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Decoupling of Imaging and Diffusion Gradients in DTI

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***Abstract*—The linear algebra framework for MR–DTI introduced in the companion manuscript is expanded to a normed space structure. The issues originating from the inclusion of imaging gradients into the MR-DTI model to obtain a fuller description are tackled by the optimization theory. A sample independent, geometric objective function based on matrix norms is defined. A parametrization of feasible diffusion gradient sets is presented so that the optimization can be carried out by making sure that the coefficient matrix for the estimation equations has full rank. The experiments are carried with the optimal gradient schemes. There are significant improvements in terms of model matching error and the lowering of the difference between eigenvalues calculated with or without the imaging gradients.**

I. INTRODUCTION

In the companion paper [1] analytic expressions for different components for the estimation of the diffusion matrix, D (represented by $d \in \mathbb{R}^6$) in MR-DTI, are given as functions of the diffusion gradient sets, g, and imaging gradients:

$$\gamma^2 \left(b\, V_g + V_{C(g)} + V_I\right) d = p. \tag{1}$$

Here V_I, is for imaging gradients, $V_D \doteq b\, V_g$ for diffusion gradients and $V_{C(g)}$ represents the cross terms.

In this manuscript, an optimization problem in the diffusion gradient space is tackled to decouple the effects of the imaging and diffusion gradients. This is accomplished in a geometric and sample independent setup.

II. DEFINITION OF THE OPTIMIZATION PROBLEM

A. Main Objective

The objective is to minimize the difference between the eigenvalues estimated with and without the incorporation of the imaging gradients. The main idea originates from seeing (1) as a matrix perturbation of V_D, $V = V_D + (V_I + V_C)$:

Theorem 1 ([2]): Let $A \in \mathbb{R}^{m\times m}$ be nonsingular and let $\tilde{A} = A + E$ be a perturbation of A. For $p \in \mathbb{R}^m$ let $A\, d = p$ and let $\|\cdot\|$ be an operator norm. If there is a vector $\tilde{d}$ such that $\tilde{A}\, \tilde{d} = p$, then

$$\frac{\|d - \tilde{d}\|}{\|\tilde{d}\|} \leq \|A^{-1}E\|. \tag{2}$$

The theorem provides in (2) an upper bound on the relative error between the entries of the diffusion matrices obtained from $V\, \tilde{d} = p$ and $V_D\, d = p$. The bound is

$$\frac{\|d - \tilde{d}\|}{\|\tilde{d}\|} \leq \|V_D^{-1}(V_I + V_C)\|. \tag{3}$$

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The appropriate norm to adopt for Theorem 1 is the Frobenius norm because for a symmetric matrix D with its representation $d \in \mathbb{R}^6$, there is a relationship with the eigenvalues:

$$\|d\|_R \doteq \sqrt{d_1^2 + d_2^2 + d_3^2 + 2(d_4^2 + d_5^2 + d_6^2)} = \left[\sum_i^3 \lambda_i^2\right]^{\frac{1}{2}}. \tag{4}$$

The compatible operator Frobenius norm is given by

$$\|V\|_R = \|R^{\frac{1}{2}}\, V\, R^{-\frac{1}{2}}\|_2 = \sqrt{r_\sigma(R^{-\frac{1}{2}}\, V^T\, R V\, R^{-\frac{1}{2}})} \tag{5}$$

with r_σ as the spectral radius of the matrix and

$$R = \begin{bmatrix} I_3 & 0 \\ 0 & 2I_3 \end{bmatrix}$$

where I_3 is 3×3 identity matrix. The Frobenius norm possesses also this important property:

Theorem 2 ([2], p. 205): Let d and $\tilde{d} \in \mathbb{R}^6$ represent two symmetric $n \times n$ matrices with eigenvalues $\lambda_1 \geq \lambda_2 \geq \cdots \geq \lambda_n$ and $\tilde{\lambda}_1 \geq \tilde{\lambda}_2 \geq \cdots \geq \tilde{\lambda}_n$ respectively. Then

$$\left[\sum_i^n (\lambda_i - \tilde{\lambda}_i)^2\right]^{\frac{1}{2}} \leq \|d - \tilde{d}\|_R.$$

