

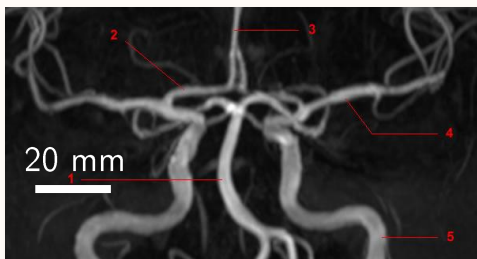
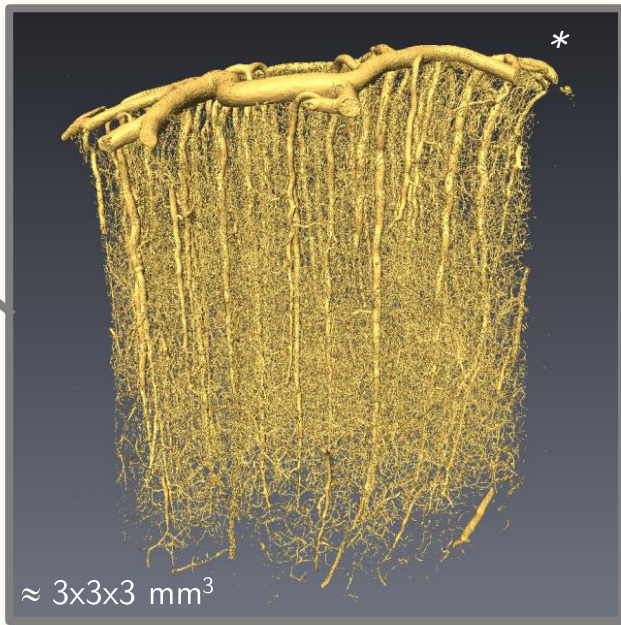
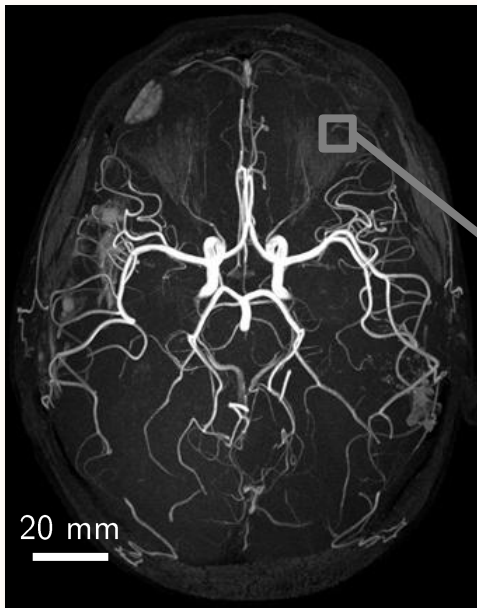
# Développements Méthodologiques pour la mesure de la Perfusion Cérébrale par IRM

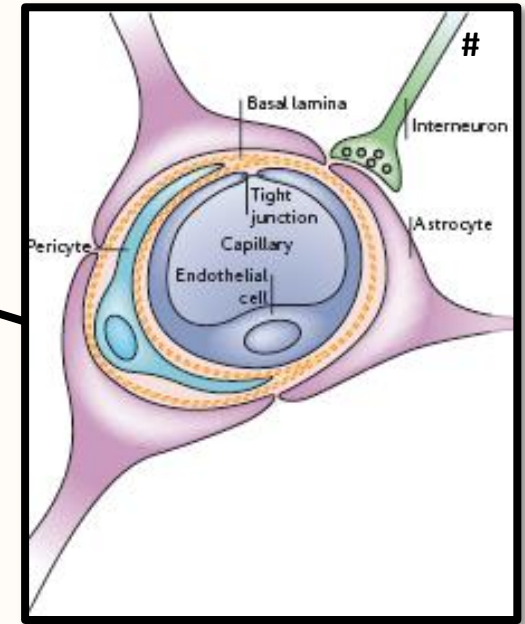
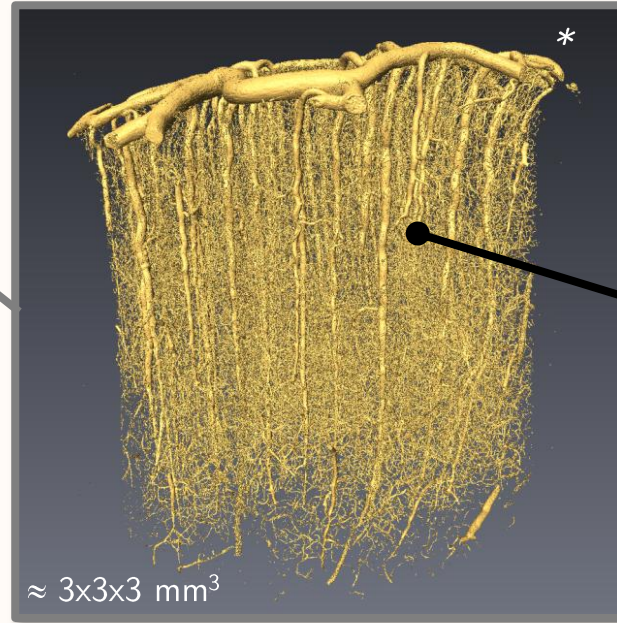
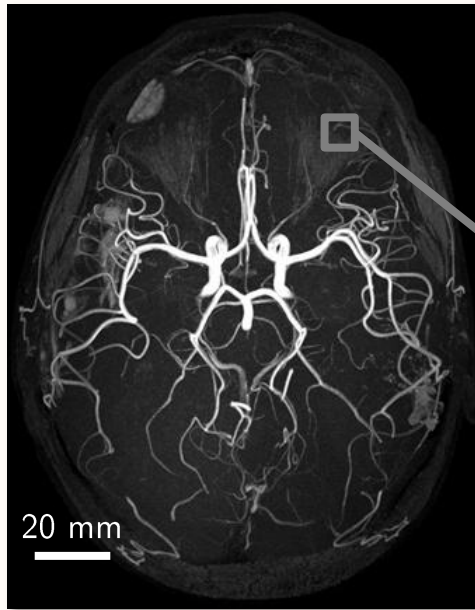
*Thèse de Doctorat soutenue par Nicolas PANNETIER  
encadré par Emmanuel BARBIER*

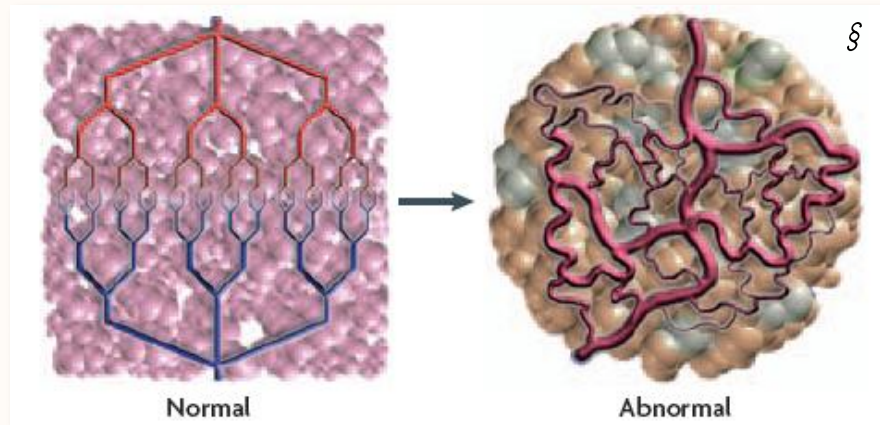
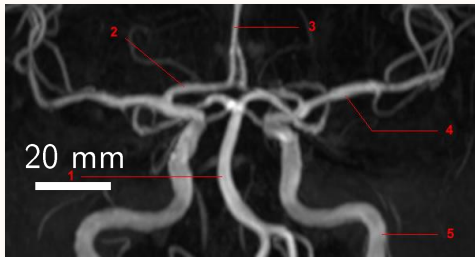
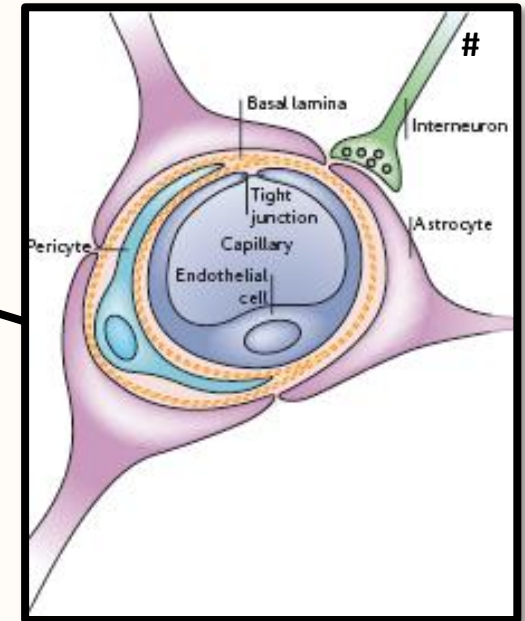
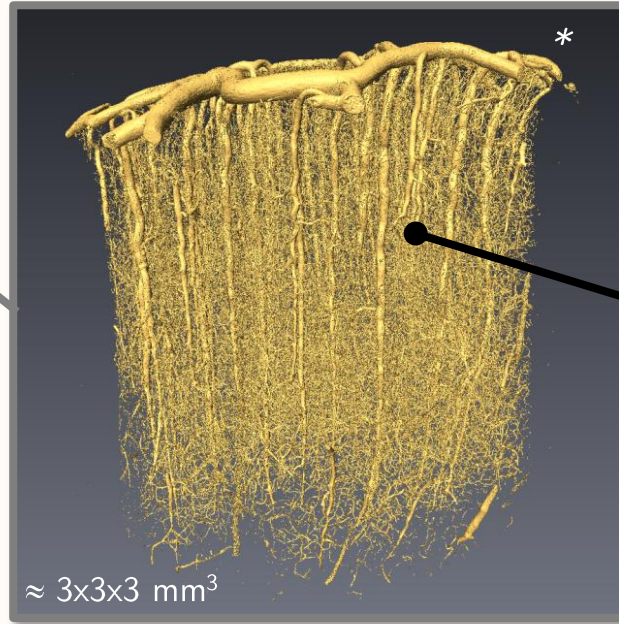
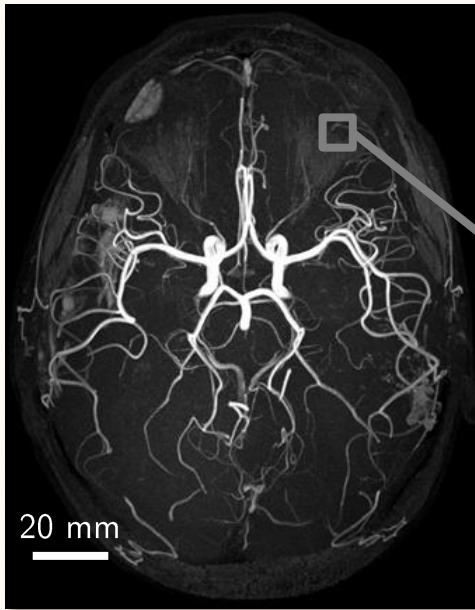
*Le 17 Décembre 2010*

devant le jury composé de : Chrit Moonen  
Ralph Sinkus  
Frank Kober  
Antoine Delon  
Emmanuel Barbier

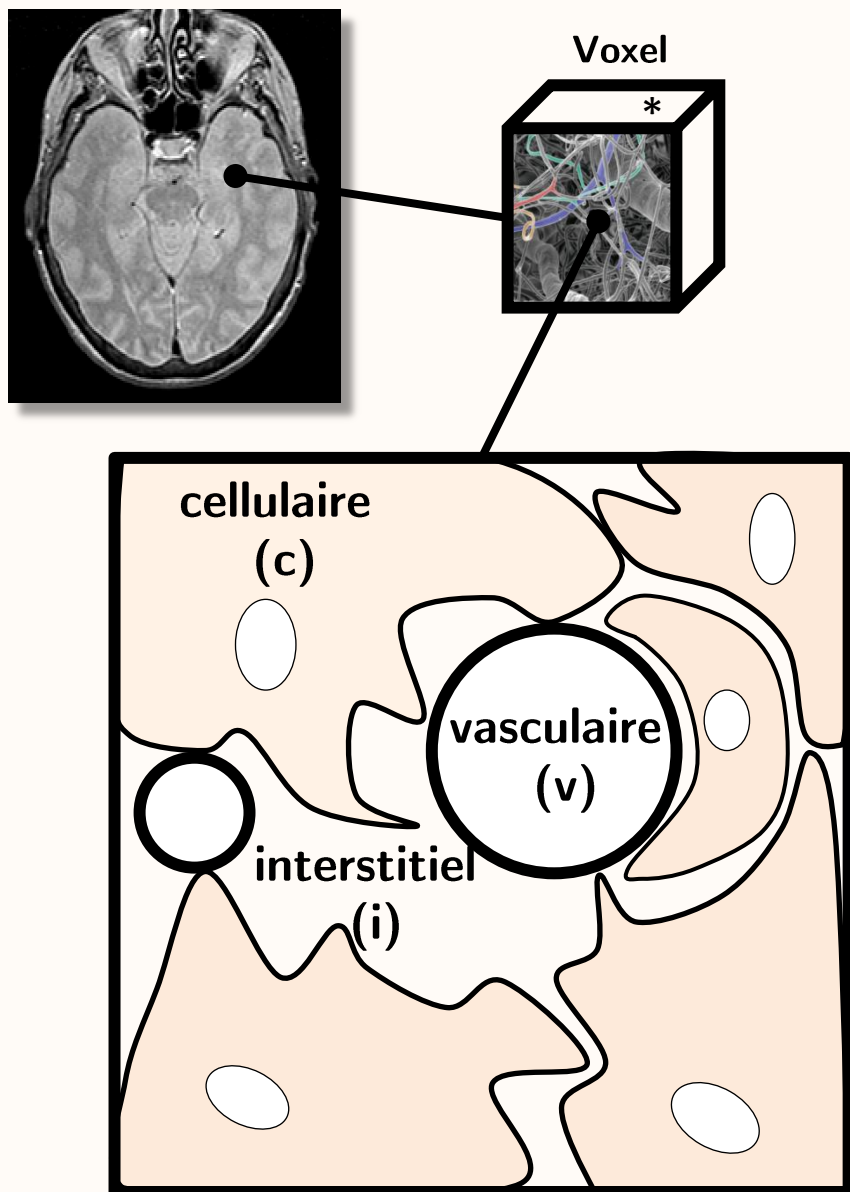
*Grenoble Institut des Neurosciences – INSERM U836 - UJF - CEA -CHU  
Equipe 5 – NeuroImagerie Fonctionnelle et Métabolique*

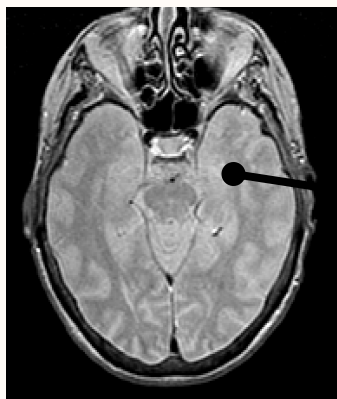




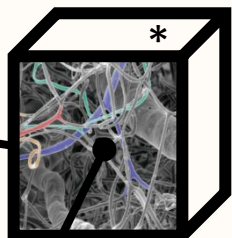


\*Guibert, Thèse de Doctorat (2009)  
# Abbott, Nat Neuro (2006)  
§ Jain, Nat Neuro (2007)



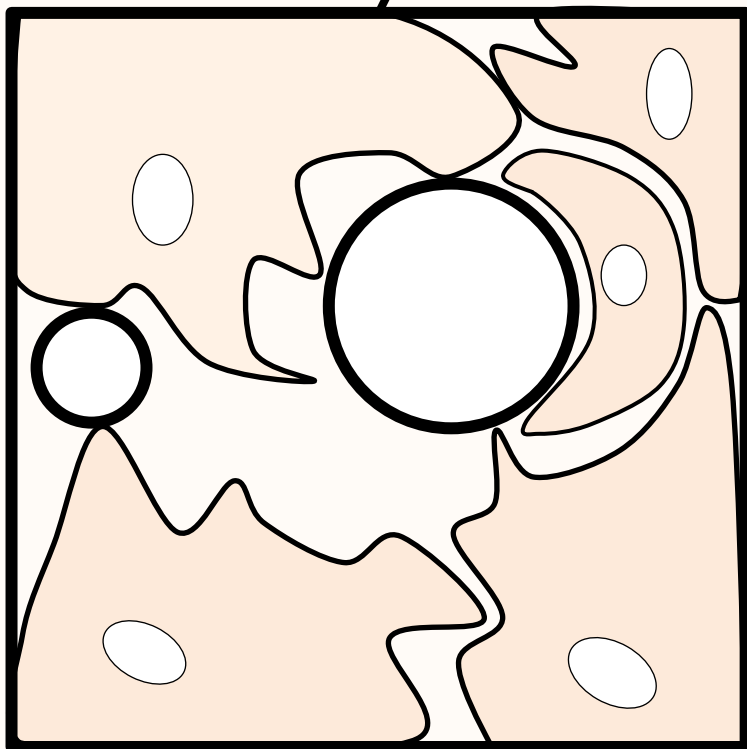


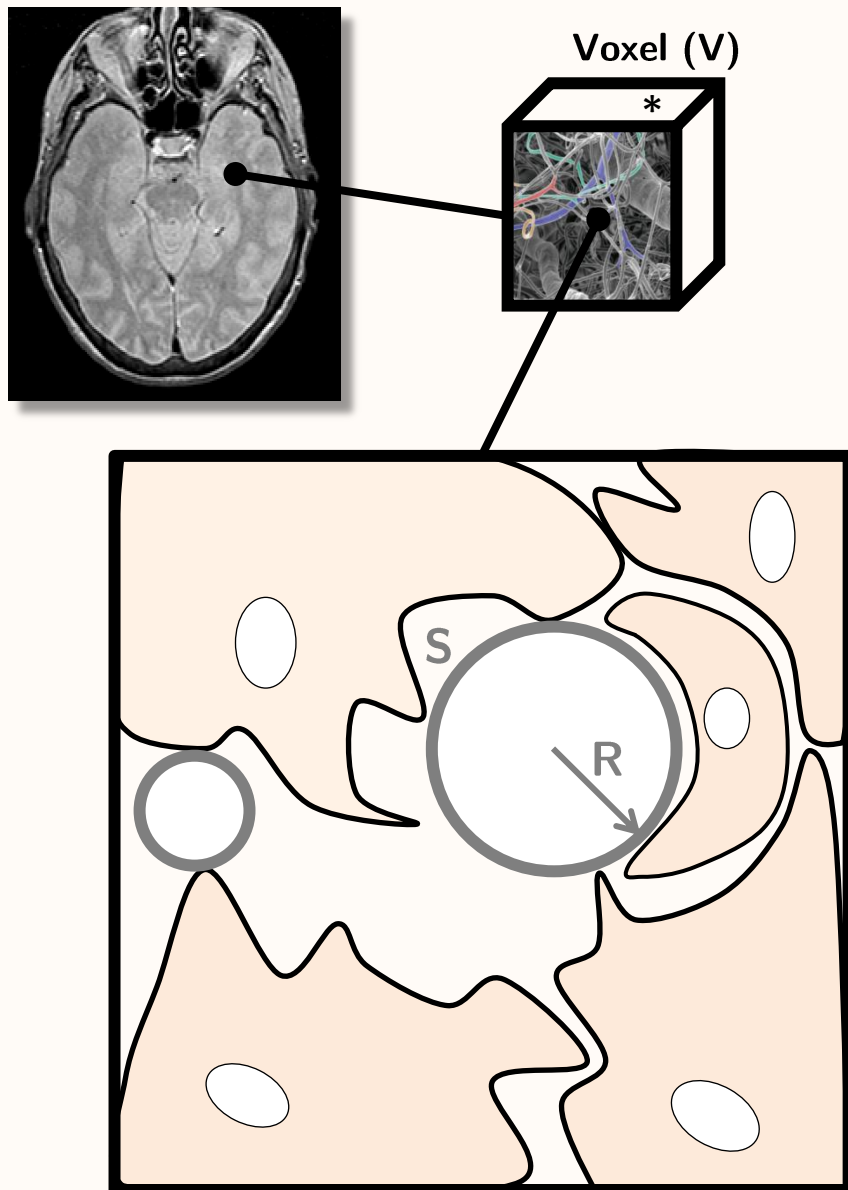
Voxel (V)



## Paramètres :

**Géométriques** ● **V** (volume de l'élément)

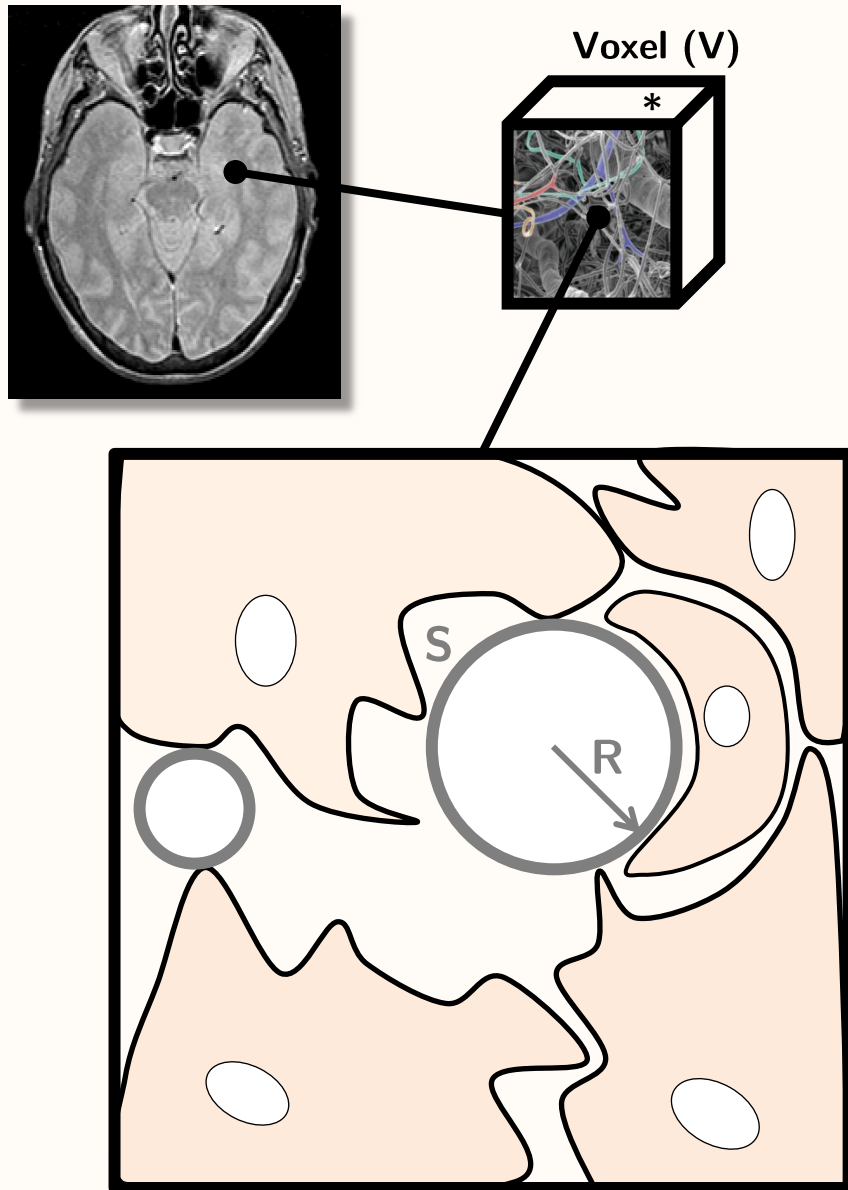




### Paramètres :

#### Géométriques

- $V$  (volume de l'élément)
- $\rho(R)$  (distribution rayon des vaisseaux)
- $\rho(S)$  (distribution surface des vaisseaux)

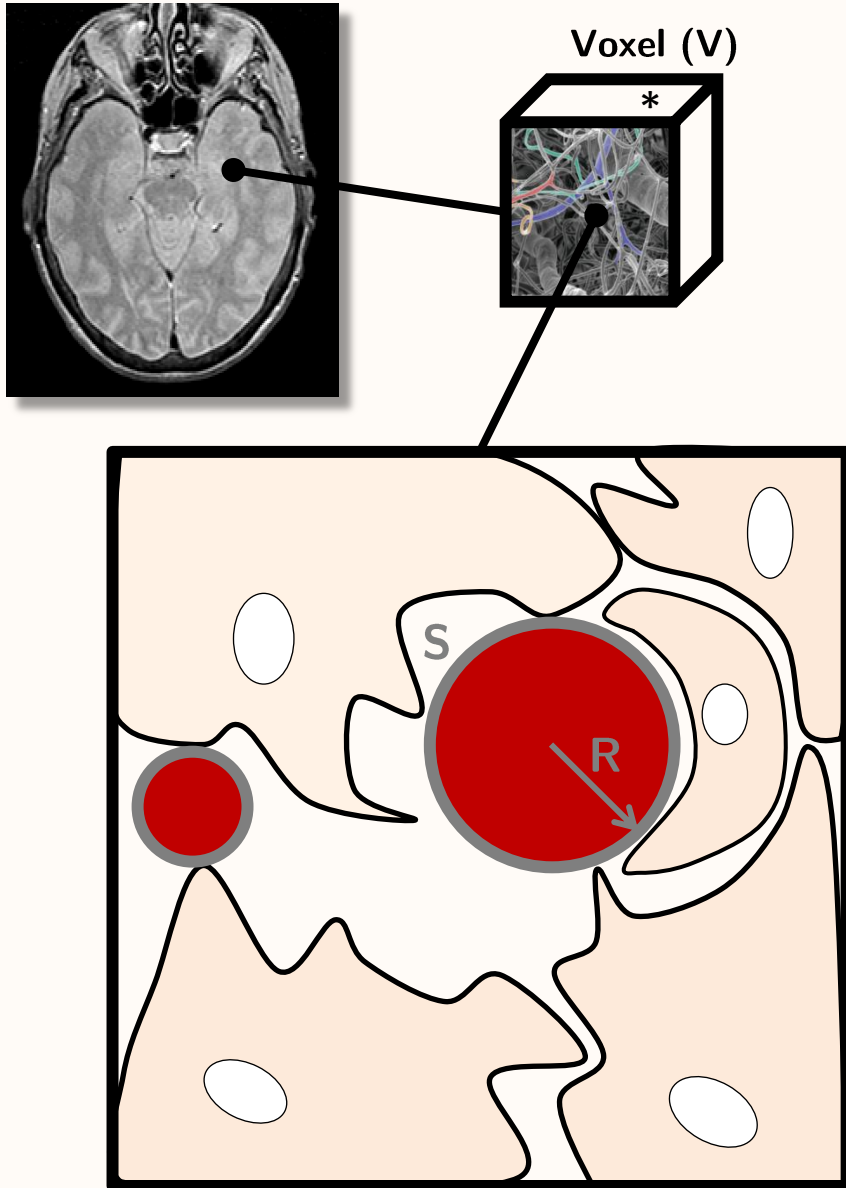


### Paramètres :

#### Géométriques

- $V$  (volume de l'élément)
- $\rho(R)$  (distribution rayon des vaisseaux)
- $\rho(S)$  (distribution surface des vaisseaux)
- ➔ **BVf** (fraction de volume sanguin, %)





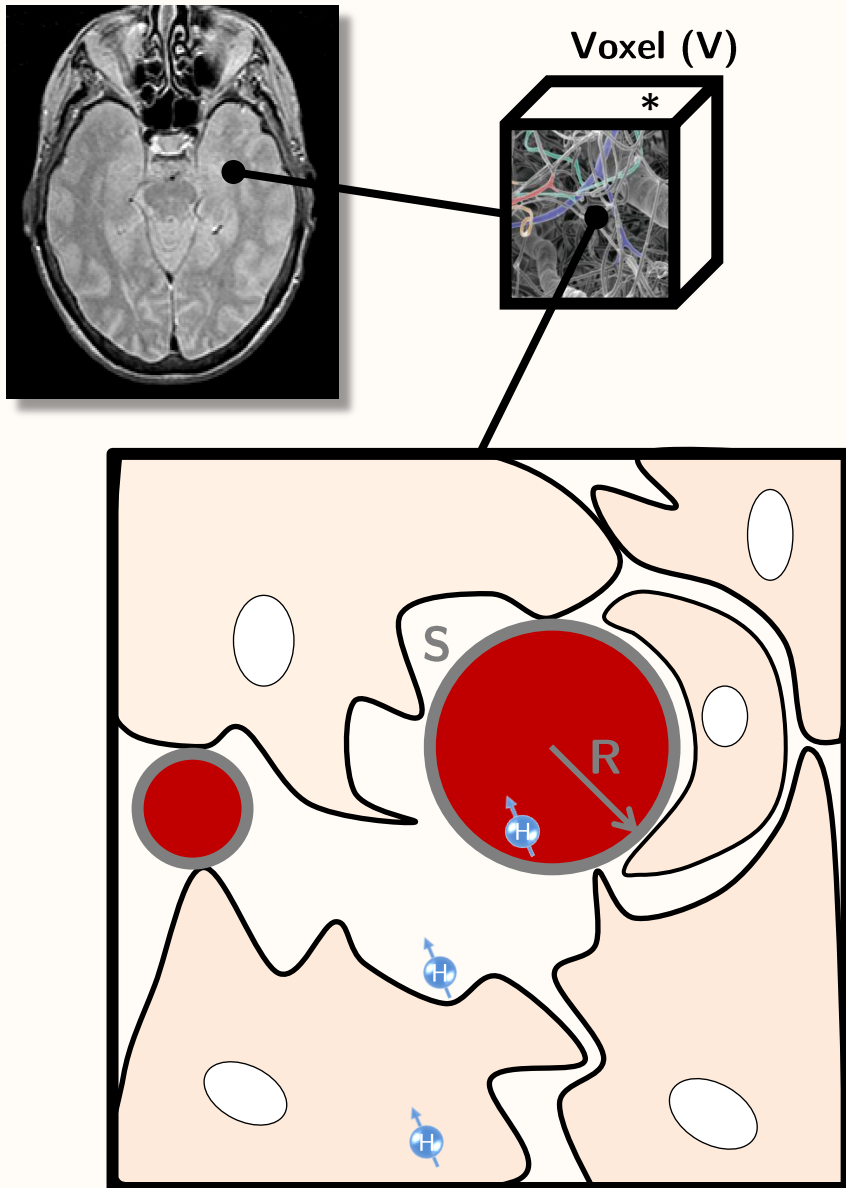
### Paramètres :

#### Géométriques

- **V** (volume de l'élément)
- $\rho(R)$  (distribution rayon des vaisseaux)
- $\rho(S)$  (distribution surface des vaisseaux)
- ➔ **BVf** (fraction de volume sanguin, %)

#### Fonctionnels

- **CBF** (débit sanguin cérébral)



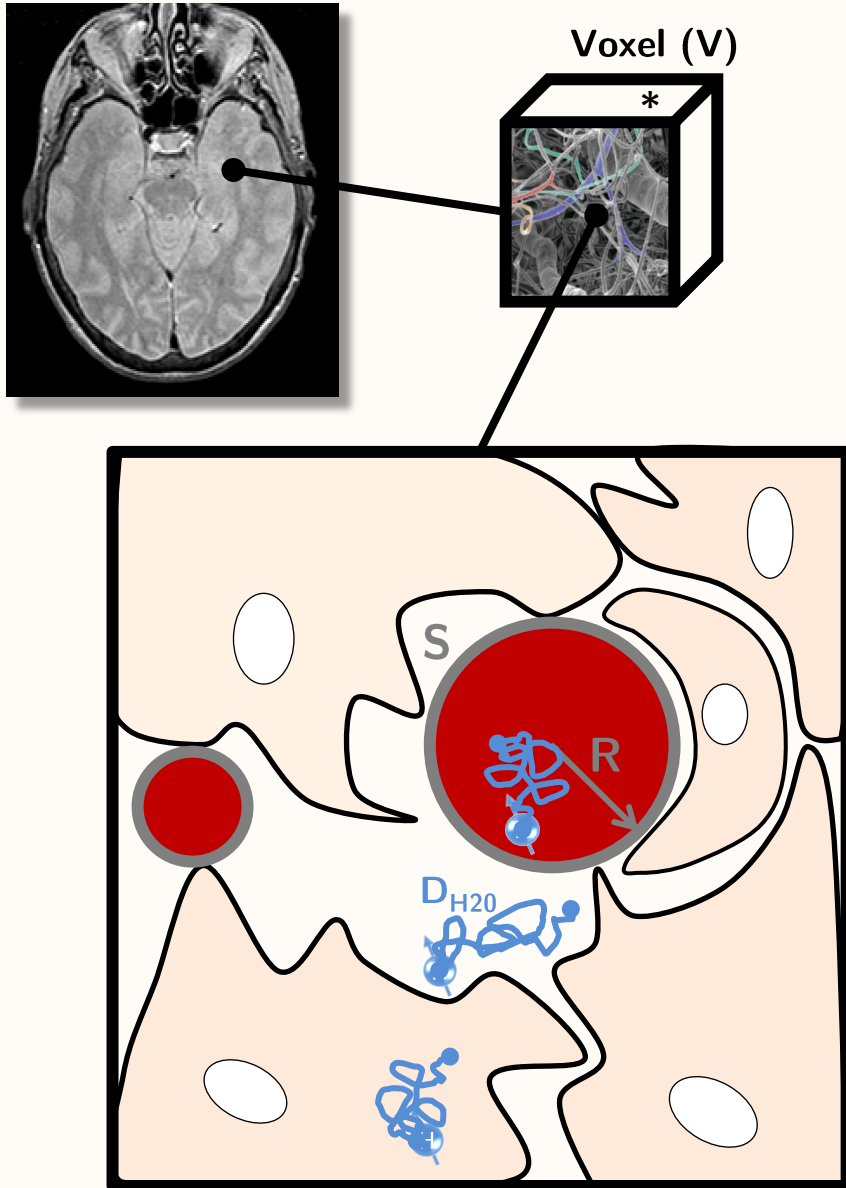
### Paramètres :

#### Géométriques

- **V** (volume de l'élément)
- $\rho(R)$  (distribution rayon des vaisseaux)
- $\rho(S)$  (distribution surface des vaisseaux)
- ➔ **BVf** (fraction de volume sanguin, %)

#### Fonctionnels

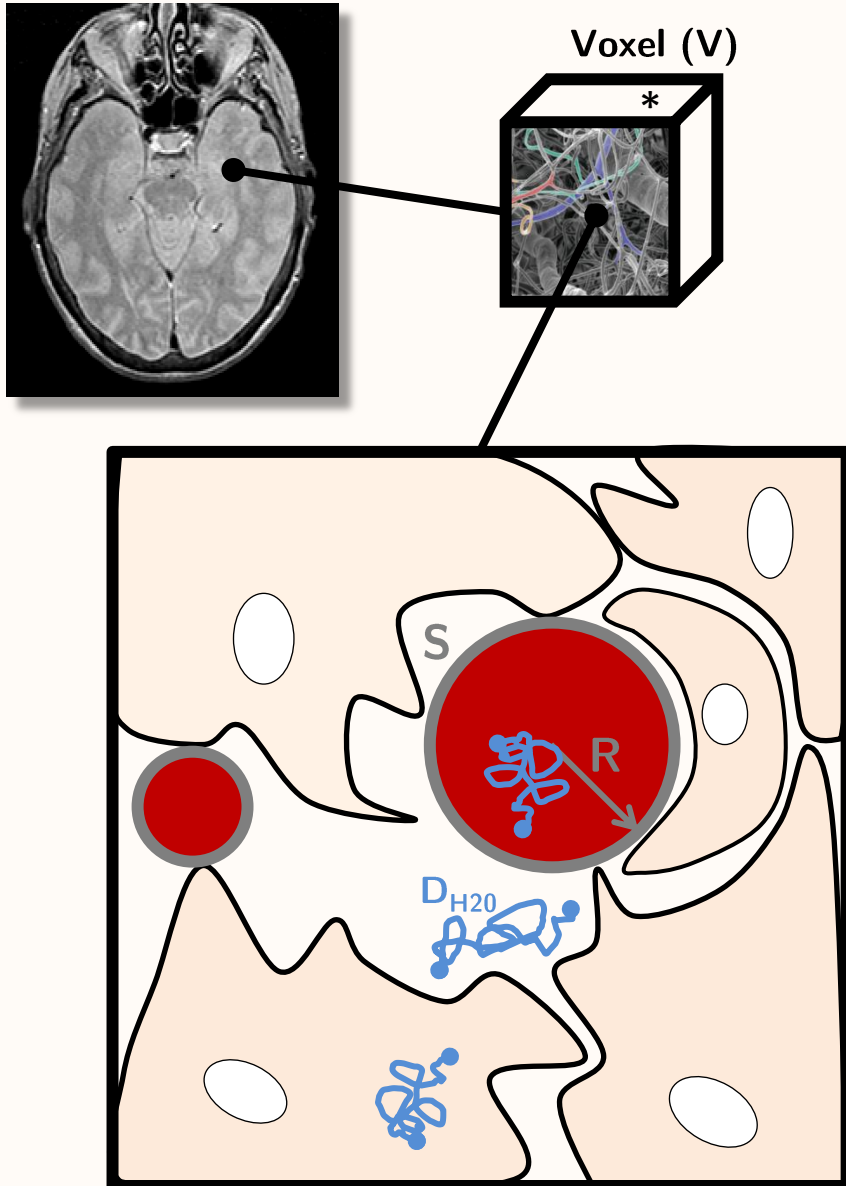
- **CBF** (débit sanguin cérébral)

Paramètres :**Géométriques**

- **V** (volume de l'élément)
- $\rho(R)$  (distribution rayon des vaisseaux)
- $\rho(S)$  (distribution surface des vaisseaux)
- ➔ **BVf** (fraction de volume sanguin, %)

**Fonctionnels**

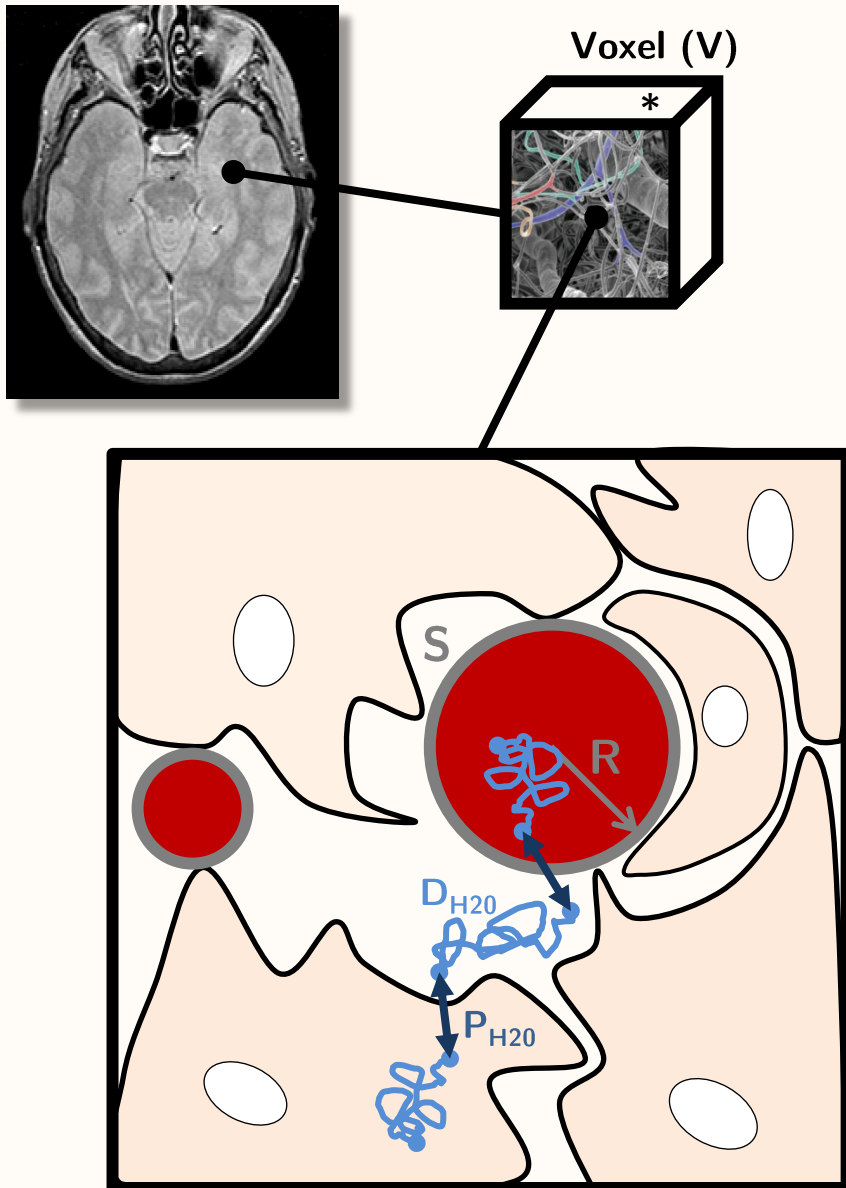
- **CBF** (débit sanguin cérébral)
- $D_{H2O}$  (diffusion de l'eau)

Paramètres :**Géométriques**

- **V** (volume de l'élément)
- $\rho(R)$  (distribution rayon des vaisseaux)
- $\rho(S)$  (distribution surface des vaisseaux)
- ➔ **BVf** (fraction de volume sanguin, %)

**Fonctionnels**

- **CBF** (débit sanguin cérébral)
- $D_{H2O}$  (diffusion de l'eau)

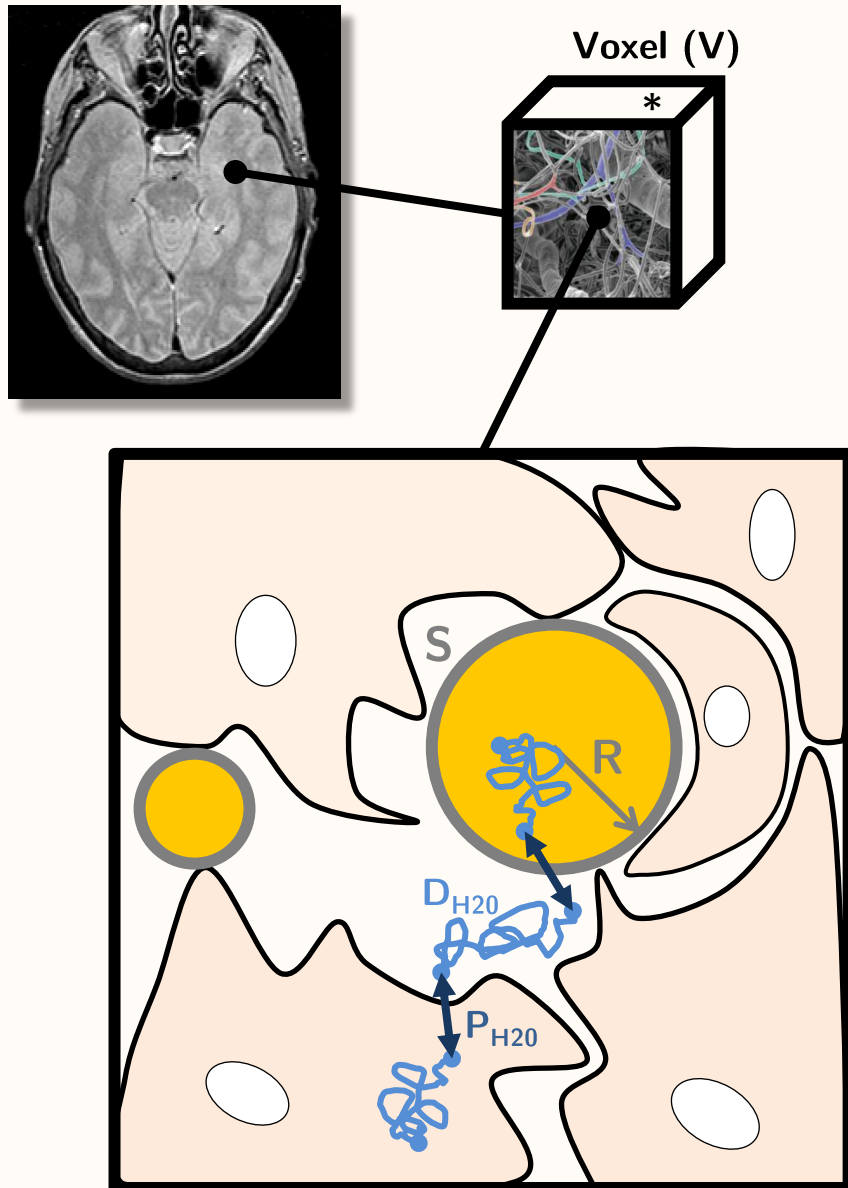
Paramètres :

## Géométriques

- $V$  (volume de l'élément)
- $\rho(R)$  (distribution rayon des vaisseaux)
- $\rho(S)$  (distribution surface des vaisseaux)
- ➔ **BVf** (fraction de volume sanguin, %)

## Fonctionnels

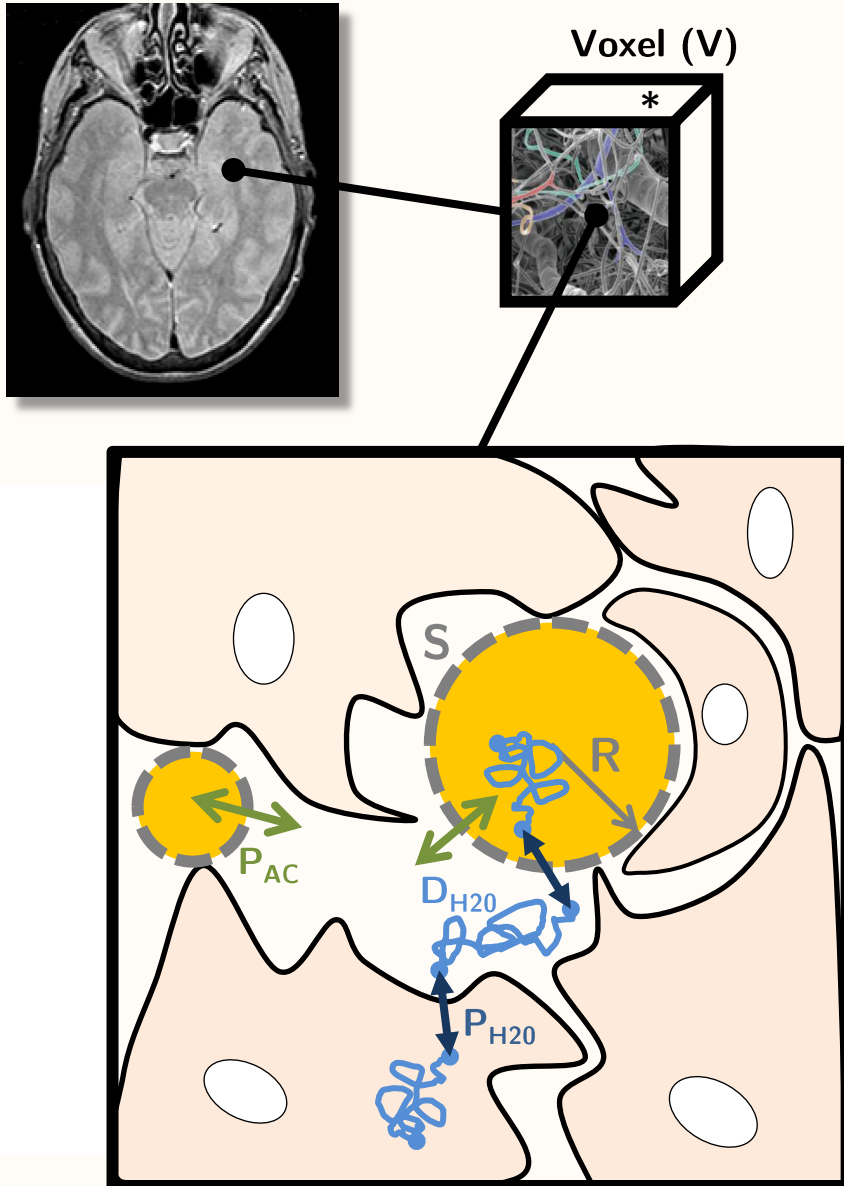
- **CBF** (débit sanguin cérébral)
- $D_{H2O}$  (diffusion de l'eau)
- $P_{H2O}$  (perméabilité des membranes à l'eau)

