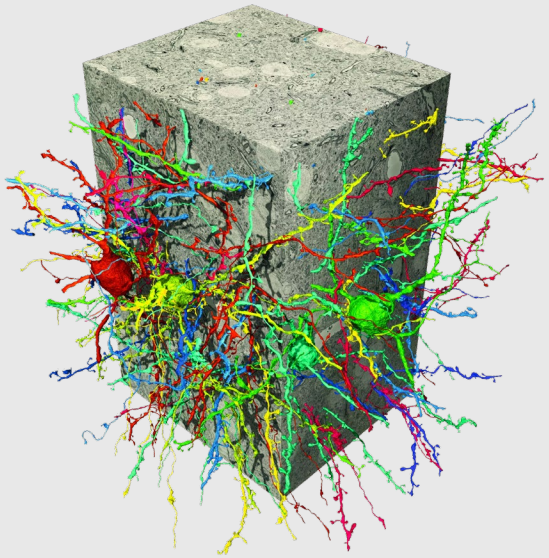


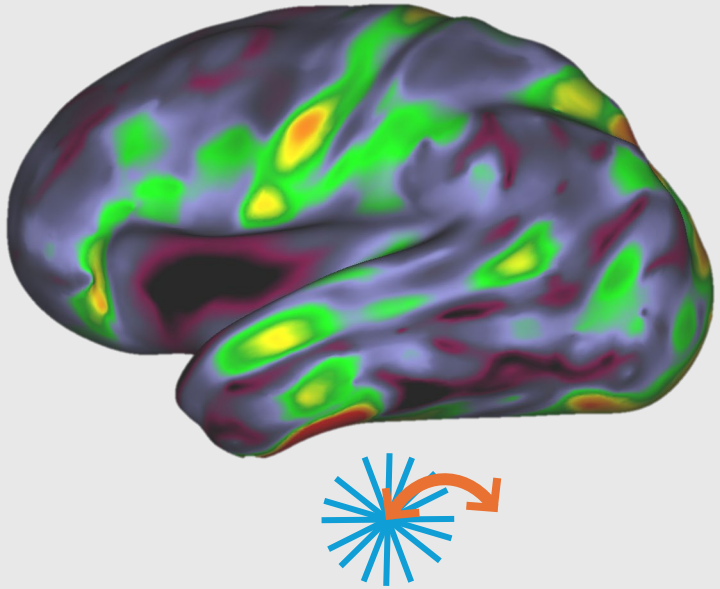
GEM

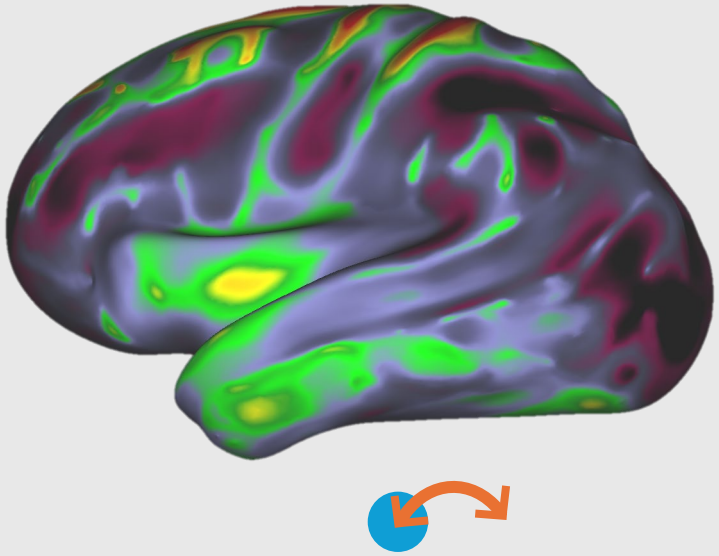
SANDI

NEXI/SMEX

SANDIX

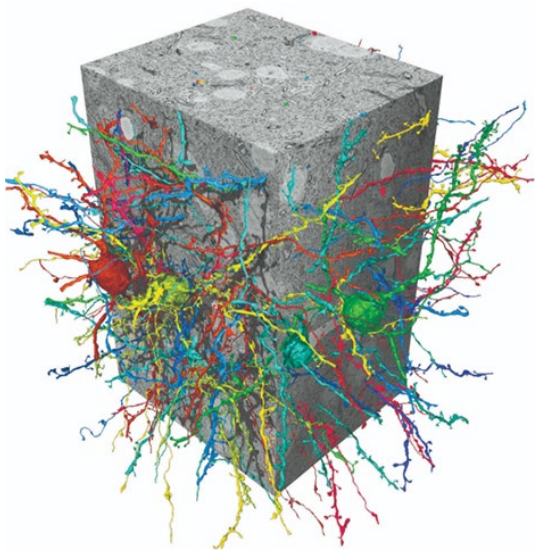
Unifying framework





Introduction

Towards a Standard Model of Gray Matter

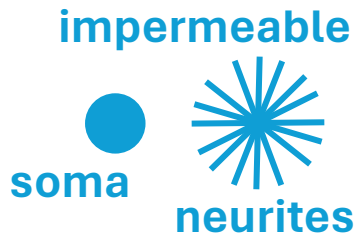


Gray matter microstructure models require:

- Water exchange across the cell membrane
- Signal contribution from cell bodies
- Non-Gaussian diffusion → structural disorder

Source : Songbird Basal Ganglia, Neurobiology/ J. Kornfeld

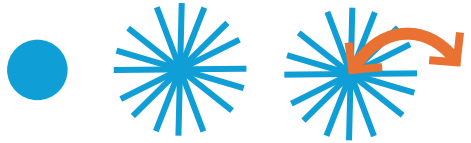
SANDI



NEXI/SMEX

SANDIX

eSANDIX



→ **soma** are still considered **impermeable**

Sources : Jelescu et al. 2022. NeuroImage
Olesen et al. 2022. NeuroImage
Palombo et al. 2020. NeuroImage

Outline

- Extending the theory to **include soma exchange**, defining a Generalized Exchange Model (GEM).
- Check the **accuracy and precision** of its parameter estimation.
- Obtain **parametric maps in the human cortex**.
- Check **consistency** with other model estimates.

