

PARAMETER ESTIMATION ANALYSIS OF DIFFUSION-WEIGHTED MRI PROTOCOLS USED FOR SOFT TISSUE FIBER RECONSTRUCTION

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INTRODUCTION

Quantitative biomedical imaging often involves the estimation of biophysically relevant parameters from a series of images by integrating our knowledge of the underlying physics of the problem into the image post-processing, thereby solving inverse problems. Since the observation that magnetic resonance imaging (MRI) can be made sensitive to water diffusion in tissues [1], a plethora of work has focused on using diffusion-weighted magnetic resonance imaging (DWMRI) to track fibers non-invasively in biological soft tissue. In the study of the central and peripheral nervous system, DWMRI can provide the distribution and orientations of neuron bundles inside elementary volumes (voxels), as well as estimates of the diffusion characteristics within brain compartments (axons, extra-axonal medium) [2], while its application in skeletal muscle studies recovers the orientation of myofiber bundles [3]. The sizes of individual axons and myofibers (both $< 50 \mu\text{m}$) typically fall under the spatial resolution used in DWMRI (about 1 mm for clinical systems), thus some modeling is required to extract quantitative sub-voxel information.

DWMRI produces maps of the echo attenuation, which depend on the local diffusion process and are indexed by a vector in \mathbf{q} -space corresponding to the experimental parameters [4]. Different modalities exist for post-processing, and diffusion tensor imaging (DTI), an anisotropic unrestricted diffusion model, is the most commonly used. DTI reconstructs the local “apparent diffusion tensor” (ADT, symmetric 3×3 matrix), by fitting the echo attenuation, E , to a 3-D Gaussian function of \mathbf{q} , E_{DTI} [2]. The fiber orientation angles are identified with the eigenvector corresponding to the ADT maximum eigenvalue. The \mathbf{q} -space sampling schemes have typically been chosen independently of the post-processing models [5]. We propose to investigate the

advantages of using model-based optimal sampling schemes for the case where it is known *a priori* that the fiber orientations are within a finite region.

METHODOLOGY

For analysis, the physical model consists of a bundle of impermeable water-filled cylindrical fibers in the voxel of interest, which is the restricted diffusion model used for the quantitative analysis of \mathbf{q} -space MRI data (QUAQ) in [6]. The analytical expression for the measured normalized echo attenuation in \mathbf{q} -space, E_{Q} , for QUAQ is obtained by solving the diffusion equation [7], and depends on four model parameters – molecular self-diffusion coefficient D , individual fiber diameter a , and orientation angles $(\theta_{\text{F}}, \phi_{\text{F}})$ – while the model parameters for E_{DTI} are the six independent coefficients of the ADT. The sensitivity coefficients for each fitting parameter at the sampling points can be computed, and arranged into a sensitivity matrix \mathbf{X} . The sampling strategy that maximizes $\chi_1 = \det(\mathbf{X}^T \mathbf{X})$, is such that the correlation of the sensitivity coefficients between parameters and the size of the confidence intervals for the estimated parameters are minimized [8]. A spacing constraint is added in the form of a metric χ_2 and a Lagrange multiplier λ , so that the final function maximized via the gradient method is $\chi = \chi_1 + \lambda \chi_2$. The sampling points are restricted to be on a sphere in \mathbf{q} -space, as in current imaging protocols.

The metric χ_1 can be normalized by using $\chi_{1,\text{min}}$, the value obtained for the minimum number of sampling locations after optimization (set S_{min} , with N_{min} locations) for which the inverse problem can be solved, and the number of model parameters M . The normalized metric, $\chi_1^* = (N_{\text{min}}/N)^M \chi_1 / \chi_{1,\text{min}}$, is such that $\chi_1^* = 1$ when the locations in S_{min} are sampled repeatedly, and allows the comparison of sampling schemes.

