On random walks and entropy in diffusion-weighted magnetic resonance imaging studies of neural tissue

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Target Audience

The scope of this study is directed at MR physicists, bioengineers, and neuroscientists interested in new tools to probe and model neural tissue with diffusion MRI.

Purpose

For Brownian motion, the characteristic function (i.e., the spatial Fourier transform of the probability distribution function) is represented by a mono-exponential decaying function with respect to time. In diffusion MRI (DWI) studies, this decay is modeled as $exp[-(bD)]$, where D is the diffusion coefficient (e.g., mm^2/s) and b is the pulse sequence controlled parameter. The random walk (RW) model is a practical approach to derive the features of Brownian motion and also predicts a mono-exponential decay for the characteristic function. However, numerous research groups have reported diffusion decay processes in neural tissues, which deviate from the mono-exponential model [1]. A generalization to the RW is the continuous time random walk (CTRW) model in which there are no *a priori* assumptions regarding the governing statistics [2]. In the CTRW framework, the characteristic function is described by the Mittag-Leffler function (MLF), which through the fractional order stretching parameter, α, is able to capture diffusion decay processes that are not mono-exponential ($\alpha < 1$). Furthermore, using entropy, $H(q,\Delta)$, we are able to quantify the 'information' in the characteristic function in order to distinguish the 'complexity' of white and gray matter regions of interest (ROIs) in neural tissue.

Methods

To evaluate the MLF and entropy parameters as potential biomarkers for biological tissue features, we performed DWI experiments on 5 fixed rat brains. For each imaging experiment, the rat brain was placed in a 20 *mm* imaging tube, immersed in Fluorinert, and secured with a magnetic susceptibility-matched plug. In this study, four pulsed gradient stimulated echo (PGSTE) DWI experiments were performed in one diffusion direction on a spectrometer (17.6 Tesla, 89 *mm* bore) with 10 b-values arrayed between 50 - 25,000 s/mm^2. The b-value array was comprised of either constant Δ (mixing time) or constant q (diffusion gradient strength) values. The two constant Δ PGSTE DWI experiments were set at Δ=20 ms and Δ=50 ms. The two constant q PGSTE DWI experiments were set at q=52 mm^{-1} and q=78 mm^{-1}. Using custom Matlab code, we fit the data to the MLF and then computed the entropy in the ROIs.

Results

The signal decay plots for the ROIs selected in the corpus callosum, thalamus, and cortex show clear divergence from the mono-exponential decay on the linear-log scale (Fig. 1). The MLF parameter, α, separated the central corpus callosum (0.42 ± 0.04), the thalamus (0.57 ± 0.07), and the cerebral cortex (0.76 ± 0.05) (Fig. 2a). The entropy, $H(q,\Delta)$, distinguished the central corpus callosum (0.93 ± 0.01), the thalamus (0.86 ± 0.01), and the cerebral cortex (0.81 ± 0.01) (Fig. 2b). We observed the best image contrast in the constant Δ=20 ms PGSTE DWI experiment, in which q was arrayed over the largest range of gradient strengths.

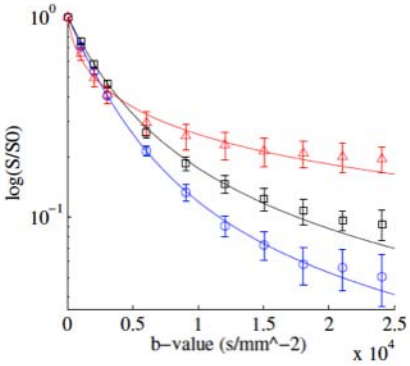

Fig. 1: Signal plots and MLF fits for the corpus callosum (red triangles), thalamus (black squares), and cortex (blue circles).

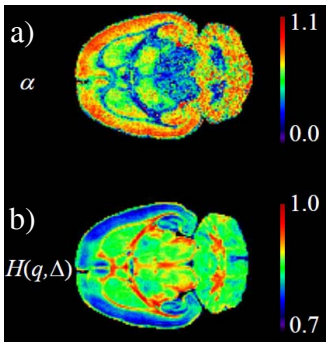

Fig. 2: Parameter maps for a) α, and b) $H(q,\Delta)$ in an axial slice through a fixed rat brain.

Discussion

In the context of CTRW theory, α is recognized as a measure of the waiting times between jumps along the diffusion path. For heterogeneous and tortuous materials, sub-diffusion is expressed when $\alpha < 1$. In this study, the selected ROIs exhibited good contrast with distinct values of α, indicating degrees of sub-diffusion. To quantify these anomalous dynamics, we applied entropy, $H(q,\Delta)$, as an overall measure of the stochastic 'uncertainty' in the CTRW characteristic function and observed the highest entropy values in the most 'complex' tissue ROIs (i.e., corpus callosum). At low b-values, the classical diffusion coefficient, D, was not able to distinguish the ROIs. However, at high b-values, both α and $H(q,\Delta)$ were able extract new 'information' about tissue from the heavy-tailed diffusion decays that are clearly not mono-exponential. Finally, our results suggest that the weighting choices of q and Δ have an observable impact on the diffusion dynamics in b-value arrayed DWI experiments.

Conclusion

We present these MLF and entropy parameters as potential biomarkers for morphology in neural tissue.

References

1. Zhou, X.J. Magn Reson Med. 2010;63(3):562-569. 2. Metzler, R. and Klafter, J. Phys Rep. 2000;39(1):1-77.