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Microstructure Mapping Lab

NEXI for the quantification of human gray matter microstructure on a clinical MRI scanner

Quentin Uhl[1], Tommaso Pavan[1], Thorsten Feiweier[2], Gian Franco Piredda[4,5], Sune N. Jespersen[3] and Ileana Jelescu[1]

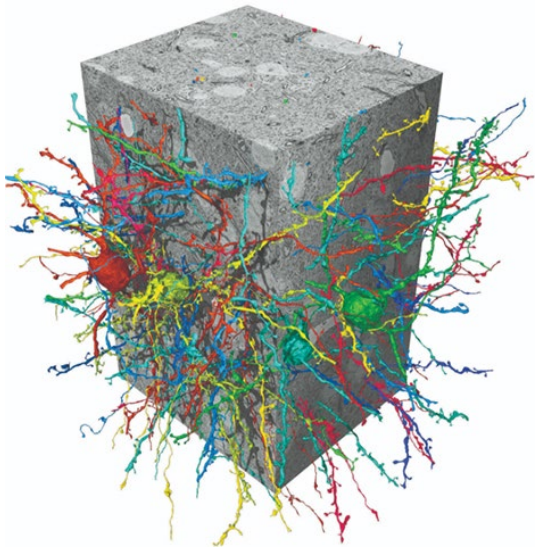
[1]Department of Radiology, Lausanne University Hospital (CHUV) and University of Lausanne, Lausanne, Switzerland
[2]Siemens Healthcare GmbH, Erlangen, Germany
[3]Center of Functionally Integrative Neuroscience (CFIN) and MINDLab, Department of Clinical Medicine, Aarhus University, Aarhus, Denmark
[4]Advanced Clinical Imaging Technology, Siemens Healthineers International AG, Lausanne, Switzerland
[5]CIBM Center for Biomedical Imaging, Geneva, Switzerland

Declaration of Financial Interests or Relationships

Speaker Name: Quentin Uhl

I have no financial interests or relationships to disclose with regard to the subject matter of this presentation.

Modeling Gray Matter…

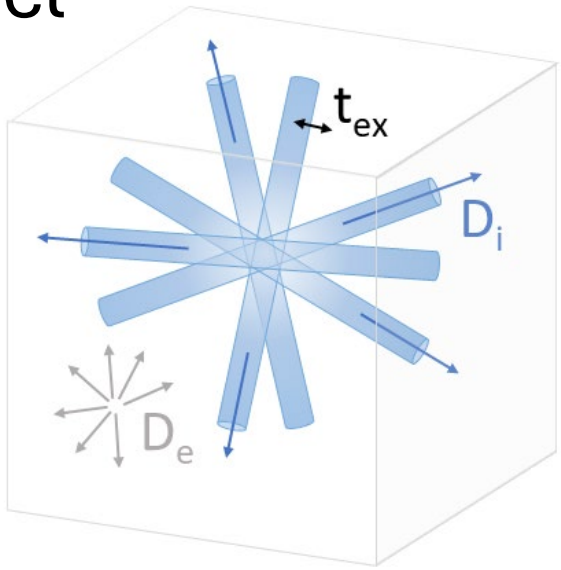


Gray matter microstructure models require:

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

Sources : Songbird Basal Ganglia, Neurobiology, J. Kornfeld
Jelescu et al. 2022. NeuroImage
Olesen et al. 2022. NeuroImage

using the Neurite Exchange Imaging (NEXI) model

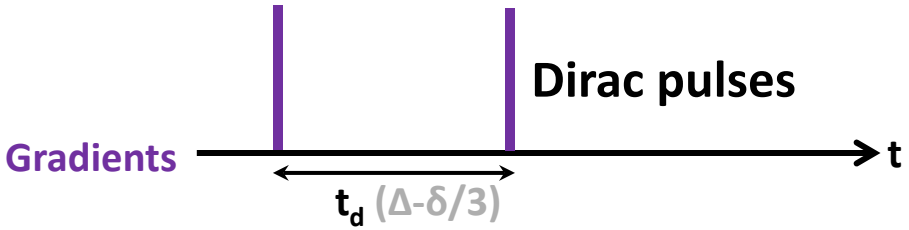


		Volume fraction
Intra-neurite space		f
Extra-neurite space		1-f

t_{ex} : exchange time
f : intra volume fraction
$D_{i/e}$: intra/extra diffusivities

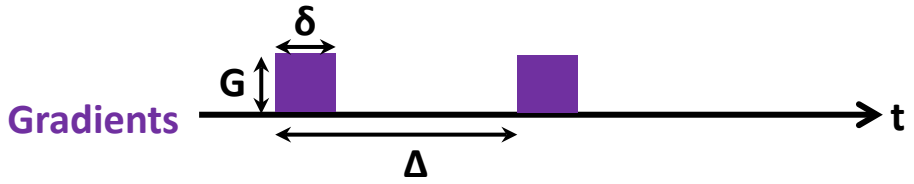
Solving the NEXI differential equation

Narrow Pulses Approximation
$NEXI_{NPA}$



- **Fast analytical solution**

Actual Wide Pulses
$NEXI_{WP}$ (a.k.a. SMEX)



