How to make sure you are using the correct gradient orientations in your diffusion MRI study

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TARGET AUDIENCE: Scientist and clinicians who are unsure whether they are using the correct gradient tables in their diffusion MRI study. **PURPOSE:** Diffusion tensor imaging (DTI) parameters derived from the tensor eigenvalues, such as fractional anisotropy (FA) and mean diffusivity (MD) are rotationally invariant, meaning that they should not change if the subject is scanned with a different angulation. Rotationally variant diffusion parameters, on the other hand, such as the principal diffusion vector (PDV) and, consequently, DTI fiber tractography will change if this angulation changes. For this type of information to be meaningful, the coordinates of the gradient orientations should use the same coordinate frame as the voxels in the diffusion weighted (DW) data set. In theory, the metadata generated by MRI scanners should provide all the necessary information to properly align the gradient table with the subject coordinate frame. In practice, however, this procedure is error-prone and highly dependent on the coordinate system conventions of the scanner's meta data, the used data file format, and even the used post-processing tool. While large gradient misalignments can be detected by visual inspection of PDV maps or tractography results, small angulations could go unnoticed and may drastically affect tractography results. In this work, we propose a convenient tool to check and correct the gradient table based on [1]. **METHODS:** *Overview:* Incorrect gradient orientations result in a loss of global fiber "connectivity", which can be determined with fiber tractography. By transforming the gradient table and measuring the fiber trajectory length, one can search for the transformation that results in the best "global connectivity" [1]. Finding the correct DW gradient settings then becomes an optimization problem similar to image registration (Fig. 1). *Transformation:* The 3D rotation of the gradient table can be parameterized as successive rotations around the main orthogonal axes resulting in a parameter vector $\boldsymbol{\theta}$ with three rotation parameters. *Metric*: The metric, which provides a measure of how well the gradient orientations match the DW images, is defined as the average trajectory length $f(\boldsymbol{\theta}, n)$, measured with whole-brain streamline DTI tractography [2], where n is the number of seed points evenly distributed over the whole brain. Since finding the optimal gradient table requires many repeated evaluations of the metric, it is imperative that this step is fast. Since whole-brain tractography is computationally intensive, several algorithmic optimizations were implemented to speed up the standard streamline DTI tractography algorithm. First, fiber tractography was performed directly in tensor space, using the Log-Euclidian framework [3]. As a result, the tensor fitting procedure needs to be performed only once for the entire data set and interpolation can be performed directly on the tensor field, greatly reducing computation time. An additional advantage is that the rotation of the gradient orientations can now be obtained by directly rotating the tensor eigenvectors, requiring only a single diffusion tensor fit for repeated metric evaluations. Second, the analytical eigenvalue decomposition proposed in [4] is used, which is much faster than standard iterative methods. Finally, to reduce computation time even further, whole brain tractography is restricted to a set of n seed points evenly distributed over the whole brain, allowing a trade-off between metric calculation speed, and precision. *Optimization*: In order to find the optimal set of rotation angles $\boldsymbol{\theta}$, a stochastic gradient ascent [5] is defined as $\boldsymbol{\theta}_{k+1} = \boldsymbol{\theta}_k + \gamma_k \nabla \tilde{f}(\boldsymbol{\theta}_k, n)$ with γ_k the scalar gain factor, $\tilde{f}(\boldsymbol{\theta}_k, n)$ the approximate average tract length resulting from whole brain tractography with rotation angles $\boldsymbol{\theta}_k$ and n randomly distributed seed points and iterations $k = 0, \ldots, K$. Note that $\tilde{f}(\boldsymbol{\theta}_k, n)$ is stochastic since each evaluation uses a different set of randomly distributed seed points. Since the approximated gradient $\nabla \tilde{f}(\boldsymbol{\theta}_k, n)$ with respect to $\boldsymbol{\theta}_k$ does not necessarily vanish close to the solution, convergence must be enforced by ensuring $\gamma_k \to 0$ as $k \to K$. In this work, $K = 150$ and $\gamma_k \equiv \gamma(k) = 100e^{-0.068k}$. Using the stochastic gradient ascent makes the optimization routine robust to spurious maxima [5], which are common, especially close to the optimum, and also allows the number of seed points n to be small, significantly speeding up the metric evaluation (we use $n = 100$). As a consequence, robustness and processing speed is much higher than in [1]. Since the gradient ascent can only find the local minimum, a multi-start approach is used. *Evaluation*: A noiseless full-brain DTI data set consisting of 6 b=0s/mm² and 60 b=1200s/mm² images was simulated with Rician noise levels ranging from 1 to 30 in the b=0s/mm² image. For each noise level, 250 noisy realizations were simulated. For each realization, the gradient table was corrupted by a random 3D rotation. After correction, quality of the gradient orientations was assessed: for each gradient orientation, the 250 estimations were averaged and the angular difference with the ground truth orientation (bias) and the 95% confidence interval (CI) were calculated as in [6]. **RESULTS:** Fig. 2A shows the average bias of the proposed method as a function of SNR. Starting from SNR=2, sub-degree accuracy is achieved. Fig. 2B shows the average 95% CI of the gradient orientations as a function of SNR. Starting from SNR=4.3, sub-degree precision is achieved. Fig. 3 shows the 250 realizations of the estimated gradients for different SNRs. At SNR=2 (Fig. 3A), the estimated orientations (colored dots) have clearly converged to the true orientations (plus signs), resulting in a small angular bias. However, dispersion of the orientations is very high, resulting in bad precision. Note, however, that SNR is defined on the b=0s/mm² image and that such data quality is unrealistically poor even for clinical data. At SNR=5, the estimated gradient orientations are tightly clustered around the true orientations resulting in both sub-degree accuracy and precision. At SNR=20, which is representative for clinical data, the estimated orientations are even more tightly clustered around the true orientations. **CONCLUSION:** Using a metric based on whole brain tractography, we have developed a fast and reliable tool to align the DW gradients with the corresponding DW images. Simulations show that our method reports the correct gradient orientations with sub-degree accuracy and precision even for data with very low SNR. Note that while the metric is based on DTI tractography, the recovered gradient orientations can be used in general diffusion MRI post-processing. This tool will be made available during the meeting as a web application.

