

From ex-vivo to in-vivo histology of human cortex with ultra-high field MRI

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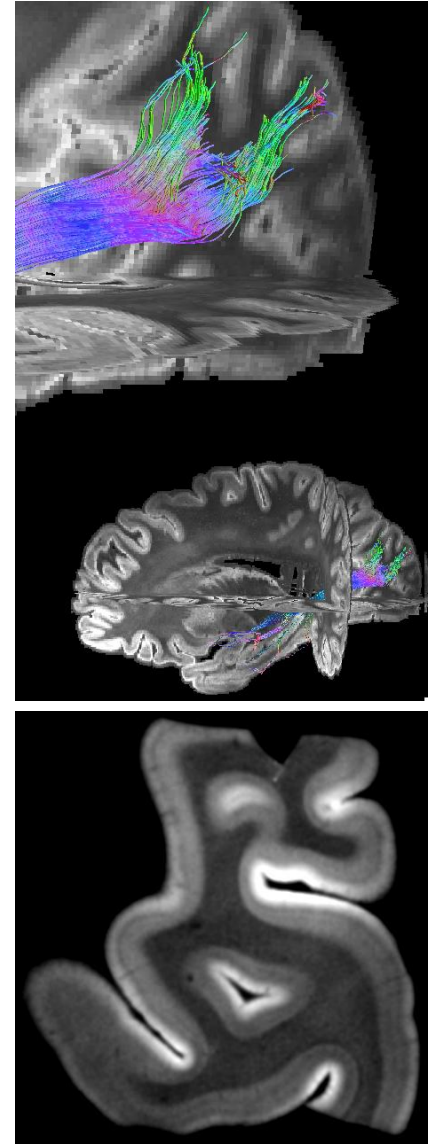
Faculty of Psychology & Neuroscience

Maastricht University

www.cbclab.org

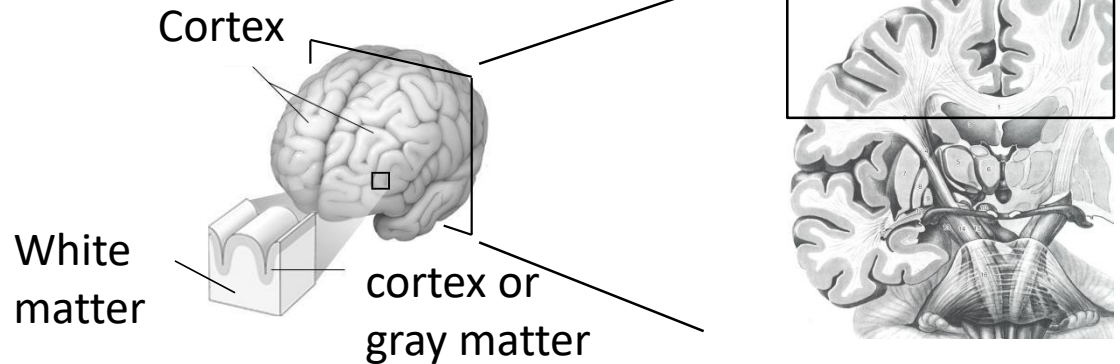
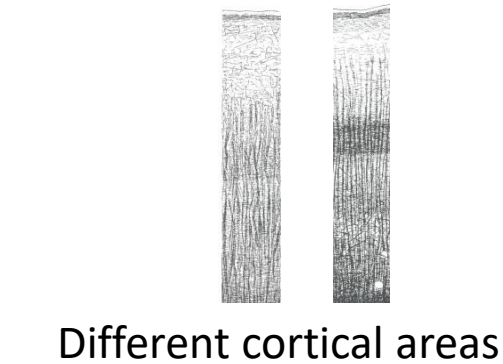
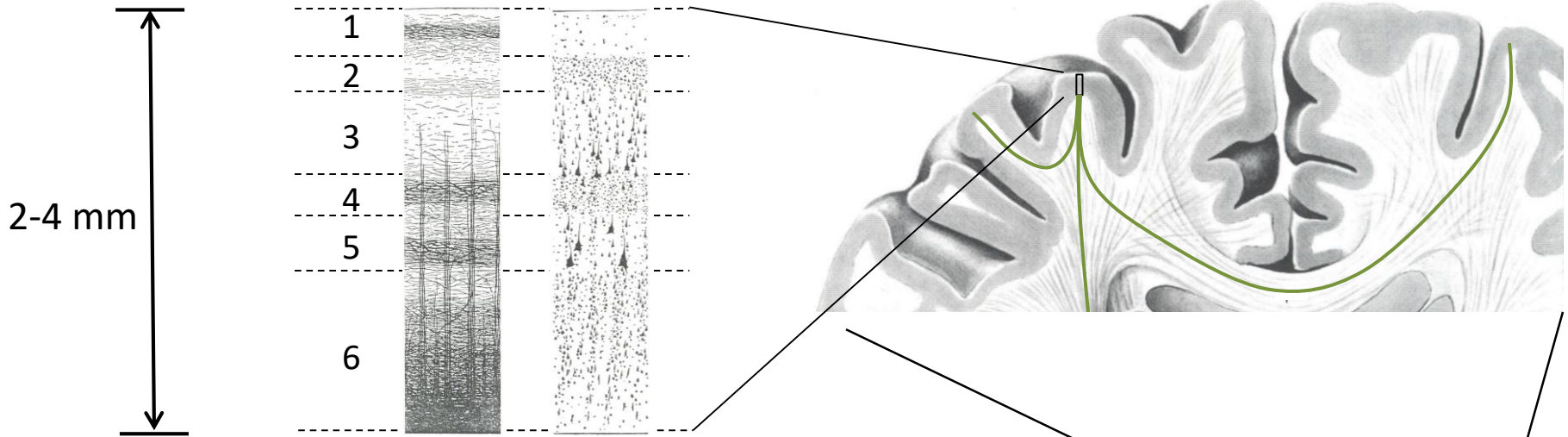
Overview

- Human cortical architecture & multiscale connectivity
- Post mortem / ex-vivo
 - Whole brain high resolution MRI
 - Macroscale
 - Intracortical diffusion imaging
 - Mesoscale
- In vivo
 - Diffusion microstructure models
 - Microscale
- Outlook & Conclusions



Human cortical architecture

myelo-architecture **cyto-architecture** **connect-architecture**

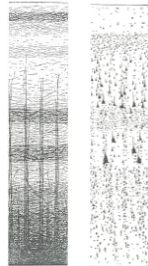


Scales of the human brain

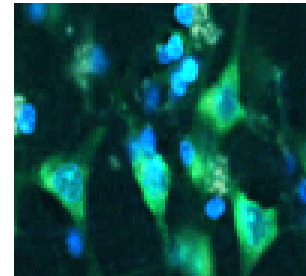
	Macroscale			Mesoscale		Microscale		Nanoscale	
μm^3 :	10^{15}	10^{12}	10^9	10^6	10^3	10^0	10^{-3}	10^{-6}	10^{-9}
μm :	10^5	10^4	10^3	10^2	10^1	10^0	10^{-1}	10^{-2}	10^{-3}
		cm	mm			μm			nm



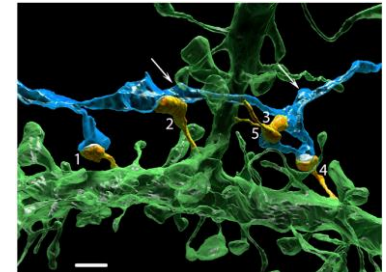
Brain



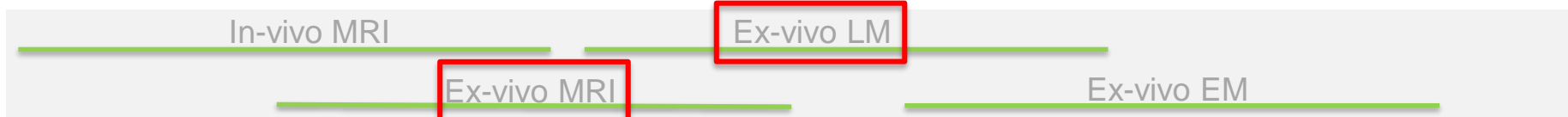
Layers



Neurons



Synapses



Human multiscale connectivity

Macroscale

Mesoscale

Microscale

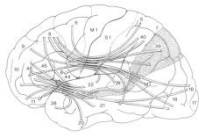
Nanoscale

In-vivo dMRI

Ex-vivo LM

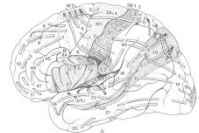
Ex-vivo dMRI

Ex-vivo EM

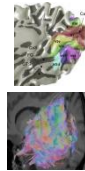


whole human brain

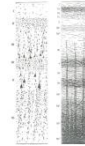
Long-range association projections



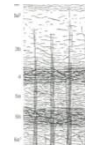
Short-range association projections



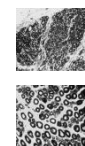
Topographic projection organization



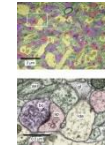
Layered Intra-cortical circuits



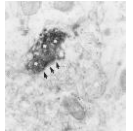
Layer of avg. large projection termination



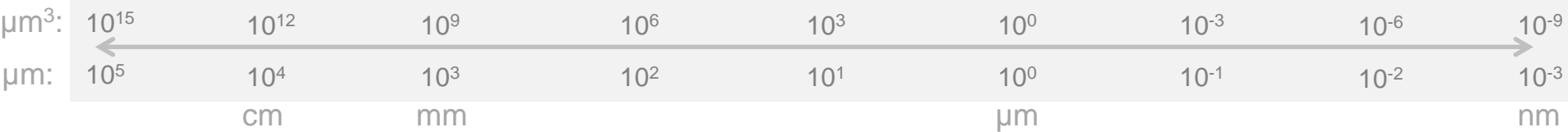
Axonal density & diameters



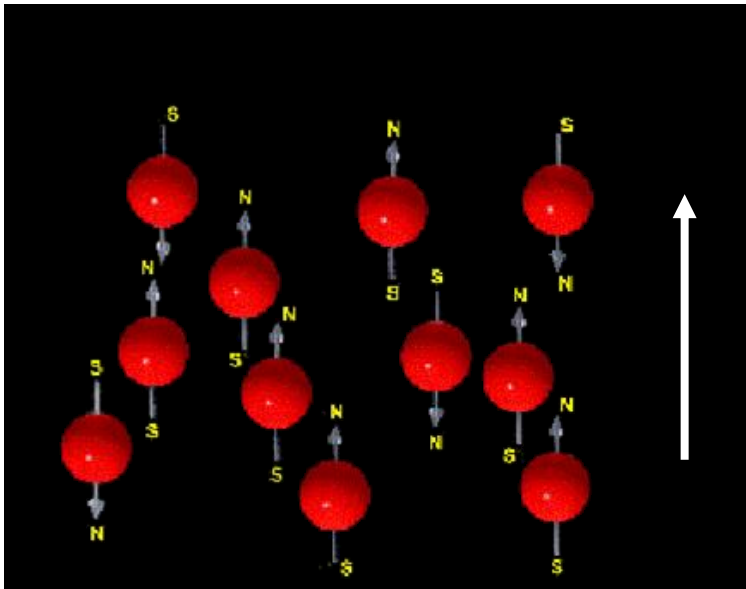
Synaptic contacts



Neuro-transmitters Receptors



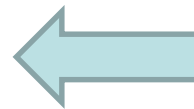
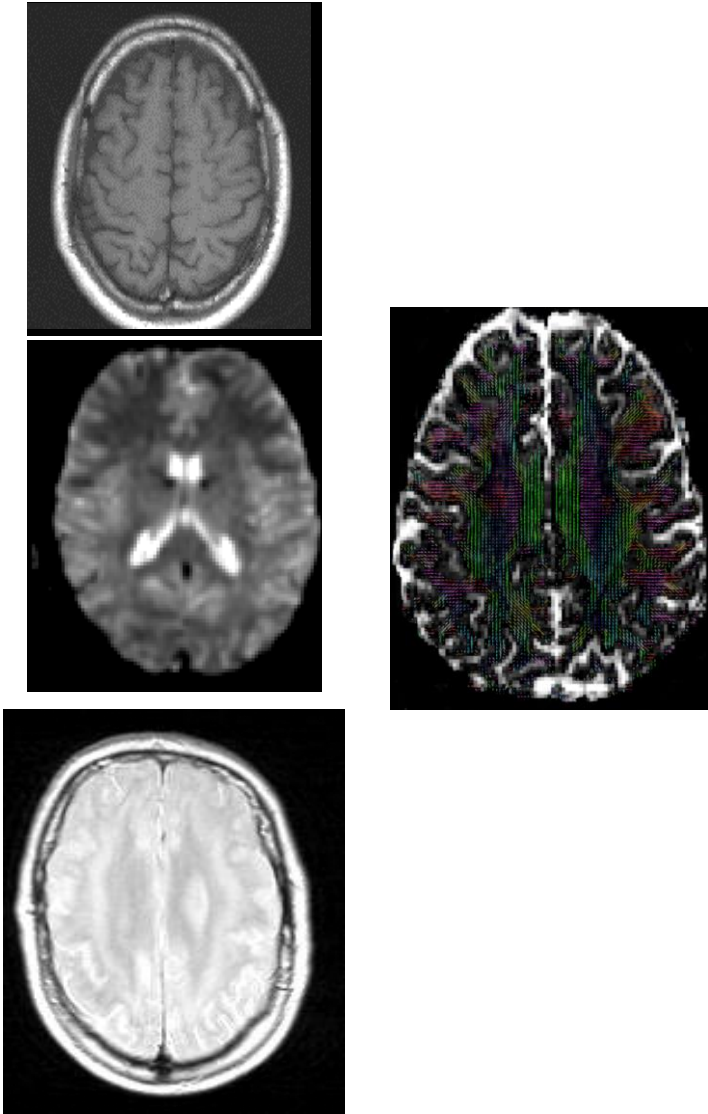
Bigger MRI magnets: why?



- The higher the field
 - 1.5T -> 3T -> 7T -> 9.4T
 - The more usable spins
 - Most often protons
 - The more signal

More MRI signal: Why?

