Q-Space Diffusion Weighted MRI Analyzed with Maximizing Rician Likelihood Improves Reliability and Tissue Contrast

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Introduction: Q-Space imaging is an analysis technique for diffusion weighted MRI (DWI) data [1] that shows great promise as a tool to study tissue microstructure [2]. Rather than simply assuming a Gaussian shape for the probability density function (PDF) for water diffusion, q-space analysis allows experimental determination of the PDF itself. The PDF is the probability that a spin diffuses a particular distance from its initial position during the DWI experiment. To date, q-space studies reported in the literature have used limited diffusion models (e.g., bi-exponential fits) to regularize noisy data prior to taking a Fourier transform to estimate the PDF. These models make *ad hoc* assumptions (e.g., censoring data near a "noise floor") and do not accurately account for the properties of Rician noise, which can be large in high b-value DWI *in vivo*. Here, we present a robust q-space M-estimator for PDFs based on a maximum likelihood (ML) method. Via simulation we show that our method, which explicitly accounts for the noise behavior in magnitude DWI data, estimates PDF-contrasts (e.g., mode probability, P0, full width at half maximum, FWHM, and the root mean square displacement, RMSD) that are closer to their true (i.e. noise-free) values. When applied to an *in vivo* DWI dataset in the human spinal cord, our method improves the reliability of PDF estimation and increases tissue contrast.

Methods: Q-space Estimation by Maximizing Rician Likelihood (QEMRL) extends a recently presented ML approach for diffusion tensor estimation [3]. The PDFs are parameterized by a positive definite mixture of Gaussian distributions that quadratically spans a physically realistic range of diffusivities ($3x10^{-5}$ to $3x10^{-3}$ mm^2/s). In this study, 15 basis functions are used. Huberization (truncation) of the likelihood measure reduces the impact of artifacts; the truncation point is adaptively determined from the data. The ML solution is numerically found by a coordinate descent Nelder-Mead simplex algorithm [3]. PDF-derived contrasts are Wiener filtered to improve the signal to noise ratio [5]. Results from QEMRL were compared to a traditional bi-exponential (Bi-Exp) q-space analysis method. The mean squared error (MSE) was computed between the results from each method and the simulated true signal. Simulations were performed with two-component exponential mixtures (with diffusivities drawn at random from $3x10^{-5}$ to $3x10^{-3}$ mm^2/s). Each simulation consisted of two repetitions of 32 data points that linearly spanned the signal decay curve from q=0 to 400 cm^{-1} at an SNR of 7:1 on the q=0 images. The QEMRL technique was also applied to DWI acquired in the human spinal cord in vivo. Four repetitions of a standard q-space DWI protocol were acquired for a healthy volunteer (male, 26 y/o) on a 3T Philips MR scanner. Briefly, 30 axial slices were acquired perpendicular to the long axis of the spinal cord covering C2 to C6 (1.3x1.3x3.0 mm, FOV=84x84x90 mm, matrix=64x64, 32 linearly spaced q-values from 0 to 414 cm^{-1}) with single-shot EPI (SENSE = 1.8, TR/TE = 7000/106 ms). To improve SNR and mitigate the impacts of artifacts, each DW image was collected with diffusion weighting along two orthogonal directions ($[G_x, G_y, G_z]$ = [1,1,0] and [1,-1,0]) with a total acquisition time of ~10 min. The SNR was ~7:1 on the q=0 images.

Results and Discussion: In simulation, QEMRL reduced the median MSE on the computed PDF by 166% (25^{th}-75^{th} quantiles: 22-600%) compared to the Bi-Exp method. For simulations that used low diffusivities (representative of white matter, WM) (**Fig. 1**). QEMRL offered less of an improvement over Bi-Exp (90%), which is to be expected as the bi-exponential model contains a parsimonious representation of the truth model when little Rician bias is present. However, for simulations that used high diffusivities (representative of gray matter, GM) (**Fig. 2**), QEMRL was able to more accurately account for the bias due to the "noise floor" and offered substantial improvements (230%). In the *in vivo* experiments, QEMRL more clearly reveals GM/WM contrast in the cervical spinal cord in the P0, FWHM, and RMSD contrasts (**Fig. 3**). QEMRL decreased scan-rescan variability in the spinal cord by 23% for P0, 18% for FWHM, and 26% for RMSD. These contrasts may be fused into a color image (**Fig. 4A**) that imparts greater information about the PDF (and tissue architecture) than any single contrast. With this visualization technique, the differences between narrow and wide PDFs and the presence of heavy tails can be readily appreciated (**Fig. 4B**).

