Biomedical Image Processing

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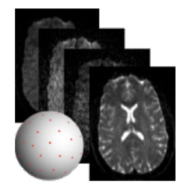
About me

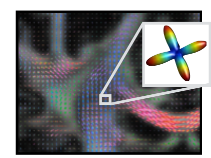
Background

- M.Sc. in *Computer Science* (Verona)
- Ph.D. in *Multimodal imaging in medicine* (Verona)
- Post-doc (EPFL, Switzerland + Sherbrooke, Canada)
- Assistant professor (Verona)

Research interests

- Diffusion MRI acquisition and reconstruction
- Fiber-tracking using convex optimization
- Applications to clinical studies

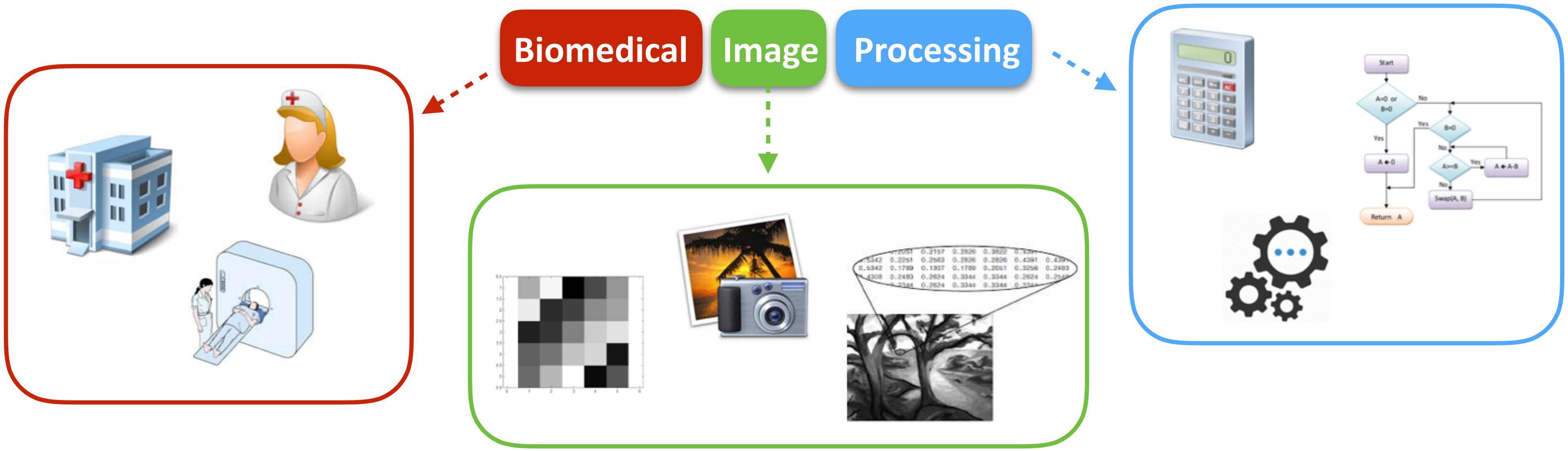




Contact

- *alessandro.daducci@univr.it*
- Office hours: Monday and Tuesday

Context and motivation

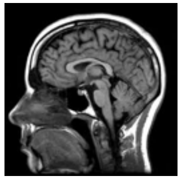


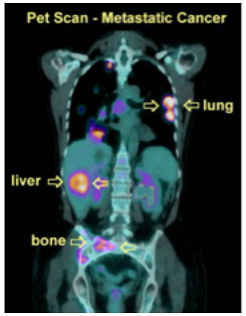
Are you in the right course?

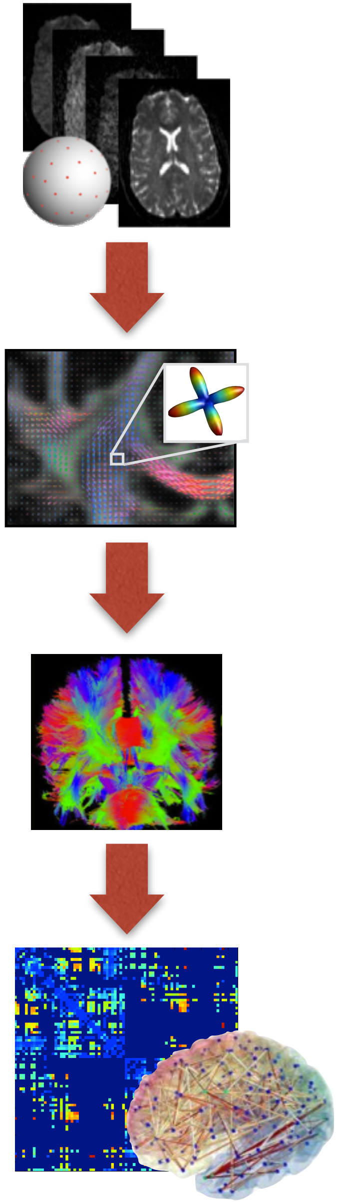
- Become an expert radiologist? ✗
- Build an x-ray scanner or develop your own RF antenna? ✗
- Learn daily life in a research imaging lab? ✓
- Apply your studies to solve concrete problems? ✓

Modules

- Introduction and basic concepts
  - modalities, resolution, file formats, metadata etc
- Image formation
  - x-rays, CT, PET, US, MRI
- Basic image processing
  - survey of standard tools
- Advanced image processing
  - focus on diffusion MRI
  - from raw data to connectivity analysis
- Laboratory
  - use software and implement algorithms (in Python)







Suggested course

- Elaborazioni di immagini (Prof. Menegaz)
- Perhaps, only first few classes (FFT)

GIORNO	ORA	TIPO	LUOGO
mercoledì	8.30 - 11.30	laboratorio	Laboratorio didattico Delta
giovedì	9.30 - 11.30	lezione	Aula B
venerdì	9.30 - 11.30	lezione	Aula B

Exam

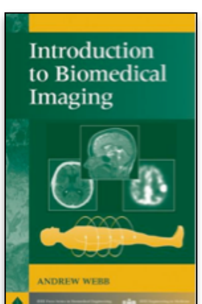
- Short report + final project (in Python)
- Possible to work in teams
- ~~Journal club (?)~~

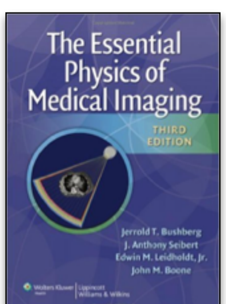
Classes schedule

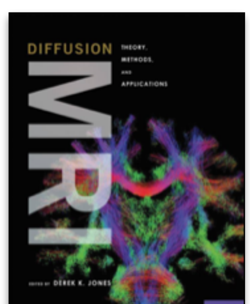
- No lab first two weeks
- Breaks? Public holidays?
- English

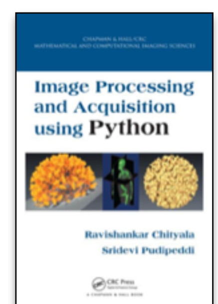
DAY	TIME	TYPE	PLACE
Monday	2:30 PM - 4:30 PM	lesson	**Lecture Hall L**
Monday	4:30 PM - 7:30 PM	laboratorio	**Laboratory Alfa**
Tuesday	12:30 PM - 2:30 PM	lesson	**Lecture Hall C**

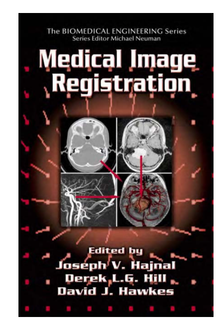
Reference books











About the course (4/4)

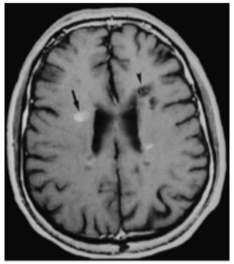
Credits (sources of material/inspiration for this course)

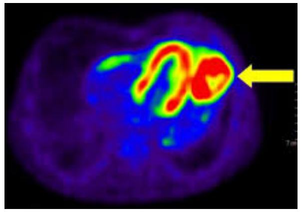
- Books
  - “**Introduction to biomedical imaging**” - A. Webb
  - “**Introduction to medical imaging - Physics, engineering and clinical applications**” - N. Barrie Smith and A. Webb
  - “**The essential physics of medical imaging**” - J. Bushberg, J. Seibert, E. Leidholdt JR, J. Boone
  - “**Image processing and acquisition using Python**” - R. Chityala and S. Pudipeddi
  - “**Medical image registration**” - J. Hajnal, D. Hill and D. Hawkes
  - “**Diffusion MRI - Theory, methods and applications**” - D. Jones
  - “**Diffusion MRI - From quantitative measurement to in-vivo neuroanatomy**” - H. Johansen-Berg and T. Behrens
- Courses
  - **Dr. Meritxell Bach Cuadra** - University of Lausanne, Switzerland
  - **Prof. Ulas Bagci** - University of Central Florida, USA
  - **Prof. Maxime Descoteaux** - Université de Sherbrooke, QC, Canada
  - **Prof. Tom Fletcher** - University of Utah, USA
  - **Dr. Gabriel Girard** - Université de Sherbrooke, QC, Canada
  - **Prof. Klaus Mueller** - Stony Brook University
- Other
  - Google images, Wikipedia and many other websites
    (sorry for not citing all contributions)

Medical vs non-medical imaging

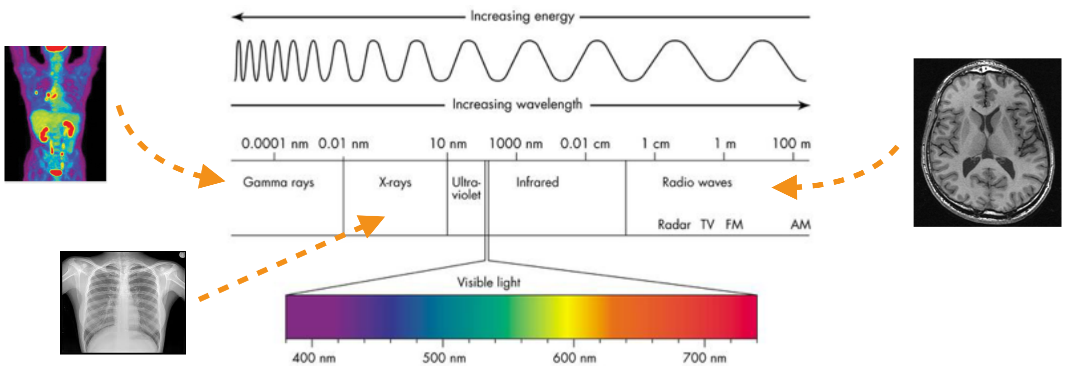
- Represent various **physical properties**

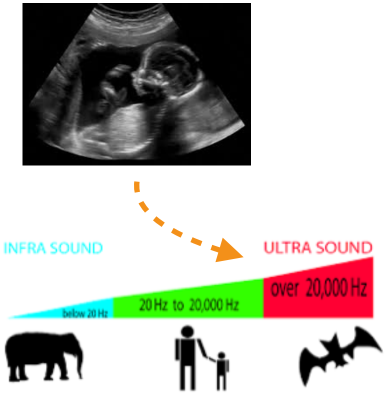




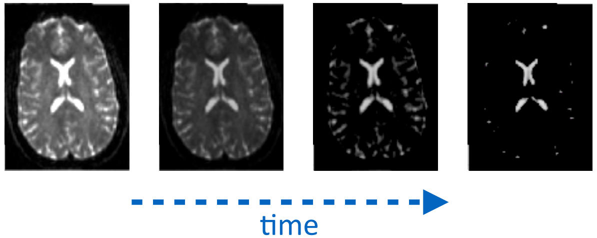


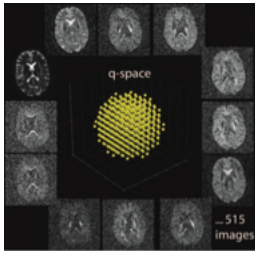
- Use **electromagnetic** and **audio** spectrums





- Are not limited to **2D**



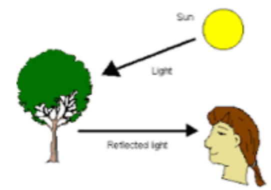


NB: diffusion MRI is a **7D modality**!