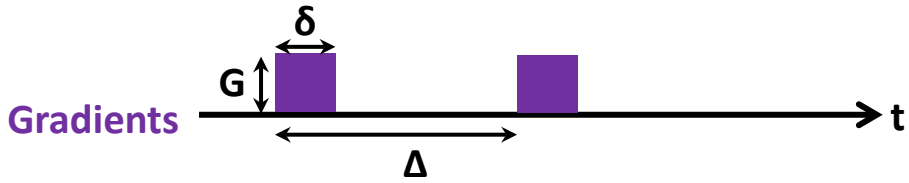
- **Computationally expensive (ODE solver) but more accurate for clinical scanners**

Both applied using preclinical scanners (short δ)

Already applied to human gray matter in vivo on CONNECTOM scanners (short δ)

Sources : NPA described in *Jelescu et al. 2022. NeuroImage*
WP described (as SMEX) in *Olesen et al. 2022. NeuroImage*
C1 : *Uhl et al. 2024. Imaging Neuroscience*
C2 : *Chan et al. ISMRM Annual Meeting 2024 #0644*

Gradient pulses: lower means longer



NEXI requires high b-values: above 5ms/µm²

$$b_{max} = \gamma^2 {G_{max}}^2 \delta^2 \left(\Delta - \frac{\delta}{3}\right)$$

	Preclinical	CONNECTOM 2.0	CONNECTOM 1.0	PRISMA
G_{max} (mT/m)	1000	500	300	80
δ (ms)	4	6	9	**16.5**

Sources : Preclinical: *Jelescu et al. 2022. NeuroImage*
C1 : *Uhl et al. 2024. Imaging Neuroscience*
C2 : *Chan et al. ISMRM Annual Meeting 2024 #0644*

Objectives

- Obtain NEXI parametric maps in the human cortex from a **clinical scanner**.
- Check whether, in the case of long gradient pulses, $NEXI_{NPA}$ approximation is **valid** and gives **equivalent** results to $NEXI_{WP}$.
- Since exchange is supposed to **reflect permeability**, investigate how would these estimates relate to **myelination** in gray matter.
- Check **consistency** with previous & ongoing studies.
- Check the **reproducibility** (scan/rescan) and **sensitivity** to variations among subjects.

Preprocessing Diffusion-Weighted Images

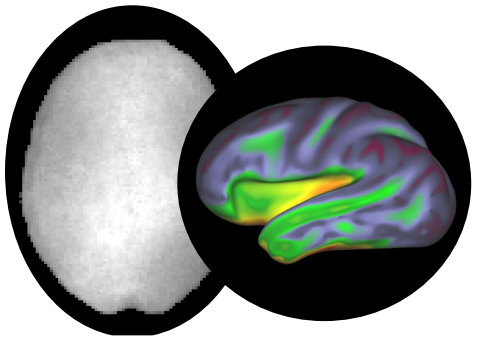
Raw data

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

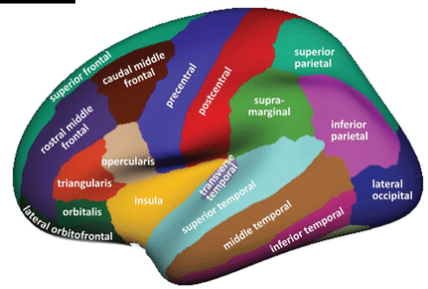
- 2 mm isotropic resolution
- b-values: from 1 to 5 ms/μm^2 (2 for short t_d)
- 4 diffusion times: from 28.3 to 65 ms
- δ = 16.5 ms, TE = 100ms

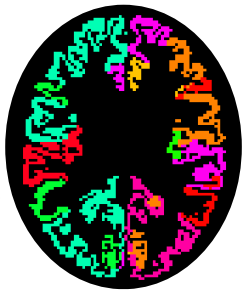
MP-PCA Denoising[1] → Gibbs ringing correction[2] → Topup[3] → Eddy currents correction[4] → Powder average → Input for NEXI fit

