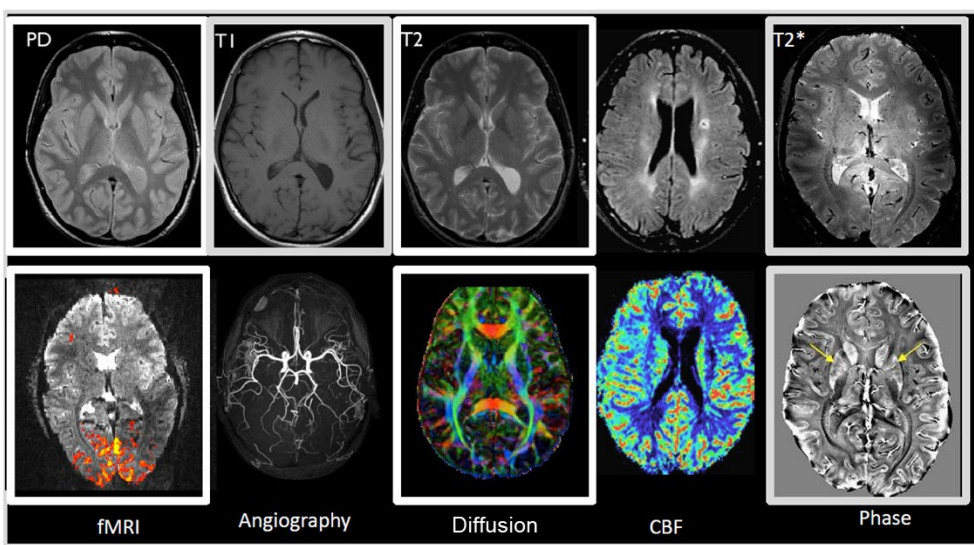
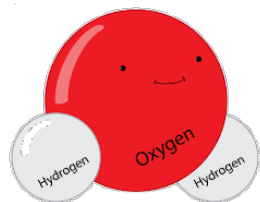


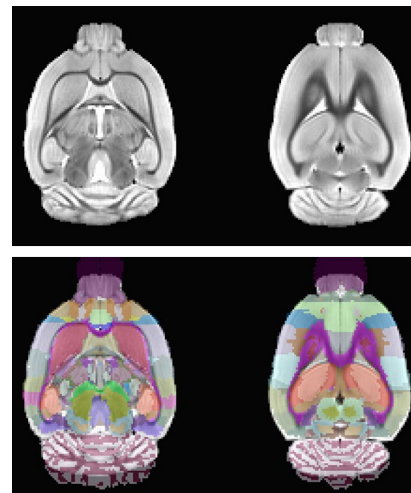
## **FROM *MRI* TO *dMRI***

*principles of diffusion*

# MRI

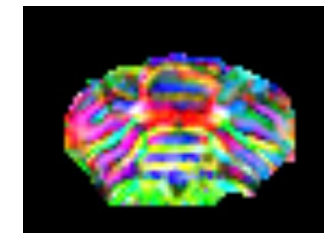
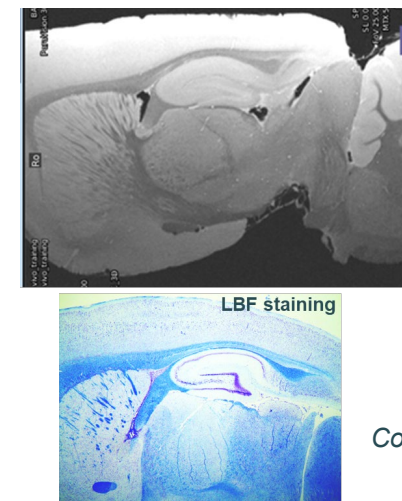


High resolution MRI: volumetry



Courtesy of Tan Toi Phan

High resolution MRI & histology



Diffusion MRI: microstructure

Courtesy of J Mosso

Courtesy of B Lanz & K Pierzchala

Courtesy of I Jelescu

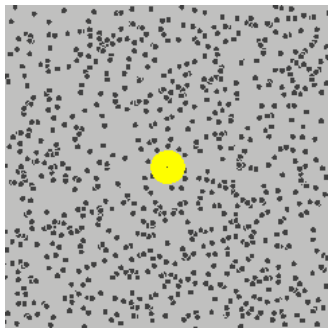
## Imaging the water - Image contrast can be manipulated to be sensitized to a variety of features:

- chemical & magnetic properties of immediate environment
- mobility of molecules
- sensitize the signal to the Brownian motion (random walk) of water molecules - **Diffusion MRI (dMRI)**
  - powerful probe of tissue **microstructure - in vivo and non-invasively**

# WHAT IS DIFFUSION



Diffusion



[https://en.wikipedia.org/wiki/Brownian\\_motion](https://en.wikipedia.org/wiki/Brownian_motion)

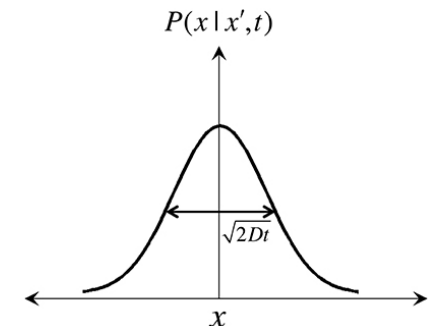
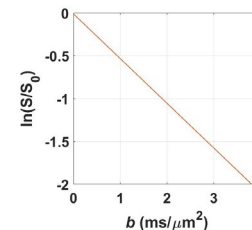
## ■ Free homogeneous medium

- random, microscopic movement of water and other small molecules due to thermal agitation
- Robert Brown – spontaneous vibration of pollen particles
- Adolf Fick - modelled diffusion as the movement of particles from a region of higher concentration to a region of lower concentration
- Albert Einstein - model the process as a statistical "random walk" with a Gaussian (normal) distribution
- Free medium diffusion is isotropic

$$\ln\left(\frac{S}{S_0}\right) \approx -b \cdot D$$

b-value

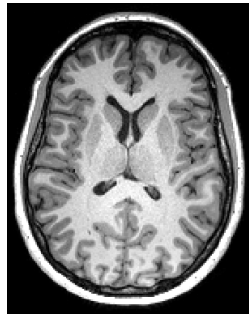
Diffusion coefficient



$$\langle x^2 \rangle = 2nDt$$

# WHAT IS DIFFUSION

MRI voxel size:  
1 – 2 mm



Typical length scale for microstructure:  
1 – 10  $\mu\text{m}$

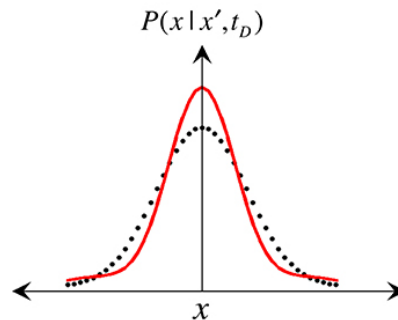


## ■ Biological tissues

### - Access microstructure

- Diffusion MRI – *sensitivity* to micron-scale features
- Biophysical modelling – *specificity* – what are these features
- Path influenced by cell membranes and other forms of restriction
- Displacement probability – non-Gaussian