Paramètres :**Géométriques**

- $V$  (volume de l'élément)
- $\rho(R)$  (distribution rayon des vaisseaux)
- $\rho(S)$  (distribution surface des vaisseaux)
- ➔ **BVf** (fraction de volume sanguin, %)

**Fonctionnels**

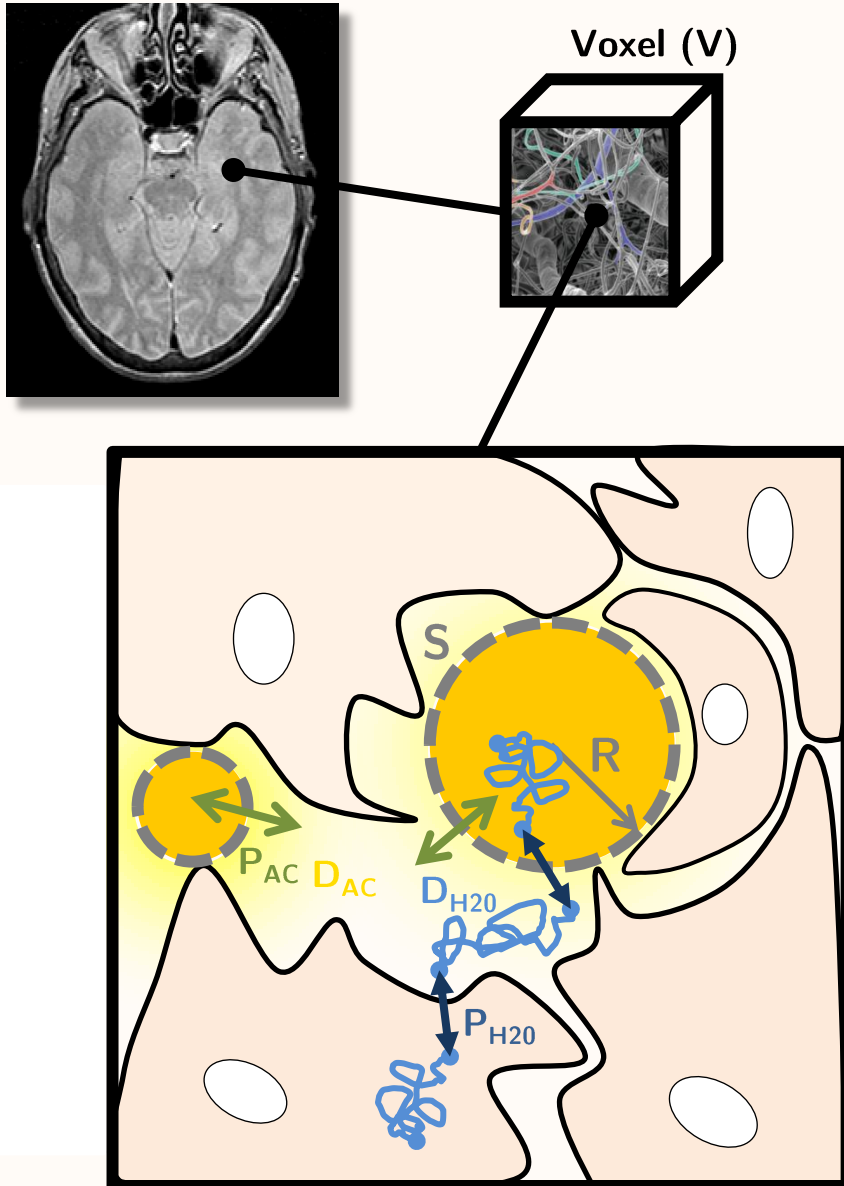
- **CBF** (débit sanguin cérébral)
- $D_{H2O}$  (diffusion de l'eau)
- $P_{H2O}$  (perméabilité des membranes à l'eau)

Paramètres :**Géométriques**

- $V$  (volume de l'élément)
- $\rho(R)$  (distribution rayon des vaisseaux)
- $\rho(S)$  (distribution surface des vaisseaux)
- ➔ **BVf** (fraction de volume sanguin, %)

**Fonctionnels**

- **CBF** (débit sanguin cérébral)
- $D_{H2O}$  (diffusion de l'eau)
- $P_{H2O}$  (perméabilité des membranes à l'eau)
- $P_{AC}$  (perméabilité de la BHE à l'AC)

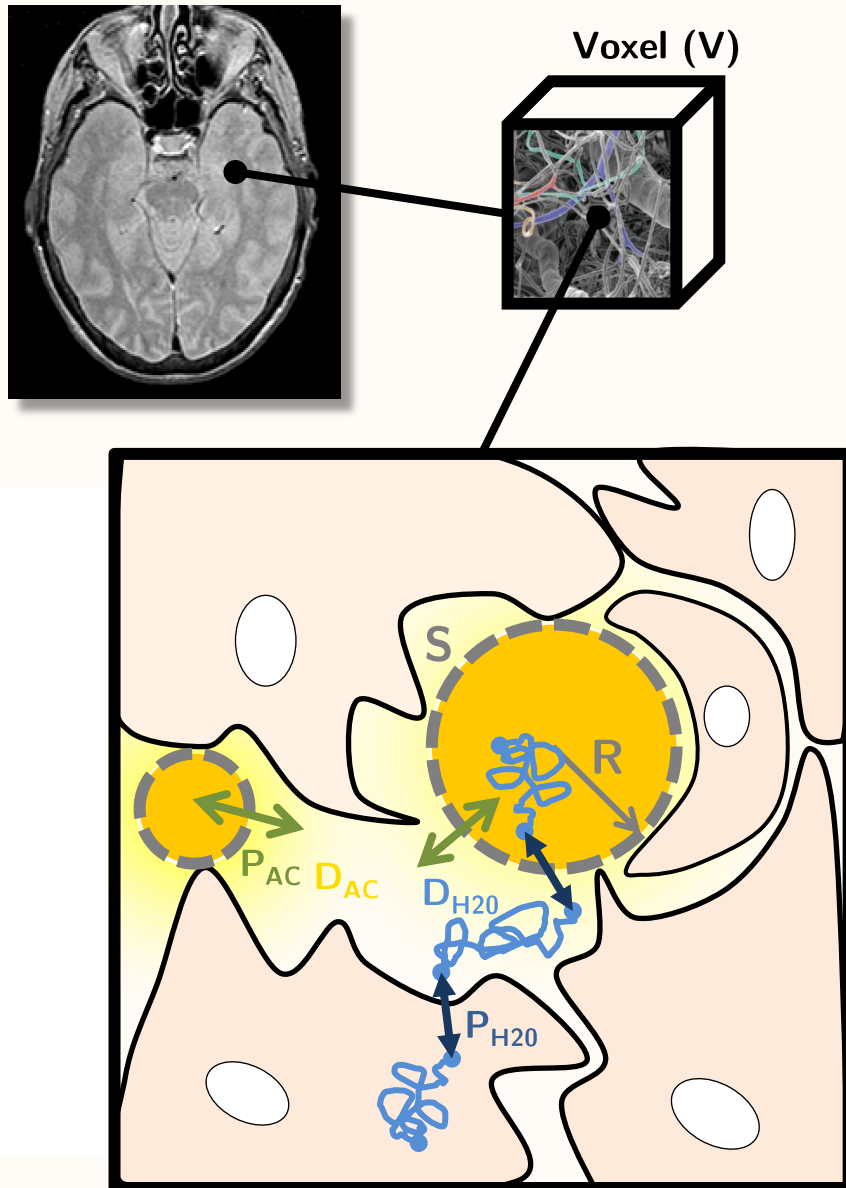
Paramètres :**Géométriques**

- **V** (volume de l'élément)
- $\rho(R)$  (distribution rayon des vaisseaux)
- $\rho(S)$  (distribution surface des vaisseaux)
- ➔ **BVf** (fraction de volume sanguin, %)

**Fonctionnels**

- **CBF** (débit sanguin cérébral)
- $D_{H2O}$  (diffusion de l'eau)
- $P_{H2O}$  (perméabilité des membranes à l'eau)
- $P_{AC}$  (perméabilité de la BHE à l'AC)
- $D_{AC}$  (diffusion de l'AC)



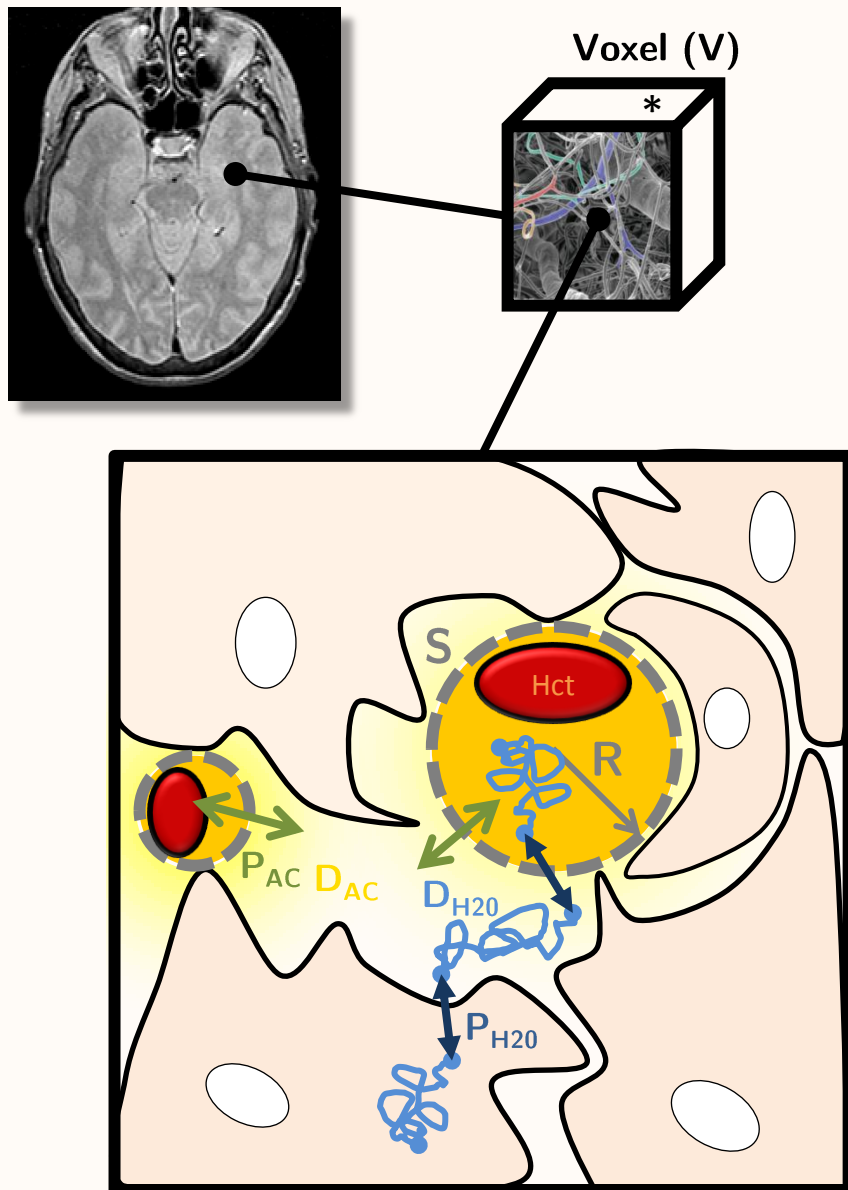
Paramètres :

## Géométriques

- $V$  (volume de l'élément)
- $\rho(R)$  (distribution rayon des vaisseaux)
- $\rho(S)$  (distribution surface des vaisseaux)
- ➔ **BVf** (fraction de volume sanguin, %)

## Fonctionnels

- **CBF** (débit sanguin cérébral)
- $D_{H2O}$  (diffusion de l'eau)
- $P_{H2O}$  (perméabilité des membranes à l'eau)
- $P_{AC}$  (perméabilité de la BHE à l'AC)
- $D_{AC}$  (diffusion de l'AC)

Paramètres :

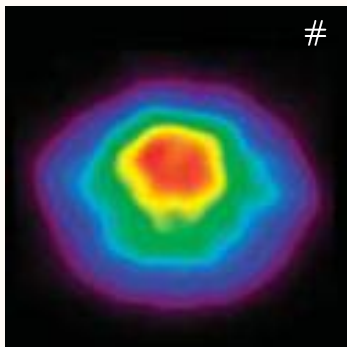
## Géométriques

- $V$  (volume de l'élément)
- $\rho(R)$  (distribution rayon des vaisseaux)
- $\rho(S)$  (distribution surface des vaisseaux)
- ➔ **BVf** (fraction de volume sanguin, %)

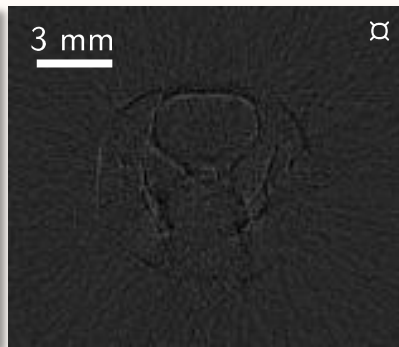
## Fonctionnels

- **CBF** (débit sanguin cérébral)
- $D_{H2O}$  (diffusion de l'eau)
- $P_{H2O}$  (perméabilité des membranes à l'eau)
- $P_{AC}$  (perméabilité de la BHE à l'AC)
- $D_{AC}$  (diffusion de l'AC)
- **Hct** (taux d'hématocrite)
- **SO<sub>2</sub>** (saturation en oxygène de l'hémoglobine)
- etc.

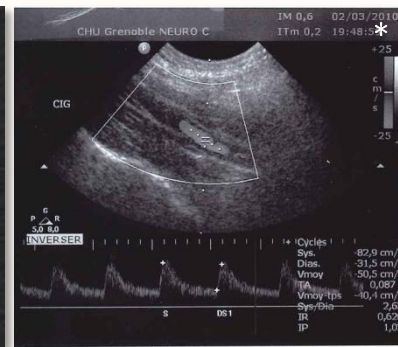
	PET – SPECT	Scanner X	Doppler	IRM
Résolution (mm <sup>3</sup> )	≈ 12	≈ 9.10 <sup>-2</sup>	N/A	≈ 5.10 <sup>-2</sup>
Irradiation (mSv)	≈ 1 – 7	≈ 2,5	/	/
CBF	X	X	X	X
BVf	X	X	X (vitesse)	X
Rayons	/	/	/	X
BHE (P <sub>AC</sub> /D <sub>AC</sub> )	X	X	/	X
O <sub>2</sub> (SO <sub>2</sub> /CMRO <sub>2</sub> )	X	/	/	X
D <sub>H2O</sub>	/	/	/	X
Quantitatif	+++	++	++	+



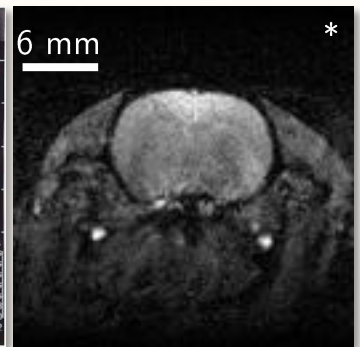
Rat



Rat  
 (Image synchrotron)




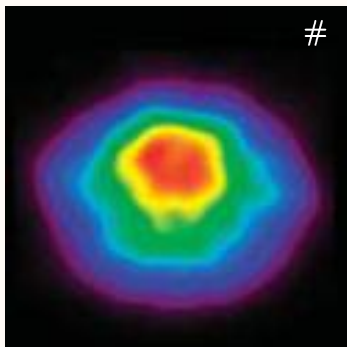
Homme



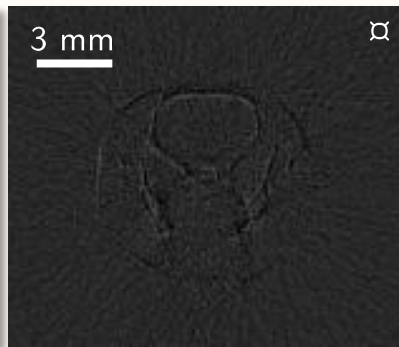
Rat

# Temma, JCBFM (2010)  
 x Collab, P Deman, GIN – Equipe 6  
 \* GIN – Equipe 5

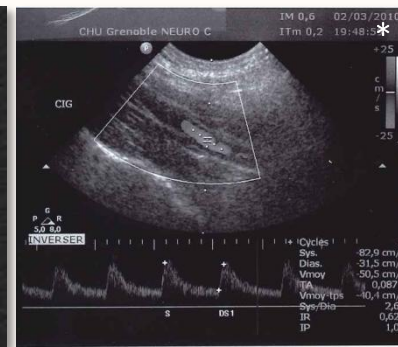
	PET – SPECT	Scanner X	Doppler	IRM
Résolution (mm <sup>3</sup> )	≈ 12	≈ 9.10 <sup>-2</sup>	N/A	≈ 5.10 <sup>-2</sup>
Irradiation (mSv)	≈ 1 – 7	≈ 2,5	/	/
CBF	X	X	X	X
BVf	X	X	X (vitesse)	X
Rayons	/	/	/	X
BHE (P <sub>AC</sub> /D <sub>AC</sub> )	X	X	/	X
O <sub>2</sub> (SO <sub>2</sub> /CMRO <sub>2</sub> )	X	/	/	X
D <sub>H2O</sub>	/	/	/	X
Quantitatif	+++	++	++	+ 



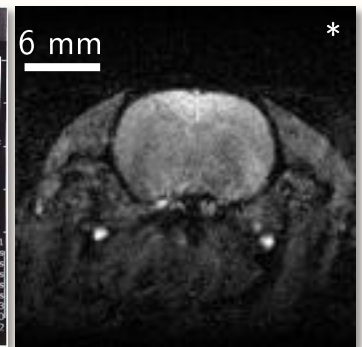
Rat



Rat  
(Image synchrotron)



Homme

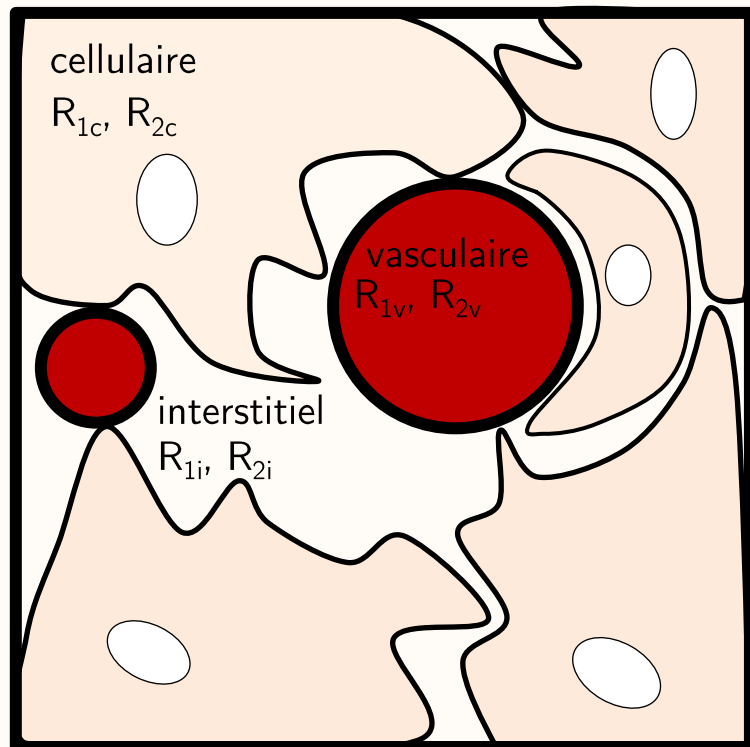


Rat

# Temma, JCBFM (2010)  
x Collab, P Deman, GIN – Equipe 6  
\* GIN – Equipe 5

$R_1$  : vitesse de relaxation longitudinale

$R_2$  : vitesse de relaxation transversale



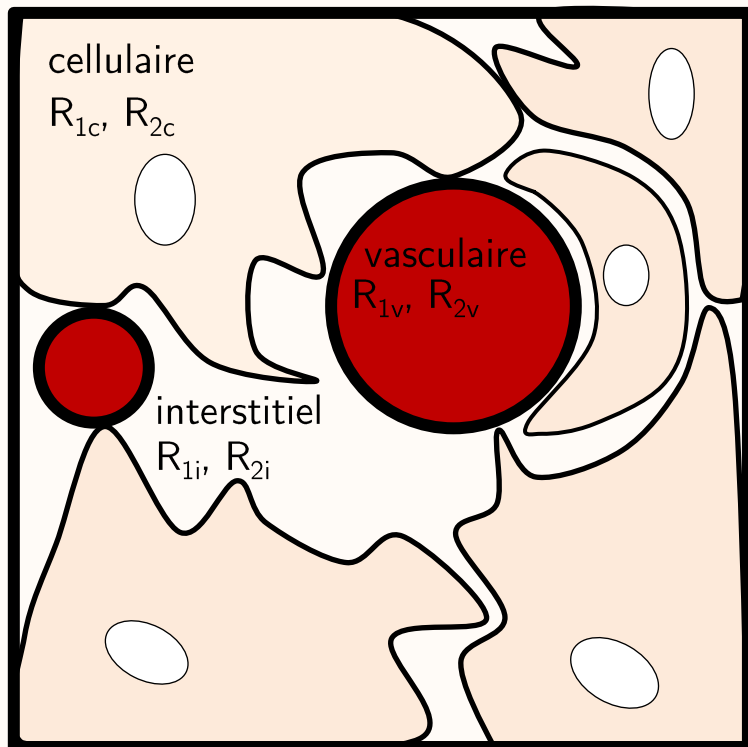
R<sub>1</sub> : vitesse de relaxation longitudinale

R<sub>2</sub> : vitesse de relaxation transversale

En écho de gradient (GE)    En écho de spin (SE)

R<sub>2</sub>\*

R<sub>2</sub>



R<sub>1</sub> : vitesse de relaxation longitudinale

R<sub>2</sub> : vitesse de relaxation transversale

~~En écho de gradient (GE)~~

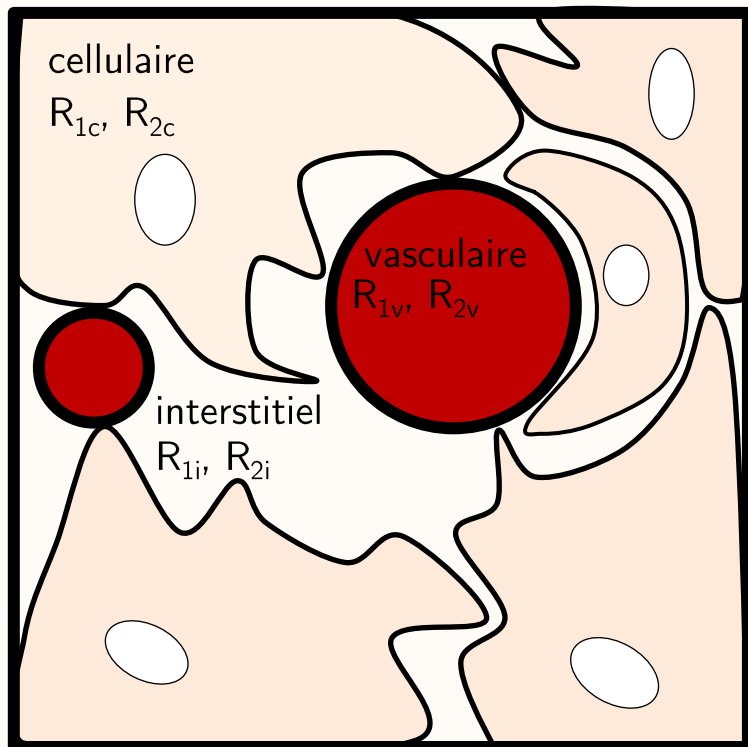
~~R<sub>2</sub><sup>\*</sup>~~

R<sub>2</sub><sup>GE</sup>

~~En écho de spin (SE)~~

~~R<sub>2</sub>~~

R<sub>2</sub><sup>SE</sup>

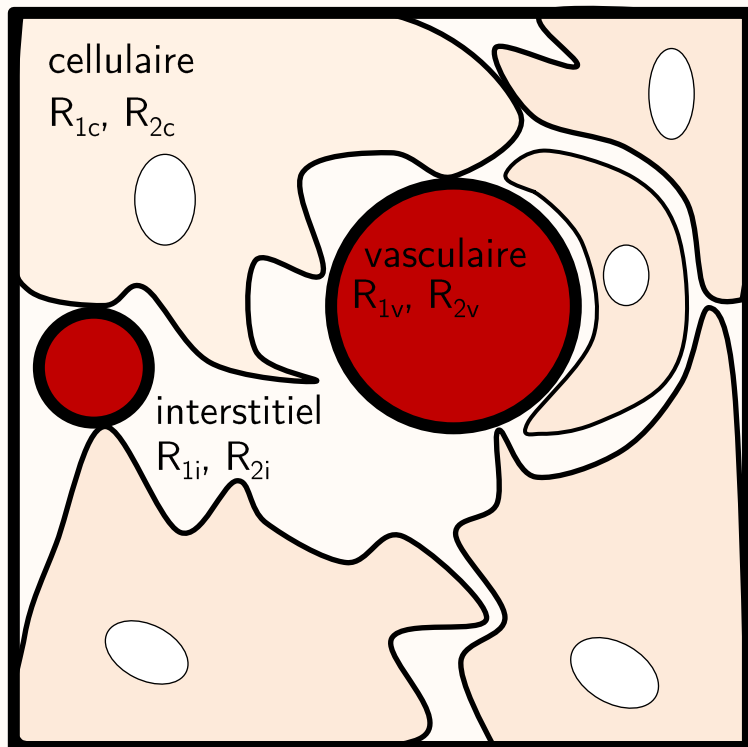


$R_1$  : vitesse de relaxation longitudinale

$R_2$  : vitesse de relaxation transversale

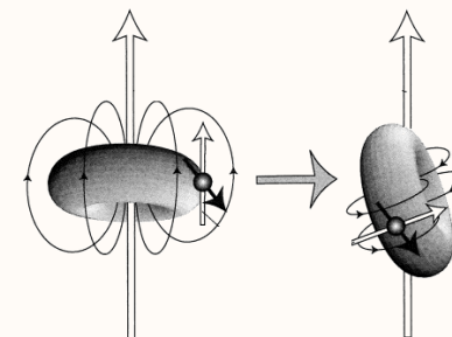
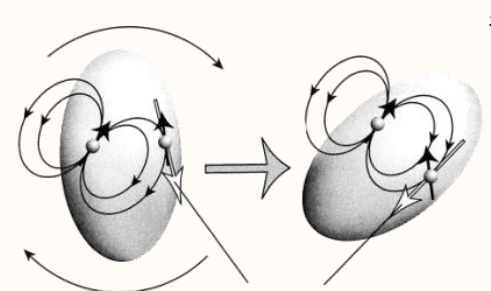
3 compartiments :  $v_v$ ,  $v_c$ ,  $v_i$  (=Porosité)

Si pas d'échange :  $R_i = v_v \cdot R_{iv} + v_c \cdot R_{ic} + v_i \cdot R_{ii}$



$$R_1 = R_{1\text{micro}}$$

$$R_2 = R_{2\text{micro}}$$



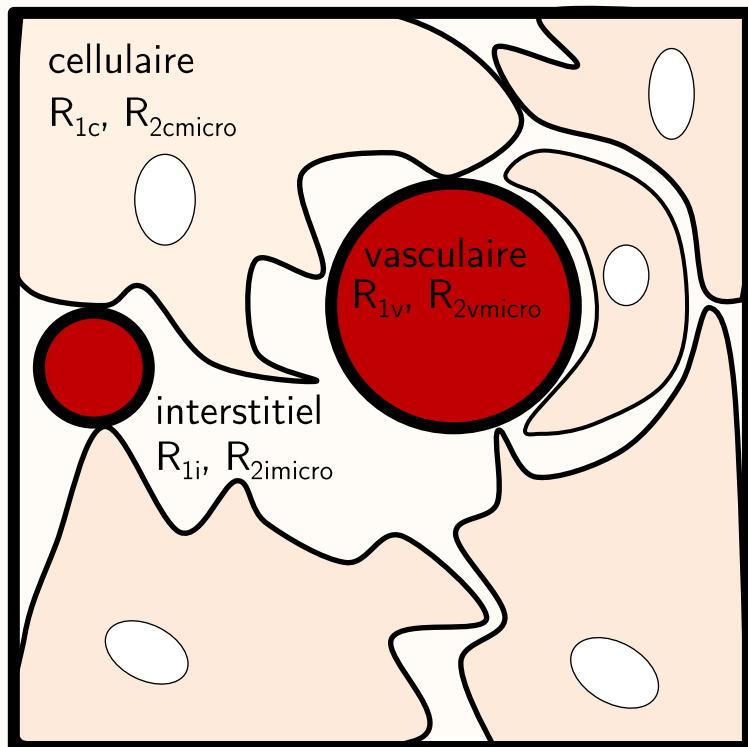


$R_1$  : vitesse de relaxation longitudinale

$R_2$  : vitesse de relaxation transversale

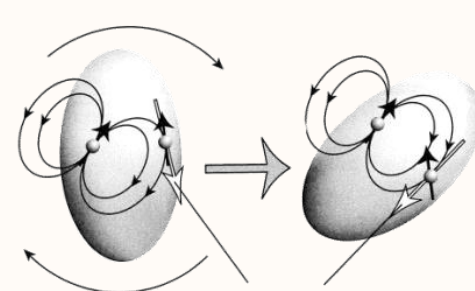
3 compartiments :  $v_v$ ,  $v_c$ ,  $v_i$  (=Porosité)

Si pas d'échange :  $R_i = v_v \cdot R_{iv} + v_c \cdot R_{ic} + v_i \cdot R_{ii}$



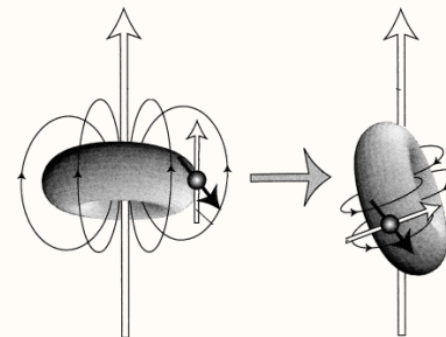
$R_1$

$R_2 = R_{2\text{micro}}$



#

Modulation du  
champ dipolaire  
local par rotation

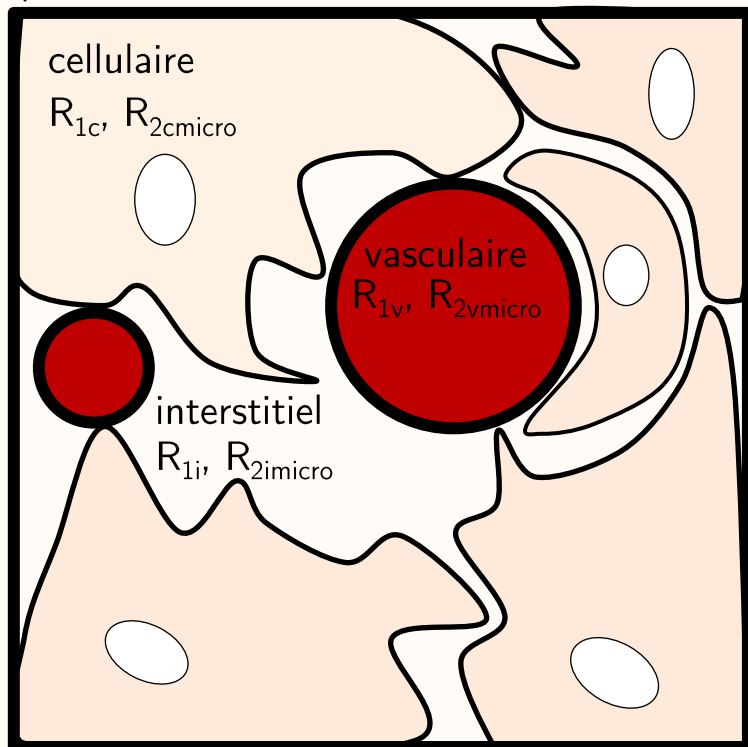
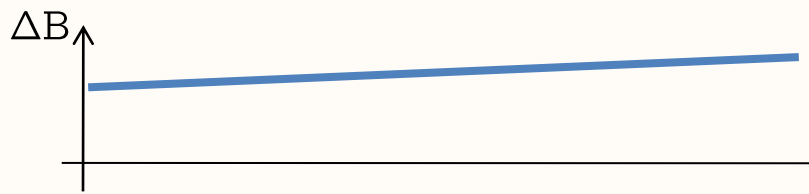


Modulation de  
l'interaction du  
décalage chimique  
par rotation

$R_1$  : vitesse de relaxation longitudinale

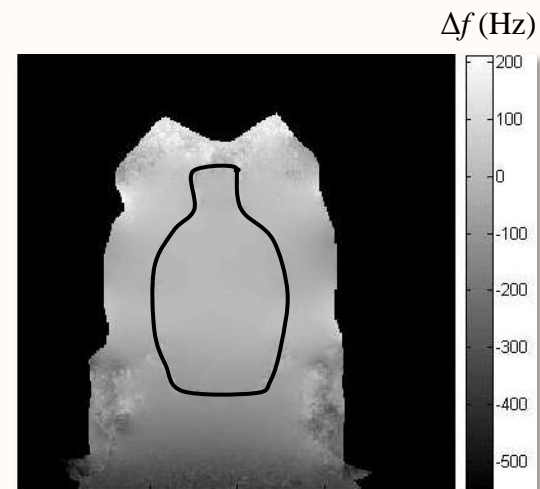
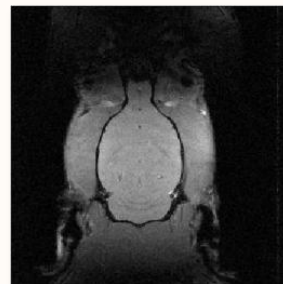
$R_2$  : vitesse de relaxation transversale

3 compartiments :  $v_v$ ,  $v_c$ ,  $v_i$  (=Porosité)



$$R_1$$

$$R_2 = R_{2\text{micro}} + R_{2\text{macro}}$$

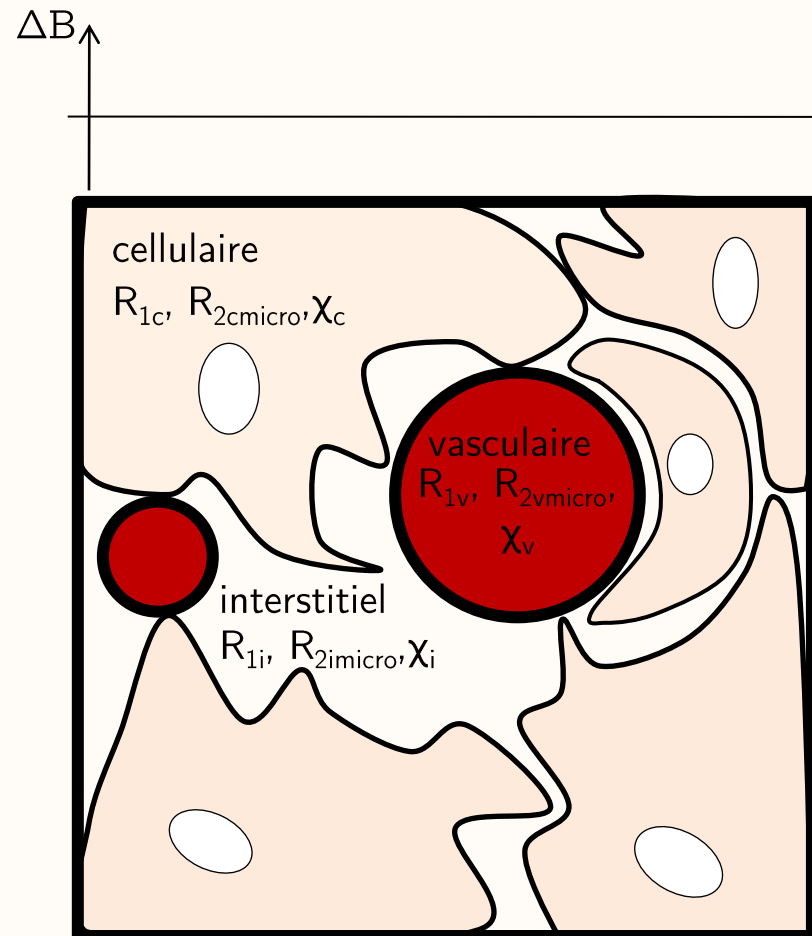


R<sub>1</sub> : vitesse de relaxation longitudinale

R<sub>2</sub> : vitesse de relaxation transversale

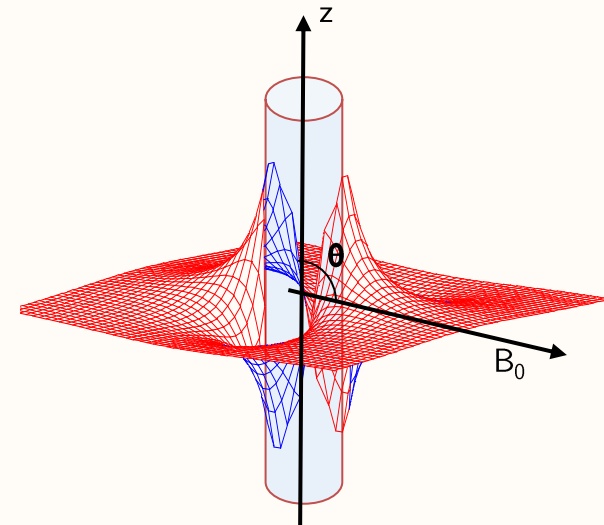
**X** : Susceptibilité magnétique

3 compartiments : v<sub>v</sub>, v<sub>c</sub>, v<sub>i</sub> (=Porosité)



R<sub>1</sub>

$$R_2 = R_{2\text{micro}} + R_{2\text{macro}}$$



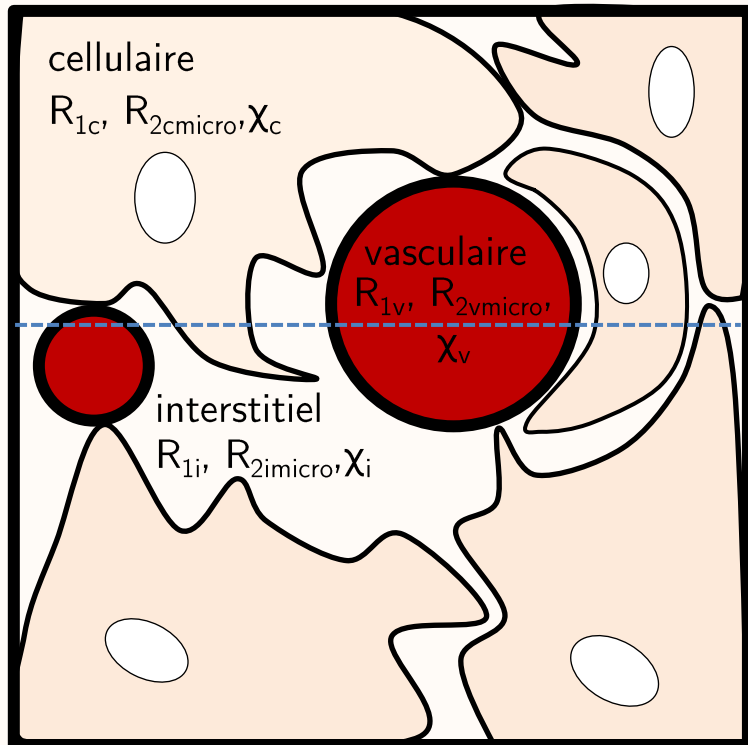
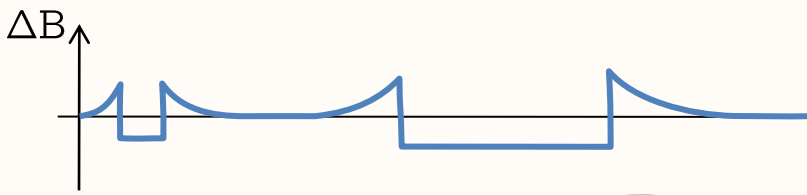
$$\delta B(\vec{\rho}; R_0, \theta, \Delta\chi) = \begin{cases} \Delta\chi B_0 \frac{R_0^2}{\rho^2} \cos(2\varphi) \sin^2\theta, & \text{pour } \rho > R_0 \\ \Delta\chi B_0 \left( \cos^2\theta - \frac{1}{3} \right), & \text{pour } \rho < R_0 \end{cases}$$

R<sub>1</sub> : vitesse de relaxation longitudinale

R<sub>2</sub> : vitesse de relaxation transversale

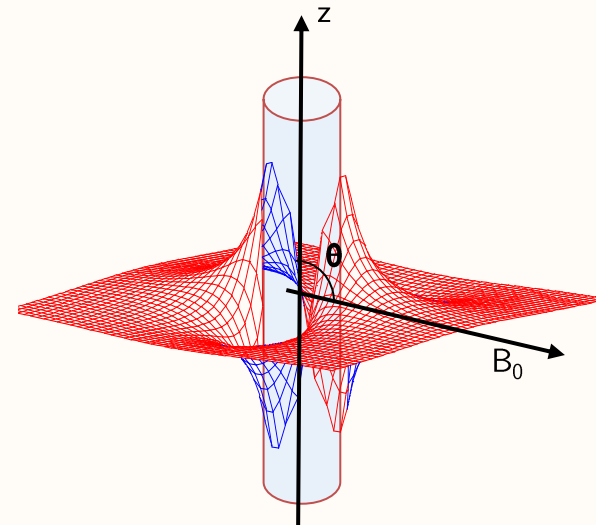
**X** : Susceptibilité magnétique

3 compartiments : v<sub>v</sub>, v<sub>c</sub>, v<sub>i</sub> (=Porosité)



R<sub>1</sub>

$$R_2 = R_{2\text{micro}} + R_{2\text{macro}}$$



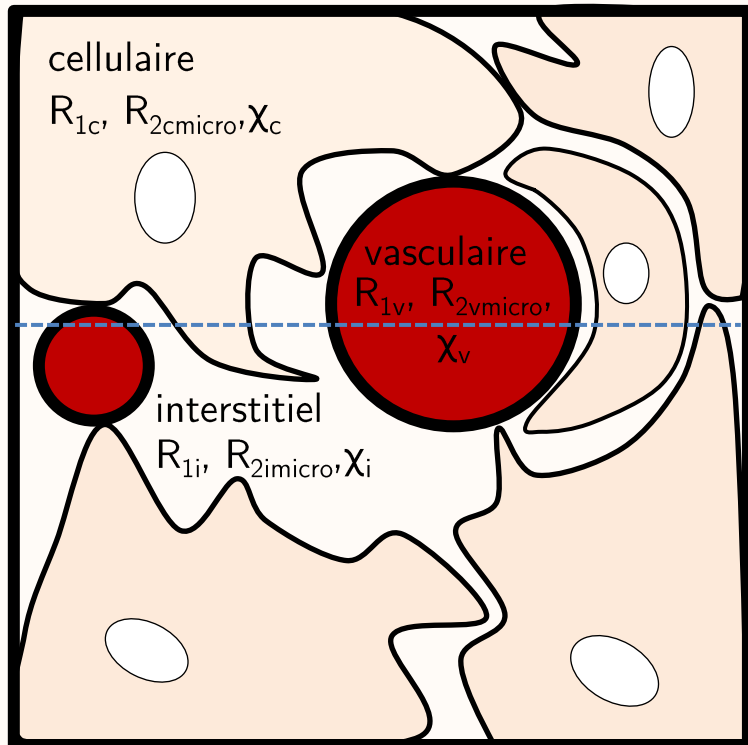
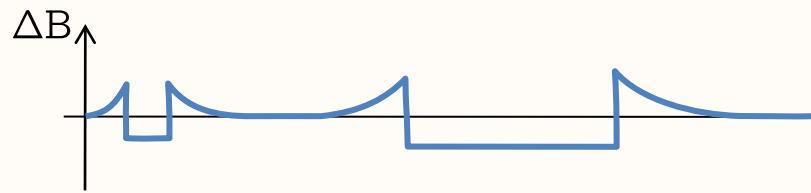
$$\delta B(\vec{\rho} ; R_0, \theta, \Delta\chi) = \begin{cases} \Delta\chi B_0 \frac{R_0^2}{\rho^2} \cos(2\varphi) \sin^2\theta, & \text{pour } \rho > R_0 \\ \Delta\chi B_0 \left( \cos^2\theta - \frac{1}{3} \right), & \text{pour } \rho < R_0 \end{cases}$$

R<sub>1</sub> : vitesse de relaxation longitudinale

R<sub>2</sub> : vitesse de relaxation transversale

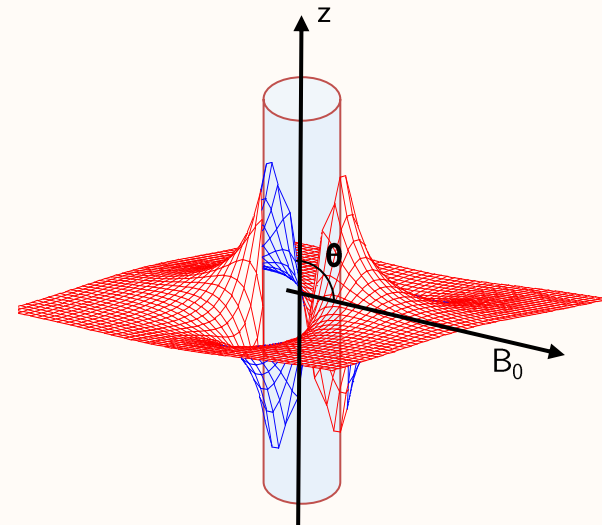
**X** : Susceptibilité magnétique

3 compartiments : v<sub>v</sub>, v<sub>c</sub>, v<sub>i</sub> (=Porosité)



