Fast and robust detection of the optimal number of fascicles in diffusion images using model averaging theory

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PURPOSE – Diffusion MRI enables non-invasive in vivo reconstruction of the white matter axon bundles hereafter referred to as fascicles. DTI is known to have a hard time depicting accurately this architecture in regions where multiple fascicles cross. New multi-compartment models [1,2,3] can unravel this issue provided that the number of fascicles is known in advance. This is a model selection problem that translates to finding the optimal number of fascicles. Recently, [4] proposed to use the generalization error to choose the best model based on its ability to predict new data that has not been used for its estimation, thus avoiding the common problem of over-fitting. Despite the excellent results obtained by this method, the generalization error needs to be estimated, which is a long process that takes up to a week on high resolution data such as the recently publicly released Human Connectome Project (HCP) data [5]. In this abstract, we introduce a new model selection approach that gives results at least as good as the generalization error with a dramatically reduced computation time, making it closer to a clinical applicability.

METHODS – We used a ball-and-cylinders diffusion model that, given an a priori number m of fascicles, predicts the diffusion weighted (DW) signal decay induced by the application of a diffusion sensitizing gradient with b-value b_j and direction $\boldsymbol{g}_j$ as $A_j^{(m)} = \left(1 - \sum_{i=1}^{m} f_i^{(m)}\right) e^{-b_j D_{iso}} + \sum_{i=1}^{m} f_i^{(m)} e^{-b_j D_\perp} e^{-b_j D_\parallel \left(\boldsymbol{g}_j^T \boldsymbol{\mu}_i^{(m)}\right)^2}$ (1), where $\boldsymbol{\mu}_i^{(m)}$ and $f_i^{(m)}$ are respectively the orientation and occupancy of the ith fascicle, $D_\parallel$ and $D_\perp$ are the fascicles' parallel and perpendicular diffusivities and $D_{iso} = 0.003$ mm^2/s is the diffusivity of free water at 37°C. We fixed $D_\parallel$ and $D_\perp$ to their averaged DTI-based value in the corpus callosum to prevent the models from describing isotropic diffusion in fascicle environments. We fitted this model for $m \in [\![1, M]\!]$ by maximizing the log-likelihood $\log L^{(m)}$ using the Gaussian approximation to the χ-distributed noise. We defined the best model as the one at minimal Kullbach-Leibler (KL) divergence to the true unknown model. Model averaging theory states [6] that such a model can be estimated by performing a weighted average of all the parameters across candidate models using Akaike's weights $a_m \propto e^{\left(AIC_{min} - AIC^{(m)}\right)/2}$, where $AIC^{(m)} = -2 \log L^{(m)} + 6m$ is the Akaike information criterion and AIC_{min} is the smallest AIC across candidate models, provided that parameters share the same interpretation in the different models. This is not the case of the orientations and occupancies defined in Eq. (1). To circumvent this issue, we can reformulate Eq. (1) as follows: $A_j^{(m)} = \left(1 - \sum_{k=1}^{M!} f_k^{(m)}\right) e^{-b_j D_{iso}} + \sum_{k=1}^{M!} f_k^{(m)} e^{-b_j D_\perp} e^{-b_j D_\parallel \left(\boldsymbol{g}_j^T \boldsymbol{\mu}_k^{(m)}\right)^2}$, where $k = (l-1)\frac{M!}{(m-1)!} + (i-1)\frac{M!}{m!} + p$, $p \in \left[\!\left[1, \frac{M!}{m!}\right]\!\right]$, $l \in [\![1, (m-1)!]\!]$, $f_k^{(m)} = \frac{m}{M!} f_i^{(m)}$ and $\boldsymbol{\mu}_k^{(m)} = \boldsymbol{\mu}_i^{(m)}$. Orientations $\boldsymbol{\mu}_k^{(m)}$ and occupancies $f_k^{(m)}$ now share the same interpretation across models and the best KL model is the M!-fascicle model with fascicle occupancies $f_k = \sum_{m=1}^{M} a_m f_k^{(m)}$ and orientations $\boldsymbol{\mu}_k$ defined as the principal eigenvector of the averaged direction cosine matrix $DCM_k = \sum_{m=1}^{M} a_m \boldsymbol{\mu}_k^{(m)} \boldsymbol{\mu}_k^{(m)^T}$. The resulting model may however poorly reflect the underlying microstructure because it can contain replicated fascicles. We thus subsequently regrouped the M! fascicles into an automatically determined number of compartments using modularity clustering [8] with the cosine similarity metric and defined the optimal number of fascicles as the number of resulting clusters.

RESULTS – We confronted the results of our method to those obtained using the generalization error [4] on two cases provided by the HCP [5]. For each case, the data consisted in 270 DW images with three different b-values at 1000, 2000 and 3000 s/mm2 and 18 non-DW images, at a spatial resolution of $1.25 \times 1.25 \times 1.25$ mm^3. We used the same ball-and-cylinders model to determine the optimal number of fascicles voxelwise using both the generalization error and our model averaging approach. We proposed for both cases a qualitative assessment of the resulting maps and a quantitative measure of overlapping by means of the generalized Dice coefficient.

DISCUSSION – Estimation of the optimal number of fascicles took almost a week using the generalization error and only three hours using model averaging theory. Fig. 1 shows coronal slices of the map of optimal number of fascicles obtained by generalization error (a,c) and by model averaging (b,d). The maps are qualitatively highly similar, which is quantitatively confirmed by a generalized Dice coefficient of 0.812 for subject #1 and 0.805 for subject #2. In addition, model averaging estimates seem to better capture known mono-fascicle regions like the basis of the cortico-spinal tract or the corpus callosum (green regions).

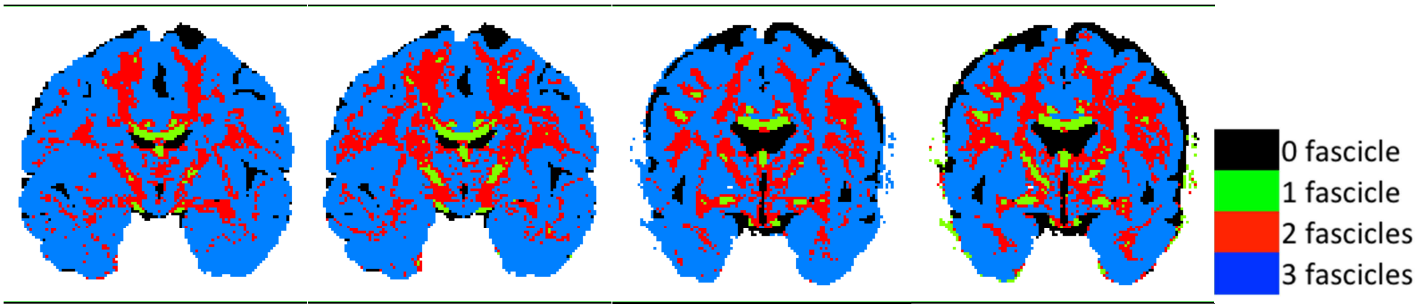

Figure 1: Coronal view of the resulting map of optimal number of fascicles for subject #1 (a,b) and subject #2 (c,d) by means of generalization error (a,c) and model averaging (b,d).

CONCLUSION – In this abstract, we showed that we were able to obtain estimates of the optimal number of fascicles in the white matter that are at least as reliable as those obtained by generalization error, with qualitatively improved delineation of mono-fascicle regions. This was achieved by a model averaging procedure, which is easily generalizable to any multi-compartment model, in a dramatically reduced computational time compared to the generalization error, making it clinically feasible.

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