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Center for Mind/Brain Sciences

Brain Diffusion MRI Introduction

Louvain-la-Neuve - Neuroimaging Workshop 2019

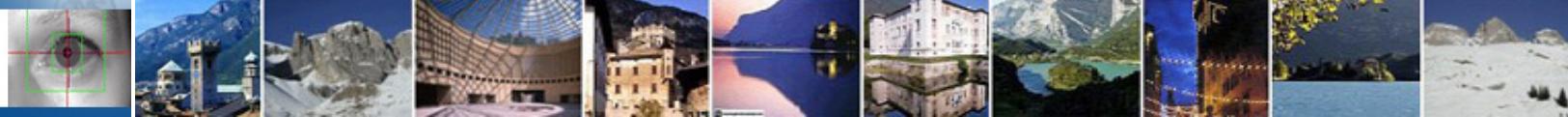
Jorge Jovicich

Center for Mind/Brain Sciences (CiMeC),
University of Trento, Rovereto, Italy

CiMeC: <https://www.cimec.unitn.it/>

MRI Lab: <http://r.unitn.it/en/cimec/mri>

E-mail: jorge.jovicich@unitn.it



Concept map for lectures

Lecture 1

NMR Signal origin

- Powerful magnet
- Radio frequency
- Magnetic field gradients

MR Image & Contrast

- Spatial encoding
- Magnetic gradients
- Pulse sequences

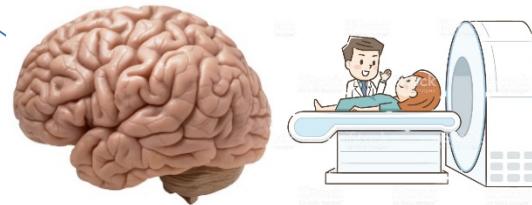
MR Safety

- Powerful magnet
- Radio frequency
- Magnetic field gradients

Lecture 2

Structural MRI

- Contrast, important parameters
- Sequences & artifacts
- Analyses & applications



Lecture 3

Diffusion MRI

- Contrast, important parameters
- Sequences & artifacts
- Analyses & applications

Lecture 4

Functional MRI

- Contrast, important parameters
- Sequences & artifacts
- Pre-processing

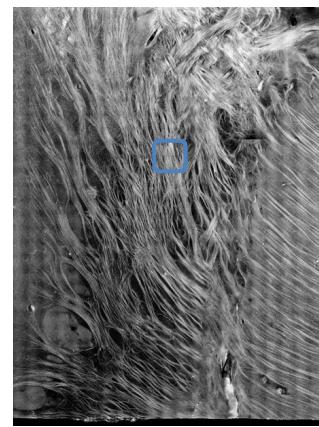
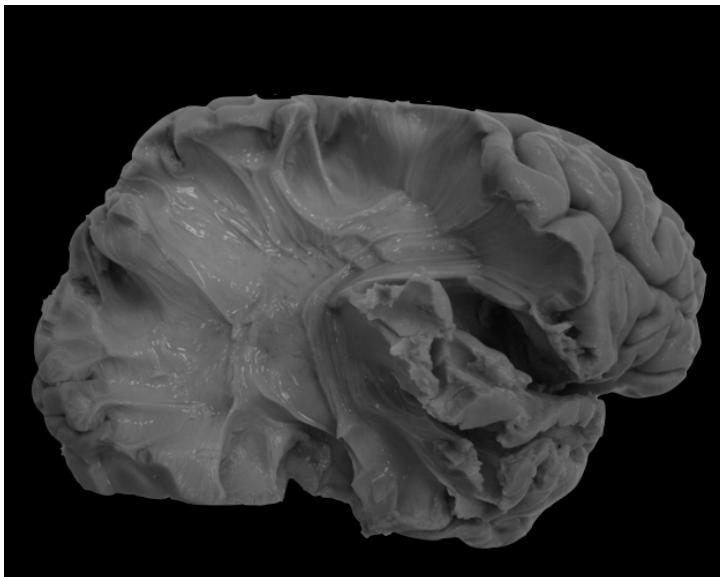
Lecture 3 outline

Brain diffusion:

- **Why do we care?**
- **How do we measure it?**
- **How do we pre-process data?**
- **Extracting information: models & challenges**

Diffusion MRI: Motivation

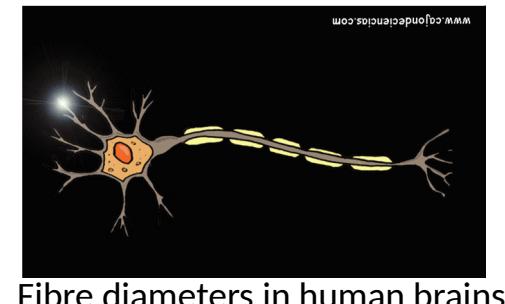
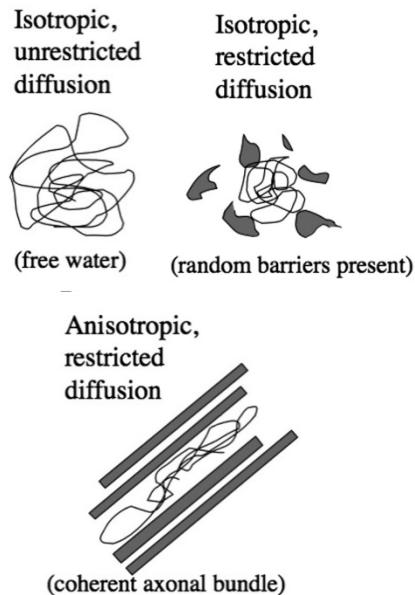
- **Brain anatomy characterization (in-vivo, non-invasive)**
 - Brain tissue microstructure (axon diameter, density, myelination, etc.)
 - White matter fibers (orientations, connections, etc.)
- **Diffusion of water molecules in tissue**
 - Reflects the local microstructural environment
 - Physical restrictions will affect diffusion magnitude and directionality
- **Diffusion MRI**
 - Contrast sensitive magnitude and direction of water diffusion
 - Models relate the NMR signal with microstructure properties



1.5cm x 1.8cm,
8.5um x 8.5um

Courtesy of Hui Wang

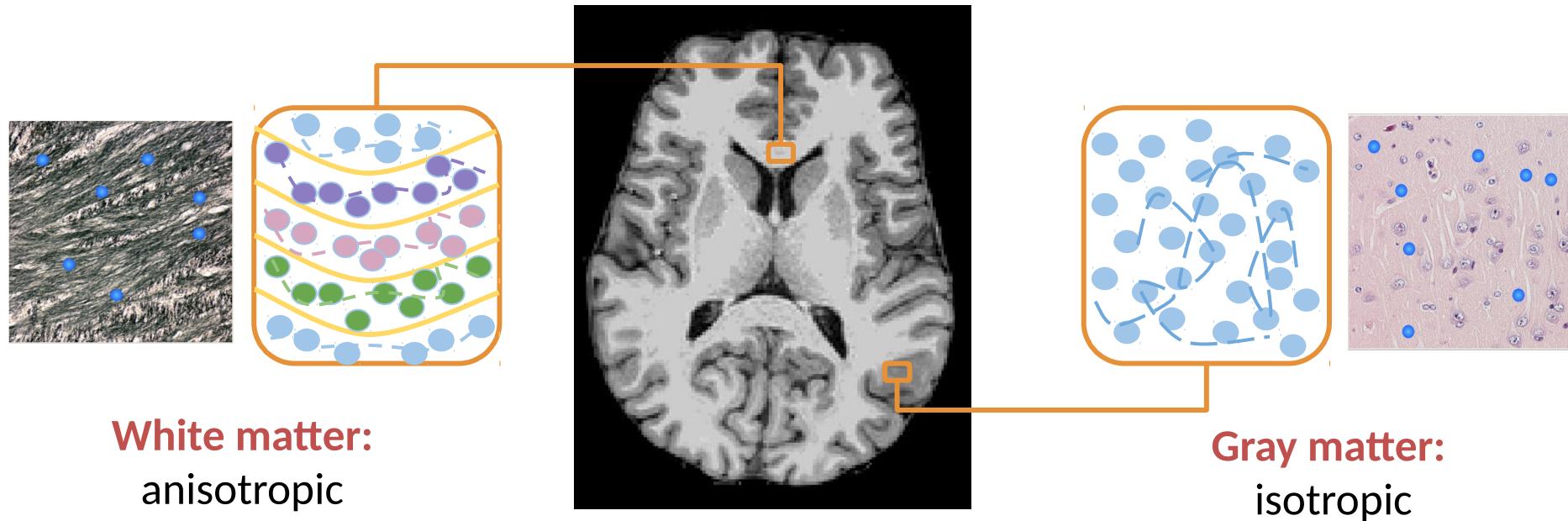
Courtesy of Viviana Silessi & Chiara Maffei



Fibre diameters in human brains
ranged from 0.16 to 9 μm
Liewald et al. 2014

Water diffusion in the brain

- **Why bother about molecular diffusion in brain?**
- Water molecules diffuse differently inside biological tissues
- We can differentiate brain tissues based on different diffusion profiles within them



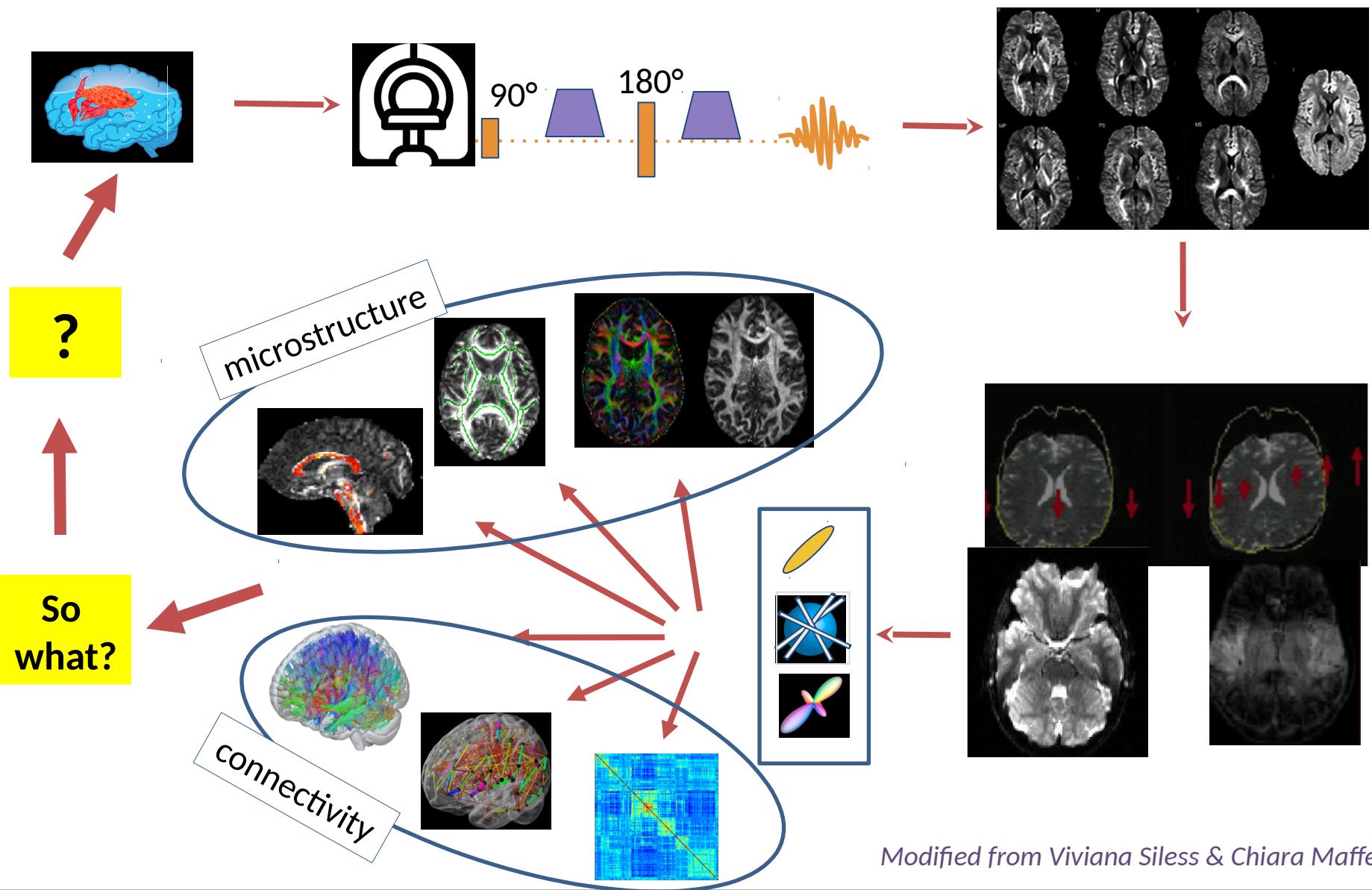
Courtesy of Viviana Silessi & Chiara Maffei

Lecture 3 outline

Brain diffusion:

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- **Why do we care?**
 - **How do we measure it?**
 - **How do we pre-process data?**
 - **Extracting information: models & challenges**

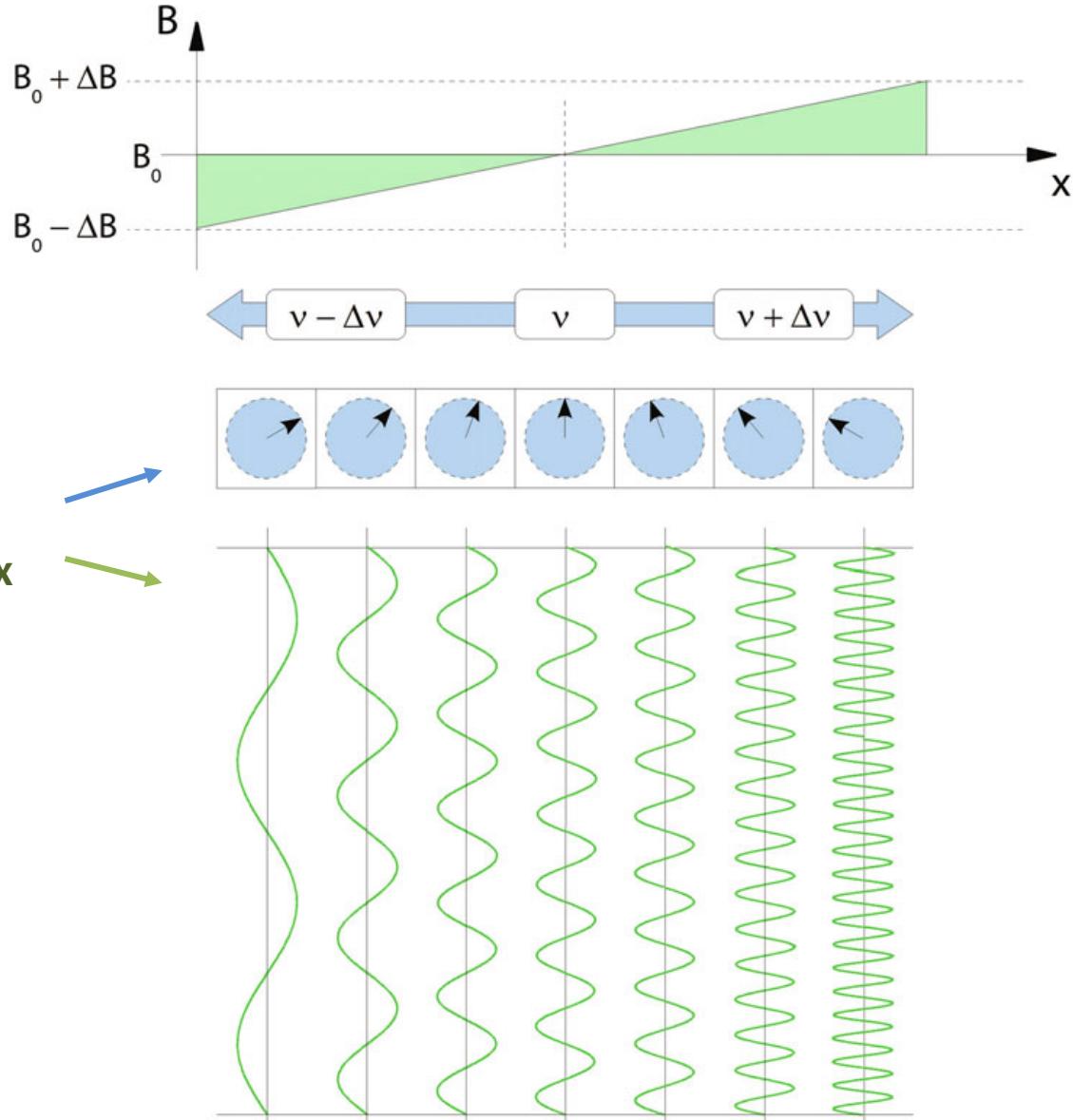
Diffusion MRI overview



Diffusion contrast: based on gradients

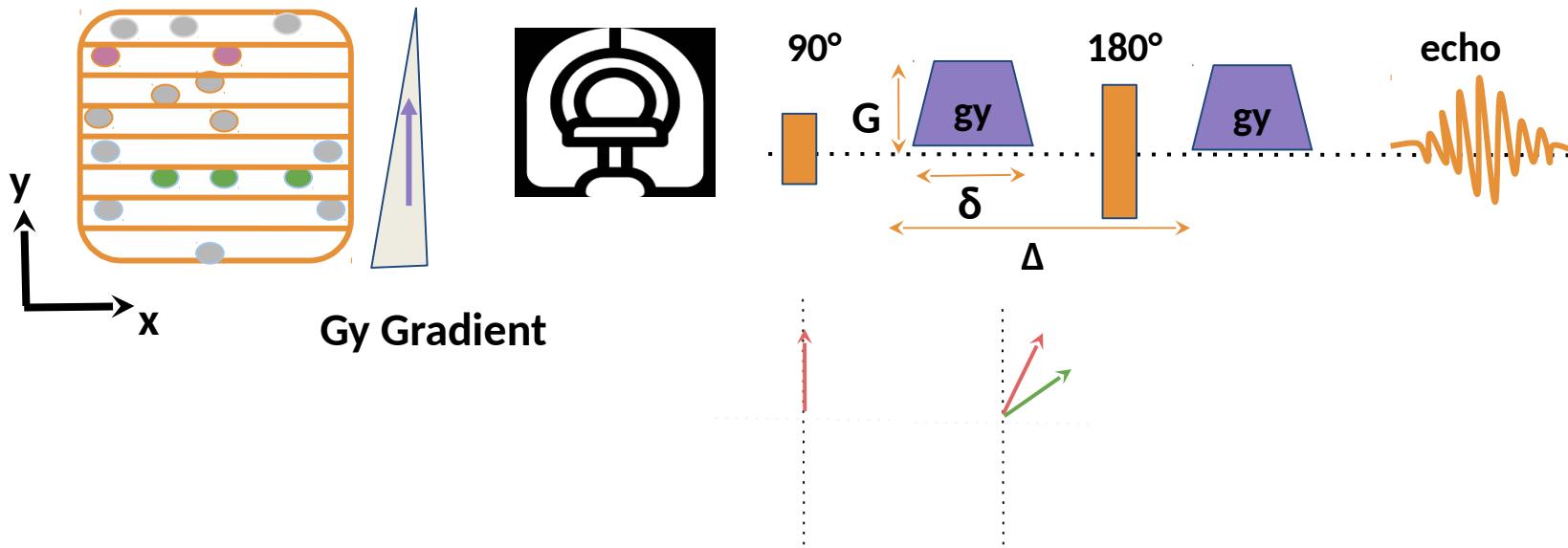
REMINDER

- Gradient along x-axis
- Two spatial-encoding possibilities for the magnetization:
 - Phase changes along x-axis
 - Frequency changes along x-axis



Diffusion MRI: how do we measure it?

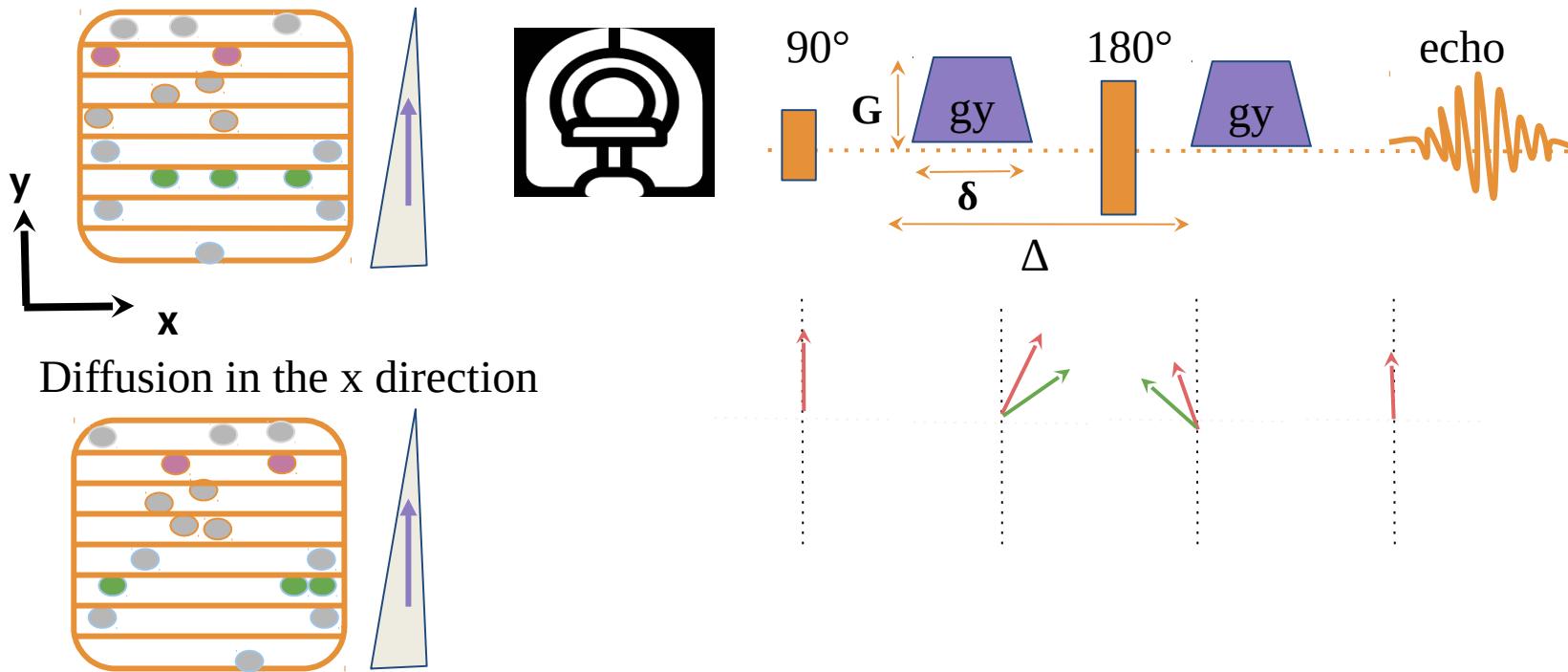
- Pulse Gradient Spin Echo sequence (PGSE)



Courtesy of Viviana Silessi & Chiara Maffei

Diffusion MRI: how do we measure it?

- Pulse Gradient Spin Echo sequence (PGSE)

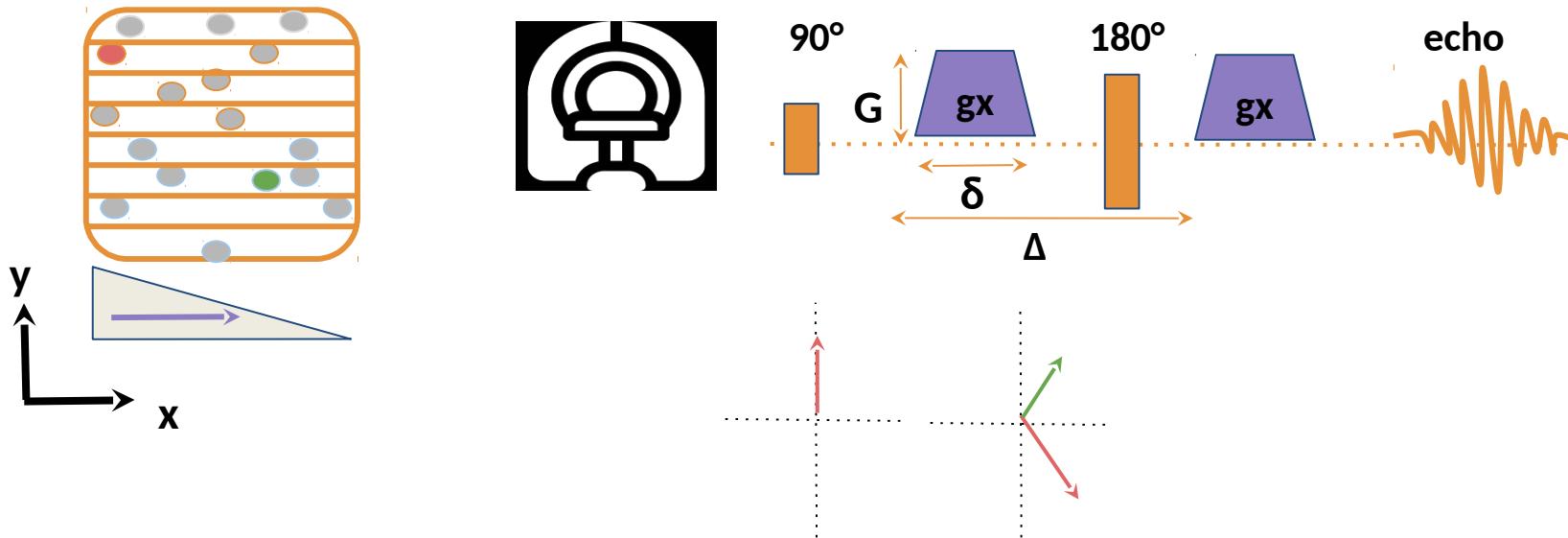


- No displacement along y-axis
- No dephasing induced by y-gradient
- No MR signal attenuation cause by diffusion y-gradient

courtesy of Viviana Silessi & Chiara Maffei

Diffusion MRI: how do we measure it?