R<sub>1</sub>

$$R_2 = R_{2\text{micro}} + R_{2\text{macro}} + R_{2\text{meso}}$$



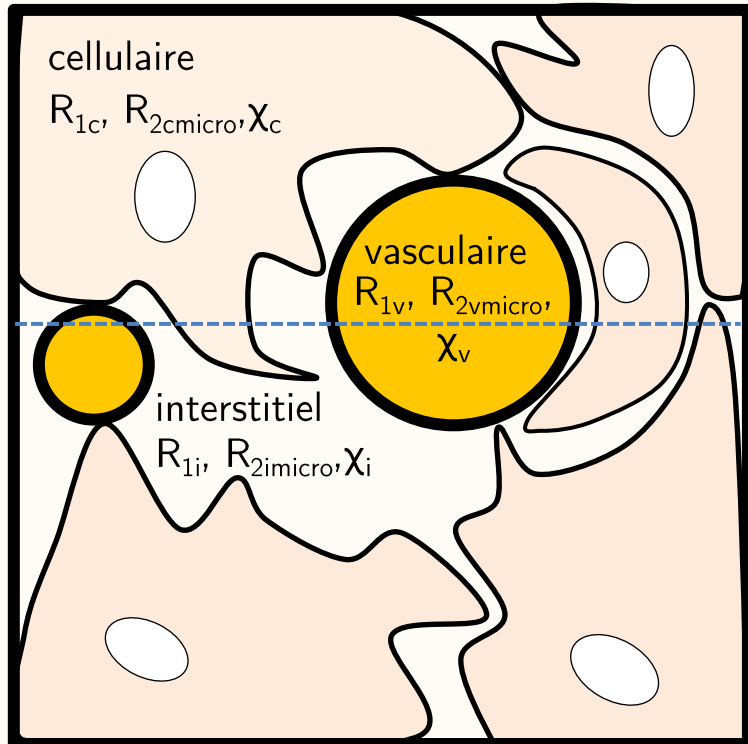
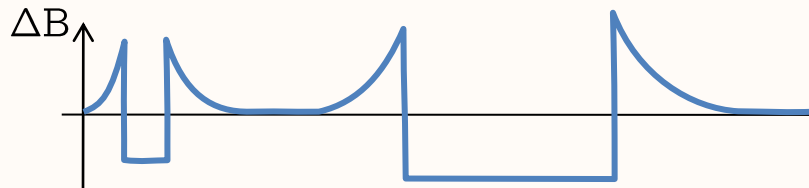
$$\delta B(\vec{\rho} ; R_0, \theta, \Delta\chi) = \begin{cases} \Delta\chi B_0 \frac{R_0^2}{\rho^2} \cos(2\varphi) \sin^2\theta, & \text{pour } \rho > R_0 \\ \Delta\chi B_0 \left( \cos^2\theta - \frac{1}{3} \right), & \text{pour } \rho < R_0 \end{cases}$$

R<sub>1</sub> : vitesse de relaxation longitudinale

R<sub>2</sub> : vitesse de relaxation transversale

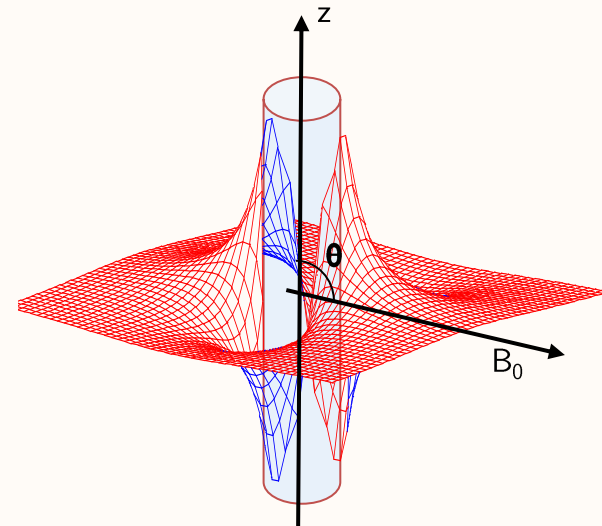
χ : Susceptibilité magnétique

3 compartiments : v<sub>v</sub>, v<sub>c</sub>, v<sub>i</sub> (=Porosité)



R<sub>1</sub>

$$R_2 = R_{2\text{micro}} + R_{2\text{macro}} + R_{2\text{meso}}$$



$$\delta B(\vec{\rho}; R_0, \theta, \Delta\chi) = \begin{cases} \Delta\chi B_0 \frac{R_0^2}{\rho^2} \cos(2\varphi) \sin^2\theta, & \text{pour } \rho > R_0 \\ \Delta\chi B_0 \left( \cos^2\theta - \frac{1}{3} \right), & \text{pour } \rho < R_0 \end{cases}$$

R1, R2,  $\chi$  : en présence d'un AC intravasculaire

$R_1$  : vitesse de relaxation longitudinale

$R_2$  : vitesse de relaxation transversale

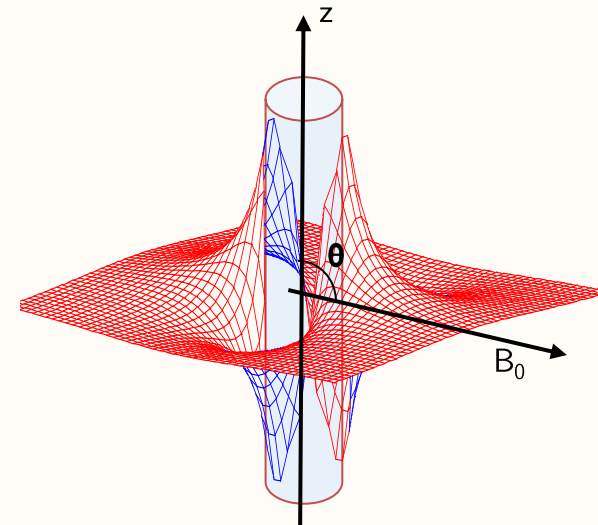
$\chi$  : Susceptibilité magnétique

3 compartiments :  $v_v, v_c, v_i$  (=Porosité)

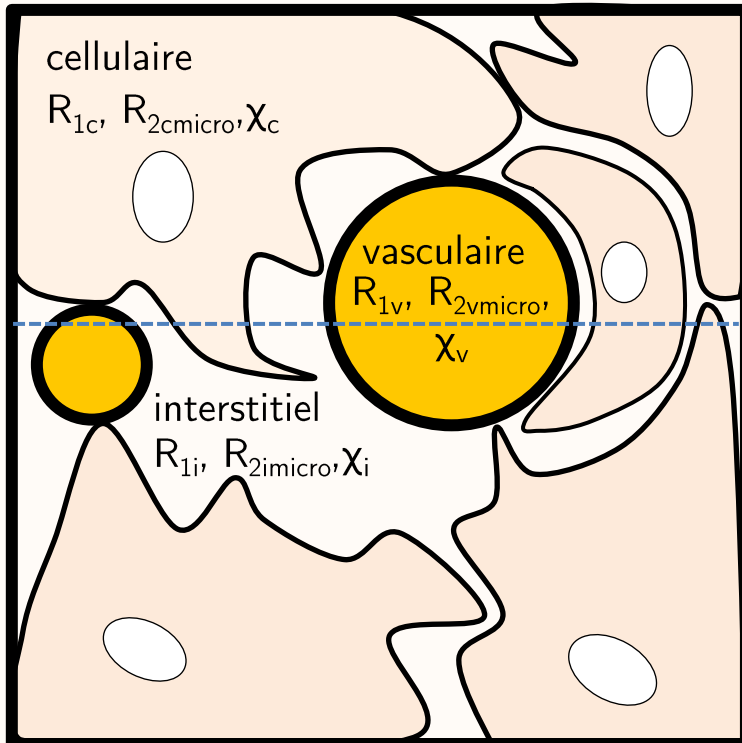
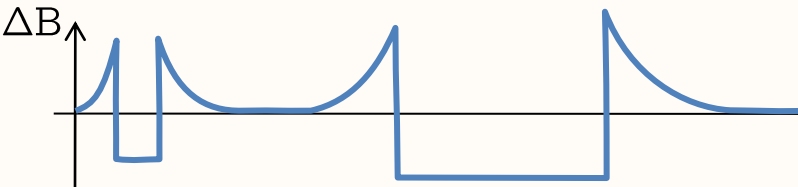
$R_{1v}, R_{2v\text{micro}}, \chi_v$   
 $\Delta\chi_{i-v}$

$R_1$

$$R_2 = R_{2\text{micro}} + R_{2\text{macro}} + R_{2\text{meso}}$$



$$\delta B(\vec{\rho} ; R_0, \theta, \Delta\chi) = \begin{cases} \Delta\chi B_0 \frac{R_0^2}{\rho^2} \cos(2\varphi) \sin^2\theta, & \text{pour } \rho > R_0 \\ \Delta\chi B_0 \left( \cos^2\theta - \frac{1}{3} \right), & \text{pour } \rho < R_0 \end{cases}$$



R1, R2,  $\chi$  : en présence d'un AC intravasculaire

$R_1$  : vitesse de relaxation longitudinale

$R_2$  : vitesse de relaxation transversale

$\chi$  : Susceptibilité magnétique

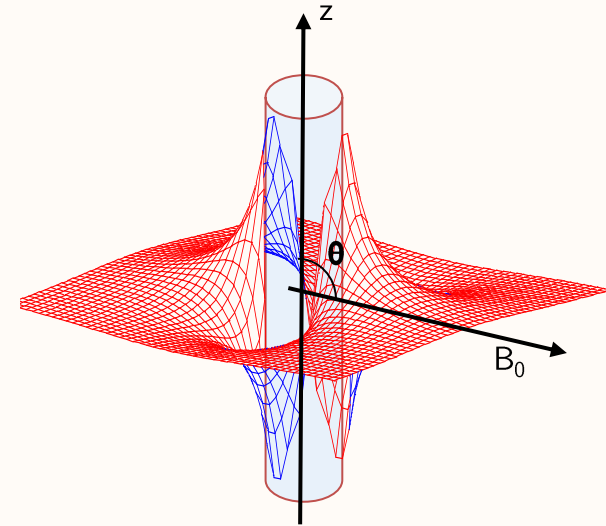
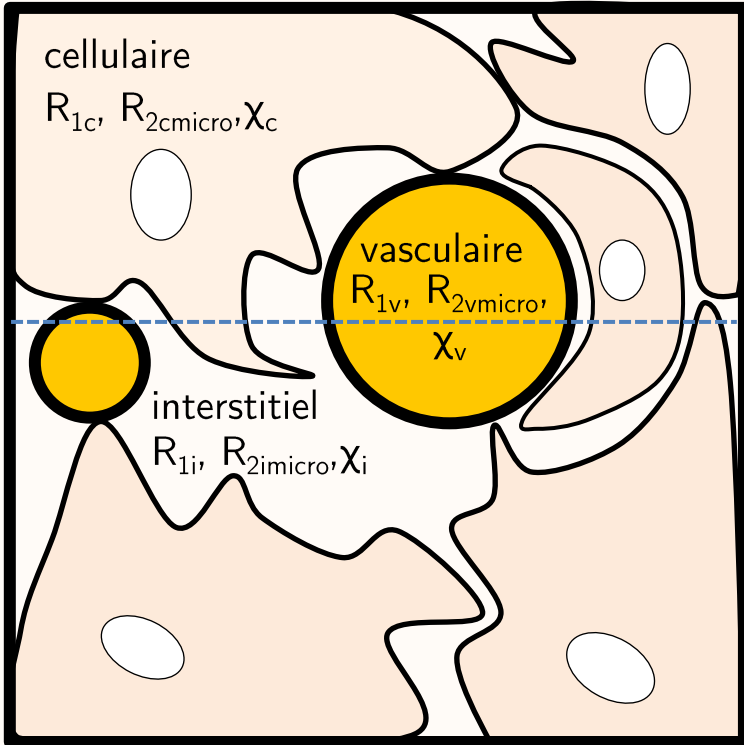
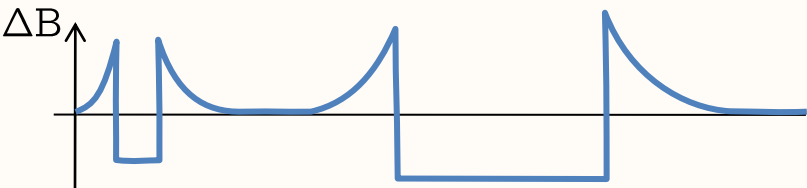
3 compartiments :  $v_v, v_c, v_i$  (=Porosité)

$$R_{1v}, R_{2v\text{micro}}, \chi_v$$

$$\Delta\chi_{i-v}$$

$$R_1 \uparrow$$

$$R_2 = R_{2\text{micro}} \uparrow + R_{2\text{macro}} + R_{2\text{meso}} \uparrow$$



$$\delta B(\vec{\rho} ; R_0, \theta, \Delta\chi) = \begin{cases} \Delta\chi B_0 \frac{R_0^2}{\rho^2} \cos(2\varphi) \sin^2\theta, & \text{pour } \rho > R_0 \\ \Delta\chi B_0 \left( \cos^2\theta - \frac{1}{3} \right), & \text{pour } \rho < R_0 \end{cases}$$



R<sub>1</sub> : vitesse de relaxation longitudinale

R<sub>2</sub> : vitesse de relaxation transversale

χ : Susceptibilité magnétique

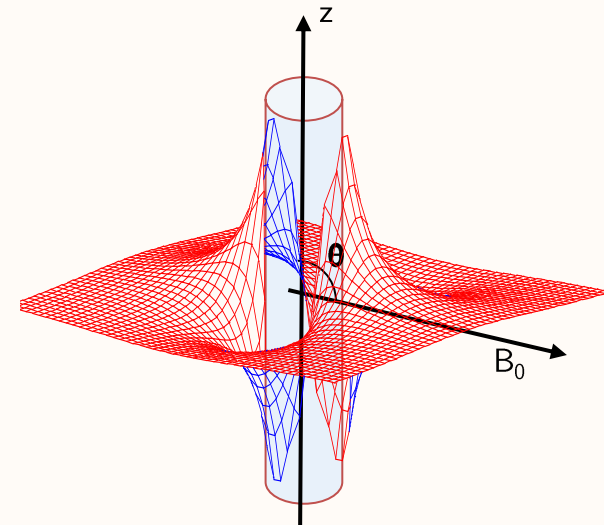
3 compartiments : v<sub>v</sub>, v<sub>c</sub>, v<sub>i</sub> (=Porosité)

$$R_{1v}, R_{2v\text{micro}}, \chi_v$$

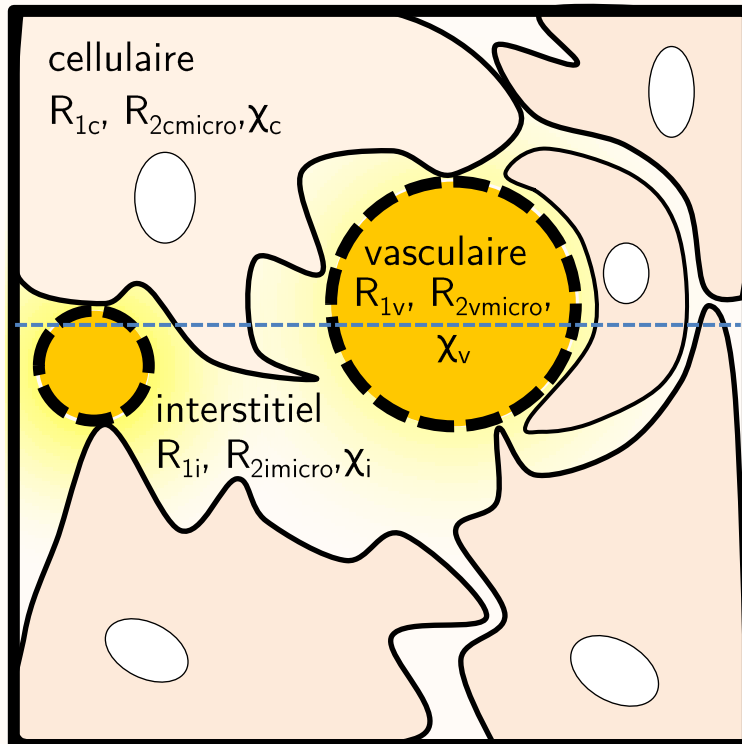
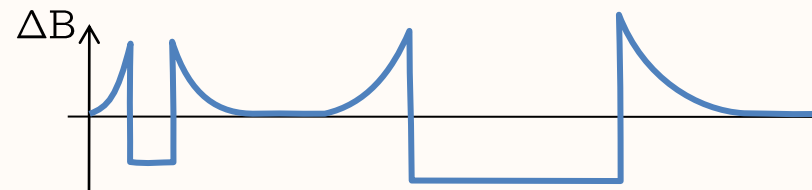
$$\Delta\chi_{i-v}$$

$$R_1$$

$$R_2 = R_{2\text{micro}} + R_{2\text{macro}} + R_{2\text{meso}}$$



$$\delta B(\vec{\rho}; R_0, \theta, \Delta\chi) = \begin{cases} \Delta\chi B_0 \frac{R_0^2}{\rho^2} \cos(2\varphi) \sin^2\theta, & \text{pour } \rho > R_0 \\ \Delta\chi B_0 \left( \cos^2\theta - \frac{1}{3} \right), & \text{pour } \rho < R_0 \end{cases}$$



R<sub>1</sub>, R<sub>2</sub>, χ : en présence d'un AC qui s'extravase

R<sub>1</sub> : vitesse de relaxation longitudinale

R<sub>2</sub> : vitesse de relaxation transversale

χ : Susceptibilité magnétique

3 compartiments : v<sub>v</sub>, v<sub>c</sub>, v<sub>i</sub> (=Porosité)

$$R_{1v}, R_{2v\text{micro}}, \chi_v \quad \uparrow$$

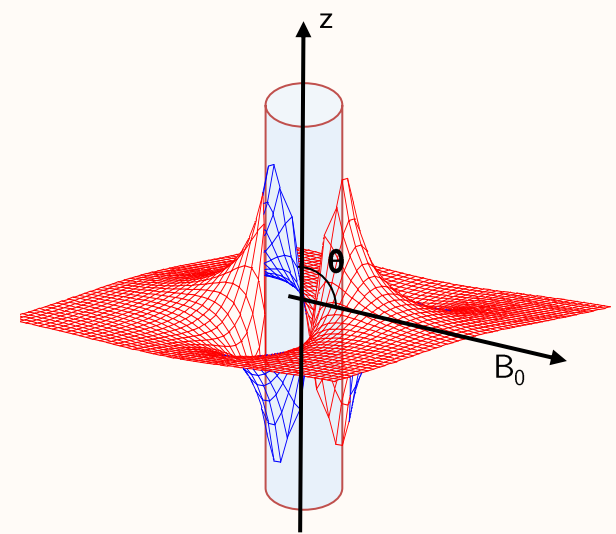
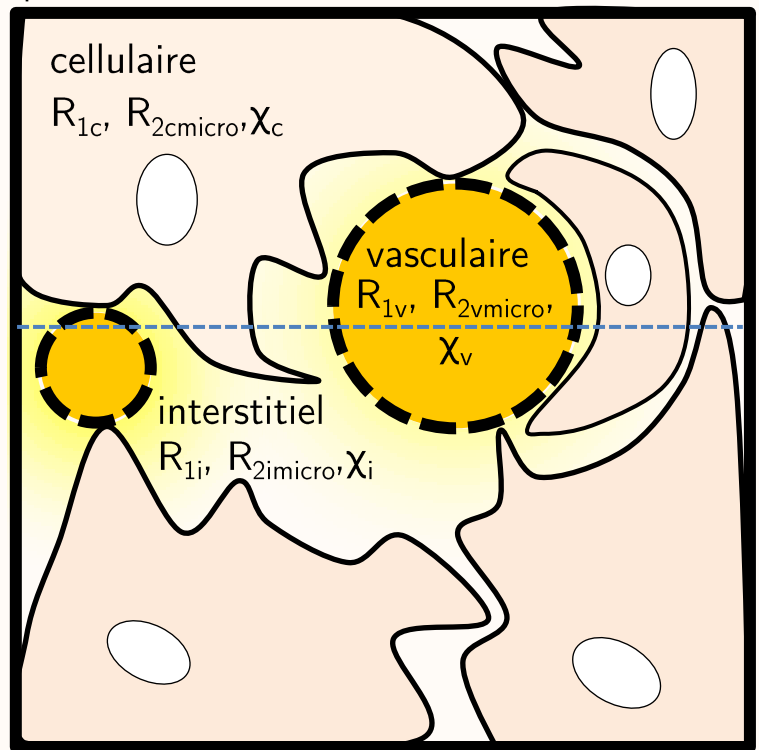
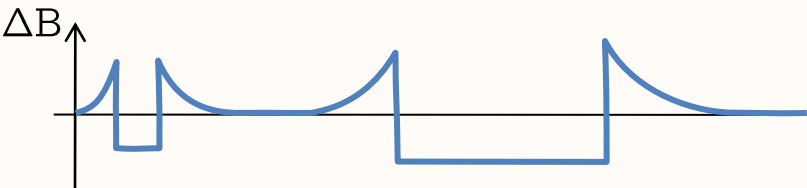
$$\Delta\chi_{i-v}$$

$$R_{1i}, R_{2vi}, \chi_i \quad \uparrow$$

$$\Delta\chi_{i-c}$$

$$R_1$$

$$R_2 = R_{2\text{micro}} + R_{2\text{macro}} + R_{2\text{meso}}$$



$$\delta B(\vec{\rho} ; R_0, \theta, \Delta\chi) = \begin{cases} \Delta\chi B_0 \frac{R_0^2}{\rho^2} \cos(2\varphi) \sin^2\theta, & \text{pour } \rho > R_0 \\ \Delta\chi B_0 \left( \cos^2\theta - \frac{1}{3} \right), & \text{pour } \rho < R_0 \end{cases}$$

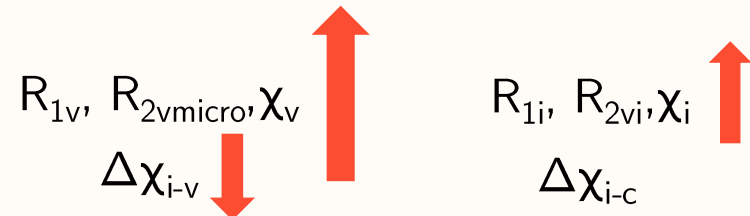
R<sub>1</sub>, R<sub>2</sub>, χ : en présence d'un AC qui s'extravase

R<sub>1</sub> : vitesse de relaxation longitudinale

R<sub>2</sub> : vitesse de relaxation transversale

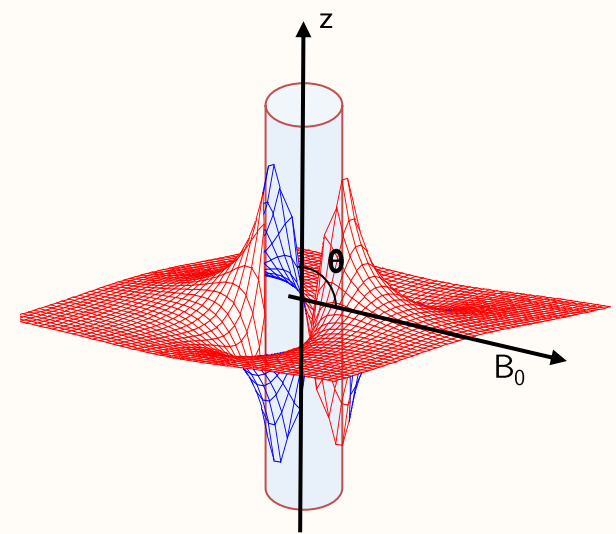
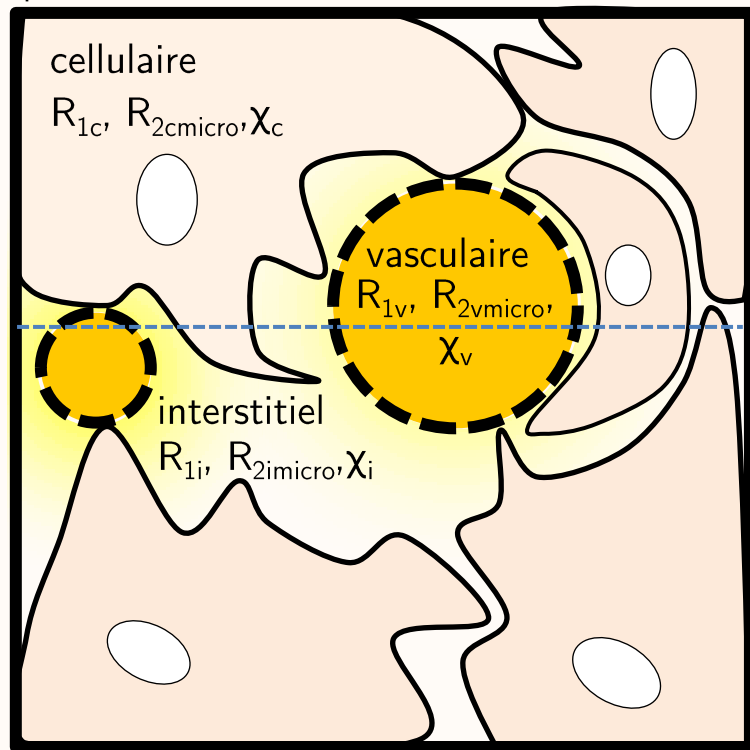
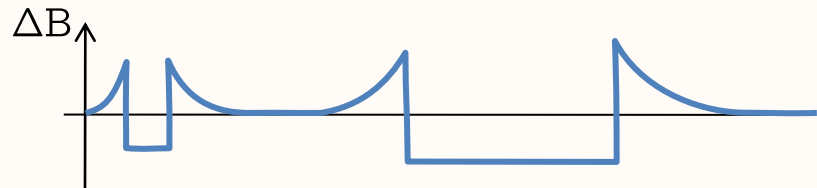
χ : Susceptibilité magnétique

3 compartiments : v<sub>v</sub>, v<sub>c</sub>, v<sub>i</sub> (=Porosité)



$$R_1$$

$$R_2 = R_{2\text{micro}} + R_{2\text{macro}} + R_{2\text{meso}}$$



$$\delta B(\vec{\rho} ; R_0, \theta, \Delta\chi) = \begin{cases} \Delta\chi B_0 \frac{R_0^2}{\rho^2} \cos(2\varphi) \sin^2\theta, & \text{pour } \rho > R_0 \\ \Delta\chi B_0 \left( \cos^2\theta - \frac{1}{3} \right), & \text{pour } \rho < R_0 \end{cases}$$

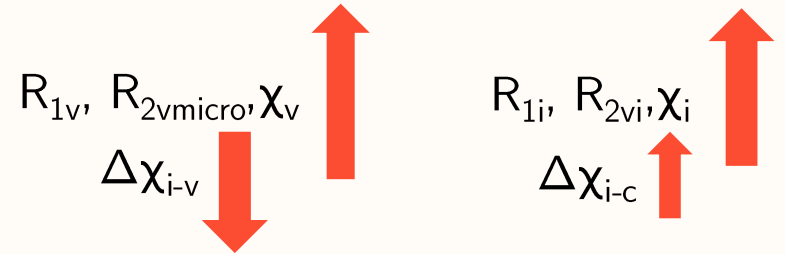
R1, R2,  $\chi$  : en présence d'un AC qui s'extravase

$R_1$  : vitesse de relaxation longitudinale

$R_2$  : vitesse de relaxation transversale

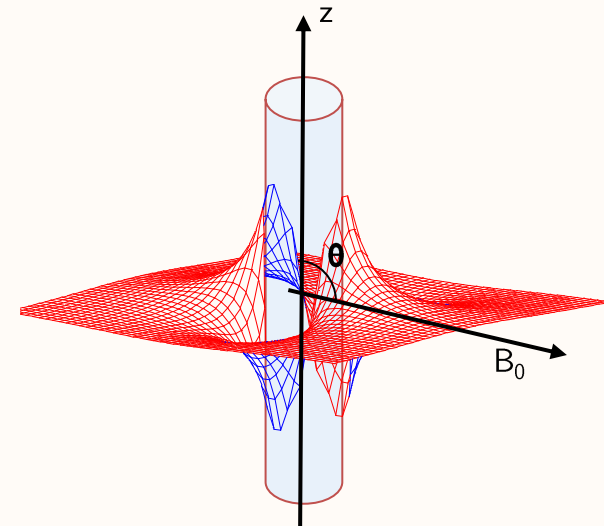
$\chi$  : Susceptibilité magnétique

3 compartiments :  $v_v, v_c, v_i$  (=Porosité)

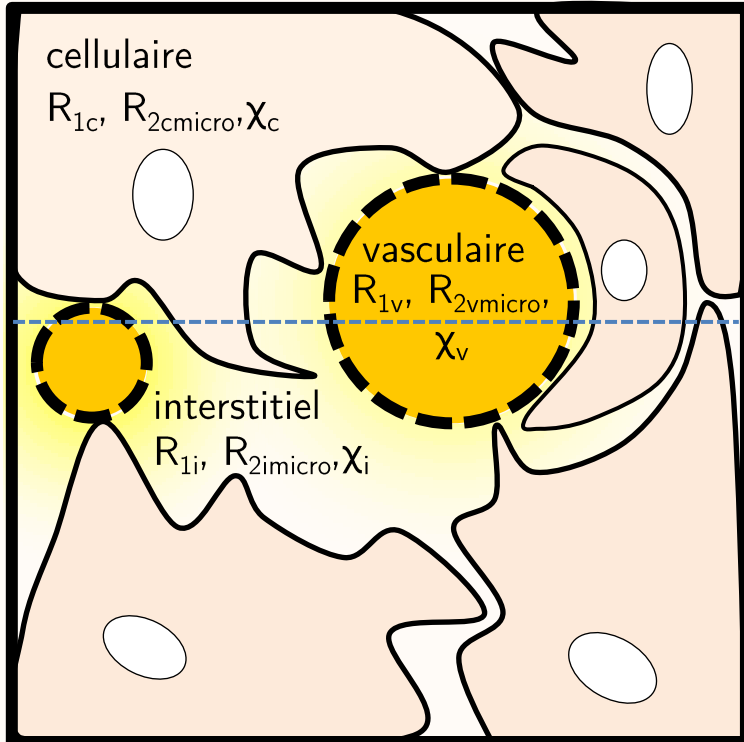
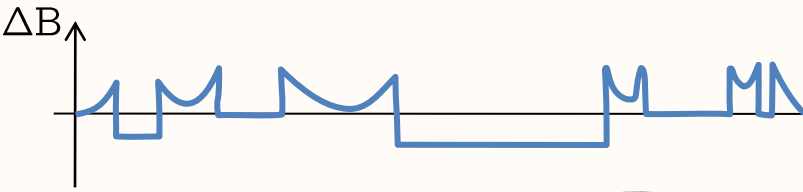


$$R_1$$

$$R_2 = R_{2\text{micro}} + R_{2\text{macro}} + R_{2\text{meso}}$$



$$\delta B(\vec{\rho} ; R_0, \theta, \Delta\chi) = \begin{cases} \Delta\chi B_0 \frac{R_0^2}{\rho^2} \cos(2\varphi) \sin^2\theta, & \text{pour } \rho > R_0 \\ \Delta\chi B_0 \left( \cos^2\theta - \frac{1}{3} \right), & \text{pour } \rho < R_0 \end{cases}$$



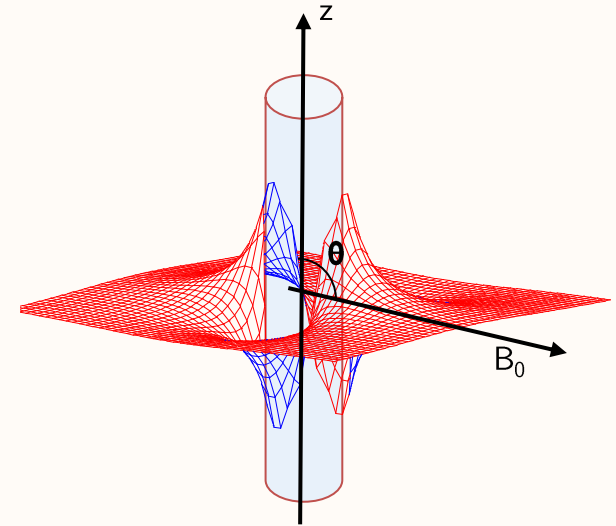
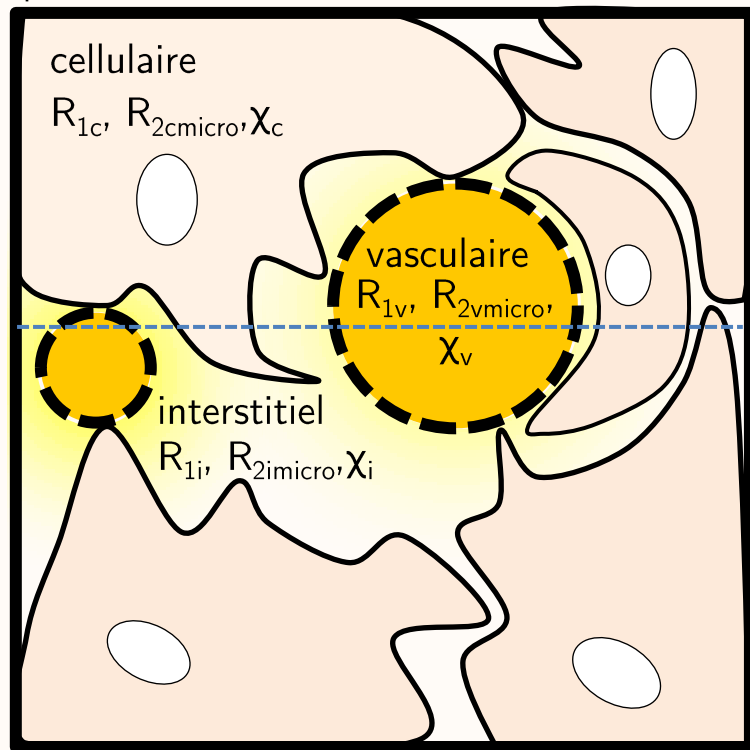
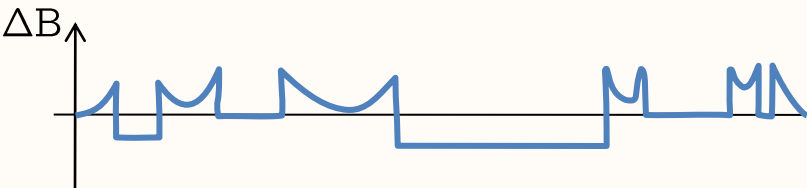
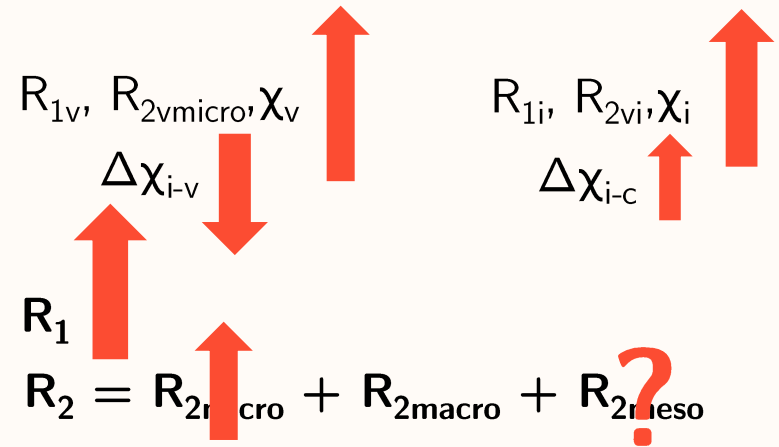
R1, R2,  $\chi$  : en présence d'un AC qui s'extravase

$R_1$  : vitesse de relaxation longitudinale

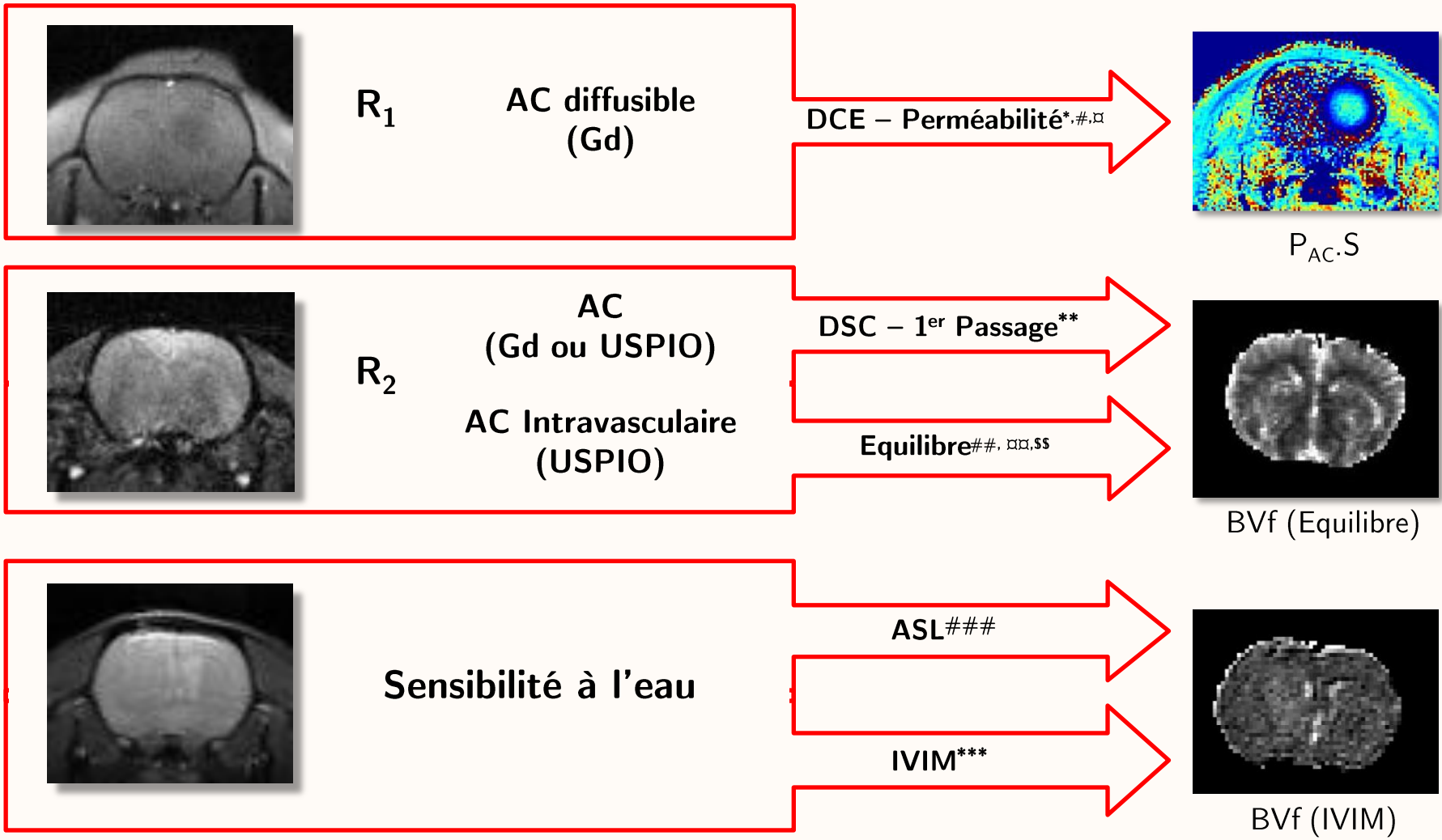
$R_2$  : vitesse de relaxation transversale

$\chi$  : Susceptibilité magnétique

3 compartiments :  $v_v, v_c, v_i$  (=Porosité)



$$\delta B(\vec{\rho} ; R_0, \theta, \Delta\chi) = \begin{cases} \Delta\chi B_0 \frac{R_0^2}{\rho^2} \cos(2\varphi) \sin^2\theta, & \text{pour } \rho > R_0 \\ \Delta\chi B_0 \left( \cos^2\theta - \frac{1}{3} \right), & \text{pour } \rho < R_0 \end{cases}$$



\*Larsson, MRM (1990)

# Tofts, MRM (1991)

□ Brix, J Comp Assit Tomogr (1991)

\*\*Zierler, Circ Res (1956)

## Yablonskiy, MRM (1994)

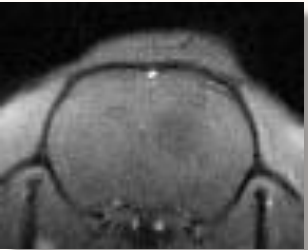
□□ Boxerman, MRM (1995)

\$\$ Troprès, MRM (2001)

\*\*\* LeBihan, MRM (1991)

### Detre, MRM (1992)

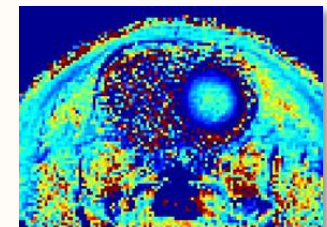
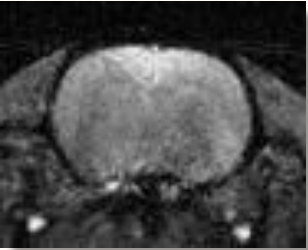
Sourbron, MRM (2009)



$R_1$

AC diffusible (Gd)

DCE – Perméabilité\*<sup>#,□</sup>

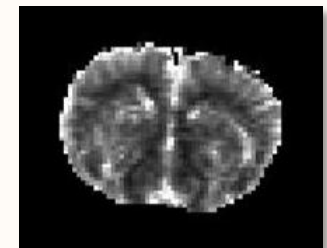
$R_2$

AC (Gd ou USPIO)  
AC Intravasculaire (USPIO)

DSC – 1<sup>er</sup> Passage\*\*

Equilibre<sup>##,□□,§§</sup>

Schmainda, AJNR (2004)  $P_{AC.S}$



BVf (Equilibre)



Sensibilité à l'eau

ASL<sup>###</sup>

IVIM<sup>\*\*\*</sup>

Zaharchuk, MRM (2010)



BVf (IVIM)

\*Larsson, MRM (1990)  
# Tofts, MRM (1991)  
□ Brix, J Comp Assit Tomogr (1991)

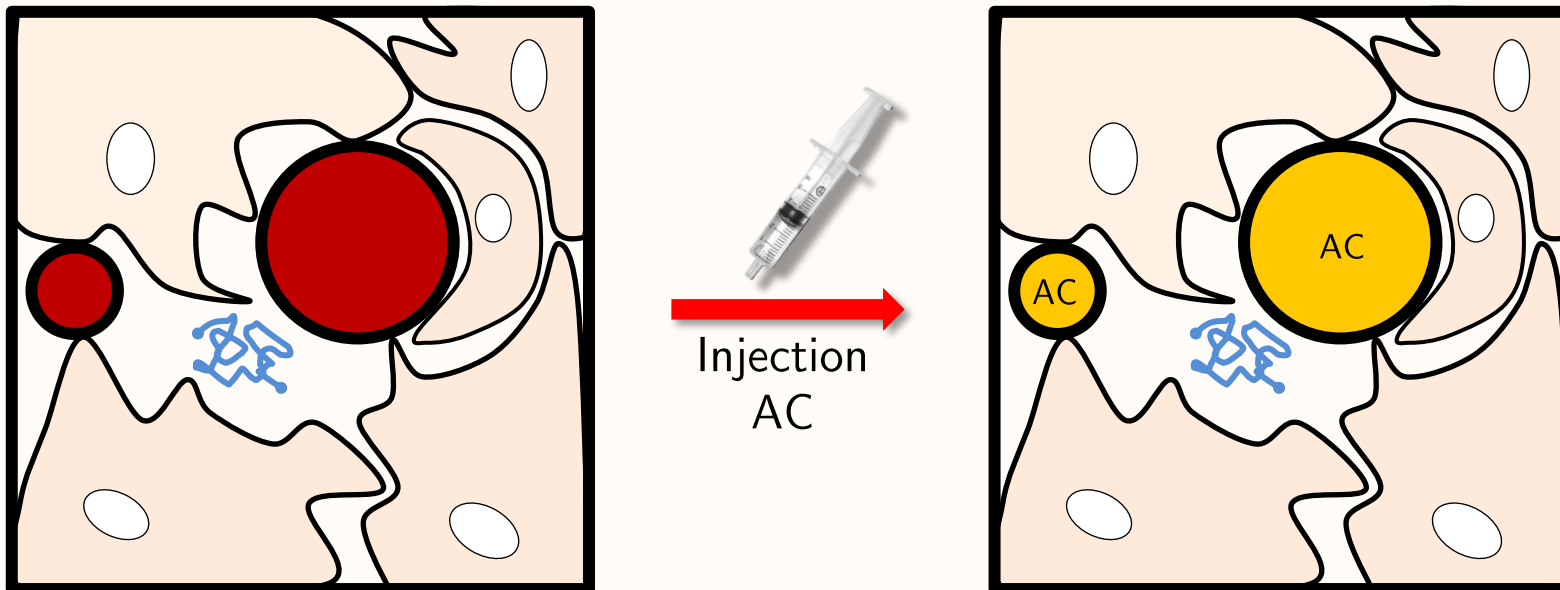
\*\*Zierler, Circ Res (1956)  
## Yablonskiy, MRM (1994)  
□□ Boxerman, MRM (1995)

§§ Troprès, MRM (2001)  
\*\*\* LeBihan, MRM (1991)  
### Detre, MRM (1992)

- ○ ○ ○ Introduction
  
- ● ○ ○ Mesure de VSI : Equilibre vs DSC
  - Théorie
  - Approche dynamique, Approche à l'équilibre
  - Matériel et méthodes
  - Résultats
  - Discussion
  
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  - Principe
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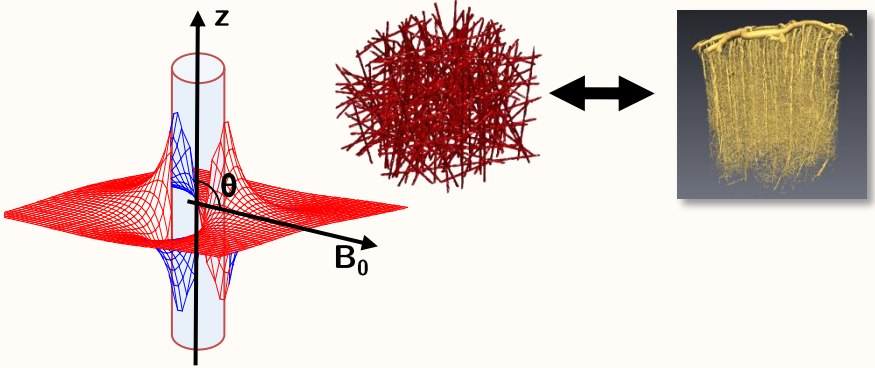


Mesure de  $R_2$  en **écho de gradient** (GE) et en **écho de spin** (SE), avec et sans AC.

