Optimizing the NEXI acquisition protocol for human gray matter microstructure mapping on a clinical MRI scanner using Explainable AI

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Introduction

We aim to optimize the acquisition protocol for parameter estimation of the NEXI model of two exchanging compartments[1,2] and demonstrate feasibility on a clinical 3T system.

The NEXI model is suited to characterize gray matter microstructure; its parameters are the **exchange time** t_{ex}, the **intra and extra-neurite apparent diffusivities** D_i and D_e and the **intra-neurite signal fraction** f.

FIGURE 1. NEXI parameters
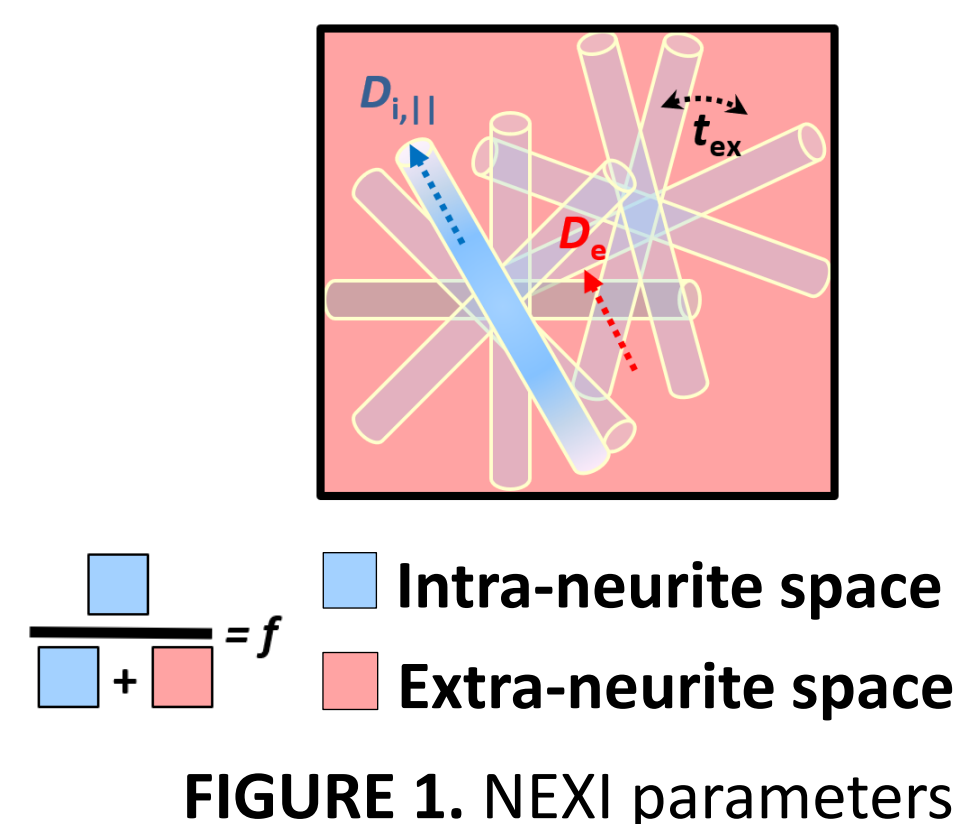
Methods

One healthy volunteer was scanned.
Acquisition:
- DWI acquired on a 3T Siemens Prisma system
- PGSE EPI sequence with N=16 (b, t) pairs among b=1, 2, 3.2, 4.44 and 5ms/μm², Δ=28.3, 36, 45, 55 and 65ms, δ=16.5ms, 4 b=0 images per Δ, 340 total dwi, at 2-mm isotropic resolution, total scan time: 35min.

