An Application of Rician Cramer-Rao Lower Bound for Optimizing Gradient Schemes in Diffusion Tensor Imaging

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Outline

- Introduction
  - DTI, Rician noise, CRLB, optimization
  - Motivation, scope for optimization
- Experiments
  - Design, DTI protocol
- Results
  - Demonstration of improvement in estimation
- Conclusion

Introduction

- Diffusion Tensor Imaging (DTI)[1] is an advanced MRI technique which can quantify diffusivity of water in tissues.

- MR signal is modeled as a function of diffusion and experimental parameters. Noise is modeled as Rician since MRI data are magnitude of complex data

- Uncertainty in estimation of diffusion parameters depends on the choice of experimental parameters that can be optimized

- A Rician CRLB-based gradient scheme optimization[2] has been proposed and experimentally validated

[1] P. J. Basser, J. Matiello, and D. Le Bihan, "MR Diffusion Tensor Spectroscopy and Imaging", *J. Biophys.*, 1994, vol. 66, p 259-267.

[2] S. Majumdar, D. C. Zhu, S. S. Udpa, L. G. Raguin, "An Optimized Diffusion Gradient Scheme for Axisymmetric Diffusion Tensor Imaging of Spinal Cord Tracts", submitted to *IEEE Transactions on Medical Imaging*, under review.

DTI Signal

DTI signal: $$E = S / S_0 = \exp(-b\mathbf{g}^T D\mathbf{g}),$$

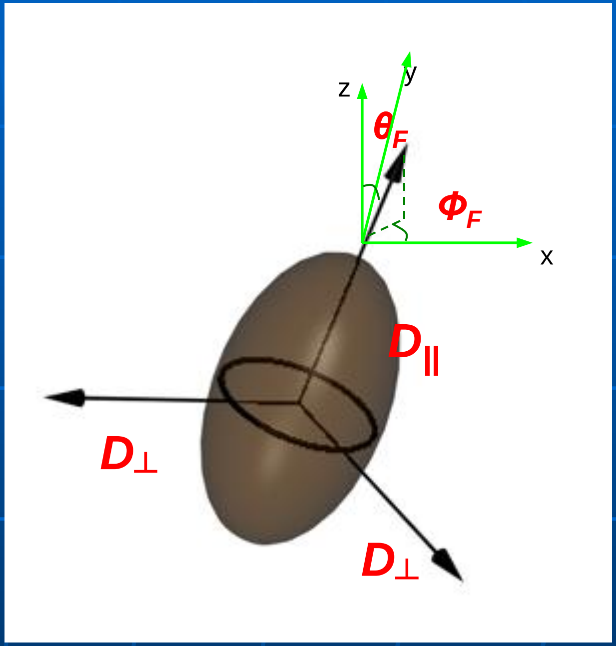
- **g** : diffusion encoding gradient direction.
- D : Diffusion tensor matrix
- S : Diffusion-weighted MRI signal
- S_0 : Normalizing signal (MRI signal with no diffusion-weighting)
- *b* : sensitivity factor ("b-factor")

$$D = R^T D_0 R \quad R = R(\theta_F, \varphi_F),$$

$$D_0 = \begin{bmatrix} D_\perp & 0 & 0 \\ 0 & D_\perp & 0 \\ 0 & 0 & D_\parallel \end{bmatrix}$$ Axisymmetric diffusion tensor

Estimation parameters:

