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Diffusion MRI Signal Reconstruction with Continuity Constraint and Optimal Regularization

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Abstract

In diffusion MRI, the reconstruction of the full Ensemble Average Propagator (EAP) provides new insights in the diffusion process and the underlying microstructure. The reconstruction of the signal in the whole Q-space is still extremely challenging however. It requires very long acquisition protocols, and robust reconstruction to cope with the very low SNR at large b -values. Several reconstruction methods were proposed recently, among which the Spherical Polar Fourier (SPF) expansion, a promising basis for signal reconstruction. Yet the reconstruction in SPF is still subject to noise and discontinuity of the reconstruction. In this work, we present a method for the reconstruction of the diffusion attenuation in the whole Q-space, with a special focus on continuity and optimal regularization. We derive a modified Spherical Polar Fourier (mSPF) basis, orthonormal and compatible with SPF, for the reconstruction of a signal with continuity constraint. We also derive the expression of a Laplace regularization operator in the basis, together with a method based on generalized cross validation for the optimal choice of the parameter. Our method results in a noticeable dimension reduction as compared with SPF. Tested on synthetic and real data, the reconstruction with this method is more robust to noise and better preserves fiber directions and crossings.

Keywords: Diffusion MRI, Laplace Regularization, Q-space imaging,

1. Introduction

In diffusion MRI, the acquisition and reconstruction of the signal attenuation on the 3D Q-space allows reconstruction of the full probability of water molecules displacement, known as the ensemble average propagator (EAP). The radial and angular information contained in the EAP opens a wide range of applications, such as the definition of new biomarkers (Cluskey and Ramsden, 2001; Piven et al., 1997), or the characterization of axon diameters in the brain white matter (Assaf et al., 2008; Özarslan et al., 2011). The reconstruction techniques are based on the acquisition of diffusion-sensitized MR signals, with the acquisition sequence described in (Stejskal and Tanner, 1965), in which a pair of diffusion encoding magnetic field gradient are applied before and after the 180° pulse. There exists a Fourier relation between the diffusion attenuation $E(\mathbf{q})$

and the EAP

$$P(\mathbf{r}) = \int_{\mathbb{R}^3} E(\mathbf{q}) e^{-2i\pi\mathbf{q}\cdot\mathbf{r}} d^3\mathbf{q}, \quad (1)$$

where the wave vector \mathbf{q} is directly related to the applied magnetic field gradient pulse magnitude, direction, and duration.

The diffusion tensor (Basser et al., 1994) is the first model historically proposed to describe the EAP. Despite its wide acceptance into the research and clinical communities, this model restricts the diffusion EAP within the family of Gaussian probability density functions, and is limited for the description of complex tissue structure. Since then, several models and methods were described to extend the results of diffusion tensor, such as high angular resolution diffusion imaging (Tuch, 2004; Descoteaux et al., 2007; Aganj et al., 2010), or higher order tensors (Özarslan and Mareci, 2003). Beyond these approaches, it is possible to reconstruct the model-free diffusion propagator, through Diffusion Spectrum Imaging (DSI) (Wedeen et al., 2005), Diffusion Propagator Imaging (DPI) (Descoteaux et al., 2011), Diffusion Order Transform (Özarslan et al., 2011) or reconstruction in Spherical Polar Fourier (SPF)

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basis (Assemlal et al., 2009). DSI relies on the sampling of the diffusion signal on a regular Cartesian grid, and reconstructs the EAP through fast Fourier transform. The main limitation of DSI is its huge demand in acquisition time, and gradient pulse strength to fulfill the Nyquist conditions (Callaghan, 1991; Tuch, 2004). DPI (Descoteaux et al., 2011) is a more natural method to describe the diffusion signal by a basis of functions solution to the 3D Laplace equation by parts. Though this method enables analytical reconstruction of the diffusion propagator, it cannot represent the diffusion signal in the whole Q-space. Indeed, DPI represents the signal using the 3D Laplace equation by part (Descoteaux et al., 2011)

$$E(q \cdot \mathbf{u}) = \sum_{l,m} \left[\frac{c_{l,m}}{q^{l+1}} + d_{l,m} q^l \right] Y_{l,m}(\mathbf{u}), \quad (2)$$

where $Y_{l,m}$ is the real, spherical harmonic function. The basis functions in DPI diverge both for $q \rightarrow 0$ and $q \rightarrow \infty$.

The SPF basis functions instead have a radial profile with a Gaussian-like decay, which is similar to the commonly observed diffusion signal. Besides, it is possible to recover the EAP (Cheng et al., 2010b) and the Orientation Distribution Function (ODF) (Cheng et al., 2010a) from the coefficients of the signal reconstructed in the SPF basis. The SPF basis is thus a unique, model-free approach for the reconstruction of the full signal E , the estimation of EAP and its derived characteristics. It has been introduced in (Assemlal et al., 2009) together with a regularization method to overcome ill-condition of the estimation problem.

However, the definition of the 3D functions of the SPF basis makes use of the parameterization $\mathbf{q} \in \mathbb{R}^3 = q \cdot \mathbf{u}$, where $q \in \mathbb{R}^+$ and $\mathbf{u} \in \mathcal{S}^2$. Near the origin, the corresponding \mathbf{u} is not unique, and we show in Section 2.1 that continuity problems near the origin may arise if this parameterization is not used with care. Adding to that, the regularization method introduced in (Assemlal et al., 2009) is based on a pair of empirical angular and radial low-pass filters. This regularization method fully relies on the choice of the basis of functions. Besides, its implementation requires to tune two separate regularization weights, which is impractical.

In this work, we propose original and efficient solutions to solve all these important problems. First, we show that continuous functions reconstructed in the classical SPF basis lie in an affine subspace which has a significantly reduced dimension. This means that the signal diffusion could be represented in this subspace with less coefficients, leading to an estimation process

with less measurements than those required when representing the signal in the classical SPF basis. Second, we propose a modified SPF (mSPF) basis, an orthonormal basis for this affine subspace, compatible with the SPF basis, but with reduced dimension and intrinsic continuity near the origin. Thus, the signal reconstructed in the mSPF will satisfy the important continuity constraint. Third, a Laplace regularization functional in the mSPF basis is proposed and minimized for a robust reconstruction of the diffusion signal. The method is analytical and ensures a fast implementation and reconstruction with continuity constraints. The Generalized Cross Validation method is applied to find the unique optimal regularization weight between the regularity of the solution and the data fit. Finally, synthetic and real data are used to illustrate and validate the proposed method. In particular, better reconstruction results with exact continuity constraints are obtained and illustrated in crossing fibers regions.

