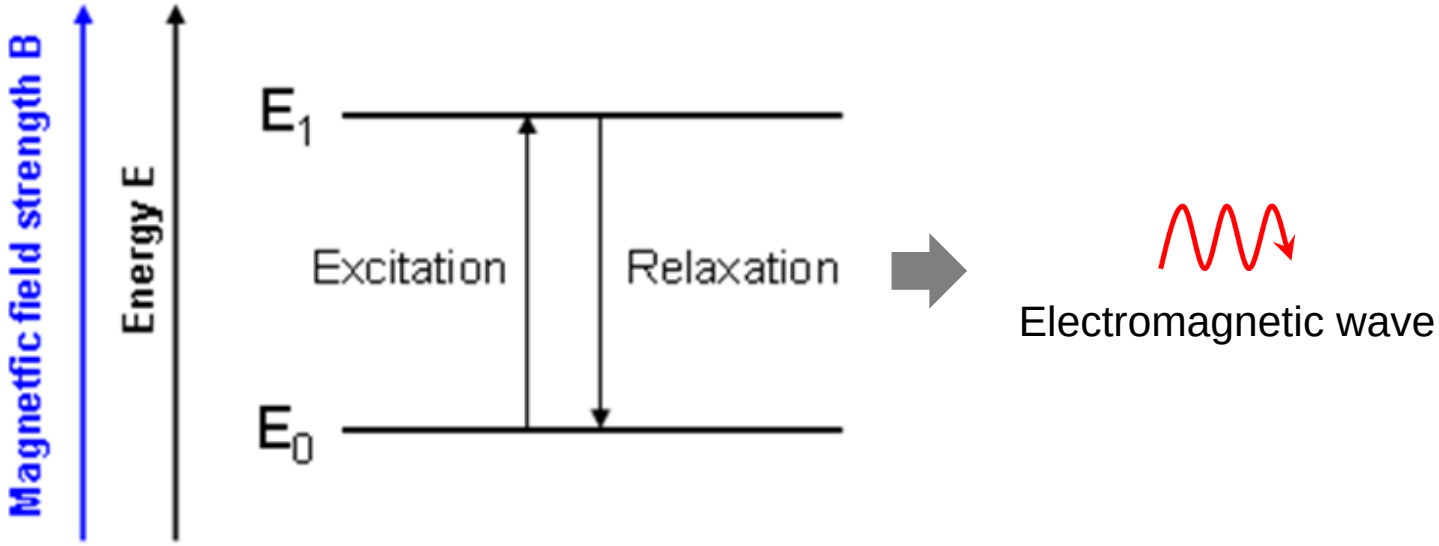
Medical/Bio Research Topics Ⅱ: Week 04 (24.09.2024)

Functional MRI: Fundamental Principles and Data Processing

기능 자기공명영상: 기본 원리 및 데이터 처리 방법

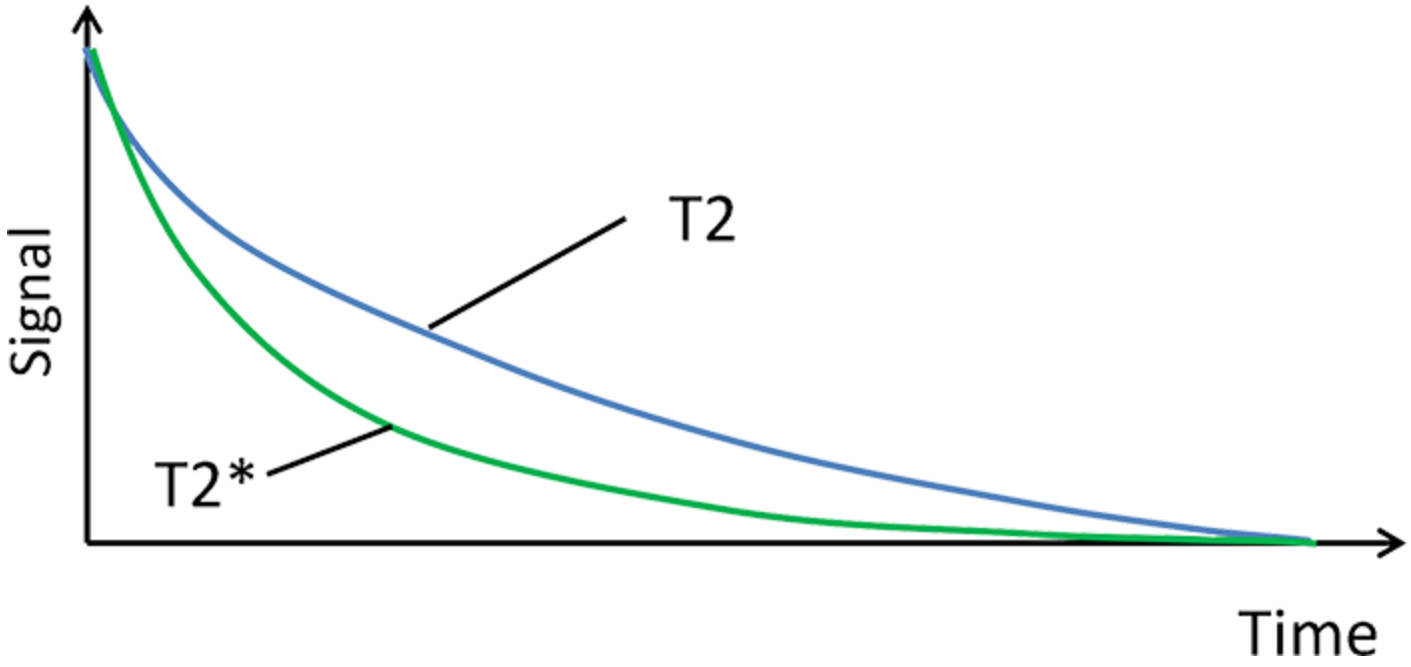
MRI Principles

- Excites hydrogen nuclei (protons) into releasing electromagnetic waves (in radio frequency) and then records the locations of the waves with high accuracy



- MRI contrast mechanisms
  - 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 particularly for fMRI
    - 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

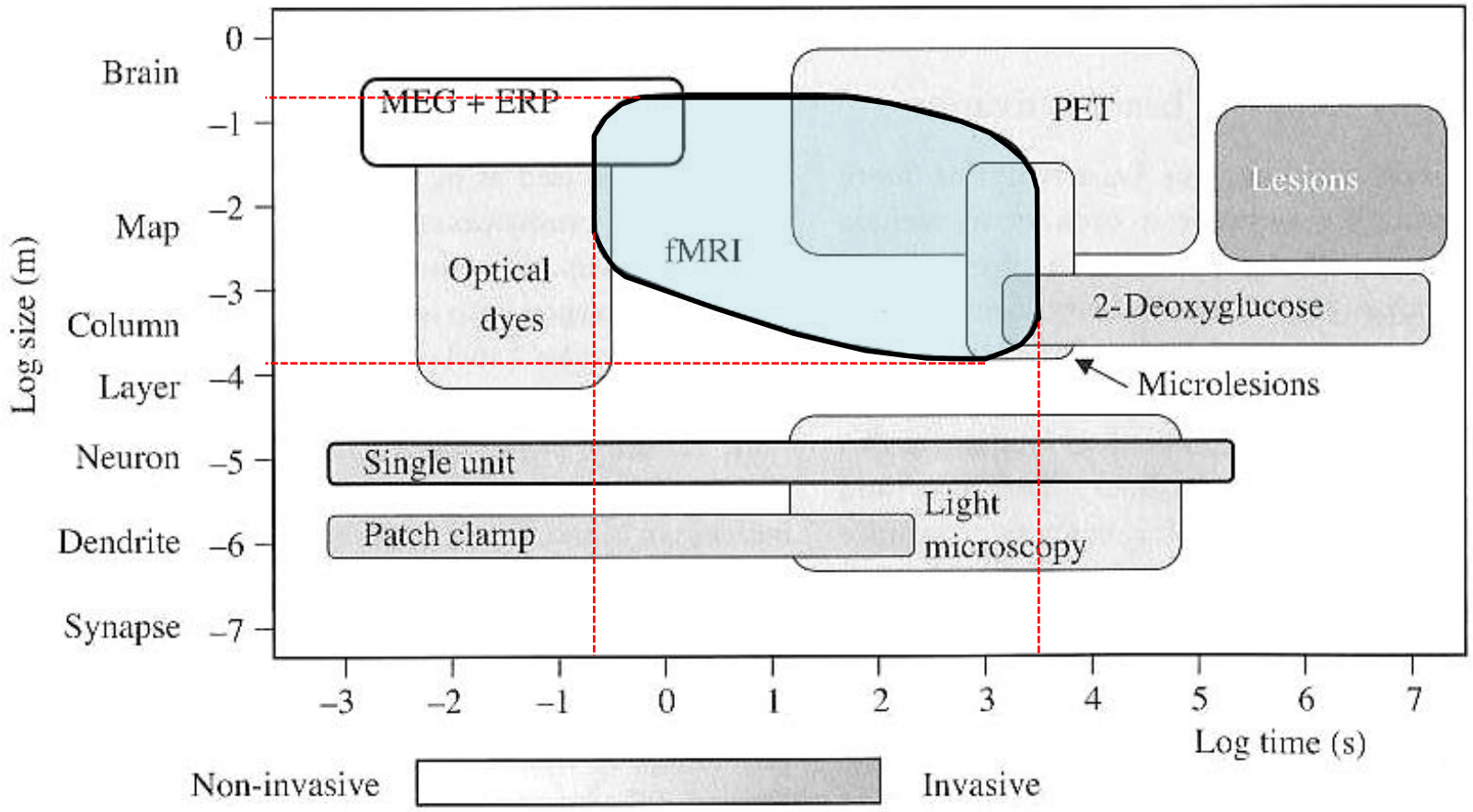


[https://www.radiologycafe.com/frcr-physics-notes/mr-imaging/t1-and-t2-signal/]

Quicker T2* decay than T2 decay

fMRI

- MRI technique primarily for measuring brain activity
  - Creates a movie that non-invasively reveals details of events over time in the brain
  - Spatially within millimetres and temporally within a window of a few seconds
- Relies on the coupling between haemodynamics (changes in blood flow, blood volume, and blood oxygenation) and neuronal activity



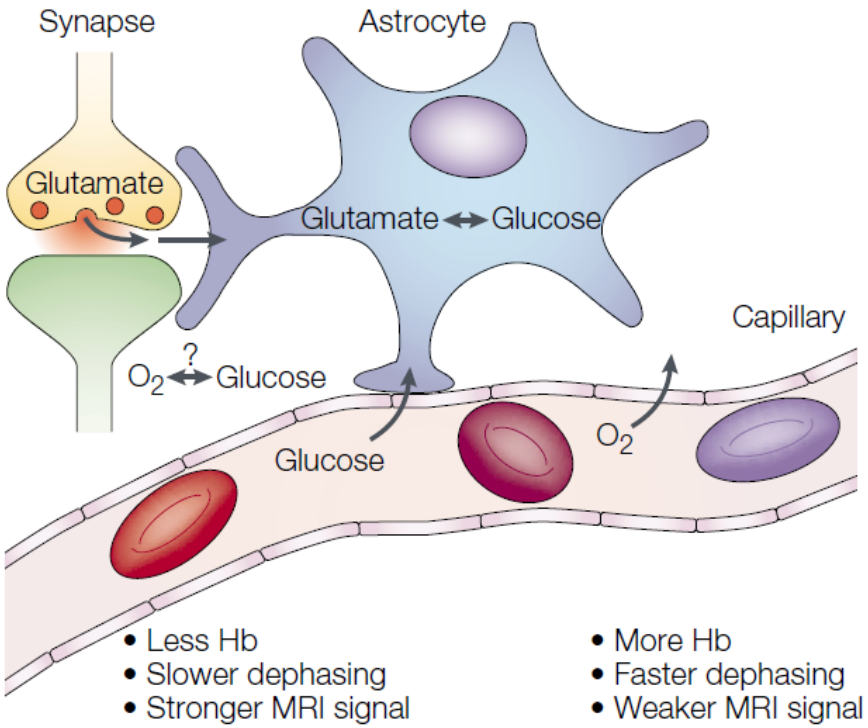
[Churchland and Sejnowski, 1988]

fMRI in comparison with other neuroscience methods

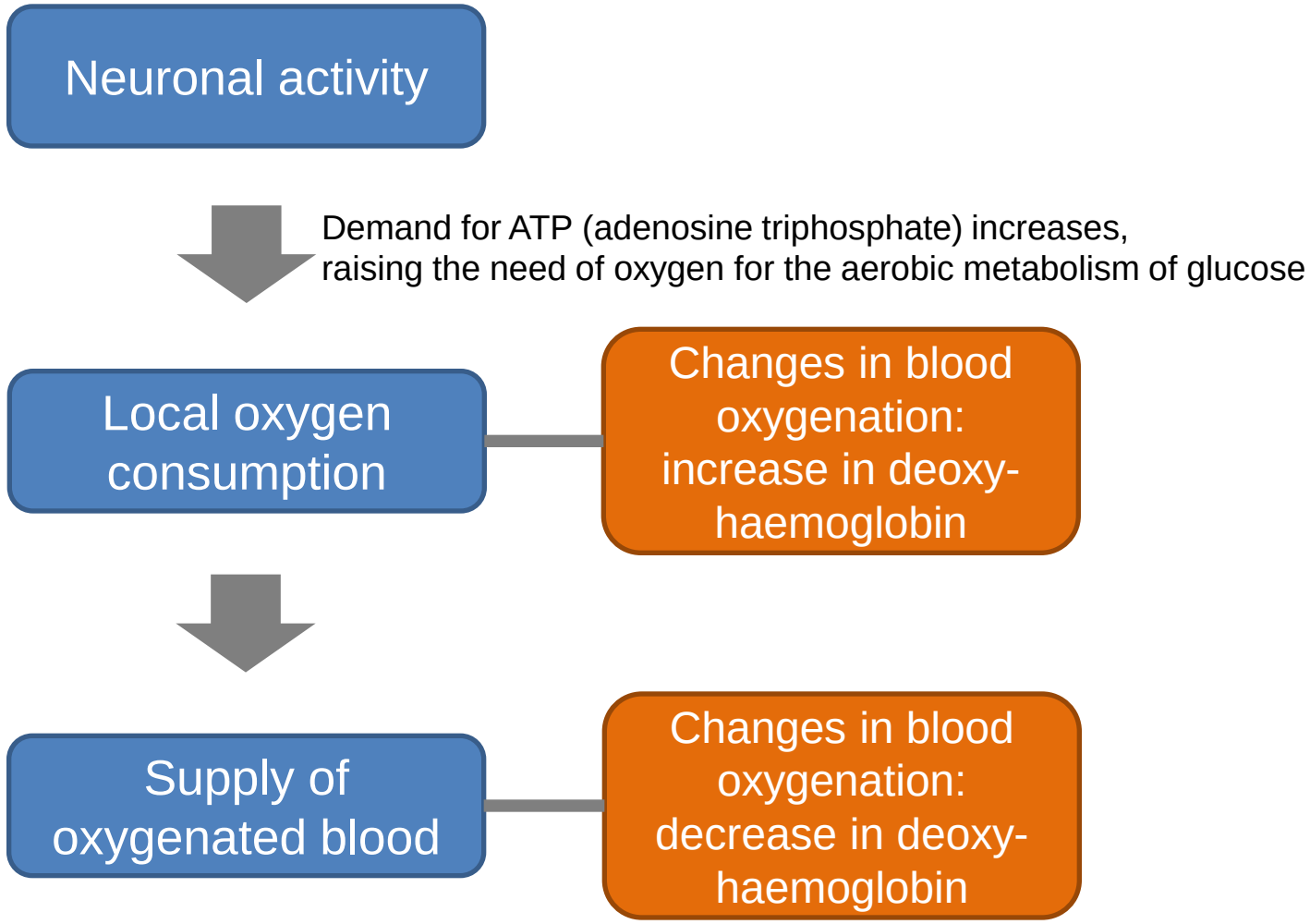
BOLD Contrast for fMRI

- BOLD contrast
  - Exploits different electromagnetic properties between blood containing oxygen (oxyhaemoglobin) and blood without oxygen (deoxyhaemoglobin)
  - Deoxyhaemoglobin (paramagnetic, thus faster relaxation) vs. oxyhaemoglobin (weakly diamagnetic)
    - Deoxyhaemoglobin concentration ↑ ➜ image intensity ↓
    - Deoxyhaemoglobin concentration ↓ ➜ image intensity ↑