Medical vs non-medical imaging (2/5)

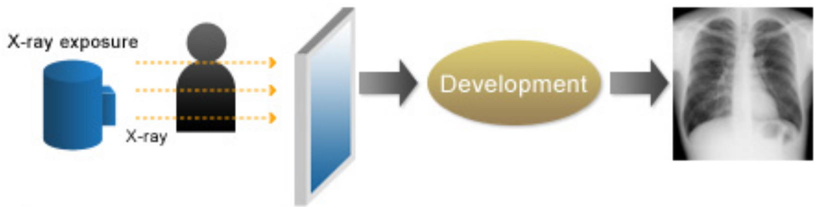
Images formed by **interaction** with tissues/organs

- Photography
  - reflection of light
- Medical imaging:
  - emission and absorption of signal
  - different mechanisms to provide contrast

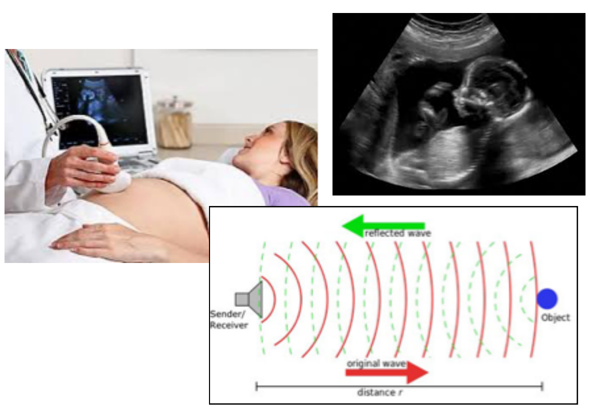


Positron Emission Tomography

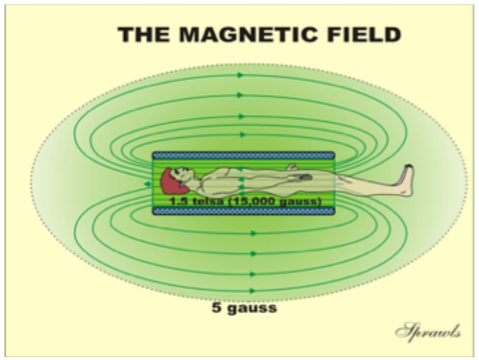
X-rays

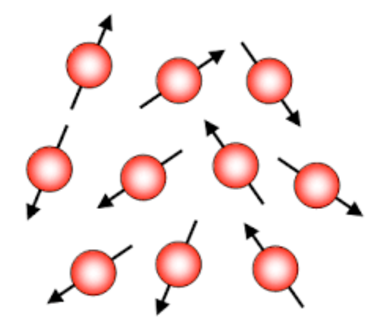


Ultrasounds



Magnetic Resonance Imaging





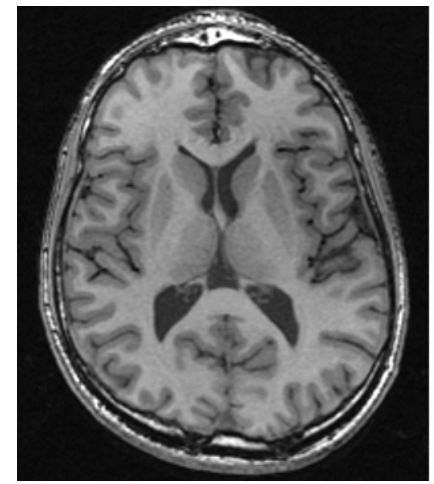
Medical vs non-medical imaging (3/5)

- Application: study "**anatomy**" or "**structure**"

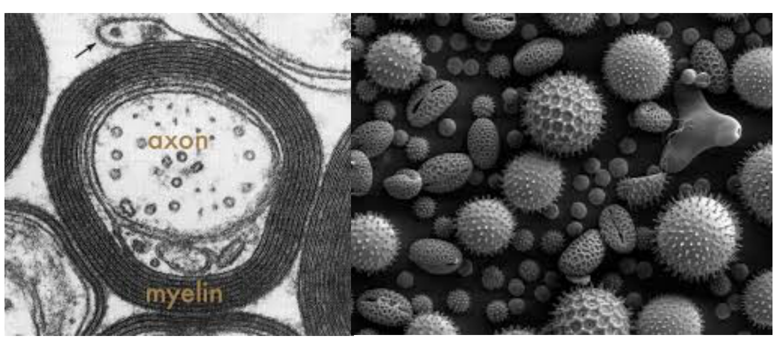
X-rays

CT

MRI



electron microscopy

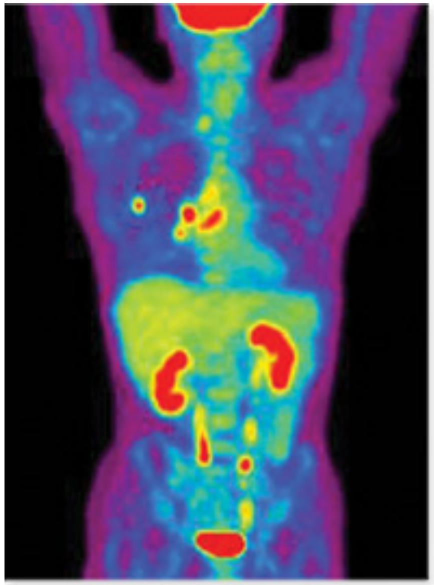


US

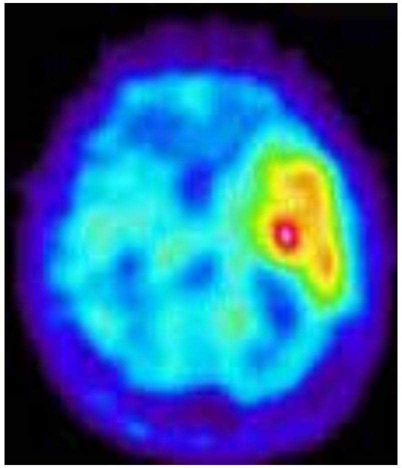
Medical vs non-medical imaging (4/5)

- Application: study "**function**" or "**activity**"

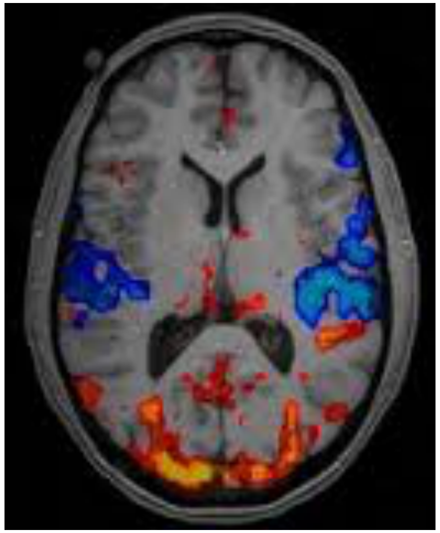
PET



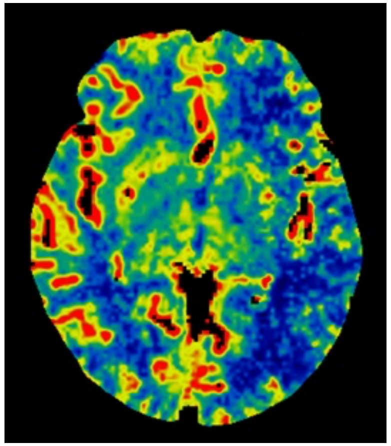
SPECT



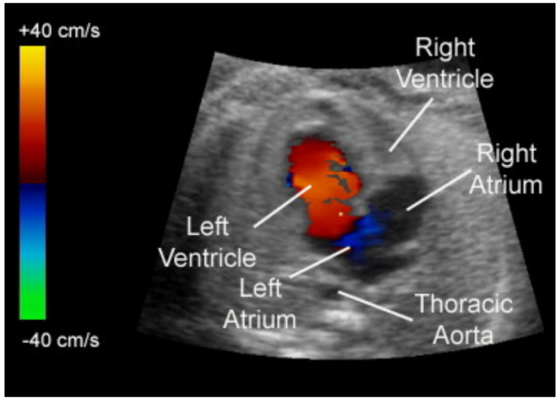
functional MRI



perfusion CT

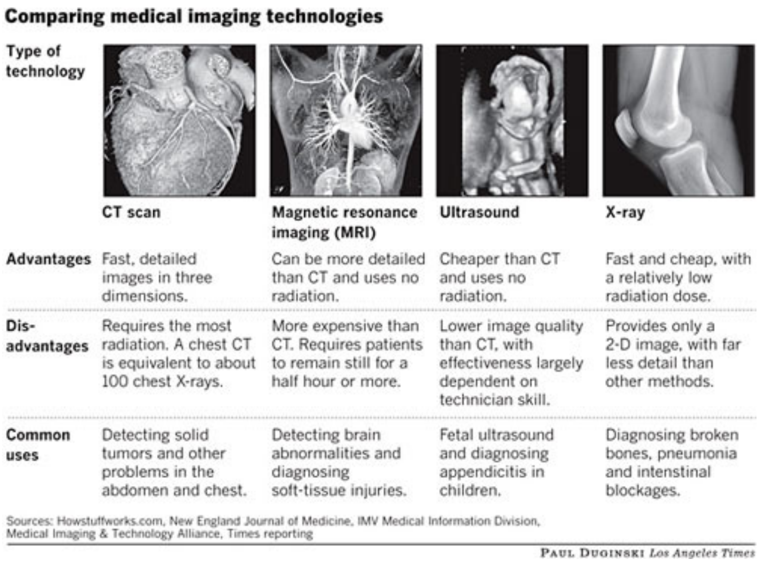


doppler US



Medical vs non-medical imaging (5/5)

- Pros and cons



Comparing medical imaging technologies

Type of technology	CT scan	Magnetic resonance imaging (MRI)	Ultrasound	X-ray
Advantages	Fast, detailed images in three dimensions.	Can be more detailed than CT and uses no radiation.	Cheaper than CT and uses no radiation.	Fast and cheap, with a relatively low radiation dose.
Dis-advantages	Requires the most radiation. A chest CT is equivalent to about 100 chest X-rays.	More expensive than CT. Requires patients to remain still for a half hour or more.	Lower image quality than CT, with effectiveness largely dependent on technician skill.	Provides only a 2-D image, with far less detail than other methods.
Common uses	Detecting solid tumors and other problems in the abdomen and chest.	Detecting brain abnormalities and diagnosing soft-tissue injuries.	Fetal ultrasound and diagnosing appendicitis in children.	Diagnosing broken bones, pneumonia and intenstinal blockages.

Sources: Howstuffworks.com, New England Journal of Medicine, IMV Medical Information Division, Medical Imaging & Technology Alliance, Times reporting

PAUL DUGINSKI *Los Angeles Times*

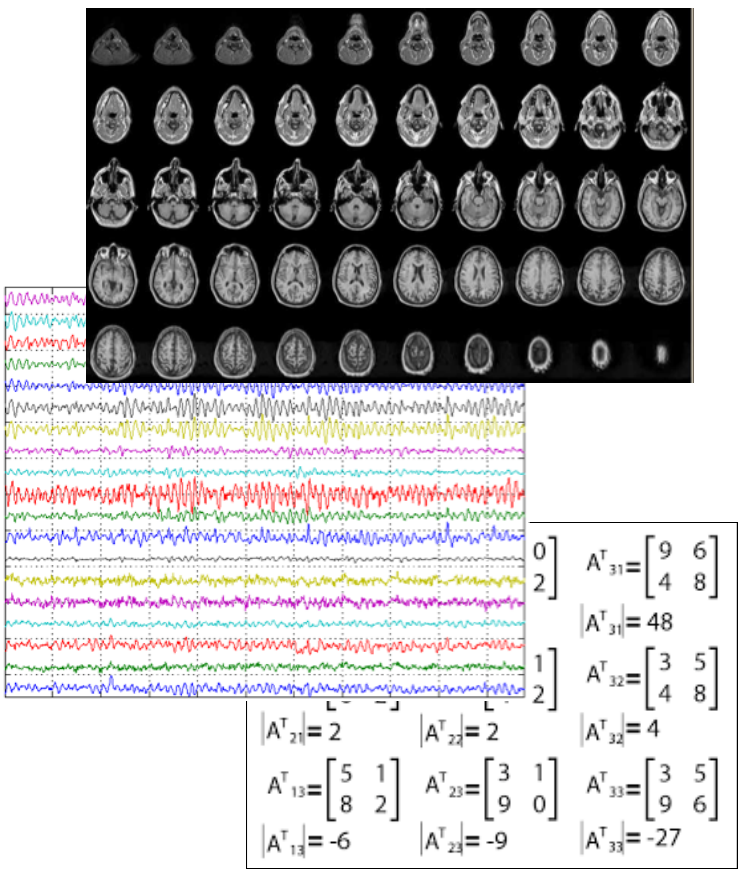
- Don't have time to see all
  - Only the most popular
    - X-rays, CT, PET, US, MRI
  - Get the idea, how they work
    - *"…we are neither doctors nor physicists, but it is* ***very important to understand how images are formed*** *and what they represent in order to properly manipulate, process and analyze them…"*

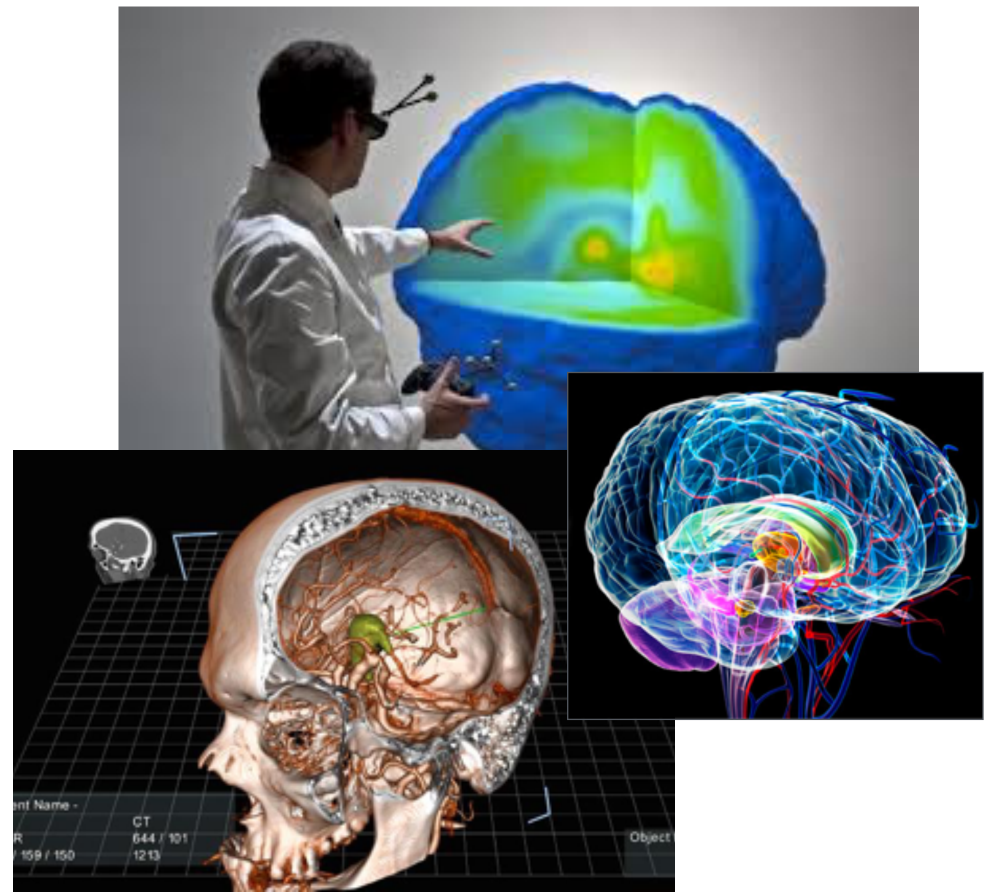
- NB: **crucial decisions** made based on **results of image analysis**
  - Life or death
  - Surgical intervention or not?
  - Treatment planning
  - ….