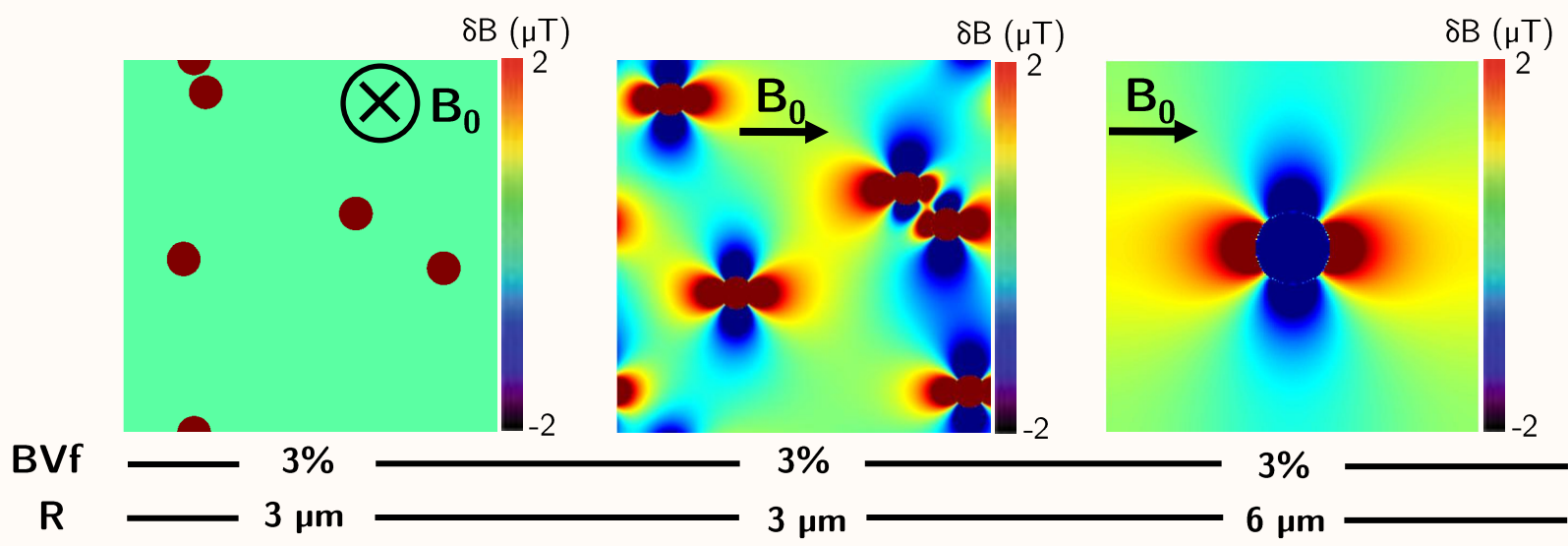
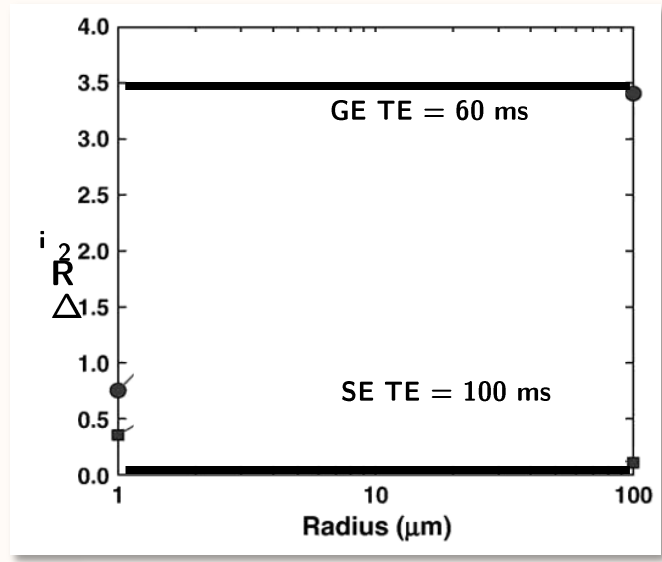
$$\text{En GE : } R_2^{\text{GE}} = R_{2\text{micro}} + R_{2\text{macro}} + R_{2\text{meso}}^{\text{GE}}$$

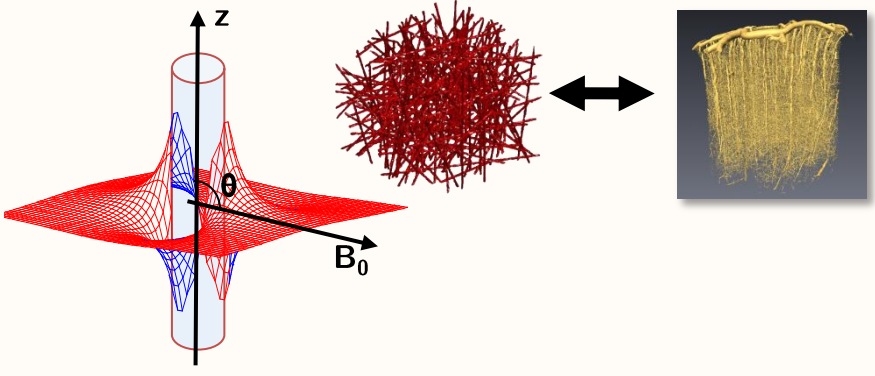
$$\text{En SE : } R_2^{\text{SE}} = R_{2\text{micro}} + R_{2\text{meso}}^{\text{SE}}$$

$$\text{Si BVf} \ll 1 : \begin{aligned} \Delta R_2^{\text{GE}} &= \Delta R_{2\text{meso}}^{\text{GE}} \\ \Delta R_2^{\text{SE}} &= \Delta R_{2\text{meso}}^{\text{SE}} \end{aligned} \neq D_{\text{H}_2\text{O}}$$

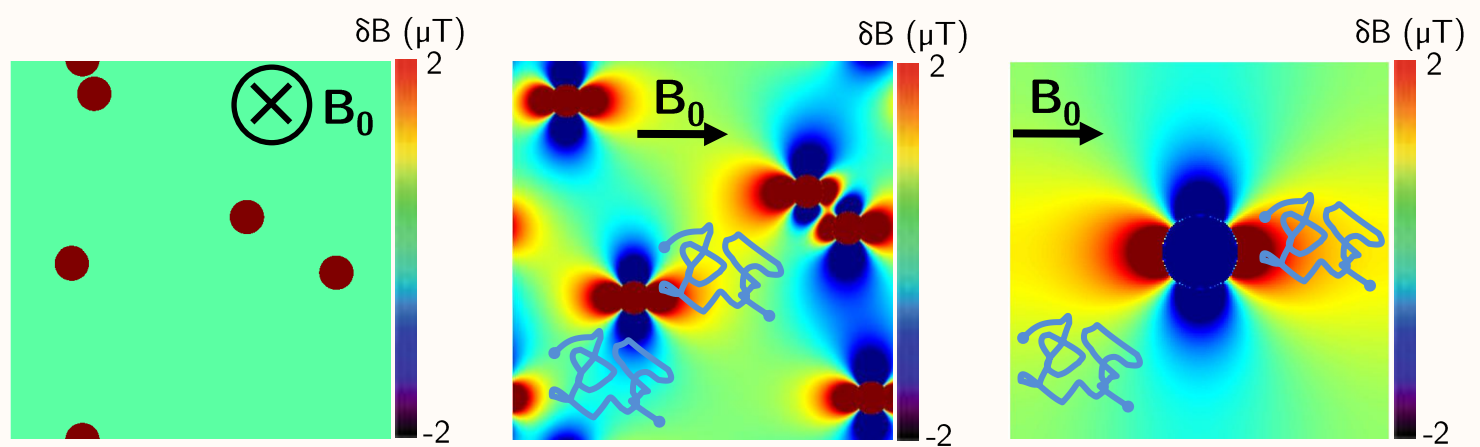
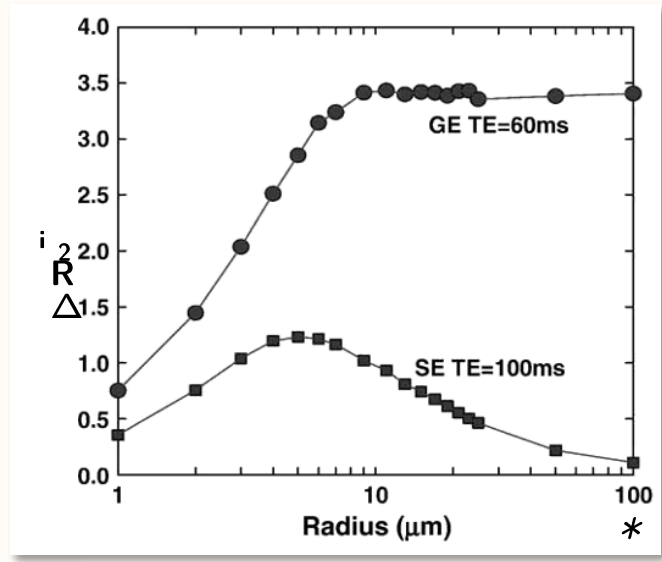


$B_0 = 4,7 \text{ T}$   
 $\Delta\chi = 0,231 \text{ ppm}$   
 $D_{H2O} = 0$



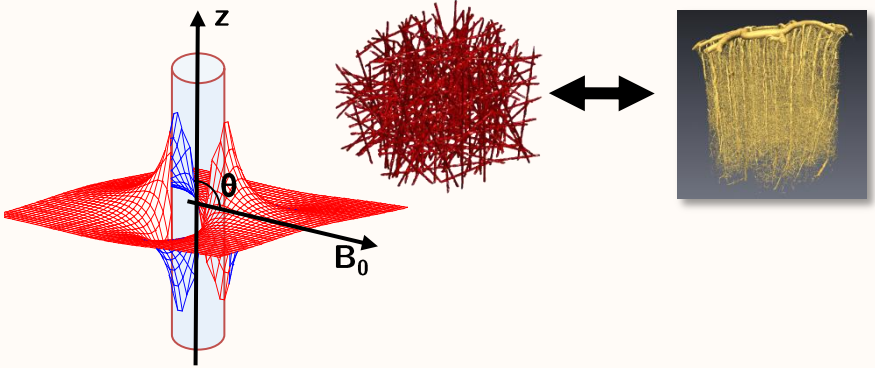


$B_0 = 4,7 \text{ T}$   
 $\Delta\chi = 0,231 \text{ ppm}$   
 $D_{H2O} = 1000 \mu\text{m}^2 \cdot \text{s}^{-1}$

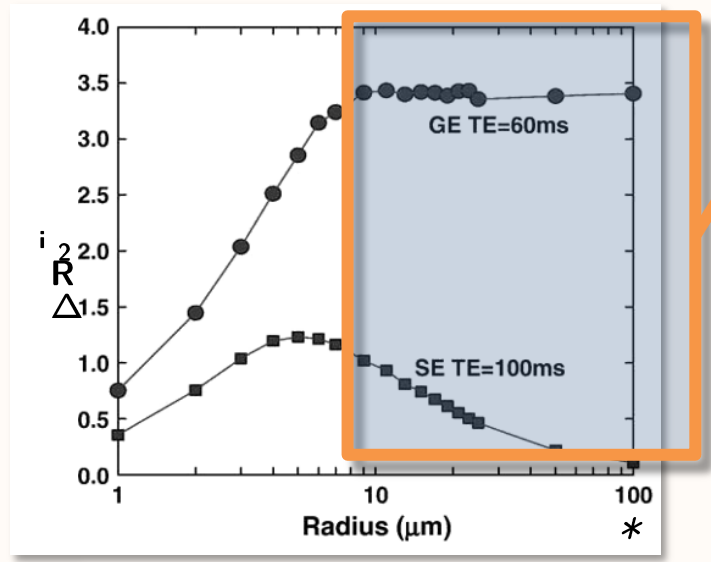


BVf 3% 3 micrometer  
 R 3% 3 micrometer  
 3% 6 micrometer

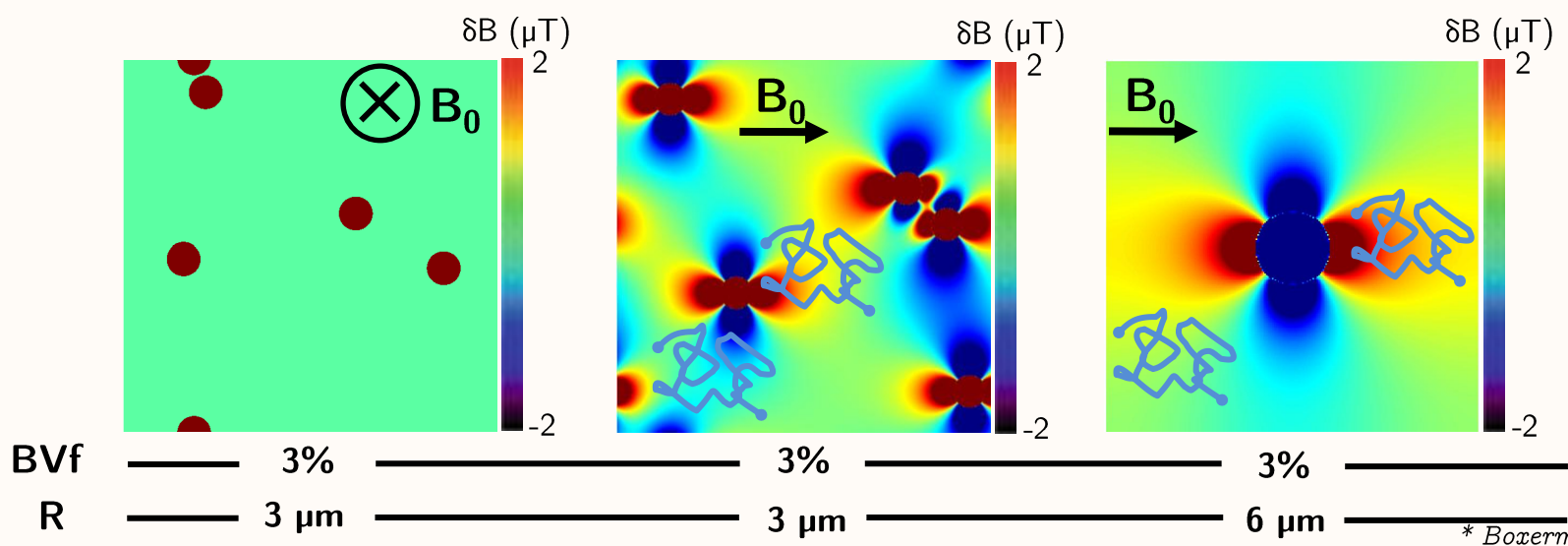
\* Boergerman, MRM (1995)



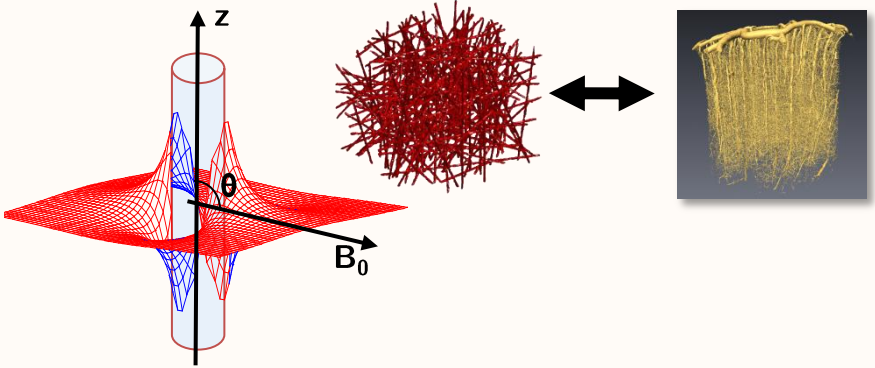
$B_0 = 4,7 \text{ T}$   
 $\Delta\chi = 0,231 \text{ ppm}$   
 $D_{H2O} = 1000 \mu\text{m}^2 \cdot \text{s}^{-1}$



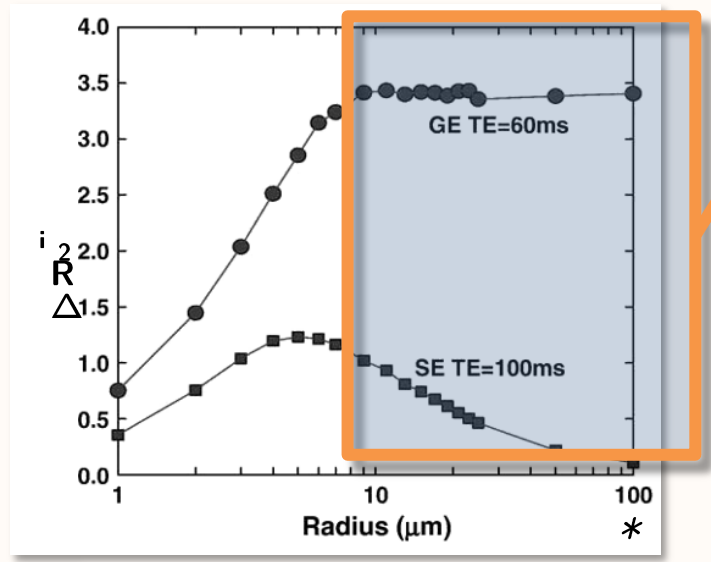
Static  
Dephasing  
Regime  
(SDR)



\* Boergerman, MRM (1995)

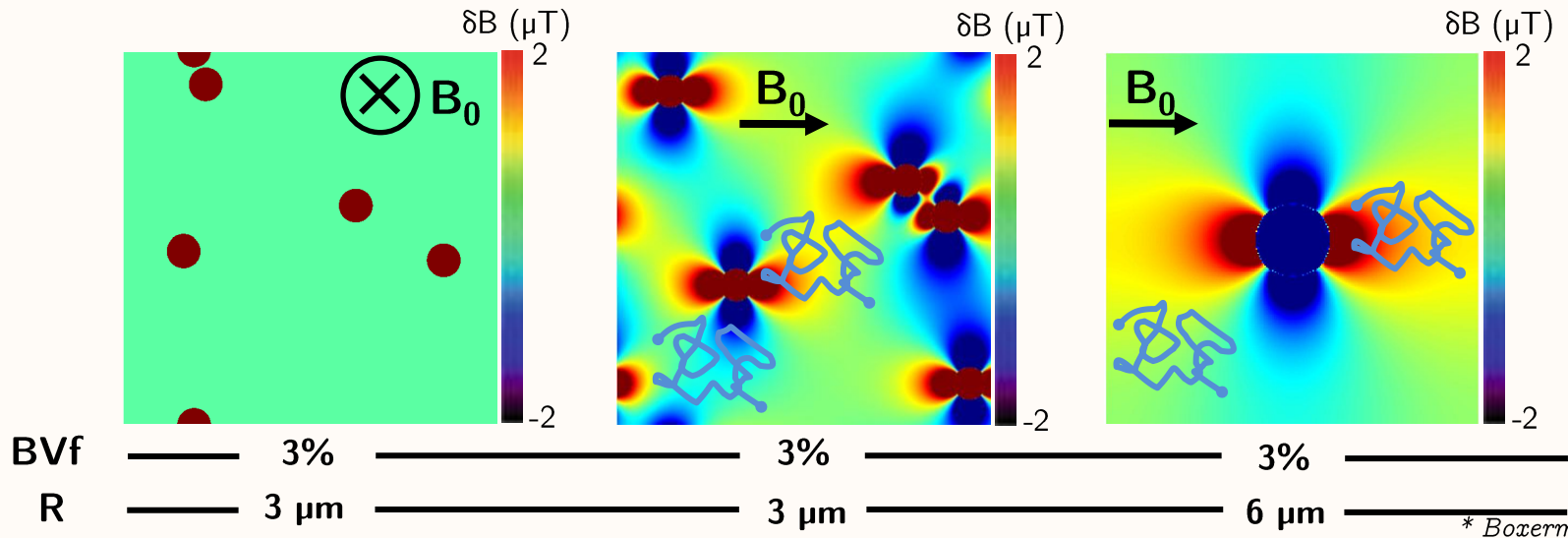


$B_0 = 4,7 \text{ T}$   
 $\Delta\chi = 0,231 \text{ ppm}$   
 $D_{H2O} = 1000 \mu\text{m}^2 \cdot \text{s}^{-1}$



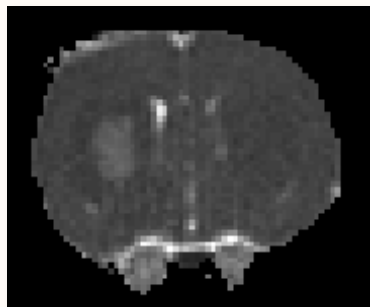
Static Dephasing Regime (SDR)

$$VSI = 1,062 \left( \frac{D_{H2O}}{\gamma \Delta\chi B_0} \right)^{1/2} \left( \frac{\Delta R_2^{GE}}{\Delta R_2^{SE}} \right)^{3/2}$$

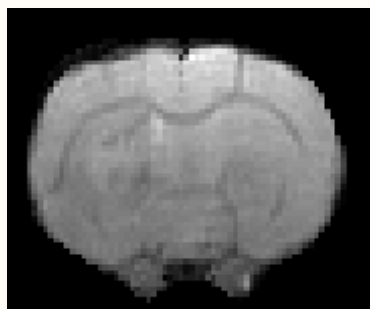


\* Boergerman, MRM (1995)

ADC

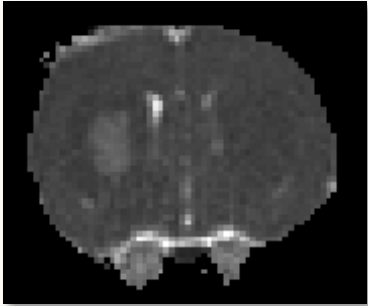
 $D_{H20}$ 

MGESE



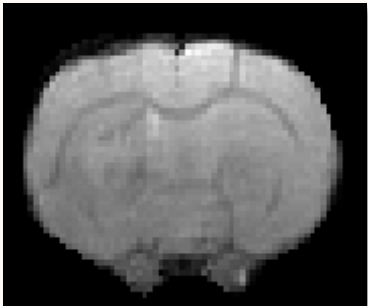
Avant :  $R_2^{GE}$  *avant*  
 $S^{SE}$  *avant*

ADC

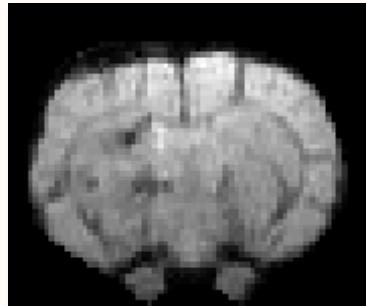


$D_{H2O}$

MGESE



MGESE



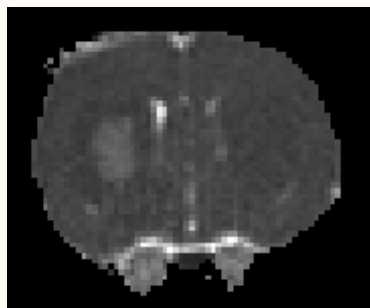
Avant :  $R_2^{GE}$  avant  
 $S^{SE}$  avant

Après :  $R_2^{GE}$  après  
 $S^{SE}$  après

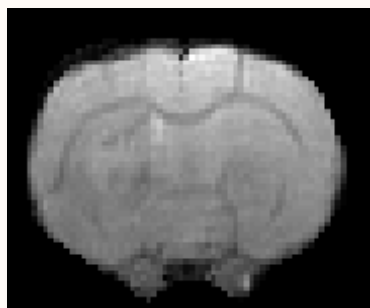




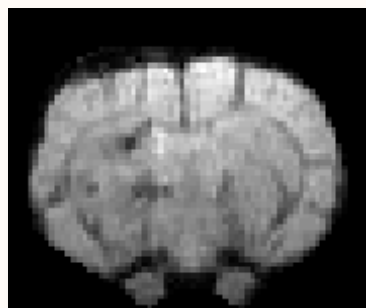
ADC

 $D_{H2O}$ 

MGSE



MGSE



Avant :  $R_2^{GE}$  avant  
 $S_{avant}^{SE}$

Après :  $R_2^{GE}$  après  
 $S_{après}^{SE}$

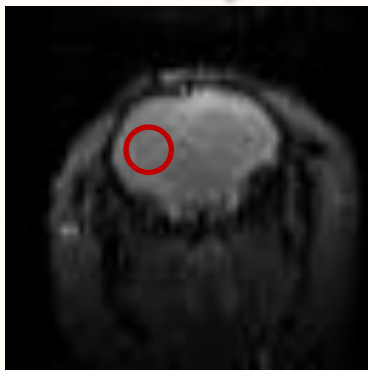
$$\Delta R_2^{GE} = R_2^{GE} \text{ avant} - R_2^{GE} \text{ après}$$

$$\Delta R_2^{SE} = -\frac{1}{T_E^{SE}} \ln \frac{S_{après}^{SE}}{S_{avant}^{SE}}$$

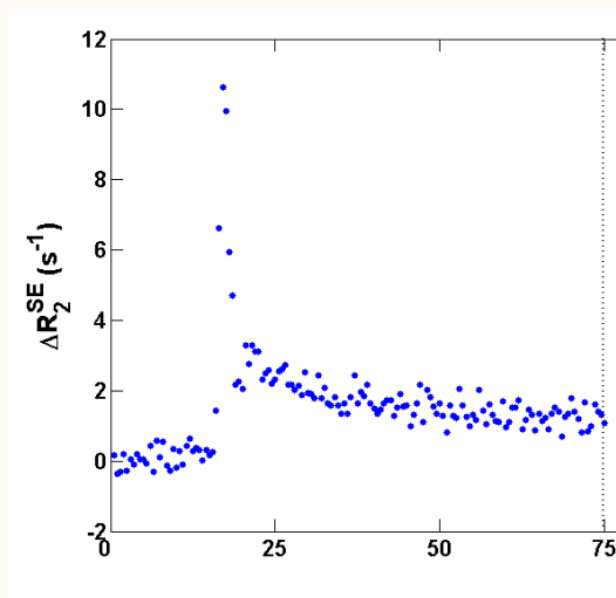
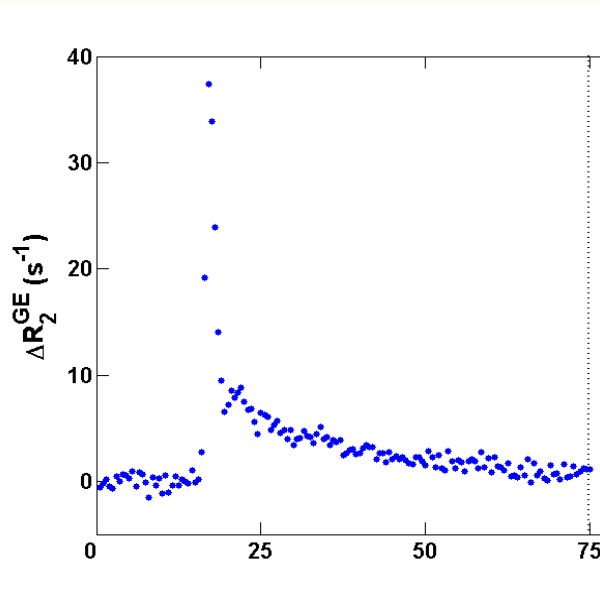
$$VSI = 1,062 \left( \frac{D_{H2O}}{\gamma \Delta \chi B_0} \right)^{1/2} \left( \frac{\Delta R_2^{GE}}{\Delta R_2^{SE}} \right)^{3/2}$$

DSC avec 1GE et 1SE

Gd



$$\Delta R_2^i(t) = -\frac{1}{T_E^i} \ln \frac{S^i(t)}{S_0^i}$$

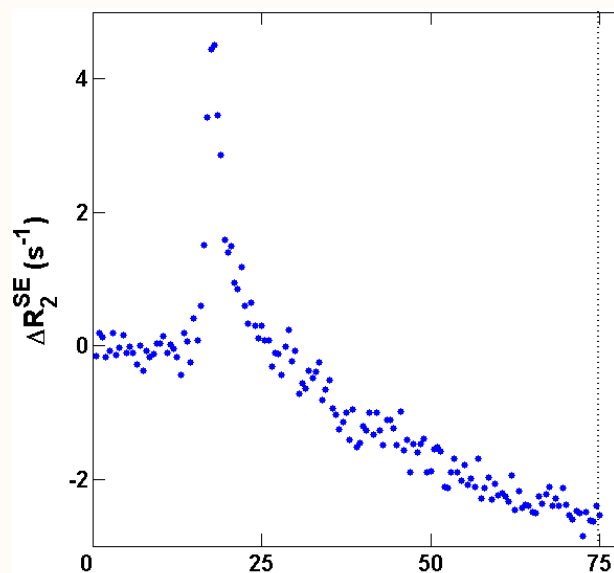
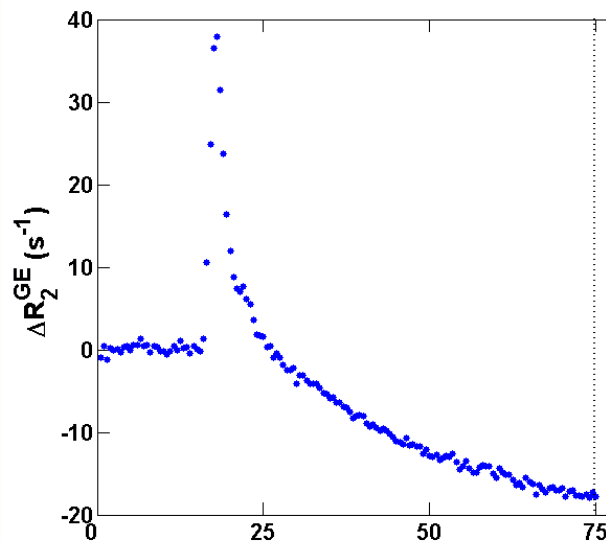


DSC avec 1GE et 1SE

Gd



$$\Delta R_2^i(t) = -\frac{1}{T_E^i} \ln \frac{S^i(t)}{S_0^i}$$

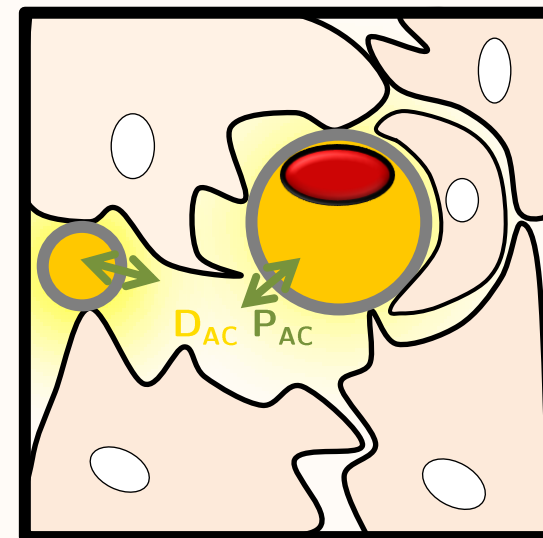
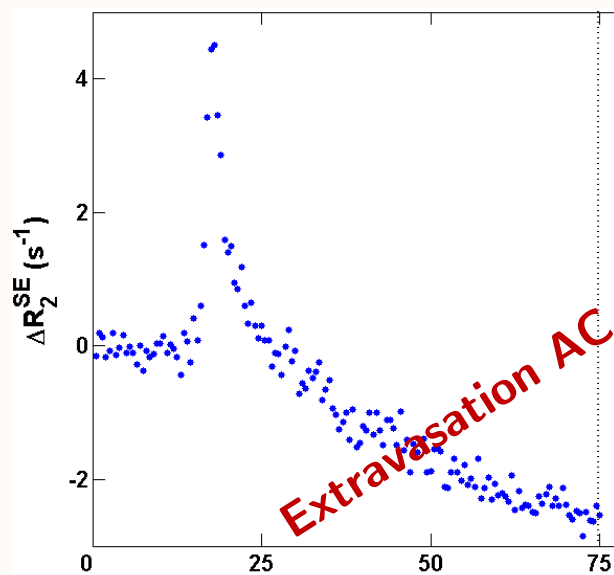
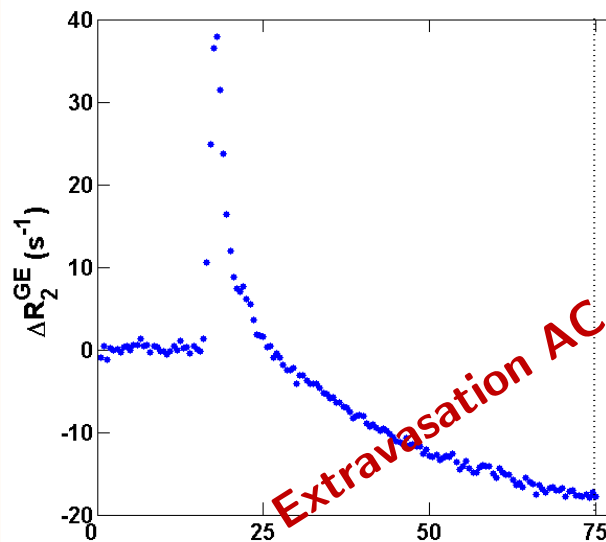


DSC avec 1GE et 1SE

Gd



$$\Delta R_2^i(t) = -\frac{1}{T_E^i} \ln \frac{S^i(t)}{S_0^i}$$



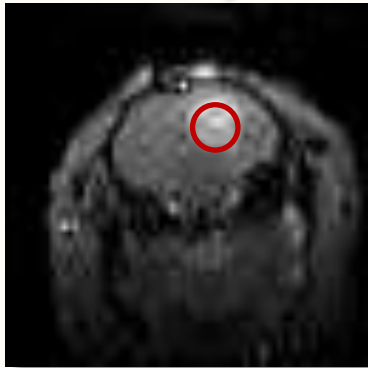
$R_1 \nearrow$

$\Delta\chi_{i-v} \searrow$  ,  $\Delta\chi_{i-c} \nearrow$

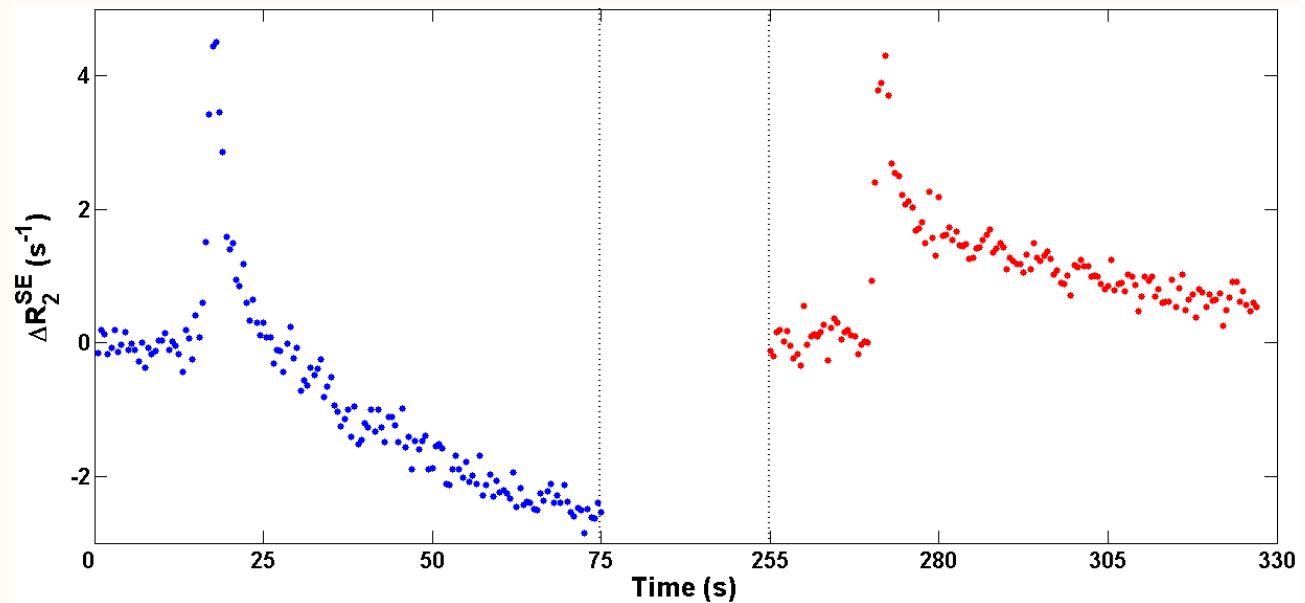
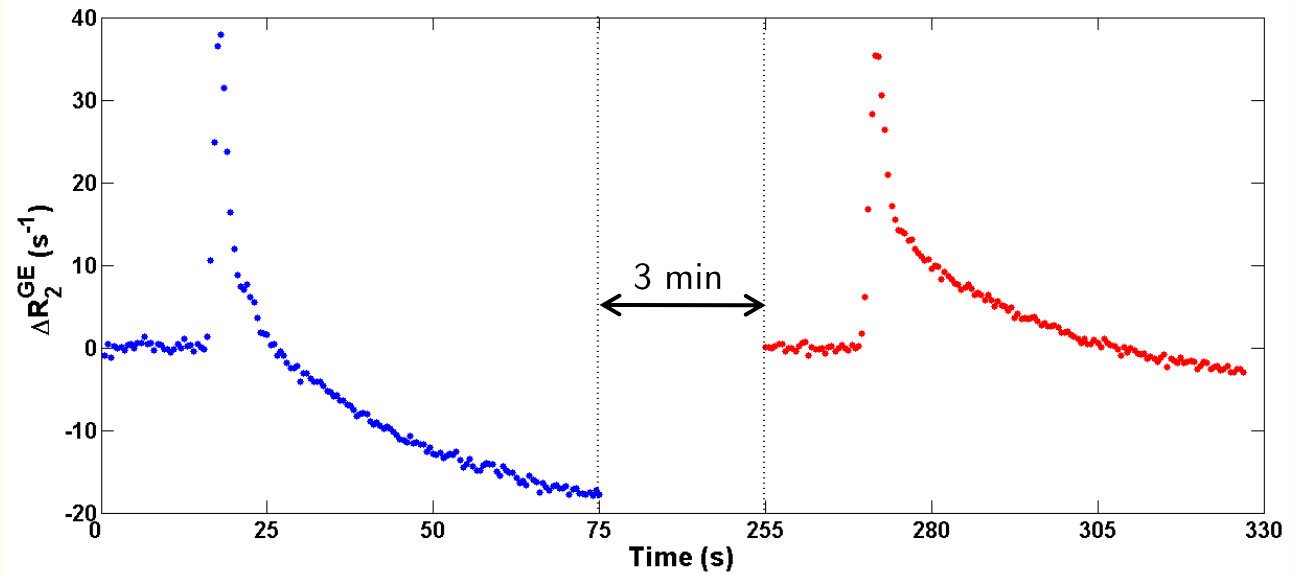
Johnson, MRM (2004)  
 Boexerman, Neuroradio (2006)  
 Sourbron, MRM (2009)  
 Maeda, Radiology(1993)  
 Barbier, JMRI (1998)  
 Heilman, MRM (2007)  
 Schmainda, AJNR(2004)  
 Paulson , Radiology(2008)

DSC avec 1GE et 1SE

Gd



$$\Delta R_2^i(t) = -\frac{1}{T_E^i} \ln \frac{S^i(t)}{S_0^i}$$



- Les deux approches fournissent-elles une mesure de VSI comparable ?

$$VSI\{USPIO\} \text{ vs } VSI\{Gd_j\}$$

- Les deux injections de Gd fournissent-elles une mesure de VSI comparable ?

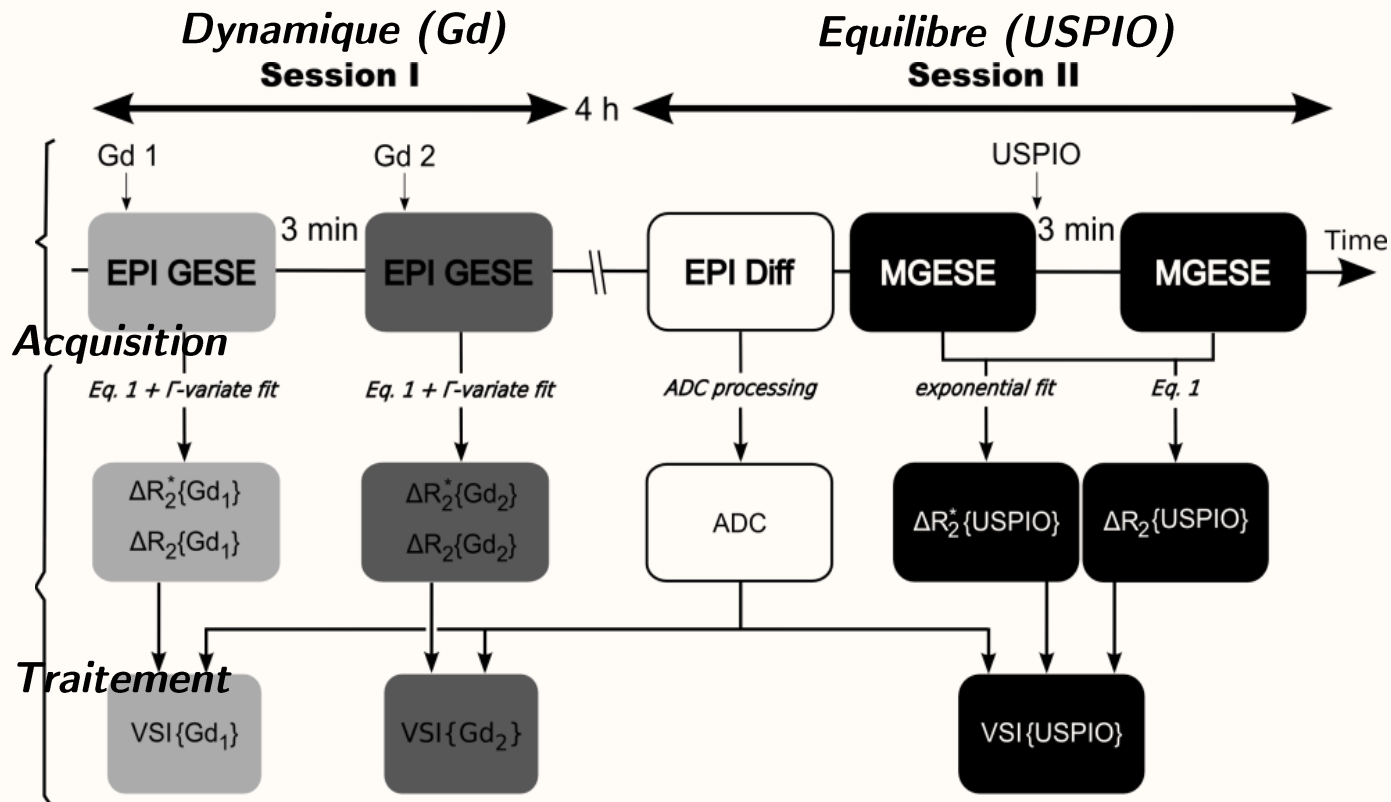
$$VSI\{Gd_1\} \text{ vs } VSI\{Gd_2\}$$

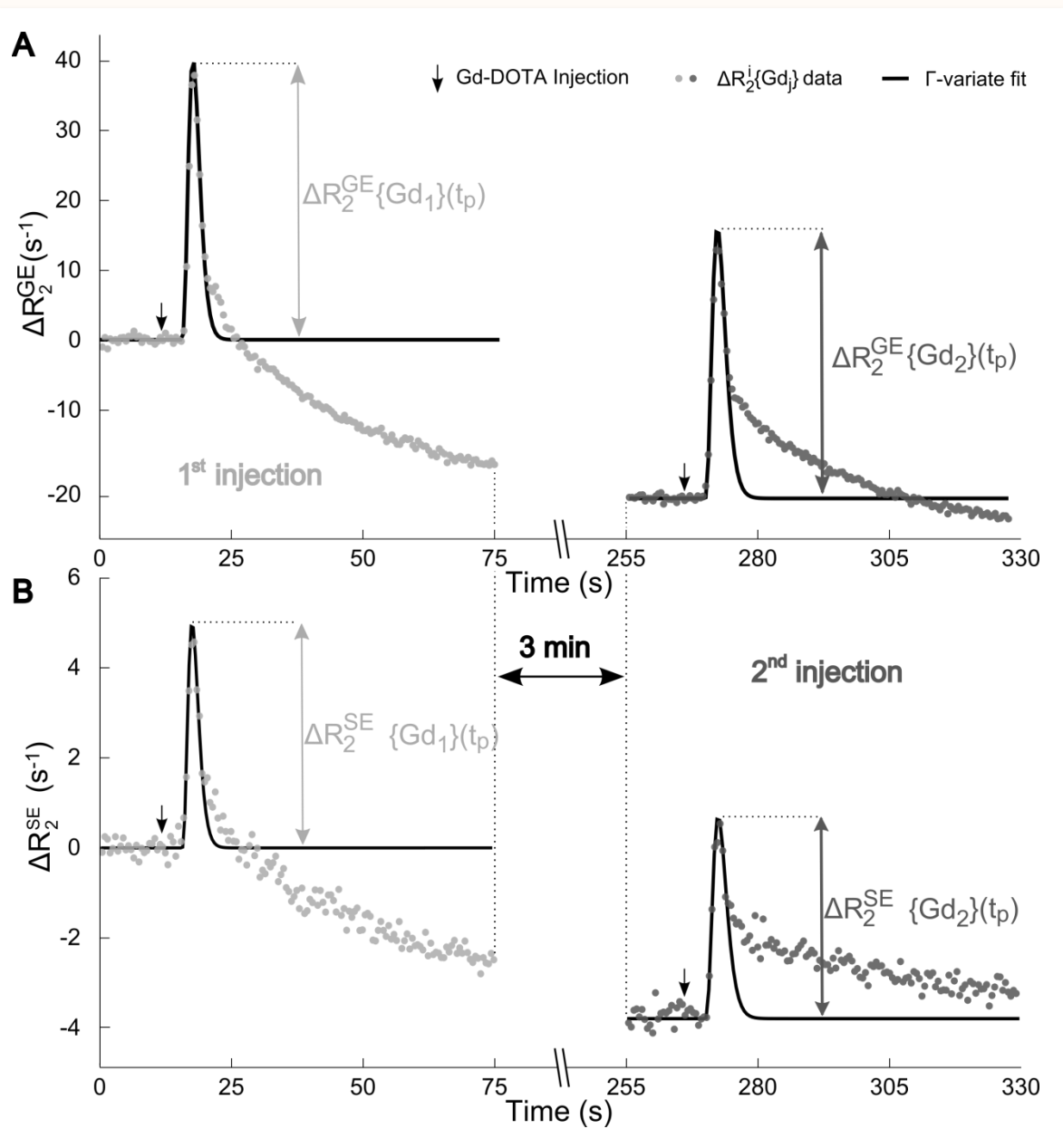
## Modèle animal

- Rats Wistar (n = 7)
- Tumeur C6 (J15 et J17)
- Anesthésie (induction 5% isoflurane – maintien 2% d'isoflurane)
- Cathéter dans la veine de la queue (injection de l'AC 200  $\mu\text{mol/kg}$ )

