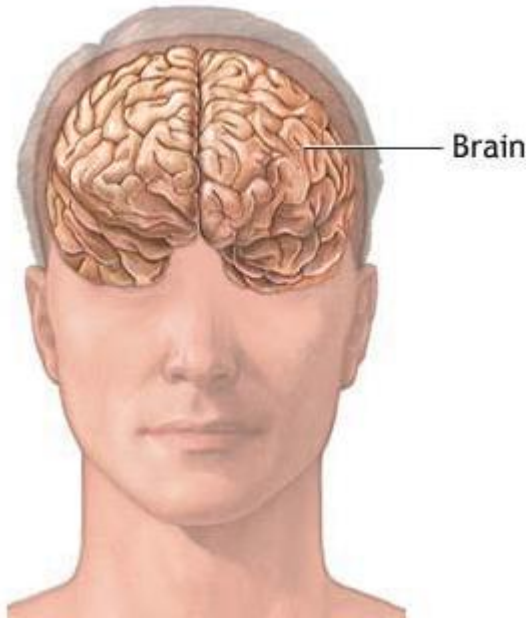
**Medical/Bio Research Topics Ⅰ: Week 15 (13.06.2024)**

# Final Evaluation and Summary

## 최종 평가 및 요약

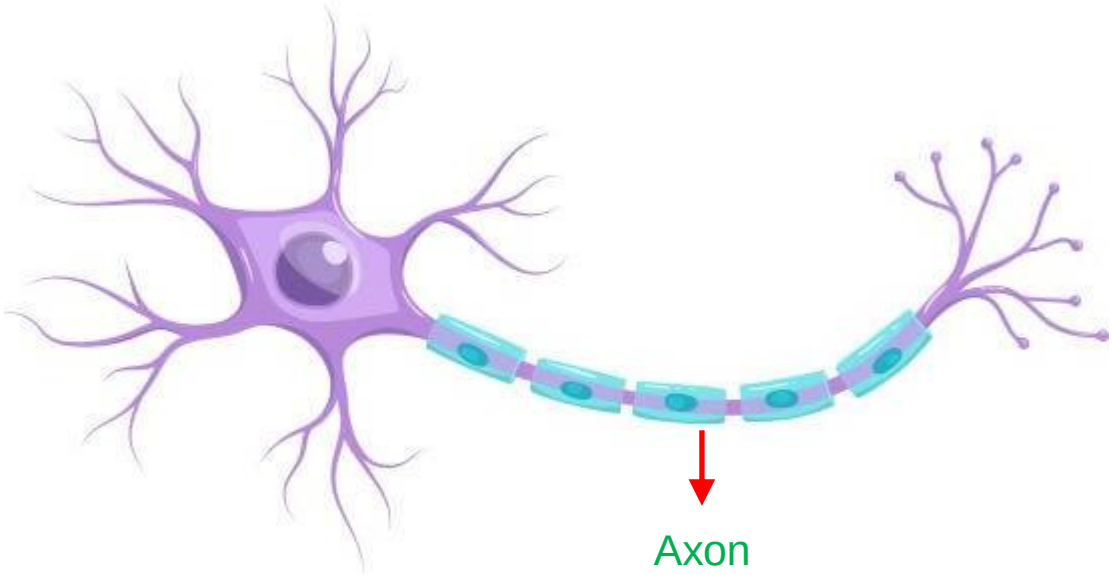
# Brain

- Center of the nervous system
- Located in the head



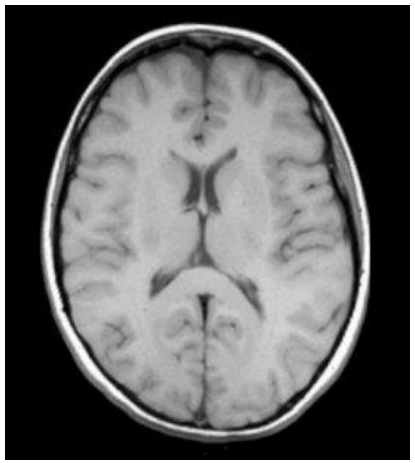

[https://medlineplus.gov/ency/imagepages/8738.htm]

- Composed of tens of billions of neurons
  - Interconnected neurons communicate with each other by axons

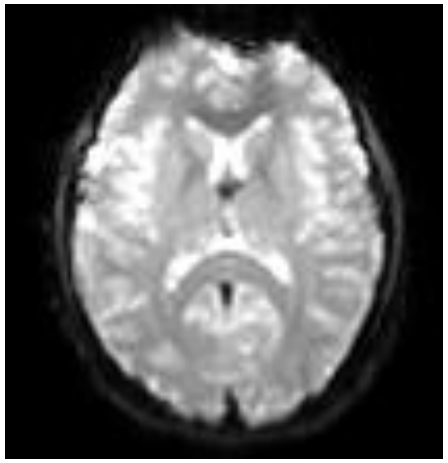


# Brain Imaging

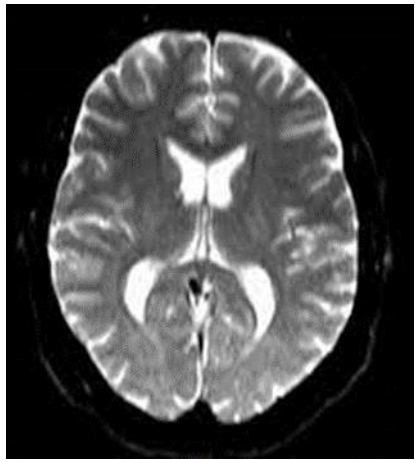
**CT**



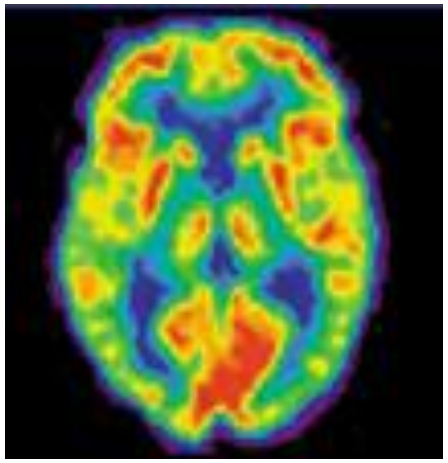
**Structural MRI**



**Functional MRI**



**Diffusion-weighted MRI**



**PET**

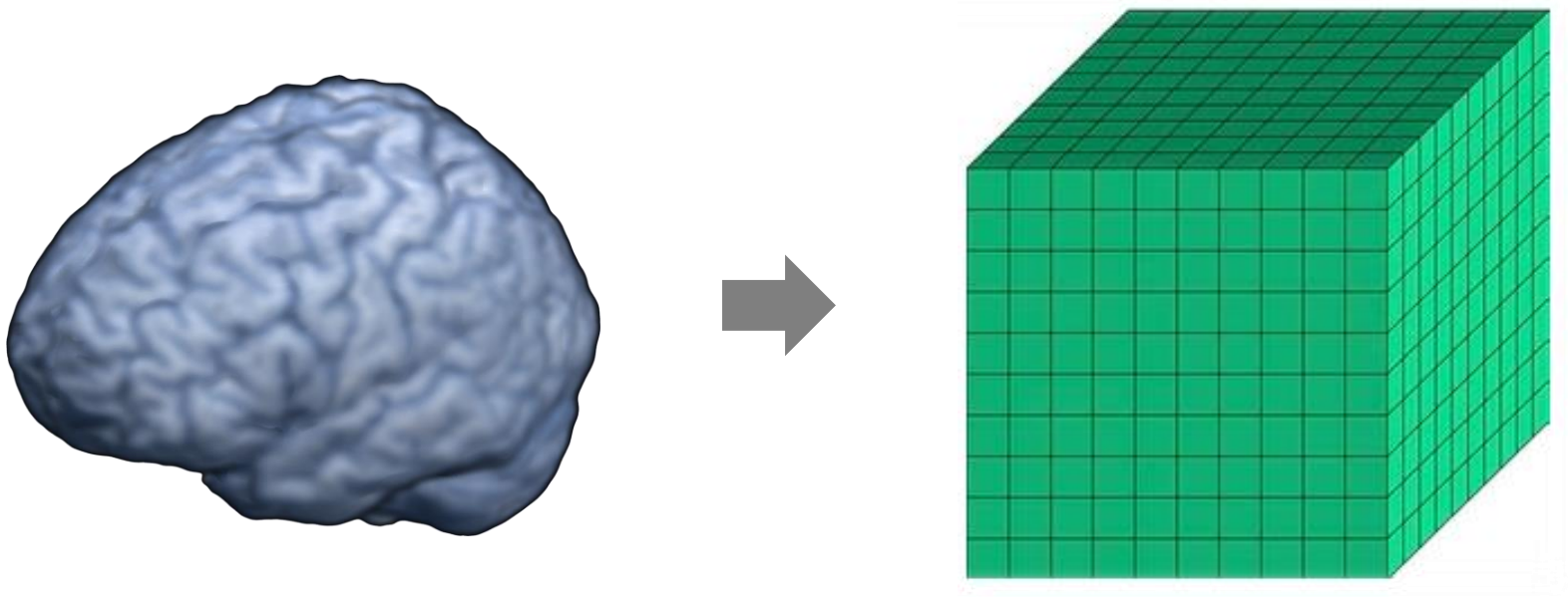
CT, Computed Tomography (컴퓨터단층촬영)
MRI, Magnetic Resonance Imaging (자기공명영상)
PET, Positron Emission Tomography (양전자방출단층촬영)

- Various techniques for imaging the structure or function of the brain
  - Computed Tomography (CT)
  - Magnetic Resonance Imaging (MRI)
    - Structural MRI (sMRI)
    - Functional MRI (fMRI)
    - Diffusion-weighted MRI (dMRI)
  - Positron Emission Tomography (PET)

- Volumetric description of the brain as a 3D array

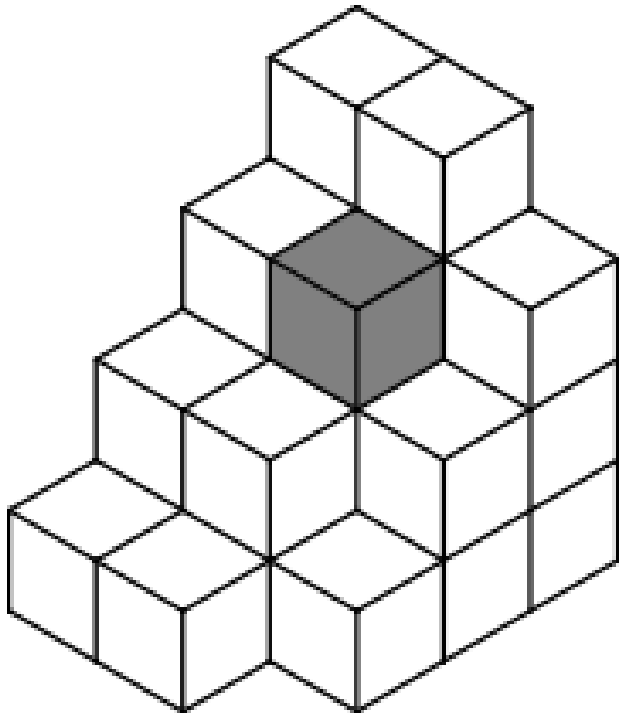
[Larobina and Murino, 2014]

  - Representation of the structure or function of the brain in the form of an array of voxels



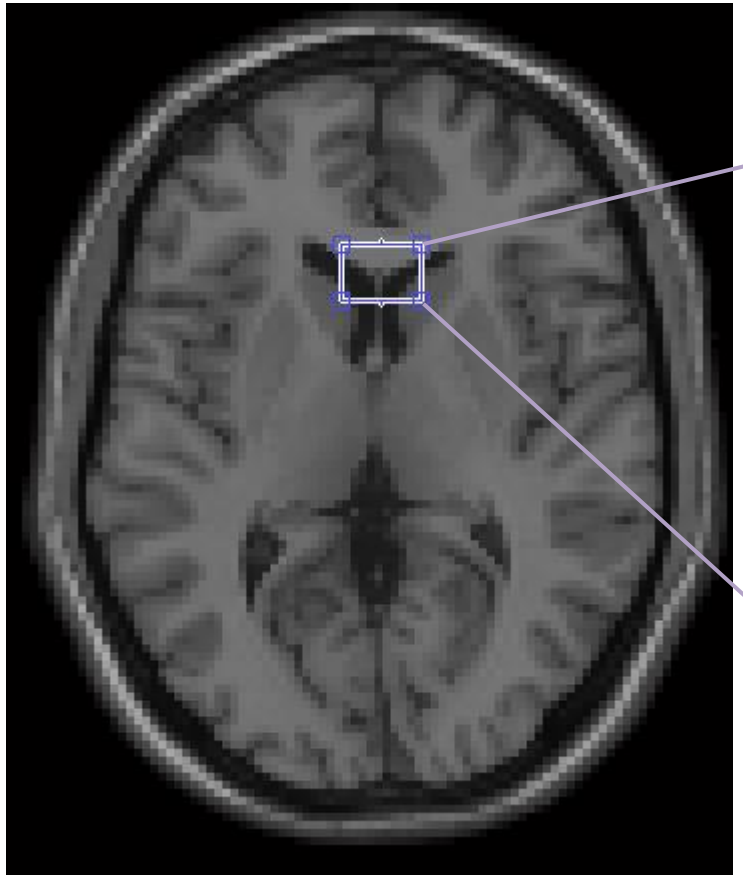
  - Discrete representation resulting from a sampling/reconstruction process that maps numerical values to positions of the space