QEMRL improves the accuracy and reliability of PDFs derived from q-space DWI by accounting for the Rician noise properties in magnitude images. Specifically, while the Rician bias at low SNR causes the PDFs computed with the Bi-Exp method to be artificially narrow (**Fig. 2**), QEMRL produces PDFs that more closely resemble the true PDF. Outlier rejection and stable numerical optimization reduce the impact of imaging artifacts and result in increased empirical q-space PDF reliability. Incidentally, QEMRL estimates a projection of the PDF onto a finite basis set, which has a physical interpretation as the mixture of diffusion compartments and may be useful as a biomarker for micro-structural changes. An additional benefit is that the basis functions in QEMRL can be analytically transformed into PDFs, without the need for a numerical Fourier transform (which can introduce ringing artifacts in data series that are truncated). It is also worth noting the GM heterogeneity in the RMSD images seen in the posterior dorsal horns compared to the dorso-lateral anterior horn, which would not be apparent if the RMSD were derived from the FWHM. This contrast may be indicative of different cytoarchitecture and structure within the gray matter, for example, due to the merging of the dorsal root collaterals. Analysis of q-space DWI data with QEMRL provides robust estimates of the PDF for diffusion. The estimation of noise properties and the removal of their influence may allow acquisition at higher spatial resolution. Through improved estimation, QEMRL permits the wealth of information in the PDF to be more fully explored and utilized to assess microstructure in both healthy and diseased tissue.

References: [1] Cory, D.G., Garroway, A.N., MRM, 1990, 14:435; [2] Cohen Y., Assaf Y., NMR in Biomed., 2002, 15:516 [3] Landman et al., MMBIA/ICCV 2007 [4] Oppenheim et al. Discrete Time Signal Processing. 1999 [5] Press et al. Numerical Recipes. 2007

Fig 1. Simulated q-Space in White Matter

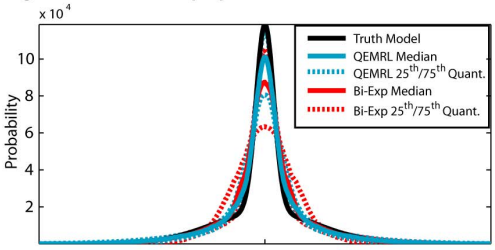


Fig 2. Simulated q-Space in Gray Matter

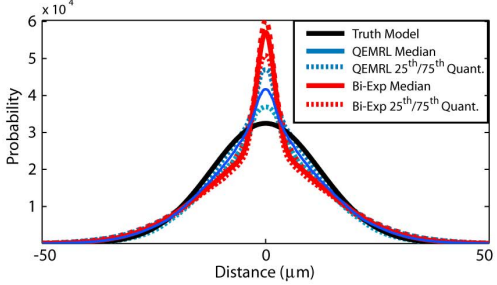
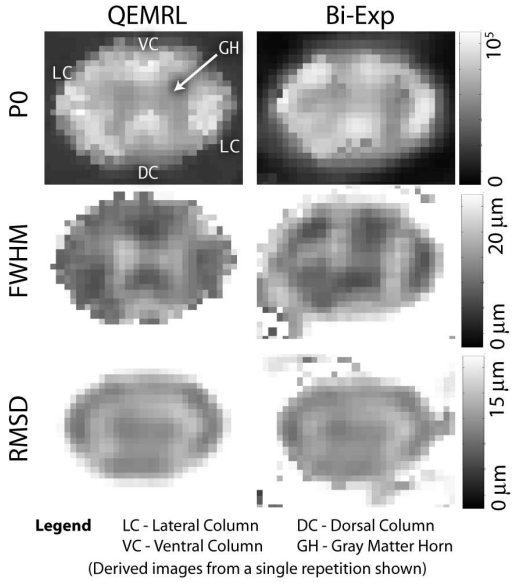
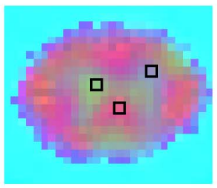


Fig 3. *In Vivo* Spinal Cord q-Space Imaging



(Derived images from a single repetition shown)

Fig 4A. PDF Interpretation



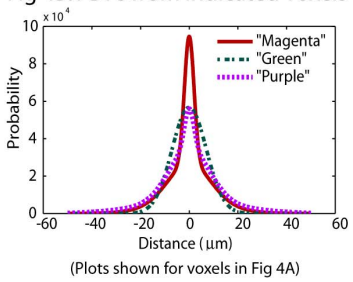
Interpretation

Magenta - Strongly restricted

Green - Weakly restricted, but few high diffusivities

Purple - Weakly restricted, with additional high diffusivities

Fig 4B. PDFs from indicated voxels



(Plots shown for voxels in Fig 4A)