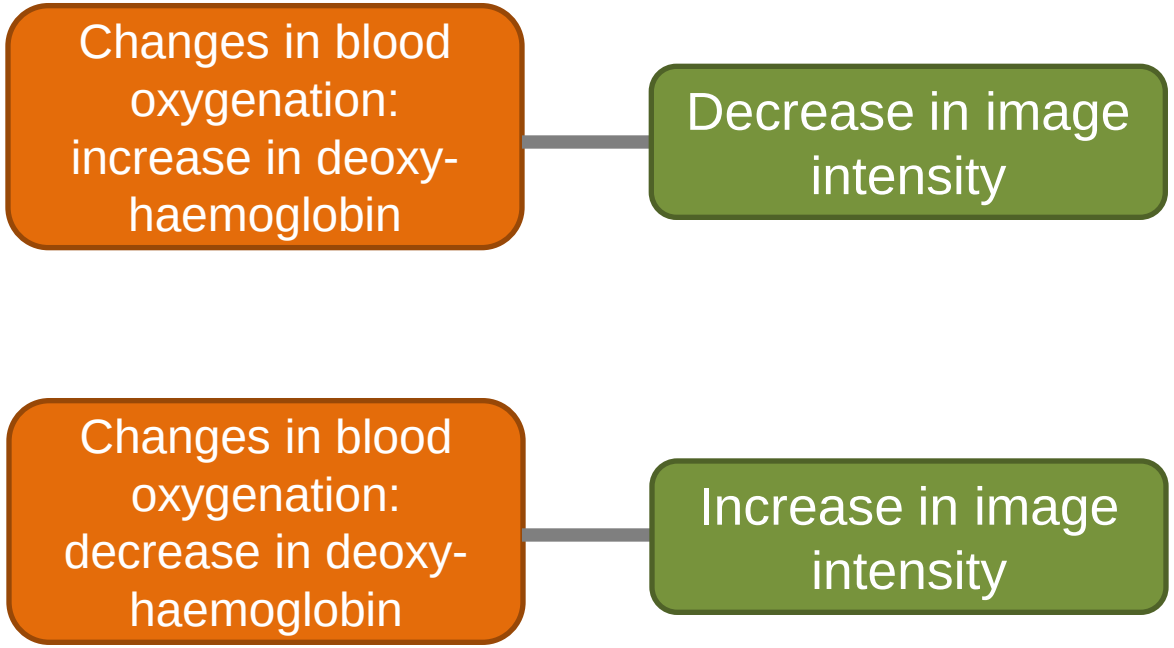
- Based on the assumption that the changing distribution of blood oxygenation in the brain correlates with neuronal activity



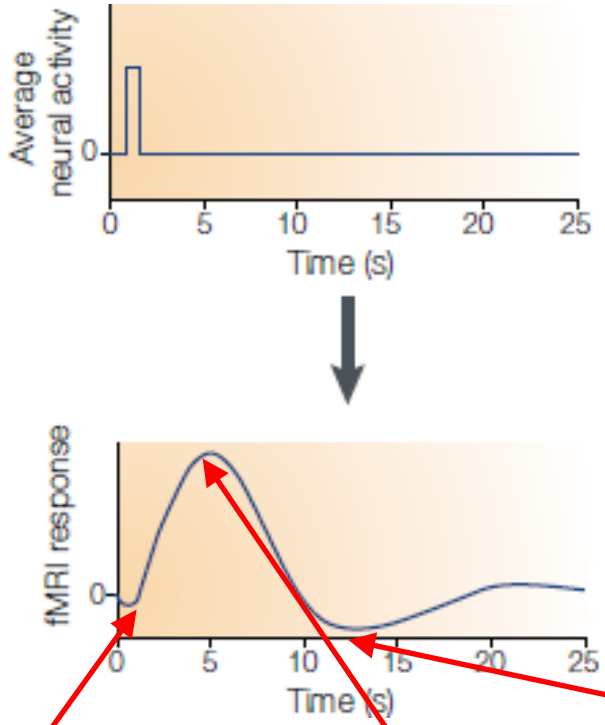
[Heeger and Ress, 2002]



Neuronal activity → changes in blood oxygenation



Changes in blood oxygenation → changes in image intensity



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

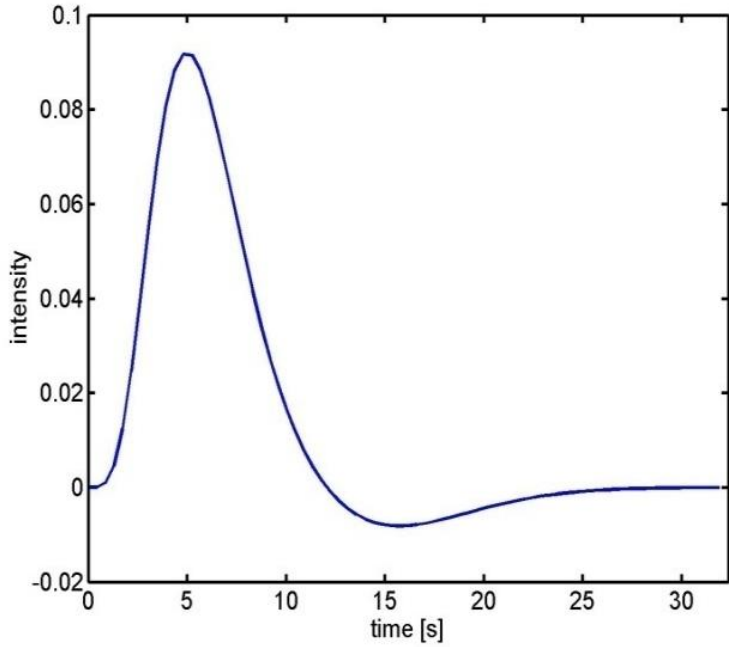
[Heeger and Ress, 2002]

Three phases of a BOLD fMRI response

Haemodynamic Response Function

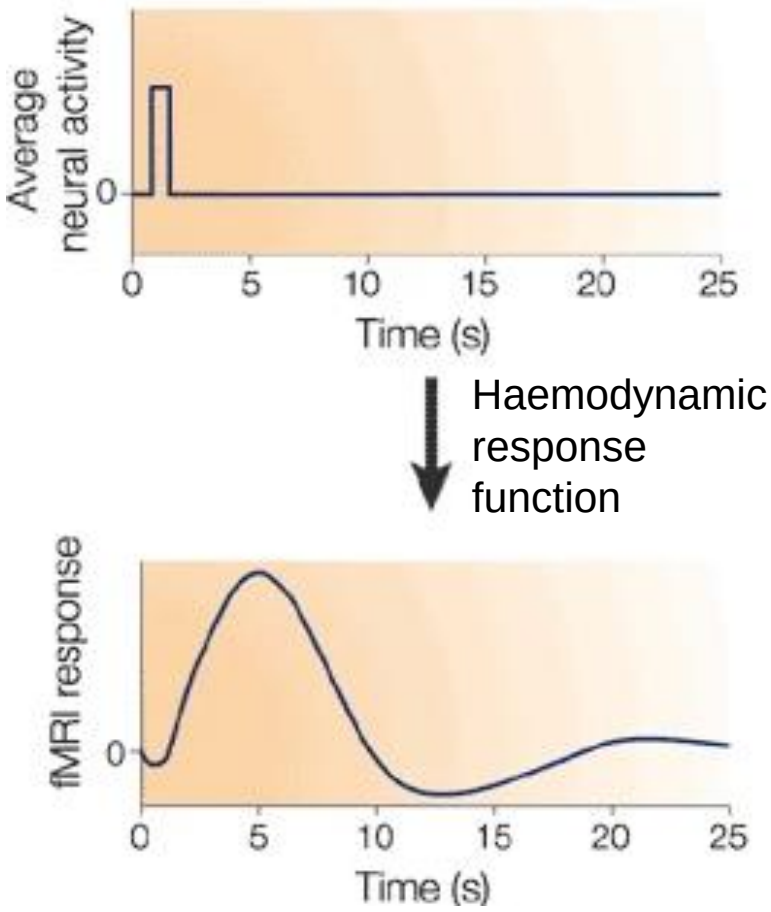
- Hypothetically characterizes the relationship between neuronal activity and an fMRI signal
  - Positive for excitatory neuronal activity
  - Much slower than underlying neuronal processes

- Models a gradual rise to peak (about 6 seconds), a long return to baseline (about 10 seconds), and a slight undershoot (about 10-15 seconds)
  - Mathematically represented by a mixture of gamma functions

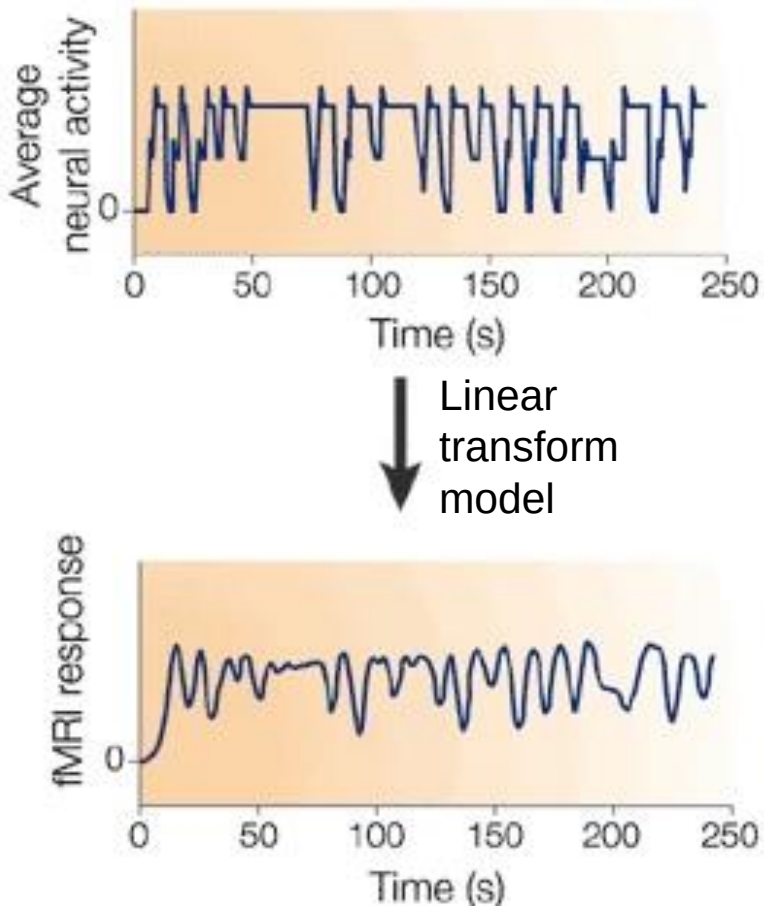


- Linear transform model
  - Predicts that an fMRI signal should sum over time
  - Enables to compute (using convolution) the time course of an fMRI signal, given a measured time course of neuronal activity
  - Simplifies the analysis and interpretation of fMRI data

Brief pulse of neuronal activity

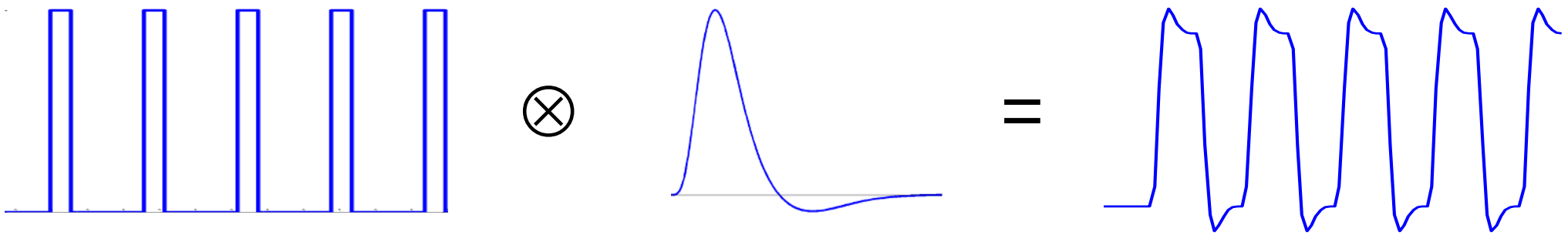


Alternating neuronal activity



[Heeger and Ress, 2002]

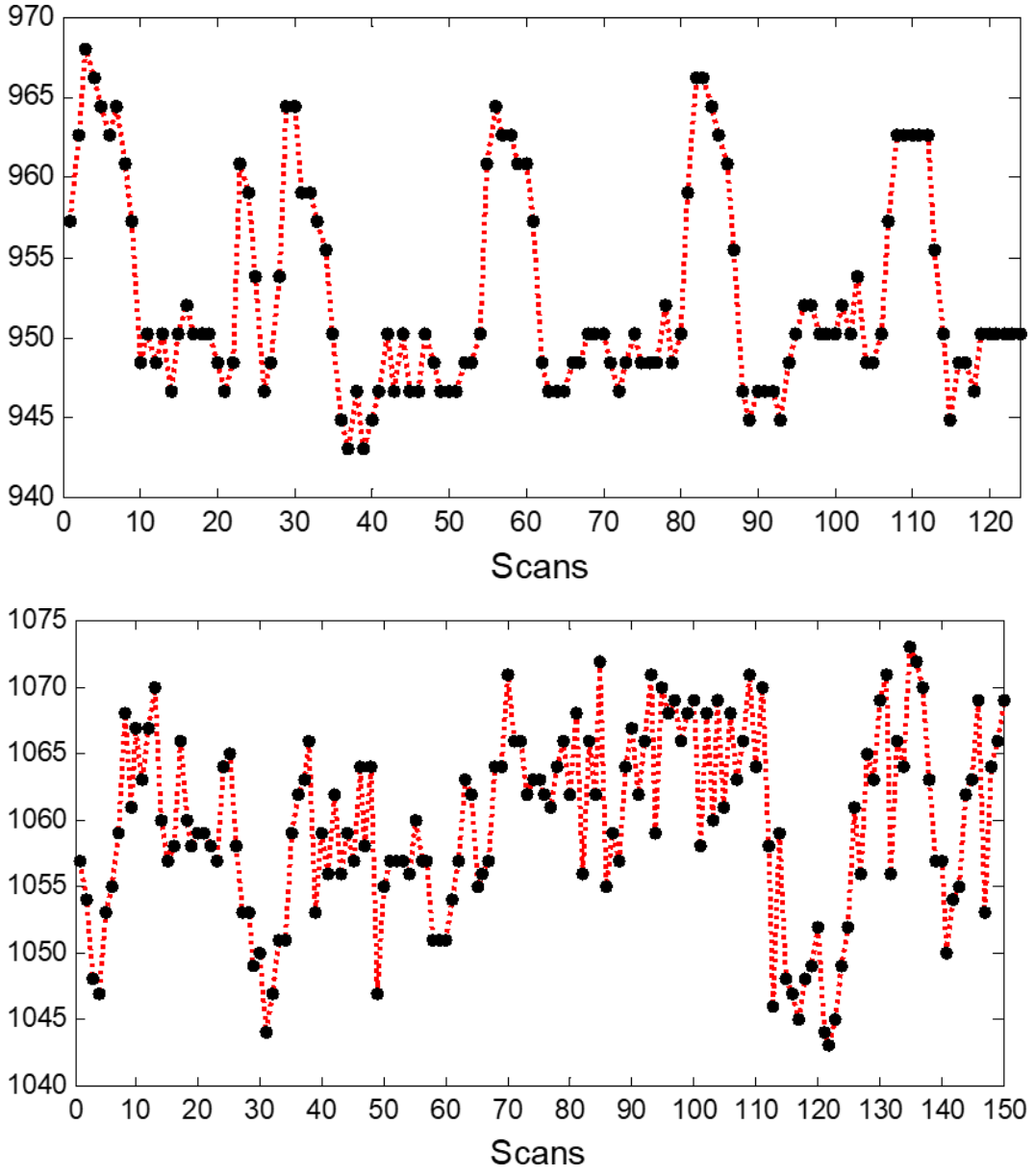
Prediction of a BOLD fMRI response



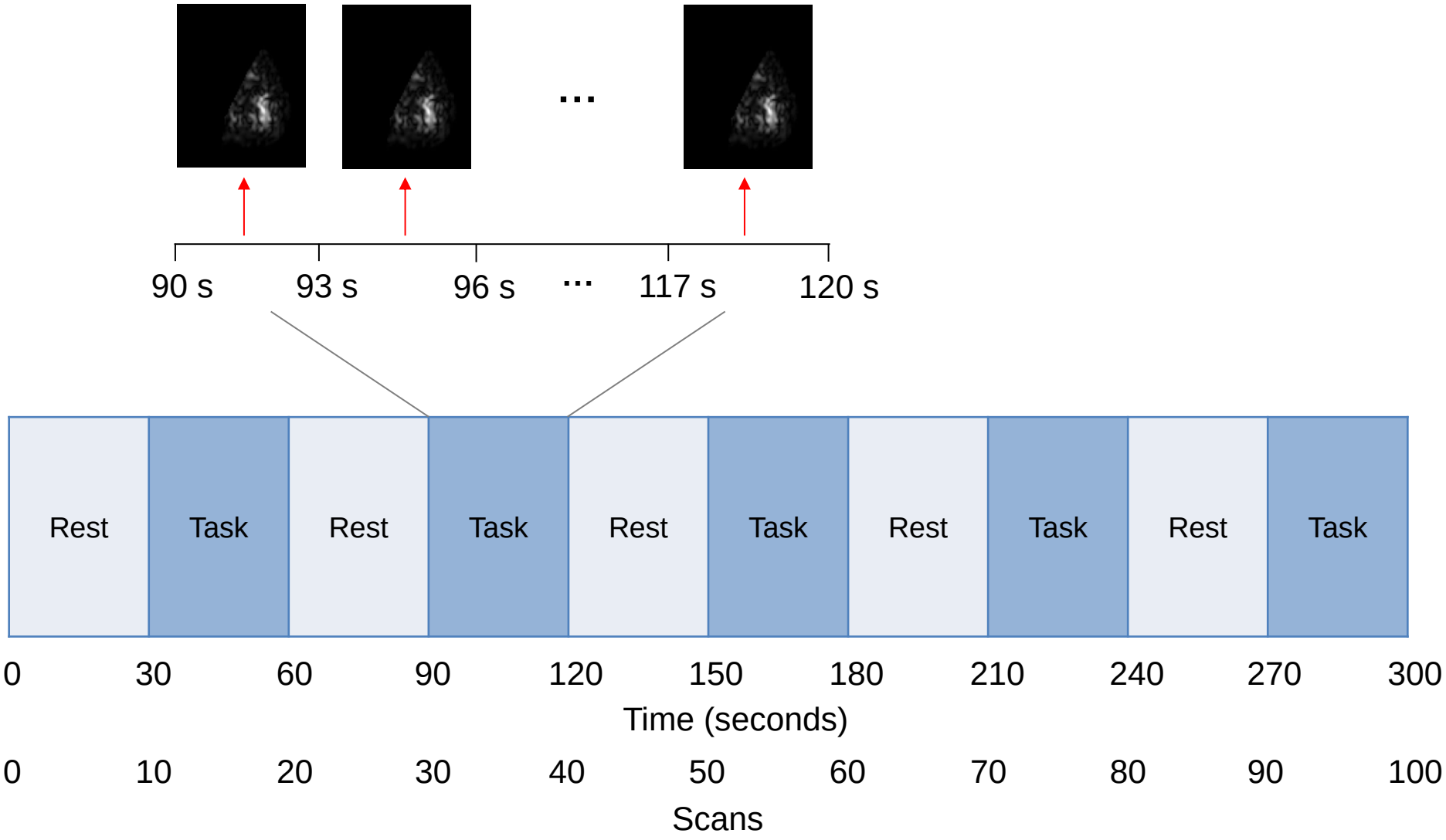
Linear transform model for predicting an fMRI time course

