Fast Monte Carlo simulations replace analytical tissue models in diffusion MRI

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Introduction

Characteristics of tissue micro-structure, such as axonal diameters (d) and membrane permeability (p), can be estimated from diffusion MRI data obtained with different diffusion times [1,2]. Micro-structural parameters are currently extracted using analytical models, based on approximations of the tissue geometry and of the measurement on that geometry [3,4]. For example, the intracellular signal is modelled using either the short-gradient-pulse (SGP) or the Gaussian-phase-distribution (GPD) approximation [5]. As a consequence, analytical models suffer from crude approximations. In this work, we propose a novel approach to the extraction of micro-structural parameters from diffusion MRI data without the use of analytical models, by using Monte Carlo simulations of particles diffusing in tissue geometries.

Theory

The theoretical signal S and the Monte-Carlo simulated signal S^* for a diffusion experiment are given by

$$S = \int_{-\infty}^{\infty} \exp(i\phi) P(\phi) d\phi, \quad S^* = \frac{1}{n}\sum_{i=1}^{n} \exp(i\phi_i) \approx S, \quad \phi_i = \left(\int_{t=0}^{T} \mathbf{r}_i(t) \cdot \gamma \mathbf{g}(t) dt \right) \in P(\phi)$$

where ϕ is the spin phase and $P(\phi)$ is the probability density for the phase angles in the measurement volume. Analytical models approximate $P(\phi)$ by assuming, for example the SGP approximation, but such approximations can be avoided by sampling $P(\phi)$ with n simulated particles. The phase ϕ_i of the i:th particle is drawn from $P(\phi)$ by simulating $\mathbf{r}_i(t)$ as a random walk and calculating ϕ_i according to the integral given above, where T is the time for the signal acquisition, γ is the gyromagnetic ratio and $\mathbf{g}(t)$ is the magnetic field gradient amplitude waveform. Note that when the magnitude $|S^*|$ is studied, a noise-floor will be introduced, given by $(\pi/n)^{1/2}/2$.

Method

To draw ϕ_i from $P(\phi)$, $\mathbf{r}_i$ was simulated by a Markov Chain as a random walk in a geometry consisting of different compartments (see Fig. 1 for a simple case). Membrane permeability, related to the intracellular exchange time (τ), was implemented as described in [6]. The simulation framework was developed in Matlab and the simulation kernel was implemented using CUDA (NVIDIA, Santa Clara, CA) to allow parallel simulations on a graphics processing unit (GPU) of a GeForce 9800 GT graphics card. The simulation framework was validated using several unit tests. For example, the intracellular signal-versus-q curve perpendicular to an impermeable cylinder was simulated, using δ/T_D = 7 µs/400 ms, and compared to the theoretical signal curve derived using the SGP approximation.

The potential of this method for evaluating diffusion MRI data was investigated by comparing synthetic signal-versus-b curves with a database of simulations. For this investigation, the database was created for the following micro-structural parameters; d = 1,2,..,10 µm, τ = 50,150,…,950 ms, intra- and extracellular ADC = 0.4, 0.6, …, 2.2 µm^2/ms and intracellular volume fraction p_i = 45,50,…,75%, for a pulsed gradient spin echo sequence (PGSE) with diffusion encoding duration δ = 30 ms and two diffusion times T_D = 30 and 60 ms. Signal-versus-b curves for each set of microstructural parameters were stored in the database, sampled with 36 b-values for each T_D, using b_{max} = 18 000 s/mm^2 ($g_{max} \approx$ 100 mT/m, i.e. obtainable on a clinical MRI scanner). Next, synthetic signal-versus-b curves S_{syn} were created by adding noise with a signal-to-noise ratio (SNR) set to 50, for the maximal signal value, for two different sets of simulated signal-versus-b curves. For these two sets, the posterior distribution $f(p_i,d,\tau,ADC \mid S_{syn}) \propto f(S_{syn} \mid p_i,d,\tau,ADC) \cdot f(p_i,d,\tau,ADC)$ was estimated, assuming a Rician signal distribution. The maximum of the posterior distribution was calculated, as well as the marginal posterior distributions for each parameters (i.e. p_i, d, τ and ADC), by integrating over the other three parameters.