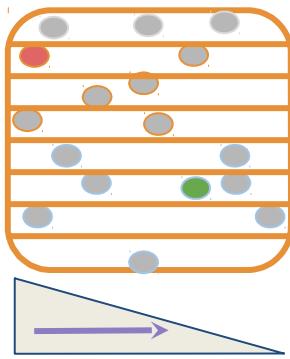
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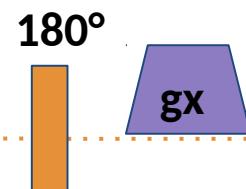
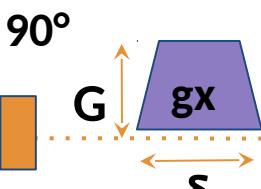
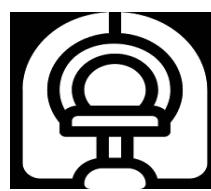
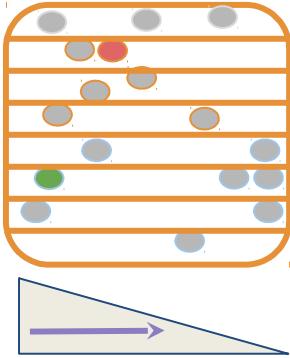
Courtesy of Viviana Silessi & Chiara Maffei

Diffusion MRI: how do we measure it?

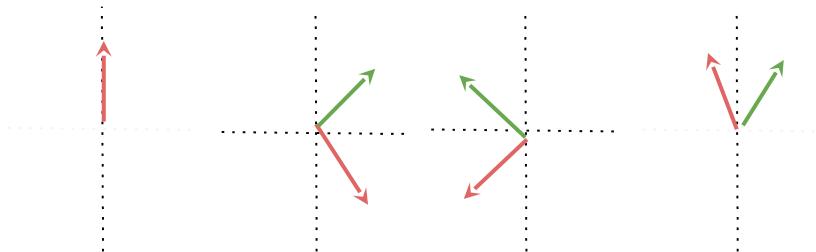
- Pulse Gradient Spin Echo sequence (PGSE)



Diffusion in the x direction



Δ

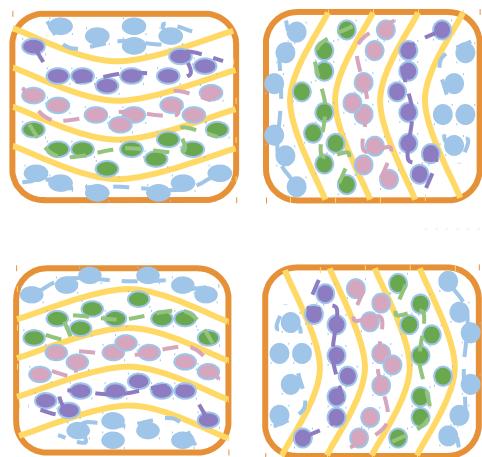


- Displacement captured by the diffusion x-gradient
- Dephasing of magnetization
- **Signal attenuation caused by diffusion gradients**

Courtesy of Viviana Siless & Chiara Maffei

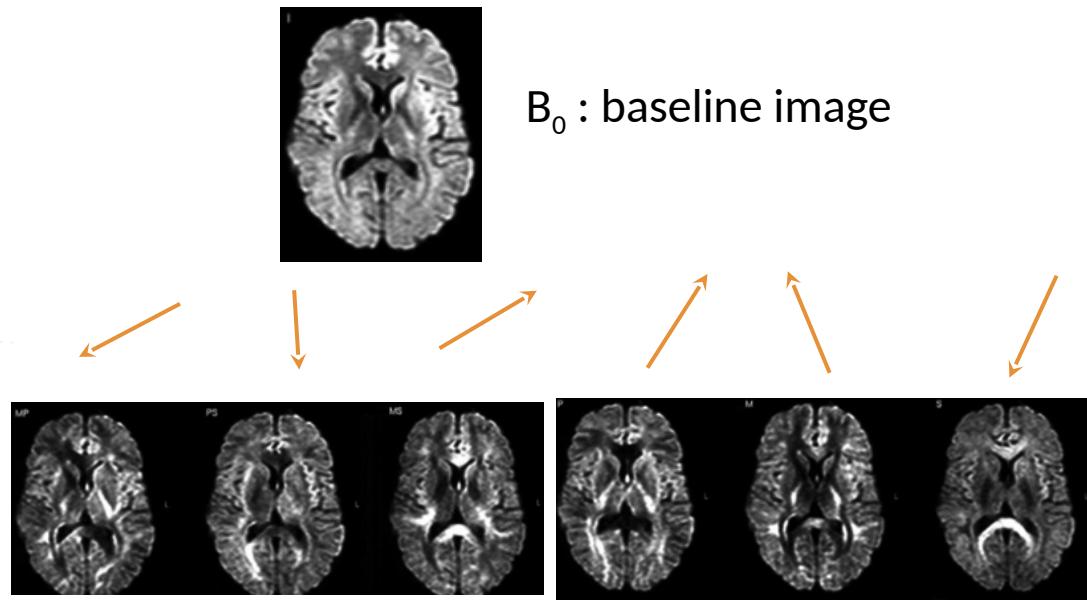
Diffusion MRI: how do we measure it?

- Many possible configurations can appear in each voxel: In one mm cubic voxel there are millions of axons of ~um resolution.
- Because of the orientation dependency in encoding diffusion, multiple diffusion directions (**b-vector**) are needed to cover the full 3D profile.



Sensitivity to diffusion in multiple directions

Multiple gradient encoding directions



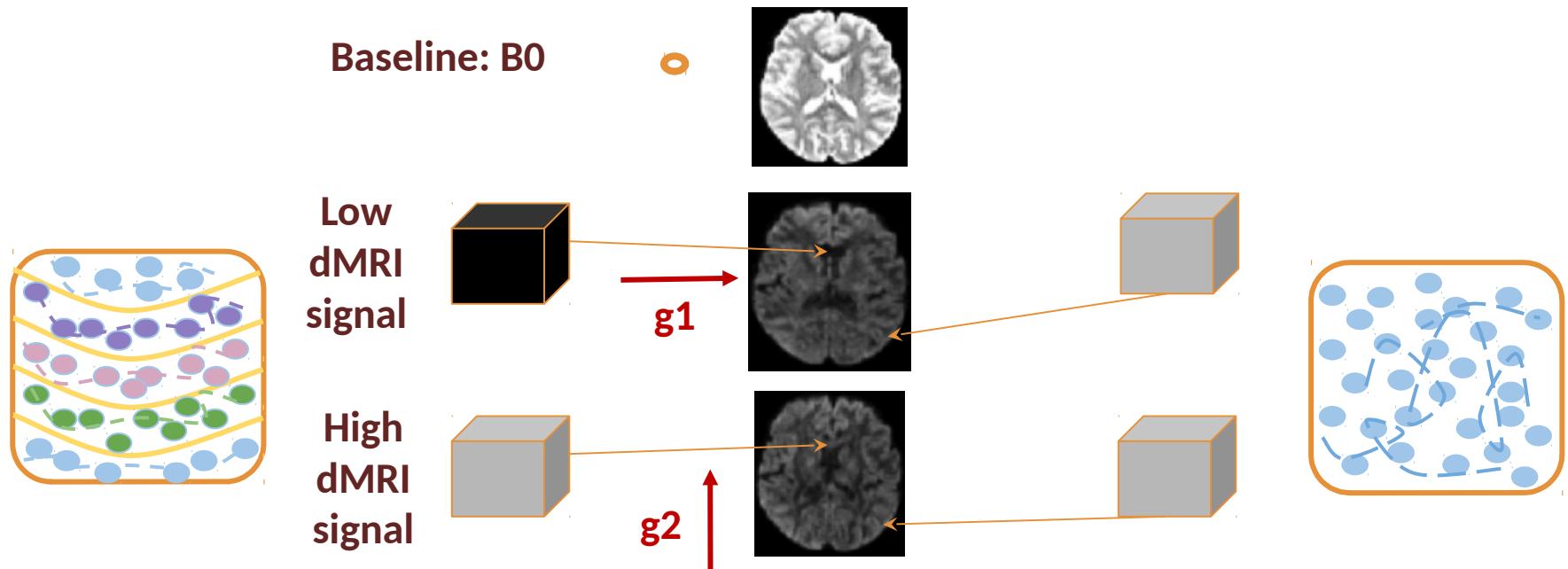
g1 g2 g3 g4 g5 g6
Diffusion weighted images (DWI)

Courtesy of Viviana Silessi & Chiara Maffei

Diffusion MRI: how do we measure it?

Diffusion encoding:

- Only along the specific direction applied
- Image intensity is attenuated depending on water diffusion for the specific direction.
- We compare each image direction to a baseline image (no direction, B0).



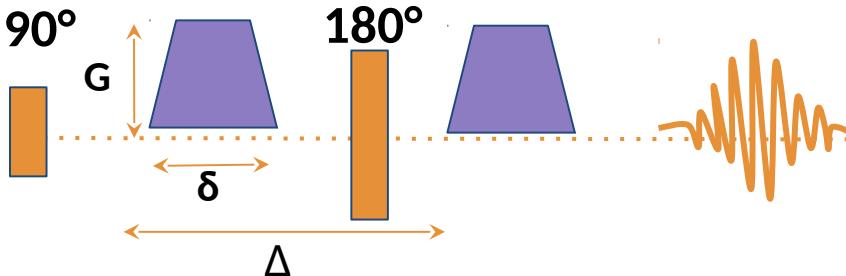
Courtesy of Viviana Silessi & Chiara Maffei

Diffusion MRI: what is the b-value?

- **MRI signal:** $S_{(b)} = S_0 e^{-bD}$
- **b-value** (diffusion weight): Measure of diffusion sensitivity
Large $b \rightarrow$ strong diffusion sensitivity
- The **b-value** depends on the sequence and acquisition parameters:

$$b = \gamma G^2 \delta^2 (\Delta - \delta/3)$$

Pulse Gradient Spin Echo sequence (PGSE)

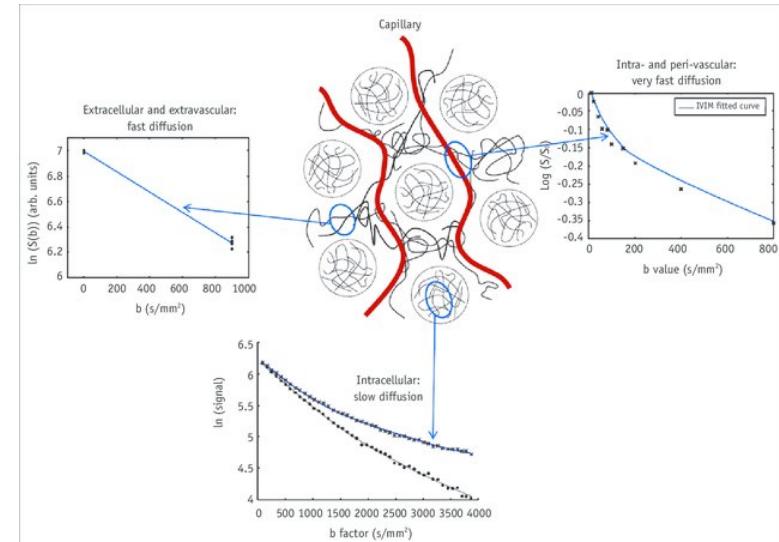


γ → gyromagnetic ratio

G → diffusion gradient strength

δ → duration of the diffusion-encoding pulse

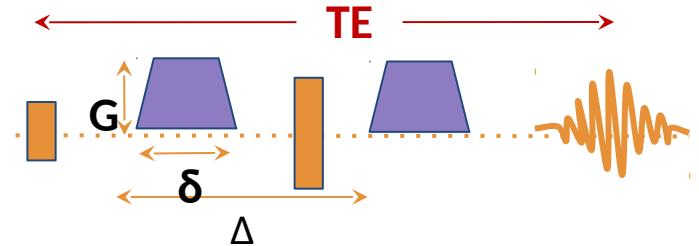
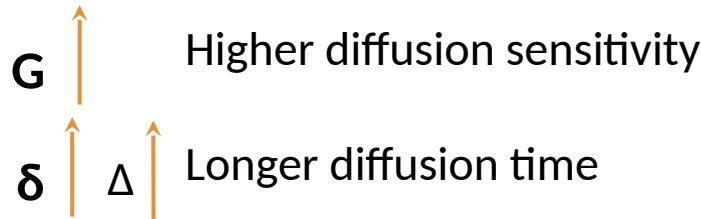
Δ → the interval between diffusion pulses



Kim & Kim 2016

Diffusion MRI: why is the b-value important?

- b-value increase \Rightarrow increased contrast between areas of higher and lower diffusivity



- Increasing the length of the diffusion-encoding gradient pulses
 \rightarrow Increased echo time (TE) \rightarrow Decreased signal-to-noise-ratio (SNR)!
- To scan with high b-value you need **STRONG** and **FAST** magnetic gradients (\$\$)

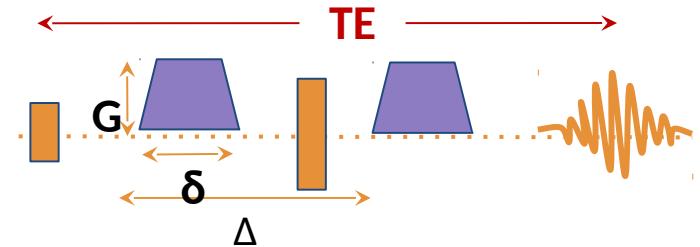
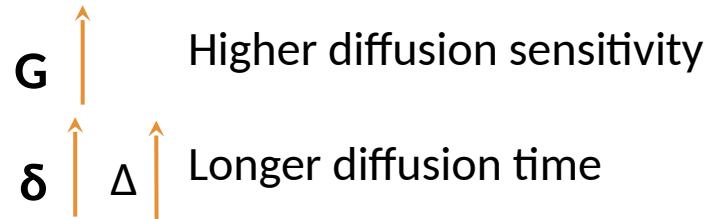
- Clinical MRI scanners \rightarrow $G_{max} = 40 \text{ mT/m}$
- Prisma scanner \rightarrow $G_{max} = 80 \text{ mT/m}$ (MGH)
- HCP scanners \rightarrow $G_{max} = 300 \text{ mT/m}$ (MGH)
- Some animal scanners \rightarrow $G_{max} = 1000 \text{ mT/m}$

G_{max}	Desired b	Needed δ	Resulting TE
40 mT/m	1000 s/mm ²	24 ms	48 ms
1000 mT/m	1000 s/mm ²	3 ms	6 ms

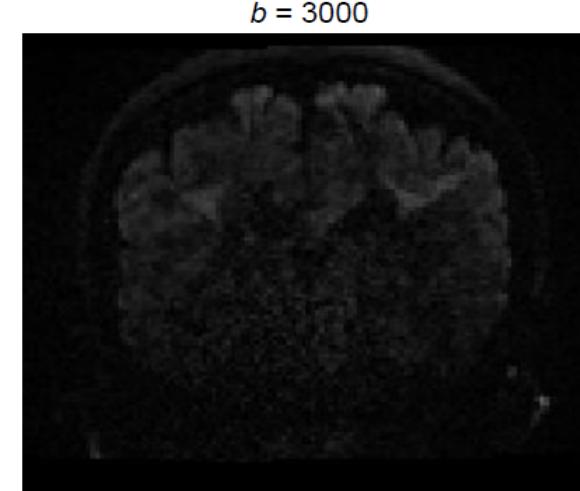
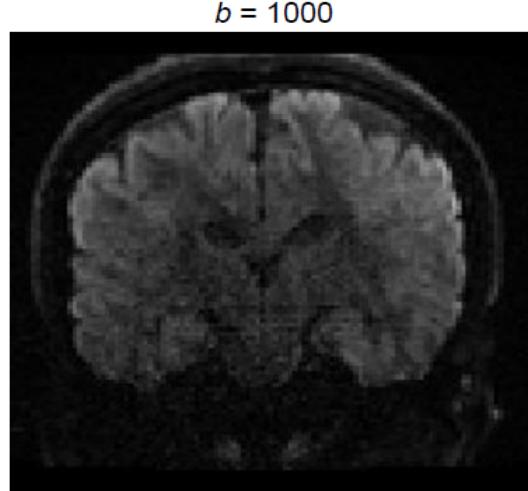
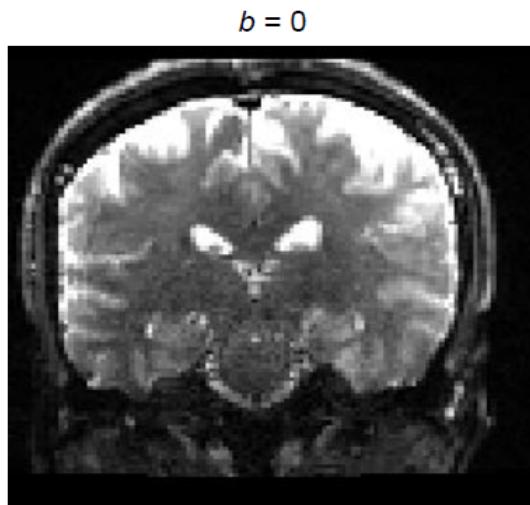
Modified from Viviana Silessi & Chiara Maffei

Diffusion MRI: why is the b-value important?

- b-value increase \Rightarrow increased contrast between areas of higher and lower diffusivity



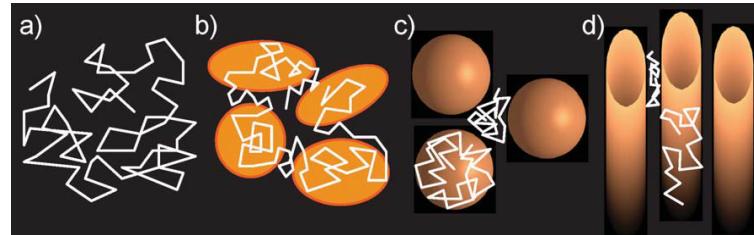
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data: Human Connectome Project

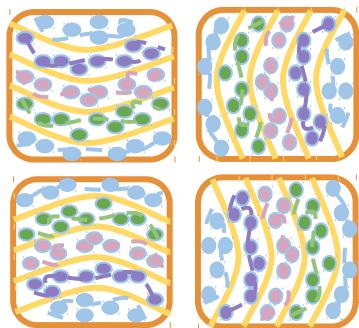
Diffusion MRI: b-value and gradient directions

- In a voxel
 - ⇒ many possible orientations for molecular diffusion
 - ⇒ many different levels of diffusion

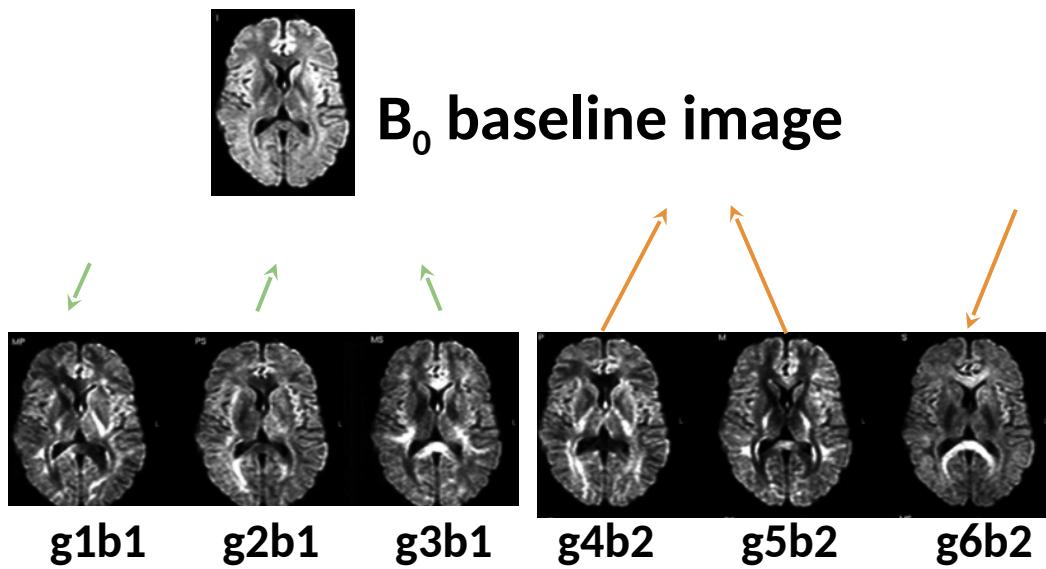


Derek Jones, 2010

- Ideally you want to acquire diffusion MRI data with
 - Different b-values (sensitivity to different ranges of diffusion)
 - Multiple gradient-encoding directions for each b-value (sensitivity in 3D space)



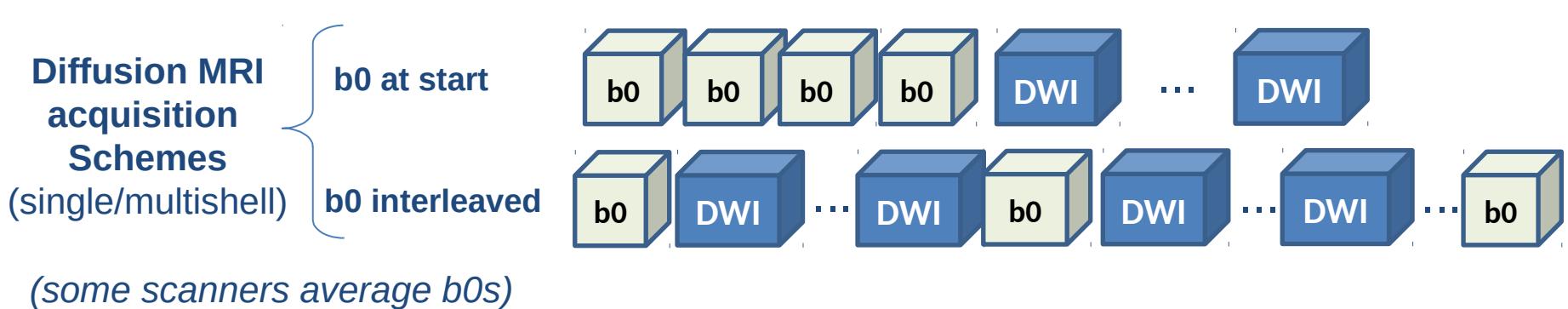
b1
—
b2



Modified from Viviana Silessi & Chiara Maffei

Diffusion MRI data structure

- Multiple 3D brain volumes, each one with fast-MRI (spin-echo Echo Planar Imaging)
- Several of them are b0 (used for diffusion estimation and for head motion correction)
- Several diffusion weighted images:
 - Single-shell: means there is one b-value for diffusion encoding, multiple gradient encoding directions
 - Multi-shell: mean there are many different shells
- Your pulse sequence defines the order in which b-values and directions are acquired