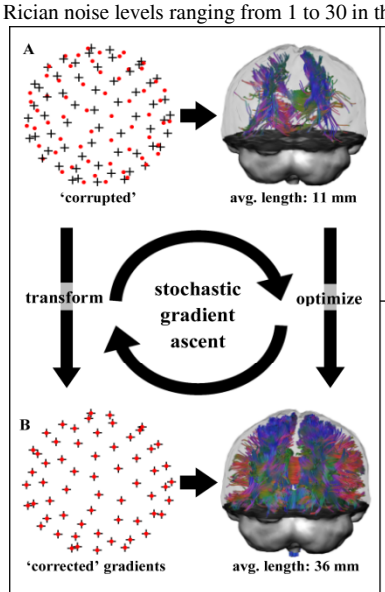


Fig. 1: Overview of the method: true (plus signs) vs. used gradient orientations (red dots) on the unit sphere (left) and the resulting whole brain tractograms (right) before (A) and after rotation correction (B) using the proposed method.

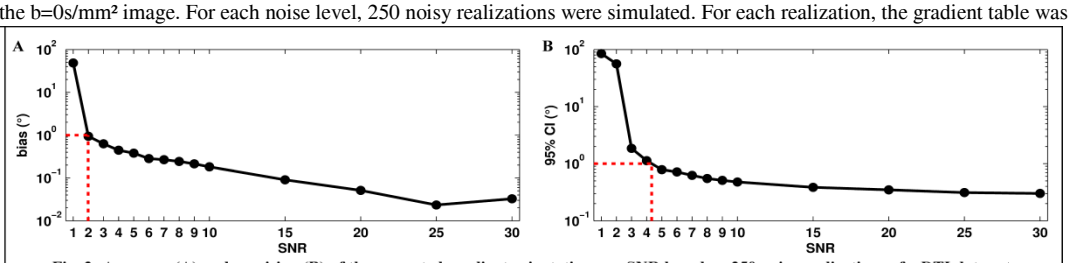
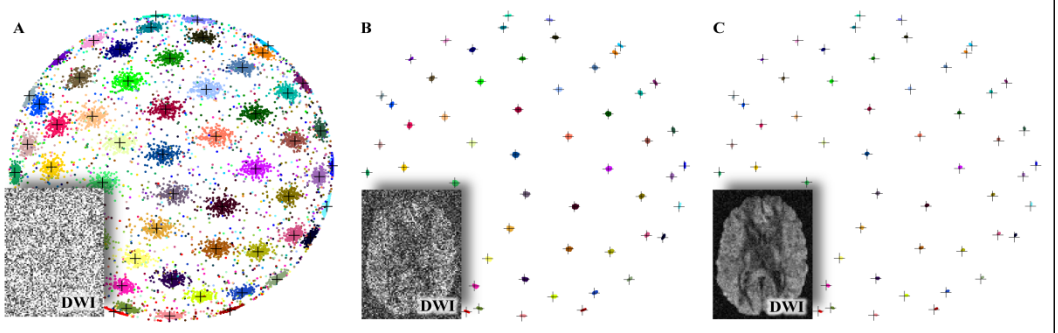


Fig. 2: Accuracy (A) and precision (B) of the corrected gradient orientations vs. SNR based on 250 noisy realizations of a DTI data set. Dashed red lines indicate at which point sub-degree accuracy and precision is achieved.



SNR: 2 bias: 0.94° 95% CI: 56.07° **SNR: 5 bias: 0.38° 95% CI: 0.78°** **SNR: 20 bias: 0.05° 95% CI: 0.35°**

Fig. 3: True (plus signs) vs. estimated gradient orientations (colored dots) for 250 noisy realizations at selected SNRs. Corresponding gradient orientations have a unique color. Data quality for each SNR can be appreciated from the b=1200s/mm² image in the lower left corner.

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