Optimal imaging parameters for fibre-orientation estimation in diffusion MRI

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Introduction This abstract investigates the optimal imaging parameters for estimating white-matter fibre orientations using diffusion MRI with a spherical sampling scheme [1]. We synthesize diffusion MRI measurements from brain tissue with one and two dominant microstructural fibre orientations using simple models of the particle-displacement density *p*. We refit the models to the synthetic data to recover the fibre orientations. In the one-fibre case, we use a zero-mean Gaussian density, as in diffusion-tensor MRI [2], and in the two-fibre case, we use a mixture of two zero-mean Gaussians, as in [3, 4]. We study the error in the fibre-orientation estimates in the presence of noise as a function of the parameters of the imaging sequence in order to identify optimal settings for brain imaging.

In earlier work, Xing et al [5] show that the optimal strategy for measuring the diffusion coefficient *d* uses a two-point sampling scheme, which acquires *N* repeated measurements at b_2 and *M* repeats at $b_1 < b_2$. For N = M = 1, $d(b_1 - b_2) = 1.11$ maximizes the signal to noise ratio of the measured *d*. As the number of available measurements increases, the optimal $d(b_1 - b_2)$ increases asymptotically to 1.28 and the optimal *N/M* tends to 3.6. Jones et al [1] extend Xing et al's analysis to measurement of the full diffusion tensor. They acquire the *N* measurements at b_2 with gradient directions spread evenly over the sphere and the *M* measurements at $b_1 = 0$. Jones et al note that higher b_2 requires higher TE, which reduces signal to noise. They model this effect (for a specific, but fairly typical, EPI-based pulse sequence) and show numerically that, for an approximately isotropic diffusion tensor D and $T_2 = 0.08$ s, the sum of the variances of the elements of D is minimum when $b_2 = 0.85 \times 3/\text{Tr}(D)$ and M/(N + M) = 0.103. Here, we use simulations to determine b_2 in Jones' spherical sampling scheme that minimizes the variance of the principal eigenvector of anisotropic diffusion tensors over a large number of independent noise trials. The simulations take into account the reduction in signal as TE increases.

Methods We assume the standard PGSE measurement sequence with EPI readout. To synthesize measurements with a particular b_2 , we choose the gradient pulse-width δ and separation Δ , TE and *k*-space-sampling fraction that maximize the signal to noise at b = 0. We fix gradient strength and image resolution and thus the time R_H required to readout the second half of *k*-space after the echo centre. The SNR at b = 0 is then $S = S_0 \exp(\text{TE/T}_2)$ (R + R_H)^{1/2}, where S_0 is a constant and R is the time available within TE to sample some or all of the first half of *k*-space. At fixed TE, a range of choices for δ and Δ provide the required *b*. We choose δ as large as possible, since this maximizes R. To select the optimal TE for *b*, we determine δ , Δ , R and hence S/S_0 separately at each TE and choose the TE that maximizes S/S_0 .

We use variations of two simple test functions: $p_1 = G(\mathbf{x}; \mathbf{D}_1, t)$ (one-fibre case) and $p_3 = a G(\mathbf{x}; \mathbf{D}_1, t) + (1 - a) G(\mathbf{x}; \mathbf{D}_2, t)$ (two-fibre case), where $a \in [0, 1]$ is a mixing parameter, $G(\bullet; \mathbf{D}, t)$ is the zero-mean Gaussian function with covariance $2t\mathbf{D}$ and the diffusion tensors are $\mathbf{D}_1 = \text{diag}(\lambda_1, \lambda_2, \lambda_2)$ and $\mathbf{D}_2 = \text{diag}(\lambda_2, \lambda_1, \lambda_2)$. By default, a = 0.5, $\lambda_1 = 1.7 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$ and $\text{Tr}(\mathbf{D}_i) = \lambda_1 + 2\lambda_2 = 2.1 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$. We synthesize data by sampling the Fourier transform *F* of *p* at each wavenumber sampled by the imaging sequence, adding a random complex number with independent real and imaginary parts drawn from $N(0, \sigma^2)$, where $\sigma = F(0)/S$, and taking the modulus.

