RUBIX: COMBINING SPATIAL RESOLUTIONS FOR BAYESIAN INFERENCE OF CROSSING FIBRES IN DIFFUSION MRI

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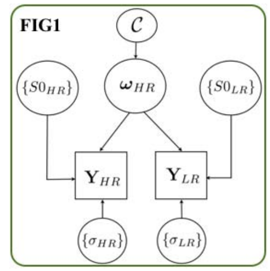
Target Audience: This work will be of immediate interest to scientists studying fibre orientation estimation and spherical deconvolution approaches for diffusion-weighted MRI data. It falls within the broader category of microstructural modelling for white matter tractography approaches.

Purpose: The trade-off between signal to noise ratio (SNR) and spatial specificity governs the choice of spatial resolution in magnetic resonance imaging (MRI); diffusion-weighted (DW) MRI is no exception. Images of lower resolution have higher signal to noise ratio, but also more partial volume artifacts. Benefits from improvements in either of those parameters have been shown. For instance, high SNR values are beneficial for robust estimation of tissue microstructure properties from the DW-MRI signal [1-3]. On the other hand, high spatial resolution reduces partial volume and allows exquisite tissue details to be revealed, as has been shown from post-mortem acquisitions [4]. Thus, an approach that combines multiple spatial resolutions could intuitively combine the benefits. In this study, we introduce a novel framework for combining multiple spatial resolutions during fibre orientation estimation. We combine all data into a single Bayesian model to estimate the underlying fibre patterns and diffusion parameters. We hypothesise that fibre crossings at the highest spatial resolution can be inferred more robustly using such a model compared to a simpler model that operates only on high-resolution data, when both approaches are matched for acquisition time.



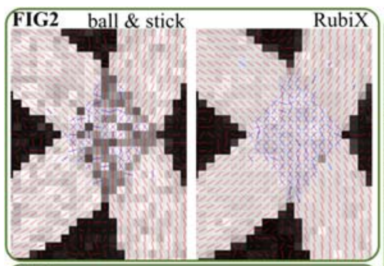
Methods: In this section we present the RubiX (Resolutions Unified for Bayesian Inference of Crossings) generative model. This is a data-fusion framework, where data from all resolutions are combined through a spatial and a local model. Priors on the model parameters impose spatial regularisation constraints that assist model identifiability when the high resolution data are of very low SNR.

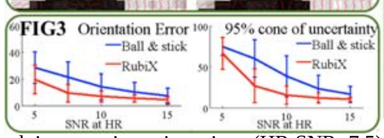
Let us assume that an object has been scanned at two different spatial resolutions. The aim is to construct a model that utilises both datasets and estimates parameters at the highest spatial resolution. Let the set of diffusion-weighted measurements at all voxels *X* of the low-resolution (LR) grid and all diffusion-sensitising directions *M* be $\mathbf{Y}_{LR}=\{y_{LR}^{XM}\}$. Let $\mathbf{Y}_{HR}=\{y_{HR}^{xm}\}$ be the set of measurements at directions *m* and voxels *x* of the high-resolution (HR) grid. Then, the RubiX mechanism can be understood by the graphical model shown in Fig.1. The data at both resolutions are generated by a model parameterised by $\boldsymbol{\omega}_{HR}$, a set of voxelwise parameters at the higher resolution grid. These parameters are restricted by the prior hyper-parameters $\boldsymbol{C}$. Different noise levels σ and baseline signals $S0$ are used for each acquisition. We treat $\boldsymbol{\omega}_{HR}$ as the set of parameters of local models that generate the predicted DW signal S_{HR}^{xm} at each HR voxel *x*. Assuming that the two spatial grids are registered to each other, we can apply a partial volume model to relate these parameters to the predicted signal at the LR grid. The partial volume model that predicts the LR signal for a voxel *X* is: $S_{LR}^{XM}/S0_{LR}^{X}=\sum_{k=1}^{K}\alpha_k S_{HR}^{kM}/S0_{HR}^{k}$. Index *k* describes the *K* HR voxels that intersect voxel *X*, each with a volume fraction α_k. The above model relates signal attenuation predictions at the LR grid with predictions at the HR grid. It should be noted that it is valid under the assumption of relatively constant proton density and relaxation times over a small neighbourhood of *K* HR voxels. The spatial model can be used in conjunction with a local model at the HR voxels to relate parameters $\boldsymbol{\omega}_{HR}$ to both LR and HR measurements. In this study, we have used the ball & stick [3], as a local model.