- Voxel: volume element or volumetric pixel
  - Analogous to a pixel in 2D space

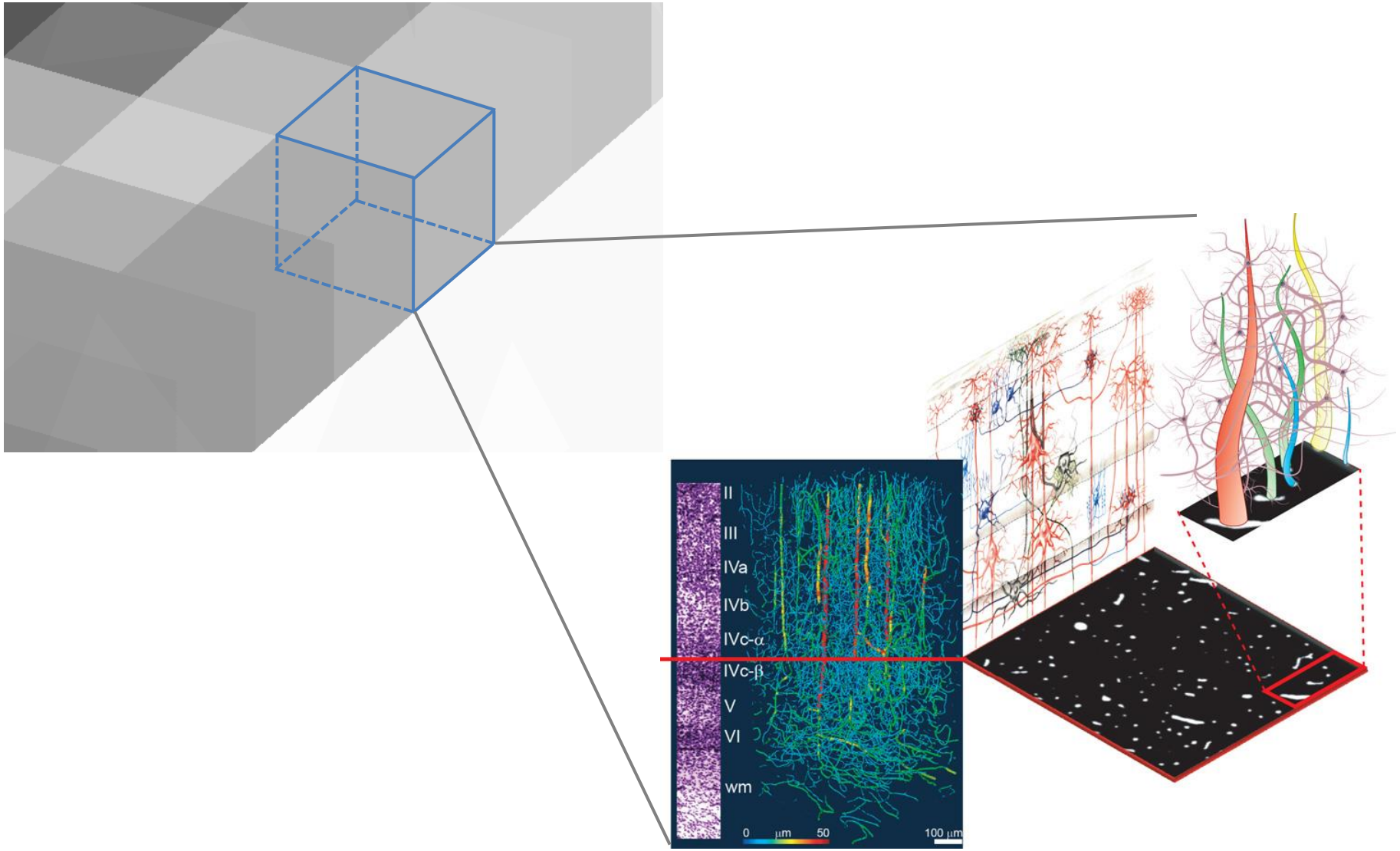


[https://en.wikipedia.org/wiki/Voxel]

– Sub-volume box with a constant value inside



| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 0.45 | 0.45 | 0.45 | 0.45 | 0.45 | 0.45 | 0.45 | 0.45 | 0.45 | 0.45 |
| 0.41 | 0.45 | 0.45 | 0.45 | 0.45 | 0.45 | 0.45 | 0.45 | 0.45 | 0.44 |
| 0.16 | 0.28 | 0.40 | 0.45 | 0.45 | 0.43 | 0.43 | 0.41 | 0.29 | 0.15 |
| 0.12 | 0.12 | 0.17 | 0.33 | 0.29 | 0.37 | 0.24 | 0.13 | 0.12 | 0.13 |
| 0.12 | 0.11 | 0.12 | 0.15 | 0.31 | 0.18 | 0.11 | 0.11 | 0.17 | 0.31 |
| 0.18 | 0.12 | 0.11 | 0.11 | 0.27 | 0.11 | 0.11 | 0.14 | 0.31 | 0.33 |
| 0.32 | 0.12 | 0.11 | 0.11 | 0.22 | 0.11 | 0.11 | 0.24 | 0.32 | 0.33 |

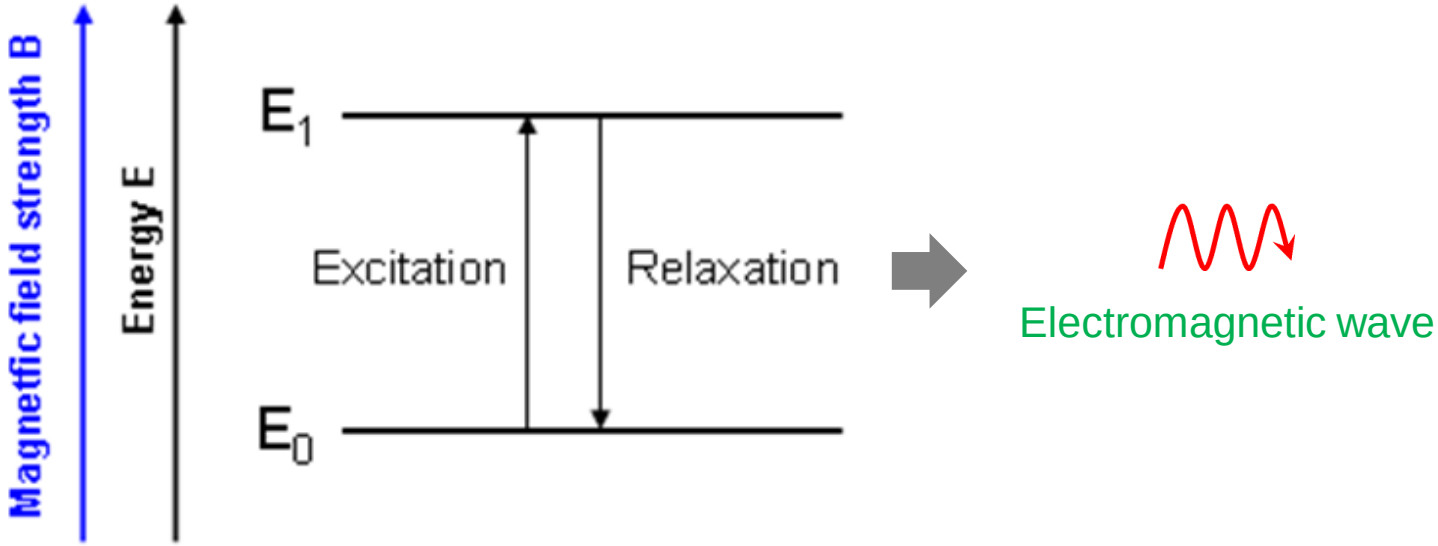



[Logothetis, 2008]

**Neuronal and vascular contents within a voxel**

# Brain MRI

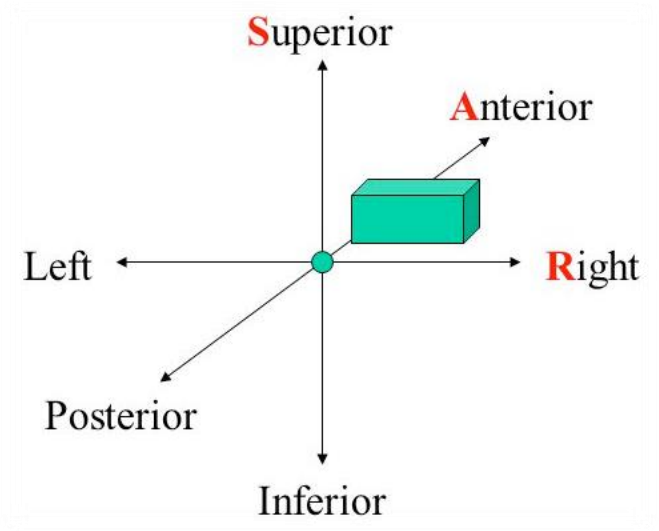
- Medical application of nuclear magnetic resonance (NMR)
  - Generates different contrasts between tissues based on the relaxation properties of hydrogen nuclei therein

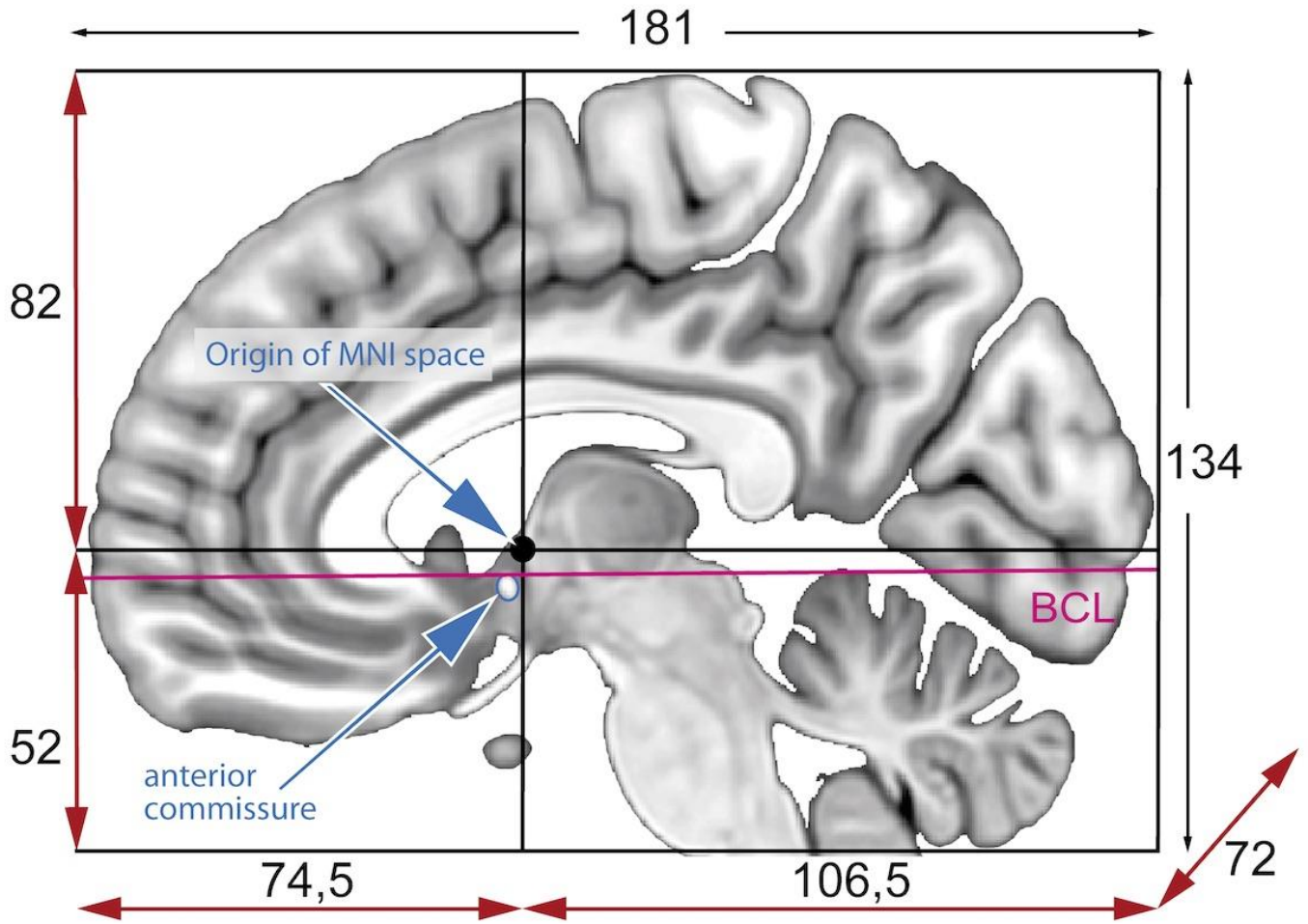


- Coordinate system
  - Reference frame in a 3D space that assigns *x*, *y*, and *z* coordinates to anatomical regions
  - Montreal Neurological Institute (MNI) coordinate system

[https://www.fieldtriptoolbox.org/faq/coordsys/]

    - Origin in the anterior commissure
    - *X*-axis from left to right
    - *Y*-axis from posterior to anterior
    - *Z*-axis points from inferior to superior
    - Used if the geometry is spatially warped to the MNI152 template brain (average of 152 T1-weighted MRI scans from young adults)