$$\beta = \{D_\parallel, D_\perp, \theta_F, \phi_F\}$$



Diffusion ellipsoid

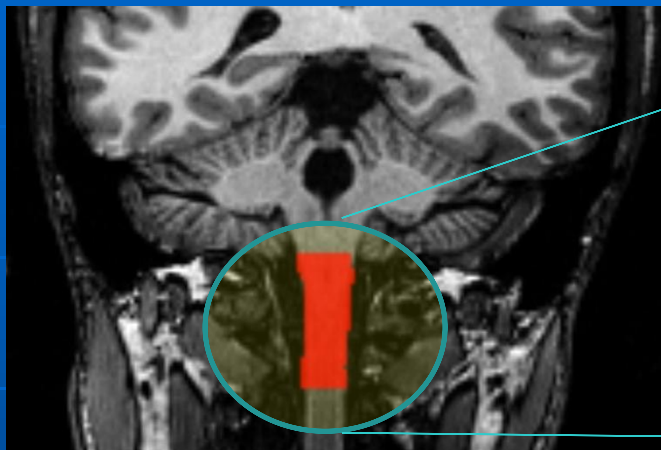
Noise model

- S, S_0 are magnitudes of complex MRI data
- Complex MRI data assume Gaussian noise, Magnitude MRI have Rician noise
- S_0 assumed to have high SNR
- Noise in DTI signal (echo attenuation), $E = S/S_0$, is also Rician

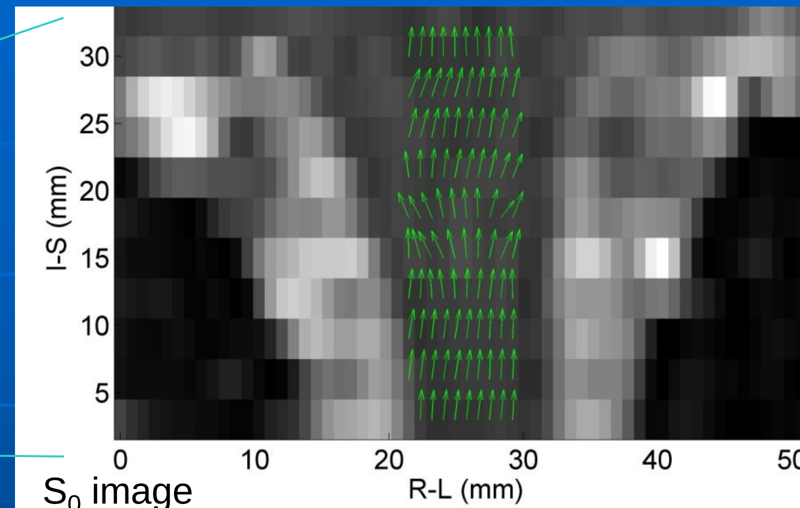
$$p(\hat{E} \mid E, \sigma^2) = \frac{\hat{E}}{\sigma^2} I_0\left(\frac{E\hat{E}}{\sigma^2}\right) \exp\left(-\frac{\hat{E}^2 + E^2}{2\sigma^2}\right)$$

I_0 is the zero-order modified Bessel function of the first kind.
$\hat{E}$ is the observed echo attenuation signal.
E is the model echo signal and σ^2 is the noise variance.

Motivation: Using *A Priori* Information

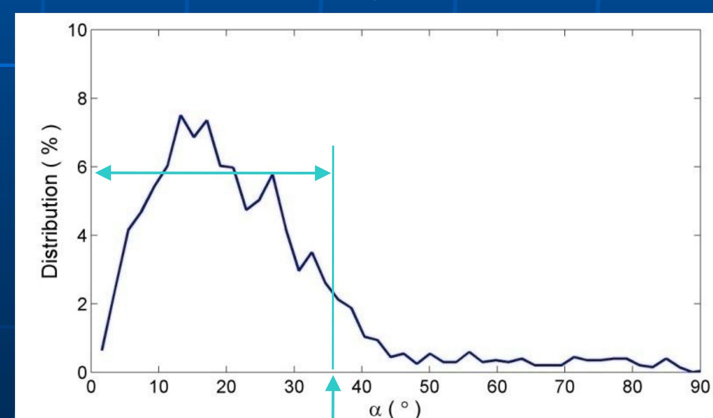


T1 image



S_0 image

For special structures such as spinal cord, most nerve fibers are oriented within ~ 35^0 of mean fiber orientation as obtained from preliminary studies.



