Rapid and Accurate NODDI Parameter Estimation with the Spherical Mean Technique

Ryan P Cabeen[1], Farshid Sepehrband[1], and Arthur W Toga[1]

[1]*Laboratory of Neuro Imaging, Stevens Neuroimaging and Informatics Institute, Keck School of Medicine of USC, Los Angeles, CA, United States*

Synopsis

Neurite orientation dispersion and density imaging (NODDI) is a widely used tool for modeling microstructure using diffusion MRI, but its computational cost can be prohibitively expensive. This work investigates the efficacy of integrating the spherical mean technique (SMT) into a non-linear optimization framework to improve NODDI parameter estimation. Through quantitative simulation, comparative, and reliability analyses, we found that integrating SMT into more traditional non-linear optimization enables rapid, accurate, and reliable estimation of neurite density and dispersion compared to other approaches.

Introduction

Neurite orientation dispersion and density imaging (NODDI) is a multi-compartment modeling technique for deriving microstructural parameters from multi-shell diffusion MRI[1]. It has been widely adopted due to its simplicity and improved biophysical specificity compared to other techniques, such as diffusion tensor modeling[2,3]; however, its computational cost can be prohibitive when datasets are large or the available compute resources are limited. While a variety of approximate accelerated fitting methods have been proposed, faster non-linear fitting approaches remain attractive due to their accuracy and flexibility for setting study specific diffusivity and incorporating priors.

The spherical mean technique (SMT) is a mathematical tool for obtaining orientationally-invariant parameters of multi-compartment models using powder averaging of the diffusion signal within each shell of the gradient encoding[4]. SMT has been previously used for neurite density estimation[5] but it has been neither systematically evaluated nor combined with dispersion estimation. Because its use may provide computational advantages, we investigated such a multi-stage approach for estimating the complete set of NODDI parameters by integrating the SMT into a typical non-linear optimization framework (NODDI-SMT). We evaluated this approach through simulation experiments, quantitative comparisons with other techniques using in vivo data, and a scan-rescan analysis of reliability across a typical population.

Methods

Datasets: Our experiments used the in vivo human scan with 1.875x1.875x2.5 mm^3 voxels and b=0,700,2000 s/mm2 released on NITRC with the NODDI toolbox[6] and 44 pairs of test-retest in vivo human scans with 1.25 mm isotropic voxels and b=0,1000,2000,3000 s/mm^2 from the Human Connectome Project[7] (HCP).

Fitting: We incorporated SMT into NODDI fitting using the following multi-stage approach: first, the neurite density index (NDI) and isotropic volume fraction (FISO) were estimated using powder averaged signals with the SMT, then the orientation dispersion index (ODI) and NDI were obtained using Powell's BOBYQA non-linear optimization algorithm[8] with the SMT parameters as initial conditions. We compared the performance of SMT fitting with two reference fitting techniques: Accelerated Microstructure Imaging via Convex Optimization[9] (AMICO), implemented using the publicly available Python code[10] and non-linear least squares (NLLS) using BOBYQA with fixed initial conditions.

Experiments: We evaluated this technique using three experiments. First, we evaluated the accuracy of NLLS and SMT fitting across several levels of Rician noise (Fig 1). We simulated diffusion MR signals from a variety of typical NODDI parameter sets and assessed the error from NLLS and SMT fitting. Second, we evaluated consistency among AMICO, NLLS, and SMT-based fitting approaches by comparing their runtimes, parameter estimates, and residual fitting errors with NITRC data (Figs. 2,3), and excluded voxels that were mostly free water from the analysis. Third, we evaluated scan-rescan reliability using the coefficient of variation (CV) and intra-class correlation (ICC) with HCP data (Figs. 4,5) using averages from regions-of-interest from the Johns Hopkins and Desikan-Killiany white matter atlases coregistered using DTI-TK[11].

