PARAMETERS ESTIMATION FOR WHITE MATTER MICROSTRUCTURE MODELS USING VARIABLE PROJECTION METHOD AND STOCHASTIC GLOBAL SEARCH ALGORITHMS

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Target audience: Scientists interested in computational methods for white matter microstructure mapping from diffusion MRI.

Purpose: Biophysical models of brain tissues are becoming increasingly important to extract quantities directly related to axonal architecture (*e.g.* diameter, density) [1]. Here, we introduce an improved computational procedure for tissue microstructure models to extract such quantities from diffusion MRI data. The parameters of multi-compartment models, which describe the underlining structure of the brain white matter, do not relate linearly to MRI measurements. Moreover, these functions are not simple enough to constitute well-posed optimization problems for parameter estimation. Consequently, any fitting procedure using gradient-based methods depends largely on a very good initial guess, as for instance in CAMINO [2]. Currently, simpler models (such as the diffusion tensor) are being used to find this initial guess. Therefore, before estimating a three-compartment tissue model parameters (as given below), one ends up estimating five to six simpler models parameters. Markov chain Monte Carlo (as used in CAMINO [2] and in [3]) substantially increases the probability of finding global minimum but adds to the overall estimation time. Our Non-linear Least Squares (NLLS) optimization problem is of the following form:

$$min_{R,\theta,\phi,f1,f2,f3} \quad \left\| y - \left(f_1 e^{-A_{cylinder}(R,\theta,\phi)} + f_2 e^{-A_{Zepplin}(\theta,\phi)} + f_3 e^{-A_{Dot}}\right)\right\|_2^2$$

$$such\ that\ f_1 + f_2 + f_3 = 1\ ,\ \ f_1 \geq 0\ ,\ f_2 \geq 0\ ,\ f_3 \geq 0,\ \ 0 \leq R \leq 20,\ \ 0 \leq \theta \leq 2\pi\ \ and\ \ 0 \leq \phi \leq \pi$$

Where vector 'y' has normalized MRI measurements, R is axon radius (μ-*meters*) θ and ϕ represent fiber orientation (*radians*), while f_1, f_2 and f_3 are intra-axonal, extra-axonal and isotropic volume fractions respectively. Only unknown parameters have been described here.

Methods: Our suggested algorithm is based on exploiting the separable structure of the problem as described above, through the Variable Projection Method [4]. The variable projection guarantees that the global minimum of a variable projection functional remains unchanged. Moreover, variables entering nonlinearly into the objective function are estimated separately and the problem reduces to a conditional linear least squares (CLLS) estimation. The algorithm can be summarized in the following four steps:

Variable Projection Genetic Algorithm (GA) based method

Step 1. Write NLLS objective function in terms of parameters entering nonlinearly only (R, θ and ϕ), by variable projection.

Step 2. Use Genetic Algorithm based NLLS [5] to estimate the parameters of objective function obtained in step 1.

Step 3. Using values of estimated parameters in step 2, estimate conditionally linear parameters (f_1, f_2 and f_3) with linear least squares.

Step 4. Perform constrained NLLS estimation using initial guess from step 3 to get values of conditionally linear parameters.

Results and discussion:

Evaluation on synthetic data

The suggested algorithm was tested using synthetic data generated by own model routines written in MATLAB and also with data generated by CAMINO. Data was generated with different values of SNR using a Rician noise model with different tissue models (like ZepplinCylinderDot'). Parameters were estimated using both CAMINO ('modelfit' function) and the suggested algorithm. Table 1 shows a comparison of estimated parameters from synthetic data generated by CAMINO using the 'ZepplinCylinderDot' tissue model. It can be seen that the parameters were estimated with better accuracy even at low SNR using the suggested method. In particular radius was consistently better estimated by our proposed method.

	SNR	f_1=0.5	f_1=0.3	f_1=0.2	θ = 1.54 rad	φ = 1.8 rad	R = 5 μm
CAMINO	12	0.662	0.083	0.255	1.58	-1.31	7.84
Suggested Algorithm	12	0.4906	0.2826	0.2172	1.5527	1.8379	5.1005
CAMINO	100	0.765	0.0195	0.215	1.6	-1.31	6.29
Suggested Algorithm	100	0.5017	0.2974	0.199	-1.5404	-1.3087	5.0132
CAMINO	200	0.59	0.367	0.0433	1.6	-1.31	3.49
Suggested Algorithm	200	0.501	0.2986	0.1999	1.5401	1.8316	5.007

Table 1*. Comparison of parameters estimated by CAMINO and suggested algorithm with different SNR values (Top row shows values chosen for the model parameters).*

Evaluation on brain data

Diffusion MRI data was acquired on a healthy volunteer using a Siemens 3T Skyra system with voxel size 2mm^3, and four b-values, each with 119 directions and 18 additional b=0 volumes. b-values and corresponding parameters were chosen as follows [2]: b_1=820 s.mm^{-2} ($\Delta/\delta/|G|_{max}$=17.6/9ms/98.5mT.m^{-1}); b_2=980 s.mm^{-2} ($\Delta/\delta/|G|_{max}$=55.5/5.2ms/97.1mT.m^{-1}); b_3=3010 s.mm^{-2} ($\Delta/\delta/|G|_{max}$=38.5/22.2ms/52.4mT.m^{-1}); and b_4=7600 s.mm^{-2} ($\Delta/\delta/|G|_{max}$=37.8/29.3ms/66.6mT.m^{-1}). This dataset was used for further evaluation and comparison of the suggested algorithm. The data was fitted to 'ZepplinCylinderDot' model to estimate axonal radius in corpus callosum. Results were consistent with CAMINO (Fig. 1) although the fitting procedure took about half the time required by CAMINO. It can be noticed on Fig. 1 that results obtained with our suggested method are more spatially coherent with a gradual increase in radius around the genu and splenium area. Recovered radii were also larger in the body [2]. An axial slice through the corpus callosum is presented in Fig 1 (C-D) where axonal radius and density estimates are shown.

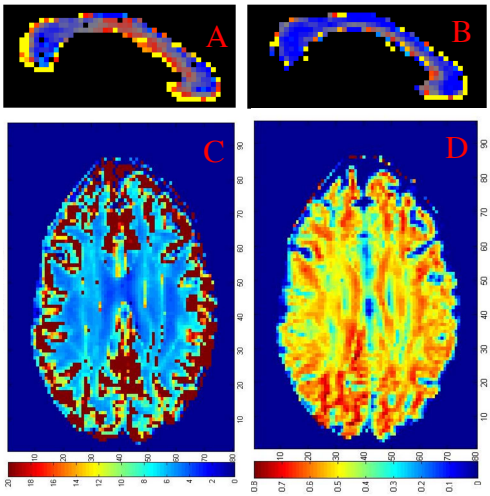

Figure 1*. (A) Axonal radius estimate by CAMINO, (B) Axonal Radius estimate by suggested algorithm, (C) Axonal diameter (0-20 μm) and (D) intra-axonal volume fraction (f_1) estimated by proposed algorithm (0 – 0.8).*

Conclusion: We suggest an iterative algorithm, based on separating the Non-linear Least Squares (NLLS) fitting problem into (i) finding non-linearly entering parameters separately using genetic algorithm and (ii) reducing the problem to CLLS for linear parameters. Convergence of this process to global minimum is absolutely independent of the starting point and requires no information of function derivatives, which leads to more robust parameters estimates.

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