

# Effect of Diffusion Gradient Pulse Duration on Fibre Orientation Estimation

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## Introduction

In the  $q$ -space formalism, the probability density function (PDF) of water molecule displacements can be obtained by performing the Fourier transform of the diffusion-weighted (DW) signals acquired as a function of the wave vector  $q$  under the short pulsed gradient (SPG) condition [1]. The displacement PDF can be utilized to estimate the dimensions of microstructures and interpret tissue states. However, the essential requirement of the SPG approximation is usually unattainable in practice. The effects of finite gradient pulse widths on the estimated displacement PDF has been studied by several groups [2-3]. It has been found that an increased diffusion gradient pulse duration ( $\delta$ ) can result in an underestimation of the compartment scale [4], but does not affect the accuracy of estimated fiber directions [5]. In this study, we propose that, unlike in  $q$ -space applications to determine spin displacement, the application of a longer  $\delta$  is actually beneficial for resolving fibre orientations, as it enhances both the DW signal and the contrast between the DW directions. We therefore investigate the relationship between  $\delta$  and the DW signal measured as a function of orientation under the same effective diffusion time ( $\Delta_{\text{eff}}$ ) for a given  $b$ -value, using both simulated and experimental data.

## Theory

When performing  $q$ -space imaging with finite  $\delta$ , the displacements that are actually estimated correspond to the distance between each spin's average position during the first DW pulse and its average position during the second DW pulse [2]. If the diffusion is restricted, the average position of the spin during each DW pulse will tend towards the centroid of the restricted compartment, and the estimated displacement should therefore tend to zero as  $\delta$  increases. In white matter fibers, the diffusion can be approximated as restricted in directions perpendicular to the fibre axis, and free along the fibre axis. In this case, increased  $\delta$  should result in reduced DW signal attenuation (and hence increased DW signal) in the transverse plane, with no change in the longitudinal DW signal attenuation. This should therefore provide improved SNR, and increased discrimination between longitudinal and transverse directions.

## Methods

**Simulations** were performed using a random walk Monte Carlo simulation to simulate 3-D water molecular diffusion within a restricted cylindrical fiber. The step size for the movement of water molecules was 0.1  $\mu\text{m}$ , and the diffusion coefficient was set at  $2 \times 10^{-3} \text{ mm}^2/\text{s}$ . A constant  $\Delta$  of 60 ms was used, while  $\delta$  was varied from 1 to 55 ms. To study the dependence on  $b$ -value, the fiber diameter was fixed at 5  $\mu\text{m}$ , and  $b$ -values ranging from 1,000 to 10,000  $\text{s}/\text{mm}^2$  were obtained by increasing the gradient intensity. To study the dependence on axonal diameter, a  $b$ -value of 5,000  $\text{s}/\text{mm}^2$  was used, and the axonal diameters of 1 to 10  $\mu\text{m}$  were studied. For each condition, noiseless DW signals were calculated along a set of 360 gradient directions spanning the plane containing the fibre direction.

**Experimental data** were acquired from a unidirectional phantom, constructed using plastic capillaries immersed in water with inner and outer diameters of 20  $\mu\text{m}$  and 90  $\mu\text{m}$ . DW images were acquired using a stimulated echo sequence on a 9.4 T MRI scanner (Bruker, Germany). A fixed TR = 2,300 ms, TE = 80.1 ms, NEX = 3, and effective diffusion time  $\Delta_{\text{eff}} (= \Delta - \delta/3) = 100 \text{ ms}$  were used. The DW datasets were acquired using  $\delta = 2, 12, \text{ and } 36 \text{ ms}$  and  $b = 1,000 \text{ and } 4,000 \text{ s}/\text{mm}^2$ . 40 DW gradient directions were applied at  $9^\circ$  intervals in the plane of the fibres.

For both the simulated and experimental data, the DW signals were normalized to the  $b=0$  intensity, and displayed as a function of the gradient direction using polar plots.

## Results

Fig. 1 and Fig. 2 show results obtained from the Monte Carlo simulation, showing that using a longer  $\delta$  results in increased transverse DW signal ( $90^\circ$  &  $270^\circ$ ), with all other parameters fixed ( $\Delta$ ,  $b$ -value, and axonal diameter). This effect was more evident at the higher  $b$ -value and for the larger axonal diameter, as shown in Fig. 1 and Fig. 2 respectively. No change was observed in the DW signal when the DW gradients were applied along the fiber axis.

