Diffusion weighted imaging challenges the neurohistology: dream or reality?

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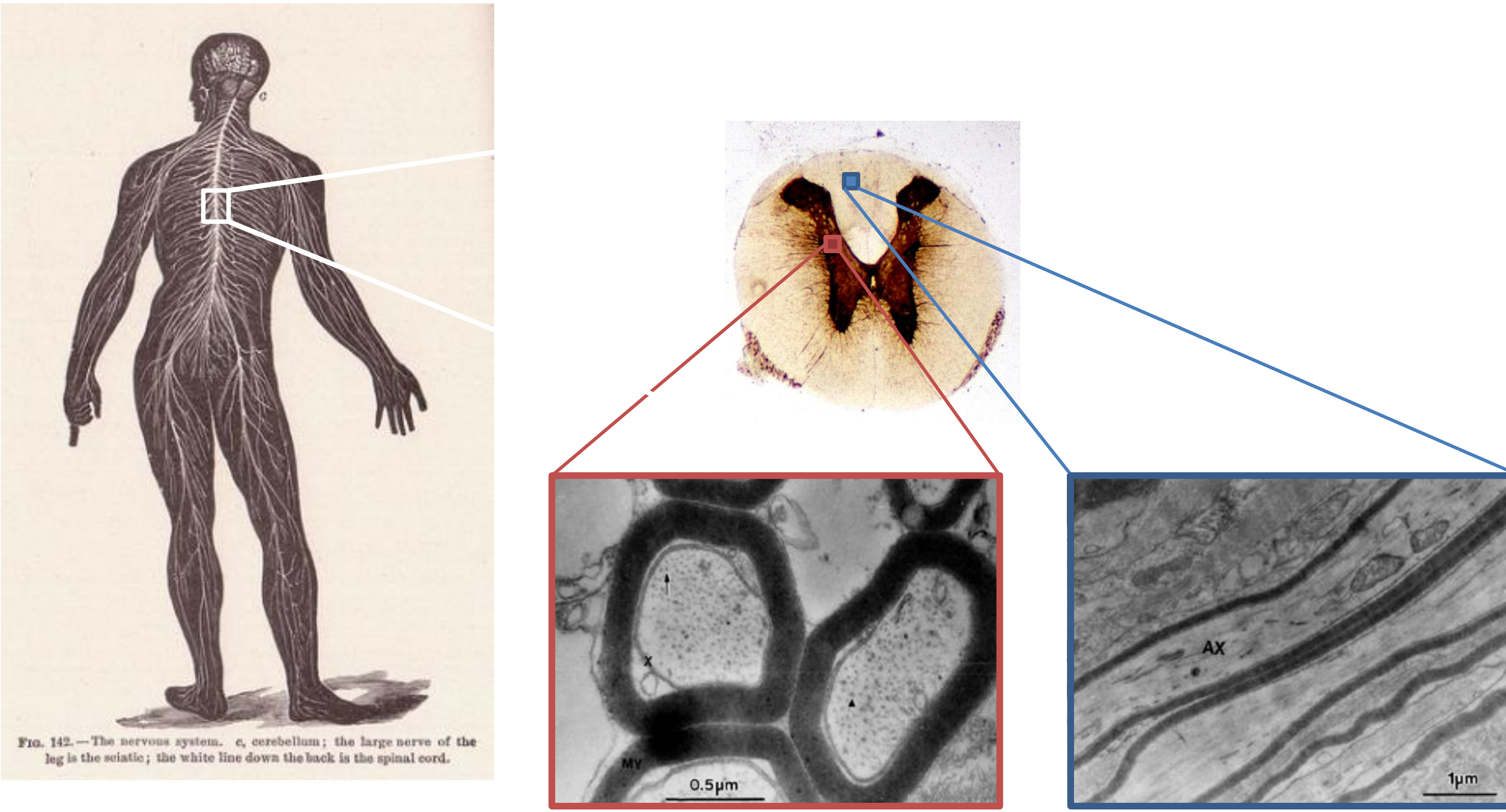
Boston Children's Hospital (Harvard, USA)
Promotors: Benoit Macq, Anne des Rieux, Bernar Gallez

04/02/2015

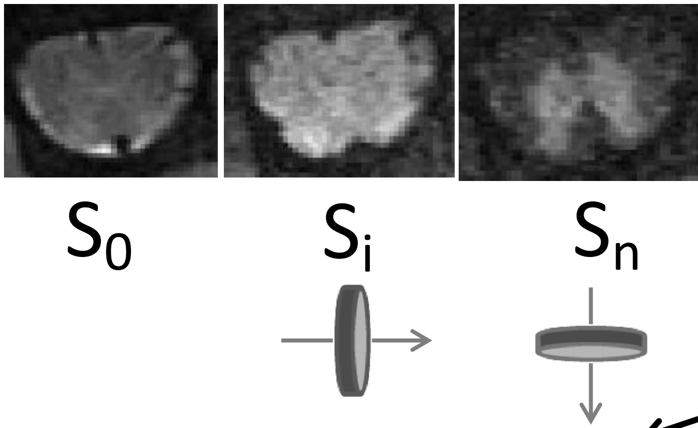
Application to the spinal cord



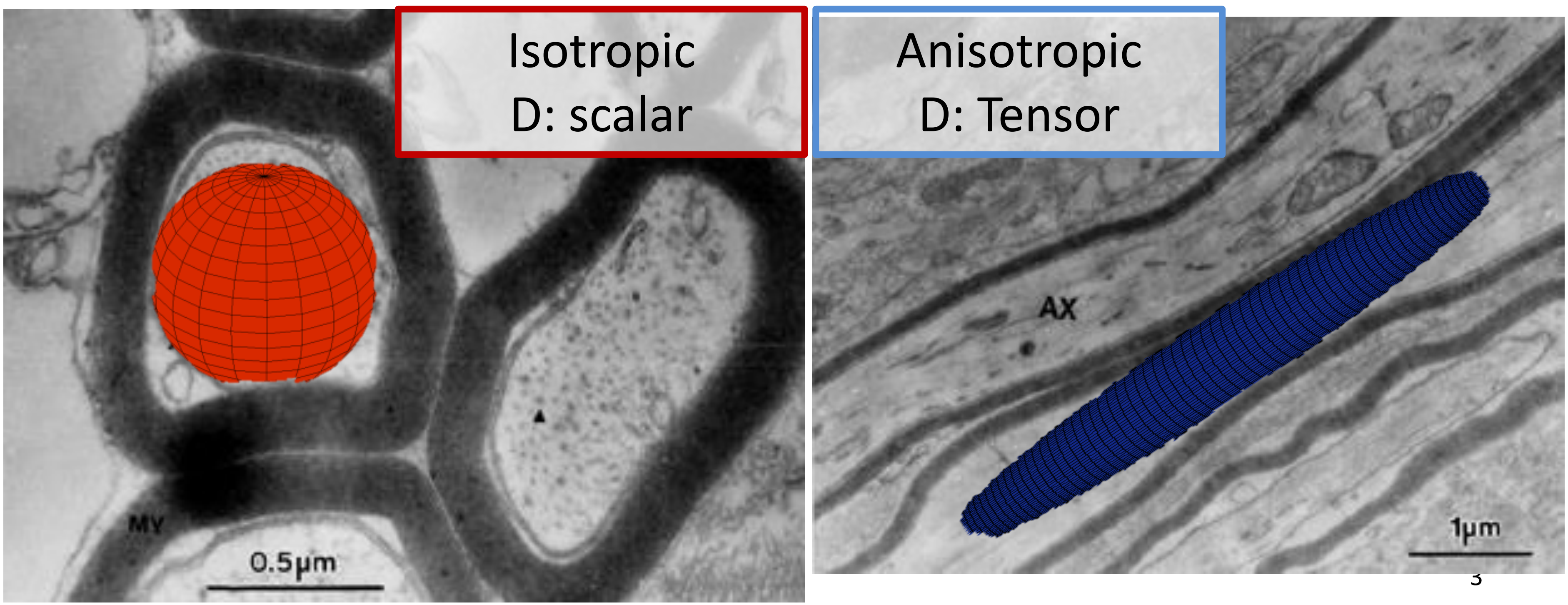
Gray Matter

White Matter

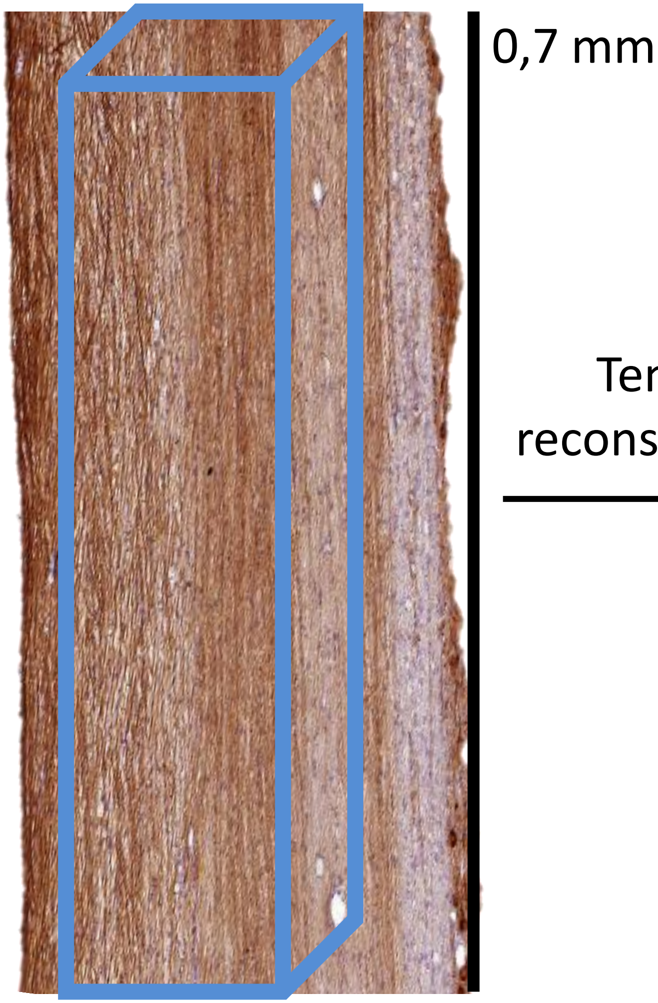
Spinal cord studied by diffusion tensor imaging



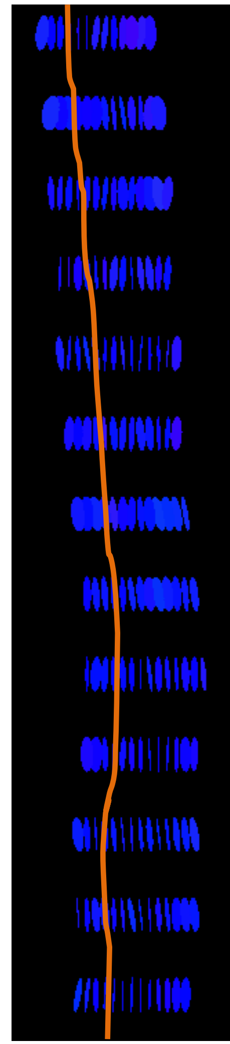
$$S_n = S_0\, e^{-b\,\boldsymbol{g}^T . \boldsymbol{D} . \boldsymbol{g}}$$



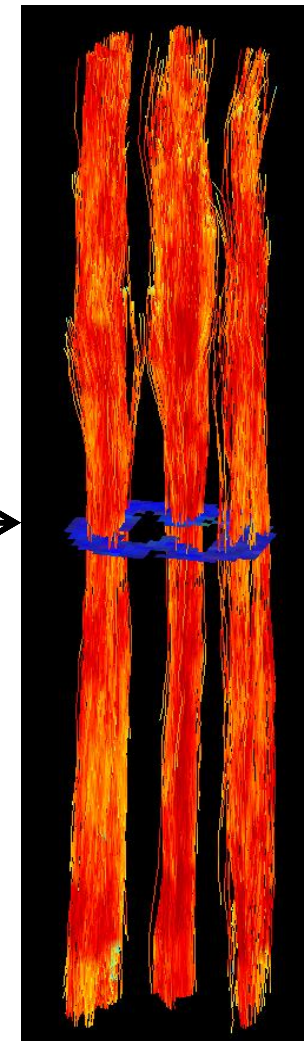
One fascicle at macro-scale resolution
(~mm, in vivo diffusion weighted imaging on human)



Tensor reconstruction



Fibers reconstruction



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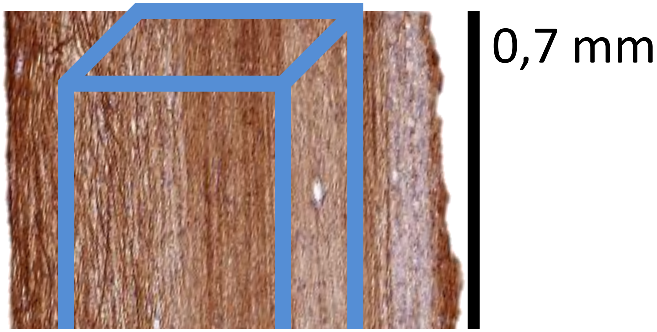
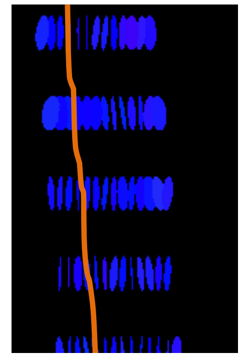
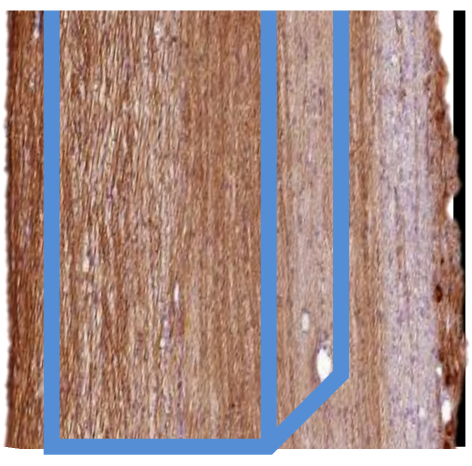
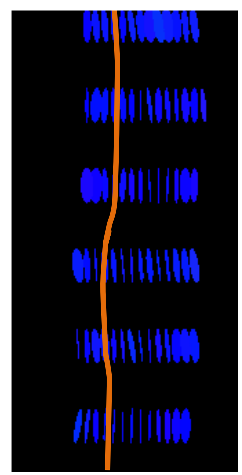


