The anisotropy of myelin magnetic susceptibility

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Purpose of study: To measure the anisotropy of the magnetic susceptibility of myelin.

High field susceptibility-weighted MRI reveals rich detail of white matter (WM) structure in human brain [1]. Myelin is thought to play an important role in this contrast, and may introduce a dependence on WM fiber orientation with the magnetic field because of its anisotropic susceptibility [2,3]. This anisotropy, quantified by the difference in susceptibility along and perpendicular to the fiber bundle of WM, has been estimated from MRI measurements to range from 0.01 to 0.027ppm [2,4], but these measurements may be imprecise due to various confounding mechanisms that may contribute to orientation dependence of the MRI signal. Thus, we aimed at providing an independent measure. Previously, the anisotropy of lipid bilayers has been estimated by studying lecithin vesicles, whose anisotropy results from a single bilayer and causes them to align with an external magnetic field [5]. This prompted us to investigate whether a similar alignment phenomenon could be observed for excised sections of white matter. For this purpose, an excised section of spinal cord with highly uniform fiber orientation was suspended in a 7T MRI magnet and its orienting behavior was studied and analyzed by constructing a magnetic torque balance [6].

Theory

$$T_m = \boldsymbol{M}\times\boldsymbol{B_0} = (\chi_\parallel-\chi_\perp)\frac{\sin(2\theta)}{2}\frac{\boldsymbol{B_0}^2}{\mu_0}V = a\sin(2\theta) \quad [1]$$

$$T_s = k(\varphi-\varphi_0) \quad [2]$$

$$T_s = T_m \Rightarrow \varphi_e = \varphi_0+\theta_e+\frac{a}{k}\sin(2\theta_e) \quad [3]$$

$$f = \frac{1}{2\pi}\sqrt{\frac{1+2(a/k)\cos(2\theta_e)}{I/k}} \quad [4]$$

The magnetic torque T_m acting on a section of spinal cord ('sample') suspended in a homogeneous magnetic field $\boldsymbol{B_0}$ depends on the anisotropy ($\chi_{//}$-$\chi_\perp$), its volume V, and the angle θ between the field and fiber axis (Eq. 1, where *a* summarizes the angle independent terms). Suspending the sample from a string in a horizontal, homogeneous magnetic field creates a torque balance (Fig.1). Rotating the suspension point of the string (by a rotator wheel) creates a string torque T_s (Eq. 2), where φ_0 is the neutral (zero torque) position of the wheel and *k* the string's torsion constant. T_s will drive the sample from its preferred orientation (θ=0) to a new equilibrium (Eq. 3; the subscript '*e*' refers to equilibrium). The net torque (T_s-T_m) and the moment of inertia (*I*) of the sample determine the oscillation frequency around θ_e. First order Taylor expansion of the equation for angular acceleration results in an approximate value for this frequency (Eq. 4). The unknowns are: $\chi_{//}$-$\chi_\perp$*(i.e. a), k, I* and φ_0; *I* can be calculated from the dimensions of the sample, fitting Eq. 3 and 4 to the observations resolves φ_0 and the torsion constants *a* and *k*.

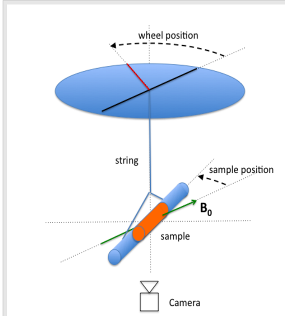

Figure 1. The experimental setup, placed in the center of the magnet. The sample in a tube is suspended by a string from a movable wheel. The angle of the wheel and the tube can be observed in real time (and recorded) with the camera placed below the device.

Methods

A 20mm section of fixed thoracic spinal cord (Fig. 2) was placed in the center of a 10mm diameter NMR tube of 95mm length. The remaining volume was filled with water. A similar tube entirely filled with water was used as a control. The tube was placed in a 13mm NMR tube which in turn was placed plastic cylinder. This cylinder was suspended in the center of a 7T MR magnet from a plastic wheel that could be rotated remotely (Fig. 1). The angle of the tube and wheel were observed with an MRI compatible video camera placed directly below the tube. The wheel was rotated stepwise in intervals of several minutes.

Combined fitting of the equilibrium angles and frequencies by a non-linear iterative optimization took into account that all three observables (wheel angle, tube angle, and frequency) have measurement errors. The white matter volume was estimated from a 3D, 375µm isotropic resolution gradient echo MR image produced on a 16T system.

Result & Discussion

The change in the tube angle (θ) over time in response to changes in wheel angle is shown in Fig. 3, for both the control and for the spinal cord. A clear orienting effect of the spinal cord is visible: while the control tube follows the wheel angle, the tube with the cord stays aligned with the $\boldsymbol{B_0}$ field to within 30 degrees. This is most clearly observed from the equilibrium angles (Fig. 4). The anisotropy in the spinal cord white matter volume magnetic susceptibility was found to be 0.024ppm. The error in this value is estimated to be around 10%, based on the error in *I,* the volume of WM and the ratio between the inertial and magnetic moments (determined from the fit). The value in brain WM may be about 20% lower because of the lower lipid content [7,8]. The resulting estimate (0.018ppm) is within the range of MRI-derived values, and close to an estimate of 0.023ppm based on the contribution of hydrocarbon chains [9]. This finding confirms the significant anisotropy of WM susceptibility reported in previous MRI studies, and furthermore provides a quantitative estimate that validates previous estimates.

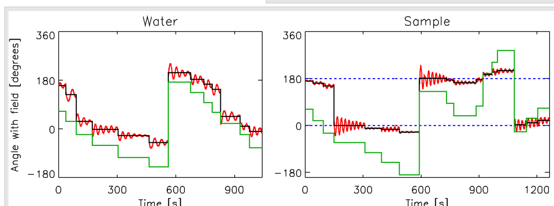

Figure 3. Angle of the tube (red) and the wheel (green) over the course of the experiment, the black line shows the fitted equilibrium angle. Left: control (water), right: spinal cord sample. It is clear the latter has a strong tendency to align with the magnetic field (angles at 0 or 180°) and oscillates faster. Each step in the wheel angle induces an oscillation around a new equilibrium.

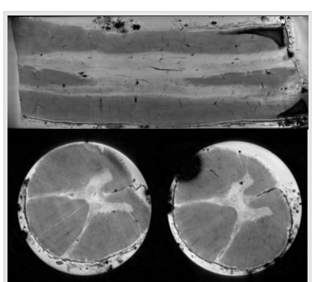

Figure 2. 375µm resolution MR images along two orientations of the spinal cord section. The WM is darker in this image and takes 92% of the volume.

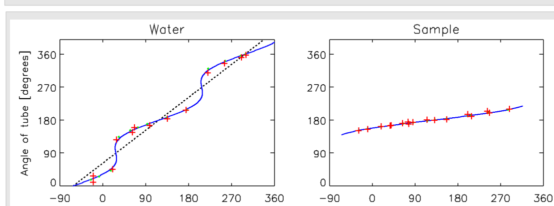

Figure 4. The equilibrium angle (vertical) versus the wheel angle (horizontal) with the fitted model in blue. Left: water control, right: spinal cord. The spinal cord angle was modified to account for 180° flips. The data points are the red crosses, the best fit (accounting for errors in wheel and tube angles) is in blue.

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