Coupled Two Compartment Diffusion Model for Estimating Water Exchange Ratio in White Matter Fiber Tracts Using Diffusion MRI

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Introduction

Axonal structure information, such as axonal density and diameter, is crucial for evaluating the status of neurological diseases with white matter damage. MRI has exhibited the ability to quantitatively estimate axonal density and diameter. However an important parameter effecting the axonal structure, the water exchange ratio (WXR) –the ratio of exchanged spins during diffusion time, Δ, between intra and extra axonal space, has not been fully investigated. Injury (such as MS, stroke, and TBI) to the axonal membrane or myelin sheath will likely change this parameter. There have been few efforts to include this factor in a proper diffusion model and then estimate it using DWMRI. In this work, we propose a model to estimate WXR within white matter fiber tracts which can be used in multi-shell DWMR imaging.

Methods

It is assumed that the fibers inside a voxel are nearly parallel and cylindrical having almost the same radius, *R*; therefore we consider that the voxels belong to a single fiber. Our proposed model is a modified and combined version of the well-known CHARMED model and the model introduced by Zhou et al[1]. It consists of two parts for intra and extra axonal spaces coupled by a parameter *k* accounting for the exchange rate: $E(q) = S(q)/S_0 = v.E^{\perp}_{in}(q).E^{\parallel}_{in}(q)E_{Xin}(g) + (1-v).E^{\perp}_{out}(q).E^{\parallel}_{out}(q).E_{Xout}(g)$

Where *v* is the axonal space fraction, *g* is the diffusion gradient, and $q=\gamma g\delta$ in which δ is the diffusing pulse width. In this work we use a more general form[2] for the diffusion signal perpendicular to the axons than the one used by CHARMED so it is not restricted to the cases in which $\delta \approx \Delta$.

$$\log E^{\perp}_{in}(q) = -\frac{2q_{\perp}^2}{\delta^2\eta^2[(112/33)^2-1]}\left\{2\delta - \frac{2+e^{-\eta(\Delta-\delta)}-2e^{-\eta\delta}-2e^{-\eta\Delta}+e^{-\eta(\Delta+\delta)}}{\eta}\right\},\quad \eta=(112/33)^2\frac{D_{in}}{R^2},\quad \log E^{\parallel}_{in}(q) = -4\pi^2(\Delta-\frac{\delta}{3})q_{\parallel}^2 D_{in},\quad \log E_{Xin}(g) = -k^2 D_{in}\Delta\, g_{\perp}/R^2$$

$$\log E^{\perp}_{out}(q) = -4\pi^2(\Delta-\frac{\delta}{3})q_{\perp}^2 D^{\perp}_{out},\quad \log E^{\parallel}_{out}(q) = -4\pi^2(\Delta-\frac{\delta}{3})q_{\parallel}^2 D^{\parallel}_{out},\quad \log E_{Xout}(g) = -k^2 D^{\perp}_{out}\Delta\, g_{\perp}/R^2$$

Here, *g* is decomposed into the parallel and perpendicular directions of the fibers, $\vec{n}$, i.e., $g^2=g_{\parallel}^2+g_{\perp}^2$. The expressions for *Ex* is inspired from the solution of the Ficks Law under the condition of $\delta \approx 0$ for a permeable membrane[2]. As we use this model for a large δ, the definition of *k* is not the same; however, we will show that this parameter is proportional to the WXR. Finally, the unknown parameters need to be estimated are: D_{in}, $D^{\perp}_{out}$, $D^{\parallel}_{out}$, *v*, *R*, and *k*. We calculate $\vec{n}$ using the common Diffusion Tensor model. The parameters are estimated using non-linear least square curve fitting method in MATLAB Optimization Toolbox (www.mathworks.com).

Results and Discussion

Simulation Data. To validate our model, we generated artificial diffusion signals using Monte Carlo simulation (10^6 times) of Random Walk process for a pack of parallel permeable cylinders. In the simulation, all parameters were set to be similar to our real MR imaging scheme. We investigated the model using the generated data with different values for *R* (1.5,2.5 μm), *v*, and also the membrane permeability, P_m (0,1,2,3,4,5,6,9,12 $\mu m/s$). The diffusion coefficients D_{in} and D_{out}, are set to 2 and 3 $\mu m^2/s$, respectively. Note that although the diffusion coefficient for the extra axonal space is identical in all directions, the apparent diffusion coefficient in the perpendicular direction is smaller than the parallel one. A white Gaussian noise was added to the signals (SNR=40) and each investigation was repeated 50 times. In Fig 1, the mean and STD values for the estimated parameters *k, r'*, and *v'* are shown for different combinations of *R*, *v*, and WXR. It can be seen that *k* has a good proportional relation to WXR which shows its capability in discriminating permeable axons as well as estimating the radius, density, and diffusion coefficients. Note that *v'* decreases as WXR increases due to the fact that *v'* corresponds to the fraction of spins trapped inside axons which decrease by increasing WXR. Although, we used the *Ex(g)* terms to compensate this, there are still a group of spins which affect the estimated values.