MRI voxel size:  
0.18 – 0.3 mm

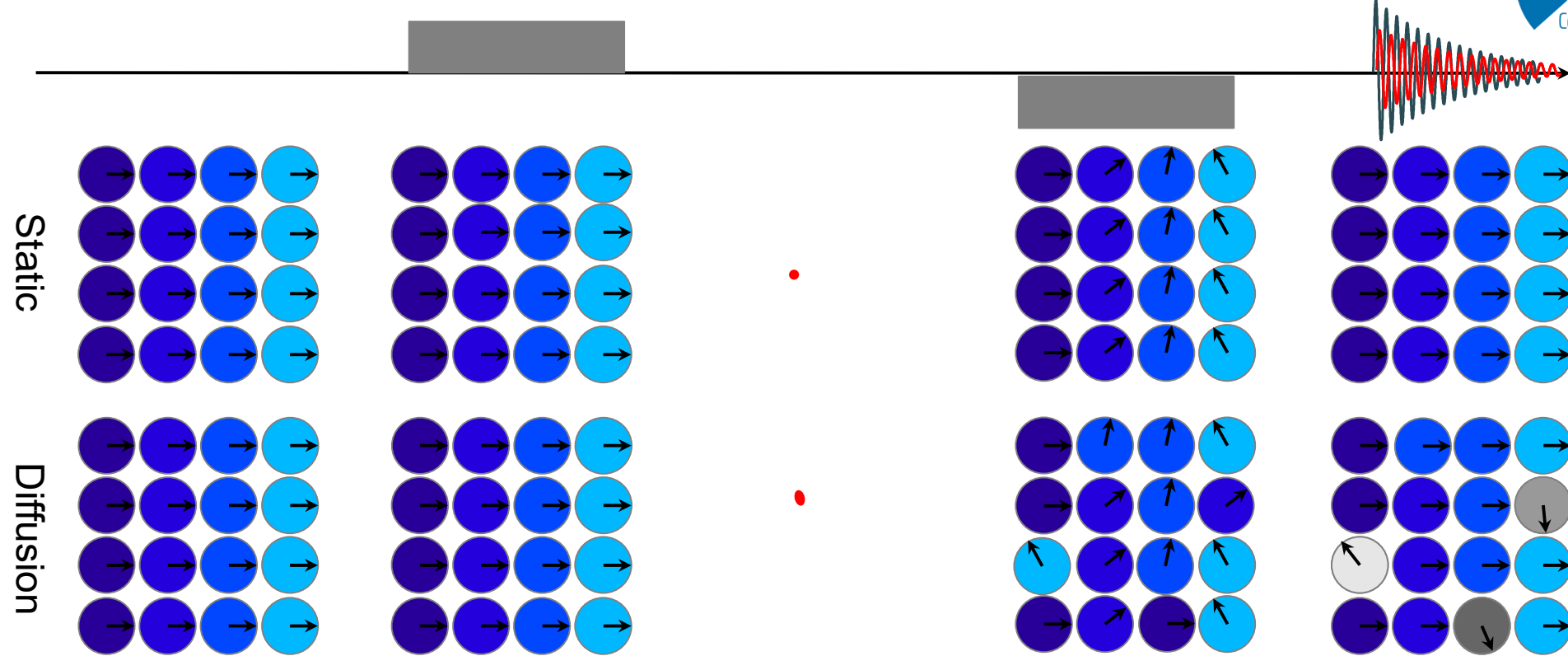


Mean displacement of water molecules :

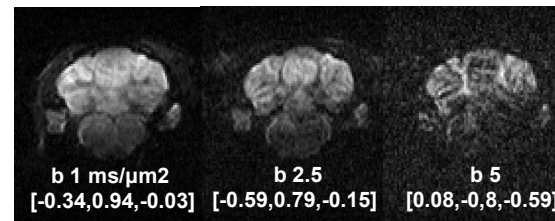
•  $t = 2 - 500 \text{ ms} \longrightarrow \sqrt{\langle x^2 \rangle} \approx 2 - 50 \mu\text{m}$

➤ Excellent probe of tissue microstructure

# HOW DO WE MAKE THE INVISIBLE VISIBLE ?

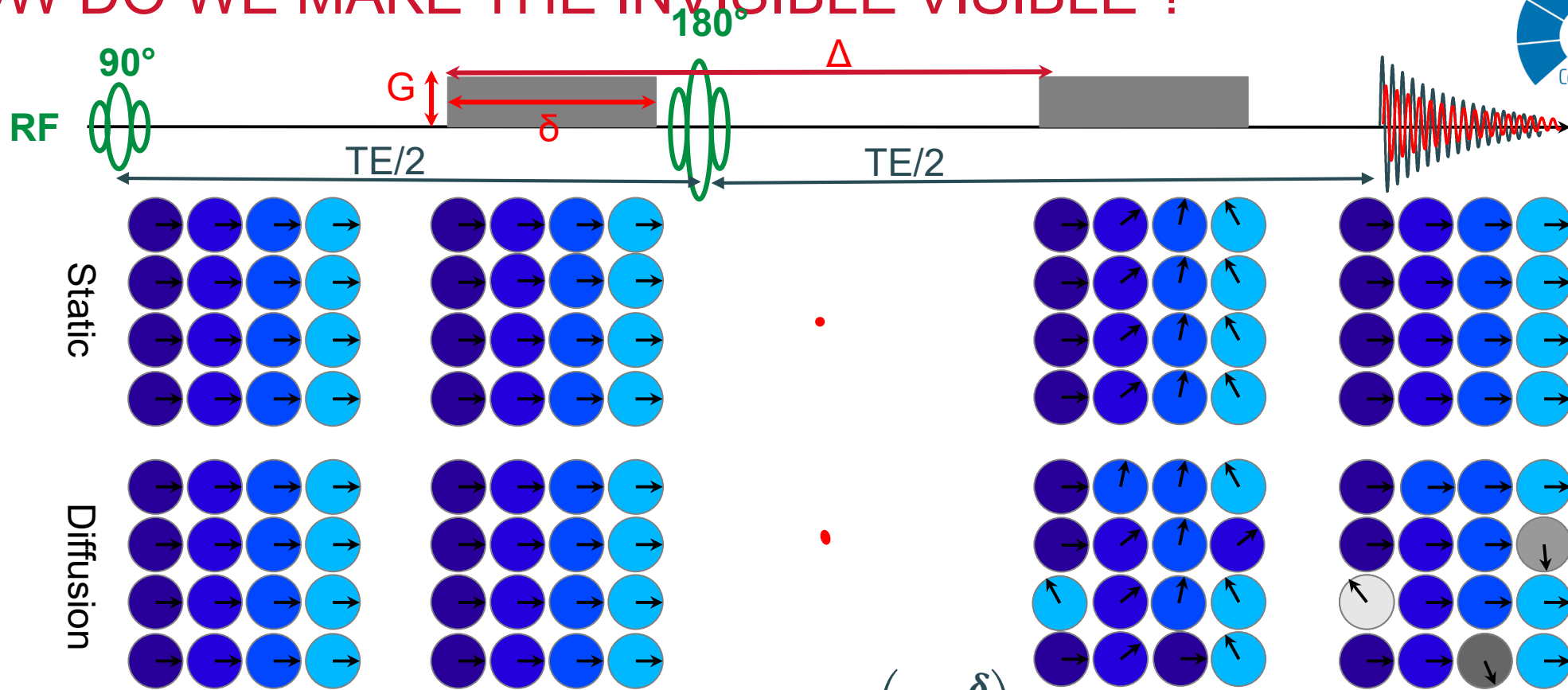


Signal attenuation due to diffusion  
 - Increases with *diffusion-weighting*  
 - Increases with **Diffusivity**



Courtesy of N Kunz & J Mosso

# HOW DO WE MAKE THE INVISIBLE VISIBLE ?



$$b = (\gamma \delta G)^2 \cdot \left( \Delta - \frac{\delta}{3} \right) = q^2 t$$