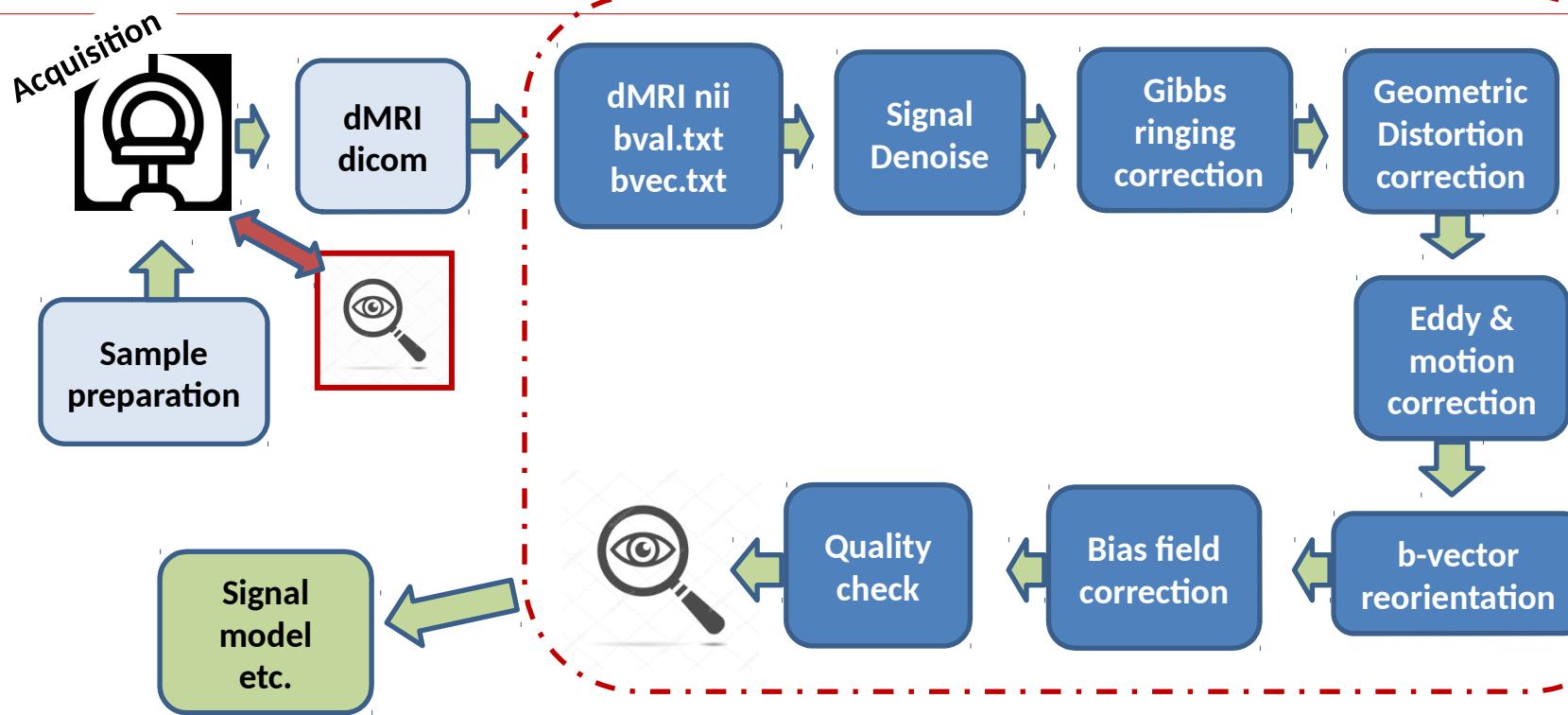
Lecture 3 outline

Brain diffusion:

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- **Why do we care?**
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Diffusion MRI pre-processing

Pre-processing: analyses steps to minimize noise, artifacts to get the «cleanest» data for models



This is a generic example
Jury out for optimal details

Various pre-processing tools available:

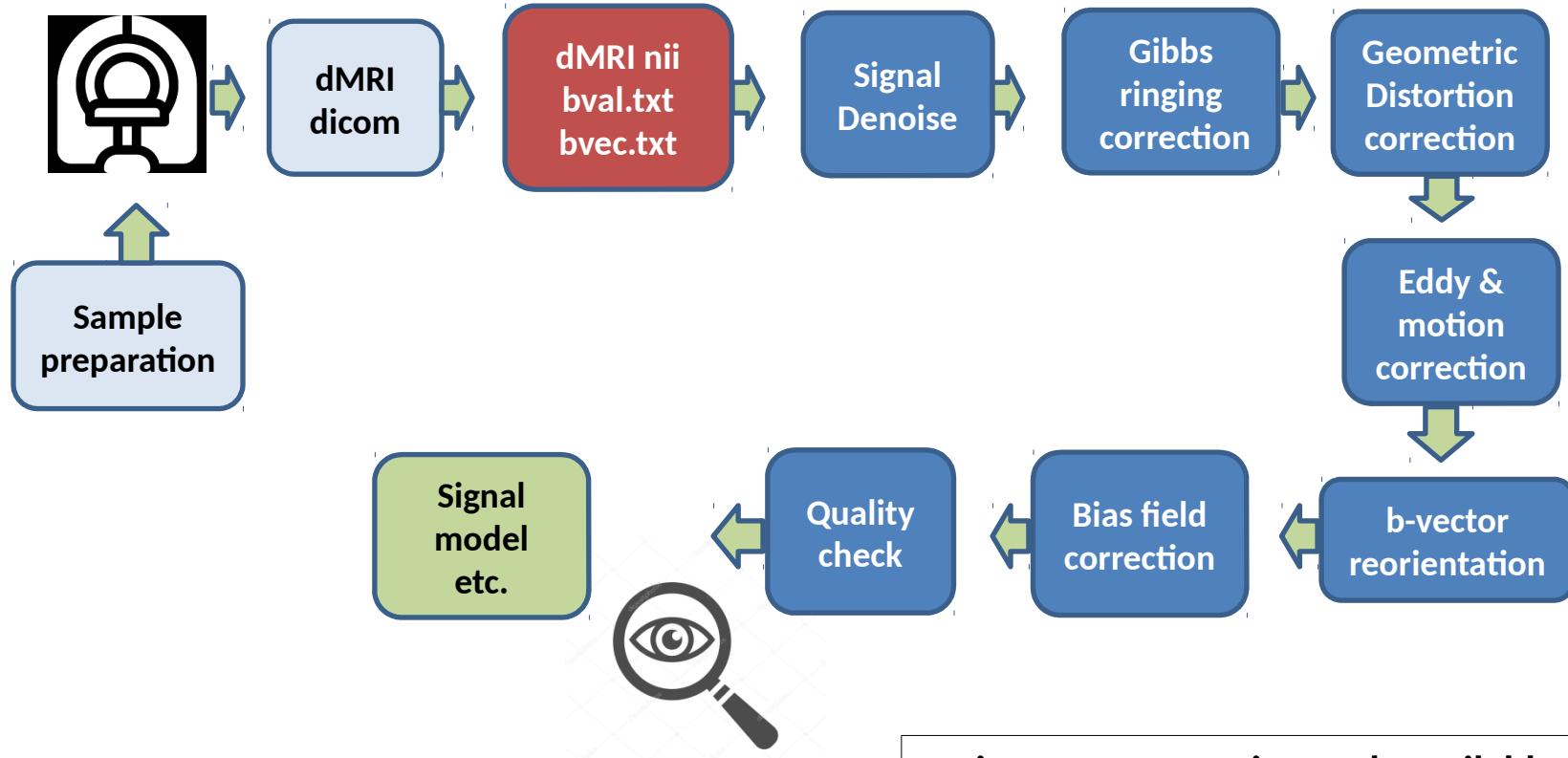
<https://tortoise.nibib.nih.gov>

<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FDT>

<https://www.mrtrix.org>

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Diffusion MRI pre-processing



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<https://www.mrtrix.org>

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Diffusion MRI: reformatting

Journal of Neuroscience Methods 264 (2016) 47–56

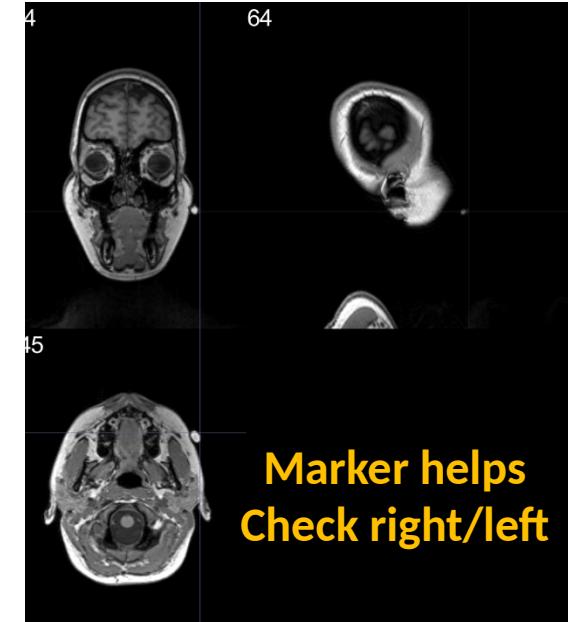
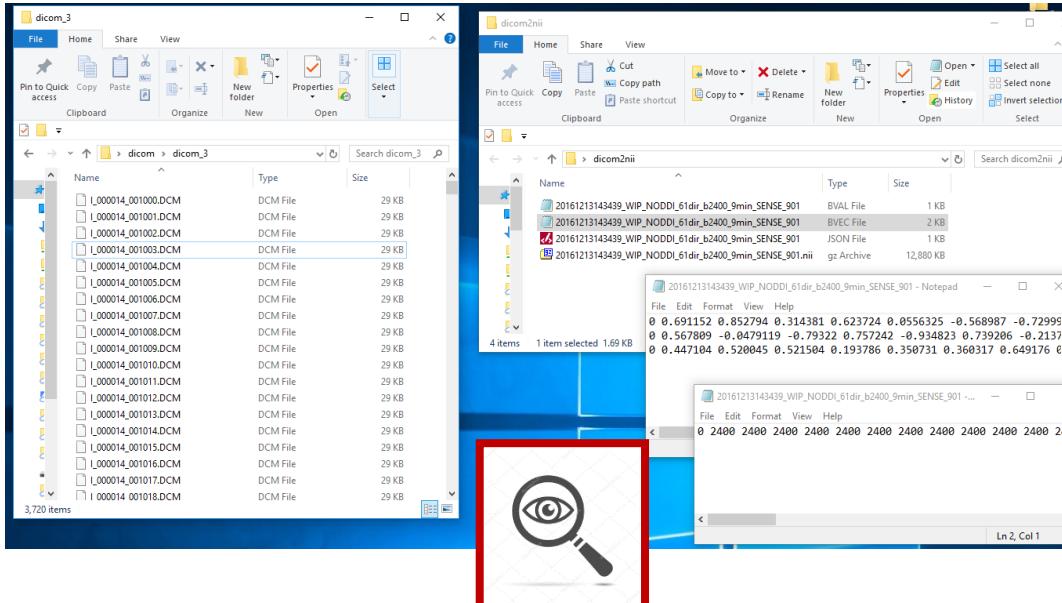


The first step for neuroimaging data analysis:
DICOM to NIfTI conversion

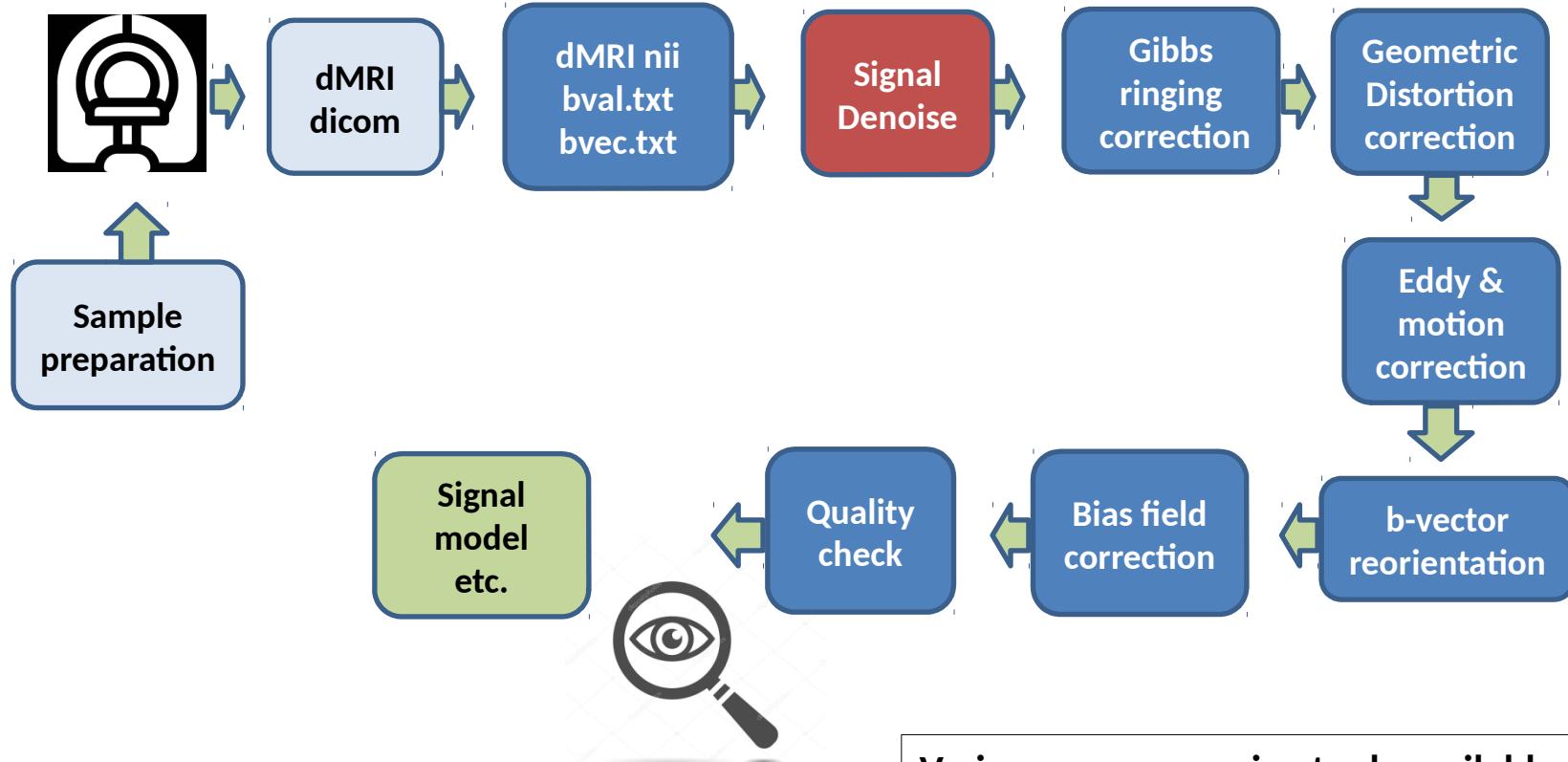


Xiangrui Li^a, Paul S. Morgan^b, John Ashburner^c, Jolinda Smith^d, Christopher Rorden^{c,*}

dicom2nii



Diffusion MRI pre-processing



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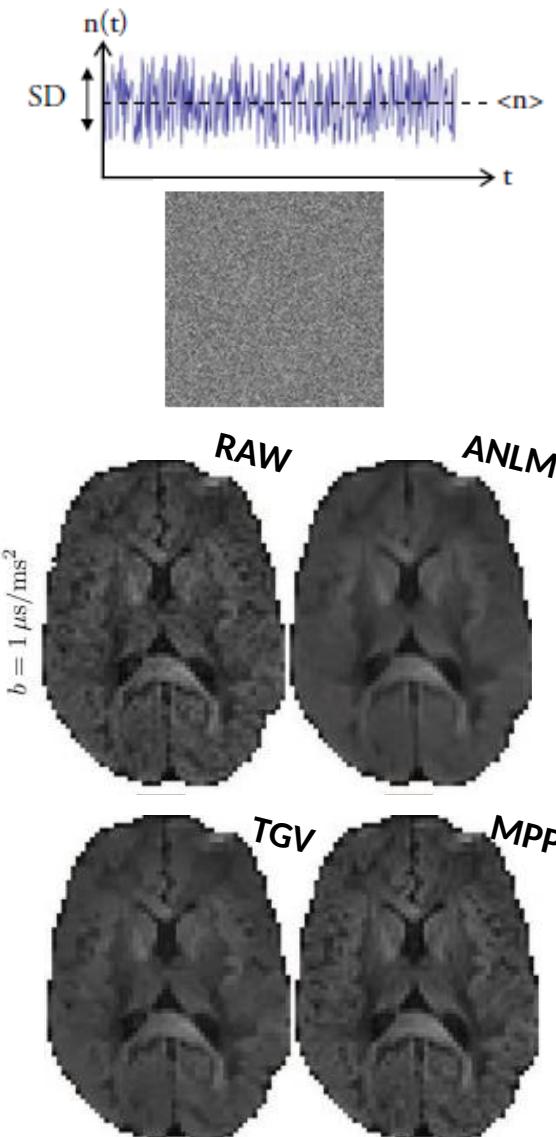
<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FDT>

<https://www.mrtrix.org>

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Diffusion MRI: Signal denoising

- **Thermal noise sources**
 - Detection system: random electron motion in electronic
 - Sample: random spin fluctuations
- **Noise in diffusion MR signal**
 - Will propagate through analysis & modelling
 - Will affect accuracy and reproducibility
 - Need to optimize SNR with acquisition parameter choices
- **Post processing noise reduction**
 - Smoothing
 - Blurs image, spatial resolution loss
 - Total generalized variation regularization
 - Preserve edges
 - Regularization parameter dependent
 - Principal component analysis
 - Uses data redundancy
 - Preserves accuracy and spatial resolution
 - Identifies + eliminates noise-only components



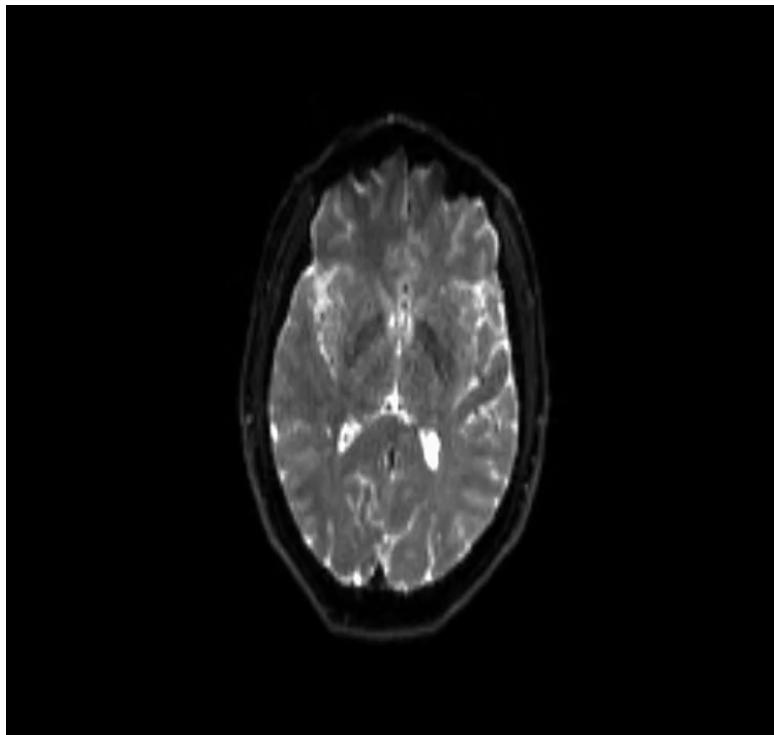
Manjon et al. Med. Image Anal.c 2008

Rudin et al. D: Nonlinear Phenomena, 1992

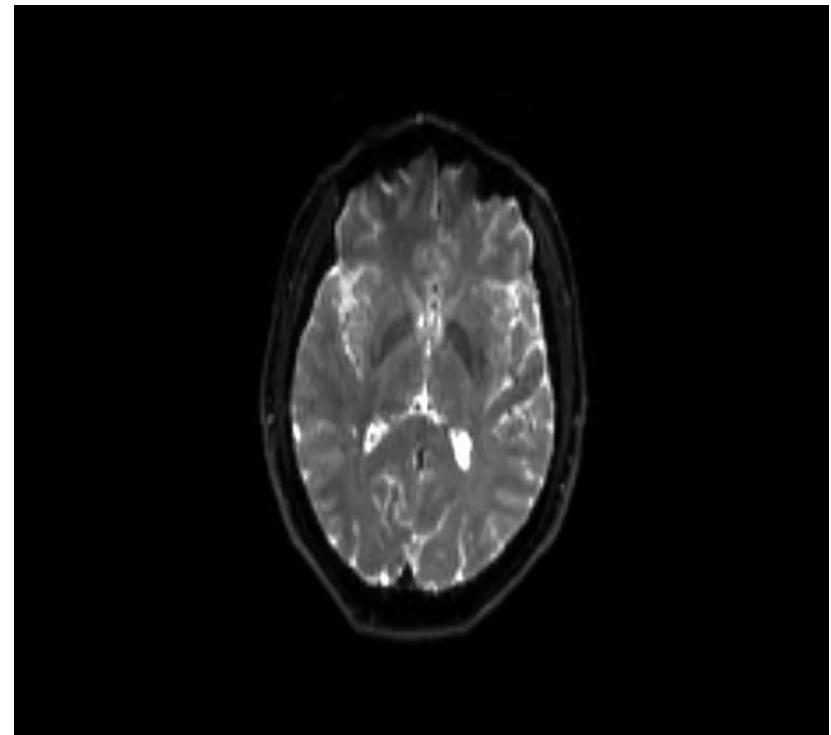
Hotelling, J. Educ. Psychol., 1933

Veraart et al. NeuroImage, 2016

Diffusion MRI: Signal denoising



Raw data

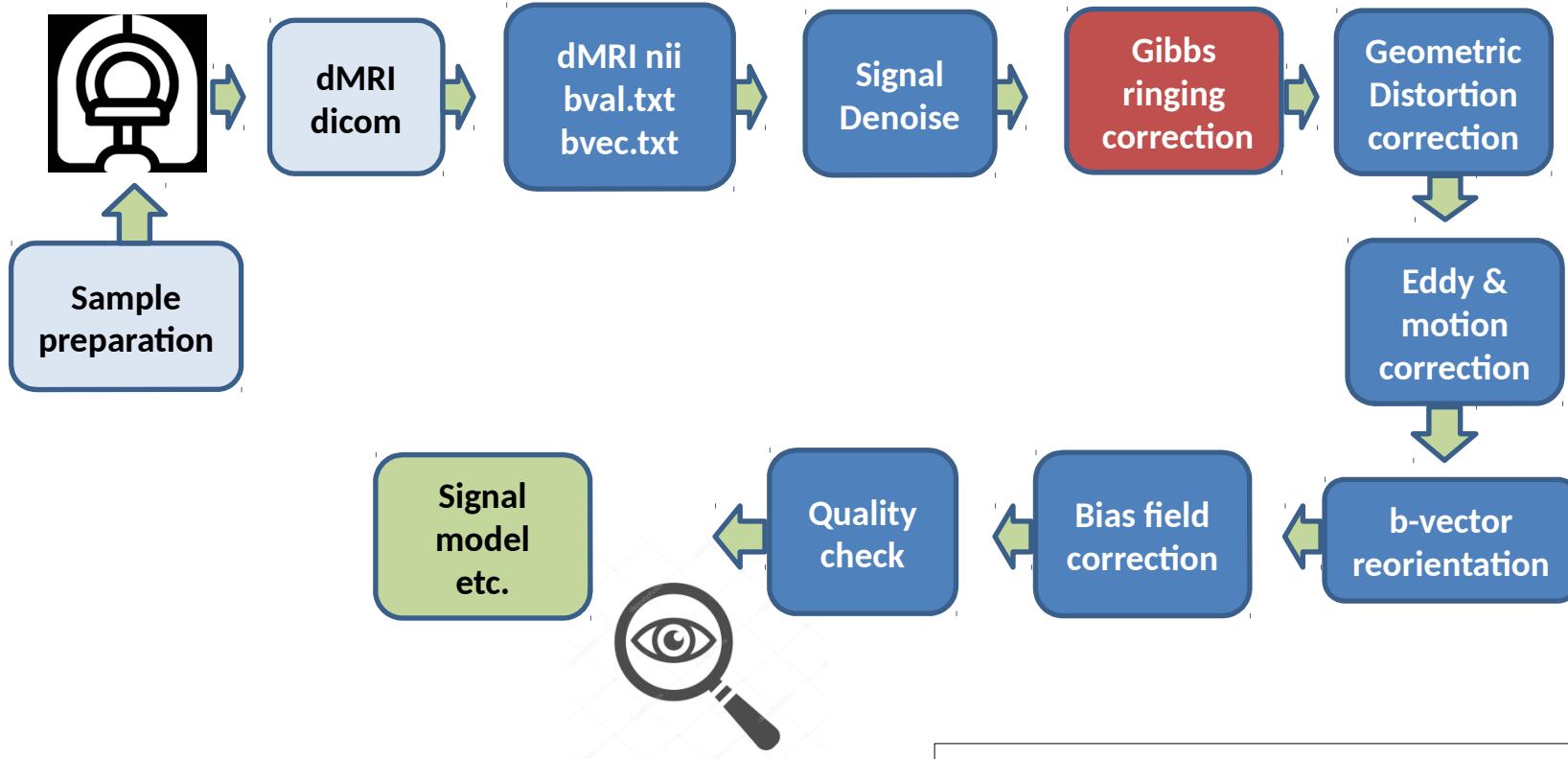


MPPCA denoised data

3T Siemens Prisma example (1.8mm isotropic, TE=72ms, TR=5.2s)

