Error Propagation Framework for Diffusion Tensor Imaging

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INTRODUCTION In a typical Diffusion Tensor Imaging (DTI) experiment, generally only one estimate of a tensor is obtained in each voxel. Since the tensor estimate itself is derived from the noisy diffusion-weighted (DW) signals, here we derive the SD of the tensor and tensor-derived quantities by error propagation from the DW signals. This error propagation technique relies on the nonlinear least squares (NLS) objective function of DTI. This proposed technique is shown to produce precise estimate of the SD of FA. The simulation results show that the variability in tensor-derived quantities is largely due to the variability in the reference signal if the DTI model includes the reference signal as a parameter to be estimated. A simple procedure is provided to ameliorate this problem.

METHODS Let $f = \frac{1}{2}\sum_{i=1}^{n}(s_i - \alpha \mathrm{Exp}(\sum_{j=1}^{6} X_{ij}\beta_j))^2$ be the NLS objective function where s_i and α are the DW and reference signals, respectively. The DTI design matrix is $\mathbf{X}$ and $\boldsymbol{\beta} = [D_{xx}, D_{yy}, D_{zz}, D_{xy}, D_{yz}, D_{xz}]^T$ is the diffusion tensor parameter vector. Let g be any smooth function of $\boldsymbol{\beta}$ and let $\hat{\boldsymbol{\beta}}$ be the NLS estimate. The connection between the uncertainty of g and of f can be represented pictorially. We first translate our coordinates to a region around $f(\hat{\boldsymbol{\beta}})$ and examine the mapping of the variability of f to a region around $g(\hat{\boldsymbol{\beta}})$ (Fig 1 A-B). By 2nd-order Taylor expansion, the change in f is $\Delta f(\boldsymbol{\delta}) = f(\hat{\boldsymbol{\beta}} + \boldsymbol{\delta}) - f(\hat{\boldsymbol{\beta}}) \approx \frac{1}{2}\boldsymbol{\delta}^T \nabla^2 f(\hat{\boldsymbol{\beta}})\boldsymbol{\delta}$ where $\boldsymbol{\delta}(\boldsymbol{\beta}) \equiv \boldsymbol{\beta} - \hat{\boldsymbol{\beta}}$ and $\nabla f(\hat{\boldsymbol{\beta}}) = \mathbf{0}$ because $\hat{\boldsymbol{\beta}}$ minimises f (Fig 1C). By 1st-order Taylor expansion, the change in g is $\Delta g(\boldsymbol{\eta}) = g(\hat{\boldsymbol{\beta}} + \boldsymbol{\eta}) - g(\hat{\boldsymbol{\beta}}) \approx \nabla_{\boldsymbol{\eta}}^T g \boldsymbol{\eta}$, where $\boldsymbol{\eta}$ is defined later. The Hessian matrix $\nabla^2 f$ is positive definite at $\hat{\boldsymbol{\beta}}$ and can be written as $\nabla^2 f(\hat{\boldsymbol{\beta}}) = \mathbf{Q}\boldsymbol{\Lambda}^{\frac{1}{2}}(\mathbf{Q}\boldsymbol{\Lambda}^{\frac{1}{2}})^T$ where $\mathbf{Q}$ is orthogonal and $\boldsymbol{\Lambda}$ is diagonal with positive elements. Therefore, $\Delta f(\boldsymbol{\eta}) = \frac{1}{2}\boldsymbol{\eta}^T\boldsymbol{\eta}$ where $\boldsymbol{\eta} \equiv (\mathbf{Q}\boldsymbol{\Lambda}^{\frac{1}{2}})^T\boldsymbol{\delta}$. In the $\boldsymbol{\eta}$ system, the change in f looks uniform in all directions of $\boldsymbol{\eta}$ since $\Delta f(\boldsymbol{\eta}) = \frac{1}{2}\boldsymbol{\eta}^T\boldsymbol{\eta}$ is the equation of a hyper-sphere (Fig 1E). To measure $\Delta g(\boldsymbol{\eta})$, $\boldsymbol{\eta}$ has to satisfy $\Delta f(\boldsymbol{\eta}) = \frac{1}{2}\boldsymbol{\eta}^T\boldsymbol{\eta}$ and be parallel to $\nabla_{\boldsymbol{\eta}} g$. Therefore, $\Delta g(\boldsymbol{\eta}) \approx (2\Delta f(\boldsymbol{\eta}))^{\frac{1}{2}} \| \nabla_{\boldsymbol{\eta}} g \|$ (Fig 1F). By a change of variable from $\boldsymbol{\eta}$ back to $\boldsymbol{\delta}(\boldsymbol{\beta})$ (Fig 1D-F), we arrive at the error propagation equation [1, 2]: $\Delta g(\boldsymbol{\delta})^2 \approx 2\Delta f(\boldsymbol{\delta}) \nabla_{\boldsymbol{\beta}}^T g(\hat{\boldsymbol{\beta}})[\nabla^2 f(\hat{\boldsymbol{\beta}})]^{-1}\nabla_{\boldsymbol{\beta}} g(\hat{\boldsymbol{\beta}})$. There is freedom in the choice of $\Delta f(\boldsymbol{\delta})$; we have adopted the following definition $\Delta f(\boldsymbol{\delta}) \equiv f(\hat{\boldsymbol{\beta}})/(n-p)$ where n-p is the number of degrees of freedom. This definition is convenient and intuitive because $2\Delta f(\hat{\boldsymbol{\beta}})/(n-p)$ is an estimate of the variance of the DW signals and, therefore, $\Delta g(\boldsymbol{\delta})^2$ is the variance estimate of g. The choice of p is 6 or 7 depending on whether the reference signal, α, is to be estimated.

