A Bayesian framework for modelling the regional variation of white matter microstructure

Gemma L Morgan[1]
g.morgan@cs.ucl.ac.uk
Hui Zhang[1]

Brandon Whitcher[2]

Daniel C Alexander[1]

[1] Centre for Medical Image Computing
Department of Computer Science
University College London
London, UK

[2] Clinical Imaging Centre
GlaxoSmithKline
London, UK

Abstract

We present a Bayesian framework for the group-wise comparison of the regional variation of tissue parameters estimated from diffusion-weighted MRI (DW-MRI) over an anatomical region of interest (ROI). The regional variation model (RVM) fits a geometric model of parameter variation directly to the DW-MRI signals which captures the spatial changes in a natural way as well as reducing the effects of noise. We use the technique to localise tissue changes due to healthy aging in the mid-sagittal CC and detect increases in diffusivity in the genu and splenium of the older group.

1 Introduction

Diffusion-weighted MRI (DW-MRI) is a powerful, non-invasive imaging tool which measures the displacement of water molecules in vivo [6]. Because the paths of water molecules are influenced by the shape and structure of the environment in which they move, DW-MRI is a very sensitive probe for measuring tissue microstructure and is used extensively to study white matter (WM) in the brain. Indices that reflect tissue microstructure, such as diffusivity, fibre orientation and anisotropy, can be estimated by fitting models of the diffusion MR signal to the measured signals. These models are typically fit to each individual voxel of data, which means that parameter estimates are often affected by noise. This can be problematic when performing group-wise studies to compare these indices between populations, particularly for voxel-wise techniques such as voxel based morphometry (VBM) [2] or tract-specific spatial statistics (TBSS) [7]. Region of interest (ROI) studies try to overcome the effects of noise by averaging indices over a particular feature or tract, but lose useful information about the spatial localisation of tissue changes in the process.

In this paper we introduce a Bayesian framework, the regional variation model (RVM), that improves estimates of white matter microstructure by using the spatial coherence of

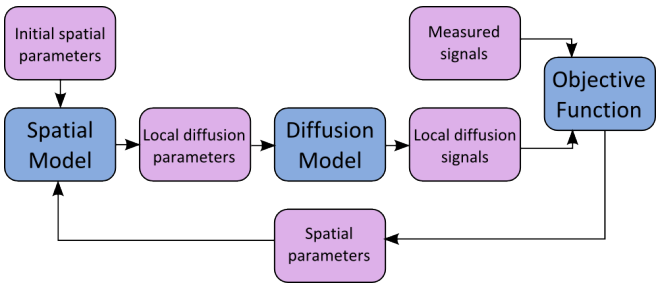

Figure 1: The pipeline for the RVM. The spatial model maps onto the ROI to provide microstructure parameters in each voxel. The diffusion model predicts MR signals, which are compared to the measured signals. The spatial model is updated until the most likely set of parameters is found.

specific WM structures to constrain the fitting. Curves or surfaces are used to represent the variation of microstructure parameters throughout the tracts and are fit directly to the diffusion-weighted signals across the whole ROI simultaneously using a smoothing prior to reduce noise effects. The resulting curves or surfaces can be used in group-wise testing to localise tissue changes between populations whilst overcoming the limitations of noise. Unlike traditional ROI analysis, we obtain a continuous representation of the parameter variation. Unlike VBM or TBSS, the RVM can detect differences in global trends of parameters and exploit the local coherence of parameter values in a natural way.

2 Methods

The RVM framework estimates microstructure parameters across an ROI using the local spatial neighbourhood to constrain the fitting. A forward model predicts the DW-MRI signals in every voxel in the region using a set of curves, the spatial model, to control the regional variation of microstructure parameters across the ROI. The key components of the method are the spatial model, which predicts diffusion model parameters in every voxel, and the diffusion model, which calculates the diffusion MR signals from the predicted parameters. The optimal spatial model is determined by finding the most likely curves of parameter variation, given the data. The framework is independent of the choice of diffusion model, spatial model and optimisation strategy. In the next sections, we describe a potential implementation using a simple diffusion model, which we use throughout this work. We show an overview of the whole pipeline in figure 1.