2. Theory

The Spherical Polar Fourier basis was recently introduced in (Assemlal et al., 2009) to reconstruct the diffusion signal in the complete 3D space. The functions $B_{n,l,m}$ of this basis are defined as the product of a radial and an angular function

$$B_{n,l,m}(q \cdot \mathbf{u}) = R_n(q) Y_{l,m}(\mathbf{u}). \quad (3)$$

$Y_{l,m}$ is the real, symmetric spherical harmonic introduced in (Descoteaux et al., 2006), and the radial function R_n is reported below for the record

$$R_n(q) = \kappa_n L_n^{1/2} \left(\frac{q^2}{\zeta} \right) \exp \left(-\frac{q^2}{2\zeta} \right) \quad (4)$$

$$\kappa_n = \sqrt{\frac{2}{\zeta^{3/2}} \frac{n!}{\Gamma(n+3/2)}}, \quad (5)$$

where $L_n^{1/2}$ is the generalized Laguerre polynomial, and Γ is the Gamma function $\Gamma(z) = \int_0^\infty t^{z-1} e^{-t} dt$. We use $\Omega_{N,L}$ to denote the linear space of functions spanned by the truncated basis $\{B_{n,l,m}, n \leq N, l \leq L, |m| \leq l\}$. The choice of the scale factor ζ can be related to the mean diffusivity of the measured data. Several strategies were proposed in Assemlal et al. (2009), here and throughout the experiments, we retain

$$\zeta = \frac{1}{8\pi^2 \tau D}, \quad (6)$$

where τ is the diffusion time, and D is the mean diffusivity.

The SPF basis is orthonormal for the dot product

$$\langle f, g \rangle = \int_{\mathbb{R}^3} f(\mathbf{q})g(\mathbf{q})d^3\mathbf{q}. \quad (7)$$

The construction of this basis was motivated by the need for a complete orthonormal basis of antipodally symmetric and real functions. Besides, the radial profiles R_n have a quasi-Gaussian decay, so that even a low radial truncation order leads to an accurate reconstruction and extrapolation beyond the sampling domain of the diffusion weighted attenuation $E(\mathbf{q})$. From the reconstruction of the signal in this basis, we can estimate the EAP following Cheng et al. (2010b) and the ODF following Cheng et al. (2010a).

However, a closer look at the functions $B_{n,l,m}$ near the origin reveals rapid oscillations and a discontinuity. Moreover, by definition the value of the attenuation E is equal to 1 when $\mathbf{q} = \mathbf{0}$, but there is nothing in the SPF basis to impose this. In this work, we show that the subset of functions verifying these properties of continuity and imposed value at the origin is an affine subspace of $\Omega_{N,L}$. We propose mSPF, an orthonormal basis for this subspace, and we give for convenience the relation between this modified SPF (mSPF) basis and the SPF basis $B_{n,l,m}$ introduced in Assemlal et al. (2009).

We also derive the Laplacian regularization functional expression in the mSPF basis, for a robust reconstruction of the diffusion signal. Indeed, the dimension of the basis grows rapidly with the angular and radial orders, and diffusion weighted images have a very low SNR. For the reconstruction of a smooth function, the Laplacian operator is a commonly proposed approach for regularization (Descoteaux et al., 2007). We derive the calculation of the Laplacian operator in the mSPF basis. The method is analytical, which ensures a fast implementation and reconstruction.

In this section, we use indifferently a notation with three indices for the bases elements, such as $B_{n,l,m}$, or a notation with a simple index i , convenient for matrix notation. The link between both indexing systems is given by the functions $n(i)$, $l(i)$ and $m(i)$.

2.1. Continuity in $\Omega_{N,L}$

Theorem 1. *A function $f = \sum_{n,l,m} a_{n,l,m} B_{n,l,m}$ of the SPF basis is continuous if and only if*

$$\forall l > 0, \forall |m| \leq l, \sum_n a_{n,l,m} R_n(0) = 0. \quad (8)$$

The proof of this theorem is detailed in Appendix A. The linear constraint in Eq. 8 imposes that the polynomial part of $f_{l,m} = \sum_n a_{n,l,m} R_n$ has no constant term.

This linear constraint can be imposed while estimating the coefficients by constrained least squares estimation. Alternatively, we will derive a new basis of functions to span the subspace of continuous functions. This approach greatly simplifies the Laplace regularization formulation and implementation, as we show in the next section.

In addition to this continuity constraint, we emphasize that the diffusion attenuation signal is defined as $E(\mathbf{q}) = S(\mathbf{q})/S(\mathbf{0})$, and therefore should verify

$$f(\mathbf{0}) = 1. \quad (9)$$

The set of continuous functions in $\Omega_{N,L}$ verifying Eq. 9 is the solution of an inhomogeneous linear equation, and therefore is an affine subspace of $\Omega_{N,L}$. This affine space is fully characterized by an underlying linear subspace, and an origin. It is underlain by $\Omega_{N,L}^0$, the kernel of the associated homogeneous equation $f(\mathbf{0}) = 0$. As for the origin of the affine subspace, we can choose any solution of Eq. 9. For the sake of simplicity, we choose a simple Gaussian as the origin.

To sum up, any function $f \in \Omega_{N,L}$ verifying the continuity property, together with the property $f(\mathbf{0}) = 1$ can be expressed as

$$f(\mathbf{q}) = \exp\left(-\frac{\|\mathbf{q}\|^2}{2\zeta}\right) + \sum_{n,l,m} x_{n,l,m} C_{n,l,m}(\mathbf{q}), \quad (10)$$

where $\{C_{n,l,m}\}$ is a basis of $\Omega_{N,L}^0$, the subspace of continuous functions f in $\Omega_{N,L}$ verifying $f(\mathbf{0}) = 0$. In the remaining of this section, we give a construction for the orthogonal basis $\{C_{n,l,m}\}$.

We first construct a basis of radial functions $\{F_n\}$, expressed as $F_n(q) = \chi_n q^2 / \zeta P_n(q^2 / \zeta) \exp(-q^2 / 2\zeta)$. This verifies $F_n(0) = 0$; the polynomials P_n and the normalization constant χ_n are to determine, provided that the following orthogonality property is fulfilled

$$\langle F_n, F_p \rangle_{\mathbb{R}^3} = \int_0^\infty F_n(q) F_p(q) q^2 dq = \delta_{n,p}. \quad (11)$$

The substitution $u = q^2 / \zeta$ in Eq. 11 gives

$$\int_0^\infty \chi_n \chi_m \frac{\zeta^{3/2}}{2} P_n(u) P_p(u) u^{5/2} e^{-u} du = \delta_{n,p}. \quad (12)$$

The generalized Laguerre polynomial $L_n^{5/2}$ suits this orthogonality property. Finally the modified radial basis functions are

$$F_n(q) = \chi_n \frac{q^2}{\zeta} L_n^{5/2} \left(\frac{q^2}{\zeta} \right) e^{-q^2 / 2\zeta}, \quad (13)$$

205 and the normalization constant

$$\chi_n = \sqrt{\frac{2}{\zeta^{3/2}} \frac{n!}{\Gamma(n+7/2)}}. \quad (14)$$

206 The diffusion attenuation $E(\mathbf{q}) = \exp(-\|\mathbf{q}\|^2/2\zeta)$ is re-
207 constructed through the functions

$$C_{n,l,m}(\mathbf{q}) = F_n(\|\mathbf{q}\|) Y_{l,m} \left(\frac{\mathbf{q}}{\|\mathbf{q}\|} \right). \quad (15)$$

208 The family of functions $\{C_{n,l,m}, n = 0 \dots N-1, l =$
209 $0 \dots L, m = -l \dots l\}$ is the modified SPF (mSPF) basis,
210 an orthonormal basis of $\Omega_{N,L}^0$.