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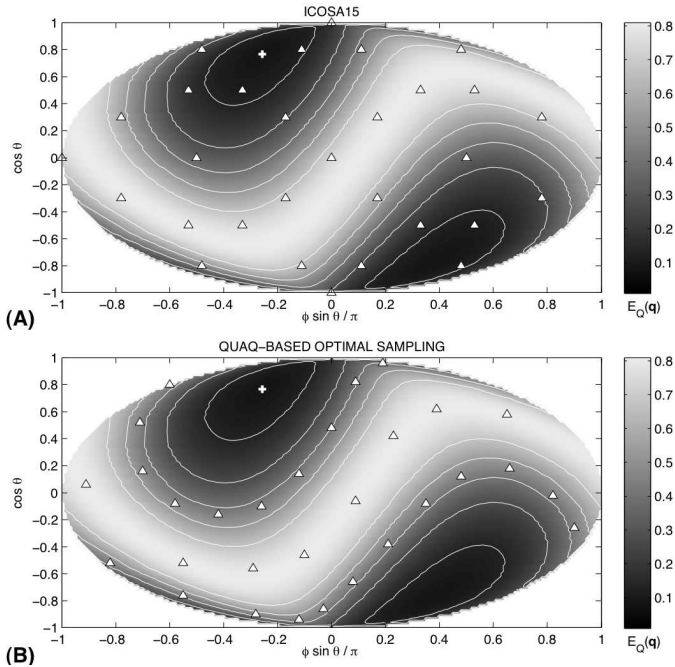


Figure 1. 30-point sampling schemes on a sphere in q -space: (A) ICOSA15; (B) QUAQ-based optimal sampling. The cross indicates the fiber orientation used for optimization.

RESULTS

The resulting model-based optimized sampling strategy using 30 q vectors for the QUAQ model is shown in Fig. 1 ($\lambda = 0.25$), and compared with a relatively uniform sampling scheme (based on an icosahedron, ICOSA15). The improvement ratio for χ_1 between the optimal sampling to ICOSA15 is 2.79. Monte Carlo simulations using 400 trials reveal that the QUAQ-optimized sampling scheme leads to a significant improvement in terms of the spread of the results for the fiber orientations of about 30%.

Model-based optimal sampling strategies would be used when *a priori* knowledge that the fiber orientations are within a finite region is available. They can be compared to existing protocols by plotting the value of χ_1^* , which only depends on the angle α between the fiber orientation used for the optimization and the actual fiber orientation, as in Fig. 2 (by symmetry, $\alpha \in [0, \frac{\pi}{2}]$). ICOSA15 is used for any fiber orientation, and χ_1^* varies between 0.3 and 0.5. The QUAQ-based optimal sampling scheme yields χ_1^* values that are above 0.3 for deviation angles $\alpha \leq \frac{2\pi}{5}$, and χ_1^* values that are above 0.5 for deviation angles $\alpha \leq \frac{\pi}{8}$.

Model-based optimized sampling schemes appear to be more sensitive than traditional sampling schemes for a large range of possible fiber orientations, and therefore can produce parameter estimates with higher confidence. Experiments will be performed at the Biomedical Imaging Research Center at MSU (<http://www.birc.msu.edu>) for validation.

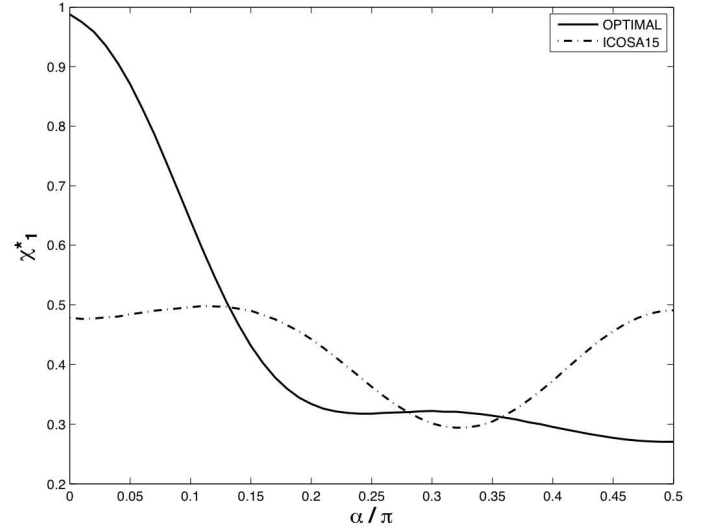


Figure 2. χ_1^* as a function of angle α between the assumed and actual fiber orientation for ICOSA15 (dashed line) and QUAQ-based optimal sampling (solid line).

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