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Robust and fast nonlinear optimization of diffusion MRI microstructure models

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ABSTRACT

Advances in biophysical multi-compartment modeling for diffusion MRI (dMRI) have gained popularity because of greater specificity than DTI in relating the dMRI signal to underlying cellular microstructure. A large range of these diffusion microstructure models have been developed and each of the popular models comes with its own, often different, optimization algorithm, noise model and initialization strategy to estimate its parameter maps. Since data fit, accuracy and precision is hard to verify, this creates additional challenges to comparability and generalization of results from diffusion microstructure models. In addition, non-linear optimization is computationally expensive leading to very long run times, which can be prohibitive in large group or population studies. In this technical note we investigate the performance of several optimization algorithms and initialization strategies over a few of the most popular diffusion microstructure models, including NODDI and CHARMED. We evaluate whether a single well performing optimization approach exists that could be applied to many models and would equate both run time and fit aspects. All models, algorithms and strategies were implemented on the Graphics Processing Unit (GPU) to remove run time constraints, with which we achieve whole brain dataset fits in seconds to minutes. We then evaluated fit, accuracy, precision and run time for different models of differing complexity against three common optimization algorithms and three parameter initialization strategies. Variability of the achieved quality of fit in actual data was evaluated on ten subjects of each of two population studies with a different acquisition protocol. We find that optimization algorithms and multi-step optimization approaches have a considerable influence on performance and stability over subjects and over acquisition protocols. The gradient-free Powell conjugate-direction algorithm was found to outperform other common algorithms in terms of run time, fit, accuracy and precision. Parameter initialization approaches were found to be relevant especially for more complex models, such as those involving several fiber orientations per voxel. For these, a fitting cascade initializing or fixing parameter values in a later optimization step from simpler models in an earlier optimization step further improved run time, fit, accuracy and precision compared to a single step fit. This establishes and makes available standards by which robust fit and accuracy can be achieved in shorter run times. This is especially relevant for the use of diffusion microstructure modeling in large group or population studies and in combining microstructure parameter maps with tractography results.

Introduction

Diffusion MRI (dMRI) is a tool for investigating the microstructure of biological tissue by probing the self-diffusion of water (Bihan et al. 1986). The conventional method for the analysis of white matter in dMRI imaging is the tensor model in Diffusion Tensor Imaging (DTI; Basser et al. 1994). DTI has shown to be sensitive to microstructural changes due to, for example, development (Pfefferbaum et al. 2000; Neil et al. 2002; Assaf and Pasternak 2008; Lebel et al. 2010) and pathology (Werring et al. 1999; Horsfield and Jones 2002; Sotak 2002; Sundgren et al. 2004). Although sensitive, DTI indices such as Fractional Anisotropy (FA) are also unspecific, since differences in FA can reflect different axonal properties such as axon density, diameter distribution and myelination (Beaulieu 2002; Assaf et al. 2004; Assaf and Pasternak 2008; Jones et al. 2013; Santis et al. 2014).

Recently, advances in biophysical multi-compartment modeling have gained popularity because they possess greater specificity than DTI in relating the dMRI signal to the underlying cellular microstructure (Assaf et al., 2004; Assaf and Basser, 2005; Assaf et al., 2008; Alexander et al., 2010; Panagiotaki et al., 2012; Zhang et al., 2012;

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Assaf et al., 2013; Fieremans et al., 2013; De Santis et al., 2014; Santis et al., 2014; Jelescu et al., 2015). In these diffusion microstructure models the diffusion weighted signal is expressed as a combination of one or more biophysically inspired compartments. Although the compartment models are based on simple geometric shapes, and a strong assumption of no inter-compartment exchange is made (cf; Nilsson et al. 2013; Li et al. 2016), these models can provide specific measures such as fiber density, orientation dispersion, and axonal diameter distributions and have been shown to be sensitive to specific white matter alterations due to development (e.g. Kunz et al., 2014; Jelescu et al., 2015) and pathology (Bergers et al., 2002; Fieremans et al., 2013; Benitez et al., 2014; Timmers et al., 2015; Wen et al., 2015; Kamagata et al., 2016).