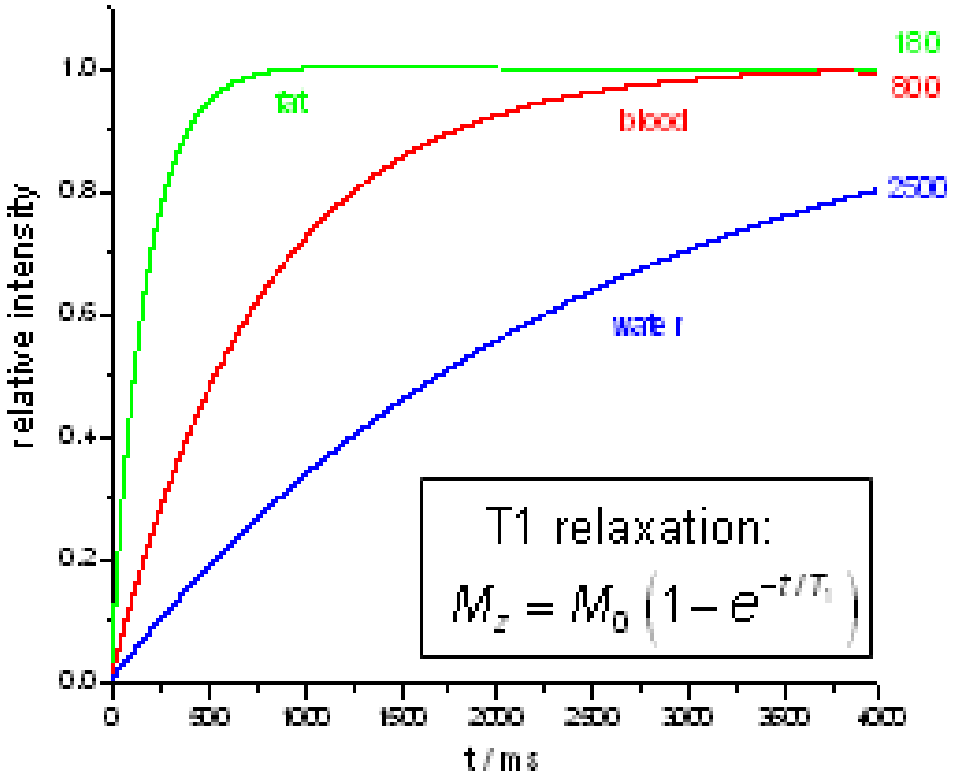

[https://carpentries-incubator.github.io/SDC-BIDS-sMRI/03-Image_Spatial_Normalization/index.html]

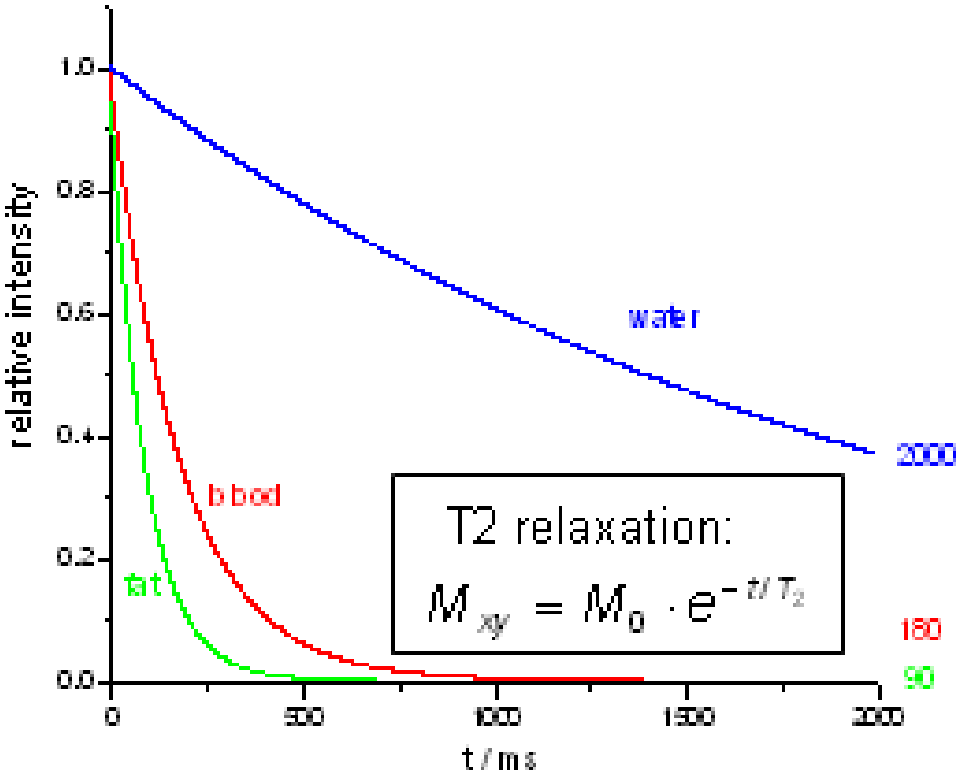
**MNI coordinate system**

- File format
  - Provides a standardized way to store the information describing an image in a computer file [Larobina and Murino, 2014]
  - Major file formats
    - Digital Imaging and Communications in Medicine (DICOM)
      - Default file fomat for acquisition
    - Neuroimaging Informatics Technology Initiative (NIfTI)
      - Default file format for analysis

# Structural MRI (sMRI): Principles

- MRI technique primarily for examining the anatomy and pathology of the brain
  - T1-weighted contrast
    - Predominately determined by T1 differences between tissues
  - T2-weighted contrast
    - Predominately determined by T2 differences between tissues
  - Fluid Attenuated Inversion Recovery (FLAIR) contrast
    - Dampens ventricular cerebrospinal fluid signals, causing the highest signals from certain brain parenchymal abnormalities

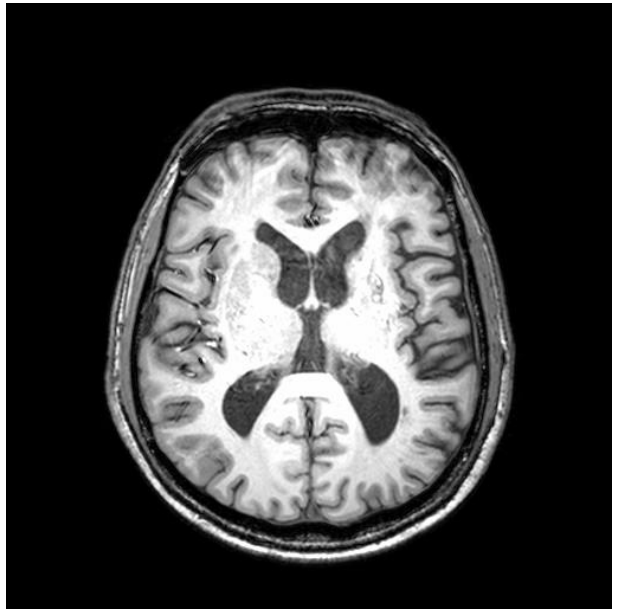



[Pollacco, 2016]

**Differences in T1 and T2 relaxation times between tissues**

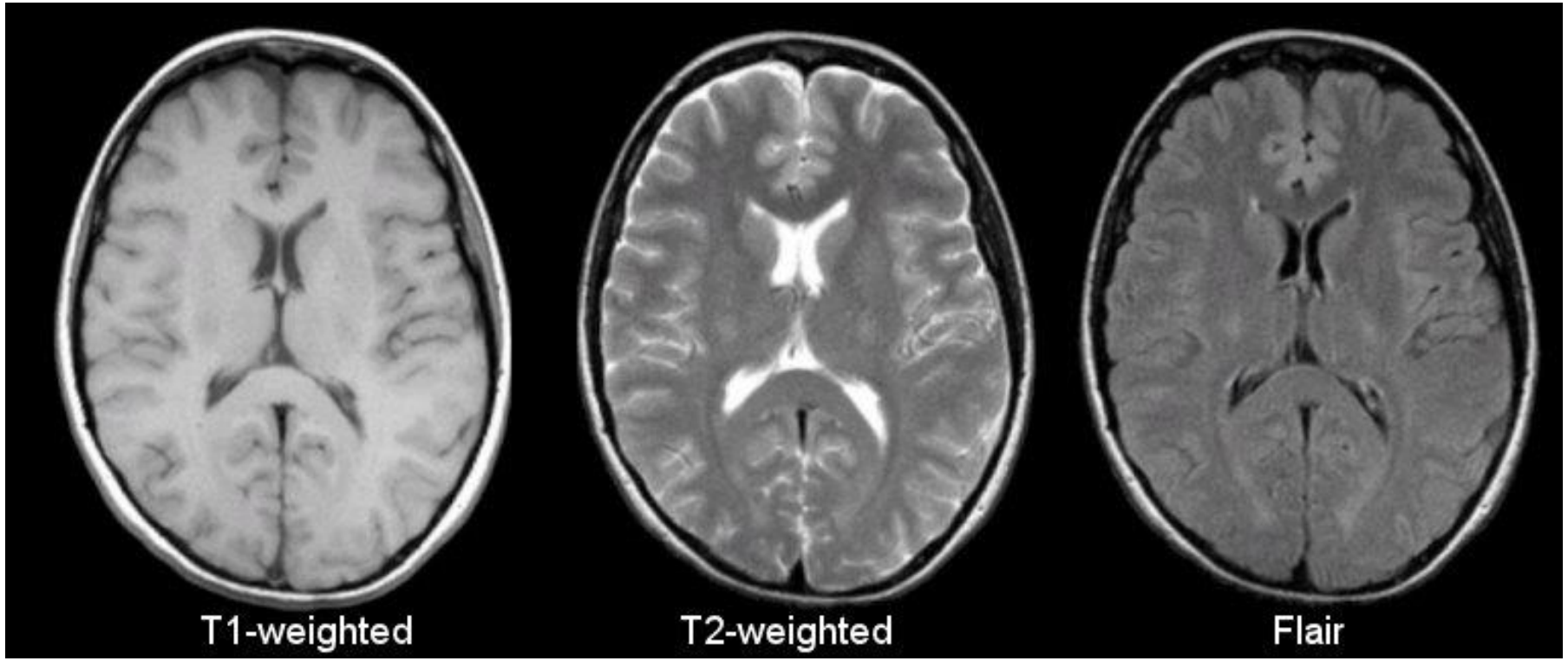
- White matter (nerve fibres) has a very short T1 and relaxes rapidly
- Cerebrospinal fluid has a long T1 and relaxes slowly
- Grey matter (neuron congregations) has an intermediate T1 and relaxes at an intermediate rate



Producing an image
at a time when the curves are widely separated
between the tissues

- White matter contributes to lighter voxels
- Cerebrospinal fluid contributes to darker voxels
- Grey matter contributes to voxels with intermediate shades of grey

**T1-weighted contrast**

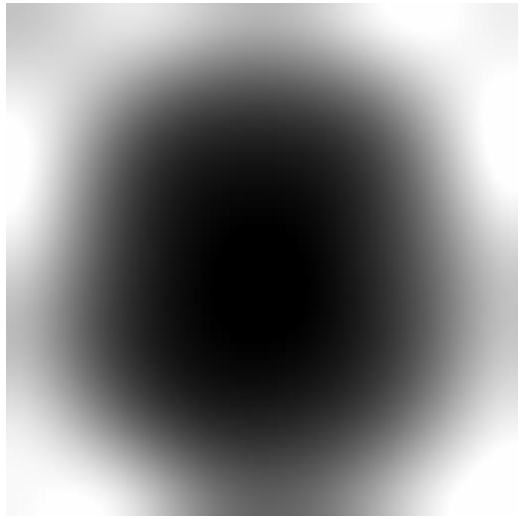



[https://case.edu/med/neurology/NR/MRI Basics.htm]

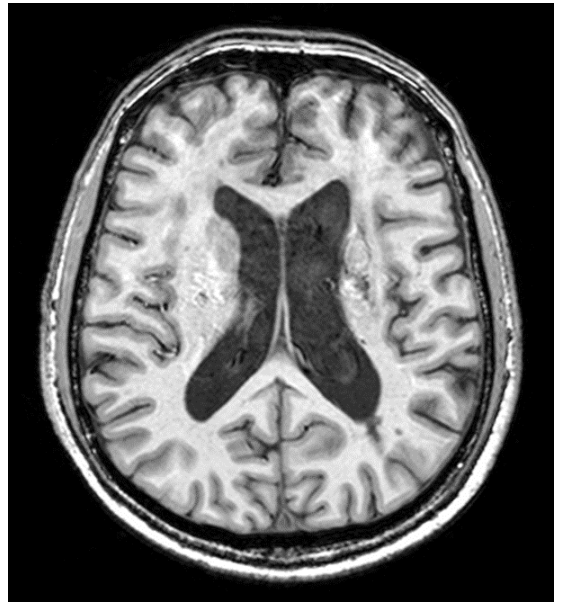
**Different contrasts of the brain: T1-weighted, T2-weighted, and FLAIR**

# sMRI: Data Processing

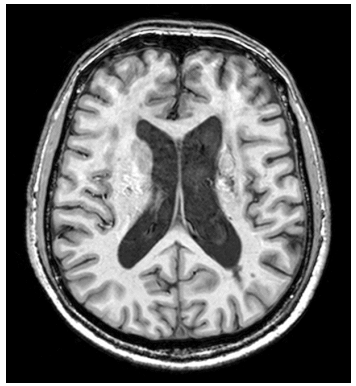
- Preprocessing
  - Correction for intensity non-uniformity (bias field)
  - Segmentation
    - Classifies an image into the non-brain and brain and, furthermore, the brain into different tissues usually including grey matter, white matter, and cerebrospinal fluid
  - Normalisation
    - Transforms an image from a native space to the standard space



Intensity non-uniformity



**Correction for intensity non-uniformity**



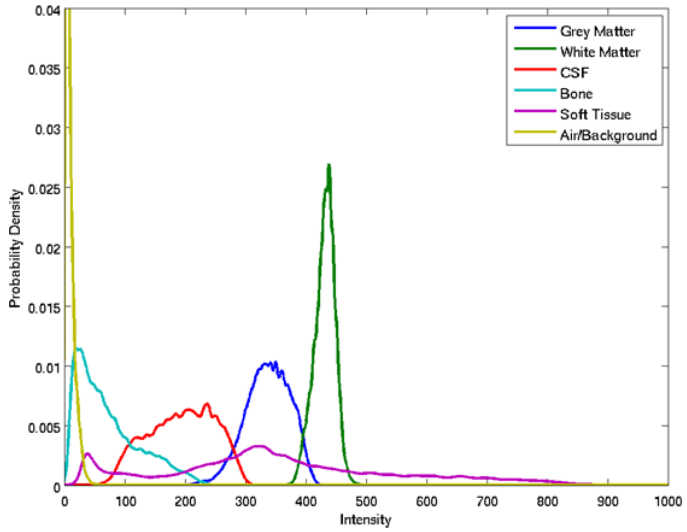
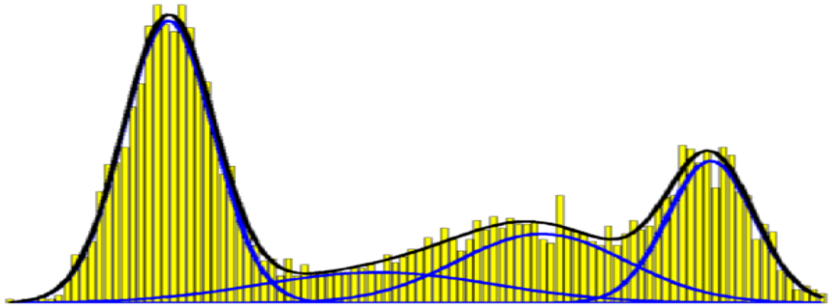