211 The coefficients $x_{n,l,m}$ are estimated by minimization
212 of the squared error criterion $\|\mathbf{y} - \mathbf{H}\mathbf{x}\|^2$, where \mathbf{y} is the
213 vector of observations $y_k = E(\mathbf{q}_k) = \exp(-\|\mathbf{q}_k\|^2/2\zeta)$
214 measured at wave vectors \mathbf{q}_k . The observation matrix
215 has entries $H_{k,i} = C_{n(i),l(i),m(i)}(\mathbf{q}_k)$.

216 This new space has a substantially reduced dimension:
217 $\dim(\Omega_{N,L}) = (N+1) \cdot L(L+1)/2$, whereas
218 $\dim(\Omega_{N,L}^0) = N \cdot L(L+1)/2$. This dimension reduction
219 comes from the two systems of linear constraints
220 of Eq. 8 ($L(L+1)/2 - 1$ equations), and Eq. 9 (1 equation).
221 As an example, when the angular truncation order
222 $L = 4$ is used, the reconstruction in $\Omega_{N,L}^0$ requires 15 less
223 coefficients, to represent the same signal. This simplifies
224 the implementation, reduces the demand in storage capacity,
225 and improves computational efficiency.

226 2.2. Link with the SPF basis

227 In this section we give the link between SPF and
228 mSPF bases. This relationship is useful as SPF (As-
229 semlal et al., 2009) is a now a state-of-the-art method in
230 diffusion MRI. We can therefore reconstruct the ensemble
231 average propagator (EAP) following Cheng et al. (2010b),
232 the orientation distribution function (ODF) following Cheng et al. (2010a),
233 or the apparent fiber population dispersion following Assemlal et al. (2011).
234 The SPF basis is built on Laguerre polynomials $L_n^{1/2}$ while
235 we use $L_n^{5/2}$ in this work. Using the recurrence relations
236 between Laguerre polynomials detailed in (Abramowitz
237 and Stegun, 1970, p. 783), we have:

$$F_n(q) = \sum_{i=0}^n \frac{3\chi_n}{2\kappa_i} R_i(q) - \frac{(n+1)\chi_n}{\kappa_{n+1}} R_{n+1}(q). \quad (16)$$

238 If the function $f(\mathbf{q}) = E(\mathbf{q}) = \exp(-\|\mathbf{q}\|^2/2\zeta)$ is expressed
239 in this basis, $f(\mathbf{q}) = \sum x_{n,l,m} C_{n,l,m}(\mathbf{q})$, then the
240 coefficients $a_{n,l,m}$ of E in the SPF basis are obtained by
241

242 $\mathbf{a} = \mathbf{M}\mathbf{x} + \mathbf{a}^0$, where

$$M_{ij} = \delta_{l(i),l(j)} \delta_{m(i),m(j)} \cdot \begin{cases} \frac{3\chi_{n(j)}}{2\kappa_{n(i)}} & n(i) \leq n(j) \\ -\frac{n(i)\chi_{n(j)}}{\kappa_{n(i)}} & n(i) = n(j) + 1 \\ 0 & n(i) > n(j) + 1 \end{cases}$$

243 and $\mathbf{a}^0 = [\sqrt{4\pi}/\kappa_0 \ 0 \ 0 \ \dots]^T$, as $\exp(-\|\mathbf{q}\|^2/2\zeta) =$
244 $\sqrt{4\pi}/\kappa_0 B_{0,0,0}(\mathbf{q})$.

245 \mathbf{M} is the change-of-basis matrix from mSPF to SPF,
246 two orthonormal bases. Therefore, this matrix is orthog-
247 onal: the orthogonal projection of any function in $\Omega_{N,L}$,
248 represented by its coefficients \mathbf{a} in the SPF basis, onto
249 the subspace $\Omega_{N,L}^0$ has coefficients $\mathbf{x} = \mathbf{M}^T \mathbf{a}$.

250 2.3. Laplace regularization in the mSPF basis

251 In this section, we propose to introduce a regulariza-
252 tion term in the fitting procedure. We choose as a regu-
253 larization functional

$$U(\mathbf{x}) = \int_{\mathbb{R}^3} |\Delta E_{\mathbf{x}}(\mathbf{q})|^2 d^3 \mathbf{q}, \quad (17)$$

254 where $E_{\mathbf{x}}(\mathbf{q}) = \exp(-\|\mathbf{q}_k\|^2/2\zeta) + \sum_i x_i C_i(\mathbf{q})$ is the recon-
255 structed signal. This continuous operator is rotational
256 invariant, and independent on the choice of a specific
257 basis. Besides, the Laplace operator was already ap-
258 plied successfully for several applications ranging from
259 natural image denoising (You and Kaveh, 2000; Chan
260 and Shen, 2005) to diffusion MRI analysis (Descoteaux
261 et al., 2007; Koay et al., 2009; Descoteaux et al., 2010).

262 We minimize $\|\mathbf{y} - \mathbf{H}\mathbf{x}\|^2 + \lambda U(\mathbf{x})$, where the observa-
263 tions are $y_k = E(\mathbf{q}_k) = \exp(-\|\mathbf{q}_k\|^2/2\zeta)$ and \mathbf{H} is the ob-
264 servation matrix. In this section, we write the Laplace
265 penalization as a quadratic form

$$U(\mathbf{x}) = (\mathbf{x} - \mathbf{x}_0)^T \mathbf{\Lambda} (\mathbf{x} - \mathbf{x}_0) + U_0. \quad (18)$$

266 Hence the penalized least squares has a unique mini-
267 mum

$$\hat{\mathbf{x}} = \mathbf{x}_0 + (\mathbf{H}^T \mathbf{H} + \lambda \mathbf{\Lambda})^{-1} (\mathbf{y} - \mathbf{H}\mathbf{x}_0). \quad (19)$$

268 In what follows, we give explicit directions how to com-
269 pute the matrix $\mathbf{\Lambda}$ and the vector \mathbf{x}_0 .

