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## Optimal real-time estimation in diffusion tensor imaging

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## Abstract

Diffusion tensor imaging (DTI) constitutes the most used paradigm among the diffusion-weighted magnetic resonance imaging (DW-MRI) techniques due to its simplicity and application potential. Recently, real-time estimation in DW-MRI has deserved special attention, with several proposals aiming at the estimation of meaningful diffusion parameters during the repetition time of the acquisition sequence. Specifically focusing on DTI, the underlying model of the noise present in the acquired data is not taken into account, leading to a suboptimal estimation of the diffusion tensor. In this paper, we propose an optimal real-time estimation framework for DTI reconstruction in single-coil acquisitions. By including an online estimation of the time-changing noise variance associated to the acquisition process, the proposed method achieves the sequential best linear unbiased estimator. Results on both synthetic and real data show that our method outperforms those so far proposed, reaching the best performance of the existing proposals by processing a substantially lower number of diffusion images.

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## 1. Introduction

Magnetic resonance imaging (MRI) allows for easily identifying the anatomical structures of the brain in vivo. However, with this modality, the white matter appears as a homogeneous region, which hides the complex microarchitecture and connectivity of the nervous fibers comprised in this tissue. Diffusion-weighted MRI (DW-MRI) is intended to overcome this drawback, taking advantage of the diffusion of water molecules along the myelinated fiber bundles in the white matter.

The three-dimensional diffusion probability displacement function (PDF) or diffusion propagator of water molecules

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can be inferred from DW-MRI by acquiring a number of diffusion-sensitized images along different orientations of the sampling space. DW-MRI leads to diffusion-direction-dependent image intensities. In the case of anisotropic water diffusion, these intensities will be low if the measurement gradient direction is aligned with the major direction of diffusion and high for diffusion directions orthogonal to the measurement gradient direction.

The number of required diffusion-weighted images (DWIs) depends on how the diffusion is modeled. The well-known diffusion tensor (DT) model assumes a Gaussian PDF and requires at least six DWIs plus an additional unweighted image. Since the physics of the problem impose the radial symmetry of the diffusion, the entire process can be described in terms of the  $3\times3$  covariance matrix of a Gaussian random variable. As such, the covariance matrix is positive, definite and symmetric, so it has only six degrees of freedom. This matrix is the diffusion tensor, and those techniques oriented to compute and represent it (or parameters derived from it) at each location of a three-dimensional volume are gathered under the denomination of DT (magnetic resonance) imaging (DT-MRI or DTI). Due to

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the six degrees of freedom of the DT, it may be determined from six independent gradient directions (thus, the need for six DWIs [1]). Nevertheless, it is very common to acquire a higher number of directions (DWIs) to improve the robustness of the estimation [2].

A number of techniques have been recently developed in order to overcome the limitations of the DT model. These limitations are imposed by the Gaussian assumption, which cannot properly model fiber bundle crossing (diffusion in two or more principal directions). The group of methods known as high angular resolution diffusion imaging (HARDI) goes beyond these limitations and ranges from more or less immediate extensions of the DT model to multitensor models [3-5], continuous distributions of tensors based on deconvolution approaches [6-10] or generalized tensor models [11], to even more general, nonparametric techniques [12,13] like the popular Q-ball [14,15] or the recent improvements including solid-angle considerations [16-18]. Recently, multishell approaches [18-20] have allowed to overcome some of the limitations of HARDI techniques at the expense of acquiring far more diffusion directions.

Robust estimation in DTI usually requires long acquisition times due to the increase in the number of DWIs needed. Acquisitions may be even longer for HARDI or multishell techniques [21,22]. This can be problematic when there is an excessive motion of the patient undergoing the scan (a frequent situation for neurological patients or children who cannot be sedated). Severe motion during the scan can force it to be aborted or render the acquired DWIs useless. Thus, one would like to make only as few acquisitions as possible. An estimation framework providing real-time estimates as new DWIs are available would allow online checking of the quality of the estimations. This would deliver immediate feedback to help the practitioner decide whether the acquisition is sufficiently acceptable to stop the procedure.

Poupon et al. [21,22] proposed an interesting approach based on the Kalman filter for real-time estimation of the DT and the orientation distribution function (ODF) obtained from Q-ball imaging. The DT model, provided that certain signal-to-noise ratio (SNR) conditions are met and no positivity constraints exist, is linear and easily fits into the Kalman filtering framework. As for the reconstruction of the ODF following [23], Deriche et al. [24] demonstrated that the approach in Refs. [21,22] was suboptimal and proposed a regularized Kalman filter that nicely addressed this issue. Brion et al. [25,26] recently proposed an improved version of the filters in Refs. [21,22,24]. In their work, the acquired DWIs are previously denoised in real time by means of the signal estimator proposed in Ref. [27]. This way, the Kalman filter benefits from the higher SNR of the observed data, yielding a performance improvement for both DT and ODF estimation.

The authors of Refs. [21,22], however, focus on the realtime aspect of the general algorithm, and thus, they do not elaborate on the specific noise statistics of the DT model. In their estimator, the same variance is considered for each logarithmic DWI signal (log-DWI hereafter), and this turns out not to be true [2,28]. With this constant variance assumption, the estimator proposed in Refs. [21,22] behaves as a sequential ordinary least squares (OLS) algorithm, which is suboptimal for this application. The method in Refs. [25,26] also behaves as a sequential OLS since it considers that the noise variance after signal restoration is the same for all the restored log-DWIs. If this assumption is not valid before signal denoising, it will remain the same for the restored data. Thus, the OLS is also suboptimal in this case.

The batch (offline) OLS estimator can be shown to be the best linear unbiased estimator (BLUE) for the linear model provided that the underlying noise is uncorrelated (with the same variance for each log-DWI) and has zero mean [29]. For single-coil acquisitions, where the signal can be modeled as Rician [30], the noise in each gradient image is assumed to be independent, but the variance suffers nonnegligible changes across log-DWIs. Salvador et al. [2] proposed an improvement to DT estimation in single-coil acquisitions based on LS. Since no constant variance can be assumed, those measurements with higher noise variance are less reliable. A strategy giving higher relevance (weight) to those samples with lower variance would be preferable instead. Thus, the proposal in Ref. [2] was based on the weighted least squares (WLS) estimator, which is in fact the BLUE under these conditions<sup>1</sup>.

It can be demonstrated that the optimal weights for the WLS estimator are the inverses of the noise variances associated to each log-DWI measurement, so a formal noise characterization of the linearized DT model is necessary. In Ref. [2], this problem was solved by assuming that the variance of the logarithmic observations in the Rician model is inversely proportional to the squared amplitude of the corresponding DWI signal. Though the authors only provided empirical evidence, it is an excellent approach which has been analytically solved in Ref. [28]. When the data have been previously denoised, the noise characterization depends on the specific filter employed for restoration, although, in most practical cases, the dependence with the DWI amplitudes remains the same.

In this paper, we address the problem of optimal real-time estimation in single-coil DT-MRI acquisitions. A strategy based on real-time signal restoration is proposed to incorporate time-varying noise information to the online estimation process. Based on this strategy, we propose a sequential WLS estimation framework which can be used with either directly measured data or the real-time restored data as inputs, achieving the BLUE in both contexts. A comparative analysis over both synthetic and real data shows

<sup>&</sup>lt;sup>1</sup> In the case of simultaneous acquisition and parallel reconstruction schemes (pMRI), the noise is no longer Rician [31–33], and the bias in WLS estimation is relevant as shown in Ref. [28]. Thus, although the WLS is still applicable, it is not the BLUE for pMRI schemes.

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