Experimental fMRI

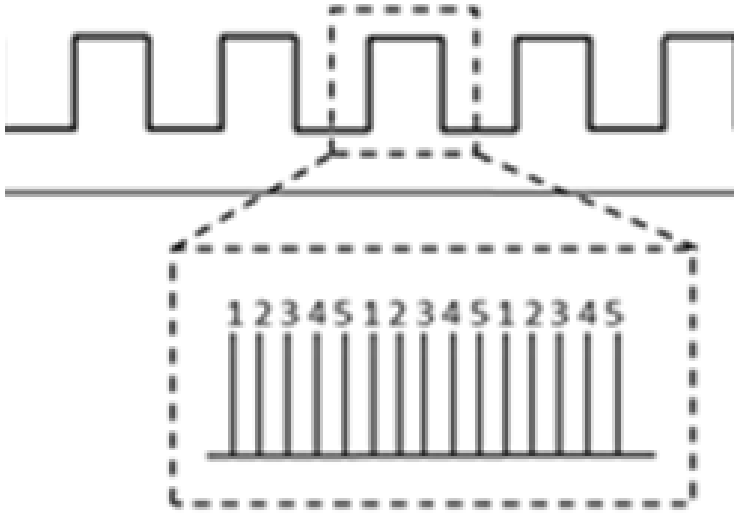
- Task-based fMRI
  - Given an overt task or external stimuli
  - The brain exhibits task-related activity
- Resting state fMRI
  - With wakefulness maintained but structural thinking (e.g., counting) avoided
  - The brain exhibits spontaneous fluctuations in activity



Time series from the same location for task-based vs. resting state fMRI

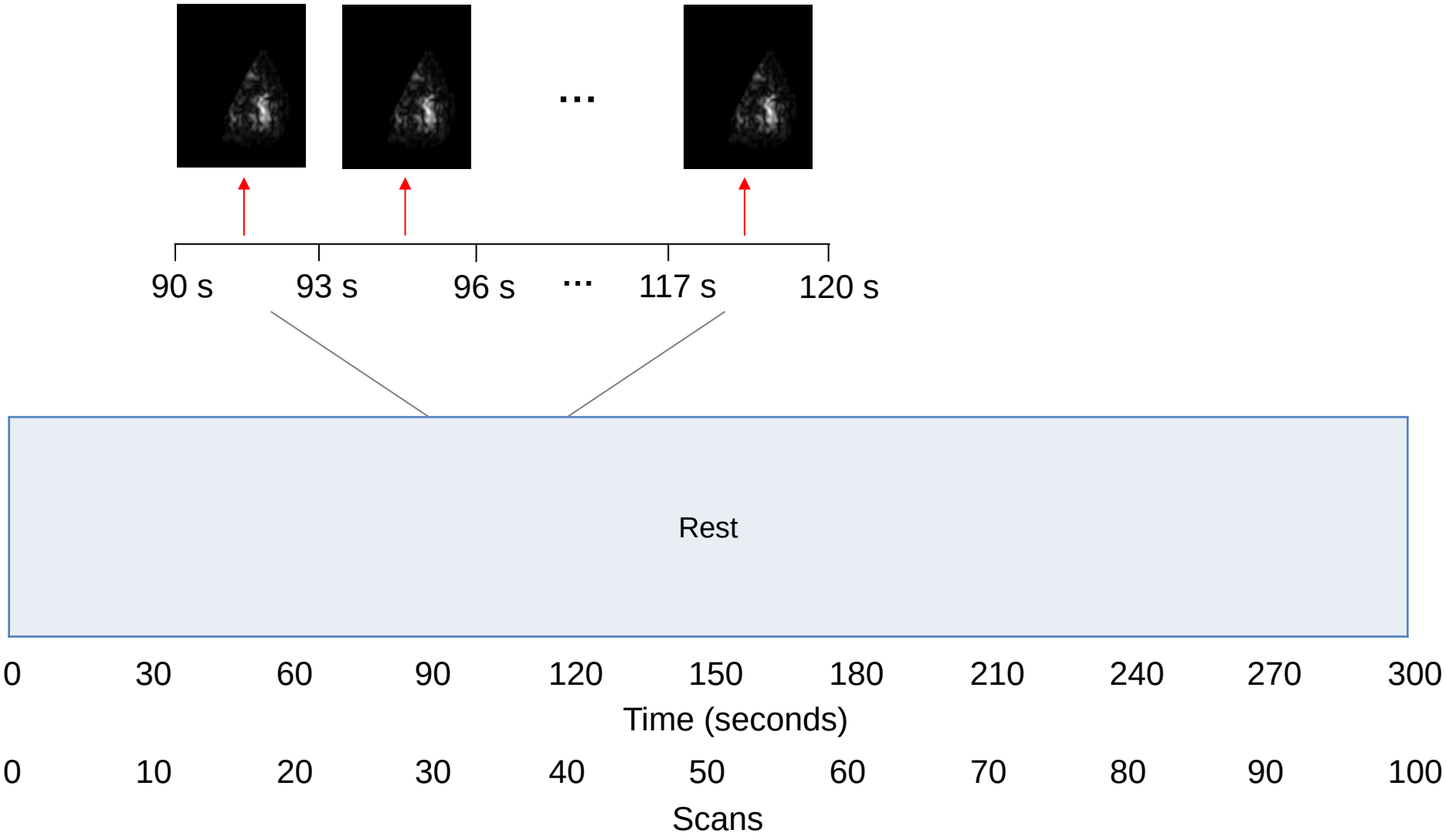


Example of task-based fMRI



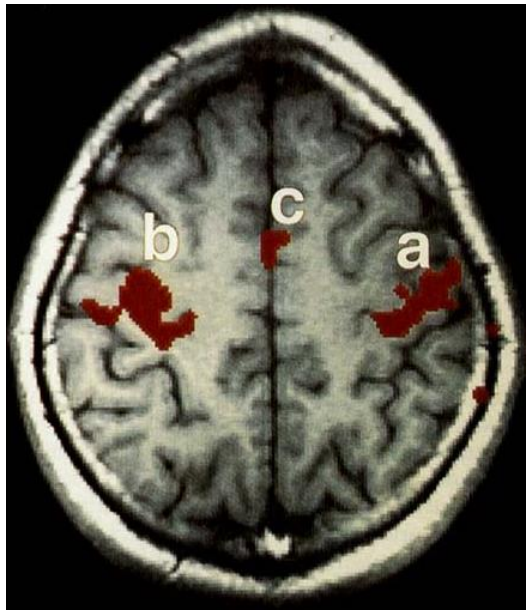
[Manon et al., 2023]

Sequential hand grip task for fMRI



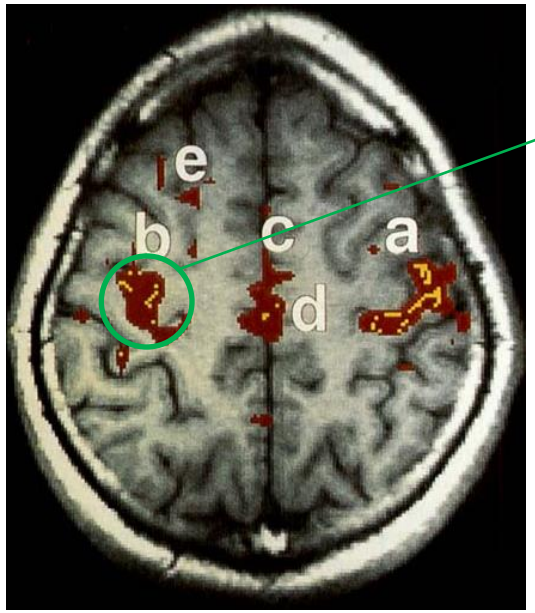
Example of resting state fMRI

Task-based fMRI

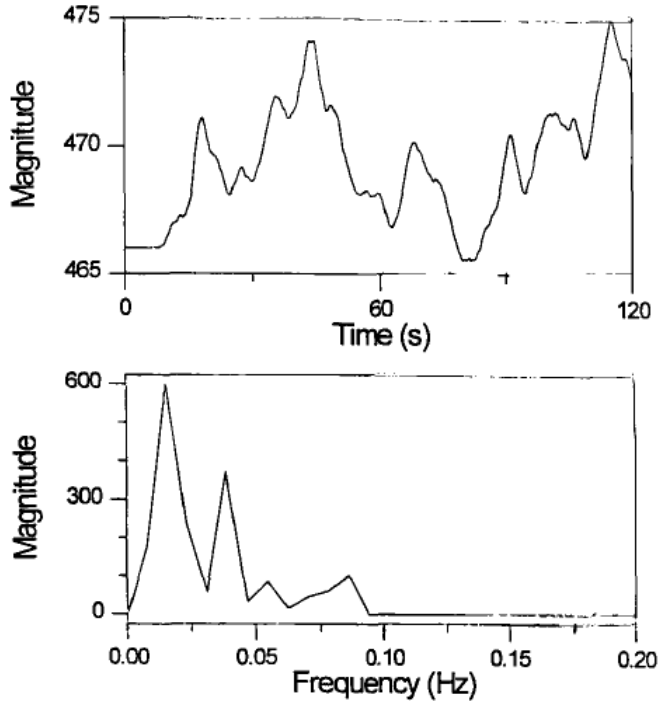


Finger movement-induced activation

Resting state fMRI

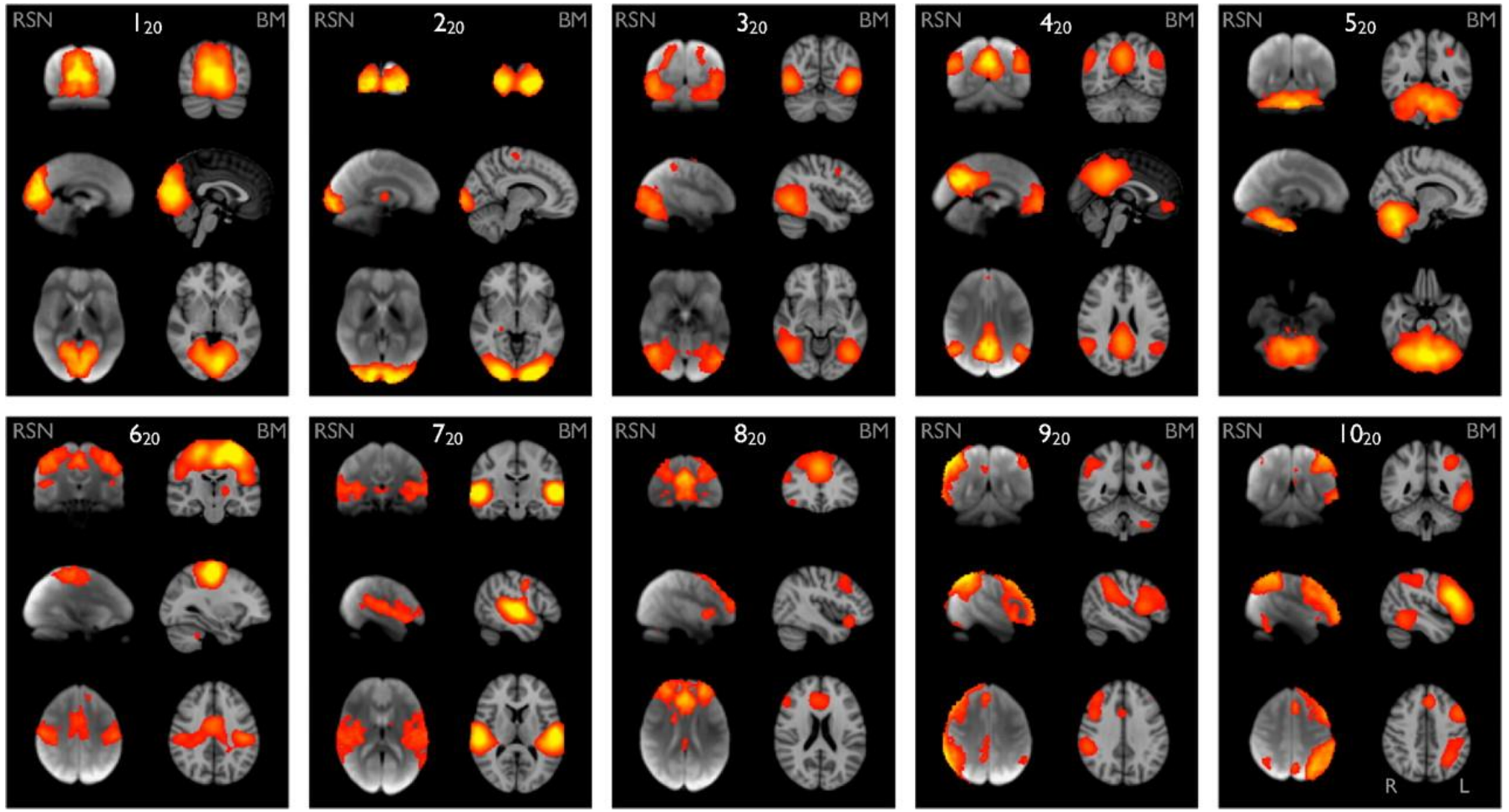


Correlation with the representative time series



[Biswal et al., 1995]

Correspondence between task-based and resting state fMRI: sensorimotor network



Resting state fMRI

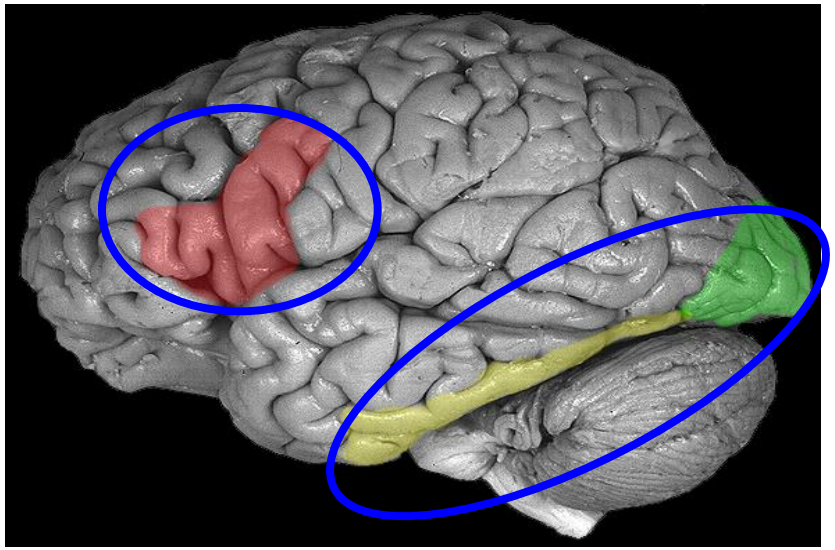
Task-based fMRI

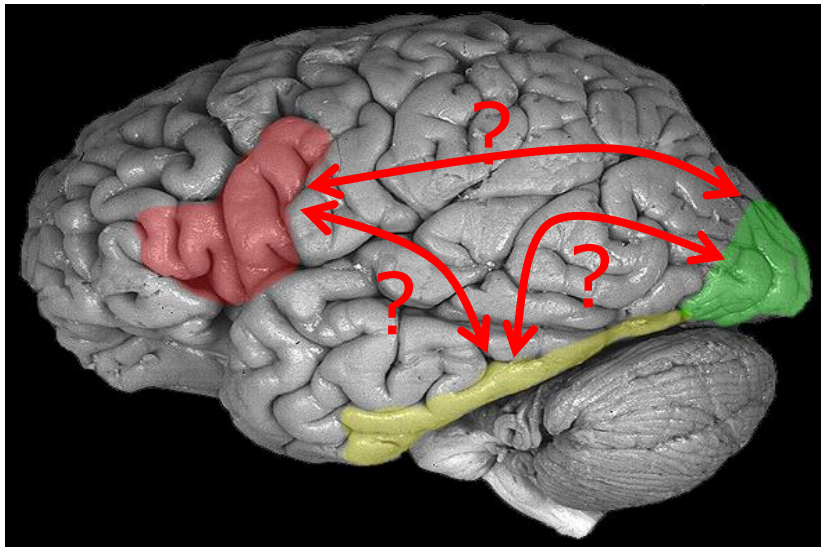
[Smith et al., 2009]