Real Data. To show the capability of the model to discriminate between injured and normal tissue, we scanned 6 ex-vivo rat brains, that suffered from TBI on the right side of the brain, using a Varian 7 Tesla with maximum applied gradient amplitude of 290mT/m. HYDI data sampling scheme with 125 diffusion gradient directions in 5 shells (6, 21, 24, 24, 50 directions with b-values of 360, 1440, 3240, 5760, 9000s/mm2, respectively, along with a reference T2 weighted B0 image) was chosen to be performed using a PGSE sequence with TR/TE/Δ/δ = 1500/40/18/10 ms and 5 averages. The FOV was 24 mm and 1mm slice thickness resulting in a 128x128 imaging matrix with 13 slices. Ex-vivo MRI scans were preformed 7 weeks after TBI. The resulting images were smoothed using a 3by3 Gaussian filter to reduce the noise. For each brain, the Corpus Callosum (CC) fiber tract was segmented manually and divided into 3 parts: left, center, and right for comparison. The reprehensive estimated map of *k* (overlaid on FA map) is shown in Fig 2 just for one of our TBI cases due to the space limitation. As it can be seen, there is a clear contrast between the injured (right) and normal (left) parts of the CC. The quantitative values for the estimated parameters are shown in Table 1.

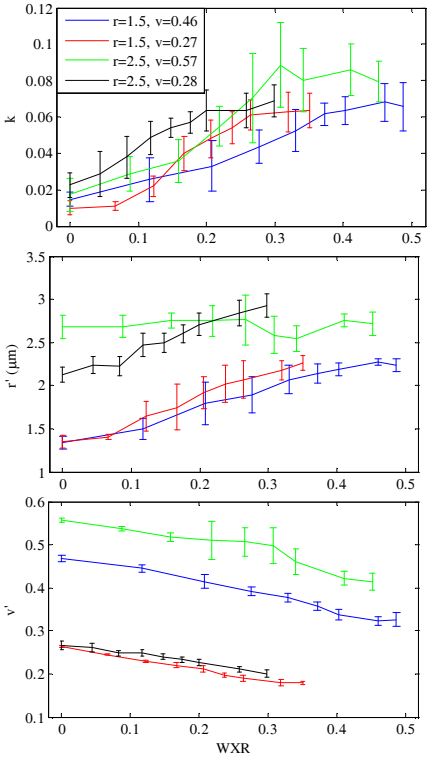

Fig 1. Mean and STD values of the estimated parameters. Note that *k* is almost linearly proportional to the WXR independent of the values of *r* and *v*.

Conclusion

The proposed model can discriminate between normal and injured fiber tracts induced by TBI or other diseases which affect the exchange parameters of the tissue. This model also may be used to estimate other micro-structural parameters like radius, density, and diffusion coefficients. One of the limitations of this model is that it is valid only for single fibers. Moreover, the estimated values for *r* and *v* are still deviating from their actual values as the exchange ratio increases (see Fig. 1). This deviation may be compensated by importing new term(s) into the model in the future works.

Table 1. Overall mean and STD values of the estimated parameters for all cases in the left (normal) and right (TBI) parts of CC.

	k	*r'* (μm)	*v'*	$D^{\parallel}{}'_{out}$ ($\mu m^2/s$)	$D^{\perp}{}'_{out}$ ($\mu m^2/s$)	D'_{in} ($\mu m^2/s$)
Left	0.02±0.006	0.25±0.08	0.2±0.041	0.47±0.05	0.27±0.02	0.05±0.02
Right	0.08±0.014	0.34±0.17	0.17±0.03	0.46±0.08	0.26±0.04	0.12±0.09

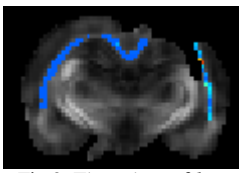

Fig 2. The values of *k* overlaid on the FA map of one TBI case.

References

1. Neuman CH. Spin echo of sp- ins diffusing in a bounded medi- um. J Chem Phys. 1974;60(11):4508-4511.
2. Zhou W, Laidlaw DH. An analytical model of diffusion and exchange of water in white matter from Diffusion-MRI and its application in measuring axon radii. ISMRM. 2009; 17:263.