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# Multi-Spherical Diffusion MRI: An in-vivo Test-Retest Study of Time-Dependent q-space Indices

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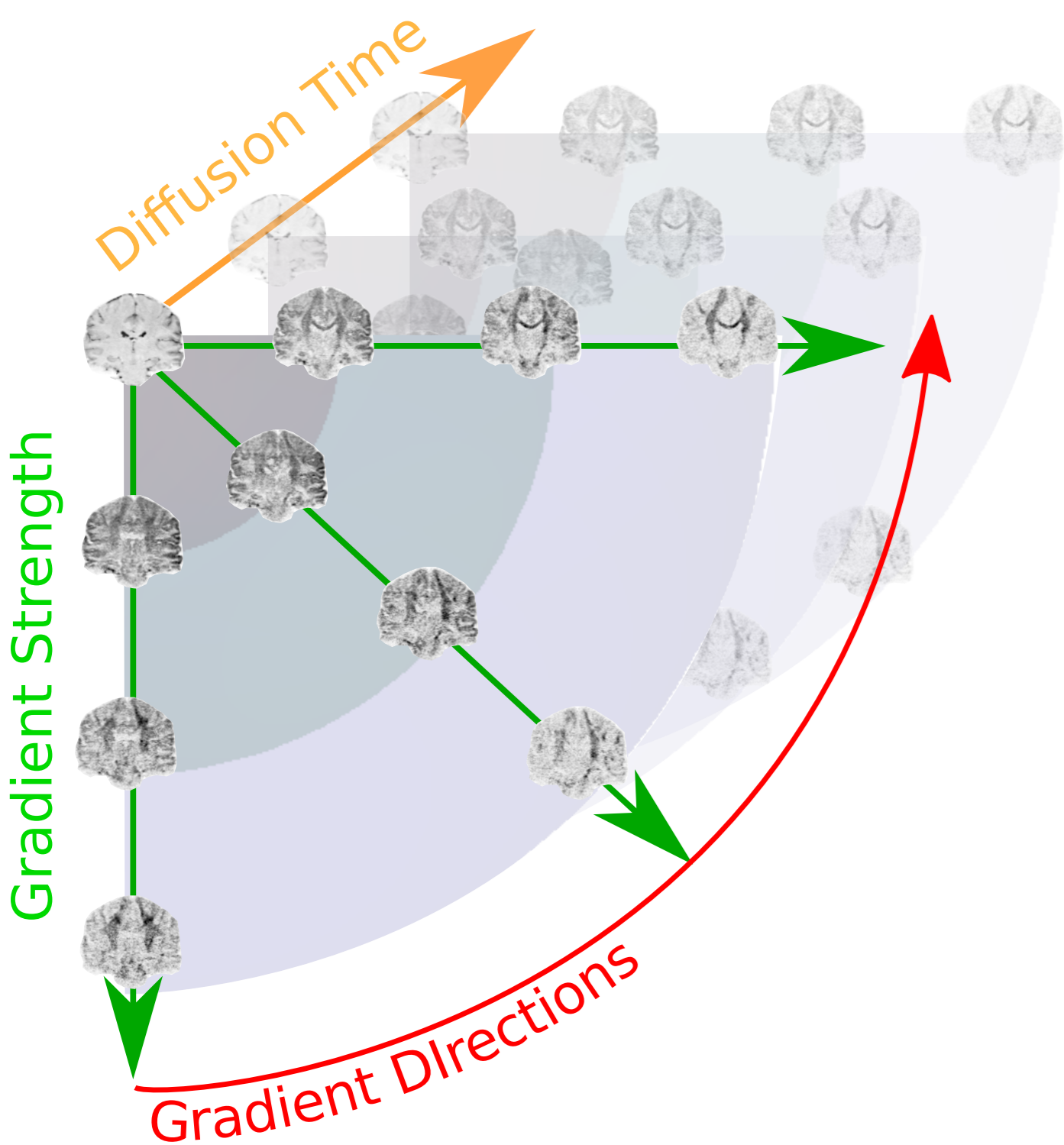
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**Abstract:** We assess the test-retest reproducibility of time-dependent q-space indices (q $\tau$ -indices) in three C57Bl6 wild-type mice. To estimate q $\tau$ -indices from the four-dimensional q $\tau$  diffusion signal - varying over 3D q-space and diffusion time - we use our recent Multi-Spherical Diffusion MRI (MS-dMRI) method. Using MS-dMRI we could reliably estimate q $\tau$ -indices for two out of three subjects, where acquisition artifacts caused the offsets of the last subject.

