Studying restricted diffusion with more accessible gradient amplitudes

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Introduction: Since its introduction in 1965, the Stejskal-Tanner (ST) pulse sequence [1] has dominated the diffusion MR studies of porous media, food products, and biological tissues. The ST signal is the Fourier transform of the ensemble-averaged propagator (EAP), a compromised version of the true diffusion propagator, which fully describes diffusion. Recently, a new gradient waveform (PROP; see Fig. 1) was introduced, capable of reconstructing the true propagator in both restricted compartments [2] and for free diffusion [3,4]. However, this method requires sampling a 2d-dimensional space (d = diffusion dimensionality), which is impractical. We introduce the reduced PROP (rPROP) technique, which matches the ST method in the number of measurements while providing additional information.

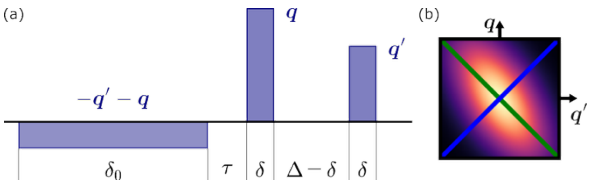

Fig. 1: (a) Propagator sensitive waveform (PROP) introduced in [2,3]. (b) 1D sampling space obtainable with PROP, ST is obtained with $q' = -q$ (green), while rPROP is obtained with $q' = q$ (blue).

In Fig. 1b, we show the qq'-plane that can be probed via the PROP method. The simulated free diffusion signal (provided in the background), is heavily suppressed in rPROP, due to the larger diffusion weighting (b -value) for the same q-value (or gradient amplitude). Since diffusion anisotropy typically arises from restricted diffusion [5], we use rPROP to detect anisotropy in samples with an overwhelming presence of isotropic diffusion. This is important for applications such as fiber-tract mapping in the brain, where the smallest trace of anisotropy could be indicative of an important connection. By taking the Fourier transform of the rPROP signal, we reconstruct the distribution of the mean value of the particles' positions at two time points defined by the two narrower pulses. This mean position distribution (MPD) is compared with the EAP available via ST.

Method: Pulse sequences featuring the rPROP and ST gradient waveforms were implemented on a 0.55T benchtop MRI system (*PureDevices*, Rimpar, Germany). To showcase the filtering effect of rPROP, data was acquired from a dairy cream (DC) sample. A two-compartment model is employed: a restricted compartment for the fat globules and a free diffusion compartment for the fluid they are suspended in. Both measurements were performed with a q_{max} of 127.3mm^{-1}. R_0 (sphere radius) was estimated from a subset of the samples (I_q in Fig. 2a) to assess whether low-to-mid q-values are sufficient to accurately extract restriction information.

The filtering capabilities of rPROP were then employed to detect anisotropy in predominantly isotropic samples. A celery stalk was scanned (with no imaging gradients) and analyzed with a multidimensional (md) approach akin to DTI. Finally, two distributions were computed for a mouse spinal cord (SC) sample. Data from both sequences were acquired with q-values ranging from 0.09 to 127.32mm^{-1}. All diffusion gradients were applied perpendicular to white matter (WM) fibers. The mean position distribution $\bar{p}_\Delta(\bar{x})$, and the displacement distribution $\bar{p}_\Delta(\Delta x)$ were then estimated via inverse Fourier Transform of the rPROP and ST signal profiles, respectively.

Results and discussion: Signals from the DC sample (Fig. 2a) shows the filtering effect of the rPROP sequence as a faster decay in the signal. The ground truth and estimated sphere's radius with ST

and rPROP were 1.9, 4.39, 2.94µm, respectively, suggesting that rPROP provided better estimates in the same I_q range [6].

