Polynomial Meta-Model of Bloch-Torrey Equation for Track-based Regularization of Microstructural Inversion

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Synopsis

A meta-model approach is presented which fits a multi-dimensional polynomial to numerical solutions of the Bloch-Torrey equation after being parameterized by microstructural and diffusion encoding parameters. This meta-model allows analytical representation of the solution space enabling analytical analysis of the space as well as reduced computational cost to solutions that do not need precise results. Possible uses of such a model are outlined, such as its use in allowing muscle tractography results to regularized by neighboring voxels in its defined muscle tract.

Introduction

Both gradient strength and diffusion time have been identified as important parameters to control when quantifying muscle microstructure with diffusion MRI.[1-4] Determining which of these encoding parameters yield the most structural information into the dMRI signal will allow more accurate estimation of microstructural parameters. Diffusion MRI is governed by the Bloch-Torrey equation which is a 2nd order PDE. Solving this equation over a realistic domain requires computationally expensive numerical solutions. Being able to interpolate between already computed points saves computational time and allows rapid solution times. In this abstract, we fit a polynomial surface to numerical solutions of the Bloch-Torrey equation to provide an analytical representation, or metamodel, of the relationship between the microstructural parameters, diffusion encoding parameters, and the dMRI signal.

Methods

Using a numerical model based on a Lattice Boltzmann Method solution of the Bloch-Torrey equation,[5] dMRI experiments were computed[6] over a domain of periodically packed hexagonal cells surrounded by a permeable membrane and embedded in an extracellular matrix. The domain was parameterized by intra- and extracellular diffusion, cell diameter, membrane permeability, and volume fraction and sampled with a Sobol sequence[7] to create 1600 parameter combinations ($D_{in,ex} \in [0.5,3]$ μm^2/ms, $a \in [10,100]$ μm, $\kappa \in [1,150]$ μm/s, $f \in [0.4, 0.95]$). PGSE sequences were simulated for 5 b-values (500, 750, 1000, 1500, and 2000 s/mm^2). At each b-value 5 diffusion times (Δ) were simulated (10, 25, 50, 75, and 100 ms) with a gradient timing of 7.5 ms. Six gradient directions were used to estimate a diffusion tensor from which fractional anisotropy (FA), mean diffusivity (MD), longitudinal diffusivity (LD) and radial diffusivity (RD) were extracted. Further simulations were performed with a single microstructural parameter varied and all other parameters held constant and for a different Sobol sequence to generate an additional 320 parameter combinations. The opensource python package Chaospy[8] was used to create a metamodel which fit microstructural and DTI encoding parameters to each of the four DTI metrics (i.e. FA = f(Din, Dex, a, κ, f, b, Δ)). Polynomials of order n were fit using least squares for n = 3, 4, and 5.

Results

Comparison of the fitted polynomial meta-model with the numerical testing data for variations of a single parameter at a time is shown in for FA Figure 1. Figure 2 shows how the Sobol testing data compares with the fitted polynomials for various orders of n. Diffusion coefficients are fit with much higher accuracy than FA. A sufficient number of points is necessary to constrain the fitted polynomial in each dimension, a criterion not satisfied for the 5th order polynomial in terms of b-value of diffusion time demonstrating the limits of such a modeling procedure.

Discussion and Conclusion

The primary goal of this abstract was to determine the feasibility and accuracy of such a metamodel representation of the Bloch-Torrey equation. While more work can be done to improve the fitting procedure, it is clearly possible to represent the overall behavior of the equation through use of such a hypersurface. The utility of such a surface is the ability to analytically represent the relationship between microstructure, DTI pulse parameters, and the resulting DTI measurements, allowing analysis of regions of high or low sensitivity to changes in parameters (Figure 3). Knowledge of parameter sensitivity is important in determining confidence intervals when estimating microstructure and can determine which diffusion encoding parameters needed to be sensitive to change in a particular microstructural parameter. Additionally, by assuming that muscle structure is smoothly and slowly varying between voxels, this surface can be used to regularize predicted microstructure. In such a system, an initial subsurface at each voxel of the possible parameters (P_i) would be generated that satisfy the condition $FA_i \cap MD_i \cap LD_i \cap RD_i$. This subsurface could then be regularized by nearby voxels by examining $P_i \cap P_j$ subject to some relaxation condition, or, if such an intersection does not exist, by examining the shortest distance between the two subsurfaces P_i and P_j. This regularization approach can be combined with tractography to regularize by voxels in the same muscle track. Histology of different muscles can create priors for allowable parameter values allowing the creation of a DTI parameter atlas which can inform such track-based microstructural inversion. The results presented in this abstract demonstrate that a metamodel representation of the Bloch-Torrey equation is possible and point to future methods of exploiting its features in bolstering microstructural estimation in skeletal muscle.