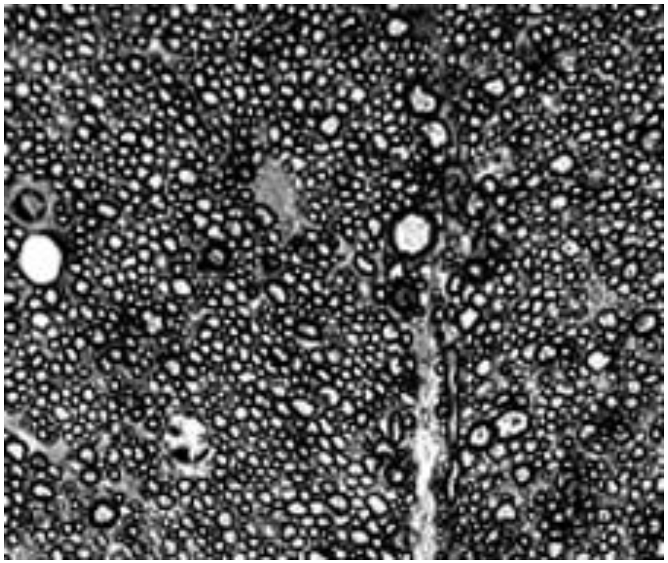


Hypothesis: spinal cord can be represented as an uniaxial fiber population in the head-feet axes

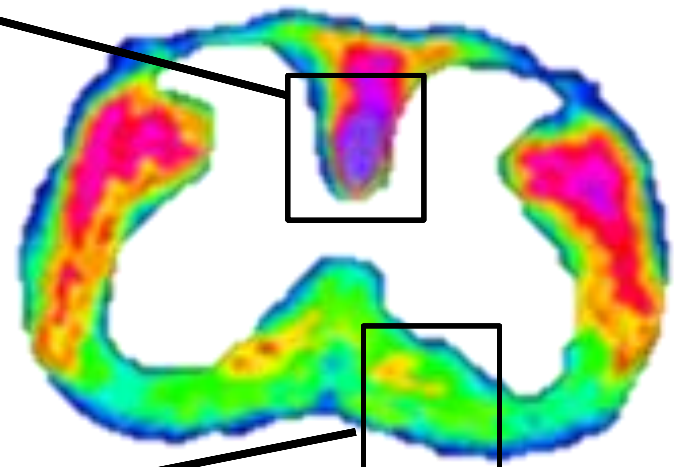




High heterogeneity at micro-scale resolution (~100μm, ex vivo diffusion weighted imaging on animals)

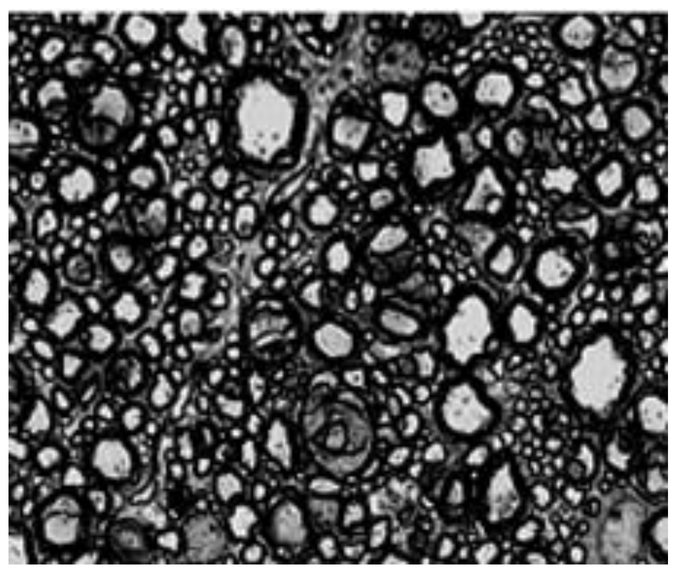


Anisotropic parameter (ZDP) correlates to the diameter of the myelin sheaths



R < 1 μm

R > 5 μm



40 μm

Ong et al, 2008, Neuroimage

Can you identify the different contribution of the heterogeneous signal for one fascicle ?

The partial (!) microstructure of the white matter in a voxel:

800 µm

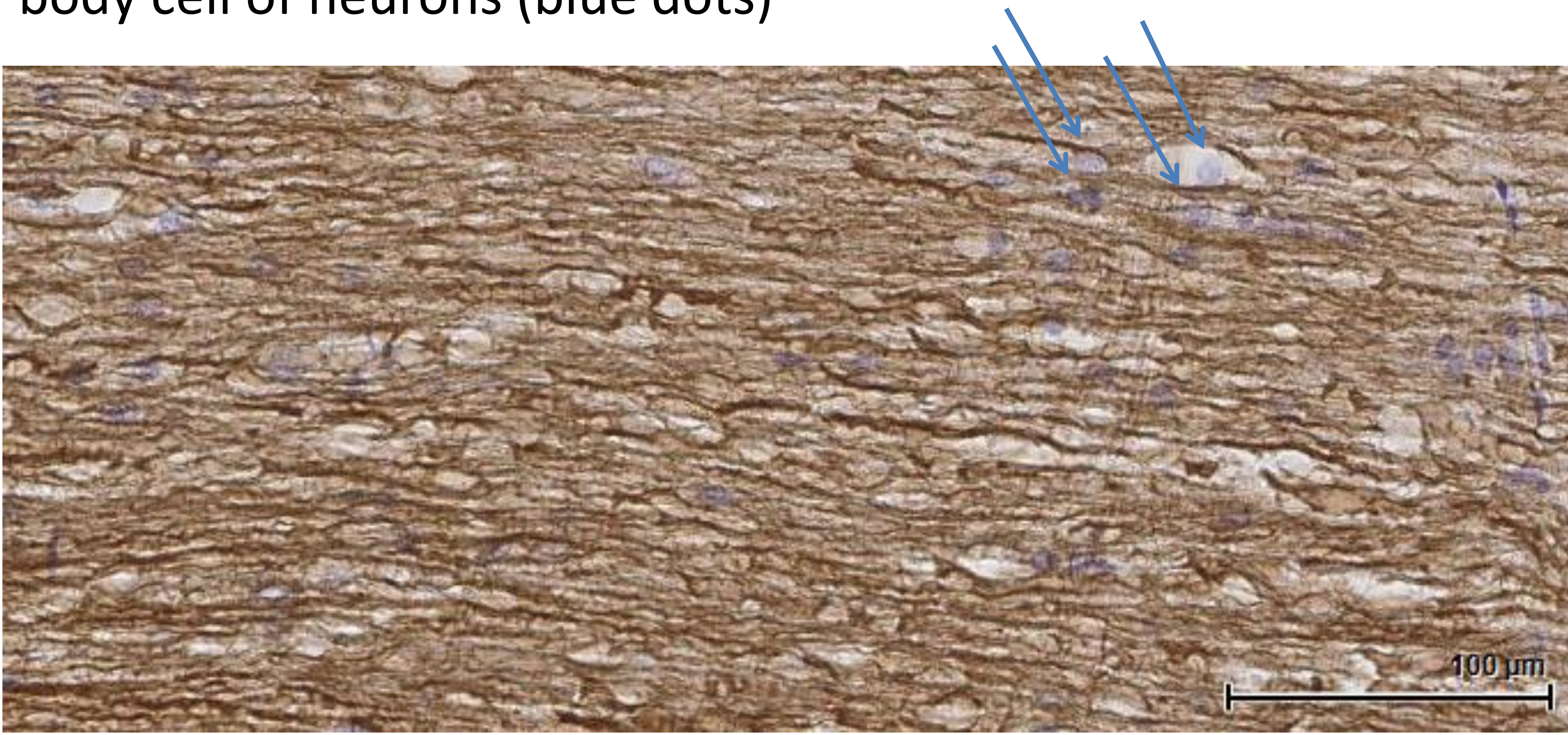
Can you identify the different contribution of the heterogeneous signal ?

The partial(!) microstructure of the white matter in a voxel: neurofilaments and the extra-cellular space

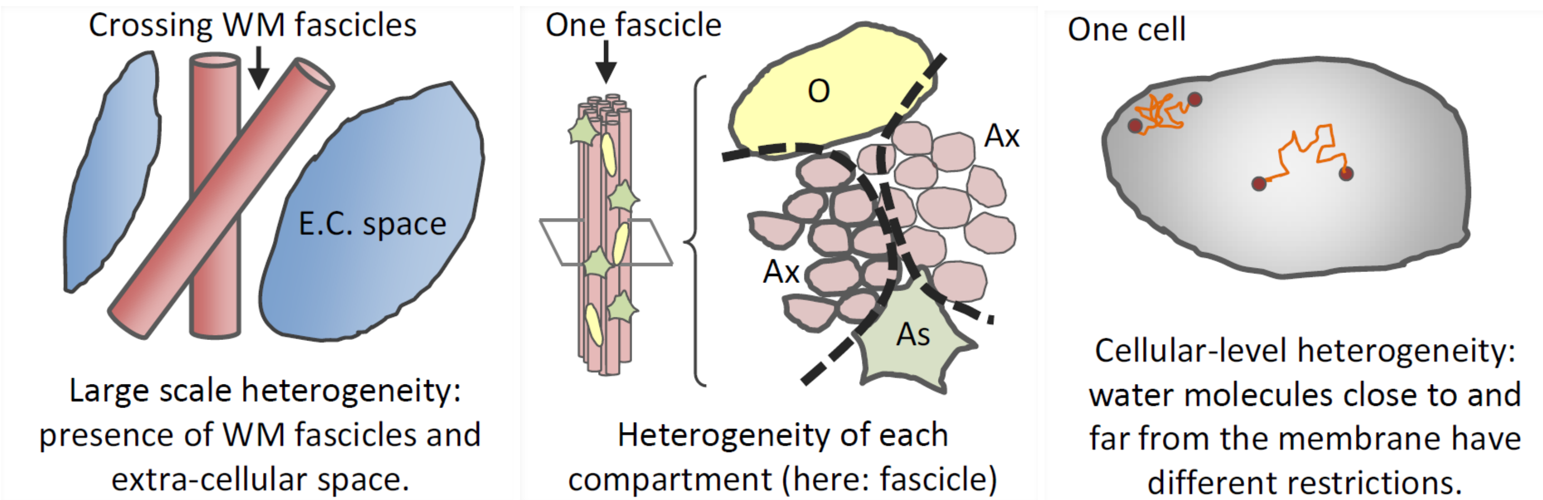
800 μm

Can you identify the different contribution of the heterogeneous signal ?

The partial(!) microstructure of the white matter in a voxel: body cell of neurons (blue dots)



Multi compartiment models taking into account the heterogeneity: DIAMOND

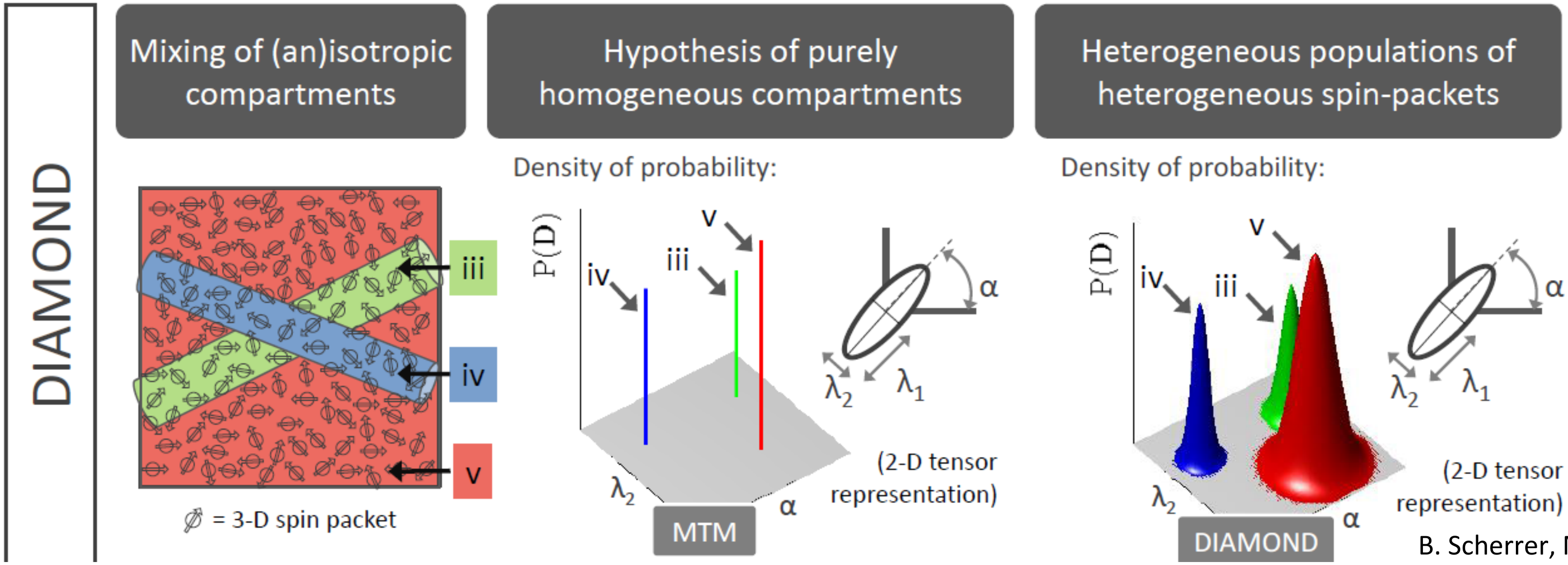


B. Scherrer, MRM, 2015

Several levels of heterogeneity can be identified with a tensorial distribution:

$$S_k = S_0 \int_{\mathbf{D} \in \mathrm{Sym}^+(3)} P\left(\mathbf{D}\right) \exp\left(-b_k \mathbf{g}_k^T \mathbf{D} \mathbf{g}_k\right) d\mathbf{D}$$

Multi compartiment models taking into account the heterogeneity: DIAMOND



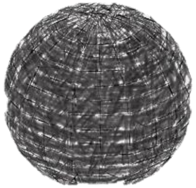
B. Scherrer, MRM, 2015

$$S_k = f_{\mathrm{free}} \mathcal{D}(\mathbf{D}^0_{\mathrm{free}}, \kappa_{\mathrm{free}}) + f_{\mathrm{iso,r}} \mathcal{D}(\mathbf{D}^0_{\mathrm{iso,r}}, \kappa_{\mathrm{iso,r}}) + \sum_{j=1}^{N_f} \left[f_{j,\mathrm{r}} \mathcal{D}(\mathbf{D}^0_{j,\mathrm{r}}, \kappa_{j,\mathrm{r}}) + f_{j,\mathrm{hin}} \mathcal{D}(\mathbf{D}^0_{j,\mathrm{hin}}, \kappa_{j,\mathrm{hin}}) \right]$$