Theory

Generalized Exchange equation

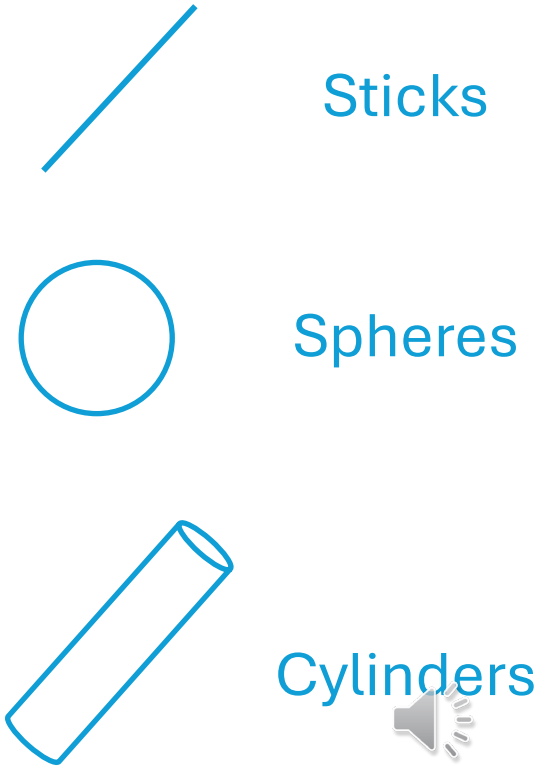
In one compartment, at the first order:

$$\frac{dS}{dt} = \frac{dS_{imper}}{dt} . \frac{S}{S_{imper}} - rS + \alpha r_{ext} S_{ext}$$

Gaussian case:

$$\frac{1}{S_{imper}} . \frac{dS_{imper}}{dt} = -q^2(t) . D$$

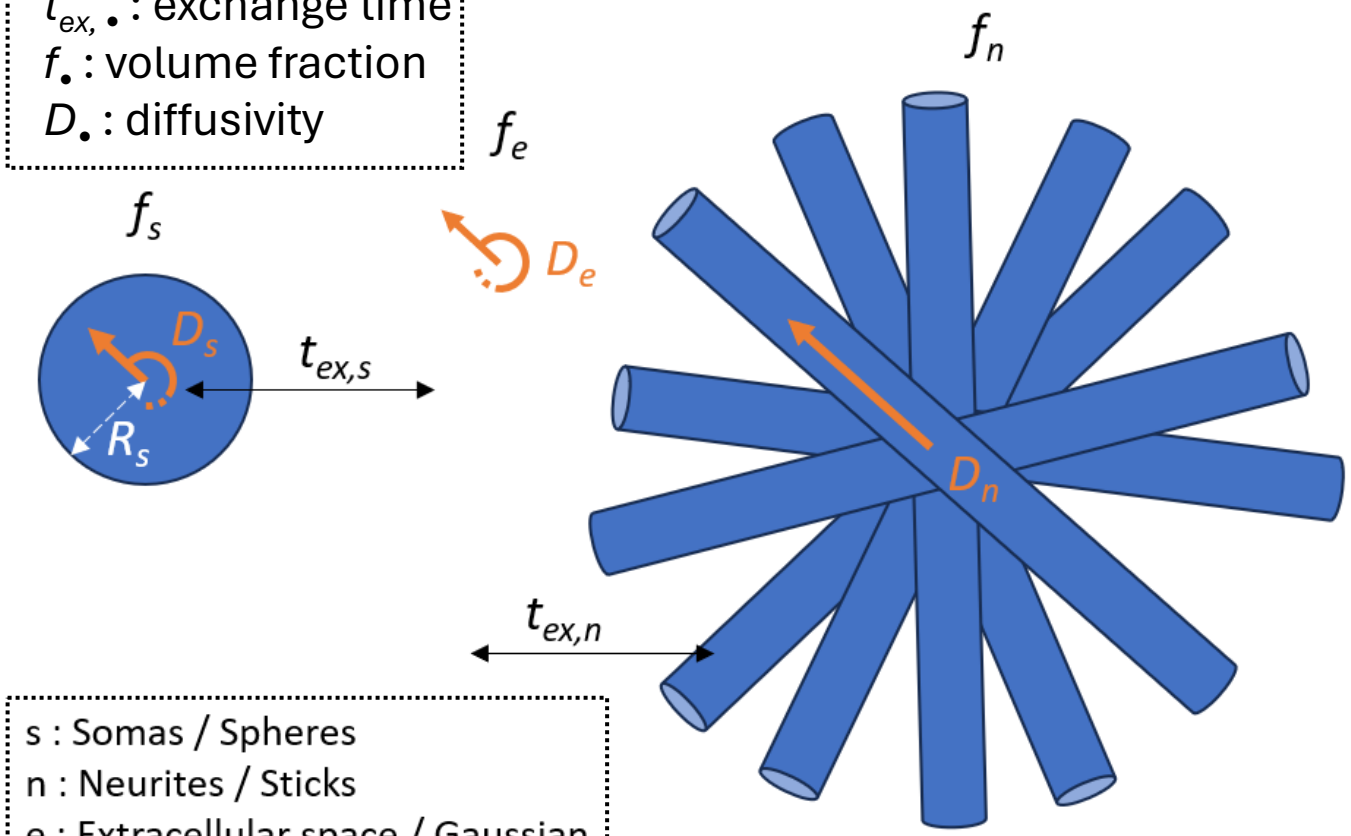
Known S_{imper} geometries



Theory

Generalized Exchange Model (GEM)