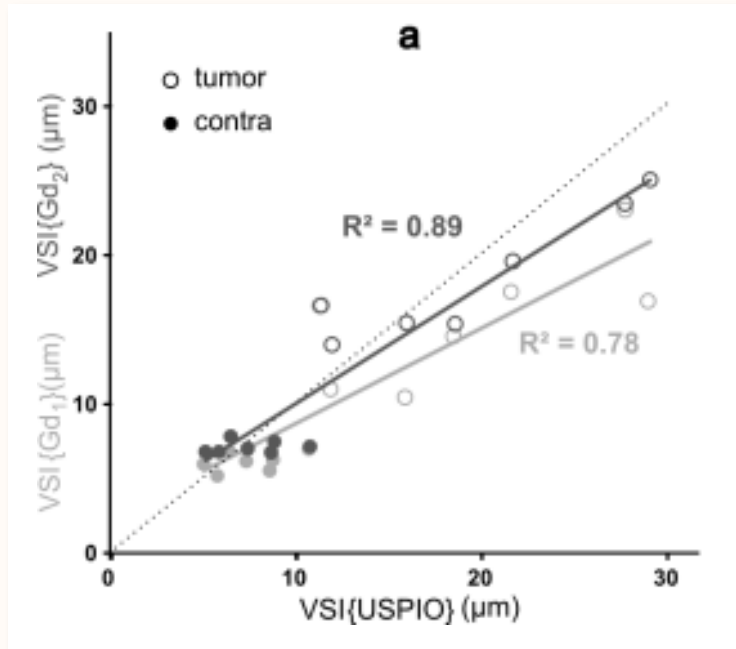
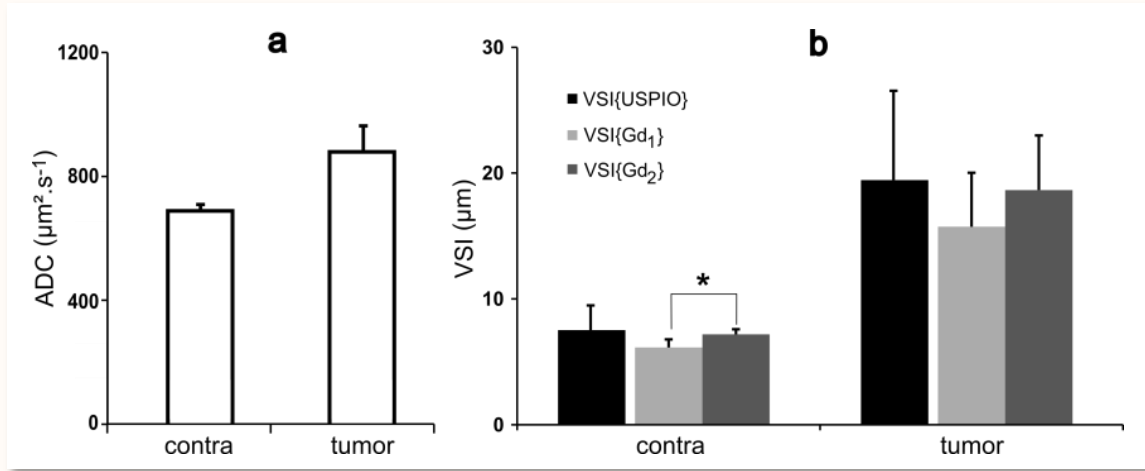
## Paramètres d'imagerie

- EPI : 1GE 1SE, simple segment (TEGE = 12 ms, TESE = 60 ms, TR = 500 ms), voxel =  $0,469 \times 0,469 \times 2 \text{ mm}^3$ )
- MGESE : 8 GE, 1 SE (TEGE/ $\Delta\text{TE}$  = 3/4 ms, TR = 2,5 s, voxel =  $0,469 \times 0,469 \times 2 \text{ mm}^3$ )

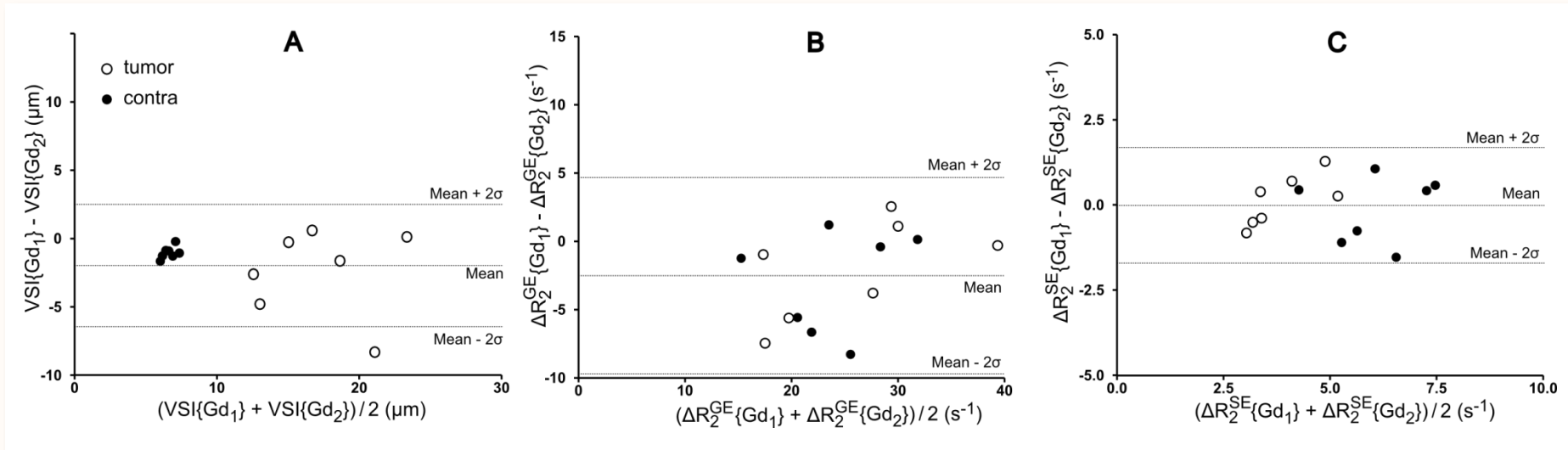






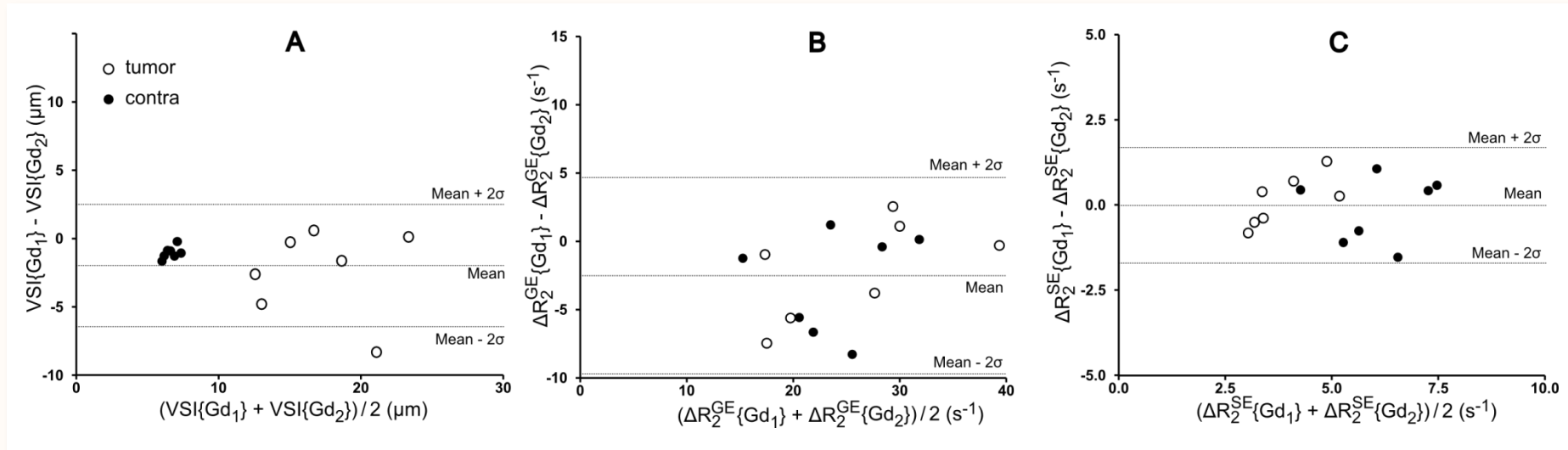


- Accord entre l'approche à l'équilibre et l'approche dynamique  
➔ Utilisation clinique ( $B_0 > 3T$ )
- VSI{Gd<sub>1</sub>} significativement différent de VSI{Gd<sub>2</sub>} dans la région controlatérale
- VSI peut être mesuré sur une simple injection



- Biais sur  $\Delta R_2^{GE}$  entre les deux injections

➔ Effet  $R_1$  différent entre les deux injections (controlatéral et tumeur) ?

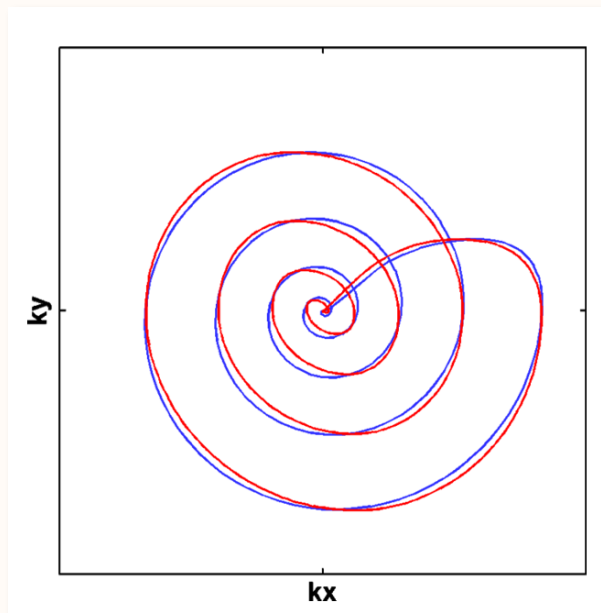


- Biais sur  $\Delta R_2^{GE}$  entre les deux injections  
 → Effet  $R_1$  différent entre les deux injections (controlatéral et tumeur) ?

**Acquisition rapide multi-échos de gradient à temps d'écho court**

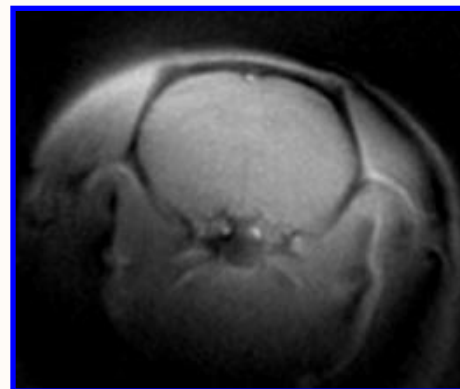
- ○ ○ ○ Introduction
  
- ● ○ ○ Mesure de VSI : Equilibre vs DSC
  - Théorie
  - Approche dynamique, Approche à l'équilibre
  - Matériel et méthodes
  - Résultats
  - Discussion
  
- ● ● ○ Séquence spirale multi-échos
  - Principe
  - Refocalisation de la trajectoire
  - Application au suivi du premier passage
  
- ● ● ● Perméabilité et diffusion : outil de simulation
  - Concept
  - Algorithme de simulation
  - Validation de l'algorithme
  - Applications  $P_{AC}$  vs  $D_{AC}$ , Porosité et  $\delta B$

1 entrelacement, 1 écho



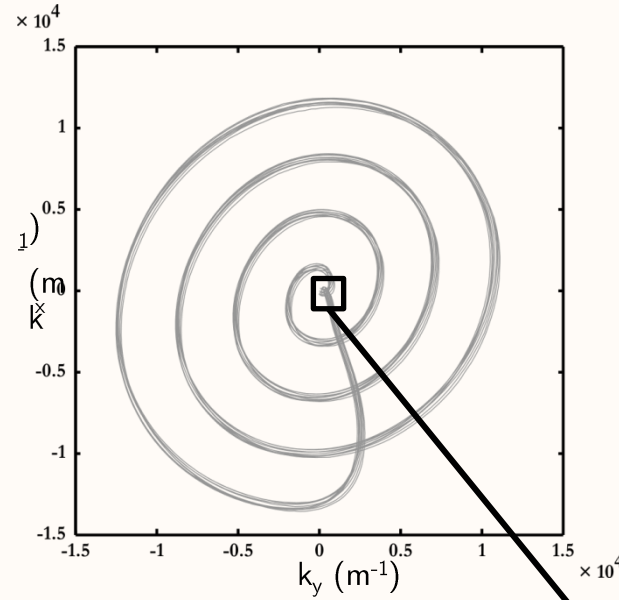
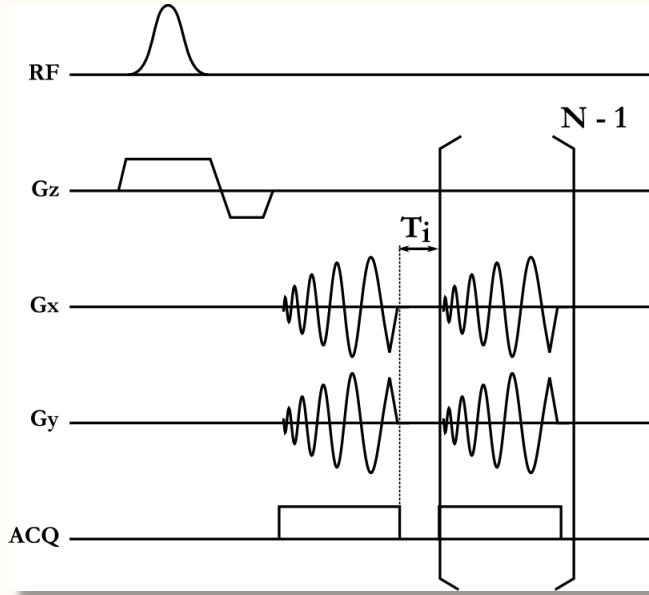
— Théorique

— Mesurée

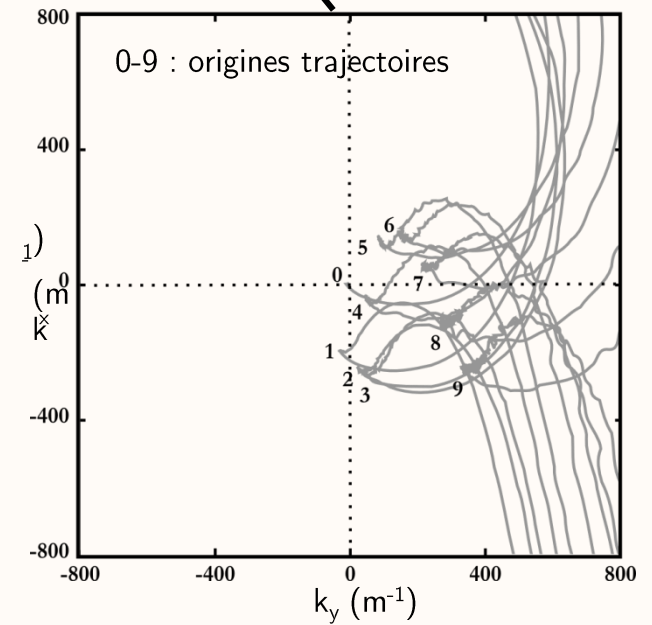


Distorsions

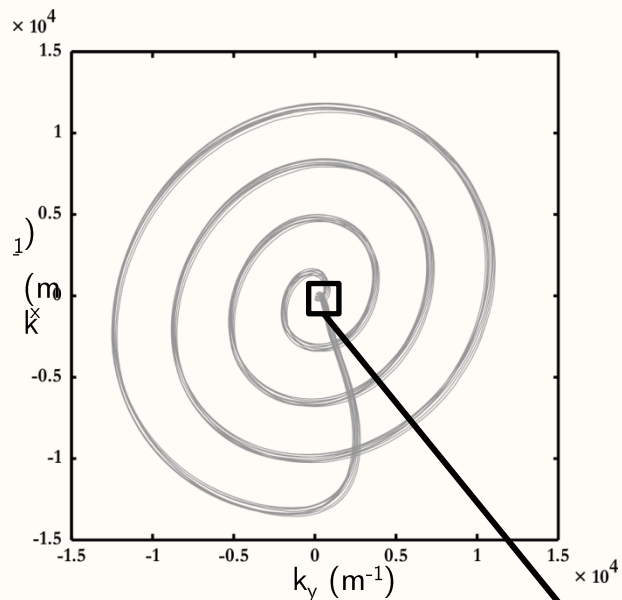
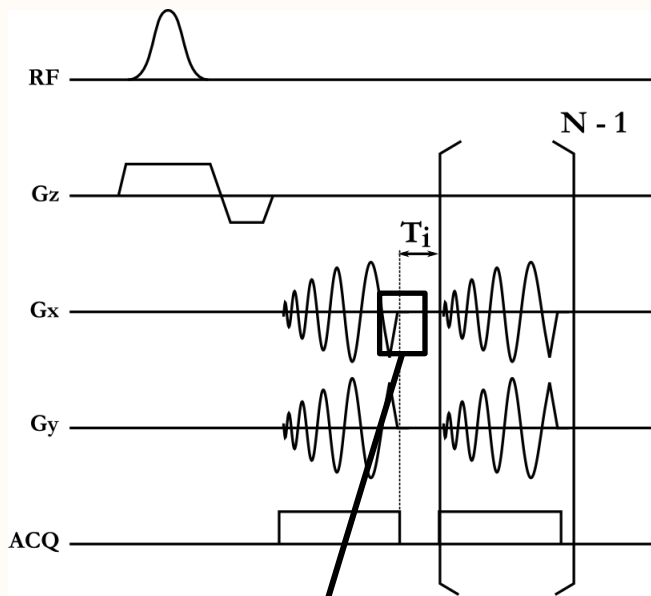
Spirale N échos



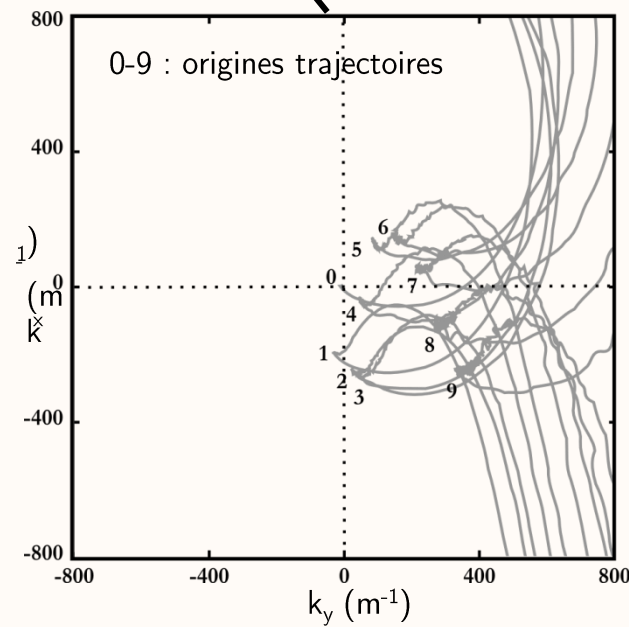
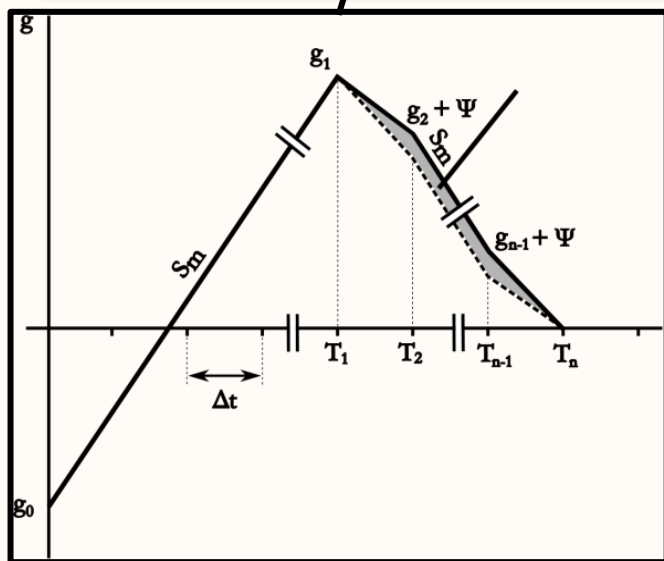
1 entrelacement  
10 échos



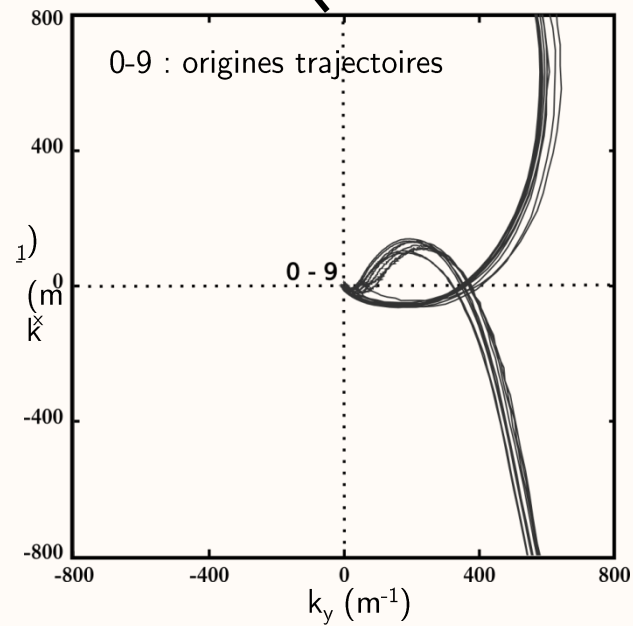
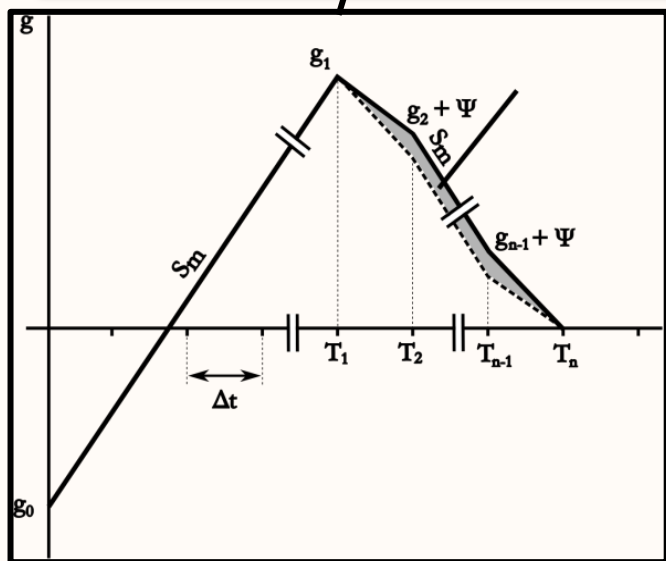
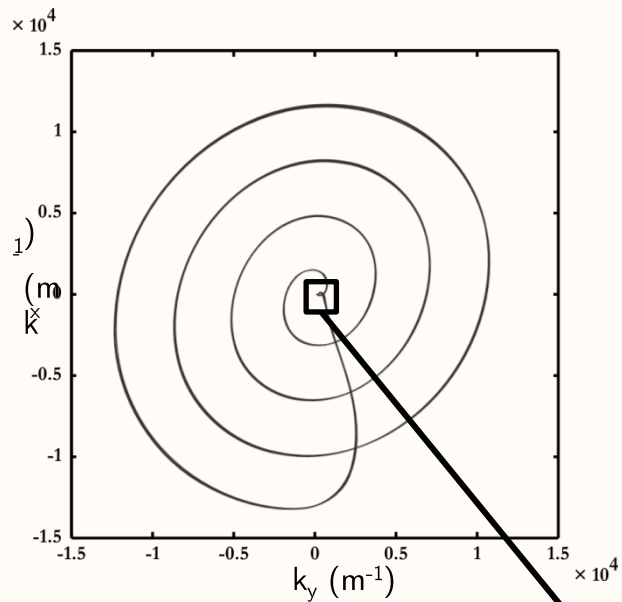
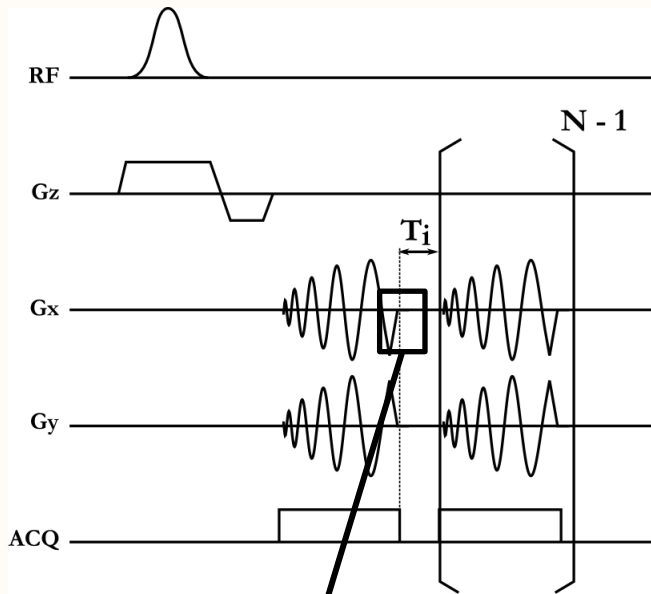
Spirale N échos



1 entrelacement  
10 échos

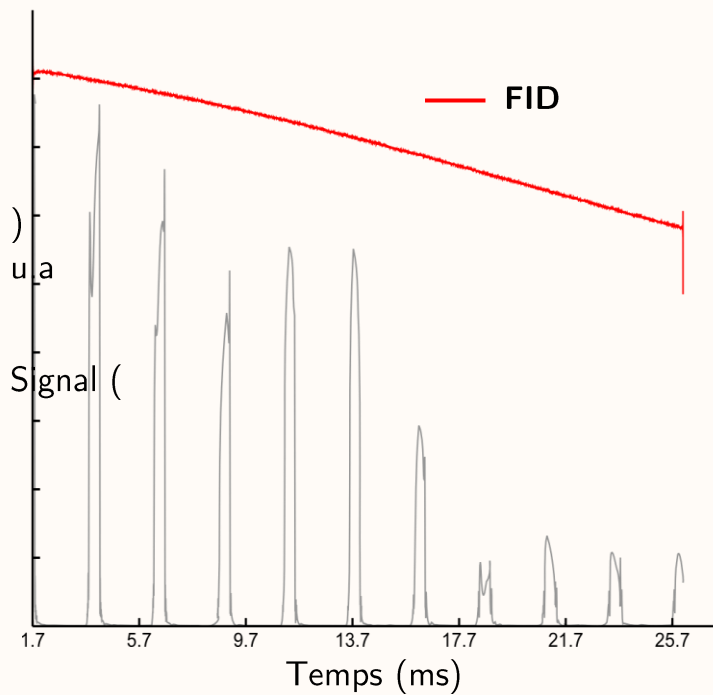


Spirale N échos

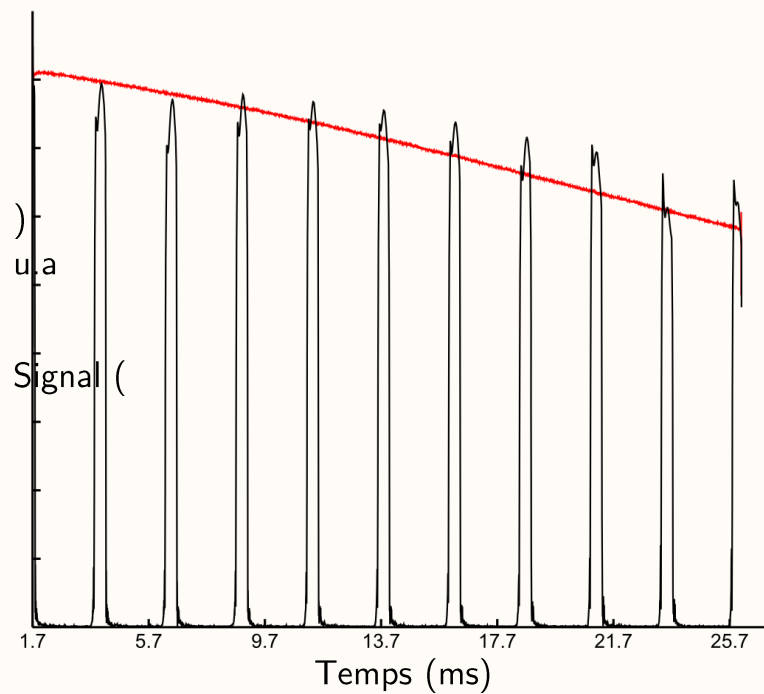




Avant correction



Après correction

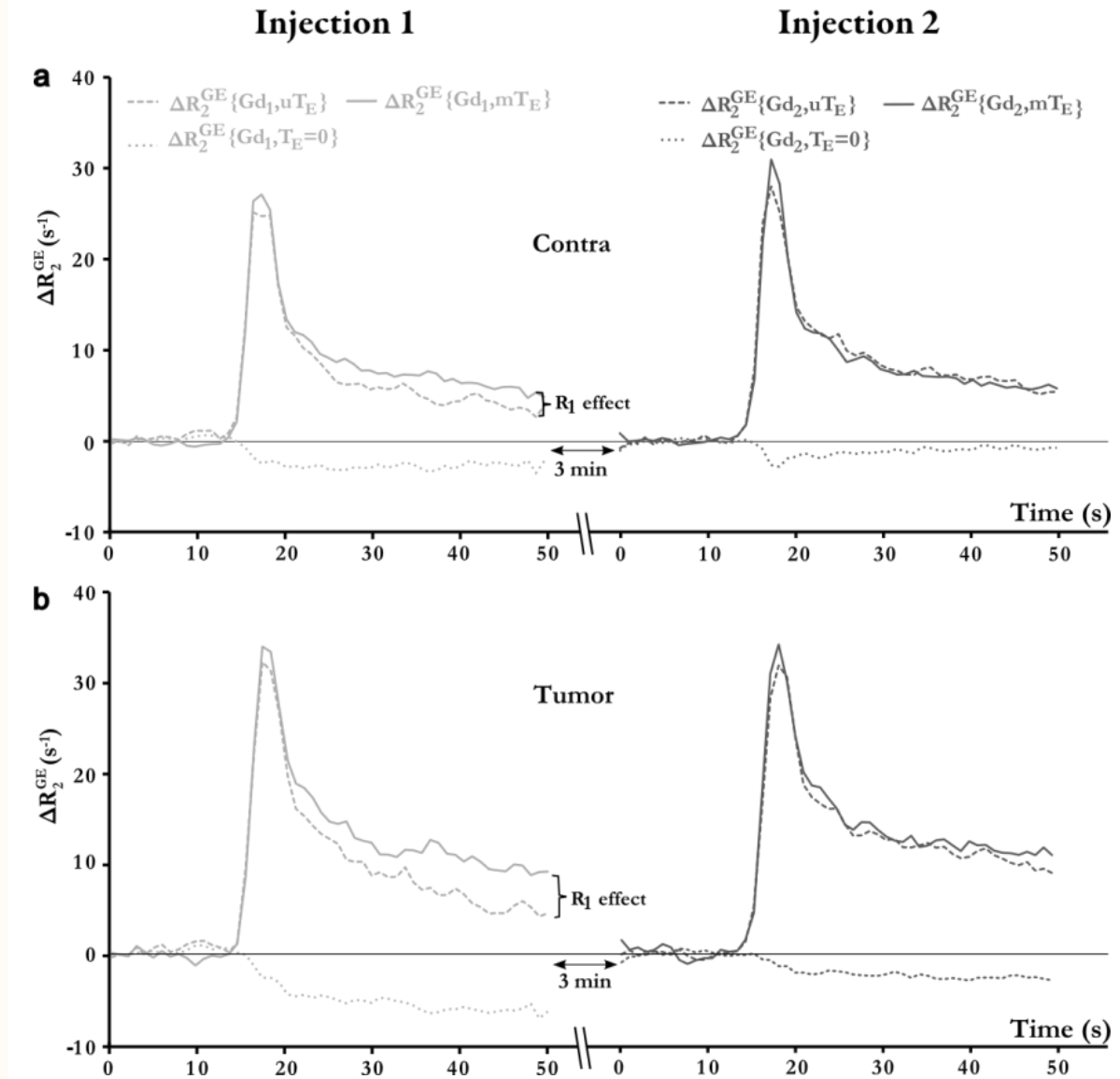


## Protocole imagerie

- Spirale, 5 GE, 2 entrelacements  
( $TE/\Delta TE = 1/12,8$  ms,  $TR = 250$  ms,  
voxel =  $0,254 \times 0,254 \times 1$  mm<sup>3</sup>)
- 2 injections de Gd

→ Pas de différence significative d'effet  $R_1$  au pic de concentration

→ Différence d'effet de relaxation  $R_1$  dans la région controlatérale entre les deux injections

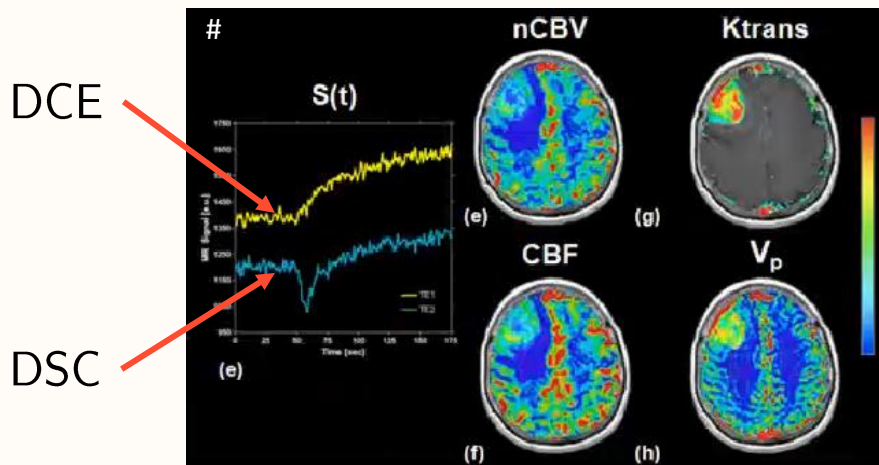


- Outil pour la caractérisation dynamique de  $R_2^{GE}$ 
  - ➔ Amélioration estimation BVf premier passage
  - ➔ VSI corrigé de  $R_1$

- Outil pour la caractérisation dynamique de  $R_2^{GE}$ 
  - ➔ Amélioration estimation BVf premier passage
  - ➔ VSI corrigé de  $R_1$

## Perspective :

Une injection, Deux contrastes

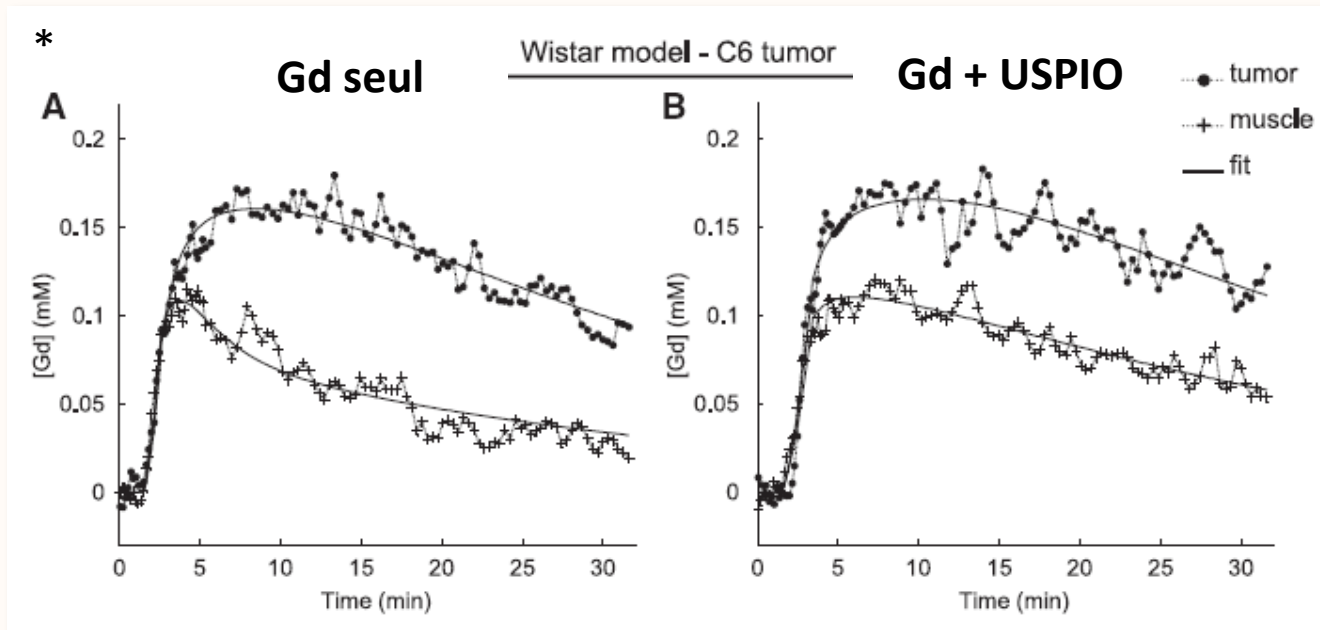
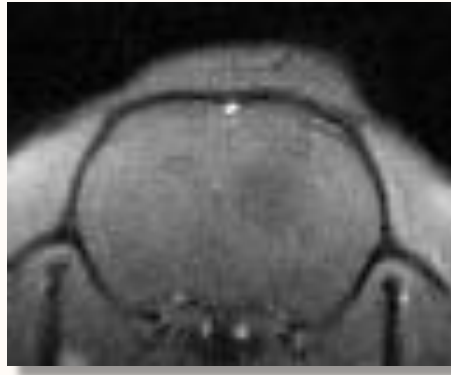


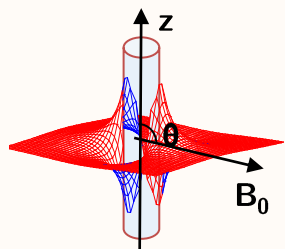
- Ajout écho de spin :
  - ➔ DCE + DSC en GE et SE (VSI) \*

**Intégrer l'ensemble de ces contrastes dans un unique modèle ?**  
**Prise en compte de la diffusion de l'AC ?**

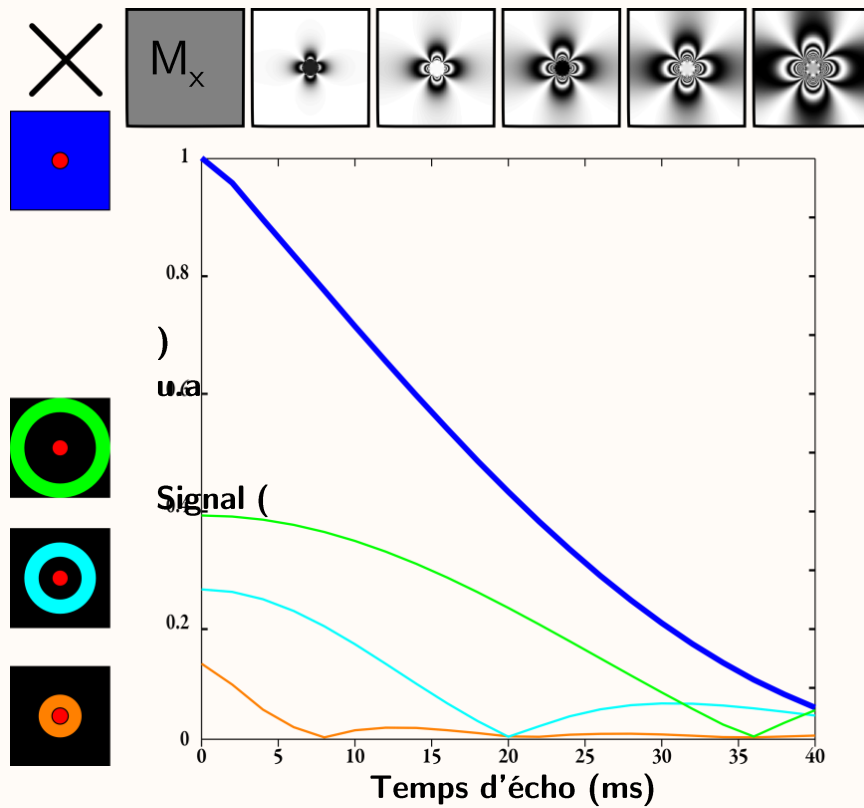
- ○ ○ ○ Introduction
  
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- *La diffusion de l'AC impacte-t-elle l'estimation de la perméabilité ?*
  - ➔ *Peut-on séparer  $D_{AC}$  et  $P_{AC}$  ?*
- *Impact de la porosité sur  $R_{2meso}$  ?*
  - ➔  $\Delta\chi_{i-c}$  vs  $\Delta\chi_{i-v}$

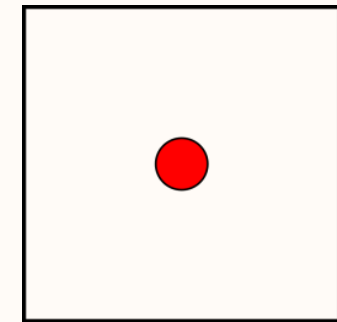
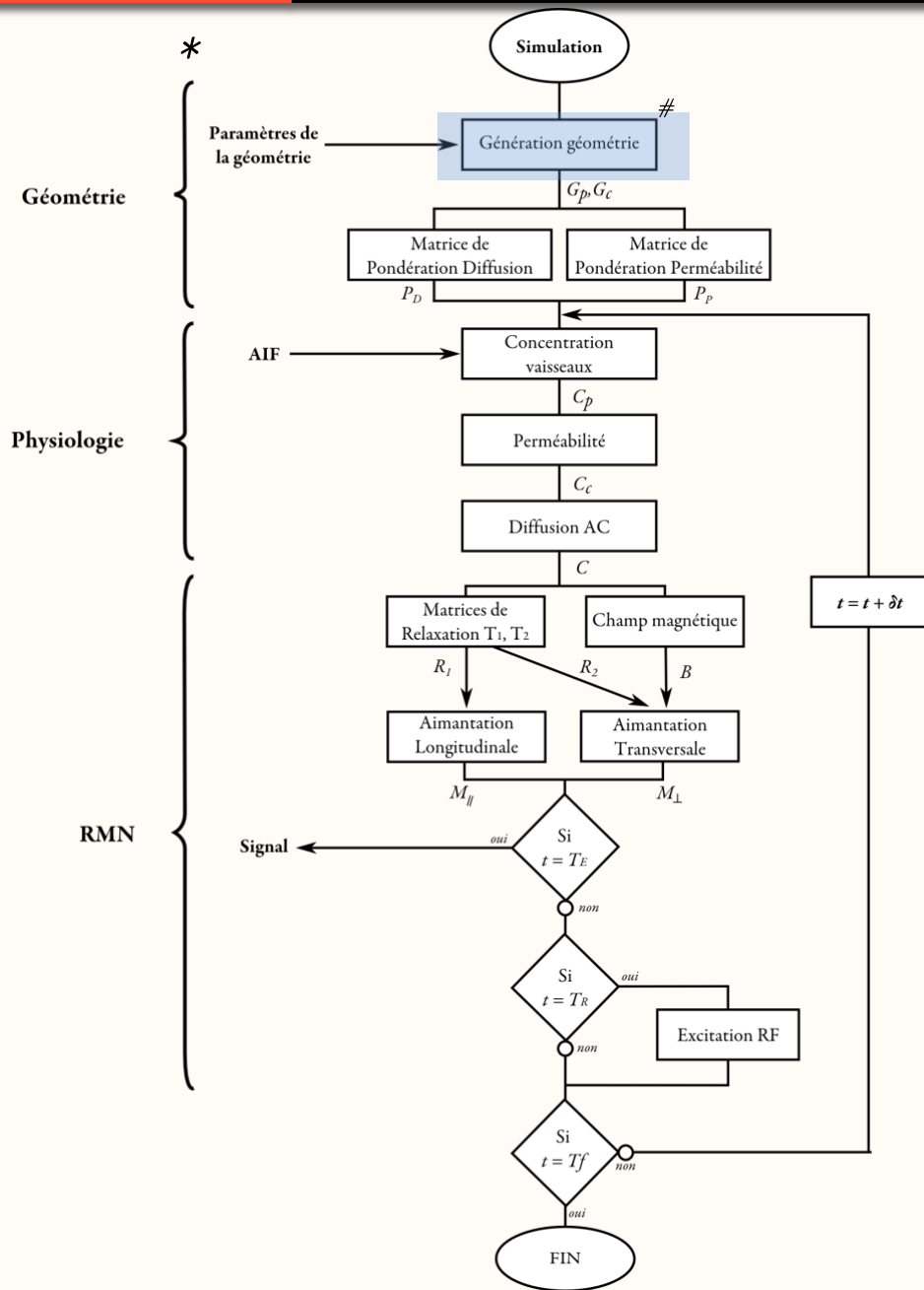




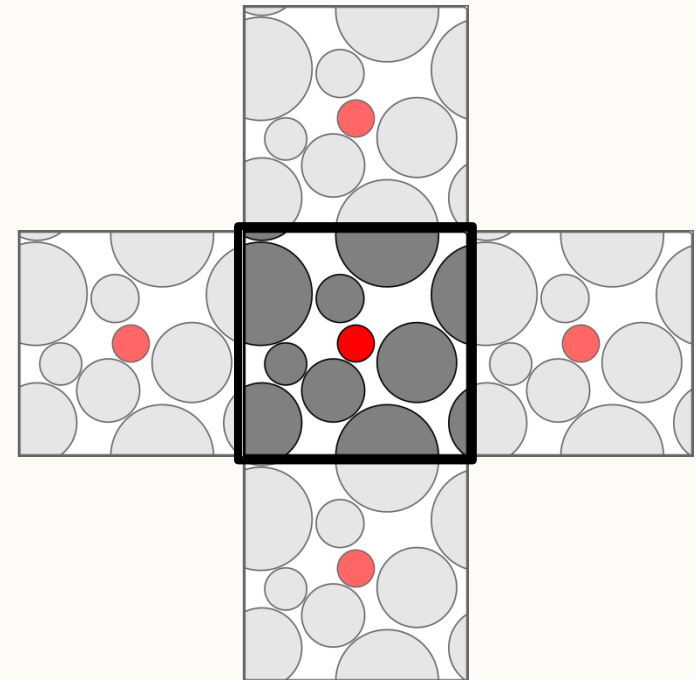
## AC intravasculaire (USPIO)