Why do we need image processing? (1/6)

- Visualization

Provide information in a form usable by doctors



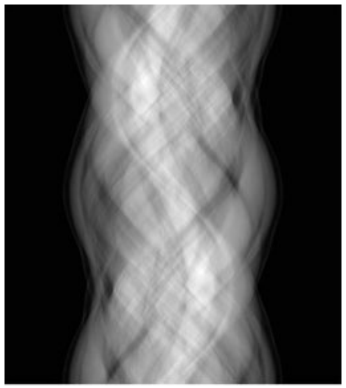


Why do we need image processing? (2/6)

Reconstruction

CT acquisition

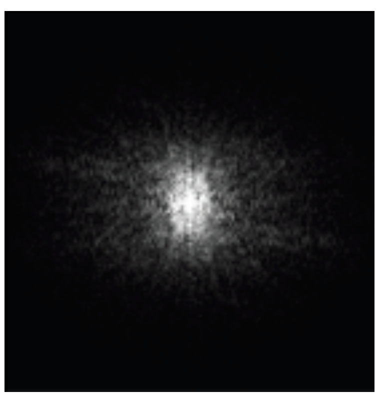
projection angle



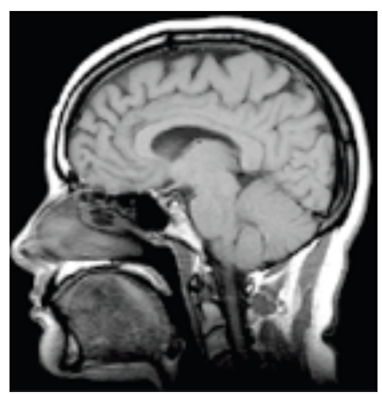
projection offset

MRI acquisition

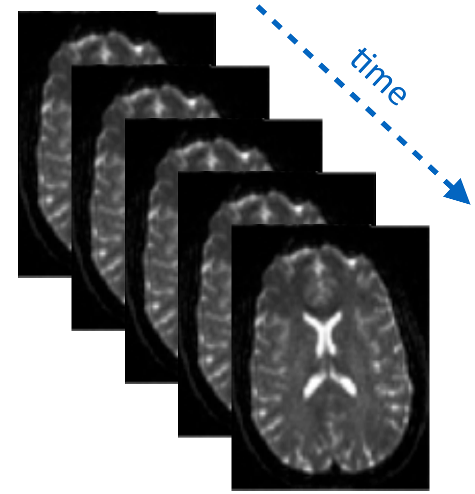
phase in y

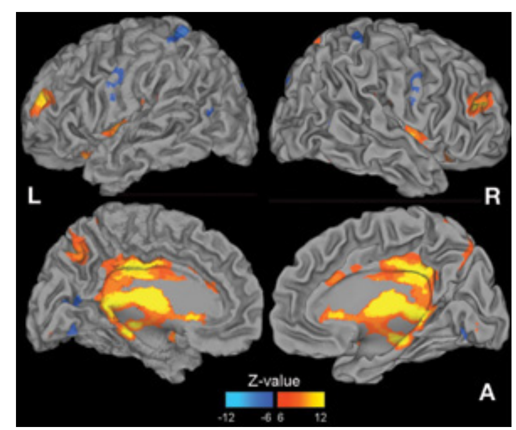


phase in x



functional activation

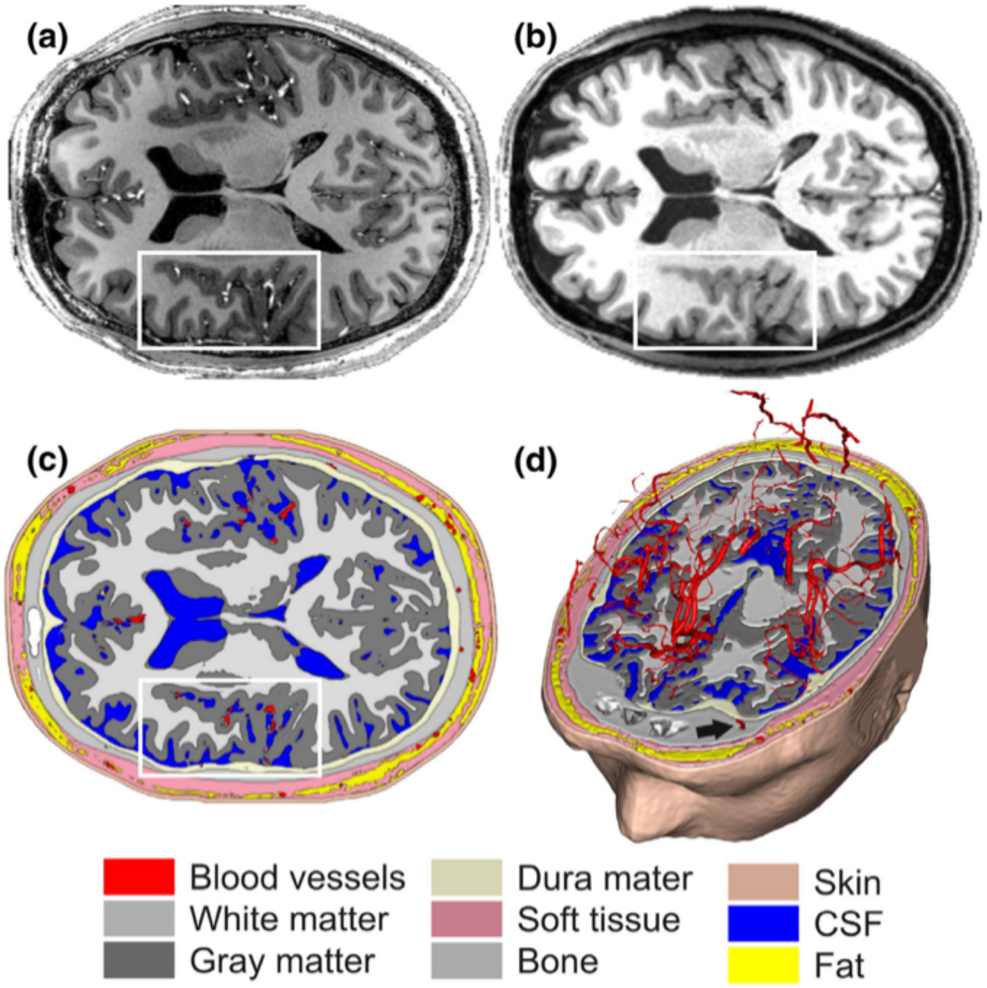




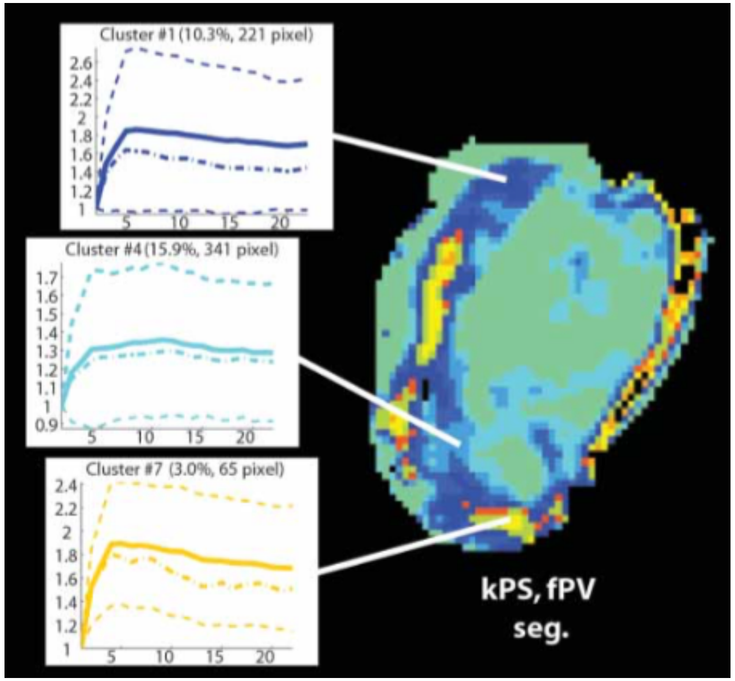
Why do we need image processing? (3/6)

