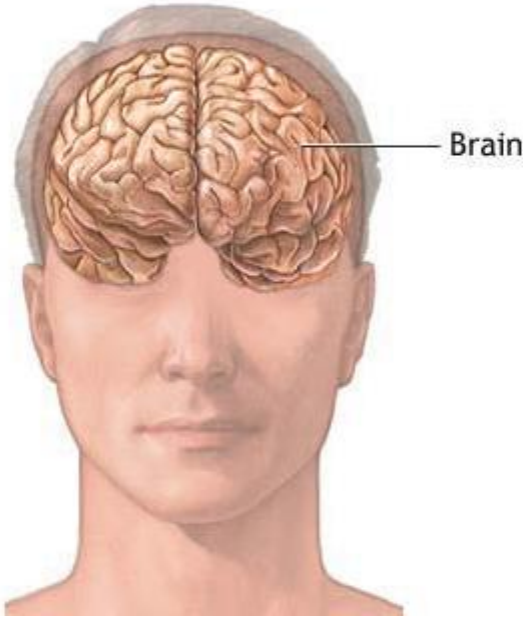
Medical/Bio Research Topics Ⅱ: Week 01 (07.09.2023)

General introduction of brain imaging

(뇌영상 소개)

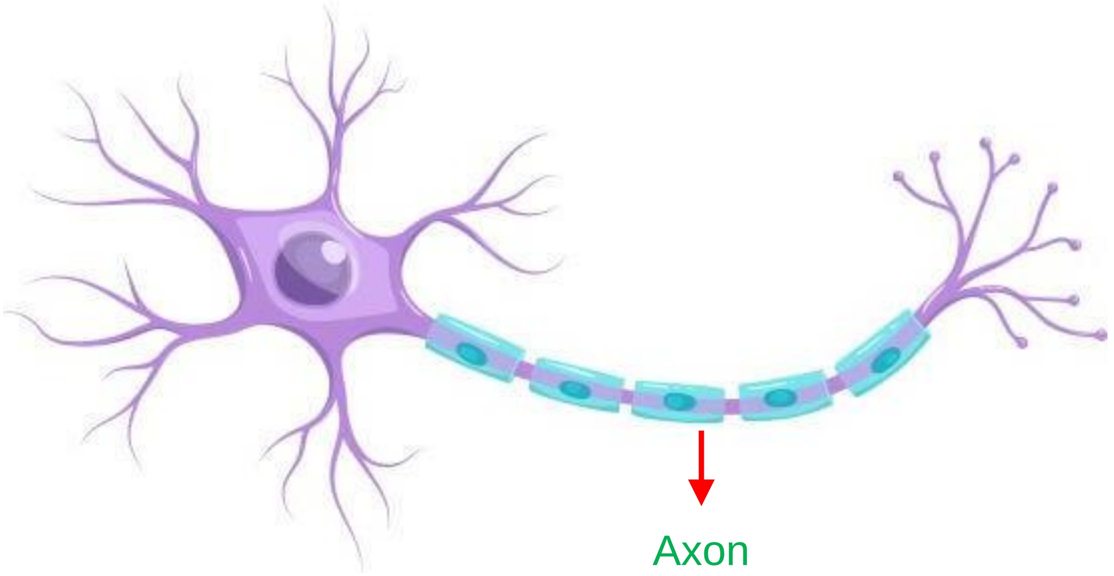
Brain

- Center of the nervous system
- Located in the head

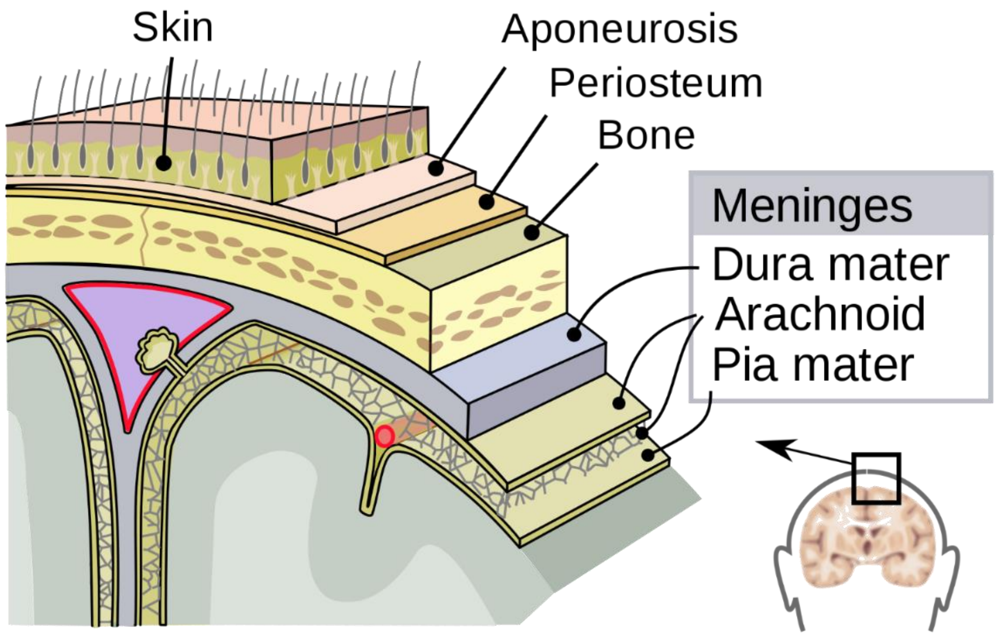


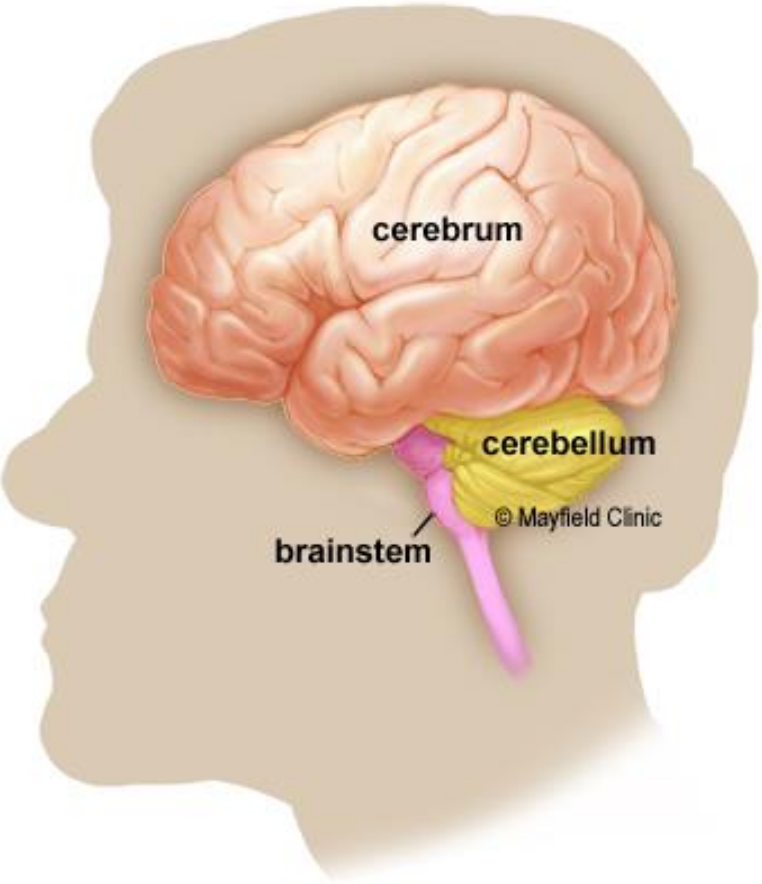
[https://medlineplus.gov/ency/imagepages/8738.htm]

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

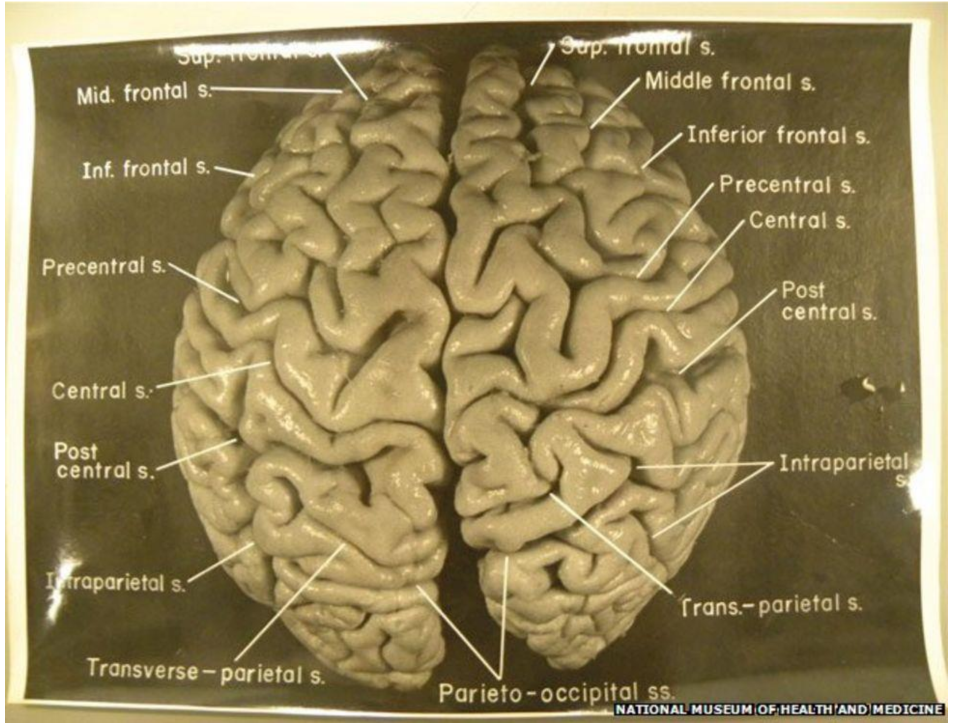


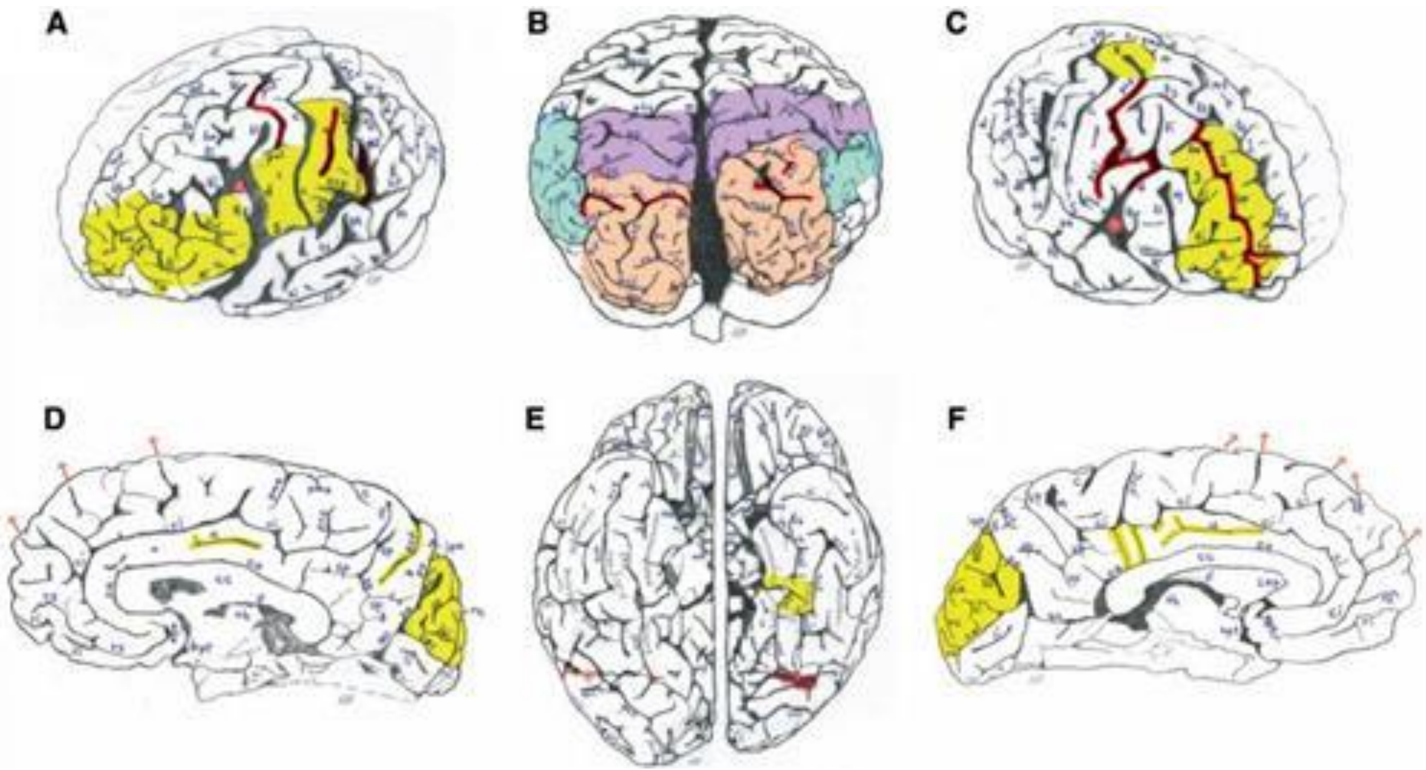
- Anatomy of the brain





[[https://www.physio-pedia.com/Meninge; https://mayfieldclinic.com/pe-anatbrain.htm]

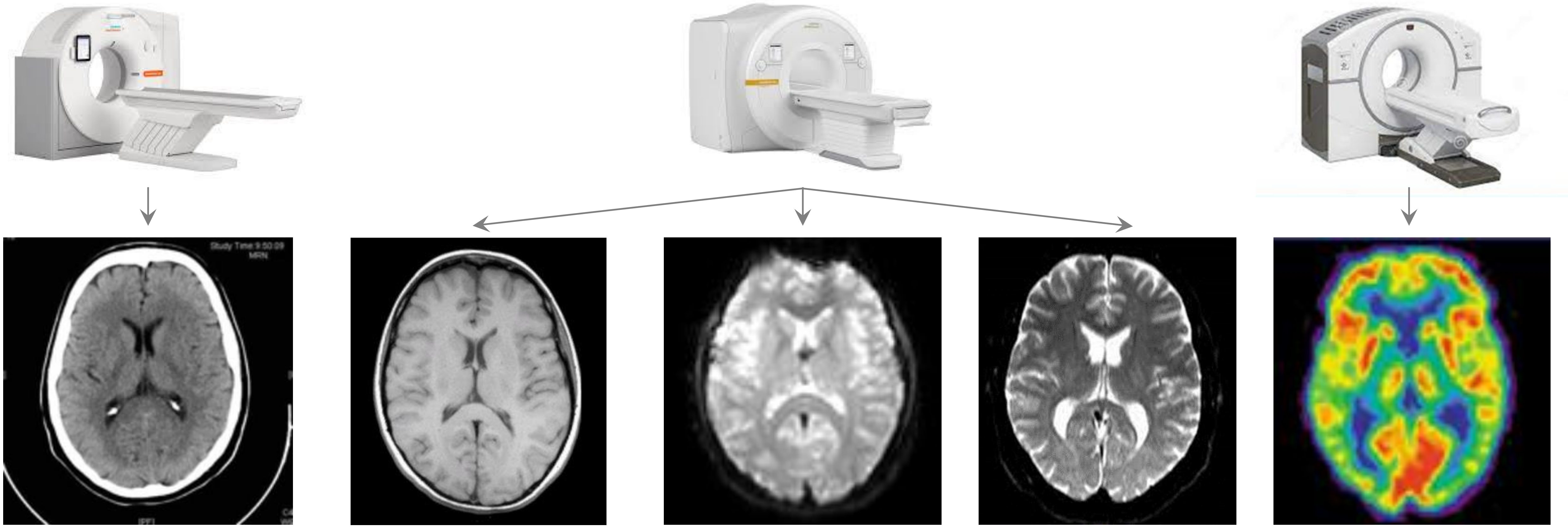




[Falk et al., 2019]

Unusual features of Einstein's brain

Brain Imaging

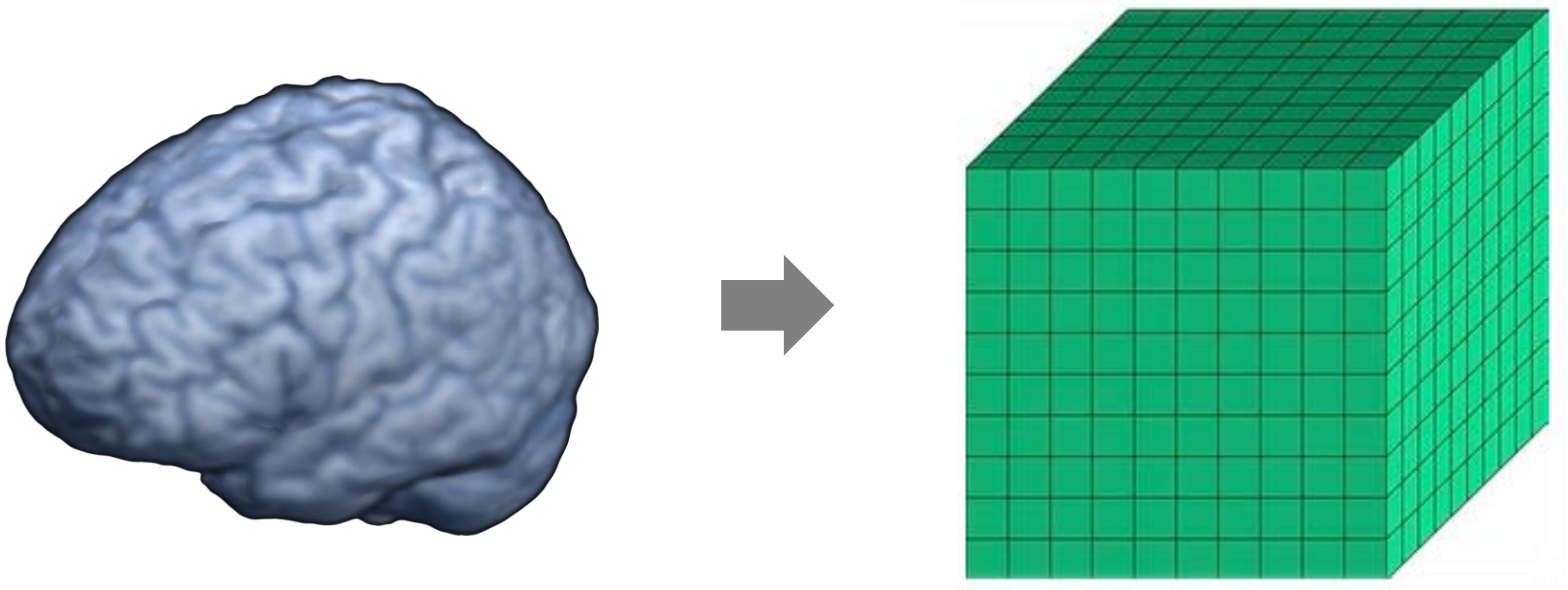


CT | Structural MRI | Functional MRI | Diffusion-weighted MRI | PET

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

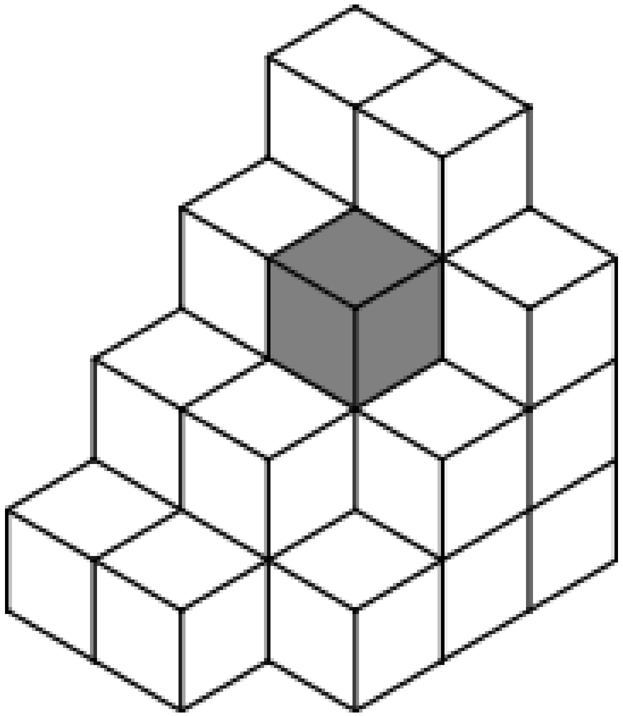
- Various techniques for imaging the structure or function of the brain
  - Computed Tomography (CT)
  - Magnetic Resonance Imaging (MRI)
    - Structural MRI (sMRI)
    - Functional MRI (fMRI)
    - Diffusion-weighted MRI (dMRI)
  - Positron Emission Tomography (PET)