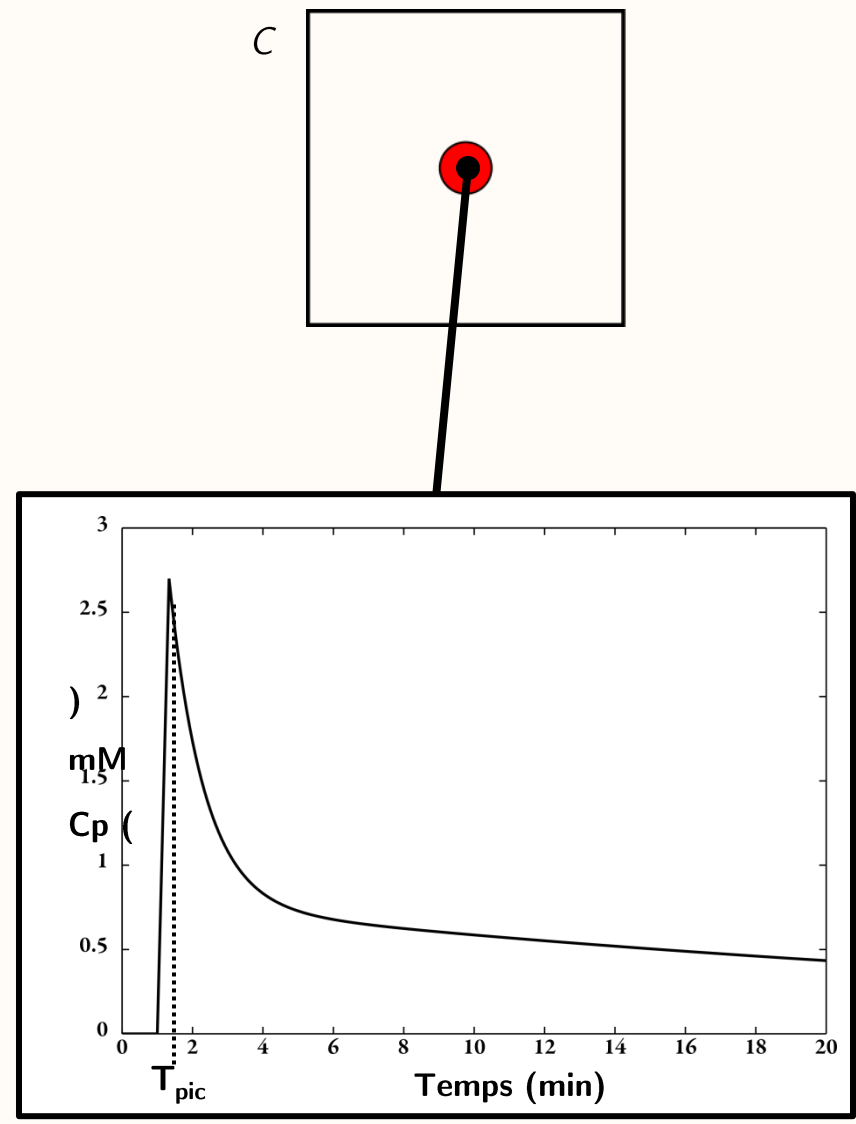
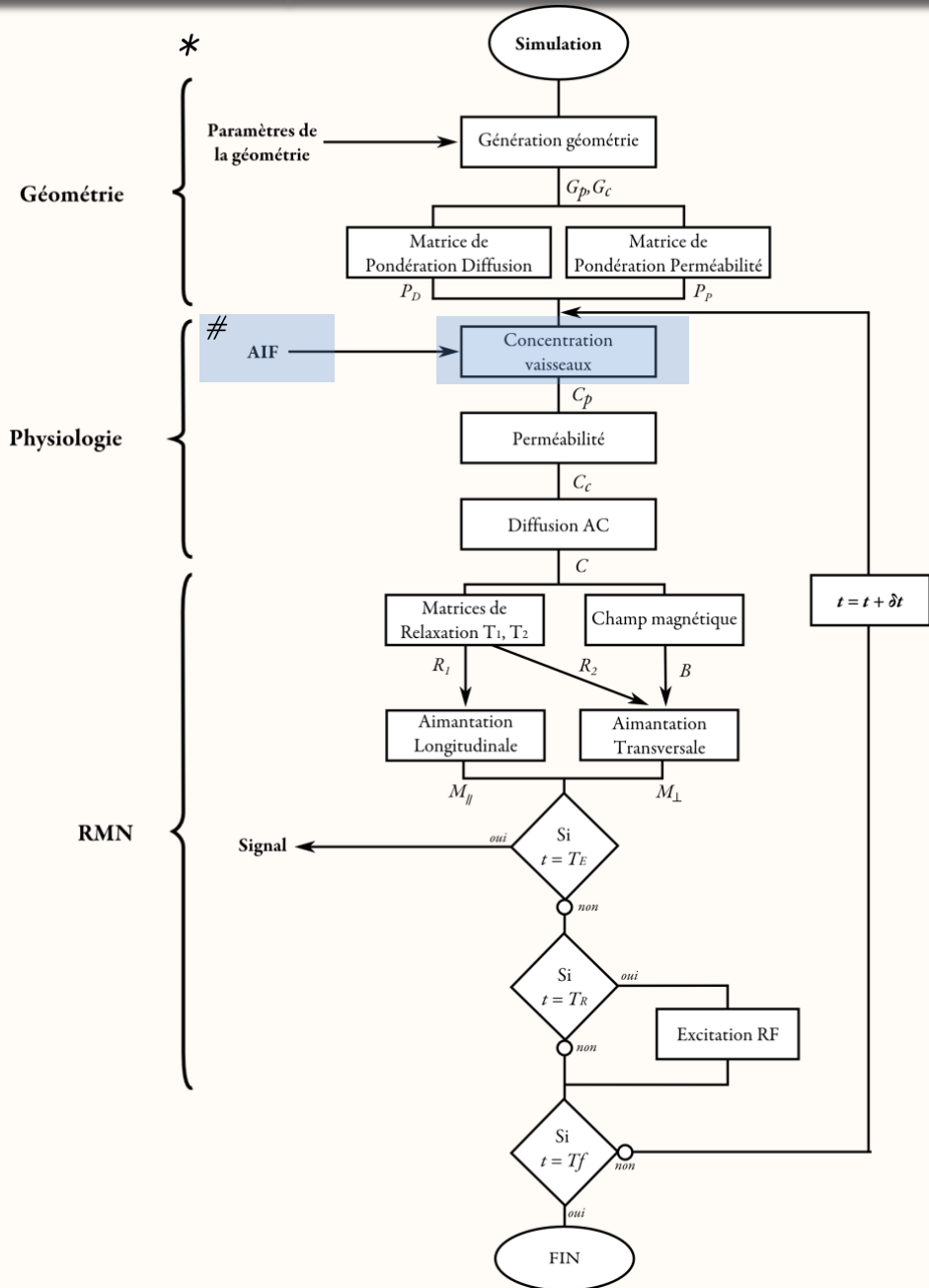
2 compartiments



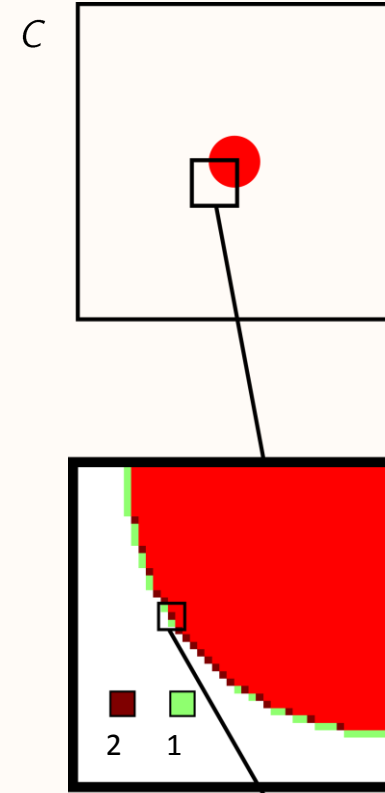
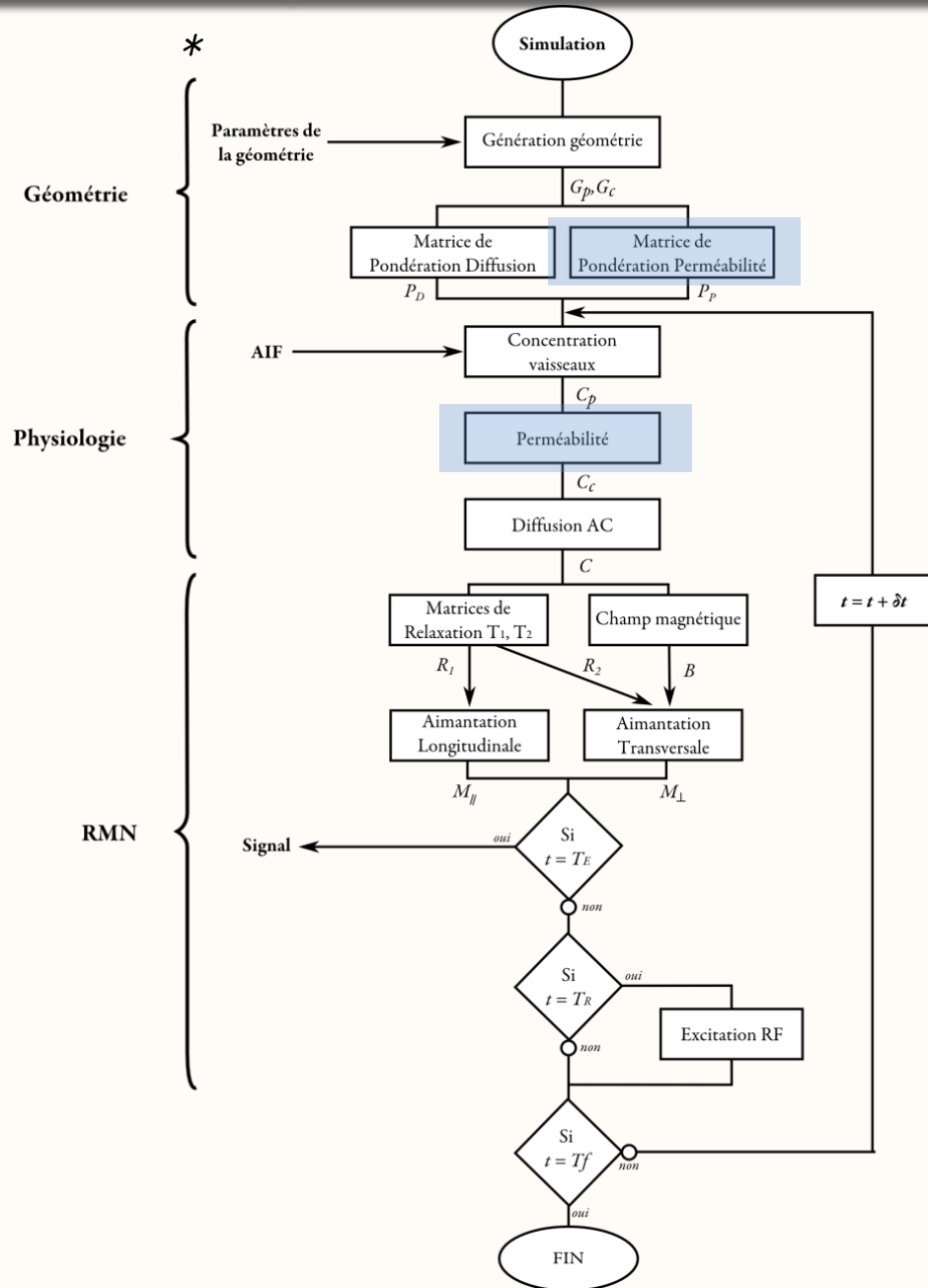
3 compartiments

# Collab F. Mauconduit – GIN Equipe 5

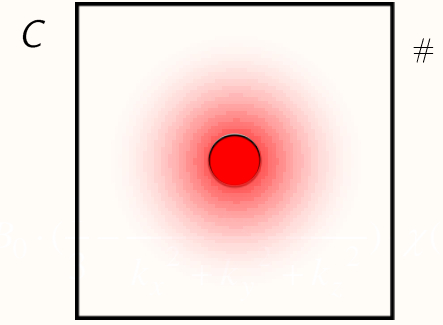
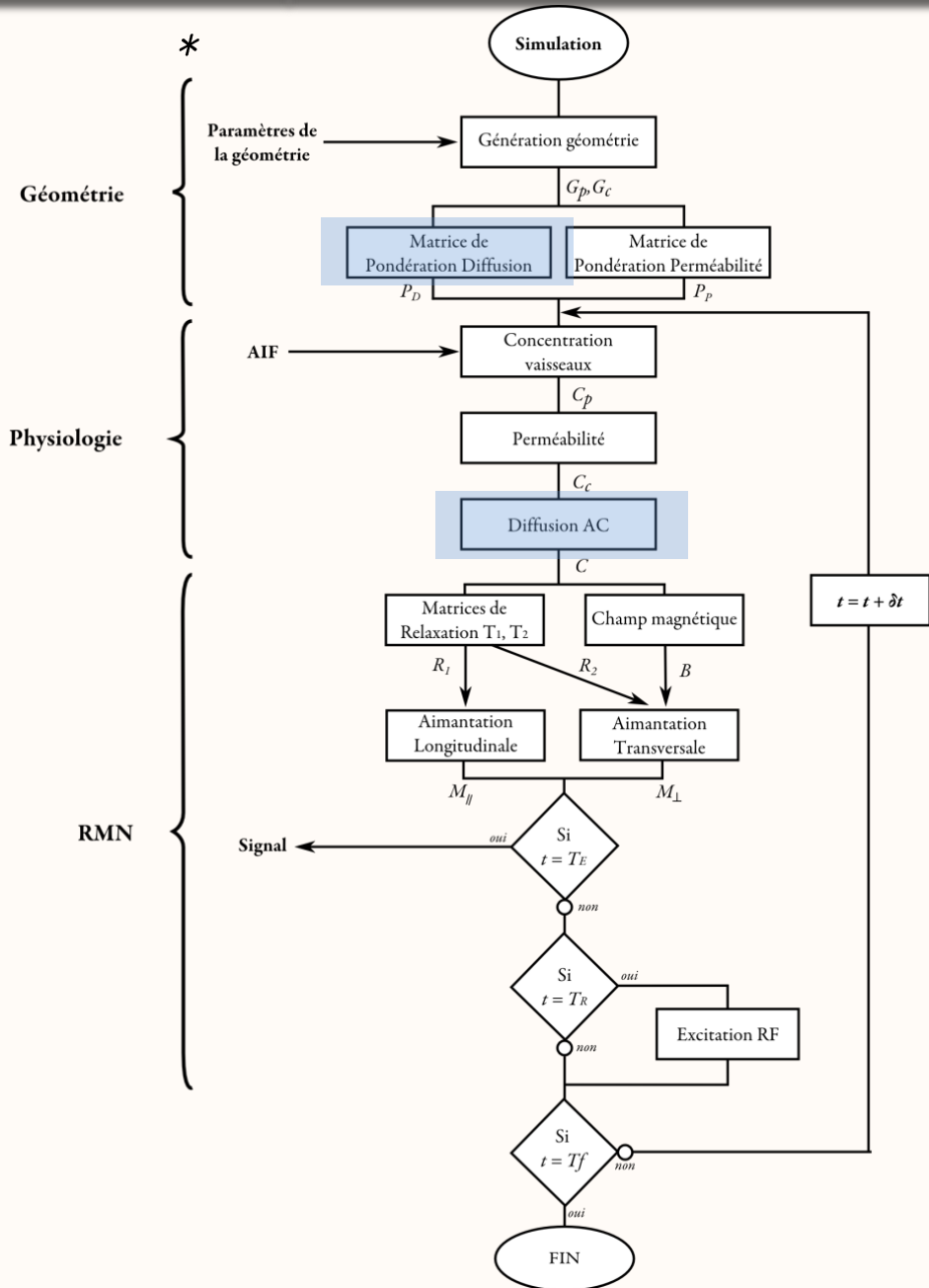
\* Collab, C. Debacker – GIN Equipe 5



\* Collab, C. Debacker – GIN Equipe 5  
# Collab, CEA-LETI-DTBS



$$\delta C_c(t) = k_{pe}(c_p(t) - C_c(t))\delta t$$

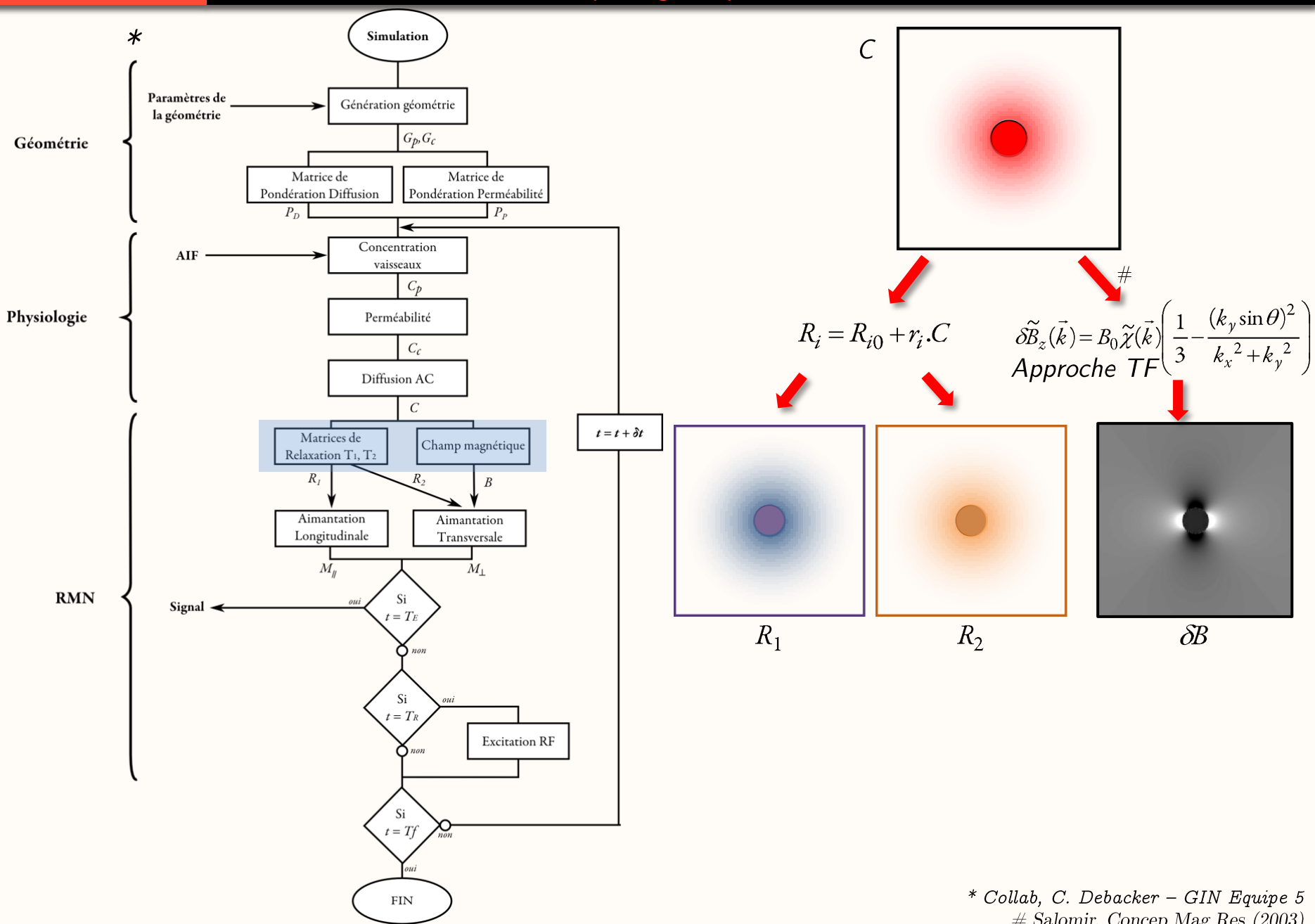


$$B_{xy}(t) = B_{xy}(t_0) + \int_{t_0}^t D_{xy}(t') \nabla^2 B_{xy}(t') dt'$$

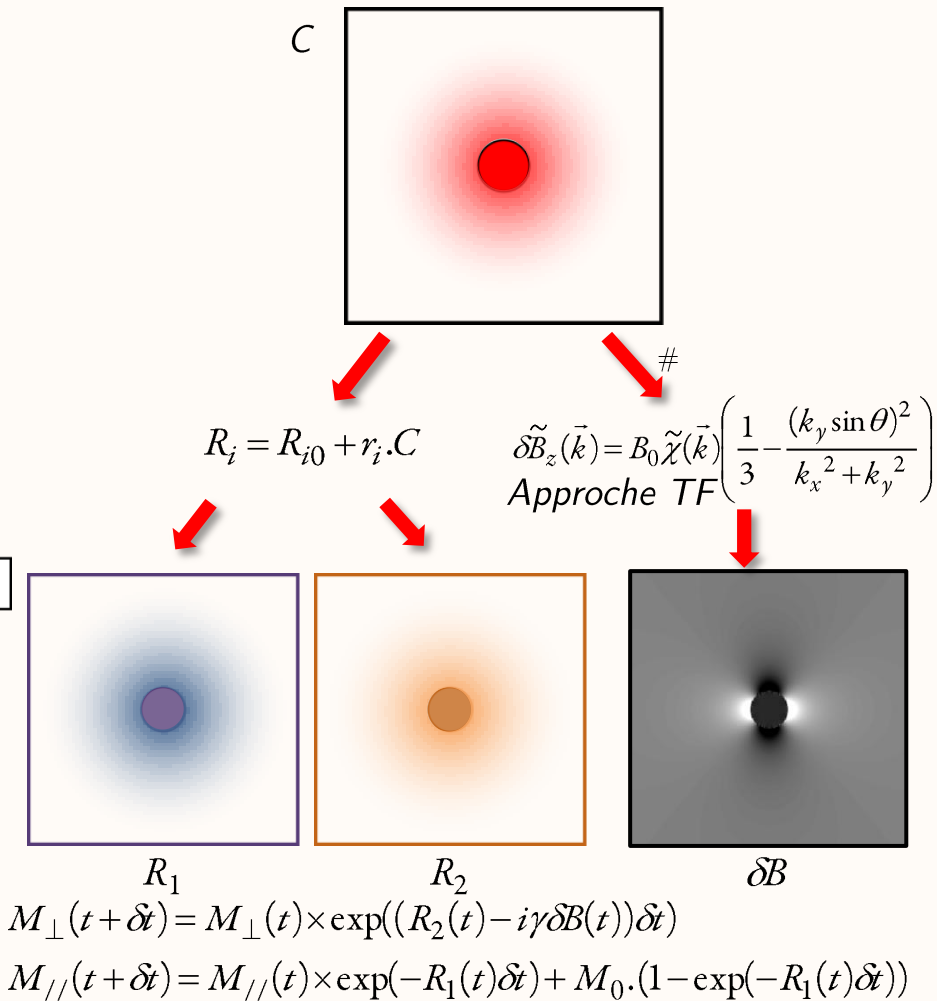
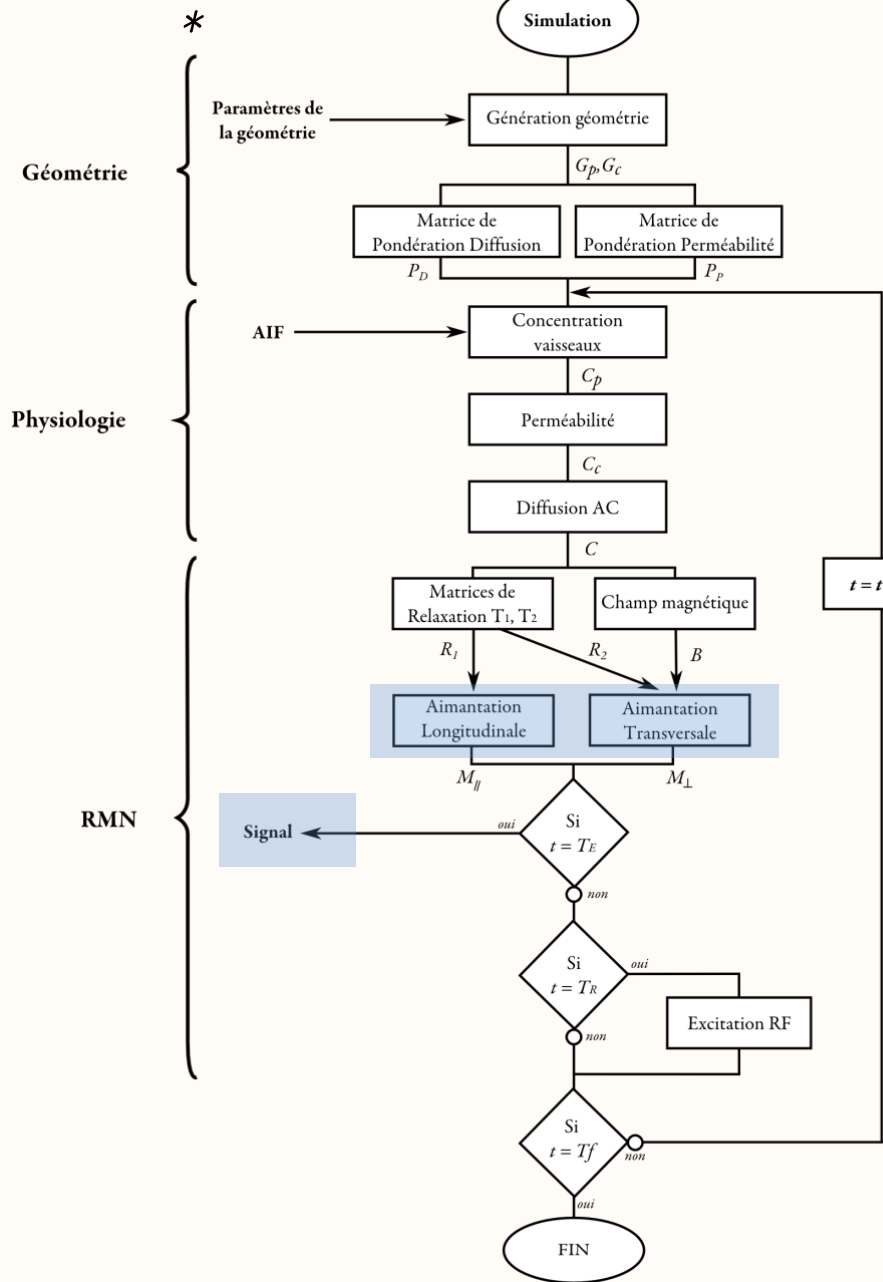
$$D_{xy} = \frac{1}{4\pi D_{AC} \delta t} \exp\left(-\frac{x^2 + y^2}{4D_{AC} \delta t}\right)$$

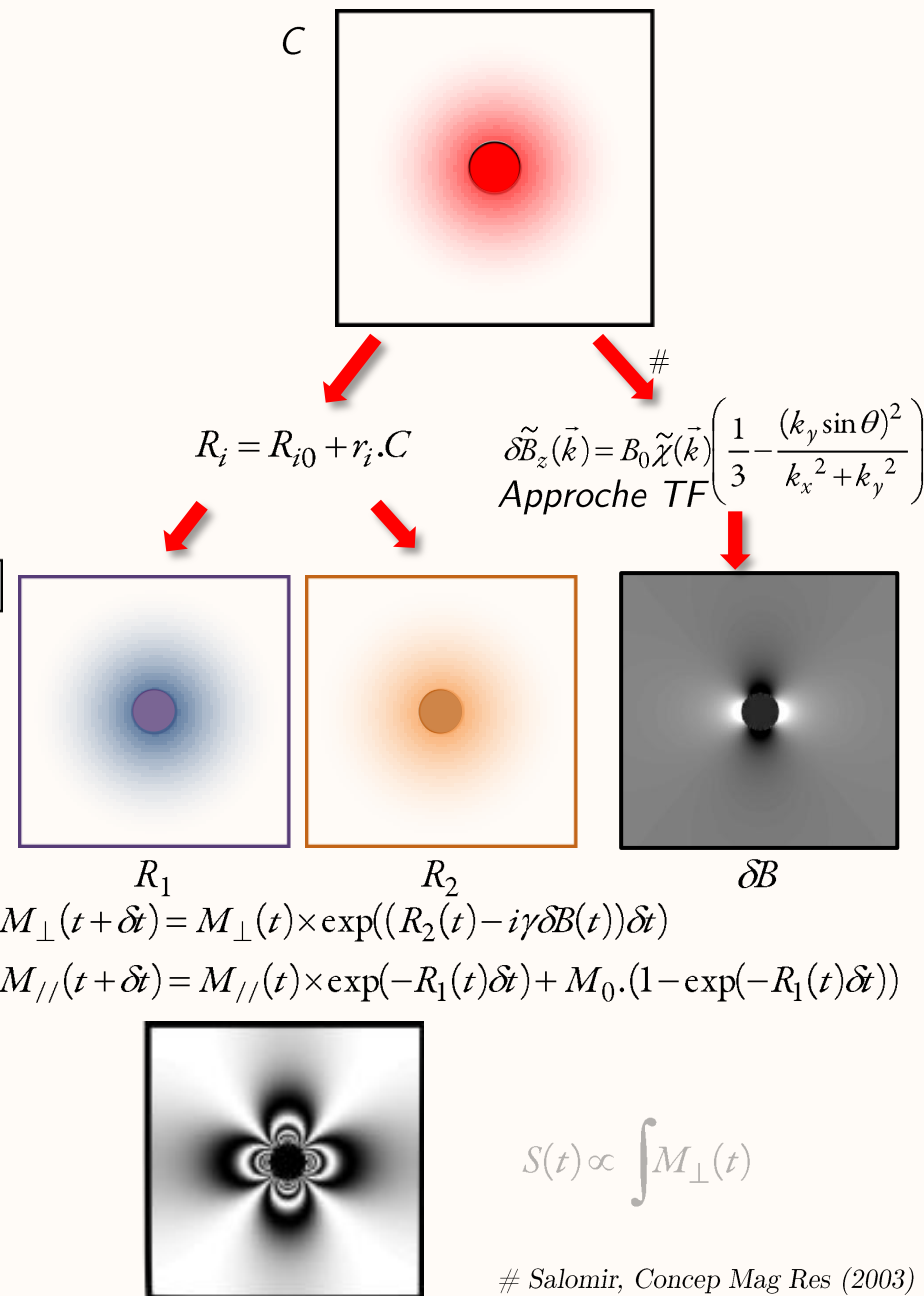
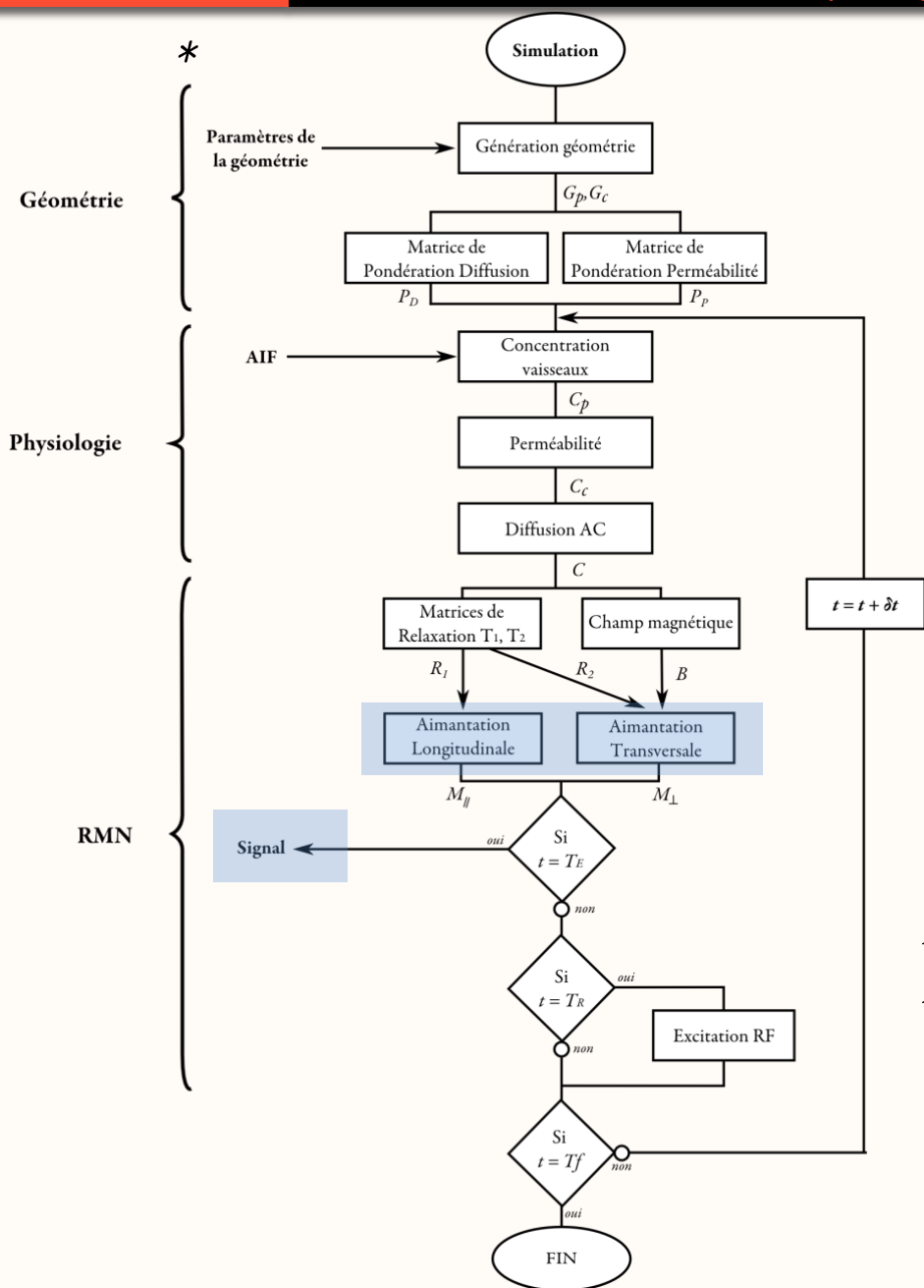
Approche convolution (TF)

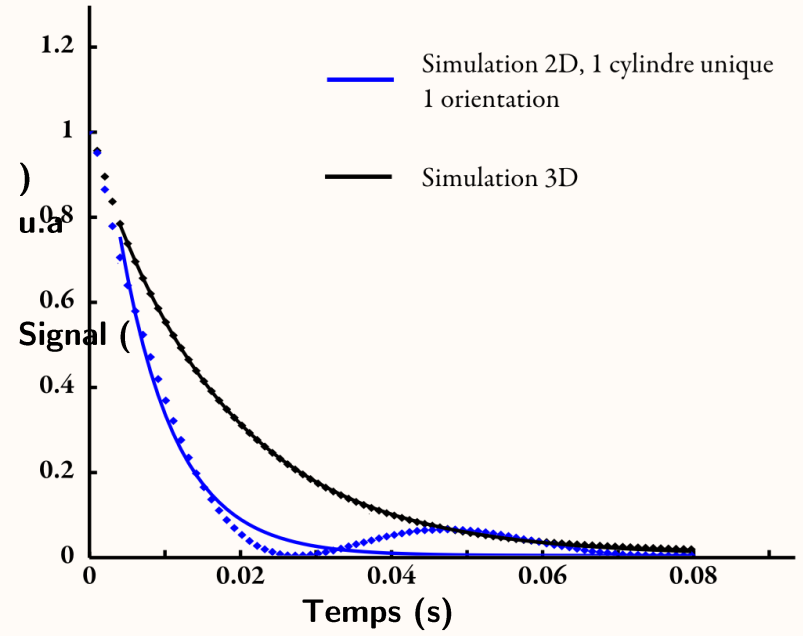
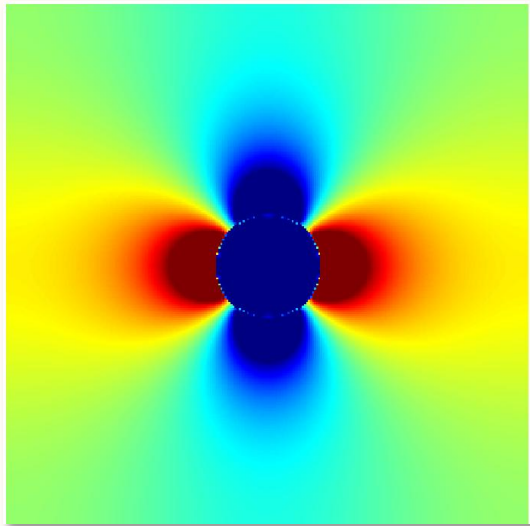
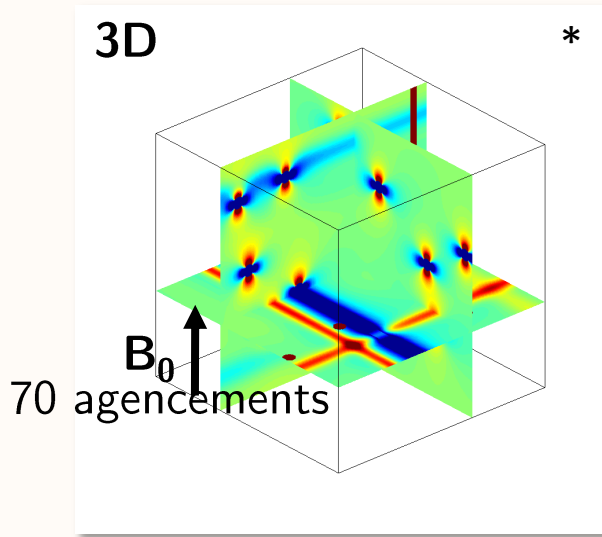
\* Collab, C. Debacker – GIN Equipe 5  
# Bandettini, J Imag Syst Techn (1995)



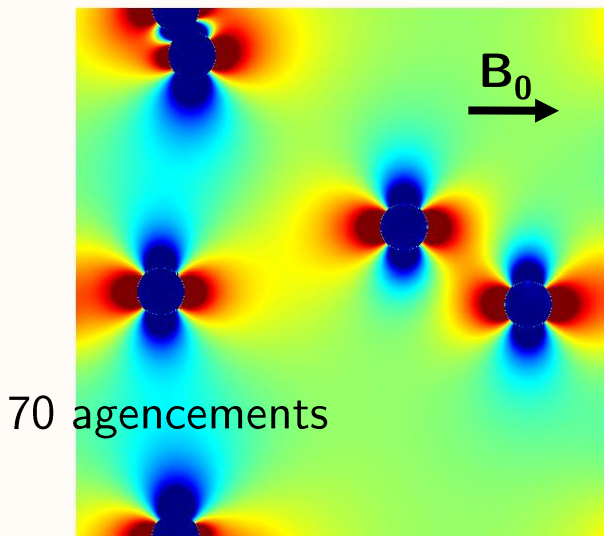
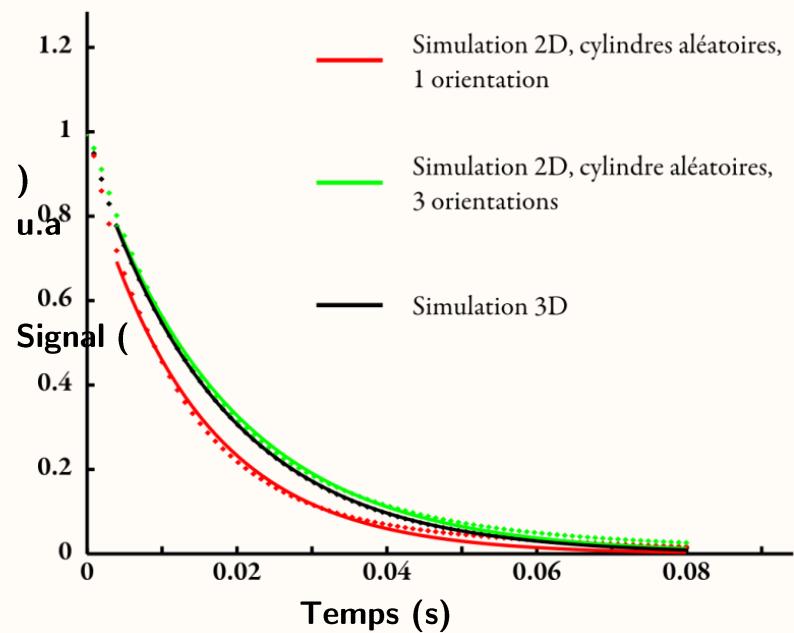
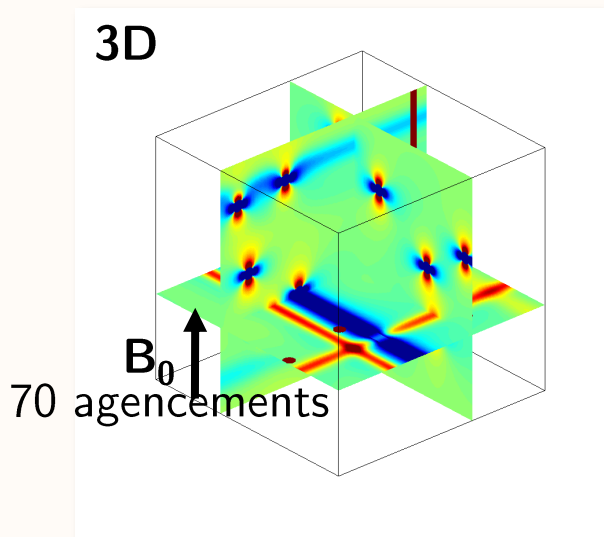
\* Collab, C. Debacker – GIN Equipe 5  
# Salomir, Concep Mag Res (2003)

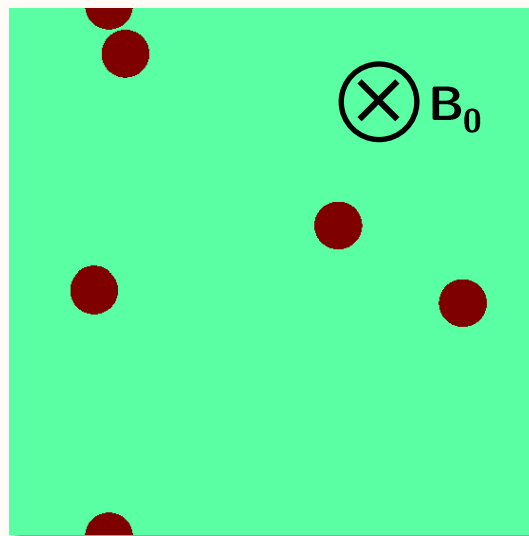
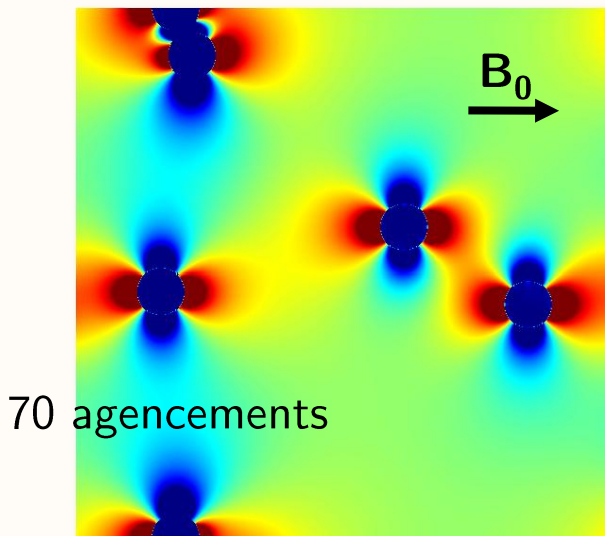
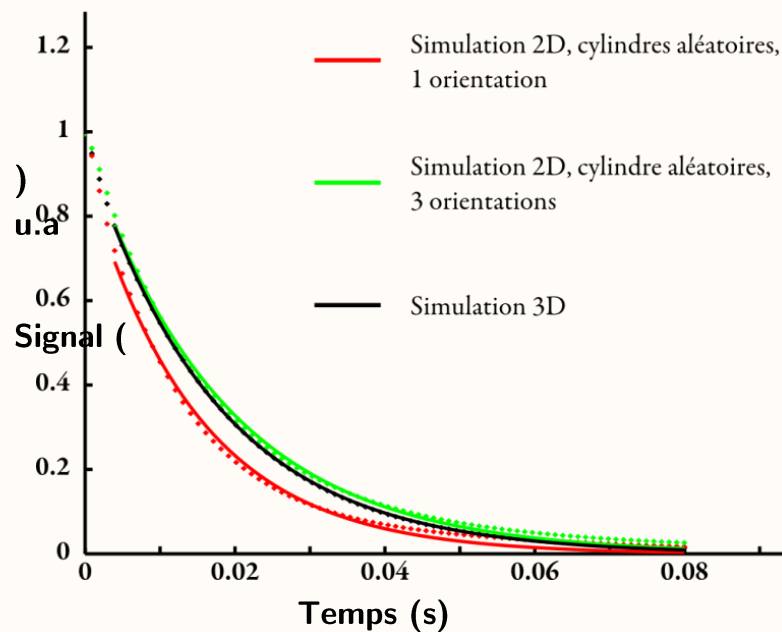
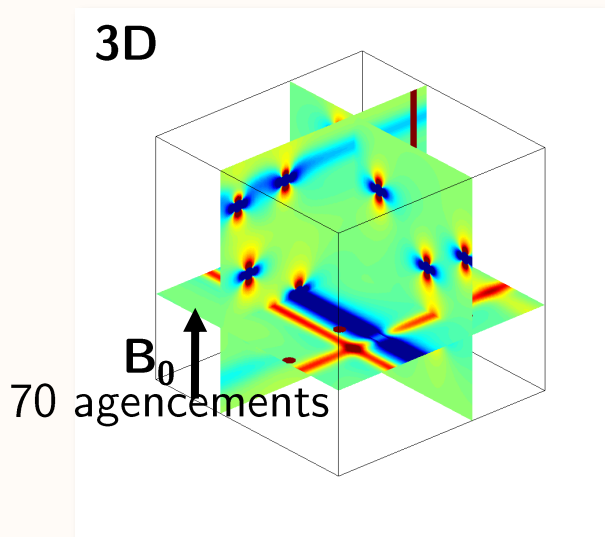