- number of b0: 5 (1 at the beginning, 4 at the end)
- number of directions per each shell: 64
- **b-values (>0): 500, 1500, 3000 s/mm²** (17 min acquisition)

Diffusion MRI pre-processing



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Jury out for optimal details

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<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FDT>

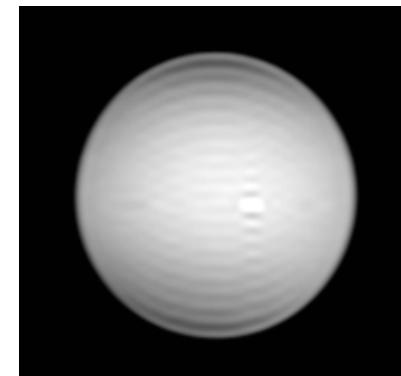
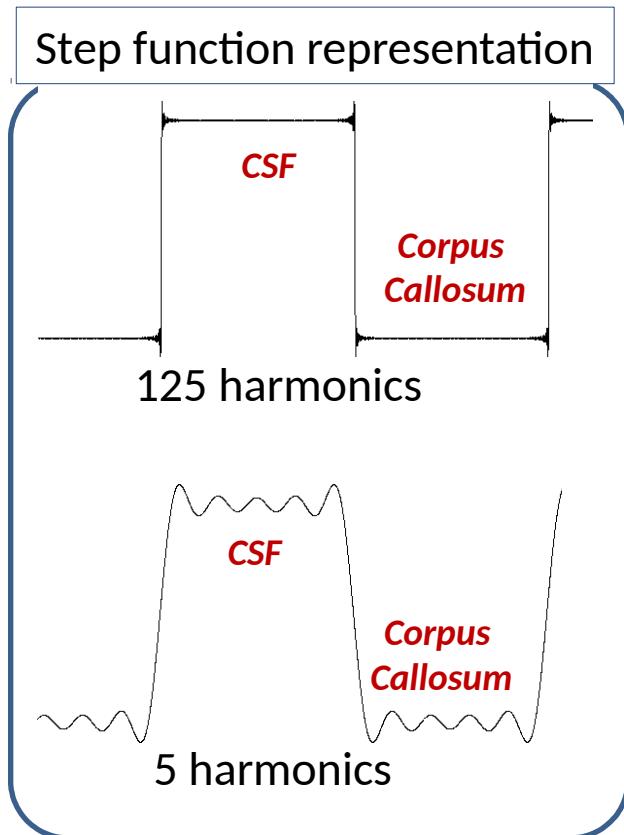
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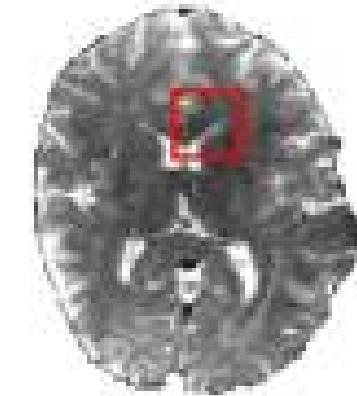
Diffusion MRI: Gibbs ringing

- **What is Gibbs ringing?**

- Every signal can be decomposed by an infinite Fourier series
- A truncated series gives an imperfect signal representation
- At signal «edges» this effect is seen as artificial signal ringing fluctuations



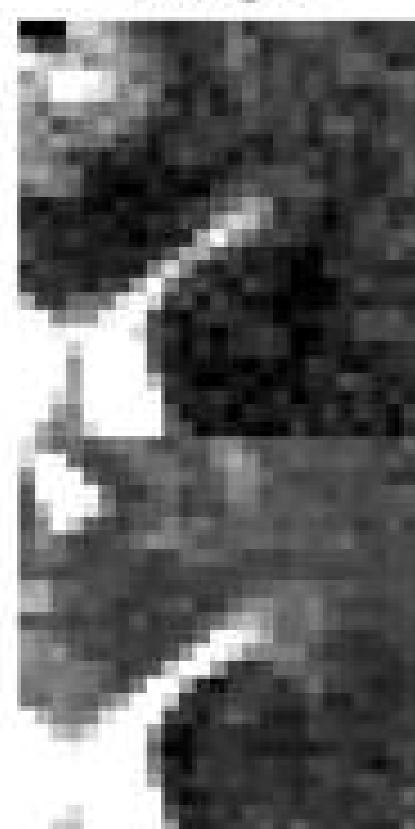
non-DW image



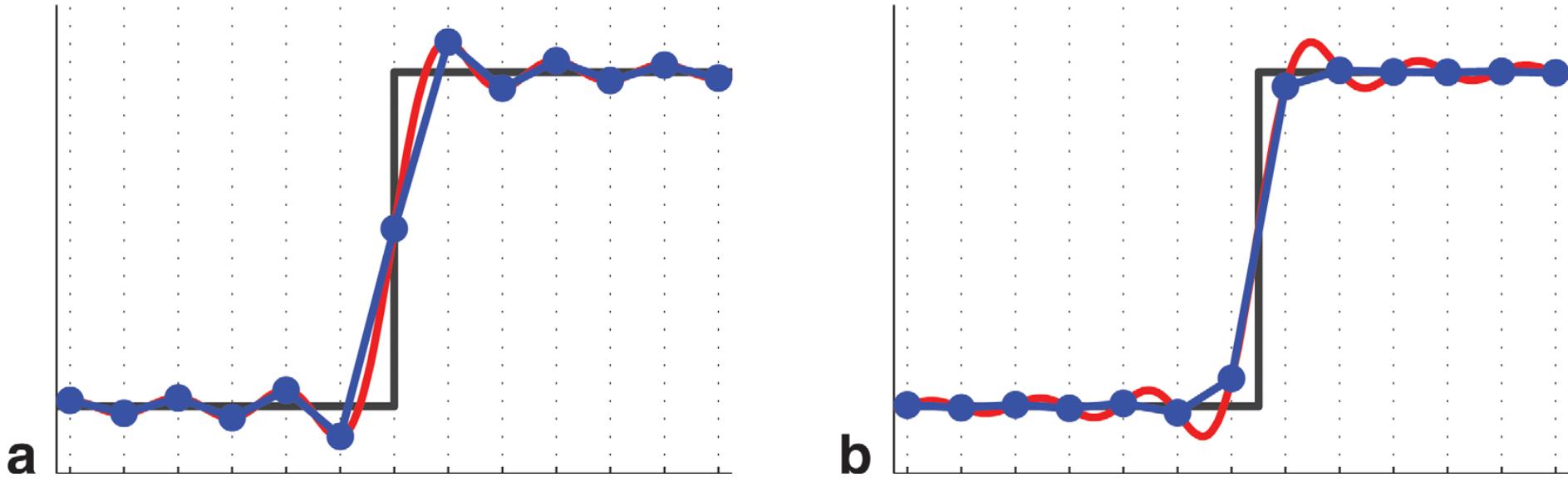
Veraart et al. MRM, 2016

non-DW image

MD



Diffusion MRI: Gibbs ringing correction

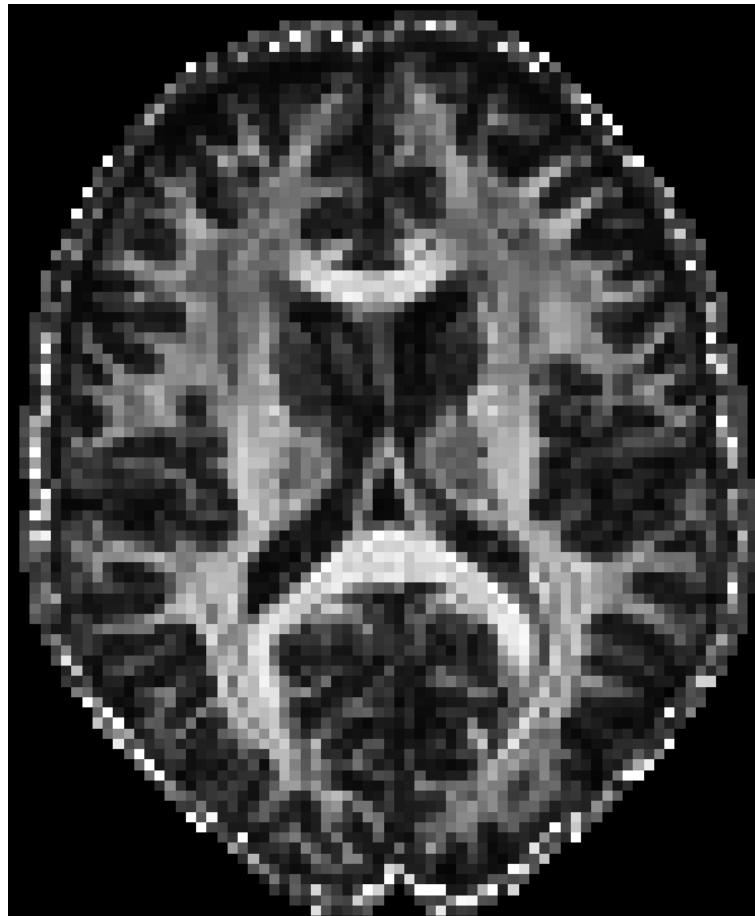


Correction: reinterpolate the image based on local, subvoxel-shifts
to sample the ringing pattern at the zero-crossings of the
oscillating sinc-function (Kellner et al., MRM 2016)
[Full k-space acquisition assumption]

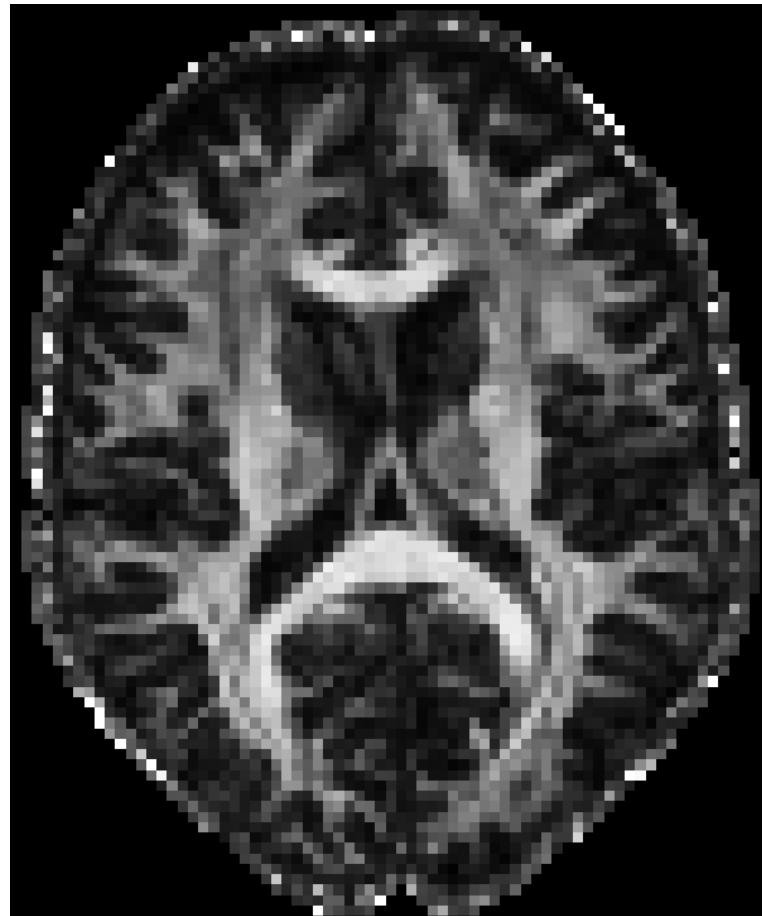
Diffusion MRI: Gibbs ringing correction

Effects on FA

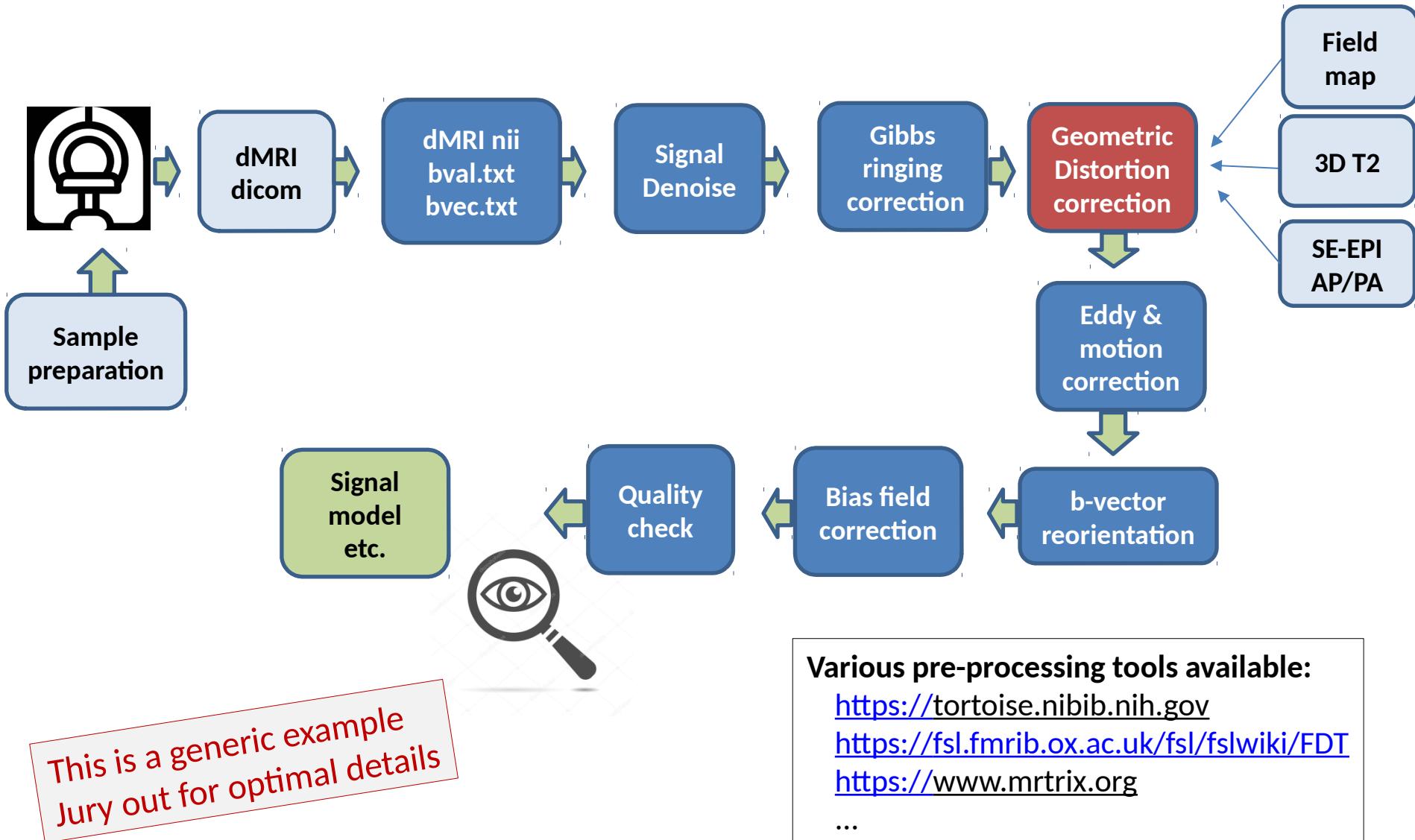
Uncorrected



Corrected



Diffusion MRI pre-processing

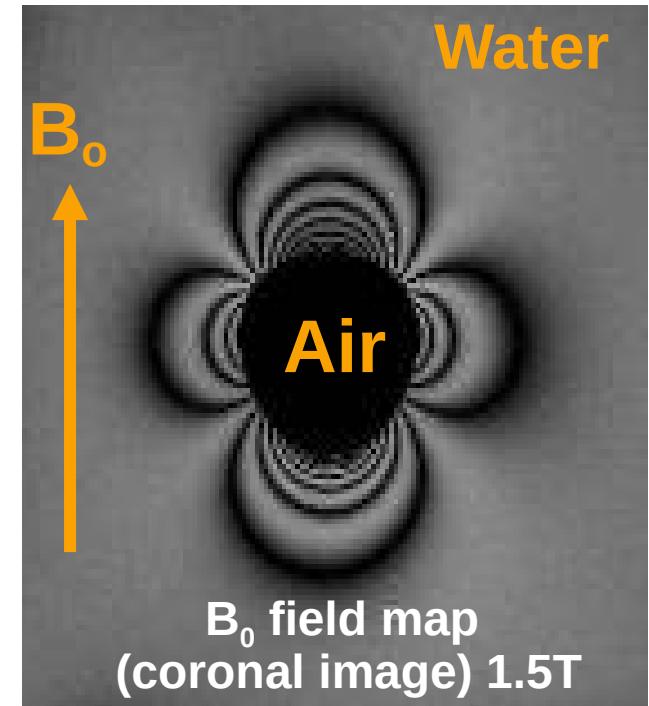
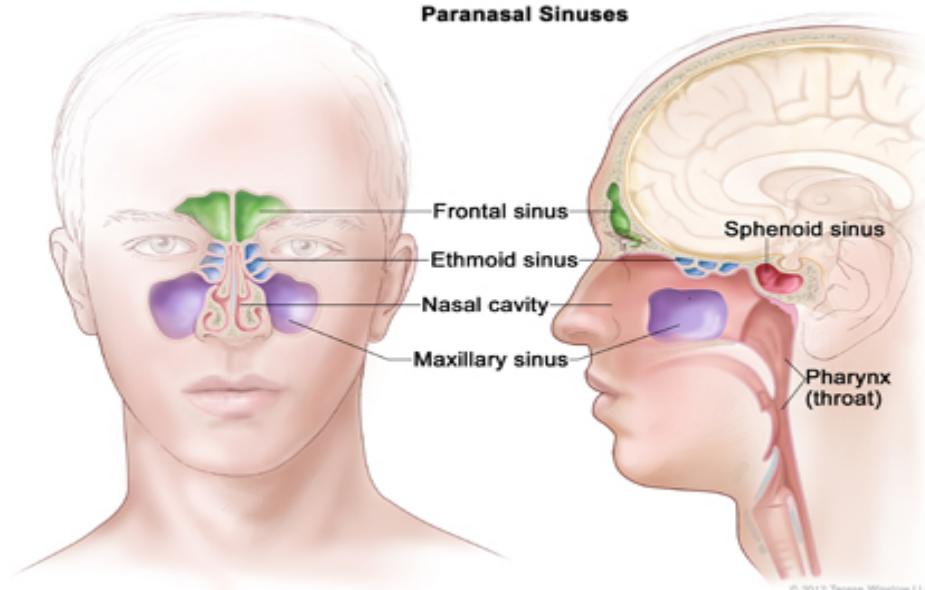


Diffusion MRI: susceptibility distortions

- Image reconstruction assumes uniform B_0 in the sample
- True field is different:

$$B(\bar{r}) = B_0 + \Delta B_0(\bar{r})$$

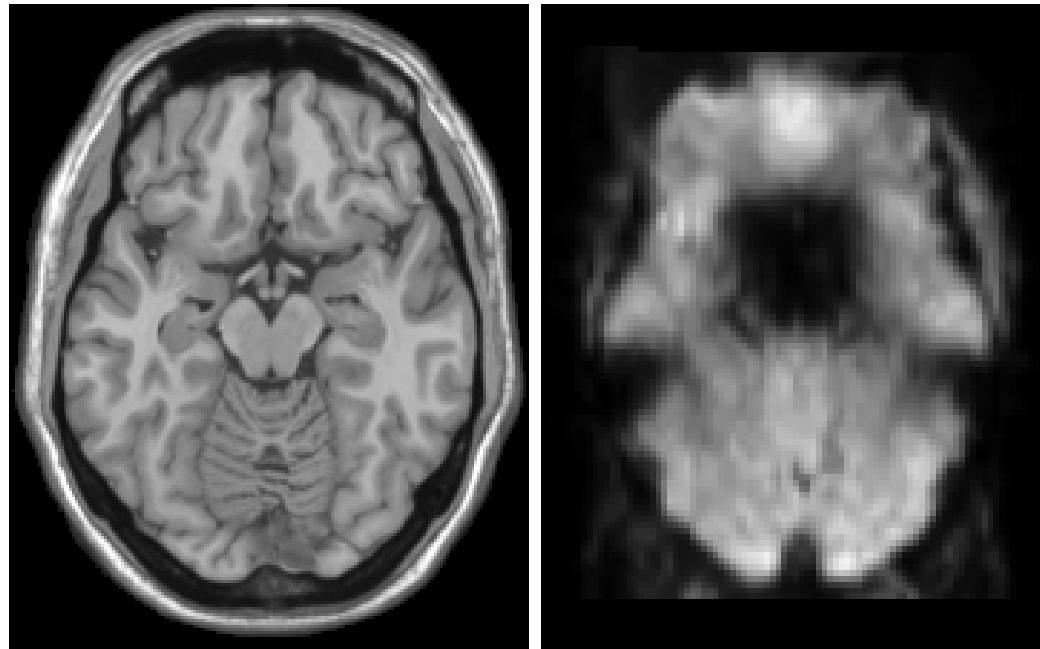
$$s(t) = \iiint_{x \ y \ z} m(x, y, z) e^{\frac{i\gamma\Delta B_0(x, y, z)t}{}} e^{-i2\pi[k_x(t)x+k_y(t)y]} dx dy dz$$



Phantom images courtesy of Larry Wald

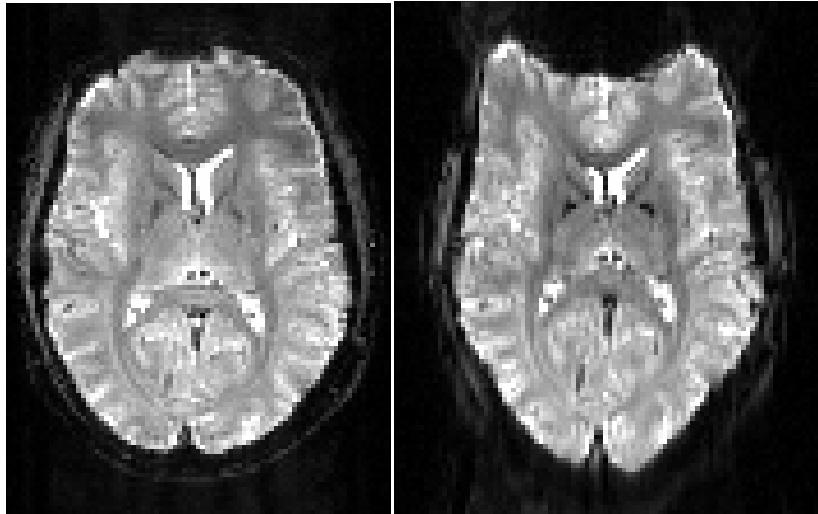
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- As a result, fast diffusion images (Echo Planar Images, EPI) show:
 - areas with signal loss (where $T2^* \ll TE$): nothing to do!



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- As a result, fast diffusion images (Echo Planar Images, EPI) show:
 - areas with signal loss (where $T2^* \ll TE$): nothing to do!
 - areas with geometric distortions: something to do!