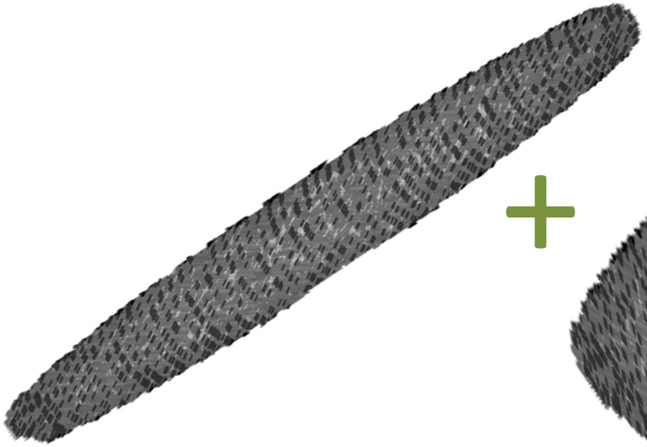
Multi compartiment models taking into account the heterogeneity: DIAMOND

$$S_k = f_{\mathrm{free}}\mathcal{D}(\mathbf{D}^0_{\mathrm{free}}, \kappa_{\mathrm{free}}) + f_{\mathrm{iso,r}}\mathcal{D}(\mathbf{D}^0_{\mathrm{iso,r}}, \kappa_{\mathrm{iso,r}}) +$$

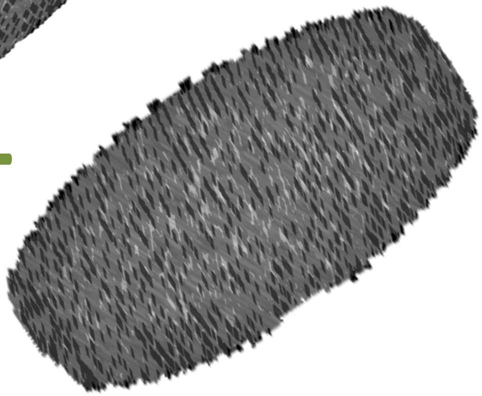
Fixed constant: $3\ 10^{-9}$



$$\left[f_{j,\mathrm{r}}\mathcal{D}(\mathbf{D}^0_{j,\mathrm{r}}, \kappa_{j,\mathrm{r}}) + f_{j,\mathrm{hin}}\mathcal{D}(\mathbf{D}^0_{j,\mathrm{hin}}, \kappa_{j,\mathrm{hin}})\right]$$



+

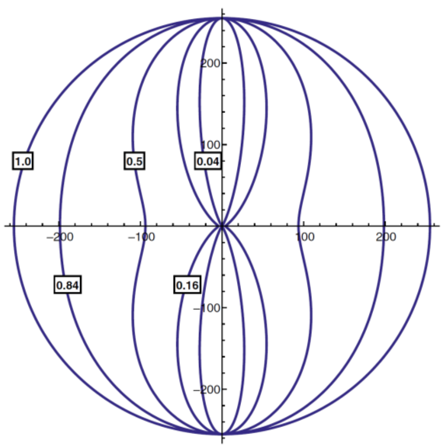


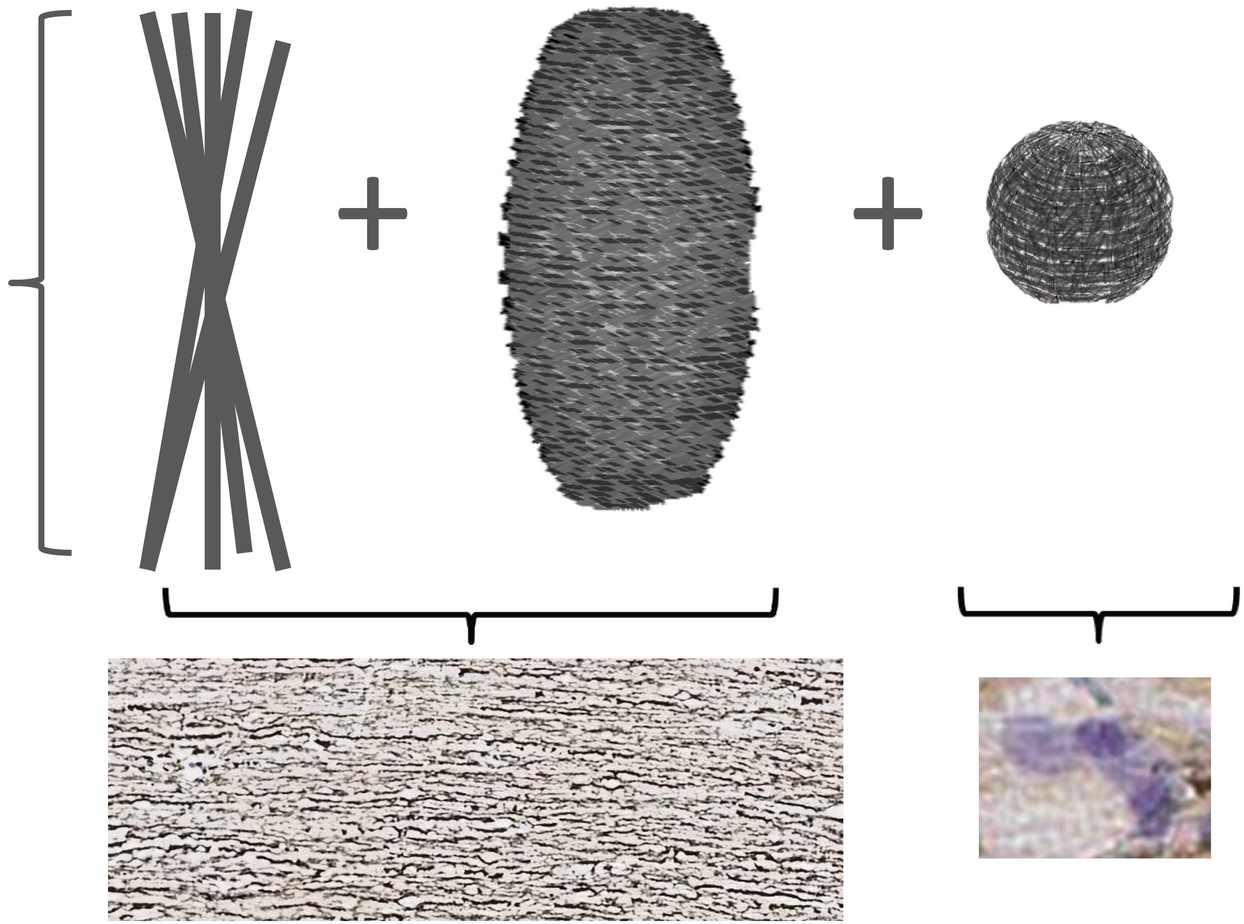
=

Multi compartiment models taking into account the heterogeneity: NODDI

$$A = (1-\nu_{iso})(\nu_{ic}A_{ic} + (1-\nu_{ic})A_{ec}) + \nu_{iso}A_{iso}$$

Watson distribution





These both models have been validated on healthy patients

⇒ evaluate these diffusion models on neuropathologies.

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⇒ evaluate these diffusion models on neuropathologies. Which model?

Define a pre-clinical model to study the Wallerian degeneration process based on imaging quality:
- reduce the bleeding effect
- control and lesion on the same slices
- limit the functional loss due to the model

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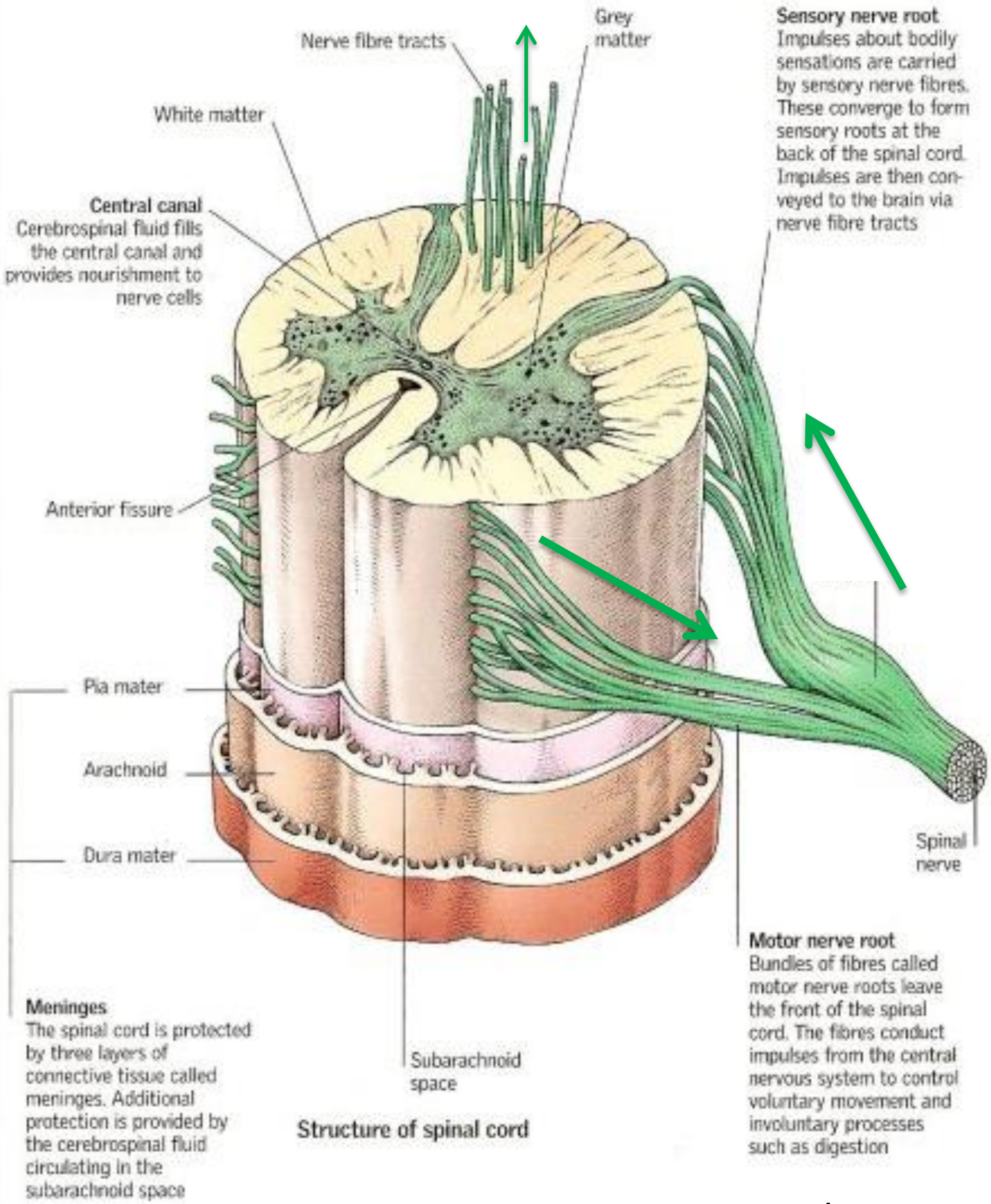
Define a pre-clinical model to study the Wallerian degeneration process based on imaging quality:

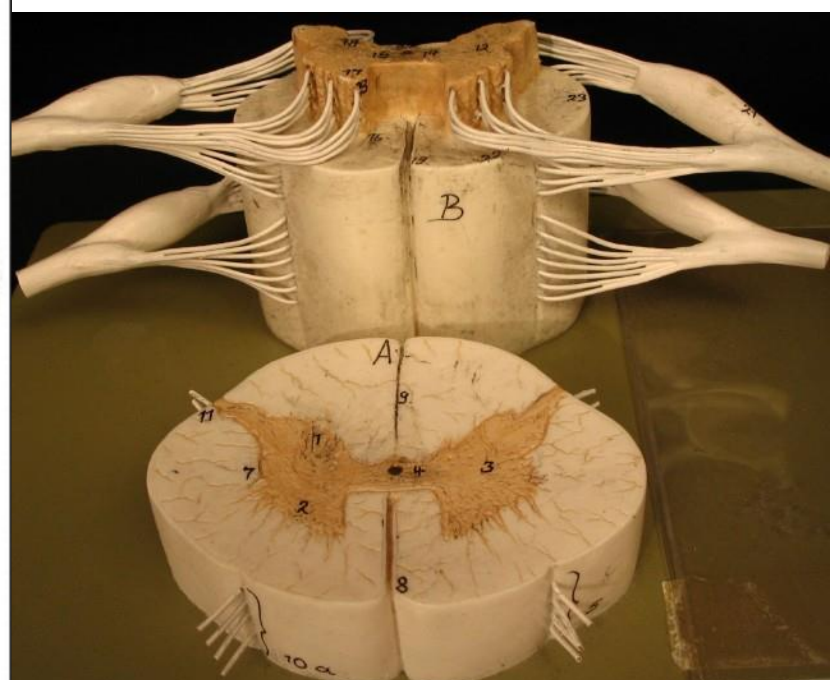
- reduce the bleeding effect
- control and lesion on the same slices
- limit the functional loss due to the model

