Supplementary Material: White Matter Tract Integrity (WMTI) Method

The theory underlying the White Matter Tract Integrity (WMTI) method is described in detail by Fieremans et al.[13] Here we give a brief synopsis of its main assumptions and equations.

A primary assumption underlying WMTI is that the axons are mostly oriented in similar directions. This is usually reasonably well satisfied in brain regions with a high fractional anisotropy (FA), and the accuracy of WMTI improves with increasing FA, as suggested by a comparison with a more comprehensive model for white matter microstructure.[77] A second assumption is that molecular exchange between the intra-axonal and extra-axonal water pools is slow in comparison to the diffusion time for the pulse sequence used to acquire the diffusion data. Inter-compartmental exchange times for white matter have been measured to be around 1 second[78], which is indeed long in comparison to typical diffusion times of about 30-40 ms for clinical MRI systems.

Of the several parameters that can be estimated with WMTI, two of the most important are the axonal water fraction (AWF) and the extra-axonal radial diffusivity ($D_{e,\perp}$). The AWF for any given voxel is estimated by the formula

$$f = \frac{K_{max}}{K_{max} + 3}, \tag{1}$$

where f is the AWF and K_{max} is the maximum of the diffusional kurtosis for that voxel over all possible diffusion directions[13]. The diffusional kurtosis is a standard diffusion parameter that is provided by diffusional kurtosis imaging[12] (DKI). The WMTI estimate for the extra-axonal radial diffusivity is then given by

$$D_{e,\perp} = D_{\perp}\left[1 + \sqrt{\frac{K_{\perp} f}{3(1-f)}}\right], \tag{2}$$

where $D_{\perp}$ is the radial diffusivity and $K_{\perp}$ is the radial kurtosis, both of which can also be obtained with DKI.