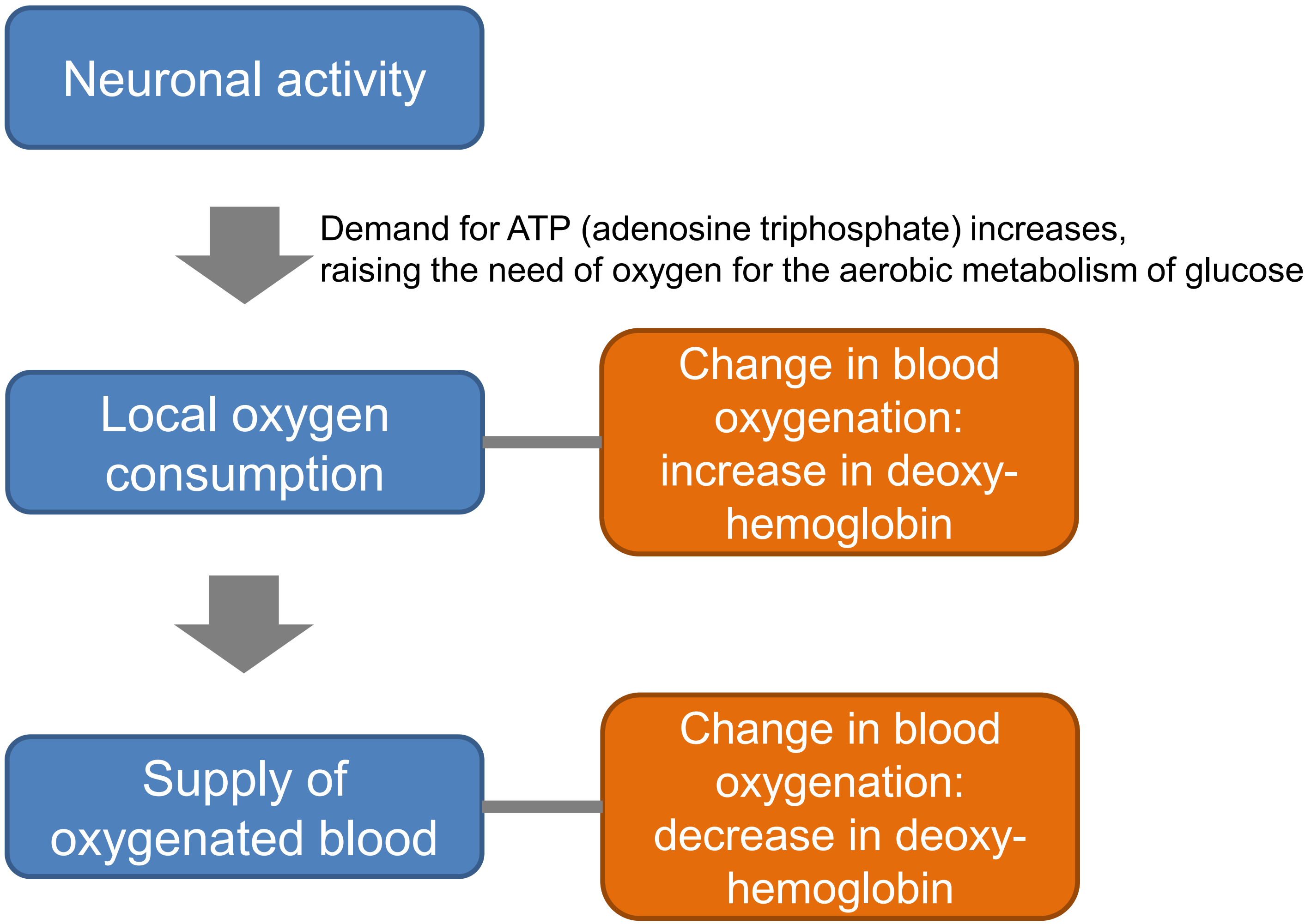
BOLD Contrast for fMRI

- BOLD contrast
  - Exploits different electromagnetic properties between blood containing oxygen (oxyhemoglobin) and blood without oxygen (deoxyhemoglobin)
  - Deoxyhemoglobin (paramagnetic, thus faster relaxation) vs. oxyhemoglobin (weakly diamagnetic)
    - Deoxyhemoglobin concentration ↑ → MRI signal intensity ↓
    - Deoxyhemoglobin concentration ↓ → MRI signal intensity ↑

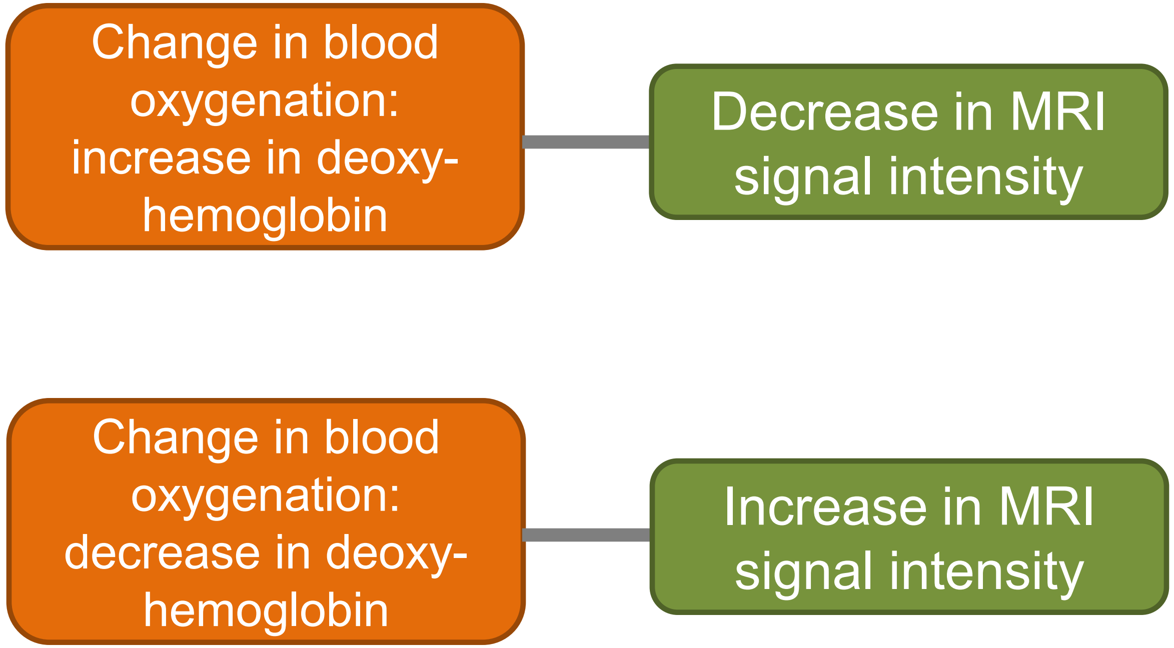
- Based on the assumption that the changing distribution of blood oxygenation in the brain correlates with neuronal activity



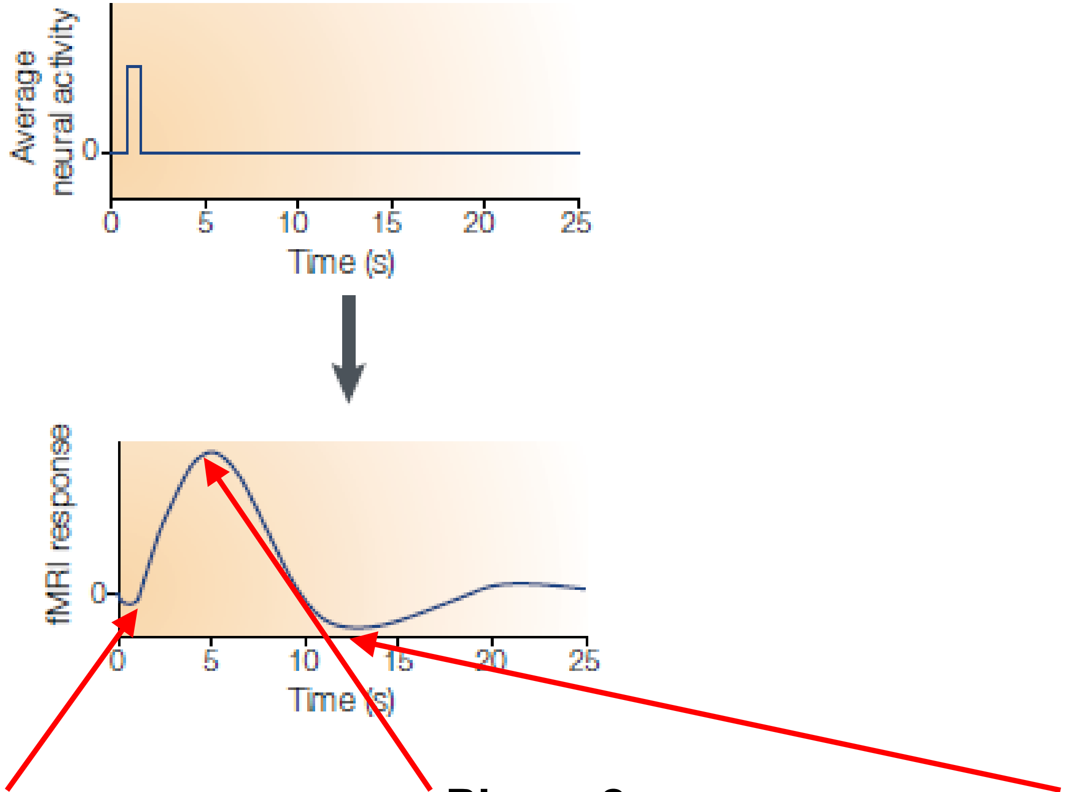
[Heeger and Ress, 2002]



Neuronal Activity → Blood Oxygenation Change



(Neuronal Activity →) Blood Oxygenation Change → MRI Signal Intensity Change



	Phase 1	**Phase 2**	**Phase 3**
Hemodynamics	Consumption of local oxygen	Oversupply of oxygenated blood	Diminished oversupply of oxygenated blood
MRI signal	Small decrease below baseline	Large increase above baseline	Decrease back to below baseline

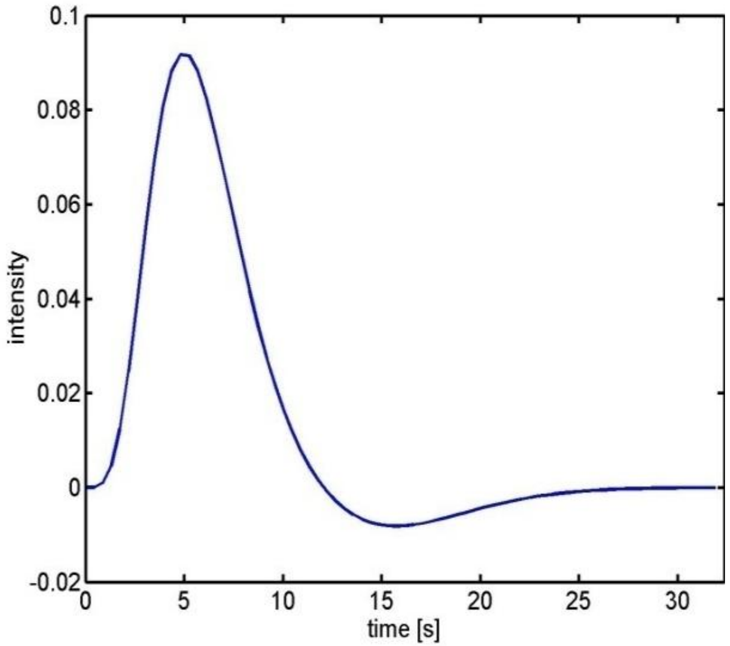
[Heeger and Ress, 2002]

Three Phases of the BOLD Response

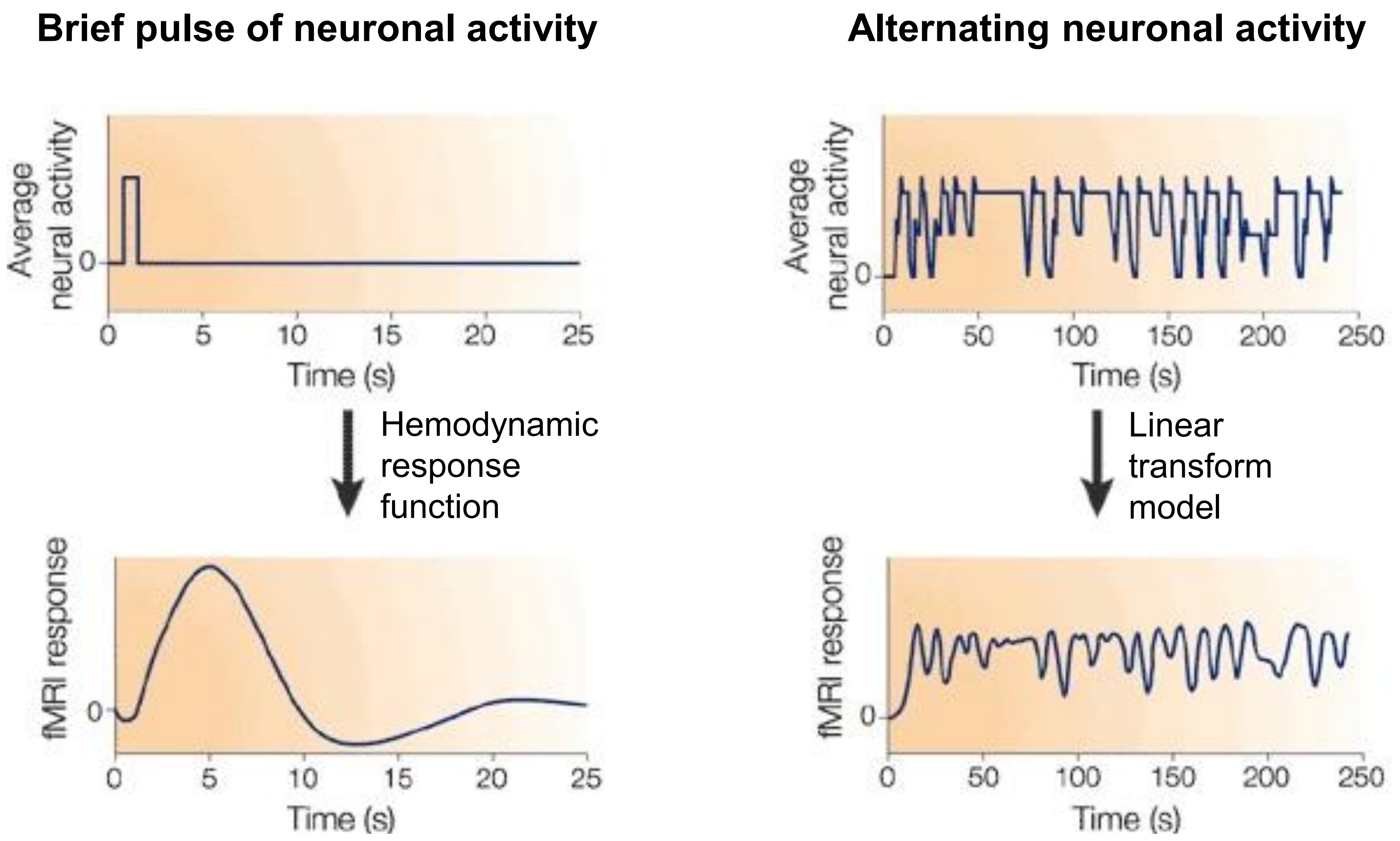
Hemodynamic Response Function

- Hypothetically characterizes the relationship between neuronal activity and the BOLD response
  - Positive for excitatory neuronal activity
  - Much slower than underlying neuronal processes

- Models a peak response at ~6 seconds, followed by return to baseline and slight undershoot, with total duration of ~20-30 seconds
  - Mathematically represented by a difference of two gamma functions

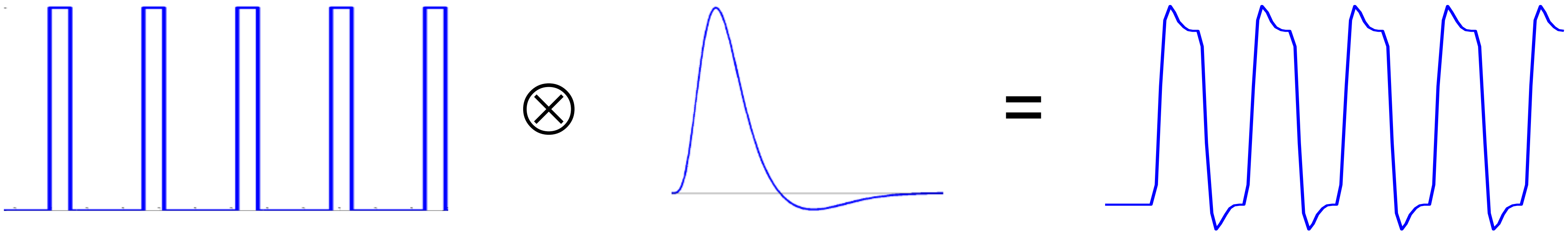


- Linear transform model
  - Predicts that BOLD responses should sum over time
  - Enables to compute BOLD response time courses using convolution
  - Simplifies BOLD signal analysis and interpretation



[Heeger and Ress, 2002]