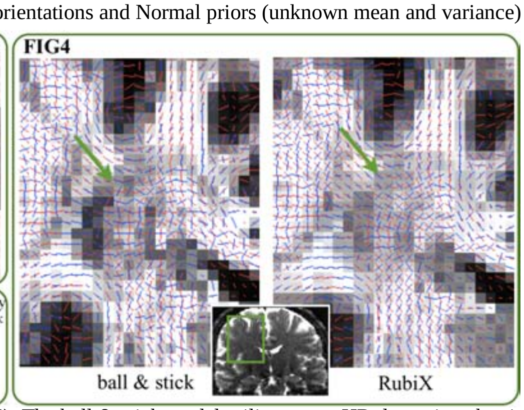
We used Bayes theorem to obtain the posterior distribution of the model parameters of interest given the HR and LR data [5]. Monte-Carlo Markov-Chain (MCMC) was utilised for parameter estimation. The conditional priors $\boldsymbol{C}$ were chosen to indirectly unify orientation, volume fraction and diffusivity estimates across the two spatial resolutions. They are imposed on parameters of the local models. The hyper-parameters of these priors are common to all *K* HR voxels intersected by the LR voxel *X* and are also estimated from the data. The model allows the values of these hyper-parameters to further propagate as constraints on the estimation of the HR model parameters. A Watson prior distribution with unknown mean and concentration was utilised for the orientations and Normal priors (unknown mean and variance) were utilised for the volume fractions and diffusivities.

Results and Discussion: RubiX model estimates were compared to estimates obtained from the ball & stick model. 180 DW directions were acquired at 1.5mm isotropic (HR) resolution on a 3T Siemens Trio system. Also, 120 DW directions were acquired at 3mm isotropic (LR) resolution (same field of view as HR). The *b* value was kept the same for HR and LR at b=1000 s/mm^2. The ball & stick model was applied to the HR dataset. RubiX was applied to the first 120 HR directions and the 120 LR directions. Notice that both approaches were *matched for acquisition time.*

A simple crossing example was also simulated. Data were generated using the ball & stick model at HR and the RubiX partial volume model at LR. Once the SNR was chosen for the HR data, the LR SNR was scaled by $8/\sqrt{2}$ [6]. Fig.2 shows the benefit of the multi-resolution RubiX approach for resolving crossing orientations (HR SNR=7.5). The ball & stick model utilises more HR datapoints, but it fails to recover the crossing area. Fig.3 shows how the mean orientation error and the 95% cone of uncertainty [7] reduces with RubiX in the crossing for various SNRs.







Similar benefits are shown for the in-vivo data (Fig.4). The RubiX estimates are less noisy and more spatially coherent at the centrum semiovale and the internal capsule. To assess accuracy of in-vivo estimates, we performed a cross-validation test. The full 180 direction HR dataset was divided into one dataset with 120 directions and another with 60 directions. We ran the ball & stick model on these datasets and used the estimates from the 120-direction one as "ground-truth". The accuracy of the 60-direction ball & stick estimates was then compared to the accuracy of the RubiX estimates obtained from 40 HR directions (subset of these 60) and 40 LR directions (to match for acquisition time). Whilst the 120-direction dataset is a noisy estimate of ground truth, this "ground-truth" is the result of twice the acquisition time as the ball & stick and RubiX analyses. The results of this comparison indicate that the RubiX estimates agree more with the "ground-truth" estimates than the ball & stick ones. For an ROI in the centrum semiovale the mean orientation error was 12.81^o for RubiX and 15.64^o for the ball & stick model. Furthermore, RubiX identified 74% of the voxels that contained a crossing, according to the "ground-truth". The ball & stick model identified 61% of these voxels.

It should be noted that the current RubiX framework cannot combine data acquired at different *b* values, due to limitations imposed by the local model. Furthermore, the employed spatial model is valid under certain assumptions and also imposes limitations. We will illustrate improvements on both aspects in a future study.

Conclusion: We have presented a model that simultaneously considers DW-MRI data acquired at multiple spatial resolutions to infer fibre orientations. RubiX combines the spatial specificity and SNR benefits of the high and low resolution grids, respectively, to estimate more robustly orientations at the highest of the available resolutions. The current study illustrates the value of spending some of the acquisition time for collecting data at a lower (than desired) spatial resolution, rather than collecting more, but noisier data only at high resolution.

References: **[1]** Tournier et al, Neuroimage 23, 1176–1185, 2004. **[2]** Sotiropoulos et al, NeuroImage 60, 1412-1425, 2012. **[3]** Behrens et al, NeuroImage 34, 144-155, 2007. **[4]** Miller et al, NeuroImage 57, pp. 167-181, 2011. **[5]** Bernardo & Smith, Bayesian Theory, Wiley, 2000. **[6]** Haacke et al, Magnetic Resonance Imaging: Physical principles and sequence design, Wiley, 1999. **[7]** Jones, Magn Reson Med 49, 7-12,2003.

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