There is a large range of diffusion microstructure models, including popular models such as Neurite Orientation Dispersion and Density Imaging model (NODDI; Zhang et al., 2012), the Combined Hindered And Restricted Model of Diffusion (CHARMED; Assaf and Basser, 2005), the White Matter Tract Integrity model (WMTI; Fieremans et al., 2013), AxCaliber (Assaf et al., 2008), the Minimal Model of White Matter Diffusion (MMWMD in ActiveAx; Alexander et al., 2010; Zhang et al. 2011), including further developments of these models like NODDIDA (Jelescu et al., 2015), Bingham NODDI (Tariq et al., 2016), diffusion time dependent CHARMED (De Santis et al. 2016) and fiber-specific T_1 CHARMED (De Santis et al., 2016).

Each of these models needs to be fitted to the dMRI data to estimate parameter maps, which is commonly accomplished using non-linear optimization. This has two major challenges. First, it is computationally expensive, quickly leading to very long run times. Second, the quality, accuracy and precision of the data fit is often uncertain. To tackle these challenges, each of the popular models comes with its own, mostly different, optimization algorithm, noise model and initialization strategy to estimate its parameter maps. This creates challenges to comparability and generalization of results from diffusion microstructure models, additional to the model formulation itself. In this technical note we investigate the performance of several optimization algorithms and initialization strategies over a few of the more popular diffusion microstructure models. We investigate whether a single well performing approach exists that could be applied to many models and that equates both run time and fit aspects. To this end, we evaluate the fit, accuracy, precision and run time for different models of differing complexity against three common optimization algorithms and three parameter initialization strategies. All models, algorithms and strategies were implemented on the GPU to remove run time constraints. Variability of the achieved quality of fit in actual data is evaluated on ten subjects of each of two large group studies with a different acquisition protocol, the MGH-USC part of the Human Connectome Project (Fan et al., 2016) and the Rhineland Study (www.rheinland-studie.de).

Methods

All biophysical compartment models, noise models / likelihood functions, as well as optimization algorithms were implemented in a python based GPU accelerated toolbox (Maastricht Diffusion Toolbox or MDT, freely available under an open source L-GPL license at https://github.com/cbclab/MDT). Its object oriented modular design allows arbitrary combinations of individual single compartment models into composite compartment models, which can then be combined with a chosen likelihood function and optimization algorithm by Python scripting. The complete multi-compartment model, likelihood function and optimization algorithm is automatically compiled into OpenCL code executable on both CPUs and GPUs (or combinations thereof).

Single compartment models

Table 1 defines the individual compartment models which are combined to construct the multi-compartment models (c.f. Panagiotaki et al., 2012; Ferizi et al., 2013) valid for (singly refocused) Pulsed Gradient Spin Echo (PGSE; Stepisnik, 1993) acquisitions.

The Tensor model was first described in (Basser et al., 1994), the Ball and Stick models are defined in (Behrens et al., 2003), NODDI_in and NODDI_ex are respectively the intra cellular and extra cellular models in (Zhang et al., 2012) and the CHARMED_in compartment is the restricted compartment defined in (Assaf et al., 2004).

Each compartment has a signal function modelling the signal $\mathbf{S}$ depending on the unit norm gradient direction vector $\mathbf{g}$ with scalar $b = (\Delta - \delta/3)(\gamma\delta G)^2$ and the vector $\mathbf{q} = \gamma\delta\mathbf{g}G/2\pi$. Here G is the gradient amplitude, Δ the time between the start of the two gradient pulses, δ the duration of the gradient pulse and γ the gyromagnetic ratio for ^{1}H in $rad{\bullet}s^{-1}{\bullet}T^{-1}$. Additionally, the CHARMED_in compartments depend on the echo time *TE*.