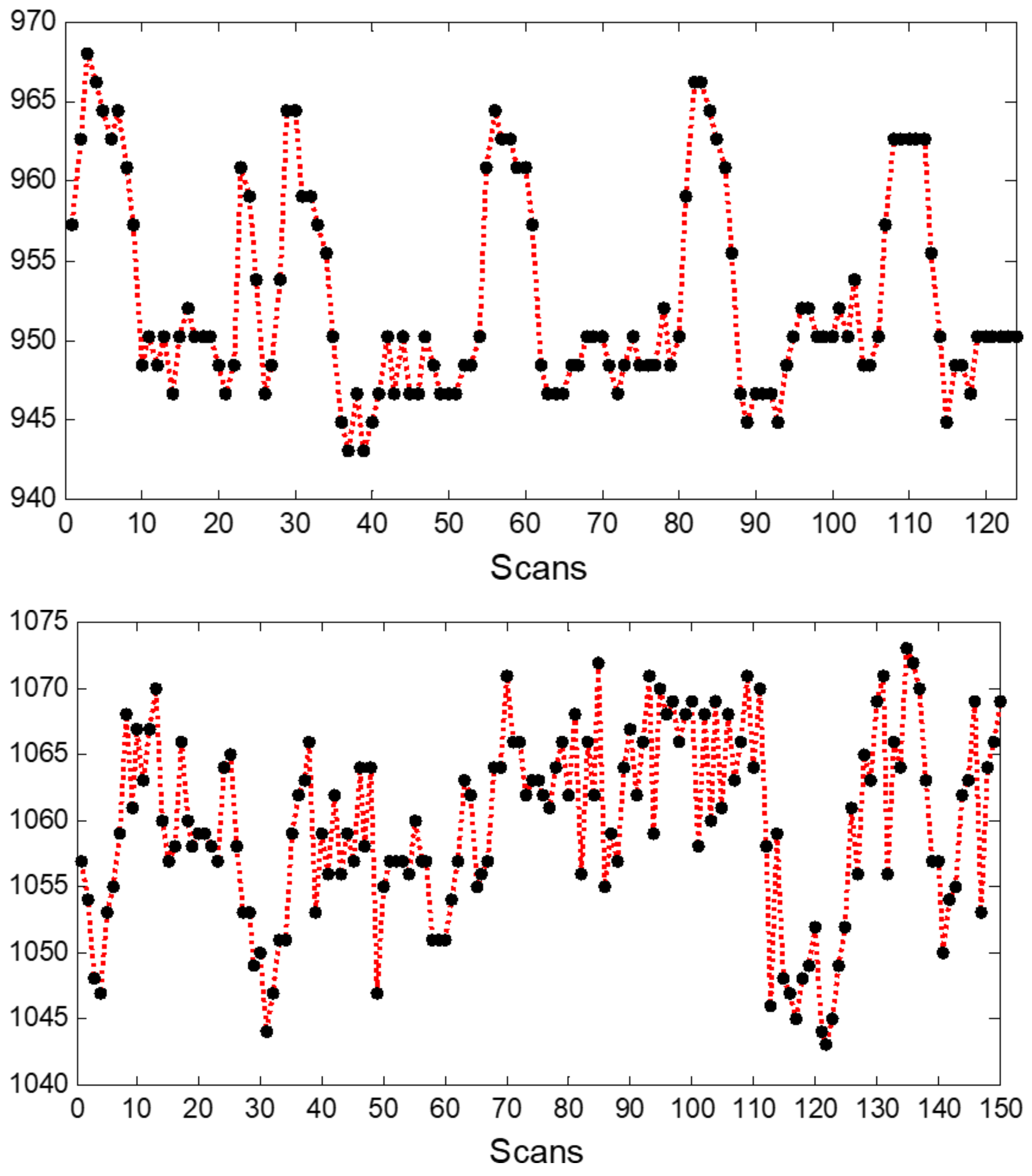
Prediction of BOLD Responses



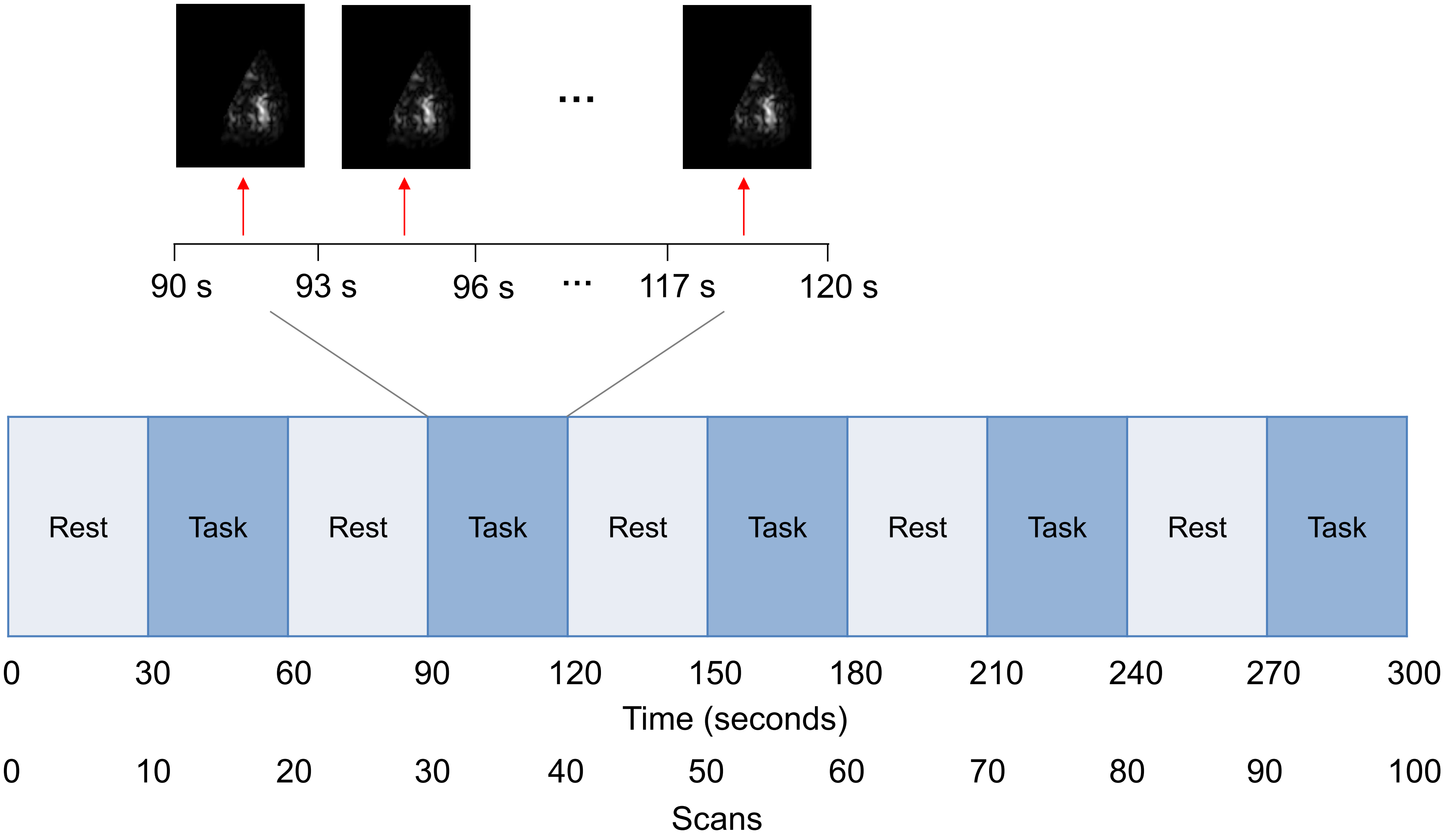
Linear Transform Model for Predicting BOLD Response Time Courses

Experimental fMRI

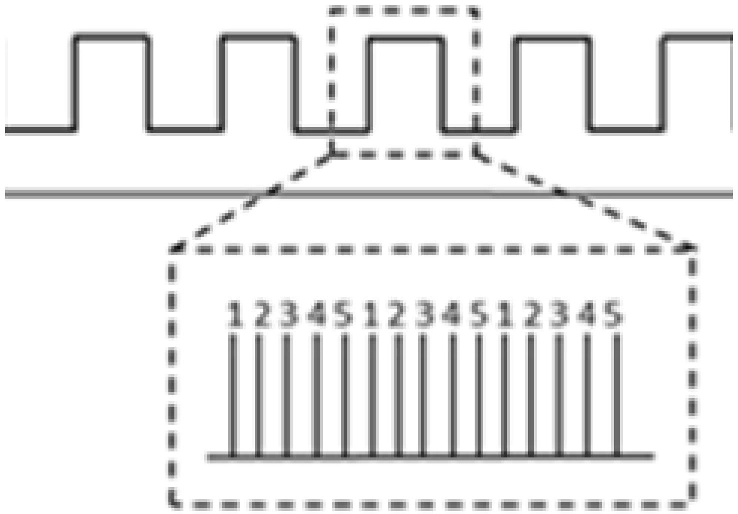
- Task-based fMRI
  - Given an overt task or external stimuli
  - The brain exhibits task-related activity
- Resting-state fMRI
  - With wakefulness maintained but structural thinking (e.g., counting) avoided
  - The brain exhibits spontaneous fluctuations in activity



Time Courses from the Same Location for Task-based vs. Resting-state fMRI

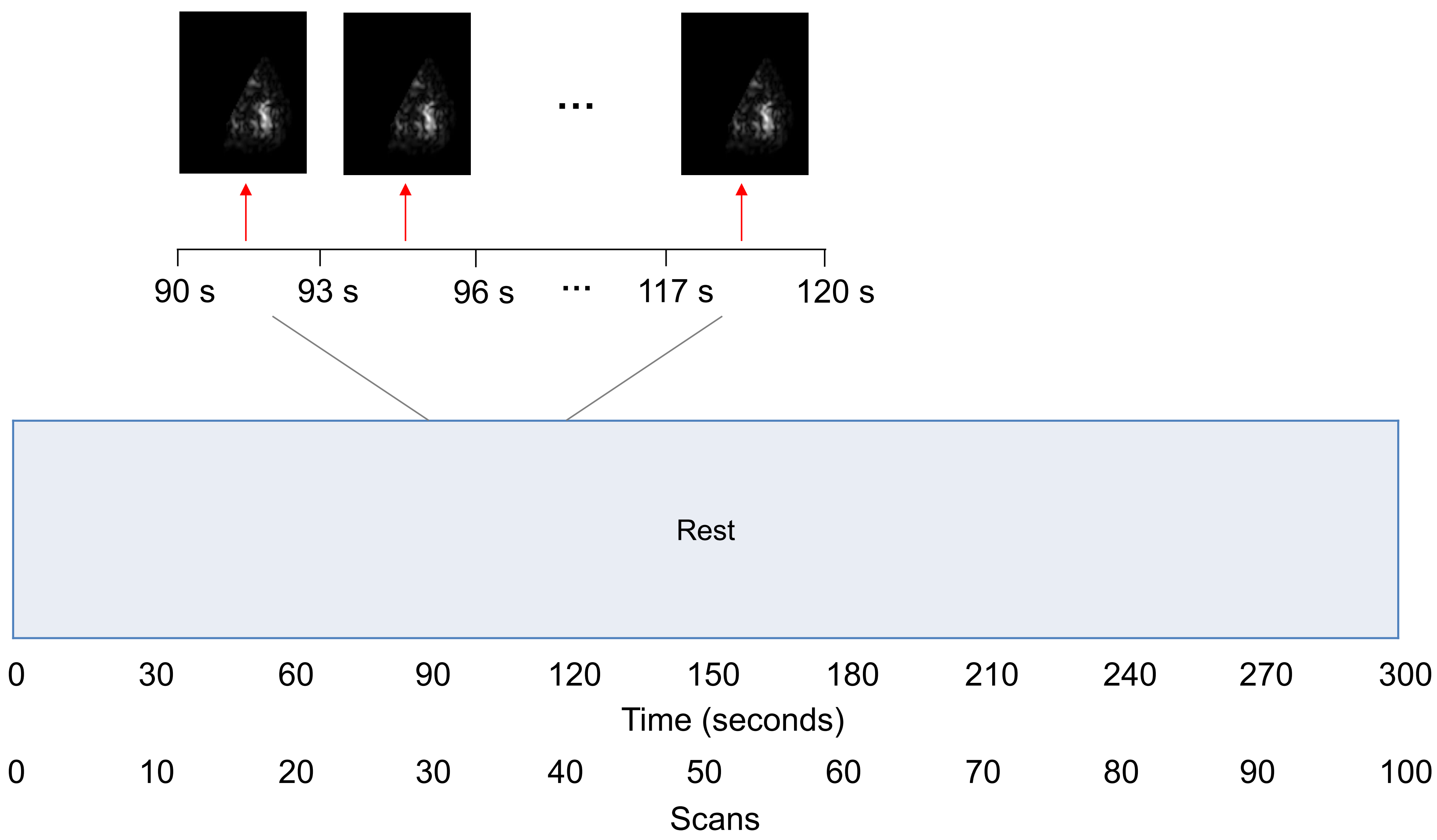


Example of Task-based fMRI



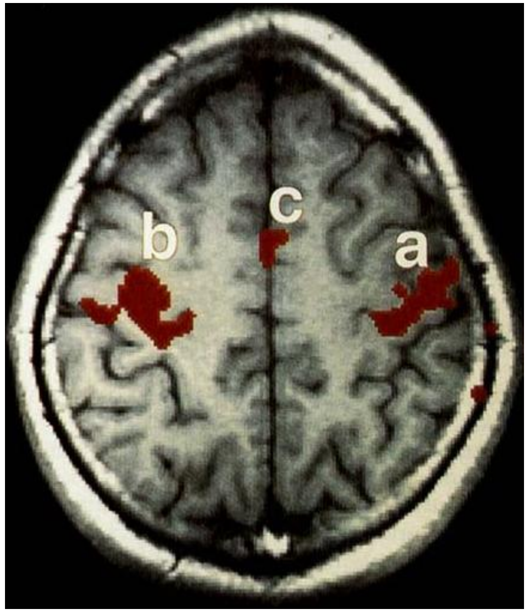
[Manon et al., 2023]

Sequential Hand Grip Task for fMRI



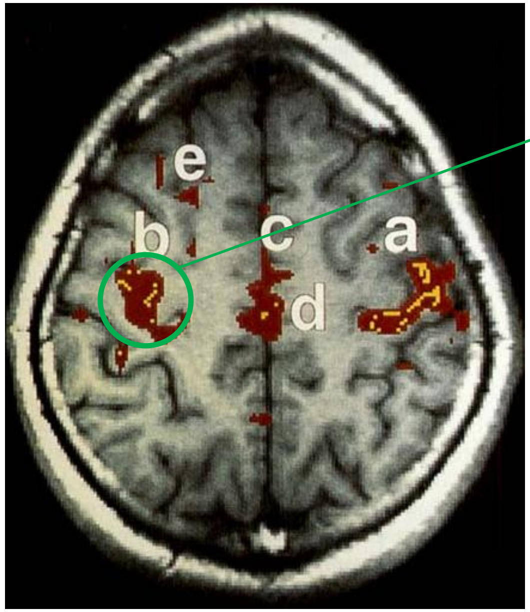
Example of Resting-state fMRI

Task-based fMRI

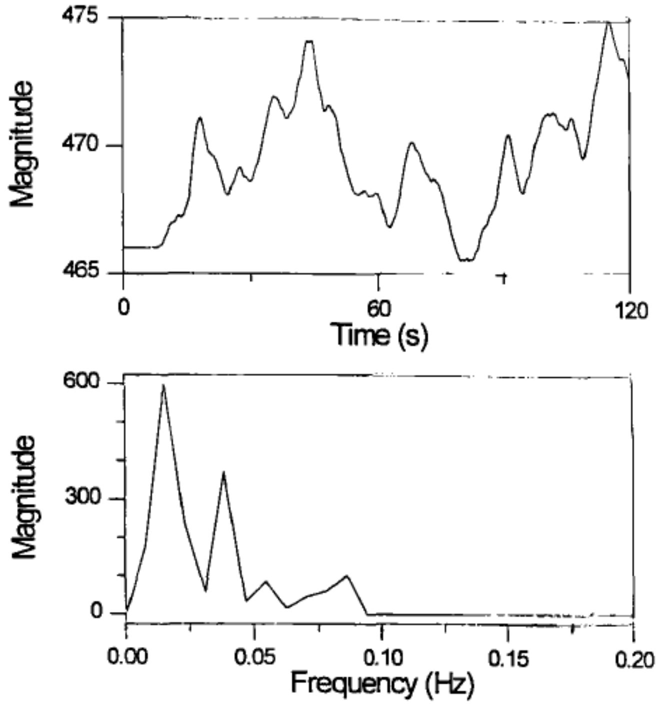


Finger movement-induced activation

Resting-state fMRI

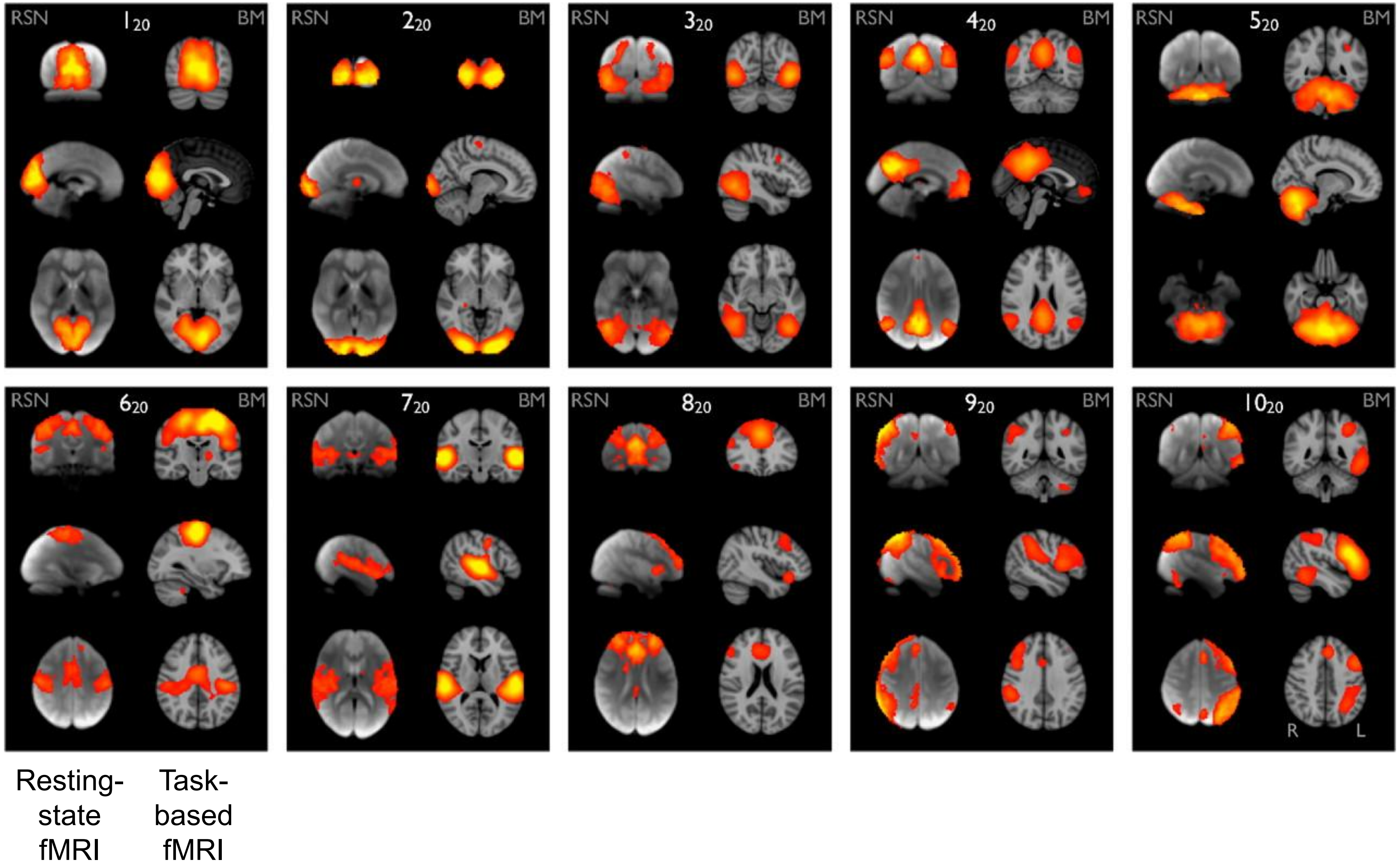


Correlation with the representative time course



[Biswal et al., 1995]

