# NODDI with dispersion anisotropy

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**PURPOSE** This work presents a technique for estimating the dispersion anisotropy in neurite orientations, using Neurite Orientation Dispersion and Density Imaging (NODDI) [1]. NODDI is a diffusion MRI technique, recently developed to directly quantify the microstructural features (density and orientation dispersion) of neurites *in vivo*, in the human brain. The parameters it provides offer higher specificity and sensitivity than standard indices from Diffusion Tensor Imaging (DTI), as shown in the preliminary application to epilepsy [2], dementia [3] and brain development [4]. One limitation of the current implementation is that it models neurite orientation dispersion with the Watson distribution, which constrains the dispersion about the dominant orientation to be isotropic (Fig. 1). This can neither accurately represent nor fully characterise the anisotropic orientation dispersion associated with complex fibre configurations, such as fanning and bending fibres. The present work develops a new NODDI model that can quantify the degree of this anisotropy and estimate the primary dispersion orientation. These features are not only important for mapping brain connectivity [5] but are also potential markers for disease diagnosis and monitoring. Using simulated and *in vivo* brain data, we assess the accuracy and precision of estimating the dispersion anisotropy using the NODDI protocol [1] and quantify the potential bias of the current NODDI model in estimating tissue microstructure.

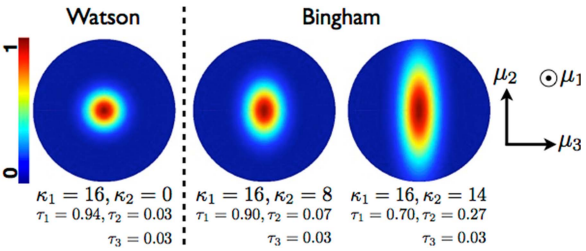


**Fig.1:** Bingham distributions: From left to right, increasing orientation dispersion anisotropy about the dominant orientation $\vec{\mu}_1$. The primary dispersion orientation is denoted by $\vec{\mu}_2$. Watson distribution is a special case.

**THEORY** NODDI model: The diffusion MR signal is modelled as the sum of contributions from the tissue, broken down into intra- and extra-neurite components; and a non-tissue compartment accounting for the CSF contamination. CSF is modelled as an isotropic compartment, while the tissue compartments account for the dispersion in the orientations of neurites as described in [1]. Similar to [6-8], we use the Bingham distribution [9] to accommodate orientation distributions of fanning and bending neurites. Bingham Distribution: This parametric distribution is the spherical analogue of 2-D Gaussian distributions. It is given by the dominant orientation $\vec{\mu}_1$, the primary dispersion orientation $\vec{\mu}_2$, and their respective concentration parameters $\kappa_1 \geq \kappa_2 \geq 0$ as shown in Fig.1. The primary dispersion orientation is orthogonal to the dominant orientation, thus requires only one more angle to be determined. Together with $\kappa_2$, the two are the only extra parameters to estimate compared to the original model that uses the Watson distribution, a special case of Bingham distribution when $\kappa_2$ is zero (Fig.1). Orientation Tensor: We compute the orientation tensor (OT), defined as the scatter matrix of a Bingham distribution [10], to enable the visualisation of Bingham distributions in terms of the familiar 3-D rendering of diffusion tensors (Fig.2). The primary and secondary eigenvectors of OT are precisely $\vec{\mu}_1$and $\vec{\mu}_2$. The corresponding eigenvalues, $1 \geq \tau_1 \geq \tau_2 \geq 1/3$, are functions of $\kappa_1$ and $\kappa_2$ [10] and reflect the relative concentration of neurites along the dominant and the primary dispersion orientations respectively. (The tertiary eigenvalue is not independent and is equal to $1 - \tau_1 - \tau_2$.) The narrow dynamic range of these parameters makes them easier to visualise than $\kappa_1$and $\kappa_2$, which range between 0 and ∞. We define the dispersion anisotropy about $\vec{\mu}_1$ in terms of the planarity measure [11], which is equal to $(\tau_2 - \tau_3)/\tau_1$: 0 for isotropic dispersion (the Watson distribution) and 1 for the maximum dispersion when $\tau_1 = \tau_2 = 0.5$.