2.1 Diffusion model

We use the ball and stick model [8], which models the total DW-MRI signal as a mixture of signals due to the restricted intra-axonal water (the stick) with volume fraction f and orientation $\mathbf{e}$ (defined by angles θ and ϕ) and the hindered extra-axonal water (the ball). Both compartments have diffusivity d. The total normalised signal A for a gradient pulse with direction $\hat{\mathbf{G}}$ and diffusion weighting may be written as

$$A = f \exp\left(-bd(\mathbf{e}\cdot\hat{\mathbf{G}})^2\right) + (1-f)\exp\left(-bd\right). \quad (1)$$

2.2 Spatial model

We represent the regional variation of the diffusion model parameters using Bayesian penalised b-splines (Bayesian P-splines) [9] as they are particularly suited to capturing local variation within data. We assume that the variation of each parameter $p \in \{f, d, \theta, \phi\}$ across the ROI can be represented as the sum of N cubic B-spline basis functions with weights $\mathbf{a}_p = [a_{p,1}\ a_{p,2}\ \ldots a_{p,N}]$. We denote the resulting curve for each parameter by C_p. If the position of the i^{th} voxel along the ROI is x_i, we can use the curves to predict the diffusion model parameters in each voxel by evaluating

$$C_p(x_i) = \sum_{n=1}^{N} a_{p,n} B_n(x_i) \tag{2}$$

for each parameter p. P-splines use a large number of equally spaced knots to define the basis functions and add a penalty term to prevent fitting to the noise. In the Bayesian P-spline approach, the penalty term is formulated as a prior probability on the basis function weights $\mathbf{a}_p$ such that

$$a_{p,i} \sim N\left(\frac{1}{2}(a_{p,i-1} + a_{p,i+1}), {\nu_p}^2\right) \tag{3}$$

where N is the Gaussian distribution. The variance parameters for each p, ${\nu_p}^2$, are fit as part of the model with inverse gamma prior probabilities such that ${\nu_p}^2 \sim IG(a,b)$. The hyperparameters are set according to the literature [9] as a=1 and b=1×10^{-5}.

2.3 Fitting the RVM

When fitting a model within the Bayesian framework, we aim to evaluate the posterior probability of the model parameters given the data $\Pr(\mathbf{a} \mid \tilde{A})$, where $\mathbf{a} = \{\mathbf{a}_f, \mathbf{a}_d, \mathbf{a}_\theta, \mathbf{a}_\phi\}$ represents all model parameters and $\tilde{A}$ is the observed data. Using Bayes' theorem, we express this as

$$\Pr(\mathbf{a}|\tilde{A}) \propto \Pr(\tilde{A}|\mathbf{a}) \Pr(\mathbf{a}|\nu^2) \Pr(\nu^2), \tag{4}$$

where $\Pr(\tilde{A} \mid \mathbf{a})$ is the probability of $\tilde{A}$ given $\mathbf{a}$, $\Pr(\mathbf{a} \mid \nu^2)$ is the prior probability of $\mathbf{a}$ given ν^2 and $\Pr(\nu^2)$ is the prior probability of ν^2. We use the Rician distribution for $\Pr(\tilde{A} \mid \mathbf{a})$, as the noise on MR magnitude images is Rice distributed. As we cannot evaluate equation 4 analytically, we use Markov Chain Monte Carlo (MCMC) techniques [10] to sample from the posterior distribution. We use a Metropolis sampler with zero mean Gaussian proposal distributions. The first 1000 samples are discarded, after which we obtain 200 samples at intervals of 20 iterations.

3 Experiments and results

We demonstrate this method on the mid-sagittal section of the CC. We choose this region as histology studies [3] show that the axon radius and density vary smoothly across the medial axis of the CC, which we hypothesise will manifest as smooth variation in parameters such as f and d.

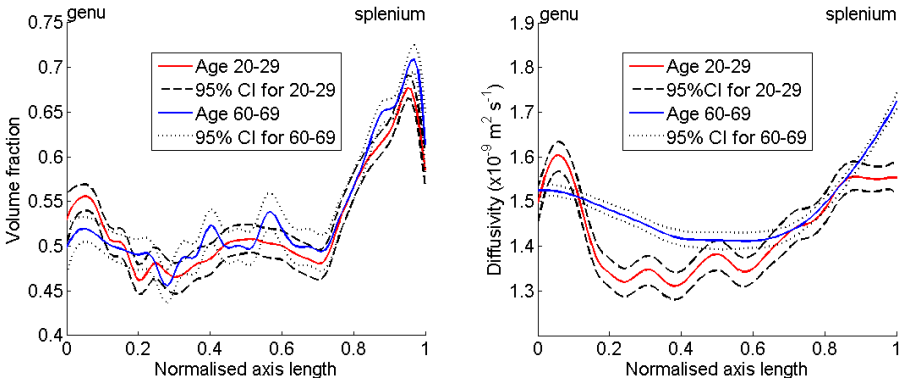

Figure 2: The mean curves and 95% CI for f (left) and d (right) for both groups of subjects.