Correspondence between Task-based and Resting-state fMRI: Sensorimotor Network

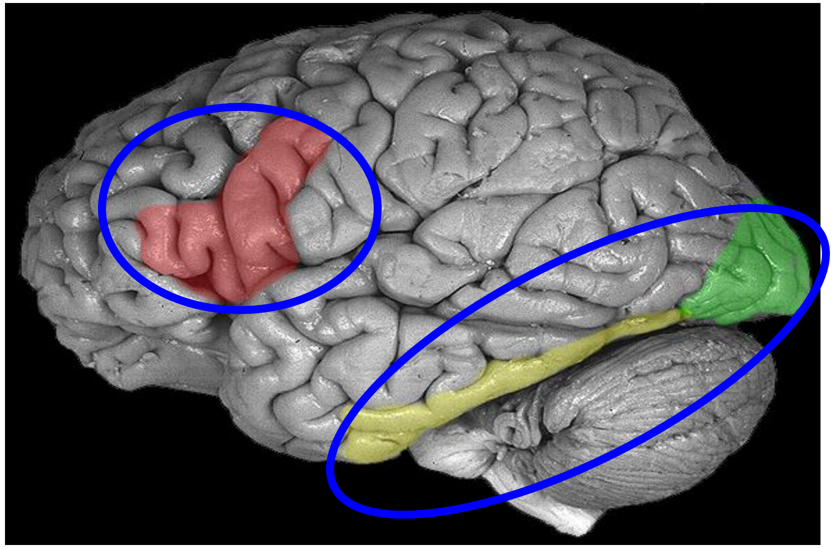


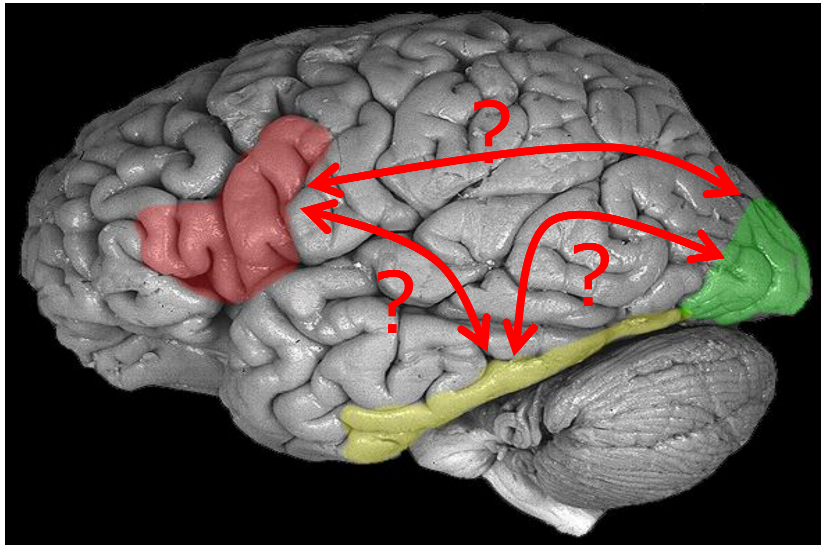
[Smith et al., 2009]

Correspondence between Task-based and Resting-state fMRI: 10 Brain Networks

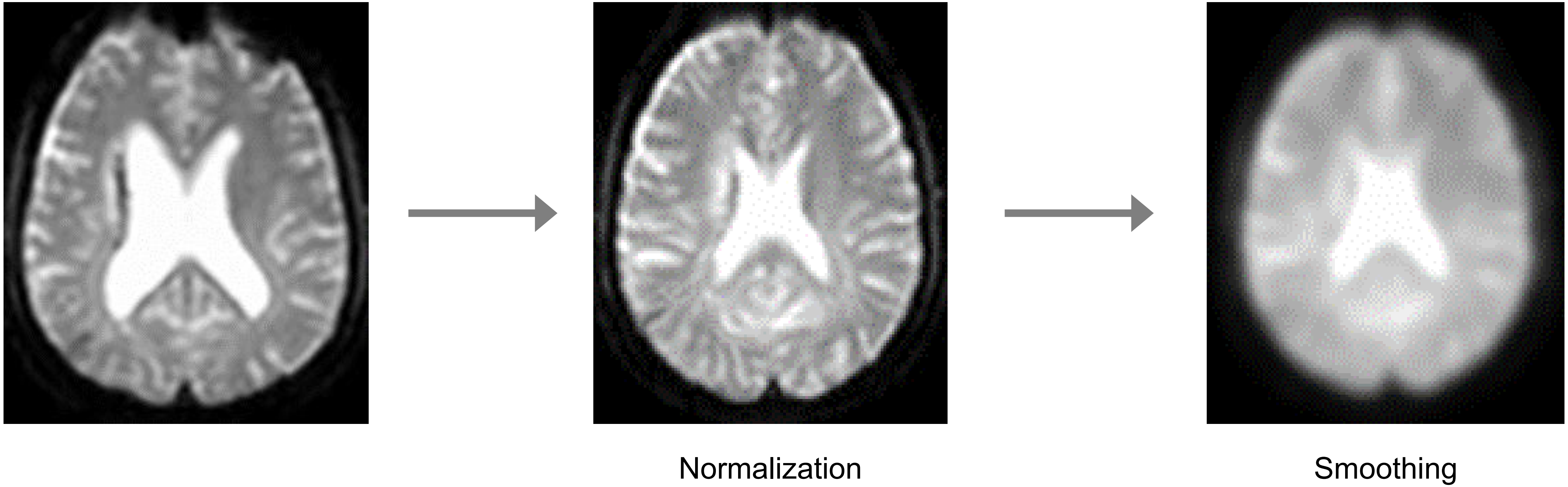
Brain Function Analysis with fMRI

- Functional segregation vs. integration
  - Related to perspectives on how brain regions communicate and work together to process information





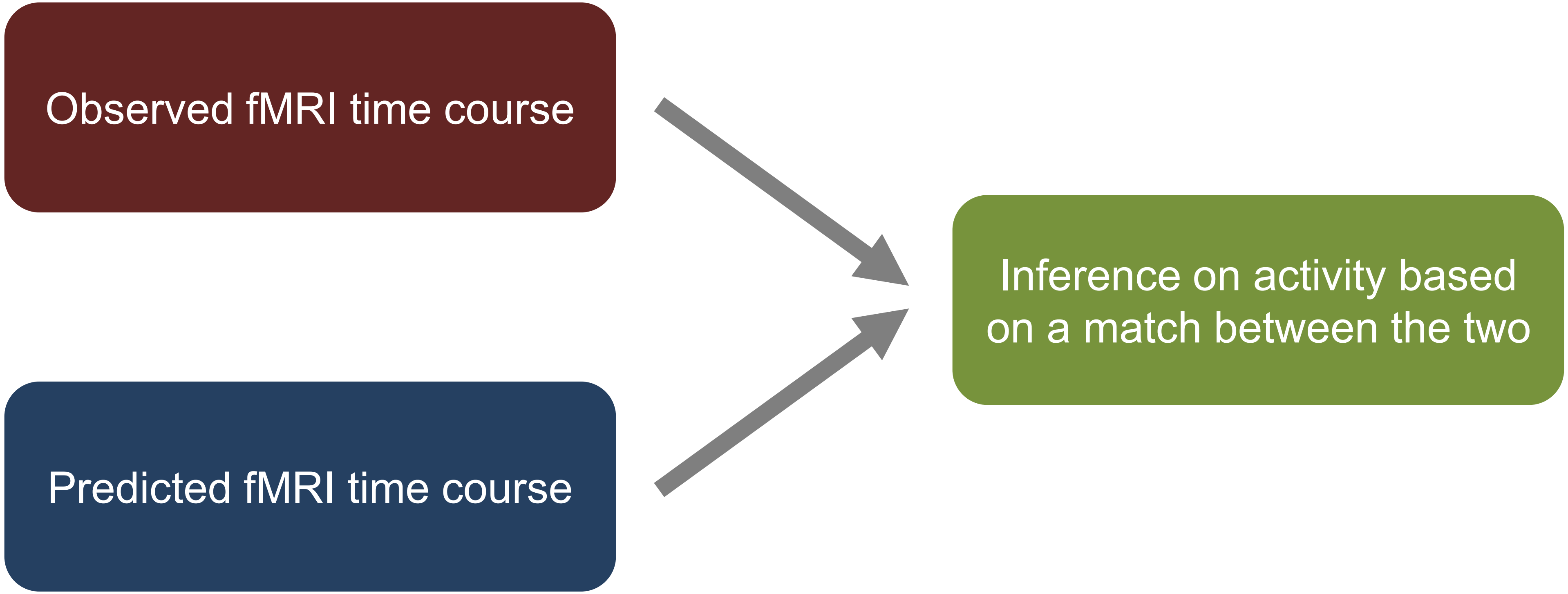
- Preprocessing before extracting and managing fMRI time courses
  - Correction for unwanted variation
    - Difference in slice timing
    - Head motion
    - Susceptibility artifact (B0 inhomogeneity-induced distortion): local variations in magnetic susceptibility between different tissues or at tissue-air interfaces, causing geometric distortions or signal loss in affected areas
  - Normalization
    - Transforms images from native space to standard space
  - Smoothing
    - Blurs images by convolving with a 3D Gaussian kernel



Preprocessing

Functional Segregation

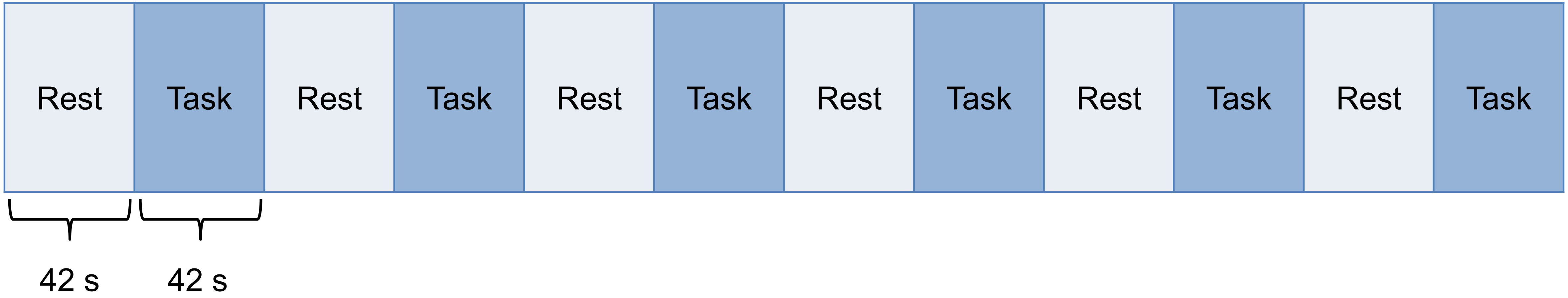
- Specialization of different brain regions for different functions
  - Based on the idea that certain tasks or processes are localized to specific regions of the brain
- In task-based fMRI:
  - Increased activity in specific brain regions during a task, as compared to a baseline, suggests those regions are specialized for the task



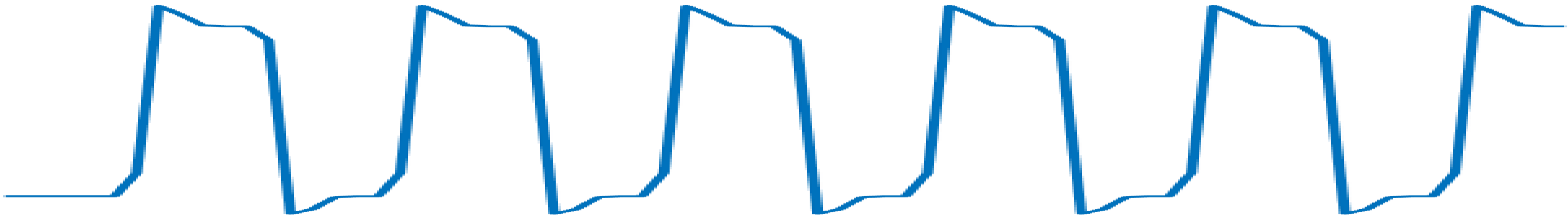
Functional Segregation Analysis in Task-based fMRI

Auditory stimulation task [https://www.fil.ion.ucl.ac.uk/spm/data/auditory/]

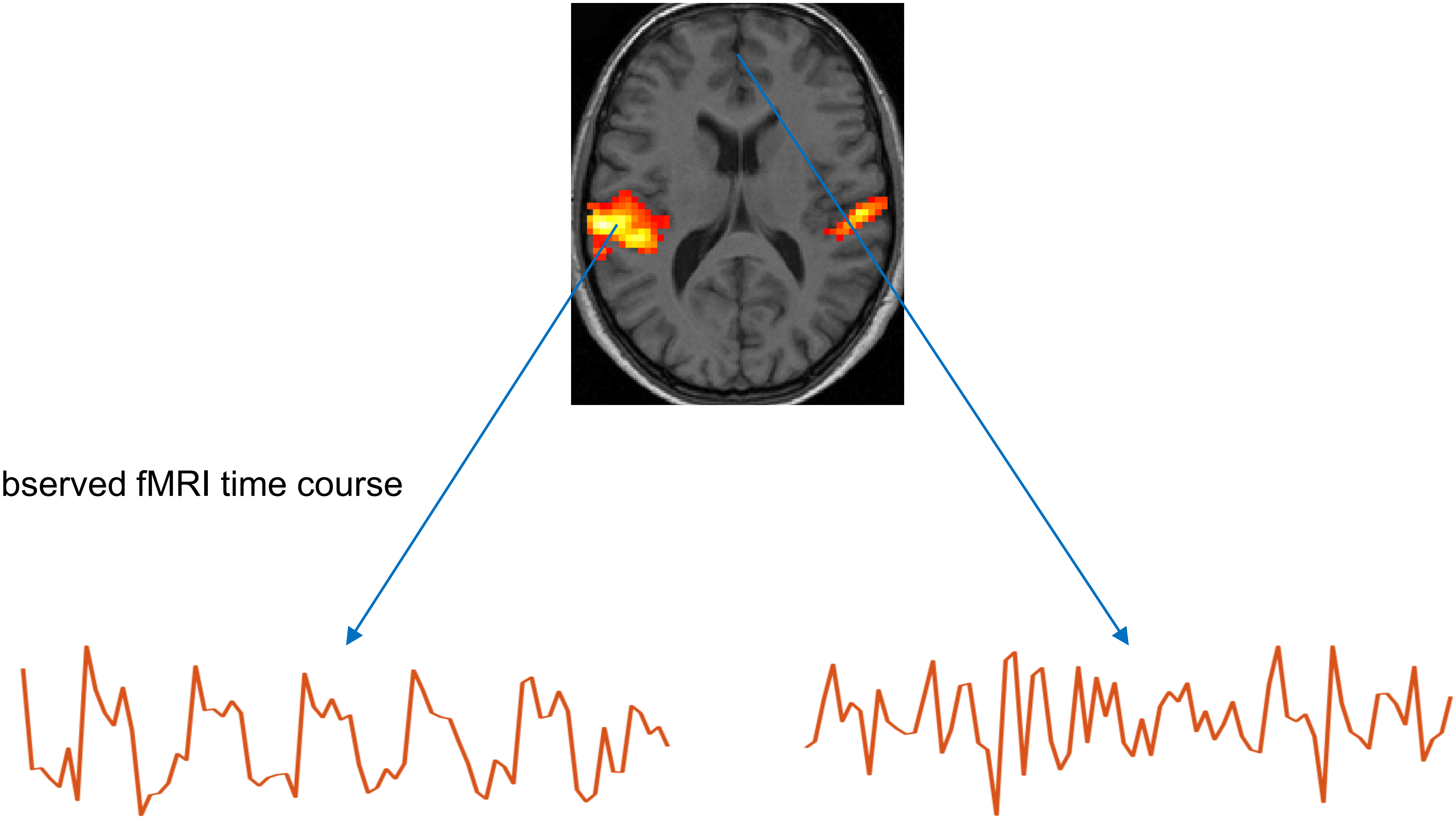
Bi-syllabic words presented binaurally at a rate of 60 per minute