- 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

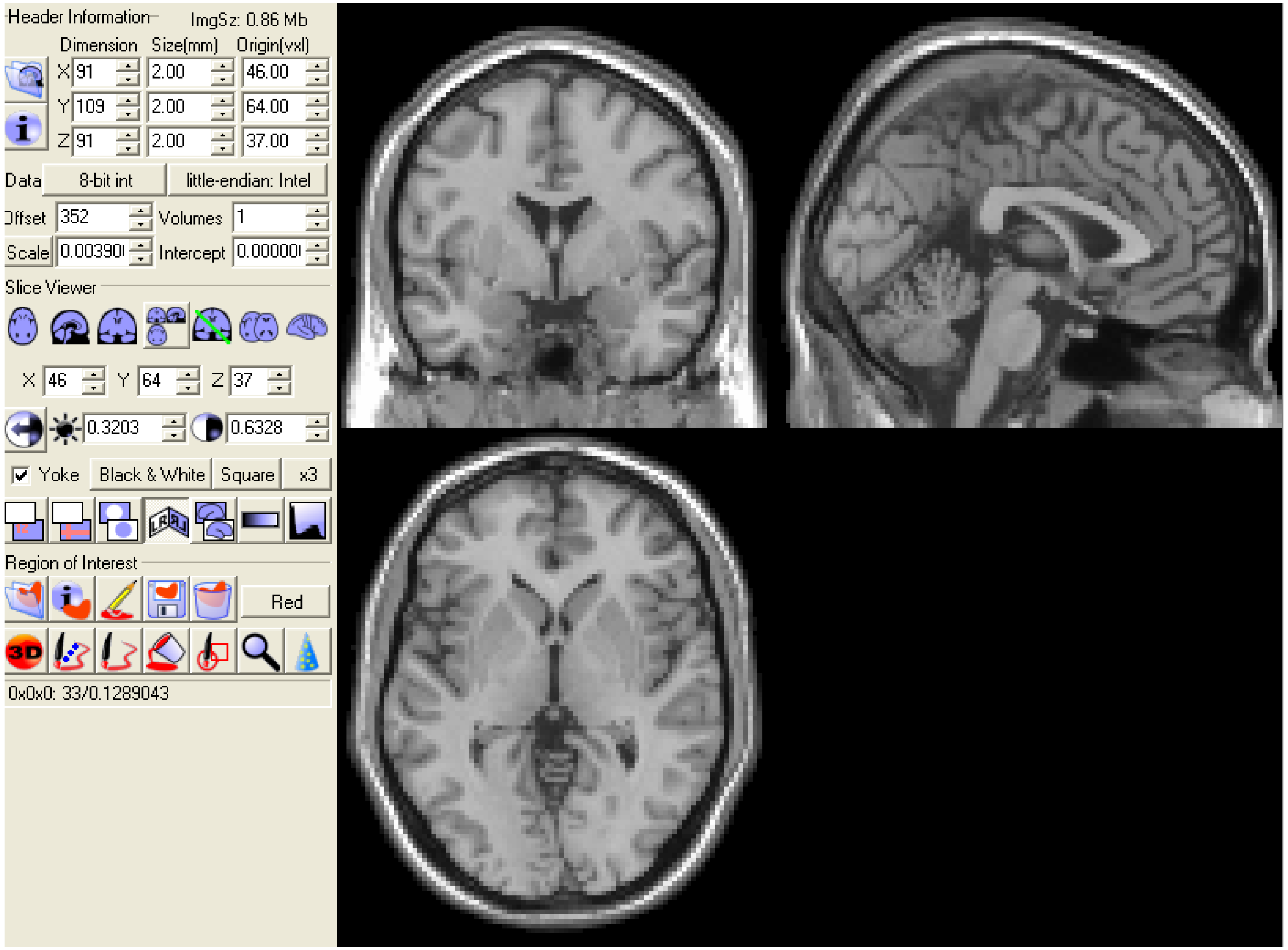


  - Discrete representation resulting from a sampling/reconstruction process that maps numerical values to positions of the space

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



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

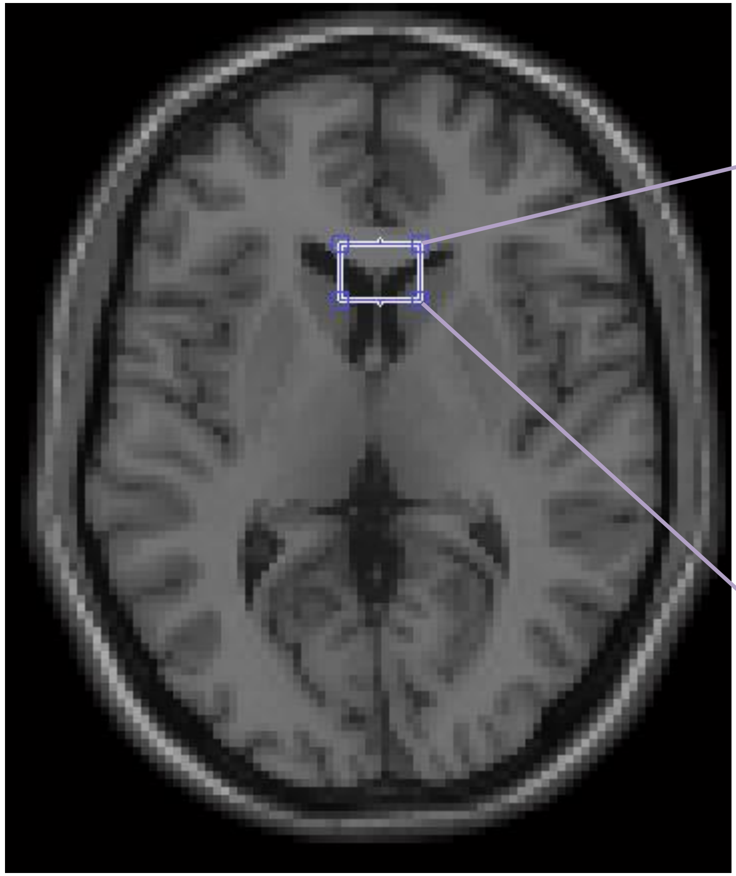


Dimensions: 91 × 109 × 91
Voxel depth: 8-bit integer
Voxel size: 2 mm × 2 mm × 2 mm
Origin: [46, 64, 37]

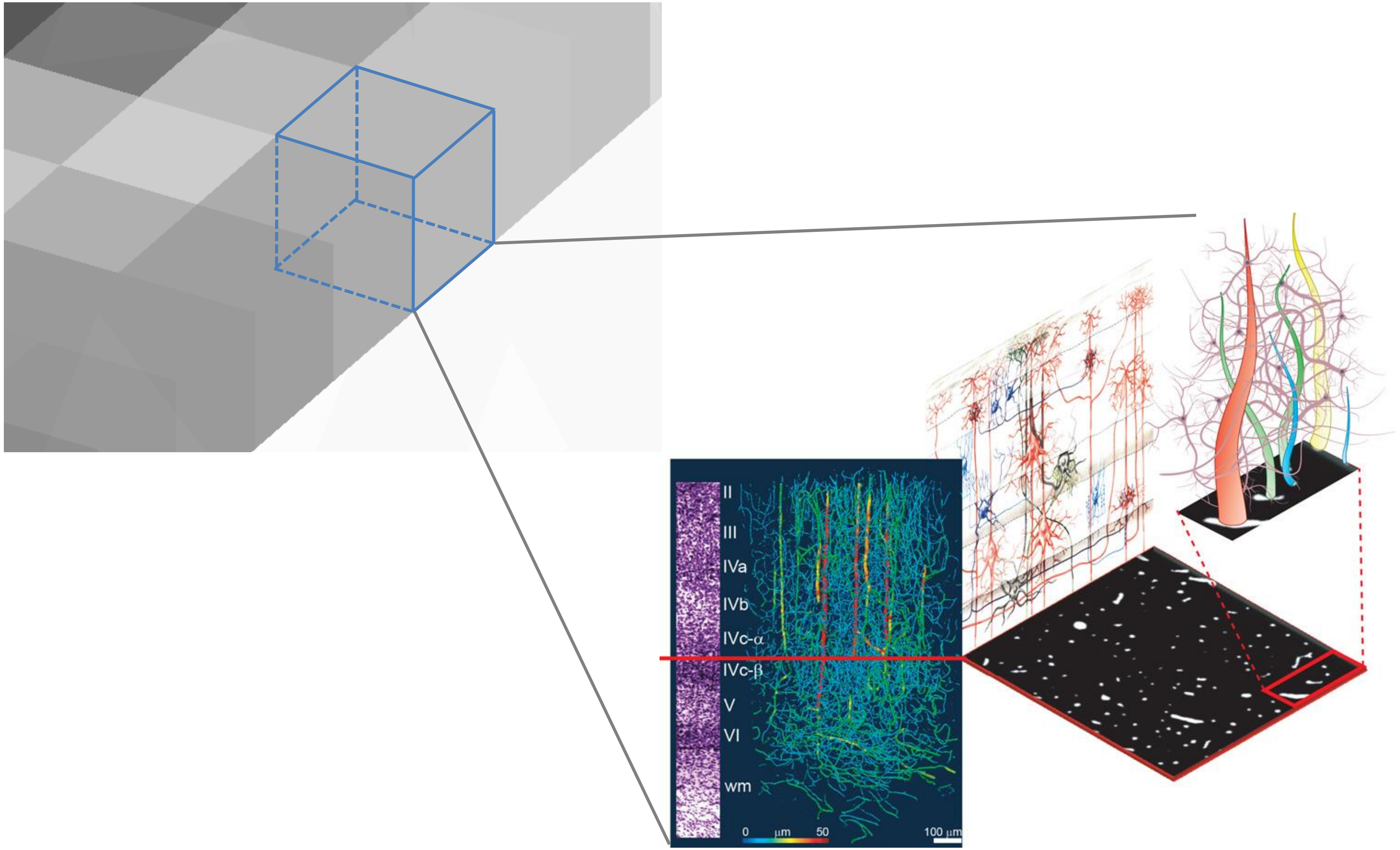
File size:
Header = 352 B
Image data = 91 × 109 × 91 × 8 bits
Total = 352 B + 902,629 B
= 902,981 B
= 0.86 MB

MRI image composed of voxels

– 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

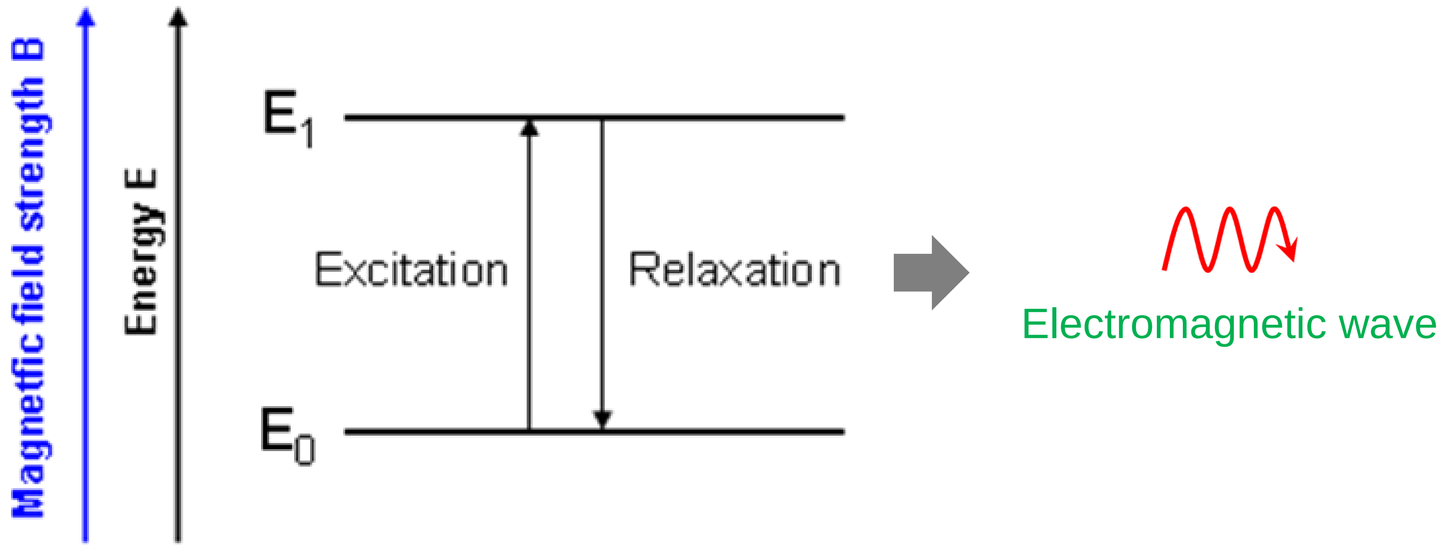


[Logothetis, 2008]

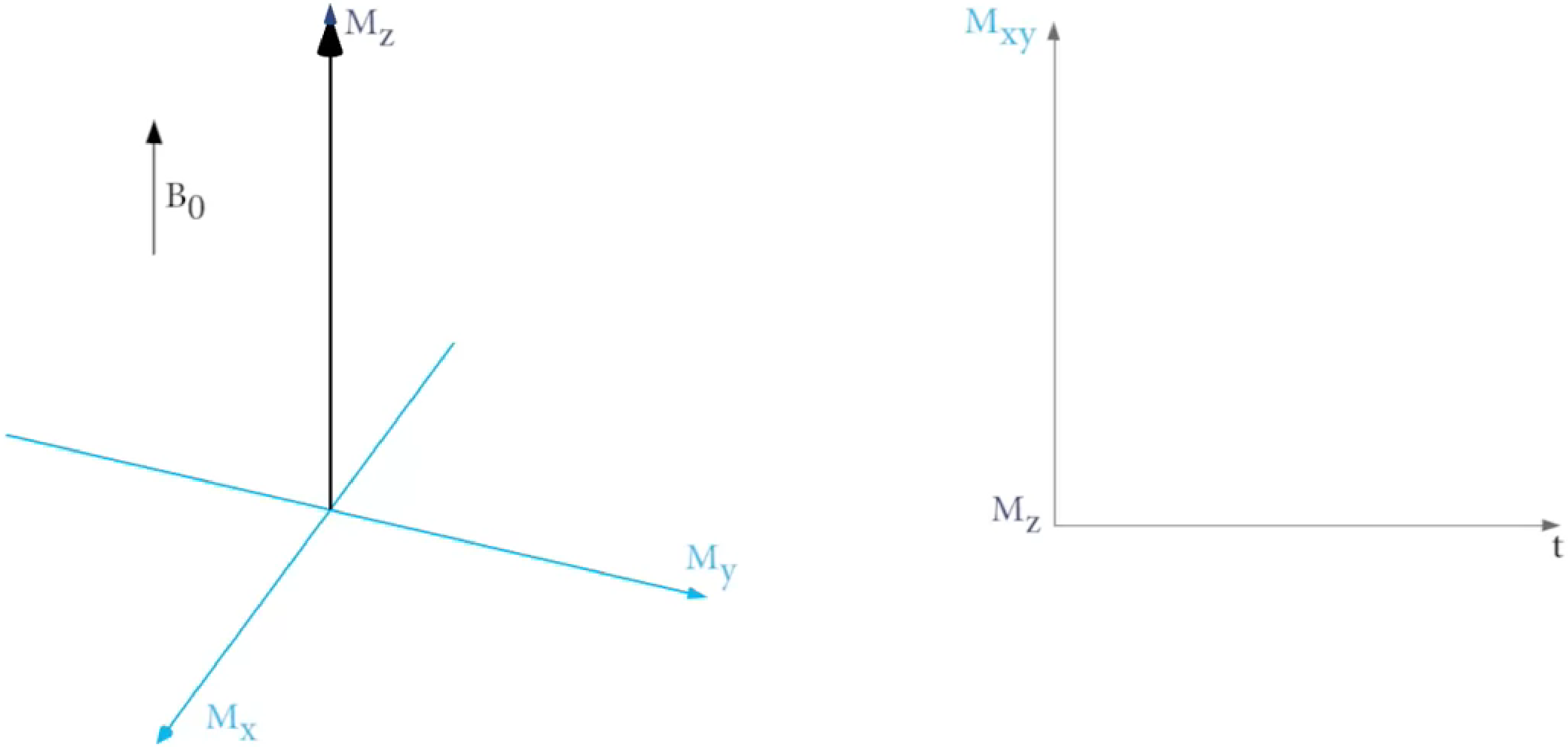
Neuronal and vascular contents within a voxel

Magnetic Resonance Imaging (MRI)