35^o : at 80% cumulative distribution

A priori spread of fiber distribution ~ 35^o

→ Optimization of gradient directions → Reduced Uncertainty

CRLB

- Cramer-Rao Bound on Variance:

$$\Sigma(\hat{\beta}) - \mathrm{I}^{-1}(\beta) \geq \mathbf{0}$$

I : Fisher Information matrix

Σ : Covariance matrix of estimates

$$\Sigma_{CR}(\beta) = \mathrm{I}^{-1}(\beta) \qquad [\mathrm{I}(\beta)]_{jk} = -\left\langle \frac{\partial^2 \ln p(\hat{E})}{\partial \beta_j \partial \beta_k} \right\rangle$$

$\langle\ \rangle$ represents the expectation operation w.r.t. $p(\hat{E})$

Any minimum variance unbiased and efficient estimator should attain the covariance bound on estimation

Rician CRLB

- Fisher information matrix for Rician noise[1]:

$$[\mathrm{I}(\beta)]_{jk} = \sum_{i=1}^{N} \frac{1}{\sigma^2} \frac{\partial E_i}{\partial \beta_j} \frac{\partial E_i}{\partial \beta_k} (E_i{}^2 - Z_i)$$

$$= \sum_{i=1}^{N} \frac{1}{\sigma^2} (E_i - W_i) \frac{\partial E_i}{\partial \beta_j} (E_i + W_i) \frac{\partial E_i}{\partial \beta_k}$$

where $W_i{}^2 = Z_i$ and $Z_i = \int_0^\infty E_i{}^2 I_1^2\left(\frac{E_i \hat{E}}{\sigma^2}\right) I_0^{-2}\left(\frac{E_i \hat{E}}{\sigma^2}\right) p(\hat{E})\, d\hat{E}$

$$\boxed{\Sigma_{CR}(\beta) = \mathrm{I}^{-1}(\beta) = \sigma^4 (\mathbf{X}_1{}^T \mathbf{X}_2)^{-1}}$$

$$[\mathbf{X}_1]_{ij} = (E_i - W_i) \frac{\partial E_i}{\partial \beta_j}$$

$$[\mathbf{X}_2]_{ij} = (E_i + W_i) \frac{\partial E_i}{\partial \beta_j}$$

[1] D. C. Alexander. A General Framework for Experiment Design in Diffusion MRI and Its Application in Measuring Direct Tissue-Microstructure Features. Mag. Res. Med., 60:439–448, 2008.

Optimization

- For a nonlinear least-squares estimation, the Cramer-Rao bound[1] on estimator covariance:

$$\Sigma_{CR} = \sigma^4 (\mathrm{X}_1{}^{\mathrm{T}} \mathrm{X}_2)^{-1}$$

Taking determinant,

$$\det \Sigma_{CR} = \frac{\sigma^{4M}}{\det(\mathrm{X}_1{}^{\mathrm{T}} \mathrm{X}_2)}$$

$$\boxed{\det \Sigma_{CR} \downarrow \; = \det(\mathrm{X}_1{}^{\mathrm{T}} \mathrm{X}_2) \uparrow}$$

<u>Optimization problem:</u> Solve for Ω_{robust} := {$\mathbf{g}_i$, $i \in$ [1, N]}, N= number of gradient directions

$$\boxed{\Omega_{robust} = \arg[\min_{\mathbf{g}} (\max_{\{\theta_F, \phi_F\} \in \Lambda} f)], \quad f = 1/\det(\mathrm{X}_1{}^{\mathrm{T}} \mathrm{X}_2)}$$

- “Minimax” technique; robust w.r.t. fiber angle
- Use of *a priori* information in *f* and *Λ* and Rician formulation

[1] S. Majumdar, D. C. Zhu, S. S. Udpa, L. G. Raguin, “An Optimized Diffusion Gradient Scheme for Axisymmetric Diffusion Tensor Imaging of Spinal Cord Tracts”, submitted to IEEE Transactions on Medical Imaging, under review.

