Monte-Carlo Simulation Software Dedicated to Diffusion Weighted MR Experiments in Neural Media

C-H. Yeh[1,2], D. Le Bihan[1], J-R. Li[1], J-F. Mangin[1], C-P. Lin[2], and C. Poupon[1]

[1]NeuroSpin, I2BM, CEA, Gif-sur-Yvette, France, [2]National Yang-Ming University, Taipei, Taiwan

Introduction

A novel simulation tool dedicated to diffusion-weighted (DW) MR experiments is described in this study. We combine a Monte Carlo Brownian dynamics simulator capable of simulating diffusion of spins in arbitrarily complex geometries with a DW signal integrator emulating various MR pulse sequences. The flexibility and ability of Monte-Carlo modeling enables us to investigate detail dynamics and mechanisms of molecular diffusion in complex systems which cannot be handled through analytical models [1-3]. Hence, we have developed software to reproduce various tissue configurations using dynamic meshes. Complicated geometries mimicking neural tissue components, such as neurons, astrocytes, axons, etc. can be emulated, as well as tissue features (e.g. cell size, density, membrane permeability) and basic diffusion mechanisms in different compartments (presence of attractors, local viscosity, membrane interactions, etc.). This framework allows to bridge the gap between elementary processes occurring at a micrometer scale and the resulting DW signal measured at millimeter scale, providing a better understanding of the features observed in DW MRI (variation of apparent diffusion coefficient (ADC) with cell size, diffusion anisotropy) and to optimize acquisition schemes for different applications (e.g. fiber-tracking algorithms).

Methods

The simulation code is implemented in C++ on a high computing PC cluster for large-scale simulations, and main features are described as following:

Cell membranes are generated using meshes in order to model different cell types with heterogeneous shapes and sizes. This module allows users to specify cell properties including the thickness, permeability, and diffusion coefficient (D) inside and close to the membrane layers. In addition, we incorporates the mesh with dynamic morphological evolution, thus it can be utilized to simulate sequential changes of tissue shapes including expansion, shrinkage, and deformation.

Diffusing particles ("spins") are modeled as random walkers which are initially randomly distributed in a three dimensional space. The average free displacement of each "spin" for an elementary time step of length dt is scaled to its associated compartmental D based on the Einstein equation, i.e. $\langle x\rangle=(6Ddt)^{1/2}$. For each simulation step, the spatial positions of particles are updated subject to a series of potential interactions: (i) In accordance with the permeability, the particle may penetrate through the related cell membrane or be elastically reflected. (ii) The diffusivity of the particle may be modified into that of the interacting membrane layers.

The MR pulse sequence module is flexible to model a variety of pulse sequences with different combinations of radio frequency (RF) and gradient pulses. The gradient pulse is characterized using a trapezoid model in our current implementation but can, of course, be extended to fit any shapes. Parameters including the magnitude (g), the rising and descending ramp times, the duration (δ) and separation (Δ) of the diffusion gradient pulses are adjustable.

DW signal of each synthetic MR voxel, $S(v)$, is computed by performing the integration numerically using the following equations:

$$S(v)=\sum_{p=1,p\subset v}^{N_{p,p\subset v}} e^{i\phi_p} \cdots\cdots\cdots(1), \qquad \phi_p = j\gamma\sum_{i=0}^{N_i}(-1)^{N_{\pi RF}(t_i)}\vec{G}(t_i)\cdot\vec{R}(t_i)dt \cdots\cdots\cdots(2).$$

In Eq. (1) ϕ_p denote the accumulated phase of the pth particle belonging to the voxel v that contains amount of N_p particles at the end of simulation. In Eq. (2), γ is the gyromagnetic ratio; N_i is the number of iterations in simulation; $N_{\pi RF}$ is the accumulated counts of refocusing pulses at the time step t_i. G and R are measured at each t_i, where G is the DW gradient vector, and R is the spatial position of the pth water molecule at the ith iteration. Users can add imaging (Rician) noise to the synthetic MR signal.