- More contrast
- Higher resolution
- More coverage
- Shorter measurement



Contrast

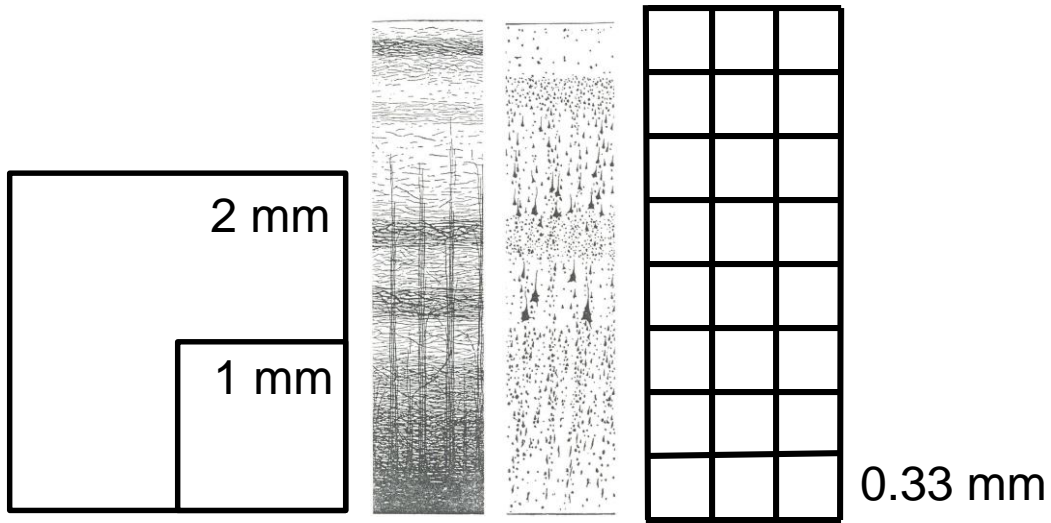
Resolution



Coverage

Acquisition Time

MRI Resolution



9.4 Tesla



7 Tesla



Ultra-high field MRI



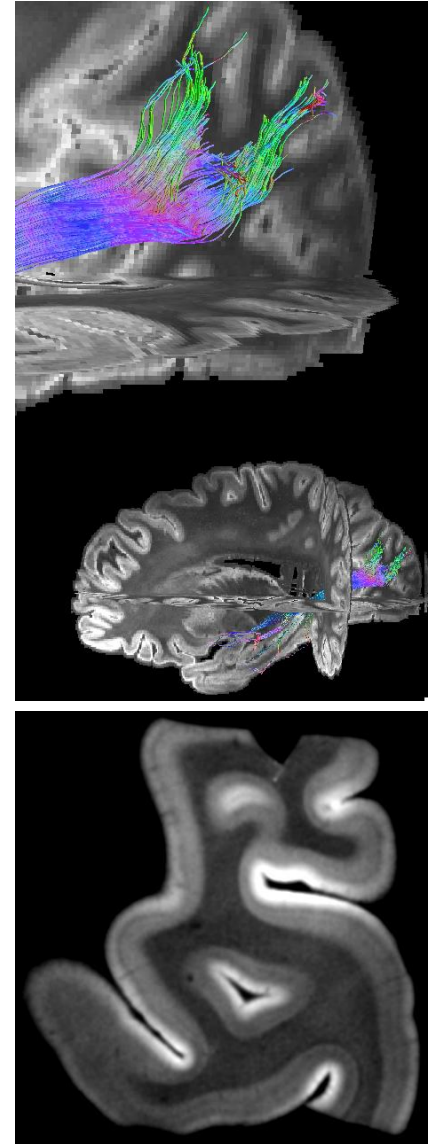
9.4T whole human brain 330 μ m isotropic



Specialized RF coils

Overview

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- In vivo
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 - Microscale
- Outlook & Conclusions



Whole human brain mesoscale anatomy & connectivity

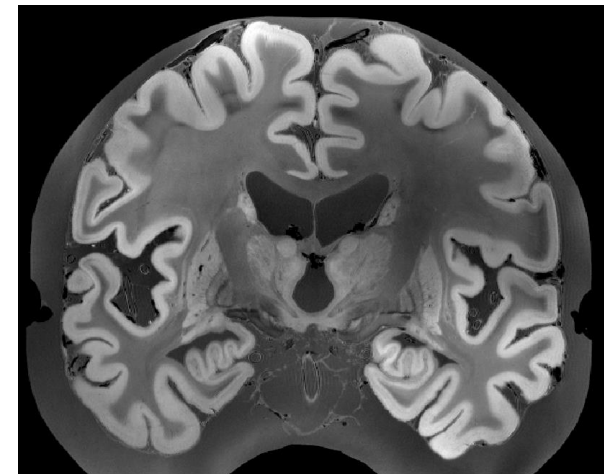
- **9.4T ex vivo human brain coil**

- For 9.4T 820cm bore system
- 8Ch pTX
- 80mT/m head gradient

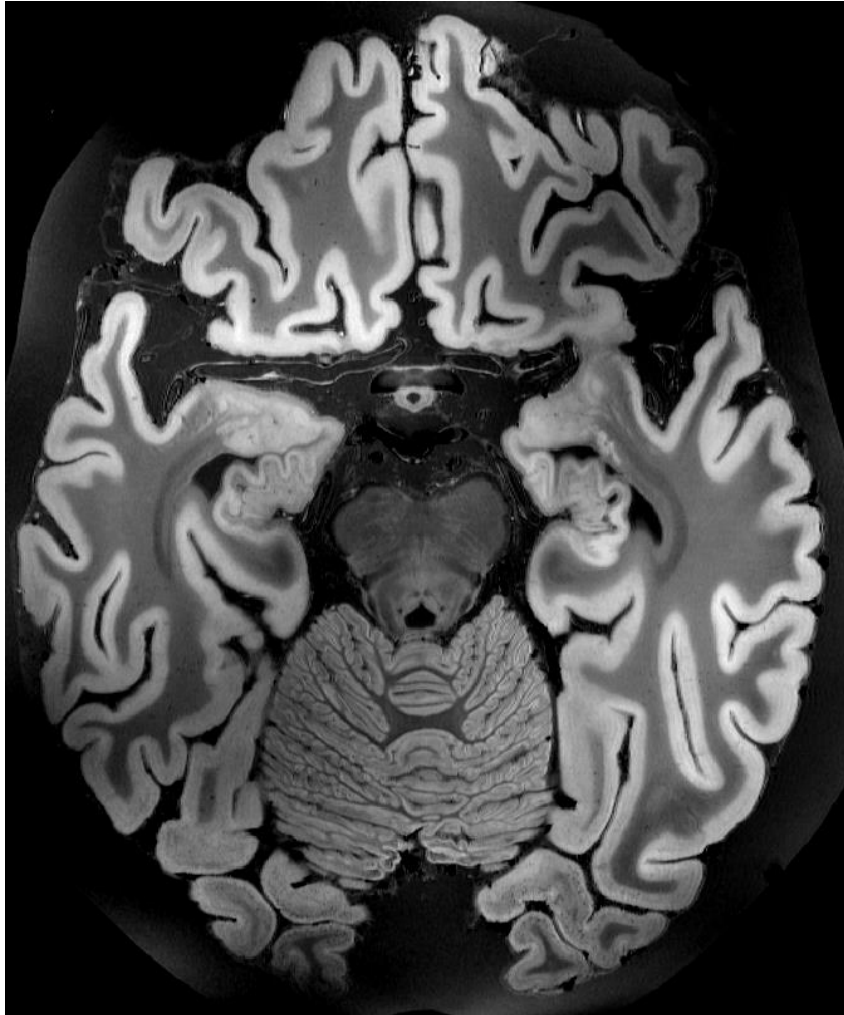


- **High-res imaging of the whole human brain**

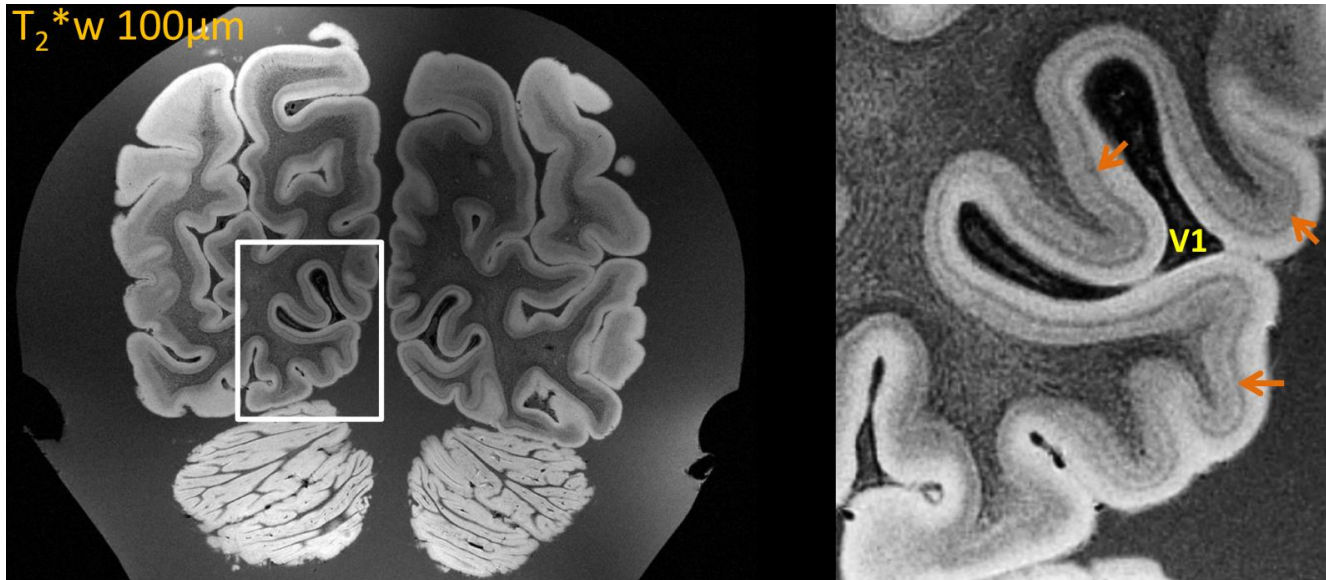
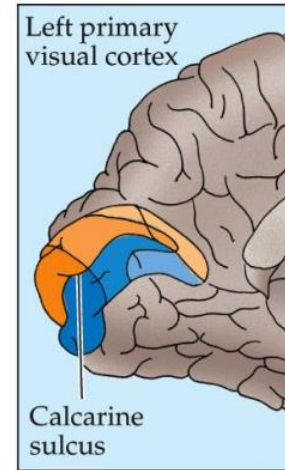
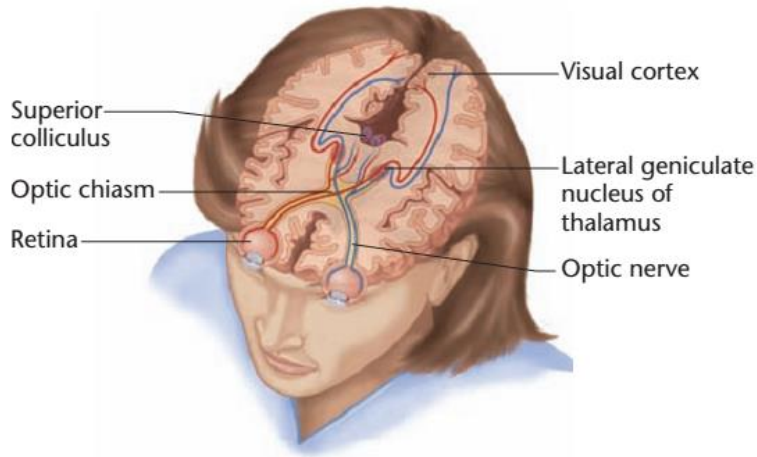
- in pTX-mode
- High SNR
- Time-efficient