$t_{ex,\bullet}$: exchange time
$f_\bullet$: volume fraction
$D_\bullet$: diffusivity



s : Somas / Spheres
n : Neurites / Sticks
e : Extracellular space / Gaussian

Compartment signal equations

$$\begin{cases} \frac{dS_s}{dt} = \frac{dS_{s,imper}}{dt} . \frac{S_s}{S_{s,imper}} - r_s S_s + \frac{f_s}{f_e} r_s S_e \\ \frac{dS_n}{dt} = -q^2(t) . D_n . (\mathbf{g} \cdot \mathbf{n})^2 . S_n - r_n S_n + \frac{f_n}{f_e} r_n S_e \\ \frac{dS_e}{dt} = -q^2(t) . D_e . S_e - r_e S_e + r_s S_s + r_n S_n \end{cases}$$

Relations between rates and fractions

$$f_e r_e = f_s r_s + f_n r_n \qquad t_{ex,s/n} = \frac{1}{r_{s/n}} \frac{f_e}{f_e + f_{s/n}}$$

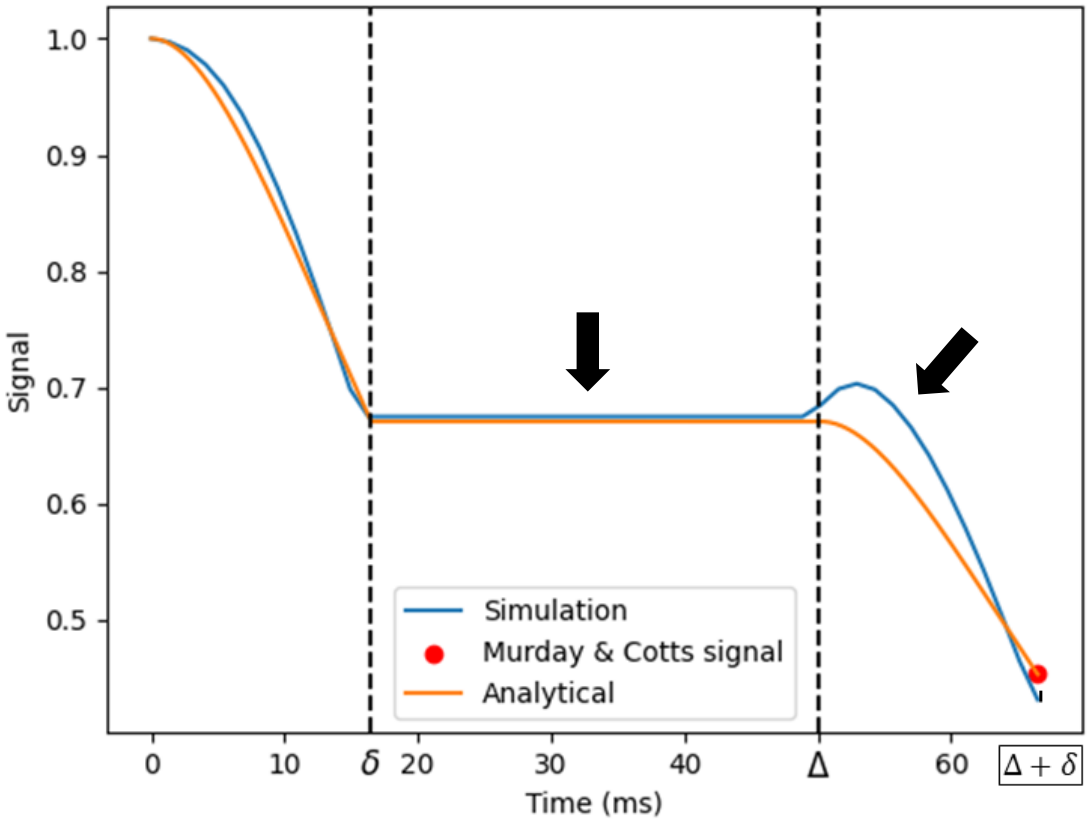
7 parameters

$t_{ex,s}$, $t_{ex,n}$, f_n, f_s, D_n, D_e, r_s
(D_s set to 3µm^2/ms)

Validation of the signal inside a sphere during PGSE

Evolution of the signal inside an impermeable sphere $S_{imper,s}(t)$

$b = 3ms/\mu m^2, \Delta = 50ms, \delta = 16.5ms, R_s = 10\mu m, D_s = 2.5\mu m^2/ms$



Simulation using MC/DC Simulator* with 50'000 walkers

Analytical expression

$$S_{imper,s}(t) = \exp\left\{-\frac{2\gamma^2 g^2}{D_{is}} \sum_1^\infty \frac{\alpha_m^{-4}}{\alpha_m^2 r_s^2 - 2} f(t)\right\}$$ with $f(t)$ defined as :

$t \in [0, \delta]$: $$f(t) = t - \frac{1 - e^{-\alpha_m^2 D_{is} t}}{\alpha_m^2 D_{is}}$$ (with $(\alpha_m r_s)^{-1} J_{\frac{3}{2}}(\alpha_m r_s) = J_{\frac{5}{2}}(\alpha_m r_s)$)