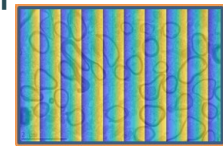
Low q



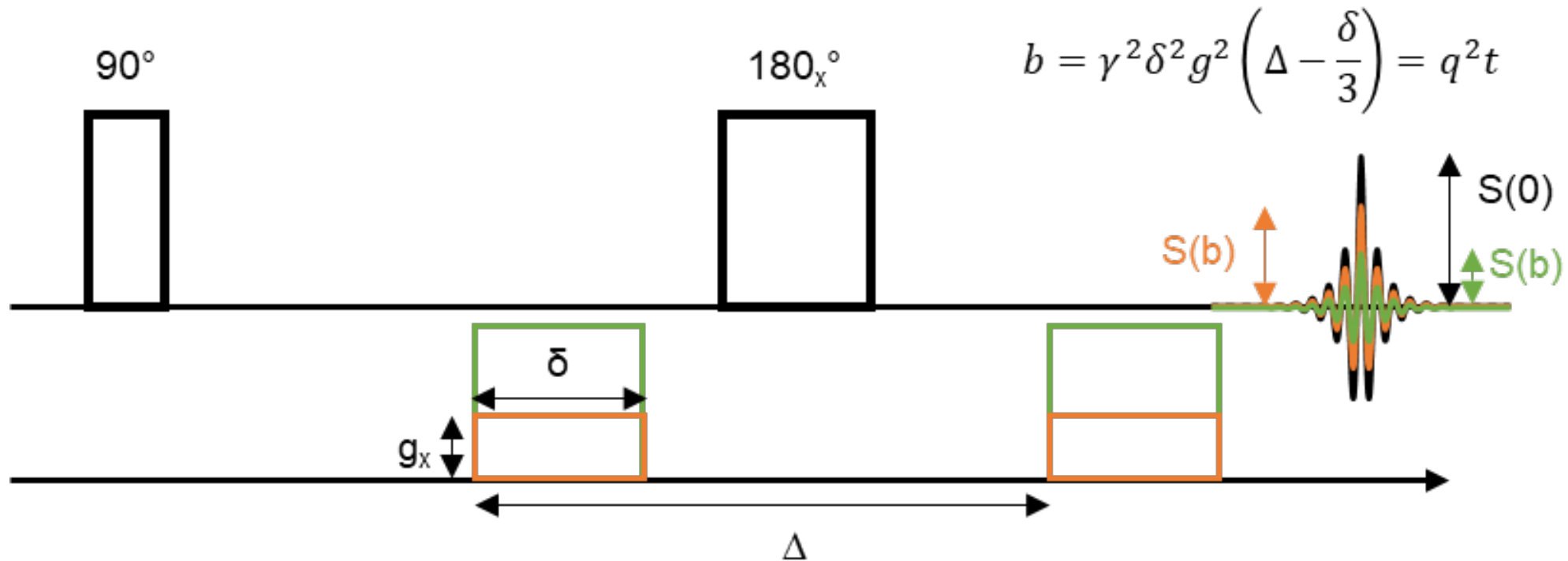
Phase warp

Diffusion time

High q

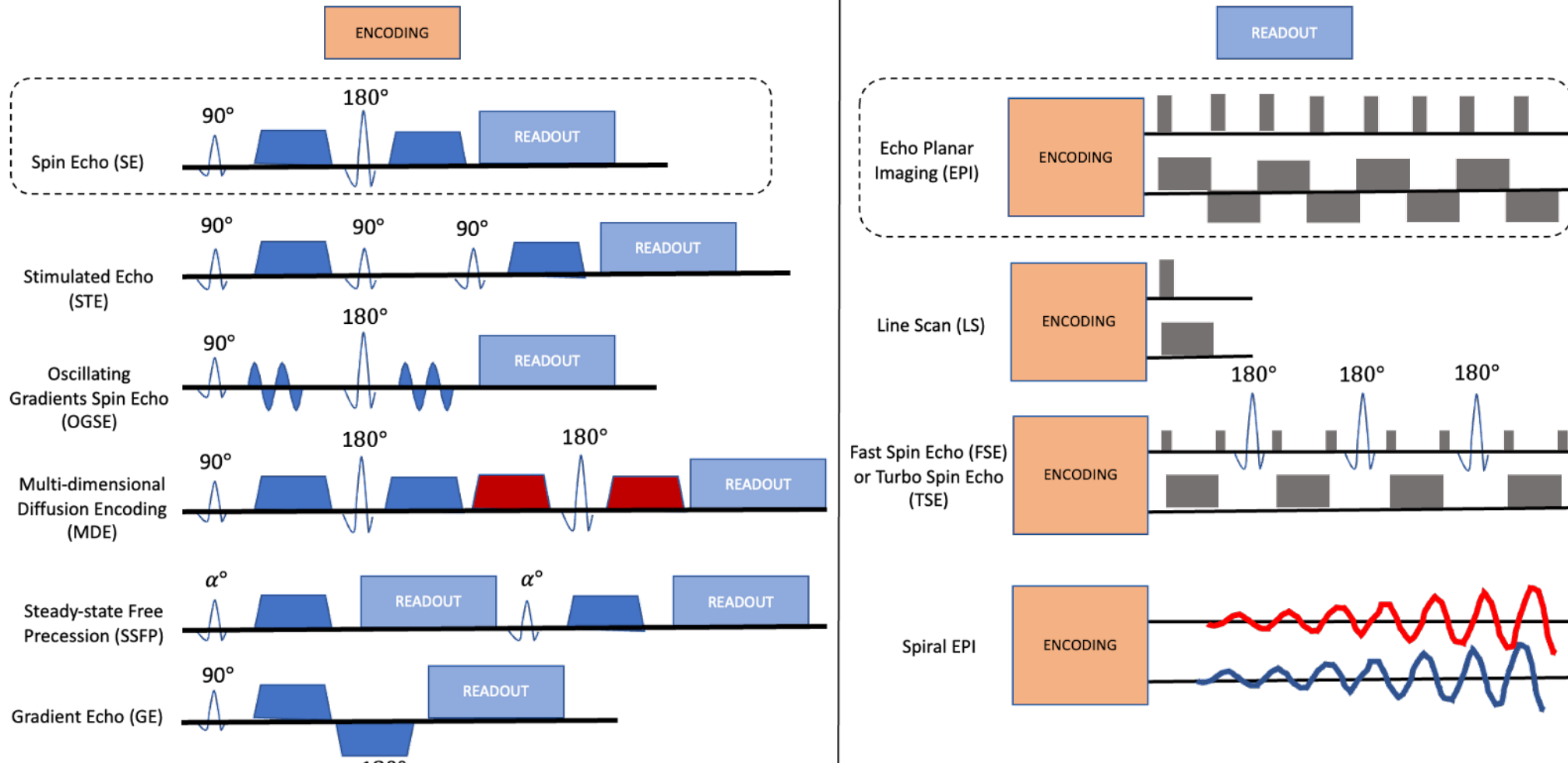


# HOW DO WE MAKE THE INVISIBLE VISIBLE ?

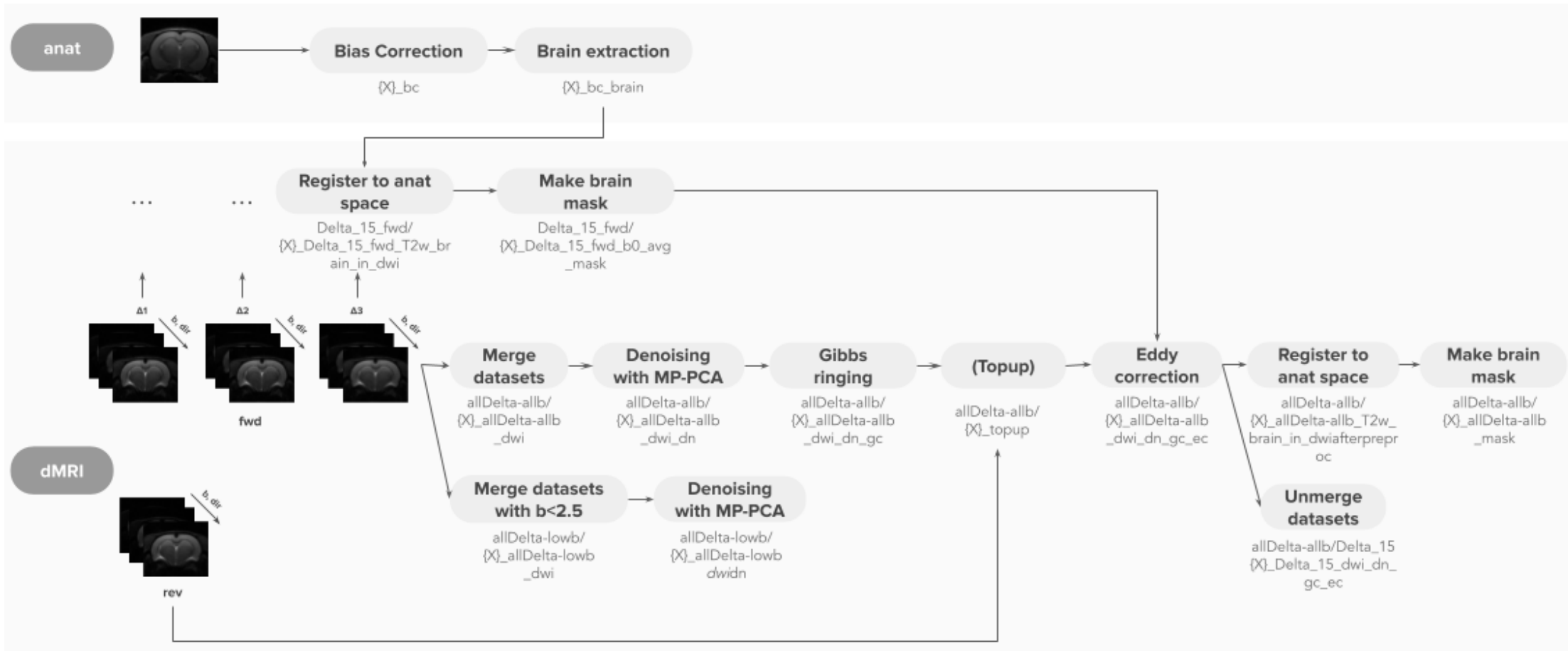


Courtesy of J Mosso

# DIFFUSION ENCODING AND IMAGE READ-OUT SCHEMES

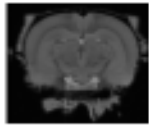


# DMRI EXAMPLE – RAT BRAIN

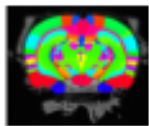


[GitHub - rita-o/dMRSI](https://github.com/rita-o/dMRSI)