The equations (3), (4) and Theorem 2 can be combined to put a bound on the relative error of eigenvalues:

$$\frac{\left[\sum_i^3 (\lambda_i - \tilde{\lambda}_i)^2\right]^{\frac{1}{2}}}{\left[\sum_i^3 \tilde{\lambda}_i^2\right]^{\frac{1}{2}}} \leq \|V_D^{-1}(V_I + V_C)\|_R. \tag{6}$$

The optimization algorithms will search for diffusion gradients that will minimize the right hand side of (6) in order to obtain schemes that are insensitive to neglecting the imaging gradients from the estimation process. It is a geometric search for schemes that are optimally 'bloomed', 'stretched' and 'oriented' with respect to the fixed imaging gradient vectors.

Note that the left hand side of the inequality (6) is unknown before the measurements and the right hand side is solely determined by the gradient directions, magnitudes and time course, thus is completely independent of measurement values. Since the expression on the right hand side does not depend on the diffusion matrix (thus neither to its eigenvalues nor to its eigenvectors), it is also completely detached from the properties of the diffusion at any given location. This is an extremely sound choice for an objective function which does not have the sample dependence (tissue properties, orientation, location in the sample etc.) of the existing optimization criterions in the literature [3], [4], [5], [6], [7].

$$M = \begin{bmatrix} P_{11}^2 & P_{12}^2 & P_{13}^2 & 2P_{11}P_{12} & 2P_{12}P_{13} & 2P_{11}P_{13} \\ P_{21}^2 & P_{22}^2 & P_{23}^2 & 2P_{21}P_{22} & 2P_{22}P_{23} & 2P_{21}P_{23} \\ P_{31}^2 & P_{32}^2 & P_{33}^2 & 2P_{31}P_{32} & 2P_{32}P_{33} & 2P_{31}P_{33} \\ P_{11}P_{21} & P_{12}P_{22} & P_{13}P_{23} & P_{12}P_{21}+P_{11}P_{22} & P_{13}P_{22}+P_{12}P_{23} & P_{13}P_{21}+P_{11}P_{23} \\ P_{21}P_{31} & P_{22}P_{32} & P_{23}P_{33} & P_{22}P_{31}+P_{21}P_{32} & P_{23}P_{32}+P_{22}P_{33} & P_{23}P_{31}+P_{21}P_{33} \\ P_{11}P_{31} & P_{12}P_{32} & P_{13}P_{33} & P_{12}P_{31}+P_{11}P_{32} & P_{13}P_{32}+P_{12}P_{33} & P_{13}P_{31}+P_{11}P_{33} \end{bmatrix} \quad (7)$$

The advantage of the formulation that separates the timings and strengths of the gradients (e.g. $V_D = b\,V_g$) in [1] becomes now clear. When the gradient pulses are approximated by boxcar functions, b defined in [1] (different than the definition used in the literature) is a factor for the timing of the gradient pulses and is independent of their strength. The optimization problem, including the constraints, can be posed and carried on the diffusion gradient sets without involving their timings.

B. Parametrization of the Feasible Search Space

Regardless how the estimation is done, with or without the incorporation of the imaging gradients, the set of diffusion gradients g has to have the corresponding V_g, i.e. V_D, full rank [8]. This is also in line with the conditions of Theorem 1. In addition, the full version of Theorem 1 in [2] asserts that provided V_D is nonsingular, if $\|V_D^{-1}(V_I + V_C)\|$ is small then the sum of all three matrices, V, will also be nonsingular.