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

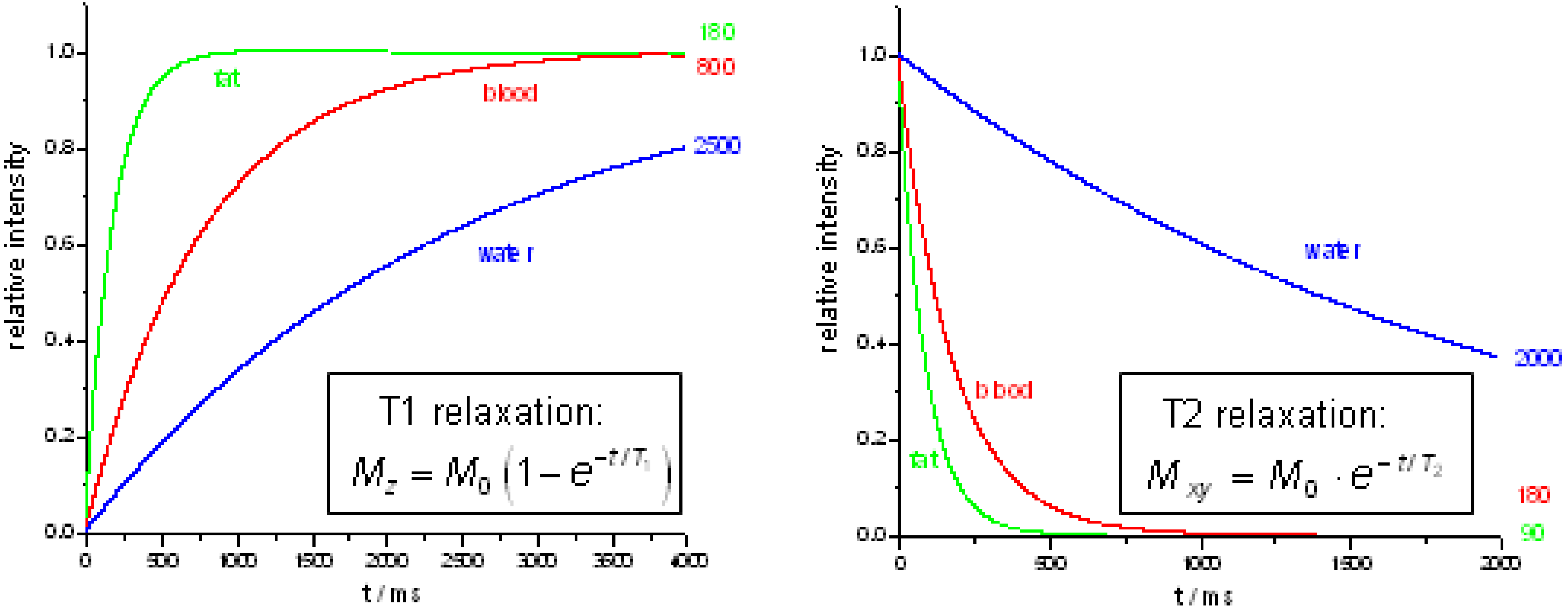


- Two different relaxation times
  - T1 (longitudinal relaxation time)
    - Time taken for hydrogen nuclei to realign with the external magnetic field
    - Spin-lattice relaxation time: time taken for the longitudinal magnetization to recover 63% (1-(1/*e*)) of its initial value
    - Water-based tissues in the 400-1200 ms range; fat-based tissues in the 100-150 ms range
  - T2 (transverse relaxation time)
    - Time taken for hydrogen nuclei to lose phase coherence among the nuclei
    - Spin-spin relaxation time: time taken for the transverse magnetization to irreversibly decay to 37% (1/*e*) of its initial value
    - Water-based tissues in the 40-200 ms range; fat-based tissues in the 10-100 ms range



[https://en.wikipedia.org/wiki/Spin-spin_relaxation]

T1 and T2 relaxation times



[Pollacco, 2016]

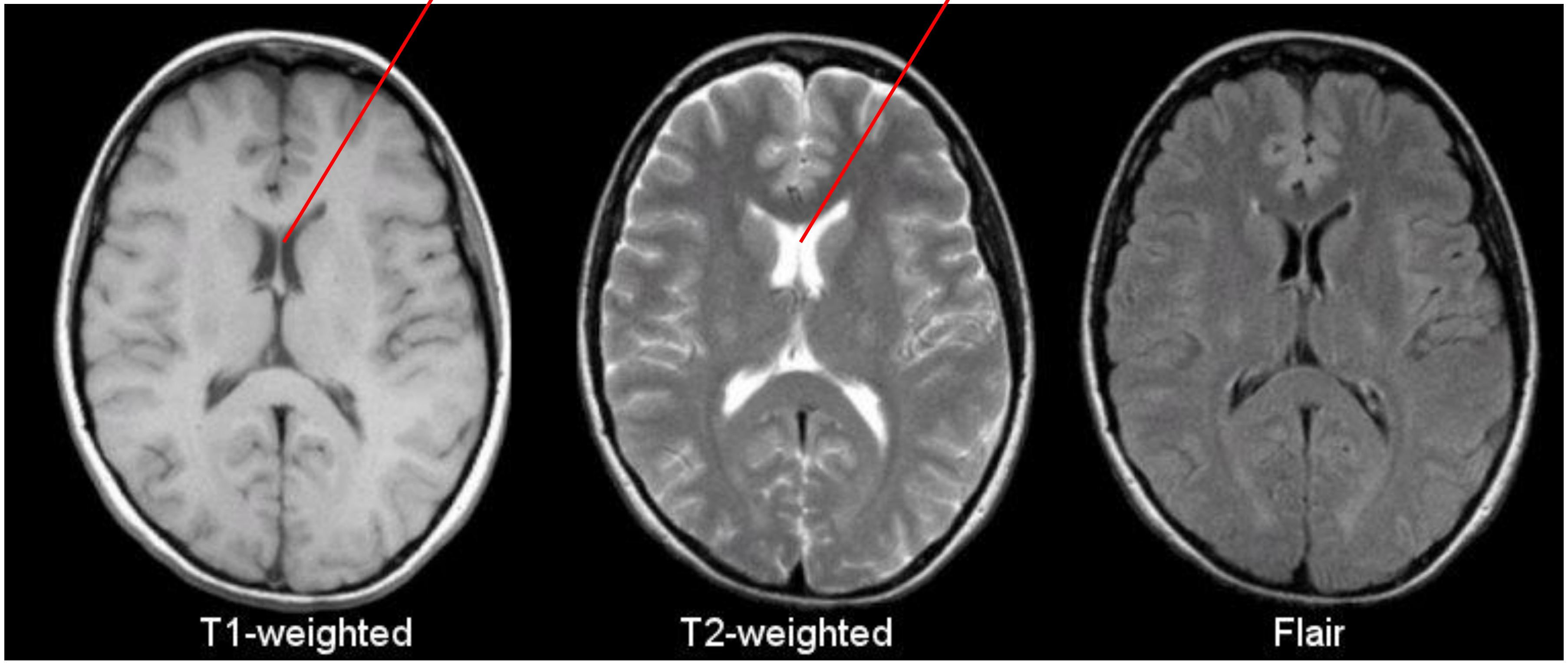
Differences in T1 and T2 relaxation times between tissues

Structural MRI (sMRI)

- MRI technique primarily for examining the anatomy and pathology of the brain
  - T1-weighted
  - T2-weighted
  - Fluid Attenuated Inversion Recovery (FLAIR)

Cerebrospinal fluid as dark

Cerebrospinal fluid as bright



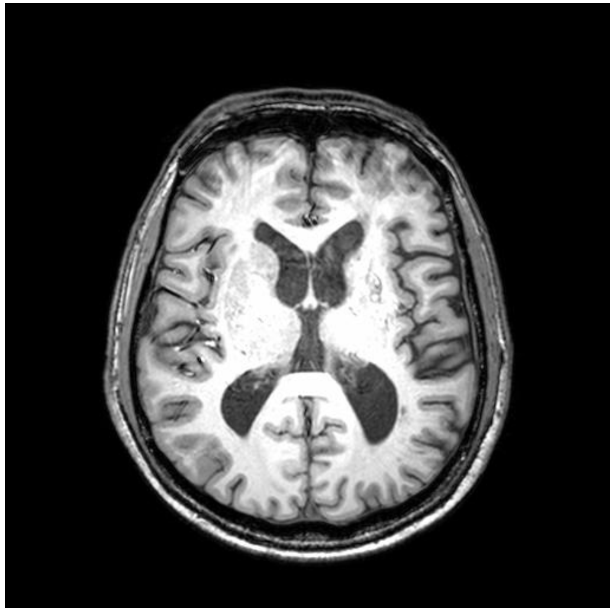
[https://case.edu/med/neurology/NR/MRI Basics.htm]

Comparison between T1-weighted, T2-weighted, and FLAIR images

- T1-weighted contrast

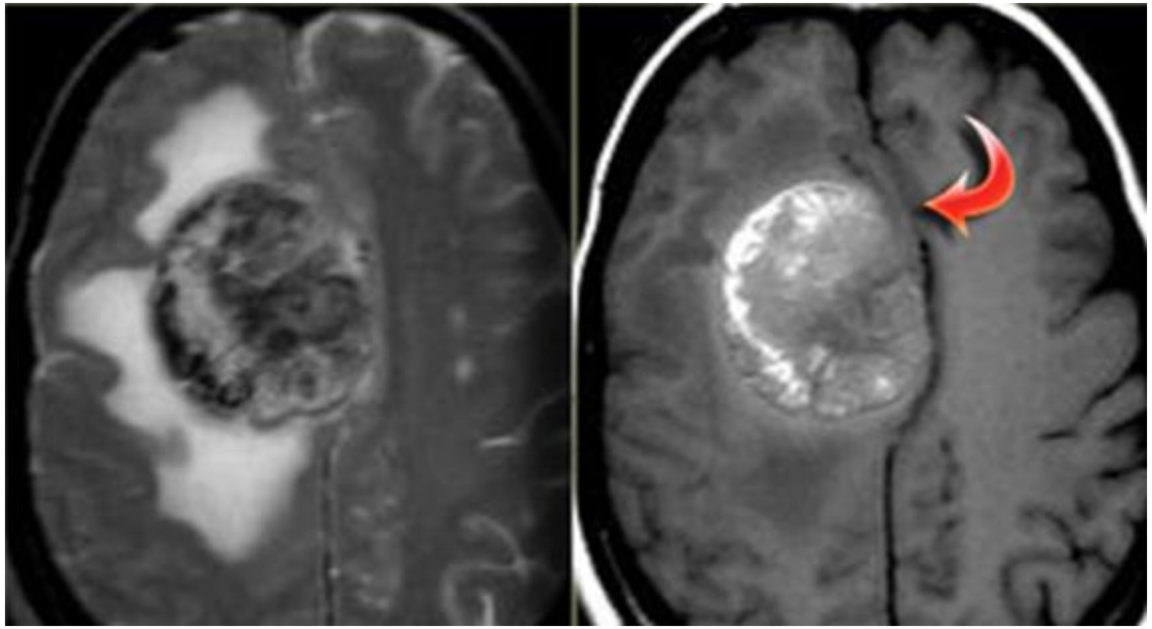
- White matter (nerve fibres) has a very short T1 and relaxes rapidly
- Cerebrospinal fluid has a long T1 and relaxes slowly
- Grey matter (neuron congregations) has an intermediate T1 and relaxes at an intermediate rate

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

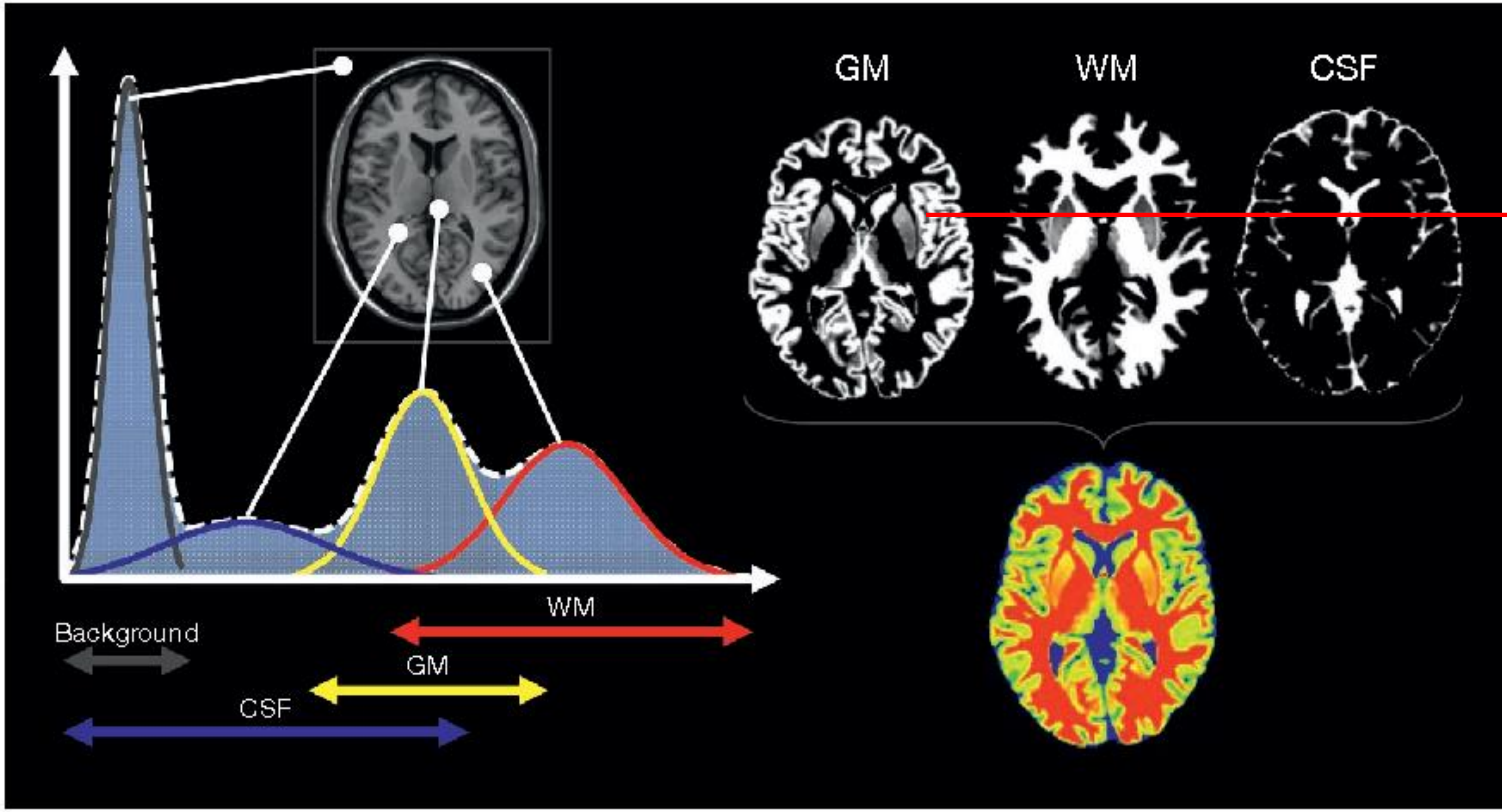
- Abnormality detection
  - Brain lesion
    - Region that has been damaged by an injury or a disease
    - Disrupts the way the brain works, causing a wide range of symptoms



[https://radiologyassistant.nl/neuroradiology/brain-tumor/systematic-approach]

Brain tumour (melanoma metastasis) on T2-weighted and T1-weighted images

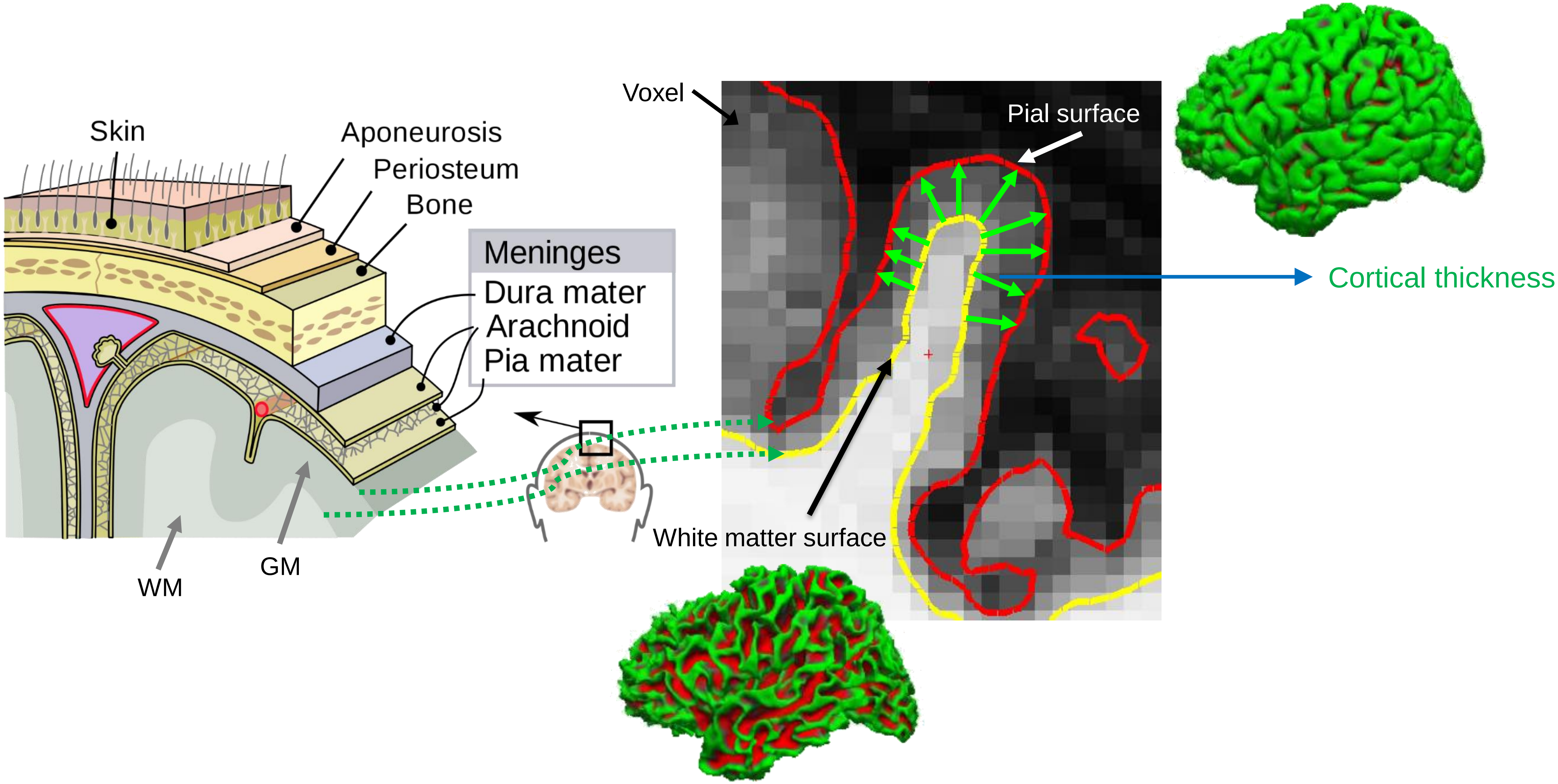
- Brain morphometry
  - Measurement of brain structures
    - Voxel-based morphometry (VBM)
      - Local differences in density or volume
      - Given that, after the segmentation of an image, each voxel contains a measure of the probability according to which it belongs to a specific segmentation class
    - Surface-based morphometry (SBM)
      - Local differences in thickness or gyrification
      - Given that, after the segmentation of an image, the boundary between different segmentation classes can be reconstructed as a surface



Grey matter volume

[Kurth et al., 2015]

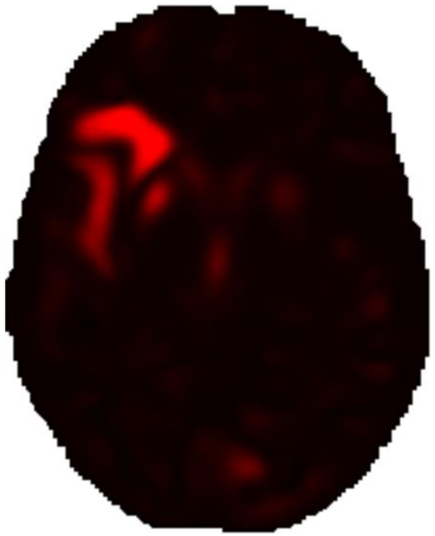
Voxel-based morphometry



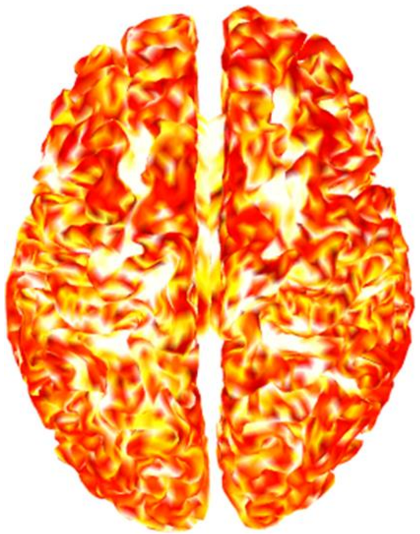
[https://www.physio-pedia.com/Meninges]