⇒ Rhizotomy, transection of the dorsal roots

Anatomy and Functions of Spinal cord

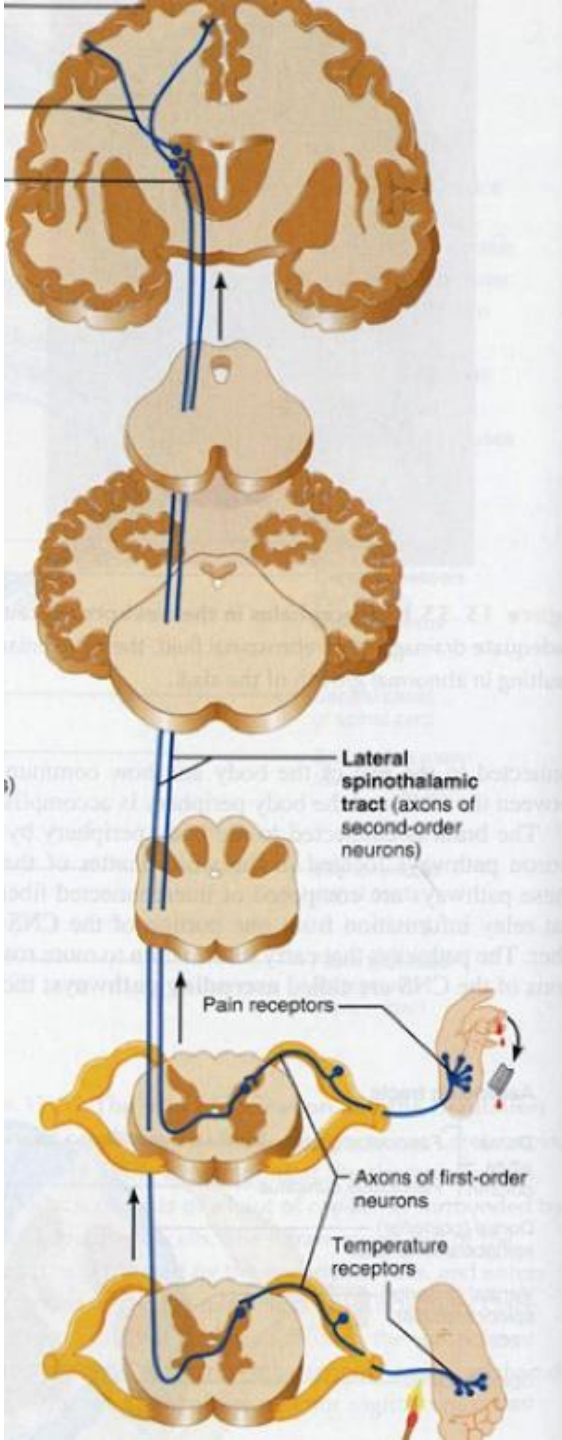


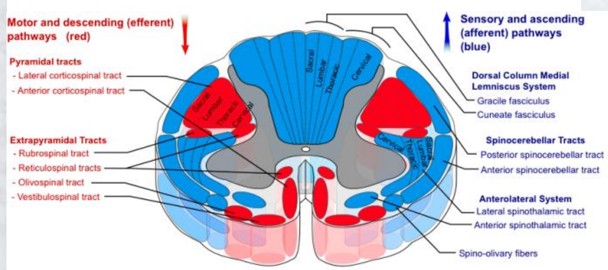
Google image

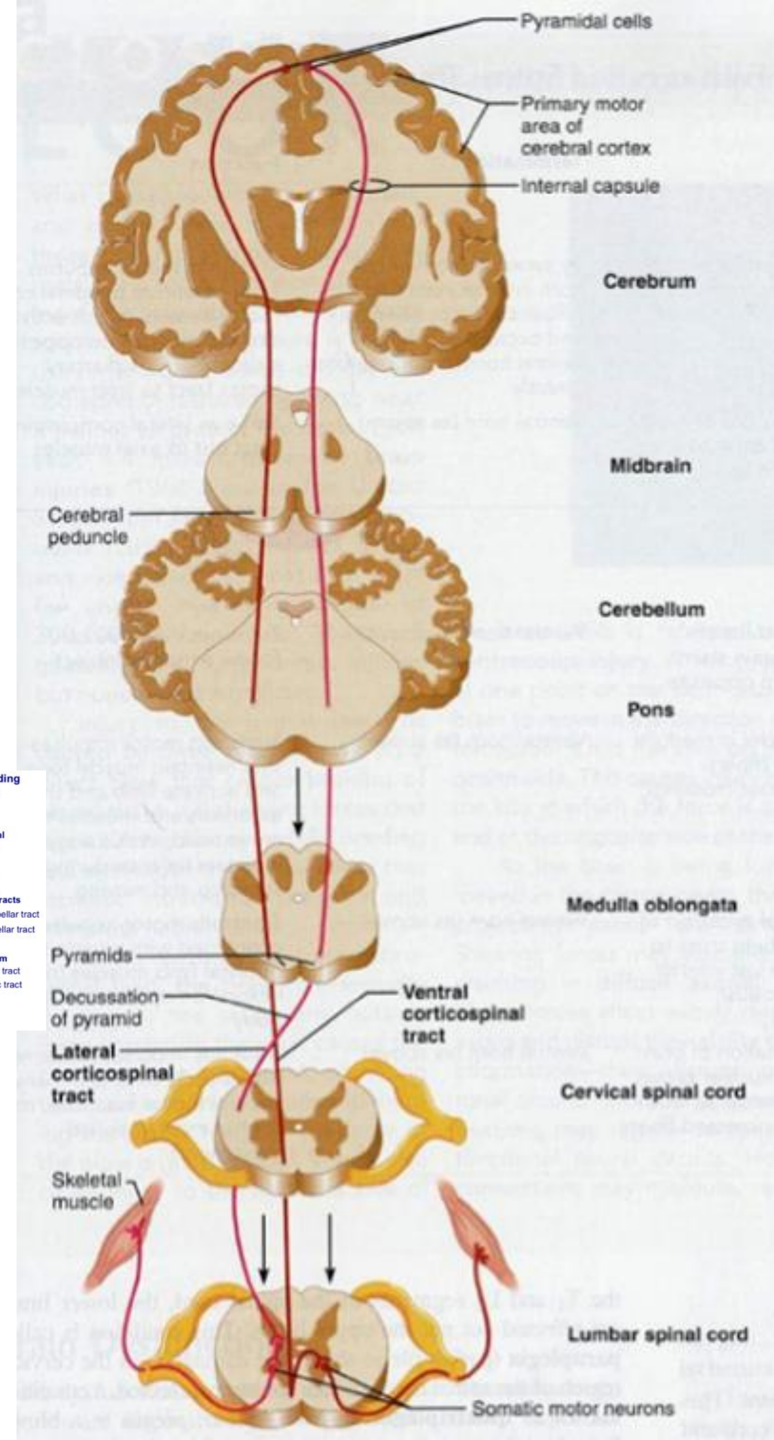


Aleksandar Jankovski, MED, UCL

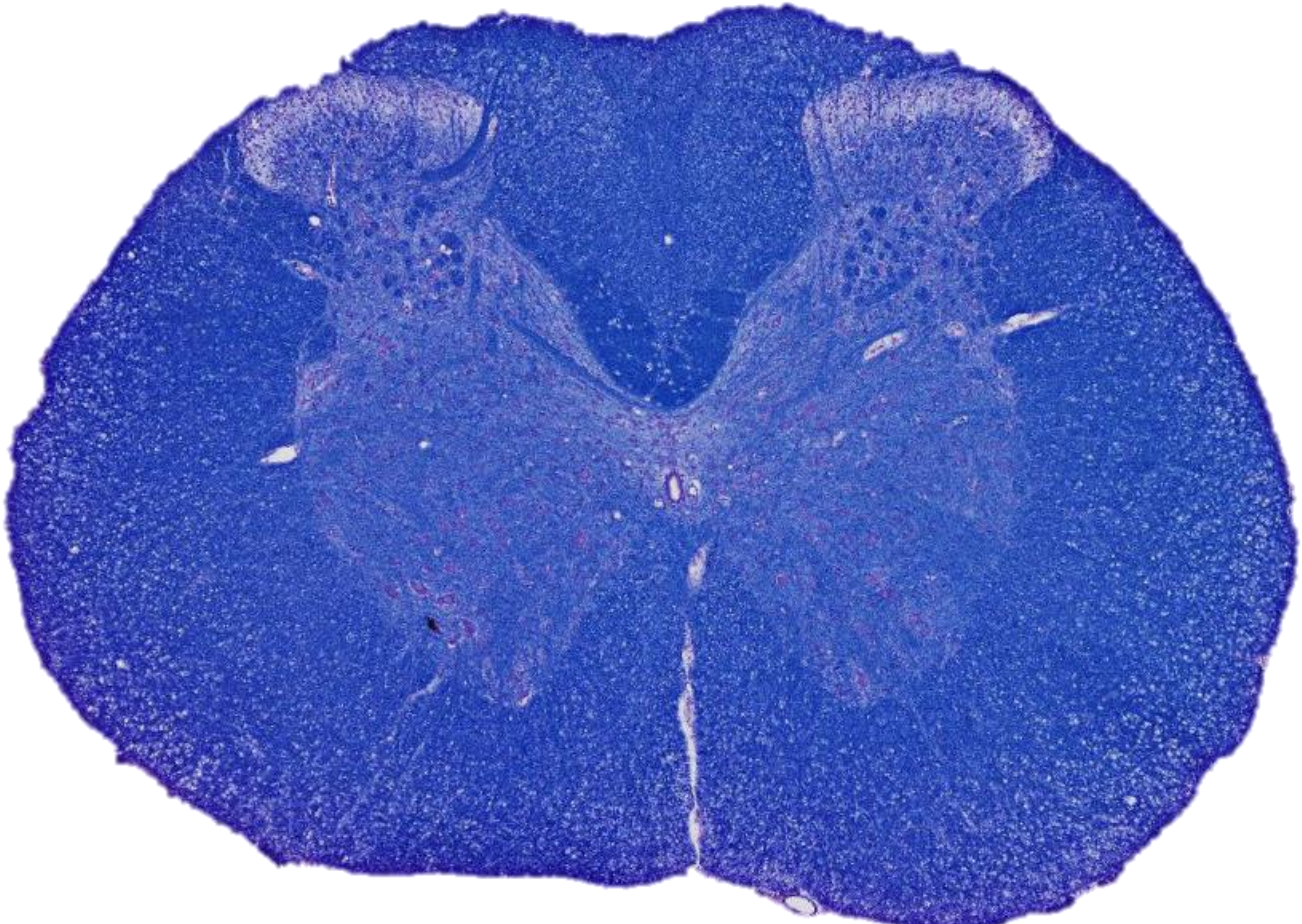
Ascending and descending pathways

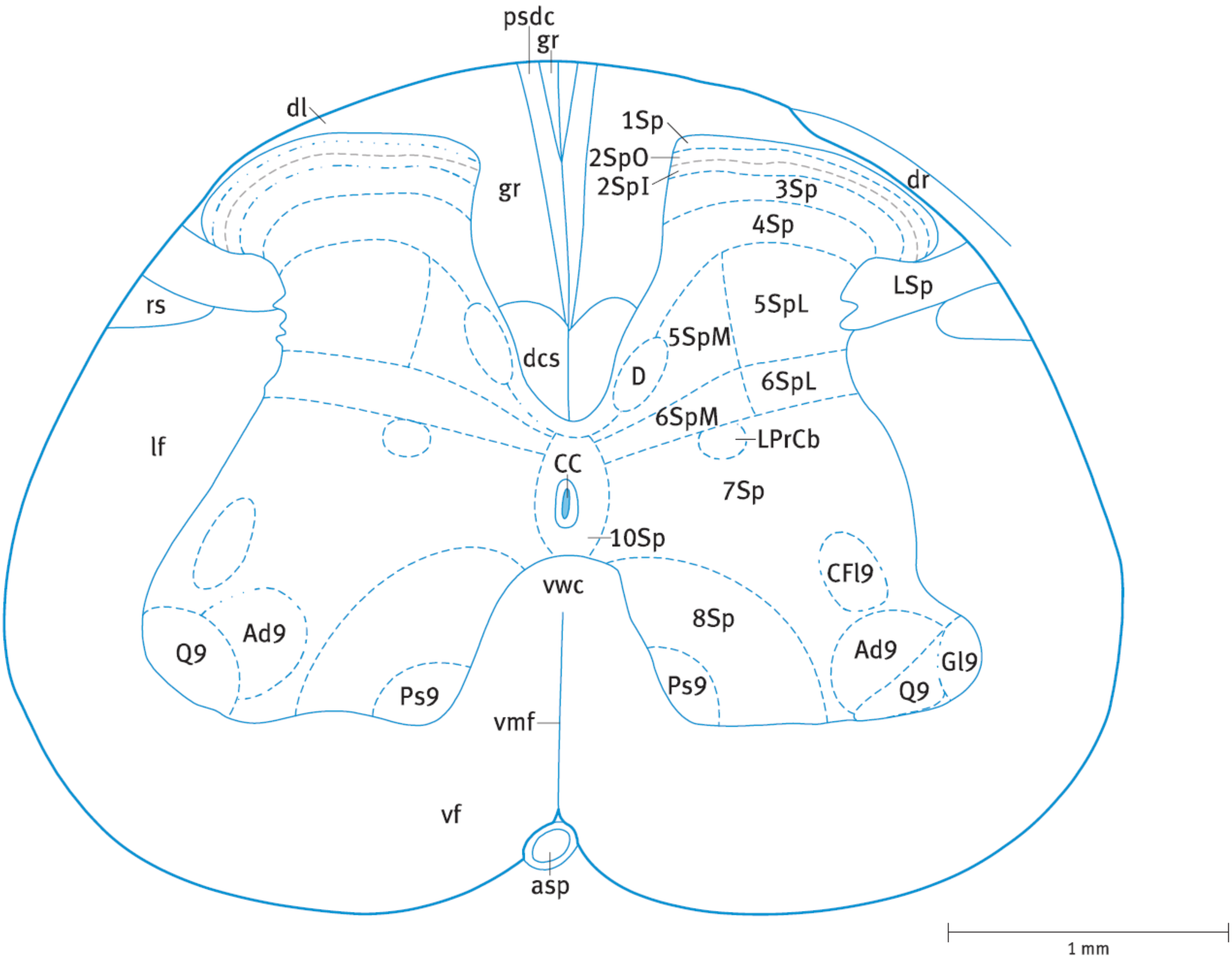






Where the Wallerian degeneration process will take effect ?