Segmentation

Quantify/study different tissues

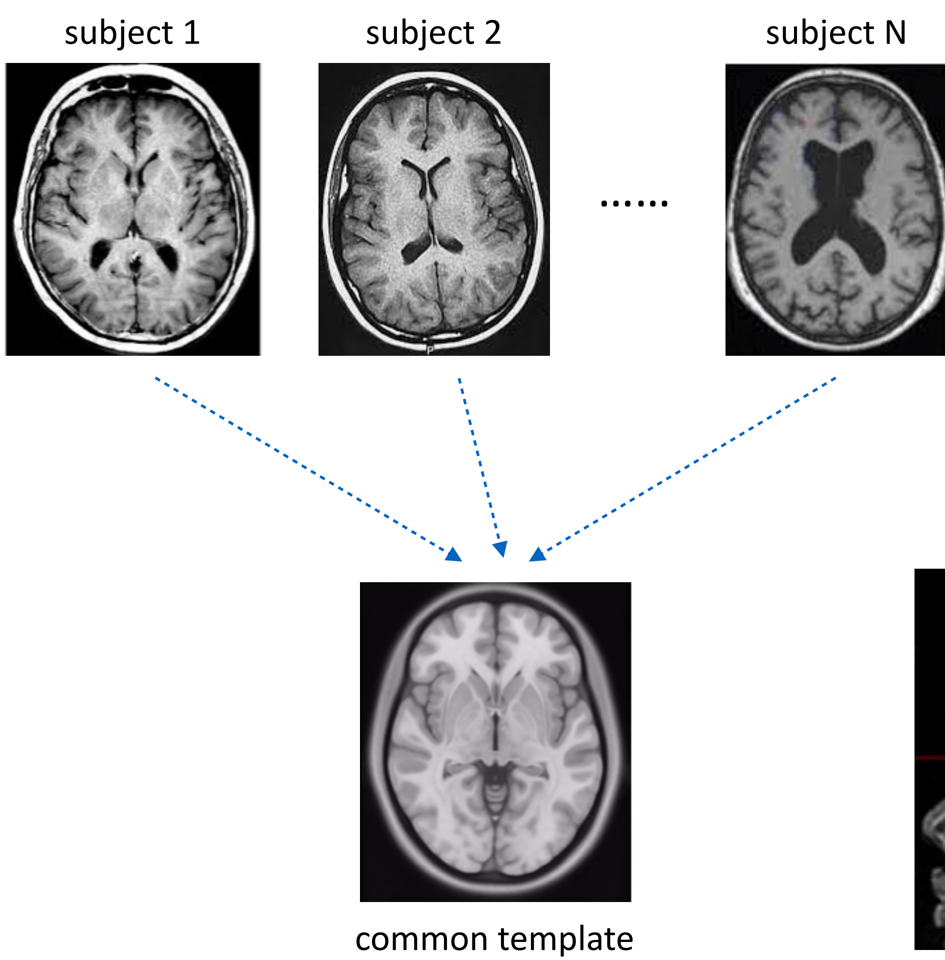


Detect tissue abnormalities

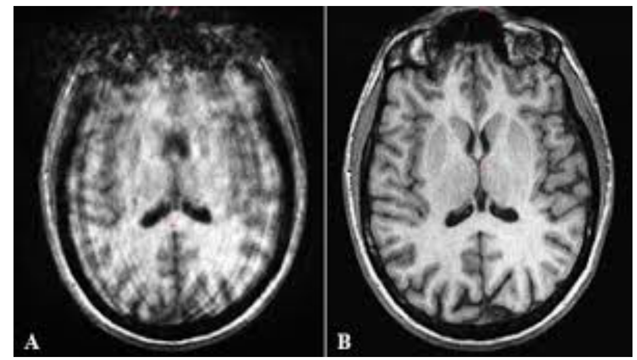


Registration

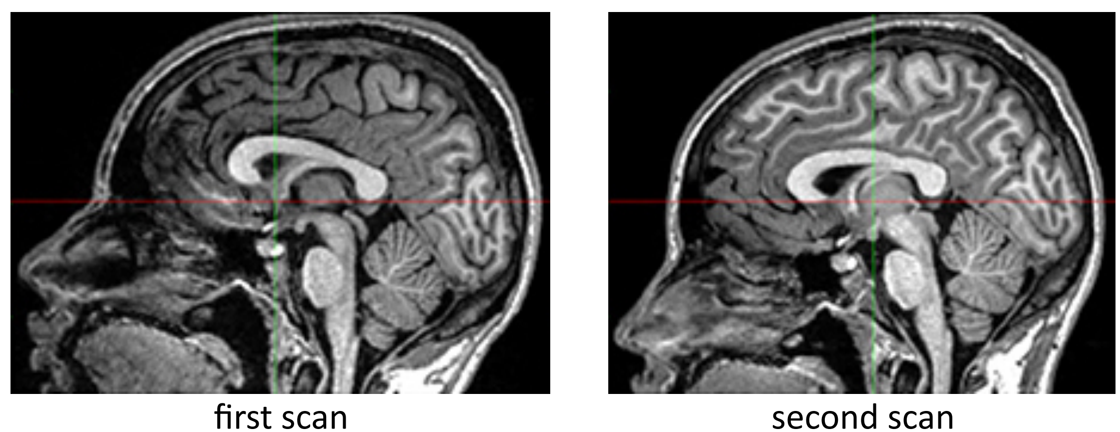
Compare different subjects



Subject motion



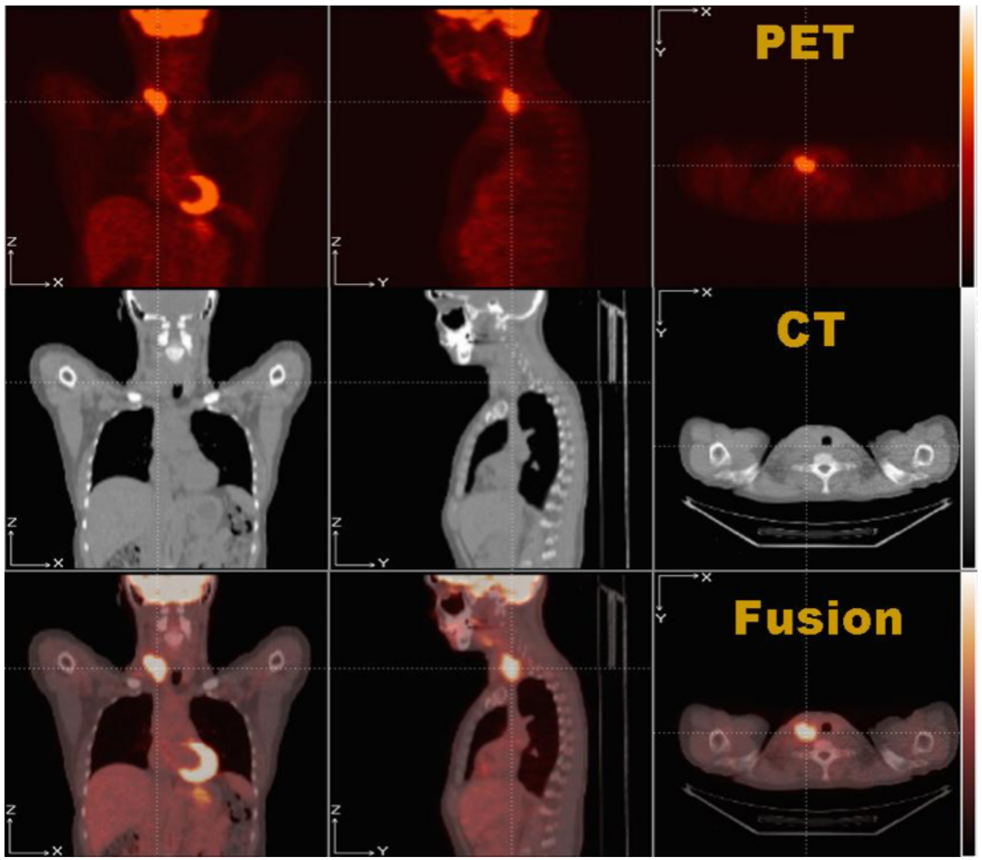
Detect changes in longitudinal studies



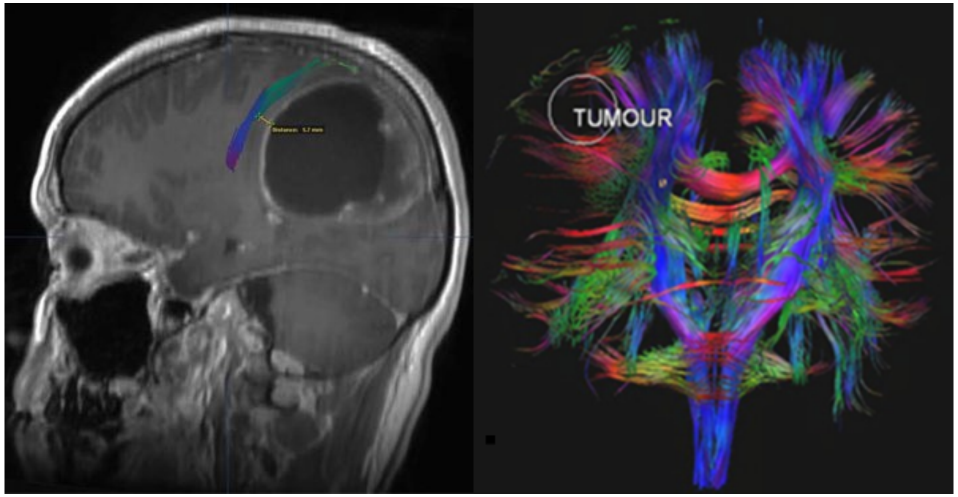
Why do we need image processing? (5/6)

- Data fusion

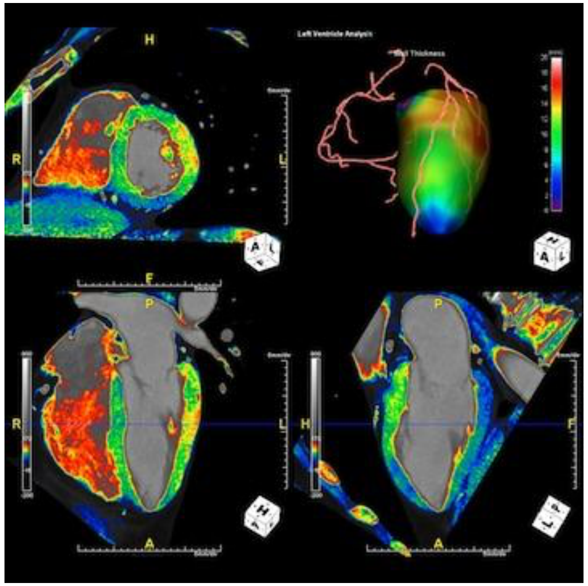
Improve accuracy



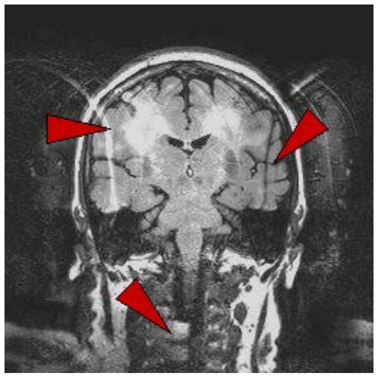
Help making decisions

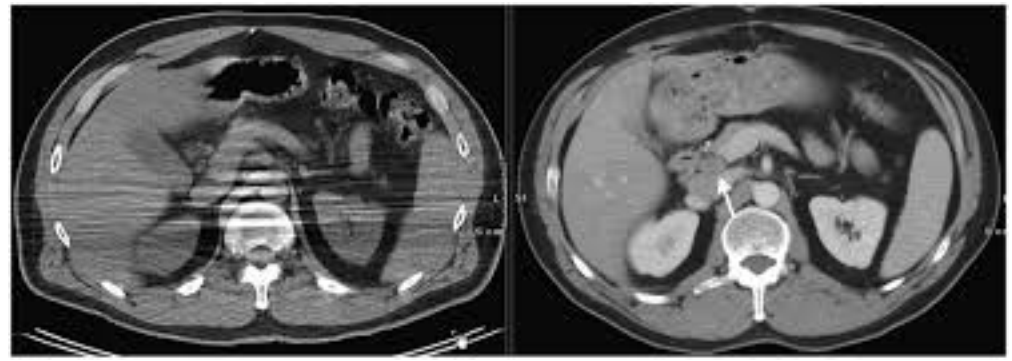


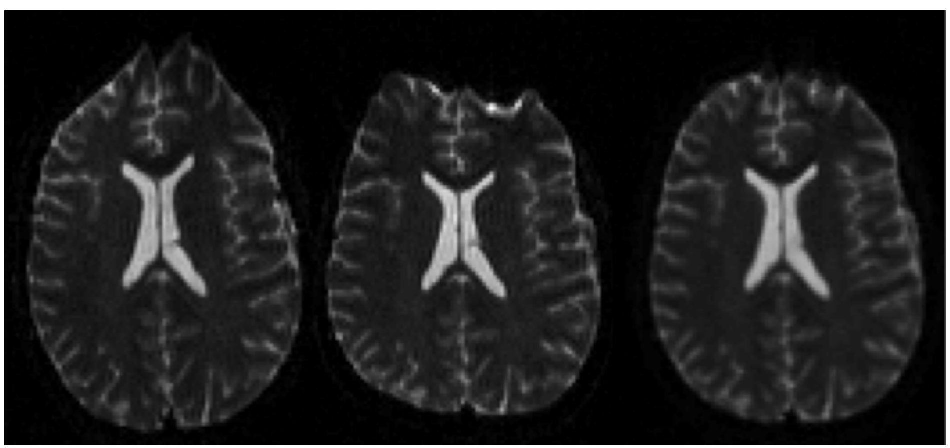
Merge different information



- Artifact correction

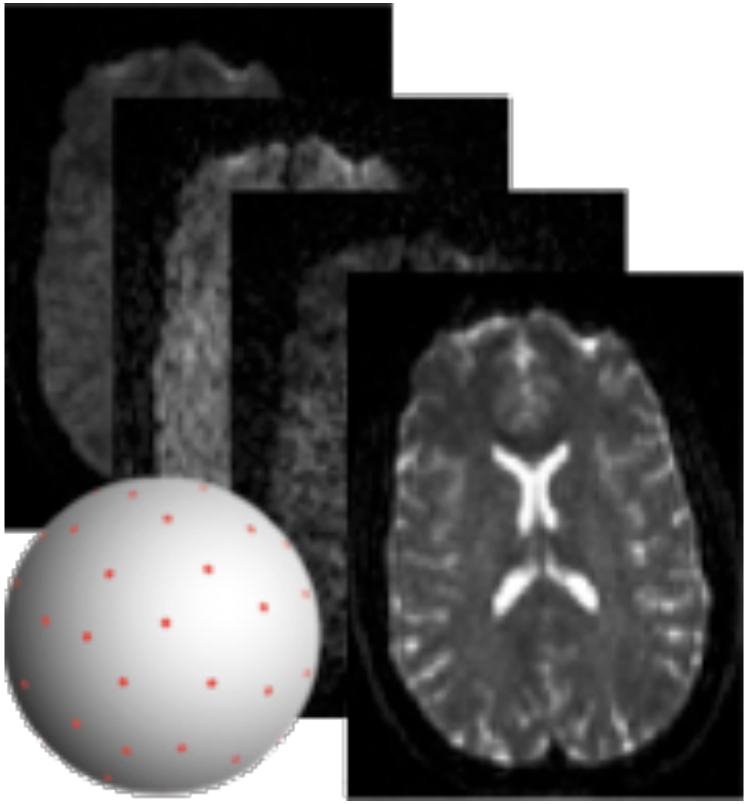






Advanced image processing (1/2)

- Connectivity analysis with **diffusion MRI**



Advanced image processing (1/2)

