

# Modelling radial and tangential fibres in the neocortex

Luke J. Edwards<sup>\*</sup>; Siawoosh Mohammadi<sup>\*,†</sup>  
Pierre-Louis Bazin<sup>‡</sup>; Michiel Kleinnijenhuis<sup>§</sup>  
Kerrin J. Pine<sup>\*</sup>, Anne-Marie van Cappellen van Walsum<sup>¶</sup>  
Hui Zhang<sup>||</sup>; Nikolaus Weiskopf<sup>\*,‡</sup>.

11 November 2015

## Synopsis

The structure of neocortical grey matter is complex due to the crossing intracortical neuronal connections involved in cortical processing. Herein we present a two-step method to capture radial and tangential fibre structure of neocortex from diffusion data: first the radial cortical orientation is extracted voxelwise using surface-based methods, and then a three-compartment diffusion model extracts radial and tangential fibre volume fractions. We demonstrate in a post mortem sample of human V1 tissue that this method captures structure known from histology and comparable diffusion models, implying potential future use as a probe of intracortical neuronal connectivity.

## Purpose

To extract histologically relevant biophysical parameters from diffusion data in neocortex using a method combining surface based techniques and a three-compartment diffusion model.

---

<sup>\*</sup>Wellcome Trust Centre for Neuroimaging, UCL Institute of Neurology, UCL, London, United Kingdom

<sup>†</sup>Institut für Systemische Neurowissenschaften, Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany

<sup>‡</sup>Department of Neurophysics, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

<sup>§</sup>FMRIB Centre, University of Oxford, Oxford, United Kingdom

<sup>¶</sup>Department of Anatomy, Donders Institute for Brain, Cognition and Behaviour, Radboud University, Nijmegen, Netherlands

<sup>||</sup>Centre for Medical Image Computing, Department of Computer Science, UCL, London, United Kingdom

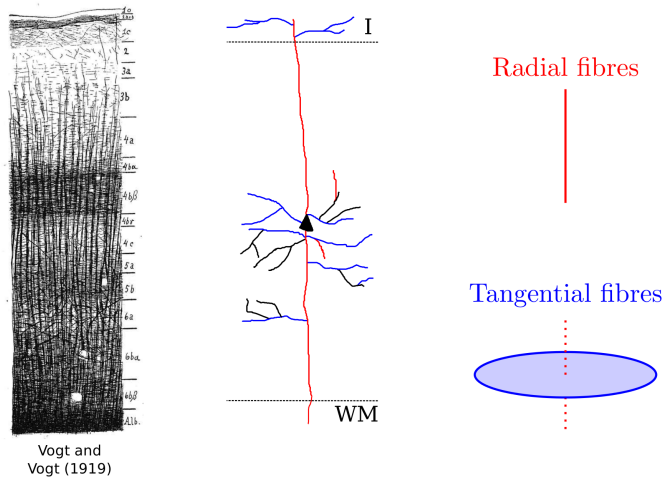


Figure 1: Schematic representation of the cortical diffusion model. The fibre structure in human neocortex (left, reproduced from Vogt and Vogt [9]) due largely to the structure of pyramidal neurons (schematically shown centre) provides rationalisation for separation into radial and tangential stick distributions (right). Markings denote cortical layers and boundaries.

## Theory

Our diffusion model consists of two types of compartment: intraneurite, and extraneurite. By modelling neocortical neurons using two populations of sticks (Figure 1)—‘radially’ distributed sticks perpendicular to the cortical surface, and ‘tangential’ sticks distributed isotropically parallel to the cortical surface—we separate the volume fraction of the intraneurite compartment into radial and tangential components. Following Zhang, et al. [1], the diffusion tensor of the extraneurite compartment is computed by averaging the relation in Szafer, et al. [2] over all stick populations. A free diffusivity parameter (assumed to be equal for intra- and extra-neurite diffusion) is also fitted, giving three parameters to be fit: radial neurite volume fraction, tangential neurite volume fraction, and diffusivity.