Preprocessing:
- Multi-shell multi-diffusion time data preprocessed jointly.
- Preprocessing steps : MP-PCA magnitude denoising[4], Gibbs ringing correction[5], distortion and eddy current correction[6], average over all the directions and normalization by the mean value of the b=0 volumes.
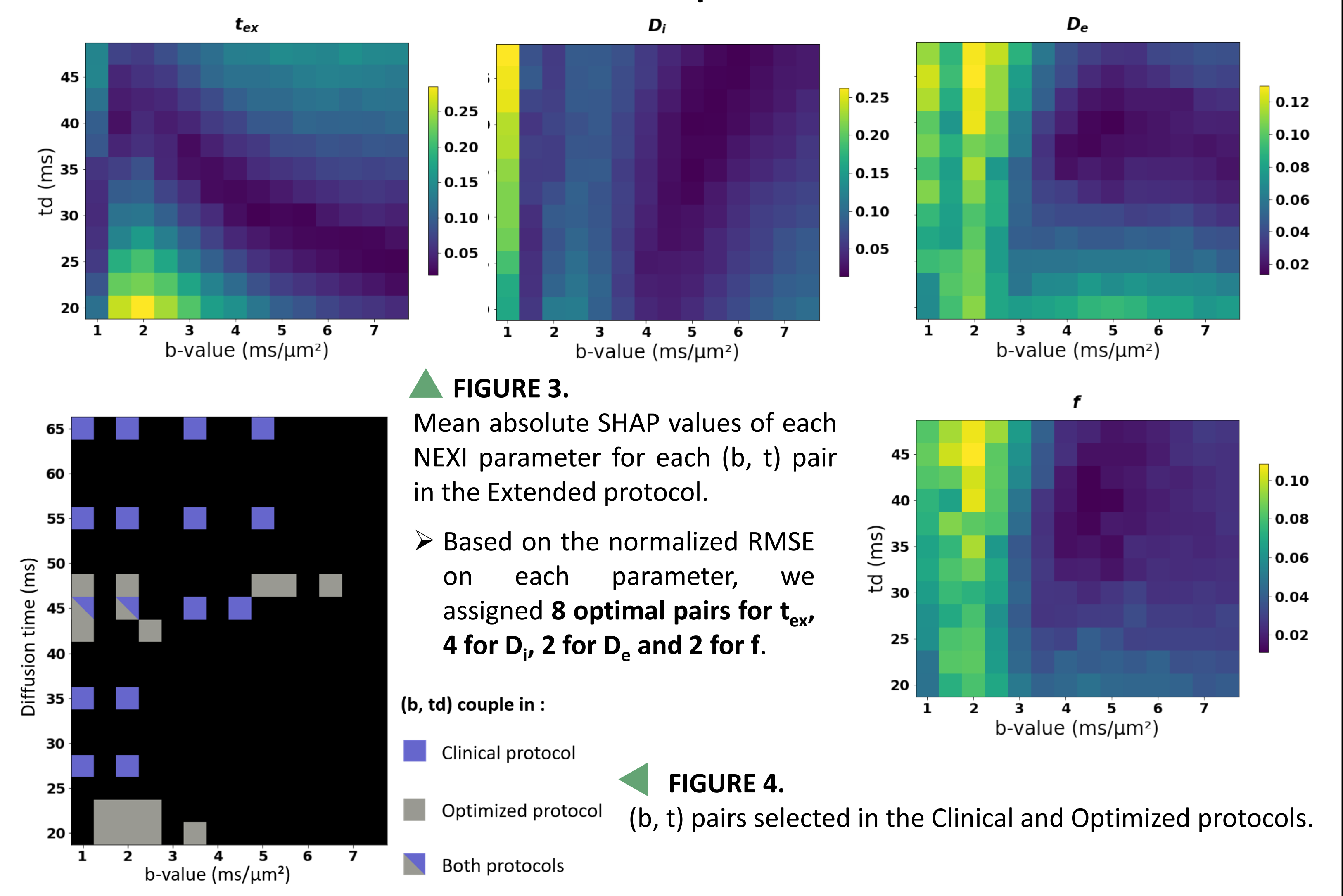
Processing:
- Fitting the NEXI model using a Multi-Layer Perceptron (MLP) of 3 hidden layers and 500 neurons per layer trained on 2.10^6 random sets (NEXI parameter combinations) and applied to a test set of 10^4 examples.
- Segmentation of the cortical ribbon ROI on the anatomical MPRAGE image using FastSurfer[7] and transformation into diffusion native space using linear registration[8] of b=0 images to MPRAGE images.

Explainable AI analysis:
- Extraction of Shapley values from an extended protocol of 12x14 (b, t) pairs using the SHAP framework[9].
- Ranking of these values to produce an optimized protocol of N=16 (b, t) pairs.
- The RMSE obtained from the clinical protocol on each parameter, normalized by their limits, gave the number of optimal pairs selected from each parameter ranked SHAP values.