Voxel shifts relative to true voxel location:

$$\Delta x = \gamma \cdot \Delta B_0(\bar{r}) \cdot FOVx \cdot \Delta tx$$

$$\Delta y = \gamma \cdot \Delta B_0(\bar{r}) \cdot FOVy \cdot \Delta ty$$

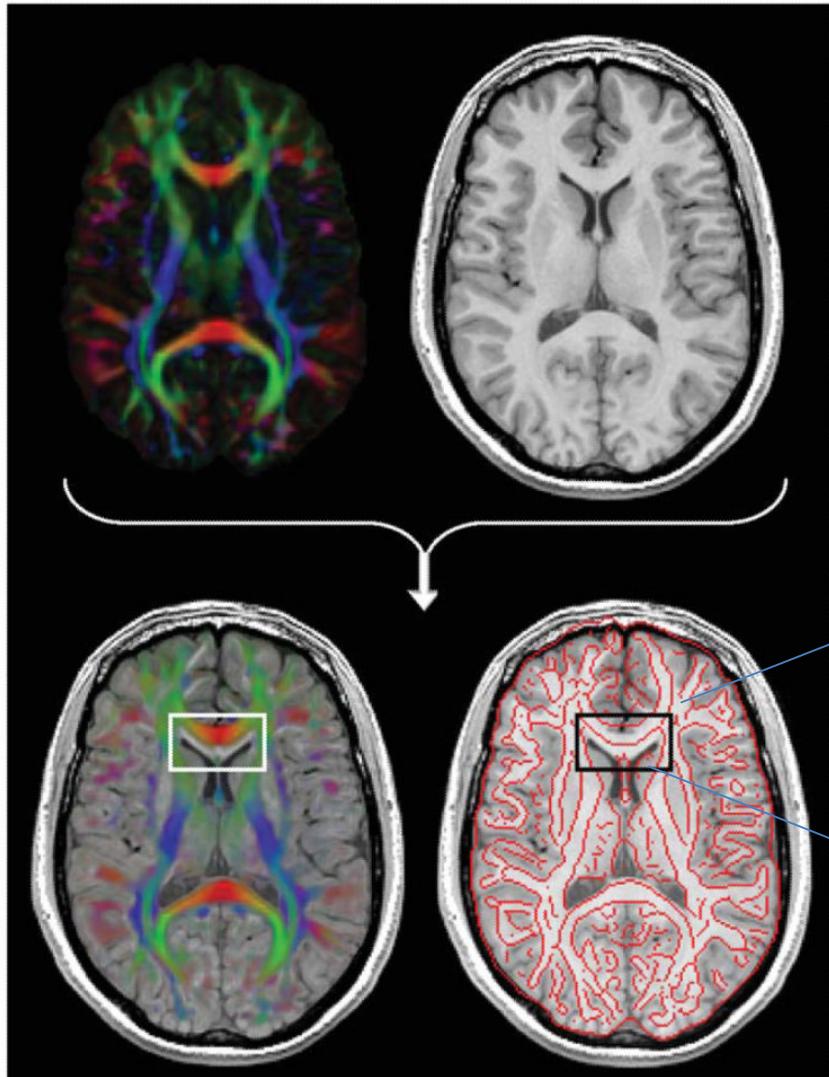
$\Delta x, \Delta y$: voxel shifts in x, y directions in mm

γ : proton gyromagnetic ratio

$FOVx, FOVy$: field of view in x, y direction in mm

$\Delta tx, \Delta ty$: sampling interval in x, y direction ($\propto 1/\text{sampling rate}$)

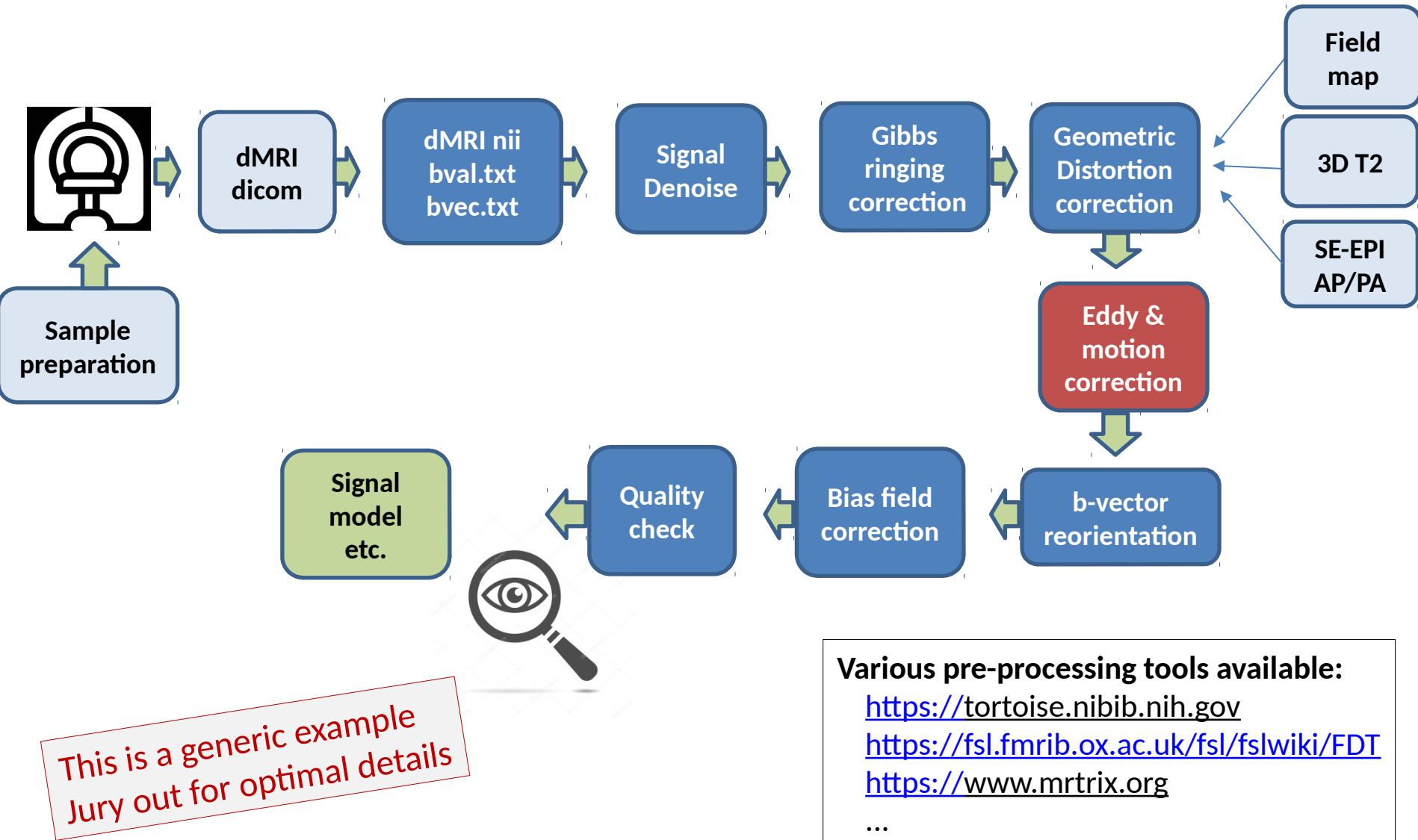
Diffusion MRI: susceptibility distortions



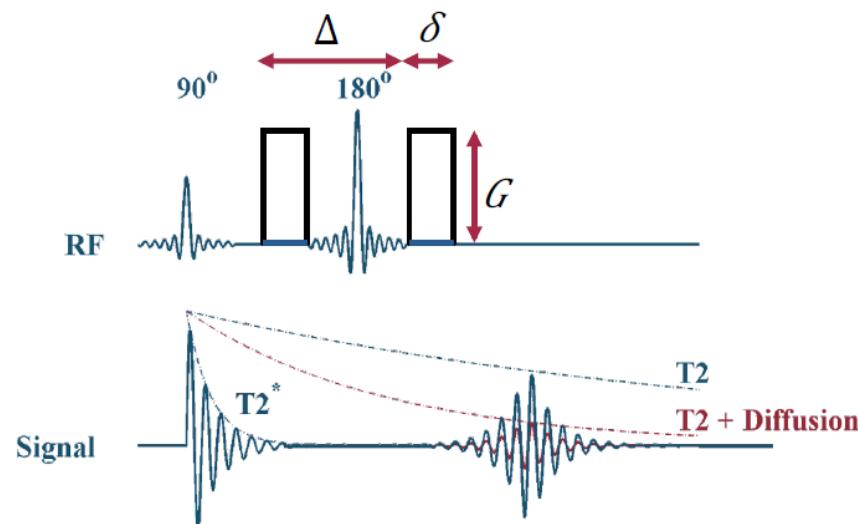
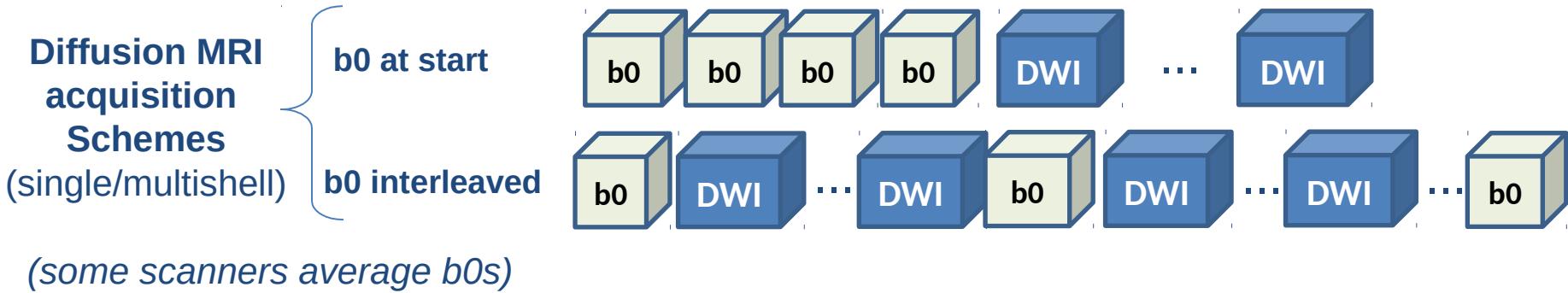
- Diffusion data overlaid on T1 anatomical
- Data are not aligned due to uncorrected distortions

Tournier et al., MRM 2011

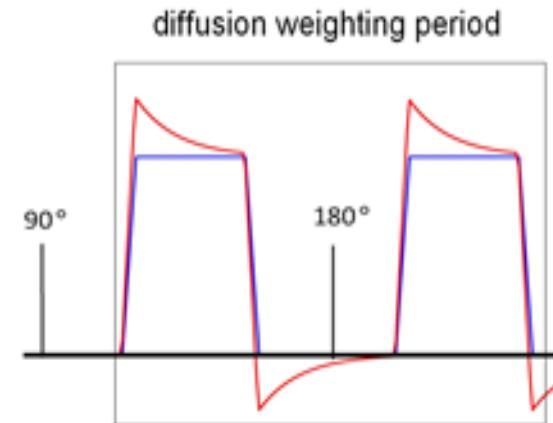
Diffusion MRI pre-processing



Diffusion MRI: Eddy and motion correction



You wish!
In reality
spins experience
another induced
gradient



Assumed gradient waveform
Effective gradient waveform

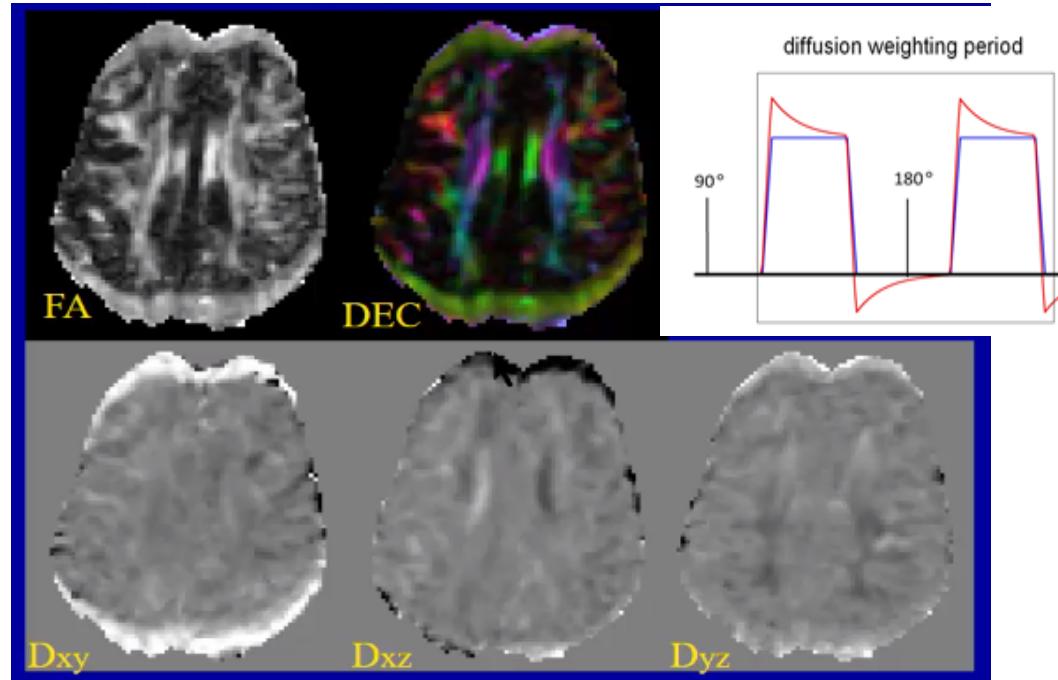
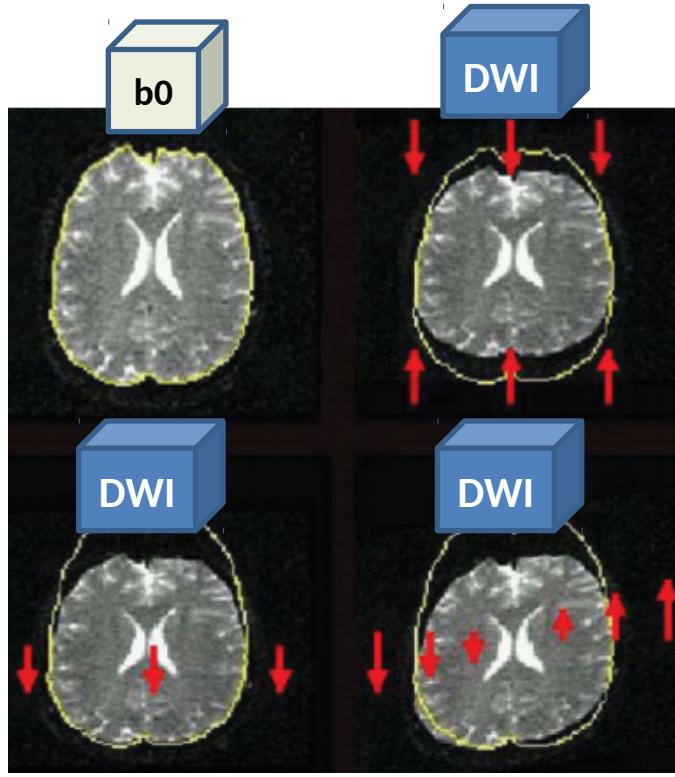
Sometimes Eddy currents are welcome



<http://mriquestions.com/eddy-current-problems.html>

Diffusion MRI: Eddy current distortions

- Electrical currents are induced inside the MRI cryostat
- They generate a magnetic field gradient that adds to the intended one
- The net gradient is incorrect leading to image geometric distortions

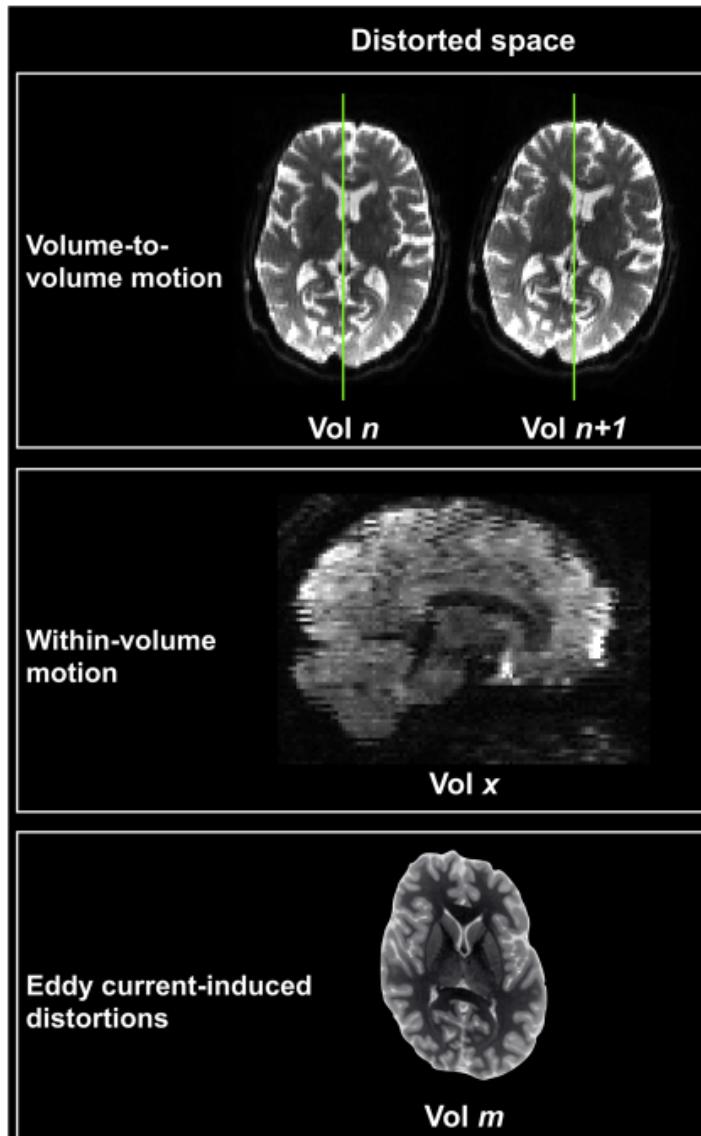


Le Bihan et al., Artifacts and pitfalls in diffusion MRI, JMRI 2006

Pierpaoli, ISMRM Diffusion, 2016

Eddy currents: strongest effects in phase-encoding direction

Diffusion MRI: head motion

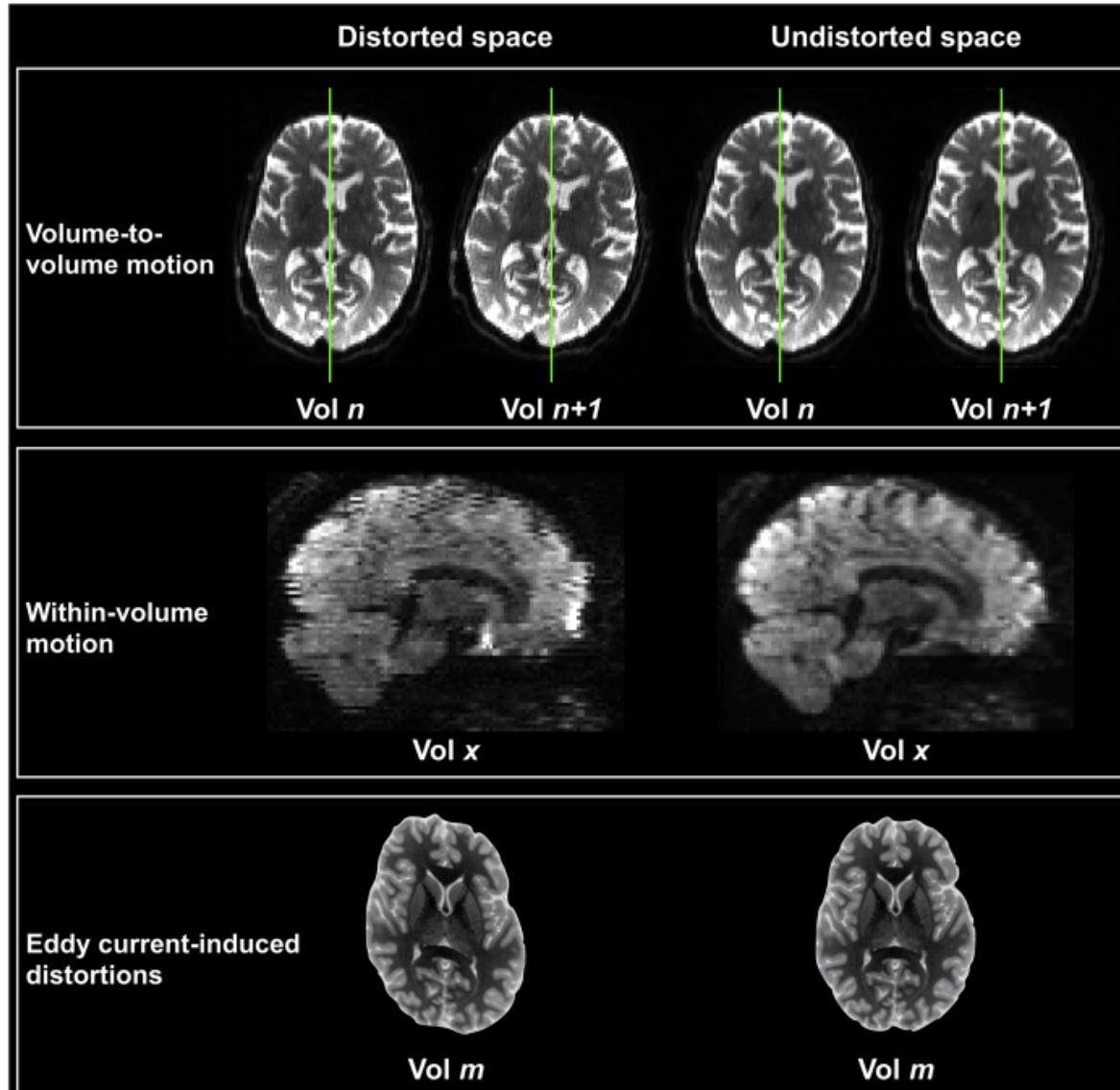


Bastiani et al., Neuroimage 2019

Minimizing head motion:

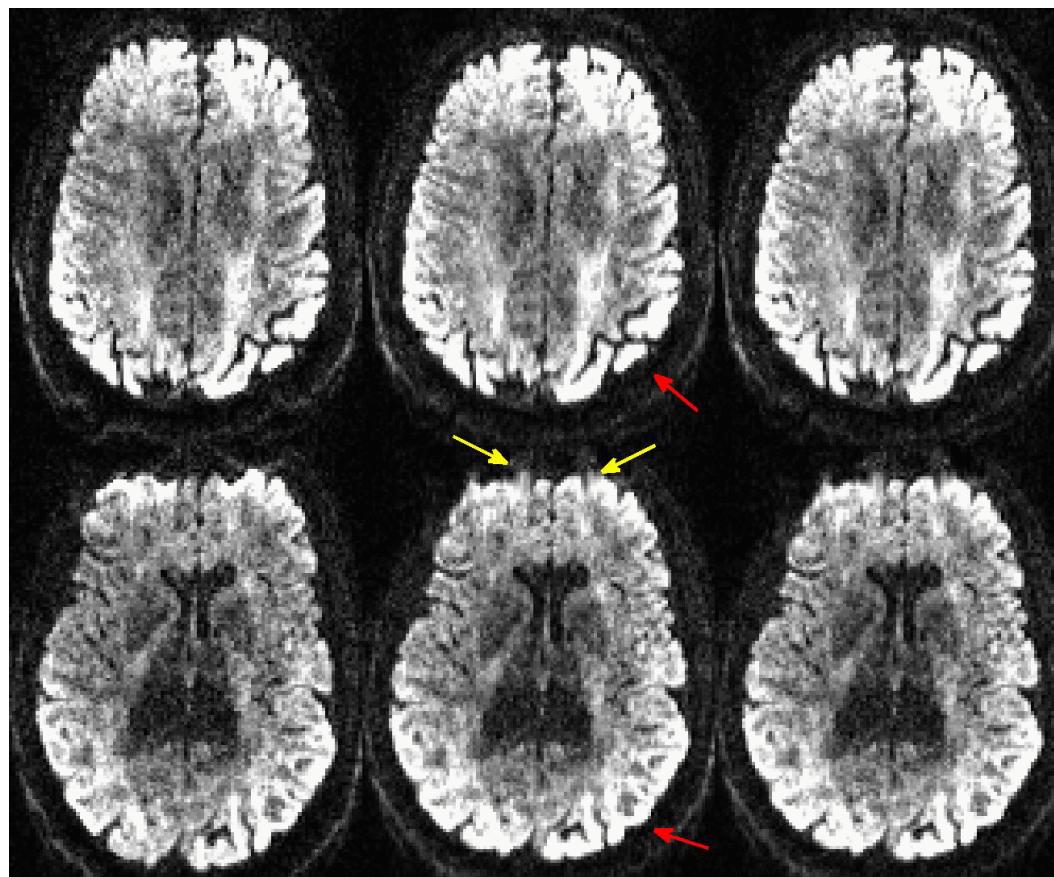
- Subject preparation
- Subject fixation
- Acquisition as short as needed
- Prospective correction
- Retrospective correction
 - Spatial model Eddy fields
 - Optimized registrations

Diffusion MRI: head motion & Eddy currents



Bastiani et al., Neuroimage 2019

Diffusion MRI: head motion & Eddy currents



Before any
correction

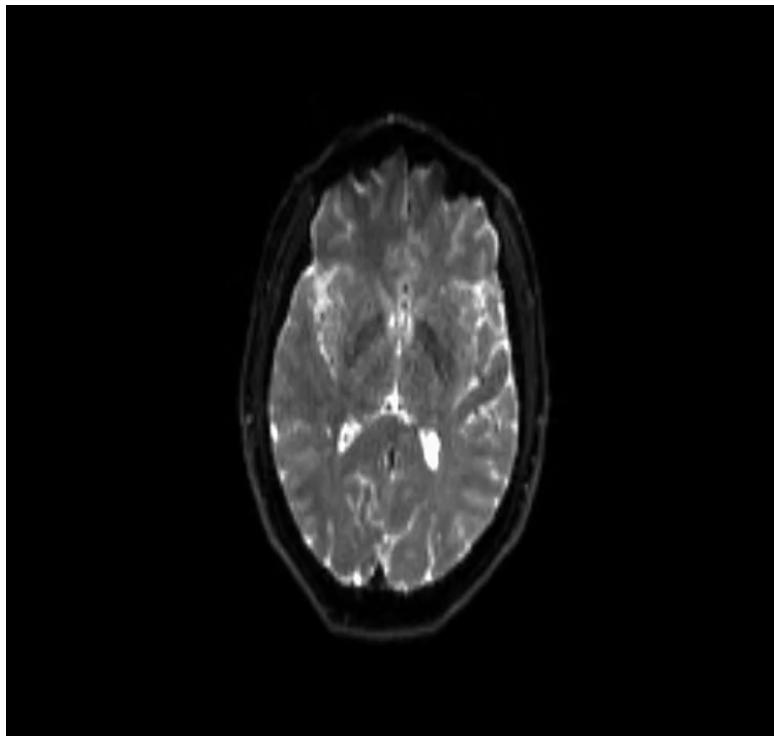
After correction for:
eddy currents,
gross subject movement,
static susceptibility map

