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## Effect of Phase Correction on DTI and q-space Metrics

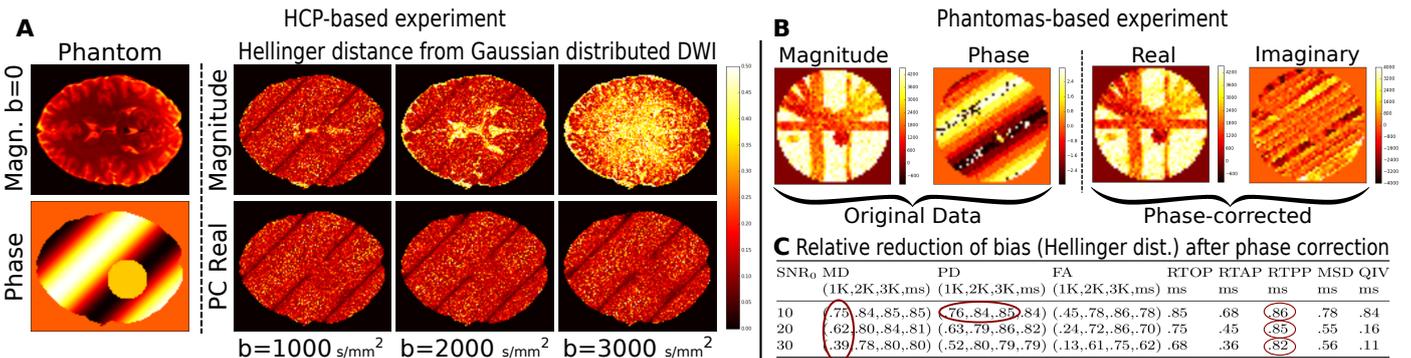
Marco Pizzolato<sup>1†</sup>, Timothé Boutelier<sup>2</sup>, Rachid Deriche<sup>1</sup>

**Introduction.** The non-Gaussian noise distribution, e.g. Rician, in magnitude Diffusion-Weighted Images (DWIs) can severely affect the estimation and reconstruction of the true diffusion signal. As a consequence, diffusion metrics computed on the estimated signal can be biased. We study the effect of phase correction, a procedure that re-establishes the Gaussianity of the noise distribution in DWIs by taking into account the corresponding phase images. We quantify the debiasing effects of phase correction in terms of diffusion signal estimation and calculated metrics. We perform *in silico* experiments based on a MGH Human Connectome Project dataset<sup>3</sup> and on a digital phantom, accounting for different acquisition schemes, diffusion-weightings, signal to noise ratios, and for metrics based on Diffusion Tensor Imaging (DTI) and on Mean Apparent Propagator Magnetic Resonance Imaging (MAP-MRI), i.e., q-space metrics. We show that phase correction is an effective tool to debias the estimation of diffusion signal and metrics from DWIs, especially at high b-values.

**Methods.** We implement a phase correction procedure based on total variation (Eichner et al. 2015). The phase correction aims to estimate the true phase of a complex DWI to subtract it from the noisy acquired phase. The estimated phase is used to perform a complex rotation of the DWI such that the real channel contains the image information plus Gaussian-distributed noise, and the imaginary channel only contains the latter. Any subsequent diffusion modeling or processing can be done on the phase-corrected real channel which, differently from the magnitude DWI, is theoretically free from the Rician bias and comply with methods (e.g. linear least squares) that assume Gaussian noise.

In the first experiment we quantify the Rician bias on a magnitude DWI at different b-values, and we compare it with that of a phase-corrected real DWI. To do so, we use a HCP dataset to create a complex DWI, which ground-truth magnitude and phase are shown in the first column of figure A. We create the ground-truth magnitude image without diffusion-sensitization,  $S(0)_{xy}$ , by averaging the 40  $b = 0$  magnitude images (for a slice of interest) of the dataset. On the same dataset, we compute the mean diffusivity image,  $MD_{xy}$ , after DTI reconstruction. For each b-value  $b \in \{1000, 2000, 3000\}$   $s/mm^2$  we calculate the ground-truth magnitude as  $S(b)_{xy} = S(0)_{xy} \exp(-b \cdot MD_{xy})$ . After creating a synthetic phase DWI that mimics a realistic scenario, we can compute, for each b-value, the real and imaginary channels of the complex DWI created by combining magnitude and phase images. We add White Gaussian Noise (WGN) with  $SNR_0 = 10$  (based on averaged  $b = 0$  image) independently on real and imaginary channels and then recompute the noisy magnitude DWI and the phase-corrected real DWI. As reference image for Gaussianity, we compute a Gaussian noisy version of the magnitude by adding WGN to the ground-truth  $S(b)_{xy}$ : this is the Gaussian DWI. We compute 1000 noisy repetition of noisy magnitude, phase-corrected real channel and Gaussian DWIs for the three tested b-values. For each pixel ( $xy$ ) of the three images we calculate the distribution of the signal over the repetitions. Figure A reports, for each b-value, the pixel-wise Hellinger distance between the signal intensity distribution of the noisy magnitude DWI and the Gaussian DWI (first row). The figure also report the same quantity but when the phase-corrected DWI is taken into account instead of the noisy magnitude (second row). A higher value (brighter color) signifies a higher distance from Gaussianity, i.e. a stronger bias.