psdc
gr
dl
1Sp
2SpO
2SpI
3Sp
dr
gr
4Sp
LSp
rs
5SpL
5SpM
dcs
D
6SpL
6SpM
LPrCb
lf
CC
7Sp
10Sp
CFl9
vwc
8Sp
Ad9
Q9
Ad9
Gl9
Ps9
Ps9
Q9
vmf
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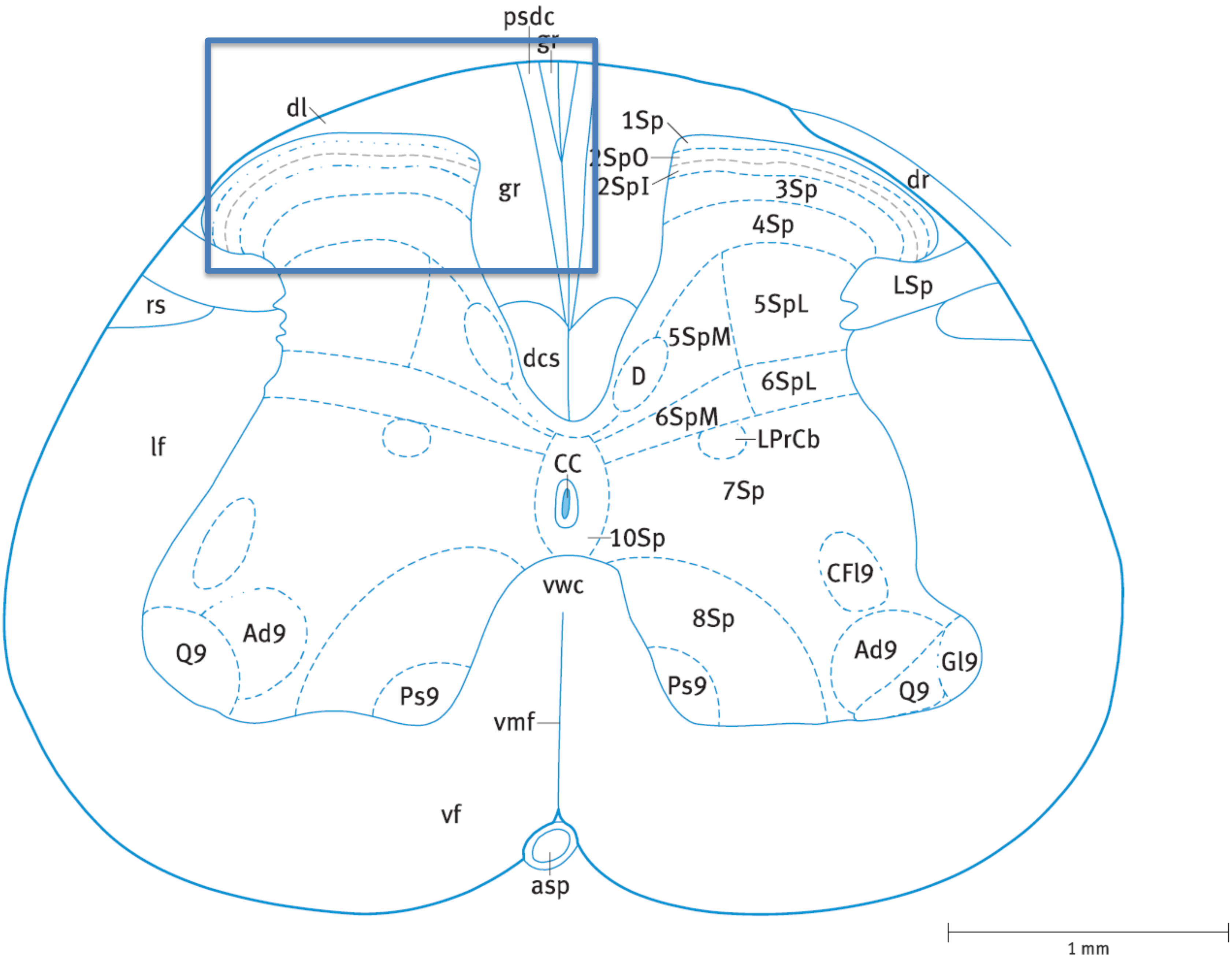
asp
1 mm


psdc
gr
dl
1Sp
2SpO
2SpI
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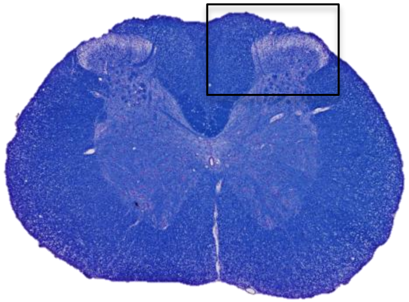
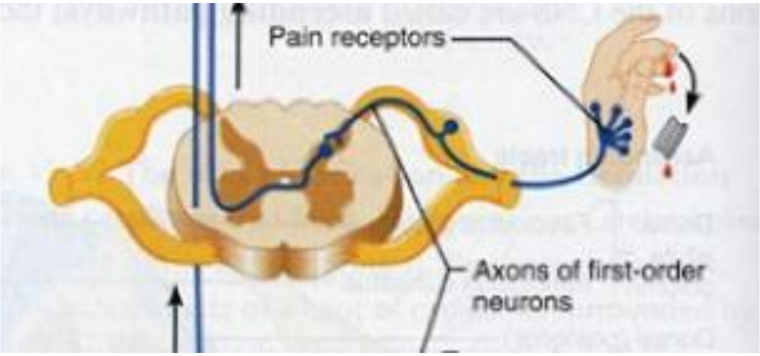
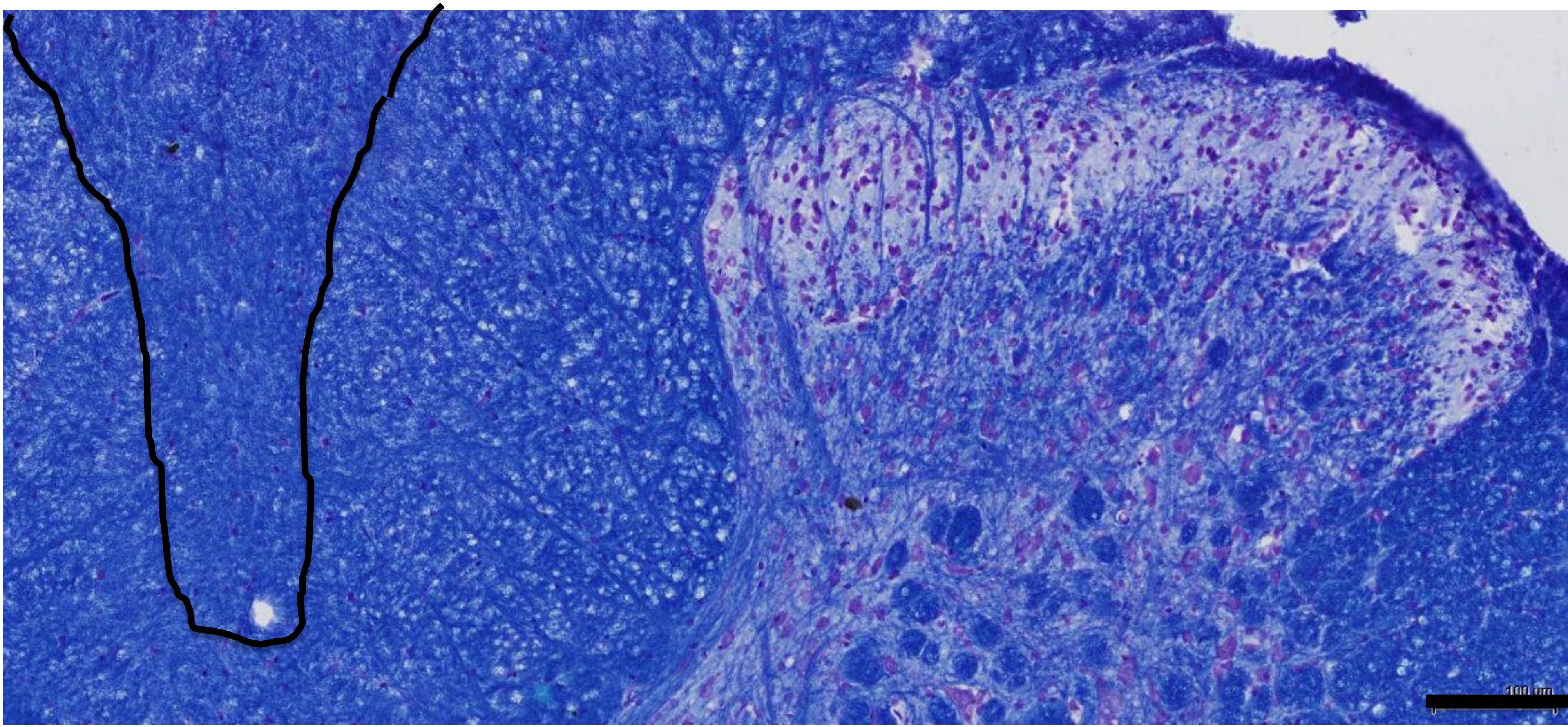
3Sp
dr
4Sp
LSp
rs
5SpL
5SpM
dcs
D
6SpL
6SpM
LPrCb
lf
CC
7Sp
10Sp
CFl9
vwc
8Sp
Ad9
Q9
Ad9
Gl9
Ps9
Ps9
Q9
vmf
vf
asp
1 mm




Pain receptors
Axons of first-order
neurons

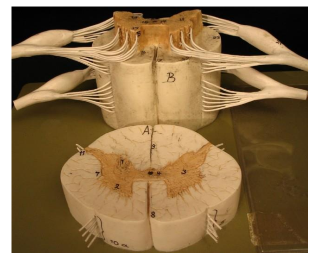


Protocol for the rhizotomy study

Healthy Rat

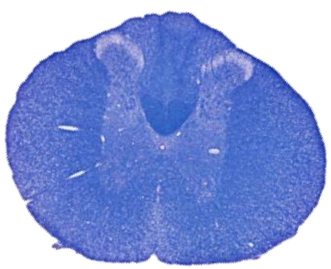
Rhizotomy

left L2-L3



... x t

- 4 days
- 13 month
- 37 days
- 50 days



Myelin (Luxol Fast Blue)

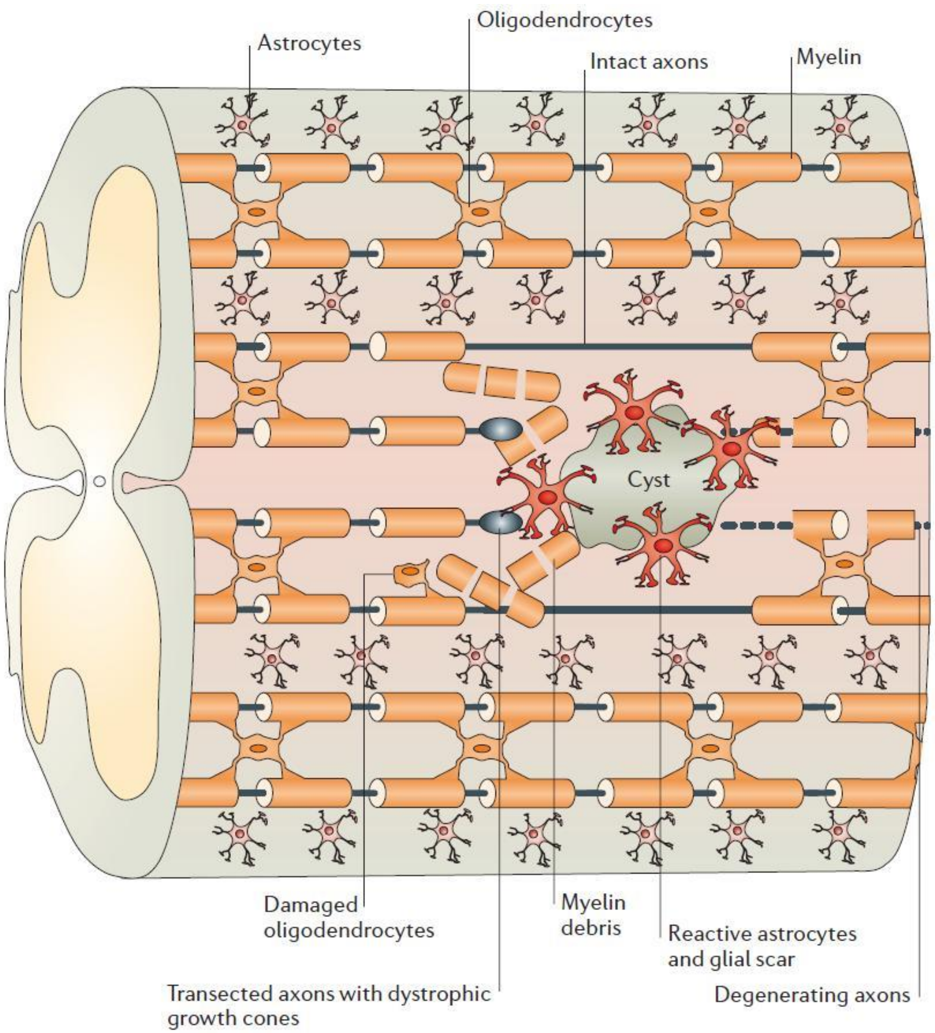
Neurofilament (SMI312)

Oligodendrocyte

Astrocyte

Microglia

Characterization of the Wallerian degeneration:

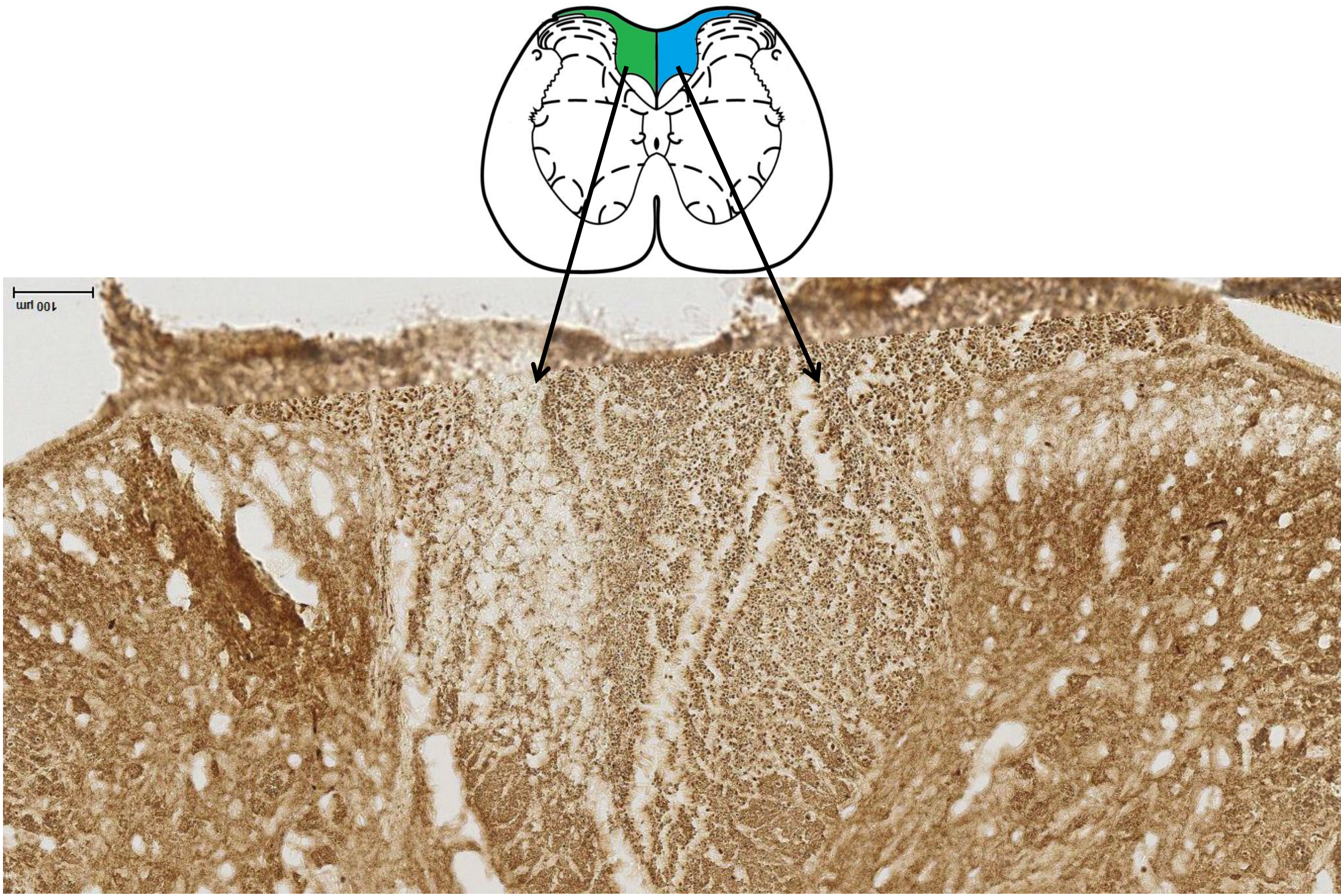


After 3 days:
- astrocyte activation
- axonal loss

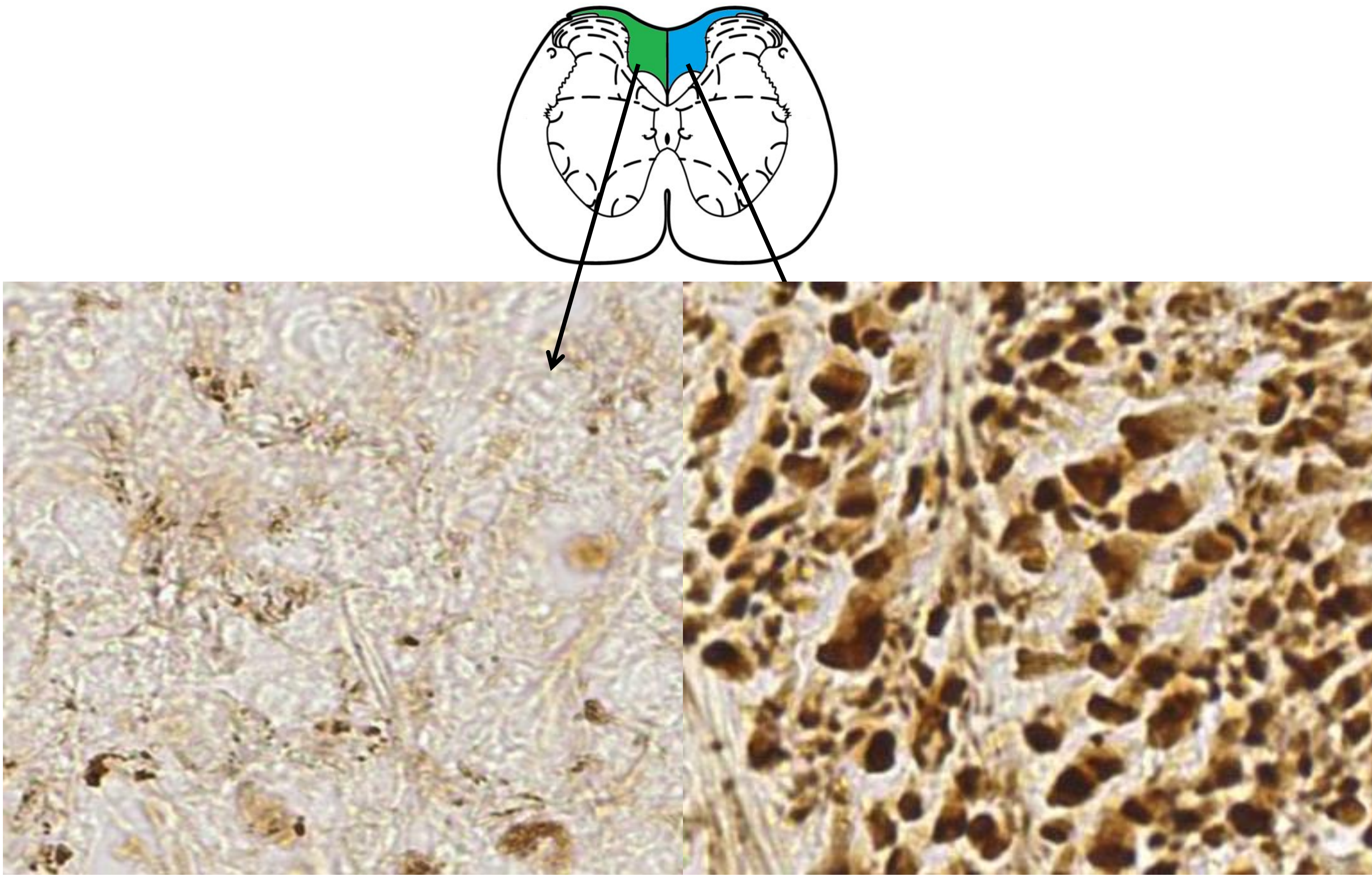
After 1 week:
- clearance of the debris
- microglia activation

After 1 month:
- demyelination
- oligodendrocyte activation ?