After correction for:
eddy currents,
gross subject movement,
dynamic susceptibility map

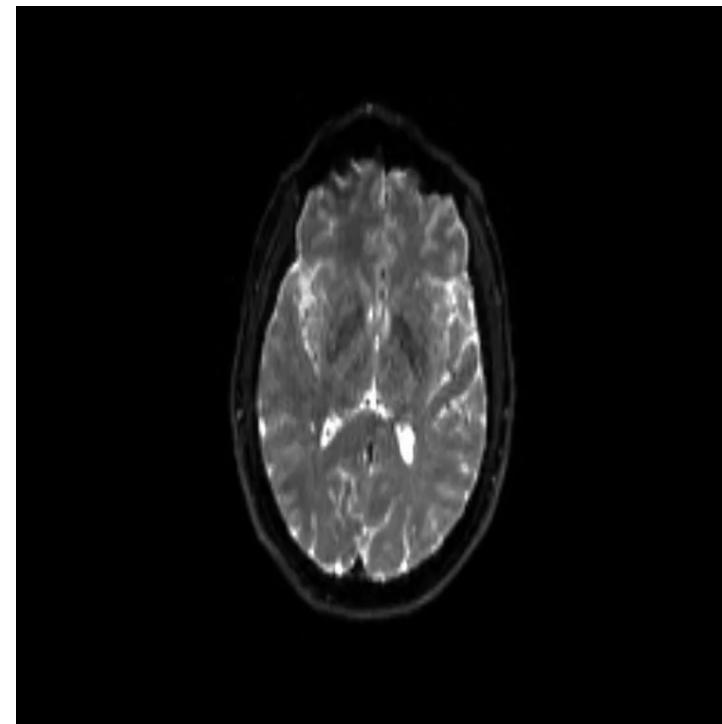
<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/eddy>

Andersson et al., Neuroimage 2018

Diffusion MRI: head motion & Eddy currents



Raw data

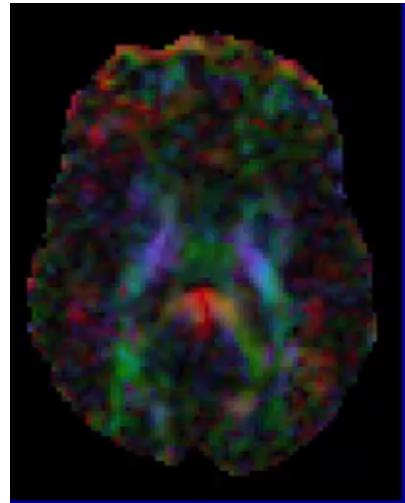


Eddy current correction

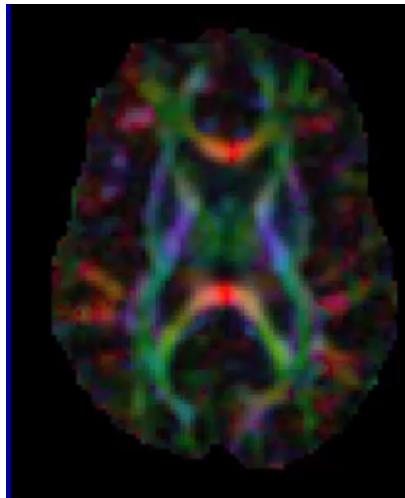
3T Siemens Prisma example:

- number of b_0 : 5 (1 at the beginning, 4 at the end)
- number of directions per each shell: 64
- b -values (>0): 500, 1500, 3000 s/mm².

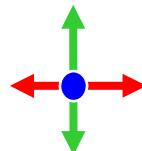
Diffusion MRI: head motion & Eddy currents



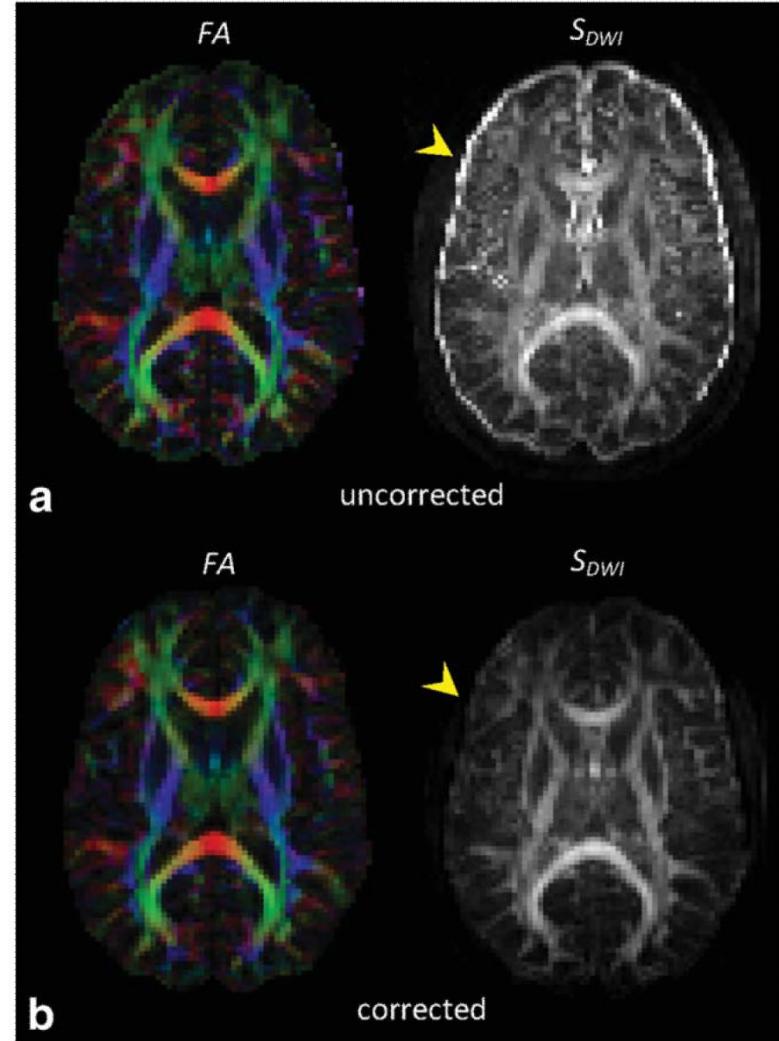
Uncorrected



corrected

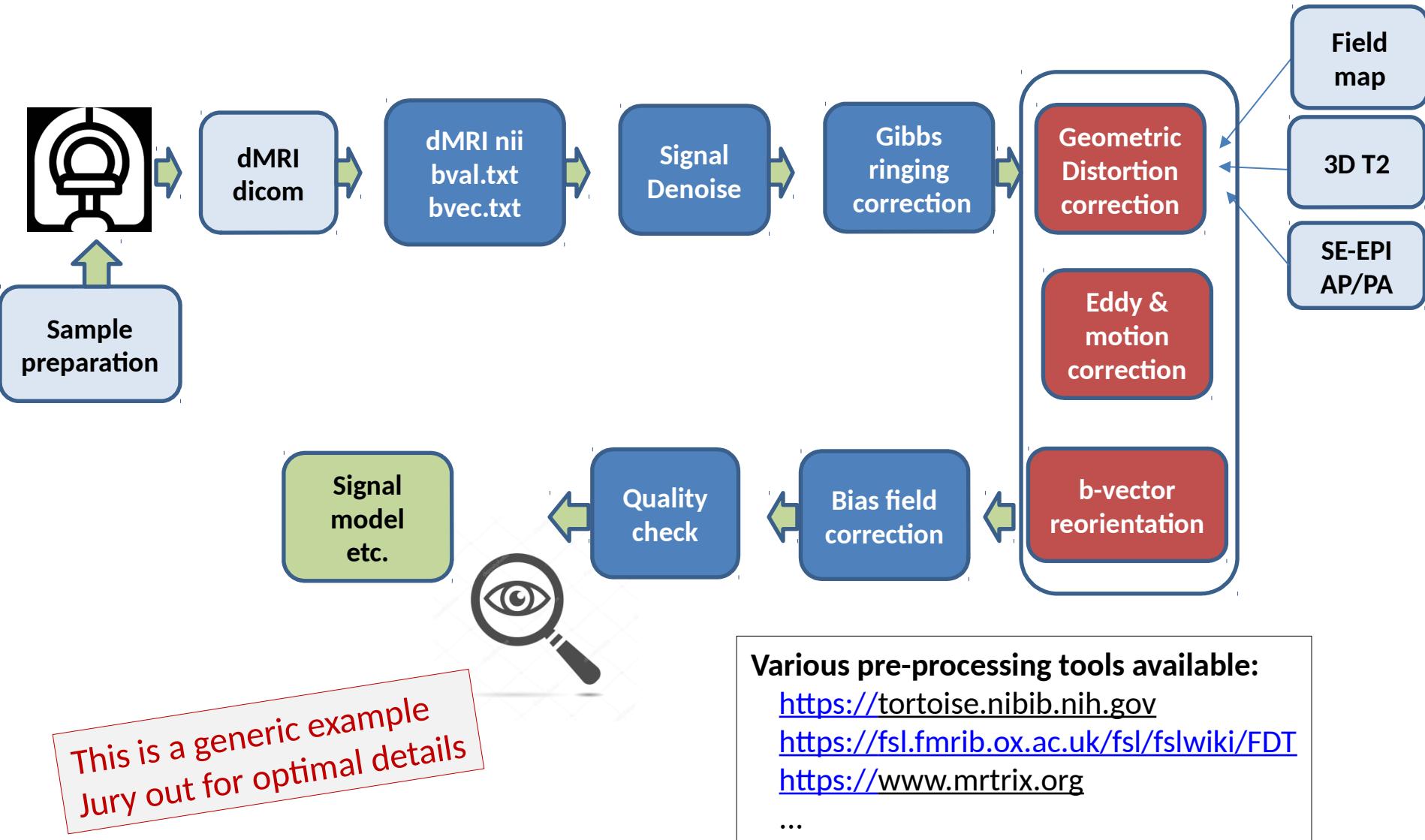


Pierpaoli, ISMRM Diffusion, 2016

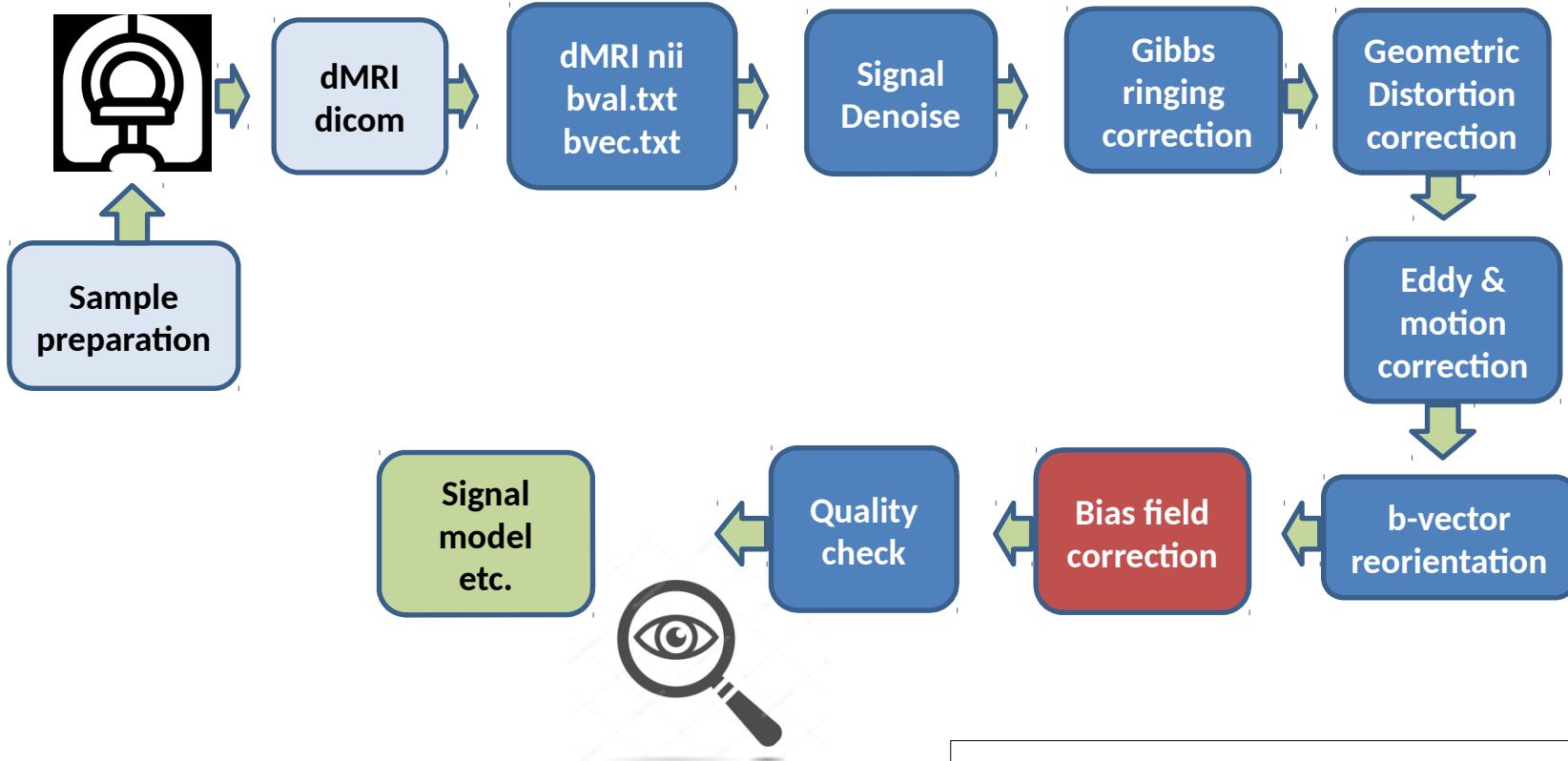


Tournier et al., MRM 2011

Diffusion MRI: pre-processing



Diffusion MRI: pre-processing



This is a generic example
Jury out for optimal details

Various pre-processing tools available:

<https://tortoise.nibib.nih.gov>

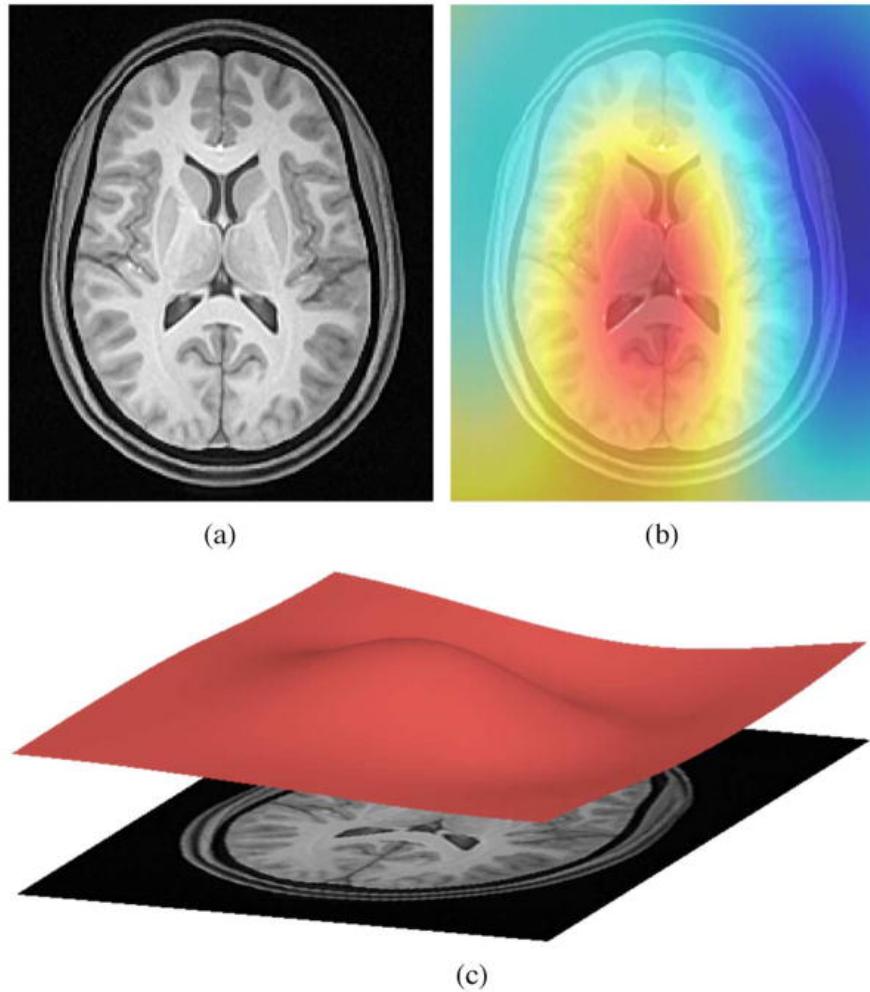
<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FDT>

<https://www.mrtrix.org>

...

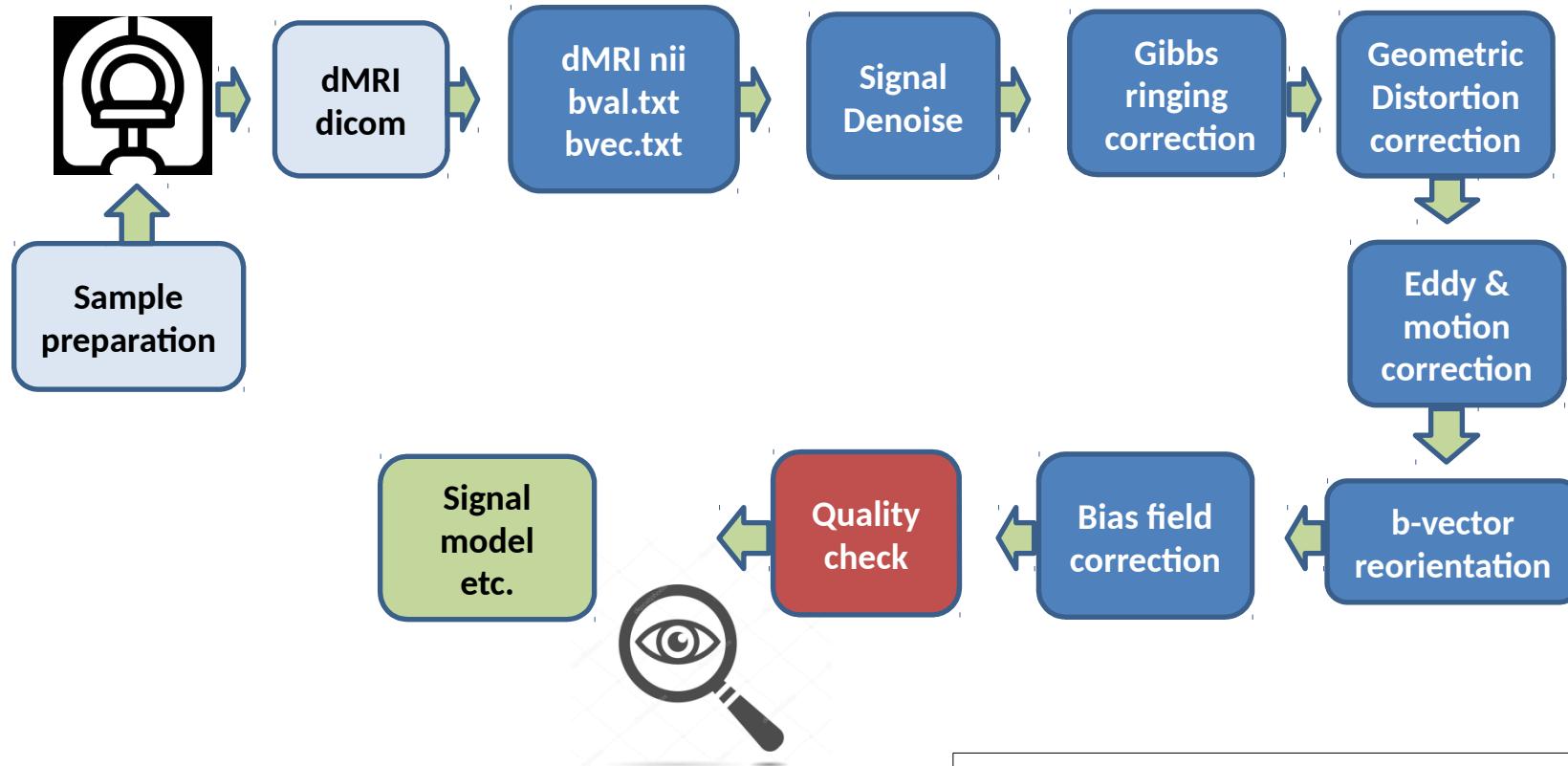
Diffusion MRI: Bias field correction

- Imperfect B1 modulation
 - Intensity modulation
- Evaluate with image intensity windowing
- Correction strategies
 - Estimate B1 map on b0
 - Apply correction to all dMRI data
 - ANTs N4 (no priors) fits smooth bias field that maximizes frequency



Tustison et al., IEEE Trans Med Imag 2010

Diffusion MRI: pre-processing



This is a generic example
Jury out for optimal details

Various pre-processing tools available:

<https://tortoise.nibib.nih.gov>

<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FDT>

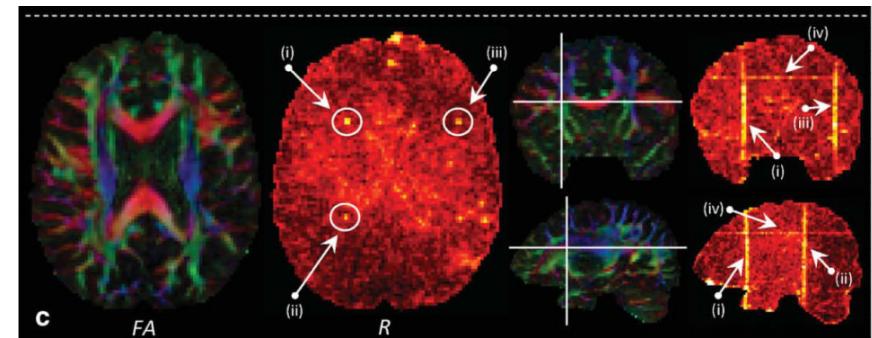
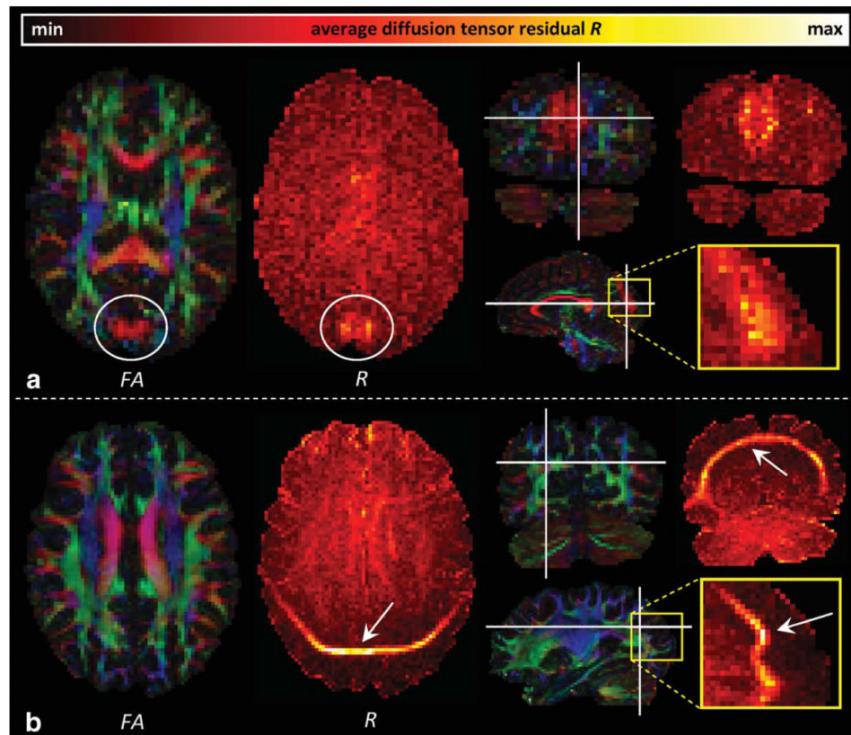
<https://www.mrtrix.org>

...

