Exchange and T2-relaxation effects in double pulsed field gradient experiments

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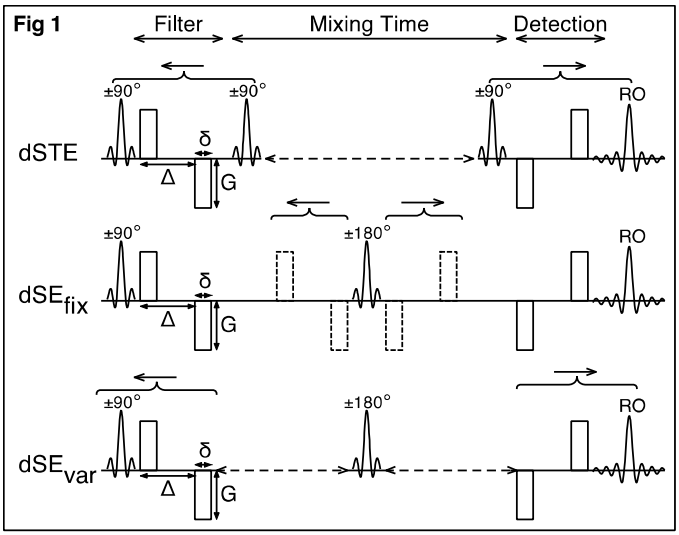
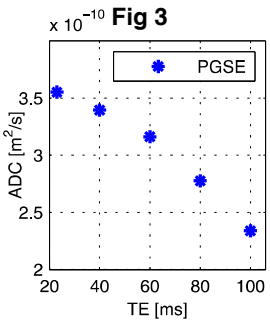
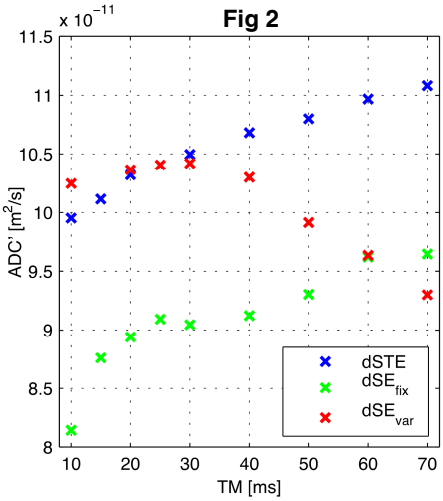
Introduction: Double Pulsed Field Gradient (dPFG) sequences have recently been used for novel tissue contrasts such as the Apparent Exchange Rate (AXR) and Compartment eccentricity[1,2]. Both stimulated echo (STE) and spin echo (SE) type sequences have been used for these kinds of experiments [1-3]. However, the effects of differences in compartment specific T1/T2 relaxation between these types of sequences are currently unknown. Here we compare effects on the mixing time (TM) dependent Apparent Diffusion Coefficient (ADC'(TM)) of either T1- or T2-relaxation during TM in dPFG type experiments using two variants of a dPFG SE (dSE) sequence and dPFG STE (dSTE) sequence. Our results indicate that differences in T2-relaxation between signal components originating from compartments with different diffusivities cause a decrease in the estimated ADC as TM or echo time (TE) are increased.

Method: A single scan session was performed in an experimental 4.7 T MRI Agilent scanner with a maximal gradient strength of 600 mT/m. A yeast cell suspension constituting a well-defined isotropic two-compartment system of densely packed cells was used for all scans. Three days prior to scanning fresh baker's yeast was mixed with tap water (3:1 weight ratio). Before scanning, the yeast was centrifuged at 2800 rpm for 15 minutes in 15-mL plastic tube and the tube was positioned in a quadrature RF transmit/receive coil. The following imaging parameters were used: Six slices with no gaps, matrix size: 128x128, voxel size: 1^3 mm^3, and a TR of 2500 ms. ADC'(TM) was estimated using three types of sequences as shown in figure 1: *i*) dSTE, *ii*) dSE with fixed echo time (TE) of 107ms (dSE_{fix}) and *iii*) dSE with minimal TE increasing with TM (dSE_{var}). How TM was varied depended upon the type of sequence as seen in Fig 1.: For *i) the dSTE sequence* by increasing the delay between the 2nd and 3rd 90°RF pulse, *ii) the dSE_{fix} sequence* by using a fixed TE and increasing the separation between the filter and detection gradients, and *iii)* the *dSE_{var} sequence* by using the minimum possible TE while increasing the separation between the filter and detection gradients. For all sequences a diffusion weighted image with both the filter and detection block applied and an image with only the filter block applied i.e. a *filtered* b_0 image, was acquired and from these the ADC'(TM) was calculated as the regular ADC. The following settings was used: b-value in both filter and detection block: 2720 s/mm^2 (gradient strength [G]: 490 mT/m, pulse duration (□): 5 ms, pulse separation (□): 8 ms), mixing time (TM): [10, 15, 20, 25, 30, 40, 50, 60, 70] ms. To further demonstrate potential effects of compartment specific T2-relaxation effects, the regular ADC was estimated at different TE using a standard diffusion weighted Pulsed Gradient Spin Echo (PGSE) sequence with the diffusion gradient position right before and after the 180°RF pulse. By increasing the delays before and after the diffusion encoding gradients TE was varied between [23, 40, 60, 80, 100] ms while keeping the diffusion encoding gradients identical for all experiments. The following settings were used: b-value: 1037 s/mm^2 (G: 300 mT/m, □: 5 ms, □: 8.11 ms). The temperature was kept at 18.4±0.7°C during all scans. The ADC'(TM) and ADC values was calculated using the mean signal from a ROI covering the central part of the yeast phantom.