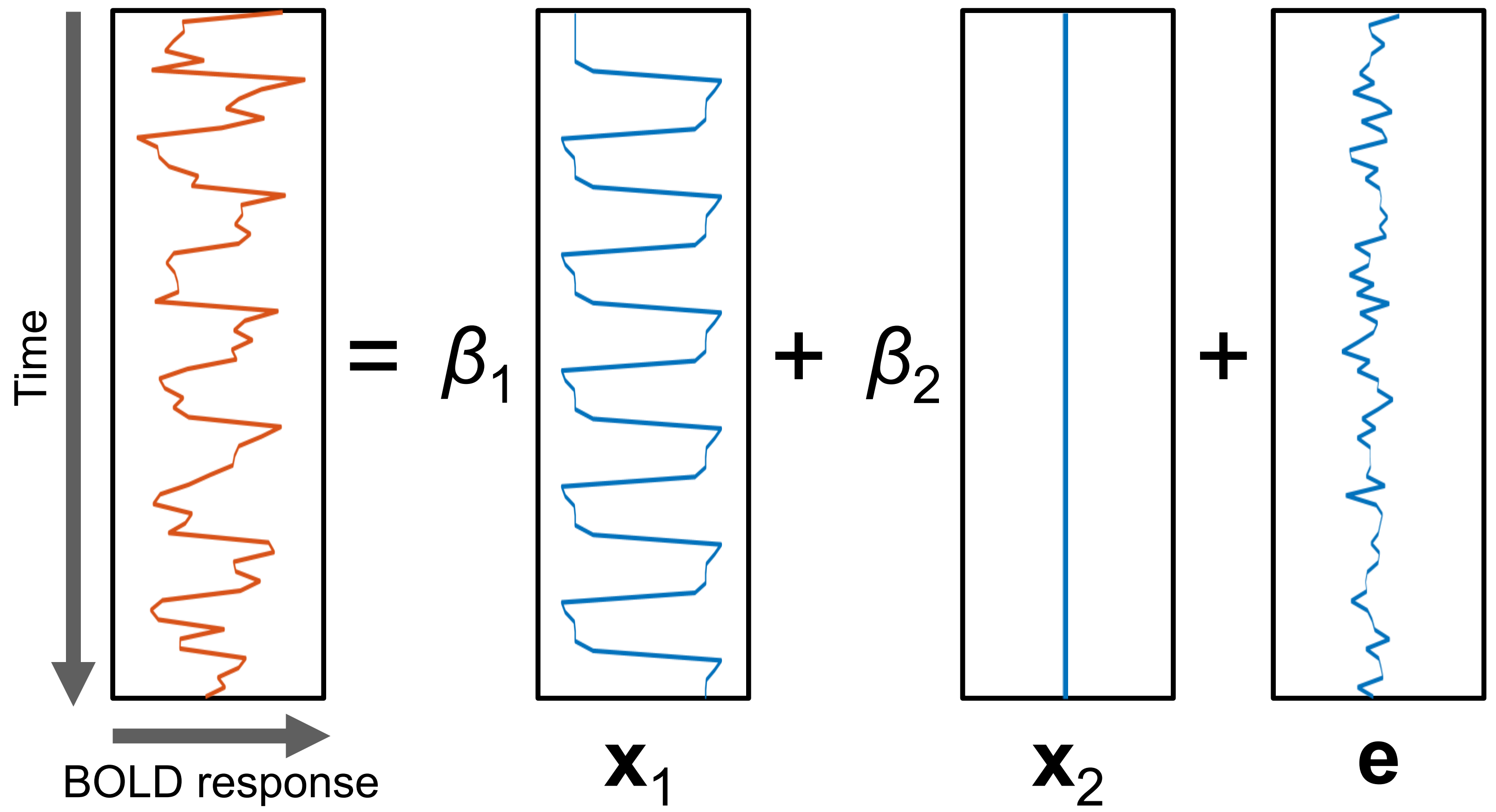


Predicted fMRI time course



Observed fMRI time course

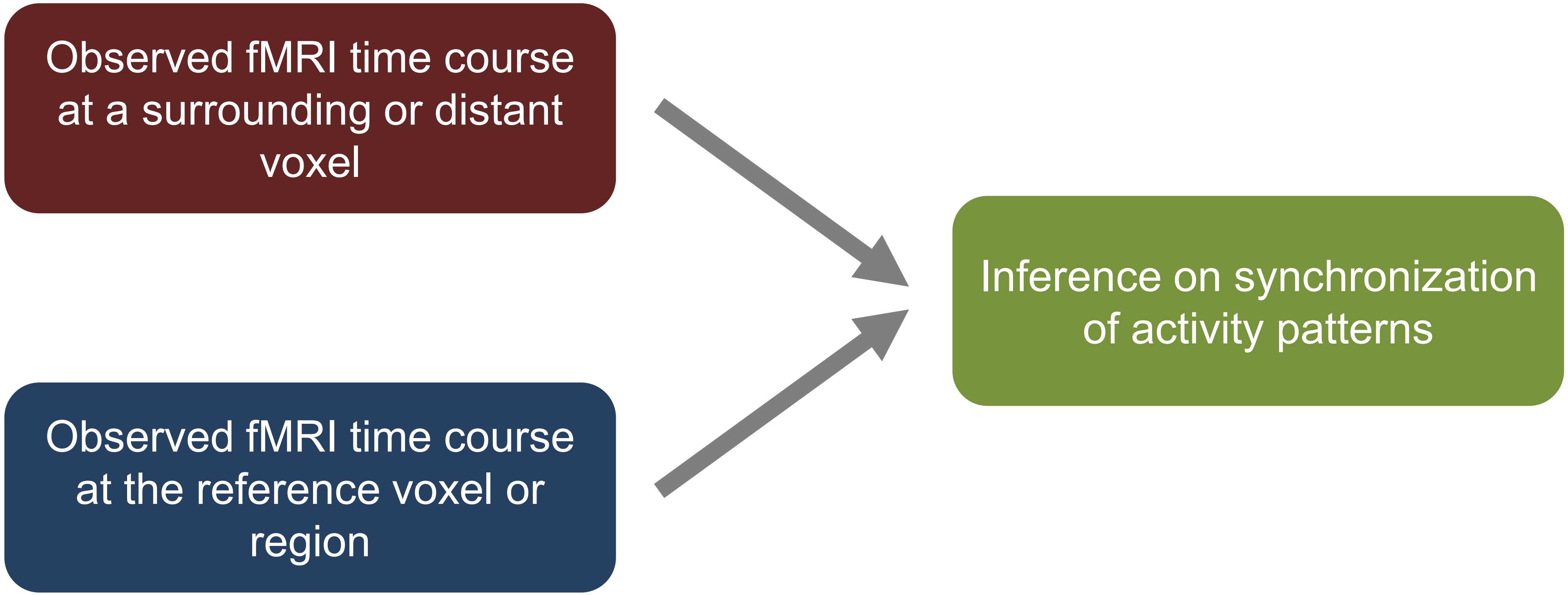




$$y = X\beta + e = x_1\beta_1 + x_2\beta_2 + e$$

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

- In resting-state fMRI:
  - Synchronized activity patterns in certain brain regions reveal functional specialization often in terms of specific brain networks (e.g., visual network, sensorimotor network, default mode network)



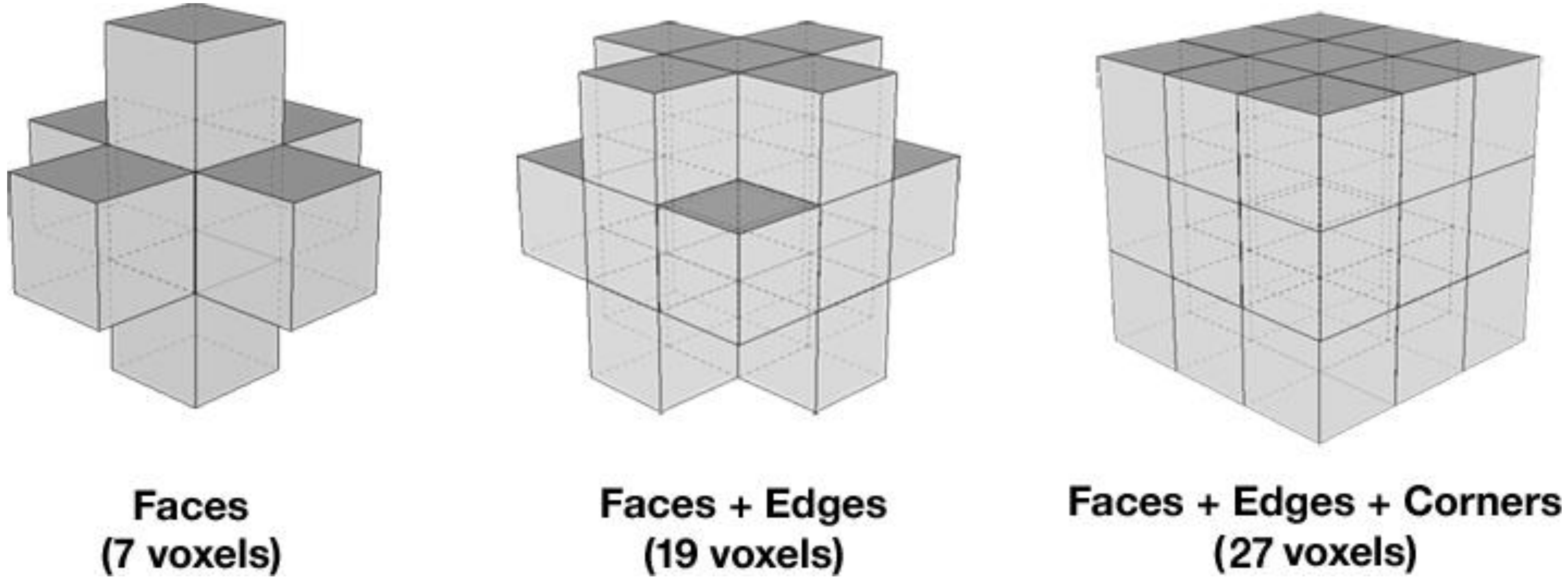
Functional Segregation Analysis in Resting-state fMRI

– Regional homogeneity [Zang et al., 2004]

- Synchronization of time courses between a given voxel and its neighbors
  - Neighbors: *K* nearest neighbors
  - Synchronization: Kendall's coefficient of concordance (KCC)

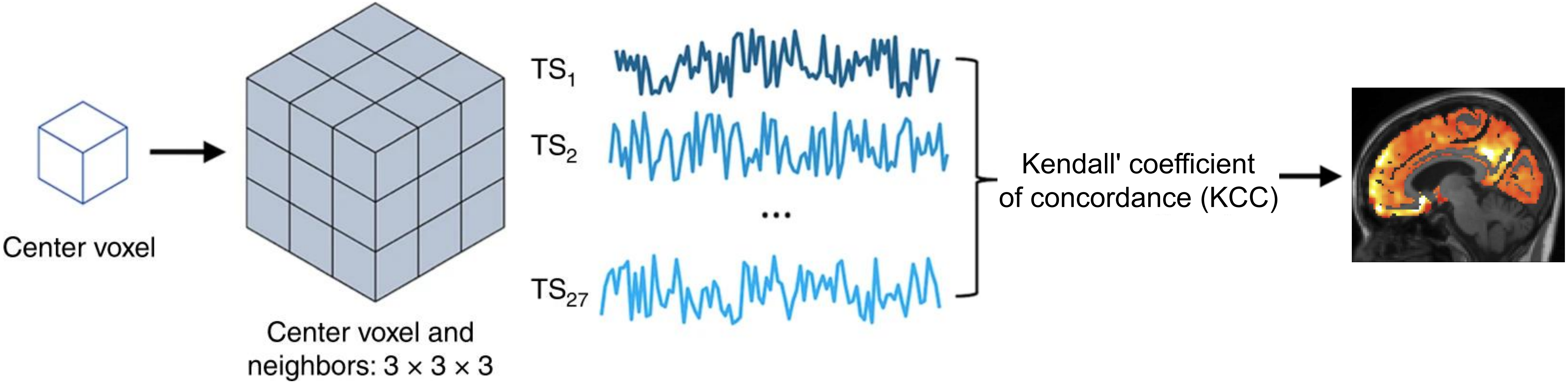
$$\mathrm{KCC} = \frac{\sum_{i=1}^{n} R_i^2 - n(\overline{R})^2}{\frac{1}{12}K^2(n^3 - n)} = 12\frac{\sum_{i=1}^{n} (\overline{R}_i)^2}{(n^3 - n)} - 3\frac{(n+1)}{(n-1)}$$

- Reveals local synchronization of spontaneous brain activity



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

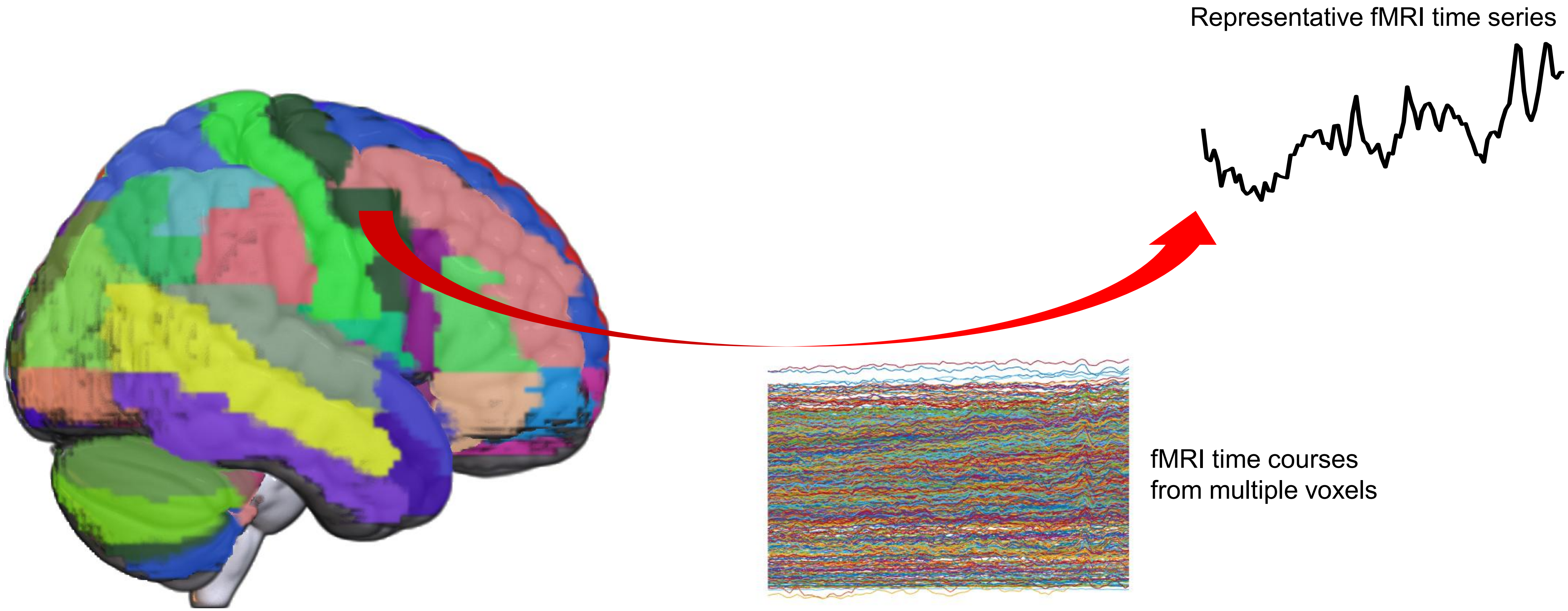
Different Definitions of Nearest Neighbors



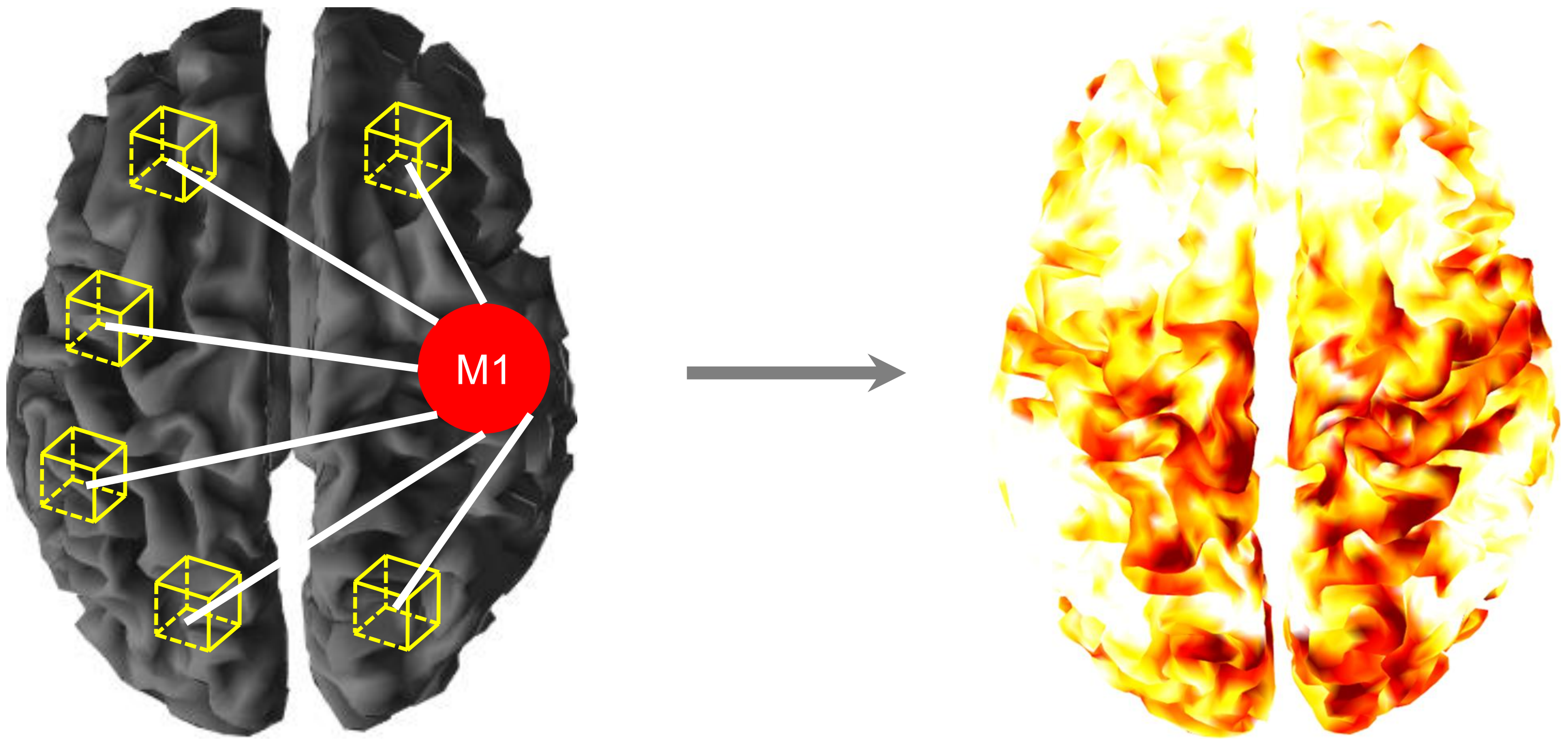
[Harrison et al., 2019]

Regional Homogeneity

- Seed-based correlation [Biswal et al., 1995]
    - Synchronization of time courses between a seed and all other voxels in the brain
        - Seed: pre-defined voxel or region
        - Synchronization: statistical association, particularly correlation
    - Identifies spontaneous brain activity patterns correlating with the seed



Extraction of an fMRI Time Course from the Seed (Primary Motor Cortex)