Noisemap



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



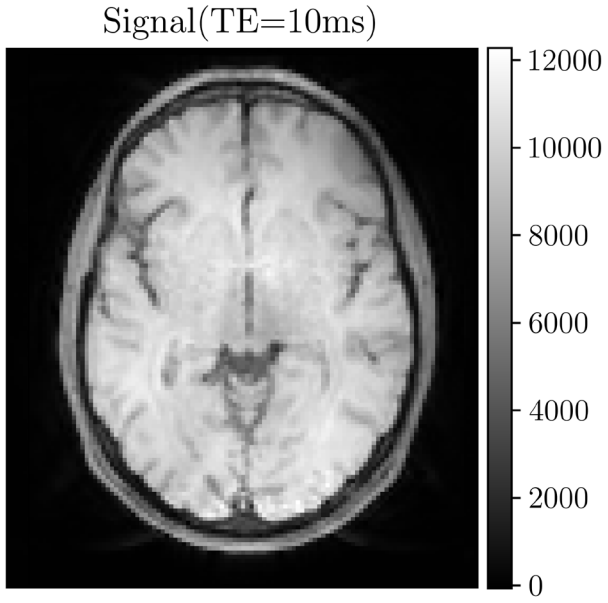


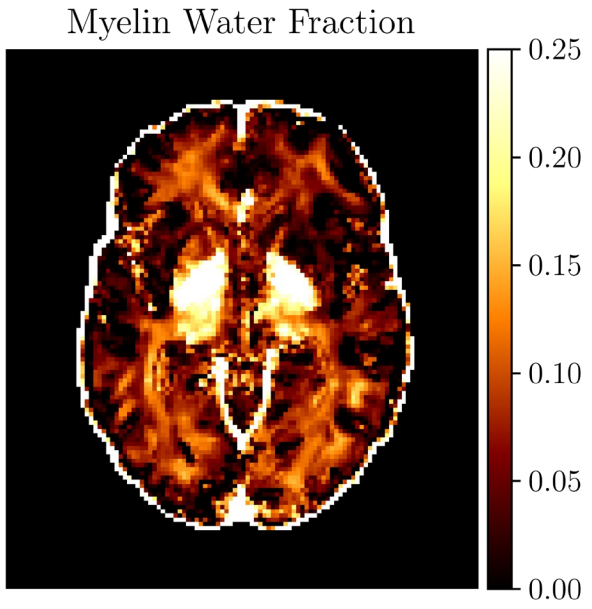
Sources : [1] Veerart, NeuroImage 2016 [2] Kellner, MRM 2016 [3] Andersson, NeuroImage 2003
[4] Andersson, NeuroImage 2016 [5] Henschel, NeuroImage 2020 [6] Avants et al., Insight j, 2009

Processing Multi-echo T2-weighted images

- Additional 10 min scan
- **GRASE** sequence (Piredda et al., 2020)
- 1.8 mm isotropic resolution

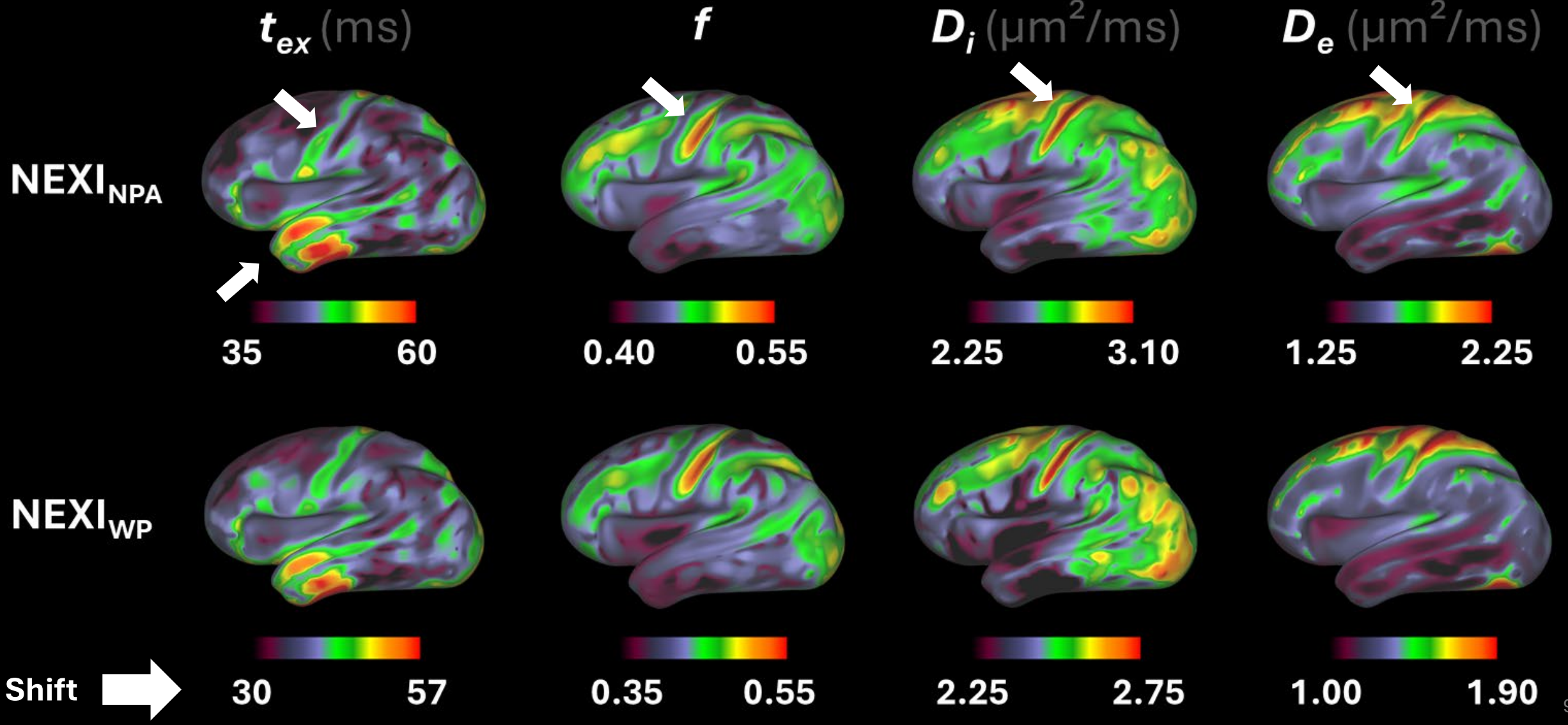
- Non-parametric T_2 relaxometry method for MWF estimation (**χ^2-I**)