Whole brain anatomy 200 μ m

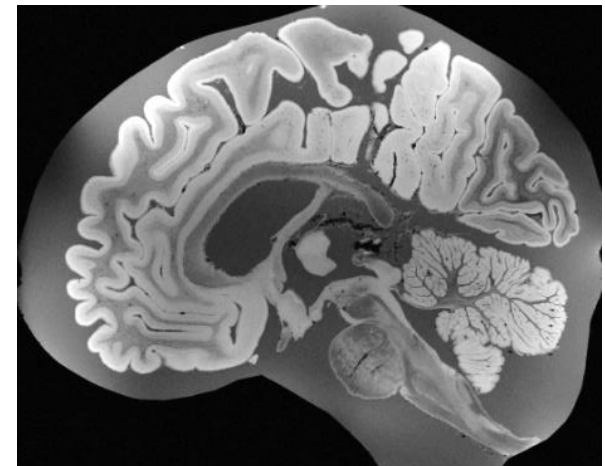
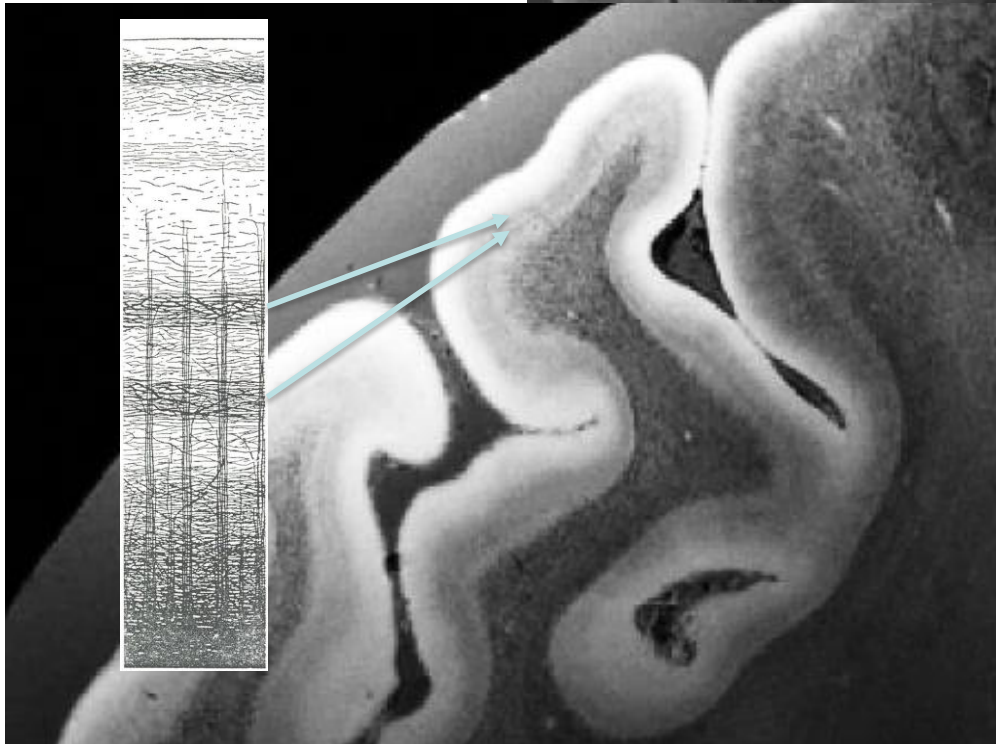
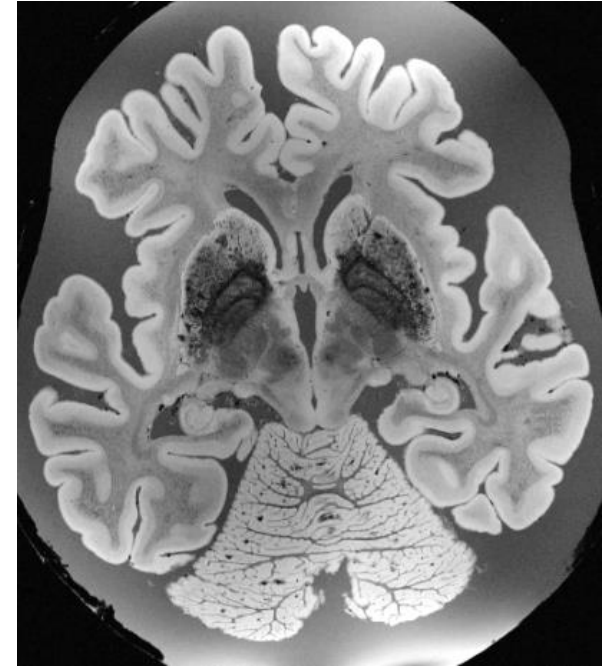
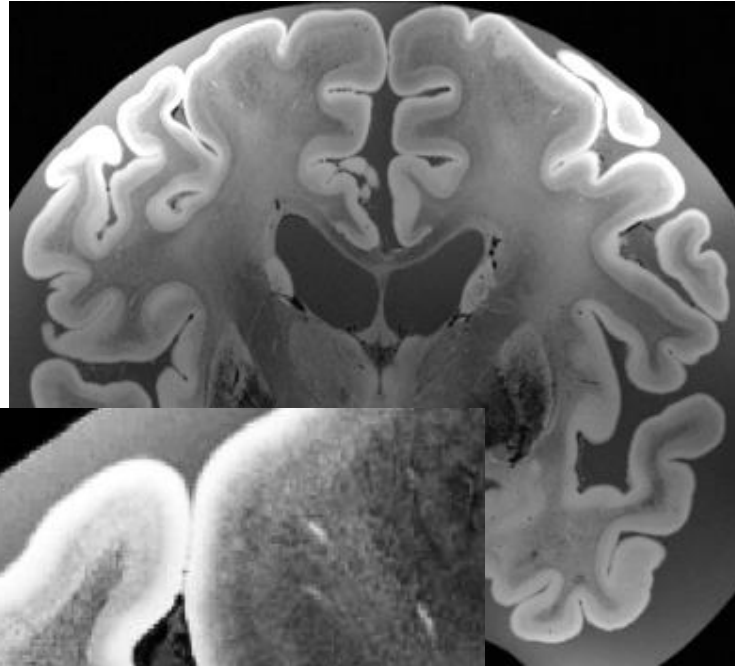


Whole brain anatomy 100 μ m

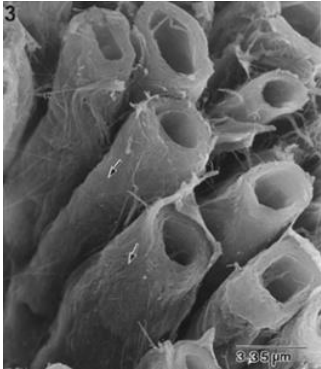


Whole brain anatomy 75 μ m

myelo-
architecture

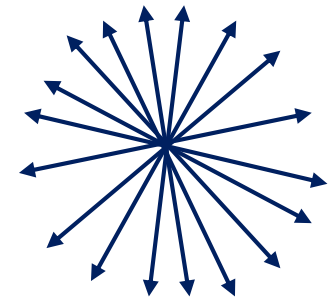
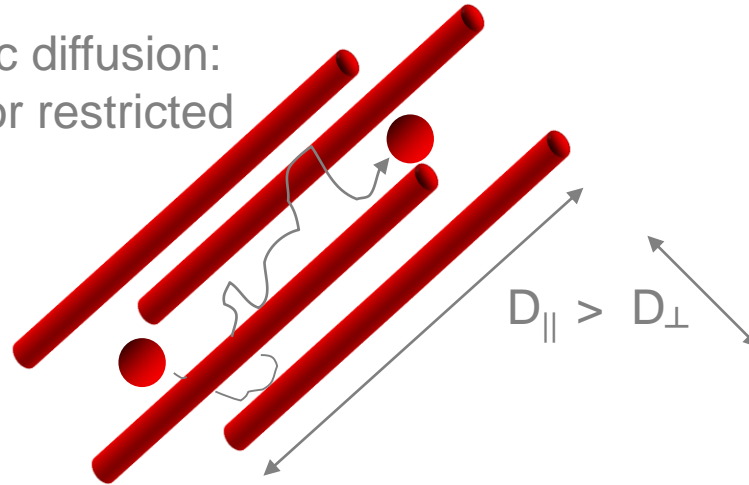


Diffusion MRI

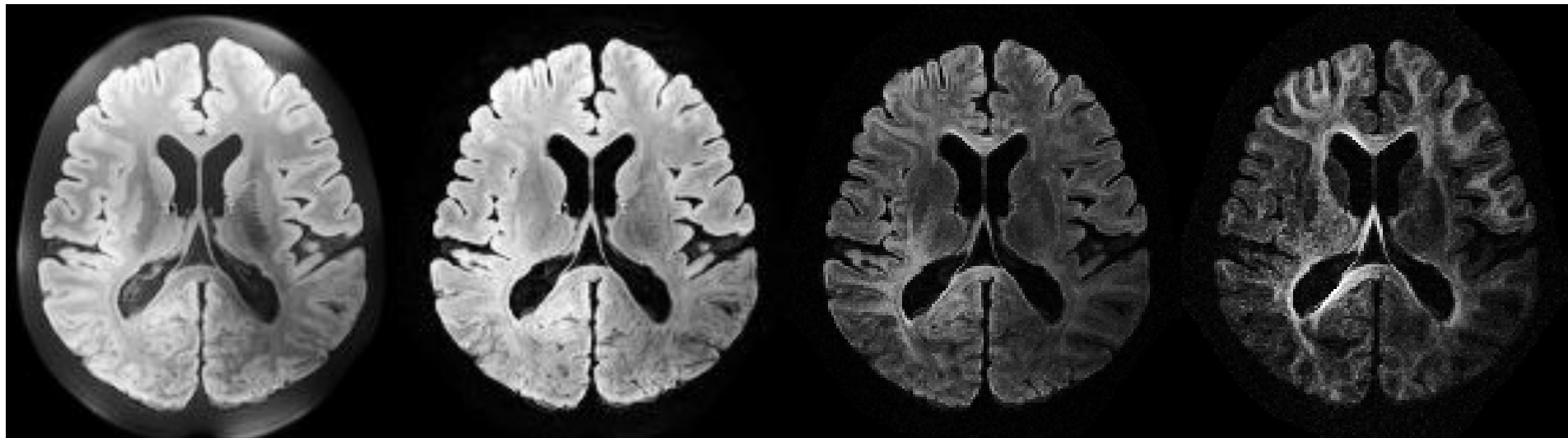


WM

Anisotropic diffusion:
hindered or restricted



Probe with diffusion
gradient directions



230 s/mm²

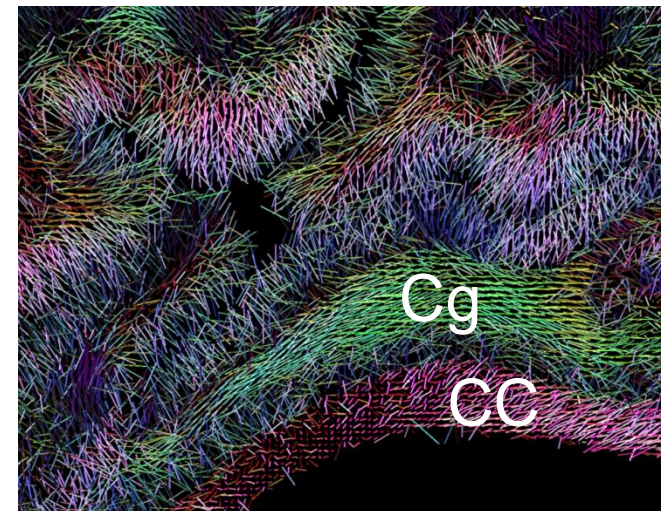
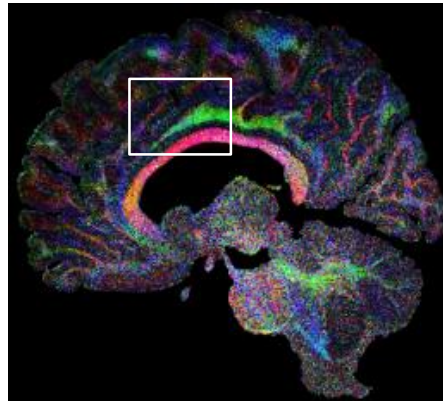
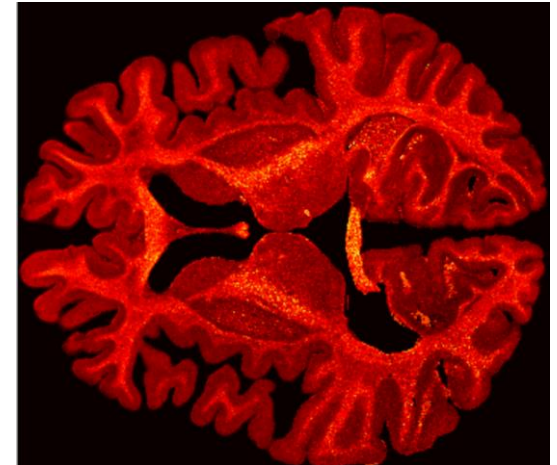
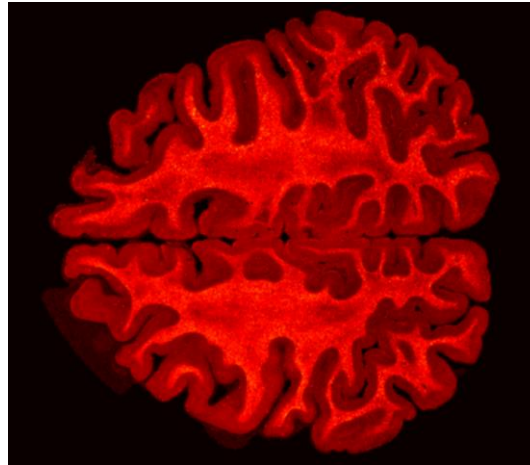
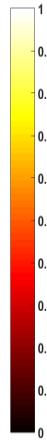
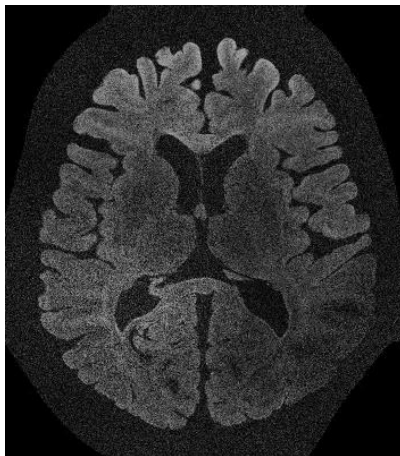
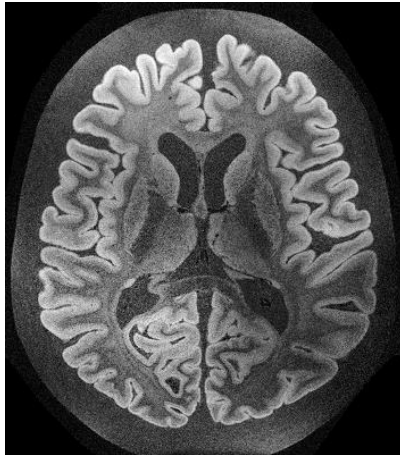
2022 s/mm²