Therefore the main constraint for the optimization problem is to guarantee the full rank condition. A parametrization is necessary to describe the set of admissible diffusion gradient vectors. It can be shown that when the set of diffusion gradient vectors

$$g = \begin{bmatrix} g_{1x} & g_{1y} & g_{1z} \\ \vdots & \vdots & \vdots \\ g_{mx} & g_{my} & g_{mz} \end{bmatrix} \in \mathbb{R}^{m\times 3}$$

is transformed to $\bar{g} = g\,P$, where P is a $3 \times m$ matrix, V_g transforms to

$$V_{\bar{g}} = V_{(gP)} = V_g\,M. \quad (8)$$

For $m = 6$, M is a function of P given in (7) with the property that $\det(M) = (\det(P))^4$. This implies that $\det(V_{\bar{g}}) = \det(V_g)\,(\det(P))^4$. In conclusion, $V_{\bar{g}}$ will be nonsingular if and only if P is, thus P is the parameter that describes the feasible gradient schemes.

The origin set, g, acts like a 'pivot' and new admissible schemes are discovered by changing P. Since P must be nonsingular, it has a polar decomposition, $P = U\,Q$, where U is an orthogonal matrix ('angle') and Q is a positive definite matrix ('magnitude') [9]. In turn Q can be parametrized by $q \in \mathbb{R}^6$ using Cholesky decomposition:

$$Q = \hat{Q}^T\hat{Q} = \begin{bmatrix} q_1 & q_4 & q_6 \\ 0 & q_2 & q_5 \\ 0 & 0 & q_3 \end{bmatrix}^T \begin{bmatrix} q_1 & q_4 & q_6 \\ 0 & q_2 & q_5 \\ 0 & 0 & q_3 \end{bmatrix},$$

and the orthogonal part of the parametrization is confined to the set of rotation matrices using the Euler angles $(\psi, \theta, \phi) \in [0, 2\pi] \times [0, \pi] \times [0, 2\pi] = \Omega$

$$U = \begin{bmatrix} \cos(\phi) & -\sin(\phi) & 0 \\ \sin(\phi) & \cos(\phi) & 0 \\ 0 & 0 & 1 \end{bmatrix} * \begin{bmatrix} 1 & 0 & 0 \\ 0 & \cos(\theta) & -\sin(\theta) \\ 0 & \sin(\theta) & \cos(\theta) \end{bmatrix} \begin{bmatrix} \cos(\psi) & -\sin(\psi) & 0 \\ \sin(\psi) & \cos(\psi) & 0 \\ 0 & 0 & 1 \end{bmatrix}.$$

Unfortunately, it is not possible to cover all the feasible diffusion gradient sets starting from a single good one. There are gradient schemes such that $g' = g\,P$ does not hold, therefore the parametrization is limited only to the congruence class of the pivot. For example, the following sets of gradients:

$$\tilde{g} = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \\ \frac{1}{\sqrt{2}} & \frac{1}{\sqrt{2}} & 0 \\ 0 & \frac{1}{\sqrt{2}} & \frac{1}{\sqrt{2}} \\ \frac{1}{\sqrt{2}} & 0 & \frac{1}{\sqrt{2}} \end{bmatrix}, \; \dot{g} = \begin{bmatrix} \frac{(1+\sqrt{5})}{2} & 1 & 0 \\ \frac{(1+\sqrt{5}}{2} & -1 & 0 \\ 0 & 1 & \frac{(1+\sqrt{5})}{2} \\ 0 & \frac{(-1-\sqrt{5})}{2} & -1 \\ -1 & 0 & \frac{(1+\sqrt{5})}{2} \\ 1 & 0 & \frac{(1+\sqrt{5})}{2} \end{bmatrix} \quad (9)$$

are not obtainable from one another. Although $M = V_{\dot{g}}^{-1}\,V_{\tilde{g}}$ exists, there is no P that provides M as in (7). In consequence, there is no way to find a global minimizer starting from a given pivot scheme using a linear parametrization.

