Partial-Volume Modelling in Diffusion MRI

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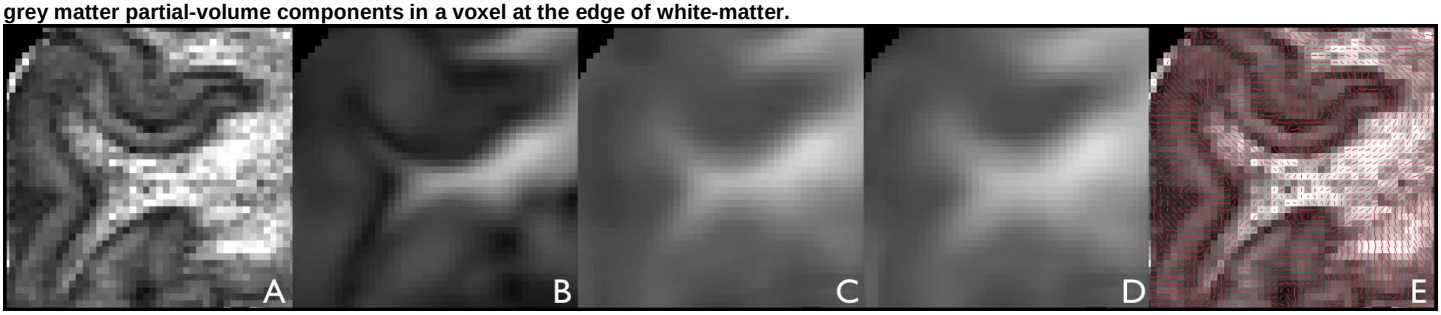
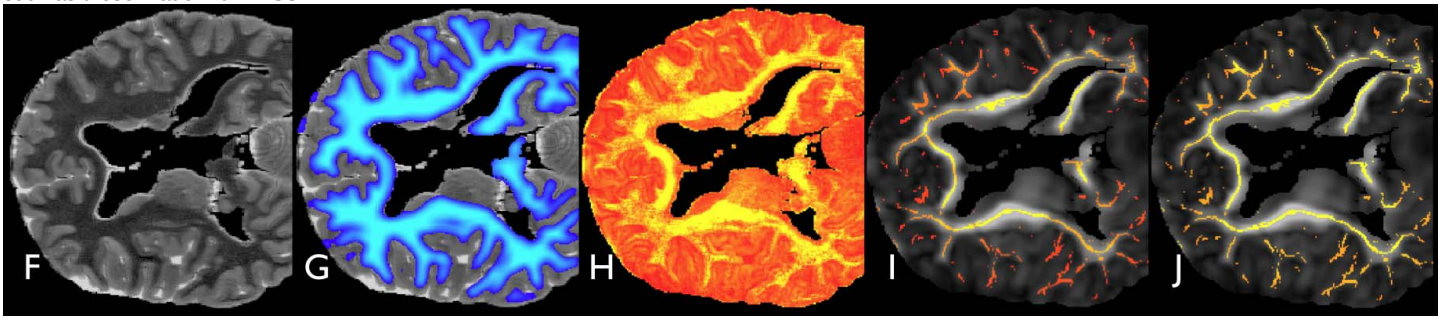
Introduction. In diffusion-based analyses of white-matter integrity (e.g., using fractional anisotropy (FA) as the primary marker), it is of concern that many tracts of interest have thickness on the same order as the data resolution; an apparent change in FA could be due to either a change in tract thickness (extent of partial-voluming) or a change in the underlying "true" FA (and that in itself can vary as a result of differing mixtures of crossing fibres). In this work we use very high-resolution diffusion data in order to test whether disambiguation of FA changes and tract thickness might be possible. We use the high-resolution data as the "gold-standard", from which to generate data at more normal resolutions for which the underlying ground-truth is known. We demonstrate the nonlinearities in the generation of the apparent FA seen at normal resolutions, and attempt to recover the underlying true FA from down-sampled data, even in thinner tracts.

Data. We acquired a high-resolution diffusion dataset from a recently-fixed *ex vivo* brain: 3T, 3D spin-echo diffusion imaging, 0.73x0.73x0.73mm, 5 repeats of 63 diffusion-encoding directions at b=3000 s/mm^2 plus the non-diffusion weighting image[1]. Data analysis was carried out using tools from FSL[2]; the individual images were corrected for eddy currents and B_0 drift using FLIRT, and the diffusion tensor model was fit using FDT.

Partial-Volume Effects in FA. We first investigated the interaction of image resolution with partial volume effects. We down-sampled the original raw diffusion data by a factor of 5 in each direction, though to maintain as much useful image information as possible, we kept the original "resolution", and replaced each voxel with the average of its 5x5x5 voxel neighbourhood. In each resulting voxel the characteristics should therefore be close to what would have been seen in data acquired at 3.5x3.5x3.5mm resolution. We then re-ran the tensor fitting to give "normal resolution" images (B). We also generated down-sampled versions of the FA in the "wrong" way, for comparison, by directly downsampling the original high-resolution FA (A, to create D). Finally, we also tested the intermediate approach of down-sampling the high-resolution tensor eigenvalues and regenerating the FA image from these (C)[3]. It is clear that resampling the raw diffusion data results in finer detail (B) than resampling the original FA (D), with resampling the original eigenvalues giving intermediate results (C). In fact, resampling the original raw data results in an apparent *thinning* of the tract. This is due to the fact that diffusion within, but at the edge of, the tract, is orthogonal to diffusion in neighbouring grey matter (see E), and only when down-sampling the data "correctly" (B) is this destructive interference seen. The processing used to generate (B) mimics what we see in real data at normal resolutions: **tracts appear thinner in a normal-resolution FA image than they really are, due to interference between the primary diffusion directions in white and grey matter partial-volume components in a voxel at the edge of white-matter.**



Disambiguating Partial-Voluming and "True" FA Change. As a convenient way to identify voxels of relevance, we applied the TBSS[4] skeletonisation algorithm to the 3.5mm FA image (I). This generated white-matter tract-centre maps with voxels that run into the finest tracts seen in the high-resolution image, allowing us to investigate the effects of partial-voluming on apparent FA. The mean diffusivity image (F) had good grey-white contrast and was fed into FAST segmentation to obtain a white-matter partial-volume estimate, which was down-sampled to 3.5mm (G). At each skeleton voxel, we therefore had 3 measures to feed into the modelling: the WM PVE fraction and the FA at "normal" 3.5mm resolution (I), and the "true underlying" FA, as sampled from the original high-resolution FA (H). The relationship between raw data and FA is highly nonlinear, as is the effect of partial-voluming at WM edges, as seen above. Together the interactions between these effects are not yet well-understood, hence we modelled true FA as a polynomial function of PVE and apparent FA. Models (up to quartic) that *only* included PVE *or* FA were unable to fit the true FA well, suggesting that both measures are needed and are therefore distinct. However, a quadratic model containing *both* was able to fit the true FA well. The *estimated* "true" FA on the skeleton in (J) clearly matches (H) more closely than (I) does, with less reduction in FA in the (partial-volumed) thinner tracts. This suggests that in normal data, if we can estimated the PVE (e.g., from the MD image, or from structural data), **it should be possible to disambiguate partial-volume effects from changes in the underlying true FA in thin partial-volumed tracts**. This will aid in the interpretation of diffusion analyses such as those made with TBSS.



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References [1]McNab, ISMRM'08. [2]www.fmrib.ox.ac.uk/fsl [3]Kindlmann, *Delineating white matter structure*, MIA, 2007. [4]Smith, *Tract-based spatial statistics*, NeuroImage, 2006.