Fig. 3 shows the results obtained from the experimental phantom. At  $b = 1,000 \text{ s}/\text{mm}^2$ , the DW signal intensity measured perpendicular to the fiber axis increased by 7.8% and 20.6% when  $\delta$  was increased from 2 ms to 12 ms and 36 ms respectively. At  $b = 4,000 \text{ s}/\text{mm}^2$ , the corresponding DW signal intensity increased further by 21.4% and 62.2% respectively. Note that the residual DW signal that can be observed along the fibre direction at  $b = 4000 \text{ s}/\text{mm}^2$  in Fig. 3 is due to Rician noise bias.

## Discussion

The results show that prolonging  $\delta$  preferentially enhances the transverse DW signal, since the diffusion is most restricted along these directions. This effect should be advantageous for estimating fiber orientations for two reasons. First, it leads to an overall increase in the DW signal. Second, it 'stretches out' the shape of the measured diffusion profile, which improves the contrast between DW orientations. This is especially beneficial for resolving crossing fibers, as this contrast is essential to discriminate between different fiber directions. Work is underway to verify this effect in sciatic nerve preparations and other biological systems.

Although a longer  $\delta$  is problematic for  $q$ -space applications, this study suggests that it is actually beneficial for estimating fiber orientations, and hence also for fiber-tracking applications. Fortunately, due to hardware limitations, DW acquisition protocols in use on current clinical scanners of necessity use  $\delta$  values that are already very long in this context.

## References

- [1] Callaghan. Principles of Nuclear Magnetic Resonance Microscopy. 1991. [2] Mitra *et al.* JMR 1995;113:94-101. [3] Linse *et al.* JMR 1995;116:77-86. [4] Caprihan *et al.* JMR 1996;118:94-102. [5] Lin *et al.* NeuroImage 2003;19:482-495.

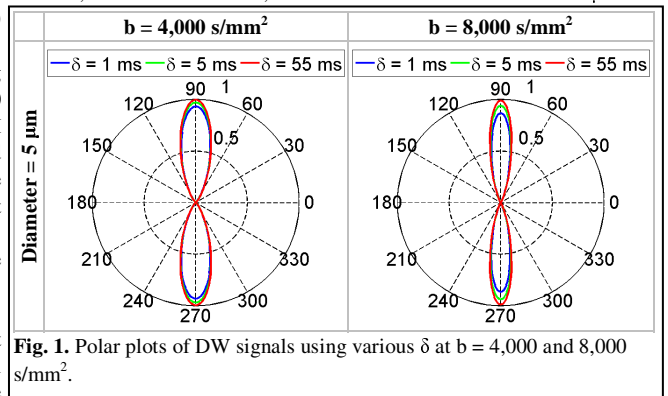


Fig. 1. Polar plots of DW signals using various  $\delta$  at  $b = 4,000$  and  $8,000 \text{ s}/\text{mm}^2$ .

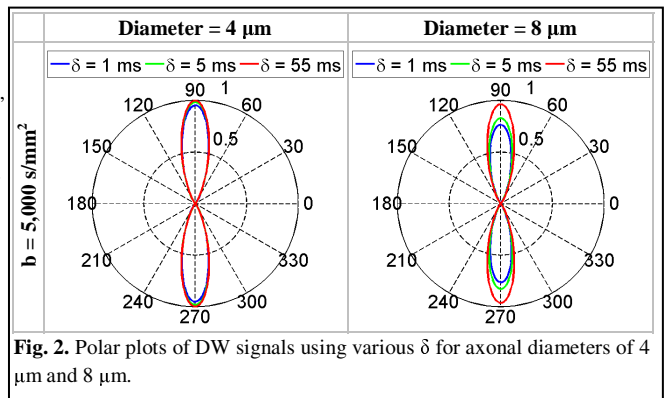


Fig. 2. Polar plots of DW signals using various  $\delta$  for axonal diameters of 4  $\mu\text{m}$  and 8  $\mu\text{m}$ .

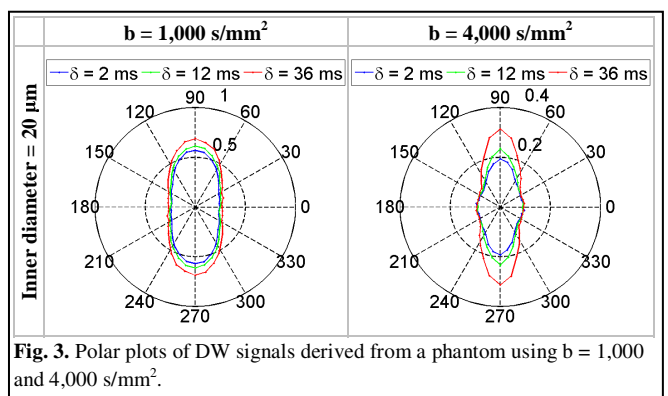


Fig. 3. Polar plots of DW signals derived from a phantom using  $b = 1,000$  and  $4,000 \text{ s}/\text{mm}^2$ .