

# Numerical Simulations of Double-Wave-Vector Diffusion-Weighting Experiments with Multiple Concatenations at Short Mixing Times

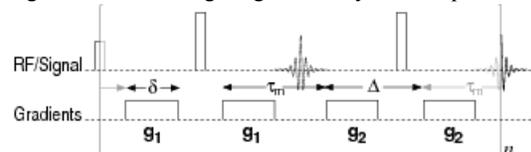
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## Introduction

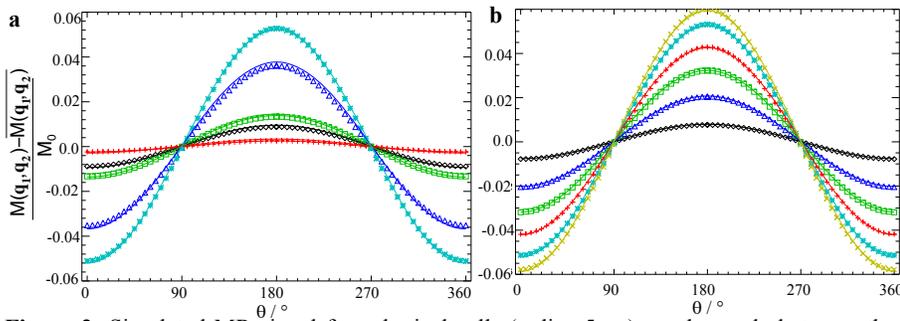
Double-wave-vector diffusion-weighting experiments where two diffusion weighting periods are applied successively in a single acquisition [1] are a promising tool to investigate tissue microstructure. For instance, cell or compartment sizes can be estimated from the signal modulation signal with the angle between the two wave vectors if a short mixing time between the two diffusion weightings is used [2,3]. Recently, multiple concatenations of the two diffusion weightings (Fig. 1) have been shown to increase this signal modulation by up to 100% if short gradient pulse durations are considered [4]. Thus, multiple concatenations are a promising approach for in vivo experiments as the long gradient pulses required on whole-body MR systems reduce the signal modulation significantly [5,6]. In this work, it is demonstrated that the increase of the modulation amplitude can be considerably higher, e.g. up to a factor of 6 for six concatenations, due to the higher diffusion-weighting efficiency of multiple concatenations which allows to shorten the gradient pulses accordingly.

**Figure 1:** Basic pulse sequence for the double wave vector experiment with multiple ( $n$ ) concatenations. The diffusion gradient directions  $g_1$  and  $g_2$  enclose an angle  $\theta$  which is varied within the experiment.



## Methods

Numerical simulations of the MR signal of spherical cells for the experiment shown in Fig. 1 were performed for  $n=1-6$  and 10000 spins using a Monte-Carlo IDL algorithm [4]. A fixed diffusion weighting, i.e. a constant  $n \cdot q^2$ , was used in comparisons with different numbers of concatenations. The maximum gradient amplitude was 40 mT/m, the diffusion time  $\Delta$  30ms, and the mixing time  $\tau_m$  identical to  $\delta$ .



**Figure 2:** Simulated MR signal for spherical cells (radius  $5\mu\text{m}$ ) vs. the angle between the two wave vectors. (a) One concatenation with a  $\delta$  of 16ms (black) and five concatenations (colors) with identical  $\delta$  and  $q=g \cdot \delta$  (blue) or constant diffusion weighting, i.e. fixed  $n \cdot q^2$ , with a  $\delta$  of 16ms (green) and about 7ms (cyan). (b) Comparison of the signal modulation for a constant  $n \cdot q^2$  with one (black) to six concatenations (yellow). The modulation amplitude increases monotonically with the number of concatenations. Lines in both subfigures represent a fit to the theoretical model [4].

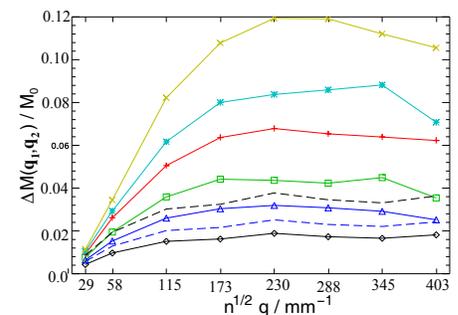
## Results and Discussion

The improvement achievable with multiple concatenations is demonstrated in Figure 2a. Compared to the simple experiment with  $n=1$  (black), an increase of the modulation amplitude by about 70% is observed for five concatenations with a reduced gradient amplitude (green) which is close to the value of 80% expected theoretically in the short-pulse approximation [4]. However, using the maximum gradient amplitude and shortening the pulse duration from 16ms to about 7ms (cyan) yields an additional factor of three. This improvement is a re-gain of the modulation decrease occurring for long gradient pulses [5,6]. Even for two concatenations (blue in Fig. 2b, green in Fig. 3), the signal modulation is more than 2.5 times that of a simple experiment with  $n=1$  (black) exceeding the theoretical expectations under the short-pulse assumption (50% increase) considerably. In Fig. 4, it is demonstrated that a comparable gain for two concatenations is observed in a large range of cell sizes.

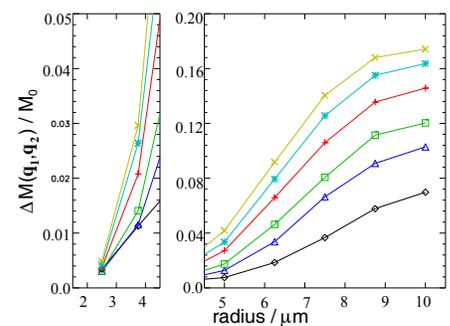
Thus, multiple concatenations may help to improve the detectability of the signal modulation and the reliability of double-wave-vector diffusion-weighted experiments with a short mixing times between the two wave vectors, in particular on whole-body MR systems.

## References

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**Figure 3:** Amplitude of the signal modulation vs.  $n^{1/2} \cdot q$  for spherical cells (radius  $5\mu\text{m}$ ) and one to six concatenations (1, 1.5, 2, 3, 4, 6). The dashed line sketches the maximum expected from the theory derived under the short-pulse assumption for a large number of concatenations, i.e. a doubling of the signal difference [4].



**Figure 4:** Amplitude of the signal modulation for spherical cells vs. the cell radius for one (black) to six (yellow) concatenations (1, 1.5, 2, 3, 4, 6). For a large number of concatenations and cell radii the signal modulation decreases because the minimum signal approaches zero.