## 1 The 4D q $\tau$ -diffusion signal

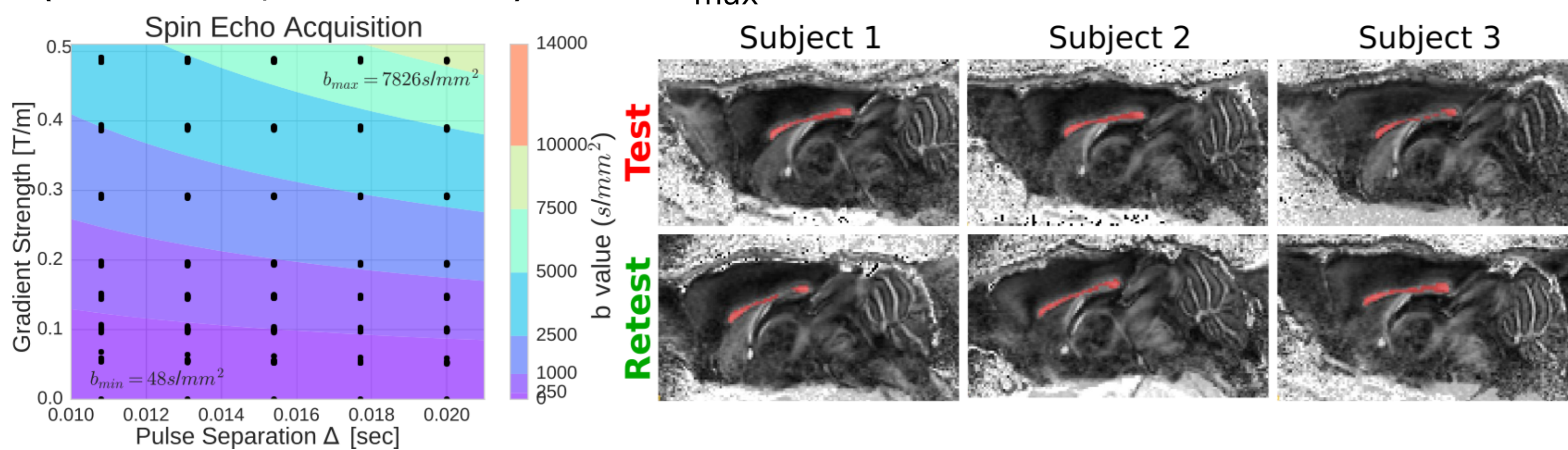


**Diffusion restriction** occurs when water diffusion is obstructed by tissue boundaries. The amount of restriction is **time-dependent**, meaning that the observed diffusion coefficient will change for varying diffusion times [1].

**Multi-Spherical dMRI (MS-dMRI)** [2] describes the q $\tau$ -diffusion signal [3] over varying:

- **Gradient strength (G)**
- **Gradient direction (g)**
- **Diffusion time ( $\tau$ )**

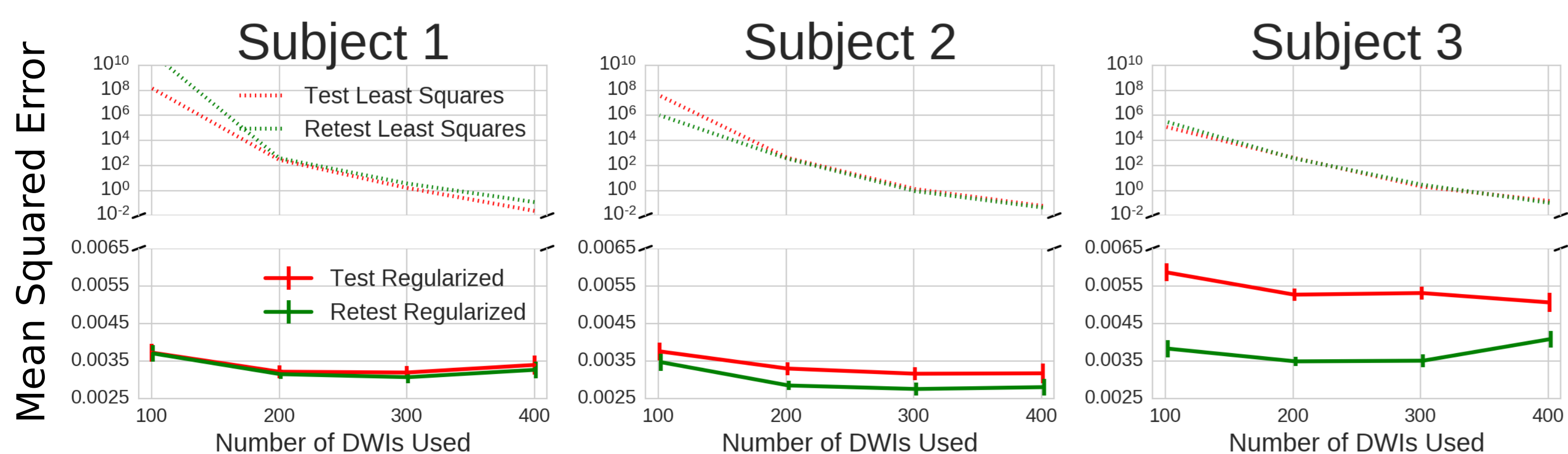
**Data Description:** We acquire 3 test-retest mouse datasets (35 shells, 580 DWIs) with  $G_{\max}=490\text{mT/m}$  and  $10.8<\tau<20\text{ms}$ .



