

Is it feasible to estimate rotation-invariant non-parametric axon diameter distributions from PGSE? Preliminary insights from regularized discrete linear modeling and simulated intra-axonal signals

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PURPOSE

dMRI Axon Diameter Distribution (ADD) mapping was first introduced by Assaf¹ through the use of non-linear optimization and a parametric model that imposed ADDs to follow a gamma distribution. Non-parametric ADD mapping was then shown to be feasible by solving a discrete linear problem of the form $Ax=y$, where A is a linear operator or dictionary, x are the ADD coefficients and y is the dMRI signal.² When using PGSE acquisitions, A is very badly conditioned, due to the similarity between signals of axons with different diameters. Benjamini et al. propose to use Double Diffusion Encoding (DDE) to reduce the condition number of A , and to solve the linear problem using standard Tikhonov regularization.² However, in order to acquire the signal in a reasonable time, both DDE and AxCaliber need dMRI signals sampled perpendicularly to the fibers, which limits the method to regions with single and known orientation. We aim at testing the feasibility of ADD mapping from standard rotation-invariant PGSE sequences using discrete linear problem formulation, as part of the Accelerated Microstructure Imaging with Convex-Optimization (AMICO) framework.³

METHODS

To test the feasibility of ADD mapping using PGSE, we focused on a simple study, which considers only the intra-axonal compartment, and tested the influence of different regularization methods on the estimated ADD. We first illustrate the ill-conditioned nature of the problem (PGSE protocol with uniform samples on 3 shells⁴: $G=[300,220,300]$ mT/m, $\Delta=[12,20,17]$ ms, $\delta=[6,7,10]$ ms). We generated the intra-axonal signal of 90'000 cylinders with gamma-distributed radii and created a dictionary of 20 atoms corresponding to cylinders with r in $[0.5, 7.0]$ μ m. Solving the problem using non-negative least-squares (NNLS) recovers coefficients close to the ground-truth ADD in the noiseless case (Figure (a)). We then contaminated the signal with 100 Gaussian noise realizations corresponding to an SNR=30, and repeated the NNLS fitting. The PGSE protocol is such that A has very high condition number (a small variation in the measured signal leads to very different ADD coefficients, as shown in Figure (b)). Tikhonov regularization can be used to stabilize the ADD by minimizing the following problem instead: $\min_{0 \leq x} \|Ax - y\|_2^2 + \lambda \|\Gamma x\|_2^2$, where Γ is a linear operator and λ ponderates the regularization. Standard Tikhonov uses $\Gamma=I$, as in¹ and shown in Figure (c). Other operators, like the discrete difference operator D , or the Laplacian L , impose continuity or smoothness respectively. We tested the performance of solving $\min_{0 \leq x} \|Ax - y\|_2^2 + \lambda (\|0.5 \cdot Dx\|_2^2 + \|0.25 \cdot Lx\|_2^2)$, which promotes continuous and smooth ADD, as shown in Figure (d). The regularization weight was tuned to minimize the ADD reconstruction error. Experiments were replicated for Gaussian distributed cylinders (Figure (e)) to test if similar results could be obtained from an independent set of signals generated from another distribution.

RESULTS

Results are summarized in the following figures. The ground-truth ADD is plotted in red and recovered coefficients in blue. (a) shows the recovered ADD for NNLS fitting on the noiseless signal. Figures (b) to (d) show the mean and standard deviation for the ADD coefficients recovered over 100 signals with SNR=30. Finally, Figure (e) shows the performance of our method on the signal generated from another distribution.

DISCUSSION/CONCLUSION

Adding continuity and smoothness constrains on the ADD coefficients improve the recovered distribution. Our method, as opposed to DDE or AxCaliber, doesn't

require the acquisition to be perpendicular to the axons and is suited for rotation invariant protocols. How the presence of extra-axonal and isotropic signal contributions affect the fitting when promoting continuity and sparsity still needs to be evaluated. Furthermore, the protocol we used was optimized for mean diameter mapping.⁴ Optimizing the protocol parameters for distribution mapping might improve our results. Finally, this regularization is easily implementable in the AMICO³ framework to be used by other researchers if it appears to be of interest for the microstructure imaging community.

REFERENCES

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