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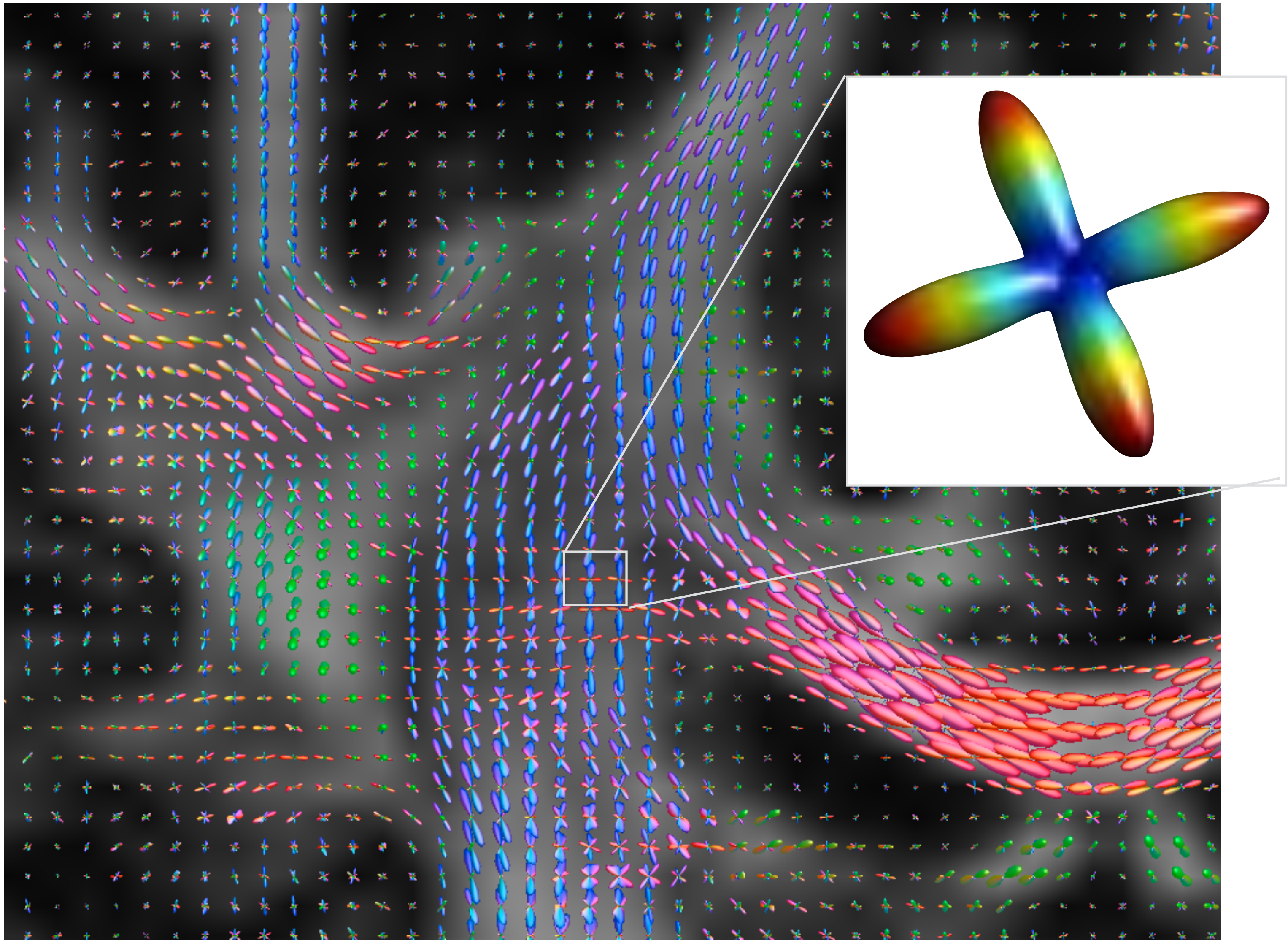

Advanced image processing (1/2)

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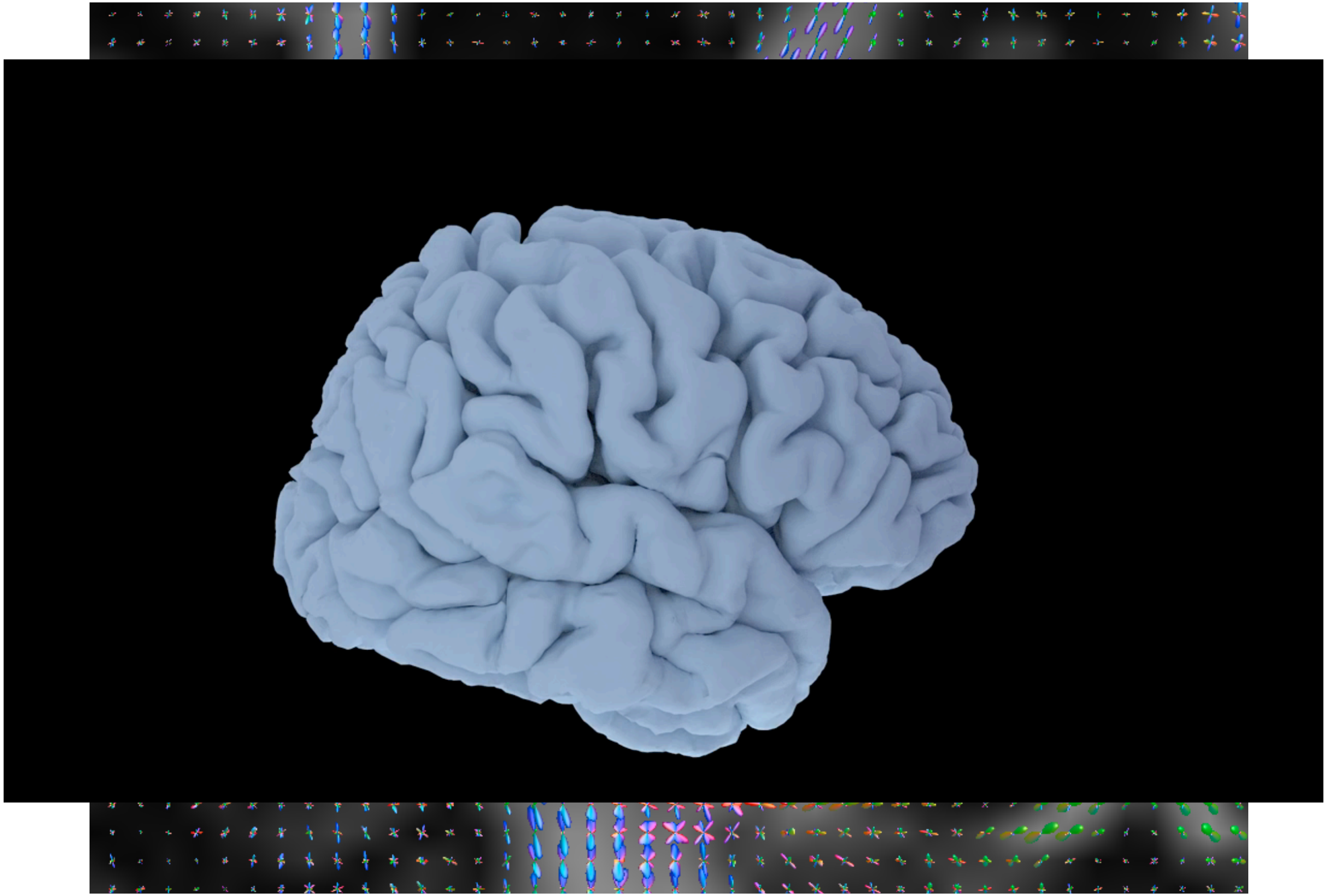
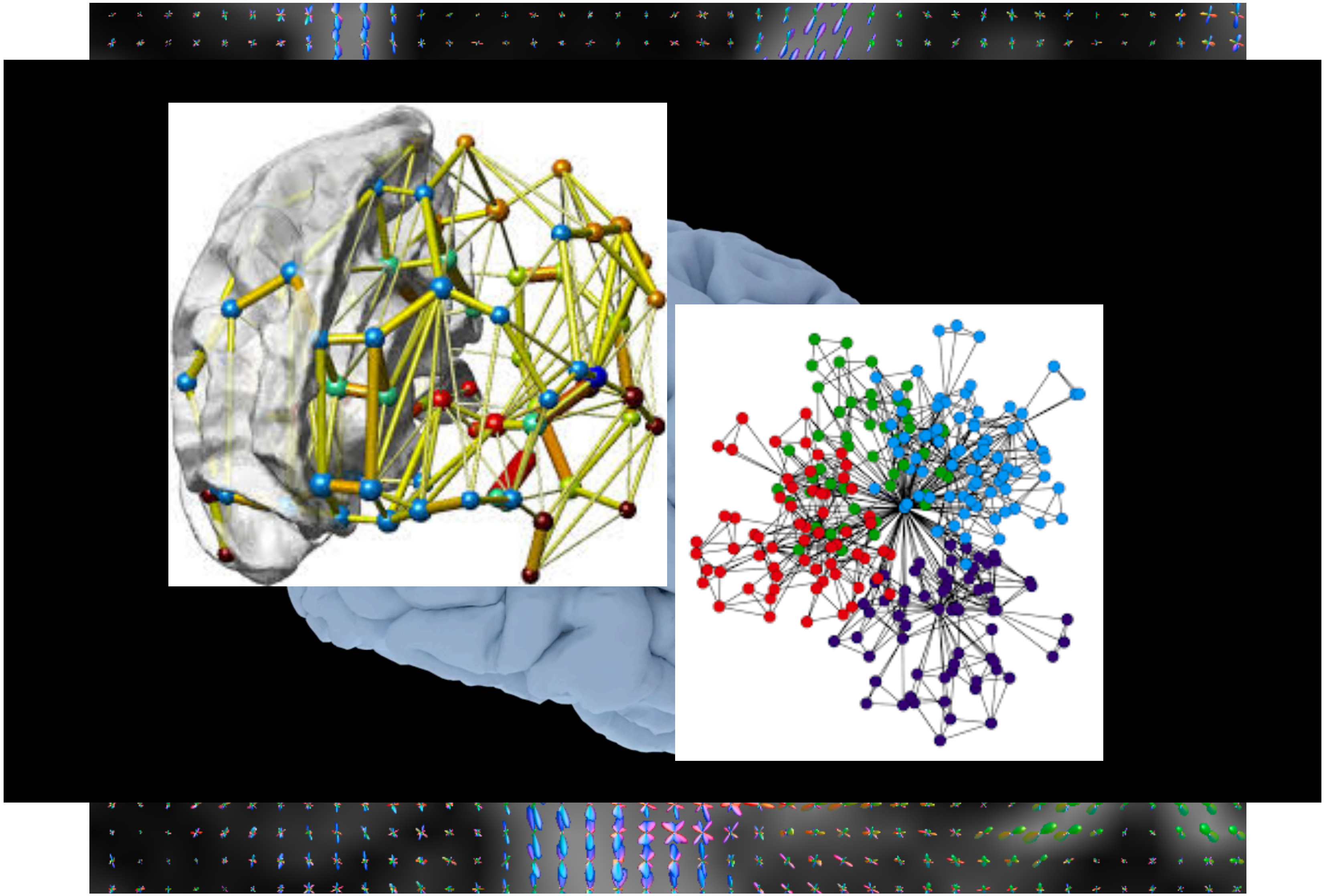


- Connectivity analysis with **diffusion MRI**

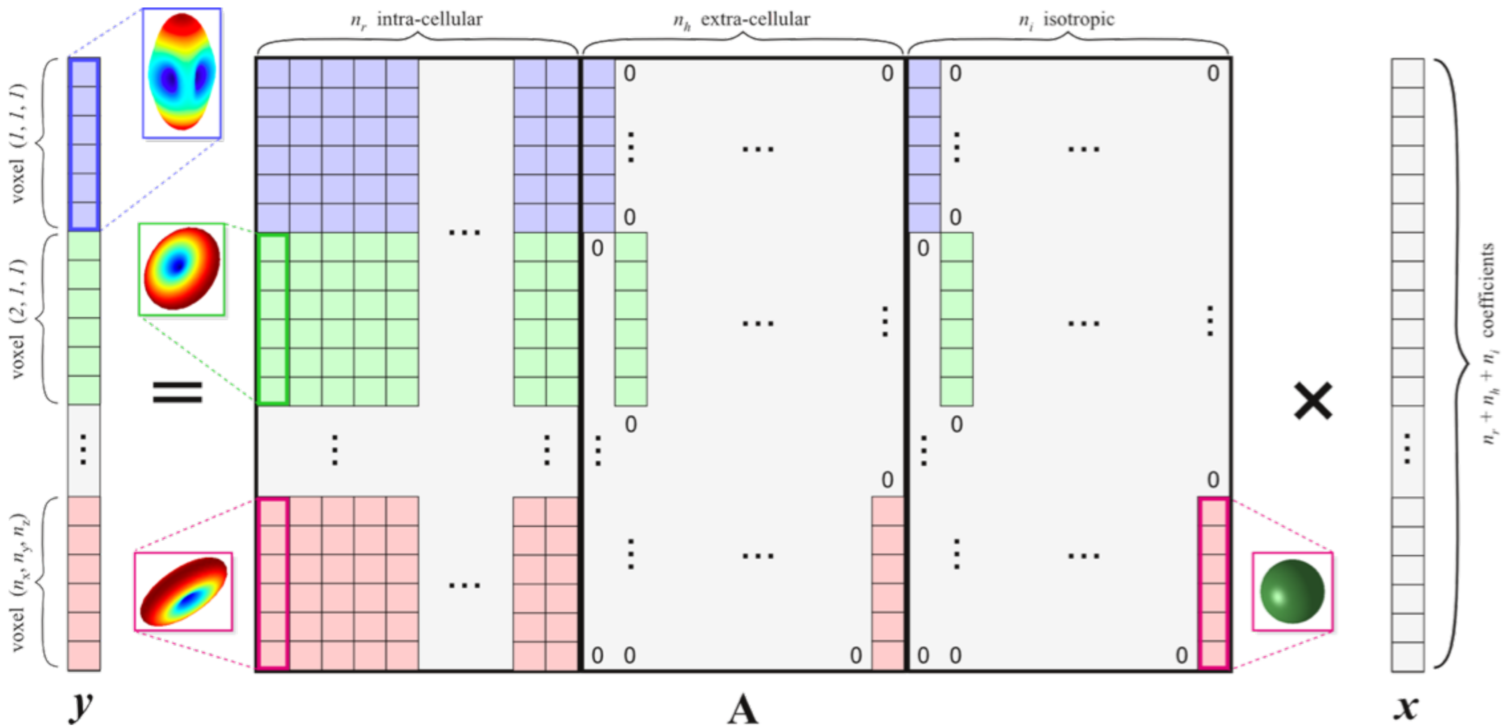


Microstructure Informed Tractography

- Tractography is <u>NOT</u> quantitative
- Combine *tractography* and *models of tissue microstructure*:

$$\underset{\mathbf{x}\geq 0}{\operatorname{argmin}} \|\mathbf{A}\mathbf{x}-\mathbf{y}\|_2^2$$