Correspondence between task-based and resting state fMRI: 10 brain networks

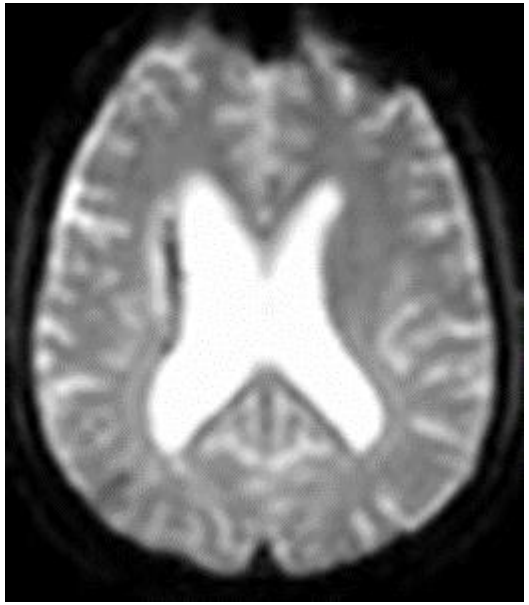
Brain Function Analysis with fMRI

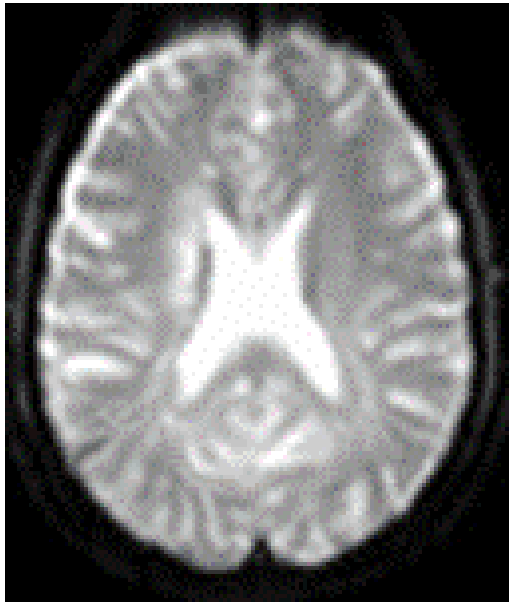
- Functional segregation vs. integration
  - Related to perspectives on how brain regions communicate and work together to process information



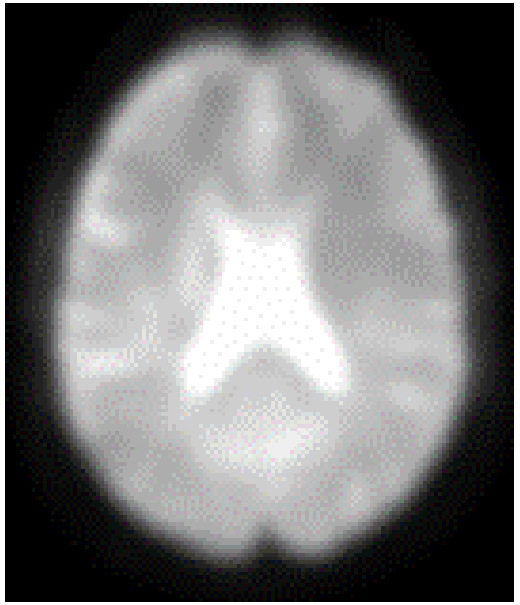


- Preprocessing before extracting and managing fMRI time series
  - Correction for unwanted variation
    - Difference in slice timing
    - Head motion
    - Susceptibility artifact (B0 inhomogeneity-induced distortion): local variations in magnetic susceptibility between different tissues or at tissue-air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





Normalisation

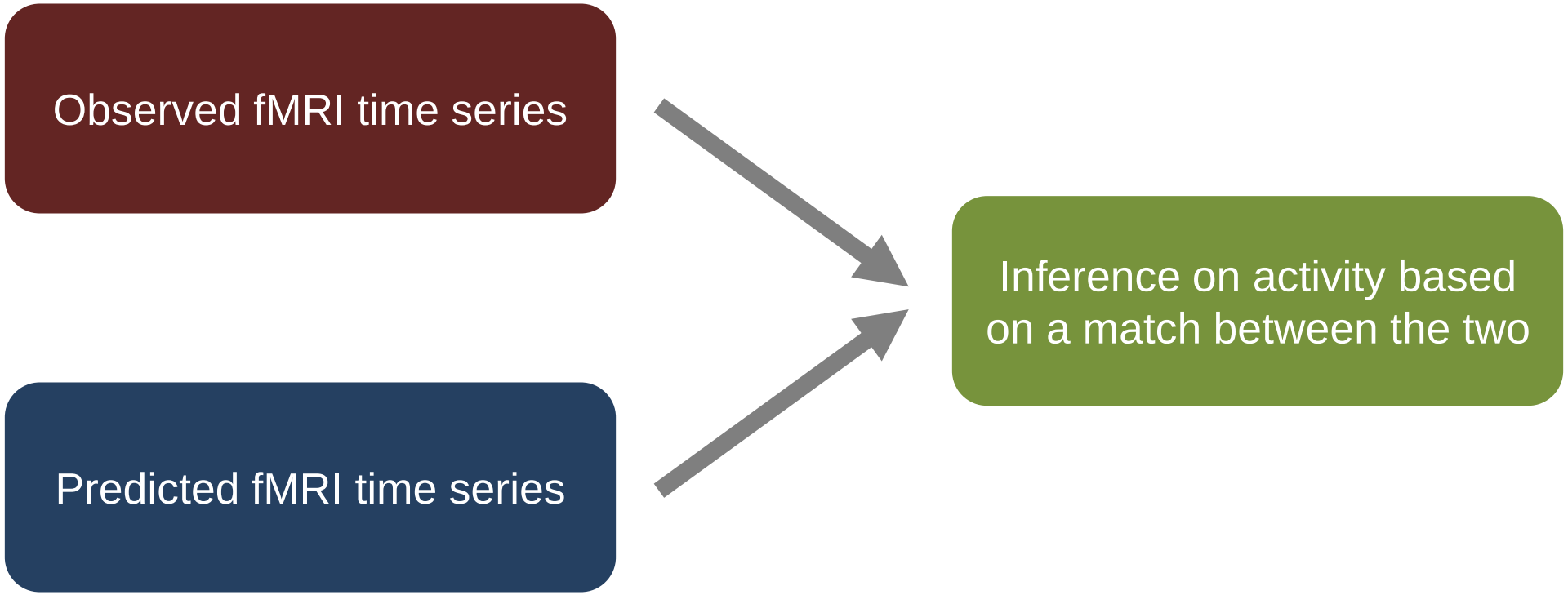


Smoothing

Preprocessing

Functional Segregation

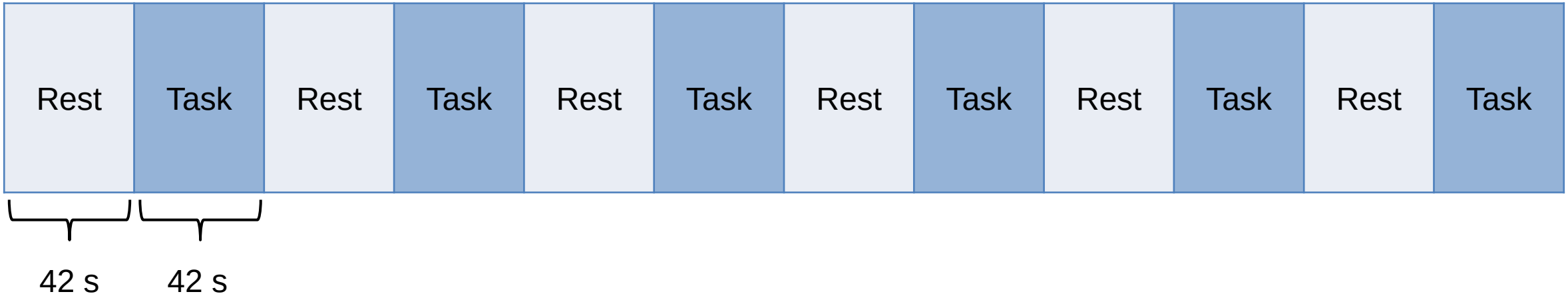
- Specialisation of different brain regions for different functions
  - Based on the idea that certain tasks or processes are localized to specific regions of the brain
- In task-based fMRI:
  - Increased activity in specific brain regions during a task, as compared to a baseline, suggests those regions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



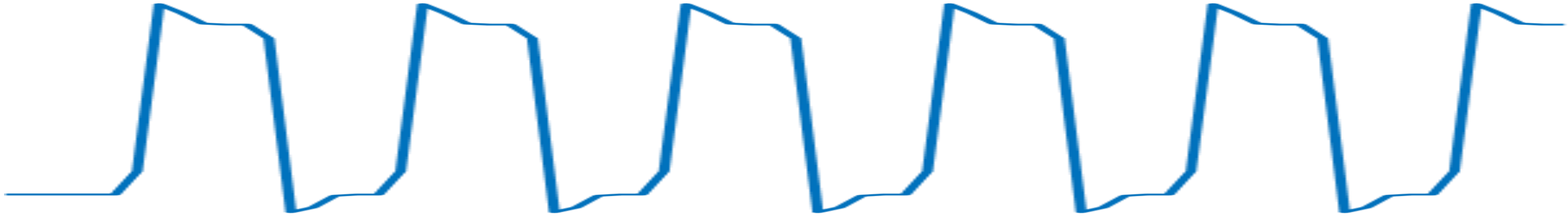
Functional segregation analysis of task-based fMRI

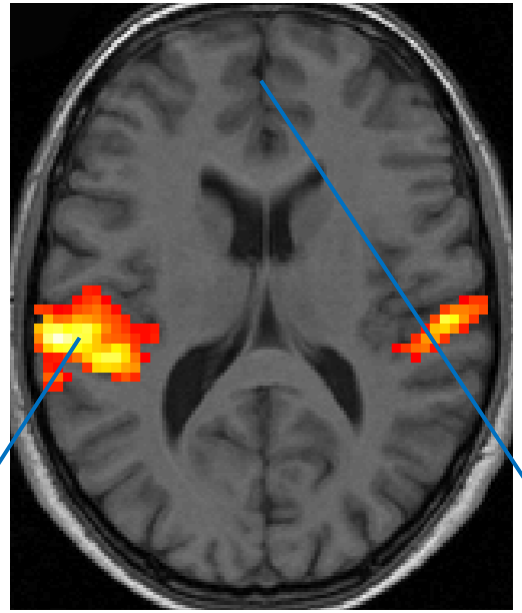
Auditory stimulation task [https://www.fil.ion.ucl.ac.uk/spm/data/auditory/]

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

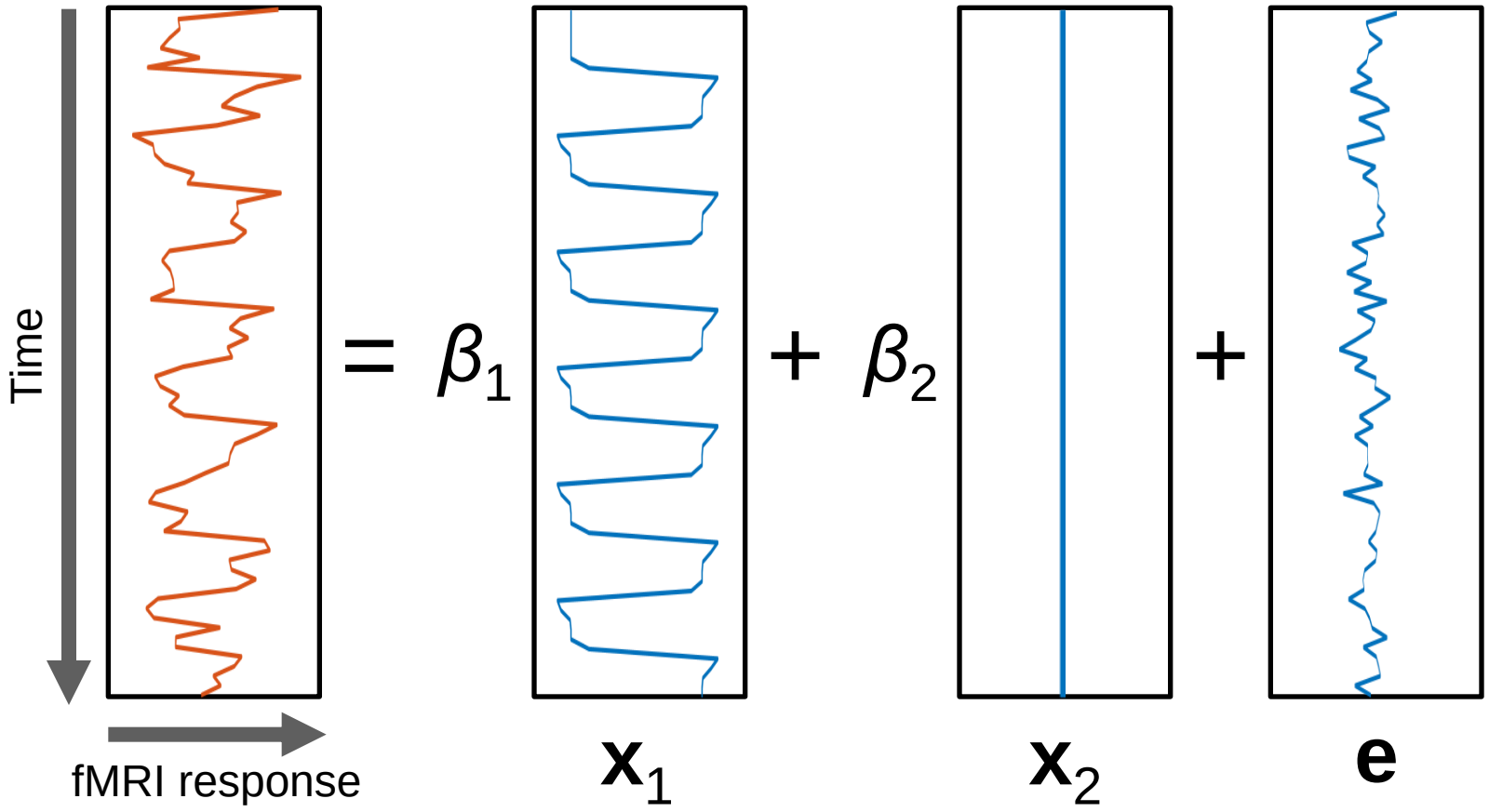


Predicted fMRI time series





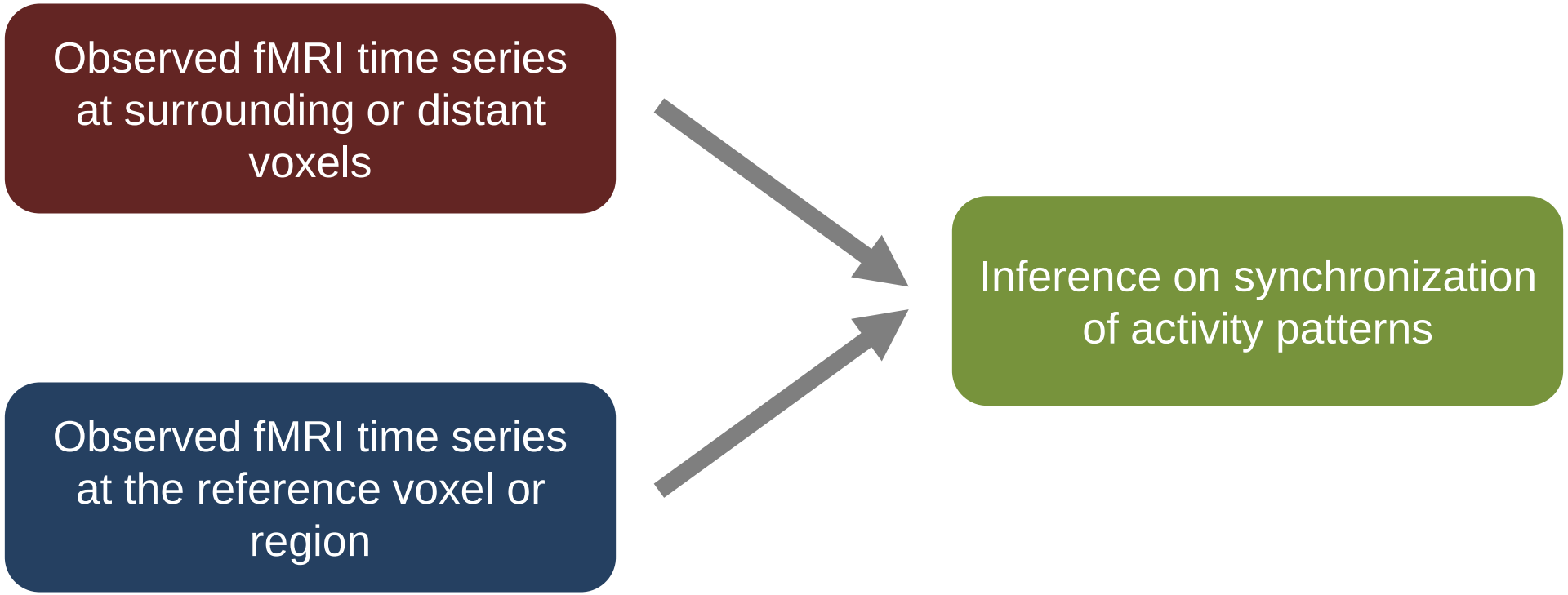
Observed fMRI time series



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

General linear model for functional segregation analysis in task-based fMRI

- 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)