Diffusion MRI: Quality check

- **Visual inspection**

- Informative but time consuming
- Look at summary metrics
 - Standard deviation map across DWI (Eddy currents)
 - Standard deviation across b0 (cardiac pulsation)
 - Diffusion tensor residual map



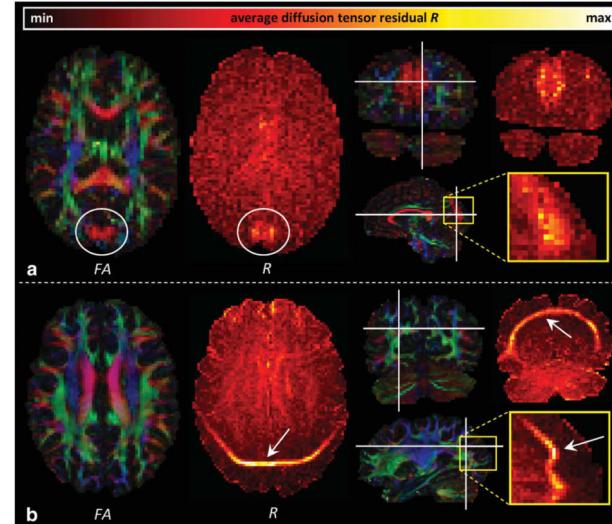
Tournier et al., MRM 2011

- a) *Bed vibrations*
- b) *Insufficient fat suppression*
- c) *RF spike/interference*

Diffusion MRI: Quality check

- **Visual inspection**

- Informative but time consuming
- Look at summary metrics
 - Standard deviation map across DWI (Eddy currents)
 - Standard deviation across b0 (cardiac pulsation)
 - Diffusion tensor residual map
 - ...



Tournier et al., MRM 2011

a) Bed vibrations

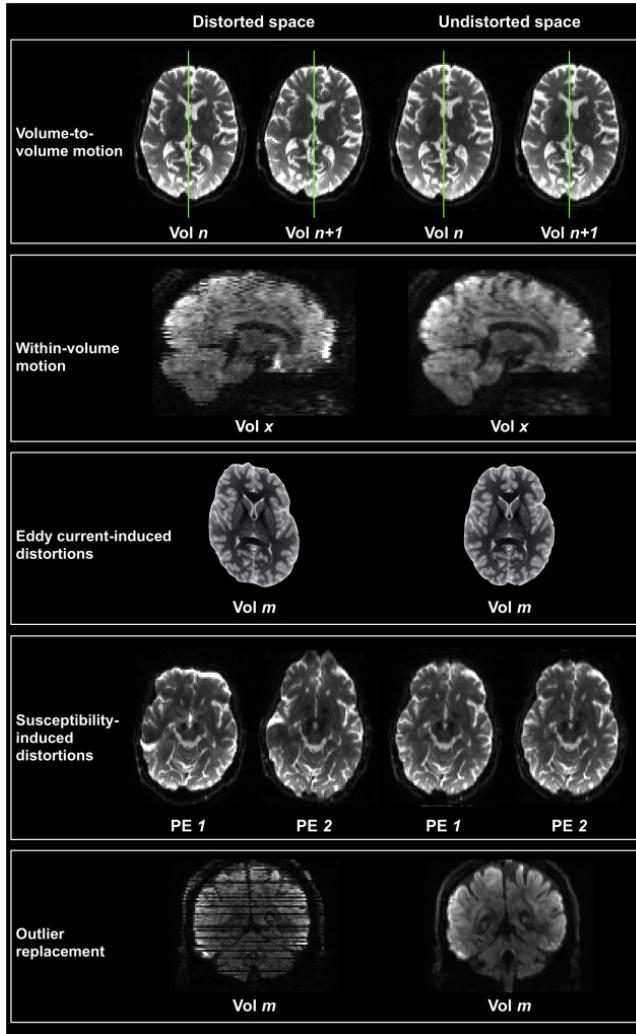
b) Insufficient fat suppression

- **Automated quality tools**

- TORTOISE (<https://www.nitrc.org/projects/tortoise>)
- DTIprep (<https://www.nitrc.org/projects/dtiprep>)
- DTI Studio (<http://dsi-studio.labsolver.org>)
- SQUAD – FSL (https://git.fmrib.ox.ac.uk/matteob/eddy_qc_release.git)
- ...

Diffusion MRI: Quality check

SQUAD - FSL (https://git.fmrib.ox.ac.uk/matteob/eddy_qc_release.git)

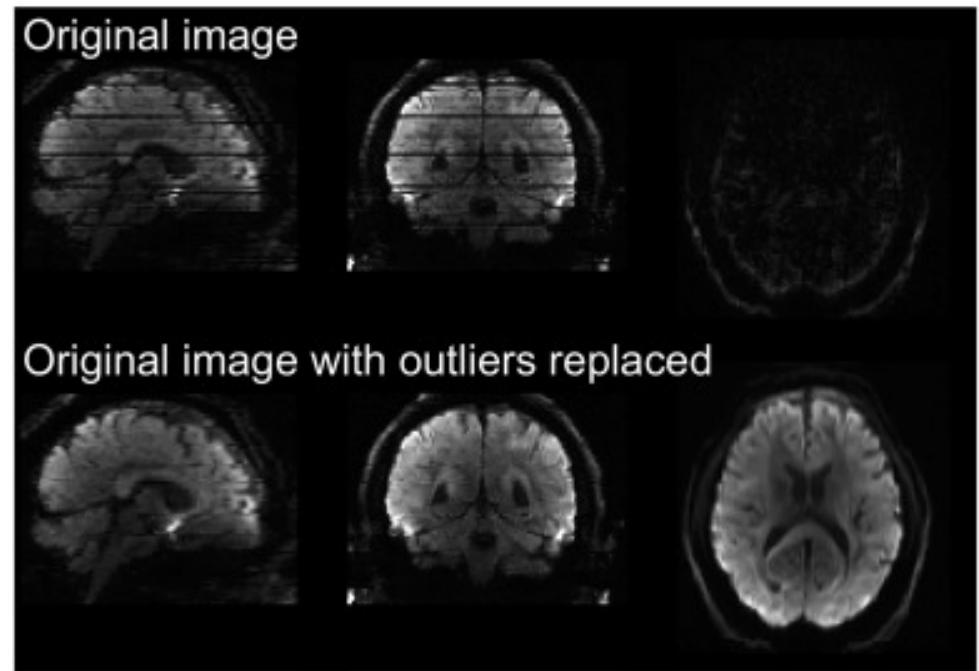
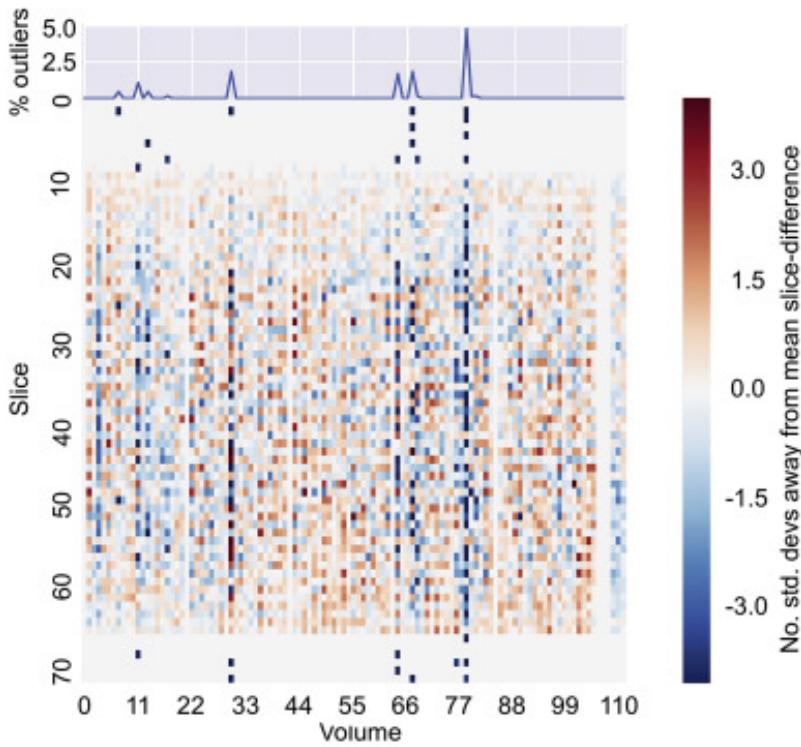


Artefact	QC metrics
<i>Volume-to-volume motion</i>	Average absolute motion (mm)
	Average relative motion (mm)
	Average x translation (mm)
	Average y translation (mm)
	Average z translation (mm)
	Average x rotation (deg)
	Average y rotation (deg)
	Average z rotation (deg)
<i>Within-volume motion</i>	Average stdev x translation (mm)
	Average stdev y translation (mm)
	Average stdev z translation (mm)
	Average stdev x rotation (deg)
	Average stdev y rotation (deg)
	Average stdev z rotation (deg)
<i>Susceptibility-induced distortions</i>	Stdev voxel displacement (mm)
<i>Eddy current-induced distortions</i>	Stdev x axis linear term (Hz/mm)
	Stdev y axis linear term (Hz/mm)
	Stdev z axis linear term (Hz/mm)
<i>Outlier replacement</i>	Total number of outliers (%)
	Volume-wise number of outliers (%)
	Outliers per b-shell (%)
	Outliers per PE dir (%)
-	Average b0 SNR
-	Average diffusion CNR per shell

Bastiani et al., Neuroimage 2019

Diffusion MRI: Quality check

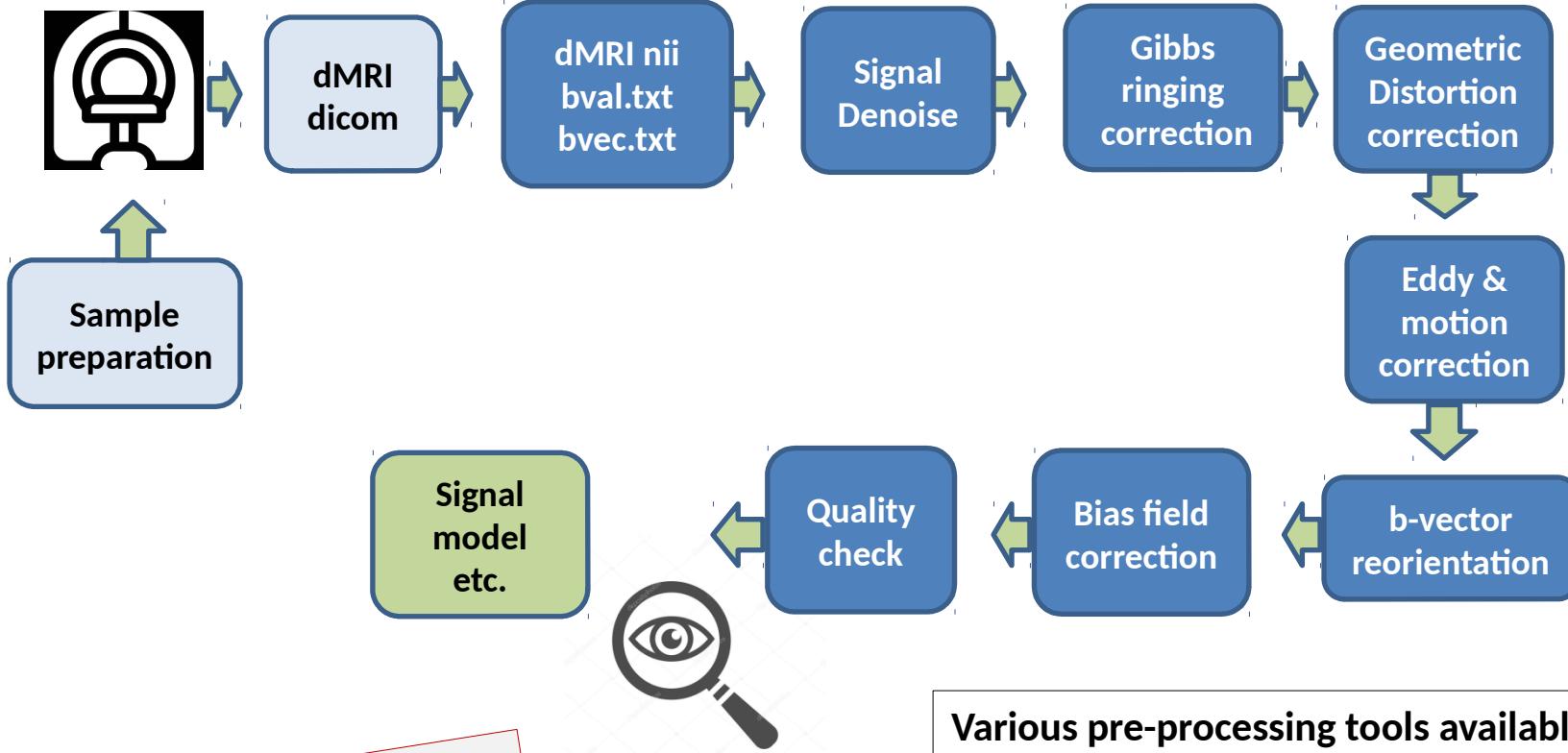
SQUAD - FSL (https://git.fmrib.ox.ac.uk/matteob/eddy_qc_release.git)



Gaussian process model used to replace an motion outlier volume with a new one

Bastiani et al., Neuroimage 2019

Diffusion MRI: pre-processing



This is a generic example
Jury out for optimal details

Various pre-processing tools available:

<https://tortoise.nibib.nih.gov>

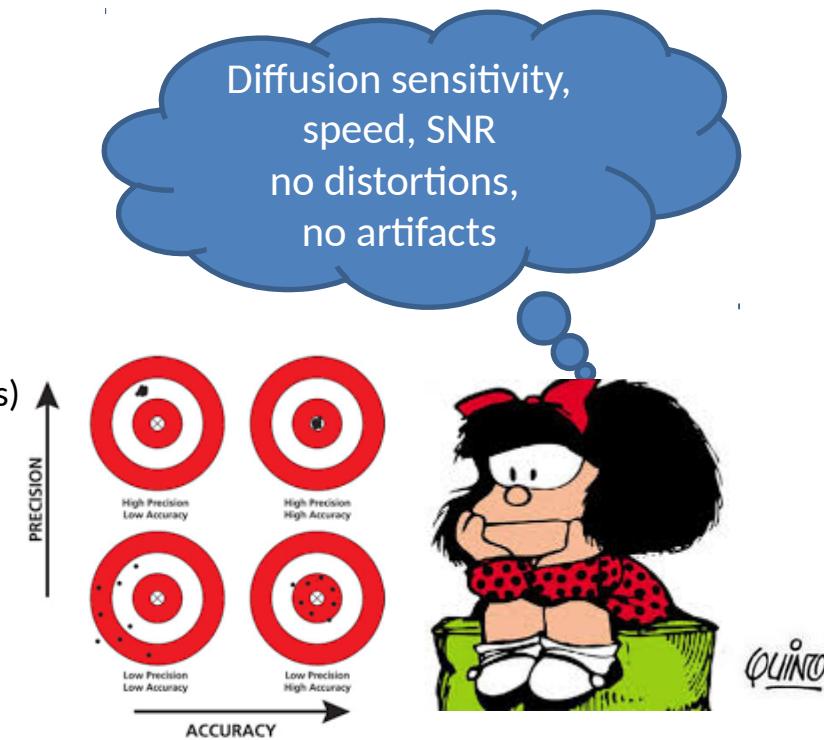
<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FDT>

<https://www.mrtrix.org>

...

Diffusion MRI: Acquisition factors

- **Diffusion sensitivity (modelling)**
 - High b-value, multiple b-values (\downarrow SNR)
 - High # directions per b-value (\uparrow acq time)
- **Maximize speed:**
 - Single-shot EPI (multishot challenges)
 - Shortest volume TR ($> 5.$ T_1 relevant tissue)
 - Simultaneous multislice (shortens TR, no SNR costs)
 - Multichannel coils (enables SMS)
 - Parallel imaging (accelerates with SNR costs, \downarrow distortions)
 - Fast and strong magnetic gradients (\$, PNS)
- **Maximize SNR**
 - Shortest TE possible (attention w. acceleration)
 - As much data as possible (\uparrow acq time)
 - Voxel size compromise with resolution
 - Postprocessing denoising
- **Minimize distortions**
 - Eddy currents distortions
 - B_0 inhomogeneity distortions
 - Gradient non-linearity distortions
- **Minimize artifacts**
 - Gradient directions check
 - Fat suppression
 - Motion correction
 - Partial volume: Isotropic voxels, whole-brain
 - Cardiac gating
 - Gibbs ringing



- *Impossible to optimize everything*
- *General guidelines*
- *Optimization details depend on goals*

Lecture 3 outline

Brain diffusion:

- Why do we care?
- How do we measure it?
- How do we pre-process data?
- Extracting information: models & challenges

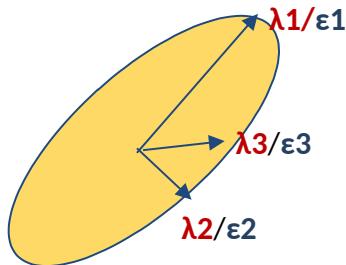


Diffusion tensor model

- A simple way of describing the directional dependence of diffusion is by using a diffusion tensor (DT)
- A DT is 3x3 symmetric, positive-definite matrix

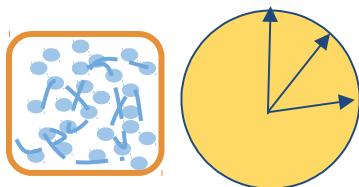
$$D = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{bmatrix}$$

Basser et al. 1994



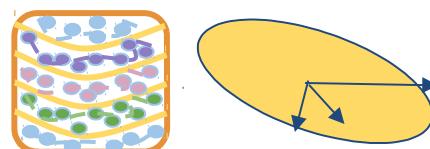
- DT has 3 positive eigenvalues: $\lambda_1 \lambda_2 \lambda_3 \rightarrow$ define the **form of DT**
- DT has 3 orthogonal eigenvectors: $\epsilon_1 \epsilon_2 \epsilon_3 \rightarrow$ define the orientation of DT

Isotropy



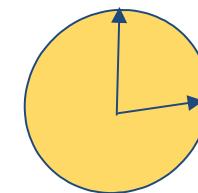
$$\lambda_1 = \lambda_2 = \lambda_3$$

Axial anisotropy



$$\lambda_1 \gg \lambda_2 \sim \lambda_3$$

Planar anisotropy



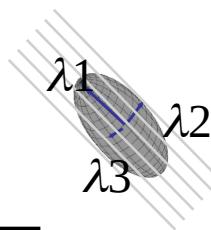
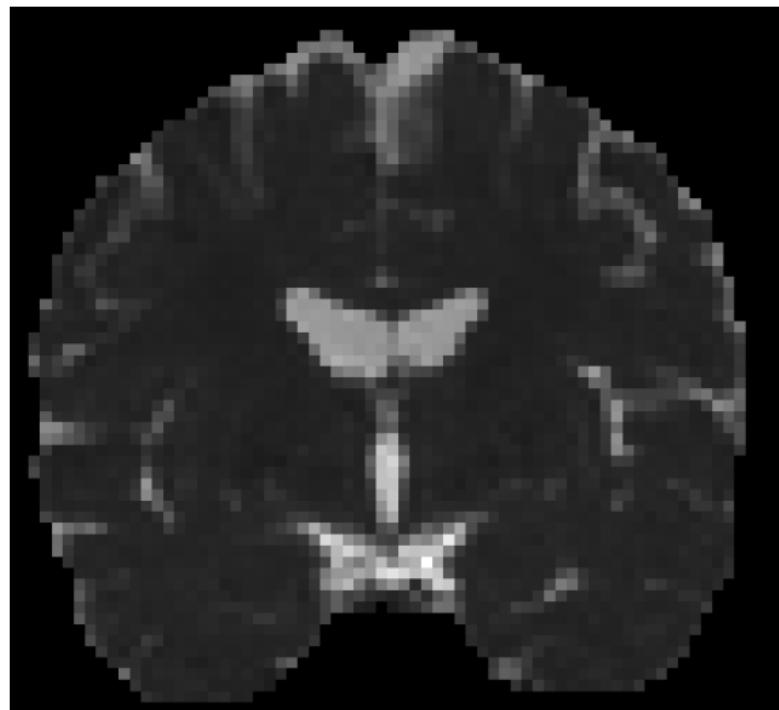
$$\lambda_1 = \lambda_2 \gg \lambda_3$$

Diffusion tensor: microstructure estimates

Fractional Anisotropy (FA)



Mean Diffusivity (MD)

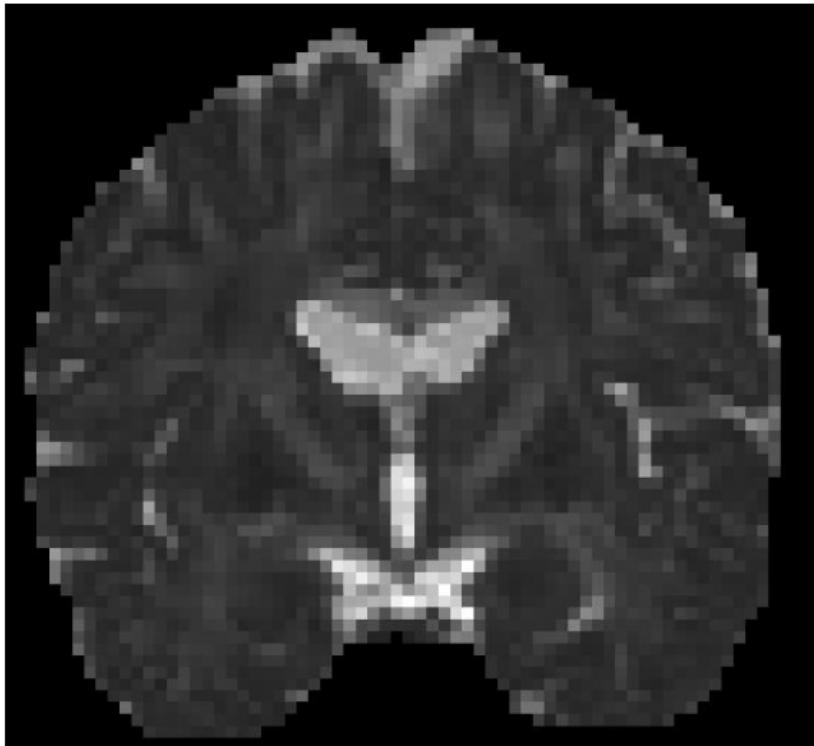


$$\frac{\sqrt{(\lambda_1 - \lambda_2)^2 + (\lambda_2 - \lambda_3)^2 + (\lambda_1 - \lambda_3)^2}}{\sqrt{2} \sqrt{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}$$

$$\frac{\lambda_1 + \lambda_2 + \lambda_3}{3}$$

Diffusion tensor: microstructure estimates

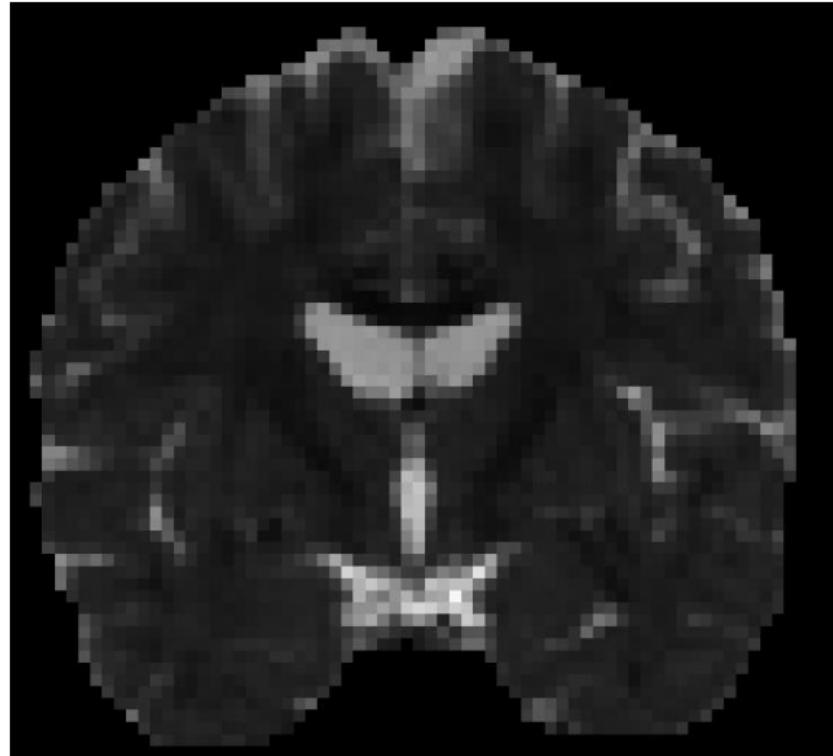
Axial diffusivity (AD)



$$AD(x,y,z) = \lambda_1(x,y,z)$$

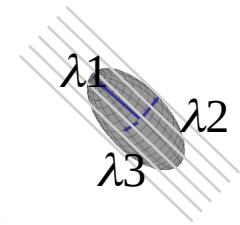
Largest eigenvalue

Radial diffusivity (RD)



$$RD(x,y,z) = [\lambda_2(x,y,z) + \lambda_3(x,y,z)]/2$$

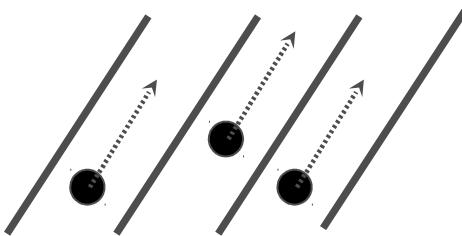
Average of two lower eigenvalues



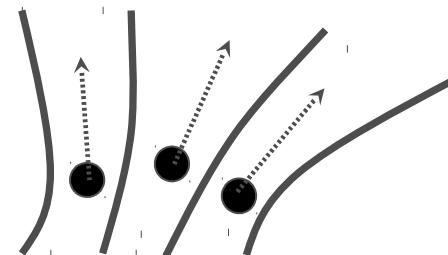
Diffusion tensor: model limitations

- Challenge interpreting diffusion tensor results
- Different biological processes may give similar estimations
- Lack of specificity in terms of microstructure interpretation

FA in group 1



FA reduction in group 2



Decrease in
axon coherence?