$t \in [\delta, \Delta]$: $$f(t) = \delta - \frac{1 - e^{-\alpha_m^2 D_{is} \delta}}{\alpha_m^2 D_{is}}$$

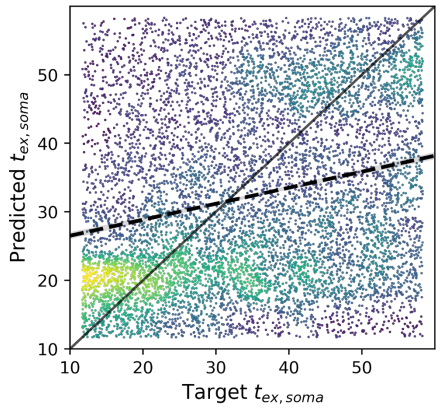
$t \in [\Delta, \Delta + \delta]$:

$$f(t) = (t - \Delta + \delta) - \frac{2 + e^{-\alpha_m^2 D_{is}(\Delta - \delta)} - e^{-\alpha_m^2 D_{is}\delta} - e^{-\alpha_m^2 D_{is}\Delta}}{\alpha_m^2 D_{is}} - \frac{e^{-\alpha_m^2 D_{is} t} - e^{-\alpha_m^2 D_{is}(t-\delta)} - e^{-\alpha_m^2 D_{is}(t-\Delta)}}{\alpha_m^2 D_{is}}$$

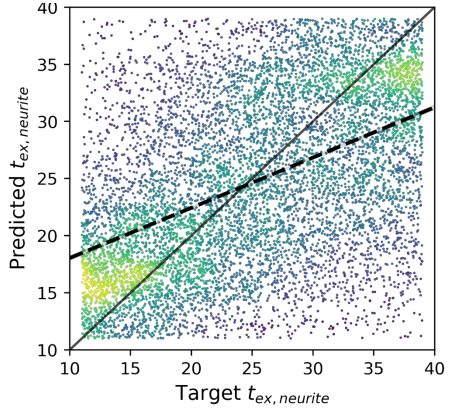
Source : Rafael-Patino et al. 2020, Front. Neuroinform.

Retrieving GEM parameters from noiseless signal…

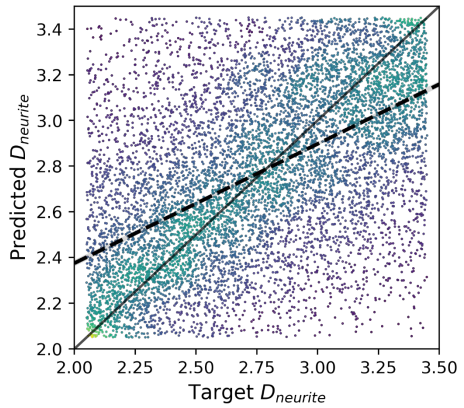
$t_{ex,soma}$ (ms)



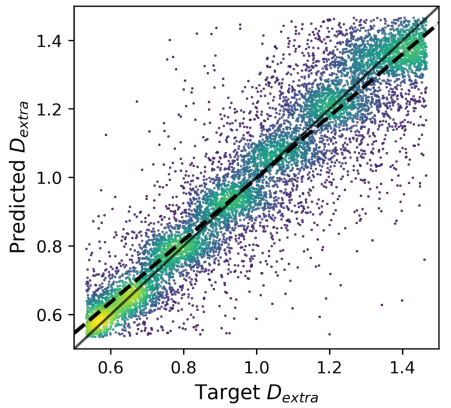
$t_{ex,neurite}$ (ms)



$D_{neurite}$ ($\mu m^2/ms$)

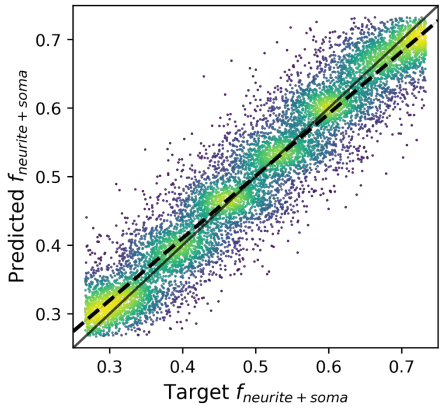


D_{extra} ($\mu m^2/ms$)

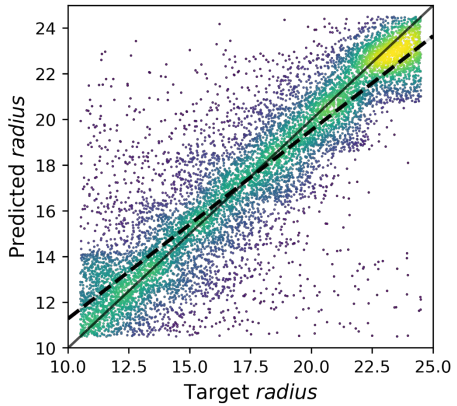


$t_{ex,\bullet}$: exchange time
$f_\bullet$: volume fraction
$D_\bullet$: diffusivity

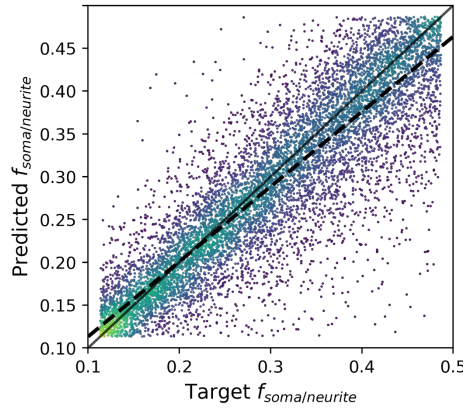
$f_{neurites+soma}$



radius (μm)