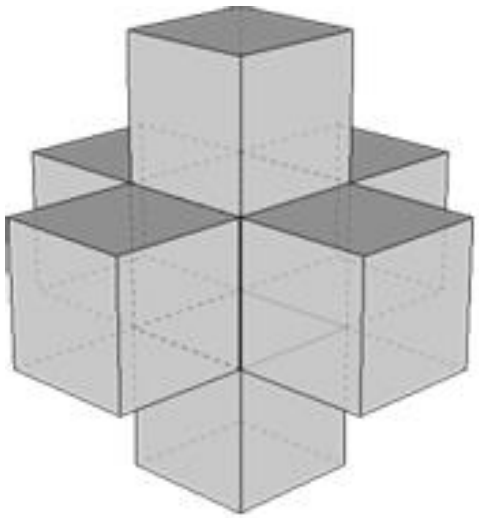
Functional segregation analysis of resting state fMRI

– Regional homogeneity [Zang et al., 2004]

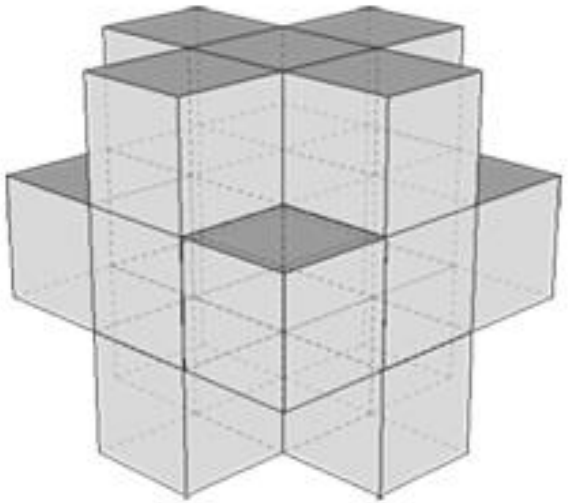
- Similarity of time series between a given voxel and its neighbours
  - Neighbours: *K* nearest neighbours
  - Synchronization: Kendall's coefficient of concordance (KCC)

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

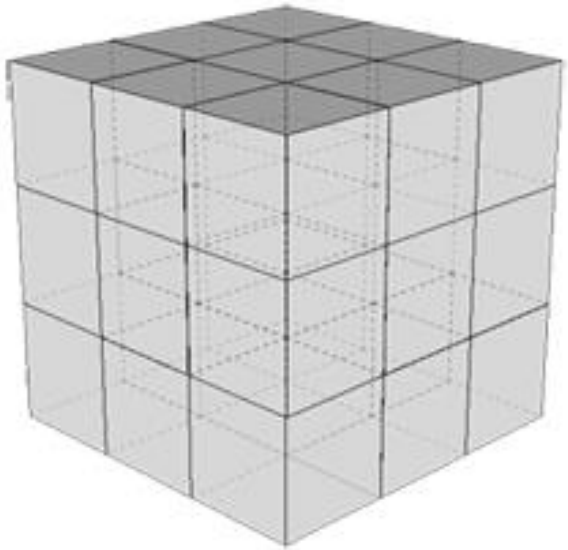
- Reveals local synchronization of spontaneous brain activity



Faces
(7 voxels)



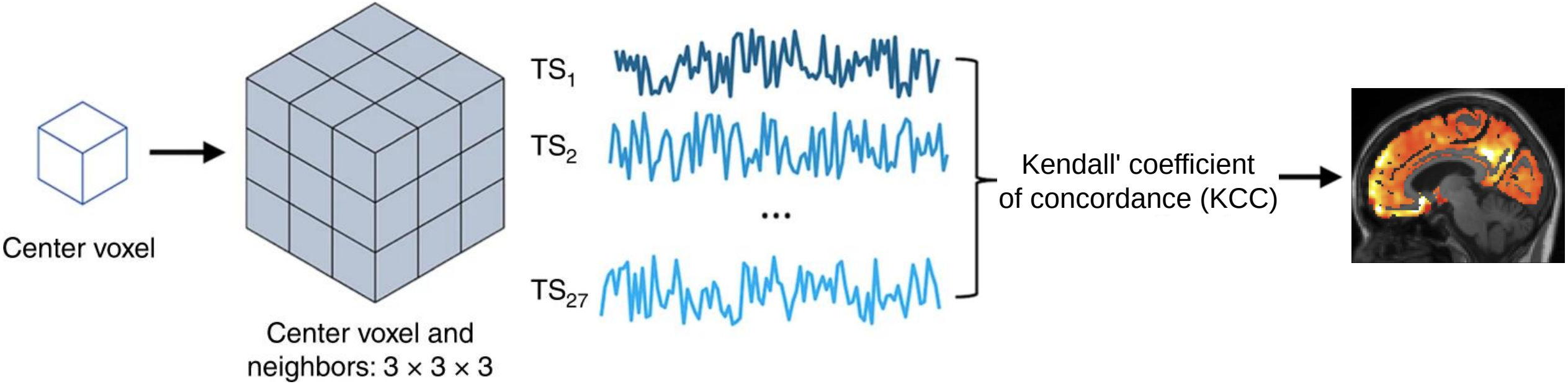
Faces + Edges
(19 voxels)



Faces + Edges + Corners
(27 voxels)

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

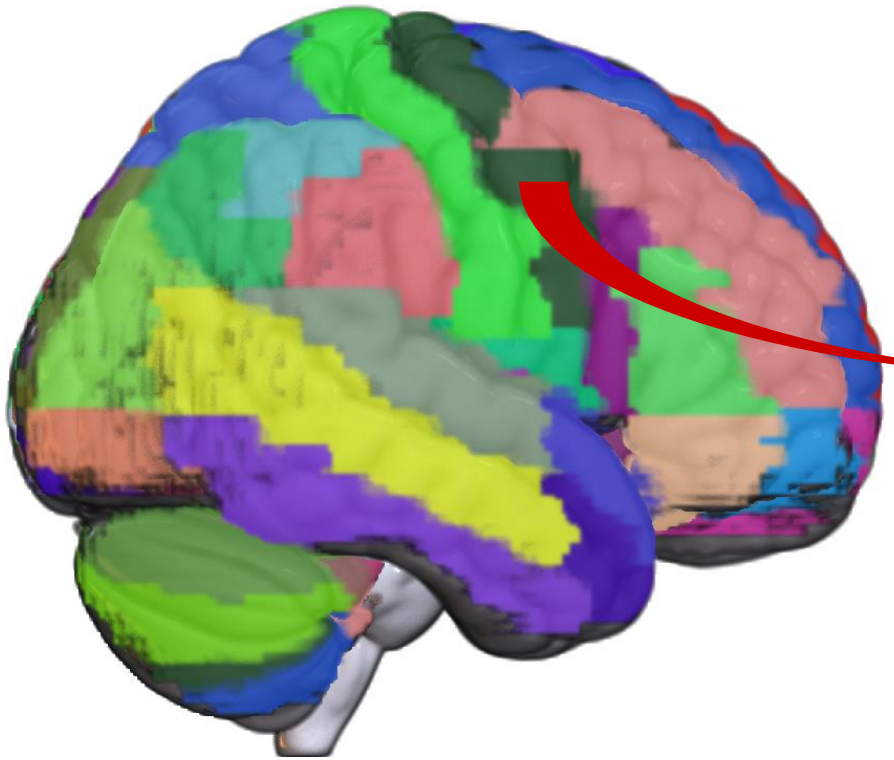
Different definitions of nearest neighbours

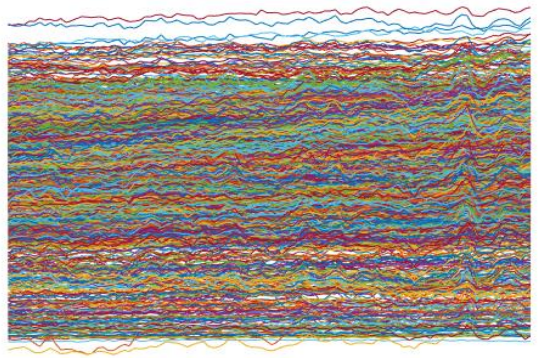


[Harrison et al., 2019]

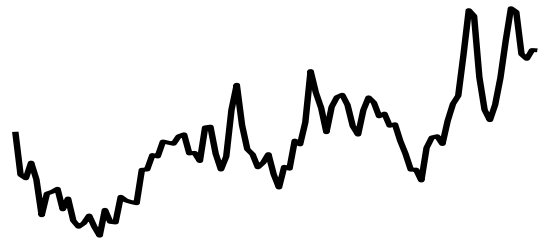
Regional homogeneity

- Seed-based correlation [Biswal et al., 1995]
  - Temporal correlation of time series between a seed and 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



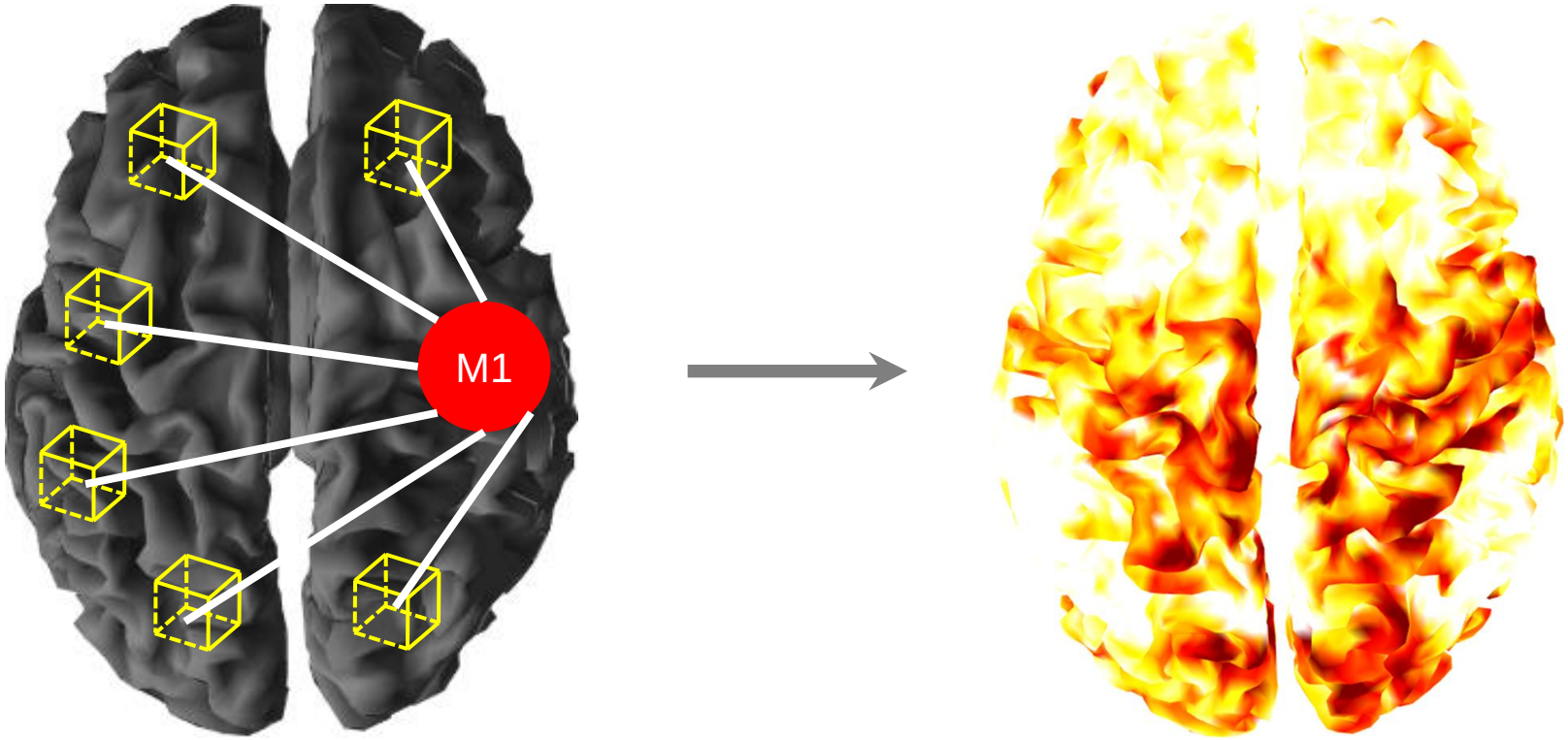


Representative fMRI time series



fMRI time seirs
from multiple voxels

Extracting fMRI time series from the seed (primary motor cortex)