## Methods

We test our model using a multi- $b$ -value  $200 \mu\text{m}$  isotropic resolution dataset of a post-mortem human V1 tissue sample from Kleinnijenhuis, et al. [3]. Data were preprocessed as described in that publication.

Radial cortical directions were estimated with CBS Tools [4] as the normal vectors to the cortical depth isosurfaces computed with an equivolume model [5] with 10 estimated depth layers, based on a GM mask manually delineated

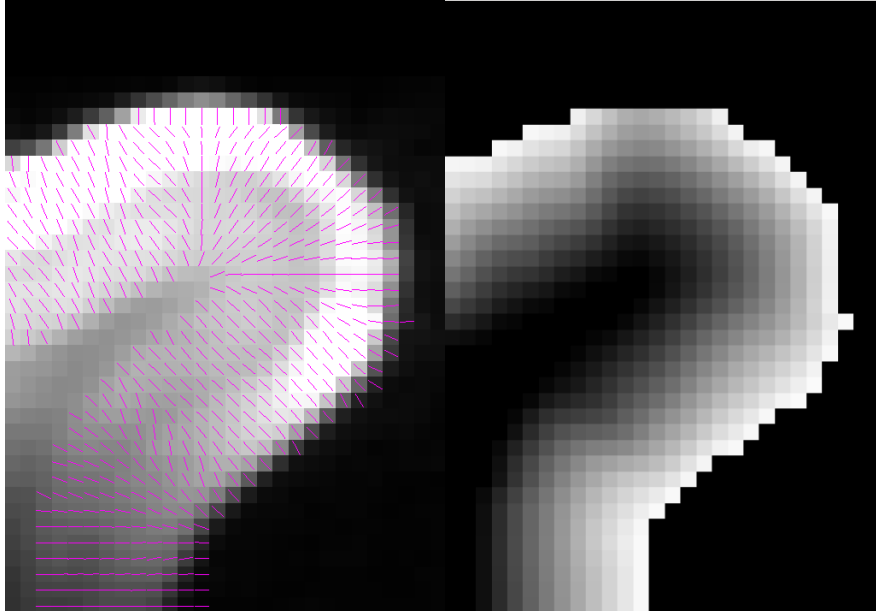


Figure 2: Orientations (left) and cortical depths (right) computed as described in Methods. Orientations are overlaid on a  $b = 0$  image, and depths range from  $[0,1]$ .

inside V1 on a  $b = 0$  image. Cortical depth values were estimated at each voxel based upon its distance to the closest two layers.

NODDI toolbox v0.9 [6] was used to implement and fit the model, with the radial direction fixed at the values computed using CBS Tools. Comparison is made to a fit using the NODDI model with standard ex vivo parameters and unfixed intraneurite diffusivity [1,7].

Cortical profiles were constructed by binning fitted parameter values into 20 equally spaced bins according to the cortical depth value of each voxel. This number of bins was chosen to include approximately 1000 voxels in each bin. The mean and standard deviation of each bin were plotted as a function of cortical depth. The cortical depth corresponding to the stria of Gennari [8,9] was demarked along a profile of cortex manually based upon a  $b = 0$  image.

## Results and discussion

Figure 2 shows the cortical depth measures and radial cortical directions computed within the GM mask, along with cortical profiles of the fitted parameters. Diffusivity varies strongly near the pial surface, reflecting partial volume effects.