We simulated two simple experiments to illustrate the potential of this software: First, we used the software to mimic water diffusion in a neural medium containing various types of neural cells. Second, we generated two fiber bundles crossing at 60-degree angle in a 0.6×0.6×0.6 mm space filled with 10^5 diffusing particles ($D = 2.0\times10^{-3}$ mm^2/s). Each bundle contained 300 cylindrical fibers with diameter of 10 μm. A high angular resolution diffusion imaging (HARDI) experiment was simulated using the following parameters: g = 40 mT/m, slew rate = 200 mT/m/s, δ/Δ = 32.97/35.97 ms, (yielding b = 3,000 s/mm^2), and 80 DW gradient orientations. Using Eq. (1), DW signal was computed by sampling on a 0.1 mm grid for a final imaging voxel size of 0.1 mm isotropic. The SNR measured on the null DW image (b = 0) was 18.4. Fiber orientations were estimated using the diffusion tensor (DT) [4] and analytical q-ball imaging (QBI) method [5].

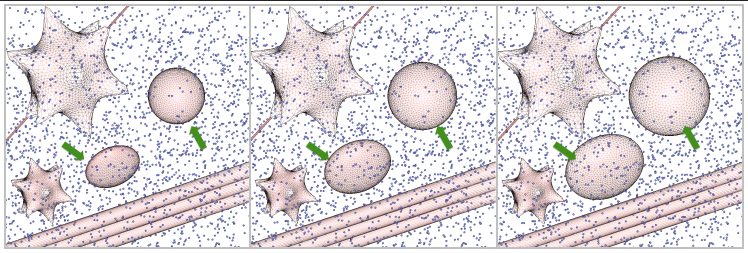

Figure 1: An example environment for the simulation of diffusion in a neural medium.

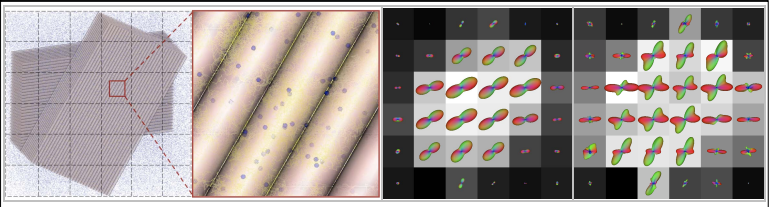

Figure 2: From left to right: (1) Mesh-based crossing fibers. (2) A zoomed area showing a certain of diffusing spins (blue spheres) and their motion trajectories (yellow curves). (3-4) ODF reconstructed using DT and analytical QBI approaches respectively.

Results & Discussion

Figure 1 shows the diffusing particles (colored in blue) and the cell membranes (colored in pink) generated using meshes to represent different neural structures. The dynamic surface evolution function was applied to the cells pointed by the green arrows to simulate cell swelling, which has been identified as an important factor in the changes of the ADC observed in acute ischemia or during neural activation [2, 6]. Figure 2 shows the simulated crossing fibers and the results of orientation distribution function (ODF) reconstructed from the synthetic DW data. ODFs were scaled to corresponding generalized fractional anisotropy (GFA) displayed as background images. The reliability of diffusion methodologies can be evaluated via the known configurations created by this software, as shown in this sample experiment. Moreover, the optimized strategies can be objectively determined by regulating features' parameters.

Conclusion

The Monte-Carlo simulation software described in this study is general and flexible to mimic diffusion in biological tissues and to generate realistic synthetic data for diffusion MRI. Since the properties of the diffusing spins and tissue structure are all manageable, this software enables investigations on the underpinning mechanisms affecting the DW signal and the consequent diffusion measured parameters (e.g. ADC and fractional anisotropy (FA) [4]). Specifically, it can be utilized to investigate mechanistic hypotheses for various scenarios (acute ischemia or neuronal activation and cell swelling, cancer and cell proliferation, axonal fiber anisotropy in complex bundles or cortex, etc.).

References

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