4036 s/mm²

8072 s/mm²

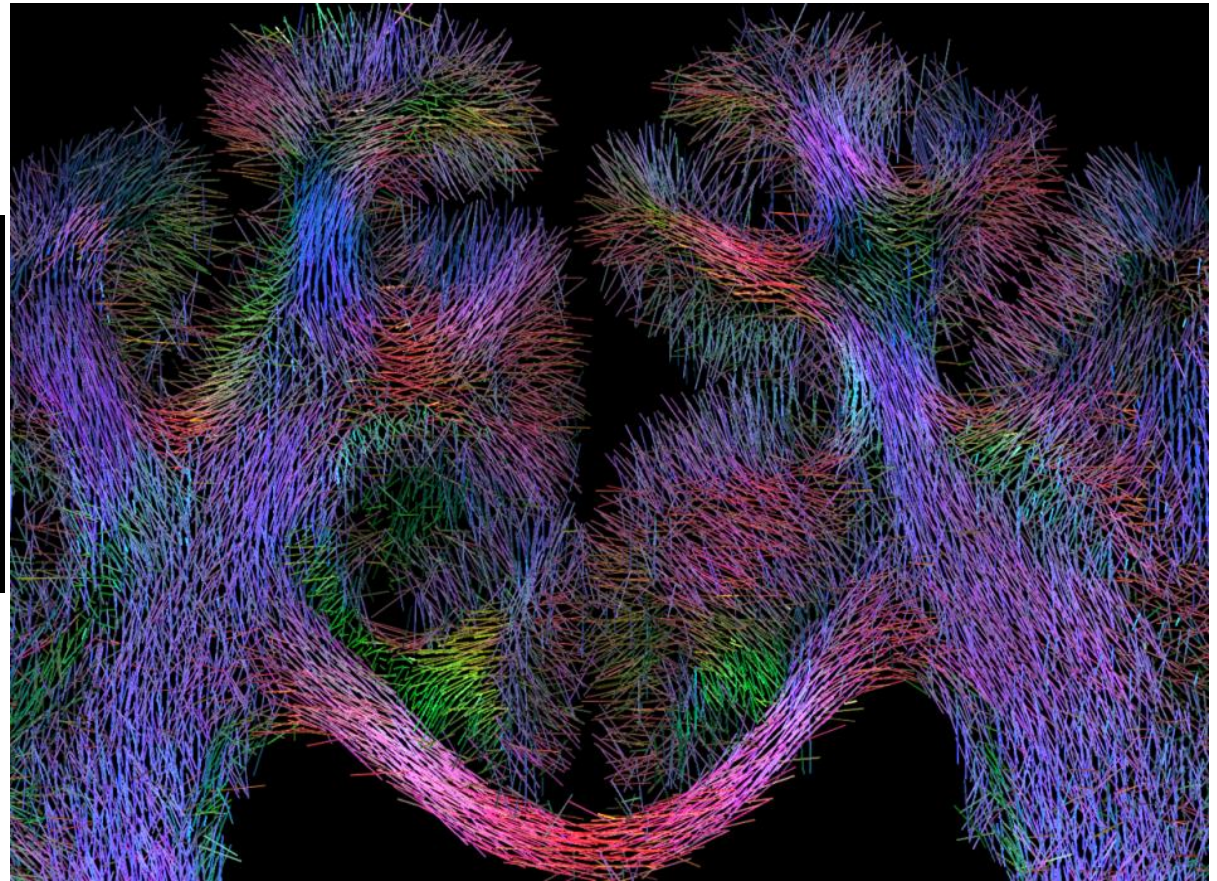
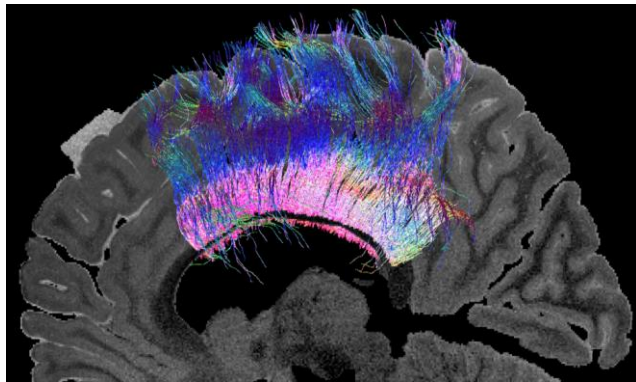
Whole brain dMRI <math>< 500\mu\text{m}</math>

9.4T, 400um



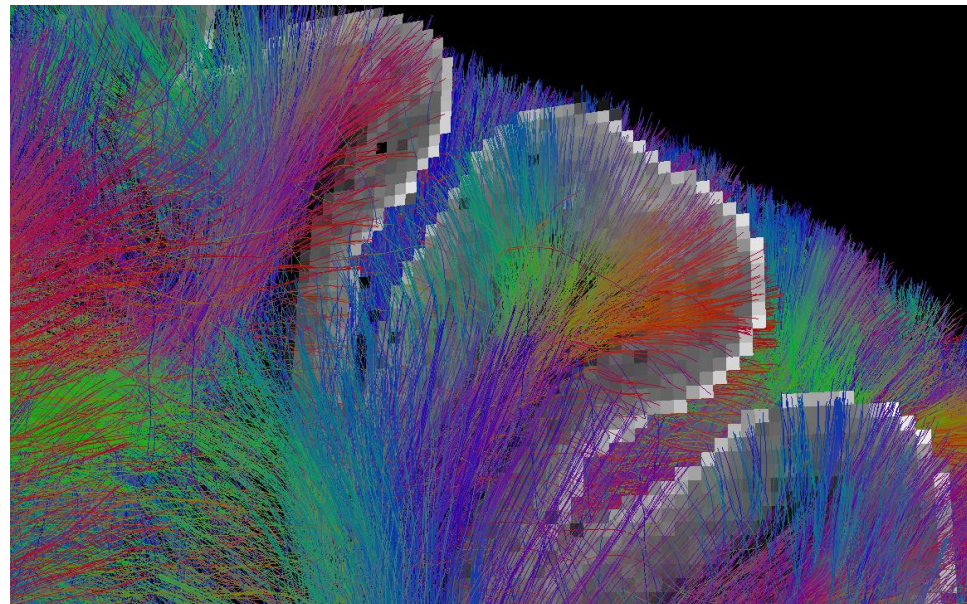
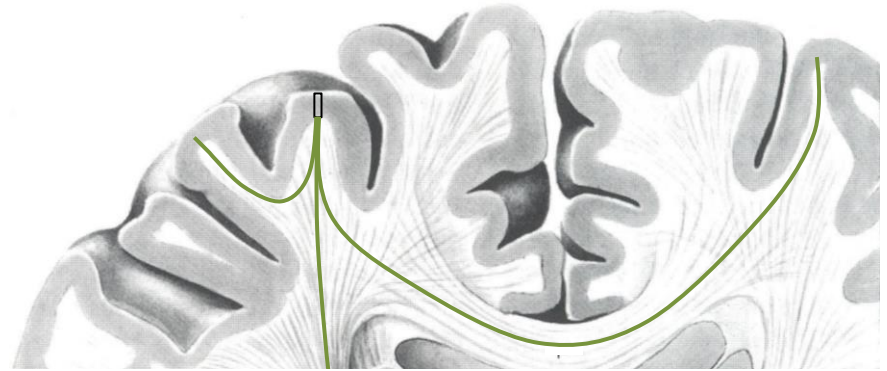
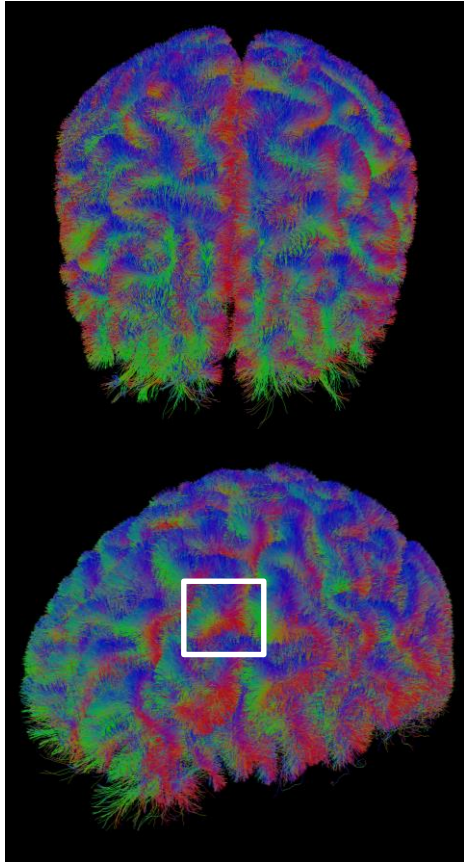
Whole brain dMRI <math>< 500\mu\text{m}</math>

9.4T, 400um



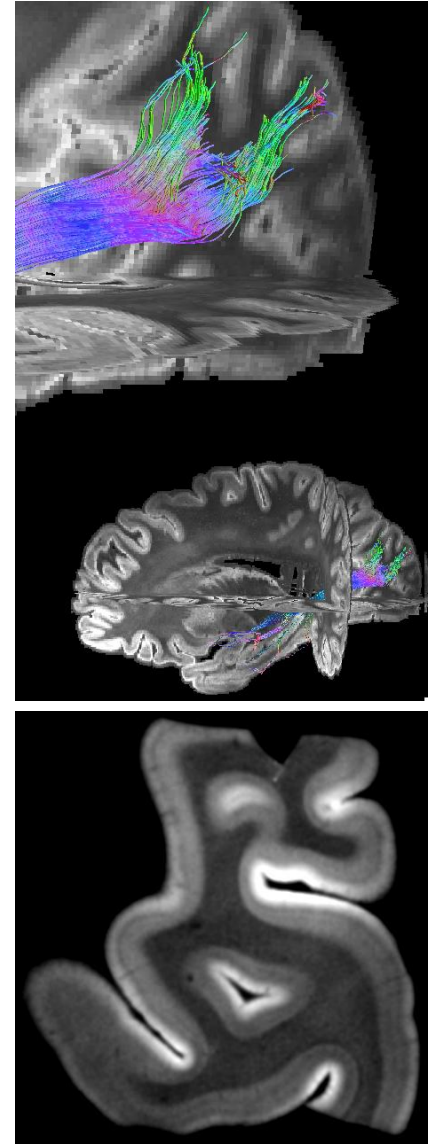
Whole brain connectivity 400 μ m

connect-
architecture



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 - Microscale
- Outlook & Conclusions



Human multiscale connectivity

Macroscale

Mesoscale

Microscale

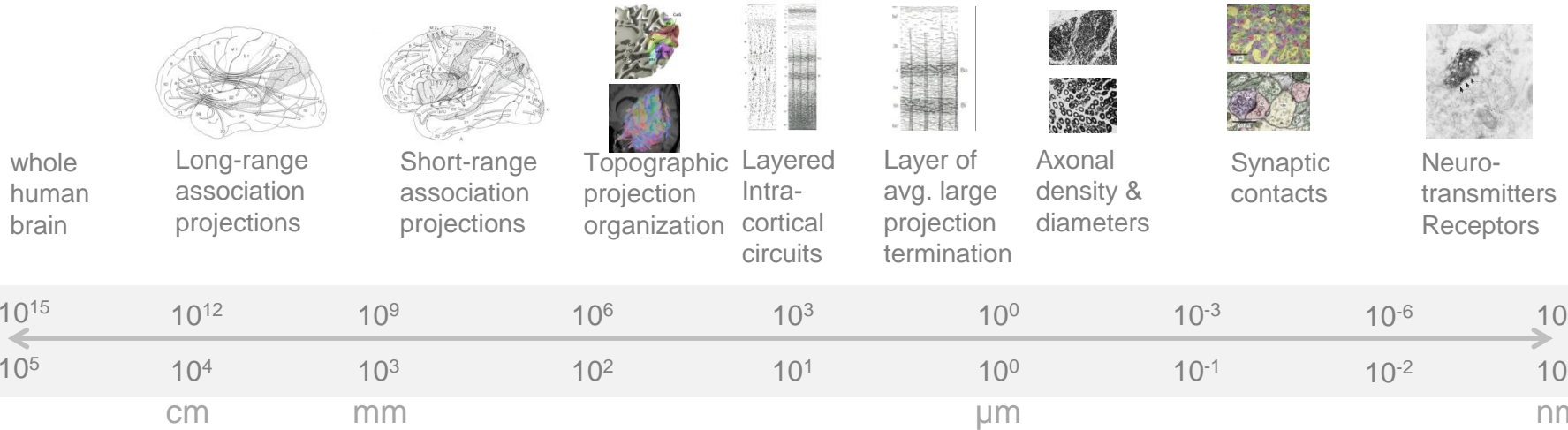
Nanoscale

In-vivo dMRI

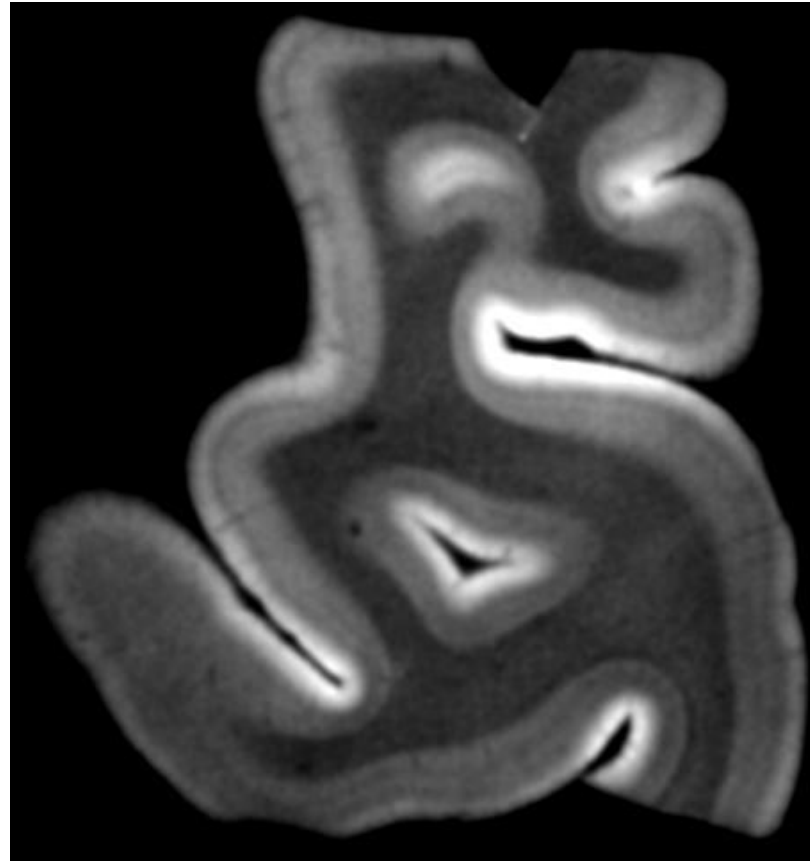
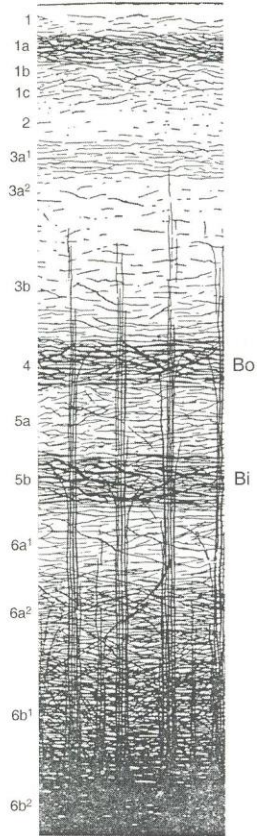
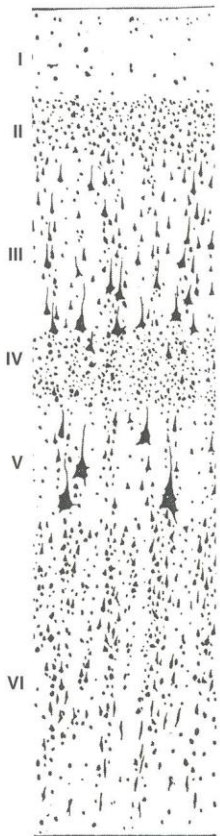
Ex-vivo LM