The stria of Gennari [8,9] can be seen prominently in both volume fractions (Figure 2), in line with previous diffusion studies [3,7,10]. Our data also show

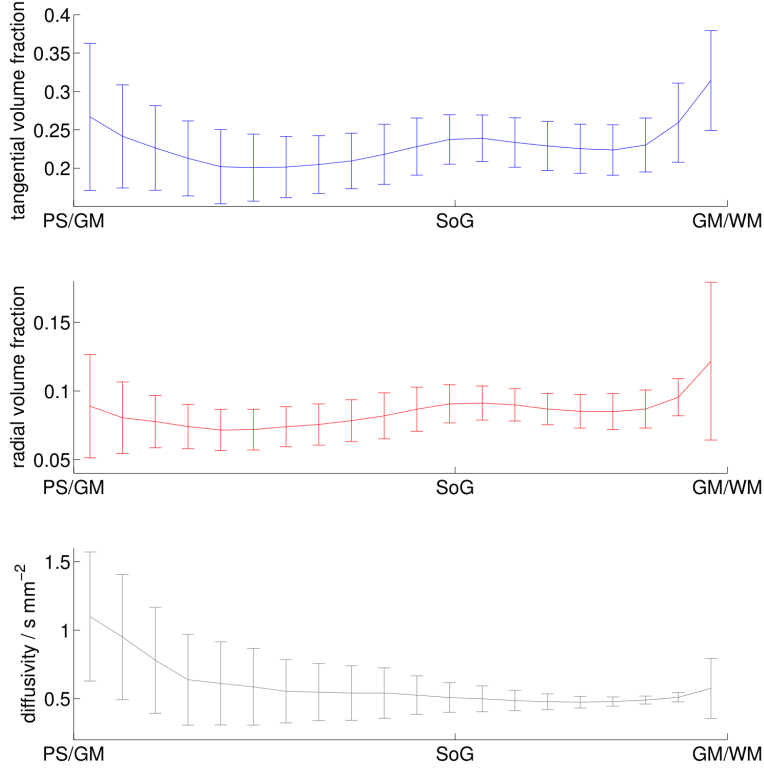


Figure 3: Plot of fitted cortical parameters as a function of depth. Borders of GM with WM and pial surface (PS) are demarked, as is the stria of Gennari (SoG). Note the different vertical axis scales.

an increase in tangential volume fraction near the pial surface border, a feature known from histology [8] and diffusion studies, though here the assumption of isotropic tangential neurite distribution means directionality of these neurites [10] could not be examined.

Figure 4 shows comparison with parameters obtained using the NODDI model, a model containing a similar overall number of fitted parameters to that presented here, where instead of two populations of sticks a single dispersed population of sticks is assumed. Although the NODDI model is not representative of the known crossing-fibre structure of neocortex, it has been shown previously to capture known neocortical features [7]. While quantitative comparison is a subject of further work, the NODDI parameters representing intraneurite volume fraction and dispersion do seem to capture the same cortical features; the

parameters generated in this work are however more readily interpretable in terms of intracortical fibre connections.

