Ground-truth and Data Synthesis of

Simulated DW-MRI Brain Data Sets for Quantitative Evaluation of Estimated Fiber Orientations

Establishment of simulation ground-truth

A 28-year-old right-handed male volunteer without any history of neurological disease was scanned on a GE 3T HDxt scanner (General Electric, Milwaukee, WI, USA), equipped with an 8-channel head coil. The subject signed an informed consent form for which the imaging protocol was approved by the Institutional Review Board of the University of Southern California.

A DW data set was acquired by a twice-refocused pulsed-gradient spin-echo (PGSE) sequence with TE/TR = 83.4 ms/16100 ms, acquisition matrix = 128x128, ASSET acceleration factor of 2, voxel size = 2.4x2.4x2.4 mm, 60 contiguous slices, 150 diffusion gradient directions with diffusion-weighting b = 1000 s/mm^2, and 10 non-diffusion weighted volumes. The acquisition took approximately 43 minutes.

Without eddy-current or motion correction[1] the diffusion data set was processed by the probabilistic multi-fiber "ball and stick" method implemented in the program 'bedpostx', a part of the diffusion toolbox in the FMRIB Software Library (FSL v5.0.2.2; http://www.fmrib.ox.ac.uk/fsl; Behrens et al., 2003; Smith et al., 2004). Up to three fibers were estimated per voxel. To reduce the possibility of false minor fibers resulting from data over-fitting, a threshold of 0.1 was applied to second and third fiber volume fractions. Images of number of fibers/voxel were inspected to ensure known crossing regions (as explored later in Sect. 3.5) retained 2 or 3 fibers after thresholding.

Our synthetic DW data sets are derived from the fiber volume fractions (f_1, f_2, f_3) and orientations ($\boldsymbol{v_1}$, $\boldsymbol{v_2}$, $\boldsymbol{v_3}$) estimated for each voxel and output by 'bedpostx'. Because of differences between the "ball and stick" model and our data synthesis equation, Eq. (1), the isotropic compartment fraction (f_0) was not used. Instead, the fiber fractions were normalized ($\sum_{k=1}^{3} f_k = 1$) and f_0 was iteratively determined per voxel: beginning with $f_0 = 0$, f_0 was gradually increased until the generalized fractional anisotropy (GFA) (Tuch, 2004) of the synthetic data reduced to within 0.00005 of the GFA of the corresponding *in-vivo* data.

Anatomical T_1-weighted SPGR images (TE/TR = 2.856 ms/7 ms) were acquired with a voxel size of 1x1x1 mm. The anatomical volume was registered to the mean non-diffusion weighted volume and subsequently segmented into white-matter (WM), gray-matter (GM) and cerebrospinal fluid (CSF) using default options in SPM (SPM v8; http://www.fil.ion.ucl.ac.uk/spm; Friston et al., 1995). The high-resolution tissue probability maps were then down-sampled by linear interpolation to the resolution of the DW data, and each voxel was classified as WM, GM, or CSF according to its most probable tissue type.

Diffusion-weighted data synthesis

Diffusion-weighted data were synthesized according to a multi-tensor model (Alexander et al., 2001; Tuch et al., 2002) accommodating three crossing fibers per voxel in addition to a free-diffusion compartment. For any given voxel the signal model is:

$$S(b, \boldsymbol{g}_j) = S_0\left[f_0 \exp(-bD_0) + (1 - f_0)\sum_{k=1}^{3} f_k \exp(-b\boldsymbol{g}_j^T \boldsymbol{D}_k \boldsymbol{g}_j)\right] \qquad (1)$$

where S_0 simulates T_2-weighting, f_0 and D_0 are the volume fraction and diffusivity, respectively, of the isotropic free-diffusion compartment, f_k and $\boldsymbol{D_k}$ are the volume fraction and diffusion tensor, respectively, of the k^{th} fiber in

[1] The diffusion-weighted data was inspected for eddy-current and motion related artifacts, and only minor artifacts were found. Even so, we evaluated eddy-current correction but the post-processing caused smoothing of the data which we considered detrimental to resolving crossing-fibers.

the voxel, b is the diffusion-weighting, and $\boldsymbol{g}_j$ is a unit vector representing the j^{th} gradient direction. Altogether the volume fractions satisfy $f_0 + (1 - f_0)\sum_{k=1}^{3} f_k = 1$.