$f_{soma\ over\ neurites}$



… with
Non-Linear Least Squares &
suboptimal
protocol and gridsearch

Methods: Preprocessing Diffusion-Weighted Images

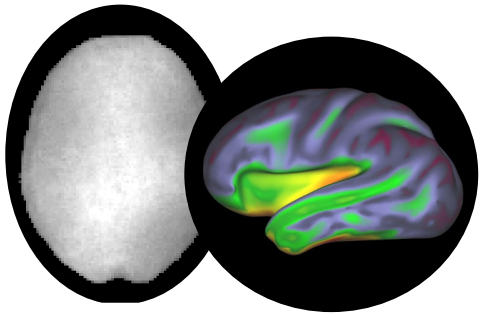
Raw data

- PRISMA scanner, 35 min scan
- 11 subjects with rescan

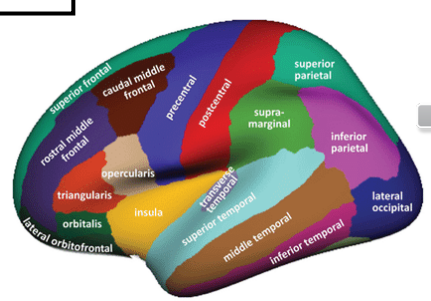
- 2 mm isotropic resolution
- b-values: from 1 to 5 ms/μm^2 (2 for short t_d)
- 4 diffusion times: from 28.3 to 65 ms
- δ = 16.5 ms, TE = 100ms

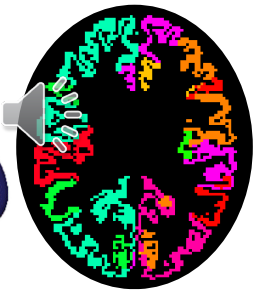
MP-PCA Denoising[1] → Gibbs ringing correction[2] → Topup[3] → Eddy currents correction[4] → Powder average → Input for NEXI fit

Noisemap



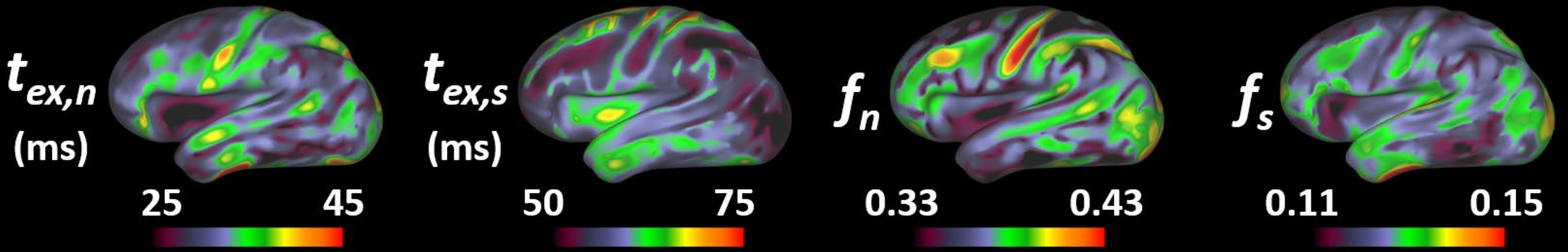
T1 → DKT Atlas segmentation[5,6] → Regions Of Interest (ROI)





Sources : [1] Veerart, NeuroImage 2016 [2] Kellner, MRM 2016 [3] Andersson, NeuroImage 2003
[4] Andersson, NeuroImage 2016 [5] Henschel, NeuroImage 2020 [6] Avants et al., Insight j, 2009