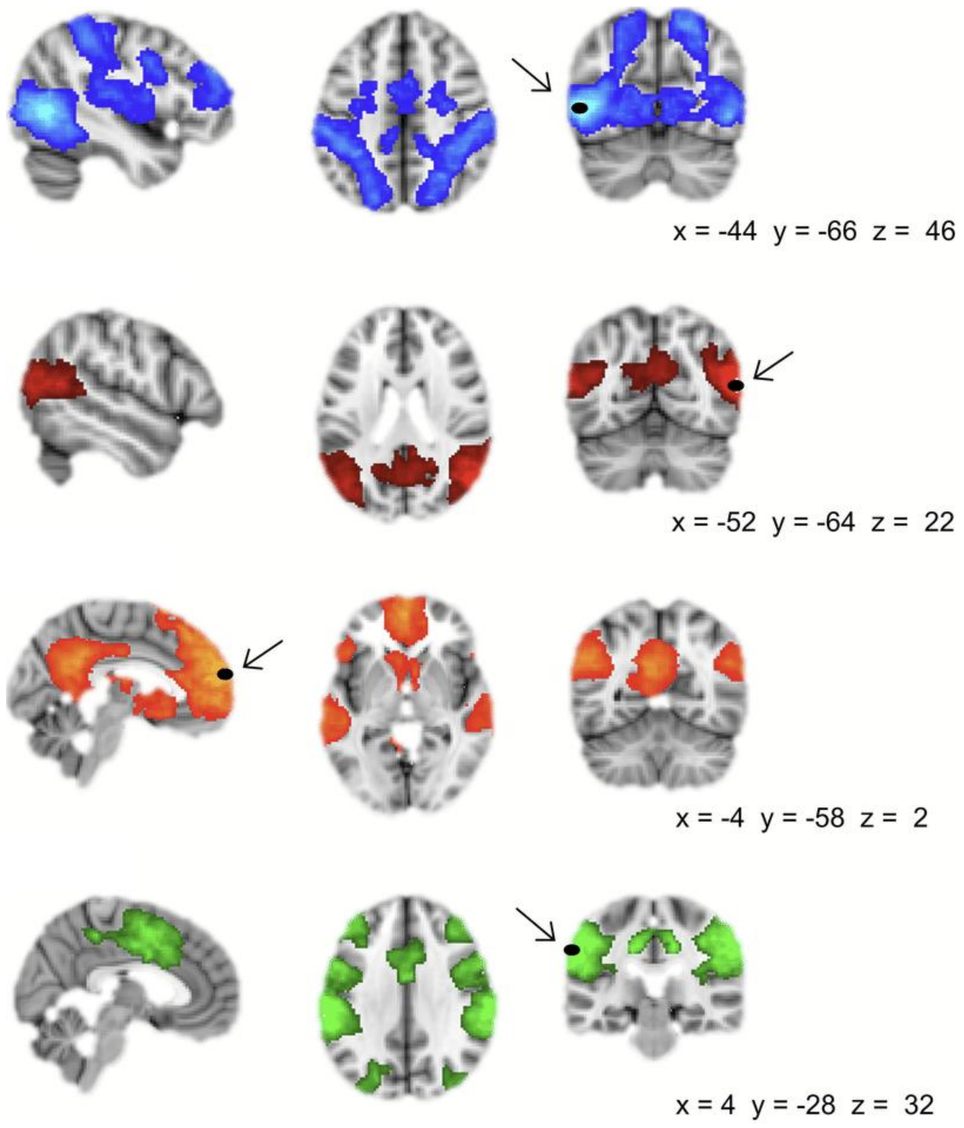
Seed-based Correlation for the Primary Motor Cortex

Left middle temporal gyrus

Right middle temporal gyrus

Left medial frontal gyrus

Left supramarginal gyrus

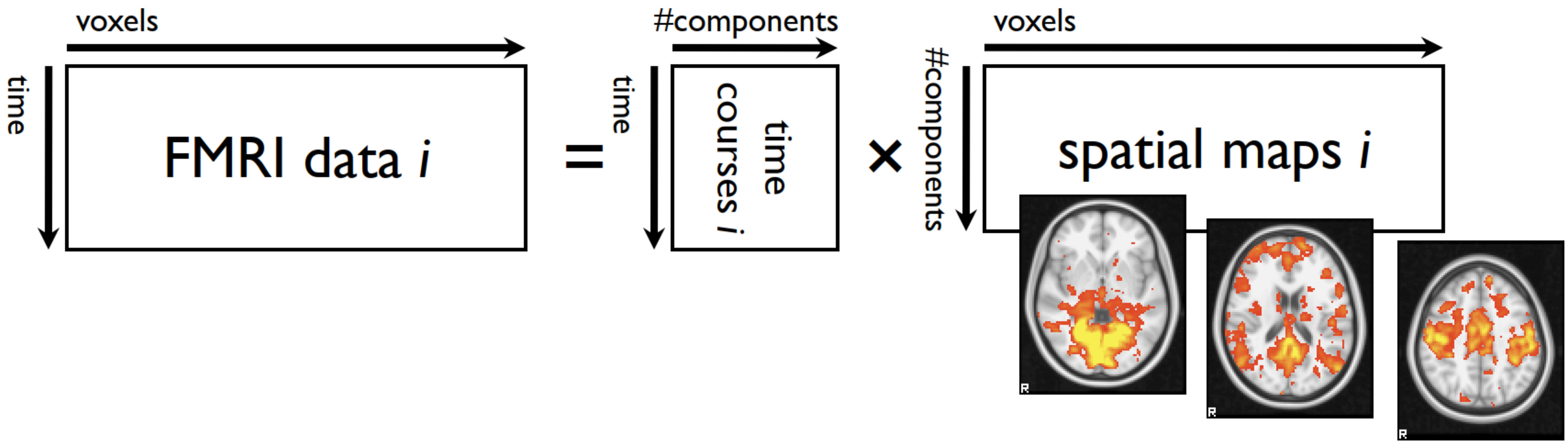


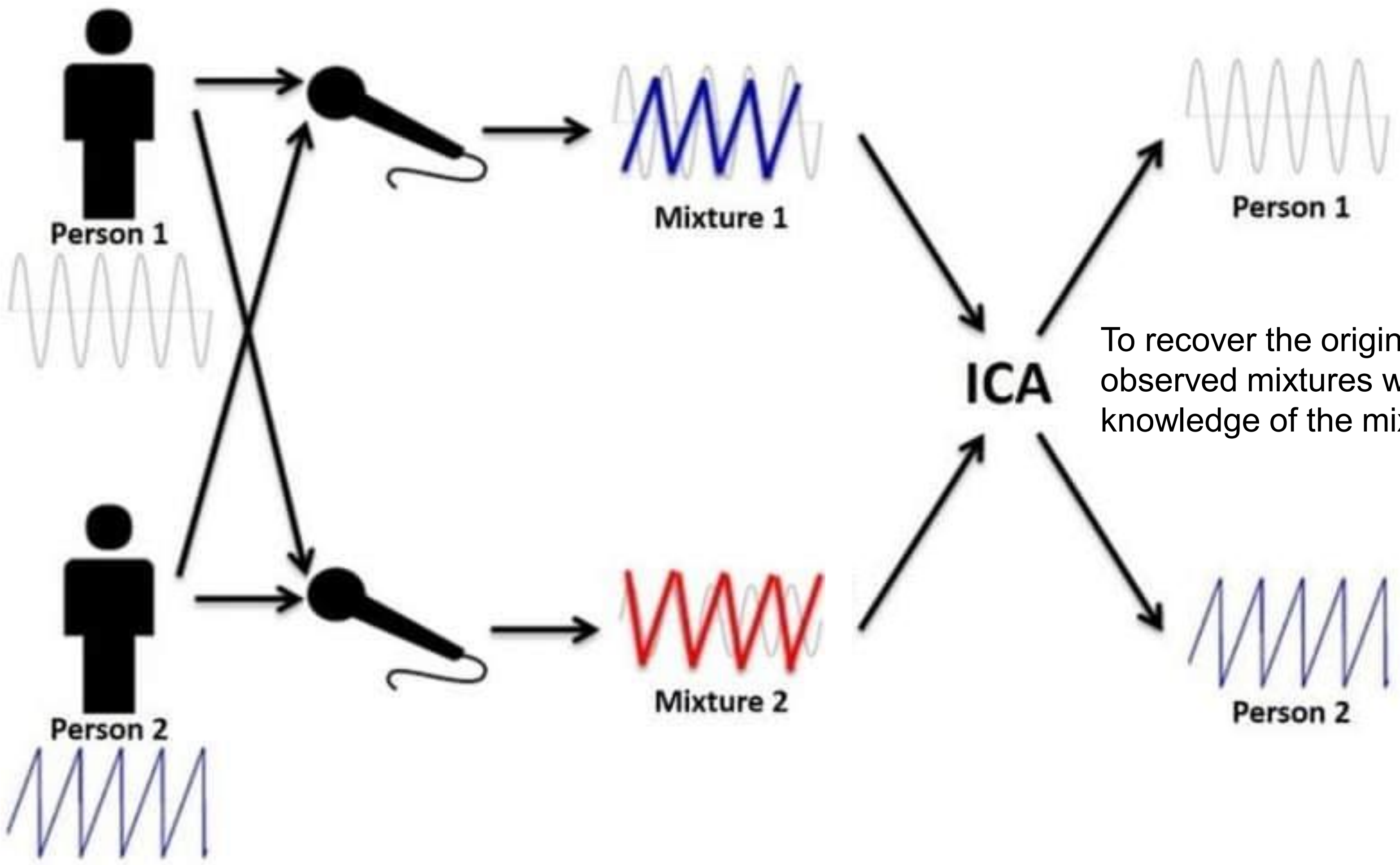
[Cousijn et al., 2014]

Time Course 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
- Explores spontaneous brain activity patterns of spatial independence

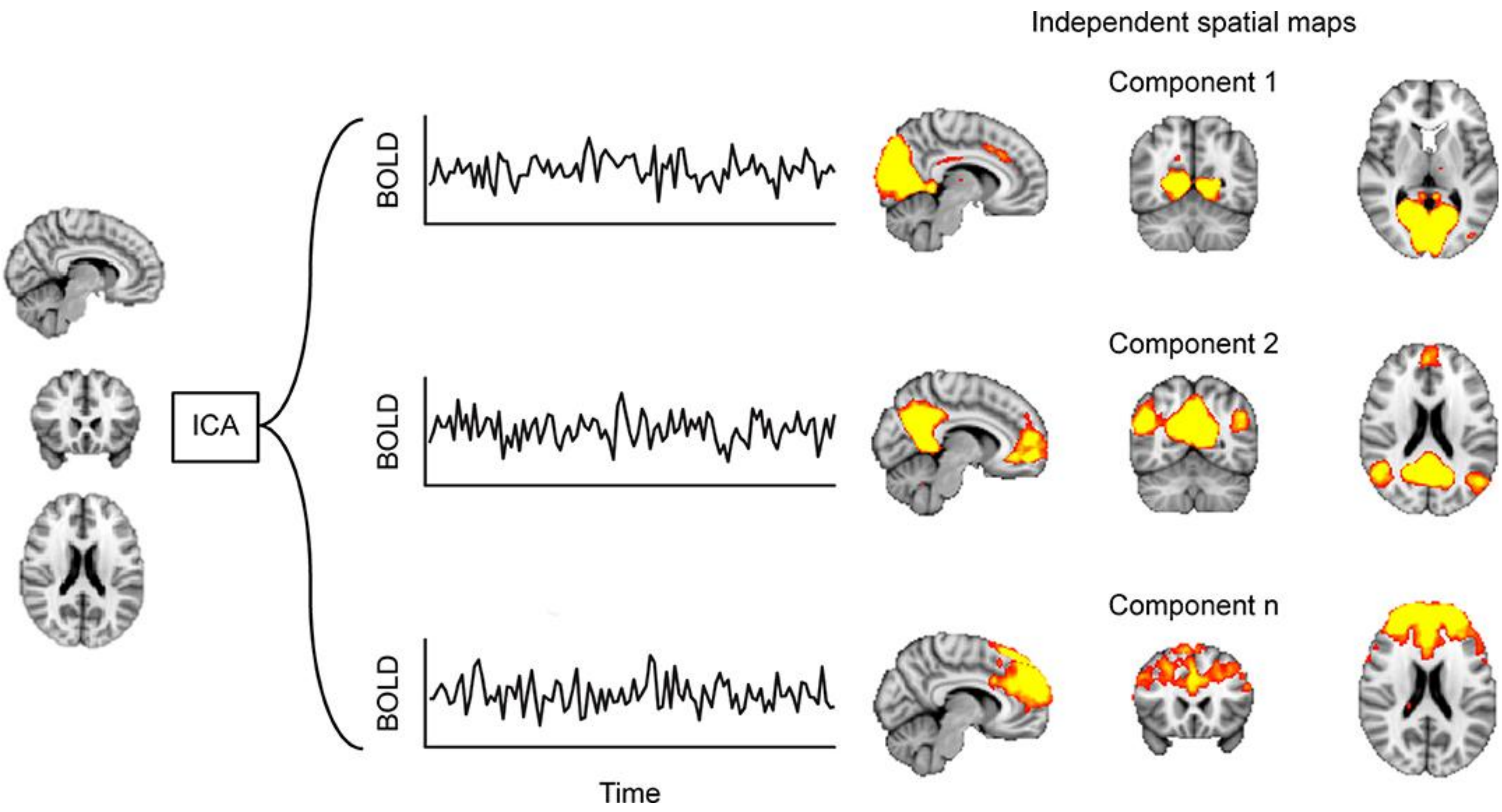




To recover the original signals from the observed mixtures without having prior knowledge of the mixing process

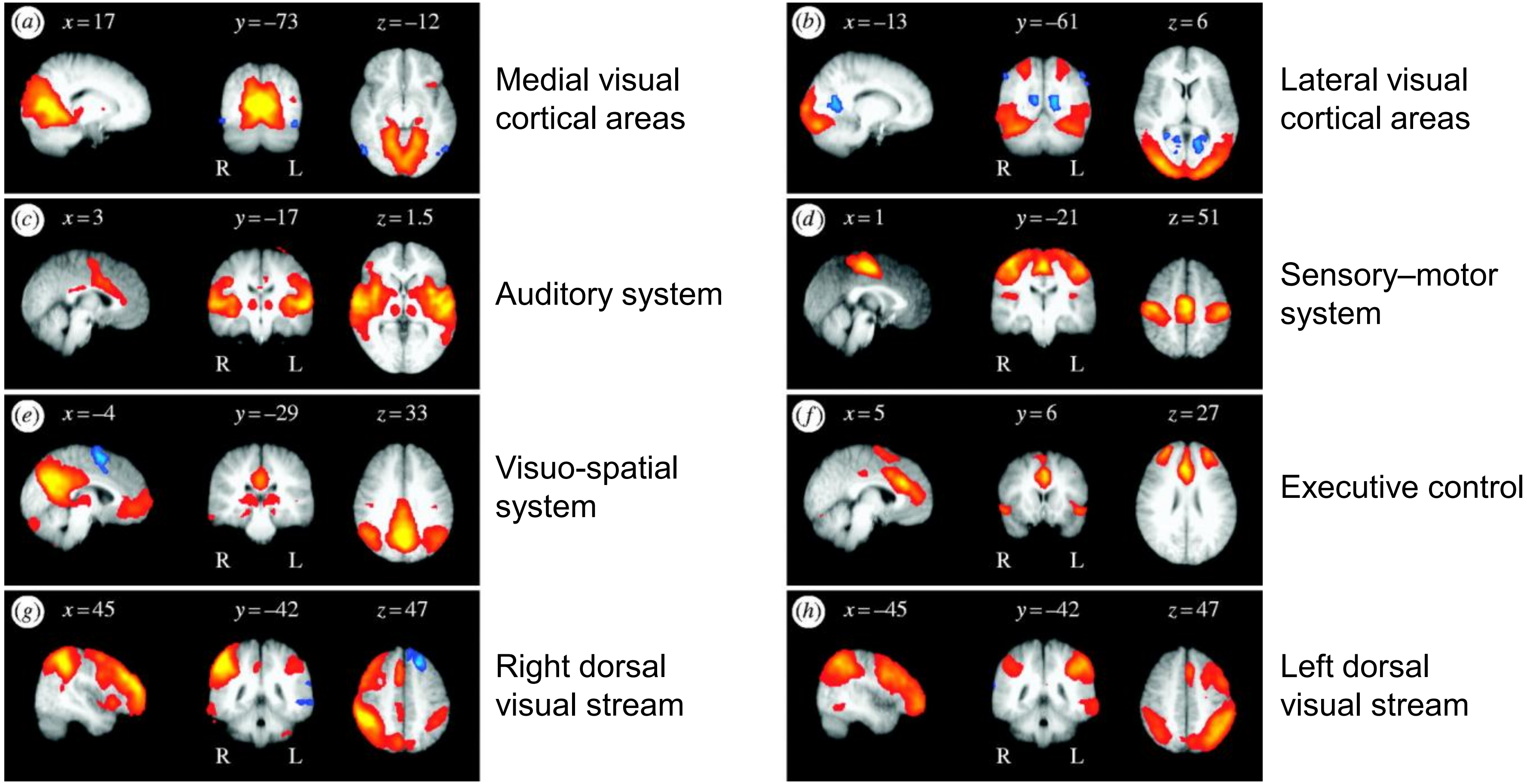
[https://vocal.com/blind-signal-separation/independent-component-analysis/]

Independent Component Analysis for the Cocktail Party Problem



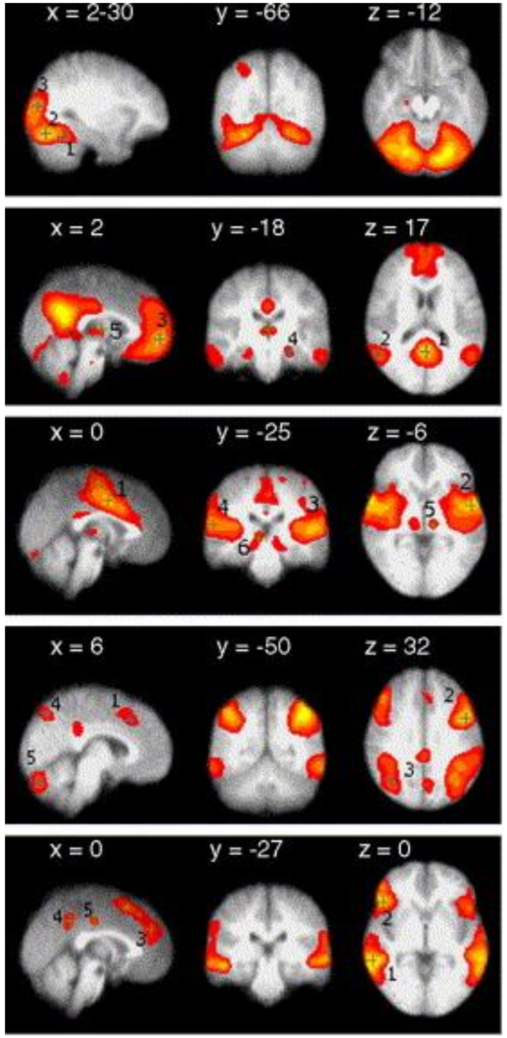
[Tahedl et al., 2018]

Independent Component Analysis of fMRI Data



[Beckmann et al., 2005]

Time Course Synchronization Explored by Independent Component Analysis (1)