Seed-based correlation for the primary motor cortex

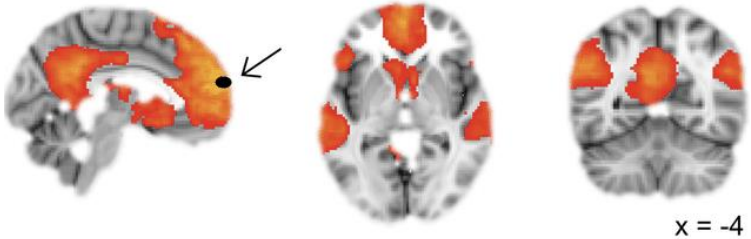
Left middle temporal gyrus

x = -44 y = -66 z = 46

Right middle temporal gyrus

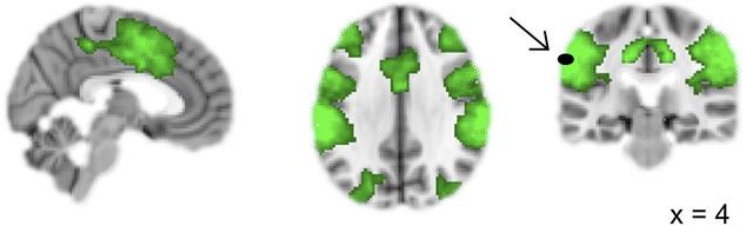
x = -52 y = -64 z = 22

Left medial frontal gyrus



x = -4 y = -58 z = 2

Left supramarginal gyrus



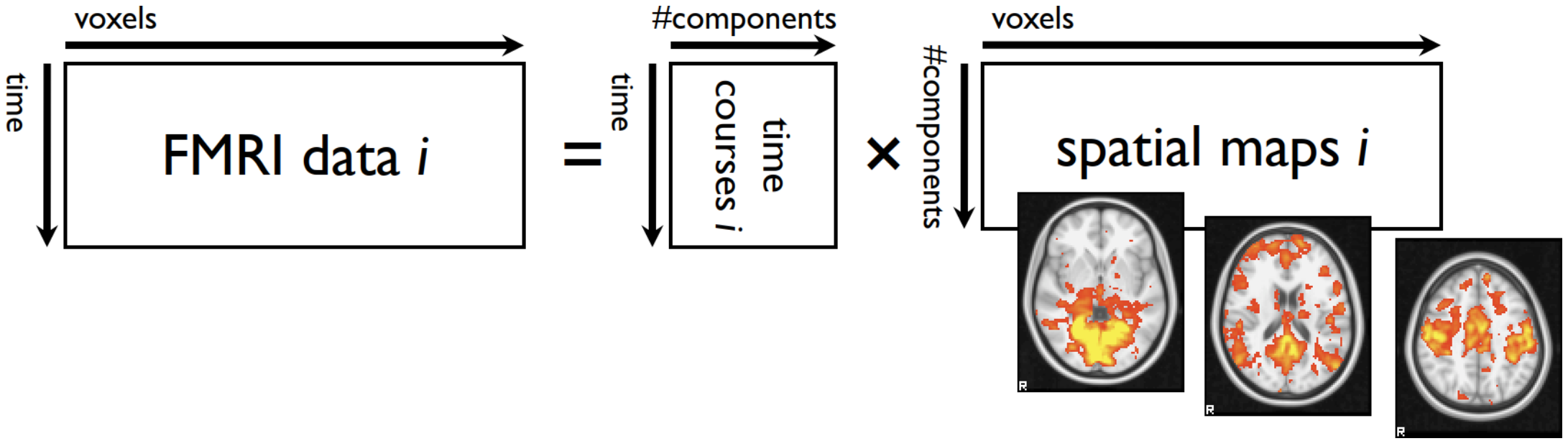
x = 4 y = -28 z = 32

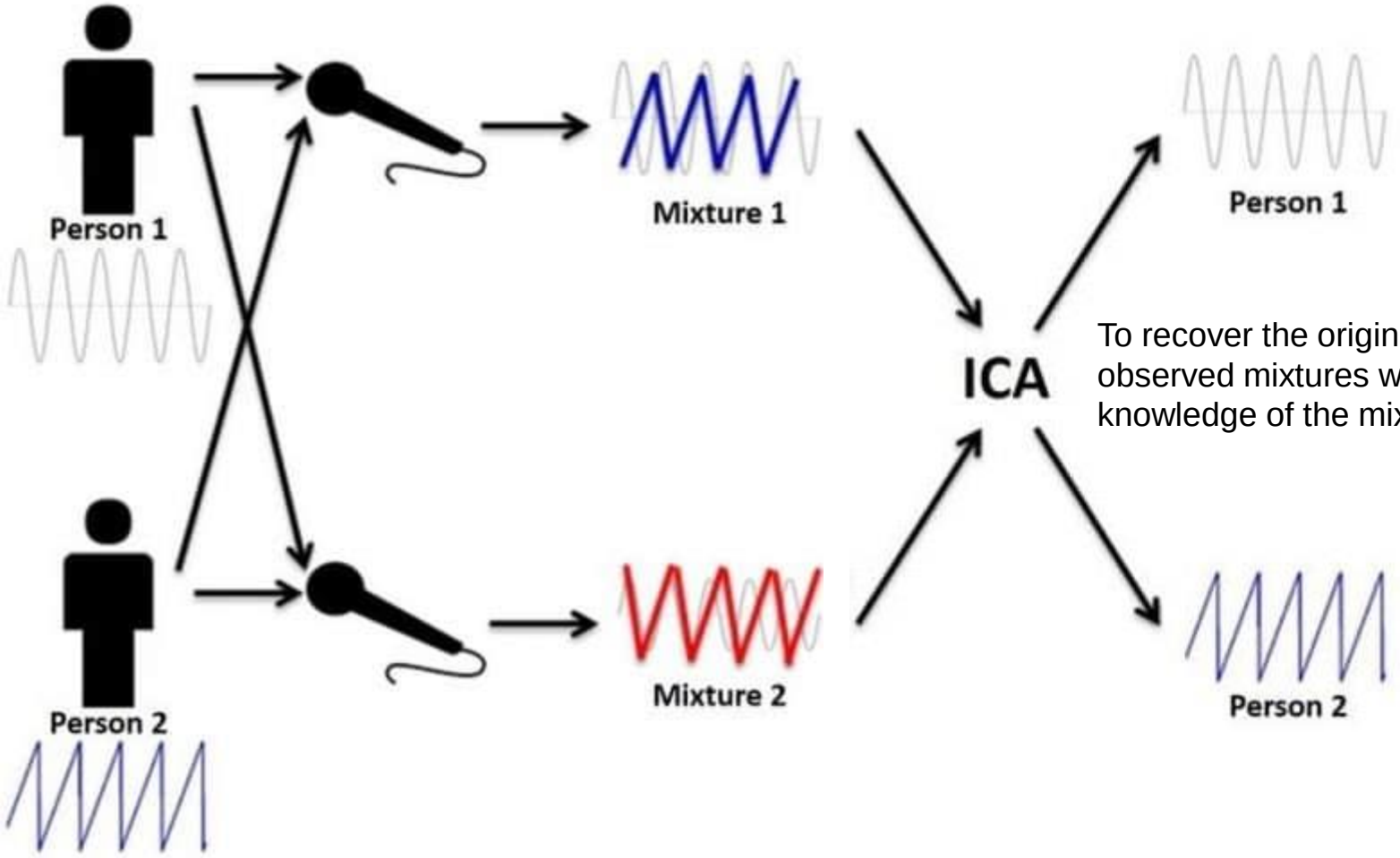
[Cousijn et al., 2014]

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
- Explores spontaneous brain activity patterns of spatial independence

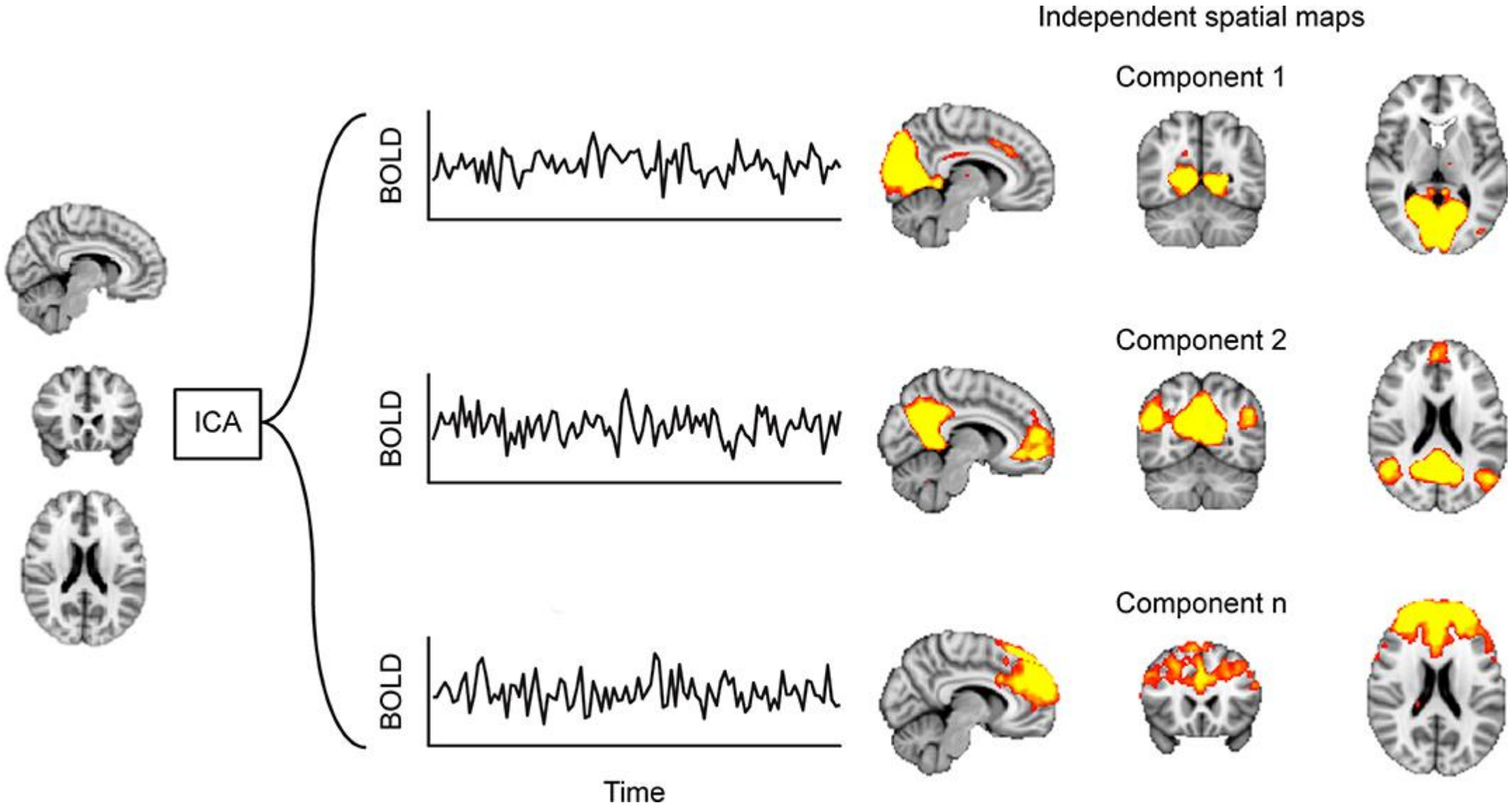




To recover the original signals from the observed mixtures without having prior knowledge of the mixing process

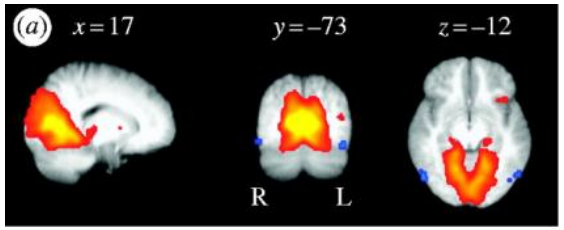
[https://vocal.com/blind-signal-separation/independent-component-analysis/]

Independent component analysis for the cocktail party problem

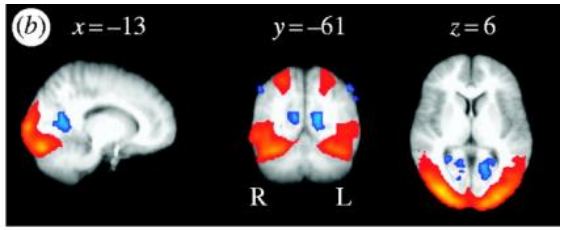


[Tahedl et al., 2018]

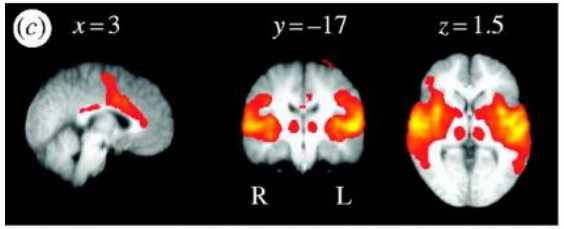
Independent component analysis of fMRI data



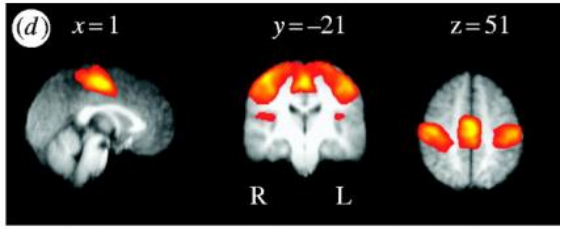
Medial visual cortical areas



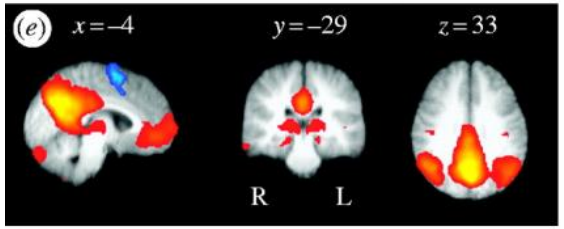
Lateral visual cortical areas



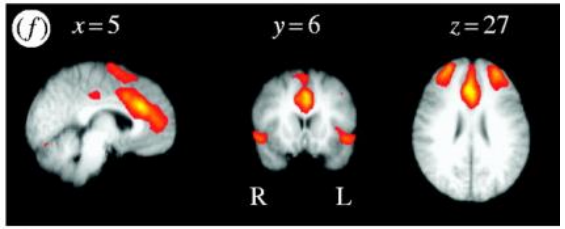
Auditory system



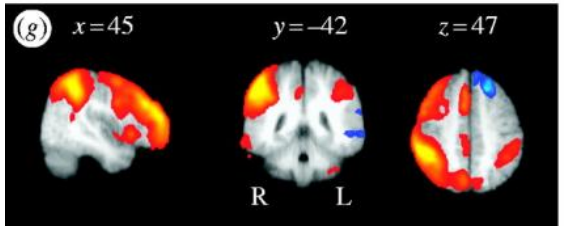
Sensory–motor system



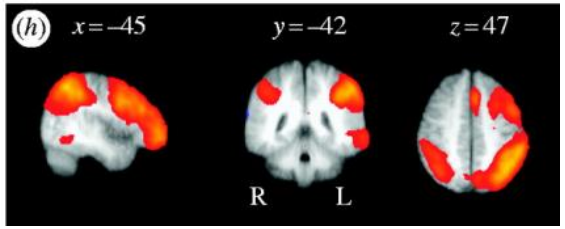
Visuo-spatial system



Executive control



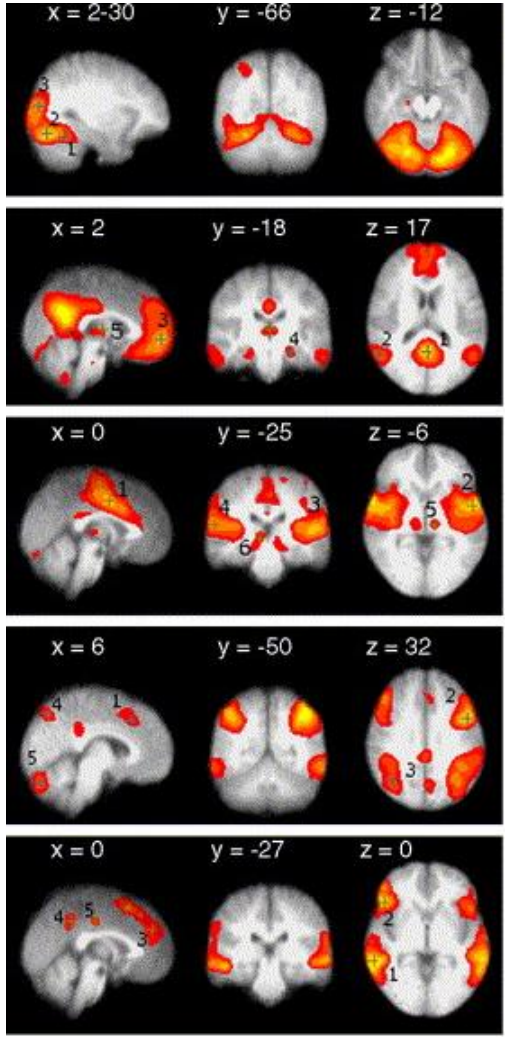
Right dorsal visual stream



Left dorsal visual stream

[Beckmann et al., 2005]

Independent components from fMRI data (1)



Visual cortical areas

Visuospatial and executive system

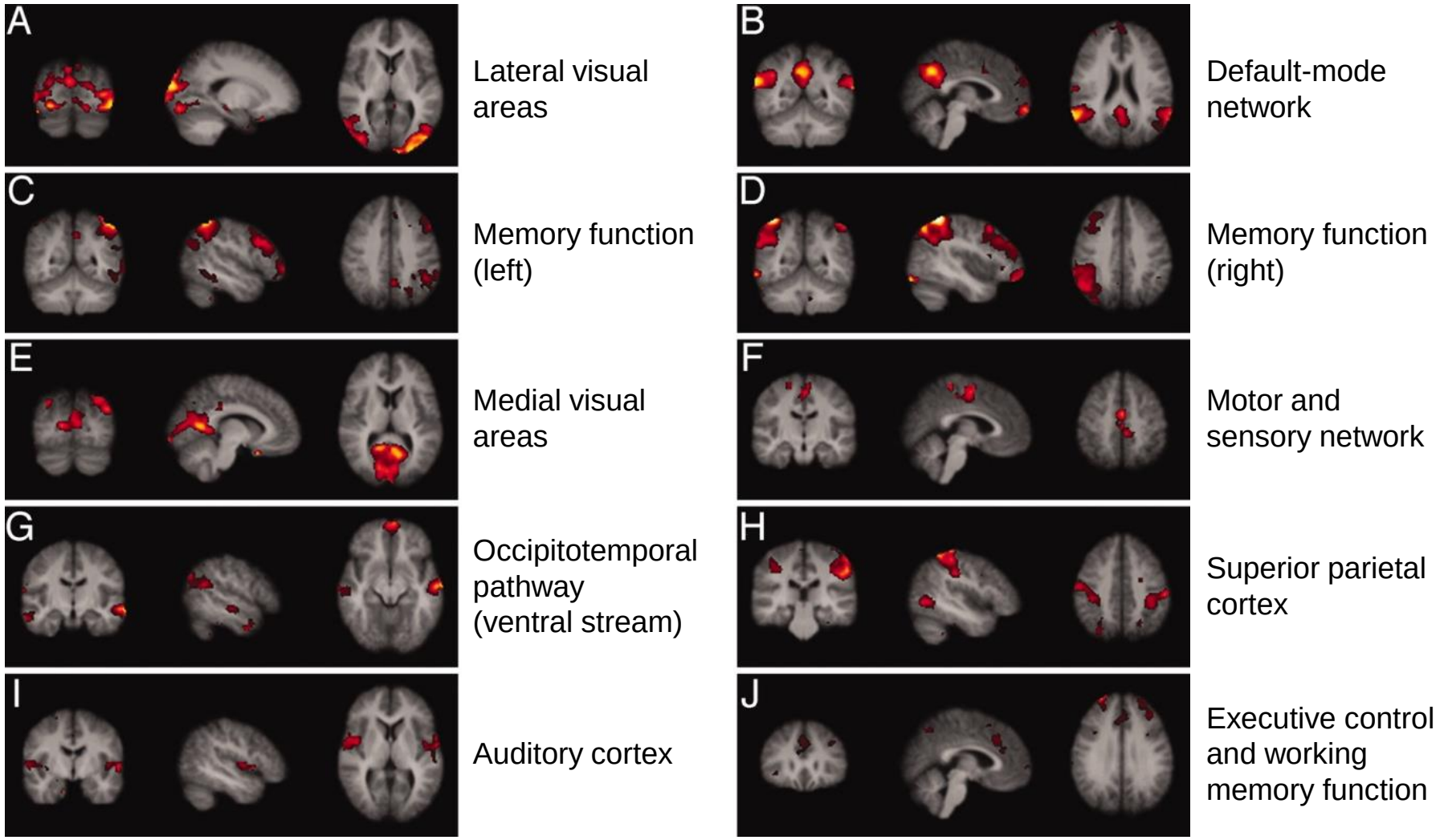
Sensory and auditory system

Dorsal pathway

Ventral pathway

[De Luca et al., 2006]