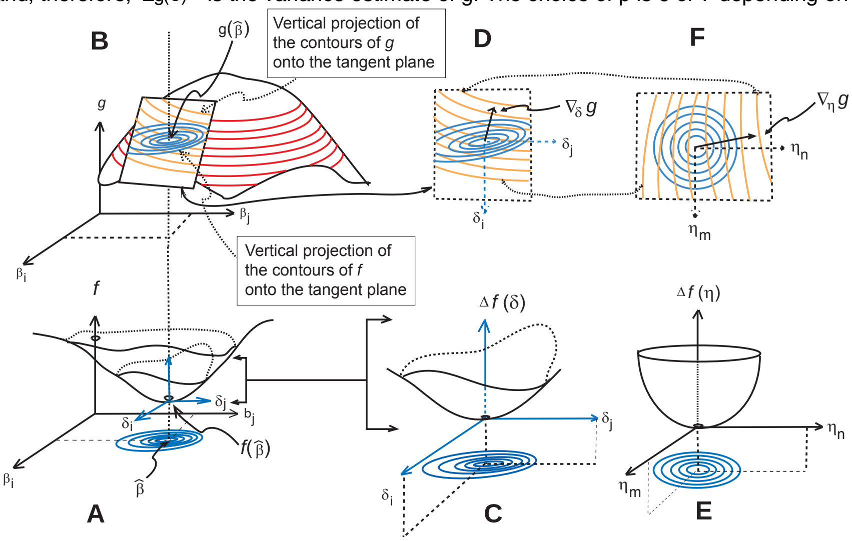

FIG 1. The pictorial representation of the error propagation framework

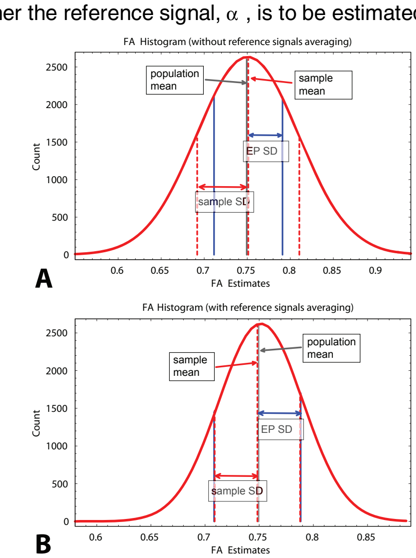

FIG 2. The FA histogram with sample SD and mean error-propagated (EP) SD of FA without reference-signal averaging (**A**), and with reference-signal averaging (**B**).

RESULTS AND DISCUSSION
We have presented a simple error propagation framework for DTI based on the nonlinear least squares objective function. This technique can be used not only to measure the variability of the tensor and tensor-derived quantities but also to guide experimental design. In terms of applications, this technique can generate the matrix perturbation used to analyze the variability of the major eigenvalue and of the eigenvector, and to DTI tractography. Regarding the design of experiments, we investigated how the variability of α affects the SD of FA. From 50,000 sets of $\{\alpha, s_1 \cdots, s_n\}$ which were generated from a single true tensor of FA = 0.74, Trace =2.19×10 mm^2/s with a 23 gradient directions of b-value = 1000 s/mm^2 and SNR=25, we carried out two procedures for comparison. The first procedure is the typical 7-parameter NLS estimation where tensor estimate is obtained directly from each set of $\{\alpha, s_1 \cdots, s_n\}$ and the sample SD of FA and mean value of the error-propagated SD's were calculated and shown in Fig 2A. The second procedure is similar to the first but each α in the 50,000 sets of $\{\alpha, s_1 \cdots, s_n\}$ is replaced by the mean value of those 50,000 α's (Fig 2B). The reduction of variability in SD of FA based on the second procedure is evident and the precision of the SD calculated from the proposed technique is noteworthy.

CONCLUSION An error propagation framework for DTI based on a NLS objective function is presented analytically and geometrically. This technique has wide applicability. Simulation results show variability in FA is mostly due to the reference signal. In other words, the design matrix for the typical 7-parameter estimation is not optimal. More studies are needed to investigate the optimal design for estimating the reference signal.

REFERENCES [1] Bevington PR et al. McGraw-Hill, New York,1992. [2] R.J. Barlow. Wiley, New York, 1989.