Visual cortical areas

Visuospatial and executive system

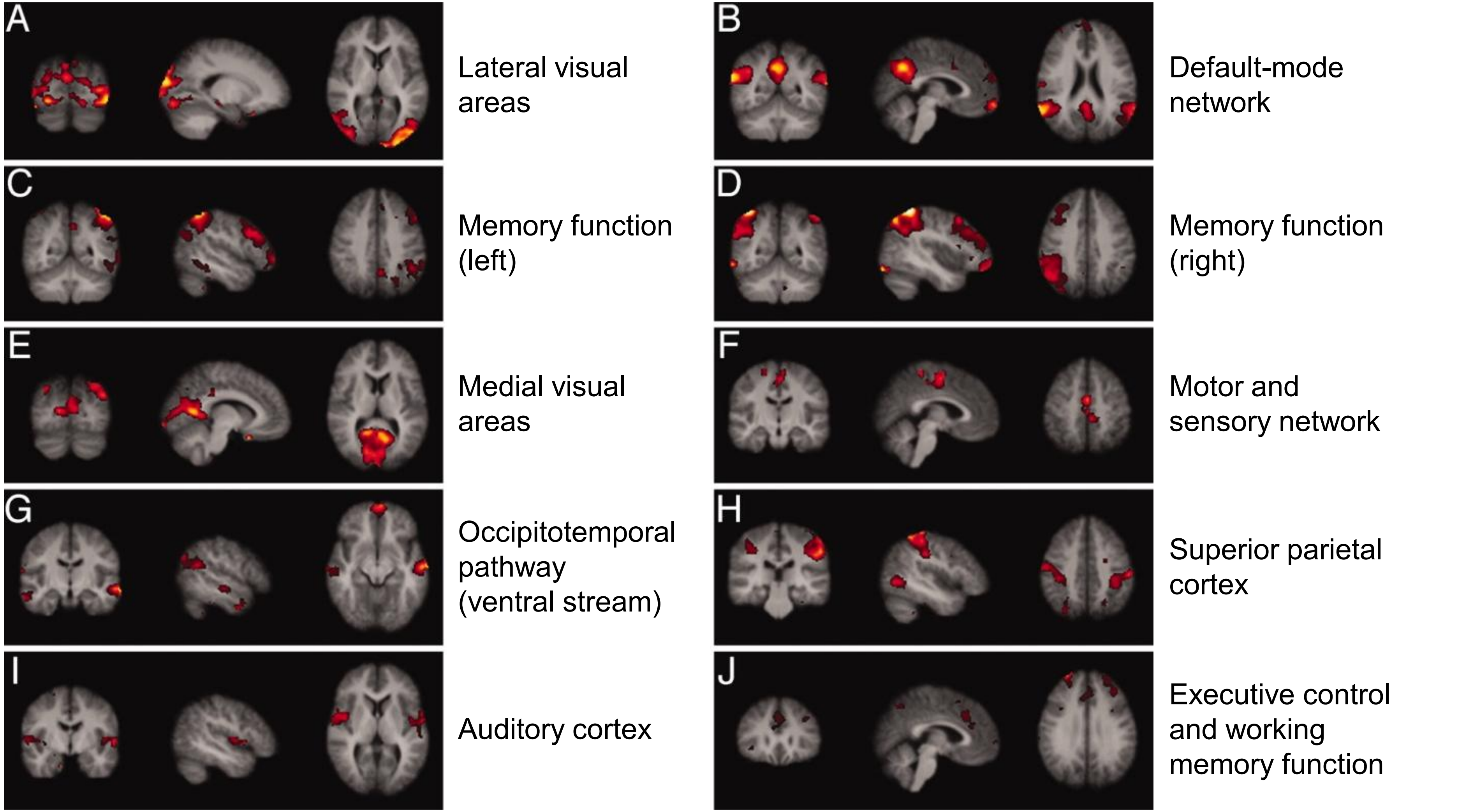
Sensory and auditory system

Dorsal pathway

Ventral pathway

[De Luca et al., 2006]

Time Course Synchronization Explored by Independent Component Analysis (2)

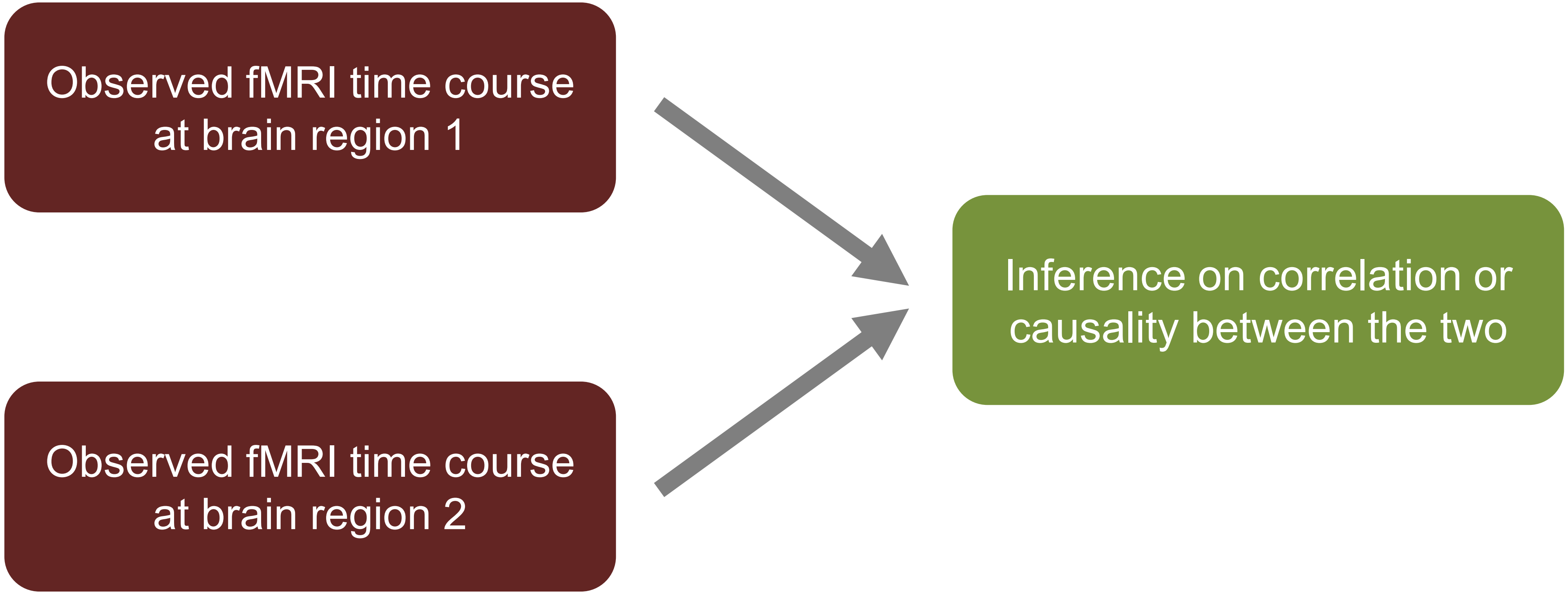


[Damoiseaux et al., 2006]

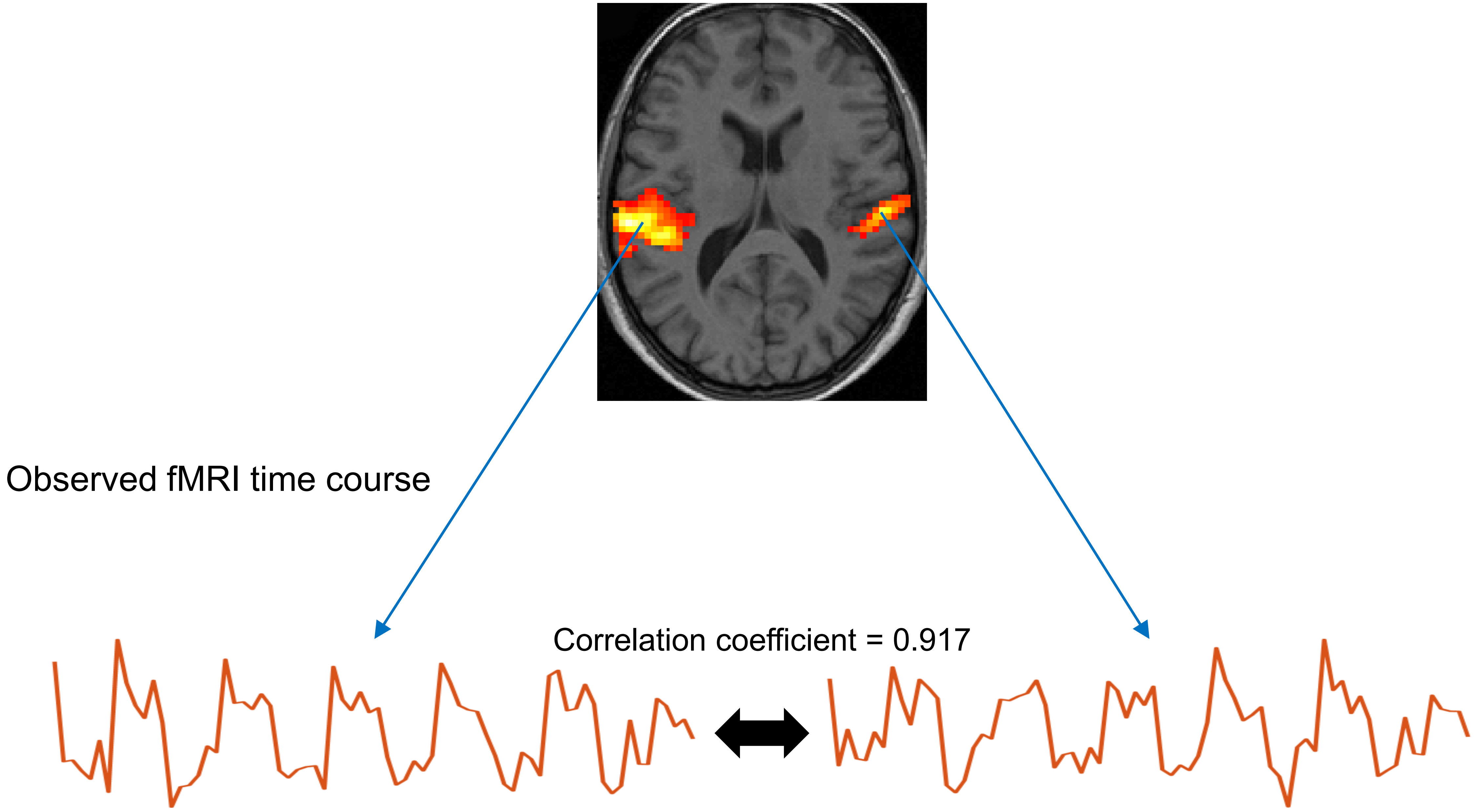
Time Course Synchronization Explored by Independent Component Analysis (3)

Functional Integration

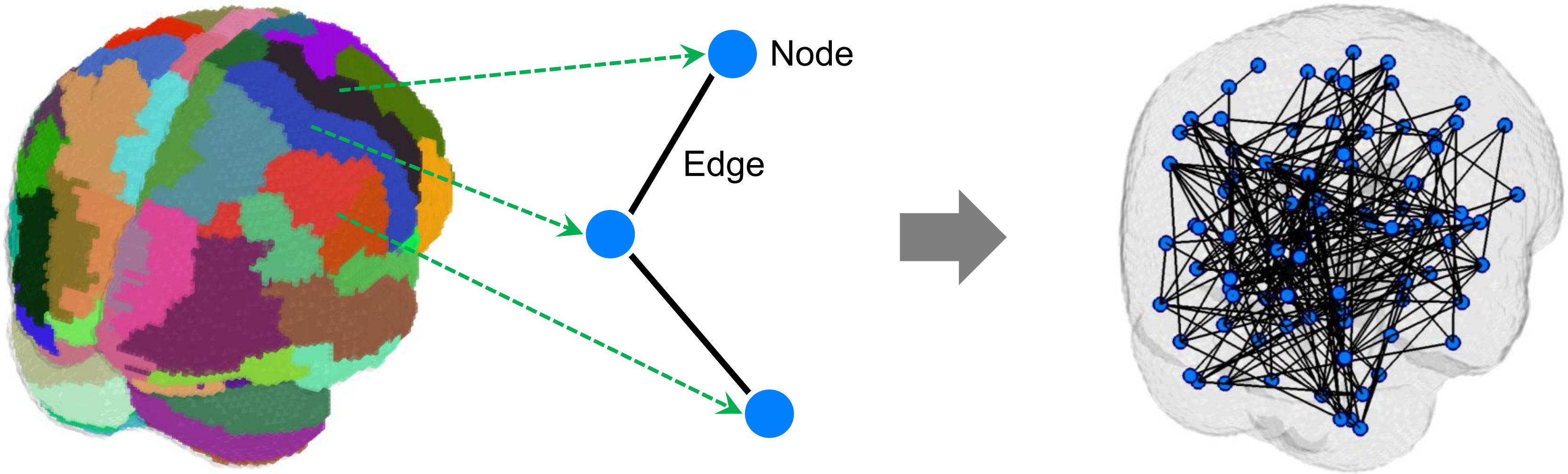
- Interaction between segregated brain regions for the integration of information across various parts of the brain
  - Based on the idea that certain tasks or processes are supported by the communication and coordination of different brain regions with each other
- In task-based and resting-state fMRI:
  - The association between time courses of activity from different brain regions reveals networks of regions that work together