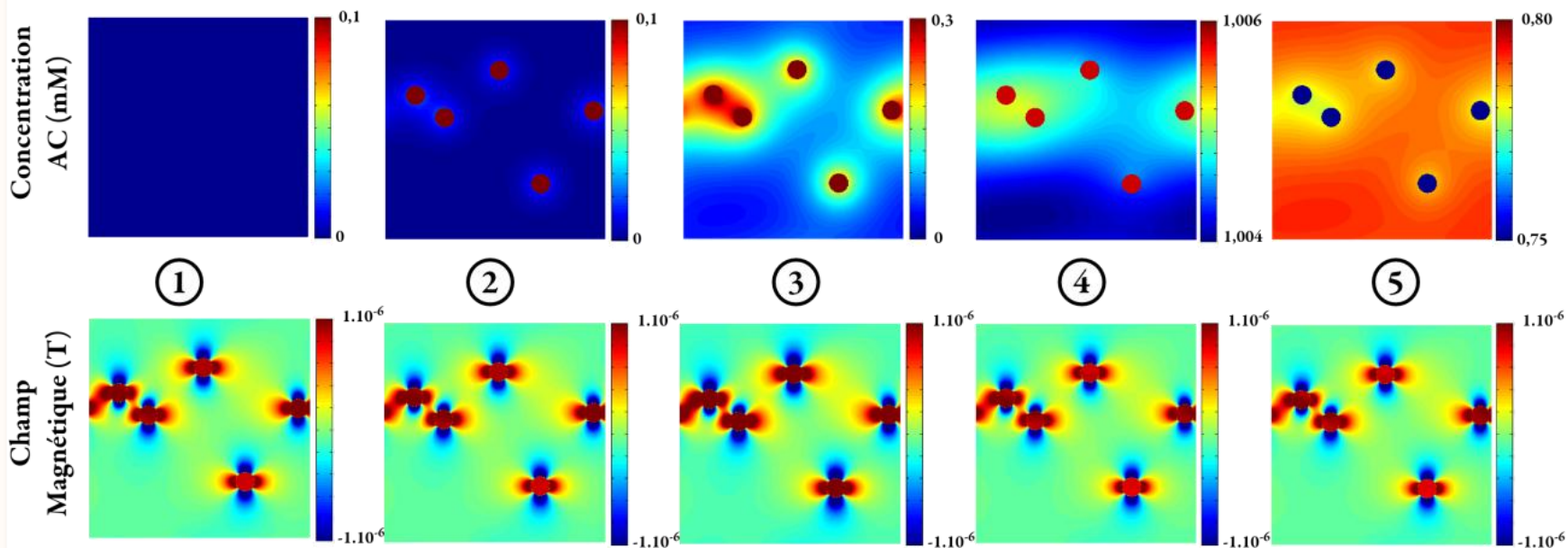
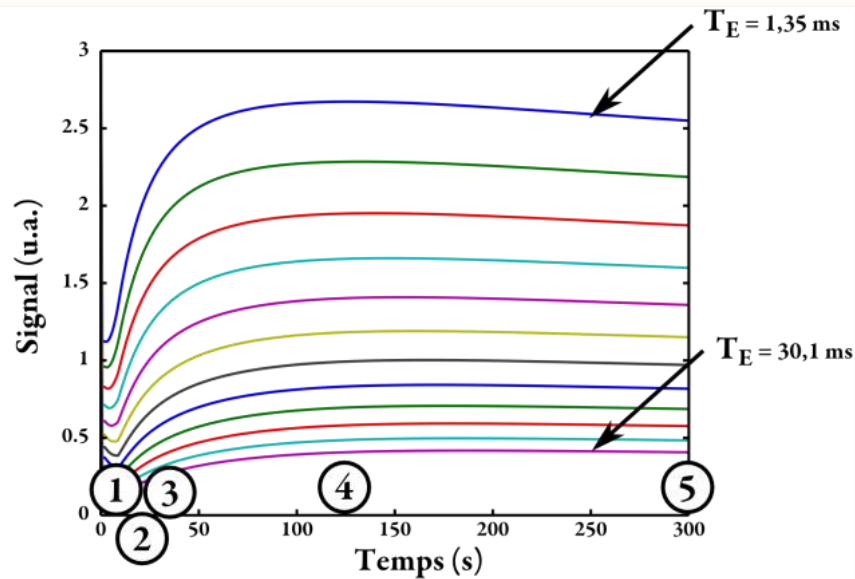
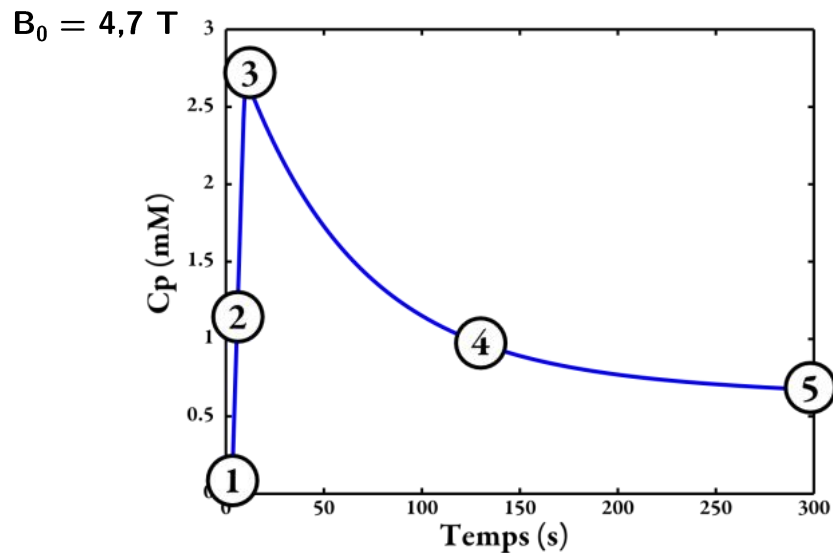


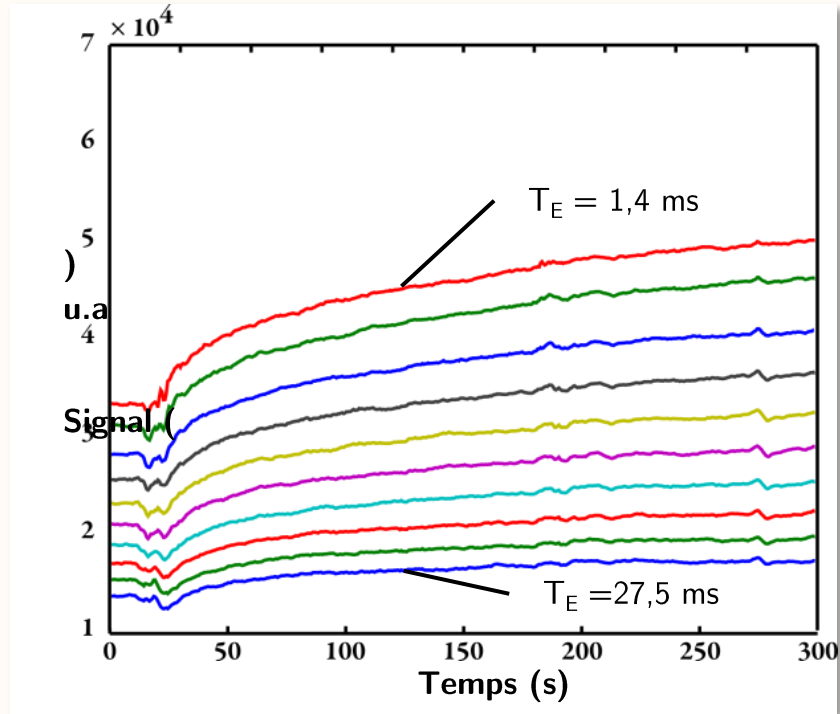
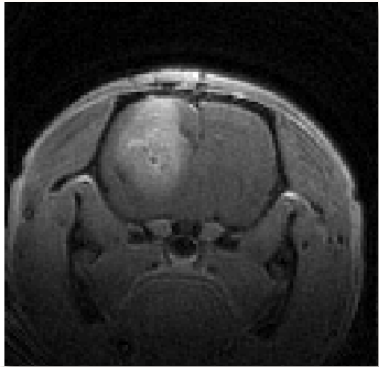


Pondération : 2/3

1/3

- *La diffusion de l'AC impacte-t-elle l'estimation de la perméabilité ?*  
→ *Peut-on séparer  $D_{AC}$  et  $P_{AC}$  ?*
- *Impact de la porosité sur  $R_{2meso}$  ?*  
→  *$\Delta\chi_{i-c}$  vs  $\Delta\chi_{i-v}$*

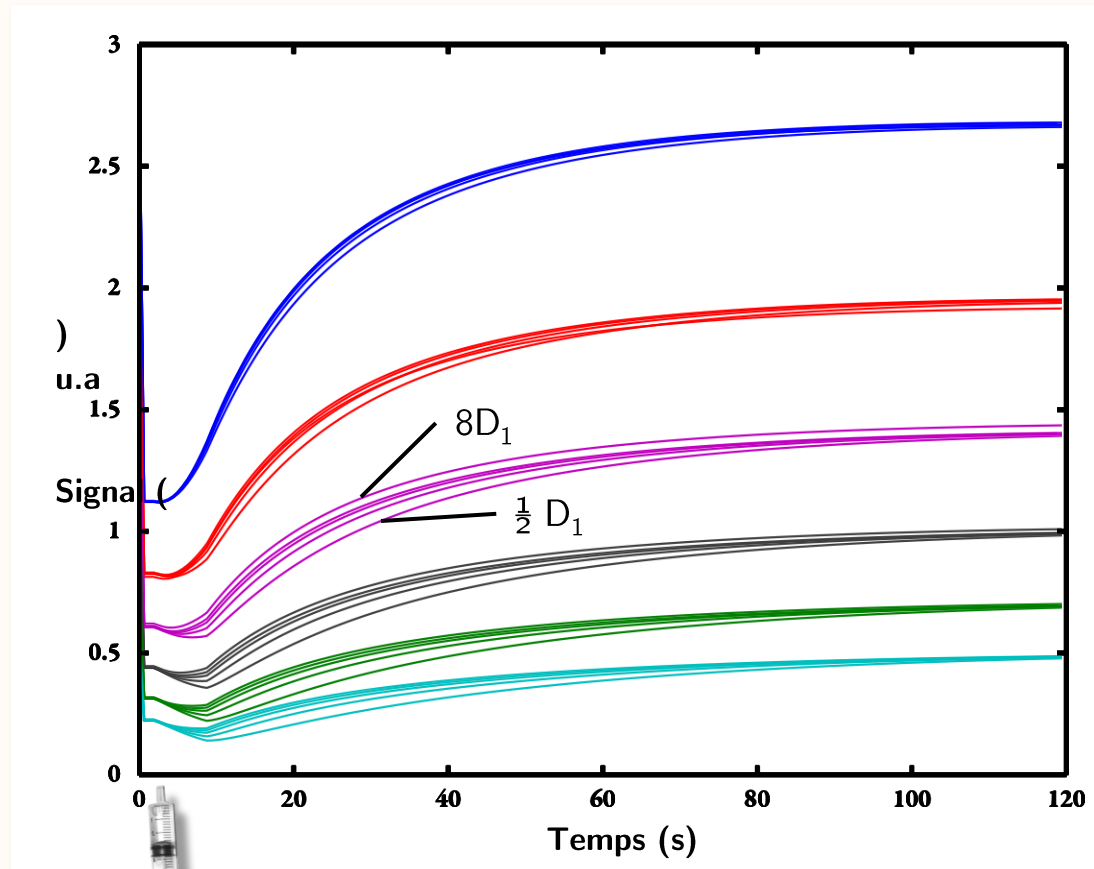




$$D_1 = D_{\text{Gd-DOTA}} = 46 \mu\text{m}^2 \cdot \text{s}^{-1} *$$

$$k_1 = 1,8 \cdot 10^{-3} \text{ s}^{-1} \#$$

$$23 \mu\text{m}^2 \cdot \text{s}^{-1} < D_{\text{AC}} < 368 \mu\text{m}^2 \cdot \text{s}^{-1}$$



$$T_E = 1,4 \text{ ms}$$

$$T_E = 6,6 \text{ ms}$$

$$T_E = 11,8 \text{ ms}$$

$$T_E = 17,1 \text{ ms}$$

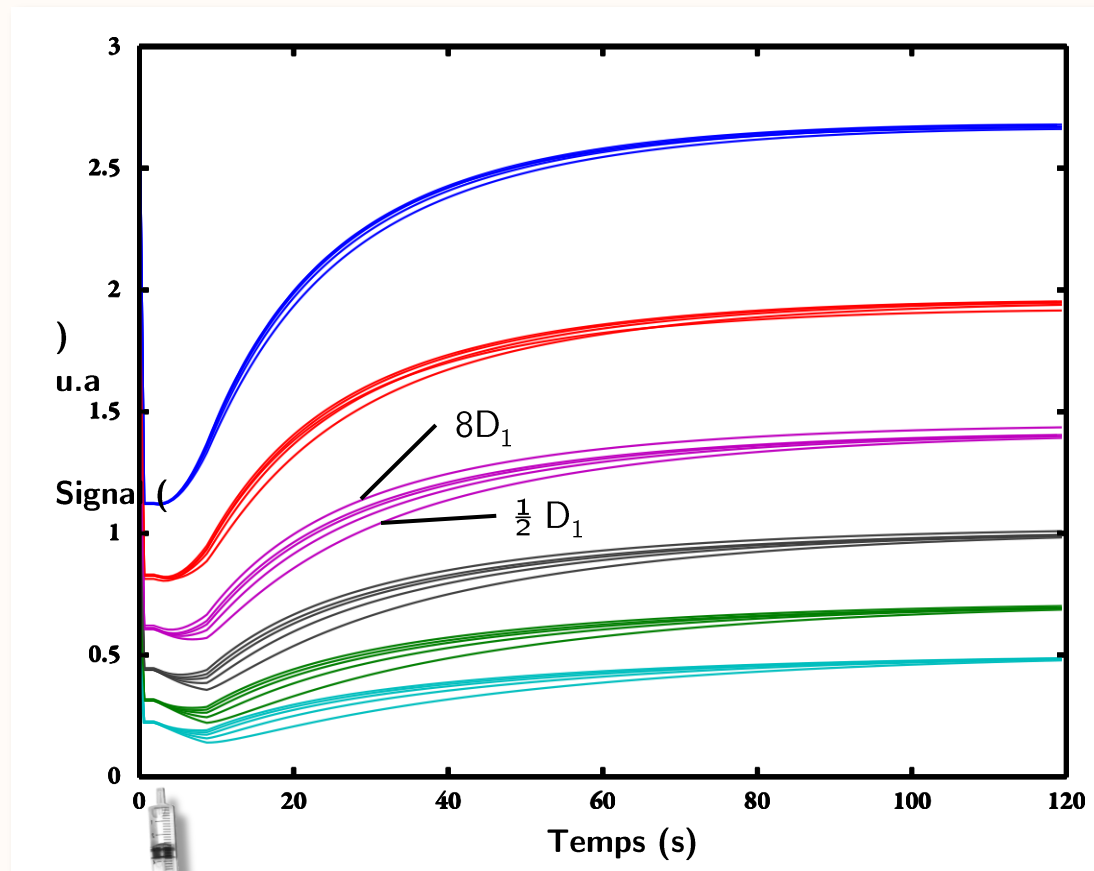
$$T_E = 22,3 \text{ ms}$$

$$T_E = 27,5 \text{ ms}$$

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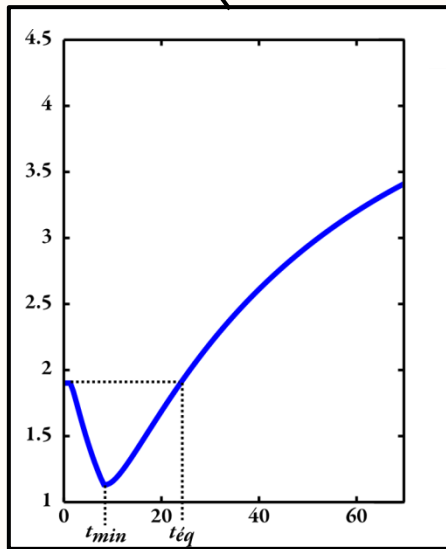
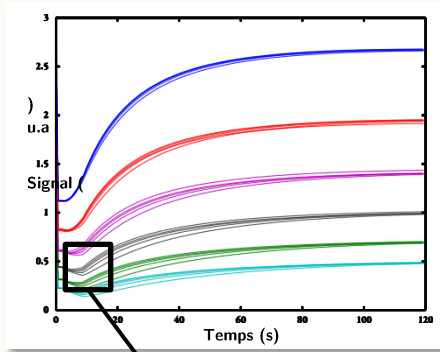
$$T_E = 11,8 \text{ ms}$$

$$T_E = 17,1 \text{ ms}$$

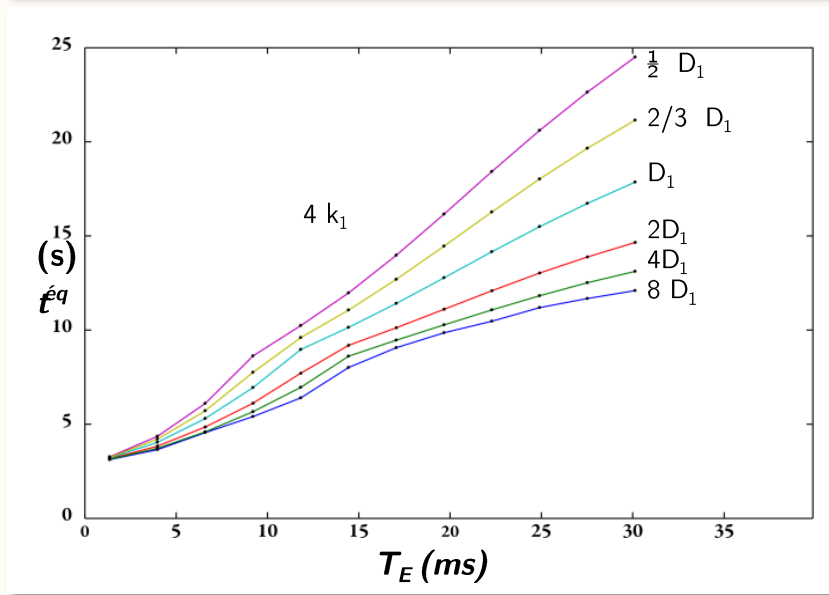
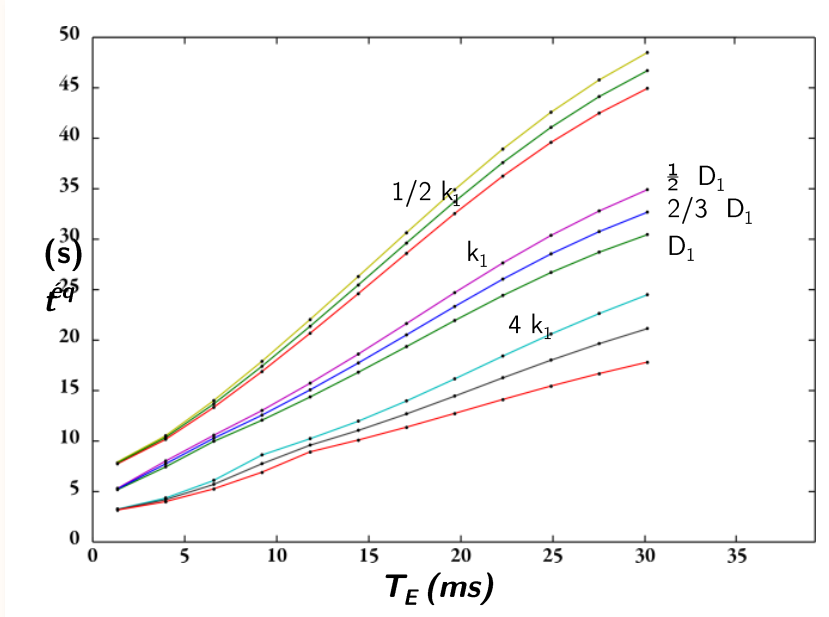
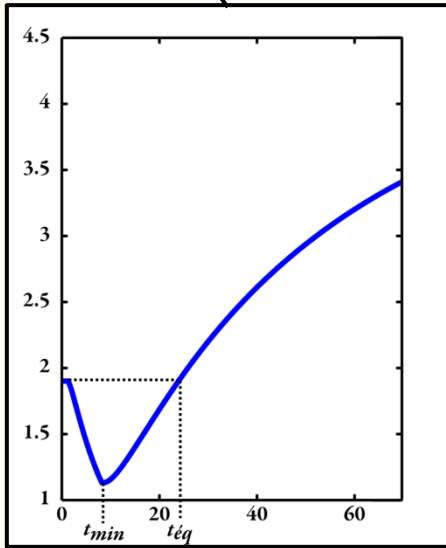
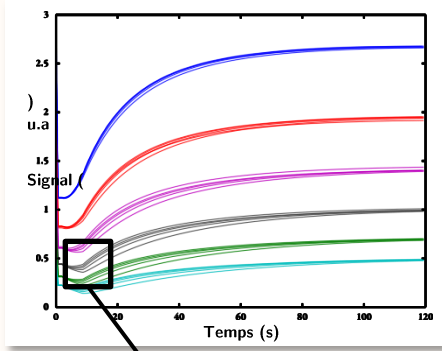
$$T_E = 22,3 \text{ ms}$$

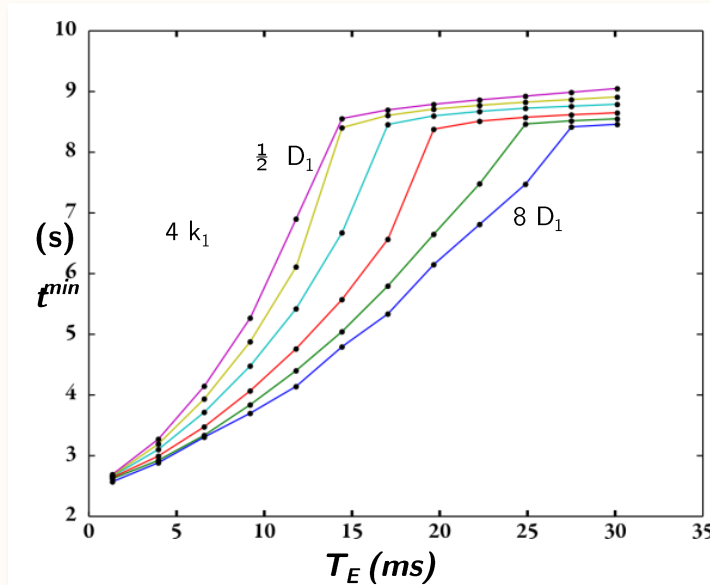
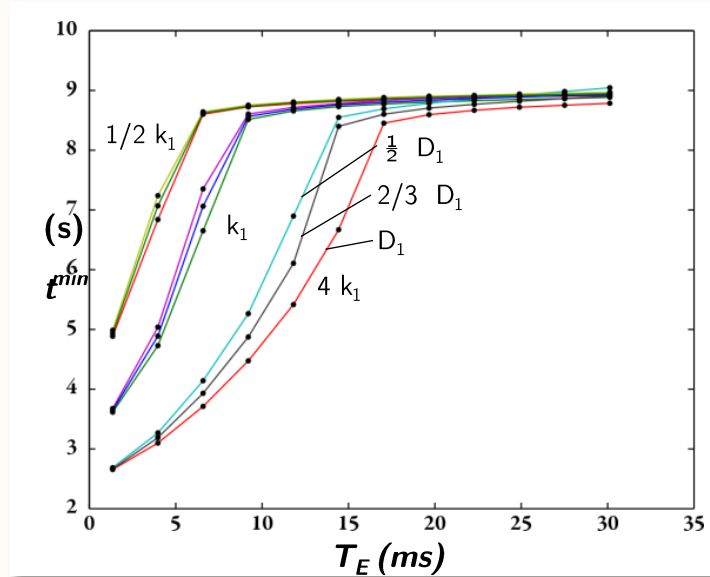
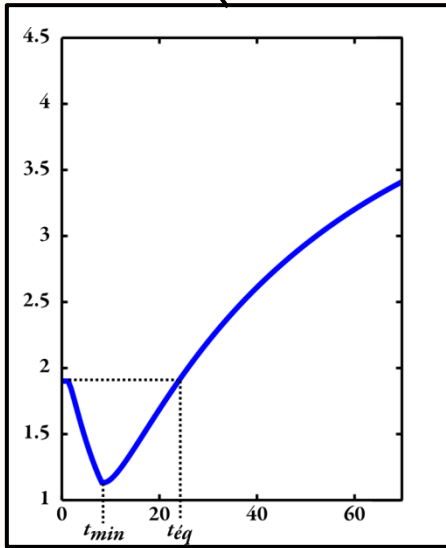
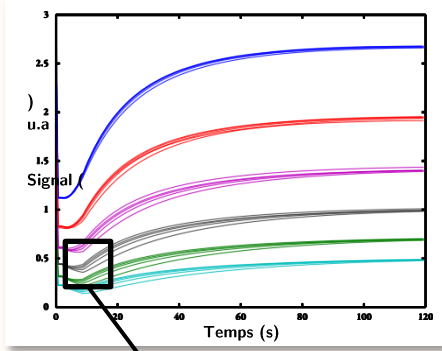
$$T_E = 27,5 \text{ ms}$$

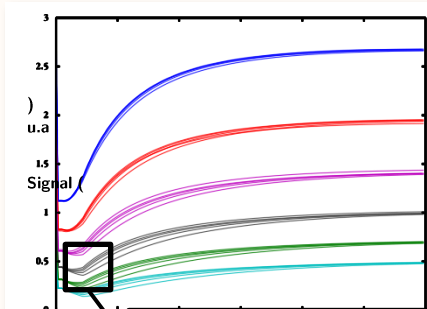
Absence d'un modèle analytique 😞



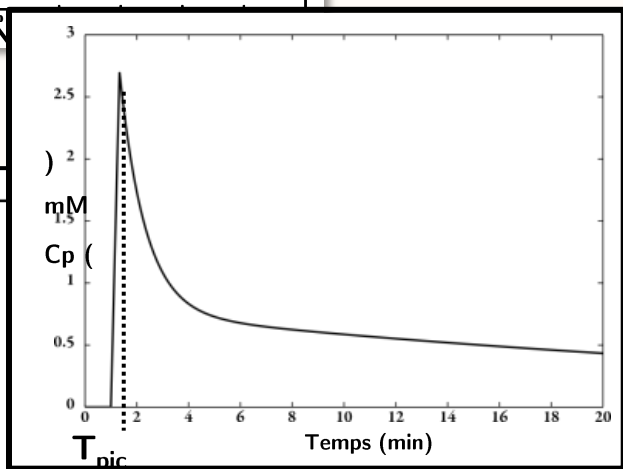




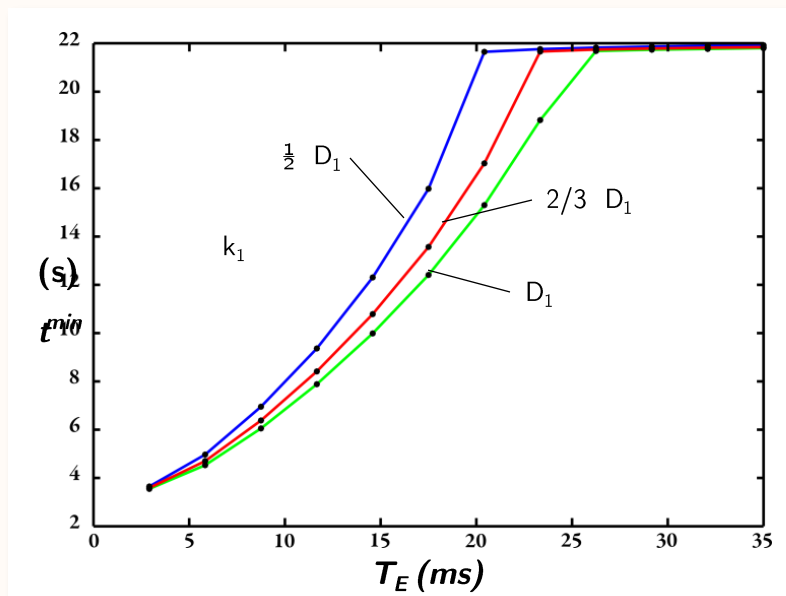
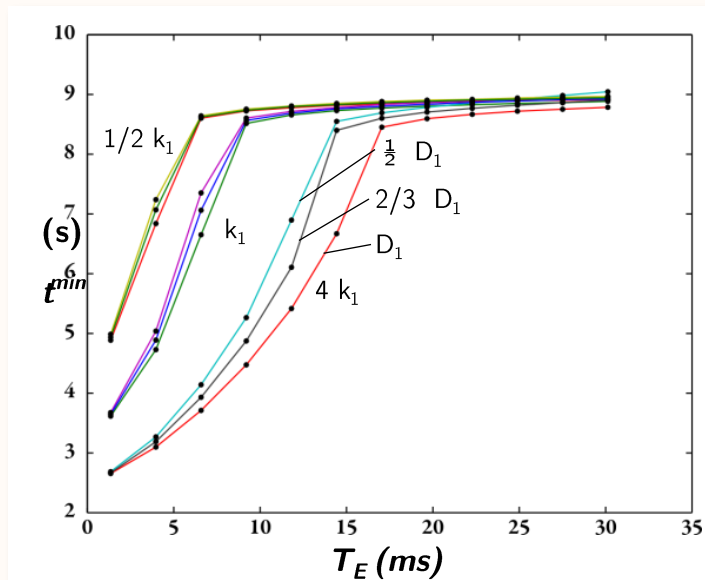
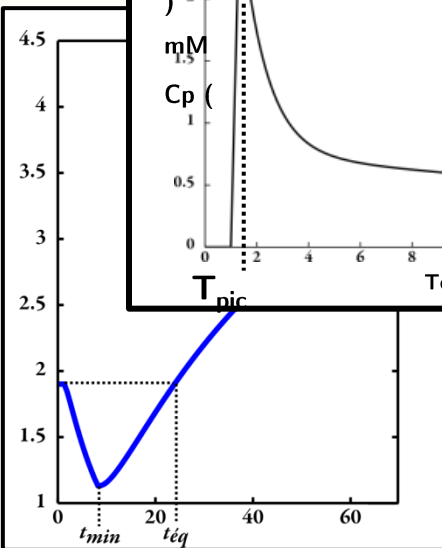




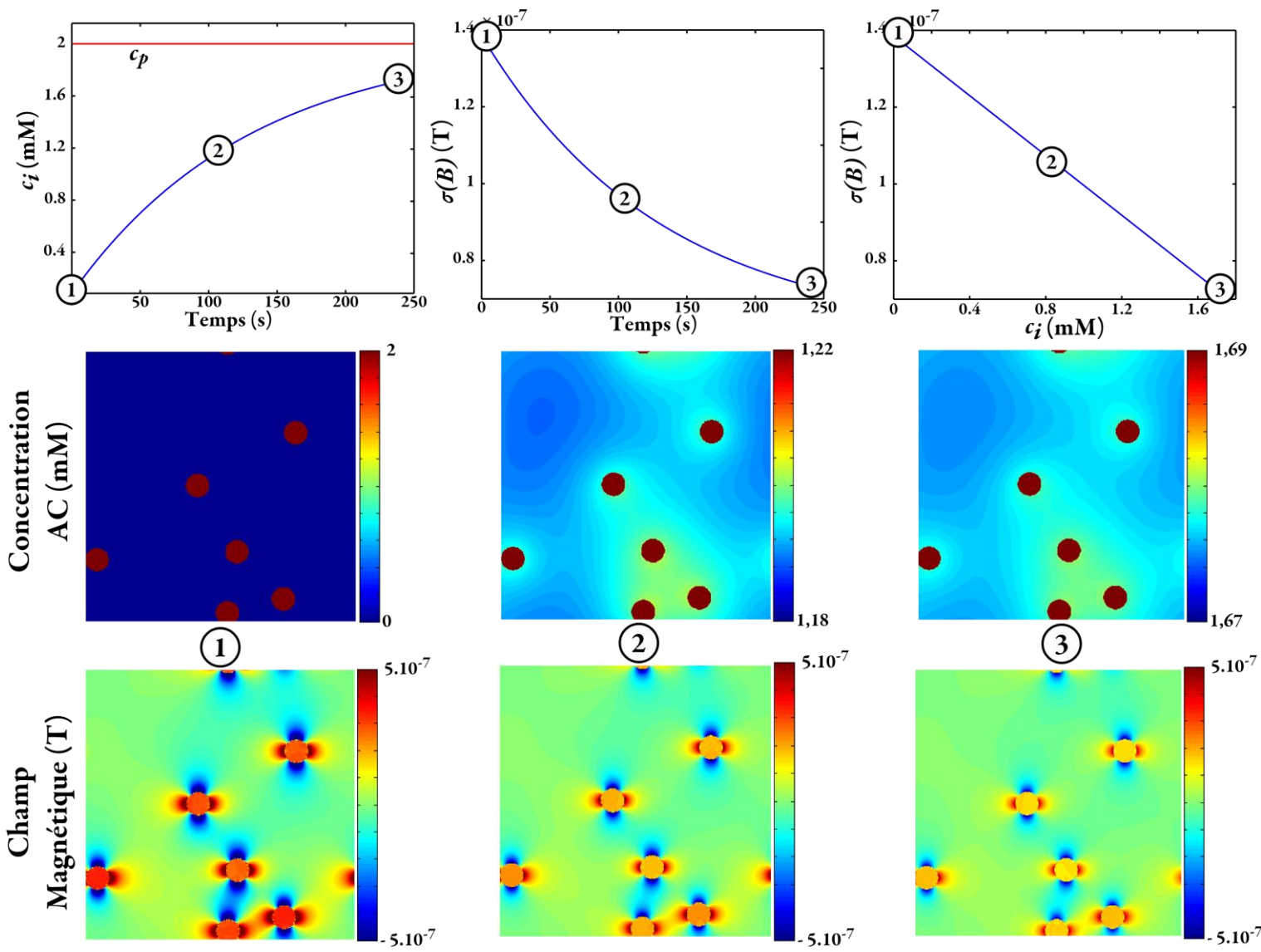
$T_{pic} = 6,7 \text{ s}$

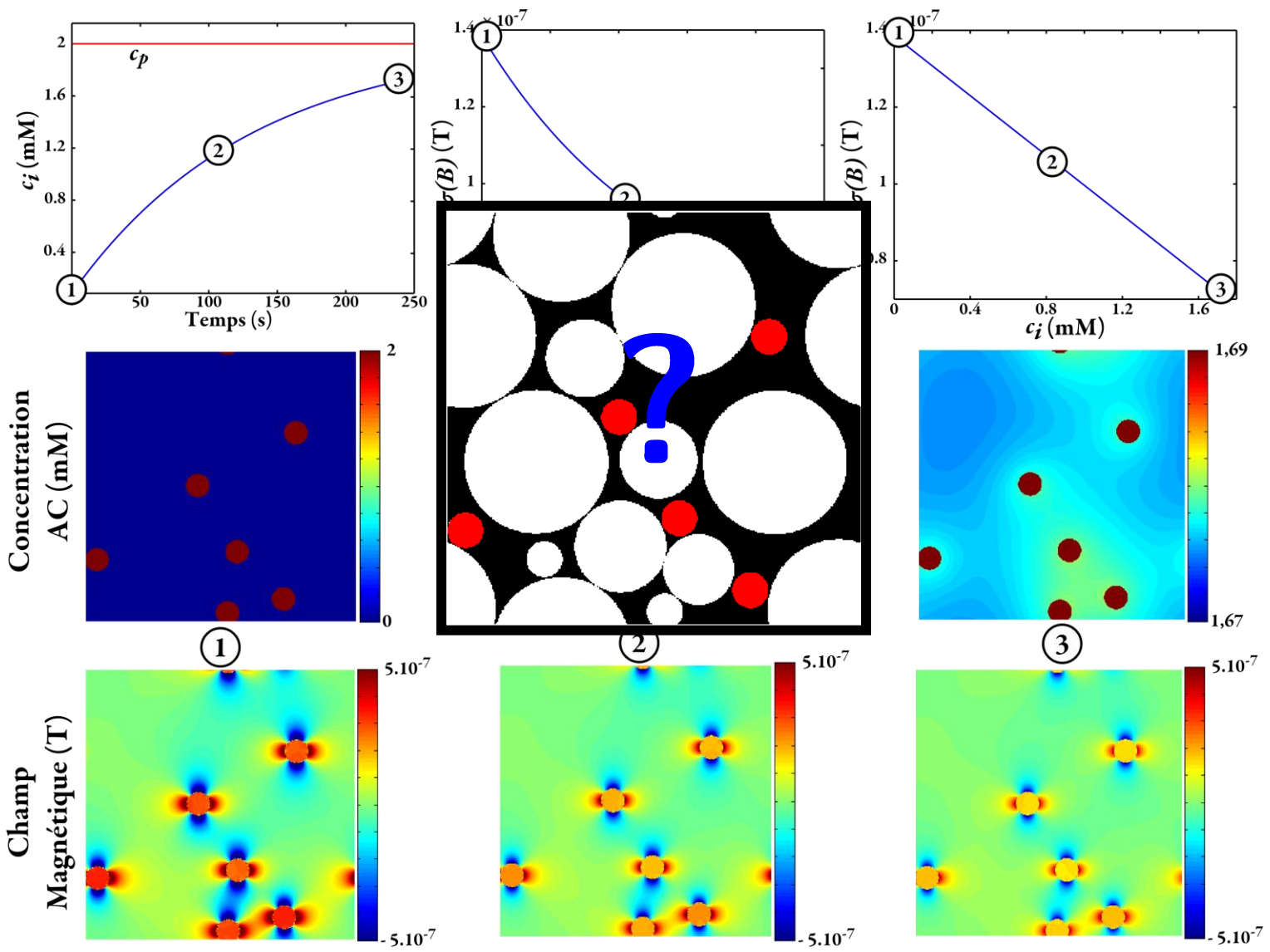


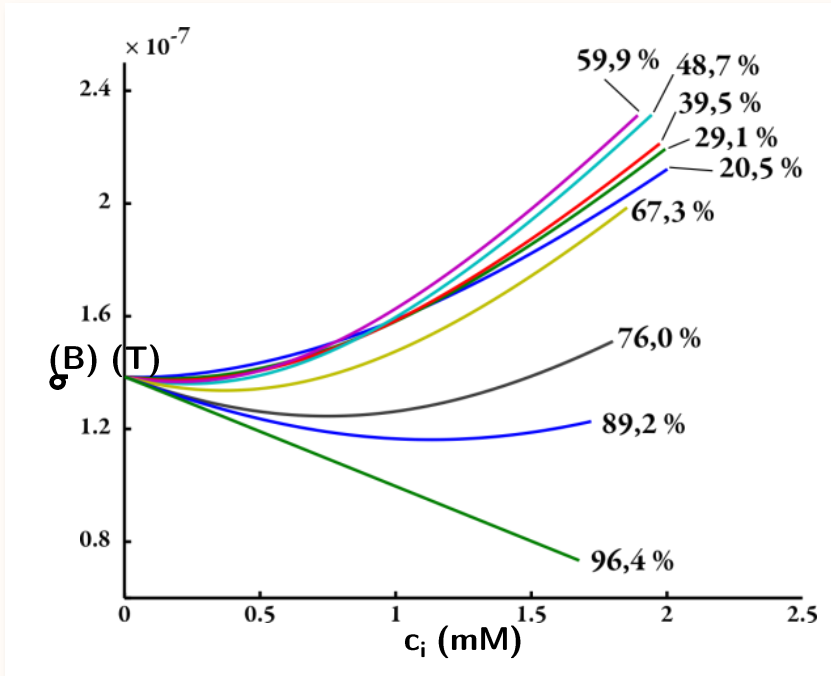
$T_{pic} = 20 \text{ s}$



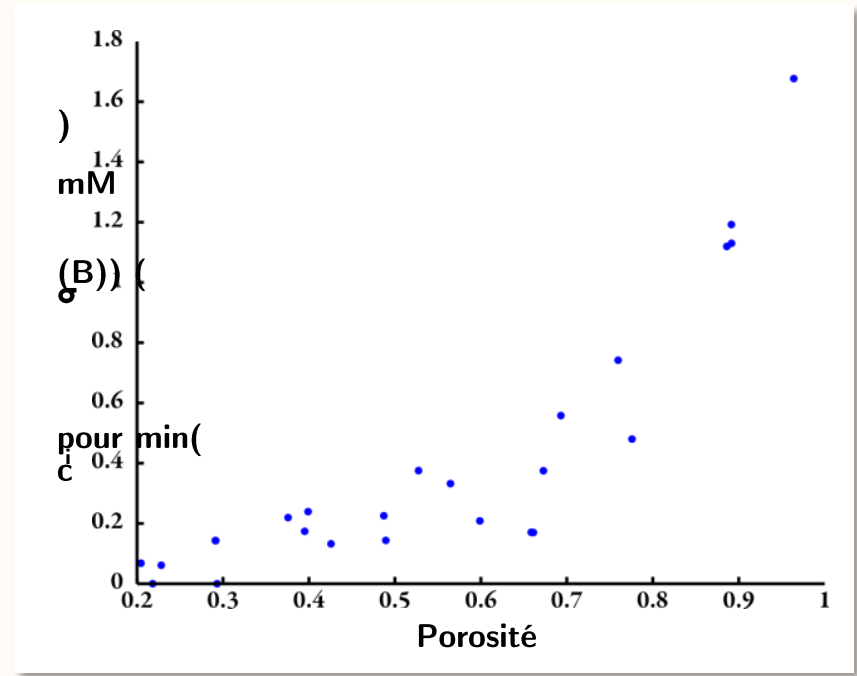
- *La diffusion de l'AC impacte-t-elle l'estimation de la perméabilité ?*  
→ *Peut-on séparer  $D_{AC}$  et  $P_{AC}$  ?*
- *Impact de la porosité sur  $R_{2meso}$  ?*  
→  $\Delta\chi_{i-c}$  vs  $\Delta\chi_{i-v}$



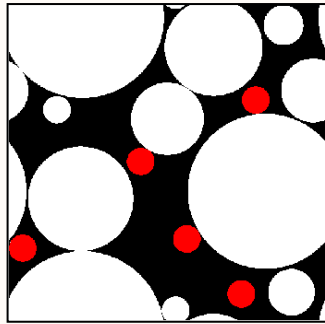




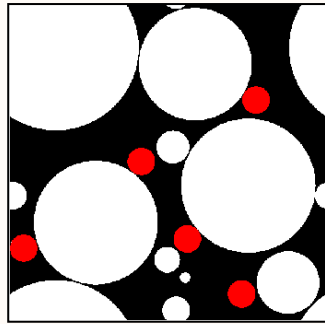
1 tirage vaisseaux X 9 porosités



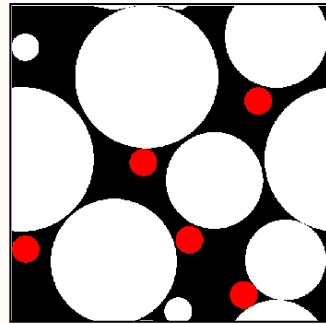
3 tirages vaisseaux X 9 porosités



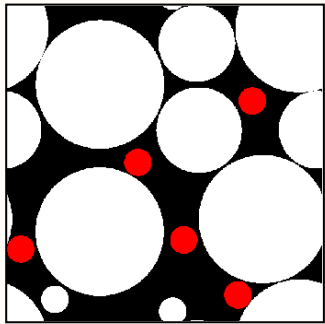
$R_{\max} = 20 \mu\text{m}$



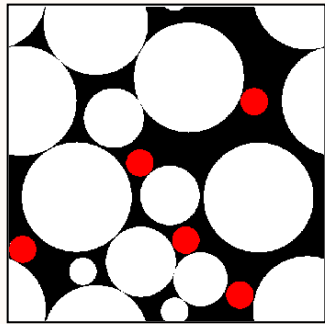
$R_{\max} = 18 \mu\text{m}$



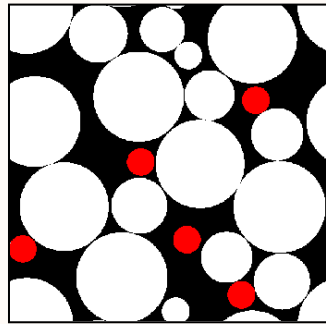
$R_{\max} = 16 \mu\text{m}$



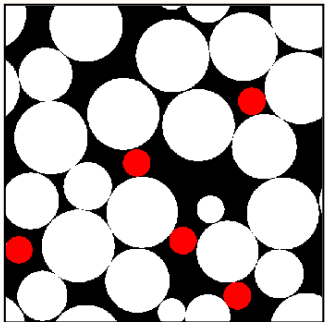
$R_{\max} = 14 \mu\text{m}$



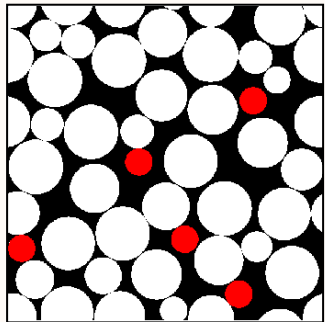
$R_{\max} = 12 \mu\text{m}$



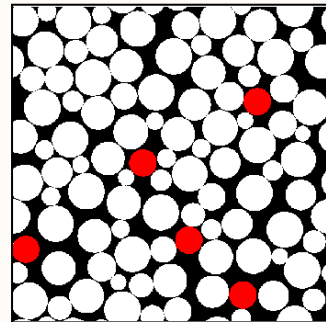
$R_{\max} = 10 \mu\text{m}$



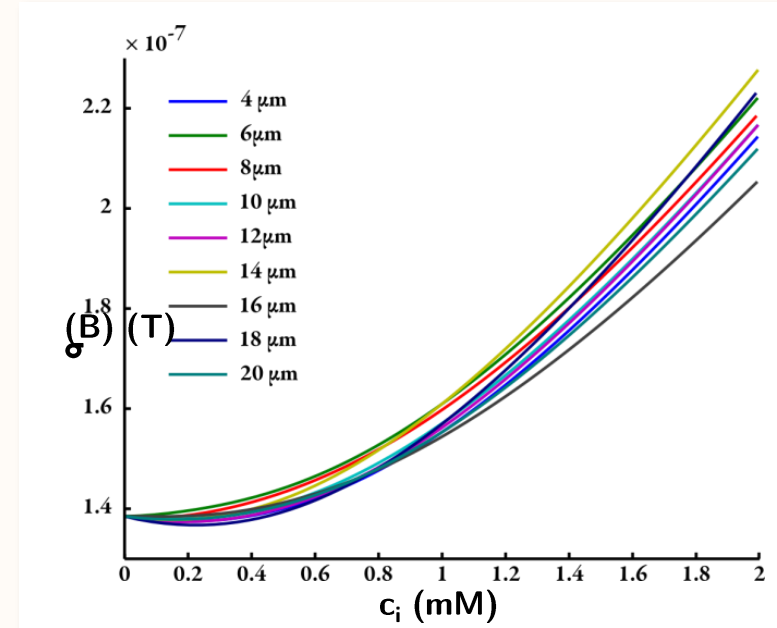
$R_{\max} = 8 \mu\text{m}$



$R_{\max} = 6 \mu\text{m}$



$R_{\max} = 4 \mu\text{m}$

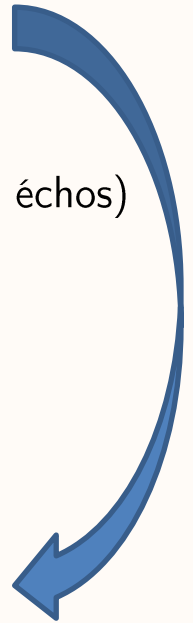




- Outil de simulation puissant pour modéliser la perfusion
  - Sensibilités  $P_{AC}$  vs  $D_{AC}$  différentes en fonction de  $T_E$ 
    - └ Nécessité d'un modèle analytique
  - Mesure de la perméabilité à  $T_E$  court – Séquence spirale
  - Rôle complexe de la porosité
    - └ Validité de la décroissance exponentielle de  $R_{2meso}$  en cas d'extravasation
    - └ Linéarité du signal en fonction de la concentration en AC
    - └ Augmenter la statistique
- Compléter le modèle en intégrant :
  - ➔  $D_{H2O}$  et  $P_{H2O}$
  - ➔ Prise en compte du CBF
- Application à différents organes

## Finalemment...

- Imbrications des phénomènes ( $R_1$ ,  $R_{2\text{meso}}$ ,  $D_{\text{H2O}}$ ,  $P_{\text{AC}}$ ,  $D_{\text{AC}}$ , ...)  
Quantification des paramètres physiologiques complexes en IRM  
→ richesse !!
- Comment l'exploiter ?
  - Développer des techniques d'acquisitions
    - Rapide (approche dynamique)
    - Multipliant les contrastes (EPI GESE, Spirale multi échos)
  - Préciser les modèles
    - En les combinant (VSI en dynamique)
    - En les prolongeant
      - Nouveaux paramètres physiologiques ( $D_{\text{AC}}$ , outil de simulation)
  - Au service de la clinique (diagnostic, suivi thérapeutique)



## Finalement...

- Imbrications des phénomènes ( $R_1$ ,  $R_{2\text{meso}}$ ,  $D_{\text{H2O}}$ ,  $P_{\text{AC}}$ ,  $D_{\text{AC}}$ , ...)  
Quantification des paramètres physiologiques complexes en IRM  
→ richesse !!