Results

Simulation results showed that SMT-based fitting had higher accuracy and robustness to noise than NLLS fitting with an 82% reduction in runtime (Fig 1). Comparative analysis showed that SMT had similar residuals and parameter estimates to NLLS fitting (Pearson's correlation > 0.99), and AMICO had higher residual error than SMT (Fig 2, 3). AMICO parameter estimates were found to exhibit discretization effects at mid-range NDI and low-range ODI values, which were not present in NLLS and SMT-based estimates. Whole brain fitting of NITRIC data with NLLS and SMT-based took 682s and 105s, respectively. AMICO took a total of 596s (237s of which were spent on optimization after building the dictionary). Reliability test showed that AMICO and SMT-based fitting had comparable reliability in NDI (ICC=0.88 and CV~2.7%), while NLLS was slightly lower (ICC=0.83, CV=2.7%). ODI estimates from NLLS and SMT-based fitting (ICC=0.91, CV=3.2%) were more reliable than AMICO (ICC=0.88, CV=6.3%) (Fig 5).

Discussion

The results indicate that the integration of SMT into a non-linear optimization framework provides improved convergence, accuracy, and reliability compared to both AMICO and NLLS. This may be explained by the regularizing effect of powder averaging, and the reduced dimensionality of the parameter search space achieved by optimizing NDI and FISO separately from ODI. While non-linear approaches are typically quite costly, the integration of SMT was found to greatly reduce the computation time, making the combination a suitable approach for using NODDI in practice.

Conclusions

Taken together, the simulation, comparison, and reliability results indicate that SMT-based fitting of NODDI parameters provides rapid and accurate estimates of both neurite density and dispersion with improvements compared to AMICO and NLLS fitting. Our implementation is available as a module in the Quantitative Imaging Toolkit[12] which is available for download online[13,14].

Acknowledgements

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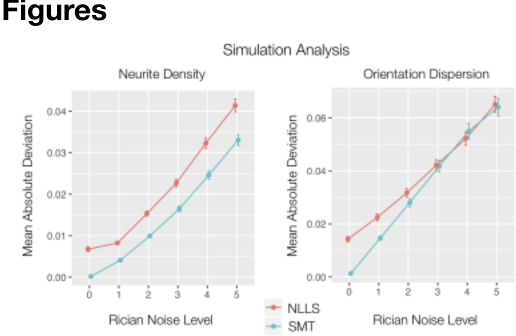
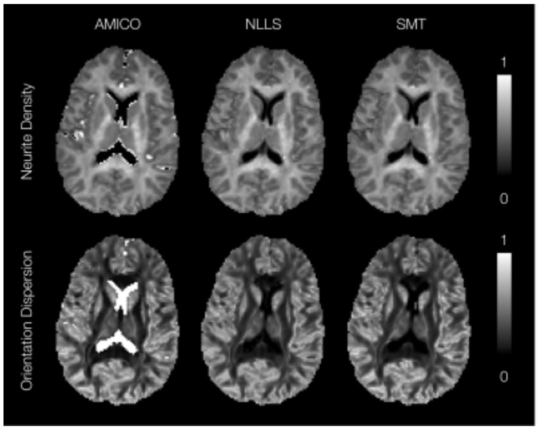
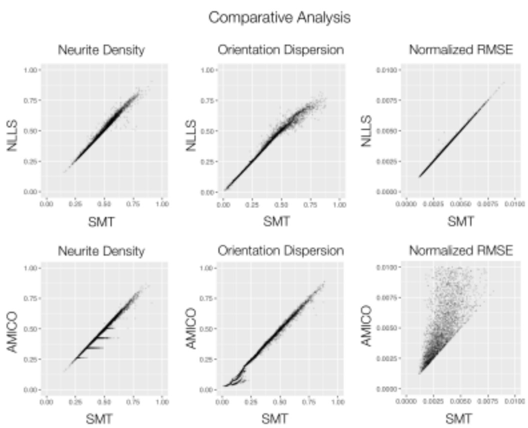
Figures