Results - Cortical maps of GEM parameters

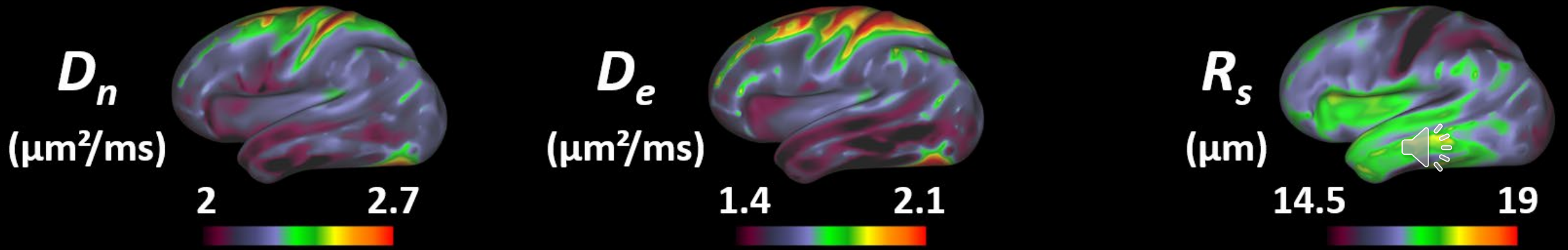


Exchange times

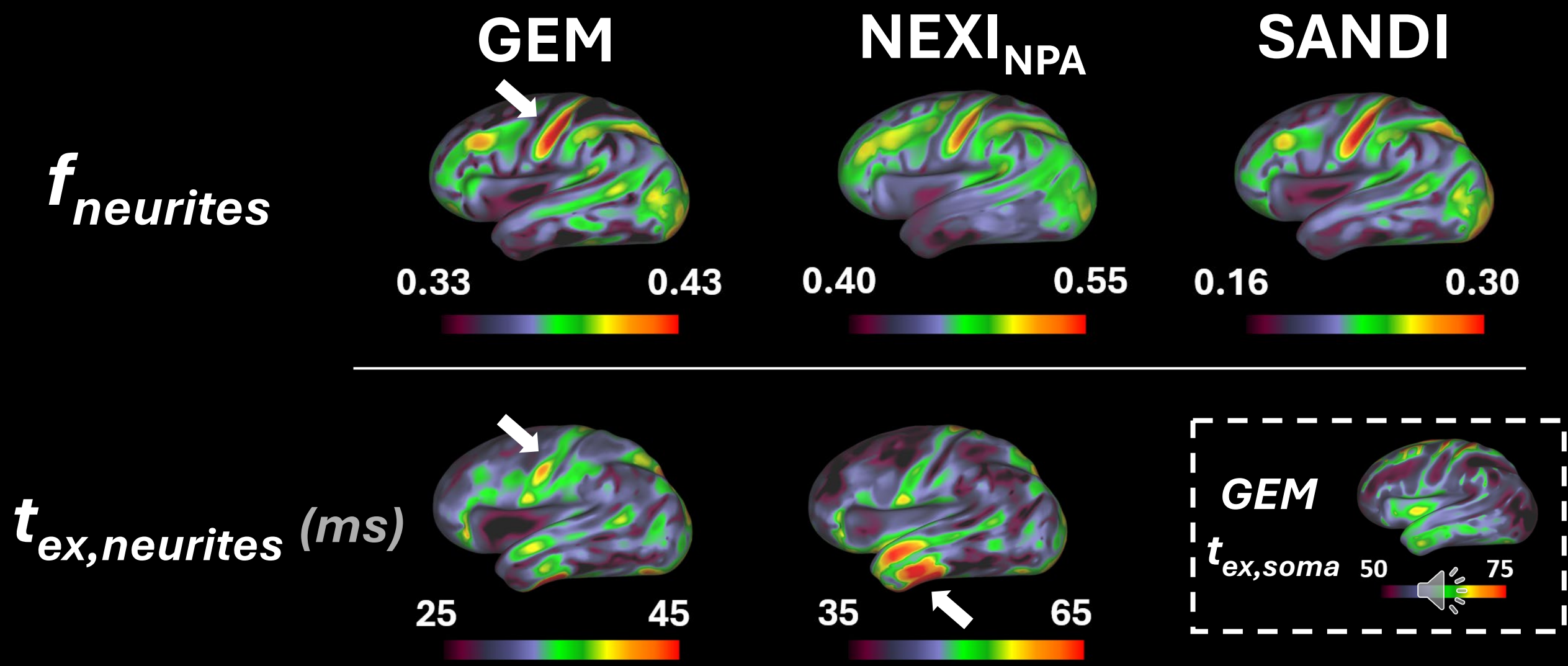
Volume fractions

Diffusivities

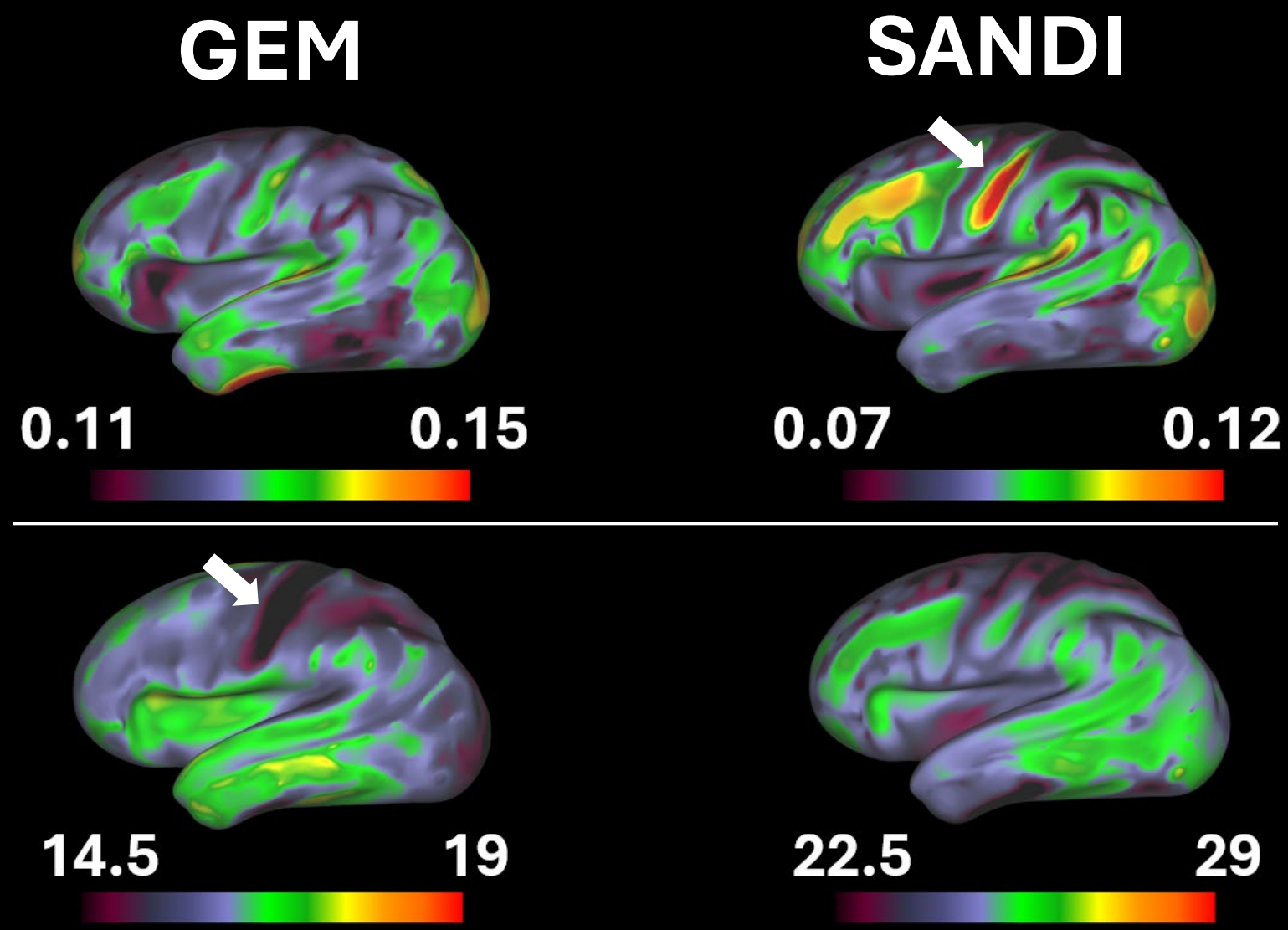
Radius

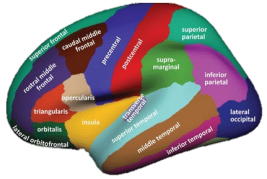


Results – Comparison with other GM model cortical maps