ROI atlas



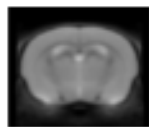
template



atlas



TPM

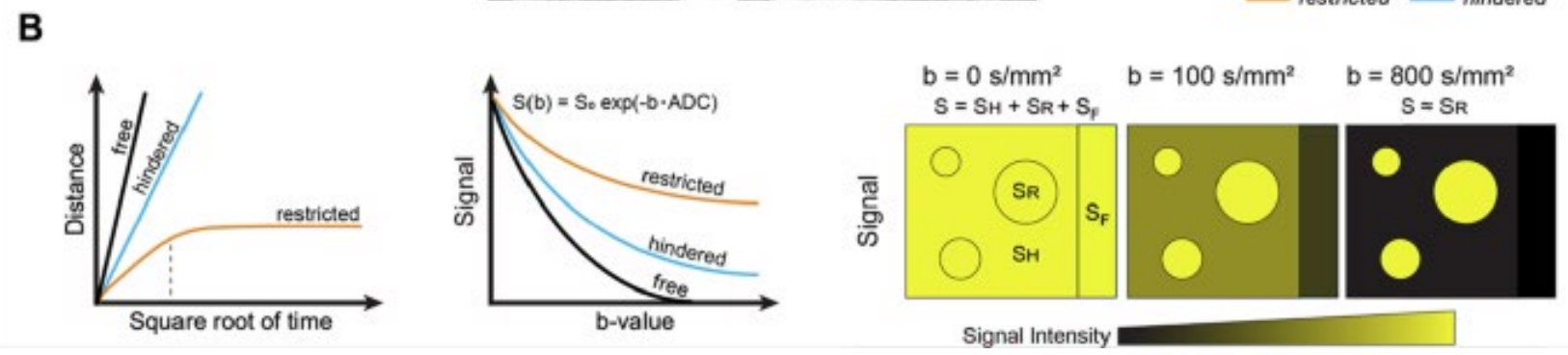
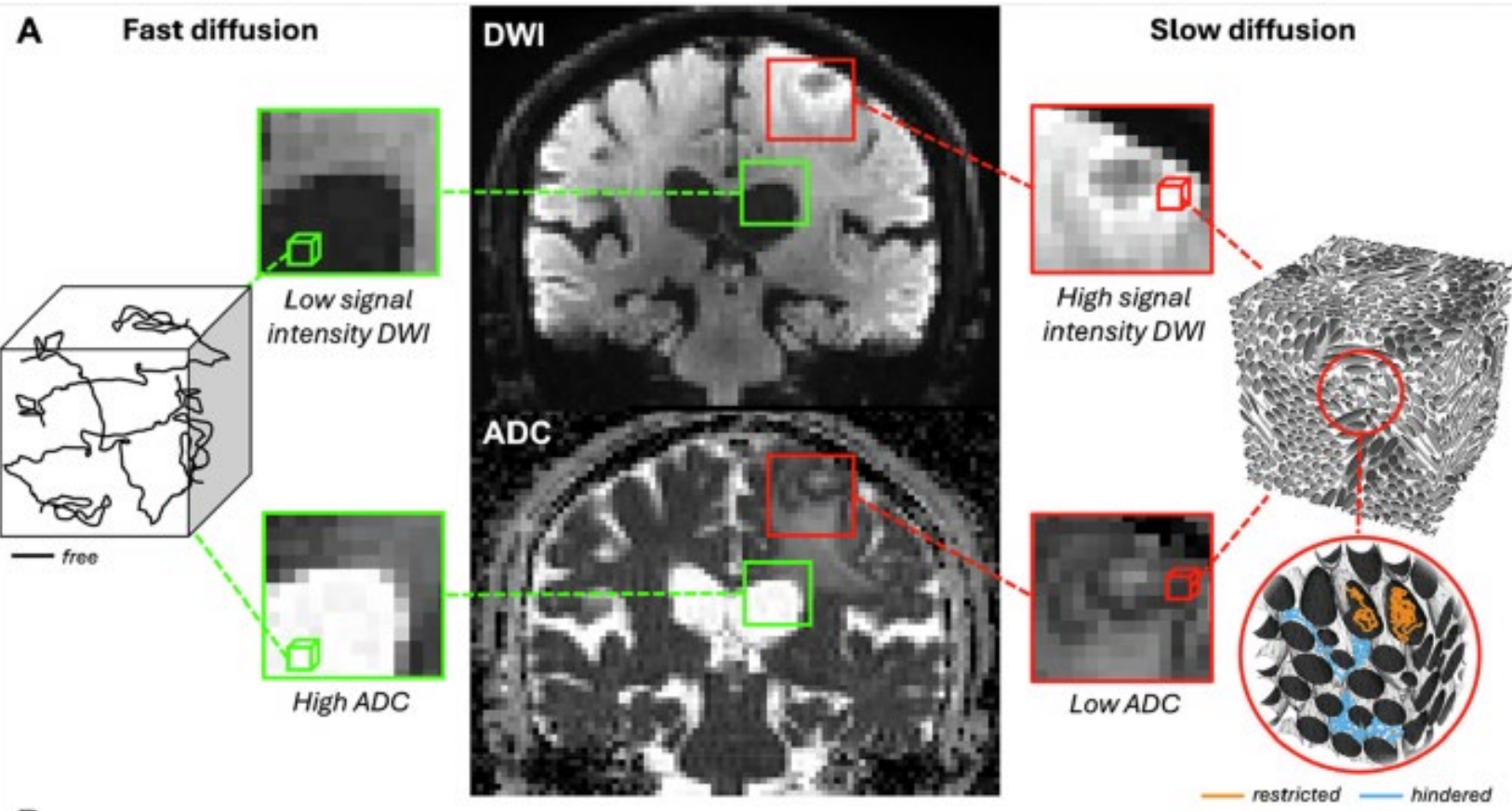


