Can AxCaliber be extended to estimate axonal radius and orientation at the same time?

J. E. Cisternas[1]
[1]Engineering and Applied Sciences, Universidad de los Andes, Santiago, RM, Chile

Introduction

One of the key ideas behind diffusion tensor (DT) imaging that explains its wide applicability, is the assumption that the diffusion of water molecules in live tissues, both inside and outside cells, is hindered in an anisotropic manner by the presence of membranes, and that mean displacement scales with square root of time. This assumption is obviously a simplification: diffusion is restricted by impermeable barriers [1] and the simple scaling doesn't hold in general. This limitation of DT can actually be used as a sign of the presence of finite scales in the tissue. Several models have been recently proposed that combine hindered and restricted diffusion and can measure direct axonal features such as density and diameter [2,3]. In particular, AxCaliber proposes a white-matter model made up of two compartments: (i) extracellular space where diffusion is hindered, and (ii) intracellular space where diffusion is restricted inside a population of impermeable cylinders of different diameters as described in [1]. AxCaliber requires previous knowledge of the axon orientation and assumes a Gamma distribution for the radii. In this work we extend AxCaliber in a non-parametric way, using a population of axons of different radii and orientations. Instead of using the computationally demanding Markov Chain Monte Carlo, we posed the estimation problem as a standard Quadratic Program, that can always be solved by fast and reliable algorithms. The feasibility of recovering multiple radii and orientations from noisy MR data is assessed using simulations.

Method

The model is composed of multiple compartments each with a population fraction. First, a discrete number of extracellular compartments modeled by diffusion tensors with principal axes oriented along a predefined set of orientations. Second, a number of intracellular compartments, modeled by impermeable cylinders of different radii a_i and orientations $\boldsymbol{u}_j$. Third, an isotropic compartment was included to account for CSF contamination [4]. Thus the basic equation for the observed diffusion signal decay is:

$$E(\mathbf{q},\Delta) = \sum_j f_j^{\mathrm{h}} E^{\mathrm{h}}(\mathbf{q},\Delta,\mathbf{u}_j) + \sum_{i,j} f_{i,j}^{\mathrm{r}} E^{\mathrm{r}}(\mathbf{q},\Delta,a_i,\mathbf{u}_j) + f^{\mathrm{csf}} E^{\mathrm{csf}}(\mathbf{q},\Delta) + \varepsilon$$

where epsilon is some additive noise and the *f*'s are the unknown population fractions. We assume other parameters, such as the extracellular mean diffusivity and anisotropy, and the intracellular diffusivity, are known. Detailed expressions for E^h, E^r and E^{csf} can be found in [3]. The problem of estimating the *f*'s can be written as the following least-squares problem:

$$\text{minimize} \quad \sum_i \left(\sum_j A_{i,j} x_j - y_i \right)^2 \quad \text{subject to } \sum_j x_j = 1 \ , \ x_j \geq 0$$

where A is a matrix relating each compartment with each observation, y is a vector containing all the MR measurements, and x is the vector of unknowns f's. This optimization problem is strictly convex [5] and can be transformed to a Quadratic Program: its unique minimizer can be found by fast and stable algorithms. There is no need of adjusting penalizations or selecting algorithmic parameters such as number of samples or number of iterations.

Results

Our simulations considered a set of 8 values for the gradient amplitude Gmax between 35e-3 and 282e-3 T/m, 9 values for the diffusion time DELTA in the range 10e-3 to 100e-3 m, a set of 16 unique orientations generated from a tesselated dodecahedron, but delta = 3.2e-3 s was kept constant. For the compartments, we considered 5 radii between 4e-6 and 20e-6 m, and the same set of 16 orientations used for the acquisitions. Data was generated using the same model plus Gaussian noise. The overdetermined system of 1152 equations and 97 unknowns was solved in 0.05 sec using the solver cvxopt [5] running in a standard desktop computer. Figs. 1 and 2 show a summary of the simulations. For each noise amplitude, 1000 independent realisations were used. Fig. 1 shows the absolute difference between the true radius (taken in the same range 4e-6 -- 20e-6 m) and the estimation. Fig. 2 shows the angle between the true orientation and the estimated one. In both figures the discretization bias was removed. Fig. 2 shows an intermediate plateau that is not well understood. The present model and the Quadratic Programming algorithm proved to be capable of recovering both axonal radii and orientation from noisy measurements.

Discussion

Previous work proved [2,3] the feasibility of axon radii estimation from diffusion weighted MR. Here we demonstrated that in principle the framework can be extended to measure not just multiple radii but multiple orientations. Future work should consider data from Monte Carlo simulation (for instance using CAMINO [6]), and from post-mortem tissue, given the long acquisition sequences demanded by the present model. We should test the robustness of the estimation under uncertainties in the diffusivities that here are assumed to be well known. We should also evaluate the possibility of measuring two or more orientations under noise, and compare with the approach of [7].

References

[1] Callaghan et al. Nature 1991. [2] Assaf et al. MRM 2004. [3] Assaf et al. MRM 2008. [4] Barazany et al. Brain 2009. [5] Boyd and Vandenberghe, Convex Optimization, Cambridge 2004. [6] Hall et al. ISMRM 2006. [7] Alexander et al. ISMRM 2009.

Fig. 1

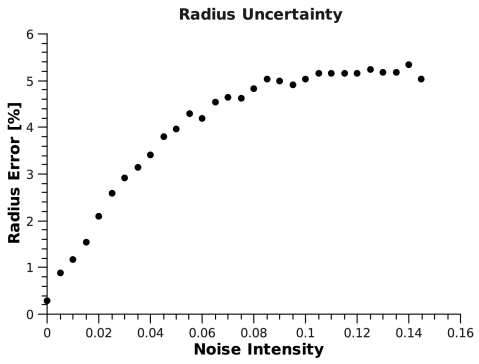

Fig. 2