

# Multi-Spherical Diffusion MRI: Breaking the Barriers of Diffusion Time

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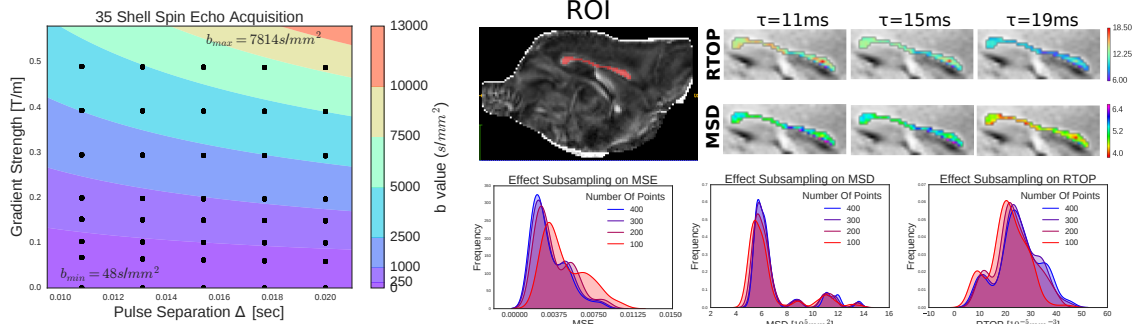
**Target Audience:** Diffusion MRI Researchers.

**PURPOSE:** Effective representation of the diffusion signal’s dependence on diffusion time is a sought-after, yet still unsolved challenge in diffusion MRI (dMRI). We propose a functional basis approach that is specifically designed to represent the dMRI signal in this four-dimensional space – varying over gradient strength, direction and diffusion time – that we call the *multi-spherical* space. In particular, we provide regularization tools imposing signal sparsity and signal smoothness to drastically reduce the number of measurements we need to probe the properties of this multi-spherical space.

**METHODS:** We represent the multi-spherical signal attenuation  $E(\mathbf{q}, \tau) = S(\mathbf{q}, \tau)/S_0$  at diffusion encoding position  $\mathbf{q}$  and diffusion time  $\tau$  using an orthogonal basis that allows to (1) represent any multi-spherical signal with a limited number of parameters  $\mathbf{c}$ , (2) impose smoothness in the signal space, (3) impose sparsity in the parameter space of the basis, and (4) respect the boundary conditions of the signal such that  $E(0, \tau) = 1$ . As we assume an infinitely short gradient pulse ( $\delta \rightarrow 0$ ), we follow Callaghan et al.’s description of time-dependent diffusion in pores and assume separability in the dependence of the dMRI signal to  $\mathbf{q}$  and  $\tau$  [1]. We represent the fitted signal attenuation using the cross-product between the spatial *Fourier* basis  $\Phi_i(\mathbf{q})$  [2] and temporal basis  $T_k(\tau)$  [3] such that we fit  $\hat{E}(\mathbf{q}, \tau; \mathbf{c}) = \sum_i^{N_q} \sum_k^{N_\tau} \mathbf{c}_{ik} \Phi_i(\mathbf{q}) T_k(\tau)$  with basis coefficients  $\mathbf{c}$  and  $N_q$  and  $N_\tau$  the number of spatial or temporal basis functions, respectively. The voxel-wise optimization is as follows:

$$\operatorname{argmin}_{\mathbf{c}} \underbrace{\iint [E(\mathbf{q}, \tau) - \hat{E}(\mathbf{q}, \tau; \mathbf{c})]^2 d\mathbf{q}d\tau}_{(1) \text{ Data Fidelity}} + \underbrace{\iint [\nabla^2 \hat{E}(\mathbf{q}, \tau; \mathbf{c})]^2 d\mathbf{q}d\tau}_{(2) \text{ Smoothness}} + \underbrace{\|\mathbf{c}\|_1}_{(3) \text{ Sparsity}}, \quad \text{subject to } \underbrace{\hat{E}(0, \tau; \mathbf{c}) = 1}_{(4) \text{ Signal Boundary}}.$$

Once the coefficients  $\mathbf{c}$  are known, we can directly estimate features of the multi-spherical *diffusion propagator*  $\hat{P}(\mathbf{R}, \tau; \mathbf{c})$  through our spatial basis’ Fourier properties [2]. We illustrate this by computing the *time-dependent* indices for the Return-To-Origin Probability (RTOP) and Mean Squared Displacement (MSD). We apply our method to an *in-vivo* spin-echo acquisition from a C57Bl6 wild-type mouse on an 11.7 Tesla Bruker scanner. An illustration of this scheme is given in the figure below, on the left. We acquire 35 different “shells” with one  $b_0$  each and a total of 400 DWIs using pulse duration  $\delta = 5ms$ . Over these shells, we measure five equispaced “ $\tau$ -shells”  $\Delta = \{10.8, 13.1, 15.4, 17.7, 20\}ms$  and seven approximately equispaced “gradient shells” between  $\{50 - 490\}mT/m$ . The voxels are of size  $100 \times 100 \times 500 \mu m$ . We manually created a brain mask and corrected the data from eddy currents and motion artifacts using FSL’s `eddy_correct`, drew a region of interest consisting of 173 voxels in the middle two slices in the corpus callosum and fitted our model.



**RESULTS:** Right next to the ROI image, we show representations of RTOP and MSD for three equispaced times points. Note that the times are not the measured ones but are interpolated from our fitted representation. As expected, we find a decrease in RTOP and an increase in MSD as time increases. Below, we show the effect of random subsampling between using 400 samples (blue) and 100 samples (red) on the fitting error (MSE), MSD and RTOP. We see that MSE is stable down to 200 samples, then suddenly increases at 100 samples. MSD is fairly stable under subsampling and RTOP becomes smaller, but remains positive as the number of samples reduces.

**DISCUSSION:** The MSE results show that our approach is able to effectively represent the multi-spherical diffusion signal of anisotropic white matter using only 200 random samples. The MSD increase and RTOP decrease over time corresponds to what we expect; as time increases, spins have more time to diffusive, covering more distance and reducing their chance of being found at the origin. The progress of these indices over time may be related to the packing of the underlying tissue [4]. When reducing samples MSD remains stable but RTOP becomes smaller, likely because the random subsampling takes samples away from the restricted diffusion direction, perpendicular to the axon axis. The basis also allows for extrapolation of  $\hat{E}(\mathbf{q}, \tau; \mathbf{c})$  before the shortest and after the longest measured  $\tau$ , but the prediction will become increasingly unreliable as the extrapolation is farther away from the measured space.

**CONCLUSION:** Our multi-spherical basis is the first of its kind in being specifically designed to represent the four-dimensional EAP and analyzing its properties. Our proposed regularization allows us to significantly reduce the number of measured samples, which may eventually bring multi-spherical diffusion MRI within the reach of clinical application.

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**References:** [1] Callaghan, Paul T. JMR Series A 113.1 (1995): 53-59. [2] Özarslan, et al. NeuroImage 78 (2013): 16-32. [3] Fick, et al. IPMI. Springer International Publishing, 2015. [4] Özarslan, et al. JMR 183.2 (2006): 315-323.