270 When $E_{\mathbf{x}}(\mathbf{q}) = \exp(-\|\mathbf{q}_k\|^2/2\zeta)$ is expressed in the
271 mSPF basis with coefficients x_i ,

$$\begin{aligned} U(\mathbf{x}) &= \int_{\mathbb{R}^3} \left(\sum_i x_i \Delta C_i(\mathbf{q}) + \Delta e^{-\|\mathbf{q}_k\|^2/2\zeta} \right)^2 d^3 \mathbf{q} \quad (20) \\ &= \sum_i \sum_j x_i x_j \int_{\mathbb{R}^3} \Delta C_i(\mathbf{q}) \cdot \Delta C_j(\mathbf{q}) d^3 \mathbf{q} \\ &\quad + 2 \sum_i x_i \int_{\mathbb{R}^3} \Delta C_i(\mathbf{q}) \cdot \Delta e^{-\|\mathbf{q}_k\|^2/2\zeta} d^3 \mathbf{q} \\ &\quad + \dots \end{aligned} \quad (21)$$

272 The constant term is discarded since it plays no role in
 273 the minimization. Thus we have the quadratic form of
 274 Eq. 18, where

$$\Lambda_{ij} = \int_{\mathbb{R}^3} \Delta C_i(\mathbf{q}) \cdot \Delta C_j(\mathbf{q}) d^3 \mathbf{q}, \quad (22)$$

275 and $\mathbf{x}_0 = \Lambda^{-1} \mathbf{v}$, with

$$v_i = \int_{\mathbb{R}^3} \Delta C_i(\mathbf{q}) \cdot \Delta e^{-\|\mathbf{q}_k\|^2/2\zeta} d^3 \mathbf{q} \quad (23)$$

276 The Laplace operator Δ can be written in spherical
 277 coordinates, with the Laplace-Beltrami operator Δ_b ,

$$\begin{aligned} \Delta C_{n,l,m}(q \mathbf{u}) = \chi_n \left(\frac{1}{q^2} \frac{\partial}{\partial q} (q^2 F'_n(q)) Y_{l,m}(\mathbf{u}) \right. \\ \left. + \frac{F_n(q)}{q^2} \Delta_b Y_{l,m}(\mathbf{u}) \right) \end{aligned} \quad (24)$$

278 Since the spherical harmonics are eigenfunctions of the
 279 Laplace-Beltrami operator with eigenvalue $-l(l+1)$, we
 280 have

$$\Delta C_{n,l,m}(q \mathbf{u}) = \chi_n \left(F''_n(q) + 2 \frac{F'_n(q)}{q} - \frac{l(l+1)F_n(q)}{q^2} \right) Y_{l,m}(\mathbf{u}) \quad (25)$$

281 As the spherical harmonics form an orthonormal basis
 282 for the canonical dot product on \mathcal{S}^2 , the entries of the
 283 matrix Λ are

$$\Lambda_{i,j} = \delta_{l(i),l(j)} \delta_{m(i),m(j)} \int_0^\infty h_i(q) h_j(q) dq, \quad (26)$$

284 where

$$h_i = \chi_{n(i)} \left(q F''_{n(i)} + 2 F'_{n(i)} - \frac{l(i)(l(i)+1)}{q} F_{n(i)} \right). \quad (27)$$

285 Similarly, the vector \mathbf{v} has entries

$$v_i = \delta_{l(i),0} \delta_{m(i),0} \int_0^\infty h_i(q) \cdot \left(\frac{q^3}{\zeta^2} - \frac{3q}{\zeta} \right) \exp\left(-\frac{q^2}{2\zeta}\right) dq. \quad (28)$$

286 The computation of the integrals in Eq. B.1 and 28 is
 287 analytical and needs no numerical integration. It is de-
 288 scribed in details in Appendix B.

289 3. Material and methods

290 3.1. Optimal regularization parameters

291 We adopted the Generalized Cross Validation (GCV)
 292 algorithm (Craven and Wahba, 1985) to find the regu-
 293 larization weight λ which guarantees the best balance
 294 between the smoothness of the reconstruction, and the

295 data fit. This algorithm, as well as the L-curve method
 296 (Hansen, 2000), have already been applied successfully
 297 for other applications in Q-ball diffusion MRI (Koay
 298 et al., 2009; Descoteaux et al., 2010, 2007). The GCV
 299 method has the major advantage to be generalizable to
 300 the situation where there is more than one λ parameter
 301 to optimize. It is the case in (Assemlal et al., 2009),
 302 where there are two regularization matrices \mathbf{N} and \mathbf{L} ,
 303 which act respectively as radial and angular low-pass
 304 filters, with corresponding weights λ_N and λ_L .

305 The GCV method is based on a one-fold cross valida-
 306 tion: among K samples, we use $K - 1$ samples to fit the
 307 model parameters, and predict the K -th left-apart sam-
 308 ple. The process is repeated K times, and the mean pre-
 309 diction error is the value we want to minimize. Fortu-
 310 nately, the mean prediction error, called the GCV func-
 311 tion, has a simple expression

$$\text{GCV}(\lambda; \mathbf{y}) = \frac{\|\mathbf{y} - \hat{\mathbf{y}}_\lambda\|^2}{K - \text{Tr}(\mathbf{S}_\lambda)}, \quad (29)$$

312 which makes this method very efficient. The matrix
 313 $\mathbf{S}_\lambda = \mathbf{H}(\mathbf{H}^T \mathbf{H} + \lambda \Lambda)^{-1} \mathbf{H}^T$ is the smoother matrix, and
 314 $\hat{\mathbf{y}}_\lambda = \mathbf{S}_\lambda \mathbf{y}$. With the GCV method, it is possible to
 315 adapt the regularization parameters to the data. How-
 316 ever, there is no analytical solution for the minimization
 317 of the GCV function and for computational efficiency,
 318 we compute the optimal λ parameters once. This choice
 319 is validated in the next section, and results show it is
 320 indeed a good compromise.

321 3.2. Synthetic and real data

322 We simulate diffusion weighted measurements with a
 323 multi-compartment Gaussian model

$$E(\mathbf{q}) = \sum_{p=1}^P \omega_p \exp(-2\pi \tau \mathbf{q}^T \mathbf{D}_p \mathbf{q}), \quad (30)$$

324 where $P \in 1, 2, 3$ is the number of compartments, ω_p is
 325 the relative compartment size and \mathbf{D}_p the corresponding
 326 diffusion tensor. The diffusion weighted signal is cor-
 327 rupted by Rician noise, with controlled variance param-
 328 eter σ . Using this diffusion model locally, we created
 329 a synthetic diffusion field simulating a sin-shaped and a
 330 straight fiber, crossing each other at 90° .

331 The wave vectors \mathbf{q}_k for synthesis are arranged on 3
 332 shells, with the strategy recently proposed in (Caruyer
 333 et al., 2011a,b). In short, this method is a generaliza-
 334 tion of the electrostatic repulsion, introduced in (Jones
 335 et al., 1999) for single Q-shell experiment design, to the
 336 multiple Q-shell case.

337 The experiments on real data were carried out on the
 338 publicly available phantom (Poupon et al., 2008; Fillard

339 et al., 2011) which served as the data for a tractography
 340 contest, held at the DMFC MICCAI workshop, London
 341 (2009). The diffusion signal was sampled on 3 Q-shells,
 342 with b -values ranging from 650 to 2000 s · mm⁻², and
 343 64 directions per shell.