template



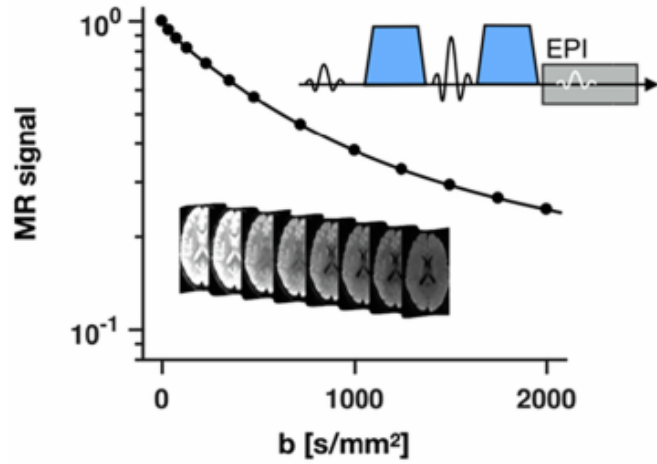
atlas



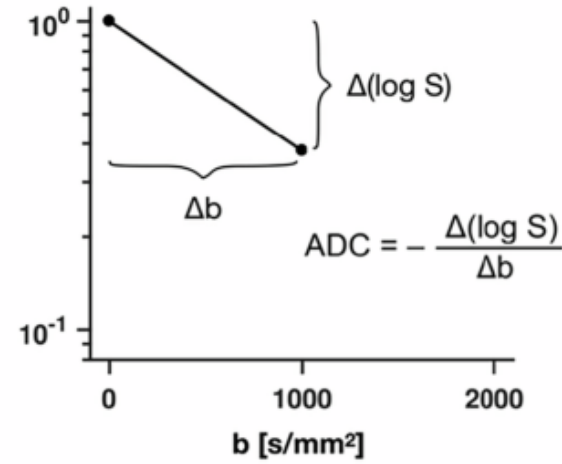


<https://link.springer.com/article/10.1007/s00330-025-12033-x>

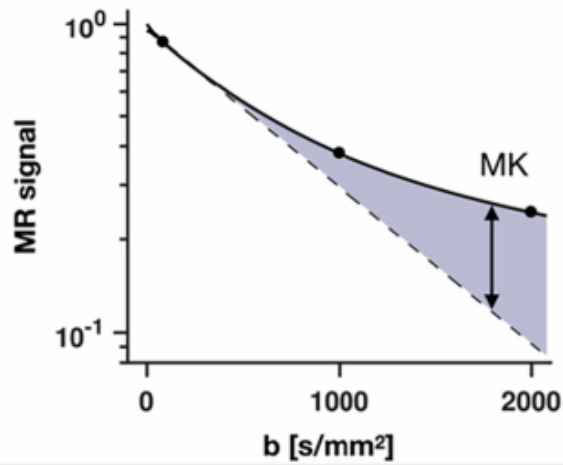
### A Diffusion MRI – signal-versus-b



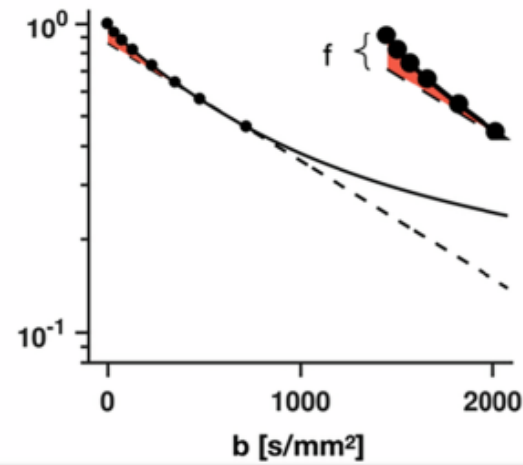
### B ADC quantification



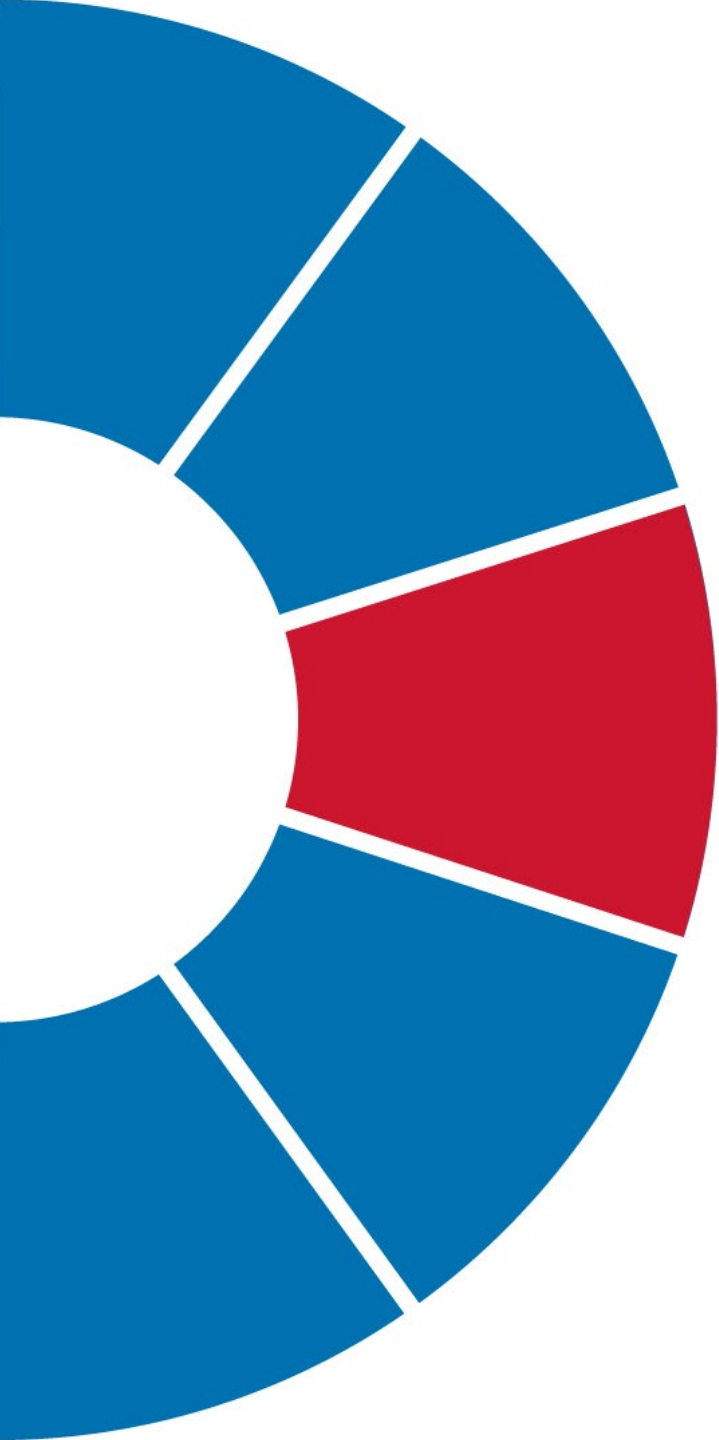
### C Diffusional Kurtosis Imaging



### D IVIM and the perfusion fraction



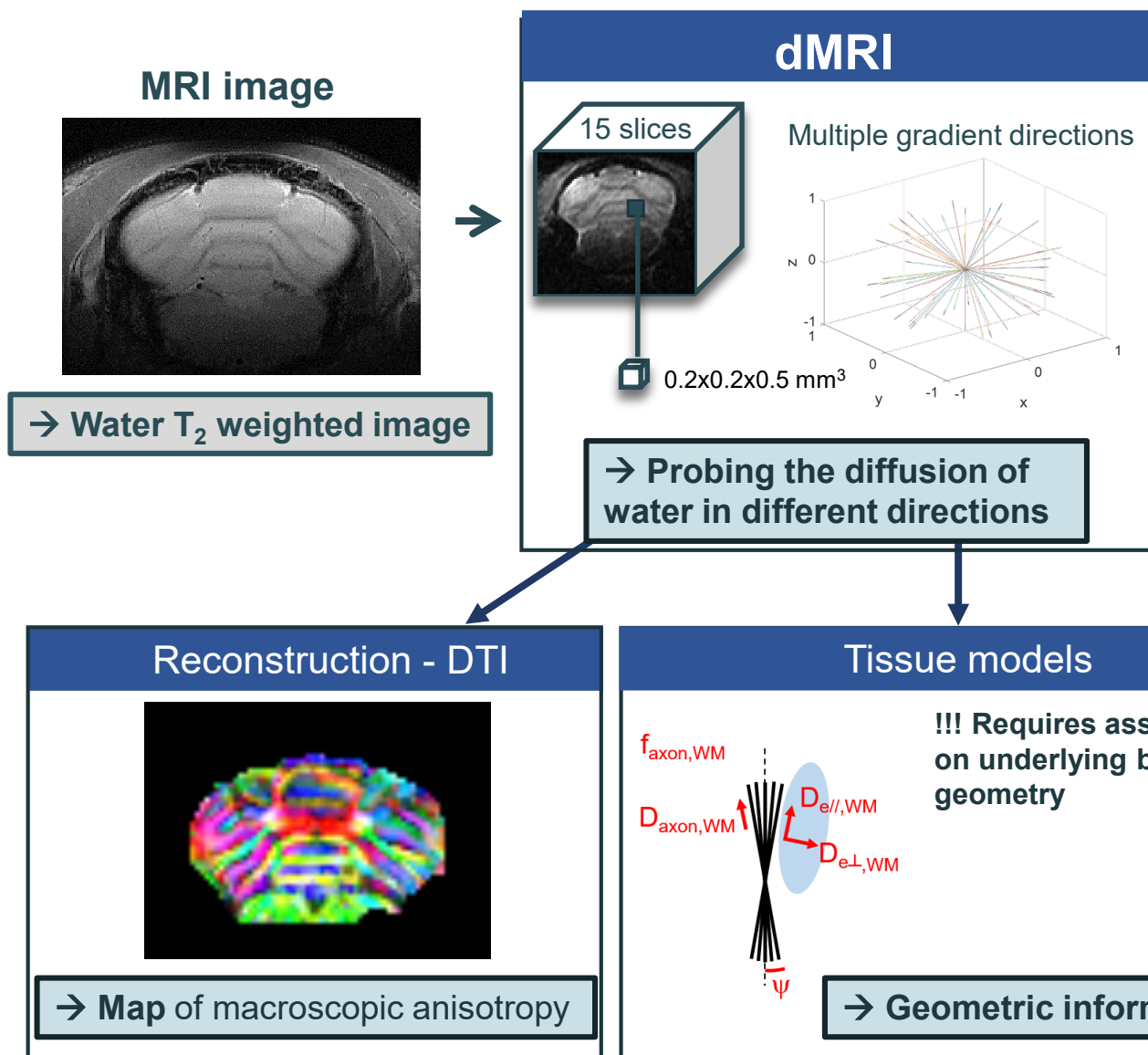
<https://link.springer.com/article/10.1007/s00330-025-12033-x>