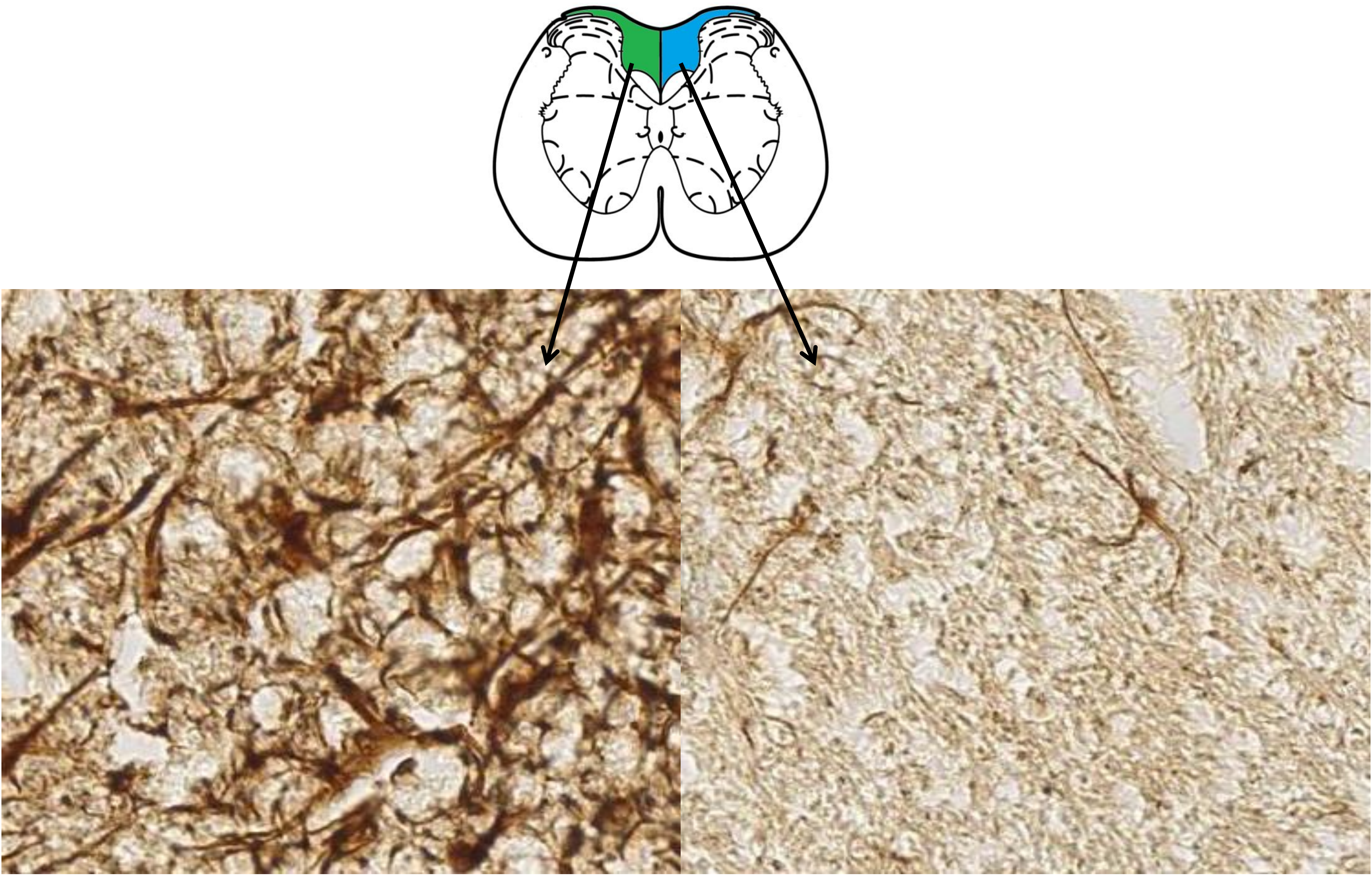
neurofilament staining: Axonal loss



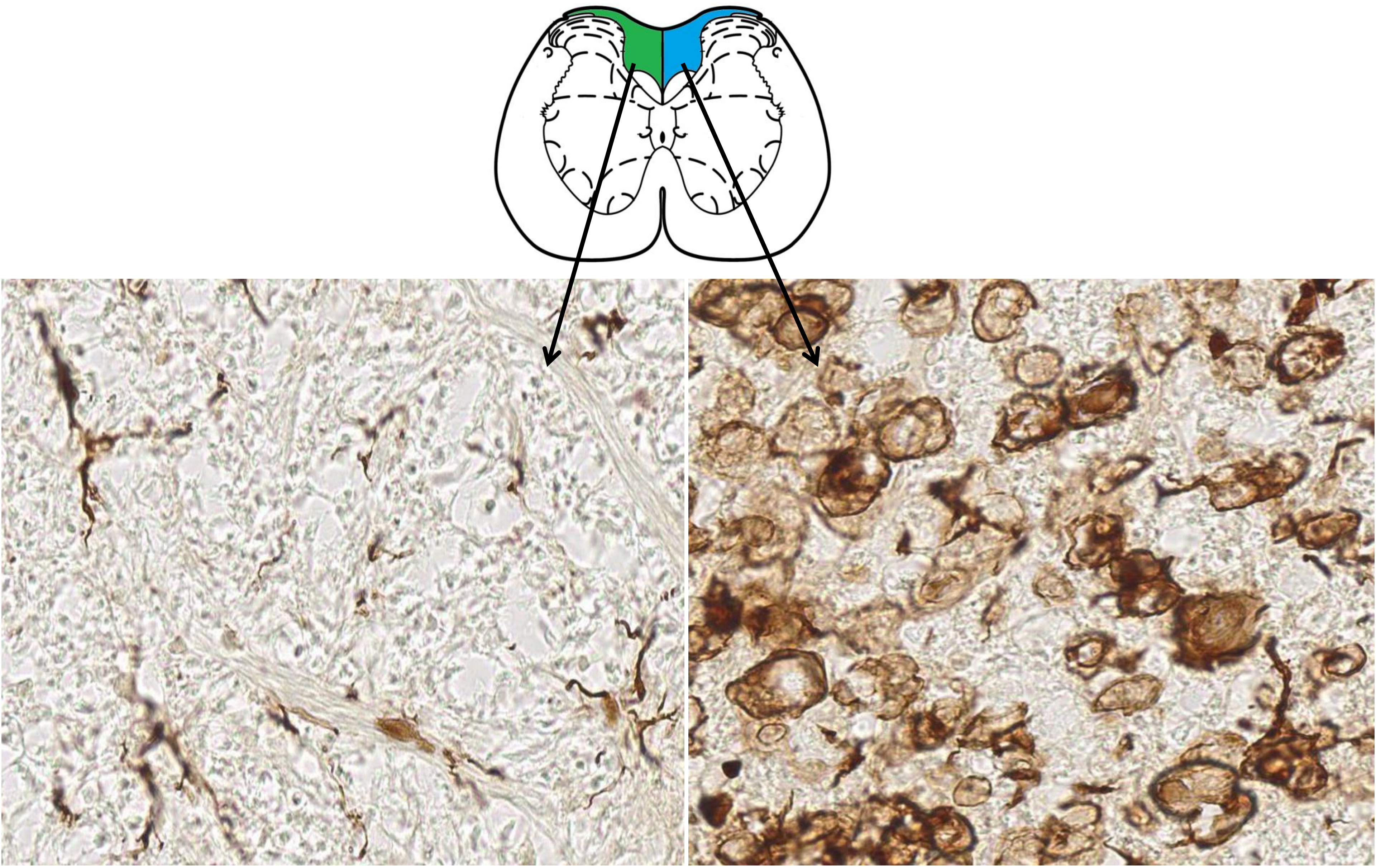
neurofilament staining: Axonal loss



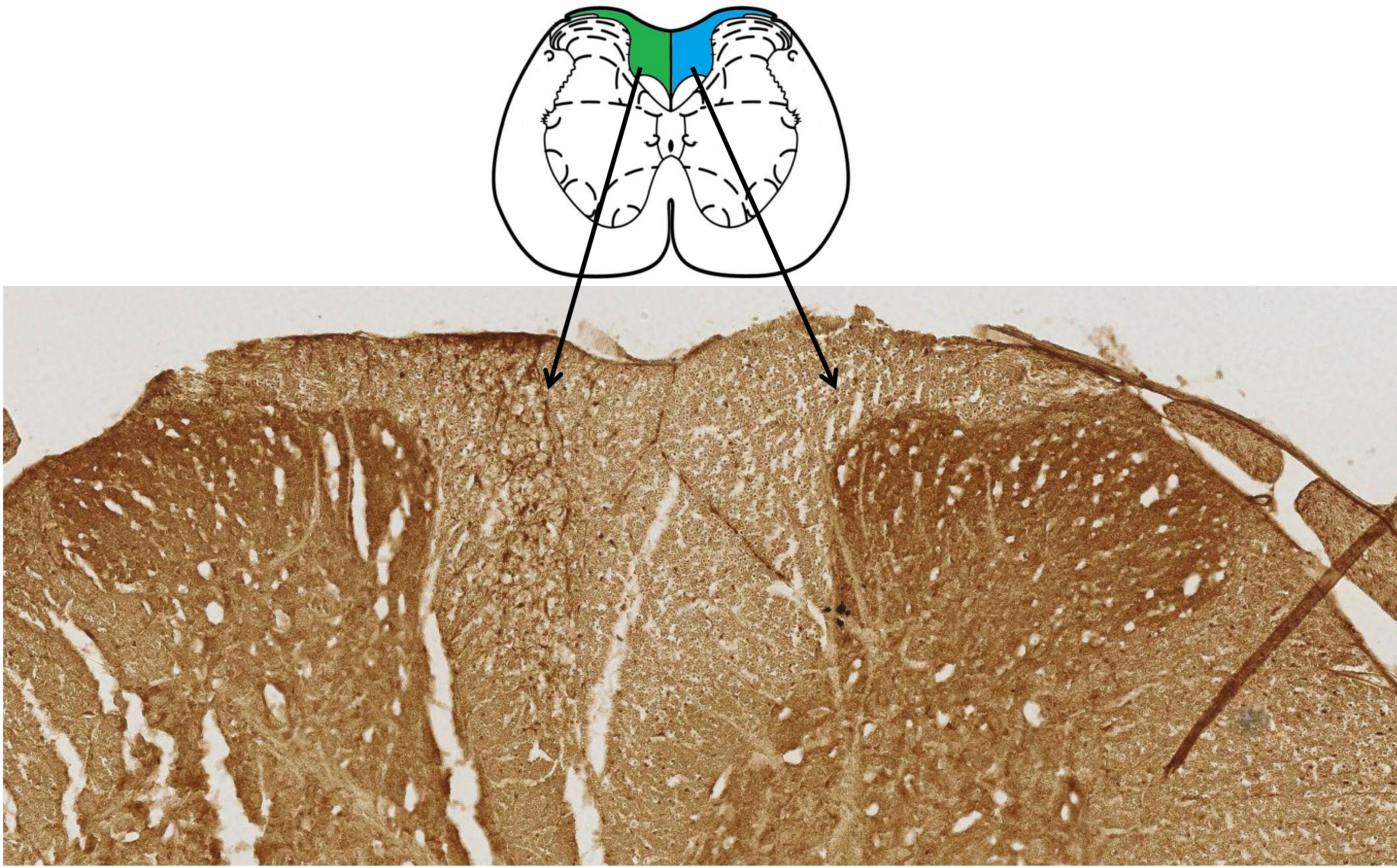
GFAP staining: astrocyte activation



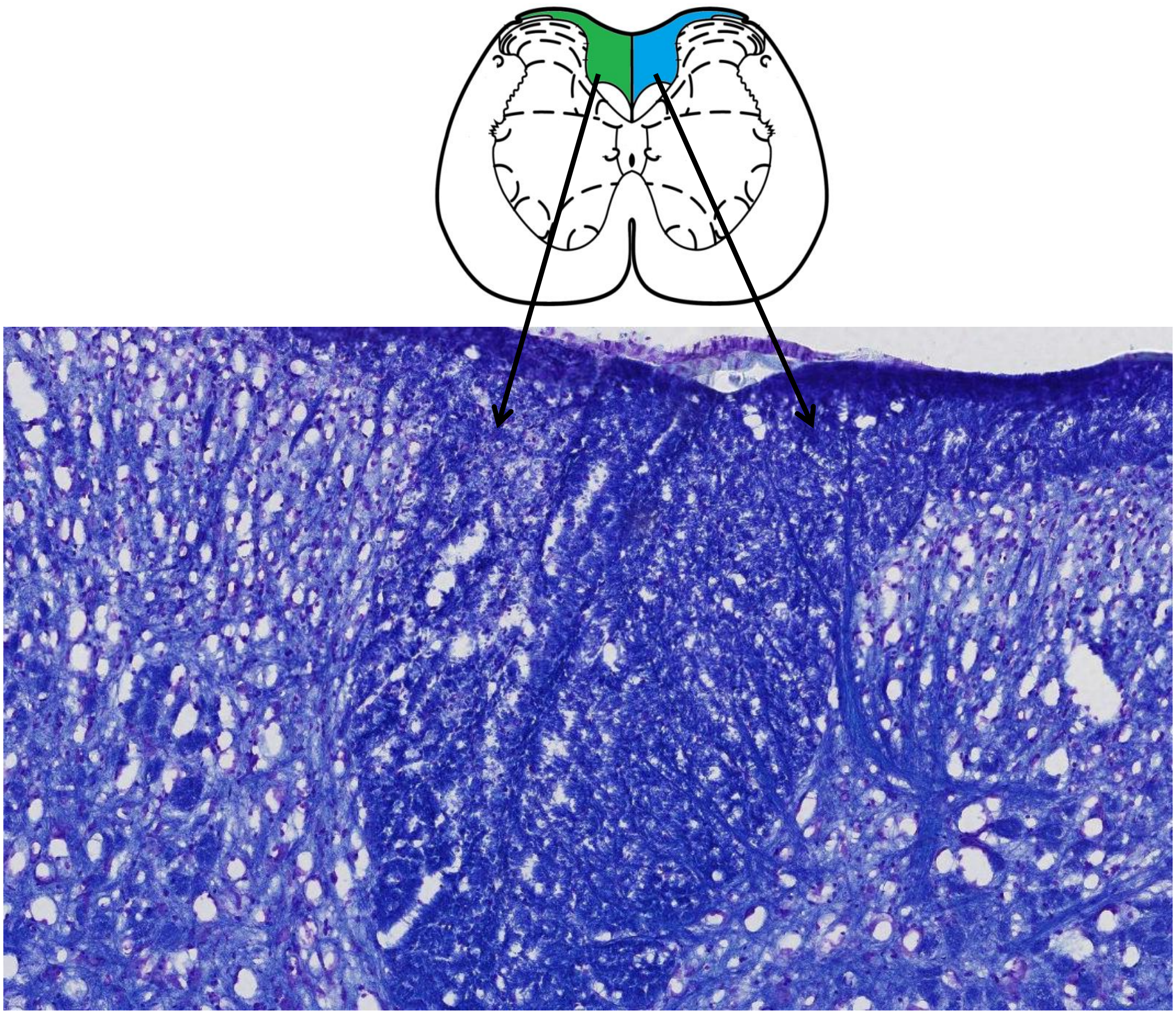
Iba1 staining: microglia activation



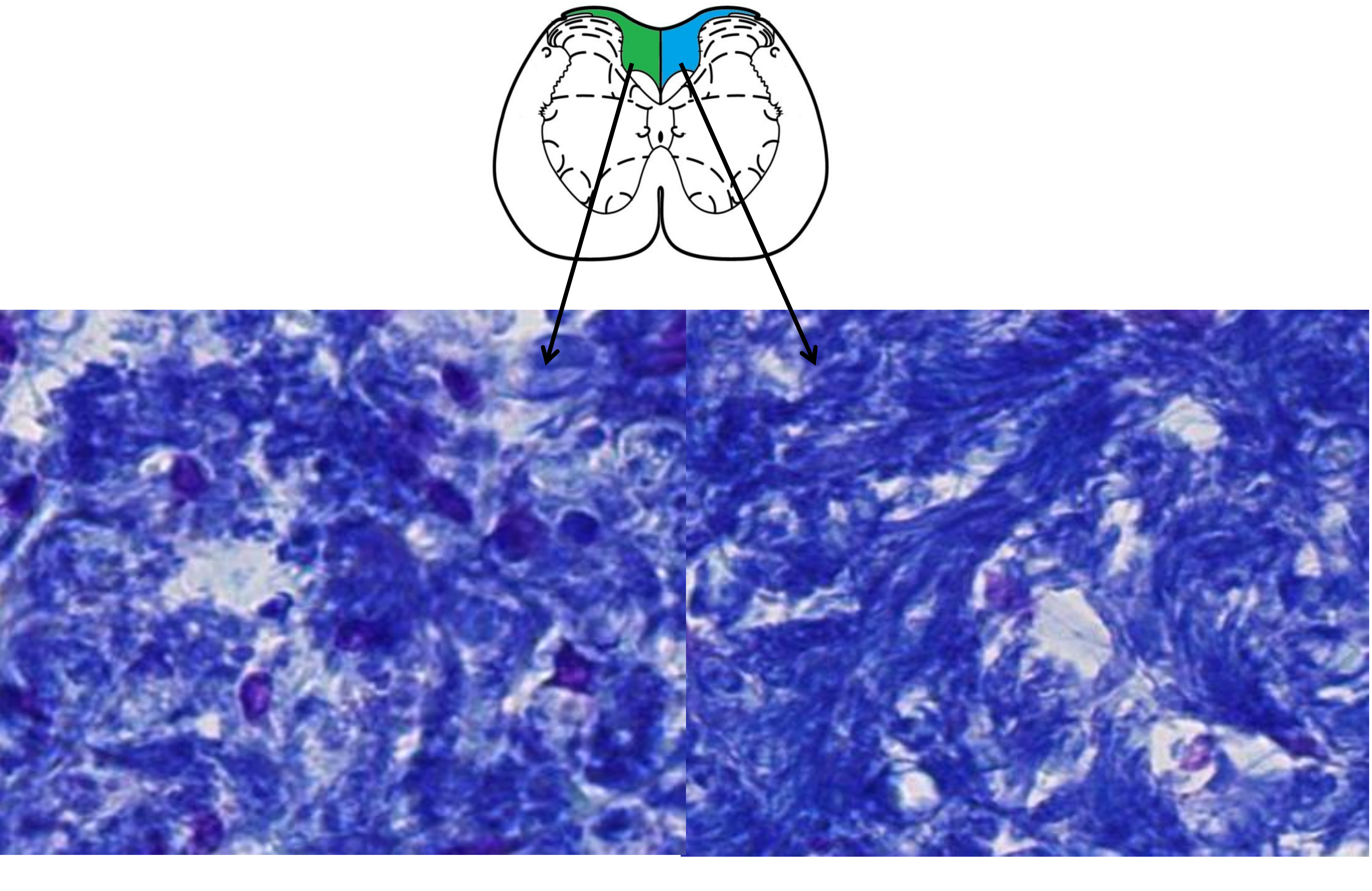
Oligodendrocyte staining: activation, migration ?