Results: ADC'(TM) values for the three sequences in Fig. 1 are seen in Fig 2. For short TM the ADC'(TM) values are comparable for dSE_{var} and dSTE whereas the values of dSE_{fix} are lower. As TM is increased, ADC'(TM) increases in a comparable way for both the dSTE and dSE_{fix} sequences due to exchange processes as previously shown[1,3]. However, for dSE_{var} at TM 30 ms ADC'(TM) start decreasing with increasing TM and gradually approaches the values of dSE_{fix}, and at TM=70 ms the two measurements are comparable. ADC values measured at different TE using a standard diffusion weighted PGSE sequence are seen in Fig 3. The measured ADC values decreases more than 30% as TE is increased from 23 to 100 ms. The ADC was not expected to be dependent on TE. Note that the higher ADC in Fig. 3 compared to ADC'(TM) in Fig. 2 are likely explained by the lower b-values used in the dwSE compared to those used in the dSTE and dSE sequences.

Discussion & Conclusion: We speculate that the decrease of ADC'(TM) in TM is explained by shorter T2-relaxation of compartment specific fast diffusion signal components, often assumed to originate from the extracellular space, effectively filtering the fast diffusing signal components as TE is increased. This explains: 1) dSTE and dSE_{fix} show comparable ADC'(TM) values at short TM where dSE_{fix} is subject to similar T2-relaxation as dSTE, 2) the ADC'(TM) values of dSE_{fix} approaches the lower values of dSE_{var} as TM increased since the T2-relaxation of dSE_{var} increases with TM, and 3) the decrease of ADC as TE is increased with otherwise identical PGSE sequence settings. Previous T2-relaxation studies in rat spinal cord, frog peripheral and frog sciatic nerve have found either the shortest T2-times in extra-axonal compartment[4], the shortest T2-times in the intra-axonal compartment[5] or non-identical T2-relaxation between the two compartments[6]. Hence the origin of the multiexponential T2-decays is not well established. If our yeast phantom is interpreted as a simple two-compartment system where the extracellular signal components are suppressed by the filter-gradients and subsequently restored due to exchange processes during TM, our data suggested that the extra-cellular signal component have shorter T2-relaxation compared to the intracellular compartment. Lastly we note that variability of ADC in TE suggests that both dPFG and regular single-shell diffusion weighted experiments with PGSE should consider the effects of differences in compartment specific T2-relaxations in the experimental design. Furthermore our results indicate that multi-shell experiments should adopt the same TE in all shells to maintain the relative T2-relaxation weighting of the individual compartments.

References: 1. Lasič et al., 2011, Apparent exchange rate mapping with diffusion MRI, MRM. 2. Jespersen et. al., 2013, Orientationally invariant metrics of apparent compartment eccentricity from double pulsed field gradient diffusion experiments, NMR in biomedicine. 3. Sønderby et. al., 2013, Apparent exchange rate imaging in anisotropic systems, MRM. 4. Peled et. al., 1999, Water diffusion, T2, and compartmentation in frog sciatic nerve, MRM. 5. Wachowicz et. al., 2002, Assignment of the T2 Components of Amphibian Peripheral Nerve to Their Microanatomical Compartments, MRM. 6. Harkins et. al., 2012, Effect of intercompartmental water exchange on the apparent myelin water fraction in multiexponential T2 measurements of rat spinal cord, MRM.