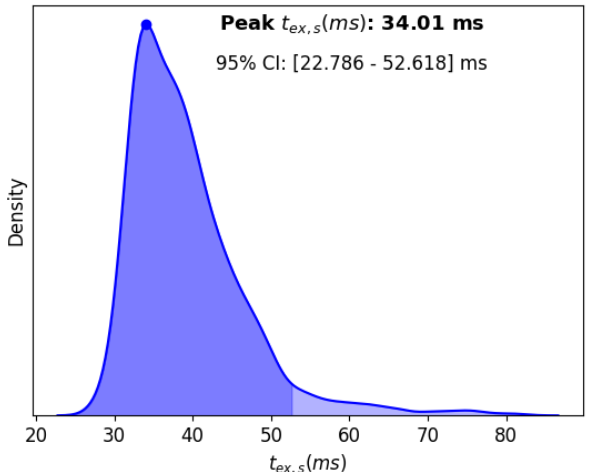
Results – Comparison with other GM model cortical maps



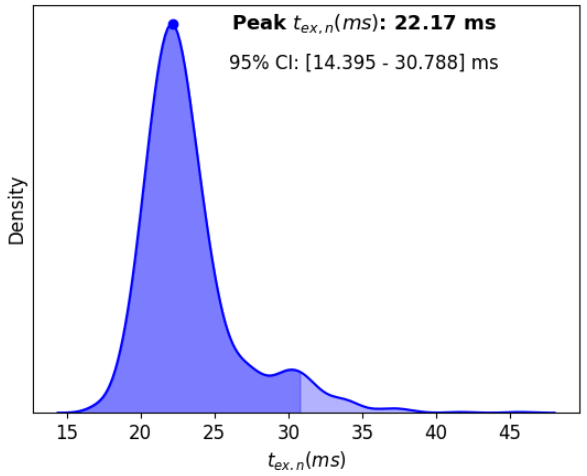


Distribution of the DKT atlas ROI medians

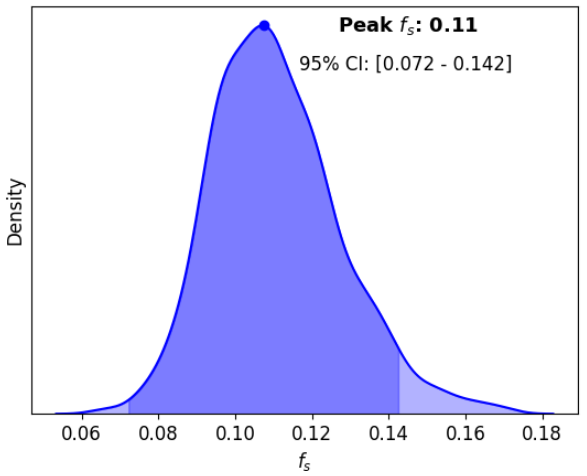
$t_{ex,soma}$ (ms)



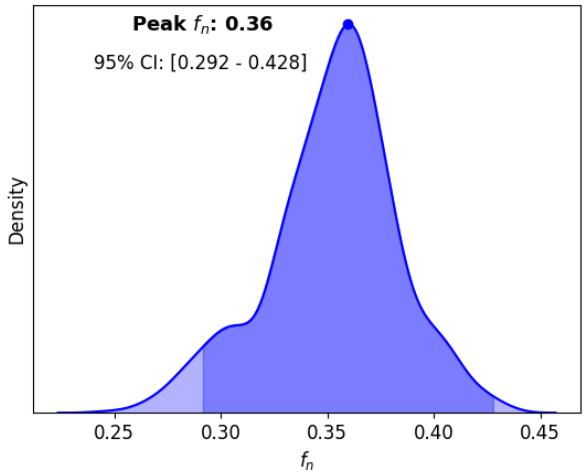
$t_{ex,neurites}$ (ms)