Ex-vivo dMRI

Ex-vivo EM

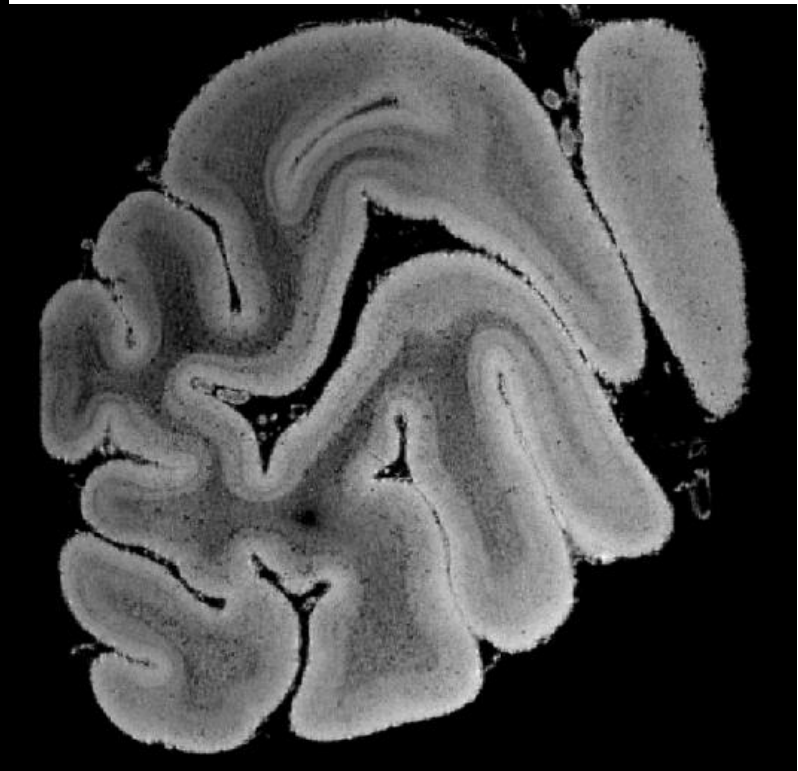
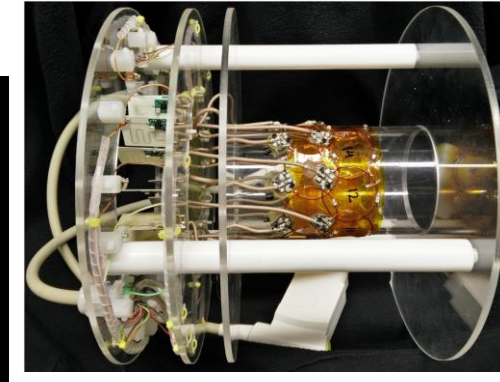
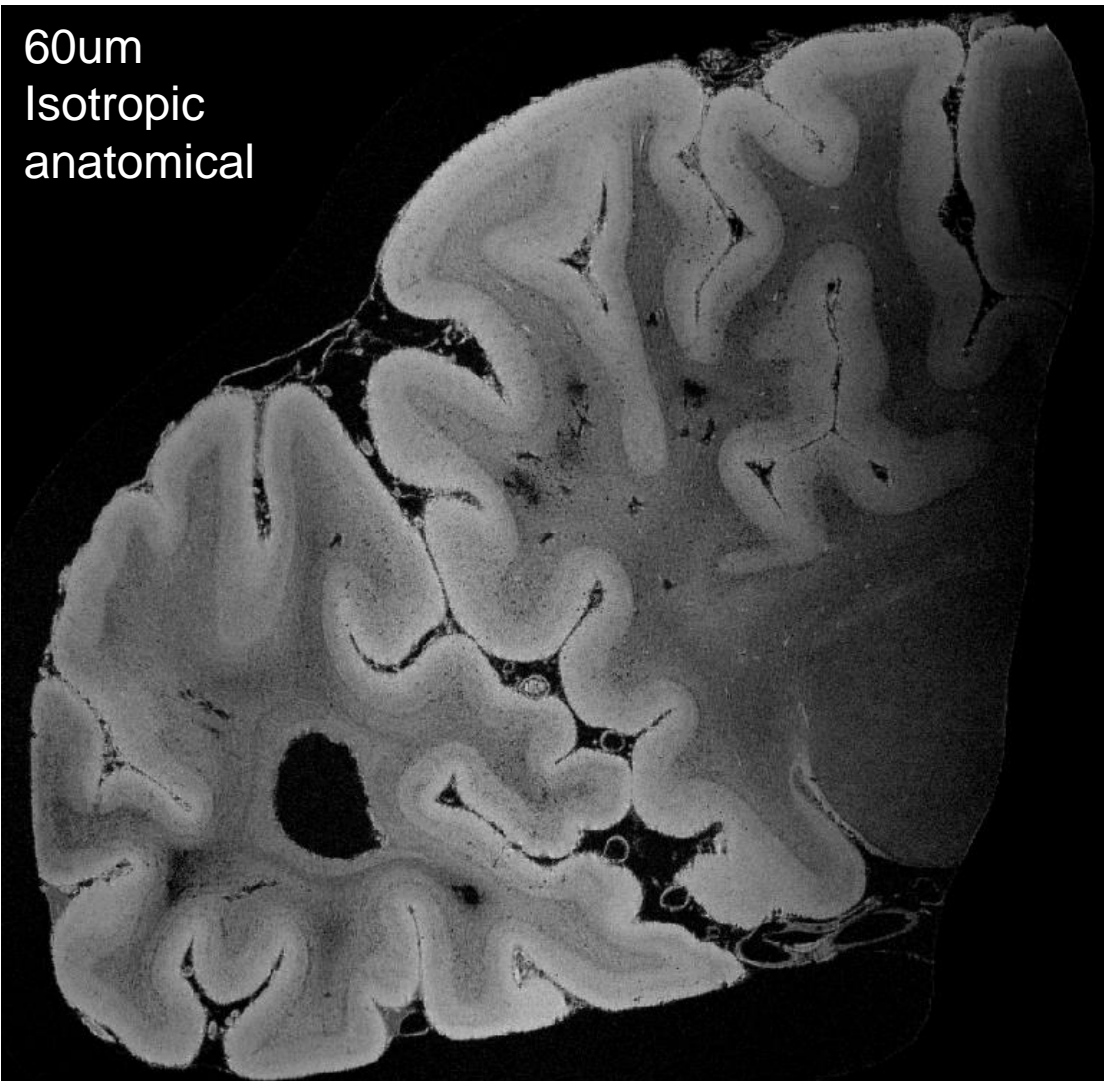


Intracortical connectivity



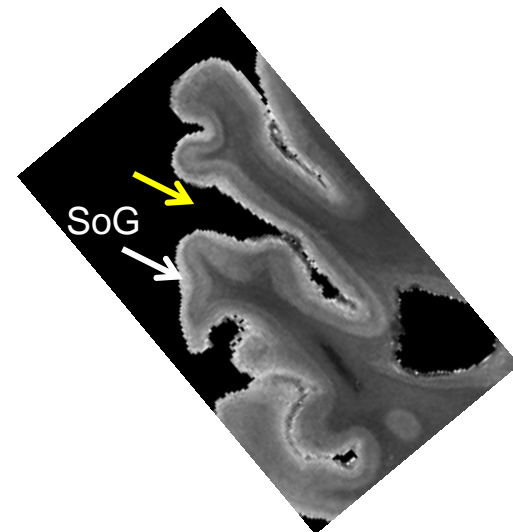
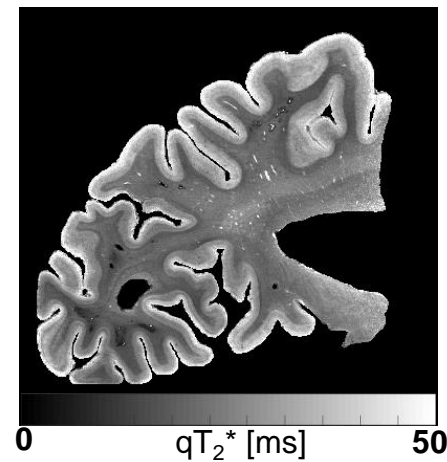
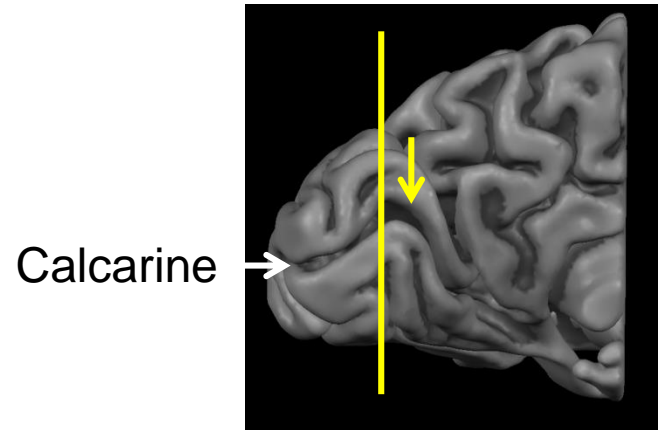
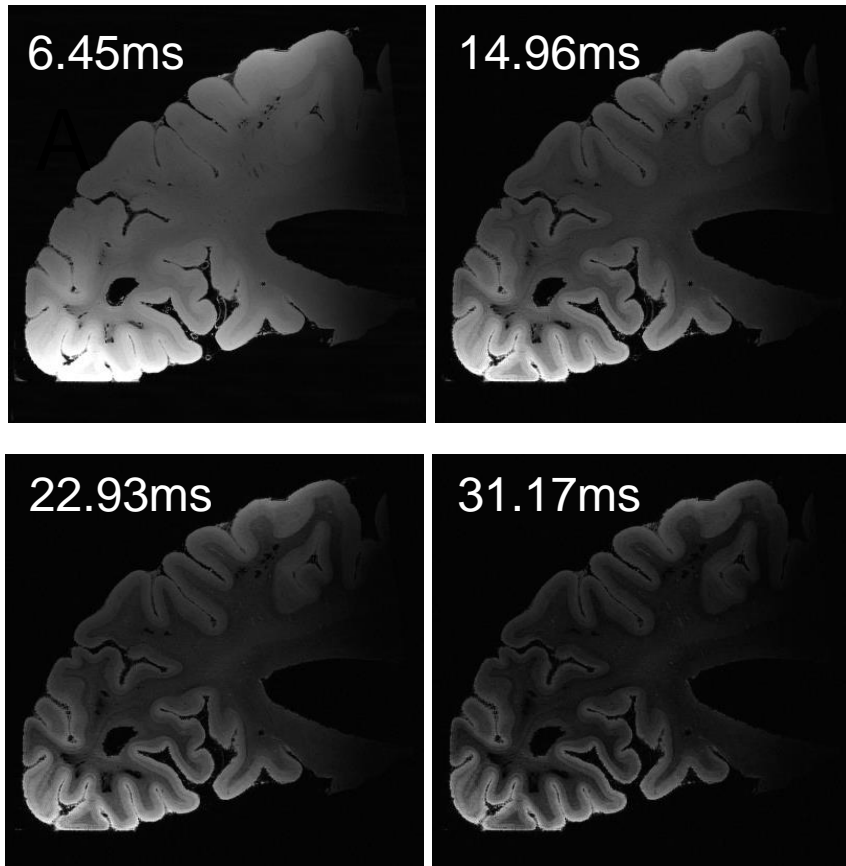
9.4T diffusion MRI, Average of 12 diffusion-weighted images, 160um in-plane