Surface-based morphometry

- Maps from sMRI



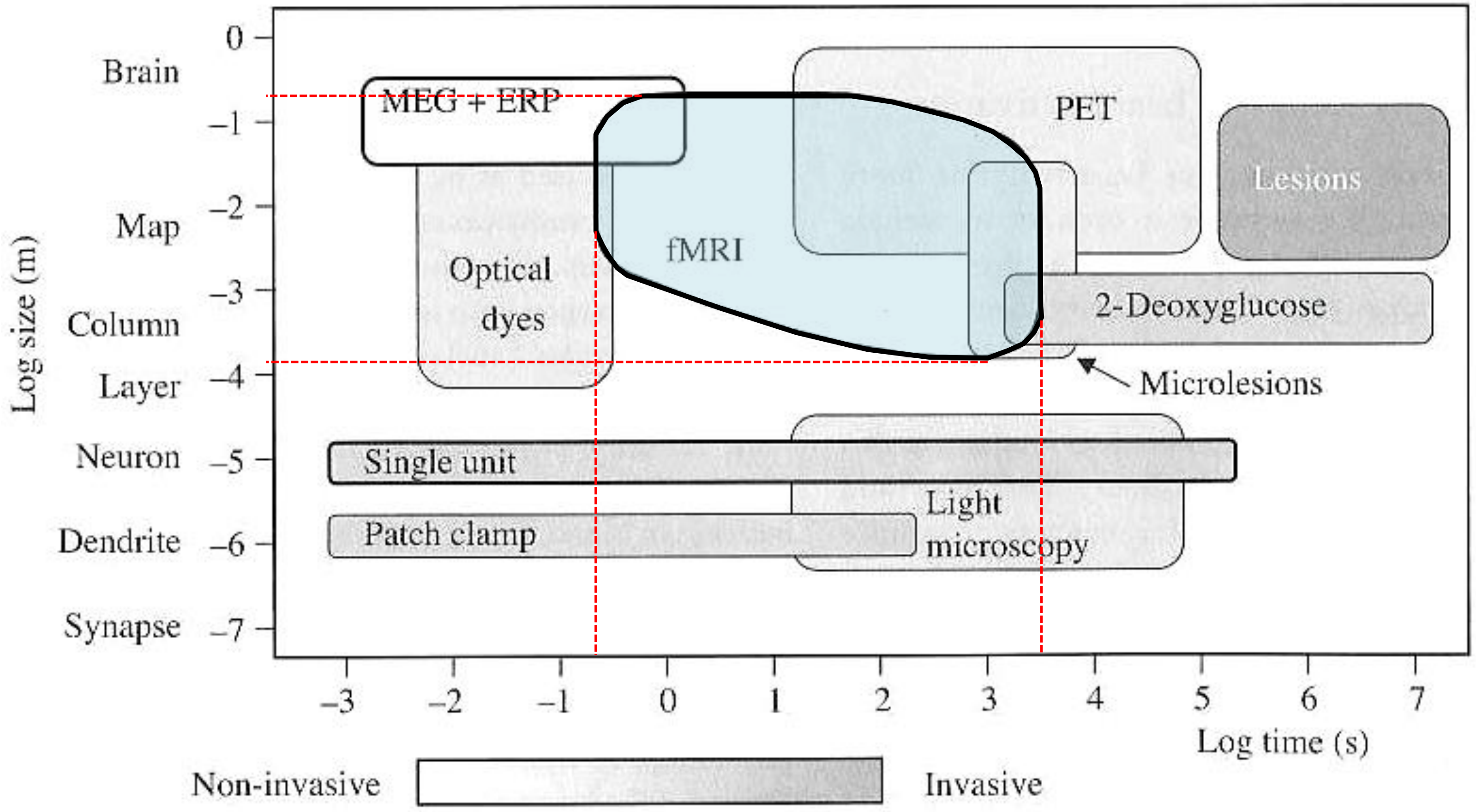
Lesion



Brain tissue volume

Functional MRI (fMRI)

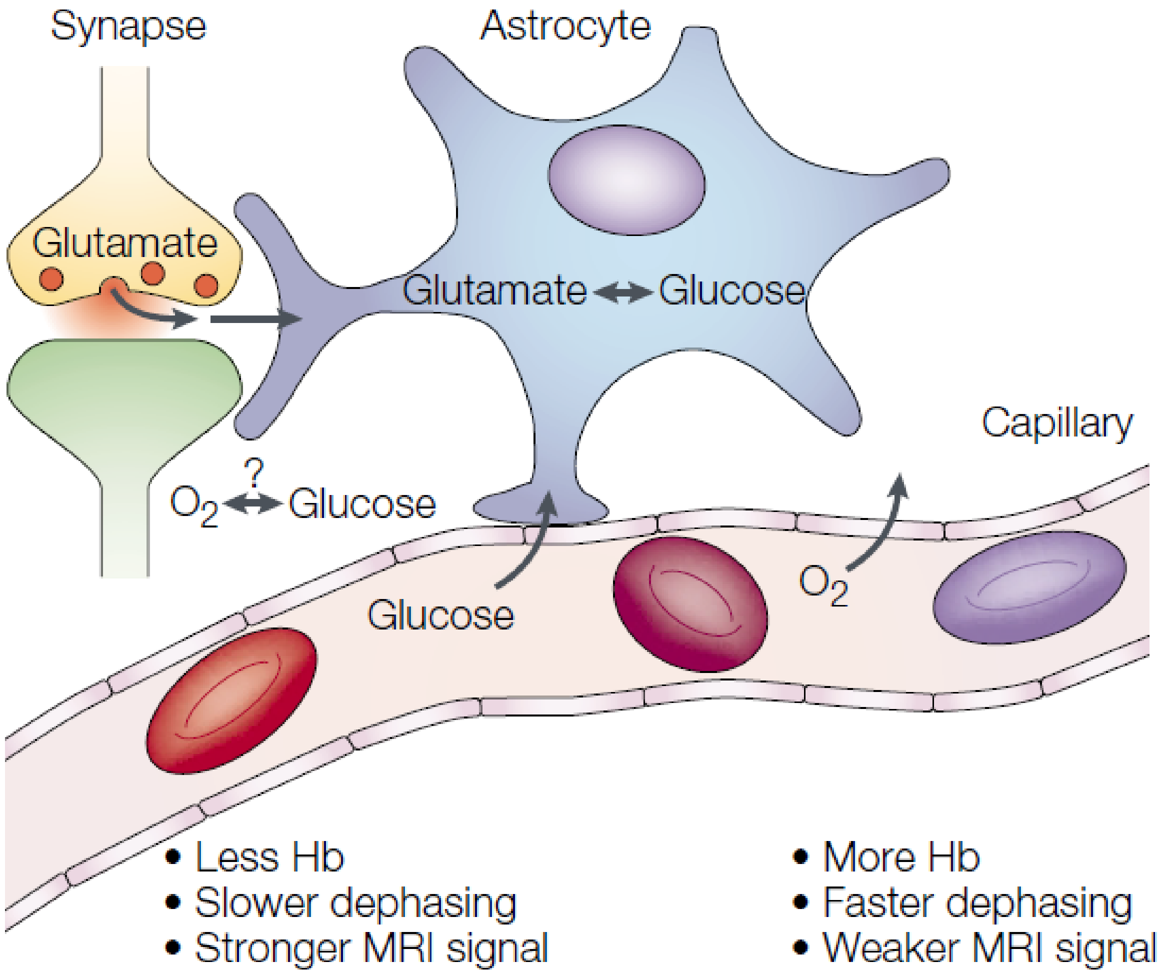
- MRI technique primarily for measuring brain activity
- Relies on the coupling between haemodynamics (changes in blood flow, blood volume, and blood oxygenation) and neuronal activity

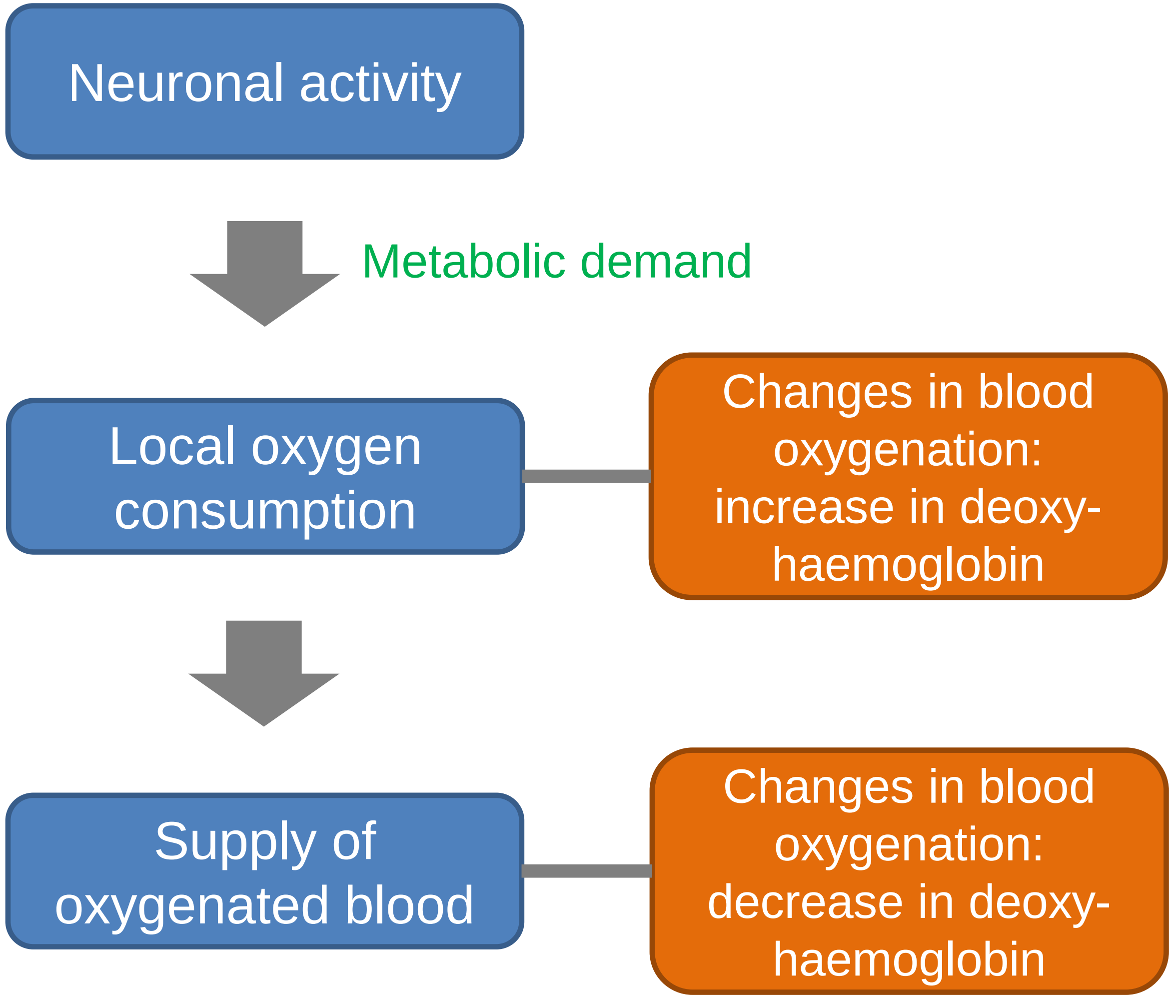


[Churchland and Sejnowski, 1988]

fMRI in comparison with other neuroscience methods

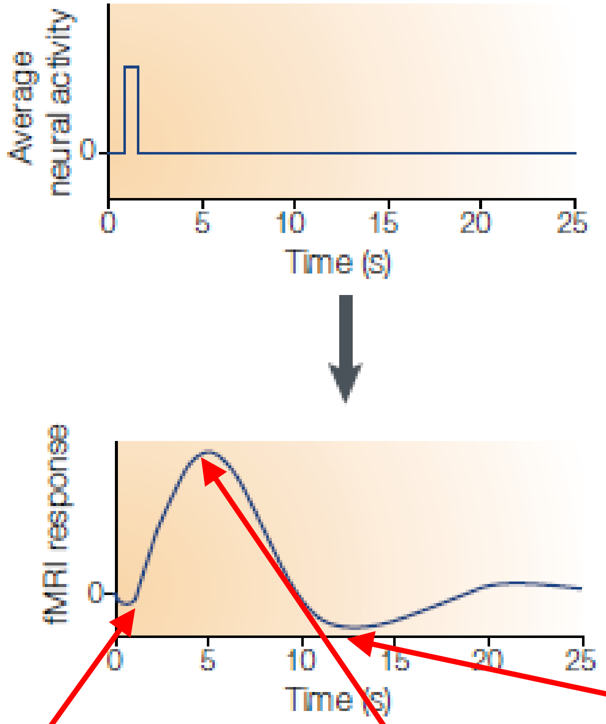
- Blood-oxygen-level dependent (BOLD) contrast
  - Exploits different electromagnetic properties between blood containing oxygen (oxyhaemoglobin) and blood without oxygen (deoxyhaemoglobin)
  - Based on the assumption that the changing distribution of blood oxygenation in the brain correlates with neuronal activity





[Heeger and Ress, 2002]

Coupling between haemodynamics and neuronal activity

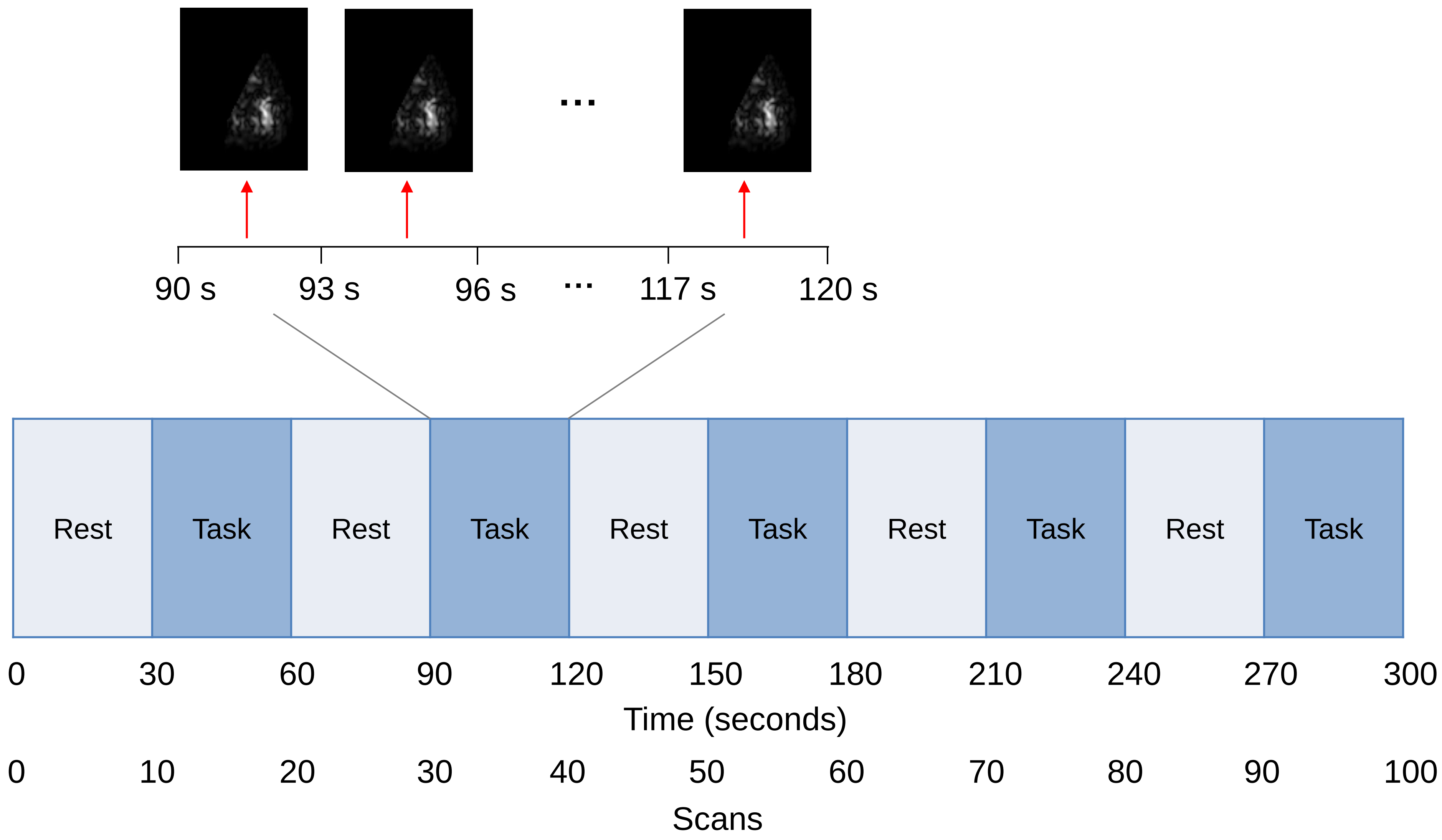


	Phase 1	Phase 2	Phase 3
Haemodynamics	Consumption of local oxygen	Oversupply of oxygenated blood	Diminished oversupply of oxygenated blood
fMRI signal	Small decrease below baseline	Large increase above baseline	Decrease back to below baseline