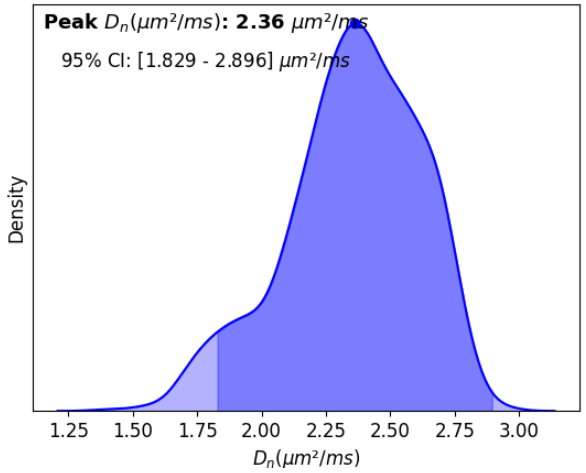
f_{soma}



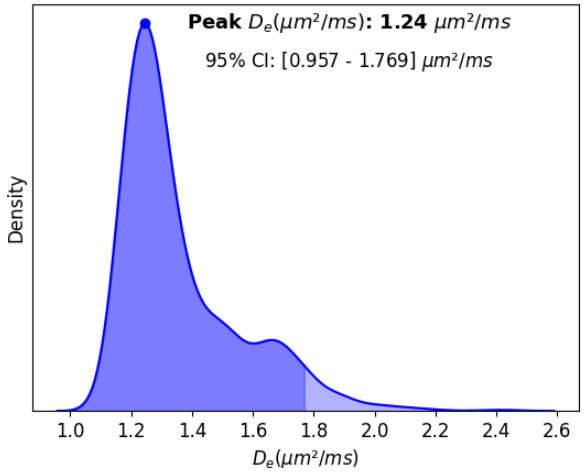
$f_{neurites}$



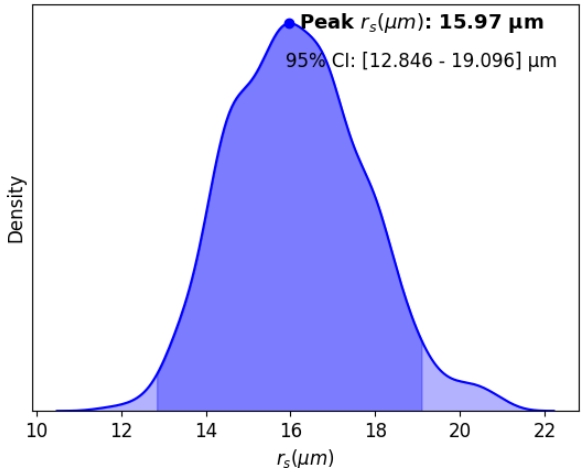
$D_{neurites}$ ($\mu m^2/ms$)



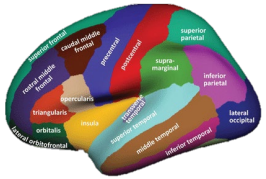
D_{extra} ($\mu m^2/ms$)



radius (μm)



$t_{ex,\bullet}$: exchange time
$f_\bullet$: volume fraction
$D_\bullet$: diffusivity



Peaks of the DKT atlas ROI medians per model

$t_{ex,\bullet}$: exchange time
$f_\bullet$: volume fraction
$D_\bullet$: diffusivity

	$t_{ex,soma}$ (ms)	$t_{ex,neurites}$ (ms)	$f_{neurites}$ (%)	f_{soma} (%)	radius (µm)	$D_{neurites}$ (µm²/ms)	D_{extra} (µm²/ms)	AICc
$NEXI_{NPA}$		**12** [1 - 37]	**48** [34 - 61]			**3.4** [2.0 - 3.5]	**1.0** [0.6 - 1.8]	**-92**
$NEXI_{WP}$		**17** [7 - 34]	**43** [33 - 53]			**2.9** [2.1 - 3.4]	**1.0** [0.7 - 1.4]	**-88**
SANDI			**21** [14 - 27]	**6** [5 - 11]	**29** [23 - 30]	**3.3** [1.9 - 3.5]	**0.8** [0.7 – 1.0]	**-79**
SANDIX		**21** [17 – 27]	**33** [27 – 38]	**8** [5 – 11]	**19** [16 – 21]	**1.4** [1.0 – 1.8]	**1.1** [0.8 – 1.8]	**-80**
GEM	**34** [23 - 53]	**22** [14 - 31]	**36** [29 - 43]	**11** [7 - 14]	**16** [13 - 19]	**2.4** [1.8 - 2.9]	**1.2** [1.0 - 1.8]	**-74**

AICc: Akaike Information criterion – the lower the better the balance btw. goodness of fit and complexity of the model

Take-home message

- GEM is a **unifying framework** for Gray Matter Microstructure modelling.
- It **extends the exchange of water** to structures with a known impermeable signal, improving specificity.
- As such, **some GEM parameters are difficult or impossible to estimate**, and require a longer protocol than the one used for NEXI estimation.
- GEM can also be used as a **validation tool for future diffusion MRI simulators** that will include inter-compartment **exchange**.

Future directions

- Some parameters could be retrieved more efficiently **when other parameters are known**. In this sense, GEM could be used as a complement to another technique.
- **Relationships between parameters** (especially the relationship between the two exchange times) could also **simplify** the fit.
- The generalized exchange equation **enables the creation of new models** to characterize other types of tissue (cells only*, thick unmyelinated fibers, and so on…).

*The CEXI model, described in Gardier et al. 2023. MRM, would then be an approximation of this model

Gray Matter Swiss Army Knife

pypi v1.1.6 | downloads 298/month | license Apache-2.0 | python 100.0% | python 3.7 | 3.8 | 3.9 | 3.10 | 3.11 | code style black

Oral #0937
Wednesday 8 May
Diffusion in Gray Matter
14h30

pip install **graymatter_swissknife**

from graymatter_swissknife import estimate_model
estimate_model(model, dwi, b, Δ, δ, noisemap)

Acknowledgments

The **Microstructure Mapping** team (Lausanne, Switzerland):

- Ileana Jelescu
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- Andreea Hertanu
- Jasmine Nguyen-Duc
- Inès de Riedmatten
- Saina Asadi
- Arthur Spencer
- Jean-Baptiste Perot

Collaborators from **Siemens**:

- Thorsten Feiweier

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