## **FROM *dMRI* TO *dMRS***

*Why we want to do it?*

# Diffusion Weighted MRI (dMRI)



?  
**1** Water is not compartment specific

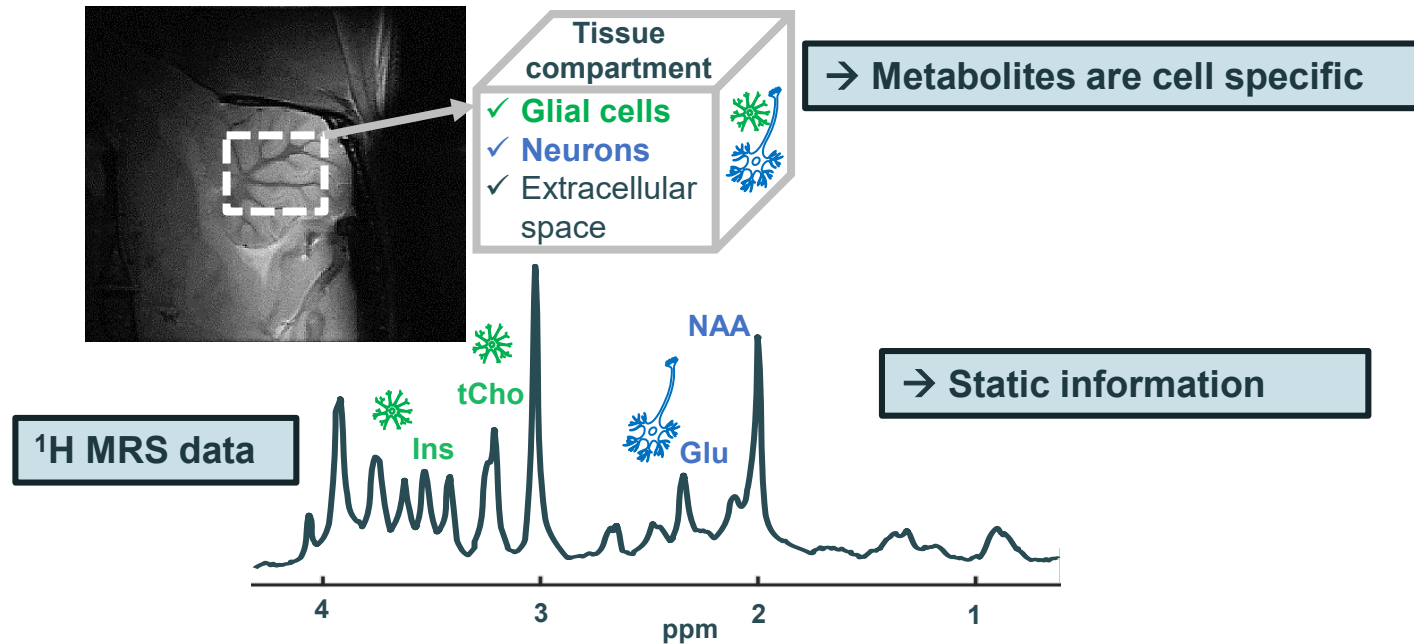
Water is everywhere!!!

?  
**2** Lack of biological proof for the assumptions underlying the tissue model

→ Example in AD (water – dMRI):

- ADC ↓ - neuronal atrophy
- ADC ↑ - reactive astrocytes
- ~ ADC ?

# Magnetic resonance spectroscopy (MRS)



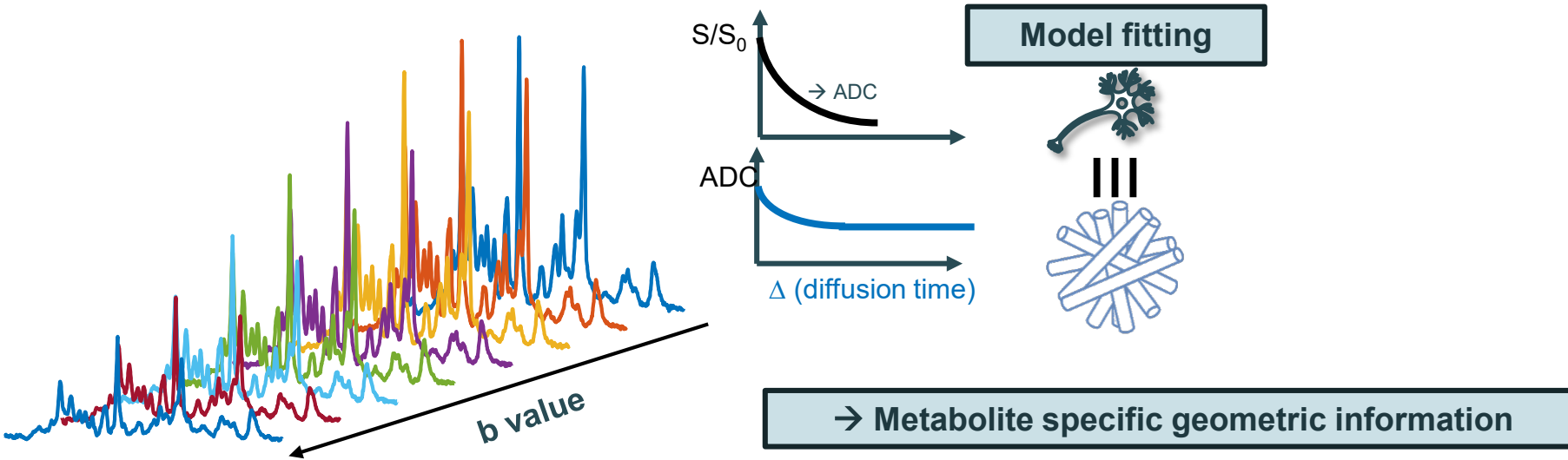
[Ins] ~ 3x higher in astrocytes compared to neurons<sup>1</sup>

[tCho] ~ 6x higher in glia compared to neurons<sup>2,3</sup>

[NAA] & [Glu], large consensus mostly in neurons

(1) Fisher S et al., *J Neurochem* 2002; (2) Urenjak J et al., *J Neurosci.* 1993; (3) Le Belle JE et al. *NMR Biomed.* 2002