- Comment l'exploiter ?

- Développer des techniques d'acquisitions

→ Rapide (approche dynamique)

→ Multipliant les contrastes (EPI GESE, Spirale multi-échos)

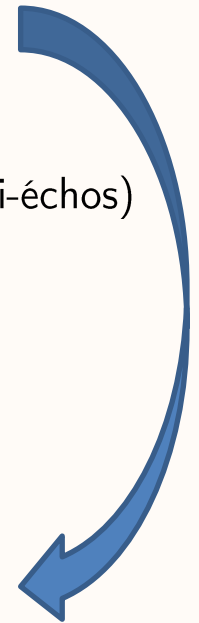
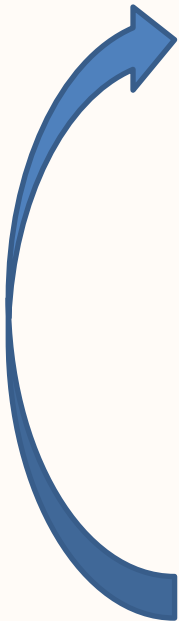
- Préciser les modèles

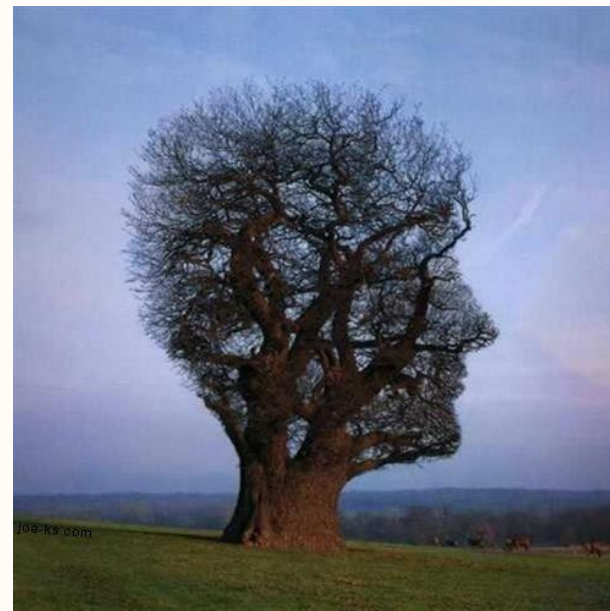
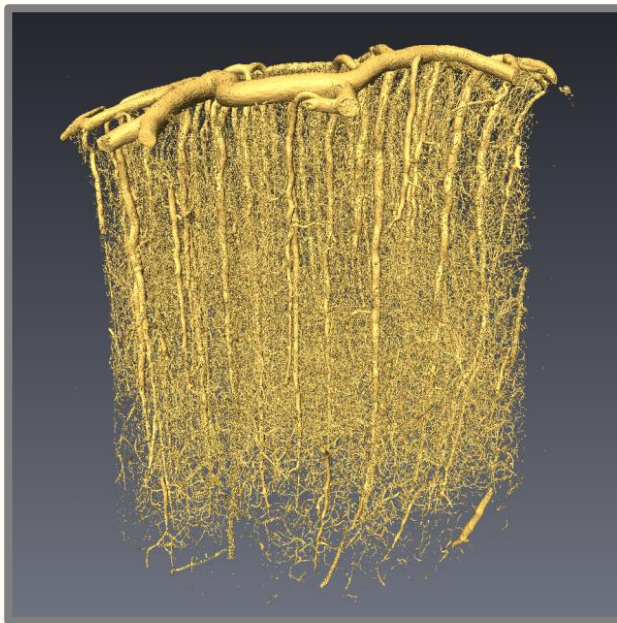
→ En les combinant (VSI en dynamique)

→ En les prolongeant

→ Nouveaux paramètres physiologiques  
( $D_{\text{AC}}$ , outil de simulation)

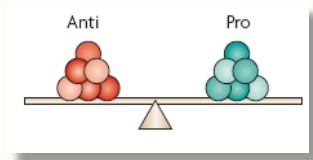
- Au service de la clinique (diagnostic, suivi thérapeutique)



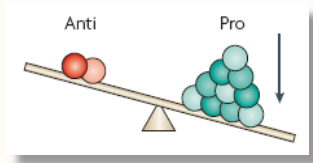




## Angiogenèse : Pro vs Anti

**Sain**

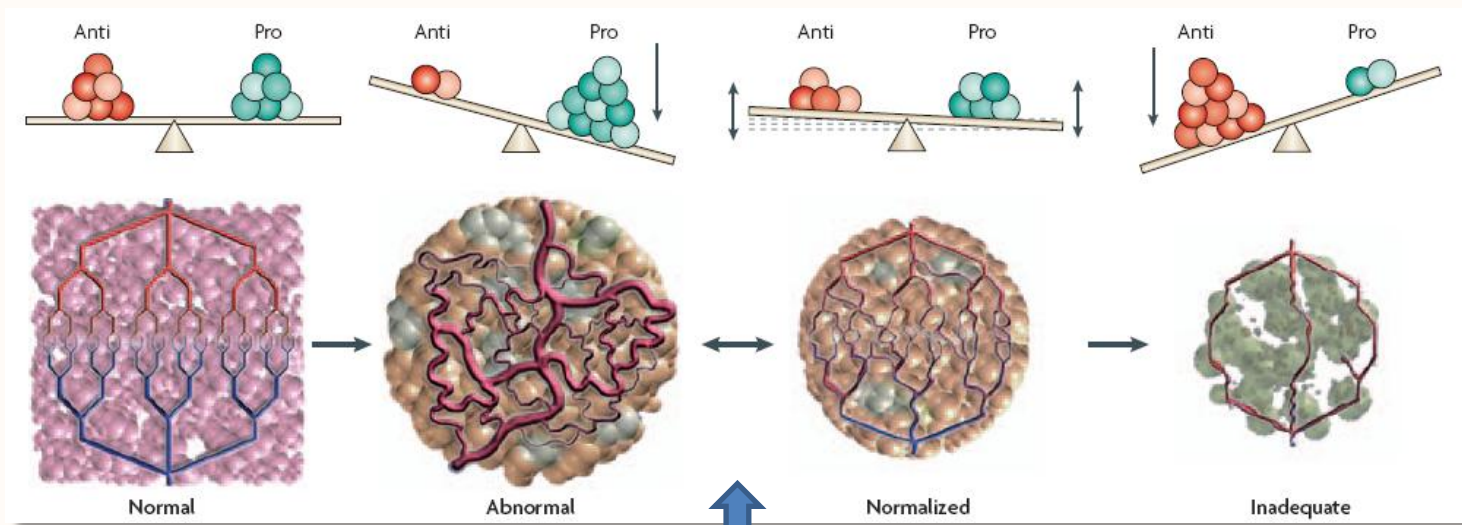
- Angiogenèse physiologique

**Pathologique**

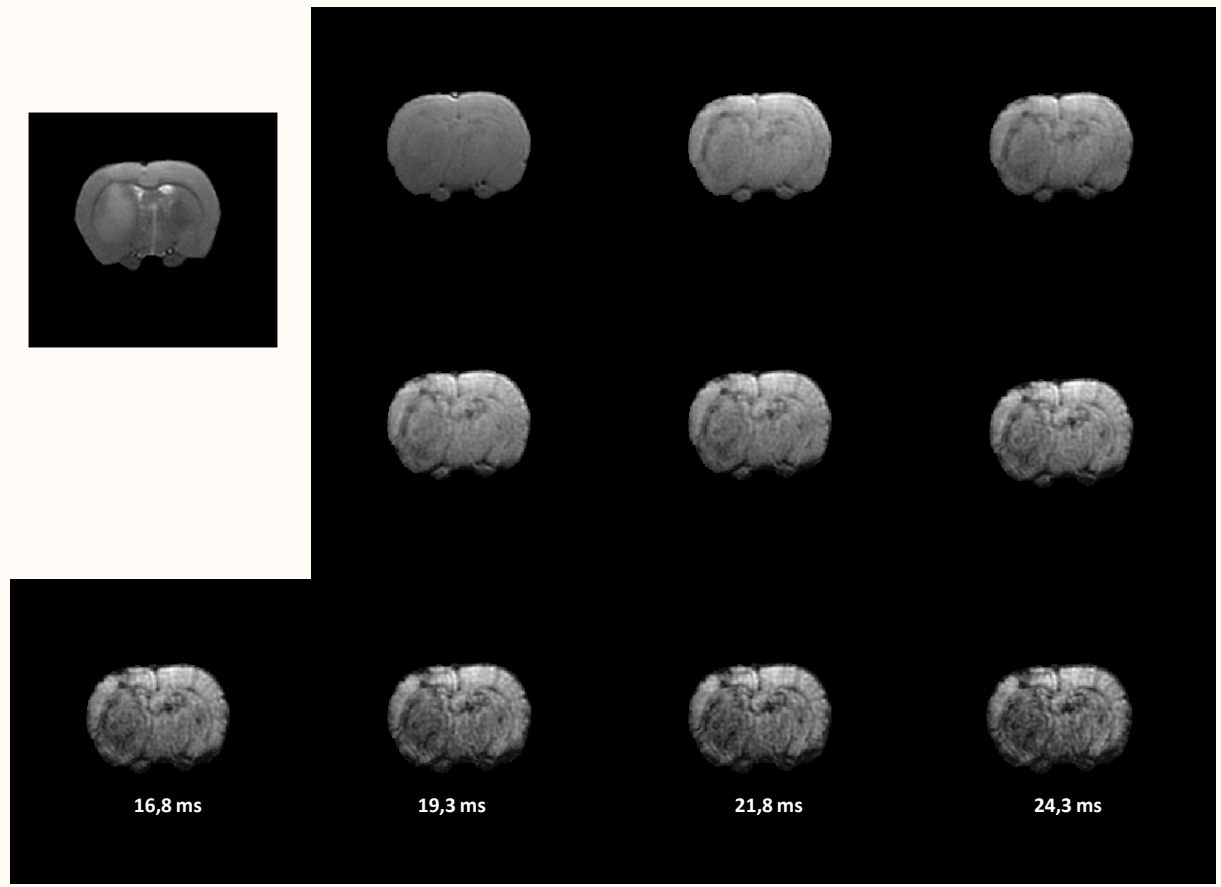
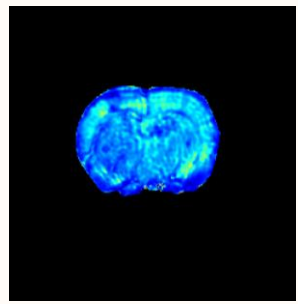
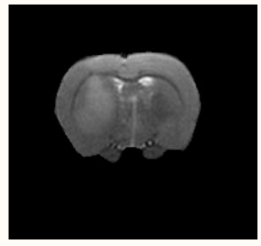
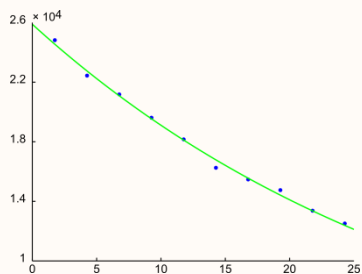
- **Tumeurs**
- Malformations vasculaires
- Obésité
- Hypertension pulmonaire primaire
- Cirrhose du foie, etc.



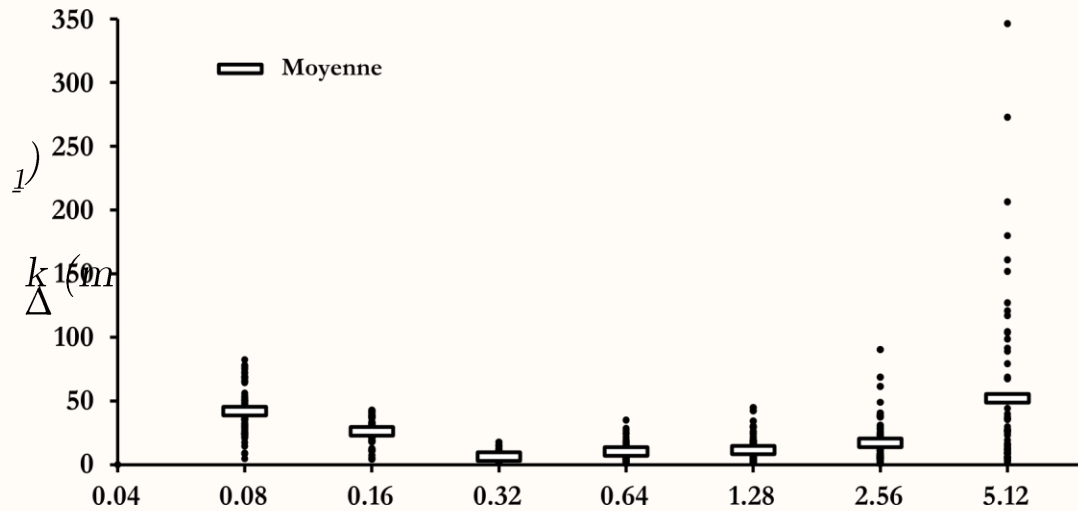
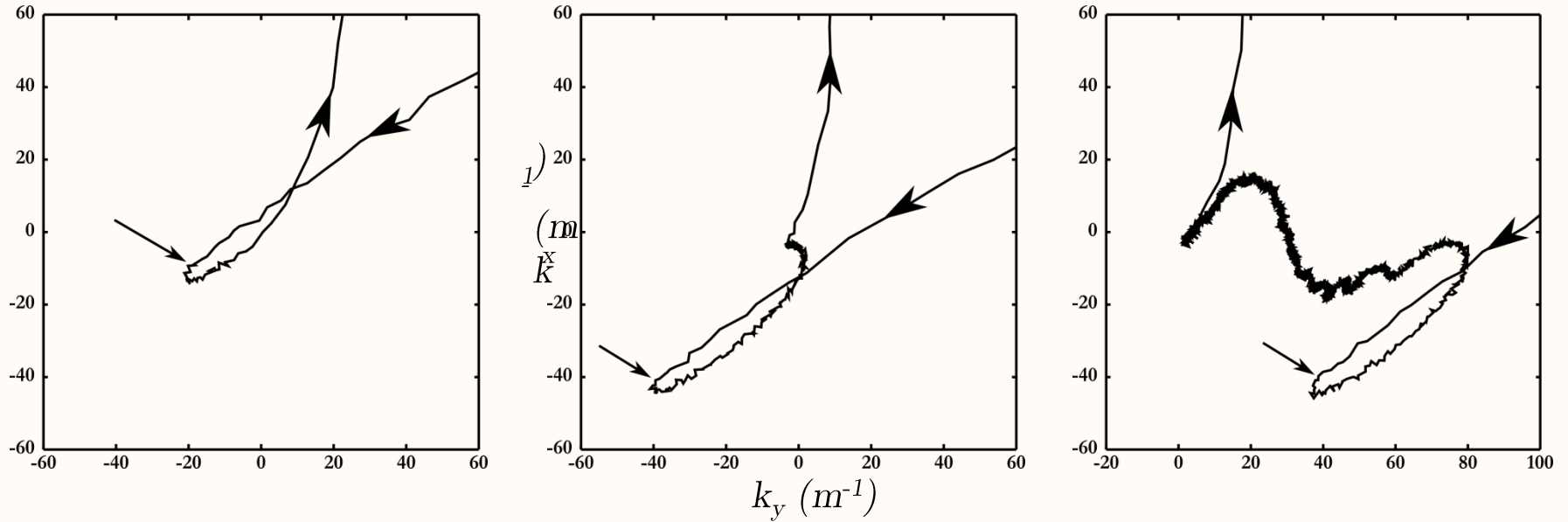
- Maladie d'Alzheimer
- Ischémie cérébrale, cardiaque
- Diabète
- Maladie de Crohn
- Perte des cheveux, etc.

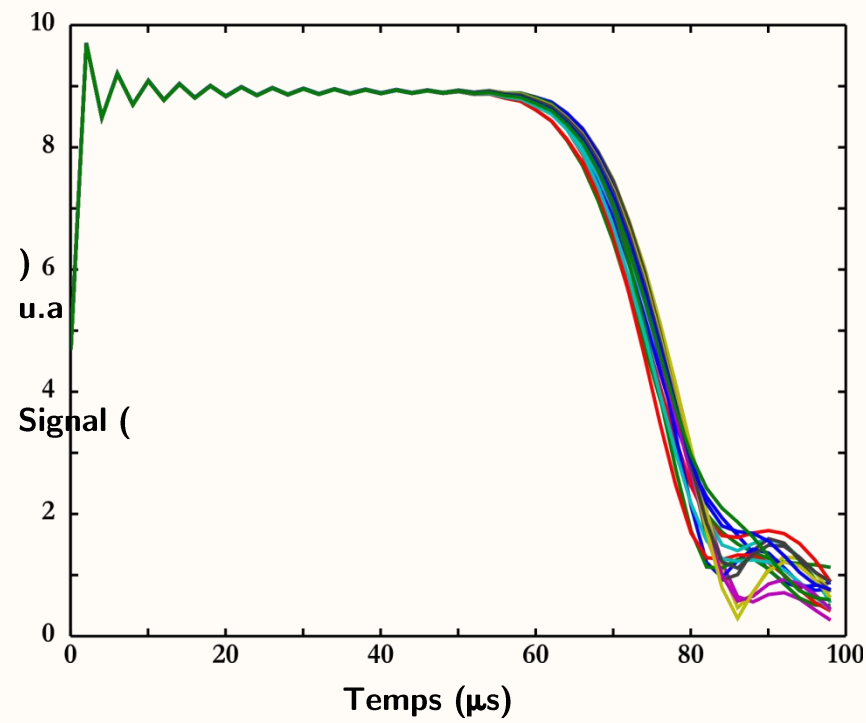
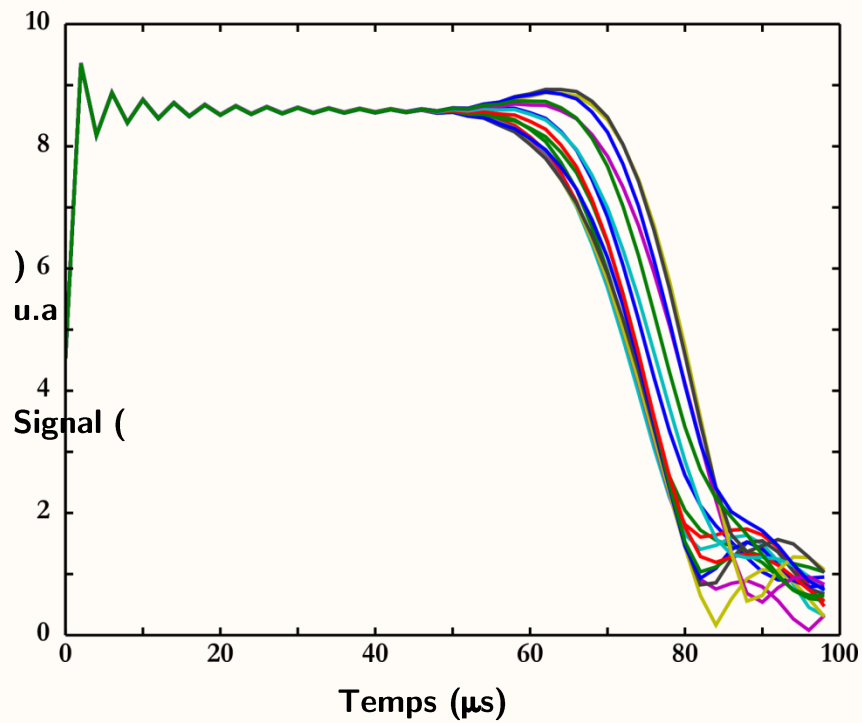


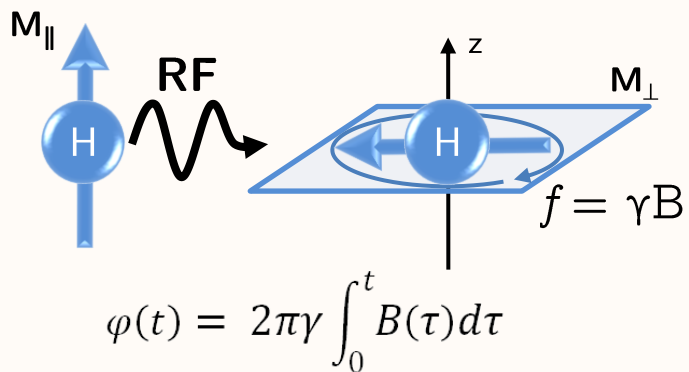
Anti-angiogénique



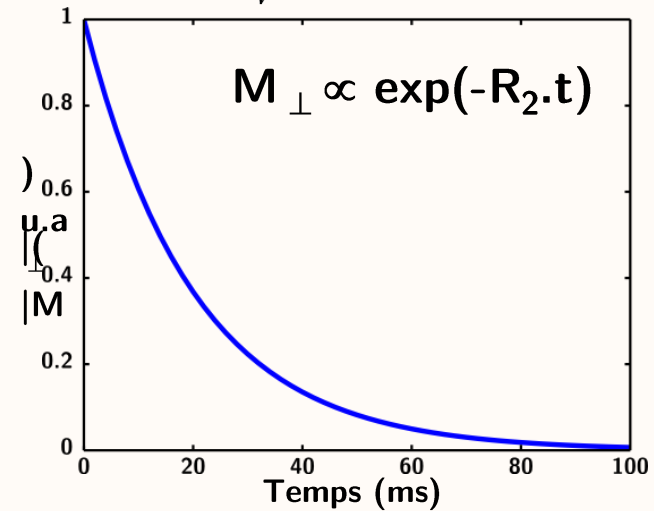




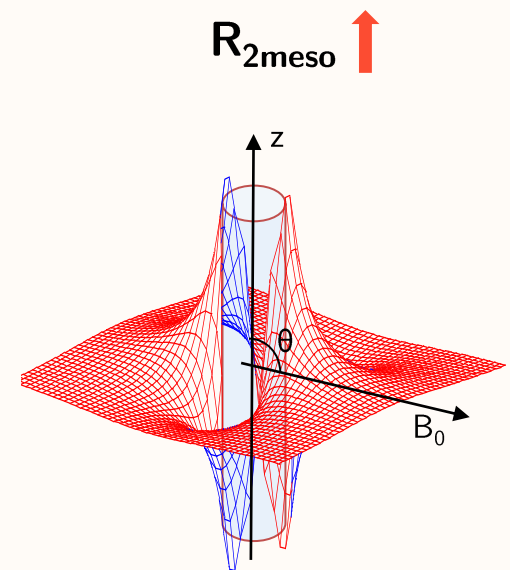
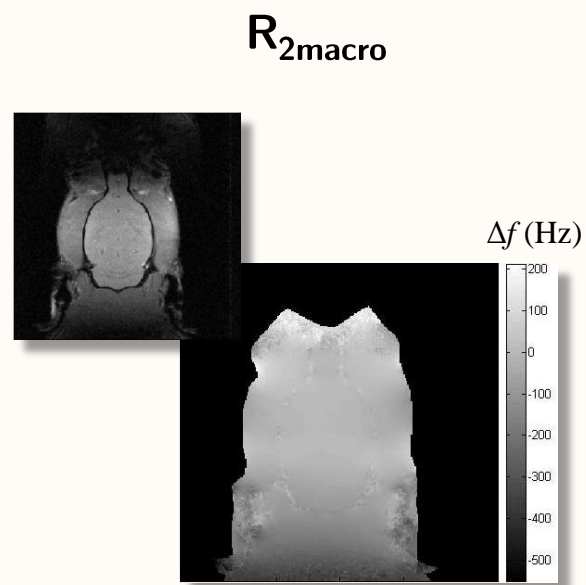
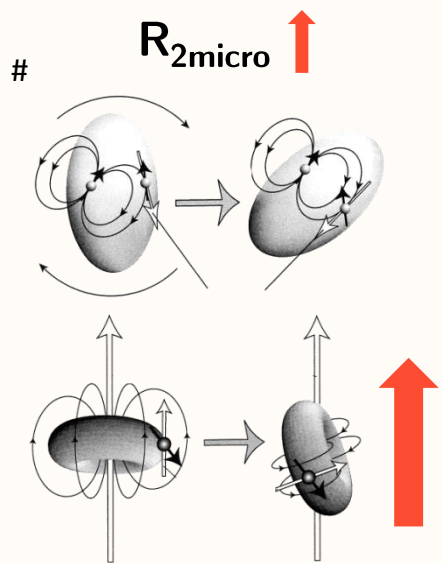




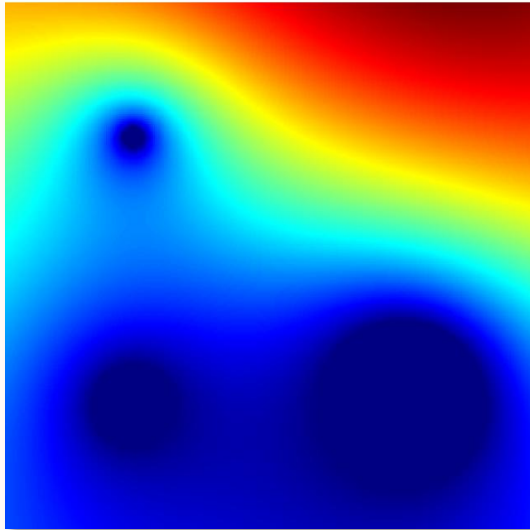
$$M_{\perp}(t) \propto \iiint_V \exp(-i\varphi(\vec{\rho}, t)) d\vec{\rho}$$



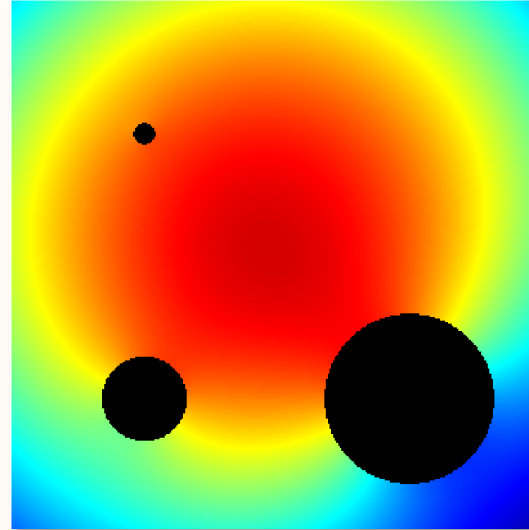
$$R_2 = R_{2\text{micro}} + R_{2\text{meso}} + R_{2\text{macro}}$$



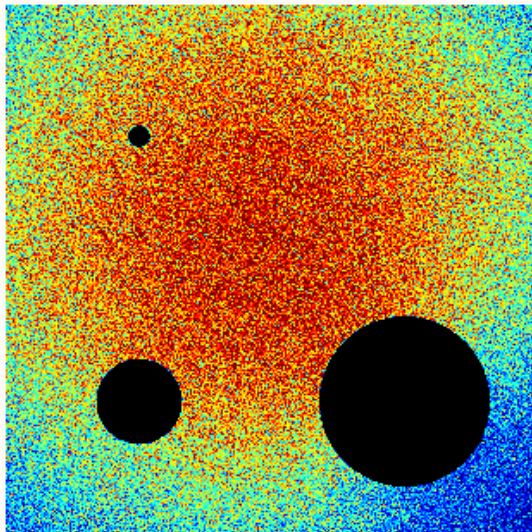
Convolution (sans pondération)



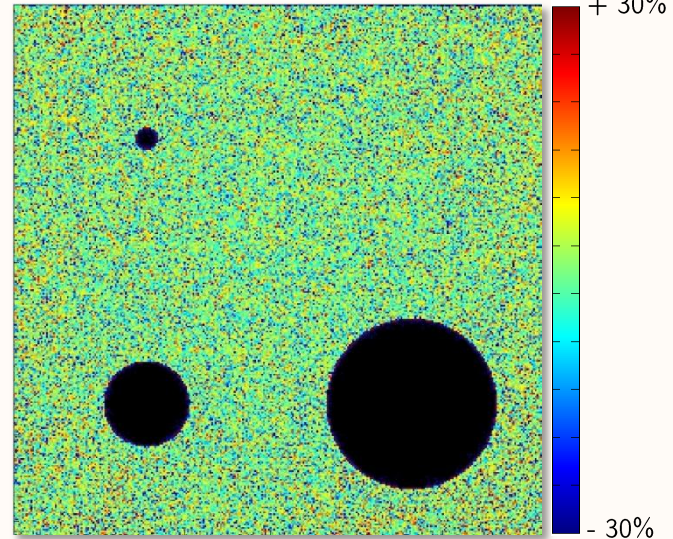
Convolution (avec pondération)

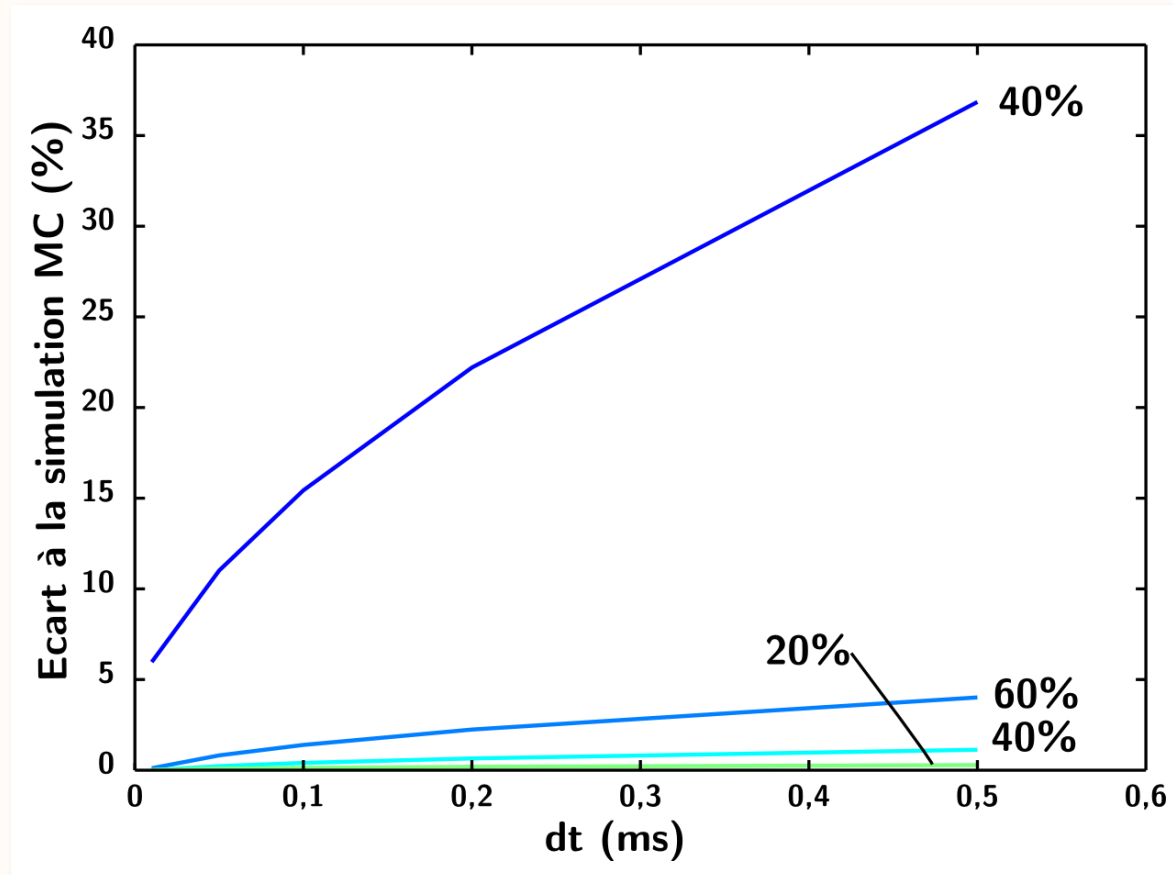


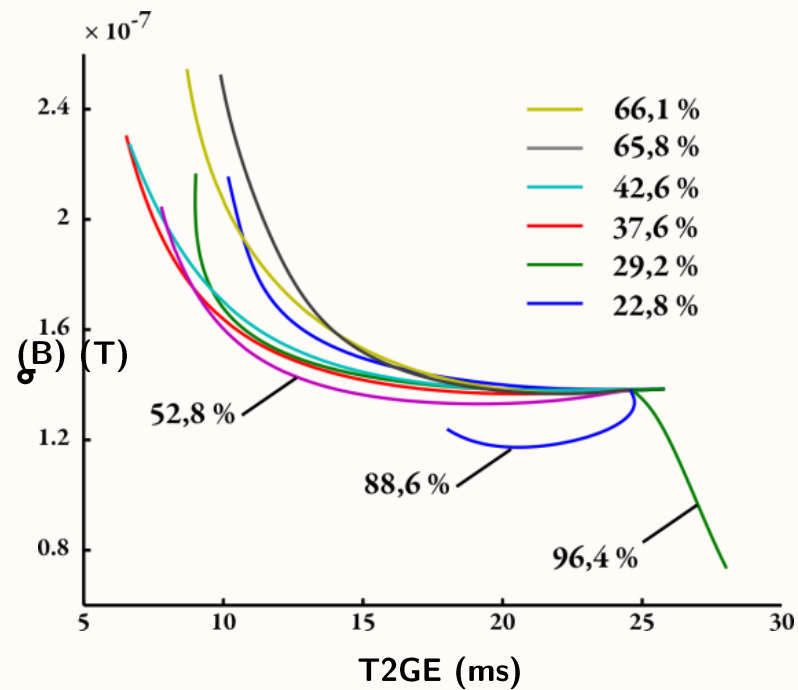
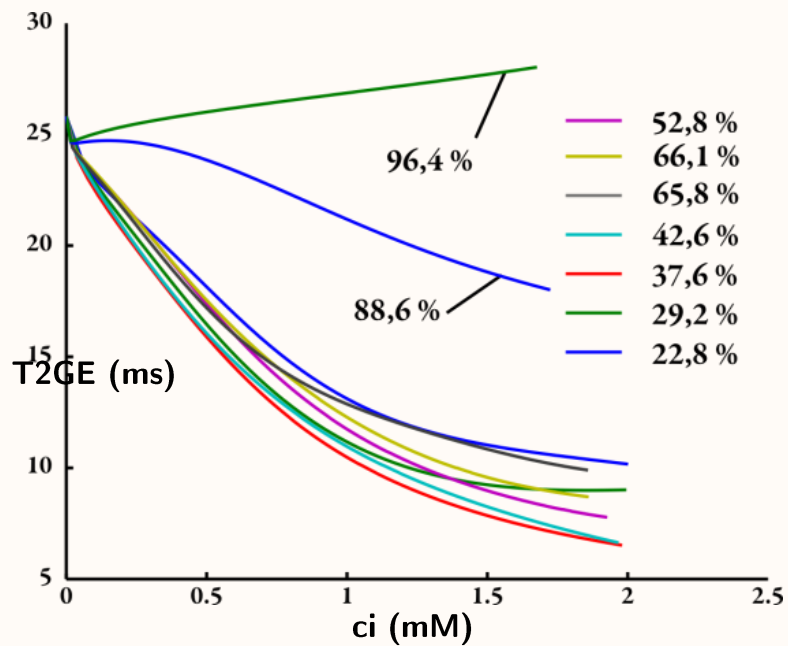
Monte Carlo

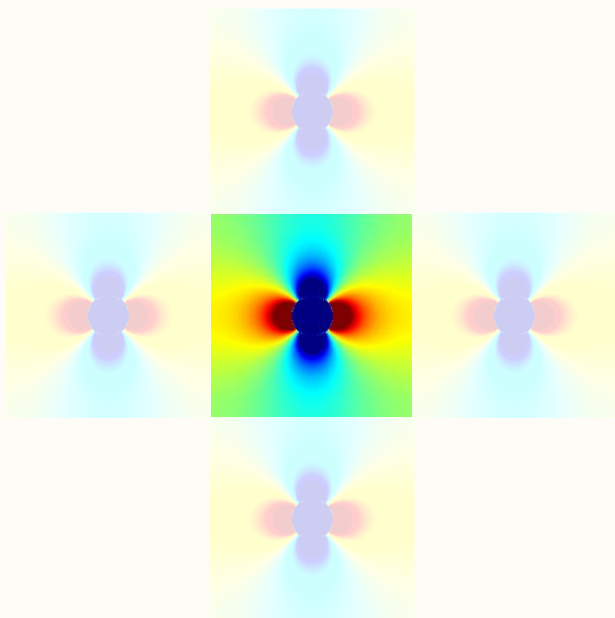
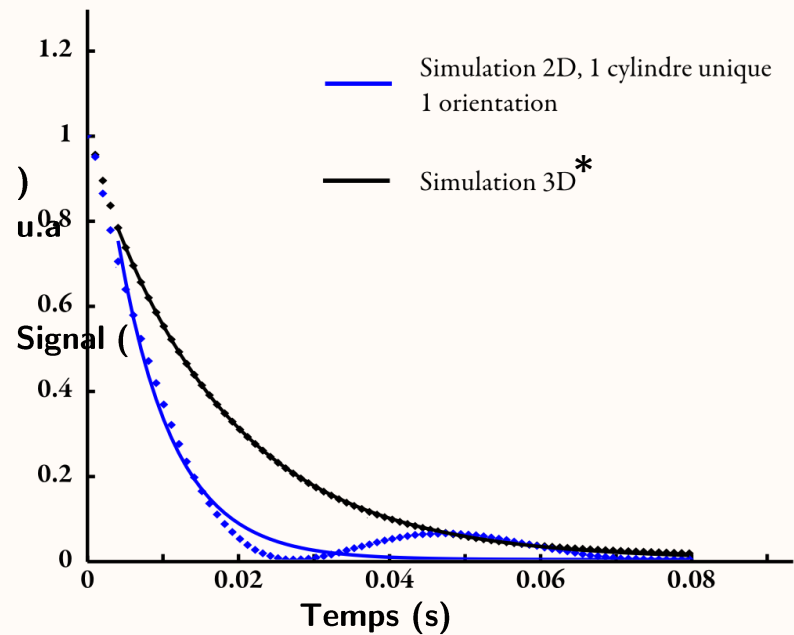
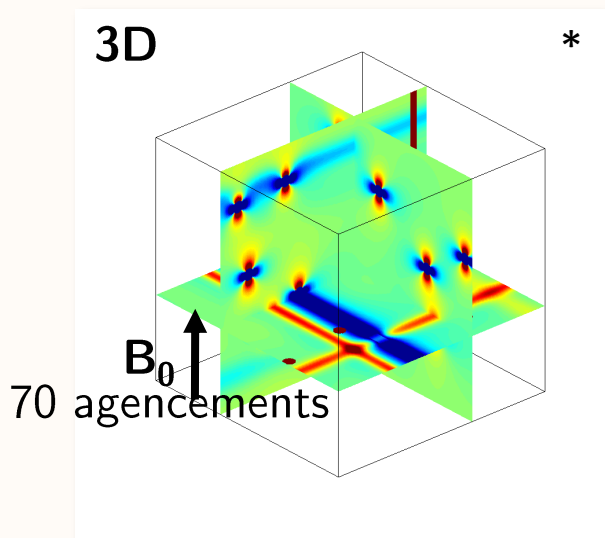


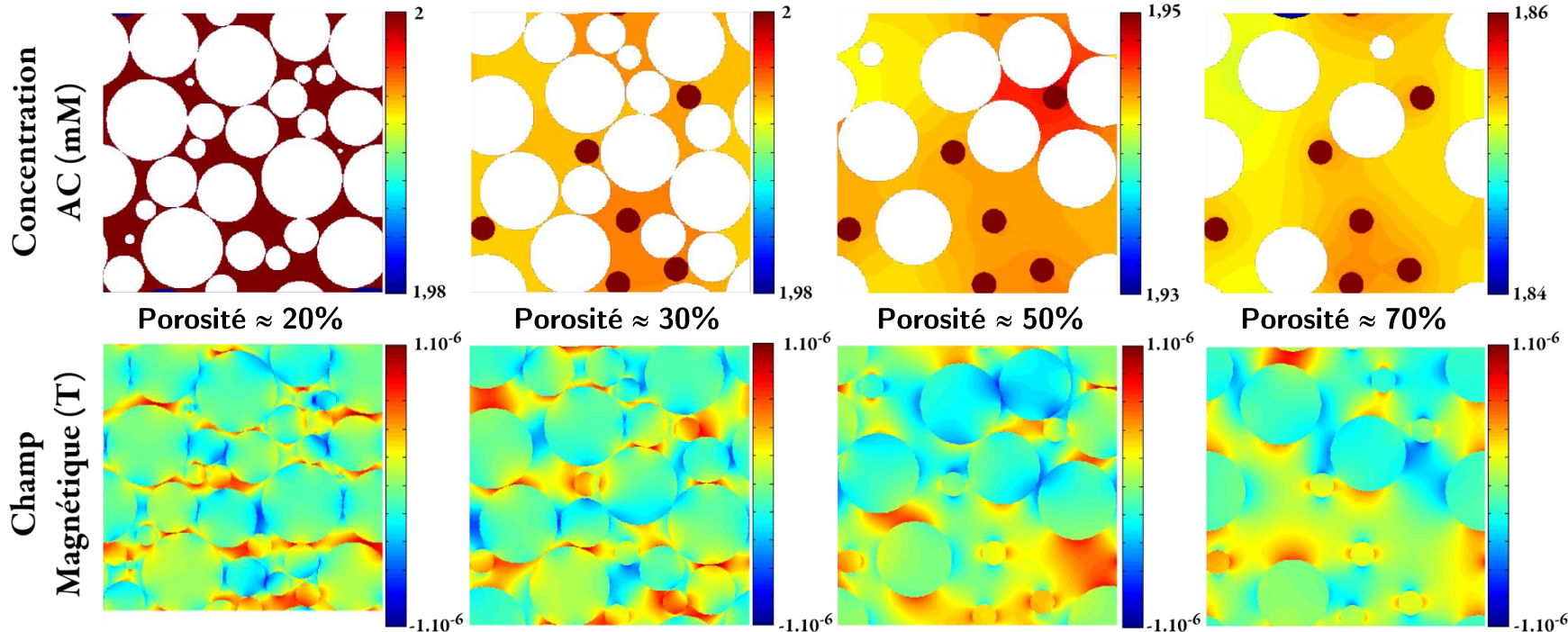
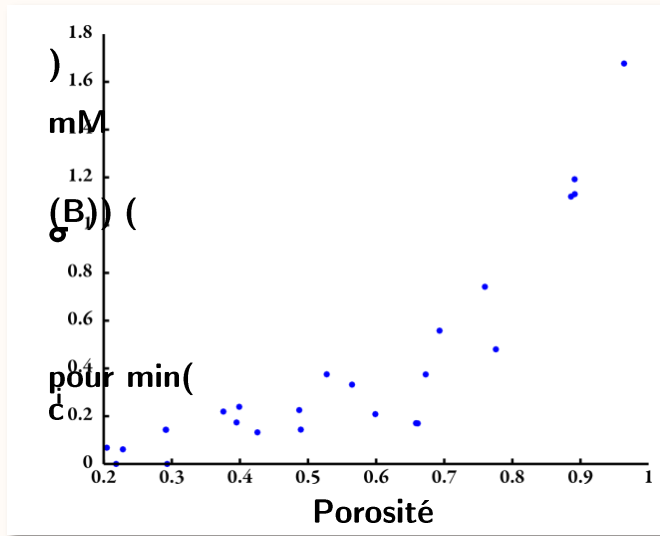
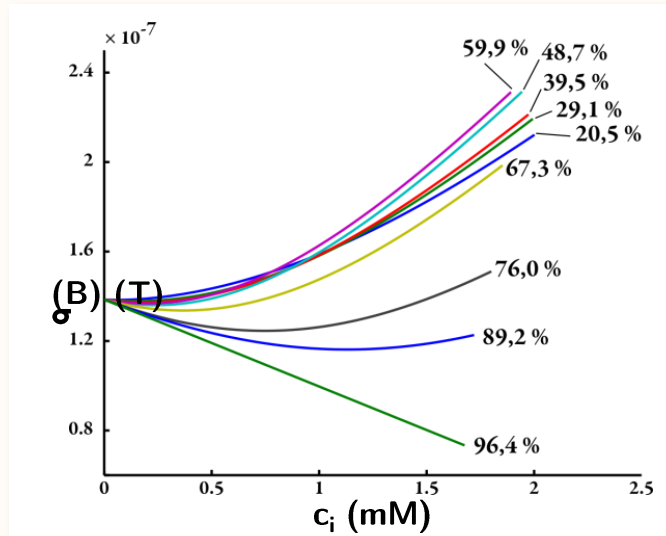
Ecart (%)



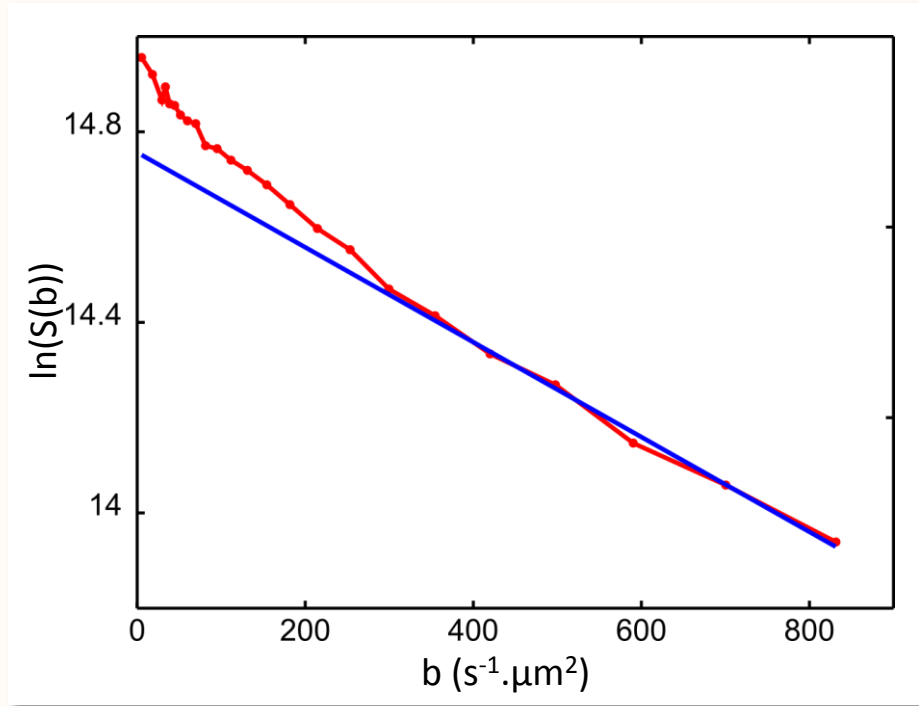
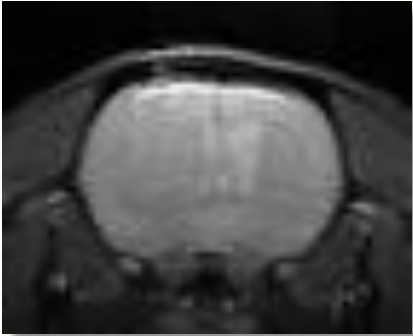


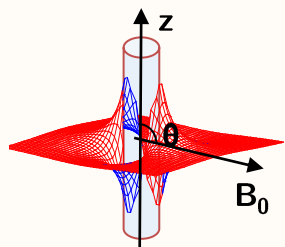












AC intravasculaire (USPIO)

