Sub-resolution Axon Microstructure Characterization Using Diffusion Fingerprints

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Abstract

the structure of axon, beading or realted to diffusion; propagator show beads. the diameter is not easy to have controversal point of transerval diffusion; we cannot see D vertical.

Diffusion correlation of D(delta) with D(2*delta) = 13-interval PFG seqeunce. egain functions; single-sided can do those too. DTI is assuming one components but really there are 2 component.

2D-experiments 2D diffusion time correaltion expeiremnt using a single direction gradient paulsen do axon connect Dx Dy

1) what ist he diffusion in axon 2) understanding our interpertion of trans/longitudnal direction. diffusion anistropy, cannot align our gradient with the axon. transversal diffusion less than calcualted or measured, compare the two direction. the alignmens issues. the transversal diffusion cannot have the diameter.

1 Introduction

Importance of understanding axon Axons are the fundamental conduits of signal communication in the nervous system [1]. Their micro-geometry, including caliber, packing density, and deviations from straight trajectories, influences conduction, functional connectivity, and reflecting to injury and disease. Noninvasive quantification of axonal microstructure therefore remains a central goal in diffusion MRI (dMRI) and diffusion NMR.

how are axon usually been modeled by NMR

Diffusion measurements probe tissue microstructure because water molecules sample restrictions imposed by cellular boundaries. The trajector of molecule assemble can be tracked to reflect the geometry of tissue.

In white matter, many microstructural models approximate intra-axonal water as sticks (effectively 1D Gaussian diffusion with $D_\perp \approx 0$) or as straight impermeable cylinders, enabling estimation of axon orientation, density, and (under specific conditions) diameter [2, 3]. The two usually used methods are CHSRMED and AxCaliber.

DTI is a microstructure biomarker of axon bundles [4, 5].

[6] showed how the undulation shape the diffusion results. [7]

Such features introduce time-dependent and waveform-dependent diffusion signatures that can confound diameter and orientation estimates, especially under practical hardware constraints on gradient amplitude, diffusion time, and echo time [8]. The diameter can be obtained from models based on those assumption [];

Real axons deviate from the idealized straight cylinder: they may exhibit undulations, beading, and caliber variations [9]. As a result, model mismatch and limited experimental sensitivity can lead to biased or weakly identifiable microstructural parameters.

what are the issues of those methods But in practice, the axons are not just a straight and narrow tube. They have features like beads, undulation ect [9]. Therefore, the based on the diffusion coefficient to have the diameter leads to strong uncertainties. Besides, because of the undulation, it is hard to find the perpendicular direction of axons trend. It is also hard to have short enough diffusion measure time to resovle the fine parameter, limited by the maximum gradient and shortest echo time contrainted by the hardware [8]. Therefore the fractional anisotropy, direction and dispersion of axon bundles are not accurate.

Our findings at short time, the molecules sense the water molecule itself, at intermediate time, the water moelcues sense the boundaries of axon, at long time the molecules sense tortuosity of medium. In axon, at short times, where $t \ll \frac{a^2}{D_0}$, follows Mitra's short-time expansions. At intermediate times, where $t \approx \frac{a^2}{D_0}$ follows Neuman cylinder model and at long times, $t \gg \frac{a^2}{D_0}$ follows Callaghan's diffusion propagator theory.

2 Results

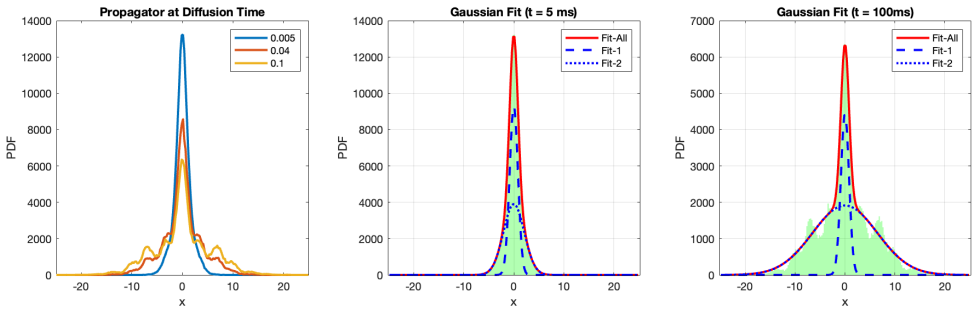

Figure 1: The simulated propagator distribution from axon 909.

The propagor shows structure details of axon. At short diffusion time, the water molecues only sense the structure with distance similar to $\sqrt{2D_0t}$. The propogator is assembly of all strucuture

features, $f(r_s)$, as in Fig. 1(b). If there is no boundary liminitation, the propagator shall be gaussian distribution. With increasing time, the molecules start to sense structures along the the axon, beads pinching and bulging along the axis. Thus we have multiple peaks on the propagator. With even longer time the molecules sense media tortuosity.

(1) Very small —x—: molecules that stayed near their origin (2) trapped in pockets / beads (3) bouncing back and forth near a boundary (4) stuck in very tortuous "loops" (5) Intermediate —x—: molecules that diffused but kept hitting obstacles so net displacement is modest (6) Large —x— (tails): molecules that happened to find relatively open, less hindered paths and accumulate long net displacements

The broad one represent the 1D diffusion model and the narrow one represent the cross section effects?

However, the water molecues begin to sense the long-distance features of the media. With sufficient long time, the molecues dynamics is mainly restricted by the medium structure, such as tortuosity.

The side peak means the sharp twist or the narrow channel of the axon. But what the superpostion of propagator means?

References

[1] Daumante Suminaite, David A Lyons, and Matthew R Livesey. Myelinated axon physiology and regulation of neural circuit function. *Glia*, 67(11):2050–2062, 2019.

[2] Yaniv Assaf and Peter J Basser. Composite hindered and restricted model of diffusion (charmed) mr imaging of the human brain. *Neuroimage*, 27(1):48–58, 2005.

[3] Yaniv Assaf, Tamar Blumenfeld-Katzir, Yossi Yovel, and Peter J Basser. Axcaliber: a method for measuring axon diameter distribution from diffusion mri. *Magnetic Resonance in Medicine: An Official Journal of the International Society for Magnetic Resonance in Medicine*, 59(6):1347–1354, 2008.

[4] Peter J Basser. Inferring microstructural features and the physiological state of tissues from diffusion-weighted images. *NMR in Biomedicine*, 8(7):333–344, 1995.

[5] Peter J Basser, James Mattiello, and Denis LeBihan. Mr diffusion tensor spectroscopy and imaging. *Biophysical journal*, 66(1):259–267, 1994.

[6] Hong-Hsi Lee, Sune N Jespersen, Els Fieremans, and Dmitry S Novikov. The impact of realistic axonal shape on axon diameter estimation using diffusion mri. *Neuroimage*, 223:117228, 2020.

[7] Dan Benjamini, Michal E Komlosh, Lynne A Holtzclaw, Uri Nevo, and Peter J Basser. White matter microstructure from nonparametric axon diameter distribution mapping. *NeuroImage*, 135:333–344, 2016.

[8] Tim B Dyrby, Lise V Sögaard, Matt G Hall, Maurice Ptito, and Daniel C Alexander. Contrast and stability of the axon diameter index from microstructure imaging with diffusion mri. *Magnetic resonance in medicine*, 70(3):711–721, 2013.

[9] Hong-Hsi Lee, Antonios Papaioannou, Sung-Lyoung Kim, Dmitry S Novikov, and Els Fieremans. A time-dependent diffusion mri signature of axon caliber variations and beading. *Communications biology*, 3(1):354, 2020.