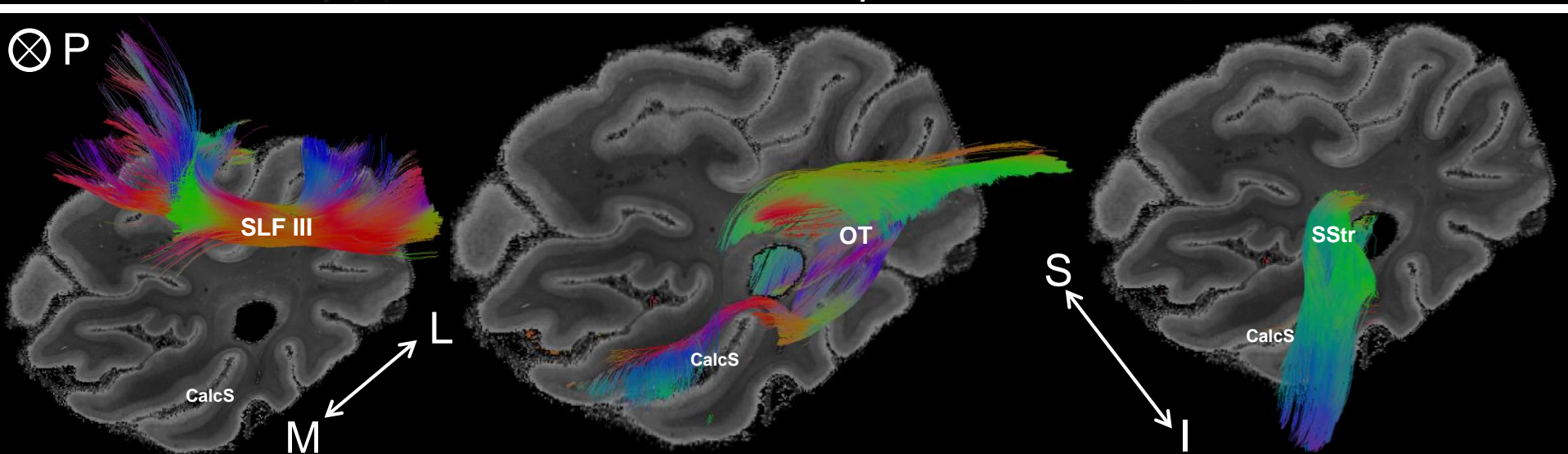
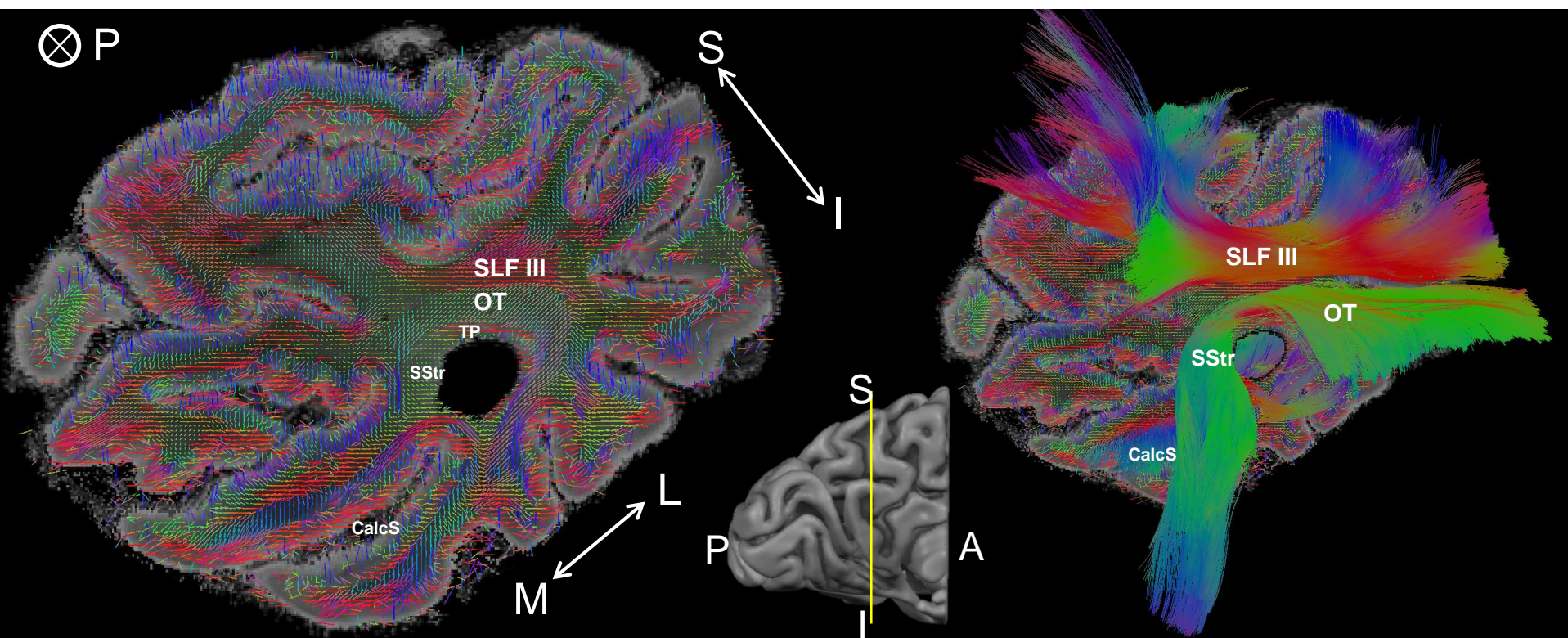
Large human samples



Anatomical imaging

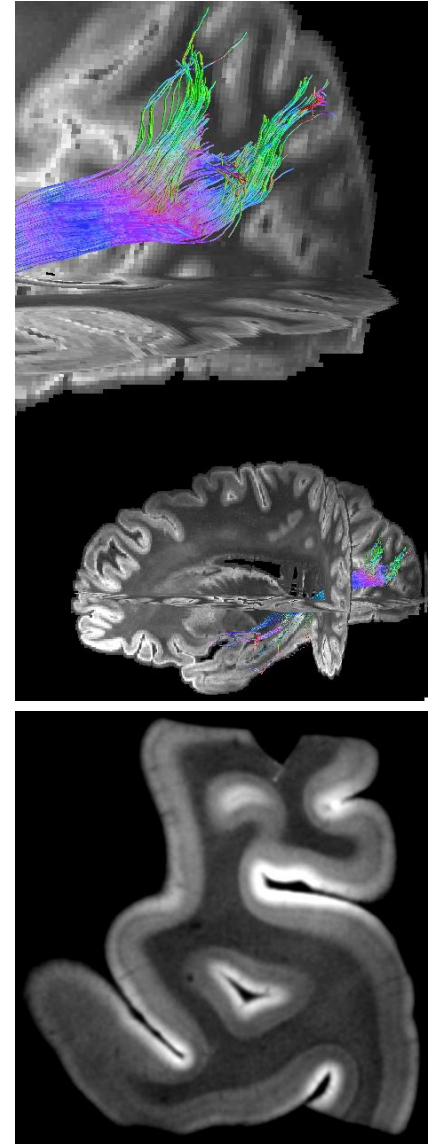
Quantitative T2*
(qT2*)





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Human multiscale connectivity

Macroscale

Mesoscale

Microscale

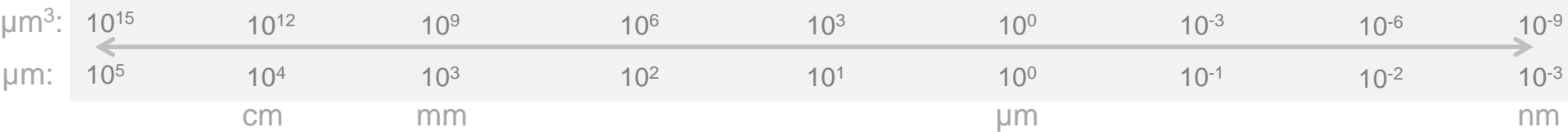
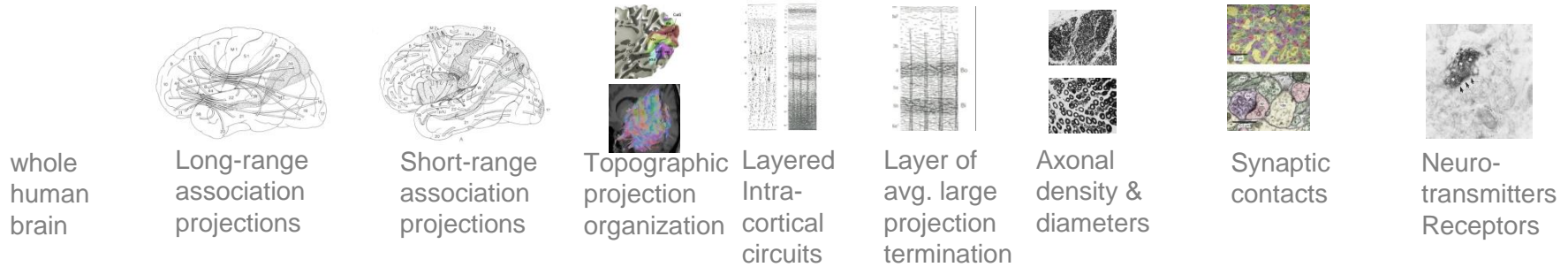
Nanoscale

In-vivo dMRI

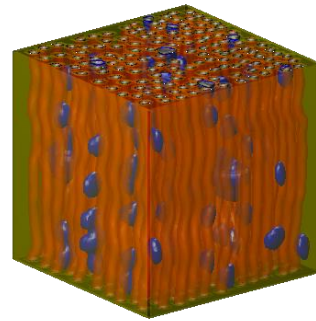
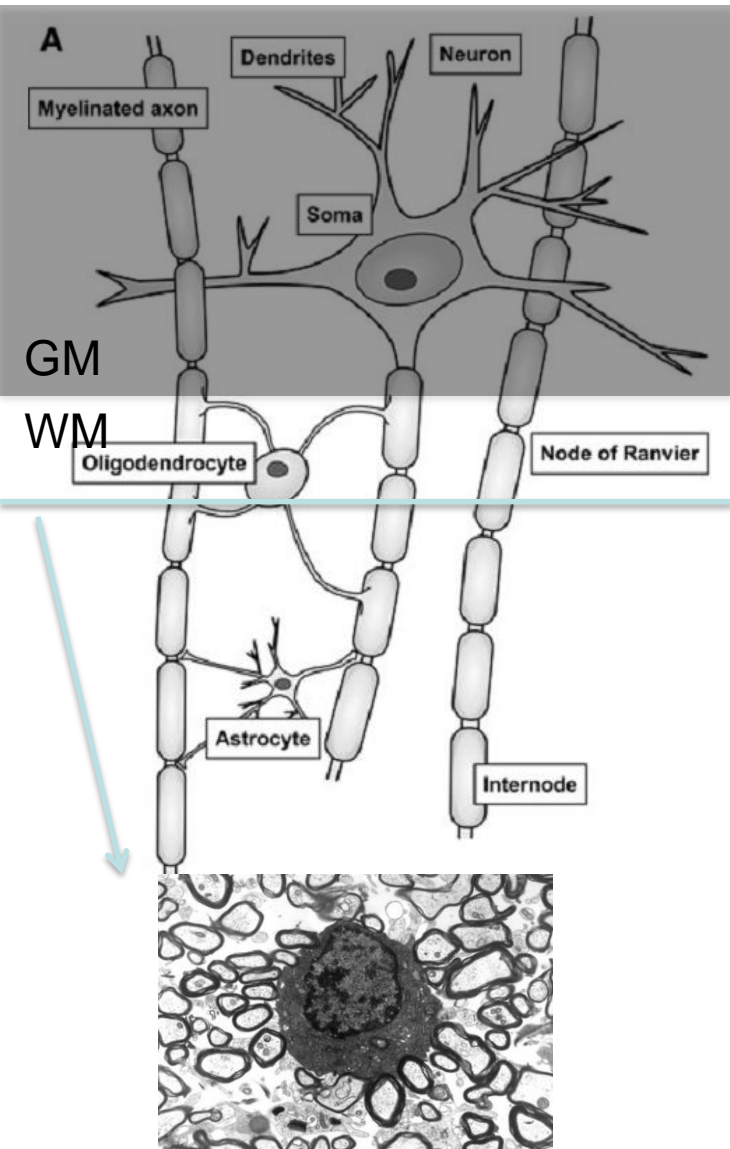
Ex-vivo LM

Ex-vivo dMRI

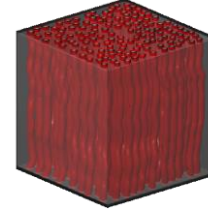
Ex-vivo EM



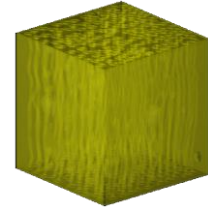
WM diffusion microstructure



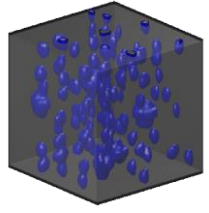
WM voxel



Intra-axon

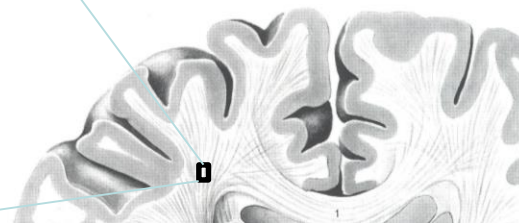


Extra-axon

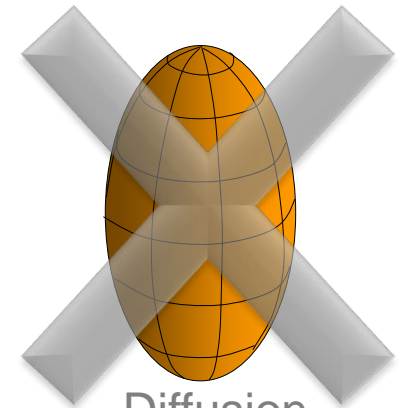


Glia cells ...