Region of Interest

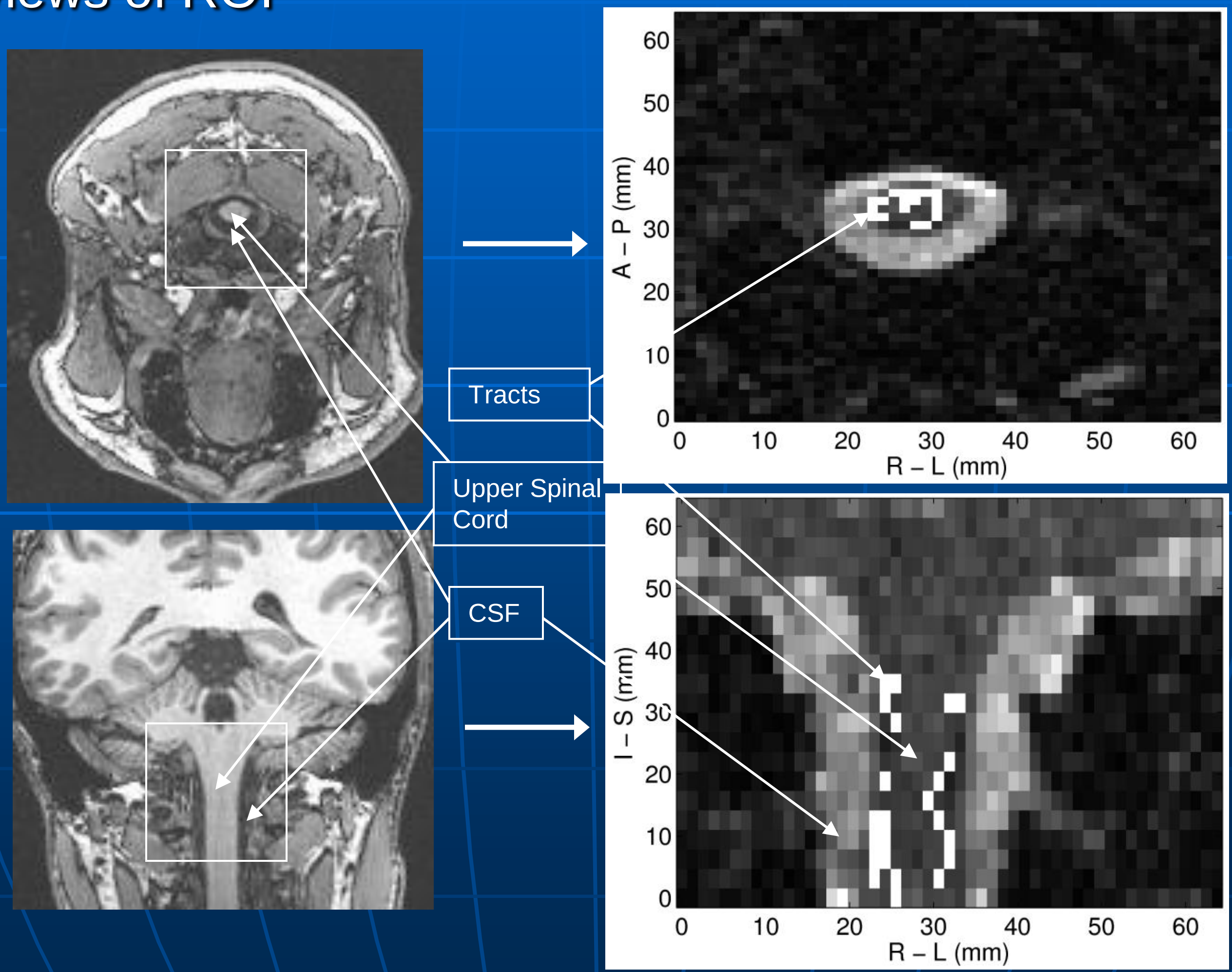
- Upper spinal cord tracts selected as imaging target
  - Simple structure, but difficult to image due to small cross-section
  - SNR issues at high resolutions due to small voxel size
  - Ideal target to apply optimized DTI procedure
    - Diffusion parameter estimates have lower overall variance
    - effective SNR improved by optimization
    - Similar high resolution imaging achieved as in standard DTI procedure

Region of Interest

- Slice views of ROI

T1 image
Axial view

T2 image
Axial view



T1 image
Coronal
view

T2 image
Coronal
view

Experiment Design

Optimization procedure:

- Preliminary scan to collect *a priori* information
- Gradient scheme optimization
- Data collection and analysis with the optimized DTI protocol

