New Mathematical Model for the Diffusion Time Dependent ADC

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Target audience

This presentation is aimed at MR physicists and medical researchers interested in diffusion Magnetic Resonance Imaging (dMRI) modeling and in interpreting the dMRI signal in terms of biological tissue microstructure.

Purpose

DMRI has been established as a useful tool to obtain voxel-level information on tissue microstructure. An important quantity measured in dMRI is the apparent diffusion coefficient (ADC), and it has been well established by *in-vivo* brain imaging experiments that the ADC depends significantly on the diffusion time (a recent reference is [1]). To aid in understanding and interpreting the experimentally measured ADC, we derive a new mathematical model of the voxel-level ADC that is diffusion time-dependent and accurate over a large range of diffusion times, using a linearization of the Bloch-Torrey equation around low b-values. The goal is to use this time-dependent ADC model in the future to identify parameters of tissue microstructure from the experimentally measured ADC at different diffusion times.

Method

The water proton magnetization in tissue, subject to diffusion-encoding magnetic field gradient pulses, can be modeled by the Bloch-Torrey equation. In a voxel Ω, we assume two compartments: Ω^e and Ω^c, the extra-cellular(e) and intra-cellular(c) compartments, with *intrinsic* diffusion coefficients D_e, D_c, respectively. The two compartments are separated by the interface Γ. Let the magnetic field gradient be G(t) and let γ be the gyromagnetic ratio of water proton, the magnetization satisfies the Bloch-Torrey equation [2] with conservation and permeability conditions on the interface Γ. The dMRI signal is sum of the magnetization over the voxel. In our approach we linearized the Bloch-Torrey equation around small b-values to obtain a macroscopic model for the ADC. We obtained that $\mathrm{ADC}(t) = v_e\sigma_e(t) + v_c\sigma_c(t)$, where v_j is the volume fraction of the compartment j, $\sigma_{j,ik}(t) := \frac{1}{v_j}\int_{\Omega_j} D_j\left(e_i\cdot e_k - \frac{\iota\gamma\int_0^t G(t)\frac{\partial}{\partial x_i}w_{j,k}(x,t)dt}{\gamma^2\int_0^t G^2(t)dt}\right), j=e,c;\ i,k=1,..,d$, are the *effective* diffusion tensors, d is the spatial dimension, ι the imaginary unit, e_i the unit vector in the canonical basis, and $w_{j,k}$ the solutions of homogeneous diffusion equations with a flux on the interface Γ: $\sigma_j\nabla w_{j,k}(x,t)\cdot\nu = \iota(\int_0^t G(t)dt)D_j e_k\cdot\nu$, where ν is the interface's external normal vector. In other words, we removed the heterogeneity of the cellular geometry from the bulk volume of the voxel and replaced it by a heterogeneity defined only on the cellular membranes (the interface between the two compartments). This allowed us to obtain an accurate simplified model of the ADC that is diffusion time-dependent.

Results and discussion

There are several known models in literature that approximate the dMRI signal or the ADC, valid in different diffusion time regimes. Our new ADC model is valid over a wider range of diffusion times than some previous macroscopic models and we illustrate this by numerical simulation on a two-dimensional cellular configuration (see Fig 1). An analytical formula for the ADC in the short diffusion time regime in presence of cellular membranes can be found in [3], which is a general case of the formula given in [4]. A long diffusion time model of the ADC can be found in [5,6]. We solved the Bloch-Torrey equation on the cellular geometry shown in Fig 1, where L=10μm, R ranges from 0.6 to 2.9μm, D_e=3×10^{-3}mm^2/s, D_c=1.6×10^{-3}mm^2/s, κ=1×10^{-5}m/s, in the diffusion-encoding gradient direction [1,0], for b-values in [0,50]s/mm^2, to compute the reference dMRI signal. The reference ADC was obtained by a linear fit of the log of the reference dMRI signal against the b-values in [0,50]s/mm^2, for several PGSE sequences where the values of Δ (time between pulses) and δ (duration of the pulses) are varied to obtain diffusion times ranging from 7μs to 120ms. A comparison of the Short Time Approximation of [3] and the Long Time Approximation of [5] and our New Model with the reference ADC over a range of diffusion times is showed on Fig 2. The results are plotted against the normalized diffusion displacement (NDD): $\sqrt{2(\Delta+\delta)D_{TL}}/R_m$, where D_{TL} is the diffusivity in the tortuosity limit, in this case D_{TL} = 1.26×10^{-3}mm^2/s, and R_m is the mean radii. We see that our new model is close to the Reference ADC over NDD ranging from 0.1 to 10, well-covering the entire range of physically possible diffusion times that can be probed using dMRI *in-vivo*.

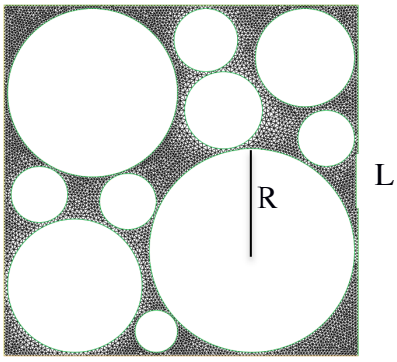

Fig 1: Geometrical configuration of cells simulated to give the ADC curves in Fig 2.

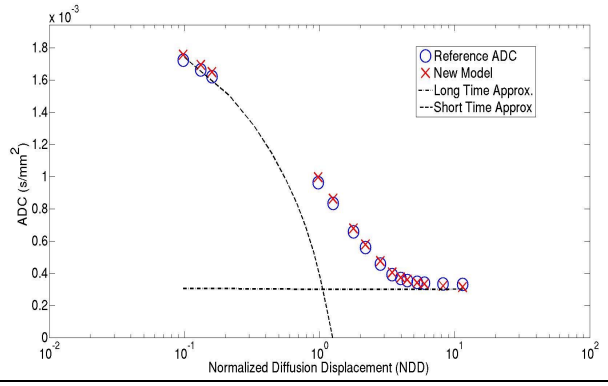

Fig 2. The ADC of the new macroscopic model is close to the reference ADC over a larger range of diffusion times.

Conclusion

We found that, over a wide range of physically possible diffusion times that can be probed using dMRI *in-vivo*, our new model for the diffusion-time dependent ADC approximates very well the reference ADC computed by solving the Bloch-Torrey equation for the water proton magnetization in a complex cellular geometry. Numerical investigation of this new model for more complex and realistic cellular geometries in three-dimensions is the subject of our next investigations. The end goal is to use this time-dependent ADC model to identify parameters of tissue microstructure from the experimentally measured ADC at several diffusion times.

References

[1] Pyatigorskaya et all 2014, Magn Reson Med 72:492-500, [2] Torrey 1956, Physical Review Online 104(3):563-565, [3] Novikov et all 2011, Nat Phys 7:508-514, [4] Mitra et all 1992, Physical Review Lett 68:3555-3558, [5] Cheng et all 1997, Proch Math Phys Eng Sci 453:145-161 [6] Coatléven et all 2014, SIAP 72(2):516-546