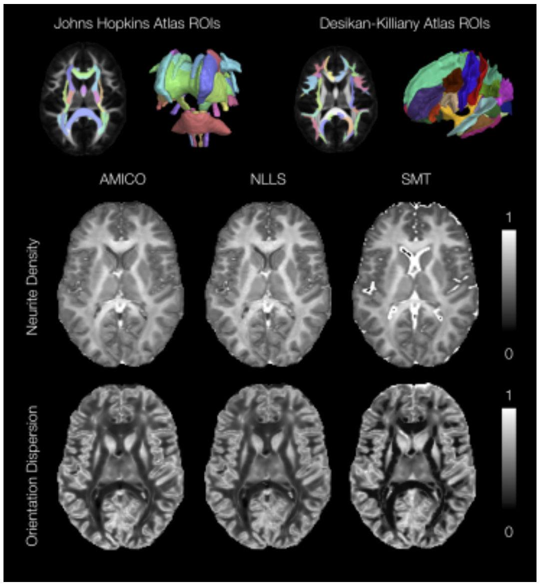
Simulation results comparing non-linear least squares (NLLS) and a multi-stage optimization framework using the spherical mean technique (SMT). The experiment synthesized 100 repetitions across Rician Noise levels={0,1,2,3,4,5} ofa simulated diffusion MR signal from typical NODDI model parameters sets including all combinations of S0=300, NDI={0.25,0.5,0.75}, ODI={0.25,0.5,0.75}. The error in estimated neurite density (Fic) and orientation dispersion (ODI) are plotted across noise levels for each method. The results show that SMT offers overall lower error and robustness to noise.



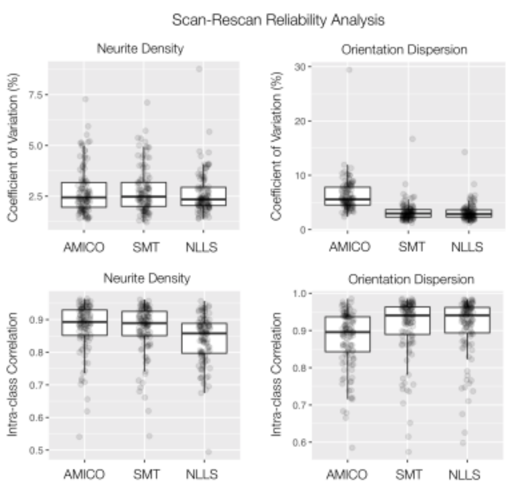
Comparative analysis of parameter maps from NITRC data estimated using AMICO, non-linear least squares (NLLS) and a multi-stage optimization framework using the spherical mean technique (SMT). The results show that SMT provides spatially homogeneous estimates than NLLS. Voxels that were less than half free water were included in a quantitative analysis.



Comparative analysis of parameter estimates and model fitting residuals obtained from AMICO, non-linear least squares (NLLS) and a multi-stage optimization framework using the spherical mean technique (SMT). The results how the agreement between SMT and NLLS in neurite density, orientation dispersion, and normalized root-mean-square residual error (NRMSE), which had Pearson's correlation coefficients of 0.991, 0.992, and 0.867, respectively. AMICO was found to have higher NRMSE than SMT and to exhibit some discretization errors for some ranges of parameters.



Example parameter maps from HCP data estimated using AMICO, non-linear least squares (NLLS) and a multi-stage optimization framework using the spherical mean technique (SMT). The first column shows the regions-of-interest used in the analysis, which were from the Johns Hopkins and Desikan-Killiany white matter atlases. This data was used for the reliability analysis.



Reliability analysis of parameters estimated using AMICO, non-linear least squares (NLLS) and a multi-stage optimization framework using the spherical mean technique (SMT). Plots of the coefficient of variation (lower is better) and intra-class correlation (higher is better) are shown, where each point represents the average performance for an individual region-of-interest. The results show that most methods had similar coefficients-of-variation in neurite density, while AMICO had lower reproducibility in orientation dispersion, and NLLS had lower intra-class correlation.