

# Extension of the double wave vector experiments at long mixing times to multiple concatenations

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MR sequences where two diffusion-weighting periods are applied successively in a single acquisition [1] seem to be a promising tool for the investigation of tissue structure on a microscopic level such as the characterization of the size and eccentricity of cells or compartments [2,3]. However, the application of these double-wave-vector diffusion-weighting (DWV) experiments [1] on whole-body MR systems is hampered by the long gradient pulses required that have been shown to reduce the signal modulation considerably [4,5].

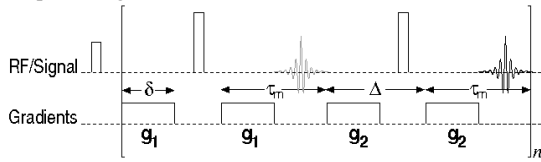
In this work, the recently presented tensor equation for DWV experiments with long mixing times  $\tau_m$  between two wave vectors [6] is extended to multiple concatenations of the two diffusion weighting periods [7] (Fig. 1). It is demonstrated by Monte Carlo simulations that the extended model yields a good approximation of the MR signals not only for infinitesimal short gradient pulses but also for typical whole-body gradient pulse durations. Most importantly, the signal modulation is increased with multiple concatenations because shorter gradient pulses can be used to achieve the desired diffusion weighting. Thus, the multiple concatenation approach may help to improve the applicability and reliability of DWV measurements with long mixing times on whole-body MR systems.

## Methods

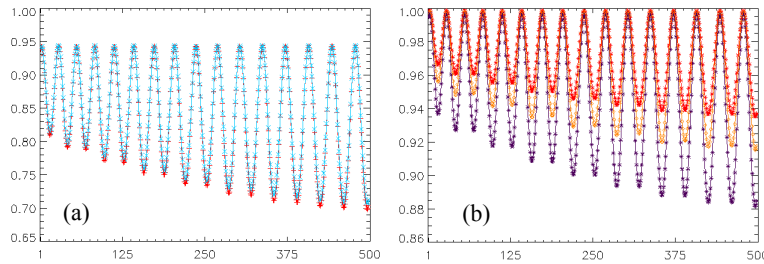
The MR signal  $M$  of spins in fully restricted isolated pores for a DWV experiment with long mixing times  $\tau_m$  and short gradient pulses is given by  $M = \sum_i |\rho_i(\theta)|^{2n} |\rho_i(\theta)|^{2n}$  [1,7] where  $n$  is the number of concatenations (Fig. 1) and  $\rho_i(q)$  is the Fourier transform of the spin density function for pore  $i$ . The generalization of the corresponding tensor model [6] then yields  $M(n, \underline{Q}) \propto 1 - 1/2 \cdot n \underline{Q}^T \underline{\tilde{T}} \underline{Q} + 1/12 \cdot \underline{\tilde{Q}}^T \underline{\tilde{U}}(n) \underline{\tilde{Q}}$  where

$$\underline{\tilde{U}}(n) = \begin{pmatrix} n \underline{\tilde{S}} + (6n^2 - 3n) \underline{\tilde{R}} & 6n^2 \underline{\tilde{R}} \\ 6n^2 \underline{\tilde{R}} & n \underline{\tilde{S}} + (6n^2 - 3n) \underline{\tilde{R}} \end{pmatrix} \text{ and } \underline{Q}, \underline{\tilde{Q}}, \underline{\tilde{T}}, \underline{\tilde{R}}, \underline{\tilde{S}} \text{ are as defined in [6], which describes the signal for arbitrary wave vectors, pore}$$

shapes, and pore orientation distributions and any number of concatenations. Monte Carlo simulations were performed for 10000 spins in parallel oriented, prolate ellipsoidal pores (semi-axes of 3, 3, and 10 $\mu$ m) as described in [6] in order to (i) confirm the theoretical results using short gradient pulses (10 $\mu$ s) and (ii) investigate their applicability to experiments on whole-body MR systems (gradient amplitude 39mT/m) with long gradient pulses. 5.4 million combinations of isotropically distributed wave vector orientations were simulated and fitted to the tensor equation with a Levenberg-Marquardt algorithm.



**Figure 1:** Example of a pulse sequence for a DWV experiment with  $n$  concatenations of the two wave vectors.



**Figure 2:** Subsets of the simulated MR signals (symbols) in ellipsoidal pores obtained for the wave vector orientation combinations and fits to the tensor equation (lines) for (a) infinitesimal short gradient pulses and  $n=1$  (blue) and  $n=5$  (red) concatenations (fixed  $nq^2 = 0.06 \text{ m}^{-2}$ ) and (b) a gradient amplitude of 39mT/m and  $n=1, 2, 5$  (fixed  $nq^2$ ), i.e. pulse durations of 24ms, 13.9ms, 10.7ms. Note the different scaling of the y-axis.

## References

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## Results and Discussion

Results for subsets of MR signals for two different concatenations acquired with the isotropic gradient direction scheme are shown in Figure 2 (symbols) together with the fits of all 5.4 million data points to the tensor equation (lines). For short gradient pulses (Fig. 2a) no significant deviations between the different numbers of concatenations as well as between the simulations and the fits are observed. Because  $nq^2$ , i.e. the diffusion weighting, was fixed, the data sets have a very similar damping. The pore-size parameters derived from the fits are in good agreement to the adopted parameters within an accuracy of below 5%. This confirms the validity of the tensor formalism extended to multiple concatenations.

The results for gradient pulse durations compatible with whole-body MR systems are shown in Fig. 2b. For the simple experiment ( $n=1$ , red) the signal modulation is considerably reduced, from about 0.24 to about 0.06, which reflects the known adverse effect of the longer gradient pulses (24ms). However, considering multiple concatenations with fixed  $nq^2$  allows to shorten the gradient pulses down to 10.7ms ( $n=5$ , violet) which is accompanied by an increase of the modulation amplitude to about 0.12. Despite the long gradient pulses, the fits are still in good agreement with the simulation results. The pore parameters derived from them show major deviations that are particularly pronounced for the standard experiment ( $n=1$ ) but are ameliorated for a larger number of concatenations. Similarly, the microscopic anisotropy measure  $MA$  [6] is obtained with an accuracy between 25% ( $n=1$ ) and 15% ( $n=5$ ).

In summary, the generalized tensor model can describe the simulated data successfully. The multiple concatenation approach leads to a distinct gain in the signal modulation due to the shorter gradient pulses that can be used to yield the same diffusion weighting. Thus, this approach may help to improve the detectibility of DWV experiments on whole-body MR systems.