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Multi-Spherical MRI: **Breaking the Boundaries of Diffusion Time**

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informatics mathematics

Abstract: Effective representation of the diffusion signal's dependence on diffusion time is a sought-after, yet still unsolved challenge in diffusion MRI. We propose a functional basis approach that is specifically designed to represent the dMRI signal in this four-dimensional space - that we call the multi-spherical space. We provide regularization tools to drastically reduce the number of measurements we need to probe the properties of this multi-spherical space.

The Multi-Spherical Space

13000

10000

7500

5000

2500

1000 250

Diffusion restriction occurs when water diffusion is obstructed by tissue

Modeling the Multi-Spherical Space

Multi-Spherical MRI uses a separable Fourier Basis to



35 Shell Spin Echo Acquisition

 $b_{max} = 7814 s/mm^2$

boundaries. The amount of restriction is **time-dependent**, meaning that the observed diffusion coefficient will change for varying diffusion times [1].

Multi-Spherical MRI [2] describes diffusion restriction by fitting the diffusion signals over varying:

- Gradient strength (G)
- Gradient direction (g)
- Diffusion time (τ)

We call this four-dimensional space the Multi-Spherical Space.

We sampled this space on 35 different "shells", varying only g, for different **G** ranging from [50-490] mT/m and τ ranging from [9.1-18.3] ms.

reconstruct diffusion propagator P(**r**,τ;**c**) from signal attenuation $E(\mathbf{q},\tau;\mathbf{c})$, represented in coefficients **c**.

$$\hat{E}(\mathbf{q},\tau;\mathbf{c}) = \sum_{i}^{N_{\mathbf{q}}} \sum_{k}^{N_{\tau}} \mathbf{c}_{ik} \Phi_{i}(\mathbf{q}) T_{k}(\tau) \quad \stackrel{\text{FT}}{\iff} \quad \hat{P}(\mathbf{r},\tau;\mathbf{c}) = \sum_{i}^{N_{\mathbf{q}}} \sum_{k}^{N_{\tau}} \mathbf{c}_{ik} \Psi_{i}(\mathbf{r}) T_{k}(\tau)$$

 $\Psi_i(\mathbf{r}) = FT(\Phi_i(\mathbf{q}))$: 3D *Fourier* basis over **q** and displacement **r** [3]. $T_m(\tau)$: Exponential diffusion time basis over τ [4].

We constrain the fitting of **c** to respect boundary conditions of the signal and impose signal smoothness and sparsity:

$$\operatorname{argmin}_{\mathbf{c}} \underbrace{\int \int \left[E(\mathbf{q},\tau) - \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(3) \operatorname{Sparsity}} + \underbrace{\int \int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \left[\nabla^2 \hat{E}(\mathbf{q},\tau;\mathbf{c}) \right]^2 d\mathbf{q} d\tau}_{(2) \operatorname{Smoothness}} + \underbrace{\int \left[\nabla^2$$

Where smoothness is imposed using **closed-form Laplacian** regularization.

Once fitted, all q-space indices [3] can be estimated for any τ . As examples we show:

- Mean Squared Displacement (MSD), related to restriction
- Return-To-Origin Probability (RTOP), related to cellularity

In-Silico results 3

We study fitting performance under random subsampling by simulating the multi-spherical diffusion signal from gammadistributed axons using Camino [5].

- Combined sparsity and Laplacian regularization produces the lowest fitting error (left).
- Time-dependent MSD and RTOP follow expected trends MSD increasing and RTOP decreasing over time - down to about 200 DWIs (right two)



Application In-vivo Mouse Data

After eddy current correction, we chose an ROI of 173 voxels in Corpus Callosum. After subsampling we find

- Stable fitting errors from 400 down to 200 DWIs
- Expected trends for time-dependent MSD and RTOP



Number of Samples

10 12 14 16 Diffusion Time [ms]

-10 0 10 20 30 40 0.00000 0.00375 0.00750 0.01125 0.0150 RTOP [10⁻⁵mm⁻³

5 **Discussion and Conclusions**

- Multi-Spherical MRI allows for the characterization of diffusion restriction through time-dependent q-space indices.
- Through signal sparsity and smoothness, our approach can represent the multi-spherical signal with less samples, allowing more realistic acquisition schemes.
- Additional signal or propagator constraints can be conveniently included in the optimization.
- Through resampling, our approach could be used as a preprocessing for other methods studying properties of the multi-spherical space, e.g. axon packing [6].

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Diffusion Time [ms]

[1] Fieremans et al. Neurolmage 129 (2016): 414-427. [2] Fick et al. CD-MRI 2016. [3] Özarslan et al. Neurolmage 78 (2013): 16-32. [4] Fick, Rutger, et al. IPMI 2015. [5] Cook et al. ISMRM, 2006. [6] Novikov et al. 111.14 (2014): 5088-5093. References

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