## 3 Test-Retest of Subsampling Fitting Error

We draw an ROI in the **corpus callosum** in each data set. We estimate the fitting error using MS-dMRI when randomly subsampling the q $\tau$ -signal down from 400 to 100 samples.

- Without regularization (dashed) the fitting error is up to 10 orders of magnitude larger than with regularization (solid).
- Only Subject 3 has inconsistent test-retest fitting errors.
- With regularization we find a **lower bound of 200 DWIs** while ensuring a low fitting error (solid lines).



## 2 Modeling the q $\tau$ -signal using MS-dMRI

MS-dMRI uses a separable **Fourier Basis** to reconstruct diffusion propagator  $P(\mathbf{r}, \tau; \mathbf{c})$  from signal attenuation  $E(\mathbf{q}, \tau; \mathbf{c})$ , represented in coefficients  $\mathbf{c}$ .

$$\hat{E}(\mathbf{q}, \tau; \mathbf{c}) = \sum_i^{N_q} \sum_k^{N_\tau} c_{ik} \Phi_i(\mathbf{q}) T_k(\tau) \xleftrightarrow{FT} \hat{P}(\mathbf{r}, \tau; \mathbf{c}) = \sum_i^{N_q} \sum_k^{N_\tau} c_{ik} \Psi_i(\mathbf{r}) T_k(\tau)$$

$\Psi_i(\mathbf{r}) = FT(\Phi_i(\mathbf{q}))$ : 3D Fourier basis over  $\mathbf{q}$  and displacement  $\mathbf{r}$  [4].

$T_m(\tau)$ : Exponential diffusion time basis over  $\tau$  [5].

We constrain the fitting of  $\mathbf{c}$  to respect boundary conditions of the signal and impose **signal smoothness and sparsity**:

$$\underset{\mathbf{c}}{\operatorname{argmin}} \left[ \int \int [E(\mathbf{q}, \tau) - \hat{E}(\mathbf{q}, \tau; \mathbf{c})]^2 d\mathbf{q}d\tau + \int \int [\nabla^2 \hat{E}(\mathbf{q}, \tau; \mathbf{c})]^2 d\mathbf{q}d\tau + \|\mathbf{c}\|_1 \right]$$