C. Hardware Constraints

Intuitively, if V_D has large entries, the effects of V_I and V_C will be reduced. Clearly, without the implementation of the constraints reflecting the hardware limits, the solution of the minimization problems tends towards stronger diffusion gradients to make V_D dominant. The main hardware constraint is the upper limit for the strength of the diffusion gradients, $G_{\max}$, imposed either by the user or by the system. The constraint, which is incorporated in the objective function below (10), guarantees that the limit is not violated.

D. Objective Function

At the heart of each optimization problem lays the choice of an adequate objective function. The analysis of the previous sections provided a foundation for minimizing the estimation differences. In addition to those, the perturbation of the measurements (e.g. due to noise) are handled by adding the R–norm condition number of V_D to the objective for increasing

the robustness. The objective function is

$$10\|(b\,V_{(gP)})^{-1}(V_I + V_{C(gP)})\|_R + b^2\,\frac{\|V_{(gP)}\|_R}{\|V_{(gP)}^{-1}\|_R} + 100\left|\max_{i=1,\cdots,m}\|g_i\,P\|_1 - G_{\max}\right|. \quad (10)$$

The last portion is the hardware constraint that confines the diffusion gradients to a cube. The choice of the weights is accomplished heuristically by trial and error. The search is performed over the parameter variables, $(\psi, \theta, \phi, q) \in \Omega \times \mathbb{R}^6$, that are the arguments of the matrix function $P(\psi, \theta, \phi, q)$ as in Section II-B.

III. Experimental Results

The experimental setup is exactly the same as in [1]. Each of the diffusion gradient schemes given in [1] with six vectors were taken as the pivot set g in the objective function (10) above and standard Matlab® Optimization Toolbox® (Mathworks, Natick, MA USA) routine *fmincon* was used.

The initial condition supplied to the numerical routines plays a crucial role in the convergence of the algorithm. For each pivot, several initial conditions obtained by changing Euler angles in the multiples of $\frac{\pi}{4}$ rad, equivalent to rotating the pivots, were evaluated. After the algorithm converged for each case, the best of the optimal solutions was picked up. The 'magnitude' of the pivot was left untouched having in mind from Section II-D that the optimization routines will easily deal with the strengths of the gradients. For Muthupallai, Downhill Simplex Minimization (DSM), Dual Gradient and Tetrahedral the initial condition $(0, 0, 0)$ has resulted in the best cost. Table I summarizes the costs at different stages of the procedure. The first row gives the optimal values after the algorithm is run and the last two rows are for the initial condition and the pivot cost values. The scheme Jones6 has the lowest cost, followed by Dual Gradient, Muthupallai and DSM.

TABLE I
Summary of Costs For Optimized Schemes

	cond6	cond*	dsm	dualgr	icosa	jones6	muthup	tetra
Opt.	25.35	5.177	4.546	4.348	9.437	4.241	4.41	12.53
Initial	40.64	20.64	13.81	34.48	21.71	12.96	19.81	45.33
Pivot	50.18	5.921	13.81	34.48	35.13	5.085	19.81	45.33

The center symmetric counterpart of the six optimal gradient vectors is added to the gradient scheme to follow NoCroT protocol and experiments were carried out on the isotropic phantom of [1]. Table II shows that the difference between the eigenvalues obtained by incorporating all the imaging gradients and neglecting them goes down in the optimal schemes with the exception of Dual Gradient scheme. This proves that the optimization goal has been reached.

