Numerical simulation of DMRI signals in a complex tissue model

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Targeted audience: Researchers interested in diffusion modeling in biological tissues and retrieving tissue structure information from DMRI data

Introduction

Diffusion MRI (DMRI) gives a measure of the average distance travelled by water molecules in a certain medium and can give useful information on tissue structure when the medium is biological tissue (see review [1]). Several models, mainly the " biexponential" model and the "kurtosis" (polynomial) model, are often used to describe DMRI signal behavior, but the link of the parameters estimated from those models with underlying tissue structure has remained elusive. We numerically simulated the MRI signal obtained with gradient spin echo (PGSE) sequence for water molecules diffusing in a two compartment tissue model consisting of permeable cells, with cylindrical and spherical shapes, and an extra-cellular space.

Theory and Method

DMRI signal was calculated at various diffusion times by numerically solving the Bloch-Torrey partial differential equation using a finite volume spatial discretization coupled with a Runge-Kutta Chebyshev time-stepping method [2]. We consider the Bloch Torrey equation for the bulk magnetization in a sample under a diffusion gradient. In the sample Ω, we assume two compartments, Ω^i and Ω^e , standing for the intra-cellular(i) and the extra-cellular(e) compartments, respectively, with intrinsic diffusion coefficients D^i, D^e. For a given magnetic field gradient combination with normalized time profile g(t), max(g(t))=1, and intensity G, the magnetization in compartment j is:

$$\frac{\partial m^j(\mathbf{x},t,|\mathbf{q})}{\partial t} = i\,g(t)(\mathbf{q}\cdot\mathbf{x})m^j(\mathbf{x},t,|\mathbf{q}) + \nabla\cdot\left(D^j\nabla m^j(\mathbf{x},t,|\mathbf{q})\right), \mathbf{x}\in\Omega^j \;, j=i,e,$$

with $\boldsymbol{q} := \gamma \boldsymbol{G}$, where γ is the gyromagnetic ratio of water proton. We impose two interface conditions on the interface between the two compartments:

$$D^j\nabla m^j(\mathbf{x},t\,|\mathbf{q})\cdot\mathbf{n}^j(\mathbf{x}) = -D^k\,\nabla m^k(\mathbf{x},t,|\mathbf{q})\cdot\mathbf{n}^k(\mathbf{x}), \qquad D^j\nabla m^j(\mathbf{x},t\,|\mathbf{q})\cdot\mathbf{n}^j(\mathbf{x}) = \kappa\left(m^j(\mathbf{x},t,|\mathbf{q}) - m^k(\mathbf{x},t|\mathbf{q})\right), \qquad \mathbf{x}\in\Gamma^{jk}.$$

The first enforces the conservation of mass and the second includes the permeability coefficient κ on the interface between the cells and the extra-cellular space. The signal is given by the integral of the magnetization over the entire sample. We simulated a PGSE sequence, with g(t) consisting of two pulses of duration δ and the time between pulses is Δ with δ=2.5 ms and Δ=5,10,20,30,40 ms on a tissue sample in three dimensions. After we obtained the simulated signal as a function of b value $b=\|\mathbf{q}\|^2\delta^2(\Delta-\delta/3)$, we computed the ADC_0 and KUR_0 by fitting the signal to a polynomial $S(b)/S_0=\exp(-bADC_o + KUR_o b^2 ADC_0^2/6)$. In addition, we fitted the signal to a bi-exponential $S(b)/S_0 = f^s e(-D^s b)+(1-f^s)e(-D^f b)$. We then observe how ADC_0, KUR_0, D^s,D^f and f^s change with the diffusion time, $\Delta-\delta/3$ and compare to experimental rat brain cortex data fitted with the biexponential and kurtosis models [3].

