# Concatenated Double Wave Vector Diffusion Weighting Experiments

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## INTRODUCTION

Double wave vector (DWV) diffusion weighting [1] is anticipated to provide a basis for assessing tissue structure in terms of cell or pore size and shape. In DWV experiments, the magnetization is prepared by two successive conventional pulsed gradient diffusion weighting periods with independent gradient direction, separated by a mixing time, $\tau_m$ (Fig. 1a). At low $\tau_m$, the signal difference between parallel and antiparallel gradient orientation for restricted diffusion depends on the mean pore size [1,2,3]. The difference is absent under conditions of free diffusion. Given the size of relevant structures in biological tissues this difference is often very small when whole body gradients are employed. This is because very long gradient pulses must be used to achieve sufficient gradient moments. Although first *in vivo* results are available [4], it is unclear whether the modulation is large enough to be routinely useful. Recently, a "concatenated version" of the DWV experiment was proposed where the double diffusion weighting is applied multiple times [5]. It should provide an antiparallel–parallel difference that is larger than would be expected from a repeated application of the original expression. Here, the predicted increase is investigated experimentally in excised pig spinal cord.

## THEORY AND METHODS

Without concatenations, the DWV-weighted signal (Fig. 1a) from randomly oriented pores of diameter $a$ depends on the angle θ between the two diffusion gradients of equal strength as [1]

$$S(q,\theta)/S_0 \approx 1-\left\langle R^2\right\rangle\frac{1}{3}q^2\left[2+\cos\theta\right] \qquad (1)$$

where $S_0$ is the signal without diffusion weighting, if $q = \gamma\delta G$ is small compared to $1/a$, if the time delay $\tau_m$ between the two weighting periods is negligible, and if $\delta << \tau_D << \Delta$ holds ($\tau_D$ mean time required for diffusion across a pore). Previous results [2,3,6,7] indicate that these conditions need not strictly be met for some of the modulation to remain. The mean squared radius of gyration, $\langle R^2\rangle$, scales with the pore size. With multiple concatenations, Eq. (1) is to be replaced by [5]

$$S(q,\theta)/S_0 \approx 1-\left\langle R^2\right\rangle\frac{1}{3}q^2\left[2n+(2n-1)\cos\theta\right] \qquad (2)$$

where $2n$ is the total number of alternating diffusion weighting periods employing $\mathbf{G}^{(1)}$ or $\mathbf{G}^{(2)}$. For $n = 1$, Eq. (2) is identical to Eq. (1). Naively, one could expect $n[2 + \cos\theta]$ in place of the square brackets in Eq. (2), as a result of applying Eq. (1) twice and retaining only terms up to 2nd order in $q$. Equation (2) predicts the modulation amplitude to increase by a factor of $(2n' - 1)/(2n - 1) = 3$ (instead of $n'/n$) when changing the number of concatenations from $n = 1$, to $n' = 2$. This is because for $\theta = \pi$ the number of sudden gradient reversals in the alternating sequence of weightings increases with $n$. In addition, the use of concatenations makes shorter gradient pulse durations possible for a given total diffusion weighting $nq^2$. Hence, the $\delta << \tau_D$ condition can more easily be met for small pore sizes, which is also associated with an enhanced modulation amplitude [3,7].

A DWV-prepared double spin echo-echo planar imaging sequence (Fig. 1) with short $\tau_m$ was applied on a 3 T whole-body MR system (Magnetom Trio, Siemens, Erlangen/Germany) to a sample of excised formalin-fixed pig spinal cord. Parameters for experiment A [B]: 2 transverse slices, 1.7×1.7×10 mm$^3$ nominal resolution, $\Delta$ = 62.36 ms [37.36 ms], $\tau_m = \delta$ + 0.6 ms, $n$ = 1, 2, $nq^2 \approx$ 10080 mm$^{-2}$ [5050 mm$^{-2}$], $TR$ = 3 s, $TE$ = 320 ms [300 ms], averaging over 8 absolute gradient directions in the $xy$ plane and 2 repetitions. The spinal cord axis was approximately aligned with the $z$ axis. When increasing $n$, δ was shortened to keep $nq^2$ constant.

## RESULTS

Figure 2 shows that the antiparallel-parallel signal difference divided by the θ-averaged signal, $[S(q,\pi) - S(q,0)]/\langle S(q,\theta)\rangle_\theta$, averaged over a region of interest in the sample, increases with the number of concatenations, $n$, although the total diffusion weighting $nq^2$ is unchanged. The relative increase is higher in the lower δ range (exp. B), consistent with a disproportionate benefit of the δ reduction [3,7]. The results suggest that concatenations in DWV experiments with short mixing time increase the modulation amplitude, albeit less than expected from Eq. (2).

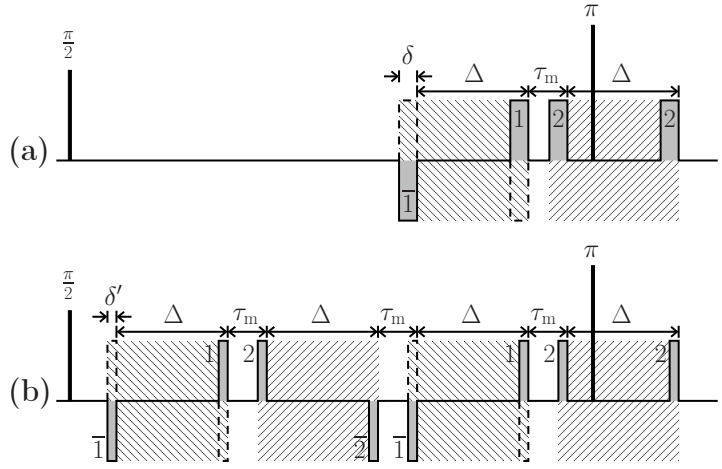


**Fig. 1:** DWV weighting sequence in the standard (a) and the concatenated version with $n = 2$ and reduced δ (b). Slice select and crusher gradients immediately before and after the refocusing RF pulse, perpendicular to the diffusion gradients, are not shown. The diffusion gradients $\mathbf{G}^{(1)}$ and $\mathbf{G}^{(2)}$ are labeled 1 and 2, respectively (a bar denotes gradient inversion). $G = |\mathbf{G}^{(1)}| = |\mathbf{G}^{(2)}|$. The solid and broken lines show $\mathbf{G}^{(1)}$ for $\theta = 0$ and π, respectively.

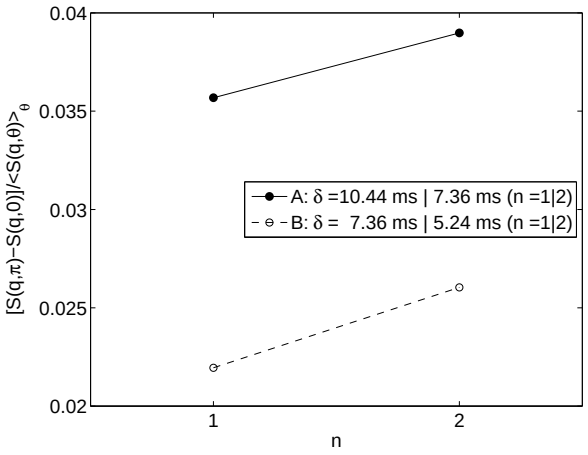


**Fig. 2:** Difference between MR signals for antiparallel and parallel gradient orientation, divided by signal average over angle θ between the gradients, versus number of concatenations, $n$. In experiments A and B, $nq^2$ was kept constant by adapting the gradient pulse duration, δ. Data averaged over a region of interest in fixed pig spinal cord.

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