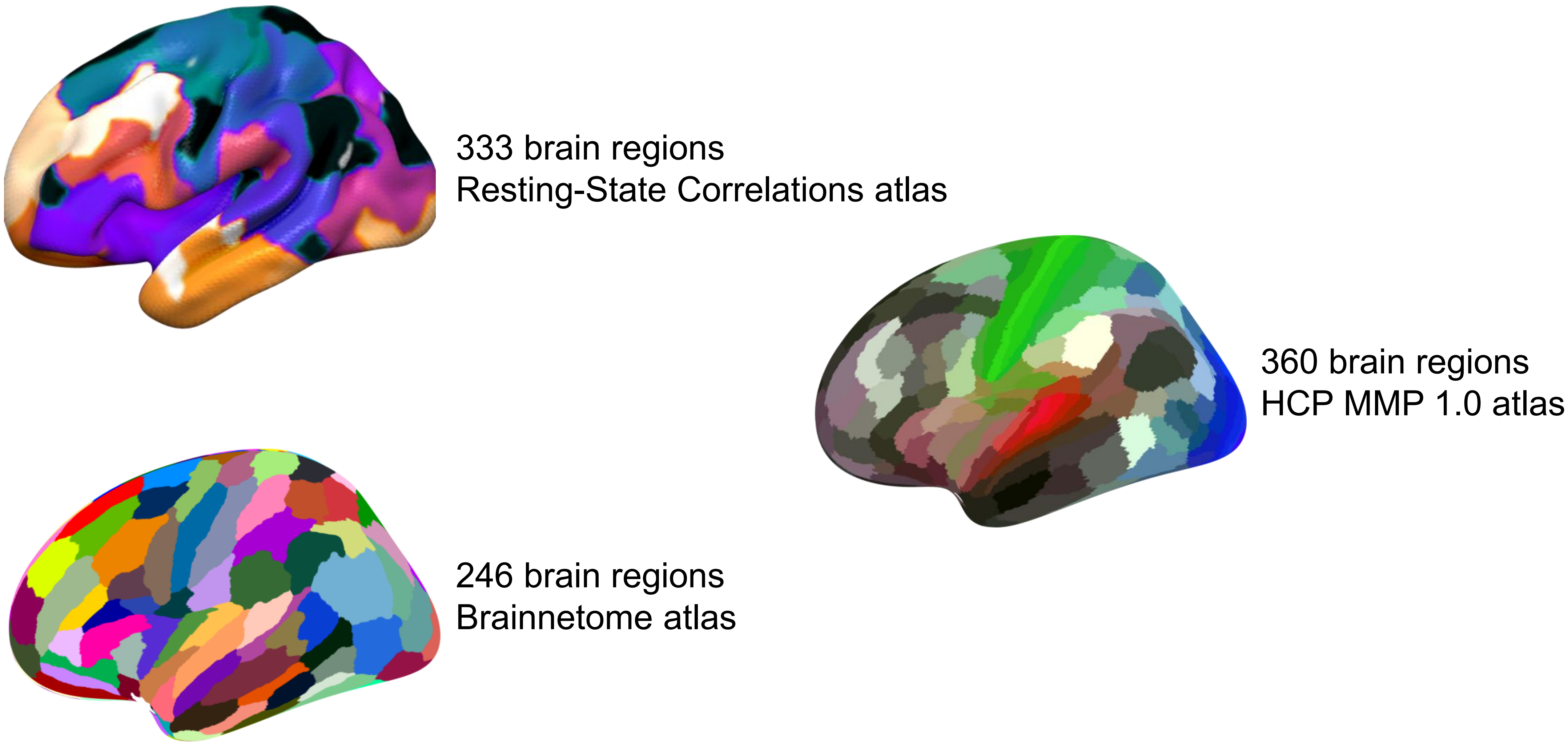


Functional Segregation Analysis in fMRI

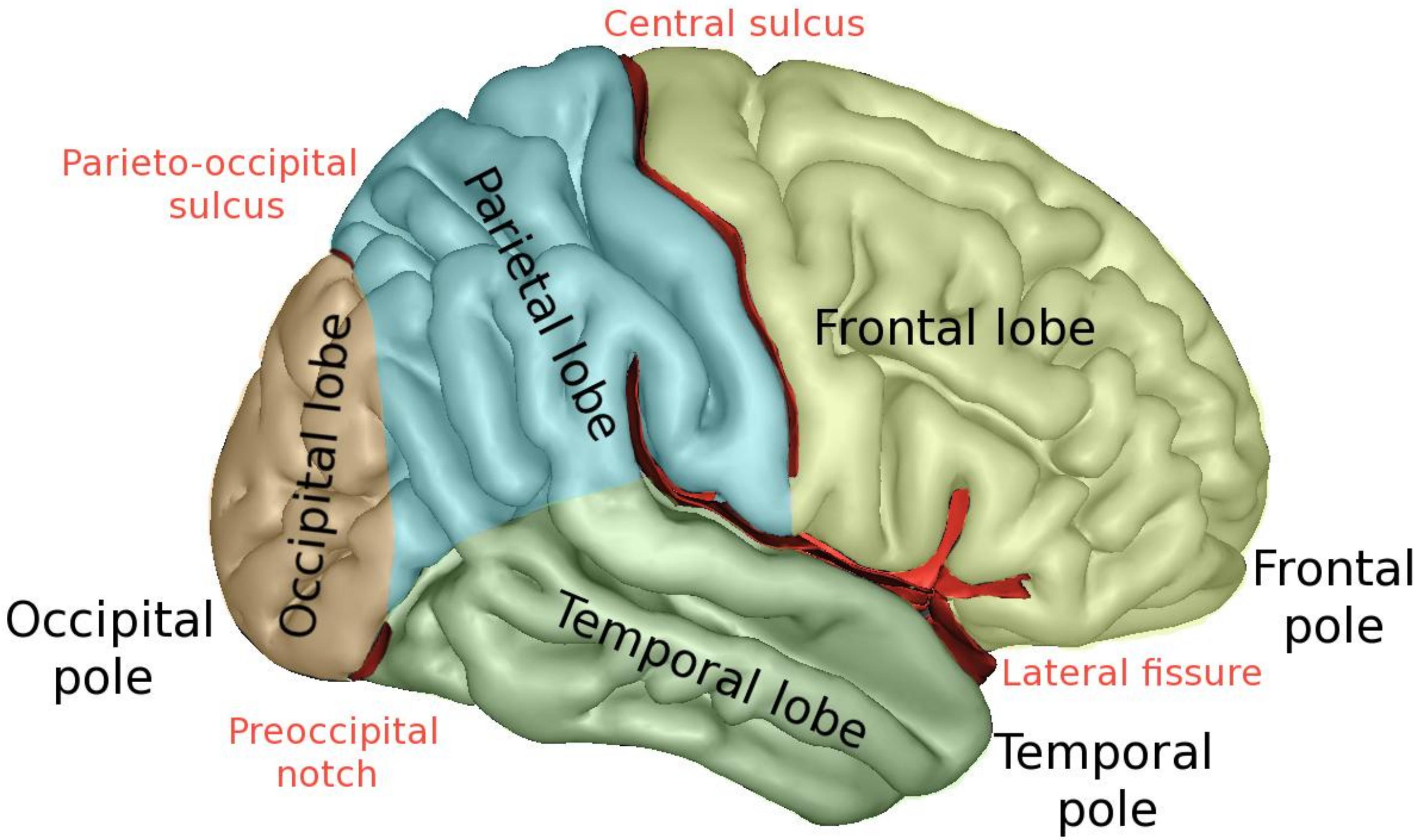

Observed fMRI time course
Correlation coefficient = 0.917

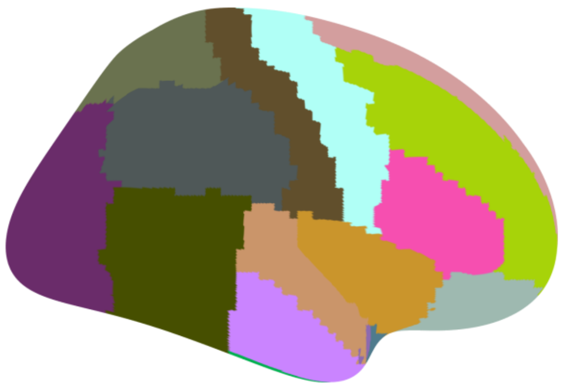
- Network
  - Set of nodes and edges
  - Functional brain network
    - Nodes: pre-defined brain regions
    - Edges: connectivity (correlation or causality) between brain regions



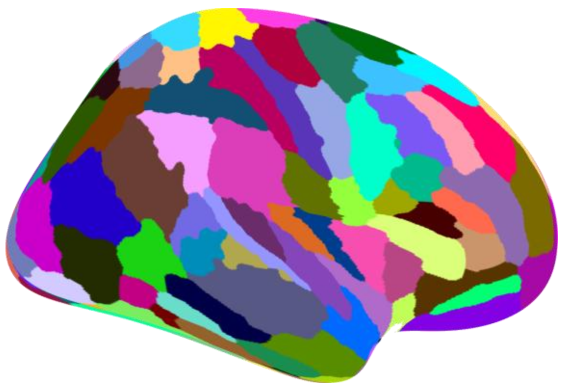


Brain Atlases Delineating Heterogeneous Nodes with Varying Definitions and Quantities





Hammers atlas



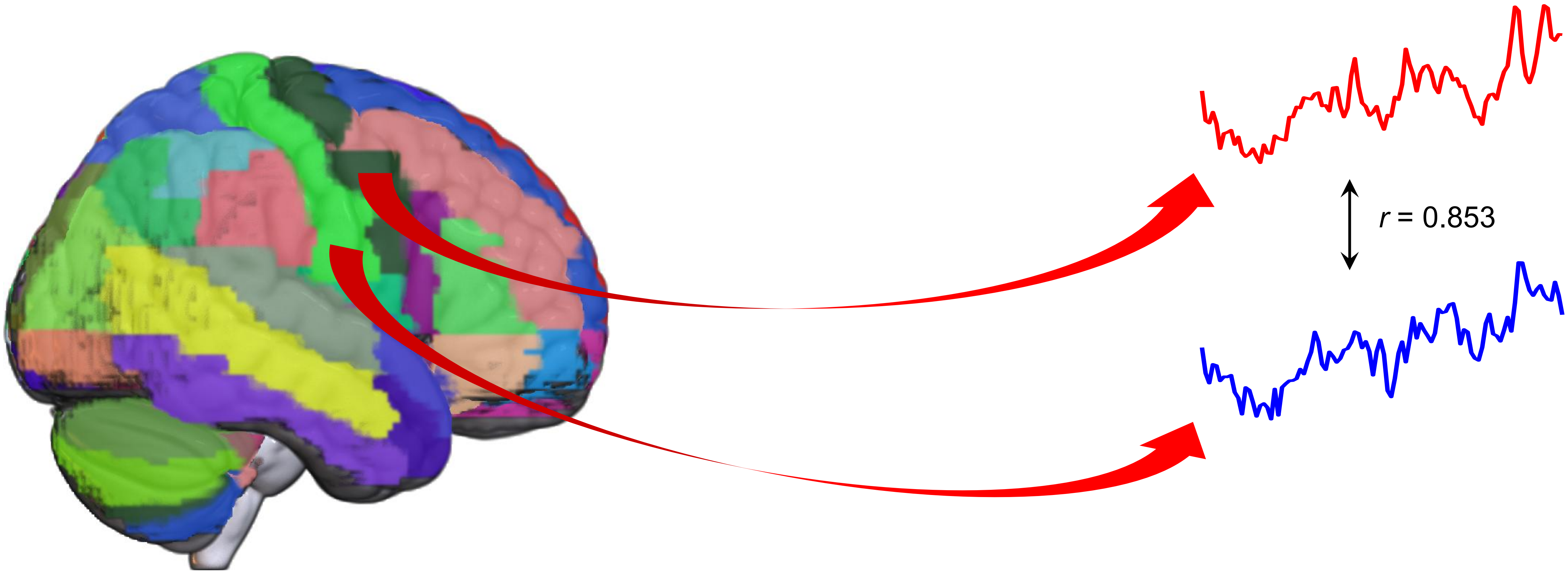
Brainnetome atlas

[https://en.wikipedia.org/wiki/Lobes_of_the_brain]

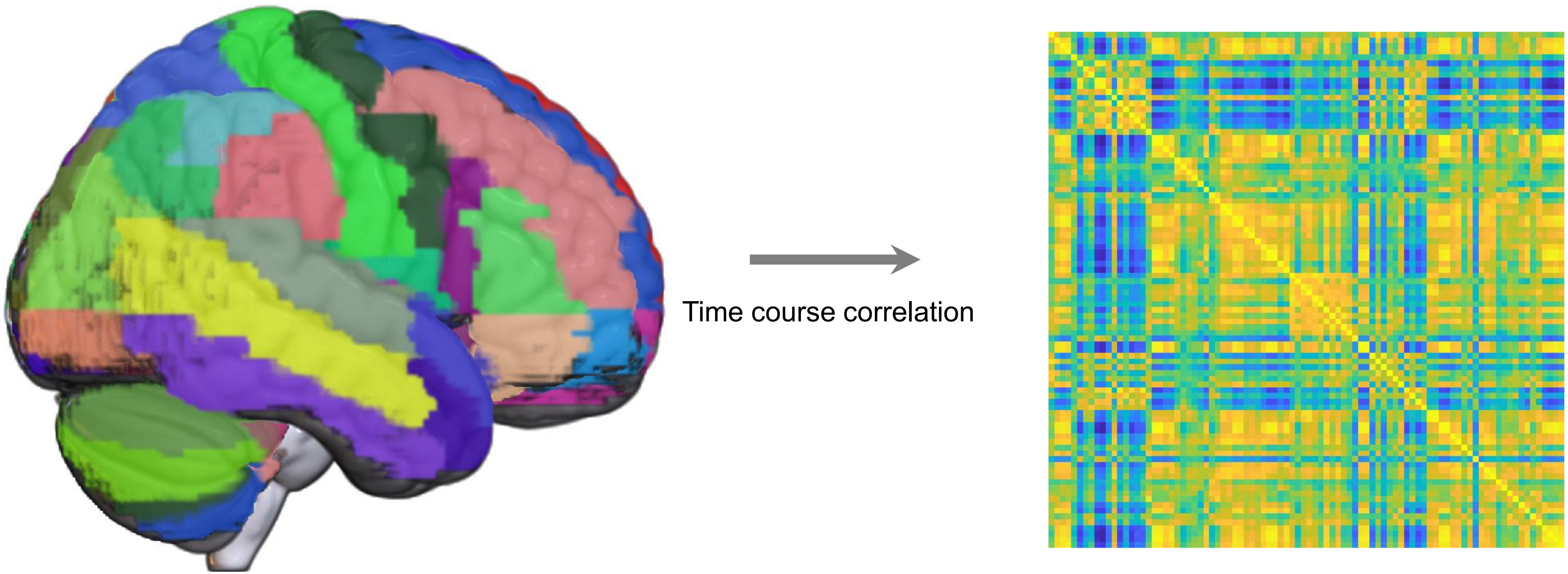
Lobes of the Brain

Hammers atlas

Brainnetome atlas

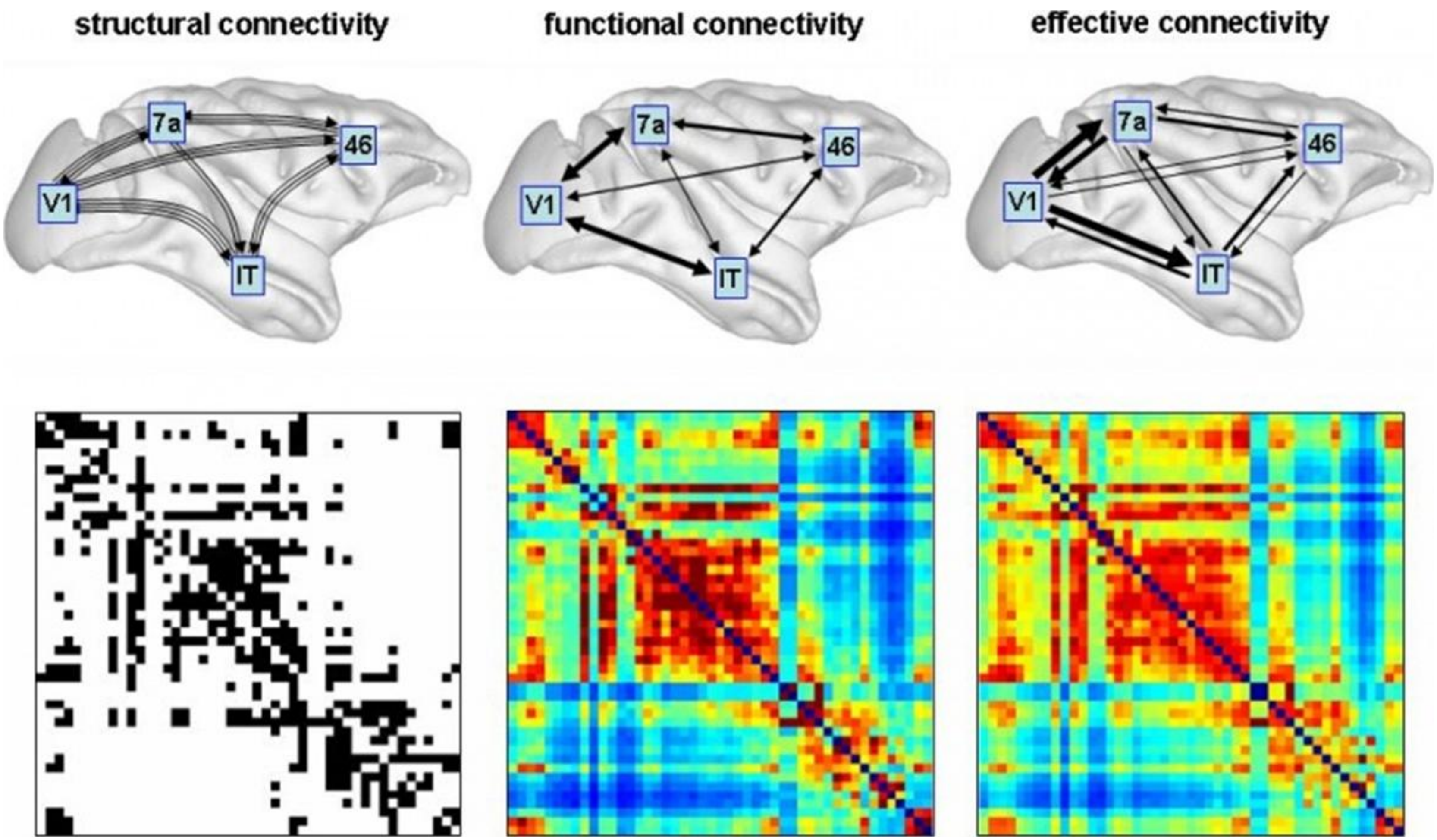


Pair-wise Correlation of Time Courses



Functional Network or Connectome

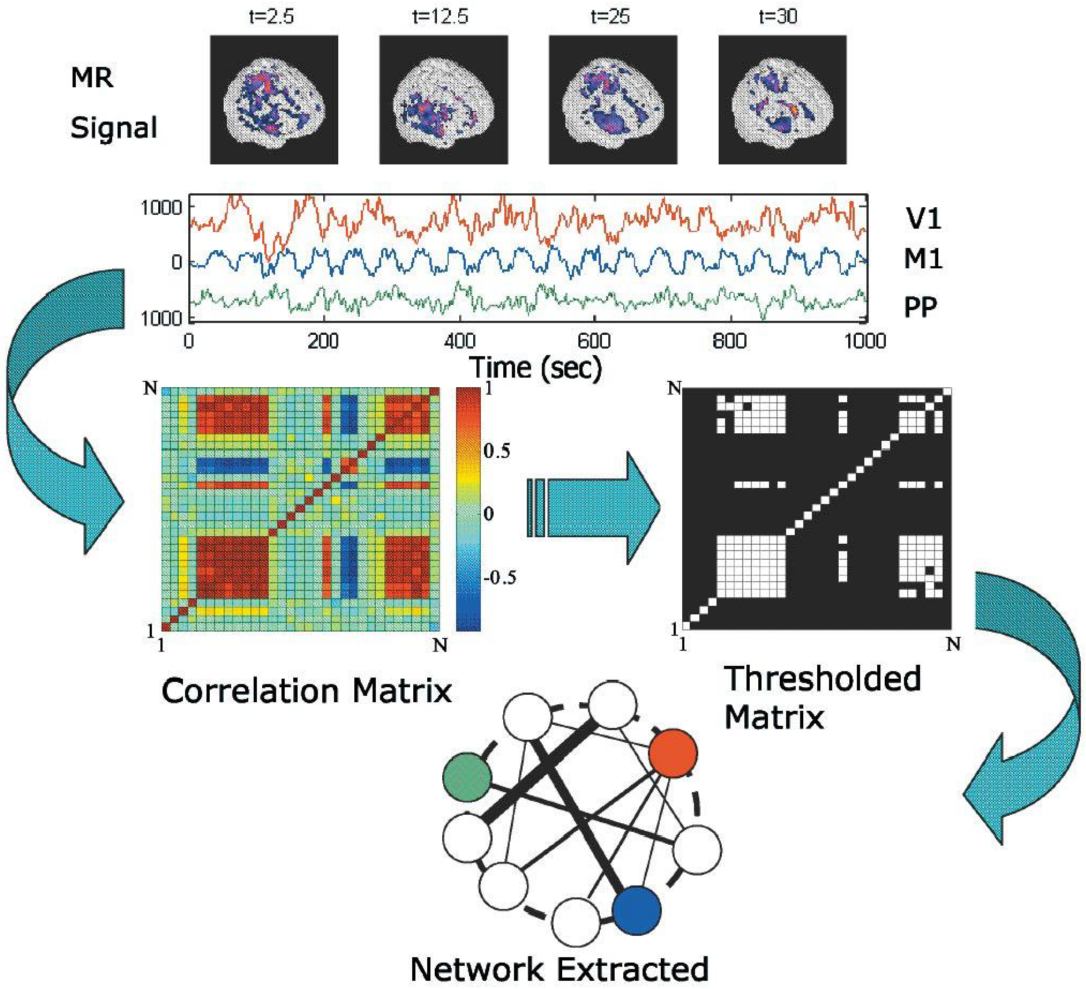
- Correlation vs. causality
  - Correlation: statistical relationship between variables
    - Claims that, given a change in one variable, there is a corresponding change in another variable
    - Can be positive (both variables increase or decrease together), negative (one variable increases while the other decreases), or zero (no relationship)
    - Does not imply causation, but simply indicates that there is a relationship between the variables
  - Causality: cause-and-effect relationship between variables
    - Claims that a change in one variable directly brings about a change in another variable
    - Much stronger assertion than correlation, often involving controlled experiments or analyses

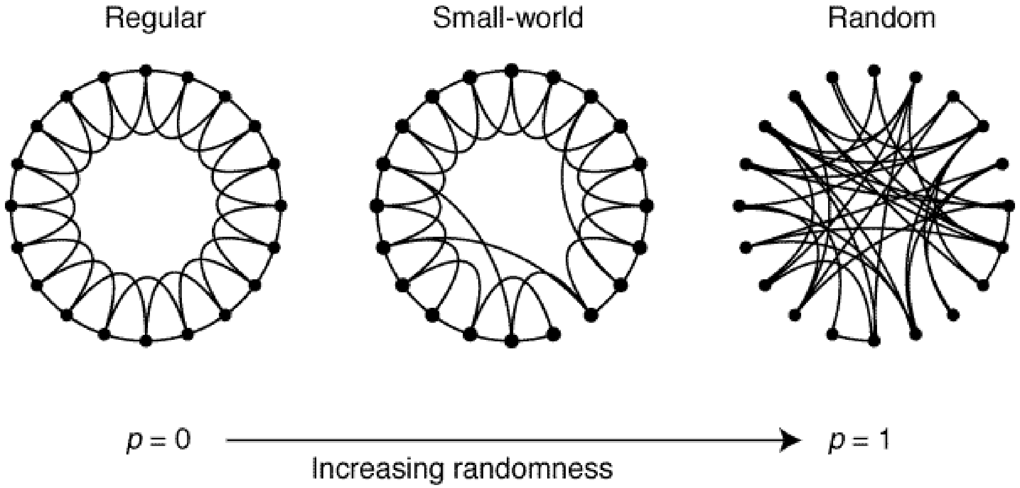


[Honey et al., 2007]