Image intensity distribution



Mixture of Gaussians model

Grey matter

White matter

Cerebrospinal fluid

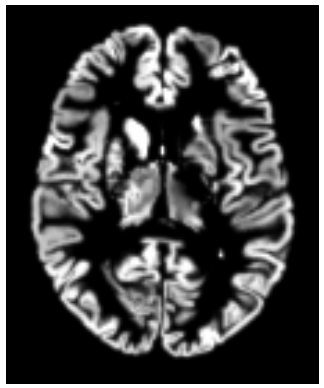
**Segmentation into different tissues**

Grey matter

White matter

Cerebrospinal fluid

Template tissue probability maps

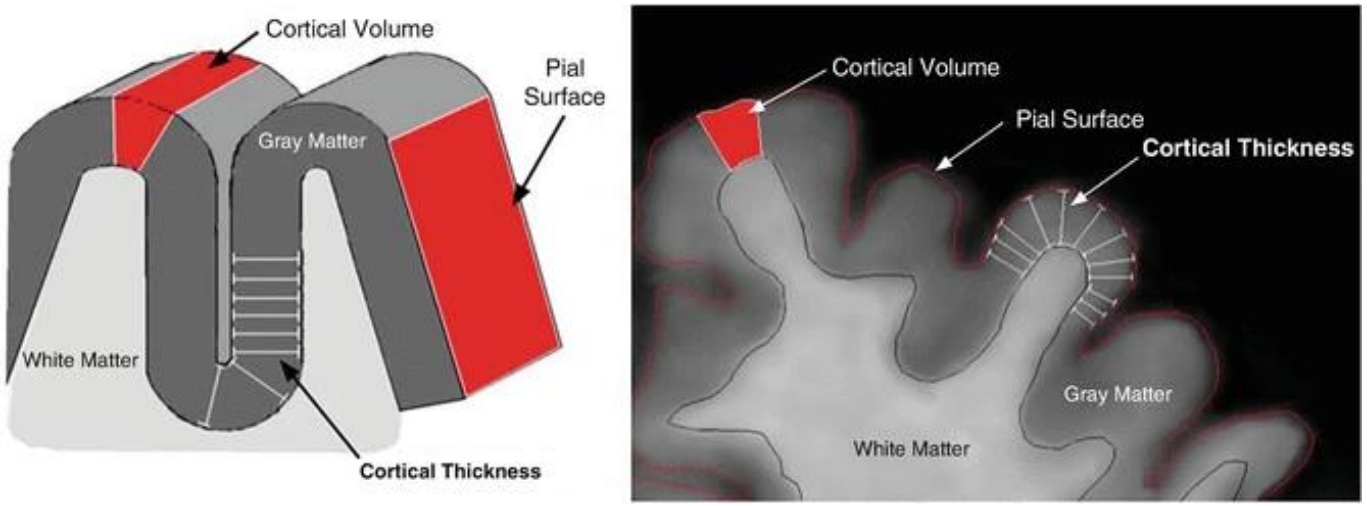


**Normalisation**

- Voxel-based morphometry
  - Grey matter volume
    - Computed by multiplying voxel-wise grey matter probability by voxel volume
    - For a grey matter probability map in the native space or its modulated one in the standard space


Grey matter volume = 0.64 × 3.375 $mm^3$
= 2.16 $mm^3$

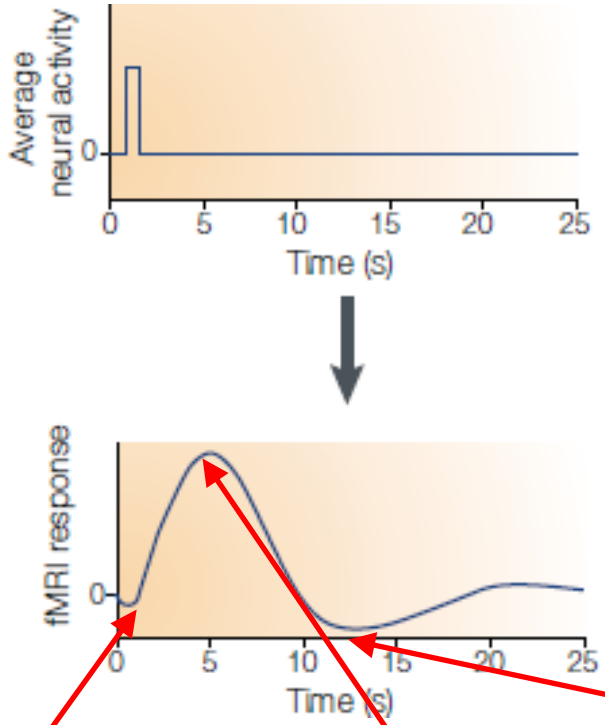
- Surface-based morphometry
  - Cortical thickness
    - Given reconstructed white matter (inner cortical boundary between grey matter and white matter) and pial (outer cortical boundary between grey matter and pia mater) surfaces
    - Distance between the inner and outer cortical boundaries




[Gale and Huff, 2017]

# Functional MRI (fMRI): Principles

- MRI technique primarily for measuring brain activity
  - Blood-oxygen-level dependent (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 ↑




| | 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 |

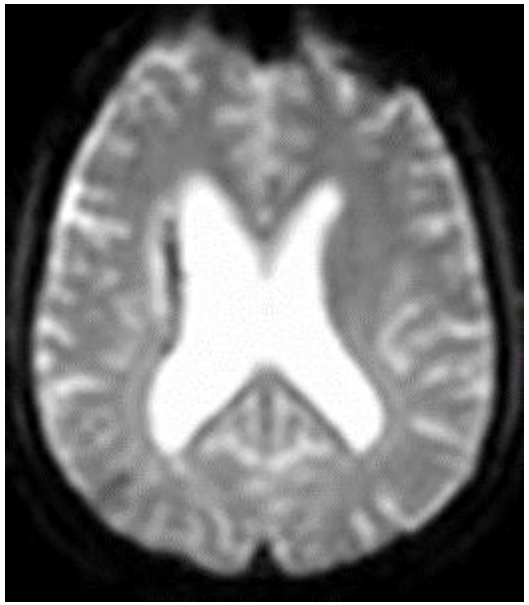
[Heeger and Ress, 2002]

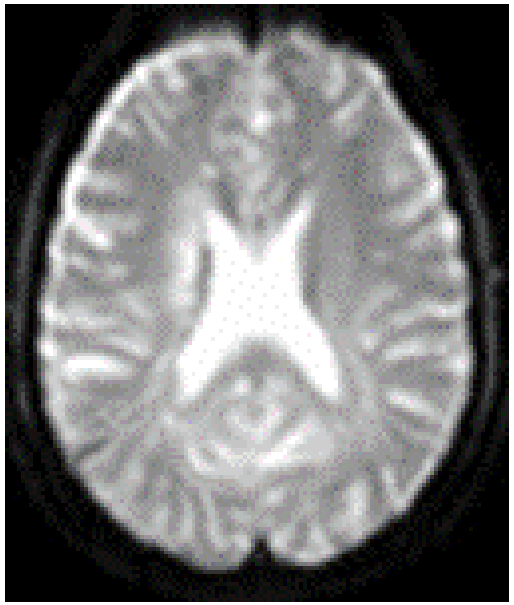
**Three phases of a BOLD fMRI response**

- 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

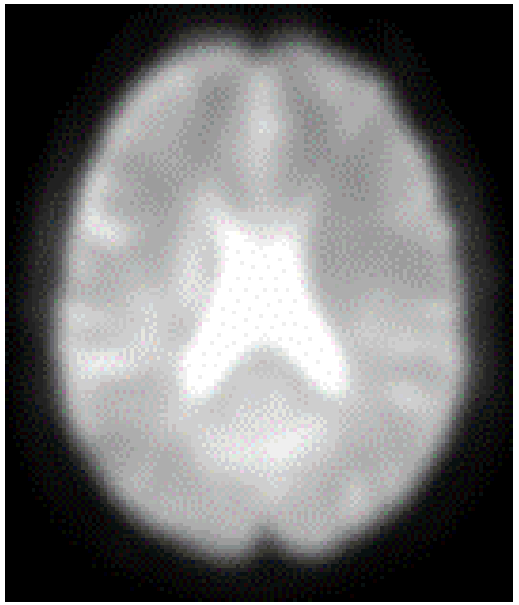
# fMRI: Data Processing

- Preprocessing
  - Correction for unwanted variation
    - Difference in slice timing
    - Head motion
    - Inhomogeneity-induced distortion
  - Normalisation
    - Transforms images from a native space to the standard space
  - Smoothing
    - Blurs images by convolving with a 3D Gaussian kernel





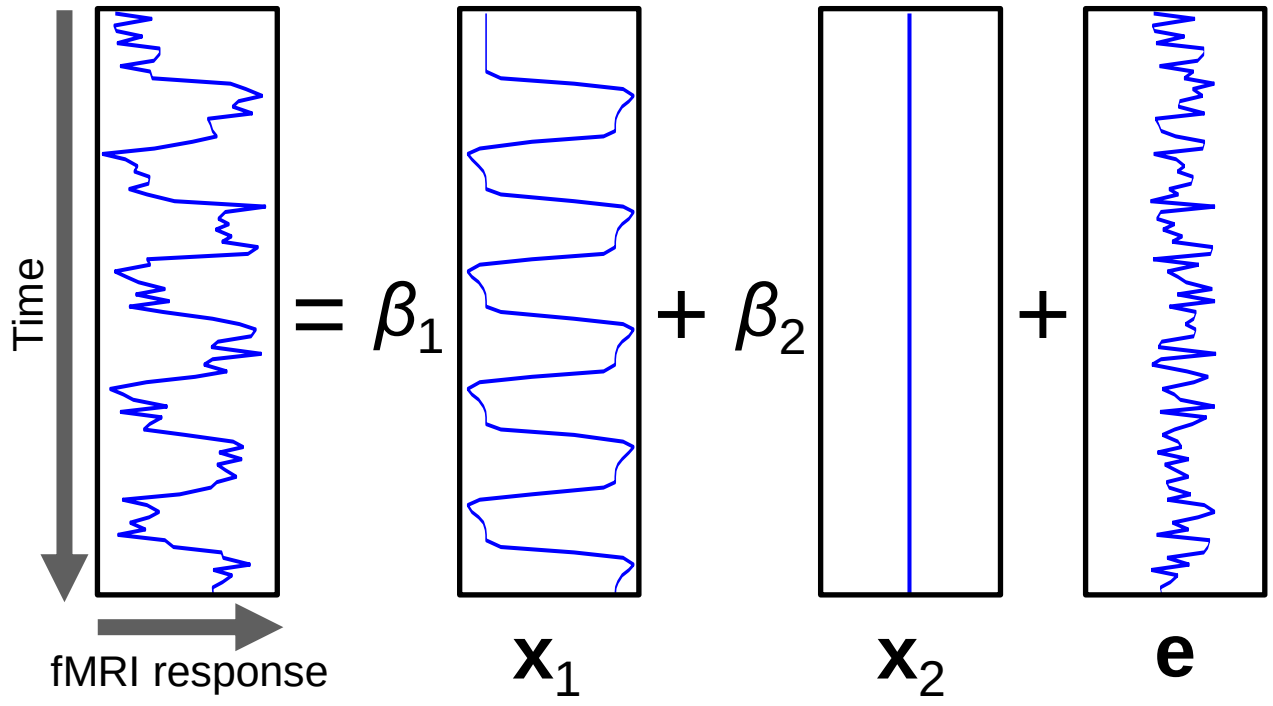
Normalisation



Smoothing

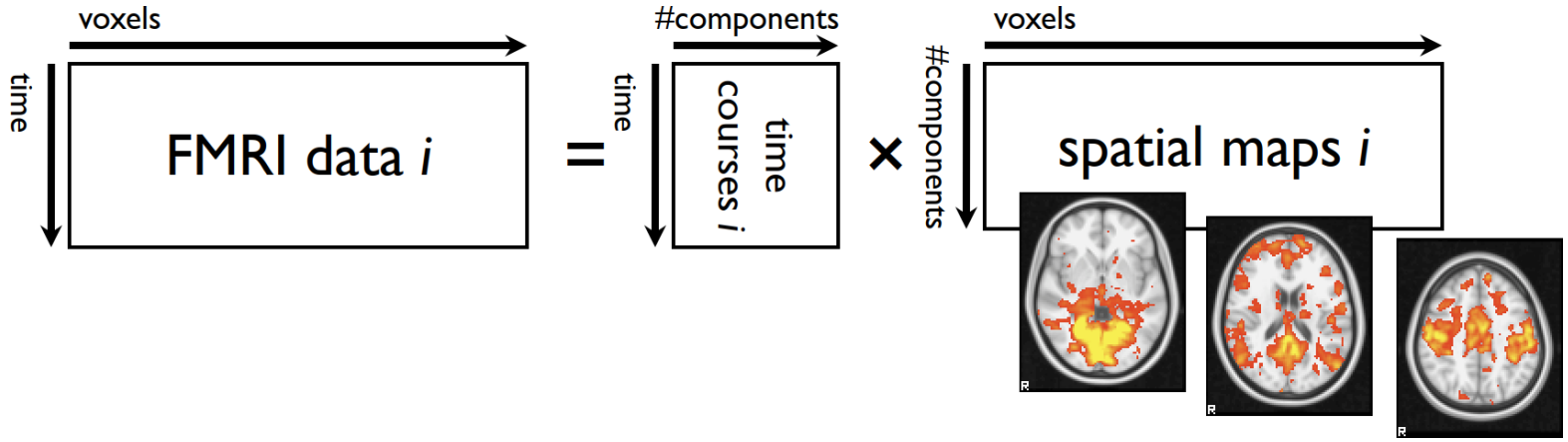
**Preprocessing**

- Functional segregation
  - Task-based fMRI
    - Mass univariate statistical analysis: observed fMRI time series ~ predicted fMRI time series + nuisance variables + error