Although not directly addressed by the objective function, it is important to see how the performance of the estimation reported in [1] has changed. Table III represents estimation results for the eigenvalues and model matching error as

TABLE II
Difference Between The Eigenvalues from V_D and V, $\lambda_i - \bar{\lambda}_i$

	!cond6	cond*	dsm	dualgr	icosa	jones6	muthup	!tetra!
Reg.	!-0.668	0.032	0.0857	0.00234	-1.78	0.061	0.0622	-1.06
Opt.	-0.178	0.0149	0.0787	0.0286	-0.219	0.0592	0.0604	-0.561
Reg.	!0.342	0.0949	0.0999	0.0227	0.325	0.0745	0.0739	-1.06
Opt.	0.202	0.0719	0.089	0.0528	0.247	0.0714	0.0707	-0.581
Reg.	!0.751	0.185	0.203	0.358	0.685	0.247	0.244	2.06
Opt.	0.433	0.205	0.154	0.114	0.401	0.166	0.162	1.11

mean±standard deviation. Exclamation point indicates the existence of negative eigenvalues. The analysis is carried by three different coefficient matrices: V, NoCroT ($V_D + V_I$) and V_D which are shown in respective rows. Only optimal Tetrahedron scheme exhibits negative eigenvalues with V. The ratios of the number of pixels with negative eigenvalues to the total number of pixels 0.0302 ($n_{roi} = 2022$). This is much lower than the ones reported for the original Tetrahedron scheme. Note that the negative eigenvalues have completely disappeared from the optimized Cond6 scheme. These observations demonstrate that robustness has improved significantly.

$\overline{FA}$ is the mean of the pixel fractional anisotropy index [10], which should be close to zero because the sample is uniform and isotropic. For the inclusion of the imaging gradients, i.e. V, optimized schemes show significant improvements compared to the non–optimal schemes given in [1]: they are consistently lower. However, for NoCroT and V_D most of the schemes worsen slightly. $\overline{FA}$ increases for Dual Gradient scheme and decreases for Icosahedron noticeably, there is a slight increase for DSM and Muthupallai but Jones6 barely changes. As in [1], $\overline{FA}$ is the lowest when all the imaging gradients are neglected from the calculations (row 3).

The standard deviation of fractional anisotropy do not change drastically between the three methods but the values from V_D and NoCroT are much closer than the ones between V_D and NoCroT as also observed in [1]. The standard deviation for the optimal schemes increases slightly for all three methods compared to non–optimal ones i.e. there is a decrease in precision after optimization. In brief, although $\overline{FA}$ values show improved results for the inclusion of all gradients, their performance for the remaining methods is worst than the non–optimal schemes.

$\bar{\lambda}_i$ ($10^{-5}\text{cm}^2/\text{s}$) are the mean eigenvalues. Overall, the eigenvalues obtained from the optimal schemes are larger. The precision is better for most of the optimal versions, specifically for DSM, Muthupallai and Icosahedron. For the rest, it is slightly worst or unchanged. Their precision follows a similar pattern as in the regular schemes: it is the best for NoCroT and the worst for V consistently. Very similar to non–optimal schemes, V_D estimates larger eigenvalues. For optimized schemes, it can not be asserted that NoCroT is a better choice for the precision of the eigenvalues since the performance fluctuates between the schemes.