344 For the experiments, we compare the diffusion signal,
 345 the ensemble average propagator (EAP) reconstructed
 346 from the SPF coefficients by the method in (Cheng et al.,
 347 2010b), and the orientation distribution function (ODF)
 348 reconstructed in constant solid angle, implementing the
 349 technique in (Cheng et al., 2010a).

350 3.3. Exact and empirical continuity constraints

351 We presented in Section 2.1 a linear constraint to im-
 352 pose the continuity of the reconstructed signal. An al-
 353 ternate solution proposed in (Cheng et al., 2010b) is to
 354 artificially add P virtual data points $\mathbf{q}_k, k = K + 1 \dots P$
 355 close to zero, verifying $E(\mathbf{q}_k) = 1$. As P goes to infin-
 356 ity, it is possible to show that the solution of this system
 357 tends to the exact solution (see Golub and Van Loan,
 358 1983, pp. 410–412). We study the convergence of this
 359 empirical continuity approach. As a measure of dis-
 360 continuity of the reconstructed signal \hat{E} about $\mathbf{0}$, we
 361 define $d(\hat{E})$ the difference between extremal values of
 362 the set $\{\lim_{q \rightarrow 0^+} \hat{E}(q\mathbf{u}), \mathbf{u} \in \mathcal{S}^2\}$. We also compare the
 363 relative difference between the solution \mathbf{c}_{AC} of the least
 364 squares problem with analytical constraint, and the so-
 365 lution $\mathbf{c}_{EC}(P)$ of the system with empirical constraint
 366 with P virtual measurements.

367 4. Results and discussion

368 4.1. Continuity constraint

369 We compare the solution \mathbf{c}_{AC} and $\mathbf{c}_{EC}(P)$, for a single
 370 Gaussian distribution. To focus on the continuity
 371 constraint, we do not impose any other kind of regular-
 372 ization. The signal is corrupted by Rician noise, with
 373 corresponding SNR = 25. An example of signal and its
 374 reconstruction is reported on Fig. 1.

375 We evaluate the difference of the signal reconstructed
 376 with exact continuity constraint and with empirical con-
 377 straint. We plot on Fig. 2 the relative squared difference
 378 between the coefficients estimated with a strict contin-
 379 uity constraint, $\hat{\mathbf{c}}_{AC}$, and the coefficients estimated with
 380 an empirical continuity constraint, $\hat{\mathbf{c}}_{EC}$. The conver-
 381 gence is pretty fast, and $P = 60$ virtual measurements
 382 give good results. This confirms the intuition in (Cheng
 383 et al., 2010b); however the minimum number of virtual
 384 measurements P for an acceptable accuracy heavily de-
 385 pends on the angular order of the SPF basis, as reported

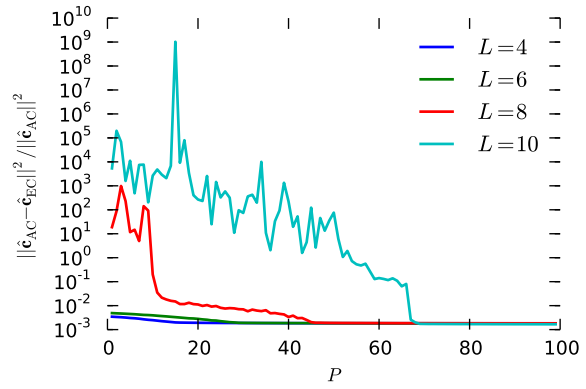


Figure 2: Relative difference between reconstruction with a strict continuity constraint, and reconstruction with a loose continuity constraint. Results on a synthetic Gaussian diffusion signal, from $K = 150$ measurements on 3 Q-shells, plus P virtual measurements at $\mathbf{q} = \mathbf{0}$, for various angular orders L of the SPF basis. Depending on the radial order, the number of additional measurements needed for an accurate reconstruction may become huge, and really impractical.

386 on Fig. 2. This makes this empirical solution imprac-
 387 tical. Besides, discontinuity is not strictly imposed: as
 388 experimented and reported on Fig. 3, the value of $d(\hat{E})$
 389 remains unacceptably high while we impose the value
 390 on $P = 150$ virtual measurements.

391 4.2. Laplace regularization

392 Laplace regularization was implemented in the mSPF
 393 basis, and we compare it with separate Laplace-
 394 Beltrami and radial low-pass filter, proposed in (Assem-
 395 lal et al., 2009). The GCV function is significantly lower
 396 for the optimal Laplace regularization (Table 1). This
 397 result suggests that Laplace regularization is more suit-
 398 able than separate Laplace-Beltrami and radial low-pass
 399 filtering. Furthermore, the optimal λ_Λ parameter does
 400 not vary much from one diffusion model to another. We
 401 can therefore select a unique λ_Λ parameter for the regu-
 402 larization of a whole volume.

403 The regularization also impacts on the extrapolation
 404 capacity of the method. Hardware limitations often re-
 405 strict the sampling to a bounded region in the Q-space.
 406 Increasing the radial order of the mSPF basis will allow
 407 better signal reconstruction within the sampled area of
 408 the Q-space. It might however introduce undesirable os-
 409 cillations outside this area, as reported on Fig. 4, where
 410 the radial truncation order was set to $N = 5$. Adding
 411 a regularization constraint greatly improves the extrap-
 412 olation of the diffusion signal. Laplace regularization
 413 performs slightly better in this task, though a more com-
 414 plete study, involving real data and outside the scope of
 415 this paper, should be carried out to further validate this.

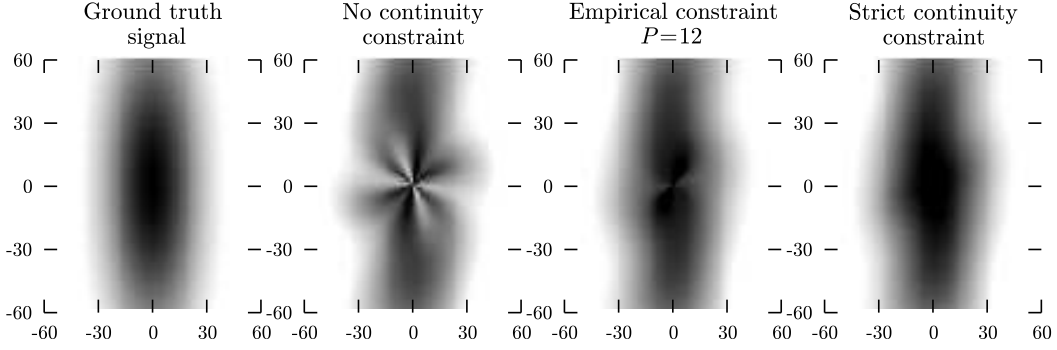


Figure 1: Diffusion signal corresponding to a single fiber oriented along the x -axis, reconstructed from 120 samples in the Q -space. The signal is shown on the (q_x, q_y) -plane, and the grey levels correspond to signal range from 0.0 (white) to 1.0 (black). q values are understood in mm^{-1} . This illustrates the discontinuity at the origin inherent to the SPF basis, and how the reconstruction in mSPF solves this problem.