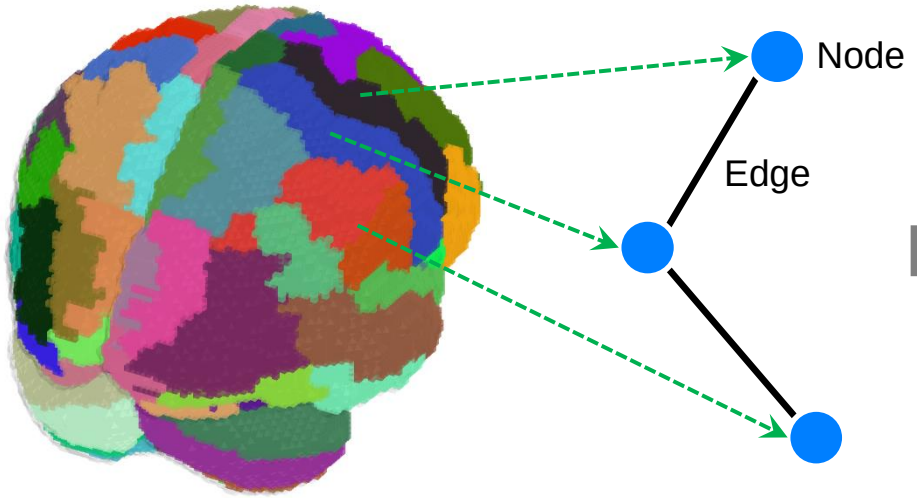


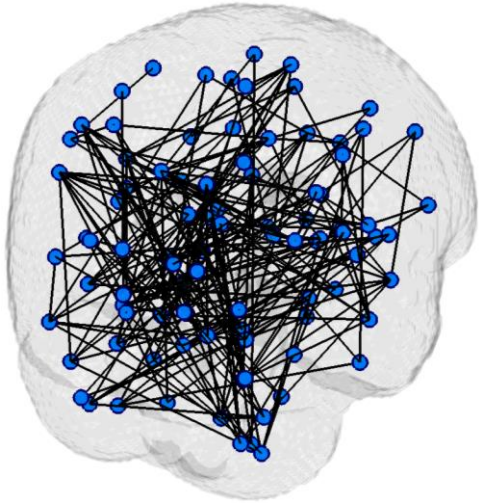
– Resting state fMRI

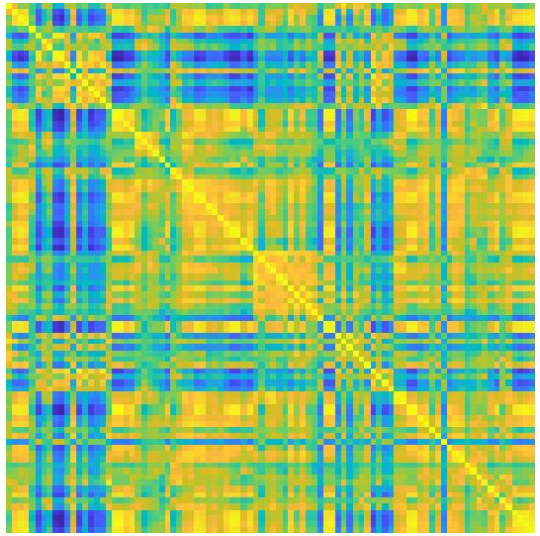
- Regional homogeneity [Zang et al., 2004]
  - Synchronization of time series between a given voxel and its neighbours
- Seed-based correlation [Biswal et al., 1995]
  - Synchronization of time series between a seed (pre-defined voxel or region) and all other voxels in the brain
- Independent component
  - Spatial map and its time course separated from fMRI data by independent component analysis (ICA)



- Functional integration
  - Functional network or connectome
    - Set of nodes and edges
      - Nodes: pre-defined regions
      - Edges: functional or effective connectivity (correlation or causality) between regions



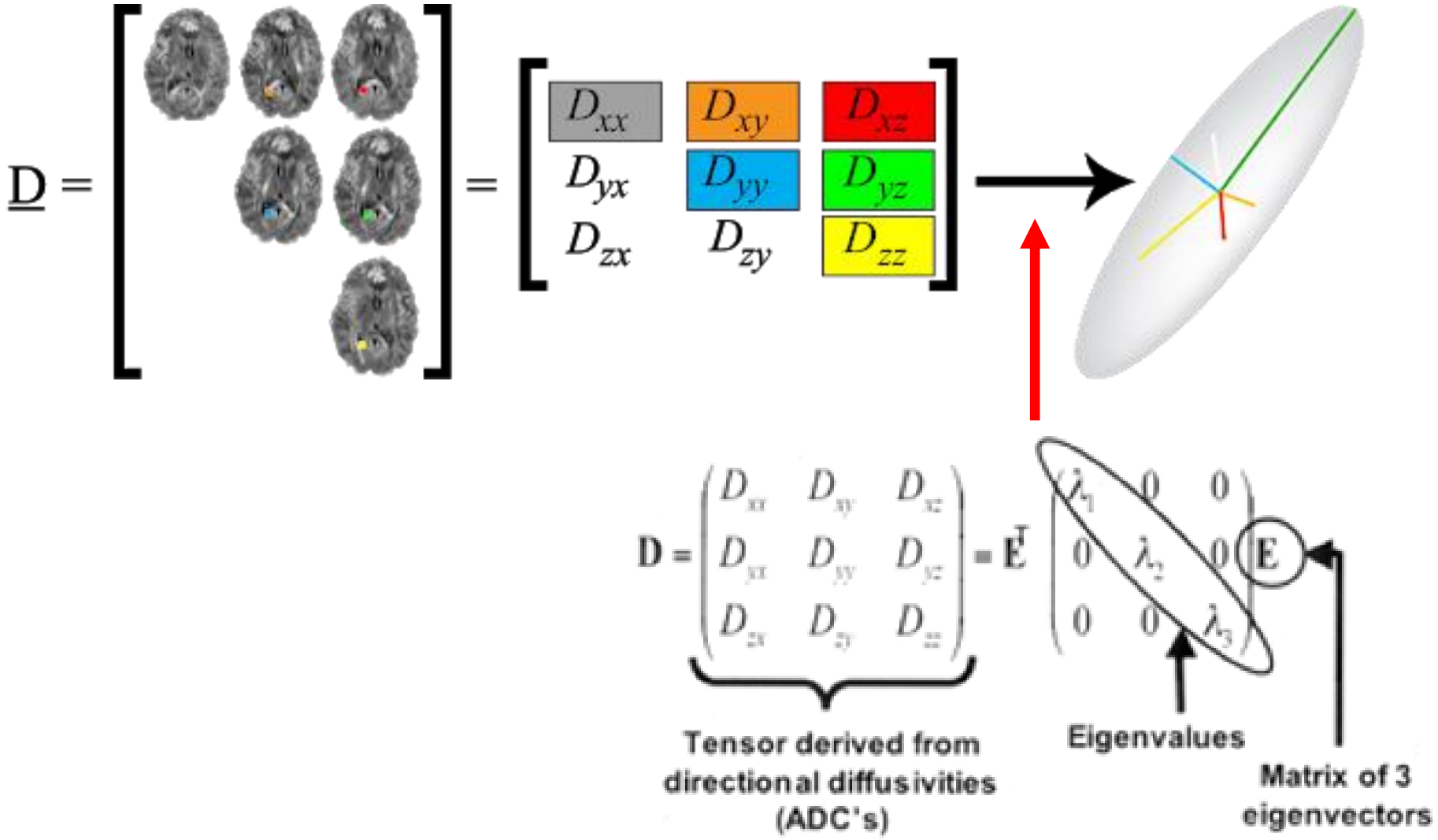





# Diffusion-weighted MRI (dMRI): Principles

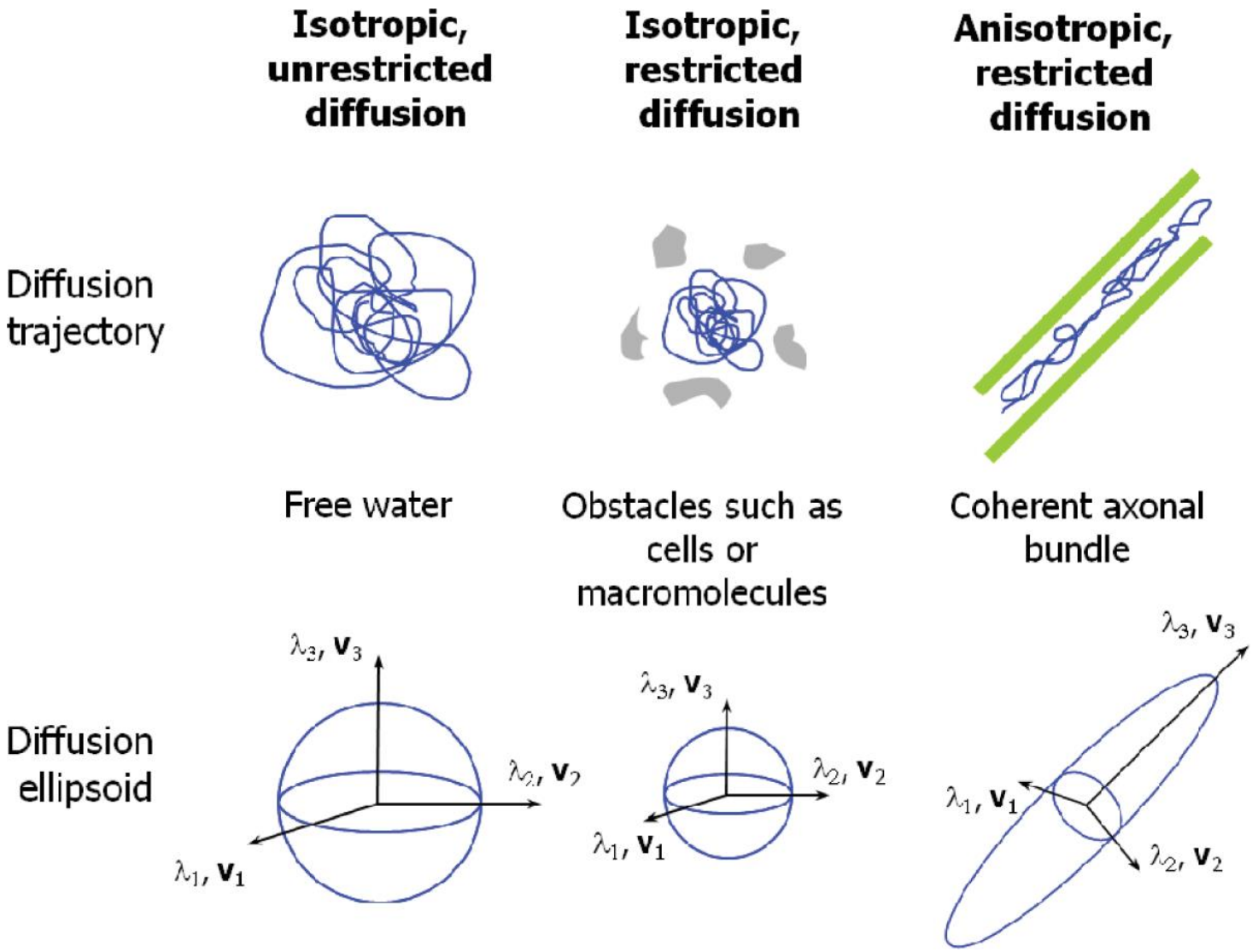
- MRI technique primarily for examining the local microstructure and anatomy of white matter
  - Diffusion-weighted contrast
    - Employs the directional dependence of water molecular diffusion dominantly in white matter composed of bundles of myelinated axons
    - Water molecular diffusion: along axon fibres (more diffusion, thus faster relaxation) vs. across axon fibres (less diffusion)
      - Water molecular diffusion ↑ ➔ image intensity ↓
      - Water molecular diffusion ↓ ➔ image intensity ↑

- Diffusion tensor model
  - Models the diffusion of water molecules as a tensor, which is a mathematical representation of the diffusion process in 3D
  - Based on the assumption that the probability density function describing the random displacement of water molecules due to diffusion is Gaussian
    - Characterized by its mean (assumed to be zero for molecular diffusion) and its variance (represented by the diffusion tensor)
  - Diagonalizing the diffusion tensor by its eigensystem (eigenvectors and eigenvalues) simplifies the model by aligning it with directions in which the diffusion measurements do not linearly interfere with each other




https://www.blog.brainsightai.com/post/from-dti-to-hardi]]

