Optimal Diffusion Tensor Imaging with Repeated Measurements

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Abstract. Several data acquisition schemes for diffusion MRI have been proposed and explored to date for the reconstruction of the 2nd order tensor. Our main contributions in this paper are: (i) the definition of a new class of sampling schemes based on repeated measurements in every sampling point; (ii) two novel schemes belonging to this class; and (iii) a new reconstruction framework for the second scheme. We also present an evaluation, based on Monte Carlo computer simulations, of the performances of these schemes relative to known optimal sampling schemes for both 2nd and 4th order tensors. The results demonstrate that tensor estimation by the proposed sampling schemes and estimation framework is more accurate and robust.

Keywords: diffusion tensor imaging, optimal sampling scheme, tensor estimation.

1 Introduction

Diffusion tensor imaging (DTI) measures the restricted diffusion of water molecules in tissues, thus revealing information about tissue micro-structure. It involves acquiring a series of diffusion-weighted images (DWIs), each acquired with diffusion sensitization along a particular gradient direction. Six or more non-collinear directions are needed to reconstruct a 2nd order tensor. The overall acquisition time needs to be compatible with in-vivo measurement. Thus, one of the most fundamental questions in DTI is how to optimally sample q-space. The classical case, i.e. single-sphere q-space sampling with a constant b-value for constructing the second order tensor, has been the subject of much study over the last decade. Two observations can be drawn from the literature: (i) it is widely accepted among researchers that sampling points should be uniformly distributed over the unit sphere (the motivation is that the SNR of the measured signal is dependent on the orientation and anisotropy of the tensor [1,2]); and (ii) it is widely accepted that more sampling points leads to more accurate tensor estimation (the motivation for acquiring more measurements is to mitigate

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noise and not to capture more directional or spatial information). Nevertheless whilst both of these sampling tenets are intuitively appealing they have not been proved. Higher reconstruction accuracy equates to reducing noise by either making additional measurements in more directions, or repeating measurements in a smaller number of directions. Research to date has been focused on the former strategy. An open question is whether, given the possibility of making N measurements, it is better to make measurements in N unique directions or to repeat measurements over a fewer number of directions. In this paper, the question is addressed for both 2nd and 4th order tensor imaging. In particular, this paper introduces a new class of sampling schemes with $r_i > 1$ repeated measurements in each direction, and proffers two sampling strategies from this class. In addition, for the second scheme, a new tensor estimation framework is proposed. The two approaches are compared to the optimal solutions of the conventional strategy of taking $r_i = 1$. The remainder of this paper is organized as follows. In the next section we discuss related work and present the general evaluation framework that is used to evaluate sampling schemes. Section 3 introduces the proposed sampling schemes and estimation framework. In section 4, Monte Carlo simulation results and comparisons with conventional optimal schemes are presented.

2 Related Work

A wide variety of diffusion tensor data sampling schemes have been proposed ranging from electrostatic repulsion (to obtain uniform sampling on the unit sphere) [1], to minimum condition number (MCN) [3] (to minimize the noise effect on the estimated tensor elements, and thus tensor-derived quantities, by minimization of the condition number of the design matrix [3] associated with the linear least squares parametric estimation of the diffusion tensor). The reader is referred to [2] for a comprehensive review of these sampling schemes.

