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#### **Atlases and generic priors for mul3-compartment mapping with diffusion MRI**

The specificity of microstructure models in diffusion MRI is limited by the quality of clinical protocols. We propose a generic statistical framework to build priors for multicompartment models, to inform estimations made from clinical acquisitions; we illustrate on a standard model of diffusion.

**Introduction**: In diffusion MRI , our ability to estimate the microstructure parameters of brain tissue models depends on the acquisition protocol. With standard clinical acquisitions, only simple models can be estimated [2].

We hereby propose an integrated method for deriving priors for multi-compartment model (MCM) estimation from high-quality databases, such as the Human Connectome Project (HCP). We present firstly the model we chose to compute priors, then the different statistical distributions adapted for each parameter, and finally the atlas we obtained.

#### **Methods:**

#### **MC model**

We focus on an MCM in which the anisotropic compartments are modeled according to diffusion tensors with fixed diffusivities,  $d_{\text{parallel}} = 1.7 \times 10^{-3}$  mm<sup>2</sup>/s and  $d_{\text{perp}} = 1.7 \times 10^{-4}$ mm<sup>2</sup>/s, ensuring the anisotropic compartments cannot be made isotropic during estimation. For the isotropic compartments, we opted to include a compartment for modeling free water diffusion (F) with dF=3.0×10−3mm<sup>2</sup>/s and one for modeling isotropic restricted diffusion (IR) in glial cells as in [3]. The MR signal predicted by such a model reads:

$$
S(i,b) \ = \ w_F e^{-bd_F} + \ w_R S_I R(b,\boldsymbol{\delta} \Delta ;\ d_S,R_S) \ + \ \sum_{j=1}^M w_j e^{-bd_{perp}e^{-b(d_{parrale!}\cdot d_{perp})}(\mu_j^T g)^2}
$$

where (i) w<sub>i</sub>'s are the volume fractions, (ii) b and g are respectively the b-value and direction defining the diffusion gradient, δ and Δ are the pulses duration and separation (iii)  $S_{IR}$  is the MR signal predicted by the IR diffusion model proposed in [3] which has two parameters: the IR diffusivity (in mm2/s) and the average cell radius (in ) and (iv)  $\mu_i$  is the direction of diffusion in the j-th anisotropic compartment.

#### **Data**

We chose such a model in regards of our data that comes from the HCP105 database [4], from the Human Connectome Project.

#### **Model for the priors**

We define priors for the parameters of this model that are common to many MCM. We used parametric distributions with appropriate support, each prior depending on the number of anisotropic compartments. The whole pipeline process is described in Figure 1. We calculated them for 0, 1, 2 and 3 anisotropic compartments. Doing this ensures that the users will ultimately be able to select the most appropriate number of compartments given the data.

For the two IR parameters  $d_s$  and  $R_s$ , we used a Gamma distribution, being the natural distribution for positive-valued data , estimated by a closed form estimator.

The prior for the volume fraction parameters,  $w_{FW}$ ,  $w_{RW}$ ,  $w_{A}$ , where  $w_{A}$  is the sum of the volume fraction of each anisotropic compartment, was computed using a Dirichlet distribution, being the most common distribution on the simplex (each weight is nonnegative and the weights sum to 1).

Last, the direction of diffusion  $\mu_i$  of the j-th compartment follows a Watson distribution, a specific case of the Bingham distribution [8].

#### **Results:**

We present here the priors we were able to obtain, for clarity we only report the specific case of M=1 anisotropic compartment. We also optimized the number M of anisotropic compartments as described in [1]. We provide a map of the mean of the model selection for our 105 subjects in Figure 2.

Figure 3 exhibits the mean and variance for IR diffusivity ds and cell radius Rs, calculated thanks to our Gamma prior.

Figure 4 shows the prior on the weight distribution parameter. The results are well related to the underlying anatomy, with a high volume fraction of free water, IR and anisotropic compartments in CSF, gray matter and white matter, respectively.

The whole pipeline shows conclusive results, therefore we are confident in the priors obtained, and we are currently working on validating the improvement they provide on our MCM estimations.

#### **Discussion & Conclusions:**

As a first step, we hereby provide atlases and priors for parameters characterizing free water, isotropic restricted diffusion and anisotropic diffusion. Our goal is to ultimately render it available and usable in a clinical context, with the most generic priors possible, usable for many different compartment models. It could also be used in a framework with deep-learning, as suggested in [7]. We expect those atlases to improve the MCM estimation, as suggested by [6].

Our work fits in with the priors developped by [9]. We wish to extend this approach by focusing on the brain microstructure, giving our results clear biological relevance. We also plan to compare our statistical-based approach to deep learning approaches such as [10]; we hypothesize that building priors with parametric distribution may help in the interpretation of results.

As for the next steps we are currently investigating, we will be using the HCP105 tracts, all reviewed by clinicians. We think we should be able to use them to improve the atlas for our anisotropic compartments priors. [5] We also are looking into the HCP MGH database, with lengthier acquisition, that may allow us to develop priors on more complex models, such as CHARMED, with a focus on the axon density.

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## **Figures:**

*Figure 1 : Description of the process pipeline. The iteration process is a way to validate our process and the improvements we get from our priors. We could ultimately get the Aikake Information Criteria to have a measure of the improvement.* 



*Figure 2 : Map of the mean optimized number of anisotropic compartments for the 105 subjects. Gray matter and CSF have* an average close to zero, while white matter voxels show a number of anisotropic compartments from 1 to 3 in complex *white matter regions.* 



*Figure 3 : Mean (left) and variance (right) of diffusivity (top, in mm<sup>2</sup>/s) and radius (bottom, in mm) of the isotropic restricted compartment.*



*Figure 4 : Mean volume fraction of the free water (top left), IR water (top right) and axons compartment (bottom left). On* the bottom right, we plotted the global variance of the volume fractions. As expected, the CSF shows high free water volume *fraction on average. Similarly, the cortex and deep gray matter structures exhibit a large IR volume fraction. And the white matter shows a large axons volume fraction.*