Cell Swelling Model Reproduces DWI Signal Change in Acute Stroke

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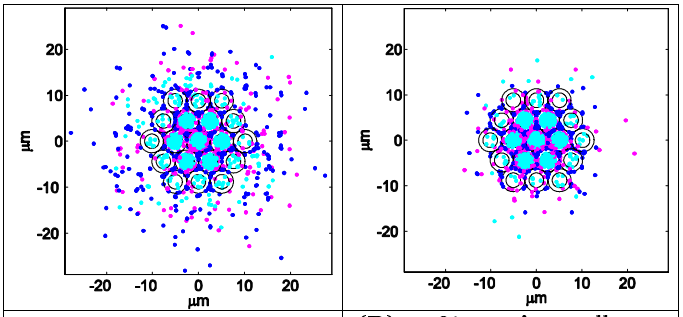
Objective: To create a model that relates the information in white matter diffusion and transverse relaxation curves to structural and functional parameters of the tissue.

Introduction

A better understanding of the biophysical origin of the MR signal would help us optimize contrast and interpret diffusion and relaxation experiments applied to white matter pathology [1,2,3]. For example in acute ischemic stroke, the apparent diffusion constant (ADC) can change by as much as 50% without T_2 changing perceptibly, but this has not yet been fully explained. There is also no quantitative theoretical basis for the widespread assumptions about a relationship existing between tissue integrity and the anisotropy measured from diffusion tensor imaging.

A 3D model has been developed that allows spin packets to diffuse, relax and exchange in a hexagonally spaced white matter construction. The whole diffusion curve can be generated for different b-values, for different pulse sequences, different gradient directions, and intrinsic diffusivities, relaxivities, permeabilities and cell dimensions. The T_2 curve is also calculated. Paradoxically, given the complexity of biological tissue, too many parameters will render any model irrelevant thus the simplicity of the model is essential.

Figure 1. Particle distribution at TE=90 ms



(A) 1% spacing between fibers: more continuous extracellular space.

(B) 0.1% spacing: cell swelling causes abuttal of fibers and less extracellular diffusion.

Method:

Particles are distributed randomly according to compartmental densities and allowed to diffuse and relax. When a particle hits a compartment boundary, it can either transfer to the new compartment, or suffer one or more "billiard ball" reflections, traversing the remainder of its trajectory in its original compartment. The proportion of particles hitting the wall that indeed transfer, is the permeability parameter set by the experimenter, which is thus made proportional to the number of wall hits, which in turn is affected by the size of the compartment and the diffusion constant. The simulated pulse sequence here is a standard spin echo diffusion-weighted sequence with Δ=60ms and δ=30ms.

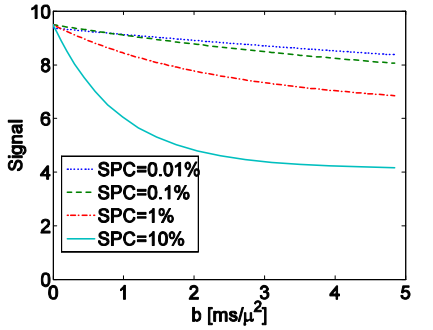


Figure 2: Transverse diffusion curves for different cell spacings

For the first application of this model, the phenomenon of acute ischemia is investigated. Cytotoxic edema leading to cell swelling is commonly held accountable for the MRI changes but the cell volume increase is thought to be not more than 10%. A potential use of the model is for optimization of DWI for differentiating cytotoxic and vasogenic edema.

Results:

Figure 1 shows two examples of spin distributions at the end of a 90 ms diffusion sequence for cells before (A) and after (B) swelling. The displayed 2000 spin packets are color-coded by compartment (actual simulations ran with 20,000 particles). The total combined volume of intracellular and extracellular space was kept the same (myelin water fixed at 13%). Due to the compactness of the tissue, the abuttal of fibers resulting from even minimal cell swelling significantly reduced the translational freedom of extracellular particles. Thus minor changes in the space between the cells drastically affected the measured transverse diffusion – see Fig. 2 and Table 1. A change in volume from 65% intracellular water (spacing=1%) to 69% intracellular (spacing=0.1%) resulted in a larger than 2-fold decrease in measured transverse diffusion. This trend was minimally influenced by the particular choice of model parameters. Manipulation of the permeability also affected measured diffusion, but to a lesser extent.

Summary

This model bridges the gap between MRI and conventional histopathology. It can predict multiexponential T_2 and DWI signals in white matter by correlating microstructural tissue changes with MRI signal. It is designed to yield insight regarding the distribution of axon sizes, their myelination status and permeability, and generally identify the cellular correlates of changes in measured diffusion and relaxation.

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References: [1] Sotak CH. *Neurochem Int.* 2004 Sep;45(4):569-82.[2] Assaf Y, Basser PJ. *Neuroimage.* 2005 Aug 1;27(1):48-58. [3] Pfeuffer J, Dreher W, Sykova E, Leibfritz D. *Magn Reson Imag.* 1998 Nov;16(9):1023-32.

Table 1: Transverse diffusion for different cell configurations

Space between fibers †	0.01%	0.1%	1%	10%
Intracellular water	69%	69%	65%	39%
Extracellular water	18%	18%	22%	49%
D transverse ‡	0.026	0.042	0.12	0.47

† Percent of fiber diameter ‡ in μ^2/ms measured at b=1000 s/mm^2