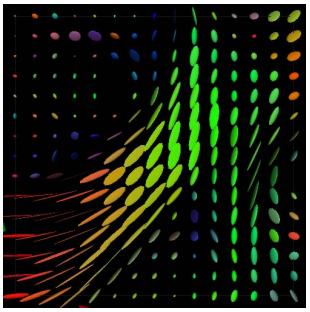

**Fig.2:** Orientation Tensor map obtained for *in vivo* data showing sharp bending of the fibres in genu of the corpus callosum

**EVALUATION** Data: The dispersion parameter estimation is assessed with diffusion MRI data of one healthy volunteer, acquired on a 3T Philips scanner ($G_{max} = 60mT/m$), using the 4-shell protocol as in [1], which includes the 2-shell NODDI protocol as a subset. The evaluation uses the estimates from the 4-shell protocol as the pseudo ground-truth. Synthetic data was additionally generated as in [1] to support the assessment with known ground-truth. Analysis: The NODDI Matlab toolbox is used for fitting. The data was fitted with both Watson and Bingham models to assess potential bias in parameter estimates with the original model. To assess the influence of acquisition protocol on parameter estimation, the proposed model was fitted to data from: 1) 4 shells, 2) NODDI shells, 3) NODDI shells with reduced orientations (half and one third), 4) b=1000 s/mm$^2$ shell, and 5) b=2000 s/mm$^2$ shell.

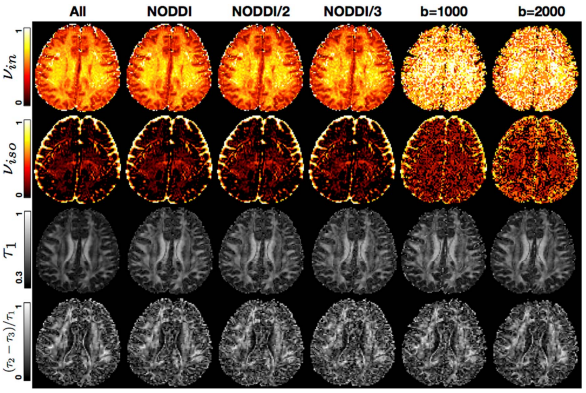


**Fig.3:** Parameter maps for the proposed NODDI model obtained for various protocols. $\tau_1$ measures the coherence of neurites about $\mu_1$, and $(\tau_2.\tau_3)/\tau_1$ the dispersion anisotropy. $v_{in}$ and $v_{iso}$ are the volume fractions of the intra-neurite and CSF compartments, respectively.

**RESULTS & DISCUSSION** Estimation of dispersion anisotropy: Fig. 2 shows the estimated OTs in the genu of the corpus callosum. For the voxels traversed by the bending fibres, the secondary eigenvector of the OTs lie in the bending plane and the tensors are wider at the more bendy part of the geometry, as expected. Fig. 3 shows the maps of key NODDI parameters, including the new dispersion anisotropy, which has the expected pattern of high values in the centrum semiovale and low values in the corpus callosum. The quality of parameter estimation is found to be comparable to that of the original model, except for the primary dispersion orientation, which is harder to estimate than the dominant orientation. Watson vs Bingham: Fig. 4 shows that the original Watson model can estimate its microstructural parameters as accurately as the proposed Bingham model, even in the presence of significant dispersion anisotropy. Synthetic data shows that the bias becomes non-negligible only when dispersion anisotropy is close to 1. Protocol comparison: Fig.3 demonstrates that the clinically feasible NODDI protocol, with 2 shells, is necessary and sufficient for estimating the parameters of the new NODDI model. Reducing the orientations sampled by the protocol can further reduce the scan time, without significantly affecting the accuracy of the estimates. Future work will investigate the reproducibility of the parameter estimates.

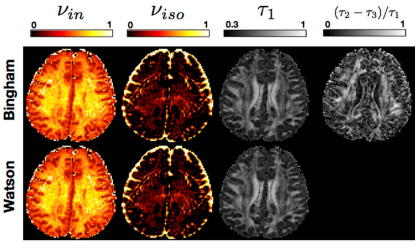


**Fig.4:** Parameter maps as Fig.3, but comparing the parameter estimates for the proposed (top) and the original (bottom) NODDI model.

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