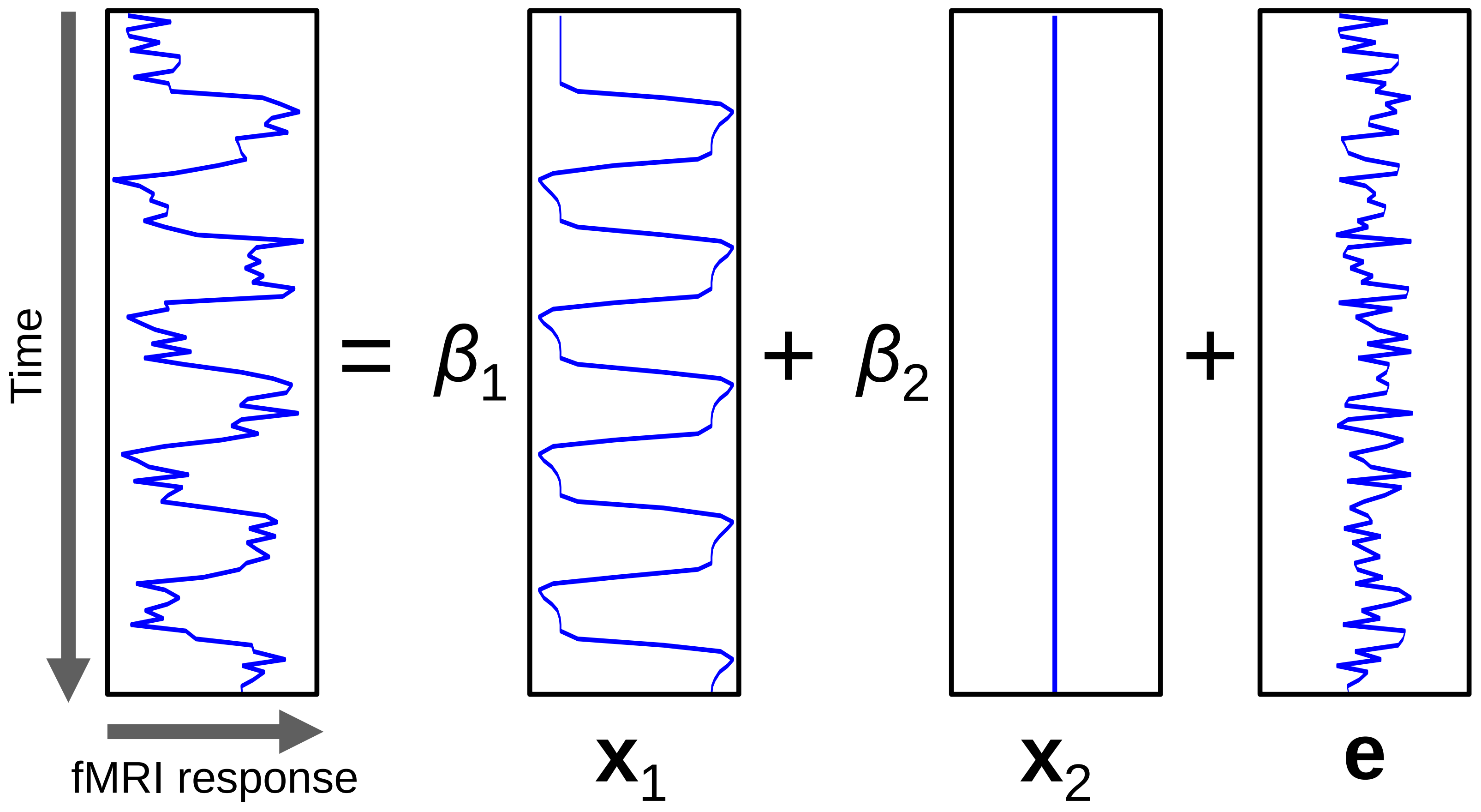
[Heeger and Ress, 2002]

Three phases of a BOLD fMRI response

- Experimental fMRI
  - Task-based fMRI
    - Given an overt task or external stimuli
  - Resting state fMRI
    - With wakefulness maintained but structural thinking (e.g., counting) avoided

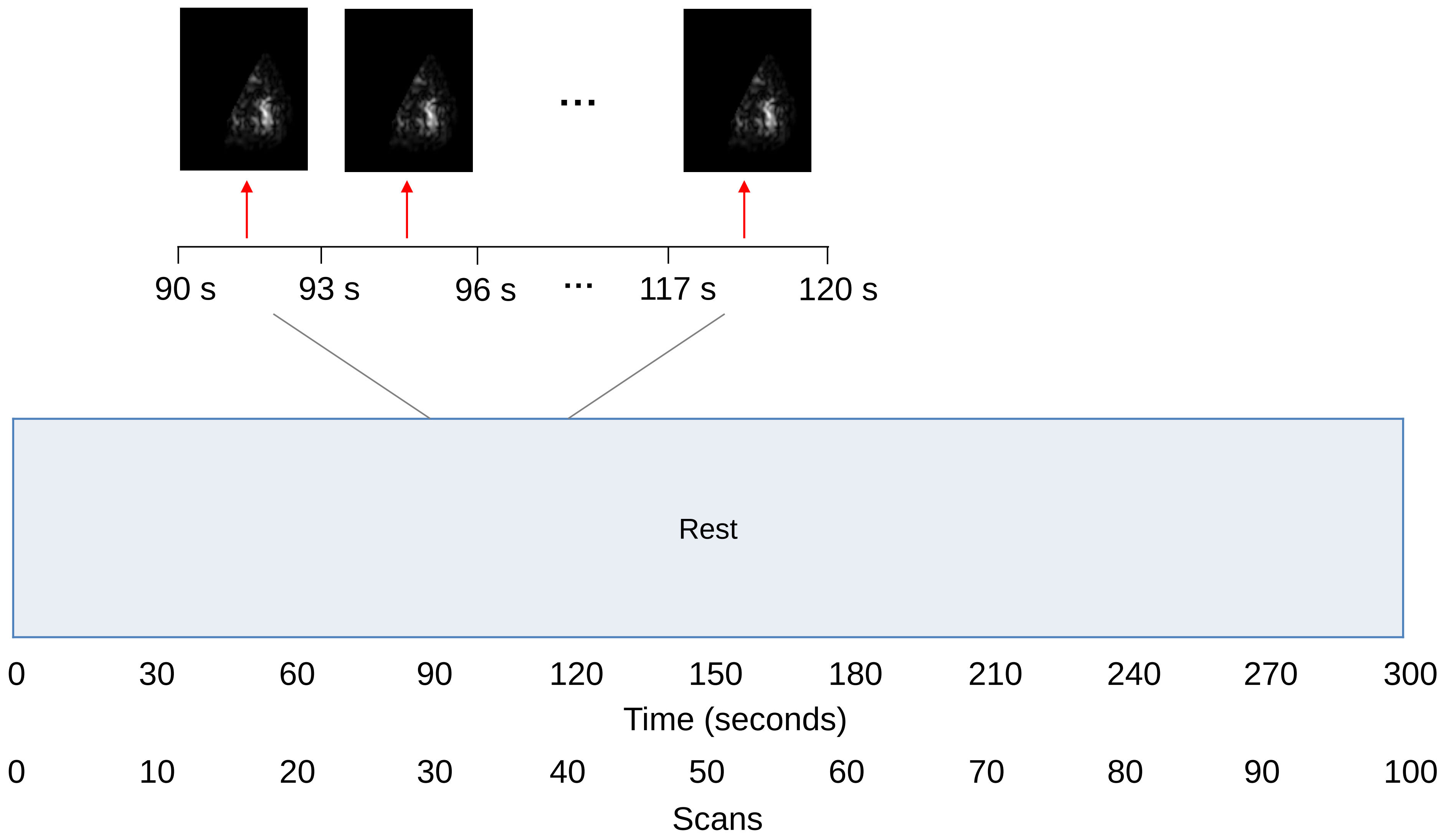


Example of task-based fMRI



$$\boldsymbol{y} = \boldsymbol{X}\boldsymbol{\beta} + \boldsymbol{e} = \boldsymbol{x}_1\boldsymbol{\beta}_1 + \boldsymbol{x}_2\boldsymbol{\beta}_2 + \boldsymbol{e}$$

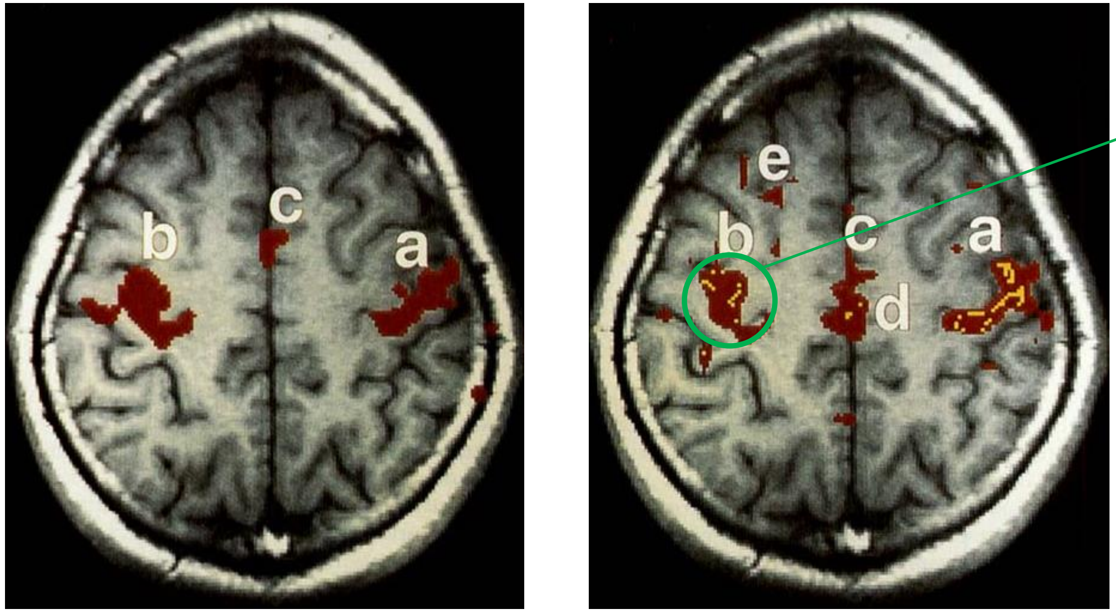
General linear model for inferring brain activation from task-based fMRI



Example of resting state fMRI

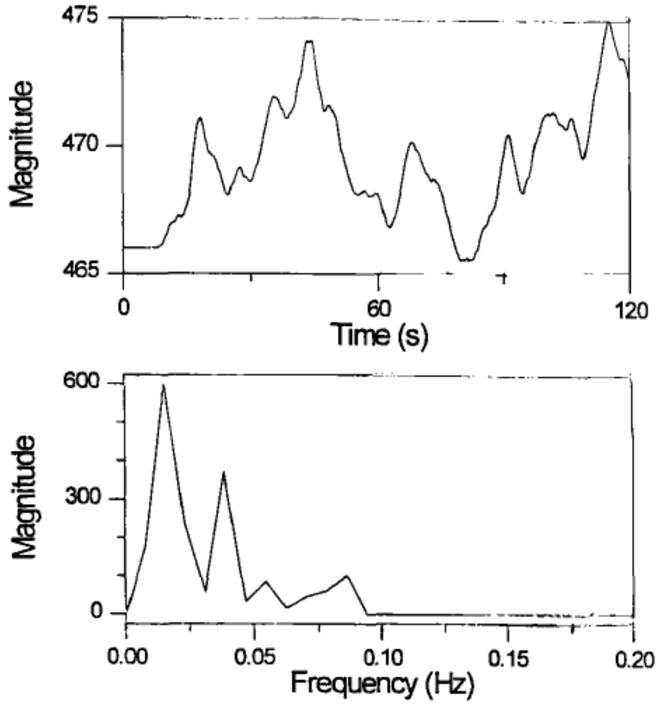
Task-based fMRI

Resting state fMRI



Finger movement-
induced activation

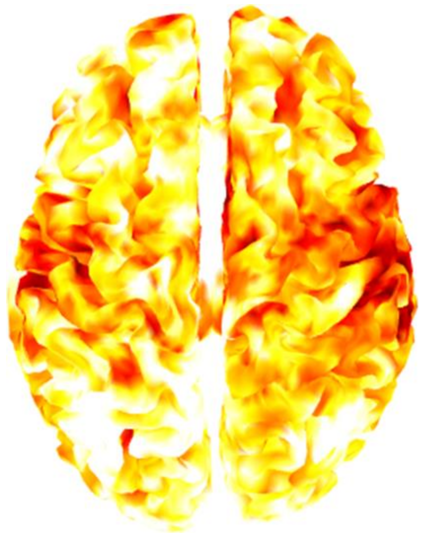
Correlation with the
representative time series



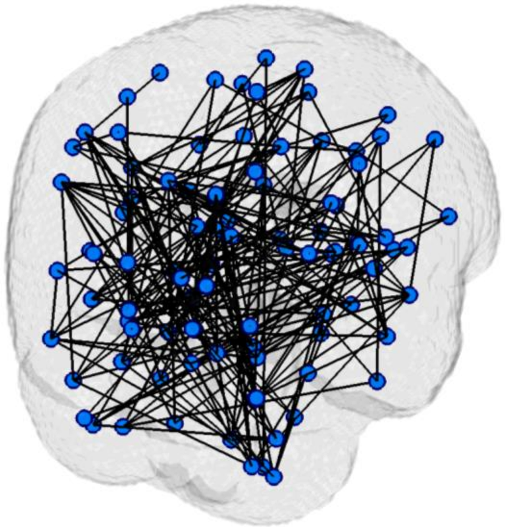
[Biswal et al., 1995]

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

- Maps from fMRI



Brain activation

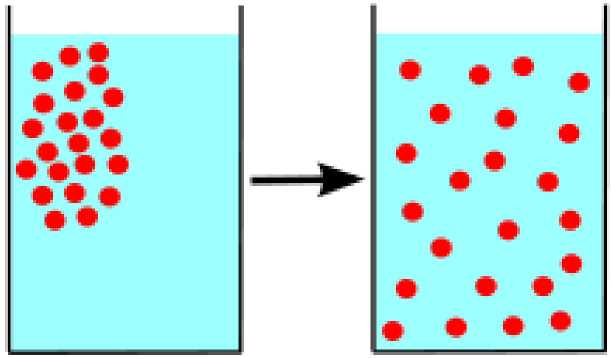


Functional connectivity

Diffusion-weighted MRI (dMRI)

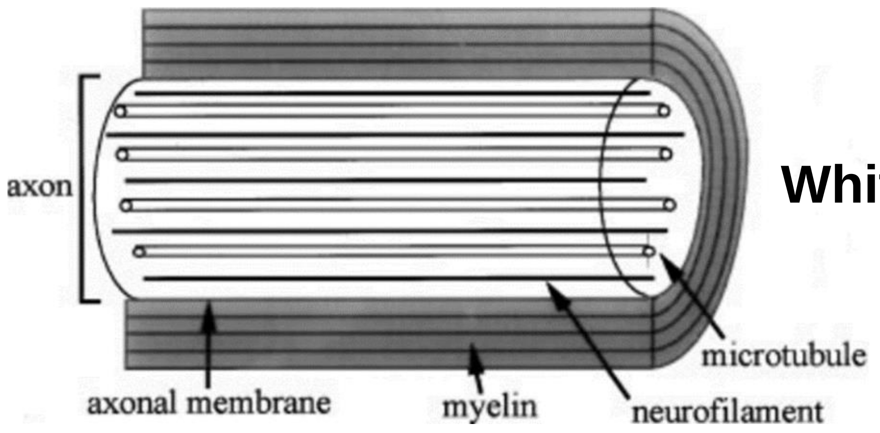
- MRI technique primarily for examining the local microstructure and connectional anatomy of the white matter
- Employs directional characteristics of diffusion

- Diffusion
  - Physical process in which particles tend to spread steadily from regions of high concentration to regions of lower concentration



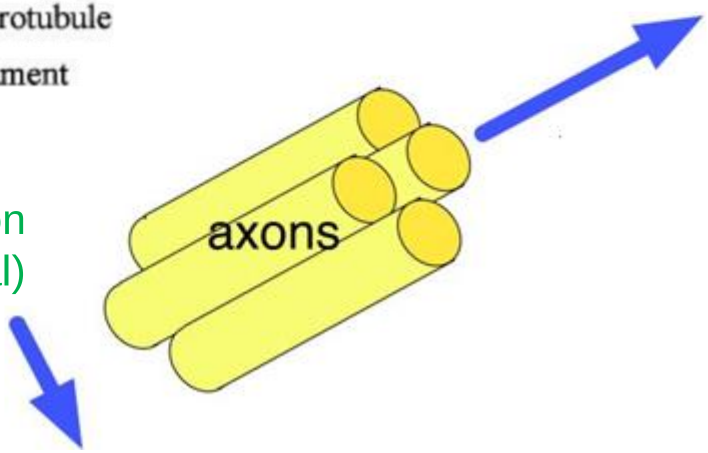
  - Movement of water molecules in a heat-driven random fashion in brain tissues
    - Unless the movement is constrained by barriers

- Diffusion-weighted contrast
  - MRI signal changes caused by diffusion



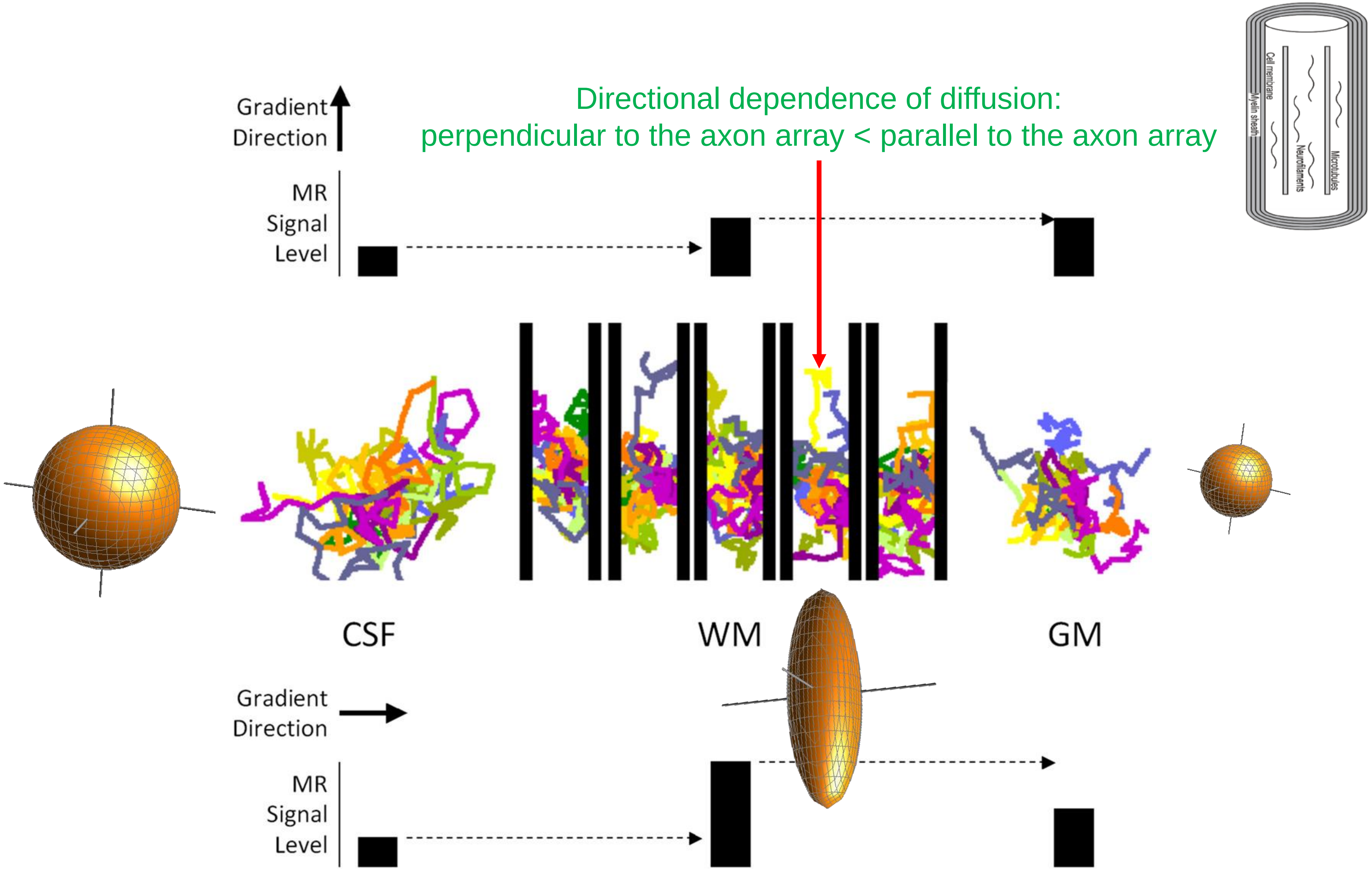
White matter

More diffusion
(More decrease in an MRI signal)



Less diffusion
(Less decrease in an MRI signal)