Simulations in [4] showed that the icosahedral sampling scheme is superior to the MCN scheme in terms of rotational invariance of the condition number (CN). Several other criteria have also been proposed to measure the optimality of sampling schemes including total tensor variance [5], interaction energy of identical charges positioned at sampling points [1], signal deviation [6], variance of tensor-derived scalars [4,7], minimum angle between pairs of encoding directions, and SNR of tensor-derived scalars [8]. However, very few studies have considered optimal sampling schemes for 4th order tensor imaging [2]. A common framework [7,9,4,6,3] to evaluate sampling schemes (mainly for the 2nd order tensor) is via Monte Carlo simulations. In particular this involves: (1) defining a diagonal tensor D_0 with a prescribed fractional anisotropy (FA) and eigenvalues; (2) rotating this initial tensor, i.e. obtaining $D = R^T D_0 R$ where R is the rotation matrix (corresponding to a rotation by Euler angles θ, ϕ and ψ); (3) simulating the diffusion signal at the sampling points defined by the scheme under evaluation using the Stejskal-Tanner [10] equation; (4) adding Rician distributed noise to the synthetic signals (to obtain a prescribed SNR); (5) using the noisy signal to obtain a reconstruction/estimate, $\hat{D}$, of D; (6) computing the optimality measure of interest; (7) repeating steps (2)-(6) N_{MC} times (for different realizations of noise); (8) recording the mean value of the optimality measure; and (9) repeating steps (2)-(8) N_R times (for different rotations). This general evaluation framework (GEF) is both well-known and widely used (typically with two 90 degree crossing fibers).

3 Proposed Work

Given that the distribution of noise in MRI magnitude images is nearly Gaussian for SNR > 2 [11], and that a typical SNR value for DTI is 12.5 [12], this motivates repetition of measurements on the same sampling points followed by averaging. To the authors' knowledge, only two papers have considered sampling schemes with repeated measurements [7,4] (in order to fairly compare with other sampling schemes with more sampling points but not to study noise mitigation by repeated measurements). Let $Name/N_u/r$ denote a gradient encoding scheme (GES) with N_u unique sampling points and r repetitions per point. To study the effect of noise mitigation by repeated measurements one should compare $X/\frac{N}{r}/r$ with $X/N/1$. There is only one such a comparison in [4] with the variance of FA as the only measure of optimality. This implies that in [4,7] the purpose was not to study noise mitigation by repeated measurements. We continue by briefly describing the commonly used reconstruction framework. The basic Stejskal-Tanner equation for diffusion MRI signal attenuation is [10]

$$-\frac{1}{b}\ln\left(\frac{S}{S_0}\right) = d(\mathbf{g}) \tag{1}$$

where $d(\mathbf{g})$ is the diffusivity function, S is the measured signal when the diffusion sensitizing gradient is applied in the direction $\mathbf{g}$, S_0 is the observed signal in the absence of such a gradient, and b is the diffusion weighting taken to be constant over all measurements. The diffusivity function $d(\mathbf{g})$ is modeled using even order (m) symmetric tensors as follows

$$d(\mathbf{g}) = \sum_{i=0}^{m}\sum_{j=0}^{m-i} t_{ij}\mu_{ijm} g_1^i g_2^j g_3^{m-i-j} \tag{2}$$

where $\mathbf{g} = [g_1\ g_2\ g_3]^T$, $\mu_{ijm} = {}^{m!}/_{i!j!(m-i-j)!}$, and the t_{ij} denote $n = (m+1)(m+2)/2$ distinct entries of the m-th order tensor. The diffusivity function is expressed as the inner product $d(\mathbf{g}) = \mathbf{t}^T\hat{\mathbf{g}}$ where $\hat{\mathbf{g}} = [g_3^m\ mg_2g_3^{m-1}\ 0.5m(m-1)g_2^2g_3^{m-2} \cdots\ g_1^m]^T$ and $\mathbf{t} = [t_{00}\ t_{01} \cdots\ t_{m0}]$. Note that both vectors $\mathbf{t}$ and $\hat{\mathbf{g}}$ are vectors in $\mathbb{R}^n$ and $d(\mathbf{g},\mathbf{t}) = d(\mathbf{g})$ is used for simplification. Given measurements in $N \geq n$ different directions $\mathbf{g}_k$ the tensor estimation problem is then formulated as

$$\min\ \sum_{k=1}^{N}(d_k - \hat{d}_k)^2, \quad \text{s.t. } d(\mathbf{g}) \geq 0 \tag{3}$$

where $d_k = d(\mathbf{g}_k)$ are the values predicted by the model, and $\hat{d}_k = -b^{-1}\ln(S_k/S_0)$ are the measured values.