Compartments

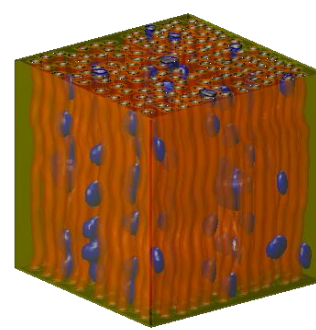
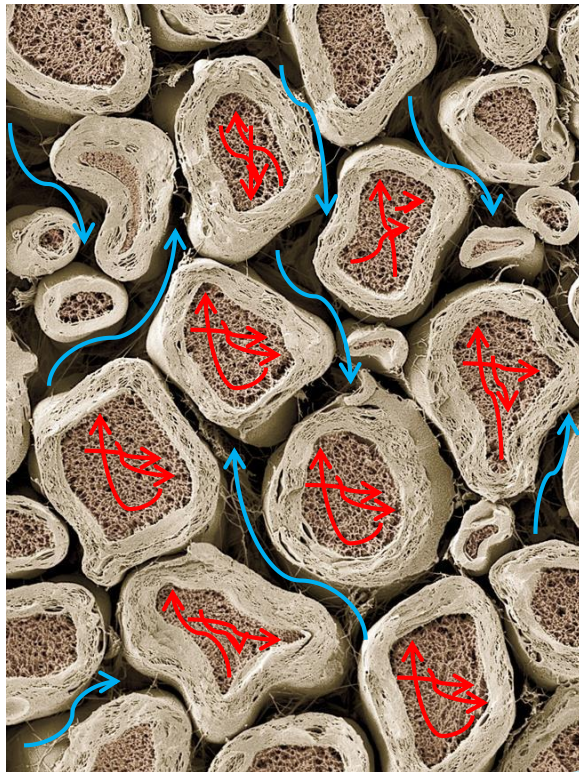


White matter

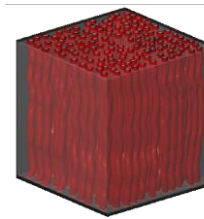


Diffusion tensor

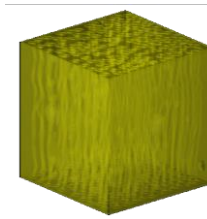
WM diffusion microstructure



WM voxel



Intra-axon

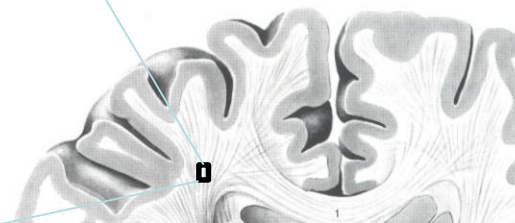


Extra-axon



$$E(\mathbf{q}, \Delta) = f_r * E_r(\mathbf{q}, \Delta) + f_h * E_h(\mathbf{q}, \Delta)$$

Intra-axonal Extra-axonal



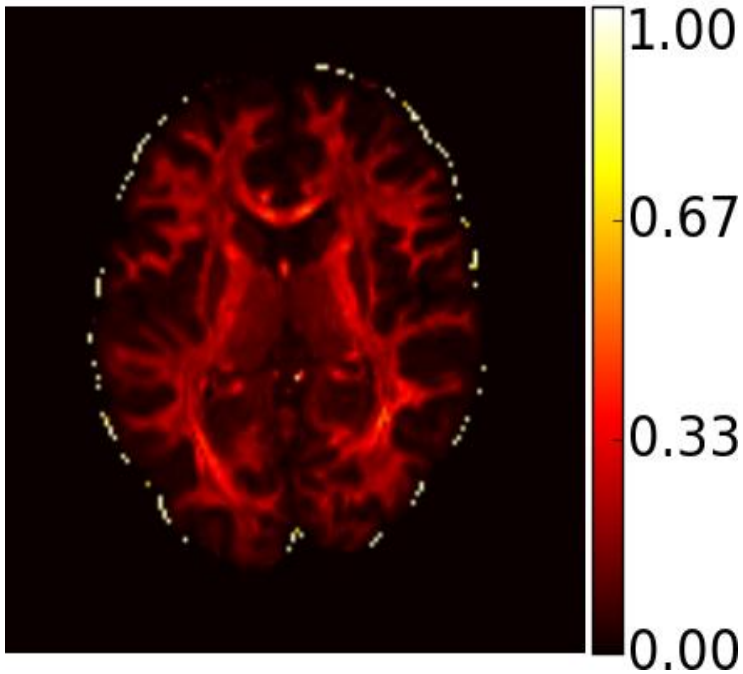
White matter

CHARMED

Assaf et al., 2004, 2005

WM diffusion microstructure

FR

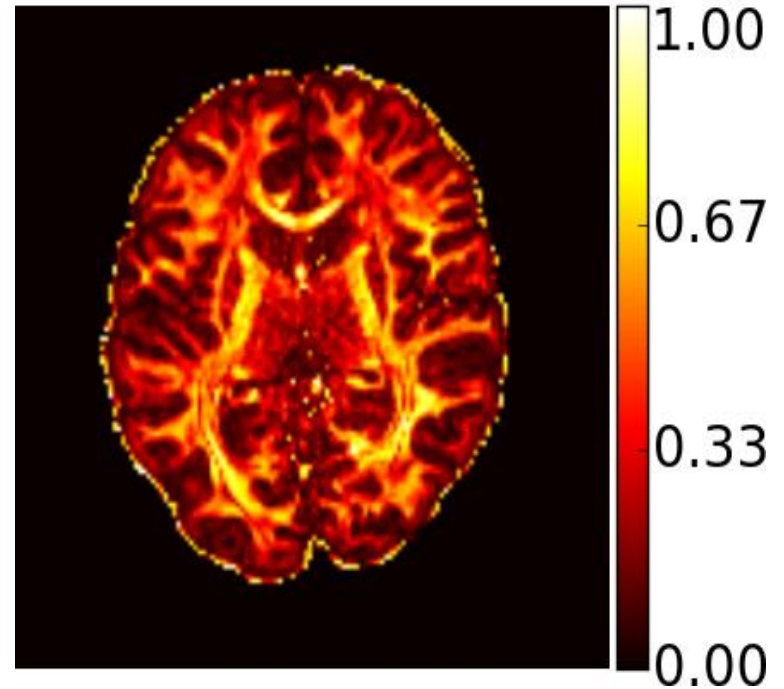


1. Crossing fibers
2. Fiber density (FR)

CHARMED

Assaf et al., 2004, 2005

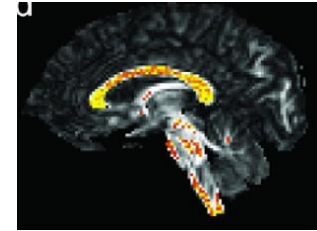
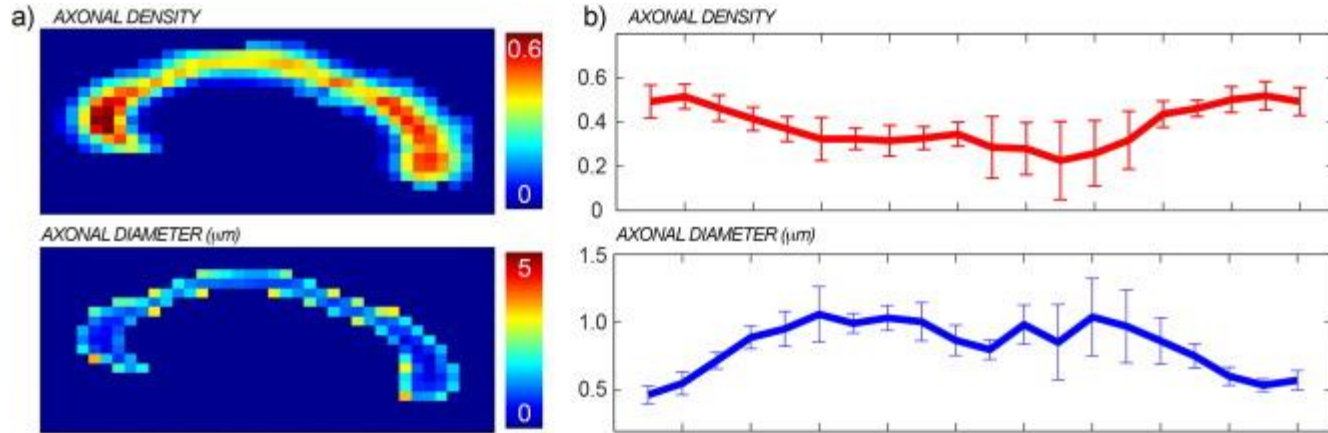
FA



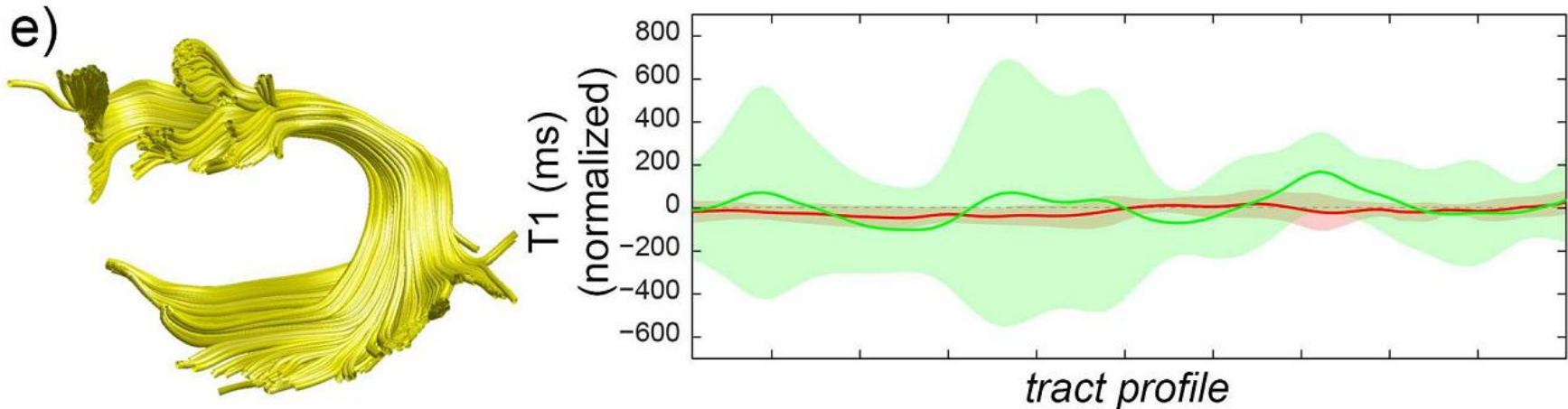
1. No crossing fibers
2. No specificity in FA

DTI

Axonal density, diameters, myelination



Human 7T
Diffusion data

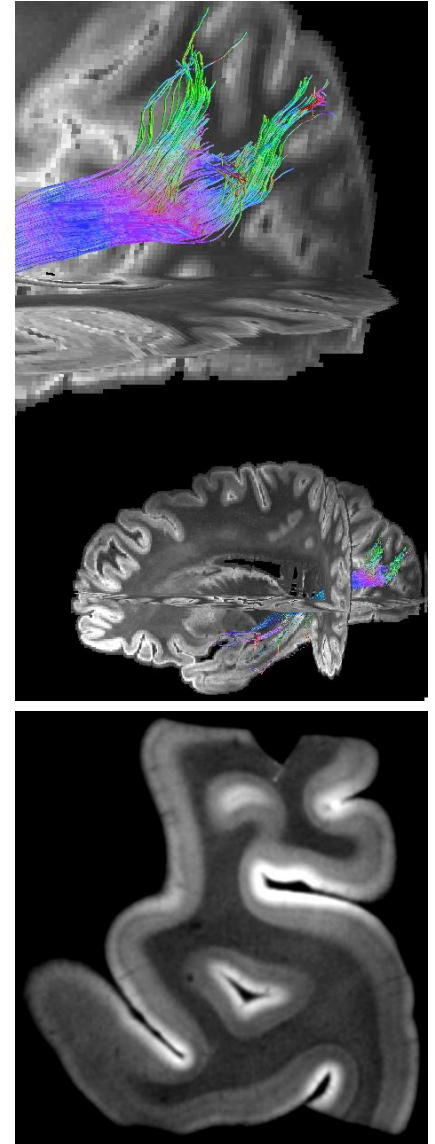


Open source toolbox:
github.com/cbclab/MDT

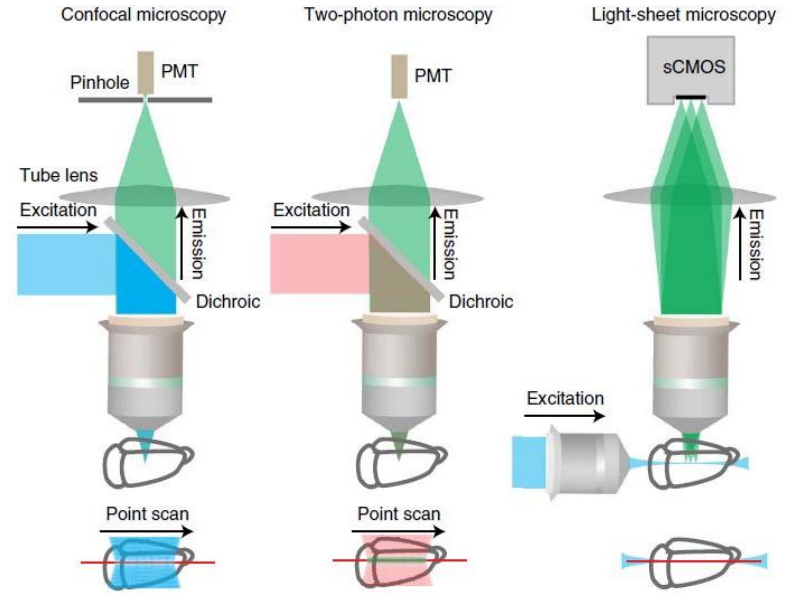
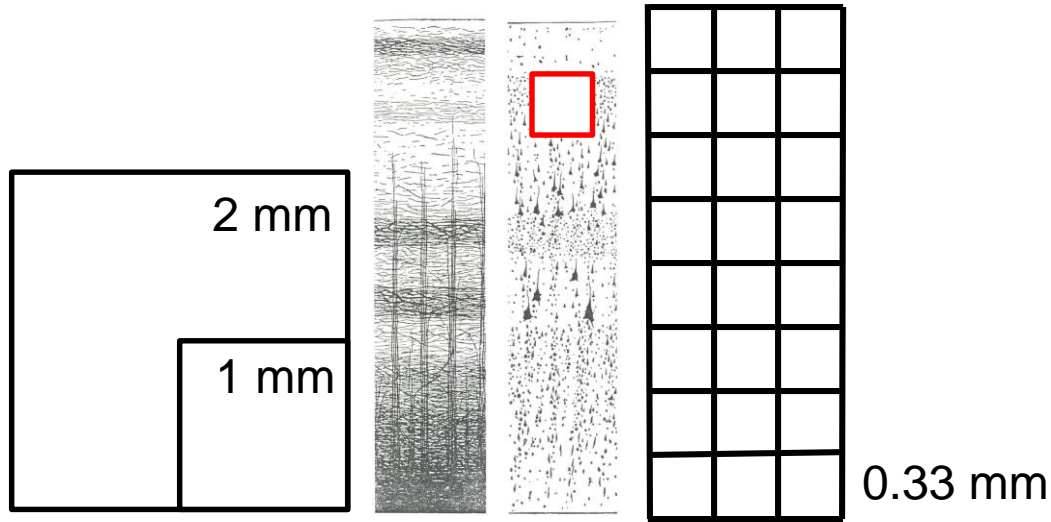
Santis et al., Neuroimage, 2016a, 2016b

Overview

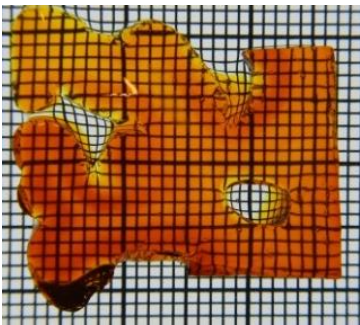
- Human cortical architecture & multiscale connectivity
- Post mortem / ex-vivo
 - Whole brain high resolution MRI
 - Macro- to mesoscale
 - Intracortical diffusion imaging
 - Mesoscale
- In vivo
 - Diffusion microstructure models
 - Microscale
- Outlook & Conclusions