3.1 Data acquisition, pre-processing and spline fitting

In this study, our diffusion MRI data sets are drawn from the large IXI database (www.brain-development.org). We use data from 30 subjects who divide into two distinct groups: 20-29 years old (9F, 6M) and 60-69 years old (9F, 6M). All data were acquired on a 3T scanner using 15 gradient directions (b=1000 s mm^{-2}) and 1 b=0 s mm^{-2} measurement.

Prior to fitting the RVM we extract the mid-sagittal slice and segment the CC by thresholding the FA maps (FA $>$0.35) and performing connected component analysis. The medial axis of the CC is identified using continuous medial representation (cm-rep) [4], after which we use a simple nearest neighbour approach to allocate each voxel in the ROI a distance along the medial axis (normalised on the interval [0,1]).

We initalise the parameters as follows. Due to the coherent orientation of fibres across the mid-sagittal CC, we model the variation of θ and ϕ using one 1^{st} order b-spline basis function each, which is defined using one knot point at either end of the medial axis, i.e. the angles are fit as constants across the ROI. We fit the angles rather than fixing them in order the capture the variance of fibre orientation. Initial values for θ and ϕ are determined from the principal eigenvectors of the diffusion tensor in all voxels in the ROI. The splines modelling the variation of f and d across the CC are fit using 26 cubic b-splines defined over 30 equally spaced knots. The 26 weighting coefficents for f are initially set to 0.7 and the 26 coefficients for d initialised at 1.7×10^{-9} m^2 s^{-1}, which are physically realistic values.

As we are interested in determining the changes in f and d due to age, we fit the RVM for each group to obtain mean curves. The samples obtained during MCMC provide a simple yet powerful way of determining confidence intervals (CI) on the mean curves for f and d obtained for each group. By comparing the mean curves and CI between groups, we can detect regions of significant differences between populations.

3.2 Results

Figure 2 shows the mean curves and 95% CI for f and d by group. The curves for f in show that the variation of volume fraction along the CC is consistent regardless of age group and there are no significant differencs between the groups. In constrast, the curves for d show marked variation in both shape and magnitude. The older group has significantly higher diffusivity in the posterior genu, anterior midbody and posterior splenium, although we also observe a small peak in the diffusivity in the younger group in the anterior genu.

4 Discussion

We have presented a regional variation model of white matter microstructure which estimates the variation of diffusion model parameters across an ROI directly from the DW-MRI signals. When fit to a data with two distinct age groups, the RVM detects increases in d in the CC in older subjects, in agreement with previous studies [5]. Our method is able to show that the spatial pattern of d, not just its magnitude, changes with age. Tracking these regional changes may provide important information about ageing as well as disease pathologies. However, the ball and stick model is a simple model and cannot determine the specific tissue changes that are occurring. In future, we plan to incorporate more complex models of diffusion into the RVM framework, allowing us to investigate more fundamental tissue properties such as axon radius and density [1]. The RVM naturally pools information across the ROI, enhancing sensitivity to these hard to estimate parameters. This approach could also be extended to more complex white matter tracts such as the whole CC or the corticospinal tract, using cm-rep [11] to characterise the shape of the medial axes or surfaces.

References

[1] D. C. Alexander. Orientationally invariant indices of axon diameter and density from diffusion mri. *NeuroImage*, 52(4):1374–1389, 2010.

[2] J. Ashburner and K. J. Friston. Voxel-based morphometry - the methods. *NeuroImage*, 11:805–821, 2000.

[3] F. Aboitiz et al. Fiber composition of the human corpus callosum. *Brain Research*, 598:143–153, 1992.

[4] H. Sun et al. Shape-based normalization of the corpus callosum for dti connectivity analysis. *IEEE Transactions on Medical Imaging*, 26:1166–1178, 2007.

[5] M. Otaa et al. Age-related degeneration of corpus callosum measured with diffusion tensor imaging. *NeuroImage*, 31:1445–1452, 2006.

[6] P. J. Basser et al. MR diffusion tensor spectroscopy and imaging. *Biophysical Journal*, 66:259–267, 1994.

[7] S. Smith et al. Tract-based spatial statistics: Voxelwise analysis of multisubject diffusion data. *NeuroImage*, 31:1487–1505, 2006.

[8] T. E. J. Behrens et al. Characterization and propagation of uncertainty in diffusion weighted mr imaging. *Magnetic Resonance in Medicine*, 50:1077–1088, 2003.

[9] S. Lang and A. Brezger. Bayesian p-splines. *J Comp Graph Stat*, 13:183–212, 2004.

[10] S. Richardson W. Gilks and D. Spiegelhalter, editors. *Markov Chain Monte Carlo in Practice*. Chapman and Hall, 1996.

[11] P. A. Yushkevich. Continuous medial representation for anatomical objects. *IEEE Transactions on Medical Imaging*, 25:1547–1564, 2006.