Experiment Design

- Preliminary scan to collect *a priori* information:
  - Obtain an approximate
    - mean of model parameters
    - range of fiber orientations
  - Used to compute inputs for gradient optimization procedure
- Scan protocol: Short DTI (1 min 52 s), 15 diffusion directions, b = 1000 $s^{-1}mm^2$, MF15
- Post-processing: ROI extraction, computation of the mean of model parameters and fiber angular range

Experiment Design

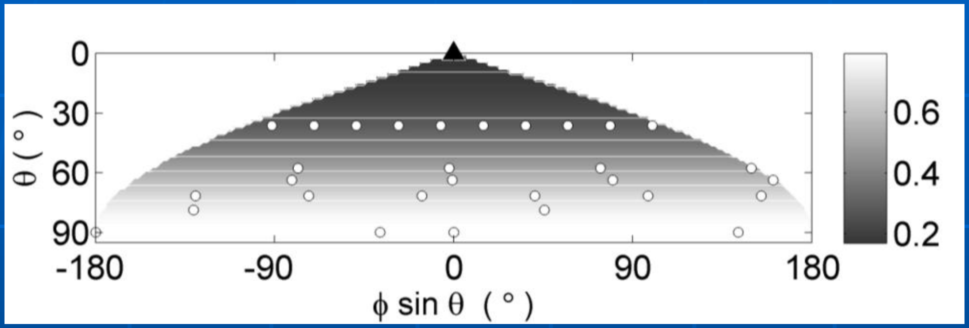
- Gradient scheme optimization
  - Solve for Ω_{robust}

$$\Omega_{robust} = \arg[\min_{\mathbf{g}}(\max_{\{\theta_F,\phi_F\}\in\Lambda} f)], \quad f = 1/\det(\mathbf{X}_1{}^T\mathbf{X}_2)$$

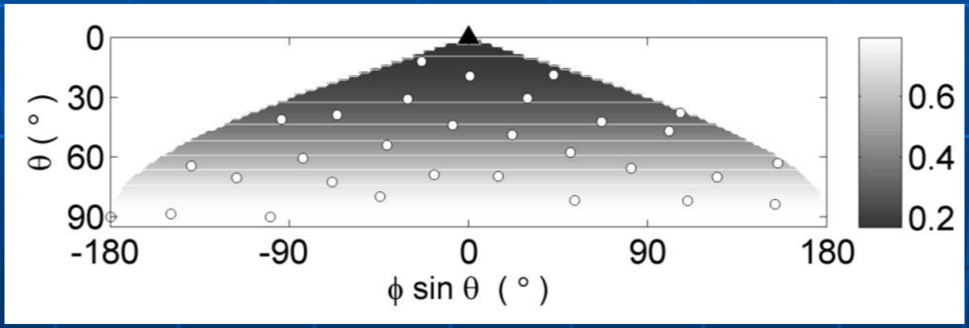
- $X_1(\beta, \Omega)$, $X_2(\beta, \Omega)$: functions of both model parameters (β) and gradient scheme (Ω)
- Mean of model parameters from preliminary scan used as β
- Λ : range of fiber angles also computed from preliminary scan

Experiment Design

- Gradient schemes (OPT30 and MF30):



OPT30 scheme (Λ = 35º)