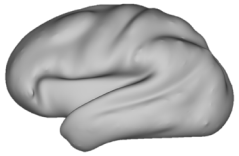




Sources : Piredda et al., Magnetic Resonance in Medicine, 2020
Jorge Canales-Rodríguez et al., Medical Image Analysis, 2021
Jorge Canales-Rodríguez et al., NeuroImage, 2021

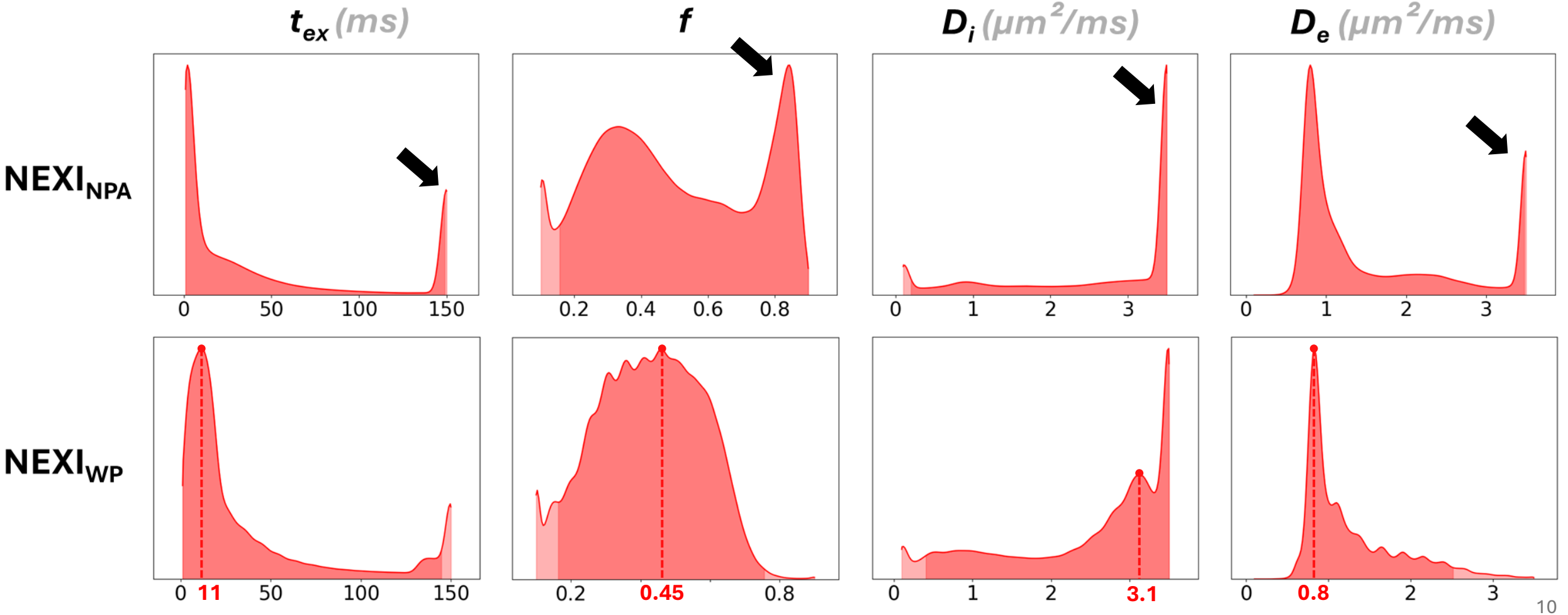
Results - Cortical maps of NEXI parameters