Images of the celery sample featuring diffusion encoding gradients applied perpendicular to phloem and xylem cells in vascular channels are shown in Fig. 2b. For the same gradient amplitude, soma regions are attenuated much faster with rPROP than with ST. The tensor ellipsoids [7] from mdrPROP and mdST show their main eigenvector aligned along the orientation of the vascular channels, though the one obtained from mdST shows a slight tilt ($\sim$7.3°). Furthermore, the tensor obtained with rPROP data features a higher fractional anisotropy (FA $\sim$ 0.13), than the one obtained with ST data (FA $\sim$ 0.09). Detecting anisotropy as done here is a very challenging task for any technique, as the anisotropic vascular channels barely constitute 2% (volume-wise) or 4% (signal-wise) of the total sample. Thus, it is remarkable that the tensor obtained with rPROP featured a higher FA and maintained the correct main diffusion direction. It is expected that more comparable results could be obtained had the ST signals been acquired with the same b-value rather than the same gradient amplitude as was done here. However, this would require a significant increase in gradient amplitude (approximately twice as large while maintaining the timing parameters employed here). These results show that with rPROP it is possible to probe anisotropy more conveniently even in very challenging environments. Finally, images of the SC sample are shown in Fig. 2c along with the computed distributions. In both distributions, GM features wider lobes when compared to WM. However, the differences between the two regions are more conspicuous for the mean position distribution.

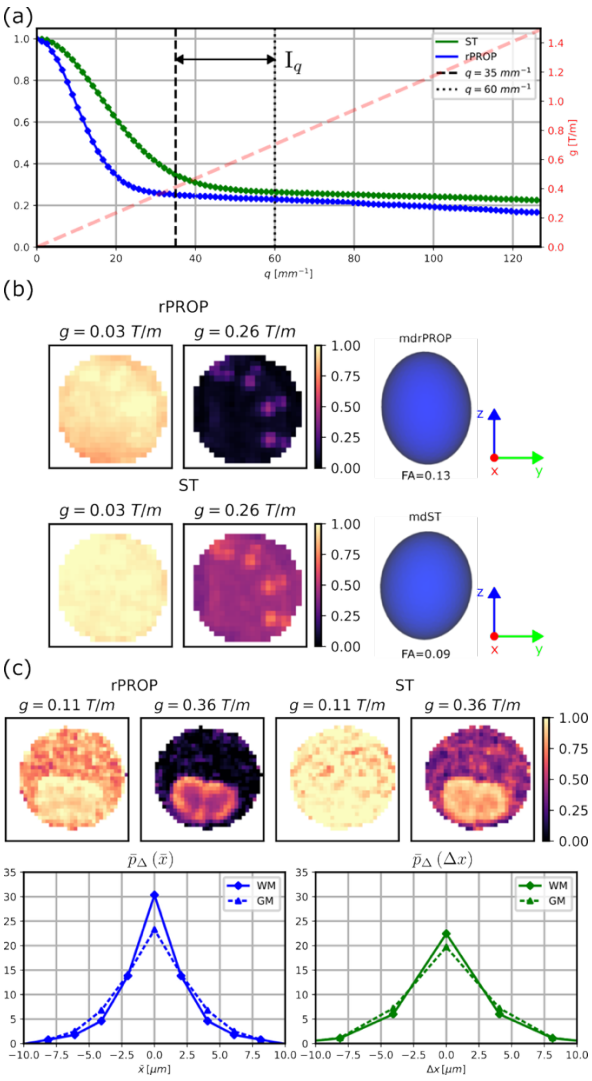

Fig. 2: (a) Signals obtained from the DC sample with ST (green) and rPROP (blue). Timing parameters: δ=2ms and Δ=30ms, δ_0=35ms, and τ=1ms. (b) Images of the celery sample acquired with rPROP and ST, and estimated ellipsoids. Timing parameters: δ=2ms and Δ=20ms, δ_0=30ms, and τ=3ms. (c) Images of the SC sample acquired with rPROP and ST sequences, and estimated mean position (blue) and mean displacement (green) distributions for voxels corresponding to white and gray matter. Timing parameters: δ =2ms and Δ =10ms, δ_0 =10ms, and τ=1ms.

Conclusion: In this work, we presented a new diffusion acquisition and analysis framework (rPROP), and showed its superiority over the ST measurements at elucidating the typically more interesting restricted compartments in complex specimens thanks to its inherently high diffusion weightings. As such, the rPROP method could be a viable alternative to the Stejskal-Tanner measurements in all characterization studies.

References: [1] Stejskal & Tanner, J. Chem. Phys. (1965). [2] Özarslan, Yolcu, Ordinola, Boito, Dela Haije, Højgaard, & Herberthson, J. Chem. Phys. (2023). [3] Özarslan, ISMRM (2021). [4] Ordinola & Özarslan, ArXiv (2021). [5] Beaulieu, NMR. Biomed. (2002). [6] Hinrichs & Kessler, J. Food. Sci. (1997). [7] Basser, Mattiello, & LeBihan, Biophys. J. (1994).