MF30 scheme

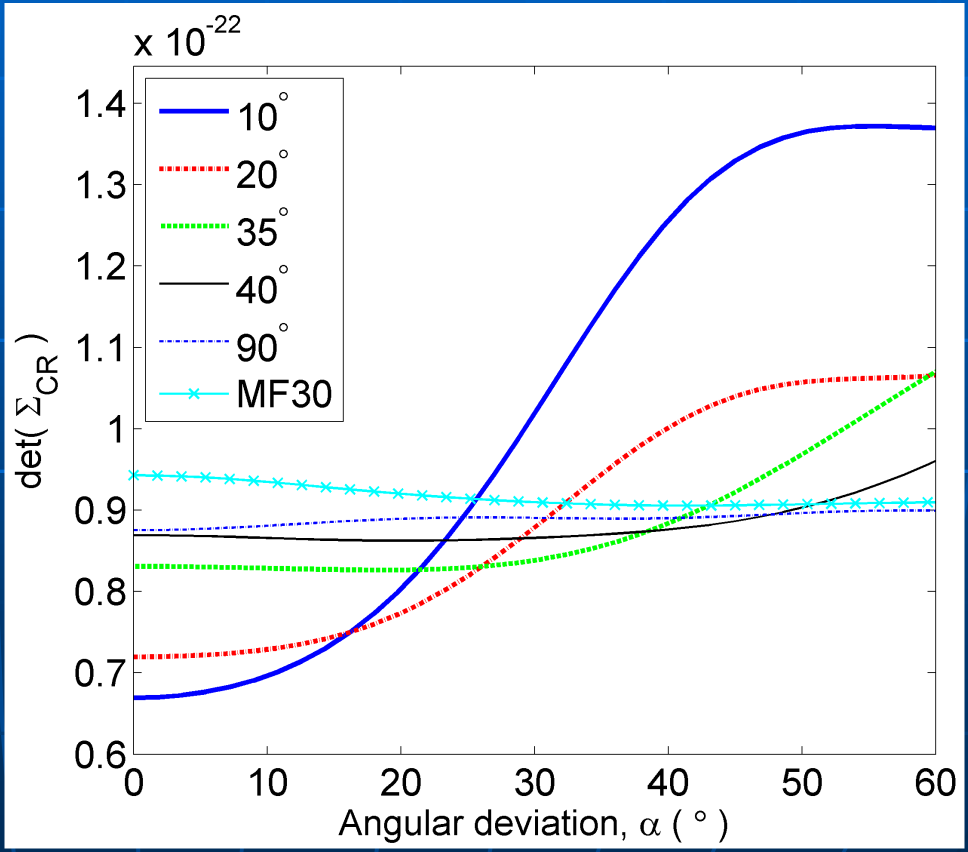
Gradient directions (white circles) on 2D (opened hemisphere), underlaying echo signal for range of gradient directions (g = {θ,φ}). Black triangle represents the mean fiber orientation.

Experiment Design

- Optimized scheme performance prediction using CRLB

Small Λ = Specific performance w.r.t. fiber angle

Large Λ = Generic performance w.r.t. fiber angle



Variation of overall uncertainty for 30-direction optimal gradient schemes with changing cone angles (Λ = [10º − 90º]) and the MF30 scheme for the Rician noise case. Noise level, σ = 0.1.

Experiment Design

- Data collection and analysis with the optimized DTI protocol
  - DTI scan protocol using optimized gradient scheme: full DTI (7 min 21 s), 30 diffusion directions, b = 1000 $s^{-1}mm^2$, OPT30 scheme (for test). MF30 (for comparison).
  - Dataset: 6 DTI dataset for OPT30 and MF30 each; bootstrapped to 6000 datasets for variance computation. Maximum likelihood estimator used for estimation

Analysis

- What to expect:
  - Reduction in uncertainty in parameter estimation
  - Rician CRLB-based predicted performance match estimation
- What is the effect on:
  - Bias
  - Overall SNR of the image dataset
- What are the sources of error?

