Validation of models for the diffusion weighted MR signal in brain white matter

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Introduction

In brain white matter (WM), barriers of axonal membranes and myelin sheets are responsible for anisotropic diffusion. The diffusion is restricted and consequently the diffusion weighted (DW) MR signal as a function of the b-factor cannot be described accurately by a mono-exponential function. Numerous studies suggest describing the DW MR signal by a bi-exponential function since this fits the data well [1]. Yet, the underlying physical meaning of this model remains unclear [2]. In this study, Monte Carlo simulations are performed in a fiber geometry similar to those observed in brain WM. Various models for the DW-MR signal are evaluated.

Methods

Random walk simulations: The diffusion process was modeled by Monte Carlo (MC) simulation of 3.0×10^5 random walkers as described in [3]. The diffusion took place in a packing made of long parallel aligned cylinders with diameters (10 µm ± 3.5 µm) and density (79.5%) chosen similar to those observed in brain WM [1]. The diffusion coefficients were chosen similar to those described in the literature for the intra- and extracellular space in brain white matter [1]: 1.0×10^{-9} m^2/s inside the cylinders and 2.5×10^{-9} m^2/s outside the cylinders. There was no exchange between the inside and outside of the cylinders.

The first and higher order moments of the total traveled distance in the direction perpendicular to the fibers were used to calculate the apparent diffusion coefficient (ADC) and apparent diffusion kurtosis (ADK). The DW MR signal S(b) itself is also simulated by incorporating the phase accumulation of the spins. Varying diffusion gradients were applied during a time δ of 0.7 ms. Different diffusion times Δ (from 2 ms up to 100 ms) were considered. The corresponding b-factors ranged from 0 up to 3500 s/mm^2.

The diffusion process and the DW MR signal have been simulated inside and outside the cylinders simultaneously to obtain the ADC, ADK and S(b). In addition, the diffusion has been simulated separately inside and outside the cylinders to obtain the corresponding ADC_{IN} and ADC_{EX}.

Evaluation of diffusion models: The following functions were fitted to the simulated S(b)/S(0)-curve using a Levenberg-Marquardt algorithm:

- Bi-exponential form:

$$\frac{S(b)}{S(0)} = \alpha e^{-bD_{slow}} + (1-\alpha)e^{-bD_{fast}}$$

The fitted values for α, D_{slow} and D_{fast} were compared to the theoretical value of $\alpha = 0.80$ and the simulated values ADC_{IN} and ADC_{EX} for the diffusion inside and outside the cylinders.

- Cumulant expansion form [2]:

$$\ln\left(\frac{S(b)}{S(0)}\right) = C_1 b + C_2 b^2 + C_3 b^3 + \ldots$$

The termination of this series after the Nth order term is called the b^N cumulant form. The coefficients of the 1st and 2nd order yield the ADC and ADK: $C_1 = -ADC$, $C_2 = ADK \cdot ADC^2/6$ [4].

The convergence of this series is investigated by fitting polynomials of the order N = 1 up to 4 to *ln(S)* considering increasing b-intervals: ([0-500m^2/s] up to [0-3500m^2/s]). The fitted values were then compared to the simulated values for the ADC and ADK.

Results

For all Δ, the datasets S(b) could be fitted to the bi-exponential model with a correlation coefficient of minimum 0.9999. Figure 1 shows the comparison between the fitted and simulated values for α, D_{slow} and D_{fast}. α, ADC_{fast} and ADC_{slow} are underestimated, especially at short diffusion times and when including large b-intervals.

Fitting results of the ADC and ADK using the cumulant expansion b^N are shown in figure 2 and 3 respectively for increasing order N. The cumulant expansion fits of S(b) with the highest correlation coefficients resulted in fitted values for the ADC and ADK which were the closest to the simulated values. The minimum order N to obtain a good agreement between fitted and simulated values for the ADC and ADK increases with increasing b-interval of the fit.

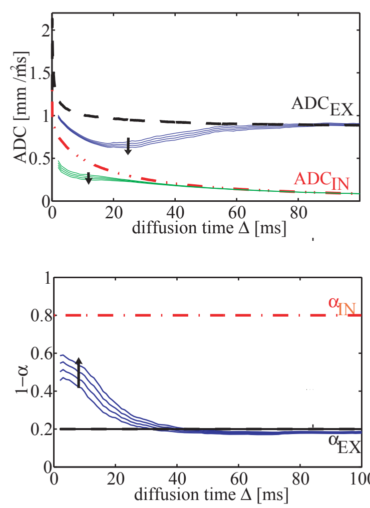

Figure 1: bi-exponential fitting results. The fraction (1-α) is compared to the theoretical fraction of the cylinder packing α_{EX}. D_{slow} and D_{fast} are compared to the simulated values D_{IN} and D_{EX} (dotted lines). The arrow indicates increasing b-interval: [0-500 s/mm^2] up to [0-3500 s/mm^2]

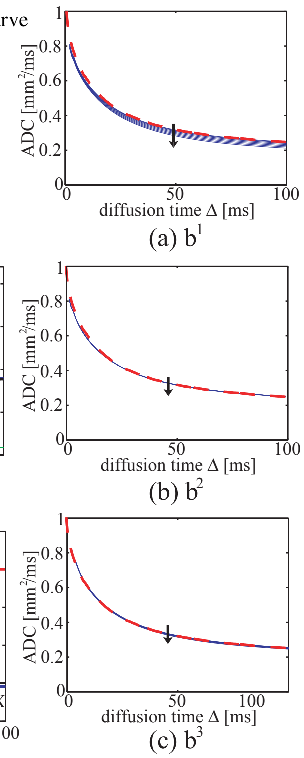

Figure 2: fitting results of the ADC using the cumulant expansion form b^N: for increasing order (N = 1 up to 3) in comparison to the simulated value (dotted line). The arrow indicates increasing b-interval: [0-500 s/mm^2] up to [0-3500 s/mm^2]

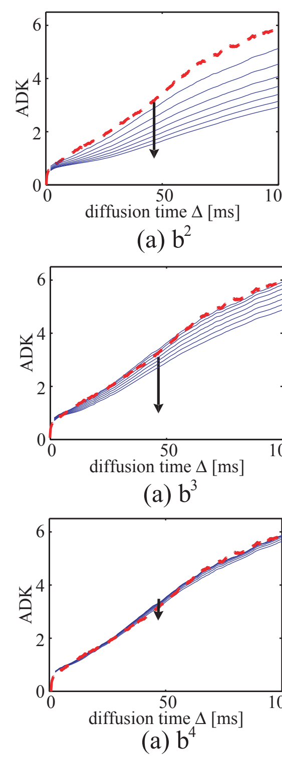

Figure 3: fitting results of the ADK using the cumulant expansion form b^N: for increasing order (N = 2 up to 4) in comparison to the simulated value (dotted line). The arrow indicates increasing b-interval: [0-500 s/mm^2] up to [0-3500 s/mm^2].

Discussion and Conclusion

The good accuracy of the bi-exponential fit does not prove the validity of the model since there is a significant dependence on the considered b-interval and diffusion time. The cumulant expansion form provides a useful alternative. When including higher order terms, the diffusion coefficient and kurtosis can be accurately fitted. The cumulant expansion form b^3 might be a better option to fit the DW MR signal in b-intervals in the range of [0-2500s/mm^2] provided the dataset has a sufficiently high signal-to-noise ratio.

References

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