Large scale optimization:
size(A) ≈ $10^7 \times 10^7$

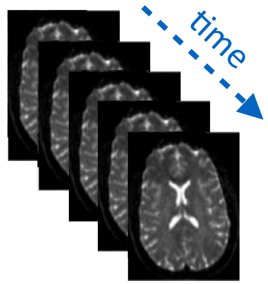


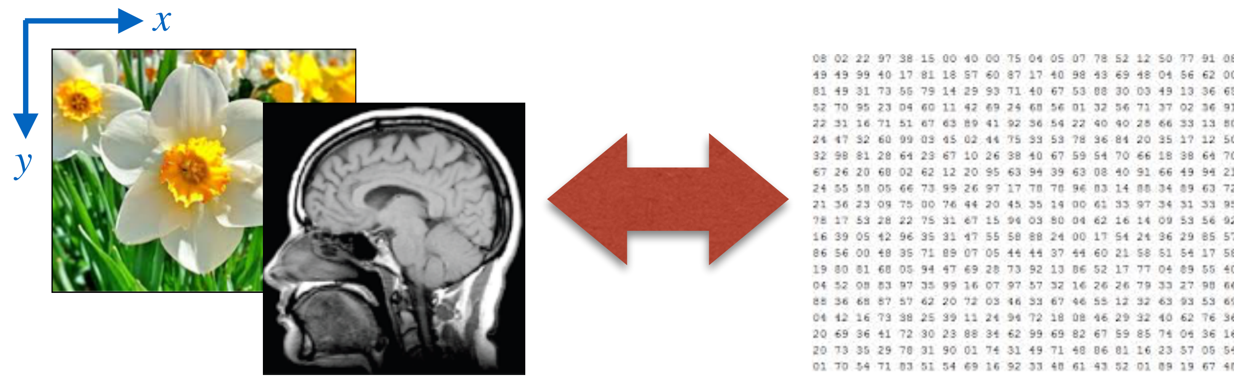
Basic concepts

What is an image? (1/2)

Array of numbers

- $f(x, y) \in \mathbb{N}^2 \mapsto \mathbb{R}$
- Not limited to **2D**

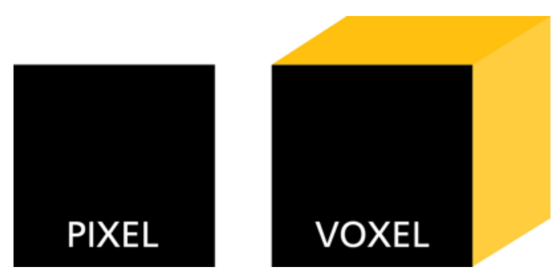




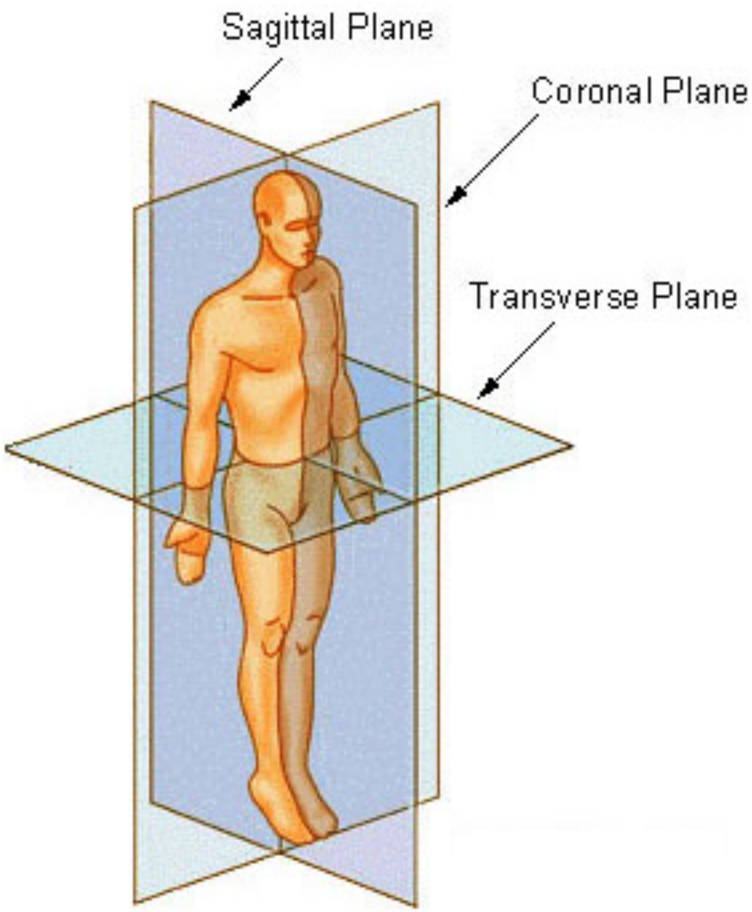
- Not limited to **single values** or **real values**

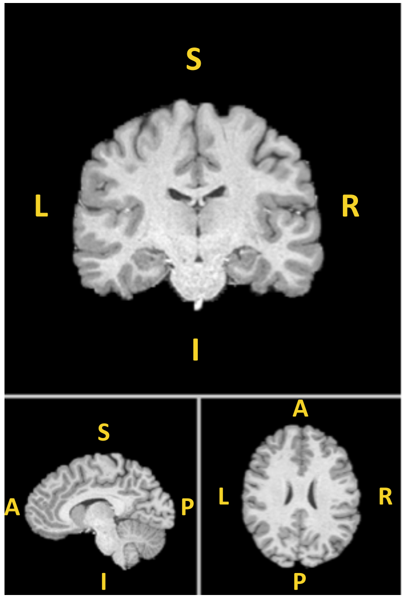
Pixel vs voxel

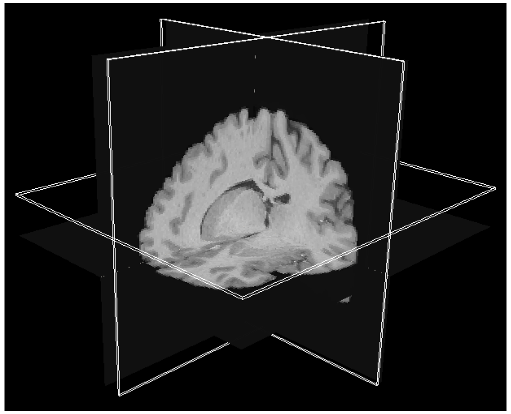
- *Pixel* = “picture element”
- *Voxel* = “volume element”



- Medical images usually displayed by **anatomical planes**
  - Sagittal
    - divides *left* (L) and *right* (R)
  - Coronal
    - divides *anterior* (A) and *posterior* (P)
  - Transverse (or axial)
    - divides *superior* (S) and *inferior* (I)



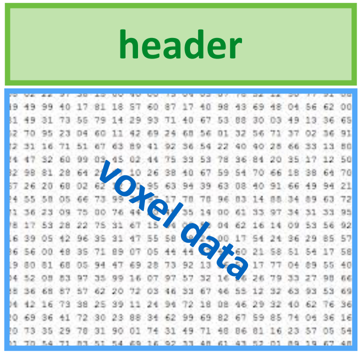




Important image properties

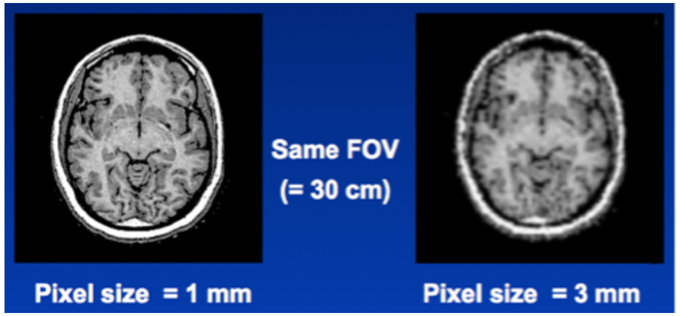
Metadata is required for **correct interpretation**

- Which parameters were used to produce the image?
- How was the patient positioned inside the scanner?
- How is data stored?
- Patient name, age, sex?

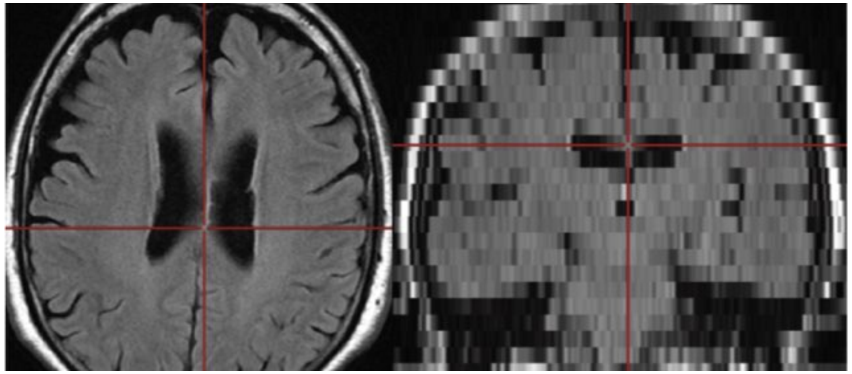


Field of view (FOV)

- Matrix size
  - Number of voxels in each dimension (e.g. 128 x 128 x 40)
- Spatial resolution
  - Physical dimension of voxel (2.0 x 2.0 x 5.0 mm)
- Note:



Acquisition can be anisotropic!



A-P : high resolution
L-R : high resolution

I-S : low resolution

NB: *acquisition* vs *image* spatial resolution

Acquisition

- **Nominal** ability to resolve fine details → intrinsic blur
- Point spread function (PSF) = response of an imaging system to a point source
- *High* resolution = distinguish *smaller* objects

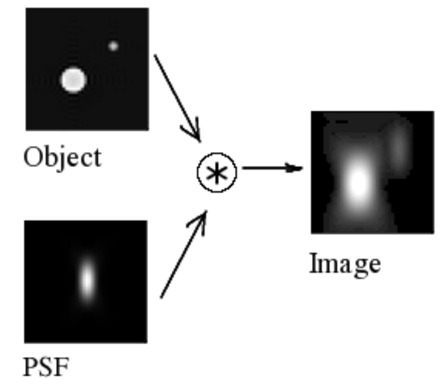
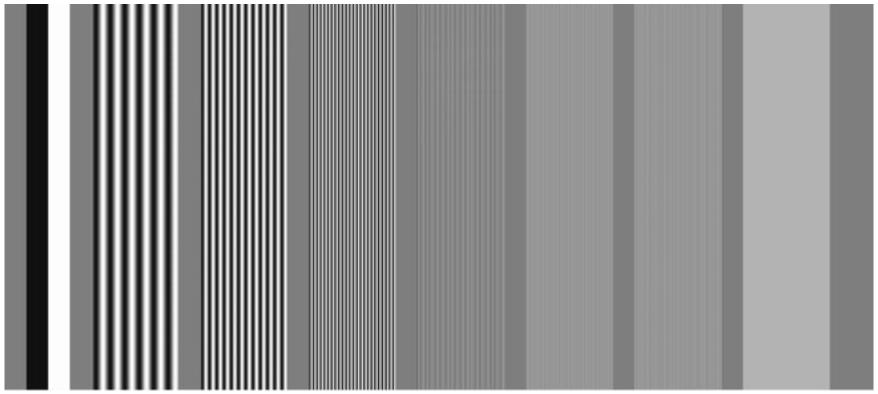


TABLE 1-1 THE LIMITING SPATIAL RESOLUTIONS OF VARIOUS MEDICAL IMAGING MODALITIES. THE RESOLUTION LEVELS ACHIEVED IN *TYPICAL* CLINICAL USAGE OF THE MODALITY ARE LISTED