	1 fiber	2 fibers, 90°	2 fibers, 60°
$(\lambda_L^0, \lambda_N^0)$	$(4.0 \cdot 10^{-7}, 8.1 \cdot 10^{-9})$	$(3.2 \cdot 10^{-7}, 1.2 \cdot 10^{-8})$	$(5.1 \cdot 10^{-8}, 5.5 \cdot 10^{-8})$
$\text{GCV}_{L,N}^0$	$5.7 \cdot 10^{-1}$	$3.4 \cdot 10^{-1}$	$4.8 \cdot 10^{-1}$
λ_Λ^0	$1.6 \cdot 10^{-1}$	$1.7 \cdot 10^{-1}$	$2.4 \cdot 10^{-1}$
GCV_Λ^0	$5.3 \cdot 10^{-1}$	$3.1 \cdot 10^{-1}$	$4.2 \cdot 10^{-1}$

Table 1: Optimal λ parameters and corresponding GCV minimum, for various synthetic diffusion models. The sampling consists in 200 diffusion weighted measurements on 3 Q -shells, with a max b -value of $3000\text{s} \cdot \text{mm}^{-2}$. Radial and angular orders were set to 5 and 6, respectively. 1st row: separate Laplace-Beltrami and radial low-pass filter smoothing, 2nd row: Laplace regularization.

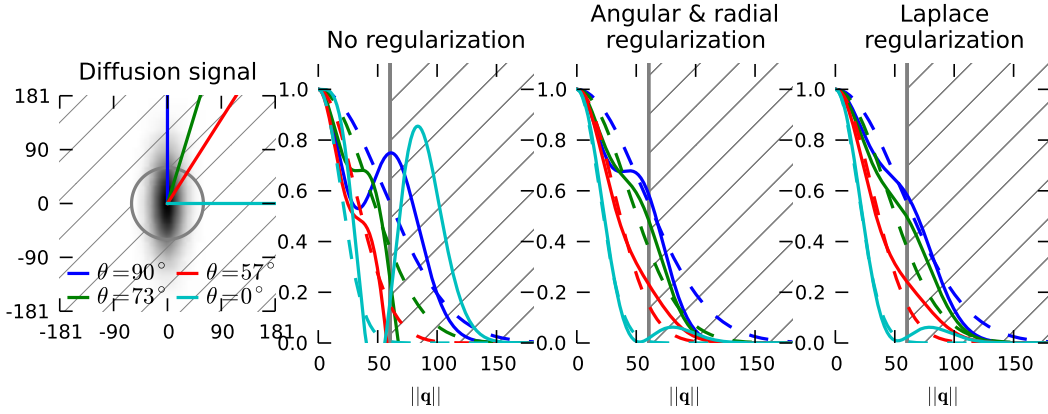


Figure 4: Reconstruction and extrapolation of a diffusion signal, for a Gaussian diffusion model, from 120 measurements on 3 Q -shells. We plot the reconstructed (solid lines) and ground truth (dashed lines) radial profiles of the signal on selected lines in the Q -space. The maximum q value of the sampling scheme was set to 60mm^{-1} , the hatched area represents the no-sample area. We compare the reconstruction without regularization, with separate Laplace-Beltrami and radial filter, and with Laplace regularization. Laplace regularization performs better in smoothing radial profiles, and we avoid oscillations outside the sampling area.

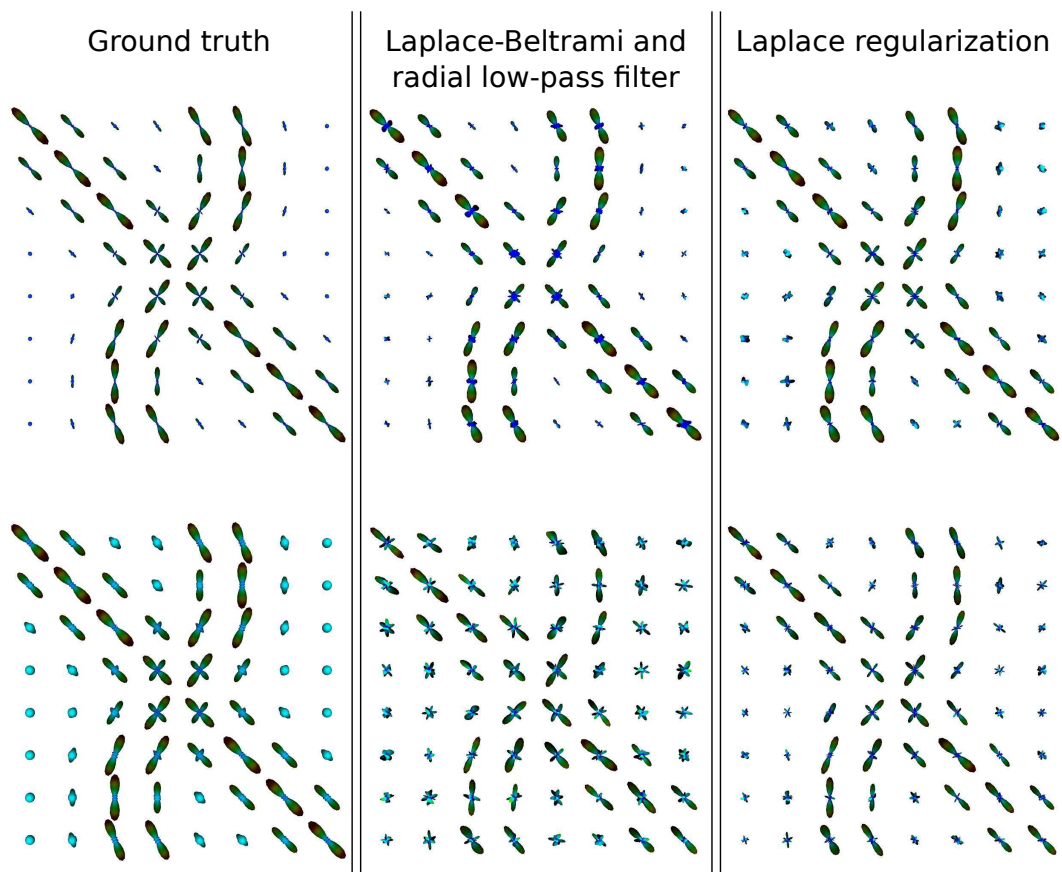


Figure 5: Reconstruction of a diffusion propagator field, from 120 measurements on 3 shells (max b -value was $3000\text{s} \cdot \text{mm}^{-2}$). We compare the diffusion EAP profile (top row) $P(r_0\mathbf{u})$, for $r_0 = 15\mu\text{m}$, and the diffusion ODF $\psi(\mathbf{u})$ (bottom row). Fiber crossing are better resolved with Laplace regularization, and isotropic regions are smoother.