**Diffusion tensor and its ellipsoid representation**



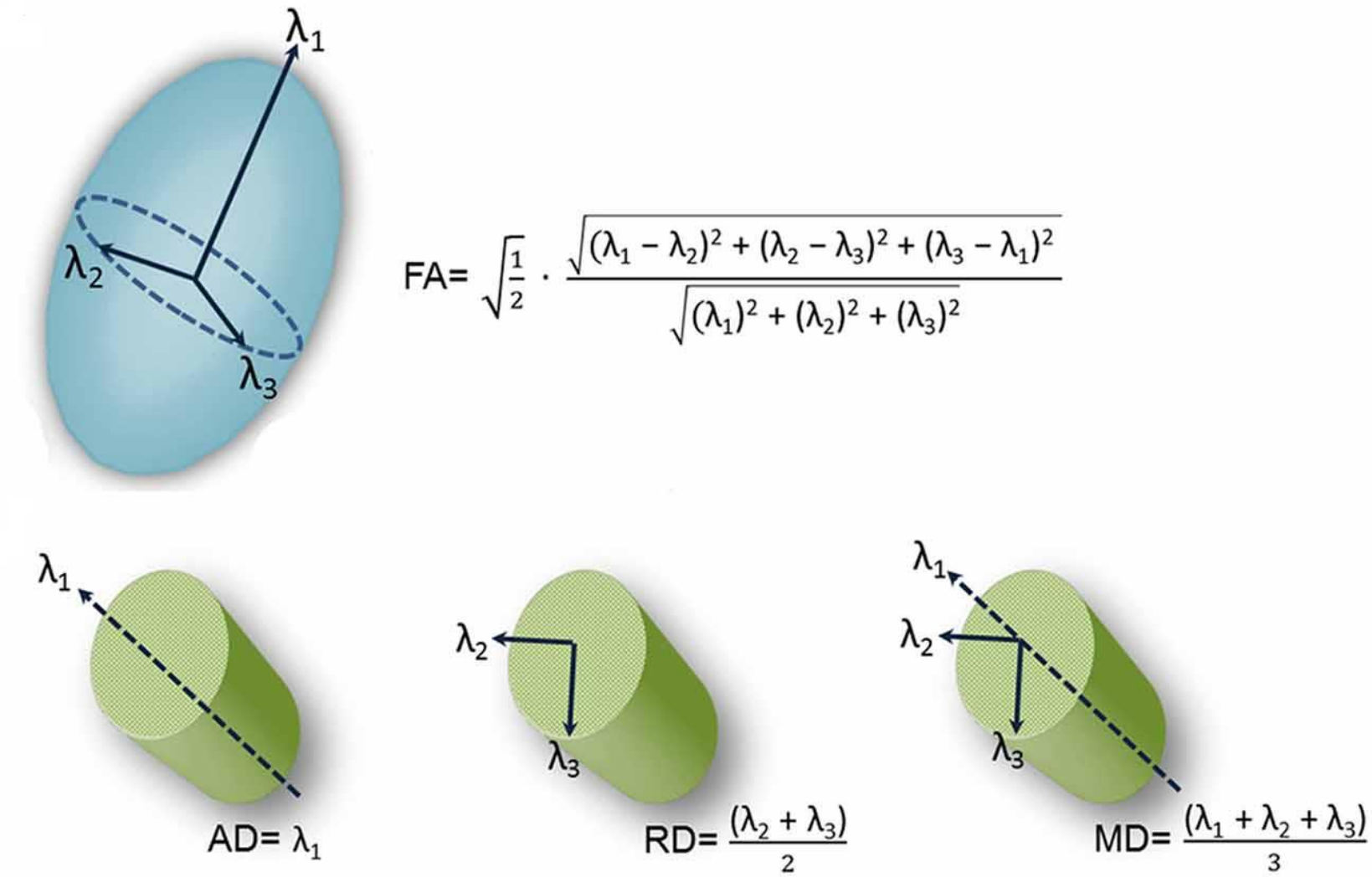

[Geva et al., 2011]

**Isotropic and anisotropic diffusion represented by ellipsoids**

# dMRI: Data Processing

- Preprocessing
  - Correction for unwanted variation
    - Head motion
    - Eddy current-induced distortion
    - Inhomogeneity-induced distortion

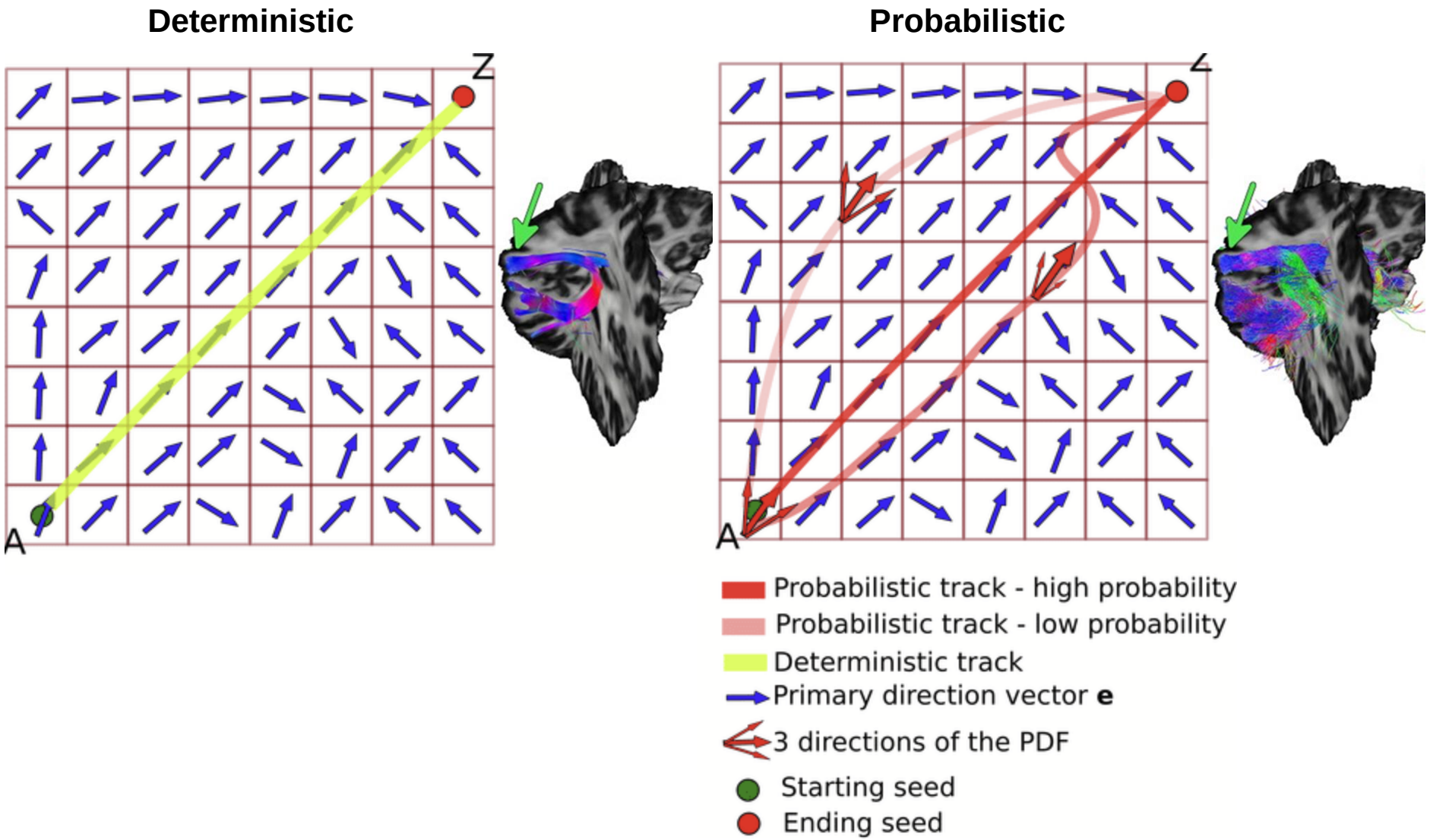
- White matter microstructure
  - Quantified by measures of diffusion properties derived from the diffusion tensor
    - Fractional anisotropy (FA)
      - Indicates the degree of diffusion anisotropy within a voxel
    - Mean diffusivity (MD)
      - Represents the overall diffusivity within a voxel
    - Axial diffusivity (AD)
    - Radial diffusivity (RD)




[DeSouza et al., 2016]

**Diffusion tensor-derived measures**

- White matter tractography
  - Maps and visualizes the pathways of white matter tracts in the brain
    - Based on how strongly and in what directions water molecules diffuse given physical constraints in the brain
  - Fibre tracking (process of tracing the pathways of white matter tracts) in a deterministic (by following the primary direction of diffusion consistently) or probabilistic (by considering the uncertainty in estimates of the diffusion direction) way

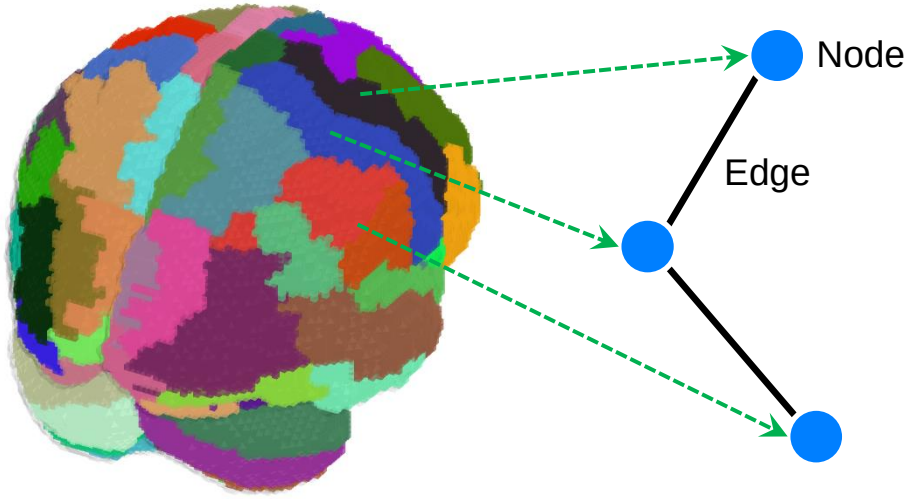


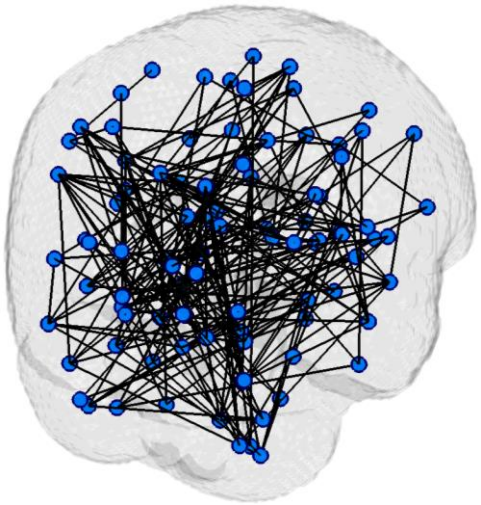

[Garyfallidis, 2012, Schreiber et al., 2014]

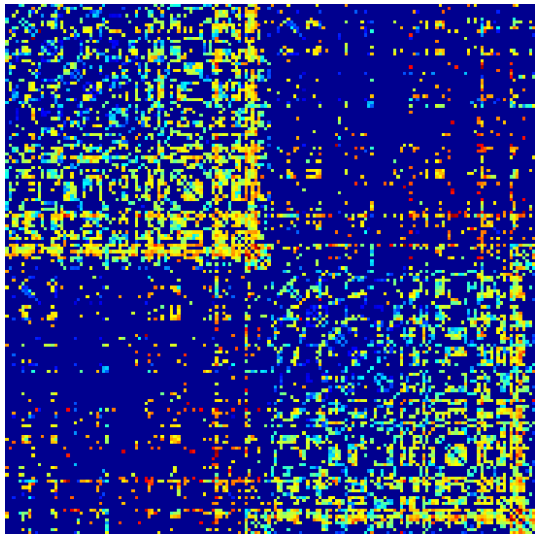
**Deterministic and probabilistic ways for white matter tractography**

– Structural network or connectome

- Set of nodes and edges
  - Nodes: pre-defined regions
  - Edges: structural connectivity (white matter fibre tracts: tract count or diffusion tensor-derived measures) between regions