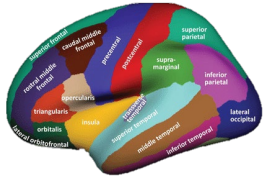




Distribution across the whole cortex

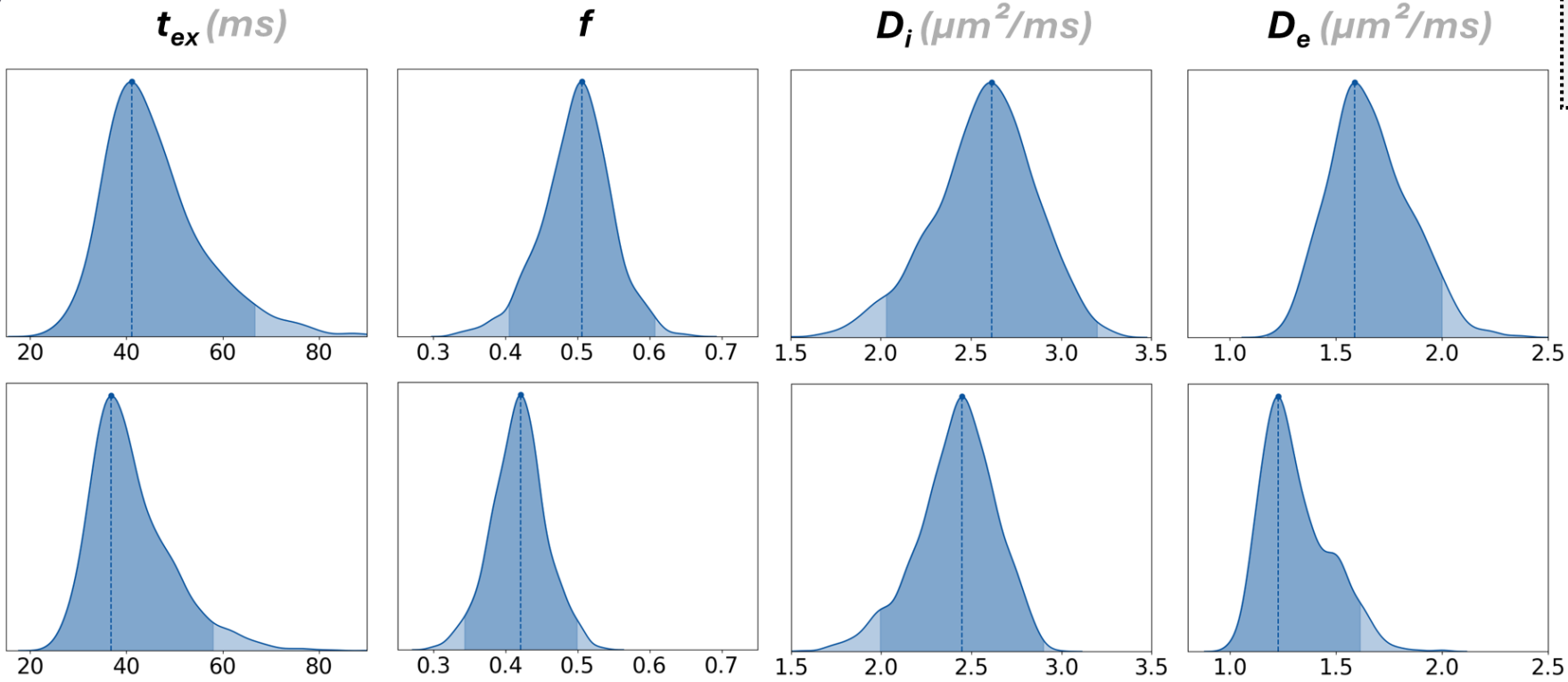
t_{ex} : exchange time
f : intra volume fraction
$D_{i/e}$: in./ex. diffusivities

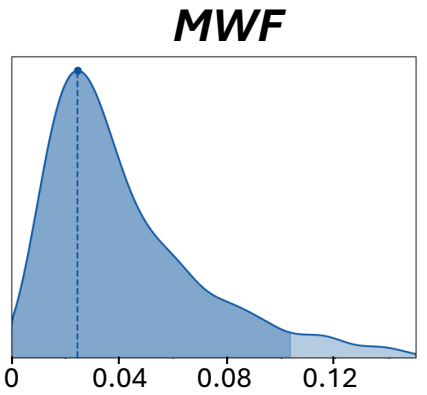




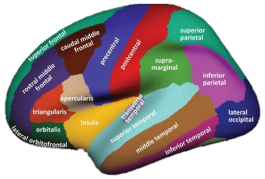
Distribution of the DKT atlas ROI means

t_{ex} : exchange time
f : intra volume fraction
$D_{i/e}$: in./ex. diffusivities





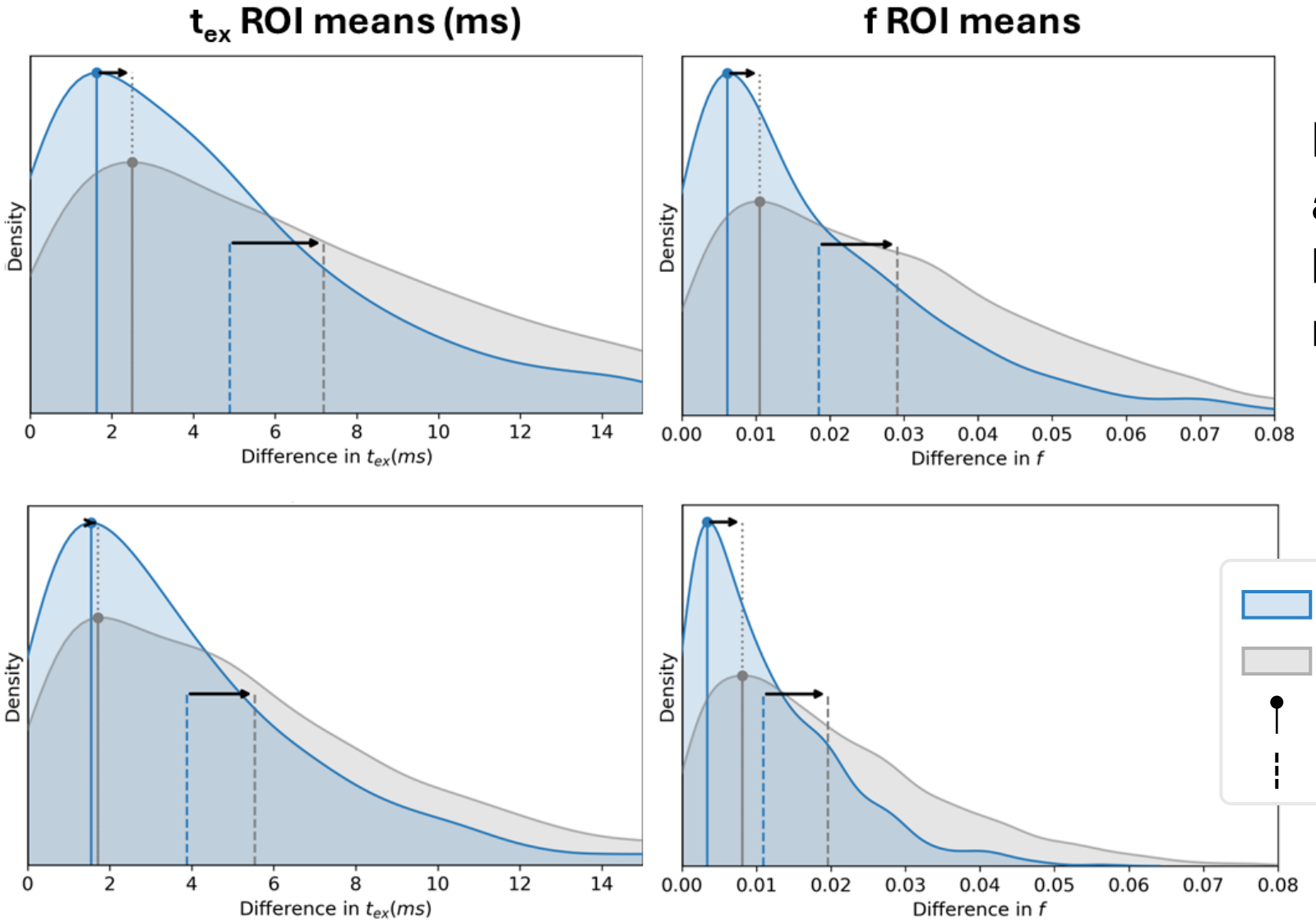
	t_{ex} (ms)	f	D_i (μm²/ms)	D_e (μm²/ms)	AICc	MWF
NEXI$_{NPA}$	**41.1** [15.5 - 66.7]	**0.51** [0.41 - 0.61]	**2.61** [2.03 - 3.20]	**1.59** [1.18 - 2.00]	**-93** [-99 , -84]	**0.024** [0.000 - 0.103]
NEXI$_{WP}$	**36.8** [17.6 - 58.0]	**0.42** [0.34 - 0.50]	**2.45** [1.99 - 2.90]	**1.23** [0.88 - 1.61]	**-88** [-94 , -81]	