In the second experiment, we create noisy complex DWIs by generating the ground truth magnitude with Phantomas<sup>4</sup> (Caruyer et al. ISMRM'14), and by artificially creating realistic phase images. A slice of the noisy magnitude and phase is shown in the "Original Data" of figure B. The same image depicts the "Phase-corrected" real and imaginary DWIs. As for the first experiment, we consider three versions of the data: noisy (Rician) magnitude, phase-corrected and Gaussian DWIs. We generate noisy data with  $SNR_0 \in \{10, 20, 30\}$   $s/mm^2$  for three single-shell 53 directions schemes,  $b \in \{1000, 2000, 3000\}$   $s/mm^2$  (1K, 2K, 3K in table C), and for the corresponding multi-shell combination of them (ms in table C). We perform DTI reconstruction for each scheme (1K, 2K, 3K and ms), and MAP-MRI for the multi-shell one (ms). Since the noise in the phase-corrected images is Gaussian-distributed, the signal can assume negative values: we impose non-negativity of the signal while performing DTI, and positivity of the Ensemble Average Propagator for MAP-MRI, while applying Laplacian regularization (Fick et al. 2016). We select a mask of fibers within the phantom and compute DTI and MAP-MRI metrics for each voxel in the mask: mean (MD) and principal (PD) diffusivity, fractional anisotropy (FA), return to origin (RTOP), axis (RTAP), and plane (RTPP) probabilities, mean squared displacement (MSD) and q-space inverse variance (QIV). We compute the distribution of each metric calculated on the noisy magnitude, phase-corrected, and Gaussian DWIs. Again, we use the Hellinger distance to quantify the distance from Gaussianity. For each metric we compute the distance between its distribution calculated on the noisy magnitude DWIs and the one calculated on the Gaussian DWIs; similarly, we compute the same distance between phase-corrected and Gaussian derived distributions. Table C reports, for each metric, the maximum theoretical relative reduction [0,1] in distance from Gaussianity, obtained after phase correction, compared to the use of the noisy magnitude DWIs. This is reported for each  $SNR_0$  and acquisition scheme (1K, 2K, 3K, ms).



**Results and Discussion.** Results for the first experiment (HCP-based) in figure A show that in the case of a magnitude DWI the bias due to non-Gaussianity, i.e. the Hellinger distance, increases with the b-value. Indeed, at high b-values the DW signal is low, especially in the absence of underlying tissue restrictions of the diffusion process. This causes also the effective SNR to be low, which is when the Rician distribution of the noisy data diverges ( $SNR < 5$ ) from a Gaussian one. On the other hand, phase correction removes the bias and keeps it stable at any b-value ("PC real" in figure A). Results for the second experiment (see figure B and table C) report that, given a metric, e.g. MD, and an acquisition scheme, e.g. 1K, the debiasing effect of phase correction increases with the amount of noise, i.e. the decrease of  $SNR_0$ . The debiasing effect of phase correction for a given metric, e.g. PD, and  $SNR_0$ , e.g. 10, increases with the b-value (1K, 2K, 3K), as also demonstrated by the first experiment. Moreover, we note that metrics that are highly related to signal measured along the less restricted diffusion direction, i.e., low intensity signal, such as PD for DTI and RTPP for MAP-MRI, benefit more than others of phase correction.

**Conclusions.** Phase correction is a useful tool for restoring the Gaussianity of the noise distribution in DWIs. We quantified its effect directly on the distribution of the diffusion signal and of the metrics computed via DTI and MAP-MRI. Since research in diffusion MRI goes towards higher b-values and resolutions, i.e. lower SNR, phase correction is a suitable technique to pre-process the DWIs. Indeed, our results show that phase-correction helps debiasing especially in low SNR regime.

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<sup>3</sup>Data for this project was provided by the MGH-USC Human Connectome Project.

<sup>4</sup>[https://github.com/ecaruyer/phantomas/blob/master/examples/isbi\\_challenge\\_2013.txt](https://github.com/ecaruyer/phantomas/blob/master/examples/isbi_challenge_2013.txt)