Each fiber's diffusion tensor, $\boldsymbol{D}_k$, was computed by rotating a default single tensor, $\boldsymbol{D}_{\boldsymbol{x}}$. That is $\boldsymbol{D}_k = \boldsymbol{R}_{\boldsymbol{x}}(\boldsymbol{v}_k)\boldsymbol{D}_{\boldsymbol{x}}\boldsymbol{R}_{\boldsymbol{x}}(\boldsymbol{v}_k)^T$, where $\boldsymbol{v}$ is a vector defining the desired fiber orientation, $\boldsymbol{R}_{\boldsymbol{x}}(\boldsymbol{v})$ is the rotation matrix that aligns the vector $\boldsymbol{x} = [1\ 0\ 0]^T$ oriented along the *x*-axis to $\boldsymbol{v}$, and $\boldsymbol{D}_{\boldsymbol{x}}$ is the single-fiber tensor model with diffusivities in orthogonal directions given by $\lambda_{1,2,3}$.

$$\boldsymbol{R}_{\boldsymbol{x}}(\boldsymbol{v}) = \frac{(\boldsymbol{x}+\boldsymbol{v})(\boldsymbol{x}+\boldsymbol{v})^T}{(\boldsymbol{x}^T\boldsymbol{v}+\mathbf{1})} - \boldsymbol{I} \tag{2}$$

$$\boldsymbol{D}_{\boldsymbol{x}} = \begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix} \tag{3}$$

Complex Gaussian noise was added to the synthesized signal, S, to achieve a Rician distribution of noisy magnitude diffusion data (Gudbjartsson and Patz, 1995):

$$E(b, \boldsymbol{g}_j) = \sqrt{\left(S(b, \boldsymbol{g}_j) + \frac{n_1}{\sqrt{2}}\right)^2 + \left(\frac{n_2}{\sqrt{2}}\right)^2} \tag{4}$$

where n_1 and n_2 are independent and identically distributed Gaussian random variables with zero mean and standard deviation $\sigma_n = \mu_{S_0}/SNR$, in which μ_{S_0} is the mean signal from a homogeneous white-matter region of the S_0 non-diffusion weighted image, and *SNR* is the desired signal-to-noise ratio of the magnitude image, E.

References

Alexander, A. L., Hasan, K. M., Lazar, M., Tsuruda, J. S., & Parker, D. L. (2001). Analysis of partial volume effects in diffusion-tensor MRI. *Magnetic Resonance in Medicine*, *45*(5), 770-780.

Behrens, T. E. J., Woolrich, M. W., Jenkinson, M., Johansen-Berg, H., Nunes, R. G., Clare, S., Matthews, P.M., Brady, J.M., & Smith, S. M. (2003). Characterization and propagation of uncertainty in diffusion-weighted MR imaging. *Magnetic Resonance in Medicine, 50*(5), 1077-1088.

Friston, K., Ashburner, J., Frith, C. D., Poline, J. B., Heather, J. D., & Frackowiak, R. S. (1995). Spatial registration and normalization of images. *Human brain mapping*, *3*(3), 165-189.

Gudbjartsson, H., & Patz, S. (1995). The Rician distribution of noisy MRI data. *Magnetic Resonance in Medicine*, *34*(6), 910-914.

Smith, S. M., Jenkinson, M., Woolrich, M. W., Beckmann, C. F., Behrens, T. E., Johansen-Berg, H., ... & Matthews, P. M. (2004). Advances in functional and structural MR image analysis and implementation as FSL. *NeuroImage*, *23*, S208-S219.

Tuch, D. S., Reese, T. G., Wiegell, M. R., Makris, N., Belliveau, J. W., & Wedeen, V. J. (2002). High angular resolution diffusion imaging reveals intravoxel white matter fiber heterogeneity. *Magnetic Resonance in Medicine*, *48*(4), 577-582.

Tuch, D. S. (2004). Q-ball imaging. *Magnetic Resonance in Medicine*, *52*(6), 1358-1372.