NEXI parametric maps

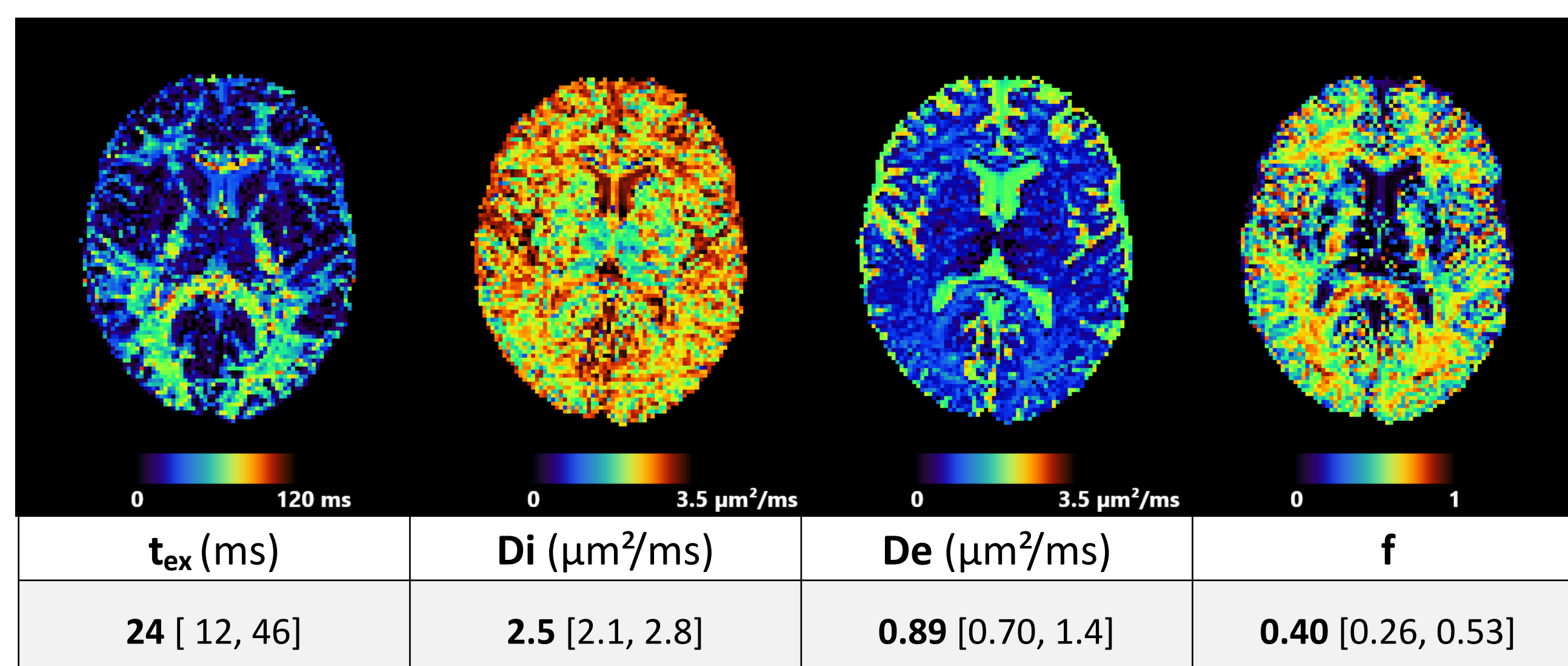| t_{ex} (ms)	Di (μm²/ms)	De (μm²/ms)	f
24 [12, 46]	**2.5** [2.1, 2.8]	**0.89** [0.70, 1.4]	**0.40** [0.26, 0.53]

FIGURE 2. Axial slice of NEXI parametric maps in our subject with, below, the median and quartiles of the estimations on the cortical ribbon, showed on the right.
➤ These are the first microstructure maps of the NEXI model estimated in the **human brain** on a **"standard" clinical scanner.**
➤ Typical NEXI parameter values in the cortex are **consistent with previous estimates** in the **rat cortex**[1.]

Protocol Optimization

FIGURE 3.
Mean absolute SHAP values of each NEXI parameter for each (b, t) pair in the Extended protocol.

➤ Based on the normalized RMSE on each parameter, we assigned **8 optimal pairs for t_{ex}, 4 for D_i, 2 for D_e and 2 for f.**

(b, td) couple in :
- ▪ Clinical protocol
- ▪ Optimized protocol
- ▪ Both protocols

FIGURE 4.
(b, t) pairs selected in the Clinical and Optimized protocols.

MLP Scores

	t_{ex} (ms)	Di (μm²/ms)	De (μm²/ms)	f
Clinical Protocol MAE	27.457	0.423	0.351	0.083
Optimized Protocol MAE	25.496	0.419	0.330	0.076

TABLE 1. Mean Absolute Error of the MLP with each input protocol
➤ These scores are very similar, we can note a **small improvement of 2ms** in t_{ex} MAE with the optimized protocol.

➤ This marginal reduction **does not allow us to prefer one protocol** over the other, especially as some pairs of the Optimized protocol are **difficult to achieve** on a clinical system, due to gradient limitations.

Summary

- We developed an **optimization method of MRI protocols** using Explainable AI.

- The limit on NEXI parameter estimation precision and accuracy is however largely **driven by the model** and the **type of measurements available**.

- Our clinical acquisition protocol feasible on a 3T system with 80 mT/m gradients **already yields reasonable NEXI microstructure maps** in the human brain.

References

[1] Jelescu, Neuroimage 2022 [2] Olesen, NeuroImage 2022 [3] Lundberg and Lee, NIPS 2017 [4] Veraart, NeuroImage 2016 [5] Kellner, MRM 2016 [6] Andersson, NeuroImage 2016, [7] Henschel, NeuroImage 2020 [8] Avants et al., Insight j, 2009, [9] Lundberg and Lee, NIPS 2017.

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