# Diffusion Weighted MRS (dMRS)



**! Metabolite specific = cell specific information**

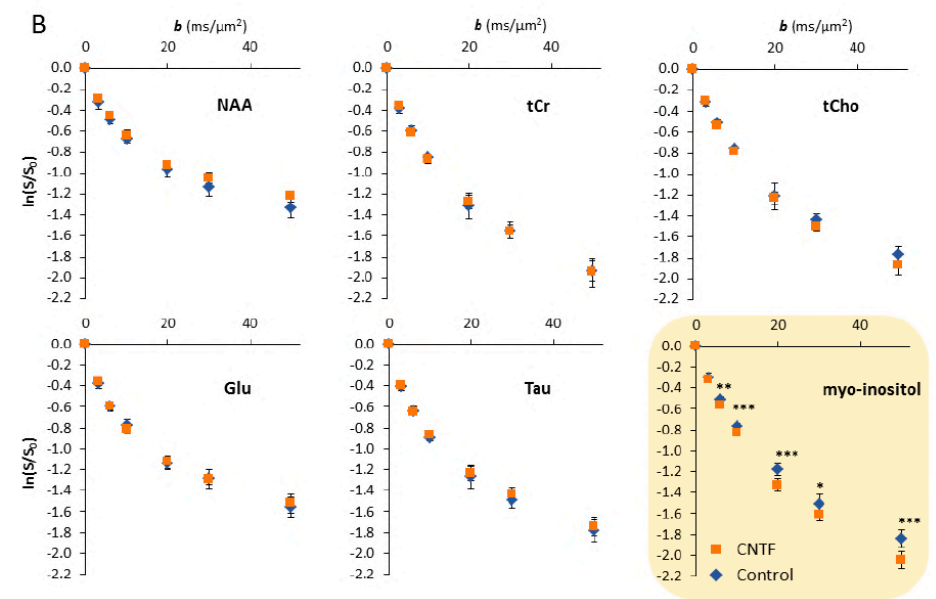
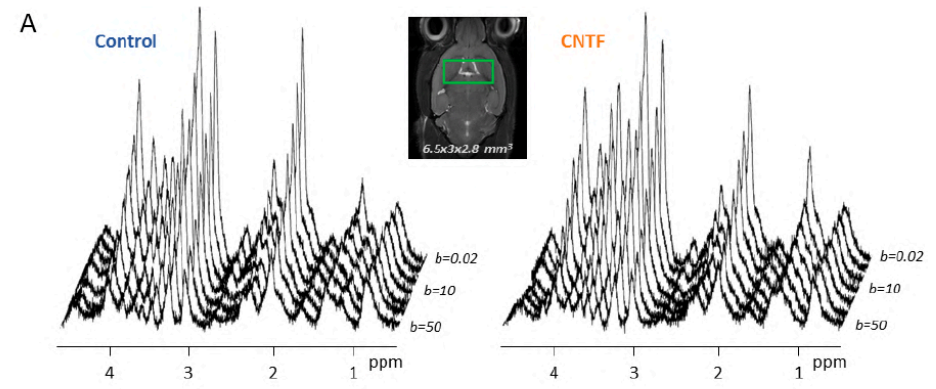
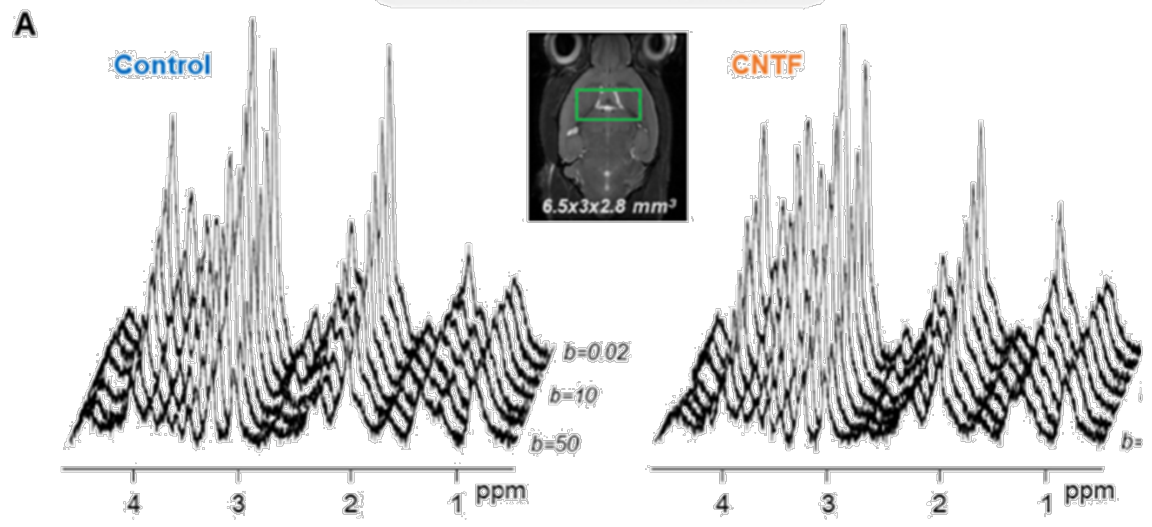
- ✓ Cellular morphology
- ✓ Cytosol viscosity
- ✓ Tortuosity
- ✓ .....

- ☺ High compartmental and cell specific information
- ☺ Intracellular
- ☹ Low sensitivity, loss spatial resolution – 1 single fairly big voxel

Palombo M. et al. *Neuroimage* (2017)

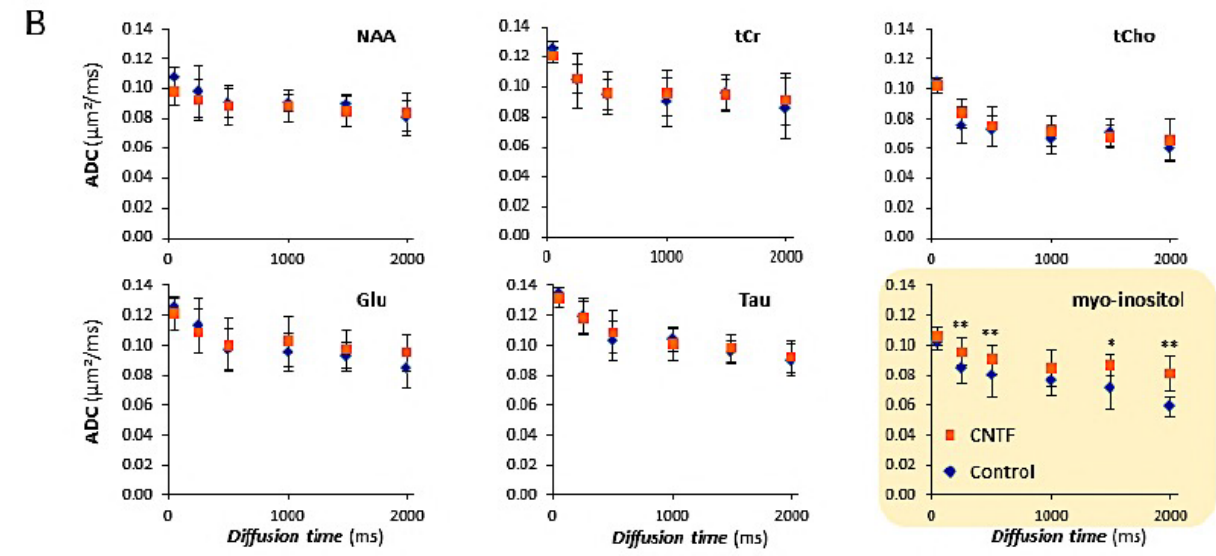
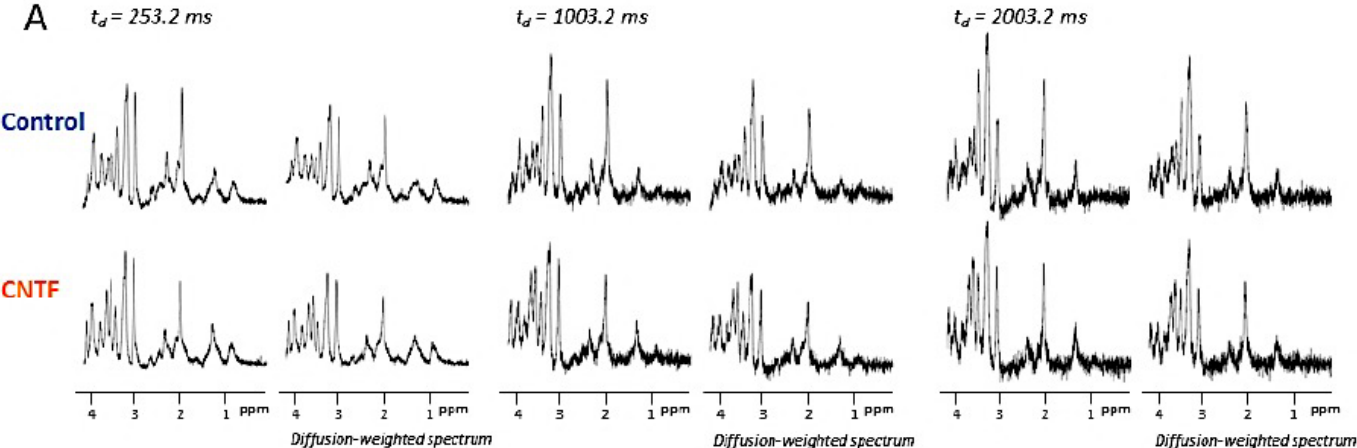


**Experiment 1:  $t_d \lesssim 80$  ms;  $b \gg 1$  ms/ $\mu\text{m}^2$**   
Segments and soma diameter



[Diffusion-weighted magnetic resonance spectroscopy enables cell-specific monitoring of astrocyte reactivity in vivo - PubMed \(nih.gov\)](#)