$\bar{\chi}$, the mean of the pixel residuals [1], is the most impor-

TABLE III
SUMMARY OF ANALYSIS RESULTS FOR OPTIMIZED SCHEMES

		cond6	cond*	dsm	dualgr	icosa	jones6	muthup	tetra
$\overline{FA}$	V	0.315±0.081	0.127±0.034	0.0772±0.0192	0.0985±0.0289	0.263±0.0462	0.0854±0.0198	0.0842±0.0203	!–!
	NoCroT	0.138±0.0729	0.0701±0.0256	0.0545±0.0175	0.0733±0.0264	0.0762±0.0301	0.0545±0.0184	0.0537±0.0174	0.148±0.0719
	V_D	0.133±0.0693	0.0682±0.0249	0.0521±0.0169	0.0713±0.0257	0.0754±0.029	0.0509±0.0173	0.0516±0.0168	0.145±0.0703
$\bar{\lambda}_1$	V	2.26±0.207	1.95±0.061	1.86±0.0453	1.95±0.0661	2.21±0.109	1.88±0.0461	1.89±0.0462	!2.68±0.194!
	NoCroT	2.01±0.135	1.92±0.0625	1.87±0.0449	1.94±0.0649	1.93±0.071	1.87±0.0471	1.88±0.0452	2.08±0.162
	V_D	2.08±0.135	1.97±0.0613	1.94±0.0457	1.98±0.0653	1.99±0.0699	1.94±0.0477	1.95±0.046	2.12±0.162
$\bar{\lambda}_2$	V	1.64±0.0993	1.77±0.0674	1.76±0.0416	1.8±0.0578	1.61±0.107	1.78±0.0451	1.78±0.0442	!2.42±0.176!
	NoCroT	1.77±0.0975	1.79±0.0476	1.77±0.0386	1.8±0.0495	1.79±0.046	1.78±0.0385	1.79±0.038	1.8±0.098
	V_D	1.85±0.105	1.84±0.0479	1.85±0.0395	1.85±0.0501	1.86±0.0481	1.85±0.0387	1.85±0.0387	1.84±0.0988
$\bar{\lambda}_3$	V	1.17±0.133	1.52±0.0772	1.6±0.0448	1.61±0.0647	1.32±0.0638	1.59±0.0482	1.6±0.0483	!0.487±0.248!
	NoCroT	1.53±0.139	1.67±0.0563	1.68±0.0413	1.68±0.0556	1.66±0.0603	1.68±0.0437	1.7±0.0419	1.55±0.133
	V_D	1.6±0.137	1.72±0.0577	1.75±0.0418	1.72±0.0554	1.72±0.0627	1.76±0.0433	1.76±0.0423	1.59±0.133
$\bar{\chi}$	V	791±60	697±55.4	966±64.8	559±52.1	1050±76.5	946±62.9	886±58.6	411±53.4
	NoCroT	438±51.2	387±50.4	510±54.4	305±48.5	537±58.1	502±53.6	470±50.7	244±47.6
	V_D	438±51.2	387±50.4	510±54.4	305±48.5	537±58.1	502±53.6	470±50.7	244±47.6

tant criterion since it measures the adequacy of the model matching. The addition of the R–norm condition number to the objective function assisted in the significant reduction of the model matching error in the optimal schemes. Despite that, it should be noted that the model matching error for V, that theoretically encompasses all the effects of the gradients, is still larger compared to the less 'correct' models.

IV. CONCLUSION

By expanding the linear algebraic framework of [1] to a normed vector space, a sample independent, robust and geometric optimization problem encompassing the hardware limitations and guaranteeing the feasibility of the diffusion gradient vectors was defined. The program succeeded in finding optimal diffusion gradient schemes that reduced the difference between eigenvalues obtained from the full incorporation and full exclusion of the imaging gradients in MR–DTI estimation, thus making the latter justifiable even under the conditions where the imaging gradients have high values. More importantly, the data obtained using the optimal schemes fit the DTI model much better than the non–optimal schemes.

When the results of the estimation is analyzed, however, there is a slight increase in the fractional anisotropy for the optimal schemes in general. One would expect that with better model matching the fractional anisotropy should get closer to zero for an isotropic sample. Considering the fact that all the experiments (with non–optimal and optimal schemes) were carried consecutively i.e. under the same conditions, this issue must be addressed by investigating new strategies for gradient schemes based on the data obtained with large number of diffusion gradients.

After the investigation of the effects of all gradients on the eigenvalues, the natural next step is the investigation of the eigenvectors which is essential for fiber tracking. The choice of an objective function that will be independent of sample properties (e.g. fiber orientation) is a significant challenge.

The linear parametrization of the feasible set of diffusion gradient schemes results in a disconnected description so the optimal solutions are limited to the congruence classes. The proof of the fact that the feasible set is a connected manifold is beyond the scope of this manuscript. If this can be shown then a nonlinear parametrization will provide the possibility of finding a global optimizer.

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