3.1 Optimality Measures

$\mathbf{G} = [\hat{\mathbf{g}}_1 \; \hat{\mathbf{g}}_2 \cdots \; \hat{\mathbf{g}}_N]^T$ is the design matrix associated with the least squares (LS) estimation of the diffusion tensor. Its CN, $k(\mathbf{G})$ is widely used to measure the optimality of a sampling scheme. Alternatively the CN of the information matrix $B = \mathbf{G}^T\mathbf{G}$ is used ($k(\mathbf{G}) = \sqrt{k(B)}$) [4]. Nevertheless these CNs do not give the full picture [2]. For this reason herein we use two optimality measures: CN and signal deviation. An interesting property of the CN is that the CN of a scheme consisting of N_u unique directions is the same as that for a scheme in which repeated measurements are made in these N_u directions (the proof is easily obtained by constructing the information matrix). The signal deviation for an estimation procedure is given by [6]

$$S_{\text{dev}} = \frac{1}{N}\sum_{i=1}^{N} |S_i - \hat{S}_i| \tag{4}$$

where S_i is the noise-free synthetic signal and $\hat{S}_i$ is the signal reconstructed from the estimated tensor.

3.2 First Scheme

Herein we describe our first solution for determining an optimal sampling scheme. It is based on the idea that if we can only make a fixed number of measurements then we should make repeated measurements in some optimal sampling points instead of seeking to acquire measurements in more unique directions. This strategy is motivated by the following facts: (i) as long as our reconstruction framework has only n free parameters, increasing the number of sampling points does not lead to the acquisition of more directional/spatial information; (ii) the acquisition of more samples and the application of LS estimation methods mitigates noise (as noted above for SNR > 2 the noise is nearly Gaussian and so repeated measurements also leads to improved SNR); and (iii) the CN is invariant under repetitions.

Given that the icosahedral scheme is widely accepted as an optimal sampling scheme for both 2nd and 4th [6] order DTI we used this scheme as a the basis for our experiments. In particular we chose to compare measurement over N_u unique directions with repeated measurements (up to a total of N_u) over only 6 directions. Hereinafter this sampling strategy is called 'S1'. We used the algorithm proposed in [13] to estimate diffusion tensors for this strategy.

3.3 Second Scheme and Its Reconstruction Framework

Herein we describe our second solution for determining an optimal sampling scheme, applicable for 2nd order tensors. In conventional tensor estimation frameworks, all tensor elements are estimated at the same time. We propose a new estimation framework by splitting the tensor estimation into two steps as follows. From (2) it can be seen that we can directly measure the diagonal elements of the

2nd order tensor by applying only three gradient directions. This defines the first step of our second scheme

$$\text{GES}_{\text{step1}} : \{d([1\,0\,0]) = t_{20},\, d([0\,1\,0]) = t_{02},\, d([0\,0\,1]) = t_{00}\}\,. \tag{5}$$

The motivation for these choices is to obtain CN=1. These directions can of course be repeated several times. Once the diagonal elements of the diffusion tensor are obtained (from above), another set of three sampling points are measured to estimate the off-diagonal elements. The **G** matrix for estimation of the off-diagonal elements is

$$\mathbf{G}_{\text{step2}} = \begin{bmatrix} g_{x1}g_{y1} & g_{x1}g_{z1} & g_{y1}g_{z1} \\ g_{x2}g_{y2} & g_{x2}g_{z2} & g_{y2}g_{z2} \\ g_{x2}g_{y2} & g_{x2}g_{z2} & g_{y2}g_{z2} \end{bmatrix}. \tag{6}$$

We minimized the condition number of (6) using particle swarm optimization [14] to obtain the sampling points for this step. We acknowledge that other optimization schemes could be used at this step. The outcome is that many solutions lead to a CN equal to one. One example is