(1) Data Fidelity (2) Smoothness (3) Sparsity

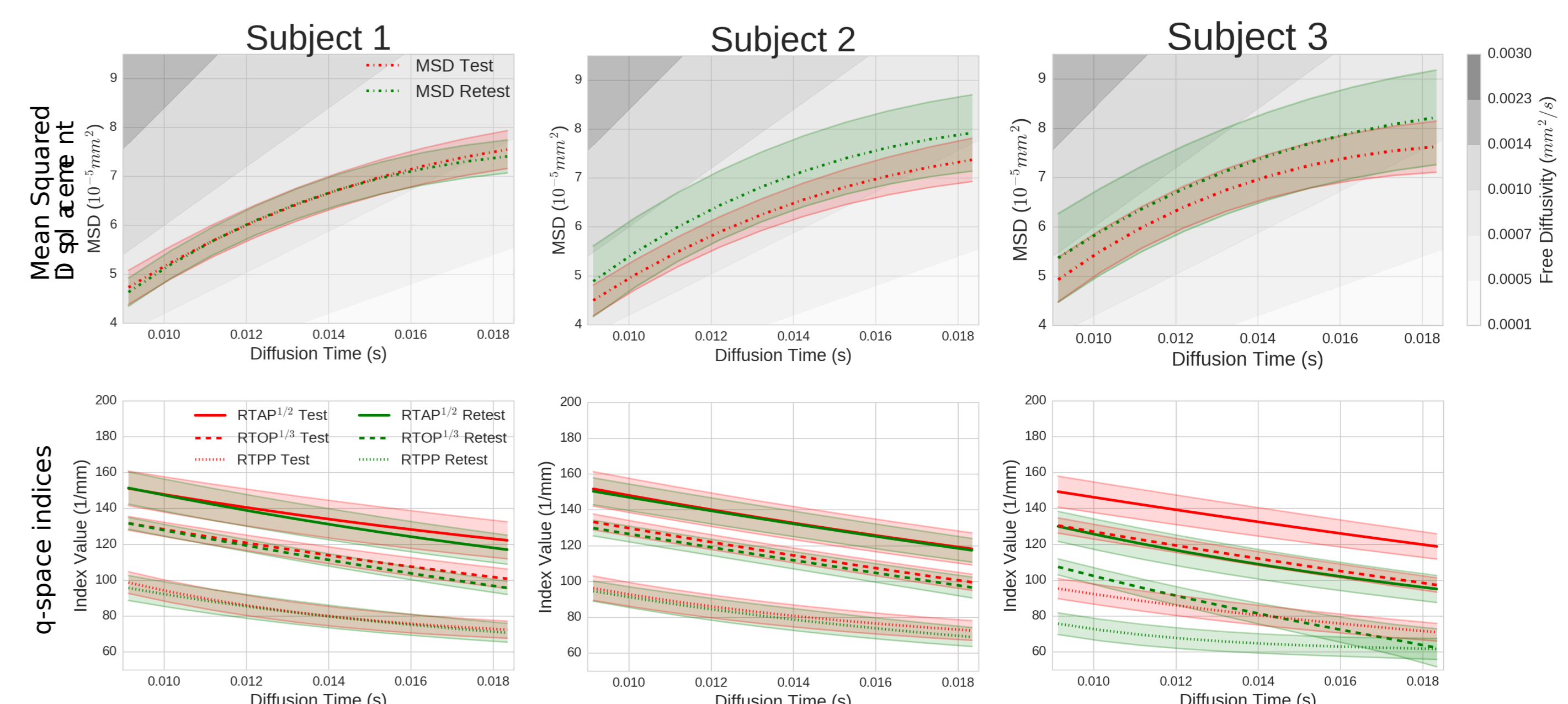
Once fitted, we can estimate, for any  $\tau$ , the q-space indices Mean Squared Displacement (MSD) and Return-to-Origin, Axis and Plane Probability (RTOP, RTAP, RTPP) [4]:

- MSD: related to restriction
- RTAP: perpendicular restriction
- RTOP: related to cellularity
- RTPP: parallel restriction

## 4 Test-Retest of q $\tau$ -index Estimation

Using the whole data, we estimate the progress of the average MSD, RTOP, RTAP and RTPP and 0.75 standard deviation over time. The gray tones show MSD isolines for different free diffusion coefficients. Notice the non-Gaussian MSD progress.

- Subject 1: Great test-retest reproducibility all indices.
- Subject 2: Similar overlap for RTXP indices, small offset MSD.
- Subject 3: Offset for both RTXP indices and MSD.



## 5 Discussion and Conclusions

- We studied the test-retest reproducibility of fitting error and q $\tau$ -index estimation in the corpus callosum of three mice.
- Through signal sparsity and smoothness, MS-dMRI can represent the q $\tau$ -signal using only 200 samples, allowing more realistic acquisition schemes.
- The acquisition protocol can still be improved to avoid excessive acquisition noise like in Subject 3.
- Overall, we found that MS-dMRI can robustly and consistently estimate q $\tau$ -indices in in-vivo acquisitions, underlining its feasibility to estimate  $\tau$ -dependent features.

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## References

- [1] Fieremans et al. NeuroImage 129 (2016): 414-427. [2] Fick et al. CD-MRI 2016. [3] Novikov et al. arXIV:1612.02059 (2016) [4] Özarslan et al. NeuroImage 78 (2013): 16-32. [5] Fick et al. IPMI 2015.