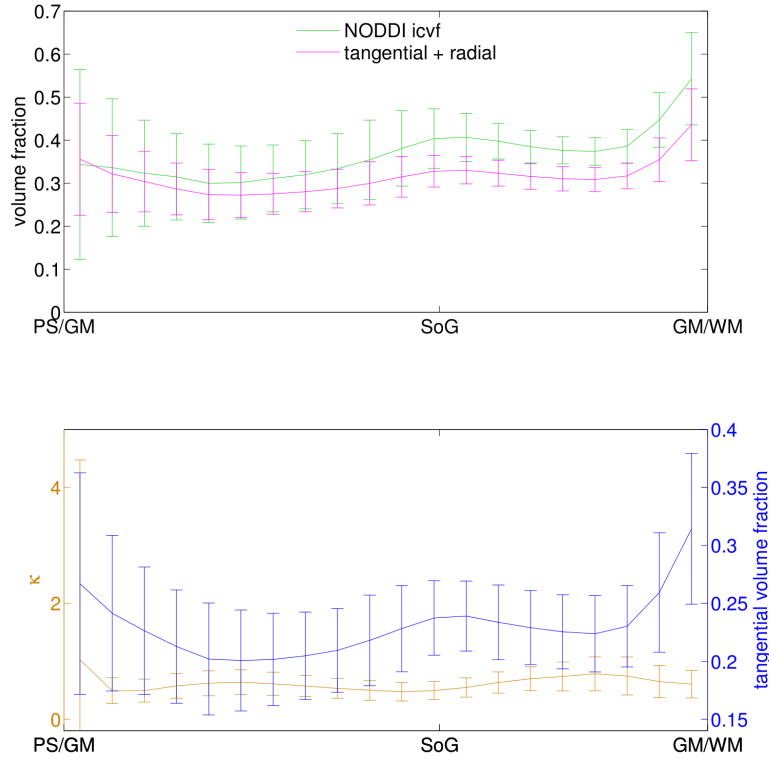


Figure 4: Comparison to NODDI parameters icvf (intra-neurite volume fraction)  $\kappa$ . Lower  $\kappa$  means greater dispersion about the main fibre orientation. As expected,  $\kappa$  decreases with increasing tangential volume fraction. Borders of GM with WM and pial surface (PS) are demarked, as is the stria of Gennari (SoG).

The model presented here is intentionally very simple, ignoring effects including the known anisotropy of cortical layer I neurites [10], exchange, and oblique neurites [8,9]. Given the present model's simplicity, and the rich amount of information contained in the diffusion signal, further work will investigate their inclusion. However, the validation presented here already outlines the interest of this model, in particular for in vivo studies of intracortical anatomy and connectivity.

## Conclusions

We have demonstrated that a diffusion model with only three fitted parameters can capture radial and tangential features of neocortical structure. Further studies will interrogate their meaning, particularly how well they represent intracortical collaterals and association fibres.

## Acknowledgements

The research leading to these results has received funding from the European Research Council under the European Union's Seventh Framework Programme (FP7/2007–2013) / ERC grant agreement n° 616905. The Wellcome Trust Centre for Neuroimaging is supported by core funding from the Wellcome Trust 0915/Z/10/Z. HZ would like to acknowledge EPSRC EP/L022680/1 for funding.

## References

1. Hui Zhang, Torben Schneider, Claudia A. Wheeler-Kingshott, Daniel C. Alexander; NODDI: Practical in vivo neurite orientation dispersion and density imaging of the human brain; *NeuroImage* (2012); doi:10.1016/j.neuroimage.2012.03.072
2. A. Szafer, J. Zhong, J.C. Gore; Theoretical model for water diffusion in tissues; *Magnetic Resonance in Medicine* (1995).
3. Michiel Kleinnijenhuis, Valerio Zerbi, Benno Küsters, Cornelis H. Slump, Markus Barth, Anne-Marie van Cappellen van Walsum; Layer-specific diffusion weighted imaging in human primary visual cortex in vitro; *Cortex* (2013); doi:10.1016/j.cortex.2012.11.015
4. Available from: <https://www.nitrc.org/projects/cbs-tools/>
5. M.D. Waehnert, J. Dinse, M. Weiss, M.N. Streicher, P. Waehnert, Stefan Geyer, Robert Turner, Pierre-Louis Bazin; Anatomically motivated modeling of cortical laminae; *NeuroImage* (2014) doi:10.1016/j.neuroimage.2013.03.078
6. Available from: [http://www.nitrc.org/projects/noddi\\_toolbox/](http://www.nitrc.org/projects/noddi_toolbox/)
7. Michiel Kleinnijenhuis; Imaging fibres in the brain; PhD thesis; Radboud Universiteit Nijmegen (2014).
8. S. Ramón y Cajal; *Studien über die Hirnrinde des Menschen v. 1* (1900); Johann Ambrosius Barth.
9. Cécile Vogt, Oskar Vogt; *Allgemeinere Ergebnisse unserer Hirnforschung*; *Journal für Psychologie und Neurologie* (1909).
10. Christoph W.U. Leuze, Alfred Anwander, Pierre-Louis Bazin, Bibek Dhital, Carsten Stüber, Katja Reimann, Stefan Geyer, Robert Turner; Layer-Specific Intracortical Connectivity Revealed with Diffusion MRI; *Cerebral Cortex* (2014); doi:10.1093/cercor/bhs311