Reproducibility

$NEXI_{NPA}$

$NEXI_{WP}$



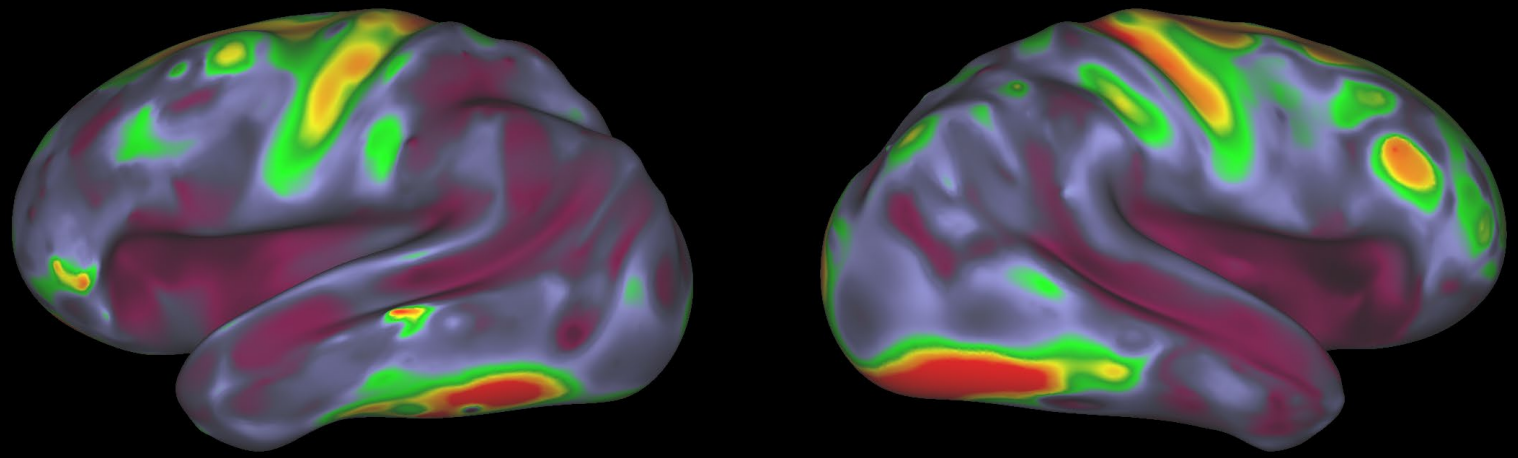
Distributions of absolute differences between DKT ROI mean estimations

- Between Scan/Rescan
- Between Subjects
- Peak of the distribution
- Mean of the distribution