**Experiment 2:  $t_d \gg 10$  ms;  $b \lesssim 5$  ms/ $\mu\text{m}^2$  → Segments length and branching**



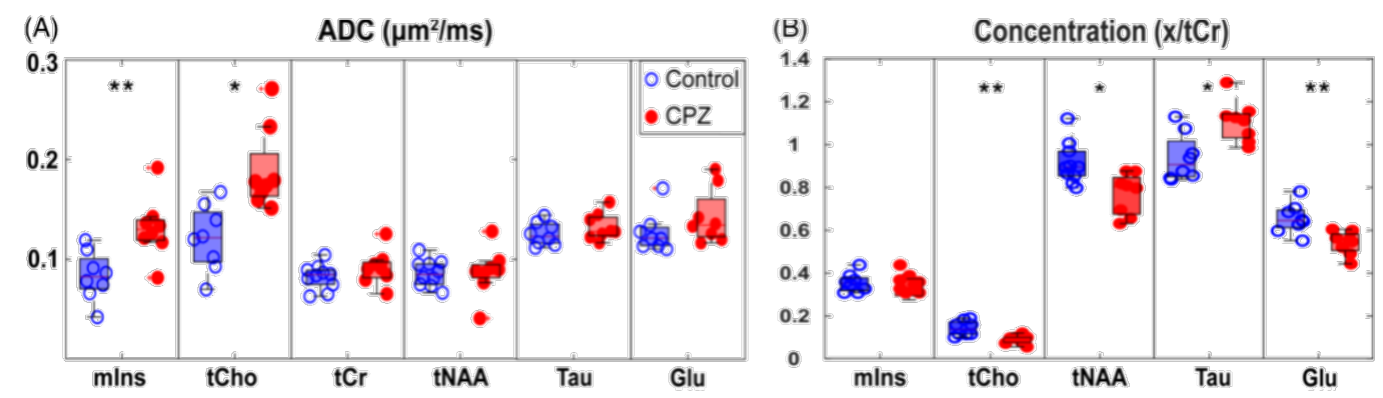
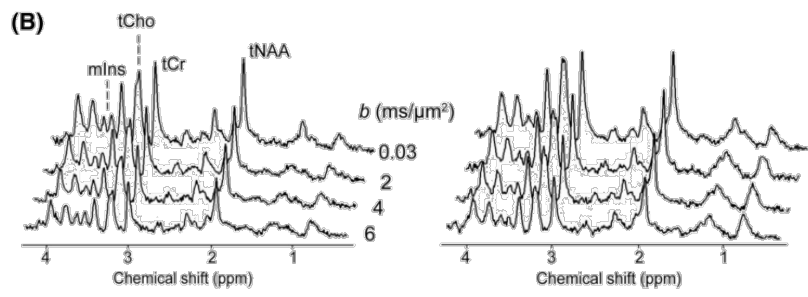
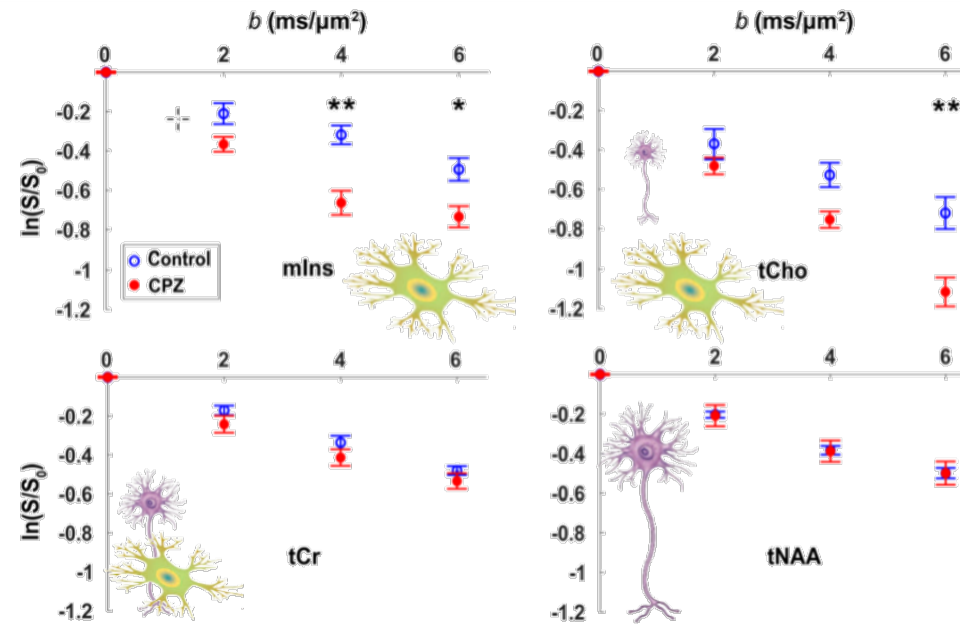
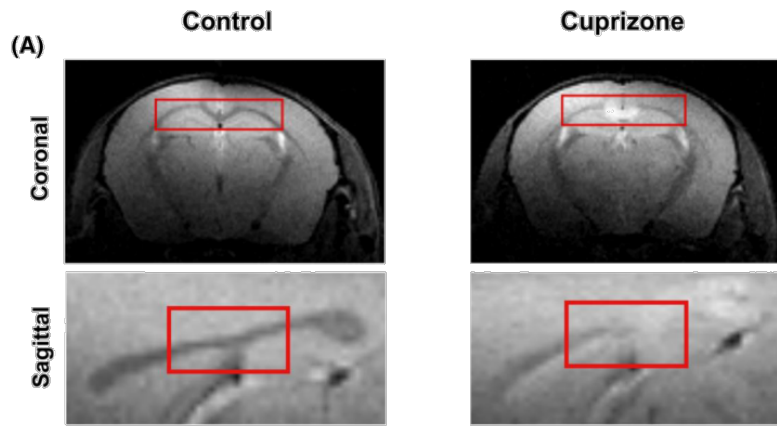
**Experiment 1**

		$R_{\text{soma}}$ ( $\mu\text{m}$ )	Variation (%)	$R_{\text{fiber}}$ ( $\mu\text{m}$ )	Variation (%)	$D_{\text{intra}}$ ( $\mu\text{m}^2/\text{ms}$ )	Variation (%)
Histology	CTR	3.7 ( $\pm 1.2$ )	+29 [**]	0.50 ( $\pm 0.08$ )	+20 [**]	n.a.	n.a.
	CNTF	4.9 ( $\pm 0.9$ )		0.60 ( $\pm 0.13$ )		n.a.	
Synthetic (from Ins)	CTR	3.80 ( $\pm 0.06$ )	+23 [***]	0.58 ( $\pm 0.02$ )	+47 [***]	0.375 ( $\pm 0.006$ )	-1 [n.s.]
	CNTF	4.66 ( $\pm 0.07$ )		0.85 ( $\pm 0.02$ )		0.372 ( $\pm 0.005$ )	

**Experiment 2**

		$L_{\text{segment}}$ ( $\mu\text{m}$ )	Variation (%)	Branch Order	Variation (%)	$D_{\text{intra}}$ ( $\mu\text{m}^2/\text{ms}$ )	Variation (%)
Histology	CTR	15 ( $\pm 5$ )	+67 [***]	6 ( $\pm 4$ )	-33 [n.s.]	n.a.	n.a.
	CNTF	25 ( $\pm 7$ )		4 ( $\pm 2$ )		n.a.	
Synthetic (from Ins)	CTR	29 ( $\pm 10$ )	+103 [***]	6 ( $\pm 5$ )	-17 [n.s.]	0.376 ( $\pm 0.008$ )	-2 [n.s.]
	CNTF	59 ( $\pm 10$ )		5 ( $\pm 5$ )		0.369 ( $\pm 0.005$ )	

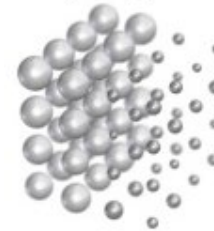
Diffusion-weighted magnetic resonance spectroscopy enables cell-specific monitoring of astrocyte reactivity in vivo - PubMed (nih.gov)



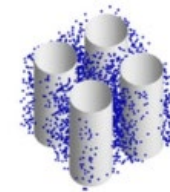
Inflammation-driven glial alterations in the cuprizone mouse model probed with diffusion-weighted magnetic resonance spectroscopy at 11.7 T - PubMed (nih.gov)

- “Diffusion MRI”  $\neq$  “DTI”
- (Free) Diffusivity  $\neq$  ADC
- In anisotropic tissue: MD  $\neq$  ADC
- Units!

- Anisotropy  $\neq$  non-Gaussian diffusion



Isotropic diffusion  
Non-Gaussian (restricted compartments)



Anisotropic diffusion  
yet Gaussian in each direction

“widespread”		“natural choice”	
Diffusion coefficient	b-value	Diffusion coefficient	b-value
mm <sup>2</sup> /s	s/mm <sup>2</sup>	μm <sup>2</sup> /ms	ms/μm <sup>2</sup>
3 · 10 <sup>-3</sup>	1000	3	1
4 · 10 <sup>-4</sup>	10'000	0.4	10