MODALITY	SPATIAL RESOLUTION (mm)	COMMENTS
Screen film radiography	0.08	Limited by focal spot size and detector resolution
Digital radiography	0.17	Limited by size of detector elements and focal spot size
Fluoroscopy	0.125	Limited by detector resolution and focal spot size
Screen film mammography	0.03	Highest resolution modality in radiology, limited by same factors as in screen film radiography
Digital mammography	0.05–0.10	Limited by same factors as digital radiography
Computed tomography	0.3	About ½ mm pixels
Nuclear medicine planar imaging	2.5 (detector face), 5 (10 cm from detector)	Spatial resolution degrades substantially with distance from detector
Single photon emission computed tomography	7	Spatial resolution worst towards the center of cross-sectional image slice
Positron emission tomography	5	Better spatial resolution than the other nuclear imaging modalities
Magnetic resonance imaging	1.0	Resolution can improve at higher magnetic fields
Ultrasound imaging (5 MHz)	0.3	Limited by wavelength of sound

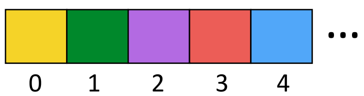


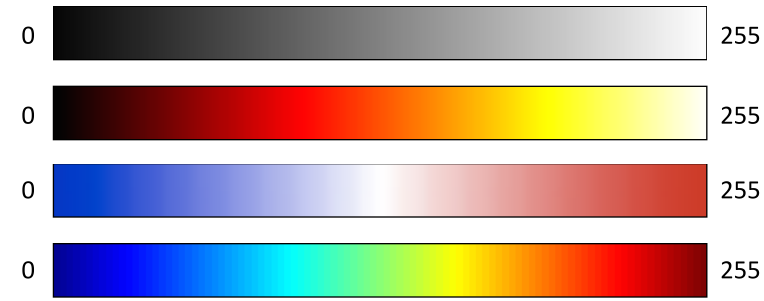
Image

- **Actual** resolution used for current acquisition
- Image resolution > acquisition resolution

Photometric interpretation

- **Grayscale** (e.g. CT and MRI)
  - intensity of physical phenomenon, no color information
  - color is associated when displaying using *colormaps*
- **Color palette** (e.g. SPECT and PET)
  - image must be displayed with color *stored* in the voxel





NB: attention to *jet/rainbow* colormap

Pixel/voxel depth

- Number of bits to encode the information in each voxel
- Typical data types:
  - signed/unsigned byte (8-bit)
  - signed/unsigned short (16-bit)
  - signed/unsigned int (32-bit)
  - float (32-bit) and double (64-bit)
- Not very common:
  - signed/unsigned long (64-bit), complex (64-bit) etc

Important image properties (4/5)

NB: **typical mistakes** when opening a dataset

- Signed or unsigned?

  129 = *10000001* → = 129 unsigned; = -1 signed

- Endian-ness?

  16-bit integer
  two bytes (*b1* and *b2*) → *b1* *b2* (big-endian) or *b2* *b1* (little-endian)

  1025 = *00000100* *00000001* →
  - *00000100* *00000001* = 1025 — big-endian (many scanner workstations)
  - *00000001* *00000100* = 260 — little-endian (intel x86 and x86-64)

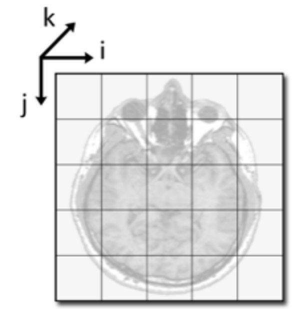
- Is data scaled?
  - Often, values are stored as *integers* but *scaling parameters* are given in the header

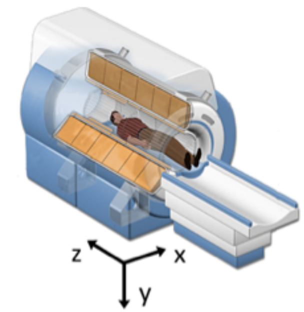
    stored *232* (unsigned 8-bit) + [Scaling slope: **10.0**, Scaling intercept: **0.5**] → *2320.5* (float 32-bit) intended

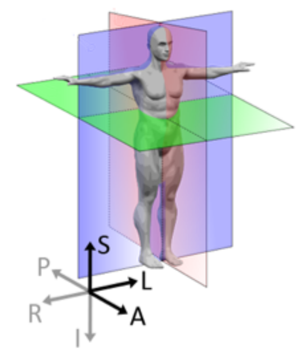
  - **NB**: always perform post-processing in float!

Coordinate systems

- **Image** space (*i, j, k*)
  - voxel indices, no notion of "*physical dimensions*"
- **World** space (*x, y, z*)
  - actual coordinates [in *mm*] w.r.t. the scanner
  - scaling, rotation and translation
- **Patient** space (*L, A, S*)
  - coordinates w.r.t. anatomical planes





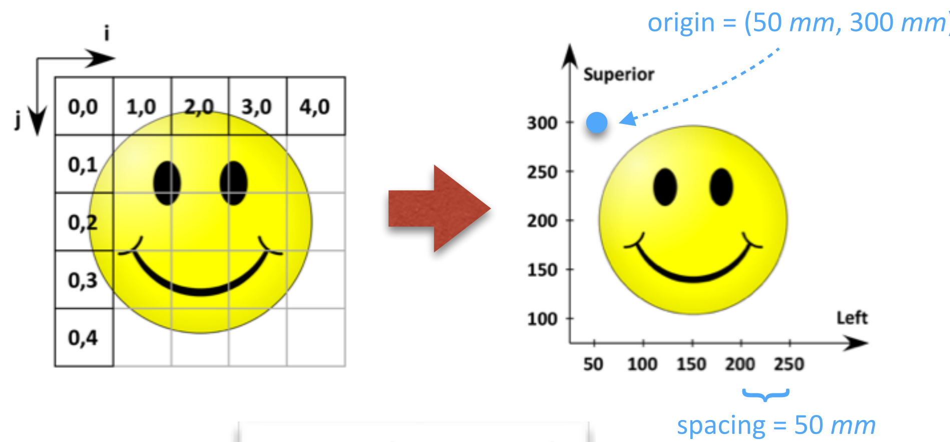


Transformation matrix

rotation/scale translation

$$\begin{pmatrix} x_1 \\ x_2 \\ x_3 \\ 1 \end{pmatrix} = \begin{pmatrix} A_{11} & A_{12} & A_{13} & t_1 \\ A_{21} & A_{22} & A_{23} & t_2 \\ A_{31} & A_{32} & A_{33} & t_3 \\ 0 & 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} i \\ j \\ k \\ 1 \end{pmatrix}$$

- Homogeneous coordinates
- Stored in the header



$$IJtoLS = \begin{pmatrix} 50 & 0 & 50 \\ 0 & -50 & 300 \\ 0 & 0 & 1 \end{pmatrix}$$

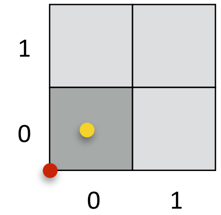
The mess with the orientation (1/2)

It is **really a mess**!

- Every software/processing pipeline uses different conventions
- Causes lots of *headaches* and *problems* in the analysis

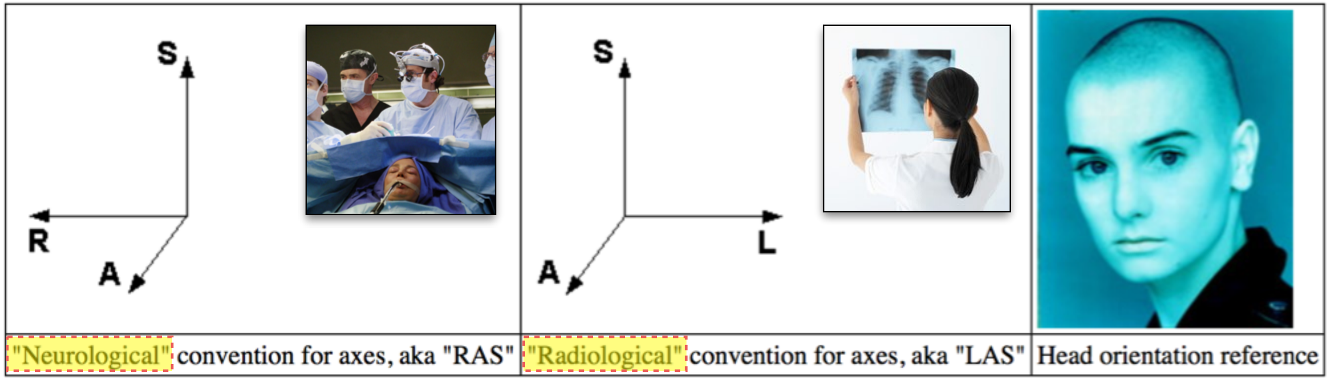
Example 1: where is the origin?

- *Center* of voxel?
- Its *corner*?
- Indices start from “0” (c++, python) or “1” (matlab)?



What is the coordinate **(0,0)**?

Example 2: *neurological* or *radiological*?



“right” is “right”

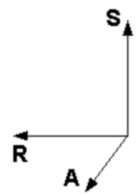
“right” is “left”

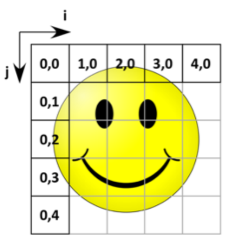
The mess with the orientation (2/2)

- When displayed, images are **flipped**
- **Transformation** matrix is different

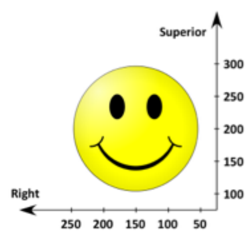
neurological

NB: *right-hand* coordinate system



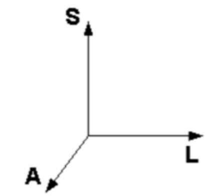


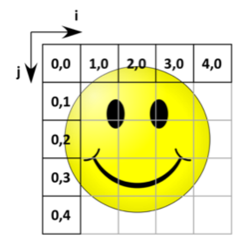
$$IJtoRS = \begin{pmatrix} -50 & 0 & 250 \\ 0 & -50 & 300 \\ 0 & 0 & 1 \end{pmatrix}$$



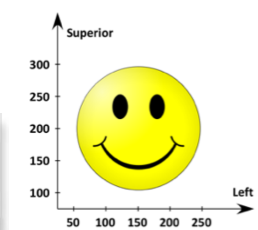
radiological

NB: *left-hand* coordinate system





$$IJtoLS = \begin{pmatrix} 50 & 0 & 50 \\ 0 & -50 & 300 \\ 0 & 0 & 1 \end{pmatrix}$$



Many more sources of confusion!

- Sometimes, the orientation stored in the header is **wrong**!
- **Terminology**: “RAS” for some people is “LPI”
- Some software use **ad-hoc fields** to change this behavior
  e.g. “qfac” (see description at *https://nifti.nimh.nih.gov/pub/dist/src/niftilib/nifti1.h*)
- ...

File formats (1/3)

Two categories:

- Standardize **images produced** by different modalities
  e.g. *DICOM*
- Facilitate **post-processing** pipelines
  e.g. *Analyze, NIFTI, MINC* etc

Summary of main characteristics:

Format	Header	Extension	Data types
Analyze	Fixed-length: 348 byte binary format	.img and .hdr	Unsigned integer (8-bit), signed integer (16-, 32-bit), float (32-, 64-bit), complex (64-bit)
Nifti	Fixed-length: 352 byte binary format[a] (348 byte in the case of data stored as .img and .hdr)	.nii	Signed and unsigned integer (from 8- to 64-bit), float (from 32- to 128-bit), complex (from 64- to 256-bit)
Minc	Extensible binary format	.mnc	Signed and unsigned integer (from 8- to 32-bit), float (32-, 64-bit), complex (32-, 64-bit)
Dicom	Variable length binary format	.dcm	Signed and unsigned integer, (8-, 16-bit; 32-bit only allowed for radiotherapy dose), float not supported

most diffuse for post-processing

most diffuse on scanners

Not all the software support all the specified data types. Dicom, Analyze, and Nifti support color RGB 24-bit; Nifti also supports RGBA 32-bit (RGB plus an alpha-channel)

[a] Nifti has a mechanism to extend the header

DICOM (1993)

- **International standard** for medical images and related information (ISO 12052)
- *"…an image separated from its metadata is meaningless as medical image…"*
- *Most complete* description of the data
- Self-contained
  - from the image, an experiment can be repeated!
- Data sharing
  - Picture Archiving and Communication System (PACS)
- Notes:
  - too much for *post-processing*
  - remember to *anonymize data* before sharing
  - not really standard (different vendors use different fields)
  - store only integers