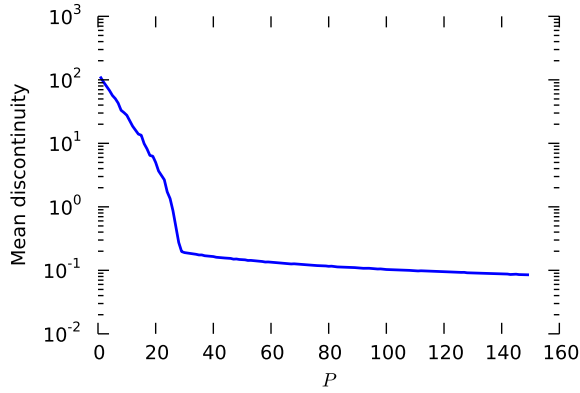


Figure 3: Discontinuity, measured about the origin, of a synthetic Gaussian diffusion signal, reconstructed from K measurements on 3 Q-shells, plus P virtual measurements at $\mathbf{q} = \mathbf{0}$. The discontinuity remains very high, even for a large number of additional, virtual measurements ($P = 150$).

We also compare the reconstruction with both regularization constraints on our synthetic diffusion field in Fig. 5. Laplace regularization performs better in crossing fiber regions, and the results show better directional coherence. Besides, in isotropic regions, the reconstructed ODFs have a smoother profile than with separate Laplace-Beltrami and radial filtering.

Similar results are obtained on the real data experiment, depicted on Fig. 6. We have overlaid the ground truth fiber orientations, as provided by Fillard et al. (2011). The reconstruction results with optimal Laplace regularization show slightly sharper EAP and ODF profiles. We acknowledge that the reconstruction of this dataset was very challenging, due to the low anisotropy of the signal.

5. Conclusions

We have proposed a novel orthonormal basis for the reconstruction of the diffusion signal in the complete 3D Q-space, based on Gaussian-Laguerre functions. This new method enables the reconstruction of a continuous signal, with known value at the origin. This mathematical constraint results in a dimension reduction with respect to the SPF basis, and a better reconstruction of the diffusion signal at the same sampling rate. This also greatly simplifies the reconstruction method, and reduces the associated computational cost as the continuity constraint is naturally imposed. The mSPF basis is presented with its linear relation to the SPF basis for convenience, so that the methods of SPF imaging directly transpose to mSPF.

We also derive a regularization functional based on the Laplace operator, together with its analytical expression in the mSPF basis. This is shown to be mathematically and practically better than separate Laplace-Beltrami and radial low-pass filtering. The experiments on simulations and real data show good results, for the reconstruction and extrapolation of the radial profile. The angular profile reconstruction is more robust to noise, and better detection of fiber crossing is reported.

Appendix A. Necessary and sufficient condition for the continuity

In this appendix, we give a proof of Theorem 1, relative to the continuity of a function $f \in \Omega_{N,L}$, expressed as a sum of SPF functions.

Appendix A.1. Necessary condition

A necessary condition for the continuity of the function f is that the restriction of f to any line in \mathbb{R}^3 must be continuous about 0. For $\mathbf{u} \in S^2$ and $q \in \mathbb{R}$, we note $f_{\mathbf{u}}(q) = f(q\mathbf{u})$ the restriction of f to the line of direction \mathbf{u} .

$$\lim_{q \rightarrow 0^+} f_{\mathbf{u}}(q) = f_{\mathbf{u}}(0) = f(\mathbf{0}) \quad (\text{A.1})$$

$$\Rightarrow \sum_{n,l,m} a_{n,l,m} R_n(0) Y_{l,m}(\mathbf{u}) = f(\mathbf{0}) \quad (\text{A.2})$$

$$\Rightarrow \sum_{l,m} \left(\sum_{n=0}^N a_{n,l,m} R_n(0) \right) Y_{l,m}(\mathbf{u}) = f(\mathbf{0}). \quad (\text{A.3})$$

Eq. A.3 must hold for any $\mathbf{u} \in S^2$. The left hand part is written as a sum of spherical harmonic functions, while the right hand part does not depend on \mathbf{u} .

The only constant function in the Spherical Harmonics basis is $Y_{0,0}$. Hence all the spherical harmonic coefficients in Eq. A.3 must be zero, except for $l = m = 0$.

$$\forall l > 0, \forall m \text{ s. t. } |m| \leq l, \sum_{n=0}^N a_{n,l,m} R_n(0) = 0 \quad (\text{A.4})$$

Appendix A.2. Sufficient condition

Now we show that if the necessary condition in Eq. A.4 is met, then the function f is continuous about $\mathbf{0}$. We can write f as a finite sum of functions $f_{l,m} = \sum_n a_{n,l,m} B_{n,l,m}$. If we prove the continuity of $f_{l,m}$, for any $0 \leq l \leq L$ and any $-l \leq m \leq l$, then by linearity we prove the continuity of f .

The continuity of f_{00} is direct, as the Gauss-Laguerre functions are continuous and Y_{00} is constant. Next, we