Result - Myelin quantification

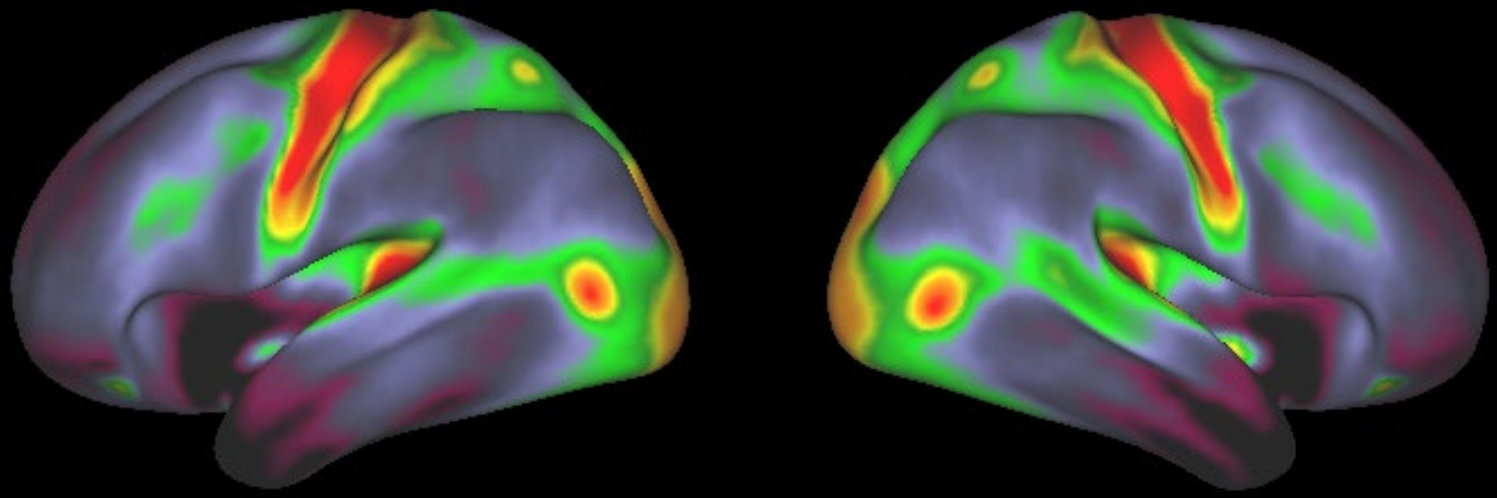
MWF

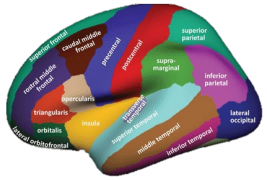
0 0.15



Another technique

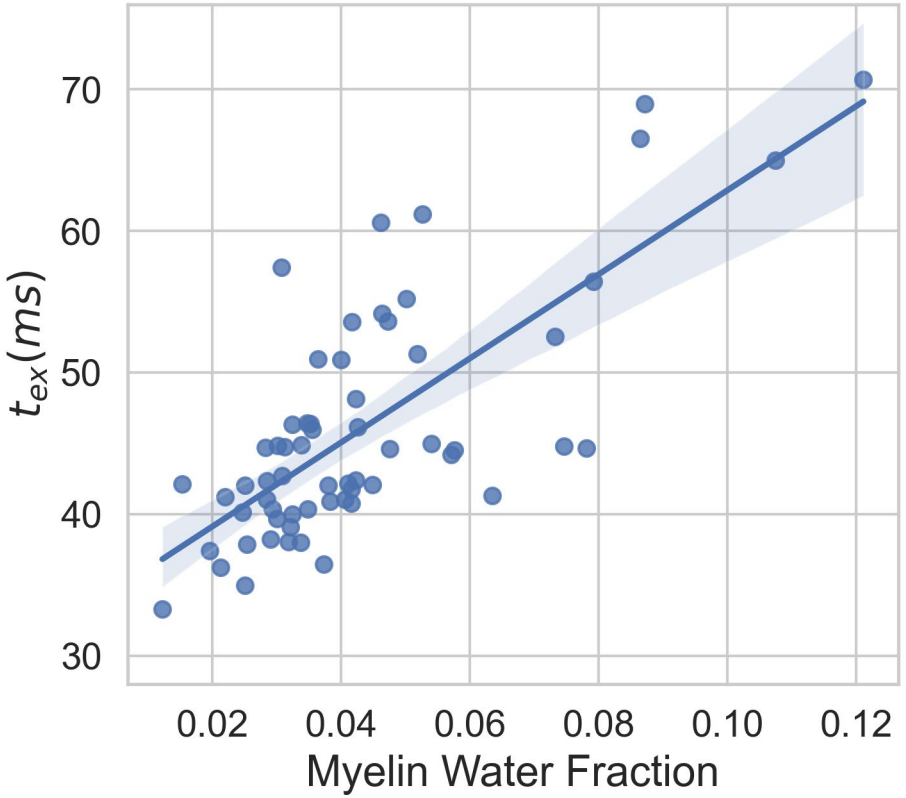
Myelin Map
T_1 / T_2
(Glasser et al.)