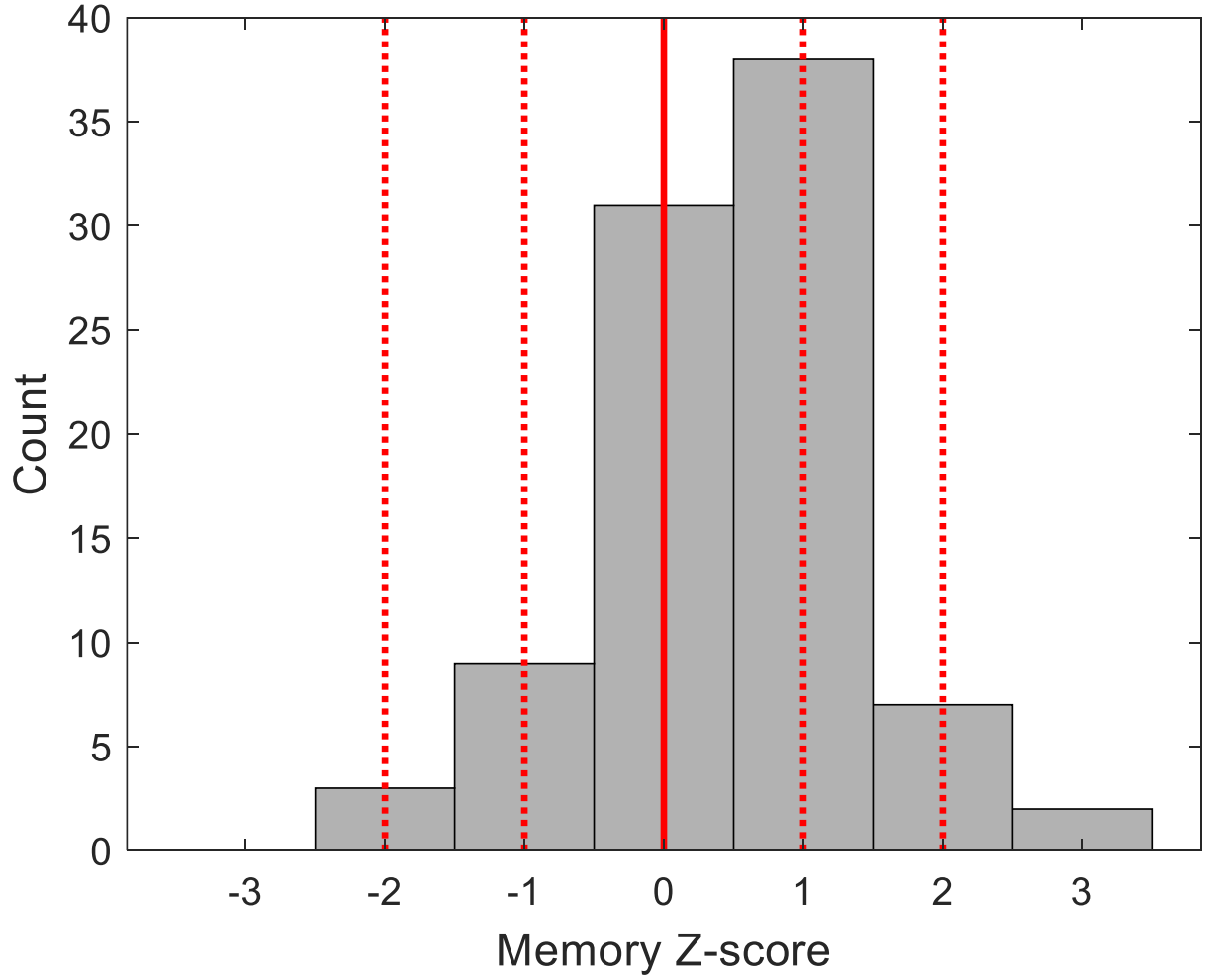




# Hands-on Machine Learning (1): Predicting Memory Performance

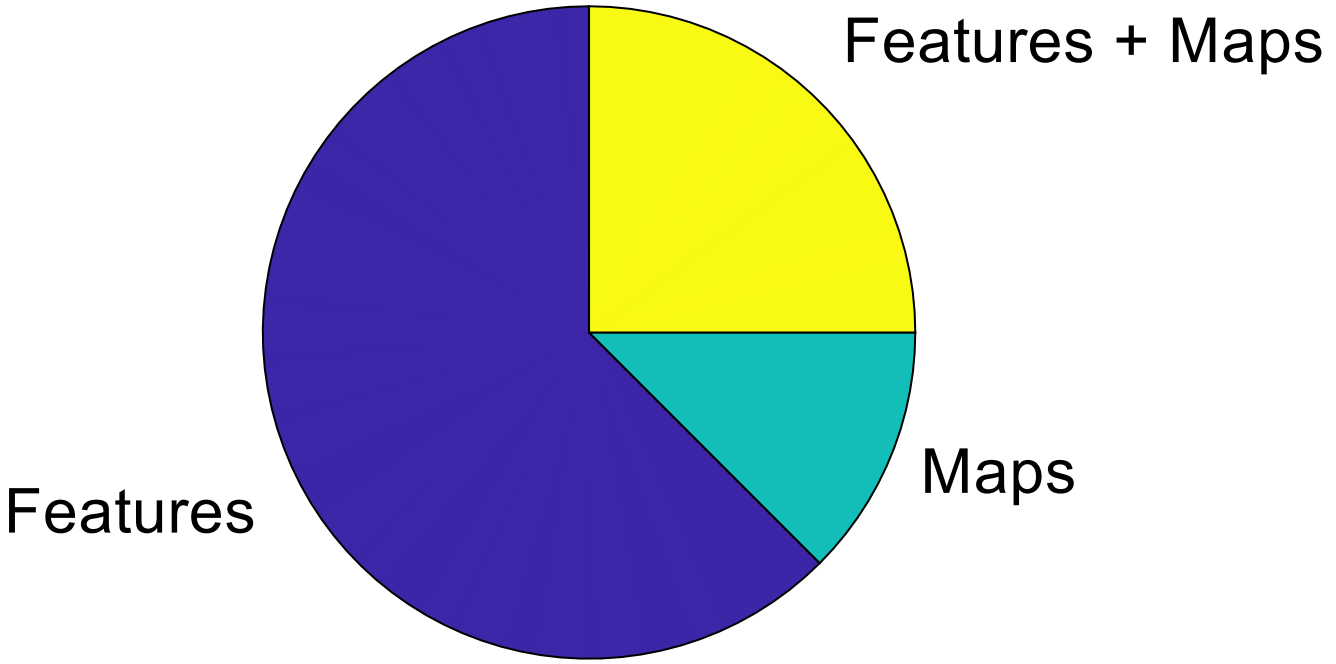
- Memory
  - Fundamental brain function that encompasses the processes of encoding, storing, and retrieving information
  - Decline in certain types of memory abilities, particularly those related to episodic and working memory, in normal ageing
- Subjects ($n$ = 90)
  - Age: 72.2±5.5 years
  - Sex: 75 females and 15 males
  - Years of education: 10.5±3.6 year



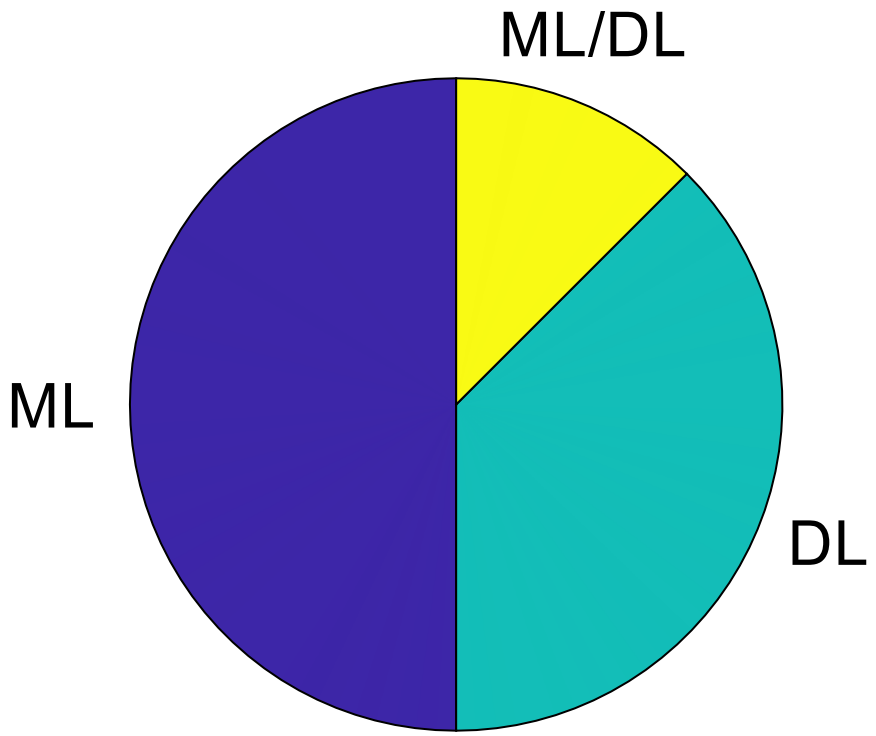

**Distribution of memory performance scores for subjects**

- Task: predicting memory performance
  - Dataset from locally acquired data
    - sMRI, resting state fMRI, and dMRI
    - Demographic information including age, sex, and years of education
    - Memory performance scores
  - Training ($n$ = 80) and test ($n$ = 10) sets
  - Input maps/features
    - Grey matter and white matter maps/features from sMRI
    - Regional homogeneity and posterior cingulate gyrus-based correlation maps/features from resting state fMRI
    - Fractional anisotropy and mean diffusivity maps/features from dMRI