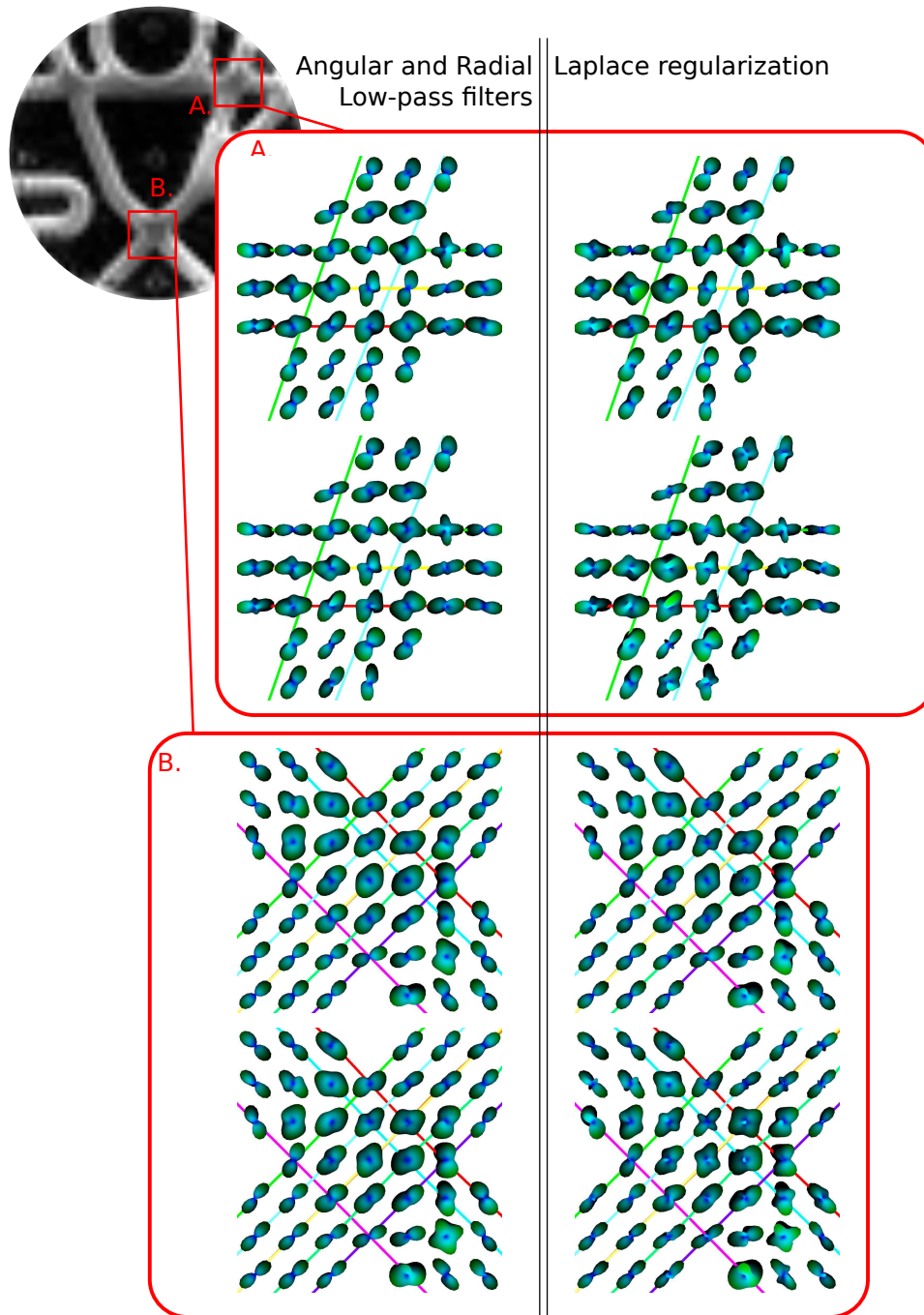


Figure 6: Diffusion ODF and EAP profiles reconstructed from the diffusion MRI data of the fiber cup. Zooms on crossing regions A and B are displayed. Within each block: EAP profile $P(r_0\mathbf{u})$, for $r_0 = 17\mu\text{m}$ (top row) and diffusion ODF reconstructed in constant solid angle $\psi(\mathbf{u})$ (bottom row). The left column corresponds to a reconstruction with separate angular and radial low-pass filters, while the right column is the reconstruction with Laplace regularization. The EAP profiles and ODF reconstructed with Laplace regularization are somehow sharper in crossing regions.

481 consider $0 < l \leq L$ and $-l \leq m \leq l$. By continuity of R_n , 502
 482 we can write $\forall \epsilon' > 0, \exists \alpha > 0$ such that

$$|q| < \alpha \Rightarrow \left\| \sum_{n=0}^N a_{n,l,m} R_n(q) \right\| < \epsilon'. \quad (\text{A.5})$$

483 This is true for $\epsilon' = \epsilon / \|Y_{l,m}\|_\infty$. Besides,

$$\forall \mathbf{u} \in S^2, \frac{|Y_{l,m}(\mathbf{u})|}{\|Y_{l,m}\|_\infty} \leq 1, \quad (\text{A.6})$$

484 hence

$$\begin{aligned} \forall \mathbf{u} \in S^2, |q| < \alpha \Rightarrow \\ \left\| \sum_{n=0}^N a_{n,l,m} R_n(q) \right\| \frac{\|Y_{l,m}(\mathbf{u})\|}{\|Y_{l,m}\|_\infty} < \frac{\epsilon}{\|Y_{l,m}\|_\infty}. \end{aligned} \quad (\text{A.7})$$

$$(\text{A.8})$$

485 This proves the continuity of $f_{l,m}$ about $\mathbf{0}$, and by linear-
 486 ity the continuity of f .

487 Appendix B. Laplace regularization matrix

488 In this appendix, we derive the general expression of
 489 the Laplace regularization matrix Λ in the mSPF basis.
 490 The entries of the matrix Λ are

$$\Lambda_{i,j} = \delta_{l(i),l(j)} \delta_{m(i),m(j)} \int_0^\infty h_i(q) h_j(q) dq, \quad (\text{B.1})$$

491 where

$$h_i = \chi_{n(i)} \left(q F''_{n(i)} + 2F'_{n(i)} - \frac{l(i)(l(i)+1)}{q} F_{n(i)} \right). \quad (\text{B.2})$$

492 The function h_i can be written as

$$h_i(q) = \chi_{n(i)} \frac{q}{\zeta} \exp\left(-\frac{q^2}{2\zeta}\right) G_{n(i),l(i)}\left(\frac{q^2}{\zeta}\right), \quad (\text{B.3})$$

493 where $G_{n,l} = \sum_k g_k^{n,l} X^k$ is a polynomial. It is hard
 494 to express the coefficients $g_k^{n,l}$ in a compact form. In-
 495 stead of manually deriving these coefficients, we com-
 496 pute them using polynomial algebra facilities, provided
 497 in the SciPy library (Jones et al., 2001) in PythonTM.
 498 The coefficients $g_k^{n,l}$ are algebraically computed on de-
 499 mand as it involves simple operation on polynomials:
 500 derivation and addition. The first coefficients are tabu-
 501 lated here for convenience.

k	$G_{0,l}$	$G_{1,l}$	$G_{2,l}$
0	$6 - l(l+1)$	$7(3 - l(l+1)/2)$	$15.75(3 - l(l+1)/2)$
1	-7	$-44.5 + l(l+1)$	$-145.125 + 4.5l(l+1)$
2	1	14.5	$78.375 - l(l+1)/2$
3		-1	-12
4			0.5

Hence the integrand $h_i(q)h_j(q)$ can be written as

$$h_i(q)h_j(q) = \frac{\chi_{n(i)}\chi_{n(j)}}{\zeta} \exp\left(-\frac{q^2}{\zeta}\right) T_{i,j}\left(\frac{q^2}{\zeta}\right) \quad (\text{B.4})$$

503 where $T_{i,j}(X)$ is the polynomial $XG_{n(i),l(i)}(X)G_{n(j),l(j)}(X)$.
 504 The coefficients $a_k^{i,j}$ of $T_{i,j}$ are simply obtained from the
 505 coefficients of $G_{n(i),l(i)}$ and $G_{n(j),l(j)}$. Therefore, the en-
 506 tries of the regularization matrix are

$$\begin{aligned} \Lambda_{i,j} &= \frac{\chi_{n(i)}\chi_{n(j)}}{\zeta} \sum_{k=0}^d a_k^{i,j} \int_0^\infty \exp(-q^2/\zeta) \left(\frac{q^2}{\zeta}\right)^k dq \\ &= \frac{\chi_{n(i)}\chi_{n(j)}}{2\sqrt{\zeta}} \sum_{k=0}^d a_k^{i,j} \Gamma(k+1/2). \end{aligned} \quad (\text{B.5})$$

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