Independent components from fMRI data (2)

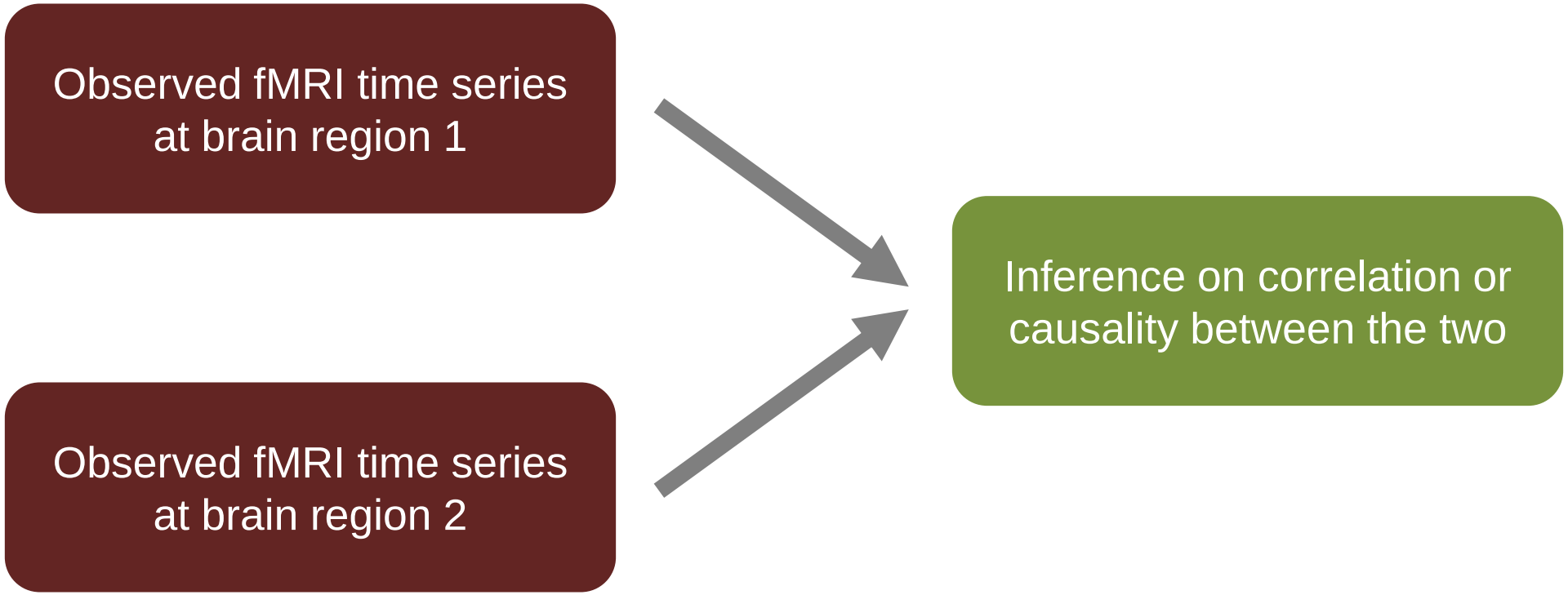


[Damoiseaux et al., 2006]

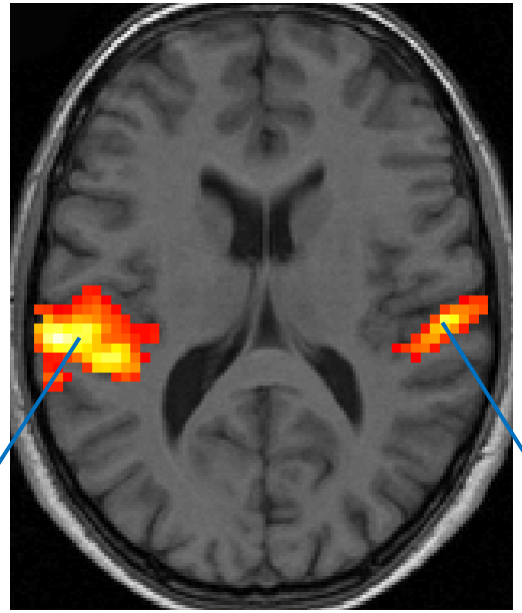
Independent components from fMRI data (3)

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 series of activity from different brain regions reveals networks of regions that work together