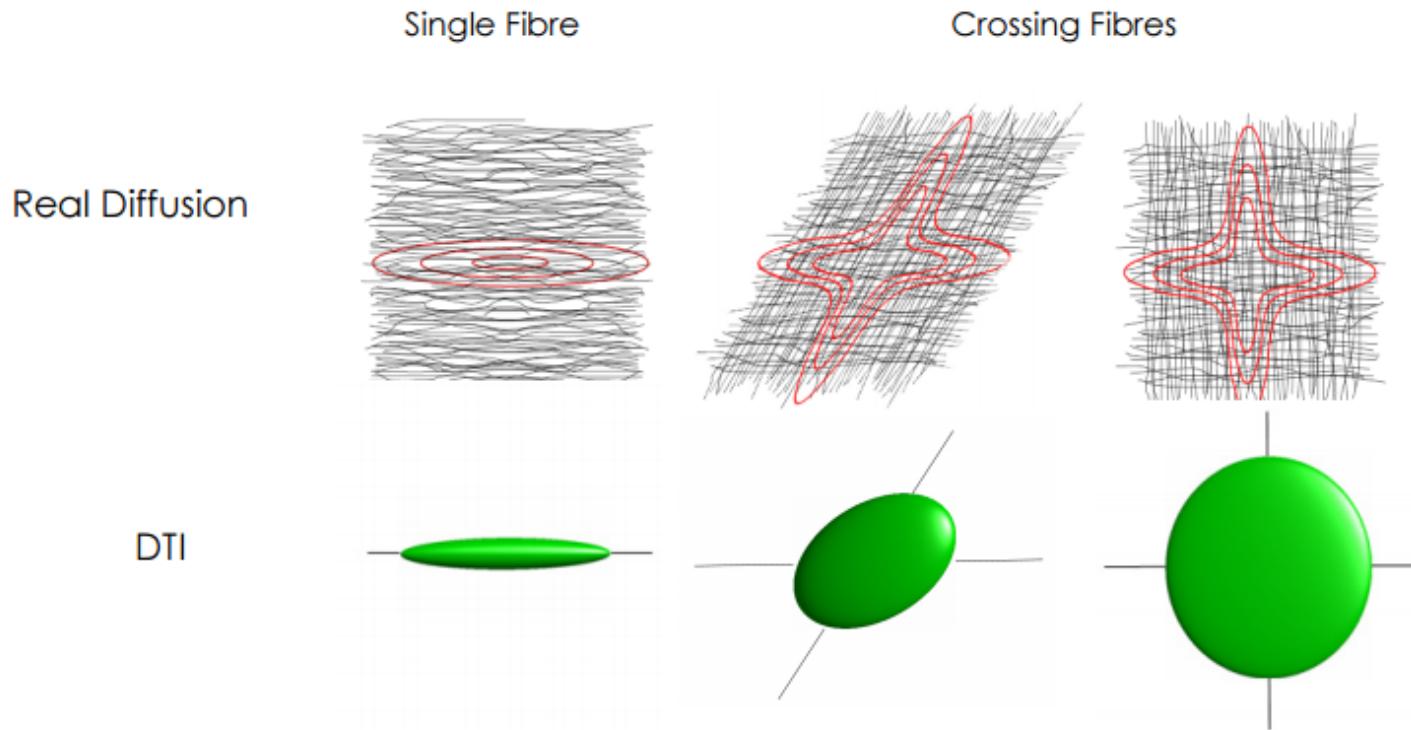
Both?

Decrease in
myelin?

DTI white matter changes are not specific to the candidate cellular
and molecular mechanisms driving the changes

Diffusion tensor: microstructure estimates

Errors in areas with fiber crossing

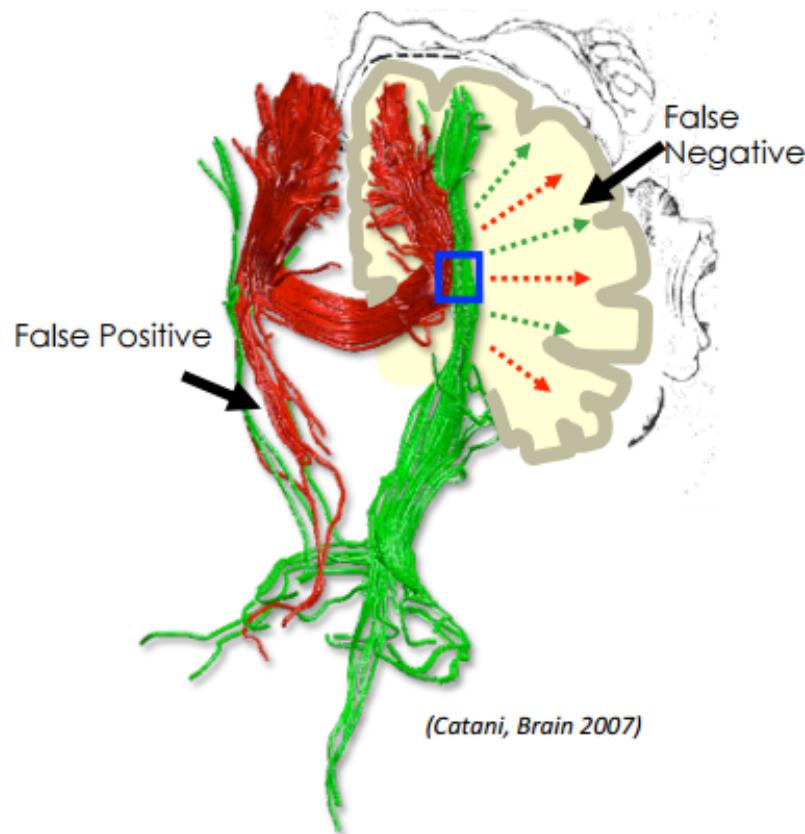


[DellAcqua Flavio, HBM 2015](#)

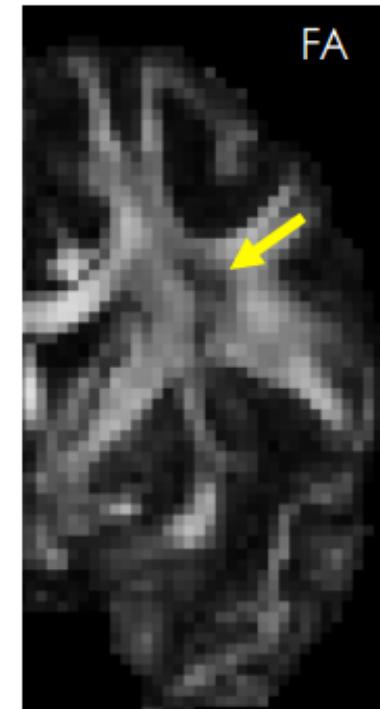
Diffusion tensor: microstructure estimates

- Areas with strong fiber crossing: wrong scalar estimations
- Low fractional anisotropy (FA)

Tractography



Maps



[DellAcqua Flavio, HBM 2015](#)

Beyond the diffusion tensor

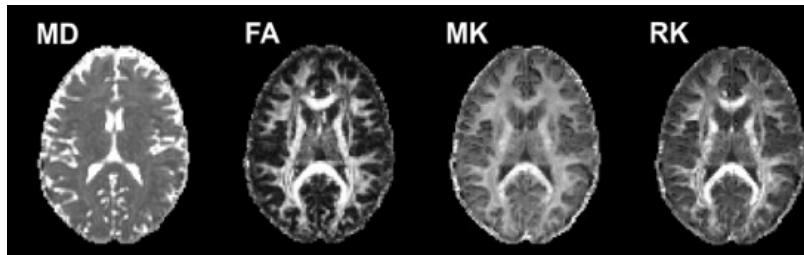
Spherical Deconvolution (single and multishell):

- Voxel signal response decomposed by stick responses with a fiber Orientation Density Function (fODF)



Diffusion Kurtosis Imaging (multishell):

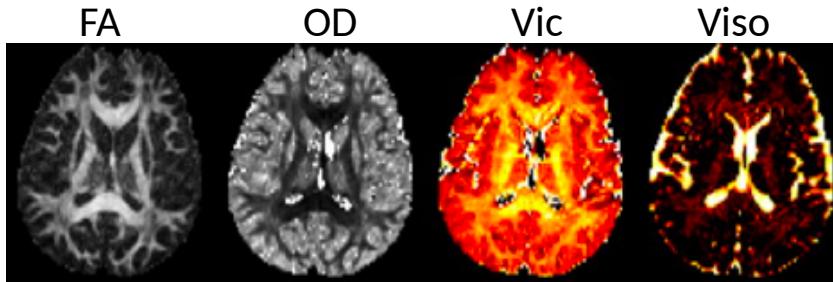
- Estimates the non-Gaussianity of the voxel 4th order tensor!



Steven et al. 2014

NODDI (multishell):

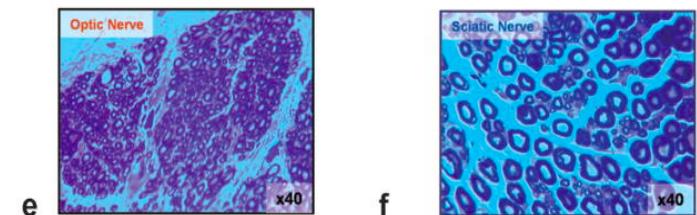
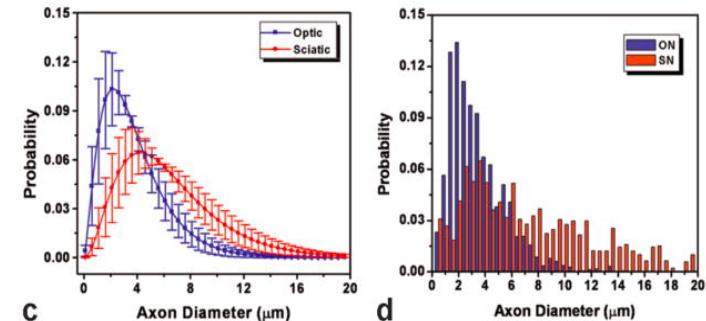
- Estimates the orientation and dispersion of axons



Zhang et al. 2012

AxCaliber (multishell):

- Measures axon diameter distribution



Assaf et al. 2008

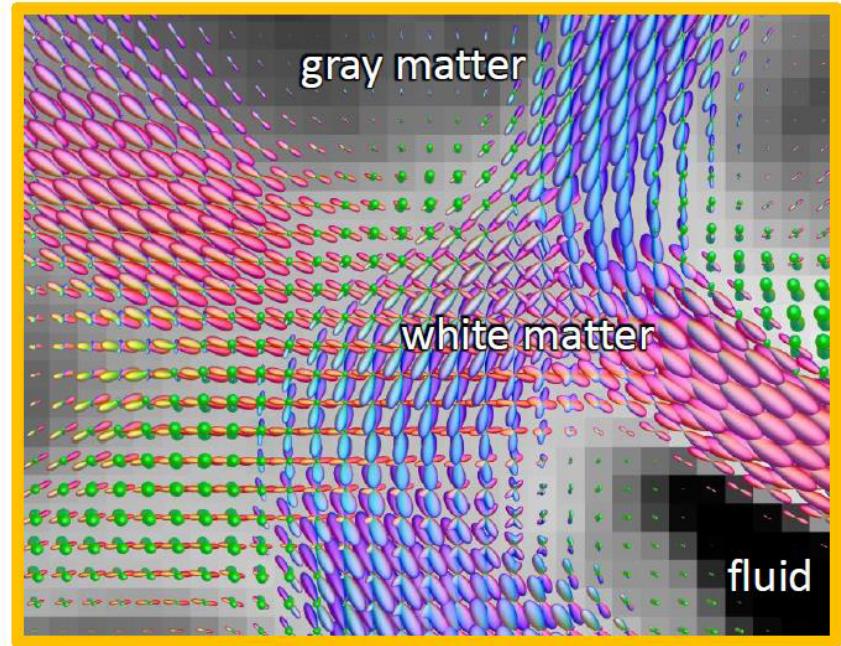
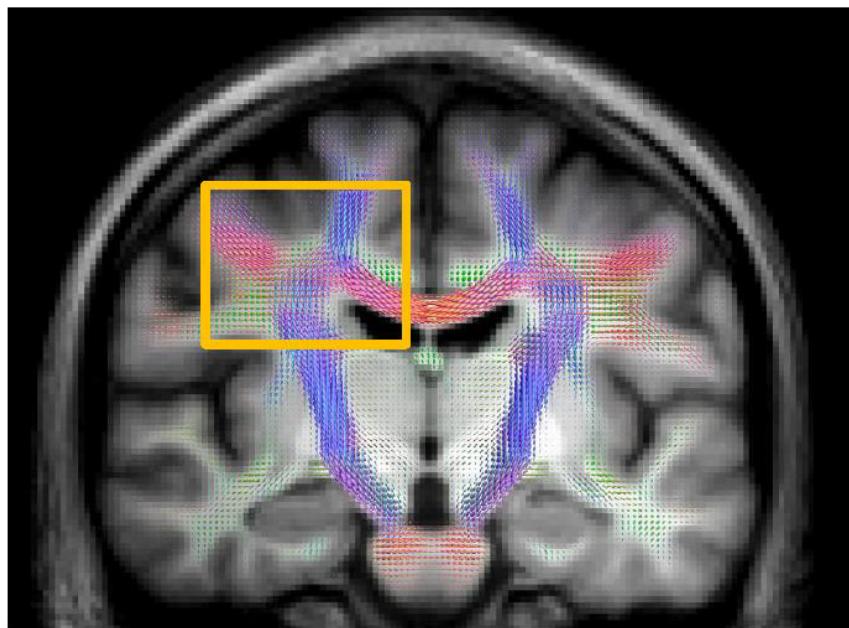
OD: orientation dispersion

V_{IC} : volume fraction of intracellular compartment

V_{ISO} : volume fraction of isotropic CSF

Diffusion MRI: Tractography

From local fiber orientations...

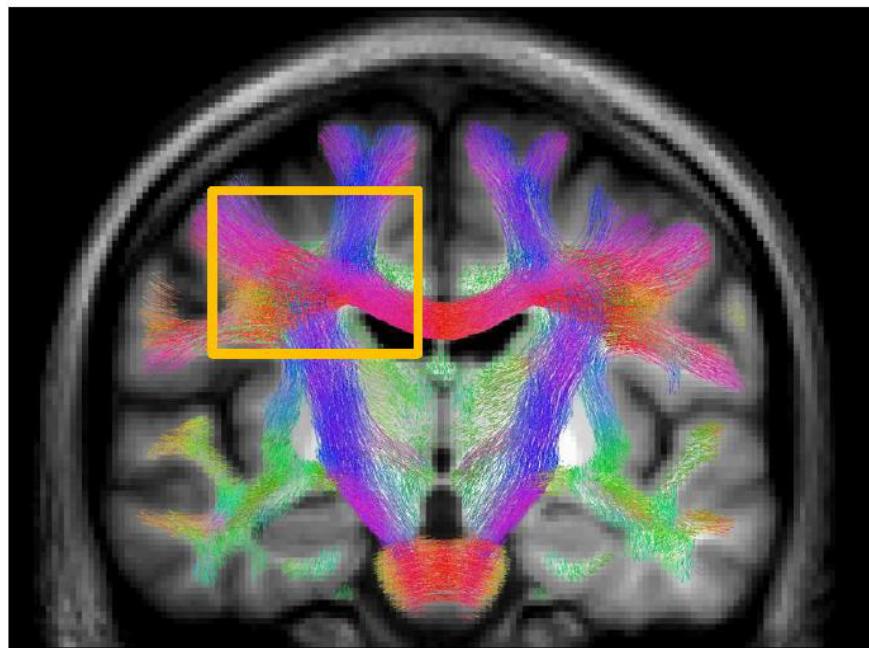


amount of white matter fibers as a function of orientation

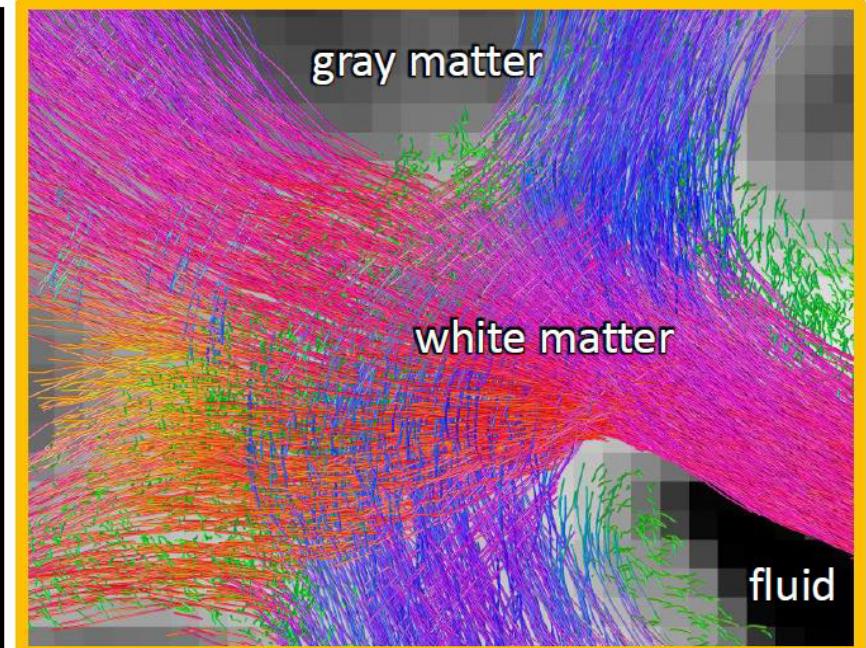
Jeurissen et al., NeuroImage, 2014

Concept map for lectures

... to long-range brain connections



white matter fiber connections



Outline of tractography concepts

Tractography variables

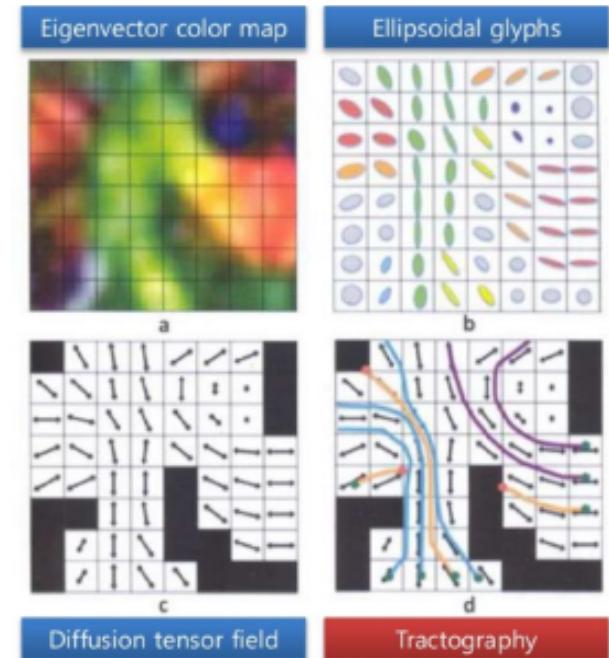
- Streamlines, seeds, step-size, interpolation
- Starting and stopping criteria
- Algorithm: deterministic vs. Probabilistic

Introduced by:
Basser, 1998
Mori et al., 1998

Nice review:
Jeurissen et al., 2017

Tractography quantification

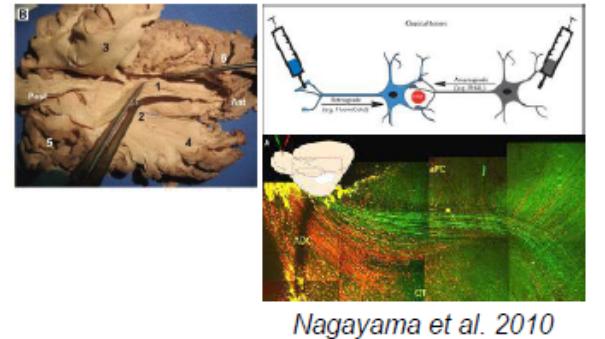
- Voxel-wise track counts (Track Density Imaging)
- Structural connection strength
- Both have issues:
 - Biases to longer tracks
 - Biases to simpler tracks
 - Errors from noise & modelling



Brain diffusion MRI challenges

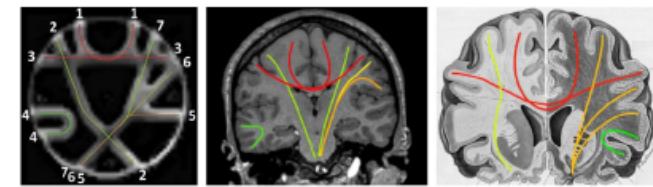
Validation

- Ex-vivo brain (histology, dissection, axial tracings)
- Phantom (digital, physical)

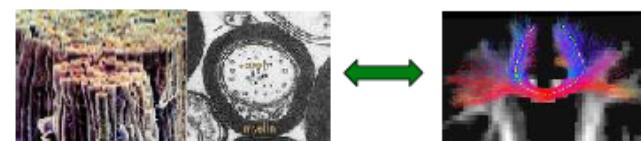


Quantification

- What is connection strength? (#, volume of streamlines)
- Integrated data from multiple modalities (T1, FA, myelin, etc)
- Evaluation of quantitative maps along tracts
- Promises: use morphology to estimate topology



Poupon et al., 2010



Microstructure Informed Tractography: Pitfalls and Open Challenges

Alessandro Dadoeli^{1,2,3*}, Alessandro Dal Pai⁴, Maxime Descoteaux³ and Jean-Philippe Thiran^{1,2}

Literature recommendations include

Papers

- Tournier. **Diffusion MRI in the brain - Theory and concepts.** *Prog Nucl Magn Reson Spectrosc.* 2019;112-113:1-16
- Maier-Han et al., **The challenge of mapping the human connectome based on diffusion tractography.** *Nat Comm.* 2017;8(1):1349.
- Jeurissen et al., **Diffusion MRI fiber tractography of the brain.** *NMR Biomed.* 2019;32(4):e3785
- Le Bihan D, Iima M. **Diffusion MRI: What Water Tells Us about Biological Tissues.** *PLoS Biol.* 2015 Jul 23;13(7):e1002203
- [Microstructural imaging](#)
- ...
- <http://www.ncbi.nlm.nih.gov/pmc/?term=diffusion+mri+review>

Web materials:

- OHBM Educational Series: <https://www.pathlms.com/ohbm/courses/>
- <https://www.ohbmbrainmappingblog.com/blog/ohbm-on-demand-how-to-diffusion-mri>
- ISMRM Educational Series
 - <https://www.ismrm.org/online-education-program/diffusion-perfusion-fMRI-videos/>
 - <https://www.youtube.com/watch?v=yIuL093GMMA>
 - ...

Concept map for lectures

Lecture 1

NMR Signal origin

- Powerful magnet
- Radio frequency
- Magnetic field gradients

MR Image & Contrast

- Spatial encoding
- Magnetic gradients
- Pulse sequences

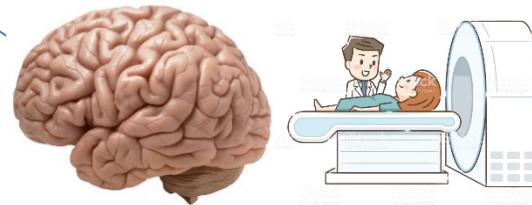
MR Safety

- Powerful magnet
- Radio frequency
- Magnetic field gradients

Lecture 2

Structural MRI

- Contrast, important parameters
- Sequences & artifacts
- Analyses & applications



Lecture 3

Diffusion MRI

- Contrast, important parameters
- Sequences & artifacts
- Analyses & applications

Lecture 4

Functional MRI

- Contrast, important parameters
- Sequences & artifacts
- Pre-processing