Results and discussion

The tissue model consisted of randomly placed and oriented cylindrical cells (with diameter of 3 microns) and randomly placed spherical cells (of diameter 8 microns) (Fig1). The total volume fraction occupied by all the cells is 83% percent of total tissue volume with 43% in the cylinders. The intrinsic intra- and extracellular diffusion coefficients were set to $D^e=D^i$ = 3x10-3 mm^2/s and the permeability between the cells and the extra-cellular space, κ, was set to three different values: $1x10^{-5}$,$3x10^{-5}$ or $5x10^{-5}$ mm/ms in three different simulations. The total tissue volume is contained in a computational box measuring 175 microns on each side and pseudo-periodic boundary conditions were enforced on the faces of the computational box to mimic the effect of periodically repeating the tissue volume infinitely in all three coordinate directions. We see that ADC_0 decreases as the diffusion time increases. KUR_0 increases and then decreases for the two higher permeabilities, and it increases continuously for the lowest permeability. D^s and D^f are relatively steady for all diffusion times, whereas f^s increases sharply from 5ms to 20ms, and then it increases very slowly for the lowest permeability, and starts to decrease for the two higher permeabilities. These simulate results are very consistent with earlier findings in the rat brain cortex [3] where D^s and D^f are found to be steady with diffusion time (at $0.3x10^{-3}$ mm^2/s and $0.9x10^{-3}$ mm^2/s, respectively, very close to our simulation results) and that f^s increases sharply from 5ms to 20 ms (rat cortex in vivo): At the highest permeability our simulated f^s goes from 0.2 to 0.4 and then decreases slightly and at the lowest permeability our simulated f^s increases continuously from 0.2 to 0.6. Our results are very close to experimental results of [3] (continuous increase from 0.2 to 0.4) taking $\kappa=3x10^{-5}$. The slight difference may be due to the fact our cylindrical cells are larger in diameter than the average neurons (1.5-2 microns in diameter) and they are blocked where cells cross each other so the diffusion distance along a cylinder is shorter than the true value. We plan to simulate smaller diameter cylindrical cells (diameter of 1.5 microns) that do not cross each other in the near future but this requires more work to generate the geometrical meshes. Through these current and future numerical simulations we hope to show that the two compartments Bloch-Torrey PDE model have the potential to explain, in a reasonable and consistent way, a part of the provenance of the DMRI signal of cerebral tissue in vivo.

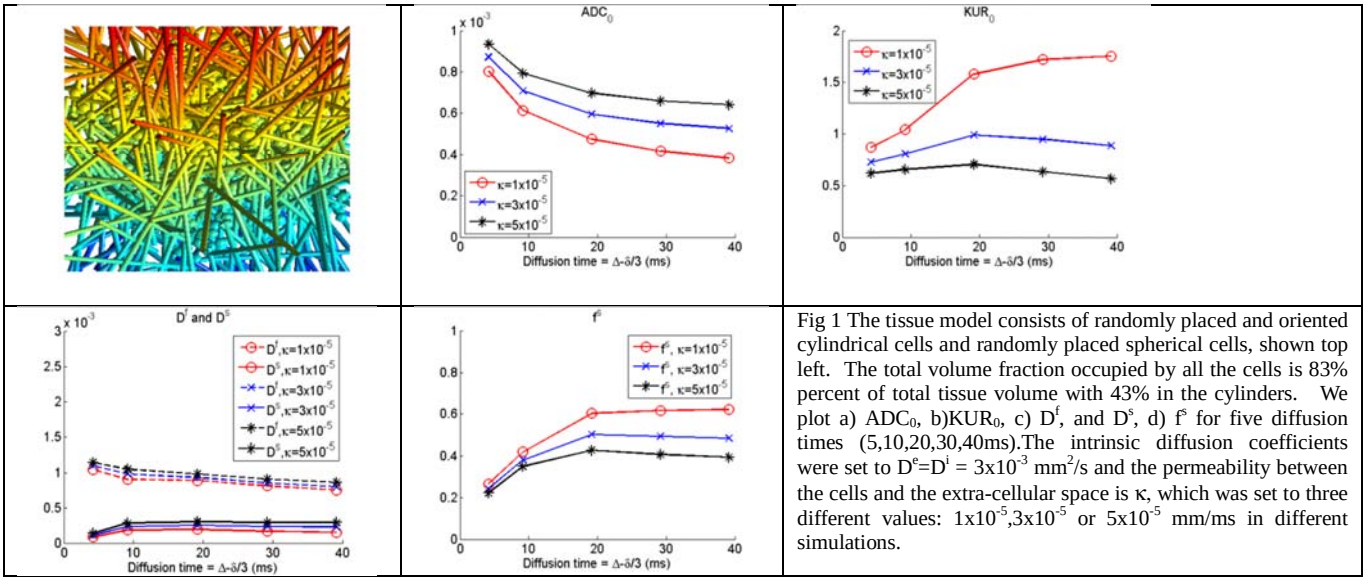

Fig 1 The tissue model consists of randomly placed and oriented cylindrical cells and randomly placed spherical cells, shown top left. The total volume fraction occupied by all the cells is 83% percent of total tissue volume with 43% in the cylinders. We plot a) ADC_0, b)KUR_0, c) D^f, and D^s, d) f^s for five diffusion times (5,10,20,30,40ms).The intrinsic diffusion coefficients were set to $D^e=D^i$ = $3x10^{-3}$ mm^2/s and the permeability between the cells and the extra-cellular space is κ, which was set to three different values: $1x10^{-5}$,$3x10^{-5}$ or $5x10^{-5}$ mm/ms in different simulations.

References [1] Le Bihan 2007 Phys Med Bio 52. [2] Sommeijer B. P. et al. JCAM (1998), 88(2):315–326. [3] Pyatigorskaya et al 2012, ISMRM abstract 2652, Melbourne.