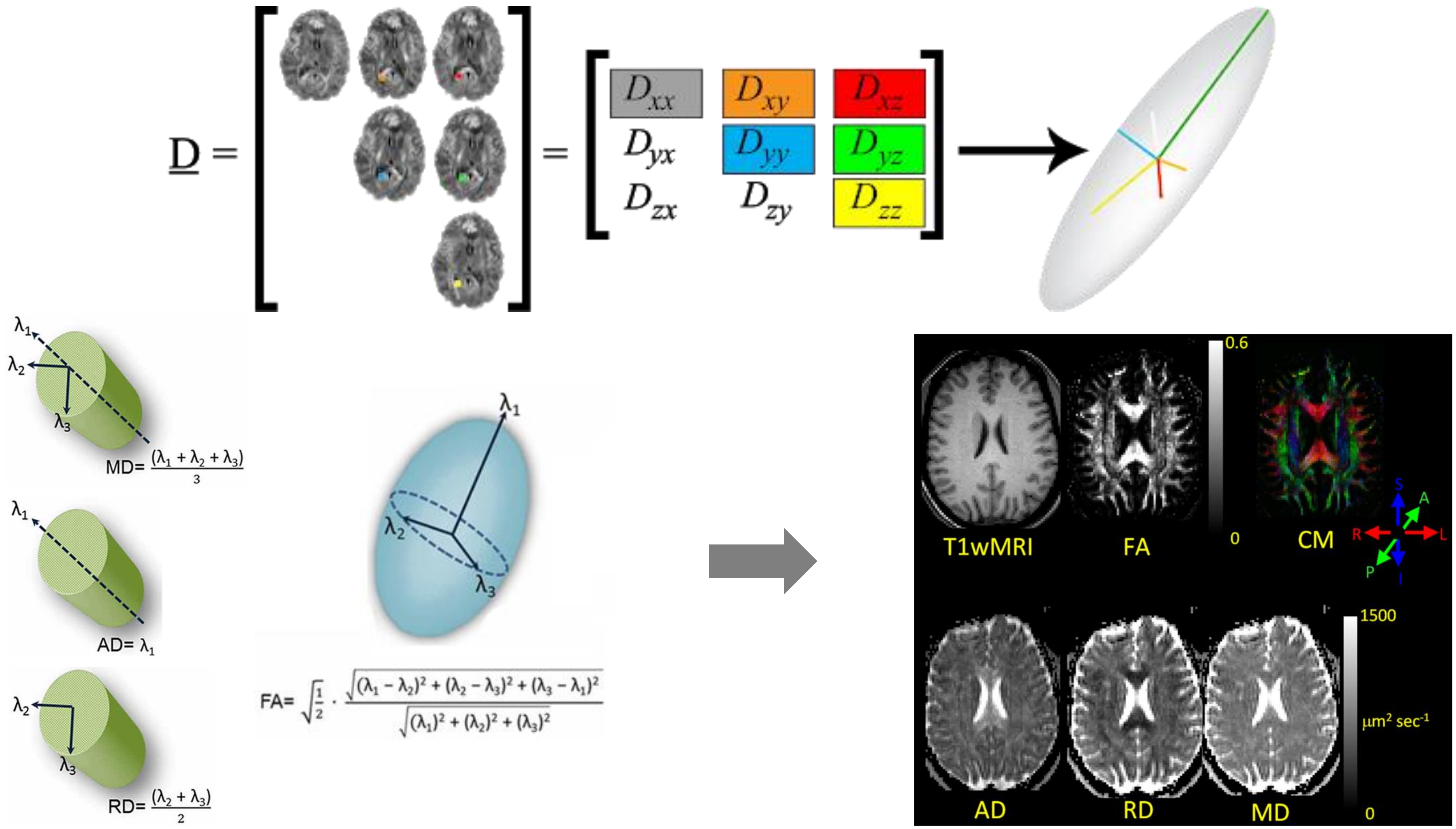
[O'Donnell and Westin, 2011]



[Alger, 2012]

Directional impact of water molecular diffusion on MRI signal changes

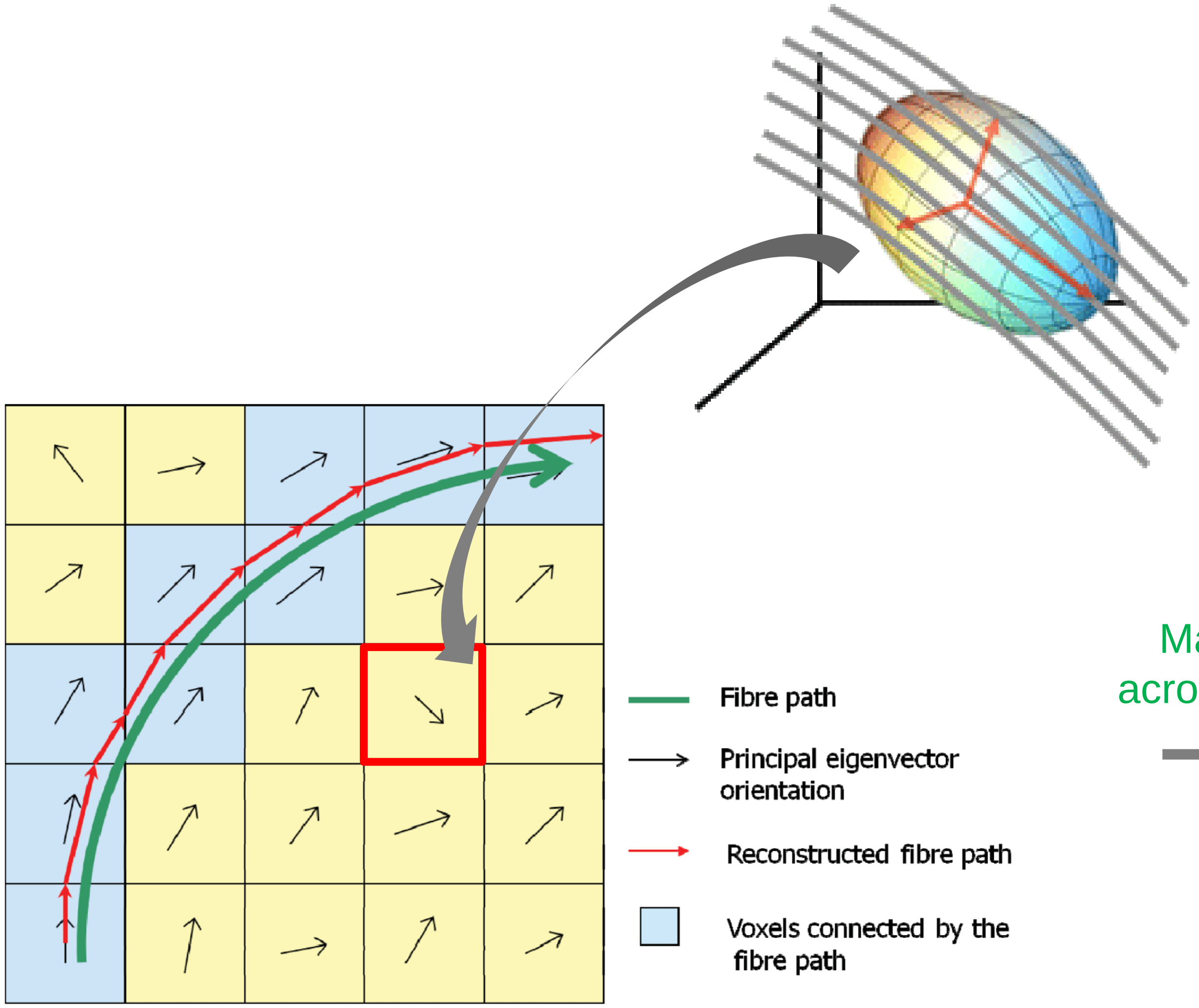
- Diffusion tensor model
  - Represents the directional dependence of water molecular diffusion by a diagonalized matrix (diffusion tensor) or an ellipsoid for each voxel
  - Based on the assumption that the diffusion process can be described by a Gaussian distribution
- Diffusion tensor-derived measures
  - Mean Diffusivity (MD), Axial Diffusivity (AD), and Radial Diffusivity (RD)
  - Fractional Anisotropy (FA)



[DeSouza et al., 2016; Alger, 2012]

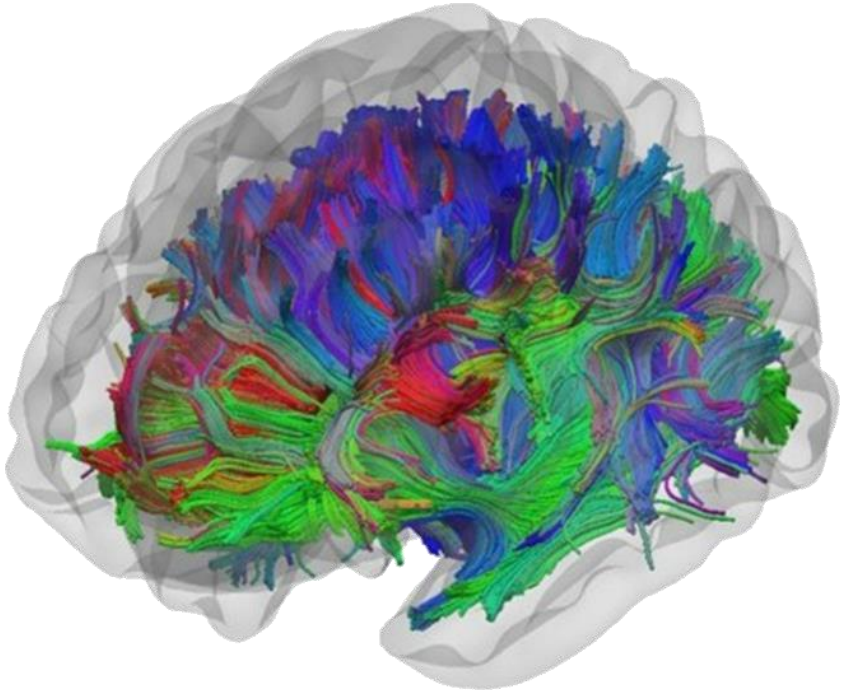
Diffusion tensor-derived measures

- White matter tractography
  - Based on how strongly and in what directions water molecules diffuse given physical constraints in the brain
  - Generates streamlines from the continuity in the local estimates of fibre directions as a proxy of white matter connectivity
    - Deterministic vs. probabilistic approaches



Streamlines based on common directions of water molecular diffusion

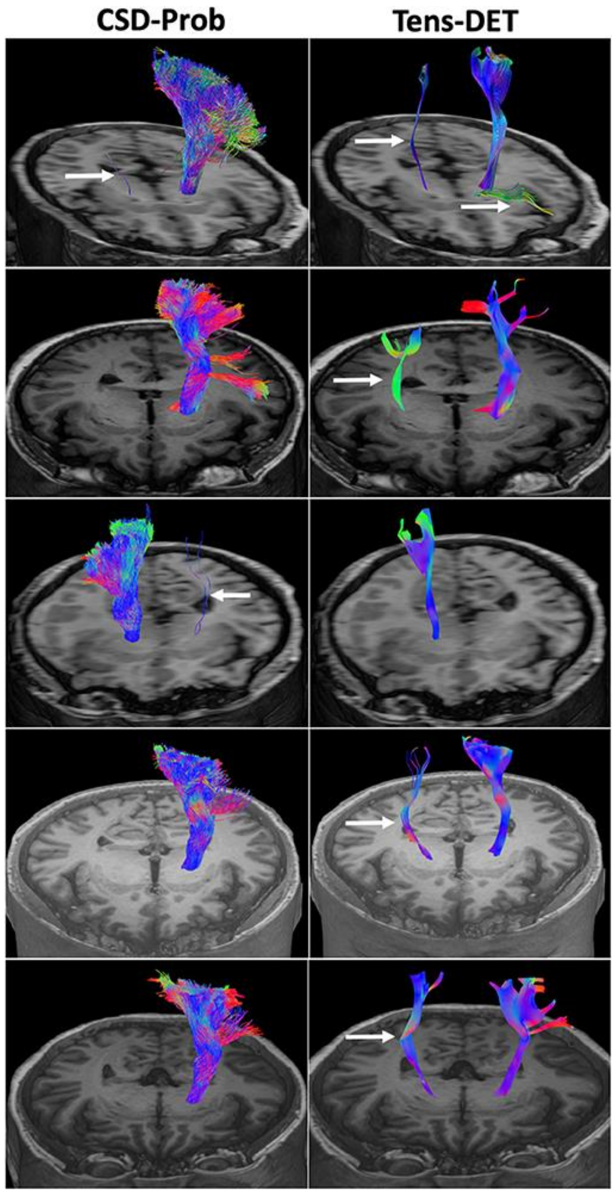
Many times across the brain



White matter tractogram

[Geva et al.,2011]

White matter tractography

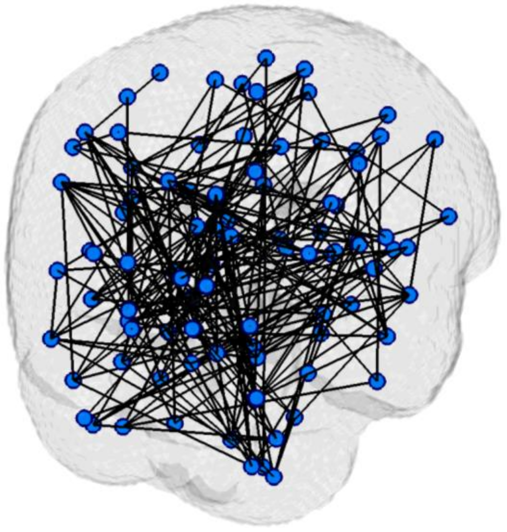


[Sheng et al., 2021]]

Comparison of probabilistic vs. deterministic approaches to white matter tractography

- Maps from dMRI

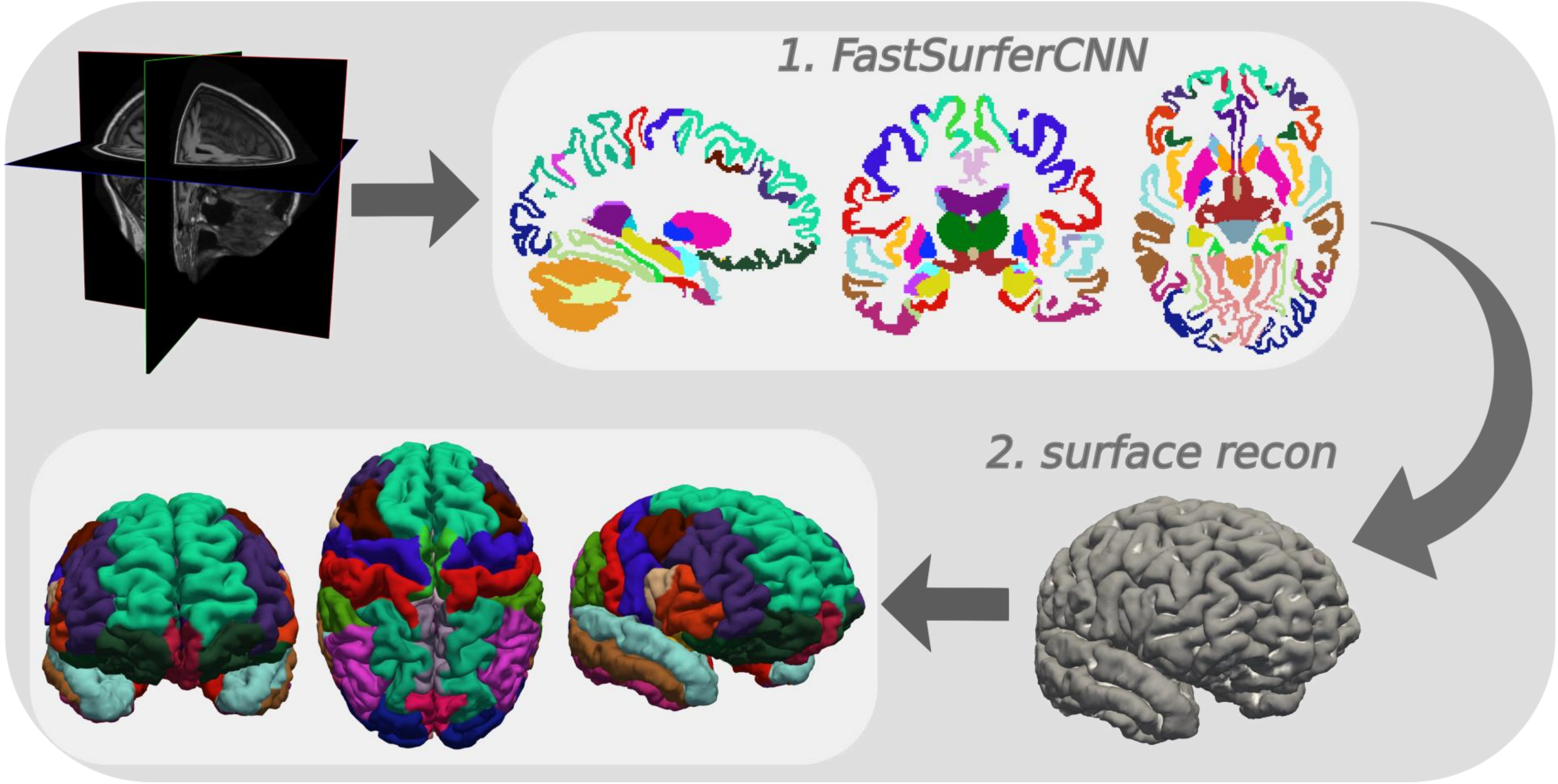
White matter microstructure



Structural connectivity

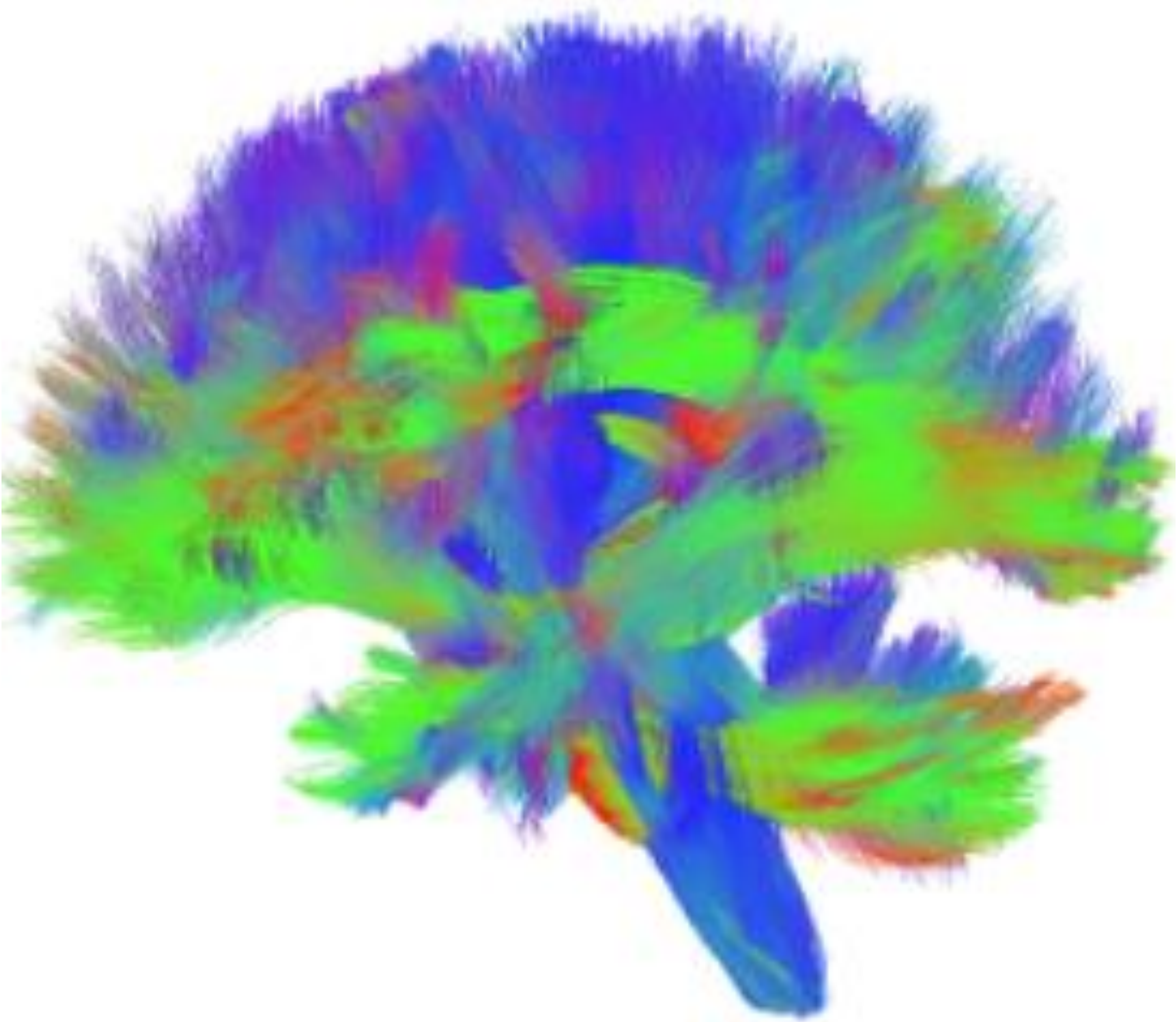
Machine Learning Application of Brain Imaging: Main Challenges