Acknowledgements

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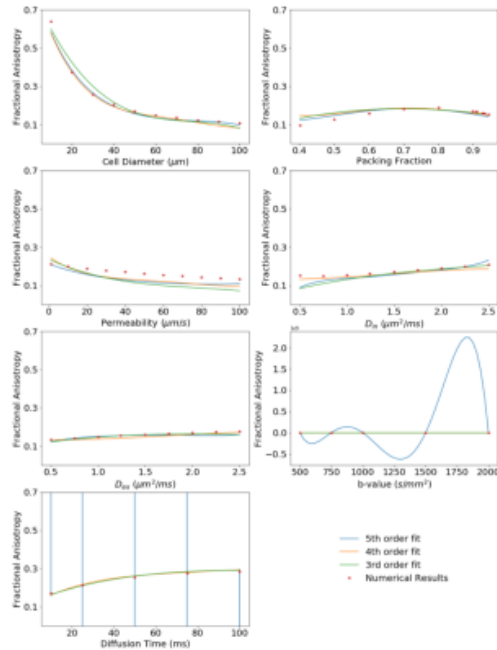
Figures

Figure 1: Metamodel surfaces of FA for 3rd, 4th, and 5th order polynomials compared with numerical simulations not used in the fitting of the model. All parameters, other than the one being varied in each graph, are held at some mean value. Poor results for varying b-value and diffusion time are due to fitting a 5th order polynomial to five points. Simulating more diffusion times and b-values will eliminate poor fit.
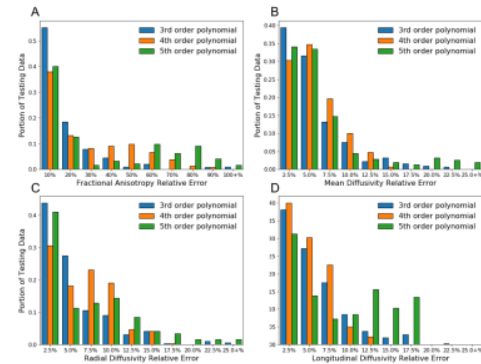

Figure 2: Histogram of Meta-model relative error compared with the Sobol testing set. For fitted models to A) FA, B) MD, C) RD and D) LD. In A) only FA values above 0.05 are compared to avoid normalization by a true FA close to zero. The majority of all the 320 parameters sets compared are within 10% of the true value. Generating more training data may lead to increased accuracy of higher dimension polynomials though at the same time will incur increased computational cost during the simulations and fitting steps.
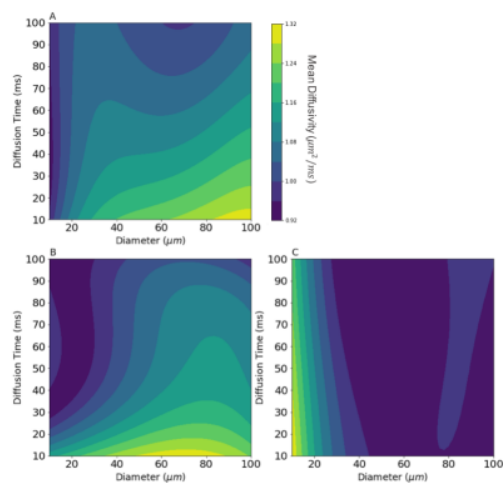
Figure 3: A) Map of FA for different cell diameters and diffusion times. B) Map of the absolute value of derivative of FA with respect to Diffusion time and C) Map of the absolute value of derivative of FA with respect to cell diameter. In B) and C), darker areas denote the derivative in that location is lower meaning that for a change in that parameter, FA will not change much, conversely, brighter areas denote higher derivative values, so a smaller change in a parameter will correspond with a larger change in FA.