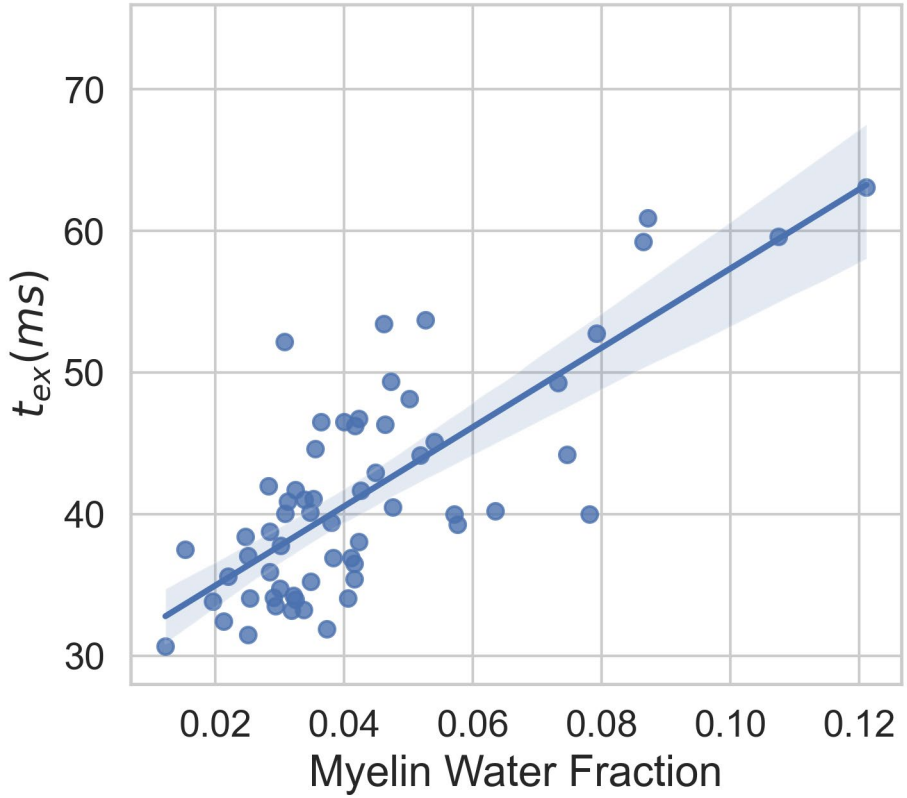


Correlation between the estimated exchange time and MWF

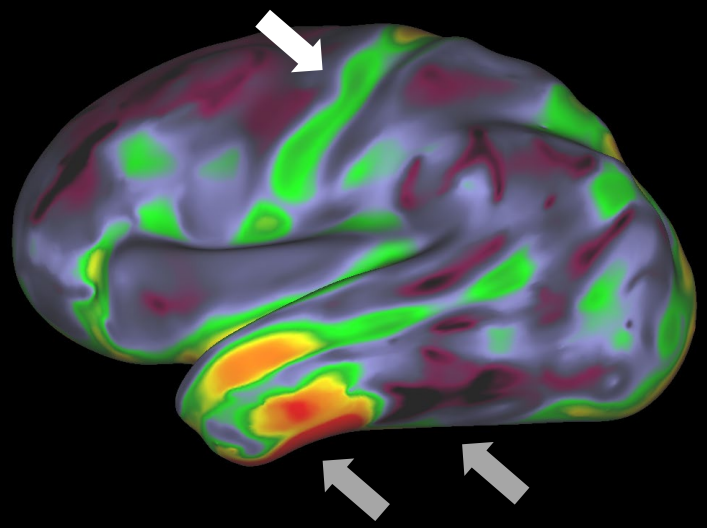
$NEXI_{NPA}$: r=0.74 (p=4e-12)



$NEXI_{WP}$: r=0.79 (p=3e-14)

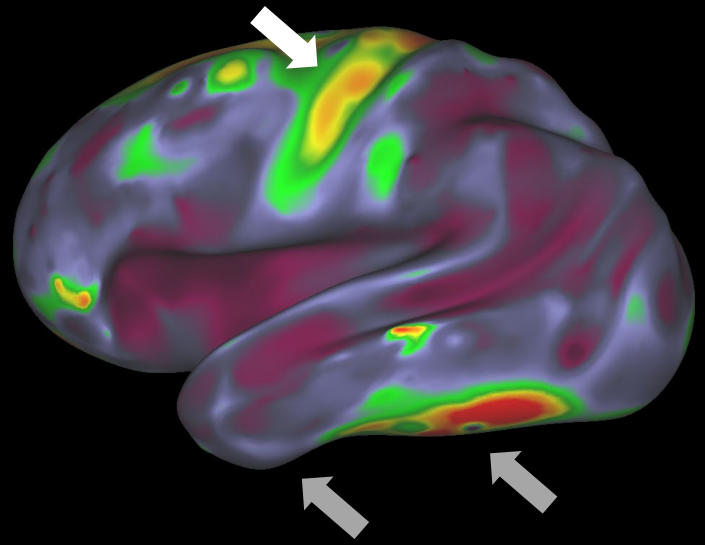


Cortical maps from DKT-correlated parameters



$NEXI_{WP}$ t_{ex} (ms)

30 57



MWF

0 0.15

Take-home message

- The first NEXI parametric maps in the human cortex from a **clinical scanner**.
- For the microstructure parameter **patterns**, **$NEXI_{NPA}$** is enough.
- For a **more theoretically comprehensive approach**, or studies with **multiple scanners** and different δ, **$NEXI_{WP}$** is more appropriate.
- Out of all NEXI parameters, **t_{ex} correlates the best** with a **myelin** quantification method.
- Our results are **consistent** with previous & ongoing studies.
  Notably, mean t_{ex} is around **40 ms**, with a peak in the distribution around **10-15 ms**.
- Good scan-rescan **reproducibility** + **sensitivity** to variations among subjects.

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

Poster #3455

pip install **graymatter_swissknife**

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

Acknowledgments

Microstructure Mapping Lab

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