Modes of Brain Connectivity

- Graph-theoretical analysis
  - Characterizes the topological properties of functional brain networks
    - Connection topology of the brain
    - Efficiency of information transfer within the brain
    - Key regions in the brain.
    - Brain's resilience to damage or attack

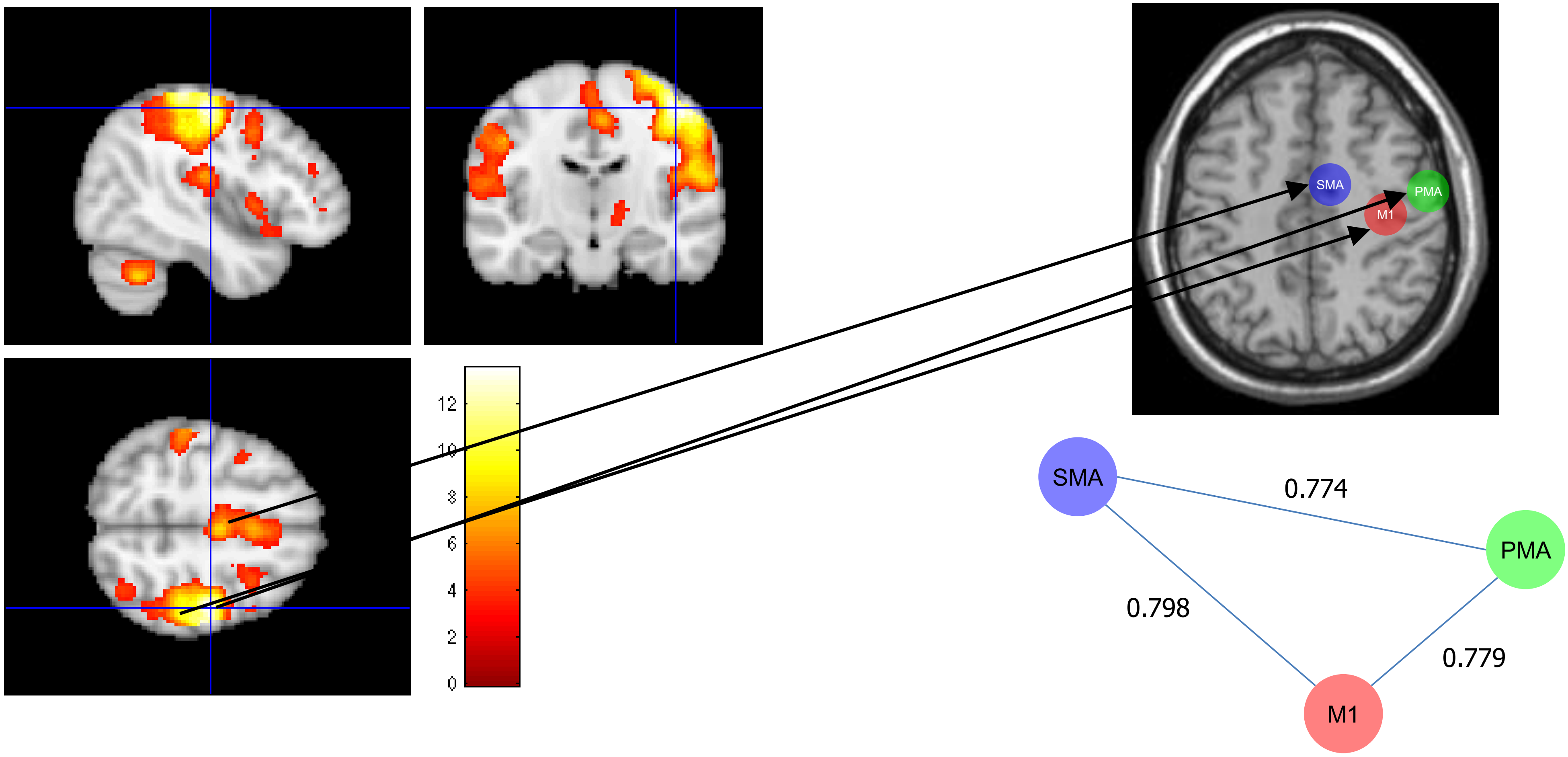




[Eguíluz et al., 2005; Watts and Strogatz, 1998]

Functional Brain Network and Its Topological Properties

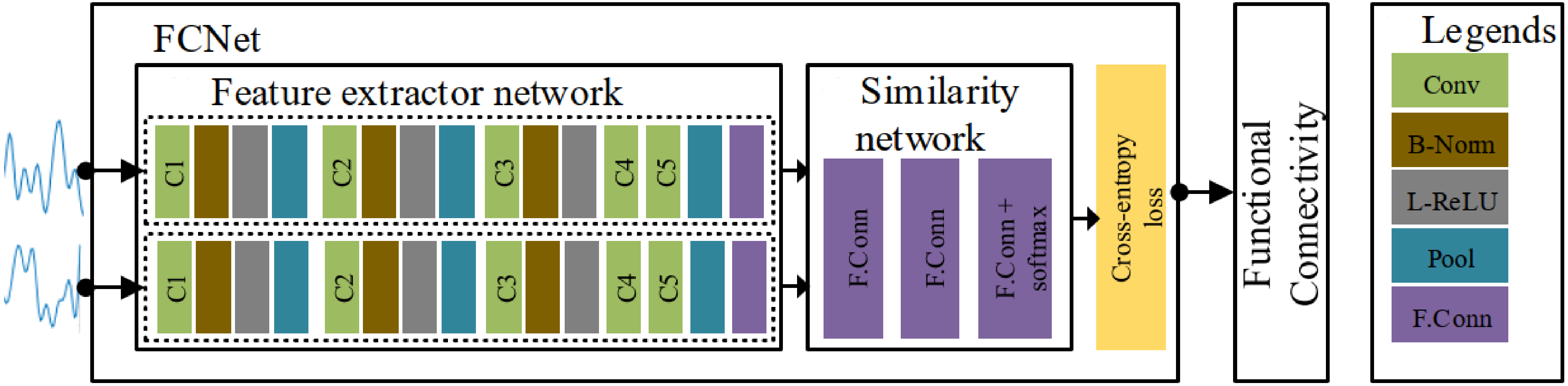
- Complementary roles of functional segregation and integration
  - Exhibited as a dynamic interplay between functional segregation and integration in the brain
    - Certain tasks may require highly specialized processing within specific regions (segregation), while the coordination and combination of information from these regions are necessary for holistic processing and decision-making (integration)
  - Explored by fMRI to gain insights into how functional segregation and integration contribute to various functions and how they may be disrupted in neurological and psychiatric disorders



Functional Segregation and Integration Contributing to Motor Function

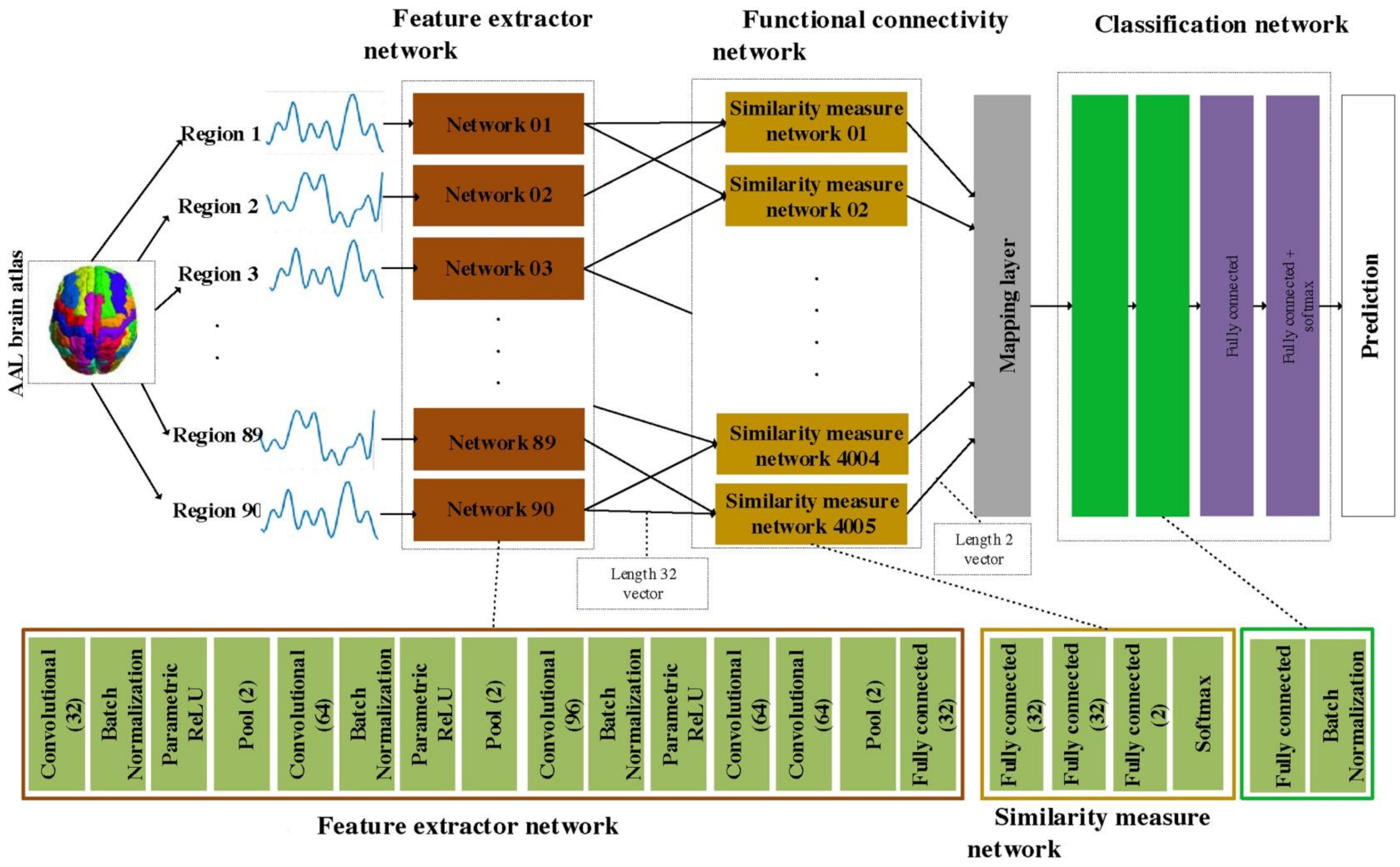
Automated Functional Connectivity Extraction

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



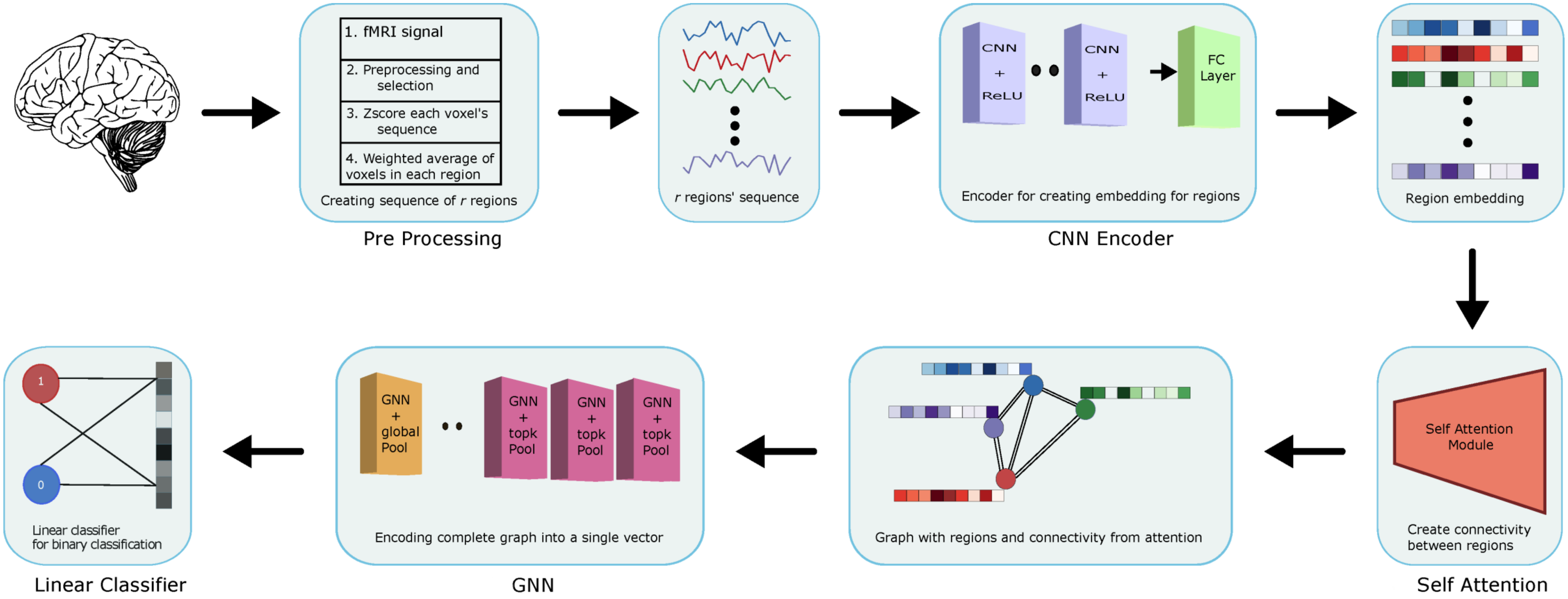
[Riaz et al., 2017]

FCNet: Functional Connectivity Extraction



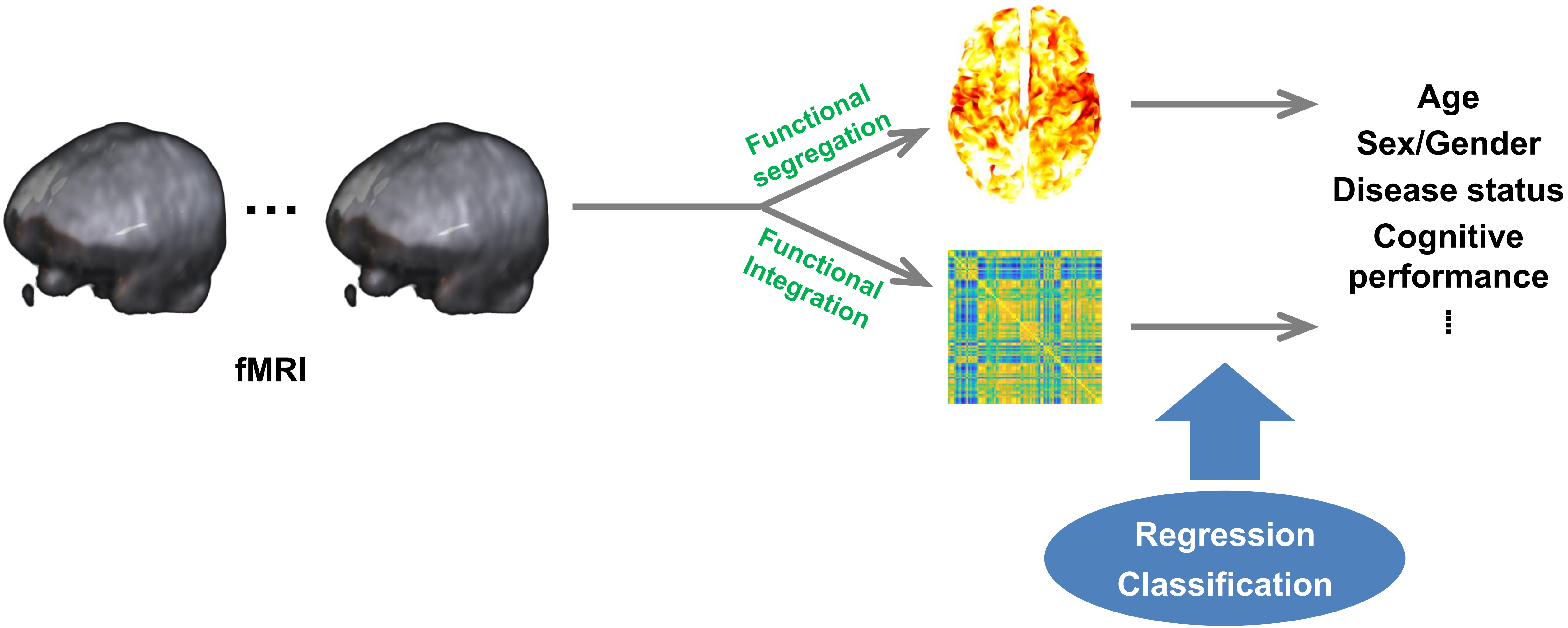
[Riaz et al., 2020]

DeepFMRI: Functional Connectivity Extraction



[Mahmood et al., 2021]

BrainGNN: Functional Connectivity Extraction



fMRI
Functional segregation
Functional Integration
Age
Sex/Gender
Disease status
Cognitive performance
Regression
Classification

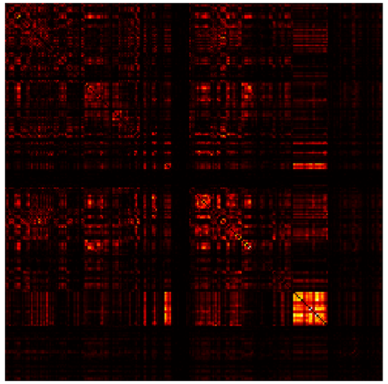
Sex Classification

$P(Y|X) = P(\text{sex} \mid \{\text{Net\_FC}, \text{Net\_EC}\})$

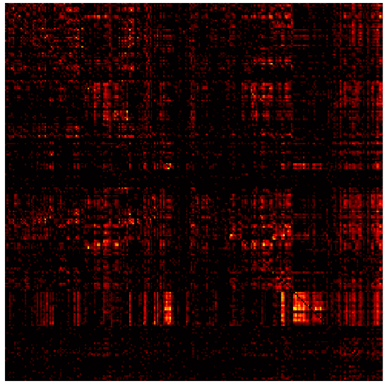
where X = functional and effective connectivity networks: Net_FC, Net_GC $\in \mathbb{R}^{N \times N}$

and Y = sex

Functional connectivity network



Effective connectivity network



→ Sex

Multi-graph Input for Sex Classification