To reconstruct the fibre orientations in each trial, we find the least-squares fit diffusion tensor to the log synthetic measurements in the one fibre case, as in [1]. In the two-fibre case, we find the least-squares fit pair of diffusion tensors and mixing parameter using one run of a Levenburg-Marquardt algorithm. The optimisation starts from equally mixed, cylindrically symmetric diffusion tensors with principal eigenvectors along the first two eigenvectors of the single tensor fit to the log measurements. In each case, the principal eigenvectors of the fitted diffusion tensors provide fibre-orientation estimates.

To assess reconstruction quality, we compute the concentration of the fibre-orientation estimates over 10,000 trials. To find the concentration of a population of directions $\mathbf{x}_1, ..., \mathbf{x}_n$, we compute the mean dyadic tensor $\mathbf{Y} = \Sigma_i \mathbf{x}_i \mathbf{x}_i^T$ and take the largest eigenvalue κ_i , which is zero for isotropically distributed directions and one for a population of equal directions. We repeat each experiment over 500 random rotations of the test function and compute the mean, maximum and minimum κ_i . For a better comparison scale, we use $\gamma(\kappa_i) = -\log(1 - \kappa_i)$ as the direction-concentration statistic.

Experiments and Results We consider a sequence running on a scanner with maximum gradient strength 0.04 T m⁻¹, 90° and 180° pulse durations 0.014 s and 0.004 s, respectively, and $R_H = 0.026$ s. Figure 1 shows S/S_0 as a function of TE for each $b_2 \in \{0.5, 0.75, 1.0, 1.5, 2.0, 2.5, 3.0, 4.0, 5.0, 6.0\} \times 10^9$ s m⁻² (top curve to bottom superpotential to the problem of PL is just below 0.2 at the problem of the p

curve) with $T_2 = 0.08$ s. The value of R/R_H is just below 0.3 at the peak for each b_2 . We have run many experiments to investigate the dependence of the optimal b_2 on various parameters of the imaging process. For example, Figure 2 shows the direction concentration in the one-fibre case, as a function of b_2 , for various values of N + M. For the results in Figure 2, we set $T_2 = 0.08$ s and estimate S_0 from scanner data; S=20 when $b_2 = 1.0 \times 10^9$ s m². The concentration peaks at $b_2 = 0.75 \times 10^9$ s m² and this optimum appears independent of N + M. Figure 3 shows results from a similar experiment in the two-fibre case; again the optimum is independent of N + M, but is now at $b_2 = 2.5 \times 10^9$ s m². Similar experiments show that the optimum b_2 changes little if we vary S_0 , λ_1 with Tr(D₁) fixed, T₂, or the gradient strength. In the two-fibre case, the optimum b_2 has little dependence on the mixing parameter *a* or the angle between the fibre orientations. In both cases, the optimum b_2 is highly dependent on Tr(D₁). Preliminary tests with the three fibres suggest an optimum $b_2 = 2.0 \times 10^9$ s m² in the one-fibre case and $b_2 = 2.0 \times 10^9$ s m² in the two-fibre case. The *N/M* that minimizes FA variance is FA dependent.

Conclusions and Further Work The simulations suggest that the optimal value of b in a spherical acquisition scheme is well-defined for specific tissue diffusivity in the one and two-fibre cases, but is higher for the multiple-

fibre case than for the one-fibre case, and has only very weak dependence on other tissue properties and imaging parameters. To optimise a sequence for both the one and two fibre cases, we must choose a compromise between their individual optima. However, Brihuega-Moreno et al [6] note that Xing et al's two-point sampling scheme is not optimal for measuring a range of diffusion coefficients. By extension, spherical acquisition schemes are unlikely to be optimal for measuring anisotropic diffusion tensors. A better compromise for reconstructing one and two fibres will likely come from relaxing the constraint that the N measurements with non-zero b have equal b. **References**

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Figure 1. Plots relative signal to noise against TE for various b-values.



Figure 2. Plots the direction concentration against b_2 in the one-fibre case for N=28, M=3 (×); N=46, M=5 (•); N=64, M=7 (□); N=82, M=9 (∇); N=100, M=11(+); and N=246, M=27 (0).



Figure 3. Plots the direction concentration against b_2 in the twofibre case. The key follows figure 2.