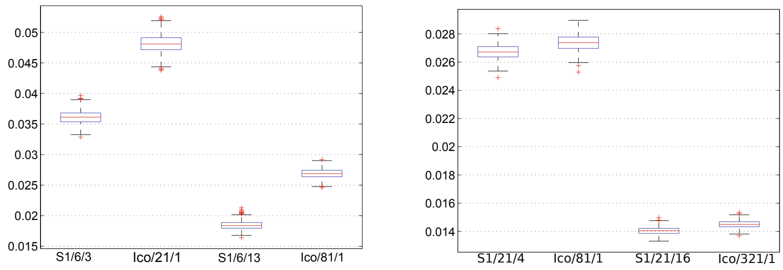
$$\text{GES}_{\text{step2}} = \{[0.10\ -0.75\ -0.65]\,, [-0.65\ -0.10\ -0.75]\,, [-0.75\,0.65\ -0.10]\}$$

that is used in our experiments. Hereinafter we call this scheme 'S2'. For a DTI data acquisition scheme with $N = 30$ measurements this implies that one may sample these six points five times (denoted as S2/6/5). Other repetition variations are also possible. For example, if $N = 21$ then four repetitions of $\text{GES}_{\text{step1}}$ and three repetitions of $\text{GES}_{\text{step2}}$ is a possibility (S2/6/4,3). Let r_{s1} and r_{s2} be the number of repetitions for each step respectively. First we simply average the measured signal to estimate the diagonal elements of the diffusion tensor (averaging is done over signals acquired by $\text{GES}_{\text{step1}}$). Substituting in the known diagonal elements yields a system of linear equations in three unknowns (off-diagonal elements). The system is overdetermined (because $r_{\text{s2}} > 1$) and is solved using LS. The motivation for this scheme is to keep CN=1 all the way through, and to employ the repetition idea from 'S1'.

4 Simulations

4.1 Simulation Setup

The measurements of diffusion signal magnitude can be modeled as [15]: $S(\mathbf{g}_i) = |A(\mathbf{g}_i) + w|,\ \ i = 1, \ldots, N$ where w is Rician distributed random noise with standard deviation σ, $A(\mathbf{g}_i) = \sum_{j=1}^{u} \frac{S_0}{u} \exp(-b\mathbf{g}_i^T D_j \mathbf{g}_i)$ is the ideal signal (without noise) from a voxel containing u fiber bundles and D_j is the 2nd order diffusion tensor for the j-th fiber. Synthetic data were generated using this model with the the following setup: $N \in \{6, ..., 321\}$, $b = 1500\,\text{sec}/(\text{mm}^2)$, $D_1 = \text{diag}(17, 1, 1) \times 10^{-4}$ $(\text{mm}^2)/\text{sec}$, $D_2 = \text{diag}(1, 17, 1) \times 10^{-4}$ $(\text{mm}^2)/\text{sec}$, $u \in \{1, 2\}$, SNR = 12.5 (a typical level of noise [12]) and $N_{\text{MC}} = 100$. In all



(a) (b)

Fig. 1. A comparison between our proposed scheme 'S1' and 'Ico' based on signal deviation statistics. (a) 2nd order tensor and one fiber bundle ($m = 2, u = 1$); (b) 4th order tensor and two fiber bundles ($m = 4, u = 2$). Our proposed 'S1' outperforms 'Ico' in terms of accuracy and robustness.

experiments the optimality measure was computed for $N_R = 441$ different rotations. Given the axial symmetry of the diffusion ellipsoid rotation angle, ψ was set to zero in all simulations [9]. The space of possible rotations over θ and ϕ was uniformly sampled with 21 steps (both in the interval $[0, 2\pi]$).