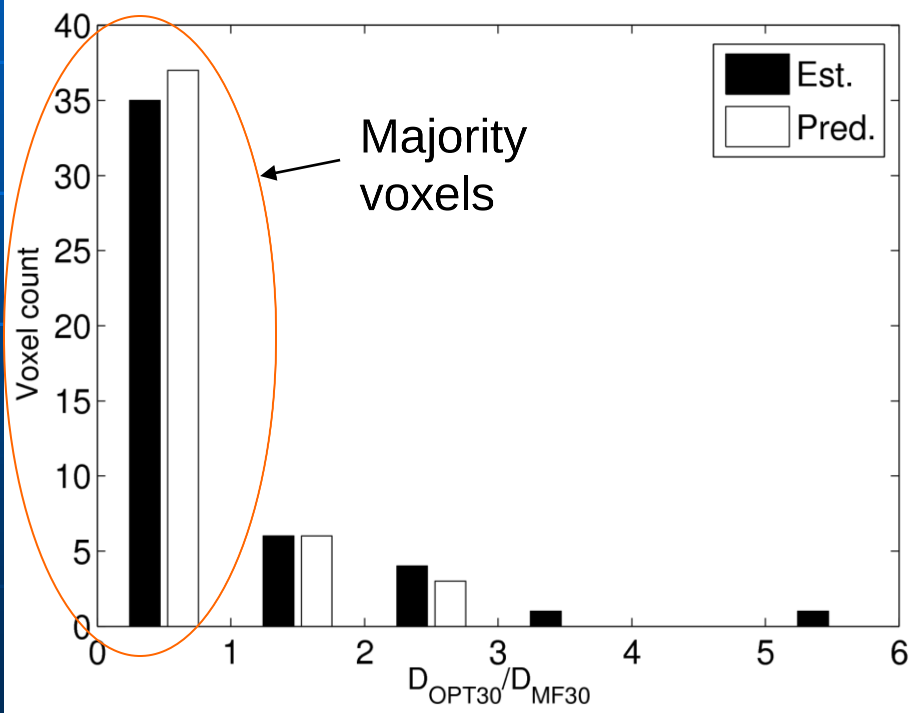
Results

- Reduction in estimation uncertainty: $D_{OPT30} / D_{MF30} < 1$

$$D = \begin{cases} \det \Sigma, \text{for estimation} \\ \det \Sigma_{CRLB}, \text{for prediction} \end{cases}$$

D_{OPT30} = OPT30 scheme

D_{MF30} = MF30 scheme



Voxel distributions w.r.t. ratio of overall uncertainty (D_{OPT30} /D_{MF30}) for one subject. We find that the majority of voxels lie in the less than unity range and are predicted so based on CRLB values.

Results

- Estimation results:
  - Total spinal cord tract voxels selected = 46
  - Percentage success in voxels = 76 %
  - Predicted percentage success = 80 %
  - Mean D_{OPT30}/D_{MF30} in successful voxels = 0.346 (< 1)
  - Mean D_{OPT30}/D_{MF30} in successful voxels = 0.361 (< 1)
- Effect on bias and SNR:
  - Mean angular deviation for OPT30 = $2.9^{o} \pm 1.8^{o}$
  - Mean angular deviation for MF30 = $3.0^{o} \pm 1.2^{o}$
  - Mean diffusivity $D_{||}$ for OPT30 = 2.354×10^{-3} mm^2 s^{-1}
  - Mean diffusivity $D_{||}$ for MF30 = 2.334×10^{-3} mm^2 s^{-1}
  - Mean diffusivity $D_{\perp}$ for OPT30 = 0.259×10^{-3} mm^2 s^{-1}
  - Mean diffusivity $D_{\perp}$ for MF30 = 0.269×10^{-3} mm^2 s^{-1}
  - Mean effective SNR for OPT30 = 5.514
  - Mean effective SNR for MF30 = 5.079

Discussion

- Sources of error:
  - Crossing fiber effects
    - DTI signal formulation models single fiber
    - Crossing fibers at neuronal junctions in the spinal cord will introduce errors/uncertainty in estimation
    - Possible solution: Use model-based crossing fiber signal formulation (BEDPOST) or model-free formulation (Q-ball imaging)
  - Partial volume effects
    - Heterogeneity within voxel: Voxel partially on the tract tissue (white matter), the grey matter (neuron cell bodies) or CSF
    - DTI signal gets averaged within voxel over the various tissue types
    - Possible solution: Incorporate volume fraction in the voxel for white and grey matter and model expected signal from each separately

Conclusion

- Majority of the voxels selected in the upper spinal cord tracts show reduction in uncertainty using OPT30 as compared to MF30(standard) using the Rician CRLB-based optimization
- Performance of the optimized gradient scheme can be predicted before conducting the experiment using the Rician CRLB formulation
- Optimized gradient scheme can be designed to perform for a range of fiber orientations which is obtained from prior information
- Optimized scheme does not affect the bias differently from the standard MF30 scheme and provides better effective SNR
- Reduced estimation uncertainty can imply applications in spinal cord MRI studies for detection of diseases, such as multiple sclerosis and myelopathy

Thank you!