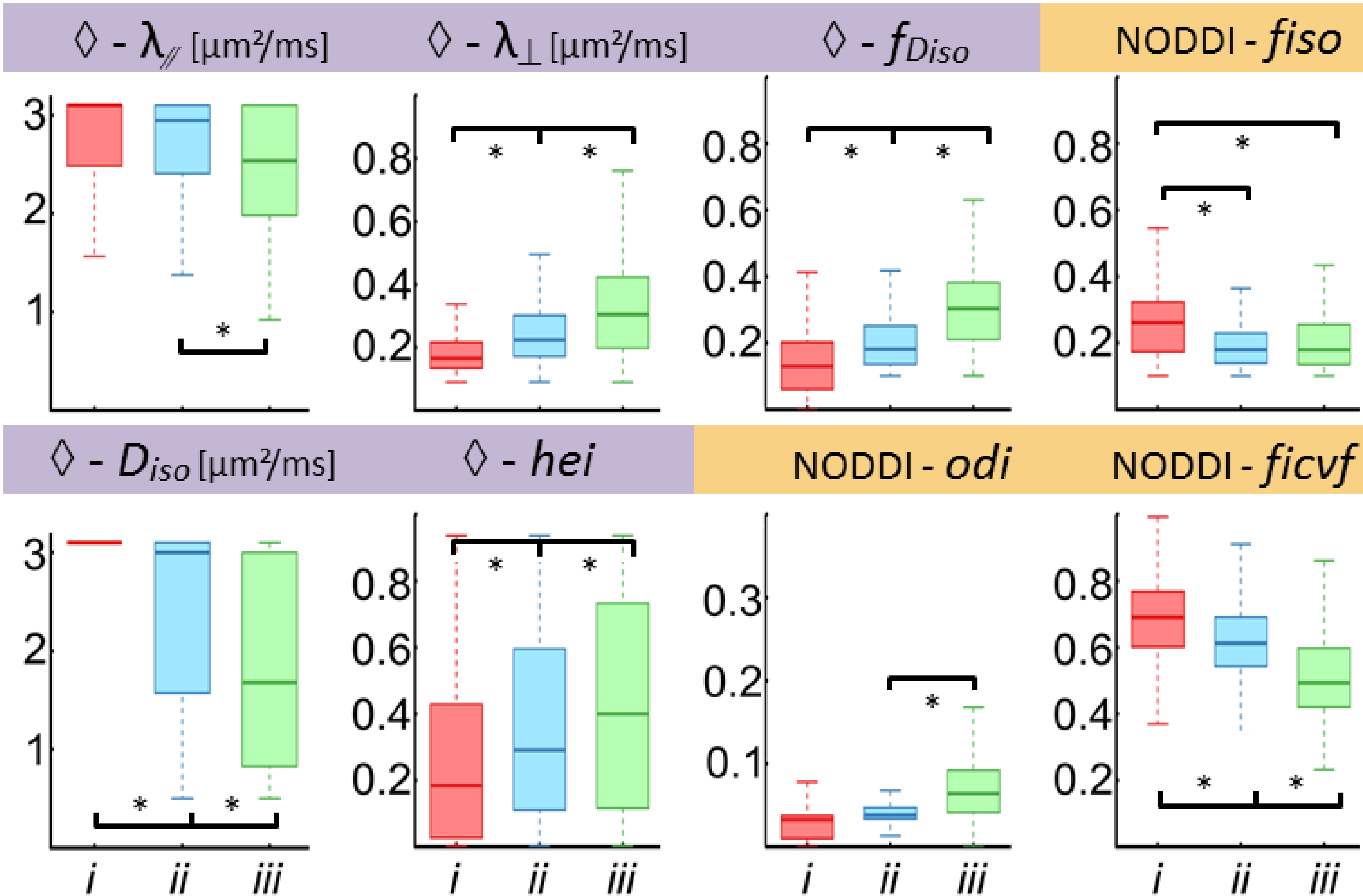
Myelin staining: demyelination



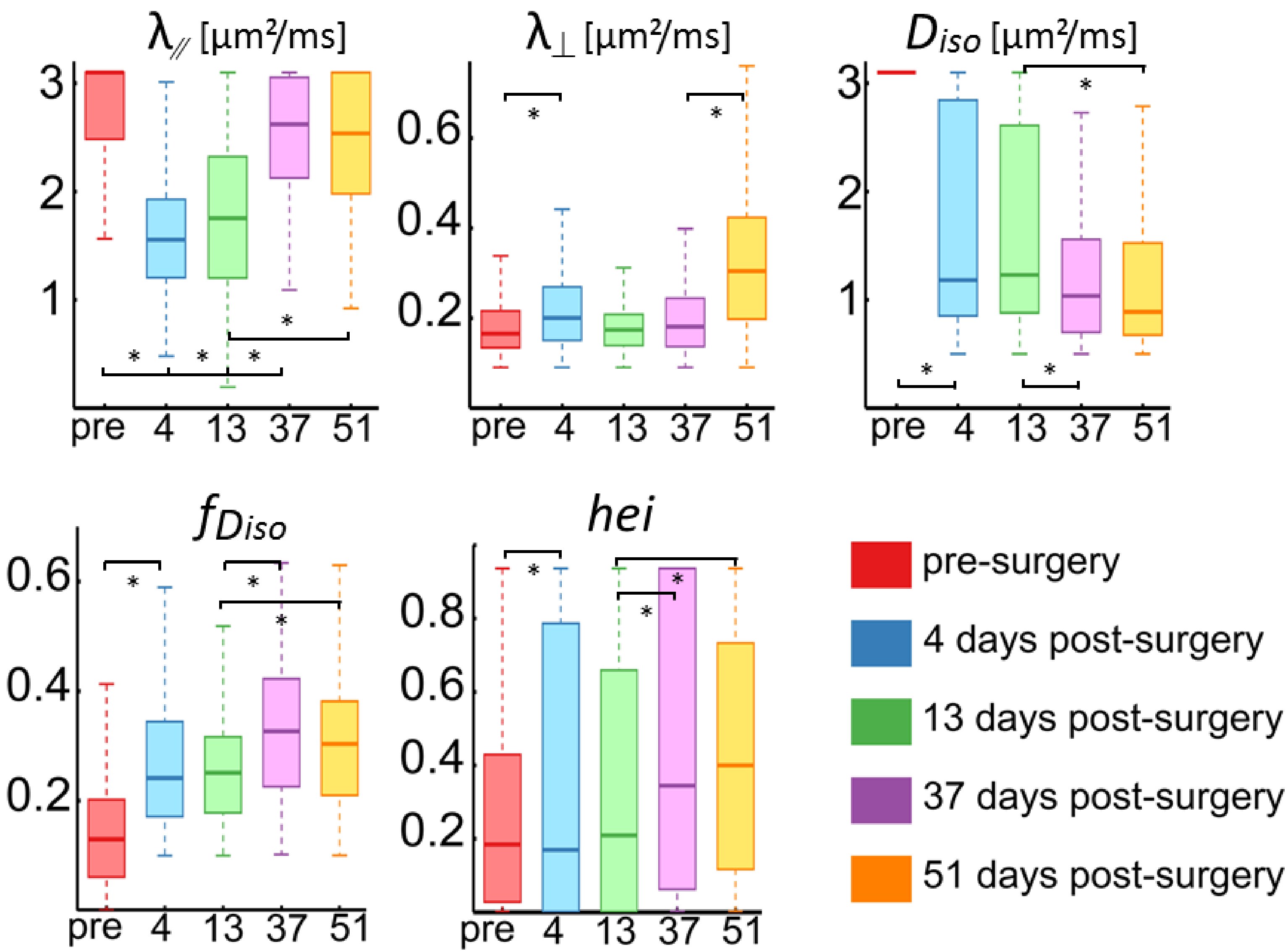
Myelin staining: demyelination



Results for DIAMOND and NODDI



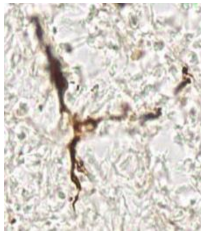
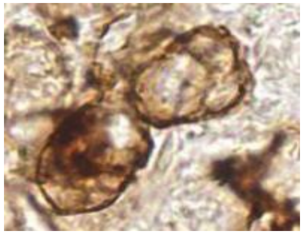
Longitudinal evolution for DIAMOND



Approach of multicompartiment model + heterogeneous parameter?

Can we define other structure ?

- yes, all structure can be studied

-> develop a dictionary  or 

How can we fix the number of compartiment ?

- cross-validation method

-> rapid and robust optimization method

The signal in the CNS can be generalized as :

(J-P. Thiran, Neuroimage, 105 (2015) p32-44)

n_h extra-cellular

$$S(\boldsymbol{q}) = \underbrace{f^{\text{IC}} R^{\text{IC}}(\boldsymbol{q})}_{\text{restricted}} + \underbrace{f^{\text{EC}} R^{\text{EC}}(\boldsymbol{q})}_{\text{hindered}} + \underbrace{f^{\text{ISO}} R^{\text{ISO}}(\boldsymbol{q})}_{\text{isotropic}}$$

n_i isotropic

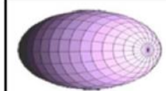
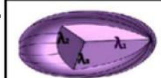
n_r intra-cellular

with the condition : $n_i + n_h + n_r = 1$

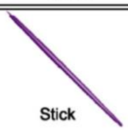
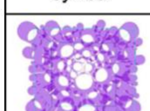
The signal in the CNS can be generalized as :

(J-P. Thiran, Neuroimage, 105 (2015) p32-44 and Alexander. Neuroimage. 54 (2012))

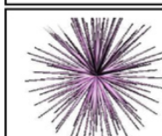
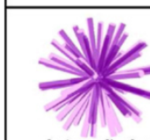
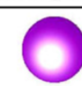
$$\mathbf{q} = \frac{\gamma}{2\pi} \int \boldsymbol{G}\, dt$$

Model	Form	Degrees of freedom
 Ball	$\mathbf{D} = d\mathbf{I}$	d
 Zeppelin	$\mathbf{D} = \alpha \mathbf{n}\mathbf{n}^T + \beta \mathbf{I},\ d_{\parallel} = \alpha + \beta, d_{\perp} = \beta$	$d_{\parallel}, d_{\perp}, \theta, \phi$
 Tensor	$\mathbf{D} = d_{\parallel}\mathbf{n}\mathbf{n}^T + d_{\perp_1}\mathbf{n}_{\perp_1}\mathbf{n}_{\perp_1}^T + d_{\perp_2}\mathbf{n}_{\perp_2}\mathbf{n}_{\perp_2}^T$	$d_{\parallel}, d_{\perp_1}, d_{\perp_2}, \theta, \phi, \alpha$

$$S(\boldsymbol{q}) = \underbrace{f^{\mathrm{IC}} R^{\mathrm{IC}}(\boldsymbol{q})}_{\text{restricted}} + \underbrace{f^{\mathrm{EC}} R^{\mathrm{EC}}(\boldsymbol{q})}_{\text{hindered}} + \underbrace{f^{\mathrm{ISO}} R^{\mathrm{ISO}}(\boldsymbol{q})}_{\text{isotropic}}$$

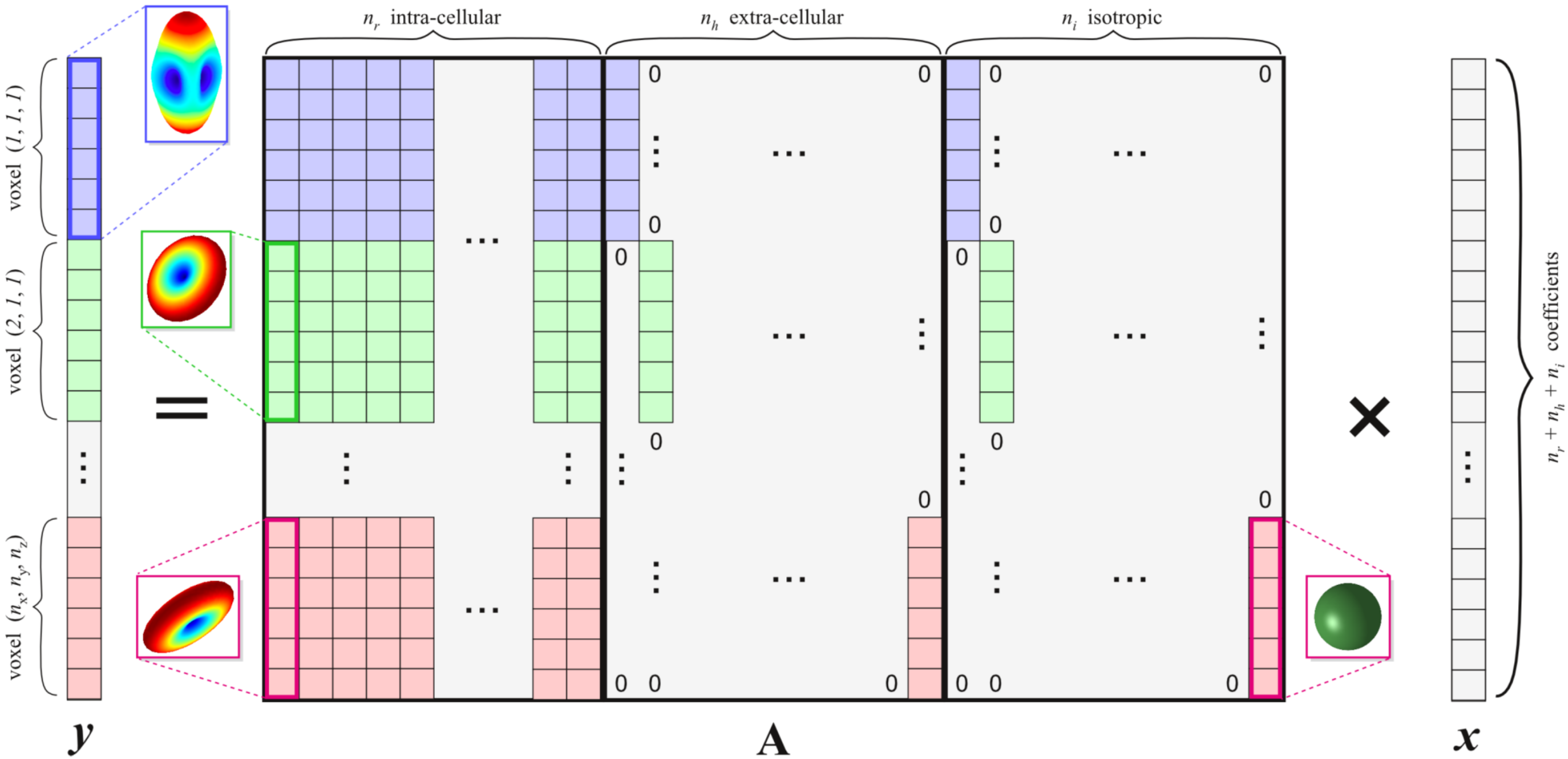
Intra-Axonal compartments		
Model	Form	Degrees of freedom
 Stick	$S = \exp(-bd(\mathbf{n}\cdot\mathbf{G})^2)$	d, θ, ϕ
 Cylinder	GPD approx.	d, θ, ϕ, R
 GDRCylinders	$P(R; k, \vartheta) = \frac{R^{k-1} e^{\frac{-R}{\vartheta}}}{\Gamma(k)\vartheta^k}$	$d, \theta, \phi, k, \vartheta$

with the condition : n_i

Model	Form	Degrees of freedom
 Astrosticks	$S_G = \int S_r p(\mathbf{n}) d\mathbf{n},\ R = 0$	d
 Astrocylinders	$S_G = \int S_r p(\mathbf{n}) d\mathbf{n},\ R > 0$	d, R
 Sphere	GPD approx. $R_s > 0$	d, R_s
 Dot	$R = 0, S = 1$	-

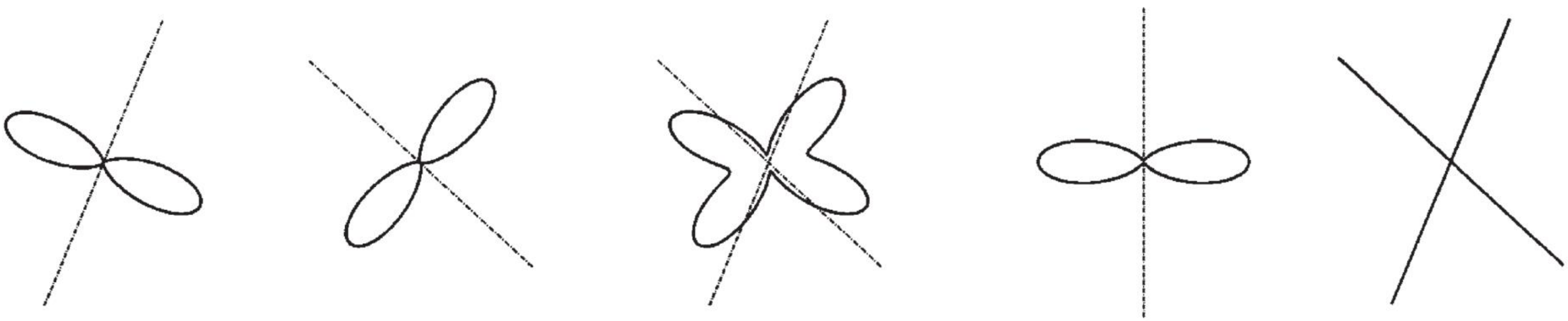
Generate a dictionary in all directions of the acquisition for each compartiment:

(J-P. Thiran, Neuroimage, 105 (2015) p32-44 and Alexander, Neuroimage, 54 (2012))



Use the prior of the fiber directions to optimize the problem:

(J-P. Thiran, Neuroimage, 105 (2015) p32-44 and Tournier, Neuroimage, 23 (2004))



$$f_1 S_1(\theta,\phi) \quad + \quad f_2 S_2(\theta,\phi) \quad = \quad S(\theta,\phi) \quad = \quad R(\theta) \quad \otimes \quad F(\theta,\phi)$$

compartiment model

known

Fiber orientation distribution (FOD)

Use the prior of the fiber directions to optimize the problem:

(J-P. Thiran, Neuroimage, 105 (2015) p32-44 and Alexander, Neuroimage, 54 (2012))

$$\underset{\mathbf{x}\geq 0}{\operatorname{argmin}} \frac{1}{2}\|\widetilde{\Phi}_A \mathbf{x} - \mathbf{y}\|_2^2 + \lambda \frac{1}{2}\|\mathbf{x}\|_2^2$$

solve with Lasso algorithm with spams toolbox

$\widetilde{\Phi}_A$ → dictionary

$\mathbf{x}$ → fractions [n_i / n_h / n_r]

⇨ do not use the condition: $n_i + n_h + n_r = 1$

Thank you for your attention