4.2 Simulation Results

As mentioned earlier, repetitions do not change the CN. The CN of the icosahedral scheme for 2nd order tensor reconstruction is rotationally invariant and equal to 1.5811 [4]. In the case of the 4th order tensor the CN is not rotationally invariant but has a mean less than 7 (dependent on N_u) [6].

Following the GEF introduced in section 2, we report summary statistics for the optimality measure at step (9); i.e. statistics summarizing the mean signal deviation (S_{dev}) over all possible rotations of the tensor. Figure 1 shows a comparison of the signal deviation statistics for our proposed 'S1' relative to the icosahedral (denoted 'Ico') sampling scheme [4]. Figure 1(a) shows that 'S1' yields more accurate and robust reconstruction compared to 'Ico' for the 2nd order tensor ($m = 2$) and one fiber bundle ($u = 1$). Notably these results are obtained in a shorter scanning time (fewer measurements). Figure 1(b) shows that 'S1' yields slightly improved reconstruction for the 4th order tensor and two crossing fiber bundles ($m = 4, u = 2$). Figure 2 shows comparisons of 'S1' versus 'S2', and 'S2' versus 'Ico' for $m = 2, u = 1$. Our proposed sampling scheme, 'S2' is much better than 'Ico' in terms of reconstruction accuracy and robustness ($N = 21, 81$, see columns (b) and (d)). Also for a smaller number of measurements ($N = 18$), 'S1' is slightly better than 'S2'. However, as N increases they show approximately the same performance (see columns (a) and (c)).

4.3 Discussion

We acknowledge that our results are based on simulations. It is noteworthy, however, that [3,5,9,13] found that the GEF results correlate with that of real brain data (RBD). We are not aware of publications to the contrary. This would suggest that our results should similarly hold for RBD. Indeed this will be the subject of future investigation. It should be noted that the quality of the results on RBD ultimately depends on the achievable SNR that in turn depends on the magnetic field strength and spatial resolution [8]. Thus such results must be complemented with simulation results. Given that the two proposed schemes outperform existing schemes on synthetic data, a similar conclusion is anticipated for RBD based on the above reasoning. Even if this were not the case, this would provide new insight/caution to the diffusion MRI community with respect to its use of the GEF.

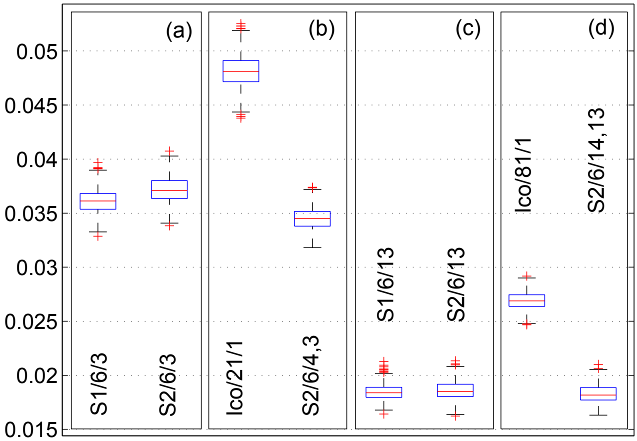


Fig. 2. 'S1' versus 'S2' (columns (a) and (c)) and 'S2' versus 'Ico' (columns (b) and (d)) for $u = 1, m = 2$. Our proposed 'S2' outperforms 'Ico' in terms of accuracy and robustness.

5 Conclusion

We proposed two new sampling schemes for diffusion tensor imaging. The first scheme utilizes repeated measurements along the directions prescribed by the icosahedral scheme in the conventional estimation framework. The second scheme uses repeated measurements of a new sampling scheme in a new estimation framework. These two schemes were evaluated and compared with known optimal sampling schemes using Monte Carlo computer simulations. Our results demonstrate that the two proposed schemes are superior in terms of accuracy and robustness. Although preliminary, these results suggest that this approach may have a significant impact on DWI acquisition protocols. Future work includes validating these results using real human brain data.

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