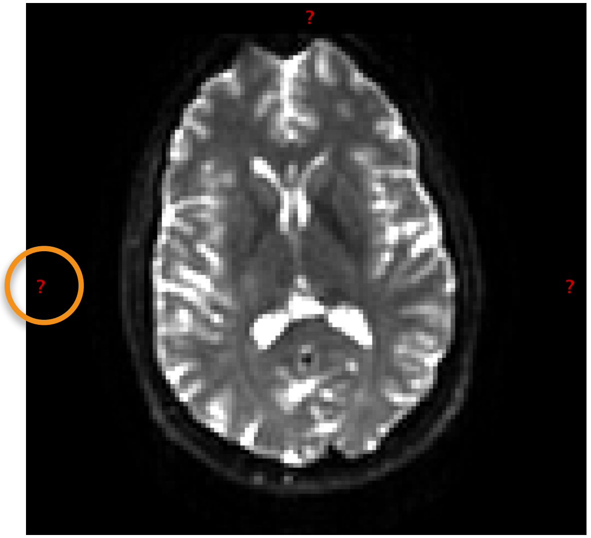

```
(0008,0022) Acquisition Date [20161012]
(0008,0023) Content Date [20161012]
(0008,0030) Study Time [135549.133000]
(0008,0031) Series Time [141430.792000]
(0008,0032) Acquisition Time [141640.767500]
(0008,0033) Content Time [141750.818000]
(0008,0050) Accession Number []
(0008,0060) Modality [MR]
(0008,0061) Modalities in Study [MR]
(0008,0070) Manufacturer [SIEMENS]
(0008,0080) Institution Name [Radiologie CHUV]
(0008,0081) Institution Address [Rue du Bugnon 21,Lausanne,District,CH,1011]
(0008,0090) Referring Physician's Name []
(0008,1010) Station Name [MRAWP67014]
```

```
(0010,0010) Patient's Name [BERCLAZ_V_DIFF_PH]
(0010,0020) Patient ID [16.10.12-13:55:14-DST-1.3.12.2.1107.5.2.43.67014]
(0010,0021) Issuer of Patient ID []
(0010,0030) Patient's Birth Date [19790115]
(0010,0040) Patient's Sex [F]
(0010,1010) Patient's Age [037Y]
(0010,1020) Patient's Size [1.77]
(0010,1030) Patient's Weight [75]
(0018,0015) Body Part Examined [BRAIN]
```

```
(0018,0020) Scanning Sequence [EP]
(0018,0021) Sequence Variant [SK,SP]
(0018,0022) Scan Options [PFP,FS]
(0018,0023) MR Acquisition Type [2D]
(0018,0024) Sequence Name [*ep_b2000#49]
(0018,0025) Angio Flag [N]
(0018,0050) Slice Thickness [1.6000000238419]
(0018,0080) Repetition Time [5100]
(0018,0081) Echo Time [80]
(0018,0083) Number of Averages [1]
(0018,0084) Imaging Frequency [123.251798]
(0018,0085) Imaged Nucleus [1H]
```

Analyze (1990)

- Designed for **multi-dimensional data**
- **Separates** *data* (.img) from *metadata* (.hdr)
- Not possible to establish **image orientation**



NIFTI (2000)

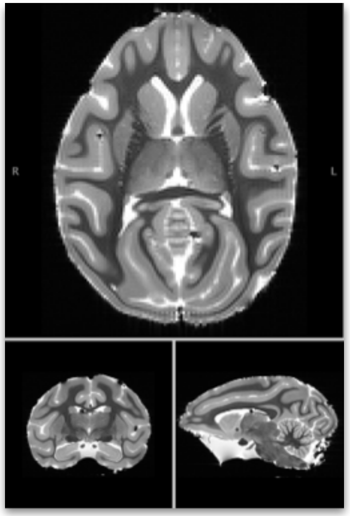
- Revised version of *Analyze*
- **Standard de-facto** in neuroimaging research (.nii)
- Supports **compression** (.nii.gz)
- Double way to store **orientation**:
  - "qform": to *world space* coordinates
  - "sform": to *standard space* coordinates, e.g. common template

```
Quaternion Parameters:  b = 0.0  c = 0.0  d = 1.0
Quaternion Offsets:  x = 80.0  y = 80.0  z = 85.0
S-Form Parameters X: -1.0, 0.0, -0.0, 80.0
S-Form Parameters Y: 0.0, -1.0, -0.0, 80.0
S-Form Parameters Z: 0.0, 0.0, -1.0, 85.0
```

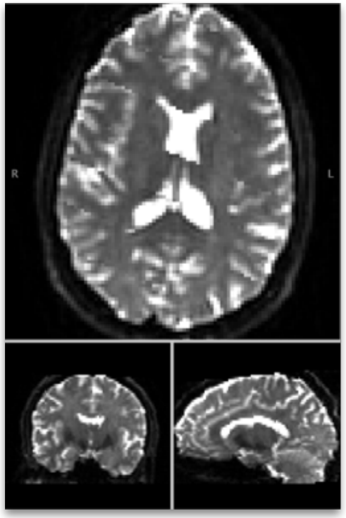
- Default file format of most **software packages**:
  - FSL, SPM, ITK Snap, 3D Slicer, ITK & VTK, nipy, etc

Trade-off between *quality* and *patient comfort*

- usually, higher quality requires longer acquisitions



Monkey :
- *ex-vivo*
- *1 week*



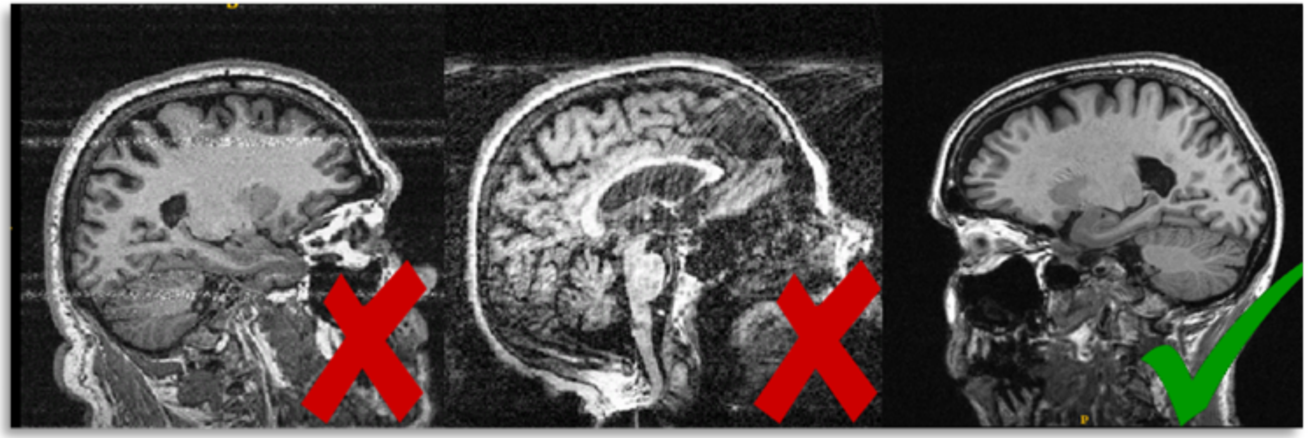
Human :
- *in-vivo*
- *25 minutes*

Main criteria for **quality assessment**:

1) Presence of artifacts
2) Spatial resolution
3) Noise level
4) Image contrast

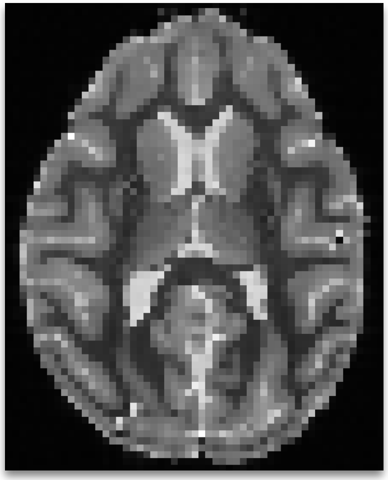
Image quality (2/4)

1) Presence of **artifacts**



2) Spatial **resolution**

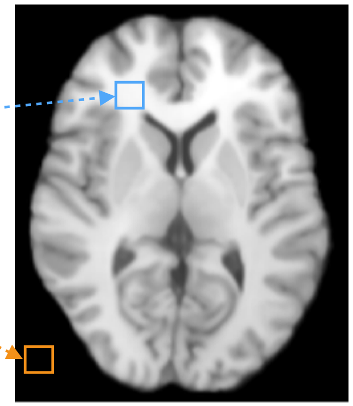
0.5 x 0.5 x 0.5 mm



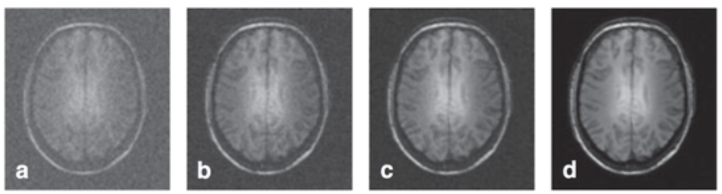
1.0 x 1.0 x 1.0 mm

3) **Signal-to-noise** ratio

- Many different definitions
- A common one is: $\mathrm{SNR} = \frac{\mu_\mathrm{S}}{\sigma_\mathrm{N}}$



- Averaging improves SNR:



4) **Contrast-to-noise** ratio

- Common definition:

$$\mathrm{CNR}_\mathrm{AB} = \frac{C_\mathrm{AB}}{\sigma_\mathrm{N}} = \frac{|S_\mathrm{A} - S_\mathrm{B}|}{\sigma_\mathrm{N}}$$

where $\mathrm{C}_\mathrm{AB} = |S_\mathrm{A} - S_\mathrm{B}|$ is the contrast between region *A* and *B*

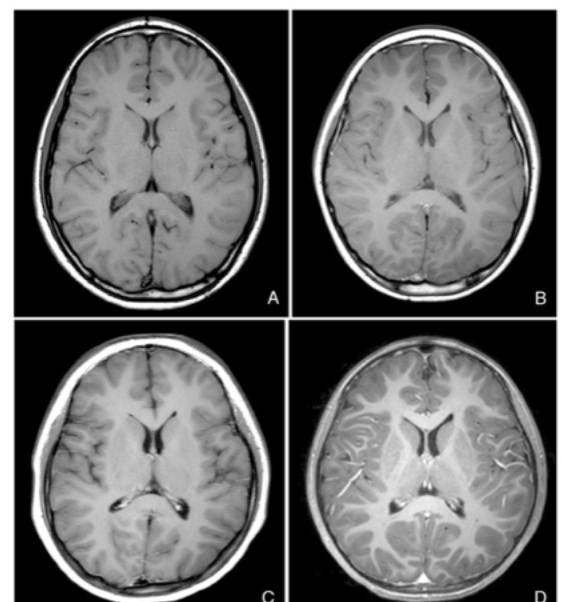
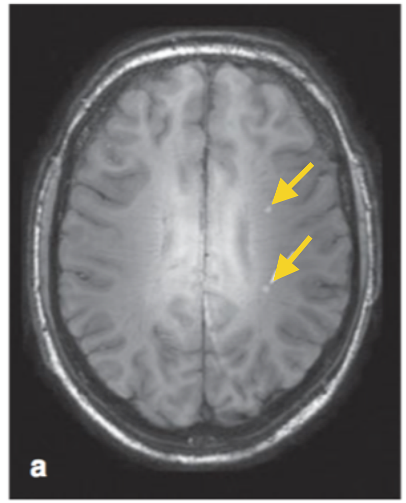
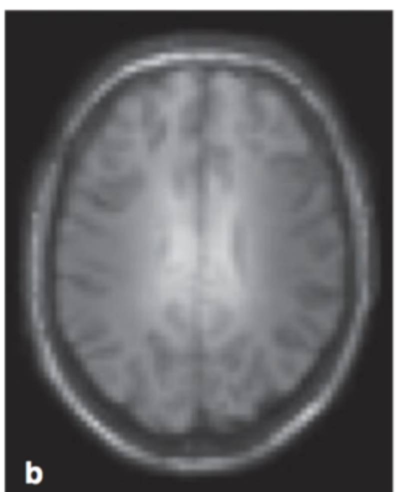


Image quality (4/4)

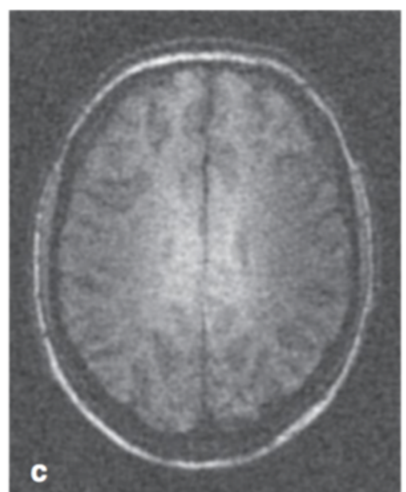
- All factors **affect diagnostic power**:



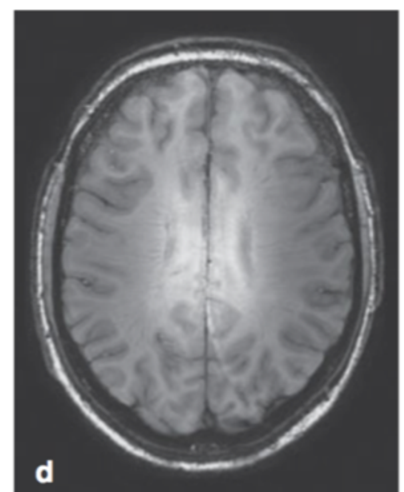
multiple sclerosis lesions
are visible
in the original image



lower resolution



lower SNR



reduced CNR