Results

The simulation framework showed the expected results in all validation steps, demonstrated for one example in Fig. 2. Generation of the database, with simulations of 7000 different combinations of micro-structural parameters for two diffusion times with 21504 particles in each simulation, took 8 hours. This database was then used for all subsequent analyses. The position of the maxima of the posterior distribution corresponded well to the simulated for both of the two sets. Generating the posterior distribution and finding its maxima took about two seconds. Figure 3 shows the marginal posterior distributions of the four different model-parameters.

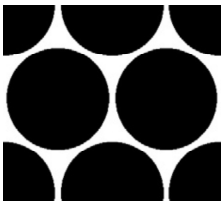

Fig. 1. Example of a simple simulation geometry with intra- and extracellular compartments.

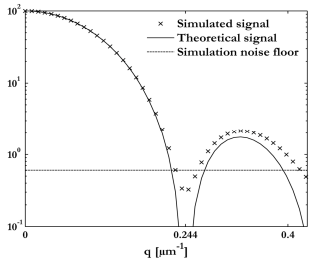

Fig. 2. The simulated intracellular signal perpendicular to an impermeable cylinder is similar to the theoretical, except when the signal drops into the noise-floor.

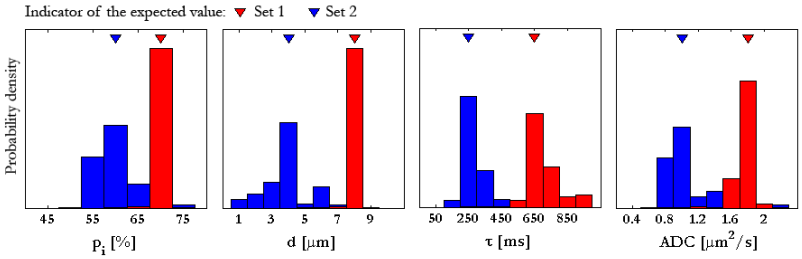

Fig. 3. Marginal posterior probability distributions for p_i, d, τ and ADC, for the simulations performed with p_i = 70%, d = 8 µm, τ = 650 ms and ADC = 1.8 µm^2/ms (red), as well as p_i = 60%, d = 4 µm, τ = 250 ms and ADC = 1.0 µm^2/ms (blue). The maximum of the posterior distributions correlated with the theoretical values, indicated by the coloured triangles. The plots also show the accuracy of the measurement, simulated using SNR = 50. A higher SNR would give sharper peaks.

Discussion and conclusion

The demonstrated examples were based on a PGSE sequence and a simple geometry (Fig. 1), but the software supports simulations of arbitrary gradient waveforms and irregular geometries. The framework was thoroughly validated, see example in Fig. 2. The simulation framework can be obtained from the authors on request.

Evaluating diffusion MRI data using fast Monte-Carlo simulations instead of analytical models was demonstrated to be fruitful - the maxima of the posterior distribution given noisy signal-versus-b curves yielded the expected set of micro-structural parameters (Fig. 3). Moreover, our experience shows that once the database is generated, this evaluation technique is generally faster than non-linear fitting of analytical models.

The accuracy of diffusion MRI measurements can be interpreted from the marginal posterior distributions. For example, an experiment with too low b_{max} or too low SNR, would yield broad and non-specific peaks in the posterior distributions. This tendency is seen, for example, for p_i (blue) or for τ (red) in Fig. 3. Note that these simulations show that extractions of micro-structural parameters using a clinical MRI scanner are feasible, in agreement with Alexander [4].

In conclusion, this novel approach improves the determination of the most accurate micro-structural parameters and enhances the interpretation of diffusion MRI experiments by replacing analytical models with fast Monte-Carlo simulations.

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