- Developing methodological approaches for analyzing brain imaging data
  - Surface-based morphometry
  - White matter tractography



[https://github.com/Deep-MI/FastSurfer]

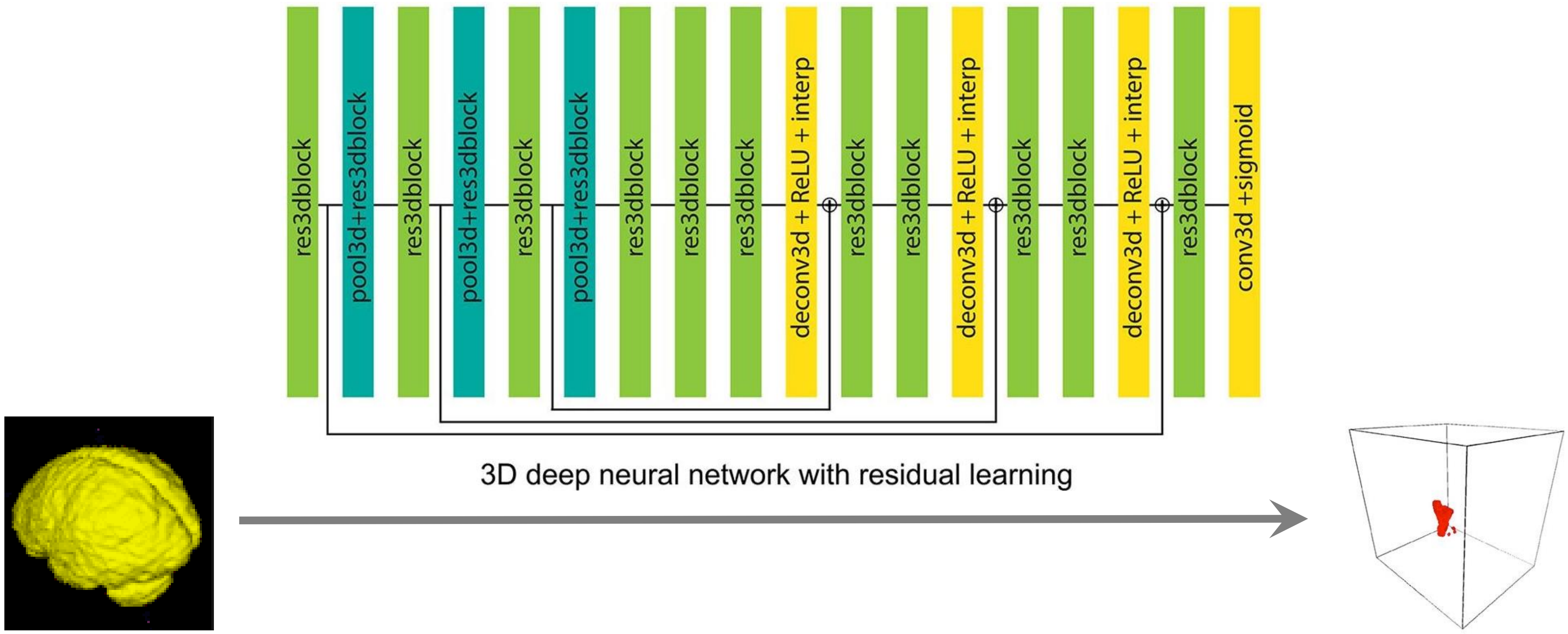
Surface-based morphometry using FastSurfer



[https://github.com/itaybenou/DeepTract]

White matter tractography using DeepTract

- Applying machine learning methods for facilitating the workflow or assisting in prediction in clinical practice
  - Disease detection and management based on the classification, detection, or segmentation of abnormalities in the brain
  - Diagnostic or prognostic prediction

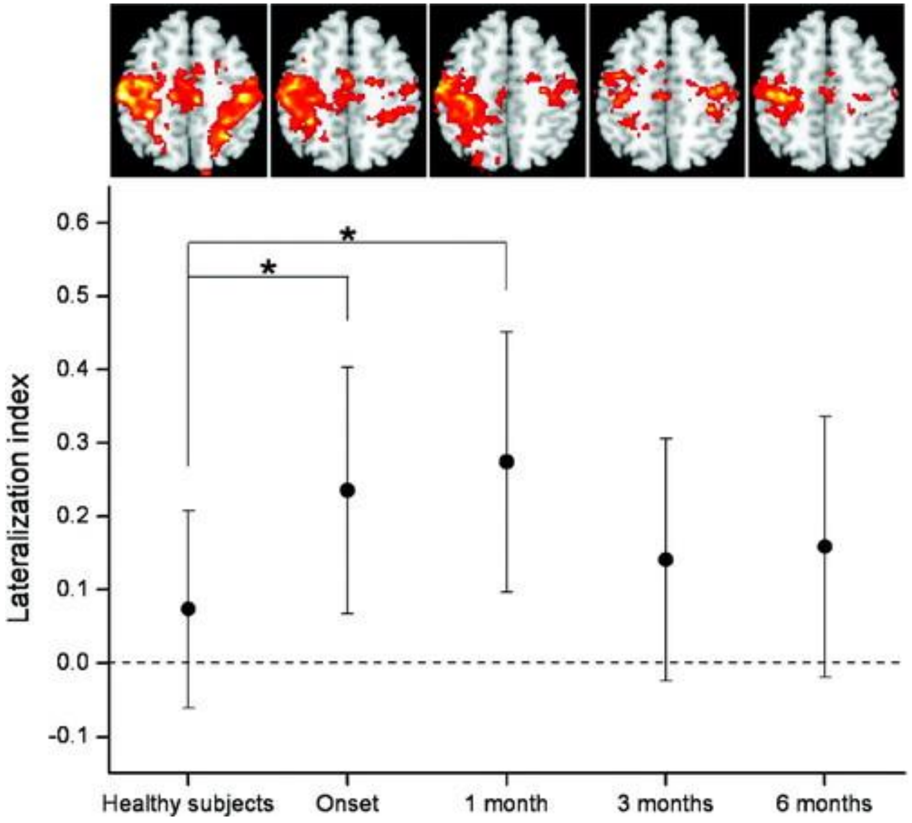


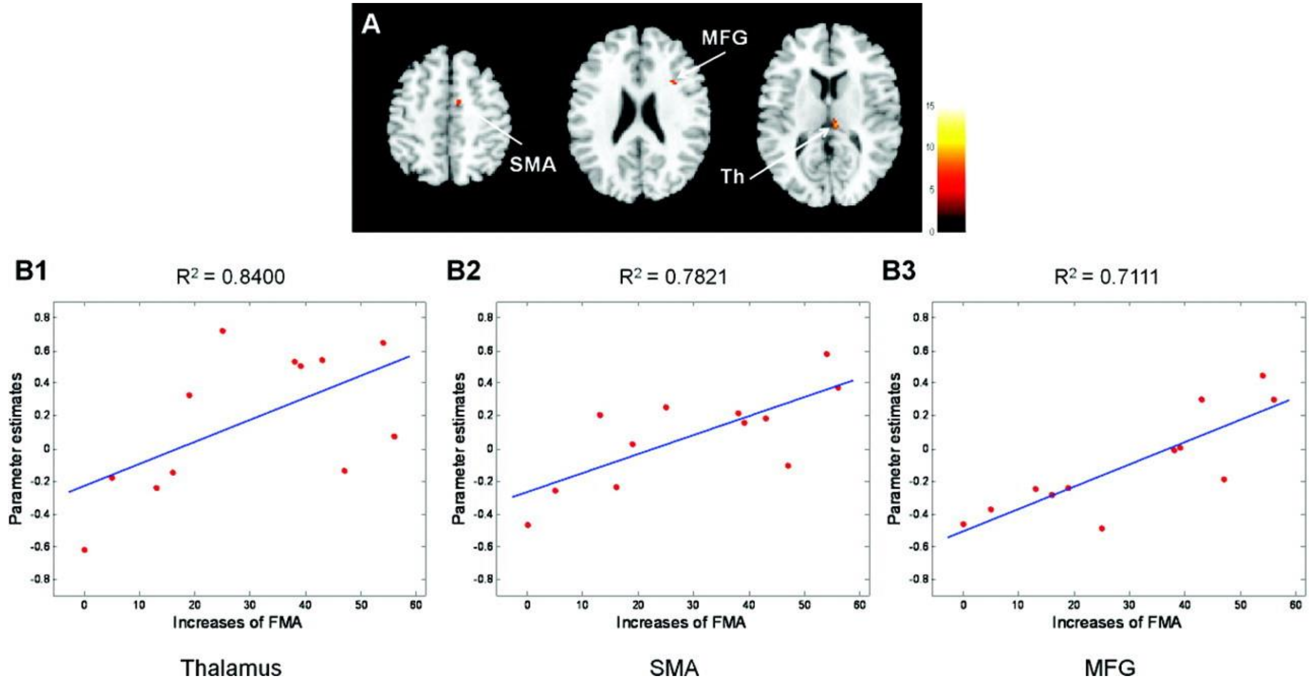
[Tomita et al., 2020]

Automatic segmentation of a stroke lesion

Diagnostic or Prognostic Prediction

- Conventional clinical MRI studies
  - By applying statistical inferences

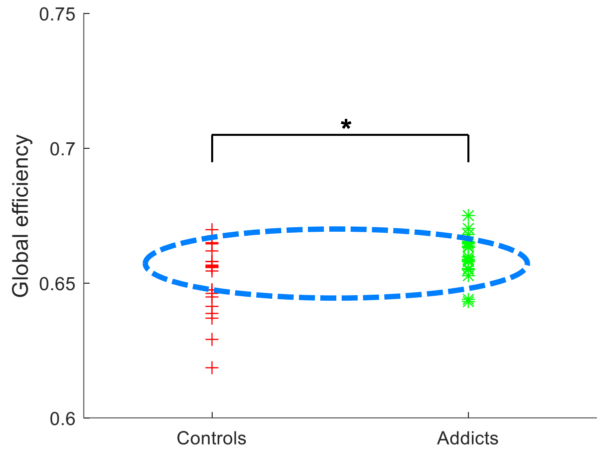


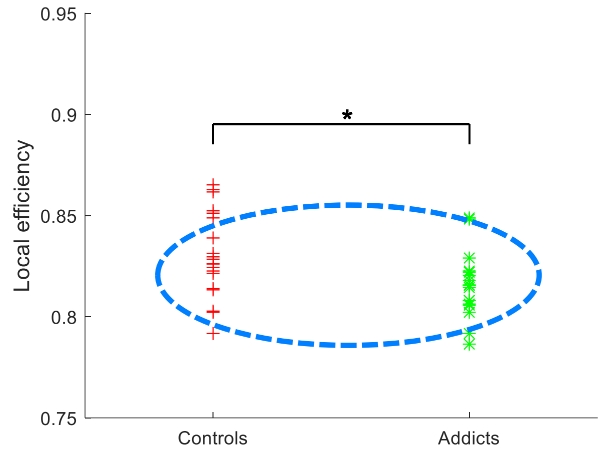


[Park et al., 2011]

Statistical inferences on brain changes after stroke

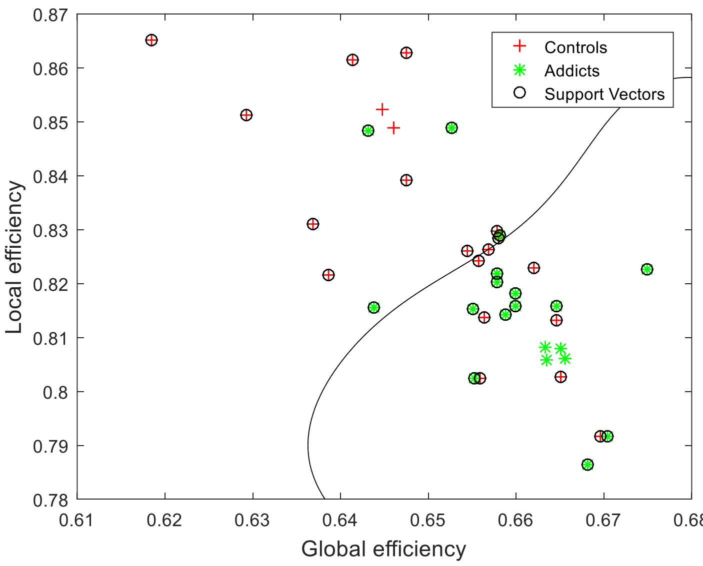
• Classification beyond describing group differences



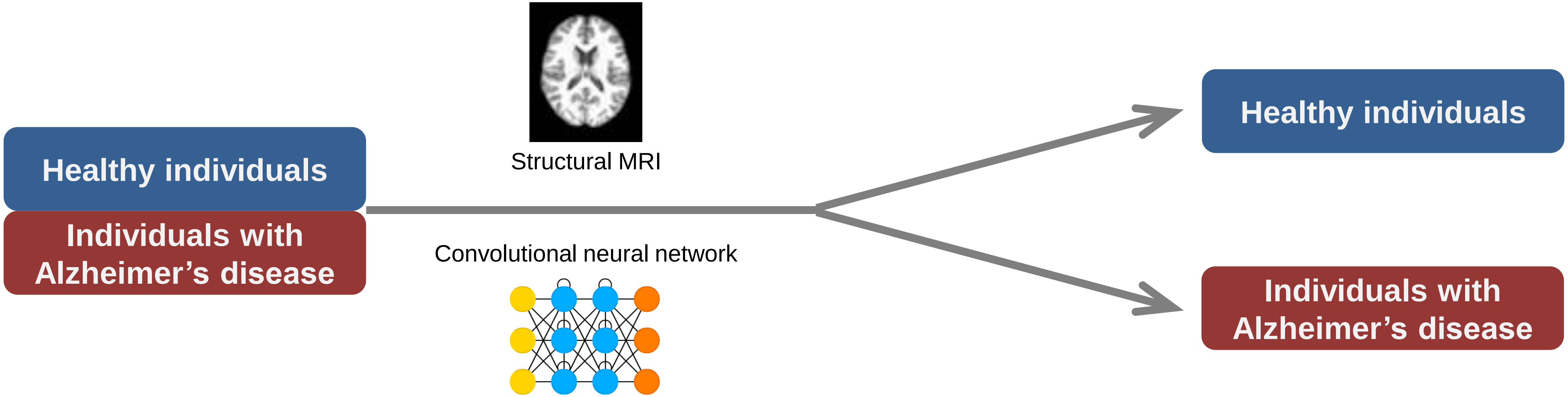


[Park et al., 2017]