- Model generation

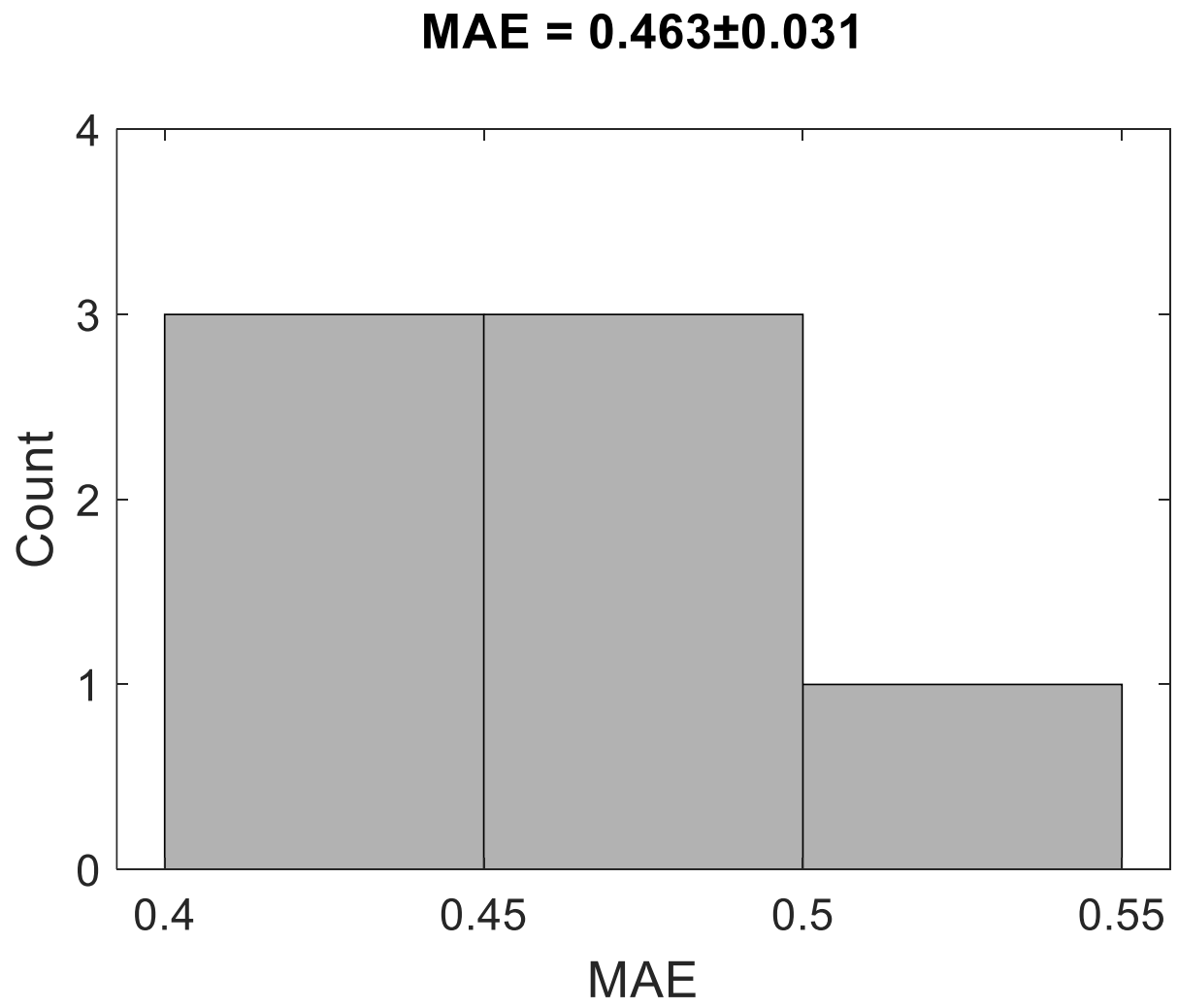



**Data types**



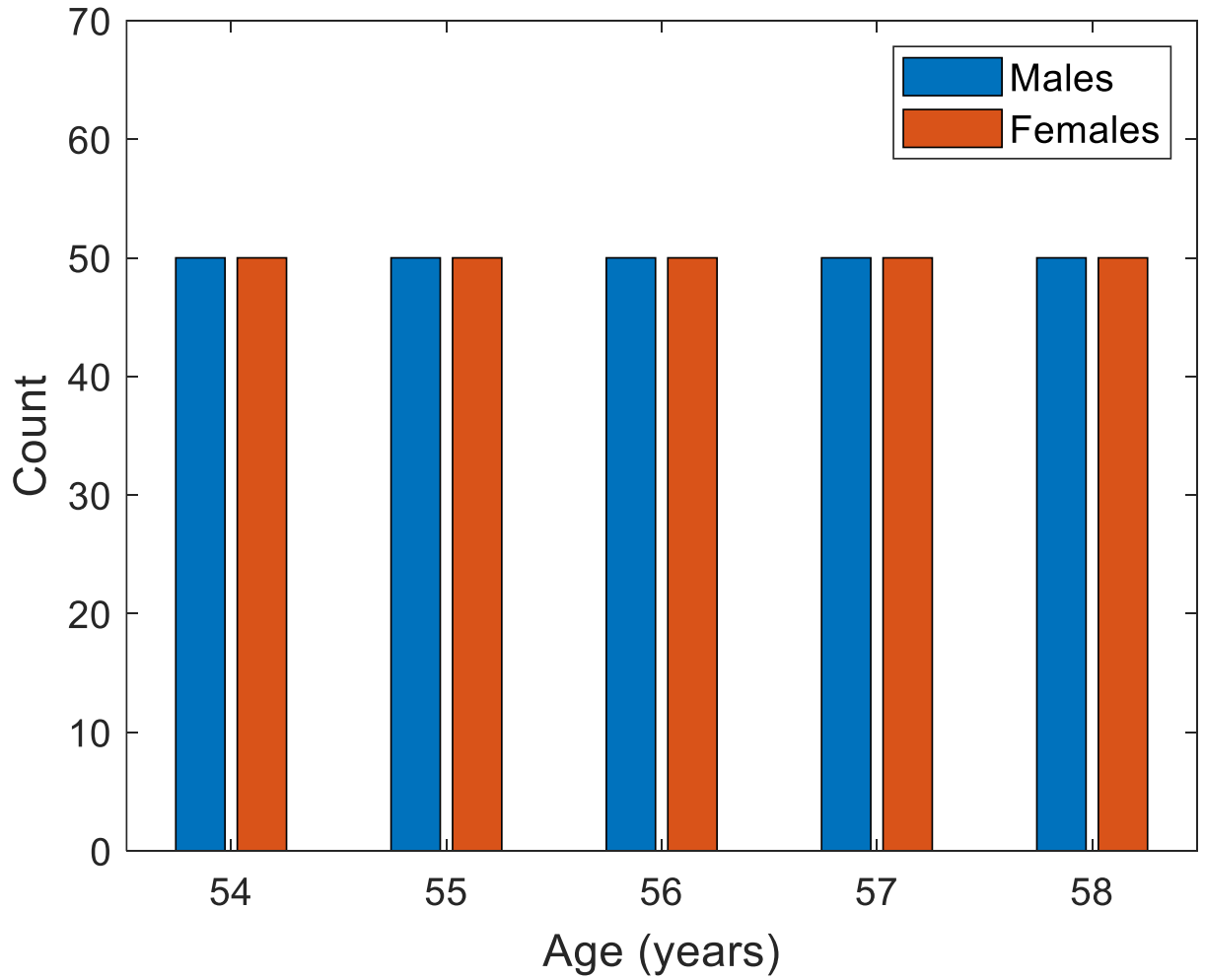

**Learning paradigms**

– Predictive performance (mean absolute error (MAE)) on the test set



# Hands-on Machine Learning (2): Predicting Sex

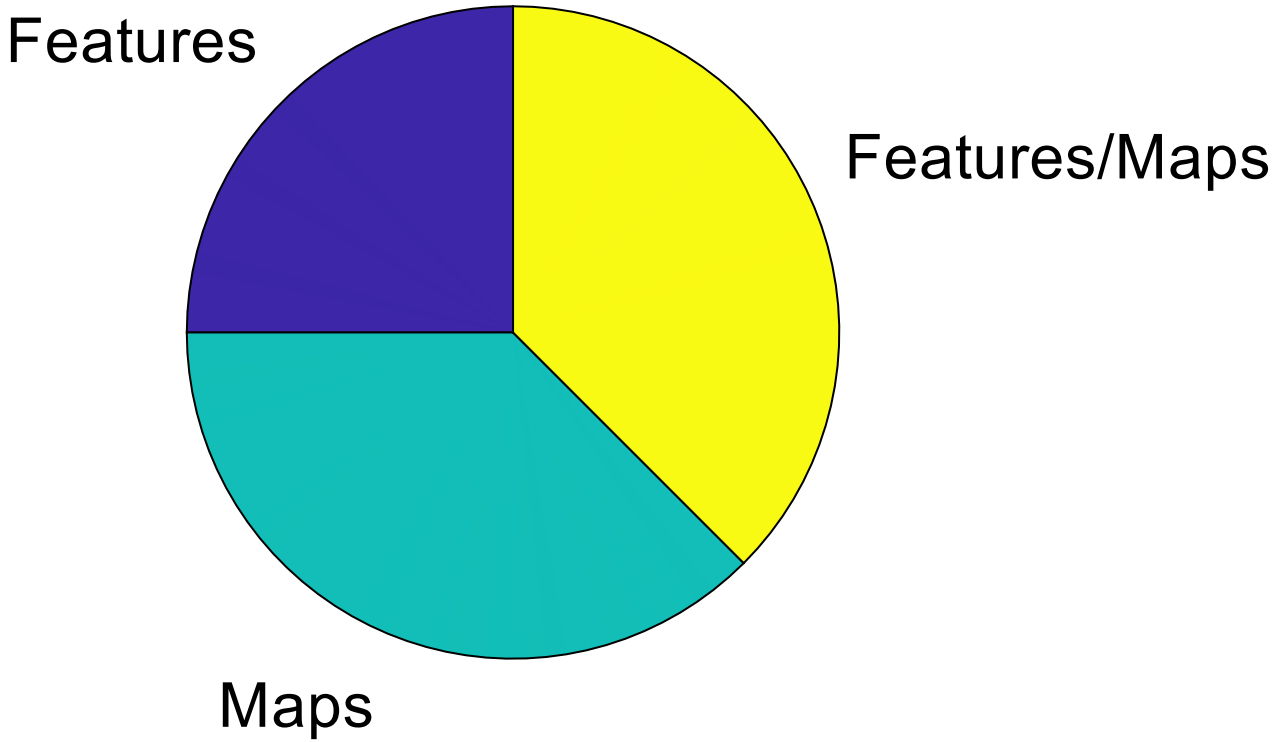
- Sex
  - Typically refers to the biological and physiological characteristics that define males and females
  - Determined by biological factors, primarily chromosomal (XX for females, XY for males) and anatomical differences
- Subjects ($n$ = 500)
  - Age and sex: 50 females and 50 males for each age from 54 to 58 years



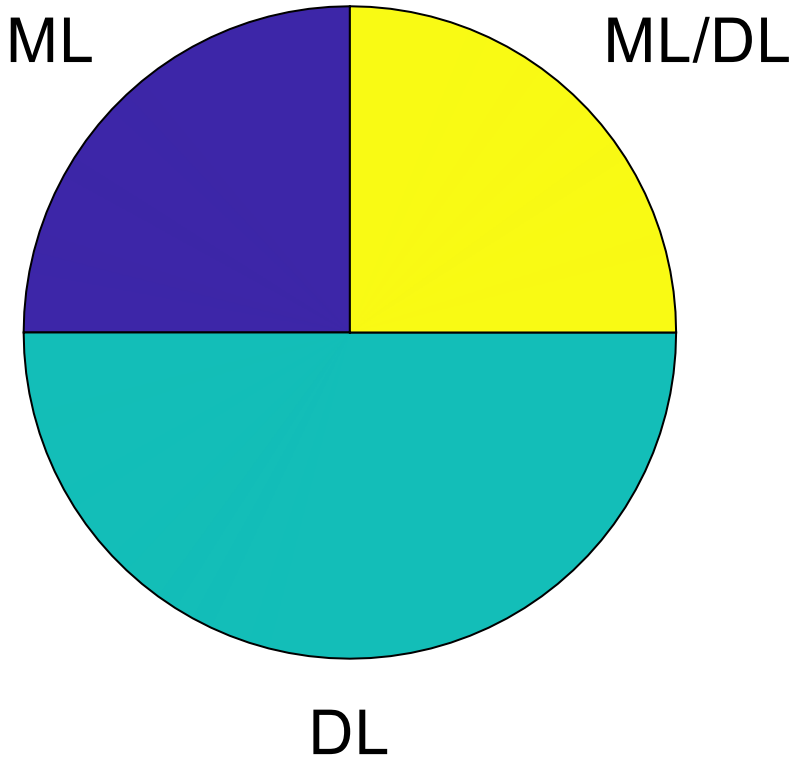

**Sex distribution across ages for subjects**

- Task: predicting sex
  - Dataset from UK Biobank (https://www.ukbiobank.ac.uk/)
    - sMRI, resting state fMRI, and dMRI
    - Demographic information including sex and age
  - Training ($n$ = 450) and test ($n$ = 50) sets
  - Input maps/features
    - Grey matter and white matter maps/features from sMRI
    - Default mode network maps/features from resting state fMRI
    - Fractional anisotropy and mean diffusivity maps/features from dMRI

- Model generation

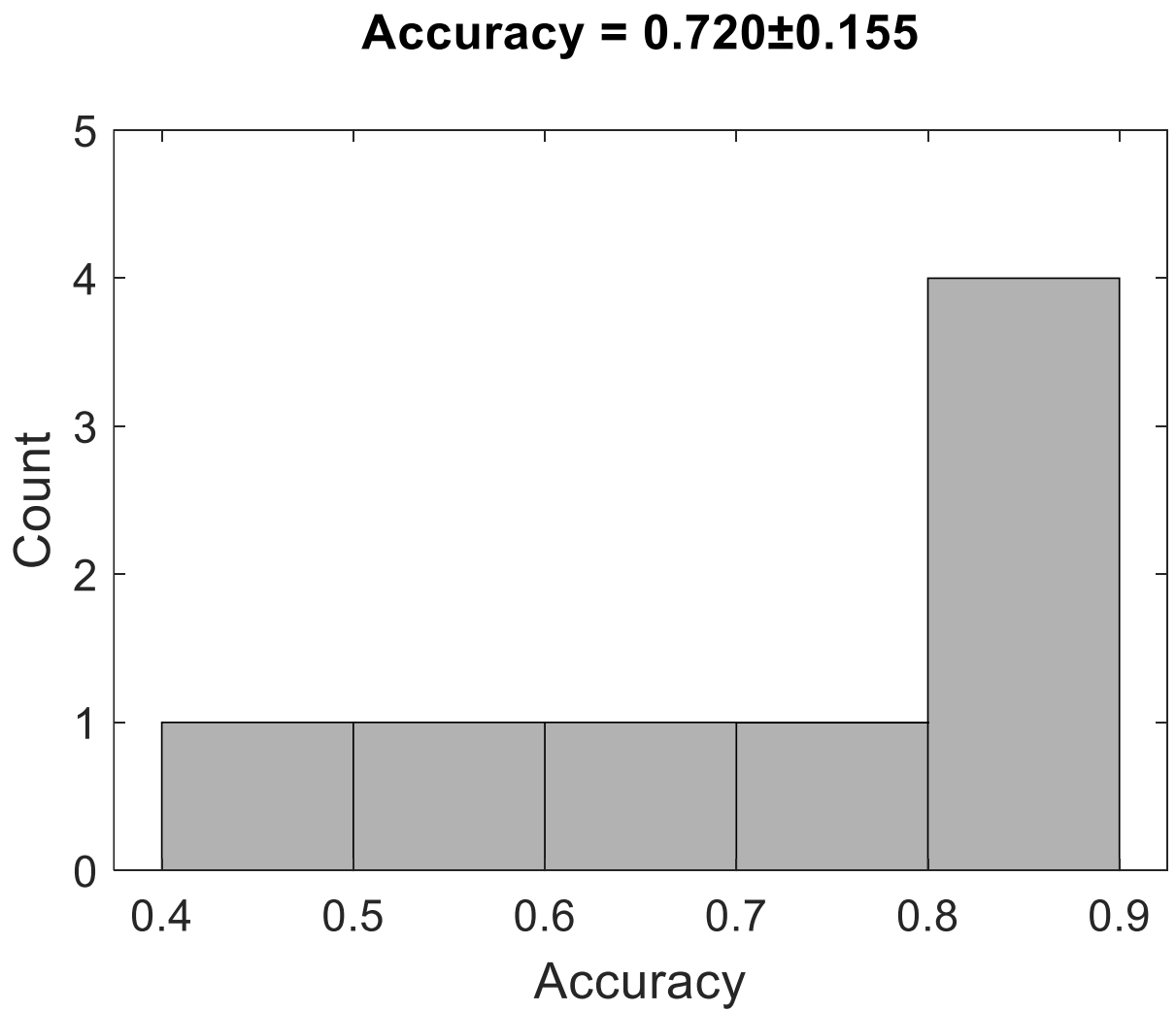



**Data types**

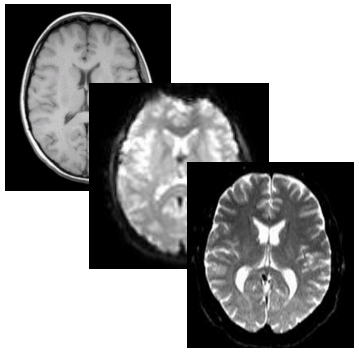


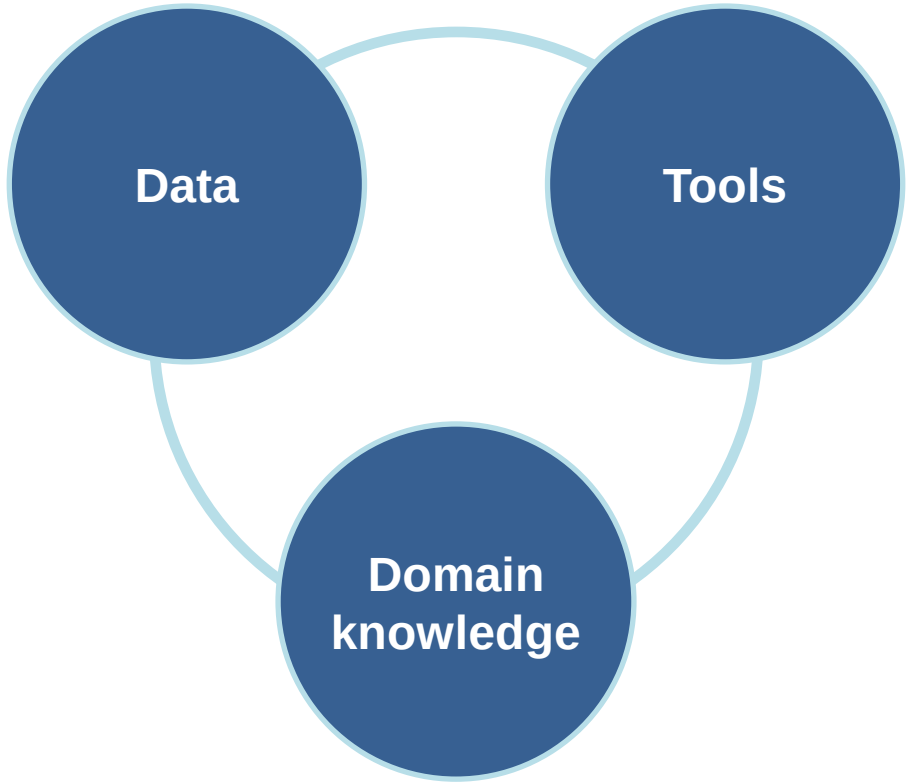

**Learning paradigms**

– Predictive performance (accuracy) on the test set



# Summary: MRI Data Predictive Analytics






MATLAB

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