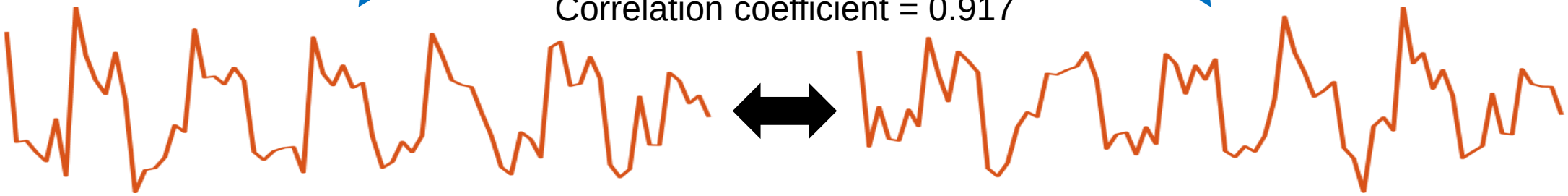


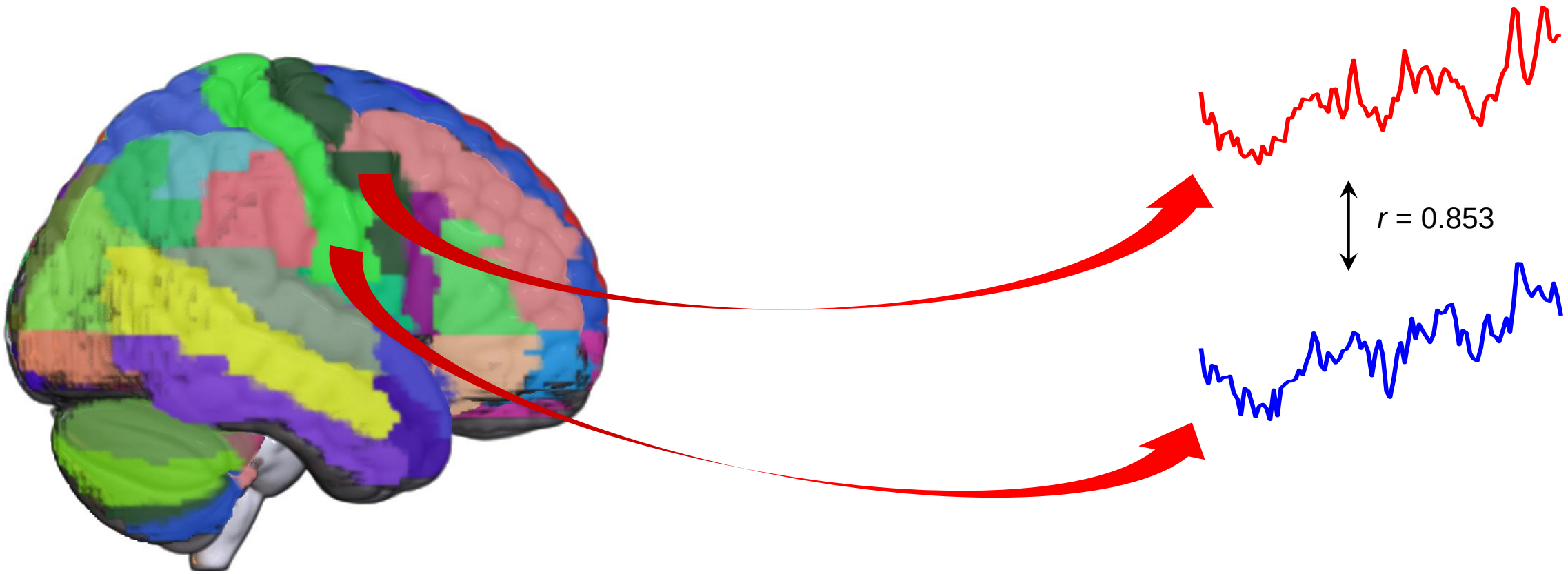
Functional segregation analysis of fMRI



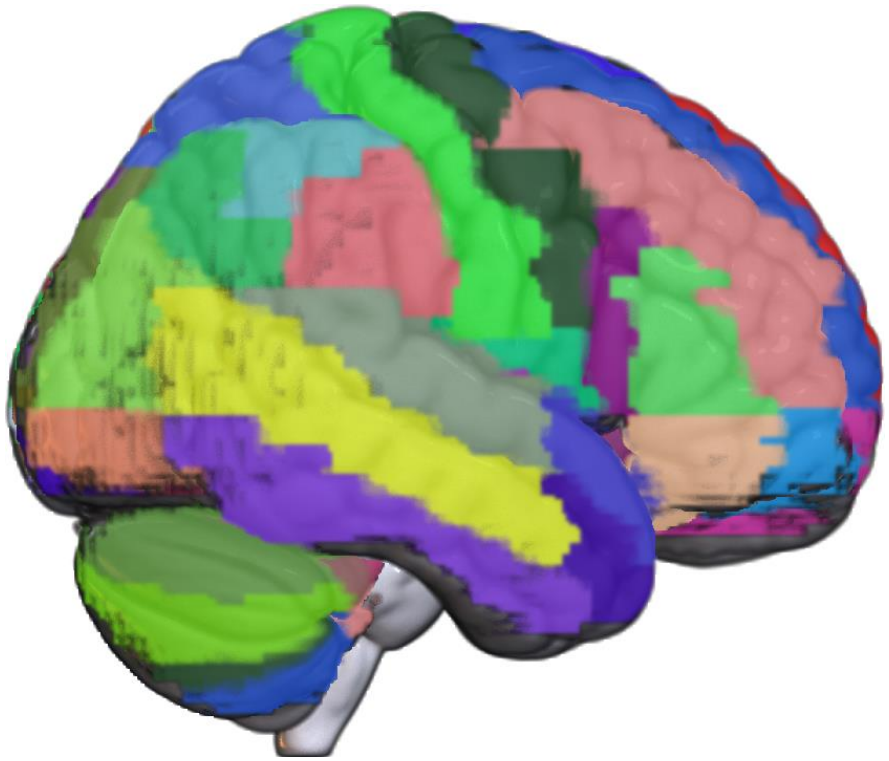
Observed fMRI time series

Correlation coefficient = 0.917

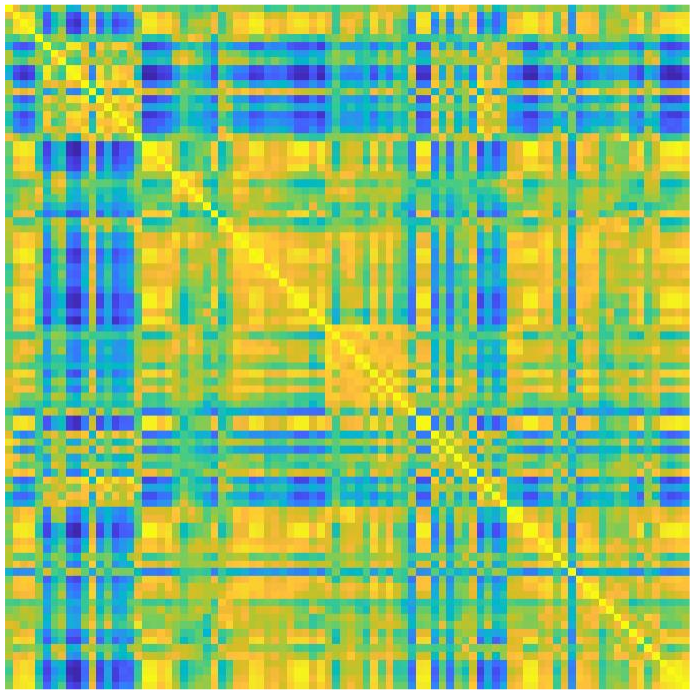




Pair-wise correlation of time series

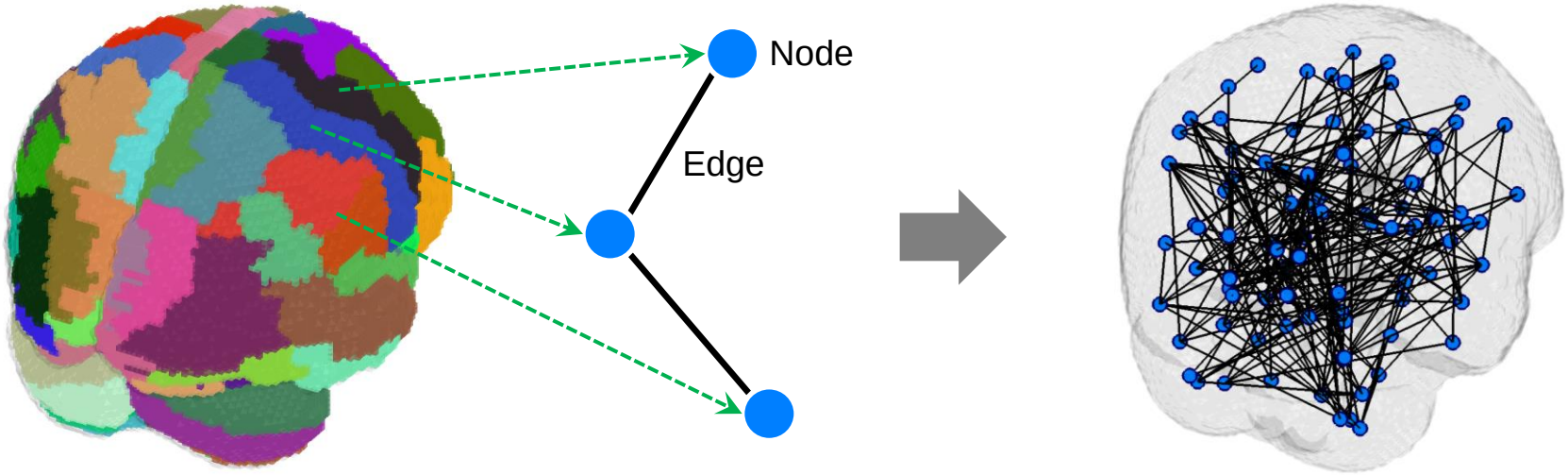


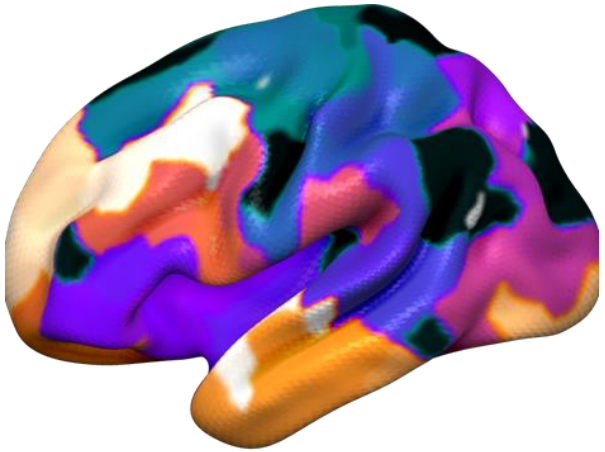
Time series correlation



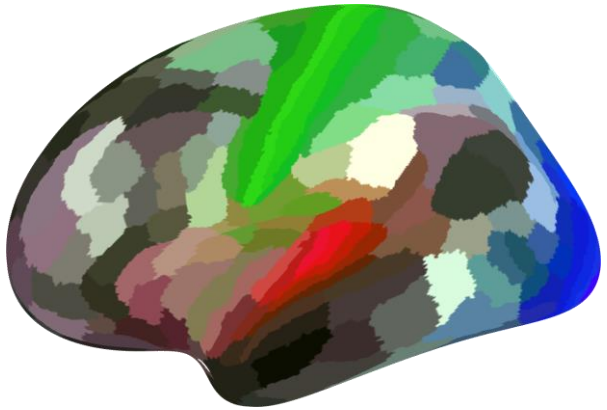
Functional brain network

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

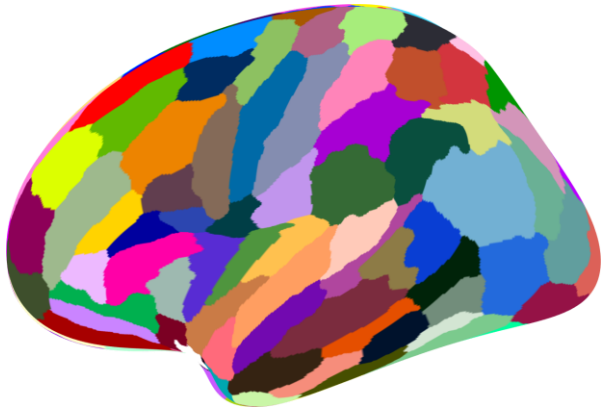




333 brain regions
Resting-State Correlations atlas

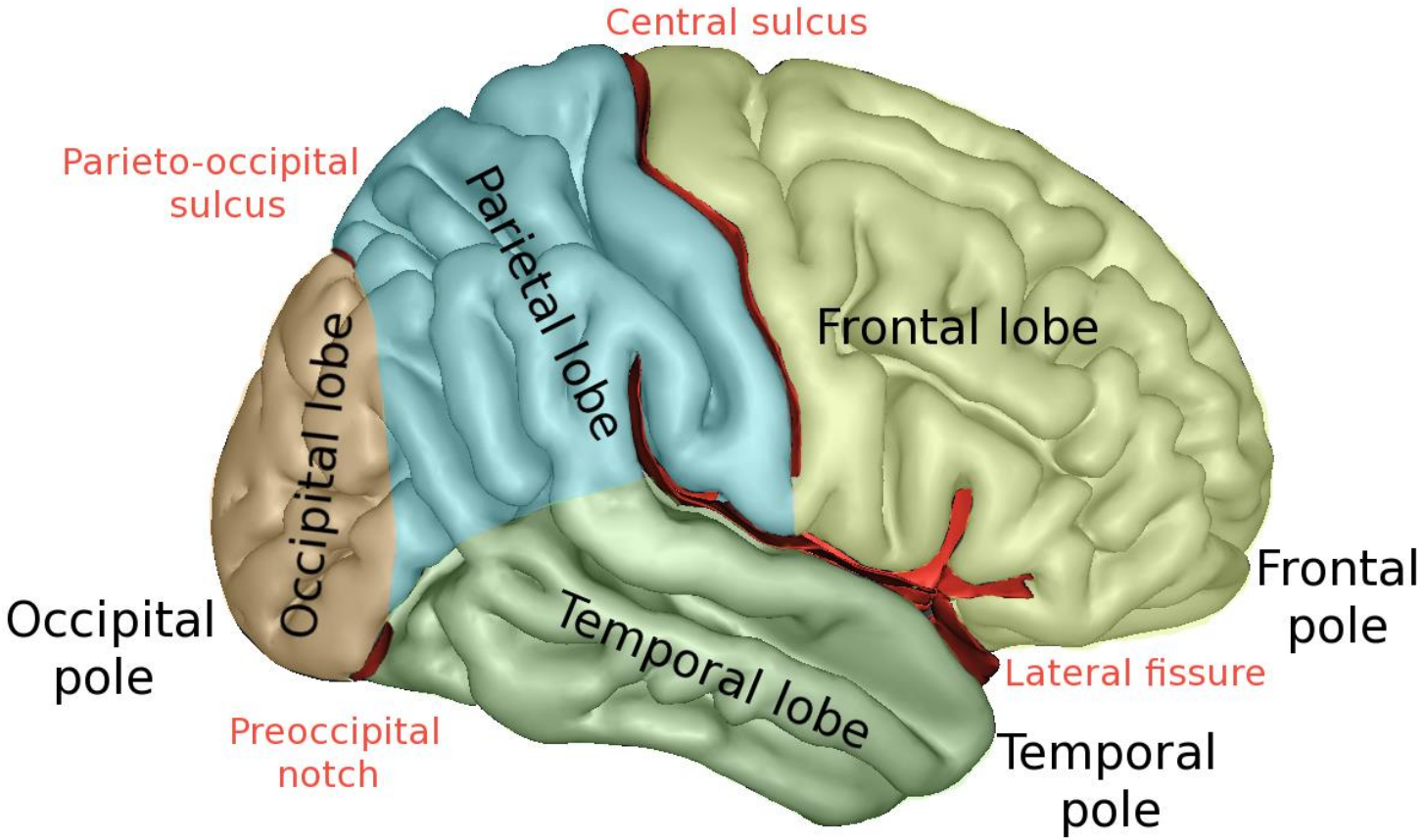


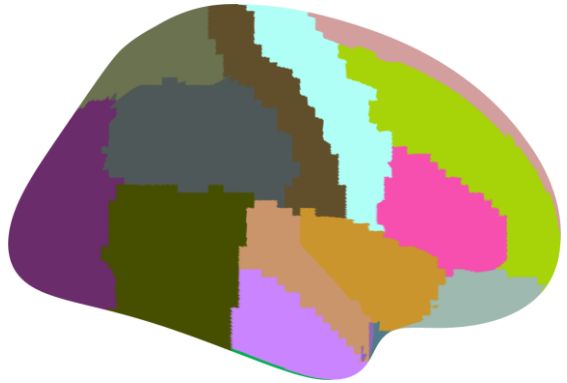
360 brain regions
HCP MMP 1.0 atlas



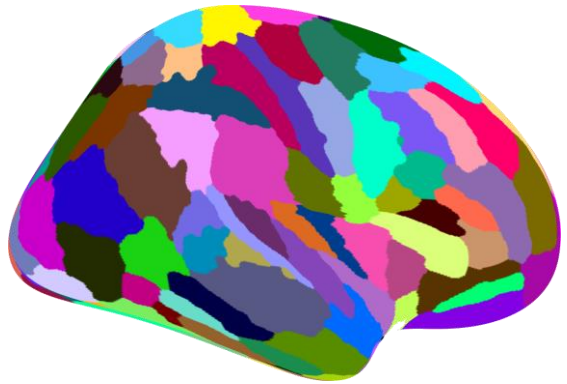
246 brain regions
Brainnetome atlas

Brain atlases delineating heterogeneous nodes with varying definitions and quantities





Hammers atlas



Brainnetome atlas

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

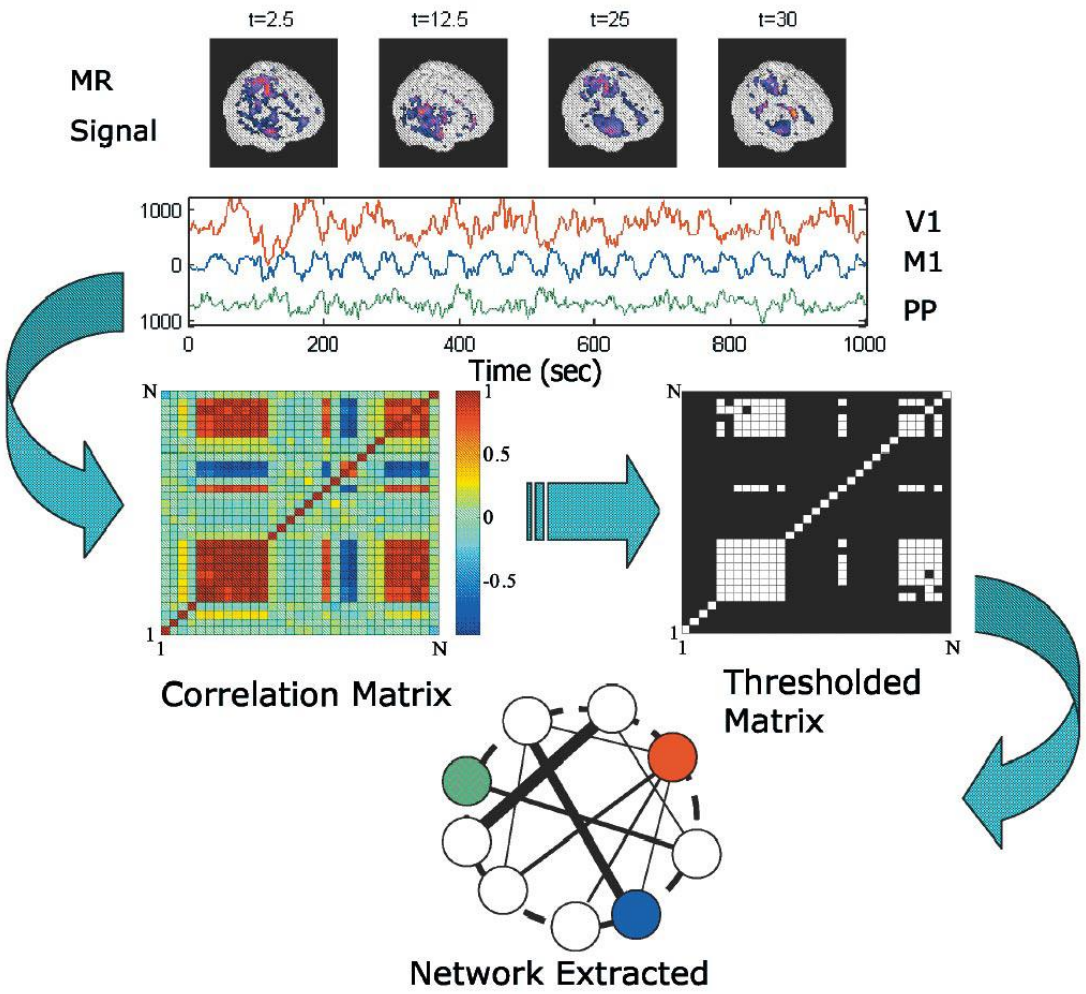
Lobes of the brain

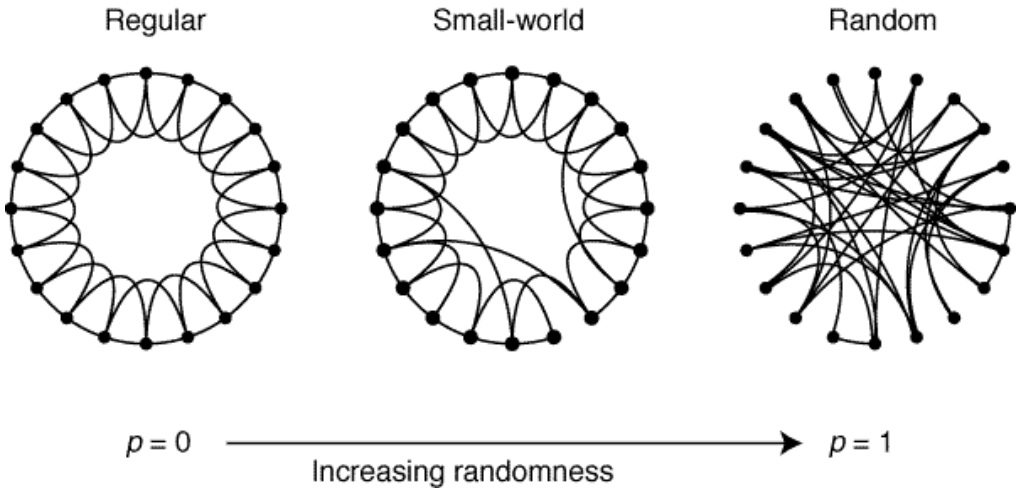
Hammers atlas

Brainnetome atlas

- 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

- Graph-theoretical analysis
  - Characterize 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

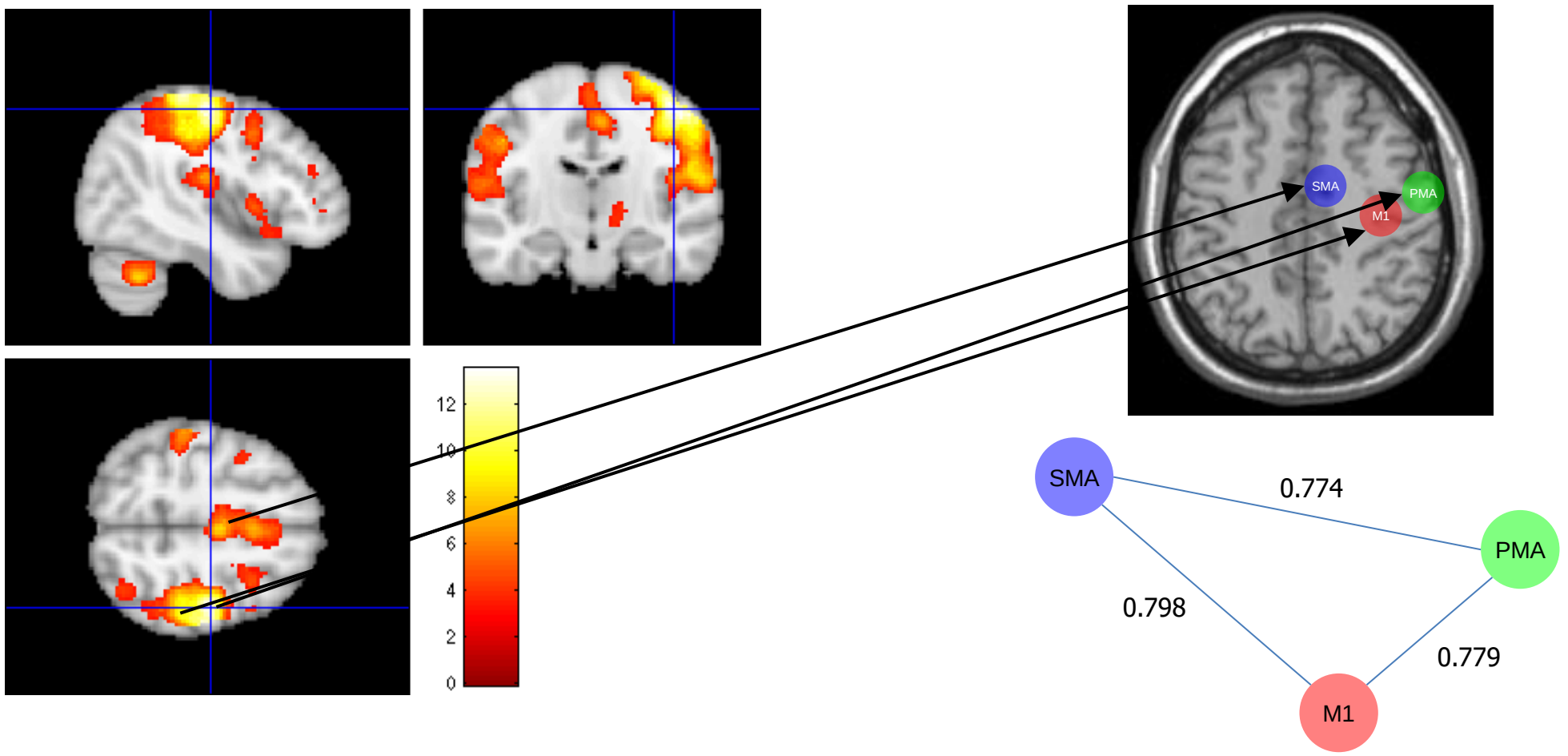




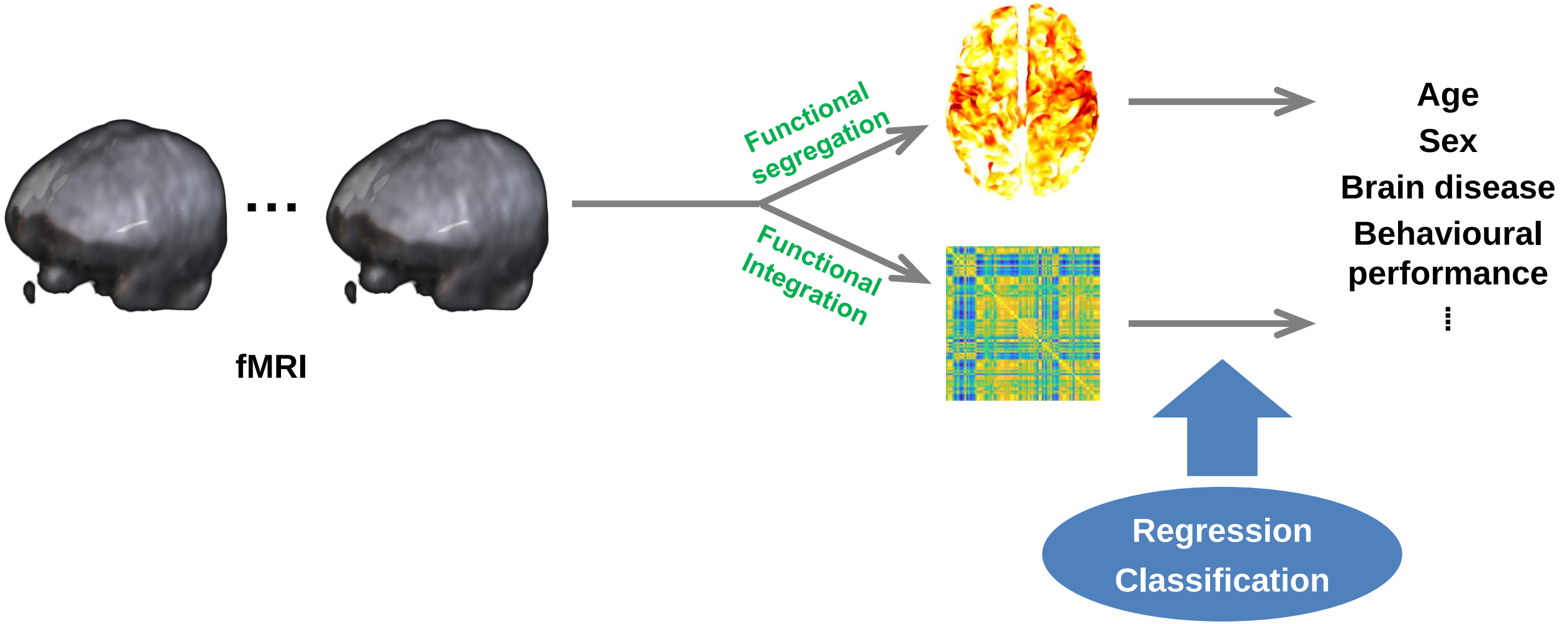
[Eguíluz et al., 2005; Watts and Strogatz, 1998]

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


Functional segregation
Functional Integration
Age
Sex
Brain disease
Behavioural performance
fMRI
Regression
Classification