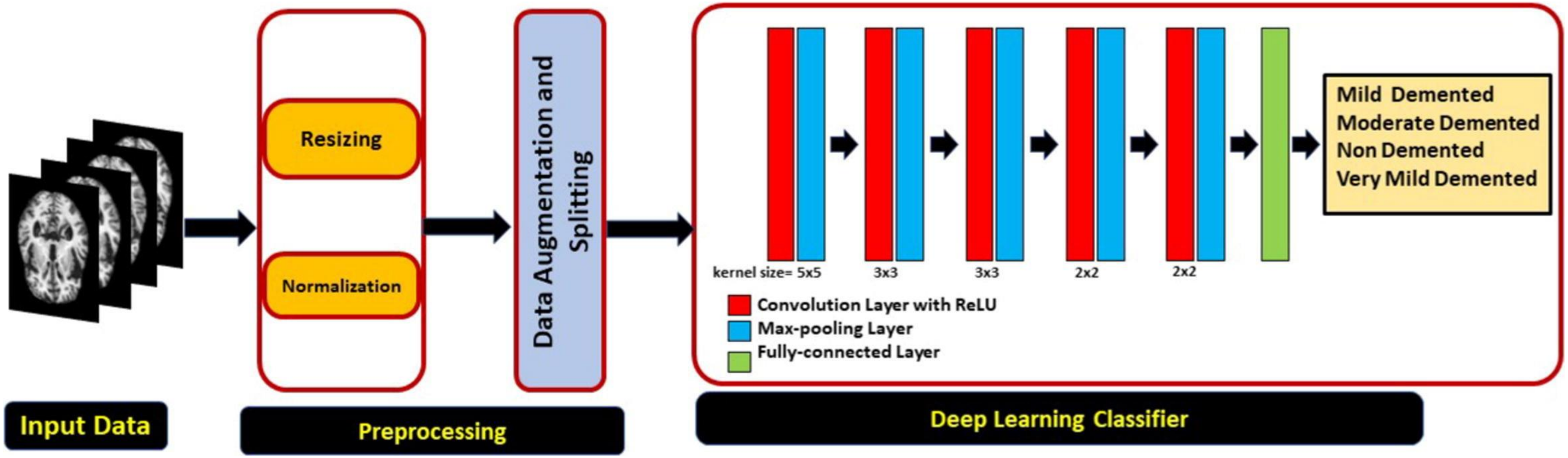
Individualized prediction



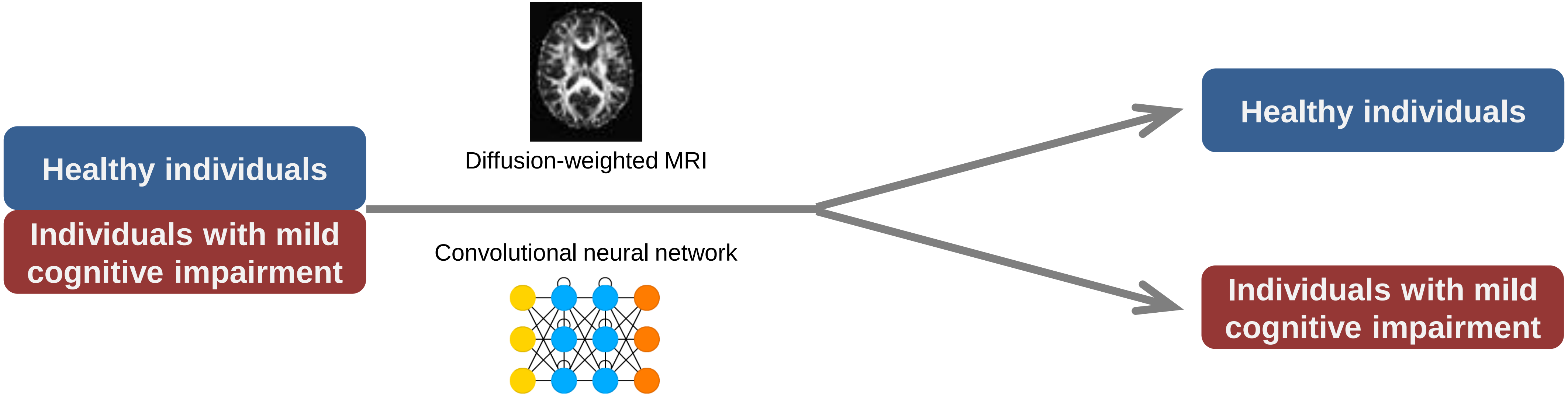
- Diagnostic prediction



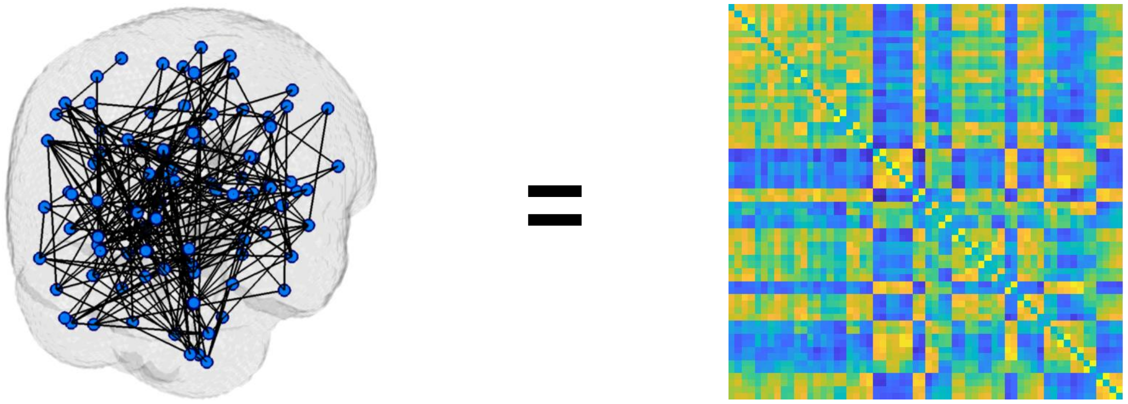
[EL-Geneedy et al., 2023]

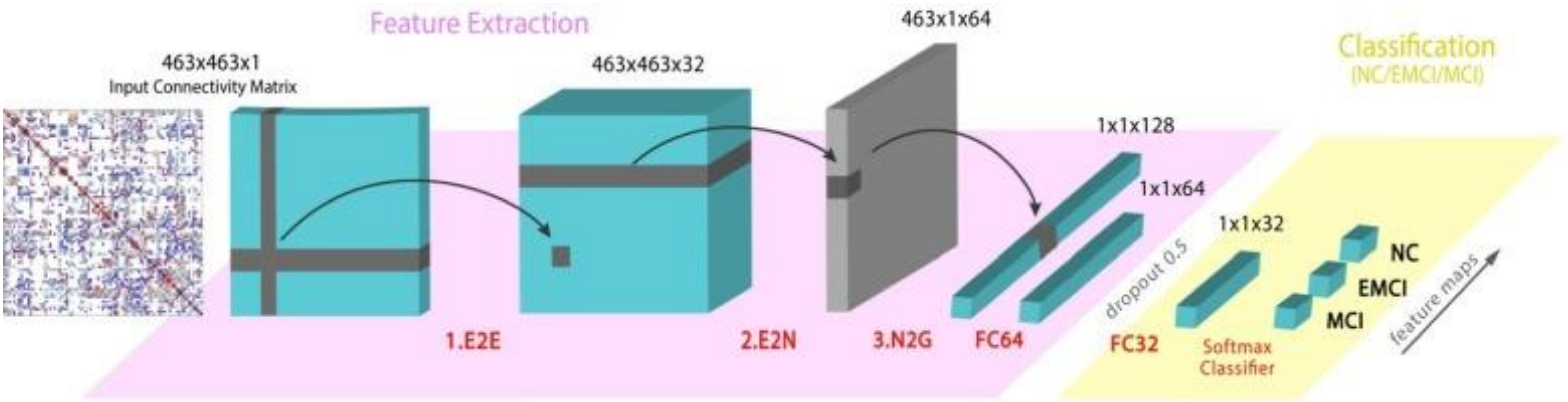


[EL-Geneedy et al., 2023]



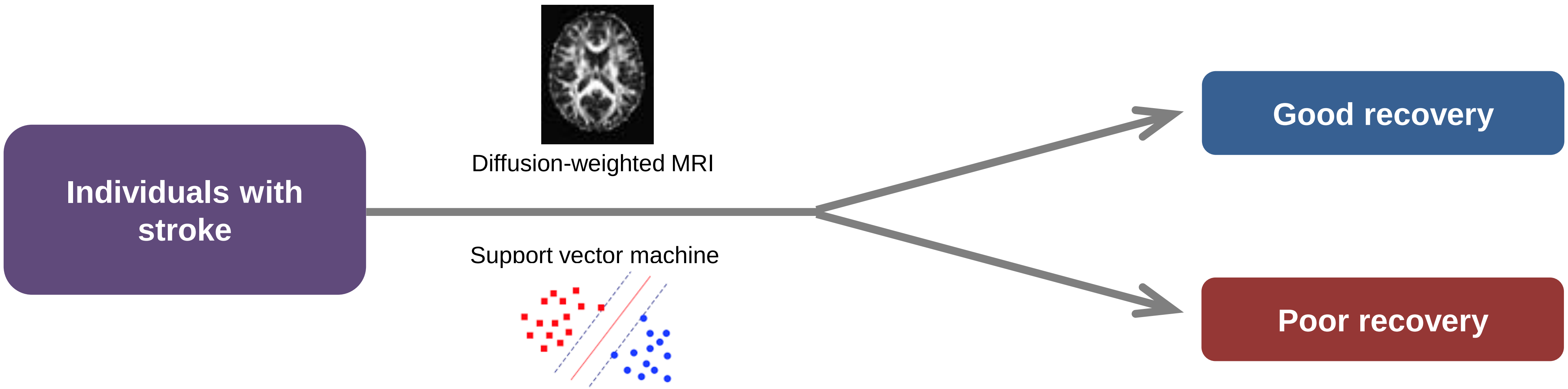
[Kolahkaj et al., 2023]



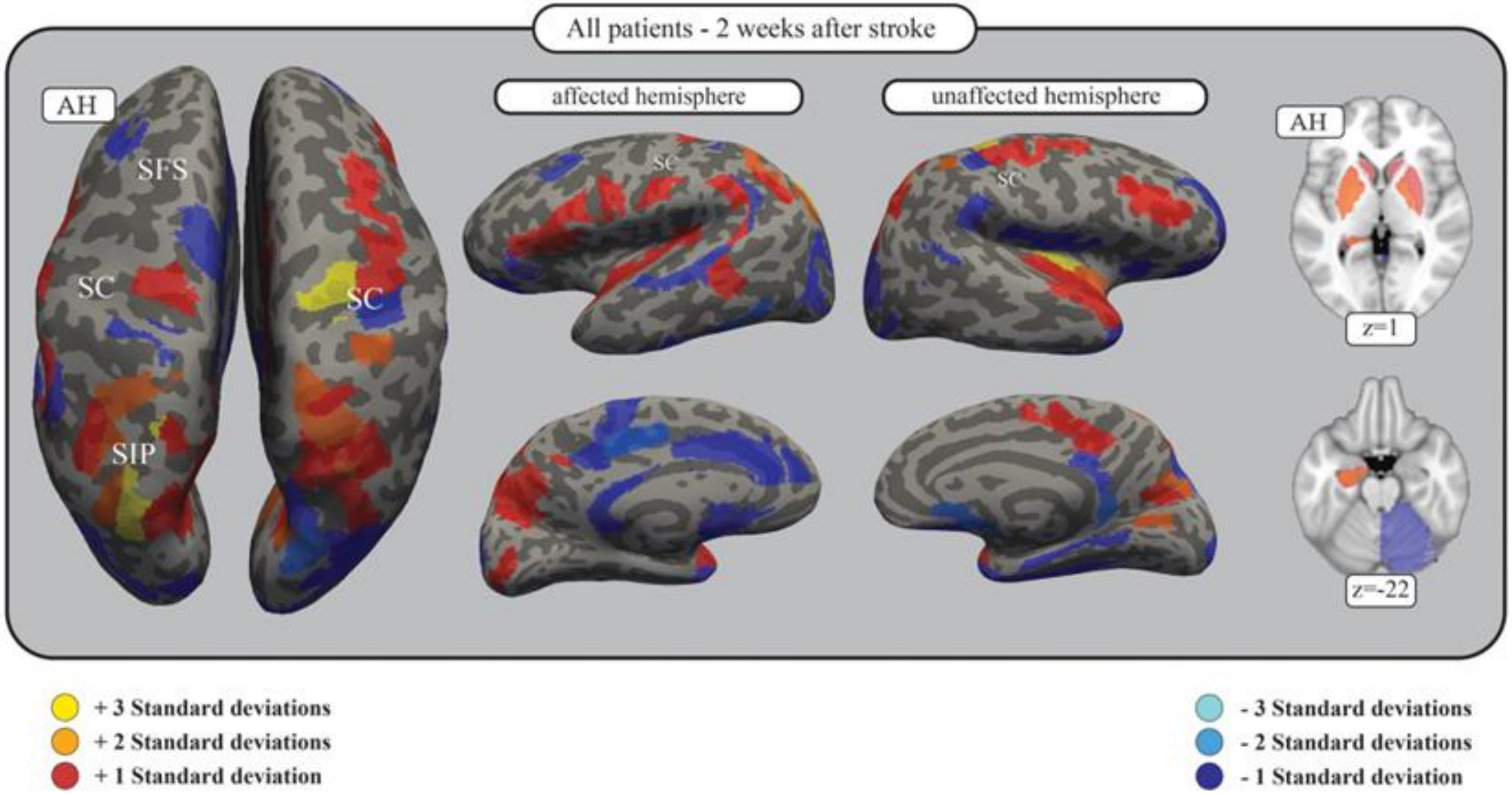


[Kolahkaj et al., 2023]

- Prognostic prediction



[Koch et al., 2021]



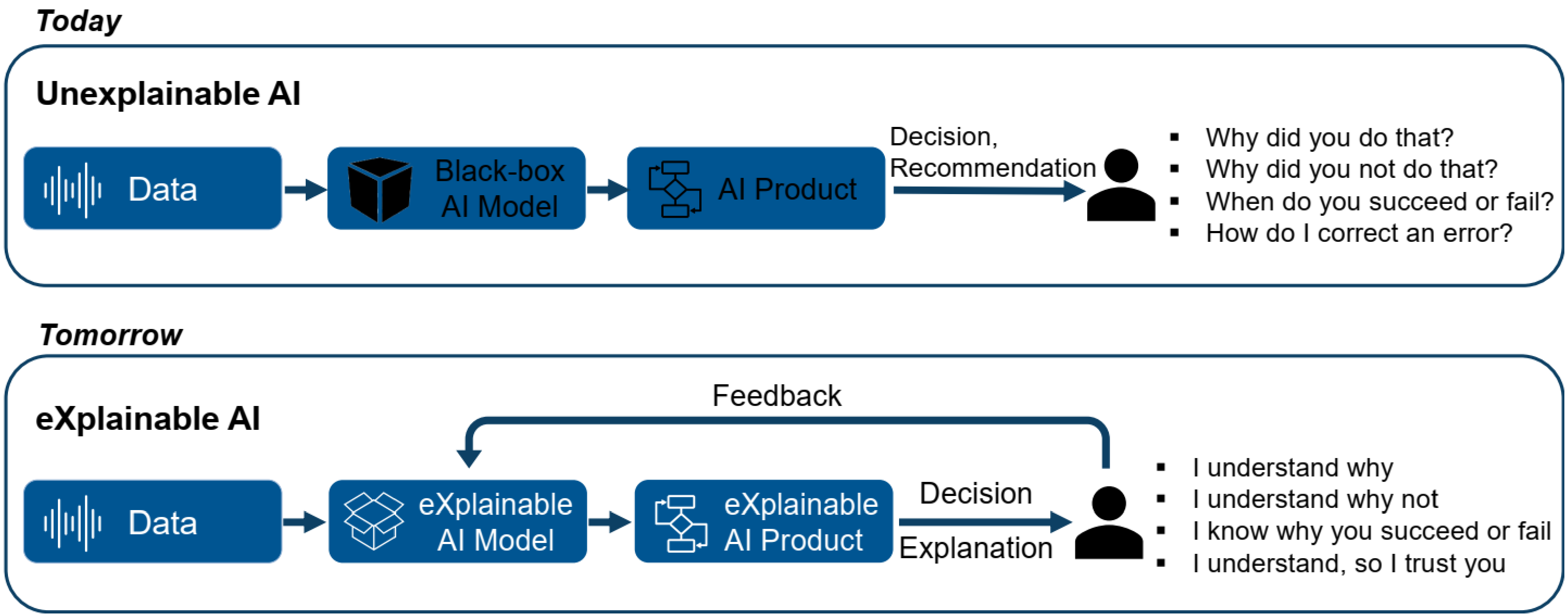
[Koch et al., 2021]

Machine Learning in Clinical Practice

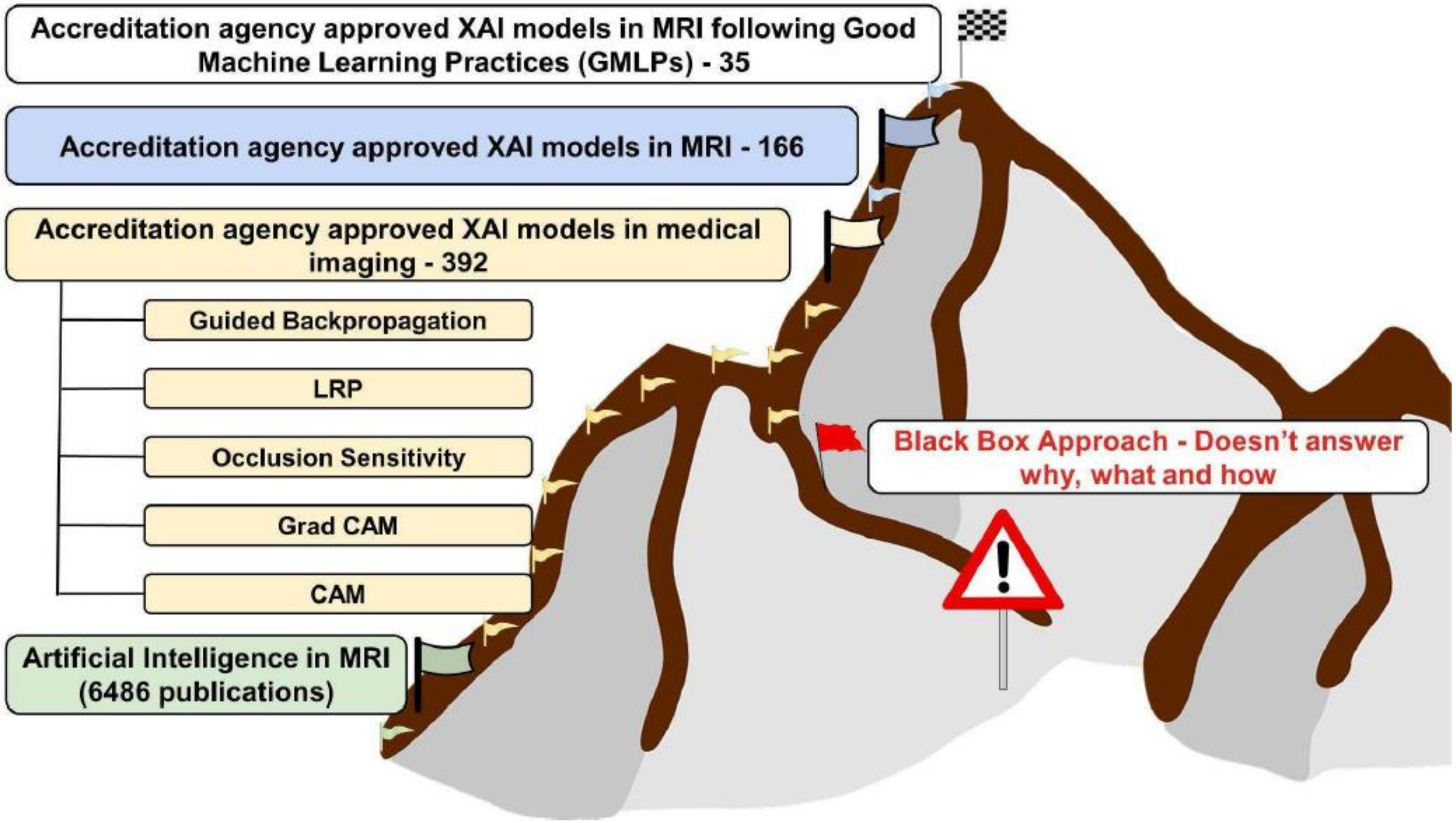
- Good Machine Learning Practices (GMLPs)
- Explainable artificial intelligence (XAI)
  - For visualizing and interpreting machine learning predictions
  - Article 15 GDPR (General Data Protection Regulation) [https://gdpr-info.eu/art-15-gdpr]: right of access by the data subject
    - Patients have the right to request an explanation for how a given diagnosis was reached

Checklist of GMLPs for brain MRI		
1.	Are neuroradiologists, neuroimaging scientists, MR technician and data scientist working together throughout the whole life cycle of the product?	
2.	Is the patient's personal information anonymous in the brain MR images?	
3.	Is the metadata being filled for each patient scan with proper details of all parameters?	
4.	Does training and testing MR datasets contain different scans? There shouldn't be any common scan in both datasets.	
5.	Does reference MR dataset for validation of model have completely unique scans with same parameters as training and testing dataset?	
6.	Are you using the model for segmenting brain structures from the specific contrast for which it has been trained for? If so, don't use it for other contrasts.	
7.	Is the output of the model accepted and readable by the neuroradiologist?	
8.	Has the model been tested in the neuroradiology department under the supervision of an expert neuroradiologist before deployment?	
9.	Are the precautions and potential dangers of using the model explicitly mentioned?	
10.	Is the model being updated frequently for incorporating the changes in the new scans that may occur naturally?	

[https://doi.org/10.48550/arXiv.2301.01241]



[MathWorks Online Seminar: eXplainable AI and AI V&V]



[https://doi.org/10.48550/arXiv.2301.01241]

Demands for machine learning in clinical practice

biobank uk

ADNI
Alzheimer's Disease Neuroimaging Initiative

Human Connectome Project