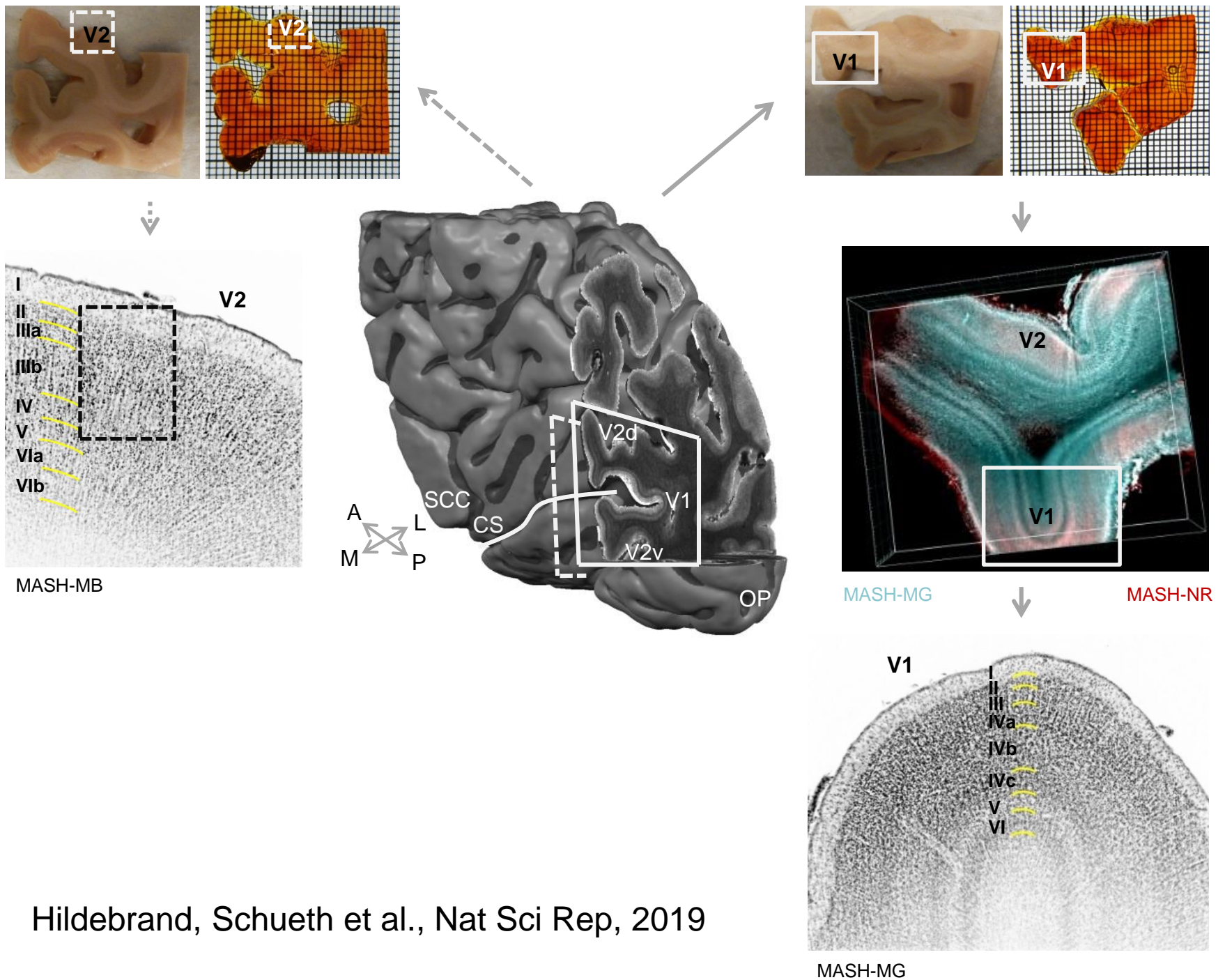
Light Microscopy FoV, Speed

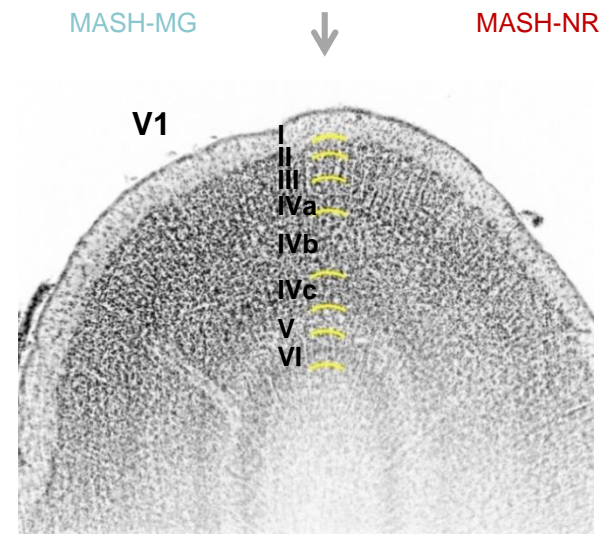
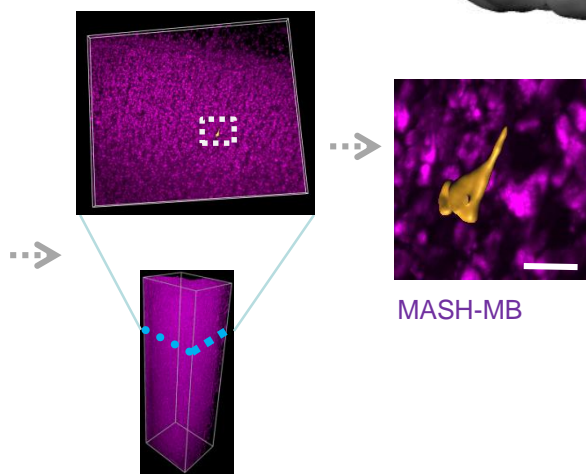
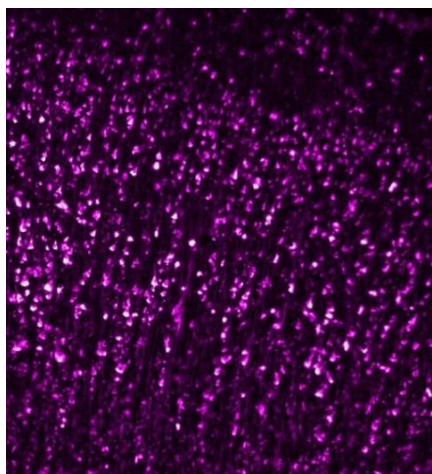
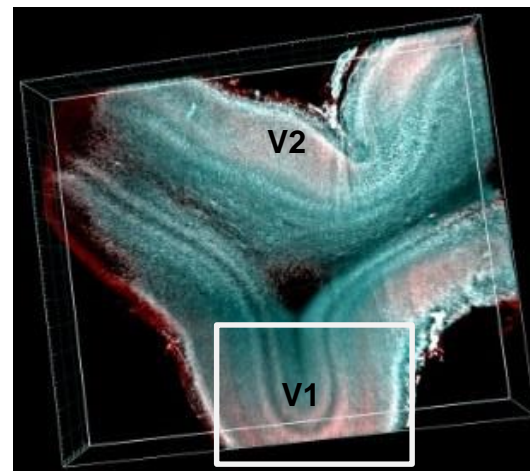
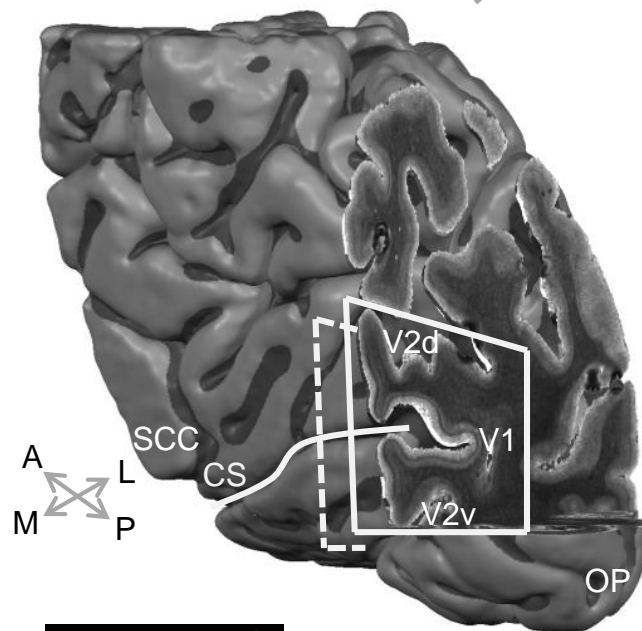
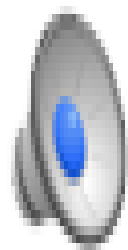
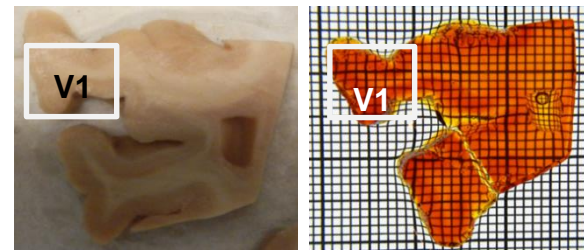
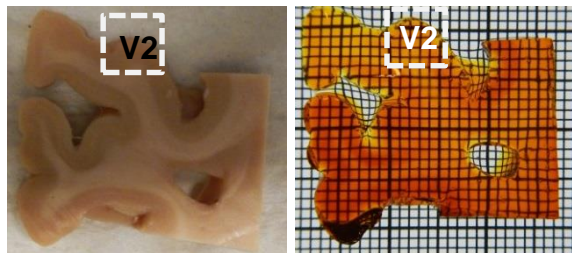


Tomer et al., Nat Prot, 2014



Tissue clearing



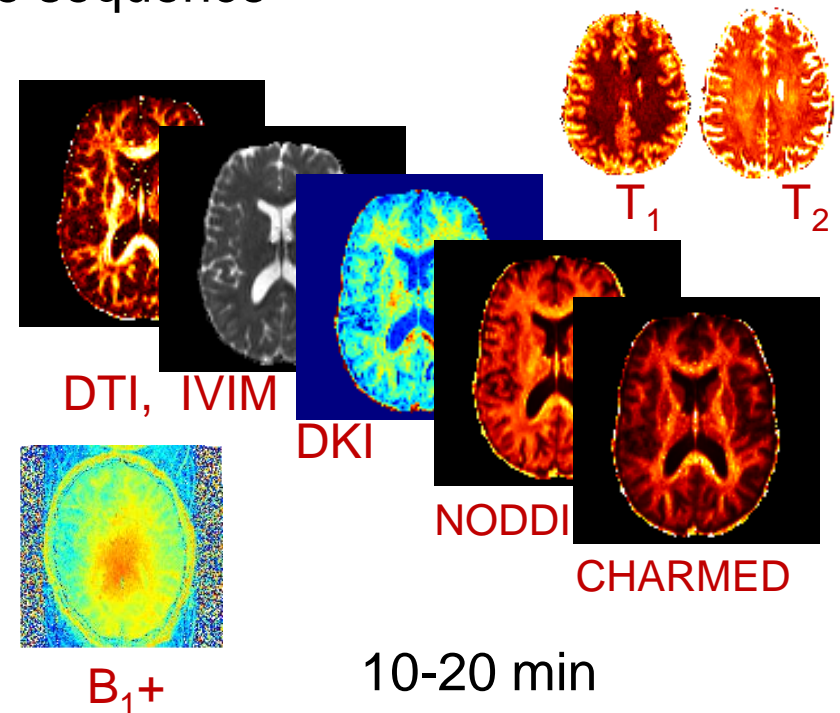


MASH-MB

MASH-MG

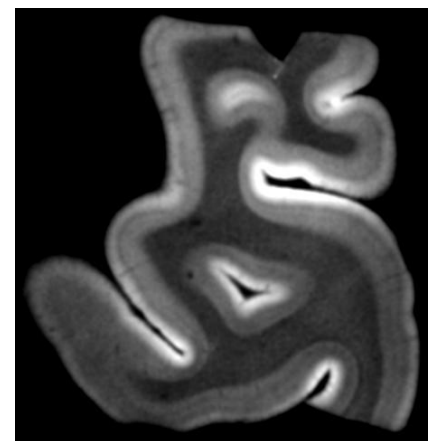
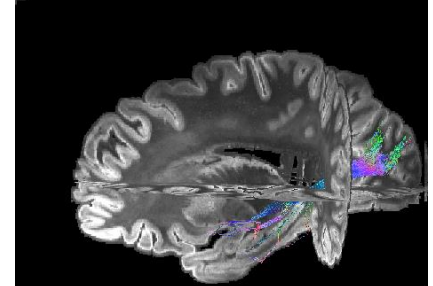
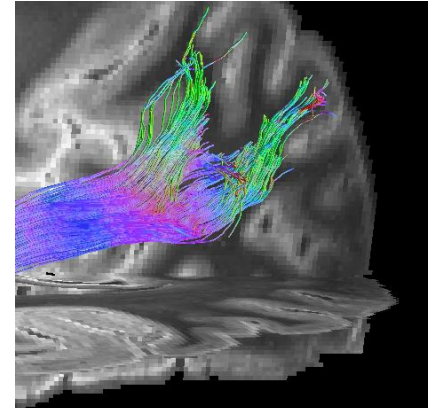
MESMERISED

- **In vivo multi-contrast MR imaging**
 - New levels of acquisition **speed**
 - **Quantitative** mapping
 - **Many contrasts** with the same sequence



Conclusions

- **Post mortem diffusion MRI**
 - Delivers high **resolution**
 - In situ **histological validation**
 - Can take **connectomics** into the **mesoscale** of the cortex
- **In-vivo cortical dMRI**
 - Limited by resolution
 - But is steadily improving
- **Diffusion microstructure modeling**
 - Increases **specificity**
 - Axonal density, diameters of crossing fibers
 - Extended **acquisitions**
 - More sophistication **modeling**



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