Disregarding fixing of parameter values discussed below, the modelled fiber orientations $\mathbf{n}$ are optimized as spherical coordinates using the free parameters θ and ϕ with scalar d for the diffusivity. Some models have more than one diffusivity, these are all optimized

Table 1
The single compartment models, see Table 2 for an overview of the optimizable parameters. The primary direction of diffusivity $\mathbf{n}$, is parameterized using polar coordinates with angles θ, ϕ and radius d. The variables b, $\mathbf{g}$, $\mathbf{q}$, Δ,δ, G and TE are sequence settings. In the Tensor compartment, the function $rotate(\boldsymbol{n},\psi)$ rotates the Tensor around $\boldsymbol{n}$ by the angle ψ. In the NODDI models, the function $f(\boldsymbol{n}, \kappa)d\boldsymbol{n}$ gives the probability of finding fiber bundles along orientation $\boldsymbol{n}$ using a Watson distribution with parameter κ integrated over the unit sphere $\mathbb{S}^2$. In the NODDI_ex model, the diffusion tensor $D(\boldsymbol{n})$ is defined as a cylindrically symmetric Tensor (alike the Tensor in this table except for the symmetry). In the CHARMED_in compartment N is the number of gamma cylinders used, v_i is the weight per gamma distributed cylinders and R_i is the radius per cylinder. In previous work $|\boldsymbol{q}|^2(\boldsymbol{n}{\bullet}\boldsymbol{g})^2$ is sometimes denoted as $|\boldsymbol{q}_{\parallel}|^2$ and $|\boldsymbol{q}|^2(\boldsymbol{I}-(\boldsymbol{n}{\bullet}\boldsymbol{g})^2$ as $|\boldsymbol{q}_{\perp}|^2$, we inlined these identities here in the CHARMED_in equation.

Compartment	Signal function	Compartment model parameters
Tensor	$\mathbf{S} = e^{-b\,(d_{\parallel}(\mathbf{n}\bullet\mathbf{g})^2 + \ d_{\perp_1}(\mathbf{n}_{\perp_1}\bullet\mathbf{g})^2 + d_{\perp_2}(\mathbf{n}_{\perp_2}\bullet\mathbf{g})^2)}$ $\mathbf{n}_{\perp_1} = \text{rotate}(\mathbf{n},\psi)$ $\mathbf{n}_{\perp_2} = \mathbf{n}\times\mathbf{n}_{\perp_1}$	$d_{\parallel}$, $d_{\perp_1}$, $d_{\perp_2}$,θ, ϕ, ψ
Ball	$\mathbf{S} = e^{-bd}$	d
Stick	$\mathbf{S} = e^{-bd\,(\mathbf{n}\bullet\mathbf{g})^2}$	d, θ, ϕ
NODDI_in	$\mathbf{S} = \int_{\mathbb{S}^2} f(\mathbf{n}, \kappa) e^{-bd\,(\mathbf{n}\bullet\mathbf{g})^2} d\mathbf{n}$	d, θ, ϕ, κ
NODDI_ex	$\mathbf{S} = e^{-b\mathbf{g}^{\mathrm{T}}\left(\int_{\mathbb{S}^2} f(\mathbf{n}, \kappa) D(\mathbf{n}) d\mathbf{n}\right)\mathbf{g}}$	$d_{\parallel}$, $d_{\perp}$,θ, ϕ, κ
CHARMED_in	$\mathbf{S} = \sum_{i=1}^{\mathrm{N}} v_i [\mathrm{S}_{\parallel}(\mathbf{q}, \Delta)\cdot \mathrm{S}_{\perp i}(\mathbf{q}, \mathrm{TE})]$ $\mathrm{S}_{\parallel}(\mathbf{q}, \Delta) = e^{-4\pi^2 \lvert\mathbf{q}\rvert^2 (\mathbf{n}\bullet\mathbf{g})^2 (\Delta - \delta/3) d}$ $\mathrm{S}_{\perp i}(\mathbf{q}, \mathrm{TE}) = e^{-\left(4\pi^2 \lvert\mathbf{q}\rvert^2 (\boldsymbol{I}-(\mathbf{n}\bullet\mathbf{g})^2) \mathrm{R}_i^4 / \left(\frac{d\bullet \mathrm{TE}}{2}\right)\right)\left(\frac{7}{96}\right)\left(2-\left(\frac{99}{112}\right) R_i^2 / \left(\frac{d\bullet \mathrm{TE}}{2}\right)\right)}$	d, θ, ϕ